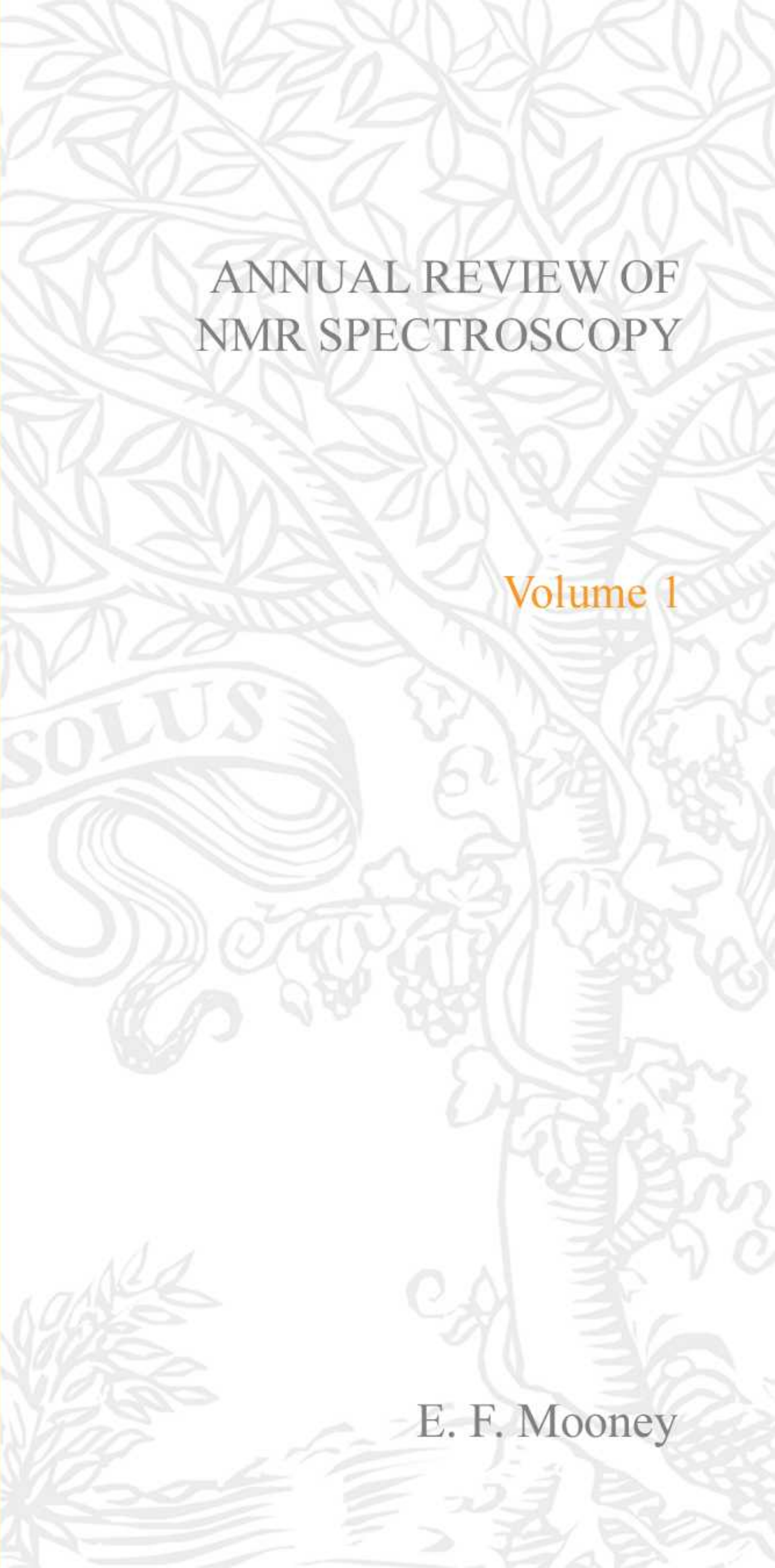

ANNUAL REVIEW OF NMR SPECTROSCOPY

Volume 1

E. F. Mooney

ANNUAL REVIEW OF

NMR SPECTROSCOPY

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Edited by

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PREFACE

The *Annual Reviews of N.M.R. Spectroscopy* are intended to assist organic, inorganic and analytical chemists, as well as n.m.r. spectroscopists, in keeping abreast with what is one of the most rapidly expanding techniques being used in every branch of chemistry. The reviews will be essentially of two kinds: one will be specifically review articles summarizing the work that has been published on a particular topic over a period of time; the other will deal with some specialized aspect that is either capable of more extensive application or is thought to be of more than general interest. Volume 1 covers the literature up to the end of 1966.

I am sure many will have raised their hands in horror at the thought of yet another book having the title *Annual Review of*, or *Progress in*, chemistry. However, so many of my colleagues thought that such a book in the field of n.m.r., written expressly with the practising chemist in mind, would be invaluable, that we have launched the present series.

It will be immediately apparent to all those who are familiar with the *Annual Reviews of the Chemical Society* that the format of this series is based upon these long-established reviews. It is anticipated that the yearly feature will be the general review of proton n.m.r., and other topics, for example fluorine-19 n.m.r. spectroscopy and conformational analysis, will be reviewed every two or three years as seems appropriate.

Although it will not be long before much of our information retrieval is computerized, it will still be necessary to read papers and review articles. It is the firm contention of many of us that works such as annual reviews will serve a useful purpose for many years to come, for it is so often the odd comment in such a review that proves to be of great value. It is for this reason, that the Index has been made comprehensive.

I would like to thank all the contributors to this present volume especially for their care and diligence in the preparation of their manuscripts, which has made my task such a pleasure. Finally, I must express my gratitude to so many of my friends and colleagues for all the encouragement they have given to me.

ERIC F. MOONEY

Birmingham,
November, 1967

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General Review of Proton Magnetic Resonance

RICHARD A. Y. JONES

School of Chemical Sciences, University of East Anglia, Norwich, England

I. INTRODUCTION

THE USES of proton magnetic resonance (p.m.r.) spectroscopy are increasing more and more rapidly. This review is intended to cover the calendar year 1966 and the early months of 1967; during this time, at a conservative estimate, some 4000 published papers contained significant p.m.r. studies and many more contained minor references to their use. It is clear, therefore, that this review can only cover a small part of the field, and many subjects are treated here only very briefly or are omitted altogether. In particular I shall not discuss some topics that are treated elsewhere in this volume or are planned for the next volume in this series. I shall also pay scant attention to those papers which contain only the more routine applications of p.m.r. to straightforward problems of structure determination. Other omissions will become obvious to the reader searching, for example, for discussions of broad-line spectra, of spin-echo measurements or of applications of the Overhauser effect. I have devoted most attention to various aspects of certain specific topics in which p.m.r. has played a large rôle: stereochemistry, kinetics and equilibrium, molecular association, studies of aromaticity. A considerable part of the Section on general structural determinations is devoted to studies in organometallic chemistry, where p.m.r. has proved widely useful. Some recent studies on coupling constants are discussed in Section VII. These subjects are not mutually exclusive; there are papers, for example, dealing with the kinetics of a stereochemical process in organometallic chemistry as studied by coupling-constant measurements! For all confusion that this may cause, I apologize.

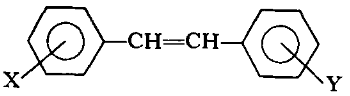
II. STEREOCHEMISTRY: CONFIGURATION AND CONFORMATION

The dividing line between configuration and conformation is a little vague when the phenomenon is studied by n.m.r. It is better to consider three categories of compounds: if the isomers are long-lived according to the n.m.r. time scale, we are interested merely in a characterization of and distinction between the isomers, their relative populations, if important, being determined by simple integration of the spectrum. At the other extreme are the rapidly interconverting conformers, for example most simple substituted ethanes, where we may merely wish to know which conformer is preferred or we may employ more subtle techniques to discover the position of the conformational equilibrium. Intermediate are those in which the rates of interconversion of isomers are comparable with the n.m.r. time scale (typically, rate processes involving half-lives ~0·01–1 sec.). At low temperatures the spectrum is a superimposition of those of the individual isomers and at high temperatures it is a weighted average of the separate spectra. Observation of the temperature at which two peaks coalesce can give the activation energy; a more detailed study of the change of shape of lines with temperature will reveal the other thermodynamic parameters of activation. All three cases will be considered in this Section. For convenience acyclic and cyclic systems are considered separately.

A. Acyclic systems

1. *Non-interconverting isomers*

The use of p.m.r. to differentiate between *cis* and *trans* isomers of olefins, either by the larger coupling between *trans* vicinal protons in 1,2-disubstituted olefins or by a characteristic chemical shift difference between isomers, is now well established and needs little further illustration. One example, which incorporates both techniques, will suffice. In substituted stilbenes (**1**)[1] the signals from the olefinic protons of *cis* compounds are always to higher field than their *trans* isomers, being shielded by the anisotropic magnetic fields of the non-coplanar benzene rings. A correlation between shift and the Taft combination $0{\cdot}4\sigma_I + 0{\cdot}7\sigma_R$ was observed. In all cases the ratio of coupling constants J_{trans}/J_{cis} was about 1·3. Similar approaches may be used for other types of double-bonded systems, for example, the pyrazolone azomethine dyes (**2**, **3**)[2] where the *syn*-isomer is distinguished by the low field signal from the aromatic proton Ⓗ, at about $\tau = 1{\cdot}7$, deshielded by the neighbouring carbonyl group.



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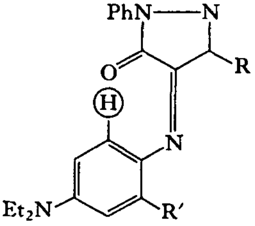

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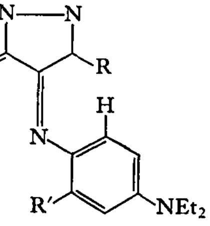

anti

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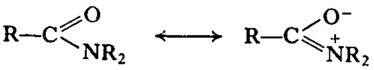
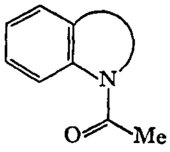
In systems containing partial double bonds, such as the C–N bond of amides (**4** ↔ **5**), rotation may be slow on the n.m.r. time scale, particularly when there is extra hindrance to rotation from steric interactions.



4 **5**

The spectrum indicates the presence of separate isomers for *N*-acyldihydroindoles and tetrahydroquinolines (**6**, **7**),[3] *o*-substituted formanilides[4] (**8**, **9**), and bis-amides, ($R{\cdot}CO{\cdot}NR'{\cdot}CH_2{\cdot}CH_2{\cdot}NR'{\cdot}CO{\cdot}R$), in which *cis–cis*, *trans–trans*, and *cis–trans* isomers coexist.[5]



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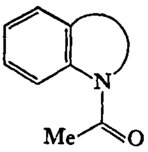

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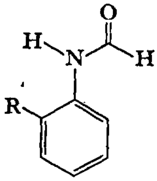

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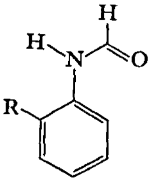

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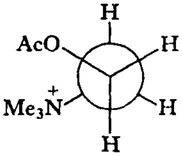
2. *Rapidly interconverting isomers*

(a) *Conformational preference.* The preferred conformation of a substituted ethane may frequently be determined by comparing the values of the vicinal coupling constants, $J_{\text{H-C-C-H}}$, with those calculated by the Karplus relation[6] or suitable modifications thereof[7, 8] for each rotamer. By this means, it has been shown that acetyl choline exists predominantly in the *gauche* conformation (**10**),[9] and the preferred conformations of the side chain of C_{20} substituted pregnanes have been determined.[10]



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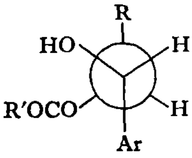
In a series of diastereomeric β-hydroxy esters of general formula Ar•CHOH•CHR•COOR′ the variation of J_{vic} with the nature of the group R was studied.[11] In *threo* isomers J_{vic} falls from 8·6 c./sec. for R = Me to 4·5 for R = Bu^t, whereas for the *erythro* isomer J_{vic} increases from 4·7 to 10·1. This is ascribed to preference for the *gauche* conformer (**11**) of the *threo* form and for the *anti* conformer (**12**) of the *erythro* form when R is a bulky group. Similar work for other diastereomeric phenylethyl systems has been reported.[12] Some elegant studies[13, 14] on 1,1,2-trisubstituted ethanes have been carried out by selectively replacing one or other



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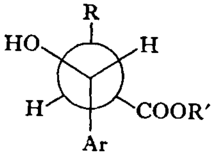

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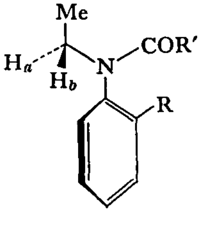
of the two non-equivalent† 2-protons by deuterium to separate the two vicinal coupling constants. The vicinal coupling across the central carbon–carbon bond of 1,3-dienols (RCH:CH–CH:CHOR′) indicates that these exist in the s-*trans*-conformation.[16]

An alternative approach to determining preferred conformation is to use chemical shift information rather than coupling constants. In *o*-substituted *N*-ethyl anilides (**13**) and similar compounds[17,18] the mere fact that the two protons *a* and *b* of the ethyl methylene group are non-equivalent shows that the preferred conformation is non-planar, as shown, and the two protons are differently shielded by the aromatic ring. A similar differential shielding in the preferred conformer of the oxazolthione (**14**, τ values indicated) was used[19] to determine the absolute configuration of the derived α-monodeuterated benzylamine.



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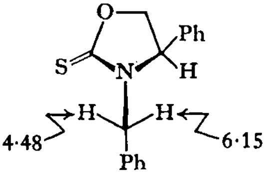

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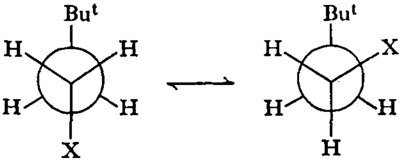
Differential shielding in biphenyls,[20] phenylpyridazines,[21] substituted styrenes,[22,23] and *o*-substituted formanilides[4] has similarly been used to study twisting from coplanarity.

(b) *Conformational equilibrium.* The equilibrium between the *anti* (**15**) and *gauche* (**16**) conformers of a series of 3,3-dimethylbutyl compounds has been studied by a detailed investigation of the variation of the vicinal coupling constants with temperature[24] and the theory has been clearly and fully discussed.[24] Some more approximate relationships between conformational equilibrium constant and vicinal couplings have also been derived.[24–26] Equilibrium constants have



15 **16**

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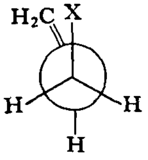
† For a review of non-equivalence in n.m.r. see Martin and Martin.[15]

thus been established both for substituted ethanes[26] and quite extensively for rotations about sp^3–sp^2 carbon–carbon bonds. For allyl halides a relationship $n = 1{\cdot}2 + 0{\cdot}16\ J_{vic}$ has been derived,[27] where n is the population of the *cis* conformer (**17**). Variable temperature studies of both coupling constant[28–30]



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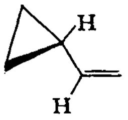

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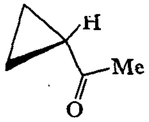

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and chemical shift[28] of vinylcyclopropane have established that the s-*trans*-conformer (**18**) is about 1 kcal./mole more stable than the s-*gauche*-, whereas for methyl cyclopropyl ketones the s-*cis*-conformer (**19**) is generally more favoured,[31] the equilibrium constant depending on the nature of substituents. Other systems that have been studied include oxime ethers[32] and phenyl hydrazones[33] ($R_2CH{\cdot}CH{:}NX$; X = OMe, NHPh), α,β-unsaturated ketones[34] and acryloyl fluoride.[35]

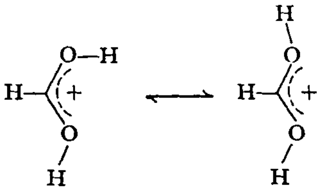
As Snyder[36] has pointed out efforts to improve the correlation of observed vicinal coupling constants with conformational equilibrium have been hampered by lack of reliable values for the *gauche* and *anti* coupling constants of the individual conformers. Studies[37, 38] on the effect of medium on rotamer energies which have allowed the reverse calculation from J_{obs} to J_g and J_a will help in this field.

3. *Hindered rotation and energy barriers*

The simplest studies merely note a qualitative change in spectrum with temperature to show hindered rotation, maybe together with a determination of equilibrium constant from an integrated low-temperature spectrum.

There is hindered rotation in the cations derived from formic acid (**20**, **21**)[39] and anisole (**22**),[40] in amides,[41–43] and in formamidines,[44] where the ease of rotation is strongly solvent dependent.

When the coalescence temperature is observed activation energies for the rotation may be derived. At room temperature the cumulene (**23**, **24**) exhibits separate peaks for the two t-butyl groups separated by 4 c./sec. in the 100 Mc./sec. spectrum. They coalesce at 100°C from which a value of $\Delta G^{\ddagger} = 20$ kcal./mole may be derived.[45] In a similar manner activation energies for rotation about carbon–nitrogen double bonds in various imino-compounds were derived.[46, 47] More frequently studied are rotations about partial double bonds, for example in amides,[48] thioamides,[49] amidinium salts,[50] enamines,[51] hydrazones,[51] hydrazides,[52] nitrosamines,[53] nitrites,[54] diazoketones[55] and phosphine ylids.[56]



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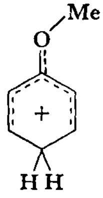

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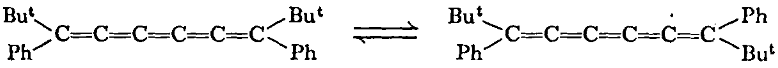
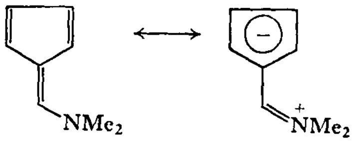


23 **24**

In 6-dimethylaminofulvenes (**25**) rotation about the carbon–nitrogen bond depends on the nature of substituents on the fulvene ring, −M groups increasing the contribution from the mesomeric form (**26**).[57] The substituted benzamide (**27**) exhibits four methoxyl signals in t-butylbenzene solution at 60°C, these coalesce, first into two at 130°C and finally into a single line at 165°C. This is attributed[58] to separate rotation barriers about the carbonyl–nitrogen and aryl–carbonyl bonds, both barriers being over 20 kcal./mole. In the carbamate (**28**) rotation about the carbon–oxygen bond is, surprisingly, more hindered than about carbon–nitrogen.[59]



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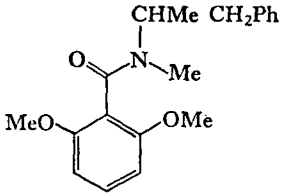

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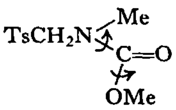

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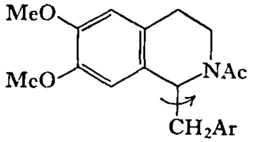
Fairly high energy barriers to rotation about carbon–carbon single bonds have been observed in sterically hindered systems, such as the benzyl isoquinolines (**29**)[60] and even more in the benzobicyclo-octatriene system (**30**)[61] where the three methyl groups appear as two peaks, of relative area 2:1 up to about 200°C.



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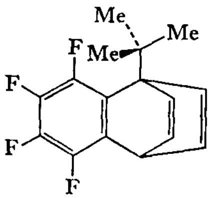

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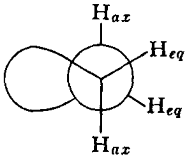
The most sophisticated studies of rate processes deriving enthalpy and entropy of activation, are exemplified by an investigation of hindered rotation about the aryl–nitroso bond in *p*-nitrosodimethylaniline.[62]

B. Cyclic systems

1. *Configuration*

(a) *Six-membered rings.* In principle, the vicinal coupling constants allow an easy distinction between an equatorial and an axial hydrogen atom because of the difference in dihedral angles involved. Typically J_{ax-ax} is about 10 c./sec., J_{ax-eq} and J_{eq-eq} both about 3 (cf. **31**). This property is widely used in rigid-ring systems (e.g., steroids[63, 64] and rotenoids[65]) and in rings which bear bulky substituents and which therefore exist predominantly in one conformation. It has proved particularly valuable in stereochemical studies of substituted flavans (**32**) and related compounds;[66–74] this subject has been recently reviewed.[75]



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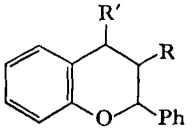

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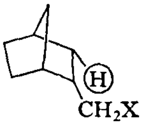
A second approach to configurational assignment in cyclohexanes is to make use of the differential shielding of axial and equatorial substituents arising from the magnetic anisotropy of the ring and of other substituents. The application of this method to alkyl-cyclohexanes[76, 77] and -decalins[77, 78] has been discussed in some detail. The configurations of hydroxy-and keto-steroids[79–81] and -decalins[82] may be determined from the observed chemical shifts of the angular methyl groups[79, 80, 82] or of some of the ring protons.[81] The *endo*-3-proton, Ⓗ, is shifted to abnormally high field (9·3–9·5 τ) in derivatives of *endo*-2-methylnorbornane (**33**) and the corresponding norbornenes (**34**).[83] One of the geminal cyclopropane protons, Ⓗ, is very strongly deshielded (7·3–7·7 τ; cf. 9 τ for the other geminal proton) in the benzotricyclo-octenol (**35**) and its ethers and esters.[84]



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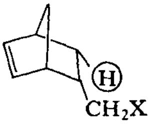

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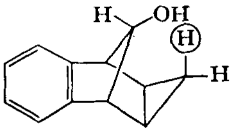

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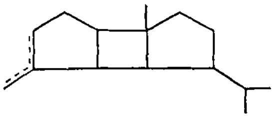
(b) *Rings other than six-membered.* Similar principles apply to the configurational assignment of rings other than six-membered. In oxirans,[85] cyclobutanes,[86] tetrahydrofurans[87] and pyrrolidones,[88] the *cis* vicinal coupling constant is greater than in the *trans*-isomer. The nature of the ring fusions in the sesquiterpenes α- and β-bourbonene (**36**, double bond at one or other of dotted lines) was derived from coupling constant measurements.[89] Chemical shift measurements



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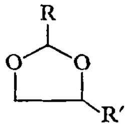

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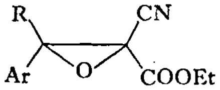

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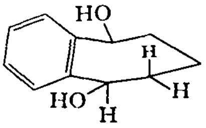
allow a distinction between *cis*- and *trans*-2,4-disubstituted dioxolans (**37**) on the basis that the 2-proton occurs at higher field in the *cis* isomer.[90] The protons of the ester group of tetrasubstituted oxirans are more shielded when they are *cis* to an aryl substituent (as **38**) than when *trans*.[91]

Stereochemically specific solvation effects may be used to assign configuration. In benzoyl-cyclopropanes and -aziridines such solvation in benzene shifts protons *trans* to the benzoyl group strongly upfield from their position in deuterochloroform or carbon tetrachloride; *cis* protons are less affected and shifted mostly downfield.[92] Similar results have been reported for other cyclopropane derivatives.[93] Differential solvent effects distinguish between *cis*- and *trans*-2,5-dimethoxytetrahydrofuran and dimethoxy-2,5-dihydrofuran, because a benzene molecule can more readily approach the unhindered side of the *trans*-isomer.[94]

2. *Conformational preference and conformational equilibrium*

When a molecule exists predominantly in one conformation this may usually be determined by analysis of coupling constants or chemical shifts, as described above for configurational analysis. *cis*-3,7-Dihydroxybenzocycloheptene exists in the chair conformation (**39**); the axial 3- and 7-protons appear as doublets coupled only to the *trans* axial protons on the adjacent carbon atoms; the vanishingly small *cis* coupling defines the dihedral angle and therefore the conformation.[95] Likewise the very small value for $J_{1,2a}$ in both *cis*- and *trans*-3-substituted bicyclo[3,1,0]octanes suggests a boat conformation (**40**).[96] Twisted boat conformations exist in the diterpenoid kaurenolides[97] and in the cyclohexane ring



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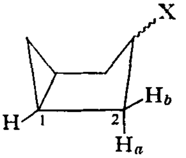

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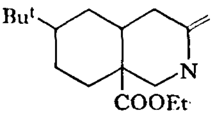

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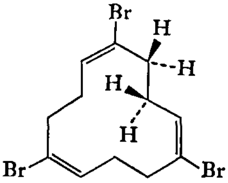
of the decahydroisoquinolone (**41**).[98] The preferred conformation of the cyclohexene ring A of 3-substituted $\Delta^{5(10)}$ steroids has been determined from the width of the 3-proton line, even though the coupling could not be completely resolved.[99] The coupling constants in 1,5,9-tribromocyclododeca-1,5-9-triene (**42**) suggest an s-*trans*-conformation (probably slightly skewed) about the three CH_2–CH_2 bonds.[100]



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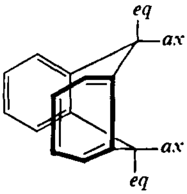

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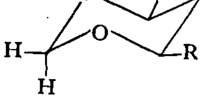
Chemical-shift correlations have also been used in conformational studies, frequently in conjunction with measurements of coupling constants. The chemical shift of the hydroxyl proton of cyclohexanols in dimethylsulphoxide solution depends on conformation.[101] The differential shielding of the pseudo-axial and pseudo-equatorial substituents in 9,10-dihydroanthracenes (**43**) has been used to study their conformations.[102, 103] The conformation of substituents on puckered cyclobutane rings affects the chemical shifts of the ring protons.[104] A fascinating, but rather inexplicable, linear correlation has been found[105] between the chemical-shift difference between the two 2-protons of the 1,3-dioxans (**44**) and the total number of carbon atoms attached to the α-carbon atoms of R and R′.



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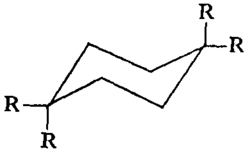
Among other systems studied have been cyclohexanetriols[106] (a comprehensive configurational and conformational study), piperidines[107] and decahydroquinolines[108] (where conformational possibilities are increased by the possibility of pyramidal inversion about nitrogen), 2-halogenotetrahydropyrans[109, 110] and 1,4-dioxenes.[111]

The position of the equilibrium between two conformers may be determined by comparing the observed average spectrum with the spectra of the individual conformers, which may be obtained by going to low enough temperatures to "freeze" the equilibrium process, or be estimated from conformationally rigid-model compounds. In this way the free-energy difference between the two chair forms of several substituted cyclohexanes has been determined.[112–118]

3. *Ring inversions and energy barriers*

(a) *Six-membered rings.* The same principles and methods as were outlined above for determination of energy barriers in acyclic systems apply also to ring inversions. 1,1,4,4-Tetramethyl- and 1,1,4,4-tetramethoxy-cyclohexane (**45**; R = Me, OMe, respectively) both have two separate methyl signals at low temperature (corresponding to the axial and equatorial R groups) which coalesce on warming as the chair–chair inversion of the cyclohexane ring renders all four methyl groups, on the average, equivalent.[119–121]



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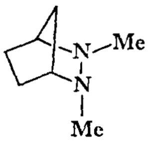
Thermodynamic activation parameters have been derived from the change of line shape with temperature.[120, 121] The inversions of cyclohexane-d_{11}[122] and of deuterated[123] and 9,10-disubstituted[124] *cis*-decalins have similarly been studied.

Ring inversions in hetero-substituted cyclohexanes have been studied, and activation parameters for piperidine,[125] piperazines,[121, 126] morpholines,[126] 1,3-dioxans,[127] hexahydropyrimidines,[128] hexahydro-1,3,5-triazines,[128, 129] and pentamethylene sulphoxide[130] reported. Particular attention has been paid by several workers to mono- and bicyclic-compounds containing the piperidazine system. In the simplest cases, such as the diazabicycloheptane (**46**)[131, 132] and related compounds,[133] the only processes involved are the pyramidal inversions about the nitrogen atoms, which are probably consecutive and synchronous. Additional complications arise in unbridged systems (as **47**, **48**) when inversion of the ring is also possible.[133, 134] When the nitrogen atoms form part of a diacylhydrazide system (as **49**) they become sp^2 hybridized, so that pyramidal inversion is no longer possible, but now there is the possibility of hindered rotation about the nitrogen–carbonyl bonds. Ring inversion and hindered rotation have different averaging effects on the p.m.r. spectra and may thus be examined separately.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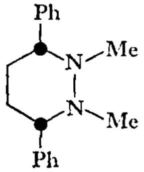
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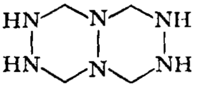
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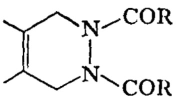
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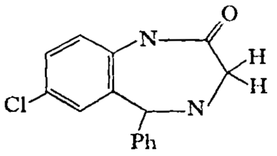
Despite some dissension[135] (cf. Korsch and Riggs[52]), it appears that in most cases the ring inversion ($\Delta G^{\ddagger}$ typically 20 kcal./mole) is a slower process than nitrogen-carbonyl rotation[136–138] ($\Delta G^{\ddagger}$ typically 15 kcal./mole). Examples of the opposite order are known.[136]

(b) *Rings other than six-membered.* The energy barrier to nitrogen inversion in *N*-substituted aziridines depends on the degree of conjugation between nitrogen and substituent.[139] Inversion in the diazepinone (**50**) was studied by the temperature variation of the spectrum of the methylene group.[140] Several eight-membered ring compounds have been studied, including alkyl[141] and deuterated cyclooctanes,[142] the heterocyclic compounds (**51**; $Z = S$, Se),[143] cyclo-octatrienone,[144] and the fused ring system (**52**).[145] In all cases it was possible to suggest preferred conformations for the eight-membered ring, as well as to investigate inversion processes. The twelve-membered ring compounds tri-*o*-thymotide (**53**; $R = Me$,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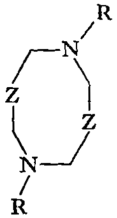
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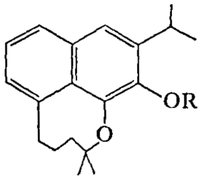
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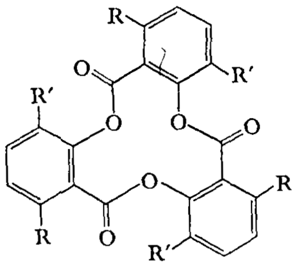
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$R' = Pr^i$) and tri-*o*-carvacrotide (**53**; $R = Pr^i$, $R' = Me$) can exist in two conformations, the propeller (*P*), in which all the arylmethyl groups are equivalent, and the helical (*H*), in which they are all non-equivalent; each conformer can exist in enantiomeric forms (P^*, H^*). Activation parameters for the interconversion equilibria, $P \rightleftharpoons H \rightleftharpoons H^* \rightleftharpoons P^*$, have been determined by variable temperature p.m.r., based on an unambiguous assignment of the arylmethyl signals to the different conformers.[146, 147]

III. KINETICS AND EQUILIBRIUM

The section on stereochemistry has contained many examples of the use of p.m.r. in studies of kinetics and equilibrium. The present Section extends the discussion to other fields. A brief review of some aspects of the subject has recently been published.[148]

A. Slow reactions

Reactions that take place slowly may be followed simply by observing the change of spectrum with time. P.m.r. has been particularly useful for following hydrogen–deuterium exchange processes, and has been applied to ring-proton exchange in the cations of several sulphur and nitrogen five-membered heterocycles,[149, 150] exchange of methyl protons in substituted pyridines and pyrimidines,[151] and to exchange in enammonium salts.[152] The reaction of benzyl fluoride with formic acid to give benzyl formate was followed by observing the replacement of a doublet for the methylene protons (coupled to fluorine) by a singlet.[153]

In many cases the mechanism of the reaction may be elucidated by observing the spectra of intermediates. The mercury-catalysed equilibrium—

$$\mathrm{PhCOOH + AcOCH{:}CH_2 \rightleftharpoons PhCOOCH{:}CH_2 + AcOH}$$

proceeds via the intermediate mercuri compound (**54**).[154] The thermodynamically stable product of the addition of amines to acetylenic sulphones is the *trans* olefin, but this is formed by isomerization of the kinetic *cis* product.[155]

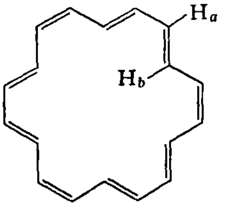
$\mathrm{(PhCOO)(AcO)CH.CH_2.HgOAc}$

54

B. Exchange and double resonance

If two protons are exchanging environments by a chemical or stereochemical process, sufficiently slowly for separate signals to be seen in the n.m.r. spectrum, then strong irradiation at the frequency of one of the lines may cause a collapse or partial collapse of the other, as the saturated population of spin states is transferred by the exchange process.[156] This has been observed for intermolecular and intramolecular processes. Proton exchange between alcohols has been studied to examine the effect on coupling constants.[157] The exchange between traces of water impurity in commercial deuterochloroform and the hydroxyl proton of phenols has been used to diagnose the signal of the latter by noting which line collapses when the small water peak at $\tau \approx 8{\cdot}5$ is irradiated.[158]

At 20°C the spectrum of [18]annulene (**55**) shows lines at $1{\cdot}2\,\tau$ and $13{\cdot}0\,\tau$ due to the outer (*a*) and inner (*b*) protons, respectively. Irradiation of one causes the other to collapse because of internal rotation.[159]



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Rotation in *p*-nitrosodimethylaniline has also been studied.[159] If the exchange process has a life time of the order of seconds, its kinetics may be determined by observing the rate of collapse of the second peak after irradiation of the first and its rate of recovery when the irradiation is switched off. The activation parameters for the chair–chair interconversion of cyclohexane-d_{11} have been determined in this way.[122]

C. Other kinetic measurements

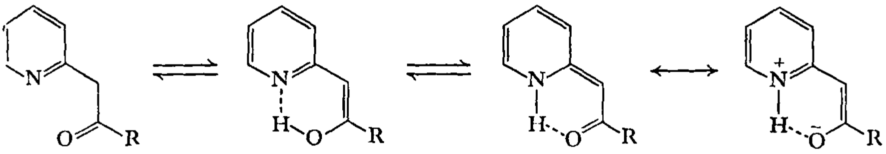
The collapse of spin-coupling between one proton and another that is exchanging rapidly can be used to obtain kinetic parameters for the exchange. Rates of proton exchange of ammonium salts have been related to ion pairing[160] and to salt effects.[161] Proton exchange rates in substituted guanidinium ions[162] and in peptides[163] have been studied.

The rates of exchange of ligands between a co-ordinated site and bulk solvent have been studied by line-shape measurements;[164–171] variable temperature effects allow separation of enthalpy and entropy of activation.[166, 167] Ligands studied include water,[164] dimethylformamide,[165, 166] β-diketones,[167] EDTA and similar chelating agents,[168–170] and triphenylphosphine.[171] The kinetics of ligand "scrambling" reactions involving Group III metal alkyls,[172, 173] alkylsilicon and alkylgermanium halides,[174, 175] and mixed trimethylantimony halides[176] have been studied by observing the coalescence of the signals from the alkyl groups at temperatures sufficient to render them equivalent on the n.m.r. time scale.

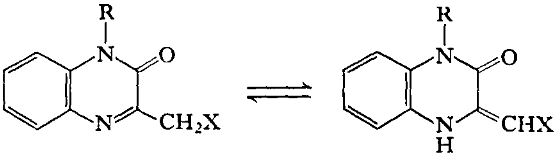
D. Slow equilibria

The position of equilibrium between slowly interconverting systems (on the n.m.r. time scale) is simply determined by integrating peaks due to the separate compounds.

Integrated spectra of a series of β-diketones have been measured at various temperatures; the change in equilibrium constant revealed entropy and enthalpy differences between the keto and enol tautomers.[177] Keto–enol tautomerism has also been studied in seven- to ten-membered ring keto-esters.[178] A detailed analysis of the spectra of picolyl ketones (**56**⇌**57**; $R = Pr^i$, Ph) reveals small lines which can only be explained by supposing that a small amount of the pyridomethine tautomer (**58**) is present.[179] Similar prototropic shifts between ring and side-chain have been observed in several quinolines, quinoxolines (as **59**⇌**60**) and benzoxazones.[180] The tautomeric equilibrium constant depends on the solvent as well as on the nature of X.[180] The ring-chain tautomerism between the tetrazolopurines (**61**, **63**, **65**) and the corresponding purinylazides (**62**, **64**) has been studied by p.m.r.[181] Equilibria involving addition to carbonyl groups (**66**⇌**67**) have been studied by p.m.r. because the signals of the R and R′ groups usually shift significantly from ketone to adduct.[182,183] (^{17}O magnetic resonance may also be used.[182]) The method can be more accurate than the usual ultraviolet measurements, and can detect the nature of the species present in more complex equilibria.[183] The covalent hydration of heteroaromatic bases and their cations has been studied.[184,185]

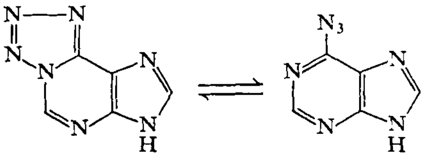


56 **57** **58**



59 **60**

The kinetics of ligand exchange and "scrambling" reactions were mentioned above. The equilibria of such reactions can readily be determined from relative peak areas.[186–189]



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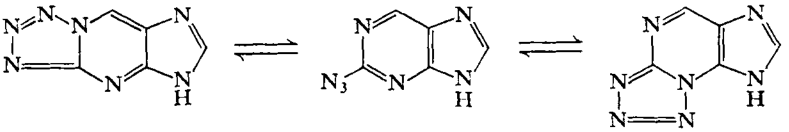
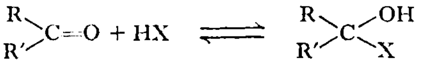


63 **64** **65**



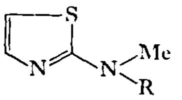
$$\mathrm{RR'C{=}O} + \mathrm{HX} \rightleftharpoons \mathrm{RR'C(OH)X}$$

66 **67**

E. Fast equilibria

The p.m.r. spectrum of a rapidly equilibrating mixture is the weighted average of the spectra of the separate components rather than a superimposition of them. The equilibrium constant can be determined from the known or estimated spectra of the components.

Fast tautomeric equilibria are studied by using non-tautomeric model compounds, e.g., the two *N*-methyl derivatives (**68**, **70**) as models for the amino (**69**) and imino (**71**) forms of *N*-substituted 2-aminothiazoles.[190] Similar studies have been reported for aminoquinolines,[191] pyrazoles[192] and dihydroxypyrimidines.[193]



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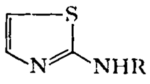

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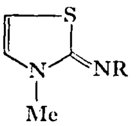

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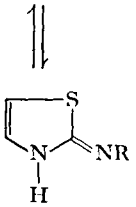

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P.m.r. has been used to determine the relative pK_a values of weak acids, such as substituted anilines[194] and hydrides of germanium, phosphorus and arsenic,[195] by setting up the equilibrium—

$$HA + B^- \rightleftharpoons HB + A^-$$

in sodium amide–liquid ammonia and determining the ratios $[HA]/[A^-]$ and $[HB]/[B^-]$ by interpolation of observed chemical shifts between those of the free acid and the conjugate base. Relative carbonium ion stabilities have similarly been determined from the equilibrium—

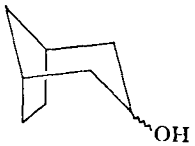
$$R^+ + R'Y \rightleftharpoons R'^+ + RY$$

where RY and R'Y are suitable covalent carbonium ion precursors.[196]

IV. SOLVENT EFFECTS AND MOLECULAR ASSOCIATION

A. Hydrogen bonding

The large downfield shift of the signal from a proton involved in a hydrogen bond is useful for both qualitative and quantitative studies. The temperature dependence of the water peak has been correlated with various theories of water structure.[197] The disruption of the structure of water,[198,199] of ammonia[200] and of methanol[201] by added electrolytes has been studied. The hydrogen-bonded self-association of alcohols,[202] thiols[203,204] and of tropolones[205] has been studied by the temperature or concentration dependence of the OH or SH protons and association constants and possible structures for the associated species derived. The isomeric *cis*- and *trans*-bicyclo-octanols (**72**) can be distinguished by their characteristic changes of OH proton shift with concentration, which arise because of the different ways in which the isomeric molecules can aggregate.[206]



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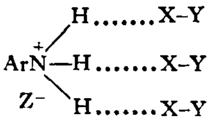
Hydrogen bonding between phenol and organic bases has been studied and the use of the p.m.r. method for estimating the enthalpy of association discussed.[207] The chemical shift of the acidic proton of a substituted tropolone when hydrogen bonded to pyridine correlates linearly with its pK_a value.[208] The SH proton of thiols forms a hydrogen bond with amines, ethers, ketones and sulphides, but in chloroform solution the thiol sulphur atom acts as an acceptor for a hydrogen bond with the chloroform hydrogen.[209] Strong hydrogen bonding between phenols and hexamethylphosphoramide has been used[210] to analyse mixed phenols because the OH protons of the separate components give separate, resolved, concentration independent, characteristic peaks in the region -3 to $+2\tau$. In dimethylsulphoxide the chemical shift of the hydrogen-bonded hydroxyl proton of oximes is characteristic of their *syn* or *anti* configuration.[211]

Hydrogen bonding may produce shifts in the p.m.r. signals of protons other than that directly involved in the hydrogen bond, and such shifts may be correlated with changes in electron distribution and charge density. The change in the chemical-shift differences between the α and β and β and γ protons of pyridine on dissolution in methanol or deuterium oxide is about equal to the theoretical contribution from the electrostatic effect of the nitrogen lone pair;[212] hydrogen bonding must effectively remove this contribution. The electron distributions in hydrogen-bonded and protonated pyridine *N*-oxides has been compared with the corresponding pyridines.[213] In polar solvents, the charge distribution around the ring of trialkyl anilinium salts, $\mathrm{Ar\overset{+}{N}R_3}$, shows that the positive centre exerts a strong inductive effect, but this is totally lacking in the unsubstituted $\mathrm{Ar\overset{+}{N}H_3}$ compounds.[214] This is ascribed to ion-pair formation and hydrogen-bonded solvation in the latter case (as **73**; X–Y = solvent, Z^- = salt anion) which effectively neutralize the effect of the positive charge.[214] The influence of hydrogen bonding on the chemical shifts of a wide range of aliphatic oxygen and nitrogen compounds in acidic media has been tabulated.[215]



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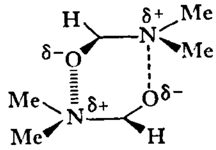
B. Non-hydrogen bonding

A stereospecific association between two molecules—either self-association or between solvent and solute—will probably cause changes in chemical shift from the unassociated molecules, particularly if the association involves large changes in electron distribution or if the molecules involved are magnetically very anisotropic. The upfield shift of the signal due to the methyl group *cis* to the oxygen atom in dimethylformamide as the medium changes from dilute carbon tetrachloride solution to pure liquid is interpreted in terms of a dimeric complex (**74**) in which the *cis*-methyl group of one molecule is shielded by the anisotropic carbonyl bond of the other.[216] Similar associations have been suggested for acridine orange[217,218] (2,8-bisdimethylaminoacridine) and in coproporphyrin tetramethyl esters.[219] The change of chemical shifts with temperature as well as



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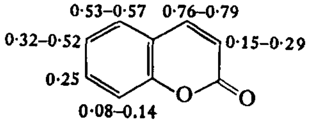
with concentration have been used to determine the thermodynamic parameters of self-association in aromatic aldehydes.[220, 221]

The relative strengths of Lewis acids towards donor solvents[222–226] (and vice versa[227]) have been determined in several cases by correlating changes in chemical shift with electron distribution. The order $BI_3 > BBr_3 > BCl_3 > BF_3$ has been found for the acceptor strength of boron halides.[222–224]

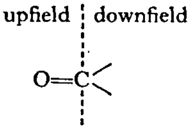
It has been suggested, however, that chemical-shift changes do not necessarily provide a good criterion of complex stability.[226]

The shifts caused by aromatic solvents, and benzene in particular, have been widely discussed in terms both of the mechanism of solvation and of the application of such solvent shifts in structural and stereochemical studies. In general,[228] benzene will interact at an electron-deficient site in a solute molecule. The relative orientation of benzene and solute molecules is governed by local dipolar interactions, but will generally be non-coplanar so that the benzene molecule is as far removed as possible from the negative end of solute dipoles.[228] Particular attention has been paid to these shifts in ketones[229–232] (especially steroidal ketones[233–235]), quinones,[236, 237] and methoxy compounds.[238, 239] The difference between the chemical shifts of ring protons in coumarins when measured in benzene or benzene-d_6 and in deuterochloroform (written as $\Delta^{CDCl_3}_{C_6H_6}$) are characteristic of position,[240] as illustrated in (75), where values for $\Delta^{CDCl_3}_{C_6H_6}$ are indicated in parts



75

per million. Shifts of similar magnitude are observed for the methyl group protons of methyl coumarins.[240] The temperature dependence of solvent shifts has been used to obtain thermodynamic association parameters.[234, 238] The change with temperature in the shift of the signals of α,β-unsaturated ketones in toluene-d_8 solution correlates roughly, but not precisely with $\Delta^{CCl_4}_{toluene}$ for the same compounds.[231] Protons that are situated to the left of the plane drawn through the carbon atom perpendicular to the carbonyl bond (76) are shifted upfield by an increase in temperature, those to the right downfield.[231] *trans*-Propenyl methyl



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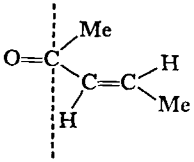

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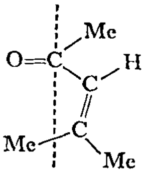

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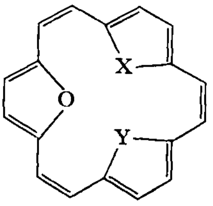
ketone exists in the s-*trans*-conformation (**77**), as shown by the strong downfield shift of the signals from the hydrogen atom and methyl group on the β-carbon. But in isobutenyl methyl ketone (mesityl oxide) the s-*cis*-conformation (**78**) is preferred, and the *cis*-β-methyl group is shifted upfield.[231]

V. RING CURRENTS AND AROMATICITY

The concept of magnetically induced ring currents in closed π-electron systems (despite recent iconoclastic suggestions denying their existence[241]) is widely used as a criterion of aromaticity. An evaluation of previous attempts to determine the magnitude of ring currents from p.m.r. chemical-shift measurements concludes that it is a good criterion although it does not always correlate directly with other aromatic properties such as resonance energy or reactivity.[242] The low-field chemical shifts, all below $2\,\tau$ observed for [18]annulene trioxide[243] (**79**; $X=Y=O$) and [18]annulene dioxide sulphide[244] (**79**; $X=O$, $Y=S$) are good evidence for the aromatic character of these compounds, but [18]annulene oxide disulphide (**79**; $X=Y=S$) is probably non-planar and non-aromatic[245] with chemical shifts above $3\,\tau$. The bridged [14]annulene (**80**) has a spectrum in accord with delocalized 14π-electrons.[246] The lowest field signals in the p.m.r. spectrum of the pure keto-compound (**81**) are in the region 3·0–4·5 τ. Base catalyses the tautomerism with the bridged [10]annulene enol (**82**); in the tautomeric mixture the ring protons are deshielded to 2·0–3·7 τ showing the aromatic nature of the enol form.[247] The high-field signal for the methylene protons of the vinylidene bridged annulene (**83**) is consistent with the existence of a ring current, since the methylene group falls into the shielded region.[248] The un-



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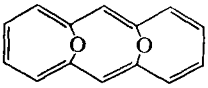

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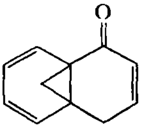

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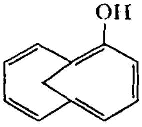

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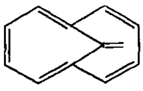

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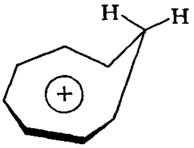
precedentedly large chemical-shift difference of nearly 6 p.p.m. between the signals from the two geminal methylene protons of the homotropylium cation[249] suggests the existence of a ring current involving the other carbon atoms (**84**);



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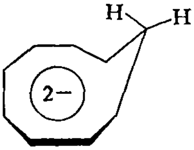

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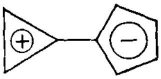
a smaller separation of 2 p.p.m. in the cyclononatetraenyl dianion[250] may similarly indicate a homoaromatic 10π system (**85**). There appears to be appreciable electron transfer, corresponding to the 2π–6π dipolar structure (**86**), in pentatrifulvalene,[251] but there is little evidence of delocalization in other fulvenes.[252, 253] P.m.r. is useful for measuring aromaticity in the dibenzoheptafulvene and dibenzotropone series[254] (**87**; $X=CH_2$, O, respectively). The tricyclic 18π-electron system (**88**) is non-aromatic containing non-planar eight-membered rings.[255]



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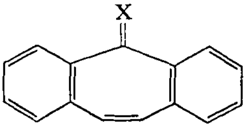

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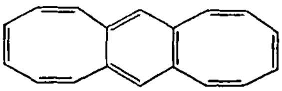

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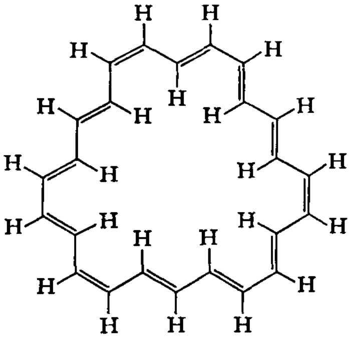
There has been recent interest in the so-called anti-Hückel annulenes, containing 4nπ-electron systems. Quantum mechanical theory predicts a *paramagnetic* ring current in these compounds,[256] which would lead to low-field signals for inner protons and high-field for outer, just the opposite of what is found for Hückel annulenes. This has now been observed in several cases.[256–259] [24]Annulene (**89** or **90**) shows a single line in its p.m.r. spectrum at 40°C, but at −80°C there are two lines, the smaller at about −2 τ and the larger at +5·3 τ. It is clear that the smaller peak must be due to the inner protons, but the integration was not accurate enough to distinguish between the two possible structures.[257]



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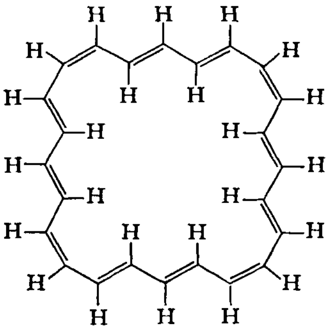

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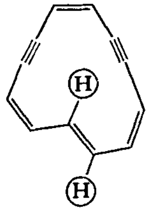

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The spectrum of bisdehydro[12]annulene (**91**) contains a signal at $-0{\cdot}9\,\tau$, which is probably due to the inner and outer protons Ⓗ in rapid equilibrium.[256] Since the outer proton should be at about $+5{\cdot}5\,\tau$ (the other signal due to the other six outer protons is between 5 and $5{\cdot}8\,\tau$), this suggests[256] the inner proton signal would be at about $-6{\cdot}4\,\tau$.

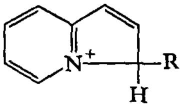
VI. GENERAL STRUCTURAL DETERMINATION

A. Correlation tables

The basis of most applications of p.m.r. to the determination of structure is still the more or less empirical correlation between structure and chemical shift. Many correlation tables, both generalized and those dealing with specific types of compounds, are published. A convenient chart[260] indicates approximate chemical shift ranges (on both τ and δ scales) for nearly 100 differently situated hydrogen atoms. More detailed tables include: olefins,[261, 262] unsaturated fatty acids,[263] polyhydric alcohols and hydroxy acids,[264] acylcyclopropanes and aziridines,[92] cyclobutanes,[86] steroids and terpenes and related compounds,[64, 97, 233, 235, 265–271] dibenzobicyclo[2,2,2]octadienes,[272] various nitrogen-containing compounds,[273] alkylbenzenes[274] and other aromatic hydrocarbons,[275, 276] quinones,[236, 277] phenols,[278] cyclic enamines and iminium salts,[279] vinylfurans,[243] polycondensed aza-aromatic compounds,[275] pyrazoles,[192, 280] thiazoles,[281] quinazolines[282] and benzotriazoles.[283] Additive substituent constants, whereby unknown chemical shifts may be estimated from known values for similar compounds, are particularly valuable. Some have been derived from the tabulations above for: vinyl protons in olefins,[262] ring protons in cyclobutanes,[86] alkylbenzenes[274] and phenols,[278] various nitrogen-containing compounds[273] and the 4-proton of pyrazoles.[192]

B. Protonation studies

P.m.r. spectroscopy is particularly appropriate for determining the precise structure of protonated bases because of the possibility of observing spin-coupled interactions between the added proton and its neighbours. Indolizines unsubstituted in the 3-position protonate almost exclusively to give the 3*H*-indolizinium cation (**92**; R = H); in 3-alkylindolizines a mixture of the 3*H* and 1*H* (**93**) ions is formed in a ratio which depends on the acid.[284, 285] The distinction is made on the basis of the coupling of the R group and on chemical-shift differences; the positive nitrogen atom exerts a greater deshielding influence on the adjacent 3-position than on the 1-position. In thiophens, on the other hand, protonation is invariably in the α-position, even in 2,5-disubstituted compounds.[286] Protonation of pteridines,[287] iminopyrrolidines[288] and nitroguanidines[289] has similarly been studied. The change in the H–N–Me spin coupling with pH may be used to distinguish between different types of *N*-substituted methylamines.[290] Methoxybenzenes may protonate (exclusively sometimes) on oxygen rather than carbon.[291] The downfield shifts of the methyl group protons in methylcyclohexanones when the hydroxonium ion is formed are characteristic both of the position on the ring and of the conformation of the methyl group.[292] In $FSO_2OH/SbF_5/SO_2$, which ionizes tertiary and many secondary alcohols to stable carbonium ions, primary and some secondary alcohols merely protonate.[293] Proton exchange in this medium is slow; deuteromethanol is protonated to $\mathrm{Me\overset{+}{O}DH}$ in which the methyl signal is a doublet, coupled to the single proton on the oxygen atom.[293]



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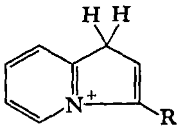

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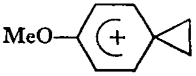
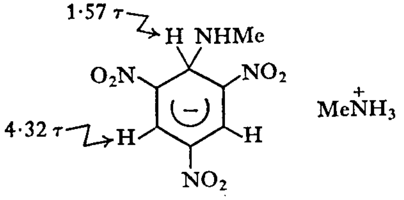
C. Carbonium ions and carbanions

Olah and his co-workers have made very extensive studies of stable carbonium ions and have made much use of p.m.r. to diagnose and characterize them. Thus fluorodimethylcarbonium ion ($Me_2\overset{+}{C}F$) is readily characterized both by the large downfield shift of the signal from the methyl protons compared with the precursor (Me_2CF_2)—from 8·64 to 6·07τ—but also by the increase in coupling constant—from 19 to 26 c./sec.—consequent on the rehybridization of the carbon.[294] A number of phenylethyl cations have been studied.[295] They can all be classified as static (e.g., $Ph_2\overset{+}{C}R$) or as equilibrating mixtures (e.g., $PhCMe_2{\cdot}\overset{+}{C}Me_2 \rightleftharpoons Me_2\overset{+}{C}{\cdot}CMe_2Ph$) with no evidence of the bridged phenonium ion structures that exist when there are strongly electron-donating substituents on the ring[296] (e.g., **94**). Other work on carbonium ions is described in references 297–301. Olah and Pittman have reviewed the uses of spectroscopy in studying alkyl



94

carbonium ions.[302] The large upfield shift experienced by the aromatic-ring protons on the formation of Meisenheimer and similar complexes has been used in their structural determination.[303–306] When 1,3,5-trinitrobenzene is mixed with increasing proportions of methylamine[303] the signal from the aromatic protons (initially at 0·8τ) moves upfield linearly with the amine:trinitrobenzene mole ratio until this is 2:1, when the signal has reached 3·4τ. Further addition of amine causes the peak to split into two lines, at 1·57 and 4·32τ of relative areas 1:2 (weighted average, 3·4τ), which are then not altered by further addition of amine. This is interpreted as showing the formation of a 2:1 amine trinitrobenzene ionic complex (**95**).[303]



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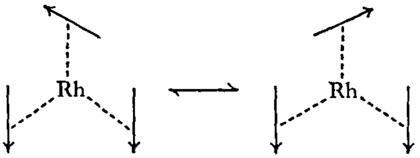
D. Organometallic and inorganic compounds

The structure of metal-allyls has been extensively investigated. In triallylrhodium all three allyl groups are non-equivalent at low temperatures,[307] but two of them become equivalent to each other[307, 308] at 10°C, which implies an equilibrium of the type (**96**$\rightleftharpoons$**97**).[307]



96 **97**

Allyl groups may form either π or σ metal–allyl bonds—cyclopentadienyldiallylrhodium, for example, contains one π-bonded and one σ-bonded allyl group[309]—but the possibility of an intermediate type of bond, perhaps involved in rapid equilibration (as **98**)[310] is somewhat controversial. There is evidence from the p.m.r. spectrum of the vinyl protons that in several cases a π-allyl group is unsymmetrically bonded to the metal,[309, 311] as with bisdiallylrhodium chloride (**99**), in which the *trans* metal–carbon bonds are probably longer than the *cis*.[309]

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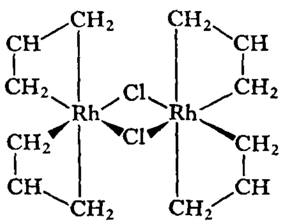

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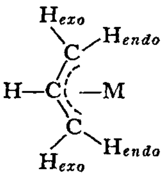

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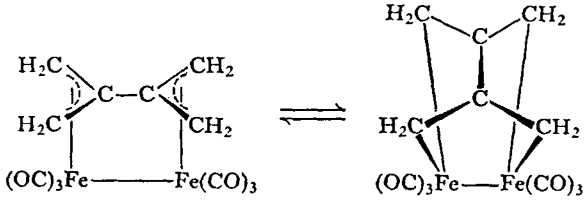
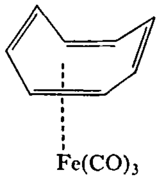
It is also clear from variable temperature studies that the *exo* and *endo* hydrogens (see **100**) of allyl groups can interchange their positions, because the spectrum changes from an AM_2X_2 pattern to an AX_4 pattern with increasing temperature,[312] but this can be accounted for by hindered internal rotation without invoking "dynamic bonding" as in (**98**) (cf. Becconsall *et al.*[313] and Vrieze and his coworkers[314, 315]). A novel type of π-allyl complex, obtained from allene with iron and cobalt carbonyls, appears to be a valence-bond tautomer (as **101**$\rightleftharpoons$**102**).[317]



101 **102**

The bonding in cyclo-octatetraene metal carbonyls has been studied by variable-temperature p.m.r. The signal in cyclo-octatetraene iron tricarbonyl splits into two equal lines at low temperature. The suggestion that this implies a 1,5-diene–metal bond (**103**)[318] is probably more realistic than the equilibrating structure (**104**)[319] which involves a geometrically impossible disposition of the carbon–carbon double bonds. Cyclo-octatetraene molybdenum tricarbonyl shows



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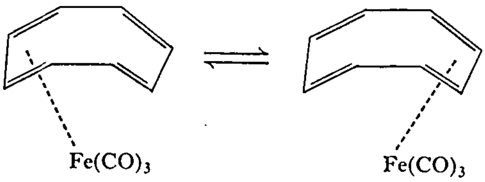

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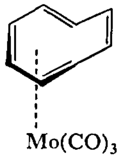
p.m.r. signals for four types of proton at low temperatures, suggesting a π-triene complex (**105**, τ-values indicated); the collapse to a single line at room temperature implies rapid equilibration by valence-bond tautomerism.[320] On the other hand the extremely complex behaviour of the spectrum of 1,3,5,7-tetramethylcyclo-octatetraene molybdenum tricarbonyl with changing temperature has been interpreted[321] in terms of a π-diene complex at low temperature (**106**). The



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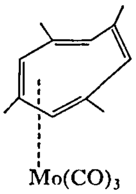

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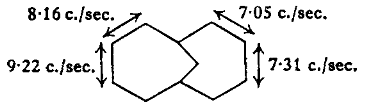
chromium tricarbonyl complex of the bridged annulene, 1,6-methanocyclodecapentaene, involves unsymmetrical bonding with the chromium atom attached to one half of the ten-membered ring.[322, 323] But the values of the *ortho* coupling constants (indicated in **107**) suggest that there is still extensive 10π-delocalization rather than a 6π-diene structure (**108**).[322] Metallocene spectra have been widely used in structural studies.[324–329] Additivity rules for estimating chemical shifts



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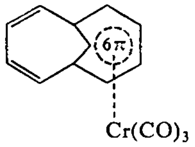

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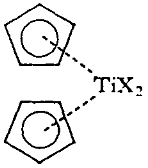
of substituted ferrocenes have been suggested.[324] In the titanocenes (**109**) there is p.m.r. evidence of hindered ring rotation when the ligands X are bulky.[325]



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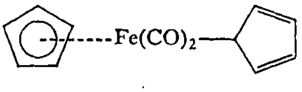


110

At room temperature all five protons of the σ-ring of σ-cyclopentadienyl-π-cyclopentadienyliron dicarbonyl (**110**) are equivalent.[330] A detailed consideration of the unsymmetrical way in which the spectrum from this ring breaks up as the temperature is lowered indicates that the equilibration takes place via a series of 1,2-shifts.[330] P.m.r. may be useful in determining the stereochemical disposition of ligands in inorganic and organometallic complexes. In ruthenium and nickel complexes with dimethylphenylphosphine[331] the methyl group chemical shift has been correlated with stereochemistry. Penta-*p*-tolyl derivatives of phosphorus, arsenic and antimony show only one methyl group signal at room temperature, because of equilibration of the ligand positions in the trigonal bipyramid.[332] 3,3-Dimethylbutyl compounds of lithium, magnesium and zinc exhibit configurational inversion at the α-methylene groups, as shown by variable-temperature studies, but the corresponding aluminium and mercury compounds are configurationally stable.[333] The chemical shifts in these compounds correlate well with metal electronegativity.[333] Slow inversion about the sulphur atom causes *cis–trans* isomerism about the C_2S_2Pt ring of the $MeSCH_2CH_2SMe$ complex with $PtCl_2$, in which two separate methyl group signals are seen in the room-temperature spectrum.[334] Bidentate and tetradentate liganding in EDTA complexes of palladium^{II} may be distinguished because of separate signals from bonded and non-bonded acetate groups.[335]

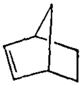
VII. COUPLING-CONSTANT CORRELATIONS

A. Long-range couplings

The magnitude of proton–proton spin-coupled interactions through more than three bonds depends on several factors. An important one is the conformation taken up by the bonds between the interacting nuclei; a W or zig-zag all s-*trans*-conformation leads to large couplings. For four-bond couplings (designated ^4J) a correlation of the type—

$$^4J = A\cos^2\phi'\cos^2\phi'' - B$$

has been derived[336] from a study of the couplings in norbornenes (**111**); A and B are constants, the magnitude of A varying according as ϕ' and ϕ'' are acute or obtuse; ϕ' and ϕ'' are the dihedral angles illustrated in (**112**). This property has been used in several stereochemical assignments. In *cis* fused 9-methyldecalins (e.g. 5β-steroids, **113**) and N-methylquinolizidinium ions (**114**) there is only one proton coupled to the angular methyl group by the W path, but in the *trans* fused isomers there are three (**115**, **116**). The long-range coupling in these compounds cannot be resolved, but is reflected in the line widths for the angular methyl group, which are much greater for the *trans* fused isomers than for the *cis*.[337, 338] In some tetra-substituted cyclopentanes[339] (e.g., **117**) the relative conformations are such that ^4J may be greater than ^3J.



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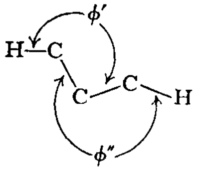

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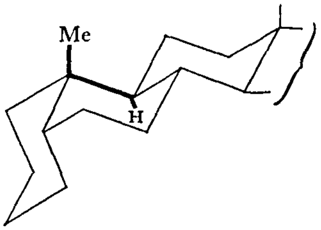

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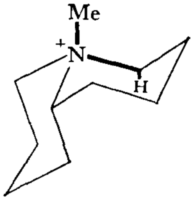

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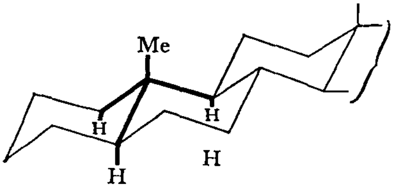

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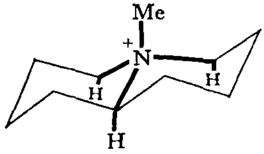

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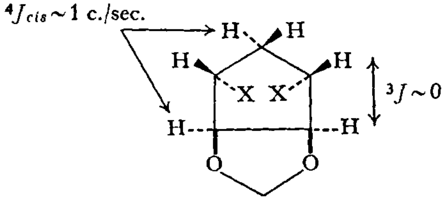
However, conformation is not the only factor. Direct, "through-space" interactions will play a part when the interacting nuclei are close together, as with geminal dimethyl groups.[340–342] The change in ^4J of acetone with changing polarity of the carbonyl bond can only be explained by supposing such direct interactions to be important and of opposite sign to the electron-coupled inter-



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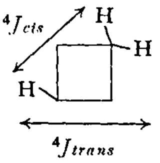
actions.[340] This is in agreement with observations that in cyclobutanes $^4J_{cis}$ and $^4J_{trans}$ (cf. **118**) have opposite sign.[343] The fluorine–proton couplings between the *ortho* fluorine atom Ⓕ and the R group in the benzobicyclo-octadienes (**119**) are larger for ^6J (R = OMe, NMe$_2$, CMe$_3$) and ^5J (R = Me) than they are for ^4J (R = H), again suggesting direct interactions.[61]



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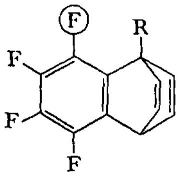

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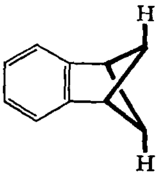
A third factor in determining the magnitude of long-range couplings is the number of paths available between the interacting protons.[344] The benzobicyclohexene (**120**) shows a very large ^4J of 5·4 c./sec. which is partly accounted for by the two separate four-bond W paths between the protons.[345] ^5J in the tricyclo-octene (**121**) is 2·6 c./sec. and the double path is again present.[346] The introduction of double bonds or heteroatoms into the path between the interacting protons



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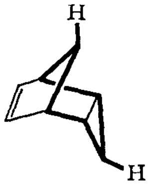

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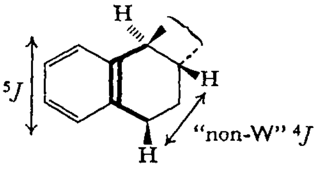

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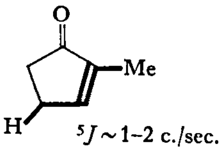
also increases the coupling. ^5J in some A aromatic steroids (**122**) is significant though the "non-W" ^4J is not observed.[347] In methyl acetate[348] the two methyl groups are coupled (^5J) by 0·2 c./sec. Other five-bond couplings are illustrated in (**123**),[349] (**124**),[350] (**125**).[351]



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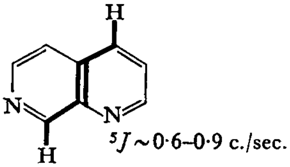

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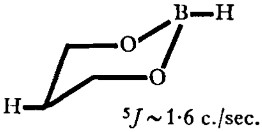

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B. Substituent effects

Several correlations have been suggested between coupling constants in a molecule and the electronegativity of substituents. In systems H—C—N—H the coupling constant decreases with increasing electronegativity of substituents on the nitrogen atom,[352] which is similar to the effect which has been known for some time in H—C—C—H systems; on the other hand H—C—O—H couplings increase with increasing electronegativity of substituents,[353] and correlate linearly with σ^*. In β-substituted systems[354] (HC•CH•CX) the vicinal coupling constant also increases with increasing electronegativity of X, and tentative evidence that this is reversed again with γ-substituents implies that the effect alternates with the number of intervening bonds.[354] In the aromatic series, the *ortho* coupling constant between the 2- and 3-protons correlates fairly well with the electronegativity of the substituent in mono-substituted benzenes from 6·7 c./sec. for phenyl-lithium to 8·4 c./sec. for fluorobenzene.[355, 356] Other couplings involving the 2-proton correlate less well and those involving only the *meta*- and *para*-protons not at all.[355] A linear correlation of the type—

$$\Delta_X = n_X J + t_X$$

has been observed in aromatic systems where J is an *ortho* coupling constant, Δ_X is the change in shift of one of the coupled protons when the other is replaced by a substituent X, and n_X and t_X are constants for a given substituent.[357]

C. Other correlations

A comprehensive survey of the factors that affect geminal coupling constants has been published. It is based on almost one thousand values, many of which are tabulated.[358]

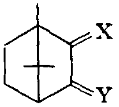
The dependence of H—C—C—F coupling constants on dihedral angle appears to follow the same pattern as for H—C—C—H couplings.[359]

An interesting correlation has been suggested for a molecule R–Ⓗ between the coupling between the hydrogen atom Ⓗ and another nucleus in R and the spin density at that nucleus in the radical R• as measured by electron spin resonance couplings. This has been demonstrated for several RR'MeCH systems with a ratio 3·1 to 3·6 c./sec. to 1 gauss.[360]

VIII. MISCELLANEOUS

A. Diamagnetic anisotropy

The subject has been reviewed.[361] The anistropic effect of the *syn*- or *anti*-oxime group in camphor derivatives (**126**; X, Y=O, NOH, NPh, CHOH) is similar to that of the *cis*- or *trans*-enol group, implying that the differential shielding between the *syn*- and *anti*-oxime groups arises from the anisotropy of the hydroxyl group and not from the nitrogen lone pair.[362] The chemical-shift differences between the geminal methyl groups of pinane derivatives (as **127**) suggest that the anisotropic effect of a puckered cyclobutane ring is as in (**128**).[363] The anisotropy of the nitrosamine group has been studied.[364] The substituent effects in ethylgermanium halides, hydrides and oxides,[365] and in methylphenyldisiloxanes[366] are probably too great to be accounted for by inductive effects and are ascribed to substituent anisotropy.



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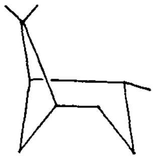

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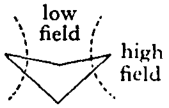

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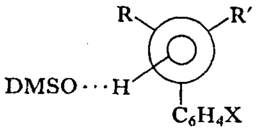
B. Hammett function correlations

In dimethylsulphoxide solution, the chemical shift of the hydroxylic proton of substituted benzyl alcohols ($X{\cdot}C_6H_4{\cdot}CRR'{\cdot}OH$) correlates well with σ_X. The variation of ρ with the nature of R and R′ suggests that transmission of substituent effects is better in the *gauche* conformation (**129**) than in the *anti* (**130**).[367] In the case of phenols in dimethylsulphoxide solution the change in hydroxyl chemical shift with substituent correlates very well with σ ($\rho = 1{\cdot}536$); this affords a very simple method for determining σ.[368] $\Delta^{\mathrm{CDCl_3}}_{\mathrm{C_6H_6}}$ for the *N*-methyl protons of *para*-substituted dimethylanilines correlates[369] with σ^-. The transmission of electronic



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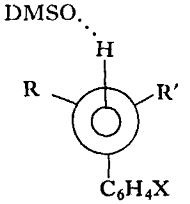

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effects through carbon, oxygen and sulphur has been studied by correlating chemical shifts for substituted toluenes, acetophenones and thioanisoles with σ values and extracting ρ values for the three series.[370]

C. Other topics

Chemical-shift measurements used as a measure of electron density have been used to suggest (p–d) π-bonding in phosphorus-carbon,[371] sulphur-carbon[372] and silicon-oxygen[373] bonds.

The variation with pH in the chemical shift of ring protons of histidine residues in peptides has been used to make tentative assignments of peaks in the high-resolution spectrum of ribonuclease to particular histidine residues.[374] Aminoacid sequences in di- and tripeptides have been determined by a similar method.[375]

The use of ^{13}C satellite peaks in a p.m.r. spectrum to detect the position of isotopic substitution in a molecule has allowed the use of ^{13}C instead of ^{14}C as a tracer isotope, and avoids the need for degradative analysis.[376]

REFERENCES

1. H. Güsten and M. Salzwedel, *Tetrahedron,* 1967, **23**, 173, 187.
2. P. J. S. Pauwels, *J. Amer. Chem. Soc.*, 1967, **89**, 580.
3. K. Nagarajan, M. D. Nair and P. M. Pillai, *Tetrahedron,* 1967, **23**, 1683.
4. I. D. Rae, *Canad. J. Chem.*, 1966, **44**, 1334.
5. T. H. Siddall, *J. Mol. Spectroscopy,* 1966, **20**, 183.
6. M. Karplus, *J. Chem. Phys.*, 1959, **30**, 11.
7. R. J. Abraham and W. A. Thomas, *J. Chem. Soc.*, 1964, 3739 and references therein.
8. M. Anteunis, *Bull. Soc. chim. belges,* 1966, **75**, 413.
9. C. C. J. Culvenor and N. S. Ham, *Chem. Comm.*, 1966, 537.
10. H. Lee, N. S. Bhacca and M. E. Wolff, *J. Org. Chem.*, 1966, **31**, 2692.
11. J. Canceill, J. J. Basselier and J. Jacques, *Bull. Soc. chim. France,* 1967, 1024.
12. C. A. Kingsbury and W. B. Thornton, *J. Org. Chem.*, 1966, **31**, 1000.
13. L. M. Jackman and N. S. Bowman, *J. Amer. Chem. Soc.*, 1966, **88**, 5565.
14. M. Buza and E. I. Snyder, *J. Amer. Chem. Soc.*, 1966, **88**, 1161.
15. M. L. Martin and G-J. Martin, *Bull. Soc. chim. France,* 1966, 2117.
16. G-J. Martin, J-P. Gouesnard and M. Martin, *Compt. rend.* [C], 1967, **264**, 794.
17. T. H. Siddall and C. A. Prohaska, *J. Amer. Chem. Soc.*, 1966, **88**, 1172.
18. T. H. Siddall, *J. Org. Chem.*, 1966, **31**, 3719.
19. H. Gerlach, *Helv. Chim. Acta,* 1966, **49**, 2481.
20. R. E. Mayo and J. H. Goldstein, *Mol. Phys.*, 1966, **10**, 301.
21. I. Crossland, *Acta Chem. Scand.*, 1966, **20**, 258.
22. G. P. Newsoroff and S. Sternhell, *Austral. J. Chem.*, 1966, **19**, 1667.
23. T. Hayashi, *J. Org. Chem.*, 1966, **31**, 3253.
24. G. M. Whitesides, J. P. Sevenair and R. W. Goetz, *J. Amer. Chem. Soc.*, 1967, **89**, 1135.
25. E. I. Snyder, *J. Amer. Chem. Soc.*, 1966, **88**, 1165.
26. C. A. Kingsbury and D. C. Best, *J. Org. Chem.*, 1967, **32**, 6.
27. R. E. Rondeau and L. A. Harrah, *J. Mol. Spectroscopy,* 1966, **21**, 332.

28. G. R. DeMare and J. S. Martin, *J. Amer. Chem. Soc.*, 1966, **88**, 5033.
29. H. Günther and D. Wendisch, *Angew. Chem.*, 1966, **78**, 266.
30. W. Lüttke and A. de Meijere, *Angew. Chem.*, 1966, **78**, 544 (*Internat. Ed.*, 1966, **5**, 512).
31. J-L. Pierre and P. Arnaud, *Bull. Soc. chim. France*, 1966, 1690.
32. G. J. Karabatsos and N. Hsi, *Tetrahedron*, 1967, **23**, 1079.
33. G. J. Karabatsos and K. L. Krumel, *Tetrahedron*, 1967, **23**, 1097.
34. R. Barlet, J-L. Pierre and P. Arnaud, *Compt. rend.* [*C*], 1966, **262**, 855.
35. D. K. Foster, *J. Amer. Chem. Soc.*, 1966, **88**, 5067.
36. E. I. Snyder, *J. Amer. Chem. Soc.*, 1966, **88**, 1155.
37. R. J. Abraham, L. Cavalli and K. G. R. Pachler, *Mol. Phys.*, 1966, **11**, 471.
38. R. J. Abraham and M. A. Cooper, *J. Chem. Soc. B*, 1967, 202.
39. H. Hogeveen, A. F. Bickel, C. W. Hilbers, E. L. Mackor and C. MacLean, *Chem. Comm.*, 1966, 898.
40. D. M. Brouwer, E. L. Mackor and C. Maclean, *Rev. Trav. chim.*, 1966, **85**, 114.
41. T. H. Siddall and M. L. Good, *Bull. Chem. Soc. Japan*, 1966, **39**, 1619.
42. D. M. Lynch and W. Cole, *J. Org. Chem.*, 1966, **31**, 3337.
43. T. H. Siddall and R. H. Garner, *Canad. J. Chem.*, 1966, **44**, 2387.
44. J. P. Marsh and L. Goodman, *Tetrahedron Letters*, 1967, 683.
45. R. Kuhn, B. Schulz and J. C. Jochims, *Angew. Chem.*, 1966, **78**, 449.
46. D. Y. Curtin, E. J. Grubbs and C. G. McCarty, *J. Amer. Chem. Soc.*, 1966, **88**, 2775.
47. N. P. Marullo and E. H. Wagener, *J. Amer. Chem. Soc.*, 1966, **88**, 5034.
48. D. G. Gehring, W. A. Mosher and G. S. Reddy, *J. Org. Chem.*, 1966, **31**, 3436.
49. W. Walter, G. Maerten and H. Rose, *Annalen*, 1966, **691**, 25.
50. L. Bauer, C. L. Bell, K. R. Sandberg and A. P. Parulkar, *J. Org. Chem.*, 1967, **32**, 376.
51. A. Mannschreck and U. Koelle, *Tetrahedron Letters*, 1967, 863.
52. B. H. Korsch and N. V. Riggs, *Tetrahedron Letters*, 1966, 5897.
53. A. Mannschreck, H. Munsch and A. Matheus, *Angew. Chem.*, 1966, **78**, 751 (*Internat. Ed.*, 1966, **5**, 728).
54. B. Bak, P. O. Jensen and K. Schaumberg, *J. Mol. Spectroscopy*, 1966, **20**, 1.
55. F. Kaplan and G. K. Meloy, *J. Amer. Chem. Soc.*, 1966, **88**, 950.
56. H. J. Bestmann, G. Joachim, I. Lengyel, J. F. M. Oth, R. Merenyi and H. Weitkamp, *Tetrahedron Letters*, 1966, 3355.
57. A. P. Downing, W. D. Ollis and I. O. Sutherland, *Chem. Comm.*, 1967, 143.
58. T. H. Siddall and R. H. Garner, *Tetrahedron Letters*, 1966, 3513.
59. S. van der Werf, T. Olijnsma and J. B. F. N. Engberts, *Tetrahedron Letters*, 1967, 689.
60. G. Fraenkel, M. P. Cava and D. R. Dalton, *J. Amer. Chem. Soc.*, 1967, **89**, 329.
61. J. P. N. Brewer, H. Heaney and B. A. Marples, *Chem. Comm.*, 1967, 27.
62. P. K. Korver, P. J. van der Haak and T. J. de Boer, *Tetrahedron*, 1966, **22**, 3157.
63. H. Hirschmann, F. B. Hirschmann and A. P. Zala, *J. Org. Chem.*, 1966, **31**, 375.
64. H. Lee and M. E. Wolff, *J. Org. Chem.*, 1967, **32**, 192.
65. D. J. Adam, L. Crombie and D. A. Whiting, *J. Chem. Soc. C*, 1966, 542.
66. C. A. Anirudhan, D. W. Mathieson and W. B. Whalley, *J. Chem. Soc. C*, 1966, 634.

67. B. J. Bolger, A. Hirwe, K. G. Marathe, E. M. Philbin, M. A. Vickars and C. P. Lillya, *Tetrahedron*, 1966, **22**, 621.
68. J. Brugidon and H. Christol, *Bull. Soc. chim. France*, 1966, 1974.
69. J. W. Clark-Lewis and D. C. Skingle, *Chem. Comm.*, 1967, 251.
70. S. E. Drewes and D. G. Roux, *Biochem. J.*, 1966, **98**, 493.
71. S. E. Drewes, D. G. Roux, H. M. Saayman, J. Feeney and S. H. Eggers, *Chem. Comm.*, 1966, 370.
72. C. P. Falshaw, W. D. Ollis, J. A. Moore and K. Magnus, *Tetrahedron Supplement 7*, 1966, 333.
73. G. F. Katekar, *Austral. J. Chem.*, 1966, **19**, 1251.
74. S. Yamaguchi, S. Ito, A. Nakamura and N. Inoue, *Bull. Chem. Soc. Japan*, 1966, **39**, 622.
75. A. Grouiller, *Bull. Soc. chim. France*, 1966, 2405.
76. A. Segree and J. I. Musher, *J. Amer. Chem. Soc.*, 1967, **89**, 706.
77. H. Booth, *Tetrahedron*, 1966, **22**, 615.
78. E. N. Banas, A. W. Weitkamp and N. S. Bhacca, *Analyt. Chem.*, 1966, **38**, 1783.
79. A. D. Cross, *Biochem. J.*, 1966, **100**, 238.
80. A. Smit and J. Bakker, *Rec. Trav. chim.*, 1966, **85**, 731.
81. D. N. Jones and D. E. Kime, *J. Chem. Soc. C*, 1966, 846.
82. K. L. Williamson, L. R. Sloan, T. Howell and T. A. Spencer, *J. Org. Chem.*, 1966, **31**, 436.
83. R. G. Foster and M. C. McIvor, *Chem. Comm.*, 1967, 280.
84. M. A. Battiste and M. E. Brennan, *Tetrahedron Letters*, 1966, 5857.
85. G. G. Lyle and L. K. Keefer, *J. Org. Chem.*, 1966, **31**, 3921.
86. H. Weitkamp and F. Korte, *Tetrahedron Supplement 7*, 1966, 75.
87. A. Zysman, G. Dana and J. Weimann, *Bull. Soc. chim. France*, 1967, 1019.
88. H. W. Heine, R. Peavy and A. J. Durbetaki, *J. Org. Chem.*, 1966, **31**, 3924.
89. J. Křepinský, Z. Samek, F. Šorm, D. Lamparsky, P. Ochsner and Y-R. Naves, *Tetrahedron Supplement 8*, 1966, 53.
90. N. Baggett, J. M. Duxbury, A. B. Foster and J. M. Webber, *J. Chem. Soc. C*, 1966, 208.
91. A. Robert, *Compt. rend.* [*C*], 1966, **263**, 1439.
92. D. W. Boykin, A. B. Turner and R. E. Lutz, *Tetrahedron Letters*, 1967, 817.
93. J. Seyden-Penne, T. Strzalko and M. Plat, *Tetrahedron Letters*, 1966, 3611.
94. Y. Aito, T. Matsuo and C. Aso, *Bull. Chem. Soc. Japan*, 1967, **40**, 130.
95. G. L. Buchanan and J. M. McCrae, *Tetrahedron*, 1967, **23**, 279.
96. S. Winstein, E. C. Friedrich, R. Baker and Yang-i Lin, *Tetrahedron Supplement 8*, 1966, 621.
97. J. R. Hanson, *Tetrahedron*, 1966, **22**, 1701.
98. R. A. Abramovitch and D. L. Struble, *Chem. Comm.*, 1966, 150.
99. S. G. Levine, N. H. Eudy and C. F. Leffler, *J. Org. Chem.*, 1966, **31**, 3995.
100. S. Castellano and K. G. Untch, *J. Amer. Chem. Soc.*, 1966, **88**, 4238.
101. C. P. Rader, *J. Amer. Chem. Soc.*, 1966, **88**, 1713.
102. W. Carruthers and G. E. Hall, *J. Chem. Soc. B*, 1966, 861.
103. J-C. Cognacq, M-P. Simonnin, W. Chodkiewicz and P. Cadiot, *Compt. rend.* [*C*], 1967, **264**, 915.
104. I. Lillien and R. A. Doughty, *J. Amer. Chem. Soc.*, 1967, **89**, 155.
105. D. Tavernier and M. Anteunis, *Tetrahedron Letters*, 1966, 5851.

106. G. E. McCasland, M. O. Naumann and L. J. Durham, *J. Org. Chem.*, 1966, **31**, 3079.
107. H. Booth and J. H. Little, *Tetrahedron*, 1967, **23**, 291.
108. H. Booth and A. H. Bostock, *Chem. Comm.*, 1967, 177.
109. G. E. Booth and R. J. Ouellette, *J. Org. Chem.*, 1966, **31**, 544.
110. C. B. Anderson and D. T. Sepp, *J. Org. Chem.*, 1967, **32**, 607.
111. G. Pfundt and S. Farid, *Tetrahedron*, 1966, **22**, 2237.
112. G. W. Buchanan and J. B. Stothers, *Chem. Comm.*, 1967, 179.
113. N. C. Franklin and H. Feltkamp, *Tetrahedron*, 1966, **22**, 2801.
114. R. J. Ouellette, K. Liptak and G. E. Booth, *J. Org. Chem.*, 1966, **31**, 546.
115. J. C. Celotti, J. Reisse and G. Chiurdoglu, *Tetrahedron*, 1966, **22**, 2249.
116. J. J. Uebel and H. W. Goodwin, *J. Org. Chem.*, 1966, **31**, 2040.
117. H. Bodot, D. D. Dicko and Y. Gounelle, *Bull. Soc. chim. France*, 1967, 870.
118. T. A. Crabb and R. F. Newton, *Chem. and Ind.*, 1966, 339.
119. W. Reusch and D. F. Anderson, *Tetrahedron*, 1966, **22**, 583.
120. R. W. Murray and M. L. Kaplan, *Tetrahedron*, 1967, **23**, 1575.
121. R. J. Abraham and D. B. Macdonald, *Chem. Comm.*, 1966, 188.
122. F. A. L. Anet and A. J. R. Bourn, *J. Amer. Chem. Soc.*, 1967, **89**, 760.
123. F. R. Jenson and B. H. Beck, *Tetrahedron Letters*, 1966, 4523.
124. J. Altman, H. Gilboa, D. Ginsburg and A. Loewenstein, *Tetrahedron Letters*, 1967, 1329.
125. J. B. Lambert and R. G. Keske, *J. Amer. Chem. Soc.*, 1966, **88**, 620.
126. R. K. Harris and R. A. Spragg, *Chem. Comm.*, 1966, 314.
127. J. E. Anderson and J. C. D. Brand, *Trans. Faraday Soc.*, 1966, **62**, 39.
128. F. G. Riddell and J. M. Lehn, *Chem. Comm.*, 1966, 375.
129. R. F. Farmer and J. Hamer, *Chem. Comm.*, 1966, 866.
130. J. B. Lambert and R. G. Keske, *J. Org. Chem.*, 1966, **31**, 3429.
131. E. L. Allred, C. L. Anderson, R. L. Miller and A. L. Johnson, *Tetrahedron Letters*, 1967, 525.
132. J. E. Anderson and J. M. Lehn, *J. Amer. Chem. Soc.*, 1967, **89**, 81.
133. J. E. Anderson and J. M. Lehn, *Bull. Soc. chim. France*, 1966, 2402.
134. J. P. Kintzinger, J. M. Lehn and J. Wagner, *Chem. Comm.*, 1967, 206.
135. C. H. Bushweller, *Chem. Comm.*, 1966, 80.
136. B. J. Price, I. O. Sutherland and F. G. Williamson, *Tetrahedron*, 1966, **22**, 3477.
137. R. Daniels and K. A. Roseman, *Chem. Comm.*, 1966, 429.
138. B. J. Price, R. V. Smallman and I. O. Sutherland, *Chem. Comm.*, 1966, 319.
139. F. A. L. Anet and J. M. Osyany, *J. Amer. Chem. Soc.*, 1967, **89**, 352.
140. P. Linscheid and J. M. Lehn, *Bull. Soc. chim. France*, 1967, 992.
141. F. A. L. Anet and M. St. Jacques, *J. Amer. Chem. Soc.*, 1966, **88**, 2586.
142. F. A. L. Anet and M. St. Jacques, *J. Amer. Chem. Soc.*, 1966, **88**, 2585.
143. J. M. Lehn and F. G. Riddell, *Chem. Comm.*, 1966, 803.
144. C. Ganter, S. M. Pokras and J. D. Roberts, *J. Amer. Chem. Soc.*, 1966, **88**, 4235.
145. F. Conti, C. H. Eugster and W. von Philipsborn, *Helv. Chim. Acta*, 1966, **49**, 2267.
146. W. D. Ollis and I. O. Sutherland, *Chem. Comm.*, 1966, 402.
147. A. P. Downing, W. D. Ollis and I. O. Sutherland, *Chem. Comm.*, 1967, 171.
148. R. J. Day and C. N. Reilley, *Analyt. Chem.*, 1966, **38**, 1323.
149. H. A. Staab, H. Imgartinger, A. Mannschreck and M. T. Wu, *Annalen*, 1966, **695**, 55.

150. R. A. Olofson and J. M. Landesberg, *J. Amer. Chem. Soc.*, 1966, **88**, 4263, 4265.
151. T. J. Batterham, D. J. Brown and M. N. Paddon-Row, *J. Chem. Soc. B*, 1967, 171.
152. M. Saunders and E. H. Gold, *J. Amer. Chem. Soc.*, 1966, **88**, 3376.
153. J. J. Delpuech and C. Beguin, *Bull. Soc. chim. France*, 1967, 791.
154. G. Slinckx and G. Smets, *Tetrahedron*, 1966, **22**, 3163.
155. W. E. Truce and D. G. Brady, *J. Org. Chem.*, 1966, **31**, 3543.
156. S. Fórsen and R. A. Hoffmann, *Acta Chem. Scand.*, 1963, **17**, 1787; *J. Chem. Phys.*, 1963, **39**, 2892.
157. B. M. Fung and R. D. Stolow, *Chem. Comm.*, 1967, 257.
158. J. Feeney and A. Heinrich, *Chem. Comm.*, 1966, 295.
159. I. C. Calder, P. J. Garratt and F. Sondheimer, *Chem. Comm.*, 1967, 41.
160. M. Cocivera, *J. Amer. Chem. Soc.*, 1966, **88**, 672.
161. M. Cocivera, *J. Amer. Chem. Soc.*, 1966, **88**, 677.
162. J. U. Lowe, R. D. Barefoot and A. S. Tompa, *J. Org. Chem.*, 1966, **31**, 3315.
163. M. Sheinblatt, *J. Amer. Chem. Soc.*, 1966, **88**, 2123.
164. T. J. Swift and T. A. Stephenson, *Inorg. Chem.*, 1966, **5**, 1100.
165. A. Fratiello, R. Schuster and D. P. Miller, *Mol. Phys.*, 1966, **11**, 597; 1967, **12**, 111.
166. N. A. Matwiyoff, *Inorg. Chem.*, 1966, **5**, 788.
167. A. C. Adams and E. M. Larsen, *Inorg. Chem.*, 1966, **5**, 814.
168. J. L. Sudmeier and C. N. Reilley, *Inorg. Chem.*, 1966, **5**, 1047.
169. R. J. Kula and D. L. Rabenstein, *J. Amer. Chem. Soc.*, 1967, **89**, 552.
170. R. J. Kula and G. H. Reed, *Analyt. Chem.*, 1966, **38**, 697.
171. W. De W. Horrocks and L. H. Pignolet, *J. Amer. Chem. Soc.*, 1966, **88**, 5929.
172. K. C. Williams and T. L. Brown, *J. Amer. Chem. Soc.*, 1966, **88**, 4134.
173. K. C. Williams and T. L. Brown, *J. Amer. Chem. Soc.*, 1966, **88**, 5460.
174. K. Moedritzer and J. R. van Wazer, *Inorg. Chem.*, 1966, **5**, 547.
175. K. Moedritzer and J. R. van Wazer, *J. Inorg. Nuclear Chem.*, 1966, **28**, 957.
176. G. C. Long, C. G. Moreland, G. O. Doak and M. Miller, *Inorg. Chem.*, 1966, **5**, 1358.
177. G. Allen and R. A. Dwek, *J. Chem. Soc. B*, 1966, 161.
178. L. A. Paquette and R. W. Begland, *J. Amer. Chem. Soc.*, 1966, **88**, 4685.
179. G. Klose and K. Arnold, *Mol. Phys.*, 1966, **11**, 1.
180. R. Mondelli and L. Merlini, *Tetrahedron*, 1966, **22**, 3253.
181. C. Temple, M. C. Thorpe, W. C. Coburn and J. A. Montgomery, *J. Org. Chem.*, 1966, **31**, 935.
182. P. Greenzaid, Z. Luz and D. Samuel, *J. Amer. Chem. Soc.*, 1967, **89**, 749, 756.
183. D. L. Hooper, *J. Chem. Soc. B*, 1967, 169.
184. J. W. Bunting and D. D. Perrin, *J. Chem. Soc. B*, 1966, 433.
185. A. Albert, T. J. Batterham and J. J. McCormack, *J. Chem. Soc. B*, 1966, 1105.
186. A. C. Adams and E. M. Larsen, *Inorg. Chem.*, 1966, **5**, 228.
187. K. Moedritzer and J. R. van Wazer, *J. Organomet. Chem.*, 1966, **6**, 242.
188. E. V. von den Berghe and G. P. van der Kelen, *J. Organomet. Chem.*, 1966, **6**, 515, 522.
189. K. Moedritzer and J. R. van Wazer, *Inorg. Chem.*, 1966, **5**, 1254.
190. L. M. Werbel, *Chem. and Ind.*, 1966, 1634.
191. J. Renault and J-C. Cartron, *Compt. rend.* [*C*], 1966, **262**, 1161.
192. L. G. Tensmeyer and C. Ainsworth, *J. Org. Chem.*, 1966, **31**, 1878.

193. G. M. Kheifets, N. V. Khromov-Borisov, A. I. Koltsov and M. V. Volkenstein, *Tetrahedron*, 1967, **23**, 1197.
194. T. Birchall and W. L. Jolly, *J. Amer. Chem. Soc.*, 1966, **88**, 5439.
195. T. Birchall and W. L. Jolly, *Inorg. Chem.*, 1966, **5**, 2177.
196. A. E. Young, V. R. Sandel and H. H. Freedman, *J. Amer. Chem. Soc.*, 1966, **88**, 4532.
197. H. H. Rüterjans and H. A. Scheraga, *J. Chem. Phys.*, 1966, **45**, 3296.
198. R. E. Glick, W. E. Stewart and K. C. Tewari, *J. Chem. Phys.*, 1966, **45**, 4049.
199. E. R. Malinowski, P. S. Knapp and B. Fever, *J. Chem. Phys.*, 1966, **45**, 4274.
200. A. L. Allred and R. N. Wendricks, *J. Chem. Soc. A*, 1966, 778.
201. R. M. Hammaker and R. M. Clegg, *J. Mol. Spectroscopy*, 1967, **22**, 109.
202. J. Feeney and S. M. Walker, *J. Chem. Soc. A*, 1966, 1148.
203. M-M. Rousselot, *Compt. rend.* [*C*], 1966, **262**, 26.
204. S. H. Marcus and S. I. Miller, *J. Amer. Chem. Soc.*, 1966, **88**, 3719.
205. Y. Ikegami, T. Ikenoue and S. Seto, *Tohoku Daigaku Hisuiyoeki Kagaku Kenkyusho Hokoku* (*Bull. Chem. Res. Inst. Non-Aq. Sol. Tohoku Univ.*), 1966, **15**, 103.
206. W. Kraus and H. Suhr, *Annalen*, 1966, **695**, 27.
207. D. P. Eyman and R-S. Drago, *J. Amer. Chem. Soc.*, 1966, **88**, 1617.
208. Y. Ikegami, T. Ikenoue and S. Seto, *Tohoku Daigaku Hisuiyoeki Kagaku Kenkyusho Kokoku* (*Bull. Chem. Res. Inst. Non-aq. Sol. Tohoku Univ.*), 1966, **15**, 111.
209. M-M. Rousselot and M. Martin, *Compt. rend.* [*C*], 1966, **262**, 1445.
210. M. W. Dietrich, J. S. Nash and R. E. Keller, *Analyt. Chem.*, 1966, **38**, 1479.
211. G. G. Kleinspehn, J. A. Jung and S. A. Studniarz, *J. Org. Chem.*, 1967, **32**, 460.
212. T. M. Spotswood and C. I. Tanzer, *Tetrahedron Letters*, 1967, 911.
213. R. A. Abramovitch and J. B. Davis, *J. Chem. Soc. B*, 1966, 1137.
214. G. Fraenkel and J. P. Kim, *J. Amer. Chem. Soc.*, 1966, **88**, 4203.
215. P. E. Peterson, *J. Org. Chem.*, 1966, **31**, 439.
216. T. Yonezawa and I. Morishima, *Bull. Chem. Soc. Japan*, 1966, **39**, 2346.
217. D. J. Blears and S. S. Danyluk, *J. Amer. Chem. Soc.*, 1966, **88**, 1084.
218. D. J. Blears and S. S. Danyluk, *J. Amer. Chem. Soc.*, 1967, **89**, 21.
219. R. J. Abraham, P. A. Burbidge, A. H. Jackson and D. B. Macdonald, *J. Chem. Soc. B*, 1966, 620.
220. R. E. Klinck and J. B. Stothers, *Canad. J. Chem.*, 1966, **44**, 37.
221. Gurudata, R. E. Klinck and J. B. Stothers, *Canad. J. Chem.*, 1967, **45**, 213.
222. A. G. Massey and A. J. Park, *J. Organomet. Chem.*, 1966, **5**, 218.
223. J. M. Miller and M. Onyszchuk, *Canad. J. Chem.*, 1966, **44**, 899.
224. D. J. Pasto and P. Balasubramaniyan, *J. Amer. Chem. Soc.*, 1967, **89**, 295.
225. Sung Mao Wang and N. C. Li, *J. Amer. Chem. Soc.*, 1966, **88**, 4592.
226. N. N. Greenwood and T. S. Srivastava, *J. Chem. Soc. A*, 1966, 703.
227. V. Gutman, E. Wychera and F. Mairinger, *Monatsh.*, 1966, **97**, 1265.
228. J. Ronayne and D. H. Williams, *Chem. Comm.*, 1966, 712.
229. M. Fétizon, J. Goré, P. Laszlo and B. Waegell, *J. Org. Chem.*, 1966, **31**, 4047.
230. Y. Fujise and S. Itô, *Chem. Pharm. Bull.* (*Tokyo*), 1966, **14**, 797.
231. J. Ronayne, M. V. Sargent and D. H. Williams, *J. Amer. Chem. Soc.*, 1966, **88**, 5288.
232. J. D. Connolly and R. McCrindle, *J. Chem. Soc. C*, 1966, 1613.
233. D. H. Williams and D. A. Wilson, *J. Chem. Soc. B*, 1966, 144.

234. P. Laszlo and D. H. Williams, *J. Amer. Chem. Soc.*, 1966, **88**, 2799.
235. P. C. Cherry, W. R. T. Cottrell, G. D. Meakins and E. E. Richards, *J. Chem. Soc. C*, 1967, 181.
236. J. H. Bowie, D. W. Cameron, P. E. Schutz, D. H. Williams and N. S. Bhacca, *Tetrahedron*, 1966, **22**, 1771.
237. R. Foster and C. A. Fyfe, *Trans. Faraday Soc.*, 1966, **62**, 1400.
238. J. H. Bowie, J. Ronayne and D. H. Williams, *J. Chem. Soc. B*, 1966, 785.
239. H. M. Fales and K. S. Warren, *J. Org. Chem.*, 1967, **32**, 501.
240. R. Grigg, J. A. Knight and P. Roffey, *Tetrahedron*, 1966, **22**, 3301.
241. J. I. Musher, *J. Chem. Phys.*, 1967, **46**, 1219 and references therein.
242. R. J. Abraham and W. A. Thomas, *J. Chem. Soc. B*, 1966, 127.
243. G. M. Badger, J. A. Elix and G. E. Lewis, *Austral. J. Chem.*, 1966, **19**, 1221.
244. G. M. Badger, G. E. Lewis and U. P. Sing, *Austral. J. Chem.*, 1966, **19**, 1461.
245. G. M. Badger, G. E. Lewis and U. P. Sing, *Austral. J. Chem.*, 1966, **19**, 257.
246. E. Vogel, M. Biskup, A. Vogel and H. Gunther, *Angew. Chem.*, 1966, **78**, 755 (*Internat. Ed.*, 1966, **5**, 734).
247. E. Vogel, W. Schröck and W. A. Böll, *Angew. Chem.*, 1966, **78**, 753 (*Internat. Ed.*, 1966, **5**, 732).
248. E. Vogel, F. Weyres, H. Lepper and V. Rautenstrauch, *Angew. Chem.*, 1966, **78**, 754 (*Internat. Ed.*, 1966, **5**, 732).
249. C. E. Keller and R. Petitt, *J. Amer. Chem. Soc.*, 1966, **88**, 604, 606.
250. M. Ogliaruso, R. Riecke and S. Winstein, *J. Amer. Chem. Soc.*, 1966, **88**, 4731.
251. A. S. Kende, P. T. Izzo and P. T. MacGregor, *J. Amer. Chem. Soc.*, 1966, **88**, 3359.
252. D. Meuche, *Helv. Chim. Acta*, 1966, **49**, 1278.
253. M. L. Heffernan and A. J. Jones, *Austral. J. Chem.*, 1966, **19**, 1813.
254. M. Rabinovitz, I. Agranat and E. D. Bergmann, *Tetrahedron*, 1966, **22**, 225.
255. J. A. Elix, M. V. Sargent and F. Sondheimer, *Chem. Comm.*, 1966, 509.
256. J. A. Pople and K. G. Untch, *J. Amer. Chem. Soc.*, 1966, **88**, 4811.
257. I. C. Calder and F. Sondheimer, *Chem. Comm.*, 1966, 904.
258. K. G. Untch and D. C. Wysocki, *J. Amer. Chem. Soc.*, 1966, **88**, 2608.
259. G. Schröder and J. F. M. Oth, *Tetrahedron Letters*, 1966, 4083.
260. E. Mohacsi, *Analyst*, 1966, **91**, 57.
261. F. C. Stehling and K. W. Barlz, *Analyt. Chem.*, 1966, **38**, 1467.
262. C. Pascual, J. Meier and W. Simon, *Helv. Chim. Acta*, 1966, **49**, 164.
263. J. M. Purcell, S. G. Morris and H. Susi, *Analyt. Chem.*, 1966, **38**, 588.
264. D. T. Sawyer and J. R. Brannan, *Analyt. Chem.*, 1966, **38**, 192.
265. A. Romo de Vivar, L. Rodriquez-Hahn, J. Romo, M. V. Lakshmikantham, R. N. Mirrington, J. Kagan and W. Herz, *Tetrahedron*, 1966, **22**, 3279.
266. H. Hugel, A. C. Oehlschlager and G. Ourisson, *Tetrahedron Supplement 8*, 1966, 203.
267. B. Tursch, R. Savoir, R. Ottinger and G. Chiurdoglu, *Tetrahedron Letters*, 1967, 539.
268. B. Tursch, R. Savoir and G. Chiurdoglu, *Bull. Soc. chim. belges*, 1966, **75**, 107.
269. G. F. H. Green, J. E. Page and S. E. Staniforth, *J. Chem. Soc. B*, 1966, 807.
270. G. J. W. Breen, E. Ritchie, W. T. L. Sidwell and W. C. Taylor, *Austral. J. Chem.*, 1966, **19**, 455.
271. A. Gaudemer, *Bull. Soc. chim. France*, 1967, 406.

272. S. J. Cristol, T. W. Russell, J. R. Mohrig and D. E. Plorde, *J. Org. Chem.*, 1966, **31**, 581.
273. G. Slomp and J. G. Lindberg, *Analyt. Chem.*, 1967, **39**, 60.
274. N. Van Meurs, *Rec. Trav. chim.*, 1967, **86**, 111.
275. R. H. Martin, N. Defay, F. Geerts-Evrard and D. Bogaert-Verhoogen, *Tetrahedron Supplement 8*, 1966, 181.
276. F. Fu-Hsie Yew and B. J. Mair, *Analyt. Chem.*, 1966, **38**, 231.
277. R. E. Moore and P. J. Scheuer, *J. Org. Chem.*, 1966, **31**, 3273.
278. J. A. Ballantine and C. T. Pillinger, *Tetrahedron*, 1967, **23**, 1691.
279. M. G. Reinecke and L. R. Kray, *J. Org. Chem.*, 1966, **31**, 4215.
280. J. Elguero, R. Jacquier and H. C. N. Tien Duc, *Bull. Soc. chim. France*, 1966, 3727.
281. G. Borgen and S. Gronowitz, *Acta. Chem. Scand.*, 1966, **20**, 2593.
282. A. R. Katritzky, R. E. Reavill and F. J. Swinbourne, *J. Chem. Soc. B*, 1966, 351.
283. K. T. Potts, H. R. Burton, T. H. Crawford and S. W. Thomas, *J.Org. Chem.*, 1966, **31**, 3522.
284. M. Fraser, S. McKenzie and D. H. Reid, *J. Chem. Soc. B*, 1966, 44.
285. W. L. F. Armarego, *J. Chem. Soc. B*, 1966, 191.
286. H. Hogeveen, *Rec. Trav. chim.*, 1966, **85**, 1072.
287. A. Dieffenbacher, R. Mondelli and W. von Philipsborn, *Helv. Chim. Acta*, 1966, **49**, 1355.
288. R. Kwok and P. Pranc, *J. Org. Chem.*, 1967, **32**, 738.
289. J. C. Lockhart, *J. Chem. Soc. B*, 1966, 1174.
290. M. Freifelder, R. W. Mattoon and R. W. Kriese, *J. Org. Chem.*, 1966, **31**, 1196.
291. D. M. Brouwer, E. L. Mackor and C. Maclean, *Rec. Trav. chim.*, 1966, **85**, 109.
292. T. D. J. D'Silva and H. J. Ringold, *Tetrahedron Letters*, 1967, 1505.
293. G. A. Olah and E. Namanworth, *J. Amer. Chem. Soc.*, 1966, **88**, 5327.
294. G. A. Olah, R. D. Chambers and M. Comisarow, *J. Amer. Chem. Soc.*, 1967, **89**, 1268.
295. G. A. Olah, C. U. Pittman, E. Namanworth and M. B. Comisarow, *J. Amer. Chem. Soc.*, 1966, **88**, 5571.
296. G. A. Olah, E. Namanworth, M. B. Comisarow and B. Ramsey, *J. Amer. Chem. Soc.*, 1967, **89**, 711.
297. C. A. Cupas, M. B. Comisarow and G. A. Olah, *J. Amer. Chem. Soc.*, 1966, **88**, 361.
298. G. A. Olah, C. A. Cupas and M. B. Comisarow, *J. Amer. Chem. Soc.*, 1966, **88**, 362.
299. G. A. Olah, C. U. Pittman and T. S. Sorensen, *J. Amer. Chem. Soc.*, 1966, **88**, 2331.
300. G. A. Olah and M. B. Comisarow, *J. Amer. Chem. Soc.*, 1966, **88**, 4442.
301. J. M. Bollinger, C. A. Kupas, K. J. Friday, M. L. Woolfe and G. A. Olah, *J. Amer. Chem. Soc.*, 1967, **89**, 156.
302. G. A. Olah and C. U. Pittman, *Adv. Phys. Org. Chem.*, 1966, **4**, 305.
303. M. R. Crampton and V. Gold, *J. Chem. Soc. B*, 1967, 23.
304. R. Foster and C. A. Fyfe, *J. Chem. Soc. B*, 1966, 53.
305. R. Foster, C. A. Fyfe, P. H. Emslie and M. I. Foreman, *Tetrahedron*, 1967, **23**, 227.
306. K. L. Servis, *J. Amer. Chem. Soc.*, 1967, **89**, 1508.

307. J. K. Becconsall and S. O'Brien, *Chem. Comm.*, 1966, 720.
308. J. Powell and B. L. Shaw, *Chem. Comm.*, 1966, 323.
309. J. Powell and B. L. Shaw, *Chem. Comm.*, 1966, 236.
310. K. C. Ramey and G. L. Statton, *J. Amer. Chem. Soc.*, 1966, **88**, 4387.
311. B. Bogdanović, H. Bönnemann and G. Wilke, *Angew. Chem.*, 1966, **78**, 591.
312. J. K. Becconsall and S. O'Brien, *Chem. Comm.*, 1966, 302.
313. J. K. Becconsall, B. E. Job and S. O'Brien, *J. Chem. Soc. A*, 1967, 423.
314. H. C. Volger and K. Vrieze, *J. Organomet. Chem.*, 1966, **6**, 297.
315. K. Vrieze, P. Cossee, C. MacLean and C. W. Hilbers, *J. Organomet. Chem.*, 1966, **6**, 672.
316. K. Vrieze, C. MacLean, P. Cossee and C. W. Hilbers, *Rec. Trav. chim.*, 1966, **85**, 1077.
317. A. Nakamura, *Bull. Chem. Soc. Japan*, 1966, **39**, 543.
318. F. A. Cotton, A. Davison and J. W. Faller, *J. Amer. Chem. Soc.*, 1966, **88**, 4507.
319. C. E. Keller, B. A. Shoulders and R. Pettit, *J. Amer. Chem. Soc.*, 1966, **88**, 4760.
320. C. G. Kreiter, A. Maasbol, F. A. L. Anet, H. D. Kaesz and S. Winstein, *J. Amer. Chem. Soc.*, 1966, **88**, 3444.
321. F. A. Cotton, J. W. Faller and A. Musco, *J. Amer. Chem. Soc.*, 1966, **88**, 4507.
322. H. Gunther and W. Grimme, *Angew. Chem.*, 1966, **78**, 1063 (*Internat. Ed.*, 1966, **5**, 1043).
323. E. O. Fischer, H. Rühle, E. Vogel and W. Grimme, *Angew. Chem.*, 1966, **78**, 548.
324. J. Tirouflet, G. Tainturier and H. Singer, *Bull. Soc. chim. France*, 1966, 2565.
325. A. N. Nesmeyanov, E. I. Fedin, O. V. Nogina, N. S. Kochetkova, V. A. Dubovitsky and P. V. Petrovsky, *Tetrahedron Supplement 8*, 1966, 389.
326. M. Cais, J. J. Danneberg, A. Eisenstadt, M. I. Levenberg and J. H. Richards, *Tetrahedron Letters*, 1966, 1695.
327. H. Watanabe, I. Motoyama and K. Hata, *Bull. Chem. Soc. Japan*, 1966, **39**, 790.
328. R. S. P. Coutts, J. R. Surtees, J. M. Swan and P. C. Wailes, *Austral. J. Chem.*, 1966, **19**, 1377.
329. T. J. Katz and J. J. Mrowca, *J. Amer. Chem. Soc.*, 1967, **89**, 1105.
330. M. J. Bennett, F. A. Cotton, A. Davison, J. W. Faller, S. J. Lippard and S. M. Morehouse, *J. Amer. Chem. Soc.*, 1966, **88**, 4371.
331. J. M. Jenkins, M. S. Lupin and B. L. Shaw, *J. Chem. Soc. A*, 1966, 1787, 1793.
332. D. Hellwinkel, *Angew. Chem.*, 1966, **78**, 749.
333. M. Witanowski and J. D. Roberts, *J. Amer. Chem. Soc.*, 1966, **88**, 737.
334. E. W. Abel, R. P. Bush, F. J. Hopton and C. R. Jenkins, *Chem. Comm.*, 1966, 58.
335. Y. O. Aochi and D. T. Sawyer, *Inorg. Chem.*, 1966, **5**, 2085.
336. V. F. Bystrov and A. U. Stepanyants, *J. Mol. Spectroscopy*, 1966, **21**, 241.
337. K. L. Williamson, T. Howell and T. A. Spencer, *J. Amer. Chem. Soc.*, 1966, **88**, 325.
338. C. W. Shoppee, F. P. Johnson, R. E. Lack, J. S. Shannon and S. Sternhell, *Tetrahedron Supplement 8*, 1966, 421.
339. H. Z. Sable, W. M. Ritchey and J. E. Nordlander, *J. Org. Chem.*, 1966, **31**, 3771.

340. W. H. de Jev, R. Deen and J. Smidt, *Rec. Trav. chim.*, 1967, **86**, 33.
341. W. J. Mijs, *Rec. Trav. chim.*, 1967, **86**, 220.
342. C. Pascual and W. Simon, *Helv. Chim. Acta*, 1967, **50**, 94.
343. C-H. Krauch, S. Farid and G. O. Schenck, *Chem. Ber.*, 1966, **99**, 625.
344. K. Takahashi, *Bull. Chem. Soc. Japan*, 1966, **39**, 2782.
345. M. Pomerantz, *J. Amer. Chem. Soc.*, 1966, **88**, 5349.
346. K. Tori and M. Ohtsuru, *Chem. Comm.*, 1966, 886.
347. F. P. Johnson, A. Melera and S. Sternhell, *Austral. J. Chem.*, 1966, **19**, 1523.
348. K. Hayamizo and O. Yamamoto, *J. Mol. Spectroscopy*, 1967, **22**, 119.
349. C. M. Cimarusti and J. Wolinsky, *J. Org. Chem.*, 1966, **31**, 4118.
350. W. W. Paudler and T. J. Kress, *Chem. and Ind.*, 1966, 1557.
351. W. G. Woods and P. L. Strong, *J. Amer. Chem. Soc.*, 1966, **88**, 4667.
352. I. D. Rae, *Austral. J. Chem.*, 1966, **19**, 1983.
353. W. B. Moniz, C. F. Poranski and T. N. Hall, *J. Amer. Chem. Soc.*, 1966, **88**, 190.
354. A. D. Cohen and T. Schaefer, *Mol. Phys.*, 1966, **10**, 209.
355. S. Castellano and C. Sun, *J. Amer. Chem. Soc.*, 1966, **88**, 4741.
356. R. R. Fraser, *Canad. J. Chem.*, 1966, **44**, 2737.
357. A. R. Katritzky, B. Ternai and G. J. T. Tiddy, *Tetrahedron Letters*, 1966, 1713.
358. R. C. Cookson, T. A. Crabb, J. J. Frankel and J. Hudec, *Tetrahedron Supplement* 7, 1966, 355.
359. K. L. Williamson, Y-F. Li, F. H. Hall and S. Swager, *J. Amer. Chem. Soc.*, 1966, **88**, 5678.
360. W. T. Dixon, *Chem. Comm.*, 1966, 870.
361. J-L. Pierre, *Ann. Chim. (France)* [14], 1966, **1**, 187.
362. A. Daniel and A. A. Pavia, *Tetrahedron Letters*, 1967, 1145.
363. N. Nakagawa and S. Saito, *Tetrahedron Letters*, 1967, 1003.
364. Y. L. Chow, *Angew. Chem.*, 1967, **79**, 51 (*Internat. Ed.*, 1967, **6**, 75).
365. R. M. Mackay and R. Watt, *J. Organomet. Chem.*, 1966, **6**, 336.
366. J. Homer, A. W. Jarvie, A. Holt and H. J. Hickton, *J. Chem. Soc. B*, 1967, 67.
367. R. J. Oullette, D. L. Marks and D. Miller, *J. Amer. Chem. Soc.*, 1967, **89**, 913.
368. J. G. Traynham and G. A. Knesel, *J. Org. Chem.*, 1966, **31**, 3350.
369. I. D. Rae and L. K. Dyall, *Austral. J. Chem.*, 1966, **19**, 835.
370. S. H. Marcus, W. F. Reynolds and S. I. Miller, *J. Org. Chem.*, 1966, **31**, 1872.
371. W. Drenth and D. Rosenberg, *Rec. Trav. chim.*, 1967, **86**, 26.
372. M. C. Caserio, R. E. Pratt and R. J. Holland, *J. Amer. Chem. Soc.*, 1966, **88**, 5747.
373. T. Ostdick and P. A. McCusker, *Inorg. Chem.*, 1967, **6**, 98.
374. J. H. Bradbury and H. A. Scheraga, *J. Amer. Chem. Soc.*, 1966, **88**, 4240.
375. M. Sheinblatt, *J. Amer. Chem. Soc.*, 1966, **88**, 2845.
376. M. Tanabe and G. Detre, *J. Amer. Chem. Soc.*, 1966, **88**, 4515.

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Nuclear Magnetic Resonance Spectroscopy in Conformational Analysis

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IN THE last twenty years, the development in the fields of n.m.r. spectroscopy and conformational analysis has followed a somewhat parallel course, as reflected in the rapidly increasing number of published papers dealing with these topics. It is now established that n.m.r. spectroscopy provides more information about the shape of molecules in solution than any other physical method, with the possible exception of microwave spectroscopy, which at present can be applied only to rather simple small molecules in the gas phase.

This review attempts to convey the more important developments in the field between 1964 and the present time, and to assess the present capabilities and potential of the n.m.r. method as a probe in conformational analysis. It is clear that the potential is by no means exhausted, and that with the better instrumentation now available, the spectroscopy of other nuclei, such as carbon-13, will play an increasing rôle in the determination of conformational information in the future.

The large field of carbohydrate conformations is not included in this review, as it will be dealt with in its own right as a single review in Volume 2 of "Annual Reviews of N.M.R. Spectroscopy".

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I. MEASUREMENT OF RAPID CHEMICAL EXCHANGE PROCESSES IN SOLUTION

In recent years, n.m.r. spectroscopy has proved invaluable in the study of fast-exchange-rate processes in both cyclic and acyclic molecules. With the development of commercial instruments with accurate temperature control, many mobile compounds have been examined in the range $-180°$ to $+200°$C. Unfortunately, where energy barriers to rotation or inversion are less than 5 kcal./mole, the lower limit of temperature attainable is still too high for appreciable slowing down of the exchange rate between sites. Therefore many ethane derivatives, and the more mobile cyclic systems such as cyclohexanone cannot be "frozen out" by using present techniques. Information concerning rotation or inversion in such molecules must be obtained by extrapolation of chemical shifts and coupling constants or by use of microwave spectroscopy. However, there are many compounds where steric and/or electronic factors combine to raise the energy barrier between sites so that the thermodynamic parameters governing the exchange may be determined.

Several very comprehensive reviews[1–5] have been published on the subject of ring inversions and rate processes in general, and it is not necessary to repeat data already recorded in these papers, but rather to add to it, in the light of more recent work.

Four techniques have been used to measure exchange rates by n.m.r. spectroscopy, namely the steady-state or high-resolution technique, the spin-echo,[6] double-resonance[7] and the fast-passage[8] method, of which the first two are by far the most commonly used. As spin-echo spectrometers are not at present readily available, the high-resolution method is used by the majority of workers.

The theory for the exchange between sites of equal energy is reasonably well established, and great detail is not required here. The appearance of the high-resolution spectrum of an inverting molecule is governed by the rate of exchange and the internal chemical shift between nuclei in different sites. In cyclohexane-d_{11} for example,[9] the spectrum at 60 Mc./sec. alters from a sharp singlet at room temperature, where fast exchange is taking place, to a sharp doublet at $-100°$C ($\delta_{ab}=28$ c./sec.), where the exchange rate is very slow compared to the n.m.r. time scale. This of course disregards any internuclear H–D coupling, which is removed by double irradiation at the deuterium frequency. In the low-temperature spectrum, the high-field peak is due to the conformer with axial hydrogen and the low-field peak to the conformer with equatorial hydrogen. By studying the spectrum at various intermediate temperatures, it is possible to obtain values of the rate constant for each temperature. Application of the Arrhenius equation follows—

$$K = A\exp(-E_a/RT) \qquad (1)$$

where K is the rate constant, A the pre-exponential factor, E_a the energy of activation of the exchange, R the molar gas constant and T the absolute temperature. By plotting a graph of $\log K$ against $1/T$, a straight line is obtained, from the slope of which E_a is determined. The other thermodynamic parameters can also be determined using the following equation—

$$K = \frac{K_B}{h} T \exp(-\Delta G^{\ddagger}_{cb}/RT) \tag{2}$$

(assuming a transmission coefficient of 1)

where K_B is Boltzmann's constant, h is Planck's constant and $\Delta G^{\ddagger}_{cb}$ is the free energy of activation for the chair-to-boat equilibrium. The enthalpy of activation $\Delta H^{\ddagger}$ is given by—

$$\Delta H^{\ddagger} = E_a - RT \tag{3}$$

and the entropy of activation $\Delta S^{\ddagger}_{cb}$ by—

$$\Delta S^{\ddagger}_{cb} = (\Delta H^{\ddagger} - \Delta G^{\ddagger}_{cb})/T \tag{4}$$

Many workers merely measure the "coalescence" temperature, T_c, at which the rate of exchange is given by—

$$K = \frac{\pi \delta_{0\,\mathrm{AB}}}{\sqrt{2}} \tag{5}$$

where $\delta_{0\,\mathrm{AB}}$ is the maximum shift between the spectra of the nuclei in different sites. Substituting the value for K in equation (2), with $T = T_c$, a value for the free energy of activation at that temperature is obtained. However, for a full kinetic treatment, the rate of exchange must be measured over as wide a range of temperature as possible. Above the coalescence temperature, the line width is a measure of the rate of exchange using the fast-exchange approximation—

$$K = \frac{\pi \delta^2_{0\,\mathrm{AB}}}{2\delta\nu} \tag{6}$$

where $\delta\nu$ is the line width due to exchange broadening, and $\delta_{0\,\mathrm{AB}}$ the maximum difference between the two site resonances at very slow exchange. Below coalescence, the doublet separation is a measure of the rate of exchange, using the approximation—

$$K = \pi[\tfrac{1}{2}(\delta^2_{0\,\mathrm{AB}} - \delta^2_{\mathrm{AB}})]^{1/2} \tag{7}$$

where $\delta_{0\,\mathrm{AB}}$ is the maximum chemical shift difference, and δ_{AB} is the shift at any temperature below coalescence. Anet and Bourn[9] in a very careful analysis of cyclohexane-d_{11}, used the double-resonance method[7] to measure very slow rates of exchange, and thereby increase the temperature range over which rates were measurable. The parameters obtained are recorded in Table I, together

TABLE I

Cyclohexane inversion parameters

Compound	Method	E_a, kcal./mole	$\Delta H^{\ddagger}$, kcal./mole	$\Delta G^{\ddagger}_{cb}$, kcal./mole	$\Delta S^{\ddagger}_{cb}$, entropy units	Ref.
C_6H_{12}	Steady state	..	5·9	10·1	..	10
C_6H_{12}	Steady state	..	9·0 ± 0·2	10·3	−6·5 ± 1·0	11
C_6H_{12}	Spin echo	..	11·5	10·7	4·9	12
C_6H_{12}	Spin echo	9·5	9·1 ± 0·5	10·3	−5·8 ± 2·4	13
C_6HD_{11}	Spin echo	9·5	9·1 ± 0·1	10·3	−5·8 ± 0·4	13
C_6HD_{11}	Steady state	11·3	10·9 ± 0·6	10·3	2·9 ± 2·3	14
C_6HD_{11}	Steady state	11·3	10·5 ± 0·5	10·2	1·4 ± 1·0	15, 16
C_6HD_{11}	Steady state, double resonance	11·24	10·8	10·22	2·8	9

Note: *cb* refers to the chair-to-boat inversion process.

with the results from previous high-resolution and spin-echo studies on cyclohexane and cyclohexane-d_{11}. The agreement is excellent for the free energy of activation, but there is a discrepancy in the values obtained for $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ by the high-resolution and spin-echo methods. Allerhand *et al.*[17] maintain that systematic errors in measuring the rates and/or temperatures are present in the high-resolution method, but the accuracy in measurement of Anet and Bourn's latest work would appear to minimize such errors. At present, the discrepancy is still unresolved, but it is clear that care must be taken in placing too much reliance on published enthalpies and entropies of activation. It is clear that other factors, such as vibrational and rotational contributions to the entropy of activation, should be taken into account, as it seems insufficient to rely on symmetry considerations alone. The suggestion[18] that the discrepancies may be due to a nuclear Overhauser effect, caused by the strong deuterium decoupling in the high-resolution method has been discounted.[9]

So far, internuclear coupling has not been significant in this discussion. Fluorine has been used as a label in cyclohexane by several groups[19–21] as ^{19}F chemical shifts are in general very much larger than their ^{1}H counterparts. Unfortunately, proton–fluorine and fluorine–fluorine coupling constants are correspondingly much larger than their proton–proton counterparts, and must be taken into account, using a full density matrix-line shape analysis.[22, 23]

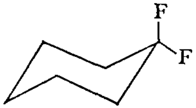
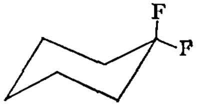
The ^{19}F spectrum of 1,1-difluorocyclohexane has been studied at low temperatures,[6, 21] where the axial and equatorial fluorine nuclei appear as an AB quartet at 56·4 Mc./sec. ($\delta_{AB}=884{\cdot}5$ c./sec. at $-93{\cdot}0$°C in CS_2 solution, $J_{AB}=236{\cdot}0$ c./sec.). Using a computer programme to obtain the best fit to the observed line shapes at various temperatures, by employing the appropriate density matrix equations, it is shown[21] that ^{1}H–^{19}F coupling cannot be ignored at the critical temperatures where H–F broadening is no longer negligible compared with exchange broadening. Table II records the results obtained for fluorinated analogues of cyclohexane. $\Delta G^{\ddagger}_{cb}$ is in general less by a factor of 1 → 3 kcal./mole than in the corresponding proton derivatives, and $\Delta S^{\ddagger}_{cb}$ is in general found to be negative, becoming more so as the number of fluorine atoms in the ring is increased.

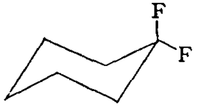
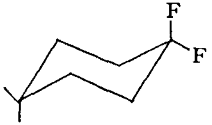
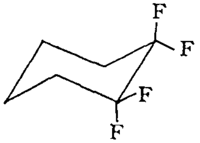
The complexity caused by internuclear coupling may also be removed by symmetrical substitution of methyl groups, or methoxyl groups in the ring and examining the spectrum of the methyl protons at various temperatures. Abraham and Macdonald[18] examined 1,1,4,4-tetramethoxy cyclohexane using methods similar to those of Anet, and found the parameters: $\Delta G^{\ddagger}_{cb}=10{\cdot}5\pm0{\cdot}4$ kcal./mole; $\Delta H^{\ddagger}=8{\cdot}6\pm1{\cdot}2$ kcal./mole; and $\Delta S^{\ddagger}_{cb}=-9{\cdot}5\pm6$ entropy units (e.u.), the large negative entropy of activation being in agreement with spin-echo work on cyclohexane itself. 1,1,4,4-Tetramethylcyclohexane has also been examined,[27, 28] but only $\Delta G^{\ddagger}_{cb}=11{\cdot}6$ kcal./mole was reported.

Many six-membered heterocyclic molecules have been investigated, and some of the results are reported in Table III. Inspection of the Table leads to the

TABLE II

Fluorinated analogues of cyclohexane

Compound	Method	E_a, kcal./mole	$\Delta H^{\ddagger}$, kcal./mole	$\Delta G^{\ddagger}_{cb}$, kcal./mole	$\Delta S^{\ddagger}_{cb}$, entropy units	Ref.
C_6F_{12}	Steady state	8·1 ± 0·3	10·9	7·5 ± 0·3†	−10·2†	24
C_6F_{12}	Spin echo	10·5 ± 0·2	11·2	9·9 ± 0·2†	−4·4†	25
	Steady state	9·5 ± 0·1	9·04	9·5	−3·3	6, 20
	Spin echo	9·8 ± 0·1	9·34	9·5	−0·6	6, 20

	Steady state	10·9 ± 0·4	10·43	9·71	3·0 ± 2	21
	Steady state	9·4 ± 0·5	8·87	10·18	−5·4 ± 2	21
	Steady state	8·0 ± 0·3	7·51	10·87	−13·6 ± 2	21
$C_6H_{11}F$‡	Steady state	ae ..	9·40	9·90 ± 0·05	−0·08	26
		ea ..	9·87	10·14 ± 0·05	−1·13	

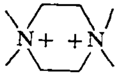
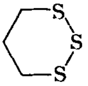
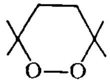
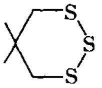
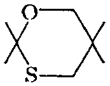
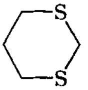
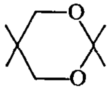
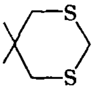
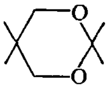
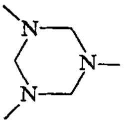
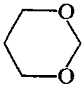
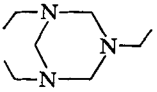
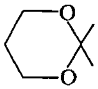
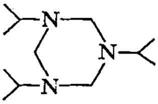
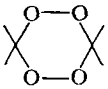
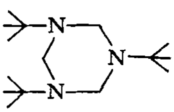
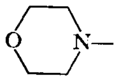
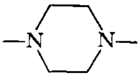
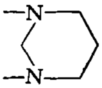
---

† Given for the chair–chair process.

‡ Two sets of parameters are given, as there is a small energy difference $\Delta G^\circ_{218^\circ K} = 242 \pm 12$ cal./mole favouring the conformer with equatorial fluorine.

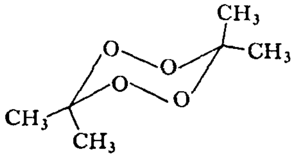
TABLE III

Six-membered heterocyclic rings

Compound	$\Delta G^{\ddagger}_{cb}$, kcal./mole†	Ref.	Compound	$\Delta G^{\ddagger}_{cb}$, kcal./mole†	Ref.
	12·9	18		13·2	33
	14·3	29		14·7	33
	11·5	29		11·0	33
	10·8	29		11·6	33
	8·2	30		12·6	34
	9·0	30		12·0	34
	10·5	30		11·3	34
	15·0	31		10·0	34
	11·5	32			
	12·6	32		12·8	35

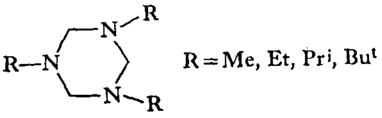
† In many cases, other thermodynamic parameters are recorded, but for reasons discussed in the text, $\Delta G^{\ddagger}_{cb}$ is the only parameter to be estimated with accuracy good enough for a comparative table of energy barriers to inversion (errors generally < 1 kcal./mole).

conclusion that the presence of oxygen in the ring tends to lower the barrier to inversion, whereas sulphur and nitrogen raise it. However, if the hetero atoms



1

are adjacent in the ring, as in acetone diperoxide (**1**),[31] the inversion barrier is raised considerably. In the case of two adjacent nitrogen atoms carrying substituents, an even greater effect is apparent, which is discussed later in this text.

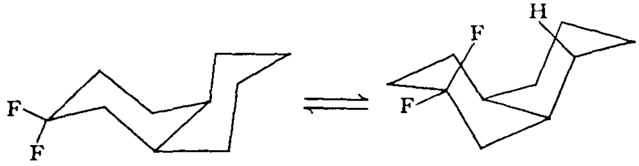


2

In the series of compounds (**2**) two interesting points emerge;[34] (a) the lowering of $\Delta G^{\ddagger}_{cb}$ as the bulk of the group R is increased, (b) the large chemical-shift difference between the geminal ring protons at low temperatures.

A. Decalin and its derivatives

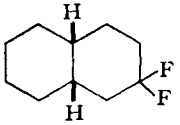
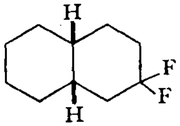
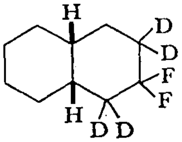
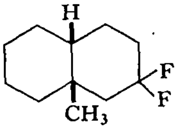
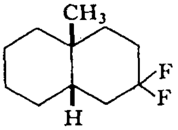
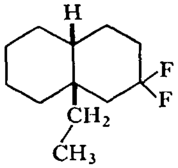
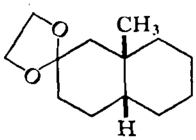
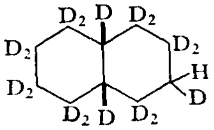
cis-Decalin was thought to be a very mobile system, as the n.m.r. spectrum showed no broadening effect at very low temperatures.[36] This must be due to fortuitous magnetic equivalence of the axial and equatorial protons.[19] Jensen and Beck[37] recently measured the free energy of activation for *cis*-decalin with all but one proton (on C_2) replaced by deuterium. They found a maximum value for $\Delta G^{\ddagger}$ of 12·85 ± 0·2 kcal./mole. Fluorine again is extremely useful as a label in *cis*-decalin,[19] and the results for some fluorinated derivatives are shown in Table IV. The inversion takes place between the two possible chair–chair forms (**3A**) and (**3B**) which are not necessarily equal in energy, as the non-bonded interactions in (**3B**) between axial fluorine and the proton on C_8 are not present in (**3A**).



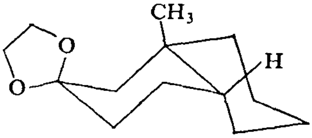
3A **3B**

TABLE IV

cis-Decalin and derivatives

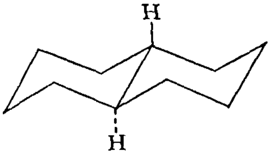
Compound	Solvent	E_a	$\Delta G^{\ddagger}$, kcal./mole	$\Delta S^{\ddagger}$, entropy units	Ref.
	Acetone	15·0 ± 0·9	12·2	8 ± 5	39
		14·5 ± 0·9	11·6	8 ± 5	
	Propene	14·6 ± 0·7	12·2	6 ± 3	39
		13·9 ± 0·7	11·6	6 ± 3	
	Propene	13·4 ± 0·8	12·4	2 ± 3	39
		13·4 ± 0·9	11·8	4 ± 3	
	Propene	9·1 ± 0·6	12·1	−13 ± 3	39
		9·2 ± 0·6	12·0	−12 ± 3	
	Acetone	10·6 ± 0·6	12·8	−10 ± 3	39
		10·4 ± 0·6	12·1	−9 ± 3	
	Acetone	9·5 ± 0·5	11·8	−11 ± 4	39
		9·5 ± 0·5	11·8	−11 ± 4	
	$CDCl_3$	..	12·5	..	38
	CS_2	..	12·85	..	37

Riddell and Robinson[38] found the methyl resonance of (**4**) split into two bands at −60°C. From the coalescence temperature they estimated a value for the free energy of activation of 12·5 kcal./mole, in good agreement with the results for other *cis*-decalin derivatives (see Table IV).



4

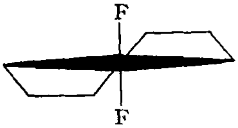
trans-Decalin, (**5**), however, exists in one rigid form only, and its n.m.r. spectrum is temperature independent.



5

B. Larger rings

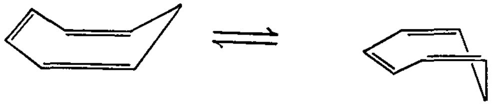
Cycloheptane appears to be a very flexible ring system, probably because pseudorotation rather than inversion is preferred. 1,1-Difluorocycloheptane shows no AB quartet at low temperatures in the ^{19}F spectrum, suggesting two possibilities. Either rapid inversion is still taking place at low temperatures, or the "frozen out" conformation is symmetrical (**6**) and the fluorine nuclei therefore magnetically equivalent. Some success was achieved with 1,1-difluoro-4,4-dimethylcycloheptane,[19] which "froze out" below −163°C. A preliminary line-shape analysis indicated an activation energy E_a of approximately 6 kcal./mole.



6

A series of seven-membered rings of the 1,2-benzcycloheptane and 1,2,3,4-dibenzcycloheptane type have been examined,[40–42] and the free energies of activation calculated from the coalescence temperature of various exchanging sites. The compounds are listed in Table V. Widely varying values of $\Delta G^{\ddagger}$ are reported from measurements of the rate of inversion of the seven-membered rings at the coalescence temperature.

Cycloheptatriene has been examined by Anet,[43] and by Jensen and Smith.[44] They concluded that the conformational equilibrium lay between two tub-like



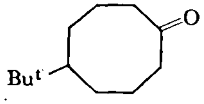
7A **7B**

forms (**7A**) and (**7B**). $\Delta F^{\ddagger}$ was reported as 6·1 kcal./mole at $-143°$ and $5{\cdot}7 \pm 0{\cdot}1$ kcal./mole, respectively. Lambert *et al.*[45] however, examined 1,1-ditrifluoromethyl-2,4,6-cycloheptatriene, and found no change in the ^{19}F spectrum down to -185°C.

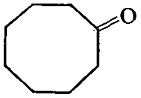
Cyclo-octane, however, appears to be a far less mobile system, and Anet and Hartmann[46] have published some elegant work on heavily-deuterated cyclo-octanes. For example, in cyclo-octane-d_{15} $\Delta G^{\ddagger} = 8{\cdot}1$ kcal./mole, $E_a = 7{\cdot}7 \pm 0{\cdot}3$ kcal./mole and $\Delta S^{\ddagger} = 4{\cdot}4$ e.u. They conclude, from coupling-constant data on cyclo-octane with all but two positions deuterated, that the predominant conformations are the boat–chair (**8A**) and the twist-boat–chair (**8B**).

8A **8B**

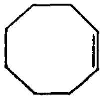
Similar conclusions were reached with t-butyl and methyl cyclo-octane, from their low-temperature n.m.r. spectra.[47] Of the five cyclo-octane derivatives



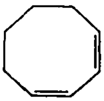
9



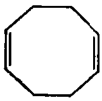
10



11



12

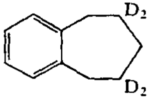
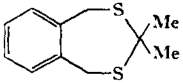
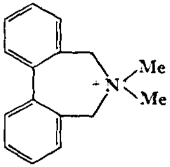
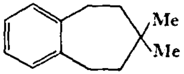
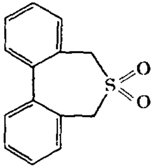
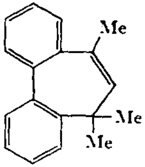
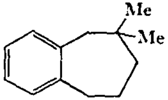
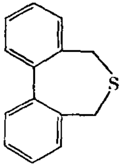
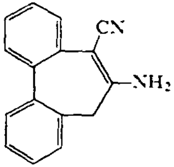
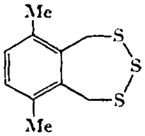
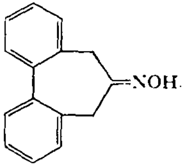
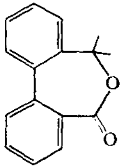
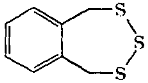
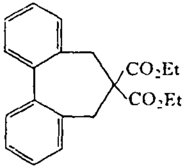
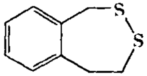


13

(**9**), (**10**), (**11**), (**12**), and (**13**), (**9**) showed two t-butyl bands at -120°C, and (**10**), (**11**) and (**12**) showed slightly temperature-dependent spectra.[48] Cyclo-octatrienone (**14**),[49] however, as well as being in valence-bond isomerization with (**15**), is also inverting between two conformations. From an Arrhenius graph, $E_a = 11{\cdot}9 \pm 0{\cdot}5$ kcal./mole, which is comparable with cyclo-octatetraene[50] ($E_a = 13{\cdot}7$ kcal./mole) and monofluorocyclo-octatetraene[51] ($E_a \sim 12$ kcal./mole),

TABLE V

Seven-membered unsaturated rings

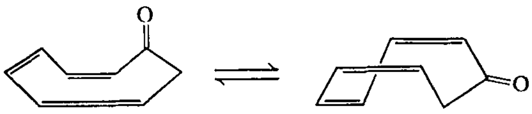
Compound	$\Delta G^{\ddagger}$, kcal./mole	Ref.	Compound	$\Delta G^{\ddagger}$, kcal./mole	Ref.	Compound	$\Delta G^{\ddagger}$, kcal./mole	Ref.
	10·9	40		12·4	29		13·4	42
	11·8	40		18·2	42		18·8	42
	11·5	40		15·5	42		17·9	42
	19·8 (11·5)†	41		13·5	42		12·3	42
	17·4 (10)	33		14·0	42			
	13·5 (10·4)	41						

† Two rate processes apparently take place in the sulphur rings. inversion and pseudo-rotation. The free energy of activation for the latter process is given in brackets.

95% **14**

5% **15**

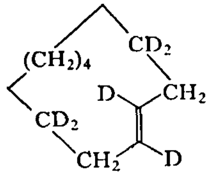
although fluctuation of bonds (valence-bond isomerization) is thought to be important in the latter two compounds.[63] Ganter *et al.*[49] propose the two conformations (**16A**) and (**16B**) for the inversion.



16A

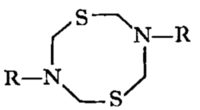
16B

trans-Hexadeuterocyclodecene (**17**) also "freezes out" at low temperatures.[53] Observing the allylic protons, the rotation of the double bond through the loop of the ring gives the activation energy $\Delta G^{\ddagger} = 10{\cdot}7 \pm 6{\cdot}3$ kcal./mole.

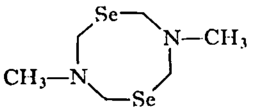


17

A heterocyclic eight-membered ring with selenium or sulphur with nitrogen present in the ring has been examined at low temperatures [(**18**) and (**19**), respectively].[54] As in compounds of type (**2**), the barrier to inversion ($\Delta G^{\ddagger}$) is



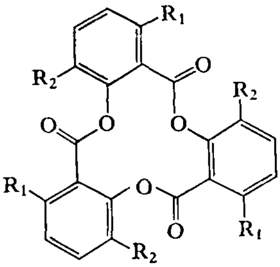
18



19

reduced as the size of the substituent R is increased. The inversion process is interpreted as being between either crown conformations, or crown and chair-boat conformations.

Turning to even larger macrocyclic rings, two unusual twelve-membered rings have recently been shown to exhibit temperature-dependent n.m.r. spectra. These are tri-*o*-thymotide[55] (**20**) and tri-*o*-carvacrotide (**21**).[56]



20 $R_1 = Me$; $R_2 = Pr^i$
21 $R_1 = Pr^i$; $R_2 = Me$

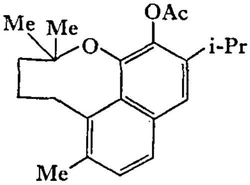
The methyl groups of the isopropyl substituents are magnetically non-equivalent, owing to the asymmetry of the twelve-membered ring, which can adopt the "propeller" or the "helix" conformations, to describe the arrangements adopted by the benzene rings in these molecules. At low temperature, where inversion is slow, there are theoretically eight types of isopropyl methyl groups associated with the propeller conformation and the helical conformation. Not surprisingly, not all of these are observed due to chemical shift equivalence in tri-*o*-thymotide. However, in tri-*o*-carvacrotide, this complex situation is somewhat resolved, as the aromatic methyl groups show non-equivalence, with four peaks at 10°C, two at 55°C and one at 100°C. The four methyl resonances are assigned to three non-equivalent methyl groups in the helical conformation, and the larger peak to three equivalent methyl groups in the symmetrical propeller conformation. A detailed line shape comparison, based on the McConnell equations[57] enabled the rate constants for methyl-site exchange to be determined, and the energies of activation for the three rate processes to be calculated—

Propeller → helix:
$E_a = 22{\cdot}8 \pm 1{\cdot}5$ kcal./mole, $\Delta G^{\ddagger} = 20{\cdot}6 \pm 0{\cdot}2$ kcal./mole.

Helix → propeller:
$E_a = 22{\cdot}8 \pm 1{\cdot}5$ kcal./mole, $\Delta G^{\ddagger} = 20{\cdot}3 \pm 0{\cdot}2$ kcal./mole.

Helix → helix:
$E_a = 21{\cdot}4 \pm 1{\cdot}3$ kcal./mole, $\Delta G^{\ddagger} = 17{\cdot}6 \pm 0{\cdot}2$ kcal./mole.

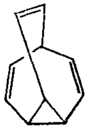
The isopropyl group has also been used as a probe by Conti *et al.*[58] in their examination of (**22**). The two doublets due to the isopropyl methyls collapse to a single doublet at 90°C, and coalescence of the geminal methyl peaks is observed above 150°C.



22

The annulenes of general formula C_nH_n have also been shown to undergo a fast conformational isomerization at room temperature. Low-temperature n.m.r. spectra show a very interesting difference between the $4n$ and $4n+2$ annulenes. The outer protons of [16]-,[59] and [24]-annulene[60] absorb at 4·60 and 5·27τ, respectively, and the inner protons at −0·43τ and −2·9 to −1·2τ, respectively (at low temperatures). [14]-[61] and [18]-annulenes,[60] however, exhibit very different spectra at −60°C with the outer protons appearing at low field (2·4 and 0·72τ) and the inner protons at very high field (10·0 and 12·99τ, respectively). This remarkable difference between the Hückel and non-Hückel annulenes has been explained theoretically recently.[62] At high temperatures, the annulene rings appear either to be turning inside-out, or else undergoing fast valence-bond isomerization. At present, the activation parameters for these inversion processes have not been accurately measured.

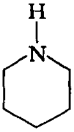
Bullvalene (**23**), which is known to undergo fast reversible valence-bond isomerization with rapid fluctuation of bonds at room temperature,[63] has been examined using both high-resolution[64] and spin-echo techniques.[52] The energy of activation determined by the two methods is 11·8 and 12·8 kcal./mole, respectively.



23

C. Slow nitrogen inversion in heterocyclic rings

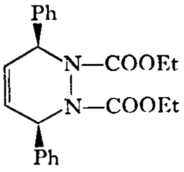
In simple cyclic amines such as piperidine (**24**), the rate of inversion about the nitrogen is very much more rapid than the normal chair–chair equilibrium, and is still fast at low temperatures relative to the n.m.r. time scale.



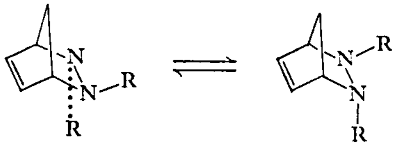
24

Exceptions to this rule are well established for the aziridine ring,[65] where the inversion rate is very much slower than normal, but other cases involving amine nitrogen atoms are rare.[66]

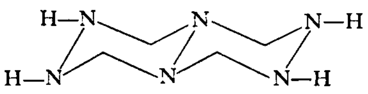
Recently, Lehn and his co-workers have synthesized and investigated a series of compounds containing two adjacent nitrogen atoms in a ring, and where the rate of inversion of the nitrogen atoms is very hindered.[67–70] The first compound of this type (**25**) appears to be undergoing several exchange processes: inversion of the cyclohexene type of ring between two half-chair forms; inversion at the nitrogen atoms and slow rotation about the $>N{-}C^{\nearrow O}$ bond.[67] Bushweller[71] has criticized Lehn's interpretation of the results obtained from low-temperature spectra, disputing the large free energy of activation proposed for the ring inversion. Later work, however,[72] together with further examples of this type without the confusing element of the $>N{-}C^{\nearrow O}$ bond present seem to confirm the very large energy barrier found in these compounds. Table VI records the results for this series of compounds in which the inversion is thought to be a synchronous process involving both nitrogens as shown below (**26A**) → (**26B**).[69] The latest examples of this type are provided by the decalin type of compound (**27**) and (**28**).[70]



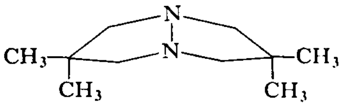
25



26A **26B**



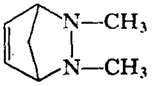
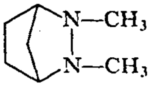
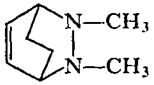
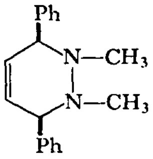
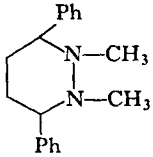
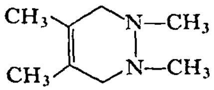
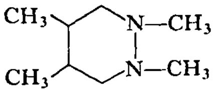
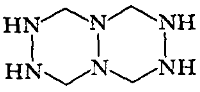
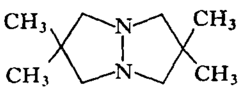
27



28

TABLE VI

Examples of slow, synchronous nitrogen inversion

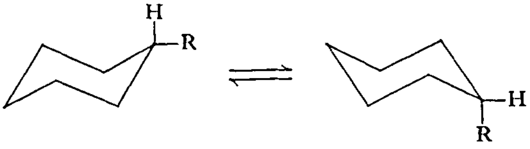
Compound	Solvent	$\Delta H^{\ddagger}$, kcal./mole	$\Delta G^{\ddagger}$, kcal./mole	$\Delta S^{\ddagger}$, entropy units	Ref.
	$CDCl_3$	16·9 ± 0·6	14·5 ± 0·2	8·3 ± 2·1	69
	Pentane	16·2 ± 0·8	13·9 ± 0·2	7·6 ± 2·6	
	$CDCl_3$	14·8 ± 0·5	13·0 ± 0·2	6·0 ± 2·0	69
	Pentane	15·7 ± 1·0	12·6 ± 0·4	11·5 ± 4·0	
	$CDCl_3$	14·9 ± 0·8	12·2 ± 0·2	10·0 ± 3·0	69
	Pentane	12·4 ± 0·6	11·8 ± 0·3	2·8 ± 2·5	
	$CDCl_3$	..	13·8†	..	68
	$CDCl_3$	..	11·2†	..	68
	$CDCl_3$	..	12·6†	..	68
	$CDCl_3$	..	12·3†	..	68
	$CDCl_3$	..	16·6 ± 0·2†	..	70
	$CDCl_3$	..	12·1 ± 0·2†	..	70

† Measured from the coalescence temperature, T_c, of the methyl resonances.

D. Free-energy differences between conformers

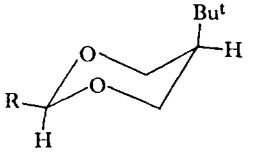
So far in this review, little has been said about the inversion between conformers of unequal energy. The line-shape treatment in the determination of thermodynamic parameters in the latter case is naturally much more complex, and different activation parameters are obtained for each path of inversion. However, if the inversion rate between sites is slow enough that the spectrum of the individual conformers is observed, then the relative areas of the peaks for each conformer are equal to the relative populations of sites at that temperature. In a monosubstituted cyclohexane, for example if the mole fractions of the two conformations are (p) and ($1-p$), then—

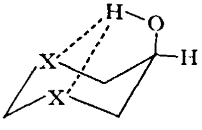
$$p/(1-p) = \exp(-\Delta G^\circ/RT)$$



p $1-p$

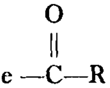
where ΔG° is the free-energy difference between the two conformations at a temperature T °K, and is therefore a measure of the difference in energy or A value of the substituent when axial or equatorial. Most substituents prefer the equatorial position, as 1,3-non-bonded interactions raise the energy for an axial substituent. Comprehensive lists of A values have been published,[74, 74a] which need not be repeated here. The free-energy differences appear to depend on the solvent used as well as temperature, so care must be taken in using published values too liberally. In the case of heterocyclic compounds, quite different free-energy differences may be obtained. Evidence for an axial t-butyl group in 1,3-dioxan derivatives (**29**) has been reported,[75] and the hydroxyl group very often prefers the axial position if a hetero-atom is present in the ring to which it can hydrogen bond (**30**).





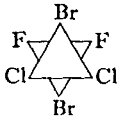
X = O, S or N

29 **30**

A more accurate method of estimating free-energy differences is by measuring the vicinal coupling constants of the protons α and β to the substituent. This process will be discussed later in the text. Jensen and Bushweller[76] have recently reported the isolation of the separate conformations of monochlorocyclohexane, and trideuteromethoxycyclohexane in solution. Chlorocyclohexane is cooled down to −150°C and preferential crystallization of the equatorial conformer takes place. With careful cooling and removal of the mother liquor, the equatorial conformer is isolated and can be redissolved, the spectrum obtained being that of the pure equatorial conformer. The very slow rate of interconversion is indicated by the absence in the spectrum of any of the axial conformer after an hour at −150°C. This technique clearly holds much scope for the accurate measurement of activation parameters for such molecules starting from the single, pure conformations, and may also apply to suitably substituted ethanes. The same workers report an A value for $—OCD_3$ of $0{\cdot}56 \pm 0{\cdot}02$ kcal./mole at −96°C. Another hitherto unknown A value is that for the formyl group, which is estimated from chemical-shift measurements to be $1{\cdot}35 \pm 0{\cdot}1$ kcal./mole,[73] a value similar to that of other substituents of the  $—\overset{\overset{\displaystyle O}{\|}}{C}—R$ type.

E. Barriers to rotation in acyclic molecules

Very little work has been published on the low-temperature spectra of substituted ethanes, since the elegant paper by Newmark and Sederholm,[77] who "froze out" the separate rotamer forms of various heavily halogenated ethanes at low temperatures. When protons are replaced by such bulky groups as bromine in ethane, the barrier to rotation is consequently raised by as much as 7 kcal./mole, depending on the number and nature of the substituents. In monosubstituted ethanes, however, and in ethane itself, the barrier is only ~ 3 kcal./mole. However, information can be obtained from the variation in coupling constants over the limited temperature range available, and this is discussed later. The three rotamers of $CF_2Br{\cdot}CCl_2Br$ are shown below (**31**), (**32**) and (**33**). Forms (**32**) and (**33**) are



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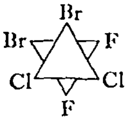

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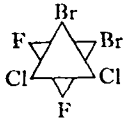
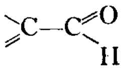
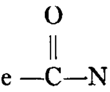


33

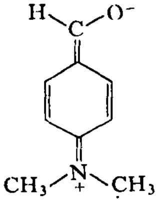
mirror images, and give identical *AB* quartets at low temperature, whereas (**31**), in which the two fluorine nuclei are equivalent, gives a single line. The respective areas of the two sets of peaks show that forms (**32**) or (**33**) are 320 ± 20 cal./mole higher in energy than (**31**).

There are two cases where rotation about a "single bond" is slow enough for temperature experiments to be successful—

(a) Rotation about the  $>C{-}C\overset{\nearrow O}{\underset{\searrow H}{}}$ bond in aromatic aldehydes, and

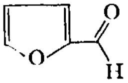
(b) Rotation about the  $-\overset{O}{\overset{\|}{C}}-N$ bond in amides.

Anet and Ahmad[78] examined benzaldehyde at low temperatures, coalescence occurring at -123°C, leading to a value of $\Delta F^{\neq} = 7{\cdot}9$ kcal./mole. *p*-Dimethylaminobenzaldehyde, however, is much less mobile, owing to contribution of

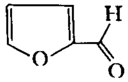


34

mesomeric forms of the type (**34**). The barrier to rotation in this compound was estimated to be 10·8 kcal./mole and that in anisaldehyde to be 9·2 kcal./mole. Dahlqvist and Forsén,[79] in some accurate low-temperature experiments on furfural, determined not only the barriers to rotation in the aldehyde, and the enthalpy and entropy of activation for each of the two rotamers (**35A**) and (**35B**), but also the free-energy differences between them, (**35B**) being of higher energy by ca. 0·6 kcal./mole.

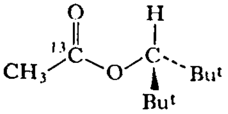


35A



35B

The barrier to rotation in dimethyl formamide has been measured by several workers, and values have been quoted over a wide range (7–24 kcal./mole).[80–82] Using the temperature dependence of the chemical shift between the *N*-substituents in several *N*,*N*-dialkyl amides, Whittaker and Siegel[81, 82] found that solvent plays a dominant rôle in the exchange, and suggested that the discrepancies may be due to other processes taking place; e.g., the breaking of solvent–amide complexes as well as rotation about the $O{\Large\geqq}C{-}N$ bond. Dipolar association may at least qualitatively explain the results. Separate isomers of a high-molecular-weight formamide derivative have been claimed to be isolated, with different melting points and different molecular rotations.[83] Rotational isomerism in acetates has also been examined,[84] again using the temperature dependence of coupling constants within the molecule $\left(J_{^{13}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{—O—C}H}\right)$. It was found that all the acetates examined appeared to be rotating about the $\text{—}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{—O—}$ bond at normal temperatures except for the di-t-butyl derivative (**36**), which showed no temperature dependence of $J_{^{13}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{—O—C}H}$, indicating a locked configuration. Two rate processes have been postulated for the benzamide derivative (**37**), slow rotation about the $\text{—}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{—C}$ and the $\text{—}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{—N}$ bonds, both energy barriers being in excess of 20 kcal./mole.[85] Slow rotation again occurs in *N*,*N*-dimethyl-*p*-nitrosoaniline, with a coalescence temperature of 30°C.[86]



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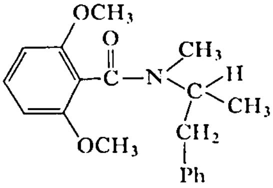
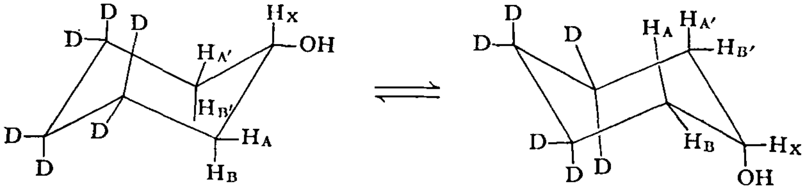


37

F. Coupling constants in mobile systems

So far we have discussed the use of chemical shifts to determine conformational equilibria, but have not in the main described how coupling constants may be used in a similar manner. In a compound rapidly exchanging between sites, the coupling constants in the molecule as well as the chemical shifts are time averaged.

The dependence of vicinal and longer-range H–H coupling constants on the spatial configuration within the molecule is now well established. In the case of cyclic molecules, a good example was provided by Anet[87] with 3,3′,4,4′,5,5′-hexadeuterocyclohexanol, (**38**), and the *cis*- and *trans*-4-t-butyl derivatives.



38A **38** **38B**

The protons in (**38**), excluding couplings to deuterium which are removed by decoupling at the deuterium frequency, and to the hydroxyl proton, which is removed by exchange, approximate in the general nomenclature to an $(AB)_2X$ arrangement, assuming the cross-ring couplings to be small enough to be negligible. If the mole fractions of the two conformations are p and $(1-p)$, respectively, then it follows that—

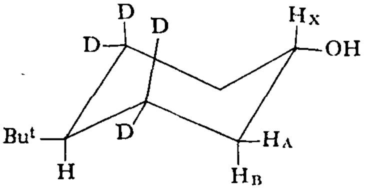
$$\langle J_{AX}\rangle = pJ_{AX(A)}+(1-p)J_{AX(B)} \tag{8}$$

$$\langle J_{BX}\rangle = pJ_{BX(A)}+(1-p)J_{BX(B)} \tag{9}$$

where $\langle J_{AX}\rangle$ and $\langle J_{BX}\rangle$ are the time-averaged observed coupling constants, and $J_{AX(A)}$, $J_{AX(B)}$ the AX couplings in the separate conformers. Also—

$$p/(1-p) = \exp(-\Delta G^{\circ}/RT) \tag{10}$$

$J_{AX(A)}$ and $J_{BX(A)}$ can be substituted by the AX and BX coupling constants in the *trans*-t-butyl derivative (**39**) and $J_{AX(B)}$ and $J_{BX(B)}$ to the couplings in the *cis*-derivative (**40**).



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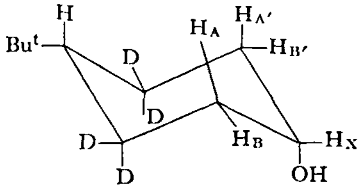


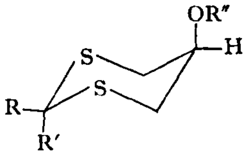
40

This treatment assumes that the t-butyl group has no effect on the vicinal coupling constants at the other end of the ring, but appears to hold reasonably well in most cases. Summing equations (8) and (9), one obtains—

$$\langle J_{AX}+J_{BX}\rangle = p(J_{AX}+J_{BX})_{(A)}+(1-p)(J_{AX}+J_{BX})_{(B)} \tag{11}$$

This relationship is very useful for undeuterated compounds, where only the sum of the observed couplings $(J_{AX}+J_{BX})$ is obtained from the X proton spectrum (in general $(J_{AX}+J_{BX})$ is equal to half the distance between the outermost lines in the X multiplet). Using equation (11) a value of p can then be obtained, if the sum is known for the rigid conformers with a large locking group in the 4-positions. In theory, this process can be applied also to the chemical shifts, but in practice, the 4-substituent appears to affect the chemical shifts much more than the coupling constants, and the results are less meaningful. Feltkamp and Franklin have used this method for determining ΔG° for nitrocyclohexane[88] ($1{\cdot}02 \pm 0{\cdot}15$ kcal./mole) and cyclohexylamine (1·2 kcal./mole).[89, 90] In measuring the band width of the X proton multiplet, care should be taken to avoid cases in which strong coupling of the A and B protons causes second-order effects, often called "virtual coupling" owing to the presence of combination lines in the X multiplet, which may possibly affect the total band width measured, and give a value of $J_{AX}+J_{BX}$ which is erroneous. The same workers[74] have recently reviewed the general method very comprehensively.† Trager and Huitric[91] examined nitrocyclohexane deuterated in the 3 and 5 positions, and the corresponding *cis*- and *trans*-4-t-butyl derivatives, in various solvents, and found a value of $\Delta G^\circ = 0{\cdot}78 \pm 0{\cdot}10$ kcal./mole. It is thought that the free-energy differences for two substituents widely separated in the ring are additive within experimental error. Using this established assumption, Feltkamp and Franklin also examined *cis*-4-methyl nitrocyclohexane,[88] and found $\Delta G^\circ_{CH_3} - \Delta G^\circ_{NO_2} = 0{\cdot}4$ kcal./mole. Further examples of this type, where the conformational equilibrium is determined by using either the sum of the vicinal coupling constants in a C–C fragment of the molecule concerned, or better, the separate coupling constants from a full analysis, include the *cis*- and *trans*-1,4-cyclohexanediols,[92] 4-hydroxycyclohexanone,[93] a number of monosubstituted cyclohexanes,[94] and α-halocyclohexanones.[95]

Another method for reducing the complexity of the spectra of cyclohexane derivatives, is to substitute hetero-atoms in the ring. A series of 1,3-dithians (**41**) was examined,[96, 97] in order to determine the effect of the bulky hetero-atoms on the conformational equilibria.



41

	R	R′	R″		R	R′	R″
(A)	Ph	H	H	**(G)**	CH_3	CH_3	H
(B)	H	Ph	H	**(H)**	CH_3	CH_3	Ac
(C)	Ph	H	Ac	**(I)**	Bu^t	H	H
(D)	H	Ph	Ac	**(J)**	H	Bu^t	H
(E)	H	H	H	**(K)**	Bu^t	H	Ac
(F)	H	H	Ac	**(L)**	H	Bu^t	Ac

In agreement with infrared results it is found that the hydroxyl group prefers the axial position in all cases, unless held equatorial by a bulky 2-substituent. The strong intramolecular hydrogen bond formed stabilizes the axial –OH conformer of (**41E**) to the extent of 0·5 kcal./mole,[97, 98] in striking contrast to cyclohexanol, where the equatorial conformer is favoured by 0·7 kcal./mole.[87]

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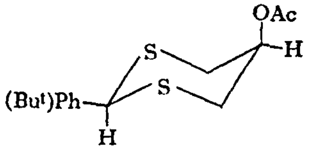
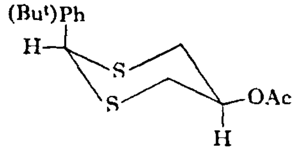
† See also ref. 74a.

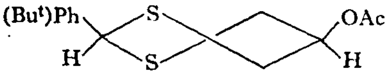
In the case of the acetate, the normal situation holds, and the equatorial conformer is favoured ($\Delta G^\circ_{(41\mathrm{F})} = 1{\cdot}03$ kcal./mole). It is interesting to note that in (**41B**), (**41D**) and (**41L**) neither the phenyl nor the t-butyl groups will "lock" the molecule, as extensive line broadening occurs at low temperature in all three compounds at −80°C. This suggests that one of two possible conformations (**ii**) or (**iii**) is in equilibrium with (**i**). The spectrum of (**41B**) is also temperature dependent, and it is estimated that up to 25% of the conformer with axial Ph– and –OH is present in $CDCl_3$ at room temperature.[96] The lowering of the free-energy differences for 2-substituents has also been noted by Baggett *et al.*,[99] who showed (by infrared spectroscopy) that changing the 2-substituent from methyl to ethyl to isopropyl to phenyl only slightly affected the ratio of the populations of the conformers of 5-hydroxy-1,3-dioxan.† Kalff and Havinga[104] have also studied the conformation of some 2-substituted-1,3-dithians. Similar free-energy differences for the phenyl group were quoted as found previously by Abraham and Thomas, although different reasons are suggested for the phenomenon. Among the many other examples reported of investigations into the conformations of heterocyclic rings using coupling-constant data, some of the most interesting cases involve the 1,4-dioxan ring. Pfundt and Farid[105] examined the equilibria between the "half chair" conformations of (**42**), showing that although the phenyl



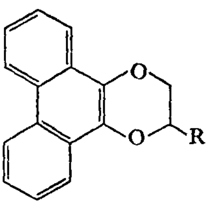
i



ii



iii



R = Phenyl, naphthyl, OEt, Cl, SEt.

42

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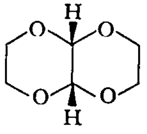
† Extensive work on the conformation of the 1,3-dioxan ring has been reported by Delmau and Duplan[100, 101] and Delmau[102] and in the papers referred to by Ramey and Messick.[103]

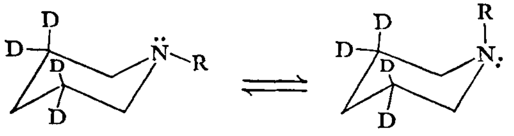
and naphthyl substituents are almost exclusively equatorial, the conformer with the substituent axial becomes increasingly predominant as the group R decreases in bulk.

cis-2,3-Dichloro-1,4-dioxan, previously assigned wrongly as the *trans* isomer,[106, 107] has been shown to be inverting rapidly between two chair conformations of equal energy.[108–110] Other *cis*-2,3-disubstituted 1,4-dioxans have been shown to adopt similar conformations, including the interesting molecule (**43**).[110]



43

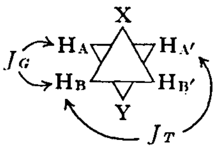
Before leaving heterocyclic rings, some mention should be made of the attempts to measure the conformational preference of the lone pair of electrons in piperidine (**44**) and similar molecules. Although the literature on this subject is voluminous,[111] conflicting evidence using spectroscopic methods made the situation unsatisfactory, until a recent paper by Lambert and Keske explained some of the anomalies.[111] Using the chemical shifts of the α protons in several 3,3,5,5-tetradeuterated piperidines with various *N*-substituents, they found the order of "effective bulk" of the *N*-substituents to be $CH_3 >$ lone pair $>$ H. In other words the predominant species in piperidine itself is (**44B**), whereas the reverse is true when the *N*-substituent is larger than hydrogen.



44A **44B**

R=H, CH_3

The same process with time-averaged coupling constants can be used for acyclic molecules, but for chains longer than two carbon atoms, the treatment



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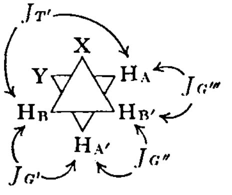
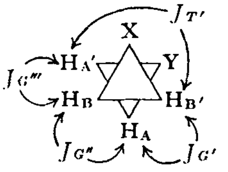


ii



iii

becomes forbiddingly complex, except where favourable substitution is made to simplify matters. In a 1,2-disubstituted ethane, $X \cdot CH_2 \cdot CH_2 \cdot Y$, there are three possible eclipsed rotational isomers, one *trans* and two *gauche* forms. In each of these isomers, the geminal protons are magnetically non-equivalent, as there are always two different vicinal coupling constants. As the two isomers **ii** and **iii** are energetically equivalent, the observed coupling constants J_{AB} and $J_{AB'}$ are given by—

$$\langle J_{AB} \rangle = n_T J_G + \tfrac{1}{2} n_G (J_{G''} + J_{T'}) = \langle J_{A'B'} \rangle \tag{12}$$

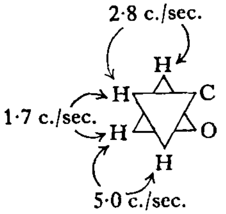
$$\langle J_{AB'} \rangle = n_T J_T + \tfrac{1}{2} n_G (J_{G'} + J_{G''}) = \langle J_{A'B} \rangle \tag{13}$$

$$\approx n_T J_T + n_G J_G \tag{14}$$

where $$n_T + n_G = 1 \tag{15}$$

and $$n_G / n_T = 2 \exp(-\Delta E / RT) \tag{16}$$

where n is the mole fraction of the isomer considered, and ΔE is the excess energy of the *gauche* isomer. However, to assume $J_G = J_{G'} = J_{G''}$ in such molecules is very hazardous as shown by the coupling constants in the C_5–C_6

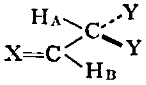


45

fragment of 4-phenyl-1,3-dioxan (**45**).[103] This remarkably demonstrates the wide variation in vicinal couplings for dihedral angles of ca. 60°. Whatever the angle of buckle of the ring, the dihedral angle for the nuclei where $J = 2 \cdot 8$ c./sec. is always the same as that for the two where $J = 5 \cdot 0$ c./sec. The recent rule proposed by Booth[112] and Bhacca and Williams[113] and extended by Abraham *et al.*[114] suggests that the electronegativity of the substituents have a minimum effect on J_G unless they are in a planar, *trans* arrangement with one of the coupling protons. However, it is clear that small changes in dihedral angle can influence J_G to a large extent, as it is in the region of $\phi = 60°$ that the slope of the $\cos^2\phi$ curve is steepest.

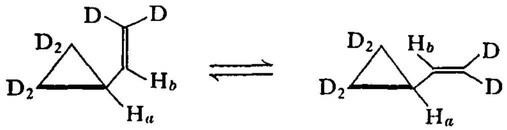
The rotational isomerism about the C—C bond in 1,2-disubstituted ethanes[115–117] and in 1,1,2-trisubstituted ethanes[117, 118] has been investigated thoroughly by the n.m.r. technique, measuring the variation in coupling constants at various temperatures and in solvents of different dielectric constant. It has been shown that in 1,2-dihalogenated ethanes, the *gauche* isomer is often the more stable form, depending on the solvent used. Dipolar interactions appear to be more important than non-bonded interactions in the latter case, and temperature variations in coupling constants can give misleading results, owing to the very small changes observed in the usual temperature ranges employed.

Recently, a calculation of the dipolar and quadrupolar electric fields of substituted ethanes, and their dependence on the dielectric constant of the medium has been used to derive the vicinal proton–proton and proton–fluorine coupling constants of the individual rotational isomers of several halogenated ethanes, from the solvent and temperature dependence of the couplings.[114, 119] It is pointed out in this work that on the basis of this theory, the results of some earlier workers need to be modified. Gutowsky *et al.*[120] interpreted the temperature variation of the proton–proton coupling of $CHCl_2 \cdot CHCl_2$ in terms of a constant energy difference between the *trans* and *gauche* isomers in the liquid phase of $-1{\cdot}1$ kcal./mole, and couplings for the two isomers $J_g = 2{\cdot}01$ and $J_t = 16{\cdot}35$ c./sec. The latest theory applied to Gutowsky's results using a value for the energy difference between the rotamers in the gas phase of 0 kcal./mol., and *not* assuming ΔE constant for the liquid phase, gives $J_g = 2{\cdot}2$ and $J_t = 10{\cdot}4$ c./sec., the latter being a much more reasonable value for a dihedral angle of 180°. The most unambiguous method of determining the coupling constants in individual rotational isomers is still to measure the couplings of the isomers directly at very low temperatures, but as this can be achieved with only heavily substituted ethane derivatives,[77] a theory using the solvent or temperature dependence of the spectra of less substituted molecules is the only alternative at present. The consistency of the results so far obtained is therefore heartening, and further applications of the theory are clearly possible with other simple acyclic molecules.



46

In the compounds of type (**46**) with X=O or —CR_2, the population of the preferred rotational isomers varies with temperature, and so therefore does the coupling constant J_{AB}. A simple example of this type is provided by vinylcyclopropane (**47**), deuterated as shown,[121] for which—

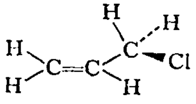


47

$$\langle J_{ab}\rangle = pJ_{ab_{cis}} + (1-p)J_{ab_{trans}} \tag{17}$$

where $$p(1-p) = \exp(\Delta H/RT) \quad (\text{assuming } \Delta S \approx 0) \tag{18}$$

The s-*trans*-conformation is therefore found to be the energy-poorer by ca. 1·1 kcal./mole. Similar considerations have been applied to the halopropenes by Bothner-By *et al.*[122, 123] For allyl chloride (**48**) $\Delta H = 100 \pm 30$ cal./mole (*gauche* isomer favoured), whereas in allyl fluoride (**49**) the *trans* is favoured by 166 ± 67 cal./mole. In allylidene fluoride (**50**), however, and allylidene chloride (**51**), the *gauche* isomer is favoured. The favouring of one rotamer over another appears to depend on the polarity of the —C—X bond, where X is chlorine or fluorine. Further examples of this type are aliphatic aldehydes (**52**). Abraham and Pople[124] first reported the unusual phenomenon in propionaldehyde, where the methyl group prefers to be eclipsed by the carbonyl group.



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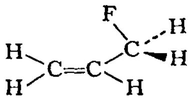

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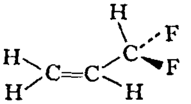

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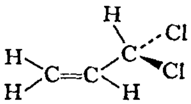

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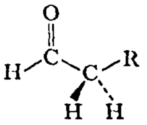
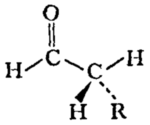
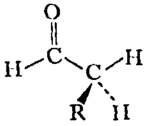


52A



52B



52C

Karabatsos and Hsi[125] extended this investigation by measuring the vicinal H–H coupling constant at various temperatures in the series $R\cdot CH_2\cdot CHO$. In the neat liquids, where R is methyl, ethyl, n-propyl, n-pentyl, isopropyl or phenyl, the energy difference favouring the *trans* rotamer (**52A**) is 800, 700, 600, 500, 400 and 300 cal./mole, respectively. Where R is t-butyl the *gauche* isomer (**52B**) or (**52C**) is more stable by 250 cal./mole. The population of the *gauche* isomer increases with increase in solvent polarity with the exception of phenylacetaldehyde when it decreases. Further investigations using ^{13}C–C–C–H coupling constants will be discussed later.

II. THE VALIDITY OF THE KARPLUS EQUATION

It is now 8 years since Karplus first proposed the relationship between the vicinal coupling constants in saturated systems, and the dihedral angle between the coupling protons.[126] The relationship can be expressed in the form—

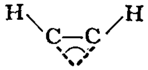
$$J_1 = K_1 \cos^2\phi + c \qquad 0 \leqslant \phi \leqslant 90^\circ \tag{19}$$

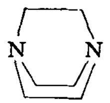
$$J_2 = K_2 \cos^2\phi + c \qquad 90^\circ \leqslant \phi \leqslant 180^\circ \tag{20}$$

where K_1 and K_2 are constants depending on the nature of the C–C fragment, and c is a constant which is generally very small or zero.

Following the vast number of papers published using this relationship in a quantitative or semi-quantitative manner, Karplus[127] warned against the too liberal use of the $\cos^2\phi$ law, and reported a second more refined calculation—

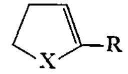
$$J_{\mathrm{HH}} = A + B\cos\phi + C\cos 2\phi \tag{21}$$

pointing out the assumptions made, and the fact that other parameters, including the electronegativity of the substituents on the C—C fragment, and the  angle may affect the coupling constant considerably. From data published in the last few years, however, it is now well established that in most saturated, unstrained systems the coupling constants over three bonds between protons follow the $\cos^2\phi$ rule closely. Thus, axial–axial couplings in cyclohexane rings where ϕ is 180° almost always lie in the range 8–14 c./sec., whereas axial–equatorial and equatorial–equatorial couplings ($\phi \approx 60^\circ$) lie generally in the range 0–6 c./sec. For dihedral angles of near 90°, the coupling as predicted is usually $\leqslant 2$ c./sec. The maximum variations are found for angles of the order of 60°, where the slope of the curve plotting ϕ against $\cos^2\phi$ is greatest. It is found in practice, that J_{ax-eq} is almost invariably greater in magnitude than J_{eq-eq}, a fact which is explained by the electronegativity effect already mentioned. In testing the theory for a dihedral angle of 0°, Macdonald[128] measured the vicinal couplings in 1,4-diazabicyclo[2,2,2]octane (**53**) in which the six-membered rings are held in the boat conformation where he found by an analysis of the ^{13}C satellites in the proton spectrum, that $J_{cis}(=J_{0}^{\circ}) = 9{\cdot}27$ c./sec. An unusually large J_{trans} coupling of 5·93 c./sec. is difficult to explain.



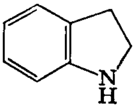
53

Further anomalies have been noted by Abraham and Thomas,[129] in a study of the spectra of near-planar five-membered rings of the type (**54**). In the CH_2—CH_2 fragment as in compound (**53**), the *cis* ($\phi = 0°$) coupling in these molecules is large, (8–10 c./sec.), but the *trans* coupling ($\phi \approx 120°$) is also large (6–9 c./sec.). The authors attribute the large *trans* coupling to the possible effect of the lone pair of electrons on the hetero-atom, the *p* orbital of which can overlap in a planar ring with the C–H orbitals on the adjacent carbon atom. This fact is verified to a certain extent by comparing the coupling constants in indoline (**55**) with those in the quaternary salt (**56**) where the lone pair of electrons is removed—



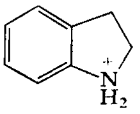
$X = O, S, N$
$R = H, CH_3$

54



$J_{trans} = 8{\cdot}43$ c./sec.
$J_{cis} = 8{\cdot}43$ c./sec.

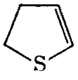
55



$J_{trans} = 6{\cdot}63$ c./sec.
$J_{cis} = 8{\cdot}99$ c./sec.

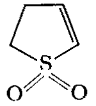
56

Similarly, in 2,3-dihydrothiophen (**57**), and the sulphone (**58**), the same effect is observed—



$J_{trans} = 7{\cdot}51$ c./sec.
$J_{cis} = 9{\cdot}96$ c./sec.

57

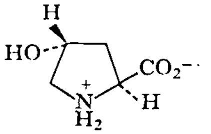


$J_{trans} = 4{\cdot}18$ c./sec.
$J_{cis} = 8{\cdot}97$ c./sec.

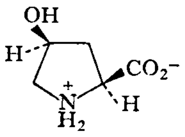
58

It is assumed that the larger coupling constant is always between the eclipsed protons, as found experimentally by Anet for the 2,3-dimethylindolines.[130] Even when the lone pair(s) is removed, J_{trans} is still relatively large, showing that the other effects are present in these planar rings. Erickson[131] has found similar effects in a series of substituted succinic anhydrides, in which J_{trans} is again larger than expected, but is considerably reduced on hydrolysis to the diacid. This suggests that the large *trans* couplings are due not only to lone-pair effects, which are absent in this case, but also to other factors, such as the variation in the internal angles in these planar rings.

In saturated five-membered rings, however, which are not planar molecules, the usual Karplus relationship applies. 4-Hydroxyproline (**59**) and 4-allohydroxyproline (**60**) are excellent compounds of this type for analysis,[132, 133] as are substituted tetrahydrofurans which were examined by Gagnaire.[134]

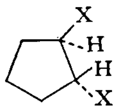


59



60

In neutral or acid solution, from an analysis of the coupling constants, the prolines appear to adopt a highly buckled rigid conformation,[132] but in alkali, as the anions, this rigidity disappears and the coupling constants are the weighted mean of two or more conformations.[133] An attempt has been made to rationalize the pseudorotation in the cyclopentane ring in an examination of the n.m.r. spectra of *trans* 1,2-dihalogenated cyclopentane (**61**).[135] The spectrum of the protons α to the halogen approximates to the X multiplet of an ABX pattern, from which $J_{AX}+J_{BX}$ is readily obtained. From the values of the latter in a variety of solvents and at different temperatures, it is concluded that the halogens prefer to be "diaxial", even in highly polar solvents.



X = Cl, Br

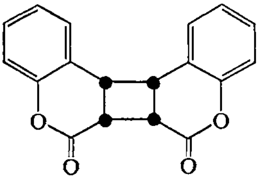
61

A. Four-membered rings

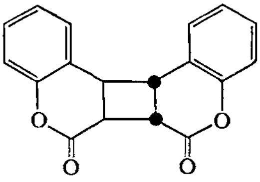
In a recent review on the detailed analysis of the n.m.r. spectra of 20 cyclobutane derivatives,[136] it was shown that the differences between the *cis* and *trans* coupling constants is often small, though J_{cis} was always found to be greater than J_{trans}. The ranges of magnitude found are: J_{gem}, -11 to -14 c./sec.: J_{cis} $+8$ to $+12$ c./sec.: J_{trans}, $+8$ to $+10$ c./sec. Similar values were found in the four isomers formed by photo-dimerization of coumarin (**62A–62D**).[137]

This would appear to indicate that the $\cos^2\phi$ rule does not hold in the case of the more strained cyclobutane ring, but recent reports on the natural product anemonin (**63**)[138] and 3-chlorothietane (**64**)[139] suggest otherwise.

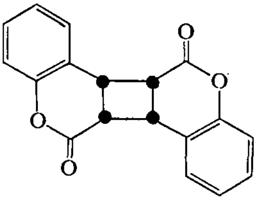
The *cis* and *trans* coupling constants in (**63**) are (c./sec.): $J_{AB'}=10{\cdot}19$; $J_{AA'}=10{\cdot}72$; $J_{BB'}=2{\cdot}24$. Moriarty and co-workers[138, 140] used these values in adjusted Karplus equations, and estimated the angle of twist in the four-membered ring to be between 9° and 11°, in excellent agreement with X-ray data of the same



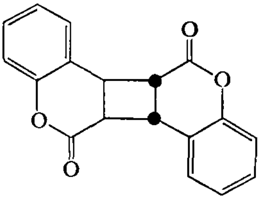
62A



62B

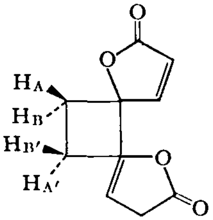


62C



62D

molecule (9·9 ± 0·3°). Similarly, the vicinal couplings in (**64**) ($J_{13} = J_{23} = 7{\cdot}67$ c./sec.; $J_{34} = J_{35} = 9{\cdot}34$ c./sec.), are again in reasonable agreement with the couplings predicted by using the known dihedral angles of the puckered molecule,



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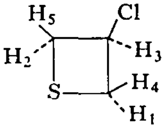
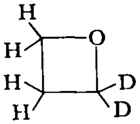


64

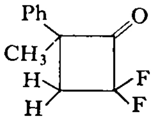
chlorocyclobutane.[141] The vicinal coupling constants in the planar molecule cyclobutanone have been measured by computer iterative analysis,[142] yielding the values 10·02 and 6·35 c./sec., in reasonable agreement with previous results using substituted cyclobutanones.[143] Trimethylene oxide (**65**), deuterated in the C_2 position, has been analysed as an AA′BB′ spectrum,[144] and the vicinal coupling constants obtained, 8·65 and 6·87 c./sec., are again of the same order as in the above examples.



65

The near-equality of J_{cis} and J_{trans} in many four-membered rings may be due to the fast conformational averaging in the molecule, which tends to equalize the two 3-bond couplings.

It appears that the Karplus equation can be applied safely to most unstrained, saturated five- or six-membered rings (or larger) as long as account is taken of the electronegativity of substituents. In three- and four-membered rings, the treatment is less satisfactory, with certain exceptions, although in most cases $J_{cis} > J_{trans}$. Excellent evidence for the inversion or pseudorotation between conformations in cyclobutanes has been reported by Lambert and Roberts,[145] who examined the ^{19}F chemical-shift differences between geminal fluorine nuclei, and also the ^{1}H–^{19}F vicinal coupling as functions of temperature. The latter couplings appear to follow a relationship similar to the Karplus dihedral-angle dependence. Temperature dependence was found in all but the cyclobutanone (**66**), suggesting a rigid planar structure for the latter molecule.

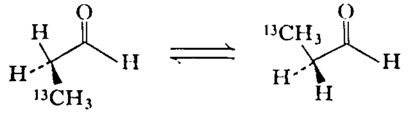


66

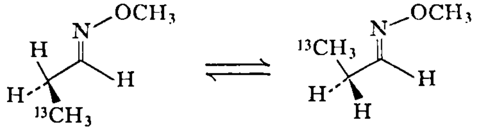
Before leaving the angular dependence of vicinal coupling constants, it should be noted that the theory appears to hold reasonably well for couplings of protons with other nuclei, notably ^{19}F, ^{13}C and ^{31}P. Williamson *et al.*[146] have recently examined the spectra of several rigid molecules containing hydrogen and fluorine separated by three bonds. For dihedral angles of 0°, the coupling constant lay between 10·55 and 30·8 c./sec., for 60° $J_{HF} = 3{\cdot}8$ or 6·0 c./sec., and for 90° small couplings of the order of 2 c./sec. were noted. In 1-chloro-2-fluoroethane and 1-bromo-2-fluoroethane, J_{trans} was found to be 53 c./sec. and J_{gauche} equal to 3·0 and 3·8 c./sec., respectively.[114] The values for J_{trans} appear to be affected strongly by the electronegativity of the accompanying substituents, since, for example, J_{trans} and J_{gauche} in $CHBrCl{\cdot}CF_2Br$ are: (a), J_{trans} 18·9, $J_{gauche} < 2$ c./sec.; (b), J_{trans} 18·5, $J_{gauche} < 2$ c./sec.; and (c), J_{gauche} 1·8, J'_{gauche} 3·4 c./sec., from the low-temperature spectrum of the three rotational isomers.[77]

Further examples of this type are provided in fluorinated cyclohexanes[147] and also in fluorinated carbohydrates.[148] Fluorine–fluorine couplings over three bonds on the other hand, seem to bear no relation to dihedral angles between the C–F bonds. ^{13}C–C–C–*H* coupling constants have been measured in propionaldehyde-3-^{13}C and the corresponding methylated oxime (**67**) and (**68**), respectively.[149]

Previous work has established that $\Delta H_{A\to B} = -800$ cal./mole and $\Delta H_{C\to D} = +390$ cal./mole, assuming $\Delta S = 0$. If $J_{trans\,^{13}CCCH} > J_{cis\,^{13}CCCH}$, an increase in

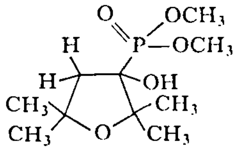


67A **67B**



68C **68D**

temperature should decrease $J_{^{13}CCCH}$ in (**67**) and increase it in (**68**). This is found in practice, as the coupling in (**67**) decreases from 2·65 to 2·30 c./sec. between $-35°C$ and $+45°C$, whereas in (**68**) J increases over a similar range from 2·65 to 3·00 c./sec. Extrapolation of these results leads to values of J_T and J_G of 3·5 and 0·2 c./sec. in (**67**), respectively, and 7·8 and 0·7 c./sec. in (**68**), respectively. Hydrogen–phosphorus couplings again seem to follow the same relationship in the examples provided by Benezra and Ourisson,[150] e.g., (**69**), in which $^3J_{HP}=7$ c./sec. and $\leqslant 0{\cdot}5$ c./sec. for dihedral angles of 30° and 90°, respectively. There is



69

no reason why the angular dependence of vicinal coupling constants should not be extended to *H*—C—O—*H* and *H*—C—N—*H* coupling constants. Some evidence for the former case has been provided by Rader,[151] who examined a series of cyclohexanol derivatives in dry carbon tetrachloride or dimethylsulphoxide, in which intermolecular exchange of the hydroxyl proton is prevented. In all cases the chemical shift of the axial —OH is to higher field than for the corresponding equatorial —OH. It follows from examination of the rotational isomerism about the C—O bond that J_{HCOH} should be larger for the conformers with equatorial —OH than for those with axial —OH. This is found in practice, though the difference between the coupling constants for the two conformations is small (≈ 2 c./sec.). Similar considerations apply to *H*—C—N—*H* coupling constants,[152] though these are often obscured by the quadrupolar broadening of the nitrogen atom. However, the method has some potential for future measurements of the conformations of polypeptides in solution.

B. Geminal coupling constants in methylene groups

The factors affecting the geminal coupling constant between protons have been extensively reviewed recently.[153] The range of coupling constants reported, $-22\cdot3$ to $+42$ c./sec., indicates that some of the many factors affecting the coupling could possibly be used as a probe in determining conformations of molecules. An important paper by Pople and Bothner-By,[154] outlining a molecular-orbital treatment of the two-bond coupling, accounts for the sign and magnitude of most of the coupling constants given in the review. Although so far, little use has been made of the geminal coupling constant in conformational analysis, the sensitivity of $^2J_{HH}$ to environment has clearly great potential for future investigation.

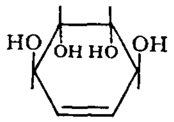
C. Long-range coupling constants over four or more bonds

Spin–spin coupling constants between protons fall off in magnitude rapidly as the number of intervening bonds increases. However, with the improvement in resolution attainable with modern n.m.r. spectrometers, couplings over four and more bonds in organic compounds are now resolved with ease. Theoretical treatment of these interactions, together with empirical correlations have been published, and a recent review on the subject has clarified the situation in its present state.[155]

Whereas the absolute signs of geminal coupling constants between protons can be positive or negative, but usually the latter, and vicinal H–H couplings are positive almost without exception, four-bond couplings have been found to be of either sign, depending on the steric environment of the coupling protons. It is often possible to determine the signs of these coupling constants relative to those of known sign, either by complete analysis of complex spectra, or by spin-decoupling experiments. In conformational analysis, coupling over four bonds in saturated C—C—C fragments are the most important, and in addition, allylic and homoallylic coupling constants, over four and five bonds, respectively, are often used as a conformational probe. The anomalously large splittings found in strained bicyclic compounds are of great interest theoretically, but as little is known about the mechanisms involved, they will not be discussed in this review.

The p.m.r. spectra of the six isomeric conduritols (cyclohexenetetrols) (**70**) to (**75**), have been analysed in detail.[156]

The coupling constants in these molecules provide an excellent test of current theories, as vicinal, allylic, homoallylic and couplings over four saturated bonds are found. In all six cases, the vicinal coupling constants are consistent with "half-chair" conformations either in one single conformation as in conduritols (**71**) and (**75**) or inverting between the two possible forms [conduritols (**70**), (**72**), (**73**) and (**74**)], depending on the number of equatorial hydroxyl groups in each conformation.



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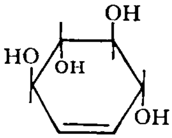

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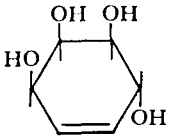

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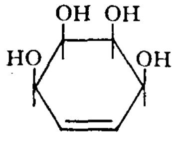

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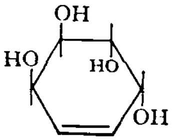

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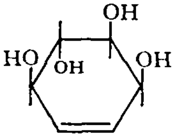

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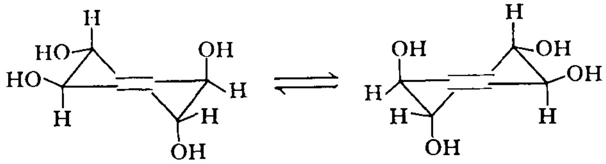
Theory predicts that allylic $(\mathrm{C}H\cdot\mathrm{C}{=}\mathrm{C}H)$ coupling constants exhibit angular dependence.[157] The couplings which are due mainly to σ–π interactions, are proportional to the overlap of the π orbital of the double bond and the 1*s* orbital of the saturated C—H proton. This overlap is proportional to $\cos^2\phi$, where ϕ is the dihedral angle between the C—H proton and the π orbital. More conveniently, the coupling is proportional to $\sin^2\phi'$, if ϕ' is the dihedral angle between the C—H bond and the plane of the olefinic group. Considerable evidence has been accumulated supporting this angular dependence.[155, 158] The two values of the allylic coupling in the conduritols, therefore, should be proportional to $\sin^2 45°$ and $\sin^2 75°$, i.e., 0·5 and 0·9. The observed values, −0·5 and −2·1 c./sec., therefore exhibit a larger variation than expected. This must be due to a contribution to the coupling through σ bonds, which can add to or subtract from the σ–π interaction, depending on the orientation of the protons.



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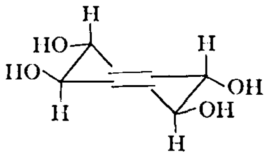

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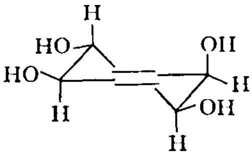


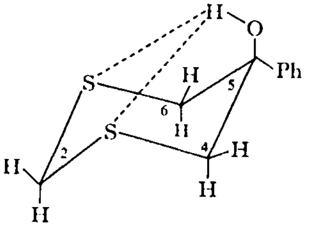
75

Homoallylic coupling constants are also considered to arise from σ–π interactions.[159] Since two dihedral angles are now involved, the coupling should be proportional to $\sin^2\phi_1'.\sin^2\phi_2'$, where ϕ' is as defined for the allylic coupling. The couplings in the conduritols again support the predictions qualitatively, but again show greater variation than expected. $J_{e'e'} = 0$, $J_{e'a'} = 1{\cdot}3$ and $J_{a'a'} = 3{\cdot}0$ c./sec., where e' and a' refer to pseudo-equatorial and pseudo-axial protons, respectively. It is unlikely that a σ bond contribution is present in this case, as such a coupling would be negligible over five bonds. These long-range coupling constants may also be affected by the electron-withdrawing effect of the hydroxyl substituents.

In agreement with Barfields's predictions for couplings over four single bonds,[160] small negative couplings are observed for both protons axially orientated ($J_{a'a} = -0{\cdot}2$ c./sec.), and larger positive coupling constants for both protons equatorial ($J_{e'e} = +1{\cdot}2$ c./sec.). The intermediate couplings $J_{e'a}$ and $J_{a'e}$ are $-0{\cdot}8$ and $+0{\cdot}4$ c./sec., the value $-0{\cdot}8$ being anomalously low. The theoretical graphs[160] are approximated by the equation—

$$^{4}J_{\mathrm{HH}} = \cos^2\phi_1 + \cos^2\phi_2 - 0{\cdot}8 \text{ c./sec.} \qquad (22)$$

where ϕ_1 and ϕ_2 are the two ${}^{\mathrm{H}}\diagdown\mathrm{C}{-}\mathrm{C}\diagup^{\mathrm{C}}$ dihedral angles; equation (22) reproduces the observed couplings in good agreement. The maximum positive coupling is always found to exist between protons in the coplanar W configuration. An example of this type is illustrated by the spectrum of the ring protons of 5-hydroxy-5-phenyl-1,3-dithian (**76**), which is shown in Fig. 1.



76

This molecule is held rigid by the preference of the hydroxyl group for the axial position, in which it can hydrogen-bond intramolecularly with either of the sulphur atoms, and by the known preference of the phenyl group for the equatorial position. In methylene groups adjacent to sulphur in a six-membered ring, the axial proton is usually deshielded relative to the equatorial proton.[97, 161] Therefore the assignment of the protons in Fig. 1 is clear, and indicates the strong coupling of the equatorial protons on C_4 and C_6 with the C_2 equatorial proton, leading to the well-resolved triplets in the high-field part of the AB quartet

($^4J_{HH}=1·85$ c./sec., $J_{AB_{gem}}=13·5$ c./sec.). Analysing the spectrum of the C_4 and C_6 protons as an AA′BB′X case, a further coupling is noted between the equatorial protons on these carbon atoms ($^4J_{HH}=1·6$ c./sec., $J_{AB_{gem}}=13·5$ c./sec.). Similar enhanced four-bond couplings have been determined in several 1,3-dioxan derivatives.[103] No observable coupling between equatorial and axial, or axial and axial protons over four bonds is found in (**76**). Larger coupling constants than usual are also found across the carbonyl group of ketones,[162–164] and can be explained by a σ–π contribution adding to the normal W σ bond mechanism. Such couplings have been used to predict the conformational equilibria of various α-bromocyclohexanone derivatives, in which the bromine atom prefers the axial orientation in solvents of low dielectric constant, and the equatorial position in solvents of high dielectric constant.[163, 164]

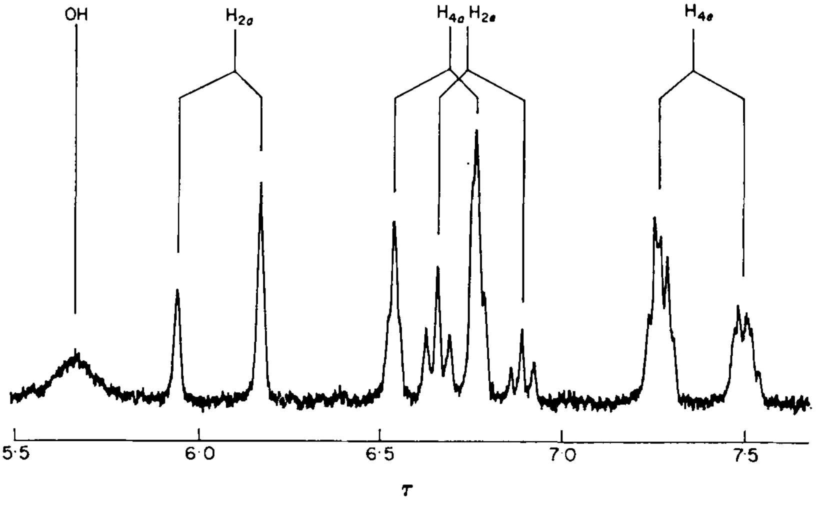
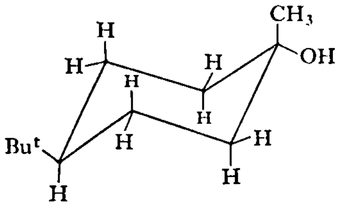


FIG. 1. The p.m.r. spectrum of the ring protons of 5-hydroxy-5-phenyl-1,3-dithian in $CDCl_3$ solution.

The four-bond coupling constant has been shown to be of great importance in the decalin and steroid field. The band widths of the spectra of tertiary methyl groups have been shown to be highly dependent on the orientation of the methyl group, the line widths being significantly greater for axial-methyl resonances.[165–169] A simple example is provided by the two compounds (**77**) and (**78**),[165] in which the band widths at half height of the CH_3 peaks are 1·0–1·3 c./sec. and 0·6–0·7 c./sec., respectively, relative to TMS (0·4–0·5 c./sec.). This difference can only be caused by coupling over four bonds being preferential for the axial methyl group, in which the W rule is followed to a greater extent than for the



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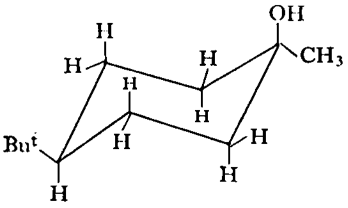
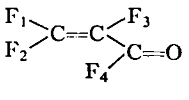


78

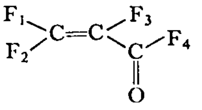
equatorial conformer. Robinson[166] and Williamson *et al.*[169] have shown that in *cis*- and *trans*-decalin derivatives, when a methyl group is present on the ring junction, the band widths of the methyl resonance are much greater for the *trans* fused ring in which three protons are ideally situated for maximum coupling with the methyl protons, than for the *cis* fused rings, in which only one proton is so situated. Results for a larger number of steroid derivatives support this general phenomenon.[167] The long-range splittings are not always resolved, often because complex second-order effects caused by strong coupling between the ring geminal and vicinal protons, tend to complicate the methyl spectrum in some cases.

D. "Through-space" coupling constants

All the coupling constants mentioned so far in this review are thought to originate via a through-bond mechanism. Many coupling constants have been measured, notably between fluorine nuclei, in which the coupling nuclei are separated by several bonds, yet are relatively close in space.[170, 171] One of the first examples of this type was reported by Ramey and Brey[170] who succeeded in "freezing out" the two rotamers (**A**) and (**B**) of perfluoroacrolein (**79**). In



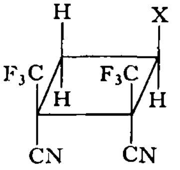
79A



79B

(**79A**), $J_{24}=84{\cdot}5$ c./sec. and $J_{14}<2$ c./sec., whereas in (**79B**), $J_{24}<2$ c./sec. and $J_{14}=41{\cdot}6$ c./sec.

It is found that in the s-*trans*-conformation, the four-bond coupling J_{24} is very large, whereas in the s-*cis*-form, the coupling is much reduced. This would seem to indicate that other factors are contributing to the coupling as well as the normal σ–π interaction, that is, a contribution "through space" could be involved. Convincing evidence for "through-space" coupling was reported by Ng and Sederholm[172] for the coupling between adjacent trifluoromethyl groups over five bonds. For example, in the cyclobutane structures [(**80**) and (**81**)], the F–F coupling is ca. 12 c./sec. for the *cis*-orientated derivative and ca. 0 c./sec. for



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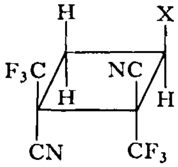
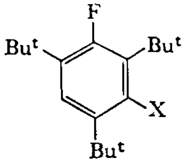


81

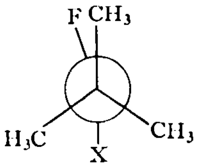
the *trans* derivative. Arguments for and against "through-space" coupling constants have been advanced[172–180] and until recently, the situation was rather confused. The answer lies in the synthesis and examination of suitable model compounds, in which the spatial configuration of the coupling nuclei is known accurately. In an investigation of proton–fluorine couplings over five bonds, a series of substituted 2,4,6-tri-t-butyl-1-fluorobenzenes has been prepared (**82**), where X is a substituent of varying bulk.[180]



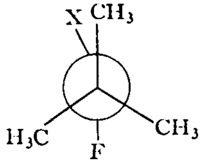
$X = H, \overset{+}{N}H_3, NO_2, OH, NH_2, Br$

82

It is found that the coupling between the fluorine and the β protons of the 2-t-butyl group is markedly increased, as X is increased in size (0·9 c./sec. for X=H to 4·2 c./sec. for X=Br) whereas the coupling to the β protons in the 6-t-butyl group remains relatively constant (0·9–1·3 c./sec.). This can be explained by regarding the configuration of the 2-t-butyl group. The two possible rotational isomers are shown below as (**i**) and (**ii**).



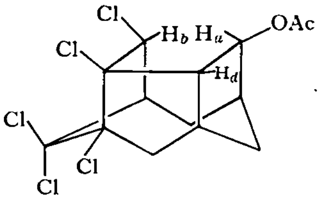
i



ii

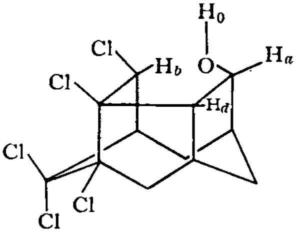
As X is increased in size, the rotamer (**ii**) becomes more unfavourable, as the substituent is eclipsed by a methyl group. In (**i**), the CH_3 eclipsing the fluorine atom is clearly closer in space than in (**ii**), so if a "through-space" mechanism is possible, the coupling should be consequently enhanced, as found in practice.

A very stringent test of the "through-space" coupling hypothesis with regard to proton–proton couplings has been reported by Anet *et al.*[181] Two of the cage compounds investigated are the molecules (**83**) and (**84**).



$J_{ab} < 1$ c./sec.

83



$J_{b0} = 1{\cdot}1$ c./sec.

$J_{ab} = 0{\cdot}24$ c./sec.

84

It is shown that coupling between the non-bonded protons H_a and H_b in (**83**) is negligible, but in (**84**), H_b couples to both H_0 and H_a to the extent of 1·1 and 0·24 c./sec., respectively. As any through-bond mechanism can be disregarded, the couplings must take place via the unshared electrons on the oxygen atom. Unfortunately, a weak hydrogen bond between H_b and oxygen cannot be ruled out entirely, although unusual for a saturated monohalo carbon atom. In the compound with chlorine replaced by hydrogen, much smaller couplings are found, in accordance with the replacement of electrons into the C—H_b bond and consequent lack of formation of a hydrogen bond. In normal, less strained molecules, therefore, proton–proton couplings through space must be negligible, although the same cannot be said for H–F and F–F coupling constants, which, at the present time, appear to couple strongly when the nuclei are close in space and separated by four or more bonds. At present however, the magnitude of such couplings appears not to depend on the internuclear separation,[174] and the mechanism is still therefore not known.

III. SUMMARY

In this review, the wide range of methods by which n.m.r. spectroscopy can be used to solve conformational problems has been discussed. It has not been possible to mention all of the work published in this field in the last 2 years. However, it has been shown that in general, current theories regarding chemical shifts and coupling constants in inverting or rigid molecules can be applied with success to obtain useful conformational information, and that the n.m.r. method is now probably the most valuable tool in this important topic.

For the future, the n.m.r. spectra of other nuclei will clearly become more popular, as instrumentation in that direction improves. The carbon-13 nucleus is likely to provide the most rewarding information. Pioneering work by Stothers[182] and Stothers and Lauterbur[183] and others in this field, indicate that ^{13}C chemical shifts and coupling constants are extremely sensitive to steric environment, and that once the problems of low abundance and sensitivity are overcome, and routine ^{13}C spectra can be obtained, the field should prove extremely profitable.

Although the thermodynamic parameters for exchange processes between conformations can be measured with an accuracy unparalleled by any other physical method, published values for the enthalpies and entropies of activation for these processes must still be regarded with caution, until the current discrepancies between results obtained by the high-resolution and spin-echo techniques are resolved. However, good agreement has been shown between the two methods in the measurement of free energies of activation for the inversion processes. Again, better instrumentation will help to iron out the systematic errors inherent in the high-resolution and spin-echo techniques.

REFERENCES

1. J. E. Anderson, *Quart. Rev.*, 1965, **19**, 426.
2. C. S. Johnson, Jr., *Adv. Magnetic Resonance*, 1965, **1**, 33.
3. L. W. Reeves, *Adv. Phys. Org. Chem.*, 1965, **3**, 187.
4. A. Loewenstein and T. M. Connor, *Ber. Bunsen Gesellschaft phys. Chem.*, 1963, **67**, 280.
5. J. W. Emsley, J. Feeney and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy", Vol. 1, Chap. 9. Pergamon Press, London, 1965.
6. J. Jonas, A. Allerhand and H. S. Gutowsky, *J. Chem. Phys.*, 1965, **42**, 3396.
7. S. Forsén and R. A. Hoffman, *J. Chem. Phys.*, 1963, **39**, 2892.
8. S. Meiboom, *J. Chem. Phys.*, 1961, **34**, 375.
9. F. A. L. Anet and A. J. R. Bourn, *J. Amer. Chem. Soc.*, 1967, **89**, 760, and references therein.
10. F. R. Jensen, D. S. Noyce, C. H. Sederholm and A. J. Berlin, *J. Amer. Chem. Soc.*, 1962, **84**, 386.
11. R. K. Harris and N. Sheppard, *Proc. Chem. Soc.*, 1961, 418.
12. S. Meiboom, *In* "American Chemical Society Symposium on High Resolution n.m.r. Spectroscopy", July, 1962.
13. A. Allerhand, F.-M. Chen and H. S. Gutowsky, *J. Chem. Phys.*, 1965, **42**, 3040.
14. F. A. L. Anet, M. Ahmad and L. D. Hall, *Proc. Chem. Soc.*, 1964, 145.
15. F. A. Bovey, F. P. Hood, E. W. Anderson and R. L. Kornegay, *J. Chem. Phys.*, 1964, **41**, 2041.
16. F. A. Bovey, F. P. Hood, E. W. Anderson and R. L. Kornegay, *Proc. Chem. Soc.*, 1964, 146.
17. A. Allerhand, H. S. Gutowsky, J. Jonas and R. A. Meinzer, *J. Amer. Chem. Soc.*, 1966, **88**, 3185.
18. R. J. Abraham and D. B. Macdonald, *Chem. Comm.*, 1966, 188.
19. J. D. Roberts, *Chem. in Britain*, 1966, **2**, 529.
20. A. Allerhand and H. S. Gutowsky, *J. Chem. Phys.*, 1965, **42**, 4203.
21. S. L. Spassov, D. L. Griffith, E. S. Glazer, K. Nagarajan and J. D. Roberts, *J. Amer. Chem. Soc.*, 1967, **89**, 88.
22. H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, 1956, **25**, 1228.

23. S. Alexander, *J. Chem. Phys.*, 1962, **37**, 967, 974.
24. G. V. D. Tiers, *Proc. Chem. Soc.*, 1960, 389.
25. H. S. Gutowsky and F.-M. Chen, *J. Phys. Chem.*, 1965, **69**, 3216.
26. F. A. Bovey, E. W. Anderson, F. P. Hood and R. L. Kornegay, *J. Chem. Phys.*, 1964, **40**, 3099.
27. H. Friebolin, W. Faisst, H. G. Schmid and S. Kabuss, *Tetrahedron Letters*, 1966, 1317.
28. W. Reusch and D. F. Anderson, *Tetrahedron*, 1966, **22**, 583.
29. H. G. Schmid, H. Friebolin, S. Kabuss and R. Mecke, *Spectrochim. Acta*, 1966, **22**, 623.
30. J. E. Anderson and J. C. D. Brand, *Trans. Faraday Soc.*, 1966, **62**, 39.
31. R. W. Murray, P. R. Story and M. L. Kaplan, *J. Amer. Chem. Soc.*, 1966, **88**, 526.
32. R. K. Harris and R. A. Spragg, *Chem. Comm.*, 1966, 314.
33. S. Kabuss, A. Lüttringhaus, H. Friebolin and R. Mecke, *Z. Naturforsch.*, 1966, **21B**, 320.
34. F. G. Riddell and J. M. Lehn, *Chem. Comm.*, 1966, 375.
35. R. F. Farmer and J. Hamer, *Chem. Comm.*, 1966, 866.
36. N. Muller and W. C. Tosch, *J. Chem. Phys.*, 1962, **37**, 1167.
37. F. R. Jensen and B. H. Beck, *Tetrahedron Letters*, 1966, 4523.
38. F. G. Riddell and M. J. T. Robinson, *Chem. Comm.*, 1965, 227.
39. J. T. Gerig and J. D. Roberts, *J. Amer. Chem. Soc.*, 1966, **88**, 2791.
40. S. Kabuss, H. Friebolin and H. G. Schmid, *Tetrahedron Letters*, 1965, 469.
41. S. Kabuss, A. Lüttringhaus, H. Friebolin, H. G. Schmid and R. Mecke, *Tetrahedron Letters*, 1966, 719.
42. I. O. Sutherland and M. V. J. Ramsey, *Tetrahedron*, 1965, **21**, 3401.
43. F. A. L. Anet, *J. Amer. Chem. Soc.*, 1964, **86**, 458.
44. F. R. Jensen and L. A. Smith, *J. Amer. Chem. Soc.*, 1964, **86**, 956.
45. J. B. Lambert, L. J. Durham, P. Lepoutere and J. D. Roberts, *J. Amer. Chem. Soc.*, 1965, **87**, 3896.
46. F. A. L. Anet and J. S. Hartman, *J. Amer. Chem. Soc.*, 1963, **85**, 1204.
47. F. A. L. Anet and M. St. Jacques, *J. Amer. Chem. Soc.*, 1966, **88**, 2586.
48. M. St. Jacques, M. A. Brown and F. A. L. Anet, *Tetrahedron Letters*, 1966, 5947.
49. C. Ganter, S. M. Pokras and J. D. Roberts, *J. Amer. Chem. Soc.*, 1966, **88**, 4235.
50. F. A. L. Anet, *J. Amer. Chem. Soc.*, 1962, **84**, 671.
51. D. E. Gwynn, G. M. Whitesides and J. D. Roberts, *J. Amer. Chem. Soc.*, 1965, **87**, 2862.
52. A. Allerhand and H. S. Gutowsky, *J. Amer. Chem. Soc.*, 1965, **87**, 4092.
53. G. Binsch and J. D. Roberts, *J. Amer. Chem. Soc.*, 1965, **87**, 5157.
54. J. M. Lehn and F. G. Riddell, *Chem. Comm.*, 1966, 803.
55. W. D. Ollis and I. O. Sutherland, *Chem. Comm.*, 1966, 402.
56. A. P. Downing, W. D. Ollis and I. O. Sutherland, *Chem. Comm.*, 1967, 171.
57. H. M. McConnell, *J. Chem. Phys.*, 1958, **28**, 430.
58. F. Conti, C. H. Eugster and W. von Philipsborn, *Helv. Chim. Acta*, 1966, **49**, 2267.
59. G. Schroder and J. F. M. Oth, *Tetrahedron Letters*, 1966, 4083.
60. I. C. Calder and F. Sondheimer, *Chem. Comm.*, 1966, 904.
61. Y. Gaoni, A. Melera, F. Sondheimer and R. Wolovsky, *Proc. Chem. Soc.*, 1964, 397.

62. J. A. Pople and K. G. Untch, *J. Amer. Chem. Soc.*, 1966, **88**, 4811.
63. G. Schröder, *Angew. Chem. Internat. Ed.*, 1965, **4**, 752.
64. J. B. Lambert, *Tetrahedron Letters*, 1963, 1901.
65. A. T. Bottini, R. L. Van Etten and A. J. Davidson, *J. Amer. Chem. Soc.*, 1965, **87**, 755 and references therein.
66. D. L. Griffith and J. D. Roberts, *J. Amer. Chem. Soc.*, 1965, **87**, 4089.
67. J. C. Breliere and J. M. Lehn, *Chem. Comm.*, 1965, 426.
68. J. E. Anderson and J. M. Lehn, *Bull. Soc. chim. France*, 1966, 2402.
69. J. E. Anderson and J. M. Lehn, *J. Amer. Chem. Soc.*, 1967, **89**, 81.
70. J. P. Kintzinger, J. M. Lehn and J. Wagner, *Chem. Comm.*, 1967, 206.
71. C. H. Bushweller, *Chem. Comm.*, 1966, 80.
72. B. J. Price, R. V. Smallman and I. O. Sutherland, *Chem. Comm.*, 1966, 319.
73. G. W. Buchanan and J. B. Stothers, *Chem. Comm.*, 1967, 179.
74. N. C. Franklin and H. Feltkamp, *Angew. Chem. Internat. Ed.*, 1965, **4**, 774.
74a. E. L. Eliel, *Angew. Chem. Internat. Ed.*, 1965, **4**, 761.
75. E. L. Eliel and M. C. Knoeber, *J. Amer. Chem. Soc.*, 1966, **88**, 5347.
76. F. R. Jensen and C. H. Bushweller, *J. Amer. Chem. Soc.*, 1966, **88**, 4279.
77. R. A. Newmark and C. H. Sederholm, *J. Chem. Phys.*, 1965, **43**, 602.
78. F. A. L. Anet and M. U. Ahmad, *J. Amer. Chem. Soc.*, 1964, **86**, 119.
79. K. I. Dahlqvist and S. Forsén, *J. Phys. Chem.*, 1965, **69**, 4062.
80. A. G. Whittaker and S. Siegel, *J. Chem. Phys.*, 1965, **43**, 1575.
81. A. G. Whittaker and S. Siegel, *J. Chem. Phys.*, 1965, **42**, 3320.
82. R. M. Hammaker and B. A. Gugler, *J. Mol. Spectroscopy*, 1965, **17**, 356.
83. L. Toldy and L. Radics, *Tetrahedron Letters*, 1966, 4753.
84. G. J. Karabatsos, N. Hsi and C. E. Orzech, Jr., *Tetrahedron Letters*, 1966, 4639.
85. T. H. Siddall, III, and R. H. Garner, *Tetrahedron Letters*, 1966, 3513.
86. P. K. Korver, P. J. Van der Haak and T. J. de Boer, *Tetrahedron*, 1966, **22**, 3157.
87. F. A. L. Anet, *J. Amer. Chem. Soc.*, 1962, **84**, 1053.
88. H. Feltkamp and N. C. Franklin, *J. Amer. Chem. Soc.*, 1965, **87**, 1616.
89. H. Feltkamp, N. C. Franklin, K. D. Thomas and W. Brügel, *Annalen*, 1965, **683**, 64.
90. H. Booth, N. C. Franklin and G. C. Gidley, *Tetrahedron*, 1965, **21**, 1077.
91. W. F. Trager and A. C. Huitric, *J. Org. Chem.*, 1965, **30**, 3257.
92. W. F. Trager, B. J. Nist and A. C. Huitric, *Tetrahedron Letters*, 1965, 267.
93. W. F. Trager, B. J. Nist and A. C. Huitric, *Tetrahedron Letters*, 1965, 2931.
94. H. Booth, *Tetrahedron*, 1964, **20**, 2211.
95. C.-Y. Chen and R. J. W. Le Fèvre, *J. Chem. Soc.*, 1965, 3700.
96. R. J. Abraham and W. A. Thomas, *J. Chem. Soc.*, 1965, 335.
97. W. A. Thomas, Ph.D. Thesis, University of Liverpool, 1965.
98. A. Lüttringhaus, S. Kabuss, H. Prinzbach and F. Langenbucher, *Annalen*, 1962, **653**, 195.
99. N. Baggett, M. A. Bukhari, A. B. Foster, J. Lehmann and J. M. Webber, *J. Chem. Soc.*, 1963, 4157.
100. J. Delmau and J. Duplan, *Tetrahedron Letters*, 1966, 2693.
101. J. Delmau and J. Duplan, *Tetrahedron Letters*, 1966, 559.
102. J. Delmau, *Compt. Rend. Congr. Natl. Soc. Sarentes Sect. Sci.*, 1964, **90**, 123.
103. K. C. Ramey and J. Messick, *Tetrahedron Letters*, 1965, 4423.
104. H. T. Kalff and E. Havinga, *Rec. Trav. chim.*, 1966, **85**, 467.
105. G. Pfundt and S. Farid, *Tetrahedron*, 1966, **22**, 2237.
106. E. Caspi, T. A. Wittstruck and D. M. Piatak, *J. Org. Chem.*, 1962, **27**, 3183.

107. C.-Y. Chen and R. J. W. Le Fèvre, *J. Chem. Soc.*, 1965, 558.
108. R. R. Frazer and C. Reyes-Zamora, *Canad. J. Chem.*, 1965, **43**, 3445.
109. D. Jung, *Chem. Ber.*, 1966, **99**, 566.
110. C. Altona and E. Havinga, *Tetrahedron*, 1966, **22**, 2275.
111. J. B. Lambert and R. G. Keske, *J. Amer. Chem. Soc.*, 1966, **88**, 620 and references therein.
112. H. Booth, *Tetrahedron Letters*, 1965, 411.
113. N. S. Bhacca and D. H. Williams, "Applications of N.M.R. Spectroscopy in Chemistry", p. 144. Holden-Day, San Francisco, 1964.
114. R. J. Abraham, L. Cavalli and K. G. R. Pachler, *Mol. Phys.*, 1966, **11**, 471.
115. R. J. Abraham and K. G. R. Pachler, *Mol. Phys.*, 1963, **7**, 165.
116. R. J. Abraham and L. Cavalli, *Mol. Phys.*, 1965, **9**, 67.
117. D. Jung and A. A. Bothner-By, *J. Amer. Chem. Soc.*, 1964, **86**, 4025.
118. E. I. Snyder, *J. Amer. Chem. Soc.*, 1966, **88**, 1155, 1161, 1165.
119. R. J. Abraham and M. A. Cooper, *Chem. Comm.*, 1966, 588.
120. H. S. Gutowsky, G. G. Belford and P. E. McMahon, *J. Chem. Phys.*, 1962, **36**, 3353.
121. W. Lüttke and A. de Meijere, *Angew. Chem. Internat. Ed.*, 1966, **5**, 512.
122. A. A. Bothner-By, S. Castellano and H. Günther, *J. Amer. Chem. Soc.*, 1965, **87**, 2439.
123. A. A. Bothner-By, S. Castellano, S. J. Ebersole and H. Günther, *J. Amer. Chem. Soc.*, 1966, **88**, 2466.
124. R. J. Abraham and J. A. Pople, *Mol. Phys.*, 1960, **3**, 609.
125. G. J. Karabatsos and N. Hsi, *J. Amer. Chem. Soc.*, 1965, **87**, 2864.
126. M. Karplus, *J. Chem. Phys.*, 1959, **30**, 11.
127. M. Karplus, *J. Amer. Chem. Soc.*, 1963, **85**, 2870.
128. D. B. Macdonald, Ph.D. Thesis, University of Liverpool, 1966.
129. R. J. Abraham and W. A. Thomas, *Chem. Comm.*, 1965, 431.
130. F. A. L. Anet and J. M. Muchowski, *Chem. and Ind.*, 1963, 81.
131. L. E. Erickson, *J. Amer. Chem. Soc.*, 1965, **87**, 1867.
132. R. J. Abraham and K. A. McLauchlan, *Mol. Phys.*, 1962, **5**, 195, 513.
133. R. J. Abraham and W. A. Thomas, *J. Chem. Soc.*, 1964, 3739.
134. D. Gagnaire and P. Vottero, *Bull. Soc. chim. France*, 1963, 2779.
135. C. Altona, H. R. Buys and E. Havinga, *Rec. Trav. chim.*, 1966, **85**, 983.
136. H. Weitkamp and F. Korte, *Tetrahedron Supplement* 7, 1966, 75.
137. C. H. Krauch, S. Farid and G. O. Schenck, *Chem. Ber.*, 1966, **99**, 625.
138. E. Lustig and R. M. Moriarty, *J. Amer. Chem. Soc.*, 1965, **87**, 3252.
139. W. D. Keller, T. R. Lusebrink and C. H. Sederholm, *J. Chem. Phys.*, 1966, **44**, 782.
140. R. M. Moriarty, C. R. Romain, I. L. Karle and J. Karle, *J. Amer. Chem. Soc.*, 1965, **87**, 3251.
141. H. Kim, Ph.D. Thesis, University of California, 1964.
142. B. Braillon and J. Barbet, *Compt. rend.*, 1965, **261**, 1967.
143. B. Braillon, J. Salaün, J. Gore and J.-M. Conia, *Bull. Soc. chim. France*, 1964, 1981.
144. E. Lustig, E. P. Ragelis and N. Duy, *Spectrochim. Acta*, 1967, **23A**, 133.
145. J. B. Lambert and J. D. Roberts, *J. Amer. Chem. Soc.*, 1965, **87**, 3884, 3891.
146. K. L. Williamson, Y.-F. Li, F. H. Hall and S. Swager, *J. Amer. Chem. Soc.*, 1966, **88**, 5678.
147. A. Peake and L. F. Thomas, *Trans. Faraday Soc.*, 1966, **62**, 2980.

148. L. D. Hall and J. F. Manville, *Chem. and Ind.*, 1965, 991.
149. G. J. Karabatsos, C. E. Orzech, Jr., and N. Hsi, *J. Amer. Chem. Soc.*, 1966, **88**, 1817.
150. C. Benezra and G. Ourisson, *Bull. Soc. chim. France*, 1966, 1825.
151. C. P. Rader, *J. Amer. Chem. Soc.*, 1966, **88**, 1713.
152. P. Rouillier, J. Delmau, J. Duplan and C. Nofre, *Tetrahedron Letters*, 1966, 4189.
153. R. C. Cookson, T. A. Crabb, J. J. Frankel and J. Hudec, *Tetrahedron Supplement* 7, 1966, 355.
154. J. A. Pople and A. A. Bothner-By, *J. Chem. Phys.*, 1965, **42**, 1339.
155. S. Sternhell, *Rev. Pure Appl. Chem.* (*Australia*), 1964, **14**, 15.
156. R. J. Abraham, H. Gottschalck, H. Paulsen and W. A. Thomas, *J. Chem. Soc.*, 1965, 6268.
157. J. A. Pople, W. G. Schneider and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance", Chap. 8. McGraw-Hill, London, 1959.
158. D. Brookes, S. Sternhell, B. K. Tidd and W. B. Turner, *Austral. J. Chem.*, 1965, **18**, 373.
159. M. Karplus, *J. Chem. Phys.*, 1960, **33**, 1842.
160. M. Barfield, *J. Chem. Phys.*, 1964, **41**, 3825.
161. E. Campaigne, N. F. Chamberlain and B. E. Edwards, *J. Org. Chem.*, 1962, **27**, 135.
162. J. R. Holmes and D. Kivelson, *J. Amer. Chem. Soc.*, 1961, **83**, 2959.
163. H. Dürr, G. Ourisson and B. Waegell, *Chem. Ber.*, 1965, **98**, 1858.
164. H. Dürr, *Ber. Bunsen Gesellschaft Phys. Chem.*, 1965, **69**, 641.
165. C. W. Shoppee, F. P. Johnson, R. E. Lack and S. Sternhell, *Chem. Comm.*, 1965, 347.
166. M. J. T. Robinson, *Tetrahedron Letters*, 1965, 1685.
167. N. S. Bhacca, J. E. Gurst and D. H. Williams, *J. Amer. Chem. Soc.*, 1965, **87**, 302.
168. A. Rassat, C. W. Jefford, J. M. Lehn and B. Waegell, *Tetrahedron Letters*, 1964, 233.
169. K. L. Williamson, T. Howell and T. A. Spencer, *J. Amer. Chem. Soc.*, 1966, **88**, 325.
170. K. C. Ramey and W. S. Brey, *J. Chem. Phys.*, 1964, **40**, 2349.
171. N. Boden, J. W. Emsley, J. Feeney and L. H. Sutcliffe, *Proc. Roy. Soc.*, 1964, **A282**, 559.
172. S. Ng and C. H. Sederholm, *J. Chem. Phys.*, 1964, **40**, 2090.
173. L. Petrakis and C. H. Sederholm, *J. Chem. Phys.*, 1961, **35**, 1243.
174. N. Boden, J. Feeney and L. H. Sutcliffe, *J. Chem. Soc.*, 1965, 3482.
175. K. L. Servis and J. D. Roberts, *J. Amer. Chem. Soc.*, 1965, **87**, 1339.
176. A. D. Cross, *J. Amer. Chem. Soc.*, 1964, **86**, 4011.
177. A. D. Cross and P. W. Landis, *J. Amer. Chem. Soc.*, 1964, **86**, 4005.
178. A. Lewin, *J. Amer. Chem. Soc.*, 1964, **86**, 2303.
179. J. Burdon, *Tetrahedron*, 1965, **21**, 1101.
180. P. C. Myhre, J. W. Edmonds and J. D. Kruger, *J. Amer. Chem. Soc.*, 1966, **88**, 2459.
181. F. A. L. Anet, A. J. R. Bourn, P. Carter and S. Winstein, *J. Amer. Chem. Soc.*, 1965, **87**, 5249.
182. J. B. Stothers, *Quart. Rev.*, 1965, **19**, 144.
183. J. B. Stothers and P. C. Lauterbur, *Canad. J. Chem.*, 1964, **42**, 1563.

The Interpretation of High-Resolution Nuclear Magnetic Resonance Spectra

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I. REFERENCES AND INTENTION

THE SUBJECT of spectral interpretation is having a spate of review coverage at the present time, so that initially a "review of reviews" will not be out of place, if only to introduce a few key references of which frequent mention will be made. At the level of massive compilation, Emsley *et al.*[1] have covered in a 200-page chapter and appendix all the literature to the end of 1963 (and some references for 1964). For the reader with some mathematical inclination a very thorough account of spectral analysis by Corio[2] has recently been published, and the review by Hoffman[3] gives a concise overall picture. Several of the more important experimental and mathematical techniques for dealing with complex spectra have been, or are about to be, reviewed individually. Computer techniques in spectral analysis have been reviewed succinctly by Swalen,[4] and the procedure of sub-spectral analysis is shortly to be reviewed by its chief exponents Diehl *et al.*[5] Double (and triple) resonance is one of the most powerful experimental techniques now used to assist in spectral interpretation; this has been reviewed at some length by Hoffman and Forsén,[6] and is the subject of a separate article in this volume by W. McFarlane (p. 135).

The present article is intended primarily as a general account for inorganic and organic chemists with some, but not specialist, knowledge of n.m.r. In addition to analysis as such, a Section is included on theoretical principles at an elementary level, to provide some insight into the structure of high-resolution spectra. Details of the calculations involved are set out very clearly for a few illustrative examples in an account by Roberts.[7] A secondary purpose of this article is to mention some recent advances and to amplify a few points treated cursorily elsewhere.

II. PARAMETERS OF THE SPECTRUM

The content of n.m.r. spectral interpretation will now be defined. If the infrared vibration–rotation spectrum of a diatomic molecule is analysed, the results are expressed most simply in terms of a few molecular constants—rotational, anharmonicity, vibrational, etc.—and these would determine, with the appropriate quantum numbers, the vibrational–rotational energy levels. These are phenomenological parameters, introduced for mathematical convenience. Sometimes such parameters are related very simply to more fundamental properties (for example the rotational constant to the atomic masses and bond lengths) but more often they involve detailed molecular electronic wave functions; so that further breakdown, or conversely prediction from first principles, involves gross approximations to simplify the mathematics. Such constants are nevertheless extremely useful as a general guide to molecular structure. The same approach is adopted in n.m.r.; high-resolution (liquid or gas phase) spectra usually of "spin $\frac{1}{2}$" nuclei (see next Section), can be expressed in terms of two phenomenological parameters alone—the chemical shift (ν_i, ν_j etc. for nuclei i, j etc.) and the spin coupling constant (J_{ij} between nuclei i, j). The chemical shift as measured or calculated directly from a spectrum is the frequency separation, usually in c./sec., from a selected reference signal, e.g., TMS for ^1H spectra. As such it is directly proportional to the applied magnetic field (H_0), in contrast to J_{ij} which is independent of H_0. The shift is often expressed instead as a fraction of the oscillator r.f. frequency, to produce a field-independent value (e.g., the τ scale). The shielding constant is a tensor quantity, and under the conditions of a high-resolution spectrum one is measuring the average value of the chemical shift for all orientations of the molecule (rapid tumbling) relative to the external field.

Chemical shifts, and sometimes coupling constants, are measurably affected by extramolecular environment, so that strictly they are molecular constants only in the vapour state or (more practicably) when extrapolated to high dilution in an inert solvent. If this is not the case, the concentration and nature of the solvent should always be specified.

The main interpretative problem is, then, the deduction of these phenomenological parameters from the spectrum (remembering that coupling constants may be either positive or negative). To these parameters may be added the relative number of nuclei at each chemical shift. The interpretation is sometimes evident on cursory inspection, or with the supplementary help of a simple experiment such as double resonance or a change of solvent. Alternatively, to obtain the required information it may be necessary to carry out a formal mathematical analysis, which may be anything from a simple slide-rule calculation to lengthy electronic computation. It is important to note that formal analysis does not always enable one to identify particular chemical shifts with particular environments within the molecular species (singular or plural) causing the spectrum—see also next Section. Interpretation in its fullest sense will include an attempt to relate the parameters to chemical structures, using data on similar compounds where available.

In analysis, the positions and relative intensities of the spectral lines are considered, but not usually their width. Characteristically the spectra of spin $\frac{1}{2}$ nuclei have very narrow lines under normal high-resolution conditions, owing to inefficiency of the mechanisms for nuclear-spin relaxation. Often, the minimum line width observed is determined rather by inhomogeneities in the external magnetic field and all lines in the spectrum have approximately the same apparent width. Relative heights then give a reasonable and quick estimate of the relative intensities of well-resolved lines, but are misleading if there is significant overlap. Computer programmes for the breakdown of overlapping lines or synthesis of an experimental line envelope are mentioned later. If differences in line width are observed, these can be used to obtain extra information. In the first place, such differences can be created artificially by adding a paramagnetic material, thereby shortening the relaxation time associated with each line and broadening it to the state at which field inhomogeneity ceases to be the decisive factor. This is referred to later; it is not a part of normal analysis procedure. Differences in width observed with no paramagnetic addition may reflect differences in relaxation times, unresolved spin coupling, or time-dependent processes such as internal rotation or chemical exchange. In the last case, broadening occurs over a certain range of rate constants (see below), when the latter can be evaluated by analysis of line shape using the Bloch equations.[1] The presence of an electric quadrupole moment can cause considerable line broadening. Such a moment is possessed by nuclei of spin greater than $\frac{1}{2}$, and can cause strong spin-lattice relaxation and line broadening through interaction with the fluctuating electric field gradient at the nucleus.

The line widths are then a source of information about local symmetry. Lines due to resonance of spin $> \frac{1}{2}$ nuclei in an unsymmetrical environment are often so broad that they cannot be considered as "high-resolution" spectra. Lines due to spin $\frac{1}{2}$ nuclei in proximity to a nuclear quadrupole are less affected but can still be significantly broadened (e.g., a non-exchanging H directly bound to ^{14}N).

It is important to note the conditions under which coupling between two nuclei can occur. First, since the interaction is transmitted via a perturbation of the electron wave function, the nuclei must be in the same molecule. Second, the nuclei must experience a constant interaction over a time interval which is long compared to the reciprocal of the coupling constant expressed in frequency units (c./sec.). A chemical exchange process which separates a given pair of nuclei in a time shorter than this will effectively remove the spin coupling. Furthermore, even if the nuclei remain in the same molecule, the energy states must be constant over the critical time interval; i.e., the relaxation times of both nuclei must be sufficiently long. For this reason coupling involving a nucleus of spin $> \frac{1}{2}$ is often not observable; here, relaxation via the electric quadrupole moment is too rapid unless either the moment or the local electric field gradient is small. For example, bound chlorine is always in a highly asymmetric environment, so that coupling to ^{35}Cl ($I = \frac{3}{2}$) is not observed.

Both chemical shifts and coupling constants are subject also to time averaging. Rapid intramolecular motion between conformers in which a particular nucleus has different chemical shifts or coupling interactions will produce a spectrum appropriate to the time average only of these parameters. Slow interconversion produces a superposition of the conformer spectra, and intermediate rates produce a line-broadened spectrum as noted earlier. Rapid intermolecular exchange averages chemical shifts in a similar way, but completely removes the effect of spin coupling as mentioned above.

III. NOTATION AND SYMMETRY

Discussion of an n.m.r. spectrum is greatly helped by a notation designating the number of chemical shift and coupling parameters affecting the spectrum, and their interrelation. Each designation defines a type of "spin system", whose spectra have many features in common and present basically the same analytical problem. Systematic notation has been adopted only in the case of spin $\frac{1}{2}$ nuclei, which account for most high-resolution spectra. Several notations have been used, all of which follow the original proposal of Bernstein *et al.* in Emsley *et al.*,[1] (p. 283), in the use of capital letters to denote nuclei within a spin-coupled system. A different letter is used for each chemical shift. Letters close in the alphabet (A, B, C...) are used if coupling between the relevant nuclei is of the same order of magnitude as their separation in chemical shift, and widely separated letters (A, M, P, X...) are used to signify relatively large shift separations.

It often happens that two or more spin-coupled nuclei (i.e., in the same molecule) have the same chemical shift. It is important analytically to differentiate between (a) complete equivalence, and (b) chemical-shift equivalence only, of such a group of nuclei. Complete equivalence, (a), requires equality of chemical shifts plus "spin-coupling equivalence", which means that each member of the group must be coupled equally to all the nuclei at any other chemical shift, e.g., the A nuclei are completely equivalent if there is only one value for J_{AB}, one value for J_{AC}, and so on. It is in practice always due to symmetry conditions. Chemical-shift equivalence without spin-coupling equivalence, (b), is usually symmetry-produced, which implies equality of some of the inter-group couplings, but is occasionally due to a chance coincidence irrespective of symmetry.

It is useful to have a notation that will distinguish between these possibilities. The original scheme of Bernstein *et al.* did not do so, but simply indicated the number of spin-coupled nuclei at a given chemical shift as a subscript. Several modifications have been proposed, and that of Richards and Schaefer is at present most widely adopted (ref. 1, p. 283). In this, subscripts are used only to denote completely equivalent nuclei, (a). In case (b), nuclei that have the same shift but are not completely equivalent are distinguished by single or multiple primes. For example, the ring protons of a *p*-disubstituted benzene (RC_6H_4R', $R \neq R'$, see formula 3, p. 116), are described as an AA'BB' system since $J_{AB} \neq J_{AB'}$. The notation A_2B_2 is reserved for the case $J_{AB} = J_{AB'}$. It is very unlikely that the case AA'BB' will arise through chance coincidence of shifts, so this notation is always assumed to apply to the symmetry-determined situation (as in the example) in which $J_{AB} = J_{A'B'}$ and $J_{AB'} = J_{A'B}$, unless specifically excluded. It is unfortunate that information of this kind should be implicit rather than explicit in the notation. A recent survey by Haigh[8] points out also that the above notation is cumbersome when applied to complex systems of high symmetry, and proposes a new notation to avoid these disadvantages.

The proposed notation of Haigh[8] is based on the use of square brackets to enclose any part of a spin system within which there is spin-coupling equivalence. An outer subscript indicates that the sub-system enclosed is repeated elsewhere in the spin system due to symmetry, i.e., together with all the couplings "across" the bracket as well as within it. Brackets within brackets are used whenever possible, so that the number of non-identical coupling constants in the system is indicated explicitly. Thus, in the previous example, the symmetry-determined AA'BB' system of Richards and Schaefer becomes $[AB]_2$, and the A_2B_2 case of complete equivalence becomes $[A_2B_2]$. Haigh also proposes that the completely bracket-free notation be retained in the original sense of Bernstein *et al.* as a general term with no implication as to symmetry or coupling constants. In this sense, A_2B_2 includes both the above cases and also chance coincidence of shifts. The advantages of the new proposals are best seen in a relatively complicated but highly symmetrical case such as anthracene, $C_{14}H_{10}$. This proton-spin system

TABLE I

Spin system R & S	H	Parameters	Maximum No. of lines	Largest sub-matrix	Lines given explicitly
Two spins					
	AB	$2\,(J_{AB}, \Delta\nu_{AB})$	$(2)(2)+0=4$	2×2	All
	AX	$2\,(J_{AX}, \Delta\nu_{AX})$	$(2)(2)+0=4$	1×1	All
Three spins					
	ABC	$5\,(J_{AB}, J_{AC}, J_{BC}, \Delta\nu_{AB}, \Delta\nu_{BC})$	$(4)(4)(4)+3=15$	3×3	None
	ABX	$5\,(C\rightarrow X)$	$(4)(4)(4)+2=14$	2×2	All
	AMX	$5\,(B\rightarrow M, C\rightarrow X)$	$(4)(4)(4)+0=12$	1×1	All
ABB′	AB_2	$4\,(J_{AB}, J_{AB'}, J_{BB'}, \Delta\nu_{AB})$	$(4)(8)+3=15$	3×3	None
AXX′	AX_2	$4\,(B\rightarrow X)$	$(3)(8)+2=13$	2×2	All
AB_2	$[AB_2]$	$2\,(J_{AB}, \Delta\nu_{AB})$	$(4)(4)+1=9$	2×2	All
AX_2	$[AX_2]$	$2\,(J_{AX}, \Delta\nu_{AX})$	$(3)(2)+0=5$	1×1	All
Four spins					
	ABCD	$9\,(J_{AB}, J_{AC}, J_{AD}, J_{BC}, J_{BD}, J_{CD}, \Delta\nu_{AB}, \Delta\nu_{BC}, \Delta\nu_{CD})$	$(8)(8)(8)(8)+24=56$	6×6	None
	ABCX	$9\,(D\rightarrow X)$	$(8)(8)(8)(8)+18=50$	3×3	Two
	ABXY	$9\,(C\rightarrow X, D\rightarrow Y)$	$(8)(8)(8)(8)+16=48$	4×4	16
	ABMX	$9\,(C\rightarrow M, D\rightarrow X)$	$(8)(8)(8)(8)+8=40$	2×2	All
	AMPX	$9\,(B\rightarrow M, C\rightarrow P, D\rightarrow X)$	$(8)(8)(8)(8)+0=32$	1×1	All
ABC_2	$[ABC_2]$	$5\,(J_{AB}, J_{AC}, J_{BC}, \Delta\nu_{AB}, \Delta\nu_{BC})$	$(8)(8)(8)+10=34$	4×4	Four
ABX_2	$[ABX_2]$	$5\,(C\rightarrow X)$	$(6)(6)(6)+4=22$	2×2	All
AB_2X	$[AB_2X]$	$5\,(C\rightarrow X)$	$(8)(8)(8)+6=30$	2×2	All
AMX_2	$[AMX_2]$	$5\,(B\rightarrow M, C\rightarrow X)$	$(6)(6)(4)+0=16$	1×1	All
AB_3	$[AB_3]$	$2\,(J_{AB}, \Delta\nu_{AB})$	$(6)(8)+2=16$	2×2	All
AX_3	$[AX_3]$	$2\,(J_{AX}, \Delta\nu_{AX})$	$(4)(2)+0=6$	1×1	All
AA′BB′	$[AB]_2$	$5\,(J_{AA'}, J_{AB}, J_{AB'}, J_{BB'}, \Delta\nu_{AB})$	$(12)(12)=24$	4×4	Half, (6)(6)
AA′XX′	$[AX]_2$	$5\,(B\rightarrow X)$	$(10)(10)=20$	2×2	All
A_2B_2	$[A_2B_2]$	$2\,(J_{AB}, \Delta\nu_{AB})$	$(7)(7)+4=18$	3×3	Six
A_2X_2	$[A_2X_2]$	$2\,(J_{AX}, \Delta\nu_{AX})$	$(3)(3)+0=6$	1×1	All

Main analytical features of some of the simpler spin systems

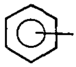
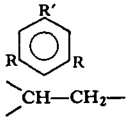
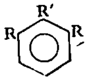
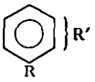
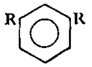
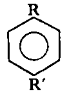
Recognition and analysis		Examples and occurrence
(†) [1*, 7, 14*, 15*]. Symmetrical quartet		Common
First order		HF
Usually recognizable by relatively small number of lines. Many special methods (see text). [1, 15*]		Very common, e.g., $CH_2{=}CHR$,  R, R′, R″
[1, 7, 15*]. Relative signs of J_{AX}, J_{BX} but not J_{AB}		
First order		
As ABC. [15*, 42*]		Rare; only by chance coincidence of shifts
(†) [1*, 7*, 14*, 15*]. Line at ν_A		 
First order		
[1]; *J. chem. Phys.*, 1962, 27, 2603		 
[1, 1a, 65*]. abc sub-spectra. ν_X average of two strong lines		$CH_2{=}CHF$
[1a]. If $J_{XY} = 0$, system simplifies (to ABMX)		
[1a]		
First order		
[1a]; *J. Mol. Spectroscopy*, 1963, 10, 250		
[1]		
[1a]; *J. Chem. Phys.*, 1961, 34, 1846; 1966, 44, 4305. Two [ab₂] sub-spectra		$RHC{=}CH{-}CH_2\left\{\begin{matrix}R\\R'\end{matrix}\right.$
First order		
(†) [1*, 15*, 19]. ab and [ab₂] sub-spectra		$\left.\begin{matrix}CH_3SH\\RPF_3\end{matrix}\right\}CH_3CHR\left\{\begin{matrix}R\\R'\end{matrix}\right.$
First order		
[1, 65, 66*, 67*]; *Canad. J. Chem.*, 1966, 44, 1211. Useful sub-spectra. Cannot differentiate $J_{AA'}$ from $J_{BB'}$, or J_{AB} from $J_{AB'}$	Completely symmetrical about centre	  $R = \left\}\begin{matrix}NH\\O\\S\end{matrix}\right.$
[1, 7, 66*]. Two strong lines spaced by $\lvert J_{AX}+J_{AX'}\rvert$. No relative signs $J_{AA'}$, $J_{XX'}$. Cannot differentiate $J_{AA'}$, $J_{XX'}$ or J_{AX}, $J_{AX'}$		$RCH_2{-}CH_2R'$
(†) [1*, 14*, 15*]		SF_4, CH_2F_2 } exact cases are rare
First order		

TABLE I—*Continued*

Spin system R & S	Spin system H	Parameters	Maximum No. of lines	Largest sub-matrix	Lines given explicitly
Higher spins					
(Brief selection only)					
ABCDE		14 ($J_{AB}, J_{AC}, J_{AD}, J_{AE}, J_{BC}, J_{BD}, J_{BE}, J_{CD}, J_{CE}, J_{DE}, \Delta\nu_{AB}, \Delta\nu_{BC}, \Delta\nu_{CD}, \Delta\nu_{DE}$)	(16)(16)(16)(16)(16) +130=210	10 × 10	None
AA′BB′C	[[AB]$_2$C]	8 ($J_{AA'}, J_{AB}, J_{AB'}, J_{AC}, J_{BB'}, J_{BC}, \Delta\nu_{AB}, \Delta\nu_{BC}$)	(24)(24)(16)+46=110	6 × 6	None
AA′BB′X	[[AB]$_2$X]	8 (C → X)	(24)(24)(15)+32=95	4 × 4	(12)(12)(11) +10=45
ABB′XX′	[[BX]$_2$A]	8 (C → A, A → X)	(20)(24)(24)+20=88	3 × 3	(8)(8)(4) +2=22
$A_2A_2'X$	A_4X or [AA′]$_2$X	6 ($J_{AA}, J_{AA'}, J_{A'A'}, J_{AX}, J_{A'X}, \Delta\nu_{AX}$)	(56)(35)=91	4 × 4	(24)(19)
ABX_3	[ABX_3]	5 ($J_{AB}, J_{AX}, J_{BX}, \Delta\nu_{AB}, \Delta\nu_{BX}$)	(8)(8)(8)+6=30	2 × 2	All
A_2B_3	[A_2B_3]	2 ($J_{AB}, \Delta\nu_{AB}$)	(12)(13)+9=34	3 × 3	25
AB_4	[AB_4]	2 ($J_{AB}, \Delta\nu_{AB}$)	(9)(12)+4=25	Effectively, 2 × 2	All
AB_6	[AB_6]	2 ($J_{AB}, \Delta\nu_{AB}$)	(16)(24)+9=49	2 × 2	All
$X_nAA'X_n'$	[X_nA]$_2$	5 ($J_{AA'}, J_{AX}, J_{AX'}, J_{XX'}, \Delta\nu_{AX}$)	. .	. .	. .
ABCDEFGH		34 J's and 7 $\Delta\nu$'s	(1024)+10,416=11,440	. .	None

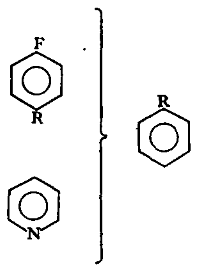
NOTES ON TABLE I

Spin system: R & S = notation of Richards and Schaefer. H = notation of Haigh (see text).

Parameters: Listed as J and $\Delta\nu$ parameters which affect the spectrum.

Maximum No. of lines: i.e., in a fully resolved spectrum. Transitions which are necessarily coincident are not counted separately, but listed as one line. Usually, relatively few only of the combination lines are seen. Brackets, where applicable, indicate the formal assignment of "fundamental" lines in accordance with extrapolated high-field behaviour. They refer to each chemical shift in alphabetical sequence, and represent spin multiplets in weakly coupled spectra only.

Largest sub-matrix: of the spin-coupling Hamiltonian. This is for a representation which gives maximum factorization.

Recognition and analysis	Examples and occurrence
Difficult; *Proc. Ind. Acad. Sci.*, 1965, **61A**, 80	
[1a]; *Proc. Ind. Acad. Sci.*, 1962, **56A**, 86; *J. Chem. Phys.*, 1961, **34**, 1460	
[1, 1a, 18]; *Acta Chem. Scand.*, 1964, **18**, 1767: Two $[ab]_2$ sub-spectra. Strong line (2 transitions) at ν_X	
Canad. J. Chem., 1966, **44**, 1725 (AB_2X_2); 1965, **43**, 81; 1957, **35**, 1487; *Spectrochim. Acta*, 1966, **22**, 1964. $[ab_2]$ and abc sub-spectra. Strong line at ν_X	
Canad. J. Chem., 1963, **41**, 2774 (assumes $J_{AA} = J_{A'A'}$)	Cyclopropylamine at critical concentration
[1a, 65]. *J. Chem. Phys.*, 1960, **33**, 1794.* Strong X doublet of separation $\lvert J_{AX}+J_{BX}\rvert$. No relative sign J_{AB}	$RCH{=}CH{-}CH_3$
(†). [1*, 14, 15*]. For $(CH_3CH_2)_nX$ see *J. Chem. Phys.*, 1964, **34**, 1049	RCH_2CH_3
(†) [1*, 15*]. Line at ν_A. $[ab]_2$ sub-spectra	SF_5Cl
(†) [1a]: (cf. n-propyl; *J. Chem. Phys.*, 1961, **34**, 1094)	$RCH(CH_3)_2$
[1a, 33–36]; X region dominated by doublet of separation $\lvert J_{AX}+J_{AX'}\rvert$	See text
Give up!	

Lines given explicitly: i.e., in terms of the parameters by simple closed algebraic expressions. Neither of the connected spin states involves a sub-matrix of order greater than 2.

Recognition and analysis: (†) denotes spectra whose appearance is determined by a single $J/\Delta\nu$ ratio (see text p. 127). First-order spectra are symmetrical multiplets, predictable from a branching diagram (see text). References are given to sources of other references where convenient, rather than to original papers. Those which include illustrative series of calculated spectra are denoted (*). A useful compilation of references, slightly more recent than that of Emsley *et al.*[1] is given by Suhr.[65]

Examples and occurrence: R and R′ (≠R) are substituents that do not contribute to the spin system.

would be BB′AA′CC′A″A‴B″B‴ according to Richards and Schaefer, and $[[AB]_2C]_2$ according to Haigh. The latter notation implies specifically that there are 15 distinct coupling constants, comprising three J_{AA}'s, three J_{BB}'s, one J_{CC}, four J_{AB}'s, two J_{AC}'s and two J_{BC}'s. Further labelling is necessary if it is required to differentiate between the individual J_{AA}'s etc., and must be related to a labelled diagram (the notation of Richards and Schaefer has a minor advantage here in that the additional labelling is already provided by the use of primes). Both notations are indicated in Table I, and that of Haigh is used in the text unless there is obvious reference to the contrary.

IV. PRELIMINARY STUDY OF A COMPLEX SPECTRUM: CONSIDERATION OF FIRST-ORDER INTERACTIONS

Clearly, there is no point in carrying out a detailed mathematical analysis of a difficult n.m.r. spectrum if the information one wants can be extracted reliably without it. This Section is an attempt to show how one may often obtain useful information by inspection or with a few simple additional experiments.

A spectrum may, of course, be complex for one or two reasons; either the whole pattern (or most of it) is due to a single molecular species, or there are several components each contributing a relatively simple part of the spectrum. Deciding between these (and assigning groups of lines generally) is less of a problem than in some other forms of spectroscopy because of the useful "counting property" of n.m.r. spectra run at sufficiently low r.f. power level, i.e., in absence of differential saturation effects. The total intensity of an n.m.r. signal is then directly proportional to the number of nuclei causing it. This applies equally to separate molecular species and to individual multiplets within the spectrum of a single species. In the latter case, deviations may occur if the system is rather strongly coupled, but are insignificant if the multiplets are not too far from the first-order condition.[9] In many cases it will be known before running the spectrum whether one has essentially a mixture or a pure compound. If the compound is known to be reasonably pure it can be assumed, in view of the counting property, that all high and moderate intensity lines belong to that compound. This is not the case with very weak lines, and it may be quite difficult to decide without a complete analysis if these are due to traces of impurity or are so-called "combination" lines in the spectrum of the major component. However, it has been pointed out that the relative ease of saturation forms a basis for differentiation. Lines observed from traces of an impurity are its most strongly allowed transitions, and are therefore more easily saturated on increasing the r.f. power than are weakly allowed transitions of a more abundant compound.[10] Weak "spinning side bands" or satellite spectra (e.g., of protons directly bonded to ^{13}C in 1% natural abundance) are another possible source of confusion, but they always occur symmetrically to either side of a strong spectral line, often that of the solvent. Spinning side bands can always be recognized by their displacement on changing the spinning frequency of the sample tube.

A completely first-order spectrum is by far the easiest to interpret, since most information can be extracted by cursory examination and measurement. The first-order condition is that in which all groups of completely equivalent nuclei in the system are separated by a chemical shift that is large compared to the coupling constant between them. Most spin systems tend to a first-order condition if the external field, H_0, is progressively increased—the exceptions being those involving chemical-shift equivalence without spin-coupling equivalence (see previous Section). Hence there is usually a distinct advantage in using as high a field as possible in order to pull the spectrum out towards the first-order condition. A first-order spectrum consists of several completely symmetrical multiplet patterns (some of which may be a single line) centred upon each chemical shift—and is among the most striking to be found anywhere in spectroscopy. The theoretical basis for this simplicity is outlined in the next Section; for practical purposes the appearance of each multiplet—number of lines, spacing and relative intensities—can always be explained simply by a "branching diagram" tracing the origin of the splittings (Fig. 1). One starts with a single line at each chemical shift (the so-called "zero order" spectrum), the relative intensities of the lines being given by the counting property. The coupling interactions are now introduced one at a time by successive line splitting equal in magnitude to the coupling constant. Consider the case of nuclei of spin $\frac{1}{2}$. The original line at any particular shift is first split into a doublet (the intensity is shared equally) by the first nucleus to be coupled to it, then each component into a further doublet by the second coupled nucleus, and so on. For example, an AX spectrum will have A and X doublets; and an AMX spectrum will have three quartets, all lines being of equal intensity (Fig. 1a). If some chemical shifts are shared by more than one equivalent nucleus per molecule, then the splitting rules predict a re-coalescence of lines towards the centre of each multiplet, with adding of intensities (Fig. 1b). Some of the most distinctive patterns (regularly spaced 1:2:1 triplets, 1:3:3:1 quartets, 1:4:6:4:1 quintets, 1:5:10:10:5:1 sextets etc.) are produced in this way, and are easily interpreted as coupling to one other group of n equivalent nuclei. The number of components $(n+1)$ in the multiplet is determined by the number of nuclei causing the splitting (n), and is not affected by the number of nuclei in the group whose resonance is being considered. This is because coupling within a group of completely equivalent nuclei has no effect on any n.m.r. spectrum, whether first order or not (see next Section). For example, P–F coupling in PF_3 causes a ^{31}P 1:3:3:1 quartet and a ^{19}F doublet, but J_{FF} has no effect on the spectrum. First-order interactions with nuclei of spin $>\frac{1}{2}$ can also be predicted with a branching diagram, remembering that each coupling causes in general a splitting into $(2I+1)$ components of equal intensity. For example, the ^{19}F spectrum of NF_3 is a 1:1:1 triplet due to coupling to ^{14}N, which has $I=1$. This pattern differs from the 1:2:1 triplet, which would be caused by coupling to two equivalent spin ½ nuclei, (e.g., a CH_2 group) since the F nuclei "see" the three orientations of the ^{14}N nucleus (next Section) with equal probability. In terms of the composite-particle approach described later, the 1:1:1 triplet may be regarded as part of the 1:2:1 triplet, lacking one central component since the component spins within the ^{14}N nucleus cannot be antiparallel. It has been noted above that coupling to nuclei of spin >½ is observed only in favourable cases.

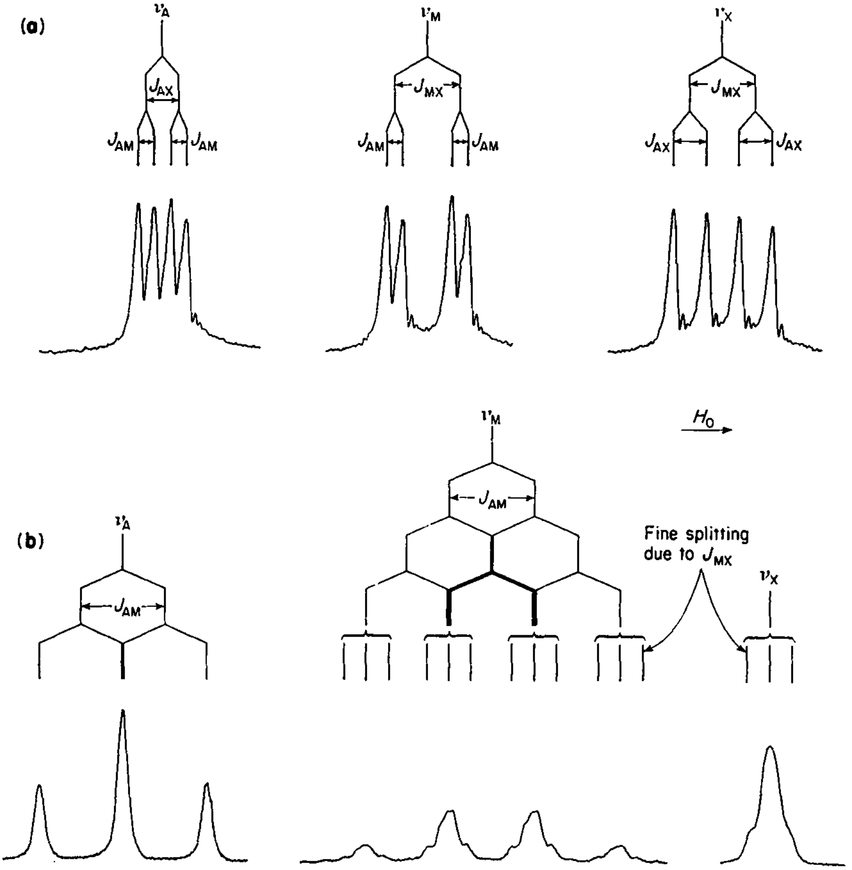


FIG. 1. First-order splitting diagrams. (a) 100 Mc./sec. ring proton spectrum of 2-furoic acid in acetone. Close to AMX. "Ringing" has been partially suppressed for clarity. (b) 94·1 Mc./sec. fluorine spectrum of perfluorobutyric acid $CF_3CF_2CF_2COOH$.† $A_3M_2X_2$ case ($A = \gamma$, $M = \alpha$, $X = \beta$). Splitting diagram shown for the largest coupling, J_{AM}, only (N.B. this is between nuclei in the α and γ positions). Each component of the B quartet is further split by J_{MX} into a poorly resolved triplet. J_{AX} is undetectable.

† I am indebted to Dr. J. D. Smith (University of Sussex) for this sample.

Starting from an experimental first-order spectrum, it is easy to reverse the above procedure to find the parameters, with the important restriction that the relative signs of the coupling constants remain indeterminate. Also, if two inter-group couplings were very similar, it might not be possible to tell by inspection which groups were coupled to which. Both questions can be answered by double-resonance experiments, in which two r.f. frequencies are applied simultaneously. The "irradiating" field (H_2) is held constant at a pre-selected point in the spectrum whilst the other (H_1) is used to record the rest of the spectrum; for practical considerations it is easier to scan by frequency sweep of the H_1 field, rather than by changing the main H_0 field as in a single-resonance experiment. Another application is illustrated below. Coupling ambiguity is resolved by H_2 irradiation at the centre of one of the multiplets in question, of sufficient intensity to completely decouple the nuclei concerned from the rest of the spin system. This causes a collapse (coalescence), in other parts of the spectrum, of line splittings which were due to coupling to the irradiated group. Relative signs of J's in a first-order spectrum with three or more chemical shifts, can be found by selective partial decoupling experiments. Weak irradiation between two components of a multiplet then collapses some, but not all, of the line splittings associated with the same coupling in other parts of the spectrum. The lines collapsed are those sharing an energy level in common with the pair being irradiated. Deduction of relative signs in the AMX case is given in detail by Emsley *et al.*,[1] p. 466 and by Hoffman and Forsén,[6] p. 143. In a single resonance experiment with H_1 power much increased to saturate the normal spectrum, it is replaced by a new set of sharp "multiple-quantum" transitions which can also give relative sign information.[1]

Interactions which depart somewhat from the first-order condition are found more often than those that are rigorously first order. This applies particularly to proton n.m.r., where the usual range of chemical shifts is relatively small—although much extended by the "contact-shift" mechanism in the case of ligands attached to a paramagnetic transition metal atom. However, a first-order interpretation of a weak coupling interaction, not too far from the first-order condition, will often yield sufficiently accurate parameters. Slight departures from first order are in fact quite useful in deciding which groups are coupled to which if this is not seen unambiguously from the property of repeated spacings. This is because such an interaction causes a distortion of the first-order intensity pattern within a multiplet, so that the components closest to the group causing the splitting, gain in intensity at the expense of those furthest away. This slanting appearance is generally a more sensitive indication of departure from first-order behaviour (being easily detectable at $J:\Delta\nu\approx 1:20$; Bible,[11] p. 77) than the resolution of second-order splitting, development of combination lines or distortion of line spacings. If three or more chemical shifts are involved, finer details of the intensity distribution are affected also by the relative signs of the coupling constants to an extent that increases progressively with the coupling strength.

The slanting appearance is apparent in the X quartet of Fig. 1(a) and in Fig. 2. In the latter, for example, the doublets centred at 3·30τ and 3·84τ are clearly coupled to each other, making up an AB quartet. The doublet at 5·18τ is an apparent exception which provides a note of caution (see below). If in doubt, coupling information in a weakly coupled system can always be confirmed by a spin-decoupling experiment as for first-order spectra.

It is readily seen from Table I that the complexity of a n.m.r. spectrum increases very rapidly with increasing number of spin-coupled nuclei (unless the whole forms a group of high local symmetry). One often obtains, therefore, n.m.r. spectra that are so complicated (generally through incomplete resolution of closely packed lines) as to make a complete formal analysis quite impracticable. In fact, in any complicated n.m.r. spectrum it is quite pointless to attempt a full analysis if the required information can be found reliably by simpler means. Often, an approximate first-order interpretation of selected features of the spectrum will yield valuable information very easily, and this can be extended and made more reliable by a few double-resonance experiments under spin-decoupling conditions. This is illustrated by the 100 Mc./sec. p.m.r. spectrum of santonin in Fig. 2.† The same remarks apply to any complicated organic molecule, e.g., a steroid. Most aliphatic protons attached to skeletal carbon atoms have similar chemical shifts and form a strongly coupled group of lines at 7·4–9·0τ, for the most part incompletely resolved. In the present state of the art, it is a waste of time trying to analyse this part of the spectrum, at least in the more complex case of a steroid, although it is of use in "fingerprinting" compounds. Features that stand out clearly are either due to simpler spin systems that are isolated (in a spin-coupling sense) within the molecule and can be analysed separately, or else they "belong" to the main spin system of the aliphatic skeletal protons but are so displaced as to have approximately first-order interactions with it. The AB pattern of the olefinic protons at 3–4τ is of the former type; also the angular methyl peaks (A_3 single-line spectra). The doublet centred at 5·18τ illustrates the latter, being a single proton A (seen from the integral trace) coupled to another proton X within the range 7·4–9·0τ. The coupling J_{AX} can be found to a good approximation on a first-order basis, even though X is presumably coupled to other nuclei also. Further, the hidden chemical shift ν_X can be found by spin decoupling (Fig. 2, insets). A very rough indication is first obtained by siting the H_2 field at 5·18τ and observing which region of the 7·4–9·0τ complex is most affected. The H_2 field is then re-sited in the region indicated, and its position and amplitude adjusted to obtain optimum collapse of the 5·18τ doublet. This position (8·20τ) is the best estimate of ν_X. The slightly greater height of the low-field component of the doublet appears to be a real effect, and as such is rather unexpected. However, this does not reflect a difference in intensity, as the higher-

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† I am indebted to Dr J. R. Hanson (University of Sussex) for this sample, and for discussion.

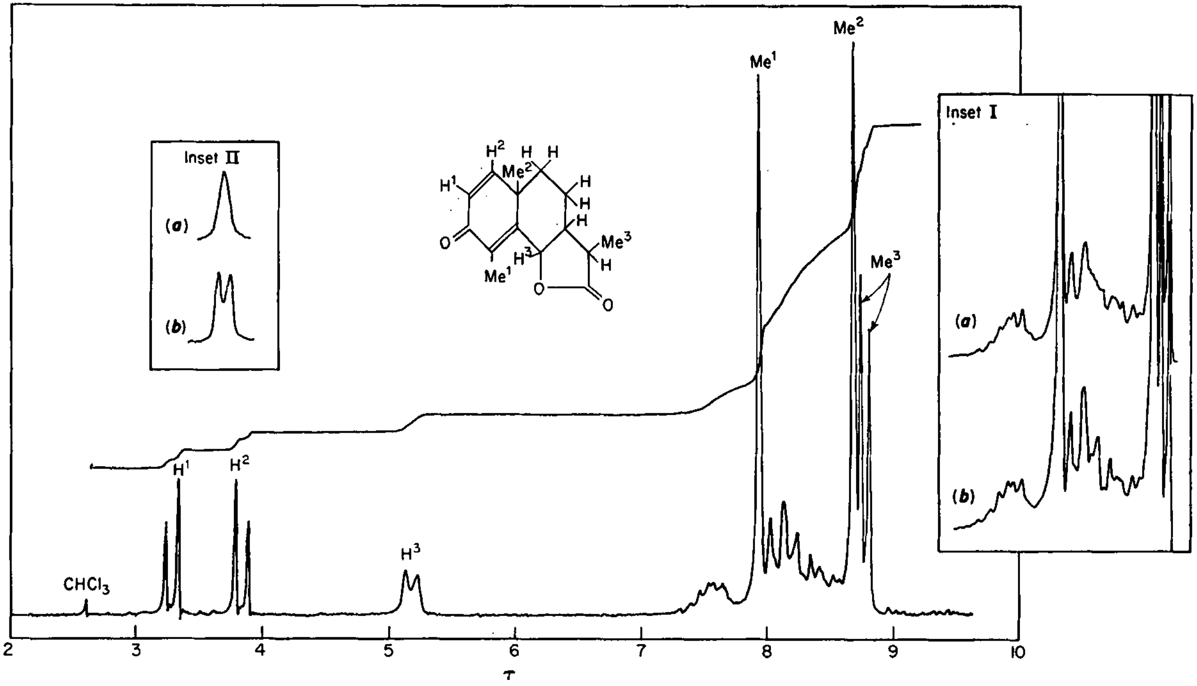

FIG. 2. Proton resonance spectrum of Santonin in $CDCl_3$, at 100 Mc./sec. with integral trace. Inset I, high-field proton region (*a*) with, (*b*) without irradiation at 5·18τ. Inset II, 5·18τ doublet (*a*) with, (*b*) without, irradiation at 8·20τ.

field component is slightly broader. This is probably due to slight virtual coupling (see later) to other ring protons adjacent to X; there is also a small (real) coupling between A and the methyl group at 7·94τ which can be detected at 60 Mc./sec. by the doublet fine structure of the latter.

V. THEORY OF SPECTRA: THE EIGENSTATE PROBLEM

This Section is concerned mainly with the converse of the analytical approach; given a set of chemical shift (ν_i) and coupling (J_{ij}) parameters, how do these decide the appearance of the spectrum? This is, of course, highly relevant to analysis since it determines the parameters that can be found from a spectrum and the best method to be used. As in other forms of spectroscopy, the problem is that of solving the time-independent Schrödinger equation $\mathscr{H}\psi = E\psi$ to find the allowed energies (E) and eigenfunctions (ψ) that constitute eigenstates of the quantum mechanical Hamiltonian operator. The spectrum then follows: a transition between states m and n gives rise to a spectral line whose position and intensity are determined respectively by the energy gap ($h\nu = \Delta E = |E_n - E_m|$) and the wave functions ψ_m, ψ_n.

The effective Hamiltonian for a nuclear spin system under "high-resolution" conditions, expressed in terms of ν_i and J_{ij}, is simply as follows—

$$\mathscr{H} = \underbrace{\sum_i \nu_i \mathscr{I}_{z(i)}}_{(\mathscr{H}^\circ)} + \underbrace{\sum_{i<j}\sum J_{ij}\mathscr{I}_i . \mathscr{I}_j}_{(\mathscr{H}')} \qquad (1)$$

$\mathscr{H}^\circ$ is termed the "external-field" part of the Hamiltonian, since it refers to interaction with H_0, and $\mathscr{H}'$ refers to the spin-coupling effect. The form of the operator, and the solution of the wave equation, are now discussed with special reference to spin $\frac{1}{2}$ nuclei.

A. The single nucleus: spin angular momentum

Consider first the simplest possible case of a single nucleus, where there is no spin coupling part to the Hamiltonian. The key to understanding n.m.r. spectra is the spin quantum number (I), often just called the "spin", of the nuclear species involved. This number, which may be a half integer or integer, is characteristic of an isotope rather than of an element, and depends on the internal structure of the nucleus. (An excited nuclear state may have a different spin from the normal ground state; however; in n.m.r. one is concerned only with the latter.†) Basically, the spin quantum number defines the length of the angular momentum vector $\bar{I}$ associated with the spinning nucleus, by the equation $\bar{I} = \sqrt{I(I+1)}$ units of $h/2\pi$

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† It is relevant to inorganic chemists that the ground and excited Mössbauer states of the ^{57}Fe nucleus have spin of $\frac{1}{2}$ and $\frac{3}{2}$, respectively.

(a.m. units). In the n.m.r. experiment, the nuclei are subjected to a strong magnetic field (H_0), which constitutes a well defined axis, conventionally the z axis with the lines of force taken to be in the negative z direction. According to the quantum mechanical theory of spin, the scalar projection of $\bar{I}$ upon the z axis (I_z) then has only certain well defined values, but there must be uncertainty in the components of $\bar{I}$ measured along any other axis, e.g., I_x, I_y in a Cartesian co-ordinate system. Classically, this corresponds to precession of the $\bar{I}$ vector about the z axis. The quantum mechanically "allowed" values of I_z are $I, I-1, I-2 \ldots -I+1, -I$ a.m. units; a total of $(2I+1)$ projections.† For example, if $I=\frac{1}{2}$, the two allowed projections are $+\frac{1}{2}$ and $-\frac{1}{2}$ a.m. units. In the quantum theory, observed values of any physical quantity should be regarded as eigenvalues (λ) obtained by solving the wave equation $\mathscr{O}_\psi=\lambda_\psi$ for the corresponding operator $\mathscr{O}$. Here, I_z are the eigenvalues of the operator $\mathscr{I}_z$.‡ The wave functions corresponding to these are represented conveniently by the symbols α and β, i.e., the solutions are $\mathscr{I}_z\alpha=+\frac{1}{2}\alpha$ and $\mathscr{I}_z\beta=-\frac{1}{2}\beta$. The analogous operators $\mathscr{I}_x$ and $\mathscr{I}_y$, however, cannot leave the functions α or β unchanged, since there are no solutions to the equations $\mathscr{I}_x\psi=\lambda_\psi$ or $\mathscr{I}_y\psi=\lambda_\psi$ when there is quantization along the z axis. Instead, by analogy to the Pauli treatment of electron spin, one may write $\mathscr{I}_x\alpha=\frac{1}{2}\beta$; $\mathscr{I}_x\beta=\frac{1}{2}\alpha$; $\mathscr{I}_y\alpha=\frac{1}{2}i\beta$, and $\mathscr{I}_y\beta=-\frac{1}{2}i\alpha$. Since I_x, I_y and I_z cannot be simultaneously measured, one cannot uniquely define the spatial direction of the spin vector $\bar{I}$ at any instant. However, the square of $\bar{I}$, as defined by $\bar{I}^2=\bar{I}.I=I_x^2+I_y^2+I_z^2$, is a scalar quantity, completely specified by its magnitude $I(I+1)$. In the case of a single nucleus, therefore, the corresponding operator $\mathscr{I}^2$ has simultaneous eigenstates with $\mathscr{I}_z$. For the spin $\frac{1}{2}$ case, $\mathscr{I}^2\alpha=\mathscr{I}_x^2\alpha+\mathscr{I}_y^2\alpha+\mathscr{I}_z^2\alpha=(\frac{1}{4}+\frac{1}{4}+\frac{1}{4})\alpha=\frac{3}{4}\alpha$; similarly $\mathscr{I}^2\beta=\frac{3}{4}\beta$.

A second consequence of nuclear spin is the presence of a magnetic dipole moment in the same direction as the "axis of spin" (this is the classical picture; more exactly, the directions of the spin angular momentum and magnetic moment vectors coincide). Each of the $(2I+1)$ projections of angular momentum upon the z axis therefore has a different orientation of the nuclear magnetic moment relative to H_0, and hence a different energy of interaction with it. This simultaneous quantization of I_z and energy (E) produces $(2I+1)$ discrete energy levels, which are equally spaced (Fig. 3). The simplest way of denoting the energies is in terms of the chemical shift ν, e.g., $+\frac{1}{2}\nu$ and $-\frac{1}{2}\nu$ in the case $I=\frac{1}{2}$. These are accordingly the eigenvalues of $\mathscr{H}$. Thus $\mathscr{H}$ and $\mathscr{I}_z$ have simultaneous

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† Note that the largest projection I is smaller than the total vector length $\sqrt{I(I+1)}$—i.e., the latter is not allowed to be oriented directly along the z axis, since this would correspond to simultaneous knowledge of I_x, I_y (both zero) and I_z.

‡ Spin operators are denoted here by script $\mathscr{I}$, and their eigenvalues by the capital I, with the same subscripts, superscripts etc. Vector operators and observables have a bar above. I, by itself, denotes the nuclear spin quantum number.

eigenstates, and α and β are eigenfunctions of both.† The Hamiltonian can be written as $\mathscr{H} = \nu\mathscr{I}_z$, being the simplest case of equation (1), and the solutions to the Schrödinger equation are $\mathscr{H}\alpha = +\frac{1}{2}\nu\alpha$ and $\mathscr{H}\beta = -\frac{1}{2}\nu\beta$. Both $\mathscr{H}$ and $\mathscr{I}_z$ correspond to real, physical observables (they are "Hermetian"), and this requires that eigenfunctions associated with different eigenvalues must be mutually exclusive or "orthogonal", i.e., $\int \alpha\beta \, d\tau = 0$, the integral being taken without limits (i.e., over all "spin space"). In the convenient notation adapted from Dirac, this becomes $\langle\alpha|\beta\rangle = 0$. It is also convenient to consider α and β as "normalized" functions, i.e., $\langle\alpha|\alpha\rangle = \langle\beta|\beta\rangle =$ unity.

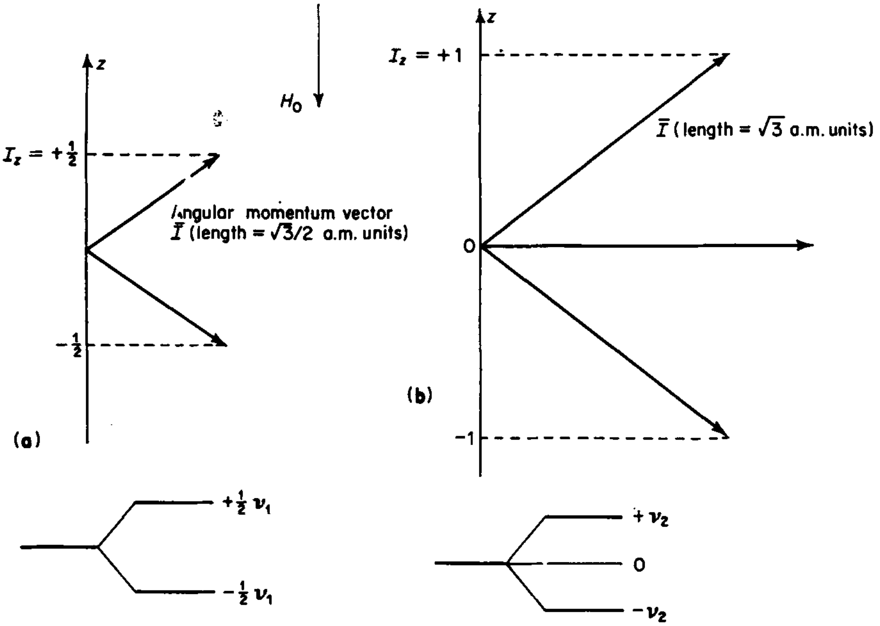

FIG. 3. Quantization of angular momentum along z axis defined by H_0; energy-level splitting ($\propto H_0$). Nucleus with: (*a*), $I = \frac{1}{2}$; (*b*), $I = 1$.

B. Multi-spin systems

Multi-spin systems are those where the molecule contains more than one "magnetically active" nucleus. If there is no interaction between the nuclei, the eigenstate problem is no more difficult than that for a single nucleus. The total energy of the system is the sum of that for each nucleus separately, the external field Hamiltonian being a summation of single-nucleus operator terms, $\mathscr{H}^0 = \sum_i \nu_i \mathscr{I}_{z(i)}$ (see equation 1). Similarly, the total angular momentum projec-

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† Any pair of operators (P,Q) which have a complete set of simultaneous eigenstates are said to "commute," and must obey the relationship $P(Q\psi) = Q(P\psi)$ for any function ψ. Here, $\mathscr{I}_z$ commutes with $\mathscr{H}$. From the previous paragraph, the total spin operator $\overline{\mathscr{I}}$ for a single nucleus does not commute with $\mathscr{I}_z$ or $\mathscr{H}$, but $\overline{\mathscr{I}}^2$ commutes with both.

tion upon the z axis, often denoted F_z, is given by $\sum_i I_{z(i)}$. These can be considered as eigenfunctions of the operator $\mathscr{F}_z$. This and $\mathscr{H}$ have simultaneous eigenfunctions, which are simple products of those for the separate nuclei. For n nuclei of spin $\frac{1}{2}$, there are 2^n eigenstates. If $n=2$, the four product functions are $\alpha_1\alpha_2$, $\alpha_1\beta_2$, $\beta_1\alpha_2$ and $\beta_1\beta_2$, the subscripts being usually omitted. These are orthogonal and normalized (orthonormal) as in the single nucleus case. The energies are $\frac{1}{2}(\nu_1+\nu_2)$, $\frac{1}{2}(\nu_1-\nu_2)$, $\frac{1}{2}(-\nu_1+\nu_2)$ and $\frac{1}{2}(-\nu_1-\nu_2)$, and the F_z values are $+1$, 0, 0 and -1, respectively.

In general, however, there is finite spin coupling to be considered. It is found that, in order to explain the appearance of n.m.r. spectra, the interaction between two spin coupled nuclei i, j must be proportional to the scalar (dot) product of their angular momentum vectors, $\bar{I}_i.\bar{I}_j = I_{x(i)}I_{x(j)} + I_{y(i)}I_{y(j)} + I_{z(i)}I_{z(j)}$. This corresponds to inclusion in the quantum-mechanical Hamiltonian of an operator term $J_{ij}\mathscr{I}_i\cdot\mathscr{I}_j$. If there are more than two nuclei, the interactions are summed over each pair, giving $\mathscr{H}' = \sum_{i<j}\sum J_{ij}\mathscr{I}_i\cdot\mathscr{I}_j$. The coupling constants J_{ij} are introduced as constants of proportionality. The eigenstate problem is now to find acceptable solutions to the wave equation $\mathscr{H}\Psi = E\Psi$, where $\mathscr{H}$ is the total Hamiltonian $\mathscr{H}^\circ + \mathscr{H}'$. One first devises a general wave function sufficiently flexible (through variable coefficients) to represent all possible eigenfunctions Ψ, and then finds values of the coefficients that will satisfy the wave equation. Fortunately, with the simple form of the phenomenological Hamiltonian it is easy to devise general functions which can accommodate all *exact* solutions. The simplest representation is the expansion $\Psi = c_1\psi_1 + c_2\psi_2 + \ldots c_n\psi_n = \sum_n c_n\psi_n$ where $\psi_1\ldots\psi_n$ are the simple product functions (which constitute a complete orthonormal set), and $c_1\ldots c_n$ are the mixing coefficients. There are two advantages in using these product functions as the basis of the representation: (1), they are already eigenfunctions of $\mathscr{H}^\circ$; (2), they are also eigenfunctions of $\mathscr{F}_z$, which commutes with the total Hamiltonian. The eigenstate problem is then conveniently reformulated as follows. Multiplying each side of the wave equation—

$$\mathscr{H}\sum_n c_n\psi_n = E\sum_n c_n\psi_n$$

by any function ψ_m of the basis set, and integrating over spin space gives—

$$\int \psi_m\mathscr{H}\sum_n c_n\psi_n\,\mathrm{d}\tau = E\sum_n c_n\int\psi_m\psi_n\,\mathrm{d}\tau = Ec_n\delta_{mn}$$

where $\delta_{mn}=1$ if $m=n$, and $=0$ if $m\neq n$ (Kroeneker delta), since ψ_m and ψ_n are members of an orthonormal set. The left-hand side involves a series of integrals $\int\psi_m\mathscr{H}\psi_n\,\mathrm{d}\tau$, or $\langle\psi_m|\mathscr{H}|\psi_n\rangle$ in the Dirac notation. These are "elements" of the Hamiltonian, and denoted $\mathscr{H}_{mn}$. The equation becomes—

$$\sum_n c_n\mathscr{H}_{mn} = Ec_n\delta_{mn},$$

or, re-arranging—

$$\sum_n (\mathscr{H}_{mn}-\delta_{mn}E)c_n = 0$$

A secular equation of this kind can be written for each value of m between 1 and n, and the problem becomes that of solving the equations to find sets of E, c_n that satisfy them simultaneously. Values of E may be found first by solving the determinantal equation $|\mathscr{H}_{mn}-\delta_{mn}E|=0$, and then the c_n values may be found by back substitution. Alternatively, the problem can be stated in its equivalent matrix form (e.g., for computer handling). The elements $\mathscr{H}_{mn}$ form a square symmetric matrix, that can be converted to diagonal form (all off-diagonal elements $m\neq n$ reduced to zero) by a suitable (unitary) transformation $\mathscr{A}^{-1}\mathscr{H}\mathscr{A}$. Elements of the diagonalized matrix are then the allowed energies $E_1\ldots E_n$, and the columns of the transformation matrix $\mathscr{A}$ are the coefficients (c's) of the corresponding eigenfunctions.

The matrix elements $\mathscr{H}_{mn}$ must first be expressed in terms of the J and ν parameters for the problem. Each element has two possible contributions, $\langle\psi_m|\mathscr{H}^\circ|\psi_n\rangle+\langle\psi_m|\mathscr{H}'|\psi_n\rangle$. Since ψ_m, ψ_n are already eigenfunctions of $\mathscr{H}^\circ$, there are no off-diagonal contributions $\mathscr{H}^\circ_{mn}$ $(m\neq n)$, and the diagonal terms $(m=n)$ are the eigenvalues of $\mathscr{H}^\circ$ discussed earlier. To evaluate elements of the spin-coupling part $\mathscr{H}'=\sum\sum_{i<j} J_{ij}\mathscr{I}_j\cdot\mathscr{I}_i$ one uses the expanded form of the angular-momentum operator product—

$$\mathscr{I}_i\cdot\mathscr{I}_j = \mathscr{I}_{x(i)}\mathscr{I}_{x(j)}+\mathscr{I}_{y(i)}\mathscr{I}_{y(j)}+\mathscr{I}_{z(i)}\mathscr{I}_{z(j)}$$

It must be remembered that $\mathscr{I}_i$ operates *only* on nucleus i, and $\mathscr{I}_j$ on nucleus j. Some elements of $\mathscr{H}'$ for the case of two spin $\frac{1}{2}$ nuclei are now worked out. First, a diagonal element—

$$\begin{aligned}\langle\alpha_1\alpha_2|\mathscr{H}'|\alpha_1\alpha_2\rangle &= J_{12}\{\langle\alpha\alpha|\mathscr{I}_{x_1}\mathscr{I}_{x_2}+\mathscr{I}_{y_1}\mathscr{I}_{y_2}+\mathscr{I}_{z_1}\mathscr{I}_{z_2}|\alpha\alpha\rangle\}\\ &= J_{12}\{\tfrac{1}{4}\langle\alpha\alpha|\beta\beta\rangle+\tfrac{1}{4}\langle\alpha\alpha|\beta\beta\rangle+\tfrac{1}{4}\langle\alpha\alpha|\alpha\alpha\rangle\}\\ &= J_{12}(0+0+\tfrac{1}{4})\end{aligned}$$

Extending to the general case of >2 nuclei (spin $\frac{1}{2}$)—

$$\mathscr{H}'_{mn}(m=n) = \tfrac{1}{4}\sum\sum_{i<j} J_{ij}T_{ij},$$

where $T_{ij}=+1$ if spins of nuclei i, j are parallel (both α or both β) and $T_{ij}=-1$ if spins of nuclei i, j are antiparallel (one α, one β).

Now two off-diagonal elements, $(m\neq n)$—

$$\begin{aligned}\langle\alpha\alpha|\mathscr{H}'|\alpha\beta\rangle &= J_{12}\{\tfrac{1}{4}\langle\alpha\alpha|\beta\alpha\rangle+\tfrac{1}{4}\langle\alpha\alpha|\beta\alpha\rangle+\tfrac{1}{4}\langle\alpha\alpha|\alpha\beta\rangle\}\\ &= 0+0+0\end{aligned}$$

$$\begin{aligned}\langle\alpha\beta|\mathscr{H}'|\beta\alpha\rangle &= J_{12}\{\tfrac{1}{4}\langle\alpha\beta|\alpha\beta\rangle+\tfrac{1}{4}\langle\alpha\beta|\alpha\beta\rangle+\tfrac{1}{4}\langle\alpha\beta|\beta\alpha\rangle\}\\ &= J_{12}(\tfrac{1}{4}+\tfrac{1}{4}+0)\end{aligned}$$

If there are more than two nuclei of spin $\frac{1}{2}$, $\mathscr{H}'_{mn}$ $(m \neq n) = \frac{1}{2}J_{ij}U$† where $U = +1$ if the basis functions ψ_m, ψ_n differ in the spins of two nuclei i, j *only*, and $U = 0$ otherwise. The presence of a finite off-diagonal element $\mathscr{H}'_{mn}$ means that the basis functions, ψ_m and ψ_n, are not eigenfunctions of $\mathscr{H}'$ (and hence of the total $\mathscr{H}$), but are mixed together in formulating the latter. Note that $\mathscr{H}'_{mn} = \mathscr{H}'_{nm}$, i.e., the matrix is symmetrical about its principal diagonal.

The examples illustrate one of the main advantages in using basis functions that are eigenfunctions of the total $\mathscr{F}_z$ operator, $\sum_i \mathscr{I}_{z(i)}$. This commutes with the total Hamiltonian, so that the value of $\sum I_z = F_z$ is sharply defined both in the basis functions and in the eigenfunctions of $\mathscr{H}$. Hence mixing can occur only between basis functions having the same F_z value. This allows an important factorization of the secular equations, which is equivalent to breaking down the $(n \times n)$ Hamiltonian matrix into smaller, non-interacting sub-matrices that can be diagonalized separately. Thus, in the 2-spin case, the only possible off-diagonal element is that connecting $\alpha\beta$ and $\beta\alpha$ $(F_z = 0)$, and the problem is reduced from a (4×4) matrix to two (1×1) and one (2×2) interactions, with $\alpha\alpha$ and $\beta\beta$ already eigenfunctions of $\mathscr{H}$ (see Fig. 2). Similarly, in the 3-spin case the (8×8) interaction is reduced to two (1×1) and two (3×3) interactions (Fig. 4).

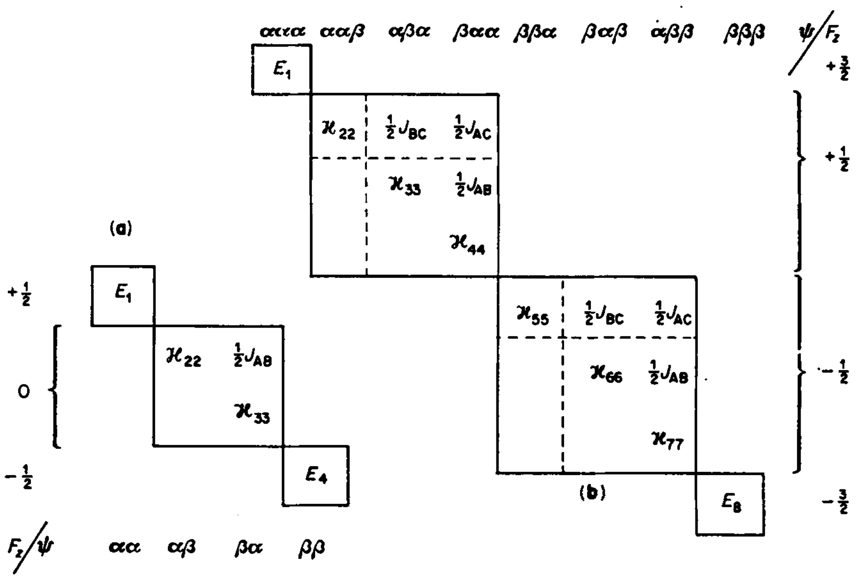

FIG. 4. Matrix representation of the nuclear spin Hamiltonian in (*a*) the two-spin case AB and (*b*) the three-spin case ABC. Further breakdown in the ABX case is indicated by dashed lines.

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† There are misprints in the rules as given by Emsley *et al.*,[1] p. 306.

The AB and ABC cases present analytical problems of a different order of magnitude, being illustrative of two general types of system in this respect. In the former, the largest sub-matrix to be diagonalized is (2 × 2); this corresponds to solution of quadratic secular equations, the roots of which can be expressed in a very simple closed algebraic form. Consequently, the energy levels and eigenfunctions, and hence the transition energies and intensities, can all be related to the J and ν parameters by simple algebraic expressions. Conversely, in this and other such cases it is usually simple to work backwards through the algebra to extract the parameters from an experimental spectrum (see later). In the ABC case, the largest sub-matrix is (3 × 3), which corresponds to cubic secular equations. It is possible to express the roots of a cubic equation in closed algebraic form, but this is much more cumbersome than for a quadratic, and the converse analysis is correspondingly difficult. This and all other interactions greater than (2 × 2) are most easily solved by successive numerical approximation or systematic matrix diagonalization with a computer. There is always great analytical advantage in choosing conditions so as to minimize the interactions which have to be considered.

C. The X approximation

The X approximation can be defined as the neglect of off-diagonal elements connecting diagonal elements of widely different numerical values, i.e., $\mathscr{H}_{mn} \ll |\mathscr{H}_{nn} - \mathscr{H}_{mm}|$. The familiar "first-order" treatment is the extreme case in which *all* the off-diagonal elements are neglected. The eigenfunctions and energies are then simply the basis functions and diagonal elements, respectively, and the presence of $\pm\frac{1}{4}J_{ij}$ terms in the latter causes the characteristic spectral property of repeated spacings equal to the coupling constants (this amounts to a first-order perturbation of the uncoupled system).

More often, *some* of the coupling interactions are weak ($J_{ij} \ll |\nu_i - \nu_j|$). The $\frac{1}{2}J_{ij}$ term may then be neglected wherever it occurs as an off-diagonal element, since the difference between the connected diagonal elements includes the quantity $|\nu_i - \nu_j|$. This produces valuable additional factorization of the secular equations. For example, in going from ABC to ABX, each (3 × 3) sub-matrix block is broken down into a (1 × 1) and a (2 × 2) interaction, so that all eigenstates can be expressed in simple algebraic form (Fig. 4).

An alternative method that has sometimes been used for systems that give nearly, but not quite, first-order spectra is to retain all the off-diagonal elements, but to treat them approximately as a small perturbation upon the first-order system. This "weak-coupling" perturbation treatment is usually taken to second order, for which the correction terms to the line positions and intensities are quite manageable. Transitions coincident in the first-order limit are generally slightly separated, this being termed "second-order splitting" (e.g., ethyl group proton spectra often approximate to A_2X_3 but with second-order splitting).

Similarly, an ABC case close to ABX could be treated as a perturbation (sometimes denoted ABK) of the latter.

D. Symmetry factorization and composite particles

A further simplification of the eigenstate problem is possible if the spin system possesses effective symmetry, which is often due to rapid internal rotation.

Many cases are discussed conveniently in terms of the total angular momentum, $\bar{I}_G$, of a group of nuclei. As for a single nucleus, more interest attaches to the square of this quantity, $\bar{I}_G^2$, defined as—

$$\bar{I}_G^2 = \bar{I}_G.\bar{I}_G = \left(\sum_i I_{x(i)}\right)^2 + \left(\sum_i I_{y(i)}\right)^2 + \left(\sum_i I_{z(i)}\right)^2$$

Stationary values of $\bar{I}_G^2$ are found as eigenvalues of the corresponding operator $\mathscr{I}_G^2$ which may be expanded in terms of $\mathscr{I}_x$, $\mathscr{I}_y$ and $\mathscr{I}_z$ as above, or more conveniently as—

$$\begin{aligned}\mathscr{I}_G^2 &= \sum_i \mathscr{I}_i^2 + 2\sum\sum_{i<j} \mathscr{I}_i.\mathscr{I}_j \\ &= \sum_i \mathscr{I}_i^2 + 2\sum\sum_{i<j} (\mathscr{I}_{x(i)}\mathscr{I}_{x(j)} + \mathscr{I}_{y(i)}\mathscr{I}_{y(j)} + \mathscr{I}_{z(i)}\mathscr{I}_{z(j)}).\end{aligned}$$

Analogously to the single-nucleus case, the allowed values of $\bar{I}_G^2$ are $I_G\,(I_G+1)$, where I_G is the total spin quantum number for the group. For n nuclei of spin $\frac{1}{2}$, I_G can have any of the values $\frac{1}{2}n$, $\frac{1}{2}n-1$, $\frac{1}{2}n-2 \ldots \frac{1}{2}$ (if n is even) or 0 (if n is odd). For example, a group of two such nuclei can have $\bar{I}_G^2=2$ or 0 corresponding to $I_G=1$ or 0; and for three nuclei $\bar{I}_G^2=\frac{15}{4}$ or $\frac{3}{4}$, corresponding to $I_G=\frac{3}{2}$ or $\frac{1}{2}$. The above applies irrespective of how the group G is composed—it might be a part or the whole of the spin system within a molecule (the latter will be denoted by subscript T instead of G). For a system of isolated nuclei as for a single nucleus, each energy state has a sharply defined $\bar{I}_T^2$. However, $\mathscr{I}_T^2$ does not in general commute with $\mathscr{H}$ if spin coupling is present, and neither does $\mathscr{I}_G^2$ for part of a spin-coupled system chosen at random.

Suppose now that effective symmetry of the spin system produces complete equivalence of certain of the nuclei. A valuable simplification of the $\mathscr{H}$ eigenstate problem is then effected by treating each group of completely equivalent nuclei as a composite particle (to treat the whole spin system in this way, some of the composite particles may be only single nuclei). The Hamiltonian may then be written in the simplified form—

$$\mathscr{H} = \sum_G \nu_G \mathscr{I}_{z(G)} + \sum\sum_{G<G'} J_{GG'}\mathscr{I}_G.\mathscr{I}_{G'}$$

the second term being a summation over all pairs of composite particles G, G'. This is possible since there is only one coupling constant $J_{GG'}$ between members of groups G, G'; also, intra-group terms in J_{GG} and $J_{GG'}$ have no effect on the spectrum and are omitted (for a formal proof of this statement, see Emsley *et al.*,[1] p. 307 or Carrington and McLachlan,[12] p. 51). Thus, no distinction need be drawn between a single nucleus and a composite particle G of >1 nucleus, and since $\mathscr{I}^2$ for the former commutes with $\mathscr{H}$ so does $\mathscr{I}_G^2$ for the latter. (If all the nuclei have identical shifts, then one has the special case in which $\mathscr{I}_G^2$ is synonymous with $\mathscr{I}_T^2$). In spin systems of this kind, the simple product functions are not in general eigenfunctions of $\mathscr{I}_G^2$. It is advantageous in such cases to change the basis of representation of the Hamiltonian, replacing the simple product functions by linear combinations chosen to be eigenfunctions of $\mathscr{I}_G^2$ for each group in the spin system, as well as of $\mathscr{F}_z$. Consider, for example, a group of two equivalent spin $\frac{1}{2}$ nuclei (designated B). The operation of $\mathscr{I}_B^2$ $(=\mathscr{I}_G^2$ with $G=$the two B nuclei) upon the simple product function $\beta\beta$, for example, yields—

$$\begin{aligned}\mathscr{I}_B^2|\beta\beta\rangle &= |\mathscr{I}_1^2+\mathscr{I}_2^2|\beta\beta\rangle+2|\mathscr{I}_{x_1}\mathscr{I}_{x_2}+\mathscr{I}_{y_1}\mathscr{I}_{y_2}+\mathscr{I}_{z_1}\mathscr{I}_{z_2}|\beta\beta\rangle\\ &= (\tfrac{3}{4}+\tfrac{3}{4})\beta\beta+2(\tfrac{1}{4}\alpha\alpha-\tfrac{1}{4}\alpha\alpha+\tfrac{1}{4}\beta\beta) = 2\beta\beta\end{aligned}$$

Therefore, the function $\beta\beta$ is already an eigenfunction of $\mathscr{I}_B^2$, of eigenvalue 2; the same applies to $\alpha\alpha$. If the same operation is performed on $\alpha\beta$ or $\beta\alpha$, it will be found that they are altered to $\beta\alpha$ and $\alpha\beta$, respectively, so that these are not eigenfunctions of $\mathscr{I}_B^2$. However, their sum and difference $1/(\sqrt{2})(\alpha\beta+\beta\alpha)$ and $1/(\sqrt{2})(\alpha\beta-\beta\alpha)$ will be left unchanged, and are eigenfunctions of $\mathscr{I}_B^2$, having eigenvalues $\bar{I}_B^2=2$ and 0, respectively. The factors $1/\sqrt{2}$ ensure that the functions are still normalized.

The new set of basis functions for the system $[AB_2]$, for example, is then obtained by combining each of the possible spin functions for A with each of the above spin functions for the two B nuclei, as in Fig. 5. The spin of A is unaffected by the operator $\mathscr{I}_B^2$, so all members of the new basis set are still eigenfunctions of the latter. One is in effect taking advantage of the symmetry of the spin system; the three ("triplet state") functions of $\bar{I}_B^2=2$ are "symmetrical" to interchange of the B_1 and B_2 (reflection through the plane of symmetry shown in Fig. 5). The "singlet" function $\alpha[1/(\sqrt{2})](\alpha_1\beta_2-\beta_1\alpha_2)$ of $\bar{I}_B^2=0$ is "antisymmetric", giving—

$$\alpha\frac{1}{\sqrt{2}}(\alpha_2\beta_1-\beta_2\alpha_1) \equiv -\alpha\frac{1}{\sqrt{2}}(\alpha_1\beta_2-\beta_1\alpha_2).$$

The advantage to the $\mathscr{H}$ eigenstate problem is the additional factorization that is possible; mixing is forbidden, not only between states of different F_z, but also between states of different $\bar{I}_G^2$ since both observables remain sharply defined. In the $[AB_2]$ case, each (3×3) sub-matrix of ABC is reduced to a (1×1) and a (2×2) interaction (Fig. 5), and the whole spectrum can be expressed in simple algebraic form. This applies to all cases $[AB_q]$, where q is any integer; and the largest interaction in $[A_pB_q]$ $(p<q)$ is reduced to order $(p+1)$ by choosing the

basis to be eigenfunctions simultaneously of $\sum_i \mathscr{F}_{z(i)}$, $\mathscr{I}_A^2$ and $\mathscr{I}_B^2$. Further, it may not even be necessary to write out the new basis functions explicitly to predict the appearance of the spectrum, in view of the second selection rule given below. The analytical advantages of the composite-particle method are discussed later. Finally, it should be noted that systems involving nuclei of spin $> \frac{1}{2}$ are accommodated very easily as special cases of the scheme for spin $\frac{1}{2}$ nuclei, e.g., the deuterium nucleus ($I=1$) can be treated as a composite particle (G) of two equivalent spin $\frac{1}{2}$ nuclei, but without states in which $\bar{I}_G^2=0$. There is no loss of generality, therefore, in restricting discussion of the eigenstate problem to spin $\frac{1}{2}$ nuclei.

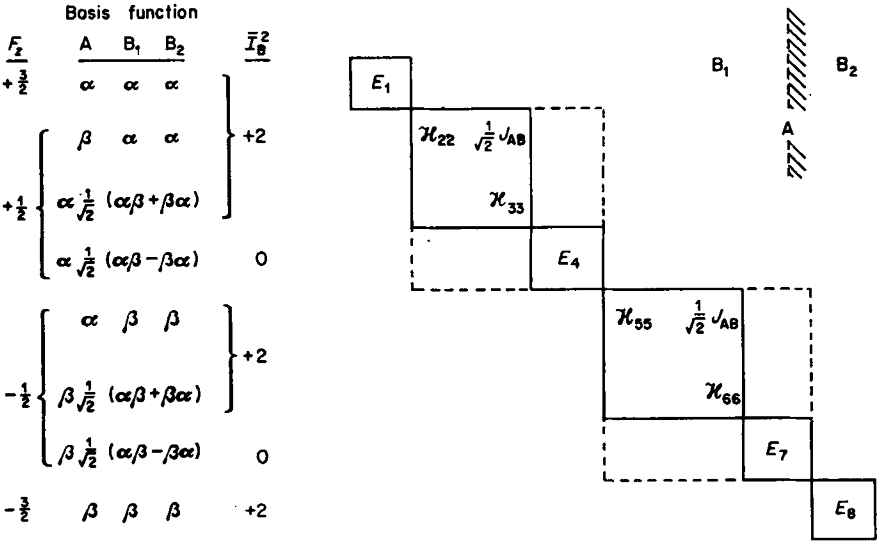
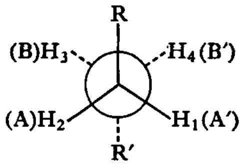


FIG. 5. Matrix representation of the spin-coupling Hamiltonian for the case [AB$_2$]. That for ABC is indicated by dashed lines.

If the effective symmetry of the spin system produces complete equivalence of all the nuclei at a given chemical shift, then the composite-particle approach is the simplest. However, if there is non-accidental (i.e., symmetry produced) equivalence of chemical shifts, but not of spin coupling, then the symmetry properties must be considered explicitly. The term "effective symmetry" is used, since symmetry simplification in an n.m.r. spectrum is often due to rapid interconversion of conformers, e.g., by rotation about a single bond. The spectrum is then governed only by the time-average values of the parameters (see above), and may be simpler than that which would be expected from the symmetry of any one of the conformers alone. In some cases, the effective symmetry is the same as the symmetry of one of the conformers, and it is then easier to visualize the problem in terms of the latter. An example is the proton resonance of a 1,2-disubstituted ethane $RCH_2 \cdot CH_2R'$, which on rapid rotation about the C—C bond has the effective symmetry of the spin system $[AB]_2$ or $[AX]_2$. This is also the symmetry of the *trans* conformer (**1**), although not of the *gauche* forms (e.g., **2**),



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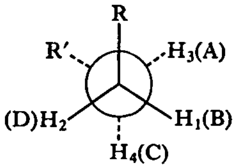

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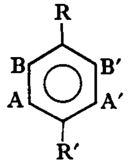

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so it is convenient to regard, say, the reflection σ_v as a symmetry operation of the free rotation case as well as of the frozen *trans* conformer (**1**). Case (**3**) has the same symmetry (C_{2v}) with no averaging. In general, the group of symmetry operations applicable to any n.m.r. system should strictly be defined as the group of all permutations of nuclear labels that do not permute the effective spectral parameters.[13] A simplification in the $\mathscr{H}$ eigenstate problem can then be brought about by choosing a set of basis functions that are eigenfunctions of as many of the symmetry operators as possible. To be more precise, the functions are selected so that they can be divided into sets, each of which forms the basis for an irreducible representation of the group of symmetry operations, i.e., a function from any set is transformed by any of the symmetry operations either into itself, if it is an eigenfunction of that operator, or into a linear combination of functions from the same set only. Now the Hamiltonian is invariant under any symmetry operation, i.e., the energy is not altered and the symmetry operators commute with $\mathscr{H}$. Therefore, only those basis functions that belong to the same irreducible representation can mix, just as mixing is restricted to states of the same F_z value. The $[AB_2]$ system (above) provides an example; the basis functions selected by the composite particle method are also eigenfunctions of the reflection σ_v, which interchanges the B nuclei. The possible eigenvalues of this operator are $+1$, corresponding to the symmetric basis functions ($\sigma_v\psi = \psi$), and -1, corresponding to the antisymmetric function ($\sigma_v\psi = -\psi$). Basis functions can similarly be constructed to be eigenfunctions of σ_v in the case $[AB]_2$, where the composite-particle approach could not have been used instead. They are in fact all combinations of singlet and triplet functions for the two A nuclei and for the two B nuclei (Fig. 1c). Applying also the F_z non-mixing rule, the largest remaining sub-matrix in the Hamiltonian is (4×4). In $[AX]_2$, this is further reduced to (2×2).

E. Transition probability

Absolute n.m.r. line intensities are not measured, since all information relevant to analysis can be found from the relative intensities (transition probabilities) of lines recorded at constant r.f. power level (H_1 amplitude). Consider first a system of isolated nuclei. An oscillating magnetic field H_1, applied at right angles to H_0 and at the correct frequency $\nu=\Delta E/h$, can interact with the nuclear magnetic dipole moment and induce transitions between different spin states. Since $H_1 \ll H_0$, it can be assumed that spin quantization is maintained along the z axis defined by H_0, so that the transitions for spin $\frac{1}{2}$ nuclei, for example, are simply $\alpha\rightarrow\beta$ or $\beta\rightarrow\alpha$. These "spin flips" are induced with equal probability, apart from population weighting, which is all-important for observation of a net absorption signal. Since $\mathscr{I}_x$ changes the function α to β and vice versa, the results may be expressed conveniently in terms of this operator equivalence. Thus, a finite transition probability is associated with a finite "transition moment" $\langle\alpha|\mathscr{I}_x|\beta\rangle=\langle\beta|\mathscr{I}_x|\alpha\rangle$, being the matrix element of $\mathscr{I}_x$ between the functions involved. The absolute probability will involve also the magnitude of the magnetic dipole moment, but this is here omitted. Extending to systems of several spin-coupled nuclei, the probability of induced transition between states of eigenfunctions Ψ_m, Ψ_n is proportional to

$$\left\langle \Psi_m \middle| \sum_i \mathscr{I}_{x(i)} \middle| \Psi_n \right\rangle^2$$

Note that the square avoids negative values. To evaluate the intensity of the transition $m\rightarrow n$, the wave functions are expanded in terms of the basis functions, and each element of the transition moment is evaluated separately, remembering that $\mathscr{I}_{x(i)}$ operates only on the spin of the ith nucleus. Consequently, the transition moment can have finite elements only between basis functions differing in the spin of one nucleus, e.g.—

$$\langle\alpha\alpha|\mathscr{I}_{x_1}+\mathscr{I}_{x_2}|\beta\alpha\rangle = \tfrac{1}{2}\langle\alpha\alpha|\alpha\alpha\rangle+\tfrac{1}{2}\langle\alpha\alpha|\beta\beta\rangle = \tfrac{1}{2}+0$$

but—

$$\langle\alpha\alpha|\mathscr{I}_{x_1}+\mathscr{I}_{x_2}|\beta\beta\rangle = \tfrac{1}{2}\langle\alpha\alpha|\alpha\beta\rangle+\tfrac{1}{2}\langle\alpha\alpha|\beta\alpha\rangle = 0+0$$

This gives a "selection rule"—

$$\Delta F_z = \pm 1$$

for allowed transitions, which are thereby restricted to states associated with adjacent $\mathscr{H}$ sub-matrices.

Effective symmetry within the spin system produces further restrictions. If this causes complete equivalence of certain nuclei (group G), then it was seen above that Ψ_m and Ψ_n must be eigenfunctions of $\bar{\mathscr{I}}_G^2$. Now from the general properties of spin, $\sum \mathscr{I}_{x(G)}$ carried over all members of G, commutes with $\bar{\mathscr{I}}_G^2$. Thus $\langle\Psi_m|\sum \mathscr{I}_{x(G)}|\Psi_n\rangle$ is zero unless Ψ_m, Ψ_n have the same value of $\bar{I}_G^2$. Combined with the fact that the transition moment can have finite elements only between functions differing in the spin of one nucleus, this suffices to define a second selection rule—

$$\Delta\bar{I}_G^2 = 0$$

If the symmetry does not produce complete equivalence, then this is replaced by the statement that Ψ_m and Ψ_n must have the same symmetry properties (i.e., must belong to the same irreducible representation of the group of symmetry operations). These considerations often lead to a considerable simplification both in the appearance of a spectrum and its interpretation (see Table).

The simple intensity ratios of a first-order spectrum are distorted in the non-first-order condition due to the additional (positive or negative) contributions to each transition moment. For example, the A transition $\alpha\alpha \leftrightarrow \beta\alpha$ of the AX case has a transition moment—

$$\langle\alpha\alpha|\mathscr{I}_{x_1}+\mathscr{I}_{x_2}|c_1\beta\alpha+c_2\alpha\beta\rangle = \tfrac{1}{2}c_1\langle\alpha\alpha|\alpha\alpha\rangle+\tfrac{1}{2}c_2\langle\alpha\alpha|\alpha\alpha\rangle = \tfrac{1}{2}(c_1+c_2)$$

in the AB case. The transition now involves some spin-change character of both nuclei, but is still conveniently classified as an A transition from its "label" in the first-order limit, and since $c_1 > c_2$. Combination lines are those that have finite intensity only on mixing of states that were eigenfunctions in the high-field limit. At least three spin-coupled nuclei are required; for example, the three transitions $\alpha\alpha\beta \leftrightarrow \beta\beta\alpha$, $\alpha\beta\alpha \leftrightarrow \beta\alpha\beta$ and $\beta\alpha\alpha \leftrightarrow \alpha\beta\beta$ are forbidden in AMX, but the transition moment has finite cross-terms between the mixed ABC functions. To differentiate between combination lines and those that have finite intensity in the high-field limit, the latter are sometimes called "fundamental" lines. This is adopted here, but is not a particularly happy choice of nomenclature, being borrowed from infrared spectroscopy.

An alternative derivation of transition intensities has been given by Corio[14] in terms of "raising" and "lowering" operators $\mathscr{I}^+$ and $\mathscr{I}^-$, defined by $\mathscr{I}^+\alpha=0$; $\mathscr{I}^+\beta=\alpha$; $\mathscr{I}^-\alpha=\beta$; $\mathscr{I}^-\beta=0$.

VI. ASPECTS OF ANALYSIS

A. General comments

The calculation of the spectrum corresponding to a given set of ν and J parameters is straightforward, in that systematic application of a sequence of mathematical steps will always yield a unique answer. The length of the calculation will often preclude "longhand" solution, but the problem is ideally suited to automatic computation (see later) since it is easy to "write" a programme that will deal with any set of parameters within the capacity of the computer. The analytical requirement of finding the parameters from an experimental spectrum is by no means as straightforward, and each case should be considered on its merits. Two general types of approach may be adopted, classified by Hoffman as "direct" and "indirect" methods[3]—these terms are used in a different sense by Primas (*loc. cit.*). By the "direct" approach is meant the systematic calculation of the parameters from the spectrum; the converse of the previous Section. It may be noted immediately that most methods so far devised for direct analysis depend explicitly on the properties of the particular spin system, and are less amenable to automatic computation. The "indirect" approach proceeds from a set of trial parameters, chosen by a preliminary approximate treatment, or by inspired guesswork. A spectrum is calculated from these, and on the basis of disagreement with the experimental spectrum the parameters are modified. One then seeks to converge on the correct solution by an iterative procedure of successive approximations until experimental and calculated spectra agree in all respects. This approach is inherently more suited to computer analysis, in that a single programme can be made applicable to any spin system (again, within the capacity of the computer). The ready availability of such programmes through the kind offices of their authors offers a relatively painless way of analysing a spectrum, without any detailed assignment of lines and with very little knowledge of the underlying principles. This has made the indirect method much the more popular approach within the past few years; so much so that it is legitimate to enquire whether the direct method still presents any advantages other than applicability on a lengthy train journey. Often a compromise is most effective. A disadvantage of the indirect method is that the starting parameters must be reasonably close to the solution for convergence to occur. Also, experimental recording errors necessitate acceptance of a finite measure of disagreement between the finally calculated and experimental spectra, and in unfortunate cases the latter may be matched to within this error by two or more quite different sets of parameters (see under "ABC Spectra" below). Since the solution obtained by the indirect method will be that which is closest to the input parameters, choice of the latter introduces a subjective element, i.e., there is a tendency to obtain the answer one expects. It is easier to guard against this by direct analysis, which if properly applied should make one aware of any alternative solution. If, therefore, direct analysis gives simple rules for finding exact possibilities for the parameters, these should be applied. Any parameters that remain indeterminate can then be sought by the indirect method. Even if all the parameters have been found directly, it is strongly advisable to back-calculate the spectrum, including the line intensities, as a check on the calculation. This also checks that the spectrum is in fact compatible with the spin system that was assumed. A standard non-iterative computer programme is extremely useful for this purpose.

B. Direct methods

As explained earlier, the direct approach is applicable mainly to those cases in which most spin states involve interactions no greater than (2 × 2), after maximum factorization of the secular equations. It has long been a popular exercise amongst exponents of n.m.r. to produce algebraic treatments of specific spin systems of this kind, so that all cases of likely, and some of unlikely, occurrence are scattered through the literature with a fair measure of duplication. Recourse to the original literature is often made unnecessary by compendia such as that of Emsley *et al.*[1] It is pointless to repeat here a detailed discussion of the many individual spin systems, and the Table is an attempt to summarize the main analytical features of some of the simpler cases. It is intended to cover all likely systems of two, three and four spin $\frac{1}{2}$ nuclei. Thereafter, only a selection of the many possibilities is included. Cases denoted † are of the general type $[A_pB_q]$; these spectra are particularly easy to recognize and analyse with the aid of the literature. They depend on J_{AB} and $\Delta\nu_{AB}$ only, alternatively expressed as the ratio $J_{AB}/\Delta\nu_{AB}$ and a trivial scaling parameter. It is possible, therefore, to present all possible appearances of the spectrum in graphical or tabular form, or as a series of diagrammatic spectra calculated for representative values of this ratio. The conformity of an experimental spectrum can then be checked easily by comparison, with interpolation between the calculated spectra if necessary. Two very useful references for this purpose are the classic article by Corio,[14] and a collection of computer print-out spectra, with a small broadening function applied, by Wiberg and Nist.[15] The latter includes also some multi-parameter spectra, e.g., ABC and AA′BB′, which might be misleading in that it is not practicable to illustrate all possible parameters. For example, the lack of cases with a large negative coupling constant is a shortcoming in view of subsequent experimental results.

In direct analysis, each obtainable parameter is usually found from certain experimental line positions, each of which is associated with an algebraic function of this and other parameters. A partial or complete line assignment, i.e., the matching of experimental lines to theoretical counterparts, is therefore an essential feature of this form of analysis (also of one form of indirect analysis requiring a set of experimental energy levels). It is always possible to assign the lines in more than one way, in each of which the line positions satisfy the necessary interrelationships. This in turn leads to ambiguity in the derived sets of parameters. In so far as interactions no larger than (2 × 2) are concerned (i.e., the cases to which direct analysis is usually applied) the situation seems to be straightforward; each line assignment leads by direct analysis to one set of parameters, and each set is in general different. (The situation is less straightforward in more complex systems; see "ABC" below.) Further, each set of parameters corresponds to a different intensity pattern (except in the case of first-order spectra), and since only one will agree exactly with experiment, this forms a basis for resolving the ambiguities. Several causes of ambiguity can be traced. The commonest, which occurs with all spectra, and is the sole cause in first-order and weakly coupled systems, will for want of a better name be called the "sign reversal" ambiguity. Different assignments are here inter-related by pairwise interchanges in the labelling of certain "fundamental" lines. The manner in which they are related is seen most easily by considering first-order spectra, where the assignments correspond simply to different sign permutations of the coupling constants (although these cannot be differentiated on an intensity basis). Ambiguity in non-first-order spectra can be described in similar terms, although the derived sets of parameters differ usually by more than just the appropriate sign reversals, being changed also in magnitude. Complete sign reversal of all the coupling constants, of course, leaves the intensity pattern unchanged, but relative signs can in general be differentiated. This does not apply to coupling between completely equivalent nuclei; for example, spectra of type $[A_pB_q]$ are affected only by the coupling constant J_{AB}, so that its sign relative to the "invisible" constants J_{AA}, J_{BB} cannot be found. Other ambiguities, particular to the spin system, sometimes arise in non-first-order spectra. For example, an $[AB]_2$ or $[AX]_2$ analysis has certain inherent limitations (see Table) owing to the symmetry of the spectrum. Confusion between "fundamental" and "combination" lines is discussed below in relation to ABC spectra. A simpler example is an ABX spectrum in which $\nu_A \approx \nu_B$, when the X region contains six lines in which the two combination lines may be confused with the X quartet; in this case, the ambiguity can be resolved with the help of intensity sum rules.[1]

Experimental modification of the spectrum can be of great help in assignment, and methods are reviewed by Hoffman,[3] p. 548. The most important of these is a further application of double resonance; "tickling" a single line with a very weak H_2 field causes additional splitting of other lines having an energy level in common with the first. Techniques involving a simplification of the spectrum are mentioned later.

The method of spectral moments permits, in principle, direct analysis without any line assignment. It is rarely used in practice since it depends essentially on very accurate intensity measurements, particularly of outlying lines which tend to be weak (Hoffman,[3] p. 545). Use of a time-averaging computer (CAT—see below) will lessen this disadvantage, although there will still be the initial difficulty of eliminating any impurity peaks.

Earlier mention has been made of perturbation treatment of systems that depart slightly from a more readily soluble case. Such treatment of weak coupling interactions, i.e., those close to first order, is not likely to be applied when an exact solution can be obtained by computer. It is also possible to treat very strongly coupled spectra by introducing small chemical-shift differences as perturbations upon the state of coincident shifts. The single-line spectrum of the latter is thereby split into several strong components, whereas the remaining lines of the general spectrum appear with much lower intensities. This approach directs attention to the few strong lines dominating a strongly coupled spectrum, and to the possibility of assigning them and obtaining certain parameters without requiring the weaker lines, some of which may not be observable. The $[A_pB_q]$[16] and ABC[17] cases have been considered.

C. Sub-spectral analysis

It was seen earlier that effective symmetry of the spin system permits formulation of non-mixing and selection rules. Mixing of basis functions and transitions between stationary states are permitted only within the same irreducible representation of the symmetry group; also the functions must belong to the same value of $\bar{I}_G^2$ for any composite particle G. The resulting factorization of the secular equations has already been discussed. A further analytical aspect that has attracted recent attention is the facility thereby offered of dividing the spectrum up into completely non-interacting, although overlapping, sub-spectra associated with different symmetry properties. If such sub-spectra can be reliably picked out from the total pattern, they can be analysed quite independently of the rest of the spectrum. The parameters affecting a sub-spectrum could then be obtained more easily than by analysis of the complete spectrum. Often such sub-spectral analysis may be stopped short of complete analysis at a stage where all possible parameters have been found. Frequently, a sub-spectrum has exactly the properties of some simpler spin system and can be described by the same notation, except that lower-case letters (a, b, c etc.) are often used instead of capitals.

The composite-particle approach to sub-spectral analysis is exemplified by the simple case $[AB_3]$. Those eigenstates in which the composite particle B_3 has $\bar{I}_B=\frac{1}{2}$ are indistinguishable from those of two spin $\frac{1}{2}$ nuclei A, B. Consequently, the spectrum contains a four-line "ab" sub-spectrum that yields all the parameters (J_{AB}, ν_A, ν_B) that could be found from a complete analysis. In general, the spectrum of $[AB_n]$ contains all sub-spectra $[ab_x]$ where $x=1, 2, 3\ldots n$ if n is odd, and $x=0, 2, 4\ldots n$ if n is even (Emsley *et al.*,[1] p. 342). In the latter case, the sub-spectrum for $x=0$ is a single line, being the transition between the two states for which $\bar{I}_B=0$ (as in $[AB_2]$, Fig. 5). This always coincides with the chemical shift ν_A. Spectra $[A_pB_q]$ where $p>1$ contain all sub-spectra $[a_xb_y]$ where x and y have the same parity (odd or even) as p and q, respectively (Emsley *et al.*,[1] p. 244).

A second approach to sub-spectral analysis is the effective frequency method, which is applicable under conditions in which the X approximation is valid. For example, the AB region of an ABX spectrum is affected by X only through the presence of J_{AX} and J_{BX} in the diagonal elements of the Hamiltonian, where their effect is indistinguishable from that of a chemical-shift displacement. This is equivalent to replacing ν_A by effective frequencies $\nu_A^{*}=\nu_A\pm\frac{1}{2}J_{AX}$, and

ν_B by $\nu_B^* = \nu_B \pm \frac{1}{2}J_{BX}$. The positive sign applies to that half of the molecules in which, at a given instant, X has spin α; the negative sign applies to the other half, in which X has spin β. In each case, inclusion of J_{AB} produces an ab sub-spectrum appropriate to the values of ν_A^* and ν_B^*. Thus the eight lines in the A, B region may be grouped into two overlapping quartets, so that each has the pattern of a two-spin AB system (note that this grouping is not the same as that into an A quartet and a B quartet). The strength of coupling in the two ab sub-spectra is different, since $\nu_A^* - \nu_B^*$ is—

$$\nu_A - \nu_B + \tfrac{1}{2}(J_{AX} - J_{BX}) \quad \text{when X has spin } \alpha$$

and—

$$\nu_A - \nu_B - \tfrac{1}{2}(J_{AX} - J_{BX}) \quad \text{when X has spin } \beta$$

A more general procedure has been recently developed[18, 19] that includes both the above as special cases, and a few recent papers are those of Jones and Williams,[18] Diehl *et al.*,[19] Diehl and Trautmann[20] and Hirst *et al.*[21] Sub-spectral analysis is likely to be most useful in moderately complex cases of known high symmetry, e.g., $[[AB]_2X]$,[18] where extensive breakdown of a complicated pattern of lines can be achieved without too much difficulty in picking out sub-spectra which are known to be present. A generalized computer procedure for systematically obtaining sub-spectra would be useful in this respect.

D. The general three-spin case, ABC

This has received a great deal of attention from the analytical standpoint, some of the reasons being discussed by Hoffman,[3] p. 547. It is of common occurrence, and as there are no more than 15 lines, with repeated spacings, the spectrum is often well resolved even when quite strongly coupled. Further, it is often worth expending some trouble over the analysis, as it is the simplest spin system in which the relative signs of all the coupling constants can be found without double resonance (which is readily applicable only to weakly coupled systems). Factorization according to F_z values leaves two (3×3) sub-matrices to be diagonalized, for which a general algebraic treatment is more lengthy than for (2×2) interactions. However, there are regularities in the spectrum, expressed as frequency and intensity sum rules, which can be used to expedite the solution. Moreover, the whole system involves only eight spin energy levels.

Accordingly, several analytical schemes, both direct and indirect, have been either devised specifically for, or applied mainly to, the ABC case. Procedures for indirect analysis include those of Swalen and Reilly,[22] based on convergence to a set of energy levels derived from the spectrum; and of Arata *et al.*[23] and Yamamoto and Fujiwara,[24] who employ simultaneously line intensities and positions. Procedures for direct analysis are due to Brügel *et al.*,[25] Whitman,[26] Sudanshu,[27] and Castellano and Waugh.[28] The last is reproduced in detail by Emsley *et al.*,[1] and a useful simplified modification is given by Liang.[29] This is a blend of direct and indirect analysis, whereby guesses for the quantity $(\nu_A^2 + \nu_B^2 + \nu_C^2)$ are combined with experimental energy levels to obtain $(J_{AB}^2 + J_{BC}^2 + J_{CA}^2)$ by two routes. A state of internal consistency can be found after a few guesses by graphical intersection, from which the parameters can be easily found.

Ambiguities in the interpretation of ABC spectra have been much studied. The situation is appreciably more complex than for any case composed of (2 × 2) interactions, yet is still simple enough for the problem to be exhaustively treated. These ambiguities offer a salutary lesson as to what might happen with larger spin systems, although the ABC case may be one of the most difficult in this respect, since it is less over-determined[3] (i.e., these are relatively few experimental lines for the number of parameters). In weakly coupled systems, the only ambiguities are of the "sign reversal" type described above. There are four line assignments that would correspond to relative sign permutations of the coupling constants on a first-order basis (we will neglect assignments differing in absolute signs). Generally, although not always, four sets of parameters can then be obtained, one for each line assignment, which are fairly close to the first-order values. These may not be the only solutions compatible with the line positions, but will include the correct one, which can then be selected on the basis of intensities. Analysis of strongly coupled ABC cases, however, is much more difficult. In the first place, although all the properties of repeated spacings of the AMX case are retained,[1] the correct parameters may be quite different from those expected on a first-order basis. This shows up a disadvantage of indirect analysis, since a search for solutions in a restricted region of "parameter space", which is sufficient for weakly coupled spectra, may here not include the correct solution. Secondly, ambiguities in assignment are multiplied by the presence of one or more combination lines towards the centre of the spectrum. They may gain intensity until they are comparable to nearby "fundamental" lines and cannot be differentiated on sight. The most thorough study of ambiguities in ABC spectra is that of Castellano and Waugh.[28] They show that there are 15 ways of grouping the lines into A, B and C quartets and three combination lines, such that the usual spacing rules are obeyed. Although the correct grouping is immediately obvious in weakly coupled spectra, this is not so in strongly coupled cases; however, application of intensity sum rules makes it possible to eliminate many of the incorrect groupings at an early stage.[17,28] Each grouping can be given four line assignments (again, neglecting those that would correspond to a complete reversal of the signs of the coupling constants), and from each assignment can be derived a set of energy levels, giving a total of 60. Of these, however, only ten are physically distinguishable. Cavanaugh[30] has pointed out that it is possible to derive all ten sets of energy levels from a single grouping into quartets and combination lines, and a programmed least-squares procedure for generating them has been described by Emerson and Cohen.[31] The direct analytical method of Castellano and Waugh[28] relates the parameters to the energy level set ultimately by quartic equations, from which they infer that $4 \times 10 = 40$ sets of parameters are in principle consistent with the experimental line positions. In practice, several of these turn out to have an imaginary part, and are rejected since eigenstates of the Hamiltonian must be entirely real. It appears that this criterion must be used with care, since Cavanaugh[32] has reported a case where the correct solution was derived with a small imaginary component, due to very minor experimental errors in the line positions. This is exceptional, and one would expect it to arise only in certain strongly coupled cases. This may occur when two energy levels are close together (near what is conventionally regarded as a "cross-over point"), which is a situation known to cause trouble in analysis. The derived parameters are then very sensitive to minor changes in the measured line positions, and indirect methods of analysis are at a particular disadvantage since iteration may converge on a wrong solution, or fail to converge at all, unless the starting parameters are very close to the correct ones. It appears that the calculated intensity pattern should always differ for each set of parameters which matches the (non-first-order) line positions. In most cases that are not too close to the first-order condition, this allows the correct solution to be decided. Occasionally, it has been found that two sets of parameters match an ABC spectrum equally well, and it is then necessary to modify the spectrum by changing the solvent or the magnetic field.

E. Deceptively simple spectra

The ambiguities of interpretation that occur in most spectra involve a choice between a small number of discrete solutions. These are considered above. Spectra that are termed "deceptively simple" present quite a different problem in ambiguity. They are insensitive to certain parametric changes, and so can be matched to within experimental error by sets of parameters that are continuously variable over a range in at least one degree of freedom. The spectra characteristically have fewer lines than normally expected for the appropriate spin system, owing to close crowding of some of the transitions into a lesser number of experimentally unresolved lines. This gives them the appearance of the spectrum of a simpler spin system, and they are liable to be misinterpreted as such.

Most cases of deceptively simple spectra are those in which several non-equivalent nuclei function as if they were a completely equivalent group in their apparent couplings to nuclei outside the group. In general, this is observed when two conditions are fulfilled. The mutual coupling of any two nuclei within the "group" must be large compared to (i) their chemical shift separation, i.e., the group is strongly coupled, and (ii) the difference between their couplings to any nucleus outside the group. Only the average coupling between members of the group and a nucleus outside it can then be found. The simplest example is ABX; if $|J_{AB}|$ is large compared to both $|\nu_A - \nu_B|$ and $|J_{AX} - J_{BX}|$, the spectrum approximates to the five-line pattern associated with $[A_2X]$ and may be mistaken for it. The inference $J_{AX} = J_{BX}$ could then be quite wrong. If this is suspected (e.g., from a hint of additional splitting) the spectrum should be re-examined at a very different magnetic field, or an attempt made to separate ν_A and ν_B by changing the solvent. If condition (i) but not (ii) is fulfilled, the X region again approximates to a deceptive 1:2:1 triplet, but the inference $J_{AX} = J_{BX}$ would be refuted by the eight-line AB region. It may be noted that the case of two coincident

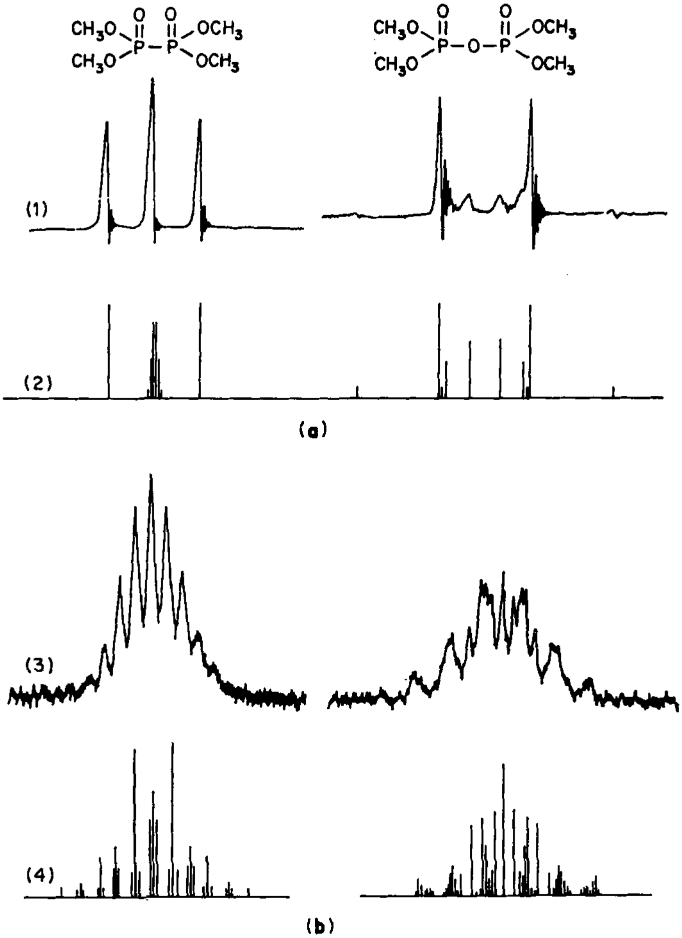

FIG. 6. N.m.r. spectra of tetramethyl hypophosphate (left) and tetramethyl pyrophosphate (right): (a), proton spectra at 60 Mc./sec.; (b) ^{31}P spectra at 25 Mc./sec. Curves 1 and 3, experimental; curves 2 and 4, calculated (for parameters, see text). (From Mowthorpe and Chapman.[38])

shifts, AA′X in the notation of Richards and Schaefer, satisfies (i) but not necessarily (ii). The three-spin case and analogous situations in the ABXY and $[AX]_2$ systems are described by Cavanaugh.[30] Additional requirements are necessary in a system possessing symmetry. Deceptively simple spectra in the cases $AA'XX' \equiv [AX]_2$[30, 31] and $AA'BB' \equiv [AB]_2$[32] have often been misinterpreted. Denoting the dissimilar J_{AB} values as $J_{AB(1)}$ and $J_{AB(2)}$, the spectrum of $[AB]_2$ reduces to that of $[A_2B_2]$ if both $|J_{AA}+J_{BB}|$ *and* $|J_{AA}-J_{BB}|$ are large compared to $|J_{AB(1)}-J_{AB(2)}|$. The case $[AX]_2$ reduces to $[A_2X_2]$ under similar conditions. Harris,[33, 34] Harris and Woodman[35] and Finer and Harris[36] have shown, in a treatment that assumes J_{XX} is small or zero, that the more general case $X_nAA'X'_n \equiv [AX_n]_2$ always approximates to $[A_2X_{2n}]$ if $|J_{AA}|$ is large compared to $|J_{AX(1)}-J_{AX(2)}|$. The X region then approaches a 1:2:1 triplet, although the composite central component is often detectably broader than the outer ones. Spectra of type $[AX_n]_2$ are often encountered in phosphorus compounds, e.g., complexes of $P(CH_3)_3$ or PF_3 with a non-metal or transition metal. The combined spectra of ^{31}P and ^{1}H or ^{19}F vary greatly in appearance according to the wide variation in J_{PP} (for some references, see Mavel[37]). This is well illustrated also by the spectra of tetramethyl hypophosphate $[(MeO)_2PO]_2$ and pyrophosphate $[(MeO)_2PO]_2O$ in Fig. 6.[38] The latter gives a complex spectrum ($J_{PH}=11{\cdot}6$ c./sec.; $J_{PP}=14{\cdot}3$ c./sec.), whereas that of the hypophosphate is deceptively simple owing to the greatly enhanced coupling between the directly bonded phosphorus atoms ($J_{PH}=11{\cdot}2$ c./sec.; $J_{PP}\approx 200$ c./sec.). Some recent examples are given by Harris *et al.*[39] and Carty and Harris.[40] An account of deceptively simple spectra in systems $[A_mB_n\ldots M_pX_q]$ has been given by Diehl, in terms of effective frequencies.[41]

F. Virtual coupling

As a corollary, spectra are occasionally more complex than might be expected from naïve consideration. Musher and Corey[42] first pointed out that the group of lines assigned to some particular nucleus in a spin-coupled system may contain splittings due to the presence of another nucleus which is not directly coupled to the first. The effect is most obvious when one or other of the nuclei concerned is isolated in chemical shift from the rest of the spectrum, but is in no way restricted to this situation. The simplest case is that of ABX, in which there are no exact coincidences among the four fundamental X lines (or the eight A, B lines) even if J_{AX}, for example, is identically zero. The spacing common to the A and X quartets is conveniently termed a "virtual coupling" between A and X. It may be seen as a general consequence of the lack of identity between coupling constants and line spacings in a spectrum with non-first-order interactions. This suggests that virtual coupling should be a very widespread phenomenon in many kinds of spin system, but it is undetectably small unless certain conditions are fulfilled. In the ABX case, the condition usually quoted is that the A and B nuclei should be strongly coupled, i.e., $J_{AB} \gg |\nu_A - \nu_B|$, although relatively weak A, B coupling may suffice if J_{BX} is particularly large.[43] The former condition thus approaches that for a deceptively simple ABX spectrum; the situation in which X is apparently coupled equally to A and B emerges as a limiting case with yet stronger A, B coupling, even if J_{AX} is still zero. Virtual coupling effects large enough to produce resolvable line splitting in a "first-order" multiplet are not encountered very often in practice, but improved resolution is revealing smaller effects as unresolved line broadening.[43, 44] A further complication of virtual coupling in systems of more than three nuclei is that the additional line broadening or splitting may differ for different lines assigned to the same nucleus. Moreover, if some of the lines arise from transitions between unmixed states, they will remain sharp and completely unaffected by virtual coupling. This is differentiated as "partial virtual coupling", and has been investigated systematically in the simplest case ABMX.[43, 44] From this, Khan *et al.*[44] conclude that significant partial virtual coupling can arise between two weakly coupled groups in a spin system, provided that each group is coupled to at least one member of a pair of nuclei which are strongly coupled to each other. It is pointed out[43, 44] that the concept of effective frequencies is a useful one in discussing virtual coupling. An interesting example has been reported[45] in the α proton resonance in alkyl fluorides $F[CH_2]_nCH_3$, which consists of two triplets due to first-order interactions with F and β H. Of these the high-field triplet alone is often broadened due to partial virtual coupling between the α and γ protons. The chemical-shift difference between the β and γ protons is large compared to $J_{\beta\gamma}$, but inclusion of $J_{F\beta}$ produces two effective β shifts, of which the higher-field value is close to that of the γ protons. Thus the β protons are in effect strongly coupled to γ in half the molecules, and since $J_{\alpha\beta}$ is finite this causes virtual coupling between the α and γ protons even though $J_{\alpha\gamma}$ is close to zero. Since $J_{F\alpha}$ and $J_{F\beta}$ have the same sign, the molecules with virtual coupling are those producing the high-field α H triplet, which is accordingly broadened.

G. The methylene non-equivalence case

Although well known, this is mentioned briefly here as another situation in which an unexpectedly complex spectrum is obtained. An environment of low symmetry causes a doubling of the proton resonance lines of a methylene group, whose nuclei are rendered slightly non-equivalent. A similar effect can be observed in the methyl–proton doublet of an isopropyl group. Proximity to an asymmetric centre is a sufficient, but not necessary, condition for this, as there are several other situations in which non-equivalence can be observed. These have recently been reviewed by Martin and Martin.[46] As an example, methylene protons in a group R_1 are non-equivalent in compounds of type $CR_1R_1R_2R_3$ since they experience the effective asymmetry of the grouping $-(R_1R_2R_3)$. If the central carbon atom is replaced by other nuclei (e.g., S, P) a directed lone pair may replace R_2 or R_3. Non-equivalence of this kind should exist in a case of completely free internal rotation, although in practice much of the observed effect may be associated with a preferred conformation.

H. Computer methods

The principal, but by no means the only, application of electronic computation to n.m.r. is in the indirect analysis of a spectrum by iteration. The nature of indirect analysis is described earlier, with some remarks on its applicability *vis-à-vis* the direct approach. Some computer methods are now mentioned briefly, and for a comprehensive account the reader is referred to the recent discussion by Swalen.[4]

The simplest kind of programme used in n.m.r. analysis is for the straightforward calculation of the spectrum corresponding to a given set of parameters. Such a programme has two main uses. First, it is an efficient check on a direct analysis by calculating the relative line intensities, which is always tedious by longhand calculation. Second, and more important, it provides an exploratory trial-and-error way of getting rough agreement between calculated and experimental spectra as a starting point for iterative solution. Although the basic programme is straightforward, there is scope for ingenuity in the mode of presentation of the results, and in economical use of store capacity and computer time (the last factor is less important here than in iterative programmes where an unknown and possibly large number of computational cycles is involved). For example, the widely used LAOCOON II Part 1 of Castellano and Bothner-By[47] utilizes factorization according to total F_z values to reduce the order of the matrices, but the range of applicability can be significantly increased without further store requirements by introducing symmetry factorization as well. This is used by Woodman and Harris[48] in their programme UEANMR II, which increases the range typically from seven up to ten spin $\frac{1}{2}$ nuclei in spin systems with symmetry, and also permits inclusion of nuclei of spin $>\frac{1}{2}$. Various MRPLOT sub-routines allow presentation directly as a "stick" diagram (cf. calculated spectra in Fig. 6), or in tabular or continuous-line graphical form with a Lorentzian broadening function applied. A rather different histogram presentation is used by Wiberg and Nist.[15]

Indirect analysis of a spectrum by iteration may seek convergence either to the spectrum itself, or to a set of energy levels derived from it. The latter approach is used by Swalen and Reilly[22] in the programme NMREN, which derives the experimental energy levels from a given assignment of the spectrum, and NMRIT, which carries out the iteration from a set of starting parameters. A later modification takes account of symmetry.[68] Use of energy levels has an advantage in making one aware of ambiguous solutions that are associated with different line assignments. Also, an energy level is usually common to several spectral lines and so can be found to greater accuracy than a single line position. However, the necessity for at least partial line assignment makes the method often impracticable in complex cases, especially those of low symmetry. Of help in this respect is a recent programme (ASSIGN) that generates all line assignments compatible with the known intensity sum and spacing rules for a given spectrum.[49]

The same authors describe (*loc. cit.*) a procedure (DECOMP) for obtaining more accurate information about the intensity and position of overlapping lines than can be made by visual estimate. The latter provides the input data to a programme that calculates the line envelope corresponding to a given shape and width, compares this with the experimental line envelope, and varies the positions and intensities to optimize agreement. If this is inadequate, an additional line may be introduced in each region of discrepancy and the iteration repeated. A special feature is the selection of an empirical line shape best suited to the individual spectrum. Often this is neither exactly Gaussian nor Lorentzian even under ideal conditions, and also is rendered slightly asymmetric ("skewed") by the finite sweep rate of the recording.

The second method of indirect analysis is to seek convergence on selected features of the experimental spectrum. This has the great practical advantage of involving no line assignment (except in very general terms for selecting the starting parameters), and is often the only realistic approach to a complex spectrum. In principle, it is preferable to use line position and intensity data simultaneously during the iteration, as suggested by Arata *et al.*[23] and Yamamoto and Fujiwara,[24] but in practice the relatively low accuracy of n.m.r. intensity measurements has discouraged this. Most analyses have compared the calculated and experimental intensity pattern only as a final check on the solution. A widely used procedure of this type is that of Castellano and Bothner-By, as LAOCOON II part 2,[47] recently modified and combined with Part 1 as LAOCN3.[50] The speed of convergence has been shown to be comparable to that using the method of Swalen and Reilly, in cases where both are applicable.[51] Not all the experimental lines need be used in the iteration. Trial-and-error calculations are first necessary to select the starting parameters, and to obtain sufficient agreement with experiment to be able to recognize the theoretical counterparts of several experimental lines. The most useful experimental lines for this purpose are those that can be correlated with a single theoretical transition, sufficiently removed from any others of comparable intensity as to avoid possible confusion between them. In strongly coupled spectra, such lines are usually found in the outlying parts of the spectrum, since the strong central ones are superpositions of several components. The iteration is then carried out to a least-squares fit with the selected lines, and the rest of the spectrum, including the relative line intensities, is generated finally as a check on the solution. This leaves unanswered the vexed question of whether more than one set of parameters may reproduce the spectrum adequately, and an incorrect one accepted. Such ambiguity has been demonstrated occasionally in

ABC cases (see above), and cannot be ruled out in more complex cases. In the absence of further information one can at best adopt, in current parlance, a pragmatic approach; if the parameters reproduce a non-first-order spectrum adequately at several widely different magnetic fields, then it is very likely, if not certain, that they are correct.

Details of the iterative procedure vary with the programme. Typically, the partial derivatives $\partial\nu_i/\partial p_j$ are found in the region of the input parameters, i.e., the rate of change of the ith experimental feature to be used (here, line position ν_i) with the jth parameter p_j. For small, finite changes, one then assumes—

$$\Delta\nu_i = \frac{\partial\nu_i}{\partial p_j}\Delta p_j$$

At each cycle of the iteration, one seeks to correct each parameter by the amount required to produce agreement with experiment, i.e.—

$$\sum_j \frac{\partial\nu_i}{\partial p_j}\Delta p_j = (\nu_{\text{obs}} - \nu_{\text{calc}})_i$$

for each selected line position ν_i. In matrix form—

$$\mathscr{D}\Delta = N$$

where $\mathscr{D}$ is the $(i \times j)$ matrix of the partial differentials, Δ is a row matrix (vector) of corrections to the j parameters, and N is the column matrix of i line position errors.[47] As long as $i > j$, the equations are over-determined. If the initial guess is not a good one, it will be necessary periodically to recalculate the partial differentials. Usually, a best least-squares fit to the experimental features is sought rather than exact agreement.

I. Experimental aids to interpretation

The most significant instrumental advance of recent years has been the development of double resonance, now a routine technique. This has many applications in spectral analysis, and some are described briefly in this article. Multiple quantum transitions have also been mentioned. The major limitation of n.m.r. relative to other forms of spectroscopy has always been its low sensitivity, owing to the small differences in population in a thermal distribution of spins. Many possibilities for sensitivity enhancement have been reviewed recently by Ernst.[52] The technique likely to make most impact on routine n.m.r. work is that of time averaging to separate the signal from electronic noise. Many fast scans are stored in a computer attachment (CAT = Computer of Average Transients) and superimposed, when signals add coherently, but noise adds randomly and tends to cancel out. Assuming there is no coherence between the noise on successive scans, the resulting signal-to-noise ratio increases as the square root of the number of scans taken (see p. 227).

Isotopic substitution is a valuable technique in n.m.r. analysis, and is described in Emsley *et al.*,[1] p. 445 and Hoffman,[3] p. 548. It is used most often to simplify complex spectra, by removing certain magnetically active nuclei from the spin system (notably, replacement of H by D). Conversely, it is sometimes used to generate non-equivalence, converting a single line spectrum into a useful pattern. Satellite spectra, spectra due to magnetically active isotopes in low natural abundance (e.g., ^{13}C, ^{29}Si), are often conveniently used instead.

Variation in the external magnetic field or the solvent is used to alter the strength of coupling in a spectrum. The former has the advantage of altering the chemical shifts in a completely predictable manner, while leaving the coupling constants unchanged. A recent example of the use of a low magnetic field (1·5 kgauss) in determining the relative signs of coupling constants, is given by Moniz and Lustig.[53]

Differential solvent effects upon chemical shifts have often been used on an *ad hoc* basis to change the appearance of a spectrum and help in its interpretation. For example, change from an aliphatic to an aromatic solvent alters shifts by association, and pyridine-d_5 is a preferred solvent for steroids. The most systematic use of solvent effects in analysis has been made by Freeman and Bhacca,[54] who point out a close parallelism with double resonance in the production of line splittings and collapse by small successive changes in mixed solvent composition, and the very high degree of control one has in the latter. Freeman has also used temperature variation in a similar way.[55] Of recent interest is the use of optically active solvents by Pirkle[56] to obtain distinct ^{19}F and ^{1}H resonance spectra from the components of an enantiomeric mixture.

In principle, more information can be obtained from n.m.r. spectra in anisotropic conditions, where the directional character of the chemical shift would become apparent, and coupling interactions other than the simple scalar product $\bar{I}_i . \bar{I}_j$ would be involved. In solids, the direct "through-space" nuclear spin–spin interactions dominate to such an extent as to obscure all other information, but it is possible to create an anisotropic environment in solution. Application of a strong electric field gradient to a polar liquid, for example, can yield information about the absolute sign of coupling constants.[57] Treatment of such cases requires a more complicated Hamiltonian than "normal" n.m.r. spectra.[58] Of recent interest too is the discovery that compounds dissolved in the nematic "mesophase" of liquid crystal solvents yield highly resolved n.m.r. spectra in an anisotropic environment.[59] This technique has also been used for absolute sign determination.[60] Use of relative line widths has been mentioned earlier. If the lines are too narrow, they may be broadened by use of a viscous solvent or a paramagnetic species, such as DPPH, to ensure that their relative widths reflect differences in relaxation times. The relative broadening pattern depends on the dominant mechanism for spin relaxation and can be used to investigate this. If the latter is established, the method can be used both for relative and (in principle) absolute sign determination of coupling constants. Theory and application to some simple spin systems are discussed in recent papers.[61–64]

REFERENCES

1. J. W. Emsley, J. Feeney and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy", Vol. 1, Chap. 8, pp. 280–480, and (a) Appendix I, pp. 661–663. Pergamon, London, 1965.
2. P. L. Corio, "Structure of High Resolution N.M.R. Spectra". Academic Press, London, 1967.
3. R. A. Hoffman, *Pure Appl. Chem.*, 1965, **11**, 543.
4. J. D. Swalen, *Progr. N.M.R. Spectroscopy*, 1966, **1**, 205.
5. P. Diehl, R. F. Jones and R. K. Harris, *Progr. N.M.R. Spectroscopy*, 1968, **3**, 1.
6. R. A. Hoffman and S. Forsén, *Progr. N.M.R. Spectroscopy*, 1966, **1**, 15.
7. J. D. Roberts, "An Introduction to Spin–Spin Splitting in High Resolution N.M.R. Spectra". Benjamin, New York, 1961.
8. C. W. Haigh, private communication.
9. E. O. Bishop and C. N. Banwell, to be published.
10. E. G. Finer and R. K. Harris, *Mol. Phys.*, 1967, **12**, 461.
11. R. H. Bible, "Interpretation of N.M.R. Spectra, An Empirical Approach". Plenum Press, New York, 1965.
12. A. Carrington and A. D. McLachlan, "Introduction to Magnetic Resonance". Harper and Row, New York, 1967.
13. C. M. Woodman, *Mol. Phys.*, 1966, **11**, 109.
14. P. L. Corio, *Chem. Rev.* 1960, **60**, 363.
15. K. B. Wiberg and B. J. Nist, "Interpretation of N.M.R. Spectra". Benjamin, New York, 1962.
16. J. S. Waugh and E. L. Wei, *J. Chem. Phys.*, 1965, **43**, 2308.
17. E. O. Bishop, *Mol. Phys.*, 1965, **10**, 45.
18. R. G. Jones and R. L. Williams, *Spectrochim. Acta*, 1967, **23A**, 15.
19. P. Diehl, R. G. Jones and H. J. Bernstein, *Canad. J. Chem.*, 1965, **45**, 81.
20. P. Diehl and D. Trautmann, *Mol. Phys.*, 1966, **11**, 531.
21. R. C. Hirst, D. M. Grant and E. G. Paul, *J. Chem. Phys.*, 1966, **44**, 4305.
22. J. D. Swalen and C. A. Reilly, *J. Chem. Phys.*, 1962, **37**, 21.
23. Y. Arata, H. Shimizu and S. Fujiwara, *J. Chem. Phys.*, 1962, **36**, 1951.
24. T. Yamamoto and S. Fujiwara, *Bull. Chem. Soc. Japan*, 1966, **39**, 333.
25. W. Brügel, T. Ankel and F. Krückeberg, *Z. Elektrochem.*, 1960, **64**, 1121.
26. D. R. Whitman, *J. Mol. Spectroscopy*, 1963, **10**, 250.
27. S. Sudhanshu, *Proc. Indian Acad. Sci.*, 1961, **54A**, 13.
28. S. Castellano and J. S. Waugh, *J. Chem. Phys.*, 1961, **34**, 295; 1961, **35**, 1900.
29. X-T. Liang, *Sci. Sinica*, 1964, **13**, 589.
30. J. R. Cavanaugh, *J. Chem. Phys.*, 1963, **39**, 2378.
31. M. T. Emerson and S. M. Cohen, *J. Mol. Spectroscopy*, 1966, **20**, 159.
32. J. R. Cavanaugh, *J. Chem. Phys.*, 1964, **40**, 248.
33. R. K. Harris, *Canad. J. Chem.*, 1964, **42**, 2275.
34. R. K. Harris, *Inorg. Chem.*, 1966, **5**, 701.

35. R. K. Harris and C. M. Woodman, *Mol. Phys.*, 1966, **10**, 437.
36. E. G. Finer and R. K. Harris, *Mol. Phys.*, 1967, **12**, 457.
37. G. Mavel, *Progr. N.M.R. Spectroscopy*, 1966, **1**, 273.
38. D. J. Mowthorpe and A. C. Chapman, *Spectrochim. Acta*, 1967, **23A**, 451.
39. R. K. Harris, A. R. Katritzky, S. Musierowicz and B. Ternai, *J. Chem. Soc. A*, 1967, 37.
40. A. J. Carty and R. K. Harris, *Chem. Comm.*, 1967, 234.
41. P. Diehl, *Helv. Chim. Acta*, 1964, **47**, 1.
42. J. I. Musher and E. J. Corey, *Tetrahedron*, 1962, **18**, 791.
43. P. Diehl, 1965, private communication.
44. A. A. Khan, S. Rodman and R. A. Hoffman, *Acta. Chem. Scand.*, 1967, **21**, 63.
45. D. C. Hooper, N. Sheppard and C. M. Woodman, *J. Chem. Phys.*, 1966, **45**, 398.
46. M. L. Martin and G. J. Martin, *Bull. Soc. chim. France*, 1966, 2117.
47. S. Castellano and A. A. Bothner-By, *J. Chem. Phys.*, 1964, **41**, 3863.
48. C. M. Woodman and R. K. Harris, 1967, private communication.
49. W. D. Keller, T. R. Lusebrink and C. D. Sederholm, *J. Chem. Phys.*, 1966, **44**, 782.
50. A. A. Bothner-By and S. Castellano, 1967, private communication.
51. Y. Kato and A. Saika, *J. Chem. Phys.*, 1966, **44**, 2824.
52. R. R. Ernst, *Adv. Magnetic Resonance*, 1966, **2**, 1.
53. W. B. Moniz and E. Lustig, *J. Chem. Phys.*, 1967, **46**, 366.
54. R. Freeman and N. S. Bhacca, *J. Chem. Phys.*, 1966, **45**, 3795.
55. R. Freeman, *Mol. Phys.*, 1966, **11**, 505.
56. W. H. Pirkle, *J. Amer. Chem. Soc.*, 1966, **88**, 1837; T. G. Burlingame and W. H. Pirkle, *ibid.*, 4294.
57. A. D. Buckingham and K. McLauchlan, *Proc. Chem. Soc.*, 1963, 114.
58. A. D. Buckingham and J. A. Pople, *Trans. Faraday Soc.*, 1963, **59**, 2421; J. D. Macomber and J. S. Waugh, *J. Chem. Phys.*, 1965, **45**, 985.
59. L. C. Snyder, *J. Chem. Phys.*, 1965, **43**, 4041; G. R. Luckhurst, *Österr. Chem.-Ztg.*, 1967, **68**, 113.
60. A. Saupe and G. Englert, *Phys. Rev. Letters*, 1964, **11**, 462; A. Saupe, *Z. Naturforsch*, 1965, **19A**, 161; **20**, 572.
61. R. M. Lynden-Bell, *Proc. Roy. Soc.*, 1965, **286A**, 337.
62. R. M. Lynden-Bell, "Molecular Relaxation Processes", Chemical Society Special Publication No. 20, 1966, p. 151.
63. J. M. Anderson, *Mol. Phys.*, 1964, **8**, 505.
64. P. W. Atkins, R. A. Dwek, J. G. Kenworthy and R. E. Richards, *Mol. Phys.*, 1967, **12**, 125.
65. H. Suhr, "Anwendungen der Kernmagnetischen Resonanz in der Organischen Chemie", pp. 71–73. Springer-Verlag, Berlin, 1965.
66. D. M. Grant, R. C. Hirst and H. S. Gutowsky, *J. Chem. Phys.*, 1963, **38**, 470.
67. D. M. Grant and H. S. Gutowsky, *J. Chem. Phys.*, 1961, **34**, 699; R. C. Hirst and D. M. Grant, *J. Chem. Phys.*, 1964, **40**, 1909.
68. R. C. Ferguson and D. W. Marquardt, *J. Chem. Phys.* 1964, **41**, 2087.

Heteronuclear Magnetic Double Resonance

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I. INTRODUCTION

In a magnetic double-resonance experiment transitions between the energy levels of a nuclear spin system are studied in the presence of two oscillatory r.f. fields. Detection is usually performed at the same frequency as one of these fields, which will be referred to as the observing field, and the transitions irradiated by this field will be those of the observed nucleus. The second r.f. field will be applied generally at or near the resonant frequency of another nucleus in the system. In tightly coupled spin systems these distinctions between the observed and other nuclei may not be valid.

The terms homonuclear and heteronuclear are used according to whether the observed and other irradiated nucleus are of the same or different species. In practice this means that two different magnetogyric ratios are involved in heteronuclear double resonance, so that the chemical shift between the observed and other irradiated nucleus will always be large.

Comprehensive reviews of the theory and practice of magnetic double resonance have been published by Baldeschwieler and Randall,[1] and by Hoffman and Forsén,[2] and there is a short review by Evans.[3] The first of these reviews is devoted mainly to heteronuclear experiments and the second mainly to proton–proton double resonance. In the present article attention will be concentrated on chemical applications of heteronuclear double resonance.

A. Terminology

The static magnetic field will be denoted by H_0, the observing field by H_1 and the other r.f. field by H_2. ν_1 and ν_2 will be used for the frequencies of H_1 and H_2, respectively. A convenient descriptive notation introduced by Baldeschwieler and Randall[1] is: A–{X}, where ν_1 is close to the resonant frequency of nucleus A and ν_2 is close to the resonant frequency of X. The term decoupling will be applied to experiments in which H_2 brings about a complete collapse of the multiplet structure displayed by the A resonance as a result of spin–spin coupling to X. The term tickling will be used when individual transitions of the X nucleus are selectively irradiated.

B. Instrumentation

Several groups of workers have constructed spectrometers specifically intended for heteronuclear double-resonance experiments,[4] but for general chemical purposes it is probably more convenient to use a modified version of a commercial instrument.[5,6,7] The second r.f. field, H_2, may be introduced into the probe either by winding an extra transmitter coil,[4] or by double-tuning the existing transmitter coil.[8,9] In the latter case it is necessary to incorporate a blocking circuit with a high dynamic impedance at ν_1 to isolate the r.f. oscillator of the spectrometer from the source of H_2. A circuit[9] that has been used in conjunction with the Varian HA 100 spectrometer is shown in Fig. 1.

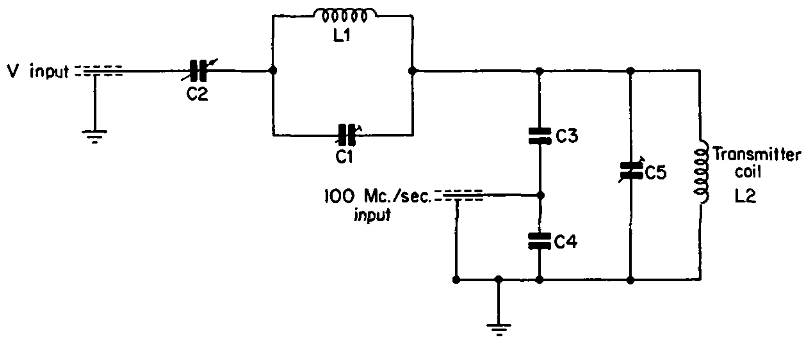

FIG. 1. Circuit diagram for double tuning of probe of Varian HA 100 spectrometer.

The most satisfactory source of the second r.f. is a frequency synthesizer such as the Rohde and Schwarz model XUA or the Schomandl ND30M. Ideally the master oscillators of the spectrometer and the frequency synthesizer should be locked together, otherwise drifts of one relative to the other will reduce the potential accuracy of the experiments. Systems for doing this have been described by Freeman[10] and by Charles[11] (see Figs. 2 and 3). It is also possible to derive

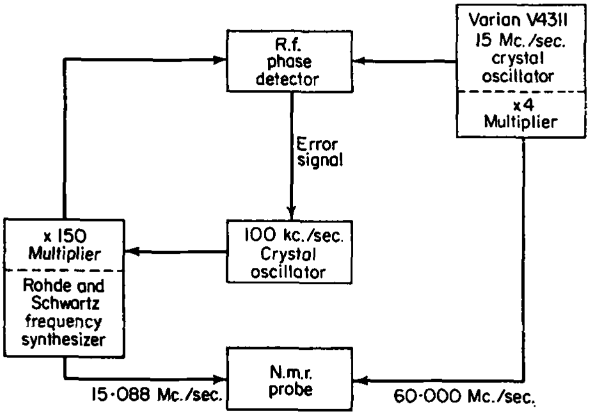

FIG. 2. Block diagram of a system used to drive proton and ^{13}C excitation frequencies from the master 15 Mc./sec. crystal controlled oscillator. (From Freeman.[12])

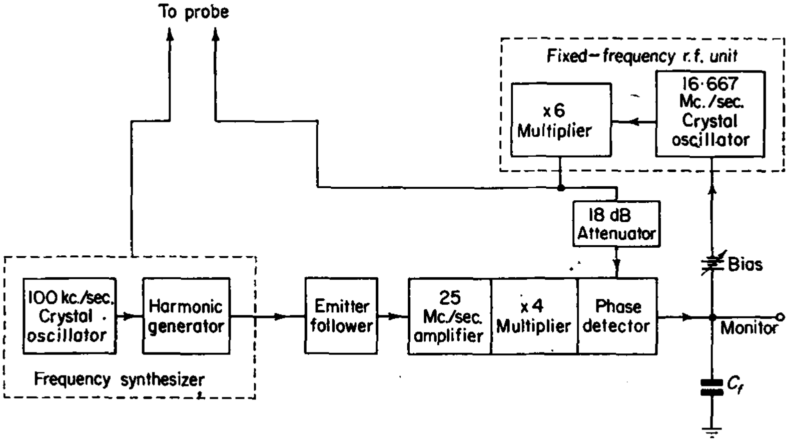

FIG. 3. Block diagram of locked oscillator system due to Charles[11] using the Varian HA 100 spectrometer and a Rohde and Schwarz frequency synthesizer model XUA.

H_2 from a very stable r.f. oscillator (preferably locked to the oscillator of the spectrometer) which is frequency modulated by an r.f. oscillator to give a variable sideband at the appropriate frequency for the double-resonance experiments.[5] Allen *et al.*[13] have used an ingenious method of frequency division together with modulation to obtain H_2 from the master oscillator of the spectrometer. This avoids the need for separate locking circuits, but the simplicity of the overall circuitry depends on the ratio γ_A/γ_X of the magnetogyric ratios of the two nuclear species.

C. The effect of the second r.f. field

If H_2 is sufficiently large its effect will be to wash-out the spin coupling between A and X, so that the resonance due to A will appear as a single line rather than as a multiplet. This has been regarded as a saturation phenomenon, but this view is incorrect, since the condition for complete decoupling is that $J_{A-X} < \gamma_X H_2/2\pi$, whereas for saturation the condition is—

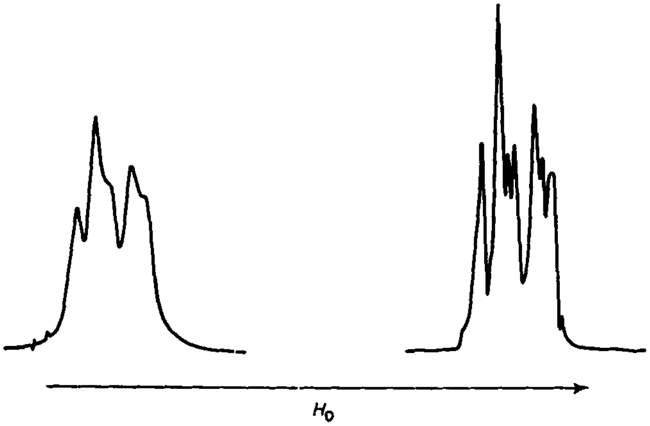

FIG. 4. α Proton resonance of pyridine (pure liquid) at 40 Mc./sec. without and with double resonance. (From Baldeschwieler and Randall.[14])

$$\gamma_X^2 H_2^2 (T_1 T_2)_X \gg 1$$

Although complete decoupling is commonly used in homonuclear ^1H-$\{^1H\}$ experiments where the coupling constants seldom exceed 20 c./sec. and it is easy to generate adequate r.f. fields in the probe, it is often difficult to apply a sufficiently large H_2 to completely wash-out the large couplings that are sometimes found in heteronuclear systems. Heteronuclear double-resonance experiments of the type ^1H-$\{X\}$ involving large values of H_2 are of greatest use when X has a spin greater than ½. Quadrupole relaxation effects, associated with X may then cause broadening of the lines in the ^1H spectrum and features of interest may be obscured. Irradiation at the frequency of the X resonance will remove this broadening in addition to washing-out the coupling J_{X-H}. An example of this for $X = {}^{14}N$ ($I = 1$) in pyridine is shown in Fig. 4.

Double-resonance experiments of the type X-$\{^1H\}$ with a field large enough to remove the X–H coupling is often useful when detection of the signals due to

X is difficult, as the entire intensity of the X resonance can then be concentrated into a single line.

It is important to distinguish between the results of field-sweep and frequency-sweep double-resonance experiments. In much of the earlier work, the A spectrum was recorded by sweeping H_0 and maintaining H_1 and H_2 constant. Consequently the position of H_2 relative to the resonant frequency of X varies throughout the experiment, and the interpretation of the results may not be simple. This may not be a serious drawback in experiments in which H_2 is large and H_0 is swept over only a small range to record the relevant part of the A spectrum. However, if smaller values of H_2 are used so as to selectively irradiate different parts of the X spectrum it is desirable to hold H_0 constant and record the A spectrum by sweeping H_1. The advent of spectrometers employing audiomodulation of the magnetic field and of field-frequency locking systems has made frequency-sweep experiments readily available, and this mode of operation should be used whenever possible. If it is necessary to operate in field-sweep mode some of the difficulties of interpretation can be avoided by sweeping H_2 as H_0 is varied, so ν_2 maintains the same relationship to the resonant frequency of X throughout the experiment.

It is also possible to perform a double-resonance experiment in which H_0 and H_1 are kept constant (usually at values that correspond to an A transition) and H_2 is varied. This kind of experiment has been termed INDOR (internuclear double resonance) and requires some form of field-frequency stabilization to maintain the correct relation between H_0 and H_1. It is also necessary to use rather low levels of H_1 in order to avoid saturation of the A nuclei.

When the amplitude of H_2 is less than is needed for complete decoupling quite complicated spectra result. Baldeschwieler[15] has calculated the spectra expected in the A_nX case for values of $\gamma_X H_2/2\pi \sim 0{\cdot}2\ J_{AX}$, and has obtained confirmation of the theory from experiments on $^{14}NH_4^+$ and $^{15}NH_4^+$. The spectra obtained in field-sweep experiments are more sensitive to small variations of H_2 in the neighbourhood of an X transition than those obtained by sweeping H_1. Consequently more accurate values of the chemical shift of X can be obtained from field-sweep experiments when intermediate amplitudes of H_2 are used. The results to be expected from double-resonance experiments using intermediate amplitudes of H_2 have been presented graphically by Anderson and Freeman[16] for A_mX_n systems where m and n can range from 1 to 3. It is convenient to define two dimensionless parameters—

$$\Delta = (\nu_2 - \nu_X)/J_{AX} \quad \text{and} \quad \Omega = (\nu_1 - \nu_A)/J_{AX}$$

and Fig. 5 shows the transition probabilities and frequencies as a function of the offset parameter for an AX system when $\gamma_X H_2/2\pi = 0{\cdot}2\ J_{AX}$. We can predict the results of a frequency-sweep experiment (i.e., H_0 and Δ constant) by drawing a vertical line at the appropriate value of Δ; the intercepts of this line with the curves of Fig. 5 then give the frequencies (in terms of Ω) and transition probabilities of the lines that will be observed in the A spectrum. An INDOR experiment (i.e., H_0 and Ω constant) would be represented by a horizontal line at height Ω; and a field-sweep experiment by a line of slope γ_A/γ_X and passing through the point $\Omega=0$, $\Delta=[(\nu_A-\nu_X)-(\nu_1-\nu_2)]/J_{AX}$.

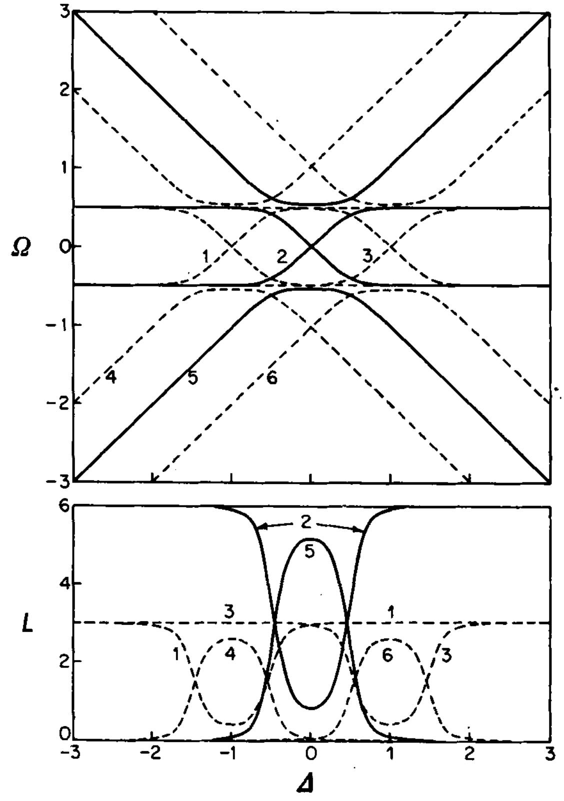

Fig. 5. The transition frequencies Ω and intensities L of the A resonance plotted against the offset parameter Δ for an AX system (full lines) and an A_3X system (full and broken lines) for $H_2/2\pi=0{\cdot}2J$. (From Anderson and Freeman.[16])

D. Tickling

If H_2 is very weak the results of a frequency-sweep double-resonance experiment will be indistinguishable from those of a single-resonance one unless $|\Delta|\sim 0{\cdot}5$; that is unless H_2 is set very close to an X transition. In these circumstances it is often possible to irradiate selectively individual transitions of the X nucleus and the description of the results is particularly simple. This is the procedure known as "tickling", and Freeman and Anderson[17] have again presented the results graphically and formulated a set of generally applicable rules. These are—

1. Any transition that has an energy level in common with the transition excited by H_2 will be split into a doublet.

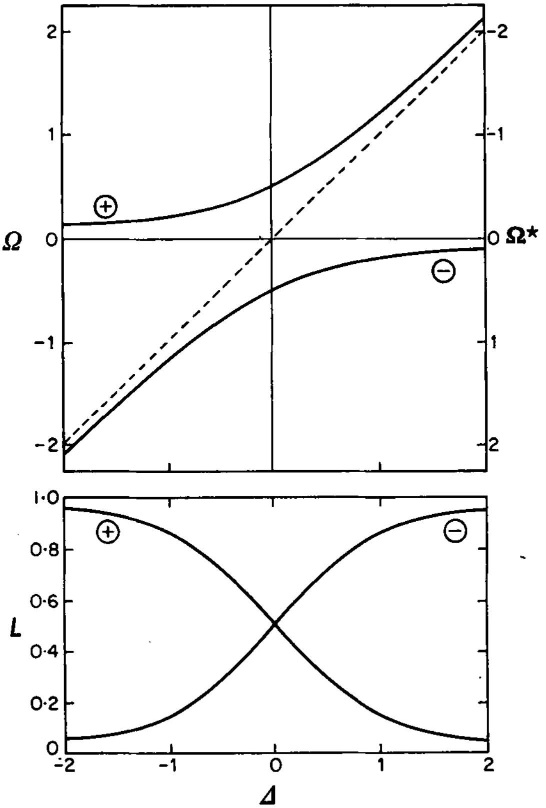

Fig. 6. The transition frequencies Ω and relative intensities L of the two components of the doublet observed when a weak r.f. field is applied near a second transition which has a common energy level. This is for the situation $\Lambda = 0$, while for $\Lambda = 2$ the reversed scale Ω^* should be used. The amount by which the second r.f. field is off resonance is represented by Δ. (From Freeman and Anderson.[17])

2. Of the three energy leads involved one is common; of the other two the spin quantum numbers must either be the same or differ by two units. In the former case the doublet will be well resolved, and in the latter poorly resolved, provided that the line-width of the observed spectrum is governed by the magnetic field inhomogeneity.
3. The magnitude of the splitting in the well resolved doublets is proportional

to the amplitude of H_2 and the square root of the intensity of the line perturbed by H_2.

The diagrams of Fig. 6 can be used to obtain the positions and intensities of the two components of the doublet produced when H_2 is offset from the line perturbed in the X spectrum. In this case the dimensionless parameters Δ and Ω are defined by—

$$\Delta = (\nu_2 - \nu_X)/2\gamma_X H_2 \lambda_X$$

and

$$\Omega = (\nu_1 - \nu_A)/2\gamma_X H_2 \lambda_X$$

where λ_X is the transition probability of the perturbed X transition. Note that J_{AX} does not enter into these expressions; the size of J_{AX} is important only in determining how large an amplitude of H_2 may be used without perturbing more than one X transition.

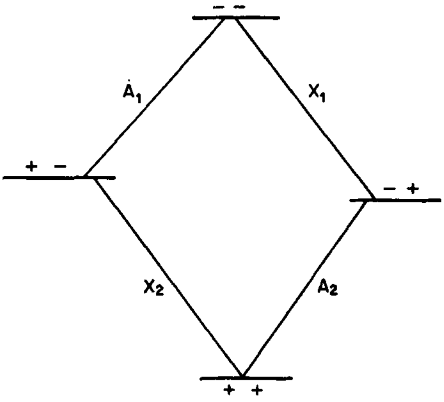

FIG. 7. Energy-level diagram for an AX system in which A and X are of spin $I = \frac{1}{2}$, and have magnetogyric ratios of the same sign.

The application of rule 2 can be illustrated by considering Fig. 7, which shows the energy-level diagram for an AX spin system in which both A and X have spin $I = \frac{1}{2}$. By rule 1 irradiation of line X_1 with a weak field should split lines A_1 and A_2 into doublets. The energy level that A_1 and X_1 have in common is $[- -]$, and the other two energy levels ($[+ -]$ and $[- +]$) involved with this pair of transitions have the same spin quantum number. Such a pair of transitions are said to be regressive, and by rule 2 the doublet splitting of A_1 should be well resolved. A_2 and X_1 have $[- +]$ as their common energy level, and the two remaining energy levels ($[- -]$ and $[+ +]$) differ in spin quantum number so that the doublet splitting of A_2 should be poorly resolved. Transitions related in this way are said to be progressive.

In many applications of heteronuclear double resonance no additional information is gained by distinguishing between progressive and regressive transitions, but it is possible to obtain optimum tickling frequencies more accurately by measurements on regressive pairs of transitions.

An important effect of the second irradiating field in double-resonance experiments in general is to change the populations of the energy levels involved. This has been called a generalized Overhauser effect by Hoffman and Forsén,[2] and the reader is referred to these authors for a full discussion. A proper quantitative treatment is complicated because the results depend on the relaxation mechanism of the different nuclei involved, but for heteronuclear experiments of the type ^1H–{X} the effects can often be ignored. This is because the relaxation time of the X nucleus is frequently much longer than that of the proton, and in these circumstances saturation of an X transition will have little effect upon the line intensities in the ^1H spectrum. If the relaxation time of X is shorter than or at any rate comparable with that of ^1H, nuclear Overhauser effects will be observed in the proton spectrum.[18]

The nuclear Overhauser effect may be useful in X–{^1H} experiments as a welcome increase in the intensity of the X lines can often be achieved. Thus Paul and Grant[19] have improved ^{13}C signal-to-noise ratios by using proton double irradiation; not only is all the intensity concentrated in a single line by multiplet collapse, but an Overhauser enhancement is also obtained.

II. SPECIFIC APPLICATIONS

The earlier literature has been covered well by Baldeschwieler and Randall,[1] and attention here will be restricted to more recent developments. We shall classify the results according to the type of experiment performed rather than by the particular nuclei involved.

A. Experiments involving large values of H_2

Most of the experiments considered by Baldeschweiler and Randall[1] were of this type, and the object generally was to remove the effects of quadrupole broadening. It is common practice to simplify the spectra of fairly large organic molecules by deuterium labelling; this procedure has the disadvantage that the ^1H spectrum of the deuterated compound may still be complicated by the effects of ^1H–^2D spin coupling, and this undesirable feature can be removed by irradiation at the ^2D resonant frequency. Since deuterium-to-proton coupling constants are smaller than proton–proton ones by a factor of 0·154 it is never necessary to wash-out couplings of more than ca. 3 c./sec. and quite moderate levels of H_2 can be used. In this way undesirable heating effects are avoided. Alternatively a less stable source of the deuterium frequency may be used and adequate amplitude will still be attainable.

Typical of the use to which deuterium double irradiation has been put is Anet and Hartman's ^{1}H-{^{2}D} experiments[20] which simplified the spectrum of deuterated cyclo-octane, $C_8H_{15}D$, and so enabled the value of 8·1 kcal./mole. for the free energy of activation of the inversion process to be obtained. The inversion process in cyclohexane has been studied similarly by Bovey *et al.*, and typical spectra[21] are shown in Fig. 8. In this case the work was extended to cover cyclohexyl fluoride in which the greater chemical-shift difference between the axial and equatorial positions of the ^{19}F nucleus enabled the inversion process to be followed over a wider temperature range. Irradiation at the proton resonance frequency was used to simplify the ^{19}F spectra. It is necessary to exercise care in extracting quantitative data from decoupled spectra as the application of the second r.f. field can cause shifts in the position of the lines in the observed spectrum.[22, 23]

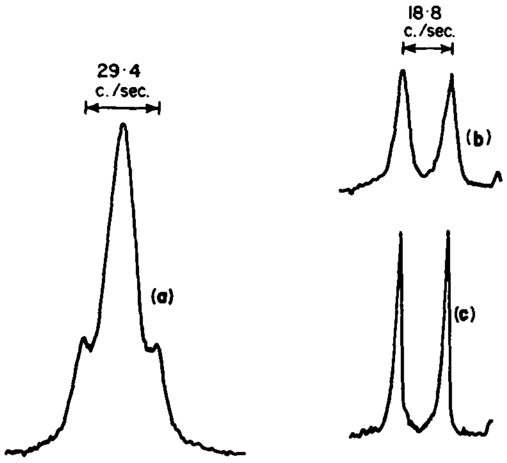

FIG. 8. Cyclo-octane at −135°C; (a) C_8H_{16}; (b) $C_8D_{15}H$; (c) $C_8D_{15}H$, D decoupled. (From Anet and Hartman.[20])

Both naturally occurring isotopes of boron (^{10}B, $I=3$, abundance 18·8%; ^{11}B, $I=\frac{3}{2}$, abundance 81·2%) have nuclear quadrupole moments, and the relaxation effects of these complicate the interpretation of both the ^{1}H and the ^{11}B spectra of boranes and related compounds. The classic work in this field is that of Shoolery[24] who used ^{11}B irradiation to simplify the proton spectrum of diborane and show the presence of two kinds of proton (bridging and terminal) in the expected 1:2 ratio. Shoolery[24] also used ^{11}B irradiation to show that the four components of the ^{1}H spectrum of sodium borohydride arise as a result of spin coupling between ^{1}H and ^{11}B.

More recently Lindner and Onak[25] have used ^{11}B decoupling to simplify the proton spectra of alkyldiboranes and to check assignments. Vickers *et al.*[26] have used ^1H decoupling experiments to improve the quality of ^{11}B spectra. *p*-Carborane ($C_2B_{10}H_{12}$) is an icosahedral network of boron atoms which incorporates two carbon atoms at opposite ends of a diameter. Its ^{11}B spectrum at 19·3 Mc./sec. is a 1:1 doublet with a separation of 166 c./sec. which is collapsed to a single line by irradiation at the proton resonant frequency (60 Mc./sec.). This indicates that the 166 c./sec. splitting is due to ^{11}B–^1H spin coupling and that all the boron atoms are equivalent, a result which was confirmed by obtaining the boron spectrum at 64·12 Mc./sec. (using a cryogenic magnet) when the splitting was unchanged. The *o*- and *m*-carboranes have more complicated ^{11}B spectra and ^1H decoupling enabled tentative assignments to be made.

An interesting application of double resonance to boron n.m.r. is the work of Norman and Schaeffer[27] on Na^+ $B_3H_8^-$ and B_4H_{10}. They used samples enriched in ^{10}B, so that the two isotopes were present in comparable amounts, and used ^{11}B–^{10}B experiments to confirm the existence of ^{11}B–^{10}B coupling. Some typical results are shown in Fig. 9. It was not possible to determine the magnitude of $J_{(^{11}B-^{10}B)}$ from the experiments.

Muetterties and co-workers[28–30] have made extensive use of boron and ^1H decoupling experiments in their work on icosahedral boron compounds, and the ^{11}B spectrum of tetraborane has been analysed with the aid of proton decoupling.[31]

The use of proton spin decoupling for improving the intensity of ^{13}C spectra has already been mentioned,[19] and the technique has also been used by Dhami and Stothers[32] in studies of acetophenones and styrenes; further details can be obtained from the review of ^{13}C n.m.r. spectroscopy by Stothers.[33]

The proton spectra of nitrogen-containing compounds are often broadened by the quadrupole moment of ^{14}N (spin $I=\frac{1}{2}$, abundance 99·5%) and double irradiation at the ^{14}N resonant frequency can be used to improve their quality. Examples of this technique are Rochow's work[34] on silicon–nitrogen compounds, and Kamei's study[35] of amides. Irradiation with a ^{14}N field large enough to raise the sample temperature by 35°C was used by Castellano *et al.*[36] as a preliminary to a complete AA′BB′C analysis of the ^1H spectrum of pyridine, and the subject is also dealt with in an article in *Chemical and Engineering News*.[37] Figure 4 shows the ^1H spectrum of pyridine with ^{14}N decoupled.

The foregoing examples of double-resonance experiments involving non-selective irradiation of the X transitions are not intended to form a complete list; rather an attempt has been made to indicate the kind of problem in which the technique may be helpful.

B. The measurement of chemical shifts

One of the main difficulties encountered in the measurement of chemical shifts of nuclei other than ^1H and ^{19}F is the low sensitivity to n.m.r. detection of most

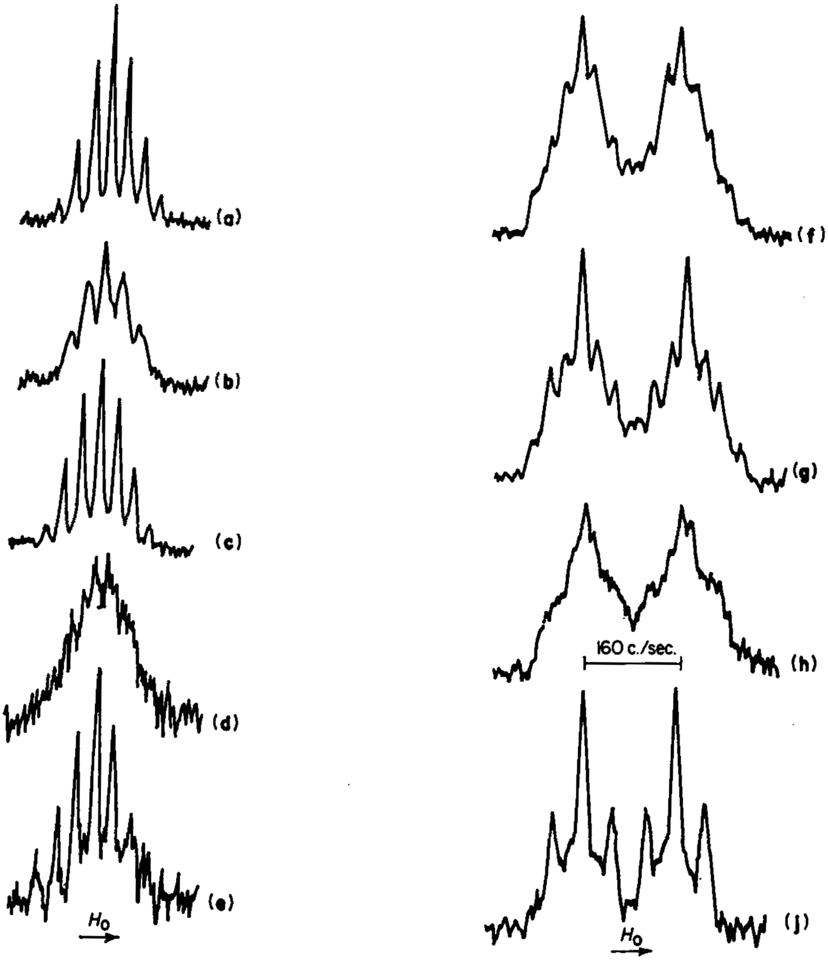

FIG. 9. (*a*)–(*e*). ^{11}B n.m.r. spectra. NaB_3H_8–diethyl ether solution; (*a*), 2% ^{10}B–98% ^{11}B; (*b*), 61% ^{10}B–39% ^{11}B; (*c*), 61% ^{10}B–39% ^{11}B, ^{11}B–$\{^{10}B\}$ decoupled; (*d*), 85% ^{10}B–15% ^{11}B; (*e*), 85% ^{10}B–15% ^{11}B, ^{11}B–$\{^{10}B\}$ decoupled. (*f*)–(*j*). ^{11}B n.m.r. spectra of B_4H_{10}; (*f*), 18·8% ^{10}B–81·2% ^{11}B; (*g*), 18·8% ^{10}B–81·2% ^{11}B, ^{11}B–$\{^{10}B\}$ decoupled; (*h*), 61% ^{10}B–39% ^{11}B; (*j*), 61% ^{10}B–39% ^{11}B, ^{11}B–$\{^{10}B\}$ decoupled. (From Norman and Schaeffer.[27])

nuclei compared with the proton. Typical values of relative sensitivities at constant field are: ^1H, 1·00; ^{13}C, 0·016; ^{14}N, 0·001; ^{31}P, 0·07. Further, many nuclei have unfavourable relaxation times and are readily saturated. By observing the proton (or ^{19}F) spectra of compounds that contain the nucleus of interest coupled to ^1H, and simultaneously irradiating at the resonant frequency of the other nucleus, it is possible to use the inherent sensitivity and favourable relaxation time of the proton for the determination of the heteronuclear parameters. In favourable cases, line positions can be determined to better than ±0·1 c./sec. by this method, and the only requirement is that the ^1H spectrum should display spin-coupling to the nucleus of interest. So far most of the work has been done on ^{13}C and ^{14}N chemical shifts, but it is likely that the method will be valuable for many nuclei.

Becconsall and Hampson[38] have examined ^{13}C chemical shifts of the methyl group in the polar molecules methyl iodide and acetonitrile dissolved in various solvents, and were able to get results to ±2 c./sec. (0·08 p.p.m.) at concentrations as low as 10% molar with specimens containing ^{13}C in natural abundance (1·1%). Matthias and Hampson[39] have also studied the ^{14}N shifts of amides in various solvents, although in this case the precision of the measurements was reduced by the broadening of both the ^1H and the ^{14}N lines owing to the quadrupole of the ^{14}N. Other ^{14}N work is by Baldeschwieler and Randall,[14] and Stothers and Robinson[40] have measured ^{31}P chemical shifts in organophosphorus compounds by irradiating at the ^{31}P resonant frequency.

There are occasional examples of applications of the technique to other nuclei: the ^{129}Xe chemical shift[41] in $XeOF_4$ is 274 p.p.m. to the high field of that in XeF_4; the ^{195}Pt chemical shift[42] of *cis*-$(Et_3P)_2PtCl_2$ is 552 p.p.m. to the high field of the *trans* isomer; the ^{207}Pb chemical shift[43] of Me_4Pb is 62 p.p.m. to the high field of Et_4Pb. It is not even essential to identify completely the origins of the lines in the proton spectrum to obtain useful results. Thus Davies *et al.*[44] have obtained ^{119}Sn chemical shifts to ±1 p.p.m. in $(C_4H_9)_2SnCl_2$ and related compounds, even though it was not clear whether the observed ^1H lines were given by the α or the β protons of the butyl groups. It must be borne in mind that solvent effects can be very large for the heavier nuclei, and it is doubtful whether measurements of chemical shifts to closer than say 1 p.p.m. are of much value.

The question of the best way of presenting chemical-shift data has received some attention, but as yet general agreement has not been reached. Apart from the obvious course of referring the observed frequencies to one of the accepted standards for the particular nucleus concerned, there is the attractive possibility of relating the resonant frequencies of all nuclei to a single standard. A popular choice for this standard is the resonance of the protons in tetramethylsilane, and this has been used by Freeman and Anderson[17] who quote $\nu(^{13}C)/\nu(^1H_{TMS}) = 0{\cdot}251{,}462{,}230 \pm 0{\cdot}000{,}000{,}003$ for $CHBr_2CHBr_2$. The data needed to deduce this ratio for ^{13}C in TMS itself have been given by McLauchlan,[45] and for ^{29}Si by Dean and McFarlane.[46] The advent of commercial spectrometers operating at a proton frequency of 100 Mc./sec. and equipped with field-frequency stabilization makes it convenient to quote the data in the form of the resonant frequency of the nucleus in a magnetic field of a strength corresponding to a TMS proton resonance at exactly 100 Mc./sec. The raw data will often be obtained in a field slightly different from this and the conversion formula—

$$
\begin{aligned}
X_{TMS} &= 10^8 X_{obs}/(10^8+f-100\delta) \\
&\approx X_{obs}(1-(f-100\delta)/10^8)
\end{aligned}
$$

may be used. Here X_{TMS} is the required frequency at a field corresponding to a TMS proton resonance of exactly 100 Mc./sec.; X_{obs} is the resonant frequency actually recorded; δ is the chemical shift relative to TMS of the protons used to supply the signal that actuates the field-frequency locking circuits (i.e., $\delta = 10 -$ the τ value); and (10^8+f) is the frequency at which this locking signal is obtained. The above formula is applicable to results obtained either by INDOR (H_0 and ν_1 constant) or by frequency-sweep (H_0 and ν_2 constant in a particular run) experiments. δ, the chemical shift of the locking compound, is included in the above formula because it is not always convenient to add T.M.S. to the sample. Errors in the value of δ are seldom important, as they are unlikely to exceed 1 p.p.m. and will affect the chemical shift of X by just this amount.

TABLE I

Values of X_{TMS} for selected nuclei

Nucleus	Compound	Conditions	X_{TMS}, c./sec.	Reference
^{13}C	$CH_3{}^{13}COOH$*	..	25,149,280	45
^{14}N	CH_3NC	Neat	7,224,570	47
^{29}Si	$(CH_3)_4Si$	Neat	19,867,220	46
^{31}P	85% H_3PO_4*	..	40,480,740	48
^{77}Se	$(CH_3)_2Se$	Neat	19,097,550	49
^{125}Te	$(CH_3)_2Te$	Neat	31,539,860	49
^{117}Sn	$(CH_3)_4Sn$	20% CCl_4	35,632,290	50
^{119}Sn	$(CH_3)_4Sn$	20% CCl_4	37,290,660	50
^{195}Pt	*cis*[$(Et_3P)_2PtCl_2$]	CH_2Cl_2 solution	21,401,000	42
^{199}Hg	$(CH_3)_2Hg$	Neat	17,910,670	51
^{207}Pb	$(CH_3)_4Pb$	Neat	20,920,680	43

The chemical shifts of the heavier elements are often very large and may occasion a rather lengthy initial search procedure, particularly as accurate values of the magnetogyric ratios may not be available. Table I is a collection of values of X_{TMS} for different nuclei assembled from various sources. It is not intended to be definitive, but may serve to reduce the time needed to locate the resonant frequencies of certain nuclei.

In several cases (indicated by an asterisk) the data were not obtained by a double-resonance experiment performed on the compound quoted, but known values of chemical shifts obtained by single resonance were used to relate measured frequencies to those given in the Table. It must be remembered that a change in the chemical shift of a particular nucleus to higher field will result in a decrease in the value of X_{TMS}

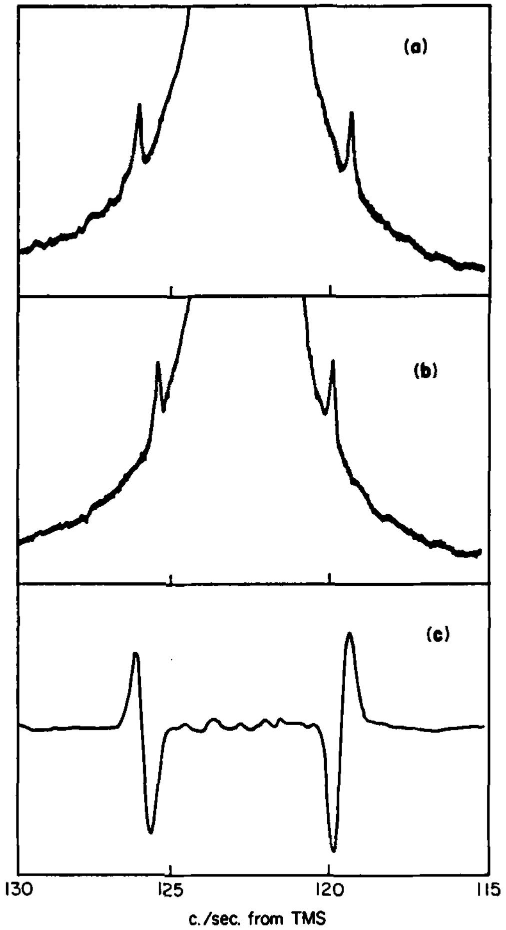

FIG. 10. Methyl proton resonance of acetic acid: (a), unperturbed spectrum; (b), with ^{13}C irradiation; (c), with pulsed ^{13}C irradiation. (From Freeman.[53])

One of the most attractive features of the double-resonance method of measuring chemical shifts is that a single suitably modified spectrometer can be used for all nuclei, only provided that the ^{1}H (or ^{19}F) spectrum of the compound studied displays X–^{1}H (X–^{19}F) spin coupling. In many compounds containing rare isotopic species of low atomic number (especially ^{13}C) the satellite lines of interest in the proton spectrum may be hidden by the strong signal that is given by the protons in molecules containing non-magnetic isotopes of X. Anderson[52] has shown that if H_2 is modulated at, say, 2000 c./sec. the effects of this modulation will be transferred only to the resonance of protons in molecules that contain the magnetic species. In the particular case of carbon, most protons are associated with ^{12}C atoms, and their resonance is unaffected by the modulation. The resonance of protons associated with ^{13}C atoms is modified by the modulation, and by employing a suitable detection technique it is possible to observe signals derived from them only. Such an arrangement has been described as an "isotope filter". In the slow-pulse modulation technique of Freeman,[53] H_2 is switched on and off at 2-sec. intervals (i.e., it is modulated with a square wave of frequency 0·25 c./sec.) and the output to the spectrometer recorder is continually inverted in phase with the pulsing of H_2. A long time constant filter (say 10 sec.) is included in the recorder output so that the proton signal from molecules that are unaffected by H_2 (i.e., those containing no ^{13}C) is effectively cancelled to zero. If H_2 is at or near a ^{13}C transition, the associated proton lines will be of different appearance according as to whether H_2 is off or on, and will not be cancelled out by the recorder arrangements. Experiments may be performed either by keeping ν_2 constant and sweeping H_1, in which case the "hidden" ^{13}C proton satellite lines will be brought to light, or by an INDOR technique in which ν_1 is maintained constant at a position corresponding to one of the "hidden" satellite lines and H_2 is swept; the excursions of the recorder pen then represent the ^{13}C spectrum. Typical results are presented in Figs. 10 and 11. In Fig. 10(a) the proton resonance

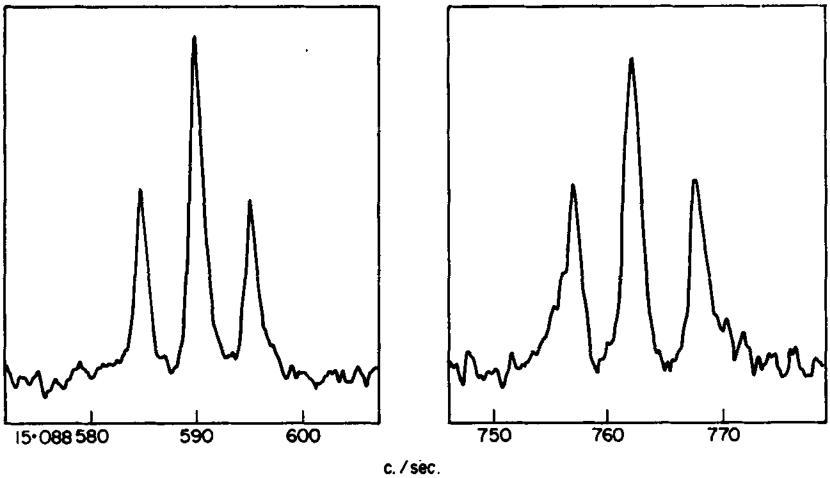

FIG. 11. ^{13}C Index spectrum of 1,3,5-$C_6H_3Cl_3$ using slow-pulsed modulation. (From Freeman.[53])

of acetic acid in the region of the methyl group is shown. The two ^{13}C satellite lines arising from molecules $CH_3{}^{13}COOH$ are in fact not quite "hidden", but this serves to make the explanation of the experiment clearer. In Fig. 10(b) irradiation of ^{13}C off-resonance causes the satellites to move in towards the centre. In Fig. 10(c), H_2 is slowly pulsed and the signal is inverted synchronously with the pulses: the resonance from ^{12}C molecules is suppressed. Figure 11 shows the INDOR spectrum obtained by monitoring an appropriate ("hidden") ^{13}C satellite line in the proton spectrum of 1,3,5-trichlorobenzene, and using slow-pulsed modulation of the ^{13}C irradiating frequency; the expected 1:2:1 triplet is obtained.

Experiments of the type outlined above should also be applicable to other nuclei such as ^{29}Si and ^{15}N; their main disadvantage is that they are rather time consuming as sweep rates of ca. 0·01 c./sec.[2] are needed.

C. Experiments involving selective irradiation

Theoretical calculations yield both a sign and a magnitude for spin–spin coupling constants, and double-resonance experiments provide an important unequivocal way of comparing the signs. The determination of the absolute sign of a coupling constant cannot be accomplished by double-resonance experiments alone, but there are good reasons for believing that the $^{13}C{-}^{1}H$ coupling constant is absolutely positive, and a positive value will be adopted in the sequel. The first application of double-resonance techniques to the determination of the relative signs of coupling constants was by Evans[54, 55] who used homonuclear proton decoupling to show that ${}^3J_{(^{205}Tl-CH_2)}$ and ${}^4J_{(^{205}Tl\cdots CH_3)}$ in Et_2Tl^+ are of opposite sign. In order to relate the signs of these to ${}^3J_{(H\cdots H)}$ which is known to be positive[56] it would be necessary to perform a $^{1}H{-}\{^{205}Tl\}$ experiment and this has apparently not been done, although comparison with other heavy nuclei suggests that the geminal coupling is negative. The reader is referred to Hoffman and Forsén's review[2] for a thorough discussion of the use of double resonance for determining the relative signs of coupling constants, and only a few salient points will be mentioned here.

Consider an AMX system where A, M and X are of spin $I = \frac{1}{2}$ and have positive magnetogyric ratios. Suppose further that $J_{(A-X)}$ is much smaller than the other two coupling constants. The magnetic resonance spectrum will then appear as shown in Fig. 12, in which the transitions of a particular nucleus are numbered in order of increasing frequency. We can divide the A and X parts of this spectrum into two sub-spectra corresponding to opposite spin states of the M nucleus. If $J_{(A-M)}$ and $J_{(X-M)}$ are of the same sign then lines A_1, A_2, X_1 and X_2 will belong to the same sub-spectrum, whereas if the two coupling constants are opposite in sign A_1, A_2, X_3 and X_4 will be members of the same sub-spectrum. If the second r.f. field, H_2, is applied at the centre of A_1, A_2 with sufficient amplitude to wash out $J_{(A-X)}$ either X_1 and X_2 or X_3 and X_4 will collapse to a single line, depending on the sign relationship of $J_{(\mathrm{A-M})}$ and $J_{(\mathrm{X-M})}$. With coupling constants of about the size indicated in Fig. 12, this experiment would be successful irrespective of whether a field- or frequency-sweep mode of operation were used to record the X spectrum. In order to compare the signs of $J_{(\mathrm{A-X})}$ and $J_{(\mathrm{M-X})}$ it would be necessary to use a field H_2 large enough to wash out the coupling $J_{(\mathrm{A-M})}$, and to distinguish the effects of applying H_2 at the mid-points of $\mathrm{A}_1, \mathrm{A}_3$ and $\mathrm{A}_2, \mathrm{A}_4$; this might be difficult if $J_{(\mathrm{A-X})}$ is small. The signs of $J_{(\mathrm{A-X})}$ and $J_{(\mathrm{A-M})}$ could be compared by similarly observing the X transitions and applying a field large enough to collapse the splitting due to $J_{(\mathrm{M-X})}$ to the M transitions. Thus in a double-irradiation experiment on a system AMX in which A transitions are irradiated and the X spectrum is observed or vice versa, the signs of $J_{(\mathrm{A-M})}$ and $J_{(\mathrm{X-M})}$ are compared; that is the nucleus which is neither observed nor irradiated figures in each coupling constant. In order to obtain the relative signs of all three coupling constants, two experiments are necessary, and each nucleus must be perturbed (by either H_1 or H_2) at least once. If the magnetogyric ratios of the observed and irradiated nuclei are of opposite sign, the above conclusions regarding the signs of the coupling constants will be reversed, but the sign of γ for the nucleus which is neither observed nor irradiated will not affect the results.

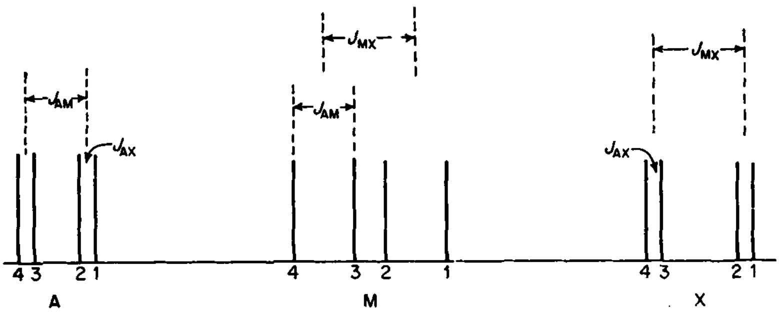

FIG. 12. Schematic diagram of an AMX system for three spins of $I = \frac{1}{2}$. The chemical shifts are drawn to a reduced scale.

An important heteronuclear experiment depending upon the above arguments was performed by Lauterbur and Kurland[57] in 1962. There were strong theoretical reasons[58] (which have since received experimental support[59–61]) for supposing that $J_{(^{13}\mathrm{C}-^{1}\mathrm{H})}$ is positive and it was desirable to know the sign of the vicinal proton–proton coupling in olefins. The compound studied was *cis*-1,2-dichloroethylene containing ^{13}C in natural abundance, so that about 2% of the molecules were of the type $\mathrm{HCl}^{13}\mathrm{C}{=}\mathrm{CHCl}$. Figure 13 shows the ^{13}C and ^{1}H spectra of these molecules schematically; lines B_1–B_4 appear as shoulders of the resonance given by molecules containing no ^{13}C. Irradiation of $\mathrm{C}_3, \mathrm{C}_4$ brought about a collapse of $\mathrm{B}_2, \mathrm{B}_4$, and irradiation of $\mathrm{C}_1, \mathrm{C}_2$ similarly affected $\mathrm{B}_1, \mathrm{B}_3$. $^{3}J_{(\mathrm{H}\cdots\mathrm{H})}$ and

$^1J_{(C-H)}$ are thus of the same sign, i.e., positive. Similar techniques have been applied to other molecules, in CH_3SiHCl_2 and related compounds. Danyluk[62] has shown that the direct ^{29}Si–H and vicinal H···H couplings are of opposite sign (^{29}Si is negative) and in analogous fluorine compounds[63] the direct ^{29}Si–^{19}F and vicinal H···^{19}F couplings are of like sign.

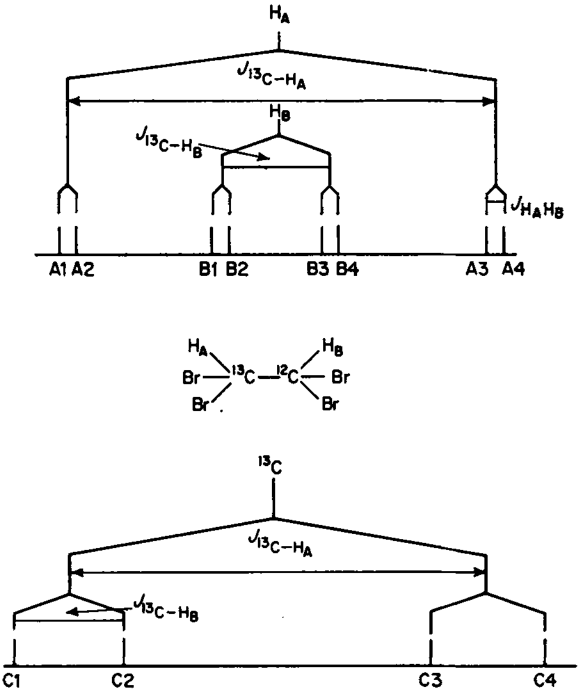

FIG. 13. Schematic diagram of the proton and ^{13}C n.m.r. spectra of 1,1,2,2-tetrabromoethane. Transitions have been labelled in order of increasing field H_0. The schematic diagrams above are also valid for the proton and ^{13}C spectra of *cis*-dichloroethylene containing one ^{13}C nucleus in each molecule ($ClH_A{}^{13}C = {}^{12}CH_BCl$). (From Hoffman and Forsén.[2])

An early experiment of this type was by Tiers[64] who showed that the ^{13}C–H and ^{13}C–^{19}F coupling constants in $CHFCl_2$ are of opposite sign by a ^1H–^{19}F decoupling experiment. Homonuclear experiments can then be used to relate the sign of $J_{(H-F)}$ in this molecule to one of these coupling constants. A study of the relaxation of the ^{19}F transitions in $CHFCl_2$ has shown that $J_{(H-F)}$ in this molecule is positive,[61] and it follows that $J_{(^{13}C-H)}$ is also positive in agreement with theoretical prediction[58] and earlier experimental work.[59, 60]

The proton spectra of the triethyl esters of phosphorous and phosphoric acids display coupling of about 8 c./sec. between the ^{31}P nucleus and the methylene protons, and also a long-range coupling of ca. 0·8 c./sec. between ^{31}P and the methyl protons.[65] Irradiation of the ^{31}P spectrum of the phosphite collapses this latter splitting and a comparison of the optimum decoupling frequencies for the different parts of the triplet arising from vicinal H···H coupling shows that $^3J_{(^{31}P\cdots CH_2)}$ and $^3J_{(H\cdots H)}$ are of like sign. A similar result was obtained for the phosphate and an analysis[66] of the spectra had earlier shown that $^3J_{(^{31}P\cdots CH_2)}$ and $^4J_{(^{31}P\cdots CH_3)}$ were of opposite sign in the phosphite and like sign in the phosphate, so that the only negative coupling in these two systems is the 4-bond $^{31}P\cdots H$ one in the phosphite.

The chemical shift between the two kinds of proton in methyl phosphine, CH_3PH_2 is quite small and the spectrum is not first order. Manatt *et al.*[67] have shown by analysis that the two ^{31}P–H coupling constants in this molecule are of the same sign and used ^{31}P decoupling to show that this sign is also the same as that of the vicinal H···H coupling. There is evidence that they are all absolutely positive. Other workers[68] have also compared the two ^{31}P–H coupling constants by analysis of the spectrum, but were unable to reach any conclusions regarding the absolute signs. This indicates the advantages of having heteronuclear double-resonance facilities available.

A relative-sign determination by spin decoupling may not be feasible if it would be necessary to wash out a coupling that is large compared with the separation between the positions that must be distinguished. An example is CH_3SiHCl_2 in which Danyluk[62] was able to compare $J_{(^{29}Si-H)}$ (-281 c./sec.) with $^3J_{(H\cdots H)}$ by collapsing $^2J_{(^{29}Si-CH_3)}$ (8·0 c./sec.), but could not compare the signs of the last two coupling constants. By using magnitudes of H_2 comparable with the line width, i.e., "tickling", individual transitions can be identified and assigned to an energy-level diagram that can then be used to give the relative signs of the coupling constants. An early application of this technique to heteronuclear work is Freeman and Anderson's study[17] of $CHBr_2CHBr_2$ containing ^{13}C in natural abundance. Molecules of the type $CHBr_2{}^{13}CHBr_2$ are present in ca. 2·2% abundance and in them $^1J_{(^{13}C-H)} = 181$ c./sec. The outer satellites in the proton spectrum of the compound arise from these molecules and are doublets with a splitting of $^3J_{(H\cdots H)} = 2{\cdot}9$ c./sec. Observation of the high-field components of these doublets showed that they were perturbed by ^{13}C tickling frequencies of 15,087,381·5 and 15,087,562·5 c./sec. (the ^1H spectrum was recorded at 60 Mc./sec.). The low-field components were perturbed by frequencies of 15,087,382·6 and 15,087,563·1 c./sec. This shows that $^2J_{(^{13}C\cdots H)}$ has a magnitude of 1·1 c./sec., a result unobtainable directly from the proton spectrum, since the relevant lines are hidden by the signal from molecules containing no ^{13}C, and that the signs of $^3J_{(H\cdots H)}$ and $^2J_{(^{13}C\cdots H)}$ are the same. A single experiment thus gives the positions of all of the lines in the ^{13}C spectrum with a precision of better than 1 in 10^8, and permits the measurement of coupling constants in the ^{13}C

spectrum that would normally be unobservable. A knowledge of the value of $^2J_{(^{13}C\cdots H)}$ allowed calculation of the exact positions of the "inner" satellites in the proton spectrum; these two positions were monitored in turn and the ^{13}C tickling field was swept through the appropriate range (i.e., an INDOR experiment was performed), and the signs of $^3J_{(H\cdots H)}$ and $^1J_{(^{13}C-H)}$ were found to be the same.

It has been found convenient[17] to represent the single quantum transitions of an AMX system by the twelve edges of a cube placed with a body diagonal (representing a triple quantum transition) vertical. The eight vertices correspond to the energy levels of the spins in a magnetic field that is directed along the vertical, and the appropriate numbering of the transitions for the case where all the coupling constants (and all the magnetogyric ratios) are of the same sign is shown in Fig. 13. The application of Freeman and Anderson's rules[17] regarding the behaviour of connected transitions in tickling experiments then makes it possible to deduce the labelling of the cube for a particular spin system from a set of double-irradiation experiments. Many workers find it easier to deduce the relative signs of the coupling constants directly from the tickling experiments, and then use these to construct the appropriate energy-level diagram if this is required. For systems in which some of the energy levels and transitions are degenerate it is often important to have the energy-level diagram (see later), but in other cases it may not be necessary.

Whipple *et al.*[69] have performed $^1H-\{^{11}B\}$ and $^{19}F-\{^{11}B\}$ tickling experiments on HBF_2 that established the positions of the ^{11}B lines to within 1 c./sec. (the boron spectrum was not examined directly) and constructed the energy-level diagram. It is likely that the direct $^{11}B-H$ coupling constant in this molecule is positive, and on this basis the signs of the other coupling constants are: $J_{(^{11}B-^{19}F)}$ negative; $J_{(^{19}F\cdots H)}$ positive.

In an exhaustive ^{13}C double-resonance study of vinyl cyanide Freeman[12] was able to determine ^{13}C line positions to within ±0·01 c./sec. and used the results to check the validity of a computer analysis of the ABC proton spectrum. Precision of this order can be attained only in exceptional circumstances. A special feature of the work was that the combination lines in the ^{13}C spectrum (corresponding to ^{13}C transitions with a simultaneous spin inversion of two protons) were detected by using higher amplitudes of H_2.

It is appropriate at this point to mention the INDOR work of Baker,[70] who has recorded the ^{13}C spectrum of trifluoroacetic acid containing ^{13}C in natural abundance by monitoring a ^{13}C satellite in the ^{19}F spectrum and sweeping the ^{13}C resonant frequency. Baker has similarly[70] obtained the ^{14}N INDOR spectrum of the ammonium ion in which the tetrahedral symmetry prevents quadrupole broadening, and has used homonuclear INDOR experiments to obtain the energy level diagram of a four-spin AKMR system.[71]

One of the most striking applications of heteronuclear tickling experiments is the measurement of coupling constants between two nuclei when neither is observed directly. An important example of this is the examination by McLauchlan *et al.*[51] of mercury dimethyl containing ^{13}C and ^{199}Hg in natural abundance (1·1 and 16·7%, respectively). In addition to a strong central line from molecular species $(^{12}CH_3)_2{}^0Hg$, the proton spectrum of this substance exhibits satellite lines due to the species $(^{12}CH_3)^{199}Hg$, $^{12}CH_3(^{13}CH_3)^0Hg$, and $^{12}CH_3(^{13}CH_3)$-^{199}Hg, the last of these being present in only 0·33% abundance. The ^1H, ^{13}C and ^{199}Hg spectra to be expected from these molecules are shown schematically in Fig. 14, and a series of ^{13}C and ^{199}Hg tickling experiments gave the positions of most of the lines. As a result of the presence of groups of equivalent protons, the tickling experiments involved the irradiation of degenerate transitions, and inspection of the energy-level diagrams in conjunction with the application of Freeman and Anderson's rules[17] indicates that only part of a proton line will be split into a doublet when a connected ^{13}C or ^{199}Hg transition is irradiated. Thus for a $^{13}CH_3$ group, irradiation of either of the outer members of the ^{13}C quartet will split 1/4 of the intensity of each of the two proton lines into a doublet, and

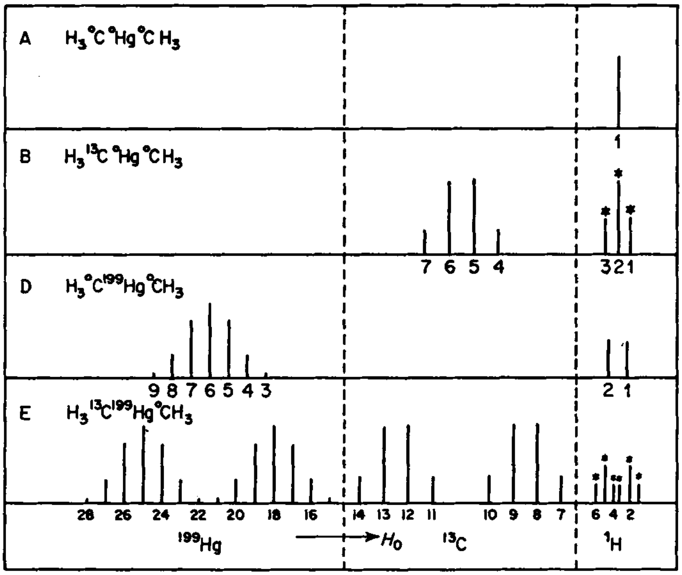

FIG. 14. A schematic representation of the spectra due to the observed species A, B, D and E from mercury dimethyl. The long-range coupling occurring between the methyl protons is too small to show on the scale of this diagram, but the lines showing quartet structure are marked with asterisks. No account has been taken of the relative abundances of the species which are given in the table. The transitions are labelled in order of increasing absolute frequency. (From McLauchlan *et al.*[51])

3/4 of the intensity will be unaffected. Irradiation of an inner line of the ^{13}C quartet will affect 3/4 of the intensity of the observed lines. These results are shown schematically in Fig. 15. In general, irradiation of a single line of the A multiplet of an AX_n system will produce a doublet splitting of a proportion of each X line equal to twice the fractional intensity of the irradiated line. Thus for molecules of the type $(CH_3)_2{}^{199}Hg$, irradiation of the lines of the mercury septet should split the following fractions of the satellite lines in the proton spectrum: 1/32; 6/32; 15/32; 20/32; 15/32; 6/32; and 1/32. The actual results of irradiating the 2nd, 3rd, 4th and 5th lines of the ^{199}Hg septet are shown in Fig. 16. Mercury dimethyl is a very suitable compound for illustrating these ideas as the value of $J_{(^{199}Hg-CH_3)} = 101{\cdot}4$ c./sec. makes it possible to use amplitudes of H_2

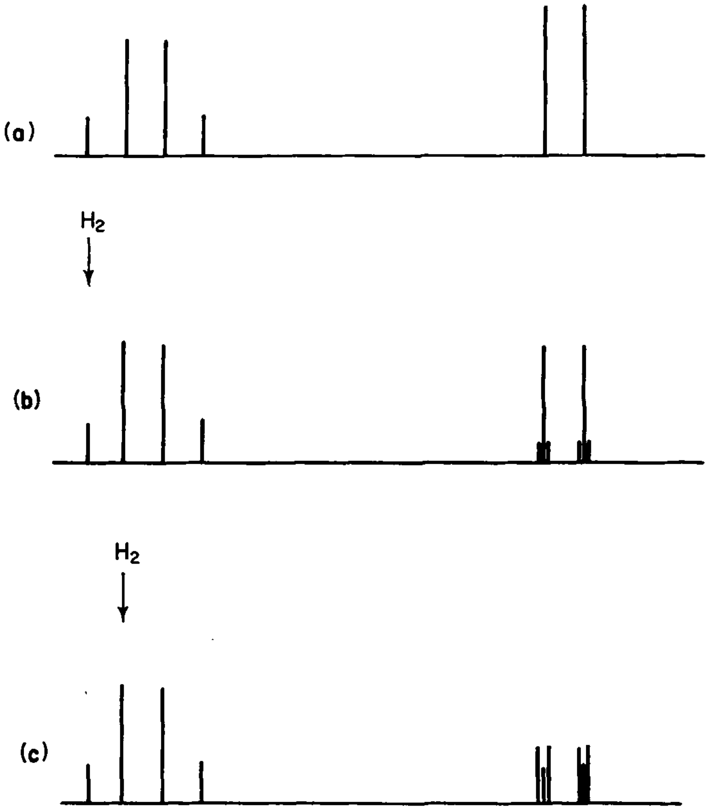

FIG. 15. Predicted effects of tickling the A part of an AX_3 spin system: (a), single-resonance spectrum; (b), outer line of the A quartet tickled; (c), inner line of the A quartet tickled.

large enough to produce substantial splittings of the observed lines without irradiating more than one ^{199}Hg transition.

Once the ^{13}C lines of species B had been located it was possible to search for the corresponding lines given by the E molecules. These were found in positions 345 c./sec. above and below the lines in the B molecules, indicating that $|J_{(^{13}C-^{199}Hg)}| = 690$ c./sec., and from their relation to the observed proton lines it was deduced that this coupling constant and $J_{(^{199}Hg-CH_3)}$ were of opposite sign. The signs of $J_{(^{13}C-^{199}Hg)}$ and $J_{(^{13}C-H)}$ were then compared by a ^{199}Hg tickling experiment. The centre of the mercury resonance of molecules D was easily found, and knowledge of the magnitude of $J_{(^{13}C-^{199}Hg)}$ made the search for the ^{199}Hg lines of species E relatively short. The numerical value of $J_{(^{13}C-^{199}Hg)}$ was confirmed, and the coupling constant was found to be positive. McLauchlan *et al.*[51] observed a long-range coupling $^4J_{(H\cdots H)}$ of 0·44 c./sec. in molecules containing a ^{13}C nucleus, but were prevented from determining its sign by drifts of their r.f. oscillators. Recently Dean and McFarlane[72] have taken advantage of the locked oscillator system designed by Charles[11] to show that this coupling is positive. The proton resonance of species E was observed, and the asymmetry that appeared as different lines of a mercury septet were irradiated showed that $^4J_{(H\cdots H)}$ and $^2J_{(^{199}Hg-CH_3)}$ were of opposite sign. The above work on mercury dimethyl has been considered in some detail as it illustrates many of the points that arise in exact heteronuclear double-resonance experiments.

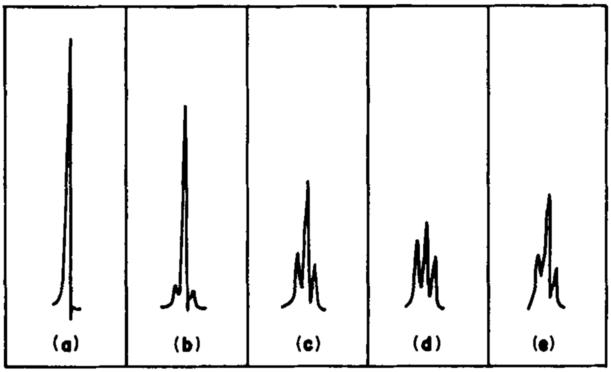

FIG. 16. Effect of tickling ^{199}Hg transitions in mercury dimethyl: (a), without irradiation in the ^{199}Hg region; (b), with irradiation of lines D_2, (c), with irradiation of line D_3; (d), with irradiation of line D_4; (e), with irradiation of line D_5. (From McLauchlan *et al.*[51])

The signs and magnitudes of several other coupling constants involving two hetero-atoms have been determined similarly, although various causes have occasionally prevented the full precision of the method from being realized. Thus in a series of organotin halides,[50] $(CH_3)_xSnX_{4-x}$, the proximity in the proton spectrum of satellite lines arising from the two tin isotopes ^{117}Sn and ^{119}Sn (abundances 7·7 and 8·7%, respectively) obscured one portion of the split-out doublet obtained in the tickling experiments and values of $J_{(^{119}Sn-^{13}C)}$ could not be obtained to closer than ±1 c./sec. In this work, a linear relation was found between $J_{(^{119}Sn-^{13}C)}$ and $J_{(^{119}Sn-CH_3)}$, but it appeared that the Fermi contact interaction was not the only term involved in the coupling constants. McLauchlan[45] has determined the magnitude and sign relative to $J_{(^{29}Si-CH_3)}$ of $J_{(^{29}Si-^{13}C)}$ in tetramethylsilane, and Dean and McFarlane[46] have shown that the sign is absolutely negative. In this work the accuracy of the measurements was reduced by the poor signal-to-noise ratio at which the relevant lines in the proton spectrum were observed, it being necessary to adopt minimum peak height as the criterion of optimum tickling frequency.

The signs and magnitudes of the directly bonded couplings between ^{13}C and the following nuclei have been determined by using the heteronuclear tickling technique: ^{13}C; ^{14}N; ^{15}N; ^{29}Si; ^{31}P; ^{77}Se; ^{117}Sn; ^{119}Sn; ^{123}Te; ^{207}Pb (see references 43, 47, 49, 50, 73, 74, 75 and 76). The results involving ^{31}P are especially interesting as the sign changes in going from P^{III} (negative) to P^{V} (positive); this is accompanied by a change in the sign of the geminal $^{31}P \cdots H$ coupling in the opposite sense.[77, 78]

The general expression for the spin–spin coupling constant between two nuclei contains the product of their magnetogyric ratios as a multiplying factor.[79] If the observed coupling constant is divided by the product of the two magnetogyric ratios, the number obtained is independent of the particular nuclei involved, and gives a measure of their electronic interaction. Different workers have proposed the inclusion of various constants in the division operation, and the system that appears to be gaining most favour is the reduced coupling constant of Pople and Santry,[80] defined as $K_{AX} = J_{AX} . 2\pi / \hbar \gamma_A \gamma_B$. Its dimensions are those of a reciprocal volume, and observed values range from 10^{19} to 10^{24} cm.$^{-3}$. Ordinary and reduced coupling constants will be of the same sign if both the γ's involved are of the same sign, otherwise they will be opposite; important nuclei that have negative magnetogyric ratios are: ^{15}N; ^{17}O; ^{29}Si; ^{73}Ge; ^{117}Sn; ^{119}Sn; and ^{125}Te. The signs and magnitudes of the reduced coupling constants between H and C and a number of directly bonded nuclei are given in Table IIA and B.†

If one of the coupling constants (say A–X) in an AMX system is vanishingly small, it is not possible to compare the signs of the other two by a double-resonance experiment unless the spectrum is not first order. This is because the A transitions corresponding to the opposite spin states of X are degenerate, so that irradiation of an X transition (also degenerate) perturbs the energy levels coherently and no effect is apparent in the A spectrum. The degeneracy can be set aside by irradiating a suitable M transition, when part of each A line (corresponding to a particular

† Adapted from a table drawn up by Dr D. H. Whiffen, F.R.S.

spin orientation of X) will be perturbed. The normal double-resonance determination of the relative signs of $J_{(A-M)}$ and $J_{(X-M)}$ by irradiating X and observing A may then be undertaken. For a fuller discussion of the principles of this type of triple-resonance experiment the reader should consult Hoffman and Forsén's review.[2] The feasibility of such an experiment has been demonstrated by Cohen *et al.*[81] in the homonuclear case, but the problem studied by them could also have been solved by analysis of the spectrum obtained at a lower field strength.[82] It was therefore of interest to examine a heteronuclear system in which the analysis method would be inapplicable, and the compound selected[83] was dimethyl phosphite, $(CH_3O)_2PH'O$, in which ^{31}P is coupled to each kind of proton, but $^4J_{(H\cdots H')}=0$.

TABLE IIA

Values of $K_{(X-H)} \times 10^{-20}$ cm.$^{-3}$

C	+41	N	+58
Si	+75 to +150	P^{III}	+40; P^{V} +120
Sn	(+)400		
Pb	(+)950		

TABLE IIB

Values of $K_{(X-C)} \times 10^{-20}$ cm.$^{-3}$

C	+45	N	+48		
Si	+87	P^{III}	−12; P^{V} +40 to +100		
				Se	−107
Sn	+300 to +700			Te	−170
Pb	+395	Hg	+1130		

A sign placed in parentheses indicates that it is probable but unconfirmed.

A homonuclear experiment in which the methoxy protons were observed and the H′ was tickled confirmed that the two ^{31}P–H coupling constants could not be compared in this way. Application of a moderately strong field to one of the two septets (separated by $J_{(^{31}P-H')}=694$ c./sec.) of the ^{31}P spectrum removed the troublesome degeneracy, and a homonuclear tickling experiment showed that the two coupling constants were of the same sign. Separate heteronuclear tickling experiments involving the ^{13}C satellites of the methoxy proton showed that $J_{(^{31}P\cdots CH_3)}$ was positive. There appears to be no record of a true heteronuclear triple irradiation experiment, i.e., one in which all three irradiating fields are applied to different nuclear species.

The next few years should see the elucidation of the signs of most spin–spin coupling constants, and it is likely that the most important applications of heteronuclear double resonance will then be to chemical-shift measurements and the determination of the magnitudes of coupling constants between nuclei with poor sensitivities to n.m.r. detection. The principal merits of the technique are versatility and precision, and the necessary modification of a spectrometer can multiply its value many times.

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REFERENCES

1. J. D. Baldeschwieler and E. W. Randall, *Chem. Rev.*, 1963, **63**, 81.
2. R. A. Hoffman and S. Forsén, *Progr. N.M.R. Spectroscopy*, 1966, **1**, 15.
3. D. F. Evans, *Lab. Practice*, January 1965, p. 57.
4. D. G. Gillies and E. W. Randall, *J. Sci. Instr.*, 1966, **43**, 466.
5. J. A. Glassel, D. W. Turner and L. M. Jackman, *Proc. Chem. Soc.*, 1961, 426.
6. A. L. Bloom and J. N. Shoolery, *Phys. Rev.*, 1956, **97**, 1261.
7. W. A. Anderson and F. A. Nelson, *J. Chem. Phys.*, 1963, **39**, 183.
8. R. C. Hopkins, *Rev. Sci. Instr.*, 1964, **35**, 1495.
9. A. Charles and W. McFarlane, to be published.
10. R. Freeman, *J. Chem. Phys.*, 1964, **40**, 3571.
11. A. Charles, *J. Sci. Instr.*, in press.
12. R. Freeman, *J. Chem. Phys.*, 1964, **40**, 3571.
13. J. H. Allen, J. K. Becconsall and D. W. Turner, *J. Sci. Instr.*, 1964, **41**, 673.
14. J. D. Baldeschwieler and E. W. Randall, *Proc. Chem. Soc.*, 1961, 303.
15. J. D. Baldeschwieler, *J. Chem. Phys.*, 1962, **36**, 152.
16. W. A. Anderson and R. Freeman, *J. Chem. Phys.*, 1962, **37**, 85.
17. R. Freeman and W. A. Anderson, *J. Chem. Phys.*, 1962, **37**, 2053.
18. R. Kaiser, Communication at Fifth Experimental N.M.R. Conference, Pittsburgh, 1964.
19. E. G. Paul and D. M. Grant, *J. Amer. Chem. Soc.*, 1964, **86**, 2977, 2984.
20. F. A. L. Anet and J. S. Hartman, *J. Amer. Chem. Soc.*, 1963, **85**, 1204; *Proc. Chem. Soc.*, 1964, 145.
21. F. A. Bovey, E. W. Anderson, F. P. Hood and R. L. Kornegay, *J. Chem. Phys.*, 1964, **40**, 3099.
22. G. Fraenkel and W. Burlant, *J. Chem. Phys.*, 1965, **42**, 3724; 1965, **43**, 4541.
23. N. Muller and R. H. Birkhahn, *J. Chem. Phys.*, 1965, **43**, 4540.
24. J. N. Shoolery, *Discuss. Faraday Soc.*, 1955, **19**, 215.
25. H. H. Lindner and T. Onak, *J. Amer. Chem. Soc.*, 1966, **88**, 1890.
26. G. D. Vickers, H. Agahigian, E. A. Reir and H. Schroeder, *Inorg. Chem.*, 1966, **5**, 693.
27. A. D. Norman and R. Schaeffer, *J. Phys. Chem.*, 1966, **70**, 1663.
28. W. H. Knoth, W. R. Hertler and E. L. Mutterties, *Inorg. Chem.*, 1965, **4**, 280, 288.
29. H. C. Miller, W. R. Hertler, E. L. Mutterties, W. H. Knoth and N .E. Miller, *Inorg. Chem.*, 1965, **4**, 1216.

30. N. E. Miller, H. C. Miller and E. L. Mutterties, *Inorg. Chem.*, 1964, **3**, 866.
31. R. C. Hopkins, J. D. Baldeschwieler, R. Schaeffer, F. N. Tebbe and A. D. Norman, *J. Chem. Phys.*, 1965, **43**, 975.
32. K. S. Dahmi and J. B. Stothers, *Canad. J. Chem.*, 1965, **43**, 479, 510.
33. J. B. Stothers, *Quart. Rev.*, 1965, **19**, 144.
34. E. G. Rochow, *Monatsh.*, 1964, **95**, 750.
35. H. Kamei, *Bull. Chem. Soc. Japan*, 1965, **38**, 1212.
36. S. Castellano, C. San and R. Kostelnik, *J. Chem. Phys.*, 1965, **46**, 327.
37. F. A. Bovey, *Chem. Eng. News*, 30 August 1965, p. 104.
38. J. K. Becconsall and P. Hampson, *Mol. Phys.*, 1965, **10**, 21.
39. A. Mathias and P. Hampson, *Mol. Phys.*, 1966, **11**, 541.
40. J. B. Stothers and J. R. Robinson, *Canad. J. Chem.*, 1964, **42**, 967.
41. T. H. Brown, E. B. Whipple and D. H. Verdier, *J. Chem. Phys.*, 1963, **38**, 3029; *Science*, 1963, **140**, 178.
42. W. McFarlane, *J. Chem. Soc.*, in press.
43. W. McFarlane, *Mol. Phys.*, in press.
44. A. G. Davies, W. McFarlane and R. F. M. White, unpublished work.
45. K. A. McLauchlan, *Mol. Phys.*, 1966, **11**, 303, 503.
46. R. R. Dean and W. McFarlane, *Mol. Phys.*, 1967, **12**, 289.
47. W. McFarlane, *J. Chem. Soc. A*, 1967, 1660.
48. W. McFarlane, *J. Chem. Soc.*, in press.
49. W. McFarlane, *Mol. Phys.*, 1967, **12**, 243.
50. W. McFarlane, *J. Chem. Soc. A*, 1967, 528.
51. K. A. McLaughlan, D. H. Whiffen and L. W. Reeves, *Mol. Phys.*, 1966, **10**, 131.
52. W. A. Anderson, *J. Chem. Phys.*, 1962, **37**, 1373.
53. R. Freeman, *J. Chem. Phys.*, 1965, **43**, 3087.
54. J. P. Maher and D. F. Evans, *Proc. Chem. Soc.*, 1961, 208.
55. D. F. Evans, *Mol. Phys.*, 1962, **5**, 183.
56. J. W. Emsley, J. Feeney and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy", Vol. 2, p. 682. Pergamon Press, London, 1966.
57. P. C. Lauterbur and R. J. Kurland, *J. Amer. Chem. Soc.*, 1962, **84**, 3405.
58. M. Karplus, *J. Amer. Chem. Soc.*, 1962, **84**, 2458.
59. A. D. Buckingham and K. A. McLauchlan, *Proc. Chem. Soc.*, 1963, 144.
60. A. Saupe and G. Englert, *Phys. Rev. Letters*, 1963, **11**, 462.
61. E. L. Mackor and C. MacLean, *J. Chem. Phys.*, 1966, **44**, 64.
62. S. Danyluk, *J. Amer. Chem. Soc.*, 1965, **87**, 2300.
63. S. Danyluk, *J. Amer. Chem. Soc.*, 1964, **86**, 4504.
64. G. v. D. Tiers, *J. Amer. Chem. Soc.*, 1962, **84**, 3972.
65. E. Duval and E. A. C. Lucken, *Mol. Phys.*, 1966, **10**, 499.
66. G. J. Bene, E. Duval, A. Finaz, G. Hochstrasser and S. Koide, *Physics Letters*, 1963, **7**, 34.
67. S. L. Manatt, G. L. Juvinall, R. I. Wagner and D. D. Elleman, *J. Amer. Chem. Soc.*, 1966, **88**, 2689.
68. G. M. Whitesides, J. L. Beauchamp and J. D. Roberts, *J. Amer. Chem. Soc.*, 1963, **85**, 2665.
69. E. B. Whipple, T. H. Brown, T. C. Farrar and T. D. Coyle, *J. Chem. Phys.*, 1965, **42**, 1841.
70. E. B. Baker, *J. Chem. Phys.*, 1962, **37**, 911.

71. E. B. Baker, *J. Chem. Phys.*, 1966, **45**, 609.
72. R. R. Dean and W. McFarlane, *Mol. Phys.*, 1967, **13**, 343.
73. K. A. McLauchlan, *Chem. Comm.*, 1965, 105.
74. D. M. Grant, *J. Amer. Chem. Soc.*, 1967, **89**, 2228.
75. W. McFarlane, *Mol. Phys.*, 1966, **10**, 603.
76. W. McFarlane, *J. Chem. Soc. A*, 1907, 1275.
77. W. McFarlane, *Chem. Comm.*, 1967, 58.
78. A. R. Cullingworth, A. Pidcock and J. D. Smith, *Chem. Comm.*, 1966, 89.
79. J. A. Pople, H. J. Bernstein and W. G. Schneider, *In* "High Resolution Nuclear Magnetic Resonance", p. 188. McGraw-Hill, New York, 1959.
80. J. A. Pople and D. P. Santry, *Mol. Phys.*, 1964, **8**, 1.
81. A. D. Cohen, R. Freeman, K. A. McLauchlan and D. H. Whiffen, *Mol. Phys.*, 1963, **7**, 45.
82. P. T. Narasimhan and M. T. Rogers, *J. Chem. Phys.*, 1960, **33**, 727.
83. W. McFarlane, *J. Chem. Soc. A*, 1967, 1167.

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The Nuclear Magnetic Resonance Spectra of Polymers

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I. INTRODUCTION

THE AIM of this review is to cover reasonably extensively the contribution of high-resolution n.m.r. spectroscopy to the study of polymer structure, particularly over the years 1963–6 inclusive. The high-resolution n.m.r. study of polymers in solution furnishes chemical information concerning polymer structure. Broad-line or wide-line n.m.r. spectroscopy uses solid materials to obtain physical information, and so is not included in this review. The polymers considered here are mostly synthetic ones; biological polymers are excluded, but there is a review of the structures of the latter.[1] Previous reviews,[2–6] with few exceptions,[7, 8] have been relatively short, although some give a good insight into the capabilities of the technique.[9, 10] This survey has been confined to work including or directly related to n.m.r. spectroscopy. The impact of stereospecific catalysts on the polymer world has created new demands for methods of studying the stereochemical configuration of polymer chains. High-resolution n.m.r. spectroscopy has become a very important method in this field through its ability to discriminate between different structures in a quantitative manner. The study of polymer configuration involves consideration of the polymer chain as sequences of meso (isotactic) and racemic (syndiotactic) monomer placements, i.e., as diads. A more detailed treatment involves isotactic, heterotactic and syndiotactic triads (regarding a heterotactic sequence as a change-over point between isotactic and syndiotactic sequences). Both these concepts fit very closely with the type of information and measurements which can be obtained from an n.m.r. spectrum. In favourable cases at least, n.m.r. provides absolute evidence for the presence of isotactic structures in polymers and assignments for other structures follow from this or alternatively from other non-n.m.r. evidence. The treatment by diads and triads analysis has been found very useful in the general interpretation of polymer structural problems in the widest sense. However, the subject is capable of more particular development as and when evidence for longer sequences e.g. tetrads may be discerned in the spectra. In such cases more specific information is forthcoming which may be used in a special way, e.g., in correlations with statistical polymerization theory.

Although n.m.r. spectroscopy is by no means the only technique for studying polymer structure, it is often the most discriminating and is fundamentally quantitative. It is probably more generally useful than X-ray diffraction, which gives absolute information on the crystallinity of ordered regions possessed by relatively few polymers. It has the advantage over i.r. spectroscopy of not requiring model compounds for quantitative work, although model compounds have often been used to help make assignments. Ideally, it should be possible to interpret an n.m.r. spectrum without assistance from additional information, and although this is sometimes the case,[6] much use has been made of evidence obtained from other techniques, particularly for the purpose of making configurational assignments. Other techniques have been classed as "qualitative" in comparison with n.m.r. spectroscopy, which reflects the power of the n.m.r. method. Although in this review correlations and comparisons between n.m.r. evidence and that given by other techniques are included only if contained in the papers being reviewed, it is not intended here to compare different physical methods of determining polymer structure. Often, evidence from other techniques may be found consistent with n.m.r. results, occasionally the reverse is true. In some instances, n.m.r. results have been used to calibrate i.r. methods.

The effectiveness of n.m.r. spectroscopy follows from the clarity or resolution of the spectra, which depends on instrument frequency, the solvent and the temperature of measurement as well as the structure of the polymer. The latter depends principally on the type of catalyst used, the temperature of polymerization and some other conditions, e.g., homogeneous or heterogeneous polymerization, presence of additives, etc. On these factors depend the whole of the subject matter as related in the second part of this review.

The principles and instrumentation of n.m.r. spectroscopy have been the subject of several textbooks and will not be considered here except as particularly required. An instrument working at a particular frequency receives signals from nuclei of the appropriate element only; in most of the cases considered here, this element is hydrogen, but fluorine spectra have been studied in a few instances. N.m.r. spectra consist of several resonance signals observed at different values of "chemical shift" that are characteristic of differently positioned nuclei in the sample under examination. The intensities of the signals arising from particular groupings are proportional to the numbers of protons in those groups, and intensity measurements may be made directly and used quantitatively. A further feature of n.m.r. spectra is the fine structure or splitting exhibited in the resonances from some groups dependent on the type of adjacent groupings. This important aspect of n.m.r. spectroscopy is illustrated particularly in its ability to show up as multiplets, magnetically non-equivalent nuclei which are chemically equivalent, as for instance the backbone methylene protons of most isotactic polymers.

These three principal features of an n.m.r. spectrum may be used to obtain information on polymer structures in the following main areas—

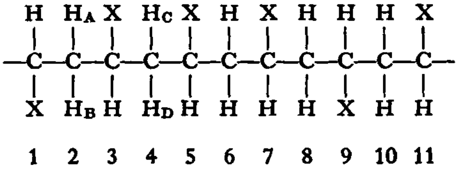
1. Compositional analysis: qualitative evidence for the presence of a particular structure or the quantitative measure of the percentage of structure A in the presence of structure B, e.g., copolymer analysis. Further evidence for the presence of A units between B units may also be forthcoming and pictures of average sequence distributions in copolymers may be derived. Speciality information, e.g., head-to-head placements, has been obtained in a few favourable instances.
2. Stereoregularity measurements concerning isotactic and syndiotactic configurations may be made quantitatively. In some instances direct n.m.r. evidence for a particular configuration may be obtained, but in other cases, although the presence of different configurations may be substantiated, the identification of these may be dependent on evidence obtained from other techniques.
3. Conformational analysis in terms of *trans* and *gauche* sequences has been accomplished for model compounds but for few polymers.

The success of the n.m.r. methods varies greatly from polymer to polymer; whilst some systems have furnished much information others have appeared relatively intractable so far.

A. Polymer-chain configuration

A vinyl polymer may be represented as a planar zig-zag extended carbon chain normal to the plane of the paper, as shown in Fig. 1.[8]

Although it is apparent that hydrogens A and B are equivalent, i.e., are in similar environments to H and X, this is not the case for hydrogens C and D, when viewed from the n.m.r. point of view. As every other carbon atom is asymmetric, the above chain may be described as *dllldl* if carbon 1 is called *d*. Carbon 5 is said to be in an isotactic position since carbons 3, 5 and 7 all have the same configuration. Carbon 9 is said to be in a syndiotactic position since its neighbours carbon 7 and carbon 11 both have the opposite configuration. Carbon 7 is said to be in the heterotactic position since carbon 5 has the same configuration but carbon 9 has the opposite configuration. These distinctions are related to information concerning the second atom removed, and involve consideration of the chain in terms of triads. The even-numbered carbons are in one of two possible positions, racemic (*r*) or *dl* or *ld* as carbon 2, or *meso* (*m*) or *dd* or *ll* as carbon 4. This involves consideration of the chain in terms of diads and it may be described as *rmmrr*.



$$\begin{array}{ccccccccccc}
H & H_A & X & H_C & X & H & X & H & H & H & X \\
| & | & | & | & | & | & | & | & | & | & | \\
-C- & C- & C- & C- & C- & C- & C- & C- & C- & C- & C- \\
| & | & | & | & | & | & | & | & | & | & | \\
X & H_B & H & H_D & H & H & H & H & X & H & H \\
 & & & & & & & & & & \\
1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 & 9 & 10 & 11
\end{array}$$

FIG. 1. Diagrammatic representation of a vinyl polymer. (From McCall and Slichter[8].)

Even stereoregular polymers are not always of very high steric purity and most polymers are composed of isotactic, heterotactic and syndiotactic sequences or may be regarded as "copolymers" of such units.[7] An atactic or random polymer has $i:h:s$ ratio tending to 25:50:25, whereas a stereoblock polymer has relatively little heterotactic content since heterotactic units occur only at "change-over points" between isotactic and syndiotactic sequences. Another way of saying this is that the sequence length, or run number, is low in polymers of low stereoregularity and high in stereoblock polymers. The values of m, r, i, h and s as obtained from n.m.r. spectra are usually normalized according to the equations[8]—

$$m+r = 1 \qquad \text{and} \qquad i+h+s = 1$$

and these values may be used in the following equations in order to calculate sequence lengths—

$$n_i = (1-i/s)/(1-ir/ms)$$
$$n_s = (1-i/s)/[(m/r)-(i/s)]$$
$$h = 2/(n_i+n_s)$$

However, it must be pointed out that only the average values of sequence lengths may be obtained from such a treatment and not information on the distributions of sequence lengths. The values of *i*, *h* and *s* have been coupled with various considerations of polymerization theories. Perhaps the simplest of these, due to Bovey and Tiers,[7] is the most generally applicable and involves the parameter σ, the probability that a polymer chain will add a monomer unit to give the same configuration as that of the last unit at its growing end. Theoretical graphs of *i*, *h* and *s* against σ have been constructed and it has been found that for methyl methacrylate free-radical polymers give "single σ" propagation whereas anionic copolymers show a different behaviour, which has been called "non-σ" propagation. For the free-radical polymerization of poly(methyl methacrylates)

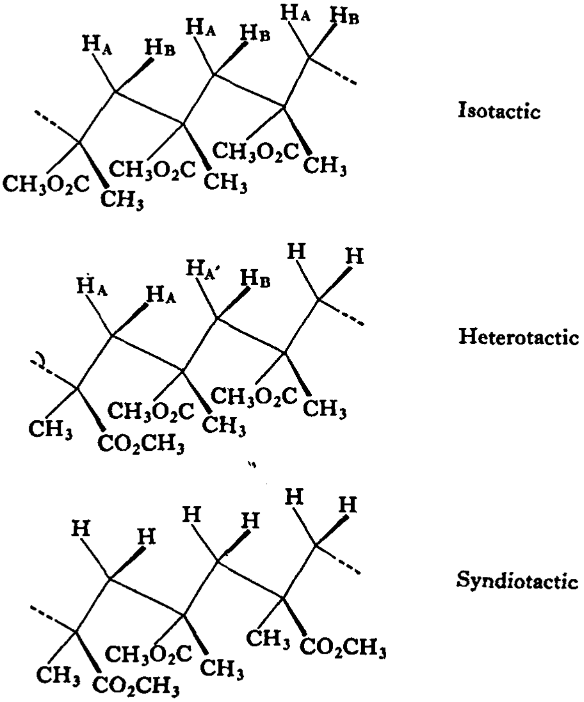


FIG. 2. Diagrammatic representation of spatial arrangements of groups in different tactic forms of poly(methyl methacrylate). (From Bovey.[13])

it has been observed that σ increases with the temperature of polymerization; and more detailed treatments have been attempted for special purposes, e.g., the demonstration of the penultimate-monomer-unit effect. More elaborate treatments involving consideration of tetrads with Bernoullian and Markoffian statistics have also been attempted.[10, 12] The equivalence or non-equivalence of the methylene protons in vinyl polymers may also be seen from Fig. 2, where the backbone is drawn as a planar zig-zag. Although the latter may be the preferred conformation for a syndiotactic polymer, an isotactic polymer tends to assume a helical *trans–gauche* conformation to avoid steric interferences between side groups;[1] this is illustrated in Fig. 3. Whilst such types of conformation have been deduced for various model compounds, similar inferences for polymers have been relatively few. Conformation, unlike configuration, is solvent and temperature dependent.

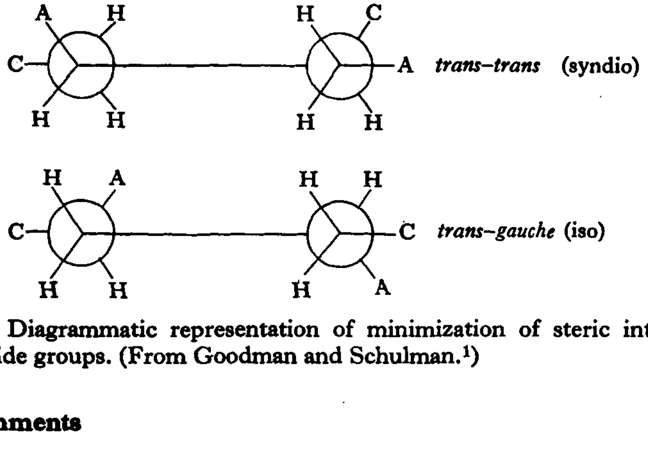


FIG. 3. Diagrammatic representation of minimization of steric interferences between side groups. (From Goodman and Schulman.[1])

B. Assignments

Two types of assignments may be distinguished: those which follow purely from n.m.r. spectra and those which are taken from non-n.m.r. evidence. An example of the former is the AB quartet signal given by a methylene group in the backbone of most isotactic polymers. This also infers that a methylene singlet signal may be attributed to syndiotactic sequences. In those cases where methylene quartets and singlets may be distinguished, it should be possible to assign the resonances of other associated groups in the monomer unit which show chemical-shift dependence on stereoregularity. For instance, the resonance of the α-methyl group in isotactic poly(methyl methacrylate) which occurs consistently with the isotactic methylene quartet is the one which lies at lowest field. This behaviour is consistent with non-n.m.r. evidence obtainable from sources which include i.r. spectroscopy, X-ray diffraction and the measurement of properties such as solubility, rate of hydrolysis, dipole moment, cloud-point temperature, melting point and other physical properties, as well as from implications such as the type of polymerization. These non-n.m.r. methods must be relied upon when n.m.r.

methods are inapplicable, and in some cases this has led to conflicting assignments being made.

Although the interpretation of some polymer spectra is now relatively trivial, in other cases major complexities remain. The spectrum of poly(vinyl chloride) shows two complicated multiplets, that for the methylene group has been interpreted in at least three different ways. Analysis of such a complicated multiplet follows the normal methods of taking values of chemical shifts, intensities and peak separations (as possible coupling constants) from the spectra for comparison with those from model spectra of the appropriate $A_xB_yC_z$ type. When a suitable match is obtained, configurational assignments may be attempted. The use of computer calculations to select the best fit from a number of calculated spectra is not uncommon. Model compounds may not always be relied upon to give an acceptable assignment.

C. Instrumental considerations

The early instruments operating at 40 Mc./sec., which served so well in establishing this subject, have now been outdated almost completely by those operating at 60 Mc./sec., which in turn are being superseded by 100 Mc./sec. instruments. One instrument of 220 Mc./sec. is reported to be in use.[14]

The ready availability of commercial 60 Mc./sec. instruments has resulted in a real flow of results in the past few years. Although 40 Mc./sec. instruments were perfectly capable of allowing tacticity determinations to be made in favourable cases, such as poly(methyl methacrylate), there are many more polymers whose proton resonances are spaced so closely that the highest possible n.m.r. frequencies are necessary to allow their elucidation. Fortunately much progress has been made at 60 Mc./sec. and indeed the greatest number of papers reviewed here concerns 60 Mc./sec. work. The advent of 100 Mc./sec. instruments is causing some of the earlier work to be repeated and generally more reliable information is being obtained in this way although many problems remain. Instruments working at 100 Mc./sec. have better resolution, and better separation of peaks is to be expected since coupling constants, unlike chemical-shift values expressed in cycles per second are not field (i.e., frequency) dependent.

The conditions under which polymer spectra have been obtained are not always stated in the literature. Generally frequencies, solvents and temperatures are stated and indeed such information is necessary for critical comparisons to be made, since these factors contribute significantly to the clarity of the spectra thus facilitating interpretation. Other experimental factors involved in obtaining spectra, e.g., scanning speed, avoiding saturation conditions, integration conditions and integral curves are rarely given in the literature, although full lists of equipment used are often to be seen. In view of this we must trust that operators are using acceptable conditions and to judge from the spectra reproduced in the literature, this is usually the case. On the other hand, integral curves are rarely seen in the literature and figures quoted for intensities must be accepted as such. Some intensity figures quoted for overlapping broad signals have raised the reviewer's eyebrows.[15] Occasionally the methods of measuring intensities have been stated and these include the use of planimeters, the weight of cut-out peaks,[16] as well as the more usual instrumental electronic methods of integration.

Similarly, the methods used for calibration of chemical shifts vary from the most careful instrumental techniques to reading off values from calibrated charts, but usually the method is not stated. Again it is necessary to accept the quoted figures, and variations between different workers appear acceptable for values of chemical shifts and coupling constants. Tetramethyl silane has been used very widely as a reference standard for chemical shift.

It is of course necessary to use solutions of polymers in order to obtain high resolution n.m.r. spectra. The solvents should preferably be without protons or deuterated, but if protonated, the signals for the solvent must not occur in the region occupied by signals from the polymer solute. The solution conditions most preferred are about 10% concentration and in the temperature range 100–150°C, although temperatures from room temperature to at least 200°C have been used. Concentrations vary from as low as 1 or 2% for a difficultly soluble polymer to 20% and occasionally more for normal solid polymers. Solution viscosity usually fixes the upper limit of concentration. Liquid polymers may be conveniently run at 50% concentration to get improved resolution compared to that in the absence of solvent. Some authors have commented on the lack of thermal stability of some polymer structures at the high temperatures used to obtain narrower line widths. Only rarely do authors complain of difficulties due to noise level but this becomes apparent at lower concentrations. Noise is also a trouble when minor amounts of a particular polymer structure is being searched for and computer devices have been used to average out the noise and to accumulate signals of low intensity which would otherwise be lost in the noise. These devices usually called CAT (Computer of Average Transients) methods make remarkable improvements in the clarity of spectra (see p. 227). The signal-to-noise ratio improvement factor attainable by the use of CAT devices is the square-root of the number of scans made of the spectrum. Although such devices have been known for 5 years, their use in the polymer field is infrequent, but the results so obtained are difficult to challenge.

The technique known as double irradiation or spin–spin decoupling has been used to simplify polymer spectra by eliminating the effect of spin coupling. This process is carried out by examining the spectrum of one type of proton while simultaneously strongly irradiating the protons that cause the complication through spin coupling with the first proton. Choice of conditions for decoupling requires some expertise, and confirmation of decoupled spectra are to be welcomed. Some decoupled spectra appear as broad singlets that could be confused with unresolved multiplets, in other cases decoupled spectra are very well resolved. Double irradiation becomes increasingly difficult as the chemical shifts of the two coupled protons come closer together as for example in polypropylene and hydride shift polyolefins. Apart from some notable exceptions,[17] the experimental details of decoupling processes are rarely reported, and in some instances spectra are not reproduced but merely described. Despite these difficulties, the power of the method cannot be denied.

Another method of reducing the complication of n.m.r. spectra is to replace particular protons with other atoms that do not give an observable signal. One way of doing this is by deuteration, although substitution by halogen might also be considered. In this way, not only is the signal of the substituted group removed from the spectrum (which allows the remaining signals to be observed without interference), but also the spin-coupling effect of the substituted group is very much reduced. Thus a double advantage is immediately gained, which is only offset by the difficulties involved in the deuteration of a specific grouping. Successive selective deuteration has been used with remarkable success in polypropylene where decoupling is inapplicable. The interpretation of spectra of deuterated materials usually follows more readily than it does for decoupled spectra, and the assignments may be made with greater certainty. One complication which may be caused by deuteration of monomers is the possibility of di-isotactic polymers (threo- and erythro-forms). The substitution of hydrogen by halogen causes movement of chemical shift of neighbouring protons which has been used to advantage in hydroxyl end-group studies in polypropylene oxides.[18, 19]

Model compounds of polymers have been used extensively in n.m.r. spectroscopy in two main ways. Firstly, to correlate chemical shifts found in polymers with those of well defined small molecules in order to identify the presence of particular groupings. Secondly, the use of more sophisticated model compounds such as isomers of the 2,4-disubstituted pentane type as models of different configurations in the correlation of splitting patterns observed in polymer spectra. The study of the second type has been extended to the 2,4,6-trisubstituted heptanes, and considerable insight into polymer conformational studies has been gained. A considerable amount of attention has been devoted to model compound studies.

Various chemical reactions have been used in order to exploit well tried situations where n.m.r. methods are at an advantage. These include the conversion of polymers such as polymethacrylonitrile and poly(butyl methacrylate) into poly(methyl methacrylate) whose stereoregularity may be determined quite readily by n.m.r. The conversion of poly(vinyl acetate) and other esters into poly(vinyl alcohol) and *vice-versa* has also been used many times. The question of the possible occurrence of racemization in such processes, particularly in the polyacrylates has been demonstrated.[20–22] The danger of changing polymer composition by accidental fractionation due to incomplete recovery of product appears to have escaped attention, although some quoted yields are far from complete. The fact that the product was obtained virtually free from the starting material is of lesser significance in comparison with fractionation problems.

Model polymers have even been made by hydrogenation of unsaturated polymers of known structure. N.m.r. spectroscopy has also been used to follow the progress of polymerization and to study the effects on polymers of various reactions, e.g., acetalization, cyclization and addition of halogen acid.

II. POLYMERS

Several general papers have appeared in the literature and these may be briefly classified into—

(a) Longer reviews.[7, 8]
(b) Other general papers.[2,3, 4,7a, 9, 10]
(c) More specialized papers such as a review of model compounds,[23] application of spin decoupling,[17] a review of copolymers[5] and an attempt to explain n.m.r. line ordering with tacticity.[6]
(d) Papers of a theoretical nature with n.m.r. applications.[24–27]

One report[6] has attempted to rationalize n.m.r. line ordering and multiplicity relating to tactic structures with the chemical structure of the polymer. The order, namely isotactic, heterotactic and syndiotactic with increasing field, was attributed to the presence of functional groups causing a shielding effect on the adjacent methylene groups, as in poly(methyl methacrylate). The reverse ordering was attributed to a de-shielding effect as occurs in poly(vinyl methyl ether). The apparent lack of ordering, as in poly(vinyl chloride) and polyacrylonitrile, was explained by the presence of groups in which anisotropic effects are orthogonal to the backbone of the chain. Moreover, it was demonstrated how bond angles, distances and magnetic susceptibilities may be used in the calculation of shielding contributions, and hence chemical shifts, for a material such as polypropylene. Although the above treatment was limited to non-aromatic polymers its appearance is welcomed since this aspect of the subject appears to have been neglected.

A. Saturated hydrocarbon polymers

1. *Polyethylene*

Most attention has been paid to the copolymers of ethylene.[9, 16, 28, 29] Polyethylene itself exhibits one resonance signal from equivalent methylene groups at about $8{\cdot}73\tau$. However more interest has centred on the measurement of the terminal methyl groups of main chains and branches in order to evaluate branching. Although this can be done normally for low-molecular-weight samples,[30] with polymers it is necessary to employ CAT equipment,[9, 31, 32] using up to 400 scans in order to obtain an accurate result. The number of methyl groups per thousand carbon atoms varying from about three or four for stereoregular samples to about 40 for "high pressure" materials (with an error of ±1 on these figures) has been recorded for commercial polymers. Signals given by small amounts of unsaturation have also been detected, at $4{\cdot}7\tau$[31, 32] and at 5·0, 5·1 and $5{\cdot}3\tau$,[9] with CAT equipment.

2. *Polypropylene*

The n.m.r. spectra of polypropylene are characterized by the very small differences in chemical shift between the various types of protons, which entails that the various resonances show extensive overlapping. Selective replacement of hydrogen by deuterium has proved to be a great help in the interpretation of the spectra.

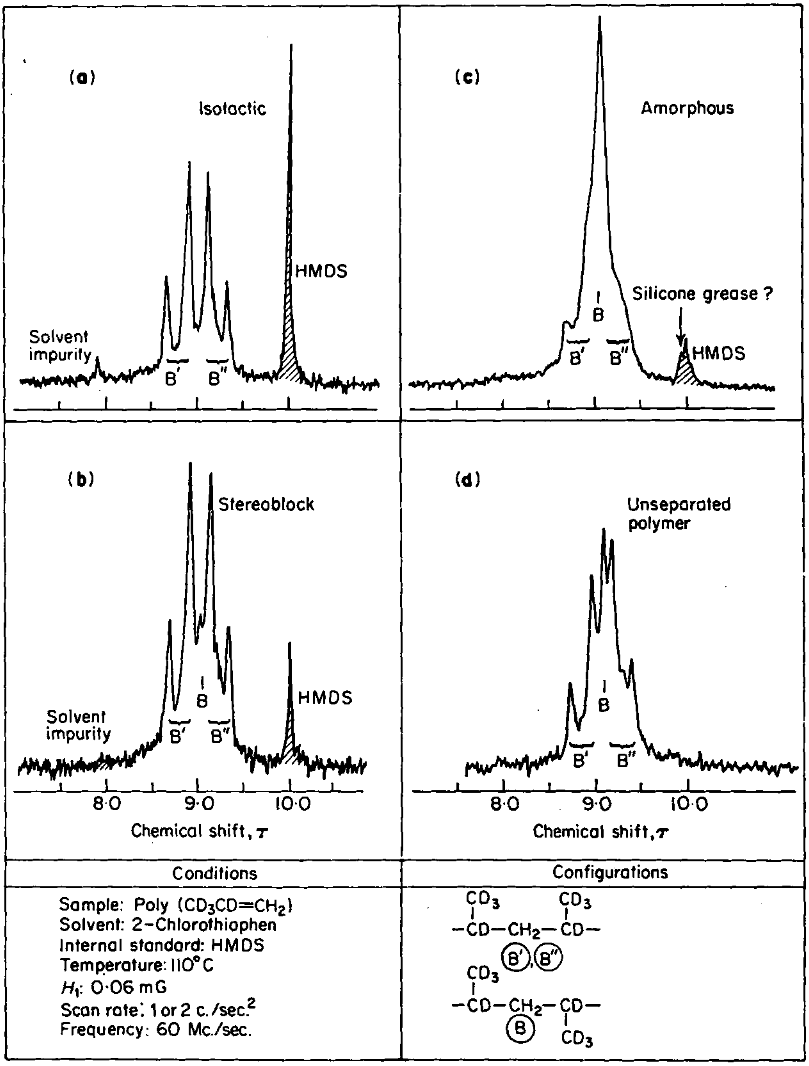
The first record of n.m.r. spectra of polypropylene attributed differences in the methylene resonances to differences in the stereoregularities of the samples;[33] comparison with calculated spectra and estimates of stereoregularity were made. In an extension of this approach thermally degraded samples were used to attain better resolution.[34] Computer calculations were made treating the isotactic methylene protons as part of an ABC_2 spectrum and the syndiotactic as part of an A_2B_2 spectrum. In this way a reasonably good fit with the experimental data was obtained and estimates of tacticity were made.

The dependence of the methylene region on stereoregularity has been confirmed from a study of partially deuterated amorphous stereoblock and isotactic fractions.[35] Such samples prepared from the deuterated monomer propene-2,3,3,3-d_4 exhibited a single resonance, a quartet with additional central resonance, and a quartet respectively for these mentioned structures (Fig. 4). Spectra of polypropene-2-d_1 and normal polypropene for these structures are also reported, in which sufficient differences can be discerned to make qualitative measurements of tacticity. Spectra of the deuterated polymers were obtained at 110°C in 2-chlorothiophene solvent at 60 Mc./sec.

The resolution of the methyl doublet into six peaks has been demonstrated[36] at 100 Mc./sec. (Fig. 5), but only four peaks could be resolved at 60 Mc./sec. for a sample of mixed tactic structures. However it was claimed that the tacticities obtained from methyl triads were in good agreement with those from the methylene diads. Measurements were made in 10% solutions in *o*-dichlorobenzene at 150°C and the syndiotactic signal was stated to appear at higher field. This evidence has been considered in greater detail,[37] and mixtures of isotactic rich and syndiotactic rich polymers have been used to simulate the spectra of so-called stereoblock polymer giving a six-peak methyl signal at 100 Mc./sec. This seems to be an unattractive method at 60 Mc./sec.

An analysis of the n.m.r. spectrum of isotactic polypropene has been carried out by reiterative treatment using a computer to calculate chemical shifts and coupling constants.[38] Agreement with simple compounds was claimed; and the unacceptable solutions were attributed to unoccupied conformations.

A complete analysis of the polypropene spectra at 60 Mc./sec. has been attempted,[39] utilizing samples deuterated in the 3,3,3- and 1,1-positions. From the deuterated samples chemical shifts were obtained namely α-H at 100 c./sec., β-CH_2 at 70 c./sec. and methyl at 55 c./sec. from TMS. Apparently the α-proton spectrum is not influenced by stereoregularity, since it appears as a simple quartet



Conditions

Sample: Poly ($CD_3CD{=}CH_2$)
Solvent: 2-Chlorothiophen
Internal standard: HMDS
Temperature: 110°C
H_1: 0·06 mG
Scan rate: 1 or 2 c./sec.^{2}
Frequency: 60 Mc./sec.

FIG. 4. N.m.r. spectrum of polypropylene-2,3,3,3-d_4. (From Stehling.[35])

in the polypropene-1,1-d_2. The methyl doublets appeared at 60·3 and 54·6 (isotactic) and 58·0 and 52·3 c./sec. (syndiotactic). The isotactic β-methylene spectrum was interpreted as 12 signals given by the AB quartet of the non-equivalent β-protons each coupled with two α-protons. This is confirmed[35] by the spectrum of polypropylene-2,3,3,3-d_4 in which the syndiotactic β-methylene signal was a triplet. The shapes of 100% iso and 100% syndio and various mixtures of these have been calculated from the observed spectra considering only the peaks appearing at 83, 76 and 70 c./sec. In this way semi-quantitative tacticity comparisons may be made that are not dependent on the availability of polymers of perfect steric purity. An "impurity" noticed in the spectra of deuterated polypropenes was attributed to the presence of branched or 1,3-addition structures.

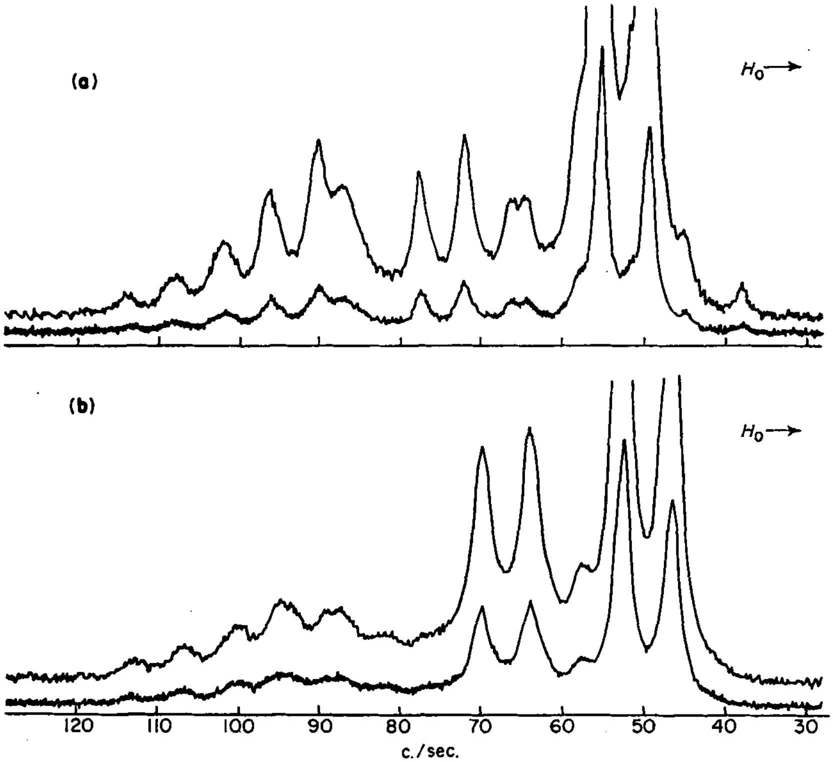


FIG. 5. N.m.r. spectra of two polypropylenes (a) isotactic (b) syndiotactic, obtained at 60 Mc./sec. as 8 wt. % solutions in o-dichlorobenzene at 150°C. HMDS internal reference at zero c./sec. (From Woodbrey.[36])

Spectra of various polypropylene samples of high steric purity have been obtained at 100 Mc./sec.[40] These include the threo and erythro di-isotactic forms of polypropene-1-d_1 which were shown to have different spectra. The methylene region has also been used[41] to study the effect of tacticity on polypropylene fractionation by the gradient elution technique. Apart from the initial (lowest molecular weight) fractions which were lower in isotactic content, the figures showed relatively little change in stereoregularity from fraction to fraction for "isotactic" and "atactic" polymers. Diphenyl ether solutions of 10% concentration were used near 200°C at 60 Mc./sec. although it was admitted that measurements at this frequency were only just adequate. It was claimed that these results were consistent with some previous reports[33, 40] but less so with another.[36]

In a report on the characterization of syndiotactic polypropylene by many techniques,[42] n.m.r. spectroscopy was mentioned briefly with the statement that 30% solutions in *o*-dichlorobenzene at 170°C and 100 Mc./sec. gave poor resolution. A further analysis of the spectrum of syndiotactic polypropylene has been reported[43] having particular regard to the conformational aspects. By comparing observed spectra with those calculated for a variety of values of coupling constants, it was concluded that rapid exchange of conformers took place under the conditions studied, namely 100–170°C.

3. *Polybutenes*

Whereas the resonances were scarcely resolved at 25 Mc./sec.,[44] two separate peaks of relative intensities 1:3 were found at 8·58 and 8·88τ in the 60 Mc./sec. spectrum.[45–48] The latter evidence was offered as proof of the generally accepted structure of polyisobutylene, *viz.* $(\text{—CH}_2\text{—CMe}_2\text{—})_n$. However, a further report[49] agreed only for Ziegler-polymerized material, since other small peaks at 9·4 and 9·6τ were claimed for boron trifluoride-initiated polymer.

4. *Hydride shift polyolefins*

Several papers have appeared on the low-temperature cationic intramolecular hydride shift polymerization of branched α-olefins. Normal polymerization gives 1,2-polymers that exhibit methyl doublets from the pendant isopropyl groups, whereas cationic polymerization gives also the non 1,2-hydride shift polymers having methyl singlets arising from geminal dimethyl groups. The chemical shifts of all these aliphatic protons are very close. This makes interpretation difficult and intensity measurements suspect; additionally the spectral differences between 1,2- and non-1,2-polymers are small, and polymers of mixed structures are obtained except at very low polymerization temperatures. In all the papers of this series, 60 Mc./sec. instruments have been used, although the better resolution of 100 Mc./sec. instruments is evidently called for, especially as deuterated samples have not been available. Various solvents have been used, carbon tetrachloride[50] and tetrachloroethylene,[48] 2-chlorothiophen at 120°C,[47] hexachlorobutadiene at 150–200°C[15, 51] and diphenyl oxide at 240°C.[52] In the later work higher temperatures appeared to give improved resolution.

Polymers of 3-methylbut-1-ene, 4-methylpent-1-ene and 5-methylhex-1-ene made at −73°C gave n.m.r. spectra that were taken to indicate all 1,3-, mostly 1,4- and about half 1,5-structures, respectively. The same monomers polymerized at 0°C gave all 1,3-, more than half 1,4- and almost nil 1,5-structures.[47] Polymerization temperatures of −130°C were found necessary to obtain polymers of predominantly 1,4- or 1,5-structure.[51] Elsewhere[46,47] spectra of this type of polyolefin have been compared with those of paraffinic model compounds and with specially prepared model polymers of 1,2-enchainment.[48] This comparison is evidently in favour of the non-1,2-structures in hydride shift polymers. The 1,2-polymer spectra show a broadened methyl signal with a scarcely resolved "twin-top" arising from the isopropyl side group.

Improved resolution was obtained for 3-methylbut-1-ene polymers using solutions in hexachlorobutadiene at 200°C.[51] Whereas the isotactic 1,2-polymer showed a well resolved methyl doublet (7 c./sec. separation), the methyl signal from the cationic polymer produced at −130°C showed essentially a singlet. The cationic polymer produced at temperatures of +25°C and above had a broadly based methyl resonance thought to be composed of six lines, which was judged to indicate about 25% of 1,2-enchainment.

For poly(4-methylpent-1-ene), the spectral differences between Ziegler 1,2- and cationic 1,4-polymers have been demonstrated,[52] and the better resolution claimed allowed clarification of the lower-field resonances. In this way the methine resonance was distinguished and estimates made of 50–80% (±10%) for the 1,4-content of the cationic polymer. Again the chemical shifts for the 1,2- and 1,4-polymers were similar, but the latter had a split methyl and larger methylene signal. It was remarked[53] that other samples prepared with aluminium chloride at −78°C were in substantial agreement with this.[47] The relatively slight differences in n.m.r. spectra of the cationic and Ziegler-catalysed vinylcyclohexane polymers have been interpreted as being due to 1,3- and 1,2-polymer structures, respectively.[15] The spectra of reference compounds and the integrals obtained on broad overlapping peaks were used to support this interpretation. Likewise it was suggested that the oligomer obtained cationically from 3-phenylbut-1-ene was, from the appearance of its n.m.r. spectrum,[54] essentially a 1,3-polymer.

The cationic polymer of 4-methylhex-1-ene obtained at 97°C,[55] was claimed to be all 1,4-structure from the examination of its n.m.r. spectrum, which showed the presence of an isolated methyl group and virtual absence of methine proton. On the other hand, the γ-initiated polymers of 3-methylbut-1-ene and 4-methylpent-1-ene obtained at −78°C as low-molecular-weight oily materials were judged to be 1,2-polymers from their i.r. and n.m.r. spectra.[50] This was as expected for free-radical polymerization.

The picture presented by this series of papers is consistent with the cationic formation of non-1,2-structures, although the difficulties involved do not allow an elegant study to be made.

5. *Other polyolefins*

The polymerization of vinylcyclopropane has been shown[56] to proceed mostly by a 1,2-mechanism when initiated by catalysts such as stannic chloride and the cyclopropane ring remains intact giving a signal near to 10τ. On the other hand, free-radical catalysts gave mostly unsaturated 1,5-polymers by ring opening. The polymerization ring-opening of cyclopentene by a particular Ziegler catalyst to give similar 1,5-polymer was also reported.[56] The virtual absence of unsaturation in the 1,2-polymer and the absence of the cyclopropane ring in the 1,5-polymer were indicated by the n.m.r. spectra.[57]

The diene 4-vinylcyclohexene has been reported to give polymers of mixed structures from various catalysts.[58] The n.m.r. evidence appears to favour some pendant cyclohexene rings and some cyclized, i.e., saturated, units.

B. Polybutadiene and other polydienes

1. *Polybutadiene*

Butadiene gives 1,4- (*cis* and *trans*) and 1,2-polymers, and the chemical shifts of these enchainments have been reported,[59] but the *cis* and *trans* forms are virtually indistinguishable at 60 Mc./sec. This has also been demonstrated at 40 Mc./sec.,[60] and the chemical shifts of various poly(1,4-sorbic acid esters) have also been given using signal intensities to help make assignments (see also Sergeyev and Karpov[44]).

Samples of variously prepared liquid polybutadienes and their partial epoxidation products have been studied by n.m.r. at 60 Mc./sec. and by near i.r. spectroscopy.[61] Although good resolution was achieved for the polybutadienes, the n.m.r. spectra of the partially epoxidized materials were broader. This has restricted the authors to the comment that the amount of "epoxidation" as measured by n.m.r. agreed with that measured by chemical analysis. No doubt more information concerning the structure of these materials could be obtained by n.m.r., but interest appeared to centre on fears for the presence of cyclized structures.

Elsewhere,[62] the n.m.r. spectrum of a free-radical-initiated polybutadiene has indicated 22–25% 1,2-content, a result in good accord with a chemical determination. This polymer sample had —$C(CH_3)_2CH_2OH$ end groups whose methyl and α-CH_2 protons appeared clearly in the spectrum at 9·20 and 6·78τ, respectively. These can be used in end group concentration measurements whereas the hydroxyl proton resonance was scarcely visible in the spectrum. The n.m.r. spectrum of a 1,2-polybutadiene has been reported[63] together with its spectrum after cyclization. Anionic telomerizations of butadiene with aromatic hydrocarbons have been reported.[64]

A spectrum has been reported of a 90% 1,2-polymer obtained from a "living" polymerization system.[65] Block copolymers with styrene have also been mentioned.[66]

2. *Poly-2,3-dimethylbuta-1,3-diene*

Both 1,4- (*cis* and *trans*) and 1,2-structures are to be expected in these polymers. From the 60 Mc./sec. spectrum[67] of a polymer prepared by lithium in pentane, the composition of 38% 1,2- 26% *cis*-1,4- and 37% *trans*-1,4- has been deduced. Only the 1,2-enchainment has olefinic protons and the assignments for *cis* and *trans* were made by analogy with polyisoprene.

It has also been indicated[68] that the polymer composition is dependent on monomer concentration; 94% *trans* was produced at low monomer concentration and 34% *trans* in bulk polymerization. The compositions obtained by using other polymerization systems are given below—

		% 1,2-	% *cis*	% *trans*
Pentane	BuLi	17	10	73
Pentane	Na	36	24	40
Pentane	K	33	20	48
Tetrahydrofuran	Li	44	27	29

3. *Polypiperylene* (*polypenta-1,3-diene*)

These polymers present five different possible enchainments, 1,4- (*cis* and *trans*), 3,4- and 1,2- having 3,4- (*cis* and *trans*). Chemical shifts obtained at 40 Mc./sec. have been quoted,[60] and these differ slightly for isotactic and syndiotactic polymers. It was also stated that the methyl signal is a singlet for the isotactic form but is a doublet of 6 c./sec. separation for the syndiotactic form, but no spectra were shown. Elsewhere,[67] was shown the 60 Mc./sec. spectrum of a lithium-polymerized piperylene, from which the structure 23% 1,2-, 10% 3,4- and 77% 1,4- was obtained. Only one olefinic peak was apparent, and in benzene solution the 1,2-methyl peak exhibited splitting with its α-olefinic proton. Another 60 Mc./sec. spectrum[69] of a polypenta-1,3-diene had six resonances from which the composition 63% 1,2- and 37% 1,4- was deduced. This spectrum had some similarities with the one mentioned previously.[67]

Again,[68] more figures of high 1,4-contents have been quoted for lithium-initiated polymers, but changing the alkali metal reduced the 1,4-content to 63% (for sodium), 81% (for potassium) and 60% (for lithium in tetrahydrofuran), respectively. In the latter two instances, about 5% 3,4-content was also detected. It has been pointed out that *cis* and *trans* forms of 1,2- and 1,4-enchainments are to be expected, but these have not been distinguished.

Another report described polymers made from stereospecific catalysts, and chemical shifts are given for materials described as 1,4-*trans* isotactic and 1,4-*cis* syndiotactic, but no n.m.r. spectra are given.[70] Infrared spectroscopy was necessary to distinguish *cis* from *trans* structures.

4. *Polycyclopentadiene*

It has been presumed that cyclopentadiene may be polymerized in the 1,4- and 1,2-enchainments, but also various other structures have been proposed. It has been pointed out[71] that the 1,2- and 1,4-forms have the same ratio of olefinic to non-olefinic protons, and that the ratio of protons in positions α and β to the double bond must serve to indicate the type of enchainment, since only one resonance was observed for the olefinic protons. Although no spectrum was shown,[71] chemical shifts have been listed and intensity measurements made for Ziegler-catalysed polycyclopentadiene and poly-3-methylcyclopentadiene. For the former the 1,4-structure was preferred, and for the latter the 1,2-structure was ruled out.

The spectrum of a polymer obtained by γ-initiated bulk polymerization at $-78°C$[72] has been shown. Only here does the olefinic resonance appear as three peaks at 4·11, 4·39 and 4·59τ. Assignments were suggested for the overlapping non-olefinic resonances, from which it was concluded that more than 80% of the additions were in the 1,4-enchainment. On the other hand a polymer catalysed by stannic chloride with trichloroacetic acid has given rise to a spectrum[73] which is apparently unlike all other polycyclopentadiene spectra in relative intensities. Here the emphasis is on the ratio of polymerized units having double bonds with protons to those without protons. Yet another method of assigning the non-olefinic protons has been suggested[74] in a study of the low-temperature cationic polymerization of cyclopentadiene, where it was claimed that the 1,2-/1,4-contents were little affected by change in solvent but more so by the nature of the catalyst.

The reference compounds 3,4- and 3,5-dimethylcyclopentenes have been used,[75] which has led to criticism of previous assignments[71,72,74] and to the conclusion that anionically polymerized samples contained about 50% 1,2-content, although the spectrum shown appears not unlike those criticized. All the spectra are similar in that three broad overlapping peaks appear for the non-olefinic protons and, except as stated,[72] the olefinic resonance is essentially only one peak. The apparent differences in structure arise from the different assignments given to the non-olefinic resonances.

C. Polyisoprenes

The chemical shifts of the different protons in the 1,4- (*cis* and *trans*), 1,2- and 3,4-enchainments of polyisoprenes have been charted, together with those for the 1,4- and 1,2-enchainments of polybutadienes.[59] It has been shown that quantitative analysis of butadiene–isoprene copolymers comprising such enchainments can be carried out reasonably accurately. This involves measuring the areas of seven peaks to most of which more than one type of proton contributes.

The peaks for the methyl and methylene adjacent to double bonds in each case do not separate completely.

The controversy concerning the steric purity of natural rubber (*cis*) and balata (*trans*) has been calmed[76] by using 100 Mc./sec. and also 60 Mc./sec. with CAT equipment. Although a commercial lithium-initiated polyisoprene showed 3,4-content in excellent accord with infrared measurement, no 3,4-content could be detected in natural polyisoprenes at 100 Mc./sec. Diluting this synthetic material with balata allowed a minimum level of 0·3% 3,4-monomer units to be determined by using the CAT method. In carbon tetrachloride solution the *cis*- and *trans*-methyl groups were discerned as separate peaks at 8·33 and 8·40τ, respectively, and 1% of *cis* in the *trans* and *vice-versa* was stated to be the minimum detection level at 100 Mc./sec. at room temperature. In this way it was demonstrated that natural *cis*- and *trans*-polyisoprenes are at least 99% *cis* and *trans*, respectively.

It has also been reported[77] that the use of benzene as solvent separates the *cis*- and *trans*-methyl peaks of polyisoprene by 0·14 p.p.m. at 60 Mc./sec., about twice as much as in carbon tetrachloride or carbon disulphide solutions. This greatly helps the analysis of these polymers, even though the chemical shifts of other types of protons showed no differences between *cis* and *trans*. As pointed out[76] the n.m.r. method for determination of *cis* and *trans* ratios is more precise than the i.r. method, but various authors infer that the i.r. method is to be preferred for the determination of small amounts of 1,2-content.

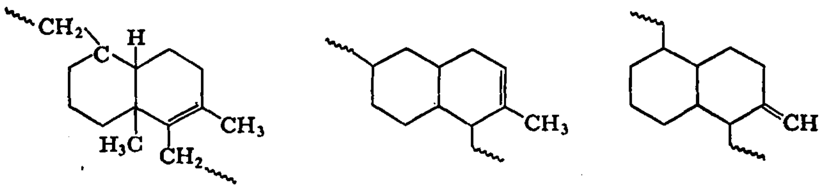
Spectra have been obtained from 1% solutions in tetrachloroethylene at room temperature and 60 Mc./sec. of polyisoprenes, prepared by using lithium in pentane and tetrahydrofuran, respectively, as catalyst.[67] The enchainments indicated for these polymers are in good agreement with the i.r. values.

The structures of anionically initiated polyisoprenes have been studied by using 56·4 Mc./sec. n.m.r. to determine the *cis*/*trans* content, together with i.r. assistance for determining the 3,4-content.[78] Although it was stated that the peaks are seldom completely resolved, n.m.r. evidence seems to be preferred to that of i.r. when divergencies arise, but it is commented that low 1,2-contents tend to be undetected by n.m.r. Apparently benzene shows some improvement in resolution over carbon tetrachloride as a solvent for non-1,4-polymers. Another n.m.r. spectrum of a polyisoprene of mixed structure has been reported,[69] and also the spectra of polyisoprenes with very high 3,4-enchainment.[63, 79] An n.m.r. spectrum of natural rubber obtained at 25 Mc./sec., has been given.[44]

The CAT technique has also been used[80] to show that a commercial synthetic *cis*-polyisoprene has a structure more closely resembling that of natural rubber than has been currently thought. The method is like a previous one[76] except that an automatic mechanical timing-sequence device for signal-to-noise ratio enhancement was used at 60 Mc./sec. for studying the olefinic proton region, complemented by CAT equipment at 100 Mc./sec. for the methyl region. Again, a commercial lithium-initiated polyisoprene was used to calibrate the minimum 3,4-content detectable, which was 0·1% in this case. In this way it was demonstrated that the synthetic *cis* polymer contained less than 0·1% 3,4- and about 0·5% *trans* content.

Barium catalysts have been reported to give 21% 3,4- and 79% 1,4-enchainments in polyisoprene,[81] the ammonia complex and barium metal affected only the 1,4- *cis*/*trans* ratios, *cis* contents of 23% and 67% were obtained, respectively.

Polyisoprenes are unusual, in that their chemical reactions have produced structures that have also been studied by n.m.r. These reactions with halogen compounds involve addition of halogen acid or cyclization, or both. There is i.r. evidence that the sulphur dioxide-catalysed *cis–trans* isomerization of polyisoprenes is not accompanied by double-bond shift. This has been confirmed[82] by i.r. and n.m.r. on deuterated polyisoprene-3-*d*. No signal at 5τ was observed; hence the double bond must stay attached to the deuterated carbon atom.



1 (48%) **2** (33%) **3** (9%)

FIG. 6. Bicyclo-structures formed from cyclization of polyisoprene.

The cyclization of 1,4-polyisoprenes by titanium tetrachloride has been studied,[83] and the n.m.r. spectrum of the cyclized products shows extensive overlapping of resonance peaks in the 7–10τ region and little residual olefinic proton resonance signal. Similar study of a cyclized pentadeuterated polyisoprene has enabled this complex resonance to be explained on the basis of the formation of bicyclo structures of the types (**1**, **2** and **3**) and 10% isolated unchanged units (see Fig. 6).

The cyclo-hydrochlorination of a high 3,4-polyisoprene containing 12% 1,4- and 9% 1,2- has been studied.[84] The product appears to be a mixture of the linear addition product to the 1,4-portions, and cyclic structures which are made from adjacent pairs of non-1,4-portions. The n.m.r. spectrum is characterized by a sharp resonance near 9τ and also one at 8·4τ. It is also stated that the hydrochlorination of 1,4-polyisoprenes is accompanied by only a small amount of cyclization, as shown by a small 9·1τ signal, and no isomerization.[85]

The addition of various halogen acids to a synthetic polyisoprene has been studied;[86] the n.m.r. spectra of the products showed the halogen atom to be attached to the carbon atom with the methyl group. The materials obtained by the lithium aluminium halide reduction of the hydrochlorinated products have n.m.r. spectra analogous to the spectra of some commercial ethylene–propylene copolymers.

The cyclization of a high 3,4-polyisoprene by using titanium tetrachloride indicated[79] that the original unsaturation was not quite completely removed and the cyclized material had peaks at 8·4 and 9·05τ, which were somewhat broad and incompletely resolved. The "cyclicity" (the number of rings fused together) of this sample, which may have been influenced by the presence of 12% 1,4- and 9% 1,2-content in the starting material, was thought to be about three.

The product of cyclization of a very high 3,4-polyisoprene which was taken to be a "ladder" polymer, i.e., one that consists almost entirely of fused methylcyclohexane rings has been studied.[63] The n.m.r. spectrum of this material showed broad absorptions in the 7–10τ region, not unlike that of another sample.[79] This result has been taken to support the contention that stereospecific diene-type polymers contain small amounts of cyclized material produced during the polymerization. In this matter, the chemical-unsaturation data may possibly be more compelling evidence than the n.m.r. spectra. These assignments for the proposed "ladder" polymers[63] have been disputed[87] and the n.m.r. evidence re-interpreted to furnish no evidence for cyclic structures in 1,2-polybutadienes, 3,4- and 1,4-polyisoprenes.

The n.m.r. spectroscopic examination of block copolymers of high 3,4-polyisoprene with high 1,2-polybutadiene and styrene has been mentioned.[66]

D. Polystyrene

The difficulty with polystyrene is to resolve the signals from the α- and β-protons.[8] It has been shown[88] that this can be achieved in aromatic solvents, where the chemical-shift difference for α- and β-protons is greater for isotactic polymer. The spectra of atactic and isotactic polystyrene-α-d_1 have been shown. It has also been shown[89] that in polystrene-β,β-d_2 the α-methine spectrum has resonances corresponding to iso-, hetero- and syndiotactic placements (see also Kern[90]).

Good resolution of α- and β-protons in isotactic polystyrene has been achieved at 60 Mc./sec. by using 15% solutions in *o*-dichlorobenzene at 200°C[91] (see Fig. 7), but the same treatment of an atactic sample gave poorly resolved spectra. The isotactic β-methylene signal was found to be a triplet and that of the α-methine hydrogen a distorted quintet, whereas both aromatic resonances also showed considerable fine structure. The β-protons in the isotactic structure appear to be coincidentally equivalent. As in a previous report,[89] the α-proton spectrum of polystyrene-β,β-d_2 showed three peaks, the lower-field one being judged due to isotactic placements; such "atactic" samples appear to be about 80% syndiotactic. The spectra of meso and racemic 2,4-diphenylpentanes were also shown; and in spite in marked differences in the β-methylene spectra of polymer and model compounds it was inferred that isotactic polystyrene has the same local conformation as the meso pentane derivative. The spectra of three stereo isomers of 2,4,6-triphenylpentanes have been obtained at 100 Mc./sec.[92]

It has been shown that the line width of the aromatic protons shows an abrupt decrease as the temperature of measurement is increased. As this change is paralleled by other changes in physical properties of solid and dissolved polystyrenes, it has been called a "transition in solution". Such transitions have been observed at 60 Mc./sec. to occur at 40–80°C and 50–60°C for atactic and isotactic samples, respectively.[93] A similar change at about 40°C was observed at 100 Mc./sec. for an isotactic polystyrene degraded ultrasonically to a molecular weight of about 5000.[94]

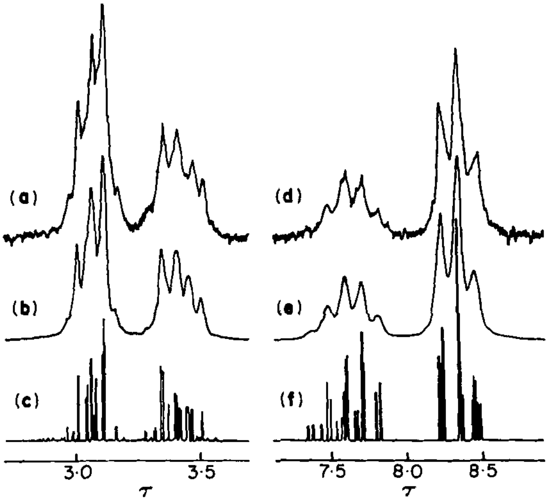


FIG. 7. Isotactic polystyrene. (a) aromatic proton spectrum, in tetrachlorethylene at 135°C. (b), calculated spectrum: $\nu_{(ortho)} - \nu_{(meta)} = 22$ c./sec.; $\nu_{(para)} - \nu_{(meta)} = 2$ c./sec.; all $J_{ortho} = 6{\cdot}5$ c./sec.; both $J_{meta} = 2{\cdot}0$ c./sec.; $J_{para} = 1{\cdot}0$ c./sec.; line width = 1·0 c./sec. (c), "stick spectrum" corresponding to (b). (d), backbone-proton spectrum, in *o*-dichlorobenzene at 200°C. (e), calculated spectrum: $\nu_\beta - \nu_\alpha = 43{\cdot}8$ c./sec.; both $J_{vic} = 7{\cdot}0$ c./sec.; $J_{gem} = 14{\cdot}0$ c./sec.; line width = 3·0 c./sec. (f), "stick spectrum" corresponding to (e). (From Bovey *et al.*[91])

E. Poly-α-methylstyrene

Earlier work had shown that the α-methyl resonance is sensitive to stereoregularity and the peak at highest field was attributed to the syndiotactic form.[7, 8] The methylene spectrum did not exhibit multiplicity and the polymers examined were mostly syndio rich. Polymers prepared from various cationic catalysts have been examined in 10% solutions in chloroform at 80°C and at 60 Mc./sec.[95] From the stereoregularities determined by n.m.r., these catalysts were arranged in order of stereo-effectiveness, which was found to be similar to that obtained by "qualitative" methods. In the apparently "twin-topped" methylene resonance, the amount of splitting was proportional to the intensity of the methyl peak attributed to syndiotactic placements. This cast doubts on the above assignment or suggested that the methylene splitting is unlike that found, for example, in poly(methyl methacrylate). Hence the assignment of the highest field peak to isotactic would be preferred, especially as this is suggested by X-ray evidence. From samples examined at 100 Mc./sec., the methylene spectrum appeared to be a singlet upon an AB quartet.[96] The predominance of the isotactic methylene signal is consistent with the highest-field methyl resonance being the isotactic signal, and the difficulty arose of assigning the other two methyl signals. A comparison of intensities with diad structures strongly supported the assignment of methyl resonances in the unusual order heterotactic, isotactic and syndiotactic with increasing field strength. Carbon disulphide was the solvent showing the best resolution of the methylene peak at 30°C in a polymer obtained from sodium naphthenide in tetrahydrofuran at −78°C. The effect of different solvents on the spectra of such samples has been described elsewhere.[11]

Two samples of poly-α-methylstyrene catalysed by boron trifluoride etherate at −70°C in hexane and in chloroform were shown to have different n.m.r. spectra.[97] By using the original assignment[95] of highest-field methyl signal for isotactic structure, these polymers were declared atactic and isotactic, respectively. The penultimate monomer unit was judged to have no effect on the stereoregularity.

This has been extended to the study of stereoregularity by using Friedel–Crafts catalysts in various solvents,[98] and solvent/non-solvent mixtures. Atactic polymer was produced in heterogeneous polymerization and isotactic in homogeneous polymerization. The stereoregularity was little affected by polarity of solvent or catalyst. Three different spectral assignments by four groups of workers can hardly be regarded as conclusive.

F. Methacrylate polymers

1. *Poly(methyl methacrylate)*

The features of the n.m.r. spectra of poly(methyl methacrylate) samples have been clearly demonstrated by Bovey[7a] (see Fig. 8) in his paper which not only established the structural characterization of this polymer, but also set the pattern of investigation for most other addition polymers. He found that in chloroform solution three α-methyl peaks appeared at 8·78, 8·95 and 9·09τ and were due to isotactic, heterotactic and syndiotactic forms, respectively. Also, the isotactic methylene signal was a quartet, whereas the syndiotactic one was a singlet. The observation of an AB quartet methylene signal is an absolute determination of the presence of isotactic structures and is independent of any other type of evidence.[7] Whereas free-radically initiated polymer was found to have an approximate *i*:*h*:*s* ratio of 10:30:60, anionic ("non-sigma") polymers could be made having either 100% iso or 90% syndio. Stereoregularity measurements on many samples have been recorded[26, 100, 101] (see also Bovey and Tiers[7] and McCall and Slichter[8]). It has been observed that increase of pressure up to 7960 kg./cm.^{2} had the effect of reducing the amount of syndiotactic sequences in free-radical polymerization, and an *i*:*h*:*s* ratio of 11:49:40 was found.[102]

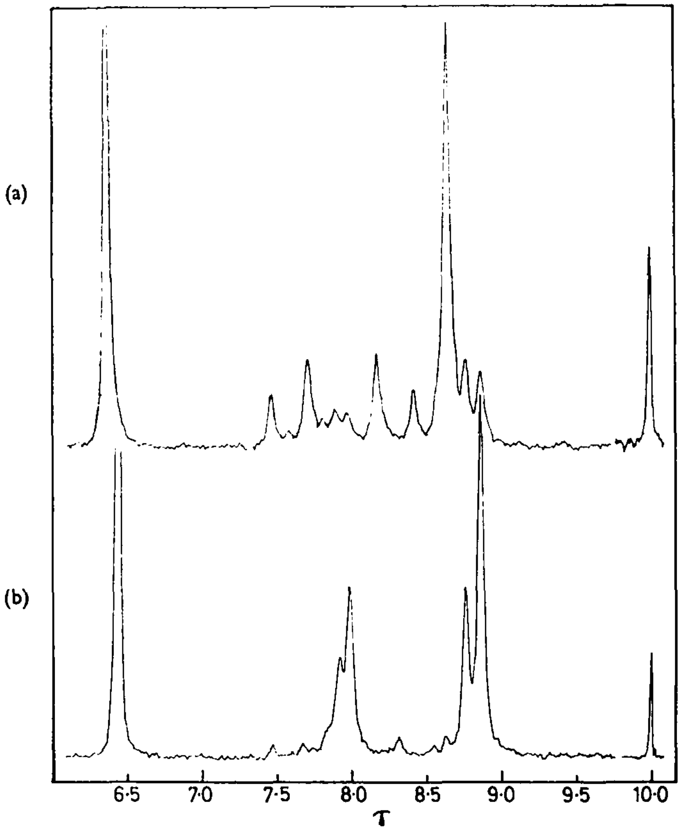
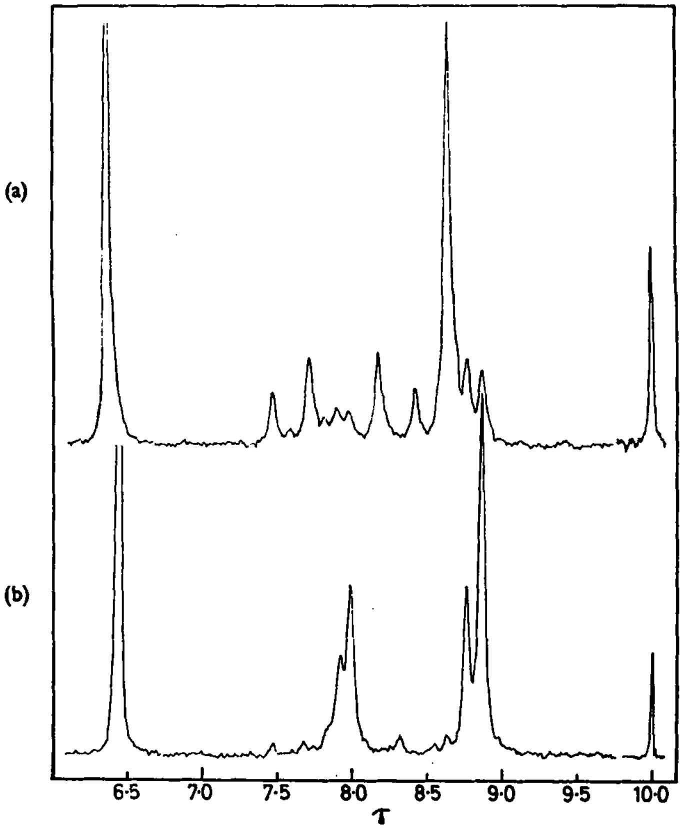


FIG. 8. 60 Mc./sec. spectrum of methyl methacrylate polymers, approximately 15% solutions in chlorobenzene; (a) predominantly isotactic polymer, recorded at 160°C; (b) predominantly syndiotactic polymer, recorded at 145°C. (From Bovey.[7a])

The findings of Bovey for free-radical polymers have been largely confirmed,[103] but by treating the *i*:*h*:*s* figures on a ternary diagram it has been suggested that anionically initiated polymers may show a stereoblock character. Also, it has been shown[104] that i.r. spectroscopy can furnish similar information on tacticity *i*:*h*:*s* ratio of 10:30:60, anionic ("non-sigma") polymers could be made having either 100% iso or 90% syndio. Stereoregularity measurements on many samples have been recorded[26, 100, 101] (see also Bovey and Tiers[7] and McCall and Slichter[8]). It has been observed that increase of pressure up to 7960 kg./cm.^{2} had the effect of reducing the amount of syndiotactic sequences in free-radical polymerization, and an *i*:*h*:*s* ratio of 11:49:40 was found.[102]



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The findings of Bovey for free-radical polymers have been largely confirmed,[103] but by treating the *i*:*h*:*s* figures on a ternary diagram it has been suggested that anionically initiated polymers may show a stereoblock character. Also, it has been shown[104] that i.r. spectroscopy can furnish similar information on tacticity evidence,[110] and an analogy with dilute solution behaviour was outlined. Also, the examination of polymers prepared with various alkali-metal compounds has been reported together with an alternative way of representing the structural parameters.[115]

The effect of zinc chloride on the free-radical polymerization of methyl methacrylate has again been studied.[116] No effect on the polymer structure was observed over the temperature range -78°C to $+150$°C, except in the case of the 1 : 1 molar mixture of monomer to zinc chloride in the absence of water, when the formation of isotactic material was favoured. This appears to clarify the earlier comments.[7]

In a study of the effect of solvent on the appearance of spectra, it has been shown[11] that in benzene solution the ester methyl group appears as three close resonances which have been assigned to isotactic, heterotactic and syndiotactic, in order of increasing field strength. The separation of the α-methyl resonances were less in aromatic solvents. Elsewhere,[117] a multiplet ester methyl signal has been reported in styrene copolymers.

Other reports concern the application of n.m.r. information to the determination of diastereosequence distribution statistics for anionic and free-radical polymers.[12, 118]

2. *Polymers of other esters of methacrylic acid*

These polymers have been studied either directly or after conversion by hydrolysis and re-esterification into poly(methyl methacrylate), which facilitates straightforward examination.

(a) *Polymers studied directly.* The polymers of methyl, ethyl and butyl methacrylates have been studied over the range of temperature of measurement from 35 to 100°C with both 40 Mc./sec. and 100 Mc./sec. instruments.[110] Better resolution was obtained at both higher temperature and higher frequency, although the values given for the polymer structures were little altered. In the ethyl ester, the α-methyl signal was seen to sharpen at a lower temperature than the C—CH$_3$ resonance of the ethyl group. In the butyl ester complete overlap of the α-methyl signal by the —C—CH$_3$ resonance of the butyl group precludes structural measurement, which is consistent with another report.[100]

Two similar papers by the same authors[119] (see also Yokota and Ishii[120, 121]) concern the polymers of benzyl, β-phenylethyl and γ-phenylpropyl methacrylates produced by free-radical initiation at 50°C. Whereas the α-methyl signals of the first and last of these showed a pattern similar to that given by an atactic poly(methyl methacrylate), the spectrum given by the poly-β-phenyl polymer indicated a highly syndiotactic structure. Attempts to make isotactic polymers by using phenylmagnesium bromide were successful for the first two esters, so also were attempts to make syndiotactic polymers using γ-irradiation at -47°C. It was concluded that the α-methyl peak is sensitive to stereoregularity in all these polymers and that the free-radical polymerization of β-phenylethyl methacrylate at 50°C does indeed produce polymer of anomalously high syndiotacticity. The β-methylene signals are not obscured by other resonances and are also considered.

(b) *Polymers studied after conversion to poly(methyl methacrylate).* The menthyl ester polymerized in a variety of ways has been studied,[122] and it appears that the introduction of a bulky alkyl group generally gives polymers of low syndiotacticity.

N.m.r. results are quoted[106] for s-butyl, t-butyl and α-methylbenzyl methacrylates polymerized at temperatures in the range −78°C to +80°C by phenylmagnesium bromide and free-radical (γ- or peroxide) initiation. The results for stereoregularity are shown graphically against temperature of polymerization together with curves for the methyl and menthyl esters. Whereas free-radical polymers show a slight decrease in syndiotacticity with increasing temperatures, the Grignard polymers show higher isotacticity at higher temperatures (although a minimum is experienced by the Grignard methyl and s-butyl polymers).

A whole range of esters including methyl, ethyl, isopropyl and t-butyl methacrylates polymerized by both free-radical and anionic initiators have been studied[123] and consideration given to the effect of the penultimate unit on stereoregularity. It was concluded that in free-radical polymers the stereoregularity was controlled by the terminal unit, but deviations from this occurred in cases with long-chain and bulky ester groups. It was also stated that hydrolysis and re-methylation do not affect the stereoregularity, and a wealth of detailed information on many polymers is given.

3. *Other methacrylate polymers*

The tacticity of allyl methacrylate polymers prepared anionically in toluene or tetrahydrofuran and mixtures of these have been reported.[124] Measurements were made at 100 Mc./sec. in *o*-dichlorobenzene solutions at 100°C, and these indicated various polymer structures from high isotactic to high syndiotactic. The allylic part of the monomer was not involved in the polymerization which was readily discerned from the n.m.r. spectra.

The spectrum of a graft copolymer of ethyl methacrylate onto a partially peroxidized poly-*p*-isopropylstyrene backbone has been presented.[125] Although the multi-technique approach of these authors is praiseworthy, in this case the n.m.r. spectrum does not show all the expected features of poly(ethyl methacrylate), but tends to show the oxidized state of the backbone. True evidence of grafting would be the appearance in the spectrum of resonances associated with the join-up points of the different polymer chains. As these entities are at very low concentration their detection under normal conditions is not favoured.

G. Polyacrylates

Although it is well known that the stereoregularity of poly(methyl methacrylate) may be determined readily by n.m.r., the case of poly(methyl acrylate) is more complicated.

From the polymers of s-butyl and t-butyl acrylates obtained by free-radical and ionic catalysts, it has been shown[126] that the poly(acrylic acids) produced by hydrolysis have different infrared spectra and the methylated acids have different n.m.r. spectra for the β-methylene protons. These differences have been attributed to different stereoregularities in the original polyacrylates. Also n.m.r. spectra were obtained directly by the appropriate polymerization of methyl acrylate, and these were similar to those obtained through conversion from the other esters.[127] The polymer prepared from ionic catalysts and expected to be isotactic also gave a rather similar n.m.r. spectrum. Also meso and racemic model compounds, spin decoupling and deuterated poly(methyl acrylate-α-d_1) have been used[128] to deduce the spectral parameters, and it was claimed that the calculated ABKL spectrum showed good agreement with the observed spectrum.

The racemization of an isotactic sample of poly(isopropyl acrylate) by an alkaline catalyst has been demonstrated[22] by the production of a sample whose n.m.r. spectrum was virtually identical with that obtained from an atactic sample. Additional evidence has been furnished for the racemization of polyacrylonitrile in the course of conversion by acid hydrolysis to poly(methyl acrylate).[20] The α-deuterated polyacrylonitrile yielded poly(methyl acrylate) having an α-proton signal. However the conversion of α-deuterated polyacrylonitrile in deuterated reagent produced poly(methyl acrylate-α-d_1) which gave a singlet at $8{\cdot}16\tau$ for the syndiotactic β-methylene protons, superimposed on a quartet for the isotactic methylenes.

α,β-Disubstituted monomers may form di-isotactic polymer structures depending on the geometry of the monomer, the presentation of the monomer to the growing chain and the type of opening (*cis* or *trans*) of the monomer double bond[1] with stereospecific catalysts. The α,β-di-deuterated acrylates are an example of this.

The backbone proton spectra of isotactic poly(isopropyl acrylate) together with that of isotactic poly(isopropyl acrylate-α-*cis*-β-d_2) (with deuterium irradiation) have been reported.[129] The latter shows singlets of approximately equal intensity corresponding to threo ($8{\cdot}32\tau$) and erythro ($7{\cdot}87\tau$) forms. From this the configuration of a polyacrylate chain was claimed to be random with respect to CHD groups and stereospecific with respect to ester groups. This infers that *cis* and *trans* opening of the monomer double bond is equally probable in the anionic polymerization by phenylmagnesium bromide in toluene at −78°C. This latter statement was not supported[130] by a study of the anionic polymerization of methyl acrylate-α,β-d_2 by lithium aluminium hydride in toluene at −78°C, since the ratio of the intensities of the isotactic methylene signals was equal to the *cis/trans* ratios of the starting monomers. A further comment on this point[1] is that anionic polymerization formed highly isotactic ester and CHD placements and an erythro relationship between substituents on adjacent carbons. However, in the free-radical polymerization of this monomer at various *cis/trans* ratios,[130] (see Fig. 9) the ratio of isotactic signal intensities tended to unity and it was concluded that both *cis* and *trans* opening of the monomer double bond then takes place. There is more evidence for *trans* opening of the double bond in the anionic polymerization of methyl acrylate.[131] Unused monomers had unchanged *cis–trans* ratio. There is a further comment on these samples.[10]

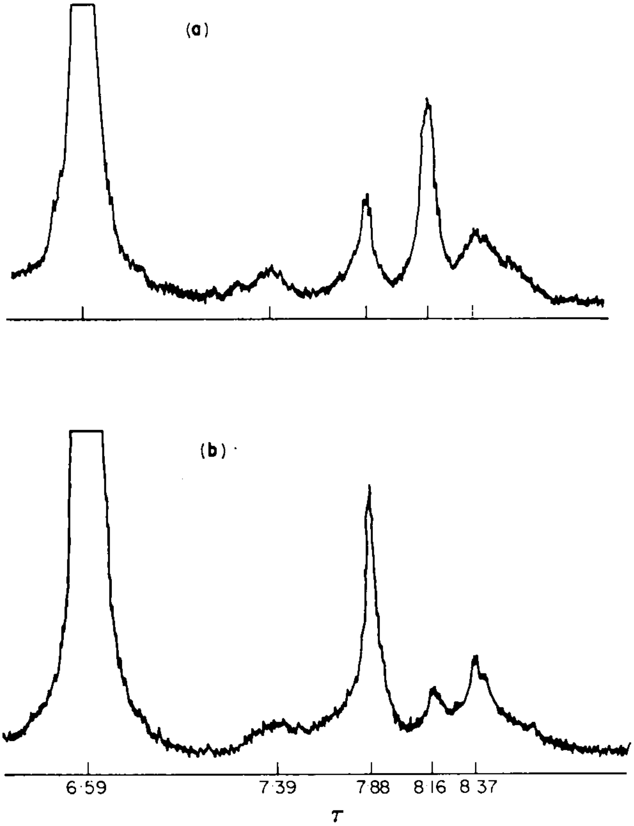


FIG. 9. N.m.r. spectra of methyl acrylate-α,β-d_2 polymers prepared with: (a), azobisisobutyronitrile in toluene at 50°C; (b) lithium aluminium hydride in toluene at −78°C. The spectra are measured on 10% solutions of the polymers in benzene. (From Yoshimo and Komiyama.[130])

The conformations of poly(alkyl acrylates) have been studied.[132] The β protons of isotactic poly(methyl acrylate-β-d_1) gave two triplets in methyl formate solution at room temperature. Interpretation of these as an A part of an AC_2 spectrum leads to the result that the *trans* conformation is as probable as the sum of the *gauche* ones. Evidence from model compounds was also presented to support this.

The n.m.r. spectra of model compounds for polyacrylate esters and acids have been reported,[133] but i.r. data was used to infer that a free-radical poly(methyl acrylate) is substantially isotactic.

In a 100 Mc./sec. examination of poly(methyl acrylate), it was reported that the isotactic methylene signal was two separate quintets centred at 8·34 and 7·90τ, whereas the syndiotactic signal was a triplet at 8·16τ. From this it was deduced that free-radical and anionic polymers had 60% and 93% isotactic content, respectively.[134]

H. Polyacrylonitrile and polymethacrylonitrile

1. *Polyacrylonitrile*

Difficulties in making suitable solutions and in attaining adequate resolution have restricted n.m.r. progress with polyacrylonitrile.

An attempt to determine the stereoregularity of a redox polyacrylonitrile by its conversion to poly(methyl acrylate)[127] resulted in a spectrum similar to that obtained from an atactic sample of poly(methyl acrylate) produced by free-radical initiation at 65°C. Isotactic-rich poly(methyl acrylate) prepared from butyllithium at −78°C and from the conversion of poly(s-butyl acrylate) made from phenylmagnesium bromide in ether at −78°C give similar n.m.r. spectra, but were different from those given by samples converted from polyacrylonitrile. This difference has been taken as justification for the claim that racemization does not occur on conversion. But the same authors have proceeded[20] to show that racemization can take place on drastic hydrolysis. Polyacrylonitrile-α-d_1 was converted to poly(methyl acrylate), the n.m.r. spectrum of which was found to possess an α-methine proton resonance, thus demonstrating the exchange of the α-proton of the polymer during conversion. Polyacrylonitrile samples thought to be syndio rich were found to be completely atactic after conversion.

Further study of racemization on conversion[21] has confirmed the latter result. It was concluded that the method is applicable to tacticity determinations in polyacrylates, poly(acrylic acids), etc., but fails to detect any differences in tacticity in polyacrylonitrile. The exchange of the α-proton takes place during the hydrolysis step, and it is presumed that racemization of polyacrylonitriles occurs in this way.

Although the separation of the meso and racemic model compounds for polyacrylonitrile (2,4-dimethylglutaronitrile) has been known for some years, it appears that n.m.r. spectroscopy has been the only means of differentiating between these isomers.[135]

A concentrated solution of sodium thiocynanate in deuterium oxide has been used as a solvent for both normal and α-deuterated polyacrylonitrile.[136] Although spectra obtained at 100°C were not too well resolved, the similarity to the spectra of poly(vinyl chloride) was apparent and so it was presumed that a similar structure (syndio rich) was applicable to the free-radical polyacrylonitrile samples. An improvement on this method is the use of deuterated dimethyl sulphoxide as solvent,[137] which gives a triplet centred at 7·83τ for the β-methylene signal and a quintet at about 6·77τ for the α-methine proton. The spectra of variously prepared samples appeared to be largely similar when obtained in this way. Samples deuterated in the α position gave a methylene singlet at 7·85τ, which was also observed at 100 Mc./sec. It was suggested that the observed methylene triplet might be two overlapping triplets corresponding to the isotactic and syndiotactic structures.

A further improvement is the use of deuterated dimethylformamide-d_7, which resolves the two methylene triplets and allows the stereoregularity to be determined.[138] Assignments were made from an examination of the meso and racemic model compounds of 2,4-dimethylglutaronitrile, the signals for the methylene protons being found centred at 8·05 and 8·08τ for meso and racemic, respectively. This suggests that the signals from the syndiotactic structure appear at higher field, which is consistent with an earlier record.[135] By the same method it was found that the methylene spectra of α-deuterated polymers were two singlets of almost equal intensity for three variously prepared samples. From this it was concluded that the polymer structures were completely random. Spectra obtained at 100 Mc./sec. and 140°C showed central methylene peaks at 7·76 and 7·79τ (with coupling constants of 7 and 6·5 c./sec.) for isotactic and syndiotactic, respectively.

Resolution of the methyl triplets has since been reported[139] in sodium thiocyanate–deuterium oxide solution at 60 Mc./sec. and 120°C for various samples showing syndiotacticity ranging from 50 to 80%. A decoupled spectrum at 100 Mc./sec. had a similar methylene spectrum to that of polyacrylonitrile-α-d_1 at 60 Mc./sec., namely a larger syndiotactic singlet having a smaller isotactic shoulder at lower field. Spectra of model compounds similar to those of a previous account[135] are also shown.

2. *Polymethacrylonitrile*

Earlier attempts to deduce the stereoregularity of polymethacrylonitrile by i.r., n.m.r. and X-ray methods had been of no avail until its conversion to poly(methyl methacrylate),[140] which was dealt with by the well established method.[99] Samples polymerized at −78°C by γ-radiation and by butyl-lithium had similar structures after conversion, i:h:s ratios of 36:64:0 and 32:55:13, respectively. The same authors[141] have also reported on two other samples prepared in bulk by free-radical catalysts at 80°C, and converted which gave i:h:s ratios of 38:52:10 and 37:51:12. The similarity of these structures with those given by the low-temperature polymers is immediately apparent, and raises doubts concerning the effectiveness of these particular catalysts in the production of stereoregular polymethacrylonitrile. However, the authors admitted that the recovery of interconverted polymer was between 50 and 76%, which does not preclude the possibility of fractionation occurring in these processes. Later figures given by the same authors[142] indicated that the converted polymers had almost completely random structure.

The above results have been questioned,[143] which has led to the direct examination of samples of polymethacrylonitrile in trifluoroacetic acid solution at 70°C and 100 Mc./sec. The resulting spectra were not of the poly(methyl methacrylate) type as expected, since only one single methyl peak could be discerned; thus the triad treatment was ruled out. The five β-methylene resonances were found to be a singlet corresponding to the syndiotactic form centred on an AB quartet resulting from the isotactic form. The polymers studied were made from organo-metallic catalysts (e.g., diethylmagnesium) and fractionated, and were judged to range from amorphous to considerably crystalline. The isotacticity increased from about 50% to 80% along with increase in crystallinity. This has been confirmed[144] by similar treatment of samples prepared by γ-initiation at both room temperature and at -78°C, and also by a diethylmagnesium catalyst at 70°C. The isotacticity was found to increase in this order, and the latter was judged to be 80% isotactic. Both reports give a value of 15–16 c./sec. for the coupling constant of the isotactic methylene AB quartet, although the chemical-shift values are not identical.

I. Polyacids and polyamides

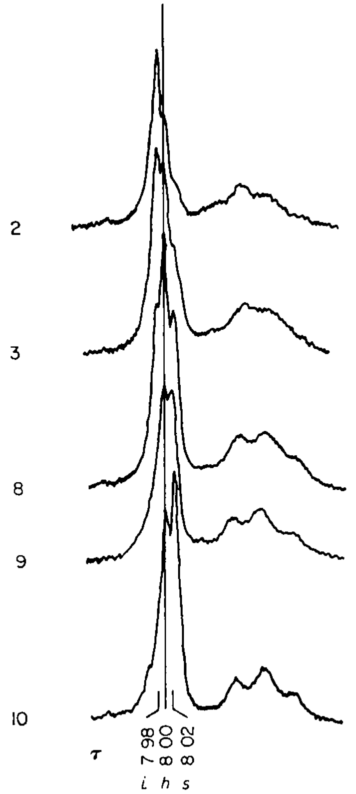
A marked dependence of polymer configuration on the pH of the polymerization medium for poly(methacrylic acid) has been demonstrated[145] by methylation of the acid and examination of the resulting poly(methyl methacrylate) in the well known manner.[99] Similarly, the dependence of stereoregularity on temperature of polymerization has been demonstrated for aqueous solutions of the free acid and its sodium salt.[108] A table of figures has been repeated elsewhere,[26] and evidence for the penultimate monomer unit effect has been considered.[146] A spectrum of polyacrylamide in aqueous solution has been reported[147] to give an amide doublet, but no amide signal was detected in polymethacrylamide. The possibilities of hydrogen bonding, proton exchange and dipolar broadening, etc., are discussed. Spectra of normal 1,2-polymethacrylamide and the 1,3-substituted polyamide structure obtained by proton migration and also of mixed structures have been obtained[148] in 12% formic acid solution at room temperature and 60 Mc./sec.

J. Poly(vinyl esters) and poly(vinyl alcohols)

1. *Poly(vinyl esters)*

Poly(vinyl acetate) has an n.m.r. spectrum consisting of three resonances for the α,β and acetate methyl protons. It has been commented that[17] the methyl resonance in poly(vinyl acetate) is split into three components, which has been taken to indicate a largely atactic structure for a free-radical initiated sample. Spin decoupling applied to the backbone protons was found of little use in the elucidation of configuration.

Spectra of poly(vinyl trifluoroacetate) obtained at 100 Mc./sec. in deutero-



i/h/s RATIO		
79	17	4
46	34	20
23	44	23
11	43	46
6	40	54

Fig. 10. N.m.r. spectra of several poly(vinyl acetates) in chloroform solutions at 60°C. Slow sweep of the methyl resonance. (From Murahashi *et al.*[154])

acetone when decoupled show the α-methylene resonance splitting into three peaks (not too well resolved) at 4·63, 4·72 and 4·78τ for isotactic, heterotactic and syndiotactic placements, respectively. These assignments were made from a sample converted from isotactic poly(vinyl methyl ether).[149] Similar examination of poly(vinyl acetate)[150] in methylene dichloride solution has shown the methyl resonance and the decoupled α-proton resonance split into partially resolved triplets at 8·02, 8·00 and 7·98τ and 5·03, 5·07 and 5·1τ for isotactic, heterotactic and syndiotactic placements, i.e., in the opposite order. However, from a study of samples of poly(vinyl formate) and isotactic poly(vinyl t-butyl ether) converted to poly(vinyl acetates),[151] as well as model compounds, it has been suggested that the assignments for the three peaks shown by the methyl resonance should be in the order isotactic, heterotactic and syndiotactic with increasing field. All the spectra shown of directly prepared poly(vinyl acetates) appear with the central peak (i.e., heterotactic) the largest. Further support for this latter assignment comes from the examination of many variously prepared samples and their correlation with infrared spectra[152, 153] and X-ray evidence[154] (see Fig. 10).

It has been claimed[155] that in the fluorine n.m.r. spectra of poly(vinyl trifluoroacetates), signals from three types of triad may be distinguished, and the results appear to show some similarity to those in certain other reports.[151, 153, 154] Also it is commented that poly(vinyl trifluoroacetate) is only slightly higher in syndiotacticity than poly(vinyl acetate) (both free-radically initiated, and both approaching atactic). The stereoregularity appears to be only slightly dependent on polymerization temperature. Evidently the most stereoregular poly(vinyl acetates) have been obtained from vinyl trimethylsilyl ether in the isotactic (86%) form by ethylaluminium chloride in toluene at −95°C, and in the syndiotactic (54%) form by stannic chloride in nitroethane at −78°C.[152–154] Apart from isotactic poly(vinyl t-butyl ether),[153, 156] most other samples show structures approaching atactic, although there is some scatter amongst the quoted values. The use of various solvents has not led to any improvement in the spectra.[11]

2. *Poly(vinyl alcohol)*

This polymer has been made from hydrolysis of various parent esters which include the acetate, trifluoroacetate and formate and from parent ethers such as t-butyl vinyl ether and vinyl trimethylsilyl ether. The alcohol samples so produced have been examined as such and also after re-esterification with different acids.

The effect of intramolecular hydrogen bonding on the conformation of poly(vinyl alcohol) in aqueous solutions has been the subject of a long account.[157]

Examination of poly(vinyl alcohol) in deuterium oxide at 37°C by double irradiation at 100 Mc./sec. showed a poorly resolved α-proton triplet signal[149, 150] assigned syndiotactic, heterotactic and isotactic in order of increasing field (like the methyl vinyl ether, but unlike the esters). Formamide, ethylene glycol and phenol have been used as solvents at 180°C to obtain 56·4 Mc./sec. spectra of a poly(vinyl alcohol). Decoupled spectra were obtained on the phenol solution and the sample was judged to be nearly atactic.[158]

The careful examination of 15% solutions at 60 Mc./sec. and 100–200°C of poly(vinyl alcohol) samples cleaved at the 1,2-diol linkages has demonstrated that the α-proton signal consists of at least nine peaks not completely resolved[159] (see Fig. 11). It has therefore been treated as three quintets, one each for syndiotactic, heterotactic and isotactic in order of increasing field. The β-methylene signal has been observed to be of six peaks and hence has been treated as two triplets (the isotactic one being at lower field) assuming the equivalence of β-protons in isotactic diads. The latter assumption is inconsistent with the results of a study of model compounds, but was dictated by polymer structures obtained by X-ray evidence for the isotacticity of the parent sample of poly(vinyl t-butyl ether). It was concluded that commercial poly(vinyl acetate) was atactic, although that obtained from the low-temperature polymerization of the trifluoroacetate was slightly syndiotactic. The inconsistencies between the behaviour of polymers and models was attributed to conformational differences. Other work[160] has given a spectral treatment apparently consistent with the above. Highly stereoregular poly(vinyl alcohols) have been obtained by various methods of polymerization of vinyl trimethylsilyl ether, as shown by the n.m.r. examination of the acetates.[152, 154] Here the polymer obtained from the trifluoroacetate was stated to be atactic.

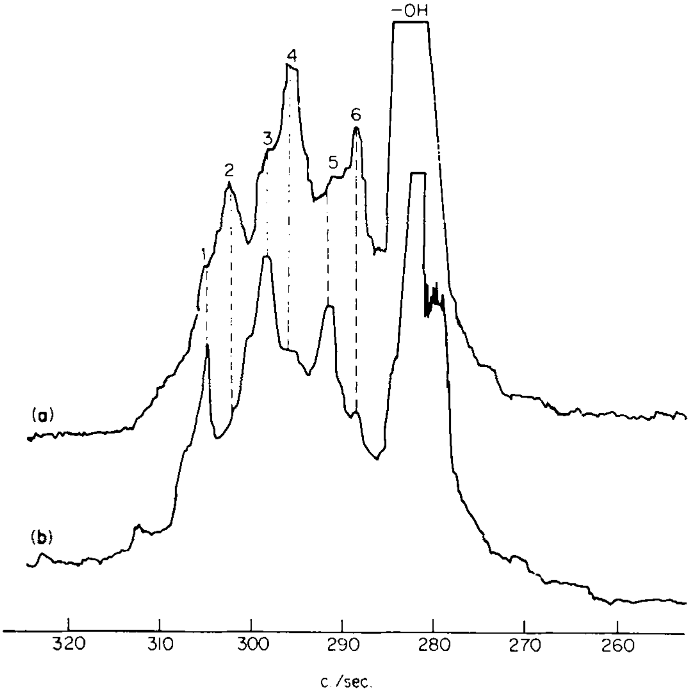


FIG. 11. N.m.r. spectra of the α protons of poly(vinyl alcohols) obtained on hydrolysis of: (a) poly(vinyl t-butyl ether); (b), poly(vinyl acetate). (From Tincher.[159])

Although variously prepared poly(vinyl alcohol) samples show obvious differences in solubility, their stereoregularity has been shown by n.m.r. to be relatively similar. The differences in solubility were attributed to differences in molecular weight and degree of branching.[161] A similar study has shown the crystallite dissolution temperature to increase with the syndiotacticity of the sample,[162] and the i.r. and n.m.r. spectra have been compared.

3. *Poly(vinyl alcohol) derivatives*

The reaction of poly(vinyl alcohol) with aldehydes is dependent on the stereoregularity of the polymer. The n.m.r. spectra of formalized model compounds show[163] significant differences which are also apparent in the spectra of formalized polymers. The formal methylene signal at about 5·3τ was shown to be a singlet and a quartet for the formalized racemic and meso 2,4,6-trihydroxyheptanes, respectively. Samples of isotactic and atactic polymers formalized to 80% showed both singlet and quartet resonances essentially in the amounts expected from the n.m.r. examination of the original poly(vinyl acetates). Reports[164, 165] on poly(vinyl acetals) feature mostly model acetals that show different spectra for the racemic and meso compounds. The rates of acetalization are widely different and dependent on stereoregularity.

K. Poly(alkyl vinyl ethers)

Differences in the n.m.r. spectra of atactic and stereoregular poly(alkyl vinyl ethers) have been detected that are paralleled by differences in i.r. spectra and other physical properties.[166] The differences were revealed mostly by the β-methylene resonances. The spectra obtained at 60 Mc./sec. from a presumably isotactic poly(methyl vinyl ether) in 10% solution in chlorobenzene at 150°C, show an α-methine quintet at 6·42τ and a complex multiplet at about 8·2τ for the β-methylene resonance.[17] On decoupling these from each other in turn, they became respectively, a singlet and an AB quartet plus a singlet. From the relative areas of the latter, the sample was shown to be 75–80% isotactic. The examination of various samples in nitromethane solution at 113°C and at 56·4 Mc./sec. has enabled the methoxy resonance to be resolved into three peaks, although the overall separation was only 1·4 c./sec.[156] From consideration of the type of catalysts, properties of polymers and X-ray evidence, the peak at highest field was assigned to the isotactic structure and peak heights were used to calculate configurations. Resolution of the methoxy signal was not so good when carbon tetrachloride, chloroform or benzene was used as solvent.

The use of 100 Mc./sec. at 37°C with 3–10% concentrations in a 27:75 molar chlorobenzene–methylene dichloride solvent mixture allowed the three methoxy signals to be seen at 6·70, 6·72 and 6·74τ[167] (see Fig. 12). The assignments given to these were the same as in an earlier report.[156] Decoupling the β-methylene signal from the α-methine proton gave an AB quartet plus a singlet, which was consistent with another report,[17] but decoupling the α- from the β-proton showed three peaks for the α-methine signal in the same ratio of intensities as found for the three methoxy signals. This latter finding appears to be an improvement on earlier work at 60 Mc./sec.[17]

In an examination of the spectra of poly(ethyl, isopropyl and isobutyl vinyl ethers), overlapping of the resonance signals did not allow unambiguous assignments to be made,[168] although decoupled spectra showed differences for differently prepared samples of the same polymer. In the case of poly(isobutyl vinyl

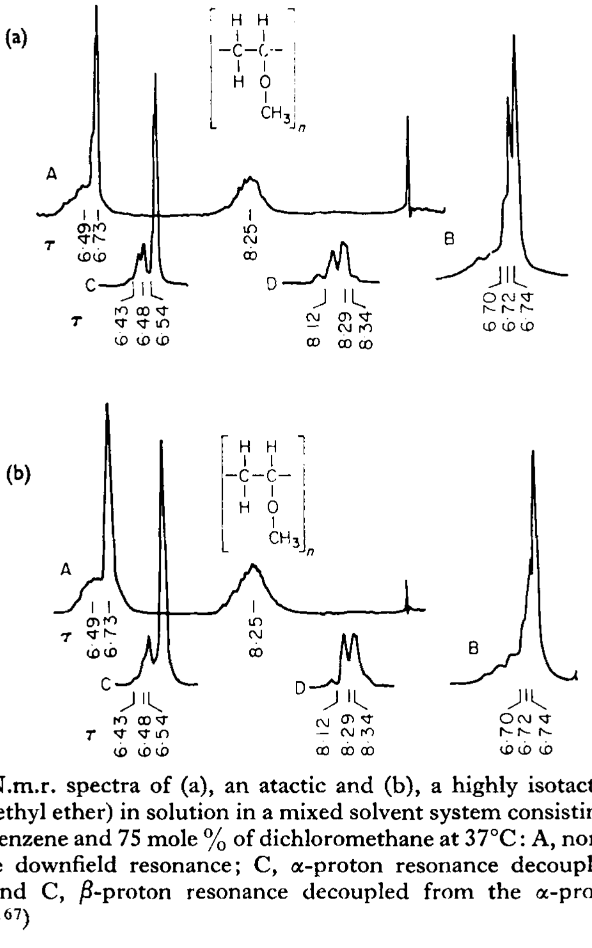


FIG. 12. N.m.r. spectra of (a), an atactic and (b), a highly isotactic sample of poly(vinyl methyl ether) in solution in a mixed solvent system consisting of 25 mole % of chlorobenzene and 75 mole % of dichloromethane at 37°C: A, normal; B, slow sweep of the downfield resonance; C, α-proton resonance decoupled from the β-protons; and C, β-proton resonance decoupled from the α-protons. (From Ramey *et al.*[167])

ether), the nature of different samples led to the unusual assignment of heterotactic, isotactic and syndiotactic triads in order of increasing field for the decoupled α-methine triplet. The spectra of poly(t-butyl vinyl ether) showed three separate resonances apparently uninfluenced by different methods of polymerization, and the decoupled α- and β-proton signals were both broad singlets. Hydrolysis of such a sample to poly(vinyl alcohol) showed a mixed structure on examination of its decoupled spectrum. A sample of poly(t-butyl vinyl ether) prepared from boron trifluoride etherate in toluene at −78°C was investigated by n.m.r. after conversion to poly(vinyl acetate).[153] It was found to have an *i*:*h*:*s* ratio of 79:14:4. Samples of poly(vinyl trimethylsilyl ether) have been treated similarly. In the boron trifluoride etherate-initiated polymerization of methyl vinyl ethers,[97] the penultimate monomer unit was found to effect the stereoregularity of the ensuing polymerisation. This has been discussed elsewhere.[156]

Only one type of spectrum has been obtained from polymers of α-methylvinyl methyl ether, and this shows three singlets.[169] All the indications are that syndiotactic polymer is formed and the absence of an AB quartet for the methylene resonance supports this. This is unlike poly(vinyl methyl ether) which tends to form isotactic-rich polymers.

L. Poly(vinyl chloride)

The n.m.r. spectrum of poly(vinyl chloride) consists of two multiplets, the analysis of which has presented greater difficulties than was suggested by earlier work. Initially, it was shown[170] that the β-methylene signal was sensitive to differences in stereoregularity and the spectrum was treated as two overlapping triplets, the one at higher field being arbitrarily assigned to syndiotactic units. However it was pointed out that the isotactic methylene protons should not be equivalent,[171] and their treatment as an AB part of an ABC_2 spectrum (and syndiotactic as an A part of an A_2B_2 spectrum) enabled calculated spectra to simulate the recorded spectra. In this way the diad content was determined, and most of the earlier results indicated the slight predominance of syndiotactic units[172] (see also McClanahan and Previtera[173]). However, it was claimed[174] that the spectrum of deuterated poly(vinyl-α-d_1 chloride) showed two singlets at 7·76 and 7·96τ in chlorobenzene at 150°C, indicating that the isotactic methylene protons are equivalent. It was also stated that the polymerization temperature has little influence on the stereoregularity, and that the polymer was believed to be stereochemically very irregular. Further, the presence of butyraldehyde during the polymerization was found to have very little influence on the stereoregularity, but its effect was thought to be in reduced branching. Another similar report features the increase in crystallinity at very low molecular weights.[175]

The decoupled spectrum of poly(vinyl chloride) shows[17] the α-signal as a triplet and the β-methylene as two singlets, which is consistent with some earlier work,[170, 174] but not with another report.[171]

A syndiotactic-rich structure has been claimed[176] for polymer prepared from t-butylmagnesium, and low-molecular-weight polymers were shown to have t-butyl and vinyl end groups.

The inconsistencies found[177] in the spectra of polymers and model compounds does little to solve the conflicting views already quoted; indeed support can be found for both points of view.[178] Amidst a mass of information may be found[177] reaffirmation that the decoupled β-methylene resonance is two singlets, and the assignment of the peaks of the decoupled α-resonance at 5·43, 5·53 and 5·69τ to syndiotactic, heterotactic and isotactic units, respectively. These latter assignments have also been put forward elsewhere,[179] and the normal α-methylene proton resonance treated as three overlapping quintets. The β-methylene resonance has been treated in two ways, assuming equivalent and non-equivalent protons in the isotactic configuration. These give rise to two triplets and four overlapping triplets on which the syndiotactic triplet is also superimposed, although it is conceded that no theory is completely satisfactory. The occurrence of chain branching has been blamed for some observed irregularities. However, the examination of deuterated poly(vinyl-α-d_1 chloride) showed four peaks unlike an AB quartet and it was concluded that the isotactic β-methylene protons are equivalent. Alternatively, it has been suggested[180] that the controversy may be resolved by a consideration of the structure in terms of tetrads, since the spectrum of deuterated poly(vinyl-α-*cis*-β-d_2 chloride) was found to consist of 10 peaks, which were assigned to the 10 possible tetrad configurations. It was shown that the appearance of the spectra depended on choice of solvent, which may account for the comment[181] that the 100 Mc./sec. α-d_1 spectra of poly(vinyl-α-d_1 chloride) shown in two other reports[179, 180] are not similar. It was claimed[180] that the decoupled methylene spectrum of poly(vinyl chloride) is like the normal spectrum of deuterated poly(vinyl-α-d_1 chloride), and also that the decoupled methylene spectrum of deuterated poly(vinyl-*trans*-β-d_1 chloride) is like the normal spectrum of deuterated poly(vinyl-α-*cis*-β-d_1 chloride).

The former claim has been disputed,[181] and the shape of the spectra of deuterated poly(vinyl-α,β-d_2 chloride) samples requiring tetrad treatment has been shown[182] to depend on the *cis–trans* content of the monomer and temperature of polymerization. Spectra of deuterated poly(vinyl-β,β-d_2 chloride) samples have three peaks attributed to syndiotactic, heterotactic and isotactic units.[182]

A consideration[181] of the β-methylene resonance of poly(vinyl chloride) as an isotactic triplet at lower field and two overlapping syndiotactic triplets treated in terms of tetrad configurations is a new departure. No figures for configurations are given. Copolymers of vinyl chloride and isopropenyl chloride made as macromolecular models of branched poly(vinyl chloride) failed to give acceptable n.m.r. spectra due to the mistaken impression that high concentration solutions were required;[183] such a praiseworthy endeavour deserves further attention.

In the latest report,[184] the decoupled α-methylene proton spectrum was shown to consist of three peaks as before, and the β-methylene resonance was treated as four isotactic triplets, one syndiotactic triplet and a further triplet assigned to irregularities in polymerization, such as branching (see Fig. 13). This is the same type of analysis as in an earlier report,[179] but line positions and assignments do not appear to be identical, especially for the structural irregularities.

The interpretation of the n.m.r. spectra of poly(vinyl chloride) was for some years regarded as a conflict between the results of Johnsen and Tincher, but with the latest work of Johnsen these differences are less apparent. It may be said that generally there is fair agreement amongst the majority of published work, as most samples appear to be well described as slightly more syndio rich than atactic, and syndiotacticity increases only slightly with decrease in temperature of polymerization. Tincher's figures tend to show some variations from, but the same overall picture as those quoted elsewhere. It appears necessary to include the consideration of structural abnormalities to explain the spectra satisfactorily.

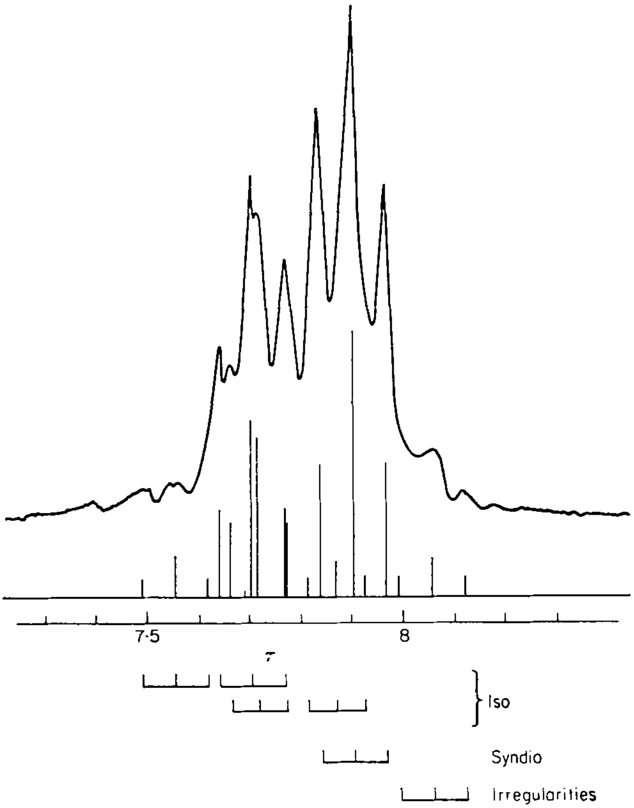


FIG. 13. The methylene resonance of poly(vinyl chloride) obtained from a 20% solution in chlorobenzene at 150°C and 100 Mc./sec. (From Bargon *et al.*[184])

M. Other halogenated polymers and copolymers

N.m.r. spectra have shown that structural irregularities in polychloroprene are more extensive than expected.[30] The well known *trans* polymer and the specially produced high *cis* polymer may be distinguished by their olefinic signals at 4·66 and 4·50τ, respectively. The 1,2- and 3,4-forms, for which there is i.r. evidence are of little significance in the n.m.r. spectra, which, on the other hand, have been shown to indicate 10–15% each of head–head and tail–tail type enchainments in the free-radical polymer, and even more in the *cis* polymer. Polychloroprene is one of the few polymers showing sequence isomerism and one of the few whose 200 Mc./sec. spectrum has been published.[9] The spectrum of poly-1,1,2-trichlorobutadiene has been reported.[185]

Free-radical polymers of 1,1 dichloro- and 1,1-dibromovinyl cyclopropane have been reported to consist of both the 1,2- and 1,5-types of addition.[56]

The spectra of poly(vinyl bromide) appear rather similar to those of poly(vinyl chloride).[186] The 60% syndiotacticity found varied little with polymerization temperature, which is also the case for poly(vinyl chloride).

The proton spectra of poly(vinyl fluoride) has been obtained at 60 Mc./sec. in benzaldehyde solution at 180°C. The α-methine resonance appeared as two quintets at 5·0τ and the β-methylene as a broad triplet at 7·9τ.[17] These have been subjected to triple irradiation, when the α-methine signal appeared as two singlets with another pair of up-field singlets attributed to head–head enchainments, whereas the β-methylene resonance remained a triplet, but was slightly better resolved. Little similarity with the spectra of poly(vinyl chloride) was apparent.

The fluorine spectra of experimental and commercial samples of poly(vinyl fluoride) have been obtained at 56·4 Mc./sec. and showed six resonances.[187] Not all of these have been assigned, but the most intense resonance at low field must be due to head-to-tail placements. The spectrum has been treated as 11 possible lines, 8 of which were thought to be due to head–head and tail–tail placements giving 26–32% of these. The proportion of "backwards additions" was found to increase linearly with increase of polymerisation temperature.

The 56·4 Mc./sec. fluorine spectra of poly(vinylidene fluoride) obtained in dimethylacetamide have been interpreted as indicating 10–12% of head–head enchainments[188] (see Fig. 14). Four resonances, only one of which is indicative of head–tail placements, have been distinguished, and detailed assignments for these have been presented.[187]

Two pairs of doublets appeared in the fluorine spectra of polychlorotrifluoroethylene,[7, 189] and these have been interpreted as arising from heterotactic and syndiotactic units. The proportions of these units appeared to be little altered by polymerization temperature, and so the n.m.r. evidence suggests an irregular configuration, whereas X-ray data suggests a regular structure.

Improved fluorine spectra of vinylidene fluoride–hexafluoropropylene copolymer have been obtained at 56·4 and 94·1 Mc./sec., which allow a more detailed investigation of the multiplicity of structural possibilities indicated by the presence of at least 12 resonances.[9] Fluorine spectra of vinylidene fluoride–chlorotrifluoroethylene copolymers have been obtained[190] at 40 Mc./sec., but these showed little or no evidence for "backwards" placements. Compositional analysis of vinylidene fluoride–chlorotrifluoroethylene copolymers has been accomplished from the proton spectra by using *o*-dichlorobenzene as internal standard in hexafluorobenzene solution at 70°C and 60 Mc./sec.[191] The figures obtained were in good agreement with other physical data and were taken to indicate a random polymer structure. They were also used as a calibration for i.r. measurements.

A copolymer of perfluoroethylene and perfluoropropylene (fluorocarbon resin) has been studied in the molten state in the absence of solvent at 310°C and 40 Mc./sec. Its fluorine spectrum consisted of three separate resonances, which indicated about 9 mole % hexafluoropropylene content.[192]

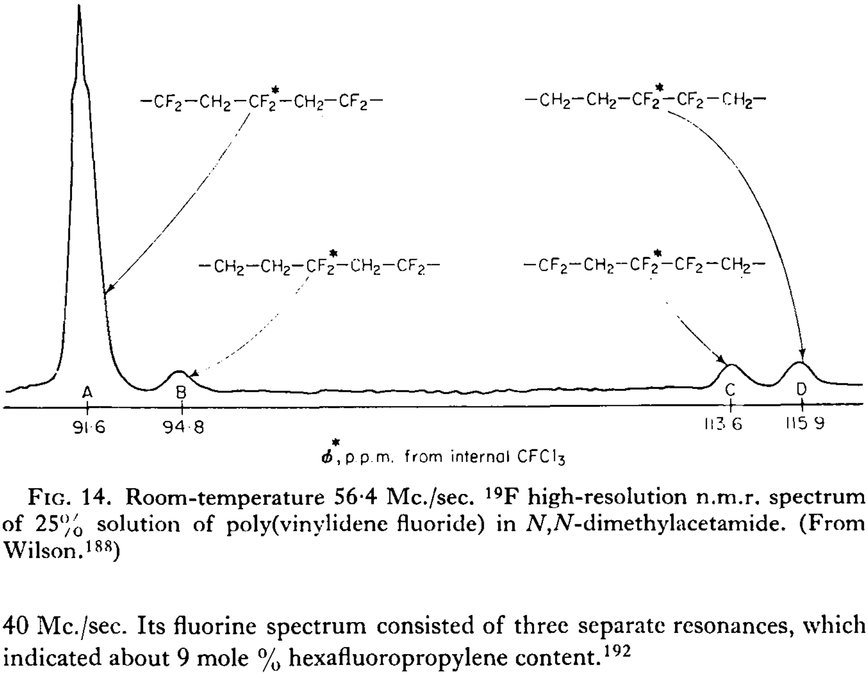


FIG. 14. Room-temperature 56·4 Mc./sec. ^{19}F high-resolution n.m.r. spectrum of 25% solution of poly(vinylidene fluoride) in *N*,*N*-dimethylacetamide. (From Wilson.[188])

Also, the γ-initiated powdery and rubbery polymers of perfluoro-1,4-pentadiene have been claimed[193] to be mixtures of 1,4- and 1,3-polymers from their fluorine spectra.

N. Alkylene oxide polymers

The single resonance of polyoxymethylene has been observed[194] in spectra obtained from chlorophenol solution and also a second resonance due to copolymerized oxyethylene units. Additional peaks present when the polymer or its solution had been subjected to high temperatures were attributed to the reaction of the solvent with formaldehyde (a product of thermal degradation of the polymer). The composition of ethylene oxide–propylene oxide copolymers has been determined by n.m.r. by using a 10% solution in carbon tetrachloride at 60 Mc./sec.[195] Hydroxyl end-group determinations in poly(alkylene oxide) polymers have been carried out[196] in pyridine solution with a trace of hydrogen chloride gas. The action of pyridine in bonding with the alcohol group moved the resonances of the methylenes adjacent to the hydroxyl away from the resonances of the other (ether-type) backbone protons and hence facilitated their measurement. The method appeared to be applicable to some polyesters. Hydroxyl contents have also been measured after reaction with phenyl isocyanate.[197] The adjacent methylene group was found to be shifted, but sometimes obscured, so measurements were made using the urethane *N*-proton in pyridine or 2,6-lutidine solution with CAT assistance. The copolymer of propylene glycol and tetrahydrofuran was stated to give only propylene glycol-type end groups.

It has been found difficult to study the tacticity of poly(propylene oxide), since the n.m.r. spectra of amorphous and crystalline samples are very similar even at 100 Mc./sec.[198] The methyl doublets are indistinguishable, and the chemical shifts of the backbone protons are very close. Spin decoupling simplified the crystalline (isotactic) backbone spectra allowing a calculated analysis to be made but this cannot be done for an amorphous sample.

The chain conformation of poly(ethylene oxide) has been studied[199] through its ^{13}C—H satellite signals. Although these are small, the splittings can be measured, and the results were interpreted as being not in accord with theory.

Both the end-groups[18] and the configuration[19] of poly(propylene oxides) have been studied as the trifluoroacetates by ^{19}F n.m.r. spectroscopy at 56·4 Mc./sec. The resonances of trifluoroacetates from primary and secondary alcohol end groups are separated by 15 c./sec. (i.e., more than the proton separation of methyl esters). The secondary trifluoroacetate esters are doublets with greater spacing at 94·1 Mc./sec., which demonstrates two distinct types of secondary end groups. The crystalline polymer showed only one of these signals, and the stereoregularity of the terminal and penultimate monomer units is implicated in the occurrence of these two signals. Model diols have been examined and a table of chemical shifts compiled. Elsewhere,[200] it has been shown that the polymerization of mono-substituted ethylene oxides proceeds exclusively through the epoxide rings, since rearranged structures were not detected.

O. Polyesters

The maleate–fumarate isomerization in the preparation of polyesters with various glycols has been studied[201] using the well-separated olefinic resonances at 3·45 and 3·02τ, respectively. The identification of the components of (uncured) polyester resins has been reported[202] (see Fig. 15), and tables of chemical shifts of constituent entities in acetone, benzene and styrene solutions recorded. Semi-quantitative results have been obtained by integration of the appropriate peaks for resins of up to four components.

The relative amounts of terephthalic and isophthalic acids in their copolymers with ethylene glycol have been determined[203] from the singlet and multiplet aromatic signals given by these two acids respectively. Only one signal for the aliphatic methylene groups was detected for either polymers or model compounds. Spectra were obtained from 5% solutions in trifluoroacetic acid at 80°C and 60 Mc./sec., and reasonably good quantitative accuracy was claimed.

The composition of copolymers made from terephthalic acid with ethylene and diethylene glycols has been determined from the differences in chemical shifts of the ether and ester-linked methylene groups in the diols.[204] Spectra were obtained in 10% solution in o-chlorophenol at 80°C and 60 Mc./sec. The pattern of the "phenylene" spectra are also reputed to be composition dependent.

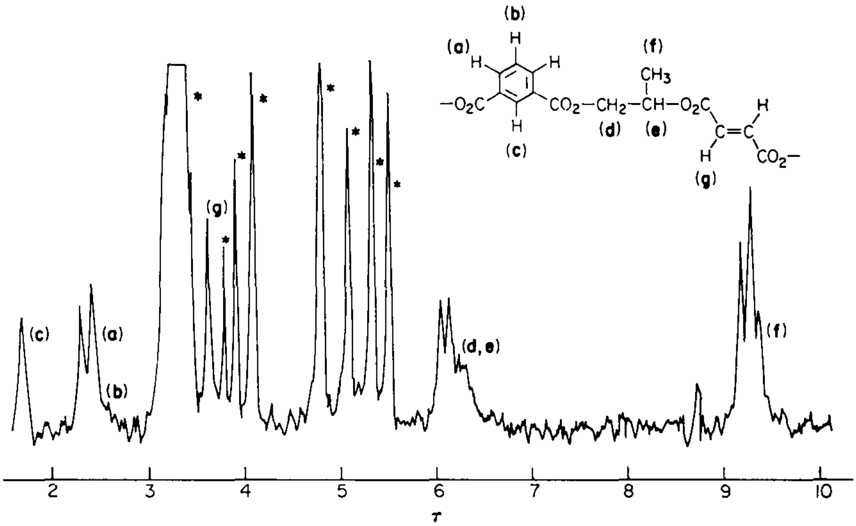


FIG. 15. N.m.r. spectrum of 3:1:4 isophthalic acid–maleic acid–propylene glycol polyester in styrene solution. Peaks marked * are due to styrene. (From Percival and Stevens.[202])

P. Resins

The application of n.m.r. spectroscopy to the study of phenol–formaldehyde type resins has been attempted with some noteworthy success. Investigations are restricted to soluble samples, but even so some reaction patterns have been established. The use of arsenic trichloride as a solvent[205] (see also Ferguson[9]) has been applied to Novolak two-step resins. The o-linked resin gave an —OH signal not shifted by the addition of hydrochloric acid gas, but which was shifted if the p-linked equivalent was also present. This solvent system is unsuitable for resols that interact and become cured. Benzyl-type hemi-formals are reported to contribute substantially to the structure of many resols,[206] and other structural information was also forthcoming from n.m.r. spectra obtained by using acetone, pyridine and dimethyl sulphoxide solvents. Acetylated products have been examined in deuterochloroform solution. These papers contain a wealth of experimental data and information virtually unobtainable by other techniques.

The positions of methylene linkages between aromatic rings in various low-molecular-weight reputedly linear polymers has been studied[207] from the shift to lower field as the linkage changes from *para–para* to *ortho–ortho*. Dimers and trimers have been well characterized. Acetone solutions at 60 Mc./sec. were used and difficulties due to paramagnetic impurities were encountered. These papers show spectra with apparently high noise level, indicating that clarification with a CAT device should be helpful.

Claimed graft copolymers of Novolacs onto various polyamide backbones have been studied by n.m.r. spectroscopy[208] in dimethyl sulphoxide solution. The spectra showed the presence of both types of polymer, but no spectral evidence of their link-up points was demonstrated. Three reports have dealt with the characterization of ion-exchange resins by n.m.r. spectroscopy,[209–211] which demonstrated a difference in chemical shift between "internal" and "external" water.

R. Other polymers

Cationically prepared polyacetaldehyde has been examined in aromatic solvents and a multiplicity of resonances for each type of proton was seen. Double irradiation at 150°C and 60 Mc./sec. gave two peaks for the methyl signal, from which it was thought that the syndiotactic form was absent.[212] Examination at 100 Mc./sec. suggested that the shoulder on the low-field side of the methyl multiplet was due to the syndiotactic form, but poor resolution precluded its measurement.[213]

Elsewhere,[192] spectra obtained from elastomeric polyacetaldehyde in tetrachloroethylene at ambient temperature and 60 Mc./sec. showed a pair of doublets that reverted on spin decoupling to two peaks. The minor one of these was at higher field and was attributed to isotactic placements, although the general conclusion was that the polymer was "highly random". It was claimed that these results were in accord with the other reports.[212, 213] It seems that the appearance of these spectra is solvent dependent.

Examination of "elastomeric" polyacetaldehyde at 200 Mc./sec. gave a peak at $8{\cdot}7\tau$ that consisted of a complex envelope of three main peaks with a shoulder at each side.[214] A proprietary "curve resolver" reduced this multiplet into five doublets of relative intensity 1:2:2:1:1 going from low to high field.

An extra peak present in branched dextran, but absent in the linear polymer, has been demonstrated,[215] and the spectra of sulphated materials have also appeared[216] (see also Ruckel and Schuerch[217]).

Spectra are given to support the 1,4-structure of the base-catalysed and the 1,2-structure of the radical-induced polymers of *p*-styrenesulphonamide.[218]

Whereas the resolution of spectra of poly-2-vinylpyridine samples in deuterochloroform at 60 Mc./sec. was sufficient to separate the α-proton resonance from the β-methylene only in the case of isotactic polymer, the spectrum of poly-4-vinylpyridine in pyridine showed only one broad peak.[219]

The spectrum of a polyethylenimine was reported to be a singlet in pure water and more complicated in acid solution, owing to protonation.[220]

Considerable detail is usually evident in the spectra of soluble polyurethanes. It has been claimed that urethane, urea, allophonate and biuret linkages may be distinguished from one another in model compounds by using polar solvents, such as dimethyl acetamide or dimethyl sulphoxide.[269] Also, cured polyurethanes after reaction with butylamine have become soluble in these solvents, and this has allowed n.m.r. spectra to be obtained.[222] Information about backbone-polymer and di-isocyanate couplers has been obtained by using arsenic trichloride as a solvent at 100°C.[9] Also, the urethane resonance has been used to study the hydroxyl content and type in alkylene polyols.[197]

Other reports feature the use of liquid polyethylene glycol as a solvent for inorganic solutes,[223] and a study of polymer–surfactant complexes.[224]

S. Model compounds

The original interest was in simple model compounds for assistance in making assignments regarding tactic structures in polymers. The 2,4-disubstituted pentanes (although of considerable interest) have not been found to be close enough to polymer structures, which has led to the study of the 2,4,6-trisubstituted heptanes. Here additional difficulties of preparation, separation and characterization have been largely overcome. Unfortunately, in some cases only n.m.r. has been successful in characterizing the isomers, whereas in others the assignments obtained have been found inapplicable in polymers. In many accounts of model compounds little or no mention is made to polymeric samples, and in some others naïve claims have been made to the effect that the model spectra showed accordance with polymer spectra.

On the other hand, there have been some careful studies of model compounds that have resulted in conformational evidence and conformational energy differences have been calculated. Table I shows the references to the subject matter of quoted work.

A review of model compounds has appeared.[23] Polymer conformations are dependent upon conditions of measurement, e.g., choice of solvent and temperature. Some results support the preference of syndiotactic structures for planar zig-zag conformations, except for poly(vinyl alcohol) where hydrogen bonding has a special effect.

TABLE I

Polymer	2,4-Pentanes	2,4,6-Heptanes
Polystyrene	91, 225	92
Poly(methyl acrylate)	128, 131, 226†	133, 227
Poly(methacrylic acid)	..	133
Polyacrylonitrile	134, 135, 138, 139, 228	..
Poly(vinyl acetate)	..	151, 229†
Poly(vinyl alcohol)	134,† 157, 159, 229,† 230,† 231,† 232†	229,† 231†
Poly(vinyl acetal)	164, 165	..
Poly(vinyl formal)	..	163
Poly(vinyl chloride)	178, 228, 233, 234, 235	178, 234, 236
Poly(vinyl bromide)	228, 234	..

† Indicates conformational information also.

III. COPOLYMERS

The spectra of copolymers have been used in one or more of the following ways—

1. For making qualitative and quantitative measurements of composition of copolymer (or mixture of homopolymers).
2. Proof of particular evidence for random copolymer structure from the presence of a signal at a particular chemical shift which is not shown by either homopolymer. Some copolymer spectra do not furnish evidence of copolymerization, i.e., linking-up of different types of units.
3. Proof of "blockiness" (i.e., non-random nature) of copolymer from the presence of a particular feature in the spectrum.
4. For making sequence distribution measurements, in terms of mixed triads, e.g., AAA, ABA, BAB etc. Some configurational information has been obtained from copolymers.

Reactivity ratios may be calculated from measurements of copolymer composition and these with other information obtained from n.m.r. spectra have been widely used in checking various theories of copolymerization. Values of reactivity ratios obtained from n.m.r. measurements have usually been quite close to those obtained from other methods of determination.

A. Styrene–methyl methacrylate copolymers

Such copolymers have been mentioned in earlier work,[7] where the well known effects of styrene blocks cleaving the aromatic signal and the random styrene units dividing the methoxyl resonance were featured, but the α-methyl signal was not resolved well enough for tacticities to be determined. Further study of random copolymers has shown that differences in chemical shifts of methoxyl and α-methyl signals from the ester could be related to the proximity of the nearest styrene units in the chain,[237] and the results were treated by using the run-number concept. More proof of copolymerization and a consideration of the methoxyl resonances have appeared.[238]

The n.m.r. method of determination of copolymer composition has been judged to be as good as i.r. methods and elemental analysis in a cloud-point titration study.[239] It has been observed that the relative proportions of the three methoxy and three α-methyl signals are dependent on the styrene content of the free-radical copolymer,[240] and it was preferred to explain this in terms of sequence distribution of monomer units rather than tacticity effects if carbon tetrachloride and not deuterobenzene were used as solvent.

Radical copolymers have been the subject of further detailed study, and the twelve triads involving composition and configuration in relation to a central methyl methacrylate unit have been divided between the three methoxy resonances[241] (see also Yamashita and Ito[117]). It was noticed that the appearance of spectra of styrene–methyl methacrylate copolymers were changed when aromatic solvents were used, and the results could not be interpreted in the manner previously described.[99, 241] It was claimed that better correlations could be made for methyl methacrylate-centred pentads. This prompted a study of styrene-phenyl methacrylate copolymers after inter-esterification to styrene–methyl methacrylate copolymers, as a means of changing the aromatic content. The spectra of these copolymers also could not be interpreted in the usual manner, and this was thought to be due to the existence of unconventional sequence distributions.

It has been pointed out that the lithium-initiated anionic copolymer does not have the same type of n.m.r. spectrum as that given by the free-radical copolymer,[242, 243] but one similar to that obtained from a mixture of homopolymers was found. This has been interpreted as evidence for block copolymerization, although no specific signal was detected for units comprising the link-up points. This has been confirmed[244] in a more detailed study using butyl-lithium initiator, but fractionation showed the presence of considerable amounts of homopolymers and small amounts of copolymer of low styrene content.[243]

An attempt to obtain a styrene–methyl methacrylate copolymer of unconventional sequence distribution has been made through the inter-esterification of a free-radical styrene–propyl methacrylate copolymer.[245] A pentad treatment was used and the results, although not consistent with those expected for conventional distributions, were not too clear-cut.

B. Other styrene copolymers

The spectral features of styrene–butadiene copolymers have been mentioned in earlier work,[7, 44] and a subsequent report related to copolymer composition and 1,2- and 1,4- butadiene enchainments,[246] but *cis*- and *trans*-1,4-butadiene units could not be distinguished.

For styrene–methylacrylate copolymers, three methoxy signals having intensities dependent on composition have been observed,[247] and comparisons have been drawn with the styrene–methyl methacrylate system.

Similarly, in a study of benzyl methacrylate–styrene copolymers,[248] the benzyl methylene signal was found to be resolved into three peaks that were analysed[241] as before for styrene–methyl methacrylate copolymers. On the other hand, a singlet benzylmethylene signal was observed for benzyl methacrylate–methyl methacrylate, copolymers indicating that the benzyl aromatic ring does not affect the shielding of these protons.[248]

An initial report on styrene–propylene copolymers showing only the aromatic spectra was not particularly convincing,[249] but in subsequent work,[250] it was claimed that the copolymerization was random and that the stereoregularity of the propylene segments was unaffected by incorporation of styrene.

A compositional analysis of acrylonitrile–styrene copolymers has been made using the α-methine signal of acrylonitrile in relation to (a) the aromatic signal and (b) the signals from the rest of the main-chain protons.[251] Numerous spectra were shown, and errors of measurement of a few per cent are quoted. In the determination of copolymerization ratios in this system, attention was focused on n.m.r. intensity measurements although it was commented that these were omitted from many published papers.[252] Copolymer composition by n.m.r. was found to be slightly different from that calculated from Kjeldahl nitrogen analysis, but it was asserted that more accurate values of reactivity ratios were obtained by the n.m.r. method.

A report on the copolymerization of styrene with isopropyl and isopropylidene oxazolones involving different enchainments of the latter appeared to be insufficiently proven by a poorly resolved n.m.r. spectrum.[253]

Triad distributions in copolymers of 1,2-diphenylethylene (D) and methylacrylate (M) have been studied[254] by using the three methoxy signals centred at approximately 6·5, 6·8 and 7·2τ, which were assigned to MMM, MMD and DMD type triads, respectively.

C. Vinyl chloride–vinyl acetate copolymers

The relative ease with which the composition of vinyl chloride–vinyl acetate copolymers may be determined by n.m.r. spectroscopy by using the well separated α-methine resonances has been pointed out,[255] and reactivity ratios have been obtained which were in good agreement with the results by other methods. In further work, the errors involved in making these measurements have been calculated[256] for three different ratios of various signal intensities from spectra obtained in different solvents. It has been observed that in cyclohexanone solution, the α-methine proton signal of copolymerized vinyl acetate appears at lower field

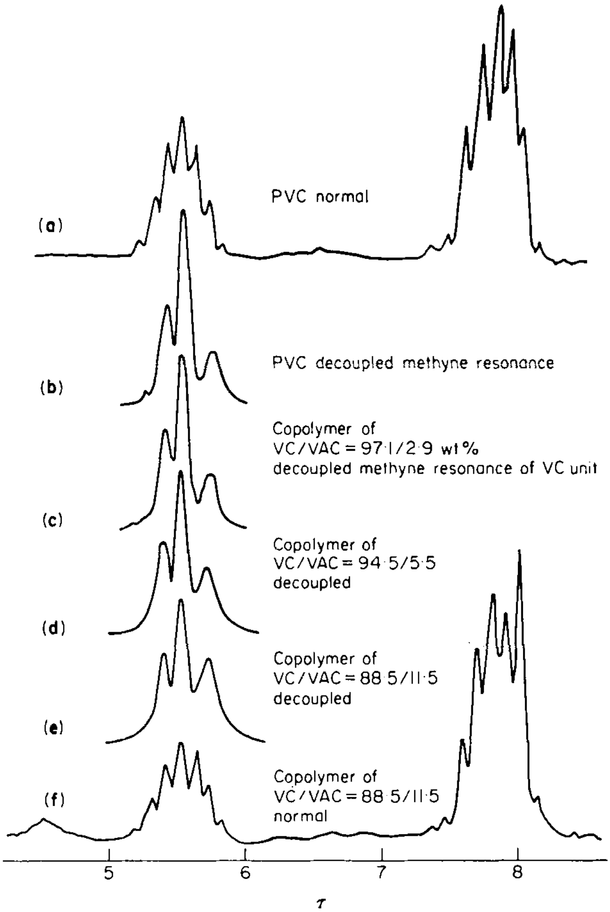


FIG. 16. Normal and decoupled spectra of poly(vinyl chloride–vinyl acetate) copolymer at 60 Mc./sec. and 150°C. PVC = poly(vinyl chloride); VC = vinyl chloride; VAC = vinyl acetate. (From Takeuchi *et al.*[221])

than that of the homopolymer. Such a shift as this has been taken as proof of copolymerization. The effect of composition on sequence distribution has been studied[221] by using the decoupled α-methine triplet of vinyl chloride to obtain tacticity data (see Fig. 16). The fraction of isotactic vinyl chloride units appeared to increase slightly with increase in vinyl acetate content.

D. Vinyl chloride–vinylidene chloride copolymers

Early work had shown the way to obtain compositional analysis of these copolymers.[172] The spectrum of poly(vinylidene chloride) has only one resonance at 6·07τ, but this is replaced by two at 6·01 and 6·17τ in the copolymers with vinyl

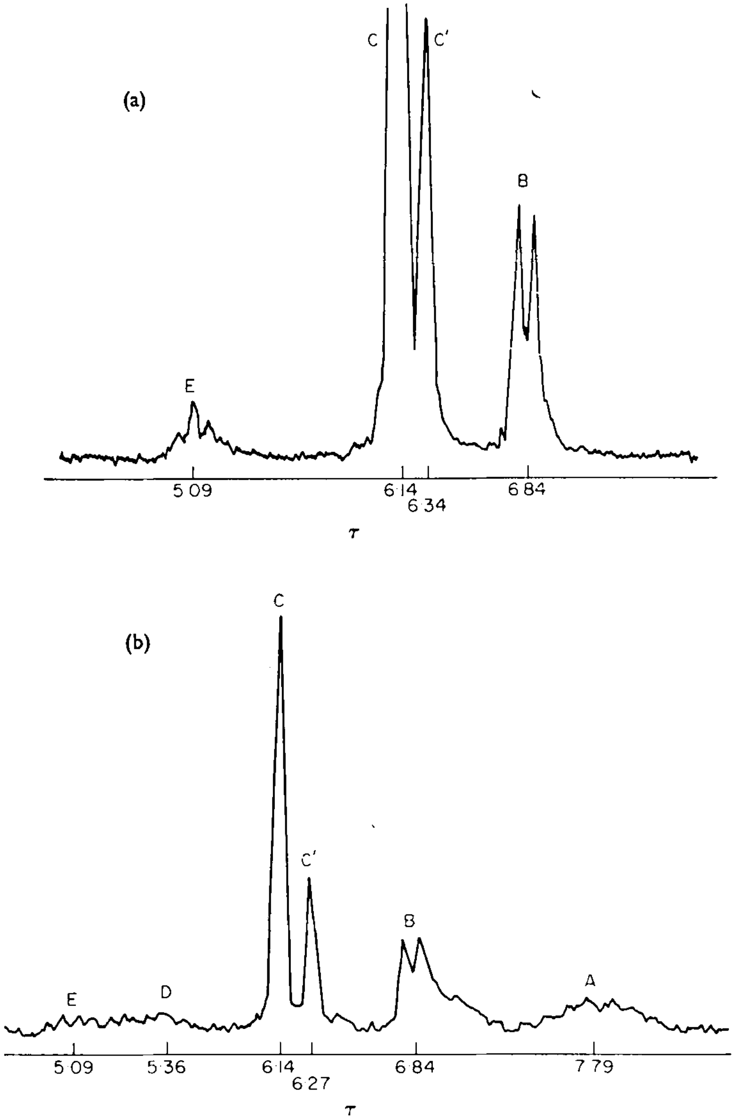


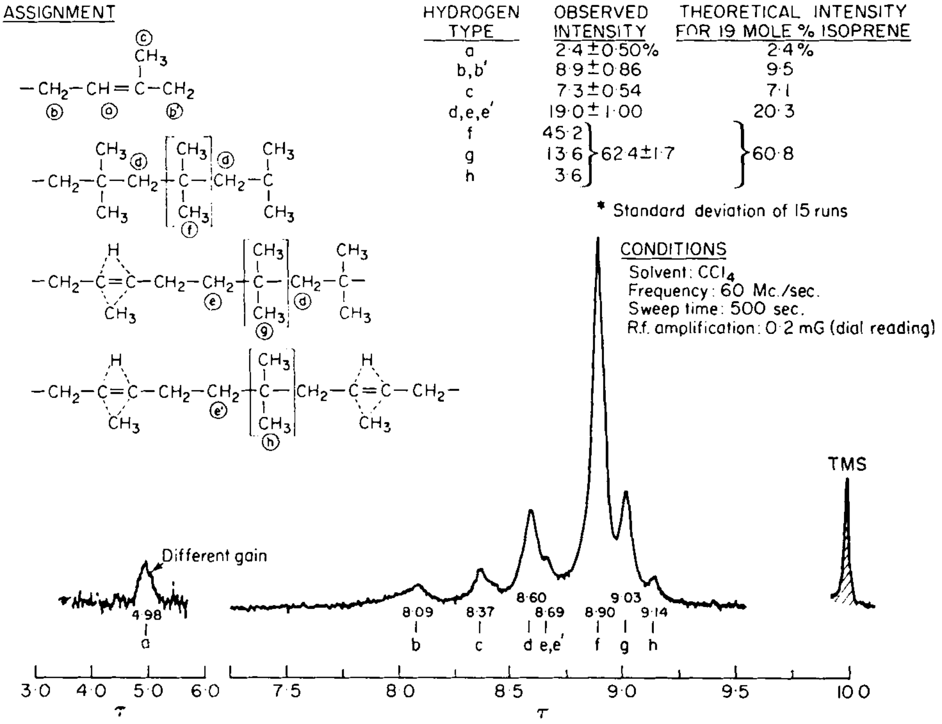
Fig. 17. N.m.r. spectra of vinyl chloride–vinylidene chloride copolymers: (a), type I copolymer; (b), type II copolymer. (From McClanahan and Previtera.[173])

chloride.[257] These signals have been attributed to the presence of head–tail and head–head placements in the copolymer. The fraction of head–head placements appeared to increase with increasing vinyl chloride content. Spectra of poly-2,3-dichlorobutadiene and its partially chlorinated derivative were used to assist in making assignments, e.g., for head–head placements. This evidence for head–head placements has been confirmed,[258] and it has also been claimed that the vinyl chloride units exist in block sequences in the copolymer, contrary to copolymerization theory. In another more detailed analysis,[173] the above conclusions were confirmed and two types of copolymer distinguished (see Fig. 17). The first type showed four resonance signals in the spectrum and was thought to be made up of head–tail and head–head vinylidene chloride sequences as well as alternating vinyl chloride–vinylidene chloride sequences. The second type has seven resonance signals and in addition to the constituent units of the first type also contains short blocks of vinyl chloride units.

Copolymers of vinyl chloride and isopropenyl chloride were reputed to be close in composition to the monomer feed ratio and have been mentioned above.[183]

E. Hydrocarbon copolymers

Most of the reported work in this Section falls into the classification of compositional analysis. Ethylene–propylene copolymers have been studied by n.m.r.



HYDROGEN TYPE	OBSERVED INTENSITY	THEORETICAL INTENSITY FOR 19 MOLE % ISOPRENE
a	2·4±0·50%	2·4%
b,b′	8·9±0·86	9·5
c	7·3±0·54	7·1
d,e,e′	19·0±1·00	20·3
f	45·2 } 62·4±1·7	} 60·8
g	13·6	
h	3·6	

* Standard deviation of 15 runs

CONDITIONS
Solvent: CCl_4
Frequency: 60 Mc./sec.
Sweep time: 500 sec.
R.f. amplification: 0·2 mG (dial reading)

FIG. 18. N.m.r. spectrum of copolymer of isobutylene and isoprene. (From Stehling and Bartz.[69])

spectroscopy and the results for composition compared with those determined by radioactive labelling of the propylene monomer.[259] It was claimed that choice of methylene peaks allows satisfactory compositional analysis to be made independent of tacticity. It is possible to infer the propylene tacticity and sequencing as is shown by the spectra of random and block copolymers. On the other hand, for copolymers greater in ethylene content, the method of weighing cut-out peak area has been preferred to that of integration when compared with i.r. determinations.[16] Elsewhere, spectra of commercial copolymers may be found.[86]

Evidence for the composition of copolymers of isobutylene, propylene and but-1-ene and but-2-ene has been given[45] in connection with a pyrolysis-gas-chromatographic study. Other information suggests that but-1-ene and but-2-ene are used up in the early stages of copolymerization with isobutylene.[260] The composition of isoprene–isobutylene copolymers may be determined by using the vinyl resonance signals only at relatively high (19 mole %) isoprene content[69] (see Fig. 18). The eight peaks which have been resolved in the spectra of such copolymers have been interpreted in terms of the distribution of monomer units. The analysis of butadiene–isoprene copolymers in terms of monomer composition and the types of enchainment of the monomers has been reported.[59, 77] There is also a report that in 1,1-diphenylethylene–2,3-dimethylbutadiene copolymers,[261] the aromatic signal was moved upfield compared with its position in the spectra of the homopolymer.

F. Other types of copolymers

The compositions of copolymers of ethylene with vinyl acetate and ethyl acylate have been determined by n.m.r. spectroscopy.[29] Results in good accord with measurements made by pyrolysis gas chromatography and oxygen neutron-activation analysis were claimed. Ferrocene has been used as an internal standard in the compositional analysis of ethylene–vinyl acetate copolymers.[28]

A wealth of data has been assembled in a study of ethylene–vinyl chloride and ethylene–vinyl acetate copolymers[262] and it was concluded that the order of addition of the next monomer unit to the polymer radical in emulsion systems does not depend on the radical type. Copolymers of vinyl acetate with dibutyl fumarate, dibutyl maleate, dioctyl maleate and 2-ethylhexyl acrylate have been examined[263] in carbon tetrachloride solution at 60 Mc./sec. for compositional analysis. Samples of known composition had been examined giving curved calibration plots of peak height with composition which were used in subsequent analysis. In these copolymers, the vinyl acetate methine proton signal appeared at $5{\cdot}3\tau$ compared with $4{\cdot}9\tau$ in the homopolymer.

Reactivity ratios have been determined from compositions obtained by n.m.r. for copolymers of methyl methacrylate with ethyl acrylate, propyl acrylate, butyl acrylate and ethyl methacrylate[264] by using the methoxyl resonance of methyl methacrylate and the signal of the methylene adjacent to the oxygen atom in the second monomer. The lack of characteristic signals for the methyl methacrylate–methyl acrylate system precluded measurements of composition. Determinations of composition have also been made for ethyl acrylate and methacrylonitrile copolymers with acrylonitrile,[252] and the values of reactivity ratios obtained are claimed to be acceptable.

The monomer distribution in copolymers of propylene oxide and maleic anhydride with various different catalysts has been studied,[265] and there is a report on the fluorine spectrum of an alternating tetrafluoroethylene–oxygen copolymer.[266]

Copolymer systems may sometimes be chosen to illustrate particular effects. Such is the case with copolymers of isobutylene (A) and vinylidene chloride (B), each of which has an isolated methylene signal. It has been shown[267] that the three regions in the spectra may be assigned to three types of diads: AA; AB; and BB. The splitting that can be seen in some of these regions allows more detailed study of sequences. Another unusual application is the use of n.m.r. spectroscopy to follow the course of copolymerization through the diminution of the olefinic proton signals.[268] The three monomers chosen were methyl methacrylate, vinyl isobutyl ether and maleic anhydride, each of which have their particular olefinic proton signals at different chemical shifts. This allowed the consumption of each monomer to be charted individually and the copolymer composition to be deduced at any instant. In this way it was shown that methyl methacrylate copolymerized easily with maleic anhydride to give an alternating copolymer, but much less readily with the vinyl ether.

IV. CONCLUDING REMARKS

The polymer-by-polymer treatment of the major part of this review prompts the following few brief remarks.

The continuous development of the n.m.r. method in the study of polymer structure has been evident in a number of ways. First, the improvement in instruments and experimental techniques, such as high-temperature probes and CAT equipment has enabled the early treatment given to poly(methyl methacrylate) to be extended to other polymers presenting more complex characteristics. Secondly, the search for different solvents in order to obtain more suitable polymer solutions has lead to progress with such intractable polymers as polyacrylonitrile. Thirdly, the efforts to interpret n.m.r. spectra in terms of sequences of greater length than triads, e.g., pentads, is noteworthy, and this appears to be receiving more attention than does the study of polymer conformation.

There are still many apparent contradictions in the interpretation of n.m.r. spectra, particularly in regard to assignments given to tactic structures. These mostly arise from non-n.m.r. implications, for example that a polymer is of a particular tactic form as suggested by evidence from other techniques or because it was made from a particular catalyst. However, in these cases the n.m.r. spectra are usually quite similar as far as can be judged from published spectra and the often incomplete information that may have been given. On the other hand, some n.m.r. spectra, such as those for poly(vinyl chloride) have received intensive treatment that has shown differences in spectral detail from which differences in interpretation (i.e., n.m.r. treatment) have arisen.

One other feature showing up in the n.m.r. results is the relatively small number of polymers possessing perfect or near-perfect steric purity; indeed quite a number of reputedly syndiotactic polymers are apparently little removed from atactic.

REFERENCES

1. M. Goodman and J. S. Schulman, *J. Polymer Sci. C*, 1966, **12**, 23.
2. A. Nishioka, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1965, **68**, 757.
3. A. S. Khachaturov, *Zavodskaya Lab.*, 1965, **31**, 948.
4. U. Johnsen, *Kolloid Z.*, 1966, **210**, 1.
5. U. Johnsen, Bunsen Gesellschaft Diskussionstagung, Ludwigshafen, 20 October 1965.
6. W. M. Ritchie and F. J. Knoll, *J. Polymer Sci. B*, 1966, **4**, 853.
7. F. A. Bovey and G. V. D. Tiers, *Fortschr. Hochpolym-Forsch.*, 1963, **3**, 139.

7a. F. A. Bovey, *Pure and Applied Chem.*, 1966, **12**, 525.

8. D. W. McCall and W. P. Slichter, *Polymer Rev.*, 1964, **6**, 321.
9. R. C. Ferguson, *Kaut & Gummi. Kunst. Plastics*, 1965, **18**, 723.
10. F. A. Bovey, SPE Technical Papers, 19 October 1966 (Palisades Section), 52–70.
11. K. C. Ramey and J. Messick, *J. Polymer Sci. A2*, 1966, **4**, 155.
12. M. Reinmöller and T. G. Fox, *Amer. Chem. Soc.*, *Polymer Preprints*, 1966, **7**, (2), 999.
13. F. A. Bovey, *Chem. Eng. News*, 30 August 1965, p. 112.
14. Anon., *Chem. Eng. News.*, 5 September 1966, p. 46.
15. J. P. Kennedy, J. J. Elliott and W. Naegele, *J. Polymer Sci. A1*, 1964, **2**, 5029.
16. L. C. Key, F. M. Trent and M. E. Lewis, *Appl. Spectroscopy*, 1966, **20**, 330.
17. F. A. Bovey, E. W. Anderson, D. C. Douglass, and J. A. Manson, *J. Chem. Phys.*, 1963, **39**, 1199.
18. S. L. Manatt, D. D. Lawson, J. D. Ingham, N. S. Rapp and J. P. Hardy, *Analyt. Chem.*, 1966, **38**, 1063.
19. J. D. Ingham, D. D. Lawson, S. L. Manatt, N. S. Rapp and J. P. Hardy, *J. Macrochem.*, 1966, **1**, 75.
20. K. Matsuzaki, T. Uryu and M. Takeuchi, *J. Polymer Sci. B*, 1965, **3**, 835.
21. J. H. Rhodes, R. Chiang and J. C. Randall, *J. Polymer Sci. B*, 1966, **4**, 393.
22. A. Ueno and C. Schuerch, *J. Polymer Sci. B*, 1965, **3**, 53.
23. Y. Fujiwara, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1965, **68**, 1352.
24. R. Chujo, International Symposium on Macromolecular Chemistry, Tokyo Kyoto, 30 September 1966. Preprints, **I**, 145, Paper 3.1.14.
25. B. D. Coleman, T. G. Fox and M. Reinmöller, *J. Polymer Sci. B*, 1966, **4**, 1029.

26. R. L. Miller, *S.P.E. Trans.*, 1963, **3**, 123.
27. A. Yamada and M. Yanagita, International Symposium on Macromolecular Chemistry, Tokyo Kyoto, 30 September 1966. Preprints, **I**, 148, Paper 3.1.15.
28. H. Y. Chen and M. E. Lewis, *Analyt. Chem.*, 1964, **36**, 1394.
29. R. S. Porter, S. W. Nicksic and J. F. Johnson, *Analyt. Chem.*, 1963, **35**, 1948.
30. R. C. Ferguson, *J. Polymer Sci. A*1, 1964, **2**, 4735.
31. Y. Kato and A. Nishioka, International Symposium on Nuclear Magnetic Resonance, Tokyo, 1–3 September 1965. Preliminary Report, Paper R–2–14.
32. A. Nishioka and Y. Kato, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1965, **68**, 1452.
33. S. Satoh, R. Chujo, T. Ozeki and E. Nagai, *J. Polymer Sci.*, 1962, **62**, s101.
34. Y. Kato and A. Nishioka, *Bull. Chem. Soc. Japan*, 1964, **37**, 1622.
35. F. C. Stehling, *J. Polymer Sci. A*1, 1964, **2**, 1815.
36. J. C. Woodbrey, *J. Polymer Sci. B*, 1964, **2**, 315.
37. J. C. Woodbrey and Q. A. Trementozzi, *J. Polymer Sci. C*, 1965, **8**, 113.
38. S. Ohnishi and K. Nukada, *J. Polymer Sci. B*, 1965, **3**, 179.
39. W. C. Tincher, *Makromol. Chem.*, 1965, **85**, 34.
40. G. Natta, E. Lombardi, A. L. Segre, A. Zambelli and A. Marinangeli, *Chimica e Industria*, 1965, **47**, 378.
41. R. S. Porter, M. J. R. Cantow and J. F. Johnson, *Makromol. Chem.*, 1966, **94**, 143.
42. J. Boor, Jnr. and E. A. Youngman, *J. Polymer Sci. A*1, 1966, **4**, 1861.
43. S. Ohnishi and K. Nukada, *J. Polymer Sci. B*, 1965, **3**, 1001.
44. N. M. Sergeyev and V. L. Karpov, *Polymer Sci.* (*U.S.S.R.*), 1964, **6**, 356.
45. E. M. Barrall, R. S. Porter and J. F. Johnson, *J. Chromatog.*, 1963, **11**, 1777.
46. K. W. Bartz and N. F. Chamberlain, *Analyt. Chem.*, 1964, **36**, 2151.
47. W. R. Edwards and N. F. Chamberlain, *J. Polymer Sci. A*1, 1963, **1**, 2299.
48. J. P. Kennedy, L. S. Minckler, G. Wanless and R. M. Thomas, *J. Polymer Sci. A*1, 1964, **2**, 2093.
49. R. Bacskai and S. J. Lapporte, *J. Polymer Sci. A*1, 1963, **1**, 2225.
50. J. P. Kennedy, K. Ueno, K. Hayashi and S. Okamura, *J. Macromolec. Chem.*, 1966, **1**, 243.
51. B. E. Hudson, Jnr., *Makromol. Chem.*, 1966, **94**, 172.
52. J. E. Goodrich and R. S. Porter, *J. Polymer Sci. B*, 1964, **2**, 353.
53. A. D. Ketley, *J. Polymer Sci. B*, 1964, **2**, 827.
54. J. P. Kennedy, C. A. Cohen and W. Naegele, *J. Polymer Sci. B*, 1964, **2**, 1159.
55. J. P. Kennedy, W. Naegele and J. J. Elliott, *J. Polymer Sci. B*, 1965, **3**, 729.
56. T. Takahashni and I. Yamashita, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1965, **68**, 869.
57. T. Takahashni and I. Yamashita, International Symposium on Macromolecular Chemistry, Tokyo Kyoto, 30 September 1966. Preprints, **II**, 5, Paper 1.2.02.
58. G. B. Butler and M. L. Miles, *J. Polymer Sci. A*1, 1965, **3**, 1609.
59. H. Y. Chen, *Analyt. Chem.*, 1962, **34**, 1134.
60. E. Lombardi and A. Segre, *Atti. Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1963, **34**, 547.
61. A. J. Durbetaki and C. M. Miles, *Analyt. Chem.*, 1965, **37**, 1231.
62. W. H. Stubbs, C. R. Gore and C. S. Marvel, *J. Polymer Sci. A*1, 1966, **4**, 1898.
63. J. L. Binder, *J. Polymer Sci. B*, 1966, **4**, 19.

64. S. Kume, H. Sake, A. Takahashi, G. Nishikawa, M. Hatano and S. Kambara, *Makromol. Chem.*, 1966, **98**, 109.
65. M. Hiraoka, T. Takase and Y. Kobayashi, International Symposium on Macromolecular Chemistry, Tokyo Kyoto, 30 September 1966. Preprints, **I**, 73, Paper 2.1.11.
66. R. J. Angelo, R. M. Ikeda and M. L. Wallach, *Polymer*, 1965, **6**, 141.
67. F. Schué and J. P. Dole-Robbe, *Bull. Soc. chim. France*, 1963, 975.
68. F. Schué, *Bull. Soc. chim. France*, 1965, 980.
69. F. C. Stehling and K. W. Bartz, *Analyt. Chem.*, 1966, **38**, 1467.
70. G. Friedman, F. Schué, M. Brini, A. Deluzarche and A. Maillard, *Bull. Soc. chim. France*, 1965, 1343.
71. S-P. S. Yen, *Amer. Chem. Soc., Polymer Reprints*, 1963, **4**, (2), 82.
72. M. A. Bonin, W. R. Busler and F. Williams, *J. Amer. Chem. Soc.*, 1965, **87**, 199.
73. A. G. Davies and A. Wassermann, *J. Polymer Sci. A*1, 1966, **4**, 1887.
74. Z. Momiyama, Y. Imanishi and T. Higashimura, *Chem. High Polymers (Japan)*, 1966, **23**, 56.
75. C. Aso, T. Kinitake, K. Ito and Y. Ishimoto, *J. Polymer Sci. B*, 1966, **4**, 701.
76. M. A. Golub, S. A. Fuqua and N. S. Bhacca, *J. Amer. Chem. Soc.*, 1962, **84**, 4981.
77. H. Y. Chen, *Analyt. Chem.*, 1962, **34**, 1793.
78. D. J. Worsfold and S. Bywater, *Canad. J. Chem.*, 1964, **42**, 2884.
79. M. A. Golub and J. Heller, *J. Polymer Sci. B*, 1966, **4**, 469.
80. H. Y. Chen, *J. Polymer Sci. B*, 1966, **4**, 891.
81. J. P. Kistler, *Bull. Soc. chim. France*, 1965, 764.
82. M. A. Golub, *J. Polymer Sci. B*, 1966, **4**, 227.
83. M. A. Golub and J. Heller, *Canad. J. Chem.*, 1963, **41**, 937.
84. M. A. Golub and J. Heller, *J. Polymer Sci. B*, 1964, **2**, 523.
85. M. A. Golub and J. Heller, *J. Polymer Sci. B*, 1964, **2**, 723.
86. K. Matsuzaki and K. Fujinami, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1965, **68**, 1456.
87. H. Y. Chen, *J. Polymer Sci. B*, 1966, **4**, 1007.
88. T. Yoshino, H. Kyogoku, J. Komiyama and Y. Manabe, *J. Chem. Phys.*, 1963, **38**, 1026.
89. S. Brownstein, S. Bywater and D. J. Worsfold, *J. Phys. Chem.*, 1962, **66**, 2067.
90. R. J. Kern, *Amer. Chem. Soc., Polymer Preprints*, 1963, **4**, (2), 324.
91. F. A. Bovey, F. P. Hood III, E. W. Anderson, and L. C. Snyder, *J. Chem. Phys.*, 1965, **42**, 3900.
92. D. Lim, M. Kolinsky, J. Petranek, D. Doskocilova and B. Schneider, *J. Polymer Sci. B*, 1966, **4**, 645.
93. K-J. Liu and R. Ullman, *Polymer*, 1965, **6**, 100.
94. G. Weill and R. Reeb, *Compt. rend.*, 1966, **263C**, 21.
95. Y. Sakurada, M. Matsumoto, K. Imai, A. Nishioka and Y. Kato, *J. Polymer Sci. B*, 1963, **1**, 633.
96. K. C. Ramey and G. L. Statton, *Makromol. Chem.*, 1965, **85**, 287.
97. Y. O. Sumi, T. Higashimura and S. Okamura, *J. Polymer Sci. A*1, **3**, 1965, 3729.
98. Y. O. Sumi, T. Higashimura and S. Okamura, *J. Polymer Sci. A*1, 1966, **4**, 923.

99. F. A. Bovey and G. V. D. Tiers, *J. Polymer Sci.*, 1960, **44**, 173.
100. N. M. Bazhenov, M. V. Vol'Kenshtein and A. S. Khachaturov, *Polymer Sci. (U.S.S.R.)*, 1964, **5**, 79.
101. T. G. Fox and H. W. Schnecko, *Polymer*, 1962, **3**, 575.
102. C. Walling and D. T. Tanner, *J. Polymer Sci. A*1, 1963, **1**, 2271.
103. Y. Kato and A. Nishioka, *Bull. Chem. Soc. Japan*, 1964, **37**, 1614.
104. Y. Kato, H. Watanabe and A. Nishioka, *Bull. Chem. Soc. Japan*, 1964, **37**, 1762.
105. N. T. Lipscomb and E. C. Weber, *J. Polymer Sci. A*1, 1965, **3**, 55.
106. K. Matsuzaki, A. Ishida, N. Tateno, T. Asakura, A. Hasegawa and K. Tameda, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1965, **68**, 852.
107. D. L. Glusker, R. A. Galluccio and R. A. Evans, *J. Amer. Chem. Soc.*, 1964, **86**, 187.
108. G. Schröder, *Makromol. Chem.*, 1966, **97**, 232.
109. Y. Kato and A. Nishioka, *J. Polymer Sci. B*, 1965, **3**, 739.
110. Y. Kato and A. Nishioka, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1965, **68**, 1461.
111. E. V. Thompson, *J. Polymer Sci. B*, 1965, **3**, 675.
112. H. Abe, K. Imai and M. Matsumoto, *J. Polymer Sci. B*, 1965, **3**, 1053.
113. H. Abe, K. Imai and M. Matsumoto, *J. Polymer Sci. B*, 1966, **4**, 589.
114. S. Brownstein and D. M. Wiles, *Canad. J. Chem.*, 1966, **44**, 153.
115. D. Lim, J. Coupek, K. Juzl, J. Baca, S. Sykora and B. Schneider, International Symposium on Macromolecular Chemistry, Tokyo Kyoto, 30 September 1966. Preprints, **I**, 140, Paper 3.1.13.
116. T. Otsu, B. Yamada and M. Imoto, *J. Macromolec. Chem.*, 1966, **1**, 61.
117. Y. Yamashita and K. Ito, International Symposium on Nuclear Magnetic Resonance, Tokyo, 1–3 September 1965. Preliminary Report, Paper R–2–16.
118. M. Reinmöller and T. G. Fox, *Amer. Chem. Soc., Polymer Preprints*, 1966, **7**, (2), 987.
119. K. Yokata and Y. Ishii, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1965, **68**, 1473.
120. K. Yokota and Y. Ishii, *J. Polymer Sci. B*, 1965, **3**, 771.
121. K. Yokota and Y. Ishii, International Symposium on Nuclear Magnetic Resonance, Tokyo, 1–3 September 1965. Preliminary Report, Paper A–3.
122. H. Sobue, K. Matsuzaki and S. Nakano, *J. Polymer Sci. A*1, 1964, **2**, 3339.
123. T. Tsuruta, T. Makimoto and H. Kanai, *J. Macromolec. Chem.*, 1966, **1**, 31.
124. D. M. Wiles and S. Brownstein, *J. Polymer Sci. B*, 1965, **3**, 951.
125. F. S. Holahan, S. S. Stivala and D. W. Levi, *J. Polymer Sci. A*1, 1965, **3**, 3993.
126. K. Matsuzaki, A. Ishida, Z. Osawa and K. Sano, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1965, **68**, 855.
127. K. Matsuzaki, T. Uryu, A. Ishida and T. Ohki, *J. Polymer Sci. A*1, 1964, **2**, 1139.
128. K. Matsuzaki, T. Uryu, K. Tameda and M. Takeuchi, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1965, **68**, 1466.
129. S. Schuerch, W. Fowells, A. Yamada, F. A. Bovey, F. P. Hood and E. W. Anderson, *J. Amer. Chem. Soc.*, 1964, **86**, 4481.
130. T. Yoshino, J. Komiyama and M. Shinomiya, *J. Amer. Chem. Soc.*, 1964, **86**, 4482.
131. T. Yoshino, M. Shinomiya and J. Komiyama, *J. Amer. Chem. Soc.*, 1965, **87**, 387.

132. T. Yoshino, Y. Kikuchi and J. Komiyama, *J. Phys. Chem.*, 1966, **70**, 1059.
133. H. G. Clark, *Makromol. Chem.*, 1965, **86**, 107.
134. K. Matsuzaki, T. Uryu, A. Ishida and M. Okada, International Symposium on Macromolecular Chemistry, Tokyo Kyoto, 30 September 1966. Preprints, **VII**, 28, Paper 2.5.08.
135. H. G. Clark, *Makromol. Chem.*, 1963, **63**, 69.
136. R. Yamadera and M. Murano, *J. Polymer Sci. B*, 1965, **3**, 821.
137. K. Matsuzaki, T. Uryu and K. Ishigure, *J. Polymer Sci. B*, 1966, **4**, 93.
138. K. Matsuzaki, T. Uryu, M. Okada, K. Ishigure, T. Ohki and M. Takeuchi, *J. Polymer Sci. B*, 1966, **4**, 487.
139. R. Yamadera and M. Murano, International Symposium on Macromolecular Chemistry, Tokyo Kyoto, 30 September 1966. Preprints, **VII**, 32, Paper 2.5.09.
140. H. Sobue, T. Uryu, K. Matsuzaki and Y. Tabata, *J. Polymer Sci. B*, 1963, **1**, 409.
141. H. Sobue, T. Uryu, K. Matsuzaki and Y. Tabata, *J. Polymer Sci. A*1, 1964, **2**, 3333.
142. K. Matsuzaki and T. Uryu, *J. Polymer Sci. B*, 1966, **4**, 255.
143. A. L. Segre, F. Ciampelli and G. Dall'asta, *J. Polymer Sci. B*, 1966, **4**, 633.
144. K. Ishigure, Y. Tabata and K. Oshima, *J. Polymer Sci. B*, 1966, **4**, 669.
145. F. A. Bovey, *J. Polymer Sci. A*1, 1963, **1**, 843.
146. M. Reinmöller and T. G. Fox, *Amer. Chem. Soc.*, *Polymer Preprints*, 1966, **7**, (2), 1005.
147. F. A. Bovey and G. V. D. Tiers, *J. Polymer Sci. A*1, 1963, **1**, 849.
148. K. Yokota, Y. Sakai and Y. Ishii, *J. Polymer Sci. B*, 1965, **3**, 839.
149. K. C. Ramey and N. D. Field, *J. Polymer Sci. B*, 1965, **3**, 63.
150. K. C. Ramey and N. D. Field, *J. Polymer Sci. B*, 1965, **3**, 69.
151. K. Fujii, Y. Fujiwara and S. Fujiwara, *Makromol. Chem.*, 1965, **89**, 278.
152. S. Murahashi, S. Nozakura, M. Sumi and K. Matsumara, *J. Polymer Sci. B*, 1966, **4**, 59.
153. S. Murahashi, S. Nazakura, M. Sumi, H. Yuki and K. Hatada, *Chem. High Polymers (Japan)*, 1966, **23**, 605.
154. S. Murahashi, S. Nazakura, M. Sumi, H. Yuki and K. Hatada, *J. Polymer Sci. B*, 1966, **4**, 65.
155. J. G. Pritchard, R. L. Vollmer, W. C. Lawrence and W. B. Black, *J. Polymer Sci. A*1, 1966, **4**, 707.
156. S. M. Brownstein and D. M. Wiles, *J. Polymer Sci. A*1, 1964, **2**, 1901.
157. H. Buc, *Ann. Chim. (France)*, 1963, **8**, 431.
158. J. Bargon, K-H. Hellwege and U. Johnsen, *Makromol. Chem.*, 1965, **85**, 291.
159. W. C. Tincher, *Macromol. Chem.*, 1965, **85**, 46.
160. H. Hayakawa, I. Yamaguchi and A. Danno, International Symposium on Nuclear Magnetic Resonance, 1–3 September 1965. Preliminary report, Paper R–2–15.
161. H. N. Friedlander, H. E. Harris and J. G. Pritchard, *J. Polymer Sci. A*1, 1966, **4**, 649.
162. H. E. Harris, J. F. Kenney, G. W. Willcockson, R. Chiang and H. N. Friedlander, *J. Polymer Sci. A*1, 1966, **4**, 665.
163. K. Fujii, K. Shibatani, Y. Fujiwara, Y. Ohyanagi, J. Ukida and M. Matsumoto, *J. Polymer Sci. B*, 1966, **4**, 787.
164. Y. Fujiwara and S. Fujiwara, *Bull. Chem. Soc. Japan*, 1964, **37**, 1010.

165. M. Matsumoto and K. Fujii, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1965, **68**, 843.
166. R. J. Kern, J. J. Hawkins and J. D. Calfee, *Makromol. Chem.*, 1963, **66**, 126.
167. K. C. Ramey, N. D. Field and I. Hasegawa, *J. Polymer Sci. B*, 1964, **2**, 865.
168. K. C. Ramey, N. D. Field and A. E. Borchert, *J. Polymer Sci. A*1, 1965, **3**, 2885.
169. M. Goodman and You-Ling Fan, *J. Amer. Chem. Soc.*, 1964, **86**, 4922.
170. U. Johnsen, *J. Polymer Sci.*, 1961, **54**, 56.
171. W. C. Tincher, *J. Polymer Sci.*, 1962, **62**, s148.
172. R. Chujo, S. Satoh, T. Ozeki and E. Nagai, *J. Polymer Sci.*, 1962, **61**, s12.
173. J. L. McClanahan and S. A. Previtera, *J. Polymer Sci. A*1, 1965, **3**, 3919.
174. F. A. Bovey and G. V. D. Tiers, *Chem. and Ind.*, 1962, 1826.
175. O. C. Böckman, *J. Polymer Sci. A*1, 1965, **3**, 3399.
176. J. Demarquay, P. Q. Tho, M. G. Hardrouyére, A. Guyot and M. Prettre, *Compt. rend.*, 1964, **259**, 3509.
177. S. Satoh, *J. Polymer Sci. A*1, 1964, **2**, 5221.
178. T. Shimanouchi, M. Tasumi and Y. Abe, *Makromol. Chem.*, 1965, **86**, 43.
179. W. C. Tincher, *Makromol. Chem.*, 1965, **85**, 20.
180. T. Yoshino and J. Komiyama, *J. Polymer Sci. B*, 1965, **3**, 311.
181. K. C. Ramey, *J. Phys. Chem.*, 1966, **70**, 2525.
182. S. Enomoto, M. Asahina and S. Satoh, *J. Polymer Sci. A*1, 1966, **4**, 1373.
183. A. A. Caraculacu, *J. Polymer Sci. A*1, 1966, **4**, 1829.
184. J. Von Bargon, K-H. Hellwege and U. Johnsen, *Makromol. Chem.*, 1966, **95**, 187.
185. A. P. Suprun and T. A. Soboleva, *Polymer Sci.* (*U.S.S.R.*), 1964, **6**, 1242.
186. M. Frata, G. Vidotto and G. Talamini, *Chimica e Industria*, 1966, **48**, 42.
187. C. W. Wilson III and E. R. Santee, Jnr., *J. Polymer Sci. C*, 1965, **8**, 97.
188. C. W. Wilson III, *J. Polymer Sci. A*1, 1963, **1**, 1305.
189. G. V. D. Tiers and F. A. Bovey, *J. Polymer Sci. A*1, 1963, **1**, 833.
190. A. S. Shashkov, F. A. Galil-Ogly and A. S. Norvikov, *Polymer Sci.* (*U.S.S.R.*), 1966, **8**, 288.
191. J. P. Sibilia and A. R. Paterson, *J. Polymer Sci. C*, 1965, **8**, 41.
192. E. G. Brame Jnr., R. S. Sudol and O. Vogl, *J. Polymer Sci. A*1, 1964, **2**, 5337.
193. J. E. Fearn, D. W. Brown and L. A. Wall, *J. Polymer Sci. A*1, 1966, **4**, 131.
194. G. Allen and R. Warren, *Chem. and Ind.*, 1964, 623.
195. A. Mathias and N. Mellor, *Analyt. Chem.*, 1966, **38**, 472.
196. T. F. Page and W. E. Bresler, *Analyt. Chem.*, 1964, **36**, 1981.
197. M. Sumi, Y. Chokki, M. Nakabayashi and K. Kodama, International Symposium on Macromolecular Chemistry, Tokyo Kyoto, 30 September 1966. Preprints, **VII**, 36, Paper 2.5.10.
198. K. C. Ramey and N. D. Field, *J. Polymer Sci. B*, 1964, **2**, 461.
199. T. M. Connor and K. A. McLauchlan, *J. Chem. Phys.*, 1965, **69**, 1888.
200. H. Haubenstock and W. Naegele, *Makromol. Chem.*, 1966, **97**, 288.
201. L. G. Curtis, D. L. Edwards, R. M. Simons, P. J. Trent and P. T. von Bramer, *Ind. Eng. Chem. Product Res. Dev.*, 1964, **3**, 218.
202. D. F. Percival and M. P. Stevens, *Analyt. Chem.*, 1964, **36**, 1574.
203. M. Murano, Y. Kaneishi and R. Yamadera, *J. Polymer Sci. A*1, 1965, **3**, 2698.
204. T. Harada and N. Ueda, *Chem. High Polymers* (*Japan*), 1965, **22**, 685.
205. H. A. Szymanski and A. Bluemle, *J. Polymer Sci. A*1, 1965, **3**, 63.

206. J. C. Woodbrey, H. P. Higginbottom and H. M. Culbertson, *J. Polymer Sci. A*1, 1965, **3**, 1079.
207. R. C. Hirst, D. M. Grant, R. E. Hoff and W. J. Burke, *J. Polymer Sci. A*1, 1965, **3**, 2091.
208. A. Ravve and C. W. Fitko, *J. Polymer Sci. A*1, 1966, **4**, 2533.
209. R. H. Dinius, M. T. Emerson and G. R. Choppin, *J. Phys. Chem.*, 1963, **67**, 1178.
210. D. Reichenberg and I. J. Lawrenson, *Trans. Faraday Soc.*, 1963, **59**, 141.
211. J. P. de Villiers and J. R. Parrish, *J. Polymer Sci. A*1, 1964, **2**, 1331.
212. J. Brandrup and M. Goodman, *J. Polymer Sci. B*, 1964, **2**, 123.
213. M. Goodman and J. Brandrup, *J. Polymer Sci. A*1, 1965, **3**, 327.
214. Anon., Du Pont Sales Brochure for 310 Curve Resolver, 1966.
215. W. M. Pasika and L. H. Cragg, *Canad. J. Chem.*, 1963, **41**, 293.
216. W. M. Pasika and L. H. Cragg, *Canad. J. Chem.*, 1963, **41**, 777.
217. E. R. Ruckel and C. Schuerch, International Symposium on Macromolecular Chemistry, Tokyo Kyoto, 30 September 1966. Preprints, **X**, 5, Paper 1.5.02.
218. N. Yoda and C. S. Marvel, *J. Polymer Sci. A*1, 1965, **3**, 2229.
219. G. Geuskens, J. C. Lubikulu and C. David, *Polymer*, 1966, **7**, 63.
220. K-J. Liu, International Symposium on Macromolecular Chemistry, Tokyo Kyoto, 30 September 1966. Preprints, **VII**, 50, Paper 2.5.15.
221. T. Takeuchi, M. Yamazaki and S. Mori, *J. Polymer Sci. B*, 1966, **4**, 695.
222. H. Okuto, *Makromol. Chem.*, 1966, **98**, 148.
223. B. J. Duke, O. W. Howarth and J. G. Kenworthy, *Nature*, 1964, **202**, 81.
224. J. F. Yan and M. B. Palmer, International Symposium on Macromolecular Chemistry, Tokyo Kyoto, 30 September 1966. Preprints, **VII**, 40, Paper 2.5.11.
225. D. Doskocilova and B. Schneider, *J. Polymer Sci. B*, 1965, **3**, 213.
226. D. Doskocilova, S. Sykora, H. Pivcova, B. Obereigner and D. Lim, International Symposium on Macromolecular Chemistry, Tokyo Kyoto, 30 September 1966. Preprints, **VII**, 24, Paper 2.5.07.
227. D. Lim, B. Obereigner and D. Doskocilova, *J. Polymer Sci. B*, 1965, **3**, 893.
228. P. E. McMahon and W. C. Tincher, *J. Mol. Spectroscopy*, 1965, **15**, 180.
229. Y. Fujiwara, S. Fujiwara and K. Fujii, *J. Polymer Sci. A*1, 1966, **4**, 257.
230. S. Fujiwara, Y. Fujiwara, K. Fujii and T. Fukoroi, International Symposium on Nuclear Magnetic Resonance, Tokyo, 1–3 September 1965. Preliminary Report, Paper R–2–13.
231. S. Fujiwara, Y. Fujiwara, K. Fujii and T. Fukoroi, *J. Mol. Spectroscopy*, 1966, **19**, 294.
232. S. Fujiwara, Y. Fujiwara and T. Fukoroi, International Symposium on Macromolecular Chemistry, Tokyo Kyoto, 30 September 1966. Preprints, **VI**, 14, Paper 2.3.06.
233. P. E. McMahon, *J. Mol. Spectroscopy*, 1965, **16**, 221.
234. H. Pivcova and B. Schneider, *Coll. Czech. Chem. Comm.*, 1966, **31**, 3154.
235. D. Doskocilova, *J. Polymer Sci. B*, 1964, **2**, 421.
236. Y. Abe, M. Tasumi, T. Shimanouchi, S. Satoh and R. Chujo, *J. Polymer Sci. A*1, 1966, **4**, 1413.
237. W. M. Ritchie, J. H. Harwood and J. V. Putsinger, *Chem. Eng. News*, 22 April 1963, p. 37.
238. Y. Kato, N. Ashikari and A. Nishioka, *Bull. Chem. Soc. Japan*, 1964, **37**, 1630.
239. V. U. Gruber and H-G. Elias, *Makromol. Chem.*, 1965, **86**, 168.
240. H. J. Harwood and W. M. Ritchie, *J. Polymer Sci. B*, 1965, **3**, 419.

241. K. Ito and Y. Yamashita, *J. Polymer Sci. B*, 1965, **3**, 625.
242. C. G. Overberger and N. Yamamoto, *J. Polymer Sci. B*, 1965, **3**, 569.
243. C. G. Overberger and N. Yamamoto, *J. Polymer Sci. A*1, 1966, **4**, 3101.
244. K. Ito and Y. Yamashita, *J. Polymer Sci. B*, 1965, **3**, 631.
245. R. G. Bauer, H. J. Harwood and W. M. Ritchie, *Amer. Chem. Soc., Polymer Preprints*, 1966, **7**, (2), 973.
246. W. L. Senn, *Analyt. Chim. Acta*, 1963, **29**, 505.
247. K. Ito and Y. Yamashita, *J. Polymer Sci. B*, 1965, **3**, 637.
248. K. Ito and Y. Yamashita, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1965, **68**, 1469.
249. N. Ashikari, T. Kanemitsu, K. Yanagisawa, K. Nakagawa, H. Okamoto, S. Kobayashi and A. Nishioka, *J. Polymer Sci. A*1, 1964, **2**, 3009.
250. S. Kobayashi, Y. Kato, H. Watanabe and A. Nishioka, *J. Polymer Sci. A*1, 1966, **4**, 245.
251. T. Takeuchi and M. Yamazaki, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1965, **68**, 1478.
252. W. M. Ritchie and L. E. Ball, *J. Polymer Sci. B*, 1966, **4**, 557.
253. Y. Iwakura, F. Toda and Y. Torii, *J. Polymer Sci. A*1, 1966, **4**, 2649.
254. K. Ito and Y. Yamashita, *J. Polymer Sci. A*1, 1966, **4**, 631.
255. N. Grassie, I. C. McNeill and I. F. McLaren, *J. Polymer Sci. B*, 1965, **3**, 897.
256. T. Takeuchi and M. Yamazaki, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1965, **68**, 931.
257. R. Chujo, S. Satoh and E. Nagai, *J. Polymer Sci. A*1, 1964, **2**, 895.
258. K. Okuda, *J. Polymer Sci. A*1, 1964, **2**, 1749.
259. R. S. Porter, *J. Polymer Sci. A*1, 1966, **4**, 189.
260. W. F. Haddon Jnr., R. S. Porter and J. F. Johnson, *J. Appl. Polymer Sci.*, 1964, **8**, 1371.
261. H. Yuki, K. Hatada and T. Inoue, International Symposium on Macromolecular Chemistry, Tokyo Kyoto, 30 September 1966. Preprints, **I**, 80, Paper 2.1.13.
262. J. Schaefer, *J. Phys. Chem.*, 1966, **70**, 1975.
263. M. W. Dietrich and R. E. Keller, *Analyt. Chem.*, 1964, **36**, 2174.
264. N. Grassie, B. J. D. Torrance, J. D. Fortune and J. D. Gemmell, *Polymer*, 1965, **6**, 653.
265. R. J. Kern and J. Schaefer, *J. Amer. Chem. Soc.*, 1967, **89**, 6.
266. F. Gozzo and G. Carraro, *Nature*, 1965, **206**, 507.
267. T. Fischer, J. B. Kinsinger and C. W. Wilson III, *J. Polymer Sci. B*, 1966, **4**, 379.
268. C. P. Haney, F. A. Johnson and M. G. Baldwin, *J. Polymer Sci. A*1, 1966, **4**, 1791.
269. M. Sumi, Y. Chokki, Y. Nakai, M. Nakabayashi and T. Kazawa, *Makromol. Chem.*, 1964, **78**, 146.

Signal-to-noise Enhancement of Nuclear Magnetic Resonance Spectra

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I. INTRODUCTION

SPECTROSCOPIC METHODS[1, 2] have been increasingly used for the identification of a substance or the elucidation of its structure. Recognizable mass, i.r., u.v. and visible spectra can be obtained from 100 μg. of material or less.[2] By comparison, n.m.r. spectroscopy requires much more material, and since the earliest days of the technique attempts[3] have been made to improve the signal-to-noise ratio.† The quantities needed to obtain a suitable conventional (single scan) high-resolution n.m.r. spectrum vary with the nucleus under investigation. For protons in other than the simplest compounds, 10–40 mg. are required when a 14,000 G spectrometer is used. The natural abundance of protons is almost 100% of the hydrogen content and, apart from tritium, the inherent sensitivity[4] is higher than that of other nuclei, for which larger samples are therefore ordinarily required. For the purposes of this Chapter, inherent sensitivity may be taken as the signal to be anticipated, for given amplification, without reference to the spectrometer noise introduced.

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† The signal-to-noise ratio (S:N) is a quantitative measure of the fact that a signal has random fluctuations imposed upon it. S:N has been defined in more than one way, but the commonest is—

$$2{\cdot}5 \times \frac{\text{peak height}}{\text{peak–peak value of noise}}$$

The relatively high inherent sensitivity of the proton, its common occurrence in organic compounds, and the availability of suitable commercial equipment explain why that nucleus is so often studied. However in this way the carbon skeleton is not directly observed, and so ^{13}C spectroscopy[5] would be more satisfactory for certain problems of organic-structure elucidation. The sample sizes required mean that this is in general impracticable without recourse to some of the methods described later. Even the amounts required for proton spectra are far larger than frequently are available. This Chapter is concerned with outlining currently available methods and possible future techniques for the enhancement of S:N.

Ordinarily the problem is that of improving[6] existing equipment, but if a new spectrometer[7, 8, 9] is being purchased, one with a high magnetic field should be considered, since the inherent sensitivity for a given nucleus theoretically[10] increases with the applied magnetic field. The theoretical improvement is not always attained, owing to various practical difficulties. In any case there are limits to the fields obtainable with iron-core magnets owing both to magnetic saturation of the metal and to the tremendously increased power consumption[11] of electromagnets. The advent[12] of suitable superconducting-magnet[13] spectrometers means that higher fields can now be obtained, with the associated bigger chemical shift separations (in c./sec.) and potential S:N. Available data suggest that for proton spectra from practical spectrometer systems the S:N approximately doubles[14, 15] from 14,000 to 23,500 gauss but that as yet there is no[15, 16] S:N improvement in using a superconducting-magnet field strength of 52,000 gauss.

II. SPECTROMETER CONDITIONS

Magnetic-field inhomogeneities, which determine resolution, can be averaged out to a certain extent by spinning the sample. Spinning is therefore important, but it is a coherent and not a random process. The resulting spinning sidebands remove signal energy from the central band and so they should be reduced in size as much as possible. Their height depends on the spinning rate, which should therefore be adjusted to the optimum.[17] Any unsteadiness in the spinning or imperfections in the sample tube sufficient to introduce significant spinning noise must be corrected. The amplifiers must be tuned to maximum S:N,† and the field homogeneity correcting coils adjusted for minimum side bands and maximum resolution. The resolution is important because, although the area of a peak is unaffected by its width, the height clearly is. It is the extent to which the peak shows above the baseline noise that determines the S:N and hence the smallest sample required. N.m.r. lines do have finite widths owing to spontaneous

† In attempting to improve S:N, either the signal can be enhanced—as is discussed in this Chapter—or the inherent noise reduced. It is often the case that most noise is introduced by the first-stage r.f. amplifier.

emission and various interaction effects,[18] but there are various factors that may cause undue line broadening. The most important of these are the presence of insoluble particles or soluble paramagnetic materials,[19] and a high viscosity[20] of the solution. The former problem can be circumvented by removal of the offending materials (for example, by degassing to remove oxygen) and the latter by a change of solvent or by altering the operating temperature to one at which the viscosity is acceptable.

There are other circumstances in which a change in the operating temperature may improve the sensitivity. In practice, sensitivity is limited for one of two reasons; either by the total quantity of sample available or by a low concentration of the nucleus under study in the suitable solvent. In the latter case raising the temperature may sufficiently increase the solubility to solve the problem. On the other hand, a higher temperature causes a more equable Boltzmann distribution of the nuclei between the energy levels, and so the signal intensity decreases; there is an inverse power dependence[10] with temperature. Published specifications[14] suggest that, relative to +40°C, the S:N is more than doubled at −100°C and halved at +150°C. This is so if the sample solubility is not decreased and if the changed viscosity does not unduly broaden the lines. It should also be noted that the S:N at a given temperature may be lowered[14] by insertion of the variable temperature accessory, so any gain must more than offset such loss.

For nuclei that readily suffer r.f. saturation,[21] rapid passage dispersion mode[22] methods may be advantageous. However, for most high-resolution work the absorption mode is to be preferred. In that case four factors affect the S:N observed: (a) the intensity of the r.f. field; (b) the rate of scan; (c) the filtering time (time constants, band widths); and (d) the nuclear relaxation times. The first three factors are under direct control, and guidance can be obtained as to the conditions to be used from experience, the instrument manufacturers and elsewhere.[4, 9, 22] The highest r.f. field strength consistent with saturation should be used. The rate of scan determines the usable r.f. field strength and also the extent of filtering that can be allowed without undue line broadening. Ordinarily there is no control over (d), but it has been suggested[23] that the addition of small amounts of a paramagnetic material may allow the use of higher r.f. field strengths. This procedure, besides broadening the lines,[19] may alter[24] the chemical shifts.

If large quantities of sample are available, but a low concentration limits the sensitivity, then a rather specialized trick of flowing samples may lead to enhancement.[25] In this way fresh samples which have not undergone r.f. saturation are continuously supplied. This method may be especially useful for nuclei, such as ^{13}C, in which inefficient nuclear relaxation occurs, when an approximately threefold enhancement[26] is feasible. The long relaxation time of ^{13}C nuclei has been turned to good advantage in another flow experiment,[27] in which the ^{13}C resonance was observed in a very weak field (11·2 gauss) by using flowing samples which had previously been polarized in a high field (ca. 10,000 gauss).

III. CURRENTLY AVAILABLE ADDITIONAL TECHNIQUES

The following discussion is principally concerned with the situation in which the sensitivity is limited by availability of the sample, which is assumed to be soluble to any necessary extent. The enhancement factor indicates the relative improvement in S:N observed using a given sample weight.

A. Microcells

In most commercial high-resolution instruments, a cylindrical sample cell is employed. For good resolution to be maintained in such a system, the ratio of the length of the liquid column to its diameter has[28] to be at least about 5–10. This makes its length large compared with that of the detector coil and by no means all the sample is effectively contributing to the signal. The column length may be reduced a certain amount by use of suitable plugs, but care must be taken to ensure that the vortex, formed in the liquid by spinning, does not extend into the coil. Alternatively the diameter (and hence the length) may be considerably reduced[28, 29] by placing the sample within a small tube inserted inside the normal one. The solution is then more concentrated, but the filling factor for the r.f. coil is worse. The overall enhancement is two- to threefold.

The most popular type of microcell is in the shape of a sphere,[30] because that approximates[31] closely to the theoretical Lorentzian cavity. The sample volume is then generally 0·03–0·05 ml. rather than the 0·2–0·4 ml. of normal cylindrical cells. Deviations from an ellipsoidal shape lead to loss of resolution owing to distortion of the magnetic field. Any differences in the bulk volume magnetic susceptibilities of the cell material and the solution accentuate this distortion. Nylon has been used for cell construction,[15] but glass is the common material. There are commercial microcells available,[15, 32, 33] but they are too expensive to be generally disposable. They also introduce large amounts of cell material into the probe area, and this may[34] have deleterious results. Each tube may need individual testing as they can vary widely. It has also been found[35] that, if a tube is suitable on one instrument (say an A-60), it is not necessarily satisfactory on another (HA-100). Again, particulate matter ruins the resolution and the solutions should[35] be filtered. These remarks may also be applicable to the other cells discussed here. Good results have been achieved[34, 36] with spheres blown on the end of small diameter glass tubing. A convenient glass lathe is[6, 34, 36] an electric motor with a hollow drive shaft through which air pressure may be applied to the developing sphere. This method gives better spheres than those made by sealing both ends of the tube[37, 38] and allowing heat expansion to blow the bulbs. In the spectrometer the tube must spin accurately about its long axis. One group of workers[34] reports little difficulty in this respect and uses a simple arrangement; another group finds more elaborate[36] precautions are necessary. It is presumably a question of experience with each system to decide which is preferable for any given spectrometer. The optimum position for the sphere in the spectrometer probe is determined by filling the sphere with a convenient material and adjusting the height for the greatest S:N. Model experiments suggest[34] that for maximum sensitivity, a given sample should be diluted in a sphere of the maximum volume consistent with the probe coil diameter. Spherical microcells yield an enhancement factor of 3–5. Figure 1 illustrates the kind of results than can be obtained. The sample may be transferred into the microcell from an i.r. solution cell,[34] which may be washed with solvent containing a suitable internal reference compound. If the sample is obtained by gas-chromatographic separation it may be trapped by any[6, 39, 40] of the methods available. Alternatively the sample can be trapped directly from the gas stream into the microcell[41] or transferred from a packed trap into[42] the microcell.

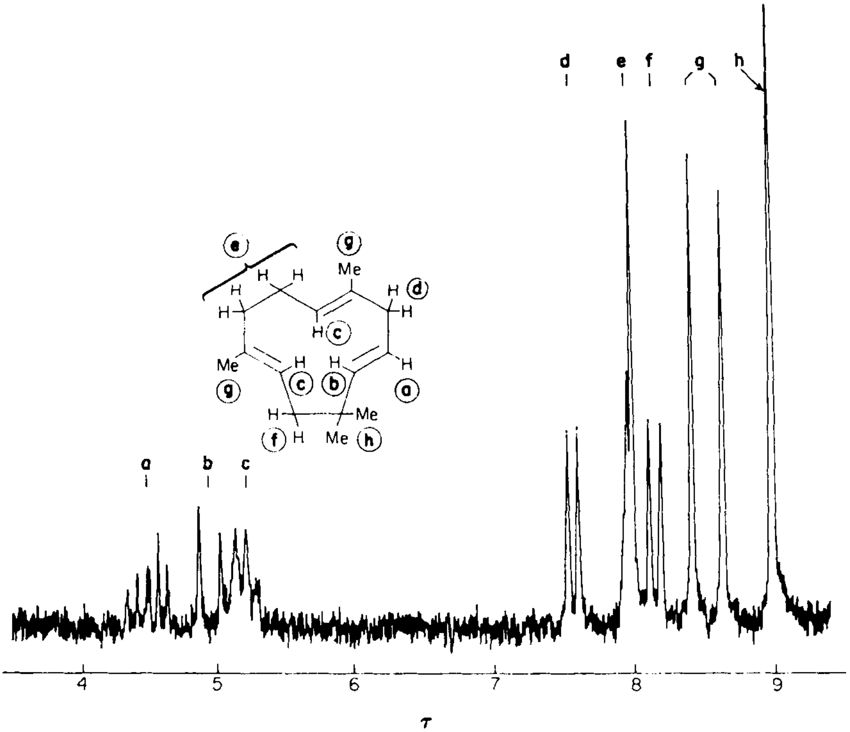

FIG. 1. Single-scan 100 Mc./sec. p.m.r. spectrum of *trans*, *trans*-humulene (0·45 mg.) in carbon tetrachloride (34 μl.) using a spherical microcell. (From Flath *et al.*[36])

B. Time-averaging methods

The commonest ways at present employed for significantly improving sensitivity trade time for better S:N. That is, a longer time is taken over the measurements, allowing the noise to average out to a certain extent. One of the simplest methods[43–46] involves collecting information from one point at a time. The magnetic field and r.f. are adjusted to correspond to the chosen point and the signal is fed to the electronic integrator circuit now commonly available on n.m.r. spectrometers. The integrating condenser charges up proportionally to the signal at that point, and the noise, which randomly adds or subtracts, relatively diminishes. After a pre-determined time the integral is recorded, the condenser discharged, and the magnetic field or r.f. adjusted by a small definite amount. The whole process is then repeated at the new point. Instead of advancing the spectrometer in discrete steps a very slow continuous scan[44, 46] may be used. In this case the integrator is collecting information over a small finite sweepwidth, the size of which is determined by the frequency of integral cancellation and the rate of scan. Figure 2 shows an example of what can be achieved by this general method. The system is best suited[44] to the study of small parts of a spectrum, since it demands a high degree of stability in both the magnetic field and the standing d.c. input to the integrator. Small baseline changes that are almost unnoticeable on an absorption spectrum may cause wild fluctuations in the integrator. Good baseline stability can be achieved by field modulation[47] and a phase-sensitive detector. The above method has been called[46] the SUPER SNAIL technique. A related method[48] is the DOG which employs a low spectral scan rate with high gain, suitable low r.f. level, and adequate filtering to reduce the response of the detection system to spectrometer noise. This method, which gives some peak distortion, does not appear to have been much used.

The most widely employed method for improving S:N involves summing (i.e., averaging) spectra digitally.[49, 50] The analogue n.m.r. spectrum is obtained under optimum conditions[51] and then digitized[52] at regular, pre-determined intervals along the magnetic-field axis. A second spectrum is then produced independently of the first, and digitized at exactly the same points. In this way n spectra are collected and the corresponding points of each added together in a computer's magnetic memory. The noise, which is non-coherent, tends to average out and the signal, which is coherent, increases in size. The theoretical[53] improvement in S:N (i.e., enhancement factor) is $\sqrt{n}$. For protons, a readily achieved enhancement is 15 obtained by summing about 250 spectra during an overnight experiment. For many other nuclei for which fast scan rates can be used, several thousand spectra may[34] readily be accumulated. The best conditions for obtaining the spectra for accumulation may not be those for the best S:N in a single scan; by sacrificing S:N for speed, far more spectra may be accumulated in a given time. Figure 3 shows ^{13}C spectra obtained in this way. The square-root sign in the enhancement factor means that the return falls off fairly rapidly. A tenfold increase in S:N entails averaging 100 spectra; to double this to twentyfold requires 400 spectra. Slow magnetic-field drifts are either compensated for by triggering the digitization from a prominent spectral peak or retrospectively[54] by ensuring that the major peaks are correctly overlapped.

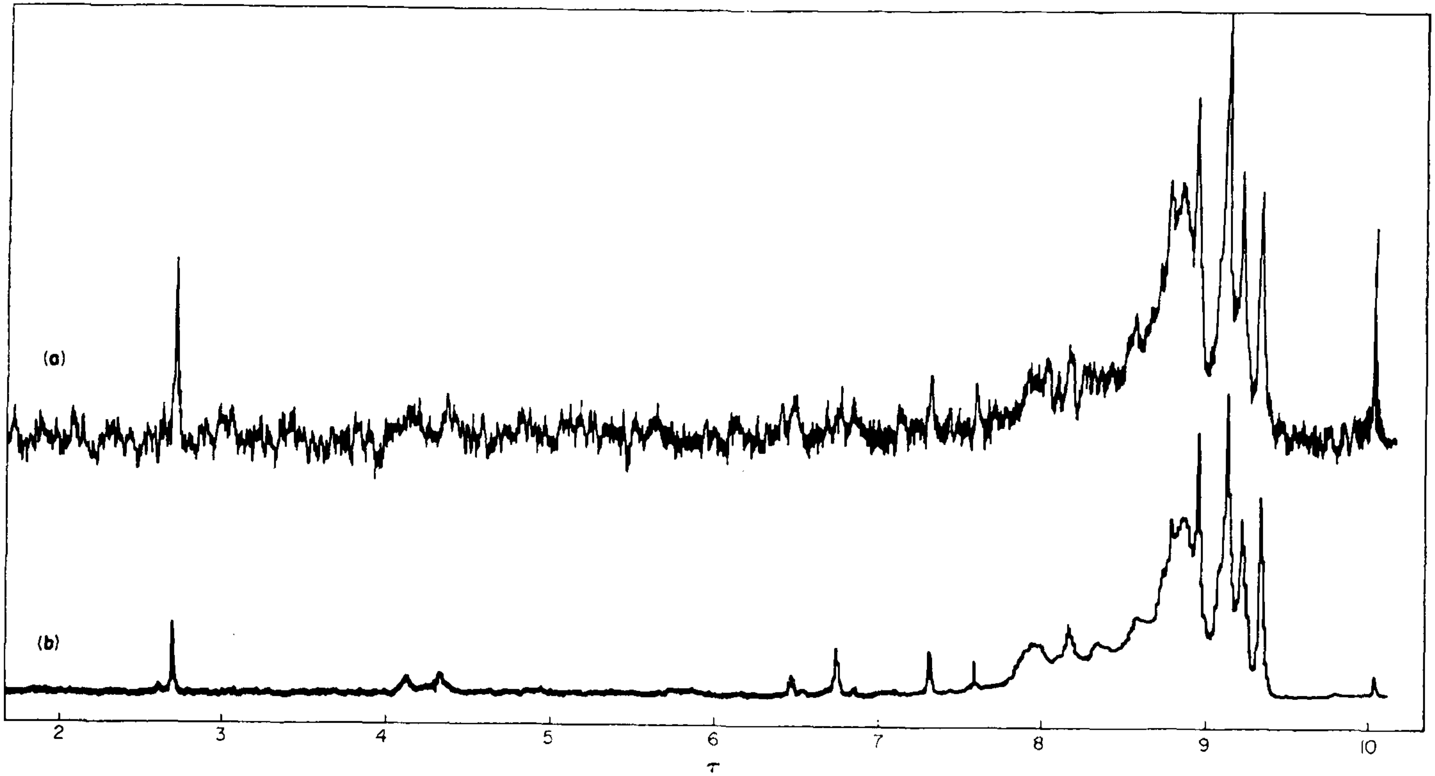

FIG. 2. Normal scan (a) and SUPER SNAIL (b) proton spectra of 2,2,4β-tribromo-5β-cholestan-3-one in deuterochloroform. (From Dehlsen and Robertson.[46])

For equipment, a small special purpose computer incorporating a digitizer and special read-in/read-out facilities is normally used. Such a system is frequently referred to as a CAT (Computer of Average Transients). Some[55] have the advantage that the contents of the memory may at any time be viewed on a built-in oscilloscope. In principle, any digital computer may be used, providing that a digitizer is available. General-purpose electronic computers cost too much in real-time computing for them ordinarily to be used in this way. One way of overcoming this problem would be to collect the analogue spectra sequentially on a magnetic tape

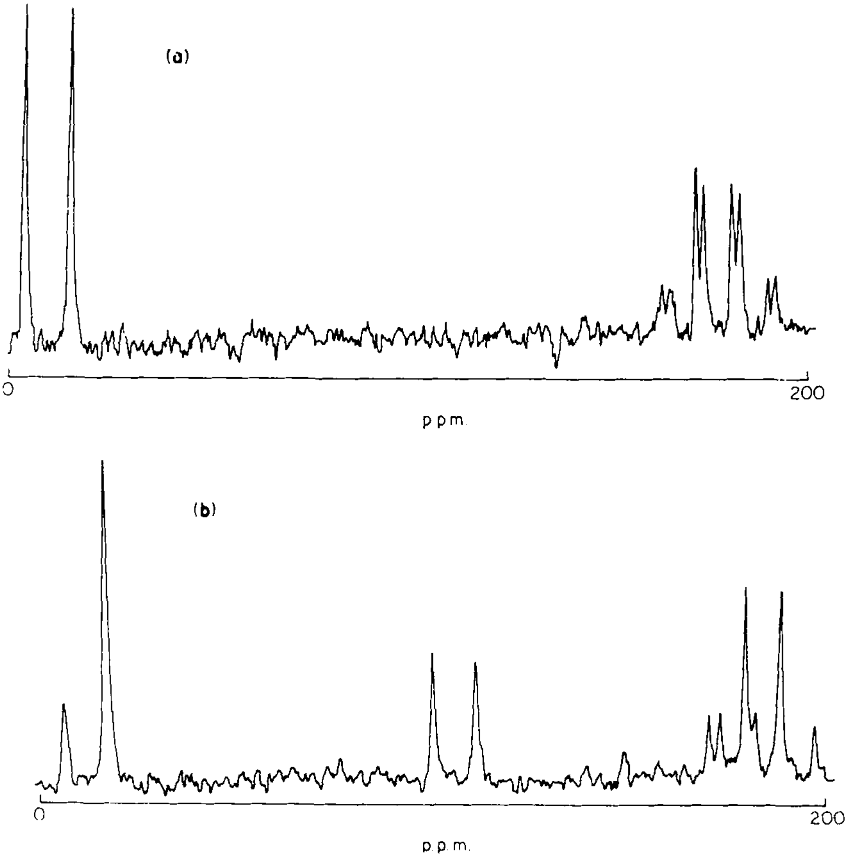

Fig. 3. The result of 256 ^{13}C spectra accumulated in 3½ hr. The ^{13}C was at natural abundance and observed at 15·1 Mc./sec.: (a), acetaldehyde; (b), acetylacetone. (These spectra were recorded in the Application Laboratory of Perkin–Elmer Ltd, with an R-10 n.m.r. spectrometer and computer accessory.)

that could subsequently be fed at a faster rate through the A–D converter into the computer. Alternatively, the spectra could be stored digitally in some computer input medium and read in quickly later. A special-purpose computer does have the advantage of convenience, and in addition it can be used for the enhancement of i.r.,[56] e.s.r. and other signals.

It is appropriate at this stage to draw attention to the dangers in using greatly enhanced spectra—

(a) The possibility of incorrect overlapping of spectra must always be considered.
(b) A large peak may, after multiple addition, digitally exceed the highest possible word length in the computer. In this case the word effectively resets to zero and the peak may appear split on display; the integrated areas will then be wrong.
(c) The sample must be stable over the long periods required for accumulation.
(d) The purity of the solvent and of the internal reference compound should be checked. Not only may impurities be present, but side bands (e.g., the so-called ^{13}C satellites in proton spectra) may be observed. However, a computer system may be used in a subtract mode as well as an add, and the solvent peaks can in principle be removed[6] in this way.

C. Other techniques

1. *Smoothing*

Mathematical curve smoothing[57] should improve S:N. This technique can be used in conjunction with the special-purpose computer referred to above. If that is incapable of further calculations, the digital data can be put onto cards or tape to be used as input to another computer.† The curve-smoothing routine operates essentially by mathematically inspecting the data and adjusting irregular points. The method sometimes appears to be unjustified,[6] but is akin to a regression analysis in which data are statistically fitted to a given algebraic expression. The value of curve smoothing after averaging several spectra is quite possibly[34, 60] marginal, although it was found useful[61] in improving a homonuclear spin decoupling experiment.

2. *Double resonance*[62]

Nuclei of inherently low sensitivity may sometimes be readily observed by means of their coupling with other nuclei of higher sensitivity. This method has been applied to ^{13}C by observing[63] changes induced in the proton spectrum

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† This data can be used for other calculations, such as resolution of overlapping curves[58] and the determination of moments,[59] as aids in spectral analysis.

while a second, strong r.f. field is swept through the ^{13}C region. Spin decoupling can anyway result in higher S:N. For example, if a ^{13}C spectrum is being observed directly[64] (as opposed to indirectly by the above method) coupling to the protons of the molecule may cause splitting or broadening of the ^{13}C resonances. If the protons are decoupled from the carbon nuclei by saturation with a second r.f. field then[62, 64] sharp signals appear in the ^{13}C spectrum. There may also be a small improvement in such a case[62, 64, 65] owing to the phenomenon known as the Overhauser effect. If one magnetic particle (e.g., an electron or a nucleus) is undergoing a transition from one energy level to another, the populations of the energy levels of a second magnetic particle are affected.[66] This means that there is a change in the number of spins that are available for observation of the magnetic resonance transition of the second particle. It can happen that there are more spins in the upper energy state than in the lower. (This corresponds to a negative spin temperature.[67]) In such a case the signal of the second particle is inverted. Dramatic Overhauser enhancements (very often negative) of two orders of magnitude are obtained in nuclear electron double-resonance experiments.[68, 69] In these, nuclear resonances are observed while the electron resonance of an added free radical is saturated. The method has not yet been widely used, probably because of the line broadening induced by the unpaired electrons and the difficulties in obtaining the high microwave power required to saturate the electron resonance.

3. *Fourier transform*

I confidently expect that this method will be considerably developed in the near future, although at present a great deal of sophisticated equipment is required. The principle of the method,[70] which is particularly applicable to high-resolution p.m.r. spectroscopy, can be understood in the following way. Consider a spectrometer operating in a frequency-sweep mode. At any given instant the frequency corresponds to only one point in the spectrum, and information is obtained only from that point. Obviously, if the entire spectrum could be studied at one time, the rate of acquisition of information would be vastly increased. This could be done by using several transmitters and receivers in a "multichannel" spectrometer. However, it transpires[70] that in effect the same end may be achieved by using particular r.f. pulse sequences. The spectrum that results is the Fourier transform of the conventional absorption spectrum, which can be generated by suitable computation. This computation has so far been performed digitally, but analogue methods should be possible. The S:N of proton spectra can be enhanced by a full order of magnitude in a given time by this method. Alternatively the time necessary to achieve a given S:N is two orders lower than that required by conventional methods. Consequently the method offers the possibility of observing rapid reactions by n.m.r. Figure 4 shows one example of what has been achieved by Fourier transform spectroscopy.

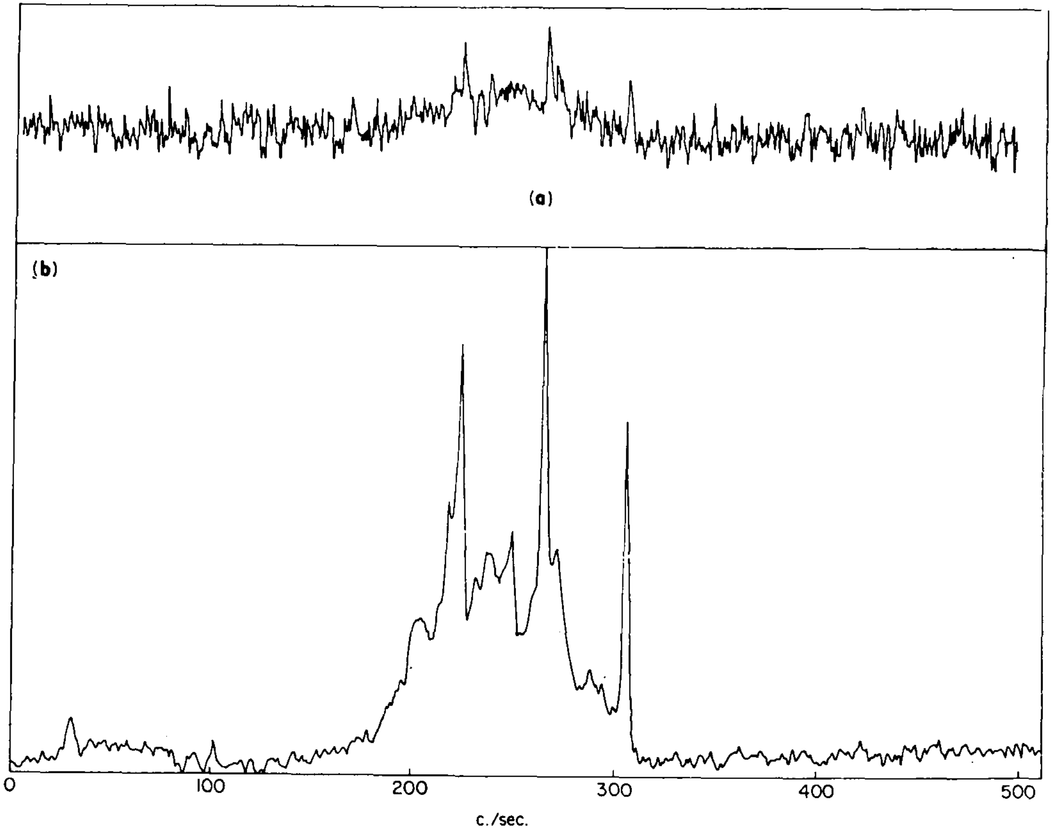

Fig. 4. Two proton spectra, each obtained in 500 sec., of a 0·011 M solution of progesterone in hexafluorobenzene: (a), conventional single scan; (b), the result of 500 pulses, 1 sec. apart, followed by a Fourier transformation. (From Ernst and Anderson.[70])

IV. SUMMARY

The sample size required to obtain suitable high resolution n.m.r. spectra can be decreased by various methods. Table I indicates the approximate quantities

TABLE I

Minimum sample quantities required for S:N = 2

Nucleus	Single run Moles sample	 Volume (ml.)	 Sample wt. (mg.) for M.W. = 250	After 1 hr. with computer. Sample wt. (mg.) (M.W. = 250)	Overnight enhancement with computer. Sample wt. (mg.) (M.W. = 250)
^{1}H	4×10^{-6}	0·4	1·0	0·25	0·065
^{19}F	6×10^{-6}	0·4	1·5	0·40	0·10
^{31}P	3×10^{-5}	0·8	7	0·35	0·09
^{11}B	8×10^{-6}	0·8	2	0·10	0·025
^{13}C (natural abundance)	5×10^{-3}	0·8	1300	200	50
^{14}N	1×10^{-3}	0·8	250	12	3

Notes

1. The above data, kindly provided by Dr J. B. Leane, apply to a Perkin-Elmer R-10 (14,092 G) spectrometer with an NS-544 accessory.
2. All figures relate to a single sharp resonance from a single nucleus. Multiplet formation reduces peak heights, in which case more sample is required.

TABLE II

Approximate enhancement factors obtainable by various methods

Method	Enhancement	Comments
Higher magnetic field	. .	See text
Lower operating temp.	< 2	Limited by viscosity and solubility changes
Microcells	2–5	Unsuitable if limited by concentration
Time-averaging	$\propto \sqrt{\text{time}}$	. .
CAT	10–100	Depends on nucleus
Curve smoothing	ca. 1–2	Theoretically higher
Overhauser	~100	Limited applicability so far
Fourier transform	10–100	Limited experience so far

nowadays required for routine spectra of various nuclei. In Table II are given the probable enhancements obtainable by the various methods discussed. These include some techniques not at present widely used, and in particular one (the Fourier-transform method) that presages a reduction in experimental time.

REFERENCES

1. "Determination of Organic Structures by Physical Methods," Vol. 2 (F. C. Nachod and W. D. Phillips, Eds.). Academic Press, New York, 1962.
2. R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds," Wiley, New York, 1963.
3. I. M. Ross and F. B. Johnson, *Nature*, 1951, **167**, 286.
4. J. A. Pople, W. G. Schneider and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, 1959.
5. J. B. Stothers, *Quart. Rev.*, 1965, **19**, 144.
6. R. E. Lundin, R. H. Elsken, R. A. Flath and R. Teranishi, *Appl. Spectroscopy Rev.*, **1**, to be published.
7. A list of spectrometer manufacturers can be drawn up by reference to other articles (cf. Refs. 2, 4, 6, 8 and 9).
8. E. Lustig, *Analyt. Chem.*, 1966, **38**, 331R.
9. J. W. Emsley, J. Feeney and L. M. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, Oxford, 1965.
10. For example, see C. P. Slichter, "Principles of Magnetic Resonance," Harper and Row, New York, 1963.
11. F. Bitter, *Rev. Sci. Instr.*, 1962, **33**, 342.
12. F. A. Nelson and H. E. Weaver, *Science*, 1964, **146**, 223.
13. A. C. Rose-Innes, *Contemporary Phys.*, 1965, **7**, 135; W. B. Sampson, P. P. Craig and M. Strongin, *Sci. Amer.*, 1967, **216**, No. 3, 114.
14. Perkin–Elmer Ltd, Beaconsfield, Bucks, England.
15. Varian Associates, Palo Alto, California, U.S.A.
16. F. A. Bovey, F. P. Hood, E. Pier and H. E. Weaver, *J. Amer. Chem. Soc.*, 1965, **87**, 2060.
17. G. A. Williams and H. S. Gutowsky, *Phys. Rev.*, 1956, **104**, 278.
18. J. A. Pople, W. G. Schneider and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," p. 28. McGraw-Hill, New York, 1959.
19. A. Kowalsky and M. Cohn, *Ann. Rev. Biochem.*, 1964, **33**, 481; H. Sternlicht, *J. Chem. Phys.*, 1965, **42**, 2250.
20. For example, see J. W. Emsley, J. Feeney and L. M. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," p. 32. Pergamon Press, Oxford, 1965.
21. For example, see J. A. Pople, W. G. Schneider and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," p. 30. McGraw-Hill, New York, 1959.
22. P. C. Lauterbur, *In* "Determination of Organic Structures by Physical Methods," Vol. 2 (F. C. Nachod and W. D. Phillips, Eds.), p. 465. Academic Press, New York, 1962.
23. L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," p. 41. Pergamon Press, Oxford, 1959.
24. R. S. Milner and L. Pratt, *Discuss. Faraday Soc.*, 1962, **34**, 88.

25. A. I. Zhernovoi and G. M. Latyshev, "Nuclear Magnetic Resonance in a Flowing Liquid" (translated by C. N. and T. I. Turton). Plenum Press, New York, 1965.
26. S. Forsen and A. Rupprecht, *J. Chem. Phys.*, 1960, **33**, 1888.
27. H. Ottavi, *In* "Magnetic and Electric Resonance and Relaxation," (J. Smidt, Ed.), p. 669. North-Holland, Amsterdam, 1963.
28. S. C. Slaymaker, *Appl. Spectroscopy*, 1967, **21**, 42.
29. S. Ito and I. Miura, *Bull. Chem. Soc. Japan*, 1965, **38**, 2197.
30. P. Higham and R. E. Richards, *Proc. Chem. Soc.*, 1958, 128.
31. E. R. Andrew, "Nuclear Magnetic Resonance," p. 78. Cambridge University Press, London, 1958.
32. Wilmad Glass Co., Buena, New Jersey, U.S.A.
33. NMR Specialties, Inc., New Kensington, Pa., U.S.A.
34. D. J. Frost, G. E. Hall, M. J. Green and J. B. Leane, *Chem. and Ind.*, 1967, 116.
35. R. E. Lundin, personal communication.
36. R. A. Flath, N. Henderson, R. E. Lundin and R. Teranishi, *Appl. Spectroscopy*, 1967, **21**, 183.
37. D. J. Frost and G. E. Hall, unpublished work.
38. J. F. Hinton and E. S. Amis, *J. Chem. Educ.*, 1966, **43**, 443.
39. R. E. Lundin, R. H. Elsken, R. A. Flath, N. Henderson, T. R. Mon and R. Teranishi, *Analyt. Chem.*, 1966, **38**, 291.
40. M. D. D. Howlett and D. Welti, *Analyst*, 1966, **91**, 291.
41. E. G. Brame, *Analyt. Chem.*, 1965, **37**, 1183.
42. I. A. Fowlis and D. Welti, *Analyst*, 1967, **92**, 639.
43. R. E. Mayo and J. H. Goldstein, *Rev. Sci. Instr.*, 1964, **35**, 1231.
44. S. E. Brown, D. A. Maguire and D. D. Perrin, *Chem. and Ind.*, 1965, 1974.
45. P. J. Huck and J. Homer, *Chem. and Ind.*, 1966, 1488.
46. D. C. Dehlsen and A. V. Robertson, *Austral. J. Chem.*, 1966, **19**, 269.
47. O. Haworth and R. E. Richards, *In* "Progress in Nuclear Magnetic Resonance Spectroscopy" (J. W. Emsley, J. Feeney, and L. H. Sutcliffe, Eds.), Vol. 1, p. 1. Pergamon Press, Oxford, 1966.
48. R. R. Ernst and H. Primas, *Discuss. Faraday Soc.*, 1962, **34**, 43.
49. O. Jardetzky, N. G. Wade and J. J. Fischer, *Nature*, 1963, **197**, 183.
50. L. C. Allen and L. F. Johnson, *J. Amer. Chem. Soc.*, 1963, **85**, 2668.
51. R. R. Ernst and W. A. Anderson, *Rev. Sci. Instr.*, 1965, **36**, 1696.
52. J. Macy, *In* "Computers in Biomedical Research," (R. W. Stacy and B. D. Waxman, Eds.), Vol. 2, p. 3. Academic Press, New York, 1965.
53. M. P. Klein and G. W. Barton, *Rev. Sci. Instr.*, 1963, **34**, 754. R. R. Ernst, *Rev. Sci. Instr.*, 1965, **36**, 1689.
54. Japan Electron Optics Laboratory Co. Ltd., Tokyo, Japan.
55. For example, those manufactured by Technical Measurement Corporation, North Haven, Connecticut, U.S.A., Northern Scientific, Inc., Madison, Wisconsin, U.S.A., and Data Laboratories, 3/7 Hatfields, London S.E.1, England.
56. M. J. D. Low and S. K. Freeman, *Analyt. Chem.*, 1967, **39**, 194.
57. A. Savitzky and M. J. E. Golay, *Analyt. Chem.*, 1964, **36**, 1627.
58. W. D. Keller, T. R. Lusebrink and C. H. Sederholm, *J. Chem. Phys.*, 1966, **44**, 782.
59. W. A. Anderson and H. M. McConnell, *J. Chem. Phys.*, 1957, **26**, 1496.
60. J. M. Read and J. H. Goldstein, *Analyt. Chem.*, 1965, **37**, 1609.

61. G. E. Hall and D. G. Roberts, *J. Chem. Soc. B*, 1966, 1109.
62. J. D. Baldeschwieler and E. W. Randall, *Chem. Rev.*, 1963, **63**, 81.
63. R. Freeman and W. A. Anderson, *J. Chem. Phys.*, 1965, **42**, 1199; J. K. Becconsall and P. Hampson, *Mol. Phys.*, 1965, **10**, 21.
64. E. G. Paul and D. M. Grant, *J. Amer. Chem. Soc.*, 1964, **86**, 2977.
65. R. Kaiser, *J. Chem. Phys.*, 1963, **39**, 2435; 1965, **42**, 1838.
66. A. Abragam, "The Principles of Nuclear Magnetism," p. 367. Oxford University Press, London 1961. R. A. Hoffman and S. Forsen, *In* "Progress in Nuclear Magnetic Resonance Spectroscopy" (J. W. Emsley, J. Feeney and L. H. Sutcliffe, Eds.), Vol. 1, p. 82. Pergamon Press, Oxford, 1966.
67. J. W. Emsley, J. Feeney and L. M. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," p. 17. Pergamon Press, Oxford, 1965.
68. R. A. Dwek, J. G. Kenworthy, and R. E. Richards, *Mol. Phys.*, 1966, **10**, 529.
69. D. J. E. Ingram, *Contemporary Phys.*, 1965, **7**, 103.
70. R. R. Ernst and W. A. Anderson, *Rev. Sci. Instr.*, 1966, **37**, 93.

Fluorine-19 Nuclear Magnetic Resonance Spectroscopy

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ALTHOUGH P.M.R. spectroscopy takes first place in importance for the organic chemist, the number of papers dealing with, and papers quoting, ^{19}F resonance studies is increasing very rapidly. This growth of interest in ^{19}F studies was bound to increase to keep pace with work on the study of the chemistry of fluorinated hydrocarbons, but a similar increase in the application is being found in the study of inorganic derivatives. Additionally some of the advantages of ^{19}F spectra, e.g., the larger chemical shifts, are being utilized in the study of such topics as conformational analysis.

In preparing this review it has been desirable to divide the subject matter but, as so often happens, the divisions chosen are not absolutely rigid.

We additionally thought that it would be more helpful to the reader to quote all chemical shifts to the same reference material, namely CCl_3F. However unlike ^1H resonance spectroscopy, there is no universally accepted standard, and many compounds, e.g., trifluoroacetic acid, hexafluorobenzene and 1,2-difluorotetrachloroethane have been used.

The chemical shifts that have been recorded by using internal CCl_3F will be quoted as ϕ^* values, other shifts quoted were obtained as indicated below—

$$\phi^{\ddagger} = \delta_{CF_3CO_2H\,(ext)} + 78{\cdot}5$$
$$\phi^{+} = \delta_{C_6F_6} + 162{\cdot}9$$
$$\phi^{a} = \delta_{CFCl_2CFCl_2} + 67{\cdot}3$$
$$\phi^{b} = \delta_{C_6H_5CF_3} + 63{\cdot}8$$

In order to simplify the extensive amount of ^{19}F data derived from compounds other than fluorocarbons and their simple derivatives, Section III has been sub-divided in the following manner.

A. Organometallics.
B. Fluorinated derivatives of the elements.
C. Complex fluoro-anions.

It is immediately apparent that some overlap will occur between the respective divisions depending upon the definition of the groups. This is probably unavoidable, but an attempt has been made to minimize the discrepancies in the following way. The organometallic section, sub-divided into the periodic groups, comprises molecules with carbon–metal bonds where the emphasis is on the fluorine atoms attached to the carbon skeleton. Generally, therefore, the chemical information is provided by the fluorocarbon part of the molecule. Section IIIB, similarly divided into the periodic groupings, generally represents molecules where fluorine is directly bonded to the element concerned. Here direct couplings and the influence of the elements on the fluorine chemical shifts are of increasing importance. Additionally, in this Section the simple perfluoroalkyl derivatives of the non-metallic elements are considered. In Section IIIC some complex fluoro-anions are discussed.

I. FLUOROHYDROCARBONS

A. Fluorinated aliphatic hydrocarbons

White,[1] in an extension of earlier studies of 2,2-difluoropropane derivatives,[2] has correlated the chemical shifts of the 2-CF_2 group of chlorinated fluoropropanes and found that a linear relationship exists between the shift of this 2-CF_2 group and the sum of the substituent electronegativities. The shifts and the coupling constants are shown in Table I. It will be noted that the shift of the terminal $CFCl_2$, or the CF_2Cl, group is substantially affected by the nature of the second terminal group. Similarly it is observed that the $^3J_{FF}$† values are very much smaller when coupling is between CF_2—CF_2 or CF_2—CF_3 groups than for CF_2—CF groups.

† The prefix n in ^nJ indicates the number of bonds over which coupling is occurring; thus in this instance $^3J_{FF}$ is the vicinal F–F coupling.

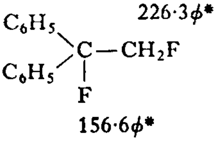
TABLE I

Chemical shifts and coupling constants of fluorinated propanes $X \cdot CF_2Y$

		Chemical shifts $\phi^{\ddagger}$			Coupling constants c./sec.		
X	Y	X	CF_2	Y	J_{XCF_2}	J_{YCF_2}	J_{XY}
CCl_3	CCl_3	..	98·07	..	..	..	..
CCl_3	$CFCl_2$	..	103·22	63·93	..	4·9	..
$CFCl_2$	$CFCl_2$	66·68	108·85	66·68	6·1	6·1	..
CF_2Cl	$CFCl_2$	64·82	114·02	70·97	<1	7·2	13·6
CF_2Cl	CF_2Cl	67·91	119·44	67·91	1·1	1·1	..
CF_3	CF_2Cl	80·91	125·61	70·01	<1	1·8	8·9
CF_3	CF_3	82·95	131·47	82·95	<1	<1	7·3

Hopkins[3] has demonstrated the simplification of calculating the n.m.r. parameters, for large spin systems by using the properties of molecular symmetry, as occurs in the ten-spin system of perfluorobutane.

Direct fluorination of 1,1-diphenylethylene afforded[4] 1,1-diphenyl-1,2-difluoroethane (**1**) and 1,1-diphenyl-1,2,2-trifluoroethane (**2**). The n.m.r. parameters are shown, and it is apparent that $^3J_{FF}$ is again smaller for the CF–CF_2 coupling than for the CF–CF coupling.



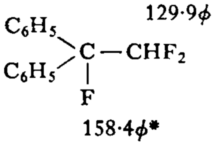
$(C_6H_5)_2CF-CH_2F$

1

$J_{HF\ gem} = 48$ c./sec.

$J_{FF} = 20$ c./sec.

$J_{HF\ vic} = 20$ c./sec.



$(C_6H_5)_2CF-CHF_2$

2

$J_{HF\ gem} = 52$ c./sec.

$J_{FF} = 12$ c./sec.

$J_{HF\ vic} = 12$ c./sec.

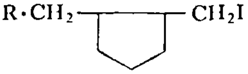
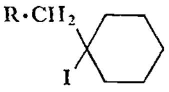
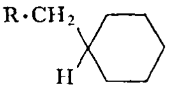
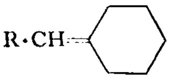
The anomalous spin coupling that is often observed in alkyl fluorides has been ascribed[5] to virtual coupling of the fluorine to the γ-proton(s). These authors showed that the ^1H spectrum of the α-CH_2 group of n-heptyl fluoride was dependent upon the field strength; no details of the ^{19}F spectrum were given.

Brace[6] has considered some reactions of perfluoroalkyl free radicals with olefins and includes in the paper the ^{19}F chemical shifts of the $CF_3 \cdot CF_2 \cdot CF_2$ groups, inserted from the perfluoroalkyl iodide used (Table II).

TABLE II

The chemical shifts of the perfluoropropyl group in some substituted hydrocarbons

$R = CF_3 \cdot CF_2 \cdot CF_2—$

	Chemical shifts in ϕ^*		
	αCF_2	βCF_2	γCF_3
	114·62	128·36	81·28
$(R \cdot CH_2 \cdot CHI)_2(CH_2)_3$	114·0–114·8	130·0	81·25
	110·59	128·85	81·23
	114·44	139·33	82·08
	106·73	129·42	82·08

B. Derivatives of fluorinated hydrocarbons

Dyer and Lee[7] have studied the ^{19}F chemical shifts and coupling constants of substituted 1,1,2-trifluoro-2-chloroethanes of the general form $CF_2Q \cdot CFHCl$ where $Q = SiMe_3$, $SiCl_3$, PMe_2, PH_2, OMe, SMe and Cl. The system was treated by an ABPX analysis as previously described;[8] the AB part of the spectrum arising from the low-field CF_2 group with a large geminal coupling in the range 142–343 c./sec. The value of this geminal coupling $[J_{AB}]$ was found to be inversely proportional to the electronegativity of the atom of group Q which is directly bonded to the CF_2 group. Fairly good correlations were obtained between the mean of the chemical shifts of A and B, namely δ_{AB}, with the electronegativities and of the chemical shift between A and B, namely $\delta_B - \delta_A$, with the reciprocal of the electronegativity (Figs. 1 and 2).

In a paper[9] describing a new method of obtaining monofluorinated-α-hydroxy-esters, the ^{19}F chemical shifts and the ^1H–^{19}F coupling constants were given to substantiate the nature of the products obtained. The parameters are shown in (**3**–**6**).

In another preparative paper[10] the direct fluorination of difluoroacetyl fluoride, resulting in the conversion of the carbonyl group to a difluoromethylene group,

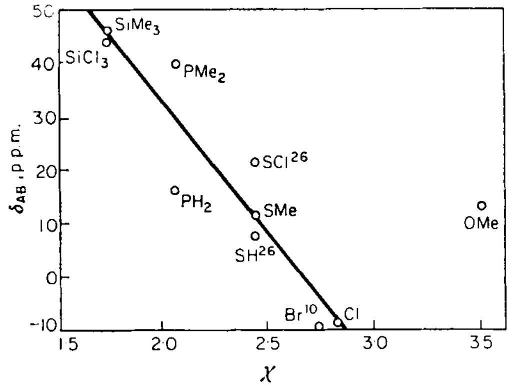


FIG. 1. Relationship of the mean chemical shifts AB to electronegativity (χ) of Q. (From Dyer and Lee.[7])

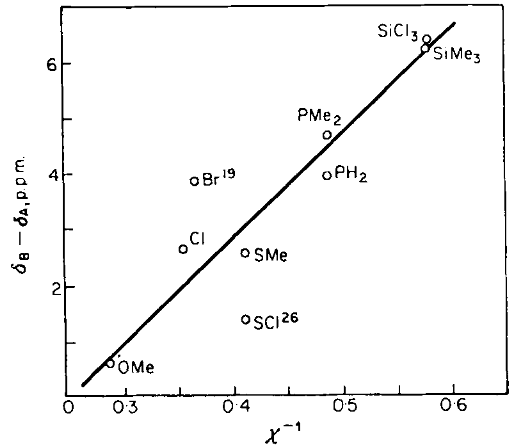


FIG. 2. Graph of $\delta_B - \delta_A$ of the CF_2 group against the reciprocal of the electronegativities of Q. (From Dyer and Lee.[7])

is described; the parameters are shown in (**7**) and were compared with those of C_2F_5OF (**8**) to substantiate the structure of (**7**).

The direct fluorination of steroidal olefins to give the *cis*-vicinal difluorides has been studied by Merritt and Stevens.[11] Fluorination of Δ^4-cholester-3-one gave the *cis*-4,5-difluoride and the ^{19}F spectrum showed resonances at 170·1 and 207·4ϕ*. The complex low-field signal was assigned to the fluorine at C_5, and the

$Me_2CF \cdot CH(OH) \cdot CO_2Me$

$152 \cdot 3\phi^*$

3

$J_{CF-CH} = 14.4$ c./sec.

$J_{CF-CH_3} = 21 \cdot 3$ c./sec.

$CH_3 \cdot CHF \cdot CH(OH) \cdot CO_2Et$

$184 \cdot 5\phi^*$

4

$J_{HF\ gem} = 47 \cdot 0$ c./sec.

$J_{CF-CH} = 16 \cdot 3$ c./sec.

$J_{CF-CH_3} = 23 \cdot 5$ c./sec.

$CH_2F \cdot C(CH_3)OH \cdot CO_2Me$

$224 \cdot 7\phi^*$

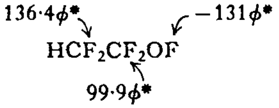
5

$J_{HF\ gem} = 47 \cdot 9$ c./sec.

$CH_2F \cdot CH(OH) \cdot CO_2Et$

$235 \cdot 9\phi^*$

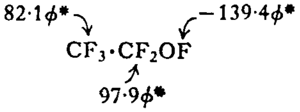
6



HCF_2CF_2OF

7

$J_{HF\ gem} = 56$ c./sec.



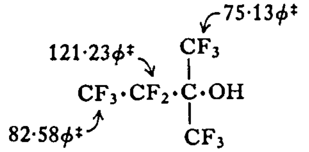
$CF_3 \cdot CF_2OF$

8

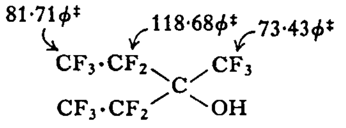
high-field signal, exhibiting a characteristic geminal HF coupling of 47 c./sec., resulted from the fluorine at C_4; the vicinal FF coupling was 12 c./sec. Fluorination of cholesteryl chloride give the 5,6-difluoride, the ^{19}F spectrum consisting of a broad band at $179 \cdot 7\phi^*$, from the fluorine at C_5, and a complex doublet at $194 \cdot 5\phi^*$, due to the fluorine at C_6 with geminal HF coupling of 40 c./sec. The cholesteryl acetate was converted to the 5α,6α-difluorocholestan-3β-ol acetate, with resonances at $178 \cdot 9\phi^*$ and $194\phi^*$, which in turn was converted to the 5α,6α-difluorocholestan-3-one, with resonance signals at 174·9 and $196\phi^*$; in each case the high-field signal was a doublet with geminal HF coupling of 46 c./sec.

The ^{19}F chemical shifts of a number of mono, di, tri, tetra and pentafluoroandrostan-2-ol and -3-one derivatives have been given by Boswell.[12]

The fluoride ion initiated reaction of fluorinated olefins with ketones and carbon dioxide have resulted in the formation of some very simple fluorinated alcohols. Thus tetrafluoroethylene with hexafluoroacetone, perfluorobutan-2-one and perfluoropentan-3-one afforded, respectively, the tertiary alcohols (**9–11**).[13] With carbon dioxide the same olefin afforded pentafluoropropionic acid, but with perfluoropropylene the perfluoroisobutyric acid (**12**) was obtained. Perfluoroisobutylene, treated with caesium fluoride in diglyme and then with carbon dioxide, affords bis(trifluoromethyl)acetic acid (**13**), but if hydrogen chloride is used in place of carbon dioxide, the tris(trifluoromethyl)methane (**14**) is obtained.[14] This may be a particularly useful method of obtaining these compounds having a tertiary hydrogen atom as it has been shown that direct fluorination of t-butyl derivatives always results in the insertion of a tertiary fluorine atom.[15]



9



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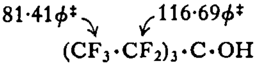
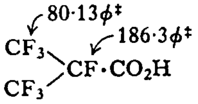
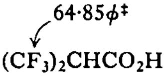

$\overset{81\cdot41\phi^{*}}{(CF_3\cdot CF_2)_3}\cdot\overset{116\cdot69\phi^{*}}{C}\cdot OH$

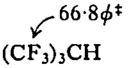
11



12

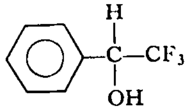

$\overset{64\cdot85\phi^{*}}{(CF_3)_2}CHCO_2H$

13


$\overset{66\cdot8\phi^{*}}{(CF_3)_3}CH$

14

Pirkle[16] has used 1-phenyl-2,2,2-trifluoroethanol (**15**) to demonstrate the general magnetic non-equivalence of enantiomorphs. In carbon tetrachloride solution only the vicinal CF–CH coupling of 6·7 c./sec. was observed, whereas in pyridine, both the vicinal coupling of 7·3 c./sec. and the coupling to the *ortho*-hydrogen atoms of the phenyl group were seen. In each case only one set of signals was observed at 4445 c./sec. (CCl_4) and 4387 c./sec. (Py) from internal CCl_3F. However, by using the optically active 1-phenylethylamine as solvent, two sets of doublets were observed, at 4374 and 4376 c./sec. from CCl_3F, which, as would be expected for the racemate, were of equal intensity. With racemic 1-phenylethylamine as solvent, only one set of signals were again observed. This author further demonstrated that by using a partially resolved sample of the trifluoroalcohol, the two sets of signals were no longer of equal intensity; the relative intensity of the signals depended upon whether the L- or D-1-phenylethylamine was used as solvent, enabling the assessment of the optional purity of the partially resolved material to be made. This was the first example reported of using the

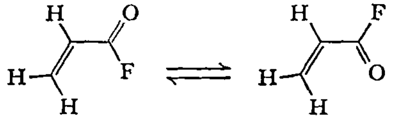


15

n.m.r. technique for the determination of optical purity of isomers. This is a sophisticated example of a selective solvent effect and in this instance the optically active solvent preferentially interacts with one of the enantiomers. This method may, however, only be applicable to fluorinated systems, since it relies upon the greater chemical-shift differences normally found for fluorine atoms (groups) in fairly similar environments.

Manatt[17] has used the greater sensitivity of chemical shift to chemical environment to classify the nature of alcohols by means of the ^{19}F chemical shifts of their trifluoroacetates. These are conveniently prepared *in situ* with trifluoroacetic anhydride, followed by removal of the excess anhydride and acid *in vacuo*. Although this is of interest, its application cannot, at the moment, be taken too rigorously, as chemical-shift differences are sometimes very small, e.g., the CF_3 resonance of *cis*- and *trans*-4-t-butylcyclohexanols differ by only 0·1 p.p.m. in dimethyl sulphoxide, but by only 0·04 p.p.m. in pentane. However, this method may be quite useful for determining isomeric purity, and could warrant further study. Indeed Manatt and his co-workers[18] have used this principle in the characterization of hydroxyl groups in polypropene oxides.

The values of the HF couplings of acryloyl fluoride are found to be temperature dependent;[19] the temperature dependence was explained in terms of rotational isomerism about C_1–C_2 (**16**, **17**). $^{3}J_{HF}$ varied from 8·10 c./sec. at +80°C to

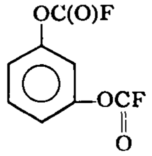


16 **17**

11·83 c./sec. at −95°C and $^{4}J_{HF\,trans}$ varied from 3·08 c./sec. at +80°C to 2·04 c./sec. at −95°C; $^{4}J_{HF\,cis}$ was essentially invariant. This data is consistent with the *s-trans* form (**16**) being the most stable; the ΔH value for the equilibrium was calculated to be 800 ± 250 cal./mole.

The ^{19}F chemical shifts of several fluorocarbonyl derivatives have been reported. The *m*- and *p*-phenylenebisfluoroformates (**18**, **19**) and 1,3,5-phenenyltrisfluoroformate (**20**) all have a ^{19}F chemical shift of 16·5ϕ^*.[20] Bis(monofluorocarbonyl)peroxide (**21**) exhibits a single, temperature-independent signal at 34·4ϕ^*. This peroxide on irradiation in the presence of sulphur dioxide gives the fluoroformylsulphuryl fluoride (**22**), which shows two resonance signals at −37·0ϕ^* (—SO_2F) and at 13·5ϕ^* (FC=O).[21]

The ^{19}F chemical shifts of the acid fluorides occur to lower field than the fluoroformates. In 3-fluoroxyperfluoropropionyl and 3-chloroperfluoropropionyl fluorides the acid fluoride shift is in the region of −25ϕ^*; the exact shifts are shown in structures (**23** and **24**).[22]



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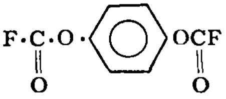

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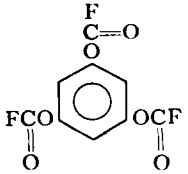

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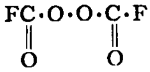
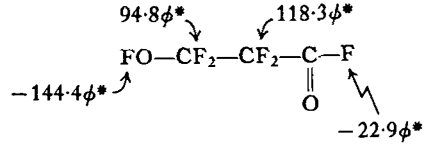


$FC(=O)\cdot O\cdot O\cdot C(=O)\cdot F$

21

$F\cdot C(=O)\cdot O\cdot SO_2F$

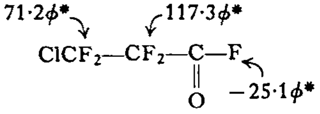
22



$FO—CF_2—CF_2—C(=O)—F$

$J_{FO\cdot CF_2} = 7\cdot 0$ c./sec.
$J_{CF_2\cdot CF_2} = 3\cdot 2$ c./sec.
$J_{FO\cdot C\cdot CF_2} = 3\cdot 5$ c./sec.
$J_{CF_2\cdot C(O)F} = 8\cdot 4$ c./sec.
$J_{CF_2\cdot C\cdot C(O)F} = 5\cdot 1$ c./sec.

23



$ClCF_2—CF_2—C(=O)—F$

$J_{ClCF_2\cdot CF_2} = 4\cdot 7$ c./sec.
$J_{CF_2\cdot C(O)F} = 8\cdot 0$ c./sec.
$J_{ClCF_2\cdot C\cdot C(O)F} = 6\cdot 5$ c./sec.

24

C. Fluoro-olefins and acetylenes

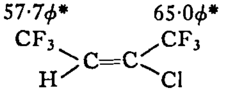
Fukuyama[22a] has analysed the spectra of mixed *cis*- and *trans*-1,2-difluoroethylene. Two sets of parameters were obtained for the A_2X_2 spin system, but the ambiguity of the assignments was removed by examining the samples in the gas phase and by making use of data from related compounds. The final parameters obtained were as shown in Table III.

TABLE III

The n.m.r. parameters of *cis*- and *trans*-1,2-difluoroethylene

	cis-Isomer	*trans*-Isomer
δ_H	3·753	2·777
δ_F	165·0φ*	186·25φ*
J_{HH}	−2·0 c./sec.	+9·5 c./sec.
J_{FF}	+18·7 c./sec.	−124·8 c./sec.
$J_{HF\,gem}$	+72·7 c./sec.	+74·3 c./sec.
$J_{HF\,vic}$	+20·4 c./sec.	+4·4 c./sec.

Several pairs of isomeric 1,1,1,4,4,4-hexafluorobut-2-enes have been studied, e.g., 2*H*,3-chloro-,[23] 2,3-bis(pentafluoroethyl)-,[24] 2,3-dichloro-[25] and 2,3-dicyano-.[26] The chemical shifts of the CF_3 groups are shown in structures (**25**–**32**); in each case the *trans* CF_3 groups are shifted to higher field.



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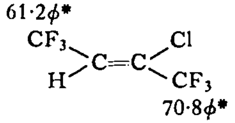

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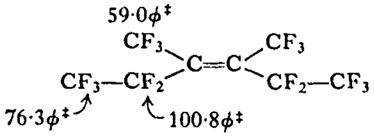

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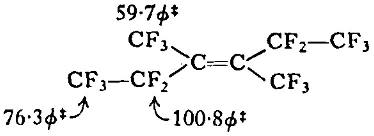

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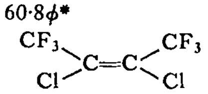

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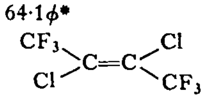

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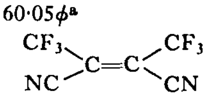

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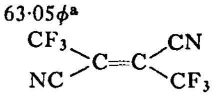
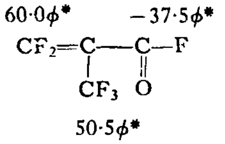


32

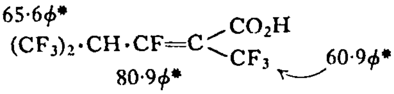
Many fluorinated derivatives of acrylic, butenoic and pentenoic acids have been prepared from bis(trifluoromethyl)keten.[27] The chemical shifts and coupling constants of some of these compounds are shown in structures (**33**–**39**).



$CF_2{=}C(CF_3)-C(=O)-F$

Pentafluoromethacryl fluoride

33

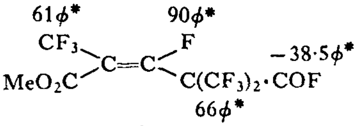


$J_{CF_3\cdot C=CF} = 31$ c./sec.

$J_{(CF_3)_2\cdot C\cdot CF} = 7{\cdot}0$ c./sec.

2,4,4-tris(trifluoromethyl)-3-fluoro-2-butenoic acid

34



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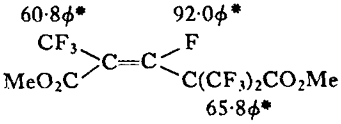

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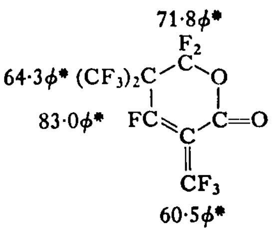

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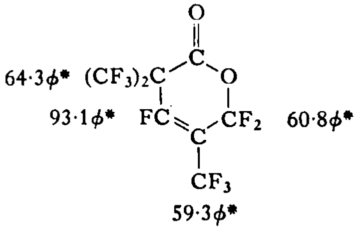

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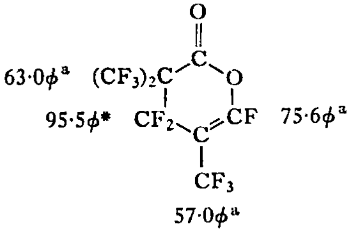

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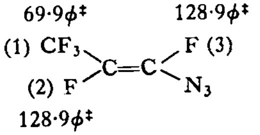
Perfluoropropenyl azide has been prepared[28] and, by the magnitude of the FF coupling, was shown to be the *trans* isomer; the shifts and coupling constants are shown in structure (**40**).



$|J_{12}| = 12$ c./sec.
$|J_{13}| = 21$ c./sec.
$|J_{23}| = 127$ c./sec.

40

Often observation of the coupling constants in fluoro-olefins is particularly useful. Barlow[29] has studied the effect of substituents on the value of the vicinal FF coupling in the 1,2-difluoroethylenes. It was possible to assign contributions due to each of the two substituents, X and Y to the *cis* and *trans* FF coupling. The substituent values are shown in Table IV.

The n.m.r. parameters of the three isomeric 1,4-dichlorotetrafluorobuta-1,3-dienes have been recorded,[30] and a trifluorobutadiene isolated from the products of the fluorination of n-butane, has been shown by n.m.r. to be the *cis*-1*H*, 1*H*, 4*H*-trifluorobuta-1,3-diene.[31] In all *cis–trans* and *trans–trans* dichloroisomers and in the trifluorobutadiene the *trans* FF coupling across the 2–3 bond was found to be in the range 34–36 c./sec.

The ^{19}F shifts and the "near" and "far" ^{13}C–F coupling constants, $J_{^{19}F-^{13}C}$ and $J_{^{19}FC-^{13}C}$ respectively, have been compared in a series of chloro- and bromo-fluoroethylenes.[32] The shifts and coupling constants are shown in Table V. A point of interest is the very large "far" ^{13}C–^{19}F coupling constant of 102·5 c./sec. The reason for this large coupling constant in the *trans* bromo-isomer is discussed.

TABLE IV

Substituent contributions to *cis* and *trans* FF coupling in 1,2-difluoroethylenes

	X or Y						
	H	I	Br	Cl	CF_3	$N(CF_3)_2$	F
$J_{cis\ FF}$	−7·9	12·5	17·5	18·8	1·6	18·1	39·0
$J_{trans\ FF}$	67·3	78·4	71·4	64·5	69·7	62·9	51·4

TABLE V

Chemical shifts and ^{13}C–^{19}F coupling constants of halogenofluoroethylenes

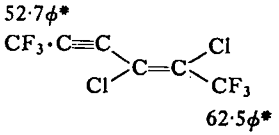
	ϕ^*	$J_{^{19}F-^{13}C}$	$J_{^{19}FC-^{13}C}$
$Br_2C{=}CFBr$	58·1	323·6	39·9
$Cl_2C{=}CFCl$	79·3	303·1	44·2
$Br_2C{=}CF_2$	79·2	289·9	43·1
$Cl_2C{=}CF_2$	88·5	288·9	43·7
cis-BrFC=CBrF	95·3	+324·7	−35·8
cis-ClFC=CClF	105·1	+299·3	−38·1
trans-BrFC=CBrF	113·0	+355·0	−102·5
trans-ClFC=CClF	119·6	+289·6	−53·9

The oxidative coupling of 3,3,3-trifluoropropyne afforded the 1,1,1,6,6,6-hexafluorohexa-2,4-diyne.[33] The ^{19}F chemical shifts of this diyne and the two isomeric (*cis* and *trans*) 2,3-dichloro-1,1,1,6,6,6-hexafluorohex-2-ene-4-ynes were given and are shown in structures (**41**–**43**).

52·0ϕ^*

$CF_3{\cdot}C{\equiv}C{-}C{\equiv}C{\cdot}CF_3$

41



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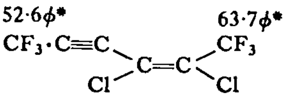

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D. Fluorinated cycloalkanes

By far the most comprehensive studies on fluorine n.m.r. spectroscopy have been concerned with the simple cyclic systems, both saturated and unsaturated.

In a study of fluorinated cyclohexanes, Peake and Thomas[34] have published details of HF and FF couplings of perfluoromethylcyclohexane and the two isomeric 1-trifluoromethyl-4*H*-decafluorocyclohexanes, all of which exist in a rigid framework since the molecules are not interconverting between two conformational forms. In summary the FF coupling constants were found to be—

$J_{\mathrm{FF}\,gem}$ 290–305 c./sec. $J_{\mathrm{F_1F_3}\,diax}$ ~27 c./sec.

$J_{\mathrm{F_1F_2}\,gauche}$ ~14 c./sec. $J_{\mathrm{F_1F_3}\,dieq}$ ~9 c./sec.

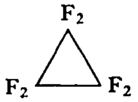
$J_{\mathrm{F_1F_2}\,trans}$ 0–3 c./sec. $J_{\mathrm{F_1F_3}\,ax-eq}$ ~1 c./sec.

The HF coupling constants were—

$J_{\mathrm{HF}\,gem}$ ~45 c./sec. $J_{\mathrm{H_1F_2}\,trans}$ ~17 c./sec.

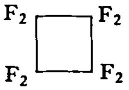
$J_{\mathrm{H_1F_2}\,gauche}$ ~6 c./sec. $J_{\mathrm{H_1F_3}}$ ~4 c./sec.

Gash and Bauer[35] have detailed the chemical-shift parameters of several fluorinated cycloalkane and cycloalkene derivatives. Although all the data on the saturated derivatives were previously available in the literature, these authors, however, draw attention to a correlation of chemical shift and ring strain. Although there is a marked effect in the case of the perfluorocyclopropane, the shift of the perfluorocyclobutane is not so different from that of the perfluorocyclopentane and cyclohexane (**44**–**47**). Their analogue may thus be an oversimplification, since the average chemical-shift values for the inverting molecules are used. The chemical shift of perfluorocyclo-octane is at substantially lower field than in (**47**), yet the bond angles in (**47**) and perfluorocyclo-octane would be expected to be of the same order of magnitude. In a preliminary note on the ^{19}F spectrum of perfluorocyclo-octane at −70°C, Peake *et al.*[36] report that a more complex spectrum than expected was obtained. In addition to the AB spectrum, ν_A 118·6ϕ^+, ν_B 121·3ϕ^+ and J_{AB}=297 c./sec., a single line at 120·8ϕ^+ was also observed. The authors point out that these observations are inconsistent with a



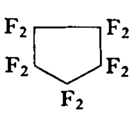
$151\phi^*$

44



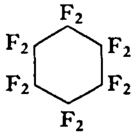
$134{\cdot}6\phi^*$

45



$132{\cdot}9\phi^*$

46

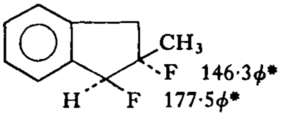


$133{\cdot}0\phi^*$

47

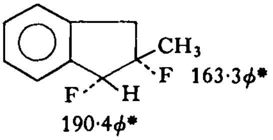
regular (D_{4d}) crown conformation for the molecule and suggest that the crown must be distorted into a D_2 form. It has been suggested that the hydrocarbon cyclo-octane also exists in a stable D_2 form and that pseudo rotation occurs as a "ripple" which causes the ring to pass through a less stable C_{2v} (extended crown) form. If the same situation occurred in perfluorocyclo-octane then half the nuclei would retain axial and the other half equatorial conformations; the authors thus suggest that inversion also occurs.

The addition of fluorine to indenes and acenaphthylenes gives the difluorobenzo- and naphthocyclopentane derivatives. In each case addition of fluorine



$J_{FF} \approx 0$ c./sec.
$J_{HF\ gem} = 56$ c./sec.
$J_{HF\ vic} = 15$ c./sec.
$J_{CH_3 \cdot F} = 22$ c./sec.
$J_{CH_3 \cdot C \cdot CF} = 4$ c./sec.

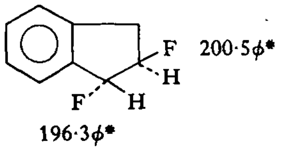
48



$J_{FF} = 8$ c./sec
$J_{HF\ gem} = 56$ c./sec.
$J_{HF\ vic} = 9$ c./sec.
$J_{CH_3 \cdot F} = 22$ c./sec.
$J_{CH_3 \cdot C \cdot CF} \approx 0$ c./sec.

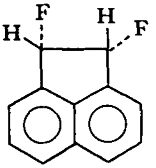
49

to the double bond is found to give both the *cis* and *trans* isomers (**48**, **49**).[37] The ^{19}F chemical shifts and coupling constants of the difluoroindane (**50**) are shown. The coupling constants of *cis*- and *trans*-1,2-difluoroacenaphthene (**51**, **52**), 1,2,2-trifluoroacenaphthene (**53**) and 1,2-difluoro-1-methylacenaphthene (**54**) are shown in Table VI. Dehydrofluorination of compounds (**51**) or (**52**) and



$J_{HF\ gem} = 56$ c./sec.
$J_{HF\ vic} = 16$ c./sec.
$J_{FF\ vic} = 4$ c./sec.

50



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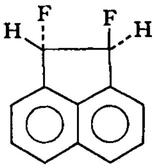

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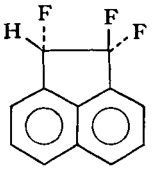

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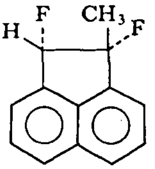


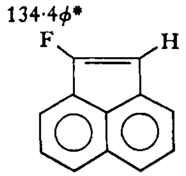
54

TABLE VI

Coupling constants (c./sec.) of fluorinated acenaphthenes

	Structure			
	(51)	**(52)**	**(53)**	**(54)**
$J_{\text{FF}\,cis}$	16·4	..	9·8	16·0
$J_{\text{FF}\,trans}$	..	0·1	1·2	..
$J_{\text{FF}\,gem}$	..	..	265·3	..
$J_{\text{HF}\,cis}$	..	19·4	12·8	..
$J_{\text{HF}\,trans}$	5·2	..	1·2	5
$J_{\text{HF}\,gem}$	54·6	52·2	53·9	54
$J_{\text{HH}\,cis}$	5·1	..	..	..
$J_{\text{HH}\,trans}$	..	0·7	..	..
$J_{\text{F—CH}_3}$	..	..	..	22

(**54**) afforded 1-fluoroacenaphthylene (**55**) and 1-fluoro-2-methylacenaphthylene (**56**), respectively; the shift of the olefinic fluorine atoms are shown on the formulae.



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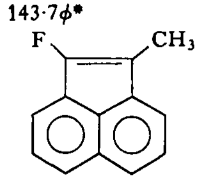
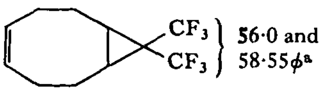


$J_{\text{CH}_3\cdot\text{F}} = 2{\cdot}8$ c./sec.

56

Bis(trifluoromethyl)diazirine reacts with olefins to afford the 1,1-bis(trifluoromethyl)cyclopropyl derivatives;[38] thus *cis,cis*-1,5-cyclo-octadiene affords compound (**57**) and *cis*- and *trans*-but-2-ene gives the two isomers (**58**) and (**59**), respectively. With cyclohexene two products are obtained (**60**, **61**).



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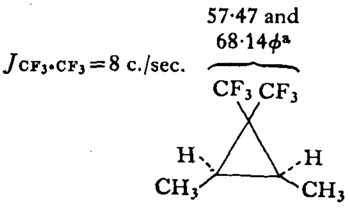

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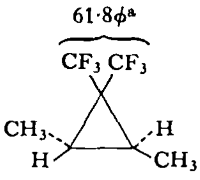

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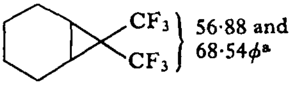

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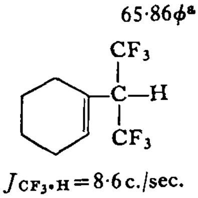

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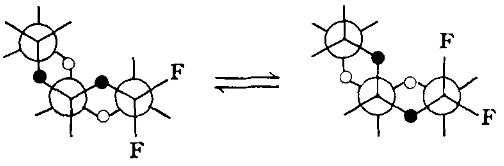
As has been previously mentioned, the larger chemical shifts experienced by the ^{19}F nucleus makes this nucleus a very convenient probe for investigating small differences in molecular environments; such a situation occurs in conformational analysis. This principle is amply demonstrated by Gerig and Roberts[39] in a study of the 2,2-difluorodecalin. The *trans* form is rigid and the ^{19}F spectrum is temperature invariant; on the other hand, the *cis* form undergoes inversion between the two double-chair forms (**62**) and (**63**). The geminal fluorine atoms

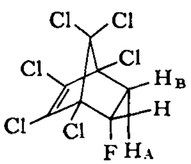


62 63

are magnetically non-equivalent and will give rise to AB spectra; the observation of the independent AB spectra of each form will depend upon the rate of interconversion. At −81°C, two distinct low-field AB doublets of the equatorial fluorines are observed, and the high-field signals of the axial fluorine atoms are considerably broadened. The rate constants of the interconversion were found by fitting the calculated spectra to those obtained experimentally. In the cases of the 1-methyl-, 3-methyl-, 6-methyl- and 6,9-dimethyl-2,2-difluoro-*cis*-decalins only, one AB spectrum was observed at each temperature studied. The application of ^{19}F spectra, of geminal difluoro-derivatives, for investigating conformational equilibrium has been fully exemplified in the 1965 Chemical Society Centenary Lecture by Professor J. D. Roberts.[40]

The conformation of perfluorocyclobutane has been re-investigated[41] to determine whether the four-membered ring is puckered (D_{2d}) or planar (D_{4h}). I.r. and Raman spectroscopy indicated that the ring was bent. The n.m.r. data was inconsistent with this, as only a single resonance signal was observed down to the freezing point of the solvent (−120°C, methylcyclohexane used as solvent); these observations are reconciled by the very low potential barrier for inversion of 1·8 kcal./mole.

The investigation of the more rigid bicyclic systems has been used to re-examine the variation of HF coupling constants with molecular geometry.[42] White[43] had earlier suggested that the vicinal HF couplings were linearly related to the dihedral angle. However, investigation of the rigid compounds (**64**–**69**) has demonstrated



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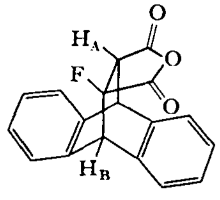

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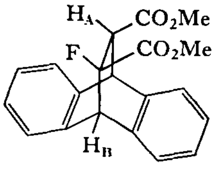

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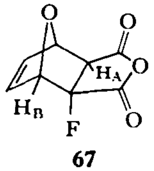

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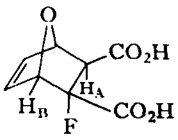

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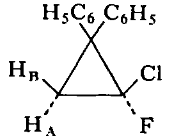


69

that the relationship of the vicinal HF coupling is very similar to that found for vicinal HH coupling and follows the relationship—

$$J_{\mathrm{HF}\,vic} = A + B\cos\Phi + C\cos 2\Phi$$

The coupling constants and the dihedral angles are shown in Table VII. The magnitude of the coupling constant is also dependent upon the bond angle, thus the increase in $J_{\mathrm{H_AF}\,vic}$ in compound (**66**) compared to the anhydride (**65**) is probably due to ring strain in the latter compound; a similar behaviour of $J_{\mathrm{H_AF}\,vic}$ is found between the anhydride (**67**) and the dicarboxylic acid (**68**).

TABLE VII

The vicinal ^{1}H–^{19}F coupling constants (c./sec.) in the conformationally rigid molecules (64–69)

	Approximate dihedral angles				
	0° (J_{AF})	60° (J_{BF})	90° (J_{BF})	120° (J_{BF})	132° (J_{BF})
(**64**)	24·7	. .	. .	12·2	. .
(**65**)	22·5	. .	. .	. .	. .
(**66**)	30·8	6·0	. .	. .	. .
(**67**)	10·55	3·8	2·3	. .	. .
(**68**)	19·8	. .	~2·0	. .	. .
(**69**)	+17·7	. .	. .	. .	+6·3

E. Fluorinated cycloalkenes

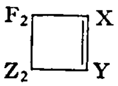
Gash and Bauer[35] have listed the ^{19}F chemical shifts of perfluorocyclobutene, pentene and hexene, together with those of some of their derivatives. There was some uncertainty in the precise assignment of the chemical shifts to the ring CF_2 groups in some of the derivatives. However by comparison with some work in our laboratory[44] on the 1-iodo- and 1-iodo-2-methoxyperfluorocyclopentenes and butenes this ambiguity has been removed. The chemical shifts are given in Tables VIII and IX.

The ^{19}F shifts of the CF_2 group of the 1,2-dichloro- and 1,2-dibromodifluorocyclopropenes, and of 1,1,2,2-tetrachlorodifluorocyclopropane have been determined and the ^{13}C–^{19}F coupling constants of these three compounds are 292 ± 3, 320 ± 5 and 313 c./sec., respectively.[45]

The ^{19}F n.m.r. spectra of two isomeric cyclobutenes, namely 3-chloro-1-chlorodifluoromethyl-3,4,4-trifluoro-2-trifluoromethylcyclobutene (**70**) and 3-chloro-3-chlorodifluoromethyl-1,4,4-trifluoro-2-trifluoromethylcyclobutene (**71**)

TABLE VIII

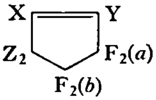
Chemical shifts of perfluorocyclobutenes



Substituents			Chemical shifts, ϕ^*				
X	Y	Z_2	X	Y	Z_2	F_2	Reference
F	F	F_2	130·4	130·4	120·3	120·3	35
I	F	F_2	..	104·52	118·7	116·8	44
I	OMe	F_2	..	..	117·18	113·67	44
F	OEt	F_2	143·0	..	116·9	119·6	35
OMe	Cl	$(OMe)_2$	..	..	..	116·8	35

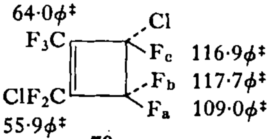
TABLE IX

Chemical shifts of perfluorocyclopentenes



Substituents			Chemical shifts, ϕ^*					
X	Y	Z_2	X	Y	Z_2	$F_2(a)$	$F_2(b)$	Reference
F	F	F_2	150·2	150·2	117·8	117·8	130·2	35
Cl	Cl	F_2	..	..	114·4	114·4	130·4	35
I	F	F_2	..	115·60	107·53	119·29	129·09	44
I	OMe	F_2	..	..	104·87	112·84	128·48	44
Cl	OMe	F_2	..	..	114·9	112·2	130·3	35
Cl	OEt	F_2	..	..	115·4	112·1	130·4	35
Cl	OPh	$(OPh)_2$	..	..	..	116·5	124·3	35

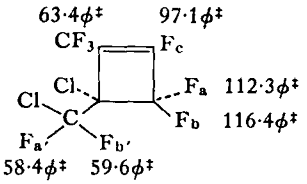
have been analysed.[46] The geminal FF coupling of the chlorodifluoromethyl group in (**71**) is 179 c./sec. compared with the geminal FF coupling of 200·3 c./sec. of the ring CF_2 group.



70

$|J_{\mathrm{CF_2Cl\cdot CF_3}}| = 6{\cdot}3$ c./sec.
$|J_{\mathrm{CF_2Cl\cdot F_c}}| = 2{\cdot}2$ c./sec.
$|J_{\mathrm{CF_2Cl\cdot F_a}}| = 2{\cdot}7$ c./sec.
$|J_{\mathrm{CF_2Cl\cdot F_b}}| = 2{\cdot}6$ c./sec.
$|J_{\mathrm{CF_3\cdot F_c}}| = 1{\cdot}9$ c./sec.

$|J_{\mathrm{CF_3\cdot F_a}}| = 2{\cdot}6$ c./sec.
$|J_{\mathrm{CF_3\cdot F_b}}| = 2{\cdot}6$ c./sec.
$|J_{\mathrm{F_aF_c}}| = 29{\cdot}1$ c./sec.
$|J_{\mathrm{F_bF_c}}| = 5{\cdot}0$ c./sec.
$|J_{\mathrm{F_aF_b}}| = 194{\cdot}5$ c./sec.

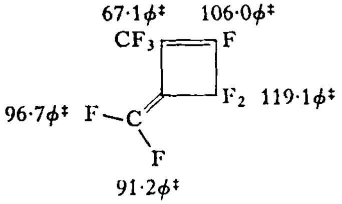


71

$|J_{\mathrm{F_{a'}F_{b'}}}| = 179$ c./sec.
$|J_{\mathrm{F_{a'}\cdot CF_3}}| = 4{\cdot}6$ c./sec.
$|J_{\mathrm{F_{b'}\cdot CF_3}}| = 2{\cdot}2$ c./sec.
$|J_{\mathrm{F_{a'}F_c}}| = 1{\cdot}4$ c./sec.
$|J_{\mathrm{F_{b'}F_c}}| = 1{\cdot}4$ c./sec.
$|J_{\mathrm{F_{a'}F_a}}| = 3{\cdot}4$ c./sec.
$|J_{\mathrm{F_{b'}F_a}}| = 3{\cdot}2$ c./sec.
$|J_{\mathrm{F_{a'}F_b}}| = 13{\cdot}3$ c./sec.
$|J_{\mathrm{F_{b'}F_b}}| = 18{\cdot}5$ c./sec.

$|J_{\mathrm{CF_3\cdot F_c}}| = 9{\cdot}5$ c./sec.
$|J_{\mathrm{CF_3\cdot F_a}}| = 2{\cdot}6$ c./sec.
$|J_{\mathrm{CF_3\cdot F_b}}| = 2{\cdot}8$ c./sec.
$|J_{\mathrm{F_aF_c}}| = 4{\cdot}1$ c./sec.
$|J_{\mathrm{F_bF_c}}| = 5{\cdot}3$ c./sec.
$|J_{\mathrm{F_{ab}}}| = 200{\cdot}3$ c./sec.

The n.m.r. parameters of two perfluoro(3-methylenecyclobutenes) have been given by Banks *et al.*[46, 47] One, the perfluoro(2-methyl-3-methylenecyclobutene)[46] (**72**) was obtained by isomerization of a dimer of tetrafluoroallene, and the second, perfluoro(1,2-dimethyl-3-methylenecyclobutene)[47] (**73**) was obtained from perfluoroallene and hexafluorobut-2-yne.



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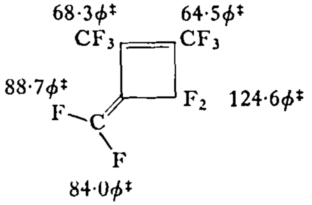
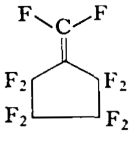


73

Photolysis of perfluorocyclohexene gave the perfluoro(methylenecyclopentane) (**74**), which, on treatment with sodium iodide in acetonitrile, gave hexafluoro-1-iodo-2-trifluoromethylcyclopentene (**75**); the shifts of both compounds were given, but no information on the coupling constants.[48]

In a paper[49] dealing with the reactions of perfluorocyclopentadiene (**76**) the ^{19}F shifts of perfluoro(tricyclo[5,2,1,0^{2,6}]deca-3,8-diene) (**77**), formed by thermal dimerization, and perfluoro(bicyclo[4,3,0]nona-2,4,7-triene) (**78**), formed by thermal breakdown of the dimer, are given. Data on 4-chloroheptafluorocyclopentene, an intermediate in the formation of the diene, are also given. In the tricyclodeca-3,8-diene the geminal FF couplings of the two CF_2 groups differ considerably, that of the bridgehead CF_2 being 180 c./sec., compared to that of the cyclopentene ring of 260 c./sec.; the geminal FF coupling of the triene (**78**) is 270 c./sec.



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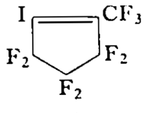

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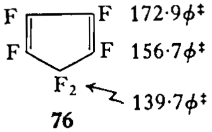

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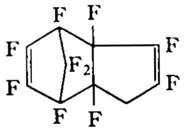

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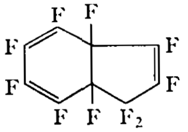


78

The reaction of 1,2-dichlorohexafluorocyclopentane and octafluorocyclohexene with sulphur trioxide and antimony pentachloride afforded mono and diketones;[50] hydrolysis of the monoketone afforded the hydroxy derivative. The ^{19}F shifts of these compounds are shown in Table X.

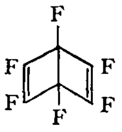
The photolysis of hexafluorobenzene vapours has been reported[51, 52] independently by two groups of workers, to give the hexafluorobicyclo[2,2,0]hexa-2,5-diene (**79**); the chemical shifts reported by these two groups of workers were

TABLE X

^{19}F chemical shifts of fluorinated cyclopentanones and cyclohexanones

Substituents		Chemical shifts, ϕ^*				
		Cyclopentanone		Cyclohexanone		
X	Z	F_2	Z	F_2	F_2'	Z
Cl	F_2	125·9	117·0	125·1	133·5	110·4
Cl	=O	124·0	. .	124·5	124·5	. .
OH	F_2	124·4	124·4	120·8	134·5	120·8

very similar, namely ~ 122ϕ for the olefinic fluorine and ~ 190·5ϕ for the tertiary fluorine. The hexa-2,5-diene with bromine gave[52] the 1,2,5,6-tetrabromohexafluorobicyclo[2,2,0]hexane (**80**). Haller[51] reported that the FF coupling in (**79**) was very similar to that previously reported[53] for (**81**).



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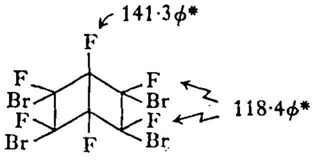

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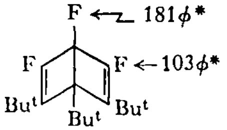
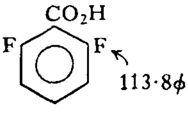


81

The FF couplings of 1,2,4-trichloroheptafluorocyclohexene[54] and of perfluorocyclohexa-1,3-diene, 1,2-dichlorohexafluoro-, 1-chloroheptafluoro-, 1-hydro-2-chlorohexafluoro- and octafluoro-cyclopentenes[55] have been considered in some detail.

F. Fluoroaromatics

The ^{19}F spectra of pentafluoroaniline, tetrafluorophenylenediamines and some nitro-derivatives of these compounds have been discussed,[56] and the shielding parameters of the amino- and nitro-groups determined. The chemical shifts of 2,6-difluorobenzoic acid (**82**) and several 1,4-disubstituted tetrafluorobenzenes (**83**–**85**), prepared via organo-lithium intermediates have also been given[57] as proof of identity of these compounds, especially in respect of the isomeric purity.



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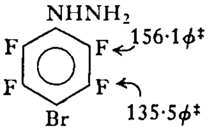

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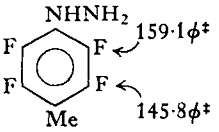

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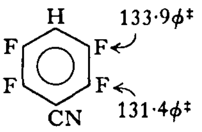
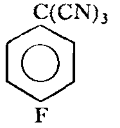


85

The ^{19}F chemical shifts of the *m*- and *p*-fluorobenzotricyanides (**86**, **87**) have been measured[58] in acetone-d_6 solution. By extrapolating the shift to infinite dilution, the resonance parameters of the tricyanomethyl —C(CN)$_3$ group have been calculated using Taft's relationships.[59]



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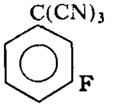

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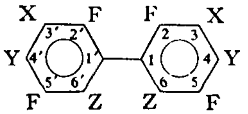
4,4′-Dihydrazino-octafluorobiphenyl has been used as an intermediate for the preparation of a range of tetrasubstituted hexafluoro- and hexasubstituted tetrafluorobiphenyls.[60] The ^{19}F chemical shifts of these compounds were recorded, but assignments were not given. The assignments shown in Table XI are based upon our own experience in this field.

TABLE XI

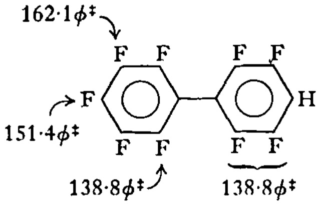
^{19}F chemical shifts of some tetra- and hexasubstituted biphenyls



Substituents				Chemical shifts, ϕ^*		
X	Y	Z	Solvent used	F_2 and F_2'	F_5 and F_5'	Z
CN	CN	F	Acetone	104·3	129·1	118·3
H	H	F	Acetone	118·2	145·1	136·7
H	H	OEt	Carbon tetrachloride	116·0	134·1	. .
H	H	OH	Acetone	118·2	142·5	. .
H	CO_2H	F	Acetone	115·5	131·8	138·9
H	CO_2Me	F	Acetone	116·4	133·0	140·7
Br	Br	F	Benzene	102·3	129·2	135·5
Br	CO_2H	F	Ethanol	106·3	132·0	140·6
CO_2H	CO_2H	F	Acetone	114·4	128·3	143·2
CO_2Me	CO_2Me	F	Acetone	114·1	127·3	142·3

Among the decomposition products of pentafluorophenylmagnesium bromide were found[61] 4*H*-nonafluorobiphenyl and 4*H*-pentafluoroterphenyl; the chemical shifts of these compounds are shown in structures (**88**) and (**89**).

The ^{19}F shifts of 4-nitrononafluorobiphenyl, 4′-nitroperfluoro-*m*-terphenyl, 4-trifluoromethylnonafluorobiphenyl, 3,4-bis(trifluoromethyl)perfluorobiphenyl and 4,′5′-bis(trifluoromethyl)perfluoro-*o*-terphenyl have been reported;[62] the shielding parameters of the nitro-, trifluoromethyl- and pentafluorophenyl-groups were also calculated.



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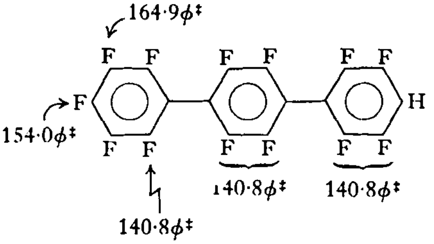
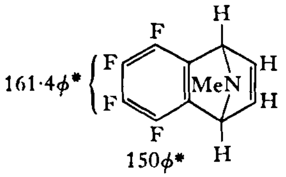


89

Some preliminary data on tetrafluorobenzyne adducts have been reported;[63, 64] one note dealt with the adducts from *N*-methylpyrrole (**90**) and durene (**91**),[63] and the second was concerned with the adduct from t-butylbenzene (**92**).[64] This



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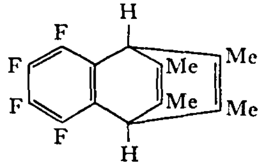

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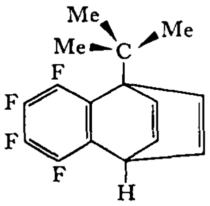

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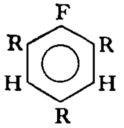
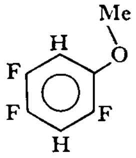
latter note was primarily concerned with the restricted rotation of the t-butyl group (see p. 8) and the long-range coupling of the methyl groups with the adjacent fluorine atom. The coupling at room temperature to two of the methyl groups is 2·9 c./sec., but at 180°C, at which temperature the methyl groups become equivalent, the HF coupling is 2·1 c./sec. It is suggested that this is evidence for "through-space" HF coupling.

Similar evidence for "through-space" HF coupling is found[65] in the investigation of the spectra of 2,4,6-trialkylfluorobenzenes of the type (**93**). It has also been suggested that the absence of OMe–F coupling in compounds of the type (**94**) is also evidence for "through-space" coupling since there is preferential orientation of the methoxy group away from the *ortho* fluorine atom;[66] this could cause



R=Et, Pr^i, Bu^t

93



94

confusion as often the multiplicity of the methoxy resonance signal is used to determine the position of substitution in fluoroaromatics.[67]

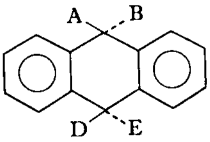
The effect of the nature of substituents upon the values of the *meta* FF coupling of fluorinated benzenes has received attention by two separate groups of workers.[68, 69]

The long-range coupling in α- and β-fluorosubstituted pentafluorostyrenes has been re-investigated[70] and, contrary to earlier reports,[71] coupling between the *para* fluorine and the α-fluorine was found to occur in every instance; only in one case was coupling observed between the *para* and β-fluorine atoms.

The ^{1}H and ^{19}F spectra of monofluorobenzene have been fully analysed[72] by treating the system as an AB_2C_2X spin system having C_{2v} symmetry. It was found that both the ^{1}H and ^{19}F shifts were solvent dependent and the ^{13}C–^{1}H and ^{13}C–^{19}F coupling constants were 160·0 ± 2·0 c./sec. and 265·5 ± 2·0 c./sec., respectively.

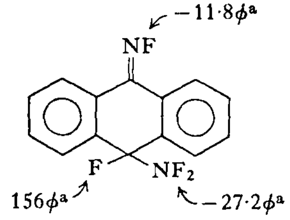
TABLE XII

^{19}F chemical shifts of 9,10-bis(difluoroamino)anthracenes



Substituents				Chemical shifts, ϕ^a				
A	B	D	E	A	B	D	E	
NF_2	H	NF_2	H	−52·6	..	−52·6	..	$J_{NF_2\text{–}H} \sim 30$ c./sec.
NF_2	H	H	NF_2	−38·3	..	..	−38·3	$J_{NF_2\text{–}H} \sim 30$ c./sec.
NF_2	Cl	NF_2	Cl	−41·7	..	−41·7	..	
NF_2	Cl	Cl	NF_2	−39·9	..	..	−39·9	
NF_2	F	NF_2	F	−25·6	150·4	−25·6	150·4	$J_{NF_2\text{–}F} \sim 7$ c./sec.
NF_2	F	F	NF_2	−26·4	131·1	131·1	−26·4	$J_{NF_2\text{–}F} \sim 16$ c./sec.

Reaction of 9,10-dibromoanthracene with tetrafluorohydrazine gives rise to a series of 9,10-difluoroamino-derivatives;[73] the shifts of these compounds are shown in Table XII. The shifts of three other derivatives, 9-fluoro-9-(difluoramino)-10-(fluorimino)- (**95**), 9,10-bis(fluorimino)- (**96**) and 9,10-difluoro- (**97**) anthracenes were also given in the paper; the shifts are as shown on the structural formulae.



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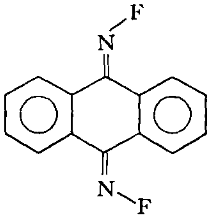
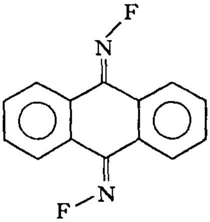


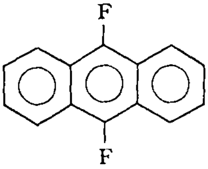
$-12{\cdot}4\phi^a$
syn-isomer

96a



$-12{\cdot}2\phi^a$
anti-isomer

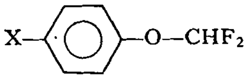
96b



$137{\cdot}0\phi^a$

97

Following the earlier work of Taft,[59] many workers have attempted to use the ^{19}F shift values of fluoroaromatics as a measure of electronic interaction of ring substituents. This approach appears to have had some success in the study of the bonding of transition-metal complexes (see p. 287). It has been shown[74] that the shift of the 4-fluorine and the value of the F_2F_4 (F_6F_4) coupling can be related to the π-electron donating or withdrawing properties of the substituent group X in pentafluoroaromatics; this is mentioned again in detail later. Another approach to the study of the electronic effects of substituents in aromatic systems has been the realization[75] of the influence on the ^{19}F shift, of the difluoromethoxy group, in *p*-substituted aryl difluoromethyl ethers of the form (**98**). There was a range of ^{19}F shifts for the —$OCHF_2$ group of some 150 c./sec. compared to a shift difference



98

of only 20 c./sec. for the ^1H signals, though the direction of the shifts was in the opposite sense.

G. Fluorocarbonium ions

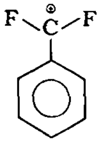
The study of ^{19}F spectra has permitted the first examples of stable fluorocarbonium ions to be detected.[76] Solutions of difluorochloromethylbenzene and diphenyldifluoromethane in antimony pentafluoride–liquid sulphur dioxide at −75°C afforded the ions (**99**) and (**100**). In each case the fluorine atom(s) were considerably deshielded compared to the parent compounds (see Table XIII).

TABLE XIII

Deshielding of ^{19}F resonance signals on the formation of the carbonium ions

		Chemical shifts, ϕ^*	
		Parent compound	Carbonium ion
Difluorochloromethylbenzene	($C_6H_5CCl_2F$)	49·4	−12·0
Diphenyldifluoromethane	($(C_6H_5)_2CF_2$)	88·5	−11·5

It is suggested that the deshielding results from the positive charge being essentially confined to the fluorine atom (e.g., as in **101**). The ^{19}F spectra of the ions are shown in the paper.



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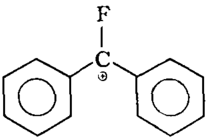

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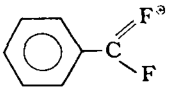

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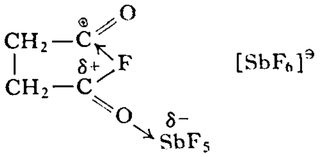


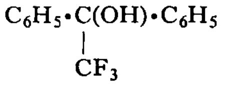
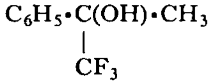
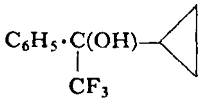
102

The ^{19}F spectra of solutions of trifluoromethylcarbinols, with one or more phenyl groups, recorded in a solvent mixture of fluorosulphonic acid, antimony pentafluoride and sulphur dioxide have been interpreted in terms of the formation of carbonium ions.[77] It was found that if two trifluoromethyl groups or phenyl groups were absent, then the alcohol was simply protonated in the solvent. The $\Delta\phi$ values, that is the difference in the ^{19}F shift of the trifluoromethyl group(s) of the parent alcohol in liquid sulphur dioxide and in the mixed solvent, are shown in Table XIV.

The ^{19}F spectra of the crystalline 1:2 complexes of dicarboxylic acid fluorides with antimony pentafluoride have been measured in liquid sulphur dioxide solution over the temperature range of $-30°$ to $-60°C$.[78] The glutaryl, adipyl, pimelyl, suberyl, azelayl and terephthaloyl complexes all showed a resonance signal due to the SbF_6^- ion at about +100 p.p.m. from external CCl_3F. The succinyl fluoride–antimony pentafluoride complex at $-60°C$ in liquid sulphur dioxide showed a triplet at $-35{\cdot}5$ p.p.m. from external CCl_3F, resulting from $F–CH_2$ coupling with a coupling constant of 5 c./sec., the antimony fluoride resonance also occurring at about +100 p.p.m. It was suggested that the structure of the succinyl fluoride complex is as shown in **(102)**.

TABLE XIV

^{19}F shifts to low field, given as $\Delta\phi$ values, of alcohols dissolved in $FSO_3H/SbF_5/SO_2$ solvent mixture

Alcohol	$\Delta\phi^+$	Inference
 $C_6H_5\cdot\underset{\underset{CF_3}{\vert}}{C}(OH)\cdot C_6H_5$	$-7{\cdot}6$	Formation of carbonium ion
 $C_6H_5\cdot\underset{\underset{CF_3}{\vert}}{C}(OH)\cdot CH_3$	$-24{\cdot}8$	
	$-9{\cdot}1$	
$C_6H_5C(OH)(CF_3)_2$	$-1{\cdot}6$	Protonation only

H. Calculation of ^{19}F chemical shifts

There has been considerable interest recently in the theoretical interpretation and prediction of ^{19}F chemical shifts. Many of the various approaches used have not been wholly satisfactory: however with the growth of the chemistry of fluorocarbons there can be no doubt that more vigorous efforts will be made in this direction.

Feeney *et al.*[79] have used an electric-field theory to calculate the ^{19}F shifts of alkanes of the type CF_3CXYZ. The chemical shift δ is given by—

$$\delta = \delta\,(\text{electronic}) + \delta\,(\text{electric})$$

and the contribution from the electric field is given by—

$$\delta\,(\text{electric}) = -A\Delta E_Z - B(\Delta E^2 + \Delta\langle E^2\rangle)$$

where E is the electric field at fluorine nucleus created by dipoles at centre of polar bonds in the molecule, E_Z is the component of this field acting along bond direction and $\langle E^2\rangle$ is the time-averaged square of electric fields produced at nucleus by fluctuating dipoles in the bonds, which is given by—

$$\langle E^2\rangle = \sum_i 3P_i I_i/r_i^6$$

where P_i is the polarizability of the electron group, I_i is the first ionization potential and r_i is the distance of fluorine atom from the C—X electron group.

A and B are constants that had the approximate values of $A \sim -10 \times 10^{-12}$ e.s.u. and $B \sim -(15\text{–}45) \times 10^{-18}$ e.s.u.

Hruska *et al.*[80] found an empirical relationship between the shifts of the *ortho*-fluorine atoms in pentafluorobenzene derivatives C_6F_5X, and a quantity Q which was defined by—

$$Q = P/Ir^3$$

where P and I are as above, but r is the C—X bond length.

Both approaches have been used by Feeney *et al.*[79] who assumed that the rotamers were freely interconverting and thus $\langle E^2\rangle$ is the weighted mean of the values for each rotamer. The correlation of $\langle E^2\rangle$ and Q with the shift of the CF_3 group in ϕ values are shown in Figs. 3 and 4, in which it is apparent that the correlation is dependent upon the degree of substitution by hydrogen. On this basis the shift of hexafluoroethane was predicted to be 93·5ϕ (from the $\langle E^2\rangle$ relationship) and 92·5ϕ (from the Q relationship).

The electric-field theory has been used[79] to calculate the ^{19}F chemical shifts of fluorinated cyclobutane derivatives; the values agreed well with those obtained experimentally by other workers. It was initially assumed that the cyclobutane ring was planar, but in the appendix the problem was reconsidered with a dihedral angle of 22° for the carbon skeleton. In this case the agreement was not so satisfactory as that for the planar model. This was thought to be due to errors in calculating the relative conformer populations.

Feeney *et al.* have used the electric-field theory to calculate the chemical shifts

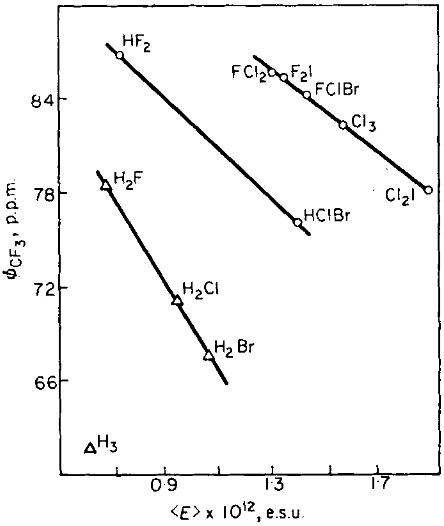


FIG. 3. Correlation of $\langle E^2 \rangle$ with fluorine chemical shifts of CF_3CXYZ-type ethanes. The points are labelled with the XYZ atoms concerned. (From Feeney *et al.*[79])

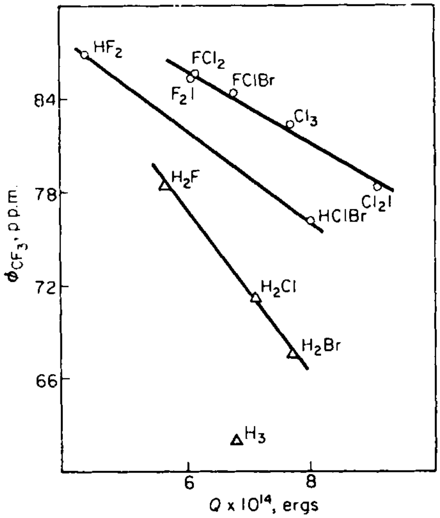


FIG. 4. Correlation of Q with fluorine chemical shifts of CF_3CXYZ-type ethanes. The points are labelled with the XYZ atoms concerned. (From Feeney *et al.*[79])

in fluorinated cyclopentenes,[81] interconverting cyclohexenes[82] and of 1,2,4-trichloroheptafluorocyclohexene.[83] The chemical shift between a fluorine atom in a substituted cyclopentene and the analogous atom in perfluorocyclopentene is given by—

$$\Delta\delta = -A\Delta E_Z - B(\Delta E^2 + \Delta\langle E^2\rangle)$$

The calculations for the 1-chloroheptafluorocyclopentene were carried out in full, but since the values of E_Z and $\langle E^2\rangle$ were found to be so small in this case, they were ignored in subsequent calculations. With two exceptions, good agreement was found between the calculated and experimentally determined shift values. The two exceptions were the 1-chloroheptafluorocyclopentene and the 1-chloro-2*H*-hexafluorocyclopentene in which the discrepancy was as much as 15 p.p.m. The deviation in the case of the olefinic fluorine arose because no allowance was made for π-electron contribution; the agreement found for the chemical-shift values of fluorine atoms attached to saturated carbon atoms supports the implication that there is no π-electron interaction in a saturated $>CF_2$ group. In the monohydro compound the deviation might have been expected since in the case of substituted 1,1,1-trifluoroethanes the value of $\langle E^2\rangle$ was dependent upon the number of hydrogens in the molecule $F_3C\cdot CXYZ$. The authors suggest that a modification of the above equation could include a new factor that would permit the superimposition of the halogen and the hydrogen correlations!

Attempts to calculate the chemical shifts of fluorobenzenes has promoted some interest. Several attempts have been made to correlate the ^{19}F chemical shifts of fluorinated benzenes with the π-electron charge densities and bond orders, and although the predicted values for the *m*- and *p*-fluorines are good, considerable deviations are found for the *o*-fluorine atoms. The large deviations found in the *o*-fluorine shifts (the "*ortho* effect") of halogenopentafluorobenzenes have been re-investigated,[84] and the effect was satisfactorily explained in terms of intramolecular electric-field contributions. However, this problem has been re-examined again by Caldow,[85] and this work would seem to have much to commend it for the organic chemist who is interested in predicting chemical-shift values. The "*ortho* effect" is now believed to arise from a Van der Waals' shift contribution; this approach has a further advantage in that the Van der Waals' shift is dependent upon the molecular geometry and thus could be a means of investigating steric effects arising from molecular overcrowding.

Emsley and Phillips[86] have studied the effect of solvents on fluorine chemical shifts and concluded that the internal reference compound used for the measurement of the shifts should be of the same chemical type and similar in size and shape to the molecules being studied. The solvent variation of the chemical shifts found in the polar molecules are discussed in terms of interaction between the solute molecules and the surrounding solvent medium.

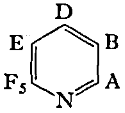
II. HETEROCYCLIC COMPOUNDS

A. Nitrogen heterocyclics

The ^{19}F chemical shifts of several fluorinated pyridine derivatives have been recorded.[87, 88] The shifts of these derivatives, all measured in acetone solution, are shown in Table XV. Investigation of the effects upon the ^{19}F chemical shifts on substituting fluorine for amino- and methoxy-groups showed that the effect was not strictly addictive, especially when nitro-groups were also present. However, because of the very large differences in the chemical shifts of the α- and β-fluorine atoms, approximately 70 p.p.m., the calculated values of the shifts for different isomers were sufficiently different to permit the ^{19}F spectra to be used for determining the position of substitution in the ring.[87]

TABLE XV

^{19}F shifts of some derivatives of perfluoropyridine

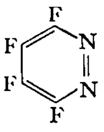


Substituent groups				Chemical shifts, ϕ^* or ϕ^+ values					
A	B	D	E	A	B	D	E	F_5	Units
F	F	F	F	87·8	161·2	133·4	161·2	87·8	ϕ^*
F	F	NH_2	F	94·7	164·6	..	164·6	94·7	ϕ^+
F	NH_2	NH_2	F	94·1	..	..	169·2	104·1	ϕ^+
NH_2	F	NH_2	F	..	164·8	..	175·9	97·1	ϕ^+
F	F	OMe	F	92·9	161·7	..	161·7	92·9	ϕ^+
OMe	F	F	F	..	164·5	140·9	171·9	91·4	ϕ^+
OMe	F	NH_2	F	..	165·3	..	171·16	97·1	ϕ^+
F	F	NO_2	F	85·4	146·3	..	146·3	85·4	ϕ^+
NH_2	F	NO_2	F	..	150·2	..	165·6	87·6	ϕ^+
F	NH_2	NO_2	F	80·1	..	..	152·7	108·4	ϕ^+
MeO	F	NO_2	F	..	147·9	..	158·7	87·4	ϕ^+
F	MeO	NO_2	F	78·1	..	..	150·5	88·8	ϕ^+
OMe	CO_2H	CO_2H	F	..	..	..	154·8	82·9	ϕ^*
F	CO_2H	F	F	65·8	..	112·4	167·0	80·9	ϕ^*
F	F	CO_2H	F	89·2	140·3	..	140·3	89·2	ϕ^*
F	CO_2H	CO_2H	F	65·5	..	..	144·4	79·1	ϕ^*

The ^{19}F chemical shifts of both perfluoroquinoline and isoquinoline, and a number of the substituted compounds, have been reported by these same authors.[88] Large *peri* FF couplings have been detected in these compounds, for example in perfluoroisoquinolines the *peri* 1–8 coupling is in the range of 60–65 c./sec. and the *peri* 4–5 coupling is about 50 c./sec. In the perfluoroquinolines the *peri* 4–5 coupling is found to be in the range of 44–50 c./sec. The recognition of these large *peri* couplings assists in identifying the position in which substitution has occurred.

The temperature dependence of the ^{19}F spectra of perfluoro-*N*-fluoropiperidine, its 2,3- and 4-trifluoromethyl derivatives and of perfluoro-*N*-fluoromorpholine have been investigated.[89] The spectra of perfluoro-*N*-fluoropiperidine over a range of temperatures were in complete accord with some earlier work[90] on this compound recorded at a lower frequency. However, in the more recent work it is stated that the equatorial fluorine atoms are more highly shielded; this assignment is contrary to the earlier work,[90] but is consistent with the assignments made in perfluorocyclohexanes.[91] While the spectra of both the perfluoro-*N*-fluoropiperidine and morpholine are temperature dependent, those of the trifluoromethyl-substituted piperidines were invariant over the temperature range of $-90°$ to $100°C$. There is also some considerable variation in the geminal FF coupling constants, where the value for the α-CF_2 group to the nitrogen are considerably smaller (185–199 c./sec.) than the β- or γ-CF_2 groups, namely 282–293 c./sec.; these latter values are similar to the geminal FF coupling of perfluorocyclohexanes, 280–290 c./sec.[34]

The ^{19}F chemical shifts of perfluoropyridazine (perfluoro-1,2-diazine) (**103**) and the 4-amino- and 4-methoxy-derivatives (**104**), obtained by nucleophilic substitution of (**103**) by ammonia and methoxide ion, respectively, have been reported[92] and are shown in Table XVI.



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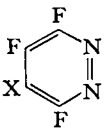
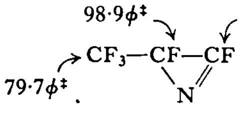


X = OMe or NH_2

104

Several simple azirine derivatives have been prepared from perfluoropropenyl azide;[28] the shifts recorded are as shown (**105–107**).



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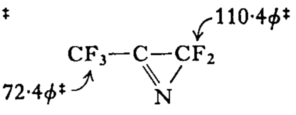

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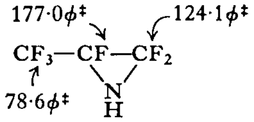

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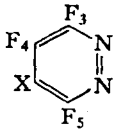
TABLE XVI

^{19}F chemical shifts of fluoro-1,2-diazines

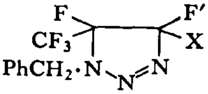


Nature of X	Chemical shifts, ϕ^+ F$_3$	F$_4$	X	F$_5$
F	83·3	144·9	144·9	83·3
—NH$_2$	92·1	154·9	. .	102·8
—OMe	89·5	149·7	. .	97·4

The reaction of benzyl azide with fluoro-olefins yields the 1-benzyl-substituted triazolines (**108**, **109**).[93] Octafluorobut-2-ene and excess of benzyl azide gave the 1-benzyl-4,5-bis(trifluoromethyl)-1,2,3-triazole (**110**) and treatment of (**108**) with tetrakis(dimethylamino)ethylene gave 1-benzyl-4-fluoro-5-trifluoromethyl-1,2,3-triazole (**111**). The chemical shifts of these compounds are shown in Tables XVII and XVIII. The triazole (**111**), on heating, afforded *N*-benzyl-2,3,3-trifluoro-2-trifluoromethylaziridine (**112**); the shifts of this compound and the isomeric *cis*- and *trans*-2,3-difluoro-2,3-bis(trifluoromethyl)aziridines are

TABLE XVII

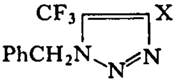
^{19}F chemical shifts of 1-benzylfluoro-1,2,3-triazolines



X	Chemical shifts, ϕ^* CF$_3$	F	F'	X
F	75·0	158·3	93·0	111·6
CF$_3$	75·0	153·0	153·0	72·0

TABLE XVIII

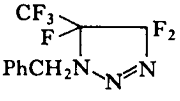
^{19}F chemical shifts of 1-benzylfluoro-1,2,3-triazoles



Substituent	Chemical shifts, ϕ^*	
X	CF_3	X
F	60·0	142·0
CF_3	59·0	55·9

shown in Table XIX. The ^{19}F shifts of a series of haloalkyldihydrotriazines are shown in Table XX.[94]

An interesting application of ^{19}F chemical shifts is in the differentiation of the α- and β-anomers of 2′-deoxy-5-(trifluoromethyl)uridines (**113**, **114**); the shifts



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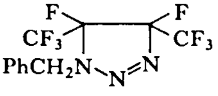

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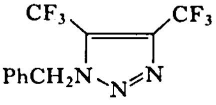

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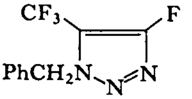

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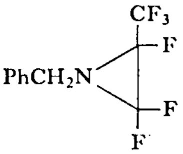

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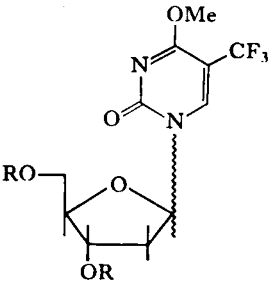

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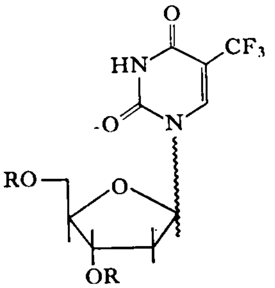

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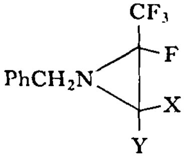
TABLE XIX

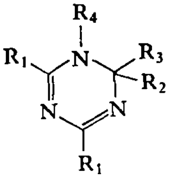
^{19}F chemical shifts of *N*-benzyl-2,3-fluoro-2-trifluoromethylaziridines



Substituents		Chemical shifts, ϕ*			
X	Y	CF_3	F	X	Y
F	F	75·9	184·9	116·6	116·6
F	CF_3	73·0	163·6	163·6	73·0
CF_3	F	75·1	177·4	75·1	177·4

TABLE XX

^{19}F chemical shifts of haloalkyldihydrotriazines



Substituents				Chemical shifts, ϕ*	
R_1	R_2	R_3	R_4	R_1	R_2
CF_3	CF_3	C_6H_5	H	73·4	80·7
$CClF_2$	$CClF_2$	C_6H_5	H	63·4	67·8
$CClF_2$	$CClF_2$	3,4-$Cl_2C_6H_3$—	H	63·4	68·1
CClF	CClF	4-ClC_6H_4—	H	62·2	66·3

are shown in Table XXI and it will be observed that the trifluoromethyl group of the α-anomer is always less shielded.[95]

In monofluorotriphosphonitrilic pentachloride (**115**) the fluorine atom couples to all three phosphorus atoms, $J_{P_AF} = 1012$ c./sec. and $J_{P_BF} = 11$ c./sec.[96]

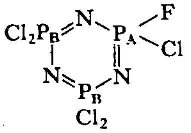
TABLE XXI

CF_3 chemical shifts of 2′-deoxy-5-(trifluoromethyl)uridines

	CF$_3$ shifts, ϕ^*	
	β-Anomer	α-Anomer
(113), $R = p\text{-}CH_3C_6H_4CO\cdot$	63·2	62·4
(114), $R = p\text{-}CH_3C_6H_4CO\cdot$	63·2	62·8
(114), $R = p\text{-}NO_2C_6H_4CO\cdot$	64·0	63·5
(114), $R = H$	64·6	64·0

B. Oxygen heterocyclics

The n.m.r. parameters of the unstable tetrafluorofuran (**116**) have been given,[97] and it is of some interest that the coupling across the oxygen atom, i.e., $J_{F_2F_5}$ is larger (20 c./sec.) than the vicinal *cis* coupling $J_{F_2F_3}$ of 15·5 c./sec. The shifts of perfluoro-1,2-dioxolane and perfluoroethylene oxide are shown in structures (**117**) and (**118**).[22]



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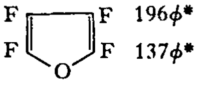

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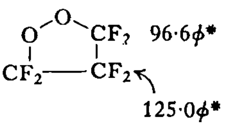

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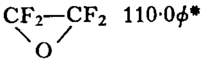

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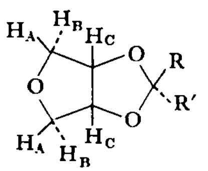
The ^{19}F spectrum of the reaction product of 3,4-dihydroxytetrahydrofuran and trifluoroacetic anhydride has revealed the existence of a stable acidic *ortho* ester.[98] The ^{19}F spectrum consisted of three signals at 85·29, 84·43 and 74·80ϕ^*; the first two signals were due to the two forms ($R = CF_3$, $R' = OH$ and $R = OH$, $R' = CF_3$)



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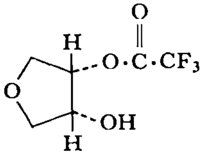


120

of the *ortho* ester (**119**) and the low-field signal was assigned to the open-chain form (**120**). These results were interpreted in terms of an equilibrium between the two cyclic and the open-chain forms in solution.

III. OTHER FLUORINE COMPOUNDS

A. Organometallics

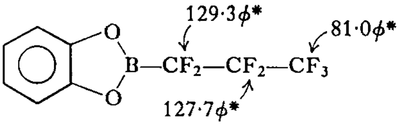
In order to rationalize the presentation of the data in this and the subsequent Section the derivatives of the elements will be dealt with in their periodic groups. Naturally the definition of organometallics is always difficult; in order to clarify the presentation and minimize the overlap, the derivatives of: magnesium; boron and aluminium; silicon and germanium; phosphorus, arsenic and antimony; and finally derivatives of the Group VII and VIII metals will be treated as separate sub-sections.

1. *Group II: magnesium*

The ^{19}F spectra of some pentafluorophenyl Grignards have been investigated[99] in order to determine the nature of these reagents in solution. The diethyl ether solution of bis(pentafluorophenyl)magnesium showed a single sharp triplet due to the 4-fluorine atom. The ethereal solution of pentafluorophenylmagnesium bromide at 22°C showed two overlapping triplets of nearly equal intensity from the 4-fluorine atom. On heating, the signals broaden and merge, and finally at 95°C a single sharp triplet is obtained; this has been interpreted in terms of rapid exchange between two molecular species. The addition of bis(pentafluorophenyl)-magnesium to the pentafluorophenylmagnesium bromide causes an enhancement of the high-field triplet and therefore this was assigned to the bis(pentafluorophenyl)magnesium, or more probably the complex $(C_6F_5)_2Mg \cdot MgBr_2$, whereas the low-field triplet is due to the pentafluorophenylmagnesium bromide. Similar observations were made on the pentafluorophenylmagnesium iodide, although in this case the lower field triplet was more intense and considerably sharper.

2. *Group III: boron and aluminium*

A short note has given some ^{19}F n.m.r. data on two perfluoropropyl derivatives of boron.[100] The two compounds investigated, namely 2-heptafluoropropylbenzo-1,3-dioxa-2-borole (**121**) and bis(dimethylamino)heptafluoropropylboron (**122**), illustrate the advantage of using fluorinated derivatives in which changes in chemical shifts are far greater than in the hydrocarbon analogues; there is a 48 p.p.m. difference in the shift of the α-fluoromethylene group of these two compounds. The spectra additionally illustrate the general phenomenon of very small vicinal FF coupling (see p. 244); the signal of the β-CF_2 group of the borole (**121**) shows no coupling to either the α-CF_2 or γ-CF_3 groups.



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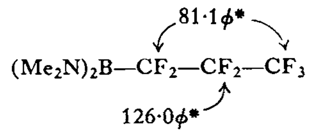

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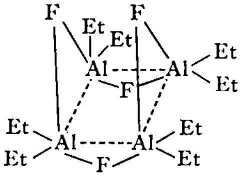

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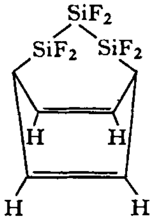
Diethylaluminium fluoride, obtained by reaction of the chloride and sodium fluoride in xylene, has been examined[101] as a 25% solution in cyclohexane at 25°C and 0°C. At both temperatures, the ^{19}F spectrum consisted of a singlet at 46·5 p.p.m. to high field of external fluorobenzene. Absence of line broadening at the lower temperature was taken to indicate that all the fluorine atoms were equivalent and it was suggested that the fluoride existed as a tetramer (**123**).

3. *Group IV: silicon and germanium*

The reaction of hexafluorobenzene with silicon difluoride gave pentafluorophenylsilicon trifluoride ($C_6F_5SiF_3$).[102] The fluorine atoms of the trifluorosilyl group couple to the two *ortho* fluorine atoms of the pentafluorophenyl groups with a coupling constant of 10·3 c./sec. Although the authors state that the fluorine of the SiF_3 group to *para* F coupling is 250 c./sec., the description of the spectrum given is not consistent with this observation. The reaction of silicon difluoride with benzene, however, affords the 2,2,3,3,4,4-hexafluoro-2,3,4-trisilabicyclo-[3,2,2]nona-6,8-diene (**124**) where the two fluorine resonances, at 130ϕ^* and 134ϕ^*, are in the ratio of 1:2.

Ethylene and silicon difluoride afford the two heterocyclic four- and six-membered compounds (**125**, **126**).[103] The ^{19}F shifts and the ^{29}Si–^{19}F coupling constants are as shown. In the four-membered ring the ^{19}F signal was a simple quintet, J_{HF} of 4·4 c./sec., but in the six-membered ring the ^{19}F signal was broad and unresolved.

1,1,2,2-Tetrafluoroethylsilane forms a pentaco-ordinate complex with trimethylamine (**127**)[104] and represents a new class of silicon complexes. The trigonal bipyramidal structure was confirmed by the equivalence of the three silyl hydrogen atoms. The chemical shifts and coupling constants of a 20% solution of the 1:1 complex in the 1,1,2,2-tetrafluoroethylsilane are intermediate between those of the complex and the parent compound (see Table XXII); this indicates that exchange is occurring in the presence of excess silane. The shift of



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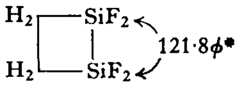
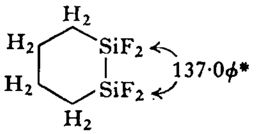


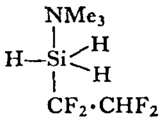
$J_{^{29}SiF} = 488$ c./sec.

125



$J_{^{29}SiF} = 380$ c./sec.

126



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the α-CF_2 resonance to high field on complex formation is explained in terms of the electron donation from the nitrogen to the silicon atom.

TABLE XXII

^{19}F chemical shifts and coupling constants of the trimethylamine complex of 1,1,2,2-tetrafluoroethylsilane (127)

	Parent silane $F_2HC{\cdot}CF_2SiH_3$	1:1 complex (**127**)	20% complex dissolved in silane
Chemical shift α-CF_2	122·5$\phi^{\ddagger}$	129·1$\phi^{\ddagger}$	123·4$\phi^{\ddagger}$
Chemical shift β-CF_2H	134·2$\phi^{\ddagger}$	134·5$\phi^{\ddagger}$	133·8$\phi^{\ddagger}$
$J_{F_\alpha SiH}$ c./sec.	10·5	11·1	10·6
$J_{F_\beta SiH}$ c./sec.	3·2	3·0	3·1
$J_{F_\alpha CH}$ c./sec.	4·9	6·5	5·2
$J_{F_\beta CH}$ c./sec.	55·8	55·7	55·6
$J_{F_\alpha F_\beta}$ c./sec.	1·6	0·7	1·6

Irradiation of pentacarbonyl(trimethylgermyl)manganese and fluorinated olefins results in the formation of a fluoroalkyl or fluoroalkenylgermanium trimethyl.[105] The pentacarbonyl and tetrafluoroethylene yield the inclusion compound, 1 - trimethylgermyl(2 - pentacarbonylmanganese)tetrafluoroethane (**128**), which shows two separate ^{19}F signals. On the other hand, reaction with trifluorochloroethylene affords the trimethyltrifluorovinylgermane (**129**). The

$(CH_3)_3GeCF_2CF_2Mn(CO)_5$ **128**

$(CH_3)_3GeCF{=}CF_2$ **129**

geminal FF coupling of 79·4 c./sec. given in this paper differs slightly from that (72 c./sec.) previously reported.[106] This point is mentioned because attempts have been made[107] to investigate the variation in the value of the geminal FF coupling of trifluorovinyl derivatives with the nature of the substituent atom M, in $F_2C{=}CF{-}M$, and errors of the magnitude of 10% could invalidate any conclusions drawn.

4. *Group V: phosphorus, arsenic and antimony*

Some preliminary chemical-shift data have been given on the two adducts obtained from the addition of phosphine and trifluoroethylene;[108] it is of interest that both of the two possible adducts, 1,2,2-trifluoro- and 1,1,2-trifluoroethylphosphine (**130**, **131**), are obtained. The reaction of phosphorus pentafluoride with acetylacetone gave the tetrafluoro(pentane-2,4-dionato) phosphorus (v) (**132**)

$CHF_2{-}CHF{-}PH_2$

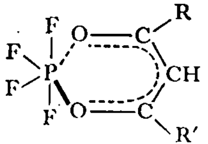
$128{\cdot}2\phi^{\ddagger}$ $195{\cdot}6\phi^{\ddagger}$

130

$CH_2F{-}CF_2{-}PH_2$

$228{\cdot}7\phi^{\ddagger}$ $96{\cdot}3\phi^{\ddagger}$

131



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in which there are two sets of magnetically different fluorine atoms.[109] The two different fluorine environments give rise to resonance signals at $53{\cdot}87\phi^{*}$ (*ax*) and $73{\cdot}81\phi^{*}$ (*eq*); the two $^{31}P{-}^{19}F$ coupling constants are 824 (*ax*) and 741 c./sec. (*eq*) and the $^{19}F{-}^{19}F$ coupling is 59·4 c./sec.

The ^{19}F n.m.r. parameters of complexes of the type NiL_4 and $Mo(CO)_nL_{6-n}$, where L is of the form R_xPF_{3-x}, in which R is F, CF_3, CCl_3, Et_2N and $C_5H_{10}N$, have been considered in some detail.[110] The shift of the PF resonance to low field (17 to 82 p.p.m.) was attributed to a large paramagnetic contribution arising from the presence of low-lying excited states in the metal–phosphorus bond; the effect is greater in the molybdenum than in the nickel complexes (see Table XXIII). The $^{31}P{-}^{19}F$ coupling of the PF_2 grouping decreases on complex formation whereas the $^{31}P{-}^{19}F$ coupling of the CF_3P group increases. For example, in CF_3PF_2 $J_{^{31}P-^{19}F} = 1245$ c./sec. and $J_{^{31}P-CF_3} = 87$ c./sec., whereas in the complex $(CF_3PF_2)_2Mo(CO)_4$ $J_{^{31}P-^{19}F} = 1172$ c./sec. and $J_{^{31}P-CF_3} = 110$ c./sec. The ^{19}F spectra of the *cis*-$[(CF_3)_2PF]_2Mo(CO)_4$, the *trans*-$[(CF_3)_2PF]_3Mo(CO)_3$, the

TABLE XXIII

^{19}F shifts of the fluorine atoms directly bonded to phosphorus in complexes NiL_4, $Mo(CO)_4L_2$ and $Mo(CO)_3L_3$

	Chemical shifts, ϕ*						
Ligand	Free ligand	NiL_4	Δ†	$Mo(CO)_4L_2$	Δ†	$Mo(CO)_3L_3$	Δ†
CF_3PF_2	104·1	72·1	−32·0	55·1	−49·0	a 52·1	−52·0
						b 56·3	−47·8
$(CF_3)_2PF$	219·0	163·3	−55·7	145·0	−74·0	a 137	−82
						b 143	−76
CCl_3PF_2	88·0	58·7	−29·3	47·9	−40·1	46·5	−41·5
Et_2NPF_2	64·8	39·4	−25·4	29·1	−35·7	..	..
$C_5H_{10}NPF_2$	66·4	39·9	−26·5	31·0	−35·4	..	..
PF_3	33·7	16·4	−17·3	2·7	−31·0	2·5	−31·2

† Shift to low field of P–F resonance on complex formation.
a = apical; b = basal.

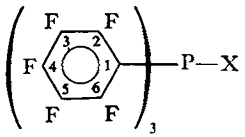
cis-$[CF_3PF_2]_2Mo(CO)_4$ and $[CF_3PF_2]_3Mo(CO)_3$ are shown in the paper. Two of these complexes, $(CF_3PF_2)_4Ni$ and $[(CF_3)_2PF]_4Ni$, have also been examined independently,[111] but the ^{19}F chemical shifts of the PF group are at lower field than reported in the above work.[110] These differences could be due to solvent effects; the latter worker[111] recorded the spectra of the neat liquid complexes while the conditions used by Barlow and Nixon[110] were not stated. This perhaps will indicate the importance, even in the short communications, of giving the conditions under which spectra were recorded, since it is very unsatisfactory to have to assume that solvent effects are responsible for discrepancies of the order of 5 to 10 p.p.m.

The investigation of the pentafluorophenyl derivatives of phosphorus has promoted some interest, especially in the study of the transmission of electronic effects along bonds. Emeléus and Miller[112] have reported the ^{19}F shifts of the tris(pentafluorophenyl)phosphine, the oxide and sulphide and of the dichlorophosphorane (see Table XXIV).

Parshall[113] demonstrated (see p. 287) that the ^{19}F shifts of monofluorophenylplatinum complexes gave information on the electronic character of the bond between the platinum and anionic ligands. This idea has been extended by Hogben *et al.*[74] in a study of pentafluorophenylphosphines and their complexes. Here a linear relationship was found between the shift of the 4-fluorine atom and the coupling constant between the 2- and 4-fluorine atoms. This relationship was used empirically to elucidate the extent of π-interaction in the organometallic compounds. This type of relationship may prove to be particularly useful, since the

TABLE XXIV

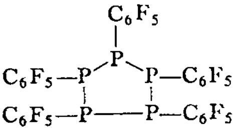
^{19}F chemical shifts of tris(pentafluorophenyl) phosphine and derivatives



X	Chemical shifts, ϕ^* F_2, F_6	 F_4	 F_3, F_5
..	130·9	149·0	160·7
=O	131·9	142·7	158·4
=S	132·1	144·7	158·8
Cl_2	128·9	146·3	158·9

^{19}F resonance signal of the 4-fluorine is easily recognized and is usually very simple, so that the shift and J_{24} may be easily obtained without complete analysis of the five-spin system. The variation of J_{24} with the shift of the 4-fluorine enables the distinction to be made between π-electron donation to the ring and withdrawal from the ring by the substituent atom or group. Large values of J_{24} and low ϕ^* values for F_4 correspond to strong π-electron acceptors, e.g., pentafluorobenzonitrile, large values of J_{24} and high ϕ^* values for F_4 correspond to π-electron donors, e.g., pentafluoroaniline, whereas low values of J_{24} and intermediate values of ϕ^* indicate a weak π-electron interaction, e.g., pentafluorotoluene.

Treatment of pentafluorophenylphosphinous dibromide with mercury afforded[114] the pentamer $(C_6F_5P)_5$ (**133**), and from consideration of the chemical



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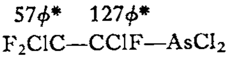
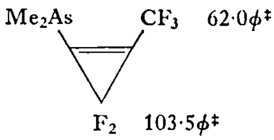


$\overset{57\phi^*}{F_2ClC}—\overset{127\phi^*}{CClF}—AsCl_2$

134



135

shifts it was concluded that the extent of π-bonding was approximately the same as in (pentafluorophenyl)diphenylphosphine, $C_6F_5P(C_6H_5)_2$.[74]

Phenyl- and methyltetrafluorophosphoranes undergo dimethylaminolysis to give the complex ion $[RPF(NMe_2)_2]^+[RPF_5]^-$; the shifts of these two salts are compared with those of $[Me_2NH_2]$ $[MePF_5]$.[115] The spectrum of the salt

TABLE XXV

^{19}F chemical shifts of pentafluorophenylarsenic derivatives

	Chemical shifts, ϕ*		
		$(C_6F_5)_2As$ $As(C_6F_5)_2$	
	$(C_6F_5As)_4$	I	II
ortho-F	125·9	133·5	133·5
meta-F	161·8	162·8	160·0
para-F	152·1	152·0	146·6

TABLE XXVI

The chemical shifts of the trifluoromethyl group of trifluoropropenylmetal alkyls

	CF_3, ϕ*
$CF_3{\cdot}C{\equiv}C{\cdot}AsMe_2$	50·6
$CF_3{\cdot}C{\equiv}C{\cdot}GeMe_3$	50·9
$CF_3{\cdot}C{\equiv}C{\cdot}SiMe_3$	51·9
$(CF_3{\cdot}C{\equiv}C)_2{\cdot}AsMe$	52·1

$[PhPF(NMe_2)_2]^+$ $[PhPF_5]^-$, recorded in acetonitrile-d_3, is shown in the paper.

Similar interest has been shown in the pentafluorophenylarsenic derivatives. The ^{19}F chemical shifts of the tetramer $(C_6F_5As)_4$ and tetrakis(pentafluorophenyl)diarsine, $(C_6F_5)_2As$ $As(C_6F_5)_2$, have been recorded[116] and are shown in Table XXV. Two species of the latter compound were recognized and these were assigned to possible *trans* and *gauche* forms.

The addition of arsenic trichloride to trifluorochloroethylene gave the 1,2,2-trifluoro-1,2-dichloroethylarsenic dichloride (**134**).[117] The two fluorine atoms of the 2-CF_2Cl-group are non-equivalent, presumably owing to restricted rotation, and the three fluorines give an ABX spectrum with J_{AB_1}, i.e., geminal FF, of 170 c./sec. and vicinal FF coupling of 16·6 c./sec. Dimethyl-3,3,3-trifluoropropynylarsine and trimethyltrifluoromethyltin react to give[118] the cyclopropenyl compound (**135**) and trimethyltin fluoride. The cyclopropenyl compound is claimed to be the first example of a cyclopropene ring attached to a metal atom. The chemical shifts of the trifluoromethyl group of four trifluoropropenyl metal alkyls are also given in this paper (see Table XXVI).

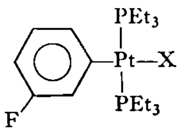
The ^{19}F chemical shifts have been used[119] to investigate the halide-exchange reactions of trimethylantimony difluoride with trimethylantimony dichloride, dibromide and di-iodide to afford the mixed halides—

$$\begin{array}{lcl}
\mathrm{Me_3SbF_2 + Me_3SbCl_2} & \rightarrow & \mathrm{Me_3SbFCl} \\
106{\cdot}1\phi^* & & 110{\cdot}9\phi^* \\
\mathrm{MeSbF_2 + Me_3SbBr_2} & \rightarrow & \mathrm{Me_3SbFBr} \\
 & & 113{\cdot}7\phi^* \\
\mathrm{Me_3SbF_2 + Me_3SbI_2} & \rightarrow & \mathrm{Me_3SbFI} \\
 & & 117{\cdot}4\phi^*
\end{array}$$

The ^{19}F chemical shifts of the antimony fluorides are shown below the respective compounds; it was stated that the shifts follow a linear relationship with the electronegativity.

5. *Group VII and VIII metals*

The utility of the type of correlations found by Pershall[113] has already been referred to above (p. 284). In this work, the ^{19}F shielding parameters of the *m*- and *p*-fluorophenylplatinum complexes (**136**) and (**137**) were used to evaluate the electronic characteristics of the metal–ligand bond in these compounds. In order to separate resonance and inductive effects, the shielding parameters of compound (**137**) were subtracted from those of compound (**136**). This difference $(\Delta p - \Delta m)_X$ for each ligand X was then subtracted from the shielding differences



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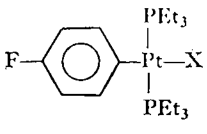

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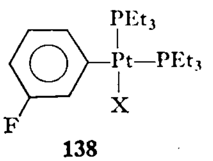

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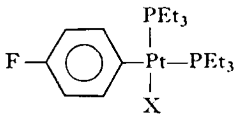

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$(\Delta p - \Delta m)_{CH_3}$ for the methyl derivative (**136** and **137**, X = Me). The shielding and the π-acceptor parameters are shown in Table XXVII. The π-acceptor parameter permitted the assessment of the π-acceptor capacity of a given ligand relative to that having no accessible π-orbitals. The shielding parameters of the corresponding *cis* compounds (**138**, **139**) are shown in Table XXVIII. However,

TABLE XXVII

^{19}F shielding and the π-acceptor parameters of fluorophenylplatinum complexes (136, 137)

X	Δm of (136) in acetone	Δm of (136) in cyclohexane	Δp of (137) in acetone	Δp of (137) in cyclohexane	π-acceptor parameter
CH_3—	3·93	4·26	11·7	11·7	0
C_6H_5—	3·46	3·72	10·9	10·9	0·3
$(C_2H_5)_3P$—	3·35	. .	. .	. .	. .
p-FC_6H_4—	3·30	3·44	10·8	10·8	0·3
$C_6H_5 \cdot C{\equiv}C$—	3·21	3·37	10·4	10·4	0·6
m-FC_6H_4—	3·07	. .	10·6	10·5	0·3
OCN— (or NCO—)	2·30	2·48	10·1	10·2	0
—CN	2·27	2·53	9·32	9·11	0·7
—Cl	2·11	2·50	10·1	10·2	−0·2
—Br	1·97	2·34	9·86	10·0	−0·1
SCN— (or NCS—)	1·75	1·90	9·29	9·20	0·2
—I	1·56	2·00	9·54	9·70	−0·2
—$SnCl_3$	−0·23	. .	6·96	. .	0·6

TABLE XXVIII

^{19}F shielding parameters for complexes (138) and (139)

X	Δm (138)	Δp (139)
C_6H_5—	3·55	11·6
p-FC_6H_4—	3·55	11·4
m-FC_6H_4—	3·44	11·2
—CN	2·85	9·48
—Cl	3·37	9·75

with these isomers, the range of values for $(\Delta p - \Delta m)$ is so large that a meaningful estimate of the π-acceptor character of the triethylphosphine group could not be made; the author concluded that π-electron interactions between *cis* ligands are much larger than those of the sigma type.

The triethylphosphine complexes of some pentafluorophenyl derivatives of nickel, palladium and platinum have also been studied[120] by using the ^{19}F shift to determine the electronic effects, and the data are compared with those presented by Parshall.[113] The chemical shifts and the ^{195}Pt–^{19}F coupling constants of the *trans*-$[(Et_3P)_2Pt(C_6F_5)X]$ (**140**) complexes, where $X = Me$, Cl, Br, I, NO_2, NCS, CN and ONO_2, are shown in Table XXIX, which includes the shift data for the complexes *trans*-$[(Et_3P)_2Pd(C_6F_5)Cl]$ and *trans*-$[(Et_3P)_2Ni(C_6F_5)Cl]$. The difference in the chemical shift of the 3- and 5-fluorine atoms and that of the 4-fluorine shown in Table XXIX is used as a criterion of the π-acceptor interaction (**28**). The π-bonding sequence was in the order $CH_3 < Cl < Br < I < NO_2 < NCS < CN < ONO_2$, which is in agreement with that obtained from other evidence, e.g., the *trans* effect. The Pt–F coupling constants are also dependent upon the nature of X in (**140**), and the authors postulate that the platinum-*ortho*-fluorine coupling constant reflects the changing bond order of the Pt–C bond.

TABLE XXIX

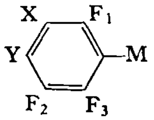
^{19}F chemical shifts and π-acceptor parameters of complexes *trans* $[Et_3P]_2M(C_6F_5)X$ (140)

		Chemical shifts, ϕ^*			
M	X	*ortho* (F_2 and F_6)	*para* F_4	*meta* (F_3 and F_5)	$(\delta_{F_4} - \delta_{F_3})$
Pt	Me	116·4	163·9	163·9	0
Pt	Cl	117·7	163·1	164·3	1·2
Pt	Br	117·3	162·4	163·8	1·4
Pt	I	117·9	161·9	163·4	1·5
Pt	NO_2	116·5	160·2	162·0	1·8
Pt	NCS	117·5	161·3	163·4	2·1
Pt	CN	117·0	160·9	163·1	2·2
Pt	ONO_2	116·9	161·1	163·6	2·5
Pd	Cl	114·3	160·8	162·5	. .
Ni	Cl	115·3	161·1	163·7	. .

The ^{19}F shifts of the substitution products obtained by the interaction of the sodium salt of $[\pi C_5H_5Fe(CO)_2]^-$ with some pentafluoro- and 1,2,3,4-tetrafluorobenzene derivatives have been reported[121] and are shown in Table XXX.

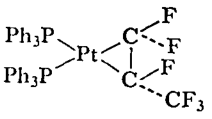
TABLE XXX

^{19}F chemical shifts of some metal carbonyl derivatives of fluorobenzenes



M	X	Y	Chemical shifts, ϕ^*			
			F_1	X	F_2	F_3
$Fe(CO)_2(\pi\text{-}C_5H_5)$	F	H	109·1	141·9	141·9	109·1
$Fe(CO)_2(\pi\text{-}C_5H_5)$	F	CN	105·9	140·8	140·8	105·9
$Fe(CO)_2(\pi\text{-}C_5H_5)$	F	CO_2Et	110·0	145·8	145·8	110·0
$Fe(CO)_2(\pi\text{-}C_5H_5)$	CN	CN	69·8	..	136·0	86·8
$Fe(CO)_2(\pi\text{-}C_5H_5)$	CO_2Et	CO_2Et	83·3	..	144·3	97·3
$Fe(CO)_2(\pi\text{-}C_5H_5)$	H	H	85·6	..	143·4	103·6
$Mn(CO)_5$	CN	CN	69·1	..	135·4	85·7
$Re(CO)_5$	CN	CN	66·2	..	134·6	83·2

Two separate groups of workers have made use of the magnitude of the geminal FF coupling constants in fluorinated olefin complexes to demonstrate the formation of carbon–metal bonds. Green *et al.*[122] have found that the geminal FF coupling of the hexafluoropropene complex with bis(triphenylphosphorus)-platinum (**141**) was 200 c./sec., which is of the order expected for the geminal FF coupling of a saturated CF_2 group. Similarly, in the complex of trifluorochloroethylene with iron tetracarbonyl (**142**),[123] analysis of the ABX spin system of the



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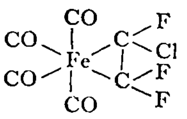

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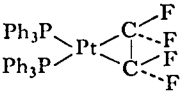
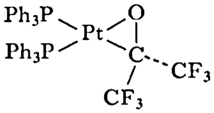
three fluorine atoms gave a geminal FF coupling of 131 c./sec. compared to the geminal FF coupling of the olefin of 78 c./sec. It was suggested that this increase in the geminal coupling reflected the increased sp^3 hybridized character of the CF_2 group. Two further platinum complexes were investigated by Green *et al.*,[122] as shown in compounds (**143**) and (**144**), and the ^{195}Pt–^{19}F and ^{31}P–^{19}F coupling constants reported are as shown.



$J_{^{195}Pt-^{19}F} = 288$ c./sec.

143



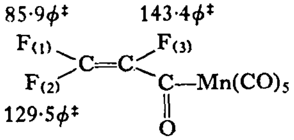
$J_{^{195}Pt-^{19}F} = 71{\cdot}5$ c./sec.

144

The reaction of dipotassium 1-hydrido-6-aquotetracyanorhodate (III), $K_2[RhH(CN)_4(H_2O)]$, with tetrafluoroethylene also resulted[124] in the formation of a σ-bonded complex, the tripotassium pentacyano-1,1,2,2-tetrafluoroethylrhodate (III), $K_3[Rh(CN)_5C_2F_4H]$ (**145**), in which the vicinal FF coupling was 5·4 c./sec., which is larger than normal; the vicinal FF coupling was not observed in the tetrafluoroethylmanganese pentacarbonyl, $HCF_2CF_2Mn(CO)_5$.[125] The rhodium–fluorine coupling constants of (**145**) were 11·1 c./sec. for Rh–F_α and 1·9 c./sec. for Rh–F_β.

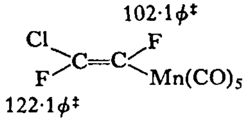
The reaction of trimethyltinpentacarbonylmanganese and trifluorochloroethylene gave three products,[126] perfluoroacryloylpentacarbonylmanganese (**146**) and *cis*- and *trans*-1,2-difluoro-2-chlorovinylpentacarbonylmanganese (**147, 148**); the chemical shifts and the FF coupling constants are shown. With trifluoroethylene, the *cis*- and *trans*-1,2-difluorovinylpentacarbonylmanganese (**149, 150**) were obtained, the full n.m.r. parameters were only given for the *cis* isomer. Trimethyltinpentacarbonylmanganese and hexafluorobuta-1,3-diene afforded[127] the *cis*-pentacarbonylmanganese complex (**151**) whose structure was established from the magnitude of the $F_{(1)}$–$F_{(2)}$ coupling constant of 34·0 c./sec. The $[\pi\text{-}C_5H_5Fe(CO)_2]^-$ anion and the hexafluorobuta-1,3-diene also gave the *cis* complex (**152**) with the $F_{(1)}$–$F_{(2)}$ coupling of 41·0 c./sec., whereas with the pentacarbonylrhenium anion, $[Re(CO)_5]^-$, the *trans* complex (**153**) is obtained exhibiting $F_{(1)}$–$F_{(2)}$ coupling of 136·5 c./sec. The pentacarbonylrhenium anion and hexafluorobut-2-yne gave two complexes.[127] One, the allenic complex (**154**) is claimed to be the first example of an allene σ-bonded to a transition metal; the ^{19}F chemical shifts and coupling constants are as shown. The second complex isolated, a dimer of the first, is a tetrafluorobutane derivative with two trifluoromethyl groups in non-equivalent positions; the structure of this complex was suggested to be as shown (**155**).

Interaction of the $[Re(CO)_5]^-$ and $[\pi\text{-}C_5H_5Fe(CO)_2]^-$ anions with 1,2-dichlorohexafluorocyclopentene results in substitution at the 1-position.[128] The ^{19}F chemical shifts and accessible coupling constants of the pentacarbonyl-σ-(2-chlorohexafluorocyclopent-1-enyl)rhenium (**156**) and of dicarbonyl-π-cyclopentadienyl-σ-(2-chlorohexafluorocyclopent-1-enyl)iron (**157**) are compared with those of 1,2-dichlorocyclopentene, Table XXI.



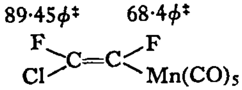
$J_{12}=92{\cdot}5$, $J_{13}=40{\cdot}6$ and $J_{23}=111{\cdot}5$ c./sec.

146



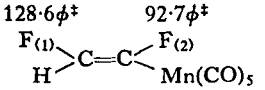
$J_{FF}=126$ c./sec.

147



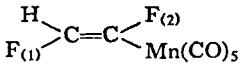
$J_{FF}=58{\cdot}5$ c./sec.

148



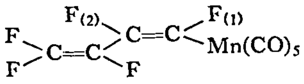
$J_{HF_1}=80{\cdot}0$, $J_{HF_2}=25{\cdot}0$ and $J_{F_1F_2}\sim 2{\cdot}4$ c./sec.

149



$J_{HF_1}=86{\cdot}5$ and $J_{H_1F_2}=10{\cdot}2$ c./sec.

150



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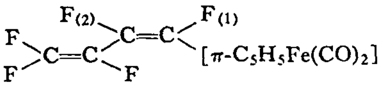

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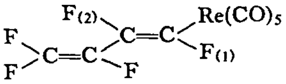

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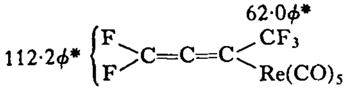
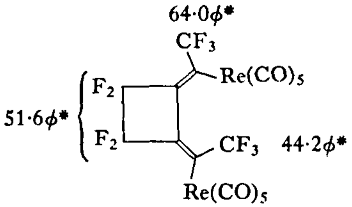


$J_{CF_3,\,CF_2}=4$ c./sec.

154



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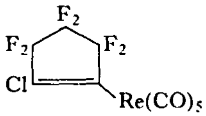

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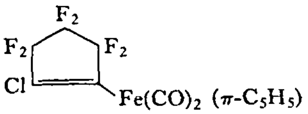

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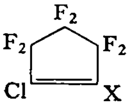
TABLE XXXI

^{19}F chemical shifts of some 2-chlorohexafluorocyclopentene derivatives



X	Chemical shifts, ϕ^*			Coupling constants	
	F_3	F_4	F_5	J_{34}, J_{45}	J_{35}
Cl	114·4	130·4	114·4	3·21	. .
$Re(CO)_5$ (**156**)	111·7	129·1	97·0	6·70	3·74
$Fe(CO)_2(\pi\text{-}C_5H_5)$ (**157**)	112·6	130·0	99·6	6·82	3·65

B. Fluorinated derivatives of the elements

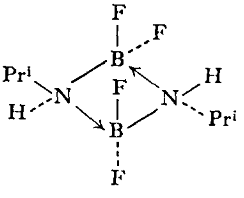
This Section is concerned with compounds in which fluorine is directly bonded to the element considered. As in the previous Section, the derivatives of a particular element will be discussed in the order of the periodic groups. Unfortunately, it is not always clear under which of the chemical divisions, inorganic or organic, compounds such as alkyl derivatives of nitrogen and alkyl and alkoxy derivatives of sulphur should be included. For clarity these types of compound are considered in this Section, so that for example under Group V, dealing with nitrogen derivatives, compounds containing the *N*-fluoro- and *N*-fluoroalkyl groupings will also be discussed.

1. *Group III*

The reaction of boron tribromide with bis(trifluoromethyl)amine to afford the bis(trifluoromethyl)aminoboron dibromide (**158**) was followed by n.m.r. spectroscopy.[129] The ^{19}F spectrum showed two resonance signals, one at $54{\cdot}6\phi^+$ with $J_{^{19}F-^{1}H}$ of 5·3 c./sec. from the parent bis(trifluoromethyl)amine and a second, single resonance signal, at $58{\cdot}4\phi^+$ due to the aminoboron dibromide. Reaction of the bis(trifluoromethyl)amine with boron trichloride did not afford the corresponding aminoboron dichloride, but gave the 1,1-dichloro-3,3,3-trifluoro-2-azaprop-1-ene (**159**) and boron trifluoride. The ^{19}F spectra of a mixture of the amine and boron trichloride showed the resonance signals of the amine, of boron

$(CF_3)_2NBBr_2$	$CF_3{\cdot}N{=}CCl_2$
158	**159**

trifluoride and the azaprop-1-ene at 57·5ϕ^+. The ^{19}F shift of the methylamine-boron trifluoride complex at 152·0ϕ^+ with $J_{^{11}B-^{19}F}$ of 16·7 c./sec., has been reported.[130] The dimeric isopropylaminoboron difluoride shows a single ^{19}F resonance signal at 157·8ϕ^* with $J_{^{11}B-^{19}F}$ of 36·7 c./sec.; the single resonance signal indicates that all the fluorine atoms are equivalent, and this has been interpreted as indicating the *trans* configuration of the isopropyl groups as shown in structure (**160**).



160

The complexes of sulpholane with boron trifluoride and phosphorus pentafluoride have been compared.[131] The ^{19}F shift of sulpholane–boron trifluoride at 144·1ϕ^* differs from these of diethyl ether–boron trifluoride (153ϕ^*) and of pyridine–boron trifluoride (149·4ϕ^*). The sulpholane–phosphorus pentafluoride complex showed a single resonance signal at 62·2ϕ^*; the loss of $^{31}P-^{19}F$ coupling is in complete contrast to the situation in phosphorus pentafluoride complexes with acetic anhydride, acetone and ethanol. For example in the ethanol–phosphorus pentafluoride the ^{19}F shift is 70·1ϕ^* and $J_{^{31}P-^{19}F}$ is 706 c./sec. It was suggested that the loss of the $^{31}P-^{19}F$ coupling is due to disproportionation of the type—

$$\text{Sulpholane} + PF_5 \rightleftharpoons PF_4^+ \text{ (solv.)} + F^- \text{ (solv.)}$$

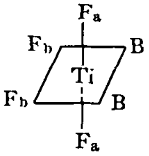
$$\text{Sulpholane} + 2PF_5 \rightleftharpoons PF_4^+ \text{ (solv.)} + PF_6^- \text{ (solv.)}$$

2. *Group IV*

The dependence of $^{29}Si-^{19}F$ coupling, in silicon tetrafluoride, upon the dispersion forces in solution has been investigated,[132] and the variation of J with H_b, the heat of vaporization of the solvent, was considered. It was found that the value of the coupling constant in trichlorofluoromethane is temperature dependent. From the graph of J against H_b, the authors considered that the variation of J could be attributed to time-varying electric fields, i.e., dispersion interactions, which alter the net electronic state of the silicon tetrafluoride. However, because of the scatter of some of the plotted points, specific interactions with donor solvents could not be completely ignored. In general it was found that the value of $J_{^{29}Si-^{19}F}$ increased as the intermolecular dispersion interactions increased.

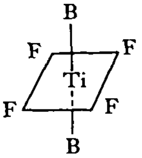
The ^{19}F spectra of hexafluorodisilane, Si_2F_6, and hexafluorodisiloxane, $(SiF_3)_2O$, have been analysed;[133] the experimental and calculated spectra of the hexafluorodisilane are shown in the paper.

The ^{19}F spectra of titanium tetrafluoride complexes have been used to identify the *cis* and *trans* adducts. Normally only the *cis* adducts (**161**) are formed, but if the ligands B have bulky groups then the *trans* adduct (**162**) has also been shown to be formed.[134] Thus the bis(pyridine-*N*-oxide)titanium tetrafluoride shows two ^{19}F resonance triplet signals, from the two environmentally different sets of fluorine atoms F_a and F_b of the *cis* isomer, at -135 and $-155\phi^*$. Bis(2-methylpyridine-*N*-oxide)titanium tetrafluoride also shows two ^{19}F triplet signals of the *cis* isomer at -130 and $155\phi^*$, but in addition exhibits a singlet signal at $-128\phi^*$, which is assigned to the *trans* isomer. Bis(2,6-dimethylpyridine-*N*-oxide)titanium tetrafluoride only shows a singlet signal in the ^{19}F spectra at $-132\phi^*$, and thus only the *trans* isomer is present; all the spectra were recorded in chloroacetonitrile solution at −40°C.



cis

161



trans

162

The ^{19}F spectrum has been used to follow the equilibrium between germanium tetrachloride and tetrafluoride at 87°C; where equilibrium was reached in 100 hr.[135]

2. *Group V*

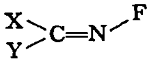
(a) *Nitrogen.* The general interest in the fluoro- and fluorocarbon derivatives of nitrogen is clearly reflected in the large number of papers on this field that have been published over the past year; only those that give ^{19}F chemical-shift data will be mentioned here.

Two independent groups of workers[136, 137] have reported the existence of the perfluoroammonium cation,[136] or tetrafluoronitronium cation[137] (NF_4^+). A hydrogen fluoride solution of $[NF_4]^+[SbF_6]^-$ exhibited a ^{19}F resonance signal at $-214{\cdot}7\phi^*$ with a ^{14}N–^{19}F coupling of 231 c./sec.[136] The data for the salt $[NF_4]^+[AsF_6]^-$ were essentially the same.[137] Similarly two independent groups have reported data on trifluoroamine oxide[138] or nitrogen oxide trifluoride[139] (F_3NO) in which the ^{19}F resonance signal is a 1:1:1 triplet at about $-365\phi^*$ with a ^{14}N–^{19}F coupling of 136 c./sec. The complexes of the amine oxide with antimony and arsenic pentafluoride were also formed[138] and the ^{19}F spectra of the complexes in hydrogen fluoride have been interpreted as indicating formation of the ionic structure $[F_2NO]^+[MF_6]^-$. The ^{19}F resonance of the $[F_2NO]^+$ ion is at $-331 \pm 3\phi^*$ and is a 4:5:4 triplet with $J_{^{14}N-^{19}F}$ of 250 c./sec. The ^{19}F signals of the anion occur at higher field, that of $[AsF_6]^-$ at $60\phi^*$ and of $[SbF_6]^-$ at $135\phi^*$.

Tetrafluorohydrazine was found to react with antimony pentafluoride in arsenic trifluoride to give a complex of the form NF_2SbF_5.[140] The ^{19}F spectra of this adduct was examined in liquid sulphur dioxide solution at −70°C and at 25°C, and the complex was additionally examined as a melt at 125°C. The ^{19}F spectrum of the adduct is shown in the paper and at low field exhibits an ABX spectrum with $\delta_A = 128{\cdot}8\phi^*$, $\delta_B = -154{\cdot}0\phi^*$ and $\delta_X = -189{\cdot}8\phi^*$ and coupling constants, $J_{AB} = 379$ c./sec., $J_{AX} = 81$ c./sec. and $J_{BX} \approx 45$ c./sec. attributed to the $[F_2NNF]^+$ ion. At high field a single resonance was observed at 25°C, but at −70°C three resonance signals were seen at 91·7, 112·7 and $134{\cdot}5\phi^*$ in the ratio 1:8:2, the spectrum being consistent with the ionic species $[Sb_2F_{11}]^-$, which had previously been identified;[141] from this the structure of the adduct was therefore concluded to be $[F_2NNF]^+[Sb_2F_{11}]^-$.

TABLE XXXII

^{19}F chemical shifts of *N*-fluoroimine derivatives



X	Y	ϕ (N–F)	X	Y	ϕ (N–F)
F	Br	−7·6†	Br	F	3·5†
F	Cl	6·8†	Cl	F	15·3†
F	F	67·0†	..	..	..
CN	F	15·3‡	F	CN	2·6‡
CN	NEt_2	35·3‡	NEt_2	CN	37·7‡
CN	CH_3	−62·1‡	CH_3	CN	−49·5‡
CN	$CH_2O{\cdot}C(O)CH_3$	1·0‡	$CH_2O{\cdot}C(O)CH_3$	CN	7·1‡
CN	CN	−90·1‡	..	..	..
CN	NH_2	30·5‡	..	..	..
CN	NHC_6H_4Cl-p	17·6	..	..	..
CN	Ph	−52·7‡	Ph	CN	−39·2‡
CN	—C(O)OMe	−70·3‡	..	..	..
CN	SF_5	−65·7‡	..	..	..

† Obtained by using internal $CClF$.

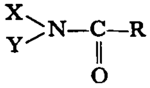
‡ Corrected from values obtained by using 1,2-difluorotetrachloroethane.

The ^{19}F shifts of perfluorourea[142] and dimethylfluoramine[143] have been reported. In the fluoramine, the fluorine atom couples to the methyl groups and the ^{19}F resonance signal was a septuplet with J_{F-CH_3} of 35 c./sec. The fluoramine hydrochloride, Me_2NFHCl, gave a broad unresolved fluorine resonance signal and the decomposition of the parent fluoramine in aqueous solution, which involves the formation of fluoride ion, was followed by the ^{19}F n.m.r. spectrum.

The reaction of tetrafluorohydrazine with tribromofluoromethane[144] and with olefins[145] gave a series of fluorimines existing as both *syn*- and *anti*-isomers. The chemical shifts of these compounds are shown in Table XXXII.

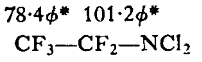
TABLE XXXIII

^{19}F chemical shifts of *N*-fluoro ureas



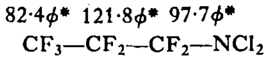
X	R	$\phi^{\ddagger}$ (N–F)
Me	NHMe	100·5
Et	NHEt	74·9
H	OEt	118·9

The direct fluorination of ureas in aqueous solution afforded the *N*-fluoro-derivatives.[146] The chemical shift of the *N*-fluoro resonance was markedly affected by the nature of the other substituents (see Table XXXIII) and it was interesting to observe that the geminal HF coupling of the —NHF group was of the same order of magnitude as the HF coupling of a >CHF group. Two molecules of chlorine monofluoride can be added across a nitrile group of fluoro-alkylnitriles to give the *N*-dichloroamines; the chemical shifts of these derivatives are shown in structures (**163**)–(**166**).[147]



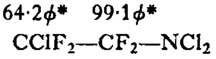
$\overset{78\cdot4\phi^*}{CF_3}—\overset{101\cdot2\phi^*}{CF_2}—NCl_2$

163



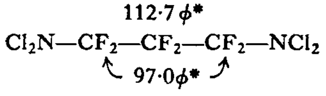
$\overset{82\cdot4\phi^*}{CF_3}—\overset{121\cdot8\phi^*}{CF_2}—\overset{97\cdot7\phi^*}{CF_2}—NCl_2$

164



$\overset{64\cdot2\phi^*}{CClF_2}—\overset{99\cdot1\phi^*}{CF_2}—NCl_2$

165



$Cl_2N—\underset{97\cdot0\phi^*}{CF_2}—\overset{112\cdot7\phi^*}{CF_2}—\underset{97\cdot0\phi^*}{CF_2}—NCl_2$

166

Methyl(bistrifluoromethyl)aminomercury (**167**), prepared by the interaction of *N*-bromobistrifluoromethylamine and dimethylmercury, shows a CF_3 resonance signal at 47·8ϕ^*; the absence of ^{19}F–^{199}Hg coupling was ascribed to intermolecular exchange of the bis(trifluoromethyl)amino group.[148] Trifluoromethylthiobis(trifluoromethyl)aminomercury (**168**), prepared from *N*-chlorobistri-

$(CF_3)_2NHgMe$
167

$(CF_3)_2NHgSCF_3$
168

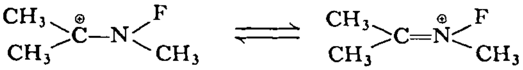
fluoromethylamine and bistrifluoromethylthiomercury, showed two ^{19}F resonance signals, that of the $(CF_3)_2N$ group at 48·0ϕ^* and of the CF_3S— group at 21·2ϕ^*. In the same paper the chemical shifts of the trifluoromethyl groups of the *N*-halobistrifluoromethylamine (see Table XXXIV) are given.[148] The shifts of two other bis(trifluoromethyl)amino-compounds have been reported.[149] Bis(trifluoromethyl(aminosulphenylmethane, $(CF_3)_2NSCH_3$, prepared from [bis(trifluoromethyl)amino]mercury and methanesulphenyl chloride, exhibits a CF_3 resonance signal at 55·8ϕ^* and J_{CH_3-F} of 0·5 c./sec. The bis(trifluoromethyl)-aminosulphenyltrifluoromethane, $(CF_3)_2NSCF_3$, obtained by irradiation of bis(trifluoromethyl)disulphide with *N*-chlorobis(trifluoromethyl)amine, shows a $(CF_3)_2N$ resonance at 58·9ϕ^* and an SCF_3 resonance at 54·7ϕ^* with J_{FF} of 3·4 c./sec.

TABLE XXXIV

Chemical shift of the trifluoromethyl groups of *N*-halobis(trifluoromethyl)amine

	ϕ^* (CF_3)
(C NF	71·3
(C NCl	64·1
(C NBr	60·7
(C NI	55·8

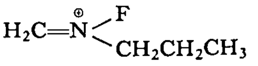
The ^{19}F spectrum of *N*-difluoro-t-butylamine in concentrated sulphuric acid showed a partially resolved quartet at $-63{\cdot}1\phi^+$ with $J_{F-CH_3\,gem}$ of 15 c./sec., and a singlet at $-38{\cdot}3\phi^+$ due to the hydrogen fluoride resonance.[150] The ^{19}F spectrum, together with the ^{1}H spectrum, was interpreted in terms of the formation of the *N*-fluoro-*N*-methylisopropylidenimonium ion (**169**). The



$$(CH_3)_2\overset{\oplus}{C}-N(F)CH_3 \rightleftharpoons (CH_3)_2C=\overset{\oplus}{N}(F)CH_3$$

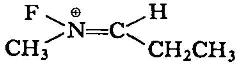
169

tetrafluoroborate salt of the ion was also prepared with a ^{19}F spectrum very similar to that described above, together with an additional signal at 146ϕ^+ from the tetrafluoroborate ion. 1,2-Alkyl group shifts were found in two other examples. 1-Difluoroaminobutane and 2-difluoroaminobutane gave the ions (**170**) and



$H_2C{=}\overset{\oplus}{N}(F)CH_2CH_2CH_3$

170

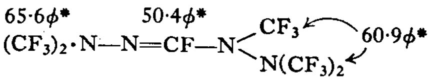


$(F)(CH_3)\overset{\oplus}{N}{=}C(H)CH_2CH_3$

171

(**171**), respectively; the ^{19}F chemical shifts and the coupling constants are shown. The spectra of the rearranged products are shown in the paper.[150]

N-Chlorobis(trifluoromethyl)amine and cyanogen chloride gave the bis(trifluoromethyl)aminocarbylamine chloride, $(CF_3)_2N{\cdot}N{=}CCl_2$, which showed a CF_3 resonance at 64·0ϕ^*. Treatment of the carbylamine with fluoride ion resulted in the formation of the dimer (**172**); the chemical shifts and couplings are as shown.[151]



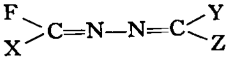
$\underset{65{\cdot}6\phi^*}{(CF_3)_2}{\cdot}N{-}N{=}\underset{50{\cdot}4\phi^*}{CF}{-}N(CF_3)N(CF_3)_2 \quad 60{\cdot}9\phi^*$

172

The chemical shifts and coupling constants of a series of fluorinated 2,3-diaza-1,3-butadienes[152] are given in Table XXXV. The geminal FF coupling constant ~70 c./sec. is larger than that normally found in fluoroalkanes, but very similar in magnitude to the geminal FF coupling of perfluorovinylmetallic compounds. The shifts of some fluorinated azo-compounds are shown in Table XXXVI.

TABLE XXXV

^{19}F chemical shifts of fluorinated-2,3-diaza-1,3-butadiene



$(F)(X)C{=}N{-}N{=}C(Y)(Z)$

			Chemical shift, ϕ^*			
X	Y	Z	X	Y	Z	F
F	F	F	74·0	52·1	74·0	52·1
F	F	Br	72·7	25·1	..	49·1
F	F	Cl	72·8	36·9	..	49·7
Br	Br	Br	..	..	..	24·4

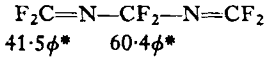
TABLE XXXVI

^{19}F chemical shifts of fluorinated azo compounds

R—N=N—R′

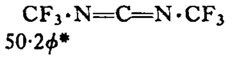
		Chemical shifts, ϕ^*	
R	R′	R	R′
CF_3	CF_3	79·7	79·7
CF_3	CF_2Br	74·5	49·1
CF_3	CF_2Cl	74·7	54·5
CF_3	CFBrCl	73·8	44·6

Irradiation of perfluoro-2,3-diazabuta-1,3-diene gave the compound (**173**), which on treatment with fluoride ion gave (**174**); the chemical shifts are as shown.[153]



$\underset{41\cdot5\phi^*}{F_2C}{=}N{-}\underset{60\cdot4\phi^*}{CF_2}{-}N{=}CF_2$

173



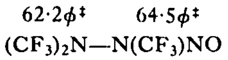
$\underset{50\cdot2\phi^*}{CF_3}\cdot N{=}C{=}N\cdot CF_3$

174

The ^{19}F chemical shifts of a series of nitroxylalkanes, formed by reaction of bis(trifluoromethyl)amine oxide and olefins,[154] hydrazines[155, 156] and amides,[156] are shown in structures (**175**)–(**191**).

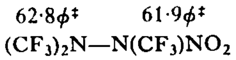
(b) *Phosphorus.* The temperature dependence of both the chemical shifts and the ^{31}P–^{19}F coupling constants of the two pentavalent trifluoro- and tetrafluorophosphines, PH_2F_3 and PHF_4, have been studied;[157] the spectra of both compounds are illustrated in the paper. A new stable hydride of pentavalent phosphorus, hydrothiophosphonyl difluoride, $S{=}PF_2H$, has been characterized and exhibits a ^{19}F resonance signal at 46·1ϕ^* with ^{31}P–^{19}F coupling of 1153·3 c./sec. and ^{19}F–^{1}H coupling of 99·0 c./sec.[158]

Two separate groups of workers have reported on the ^{19}F spectrum of diphosphorus tetrafluoride, F_4P_2. The ^{19}F signal, at 115·2ϕ^*, was stated[159] to be very complex. The spectrum recorded at −20°C is illustrated in the second paper,[160] and attention is drawn to the greater complexity of the spectrum compared with that of the isostructural H_2PPH_2. This latter paper[160] also deals with the ^{19}F spectra of μ-oxo-bisdifluorophosphine and cyanodifluorophosphine. The spectrum of μ-oxo-bisdifluorophosphine, F_2POPF_2, was found to be temperature invariant over the range of −80° to +37°C. The spectrum was treated as an



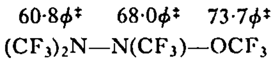
$$\overset{62{\cdot}2\phi^{\ddagger}}{(CF_3)_2N}—\overset{64{\cdot}5\phi^{\ddagger}}{N(CF_3)}NO$$

175



$$\overset{62{\cdot}8\phi^{\ddagger}}{(CF_3)_2N}—\overset{61{\cdot}9\phi^{\ddagger}}{N(CF_3)}NO_2$$

176

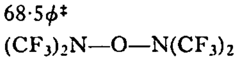


$$\overset{60{\cdot}8\phi^{\ddagger}}{(CF_3)_2N}—\overset{68{\cdot}0\phi^{\ddagger}}{N(CF_3)}—\overset{73{\cdot}7\phi^{\ddagger}}{OCF_3}$$

177

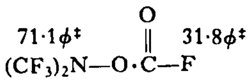
$$\overset{63{\cdot}0\phi^{\ddagger}}{(CF_3)_2}{\cdot}N—N(CF_3)_2$$

178



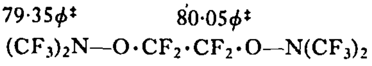
$$\overset{68{\cdot}5\phi^{\ddagger}}{(CF_3)_2N}—O—N(CF_3)_2$$

179



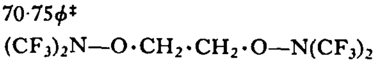
$$\overset{71{\cdot}1\phi^{\ddagger}}{(CF_3)_2N}—O{\cdot}\overset{\overset{O}{\|}}{C}—\overset{31{\cdot}8\phi^{\ddagger}}{F}$$

180



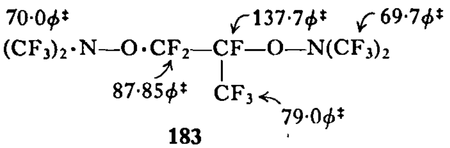
$$\overset{79{\cdot}35\phi^{\ddagger}}{(CF_3)_2N}—O{\cdot}CF_2{\cdot}\overset{80{\cdot}05\phi^{\ddagger}}{CF_2}{\cdot}O—N(CF_3)_2$$

181



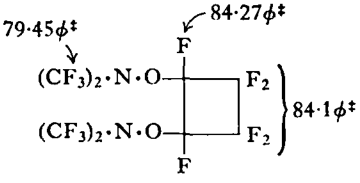
$$\overset{70{\cdot}75\phi^{\ddagger}}{(CF_3)_2N}—O{\cdot}CH_2{\cdot}CH_2{\cdot}O—N(CF_3)_2$$

182



$$\overset{70{\cdot}0\phi^{\ddagger}}{(CF_3)_2}{\cdot}N—O{\cdot}\underset{87{\cdot}85\phi^{\ddagger}}{CF_2}—\overset{137{\cdot}7\phi^{\ddagger}}{\underset{\underset{CF_3\ (79{\cdot}0\phi^{\ddagger})}{|}}{C}F}—O—\overset{69{\cdot}7\phi^{\ddagger}}{N(CF_3)_2}$$

183



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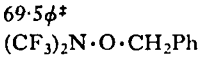
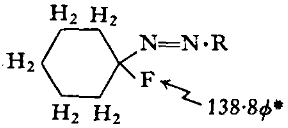


$$\overset{69{\cdot}5\phi^{\ddagger}}{(CF_3)_2N}{\cdot}O{\cdot}CH_2Ph$$

185



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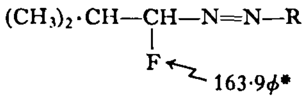
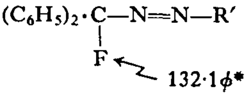


$$(CH_3)_2{\cdot}CH—\underset{\underset{F\ (163{\cdot}9\phi^{*})}{|}}{C}H—N{=}N—R$$

187



$$(C_6H_5)_2{\cdot}\underset{\underset{F\ (132{\cdot}1\phi^{*})}{|}}{C}—N{=}N—R'$$

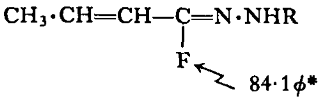
188

$C_6H_5CF{=}N—NHR''$

for $R''=R$ 83·7φ*

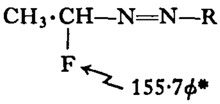
$R''=R'$ 85·2φ*

189



$$CH_3{\cdot}CH{=}CH—\underset{\underset{F\ (84{\cdot}1\phi^{*})}{|}}{C}{=}N{\cdot}NHR$$

190



$$CH_3{\cdot}\underset{\underset{F\ (155{\cdot}7\phi^{*})}{|}}{C}H—N{=}N—R$$

191

In the series (**186–191**) $R = Me_3C{\cdot}CH_2{\cdot}C(CH_3)_2—$; $R' = Me_3C—$

$X_2AA'X_2'$ spin system with the ^{19}F chemical shift at $+38{\cdot}6\phi^{+}$ with $J_{^{31}P-^{19}F}$ of 1358 c./sec. and $J_{^{31}P'-OP^{19}F}$ of -14 c./sec. The ^{19}F signal of the cyanodiflourophosphine was a doublet centred at $90{\cdot}2\phi^{+}$ with $J_{^{19}F-^{31}P}$ of 1267 c./sec.

The ^{19}F n.m.r. parameters of a series of dialkylaminofluorophosphoranes, prepared by decomposition of the dialkylaminephosphorus pentafluoride complexes, are shown in Table XXXVII.[161]

TABLE XXXVII

^{19}F chemical shifts and the ^{31}P–^{19}F coupling constants of dialkylaminofluorophosphoranes

	Shift, ϕ^{b}	$J_{^{31}P-^{19}F}$, c./sec.
PF_5, NMe_2H	80·5 (*apical*)	752
	71·1 (*eq*)	808
PF_4, NMe_2	69·1	836
$PF_3(NMe_2)_2$	55·3 (*apical*)	752
	74·0 (*eq*)	871
PF_5, NEt_2H	80·5 (*apical*)	756
	68·0 (*eq*)	813
PF_4NEt_2	68·0	868
$PF_3(NEt_2)_2$	60·8 (*apical*)	753
	58·6 (*eq*)	876
PF_4NPr_2	67·5	856

3. *Group VI*

The ^{19}F shift of dioxygen difluoride, O_2F_2, is quoted as being at $-865 \pm 10\phi^{*}$; it is suggested that the shift is not particularly concentration dependent since the variation is little more than the uncertainty in its measurement.[162]

The reaction of peroxydisulphuryldifluoride and iodine gave iodine trifluorosulphate (**192**), which has a ^{19}F resonance at 6·6 p.p.m. to low field of the ^{19}F resonance of peroxydisulphuryldifluoride.[163] The iodine trifluorosulphate has a similar structure to that of chlorine and bromine trifluorides and should therefore exhibit an AX_2 spectrum. However, even on cooling down to a temperature of −55°C, only a single resonance signal was observed. A solution of a 1:7 mixture of iodine and peroxydisulphuryldifluoride $S_2O_6F_2$ in fluorosulphonic acid showed only two ^{19}F resonance signals, over the temperature range −90° to +25°C, one due to $S_2O_6F_2$ and the second, at 1·6 p.p.m. to low field, due to $I(SO_3F)_3$ and HSO_3F, demonstrating that rapid exchange occurs between the two compounds.

Pentafluorosulphuriminosulphur difluoride (**193**) has been examined by two groups of workers,[164, 165] and like the bistrifluoromethylaminosulphur pentafluoride[166] (**194**) and the monofluoromethylsulphur pentafluoride (**195**)[149] exhibits the well-characterized AB_4 spectrum for the sulphur pentafluoride group. Several *N*-haloimino-[167] and *N*-alkyl-[168] iminosulphur derivatives have been examined and the shifts are shown in structures (**196**)–(**203**).

$I(SO_3F)_3$
192

$F_5S{-}N{=}SF_2$
193

$(CF_3)_2N{\cdot}SF_5$
194

$CH_2F{\cdot}SF_5$
195

$-43{\cdot}0\phi^*$
OSF_2NCl
196

$-37{\cdot}3\phi^*$ $113{\cdot}1\phi^*$
OSF_2NF
197

$-46{\cdot}0\phi^*$ $-15{\cdot}8\phi^*$
$O{=}SF_2{=}NCOF$
198

$-46{\cdot}3\phi^*$
SF_2NCl
199

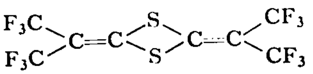
$56{\cdot}4\phi^*$
$CF_3N{=}SCl_2$
200

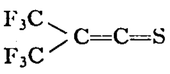
$53{\cdot}6\phi^*$
$CF_3N{=}S{=}O$
201

$86{\cdot}5\phi^*$ $96{\cdot}6\phi^*$
$CF_3{-}CF_2{-}N{=}SCl_2$
202

$86{\cdot}7\phi^*$ $90{\cdot}8\phi^*$
$CF_3{-}CF_2{-}N{=}S{=}O$
203

Tetramethyl-1,3-dithietan-Δ^{2a},Δ^{4a}-dimalonate on treatment with sulphur tetrafluoride and hydrogen fluoride gives the 2,4-bis[2,2,2-trifluoro-1-(trifluoromethyl)ethylidene]-1,3-dithietan (**204**), which shows a single resonance at $58{\cdot}9\phi^a$; this compound on heating at 650°C gave bis(trifluoromethyl)thioketen (**205**) with a single resonance signal at $58{\cdot}2\phi^a$.[169]


204


205

Many fluoroalkylfluorosulphates have been examined;[170–174] the shifts of these compounds are shown in Table XXXVIII.

TABLE XXXVIII

^{19}F chemical shifts of the $R—SO_2F$ group of the substituted fluorosulphonates

R	ϕ^*	R	ϕ^*
ClO—	-33·9	$CF_3CF_2CFCF_3$ │ O │	-51·2
—FO—	-36·3		
CF_3OO—	-37·9		
—$OOSO_2F$	-40·4		
BrO—	-41·3		
FOO—	-42·6	HO—	-65·6
—NF_2O—	-44·1		
CF_3O—	-46·8		
$CF_3C(O)\cdot O$—	-47·4	R	$\phi^‡$
$CClF_2O$—	-48·0		
—OSO_2F	-48·8	$CF_2ClCFCl$—	-43·4
$FSO_2\cdot O\cdot CF_2$—O—	-48·7	$CF_2BrCFBr$—	-43·7
C_2F_5O—	-49·6	CF_2BrCHF—	-55·5
$FSO_2\cdot O\cdot SO_2O$—	-49·6	CF_3CHF—	-48·8
$NF_2CF_2CF_2O$—	-50·4	$MeOCF_2CHF$—	-52·5
$FSO_2\cdot O\cdot CF_2CF_2$—$O$—	-50·7	$CF_2{=}CF$—	-62·0
$CF_3CBrFCFCF_3$ │ O │	-51·0	$ClCF_2\cdot O$—	-46·6
		$ClCF_2\cdot C(O)O$—	-46·1
		$CF_3CF_2C(O)O$—	-46·0
		$CF_3CF_2CF_2C(O)O$—	-45·5

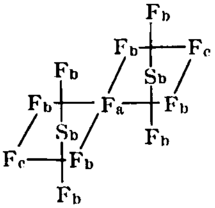
4. *Group VII*

The anomalous, low-field shift of chlorine monofluoride has recently been interpreted[175] as due to an increased paramagnetic contribution arising from a low lying $\pi^* \rightarrow \sigma^*$ excitation. The opposite electronic circulation in the two atoms results in a shift of 500 p.p.m. to low field of that theoretically expected. A similar situation cannot arise in hydrogen fluoride because of the absence of π-electrons on the hydrogen atom.

C. Complex fluoride anions

Solutions of antimony pentafluoride in hydrogen fluoride have been examined at low temperature (−60°C) and the ^{19}F spectrum showed a signal due to the SbF_6^- ion, together with three additional resonances that were assigned to the dimeric ion $[Sb_2F_{11}]^-$ **(206)**.[141] The shifts of the three different fluorine atoms were F_a at −4634, F_b at −3166 and F_c at −1918 c./sec. to low field of hydrogen fluoride. The fluorine coupling constants were $J_{F_aF_b} = 53$ c./sec. and $J_{F_bF_c} = 100$ c./sec. (see Ruff,[140] who also refers to the formation of this complex anion).

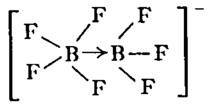
Several alkylammonium tetrafluoroborates have been found to absorb a further molecule of boron trifluoride.[176] Di-isopropylammonium tetrafluoroborate and boron trifluoride give the compound (**207**) which has a ^{19}F chemical shift of $144{\cdot}2\phi^*$ compared with $132{\cdot}6\phi^*$ for boron trifluoride and $149{\cdot}4\phi^*$ for the tetrafluoroborate ion. It is suggested that the complex ion $B_2F_7^-$ (**208**) is formed and that the equivalence is due to rapid exchange of the three fluorine atoms.



206

$[Pr^i_2NHEt]^+[BF_4, BF_3]^-$

207



208

The ^{19}F shifts of the fluoride, tetrafluoroborate and hexafluorosilicate ions have been measured in aqueous solution over a range of concentrations from 0–5 mole/kg. of water.[177] In general, there is an increased deshielding with increasing size of the cation, and it is suggested that ion-pairs are formed. In the case of the tetrafluoroborate the ^{11}B–^{19}F coupling is partially collapsed, in a similar way to that observed in the tetrafluoroarsenate ion.[178]

The complex of xenon difluoride with antimony pentafluoride $XeF_2{\cdot}2SbF_5$ shows one of the largest chemical shifts and spin-coupling constants yet recorded in ^{19}F n.m.r. spectroscopy.[179] The resonance was 1000 p.p.m. to low field of elemental fluorine, equivalent to a shift of about $-1582\phi^*$ and exhibited a ^{129}Xe–^{19}F coupling of 7234 c./sec. The corresponding xeron tetrafluoride complex XeF_4, $2SbF_5$ was not isolated, but the main ^{19}F signal was situated at essentially the same chemical shift and consisted of two overlapping triplets from two bridging and two non-bridging fluorine atoms; the ^{129}Xe–^{19}F coupling was 4000 c./sec.

A study[180] of the ^{19}F spectra of protactinium fluorides, alone and mixed with fluoride ions, has led to the recognition of the two complex ions $[PaF_6]^-$ and $[PaF_7]^{2-}$.

The concentration dependence of the ^{11}B–^{19}F coupling constant of the fluoroborate ion of sodium tetrafluoroborate, in contrast to the invariance in the corresponding ammonium salt, was interpreted as arising from ion-pair formation between the sodium and tetrafluoroborate ions. This variation has been examined[181] by using silver tetrafluoroborate in water, acetonitrile and mixed water–acetonitrile solvents. In aqueous solution the ^{11}B–^{19}F coupling is $1{\cdot}07 \pm 0{\cdot}07$ c./sec., independent of concentration, whereas in acetonitrile the coupling is $0{\cdot}39 \pm 0{\cdot}07$ c./sec. In the mixed solvent system a smooth curve is plotted for the relation of $J_{^{11}B-^{19}F}$ against percentage acetonitrile, if a change in the sign of coupling is assumed (see Fig. 5) at about 80% acetonitrile. In this solvent, the ^{19}F spectra consists of two sharp lines, the low-field signal due to the $^{10}BF_4$ ion.

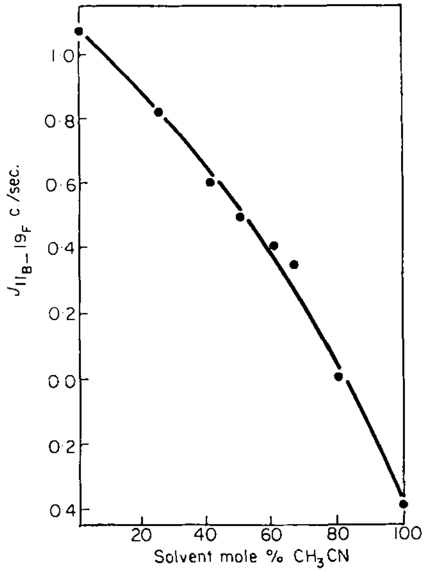


FIG. 5. Graph of $J_{^{11}B-^{19}F}$ in $AgBF_4$ against composition of water–acetonitrile solvent mixtures. (From Gillespie and Hartman.[181])

The ^{11}B–^{19}F coupling constant and the ^{19}F shift of the tetrafluoroborate ion has also been examined[182] as a function of concentration of the salt, and of solvent composition in the binary solvent systems of water–acetone, water–dioxan and water–dimethyl sulphoxide. The results found in water, water–dioxan and water–acetone have been interpreted in terms of the variation of hydrogen bonding of water to the BF_4^- ion. The behaviour in water–dimethyl sulphoxide was different, and it was suggested that there was preferential solvation of the ion by the protolysis product (solvent H^+) of dimethyl sulphoxide and water. It was found that the chemical shifts and coupling constants are directly related over the range of concentrations studied, and it was suggested that the variations arise from the same type of interaction.

REFERENCES

1. H. F. White, *Analyt. Chem.*, 1966, **38**, 625.
2. H. F. White, *Analyt. Chem.*, 1965, **37**, 403.
3. R. C. Hopkins, *J. Mol. Spectroscopy*, 1966, **20**, 321.

4. R. F. Merritt, *J. Org. Chem.*, 1966, **31**, 3871.
5. D. L. Hooper, N. Sheppard and C. M. Woodman, *J. Chem. Phys.*, 1966, **45**, 398.
6. N. O. Brace, *J. Org. Chem.*, 1966, **31**, 2879.
7. J. Dyer and J. Lee, *Trans. Faraday Soc.*, 1966, **62**, 257.
8. J. Lee and L. Sutcliffe, *Trans. Faraday Soc.*, 1959, **55**, 880.
9. R. Gardaix-Lavielle, J. Jullien and H. Stahl-Lariviere, *Bull. Soc. chim. France*, 1966, 1771.
10. J. K. Ruff, A. R. Pitochelli and M. Lustig, *J. Amer. Chem. Soc.*, 1966, **88**, 4581.
11. R. F. Merritt and T. E. Stevens, *J. Amer. Chem. Soc.*, 1966, **88**, 1822.
12. G. A. Boswell, *J. Org. Chem.*, 1966, **31**, 991.
13. D. P. Graham and V. Weinmayr, *J. Org. Chem.*, 1966, **31**, 957.
14. D. P. Graham and W. B. McCormack, *J. Org. Chem.*, 1966, **31**, 958.
15. T. N. Huckerby, Ph.D. Thesis, Birmingham University, 1966.
16. W. H. Pirkle, *J. Amer. Chem. Soc.*, 1966, **88**, 1837.
17. S. L. Manatt, *J. Amer. Chem. Soc.*, 1966, **88**, 1323.
18. S. L. Manatt, D. D. Lawson, J. D. Ingham, N. S. Rapp and J. P. Hardy, *Analyt. Chem.*, 1966, **38**, 1063.
19. D. F. Koster, *J. Amer. Chem. Soc.*, 1966, **88**, 5067.
20. K. O. Christie and A. E. Pavlath, *J. Org. Chem.*, 1966, **31**, 559.
21. W. B. Fox and G. Franz, *Inorg. Chem.*, 1966, **5**, 946.
22. J. H. Prager, *J. Org. Chem.*, 1966, **31**, 392.
22a. M. Fukuyama, *Reports Govt. Chem. Ind. Res. Inst., Tokyo*, 1966, **61**, 129.
23. D. J. Burton, R. L. Johnson and R. T. Bogan, *Canad. J. Chem.*, 1966, **44**, 635.
24. D. P. Graham, *J. Org. Chem.*, 1966, **31**, 955.
25. W. C. Soloman, L. A. Dee and D. W. Schults, *J. Org. Chem.*, 1966, **31**, 1551.
26. S. Proskov, H. E. Simmons and T. L. Cairns, *J. Amer. Chem. Soc.*, 1966, **88**, 5254.
27. D. C. England and C. G. Krespan, *J. Amer. Chem. Soc.*, 1966, **88**, 5582.
28. R. E. Banks and G. J. Moore, *J. Chem. Soc. C*, 1966, 2304.
29. M. G. Barlow, *Chem. Comm.*, 1966, 703.
30. P. Bladon, D. W. A. Sharp and J. M. Winfield, *Spectrochim. Acta*, 1966, **22**, 343.
31. T. N. Huckerby, E. F. Mooney and R. Stephens, *Tetrahedron*, 1967, **23**, 709.
32. J. Renben and A. Demiel, *J. Chem. Phys.*, 1966, **44**, 2216.
33. W. P. Norris and W. G. Finnegan, *J. Org. Chem.*, 1966, **31**, 3292.
34. A. Peake and L. F. Thomas, *Trans. Faraday Soc.*, 1966, **62**, 2980.
35. V. W. Gash and D. J. Baner, *J. Org. Chem.*, 1966, **31**, 3602.
36. A. Peake, J. A. Wyer and L. F. Thomas, *Chem. Comm.*, 1966, 95.
37. R. F. Merritt and F. A. Johnson, *J. Org. Chem.*, 1966, **31**, 1859.
38. D. M. Gale, W. J. Middleton and C. G. Krespan, *J. Amer. Chem. Soc.*, 1966, **88**, 3617.
39. J. T. Gerig and J. D. Roberts, *J. Amer. Chem. Soc.*, 1966, **88**, 2791.
40. J. D. Roberts, *Chem. in Britain*, 1966, **2**, 529.
41. R. P. Bauman and B. J. Bulkin, *J. Chem. Phys.*, 1966, **45**, 496.
42. K. L. Williamson, Yuan-Fang Li, F. H. Hall and S. Swager, *J. Amer. Chem. Soc.*, 1966, **88**, 5678.
43. H. F. White, *Analyt. Chem.*, 1965, **37**, 403.
44. S. F. Campbell and E. F. Mooney, unpublished results.
45. S. W. Tobey and R. West, *J. Amer. Chem. Soc.*, 1966, **88**, 2481.

46. R. E. Banks, M. G. Barlow, W. R. Deem, R. N. Haszeldine and D. R. Taylor, *J. Chem. Soc. C*, 1966, 981.
47. R. E. Banks, W. R. Deem, R. N. Haszeldine and D. R. Taylor, *J. Chem. Soc. C*, 1966, 2051.
48. G. Camaggi and F. Gozzo, *Chem. Comm.*, 1967, 236.
49. R. E. Banks, A. C. Harrison and R. N. Haszeldine, *J. Chem. Soc. C*, 1966, 2102.
50. R. F. Sweeney, B. Veldhuis, E. E. Gilbert, L. G. Anello, R. J. DuBois and W. J. Cunningham, *J. Org. Chem.*, 1966, **31**, 3174.
51. I. Haller, *J. Amer. Chem. Soc.*, 1966, **88**, 2070.
52. G. Cammaggi, F. Gozzo and G. Cevidalli, *Chem. Comm.*, 1966, 313.
53. H. G. Viche, R. Merenyi, J. F. M. Oth, J. R. Senders and P. Valange, *Angew. Chem. Internat. Ed.*, 1964, **3**, 755.
54. J. Feeney, L. H. Sutcliffe and S. M. Walker, *Trans. Faraday Soc.*, 1966, **62**, 2650.
55. J. Feeney, L. H. Sutcliffe and S. M. Walker, *Trans. Faraday Soc.*, 1966, **62**, 2969.
56. J. Homer and L. F. Thomas, *J. Chem. Soc. B*, 1966, 141.
57. C. Tamborski and E. J. Soloski, *J. Org. Chem.*, 1966, **31**, 746.
58. J. K. Williams, E. L. Martin and W. A. Sheppard, *J. Org. Chem.*, 1966, **31**, 919.
59. R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Anderson and G. T. Davies, *J. Amer. Chem. Soc.*, 1963, **85**, 709, 3146.
60. D. G. Holland and C. Tamborski, *J. Org. Chem.*, 1966, **31**, 280.
61. C. Tamborski, E. J. Soloski and J. P. Ward, *J. Org. Chem.*, 1966, **31**, 4230.
62. D. D. Callander, P. L. Coe and J. C. Tatlow, *Tetrahedron*, 1966, **22**, 419.
63. D. D. Callander, P. L. Coe and J. C. Tatlow, *Chem. Comm.*, 1966, 143.
64. J. P. N. Brewer, H. Heaney and B. A. Marples, *Chem. Comm.*, 1967, 27.
65. P. C. Myhre, J. W. Edmonds and J. D. Kruger, *J. Amer. Chem. Soc.*, 1966, **88**, 2459.
66. J. Burdon and W. B. Hollyhead, *J. Chem. Soc.*, 1965, 6326.
67. J. Burdon, *Tetrahedron*, 1965, **21**, 1101.
68. R. J. Abraham, D. B. Macdonald and E. S. Pepper, *Chem. Comm.*, 1966, 542.
69. A. Peake and L. F. Thomas, *Chem. Comm.*, 1966, 529.
70. D. D. Callander, P. L. Coe, M. F. S. Matough, E. F. Mooney, A. J. Uff and P. H. Winson, *Chem. Comm.*, 1966, 820.
71. N. N. Shapet'ko, N. M. Sergeev, E. M. Panov and R. S. Sorokina, *Zhur. Strukt. Khim.*, 1965, **6**, 641.
72. S. Mohanty and P. Venkateswarlu, *Mol. Phys.*, 1966, **11**, 329.
73. A. L. Logothetis, *J. Org. Chem.*, 1966, **31**, 3686.
74. M. G. Hogben, R. S. Gay and W. A. G. Graham, *J. Amer. Chem. Soc.*, 1966, **88**, 3457.
75. J. E. Baldwin and D. J. Fenoglio, *J. Phys. Chem.*, 1966, **70**, 227.
76. G. A. Olah, C. A. Cupas and M. B. Comisarow, *J. Amer. Chem. Soc.*, 1966, **88**, 362.
77. G. A. Olah and C. U. Pittman, *J. Amer. Chem. Soc.*, 1966, **88**, 3310.
78. G. A. Olah and M. B. Comisarow, *J. Amer. Chem. Soc.*, 1966, **88**, 3313.
79. J. Feeney, L. H. Sutcliffe and S. M. Walker, *Mol. Phys.*, 1966, **11**, 117.
80. F. Hruska, H. M. Hutton and T. Schaefer, *Canad. J. Chem.*, 1965, **43**, 2392.
81. J. Feeney, L. H. Sutcliffe and S. M. Walker, *Mol. Phys.*, 1966, **11**, 129.
82. J. Feeney, L. H. Sutcliffe and S. M. Walker, *Mol. Phys.*, 1966, **11**, 137.

83. J. Feeney, L. H. Sutcliffe and S. M. Walker, *Mol. Phys.*, 1966, **11**, 145.
84. N. Boden, J. W. Emsley, J. Feeney and L. H. Sutcliffe, *Mol. Phys.*, 1964, **8**, 133.
85. G. L. Caldow, *Mol. Phys.*, 1966, **11**, 71.
86. J. W. Emsley and L. Phillips, *Mol. Phys.*, 1966, **11**, 437.
87. R. D. Chambers, J. Hutchinson and W. K. R. Musgrave, *J. Chem. Soc. C*, 1966, 220.
88. R. D. Chambers, M. Hole, W. K. R. Musgrave, R. A. Storey and B. Iddon, *J. Chem. Soc. C*, 1966, 2331.
89. J. Lee and K. G. Orrell, *Trans. Faraday Soc.*, 1967, **63**, 16.
90. L. W. Reeves and E. J. Wells, *Discuss. Faraday Soc.*, 1962, **34**, 177.
91. J. Homer and L. F. Thomas, *Trans. Faraday Soc.*, 1963, **59**, 2431.
92. R. D. Chambers, J. A. M. MacBride and W. K. R. Musgrave, *Chem. and Ind.*, 1966, **22**, 904.
93. W. Carpenter, A. Haymaker and D. W. Moore, *J. Org. Chem.*, 1966, **31**, 789.
94. L. O. Moore, *J. Org. Chem.*, 1966, **31**, 3910.
95. K. J. Ryan, E. M. Acton and L. Goodman, *J. Org. Chem.*, 1966, **31**, 1181.
96. F. Heatley and S. M. Todd, *J. Chem. Soc. A*, 1966, 1152.
97. J. Burdon, J. C. Tatlow and D. F. Thomas, *Chem. Comm.*, 1966, 48.
98. P. Bladon and G. C. Forrest, *Chem. Comm.*, 1966, 481.
99. D. F. Evans and M. S. Khan, *Chem. Comm.*, 1966, 67.
100. T. Chivers, *Chem. Comm.*, 1967, 157.
101. A. W. Laubengayer and G. F. Lengnick, *Inorg. Chem.*, 1966, **5**, 503.
102. P. L. Timms, D. D. Stump, R. A. Kent and J. L. Margrave, *J. Amer. Chem. Soc.*, 1966, **88**, 940.
103. J. C. Thompson, J. L. Margrave and P. L. Timms, *Chem. Comm.*, 1966, 566.
104. D. I. Cook, R. Fields, M. Green, R. N. Haszeldine, B. R. Iles, A. Jones and M. J. Newlands, *J. Chem. Soc. A*, 1966, 887.
105. H. C. Clark, J. D. Cotton and J. H. Tsai, *Inorg. Chem.*, 1966, **5**, 1582.
106. S. Andreades, *J. Amer. Chem. Soc.*, 1962, **84**, 864.
107. C. G. Moreland and W. S. Brey, *J. Chem. Phys.*, 1966, **45**, 803.
108. R. Fields, H. Goldwhite, R. N. Haszeldine and J. Kirman, *J. Chem. Soc. C*, 1966, 2075.
109. N. M. D. Brown and P. Baldon, *Chem. Comm.*, 1966, 304.
110. C. G. Barlow and J. F. Nixon, *Inorg. Nuc. Chem. Letters*, 1966, **2**, 323.
111. A. B. Burg and G. B. Street, *Inorg. Chem.*, 1966, **5**, 1532.
112. H. J. Emeléus and J. M. Miller, *J. Inorg. Nuc. Chem.*, 1966, **28**, 662.
113. G. W. Parshall, *J. Amer. Chem. Soc.*, 1966, **88**, 704.
114. A. H. Cowley and R. P. Pinnell, *J. Amer. Chem. Soc.*, 1966, **88**, 4533.
115. G. S. Reddy and R. Schmutzler, *Inorg. Chem.*, 1966, **5**, 164.
116. M. Green and D. Kirkpatrick, *Chem. Comm.*, 1967, 57.
117. H. Goldwhite, *Inorg. Nuc. Chem. Letters*, 1966, **2**, 5.
118. W. R. Cullen and W. R. Leeder, *Inorg. Chem.*, 1966, **5**, 1004.
119. G. C. Long, C. G. Moreland, G. O. Doak and M. Miller, *Inorg. Chem.*, 1966, **5**, 1358.
120. F. J. Hopton, A. J. Rest, D. T. Rosevear and F. G. A. Stone, *J. Chem. Soc. A*, 1966, 1326.
121. M. I. Bruce and F. G. A. Stone, *J. Chem. Soc. A*, 1966, 1837.
122. M. Green, R. B. L. Osborn, A. J. Rest and F. G. A. Stone, *Chem. Comm.*, 1966, 502.

123. R. Fields, M. M. Germain, R. N. Haszeldine and P. W. Wiggans, *Chem. Comm.*, 1967, 243.
124. D. N. Lawson, M. J. Mays and G. Wilkinson, *J. Chem. Soc. A*, 1966, 52.
125. J. A. McCleverty and G. Wilkinson, *J. Chem. Soc.*, 1964, 4201.
126. H. C. Clark and J. H. Tsai, *Inorg. Chem.*, 1966, **5**, 1407.
127. M. Green, N. Mayne and F. G. A. Stone, *Chem. Comm.*, 1966, 755.
128. M. I. Bruce, P. W. Jolly and F. G. A. Stone, *J. Chem. Soc. A*, 1966, 1602.
129. N. N. Greenwood and K. A. Hooton, *J. Chem. Soc. A*, 1966, 751.
130. N. N. Greenwood, K. A. Hooton and J. Walker, *J. Chem. Soc. A*, 1966, 21.
131. J. G. Jones, *Inorg. Chem.*, 1966, **5**, 1229.
132. H. M. Hutton, E. Bock and T. Schaefer, *Canad. J. Chem.*, 1966, **44**, 2772.
133. R. B. Johannesen, T. C. Farrar, F. E. Brinckman and T. D. Coyle, *J. Chem. Phys.*, 1966, **44**, 962.
134. D. S. Dyer and R. O. Ragsdale, *Chem. Comm.*, 1966, 601.
135. G. M. Burch and J. R. van Wazer, *J. Chem. Soc. A*, 1966, 586.
136. W. E. Tolberg, R. T. Rewick, R. S. Stringham and M. E. Hill, *Inorg. Nuc. Chem. Letters*, 1966, **2**, 79.
137. K. O. Christe, J. P. Guertin and A. E. Pavlath, *Inorg. Nuc. Chem. Letters*, 1966, **2**, 83.
138. W. B. Fox, J. S. Mackenzie, N. Vanderkooi, B. Sukornick, C. A. Wamser, J. R. Holmes, R. E. Eibeck and B. B. Stewart, *J. Amer. Chem. Soc.*, 1966, **88**, 2604.
139. N. Bartlett, J. Passmore and E. J. Wells, *Chem. Comm.*, 1966, 213.
140. J. K. Ruff, *Inorg. Chem.*, 1966, **5**, 1791.
141. R. J. Gillespie and K. C. Moss, *J. Chem. Soc. A*, 1966, 1170.
142. G. W. Fraser and J. M. Shreeve, *Chem. Comm.*, 1966, 532.
143. R. A. Wiesboeck and J. K. Ruff, *Inorg. Chem.*, 1966, **5**, 1629.
144. D. H. Dybvig, *Inorg. Chem.*, 1966, **5**, 1795.
145. A. L. Logothetis and G. N. Sausen, *J. Org. Chem.*, 1966, **31**, 3689.
146. R. E. Banks, R. N. Haszeldine and J. P. Laln, *J. Chem. Soc. C*, 1966, 1514.
147. J. B. Hynes and T. E. Austin, *Inorg. Chem.*, 1966, **5**, 488.
148. R. C. Dobbie and H. J. Emeléus, *J. Chem. Soc. A*, 1966, 367.
149. H. J. Emeléus and B. W. Tattershall, *J. Inorg. Nuc. Chem.*, 1966, **28**, 1823.
150. K. Baum and H. M. Nelson, *J. Amer. Chem. Soc.*, 1966, **88**, 4459.
151. R. C. Dobbie and H. J. Emeléus, *J. Chem. Soc. A*, 1966, 933.
152. R. A. Mitsch and P. H. Ogden, *J. Org. Chem.*, 1966, **31**, 3833.
153. R. A. Mitsch and P. H. Ogden, *Chem. Comm.*, 1967, 59.
154. R. E. Banks, R. N. Haszeldine and M. J. Stevenson, *J. Chem. Soc. C*, 1966, 901.
155. R. N. Haszeldine and A. E. Tipping, *J. Chem. Soc. C*, 1966, 1236.
156. W. H. Graham, *J. Amer. Chem. Soc.*, 1966, **88**, 4677.
157. R. R. Holmes and R. N. Storey, *Inorg. Chem.*, 1966, **5**, 2146.
158. T. L. Charlton and R. G. Cavell, *Chem. Comm.*, 1966, 763.
159. M. Lustig, J. K. Ruff and C. B. Colburn, *J. Amer. Chem. Soc.*, 1966, **88**, 3875.
160. R. W. Rudolph, R. C. Taylor and R. W. Parry, *J. Amer. Chem. Soc.*, 1966, **88**, 3729.
161. D. H. Brown, G. W. Fraser and D. W. A. Sharp, *J. Chem. Soc. A*, 1966, 171.
162. N. J. Lawrence, J. S. Ogden and J. J. Turner, *Chem. Comm.*, 1966, 102.
163. R. J. Gillespie and J. B. Milne, *Inorg. Chem.*, 1966, **5**, 1236.
164. B. Cohen, T. R. Hooper and R. D. Peacock, *Chem. Comm.*, 1966, 32.

165. A. F. Clifford and J. W. Thompson, *Inorg. Chem.*, 1966, **5**, 1424.
166. R. C. Dobbie, *J. Chem. Soc. A*, 1966, 1555.
167. J. K. Ruff, *Inorg. Chem.*, 1966, **5**, 1787.
168. M. Lustig, *Inorg. Chem.*, 1966, **5**, 1317.
169. M. S. Raasch, *Chem. Comm.*, 1966, 577.
170. B. L. Earl, B. K. Hill and J. M. Shreeve, *Inorg. Chem.*, 1966, **5**, 2184.
171. F. A. Hohorst and J. M. Shreeve, *Inorg. Chem.*, 1966, **5**, 2069.
172. D. D. Desmarteau and G. H. Cady, *Inorg. Chem.*, 1966, **5**, 169.
173. J. J. Delfino and J. M. Shreeve, *Inorg. Chem.*, 1966, **5**, 308.
174. R. E. Banks, G. M. Haslam, R. N. Haszeldine and A. Peppin, *J. Chem. Soc. C*, 1966, 1171.
175. C. D. Cornwell, *J. Chem. Phys.*, 1966, **44**, 874.
176. J. J. Harris, *Inorg. Chem.*, 1966, **5**, 1627.
177. R. Haque and L. W. Reeves, *Canad. J. Chem.*, 1966, **44**, 2769.
178. E. L. Muetterties and K. J. Packer, *Proc. Chem. Soc.*, 1964, 147.
179. B. Cohen and R. D. Peacock, *J. Inorg. Nuc. Chem.*, 1966, **28**, 3056.
180. M. N. Bukhsh, J. Flegenheimer, F. M. Hall, A. G. Maddock and C. Ferreira de Miranda, *J. Inorg. Nuc. Chem.*, 1966, **28**, 421.
181. R. J. Gillespie and J. S. Hartman, *J. Chem. Phys.*, 1966, **45**, 2712.
182. R. Haque and L. W. Reeves, *J. Phys. Chem.*, 1966, **70**, 2753.

AUTHOR INDEX

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