

HIGH-RESOLUTION NUCLEAR MAGNETIC RESONANCE AND MOLECULAR STRUCTURE

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CONTENTS

I. Introduction.....	464
A. Cause of a chemical shift.....	464
B. Spin-spin coupling.....	464
C. Interaction of spin coupling and chemical shift.....	465
D. Removal of spin-coupling effects.....	466
E. Solution effects.....	467
1. Diamagnetism.....	467
2. Association.....	468
F. Standards of reference.....	468
II. Proton resonance spectra.....	471
A. Chemical shift and chemical bonding.....	471
1. Aliphatic compounds.....	471
(a) Linear compounds.....	471
(b) Cyclic compounds.....	472
2. Aromatic compounds.....	473
3. Oxygenated compounds.....	474
(a) Hydroxy compounds.....	474
(b) Carbonyl compounds.....	475
(c) Cyclic compounds.....	475
4. Compounds containing other elements.....	476
(a) Nitrogen-containing compounds.....	476
(b) Sulfur-containing compounds.....	477
(c) Halogen-containing compounds.....	477
(d) Other compounds.....	478
B. Correlation with electronegativity.....	478
C. Steric effects.....	480
D. Temperature effects.....	481
E. Examples of structure determination.....	481
III. Fluorine resonance spectra.....	482
IV. Carbon-13 resonance spectra.....	484
A. Chemical shift and chemical bonding.....	484
B. Spectra of nuclei with low abundances.....	486
C. H^1-C^{13} spin coupling.....	486
V. Phosphorus resonance spectra.....	486
VI. Resonance of other isotopes.....	488
A. Boron-11.....	489
B. Oxygen-17.....	489
C. Nitrogen.....	489
D. Silicon-29.....	490
E. Chlorine-35.....	490
F. Miscellaneous isotopes.....	491
VII. Relaxation times and chemical structure.....	491
VIII. References.....	492

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I. INTRODUCTION

A. CAUSE OF A CHEMICAL SHIFT

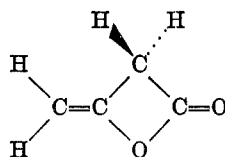
When a nucleus possessing a magnetic moment is placed in a magnetic field it may absorb and emit energy at a frequency which depends upon the magnetic moment and the strength of the field. This phenomenon has been reviewed in detail previously (6, 171, 184). There is a direct relationship between field strength and resonance frequency; hence the two will be used interchangeably in this article, depending upon convenience. However, experimental practice usually keeps the frequency constant and varies the strength of the magnetic field when high-resolution work is being done. For the purposes of this article high-resolution spectra will be those in which the natural frequency width of the resonance is usually much less than the shift caused by the chemical environment of the nucleus.

The magnetic field strength which determines the resonance frequency is the field strength at the nucleus, which may differ from the gross magnetic field in which the sample is placed. This difference is primarily due to a diamagnetic or paramagnetic shielding of the nucleus by the electrons of the inner shells and by the valence electrons (73, 96, 135). Since a change in the chemical bonding of an atom affects its share of the valence electrons, the shielding of the nucleus will be altered. Therefore the resonance frequency of a nucleus, for a given external magnetic field, will depend upon the chemical bonding of that atom. A chemical shift of the frequency of the nuclear magnetic resonance is obtained.

B. SPIN-SPIN COUPLING

In addition to the effect of the electronic environment, the resonance frequency may be affected by interaction with the spins of other nuclei (134). This causes a symmetrical splitting of the single resonance line into a multiplet. For nuclei of spin $\frac{1}{2}$ this yields, as a first approximation, a multiplet of $(n + 1)$ lines whose relative intensities are given by the coefficients of $(a + b)^n$, where n is the number of magnetically equivalent nuclei spin-spin coupled to the nucleus in question (66). If the spin of the coupled nucleus is greater than $\frac{1}{2}$, the number of lines in the multiplet may be calculated on the basis that $2I + 1$ lines are obtained for each of the n nuclei, where I is the spin of the nuclei concerned. Spin-spin coupling generally decreases with an increasing number of chemical bonds between the atoms whose nuclei are coupled, but anomalous results have been found for some fluorine compounds (148, 163).

It is important to note that atoms which have the same chemical shift need not necessarily be magnetically equivalent. Each of the vinyl protons in diketene is spin coupled to a different degree with the methylene protons (9). This arises because the vinyl protons, being in the plane of the ring, are each a different distance from the methylene protons, which are perpendicular to the plane of the ring, as shown in the formula for diketene.



Normally spin coupling between magnetically identical nuclei is not observable. However, it can be determined if the magnetically equivalent nuclei are coupled to another nucleus to different extents. An example of this situation is lead tetraethyl (11). The methyl and methylene groups have the same chemical shift but are spin coupled to a different extent with the lead nucleus. As a result, spin-coupling between the two groups of protons may be observed. When the spin-coupling with the lead nucleus is removed, in a manner described later, only a single resonance line is found. A more subtle example is the spin coupling of otherwise equivalent protons to C^{13} in natural abundance (33). Since it is very unlikely that two C^{13} atoms will be adjacent, hydrogen atoms bound to a C^{13} atom will be magnetically different from chemically identical hydrogen atoms bound to an adjacent C^{12} atom. Therefore fine structure due to spin coupling will be observed with an intensity proportional to the abundance of C^{13} . A practical consequence of this is that weak peaks may appear about the principal peak of a pure solvent such as dioxane or acetone, under high gain. Therefore the presence of weak side peaks does not necessarily mean that a solvent is impure, for nuclear magnetic resonance use, and other criteria of purity should be used.

Spin-spin coupling is thought to occur not by direct interaction of the spins through space, but rather through polarization of the bonding electrons by the nuclear spin (66). Therefore fine structure due to spin coupling is frequently useful in determining the number of magnetically equivalent nuclei attached to an atom adjacent to the one being observed. An attempt has been made to account quantitatively for at least part of the spin coupling in molecules where the magnetic shielding is highly anisotropic (131).

C. INTERACTION OF SPIN COUPLING AND CHEMICAL SHIFT

The foregoing remarks about the line shapes obtained by spin-spin coupling are strictly true only when the magnitude of the coupling is much less than the chemical shift between the coupled nuclei. This will always be the case in spin coupling of different elements but is frequently not the situation for nuclei of the same element. When the chemical shift is not large compared to the spin coupling it is necessary to treat the system by perturbation methods, or a complete solution of the Hamiltonian for the system must be done (98). Several treatments of this nature have been done on systems which are of common occurrence, and these are listed in table 1. The notation which has been developed for describing these systems will be used throughout this article (13). Nuclei of the same species for which the chemical shift difference is comparable to the spin-spin coupling are denoted by the letters A, B, C, etc. Nuclei of a different

TABLE 1
Analysis of chemical shift and spin coupling interaction

System	Molecule	Reference	System	Molecule	References
AX.....	2,3,5,6-D ₄ -fluorobenzene	(10)	AB _s	Methyl mercaptan	(1)
AB.....	S-Guaiazulene	(13)		Methyl alcohol	(80, 38)
	2-Bromo-5-chlorothiophene	(5)	A ₂ X ₂	1,1-Difluoroethylene	(98)
	Dichloroacetaldehyde	(5)		4-Pyridine-d ₁	(156)
	Acepleiadylene	(158)	ABC ₂	2,3-Dibromopropene	(5)
A ₂ X.....	2,4,6-D ₃ -fluorobenzene	(10)	A ₂ B ₂	Naphthalene	(132)
ABX.....	2,3-Lutidine	(13)		o-Dichlorobenzene	(132)
	1-Fluoro-1-chloroethylene	(99)		1-Chloro-2-bromoethane	(132)
	1,1-Difluoro-2-chloroethylene	(99)		β-Propiolactone	(5)
	3-Pyridine-d ₁	(156)		Acepleiadylene	(158)
	Diphosphite ion	(29)		X  Y	(145)
ABC.....	Chloroperfluoroethylene	(99)	AB ₂ X ₂	Pyridine	(156)
	Bromoperfluoroethylene	(99)	A ₂ B ₂ X.....	4-D-fluorobenzene	(10)
	Cyanoperfluoroethylene	(99)	A ₂ B ₂	Ethyl bromide	(5)
	Formamide	(126)		Aluminum triethyl	(27)
	3-Methylsalicylic acid	(144)		Gallium triethyl	(27)
	2,4-Dinitrochlorobenzene	(144)	A ₂ B _s	Propane	(111)
	3-Chloro-2-toluidine	(144)	A _n B _m		(5)
AB ₂	2,6-Lutidine	(13)			
	1,1,2-Trichloroethane	(5)			
	Azulene	(158)			
	3,3-Dimethyl-1-butene	(2)			
	2,6-Pyridine-d ₂	(156)			
	3-Nitrosalicylic acid	(144)			
	3-Nitro-o-xylene	(144)			
	2,5-Dichloronitrobenzene	(144)			

species, or of the same species with the resonance position well separated from A or B, are denoted by the letters X, Y, Z. A subscript is used to tell the number of nuclei of each type. For example, CH₂=CF₂ would be described as an A₂X₂ system and CHCl₂CH₂Cl as an AB₂ system.

It should be noted that the magnitude of spin coupling is independent of field strength. Therefore spectra obtained at different field strengths are frequently helpful in interpreting chemical shift and spin coupling interaction. In general it is preferable to obtain the spectra at as high a field strength as possible in order to minimize the effect of spin coupling.

D. REMOVAL OF SPIN-COUPLING EFFECTS

Since spin-coupling effects are caused by a specific orientation of a nucleus (X) to which another (A) is coupled, if the orientation of nucleus X were rapidly changed, nucleus A would only experience the average orientation of X and not its individual orientations. In other words, the spin-coupling multiplet would become a single line. This rapid reorientation can be produced by saturating nucleus X with an intense radiofrequency at its resonant frequency. This has been treated theoretically in considerable detail (15).

The most common experimental application has been in the saturation of one nuclear species while obtaining the resonance spectra of another nuclear species (16, 126). However, one example has also been reported in which one group of

protons was saturated while the spectra of a nonequivalent group of protons was being observed (5). In these cases a double-coil, induction-type method was used to observe the spectra. It would seem easier to use a single-coil, bridge-type method for observing the spectra and to use another coil, "crossed" with the first, for saturation purposes. This would remove the difficulty of protecting the receiver when very similar frequencies are used for saturation and for obtaining the resonance spectra. Such a system has been used for "wide line" spectra (149). Its adaptation to high-resolution work would only involve the usual difficulties of the single-coil method.

Nuclei with spin greater than $\frac{1}{2}$ have, in addition to a magnetic moment, a quadrupole moment. If the quadrupole moment is large, the relaxation time T_1 becomes quite small and considerable broadening of the magnetic resonance lines can occur. This broadening is often sufficient to obscure the multiplet structures expected for nuclei with spin greater than $\frac{1}{2}$ and gives instead a broad envelope.

Besides the effect of the quadrupole moment on the spectrum of the nucleus possessing it there is also an effect on nuclei spin coupled to it even when they possess no quadrupole moment. If the relaxation time of the nucleus with spin greater than $\frac{1}{2}$ is very short, it reorients rapidly and the nuclei spin coupled to it experience only the average value and therefore yield a single sharp line. This is analogous to the effect produced in double resonance experiments. If the relaxation time is long, the spin-coupled nuclei "see" the separate orientations of the other nucleus and give the usual multiplet structure. In intermediate cases the spin-spin multiplet is broadened into a wide envelope. A quantitative theory for this has been developed (130). In cases where broadening occurs by quadrupole interaction it may be removed by double resonance techniques (126).

E. SOLUTION EFFECTS

1. Diamagnetism

In addition to the shielding of the nucleus from the magnetic field by intramolecular effects, the diamagnetic susceptibility of the bulk sample changes the field from its usual value between the magnet pole pieces. Equations have been developed to give the degree of shielding (reference 6, p. 78). These depend upon the shape of the sample and assume that any individual molecule is contained within a spherical cavity. An empirical correction to this assumption must be applied (17). The resulting correction of the field is given by $H = H^0(1 - 2.60 k)$ for a cylindrical sample, where H^0 is the applied field and k is the volume magnetic susceptibility of the solution. In accurate determinations of chemical shifts it is necessary to apply this correction. However, for structure determinations where a single solvent is used, this correction can frequently be ignored (31). Table 2 lists the volume susceptibilities for several common solvents.

If the solvent has a high magnetic anisotropy the preceding calculations may frequently be in error. This is especially the case for aromatic substances, either as solvents or as solutes (17). Varying chemical shifts may also be obtained when paramagnetic ions are added to the solution (123). Although most of these

TABLE 2
Volume magnetic susceptibilities of common solvents

Solvent	Susceptibility $\times 10^{-6}$	Temperature	Reference
		$^{\circ}\text{C.}$	
Acetone.....	-0.464	20	(56)
Benzene.....	-0.617	20	(56)
Carbon disulfide.....	-0.681	30	(136)
Carbon tetrachloride.....	-0.692	20	(56)
Chloroform.....	-0.735		(56)
Cyclohexane.....	-0.631	27.5	(51)
Dioxane.....	-0.589	Room temperature	(119)
Methylene chloride.....	-0.734	20	(56)
Toluene.....	-0.628	25	(7)
Water.....	-0.719	20	(56)

effects have been observed for proton resonance spectra, some anomalous solution effects have also been observed for fluorine resonance spectra (50).

2. Association

Polar molecules in solution may frequently orient themselves in some preferred manner. Therefore the intermolecular environment, and the nuclear magnetic resonance spectra, may vary with concentration and with the nature of the solvent. This effect is most pronounced with molecules capable of forming hydrogen bonds amongst themselves or with the solvent. Studies have been made on alcohols, phenols, and acids, and the shift in the resonance position has been correlated with equilibria between hydrogen-bonded dimers through tetramers and their dissociation to monomers (12, 32, 72, 140, 150, 151). Even substances like chloroform are found to form hydrogen bonds or complexes with a wide variety of solvents (71, 81, 139). Therefore care must be taken in the interpretation of spectra where association may be suspected. If there is any doubt, the spectra should be obtained in solutions of varying concentrations and extrapolated to infinite dilution.

This shift of hydrogen-bonded protons can be used advantageously when there is an overlap of the resonance of these protons with those of another grouping in the molecule. This overlap can be removed by shifting the hydrogen-bonded protons by dilution or by addition of water, acid, or base. An interesting example is the shifting of the resonance of the hydroxyl proton in alcohols dissolved in carbon tetrachloride by the addition of chlorine gas (34). Presumably this is caused by association of the chlorine with the hydroxyl in a similar manner to the charge-transfer complexes formed by the halogens in aqueous solution.

Advantage has been taken of these shifts with solvent composition to study keto-enol tautomerism in easily enolizable compounds (76, 138). It has been found that in diethylamine and triethylamine, acetylacetone exists entirely in the enolic form (141).

F. STANDARDS OF REFERENCE

Since the long-term accuracy and reproducibility of the magnetic field are not usually sufficient, it is necessary to refer the chemical shifts to the resonance fre-

quency of the nuclei of some standard compound. If both the resonance to be determined and that of the standard compound are observed at the same time, the difference between them can be accurately determined by modulating the sweep frequency and producing side bands about the resonance peak (8). This method is preferable to a separate calibration of sweep rate, since it is independent of any transient drifting of the field.

The standard compound may be a constituent of the solution whose spectrum is being measured (an internal standard) or it may be separately enclosed (an external standard). Internal standards have the advantage that no corrections are necessary for the bulk diamagnetic susceptibility of the solution. However, there are many disadvantages to internal standards. They must not react with any of the substances in solution nor associate with them in any preferred configuration. Preferably the standard should be magnetically isotropic and have only a single resonance peak well separated from any peaks likely to be encountered in the substances being studied. Tetramethylsilane is such a standard for proton resonance spectra (177), and fluorotrichloromethane has most of these features as a standard for fluorine resonance spectra (52). Even if an internal standard possesses all of these characteristics, there is still the disadvantage that the compound studied cannot simply be recovered after its spectrum has been determined. Frequently for solids or viscous liquids the solvent is used as an internal standard.

External standards have none of these disadvantages but do have the disadvantage that for reasonably accurate work it is necessary to make a correction for the volume susceptibility of the solution being studied. This correction is large enough to cause an appreciable error, even when it is applied, in work of the highest accuracy. A common method of using an external standard is to introduce it in a sealed capillary into the tube containing the sample. However, appreciable errors may occur in this method (188, 189). A preferable procedure is to use concentric thin-walled tubing with the standard in the thin annular space between the tubes (104). It must be remembered that these procedures do not correct for the usually appreciable effects of association.

The separation between resonance peaks, in cycles, is frequently divided by the radiofrequency used and multiplied by some large number to give a dimensionless unit. This value will be independent of the radiofrequency used when chemical shifts are obtained but not for spin-spin coupling. Therefore it is preferable to tabulate spin couplings only in cycles per second. A positive sign has been given to the chemical shift when it occurs at both high and low field with respect to the standard and the result has been multiplied by 10^5 – 10^8 (17, 19, 103, 163, 177). In addition, various symbols have been used to indicate this chemical shift, with the same symbol often having different meanings for different authors. Since the symbol δ has been used most frequently and the shift is quite commonly given in parts per million, that will be done in this review. In the interests of uniformity further restrictions will be imposed on the meaning of the symbol. A positive number will indicate that the resonance of the sample occurs at a higher field than that of the standard. A superscript will be used to indicate the substance used as a standard of reference and a subscript to tell whether an

TABLE 3
Conversion formulae*

$\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = \delta_{\text{ext.}}^{\text{H}_2\text{O}} + 2.49^\dagger$	$\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = \delta_{\text{ext.}}^{\text{CH}_2\text{Cl}_2} + 1.94$
$\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = \delta_{\text{ext.}}^{\text{Si}(\text{CH}_3)_4} + 7.27$	$\delta_{\text{ext.}}^{\text{CF}_3\text{COOH}} = \delta_{\text{int.}}^{\text{CCl}_3\text{F}} - 76.64$
$\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = \delta_{\text{ext.}}^{\text{C}_6\text{H}_{12}} + 5.83$	$\delta_{\text{ext.}}^{\text{CF}_3\text{COOH}} = \delta_{\text{int.}}^{\text{C}_4\text{F}_8} + 61.49$
$\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = \delta_{\text{ext.}}^{\text{CH}_3\text{COCH}_3} + 5.18$	$\delta_{\text{ext.}}^{\text{CH}_3\text{C}\equiv\text{COH}} = \delta_{\text{ext.}}^{\text{C}_6\text{H}_6} + 50$
$\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = \delta_{\text{ext.}}^{\text{CHCl}_3} + 0.02$	

* The first part of this table was prepared from the difference in the chemical shift of the various proton compounds in dilute solution in carbon tetrachloride relative to tetramethylsilane. To convert $\delta_{\text{ext.}}^{\text{A}}$ to $\delta_{\text{int.}}^{\text{A}}$, corrections must be made for the volume magnetic susceptibility of the solution (37).

† Since water is not soluble in carbon tetrachloride, it was used externally and corrections were made for susceptibility effects.

internal or external standard was employed. Thus $\delta_{\text{int.}}^{\text{H}_2\text{O}} = +3.12$ would indicate a chemical shift of 3.12 p.p.m. to higher field than the protons in water, used as an internal standard. Similarly, $\delta_{\text{ext.}}^{\text{C}_4\text{F}_8} = -2.56$ would indicate a chemical shift of 2.56 p.p.m. to lower field than the fluorine atoms in perfluorocyclobutane, used as an external standard. Although there should be no disagreement between the values obtained using an internal or an external standard, provided the appropriate corrections for magnetic susceptibility and dilution are made, much interesting work has been done without sufficient information for these corrections to be applied.

Solvents which have often been used are carbon tetrachloride, carbon disulfide, acetone, benzene, cyclohexane, water, dichloromethane, perfluorocyclobutane, trifluoroacetic acid, and, specifically for proton resonance, completely deuterated chloroform, benzene, acetone, and water. In table 3 are given the approximate conversion factors for transposing data from one standard of reference to another. These were the numbers used to put the various measurements in a common form for this review article. By their nature these cannot be exact, but they are sufficiently accurate to indicate the region where a given type of chemically bonded nuclei will occur.

The standard for proton resonance has been chosen as $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 0.000$, in agreement with the recommendations of American Petroleum Institute Research Project 44. Water, which was often used as an external reference, was found to be unsatisfactory, since the position of its resonance line shifts 0.005 p.p.m. per °C., owing to a change in the extent of hydrogen bonding with change in temperature (177). Most of the proton chemical shifts were actually obtained relative to benzene or tetramethylsilane as internal standard and have been converted by the addition of an appropriate constant factor.

The standard for fluorine resonance has been chosen as $\delta_{\text{ext.}}^{\text{CF}_3\text{COOH}} = 0.000$, since most of the work published on chemical shifts for fluorine has been with this standard. Although it is definitely not the best standard, it will be used since there is, as yet, little agreement on a standard presentation.

II. PROTON RESONANCE SPECTRA

By far the greatest activity in high-resolution nuclear magnetic resonance has been in determining the proton resonance spectra of organic compounds. Since commercially available instruments have good sensitivity, a sample of a fraction of a millimeter is sufficient and signals can be clearly detected at a concentration of about an atom per cent.

It must be remembered that groupings bound to the same carbon atom as a proton exert a much more profound effect on the resonance position of the proton

than the type of grouping the carbon atom is in. For example, in $\text{CH}_2\text{BrCH}_2\overset{\text{O}}{\parallel}\text{CCH}_3$ the protons of the grouping $-\text{CH}_2\text{Br}$ will appear at a position characteristic of $-\text{CH}_2\text{Br}$ and not one characteristic of $-\text{CH}_2\overset{\text{O}}{\parallel}\text{C}-$. Thus care must be taken in classifying chemical shifts of small polyfunctional compounds.

A. CHEMICAL SHIFT AND CHEMICAL BONDING

The chemical shifts observed for protons tend to be smaller than for most other isotopes with a total range of about 14 p.p.m. of the applied field.

1. Aliphatic compounds

(a) Linear compounds

Protons of a methyl group attached to a saturated hydrocarbon chain have $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6}$ values from 6.23 to 6.38. Those on a methylene group in a hydrocarbon chain appear from 5.92 to 6.29, with those on highly branched chains showing the greatest shift. A tertiary hydrogen appears in the range 5.69 to 5.71. Some results for specific compounds are shown in table 4. For any given compound the resonance due to methyl protons is always found at higher field than that of methylene protons, which is at higher field than that of tertiary hydrogens. (For

TABLE 4
Chemical shift of saturated aliphatics

Compound	Protons	Chemical Shift	Reference
$(\text{CH}_3\text{CH}_2\text{CH}_2)_2\text{S}$	$-\text{CH}_3$	6.27	(179)
$(\text{CH}_3)_2\text{CHCH}_2\text{I}$	$-(\text{CH}_2)_2$	6.29	(179)
$\text{CH}_3(\text{CH}_2)_3\text{NH}_2$	$-\text{CH}_3$	6.35	(179)
$\text{CH}_3(\text{CH}_2)_5\text{CH}_3$	$-\text{CH}_3$	6.38	(179)
$(\text{CH}_3)_3\text{CCH}_2\text{CH}(\text{CH}_3)_2$	$-(\text{CH}_2)_2$	6.41	(179)
Methylcyclohexane	$-\text{CH}_3$	6.23	(31)
$[(\text{CH}_3)_2\text{C}]_2\text{CH}_2$	$-\text{CH}_2$	6.29	(179)
$\text{CH}_3(\text{CH}_2)_4\text{CH}_3$	$-(\text{CH}_2)_4$	6.02	(179)
$\text{CH}_3(\text{CH}_2)_4\text{CH}_2\text{F}$	$-(\text{CH}_2)_4$	5.92	(179)
$\text{CH}_3(\text{CH}_2)_5\text{CH}_2\text{CH}_2\text{Br}$	$-(\text{CH}_2)_5$	5.99	(179)
$(\text{CH}_3)_3\text{CH}$	$-\text{CH}$	5.71	(179)
$(\text{CH}_3)_2\text{CHCH}_2\text{Cl}$	$-\text{CH}$	5.69	(179)

TABLE 5
Chemical shift of olefins and acetylenes

Compound	Proton	Chemical Shift	Reference
$\text{CCl}_3\text{CH}_2\text{CHCH}=\text{CH}_2$ $\quad \quad \quad $ $\quad \quad \quad \text{CH}_3$	$-\text{CH}_3$	5.78	(179)
$(\text{CH}_3)_2\text{C}=\text{CHCH}_2\text{CH}_2\text{CHCH}_2\text{CHO}$ $\quad \quad \quad \quad \quad $ $\quad \quad \quad \quad \quad \text{CH}_3$	$-(\text{CH}_3)_2$	5.67	(179)
$(\text{CH}_3)_2\text{C}=\text{CHCH}_3$	$-(\text{CH}_3)_2$ and $-\text{CH}_3$	5.64	(179)
$\text{CH}_3\text{CH}=\text{CHCH}_2\text{OH}$	$-\text{CH}_3$	5.58	(179)
$\text{CH}_2=\text{CCH}_2\text{C}(\text{CH}_3)_3$	$-\text{CH}_2-$	5.36	(179)
CH_3 $ $ $\text{CH}_3-\text{CHCH}_2(\text{CH}_2)_4\text{CH}_2\text{CH}=\text{CH}_2$	$-\text{CH}_2-$	5.32	(179)
$(\text{CH}_3)_2\text{C}=\text{CH}_2$	$=\text{CH}_2$	2.67	(179)
$(\text{CH}_3)_2\text{C}=\text{CHCH}_3$	$=\text{CH}-$	2.06	(179)
$\text{HC}\equiv\text{CCH}_2\text{OH}$	$\text{HC}\equiv$	4.94	(179)
$\text{HC}\equiv\text{CCH}_2\text{Cl}$	$\text{HC}\equiv$	4.87	(179)
$(\text{C}_6\text{H}_5)_2=\text{CH}_2$	$=\text{CH}_2$	1.87	(179)

detailed information on a wide range of compounds references 31, 179, and 18 should be consulted.)

If an olefinic bond is present, the resonances are shifted to lower field. Methyl groups on an allylic carbon have $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6}$ values of about 5.78, while those on a double-bonded carbon have $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6}$ values from 5.68 to 5.58. For methylene groups on a doubly bonded carbon $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} =$ about 5.34. Protons on a double-bonded carbon appear over a wide range from $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 2.67$ to $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 2.06$. Protons on a triply bonded carbon appear at about $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 4.94$. If the multiple bond is conjugated to an aromatic ring, a carbonyl group, or another multiple bond, the resonance position will be shifted to a more negative value. Values for some specific cases are shown in table 5. If a carbonyl group is attached to one side of the double bond, protons or methyl groups on the other side of the double bond appear at lower field if they are cis to the carbonyl than if they are trans (74, 105).

(b) Cyclic compounds

On a three-membered ring the resonance position of the protons is primarily determined by the nature and position of substituents on the ring. Cyclopropane has $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 7.06$, and protons in substituted cyclopropanes would probably appear at somewhat higher values than for a corresponding situation on an aliphatic chain. The protons attached to carbon atoms of larger rings appear at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 5.59$ –5.84. In substituted cyclohexanes axial protons adjacent to bulky axial groups appear at lower field than chemically equivalent but less hindered protons (26). The substituents on substituted cyclohexanes also seem to appear at somewhat lower field when they are axial (86). It is also found that spin coupling between protons both of which are axial is greater than between an axial and an equatorial proton, while spin coupling between an axial and an equatorial proton is greater than between two equatorial protons (87).

TABLE 6
Chemical shift of cycloalkanes

Compound	Protons	Chemical Shift	Reference
Cyclopentane	$-\text{CH}_2-$	5.77	(179)
Cyclohexane	$-\text{CH}_2-$	5.84	(179)
Methylcyclohexane	CH_3-	6.36	(179)
Cyclopentene	$=\text{CH}$	1.62	(31)
1-Methylcyclohexene	$=\text{CH}$	1.98	(31)
4-Methylcyclohexene	$=\text{CH}$	1.72	(31)
1-Methylcyclopentene	$-\text{CH}_3$	5.32	(31)

TABLE 7
Chemical shift of aromatic protons

Substituent	Position	Chemical Shift	Substituent	Position	Chemical Shift
$-\text{NO}_2$	Ortho	-1.1	$-\text{CF}_3$	Ortho, meta, para	-0.2
	Meta, para	-0.6	$-\text{Cl}, -\text{Br}$	Ortho, meta, para	0.0
$-\text{SO}_2\text{Cl}$	Ortho	-1.0	$-\text{CH}_2\text{Cl}, -\text{CH}_2\text{Br}$	Ortho, meta, para	0.0
$-\text{C}(=\text{O})-$	Ortho	-0.6	$-\text{CH}_3$ or alkyl	Ortho, meta, para	0.2
	Meta, para	-0.3	$-\text{OCH}_3$	Ortho, meta, para	0.4
$-\text{CCl}_3$	Ortho	-0.6	$-\text{NH}_2$	Ortho	0.7
	Meta, para	-0.1		Meta, para	0.4
$-\text{SO}_2\text{F}$	Ortho	-0.6			
$-\text{C}\equiv\text{N}$	Ortho, meta, para	-0.2			

Methyl and methylene groups attached to a cyclic system have about the same chemical shift as those on an aliphatic chain. Values for a few typical compounds are shown in table 6. If the ring contains a double bond, the olefinic hydrogen has a chemical shift from $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 1.72$ to $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 1.62$, rather more negative than those in a straight chain. Substitution of an alkyl group for one olefinic hydrogen increases the chemical shift of the other by about 0.25 p.p.m. A methyl group on a double bond in a ring also appears at lower field than in a straight chain, usually at about $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 5.39$.

2. Aromatic compounds

Protons on an aromatic ring appear at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 0.69$ to -1.17 , but fortunately it is possible to specify the shifts in more detail. It has been shown that protons meta and para to a substituent have a more similar chemical shift than protons ortho to a substituent (37). This seems to indicate that only inductive effects of the substituent influence the chemical shift of the ring protons, whereas the usual substituent constants include a polarization effect. Table 7 lists the region in which absorption of proton resonance appears as a function of the nature and position of the substituent on the ring (37, 179). Since spin-spin coupling constants for aromatic protons are often not much smaller than chemical shifts

between the protons, complicated patterns are observed and it is difficult to get the exact chemical shifts (63, 156).

A further complication occurs with aromatic compounds. The shielding of the ring protons is thought to be greatly affected by the circular current of π electrons induced by the magnetic field (14). This theory has been refined to give better agreement with the observed spectra (67, 100). It nicely explains the spectra of cyclophanes (182) but does not fit the series $C_5H_5-Na^+$, C_6H_6 , $C_7H_7^+Br^-$ (89). The spectra of a wide variety of compounds of the ferrocene type have been reported (128).

Methyl groups on a benzene ring appear at $\delta_{ext.}^{C_6H_6} = 4.94-5.05$. Many of these shifts have been accurately determined, and no correlation is found with the Hammett or Taft σ function (178). However, there is good correlation between the chemical shift in the meta or ortho position, and that in the para position. This work was sensitive enough to detect the difference in chemical shift between the groups $-CH_3$ and $-CH_2D$ in toluene (176).

A methylene group attached to a benzene ring absorbs at about $\delta_{ext.}^{C_6H_6} = 4.7$ and a methyl group beta to an aromatic ring at about $\delta_{ext.}^{C_6H_6} = 6.1$. Alkyl groups which are further removed will appear in the same region as in a purely aliphatic compound.

3. Oxygenated compounds

(a) Hydroxy compounds

If a nucleus is rapidly exchanged between two or more different magnetic environments, its resonance absorption will be that of the average environment (62). This condition of rapid exchange is frequently encountered in protons chemically bonded to oxygen or nitrogen. This is primarily the reason why the resonance absorption of hydroxylic protons occurs over a very wide range. They may exchange among those which are hydrogen bonded and those which are not, as well as with any other exchangeable hydrogens in the molecule itself or in the solvent. If a resonance peak is thought to be due to a hydroxyl or other readily exchangeable proton, this may be confirmed by adding to the sample a small amount of water or other source of readily exchangeable hydrogen atoms. The peak will increase in intensity and shift its position if it is due to rapidly exchanging protons.

For a methyl group attached to a hydroxyl group $\delta_{ext.}^{C_6H_6} = 3.91$. A methylene group appears at about $\delta_{ext.}^{C_6H_6} = 3.61$ and a tertiary hydrogen at about $\delta_{ext.}^{C_6H_6} = 3.26$. Methyl and methylene groups beta to a hydroxyl group appear at about $\delta_{ext.}^{C_6H_6} = 5.99$ and 5.59, respectively. If further removed from the hydroxyl group, their chemical shift is in the same region as in aliphatic hydrocarbons. If the hydroxyl group is esterified all these chemical shifts are reduced, with α -methyl and α -methylene groups appearing at $\delta_{ext.}^{C_6H_6} = 3.71$ and 3.16, respectively. Little change is seen in groups which are beta or further removed from the hydroxyl group. If the hydrogen of the hydroxyl group is replaced by an alkyl group, to give an ether, there is little change in the position at which the other resonances appear. The chemical shifts for some representative compounds are shown in table 8.

TABLE 8
Chemical shift of alcohols and esters

Compound	Protons	Chemical Shift	Reference	Compound	Protons	Chemical Shift	Reference
CH ₃ OH.....	—CH ₃	3.91	(31)	(CH ₃ CH ₂ O) ₂ — succinate....	—CH ₃	6.06	(31)
CH ₃ CH ₂ OH.....	—CH ₂ —	3.61	(31)		—CH ₂	3.21	(31)
	—CH ₃	6.03	(31)	(CH ₃ O) ₂ — adipate.....	—CH ₃	3.66	(31)
(CH ₃) ₂ CHOH.....	=CH—	3.26	(31)	(CH ₃ CH ₂) ₂ O.....	—CH ₃	6.06	(31)
					—CH ₂ —	3.81	(31)

TABLE 9
Chemical shift of carbonyl compounds

Compound	Protons	Chemical Shift	Reference	Compound	Protons	Chemical Shift	Reference
C ₆ H ₅ CHO.....	—CHO	—2.69	(179)	CH ₃ COCH ₃	—CH ₃	5.19	(179)
(CH ₃) ₂ CHCHO.....	—CHO	—2.29	(179)	CH ₃ COOH.....	—CH ₃	5.21	(179)
CH ₃ CH ₂ CHO.....	—CH ₃	6.21	(31)	CH ₃ COOC ₂ H ₅	—CH ₃	5.33	(179)
	—CH ₂	4.94	(31)	CH ₃ CH ₂ COOH.....	—CH ₂ —	4.91	(31)

(b) Carbonyl

A proton attached to a carbonyl group, i.e., an aldehydic proton, is the least shielded of all normally encountered groupings. If the aldehyde group is attached to an aromatic ring it appears at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = -2.69$ to -2.37 . For an aliphatic aldehyde the region is $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = -2.44$ to -2.29 .

Methyl groups attached to a carbonyl group appear at about $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 0.1$ if alpha to the carbonyl group and at about $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 1.2$ if beta or further removed. Methylene groups appear at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = -0.2$ if alpha and 0.8 if beta. Some examples are shown in table 9.

In a molecule with a carboxylic acid grouping the resonance absorption of the acidic hydrogen may occur over a very wide range, as with hydroxyl hydrogens, since they are readily exchangeable. Methyl and methylene groups attached to this carbonyl group appear at about the same region as those attached to the carbonyl group of an aldehyde or ketone. Esterification of the carboxyl group causes little change in the position of the resonance absorption. A few representative examples are shown in table 9.

(c) Cyclic compounds

In alicyclic compounds there is some variation in the resonance position of the ring protons, depending upon the size of the ring. However, it is always found that the chemical shift will increase the further the protons are removed from the oxygen-containing functional group. Methyl groups attached to the ring are little affected by the functional group unless they are alpha to it, in which case the chemical shift is similar to that in straight-chain compounds.

Ring protons on three-membered cyclic ethers appear at about $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 4.7$. Methyl groups attached to the ring appear in the same region as with straight-

TABLE 10
Chemical shifts of cyclic oxygenated compounds

Compound	Protons	Chemical Shift	Reference
	All CH ₂	5.26	(179)
	-CH ₂ C=O Other -CH ₂	5.03 5.41	(31) (31)
	-CH -CH ₂	4.70 6.06	(31) (31)
	-CH ₂ O -CH ₂ -	3.65 5.46	(31) (31)
	-CH ₂ -CH -CH	4.77 -0.11 1.14 and 0.87	(36) (36) (36)
	-OCH ₂ -CH ₂ C=O	3.06 3.80	(179) (179)
	-OCH ₂ -CH ₂ C=O	3.00 4.97	(179) (179)

chain ethers or alcohols. In larger cyclic ethers the methylene groups furthest from the oxygen atom appear at highest field. The furan ring system has been carefully studied, and may be identified along with the extent of its substitution (36).

In γ - and δ -lactones the methylene group adjacent to the carbonyl group appears at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 4.98$, while the methylene group adjacent to the oxygen atom appears at about $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 3.04$ for β -, γ -, and δ -lactones.

Chemical shifts for some representative compounds are shown in table 10.

4. Compounds containing other elements

(a) Nitrogen-containing compounds

The hydrogen bonded to nitrogen in amines is readily exchangeable, and therefore its resonance absorption may occur over a wide range as with alcohols

TABLE 11
Proton chemical shifts in nitrogen-containing compounds

Compound	Protons	Chemical Shift	Reference	Compound	Protons	Chemical Shift	Reference
$(\text{CH}_3)_3\text{CHNH}_2$	$-\text{CH}=\text{}$	4.41	(179)	$\text{CH}_3\text{CON}(\text{CH}_2\text{CH}_3)_2$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3\text{C}- \end{array}$	5.29	(31)
	$-\text{CH}_3$	6.27	(179)		$-\text{CH}_2-$	3.91	(31)
$(\text{CH}_3\text{CH}_2)_2\text{NH}$	$-\text{CH}_2-$	4.56	(31)		$-\text{CH}_3$	6.21	(31)
$(\text{CH}_3)_3\text{N}$	$-\text{CH}_3$	5.15	(179)	$\begin{array}{c} \text{NO}_2 \\ \\ \text{CH}_3\text{CHCH}_3 \end{array}$	$-\text{CH}_3$	5.71	(179)
					$-\text{CH}=\text{}$	2.84	(179)

and acids. The rate of this exchange has been studied and was found to decrease with increasing acidity of the solution (60, 61, 91, 102). A methyl group alpha to an amino nitrogen appears at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 5.15$; if beta to an amino nitrogen it appears at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 6.21$. For a methylene group the numbers are 4.56 and 5.69. A tertiary hydrogen next to an amino group has a chemical shift of $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 4.41$.

A methyl group attached to an amide nitrogen appears at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 4.66$, and a methylene group at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 3.98$. If the methyl group is beta, it will appear at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 6.21$; if it is attached to the carbonyl group of the amide, it will appear at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 5.38$. A nitro group lowers the position of a methyl group attached to it to $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 3.00$, and a tertiary hydrogen similarly attached appears at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 2.84$. If the methyl group is one removed it is found at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 5.71$. The chemical shifts for a few representative compounds are shown in table 11.

(b) Sulfur-containing compounds

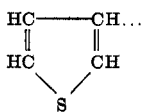
If oxygen is replaced by sulfur, the chemical shifts of protons in the analogous molecules are increased. In aliphatic thiols a methyl group appears at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 5.2, 5.9, 6.2$, and 6.3 if alpha, beta, gamma, or delta to the thiol group. For a methylene group the numbers are $4.8, 5.8$, and 6.1 if the methylene group is alpha, beta, or gamma, respectively. A tertiary hydrogen has a chemical shift of $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 4.3$ if alpha and one of 5.7 if beta to the thiol group. The chemical shifts for protons in aliphatic sulfides are very similar to those in thiols, but in disulfides they are somewhat reduced, with a methyl group appearing at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 4.8$ if alpha and 5.8 if beta to the sulfur atom.

As the oxidation number of the sulfur increases, the chemical shift of a methyl group attached to it decreases. The resonance position of dimethyl sulfide is at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 5.20$ and of dimethyl sulfoxide at 4.98 . Similarly, dimethyl sulfite appears at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 3.70$ and dimethyl sulfate at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 3.34$. The protons on a thiophene ring appear in the same region as other aromatic protons, with those alpha to the sulfur coming at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 0.1$ and those which are beta at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 0.3$. Some representative values are listed in table 12.

(c) Halogen-containing compounds

Halohydrocarbons were among the first group of compounds upon which accurate measurements of chemical shifts were made. Since the effects of bulk

TABLE 12
Miscellaneous proton chemical shifts

Compound	Protons	Chemical Shift	Reference	Compound	Protons	Chemical Shift	Reference
$(\text{CH}_3)_3\text{S}$	$-\text{CH}_3$	5.20	(179)	$\text{CH}_3\text{CH}_2\text{I}$	$-\text{CH}_2-$	4.18	(179)
$(\text{CH}_3)_2\text{CHSH}$	$-\text{CH}=\text{}$	4.26	(31)		$-\text{CH}_3$	5.42	(179)
$(\text{CH}_3\text{CH}_2)_2\text{S}_2$	$-\text{CH}_2$	4.69	(31)	$(\text{CH}_3)_2\text{CHBr}$	$-\text{CH}=\text{}$	3.08	(179)
	$-\text{CH}-\text{S}$	0.09	(179)	$\text{C}_2\text{H}_5\text{CH}_2\text{Cl}$	$-\text{CH}_2-$	3.83	(179)
	$-\text{CH}=\text{}$	0.24	(179)	$\text{ClCH}_2\text{CH}_2\text{Cl}$	$-\text{CH}_2-$	3.59	(179)

diamagnetic susceptibility and association in solution were often not fully appreciated, there are many conflicting reports of their chemical shifts in the literature (3, 19, 37, 103, 171). These effects have been sorted out, and the data of various workers are now somewhat interconvertible. For maximum uniformity the data of Tiers (179) will be used exclusively in this section.

A halogen atom attached to a carbon atom lowers the chemical shift of the hydrogen atoms attached to that carbon atom. Fluorine causes the greatest lowering and the effect is least for iodine. If more than one halogen is attached to the carbon atom, the effect is augmented. The lowering of the chemical shift is decreased for protons on carbon atoms further removed from the halogen.

These results will be treated in more detail in the following section. The shifts for some typical compounds are shown in table 12.

(d) Other compounds

Methyl groups attached to a silicon atom are the most shielded aliphatic protons that have been reported to date (177). Tetramethylsilane appears at $\delta_{\text{ext.}}^{\text{C}_6\text{H}_6} = 7.28$ and siloxanes at 7.19. There has been much work on the proton magnetic resonance spectra of boranes and substituted boranes (114, 152, 153, 165). Unfortunately there is no reference to a standard and only the number of peaks, their intensities, and their multiplicities are presented. Considerable work has been done on the chemical shift of hydrogen in binary hydrides of a large number of elements (40, 157). It is found that there are large effects due to association and magnetic susceptibility differences in the liquid state. When gaseous samples are used, the chemical shifts may be explained by a combined effect of electronegativity and magnetic anisotropy of the element bonded to the hydrogen (157).

B. CORRELATION WITH ELECTRONEGATIVITY

It would be expected that an element with high electronegativity should attract a large share of the valence electrons binding it to hydrogen, thus leaving the proton less shielded from the magnetic field. However, the magnetic anisotropy which occurs because of this dissymmetry in the electron cloud itself gives rise to a shielding effect (157). Therefore there is no simple correlation of

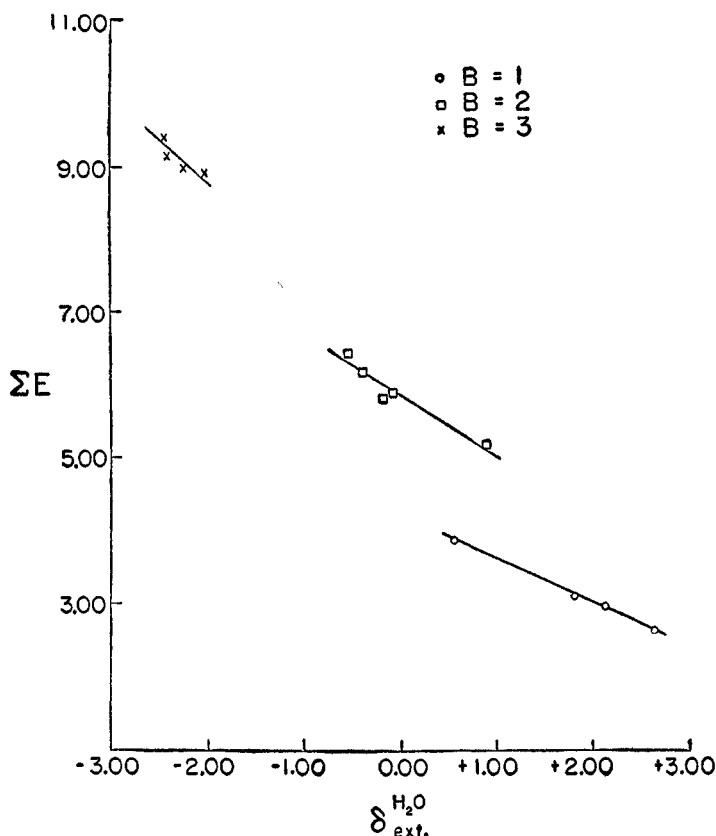


FIG. 1. Electronegativity and chemical shift

chemical shift and electronegativity for the proton resonance spectra of binary hydrides. Similarly, for methyl compounds of all the elements, differences in the geometry of the molecules and the number of unshared pairs of electrons prevent a simple correlation. However, for elements in a given column of the Periodic Table the only effect should be due to electronegativity differences. This has been observed for compounds of the type CH_AX_B , where X is a halogen, and even holds when the electronegativities of different halogens are added. The compounds where $B = 1, 2$, or 3 fall on different lines, a result which is to be expected, since the symmetry of the molecule is changed. However, the agreement within any one group is good, as shown in figure 1.

The effect of the electronegativity of a substituent attached to an aliphatic chain decreases along the chain but is not completely attenuated in the methyl hydrogen atoms of an ethyl group (19). Therefore the relative change in chemical shift of the methyl and the methylene hydrogen atoms should be sensitive to the electronegativity of the element to which the ethyl group is attached. The formula

$$\text{Electronegativity} = 0.695(\delta_{\text{CH}_3} - \delta_{\text{CH}_2}) + \text{constant}$$

fits the halogens if the constant is 1.71 (41). If the constant has a value of 2.1, good agreement is found with the electronegativities of many other elements (166). The need for two different values of the constant was attributed to the large magnetic anisotropy associated with the unshared pairs of electrons on the halogen atoms. A reversal in the relative positions of the methyl and methylene groups should occur if the electronegativity of the element bonded to the ethyl group is less than 2.1. This has been observed, and the effect has been used to investigate the effect of coordination upon the atom to which the ethyl group is attached (11, 27).

A similar type of correlation has been developed for spin-spin coupling of the methyl and methylene protons of an ethyl group, and another for spin-spin coupling of the tertiary hydrogen with the methyl protons in an isopropyl group (58).

C. STERIC EFFECTS

The actual repulsive forces between atoms which are held in close proximity is not thought to influence their nuclear resonance spectra. However, the close proximity implies a slight displacement of the atoms from the positions that they would occupy in the absence of repulsive forces. Furthermore, the close presence of another atom with its electron cloud can introduce a change in shielding, diamagnetic or paramagnetic, due to the magnetic anisotropy of that electron cloud. These effects will be called steric, although their mode of operation is slightly different from what is normally implied by that name.

The No. 4 and No. 5 hydrogen atoms in phenanthrene are considered to be displaced from the plane of the aromatic rings, owing to steric repulsion, and a shift in the position of the resonance from its calculated value is observed (142). Similarly, in ortho-substituted biphenyls there is a shift in the resonance position of the ortho protons on the unsubstituted benzene ring, owing to their interaction with the ortho substituents on the substituted benzene ring (25).

In aliphatic fluorocarbons an anomalous shift in the position of the fluorine resonance has been observed when the fluorine atom is adjacent to many iodine atoms (174, 175). This has been described as a steric effect. Bromine has been shown to have a similar effect on the proton resonance spectra of some cyclic compounds (82). Substituents on a cyclohexane ring may be held in either an equatorial or an axial position. Even if they are otherwise chemically identical they will have a different chemical shift, and therefore they must be shifted owing to a steric effect.

Protons attached to the cyclohexane ring and adjacent in space to bulky groups will appear at lower field than those which are less hindered (26). The methyl protons of acetoxy groups which are joined to the ring in an axial conformation are at lower field than those which are equatorial (86, 87). It is also found that spin-spin coupling between axial protons is considerably larger than between equatorial protons. These results hold equally well for sugars in the pyranose form and are useful in determining their conformations (87). This method has also been used to determine the conformation of the diastereois-

meric 1,3-dimethoxy-2-acetoxycyclohexanes (88). Similar effects are also seen in steroids, but it is usually possible to observe them only for methyl or acetoxy substituents on the steroid skeleton (168).

D. TEMPERATURE EFFECTS

If an external reference is being used, it is found that the position of all the peaks relative to the reference changes with temperature. This is due to a change in density and therefore in the volume diamagnetic susceptibility of the solution. Since the effect of bulk magnetic susceptibility does not influence an internal reference, there is no overall shift with temperature in these cases.

A radical change in the appearance of the proton resonance spectra of some molecules is found to occur when the temperature changes. This occurs because of a change in rate of some internal molecular motion which changes the magnetic equivalence of the protons. An extension of the Bloch equations shows that if nuclei of the same species are rapidly exchanging between different magnetic environments, the resonance absorption will be that of the average environment (62, 77, 97). The shape of the resonance line has been determined as a function of the rate of exchange and of other parameters.

Chemical reactions whose rates may be measured by this method are proton transfers of labile hydrogen atoms and slightly hindered rotation about chemical bonds. One such example is the rate of hydrogen exchange between H_2O_2 and H_2O as a function of pH (4). The rate of proton transfer between ammonia molecules in aqueous solution, and between the methylamines, has been carefully measured (60, 61, 91, 102, 113). The rate of inversion about pyramidal nitrogen in several substituted ethylenimines has also been determined (20, 22).

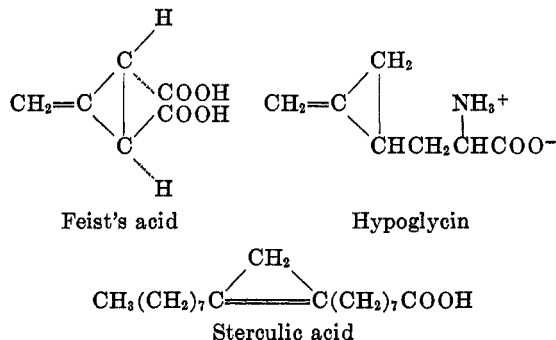
Hindered rotation can be considered to arise from two causes: the partial double-bond character of the bond being considered, or bulky groups attached to the atoms joined by the bond. The partial double-bond character of the carbon-nitrogen bond in amides, alkyl nitrites, and nitrosoamines gives rise to hindered rotation, which has been studied by the dependence of their proton resonance spectra on temperature (62, 90, 121, 124, 125).

If rotation is hindered about the carbon-carbon bond in a substituted ethane, owing to bulky substituents, otherwise equivalent groups will become different, since they may be held in specific conformations. Numerous examples of this phenomenon have been observed, and the barrier to rotation has been determined in some cases (46, 85, 167). Care must be taken in the interpretation of such spectra, since rather similar effects may be observed, even if the rotation is only slightly hindered, owing to the molecule's spending an unequal amount of time in various conformations (59, 110). The situation has been carefully analyzed to show the extent of information which may be obtained depending upon the symmetry of the molecule (129).

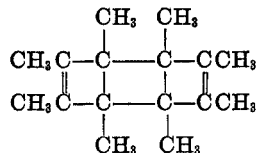
E. EXAMPLES OF STRUCTURE DETERMINATION

There are many instances of structure determinations where proton magnetic resonance has played an important role in solution of the problems. This section

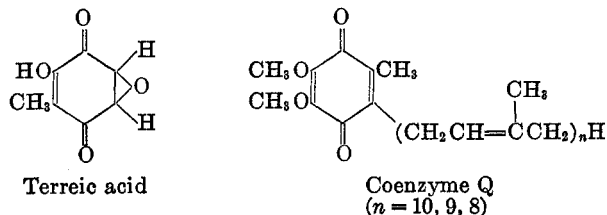
is not an exhaustive compilation of these results, but instead cites a few representative examples where proton magnetic resonance has been especially useful. The decision between a cycloheptatriene ring or a cyclopropane ring fused to a cyclohexene ring in eucarvone enol acetate and in Δ^2 -4-methylcaren-5-one has been aided by their proton resonance spectra (35). A similar uncertainty occurs in the Buchner acids and has been investigated (45). The determination of the structure of diketene has been mentioned previously (9). This technique is very valuable for cis-trans isomerism, as illustrated by the papers published on Feist's acid (21, 49, 78, 79). Other instances where it has been used for compounds containing a cyclopropane ring are sterculic acid (146), hypoglycin (147), and 2-benzoylcyclopropanepropionic acid (187).



An unusual compound whose structure was confirmed by its proton resonance spectrum is shown below (39). It has also been shown that when an aromatic



compound is protonated in strong acid an "aliphatic" methylene group is produced (93). The structures of many quinoid type compounds have been elucidated by their proton resonance spectra. Some examples are terreic acid (164), 2,6-dimethyl-3,5-dicarboethoxy-1,4-dihydropyridine (170), and coenzyme Q (186).



III. FLUORINE RESONANCE SPECTRA

The chemical shifts observed in fluorine resonance spectra are much larger than those in proton resonance spectra and may occur over a range of about

TABLE 13
Irregular fluorine chemical shifts

Substituent (X)	$-\text{CF}_3^*$	$-\text{CF}_2-$	$-\text{CF}_2\text{X}$	Reference
$-\text{I}$	1.97	40.7	-17.5	(54)
$-\text{Cl}$	4.62	48.7	-6.7	(54)
$-\text{S}-\text{S}-$	4.00	47.0	13.6	(54)
$-\text{SF}_4-$	5.0	50.0	16.5	(108)
$-\text{SF}_5$	5.0	50.7	18.8	(108)
$-\text{CN}$	5.03	51.3	30.6	(54)
$-(\text{CF}_3)_n-$	4.8	46.6	34.4	(109)
	3.60	49.1	35.0	(54)
$-\text{COCl}$	4.67	49.2	37.2	(54)
$-\text{COOC}_2\text{H}_5$	4.67	50.5	42.7	(54)
$-\text{COOH}$	4.87	50.5	43.5	(54)
$-\text{COF}$	5.35	51.3	43.5	(54)
$-\text{NF}_2$	6.4	27.1	51.1	(109)
$-\text{CF}=\text{}$	5.2	42.4	51.4	(109)
$-\text{H}$	7.48	57.0	61.2	(54)

* The chemical shifts are in parts per million from $\delta_{\text{ext.}}^{\text{CF}_3\text{COOH}} = 0.00$.

300 p.p.m. The spin-spin coupling between nonequivalent fluorine nuclei is also larger than with protons, so insufficient resolution of the spectra is rarely a problem. A characteristic property of fluorine resonance spectra is the variability of chemical shift with quite minor changes in structure. As a result it is impossible to assign the resonance frequency of a certain type of chemically bonded fluorine to a rather small region of the spectrum as with protons. The $-\text{CF}_3$ group in a perfluoro straight-chain compound may be found at $\delta_{\text{ext.}}^{\text{CF}_3\text{COOH}} = 1.97$ to 7.48, a $-\text{CF}_2-$ group adjacent to a $-\text{CF}_3$ at $\delta_{\text{ext.}}^{\text{CF}_3\text{COOH}} = 27.1$ to 57.0, and a $-\text{CF}-$ in a fluorocarbon chain at about $\delta_{\text{ext.}}^{\text{CF}_3\text{COOH}} = 110$. The effect of a substituent is not necessarily attenuated in a regular fashion as one proceeds away from it along the fluorocarbon chain. This is clearly illustrated in table 13, where the $-\text{CF}_2\text{X}$ nuclei are arranged in order of increasing shielding, but a similar order is not found in the $-\text{CF}_2-$ or $-\text{CF}_3$ groups. However, the large number of examples listed in table 13 should give an approximate idea of what to expect for other compounds of this type.

The chemical shifts of a large number of other fluorine compounds have been obtained and generalizations, sometimes based on limited data, may be obtained (52, 108, 109). In six-membered cyclic perfluoro compounds the fluorine atoms appear at about $\delta_{\text{int.}}^{\text{CF}_3\text{COOH}} = 55$, provided they are not adjacent to a hetero atom in the ring.

Fluorinated cyclobutanes have been thoroughly studied and their spectra interpreted in terms of the geometry and motion of the cyclobutane ring (122). If a $-\text{CF}_2$ group is adjacent to oxygen, it appears at $\delta_{\text{int.}}^{\text{CF}_3\text{COOH}}$ between -6.2 and 14.9. If the fluorine atom is also adjacent to a double bond, as in the grouping $-\text{C}=\text{CF}-\text{O}$, the shift is further lowered to $\delta_{\text{int.}}^{\text{CF}_3\text{COOH}} = -11.8$ to -9.4. When a $-\text{CF}_3$ group is attached to nitrogen it appears at $\delta_{\text{int.}}^{\text{CF}_3\text{COOH}} = -36.2$ to

—18.8, and for a —CF₂— group the numbers are 8.6 to 51.1. Fluorine itself attached to nitrogen appears at $\delta_{\text{int.}}^{\text{CF}_3\text{COOH}} = 36$ in $\begin{array}{c} \diagup \\ \text{N—F} \\ \diagdown \end{array}$ and at —92 in —NF₂.

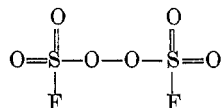
If the fluorine is attached to sulfur it appears at $\delta_{\text{int.}}^{\text{CF}_3\text{COOH}} = -105$ in (R_F)₂SF₄, and at —118.7 and —137.5 for the basal and apex atoms, respectively, in R_FSF₅.

The unpredictable behavior of chemical shifts does not continue for a fluorine substituent on an aromatic ring. In fluorobenzene the shift is $\delta_{\text{int.}}^{\text{CF}_3\text{COOH}} = 36.584$ (52), and the change in this shift with substituents on the aromatic ring agrees very well with Hammett's equation (65, 173).

A variety of alkyl silicon fluorides have been studied, and the chemical shift has been correlated with their structure (159, 160). Studies of the position of the fluorine resonance, and its temperature variations in boron trifluoride–alcohol complexes, has led to information on their stability and the establishment of a boron trifluoride “affinity” series (43, 44).

The same type of solvent effects is observed in fluorine resonance spectra as in proton resonance spectra (50). The temperature dependence of the spectra can be used to determine reaction rates (46). One elegant example was the determination of the structures of ClF₃ and IF₃ and the calculation of the activation energy for fluorine exchange in these compounds (106).

An interesting series of compounds whose structures were determined by fluorine magnetic resonance are SOF₄, SOF₆, and S₂O₆F₂ (47, 48). The compound SOF₄ had a single resonance line at $\delta_{\text{int.}}^{\text{CF}_3\text{COOH}} = 53.95$, indicating all the fluorine atoms to be equivalent. With SOF₆ there were two lines, one of intensity five at 55.49 and another of intensity one at 51.09, so that the compound can be considered as SF₅OF. A single resonance line at $\delta_{\text{int.}}^{\text{CF}_3\text{COOH}} = -115$ along with other evidence led to the assignment of the following structure to S₂O₆F₂.



IV. CARBON-13 RESONANCE SPECTRA

The nuclear magnetic resonance spectra of carbon nuclei might be expected to have as great a value in the determination of the structure of organic compounds as that shown by protons. However, owing to instrumental difficulties much less work has been done along these lines. The only stable isotope of carbon with a non-zero spin is carbon-13 with a spin of $\frac{1}{2}$. Since its natural abundance is only 1.1 per cent, one must either use enriched samples or contend with a rather low sensitivity. Despite these difficulties some excellent work has been done, and improved techniques should soon make these spectra readily accessible.

A. CHEMICAL SHIFT AND CHEMICAL BONDING

Shifts in the magnetic resonance of carbon-13 occur over a range of about 350 p.p.m. Despite this wide range the spectra are usually similar in appearance to

proton spectra in which the resolution is only fair, since the line width of the carbon-13 resonance tends to be rather broad under the conditions necessary for good signal-to-noise ratio. The spin-spin coupling with protons, or with fluorine nuclei attached to carbon, varies from 150 to 600 cycles, which amounts to at least 20 p.p.m. at the frequencies used for obtaining these spectra. Fortunately the spin-coupling pattern will usually be simple, since spin coupling of one carbon-13 nucleus with a chemically nonequivalent one is not observed unless compounds enriched in carbon-13 are used. This is because the chance of two carbon-13 nuclei being adjacent in the same molecule is very small when their abundance is only 1.1 per cent.

To date only three publications have appeared which list chemical shifts of carbon-13 (69, 83, 84). The data in this review are taken from these articles and expressed in terms of $\delta_{\text{ext.}}^{\text{CH}_3\text{COOH}} = 0.00$ for the carboxyl carbon in acetic acid, as has been done by Lauterbur (84). Although solution effects and changes due to bulk magnetic susceptibility are known to occur, no corrections have been made. Because of the large chemical shifts these corrections are likely to be quite small by comparison with their effect in proton resonance spectra.

The resonance peaks of the carbon atoms in alkanes are found in the region of $\delta_{\text{ext.}}^{\text{CH}_3\text{COOH}} = 150$ to 177, with more highly branched carbons appearing at the lower field. In cycloalkanes the range is $\delta_{\text{ext.}}^{\text{CH}_3\text{COOH}} = 145$ to 155. For aromatic and olefinic carbon atoms the resonance peaks are found between $\delta_{\text{ext.}}^{\text{CH}_3\text{COOH}} = 40$ and $\delta_{\text{ext.}}^{\text{CH}_3\text{COOH}} = 60$, with those carbon atoms having a methyl substituent appearing at lower field. Methyl groups in substituted toluenes appear in the range $\delta_{\text{ext.}}^{\text{CH}_3\text{COOH}} = 147.6$ to 164.2 and correlate very nicely with the chemical shift of the fluorine resonance in the corresponding substituted fluorobenzene. This correlation holds for ortho-substituted as well as for meta- and para-substituted compounds and is better than with either Hammett σ values or the σ_I and σ_R values of Taft (75, 172).

The chemical shifts of methyl derivatives of the elements are shown to be a function of the electronegativity of the element and the number of methyl groups attached to it. Excellent agreement has been found for $(\text{CH}_3)_n\text{X}$, where n is 1 or 4, for seven different elements. A similar type of correlation is found in CH_3AX_B , where $B = 1, 2, 3, 4$ and X is Cl, Br, I, or *O*-alkyl. The plots are similar to those in figure 1. The methyl group in substituted ethanes shows a similar behavior. In compounds of the type $(\text{CH}_3)_n\text{CH}_{(3-n)}\text{X}$ the chemical shifts of the central carbon atoms and the carbon atom of the methyl group vary regularly with n when the substituents are I, Cl, Br, OH, and NO_2 .

The chemical shift of a carbonyl carbon atom is always found at lower field than any carbon atoms which have a hydrogen bonded to them. In ketones the resonance peak appears at about $\delta_{\text{ext.}}^{\text{CH}_3\text{COOH}} = -30$ and in aldehydes at about -22 . Acids have a chemical shift of $\delta_{\text{ext.}}^{\text{CH}_3\text{COOH}} = 0$ to -5 , amides about $+5$, and anhydrides around $+11$. The carbon atom of nitriles appears in the range $\delta_{\text{ext.}}^{\text{CH}_3\text{COOH}} = 48-64$.

It is obvious from the work which has been done to date that different types of chemically bonded carbon atoms have chemical shifts grouped in different

regions. More work on model compounds is urgently needed to narrow and specialize these regions. It appears that chemical shifts of carbon-13 nuclei may be more predictable from molecular structure than those of protons or fluorine atoms.

B. SPECTRA OF NUCLEI WITH LOW ABUNDANCES

When a nucleus is present in low concentration it is necessary to use larger volumes of sample, and therefore there is a decrease in the homogeneity of the magnetic field over the sample region. It is also necessary to use a more intense radiofrequency magnetic field which, if the nuclei have a fairly long thermal relaxation time, requires one to observe the dispersion mode and to pass rapidly through the signal. All these conditions tend to increase the line width and therefore decrease the resolution.

The significant advantage of working with low abundances is the elimination of spin-spin coupling between magnetically nonequivalent atoms of the nuclear species being studied. In the case of complicated molecules this may greatly aid the interpretation of the spectrum. This technique of largely but randomly exchanging with another isotope of the element in question will probably find considerable use in the interpretation of complex spectra, especially exchange of deuterium for hydrogen.

C. H^1-C^{13} SPIN COUPLING

The magnitude of the spin coupling between carbon-13 and the protons bonded to it is somewhat diagnostic of the type of carbon atom. With few exceptions the spin coupling to saturated carbon atoms is less than 170 cycles per second, while for unsaturated carbon atoms—aromatic, olefinic, and carbonyl—it is 180 cycles per second or greater. Since there is no detectable spin coupling to elements not directly attached to the carbon atom concerned, one can unambiguously determine the number of protons, or fluorine atoms, bonded to a carbon from its spin multiplet.

It is frequently not necessary to obtain the carbon-13 magnetic resonance spectrum in order to determine its spin coupling with protons or fluorine. On examination of the proton or fluorine resonance spectra under high amplification it is often possible to observe satellites about the main peak due to the protons or fluorine nuclei whose signal is split by spin coupling with the small amount of carbon-13 available (33). This pattern may be analyzed to give the spin-spin coupling constant. In many cases, especially with aromatic compounds, these satellites are not observed, or are broad and very weak. This is due to spin coupling of these protons with other chemically equivalent, but now magnetically nonequivalent, protons in the molecule (11). This spreads the signal into a broad and weak envelope.

V. PHOSPHORUS RESONANCE SPECTRA

The chemical shifts observed in phosphorus resonance spectra vary over a range of about 700 p.p.m. (64). The resonance lines are usually narrow, and any

spin-spin coupling is often small with respect to chemical shifts so that the appearances of the spectra are similar to those of fluorine resonance spectra. Four extensive tabulations of chemical shifts for a variety of phosphorus compounds have been published (53, 64, 107, 181). They all use 85 per cent orthophosphoric acid as external reference and do not make corrections for the bulk magnetic susceptibility of the sample nor for concentration effects when solutions are employed. It has been estimated that errors due to these effects should not exceed 0.5 p.p.m., an error which can safely be ignored (107).

Compounds of phosphorus may be classified, for purposes of their resonance spectra, into those with three atoms and those with four atoms chemically bonded to the phosphorus. A much smaller range of shifts is observed with quadruply bound phosphorus, so this family will be considered first. When the phosphorus is surrounded by four oxygen atoms the resonances occur over a range of 39 p.p.m., and within that range are strongly characteristic of whether the phosphorus is at the end, in the middle, or at a branching point of the phosphorus-oxygen chain (180). The resonance of phosphate ion in solution occurs at $\delta_{\text{ext.}}^{\text{H}_3\text{PO}_4} = -5$. Phosphoric acid and alkyl orthophosphates appear at $\delta_{\text{ext.}}^{\text{H}_3\text{PO}_4} = 0$. End groups in chain phosphates are found at +5 if they exist as anions or if the hydrogen has been replaced by another group, but acidic end groups appear at +10. Phosphorus in the middle of a phosphate chain or ring appears at $\delta_{\text{ext.}}^{\text{H}_3\text{PO}_4} = 20$. Although the chemical shift of a branch-point phosphate has been reported as about $\delta_{\text{ext.}}^{\text{H}_3\text{PO}_4} = 30$, the authors caution that this may be unreliable, owing to an exchange averaging of the branching and middle groups (181). Among the lower oxidation states in phosphorus-oxygen compounds hypophosphate has a chemical shift of $\delta_{\text{ext.}}^{\text{H}_3\text{PO}_4} = -9$, hypophosphite one at -13, which is split into a triplet with separation of 553 cycles, and pyrophosphite one at -8, split into a doublet with a separation of 690 cycles. It is possible to distinguish between all these species in aqueous solution, and even to analyze quantitatively for them (28).

If an oxygen connected to a quadruply bonded phosphorus is replaced by another group, the change in chemical shift is characteristic of the replacing group and does not depend appreciably on the nature of the other groups attached to the phosphorus (182). The shift is even found to be additive, two replacing groups having twice the effect of one. The shifts caused by replacement with various groups are listed in table 14.

Replacement of oxygen by a less electronegative element causes less shielding of the phosphorus nucleus from the magnetic field. These results are opposite to simple polar-bond theory and the results obtained in proton resonance spectra. A similar effect is found in phosphoric acids and phosphonates, where organic radicals whose inductive effect tends to remove electrons increase the shielding of the phosphorus nucleus.

The chemical shift of triply connected phosphorus atoms may be found anywhere within the observed range for phosphorus compounds. However, the contribution to the chemical shift of each group attached to the phosphorus is independent and additive. Therefore by adding the contributions from each

TABLE 14
Group effects on quadruply connected phosphorus

Group	Shift per Replaced Oxygen Atom	Number of Examples	Group	Shift per Replaced Oxygen Atom	Number of Examples
	<i>p.p.m.</i>			<i>p.p.m.</i>	
H.....	-2 to -8	5	P.....	-19	1
C (aliphatic).....	-22 to -37	3	S.....	-25 to -71	8
C (aromatic).....	-6 to -19	7	Cl.....	0 to -10	5
N.....	-3 to -13	9	Se.....	-73	1
F.....	+10	1			

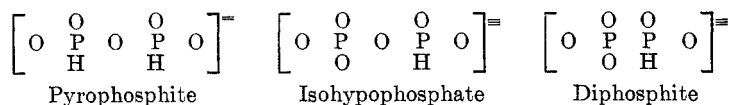
TABLE 15
Group effects on triply connected phosphorus

Group or Atom	Shift on Triply Connected Phosphorus	Group or Atom	Shift on Triply Connected Phosphorus
	<i>p.p.m.</i>		<i>p.p.m.</i>
H.....	+70	NR ₂	-50
Alkyl.....	+20	OR.....	-55
		PX ₂	-60
Phenyl.....	0	I.....	-67
S.....	-25	Cl.....	-74
F.....	-30	Br.....	-80
	-45		

group the chemical shift of a triply connected phosphorus atom may be estimated within ± 20 p.p.m. (181). The contributions for some groups are listed in table 15.

An equation has been developed for the calculation of the chemical shift of triply connected phosphorus using only the observed bond angles and the Pauling electronegativities of the atoms attached to phosphorus (107). This has been shown to be inaccurate and an improved version has been suggested (120). Even this is of little use, since good agreement is obtained only when the three substituents are identical.

The structure $(\text{RO})_2\text{POH}$ has been excluded for the acid phosphites and strong confirmation provided that the structure is $(\text{RO})_2\text{HPO}$ (29, 107). The hydrogen is spin coupled to the phosphorus with a coupling constant of 687 cycles, too large for anything but direct bonding to the phosphorus. Additional structural proofs were those of hypophosphite, isohypophosphate, and diphosphite anions.



VI. RESONANCE OF OTHER ISOTOPES

The chemical shifts in the resonance position of several other isotopes have been investigated. Although there are not yet enough data available to justify a

detailed compilation of chemical shift with molecular structure for these isotopes, the results to date appear very promising and further work should make resonance spectra of these isotopes as useful as those previously mentioned.

A. BORON-11

It is most unfortunate that so far no boron resonance spectra have been reported in which the chemical shift is related to some standard frequency. In fact, it is quite common not to even mention the amount by which the various peaks are separated. Despite this, much useful structural work has been done on the basis of the number and multiplicity of the observed resonance lines (114). Spin-spin coupling between boron and hydrogen in the boranes, which have been the principal compounds studied, greatly complicates the spectrum, and saturation of the protons in double resonance experiments is often necessary to interpret the spectra (152).

The boron-11 resonance spectra of B_5H_{11} , B_5H_9 , and $B_{10}H_{14}$ were obtained and interpreted in terms of the molecular structure of the compounds (152). A reinterpretation of the spectrum for $B_{10}H_{14}$ was shown to be necessary from the appearance of the boron-11 resonance spectrum of deuterated decaborane (185). This also cleared up the interpretation of the proton spectra of decaborane and allowed proton magnetic resonance to be used to determine the rate of hydrogen-deuterium exchange at the various sites in decaborane (162). Compounds whose structure determinations have been aided by their boron resonance spectra are B_5H_5Br , B_5H_5I , $B_{10}H_{12}I_2$, $B_{10}H_{13}Br$, $B_{10}H_{13}I$ (melting point $116^\circ C.$), $B_{10}H_{13}I$ (melting point $72^\circ C.$) (153); benzyl decaborane (169); dichloroborane ethyl etherate and deuterodichloroborane etherate (117). It is to be hoped that a large body of chemical shifts of boron-11 will soon be declassified, thus making resonance spectra of this isotope even more useful in determining molecular structure.

B. OXYGEN-17

The natural abundance of oxygen-17 is only 0.04 per cent; however, the thermal relaxation time is short enough so that the signal-to-noise ratio is not too different from that found with carbon-13 resonance spectra (183). The chemical shift of oxygen-17 occurs over a range of 690 p.p.m. and has a line width of about 0.3 gauss (30 p.p.m. in an applied field of 10,000 gauss). The resonance observed at highest field is that in water and at lowest field is that in sodium nitrite. It is interesting to note that two peaks were observed for the chemically nonequivalent oxygen atoms in ethyl nitrate and in *n*-butyl nitrite, but only a single peak was found in acetic acid and formic acid. Presumably rapid exchange of the carboxyl hydrogen atom allows only one average value to be observed.

C. NITROGEN

The position of the nitrogen resonance in various compounds may be found over a range of about 600 p.p.m.; the line width varies greatly owing to possible interaction with the quadrupole moment of the nucleus (154). Several limited compilations of chemical shifts have been published, referred to nitrate ion,

TABLE 16
Nitrogen chemical shifts

Compound or Ion	$\delta_{\text{ext.}}^{\text{NO}_2^-}$	Compound or Ion	$\delta_{\text{ext.}}^{\text{NO}_2^-}$
	<i>p.p.m.</i>		<i>p.p.m.</i>
NH_4^+	602	CH_3CN	385
$(\text{C}_2\text{H}_7)_2\text{NH}$, $(\text{C}_2\text{H}_5)_3\text{N}$	575	CN^- , CH_3SCN	380
N_2H_4	566	$\text{C}(\text{NO}_2)_4$, $\text{C}_2(\text{NO}_2)_6$	300
$(\text{CH}_3)_4\text{N}^+\text{Br}^-$	552	Pyridine.....	276
NH_3	544	N_2	268
Urea.....	536	NO_3^-	254
$\text{NH}_2\text{OH}\cdot\text{HCl}$	520	$\text{C}_6\text{H}_5\text{NO}_2$	252
Acetamide.....	498	<i>n</i> - $\text{C}_8\text{H}_7\text{NO}_2$	228
SCN^-	406		

nitrite ion, or ammonium ion as the zero of reference (68, 94, 133). Although the same compounds appear in the same general region of the spectrum, detailed agreement between the various studies is not too good. This may be due to measurement of chemical shift by alternately placing sample and standard in the probe, or to the large line width frequently encountered. Since the tabulation of Holder and Klein embraces the greatest variety of compounds, it will be listed here, but it is not necessarily the most accurate.

In addition to general surveys, specific types of nitrogen-containing compounds have been examined more carefully. Chemical shifts for NO_2^+ , NO_3^- , N_2O_5 , and HNO_3 , containing nitrogen in its 5+ oxidation state, have been determined, and studies of the exchange rate between the various species in solution have been made (115, 155). The chemical shifts for ammonia, amines, and substituted ammonium compounds have been determined, and their quadrupole relaxation and broadening have been discussed (116, 154). One example where nitrogen nuclear resonance has been used for structural investigations is the confirmation that organic cyanamides have the structure $\text{R}_2\text{N}-\text{C}\equiv\text{N}$ and that organic carbodiimides have the structure $\text{R}-\text{N}=\text{C}=\text{N}-\text{R}$ (137).

D. SILICON-29

A brief survey of the chemical shift of the resonance for silicon-29 showed a range of 140 p.p.m., including both solids and liquids (70). If a chlorine atom was bonded to the silicon the resonance line became broad and weak, and often could not be detected. More work must be done with this isotope to ascertain its usefulness, but it could quite possibly be as useful for the structure determination of condensed silicates as phosphorus resonance measurements are with condensed phosphates.

E. CHLORINE-35

Only a single publication has appeared on the chemical shift of the magnetic resonance of chlorine-35 (95). However, extensive surveys have been made of the change in chlorine-35 quadrupole coupling in different chemical environments. Since this is vaguely allied with nuclear resonance, it will be included in

this section. Excellent correlations are obtained between the quadrupole resonance frequency in substituted chlorobenzenes and the Hammett and Taft σ values for these compounds (23, 101, 172). This agreement also carries over nicely to the multichlorobenzenes, where similarly situated chlorine atoms appear in the same region (24). Similar studies have been done on chlorine-substituted pyridines, quinolines, imides, pyrimidines, and triazines, and the observed frequencies correlated with chemical properties (42, 161).

A serious disadvantage of quadrupole coupling studies is the necessity of working with solid samples and the possibility of large effects due to intermolecular interaction in the crystal. Therefore care must be exercised in drawing conclusions with compounds that crystallize in a different manner.

F. MISCELLANEOUS ISOTOPES

Bromine-81 quadrupole coupling frequencies have been determined in the multibromobenzenes and a variety of other compounds (30, 92, 161). The chemical shift of cobalt magnetic resonance spectra in fourteen cobalt complexes has been studied, along with variations due to temperature and the composition of the solvent (55). Chemical shifts of lead-207 in several of its solid ionic compounds have been measured (127) and explained theoretically (118).

VII. RELAXATION TIMES AND CHEMICAL STRUCTURE

The spin-spin relaxation time, or transverse relaxation time, or T_2 , has not been shown to give useful structural information. In high-resolution work the homogeneity of the applied magnetic field often determines the apparent T_2 for the nuclei of the sample. The spin-lattice relaxation time, or longitudinal relaxation time, or T_1 , may give useful structural information. Unless dissolved oxygen, which serves as a paramagnetic impurity, is carefully removed from the solution, the spin-lattice relaxation time will be reduced to a common value of about 2-3 sec. for all types of protons (112). In the absence of oxygen T_1 is in the neighborhood of 20 sec. for aromatic protons and 10 sec. for aliphatic protons.

The spin-lattice relaxation time is a function of the viscosity if the solution is fairly viscous, increasing with increased viscosity. However, even in solutions of low viscosity the ring and methyl protons of mesitylene showed a linear variation of T_1 with concentration (143). This linear variation has also been found for chlorobenzene, but anomalous results were obtained for phenol and are attributed to molecular association in the solution (57).

If the nucleus in question has a quadrupole moment, T_1 equals T_2 and is of little value in structure determinations (95). Nuclei, other than protons, with spin $\frac{1}{2}$ have not had their relaxation times investigated as a function of structure, and may yield interesting information.

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