Tetrahedron. 1967. Vol. 23, pp. 1817 to 1826. Pergamon Press Ltd. Printed in Northern Ireland

A PROTON MAGNETIC RESONANCE STUDY OF SOME PTEROCARPAN DERIVATIVES

THE CONFORMATION OF THE 6a,11a-DIHYDRO-6H-BENZOFURO[3,2-c][1]BENZOPYRAN RING SYSTEM

K. G. R. PACHLER
Chemical Physics Group, C.S.I.R., Pretoria, South Africa,
and
W. G. E. UNDERWOOD
University College of Rhodesia, Salisbury, Rhodesia

(*Received* 15 *August* 1966)

Abstract—The PMR spectra of four 6a,11a-dihydro-6H-benzofuro[3,2-c] [1]benzopyran derivatives have been analysed. The conformation of the heterocyclic rings has been derived from the vicinal coupling constants. Several long-range couplings have been observed. The coupling constants across four saturated bonds are compared with other reported values and theoretical calculations.

INTRODUCTION

THE pterocarpans are a group of naturally occurring heterocyclics having a 6a,11a-dihydro-6H-benzofurobenzopyran nucleus (I). The isolation of fourteen such compounds from nature has been described.[1-9] The compounds have two asymmetric centres and although it is possible to construct a Dreiding model with a *trans* junction, this is evidently a highly strained system and the relatively unstrained *cis* junction is considered more likely. Suginome[10] has concluded that the relative configuration of these centres in homopterocarpin (II) is H,H *cis* after applying the Karplus equation[11] relating the dihedral angle between two protons and their PMR coupling constant. However, this evidence is doubtful as the actual coupling constant may differ considerably from the splitting of the 11a-proton resonance used by Suginome. The absolute configuration[12] of C_{11a} in trifolirhizin (III) has recently been established as R,[13] and if the *cis* relationship is accepted, the absolute configuration of this compound is necessarily 6a,R:11a,R. As trifolirhizin can be hydrolyzed to (−)-demethylpterocarpin (IV) and this in turn converted into (−)-pterocarpin (V),[4] the absolute configuration of these three compounds is established. Of the eleven other representatives

---

[1] A. McGookin, A. Robertson and W. B. Whalley, *J. Chem. Soc.* 787 (1940).
[2] W. Cocker, T. Dahl, C. Dempsey and T. B. H. McMurry, *J. Chem. Soc.* 4906 (1962).
[3] S. Shibata and Y. Nishikawa, *Chem. and Pharm. Bull.* **11**, 167 (1963).
[4] J. B-son Bredenberg and P. K. Hietala, *Acta Chem. Scand.* **15**, 696, 936 (1961).
[5] D. R. Perrin and W. Bottomley, *J. Am. Chem. Soc.* **84**, 1919 (1962).
[6] B. L. van Duuren, *J. Org. Chem.* **26**, 5013 (1961).
[7] D. R. Perrin, *Tetrahedron Letters* 29 (1964).
[8] C. v. d. M. Brink, W. Nel, G. J. R. Rall, J. C. Weitz and K. G. R. Pachler, *J. S. African Chem. Inst.* **19**, 24 (1966).
[9] S. H. Harper, A. D. Kemp and W. G. E. Underwood, *Chem. Comm.* 309 (1965).
[10] H. Suginome and T. Iwadare, *Experientia* XVIII, 163 (1962).
[11] M. Karplus, *J. Chem. Phys.* **30**, 11 (1956).
[12] R. S. Cahn, C. K. Ingold and V. Prelog, *Experientia*, XII, 81 (1956).
[13] S. Ito, Y. Fujise and A. Mori, *Chem. Comm.* 595 (1965).

of this class, nine have high negative optical rotation and so in all probability have the same R:R configuration, whereas the remaining two, (+)-sophojaponicin[3] and (+)-pisatin[6] should have an S:S configuration. The conformation of the pterocarpans has not been studied although in order to explain the splitting of the signal due to the lone proton at C_{11a} in the PMR spectrum of pisatin (VI), Perrin and Perrin[14] have concluded that the pyran ring can exist in two energetically similar conformations.

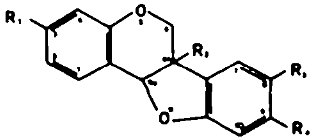


Fig. 1

I: $R_1 = R_2 = R_3 = R_4 = H$.
II: $R_1 = OMe$, $R_2 = R_3 = H$, $R_4 = OMe$.
III: $R_1 =$ O-glucose, $R_2 = H$, $R_3 + R_4 = O{-}CH_2{-}O$.
IV: $R_1 = OH$, $R_2 = H$, $R_3 + R_4 = O{-}CH_2{-}O$.
V: $R_1 = OMe$, $R_2 = H$, $R_3 + R_4 = O{-}CH_2{-}O$.
VI: $R_1 = OMe$, $R_2 = OH$, $R_3 + R_4 = O{-}CH_2{-}O$.
VII: $R_1 = OAc$, $R_2 = R_3 = H$, $R_4 = OMe$.
VIII: $R_1 = OAc$, $R_2 = H$, $R_3 + R_4 = O{-}CH_2{-}O$.

EXPERIMENTAL

The NMR spectra were recorded on a Varian A-60 spectrometer using dilute solutions in $CDCl_3$ (≤ 5 mole %) with TMS as internal reference at a probe temp of approximately 32°. The data for the analysis of the heterocyclic ring protons were averages from at least 5 recordings on an expanded scale (2 c/s·cm) calibrated by the usual sideband method.[15] The chemical shifts are quoted on the τ-scale ($\tau_{TMS} = 10{\cdot}0$). They are estimated to be in error by not more than $\pm 0{\cdot}01$ ppm. The coupling constants should be accurate to within $\pm 0{\cdot}2$ c/s. Spectra at a frequency of 100 Mc/s were recorded on a Varian HA-100 spectrometer with internal proton stabilization (TMS) at a probe temp of 30°. Spin decoupling experiments were performed in the frequency sweep mode.[16] A Hewlett-Packard audio oscillator (200 CD) and Hewlett-Packard electronic counters (521C or 5512A) were used to check the calibration of the spectrometer, to impose sidebands on the spectra, and for spin decoupling experiments.

The analyses of complex spectra have been performed on an IBM 704 computer. Direct ABC-analyses were carried out with a computer programme written according to the principles outlined by Brügel *et al.*[17] An iterative computer programme (NMRIT) was used for the analysis of the four-spin systems and energy levels were calculated with the programme NMREN.[18]

The isolation, purification and identification of the compounds, heartwood constituents of *Swartzia madagascariensis* Desv. have been reported elsewhere.[19]

ASSIGNMENT AND ANALYSIS

The NMR spectra of four pterocarpan derivatives of known structure[19] have been recorded (Fig. 1: II, V, VII, VIII).

Fig. 2 shows a 60 Mc/s spectrum of a saturated solution of Compound V in $CDCl_3$. The assignment of the methoxy and acetoxy resonances was straightforward by

---

[14] D. D. Perrin and D. R. Perrin, *J. Am. Chem. Soc.* 84, 1922 (1962).
[15] J. T. Arnold and M. E. Packard, *J. Chem. Phys.* 19, 1608 (1951).
[16] R. Freeman and D. H. Whiffen, *Proc. Phys. Soc.* 79, 794 (1962).
[17] W. Brügel, Th. Ankel and F. Krückeberg, *Z. Elektrochem.* 64, 1121 (1960).
[18] J. D. Swalen and C. A. Reilly, *J. Chem. Phys.* 37, 21 (1962).
[19] S. H. Harper, A. D. Kemp and W. G. E. Underwood, *Chem. & Ind.* 562 (1965).

comparison with other reported chemical shift data.[20,21] The methylenedioxy groups exhibited narrow AB-quartets at characteristic τ-values (~4·1). The aromatic protons in positions 1, 2 and 4 (Fig. 1) gave rise to an ABC-type three-spin spectrum. Those on the other aromatic ring showed either single resonance lines for compounds V and VIII, or constituted a second ABC-pattern for compounds II and VII. These three-spin spectra have been analyzed on a first order basis only. Comparison with three spectra analyzed with the ABC computer programme mentioned in the experimental section proved that the error in the chemical shifts is less than 0·01 ppm. The assignment of these proton resonances has been achieved by comparison with previously reported data on related compounds[6,22] and utilizing known values of substituent effects on chemical shifts[23] as well as the characteristic magnitudes of the aromatic proton-proton splittings. These data are collected in Table 1.

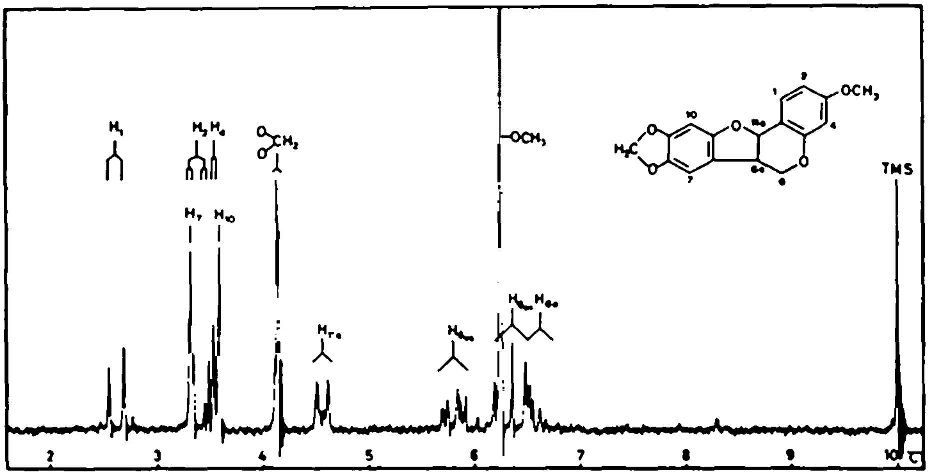


FIG. 2. 60 Mc/s NMR spectrum of compound V in chloroform-d.

The heterocyclic ring protons gave rise to a highly complex four-spin system due to strong coupling between the two protons at highest field ($J/\delta \simeq 1$). Even an approximate assignment of the spectra obtained from chloroform solutions was not possible on a first order basis. Preferential solvent shifts in benzene solution, however, lead to much simpler spectra, the analysis of which yielded a trial set of coupling constants and chemical shifts. It is well known that coupling constants are usually much less solvent-dependent than chemical shifts. Thus we calculated a number of theoretical spectra using the set of coupling constants obtained from the spectrum of the benzene solution varying the chemical shifts only. Those parameters yielding best agreement between the theoretical and the observed spectrum of the chloroform solution were then used to assign the approximately 30 resolved transitions for each of the four compounds studied by a trial and error procedure employing the computer programme NMREN. The energy levels thus obtained were then submitted to an

---

[20] NMR Spectra Catalogue, Varian Associates, Palo Alto. California.

[21] G. V. D. Tiers, *Characteristic NMR Shielding Values for Hydrogen in Organic structures. Part I: Tables of τ-Values for a variety of Organic Compounds.* Minnesota Mining and Manufacturing Co., St. Paul, Minnesota (1958).

[22] J. B-son Bredenberg and J. N. Shoolery, *Tetrahedron Letters* 285 (1961).

[23] G. W. Smith, *J. Mol. Spectroscopy* 12, 146 (1964) and Refs. quoted there.

TABLE 1. CHEMICAL SHIFTS (τ-values) AND SPIN–SPIN SPLITTINGS OF THE AROMATIC RING PROTONS

Compound	τ-values (ppm)								Splittings (c/s)
	Position on carbon skeleton								
	1	2	3	4	7	8	9	10	
V	2·62, H	3·39, H	6·27, OMe	3·55, H	3·33, H	4·13, O—CH$_2$—O		3·59, H	$S_{1,2}$ = 8·4 $S_{1,4}$ < 0·3 $S_{2,4}$ = 2·4 $S_{7,10}$ < 0·3 $^{5}J_{OCH_2O}$ = 1·3
VIII	2·52, H	3·24, H	7·75, OAc	3·31, H	3·33, H	4·13, O—CH$_2$—O		3·60, H	$S_{1,2}$ = 8·4 $S_{1,4}$ < 0·3 $S_{2,4}$ = 2·3 $S_{7,10}$ < 0·3 $^{5}J_{OCH_2O}$ = 1·3
II	2·60, H	3·39, H	6·26,* OMe	3·55, H	2·90, H	3·58, H	6·28,* OMe	3·57, H	$S_{1,2}$ = 8·5 $S_{1,4}$ < 0·3 $S_{2,4}$ = 2·4 $S_{7,8}$ = 8·8 $S_{7,10}$ < 0·3 $S_{8,10}$ = 2·7
VII	2·51, H	3·24, H	7·75, OAc	3·32, H	2·92, H	3·60, H	6·30, OMe	3·59, H	$S_{1,2}$ = 8·2 $S_{1,4}$ < 0·3 $S_{2,4}$ = 2·4 $S_{7,8}$ = 8·7 $S_{7,10}$ < 0·3 $S_{8,10}$ = 2·2

* The τ-values of these two OMe-groups may be interchanged.

iterative computer analysis as described by Swalen and Reilly.[18] The final parameters derived by this procedure are given in Table 2. The negative sign of the geminal coupling constants was a priori assumed in the assignment.

TABLE 2. CHEMICAL SHIFTS (τ-values) AND COUPLING CONSTANTS OF THE HETEROCYCLIC RING PROTONS

Compound	τ-Values (ppm)				Coupling Constants (c/s)					
	Position on Carbon Skeleton									
	11a	6 equatorial	6 axial	6a	$^{2}J_{6ax,6eq}$	$^{3}J_{6a,6ax}$	$^{3}J_{6a,6eq}$	$^{3}J_{6a,11a}$	$^{4}J_{6ax,11a}$	$^{4}J_{6eq,11a}$
V	4·55$_5$	5·81$_3$	6·37$_5$	6·57$_0$	−10·8	+10·5	+5·1	+6·9	−0·8	+0·6
VIII	4·53$_5$	5·77$_0$	6·37$_7$	6·53$_0$	−11·1	+10·7	+5·2	+7·4	−0·7	+0·5
II	4·54$_3$	5·80$_4$	6·40$_1$	6·56$_5$	−11·1	+10·8	+5·5	+7·0	−0·8	+0·6
VII	4·57$_4$	5·80$_0$	6·43$_7$	6·53$_4$	−11·0	+10·3	+5·2	+7·6	−0·9	+0·7

A spectrum of the four heterocyclic ring protons of compound V is reproduced in Fig. 3. The calculated spectrum demonstrates the good agreement achieved by the iterative analysis.

The resonance of the heterocyclic ring protons occurring at lowest field was assigned to the proton in position 11a, being next to an electronegative oxygen and an aromatic ring.[10,20,21] The proton in position 6a at highest field is identified by its strong coupling to the low field proton. The magnitude of the vicinal coupling constants identify the protons on carbon atom 6, the axial one being nearer to the proton in position 6a than to its equatorial counterpart. The strong coupling ($J/\delta \simeq 1$) between these two protons (axial on C_6 and on C_{6a}) causes the complexity of the four-spin spectrum. The overall pattern changes markedly with only slight variations of the chemical shift

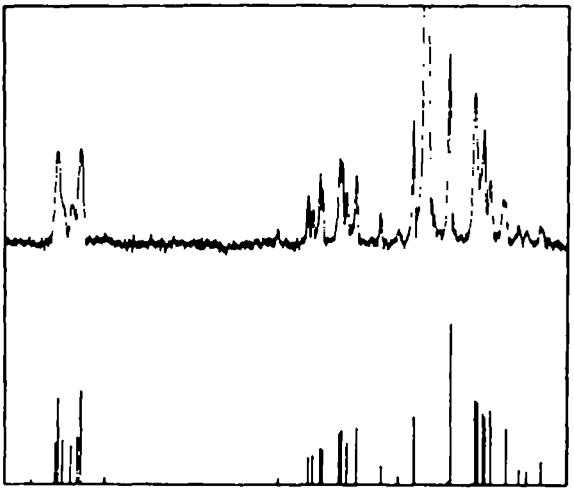


FIG. 3. Observed and calculated 60 Mc/s NMR spectrum of the heterocyclic protons of compound V.

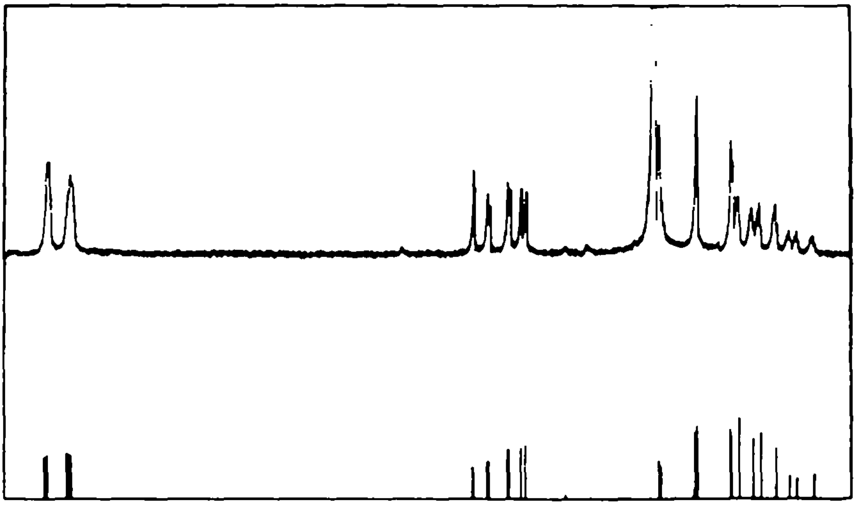


FIG. 4. Observed and calculated 100 Mc/s NMR spectrum of the heterocyclic protons of compound V.

difference between these two protons ($\nu_{6axial} - \nu_{6a}$), although the coupling constants for all four compounds are equal within experimental accuracy. The assignment of the various transitions (for all compounds investigated) differed significantly and the four sets of parameters constitute therefore independent determinations. A 100 Mc/s spectrum of compound V has been recorded and is compared with a theoretical spectrum which was calculated from the parameters obtained from the analysis of the 60 Mc/s spectrum with the chemical shifts converted to 100 Mc/s (Fig. 4).

Spin decoupling of the proton in position 11a reduced the remainder of the spectrum to a straightforward ABC-system. These experiments confirmed the assignment and analysis of the 60 Mc/s spectra unambiguously.

The resonance lines due to the proton on carbon 6a appeared to be rather broad relative to the other transitions of the four-spin system, revealing a triplet fine structure at highest resolution (Fig. 4). Double irradiation experiments showed that this proton as well as the proton on carbon 11a is coupled to aromatic protons across four and five bonds. The following long-range coupling constants have been determined: ${}^4J_{6a,7} \sim 0{\cdot}6$ c/s, ${}^5J_{6a,10} \sim 0{\cdot}5$ c/s, ${}^4J_{1,11a} \sim 0{\cdot}5$ c/s, ${}^5J_{2,11a} \leq 0{\cdot}1$ c/s and ${}^5J_{4,11a} \sim 0{\cdot}3$ c/s.

DISCUSSION

Chemical Shifts. The resonance absorption of the methoxy, acetoxy and methylenedioxy substituents agree well with other reported data.[20] The τ-values of the aromatic protons are mainly determined by the effects of the substituents attached to the aromatic ring via an oxygen atom. It has been shown[24] for a series of methoxy substituted benzenes that a linear correlation exists between the chemical shift of an aromatic proton and the π-electron density on the carbon bearing the particular proton and that the changes in the π-electron density are due to mesomeric effects influencing protons in *ortho* and *para* positions only. Empirical substituent effects on aromatic protons have been determined by a number of authors.[23] In good agreement with these data, *ortho* and *para* substituent effects of 0·5–0·6 ppm to high field for methoxy and methylenedioxy groups and *ortho* upfield shifts of 0·2–0·3 ppm for acetoxy groups are required to explain the observed τ-values. The *ortho* effect of the oxygen atom in a five-membered ring attached to an aromatic ring (such as in the dihydrobenzofuran system) is also about 0·5–0·6 ppm from this study, but it appears as if the corresponding effect of the oxygen in the six-membered heterocyclic ring of a dihydrobenzopyran system is only 0·3–0·4 ppm.

The chemical shifts of the heterocyclic ring protons also fall within the ranges where resonances of protons in similar chemical environments have been observed. Their τ-values are not very characteristic owing to the accumulation of various influences, particularly of magnetic anisotropy effects of substituents and ring current effects of neighboured benzene rings. The very similar τ-values of the axial proton in position 6 and the methine proton on the carbon atom 6a, which are responsible for the complexity of the four-spin system, is unexpected and has already led to a wrong assignment of these protons in neodulin.[6]

Geminal coupling constants. Geminal and vicinal coupling constants of protons on sp^3-hybridized carbon atoms have been shown to be of opposite sign by analysis of strongly coupled systems,[25] double irradiation experiments,[26,27] and observation of double quantum transitions.[28] The positive sign of vicinal proton–proton coupling constants has been determined by correlating these relative sign determinations with the sign of the directly bonded ^{13}C—H coupling constant,[29] which from theoretical

---

[24] A. Zweig, J. E. Lehnsen, J. E. Lancaster and M. T. Neglia, *J. Am. Chem. Soc.* **85**, 3940 (1963).

[25] F. Kaplan and J. D. Roberts, *J. Am. Chem. Soc.* **83**, 4726 (1961).

[26] R. Freeman and D. H. Whiffen, *Mol. Phys.* **4**, 321 (1961).

[27] R. Freeman and W. A. Anderson, *J. Chem. Phys.* **37**, 2053 (1962).

[28] K. A. McLauchlan and D. H. Whiffen, *Proc. Chem. Soc.* 144 (1962).

[29] P. C. Lauterbur and R. J. Kurland, *J. Am. Chem. Soc.* **84**, 3405 (1962).

considerations is very likely to be positive,[30,31] and with the directly determined sign of the *ortho* coupling in *p*-nitrotoluene.[32] Thus the assumption of a negative sign of the geminal coupling constants in the assignment of the spectra is justified. The absolute magnitude of the geminal coupling constants in the pterocarpan derivatives (10·8–11·1 c/s) is in excellent agreement with couplings observed in similar systems[33] (e.g. MeOH: $|^2J| = 10{\cdot}8$ c/s.)

Vicinal coupling constants and conformation. It has been concluded from Dreiding models that the two heterocyclic rings in the 6a,11a-dihydro-6H-benzofuran [3,2-c] [1] benzopyran system must be *cis*-fused.[10,34] There are, however, still two conformations possible as depicted in Fig. 5.

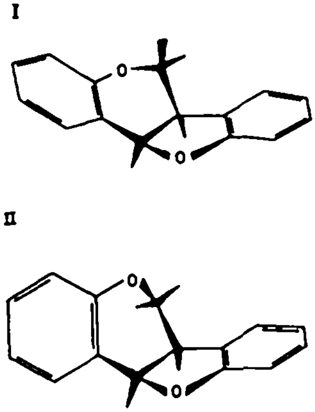


FIG. 5. The two possible conformations of (6a,R:11a,R)-6a,11a-dihydro-6H-benzofuro[3,2-c] [1]benzopyran.

The proton–proton coupling constants for these two conformers are expected to be significantly different (Table 3). Thus the conformation can be derived unambiguously from the experimentally determined coupling constants unless the molecule undergoes rapid conformational changes.

TABLE 3. EXPECTED COUPLING CONSTANTS FOR STAGGERED CONFORMATIONS

Coupling Protons	Conformation I		Conformation II	
	Dihedral Angle	Coupling Constant	Dihedral Angle	Coupling Constant
6a-11a	0°	8-9	0°	8-9
6a-6	180°	10-12	60°	2-3
6a-6′	60°	4-5	60°	2-3

---

[30] M. Karplus and D. M. Grant, *Proc. Nat. Acad. Sci. U.S.A.* 45, 1269 (1959).

[31] N. Muller and D. E. Pritchard, *J. Chem. Phys.* 31, 768, 1471 (1959).

[32] A. D. Buckingham and K. A. McLauhhlan, *Proc. Chem. Soc.* 144 (1963).

[33] H. J. Bernstein and N. Sheppard, *J. Chem. Phys.* 37, 3012 (1962).

[34] H. Suginome, *Experientia* XVIII, 161 (1962).

Table 3 gives the dihedral angles of the relevant protons for the two conformers assuming truly staggered conformations. From the theoretically calculated angle dependence of vicinal proton–proton coupling constants[11] and the knowledge on substituent effects on these couplings,[35] one would expect the coupling constants given in Table 3. The difference in gauche couplings for the two conformations is based on the observation that electronegative substituents cause a decrease of vicinal coupling constants and that they exert their maximum effect if they are *trans* and coplanar to one of the coupling protons.[35–37] In conformation I (Fig. 5), the protons H_{6a} and H_{6}, are *trans* to a hydrogen and a carbon atom respectively, while in conformation II for both gauche couplings a carbon and an oxygen atom are *trans* to the coupling protons.

Comparison of the experimentally determined coupling constants (Table 2) and the expected couplings (Table 3) shows clearly that the benzofurobenzopyran ring system of the compounds studied exists in conformation I (Fig. 5), with the six-membered ring in a staggered half-chair form joint to the planar five-membered ring. The magnitude of the observed coupling constants suggests that angle distortions are only minor. It may furthermore be concluded that the molecule very probably exists in conformation I only and that, if the molecule undergoes conformational changes between the conformers I and II [as suggested for pisatin (VI)[14]], the equilibrium will be very much in favour of the former.

The NMR spectra of other naturally occurring pterocarpan derivatives indicate[38] that these compounds exist in the same conformation (neodulin,[6] ficinin,[8] some other compounds closely related to these, and the pterocarpan derivatives described by Harper *et al.*[9]).

Long-range couplings. Barfield recently calculated the angle dependence of proton–proton coupling constants across four saturated bonds.[39] A search of the literature[40] reveals that there is insufficient data available to test whether these calculations may be used to determine the conformation of organic molecules. Some abnormally large couplings over four saturated bonds have been observed in highly strained ring systems.[40,41] For most of the small long-range couplings observed in molecules with undistorted bond angles only the magnitude is known. Long-range couplings determined for molecules of known conformation and with presumably undistorted tetrahedral bond angles are given in Table 4 together with the coupling constants expected from Barfield's calculations.

The largest coupling constant is expected for the planar zig-zag arrangement [+1·2 c/s, Group (1) in Table 4]. The average magnitude of the experimentally determined values agrees well with the predictions although the sign of these couplings is not yet known. Similarly, the absolute magnitude of long-range couplings predicted for an axial/equatorial arrangement of the interacting protons [Group (2)] and couplings in steroids involving a freely rotating methyl substituent (Group 4) is in accord with experimental observations. A few coupling constants across four bonds and

[35] H. Booth, *Tetrahedron Letters* 411 (1965).

[36] D. H. Williams and N. S. Bhacca, *J. Am. Chem. Soc.* **86**, 2742 (1964).

[37] R. J. Abraham. L. Cavalli and K. G. R. Pachler, *Mol. Phys.* submitted for publication.

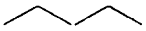
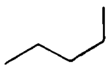
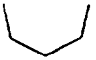
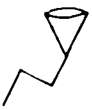
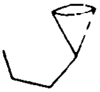
[38] K. G. R. Pachler, unpublished observation.

[39] M. Barfield, *J. Chem. Phys.* **41**, 3825 (1964).

[40] S. Sternhell, *Rev. Pure and Appl. Chem.* **14**, 15 (1964).

[41] J. Meinwald and Y. C. Meinwald, *J. Am. Chem. Soc.* **85**, 2514 (1963).

TABLE 4. OBSERVED AND CALCULATED PROTON-PROTON COUPLING CONSTANTS ACROSS FOUR SATURATED BONDS

Coupling path	Dihedral angle		$^4J_{calc.}$ (c/s)	$^4J^*_{obs.}$ (c/s)	Type of Compound	Ref.
	Φ_1	Φ_2				
1 	180°	180°	+1·2	1·0–1·3	bicyclo(2.2.1)-heptane	*a*
				1·3–1·8	hexopyranoses	*b*
				1·3–1·8	bicyclo(2.2.1)-heptane	*c*
				1·8	bicyclo(3.2.1)-octanone	*d*
				0·5–0·9	hexopyranoses	*e*
				1·1	cyclohexanone	*f*
				1·7	cyclohexane	*f*
				1·5	1,3-dioxan	*g*
				1·0	1,3-dioxan	*h*
2 	180°	60°	+0·7	0·4–0·5	1,3-dioxan	*g*
				0·45	1,3-dioxan	*h*
3 	60°	60°	−0·1	0·3–0·4	1,3-dioxan	*g*
4 	180°	0°–360°	+0·8	0·7	steroid	*i*
				1·0	steriod	*j*
5				0·65	$CH_2Br{-}CBrCH_2\Phi$	*k, l*
				0·75	$CH_2Br{-}CBr(CO_2CH_3)CH_3$	*k, l*
				+0·4	$CH_2Br{-}CHBrCH_3$	*m*
				+0·3–+0·4	$CH_2Br{-}CHBrCH_3$	*n*
6 	60°	0°–360°	+0·2	−0·35	$CH_3CHBr{-}CHBrCO_2H$	*o*
				−0·15	$CH_2Br{-}CHBrCH_3$	*n*
				−0·50	$CH_3CHBr{-}CHBrCH_3$	*p*

* Sign undetermined if not given.

---

[a] F. A. L. Anet, *Canad. J. Chem.* **39**, 789 (1961).
[b] L. D. Hall and L. Hough, *Proc. Chem. Soc.* 382 (1962).
[c] J. I. Musher, *Mol. Phys.* **6**, 93 (1963).
[d] C. W. Jefford and B. Waegell, *Tetrahedron Letters* 1981 (1963).
[e] B. Coxon, *Tetrahedron* **21**, 3481 (1965).
[f] A. Rassat, C. W. Jefford, J. M. Lehn and B. Waegell, *Tetrahedron Letters* 233 (1965).
[g] K. C. Ramey and J. Messick, *Tetrahedron Letters* 4423 (1965).
[h] J. Delmau and J. Duplau, *Tetrahedron Letters* 559 (1966).
[i] H. Wehrli, M. S. Heller, K. Schaffner and O. Jeger, *Helv. Chim. Acta* **44**, 2162 (1963).
[j] N. S. Bhacca, J. E. Gurst and D. H. Williams, *J. Am. Chem. Soc.* **87**, 302 (1965).
[k] D. R. Davies, R. P. Lutz and J. D. Roberts, *J. Am. Chem. Soc.* **83**, 246 (1961).
[l] D. R. Davies and J. D. Roberts, *J. Am. Chem. Soc.* **84**, 2252 (1962).
[m] N. S. Bhacca and R. Freeman, *J. Chem. Phys.* **38**, 1088 (1963).
[n] H. Finegold, *Proc. Chem. Soc.* 213 (1962).
[o] R. Freeman and K. G. R. Pachler, *Mol. Phys.* **5**, 85 (1962).
[p] A. A. Bothner-By and C. Naar-Colin, *J. Am. Chem. Soc.* **84**, 743 (1962).

their signs are available for substituted ethanes where one conformation is expected to be predominantly present (Groups 5 and 6). Here the observed constants for compounds with the Me group *trans* to the coupling proton vary from 0·3 c/s to 0·75 c/s with the sign positive if determined. This also compares favourably with the calculated value of +0·8 c/s. A small coupling (+0·2 c/s) is predicted if the Me group and the coupling proton are gauche to each other, but negative signs have been found experimentally varying from −0·15 c/s to −0·5 c/s.

The same pattern has been observed for the compounds studied. The coupling between the equatorial proton and the carbon atom 6 and the proton on carbon 11a having dihedral angles of 120° and 180° is predicted to be +0·7 c/s and agrees closely with the experimental value of +0·6 c/s. The other long-range coupling ($^4J_{6ax.11a}$; dihedral angles 120° and 60°) is expected to be small (+0·1 c/s) and found to be negative (−0·8 c/s). In a tetrahydrofuran derivative studied earlier[42] with dihedral angles of ca 120° one would expect small long-range couplings of approximately +0·1 c/s but negative couplings of −0·4 c/s and −0·6 c/s have been found experimentally.

Thus it appears that in undistorted saturated systems where relatively large positive long-range coupling constants across four bonds are calculated, these are actually found. In conformations, however, where the theoretical calculations predict small values, the experimental coupling constants have been found to be of negative sign.

There is a host of experimental data not fitting into this scheme, but these are taken from measurements on molecules experiencing considerable ring strain such as bicyclo[2.1.1]-hexanes, bicyclo[2.2.1]-heptanes, 3-chlorothietane,[43] a butane derivative, or compounds with epoxide rings,[44] which are quite obviously bad examples for a comparison with the theoretical results of Barfield. It should also be borne in mind that these calculations are by their nature crude approximations performed for an undistorted hydrocarbon skeleton, taking no substituent effects, no angle distortions, no bond length variations, no ring strains into account. In addition to this indirect, through-bond coupling, it has been suggested that direct, through-space effects may contribute essentially to the observed long-range couplings and these are also not included in the calculations.

[42] K. G. R. Pachler and P. L. Wessels, *J. S. African Chem. Inst.* **19**, 49 (1966).

[43] W. D. Keller, T. R. Lusebrink and C. H. Sederholm, *J. Chem. Phys.* **44**, 782 (1966).

[44] D. D. Elleman, S. L. Manatt and C. D. Pearce, *J. Chem. Phys.* **42**, 650 (1965).