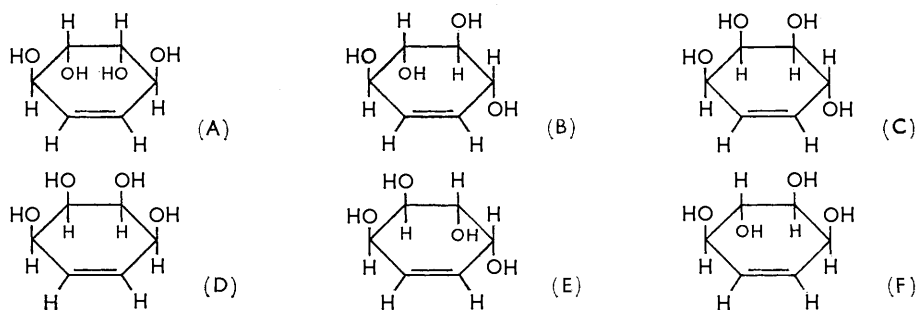


1166. The Proton Magnetic Resonance Spectra and Conformations of Cyclic Compounds. Part II.* The p.m.r. Spectra of the Conduritols

By R. J. ABRAHAM, H. GOTTSCHALCK, H. PAULSEN, and W. A. THOMAS

The proton magnetic resonance spectra of the six isomeric conduritols (1,2,3,4-tetrahydroxycyclohex-5-ene) in D₂O solution are completely analysed to give the chemical shifts and coupling constants of all the ring protons. The values of the vicinal coupling constants confirm the half-chair conformation of these compounds in solution. The allylic and homoallylic couplings obtained support present theories of their orientation dependence. Long-range coupling over four saturated bonds is also observed. This has either sign with a maximum positive value in the diequatorial orientation, and the orientation dependence agrees with other values of this coupling and also with previously unconfirmed theoretical predictions.

PROTON magnetic resonance (p.m.r.) spectroscopy has been used extensively to study a variety of stereochemical problems in the last few years, mainly by applying the $\cos^2 \phi$ relationship first proposed by Karplus,¹ to the CH-CH coupling constants of the molecule. However relatively few studies have been performed on simple cyclohexene derivatives, mainly because the p.m.r. spectra of these compounds are too complex for a complete analysis. In such cases, a careful study of the chemical shifts of those protons which can be resolved is the only practical means of obtaining useful chemical information, and this approach has been utilised successfully to study the conformations of some 6-substituted 1-phenylcyclohexenes.² The ring proton-proton coupling constants have been determined in a few cases. Analysis of the olefinic pattern in cyclohexene itself gave the couplings involving the olefinic protons,³ though the observed and calculated spectra were not in exact agreement. More detailed studies of the p.m.r. spectrum of shikimic acid⁴ demonstrated that the observed values of the ring coupling constants were consistent with a half-chair conformation, but not the boat conformation. Similar results were obtained for acetylglucal.⁵ It is of some interest to extend these isolated examples to a systematic determination of coupling constants and conformations in cyclohexene derivatives. We report here the complete analyses of the spectra of the six possible conduritol isomers (3,4,5,6-tetrahydroxycyclohex-1-ene),† A, B, C, D, E, and F.



* R. J. Abraham and W. A. Thomas, *J.*, 1965, 335, is considered as Part I.

† We shall use henceforth the accepted numbering in the conduritol field, in which these compounds are designated 1,2,3,4-tetrahydroxycyclohex-5-ene.

¹ M. Karplus, *J. Chem. Phys.*, 1959, **30**, 11.

² E. W. Garbisch, *J. Amer. Chem. Soc.*, 1963, **85**, 927.

³ G. V. Smith and H. Kriloff, *J. Amer. Chem. Soc.*, 1963, **85**, 2016.

⁴ L. D. Hall, *J. Org. Chem.*, 1964, **29**, 297.

⁵ L. D. Hall and L. F. Johnson, *Tetrahedron*, 1964, **20**, 883.

EXPERIMENTAL

The preparations of all the conduritols have been given previously,⁶ and the spectra confirmed the absence of any impurities. The spectra of the solutions in D₂O were measured on a Varian A-60 spectrometer (and in one case on a Varian HR 100 in addition), using the methyl peaks of sodium 2,2-dimethyl-2-silapentane-5-sulphonate as the internal reference (10,000 τ). All the hydroxyl protons exchange rapidly with the solvent, leaving a spectrum due to the six ring protons. The various groups in the spectrum are easily assigned, since the 2- and 3-protons are at highest field (5.9—6.4 τ), the 1- and 4-protons next (5.6—5.9 τ) and the olefinic protons at much lower field (4.1—4.4 τ). The assignment within the groups can only be made on the basis of the couplings obtained from the analysis of the spectrum.

In the unsymmetric compounds (conduritols C and F), all the protons are non-equivalent, thus the spectra are ABCDXY spectra⁷ (the vinyl protons being well separated from the other peaks). Such spectra are too complex for a full analysis, though most of the coupling constants of these molecules can be obtained by approximate methods (see below). However, the remaining isomers (A, B, D, and E) are symmetric, thus protons 1 and 4, 2 and 3, and 5 and 6 are equivalent, *i.e.*, these are A₂B₂X₂ spectra.* The general A₂B₂X₂ case is still extremely complex but it is possible to make considerable simplifications for these spectra, as follows. We may safely assume that the couplings between the 2- and 3-protons and the 5- and 6-protons are negligible. (No instances of such =CH-C-C-H couplings have yet been recorded except for epoxides and aldehydes, which are both special cases.) Also the J/δ ratio for the A₂B₂ half of the spectrum is small (*e.g.*, $J_{1,2} \sim 8$ c./sec. and $\delta_{1,2} \sim 50$ c./sec.). Thus, the groups are all weakly coupled. These factors together mean that the spectra can be treated as two separate A₂B₂ or A₂X₂ systems, *e.g.*, the 2- and 3-proton peaks will be one half an A₂B₂ system, from which all the couplings can be obtained explicitly, and similarly the olefinic spectrum will constitute one half of an A₂X₂ system. The 1- and 4-proton spectrum will in general be more complex, but this is of no consequence.

These A₂B₂ or A₂X₂ spectra are all obtained from the grouping shown. This grouping, and thus the coupling constants and spectral assignments, bear a resemblance to the well documented A₂B₂ spectra of *ortho*-disubstituted benzenes⁷ in that J_B and $J(J_{A,B})$ are the dominant couplings, J_A and $J'(J_{A,B'})$ being much smaller. The main difference is that, whilst all the couplings in the benzene ring are positive, in the conduritols they may be of either sign. In the 1H,2H,3H,4H-A₂B₂ system $J(J_{1,2})$, $J_B(J_{2,3})$, and $J_A(J_{1,4})$ are all positive,^{4,9} but $J'(J_{1,3})$ may be of either sign.^{10,11} In the 4H,5H,6H,1H-A₂X₂ system, a similar situation holds, except that $J'(J_{1,6})$ is known to be negative.⁹ Thus $N(=J+J')$ is possibly smaller than $L(=J-J')$. The magnitudes of N and L emerge uniquely from the analysis, and the results show that J' can be of either sign.

A spectrum of this type is that of the 1H, 2H, 3H, and 4H protons of conduritolo B (Figure 1), which also shows the assignments of the peaks and the calculated spectrum. The excellent agreement between the observed and calculated spectra demonstrate the validity of the above discussion.

It is of interest to note that the olefinic spectrum of this compound is a single line. This is a further example of a deceptively simple spectrum¹² in that this *does not* mean that all the couplings to the olefinic protons are zero, but merely that $N < 0.5$ c./sec., the line-width. As it is known that $J(J_{1,6})$ and $J'(J_{1,6})$ are of opposite sign, this result follows immediately when the vicinal coupling ($J_{1,6}$) is small. This phenomenon has also been noted in some Δ^3 -proline derivatives.¹³

* As these protons are chemically, but not magnetically, equivalent, some authors⁸ would classify the spectra as AA'BB'XX'.

⁶ K. Heyns, H. Gottschalck, and H. Paulsen, *Chem. Ber.*, 1962, **95**, 2660.

⁷ J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill, London, 1959.

⁸ D. R. Whitman, *J. Mol. Spectroscopy*, 1963, **10**, 250.

⁹ M. Karplus, *J. Chem. Phys.*, 1960, **33**, 1842.

¹⁰ R. Freeman and K. Pachler, *Mol. Phys.*, 1962, **5**, 85.

¹¹ M. Barfield, *J. Chem. Phys.*, 1964, **41**, 3825.

¹² R. J. Abraham and H. J. Bernstein, *Canad. J. Chem.*, 1961, **39**, 216.

¹³ A. V. Robertson and B. Witkop, *J. Amer. Chem. Soc.*, 1962, **84**, 1697.

In conduritols A and D a doublet vinyl spectrum was observed, the separation of the peaks giving again only $J + J'$. However in conduritol E the vinyl spectrum was similar to that of the A_2B_2 spectrum of Figure 1 and was analysed in a precisely similar manner.

The spectrum of conduritol C was complex and not well resolved, and thus only a first-order analysis of the spectrum was possible. However, as the separations between the peaks are much larger than the couplings, *i.e.*, they are all weakly coupled protons, the values of the splittings which could be measured will be expected to be good approximations to the true coupling constants.

In the spectrum of conduritol F, the chemical shifts are such that the 2- and 3-protons and the 5- and 6-protons form two strongly coupled AB systems. Thus, a first-order analysis is no longer possible. The 60-Mc./sec. spectrum was too complex for any analysis, but the 100-Mc./sec. spectrum could be analysed as follows. Protons 1 and 4 are well separated from the two AB systems and the value of $J_{1,4}$ (> 3 c./sec.) is small compared with the chemical shift separation of 1 and 4 (22 c./sec. at 100 Mc./sec.). Also the two AB pairs will not couple appreciably (*i.e.*, $J_{2,5}; 2,6$ and $J_{3,5}; 3,6$ are insignificant, ≈ 0). Thus, we can treat the 2,3- and 5,6-patterns as the AB regions of the two separate ABXR spectra. The theory of the general ABR_pX_q case¹⁴ shows that the AB part of these spectra can be considered as the superposition of a number of simple AB quartets, in each of which the effective chemical shift of proton A (δ'_A) depends not only on the true chemical shift (δ_A) but also on the orientation of the X and R nuclei. In the ABXR case

$$\begin{aligned}\delta'_A &= \delta_A \pm \frac{1}{2}J_{AX} \pm \frac{1}{2}J_{AR} \\ \delta'_B &= \delta_B \pm \frac{1}{2}J_{BX} \pm \frac{1}{2}J_{BR}\end{aligned}$$

and

As the positive and negative signs for the X and R nuclei have to be considered together, there will be four such quartets in the AB part of an ABXR spectrum in which

$$\begin{aligned}1. \quad & \begin{cases} \delta'_A - \delta_A = \frac{1}{2}(J_{AX} + J_{AR}); \\ \delta'_B - \delta_B = \frac{1}{2}(J_{BX} + J_{BR}); \end{cases} & 2. \quad & \begin{cases} \delta'_A - \delta_A = \frac{1}{2}(J_{AX} - J_{AR}) \\ \delta'_B - \delta_B = \frac{1}{2}(J_{BX} - J_{BR}) \end{cases} \\ 3. \quad & \begin{cases} \delta'_A - \delta_A = -\frac{1}{2}(J_{AX} - J_{AR}); \\ \delta'_B - \delta_B = -\frac{1}{2}(J_{BX} - J_{BR}) \end{cases} & 4. \quad & \begin{cases} \delta'_A - \delta_A = -\frac{1}{2}(J_{AX} + J_{AR}) \\ \delta'_B - \delta_B = -\frac{1}{2}(J_{BX} + J_{BR}) \end{cases}\end{aligned}$$

All these AB quartets will have the same coupling constant J_{AB} . Thus, the analysis of the spectrum consists in picking out these four AB quartets from the observed patterns. The 100-Mc./sec. spectrum of the two pairs of closely coupled protons, and the breakdown into the four quartets is shown in Figure 2. The relative signs of J_{AX} , J_{BX} , J_{AR} , and J_{BR} are obtained from these analyses, but not that of J_{AB} . The patterns of the R and X groups are extremely complex as they couple to both the AB systems and to each other, and the fine structure of these protons was not resolved sufficiently to justify comparison with a calculated spectrum.

The couplings and chemical shifts obtained from all these analyses are shown in Tables 1 and 2.

TABLE I
Proton chemical shifts (τ values)

Compound	1H	2H	3H	4H	5H	6H
Conduritol A	5.80	6.17		5.80	4.21	
„ B	5.83	6.56		5.83	4.39	
„ C	5.61	5.88	6.35	5.70	4.34	
„ D	5.77	6.09		5.77	4.15	
„ E	5.70	6.10		5.70	4.13	
„ F	5.92	6.39	6.43	5.70	4.11	4.19

TABLE 2

		Proton coupling constants (c./sec.)										
		$J_{1,2}$	$J_{1,3}$	$J_{1,4}$	$J_{1,5}$	$J_{1,6}$	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$	$J_{4,5}$	$J_{4,6}$	$J_{5,6}$
Conduritol A		5.4	-0.2	+1.0	1.6 ¹		2.3	-0.2	5.4	1.6 ¹		- ²
"	B	8.3	-0.3	+3.0	<0.5 ¹		10.3	-0.3	8.3	<0.5 ¹		- ²
"	C	3.0 ³	<0.5	- ²	- ²		2.1 ³	<0.5	8.1 ³	- ²		- ²
"	D	4.2	0.9	+1.6	1.7 ¹		1.6	0.9	4.2	1.7 ¹		- ²
"	E	4.3	-0.5	+0.7	-1.1	4.5	9.3	-0.5	4.3	4.5	-1.1	10.1
"	F	8.4	-0.3	-	-2.1	1.9	11.0	-0.8	4.4	5.3	-0.5	10.2

¹ $J_{1,5} + J_{1,6}$ ($J_{4,5} + J_{4,6}$). ² Indeterminate from spectrum. ³ First-order values from weakly coupled protons.

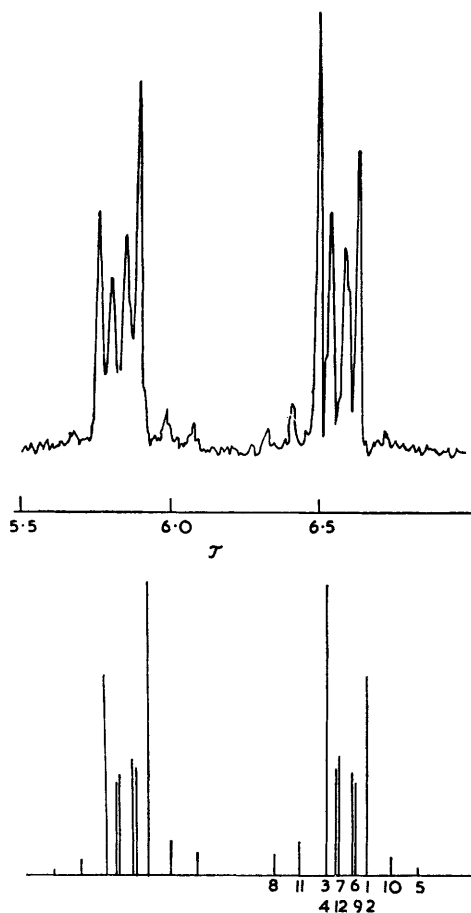


FIGURE 1. The observed and calculated A_2B_2 60-Mc./sec. spectrum of the 1-, 2-, 3-, and 4-protons of conduritol B in D_2O solution

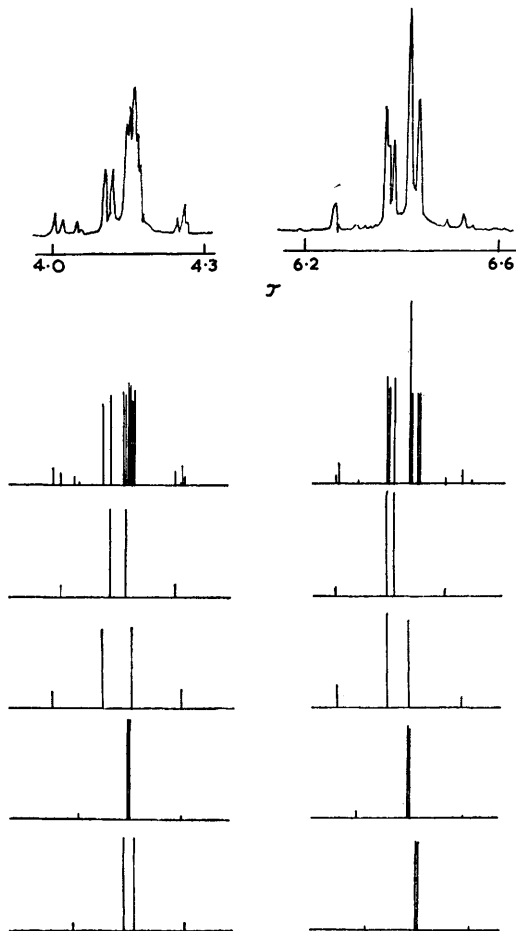
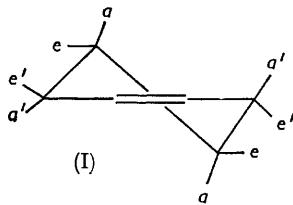


FIGURE 2. The observed and calculated 100-Mc./sec. spectrum of the 2,3- and 5,6-protons of conduritol F in D_2O solution

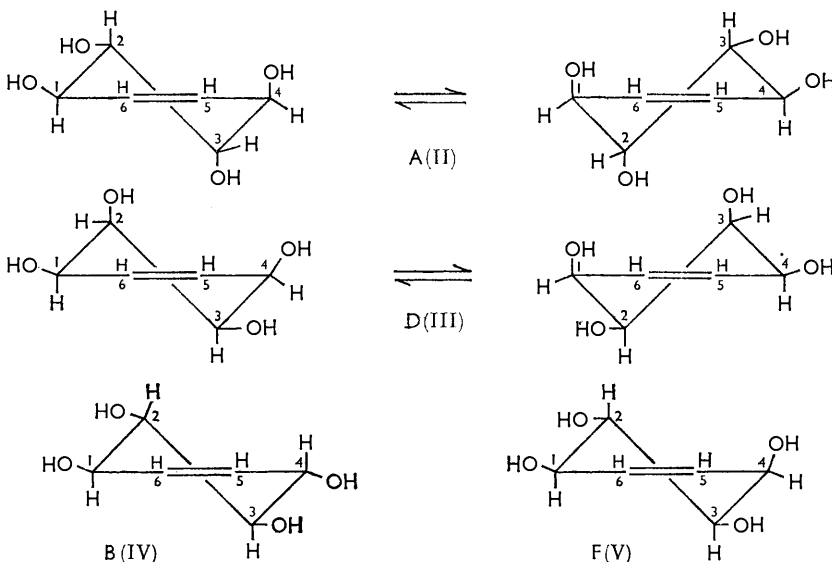
RESULTS

In order to extract the molecular constants from the results of Tables 1 and 2 it is necessary to make two basic assumptions. These are that only the half-chair conformation (I) need be

considered and that this conformation remains unchanged for all the isomers. The first assumption is reasonable on energetic grounds and will be justified later on. Strong support for the second is provided by Table 2. (We shall consider henceforth mainly the coupling constants.)



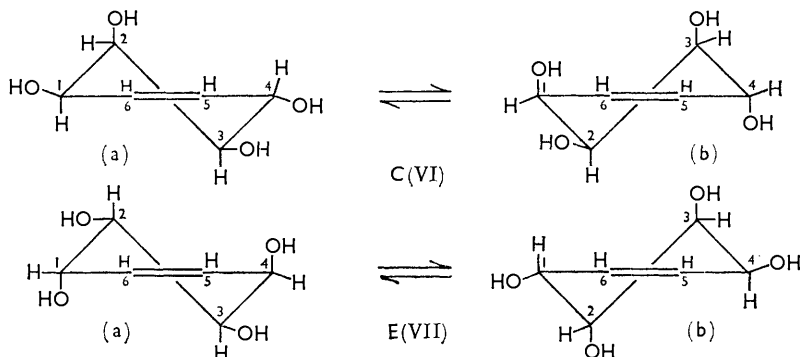
This shows that the couplings between the C-6, C-1, and C-2 protons of conduritol F are almost identical with those of the corresponding protons in conduritol B, and a similar relationship holds between the C-3, C-4, and C-5 proton couplings and those of conduritol E. As conduritol F is made up of half conduritol B and half conduritol E in unchanged stereochemical arrangement, this result confirms the invariance of the ring conformation in these compounds, and by inference for the remaining compounds. In conduritol A and D the molecules are flipping between two mirror-image conformations, shown in (II) and (III), respectively, so that the observed couplings are the average of the couplings in the two conformers. In conduritol B, with four equatorial hydroxyl groups (IV) and conduritol F (V), with the hydroxyl groups $e'ea'$, the other possible conformers are of much higher energy and thus the molecules will be largely in the conformations shown. However, in conduritols C and E the percentages of both the conformers shown in (VI) and (VII) may be appreciable, e.g., if the free-energy difference between axial and equatorial hydroxyls on C-2 and C-3 is taken to be the same as in cyclohexanol (0.7 kcal./mole)¹⁵ (which is a maximum value as the 1,3-interactions are less in the cyclohexene ring) and that between the pseudo-axial and pseudo-equatorial hydroxyls on C-1 and C-4 to be one half this value, then the free-energy differences between forms (a) and (b) would be 0.7 kcal./mole for both conduritol C and E, i.e., approximately 25% of the molecules would exist as conformers (b).



Consider the coupling constant $J_{1,2}$ ($\equiv J_{3,4}$). There will be four possible orientations of the C-1 and C-2 hydrogens, giving four coupling constants, $J_{e'a}$, $J_{e'e}$, $J_{a'a}$, and $J_{a'e}$. The results for conduritols B and F give immediately $J_{a'a}$ (twice) and $J_{e'a}$. The observed coupling in conduritol A is $\frac{1}{2}(J_{a'a} + J_{e'e})$. Using the value of $J_{a'a}$ obtained already gives the value of $J_{e'e}$. Similarly, $J_{1,2}$ in conduritol D is $\frac{1}{2}(J_{a'e} + J_{e'a})$ which gives $J_{a'e}$ from the previous value of $J_{e'a}$. These values are shown in Table 3. In conduritol E the observed value of $J_{1,2}$ ($\equiv J_{3,4}$) should lie between $J_{e'a}$ and $J_{a'e}$. This is indeed the case (Table 3). The value of J (4-3) is very close to $J_{e'a}$, but the difference between $J_{a'e}$ and $J_{e'a}$ is too small to draw any firm conclusions from this. Indeed, $J_{1,2}$ in conduritol C lies outside the expected range. The

¹⁵ E. L. Eliel and M. H. Gianni, *Tetrahedron Letters*, 1962, 97.

errors in the first-order analysis of this ill-resolved spectrum could account for a large part of this difference. However, the value of $J_{3,4}$ does lie between the two limits and here the large difference between $J_{e'e}$ and $J_{a'a}$ shows conclusively that conduritol C exists largely in form (VIa).



This breakdown is shown in Table 3 with the values for conduritols E and C shown connected to the two limiting values.

A similar breakdown can be performed for all the couplings, and the results are shown in Table 3. For $J_{2,3}$ by symmetry $J_{ae} = J_{ea}$. Therefore, there are only three possible couplings and also the couplings for conduritols A, D, and C are now merely J_{ae} . Unfortunately there is no value for J_{ee} . This would be expected to be small, so that the observed large value of $J_{2,3}$ for conduritol E demonstrates the preponderance of form (VIIa) with the axial-axial coupling. The vicinal couplings to the vinyl protons, *i.e.*, $J_{1,6}$ ($J_{4,5}$) can be treated in the same fashion, though now there are only two possibilities, $J_{H'e'}$ and $J_{H'a'}$. These are only obtained uniquely from the conduritol F couplings, though the value for conduritol E again demonstrates the preponderance of conformer (VIIa). The couplings over four and five bonds are also shown

TABLE 3

The breakdown of the coupling constants in the conduritol ring

<i>Vicinal couplings</i>								
$J_{e'e}$	$J_{1,2}, J_{3,4}$		$J_{a'a}$	J	$J_{2,3}$	J_{aa}	$J_{1,6}, J_{4,5}$	
2.4(A)	$J_{e'a}$	$J_{e'e}$	8.3(B)	$J_{ae}(=J_{ea})$	2.3(A)	10.3(B)	$J_{H'e'}$	
	4.4(F)	4.0(D)	8.4(F)		1.6(D)	11.0(F)	$J_{H'a'}$	
					2.1(C)		4.5(E)	
	4.3(E)				9.3(E)			
	3.0(C)							
	8.1(C)							
<i>Long-range couplings</i>								
	CH·C·CH ($J_{1,3}, J_{2,4}$)			Homoallylic ($J_{1,4}$)			Allylic ($J_{1,5}, J_{4,6}$)	
$J_{e'e}$	$J_{e'a}$	$J_{e'e}$	$J_{a'a}$	$J_{e'e}$	$J_{e'a}(=J_{a'e'})$	$J_{a'a'}$	$J_{H'e'}$	$J_{H'a'}$
2.1(D)	-0.8(F)	0.4(A)	-0.3(B)	ca. 0	+1.0(A)	+3.0(B)	-0.5(F)	-2.1(F)
			-0.3(F)		+1.6(D)		-1.1(E)	
					+0.7(E)			
		-0.5(E)						
		<0.5(C)						
	<0.5(C)							

in Table 3. The allylic (CH=C=CH) couplings ($J_{1,5}$ and $J_{4,6}$) are known to be of negative sign, as is observed. Again only one compound (conduritol F) gives these values uniquely, but again the value in conduritol E favours conformer (VIIa).

The values of $J_{1,5}$ and $J_{1,6}$ can now be used to calculate the sum of the couplings in condiritols A, B, and D. These calculated values are 2.3, -0.2, and 2.3 c./sec., respectively; in very good agreement with the observed values of 1.6, <0.5, and 1.7 c./sec. The homoallylic (CH=C-CH) coupling ($J_{1,4}$) has three possible values, and the value of 0.7 for condiritol E, taken with the previous results, suggests that the value for $J_{e'e'}$ is ca. 0 c./sec. The long-range coupling over four saturated bonds $J_{1,3}$ ($J_{2,4}$) is of considerable interest, as the angle variation of this coupling is not yet known. Here again the breakdown of the results leads to a set of consistent values, with those for condiritols E and C falling between the predicted limits, with once more the values for E favouring conformer (VIIa). The average of the four results for condiritol E gives ca. 20% of conformer (VIIb) present. There is only one result ($J_{1,2}$) for condiritol C, and this suggests that less than 10% of the molecule exists as conformer (VIb).

DISCUSSION

The results obtained in Table 3 can now be used to provide information on the conformation of the cyclohexene ring in the condiritols, and also to check present theories of proton-proton coupling constants. As the vicinal (CH-CH) couplings are best known, they will be considered first. A large number of investigations¹⁶⁻¹⁸ have demonstrated the general validity of the result, first derived by Karplus,¹ that these couplings are proportional to $\cos^2 \phi$, where ϕ is the dihedral angle of the two C-H bonds involved. The proportionality constants in this equation depend on the electronegativity of the substituents on the C-C fragment.¹⁹ However, a range of proportionality constants have been proposed for the same fragments and there is evidence that the $\cos^2 \phi$ law does not precisely account for all the couplings observed in steroids²⁰ and cyclohexanols²¹ (for which $J_{ac} \neq J_{ee} \approx J_{ea}$, although in the undistorted chair conformation the angles are all 60°) and in the camphane ring²² (in which $J_{2\text{endo-3endo}} \neq J_{2\text{exo-3exo}}$ although the dihedral angles should both be 0°). The general validity of the $\cos^2 \phi$ law is such that it may be used with confidence to distinguish between different conformations (such as in this case the boat and half-chair forms), though the values of the dihedral angles obtained with its use should be treated with caution.

The proportionality constants in the equation for the fragments considered, *i.e.*, C-CH(OH)·CH(OH)·C, may be obtained from compounds of known stereochemistry, *e.g.*, J_{aa} in *trans*-1,2-cyclohexanediol is 11.0 c./sec.²³ and this can be equated with J_{180° . Values for J_0 range from 8 to 9 c./sec. in the camphane-2,3-diols¹⁶ to an estimated value of 14 c./sec. in cyclohexanediol.²³ We will take 11.0 c./sec. as the mean value. It should be noted that the precise value of this coupling is not of great importance as all the angles we consider lying between 0° and 90° are ca. 50—70° and in this region the $\cos^2 \phi$ curve has a very steep slope. Thus, a change in J_0 of 1 c./sec. will make only a 1° change in the calculated dihedral angles, which is well within the limit of applicability of the $\cos^2 \phi$ law. The converse is also true and this is the reason for the large spread in the proposed values of J_0 from measurements of J_{ee} , J_{ae} , etc., which are all ca. J_{60° .

The dihedral angles obtained by the use of the equation $J = 11.0 \cos^2 \phi$ on the observed values of $J_{1,2}$ and $J_{2,3}$ are given in Table 4, which includes values for the C(6), C(1)-fragment although this is an sp^2 - sp^3 -hybridised fragment for which the Karplus theory is not strictly applicable. It is known that such CH·CH=C couplings are orientation dependent²⁴ and recently Smith and Kriloff³ have proposed $J = 10.6 \cos^2 \phi$ and $11.4 \cos^2 \phi$

¹⁶ F. A. L. Anet, *Canad. J. Chem.*, 1961, **39**, 789.

¹⁷ R. J. Abraham and K. A. McLauchlan, *Mol. Phys.*, 1962, **5**, 513.

¹⁸ H. Conroy, *Adv. Org. Chem.*, 1960, **2**, 311.

¹⁹ R. J. Abraham and K. G. R. Pachler, *Mol. Phys.*, 1963, **7**, 165.

²⁰ D. H. Williams and N. S. Bhacca, *J. Amer. Chem. Soc.*, 1964, **86**, 2742.

²¹ F. A. L. Anet, *J. Amer. Chem. Soc.*, 1962, **84**, 1053.

²² J. I. Musher, *Mol. Phys.*, 1963, **6**, 93.

²³ R. U. Lemieux and J. W. Lown, *Canad. J. Chem.*, 1964, **42**, 893.

²⁴ A. A. Bothner-By, C. Naar-Colin, and H. Günther, *J. Amer. Chem. Soc.*, 1962, **84**, 2748.

in such a fragment. For our purposes we may again take $J = 11.0 \cos^2 \phi$. Also included in Table 4 are calculated dihedral angles for the same fragments in the half-chair form of cyclohexene. In one case these angles have been derived from the calculations of Corey and Sneen,²⁵ in the other from Hall's measurements with Barton models.⁴ There is general agreement between the "observed" and calculated dihedral angles, which confirms

TABLE 4

"Observed" and calculated dihedral angles in the conduritols

	H-1, H-2 (H-3, H-4)				H-2, H-3		H-4, H-5 (H-6, H-1)	
	<i>e'a</i>	<i>e'e</i>	<i>a'a</i>	<i>a'e</i>	<i>ea</i>	<i>aa</i>	<i>He'</i>	<i>Ha'</i>
"Observed"	51	62	151	53	64	168	46	65
Corey-Sneen	59	62	178	60	69	190	43	77
Barton	50	70	170	50	60	180	40	80

unambiguously the half-chair conformations of the conduritols. However, there are a number of minor discrepancies. It is of interest to note that the approximate measurements from a Barton model are in as good agreement with the observed dihedral angles as the results of the calculations of Corey and Sneen. These calculations obtain that conformation of the cyclohexene ring which minimises the angle strain around the ring. However, they omit any explicit formulation of the Pitzer (or eclipsing strain) or of the Van der Waals repulsions between 1,3-substituents in the ring. In the derived conformation, the Pitzer strain is minimised in the 1,2-fragment (for which the angles are 60° and 180°) but not minimised in both the 2,3- (angles 70° and 190°) and 6,1-fragments (angles 43° and 77°). In the latter fragment the energy minimum (which is visualised most easily by regarding the double bond as two bent single bonds and then staggering the bonds as in ethane²⁶), would correspond to a planar ring. Thus, these interactions would have the effect of decreasing the angle of buckle of the ring. Also the 1,3-di-axial interactions would reinforce this tendency. Thus, the Corey-Sneen model is undoubtedly considerably more buckled than the actual cyclohexene ring. This is precisely what is observed in Table 4. Consideration of the differences between the observed and calculated (Corey-Sneen) dihedral angles, together with the relationships between the ring buckling and these angles, suggests that the most plausible dihedral angles in the half-chair conformation of the cyclohexene ring are C-1, C-6 ~15° (giving *He'* 45°, *Ha'* 75°), C-2, C-3 *ca.* 50°, and C-3, C-4 *ca.* 60°. These values will be used in the following discussion.

The allylic (CH·C=CH) couplings also exhibit an angular dependence. Theory predicts⁷ that these couplings, which are due to σ - π interactions, are proportional to the overlap of the π -orbital of the double bond and the 1s orbital of the saturated C-H proton. This is proportional to $\cos^2 \phi$, where ϕ is the dihedral angle between the C-H proton and the π -orbital. It is more convenient to retain the previous definition of ϕ in the C-1, C-6 fragment, *i.e.*, the dihedral angle between the C-H bond and the plane of the olefinic group. In this case, the allylic coupling will be proportional to $\sin^2 \phi$. Recently, considerable experimental evidence supporting a coupling constant variation with dihedral angle of this form has been accumulated.^{27,28} The coupling has a maximum value of *ca.* -3 c./sec. when ϕ is 90° and a near-zero value for $\phi = 0^\circ$. The explicit $\sin^2 \phi$ dependence is not fully established as yet. In Table 3 the two values of the allylic coupling ($J_{He'}$ and $J_{Ha'}$) correspond to angles of 45° and 75°, respectively, *i.e.*, the couplings should be proportional to 0.5 and 0.9. The observed couplings are -0.5 and -2.1 c./sec., a much larger variation than expected. The reason is that there is also a σ -bond coupling over four bonds. This is orientation-dependent and can be of either sign, and thus can add or subtract to the σ - π coupling (see later).

²⁵ E. J. Corey and R. A. Sneen, *J. Amer. Chem. Soc.*, 1955, **77**, 2505.

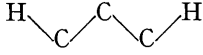
²⁶ R. J. Abraham and J. A. Pople, *Mol. Phys.*, 1960, **3**, 609.

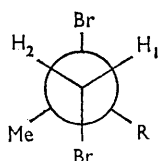
²⁷ S. Sternhell, *Rev. Pure and Appl. Chem.*, 1964, **14**, 15.

²⁸ C. N. Banwell and N. Sheppard *Discuss. Faraday Soc.*, 1962, **34**, 115.

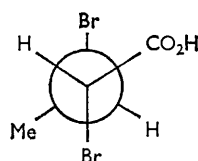
The homoallylic couplings (CH·C=C·CH) are considered to arise from the same σ - π mechanism as the allylic couplings and have a similar orientation dependence.⁹ There are now two dihedral angles involved so that the coupling will be proportional to $\sin^2 \phi_1 \cdot \sin^2 \phi_2$. Again considerable evidence has been accumulated which supports the qualitative predictions of the theory,^{27,28} *i.e.*, a maximum coupling (of *ca.* 3 c./sec.) for both dihedral angles $\sim 90^\circ$ and a zero coupling for either dihedral angle $= 0^\circ$. The homoallylic couplings observed in Table 3 support the general predictions of the theory, *e.g.*, $J_{e'e'} < J_{e'a'} < J_{a'a'}$ as expected. (This order has also been noted in other natural products with a half-chair conformation.²⁹) However, the actual values show again much more variation than would be expected on the simple theory. From the known dihedral angles we would expect the couplings to be in the ratio 0.25 : 0.5 : 0.9. The observed couplings are *ca.* 0, 1.3, and 3.0 c./sec. Proton-proton couplings over five saturated bonds have not been observed, so we may assume that no σ -coupling interaction is present here. Thus, it would appear that the homoallylic couplings decrease from the maximum value much more rapidly than would be expected on this simple σ - π theory.

Of particular interest are the couplings over four saturated bonds observed here. Although these couplings have been observed quite often for one particular orientation of the H·C·C·CH fragment, the theory of these couplings has until recently been merely speculative and no systematic experimental evidence on the stereochemical nature of the coupling has so far been obtained. The couplings which have been observed fall into three types.²⁷ (Here we exclude the very special couplings in the highly strained bicyclo-[2,1,1]hexane system^{30,31} and also couplings through an epoxide or cyclopropane ring.)

Most of the observed couplings are in systems in which the  system forms a planar zig-zag arrangement,²⁸ *e.g.*, the 1,3-diequatorial couplings in cyclohexanes³² and sugar rings³³ are well-established examples. These couplings are of *ca.* 1—2 c./sec. but of unknown sign. A second type is in the dibromopropane (VIII), in which $J_{\text{Me}} - \text{H}_1 = 0.65$ (R = Ph) and 0.75 (R = CO₂Me) and $J_{\text{Me}} - \text{H}_2 = 0$ in both cases.³⁴



(VIII)



(IX)

The third type, of much smaller magnitude, but negative in sign, is found in 2,3-dibromobutyric acid (IX) ($J_{\text{Me}} - \text{H}_1 = -0.35$ c./sec.)¹⁰ and has also been observed in a number of 2,3-disubstituted butanes, in which the coupling is of *ca.* -0.1 to -0.3 c./sec. and is between methyl and methine protons in a *gauche* orientation.^{35,36} [It should be noted that such results are not at variance with $J_{\text{Me}} - \text{H}_2 = 0$ in (VIII), as these small couplings have been obtained by the complete analyses of these strongly coupled systems, which makes it possible to detect couplings which would normally be below the limit of resolution of the spectrometer.]

In Table 3 both signs of these long-range couplings are found. In agreement with the above results, a small negative coupling is observed when the protons are in a "*gauche*

²⁹ D. W. Cameron, O. G. L. Kingston, N. Sheppard, and Lord Todd, *J.*, 1964, 98.

³⁰ J. Meinwald and A. Lewis, *J. Amer. Chem. Soc.*, 1961, **83**, 2769.

³¹ K. B. Wiberg, B. R. Lowry, and B. J. Nist, *J. Amer. Chem. Soc.*, 1962, **84**, 1594.

³² A. Rassat, C. W. Jefford, J. M. Lehn, and B. Waegell, *Tetrahedron Letters*, 1964, 233.

³³ L. D. Hall and L. Hough, *Proc. Chem. Soc.*, 1962, 362.

³⁴ D. R. Davis and J. D. Roberts, *J. Amer. Chem. Soc.*, 1962, **84**, 2252.

³⁵ F. A. L. Anet, *J. Amer. Chem. Soc.*, 1962, **84**, 747.

³⁶ A. A. Bothner-By and C. Naar-Colin, *J. Amer. Chem. Soc.*, 1962, **84**, 743.

orientation" (*i.e.*, $J_{aa'}$), and furthermore it is shown that the large coupling observed in the $e-e'$ orientation is positive. These results can be used to check a recent theory of these coupling constants proposed by Barfield.¹¹ In this theory, the coupling constant was calculated as a function of the two dihedral angles involved (*i.e.*, the two $\text{H} \backslash \text{C} - \text{C} / \text{C}$ angles). This theory predicts maximum positive coupling of *ca.* 1.2 c./sec. for both dihedral angles equal to 180° (the completely staggered form) and for angles equal to 0° , and maximum negative coupling constants of *ca.* -0.7 c./sec. for two 90° dihedral angles. The theoretical graphs are approximated by the formula $J = \cos^2 \phi_1 + \cos^2 \phi_2 - 0.8$ c./sec.

It is of considerable interest to compare the observed values of the coupling constants found in the conduritols with those predicted by this theory. The four couplings observed, *i.e.*, $J_{e'e}$, $J_{e'a}$, $J_{a'e}$, and $J_{a'a}$, which correspond to pairs of dihedral angles of 170° and 180° , 170° and 60° , 50° and 180° , and 50° and 60° are calculated on the basis of the explicit theory to be 1.1, 0.6, 0.65, and -0.4 c./sec., respectively. The above approximate equation gives 1.2, 0.4, 0.6, and -0.2 c./sec. The observed couplings are 2.1, -0.8 , 0.4, and -0.3 c./sec. Apart from the proportionality constant, the theory reproduces the observed couplings quite well except for $J_{e'a}$. This observed coupling does appear anomalous, as the difference between $J_{e'a}$ and $J_{a'e}$ would not be expected to be very large.

Thus, the reason for this exception is not at all clear. With the above information, the three classes of long-range coupling mentioned previously fall neatly into place, the large positive coupling most commonly encountered is equivalent to $J_{e'e}$, *i.e.*, $\phi_{1,2} = 180^\circ$. The smaller coupling of a methyl group oriented *trans* to a proton, as in (VIII), *i.e.*,

$\text{CH}_3 \text{---} \text{C} \backslash \text{C} / \text{H}$, is given by $\frac{1}{3}(J_{ee} + 2J_{ea})$. This is calculated as $+0.7$ c./sec., in excellent agreement with the observed values (0.65 and 0.75 c./sec.).

Finally, the much smaller coupling of a methyl group *gauche* to a methine proton, as in (IX), *i.e.*, $\text{CH}_3 \text{---} \text{C} \text{---} \text{C} \backslash \text{H}$, is given by $\frac{1}{3}(J_{ea} + 2J_{aa})$ and calculated to be -0.1 c./sec., again in good agreement with the observed values (-0.1 to -0.3 c./sec.).

It is clear that, although this theory does not give precise description of all the long-range couplings found here, the general overall agreement is such as to provide a good foundation from which more experimental evidence and theoretical calculations can be produced.

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