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STUDIES ON CYCLITOLS—XVI

CONFORMATIONAL ANALYSIS OF SUBSTITUTED CYCLOPENTANES, CYCLOPENTENES AND CYCLOPENTENE OXIDES*

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Abstract—PMR spectroscopy has been used to study the conformations at room temperature of several classes of cyclopentanoid compounds, including substituted cyclopentenes, cyclopentene oxides, tri- and tetrasubstituted cyclopentanes. The substituents are either halogens or —OR, where R is H, Ac, Bz or Me. Unlike the cyclohexanoid compounds, for most of which only the two chair forms need be considered, the cyclopentanoid compounds generally have several different conformers contributing significantly to the conformational equilibrium. The cyclopentane ring is so flexible that conformations with less than maximum puckering have little additional strain, and there appears to be considerable pseudolibration about the energy well representing a particular fully puckered conformation. The series whose conformations are most restricted is the cyclopentene oxides. Regardless of substituents, an *endo*-conformation is preferred, except for the *cis*-4-bromo-1,2-oxide which exists as an equal mixture of *endo* and *exo* conformers; all the other oxides seem to exist in fully puckered *endo* conformations. Unlike the cyclohexanes, the cyclopentanes easily tolerate 1,3-*syn* diaxial substituents, and 1,2-*trans* substituents are generally disposed diaxially rather than diequatorially; for example the tribenzoate esters of (1,3/2)-cyclopentanetriol and (1,3/2)-cyclopentenetriol contain 70–80% of all-axial conformers. The O-isopropylidene derivatives prefer conformations in which the average puckering is such that the fused dimethyldioxolane-cyclopentane ring system approximates an overall *endo*- or boat shape. Coupling constants involving oxirane protons of cyclopentene oxides are much smaller than corresponding coupling constants observed in other ring systems: oxirane-oxirane, 2·7 ± 0·3 Hz; oxirane-*cis* vicinal, 1·4 Hz; and oxirane-*trans* vicinal 0·6 Hz. The bases for all these effects are discussed.

THE factors which determine the conformation of cyclohexanoid molecules are by now fairly clearly defined, and as a result the conformational analysis of such systems usually rests on a firm basis. The same cannot yet be said about cyclopentanoid systems. Early measurements of the entropy and heat capacity of gaseous cyclopentane, as well as more recent electron diffraction studies, indicate that the molecule is puckered.[2a] Puckering of the ring changes the interior C—C—C bond angles and thus increases the angle strain, but this is offset by the decrease in eclipsing energy which results from rotation of the ethanoid units away from the fully eclipsed geometry present in the planar conformation. In their early calculations of the energies of cyclopentanoid conformations, Pitzer and Donath[2d] considered the two symmetrically puckered forms which result either from twisting one C atom out of the

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plane of the other four (C_s, envelope), or from twisting one C atom above and one below the plane of the other three C atoms (C_2, half-chair, twist*). For these two forms the curves of potential energy as a function of the amplitude of puckering were essentially identical. The conformations with minimal energy have the geometries indicated in Fig 1, which shows the dihedral angles and deformations in Å away from the principal plane of the ring. It was further shown, that for a given amplitude of puckering, the total energy was independent of the phase angle of puckering. Thus, for cyclopentane itself, 10 C_s and 10 C_2 forms of equal energy can be generated by "pseudorotation", around the ring, of the phase angle of puckering. Similar numbers of conformers are possible in furanoid systems, e.g., see Hall *et al.*[3b]

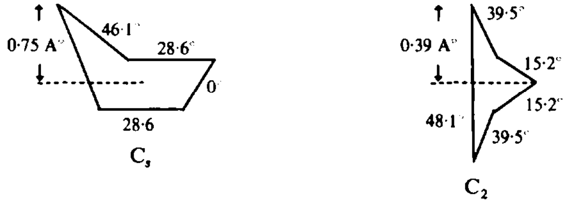

FIG 1. Minimal-energy Conformations of Cyclopentane. The indicated distances in Å refer to the displacement of one (or two) atoms from the plane defined by the other four (or three) atoms. The angles indicated refer to the dihedral angles between *cis*-vicinal bonds attached to the particular ring-bond. The values are those of Pitzer and Donath. See text for more probable values of the parameters, from recent calculations

The advent of computer calculations allowed Hendrickson[4] to remove the symmetry restrictions which earlier workers had assumed. His calculations indicated that there were many non-symmetrical conformations of cyclopentane (i.e. all C—C—C bond angles and dihedral angles unequal) representing energy wells (i.e. local energy "minima"). Altona *et al.*[5,6] noted that the torsional angles found in a given cyclopentane conformation, including both the experimental values based on X-ray data† and Hendrickson's theoretically calculated forms, were described by Eq (1). φ_j is the ring torsional angle; the parameter φ_m is the maximum possible torsional angle, and Δ is the phase angle of puckering, which locates the position of maximal puckering in the ring. If this equation is

$$\varphi_j = \varphi_m \cos\left(\frac{\Delta}{2} + j\delta\right) \qquad \text{Eq (1)}$$

$$j = 0, 1, 2, 3, 4;\ \delta = 144°$$

generally valid for cyclopentanoid systems, then any conformation can be described by the two parameters φ_m and Δ, and all the dihedral angles can be calculated by substitution of $j = 0, 1, 2, 3, 4$.

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* The symmetrical envelope and twist conformations can be described with the nomenclature suggested by Hall.[3] Envelope forms are designated by a V and twist forms by a T, with sub- and/or superscripts to denote the carbon atom(s) displaced below or above the principal plane of the ring.

† These authors[5,6] have reported X-ray and other data on ring D of a series of steroids and other molecules (in which pseudorotation is not possible), which clearly support the existence of non-symmetrical conformations in substituted cyclopentanoid systems. In the compounds they studied, the experimentally determined bond and torsional angles corresponded to unsymmetrical conformations between C_s and C_2 forms.

The model shown in Fig 1 is qualitatively correct, but the absolute values, which are taken from Pitzer and Donath[2d] should be modified in the light of more recent work. Hendrickson's calculated model[4] gives $\varphi_m = 44{\cdot}3°$; recent electron-diffraction studies* show $\varphi_m = 42 \pm 1°$. Valence-force calculations† show that for the C_s form, 41° and 25° are more reasonable than the values shown in Fig 1, and for the C_2 form the values should be 43°, 34° and 13°.

The calculations of Pitzer and Donath[2d] and of Hendrickson[4] indicated that the potential energy barriers in free cyclopentane are negligible, and that actually there is probably a continuum of minimal-energy forms which interconvert by pseudorotation. However, substituents, which change the torsional strain, will increase the potential energy barriers which restrict pseudorotation and thus some conformations will become stabilized relative to others. Pitzer and Donath[2d] calculated that a single substituent which increases two adjacent potential energy barriers would stabilize those C_s forms in which the substituent is in the most puckered part of the ring, whereas a group (e.g. CO) which lowers the adjacent potential energy barriers would stabilize C_2 forms, with the substituent in the least puckered portion of the molecule. Extension of such calculations to the *trans*-1,2-dihalogenocyclopentanes[7, 10] showed that C_2 conformations, with the halogens in the most puckered part of the ring, should be the minimal-energy forms; in these compounds the barrier to pseudorotation is about 1·2 kcal/mole. The minimal-energy C_2 form was, however, only slightly more stable (*ca* 0·2 kcal/mole) than the "nearest" C_s (envelope) forms. (In the unpublished valence force studies referred to above, Altona finds that in *trans*-1,2-dichlorocyclopentane the barrier is 1·5–1·8 kcal above the *aa* form, and in both the *aa* and *ee* forms the nearest C_s is 0·10–0·12 kcal above the minimum). These authors suggested that restricted pseudorotation, termed "pseudolibration", may occur around the minimal-energy form. The extent of pseudolibration will depend on the shape and depth of the potential energy barrier. Ouannes and Jacques[8a] have also reported similar calculations for 3-methylcyclopentanone and for the *cis*- and *trans*-3-methylcyclopentanols. 3-Methylcyclopentanone has a fairly deep (*ca* 3·6 kcal/mole) and sharp energy barrier. In contrast, the 3-methylcyclopentanols have much shallower and flatter potential energy curves, indicative of a large number of conformations which are approximately equivalent energetically, so that extensive pseudolibration is possible. The changes in torsional-energy terms which result from the introduction of a substituent(s) do not depend on the axial or equatorial orientation‡ of the substituent(s). Microwave studies on pseudorotation in such systems have recently been reviewed by Laurie.[8b]

The Karplus equation[9] (Eq 2) predicts a dependence of the vicinal coupling constants on the dihedral angle φ_{HH}. The extensive work of Altona *et al.*,[10] on the

$$J_{vic} = A\cos^2\varphi_{HH} - B\cos\varphi_{HH} + C \qquad \text{Eq (2)}$$

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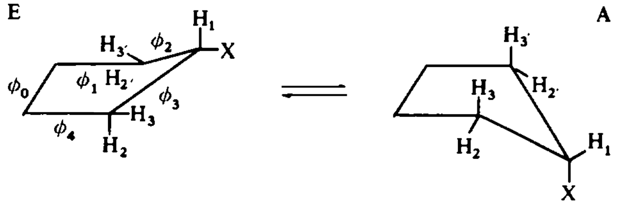
* W. J. Adams, H. J. Geise and L. S. Bartell, American Chemical Society Meeting, Columbus, Ohio, 1968. Personal communication from Dr. H. J. Geise.

† Unpublished observations of Dr. C. Altona.

‡ The "axial-equatorial" terminology used in cyclohexane has been retained, although in cyclopentanes the dihedral angles will not generally equal those in cyclohexane. If φ is the dihedral angle between *cis*-vicinal bonds, and if there is no angular deformation, then $\varphi_{ea} = \varphi$; $\varphi_{aa} = 120° + \varphi_{ea}$; $\varphi_{ee} = 120° - \varphi_{ea}$.

trans-1. 2-dihalogenocyclopentanes, suggests that in such systems the constants have the following values: $A = 9{\cdot}5$; $B = 0{\cdot}5$; $C = 0{\cdot}4$. The analogy between the polar substituted cyclopentanes studied by Altona *et al.* and the ones we have studied, suggests that it is reasonable to use the same values for the constants in Eq (2).

In conformationally mobile systems, if the rate of interconversion among conformers is sufficiently rapid, compared to the frequency differences in the chemical shifts and coupling constants, then an averaging of these values occurs in the observed spectrum.[11] The coupling constants observed will be determined by: (1) the conformational equilibrium; (2) the geometry and thus the J values of the individual conformers.



$\Delta = 180°.\ \phi_m > 0°$ $\qquad$ $\Delta = 180°.\ \phi_m < 0°$

$\phi_2 = -\phi_3$

$$J_{1,2}\,(\text{observed}) = \tfrac{1}{2}\left[X_a(J_{1,2} + J_{1,2'})_A + (1 - X_a)(J_{1,2} + J_{1,2'})_E\right]$$
$$J_{1,2} = X_a(J_{ee}) + (1 - X_a)(J_{aa}) \qquad \text{Eqn. (3)}$$

$$J_{1,3}\,(\text{observed}) = \tfrac{1}{2}\left[X_a(J_{1,3} + J_{1,3'})_A + (1 - X_a)(J_{1,3} + J_{1,3'})_E\right]$$
$$J_{1,3} = X_a(J_{ea}) + (1 - X_a)(J_{ae}) \qquad \text{Eqn. (4)}$$

$J_{aa} = J_{12}(\text{E})$; $\qquad J_{ee} = J_{12}(\text{A})$;

$J_{ae} = J_{13}(\text{E})$; $\qquad J_{ea} = J_{13}(\text{A})$

$\phi_{aa} = 120° + \phi_{ea}$; $\qquad \phi_{ee} = 120° - \phi_{ea}$

$O \leqslant \phi_{ea} \geqslant 60°$

FIG 2. Calculation of the Conformational Equilibrium Involving two Envelope Conformers. When X, the substituent on the out-of-plane carbon atom is equatorial or axial, the conformer is named E or A respectively. X_a = mole fraction of the A conformer. See text for definition of other symbols, and see footnote concerning the use of "X" with different meanings. Note that the numbering of the protons in this figure differs from the numbering indicated in the various examples in Charts 1 and 2

For a substituted cyclopentane, existing as an equilibrium mixture of envelope conformers in which the substituent is axial or equatorial (Fig 2), the observed H_1 signal will theoretically[12] be a 9-line multiplet, with average separations given by Equations (3) and (4) shown in Fig 2. If values for the individual coupling constants J_{aa}, J_{ee}, J_{ea} and J_{ae} are known, it is possible to calculate the conformational equilibrium constant from the observed coupling constants. In chair conformers of cyclohexane, the pairs of adjacent carbon atoms assume a conformation which is almost that of fully-staggered ethane. Consequently, for molecules with different X substituents,* variations in the J values of the individual conformers will be, primarily, a

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* The authors have considered the potential for confusion that is introduced by using "X" in several ways in Fig 2 and elsewhere in this paper. Nevertheless it seems better to use accepted nomenclature, i.e. "X" for an electronegative substituent (and H_x for the methine proton on the same carbon atom); X_a for the mole fraction of axial conformers; and ABX, etc. to indicate relative chemical shifts of a three spin system; than to introduce still another set of terms.

function of the electronegativity of X.[13, 14] Often the values of these coupling constants can be obtained directly from the spectra of related compounds which are conformationally homogeneous. However, in cyclopentanoid systems the values* of J_{aa}, J_{ee}, J_{ae} and J_{ea} will be a function not only of the electronegativity of X, but more importantly of the degree of puckering of the ring. This puckering will not necessarily be the same in different cyclopentanoid compounds, and will depend both on X and on any other substituents present in the molecule. Therefore, unless one assumes a particular geometric model for substituted cyclopentanes, the observed J_{cis} and J_{trans} will be a function of two unknowns, i.e. the extent of puckering and the conformational equilibrium.

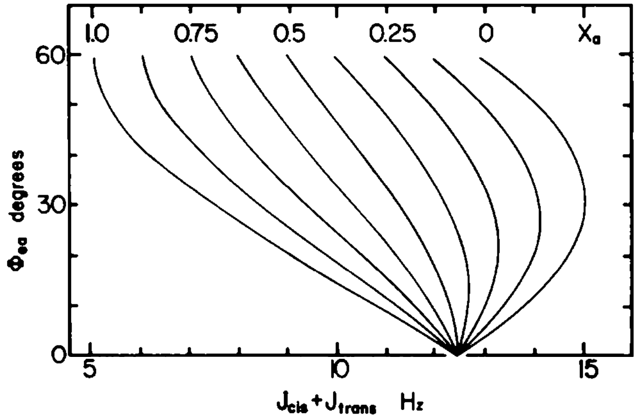

FIG 3. Dependence of J' ($= J_{cis} + J_{trans}$) on the Dihedral Angle and the Mole Fraction of Axial Conformer. For a given value of the dihedral angle ϕ_{ea} the appropriate coupling constants were calculated from the Karplus equation in the form given in the text. For each ϕ_{ea}, J' was then calculated for the different values of X_a, from the equation

$$J' = J_{ea} + (X_a)(J_{ee}) + (1 - X_a)(J_{aa}).$$

See text and Figure 2 for definition of terms

In substituted cyclohexanes J_{ea} and J_{ae} may differ by 2–3 Hz, although the dihedral angles involved are nearly the same.[15, 16] Booth[16] has rationalized this discrepancy as an orientational difference in the effect of an electronegative substituent, such that the maximum effect of the substituent on the value of J_{vic} coincides with a *trans*-coplanar system, X—C$_1$—C$_2$—H. Altona *et al.*[17] have pointed out that since the puckering in cyclopentanoid systems is generally smaller than that in cyclohexanoid systems, the difference between J_{ae} and J_{ea} will also be smaller; thus, as an approximation it can be assumed that $J_{ae} = J_{ea}$. On the basis of this approximation, Eq (4) shows that the observed $J_{1,3}$ (*cis* coupling constant) is independent of the conformational equilibrium. An appropriate form of the Karplus equation can therefore be used to estimate the dihedral angle φ_{ea} from the *cis* coupling constant, regardless of the conformational equilibrium. By further assuming that $\varphi_{aa} = 120° + \varphi_{ea}$ and $\varphi_{ee} = 120° - \varphi_{ea}$, one can calculate J_{aa} and J_{ee}. Then, from the observed *trans* coupling constant and these values of J_{aa} and J_{ee}, it is possible to calculate X_a the

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* J_{ae} and J_{ea} are the *cis* coupling constants between vicinal protons with a dihedral angle of φ_{ea}; J_{aa} is the coupling constant between *trans* vicinal protons with $\varphi_{aa} = 120° + \varphi_{ea}$; and J_{ee} is the coupling constant between *trans* vicinal protons with $\varphi_{ee} = 120° - \varphi_{ea}$.

mole fraction of conformer with axial X substituent(s), by Eq (3). In many cases the individual values of J_{cis} and J_{trans} cannot be obtained from the NMR spectrum and only their sum, J' is known. Fig 3 illustrates the dependence of J' on φ_{ae} and X_a. The figure shows that if J' is either quite large or quite small, then a reasonable estimate of X_a and φ_{ea} can be made. However, if J' has an intermediate value, then a wide range of combinations of φ_{ea} and X_a would be consistent with a particular J'.

For cyclohexanoid systems it is generally valid to assume that the conformational equilibrium involves just two conformers which differ only in the orientation of substituents, since the energies of boat and skew forms are considerably greater than those of the two chair forms. However, cyclopentanoid systems, because of the low energy barriers, can adopt a larger number of conformations. Therefore, the NMR spectrum can be interpreted only in terms of an "average conformation" characterized by consistent values of Δ, φ_m and X_a. However, if a coupling constant so calculated is found to be both unique and maximal, it will of course characterize the conformation of the compound.

A further ambiguity arises in the interpretation of the NMR spectra of non-dissymetric molecules containing enantiotopic protons.[18] In such molecules the "average conformation" may not correspond to a non-disymmetric form but rather to a DL pair of dissymetric conformations. In the example shown in Fig 2, if $\varphi_2 \neq \varphi_3$, then the protons of each pair, $H_2 - H_{2'}$ and $H_3 - H_{3'}$, would be diastereotopic, and in theory the members of each pair should be distinguishable. However, when there is rapid conformational interconversion, both protons in a pair will experience the same average environment and will therefore appear isochronous and magnetically equivalent, in a spin-coupling sense, relative to vicinal protons. Approximately the same value of X_a is calculated either from the observed average J values by treating them in the manner described above for a conformationally non-dissymetric molecule, or from the more rigorous treatment using all the individual J values indicated in the equations in Fig 2. Therefore, it is possible to learn something about the average orientation of substituents even when a full analysis is not possible. In such systems, however, unless certain assumptions are made concerning the relationship between dihedral angles, it is not possible to calculate the individual J values (and the two angles φ_2 and φ_3) from the observed coupling constants.

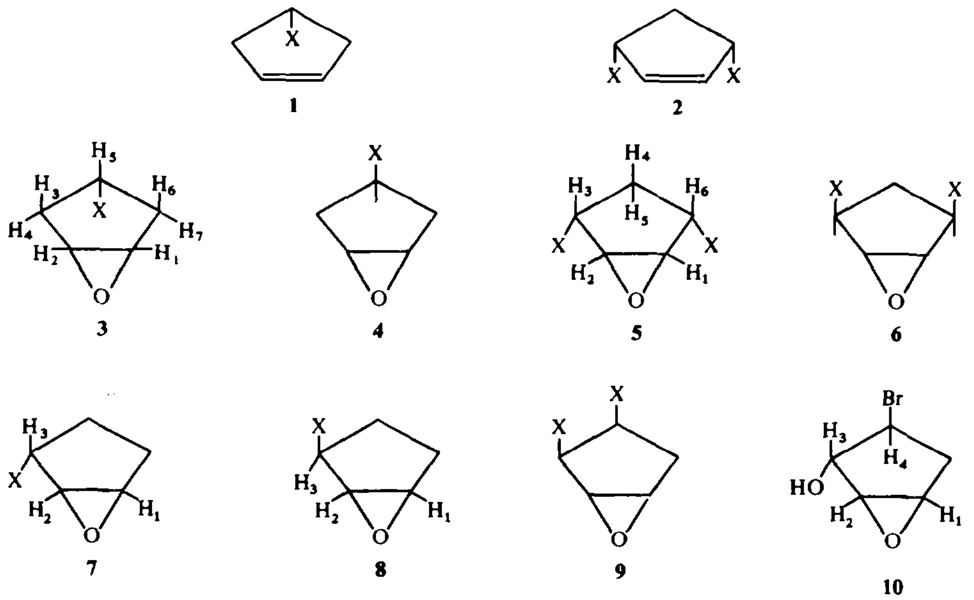
RESULTS AND DISCUSSION

Coupling constants and conformational analysis of substituted cyclopentenes and cyclopentene oxides

In cyclopentenes and cyclopentene oxides (Chart 1) the rigidity of the double bond or oxirane ring[19, 20] restricts pseudorotation, so that the only possible puckered conformations are V^4 and V_4. For a series of such compounds we have used the values of J_{cis} and J_{trans}, for coupling between methylene protons and vicinal H_x protons, to estimate the average dihedral angle between the *cis*-vicinal protons as well as the equilibrium between the V^4 and V_4 conformations. The relevant J values and the conformations are presented in Tables 1 and 2.

The coupling constants indicate that the V_4 or "boat" is the preferred conformation for the fused-ring epoxycyclopentane system (Fig 4). These results agree with those of McCullough *et al.*[21] who measured the dipole moments of a series of 4-substituted

CHART 1. SUBSTITUTED CYCLOPENTENES AND EPOXYCYCLOPENTANES



	a	b	c	d	e
X =	OH	OBz	OAc	Br	OMe

cyclopentene oxides, and concluded that the boat conformation was generally preferred. This same conformation also predominates in a variety of substituted bicyclo[3.1.0]hexane compounds which contain a cyclopropyl ring[22, 23] in place of an oxirane ring. The tendency of the substituted epoxycyclopentanes to assume a boat conformation cannot be explained consistently in terms of dipolar interactions. axial *versus* equatorial orientation. or non-bonded interactions involving the sub-

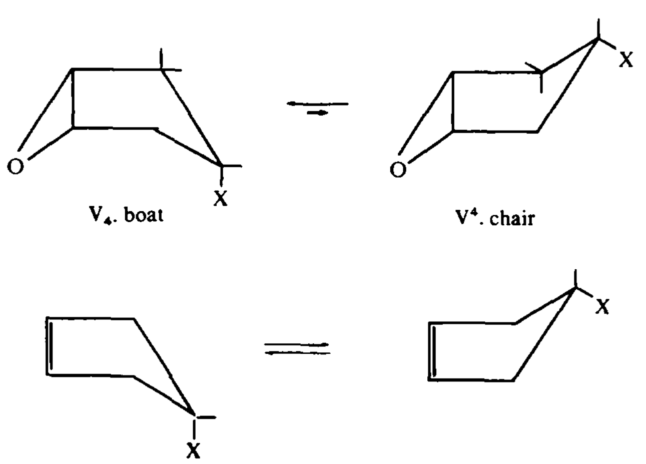


FIG 4. Conformational Equilibria in Cyclopentenes and Cyclopentene Oxides

TABLE 1. COUPLING CONSTANTS AND DERIVED CONFORMATIONS OF SUBSTITUTED CYCLOPENTENE OXIDES

Compound	J_{cis}	J_{trans}	$J_c + J_t$	ϕ_{ea} (degrees)	X_a	% V_4 or Boat conformation
3a	5·2	1·0	6·2	43	0·95	95
4a	7·3	7·0	14·3	28	0·10	90
3c			8·5			
4c	7·5	6·7	14·2	26	0·10	90
3d			8·8			
5a	7·5	8·8	16·3	26	0	100
5b	7·6	8·6	16·2	25	0	100
6d	5·7	0·9	6·6	40	0·95	95
7a			15·2		0	100
8a			15·3		1	100
7c			15·4		0	100
8c			4·8		1	100
7d			15·1		0	100
8d			5·0		1	100
7e			15·5		0	100
9c	7·5	8·2	15·7	26	0	100
10	7·5	8·8	16·3	26	0	100

J values (Hz) refer to the coupling constants between H_x protons and vicinal *cis*- or *trans*-methylene protons. See Chart 1 for identification of compounds. ϕ_{ea} = dihedral angle between H_x and the *cis*-methylene proton. calculated from

$$J_{cis} = 9{\cdot}5 \cos^2 \phi_{ea} - 0{\cdot}5 \cos \phi_{ea} + 0{\cdot}4$$

X_a = the mole fraction of conformers in which the X-substituent is oriented axially relative to the plane of the ring. Values of $X_a = 0$ or 1. and of % $V_4 = 100$. should not be taken literally. The imprecision of the measurements as well as of the constants used in the equation probably do not allow calculation of X_a to better than ± 5–10%. The values noted, then, were actually in the range where the imprecision may actually indicate $X_a > 1{\cdot}0$ or < 0. These have been reported as 1 and 0. respectively. For all compounds except **5a** the solvent was $CDCl_3$. For **5a** the solvent was CD_3OD.

stituent(s). Therefore, the boat conformation of the fused ring system must be of considerably lower energy than the chair conformation, and the preferred V_4 conformation is inherently a property of the ring system. The introduction of a substituent can reverse the relative energies, and thus change the conformation. only if there is unusually large steric or dipolar interaction in the boat conformation which is reduced in the chair conformation.

TABLE 2. COUPLING CONSTANTS AND DERIVED CONFORMATIONS FOR SUBSTITUTED CYCLOPENTENES

Compound	J_{cis}	J_{trans}	$J_c + J_t$	ϕ degrees	X_a
1a	6·2	3·3	9·5	37	0·65
1c	6·7	2·8	9·5	33	0·65
2a	6·8	5·4	12·2	32	0·36
2b	7·4	4·2	11·6	27	0·47
2d	6·2	2·0	8·2	37	0·80

Symbols are explained in Table 1.
Solvent for **1a** and **2a** was CD_3OD. For other compounds it was $CDCl_3$.
For compound **21b** in acetone. $J_{12} = J_{23} = 4{\cdot}0$ Hz. and $X_a = 0{\cdot}67$ (see text).

The substituted cyclopentenes differ from the epoxides in two ways: (a) there is no *a priori* preference for either of the possible envelope conformations; (b) the nature and position of the substituents affect the conformational equilibrium. Furthermore, as the data in Table 3 show, the conformational equilibrium for thc olefins **1c** and **2d** is shifted toward the more polar "axial" conformer in a more polar solvent. The corresponding epoxides, **4c** and **6d**, do not show this effect, indicating much less conformational mobility.

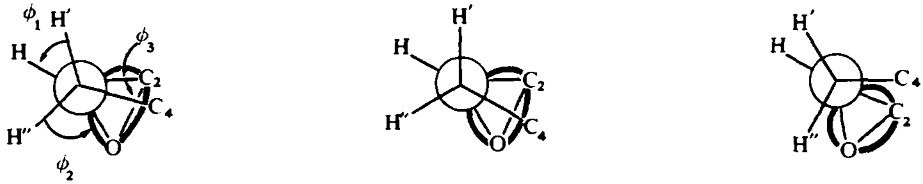
TABLE 3. EFFECT OF POLARITY OF SOLVENT ON CONFORMATIONAL EQUILIBRIUM

	CCl_4			CD_3CN		
Compound	J_{cis}	J_{trans}	X_a	J_{cis}	J_{trans}	X_a
1c	6·7	3·0	0·67	6·7	2·3	0·76
4c	7·7	7·0	0·02	7·5	7·1	0·05
2d	6·4	2·4	0·75	6·2	1·6	0·86
6d	5·2	1·1	0·96	5·5	1·0	0·96

Symbols are explained in Table 1.

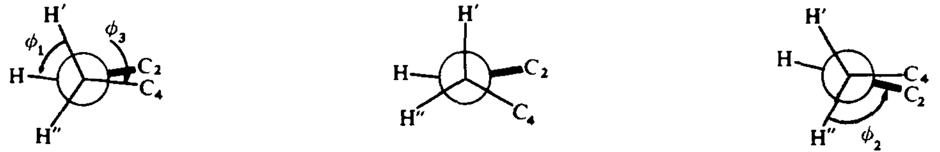
One possible explanation for this difference between the cyclopentenes and the epoxides involves the orientation of the oxirane or vinylic protons relative to the vicinal protons or substituents. Examination of Dreiding models shows that in planar cyclopentene oxide, the dihedral angle, $H\text{-}C_1\text{-}C_5\text{-}H'$(*cis*), is *ca* 40° (*cf* Fig 5). In the V_4 conformation the angle is increased to *ca.* 55°, whereas in the V^4 conformation it is decreased to *ca* 25°, a less favourable geometry. On the other hand, in planar cyclopentene each olefinic C—H bond bisects the H—C—H angle of the adjacent methylene group, producing a dihedral angle of 60°. In either puckered conformation of cyclopentene one of the C—H bonds on both C_3 and C_5 will become more nearly eclipsed with the adjacent olefinic C—H bond. Therefore, in unsubstituted cyclopentene the two possible envelope conformations are equivalent. It should be noted, however, that the internuclear distance between oxirane protons or olefinic protons and vicinal methylene protons is considerably greater than that in a saturated ethane unit. Consequently, the importance of eclipsing interactions in determining the conformation of these molecules is questionable. Indeed, Eliel has stated that "an sp^2 hybridized atom in planar surroundings is not seriously troubled by bond eclipsing".[2b] Several lines of evidence have indicated that the electrons of an oxirane ring are delocalized,[20] and Walsh[24] has suggested that the oxirane ring carbon atoms are approximately sp^2 hybridized, as he also proposed for cyclopropane. One representation of the electron density in epoxides is the "bent bond" structure[20] similar to that proposed by Coulson and Moffitt[25] for cyclopropane. In Fig 5, the shaded areas indicate the regions of major electron density about the epoxide bonds in accordance with this bent-bond formulation. McCullough *et al.*[21] have proposed that the V_4 conformation of epoxycyclopentane there is reduced interaction of the C_4—C_5 and C_5—H″ bonds (Fig 5) with the "bent" C_2—C_1 and C_1—O bonds. In the V^4 conformation these interactions would be increased, and thus this conformation would be less favorable. In cyclopentenes, however, rotation in either direction results in the same geometry about the double bond and vicinal methylene protons.

Cyclopentene Oxides



Planar V$_4$ V^4

Cyclopentenes



Planar V$_4$ V^4

Values of ϕ. degrees

	Cyclopentene Oxides			Cyclopentenes		
	Planar	V$_4$	V^4	Planar	V$_4$	V^4
ϕ_1	40	55	25	60	75	45
ϕ_2	60	75	45	120	135	105
ϕ_3	0	15	15	0	15	15

FIG 5. Newman Projections of Planar and Puckered Cyclopentene and Cyclopentene Oxide. The sketches represent projections along the C_5—C_1 bond, with C_5 in front. In all the puckered conformations the dihedral angles (C_3—C_2) − (C_4—C_5) and (C_3—C_4) − (C_5—C_1) are approximately 30°. Regions of high electron-density (the oxirane ring bonds in the case of cyclopentene oxide, and the double bond in the case of cyclopentene) are indicated by the thick lines. H is the proton attached to C_1; H' and H'' are the protons attached to C_5. *cis* and *trans* respectively to C_1—H. The dihedral angles are defined as follows: for cyclopentene oxide ϕ_1 refers to H'—C_5—C_1—H, and ϕ_2 refers to H''—C_5—C_1—O. For cyclopentene. ϕ_1 refers to H'—C_5—C_1—H. and ϕ_2 refers to H''—C_5—C_1—C_2.

There appears to be some restriction of the amplitude of this rotation, since *cis* vicinal coupling is considered to be always larger than *trans* coupling in these systems.[19c–19e]

Oxirane ring proton coupling constants

Williamson *et al.*,[26] studying monosubstituted 1,1-dichlorocyclopropanes found that the vicinal coupling constants vary with the electronegativity of the substituents. and used this as evidence that the electronic properties of the cyclopropane ring are intermediate to those of saturated and unsaturated compounds. Coupling constants for *cis* protons in epoxides are significantly smaller than those in cyclopropanes although the dihedral angle is 0° in both cases. This difference is thought to be due in part to the decreased electron density about the oxirane carbon atoms resulting from the electronegativity of the oxygen.[26, 27] The values of $J_{1,2}$ reported in Table 4

TABLE 4. COUPLING CONSTANTS INVOLVING OXIRANE PROTONS

Compound	$J_{1,2}$	$J_{2,3}$ (*cis*)	$J_{2,3}$ (*trans*)
7c	2·8	1·5	
7e	3·0	1·2	
8a	2·6		0·5
8c	2·4		0·8
8d	2·6		0·6
6d			0·5
10	3·0	1·4 (1·4)[a]	(0·7)[a]
Average	2·7	1·4	0·6

[a] These are the coupling constants between H_1 and the adjacent methylene protons on C-5.

See Chart 1 for identification of compounds and numbering of protons.

agree with the earlier observations that oxirane proton coupling constants are much smaller than those in cyclopropane compounds (J_{cis} = 8–12 Hz) or in saturated fused ring systems[13] (J_{cis} = 8–10 Hz) in which the dihedral angle is also 0°. Buss *et al.*[28] have reported an average J of 4·0 Hz for oxirane proton coupling constants in several pyranoid epoxides, and Glotter *et al.*[29a] have reported values of 6 Hz and 4 Hz for the oxirane ring proton coupling constants in both 3α-4α-epoxy-5α-hydroxy-cholestane and in the 5-β-isomer. Smaller values of $J_{1,2}$ were reported by Jefferies *et al.*[29b] in cyclopentanoid epoxides of beyerol, and the same value (average = 2·7 Hz) is found in our series. This small value of J may be due to the decreased size of the fused ring system. Laszlo and Schleyer[30] have reported that *cis* olefinic coupling constants decrease with ring size. In view of the "partial double bond" character of epoxide rings,[20, 24] it seems plausible that a similar effect might occur in fused-ring epoxides, accounting for the smaller coupling constants observed in cyclopentanoid epoxides compared to cyclohexanoid ones. It is also noteworthy that $J_{1,2}$ for epoxides is smaller than for the olefins from which they are derived, even though the dihedral angle remains at 0°; e.g. Jefferies *et al.*[29b] reported values of J = 5·5 for the olefinic protons of the cyclopentenoid moiety of the fused ring system, and J = 2–3 for the corresponding epoxides. This serves to emphasize the importance of bond angle and hydridization in determining the size of J, and the danger of relying solely on the dihedral angle.

Collins *et al.*[31a] have reported values of 3·3–4·5 Hz for the coupling of oxirane ring protons with adjacent *cis*-methine protons in 3-substituted-4,5-epoxycholestanes. Similar values were obtained by Cross [31b] for steroidal 5,6-epoxides, although the β-epoxides consistently showed weaker coupling (J = 2·1–2·7 Hz) than the α-epoxides (J = 3·3–4·1 Hz). In these epoxides the coupling of an oxirane proton with adjacent *trans*-methine or *trans*-methylene protons was too small to measure. The data in Table 4 show that, in cyclopentanoid epoxides, coupling between an oxirane proton and a *cis*-methine proton ($J^{cis}_{2,3}$) is smaller than in steroidal epoxides. We have also observed small, but measurable, couplings between an oxirane proton and an adjacent *trans*-methine proton ($J^{trans}_{2,3}$), as in Table 4 and Chart 1, compounds **6d**, **8a**, **8c**, **8d**. These differences may be due in part to the difference in the size of the carbocyclic ring, as noted above for olefins, but differences in the dihedral angles between the C—H bonds in the two types of epoxides might also account for the observed differences. Examination of Dreiding models of the steroidal 4.5-epoxides shows that in the conformations suggested by the authors[31] the dihedral angles between the oxirane C—H bonds and the vicinal methylenic C—H bonds are 25–30° (*cis*) and 90–95° (*trans*). In the V_4 conformation of the cyclopentanoid epoxides (cf. Figure 5). the *cis* dihedral angle is *ca* 40° and the *trans* dihedral angle is *ca* 80°. For these approximate dihedral angles. Equation (2) predicts that *cis*-coupling would be larger in the steroidal epoxides than in the cyclopentanoid ones. whereas the *trans* coupling would be larger in the cyclopentanoid epoxides. Although the relative values of the coupling constants observed are in agreement with those predicted. the absolute values are consistently lower than predicted from the equation. The equation. $J = 5{\cdot}1 \cos^2 \varphi$. computed by Tori *et al.*[31c] for vicinal coupling of oxirane protons in steroids. also gives values which are much larger than those we have observed in cyclopentanoid epoxides.

Coupling constants and conformational analysis of tri- and tetrasubstituted cyclopentanes

In contradistinction to the cyclopentenes and oxides. in the case of those cyclopentanoid compounds in which the number of possible conformations is not restricted. the interpretation of the coupling constants is more ambiguous. We have used the values of J_{cis} and J_{trans} for couplings involving H_x and vicinal *cis*- and *trans*-methylene protons. to estimate a value of X_a. in the manner described for the cyclopentenes and epoxides. The calculated values of X_a should be considered only as a *qualitative* measure of the average orientation of the X substituents on C_3. C_4 or C_5 relative to the general plane of the ring. A large value of X_a indicates that on the average these substituents are oriented axially. The relevant values of J and of X_a are presented in Table 5. The data indicate that there is no general preference for the substituents on C_3. C_4 or C_5 to assume an axial or equatorial orientation. For example in **13a**. **14a** and **14b** the *cis*-substituents on C_3 and C_5 are. on the average. in predominantly equatorial positions. whereas in **11b**. **13b** and **17a** the J_{trans} values indicate a larger contribution from conformations in which there are *syn*-diaxial substituents.

In the case of the all-*trans* compound **11b**. corroborating evidence of the preference for conformations with axial substituents was obtained from a different set of coupling constants. The signal of the C_2 proton is distinct from that of the other two O—C—H protons, appears as a triplet, $J_{\text{average}} = 3{\cdot}7$ Hz ($J_{\text{average}} = 1/2\,(J_{12} + J_{23})$). The average conformation was deduced by assuming that only six conformations contribute significantly. of which three (V^2. T_3^2 and T_1^2) have the substituents in axial or *quasi*-axial orientation. and three (V_2. T_2^3 and T_2^1) have equatorial or *quasi*-equatorial substituents. From the values of φ_i (Eq. 1 and Fig. 1) the values of φ_{ee}, φ_{ea} and φ_{aa} for each of the conformations were obtained. and the appropriate coupling constants calculated by Eq (2). From these theoretical values. a trial and error method* gave $X_a = 0{\cdot}69$. in reasonable agreement with the value of 0·8

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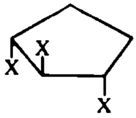
* The same result was obtained whether it was assumed that mole fraction (envelope) = mole fraction (twist), or that all three possible axial (or equatorial) conformations contributed equally to the net X_a (or X_e).

CHART 2. TRI- AND TETRASUBSTITUTED COMPOUNDS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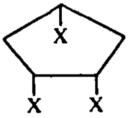
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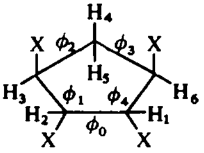
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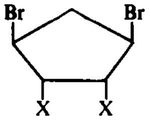
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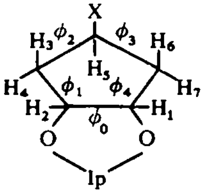
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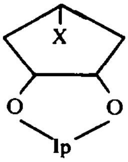
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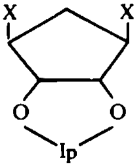
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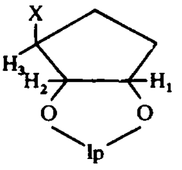
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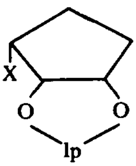
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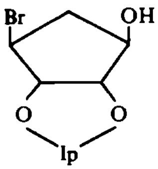
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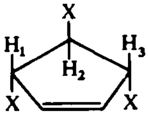
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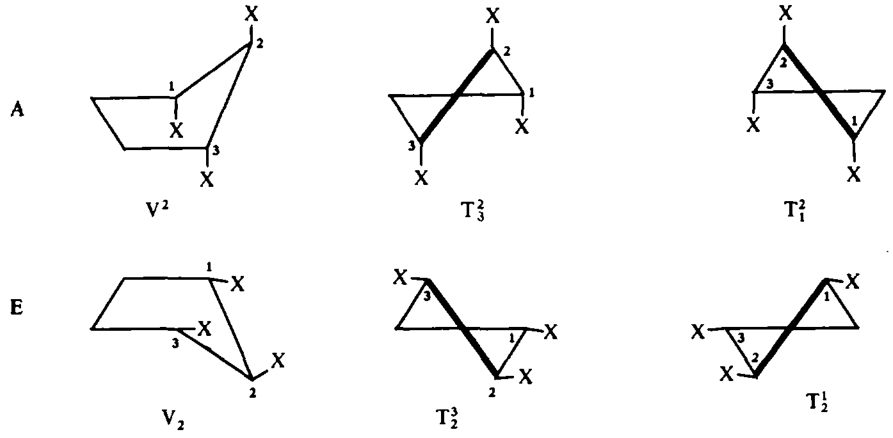
a	b	c	d	e
X = OH	OBz	OAc	Br	OMe

TABLE 5. COUPLING CONSTANTS AND AVERAGE CONFORMATIONAL PREFERENCE OF POLYSUBSTITUTED CYCLOPENTANES

Compound	$J_{1,2}$	J_{cis}	J_{trans}	$J_c + J_t$	$(X_a)^a$	Average shape[a]
11b		7·5	1·5	9·0	0·8	
12b		7·4	4·1	11·2	0·5	chair ⇄ boat
13a		7·5	6·5	14·0	0·1	chair
13b	4·7	7·8	4·0	10·4	0·5	chair ⇄ boat
14a	5·2	7·8	7·4	15·1	0	chair
14b	5·3	8·1	7·0	15·3	0	chair
Acetonides						
15a	6·0	6·0	9·3	15·3	0	boat
15b	6·5	6·3	8·8	15·1	0	boat
16b	6·1	4·7	1·2	5·9	1·0	boat
17a		4·6	2·6	7·2	0·8	boat
17b		4·9	1·1	6·0	1·0	boat
17d		6·2	3·2	7·4	0·7	boat ⇄ chair
18a	5·6			3·0	1·0	boat
19a	5·4			16·0	0	boat
20				6·2	ca. 0·9	boat

J values (Hz) other than $J_{1,2}$ refer to the coupling constants between a proton on a substituted ring carbon atom and the vicinal *cis* and *trans* methylene protons, as described in the text. The method of computing $J_{1,2}$ for isochronous protons is given in the text. The compounds are identified in Chart 2.

[a] See text for discussion of these terms.

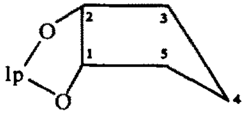


reported in Table 5. In the case of the corresponding cyclopentene derivative **21b** only the V^2 and V_2 conformations can exist. With most of the commonly used solvents, **21b** gave spectra in which most of the signals were almost isochronous. The spectrum of a solution in acetone, however, gave well-separated signals, and H_2 gave a triplet, $J = 4{\cdot}0$ Hz. From this value the mole-fraction of **21b** in the V^2 conformation is calculated to be 0·67, remarkably close to the value for **11b**, and suggesting that the same factors are operable in both cases.

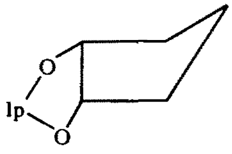
These findings agree with the conclusions of the Dutch authors[5–7] concerning the *trans*-1,2-dihalogenocyclopentanes and -indans. It would be interesting to know whether the presence of polar substituents in *trans*-1, 2, 3-disposition makes the potential well even steeper than that calculated for the 1,2-cases, and that pseudolibration would consequently be even more restricted. If that were true, the conformational equilibrium would indeed represent mainly the extreme forms indicated, rather than a whole range of forms.

Altona *et al.*[10] found that the *trans*-1,2-dihalogenocyclopentanes exist largely in diaxial conformations. The only 1–3 *syn*-diaxial interactions possible for the halogen atoms involve a H atom, which must be less serious than repulsion between vicinal C—Br dipoles. In the case of **11b** and **21b**, however, with two large groups 1,3-diaxial, the all-axial conformation is still preferred. This shows very clearly the difference between the cyclohexanoid and cyclopentanoid series. In substituted cyclohexanes, conformations with 1,3-*syn*-diaxial interactions are generally unfavorable,[2c] whereas for the cyclopentanoid series, repulsion between vicinal dipoles is more important in determining the favored conformation. The difference arises because in cyclopentanoid compounds 1,3-*syn*-diaxial substituents are not parallel, and steric and dipolar repulsion between such substituents is smaller than in corresponding cyclohexanoid compounds. Warshawsky and Fuchs[32] reached similar conclusions from a study of diphenylcyclopentanols.

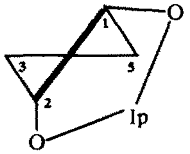
The NMR spectra of all the acetonides listed in Table 5 indicate that the average puckering is such that the fused dimethyldioxolane-cyclopentane ring system approximates an overall *endo*- or boat shape, in which C-4 of the cyclopentane ring is rotated towards, rather than away from, the dioxolane ring. In compounds **17a** and **20** conformations of this type could be stabilized by intramolecular H-bonds, but this would not be possible in the other molecules. It is difficult to assess whether this apparent consistency in the average shape of these acetonides is a consequence of the particular substituents in these compounds, or whether it is characteristic of this fused-ring system.



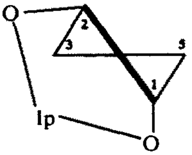
V_4



V^4



T_2^1



T_1^2

If the symmetrically substituted compounds listed in Table 5 actually existed in either the V_4 or V^4 conformations, then the dihedral angle φ_0 for H_1—C_1—C_2—H_2 would be 0°, and $J_{1,2}$ should be *ca* 9·4 Hz. The values of $J_{1,2}$ are much smaller than this and indicate that φ_0 is greater than 0°. On the other hand, if these molecules existed as a DL pair of the enantiomeric conformers, T_2^1 and T_1^2, with a dihedral angle φ_0 of 35–46° (corresponding to the observed $J_{1,2}$ values) then the dihedral angles φ_2 and φ_3, between the H_X protons and adjacent *cis*-methylenic protons would be 11–15° (from Eq 1). This would give J_{cis}, *ca* 8·5–9·0 Hz, and J_{trans} *ca* 3·0–3·5 Hz. The observed values of J_{cis} and J_{trans} are consistently outside the range predicted, and indicate that the average dihedral angle is greater. Therefore, these symmetrically substituted cyclopentanes do not appear to exist exclusively in one of the conformations (V_4, V^4, or the DL pair T_2^1 and T_1^2) in which the puckering of the ring is symmetrically oriented relative to the substituents.

Chemical shift values

In rigid systems an electronegative substituent generally exerts a greater deshielding effect on a *trans* vicinal proton than on a *cis* vicinal proton.[13,14] This generalization appears to be valid for most of the cyclopentanoid compounds which we have studied,[33] but not for **3a**, **3c**, **3d** and **16b** (see Table 6). In the spectra of these four compounds the signal for H_3 (H_6), lying *trans* to the C_4 electronegative substituent, is either upfield to or overlaps the signal of the *cis* protons H_4 (H_7). The assignment of the methylene signals in **3a** and **16b** was made on the basis of decoupling experiments which showed that the upfield methylene proton was strongly coupled to H_5 and that the downfield methylene proton was only weakly coupled to H_5. Also, in **16b** the upfield methylene proton is coupled to the dioxolane bridgehead protons, whereas the downfield methylene proton is not. Small or zero couplings

TABLE 6. PROTON CHEMICAL SHIFTS OF SYMMETRICAL CYCLOPENTENE OXIDES AND CYCLOPENTANETRIOL DERIVATIVES

Compound	δH_1	δH_3	δH_4	δH_5	$\Delta\delta H_3$	$\Delta\delta H_4$	$\Delta\delta H_A$	$\Delta\delta H_B$
3a	3·63	1·92	2·15	4·07	+0·32	−0·32	−0·55	+0·55
4a	3·48	1·60	2·47	4·09				
3c	3·52	2·14	2·14	5·23	+0·45	−0·48	−0·48	+0·45
4c	3·62	1·69	2·62	4·84				
16b	4·73	2·04	2·37	5·38	+0·24	−0·08	−0·41	+0·57
15b	4·72	1·30	2·45	5·51				
3d	3·65	ca. 2·55	ca. 2·55	4·35				
15a	4·63	1·53	2·16	4·46				

See Charts 1 and 2 for identification of compounds and numbering of protons.

$\Delta\delta H_3$ = difference in the chemical shift of H_3 in corresponding *cis*- and *trans*-isomers (δ_{cis}-δ_{trans}). Similarly for $\Delta\delta H_4$. Values are in parts per million.

H_A = vicinal methylene proton *cis* to H_X.

H_B = vicinal methylene proton *trans* to H_X.

$\Delta\delta H_A$ = the difference in chemical shifts to H_A in corresponding *cis*- and *trans*-isomers (δ_{cis}-δ_{trans}). Similarly for $\Delta\delta H_B$.

between vicinal protons *trans* to dioxolane bridgehead protons have been observed in several systems.[33–35]

The chemical shift data for these compounds can be rationalized with the earlier observations on the angular dependence of deshielding by electronegative substituents, if each pair of *cis-trans* isomers is considered together. Thus, in the spectra of the isomers in which the protons are *trans* to the C-4 electronegative substituent the H_3 and H_4 signals are downfield with respect to their positions in the spectra of the isomers in which the protons are *cis* to the substituent ($\Delta\delta$ H_3 and $\Delta\delta$ H_4 in Table 6). Apparently, both the oxirane and dioxolane ring more strongly deshield a vicinal proton *cis* to the ring (H_4), than a proton *trans* to the ring (H_3). The deshielding effect of the C_4 electronegative substituent is superimposed on this effect of the fused ring. The data for the unsymmetrical compounds listed in Table 7 further illustrate this phenomenon. In each pair of *cis-trans* isomers the H_3 signal is farther downfield when the proton is *cis* to the oxirane or dioxolane ring than when it is *trans* ($\Delta\delta$ H_3).

TABLE 7. CHEMICAL SHIFTS OF UNSYMMETRICAL CYCLOPENTENE OXIRANE AND CYCLOPENTANETRIOL DERIVATIVES

Compound	δH_1	δH_2	δH_3	$\Delta\delta H_3$
8a	3·54	3·39	4·29	+0·03
7a	3·46	3·46	4·26	
8c	3·56	3·49	5·24	+0·16
7c	3·45	3·58	5·08	
8d	3·62	3·68	4·40	+0·20
7d	3·59	3·59	4·20	
18a	4·73	4·33	4·13	+0·32
19a	4·59	4·38	3·81	

See Charts 1 and 2 for identification of compounds and numbering of protons.

$\Delta\delta H_3$ = the difference in chemical shifts of H_3 in corresponding *cis*- and *trans*-isomers (δ_{trans}-δ_{cis}).

If one considers the rings as electronegative substituents, then their apparent effect on the relative chemical shifts of vicinal *cis* and *trans* protons is opposite to that usually observed.

Unless the cyclopentane ring is in a planar conformation the various protons will be oriented differently relative to the C—C bonds of the ring, and thus differential shielding effects might be observed due to the diamagnetic anisotropy of the C—C bonds themselves.[36] As indicated earlier, the cyclopentane epoxides exist predominantly in the V_4 conformation in which a vicinal proton *trans* to the oxirane ring is *quasi*-axial and a vicinal proton *cis* to the oxirane ring is *quasi*-equatorial (Fig 4). Although the conformations of the acetonides are not as well-defined, on the average the same geometry appears to apply to the protons vicinal to the dioxolane ring in these compounds. Thus, $\Delta\delta$ H_3 in the unsymmetrical anhydrotriols and isopropylidene triols, and $\Delta\delta$ H_A and $\Delta\delta$ H_B in the symmetrical ones correspond to the difference in chemical shifts of axial and equatorial protons. The range of δ_{ae} observed in these compounds is 0·03–0·55 ppm. In cyclohexanoid systems the range of δ_{ae} which has been observed is 0·13–0·55 ppm.[37,38] Therefore, the relative chemical shifts observed for protons vicinal to an oxirane or dioxolane ring in these cyclopentanoid compounds are consistent with the generalization derived from cyclohexanes that axial protons are more shielded than corresponding equatorial protons. The puckering found in the cyclopentane derivatives is smaller than that in cyclohexanes, and thus δ_{ae} would be expected to be smaller. However, it seems unwise to ascribe any particular shielding or deshielding effect to the oxirane and dioxolane rings on the basis of a qualitative interpretation of these data. The apparently greater shielding of a vicinal proton *trans* to these fused rings may simply reflect the conformations of these compounds rather than some special shielding property of the oxirane and dioxolane rings.

EXPERIMENTAL

The syntheses of all the compounds discussed have been reported in previous publications.[39–41]

NMR spectra were determined on 5–10% solns with Varian Associates A-60 or HA-100 NMR Spectrometers. TMS or sodium 2,2-dimethyl-2-*sila*pentane-5-sulfonate was used as internal reference.

The assignment of the various NMR signals to specific protons was based on chemical shift values, integral ratios, the relative magnitude of various coupling constants, and double irradiation experiments. In the case of the unsymmetrical anhydrotriols, the assignment of H_1 and H_2 was based on the assumption that the vicinal coupling constant $J_{2,3}$ would be greater than the long-range coupling constant $J_{1,3}$. For those compounds in which the signals of the methylene protons overlap or in which the methylenic region of the spectrum is too complicated to analyze, only the sum $J_{cis} + J_{trans}$ measured from the H_X signal, has been reported. In the case of the symmetrical compounds included in Table 5, the coupling constant $J_{1,2}$, between the isochronous nuclei, H_1 and H_2, was obtained by the analysis outlined by Pople, Schneider and Bernstein[42] for AA'XX' spin-systems with $J_{AA'} = 0$ Hz. Except in those cases for which computation was actually carried out, the values of J are first-order, obtained by direct measurement of spectra recorded with an expanded sweep width.

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REFERENCES

[1] H. Z. Sable. K. A. Powell. H. Katchian. C. B. Niewoehner and S. B. Kadlec. *Tetrahedron* **26**. 1509 (1970)
[2] [a] E. L. Eliel. N. L. Allinger. S. J. Angyal and G. A. Morrison. *Conformational Analysis* p. 200 ff. Wiley. New York. N.Y. (1965).
[b] *Ibid.* p. 202;
[c] *Ibid.* pp. 51–53;
[d] K. S. Pitzer and W. E. Donath. *J. Am. Chem. Soc.* **81**. 3213 (1959)
[3] [a] L. D. Hall. *Chem. Ind.* 950 (1963)
[b] L. D. Hall. P. R. Steiner and C. Pedersen. *Canad. J. Chem.* **48**. 1155 (1970)
[4] [a] J. B. Hendrickson. *J. Am. Chem. Soc.* **83**. 4537 (1961);
[b] *J. Am. Chem. Soc.* **85**. 4059 (1963)
[5] [a] C. Altona. H. J. Geise and C. Romers. *Tetrahedron* **24**. 13 (1968);
[b] H. R. Buys and E. Havinga. *Ibid.* **24**. 4967 (1968)
[6] C. Romers, C. Altona, H. R. Buys and E. Havinga, *Topics in Stereochemistry* (Edited by E. L. Eliel and N. L. Allinger) Vol. 4, p. 39. Interscience, New York (1969)
[7] C. Altona. H. R. Buys and E. Havinga. *Rec. Trav. Chim.* **85**. 973 (1966)
[8] [a] C. Ouannes and J. Jacques. *Bull. Soc. Chim. Fr.*. 3601 (1965)
[b] V. W. Laurie. *Accts. Chem. Res.* **3**. 331 (1970)
[9] M. Karplus. *J. Chem. Phys.* **30**. 11 (1959)
[10] C. Altona. H. R. Buys. H. J. Hageman and E. Havinga. *Tetrahedron* **23**. 2265 (1967)
[11] J. W. Emsley. J. Feeney and L. H. Sutcliffe. *High Resolution Nuclear Magnetic Resonance Spectroscopy*. Vol. 1. Chapter 9. pp. 481 ff. Pergamon Press. Oxford (1965)
[12] H. Booth. *Tetrahedron* **20**. 2211 (1964)
[13] K. L. Williamson. *J. Am. Chem. Soc.* **85**. 516 (1963)
[14] P. Laszlo and P. v. R. Schleyer, *Ibid.* **85**, 2709 (1963)
[15] D. H. Williams and N. S. Bhacca. *Ibid.* **86**. 2742 (1964)
[16] H. Booth. *Tetrahedron Letters* 411 (1965)
[17] C. Altona. H. R. Buys and E. Havinga. *Rec. Trav. Chim.* **85**. 985 (1966)
[18] K. Mislow and M. Raban, *Topics in Stereochemistry* (Edited by N. L. Allinger and E. L. Eliel) Vol. 1, p. 1. Interscience, New York (1967)
[19] [a] C. W. Beckett. N. K. Freeman and K. S. Pitzer. *J. Am. Chem. Soc.* **70**. 4227 (1948);
[b] E. L. James. Dissertation. University of Pennsylvania (1963); *Diss. Abstracts* **24**. 1398 (1963);
[c] G. W. Rathjens. Jr.. *J. Chem. Phys.* **36**. 3401 (1962);
[d] H. J. Jakobsen. *Tetrahedron Letters* 1991 (1967);
[e] H. Haubenstock. P. G. Mennitt and P. E. Butler. *J. Org. Chem.* **35**. 3208 (1970)
[20] R. E. Parker and N. S. Isaacs. *Chem. Rev.* **59**. 737 (1959)
[21] J. J. McCullough. H. B. Henbest. R. J. Bishop. G. M. Glover and L. E. Sutton. *J. Chem. Soc.*. 5496 (1965)
[22] S. Winstein. E. C. Friedrich. R. Baker and L. Yang-I. *Tetrahedron. Suppl.* 8. Part II. 621 (1966)
[23] [a] P. K. Freeman. M. F. Grostic and F. A. Raymond. *J. Org. Chem.* **30**. 771 (1965);
[b] P. K. Freeman. F. A. Raymond and M. F. Grostic. *Ibid.* **32**. 24 (1967)
[24] A. D. Walsh. *Nature Lond.* **159**. 712 (1947)
[25] C. A. Coulson and W. E. Moffitt. *J. Chem. Phys.* **15**. 151 (1947)
[26] K. L. Williamson. C. A. Lanford and C. R. Nicholson. *J. Am. Chem. Soc.* **86**. 762 (1964)
[27] D. J. Patel. M. E. H. Howden and J. D. Roberts. *J. Am. Chem. Soc.* **85**. 3218 (1963)
[28] D. H. Buss. L. Hough. L. D. Hall and J. F. Manville. *Tetrahedron* **21**. 69 (1965)
[29] [a] E. Glotter. S. Greenfield and D. Lavie. *Tetrahedron Letters* 5261 (1967);
[b] P. R. Jefferies. R. S. Rosich and D. E. White. *Ibid.* 1853. (1963)
[30] P. Laszlo and P. v. R. Schleyer. *J. Am. Chem. Soc.* **85**. 2017 (1963)
[31] [a] D. J. Collins. J. J. Hobbs and S. Sternhell. *Tetrahedron Letters* 632 (1963);
[b] A. D. Cross. *J. Am. Chem. Soc.* **84**. 3206 (1962);
[c] K. Tori. T. Komeno and T. Nakagawa. *J. Org. Chem.* **29**. 1136 (1964)
[32] A. Warshawsky and B. Fuchs. *Tetrahedron* **25**. 2633 (1969)
[33] [a] H. Z. Sable. W. M. Ritchey and J. E. Nordlander. *Carbohydr. Res.* **1**. 10 (1965);
[b] *J. Org. Chem.* **31**. 3771 (1966)

[34] J. S. Brimacombe and L. C. N. Tucker. *Carbohydr. Res.* **5**, 36 (1967)
[35] W. Mackie and A. S. Perlin. *Canad. J. Chem.* **43**, 2921 (1965)
[36] L. M. Jackman. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry.* Chap. 7. MacMillan. New York. N.Y. (1959)
[37] R. U. Lemieux. R. K. Kullnig. H. J. Bernstein and W. G. Schneider. *J. Am. Chem. Soc.* **80**. 6098 (1958)
[38] E. L. Eliel. M. H. Gianni. T. H. Williams and J. B. Stothers. *Tetrahedron Letters* 741 (1962)
[39] H. Z. Sable. T. Adamson. B. Tolbert and T. Posternak. *Helv. Chim. Acta* **46**. 1157 (1963)
[40] J. A. Franks. Jr.. B. Tolbert. R. Steyn and H. Z. Sable. *J. Org. Chem.* **30**. 1440 (1965)
[41] R. Steyn and H. Z. Sable. *Tetrahedron* **25**. 3597 (1969)
[42] J. A. Pople. W. G. Schneider and H. J. Bernstein. *High Resolution Nuclear Magnetic Resonance Spectroscopy.* pp. 138 ff. McGraw-Hill. New York. N.Y. (1959)