

49. Conformational Studies of Six-membered Heterocyclic Compounds. Part I. The Proton Resonance Spectra of Some Substituted 1,3-Dithians.

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The conformational equilibria in 5-hydroxy-2,2-dimethyl-1,3-dithian, *cis*- and *trans*-5-hydroxy-2-phenyl-1,3-dithian, and the corresponding acetates are studied by proton resonance and infrared spectroscopy. The coupling constants of the individual conformers and the free-energy differences between them are obtained. The chemical shifts of axial protons in these compounds are to lower field than the corresponding equatorial protons. The free-energy differences between axial and equatorial 2-substituents in these compounds and in the analogous dioxans are shown to be much smaller than the corresponding values in the cyclohexane ring, and a possible interpretation of this is given.

THE use of proton nuclear magnetic resonance (n.m.r.) spectroscopy in the elucidation of conformational problems is now a well-established technique. However, the n.m.r. spectra of many compounds whose conformations are of interest are too complex for any detailed analysis, and this seriously restricts the amount of information which can be obtained. This is the case for most cyclohexane derivatives and it is necessary to prepare deuterated compounds, which give much less complex spectra, in order to obtain the molecular parameters from the n.m.r. spectrum.^{1,2} The introduction of one or two hetero-atoms into a six-membered ring simplifies the spectrum to such an extent that it is often possible to perform a complete analysis. Also, hetero-atoms introduce novel conformational features which are of considerable interest. In the course of an investigation into new syntheses of 1,2-dithiolium salts,³ the compounds *cis*- (I) and *trans*-5-hydroxy-2-phenyl-1,3-dithian (II), their acetates (III) and (IV),⁴ 5-hydroxy-2,2-dimethyl-1,3-dithian (V), and its acetate (VI)⁵ were prepared. It was apparent that these compounds were particularly suited to a detailed investigation, since the n.m.r. spectra are capable of complete analysis and information can be obtained by both n.m.r. and infrared (i.r.) spectroscopy.

To date, the majority of the investigations into the conformations of the 1,3-dithian and 1,3-dioxan rings have been by i.r. spectroscopy, *e.g.*, in the 5-hydroxy-derivatives, the ratio of the extinction coefficients, in dilute solution, of the free-hydroxyl to the intramolecularly bonded-hydroxyl band is a measure of the relative proportion of conformers bearing equatorial and axial hydroxyl groups. This intramolecular hydrogen bond stabilises the axial conformer to such an extent that it is more stable than the equatorial conformer in these solutions by 0.50 kcal./mole in the dithian⁶ and 1.04 kcal./mole in the dioxan,⁷

¹ Huitric, Carr, Trager, and Nist, *Tetrahedron*, 1963, **19**, 2145.

² Anet, *J. Amer. Chem. Soc.*, 1962, **84**, 1053.

³ Atkinson, Beer, and Royall, unpublished results.

⁴ Atkinson, M.Sc. Thesis, Liverpool, 1962.

⁵ Harris and Beer, unpublished results.

⁶ Lüttringhaus, Kabuss, Prinzbach, and Langenbushner, *Annalen*, 1962, **653**, 195.

⁷ Baggett, Bukhari, Foster, Lehmann, and Webber, *J.*, 1963, 4157; Barker, Brimacombe, Foster, Whiffen, and Zweifel, *Tetrahedron*, 1959, **7**, 10.

the larger value of the latter presumably being due to the greater hydrogen-bond strength of O-H...O compared to O-H...S bonds. These results are in direct contrast to cyclohexanol, in which the free-energy difference is 0.7 kcal./mole in favour of the equatorial conformer.⁸ The introduction of a 2-substituent in these 5-hydroxy-compounds will also have the opposite effect to that in the cyclohexanol series. Thus, the *cis*-isomers have been shown to exist in one stable conformer and the *trans*-isomers to be a mixture of conformers.^{6,7,9} Obviously, if the hydroxyl group is acetylated, then the more usual situation will obtain in which the *trans*-isomer would be largely one conformer and the *cis*-isomer a mixture of conformers. These general considerations are tested and verified in the following sections.

EXPERIMENTAL AND RESULTS

The n.m.r. spectra were measured on a Varian A-60 spectrometer at *ca.* 300 mg./ml. in various solvents (cf. Table 1). Dilution of the deuteriochloroform solutions gave no significant changes in the spectra. The variable-temperature spectra were obtained using the Varian V-6040 temperature probe. The infrared spectra were recorded on a Perkin-Elmer 125 spectrometer, at concentrations of less than 0.005M in various solvents.

The n.m.r. spectra of the ring protons of the *cis*- and *trans*-acetates (III) and (IV) are shown in the Figure. The assignment of the groups is trivial. Apart from the single peak of the C-2

TABLE 1.
Proton chemical shifts (τ values) and coupling constants.

Com- pound	Solvent	H-4(6)		H-5		Me	Coupling constants (c./sec.)		
		A *	B *	X	H-2		J_{AX}	J_{BX}	J_{AB}
(I)	CDCl ₃	6.74	7.09	6.10	4.93	—	1.3	4.6	13.7
	Pyridine	6.66	6.97	5.88	4.58	—	2.0	5.3	13.8
	Acetone						1.4	5.1	13.8
(II)	CDCl ₃	7.07	7.07	5.95	4.95	—	12.8 †		
	Pyridine ‡	6.67	6.77	5.53	4.48	—	10.2	3.9	13.3
	Acetone						10.4	3.9	13.7
(III)	CDCl ₃	6.88	7.00	5.02	4.92	7.86	2.4	5.9	14.4
	Pyridine	6.67	6.86	4.87	4.50	7.90	2.5	5.1	14.5
(IV)	CDCl ₃	6.98	7.08	4.83	4.86	7.97	10.8	3.6	13.4
	Pyridine	6.75	6.94	4.56	4.42	7.96	10.8	3.7	13.0
(V)	CDCl ₃	6.85	7.21	6.11	—	8.24, 8.37	1.9	5.9	14.0
(VI)	CDCl ₃	6.95	7.17	4.96	—	7.92, 8.15, 8.39	9.7	3.9	13.8

* The actual assignments (see text) are A \equiv a, B \equiv b for (I), (II), (IV), (V), and (VI); A \equiv b, B \equiv a for (III). † $J_{AX} + J_{BX}$. ‡ Contained *ca.* 10% D₂O for the ABX analysis.

proton (which can be observed in the complex C-5 proton pattern) the spectra are, in the usual nomenclature,¹⁰ A₂B₂C. This can be simplified to (AB)₂X as the cross-ring couplings between the C-4 and C-6 protons are known to be very small and the C-5-C-4(6) chemical shift is much larger than any of the corresponding couplings. Although small second-order splittings were observed, the (AB)₂X analysis was easily performed, the major difficulty being the very small chemical shift difference between the A and B protons. In one case, the *trans*-alcohol (II) in deuteriochloroform, this difference was so small that the spectrum reduced to a "deceptively simple spectrum,"¹¹ *i.e.*, a doublet AB and quintet X spectrum from which only the sum $J_{AX} + J_{BX}$ could be obtained. In the other cases, the coupling constants and chemical shifts from the (AB)₂X analyses were used to compute the full A₂B₂C spectrum. These calculated spectra are in excellent agreement with the observed spectra (see Figure), thus confirming the validity of the (AB)₂X approximation. The results of these analyses are given in Table 1. The error in the coupling constants is *ca.* ± 0.1 c./sec., and that in the chemical shifts ± 0.01 p.p.m.

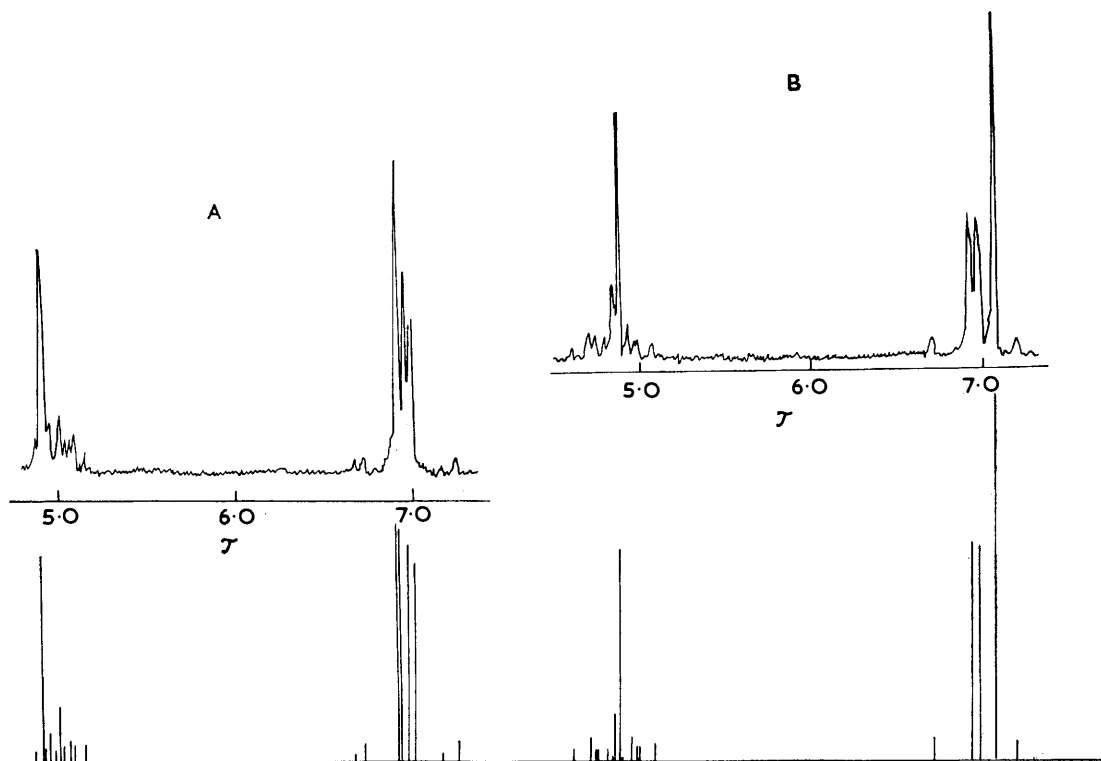
The i.r. spectrum (Table 2) of the *cis*-alcohol (I) showed only a single OH peak at 3522 cm.⁻¹ (CCl₄) of half-width 31 cm.⁻¹, which was displaced to 3510 cm.⁻¹ in chloroform solution. This

⁸ Eliel and Gianni, *Tetrahedron Letters*, 1962, 97.

⁹ Dobinson and Foster, *J.*, 1961, 2338.

¹⁰ Pople, Schneider, and Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, 1959.

¹¹ Abraham and Bernstein, *Canad. J. Chem.*, 1961, **39**, 216.



The observed and calculated 60 Mc./sec. n.m.r. spectra of the ring protons of (A) *cis*- (III) and (B) *trans*-2-phenyl-1,3-dithian-5-yl acetate (IV) in deuteriochloroform.

TABLE 2.
Infrared spectral data for OH and OH \cdots S absorption bands.

Compound	Solvent	$\nu_{\text{max.}}$ (cm. ⁻¹)		Half-height band width (cm. ⁻¹)	
		ν_{Free} (ϵ_{F}) *	ν_{Bonded} (ϵ_{B}) *	Free	Bonded
(I)	CCl ₄	—	3522(108)	—	31
	CHCl ₃ †	—	3510	—	—
	CCl ₄	3615(136)	3520(29)	28	30
(II)	CHCl ₃	3590	3498	—	—
	Hexachlorobutadiene	3608(126)	3513(17)	31	40
(V)	CCl ₄	3610(40)	3516(126)	22.5	35

* ϵ = molar extinction coefficient = $1/cl \log_{10} I_0/I$ cm.² mole⁻¹. † Resolution not good enough to measure intensities accurately in CHCl₃.

is characteristic of an O-H \cdots S intramolecular hydrogen bond,⁸ *i.e.*, compound (I) exists in these solutions solely in the conformation with an axial hydroxyl group. The spectrum of compound (II), in contrast, showed two OH bands at 3615 (the free OH position) and 3520 (CCl₄) and 3590 and 3498 cm.⁻¹ (CHCl₃), of half-widths 28 and 30 cm.⁻¹, respectively, and of integrated intensities [measured using method (I) of Ramsay^{12a}] 0.81 : 0.19 (CCl₄).

It is well known that the OH stretching band observed in intermolecular hydrogen bonds has a much greater band width, extinction coefficient, and integrated absorption coefficient than the corresponding free OH band, and there is a linear relationship between these observables.^{12b} This is not the case for intramolecular hydrogen bonds, in which it is commonly assumed that the free and bonded OH bands have equal extinction coefficients. On this basis

¹² (a) Ramsay, *J. Amer. Chem. Soc.*, 1952, **74**, 72; Jones, Ramsay, Kier, and Dobriner, *ibid.*, p. 80; (b) Pimentel and McClellan, "The Hydrogen Bond," W. H. Freeman and Co., London, 1960; (c) Krueger and Mettee, *Canad. J. Chem.*, 1964, **42**, 326.

Krueger and Mette were able to obtain a value for the entropy difference between the *gauche*- and *trans*-rotamers of 2-chloroethanol in good agreement with that found by other methods.^{12c} More direct support in the case of the OH...S bond is provided by Lüttringhaus *et al.*,⁶ who observed approximately equal extinction coefficients for the free OH band of thian-4-ol and the intramolecular bands of *cis*-5-hydroxy-2-*p*-methoxyphenyl-1,3-dithian and 3-phenylthian-3-ol, though a more rigorous parameter to use in these compounds is the integrated absorption coefficient, as the band-widths were not constant.

In the *trans*-alcohol (II) the equal band-width of the free- and bonded-hydroxyl bands further supports this assumption. Another check is provided by assuming equal integrated absorption coefficients of the bonded-hydroxyl band in the *cis*- (I) and *trans*-alcohols (II). This gives 75% of free hydroxyl in the *trans*-isomer, in excellent agreement with the earlier assumption. Thus, we conclude that the *trans*-isomer (II) is a mixture of conformers with 80% of that carrying the free (*i.e.*, equatorial) hydroxyl and 20% of that carrying the bonded (*i.e.*, axial) hydroxyl group. By exactly analogous reasoning, the proportion of free- to bonded-hydroxyl conformers in the 2,2-dimethyl alcohol (V) was estimated as 1 : 4.9, *i.e.*, 17% free-hydroxyl. The assumption of equal extinction coefficients has been used to derive the free-energy differences of the conformers in the related dioxans. However, these results are less well supported, as the published data⁷ give only extinction coefficients with no mention of the band widths or integrated intensities.

We now examine in detail the n.m.r. results (Table I) in order to determine the molecular parameters and to obtain independently the percentages of the individual conformers in the four compounds. As the proton chemical shifts are complex functions of the molecular conformation and the solvent reaction field,¹³ and the geminal coupling constants are not affected by conformational equilibria, we shall be concerned here with the vicinal (H·C·C·H) coupling constants. These are known to be independent of the solvent (for compounds of fixed conformation) but are very sensitive to conformational changes. From the i.r. results above and the absence of any concentration-dependence of the n.m.r. spectrum of the alcohol (I) in deuteriochloroform, it follows that (I) exists as a single conformer in the concentrated CDCl₃ solution studied by n.m.r. (Note that in the other solvents used this is not the case, and the coupling constants differ from those in CDCl₃.) Also, it can be safely assumed that compound (IV) exists solely as the di-equatorial conformer in any solution. Thus, the observed coupling constants for these solutions are those of the distinct conformers. This is further shown by the temperature-independence of the n.m.r. spectra of (I) and (IV) in methylene dichloride, even down to -80°. In contrast, the spectra of (II) and (III) in chloroform-pyridine and in carbon disulphide show a characteristic broadening of the lines, commencing at *ca.* -40°, typical of this type of conformational equilibrium.¹⁴ At the lowest temperature attained (-80°) the peaks were extremely broad, showing that the rate of interconversion of the isomers was still appreciable.

It is now necessary to assign the individual protons on C-4,6 in (I) and (IV). We define H_a as the proton (on C-4,6) *cis* to the 5-substituent and H_b as the *trans*-proton. This must be clearly distinguished from the nomenclature used in the analysis, in which H_A and H_B are defined as the low-field and high-field parts of the AB spectrum, respectively. In the *trans*-acetate (IV) the assignment follows immediately from the large axial-axial coupling of 10.8 c./sec., *i.e.*, J_{AX} (Table I) is J_{ax}. The assignment in (I) is not so obvious. However, examination of models, together with the existence of the strong intramolecular hydrogen bond, suggests that the ring will be bent more than 60°, and thus J_{ax} will be greater than J_{bx}, *i.e.*, J_{ax} is 4.6 and J_{bx} 1.3 c./sec. Similar coupling constants are found in the camphane-2,3-diols (J_{3-endo-4} ~ 0, J_{3-exo-4} = 4.4 c./sec.)¹⁵ in which the boat ring is also bent more than 60°. Furthermore, the alternative assignment does not lead to any consistent results in the following discussion. In the remaining compounds, (II), (III), (V), and (VI), the observed coupling constants will be the weighted mean of the couplings of the individual conformers, *i.e.*, writing ⟨J⟩ for the observed (average) coupling,

$$\langle J_{ax} \rangle = pJ_{ax} \text{ (IIa)} + (1 - p)J_{ax} \text{ (IIb)} \quad (1)$$

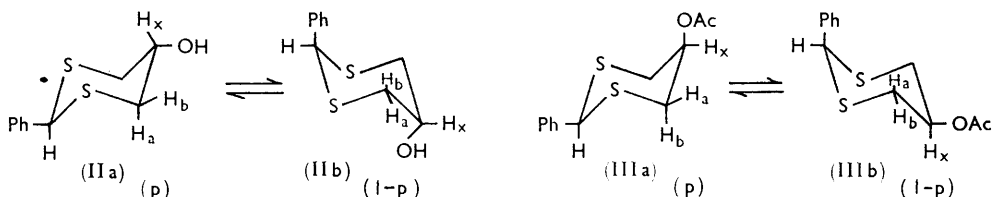
$$\langle J_{bx} \rangle = pJ_{bx} \text{ (IIa)} + (1 - p)J_{bx} \text{ (IIb)} \quad (2)$$

¹³ Buckingham, *Canad. J. Chem.*, 1960, **38**, 1960.

¹⁴ Friebolin, Kabuss, Maier, and Lüttringhaus, *Tetrahedron Letters*, 1962, 683.

¹⁵ Anet, *Canad. J. Chem.*, 1961, **39**, 789.

where (IIa) and (IIb) denote the two conformers considered and (p) and (1 - p) are the proportions of the conformers. In compound (II), the molecule may be visualised as flipping between the two chair forms (IIa) and (IIb). The large value of J_{AX} (10.3 c./sec.) (Table 1)



shows that the compound exists mainly as (IIa) in pyridine and acetone solutions and also gives the assignment of H_a and H_b [in equations (1) and (2) $\langle J_{ax} \rangle = 10.3$, $\langle J_{bx} \rangle = 3.9$ c./sec.]. However, there are still five unknowns and only two equations. Thus, it is necessary to make some further assumptions, the two most obvious being as follows.

(a) The orientation of the phenyl group will not affect significantly the buckle of the other half of the molecule. From this it follows that the coupling constants of conformer (IIb) would be identical to those of compound (I). The change from equatorial to axial phenyl would normally be expected to be accompanied by a small increase in the angle of buckle of the other half of the molecule, owing to the increased 1,3-diaxial interactions. These interactions are smaller in the dithian than in the cyclohexane ring (*vide infra*). More significantly, the ring in compound (I) must be considerably buckled in order to form the $\text{OH} \cdots \text{S}$ intramolecular hydrogen bond and therefore would be expected to be very resistant to any further increase in the angle of buckle, *i.e.*, the intramolecular hydrogen bond may be regarded as locking the conformation of this half of the molecule.

(b) Acetylation of the hydroxyl group does not affect the coupling constants of the conformers. It has been shown that this is so in molecules in which no conformational changes are possible.^{16,17} This reduces to the assumption that acetylation of the hydroxyl group does not alter the angle of buckle of the ring. It follows that the coupling constants of (IIa) will be identical to those of (IV).

If both assumptions (a) and (b) are used in equations (1) and (2), then J_{bx} would vary between 1.3 and 3.6 c./sec., [the values in (I) and (IV), respectively]. The observed value (3.9 c./sec.) shows that one of these assumptions is not strictly applicable. This is obviously (b), as otherwise the value of J_{bx} in (IIb) would need to be > 3.9 c./sec., *i.e.*, quite different from the value in (I). However, (b) is of some use as it enables the axial-axial coupling J_{ax} (IIa) to be obtained. Axial-axial couplings are insensitive to small changes in the angle of buckle. (The $\cos^2 \phi$ law¹⁸ predicts no change over the range $\pm 10^\circ$ from the classical dihedral angle of 180° .) Thus J_{ax} (IIa) may be taken to be 10.8 c./sec., the value in (IV). Using this, together with assumption (a), enables equations (1) and (2) to be solved to give J_{bx} (IIa) = 4.1 c./sec. and p 0.92 for the pyridine and acetone solutions. The relative proportions of the conformers in CDCl_3 solution can now be obtained from the sum $J_{AX} + J_{BX}$ (Table 1) to give p 0.77. This value is in excellent agreement with the infrared results (0.81 in CCl_4) when the differences in solvent and concentration are considered. This value of p is equivalent to a free-energy difference of 0.85 kcal./mole between (IIa) and (IIb).

A similar calculation can be performed on the results for the *cis*-acetate (III). Here the equilibrium between the two chair forms (IIIa) and (IIIb) gives two equations similar to (1) and (2).

The larger of the observed coupling constants (J_{BX}) must include the axial-axial coupling J_{ax} (IIIb), *i.e.*, J_{BX} is assigned as J_{ax} . The solution of these equations is obtained by assuming the coupling constants in (IIIb) to be identical to those of compound (IV), and also by using the $\cos^2 \phi$ law to relate J_{ax} (IIIa) and J_{bx} (IIIa). The coefficients in the $\cos^2 \phi$ equation,¹⁷ obtained from compounds (I) and (IV), are k_1 11.3 c./sec., k_2 10.9 c./sec. This gives two equations in the two unknowns p and ϕ [the H-C-C-H dihedral angle in (IIIa)], which can therefore be solved

¹⁶ Williamson, *J. Amer. Chem. Soc.*, 1963, **85**, 516.

¹⁷ Abraham and Pachler, *Mol. Phys.*, 1964, **7**, 165.

¹⁸ Karplus, *J. Chem. Phys.*, 1959, **30**, 11.

to give p 0.75 (CDCl_3), 0.79 (pyridine), J_{ax} (IIIa) = 3.6 c./sec., J_{bx} (IIIa) = 2.2 c./sec. The value of p is equivalent to a free-energy difference of 0.66 kcal./mole in favour of (IIIa).

The results for the 2,2-dimethyl compounds can now be used to check the above procedure, *e.g.*, in the alcohol (V) the observed coupling constants can be considered to be the weighted mean of those in the *cis*-alcohol (I) and those of conformer (IIa). This gives two equations in the one unknown, p , the fraction carrying the axial hydroxyl group. The solution of these is p 0.79 in both cases, *i.e.*, in exact agreement, and also in striking agreement with the i.r. results. This is equivalent to a free-energy difference of 0.80 kcal./mole in favour of the axial conformer. The couplings for the acetate (VI) are not in such good agreement. In particular, the value of J_{bx} (3.9 c./sec.) is outside the predicted range of 2.2 c./sec. for (IIIa) to 3.7 c./sec. for (IV). This anomaly also occurred with the *trans*-alcohol (II) and may be treated in an identical manner, *e.g.*, p , the fraction of the conformer with an equatorial acetate group, is obtained from J_{ax} , using the values in (IIIa) and (IV). This gives p 0.83, and this can be introduced into the equation for J_{bx} , using J_{bx} of (IIIa) to give $J_{bx} = 4.2$ c./sec. for the conformer with the equatorial acetate group. This value is identical to that of conformer (IIa), but differs appreciably from that of (IV). Some of this difference could be due to experimental error, but other effects appear to be present. At the moment this difference is somewhat anomalous.

Before these results are discussed it is convenient to consider the limitations of the above treatment. In particular, this assumes that boat forms of (II) and (III) are not present. These were considered by replacing (IIb) and (IIIb) by the boat conformation [(I) and (IV) and the 2,2-dimethyl compounds (V) and (VI) are much more stable than any possible boat form]. Assuming dihedral angles of 0° and 60° for a classical boat and 33° and 71° for the twisted boat,¹⁹ the corresponding coupling constants can be calculated from the $\cos^2 \phi$ law. These were incorporated into equations (1) and (2). A classical boat structure for (II), analogous to that tentatively suggested for the corresponding dioxan,⁷ gave much poorer agreement with the i.r. results. However, a twisted boat structure for the acetate (III) gave reasonable values of the coupling constants of (IIIa) and a value of p of 0.64 [equivalent to a free-energy difference of 0.35 kcal./mole in favour of conformer (IIIb)]. Although the dithian ring is more flexible than cyclohexane (*i.e.*, there is a lower barrier to ring inversion¹⁴) the destabilising axial-axial interactions will also be considerably less. Thus, the twisted boat-chair free-energy difference would not be expected to differ appreciably from the value in cyclohexane (5.7 kcal./mole).¹⁹ In this case it is difficult to see why the boat form of (III) is only 0.35 kcal./mole less stable than conformer (IIIa). Thus, we can safely neglect consideration of these boat forms at this stage.

DISCUSSION

Although the general trend of the results obtained above amply confirms the predictions given earlier, these results show some surprising features. It is noteworthy that in both compounds with a single conformation, (I) and (IV), the C-4(6) axial hydrogen resonates at lower field than the equatorial proton, in complete contrast to the generally accepted rule for cyclohexanes.²⁰ This agrees with a similar result for the α -protons in cyclohexanones,²¹ and would appear to indicate that the rule should not be considered reliable enough to assign protons in complex systems without further evidence. The vicinal coupling constants, in contrast, are in good agreement with the $\cos^2 \phi$ law, though there are only minor variations in the angles of buckle of the rings in the above compounds. The variation of these couplings with solvent are of interest, in particular as the invariance of coupling constants (or any other convenient molecular parameter) with solvent is often used as a proof of "conformational purity." Of the above compounds, only (II) and (IV) obey this rule. In (I) the hydrogen-bonding properties of the solvent are the dominant factor, but compound (III), in which no such specific effect is present and which is clearly a mixture of conformers, showed no significant variation of coupling constant with solvent. Clearly

¹⁹ Hendrickson, *J. Amer. Chem. Soc.*, 1961, **83**, 4537.

²⁰ Jackman, "Application of Nuclear Magnetic Resonance Spectroscopy to Organic Chemistry," Pergamon, London, 1959.

²¹ Wellman and Bordwell, *Tetrahedron Letters*, 1963, 1703.

this rule should not be regarded as proof of conformational purity without supporting evidence.

The free-energy differences of the isomers are of considerable interest. If the free-energy difference of 0.85 kcal./mole between conformers (IIa) and (IIb) is regarded in the usual manner²² as made up of independent contributions of the phenyl and hydroxyl groups, then the free-energy difference of -0.80 kcal./mole for the hydroxyl group in (V), which is in fair agreement with that of the parent compound (0.50 kcal./mole),⁶ gives a free-energy difference for the phenyl group of only 1.65 kcal./mole. This is very much less than the values quoted in the cyclohexane system (2.0-3.6 kcal./mole).²³ This result is confirmed by the free-energy difference between (IIIa) and (IIIb) of 0.65 kcal./mole which, taken in conjunction with the free-energy difference of the acetate group in these systems from (VI) of 1.05 kcal./mole, gives a phenyl free-energy difference of 1.70 kcal./mole.

An analogous situation holds for the 1,3-dioxan ring. The conformational free-energy differences of -1.04 kcal./mole in 5-hydroxy-1,3-dioxan and 0.68 for *trans*-5-hydroxy-2-phenyl-1,3-dioxan⁷ again give a phenyl free-energy difference of 1.70 kcal./mole. This is even more surprising as in this system the axial 2-substituent would be (in the classical chair conformation) nearer to the C-4(6) axial hydrogens than in the corresponding cyclohexane compound. The observations of Foster *et al.*,⁷ who showed that changing the 2-substituent from methyl to ethyl to isopropyl to phenyl in the *trans*-2-substituted 5-hydroxy-1,3-dioxans only slightly affected the ratio of the conformers, demonstrate that this is a general phenomenon with 2-substituents.

These low free-energy differences for the 2-phenyl group may also be contrasted with the quite normal value for the 5-acetate group. (The A value of the acetate group in cyclohexane is *ca.* 0.7 kcal./mole^{3,8}). Yet it is the axial-axial repulsions of the 5-substituent which have changed from substituent-proton interactions in the cyclohexanes to substituent-lone pair interactions in the dioxans and dithians. A possible interpretation of the low A values for the 2-substituents is that the C-O-C (C-S-C) angles are much easier to change than the C-C-C angles. Thus, in the 1,3-dioxans the angle of buckle of the C-2 part of the ring would be much less than 60°, which would increase considerably the C-2-C-4(6) axial-axial distances. This would also explain the lower barrier to ring flipping in these rings, as the chair-twisted boat interconversion only involves four successive atoms in the ring,¹⁹ which in this case would be a C·X·C·X portion

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²² Winstein and Holness, *J. Amer. Chem. Soc.*, 1955, **77**, 5562.

²³ Garbisch and Patterson, *J. Amer. Chem. Soc.*, 1963, **85**, 3228; Eliel and Rerick, *ibid.*, 1960, **82**, 1367; Allinger, Allinger, Da-Rouge, and Greenberg, *J. Org. Chem.*, 1962, **27**, 4603.