Ring Distortions in 2-Methyl-2-t-butyl Derivatives of 1,3-Dioxan, 1,3-Oxathian, and 1,3-Dithian

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The 100 MHz spectra of 2-[$^2H_3$]methyl-2-t-butyl derivatives of 1,3-dioxan, 1,3-oxathian, and 1,3-dithian, and of 2-t-butyl-1,3-oxathian have been analysed by iterative computation. Application of the *R* value treatment of vicinal coupling constants shows that the C–C–C fragment in the 1,3-dithian ring is the most distorted by the presence of the 2-axial methyl group.

RING distortion attributable to the presence of substituent groups is an established feature in conformational studies of six-membered ring compounds. Perturbation of chair geometry by an equatorial t-butyl group [1] has implications for the use of t-butyl derivatives as fixed models in conformational equilibrium studies,[2] but such distortions are small in comparison with some which occur in compounds having bulky groups occupying axial sites. In extreme cases destabilising interactions arising from an axial t-butyl group or two 1,3-diaxial substituents may cause a ring to adopt non-chair conformations and this phenomenon has been exploited for the estimation of energy differences between chair and twist forms.[3-6] Interactions arising from a single axial methyl group are less severe but ring distortion may still be significant. Thus results of an electron diffraction study have shown that 1,1-dimethylcyclohexane adopts a flatter chair

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[1] V. R. Haddon and L. M. Jackman, *Org. Magnetic Resonance*, 1973, **5**, 333; R. Parthasarathy, J. Ohrt, H. B. Kagan, and J. C. Fiaud, *Tetrahedron*, 1972, **28**, 1529; P. L. Johnson, J. P. Schaefer, V. J. James, and J. F. McConnell, *ibid.*, p. 2901; P. L. Johnson, C. J. Cheer, J. P. Schaefer, V. J. James, and F. H. Moore, *ibid.*, p. 2893; H. van Koningsveld, *Acta Cryst.*, 1972, **B28**, 1189; G. Berti, B. Macchia, F. Macchia, S. Merlino, and U. Muccini, *Tetrahedron Letters*, 1971, 3205; A. J. Jones, E. L. Eliel, D. M. Grant, M. C. Knoeber, and W. F. Bailey, *J. Amer. Chem. Soc.*, 1971, **93**, 4772; C. Altona and M. Sundaralingam, *Tetrahedron*, 1970, **26**, 925.

[2] S. Wolfe and J. R. Campbell, *Chem. Comm.*, 1967, 872; J. L. Mateos, C. Perez and H. Kwart, *ibid.*, p. 125.

[3] H. Van Bekkum, M. A. Hoefnagel, L. de Lavieter, A. Van Veen, P. E. Verkade, A. Wemmers, B. M. Wepster, J. H. Palm, L. Schäfer, H. Dekker, C. Mosselman, and G. Somsen, *Rec. Trav. chim.*, 1967, **86**, 1363

[4] R. M. Clay, G. M. Kellie, and F. G. Riddell, *J. Amer. Chem. Soc.*, 1973, **95**, 4632 and references therein.

[5] K. Pihlaja, *J.C.S. Perkin II*, 1974, 890 and references therein.

[6] K. Pihlaja and P. Pasenen, *J. Org. Chem.*, 1974, **39**, 1948 and references therein.

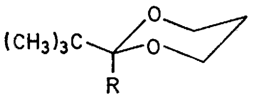
conformation (torsional angle 51.7°) [7] than cyclohexane (55.9°) [8] and coupling constant data provided the basis for an estimate of a 2° flattening of the C(4)—C(6) fragment in 2,2-dimethyl-1,3-oxathian relative to the parent ring.[9] Quantitative estimates of this type provide an insight into the relative ease and modes of ring distortions, ramifications of which may extend into seemingly unlikely areas as exemplified by recent studies on C–Bu^t bond rotation barriers.[10] The present paper assesses distortions induced by the 2-methyl groups in compounds (1)—(3) by comparing their n.m.r. data with those for the model systems (4)—(6).

TABLE 1

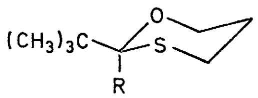
^{1}H N.m.r. parameters obtained by iterative computation [a]

Parameter [b]	Compounds (1) [c]	 (2) [d]	 (3) [e]	 (5) [f]
$\delta H\text{-}4_{ax}$	392.11 (0.02)	304.58 (0.01)	303.11 (0.01)	295.09 (0.03)
$\delta H\text{-}4_{eq}$	375.54 (0.02)	262.14 (0.01)	271.80 (0.01)	275.16 (0.02)
$\delta H\text{-}5_{ax}$	191.20 (0.01)	182.10 (0.02)	178.73 (0.01)	190.48 (0.02)
$\delta H\text{-}5_{eq}$	125.23 (0.01)	161.05 (0.02)	205.47 (0.01)	158.49 (0.02)
$\delta H\text{-}6_{ax}$	392.11 (0.02)	388.03 (0.03)	303.11 (0.01)	353.54 (0.02)
$\delta H\text{-}6_{eq}$	375.54 (0.01)	378.51 (0.03)	271.80 (0.01)	415.98 (0.03)
$J_{4ax,5ax}$	12.55 (0.02)	12.64 (0.02)	11.85 (0.02)	12.89 (0.04)
$J_{4eq,5eq}$	1.59 (0.02)	3.77 (0.02)	4.35 (0.02)	3.63 (0.03)
$J_{4ax,5eq}$	2.68 (0.02)	3.13 (0.02)	3.28 (0.02)	2.73 (0.03)
$J_{4eq,5ax}$	5.36 (0.02)	3.95 (0.02)	3.96 (0.02)	3.50 (0.03)
$J_{5ax,6ax}$	12.55 (0.02)	12.07 (0.04)	11.85 (0.02)	12.29 (0.03)
$J_{5eq,6eq}$	1.59 (0.02)	2.14 (0.04)	4.35 (0.02)	2.19 (0.03)
$J_{5ax,6eq}$	5.36 (0.02)	5.25 (0.04)	3.96 (0.02)	4.23 (0.03)
$J_{5eq,6ax}$	2.68 (0.02)	2.36 (0.04)	3.28 (0.02)	2.17 (0.03)
$J_{4ax,4eq}$	−11.31 (0.03)	−13.48 (0.02)	−14.46 (0.02)	−13.29 (0.03)
$J_{5ax,5eq}$	−12.94 (0.02)	−13.58 (0.02)	−13.54 (0.02)	−13.83 (0.03)
$J_{6ax,6eq}$	−11.31 (0.03)	−12.41 (0.04)	−14.46 (0.02)	−11.82 (0.03)
$J_{4eq,6eq}$	2.33 (0.05)	1.57 (0.03)	0.65 (0.03)	1.61 (0.04)
$J_{4ax,6ax}$	0.81 (0.04)	−0.08 (0.03)	0.03 (0.03)	−0.19 (0.03)
$J_{4ax,6eq}$	−0.57 (0.03)	−0.10 (0.03)	−0.05 (0.02)	0.07 (0.04)
$J_{4eq,6ax}$	−0.57 (0.03)	−0.31 (0.03)	−0.05 (0.02)	0.00 (0.03)

[a] Using local versions of the Laocoon III and Lacx programs. Values in parentheses are ' probable errors of parameter sets ' computed at the final iteration. [b] Chemical shifts (δ) measured in Hz downfield from Me_4Si. Coupling constants J in Hz. Spectra measured at 100 MHz. [c] 74 lines matched to observed transitions to within 0.21 Hz. R.m.s. error of fit = 0.077. [d] 128 lines matched to observed transitions to within 0.19 Hz. R.m.s. error of fit = 0.090. [e] 101 lines matched to observed transitions to within 0.17 Hz. R.m.s. error of fit = 0.084. [f] 90 lines matched to observed transitions to within 0.24 Hz. R.m.s. error of fit = 0.090.



(1) R = CH_3
(4) R = H



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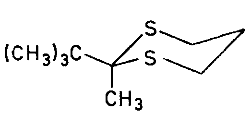
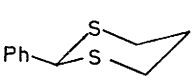


(3)



(6)

RESULTS AND DISCUSSION

The anticipated overlap of the 2-methyl group signal with the signals for the ring protons prompted us to base the study on the spectra for the 2-[$^2H_3$]methyl derivatives of (1)—(3). These spectra and that for (5) were measured at 100 MHz for solutions in $CDCl_3$ at 38°. Precise data for (4) and (6) were already available in the literature.[11,12] The parameters were refined by iterative computation using local versions of the Laocoon III or Lacx programs. Values of O Hz for $^4J_{ax,eq}$ and $^4J_{ax,ax}$, and a small positive value for $^4J_{eq,eq}$ were used as input parameters for cross-ring coupling.[12] All parameters were allowed to vary during the iterative calculation and the final root mean square error of fit was <0.1 Hz for each case. An example of the fit between the experimental and calculated spectra is given in the Figure. The computed best values and their probable errors are reported in Table 1.

The steric requirement of the bulky 2-t-butyl group is expected to lock the rings into an essentially exclusive preference for chair forms having the bulky substituent occupying the equatorial site. The assignment of the spectral parameters follows once the largest vicinal coupling constants are identified as those between two axial protons.

Comparison of the chemical shift data for (1) with those for (4), reported elsewhere,[11] and again for (2) with those for (5) shows that introduction of the axial 2-methyl group deshields the *syn*-axial protons α to ring heteroatoms but shields the corresponding equatorial protons. The effect is significantly larger when the heteroatom is

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[7] H. J. Geise, F. C. Mijlhoft, and C. Altona, *J. Mol. Structure*, 1972, **13**, 211.

[8] H. J. Geise, H. R. Buys, and F. C. Mijlhoff, *J. Mol. Structure*, 1971, **9**, 447.

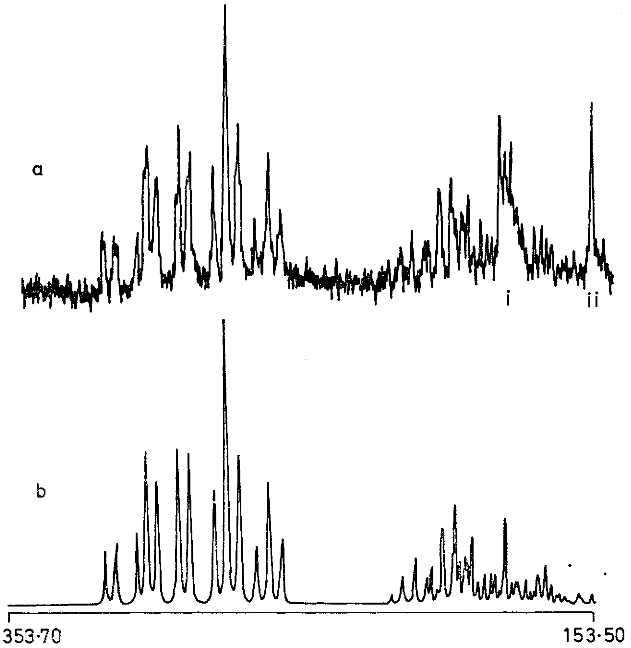
[9] N. de Wolf and H. R. Buys, *Tetrahedron Letters*, 1970, 551.

[10] P. E. Stevenson, G. Bhat, C. H. Bushweller, and W. G. Anderson, *J. Amer. Chem. Soc.*, 1974, **96**, 1067.

[11] H. R. Buys and E. L. Eliel, *Tetrahedron Letters*, 1970, 2779.

[12] H. R. Buys, *Rec. Trav. chim.*, 1970, **89**, 1244, 1253.

oxygen. In the four compounds investigated here, H-5*ax* is at lower field than H-5*eq* in all but the 1,3-dithian (3).



a, 100 MHz N.m.r. spectrum of 2-[$^2H_3$]methyl-2-t-butyl-1,3-dithian (3) (i, multiplet due to traces of the 2-[$^2H_2$]methyl-2-t-butyl analogue; ii, sideband arising from the t-butyl group signal). b, Simulated spectrum corresponding to the parameters reported for (3) in Table 1

Values for the Lambert–Buys parameter R,[13,14] the ratio $\Sigma^3J_{trans}:\Sigma^3J_{cis}$, and ψ, the weighted mean internal dihedral angle of all conformations present and calculated from Buy ’ equation, $\cos\psi = [3/(2 + 4R)]^{\frac{1}{2}}$, are reported in Table 2. Previous investigations have demonstrated that values for ψ derived using the R value method normally agree to within $0 \pm 2°$ with those obtained by other physical methods.[14]

Table 2

R Values and values for internal dihedral angles ψ

Compound	$R_{4.5}$	$R_{5.6}$	$\psi_{4.5}$ (°)	$\psi_{5.6}$ (°)
(1)	1.76		55	
(4) [11]	1.80		55	
2-*p*-Chlorophenyl-1,3-dioxan [12]	1.81		55	
(2)	2.32	1.87	59	56
(5)	2.65	2.26	61	59
(9) [12]	2.62	2.41	61	59
(3)	2.24		58	
(6) [12]	3.23		63	

1,3-*Dioxans*.—1,3-Dioxan and many of its simple derivatives exist in chair conformations which are puckered in the O–C–O region.[15] Previous applications of the R value method to data for 1,3-dioxan and (4) have shown that the equatorial 2-t-butyl substituent in the latter does not distort the C–C–C fragment.[11] Interactions to an axial methyl group in the 4-position have some small flattening effect on ring geometry.[16] In contrast, interactions experienced by a 2*ax*-Me group are expected to be quite severe [17,18] because of the puckered nature of the O–C–O fragment, and very recently Nader [19] has reported a significant flattening of this part of the ring caused by interactions to a 2*ax*-aryl group. In (1) destabilising interactions associated with the 2*ax*-Me group may be enhanced by the buttressing effect [20] of the 2*eq*-Bu^t group. Recently Bushweller *et al.*[10] proposed a flattening of the O–C–O region in (1) in a study of the Bu^t–C(2) bond rotational energy barrier.

Comparison of the present coupling constant data for (1) with that obtained elsewhere [11] for (4) shows that the introduction of the axial 2-methyl group has but little effect on the vicinal coupling constants, the greatest discrepancy being 0.36 Hz. The R values and values for ψ (Table 2) show that ring geometry about the C–C–C fragment is the same in each compound, *i.e.* strain associated with the axial 2-substituent is not relieved by flattening at this end of the ring. This conclusion is in excellent agreement with that drawn from *X*-ray structural data for a 1,3-dioxan having an axial 2-aryl group.[19] Flattening of the O–C–O region in (1) would have no effect on the observed R values and therefore it is not possible to comment on this mode of distortion.

1,3-*Oxathians*.—Simple 1,3-oxathians adopt chair forms in which the O side of the ring is probably more puckered than the S side.[21,22] Coupling constant data [21] and equilibria data [22] suggest that the ring is flattened by bulky 6-axial substituents and R value data have been reported for amongst others,[14] (7), (8),[9] and (9),[12] which demonstrate flattening of the C–C–C region in (8). Thermodynamic parameters for the chair $\rightleftharpoons$ twist interconversion have recently been established and the value for $\Delta H°$, (25.2 kJ mol^{-1}),[6] intermediate between that for 1,3-dioxans [4] and 1,3-dithians,[5] is sufficiently large to conclude that contributions from non-chair forms of (2) are negligible. Coupling constants obtained for (5) are in good agreement with those obtained elsewhere for (9),[12] demonstrating that the geometry about the C–C–C fragment is the same in each [and also very similar to that in (7) [9]]. In contrast, data for (2) show that the 2*ax*-Me group brings about a decrease in both $\psi_{4.5}$ and $\psi_{5.6}$, the latter decrease being the larger. The results, which we interpret in terms of a flattening of the

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[13] J. B. Lambert, *J. Amer. Chem. Soc.*, 1967, **89**, 1836; H. R. Buys, *Rec. Trav. chim.*, 1969, **88**, 1003.

[14] J. B. Lambert, *Accounts Chem. Res.*, 1971, **4**, 87 and references therein.

[15] A. J. de Kok and C. Romers, *Rec. Trav. chim.*, 1970, **89**, 313; for a review see E. L. Eliel, *Accounts Chem. Res.*, 1970, **3**, 1.

[16] J. Gelan, G. Swaelens, and M. Anteunis, *Bull. Soc. chim. belges*, 1970, **79**, 321.

[17] E. L. Eliel, J. R. Powers, and F. W. Nader, *Tetrahedron*, 1974, **30**, 515.

[18] K. Pihlaja and J. Heikkila, *Acta Chem. Scand.*, 1967, **21**, 2430.

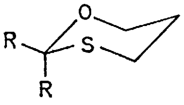
[19] F. W. Nader, *Tetrahedron Letters*, 1975, 1207, 1591.

[20] N. L. Allinger, M. A. Miller, F. A. Van Catledge, and J. A. Hirsch, *J. Amer. Chem. Soc.*, 1967, **89**, 4345.

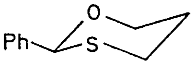
[21] J. Gelan and M. Anteunis, *Bull. Soc. chim. belges*, 1968, **77**, 423.

[22] P. Pasanen and K. Pihlaja, *Tetrahedron*, 1972, **28**, 2617 and references therein.

chair geometry are comparable with those reported by Buys[9] for the pair of compounds (7) and (8). The marginally larger distortion in (2) ($\psi_{4.5}$ 59°) relative to (8) ($\psi_{4.5}$ 60°), if real, may be due to a greater buttressing effect of the $2eq$-Bu^t group over that of the $2eq$-Me group.



(7) R = H
(8) R = CH$_3$



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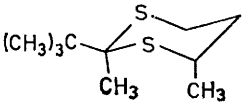

(10)

1,3-*Dithians*.—Many 1,3-dithians exist in chair conformations[23] but the low value of $\Delta H°$, 16.7 kJ mol^{-1}, for the chair $\rightleftharpoons$ twist interconversion, recently calculated by Pihlaja in a reappraisal of an interpretation of earlier data,[5] indicates that a single axial methyl group may be sufficient to cause a compound to adopt twist forms. Thus it has been suggested that up to 5% of (10) exists in non-chair forms at 298°. Coupling constant data[16,21] point to ring distortions in derivatives having a 4-axial substituent.

No precise n.m.r. data for 2-t-butyl-1,3-dithian appear to be available. In a preliminary investigation[24] of this compound we found that the signals for the protons at C-4(6) gave rise to a deceptively simple pattern which did not facilitate analysis. Rather than pursue this analysis we deemed it acceptable for the present treatment to use the data already available[12] for 2-phenyl-1,3-dithian (6), the justification for this being the very close correspondence between the R values (and values for ψ) for (5) and (9) discussed above, and again between 2-*p*-chlorophenyl-1,3-dioxan[12] and (4)[11] (Table 2). Comparison of the n.m.r. data for (3) and (6)[12] shows that introduction of the $2ax$-Me group causes marked variations in the vicinal coupling constants, in particular a decrease in $J_{4(6)ax,5ax}$ (12.4 to 11.85 Hz) and large increases in $J_{4(6)eq,5ax}$ (2.9 to 3.96 Hz) and $J_{4(6)ax,5eq}$ (2.3 to 3.28 Hz). These bring about a reduction in the R value from 3.2 to 2.2 which represents a decrease in ψ from 63 to 58°. Thus the mean geometry of the C–C–C fragments in the two 1,3-dithians is significantly different and can be rationalised in terms of a flattening of the C–C–C fragment and/or contributions from twist forms in (3). This conclusion contrasts with an assumption made elsewhere[10] that the geometry of the two compounds is the same.

Conclusions.—The present results show that distortion of the C–C–C fragment induced by the $2ax$-Me group increases in the order (1), (2), and (3). The 'A value' for the 2-methyl group in the 1,3-diheterocyclic ring systems increases in the order: 1,3-dithian, 1,3-oxathian, 1,3-dioxan,[22] and it is tempting to relate the increasing A value directly to the inflexibility of the C–C–C fragment. However, as was pointed out earlier, flattening of the X–C–Y fragment is a mode of distortion which may also occur but which is unidentifiable by the present technique, and twist forms of (3) may further complicate the picture. It is also important to note that steric interactions are not necessarily the only source of the distortion. Thus Bushweller *et al.*[10] pointed out that distortion may also arise through the repulsive interaction between the axial heteroatom lone pair and the electrons in a C-methyl bond of the t-butyl group, an interaction which will be maximised by the presence of the $2ax$-Me group.

EXPERIMENTAL

100 MHz Spectra were obtained of 10% solutions in CDCl$_3$ on a Varian HA 100 spectrometer operating at 38°. Analyses were based on 50 or 100 Hz sweepwidth spectra calibrated at 10 Hz intervals.

$[^2H_3]$*Methyl t-Butyl Ketone*.—Pinacolone (10.3 g) was heated under reflux with NaOD (2N in D$_2$O), until the n.m.r. spectrum of the compound showed exchange to be complete (>95%).

$[^2H_3]$*Methyl-2-t-butyl-1,3-dioxan*.— Propane-1,3-diol (7.2 g), and toluene-*p*-sulphonic acid (0.1 g) were shaken with D$_2$O (5 ml). Benzene (100 ml) was added and refluxed under a Dean–Stark device to dry the solution azeotropically. $[^2H_3]$Methyl t-butyl ketone (7.21 g) was added and reflux was continued until no further water was collected. The benzene solution was washed with water (1 ml), dried (MgSO$_4$), evaporated to dryness, and the residue distilled to afford the dioxan (3.1 g, 23%), b.p. 78—85° at 13 mmHg (lit.,[25] 172° at 737 mmHg)

The following were prepared as above or by a literature route: $[^2H_3]$methyl-2-t-butyl-1,3-oxathian (26%), b.p. 80° at 2.5 mmHg (lit.,[26] 49—49.5° at 0.5 mmHg) from 3-mercaptopropan-1-ol as above; $[^2H_3]$methyl-2-t-butyl-1,3-dithian (40%), m.p. 33—35° (lit.,[27] 35°), from propane-1,3-dithiol as above; 2-t-butyl-1,3-oxathian (65%), b.p. 78.82° at 20 mmHg (lit.,[26] 75° at 34 mmHg), from 3-mercaptopropan-1-ol as described in ref. 26.

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[23] E. L. Eliel and R. O. Hutchins, *J. Amer. Chem. Soc.*, 1969, **91**, 2703.

[24] K. Bergesen, B. M. Carden, and M. J. Cook, unpublished results; B. M. Carden, M.Sc. Thesis, U.E.A., 1974.

[25] E. J. Salmi and V. Rannikko, *Ber.*, 1939, **B72**, 600.

[26] E. L. Eliel and T. W. Doyle, *J. Org. Chem.*, 1970, **35**, 2716.

[27] M. J. Cook and A. P. Tonge, *J.C.S. Perkin II*, 1974, 767.