protons (which is proportional to the ratio of epimers) was effected by expansion of this area with a sweep width of 100 (two to five scans). Each expansion was integrated five times with the integrator of the instrument, so that 10–25 area values were obtained for each isomer to calculate the epimer ratio. The precision of the values obtained by this operation was estimated to be ±2%.

The ir spectra were recorded with a Perkin-Elmer Model 457 instrument.

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Conformational Analysis. XXII. Conformational Equilibria in 2-Substituted 1,3-Dioxanes[1]

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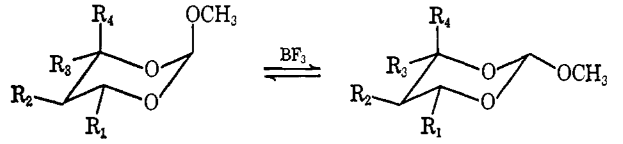
Abstract: Axial–equatorial equilibria in 13 2-substituted 1,3-dioxanes have been studied. The $-\Delta G°$ values (conformational energies) of the groups investigated (in kcal/mol) are: OMe, −0.36 to −0.62; Me, 3.98; Et, 4.04; *i*-Pr, 4.17; Ph, 3.12; *p*-FC_6H_4, 3.13; *p*-BrC_6H_4, 3.18; *p*-$CF_3C_6H_4$, 3.16; OMe/Me (*syn*-axial), 0.05; Me/Me *syn*-axial, ≥ 5.5 kcal/mol. The nmr spectra of all the compounds have been recorded and, in two cases, studied as a function of temperature. The implications of the results are discussed.

In connection with another problem[2] we had occasion to prepare a number of 2-alkoxy- and 2-alkyl-substituted 1,3-dioxanes. We have now investigated the *cis–trans* equilibria (axial–equatorial equilibria of the 2-substituent) in these compounds with the results shown in Tables I and II. The findings appear to be of sufficient interest to deserve documentation and discussion.

Table I. Equilibrium Data for 2-Methoxy-1,3-dioxanes



Compd	R_1	R_2	R_3	R_4	Equilibrium constant[a]	$\Delta G_{25}°$
II[b]	CH_3	H	H	H	0.546 ± 0.009	+0.36 ± 0.010
III	CH_3	H	CH_3	H	0.500 ± 0.014 (0.52[c])	+0.41 ± 0.016
IV	CH_3	H	CH_3	CH_3	1.084 ± 0.036 (1.06[c])	−0.05 ± 0.003
V	H	*t*-Bu	H	H	0.429 ± 0.012 (0.43[c])	+0.50 ± 0.014 (0.60[d])
I	H	H	H	H	0.35 ± 0.1[e]	+0.62 ± 0.15

[a] Solvent diethyl ether at 25°, determined by vpc, values corrected by response ratio. [b] References 3b, 4. [c] Obtained by nmr in CCl_4 solution (20%). [d] Value corrected for conformational heterogeneity. [e] Calculated from dipole moment measurements of the compound in benzene at 25°, μ = 2.24 D, μ_a = 1.953 D, μ_e = 2.910 D. The latter two values are the averages of the dipole moments of *trans*-II, -III and -IV and *cis*-II, -III, and -IV, respectively (ref 2). The error limits in this case are estimates; in all the other entries they are standard deviations.

The configurational assignments of the 2-methoxy-1,3-dioxanes, based on nmr spectra data, dipole moments, and nuclear Overhauser effects, have been discussed earlier.[2] Equilibrations were carried out by means of boron trifluoride etherate in ether;[3] equilibrium constants were determined by gas chromatography of the *cis–trans* mixtures at equilibrium and were checked by integration of distinctive nmr peaks of the components. The results are shown in Table I. Because of the "anomeric effect"[4,5] the axial isomers are generally the more stable.

The $-\Delta G°$ value for the 2-methoxy-*r*-4,*cis*-6-dimethyl-1,3-dioxanes (III),[6] −0.41 kcal/mol, is in agreement with that of −0.36 kcal/mol previously determined[3b,4] in 2-methoxy-4-methyl-1,3-dioxane (II), both diastereoisomers of which are evidently very nearly conformationally homogeneous. The value of −0.50 kcal/mol for 2-methoxy-5-*t*-butyl-1,3-dioxane (V), on the other hand, differs appreciably; moreover, as shown in Scheme I, this compound cannot be considered conformationally homogeneous and a correction must be applied to the value by taking into account that the $-\Delta G°$ value for a *t*-butyl substituent in the 5 position is only 1.4 kcal/mol[3] and thus $\Delta G°$ for the $T_1 \rightleftharpoons T_2$ equilibrium is only about 1.0 kcal/mol so that approximately 16% of the *trans* compound is in the diaxial conformation T_2.[7] The conformational energy of the

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(1) Paper XXI: E. L. Eliel and F. W. Nader, *J. Amer. Chem. Soc.*, **92**, 3045 (1970).

(2) E. L. Eliel and F. W. Nader, *ibid.*, **92**, 584 (1970).

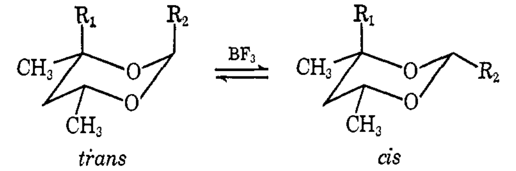
(3) (a) E. L. Eliel and M. C. Knoeber, *ibid.*, **90**, 3444 (1968); (b) M. C. Knoeber, Ph.D. Dissertation, University of Notre Dame, Notre Dame, Ind. 46556, 1967.

(4) E. L. Eliel and C. A. Giza, *J. Org. Chem.*, **33**, 3754 (1968).

(5) (a) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, New York, N. Y., 1965, p 376; (b) R. U. Lemieux in "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, New York, N. Y., 1964, Chapter 12; (c) S. J. Angyal, *Angew. Chem.*, **81**, 172 (1969); *Angew. Chem. Intern. Ed. Engl.*, **8**, 157 (1969).

(6) For use of the Beilstein nomenclature, see ref 2. See, also, IUPAC Information, Bulletin No. 35, June 1969.

Table II. Equilibrium Data of 2-Alkyl- and 2-Aryl-1,3-dioxanes

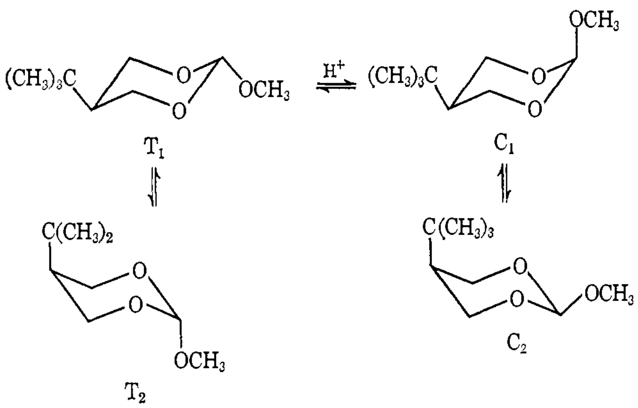


Compd	R_1	R_2	Equil const[a]	$\Delta G_{25}°$, kcal/mol[a]	$\Delta G°$ for alkylcyclohexane, kcal/mol
VI	H	Me	824 ± 90	−3.98 ± 0.09	−1.70
VII	H	Et	913 ± 47	−4.04 ± 0.04	−1.75
VIII	H	*i*-Pr	1,134 ± 93	−4.17 ± 0.05	−2.15
IX	Me	Me	⩾10,000	⩽−5.6	
X	H	Ph	193.2 ± 5.7	−3.12 ± 0.02	−3.0
			190.3 ± 4.6[b]	−3.11 ± 0.02[b]	
XI	H	*p*-FPh	196.4 ± 9.0	−3.13 ± 0.03	
			203.8 ± 5.0[b]	−3.15 ± 0.02[b]	
XII	H	*p*-CF_3Ph	205.8 ± 6.2	−3.16 ± 0.02	
			220.9 ± 5.4[b]	−3.20 ± 0.02[b]	
XIII	H	*p*-BrPh	215 ± 15[b]	−3.18 ± 0.04	

[a] 0.5–0.75 *M* ether solutions at 25°. [b] In THF.

2-methoxy substituent is to be based, of course, on the ratio C_1/T_1 rather than on the stoichiometrically determined ratio C/T (where $C = C_1 + C_2$ and $T = T_1 + T_2$). After applying the appropriate corrections, $-\Delta G°$ for the *cis–trans* equilibrium shown in Figure 1 becomes −0.57 kcal/mol.[8] If one then repeats the calculation with $-\Delta G° = -0.57$ kcal/mol (second iteration), one obtains a second corrected $-\Delta G° = -0.59$ kcal/mol. An infinite iteration value of −0.60 kcal/mol may be estimated from this calculation.

Scheme I



It is thus seen that the conformational energy of the methoxyl group in V is appreciably higher (by 0.19–0.24 kcal/mol) than that in II and III. Moreover, the conformational equilibrium in 2-methoxy-1,3-dioxane itself (I) may be estimated from its dipole moment (μ = 2.24 D) and the dipole moments[2] of *cis*-II, -III and -IV on one hand (2.88–2.92 D) and the corresponding *trans* isomers on the other (1.92–1.97 D) by use of the relationship[9] $\mu^2 = N_e\mu_e^2 + N_a\mu_a^2$; the resulting conformational free energy is 0.62 ± 0.15 kcal/mol. Thus the methoxyl group in I and V is more disposed toward the axial side than that in II and III. We ascribe this to an enhanced steric repulsion affecting axial MeO-2 in II and III by the *syn*-axial hydrogen atoms at positions 4 or 4 and 6 due to the buttressing by the equatorial methyl group or groups at these positions. This effect had been previously seen in the cyclohexane system[10] where *cis*-1,3-disubstituted compounds (e,e) are usually more stable, compared to their *trans* epimers (e,a) than are *trans*-1,4-disubstituted compounds (e,e) compared to their *cis* epimers (e,a). Allinger and coworkers have explained[11] the effect in terms of diminished ease of angular deformation of the tertiary axial hydrogen in the 3-substituted cyclohexane (4-substituted dioxane) compared to the secondary axial hydrogen in a 4-substituted cyclohexane (5-substituted dioxane).

That axial methoxyl in I, II, III, and V is preferred over equatorial is due to the anomeric effect[4,5] which has been discussed numerous times before[5] and has recently been interpreted in terms of repulsions of parallel lobes of unshared electron pairs ("rabbit-ear effect").[12] In compound IV (Table I), however, the isomer with equatorial methoxyl is preferred, although only slightly. This is clearly due to the additional steric encumbrance of the axial methoxyl in *trans*-IV caused by the *syn*-axial methyl group at C-4. Although it is not possible to calculate the magnitude of the anomeric effect in 2-methoxy-1,3-dioxanes from the present data, since the effect is always coupled with an (unknown) steric interaction[13] of the axial methoxyl at

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(7) The point can be seen in the nmr spectrum of *trans*-V: $\nu_{t\text{-Bu}}$ 55.6 Hz, $J_{4,5}$ = 9.5 Hz (a, a) and 4.5 Hz (e, a). In contrast, *cis*-V has $\nu_{t\text{-Bu}}$ 54.1 Hz, $J_{4,5}$ = 10.5 Hz (a, a) and 4.3 Hz (e, a). Typical chemical shifts at 60 MHz (ref 3) for *t*-Bu (5e) are 52.2–55.1, for *t*-Bu (5a) 62.3–63.1 Hz. Using ν_e 54 Hz, ν_a 63 Hz, *trans*-V would appear to exist in conformation T_2 to the extent of 18%. Using 10.6 Hz for $J_{4a,5a}$ (typical values[3] 10.1–12.7 Hz) and 1.5 Hz for $J_{4e,5e}$ (typical values[3] 1.4–2.3 Hz) indicates 12% T_2. These values are close to the 16% calculated.

(8) Using $-\Delta G°_{t\text{-Bu}}$ = 1.4 kcal/mol and $-\Delta G°_{OMe}$ = −0.41 kcal/mol, one obtains (Figure 1) K_c (=C_1/C_2) 21.2 and K_t (=T_1/T_2) 5.32. It follows that $C_1/(C_1 + C_2) = C_1/C$ is 0.942 and $T_1/(T_1 + T_2) = T_1/T$ = 0.842.

(9) *Cf.* ref 5a, p 159.

(10) E. L. Eliel and R. S. Ro, *J. Amer. Chem. Soc.*, **79**, 5992 (1957); E. L. Eliel and T. J. Brett, *ibid.*, **87**, 5039 (1965); E. L. Eliel, S. H. Schroeter, T. J. Brett, F. J. Biros, and J.-C. Richer, *ibid.*, **88**, 3327 (1966).

(11) N. L. Allinger, M. A. Miller, F. A. Van Catledge, and J. A. Hirsch, *J. Amer. Chem. Soc.*, **89**, 4345 (1957).

(12) *Cf.* E. L. Eliel, *Kemisk Tidskr.*, **81** (No. 6/7), 22 (1969), and papers there cited.

(13) In view of the fact that axial substituents at C-2 in 1,3-dioxanes are more crowded than corresponding substituents in cyclohexane (Table II) it is certainly not permissible to use the cyclohexane $-\Delta G°$ value of *ca.* 0.5 kcal/mol[14] for this steric interaction. The calculation of

Table III. Nmr Data of *cis*- and *trans*-2-Alkyl- and 2-Aryl-1,3-dioxanes[a]

Compd	$\nu_{H\text{-}2}$	$J_{H\text{-}2}$[b]	$\nu_{H\text{-}4/6}$	$J_{4a,5a}$	$J_{4a,5e}$	$\nu_{H\text{-}7}$
cis-VI	273	5.2	215	*c*	*c*	72
cis-VII	262	4.8	216	10.0	3.8	*c*
cis-VIII	249	4.8	215	10.8	2.8	100
cis-IX	286	5.5	235	*c*	*c*	69
cis-X	321.5		226	9.6	4.1	
cis-XI	321		227.5	10.0	3.7	
cis-XII	325		229	9.8	3.8	
cis-XIII	321		228.5	10.4	3.4	
trans-VI	310	5.8	237	10.6	3.8	80
trans-VII	290	5.7	235.5	10.2	4.2	*c*
trans-VIII	265.5	8.5	233	10.4	4.1	137
trans-IX	304	4.8	238	7.9	6.8	72.5
trans-X	360		227.5	8.3	5.7[d]	
				7.6[d]	6.5[d]	
trans-XI	372		234	8.2	5.8	
trans-XII	362		226	8.2	5.7	
trans-XIII	358		225	8.1	5.7	

[a] In hertz, at 60 MHz, CCl_4 solution, TMS as internal standard. [b] Coupling constant with alkyl. [c] Not determined. [d] Coupling obtained in CS_2 solution.

C-2, one can, by comparing the equilibrium for IV with that for II, arrive at the conclusion that the MeO/Me-4 *syn*–axial interaction in IV is more severe, by 2.46 kcal/mol than the MeO/H-4 interaction. For, if one considers the equilibrium for IV (top of Table I), one sees that

$$\mathrm{MeO/Me\text{-}4 + MeO/H\text{-}4 + Me\text{-}4/H\text{-}6} = \mathrm{Me\text{-}4\,/H\text{-}2 + Me\text{-}4/H\text{-}6} + A + 0.05 \quad \text{(i)}$$

where the slashed terms refer to *syn*–axial interactions and A is the anomeric effect. Similarly, for II

$$\mathrm{2MeO/H\text{-}4} + 0.41 = A \qquad \text{(ii)}$$

Subtracting (ii) from (i), cancelling and regrouping terms, and setting Me-4/H-2 equal to Me-2/H-4, equal to one-half the value for the conformational energy of Me-2 given in Table II (*i.e.*, 2 kcal/mol) one obtains MeO/Me-4 − MeO/H-4 = 2.46 kcal/mol. Using similar arguments, one may calculate the related value HO/Me − HO/H = 1.76 kcal/mol from data for cyclohexanols in cyclohexane solvent.[14b] (We chose OH/Me for the comparison since MeO/Me in cyclohexane is not known.) As expected, the interaction difference is greater for the 1,3-dioxane with its shorter *syn*–axial distances caused by the shortness of the C–O bonds[15] than for cyclohexane.

Equilibria for 2-alkyl-1,3-dioxanes, previously prepared[2,3] and identified as to their configuration,[2] are shown in Table II. In all cases the equatorial isomers are considerably more stable and the $-\Delta G°$ values are invariably greater than the corresponding values in substituted cyclohexanes,[16] as was to be expected on the basis of the difference in *syn*–axial distance mentioned earlier. The value for methyl represents a refinement over that published earlier[3] (3.55 kcal/mol) and is in better agreement with the calorimetric value[17] of 4.07 kcal/mol. The $-\Delta G°$ values for ethyl and isopropyl are only slightly higher than that for methyl as is to be expected if the axial groups are oriented with the methyl substituents outward and the methylene or methine hydrogens confronting the ring. As in cyclohexane,[18] this arrangement will somewhat affect the conformational entropy but will hardly alter the enthalpy part of $-\Delta G°$. It is of interest (Table III) that in *r*-2-isopropyl-*trans*-4,*trans*-6-dimethyl-1,3-dioxane the "H-inside" arrangement of the isopropyl group can actually be discerned by the unusually high $(CH_3)_2C\mathit{H}C\mathit{H}(O)_2$ coupling constant (8.5 Hz at 40° *vs.* a "normal" value for isopropyl of about 4.4 Hz) and by a marked downfield shift of the isopropyl hydrogen (141.5 Hz). We shall return to this point below.

The 2-aryl-1,3-dioxanes (Table II, X–XIII) present an anomaly. Their $-\Delta G°$ values are appreciably lower than those of the 2-alkyl analogs, contrary to what is seen in substituted cyclohexanes.[19] In fact, the $-\Delta G°$ values for 2-aryl substituents in 1,3-dioxane are barely larger than corresponding values in cyclohexane.

Some light is thrown on the situation by the coupling constants in the 4, 5, 6 region of the dioxane ring (Table III). The coupling constants of both the equatorially and axially 2-alkyl-substituted 1,3-dioxanes (VI–VIII) are in the normal[3] range of 10.1–12.7 for J_{aa} and 2.0–4.3 for J_{ae}. The coupling constants for the equatorially substituted 2-aryldioxanes (*cis*-X–*cis*-XIII) are close to this range also, but the axial epimers (*trans*-X–*trans*-XIII) have anomalously low values for J_{aa} and high values for J_{ae}. These values indicate either that the molecules exist partly in the twist–boat form, or that they are deformed chairs. Since the twist–boat form in 1,3-dioxane is about 5.7 kcal/mol less stable than the chair,[17] it seems unlikely that *trans*-X, -XI, -XII and -XIII would exist to an appreciable extent in that conformation, or else they would be less stable, *vis-á-vis* their epimers, than, in fact, they are. Thus the deformed chair conformation appears much more likely.

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the anomeric effect in 2-alkoxytetrahydropyranes on a corresponding basis, though often effected in the literature, cannot be recommended.[4]

(14) (a) F. R. Jensen, C. H. Bushweller, and B. H. Beck, *J. Amer. Chem. Soc.*, **91**, 344 (1969); (b) E. L. Eliel and E. C. Gilbert, *ibid.*, **91**, 5487 (1969).

(15) Cf. E. L. Eliel, *Accounts Chem. Res.*, **3**, 1 (1970).

(16) J. A. Hirsch in "Topics in Stereochemistry," Vol. 1, N. L. Allinger and E. L. Eliel, Ed., Interscience Publishers, New York, N. Y., 1967.

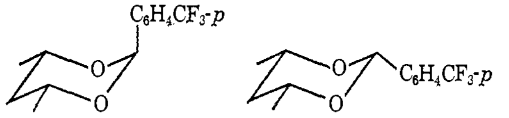
(17) K. Pihlaja and S. Luoma, *Acta Chem. Scand.*, **22**, 2401 (1968).

(18) Reference 5a, pp 61, 457.

(19) Accordingly, in 2-phenyl-2,*r*-4,*cis*-6-trimethyl-1,3-dioxane, the diastereoisomer with axial phenyl, equatorial methyl is preferred over that with equatorial phenyl, axial methyl: J. M. McKenna and W. F. Bailey, unpublished observations.

That *trans*-XII exists as a deformed chair is further supported by dipole moment data. The calculated and experimental dipole moments for *cis*- and *trans*-XII are shown in Scheme II. The experimental value for *cis*-XII agrees with the calculated, but that for *trans*-XII can be made to agree only if the molecule is deformed so that the aryl group bends outward by a considerable angle. Formally good agreement between calculated and experimental dipole moment for *trans*-XII may be attained by assuming an outward bending of the aryl group by 20°. In fact, the deformation is probably more complex, involving also flattening of the ring with a resulting change in both the magnitude and direction of the ring dipole (which is difficult to assess quantitatively).

Scheme II. Dipole Moments



μ_{exptl}	2.71 ± 0.08 D	4.50 ± 0.03 D
μ_{calcd}[a]	1.4 D	4.4 D
μ_{calcd}, aryl bent outward[b]	2.8 D	

[a] Based on the 1,3-dioxane geometry recently determined by A. J. de Kok and C. Romers, *Rec. Trav. Chim.*, in press. [b] Calculated for an outward bending of the aryl group involving a deformation of the O-C-Ar valence angle of 20°, see text.

We are thus faced with a seeming paradox. The axial 2-alkyldioxanes are beset with strong steric repulsions but appear to suffer little deformation. The corresponding 2-aryldioxanes, despite their lesser steric repulsion, seem to undergo relatively severe deformations. We can only speculate as to the cause of this phenomenon but wish to forward the following tentative hypothesis.

When a molecule is afflicted with nonbonded interactions, it will generally become deformed to minimize these interactions. The deformation, in turn, will set up angle and torsional strain and soon an energy minimum will be reached at which the total strain has the lowest possible value. If further deformation were to occur, although nonbonded interaction would diminish further, torsional and angular strain would more than make up for it. Where exactly the point of energy minimization occurs depends, of course, on the shape of the various potential curves. If the change of nonbonded energy with deformations of all possible kinds is small, then deformation cannot proceed very far before the energy minimum is reached. However, when the potential function for nonbonded interaction is steep, extensive deformation may occur on the way to the energy minimum. The two possibilities are shown in Figure 1. The solid lines show the nonbonded interaction only whereas the dashed lines represent total strain. We are assuming that for the alkyl groups, nonbonded interaction changes little with deformation (in the particular case of an axially 2-substituted dioxane probably mainly an outward bending of the substituent) and so the energy minimum is reached very soon, the minimum energy being only little less than the energy of the undeformed molecule. But for the 2-aryl compounds we assume that (perhaps because the nonbonded interaction is with the π cloud of electrons) the potential function changes steeply, and thus deformation proceeds quite far before the energy minimum is reached. Although the undeformed molecules are more strained than the corresponding alkyl compounds, the strain relief due to deformation is so great that after the deformation has occurred, the aryl compounds are actually *less* strained than their alkyl analogs.

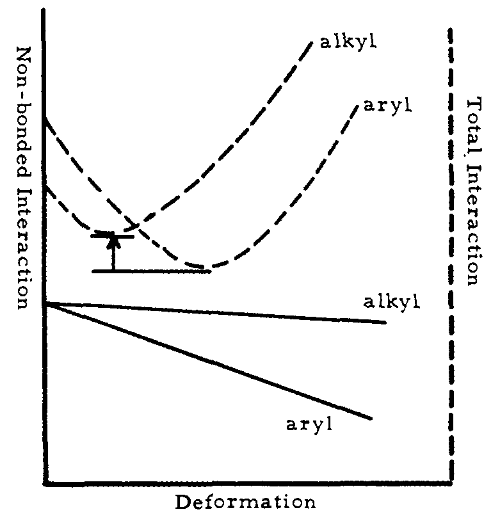
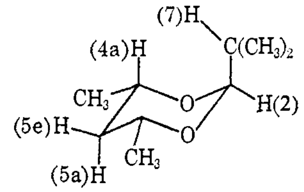


Figure 1.

Unfortunately, we have as yet little information about the exact rotational conformation of either an equatorial or an axial phenyl group at the 2 position in a 1,3-dioxane and we do not know whether the equatorial substituent is perhaps particularly strained so that the small $-\Delta G°$ value may be due to that cause rather than to a particularly stable axial conformation. Pending examination of this point and of the exact structure of axially 2-substituted 1,3-dioxanes by X-ray study (in progress) the present explanation remains quite speculative.

Various coupling constants in the axial 2-isopropyl compound (*trans*-VIII) as well as one of its chemical shifts have been studied as functions of temperature with the results shown in Table IV. The large changes

Table IV. Temperature Dependent Nmr of *trans*-VIII



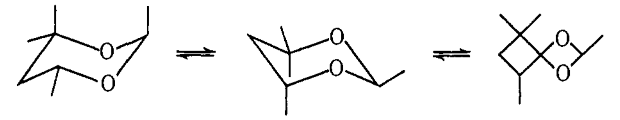
Temp, °C	Solvent	$J_{2,7}$[a]	ν_{H-7}[b]	$\nu_{H-4/6}$[b]	$J_{4a,5a}$[a,c]	$J_{4a,5e}$[a,c]
−72.5	CS_2	10.1	146	230		
−19	CS_2	9.0	141	229.5	10.7	3.9
+39	Nitrobenzene	8.5	141.5	233.5	10.6	4.0
	Pyridine	8.5	141.5	233	10.5	3.9
+80	Pyridine	7.8	136.5	235	10.4	4.2
+130	Pyridine	7.2	130.5	235	10.2	4.4
+150	Nitrobenzene	7.0	126.5	236.5	10.2	4.6
+180	Nitrobenzene	6.7	123.5	236.5	10.0	4.6

[a] In hertz, ±0.1 Hz. [b] In hertz, at 60 MHz, downfield from TMS. [c] First-order analysis.

of $\nu_{H(7)}$ (the isopropyl hydrogen) and $J_{2,7}$ (the coupling constant of the isopropyl with the anomeric hydrogen) with temperature are striking. In contrast, there is little change in $J_{4a,5a}$ and $J_{4a,5e}$, the coupling constants which are usually affected when a chair is deformed or when there is a chair–twist-boat equilibrium. Assuming extreme coupling constants of 10.5 and 4.4 Hz for $J_{2,7}$ one can calculate, from the temperature dependence shown in Table IV, a $\Delta H°$ of 2.2 kcal/mol and ΔS of 5.9 eu, for the process which occurs upon raising the temperature, assuming it is a two-component equilibrium. This result would be compatible with a chair–flexible boat equilibrium with $\Delta H°$ for this form being $4.15 + 2.2 = 6.35$ kcal/mol. However, the lack of change of $J_{4,5}$ speaks against such an interpretation. A chair–stiff boat equilibrium seems to be ruled out by the large $\Delta S°$ value. The most likely interpretation is that one is not dealing just with a two-component equilibrium but with one involving at least three components, a chair with isopropyl axial and methine-H inside, a deformed chair with isopropyl axial and isopropyl-methyl inside, and a boat (flexible or otherwise). The fact that a plot of $\nu_{H(7)}$ *vs.* $J_{2,7}$ does not define a straight line further speaks against a simple two-component equilibrium being involved in these changes.

For 2,4,4,6-tetramethyl-1,3-dioxane (IX, Table II), there is no (in effect no more than 0.01%) detectable *trans* isomer at equilibrium whence $\Delta G° \geqslant 5.5$ kcal/mol. Since the *cis* isomer already has an interaction of 2.8 kcal/mol (axial 4-Me[3]) the interaction in the *trans* must exceed 8.3 kcal/mol.[20] The coupling constant dependence on temperature shown in Table V is appreciable.[21] It appears that at 147° *trans*-IX is almost entirely in the twist-boat form and even at room temperature the apparent chair:twist-boat ratio is about 5:1. The high value of $\Delta G°$ for the *cis*-IX to *trans*-IX conversion suggests considerable residual interaction of the methyl groups remaining in the twist form of IX if Pihlaja's parameters[17] for the 1,3-dioxane skew-boat ($\Delta H° = 7.1$ cal/mol, $\Delta S° \approx 4.5$ eu) are correct. Unfortunately, thermodynamic parameters cannot be reliably calculated from the data in Table V, since once again a three-component equilibrium may be involved (see formulas at top of Table V). In fact it seems surprising that, at low temperature, the chair form with axial groups at C-2 and C-4 apparently predominates over the chair form with axial groups at C-4 and C-6, as far as can be judged from $J_{4,5}$. An alternative and perhaps more liked interpretation of the data in Table V is to assume that the molecule is in the boat form throughout the temperature range, but that the boat is relatively stiff at low temperatures with pseudorotation becoming increasingly important as the temperature is raised.

Table V. Temperature Dependent Nmr of *trans*-IX[a]



T, °C	Solvent	$J_{4,5}{}^{1,b}$	$J_{4.5}{}^{2,b}$
−83.5	CS_2	9.3	5.3
−49	CS_2	8.8	5.8
−17.5	CS_2	8.3	6.3
+39	CS_2	7.8	6.8
+39	Nitrobenzene	8.0	6.7
+80	Nitrobenzene	7.7	6.9
+129	Nitrobenzene	7.4	7.2
+147	Nitrobenzene	7.3	

[a] The chemical shifts were essentially temperature independent. [b] In hertz.

Further work regarding the skew-boat form in 1,3-dioxanes seems to be called for.

Experimental Section

2-Methoxy-1,3-dioxanes. The preparation of 2-methoxy-1,3-dioxanes and their separation is described elsewhere.[2] 2-Methoxy-1,3-dioxane (IV)[3b,4] and 2-methoxy-5-*t*-butyl-1,3-dioxane (V) (overall yield 75%) were obtained in a similar way.

As only small amounts of pure *cis*- and *trans*-V were needed the separation of the epimers was effected by preparative glpc using a Varian-Aerograph Series 1520 preparative gas chromatograph with a 20-ft, 5% FFAP on Chromosorb G column at 145° and a helium flow rate of 86 ml/min.

Anal. Calcd for $C_9H_{18}O_3$: C, 62.07; H, 10.34. Found for *cis*-V (bp 92–93° (20 mm)): C, 62.37; H, 10.28. Found for *trans*-V (bp 100–101° (20 mm)): C, 62.45; H, 10.38.

The preparation of the 2-alkyl- and 2-aryl-1,3-dioxanes VI–XIII is described in a previous paper.[2]

Equilibrations. Each pair of stereoisomers (pure *trans* and pure *cis* compound) was equilibrated in 0.5–1 M solutions (in the case of 2-alkyl-1,3-dioxanes 1.9–2.2 M solutions) in diethyl ether with BF_3, etherate as catalyst in a sealed ampoule. The mole ratio of BF_3 to substrate was *ca.* 1:10. Periodically aliquots were quenched by addition of methanolic sodium methoxide and analyzed by glpc. It was found that equilibrium in all cases studied was established after no more than 1 week at room temperature (2-alkyl and 2-aryl compounds were already equilibrated after 2–3 days).

2-Methoxy-1,3-dioxanes were analyzed on a 30-ft 6% TCEP on Chromosorb G column at 110–125°.

2-Alkyl-1,3-dioxanes were analyzed on a 20-ft 6% TCEP on firebrick column at 110–125° and 2-aryl-1,3-dioxanes on a 10-ft 20% Carbowax 20M on Chromosorb G column at 160–170°. Results are shown in Table VI.

Table VI. Equilibration Results

Compd	Equilibration time, days	Response ratio[a]	Area ratio[b]
II	7	0.959 ± 0.013	0.521 ± 0.04
III	4	0.957 ± 0.013	1.133 ± 0.05
V	10	0.951 ± 0.011[c]	0.451 ± 0.02[c]
VI	4	1.073	768 ± 84
VII	3	1.023	893 ± 47
VIII	3	1.024	1108 ± 93
IX	2	1.010	
X	3	1.120	172.5 ± 5.7 (169.9 ± 4.7)[c]
XI	3	0.953 ± 0.003	206.2 ± 9.0 (214.4 ± 5.0)[c]
XII	3	0.963	214.7 ± 6.2 (229.7 ± 5.4)[c]
XIII	3	*d*	226 ± 15[c]

[a] *trans/cis.* [b] *cis/trans.* [c] Solvent, tetrahydrofuran. [d] Assumed to be 0.95.

Compounds II–V and X–XIII were analyzed with a F & M research chromatograph, Model 810, equipped with a thermal conductivity detector maintained at 300°. For the 2-alkyl com-

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[20] A similar computation has been made by K. Pihlaja, *Acta Chem. Scand.*, 22, 716 (1968).

[21] In contrast, the coupling constants at C-4/C-5/C-6 in 2,2,4,4,6-pentamethyl-1,3-dioxane (extra methyl group at C-2 compared to IX) are relatively temperature insensitive: J. R. Powers, unpublished observations. The extra geminal methyl group seems to hold the molecule in a stiff boat form.

Table VII. Data Obtained in Measurement of Dipole Moments

Compd	R_{20}	R_M	d^{25}	μ, D
IV	131.18 ± 1.53	28.80	1.043 ± 0.002	2.24 ± 0.02
trans-XII	223.25 ± 8.20	72.55	1.094 ± 0.010	2.71 ± 0.08
cis-XII	487.73 ± 4.68	73.69	1.0785 ± 0.005	4.50 ± 0.03

pounds VI–IX an Hp research chromatograph (Hewlett Packard) equipped with flame ionization was used.

Nmr Analysis. Nmr spectra of all compounds were recorded on a Varian Associates A-60A instrument. Samples were 20–25% in CCl_4, shifts are reported in hertz downfield from tetramethylsilane (TMS) at 60 MHz. (The instrument was acquired under NSF equipment Grant GP-6875.) Low- and high-temperature spectra were recorded in a commercially available variable-temperature probe. The temperature was measured by recording the chemical shift of methanol.

Dipole Moments. Measurements were effected in benzene at 25°. Three samples of different concentrations were used. Calculations were carried out as reported previously[2] (Table VII).

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Conformational Analysis in Multisulfur Heterocycles. V. Activation Parameters for the Chair $\rightleftarrows$ Twist Equilibration in Duplodithioacetone by Direct Thermal Stereomutation and Total Nuclear Magnetic Resonance Line Shape Analysis

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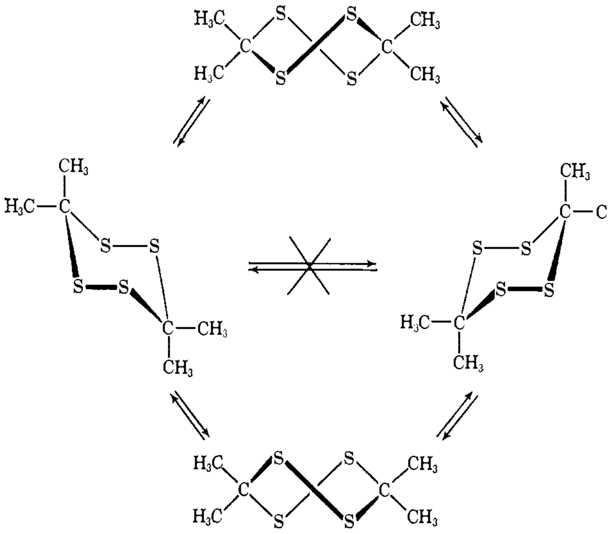
Abstract: Activation parameters for the chair-to-twist process (E_a = 16.5 ± 0.4 kcal/mole, $\Delta H^{\ddagger}$ = 15.9 ± 0.4 kcal/mole, $\Delta S^{\ddagger}$ = +1.2 ± 1.0 eu, $\Delta G^{\ddagger}$ = 15.6 ± 0.1 kcal/mole at 14°) and the twist-to-chair process (E_a = 17.4 ± 0.4 kcal/mole, $\Delta H^{\ddagger}$ = 16.5 ± 0.4 kcal/mole, $\Delta S^{\ddagger}$ = +2.8 ± 1.0 eu, $\Delta G^{\ddagger}$ = 16.0 ± 0.1 kcal/mole at 14°) in tetramethyl-*s*-tetrathiane (duplodithioacetone) have been determined by direct thermal equilibration of the pure twist conformer and by a total nmr line shape analysis at higher temperatures in carbon disulfide as solvent.

In previous reports,[2] we presented convincing evidence for a significantly lowered chair/twist energy difference in duplodithioacetone (tetramethyl-*s*-tetrathiane). Indeed, the twist is more stable than the chair. Although the twist form of cyclohexane is postulated as a discreet intermediate in the chair ⇆ chair equilibration,[3] the twist conformer of cyclohexane is too unstable to be detected by available spectroscopic techniques.

This report concerns the measurement of activation parameters for the chair ⇄ twist equilibration in duplodithioacetone (eq 1) using both the direct thermal stereomutation of the pure twist conformer[2b] at low temperatures and matching of experimental spectra to computer-generated theoretical spectra at higher temperatures. Strong evidence for the validity of total nmr line shape analysis for obtaining kinetic parameters by comparison with the direct equilibration technique is presented.



(1)

Results and Discussion

The previously reported temperature dependence of the nmr spectrum (60 MHz) of duplodithioacetone[2]

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(1) National Science Foundation Undergraduate Research Participant, Summer 1969.

(2) (a) C. H. Bushweller, *J. Am. Chem. Soc.*, **89**, 5978 (1967); (b) C. H. Bushweller, *ibid.*, **90**, 2450 (1968); (c) C. H. Bushweller, *ibid.*, **91**, 6019 (1969).

(3) F. A. L. Anet and A. J. R. Bourn, *ibid.*, **89**, 760 (1967); F. R. Jensen, D. S. Noyce, C. H. Sederholm, and A. J. Berlin, *ibid.*, **84**, 386 (1962). However, it should be noted that twist forms of *cis*-2,5-dialkyl-1,3-dithianes may be spectroscopically accessible, *e.g.*, see E. L. Eliel and R. O. Hutchins, *ibid.*, **91**, 2703 (1969). See also G. Binsch in "Topics in Stereochemistry," Vol. 3, N. L. Allinger and E. L. Eliel, Ed., Interscience Publishers, New York, N. Y., 1968.