Calorimetric Determination of the Conformational Enthalpy and Entropy of 2-Phenyl-1,3-dioxane. Effectively Free Rotation of an Equatorial 2-Phenyl Group. Conformational Equilibria in 2,2-Disubstituted 1,3-Dioxanes[1]

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Abstract: Calorimetric measurement of the heat of acid-catalyzed isomerization of axial 2-phenyl-*c*-4,*c*-6-dimethyl-1,3-dioxane (**1**) to its equatorial epimer (**2**) indicates that the conformational free energy of a phenyl group at C(2) in 1,3-dioxane ($G^\circ = -3.12 \pm 0.02$ kcal/mol) is the result of an even smaller conformational enthalpy ($\Delta H^\circ = -2.0 \pm 0.2$ kcal/mol) favoring equatorial phenyl and an unusually large conformational entropy ($\Delta S^\circ = +3.9 \pm 0.8$ eu) also favoring the equatorial isomer. Analysis of the rotameric conformations of axial and equatorial 2-phenyl-1,3-dioxanes reveals that the large ΔS° is the result of a substantial difference in the freedom of internal rotation about the C(2) to phenyl bond for each isomer: the equatorial phenyl is an effectively free rotor whereas the axial phenyl librates about an average perpendicular orientation. The low ΔH° is discussed in terms of the steric requirements of a phenyl substituent and the possible operation of an anomeric effect. The ΔG° value for 2-methyl-2-phenyl-1,3-dioxane has been determined and the large preference for axial phenyl, equatorial methyl ($\Delta G^\circ = +2.55 \pm 0.02$ kcal/mol) is understood in terms of the ΔH° and ΔS° of a 2-phenyl substituent. The ΔG° values for 2-alkyl-2-methyl-1,3-dioxanes have also been determined and are discussed.

The conformational free energies (ΔG°) for a number of 2-substituted 1,3-dioxanes have been determined by direct, acid-catalyzed equilibration of anancomeric isomers of the type shown in Scheme I.[3-6] These ΔG° values indicate that, in general, the preference of a substituent for the equatorial position at C(2) in a 1,3-dioxane is much greater than the corresponding preference in the analogous cyclohexane.[7] This finding, which is a manifestation of the short syn-axial C(2) to C(4) or C(6) distance in 1,3-dioxane,[8,9] has been discussed in terms of the geometry of the 1,3-dioxane ring.[10] An exception to this general trend has been noted for polar substituents which, because of the operation of a substantial anomeric effect, prefer to adopt the axial position at C(2) in a 1,3-dioxane.[5] In view of these results, the conformational free energies of the 2-aryl-1,3-dioxanes appear to be anomalous.[4] Thus, the conformational free energy of a 2-phenyl substituent, which was determined[4] by direct equilibration of the epimeric 2-phenyl compounds **1** and **2** (Scheme I, R = C_6H_5; A and B, respectively), is appreciably lower than that of 2-alkyl-1,3-dioxanes.[4] In fact, the ΔG° value for the 2-phenyl group[11] (-3.12 ± 0.02 kcal/mol)[4] is only slightly larger than the corresponding value for phenylcyclohexane (-3.0 kcal/mol).[7] In reporting these results, Nader and Eliel noted[4] that their explanation would necessarily remain quite speculative until more information became available about the rotameric conformations of axial and equatorial phenyl rings at the 2 position of a 1,3-dioxane. As we shall show in the sequel, the conformational free energy of a phenyl group at C(2) in 1,3-dioxane is the result of an even smaller conformational enthalpy (ΔH°) of -2.0 ± 0.2 kcal/mol favoring equatorial phenyl combined with an unusually large conformational entropy (ΔS°) of $+3.9 \pm 0.8$ eu also favoring the equatorial isomer. Indeed, the energetic situation in 2-phenyl-1,3-dioxane may be understood in terms of a small enthalpic destabilization of axial phenyl along with an intriguingly large entropic stabilization of the equatorial isomer.

Results and Discussion

In order to gain more insight into the factors affecting the conformational behavior of a 2-phenyl substituent, we have investigated the cis-trans equilibria in 2-alkyl- and 2-phenyl-2,*c*-4,*c*-6-trimethyl-1,3-dioxanes shown in Scheme II. The conformational free energies determined for these compounds are contained in Table I. Also included in the table are values deduced from the known ΔG°s of 2-monosubstituted 1,3-dioxanes[4] by assuming additivity of conformational energies. The substantial discrepancy between the experimental and additivity values is to be expected because of the additional gauche interactions present in the *gem*-disubstituted compounds.[12] The table also includes ΔG° values which were calculated taking into account the rotameric differences between monosubstituted and geminally disubstituted compounds, computing the populations of all rotamers and then evaluating the conformational enthalpy and entropy of mixing for each diastereoisomer. Analogous calculations are described in detail by Eliel and Enanoza[12] and Hutchinson et al.[13] As can be seen, this semiempirical method[14] gives reasonably good estimates of the actual free energy values for 2-ethyl-2-methyl (Table I, entry 1) and 2-isopropyl-2-methyl (Table I, entry 2). Since we have been unable to prepare the 2-*tert*-butyl-2-methyl isomer, **7,** with an axial *tert*-butyl group (cf. Experimental Section), the ΔG° value for 2-*tert*-butyl-2-methyl (cf. Table I, entry 3) represents a minimum.[15] For the most part, these results for the 2-alkyl-2-methyl equilibria compare favorably with analogous data in similar systems,[16-20] although there is some disagreement in the literature as to which isomer predominates. For the sake of continuity, this point will be discussed in the section on configurational assignments (vide infra).

In contrast to the 2-alkyl-2-methyl equilibria, which are readily understood in terms of well-known conformational principles, the 2-methyl-2-phenyl result (Table I, entry 4) is

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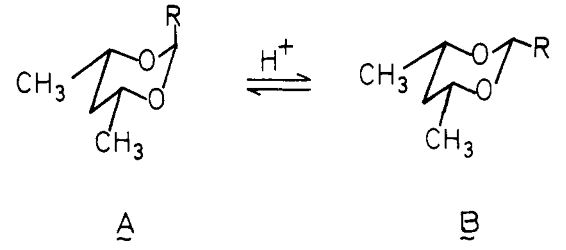
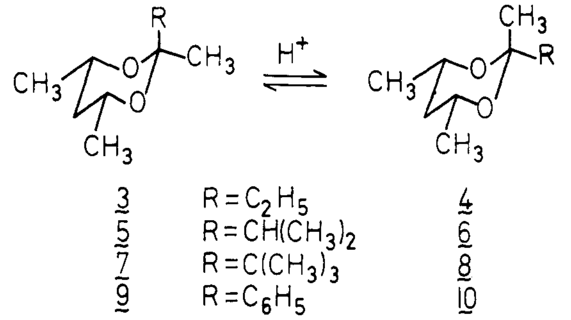
Scheme I



Scheme II



not amenable to such straightforward analysis. The measured $\Delta G°$ value, which favors the axial phenyl isomer, **9**, by 2.55 kcal/mol, is very much larger than the 0.87 kcal/mol value computed from the conformational free energies of a 2-methyl and a 2-phenyl substituent.[4] This situation is reminiscent of that in 1-methyl-1-phenylcyclohexane, where the phenyl group occupies the axial position even though its $\Delta G°$ value (−3.0 kcal/mol)[7] is significantly larger than that of methyl (−1.7 kcal/mol).[7] In view of this seeming analogy, the explanation of the 2-methyl-2-phenyl problem would appear to lie in arguments similar to those presented by Allinger and Tribble[21] in their analysis of the conformational behavior of phenylcyclohexane and 1-methyl-1-phenylcyclohexane.

In an elegant application of the molecular-mechanics method, these authors showed that the (equatorial) phenyl group of phenylcyclohexane preferentially adopts a conformation in which the aromatic ring eclipses to C(1) to H bond ("phenyl parallel" conformation)[21] in order to avoid unfavorable steric interaction between the ortho hydrogens of the equatorial phenyl and the equatorial hydrogens at C(2) and C(6) of the cyclohexane chair. In contrast, severe nonbonded interactions with the syn-axial hydrogens in axial phenylcyclohexane render the "phenyl parallel" orientation energetically unfavorable and the substituent is obliged to adopt the "phenyl perpendicular" conformation[21] in which the plane of the aromatic ring is orthogonal to the C(1) to H bond (and flatside-on to the syn-axial hydrogens). Accordingly, the steric interaction in axial phenylcyclohexane is due mainly to compression of the ortho hydrogens of the phenyl ring with the equatorial cyclohexyl hydrogens at C(2) and C(6) and only partly to syn-axial repulsion.[21] Thus, the large magnitude of $\Delta G°$ for the geometrically anisotropic phenyl ring is the result of the absence of the "ortho interaction" in the "parallel conformation" of equatorial phenyl. In 1-methyl-1-phenylcyclohexane, the energy of the "phenyl perpendicular" rotamer of axial phenyl is not affected but the geminal methyl group forces the normally "parallel" equatorial phenyl to be perpendicular to the C(1) to CH_3 bond. The attendant destabilization of equatorial phenyl (due to ortho-hydrogen compression as noted above) leads to the preference of phenyl for the axial position in 1-methyl-1-phenylcyclohexane.[21]

Scheme III

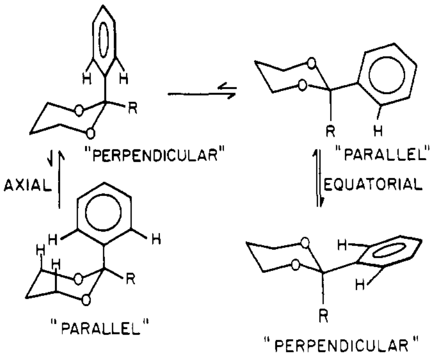


Table I. Equilibrium Data for 2-Alkyl- and 2-Phenyl-2,*c*-4,*c*-6-trimethyl-1,3-dioxanes (Scheme II)

Entry no. (compd)	$\Delta G°_{25}$(exptl),[a] kcal/mol	$\Delta G°$(add),[b] kcal/mol	$\Delta G°$(calcd)[c] kcal/mol
1 (**3**, **4**)	−0.354 ± 0.006	−0.06	−0.39
2 (**5**, **6**)	−0.62 ± 0.01	−0.19	−0.92
3 (**7**, **8**)	⩽−3.0[d]	*e*	
4 (**9**, **10**)	+2.55 ± 0.02	+0.87	*f*

[a] In diethyl ether at 25 °C. The errors are propagated standard deviations from the mean. [b] Computed by assuming additivity of conformational free energies. [c] Calculated from standard rotameric interactions (see text). [d] The axial *tert*-butyl isomer **7** was unavailable and this entry represents an estimate of the maximum value. [e] The $\Delta G°$ for a 2-*tert*-butyl group is unavailable. [f] See text.

In the 2-phenyl-1,3-dioxanes, shown diagrammatically in Scheme III, the CH_2 groups of the cyclohexane chair are replaced by bare oxygen atoms and the destabilizing ortho-hydrogen/equatorial hydrogen interactions of the "phenyl perpendicular" conformations are supplanted by far less severe ortho-hydrogen/oxygen interactions. Under these circumstances, it is tempting to attribute the unusually small conformational free energy for a phenyl substituent at C(2) in a 1,3-dioxane to the absence of significant ortho-hydrogen compression in the perpendicular rotamer of the axial phenyl isomer (Scheme III). It should be noted, however, that the Allinger and Tribble model for phenylcyclohexane[21] accounts only for enthalpic differences between axial and equatorial isomers and an explanation of the 2-phenyl-1,3-dioxane result based on this paradigm assumes that the magnitude of $\Delta G°$ is determined solely by such enthalpic interactions.[22] We shall return to this point below.

For the equatorial isomer of 2-phenyl-1,3-dioxane (Scheme III, R = H), one might expect little, if any, intrinsic rotameric preference since the ortho interactions, which are responsible for the stability of the "phenyl parallel" orientation of equatorial phenylcyclohexane, are absent in this system. In fact, x-ray analysis reveal an almost perpendicular arrangement of the equatorial phenyl ring in 2-*p*-chlorophenyl-1,3-dioxane[8] and, in contrast, an almost parallel orientation in both *r*-2-(*p*-bromophenyl)-*c*-4,*c*-6-dimethyl-1,3-dioxane[9] and *r*-2-phenyl-*c*-5-hydroxy-5-isopropyl-1,3-dioxane.[23] These results suggest that the conformation of an equatorial phenyl group at C(2) in 1,3-dioxane is determined primarily by packing forces in the solid state.[9] In the absence of a significant preference for the parallel conformation in equatorial 2-phenyl-1,3-dioxane, the Allinger and Tribble paradigm cannot, per se, account for the vastly greater than calculated proportion of axial phenyl isomer present at equilibrium in 2-methyl-2-phenyl-1,3-dioxane (Scheme III, R = CH_3). Clearly, any viable explanation for the conformational behavior of 2-phenyl-1,3-dioxane must also account for the factors responsible for the exhanced axial preference of phenyl when juxtaposed with methyl (Table I, entry 4). In an attempt to resolve this problem, we investigated the conformations of axial and equatorial 2-phenyl-1,3-dioxanes in solution.

Table II. Heat of Isomerization of *r*-2-Phenyl-*t*-4,*t*-6-dimethyl-1,3-dioxane (Solid) to *r*-2-Phenyl-*c*-4,*c*-6-dimethyl-1,3-dioxane (Soln)

Run no.	E, calib[a]	ΔR,[b] ohms	R_m,[c] ohms	Q,[d] cal	Wt, mg	Mol $\times 10^{-3}$	ΔH, kcal/mol
1	330.33	−12.855	1692.83	−2.5084	181.23	0.9427	2.661
2	329.23	−14.013	1693.58	−2.7242	216.16	1.1244	2.423
3	324.38	−14.057	1694.05	−2.6917	193.25	1.0052	2.678
4	331.19	−14.292	1693.76	−2.7945	192.46	1.0063	2.777

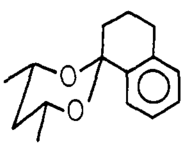
[a] Calibration constant of calorimeter with filled cell. [b] Corrected change in resistance for the isomerization. [c] Mean value of the resistance for the isomerization. [d] Heat change due to the isomerization.

Table III. Heat of Solution of *r*-2-Phenyl-*t*-4,*t*-6-dimethyl-1,3-dioxane (**1**)

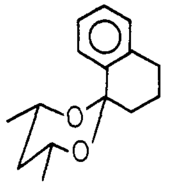
Run no.	E, calib[a]	ΔR,[b] ohms	R_m,[c] ohms	Q,[d] cal	Wt, mg	Mol $\times 10^{-3}$	ΔH, kcal/mol
1	339.00	−22.807	1713.64	−4.5119	194.87	1.0136	4.451
2	324.52	−25.119	1715.83	−4.7508	208.09	1.0824	4.389
3	332.32	−25.841	1716.33	−5.0034	207.47	1.0792	4.636
4	326.77	−23.645	1714.84	−4.5056	190.25	0.9896	4.553

[a] Calibration constant for calorimeter with filled cell. [b] Corrected change in resistance for the process. [c] Mean value of the resistance for the process. [d] Heat change upon dissolution.

The a priori unlikely parallel conformation of axial 2-phenyl-1,3-dioxane was conclusively eliminated on the following experimental grounds. It was reasoned that if this conformation did indeed contribute to the relative stability of axial 2-phenyl-1,3-dioxane, it should be possible to synthesize a 1,3-dioxane with axial phenyl "locked" into the phenyl parallel conformation by condensation of α-tetralone and *meso*-2,4-pentanediol. The two possible condensation products (A and B) are depicted below. Structure A for the single product (**11**) was established by a nuclear Overhauser study (cf. Experimental Section);[24] structure B with parallel axial phenyl was not formed at all. That axial 2-phenyl-1,3-dioxane exists in a perpendicular conformation (Scheme III) was also demonstrated in the solid state by x-ray analysis of *r*-2-(*p*-trifluoromethylphenyl)-*t*-4,*t*-6-dimethyl-1,3-dioxane.[25] Moreover, the x-ray structure is in excellent agreement with the geometry of this compound in solution as deduced from ^{1}H NMR and dipole moment studies.[4] It is worth noting that the axial phenyl substituent is found to be bent outward appreciably from an undistorted axial position[25] in both the solid state[25] and in solution.[4]



A



B

As noted above, both parallel[9,23] and perpendicular[8] conformations have been observed for equatorial 2-phenyl-1,3-dioxanes in the solid state and spectroscopic evidence is consistent with an absence of preferential orientation of the equatorial 2-phenyl in solution. Thus, the nuclear Overhauser enhancement of H(2) upon irradiation at the phenyl resonance of *r*-2-phenyl-*c*-4,*c*-6-dimethyl-1,3-dioxane (**2**) is small and independent of temperature[26] and the chemical shift of the H(2) proton of **2** in tetrachloroethylene solution is practically invariant over a 105 °C temperature range.[27] These results are in substantial agreement with a recent study of the rotamers of equatorial 2-phenyl-1,3-dioxanes[28] which concludes that the barrier to rotation of the equatorial phenyl is much lower than the corresponding barrier in the cyclohexane system.[21] We differ, however, with the conclusions drawn from Kerr constant data[29] which allege a predominance of the parallel conformer of the equatorial 2-phenyl group.[29]

The results of these investigations of phenyl rotamer preference suggest, albeit circuitously, that there is a substantial difference in rotational freedom between the axial and equatorial 2-phenyl isomers: the axial phenyl group oscillates (librates) about an average perpendicular conformation with a sizable barrier to rotation whereas the equatorial phenyl shows little preference for a particular conformation. This difference in rotational freedom implies a nontrivial entropy contribution to the conformational free energy in 2-phenyl-1,3-dioxane. Unfortunately, with so biased an equilibrium ($\Delta G° = -3.12$ kcal/mol),[4] the conformational entropy ($\Delta S°$) and enthalpy ($\Delta H°$) cannot be determined by study of the temperature dependence of $\Delta G°$. These arguments prompted us to consider direct determination of the conformational enthalpy (and hence $\Delta S°$) for 2-phenyl-1,3-dioxane by calorimetric measurement[30] of the heat of isomerization of **1** to **2** (Scheme I, R = C_6H_5).

Calorimetric Results and Discussion

The heat of isomerization of *r*-2-phenyl-*t*-4,*t*-6-dimethyl-1,3-dioxane (**1**) to *r*-2-phenyl-*c*-4,*c*-6-dimethyl-1,3-dioxane (**2**) was determined by measuring ΔH for the boron trifluoride etherate catalyzed equilibration of solid (s) **1** to **2** in 1,4-dioxane solution (soln) at 25 °C. The data are listed in Table II and give a mean value[31] of $+2.64 \pm 0.21$ kcal/mol for the isomerization. In order to have a value for the conversion of **1** in solution to **2** in solution, which is the process for which $\Delta G°$ was evaluated,[4] it was also necessary to measure the heat of solution (ΔH_{soln}) of **1** in 1,4-dioxane solvent. Dissolution of solid **1** (Table III) is a highly endothermic process with $\Delta H_{\mathrm{soln}} = +4.51 \pm 0.10$ kcal/mol. For comparison, the heat of solution of **2**, which is a liquid at 25 °C, was also measured (Table IV) and gave a value of $+0.533 \pm 0.002$ kcal/mol.

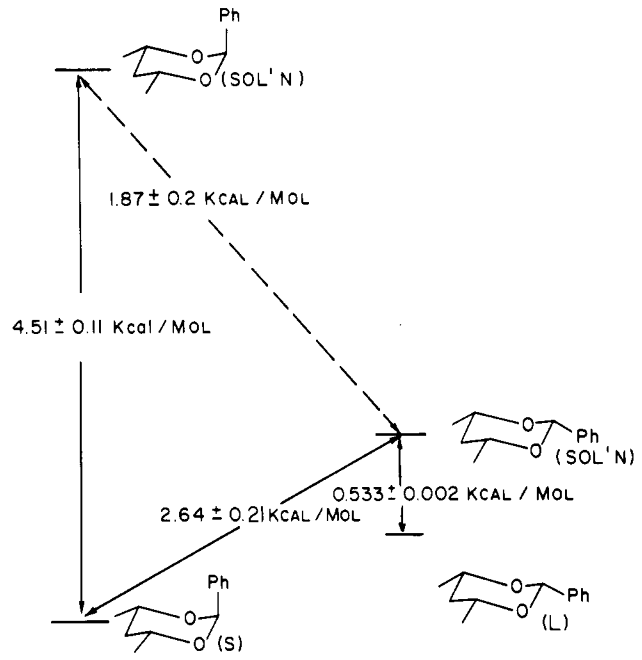
The large discrepancy between the ΔH_{soln} values for the two diastereoisomers was cause for initial concern since an accurate value for ΔH_{soln} of **1** is critical to evaluation of $\Delta H°$. A measurement of the heat of fusion (ΔH_{fus}) of **1** by differential scanning calorimetry gave a value of $+3.94 \pm 0.01$ kcal/mol and indicated that the highly endothermic ΔH_{soln} of **1** is the consequence of a large ΔH_{fus} for this compound.[32] Thus, the *hypothetical* ΔH_{soln} for liquid **1** at 25 °C is $4.51 - 3.94 = 0.57$ kcal/mol, in excellent agreement with the experimental value for the liquid epimer **2**.

Table IV. Heat of Solution of *r*-2-Phenyl-*c*-4,*c*-6-dimethyl-1,3-dioxane (**2**)

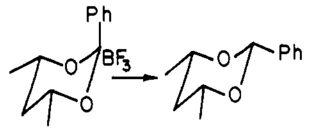
Run no.	E, calib[a]	ΔR,[b] ohms	R_m,[c] ohms	Q[d] cal	Wt, mg	Mol × 10^{-3}	ΔH, kcal/mol
1	318.50	−3.459	1697.90	−0.6488	232.59	1.2098	0.536
2	328.23	−2.693	1697.27	−0.5207	188.31	0.9795	0.532
3	310.81	−2.784	1697.33	−0.5099	184.35	0.9589	0.532

[a,b,c,d] See footnotes for Table III.

Scheme IV



Scheme V



ΔH (ISOMERIZATION) = −1.87 ± 0.2 KCAL / MOL

ISOMERIZATION PROCEEDS TO 95% COMPLETION

$\Delta H° = -2.0 \pm 0.2$ KCAL / MOL

$\Delta S° = \frac{\Delta H° - \Delta G°}{T} = +3.9 \pm 0.8$ EU

$\Delta G° = -3.12 \pm 0.02$ KCAL / MOL

The thermochemical data (Tables II–IV) are presented diagrammatically in Scheme IV from which it is seen that the enthalpy change, over the period monitored in the experiment, for the isomerization of **1** in solution to **2** in solution is −1.87 ± 0.2 kcal/mol. This value, which corresponds to conversion of pure **1** to a mixture composed of 94.9% **2** and 5.1% **1** over a 1-h time period (cf. Experimental Section), represents an incomplete isomerization. Correction of the enthalpy change to reflect complete conversion of **1** to an equilibrium mixture of **1** and **2** is straightforward since the amounts of **1** and **2** present at equilibrium are known from previous studies[4] in ether solvents (diethyl ether and tetrahydrofuran)[4] to be less than 1% **1** and more than 99% **2**. Hence, $\Delta H° = 99.5/94.9$ $(-1.87 \pm 0.2$ kcal/mol$) = -2.0 \pm 0.2$ kcal/mol.

Comparison of this low conformational enthalpy with the known $\Delta G°$ value for a 2-phenyl substituent (−3.12 ± 0.02 kcal/mol)[4] reveals a remarkably large entropic stabilization of the equatorial phenyl group relative to its axial counterpart. As shown[31] in Scheme V, $\Delta S° = +3.86 \pm 0.8$ eu.

The low $\Delta H°$ value for a 2-phenyl substituent is understandable in terms of the small steric interactions present in the perpendicular conformation of an axial 2-phenyl group (Scheme III). As noted above, compression of the ortho hydrogens of the axial 2-phenyl is minimal in this system in contrast to the situation in axial phenylcyclohexane.[21] Moreover, the axial 2-phenyl moiety bends outward to allevaite residual interaction between the ring and the syn-axial hydrogens at C(4) and C(6) until the energy of the total molecule is minimized[4] as evidenced by the solid state[25] and solution[4] studies alluded to earlier. In addition to these steric factors, there is some evidence[25] that the generalized anomeric effect[5] may contribute to the stability of an axial 2-phenyl substituent. In particular, bond lengthening associated with the anomeric effect has been invoked[25] to explain the fact that the C(2) to aryl bond length of 1.532 Å in *r*-2-(*p*-trifluoromethylphenyl)-*t*-4,*t*-6-dimethyl-1,3-dioxane[24] is 0.02–0.03 Å longer than the analogous bond in equatorial 2-phenyl-1,3-dioxanes.[8,9] Alternatively, the longer C(2) to aryl bond in the axial compound may be due to steric requirements of the substituent. Detailed analyses of the available structural data for axial 2-phenyl-1,3-dioxanes[1,4,8,9,25] have been given elsewhere[1,25] and the relation of such data to energy minimization in this system has been discussed.[1,25]

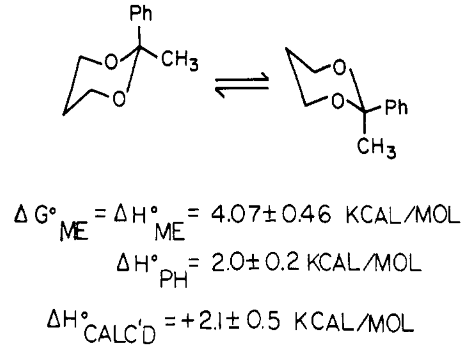
The large $\Delta S°$ term for the 2-phenyl-1,3-dioxane equilibrium is clearly the result of differences in rotation entropy between the two isomers. Since accurate atomic coordinates are available from x-ray analyses of 1,3-dioxanes having equatorial[1,8,9,23] and axial[1,25] 2-phenyl substituents, rotational entropy differences may be calculated[33,34] from the appropriate partition functions (Q). The contribution to $\Delta S°$ arising from the difference between the overall rotational entropies of the axial and equatorial isomers is negligibly small (+0.3 eu favoring the equatorial isomer).[35] Thus, $\Delta S°$ is a direct consequence of a substantial difference between the freedom of internal rotation about the C(2) to phenyl bond for each of the isomers.

To evaluate the partition functions describing entropy due to internal rotational differences, it is necessary to invoke models to represent such processes. For equatorial 2-phenyl-1,3-dioxane the simplest viable model consistent with the experimental data is that for "free" rotation which assumes a barrier to rotation much smaller than kT.[33,34] While we realize that rotation about the C(2) to phenyl bond in equatorial 2-phenyl-1,3-dioxane cannot be completely free since the V_6 barrier is clearly not symmetric, the barrier height should not be very much larger than the V_6 barrier in toluene (14 cal/mol)[36] and related molecules.[36] Within the framework of the free rotation model, the partition function for (free) internal rotation (Q_{fr}) is given by[33,34]

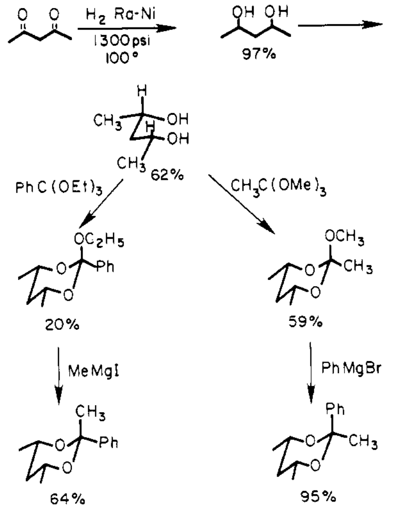
$$Q_{fr} = \frac{2.7935}{n}(10^{38} I_r T)^{1/2}$$

where I_r is the reduced moment of inertia for rotation about the bond in units of g cm^2, n is the internal symmetry number ($n = 2$ for equatorial 2-phenyl-1,3-dioxane), and T is the ab-

Scheme VI



Scheme VII



solute temperature. From the known atomic coordinates of equatorial 2-phenyl-1,3-dioxanes,[8,9] I_r is evaluated as 274.1 × 10^{-40} g cm^2 and the entropy due to internal rotation is calculated to be +8.3 eu.

The axial 2-phenyl isomer, which librates about an average perpendicular orientation (Scheme III), is adequately described by the harmonic oscillator model which assumes a barrier to internal rotation much larger than kT.[34] The entropy of internal rotation then depends on the internal symmetry number ($n = 2$), the reduced moment of inertia, and the height of the barrier to rotation.[33,34] Values of the entropy are tabulated as a function of the barrier[37] and are easily evaluated from the calculated I_r (243.2 × 10^{-40} g cm^2. We note that, if one considers physically reasonable values for the barrier, there are no circumstances for which the entropy due to internal rotation of the axial 2-phenyl group approaches the +8.3 eu value for the equatorial isomer. Within the error limits[31] of the experimental $\Delta S°$ (+3.9 ± 0.8 eu) and after correcting for the +0.3 eu contribution due to differences in overall rotational entropy,[35] the required entropy due to harmonic oscillation of the axial phenyl substituent lies in the range of 4.7 ± 0.8 eu which corresponds to rotational barrier heights in the broad range of 8–40 kcal/mol (barrier ≈ 18 kcal/mol for an entropy contribution of 4.7 eu).

A recent force-field calculation of Allinger and Chung[38] corroborates our conclusion of essentially free rotation about the C(2) to aryl bond in an equatorial 2-phenyl-1,3-dioxane. Their calculation of a zero rotational barrier[38] was interpreted in terms of a fortuitous balance between ortho-hydrogen/ring oxygen repulsion in the perpendicular conformation of an equatorial phenyl and ortho-hydrogen/H(2) repulsion in the parallel rotamer[38,45] (Scheme III).

On the basis of the preceding arguments, the 2-methyl-2-phenyl-1,3-dioxane anomaly is easily resolved. Qualitatively, introduction of a geminal methyl group at C(2) of a 2-phenyl-1,3-dioxane would impede the rotation of an equatorial phenyl ring and result in a loss of its sizable entropic stabilization but the *gem*-CH_3 would have little, if any, effect on the stability of axial phenyl in a perpendicular conformation. Indeed, it is possible to verify this contention by calculation of $\Delta H°$ for the 2-methyl-2-phenyl equilibrium and comparison of this value with the experimental $\Delta G°$ (Table I, entry 4). Since we are, in essence, attributing the anomalous $\Delta G°$ value for this equilibrium to the loss of entropic stabilization of the equatorial phenyl group, we expect the calculated $\Delta H°$ to closely approximate the experimental $\Delta G°$ of +2.55 ± 0.02 kcal/mol. For the purposes of the calculation we use the calorimetrically determined $\Delta H°$ for a 2-methyl group (4.07 ± 0.46 kcal/mol),[39] which is, in any event, identical, within experimental error, with the $\Delta G°$ value.[4] The calculated value shown in Scheme VI is in agreement with the experiment.[40]

Configurational Assignments

Assignment of configuration to the 2-phenyl-*cis*-4,*cis*-6-dimethyl-1,3-dioxanes, **9** and **10**, has been discussed.[41] The configurations of the 2-phenyl- and 2-alkyl-2,*cis*-4,*cis*-6-trimethyl-1,3-dioxanes shown in Scheme II were established by method of synthesis and from ^{1}H NMR spectral data.

The Grignard synthesis involving treatment of 2-methoxy-*r*-2,*c*-4,*c*-6-trimethyl-1,3-dioxane[41] with an appropriate RMgX, has been shown[41] to proceed in a highly stereospecific manner with retention of configuration at C(2) to give 2-R-*r*-2,*c*-4,*c*-6-trimethyl-1,3-dioxanes. In this way the configuration of at least one of each pair of diastereoisomers was established and the configuration of the epimer follows logically. Scheme VII illustrates the stereospecific synthesis[1] of both **9** and **10**.

All assignments are corroborated by ^{1}H NMR spectral evidence (cf. Experimental Section). The chemical shifts of the C(2) substituents are diagnostic of configuration since, in every instance, the protons at C(α) of the alkyl substituent are found at lower field in that diastereoisomer in which the alkyl group is axial.[3-5,41,42] Thus, there is no doubt about which isomer predominates in the equilibria tabulated in Table I.[43]

Experimental Section

Melting points and boiling points are uncorrected. Proton magnetic resonance spectra were recorded on Varian A-60A, Varian XL-100, or Jeol C 60 HL instruments and are referenced with respect to internal Me_4Si. Infrared spectra were recorded on either a Perkin-Elmer 257 or 457 grating infrared spectrometer. Preparative gas-liquid chromatography was effected with Varian Aerograph series 1520 and 2700 chromatographs equipped with 0.25-in. aluminum or stainless steel columns. Microanalyses were performed by either Midwest Microlab, Inc., or Galbraith Laboratories, Inc.

Nuclear Overhauser studies were conducted on a Varian XL-100 spectrometer in dilute carbon tetrachloride solution and the area ratios in these experiments were determined with a Keuffel and Esser Compensating Planimeter, Model 4242.

Quantities of *meso*-2,4-pentanediol were prepared as previously described.[5] The preparations of the diastereoisomeric 2-phenyl-2,*c*-4,*c*-6-trimethyl-1,3-dioxanes (**9** and **10**) have been described elsewhere.[1] The literature procedures were followed in the preparation[41] of the 2-phenyl-*c*-4,*c*-6-dimethyl-1,3-dioxanes (**1** and **2**).

All reported errors in the equilibration and calorimetric studies are propagated standard deviations from the mean (σ).[31]

General Procedure for the Preparation of Substituted 1 3-Dioxanes. This procedure represents a modification of that developed earlier by Eliel and Knoeber.[3] Equimolar amounts of carbonyl compound and *meso*-2,4-pentanediol, benzene (ca. 60 mL for a 0.1-mol run), and a catalytic quantity of *p*-toluenesulfonic acid monohydrate were placed in a round-bottom flask of appropriate size. The flask was fitted with a magnetic stirrer and a Dean-Stark trap connected to a reflux condenser protected with a drying tube. The reaction mixture was refluxed until the theoretical amount of water had collected in the trap. After cooling to room temperature, the mixture was stirred for 45 min with 1 g of anhydrous potassium carbonate to neutralize the catalyst. The mixture was filtered, the solid residue washed well with benzene, and the solvent removed at reduced pressure. The residue was either distilled, sublimed, or purified by preparative GLC to give the desired 1,3-dioxane.

2-Ethyl-*r*-2,*t*-4,*t*-6 (4) and -*r*-2,*c*-4,*c*-6 (3) -trimethyl-1,3-dioxane. Following the general procedure outlined above, 10.82 g (0.15 mol) of 2-butanone and 15.62 g (0.15 mol) of *meso*-2,4-pentanediol were condensed to give 21.62 g (92%) of a mixture of diastereoisomers, bp 145- 157 °C (760 mm). Product analysis by analytical GLC[44] indicated an isomer ratio of 62% (shorter retention time)[44] *r*-2,*t*-4,*t*-6 isomer **4** and 38% *r*-2,*c*-4,*c*-6 isomer **3**. Separation and purification of the diastereoisomers was accomplished on a 20-ft, 20% TCEP on Chromosorb P (45/60 mesh) column at 110 °C. IR spectra: *r*-2,*t*-4,*t*-6 isomer (**4**) (neat) 1370 (m), 1242 (s), 1165 (s), 1111 (s), 1042 (m), 1016 (m), 909 (m), and 850 cm^{-1} (m); *r*-2,*c*-4,*c*-6 isomer (**3**) (neat) 1369 (m), 1292 (m), 1165 (m), 1155 (s), 1111 (s), 1015 (m), 960 (m), 909 (m), and 829 cm^{-1} (m). ^{1}H NMR spectra: *r*-2,*t*-4,*t*-6 isomer (**4**) (CCl_4) δ 0.80-1.67 [overlapping multiplets, 16 H, i.e., 0.885 (t, J = 7.5 Hz, 3 H), 1.10 (d, J = 6.0 Hz; 6 H), 1.32 (s, 3 H), and 1.53 (q, J = 7.5 Hz, 2 H)], ca. 3.9 (m, 2 H); *r*-2,*c*-4,*c*-6 isomer (**3**) (CCl_4) δ 0.74-1.84 [overlapping multiplets, 16 H, i.e., 0.82 (t, J = 7.5 Hz, 3 H) 1.08 (d, J = 6.0 Hz, 6 H), 1.18 (s, 3 H), 1.75 (q, J = 7.5 Hz, 2 H)], ca. 3.80 (m, 2 H).

Anal. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.45. Found: *r*-2,*t*-4,*t*-6 isomer (**4**), C, 68.48; H, 11.45; *r*-2,*c*-4,*c*-6 isomer (**3**), C, 68.47; H, 11.37.

2-Ethyl-*r*-2,*c*-4,*c*-6-trimethyl-1,3-dioxane (3). Ethylmagnesium bromide (0.037 mol) was prepared in 20 mL of anhydrous diethyl ether. Following the general method of Eliel and Nader,[41] 5.80 g (0.034 mol) of 2-methoxy-*r*-2,*c*-4,*c*-6-trimethyl-1,3-dioxane in 10 mL of anhydrous diethyl ether was added dropwise with stirring. After stirring for 1 h[41] the resulting mixture was worked up as described.[41] Distillation of the residue afforded 2.10 g (40%) of **3** in greater than 98% isomeric purity as determined by GLC.[44] All spectral properties of the distillate were identical with those described above for pure **3**.

2-Isopropyl-*r*-2,*t*-4,*t*-6- (6) and -*r*-2,*c*-4,*c*-6- (5) trimethyl-1,3-dioxane. Condensation of 8.60 g (0.10 mol) of 3-methyl-2-butanone and 10.41 g (0.10 mol) of *meso*-2,4-pentanediol gave 12.9 g (75%) of a mixture of diastereoisomers. Analysis by GLC[44] indicated that the product mixture contained 77% (short retention time)[44] *r*-2,*t*-4,*t*-6 compound **6** and 33% *r*-2,*c*-4,*c*-6 isomer **5**. The epimers were separated and purified by preparative GLC on a 20-ft, 20% TCEP on Chromosorb P (45/60 mesh) column at 101 °C. IR spectra: *r*-2,*t*-4,*t*-6 isomer (**6**) (neat) 1379 (s), 1247 (s), 1175 (vs), 1160 (s), 1122 (s), 1080 (s), 1042 (m), 990 (w), 971 (m), 915 (s), 852 (w), and 819 cm^{-1} (s); *r*-2,*c*-4,*c*-6 isomer (**5**) (neat) 1380 (s), 1252 (m), 1179 (vs), 1169 (vs), 1125 (broad, vs), 1088 (m), 1050 (m), 1040 (m), 990 (m), 975 (m), 969 (w), 915 (2), 839 (w), and 832 cm^{-1} (w). ^{1}H NMR spectra: *r*-2,*t*-4,*t*-6 isomer (**6**) (CCl_4) δ 0.8-1.8 [overlapping multiplets, 18 H, i.e, 0.885 (d, J = 6.8 Hz, 6 H), 1.09 (d, J = 6.0 Hz,, 6 H), 1.27 (s, 3 H)], ca. 8.86 (m, 2 H); *r*-2,*c*-4,*c*-6 isomer (**5**) (CCl_4) δ 0.8-1.5 [overlapping multiplets, 17 H, i.e., 0.84 (d, J = 6.8 Hz, 6 H), 1.06 (s, 3 H), 1.07 (d, J 6.0 Hz 6 H)], 2.60 (heptet, J = 6.8 Hz, 1 H), ca. 3.82 (m, 2 H).

Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: *r*-2,*t*-4,*t*-6 isomer (**6**), C, 70.04; H, 11.57; *r*-2,*c*-4, *c*-6 isomer (**5**), C, 70.09; H, 11.52.

2-Isopropyl-*r*-2,*c*-4,*c*-6-trimethyl-1,3-dioxane (5). A solution of 9.00 g (0.056 mol) of 2-methoxy-*r*-2,*c*-4,*c*-6-trimethyl-1,3-dioxane[41] in 16 mL of anhydrous ether was added dropwise to a stirred suspension of isopropylmagnesium bromide (0.062 mol) in 30 mL of anhydrous ether. After workup,[41] the residue was flash distilled to give 2.45 g (23%) of isomerically pure **5**. All spectral properties of the distillate were identical with those reported above for this isomer.

2-*tert*-Butyl-*r*-2,*t*-4,*t*-6-trimethyl-1,3-dioxane (8). Condensation of 10.0 g (0.10 mol) of pinacolone and 10.41 g (0.10 mol) of *meso*-2,4-pentanediol afforded 14.31 g (77%) of product, bp 62-63 °C (77 mm). The product was analyzed by GLC on a variety of columns in hopes of detecting the *r*-2,*c*-4,*c*-6 isomer. The only impurity (less than 2%) in the otherwise homogeneous sample was most likely 2-*tert*-butyl-*r*-2,*t*-4,*c*-6-trimethyl-1,3-dioxane, since the diol precursor was known to contain ca. 2% *dl*-2,4-pentanediol impurity. An analytical sample was prepared by preparative GLC on a 10-ft, 20% FFAP on Chromosorb W (60/80 mesh) column at 100 °C: IR (neat) 1379 (b), 1176 (vs), 1134 (vs), 1109 (s), 1094 (s), 1051 (m), 1018 (m), 988 (m), 980 (s), 959 (s), 917 (s), 855 (m), and 799 cm^{-1} (m); ^{1}H NMR (CCl_4) δ 0.90 (s, 9 H), 1.0-1.5 (m, 2 H), 1.08 (d, J = 6.0 Hz, 6 H), 1.27 (s, 3 H), ca. 8.87 (m, 2 H).

Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 71.30; H, 11.71.

***r*-6-(7,8-Benzo)-*c*-2,*c*-4-dimethyl-1,5-dioxaspiro[5.5]undecane (11).** Condensation of 14.62 g (0.10 mol) of α-tetralone and 10.41 g (0.10 mol) of *meso*-2,4-pentanediol gave 19.72 g (85%) of product, bp 90-95 °C (0.3 mm). The product was contaminated with ca. 5% α-tetralone which was removed from a small aliquot by preparative GLC on a 4-ft, 20% FFAP on Chromosorb A (45/60 mesh) column at 189 °C. The GLC-pure product was induced to crystallize, mp 78-80 °C. The bulk of the product was seeded with a GLC-pure crystal and recrystallized twice from methanol-water to give 54% GLC-pure product, mp 78-79 °C. Three successive sublimations at 0.1 mm produced an analytically pure sample: mp 84-84.5 °C; IR (neat, supercooled, GLC-pure liquid) 1450 (m), 1380 (m), 1348 (m), 1309 (s), 1172 (vs), 1127 (vs), 1114 (vs), 957 (s), and 759 cm^{-1} (s); ^{1}H NMR (CCl_4) δ 0.9-1.4 (m, 2 H), 1.13 (d, J = 6.2 Hz, 6 H), ca. 1.80 (m, 2 H), 2.12 (m, 2 H), 2.73 (t, J = 6.0 Hz, 2 H), ca. 3.96 (m, 2 H), ca. 7.00 (m, 3 H), ca. 7.54 (m, 1 H).

Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found, 77.45; H, 8.72.

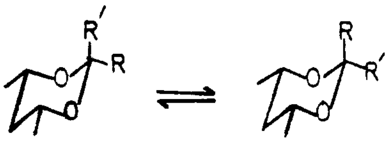
No trace of any isomeric product could be detected by GLC on several different columns in either the crude product, the distilled product, or the mother liquor concentrate from the recrystallizations. The structure of **11** was assigned on the basis of its ^{1}H NMR spectrum and double-resonance experiments.[24] Thus, irradiation of the axial H(2,4) protons (δ 3.96), which caused collapse of the 2,4-CH_3 doublet at δ 1.13 to a singlet and the H(5) multiplet to an AB pattern, resulted in an 11.5 ± 2% enhancement in the signal for the methylene protons attached to C(11) at δ 2.12. There was no enhancement of either the phenyl resonances or the benzylic protons on C(9).

Equilibratons. For each pair of diastereoisomeric 1,3-dioxanes equilibrium was approached from both the cis-rich and trans-rich sides. Solutions of the appropriate dioxane in anhydrous diethyl ether (0.1-0.3 M) were equilibrated over 10-15 beads of Amberlyst-15 (a beaded polystyrenesulfonic acid supplied by Rohm & Haas Co.) in sealed ampules under a nitrogen atmosphere at 25 °C. Periodically, ampules were opened, the ethereal solutions were neutralized by shaking with anhydrous potassium carbonate, and the samples were analyzed by GLC on a Hewlett-Packard chromatograph, Model 5750 B, equipped with a thermal conductivity detector maintained at 250 °C (injector block maintained at 220 °C). Stainless steel columns (i.d. $\frac{1}{16}$ in.) were used and helium inlet pressure was maintained at 50 psi. When the same area ratios were obtained from both the initially cis-rich and trans-rich samples, it was deemed that equilibrium had been attained. Area ratios were taken as the average of 6-10 determinations from each side and the corrected equilibrium constant was calculated from the area ratio of a given system and response ratios for the isomers which were determined at the same time and under the same conditions as the equilibrium mixture analyses. The analytical GLC data and response ratios are collected in Table V. All reported errors (Table I) are propagated standard deviations from the mean.[31]

Calorimetric and Thermochemical Data. The preparation of the compounds employed has been described elsewhere.[41] Samples of *r*-2-phenyl-*c*-4,*c*-6-dimethyl-1,3-dioxane (**2**) were purified by GLC. The *r*-2-phenyl-*t*-4,*t*-6-dimethyl-1,3-dioxane (**1**) was purified by sublimation to give GLC-pure crystals, mp 41-43 °C (lit.[41] mp 41-43 °C). Reagent grade 1,4-dioxane was distilled from lithium aluminum hydride under a nitrogen atmosphere prior to use. The isomerization of **1** to **2** was catalyzed by boron trifluoride etherate. A stock solution of 5 × 10^{-3} M boron trifluoride etherate in dry 1,4-dioxane was prepared for use in the isomerization reactions. Prior to the measurement of a heat of reaction (isomerization), the clean, dry calorimetric cell was filled with the stock solution of $BF_3{\cdot}O(C_2H_5)_2$ in 1,4-dioxane and allowed to stand for 1-2 h to remove any traces of adventitious base. The cell was then emptied and refilled with fresh 5 × 10^{-3} M $BF_3{\cdot}O(C_2H_5)_2$ in 1,4-dioxane solution for the actual calorimetric run.

The calorimetric measurements were carried out uisng an LKB Model 8700 isothermal environment submarine calorimeter. The reaction vessel had a capacity of 25 mL and was fitted with a stirrer, a thermistor as the temperature sensing element, and a heating ele-

Table V. Analytical GLC Data



R	R'	Column[a]	Temp, °C	Retention time, min R axial	 R equatorial	Response ratio
C_2H_5	CH_3	B	108	6	4	0.957 ± 0.029
i-C_3H_7	CH_3	B	121	6	4	0.998 ± 0.021
t-C_4H_9	CH_3	C	100		18	
C_6H_5	CH_3	C	171	9	21	0.922 ± 0.018

[a] The GLC columns are coded as follows: A, 6-ft 5% FFAP on Chromosorb W, 80/100 mesh; B, 20-ft 20% TCEP on Chromosorb, P, 45/60 mesh; C, 10-ft 20% Carbowax 20M on Firebrick, 80/100 mesh.

ment. The solvent, 25 mL, was placed in the reaction vessel and the reactant was sealed in a 1-mL glass ampule.

Resistance measurements were made at approximately 20-s intervals during a 6–7-min foreperiod. The ampule was broken and the resistance was measured during a 60-min reaction period (or a 5-min period for the heats of solution). Finally, the resistance was determined at approximately 20-s intervals during a 6–7-min afterperiod. After the run had been completed, the reaction vessel was cooled to the original temperature, and the above process was repeated except that a known current was passed through the heater for a precisely measured time interval.

The foreperiod data were fit to an equation of the form $R = at^3 + bt^2 + ct + d$, where R is the resistance and t is the time. The root mean square error was 0.003 ohm, which corresponds to about 0.000 03°. The resistance at the end of the foreperiod was calculated from the equation. The afterperiod data were treated similarly giving the temperature at the beginning of the afterperiod. The correction to the resistance difference due to stirring and conduction was obtained by fitting both the fore- and afterperiod data to the equation

$$\mathrm{d}R/\mathrm{d}t = R[c_1(\ln R)^2 + c_2 \ln R + c_3]$$

This equation is equivalent to

$$\mathrm{d}T/\mathrm{d}t = a_1T^2 + a_2T + a_3$$

where T is the temperature. Numerical integration of this equation over the reaction period gave the temperature correction.

The isomerization of **1** to **2** was relatively slow ($t_{1/2} \sim 13$ min) and thus a relatively long reaction period (60 min) was required. In order to estimate the error associated with this long a reaction period, two heat of solution runs were carried out for the same period of time and the results using a long reaction period of 60 min were compared with those obtained using a normal 5-min period. The average deviation in units of $\Delta R/R_\mathrm{m}$ (which is proportional to ΔT) was $\pm 2.26 \times 10^{-4}$, which corresponds to ±0.075 kcal/mol. This uncertainty is included in the reported deviation for the isomerization runs.

The values of ΔR, R_m, and the electrical calibration constant (E) determined in each run were used to compute the heat change per sample weight (Q) for each measurement [$Q = E(\Delta R/R)$]. These values, and the ΔH determined therefrom, are reported in Tables II–IV.

The extent to which the isomerization of **1** and **2** had proceeded in the 60-min reaction period was determined by GLC analysis of the mixture produced. The 1,4-dioxane solution resulting from a 60-min reaction was diluted with diethyl ether and washed with cold, aqueous 10% sodium hydroxide to remove the BF_3 catalyst. GLC analysis[44] of the ethereal solution indicated the presence of 94.9 ± 0.1% **2** and 5.1 ± 0.1% **1**. The extent to which equilibrium has been approached during the calorimetric run may be adduced from the fact that, in diethyl ether at 25 °C, there is 99+% **2** present at equilibrium.[4] Correction of the measured heat of isomerization to account for incomplete equilibration produces no meaningful change in $\Delta H°$ (i.e., the value changes from -1.87 ± 0.20 kcal/mol for 94.9% completion to -1.97 ± 0.21 kcal/mol for 100% completion).

The heat of fusion (ΔH_fus) of **1** was determined by differential scanning calorimetry using a Du Pont Model 990 Thermal Analyzer equipped with a standard cell and a hermetic sample container. Three replicate runs were made between 0 and 60 °C at a programmed heating rate of 5 °C/min. Individual curves were traced, cut out, and weighed to determine areas. Indium of 99.99% purity was used as a standard with a value of 6.79 cal/g for ΔH_fus. Direct comparison of curve weights gave three independent values for ΔH_fus of **1** (20.55, 20.44, and 20.51 cal/g) and a mean value of 3.94 ± 0.01 kcal/mol.

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(15) We note in passing that additivity of conformational free energies might be expected in this instance since both the methyl and *tert*-butyl groups are of C_{3v} symmetry (cf. ref 12). Thus, the conformational energy of a 2-*tert*-butyl group must be in excess of 7 kcal/mol.

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(27) At −25 °C the H(2) proton of **2** resonates at 5.349 ± 0.005 ppm and at 80 °C H(2) resonates at 5.315 ± 0.005 ppm. The 0.034 ± 0.007 ppm difference between these two values is probably not significant since the chemical shift of the 4,6-CH_3 doublet of **2** shows a 0.02 ± 0.01 ppm variation over this same temperature range.

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(35) The contribution to ΔS° from differences in the overall rotational entropy (ΔS°_{OR}) for axial and equatorial 2-phenyl-1,3-dioxane is evaluated from

$$\Delta S^\circ_{OR} = R[\ln Q_{OR}\ (\text{equatorial}) - \ln Q_{OR}\ (\text{axial})]$$

and Q_{OR} is given by (ref 33)

$$Q_{OR} = (0.014837/\sigma)\,(I_x\,I_y\,I_z)^{1/2}T^{3/2}$$

where $I_x\,I_y\,I_z$ are the reduced principal moments of inertia (in units of amu Å^2), T is the absolute temperature, and σ is the external symmetry number (σ = 1 for the isomeric 1,3-dioxanes).

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(43) (a) There is, apparently, a sign error in ref 19 and the isomer having an axial 2-phenyl, equatorial 2-methyl conformation is favored at equilibrium. (b) The report of a predominance of axial 2-isopropyl, equatorial 2-methyl isomer at equilibrium (ref 20) has been withdrawn; H. Lehner, private communication to E. L. Eliel (July 1977).

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Solvent Participation in Reactions. 2. Reactions of the Cystamine Anion Radical

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Abstract: First-order decomposition of the anion radical $RSSR^-$ ($RSSR^- \rightarrow RS\cdot + RS^-$) formed in cystamine solutions was studied by pulse radiolysis. The rate constants and activation energies of this reaction were determined in sucrose, glycerol, and ethanol aqueous solutions. Solvent cage effects seem to be important in more viscous media and determine the rate of separation of products. The reaction rate of electron transfer from the $RSSR^-$ radical to oxygen ($RSSR^- + O_2 \rightarrow RSSR + O_2^-$) was also determined in the same solutions. This reaction is affected by dielectric properties of solutions and enhanced in polar media.

Introduction

The kinetics of electron transfer reactions in aqueous solutions of alcohols is complex owing to ion–solvent interactions.[2a] Very often these solutions undergo structural and dielectric changes which may affect the reaction rates of reacting species.[2b] In this work the effect of composition of aqueous solutions of glycerol, sucrose, and ethanol on reactions of the cystamine anion radical was studied by observing the unimolecular decomposition reaction

$$RSSR^- \rightarrow RS\cdot + RS^- \qquad (1)$$

and electron transfer to an oxygen molecule,

$$RSSR^- + O_2 \rightarrow RSSR + O_2^- \qquad (2)$$

The cystamine anion radical, $RSSR^-$, was formed by pulse radiolysis of cystamine (RSSR) solutions in reactions with solvated electrons.

$$RSSR + e_s^- \rightarrow RSSR^- \qquad (3)$$

Cystamine (2,2′-dithiobisethylamine) dihydrochloride, $Cl^-NH_3^+CH_2CH_2SSCH_2CH_2NH_3^+Cl^-$,[3] is convenient for this study since it reacts very fast with hydrated electrons (k_3 = 4.2 × 10^{10} dm^3 mol^{-1} s^{-1})[4] and the concentration of $RSSR^-$ anion radicals can be measured accurately by pulse radiolysis. The anion radical has high molar absorptivity (λ_{max} 410 nm, a_{410} 9000 dm^3 mol^{-1} cm^{-1})[4,5] and the absorption peak is well separated from those of other radicals formed in cystamine solutions.[6]

Experimental Section

A pulse technique was used to measure the decay rates of the cystamine anion radical at 410 nm. This technique has been described previously.[7] Concentrations of several micromoles of $RSSR^-$ radicals were produced in the samples by irradiation with 20-ns pulses from a Febetron 707 (Field Emission Corp.) electron accelerator. The ab-

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