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A Microcalorimetric Determination of the Chair–Boat Enthalpy Difference in 1,3-Dioxane[1]

R. M. Clay, G. M. Kellie, and F. G. Riddell*

Contribution from the Department of Chemistry, University of Stirling, Stirling, Scotland. *Received February 21, 1973*

Abstract: A microcalorimetric technique for the study of conformational equilibria in 1,3-dioxanes is introduced and applied to two systems. The chair → 1,4-twist enthalpy difference in 1,3-dioxane is found to be 37.3 kJ mol^{-1}.

Direct measurements of heats of reaction offer a most attractive and accurate means for studying conformational equilibria. Modern microcalorimeters are especially well suited for this since they enable extremely accurate measurement of heats of reaction even in quite dilute solutions. If a chemical equilibrium A $\rightleftarrows$ B can be readily established both from pure A and from pure B, then one can measure two heat changes, ΔH_1 and ΔH_2, as A and B, respectively, are converted into the equilibrium mixture.

It follows that

$$\Delta H_{\mathrm{A}\rightarrow\mathrm{B}} = \Delta H_1 - \Delta H_2$$

and the equilibrium constant (K) is given by

$$K = -\Delta H_2/\Delta H_1$$

Thus, all three thermodynamic parameters $\Delta G°$, $\Delta H°$, and $\Delta S°$ associated with the equilibrium may be determined.

It seemed to us that the 1,3-dioxane series, in which equilibria are readily established by Lewis acids,[2] would be especially amenable to study by this technique. One particular advantage offered by microcalorimetry is that it enables heat changes to be measured for the interconversion of the least stable isomer to the more stable isomer in cases where the equilibria are so one-sided as to prohibit accurate equilibrium studies. We, therefore, hoped that direct heat measurements for a twist → chair change would settle the question of the chair–boat energy difference in 1,3-dioxane for which values ranging from 9.2 to 35.5 kJ mol^{-1} have been proposed (Table I).

Table I. Proposed Values of ΔH_{CT} for 1,3-Dioxane

ΔH_{CT}, kJ mol^{-1}	Proposed by	Date	Ref
9.2	Eliel, Allinger, Angyal, and Morrison	1965	*a*
>12.5	Anderson, Riddell, and Robinson	1967	*b*
>12.5	Riddell and Robinson	1967	3
25.9	Anteunis and Swaelens	1970	*c*
25.9	Eccleston and Wyn-Jones	1971	*d*
28.5	Pihlaja	1968	*e*
30.1	Pihlaja and Luoma	1968	*f*
30.1	Eliel	1971	*g*
33.4	Eliel and Nader	1970	*h*
35.5	Pihlaja and Jalonen	1971	*i*

[a] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1965. [b] J. E. Anderson, F. G. Riddell, and M. J. T. Robinson, *Tetrahedron Lett.*, 2017 (1967). [c] M. Anteunis and G. Swaelens, *Org. Magn. Resonance*, **2**, 389 (1970). [d] G. Eccleston and E. Wyn-Jones, *J. Chem. Soc. B*, 2469 (1971). [e] K. Pihlaja, *Acta Chem. Scand.*, **22**, 716 (1968). [f] K. Pihlaja and S. Luoma, *Acta Chem. Scand.*, 2410 (1968). [g] E. L. Eliel, *Pure Appl. Chem.*, **25**, 509 (1971). [h] F. W. Nader and E. L. Eliel, *J. Amer. Chem. Soc.*, **92**, 3050 (1970). [i] K. Pihlaja and J. Jalonen, *Org. Mass. Spectrom.*, **5**, 1361 (1961).

Experimental Section

The compounds employed were all prepared by accepted literature methods[3,4] and were purified prior to use through a 2-ft spinning band distillation unit. The purity of each compound was monitored by glc and nmr techniques and in all cases was >99%. All compounds had physical and spectroscopic properties in agreement with the literature.

An L. K. B. batch microcalorimeter with gold cells was used for the determination of thermochemical data. A Phillips chart recorder equipped with a Disc integrator enabled measurement of the peak areas with a maximum error of ±1%. In the case of 2,5-dimethyl-1,3-dioxanes, a 0.15 M solution of the 1,3-dioxane in 1,4-dioxane and a 0.12 M solution of $\mathrm{BF_3}$ in 1,4-dioxane were used. For *trans*-2,4,4,6-tetramethyl-1,3-dioxane a 0.01 M solution and a 0.02 M solution of $\mathrm{BF_3}$ in 1,4-dioxane were used.

Determinations (≤ 8) were carried out for each compound. For each determination *ca.* 1 ml of the 1,3-dioxane solution and a similar quantity of the $\mathrm{BF_3}$ solution were weighed into the microcalorimeter. On completion of each experiment, the cell was washed once with a 10% solution of pyridine in chloroform, twice with dry chloroform, and finally twice with dry ether. (Compressed air was then blown through the cell to remove residual traces of solvents.) If this sequence was not employed, in particular if the cells were not washed with a basic solvent, reproducibility of results was extremely poor. All microcalorimetric work was performed at 298°K. Small corrections for the heat of dilution of each isomer were determined and applied to each measurement.

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(1) Presented in part at the 27th Annual Calorimetry Conference (U. S. A.), Park City, Utah, July 1972.

(2) See, for example, E. L. Eliel, *Accounts Chem. Res.*, 3, 1 (1970).

(3) F. G. Riddell and M. J. T. Robinson, *Tetrahedron*, **23**, 3417 (1967).

(4) E. L. Eliel, *Pure Appl. Chem.*, **25**, 509 (1971).

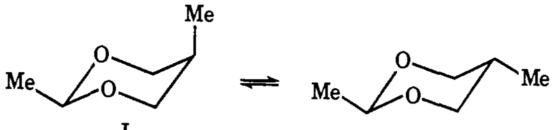
Results[5]

For 2,5-dimethyl-1,3-dioxane, ΔH_1 (cis → equilibrium mixture) = -3.20 ± 0.01 kJ mol^{-1} and ΔH_2 (trans → equilibrium mixture) = $+0.626 \pm 0.002$ kJ mol^{-1}. Therefore, $K_{298} = 5.11 \pm 0.02$; $\Delta H_{298} = 3.83 \pm 0.02$ kJ mol^{-1}; $\Delta G_{298} = -4.04 \pm 0.02$ kJ mol^{-1}; $\Delta S_{298} = +0.684 \pm 0.003$ J mol°K^{-1}.

For *trans*-2,4,4,6-tetramethyl-1,3-dioxane, ΔH_2 (trans → equilibrium mixture) = 24.37 ± 0.03 kJ mol^{-1} and ΔH_1 (cis → equilibrium mixture) was not measured (<0.1 kJ mol^{-1}). Therefore, $\Delta H_{298} = -24.37 \pm 0.03$ kJ mol^{-1}.

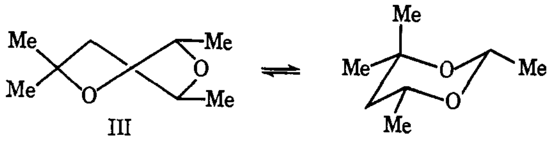
Discussion

Before attempting to estimate the enthalpy change for the twist → chair conversion in 1,3-dioxane, we first chose to examine the well-documented equilibrium between the *cis*- and *trans*-2,5-dimethyl-1,3-dioxanes (I → II).[3,6] We did this in order to standardize our techniques on a well-known system, to check the accuracy of the microcalorimetric method, and to provide additional verification of previous results. The agreement with the results published by Eliel[6] ($K = 5.11 \pm 0.04$) is most satisfactory, and verified our faith in the microcalorimetric technique.



I

II



III

IV

In our next measurement we chose to examine the diastereoisomeric 2,4,4,6-tetramethyl-1,3-dioxanes (III and IV). The trans isomer is known to exist in an anancomeric twist conformation III[7,8] while the cis isomer has a chair conformation.[2] We regard this system therefore as a reliable model for a twist → chair change in 1,3-dioxane.

Eliel attempted to measure ΔG for this system by an equilibration technique and glc analysis.[9] However, due to the extremely low amount of trans isomer at equilibrium, he was only able to estimate that ΔG was greater than 23 kJ mol^{-1} ($K > 1 \times 10^4$).[10] Because of this large free energy difference, it was only possible to measure the enthalpy of the reaction III → (III + IV), which corresponds within experimental errors to that of III → IV.

The measured heat change (-24.4 kJ mol^{-1}) corresponds to the strain released when the single 1,4-twist conformation[8] III converts to the single chair conformation IV. Strain in IV, due to an axial 4-methyl group, has been measured[11] as 12.9 kJ mol^{-1}. (While this figure is a ΔG value, ΔH should be very similar.) The enthalpy difference between the single twist conformation V and the chair conformation of 1,3-dioxane is, therefore, $24.4 + 12.9 = 37.3$ kJ mol^{-1}. This value is almost certainly an upper limit on the enthalpy change, as no allowance has been made for strain in III caused by the C(4) *gem*-dimethyl or the C(2) and C(6) pseudoequatorial methyl groups. We think it probable, however, that this strain is relatively small (<4 kJ mol^{-1}). Support for this idea comes from Hendrickson's calculations of strain in the twist forms of methylcyclohexane.[12]

Other recent estimates of the chair → twist enthalpy difference in 1,3-dioxane compare favorably with this microcalorimetric value. For example, Pihlaja[13] has recently obtained a gas-phase value of 35.5 ± 2.0 kJ mol^{-1} by use of appearance potentials in the mass spectrum. Since the trans isomer III exists predominantly in a single twist conformation, there is likely to be little entropy difference between III and IV. The free energy and enthalpy differences should be similar. This agreed with Eliel's value[9] for $\Delta G_{\text{III}\rightarrow\text{IV}}$ (< -23 kJ mol^{-1}).

From the enthalpy difference determined above, an estimate of the chair → twist free energy difference in 1,3-dioxane can be made if entropy corrections are applied. 1,3-Dioxane has six possible twist conformations and only two possible chairs. If all the twists are of the same energy, then $\Delta S_{\text{CT}} = RT \ln 3$ and, therefore, $\Delta G_{\text{CT}} = 34.6$ kJ mol^{-1}. If any one twist predominates in the twist → twist pseudorotation itinerary, then ΔS_{CT} will be somewhat smaller. Therefore, we estimate ΔG_{CT} for 1,3-dioxane to be 34 ± 2 kJ mol^{-1}.

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[5] The errors quoted on ΔH_1 and ΔH_2 are standard deviations; the errors on ΔH, ΔG, and ΔS are probable errors derived from twice the standard deviation.

[6] E. L. Eliel and M. C. Knoeber, *J. Amer. Chem. Soc.*, **90**, 3444 (1968).

[7] G. M. Kellie and F. G. Riddell, *J. Chem. Soc. B*, 1030 (1971).

[8] K. Pihlaja, G. M. Kellie, and F. G. Riddell, *J. Chem. Soc., Perkin Trans. 2*, 252 (1972).

[9] F. W. Nader and E. L. Eliel, *J. Amer. Chem. Soc.*, **92**, 3050 (1970).

[10] Subsequently, in ref 4 Powers and Eliel obtained a ΔG value for the chair–twist equilibrium, by means of a four-component equilibrium procedure, of 20.1 kJ/mol. Since the entropy of the twist probably exceeds that of the chair (*vide infra*), this figure is a minimum value for ΔH_{CT}.

[11] E. L. Eliel, personal communication; this is a revision of the value published in ref 6.

[12] J. B. Hendrickson, *J. Amer. Chem. Soc.*, **89**, 7043 (1967).

[13] K. Pihlaja and J. Jalonen, *Org. Mass. Spectrom.*, **5**, 1361 (1961).