Solvent Effects on the *cis*- and *trans*-4-t-Butylcyclohexanol Equilibrium by a New Method, using Gas-chromatographic Head-space Analysis

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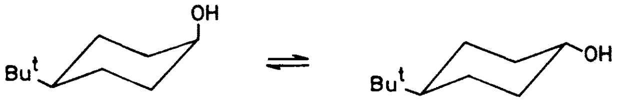
Summary Solvent effects on equilibria between configurational isomers of fixed conformation may be studied quantitatively by gas-chromatographic analysis of the head-space above solutions containing a standard ratio of the isomers; as an example, solvent effects on the *cis*- and *trans*-4-t-butylcyclohexanol equilibrium are reported.

SOLVENT effects on equilibria involving configurational isomers of fixed conformation are of interest both in their own right and because such compounds can be regarded as models for conformational isomers, *e.g.*, (**1**) ⇌ (**2**), that are in rapid equilibrium with each other. A classical method of determining solvent effects on the equilibrium constants, and hence on ΔG° values, for equilibria between isomers of fixed conformation, such as (**3**) ⇌ (**4**), is to equilibrate the isomers catalytically in various solvents, often at elevated temperatures, and then to measure the resulting isomer ratio.[1] A much more rapid and accurate method of obtaining the variation in ΔG° between solvents, $\delta\Delta G^\circ$, is simply to measure the relative retention times of the two isomers gas-chromatographically, using the given solvents as stationary phases.[2] Each of the above methods, although very useful, suffers from certain disadvantages, especially with regard to the nature of the solvents that can be used.

(1) (2)



(3) (4)

We have devised a new method of obtaining the required $\delta\Delta G^\circ$ values for the equilibrium (**3**) ⇌ (**4**), using the technique of gas-chromatographic head-space analysis. If the vapours above solutions of a given solute in solvents *a* and *b* are analysed by gas-chromatography, the solvent effect on the free energy of the solute, $\Delta G^\circ_t = \Delta G^\circ_{tb} - \Delta G^\circ_{ta}$, may be obtained through equation (1), in which D_a and D_b are the detector responses to the solute vapour above solvents *a* and *b*, and X_a and X_b are the mole fractions of the solute in the respective solutions.[3]

$$\Delta G^\circ_t = RT\ln\,[(D_b/X_b)/(D_a/X_a)] \qquad (1)$$

If equation (1) is separately applied to the isomers (**3**) and (**4**), then values of $\delta\Delta G^\circ$ may be obtained through the equation $\delta\Delta G^\circ = \Delta G^\circ_t(\mathbf{4}) - \Delta G^\circ_t(\mathbf{3})$. However, a more convenient and accurate procedure is to analyse the head-space above solutions that contain both isomers in a fixed ratio. We then have equation (2) since the ratio $(X_{a4}/X_{a3})/(X_{b4}/X_{b3})$ is unity.

$$\delta\Delta G^\circ = \Delta G^\circ_t(\mathbf{4}) - \Delta G^\circ_t(\mathbf{3}) = RT\ln\,(D_{a3}.D_{b4}/D_{a4}.D_{b3}) \qquad (2)$$

Like all methods that use head-space analysis, the procedure works best if the fixed isomers are reasonably volatile, since detector responses to the isomers in the vapour must be measured. However, to show the utility of the method, we have applied it to the equilibrium between *cis*- and *trans*-4-t-butylcyclohexanol, *i.e.*, (**3**) ⇌ (**4**), the two isomers actually being solids at room temperature.

TABLE. Values of $\delta\Delta G^\circ$, with n-hexane as the reference solvent, for the equilibrium (**3**) ⇌ (**4**), in cal mol^{-1} at 298·15 K

Solvent	$\delta\Delta G^\circ$
n-Hexane	0
Benzene	-61 ± 30[a]
Ethyl acetate	55 ± 30
Acetone	61 ± 10
Acetonitrile	62 ± 20
Me_2SO	-184 ± 15
$HCONMe_2$	-136 ± 20
Ethanol	-156 ± 20
Methanol	-275 ± 35

[a] 95% Confidence limits using Students t-test. Values are expressed in terms of the defined calorie (4·1840 J).

Values of $\delta\Delta G^\circ$ obtained through equation (2) are in the Table; n-hexane is taken as the reference solvent *a*. The solvent effect on the equilibrium (**3**) ⇌ (**4**), in terms of values of $\delta\Delta G^\circ$, is very small; this is in line with results of Eliel and Gilbert[1] who used the classical method (above) and found, *e.g.*, $\delta\Delta G^\circ$ values of -340 cal mol^{-1} on transfer from cyclohexane to propan-2-ol and to t-butyl alcohol, for the same equilibrium.† In these cases the $\delta\Delta G^\circ$ values at 298 K were extrapolated from results at higher temperatures, whereas our values are obtained directly at 298 K.

As with the previous methods[1,2] for studying solvent effects on this class of equilibria, it is also possible to obtain $\delta\Delta H^\circ$ values by the temperature variation of $\delta\Delta G^\circ$. An alternative, and we think more satisfactory, method is to determine the solvent effect on ΔH° at 298 K by direct solution calorimetry on the two separate isomers.[4] We shall discuss results in a full paper, and merely suggest now that the method of head-space analysis, especially when combined with calorimetrically determined $\delta\Delta H^\circ$ values,

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† We did not observe any dependence of the ratios D_3/D_4 on solute concentration in any of the solvents studied. This is in line with the observations of Eliel and Gilbert (ref. 1) who found no concentration dependence of ΔG° for the equilibrium (**3**) ⇌ (**4**) in cyclohexane, over the solute concentration range 0·05 to 0·20 M.

provides a valuable new method for the study of solvent effects on equilibria between configurational isomers of fixed conformation, and, indeed, on any equilibrium involving reactants and products that interconvert very slowly.

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