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A DIRECT EXPERIMENTAL AND THEORETICAL STUDY OF SOLVENT EFFECTS ON THE EQUILIBRIUM BETWEEN *trans cis* AND *trans trans* 1,2-DIBROMO-4-t-BUTYLCYCLOHEXANE

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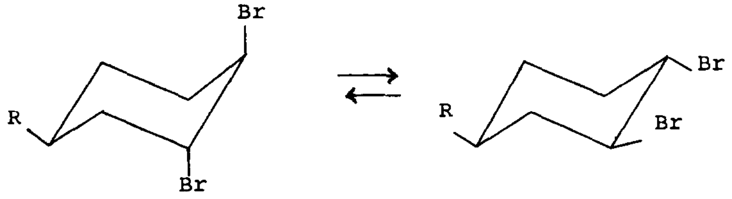
Abstract. The change in ΔG° for the equilibrium (1) $\rightleftarrows$ (2), R=t-Bu, has been measured for the gas phase and a range of solvents, thus providing a direct test of solvation theories. It is shown that reaction-field theory gives a quantitative explanation of the observed results, with the exception of the anomalous hydroxylic and aromatic solvents.

The profound effect of solvation upon almost all chemical equilibria and rates of reaction has been repeatedly emphasised by recent investigations,[1] and the need for a quantitative and general treatment of solvation has never been more necessary. Despite recent developments in Monte-Carlo methods,[2] solvation theories based on the continuum reaction-field model[3] still appear to offer the best hope of a generally applicable treatment. However, to-date there exist few absolute tests of any solvation theory, most data being restricted to particular solvents (e.g. gas-phase versus aqueous solution ionisation constants)[1] or being derived on the basis of questionable hypotheses, such as $\delta\Delta S° \sim 0$ for most I.R. and N.M.R. studies of solvent effects on conformational isomerism.[4] We present here a direct measurement of the change in free energy, $\delta\Delta G°$, for the equilibrium (1) $\rightleftarrows$ (2), R=t-Bu, between the gas phase and a variety of solvents and show that these can be given a quantitative explanation in terms of a known solvation theory.



(1) (2)

The observed values of $\delta\Delta G°$ are in Table 1. They have been obtained by the head-space analysis method[5] in which the concentration of the solute in the vapour above dilute solutions of the solute in the various solvents is determined by gas-liquid chromatography. Reisse et al[6] have previously used a method based on vapour pressure measurements to obtain $\delta\Delta G°$ values for a limited number of solvents. For transfers from cyclohexane to acetone and benzene their values[6] are -0.72 ± 0.16 and -0.82 ± 0.16 kcal mol^{-1} as compared to our values of -0.61 ± 0.05 and -0.54 ± 0.08 kcal mol^{-1} respectively.

We now use the reaction field theory to calculate the solvation free energy $-(E_v-E_s)$ of each isomer separately; E_v and E_s are the respective energies in the gas phase and in solution. The $\delta\Delta G°$ values are then obtained as $(E_v-E_s)_I - (E_v-E_s)_{II}$.[†] Details of the calculation of the (E_v-E_s) terms have been given before.[4,7] This involves the calculation of the interaction energies of the solute dipole and solute quadrupole with the solvent, the latter being regarded as a dielectric continuum of bulk dielectric constant ε_o, the only solvent parameter used in the calculations. The molecular geometry of the two solute isomers was based on the known geometry of the cyclohexane ring [d(C-C) 1.53 Å, < CCC 111.5°, θ CCCC 54.65°],[8] with the bromine substituents added using standard bond lengths and angles.[9] Solute refractive indexes and molecular volumes were calculated from constitutive additivity relationships, and thus are necessarily the same for the two isomers. The atomic charges required for the calculation of the molecular dipole and quadrupole moments were also calculated, from a general parametrisation of halo-alkane dipole moments,[10] and gave, with the above geometry, dipole moments of 3.22 D (2) and 0.93 D (1) in very good agreement with the observed values of 3.30 and 1.20 D respectively.[11] For the 4-tert-butyl compounds, as the effect of the t-butyl group is simply to decrease the solvation energy in proportion to the increase in the molecular volume, the values for the dibromocyclohexanes were multiplied by the appropriate factor (Table 1.)

Inspection of Table 1 shows that the reaction field theory gives a very good account of the observed variation in $\delta\Delta G°$ for the equilibrium (1) $\rightleftarrows$ (2), R=t-Bu, for solvents ranging from the gas phase to acetonitrile. Measurements of $\Delta G°$ have also been made[12] for the equilibrium (1) $\rightleftarrows$ (2), R=H, by direct integration of the low temperature n.m.r. spectrum, leading to a range of values from 0.98 kcal mol^{-1} (pentane) to -0.04 kcal mol^{-1} (acetone) at 208K. Our calculated value for $\delta\Delta G°$ (n-pentane→acetone)

[†] In order to avoid misunderstandings, we emphasise again that the solvation theory calculates directly the free energy of solvation.[6,7] Its' use for the calculation of enthalpies of solvation thus necessarily assumes neglect of the entropy term.

at this temperature is -0.85 kcal mol^{-1}, again in reasonable agreement with experiment. Furthermore, combination of the n.m.r. value of ΔG° in n-pentane with the calculations in Table 1 leads to an estimate of ΔG° for $(1)\rightleftarrows(2)$, R=H, in the gas phase of 1.40 kcal mol^{-1}.

Table 1 also shows the expected anomalous results from the hydroxylic solvents methanol and ethanol and also from benzene. (In this investigation CCl_4 appears to behave normally, though in common with other polyhalogenated solvents, this solvent can behave abnormally).[7] The anomalous behaviour of benzene in stabilising the more polar isomer (2) to a far greater extent than the static dielectric constant would predict is well-documented, and it has been suggested that an effective dielectric constant of 7.5 should be used for benzene.[4] This would give the correct δΔG° value here, but in the absence of any quantitative explanation of the benzene anomaly such devices must be used with extreme caution. In contrast in the hydroxylic solvents methanol and ethanol, the less polar isomer (1) is more favoured than predicted. This could be due to increased hydrogen bonding with the solvent in this isomer, although solvent structure could also be important in increasing the macroscopic dielectric constant over the microscopic (molecular) value.

Table 1. Calculated and observed values of δΔG° for the equilibrium $(1)\rightleftarrows(2)$ in kcal mol^{-1} at 298 K with cyclohexane as the reference solvent.

		$(1)\rightleftarrows(2)$ R = H			$(1)\rightleftarrows(2)$ R = t-Bu	
		$E_V - E_S$[b]		δΔG°	δΔG°	
Phase	ε_o[a]	(2)	(1)	(calc)	(calc)[c]	(obs)[d]
Gas Phase	1	0.00	0.00	0.40	0.28	0.38
Hexane	1.879	0.64	0.29	0.04	0.03	0.09
Cyclohexane	2.016	0.71	0.31	0.00	0.00	0.00
CCl_4	2.228	0.80	0.35	-0.05	-0.04	0.04
Ethyl acetate	6.02	1.55	0.64	-0.51	-0.36	-0.44
Acetone	20.49	2.02	0.80	-0.72	-0.58	-0.61
CH_3CN	36.02	2.16	0.85	-0.91	-0.64	-0.70
Benzene	2.274	0.82	0.36	-0.06	-0.04	-0.54
Ethanol	24.33	2.06	0.81	-0.85	-0.60	-0.34
Methanol	32.62	2.13	0.84	-0.89	-0.63	-0.48

[a] Dielectric constant at 298 K. [b] using calculated V_M 141.5 cm^3 mol^{-1}. [c] using V_M 200.7 cm^3 mol^{-1}. [d] This work and ref. 5.

Quite recently,[13] values of δΔG° for equilibria such as $(1)\rightleftarrows(2)$ have been correlated by the parabolic function $\delta\Delta G° = A + B\sqrt{C-X}$, where $X = (\varepsilon-1)/(2\varepsilon+1)$. Although there is a good correlation for $(1)\rightleftarrows(2)$, R = t-Bu, using this function, there is little instructive comparison to be made with the present method because of the purely empirical nature of the parabolic function. Eliel and Hofer[14] had earlier suggested that $\delta\Delta G°$ values for equilibria involving heterosubstituted 1,3-dioxanes were linearly related to the E_T parameter, but we find that for the normal solvents in Table 1 a plot of $\delta\Delta G°$(obs) against E_T is definitely curved.

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