Solvent and Gas-phase Effects on the Equilibrium between Configurational Isomers of Some 4-t-Butylcyclohexanes

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Through a combination of gas chromatographic head space analysis, gas chromatography retention times, and calorimetrically determined enthalpies of solution, the effect of various solvents, relative to the gas phase, on values of $\Delta G°$, $\Delta H°$, and $\Delta S°$ for the equilibrium between *r*-1,*t*-2-dibromo-*c*-4- and *r*-1,*t*-2-dibromo-*t*-4-t-butylcyclohexane has been determined. It is shown that the more polar diequatorial dibromo-isomer is stabilised relative to the diaxial isomer both in terms of Gibbs energy and enthalpy in polar media. Although values of $\Delta G°$, $\Delta H°$, and $\Delta S°$ for the equilibrium in nonpolar solvents approach the gas-phase values, there are still noticeable differences in these thermodynamic parameters between the gas phase and solvents such as hexane and cyclohexane. The effects of various media on $\Delta G°$ values for the equilibria between *cis*- and *trans*-4-t-butylcyclohexyl bromide and *cis*- and *trans*-4-t-butylcyclohexyl acetate have also been determined, but values of $\Delta G°$ for these two equilibria are largely independent of the reaction medium.

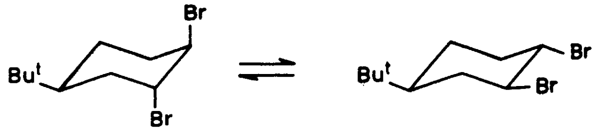
THE study of conformational and configurational equilibria for substituted cyclohexane rings has proved invaluable for developing theories concerning intramolecular interactions. However, for some systems, particularly rings bearing two polar groups, the effect of the medium can be as important as the interaction itself.[1] Thus measurement of $\Delta G°$ and $\Delta H°$ for equilibria in different solvents, and especially measurement of the change in these parameters on transfer from solution to the gas phase, is important for distinguishing between internal and external contributions to $\Delta G°$ and $\Delta H°$.

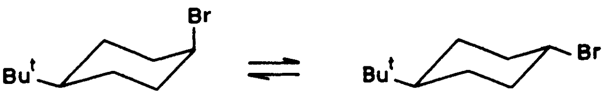
A classical method for evaluating solvent effects on conformational preference is simply to measure the appropriate equilibrium constants, and hence $\Delta G°$ values, in different solvents: for this type of work n.m.r. methods are particularly versatile.[2] It is not so easy to to apply this method to the measurement of corresponding enthalpy changes; since the $\Delta H°$ values must be obtained through the temperature variation of equilibrium constants, the error in the calculated $\Delta H°$ values using the van't Hoff method is always very much larger than the error in the primary $\Delta G°$ (or log K) values. For configurational equilibria, an attractive alternative method involves the measurement of the gas chromatographic retention times of the two configurational isomers using the solvents as the gas chromatographic stationary phases.[3] In this way changes in $\Delta G°$ ($\delta\Delta G°$) between the gas phase and the solvent stationary phase may be evaluated directly, although again the $\delta\Delta H°$ values have to be obtained using the van't Hoff method. Unfortunately the method of gas chromatographic retention times is severely limited to nonvolatile solvents that are suitable stationary phases.

Another approach altogether may be illustrated by the configurational equilibrium (1) $\rightleftharpoons$ (2). Standard thermodynamic parameters, $\Delta Q°$ where $Q = G, H, S$, *etc.*, in solvents A and B are defined as $\Delta Q°_A$ and $\Delta Q°_B$. The change in $\Delta Q°$ on transfer from a reference solvent A to the other solvent (or phase) B is then given by equation (1) in which $\Delta Q°_t$ is the change in parameter Q for the

$$\delta\Delta Q° = \Delta Q°_B - \Delta Q°_A = \Delta Q°_t(2) - \Delta Q°_t(1) \quad (1)$$

separate isomers (1) and (2).† An equation equivalent to (1) was deduced by von Halban [4] as long ago as **1909**, and since then there have been numerous applications of equation (1) to a wide variety of chemical equilibria.


(1) (2)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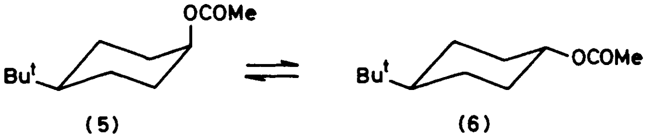
(5) (6)

Reisse *et al.*[1] have shown that if enthalpies of solution, $\Delta H°_s$, of (1) and (2) are determined separately in solvents A and B, then since $\Delta H°_t = \Delta H°_{s,B} - \Delta H°_{s,A}$ it is possible to obtain $\Delta H°_t(2)$ and $\Delta H°_t(1)$ by direct calorimetry and hence to calculate $\delta\Delta H°$ for the equilibrium (1) $\rightleftharpoons$ (2); other configurational equilibria were similarly investigated.[1] The corresponding analysis in terms of Gibbs energy proved more difficult, but Reisse *et al.*[1] succeeded in obtaining values of the Raoult's law activity coefficients, γ^{∞}, of (1) and (2) in the solvents cyclohexane, benzene, and acetone by very precise vapour

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† For a given isomer, $\Delta Q°_t = Q°_B - Q°_A$.

pressure measurements. Then since $\Delta G^\circ_t = RT\ln(\gamma^\infty_B/\gamma^\infty_A)$ it was possible to obtain values of $\delta\Delta G^\circ$ for (1) $\rightleftharpoons$ (2) on transfer from cyclohexane to benzene or acetone.[1]

As may be seen, above, few general methods for evaluating solvent effects are directly applicable to the gas phase, and data relating to the gas phase in consequence are rather rare. Although the situation is alleviated somewhat by the development of theoretical methods,[2,5] and by the extrapolation of $\delta\Delta G^\circ$ values from solution to the gas phase using various dielectric constant functions,[6,7] there is need for more experimental data on gas phase configurational equilibria. In the present paper we describe the application of gas chromatographic head space analysis (g.c.h.s.) to configurational equilibria and show how values of $\delta\Delta G^\circ$ may be obtained, not only between solvents but also between solution and the gas phase. We also use the retention time method (above) to determine $\delta\Delta G^\circ$ and, *via* the van't Hoff method, $\delta\Delta H^\circ$ values between solution and the gas phase, and show how the latter may be combined with calorimetrically determined ΔH°_t values[1] to yield $\delta\Delta H^\circ$ values between the gas phase and a wide variety of solvents.

TABLE 1

Head space analysis of the isomeric 1,2-dibromo-4-t-butylcyclohexanes (1) and (2) at 298 K

Solvent	$[(1)/(2)]_G$ [a]	σ [b]	No.	$[(1)/(2)]_S$ [c]	$-\delta\Delta G^\circ$ [d]	σ [b]
Gas phase					0	
Cyclohexane	1.623	0.073	6	0.854	380	30
Hexane	1.343	0.031	4	0.854	290	10
Squalane	2.509	0.229	12	1.060	510	40
Carbon tetrachloride	1.525	0.117	8	0.854	342	45
Ethyl acetate	3.441	0.265	6	0.854	824	45
Benzene	4.093	0.558	9	0.854	920	75
Acetone	4.524	0.288	8	0.854	987	40
Acetonitrile	5.280	0.462	11	0.854	1 077	50
Ethanol	3.440	0.112	6	0.854	717	20
Methanol	3.640	0.214	5	0.854	859	35

[a] Ratio of isomers in the head space (gas phase). [b] Standard deviations. [c] Ratio of isomers in solution. [d] In cal mol^{-1}, calculated through equation (6).

The systems we have studied are the three configurational equilibria (1) $\rightleftharpoons$ (2), (3) $\rightleftharpoons$ (4), and (5) $\rightleftharpoons$ (6). Apart from Reisse *et al.*'s work, above, on the first two of these equilibria there have been studies by Berti and his co-workers[8] who equilibrated mixtures of (1) and (2) as neat liquids at elevated temperature, and by Karger *et al.*[3] who investigated (5) $\rightleftharpoons$ (6) using the gas chromatographic retention time method referred to earlier. Under the conditions used in the present measurements, the three interconversions are all infinitely slow, but the thermodynamic parameters $\delta\Delta G^\circ$ and $\delta\Delta H^\circ$ are obviously still definable.

Gas Chromatographic Head Space Analysis.—Consider the configurational equilibrium (1) $\rightleftharpoons$ (2). In a solution sufficiently dilute that Hery's law is obeyed, the Henry's law constant of (1) in a given solvent, A, is defined as $K^H(1) = P(1)/X(1)$ where P is the vapour pressure of (1) above the solution and $X(1)$ is the mol fraction of (1) in the solution. Then for transfer of solute (1) from the gas phase to the solution, the standard Gibbs energy change is given by equation (2). A similar equation (3)

$$\Delta G^\circ_{t,A}(1) - \Delta G^\circ_{t,G}(1) = RT\ln K^H(1) \qquad (2)$$

may be written for transfer of solute (2) from the gas phase to solution in solvent A. Subtraction of equation

$$\Delta G^\circ_{t,A}(2) - \Delta G^\circ_{t,G}(2) = RT\ln K^H(2) \qquad (3)$$

(2) from (3) leads to equation (4) which can be rewritten more simply as (5). Now if the solution in solvent A

$$\Delta G^\circ_{t,A}(2) - \Delta G^\circ_{t,A}(1) - [\Delta G^\circ_{t,G}(2) - \Delta G^\circ_{t,G}(1)] = RT\ln[K^H(2)/K^H(1)] \qquad (4)$$

$$\Delta G^\circ_A - \Delta G^\circ_G = -RT\ln\left[\frac{P(1)}{P(2)}\cdot\frac{X(2)}{X(1)}\right] \qquad (5)$$

contains both isomers (1) and (2), analysis of the gas phase (head space) in equilibrium with the solution will yield the ratio $P(1)/P(2)$. The ratio $X(2)/X(1)$ of the isomers in the given solution will be identical to the ratio as made up at the start of the experiment (unless the isomers are very volatile), and therefore the difference in ΔG° for the equilibrium (1) $\rightleftharpoons$ (2) between the gas phase and solvent A may be obtained from equation (5) or (6). Through measurements in a series of solvents,

$$\delta\Delta G^\circ = \Delta G^\circ_A - \Delta G^\circ_G = -RT\ln\left[\frac{\text{ratio (1)/(2) in head space}}{\text{ratio (1)/(2) in solvent A}}\right] \qquad (6)$$

the g.c.h.s. method may obviously be used to calculate $\delta\Delta G^\circ$ values between a series of solvents, as well as from the gas phase.

Previously, the g.c.h.s. method has been used to obtain either Henry's law or Raoult's law constants for a given solute in solvents, and hence ΔG°_t values for transfer of a given solute from one solvent to another,[9-14] but this is the first report, except for our preliminary note,[15] in which equations (5) or (6) have been deduced. These represent a very simple method of obtaining $\delta\Delta G^\circ$ values for configurational equilibria, including gas phase values. Furthermore, since only ratios are measured, the method is inherently more accurate than previous g.c.h.s. methods. Results obtained for the three equilibria studied are given in Tables 1—3, with either the gas phase or cyclohexane taken as the reference medium. For the *cis*- and *trans*-4-t-butylcyclohexyl bromides, the peaks due to the *cis*- and *trans*-isomers overlapped considerably. We were able to resolve the peaks from the head space using a computer method, but were unable to analyse the pure liquid mixture or the mixture of the isomers in solution, and hence unable to obtain the isomer ratio in solution.* Although we could not calculate any $\Delta G°_A - \Delta G°_G$ values, we were still able to obtain transfers from one solvent to another (see Table 2).

TABLE 2

Head space analysis of the *cis*- and *trans*-4-t-butylcyclohexyl bromides at 333 K

Solvent	$(cis/trans)_G$	$\delta\Delta G°$ [a]
Cyclohexane	4.84	0
Ethyl acetate	4.90	10
Acetone	4.76	−10
Ethanol	4.98	20
Methanol	4.81	0

[a] In cal mol^{-1}, from cyclohexane as the reference solvent, calculated through a variant of equation (6).

For the equilibrium (1) ⇌ (2) it is possible to compare our results with those obtained previously by Reisse *et al.*[1] For the transfer from cyclohexane to benzene we find $\delta\Delta G°$ to be (-0.54 ± 0.08) kcal mol^{-1} as compared to Reisse *et al.*'s value of (-0.72 ± 0.16) kcal mol^{-1} and for the cyclohexane to acetone transfer our value of (-0.61 ± 0.05) kcal mol^{-1} may be compared to the previous value [1] of (-0.82 ± 0.16) kcal mol^{-1}. We also attempted, for this equilibrium, to obtain $\delta\Delta H°$ values for the gas phase → solution transfer using the van't Hoff method, with acetone as the solvent, but failed to obtain any reliable results. Examination of the error in $\delta\Delta H°$ due to the error in the equilibrium constant reveals that quite small errors in the latter lead to very large errors in $\delta\Delta H°$ when obtained by the van't Hoff method. One equation for assessing these errors may be expressed as $\sigma(\Delta H°) = \sqrt{2}RT^2\sigma(r)/r\Delta T$ where T is the average temperature of the measurements, ΔT is the temperature range, $\sigma(r)$ is the standard deviation in the ratio [(2)/(1) in the head space], and r is this ratio. If applied to our results using acetone solvent (Table 1) with ΔT taken as 30°, the value of $\sigma(r)$ that results in a standard deviation in $\delta\Delta G°$ of 0.04 kcal mol^{-1} leads to a corresponding standard deviation in $\delta\Delta H°$ of no less than 0.54 kcal mol^{-1}. Thus, although the g.c.h.s. method is accurate enough for most purposes in terms of $\sigma(\delta\Delta G°)$, it is not of the accuracy required for the determination of $\delta\Delta H°$ values, at least in its present form.

TABLE 3

Head space analysis of the *cis*- and *trans*-4-t-butylcyclohexyl acetates at 333 K

Solvent	$(cis/trans)_G$	σ [a]	$(cis/trans)_S$	$-\delta\Delta G°$ [b]	σ [a]
Gas phase				0	
Cyclohexane	0.638	0.024	0.395	320	20
Hexane	0.637	0.024	0.395	315	20
Ethyl acetate	0.698	0.019	0.395	375	20
Acetone	0.592	0.004	0.395	270	5
Acetonitrile	0.685	0.021	0.395	365	20
Ethanol	0.650	0.009	0.395	330	10
Methanol	0.545	0.018	0.395	210	20

[a] Standard deviations. [b] In cal mol^{-1}, calculated using corresponding equation to (6), *viz.* $\delta\Delta G° = -RT\ln[(cis/trans)_G/(cis/trans)_S]$.

Gas Chromatographic Retention Time Method.—This method is essentially that devised by Karger *et al.*[3] who applied it to a series of esters of *cis*- and *trans*-4-t-butylcyclohexanols and -4-t-butylcarboxylic acids. In the case of equilibrium (1) ⇌ (2), the value of $\Delta G°_A - \Delta G°_G$ where A is the gas chromatographic stationary phase is obtained from equation (7) in which $t(2)$ and $t(1)$ are the

$$\delta\Delta G° = \Delta G°_A - \Delta G°_G = -RT\ln\tau = -RT\ln[t(2)/t(1)] \quad (7)$$

corrected retention times, *i.e.* times measured from the air peak, of isomers (2) and (1). Karger *et al.*[3] studied their systems using conventional columns at temperatures at *ca.* 450 K, but since we wished to obtain τ values at temperatures quite close to 298 K, we used very short, rather lightly loaded chromatographic columns. Furthermore, we studied τ as a function of temperature, taking care to measure the column temperature using a series of thermocouples wrapped round the column. Results are in Table 4 for both di-isodecyl phthalate and squalane as the stationary phases. Values of $\sigma(\tau)/\tau$ are very much less than $\sigma(r)/r$, above, so that it is now possible to apply the van't Hoff method to obtain the corresponding $\Delta H°_A - \Delta H°_G$ values (Table 5). For the sets of results in both stationary phases we fitted the $\ln\tau$ values first to the simple van't Hoff function of $(1/T)$ and then to a two-parameter equation in $(1/T)$ and $(1/T)^2$, using a weighted least-squares analysis (Table 6). In the case of di-isodecyl phthalate, a good straight line was obtained for a plot of $\ln\tau$ against $(1/T)$, so that over the temperature range covered, $\delta\Delta H° = \Delta H°_A - \Delta H°_G$ is constant. However, for squalane stationary phase,

TABLE 4

Relative retention times of the isomeric 1,2-dibromo-4-t-butylcyclohexanes (1) and (2)

T/K	No. [a]	τ [b]	σ [c]
Squalane stationary phase			
409.74	9	1.557	0.020
399.37	6	1.626	0.010
388.13	6	1.730	0.017
379.50	5	1.795	0.016
369.50	5	1.876	0.017
359.80	5	1.936	0.011
349.73	5	2.028	0.034
Di-isodecyl phthalate stationary phase			
365.06	6	1.868	0.044
354.99	5	1.965	0.032
343.98	5	2.001	0.035
335.97	5	2.185	0.038

[a] Number of experiments. [b] Mean value of τ, where τ = retention time (2)/retention time (1) = retention time (di-equatorial)/retention time (diaxial). [c] σ = standard deviation of the τ value.

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* The experimental conditions for analysis of the head space or the solution differed somewhat; in the former case the overlapping peaks could be resolved by the computer method, but in the latter case they could not.

TABLE 5

Values of $\delta\Delta G^\circ$, $\delta\Delta H^\circ$, and $\delta\Delta S^\circ$ for the gas phase → stationary phase transfer of the equilibrium between the 1,2-dibromo-4-t-butylcyclohexanes [a] (1) ⇌ (2)

T/K	$-\delta\Delta G^\circ$	$-\delta\Delta H^\circ$	$-\delta\Delta S^\circ$
Squalane stationary phase			
409.74	0.36	1.50	2.8
399.37	0.39	1.43	2.6
388.13	0.42	1.35	2.4
379.50	0.44	1.28	2.2
369.50	0.46	1.20	2.0
359.80	0.48	1.12	1.8
349.73	0.49	1.03	1.5
298.15	0.53	0.48	0.2
Di-isodecyl phthalate stationary phase			
365.06	0.45	1.18	2.0
354.99	0.47	1.18	2.0
343.98	0.49	1.18	2.0
335.97	0.52	1.18	2.0
298.15	0.58	1.18	2.0

[a] $\delta\Delta G^\circ$ and $\delta\Delta H^\circ$ in kcal mol^{-1}, and $\delta\Delta S^\circ$ in cal K^{-1} mol^{-1}. Values obtained from the weighted least squares analysis (Table 6): these are slightly different from those given in ref. 15 where an unweighted analysis was used.

TABLE 6

Results of a weighted least squares analysis of the retention time data [a]

Squalane stationary phase

$$\ln \tau = -283\,024\left(\frac{1}{T/\mathrm{K}}\right)^2 + 2\,138.03\left(\frac{1}{T/\mathrm{K}}\right) - 3.0889$$

$$\frac{\Delta H^\circ}{R} = 566\,048\left(\frac{1}{T/\mathrm{K}}\right) - 2\,138.03$$

Di-isodecyl phthalate stationary phase

$$\ln \tau = 595.16\left(\frac{1}{T/\mathrm{K}}\right) - 1.0065$$

$$\frac{\Delta H^\circ}{R} = -595.16$$

[a] Weights were taken as the reciprocal of the variance of each observation weight (i) = $1/\sigma_i^2$.

this was not so, and the two parameter equation was required to fit the data. On this equation, $\delta\Delta H^\circ$ and $\delta\Delta S^\circ$ are not constant but vary with temperature (Tables 5 and 6). However, both for squalane and di-isodecyl phthalate it was possible to extrapolate all the solution parameters to 298 K, using the equations in Table 6. Over the experimental temperature range, the errors in $\sigma(\tau)$ lead to an error in $\delta\Delta G^\circ$ of *ca* 0.01 (squalane) and 0.02 kcal mol^{-1} (di-isodecyl phthalate). The extrapolated values at 298 K will be subject to greater errors, but for squalane we have been able to compare the extrapolated retention time value of -0.53 kcal mol^{-1} with the g.c.h.s. value (Table 1) of (-0.51 ± 0.04) kcal mol^{-1}, the two values being in good accord. For di-isodecyl phthalate an average value of $\sigma(\tau)/\tau$ is 0.0183 and over the temperature range studied this leads to an estimated error in $\delta\Delta H^\circ$ (Table 5) of ± 0.20 kcal mol^{-1}. It is difficult to estimate the corresponding error for the extrapolated value in the case of squalane, but from the results in Table 5 we calculate that for transfer from di-isodecyl phthalate to squalane $\delta\Delta H^\circ$ at 298 K is (-0.48 ± 1.18) = 0.70 kcal mol^{-1}, whereas from direct calorimetric measurements on the enthalpy of solution of isomers (1) and (2) separately in squalane and di-isodecyl phthalate at 298 K, we find that $\delta\Delta H^\circ$ is 0.66 kcal mol^{-1}, in excellent agreement with the value obtained from the extrapolated retention time values. We therefore conclude that for squalane, as well as for di-isodecyl phthalate, the value of $\delta\Delta H^\circ$ for the gas-phase → stationary phase transfer at 298 K is unlikely to be in error by more than 0.20 kcal mol^{-1}. In order to obtain τ values near 298 K, it was necessary to use stationary phase loadings of only 3—5%; such loadings can magnify any errors due to solute adsorption. We did not observe any pronounced peak-tailing or peak-asymmetry with the dibromides, and the excellent agreement between the $\delta\Delta G^\circ$ value of -0.53 kcal mol^{-1} from the extrapolated τ values on squalane and that of $-(0.51 \pm 0.04)$ kcal mol^{-1} from the g.c.h.s. method, suggests that no untoward effects occur with the retention time method.

General Analysis.—Values of $\delta\Delta G^\circ$ for the three equilibria studied are in Tables 1—3 and 8. The results we have for the monobromides (Table 2) although limited in number, show that there is practically no variation in ΔG° with change in solvent. Reisse *et al.*,[1] using the calorimetric method found that ΔH° for the monobromide equilibrium (3) ⇌ (4) is also rather insensitive to the medium. For the transfer from cyclohexane to acetone solvents, our g.c.h.s. value of $\delta\Delta G^\circ = -0.01$ kcal mol^{-1} may be compared with Reisse *et al.*'s value of $\delta\Delta H^\circ = 0.20$ kcal mol^{-1}. There appears to be no previous evaluation of the effect of solvent on ΔG° for the monobromide equilibrium, although there are abundant data for the related conformational equilibrium of cyclohexyl bromide.[16] Reisse [17] and Eliel [18] and their co-

TABLE 7

Enthalpies of solution of the isomeric 1,2-dibromo-4-t-butylcyclohexanes (1) and (2) in cal mol^{-1} at 298 K [a]

	ΔH°_s		ΔH°_t		
Solvent	(1)	(2)	(1)	(2)	$-\delta\Delta H^\circ$
Squalane [b]	340	750	−190	−520	330
Di-isodecyl phthalate [b]	160	−90	−370	−1 360	990
Cyclohexane [c]	530	1 270	0	0	0
Carbon tetrachloride [c]	−190	380	−720	−890	170
Benzene [c]	520	−80	−10	−1 350	1 340
Carbon disulphide [c]	400	690	−130	−580	−290
Acetone [c]	1 460	830	930	−440	1 370
Ethyl acetate [d]	860	500	330	−770	1 100

[a] The diaxial and diequatorial compounds are isomers (1) and (2) respectively. [b] This work. [c] Ref. 1. [d] This work, approximate values due to lack of material.

workers showed by n.m.r. that the latter equilibrium is also only marginally sensitive to change in solvent. This observation has been accounted for, within an electrostatic theory of solvation, on the basis of a small difference in the quadrupole terms of the two conformers.[19]

TABLE 8

Values of $\delta\Delta G^\circ$, $\delta\Delta H^\circ$, and $\delta\Delta S^\circ$ at 298 K for the equilibrium between the 1,2-dibromo-4-t-butylcyclohexanes[a] (1) $\rightleftharpoons$ (2)

Phase	$-\delta\Delta G^\circ$	$-\delta\Delta H^\circ$	$-\delta\Delta S^\circ$
Gas-phase	0	0	0
Cyclohexane	0.38	0.19	−0.6
Hexane	0.29		
Squalane	0.52[b]	0.48[c] 0.52[d]	−0.1
Carbon tetrachloride	0.34	0.36	0.1
Di-isodecyl phthalate	0.58	1.18	2.0
Ethyl acetate	0.82	1.10	0.9
Benzene	0.92	1.53	2.0
Acetone	0.99	1.56	1.9
Acetonitrile	1.08		
Ethanol	0.72		
Methanol	0.86		
Carbon disulphide		−0.10	

[a] $\delta\Delta G^\circ$ and $\delta\Delta H^\circ$ in kcal mol^{-1}, and $\delta\Delta S^\circ$ in cal K^{-1} mol^{-1}. Estimated errors are 0.05 kcal mol^{-1} in $\delta\Delta G^\circ$, 0.20 kcal mol^{-1} in $\delta\Delta H^\circ$, and 0.7 cal K^{-1} mol^{-1} in $\delta\Delta S^\circ$. Results taken from Tables 1, 5, and 7; see footnote in Table 5. [b] Average of the values from the retention time data (−0.53) and the head space analysis method (−0.51). [c] Extrapolated value from the retention time data. [d] Obtained from the value of −1.18 for the gas phase → di-isodecyl phthalate transfer, together with calorimetric value of 0.66 for the di-isodecyl phthalate → squalane transfer.

The case of the monoacetates, equilibrium (5) $\rightleftharpoons$ (6), is interesting in that although there is very little variation in ΔG° with change in solvent, there is a difference of 0.3 kcal mol^{-1} between the gas phase and solvents in general. This could possibly be due to a change in the rotamer distribution of the acetate function in the gas phase and in solution. The small variations in ΔG° with solvent are in accord with the results obtained by Karger *et al.*[3] using the gas chromatographic retention time method, and find analogy with data for the conformational equilibria of cyclohexyl acetate.[20]

As expected from the dipole moments of the diaxial (1) and diequatorial (2) dibromides, 1.2 and 3.3 D respectively, there is a large solvent effect on ΔG° for the equilibrium (1) $\rightleftharpoons$ (2) (see Table 1). The g.c.h.s. method enables, for the first time, the gas phase–solvent effect on ΔG° to be determined simply and accurately through equation (6), and we suggest that this method is now the preferred technique for the determination of solvent and gas-phase effects on ΔG° values for equilibria between any two solutes that interconvert but slowly. We have already shown[21] that the electrostatic reaction field theory gives a very good description of these solvent and gas-phase effects on ΔG° for the equilibrium (1) $\rightleftharpoons$ (2), with the exception of the anomalous solvents benzene and the alcohols. Quite recently, Zefirov and Samoshin[7] put forward an empirical parabolic function related to the solvent (or gas phase) dielectric constant, ε. When applied to the equilibrium (1) $\rightleftharpoons$ (2), for the gas phase, cyclohexane, hexane, ethyl acetate, acetone, and acetonitrile, expression (8) is obtained. Equation (8) cor-

$$\delta\Delta G^\circ/\text{cal mol}^{-1} = -3\,855.8 + 3\,888.9\,[1.0 - (\varepsilon - 1)/(2\varepsilon + 1)]^{\frac{1}{2}} \quad (8)$$

relates $\delta\Delta G^\circ$ for the six media with a standard deviation of only 33 cal mol^{-1}.* The simple Kirkwood expression (9; $A = 56.9$, $B = -2\,273.3$) also yields quite a good correlation for the six media, with a standard deviation in $\delta\Delta G^\circ$ of 47 cal mol^{-1}. Although there is no gas-phase value for the parameter[22] E_T, the $\delta\Delta G^\circ$ values for the

$$\delta\Delta G^\circ/\text{cal mol}^{-1} = A + B(\varepsilon - 1)/(2\varepsilon + 1) \quad (9)$$

five aprotic solvents, above, can be correlated with E_T (σ 69 cal mol^{-1}), and the correlation used in reverse to obtain an estimate of the gas-phase value of E_T, *viz.* 24.1, a quantity hitherto unknown.[22] Similarly, the π^* values of Kamlet and Taft[23] yield an excellent correlation of $\delta\Delta G^\circ$ for the five aprotic solvents (σ 9 cal mol^{-1}) and from the linear correlation a gas-phase value of −0.44 may be deduced for π^*. Compare previous estimates of −0.61 to −0.51.[24]

For the equilibrium (1) $\rightleftharpoons$ (2), the retention time method yields (Table 5) values of $\delta\Delta G^\circ$, $\delta\Delta H^\circ$, and $\delta\Delta S^\circ$ for the gas-phase → stationary phase transfers. As shown above, the extrapolated $\delta\Delta H^\circ$ values at 298 K are in excellent agreement with calorimetric experiments, and so we feel that the thermodynamic parameters obtained by this method are genuine and are not artefacts due to adsorption on the support, *etc.* The variation in $\delta\Delta H^\circ$ and $\delta\Delta S^\circ$ with temperature for the gas phase → squalane transfer, and consequently for the di-isodecyl phthalate → squalane transfer is an important observation, because a general method of obtaining values of ΔH° for configurational equilibria involves equilibration at high temperature and application of the van't Hoff method to the determined equilibrium constants.[25] It is then assumed that the ΔH° values obtained at high temperatures are identical to the values at 298 K. In a similar vein, values of ΔH° for conformational equilibria of cyclohexanes found at low temperatures have been equated to room temperature ΔH° values.[26] However, from the single case of equilibrium (1) $\rightleftharpoons$ (2) in squalane, it seems that the temperature invariant behaviour of ΔH° may not always be true.

One of the aims of the present work was to show how $\delta\Delta H^\circ$ values for the gas phase → stationary phase transfers may be combined with calorimetrically determined enthalpies of solution to yield gas phase → solvent $\delta\Delta H^\circ$ values. Enthalpies of solution of isomers (1) and (2) in squalane and di-isodecyl phthalate were determined

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* Professor N. S. Zefirov (personal communication) has kindly pointed out that the parabolic function $[0.5 - (\epsilon - 1)/(2\epsilon + 1)]^{\frac{1}{2}}$ correlates both the $\delta\Delta G^\circ$ and $\delta\Delta H^\circ$ values, with different slopes and intercepts for the two correlations. When applied to the six media, this parabolic function reproduces the $\delta\Delta G^\circ$ values with a standard deviation of 51 cal mol^{-1} [*cf.* the deviation of 33 cal mol^{-1} using equation (8)].

in this work, and were combined with those reported by Reisse *et al.*[1] to yield $\delta\Delta H^\circ$ values for transfer between the stationary phases and other solvents, and hence between the gas phase and other solvents (Table 7). Finally, combination of the enthalpy data with the corresponding Gibbs energies (Table 1) leads to $\delta\Delta S^\circ$ values for the equilibrium (1) $\rightleftharpoons$ (2) (Table 8). Thus the g.c.h.s. method, the retention time method, and calorimetric determinations of enthalpies of solution may all be applied to the same equilibrium to yield $\delta\Delta G^\circ$, $\delta\Delta H^\circ$, and $\delta\Delta S^\circ$ values not only between solvents but between the gas phase and solvents. In our view, the combined techniques represent a very powerful method for the determination of solvent and gas-phase effects on equilibria involving isomers that interconvert very slowly. Inspection of Table 8 shows that nonpolar solvents such as cyclohexane, hexane, or carbon tetrachloride are best models for the gas phase, and that ΔG°, ΔH°, and ΔS° for equilibrium (1) $\rightleftharpoons$ (2) in these solvents are nearest to the gas-phase values. However, when considering the overall ' spread ' of the data, there are still significant differences between these solvents and the gas phase. Thus ΔG° changes as much from the gas phase to cyclohexane as it does from cyclohexane to ethanol, illustrating the point made by Reisse *et al.*[1] that the gas phase transfers are essential in any quantitative discussion of medium effects on equilibria. The results in Table 8 show also that values of $\delta\Delta S^\circ$ are not zero and that $\delta\Delta G^\circ$ values cannot be equated to $\delta\Delta H^\circ$ values without the introduction of a considerable percentage error. Hence values of $\delta\Delta H^\circ$ cannot be used as tests of electrostatic calculations of Gibbs energy changes. Any electrostatic equations in G may be differentiated with respect to temperature to yield equations in S and thence in H. Thus from the Kirkwood expression (9), this procedure leads to the corresponding equation (10) for $\delta\Delta H^\circ$. Using the same constants, A and B, as found by application of equation (9) to $\delta\Delta G^\circ$ values, above, values of

$$\delta\Delta H^\circ/\text{cal mol}^{-1} = A + \frac{B(\varepsilon - 1)}{(2\varepsilon + 1)} - \frac{3BT}{(2\varepsilon + 1)^2} \cdot \frac{\partial\varepsilon}{\partial T} \qquad (10)$$

$\delta\Delta H^\circ$ are deduced as follows (observed values in parentheses): gas phase 60 (0), cyclohexane −530 (−190), ethyl acetate −1000 (−1 290), and acetone −1 110 (−1 560), all in cal mol at 298 K. Provided therefore that the correct equations are used, either $\delta\Delta G^\circ$ or $\delta\Delta H^\circ$ values may be used to test electrostatic theories.

EXPERIMENTAL

Mixtures of *r*-1,*t*-2-dibromo-*c*-4- and *r*-1,*t*-2-dibromo-*t*-4-t-butylcyclohexanes, b.p. 145 °C at 16 mmHg, *cis*- and *trans*-4-t-butylcyclohexyl acetates, b.p. 116 °C at 15 mmHg, and *cis*- and *trans*-4-t-butylcyclohexyl bromides, b.p. 109 °C at 15 mmHg, were prepared from commerical 4-t-butylcyclohexanol (isomer mixture) using literature procedures.[3,27] The mixture of the dibromo-compounds was separated into the two isomers by chromatography over silica gel 40 (Merck 70—230 mesh) using pentane as the eluant, and the fractions then redistilled to afford isomer (1), b.p. 65 °C at 0.1 mmHg (lit.,[8] 74 °C at 0.5 mmHg), and isomer (2), b.p. 76 °C at 0.1 mmHg, which solidified on standing (lit.,[8] m.p. 33—35 °C). Solvents were purified by standard methods.

Gas chromatographic head space analysis of the dibromides was carried out by the procedure described before.[9-11] Solutions of the isomers were made up in various solvents such that the ratio of the axial : equatorial isomers in solution was the same in each solvent (except in the case of solvent squalane); the concentration of the dibromides in the solvents was *ca.* 0.1 mol dm^{-3}. The solutions were then thermostatted at 298 K and samples (2.5 cm^3) of the head space were withdrawn and analysed by gas chromatography using a Perkin-Elmer Sigma 313 flame ionisation gas chromatograph operated at high sensitivity and fitted with a 1.5 m glass column of OV 17 at 410 K. The peak areas due to the axial and equatorial isomers were obtained by an automatic integrator fitted to the gas chromatograph. In a preliminary series of experiments using the two solvents ethanol and cyclohexane it was established that the results were independent of the concentration of the dibromides in solution over quite a wide range of concentration (0.02—0.1 mol dm^{-3}).

For head space analysis of the monoacetates and the monobromides, solutions were made up as above but the head space was sampled using a Perkin-Elmer HS6 automatic head space analyser operated at 333 K. The vapour samples were analysed using a 1.5 m glass column of 3% Dexsil 300 on Chromosorb WAW, 100—120 mesh, at 390 K. Unfortunately, the peaks due to the *cis*- and *trans*-isomers of the monobromide were not at all fully resolved either on 3% Dexsil or on any other column available. The areas of the *cis*- and *trans*-peaks were therefore found by a computer analysis of the unresolved peak by the method described by Wentworth.[28]

Relative retention times of the dibromides were obtained using a glass column (57 cm long) containing either 3% squalane on Celite or 5% di-isodecyl phthalate on Celite. The dibromide isomers were injected as a solution in acetone (0.2 µl). The temperatures of the columns were found by wrapping six thermocouples in parallel round the columns at different points. Determined in this way, the actual column temperatures often differed by several degrees from the nominal value of the oven temperature.

Enthalpies of solution of the dibromide isomers, (1) and (2), were obtained using an LKB 8700 solution calorimeter system operated as described before.[13] The final concentration of the isomer in solution was *ca.* 0.01—0.02 mol dm^{-3}. In all cases it was found that correction for the heat of breaking of empty ampoules was negligible. In these experiments, the solid dibromide (2) was not used as such, but was warmed until liquid and then left to stand. The isomer then remained liquid at room temperature for several days, and enthalpies of solution were determined using this super cooled liquid.

We are grateful to the S.R.C. for support of this work, and we thank Dr. F. Kaberia and Mr. S. M. Vather for preparing some of the compounds, and Dr. How Chiong Ling and Mrs. R. Watts for carrying out the experiments on solution calorimetry. We thank also Professors J. Reisse and N. S. Zefirov for their interest in this work.

[2/169 *Received, 28th January,* 1982]

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