Rotational Isomerism. Part XIV.[1] Medium Effects on the Conformational Equilibria of Halogenocyclohexanes

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The calculation of the solvent dependence of the conformational equilibrium in mono- and di-chloro- and -bromocyclohexanes is given and compared with experiment. The calculations are based on an electrostatic theory of solvation and the model uses a fixed cyclohexane geometry and constant C–X bond dipole moment. The model gives generally good agreement with the observed dipole moments of all the chloro- and bromo-cyclohexanes. There is no solvent dependence in cyclohexyl halides but a large solvent dependence in *trans*-1,2-, *cis*-1,3-, and *trans*-1,4-dichloro- and -dibromo-cyclohexanes. The model provides a quantitative explanation of all the observed effects. This agreement allows the prediction of the vapour state energy differences in these systems. The diaxial conformer of *trans*-1,2-dichloro- (and dibromo-) cyclohexane is the preferred conformer in the vapour phase (ΔE^v = 0·7 and 1·3 kcal mol^{-1} respectively) and this can be rationalised in terms of halogen–halogen repulsions. However, the diaxial conformer of *trans*-1,4-dichloro- (or dibromo-) cyclohexane is also the preferred conformer in the vapour phase (ΔE^v 0·8 and 0·7 kcal mol^{-1} respectively), and this has no simple rationalisation. The energy differences for benzene as solvent are anomalous in these, as in all other related equilibria, and a method of allowing for this anomaly is given.

THE determination of conformational preferences in halogenocyclohexanes has been investigated extensively in the last decade [2] due to the relative ease of obtaining reliable experimental data and the insight which such determinations give on interatomic interactions in the molecule and on reactivities in these systems.

However, in most of these investigations the influence of the solvent has not been considered explicitly, even though this may be considerable. An explanation of the solvent dependence of conformational equilibria should provide information on solvent–solute interactions and also by extrapolation a method of estimating conformational preferences in the vapour state. It is the conformational preference in the gas which must be compared with the results of theoretical calculations.

In cyclohexyl halides, which have been the most extensively studied, $-\Delta G$ ($ax \longrightarrow eq$) is remarkably independent of solvent, the range of values being virtually within the experimental error. For example Eliel obtains values for the chloride ranging between 0·34 and 0·51 kcal mol^{-1} for sixteen solvents.[3] *

In complete contrast $-\Delta G$ ($aa \longrightarrow ee$) for the *trans*-1,2-dihalogenocyclohexanes shows a pronounced dependence on the medium, varying from *ca.* −1·0 kcal mol^{-1} in non-polar media to *ca.* +0·5 kcal mol^{-1} in polar media (Table 2 and refs. therein). Obviously this is due to the very different dipole moments of the conformers, the diequatorial isomer being favoured in more polar media.

The *cis*-1,3-dihalogenocyclohexanes should also on this basis show a large solvent effect, but in the few investigations performed so far no evidence of an equilibrium has been found,[4] presumably due to the large repulsive interaction of two axial halogen atoms.

However $-\Delta G$ ($aa \longrightarrow ee$) for the *trans*-1,4-dihalogenocyclohexanes also shows a pronounced solvent dependence, varying by *ca.* 0·6 kcal mol^{-1} in different solvents (Table 3 and refs. therein), even though in this case the dipole moments and therefore dipolar interactions of both conformers are zero.

Thus it is clear that higher order terms are needed to explain these results, which to date have not been given collectively a qualitative, let alone quantitative explanation.

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* For the absolute values of ΔG, see F. R. Jensen, C. H. Bushweller, and B. H. Beck, *J. Amer. Chem. Soc.*, 1969, **91**, 344.

[1] Part XIII, R. J. Abraham and T. M. Siverns, *Tetrahedron*, 1972, **28**, 3015.

[2] J. A. Hirsch, *Topics in Stereochemistry*, 1967, **1**, 199.

[3] E. L. Eliel and R. J. L. Martin, *J. Amer. Chem. Soc.*, 1968, **90**, 689.

[4] B. Franzus and B. E. Hudson, *J. Org. Chem.*, 1963, **28**, 2238.

In previous papers of this series, a model, based on the evaluation of the molecular dipole and quadrupole fields, has been successfully applied to the calculation of the solvent dependence of rotational isomerism in halogenoethanes.[5-7] Recently this model has been extended to the 1,3-dioxan system[8] and furfuraldehyde.[1] Thus it was of interest to see whether it could account for the observed effects in halogenocyclohexanes.

The calculations of necessity evaluate the molecular dipole (and quadrupole) moments. One advantage of halogenocyclohexanes over the analogous halogenoethanes is that the dipole moments of a large number of conformationally fixed derivatives have been measured, and these provide useful checks on the model.

We show that a simple model based on a fixed cyclohexane geometry and a constant C–X bond dipole moment accounts satisfactorily for all the dipole moments of the above species and also for the solvent dependence of the equilibria. This latter allows the calculation of vapour state $-\Delta G$ values and these are discussed.

THEORY

The theory has been derived elsewhere,[5,6] thus we give here only the necessary outline, and its application to the halogenocyclohexanes.

The solvation energy of any polar molecule in state A, *i.e.* the difference between the energy in the vapour ($E^v{}_A$) and in any solvent ($E^s{}_A$) of dielectric constant ε, is obtained by calculating the molecular dipolar and quadrupolar electric fields in the solvent by classical electrostatic theory.*

This gives the expression (1) † where $x = (\varepsilon - 1)/(2\varepsilon + 1)$

$$E^s{}_A = E^v{}_A - k_A x(1 - lx) - 3h_A x/(5 - x) \qquad (1)$$

and $l = 2(n_D{}^2 - 1)/(n_D{}^2 + 2)$, n_D being the solute refractive index, and k_A and h_A are $\mu^2{}_A/a^3$ and $q^2{}_A/a^5$ respectively, μ_A and q_A being the dipole and quadrupole moments of the molecule and a the molecular radius. For two equilibrating molecular states (A and B) such as the interconverting conformers considered equation (1) becomes equation (2) where now $k = k_A - k_B$ and $h = h_A - h_B$

$$\Delta E^s = E^s{}_A - E^s{}_B = \Delta E^v - kx/(1 - lx) - 3\,hx/(5 - x) \qquad (2)$$

On our model the dipole and quadrupole moments are calculated by placing point dipoles along and at the centre of the polar bonds and a is given by $4\pi a^3/3 = M_V/N$ where M_V is the molar volume and N Avogadro's number.

Note that the energy difference $E_A - E_B$ need not only be between two stable conformers, any state of the molecule will be affected by the solvent in this manner. Thus the theory can in principle be used to predict the solvent dependence of the barrier to interconversion as well as the conformer energy difference.

In order to quantify this we need to know the molecular geometry and the dipole moments of the states involved.

The molecular geometry is taken direct from the recent determination of the cyclohexane geometry[11] together with that given previously for halogenoalkanes.[12] Buys and Geisse obtain C–C–C and C–C–C–C angles of 111·05 (±0·15)° and 55·9 (±0·3)° for cyclohexane.[11] In ref. 12 a standardised geometry for halogenoalkanes was given in which all C–C–C and C–C–X angles were 111°, all H–C–H and H–C–C angles tetrahedral, and the H–C–X angles obtained from these. As the C–C–C angle used is identical to that in cyclohexane, the standardised geometry can be used virtually unchanged for these systems. The only minor amendment is that in cyclohexane itself the C–C–C and H–C–H angles define the C–C–H angles as 109·08° and this value is used throughout.

To summarise all bond lengths are from ref. 12, all C–C–C and C–C–X angles are 111·00 and all H–C–H angles are tetrahedral. This gives the C–C–C–C dihedral angle as 56·00°, the C–C–H angle 109·08° and the H–C–X angle 105·5°.

The C–Cl and C–Br bond dipole moments are taken as 1·9 *D*, and the remaining parameters needed in equation (2) (the molar volume and *l*) are obtained directly from the experimental values of the density and refractive index.[13] The complete set of parameters used in the calculations is given in Table 1.

As the densities and refractive indices of the dichloro- and dibromo-cyclohexanes are virtually constant (Table 1), for those compounds for which there were no data, we used the average values indicated.

RESULTS AND DISCUSSION

Dipole Moments.—Unlike the corresponding ethanes, the dipole moments of the conformationally mobile halogenocyclohexanes can be estimated reasonably from conformationally fixed analogues. Thus in Table 1 the dipole moments of the *ee* and *aa* conformers of the *trans*-1,2-dihalogenocyclohexanes are obtained as the observed moments of the 2*ax*,3*ax*- and 2*eq*,3*eq*-*trans*-decalins[14] and of *aa* and *ee*-1,2-dibromo-4-t-butylcyclohexanes.[15] The values for the *cis*-1,3-dibromo- and *trans*-1,4-dibromo- and -dichloro-compounds are however the observed values for these compounds.

Also the dipole moments of those compounds which are equilibrating between two identical conformations (the *cis*-1,2-, *trans*-1,3-, and *cis*-1,4-dihalogenocyclo-

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* The calculations are in terms of the potential energy whereas the experimental data are strictly in terms of enthalpy. As we are considering only *differences* between solvents the zero-point energy, contribution of higher vibrational states and PdV terms are expected to cancel out.[9]

† A further term is given in ref. 6 which considers explicit dipole–dipole interactions. We have recently extended this to include dipole–quadrupole interactions.[10] As these terms are complex but give only minor corrections to the energy we have for simplicity omitted them here. This does not affect at all our final conclusions.

[5] R. J. Abraham and M. A. Cooper, *J. Chem. Soc.* (*B*), 1967, 202.

[6] R. J. Abraham, *J. Phys. Chem.*, 1969, **73**, 1192.

[7] R. J. Abraham and G. Gatti, *J. Chem. Soc.* (*B*), 1969, 961.

[8] R. J. Abraham, H. D. Banks, E. L. Eliel, O. Hofer, and M. K. Kaloustian, *J. Amer. Chem. Soc.*, 1972, **94**, 1913.

[9] J. Reisse, in ' Conformational Analysis,' ed. G. Chiurdoglu, Academic Press, New York, 1971.

[10] R. J. Abraham, unpublished results.

[11] H. R. Buys and H. J. Geise, *Tetrahedron Letters*, 1970, 2991.

[12] R. J. Abraham and K. Parry, *J. Chem. Soc.* (*B*), 1970, 539.

[13] ' Handbook of Chemistry and Physics,' 48th edn., Chemical Rubber Publishing Co., Cleveland, Ohio, 1968.

[14] C. Altona, H. R. Buys, H. J. Hageman, and E. Havinga, *Tetrahedron*, 1967, **23**, 2265.

[15] H. J. Hageman and E. Havinga, *Tetrahedron*, 1966, **22**, 2271.

hexanes) can be directly measured and compared with the calculated values and these are also given in Table 1.

Inspection of Table 1 shows remarkably good agreement between the observed and calculated dipole moments. The observed and calculated values are identical for the *cis*-1,2-, *trans*-1,3-, and *cis*-1,4-dihalogenocyclohexanes and the agreement with the *ee*-*trans*-1,2-dihalogeno-conformer is satisfactory when it is considered that small deformations of the cyclohexane ring may occur in the t-butyl and *trans*-decalin derivatives used for the observed value. Note that although the cyclohexane geometry is not tetrahedral, the condition that all the C–C–C and C–C–X angles are equal necessarily leads to the same calculated dipole moments for the *ea*- and *ee*-1,2-dihalogenocyclohexanes, providing some justification for the use of the dipole moment of the former as a model for the latter in obtaining the conformational preference in *trans*-1,2-dihalogenocyclohexanes.[16] The observed dipole moment for *cis*-1,3-dibromocyclohexane is identical to the calculated moment for the *ee* conformer in agreement with the calculations of Franzus and Hudson,[4] based on tetrahedral geometry, and confirm their interpretation that the molecule is entirely in this conformation.

TABLE 1

Molecular constants and calculated parameters for halogenocyclohexanes

Compound	Density (g cm^{-3})[a]	n_D[a]	Molar volume (ml)	l	Dipole moment (D) calc.	Dipole moment (D) obs.[d]	k(kcal^{-1})	h(kca mol^{-1})
1-Chloro *eq*	1·016	1·4626	116·74	0·5504	1·90	2·2	1·12	2·07
ax								1·27
1-Bromo *eq*	1·3264	1·4956	122·93	0·5838	1·90	2·2	1·07	1·84
ax								1·12
cis-1,2-Dichloro	1·2018	1·4963	127·35	0·5845	3·13	3·12	2·80	1·94
trans-1,3-Dichloro		1·49[b]	129[b]	0·5782	2·15		1·31	3·01
cis-1,4-Dichloro		1·49[b]	129[b]	0·5782	2·94	2·89	2·44	2·25
cis-1,2-Dibromo	1·803	1·5514	134·20	0·6385	3·13	3·12	2·66	1·62
trans-1,3-Dibromo		1·5472[c]	135·5[b]	0·6344	2·15	2·17[c]	1·24	2·96
cis-1,4-Dibromo	1·7714[e]	1·5476[c]	136·59	0·6348	2·94	2·92	2·31	2·18
trans-1,2-Dichloro *ee*	1·1842	1·4907	129·24	0·5789	3·13		2·76	2·28
aa					0·37	1·21	0·04	2·81
trans-1,2-Dibromo *ee*	1·784	1·5495	135·63	0·6367	3·13	3·28,[e] 3·3[g]	2·63	1·86
aa					0·37	1·15,[e] 1·19[f]	0·04	2·90
cis-1,3-Dichloro *ee*		1·49[b]	129[b]	0·5782	2·15		1·31	3·97
aa					3·78		4·03	1·45
cis-1,3-Dibromo *ee*		1·5445[c]	135·5[b]	0·6318	2·15	2·19	1·24	3·95
aa					3·78		3·84	1·16
trans-1,4-Dichloro *ee*		1·49[b]	129[b]	0·5782	0·0	0·0	0·0	9·16
aa								5·59
trans-1,4-Dibromo *ee*	1·7714[c]	1·5476[c]	136·59	0·6348	0·0	0·0, 0·55[c]	0·0	8·91
aa								5·43

[a] Ref. 13. [b] Average values, see text. [c] Ref. 4. [d] Ref. 17 unless stated otherwise. [e] 2*a*,3*a*- and 2*e*,3*e*-Dibromo-*trans*-decalin.[14] [f] *aa*-1,2-Dihalogeno-4-t-butylcyclohexanes.[15] [g] *ee*-1,2-Dibromo-4-t-butylcyclohexane.[15]

The difference in the observed and calculated dipole moment of the cyclohexyl halides is a real effect and analogous to the situation in halogenoalkanes. The dipole moments of methyl, ethyl, n-propyl, and isopropyl chlorides are 1·87, 2·03, 2·06, and 2·2 D respectively,[17] showing an almost constant effect of successive methyl substitution at the α-carbon atom and a negligible effect of β-methyl substitution. The dipole moment of cyclohexyl chloride is identical to that of isopropyl chloride in agreement with this scheme.

The only serious discrepancies in Table 1 are for the *trans*-1,2-diaxial conformers and for the *trans*-1,4-dihalogeno-compounds. The large observed dipole moment of the 1*ax*,2*ax*-dibromo-4-t-butylcyclohexane[15] and the analogous *trans*-decalin derivative[14] has been noted previously, without any real explanation for this value. Hageman and Havinga[15] note that the X–C–C–X dihedral angle would have to be reduced to *ca.* 155° to explain this dipole moment, without suggesting why this should be so. They noted also that the t-butyl group does introduce some distortion of the molecule. The steric interactions of the t-butyl substituent would increase the angle of buckle of the section with the t-butyl substituent, and hence decrease the angle of buckle of the dibromo-half, thus giving a larger dipole moment. However, the dipole moment is larger than would be given by a reasonable amount of ring buckle. Furthermore the use of this value of the dipole moment for the *trans*-1,2-dihalogeno-conformational equilibrium does not produce results in agreement with those of other investigations (see later).

Even more anomalous is the reported dipole moment of 0·55 D for *trans*-1,4-dibromocyclohexane.[4] The molecule by symmetry has a zero dipole moment in both the chair forms, there is no likelihood of any populated conformation with a large dipole moment, and there is no good reason to postulate large amplitude molecular vibrations. There is some uncertainty in this measurement as Kozima and Yoskino[18] obtain zero dipole

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[16] P. Bender, D. L. Flowers, and H. L. Goering, *J. Amer. Chem. Soc.*, 1955, **77**, 3463.

[17] A. L. McClellan, 'Tables of Experimental Dipole Moments,' Freeman, London, 1963.

[18] K. Kozima and T. Yoshino, *J. Amer. Chem. Soc.*, 1953, **75**, 166.

moment but Franzus and Boyd[4] state that their values of $P_{2\infty}$ and R_D lead to a dipole moment of 0·4 D. Both the approximations necessarily made in calculating the dipole moment from the molar polarisation and the experimental accuracy of measurement become more critical with compounds of small dipole moment. In view of the generally good agreement in Table 1 we will use in the next section values corresponding to the calculated dipole moments of all the compounds.

Solvent Dependence of the Conformational Equilibrium.—The data in Table 1 can be inserted directly into equation (2) to give the solvent dependence of the free energy difference of any equilibrium between any two of the species shown. Provided the equilibrium is truly thermodynamic then any method of measuring this is valid, thus this could include chemical equilibration, for example *cis–trans* isomerisation. However, the only extensive data available are those involving different conformers and it is this aspect we wish to consider here.

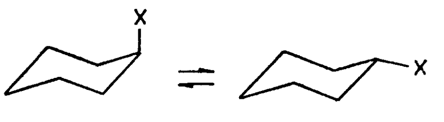
TABLE 2

Energy differences in *trans*-1,2-dihalogenocyclohexanes

Solvent	Dielectric constant	ΔE^s ($E^s_{ee} - E^s_{aa}$) (kcal mol^{-1})										
		1,2-Dichloro						1,2-Dibromo				
		Calculated	Observed[k]					Calculated	Observed[l]			
Vapour	1·0	(0·70)	0·61[c]	0·72[d]				(1·30)				
C_6H_{12}	2·0	0·15		0·72	0·41[f]			0·83	1·55[i]	0·85[f]		
CCl_4	2·2	0·08		0·58	0·37	−0·2[g]	0·0[h]	0·77	1·32	0·77	0·65[g]	0·50[h]
CS_2	2·6	−0·11	0·17	0·20	0·24			0·66	0·98	0·55	0·65	
$CHCl_3$	4·7	0·40			0·0			0·35		0·26		
Benzene	7·5[a]	−0·60	−0·43[e]		0·0	−0·65	−0·69	0·16		0·20	0·10	0·13
Pure liquid	*b*	−0·72		−0·60	0·0			0·18	0·33[j]	0·26		
Acetone	20·2	−0·86			−0·42			−0·09		−0·10	−0·10	
CH_3CN	35·9	−0·93			−0·47	−1·0		−0·15		−0·24	−0·30	
CH_3NO_2	36·5	−0·94			−0·53			−0·16		−0·32		

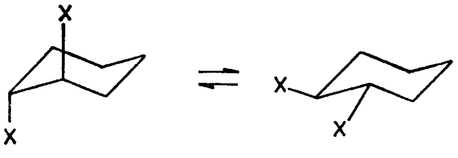
[a] See text. [b] Estimated as 10·0 for the dichloro and equal to 6·9 for the dibromo.[25] [c] Ref. 22. [d] Ref. 23. [e] For methyl acetate solution ($\varepsilon = 6{\cdot}8$). [f] Ref. 24. [g] R. U. Lemieux and J. W. Loan, *Canad. J. Chem.*, 1964, **42**, 893. [h] See text. [i] Ref. 25. [j] Y. A. Prentiss, G. M. Kuz'yants, and O. P. Ulyanova, *Russ. J. Phys. Chem.*, 1964, **38**, 708. [k] The techniques used, are, from left to right, var. temp. i.r. (2 columns); single temp. i.r.; n.m.r.; dipole moment. [l] The techniques used, are, from left to right, var. temp. i.r.; single temp. i.r.; n.m.r.; dipole moment.

Cyclohexyl halides. The first equilibrium to consider is the well documented one for cyclohexyl chloride and bromide (I). In order to calculate the solvent dependence, we merely insert the appropriate values of *k*, *h*, and *l* given in Table 1 into equation (2). This gives directly $\delta\Delta E(\Delta E^v - \Delta E^s)$ in terms of the dielectric constant of the solvent. The dipole moments (and therefore *k* values) for the axial and equatorial isomers are equal and therefore the dipolar term in equation (2) vanishes for this equilibrium. The quadrupole moments are not the same as they depend on the position of the centre of the molecule and on the distance and orientation of the bond dipole from the centre. However, in this equilibrium the quadrupole terms are small and comparable and thus the predicted influence of the medium on the equilibrium is very small. As the quadrupole term is larger for the equatorial conformer this conformer will be more stabilised in polar media. Equation (2) and Table 1 predict that the free energy difference ($-\Delta G$) of this equilibrium should increase by 0·10, 0·21, and 0·26 kcal mol^{-1} on going from the vapour to media of dielectric constant 2·0, 7·5, and 35·9. This change is virtually within the experimental error of the determinations and this is in agreement with observation. For example the systematic study of the solvent dependence of this equilibrium by Eliel[3] using the chemical shift method gave $-\Delta G^0$ values ranging from 0·34 to 0·46 kcal mol^{-1} (9 solvents) for cyclohexyl chloride, and 0·27 to 0·38 kcal mol^{-1} (8 solvents) for cyclohexyl bromide, omitting associated solvents. It may be significant that the $-\Delta G$ values for cyclohexyl chloride and fluoride (which would behave similarly) measured in the vapour state are both at the low end of the reported ranges of values[2] but the only firm conclusion is that the predicted and observed solvent dependence of this equilibrium are extremely small.



(I) X = Cl or Br

trans-1,2-*Dihalogenocyclohexanes.* The conformational equilibrium in trans-1,2-dihalogenocyclohexanes (II) has been studied by a number of different techniques and investigations. Again the effect of the medium on this equilibrium is given directly from Table 1 and equation (2). However, mere inspection of Table 1 shows that there will be now, in contrast to the monohalogenocyclohexanes, a large solvent effect, as the dipole moments of the conformers are very different but their quad-



(II) X = Cl or Br

rupole moments similar. Thus there will be considerable stabilisation of the *ee* conformer in polar media. This is indeed observed and the observed and calculated results are compared in Table 2.

In Table 2, each separate column under the observed heading gives the results obtained by different techniques of measurements. These are in order, variable temperature i.r. measurements, single temperature i.r. measurements, n.m.r. studies and dipole moment measurements. The values obtained by dipole moment measurements (*h* in Table 2) are obtained from the calculated moments for the *ee* and *aa* conformers of Table 1 with the observed dipole moments. These values are virtually identical to those given by previous workers [16] based on $\mu_{aa} = 0$ and $\mu_{ee} = \mu_{ea}$.

The dielectric constants used are those of the pure solvents at 30 °C with one notable exception. We have compared the free energy differences found in benzene solution with those calculated for a solvent of dielectric constant 7·5. It has been noted in many previous investigations of equilibria involving polar molecules that benzene invariably behaves anomalously, always preferentially stabilising the more polar isomer.[19] Three detailed comparative studies have been given recently of solvent effects. These are rotamer energy differences in halogenoethanes,[5] the relative rates of the Menshutkin reaction [20] and the free energy difference between *cis*- and *trans*-5-alkoxy-2-isopropyl-1,3-dioxans.[21] In the latter investigation Eliel and Hofer also demonstrated that toluene was analogous to benzene but that mesitylene and t-butylbenzene behaved normally.

These workers also proposed a new solvent scale, based on their $-\Delta G$ values to remove this benzene anomaly. For our purposes it is simpler to use a different value of the dielectric constant of benzene.

The value of 7·5 gives the correct answer for all three investigations considered and we use it here. This does *not* of course mean that we infer that benzene has a static dielectric constant of 7·5, merely that a large body of data is best fitted by using this value.*

For the dichloro-compound, two groups of workers [22,23] measured the energy differences by variable temperature i.r. spectroscopy and these are given together in Table 2. They agree very well in the value of ΔE^{v} obtained and the average of these values (0·70 kcal mol^{-1}) has been used together with equation (2) to obtain the calculated ΔE^{s} values shown.

In almost every measurement considered here, it is the systematic errors necessarily introduced in order to obtain the results, rather than the experimental errors, which are dominant. This is clearly shown in the very considerable differences in the ΔE values of the dichloro-compound shown in Table 2. However, these errors are minimised when one consideres the $\delta\Delta E$ values, *i.e.* the difference between two solvents measured by the same technique. These values are much more consistent and provide a better test of the theory,† for example $\delta\Delta E$ (vapour ⟶ pure liquid) observed 1·32 kcal mol^{-1} (Table 2, note *d*), calculated 1·42; $\delta\Delta E$ ($CCl_4 \longrightarrow CH_3CN$) observed 0·84 (note *f*); 0·80 (note *g*); calculated 0·85. On this basis there is excellent agreement between the observed and calculated effects.

For the dibromocyclohexane the experimental results are much more consistent. Indeed the last three columns of Table 2 giving the results of single temperature i.r. studies, n.m.r. studies, and dipole moment measurements agree to within the experimental error and also agree precisely with the calculated values. This agreement allows the prediction of the value of ΔE^{v} of 1·30 kcal mol^{-1}, which of course is not calculated by equation (2) which only gives $\delta\Delta E$ values. The results of Ul'yanova *et al.*[25] from variable temperature i.r. studies in non-polar media are the only values which are out of line for the dibromo-compound. Their values for the dichloro-compound are also anomalously high. Indeed the observed value for cyclohexane solution is the same as the gas value, an unlikely result. This discrepancy has been noted by these authors and ascribed to the use of infinitely dilute solutions, compared to the more concentrated solutions used in other investigations. This however ignores the dipole moment results which are also extrapolations to infinitely dilute solutions and in any case the difference between 5% solutions and infinitely dilute ones is very small for these solutes [0·1 kcal mol^{-1} for a 5% solution of *trans*-dichlorocyclohexane in CCl_4 from equation (2)].

The Russian school have also used the method of dilute solutions to obtain ΔE^{v}. This is essentially an extrapolation of ΔE^{s} *versus* $(\varepsilon - 1)/(2\varepsilon + 1).a^3$ and should therefore give similar results as our treatment. However, their treatment gives very different results. Their values of ΔE for the dichloro-compound in the non-polar solvents cyclohexane, CCl_4 and CS_2 (Table 2, note *d*) are, on their bases, consistent with the ΔE^{v} value; on our theory they are inconsistent.

For the dibromo-compound they obtain a ΔE^{s} value of 1·8 kcal mol^{-1} compared with our extrapolated value of 1·3, though this is based on different ΔE^{s} values.

One reason may be that following Powling and Bernstein [26] they take *a* to be the radius of the *solvent*

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* This value also removes the anomalies noted previously for benzene as solvent in the equilibration studies of 5-halogeno-2-isopropyl-1,3-dioxans.[8]

† Klaeboe *et al.*[24] state that their values should be compared in this way, and not considered as absolute values.

[19] *Cf.* P. Laslo, *Progr. N.M.R. Spectroscopy*, 1967, **3**, ch. 6; C. Altona, H. R. Buys, H. J. Hageman, and E. Havinga, *Tetrahedron*, 1967, **23**, 2265.

[20] C. Lassau and J. C. Jungers, *Bull. Soc. chim. France*, 1968, 2678.

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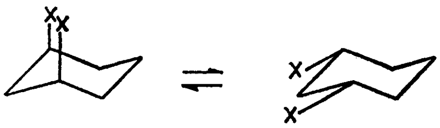
molecule. There is no theoretical justification for this procedure except for the case in which the solute is so small that it fits in the holes of the solvent lattice (*cf.* lithium in lithium iodide). This is a very rare occurrence in liquids and certainly is not valid for the systems considered here.

Furthermore the extrapolation to the gas value is much less accurate than one may expect even if the simple extrapolation with $x = (\varepsilon - 1)/(2\varepsilon + 1)$ is used. This is easily demonstrated by considering typical value of x. For ε values of 1·0 (vapour) 2·0 (C_6H_{12}) and ∞ (*e.g.* acetone) the values of x are 0, $\frac{1}{5}$, and $\frac{1}{2}$. Thus the solvation effect of cyclohexane is almost half that of acetone, and the extrapolation of ΔE from the small measured range of non-polar solvents of cyclohexane, CCl_4 and CS_2, to the vapour involves large uncertainties. A much simpler, and equally accurate method of estimating ΔE^v stems from the relationship [equation (2) and Table 2] $\delta\Delta E$ (vapour $\longrightarrow$ CS_2) = $\delta\Delta E$ (CS_2 $\longrightarrow$ acetone). Thus a measurement of ΔE in CS_2 and acetone will provide a good estimate of ΔE^v.

It is of interest to compare the calculation of the solvent effect in the above compounds with that of the corresponding 1,2-dihalogenoethanes.[7] The observed effects are very comparable. $\delta\Delta E$ (vapour $\longrightarrow$ pure liquid) for X = Cl and Br are 1·2 and 1·0 kcal mol^{-1} for the ethanes compared to 1·4 and 1·1 kcal mol^{-1} for the cyclohexanes (Table 2). Furthermore the dipole moments of the isomers are very similar (μ_g and μ_t for the ethanes are *ca.* 3·3 and 0·0 D, *cf.* Table 1). However, the details of the calculations are quite different. The much smaller molecular volume of the ethanes (78·9 and 82·5 ml, *cf.* Table 1) results in a corresponding increase in the dipole term, which is *ca.* 50% larger than in the cyclohexanes. This is compensated to a great extent in the ethanes by a large quadrupole term favouring the *trans*-isomer. In the cyclohexanes in contrast the quadrupole term is very similar in the two isomers. Thus the overall result is much the same but the detailed breakdown of the calculations quite different.

cis-1,3-*Dihalogenocyclohexanes.* The conformational equilibrium in the *cis*-1,3-dihalogenocyclohexanes (III) has not been studied systematically to any great extent, and there are no data to compare with the theoretical predictions of the solvent effect upon this equilibrium.



(III) X = Cl or Br

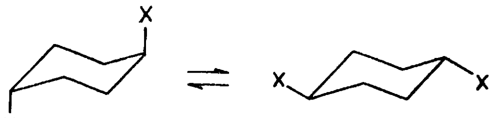
The incorporation of the k, h, and l values for these conformers given in Table 1 into equation (2) allows the prediction of the solvent dependence of this equilibrium. The diaxial conformer becomes more favoured (or more accurately less unfavoured) as the polarity of the medium increases and the equation predicts $\delta\Delta E$ (vapour $\longrightarrow$ solvent) values for the dichloro-compound for solvent dielectric constants of 2·0, 2·6, 7·5, 20·2, and 35·9 of 0·30, 0·42, 0·78, 0·95, and 1·01 kcal mol^{-1} respectively. The values for the dibromo-compound are very similar.

The observed dipole moment of *cis*-1,3-dibromocyclohexane is identical to the calculated moment for the *ee* conformer, (Table 1), thus on this basis there is virtually none of the diaxial form present. Franzus and Hudson [4] reached this conclusion and confirmed it by examining the n.m.r. spectrum of the compound at −73 °C in CS_2. No peak corresponding to the *aa* conformer could be observed, even though the corresponding *trans*-isomer showed a definite coalescence point at −33 °C, showing that the conformations were frozen out at the lower temperature. However, small amounts of the *aa* conformer could easily pass undetected, particularly if the proton resonances were near to those of the major conformer.

The absence of significant amounts of the *aa* isomer is not surprising as there is considerable 1,3-diaxial repulsion in this case. The inter-halogen distances (2·86 and 2·90 Å for X = Cl and Br) correspond to steric repulsions of *ca.* 4 and 6 kcal mol^{-1} for the two compounds, using the interatomic potentials given previously.[12] These are maximum values as torsional deformations will partially relieve this repulsion.

The interesting prediction given by the theory is that the repulsive interaction in the *aa* form can be compensated by *ca.* 1 kcal mol^{-1} of solvation energy in polar solvents and obviously the study of this equilibrium in polar solvents would seem the most profitable means of attack.

trans-1,4-*Dihalogenocyclohexanes.* The solvent dependence of the conformational equilibrium of *trans*-1,4-dihalogenocyclohexanes (IV) is of some interest, in as much as both conformers have zero dipole moment and any solvent dependence must be due to higher order terms.



(IV) X = Cl or Br

Inspection of Table 1 shows that the diequatorial conformer has a much larger quadrupole moment than the diaxial conformer and therefore will be preferentially stabilised in more polar media, and insertion of the values of h and l in Table 1 into equation (2) gives the predicted increase in energy.

There are only a few experimental observations to test these predictions. Wood and Woo observed the low temperature n.m.r. spectrum of the dichloro- and dibromo-compounds [27] and obtained the proportions of the two forms directly from the integrated areas. As the assignment of the peaks is unambiguous, due to the very different coupling constants in two conformers, this method is definite. The only limitation is the accuracy

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[27] G. Wood and E. P. Woo, *Canad. J. Chem.*, 1967, **45**, 2477.

with which the peak areas can be measured. Wood and Woo stated that there was no solvent effect in this equilibrium, but this conclusion was based on an unfortunate choice of solvents. They used [$^2H_8$]toluene and a $\frac{3}{2}$ (v/v) mixture of CD_2Cl_2 and $CDCl_3$. Toluene behaves like benzene in these equilibria, *i.e.* as if the dielectric constant was *ca.* 7·5, and the dielectric constant of the CD_2Cl_2–$CDCl_3$ mixture (solvent dielectric constants of *ca.* 14 and 6 at −70 °C) will be very similar.

However, Kozima and Yoshino[18] have observed a pronounced solvent dependence of this equilibrium using Raman spectroscopy. This technique gives $\delta\Delta E$ values on the assumption that the ratios of the intrinsic intensities of the bands due to the individual conformers are solvent independent. The absolute values of ΔE are only given by assuming a value for this ratio. This is very uncertain and we prefer to use the definitive value of ΔE (toluene) obtained by Wood and Woo with the $\delta\Delta E$ values to obtain the ΔE values in the other solvents studied. These values are given in Table 3 together with the calculated values which are obtained directly from equation (2) using a value of ΔE^v which reproduces the observed benzene result. The less detailed results for the dibromo-compound have been treated similarly.

TABLE 3

Energy differences in *trans*-1,4-dihalogenocyclohexanes

Solvent	Dielectric constant	ΔE^s ($E^s_{ee} - E^s_{aa}$) (kcal mol^{-1})					
		1,4-Dichloro			1,4-Dibromo		
		calc.	obs.		calc.		obs.
Vapour	1·0	0·80			0·70		
C_6H_{12}	2·0	0·35	0·23 [c]		0·26		
CCl_4	2·2	0·30	0·41		0·21	0·2	
Et_2O	4·3	0·03	−0·16		−0·05		
$CDCl_3$–CD_2Cl_2	11 [a]	−0·22		−0·16 [d]			
C_6H_6	7·5 [b]	−0·15	−0·16	−0·16	−0·22		−0·21 [d]
Acetone	20·2	−0·29			−0·37	−0·45	
CH_3CN	35·9	−0·34			−0·41		

[a] 2/3 Mixture. [b] See text. [c] From single temp. i.r. measurements.[18] From low temp. n.m.r.[27]

Inspection of Table 3 shows that, within the limited precision of the experimental data, there is good agreement between the observed and calculated results. This is especially pleasing in as much as this demonstrates that the procedure used to obtain the molecular quadrupole moments is a reasonable approximation. In all the other examples so far studied, the dipolar term is dominant and therefore could hide any errors in the quadrupole term.

The values of ΔE^v given in Table 3, which derive from the value in toluene solution, differ considerably from the only reported experimental values in the gas of <0·2 kcal mol^{-1} from electron diffraction measurement.[28] It should be emphasised that this discrepancy is basically an experimental one. The results of three investigations are (*a*) a very small energy difference in the gas, (*b*) a large solvent dependence of this energy difference, and (*c*) a very small energy difference in solution.

Clearly these cannot be reconciled and further experimental work is needed.

Conclusions.—The extension of the solvent effect model to the conformational equilibria in halogenocyclohexanes is shown to give generally good agreement with experiment for all the cases investigated. The calculated values have been obtained solely on the basis of the previous theory, combined with a reasonable cyclohexane geometry. It has not been necessary to introduce any modifications to the theory. The same model has been applied to the conformational equilibrium in 5-halogeno-2-isopropyl-1,3-dioxans[8] and to rotational isomerism in furfuraldehyde[1] as well as to a large number of halogenoethanes[7] and thus would appear to be generally applicable. It is however important to realise the necessary limitations of this treatment. In particular as all solvent–solute interactions are treated as arising from classical electrostatic interactions, any system in which there are specific (*i.e.* chemical) solvent–solute or solvent–solvent interactions is not covered by the theory. The obvious example is any system in which hydrogen bonding occurs, and this immediately excludes many popular solvents, in particular all the alcohols. A more subtle exception already noted is with benzene as solvent. It is clear that there are solvent–solute (and very probably solvent–solvent) interactions in benzene which are additional to the classical electrostatic forces considered in our treatment. In particular long range order in the solvent is a possible explanation.

Another apparent anomaly which however can be treated by the theory is the use of mixtures as solvents. If the solvent consists of a non-polar and polar constituent, there will be preferential solvation of any polar solute by the more polar constituent of the solvent. The energy involved is given immediately from equation (1). Any solute equilibrium will therefore not follow simple additivity laws and the mixture will appear much more polar in the equilibrium studied than the dielectric constant would indicate. For precisely similar reasons pure solvents with long hydrocarbon side chains and small polar groups will behave anomalously.

Finally it is of interest to consider the vapour-state values of ΔE obtained here. In cyclohexyl chloride and

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[28] V. A. Atkinson and O. Hassel, *Acta Chem. Scand.*, 1959, **13**, 1737.

bromide, the absence of any significant solvent effect means that the vapour-state values are virtually identical to the measured solution values which have been extensively documented and discussed. In the *trans*-1,2-dihalogenocyclohexanes in contrast the vapour-state values are very different from those observed in condensed media. The values of ΔE^{v} ($E^{\mathrm{v}}_{ee} - E^{\mathrm{v}}_{aa}$) of 0·7 and 1·3 kcal mol^{-1} for the chloro- and bromo-compounds are somewhat less than the *gauche* — *trans* energy difference in the analogous 1,2-dihalogenoethanes (1·2 and 1·7 kcal mol^{-1}).[12] The *trans*-diaxial conformers have two 1,3-diaxial H–X interactions which total by analogy with the cyclohexyl halides *ca.* 0·8 kcal mol^{-1}. Thus the results suggest that the X · · · X repulsive interactions are roughly 0·3—0·4 kcal mol^{-1} greater in the *ee* conformers than in the *gauche*-rotamers of 1,2-dihalogenoethanes, which does not appear unreasonable.

The energy differences found for the *trans*-1,4-dihalogenocyclohexanes are not consistent with any simple rationalisation. Wood and Woo[27] had previously commented on the anomalously low value of the energy difference found in solution, compared with that of the cyclohexyl halides. Table 3 shows that the anomaly in the vapour state is much greater, in that in complete contrast to the cyclohexyl halides the diaxial conformer is more stable by *ca.* 0·8 kcal mol^{-1}. If the interactions were additive this value should be reversed in sign. A possible explanation is that the electronegative halogen substituents slightly flatten that part of the cyclohexane ring, causing the diaxial hydrogen atoms to spread out and thereby reduce the additional interaction of the second axial halogen atom. The situation is similar to the 4-alkyl ketone effect in cyclohexanone.[29] Here the flattening of the ring due to the introduction of the keto-group and consequent outward motion of the axial hydrogens at C-2 and C-6 results in a marked decrease of the 1,3-diaxial interactions with a C-4 axial methyl group. However, in view of the uncertainty in the experimental results for these compounds further speculation would appear premature.

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[2/436 *Received, 25th February,* 1972]

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