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WEAK MOLECULAR INTERACTIONS—I

SOLVENT EFFECTS ON THE PROTON MAGNETIC RESONANCE SPECTRA OF t-BUTYL AND ADAMANTYL HALIDES

R. C. FORT, Jr. and T. R. LINDSTROM

Contribution from the Department of Chemistry, Kent State University, Kent, Ohio

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Abstract—The effect of aromatic solvents upon the PMR spectra of t-butyl and 1-adamantyl halides has been studied in an attempt to discover the mechanism by which the changes in chemical shift are produced. If the formation of 1:1-complexes in these solutions is assumed, the temperature dependence of the chemical shifts can be used to derive thermodynamic parameters. These parameters do not seem to respond significantly to changes in the structure of the solute or solvent. In addition freezing point diagrams give no evidence of compound formation. To explain the geometrically specific shifts which are nonetheless observed, it is suggested that the solute dipole causes a weak ordering of the solvent, which is geometrically, but not thermodynamically, equivalent to a complex.

THE changes in proton chemical shift which occur when a polar molecule is transferred from an "inert" solvent such as carbon tetrachloride to an aromatic one are often striking.[1] Moreover, these changes are usually geometrically specific; that is, only protons bearing a definite relationship to the polar function suffer a shift.[1,2] This specificity has made the solvent shifts of great value in the elucidation of natural product structures.[2]

Most commonly, a specific solute–solvent interaction is postulated as the source of this phenomenon; the solute molecule is held in such a position that the solvent ring current either reinforces or subtracts from the applied magnetic field.

In view of the usefulness of the solvent shifts in an empirical sense, and the possibility of gaining some interesting information about weak molecular interactions, we have undertaken an investigation of the association of simple polar molecules with aromatic substances. We attempt to discover whether solutions displaying the NMR solvent shifts also manifest any other properties directly attributable to the existence therein of complexes.

Our study was initiated with the 1-adamantyl halides, upon which some preliminary work had been done.[3] These molecules have a precisely defined geometry[4] which makes them particularly amenable to interaction studies. Further, the earlier examination had indicated an anomalous feature: the β-hydrogens, closest to the substituent, suffered only minor (3–8 c/s) shifts, while the γ and δ protons were substantially (25–40 c/s) shifted. As a complimentary system to adamantyl, we chose

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[1] J. A. Pople, W. G. Schneider and H. J. Bernstein, *High Resolution Nuclear Magnetic Resonance*, Chap. 16. McGraw-Hill, New York (1959).

[2] N. S. Bhacca and D. H. Williams, *Applications of NMR Spectroscopy in Organic Chemistry. Illustrations from the Steroid Field*, Chap. 7. Holden-Day, San Francisco (1964).

[3] R. C. Fort, Jr. and P. von R. Schleyer, *J. Org. Chem.* **30**, 789 (1965).

[4] R. C. Fort, Jr. and P. von R. Schleyer, *Chem. Rev.* **64**, 277 (1964).

t-butyl, the protons of which stand in the same relation to the substituent as do the β-protons in the adamantane derivatives.

RFSULTS*

Solvent shifts. Chemical shifts of the protons of t-butyl and 1-adamantyl chloride, bromide, and iodide were measured in benzene and several halobenzenes. In each case significant solvent shifts (vs. CCl_4) were seen, those for benzene solvent always being the largest. Figure 1 presents a good example. All shifts were to high field, and the extent of the shift was temperature dependent, the resonances moving further upfield as the temperature was lowered. If it is assumed (see later Discussion) that the mechanism by which the solvent shifts are generated is the formation of a weakly bound 1:1-complex, equilibrium constants and enthalpies of formation for the complex may be calculated as suggested by Abraham.[5]

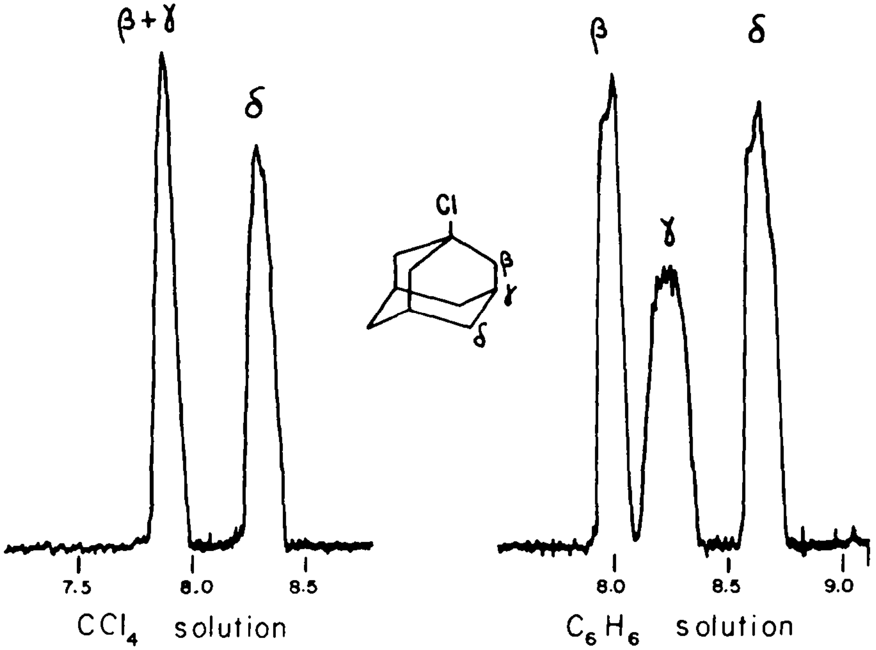

Fig. 1. Benzene solvent effect on the NMR spectrum of 1-chloroadamantane.

Briefly, the fraction of solute molecules complexed, p, (in dilute solution, so that inter-solute interactions are negligible) is given by

$$p = \frac{\delta - \delta_o}{\delta_c - \delta_o}$$

where δ = the observed chemical shift of the solute proton at temperature T in a

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* Chemical shift data for t-butyl halides and adamantyl halides may be had on application to Professor R. C. Fort.

[5] R. J. Abraham, *Mol. Phys.* **4**, 369 (1961).

complexing solvent; δ = the chemical shift of the "free" solute; and δ_c = the shift of the solute in the complex. The resonance position for a dilute solution in some inert solvent (CCl_4 in this instance) is taken as δ_o. δ_c is obtained by measuring δ as a function of temperature and extrapolating to 0° K. All of the solute molecules are assumed to be complexed at this temperature, and $\delta = \delta_c$.[6]

The equilibrium constant at any temperature is then

$$K = \frac{p}{1 - p}$$

and ΔH may be obtained as usual from the slope of a plot of log K vs. $1/T$.

In Tables 1 and 2 are presented the solvent shifts $\Delta\delta_o = \delta_{CCl_4} - \delta_{AR}$, extrapolated to 0° K,[8] and the various thermodynamic parameters obtained by the route just described. Plots of δ vs. T were reasonably linear (Fig. 2), and δ_o values could be reproduced to ±3 c/s. As expected, the solvent shifts were also concentration dependent; this factor was cancelled from studies of temperature dependence by employing solution(s) containing only 1–2 mole % of solute. Control experiments established that in this concentration range, the dilution shift is less than the error in extrapolation. The $\Delta\delta_o$ values thus actually represent the solvent shift at infinite dilution and 0° K.

TABLE 1. SOLVENT EFFECTS ON t-BUTYL HALIDE SPECTRA

Compound	Solvent	$\Delta\delta_o$, c/s[a]	K[b], m.f.$^{-1}$	$-\Delta H$, kcal.[c]	$-\Delta S$, e.u.[b]
Me_3CCl	C_6H_6	30·1	1·11	1·19	3·8
	PhF	14·9	1·69	0·86	1·8
	PhCl	17·5	1·51	0·93	2·3
	PhBr	15·1	0·92	1·19	2·7
	PhI	16·4	1·68	1·12	2·8
Me_3CBr	C_6H_6	32·5	1·15	1·23	3·8
	PhF	16·4	1·51	0·90	2·2
	PhCl	17·8	1·77	0·83	1·6
	PhBr	26·1	1·54	0·99	0·3
Me_3CI	C_6H_6	35·4	1·39	1·00	2·7
	PhF	21·4	1·82	0·88	1·8
	PhCl	24·0	1·57	0·84	1·9

[a] By extrapolation to 0° K; ±3 c/s. [b] at 25°C; [c] ±0·25 Kcal.

ΔH and ΔS were obtained in the usual fashion (Fig. 3 is an example plot of log K vs. $1/T$). The reproducibility of ±3 c/s in $\Delta\delta$ corresponds to ±0·25 kcal in ΔH and

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[6] This treatment neglects the possibility of a solute molecule being associated with more than one solvent molecule[7] (*vide infra*), and also the possibility that δ_c might be a function of temp. Thus it is probably specious to attach significance to the precise magnitude of the quantities derived.

[7] For an example of this complication, see P. J. Trotter and M. W. Hanna, *J. Am. Chem. Soc.* **88**, 3724 (1966).

[8] Shifts in CCl_4 soln were independent of temp within experimental error.

TABLE 2. SOLVENT EFFECTS ON ADAMANTYL HALIDE SPECTRA

Compound	Solvent	$\Delta\delta_o$, c/s[a]	$\Delta\delta_o$, c/s[b]	K[c], m.f.$^{-1}$	$-\Delta H$, Kcal[d]	$-\Delta S$, e.u.[c]
$C_{10}H_{15}Cl$	C_6H_6	29·0	34·5	1·18	1·09	3·3
	PhF	29·3	28·4	0·77	1·07	4·1
	PhCl	[e]	26·8	0·89	1·08	3·8
	PhI	[e]	20·3	1·51	1·07	2·3
$C_{10}H_{15}Br$	C_6H_6	33·5	35·5	1·24	0·82	2·3
	PhF	26·6	29·9	1·00	0·96	3·2
	PhCl	24·6	26·7	1·03	1·00	3·3
	PhI	[e]	20·5	1·72	1·03	1·6
$C_{10}H_{15}I$	C_6H_6	[e]	40·0	1·24	0·92	2·6
	PhF	[e]	28·9	1·05	1·01	3·3
	PhCl	[e]	27·7	1·15	1·03	3·2
	PhI	[e]	23·0	1·59	1·04	2·3

[a] For γ (bridgehead) protons, by extrapolation to 0° K; ±3 c/s.

[b] For δ (methylene) protons, by extrapolation.

[c] At 25°C; ave. for γ and δ.

[d] ±0·25 Kcal; ave.

[e] Resonance incompletely resolved.

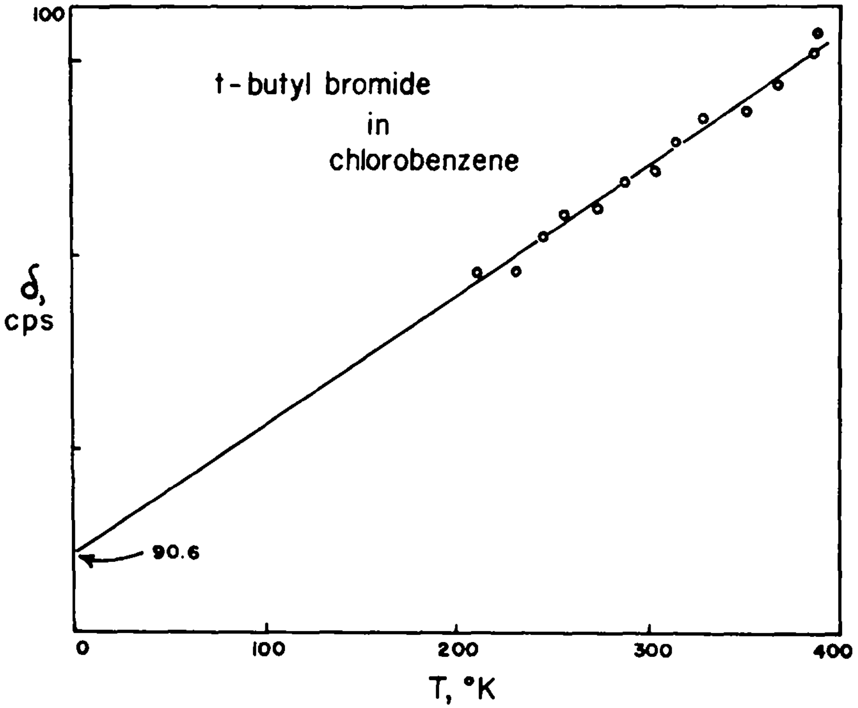

FIG. 2. Temperature dependence of the chemical shift of t-butyl bromide in chlorobenzene solution.

± 1·0 e.u. One notes that all of the values given fall within this range; that is, all are identical, within experimental error.

No data are given for the β protons of the adamantane derivatives. As remarked above, the shifts are very close to zero, and within experimental error, are invariant with temperature. In several solvents, the γ resonance was not sufficiently resolved from the β or δ to permit unambiguous assignment of chemical shift. Aside from these indicated instances, the data on the adamantanes represent averages of the values derived from γ and δ shifts. The two values were in all cases within experimental error of each other.

It was observed also that addition of an aromatic substance to a solution of alkyl halide in carbon tetrachloride gave rise to shifts of the halide resonances. For example, both benzene and naphthalene added to a dilute solution of 1-bromoadamantane induce shifts, and a plot of δ vs. [ARH]/[AdBr] is linear (Fig. 4). This is a condition which must be satisfied if a complex is to be postulated, but the converse does not hold.[7]

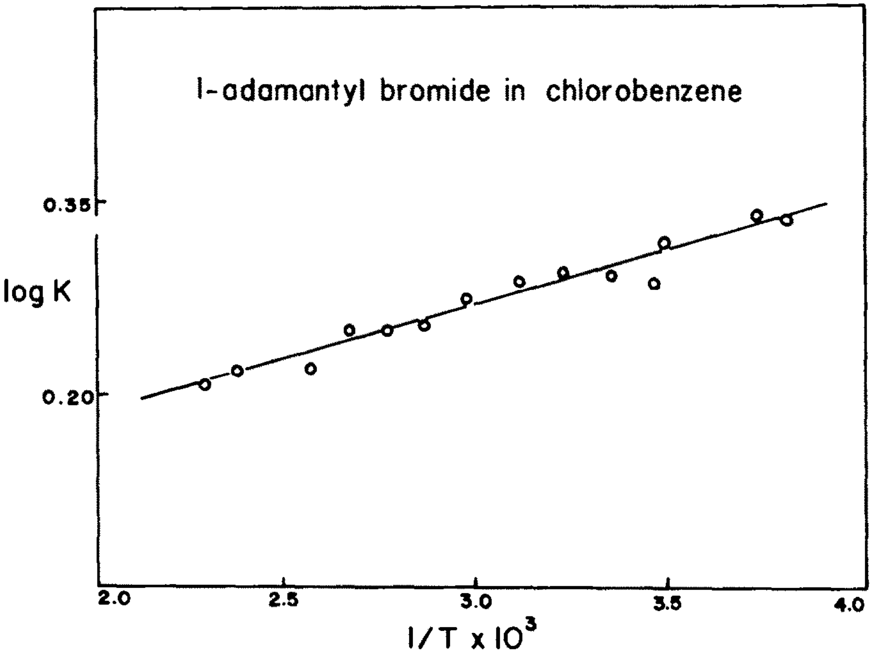

FIG. 3. Variation of equilibrium constant with temperature, 1-adamantyl bromide in chlorobenzene solution.

Freezing point diagrams. Freezing point diagrams are useful in detecting weak molecular interactions,[9] the usual observation being a maximum in the plot of freezing point against mole fraction at a mole ratio corresponding to the composition of the "compound". We have obtained such diagrams for mixtures of t-butyl chloride or bromide with benzene, fluorobenzene, and chlorobenzene. Each diagram is that of

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[9] E. g., L. W. Reeves and W. G. Schneider, *Canad. J. Chem.* 35, 251 (1957).

a typical two component eutectic, with no hint of complex formation. Although the precision of our measurements is not great (±2°C; see Experimental), the pronounced deviations from ordinary eutectic behavior observed in similar cases, such as the

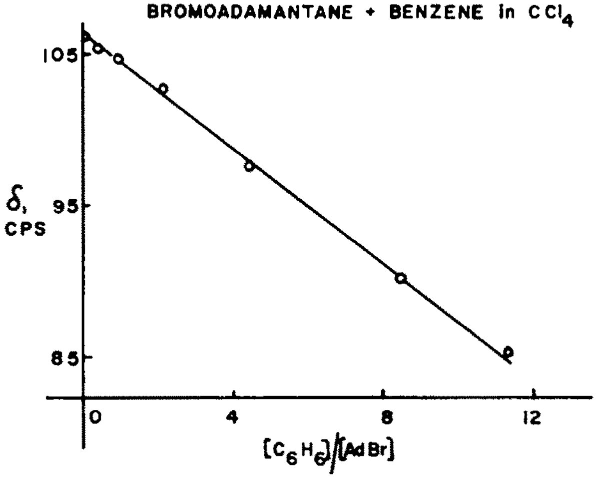

FIG. 4. "Titration curve", 1-adamantyl bromide and benzene in carbon tetrachloride.

TABLE 3. FREEZING POINT MEASUREMENTS

Mixture	Eutectic temp	Mole fraction halide
Me_3CCl–C_6H_6	−71°	0·76
Me_3CBr–C_6H_6	−65°	0·75
Me_3CCl–C_6H_5F	−77°	0·60
Me_3CBr–C_6H_5F	−80°	0·47
Me_3CCl–C_6H_5Cl	−75°	0·52
Me_3CBr–C_6H_5Cl	−78°	0·55

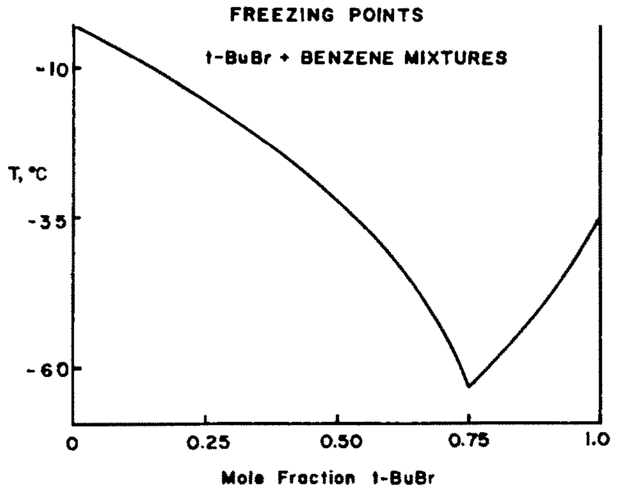

FIG. 5. Freezing point curve, system: t-butyl bromide and benzene.

benzene–hexafluorobenzene system,[10, 11] suggest that we should be able easily to detect compound formation. Table 3 and Figs 5–7 present the data.

DISCUSSION

It has been generally assumed that the solvent shifts in such systems as those investigated here are the result of complex formation.[2, 12–22] Analogy is drawn to the NMR behavior of such combinations as chloroform–benzene, in which a hydrogen bonded complex appears to exist.[9, 23–25] (Consideration of the anisotropy of the solvent susceptibility as a mechanism for the shifts is obviated by the use of an internal standard, TMS. This is particularly true since the standard and the solutes have essentially identical molecular shapes.[5, 9]). The bonding of the two components is

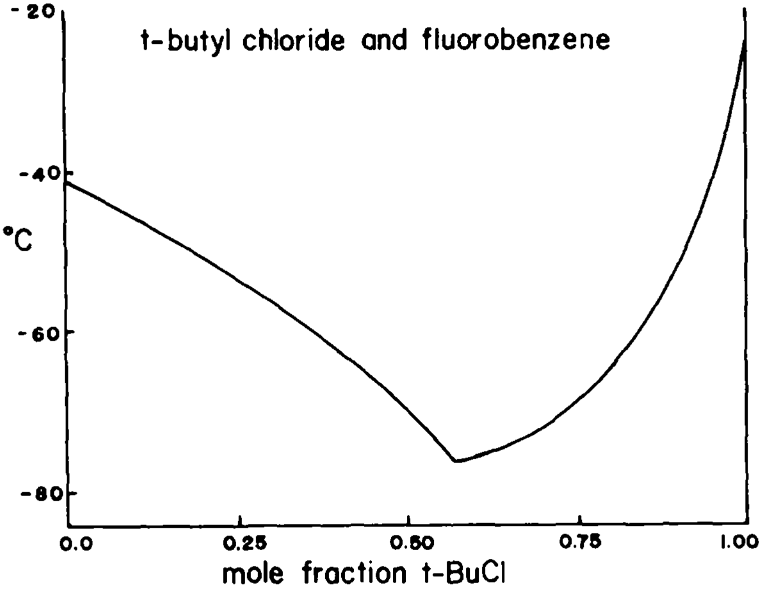

FIG. 6. Freezing point curve, system: t-butyl chloride and fluorobenzene.

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[10] W. A. Duncan and F. L. Swinton, *Trans. Farad. Soc.* **45**, 1082 (1966).

[11] We are presently carrying out NMR investigations of various systems containing hexafluorobenzene.

[12] P. Laszlo, *Bull. Soc. Chim. Fr.* 85 (1964).

[13] D. H. Williams and N. S. Bhacca, *Tetrahedron* **21**, 1641; 2021 (1965).

[14] J. E. Baldwin, *J. Org. Chem.* **30**, 2423 (1965).

[15] C. J. Timmons, *Chem. Comm.* 576 (1965).

[16] S. Bory, M. Fetizon, P. Laszlo and D. H. Williams, *Bull. Soc. Chim. Fr.* 2541 (1965).

[17] J. Seyden-Penne, T. Strazalko and M. Plat, *Tetrahedron Letters* 4597 (1965).

[18] R. E. Klinck and J. B. Stothers, *Canad. J. Chem.* **44**, 37 (1966).

[19] D. H. Williams and D. A. Wilson, *J. Chem. Soc.* (*B*), 144 (1966).

[20] A. A. Sandoval and M. W. Hanna, *J. Phys. Chem.* 7, 1203 (1966).

[21] R. G. Linck and R. E. Sievers, *Inorg. Chem.* **5**, 806 (1966).

[22] P. Laszlo and D. H. Williams, *J. Am. Chem. Soc.* **88**, 2799 (1966).

[23] P. von R. Schleyer, C. Wintner, D. S. Trifan and R. Bacskai, *Tetrahedron Letters* No. 14, 1 (1959).

[24] C. J. Creswell and A. L. Allred, *J. Phys. Chem.* **66**, 1469 (1962).

[25] We are investigating the NMR of some charge-transfer systems in hopes of developing a model for behavior of the simpler combinations discussed here.

suggested to result from polarization of the π-cloud of the aromatic by the dipole of the solute:[26] that is, a dipole-induced dipole interaction.[27] Holding the two components together in this way would cause the protons of the solute to sense the aromatic ring current, and thus experience an upfield or downfield shift depending upon their orientation relative to the aromatic molecule.

It is postulated that a complex is necessary to explain the success[16, 28] of Johnson–Bovey Treatments[29] of the induced shift. That is to say, the remarkable specificity observed for solvent induced changes in chemical shift seems to require a precisely defined relationship between the polar function of a solute molecule and an aromatic ring.

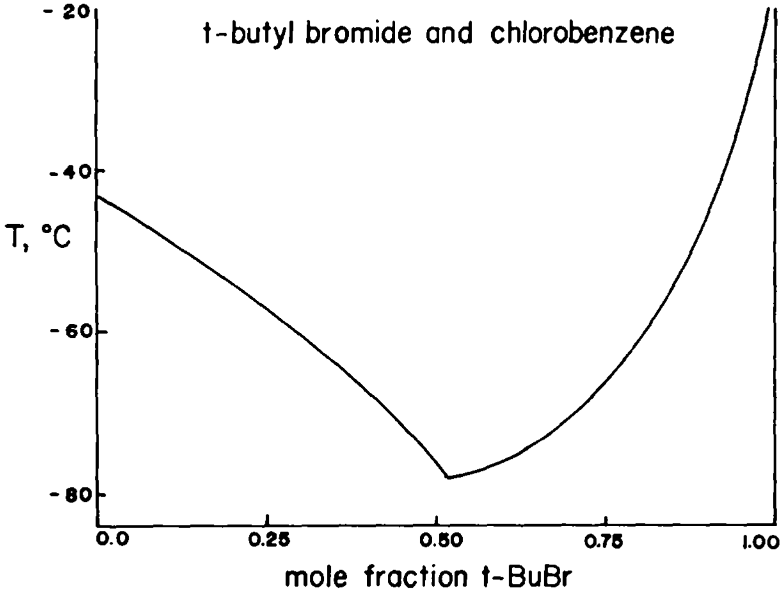

FIG. 7. Freezing point curve, system: t-butyl bromide and chlorobenzene.

Such specificity is observed in the present work. The choice of t-butyl to accompany adamantyl in this study was originally dictated by the similar geometries about the functional groups, coupled with the different overall steric situations. The comparison of the two sorts of halides leads to several interesting observations. As mentioned above, one observes no solvent shifts for the β protons of adamantane derivatives, whereas the t-butyl protons, bearing the same geometrical relationship to the substituent, are dramatically shifted. One is tempted to accommodate this result with the picture shown in Fig. 8 for adamantyl halides. The dipolar axis of the halide is very nearly parallel, about 20–25° off, to the plane of the aromatic ring, with the

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[26] It is necessary that the solute have a significant dipole moment for shifts to be observed. For example, adamantane itself has the same chemical shift in both benzene and carbon tetrachloride;[3] the shift is identical, 106·4 c/s, at 20° and 80° in benzene.

[27] W. G. Schneider, *J. Phys. Chem.* **66**, 2653 (1962).

[28] P. Laszlo and P. von R. Schleyer, *J. Am. Chem. Soc.* **86**, 1171 (1964).

[29] C. E. Johnson and F. A. Bovey, *J. Chem. Phys.* **29**, 1012 (1958).

affected γ and δ protons about 3·2–3·5 A distant.[30] The slight amount of tilt, upon whose origin we shall not speculate, is introduced in cognizance of the virtually zero effect of solvents upon the β protons. In this relative orientation, the Johnson–Bovey[29] ring current contributions reproduce well the observed benzene shifts. The picture is a reasonable one, for the benzene ring is known to have its greatest polarizability in the molecular plane.[27,31] The lesser shifts produced by the substituted aromatics may then be viewed as the result of repulsion between the two permanent dipoles, which would increase the distance between the molecules, and the known[32] reduction of ring current by electronegative substituents.

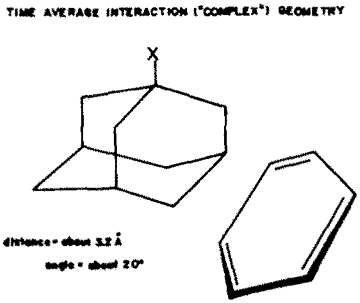

FIG. 8. Average geometry of the interaction between adamantyl halides and benzene.

Yet, continued comparison of adamantyl with t-butyl discourages such a neat picture. There appears to be no significant difference in the magnitudes of the interactions to which the two molecules give rise. Although the t-butyl shifts are in every case slightly smaller, the thermodynamic parameters do not vary in passing from adamantyl to t-butyl. This would seem to indicate that the closeness of approach of the solute dipole to the solvent molecule is not of prime importance to the solvent shifts.

A similar conclusion was reached by Connolly and McCrindle[33] from their study of hindered ketones. They pointed out that substantial solvent shifts are observed for compounds such as 2,2,6,6-tetramethylcyclohexanone which one would expect to be sterically prevented from forming a 1:1 complex.

Despite the apparent necessity[34] of postulating complex formation to explain geometrically specific shifts, and temperature dependence, and "titration" curves; and in addition to the weak objections raised above, one notes that the freezing point diagrams give no evidence of specific complexing. This would seem to be a most significant point. It might mean that the interaction is too weak to be detected by a

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[30] Baldwin[14] has pointed out that a 1:1-complex has 5 degrees of freedom, and thus five chemical shift parameters are needed to specify its geometry. Assuming for the argument of the moment that we are discussing such a complex, we have available the five shifts: those for the 4 geometrically non-equivalent types of protons in adamantyl, and that of the t-butyl model.

[31] Y. K. Syrkin and M. E. Dyatkina, *Structure of Molecules and the Chemical Bond*, Chap. 10. Butterworth, London (1950).

[32] G. G. Hall, A. Hardisson and L. M. Jackman, *Disc. Faraday Soc.* 34, 15 (1962); *Tetrahedron*, Suppl. 2, 101 (1963).

[33] J. D. Connolly and R. McCrindle, *Chem. & Ind.* 379 (1965).

[34] cf., however, Ref. 22.

relatively crude technique, a view against which we have earlier argued. Alternatively, it may indicate that the interaction does not involve a specific number of molecules.

In common with Brown and Stark[35] we prefer the latter idea. We suggest that our data are most consistent with the origin of the solvent effects being a slight structuring of the solvent about each solute molecule, a sort of "cage construction". An indeterminate number of solvent molecules would be involved, each rapidly changing places with molecules from the bulk of the solvent. Solvent organization of this kind could give the geometrical effect, on the NMR time scale, of a long-lived complex, and yet would not be thermodynamically equivalent to one. This explanation requires that our measured equilibrium constants and enthalpies have no real meaning, except perhaps to indicate the order of magnitude of the interaction, since they were based on the presumably incorrect assumption of a 1:1 stoichiometry for the solute-solvent interaction.

EXPERIMENTAL

NMR spectra were obtained with a Varian A-60 spectrometer equipped with a variable temp probe. Chemical shifts were measured by interpolation from the precalibrated chart paper: while reproducible to ±0·2 c/s, they are not considered accurate to better than ±0·5 c/s. Since spectra of adamantanes are characterized[3] by a lack of strong coupling, no difficulty was experienced in locating the centers of completely resolved peaks. Solns for temp dependence studies were 1–2 mole %, prepared by weighing appropriate amounts of material on an analytical balance. All solns contained ca. 1% TMS as internal standard, and were sealed into the usual sample tubes.

t-BuCl and t-BuBr were Eastman White Label grade reagents, and were used as received. NMR indicated no impurities. t-BuI was taken up in diethyl ether and treated with $Na_2S_2O_3$ to remove I_2, and distilled *in vacuo* (b.p. 30° at 120 mm) just before use. The solns of this substance were initially colorless, but rapidly darkened (I_2) upon exposure to light or heat. The chemical shifts were not a function of color.

The adamantyl halides were prepared according to published procedures[4] and purified until their properties agreed with literature values.

CCl_4 and benzene were spectroquality solvents; all others were reagent grade, and were distilled prior to use. Naphthalene was reagent grade.

Freezing points were determined in a small air jacketed tube, using a calibrated low temp (toluene) thermometer. Super-cooling of the mixtures and the accuracy of the thermometer limit the reliability of the freezing points to no better than ±2°. Nevertheless, the smooth trend of the curves is apparent.

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[35] T. L. Brown and K. Stark, *J. Phys. Chem.* **69**, 2479 (1965).