Aromatic Nucleophilic Exchange Reactions. Part III.[1] Dipolar Aprotic Solvent Effects

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Rates of halogen exchange between potassium iodide and 1-iodo-2,4-dinitrobenzene have been measured in six dipolar aprotic solvents and the results compared with those obtained in methanol. The effect of changing from methanol to a dipolar aprotic solvent is interpreted in terms of an initial state entropy change.

In Part II [1] we studied the effect of a series of closely related alcohol solvents on the halide exchange between potassium iodide and 1-iodo-2,4-dinitrobenzene. The effect of solvent transfer on the rate constant was adequately described in terms of the change in solvent dielectric constant.

It is well known that for transfer between protic and dipolar aprotic solvents of comparable dielectric constant, reactions between anions and dipoles are often considerably faster in the dipolar aprotic medium.[2] Such solvent effects arise principally from changes in solute–solvent interactions, a measure of which is the change in activity coefficient on solvent transfer. The ratio of the activity coefficient of a solute in a standard solvent, often taken as methanol,[3] to that in a second solvent is often called the solvent activity coefficient [4]

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[1] Part II, D. F. Maundrell, C. H. Bovington, and B. Dacre, *J.C.S. Perkin II*, 1972, 1284.

[2] A. J. Parker, *Chem. Rev.*, 1969, 1. This review contains extensive references to earlier work.

[3] R. Alexander, E. C. F. Ko, S. J. Parker, and T. J. Broxton, *J. Amer. Chem. Soc.*, 1969, **91**, 5049.

[4] A. J. Parker, *Adv. Phys. Org. Chem.*, 1967, **5**, 173.

$_m\gamma_s$. The latter is directly related to the free energy of transfer of the solute between solvents.

Attempts have been made to determine solvent activity coefficients of single ions on the basis of certain extra-thermodynamic assumptions and these have been discussed in detail by Parker and Alexander.[5] Such solvent activity coefficients are often useful in kinetic studies as a means of discriminating between initial and transition state effects and the equivalent method employing free energies of transfer has been used by Abrahams.[6] This approach allows one to determine the source of observed effects, it does not however allow their calculation in terms of solute–solvent interactions nor is it usually possible to correlate such effects on rate with any single property of the solvent. Protic–dipolar aprotic solvent effects usually reflect changes in the enthalpy rather than entropy of activation.

In this paper we present data on the iodine exchange between potassium iodide and 1-iodo-2,4-dinitrobenzene in dimethylformamide (DMF), acetonitrile (AN), hexamethylphosphoramide (HMPA), dimethyl sulphoxide (DMSO), *N*-methyl-2-pyrrolidone (NMP), and propylene carbonate (PC). We conclude that an initial state entropy effect is the most important factor contributing to the change in rate on transfer from methanol to each of these solvents.

EXPERIMENTAL

Materials.—AnalaR potassium iodide and 1-iodo-2,4-dinitrobenzene were prepared and stored as previously described.[7] The dipolar aprotic solvents which were all B.D.H. laboratory reagents were dried over 2A molecular sieves and twice distilled at reduced pressure so that no b.p.s were greater than *ca.* 100 °C.

Method.—Iodine exchange was studied as already described [7] and in this work ^{125}I was used exclusively. Exchange rates have been calculated from the familiar McKay equation [8] in the form (1) where a and b are the concentra-

$$\log (1 - F) = -Rt(a + b)/2{\cdot}303ab \qquad (1)$$

tion of potassium iodide and 1-iodo-2,4-dinitrobenzene respectively, and F is fraction of exchange at time t. If, initially there is no activity in the organic compound then $F = x_t/x_\infty$ where x_t is the specific activity of the organic compound at time t and x_∞ is the corresponding equilibrium value. Values of the latter were obtained from reaction mixtures placed in a high temperature bath. Samples were taken until the specific activity remained sensibly constant.

Side Reactions.—Certain reaction mixtures develop colours on standing at 100 °C. Also the specific activity of the organic compound, recovered from such mixtures, was seen to rise to a maximum and then decrease slowly with time. Such behaviour was noted in DMSO and HMPA. The solid recovered from a 1-iodo-2,4-dinitrobenzene–DMSO solution held at 100 °C for four days had, after recrystallisation from 2 : 1 light petroleum (b.p. 80—100)–benzene, m.p. 128 °C. No detailed analysis was performed, but a sodium fusion test indicated that sulphur was present. A test for iodine was negative. The solid recovered from a 1-iodo-2,4-dinitrobenzene–HMPA mixture held at 75 °C for four days, had m.p. 61 °C. A sodium fusion test showed the presence of phosphorus and iodine.

On the assumption that the rate of decrease of the specific activity of labelled 1-iodo-2,4-dinitrobenzene is a rough measure of the rate of side reactions we are confident that our exchange data for DMSO are reliable certainly up to 85 °C. At this temperature the specific activity remains unchanged over a period of four days. For HMPA however, the results are much less reliable. The compound recovered from a solution of labelled 1-iodo-2,4-dinitrobenzene in HMPA showed a 25% decrease in its specific activity after four days at 65 °C and a further 71% decrease over a period of three days at 70 °C. Since the halide exchange half-life is *ca.* 2—3 h at 45 °C, x_t values taken over a period of *ca.* 3 h should be quite reliable, but a large error may be present in the x_∞ value as indicated by rate constants at 45 °C of $8{\cdot}3 \times 10^{-4}$ and $4{\cdot}4 \times 10^{-4}$ l mol^{-1} s^{-1} corresponding to similar concentration conditions. We simply note that the exchange is much faster in HMPA than in the other solvents. Our method for measurement of radioactivity has been described earlier.[1] The solubility of 1-iodo-2,4-dinitrobenzene was estimated by saturating solutions at the appropriate temperature and thermostatting for at least 24 h before sampling. Spectrophotometric and gravimetric methods were used to analyse the solutions. The solubility of potassium iodide was determined by adding a sample of a saturated solution (5 ml) to water (50 ml) and titrating against silver nitrate using sodium fluoresceinate as adsorption indicator. Potassium tetraphenylboron was determined gravimetrically.

RESULTS AND DISCUSSION

Our solubility data for 1-iodo-2,4-dinitrobenzene are recorded in Table 1. Values for potassium iodide and potassium tetraphenylboron are 0·50 and 0·45M respectively in HMPA at 25 °C. Free energies of transfer are given in Table 2. Those for iodide ion have, with the exception of the HMPA values, been calculated from the data of Alexander *et al.*[3] For HMPA we have combined our solubility values for potassium iodide and potassium tetraphenylboron with that of Alexander *et al.*[3] for tetraphenylarsonium tetraphenylboron (TATB), to give the solvent activity coefficient of iodide ion; from this the transfer free energy has been calculated and is included in Table 2.

TABLE 1

Solubility of 1-iodo-2,4-dinitrobenzene

Solvent	Solubility/M (°C)	Solvent	Solubility/M (°C)
MeOH	$0{\cdot}6_2$ (45)	AN	2·5 (25)
MeOH	0·25 (25)		
PC	3·0 (25)	DMF	3·8 (25)
DMSO	5·4 (25)	NMP	2·2 (25)
HMPA	3·6 (25)		

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[5] A. J. Parker and R. Alexander, *J. Amer. Chem. Soc.*, 1968, **90**, 3313.

[6] M. H. Abrahams, *J. Chem. Soc.* (*A*), 1971, 1061 and earlier papers.

[7] C. H. Bovington, D. F. Maundrell, and B. Dacre, *J. Chem. Soc.* (*B*), 1971, 767.

[8] H. A. C. McKay, *Nature*, 1938, **142**, 99F.

Table 3 is a summary of our rate measurements, and in Table 4 derived activation parameters are listed. The agreement between $\Delta\Delta G^{\ddagger}$ values in columns 5 and 6 is an indication of the reliability of the activation parameters. Kendall *et al.*[9] record figures of $\Delta\Delta G^{\ddagger} = -13{\cdot}3$ kJ mol^{-1}, $\Delta\Delta H^{\ddagger}$ *ca.* 1·3 kJ mol^{-1}, and $\Delta(T\Delta S^{\ddagger}) = 12{\cdot}0$ kJ mol^{-1} for transfer to DMF.

TABLE 2

Initial state transfer free energies from methanol to dipolar aprotic solvent at 25 °C

Solvent	$\Delta G_t(\text{I}^-)$/ kJ mol^{-1} [a]	ΔG_t(2,4-DNIB)/ kJ mol^{-1}	ΔG_t(Initial state)/ kJ mol^{-1}
PC	17·1	−6·2	10·9
DMSO	7·4	−7·7	−0·3
HMPA	26·7	−6·6	20·1
AN	13·7	−5·8	7·9
DMF	14·8	−6·8	8·0
NMP	17·1	−5·4	11·7

[a] Data of ref. 3 and see text.

For activated S_NAr reactions in protic solvents the $T\Delta S^{\ddagger}$ terms are typically −12 to −17 kJ mol^{-1}.[9] Normally in the transfer from polar to dipolar aprotic solvent $T\Delta S^{\ddagger}$ changes little and the observed large changes in the reaction rate are attributable to decreases in $\Delta H^{\ddagger}$. On the other hand when the incoming nucleophile and leaving group are attached to the aromatic ring by second or higher row atoms then $T\Delta S^{\ddagger}$ in protic solvents is low and typically values of −25 to −29 kJ mol^{-1} [10] are observed, as for instance in the reactions of thiocyanate and iodide ion with 1-iodo-2,4-dinitrobenzene in methanol [11] (heavy atom effect). Rates of such reactions are less sensitive to solvent transfer than reactions of smaller ions such as chloride,[9] bromide,[9-12] and azide.[12]

In the present work we note that the heavy atom effect is absent in dipolar aprotic solvents and that $T\Delta S^{\ddagger}$ values are quite normal. In addition $\Delta H^{\ddagger}$ does not change appreciably on solvent transfer and may in some cases be higher in the dipolar aprotic solvents than in methanol although there is appreciable uncertainty in $\Delta\Delta H^{\ddagger}$. Changes in $T\Delta S^{\ddagger}$ may therefore be chiefly responsible for the increase in reaction rate.

TABLE 3

Second order rate constants: *a* denotes the stoicheiometric concentration of potassium iodide and *b* that of 1-iodo-2,4-dinitrobenzene in the reaction mixture

Solvent	10^2a/M	10^2b/M	T/°C	10^6k/l mol^{-1} s^{-1}
PC	5·061	2·501	85·0	480
	5·070	2·540	75·0	165
	5·000	2·539	65·0	66·5
	4·987	2·505	55·0	30·5
	4·977	2·533	45·0	5·68
	4·878	4·850	45·0	5·43
DMSO	9·989	2·492	95·0	1,208
	10·02	2·520	85·0	347
	9·994	2·502	85·0	360
	10·01	2·419	75·0	110
	10·05	2·533	65·0	31·4
	10·04	2·489	55·0	12·9
	10·01	5·00	45·0	4·45
	10·04	2·510	45·0	3·99
	5·01	2·532	45·0	4·48
	10·04	2·524	36·0	1·44
AN	6·522	2·706	70·0	107·5
	6·111	2·719	60·0	35·5
	5·997	2·505	45·0	9·63
	6·005	4·997	45·0	9·43
	3·014	2·511	45·0	7·80
	6·022	2·505	35·0	2·0
	6·013	2·516	26·0	0·50
DMF	10·00	2·506	100·0	6,810
	10·00	2·520	85·0	1,090
	9·99	2·503	65·0	195
	10·02	2·530	45·0	23·5
	10·01	5·00	45·0	20·6
	4·999	2·502	45·0	19·8
	5·008	2·502	45·0	24·8
	9·993	2·500	30·0	2·38
NMP	9·999	2·569	85·0	3,600
	10·01	2·513	75·0	1,072
	10·00	2·512	65·0	0·513
	10·01	2·534	55·0	234
	10·02	2·519	45·0	64·0
	10·04	5·013	45·0	57·2
	5·195	2·506	45·0	69·9

TABLE 4

Activation parameters

Solvent	$\Delta H^{\ddagger}$ kJ mol^{-1}	$T\Delta S^{\ddagger}$ kJ mol^{-1}	$\Delta G^{\ddagger}$ kJ mol^{-1}	$\Delta\Delta G^{\ddagger}$ [a] kJ mol^{-1}	$\Delta\Delta G^{\ddagger}$ [b] kJ mol^{-1}	$\Delta\Delta H^{\ddagger}$ kJ mol^{-1}	$\Delta(T\Delta S^{\ddagger})$ [c] kJ mol^{-1}	Initial state $\Delta\Delta G$ [d] kJ mol^{-1}
MeOH [e]	97·4 (0·5)	−22·3 (0·4)	119·7					
PC	98·0 (1·5)	−11·6 (1·5)	109·6	−10·1	−10·1	0·6	10·7	10·9
DMSO	102·7 (2·6)	−8·2 (2·5)	110·9	−8·8	−9·0	5·3	14·1	−0·3
AN	99·4 (5·8)	−10·0 (5·8)	109·4	−10·3	−10·9	2·0	12·3	7·9
DMF	98·9 (3·5)	−7·8 (3·4)	106·7	−13·0	−13·3	1·5	14·5	8·0
NMP	90·2 (4·4)	−13·4 (4·2)	103·6	−16·1	−16·1	−7·2	8·9	11·3

[a] Calculated from slope and intercept of log (k/T) against $1/T$. [b] Calculated from $\Delta\Delta G^{\ddagger} = 2{\cdot}303RT\log_{10}(k_m/k_s)$. [c] At 45 °C. [d] Initial state $\Delta\Delta G$ refers to 25 °C. [e] Values quoted are based on a combination of ours[7] and those of Kendall and Miller [*J. Chem. Soc.* (*B*), 1967, 119]. All $\Delta\Delta X$ terms refer to the transfer from methanol to the solvent. Standard errors were obtained from the slope and intercept of the line log (k/T) against $1/T$ by applying the method of least squares. Figures are given in parentheses.

Initial and Transition State Effects.—The data in Table 4 show, with the possible exception of DMSO, that we are dealing with an essentially initial state effect

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[9] F. H. Kendall, J. Miller, and R. Wong, *J. Chem. Soc.* (*B*), 1971, 1521.

[10] D. L. Hill, K. C. Ho, and J. Miller, *J. Chem. Soc.* (*B*), 1966, 2299.

[11] J. Miller, *J. Amer. Chem. Soc.*, 1963, **85**, 1628.

[12] J. Miller and A. J. Parker, *J. Amer. Chem. Soc.*, 1961, **83**, 117.

(compare columns 5 and 6 with 9). The fact that the initial state data refer to 25 whilst activation data refer to 45 °C should not affect our general conclusions. We conclude that the major reason for the increase in rate is an entropy change in the initial state.

In the case of DMF it is possible to estimate the individual contributions to the transfer entropy for 1-iodo-2,4-dinitrobenzene and iodide ion employing published results on transfer enthalpies. These have been quoted as —14·4 [13] and —15·1 [14] kJ mol^{-1} for 1-iodo-2,4-dinitrobenzene and iodide respectively.

We combine these with the corresponding transfer free energies in Table 2, columns 2 and 3 to give $\Delta(T\Delta S) = -7{\cdot}6$ for 1-iodo-2,4-dinitrobenzene and —29·9 kJ mol^{-1} for iodide ion based on the TATB assumption. Hence in combination with our kinetic result these values yield $\Delta(T\Delta S) = -23{\cdot}0$ kJ mol^{-1} for the activated complex. It is tempting to compare the latter figure with that for iodide ion and hence to suggest appreciable charge localised on iodide at the reaction centre. However in view of the extra thermodynamic assumptions necessary in the calculation of single ion transfer values [14] there is appreciable uncertainty in the above $\Delta(T\Delta S)$ figure *e.g.* if the iodide ion transfer enthalpy is based on the butylammonium assumption, then calculated values of $\Delta(T\Delta S)$ for activated complex and initial state are —16·5 and —32·0 kJ mol^{-1} respectively with iodide ion contributing —24·4 kJ mol^{-1} to the latter value. Any detailed mechanistic conclusion must therefore be treated with caution.[15]

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[13] P. Haberfield, L. Clayman, and J. S. Cooper, *J. Amer. Chem. Soc.*, 1969, **91**, 787.

[14] R. Fuchs, J. L. Bear, and R. F. Rodewald, *J. Amer. Chem. Soc.*, 1969, **91**, 5797.

[15] J. F. Coctzee and W. R. Sharpe, *J. Phys. Chem.*, 1971, 3141.