991. *Energy–Entropy Relationships in Salt Formation from Dialkylanilines and Alkyl Halides.*

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The formation of quaternary ammonium salts from dimethylaniline and alkyl halides has been followed in nitrobenzene and in nitrobenzene–chlorobenzene mixtures. The mode of decomposition of the salts has been investigated, since this affects the kinetic results. The major effect of the structure of the reactants is to change the rate through variation of E, but the value of A may also change. There is some " compensation " when the halide, the alkyl groups attached to nitrogen, and, in reactions with ethyl iodide but not in those with methyl iodide, when the ring substituents in the base are varied. Doubt is thrown on some earlier ideas about the stereochemistry of the transition complex. Use of less polar solvents increases E and the rate of the reverse reaction.

In a series of reactions involving moderate changes of structure or solvent, entropies and enthalpies of activation (or reaction) may vary. Three types of behaviour are found: (*a*) ΔS^* remains constant while ΔH^* varies, *e.g.*, when a substituent that is varied is separated from the reaction centre by a benzene ring;[1] (*b*) ΔH^* remains constant while

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[1] (*a*) Williams and Hinshelwood, *J.*, 1934, 1079; Stubbs and Hinshelwood, *J.*, 1949, S 71; Ingold and Nathan, *J.*, 1936, 222; Bradfield and Jones, *J.*, 1928, 1006, 3073; Bradfield, Jones, and Spencer, *J.*, 1931, 2907; (*b*) Venkataraman and Hinshelwood, *J.*, 1960, 4977, 4986; (*c*) Laidler, *J.*, 1938, 1786; (*d*) Evans, Watson, and Williams, *J.*, 1939, 1345.

variations in ΔS^* modify the rate, *e.g.*, when solvents are varied through a related series or a solvent is modified by pressure;[1b, 2-4] or (*c*) ΔS^* and ΔH^* both vary, large values of ΔH^* often being associated with large values of ΔS^*, so that the resulting change in rate is less than the variation of either quantity alone would indicate, and a sort of " compensation " is found;[5, 6] it is sometimes objected that this type of correlation could arise through experimental error.[5, 7]

The present paper reports a study of the formation and decomposition of quaternary ammonium salts derived from dimethylaniline, in nitrobenzene and in mixtures of chlorobenzene with nitrobenzene. Attention has been given to the variations in A and E caused by modification either of the structure of the reactants or of the solvent.

Structural modifications provided examples of all the above three types of behaviour, the major effect being due to change in E. The value of A also varies, so that there is some " compensation," when the alkyl groups attached to nitrogen, the halogen, and, in reactions with ethyl iodide, ring substituents are changed. However, when ring substituents are varied in quaternisations by methyl iodide, the value of A remains more or less constant, and a comparison of the two reaction series throws doubt upon some earlier ideas about the stereochemistry of the transition complex.

Equilibrium constants could be measured in several cases, and a consideration of these supports views of the transition complex based on the kinetic results.

Three reactions were studied in nitrobenzene–chlorobenzene mixtures. The rate of the forward reaction depends mainly on E, which rises as the proportion of chlorobenzene in the solvent increases. The rate of the reverse reaction is greater in the solvents of low polarity, leading to the unusual circumstance that slower reactions have a shorter " half-life " than faster ones.

EXPERIMENTAL

Apparatus.—Grade " A " burettes were used, and pipettes were calibrated both with water and with nitrobenzene. Thermometers were checked against others calibrated at the National Physical Laboratory and were used under the specified conditions. Thermostat-baths at 6°, 25°, 40°, 60°, 80°, and 120° were controlled within $\pm 0{\cdot}1°$. Electrically heated boilers were used at 100° and 140°, the former containing water, and the latter *m*-xylene, and to overcome variation of b. p. with barometric pressure, the temperatures of individual experiments were checked.

Materials.—" AnalaR " nitrobenzene and laboratory-grade chlorobenzene were used. Solvent mixtures were prepared by weight and were checked by their densities.

NN-Dimethyl-*p*-anisidine was prepared by Bordwell and Boutan's method.[8] Other reactants were laboratory-grade reagents, purified by distillation or recrystallisation.

Solutions of volatile reactants were prepared by addition to a weighed amount of solvent in a weighed flask and adjusted by dilution. Analysis of the solutions was not practicable, and a comparison was always made of results obtained with independently prepared solutions. The reproducibility was mostly within $\pm 2\%$, corresponding to reproducibilities in E or $\log A$ within $\pm 0{\cdot}05$. The real error may be greater, but, if so, it is probably uniform throughout and will not invalidate the comparisons made below.

Techniques.—(*a*) *Reactions.* Equal quantities, usually 10 ml., of the two reactant solutions were pipetted into ampoules which were sealed and placed in a thermostat-bath. At intervals ampoules were removed, cooled in ice, and washed, ready for analysis. With rapidly reacting systems the ampoules were cooled in ice during the filling and sealing; with the fastest reactions partly filled ampoules were cooled in ice–alcohol, and the second solution was added on top of

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[2] Grimm, Ruf, and Wolf, *Z. phys. Chem.*, 1931, *B*, **13**, 309; Pickles and Hinshelwood, *J.*, 1936, 1353.

[3] Gibson, Fawcett, and Perrin, *Proc. Roy. Soc.*, 1935, **150***A*, 223.

[4] Harris and Weale, *J.*, 1961, 146.

[5] Leffler, *J. Org. Chem.*, 1955, **20**, 1202; Blackadder and Hinshelwood, *J.*, 1958, 2721, 2728.

[6] Rüetschi, *Z. phys. Chem.* (*Frankfurt*), 1958, **14**, 277.

[7] Hammett, " Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 123; Purlee, Taft, and DeFazis, *J. Amer. Chem. Soc.*, 1955, **77**, 837.

[8] Bordwell and Boutan, *J. Amer. Chem. Soc.*, 1956, **78**, 89.

the frozen mass. The ampoules were sealed and placed in a thermostat-bath, melting and mixing quickly taking place. For work at 25° or 6° the reactant solutions were immersed in the thermostat-bath to attain the temperature of the bath before being mixed.

(*b*) *Analysis.* The basic method was extraction of the quaternary ammonium salt with water, followed by the Volhard titration of the ionisable halide with 0·02M-silver nitrate. Further reaction during the extraction was prevented by dilution with light petroleum; this also facilitated extraction since it floated the organic phase and lowered the solubility of the quaternary salt. This method, besides being somewhat tedious, was inaccurate in the earliest stages of the reaction. Conductivity has been used for following similar reactions,[9,10] and one such method [10] was adapted slightly for the present work. It proved to be of great help in measuring small amounts of reaction, besides being quicker than the extraction–titration procedure. It was not absolute, but was calibrated against the extraction–titration method for each reaction, taken, however, to an extent where accurate titration became possible. The reactions of *p*-dimethylaminobenzaldehyde gave anomalous calibration curves; this was traced to the autoxidation of the benzaldehyde (to give small amounts of perbenzoic acid, which contributed to the conductivity of the solution) and was eliminated by flushing the ampoules with oxygen-free nitrogen before and after filling.

(*c*) *Solubilities and melting points.* The solubility of several salts in nitrobenzene at 25° was measured. Equal quantities of the two reactant solutions were mixed in an ampoule, which was then sealed and kept at 25° for several weeks, in which time crystals were often formed. The mixtures were filtered into a receiver in a thermostat-bath. Aliquot parts were then analysed by extraction and titration. The residue after filtration was recrystallised to constant m. p. from ethanol–light petroleum.

Kinetic Relations.—(*a*) *Reactions in nitrobenzene.* The formation of quaternary ammonium salts based on dimethylaniline has, in the past,[1d,9–16] given good second-order constants. Some reactions in nitrobenzene have been found to be reversible,[1c,4,13] but good constants were claimed and equilibrium constants were reported.

The present work began with a study of the reaction of dimethylaniline with ethyl iodide in nitrobenzene, shown to be reversible by the rapid fall of the second-order rate constants. Equilibria were measured and equilibrium constants calculated. The rate law is

$$\mathrm{d}x/\mathrm{d}t = k_1(a - x)^2 - \mathrm{k}_2x, \tag{1}$$

where a is the initial concentration of either reactant, and x is the concentration of product at time t. If y is the value of x at equilibrium, then

$$K = k_1/k_2 = y/(a - y)^2. \tag{2}$$

These equilibrium constants gave a van't Hoff plot.

Integration of equation (1) and substitution from (2) gives

$$k_1t = \frac{2{\cdot}303y}{(a^2 - y^2)} \log\left[\frac{(a^2 - xy)y}{a^2(y - x)}\right]. \tag{3}$$

Application of this equation to the results, however, gave poor values of k_1, which fell with increasing values of x. This was traced to the influence of an " exchange " reaction. The " mixed " salt formed can decompose in two ways:

$$\mathrm{Ph{\cdot}NMe_2Et^+I^-} \rightleftharpoons \mathrm{Ph{\cdot}NMe_2 + EtI}$$

$$\mathrm{Ph{\cdot}NMe_2Et^+I^-} \rightleftharpoons \mathrm{Ph{\cdot}NMeEt + MeI}$$

The latter was found to be the more important, but the decomposition products reacted, not only with each other, but also with the initial reactants, giving a final equilibrium mixture of

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[9] Chow and Fuoss, *J. Amer. Chem. Soc.*, 1958, **80**, 1095.

[10] Preston and Jones, *J.*, 1912, 1930.

[11] Clarke, *J.*, 1910, 416.

[12] Thomas, *J.*, 1913, 594.

[13] Essex and Gelormini, *J. Amer. Chem. Soc.*, 1926, **48**, 882.

[14] Evans, Watson, and Williams, *J.*, 1939, 1348.

[15] Benkeser, DeBoer, Robinson, and Sauve, *J. Amer. Chem. Soc.*, 1956, **78**, 685.

[16] Hamann and Teplitzky, *Discuss. Faraday Soc.*, 1956, **22**, 114.

little significance. During the early stages of the reaction there is only a low concentration of the decomposition products and the appearance of ionisable halogen will be due to reaction of the initial reagents. When no " exchange " was possible, as in the reaction between ethyl iodide and a diethylaniline, or in quaternisation of a dimethylaniline with methyl iodide, the kinetic law (1) was obeyed. For the last mentioned reactions the equilibrium constants were not quite independent of the concentration, showing that there was a slight ionisation of the salt, as previously reported.[1c]

Crystals (subliming at 210—211°) were obtained in the reaction of ethyl iodide and *NN*-dimethyl-*p*-toluidine at 25° and were shown to be trimethyl-*p*-toluidinium iodide which also sublimed at 210—211°.

The reaction between methyl iodide and *N*-ethyl-*N*-methylaniline comes to a transitory equilibrium (44·5% of a quaternary salt) after 7 hours at 80°, but after a further 120 hours only 37% of salt are present. Calculations based on the first stage of the reaction and the transient equilibrium gave good rate-constants (cf. upper curve of Fig. 1). This suggests that, although most of the salt decomposes into the initial reactants, a small amount gives ethyl iodide which is initially unimportant but affects the final equilibrium. The reaction of diethylaniline with methyl iodide gave similar results.

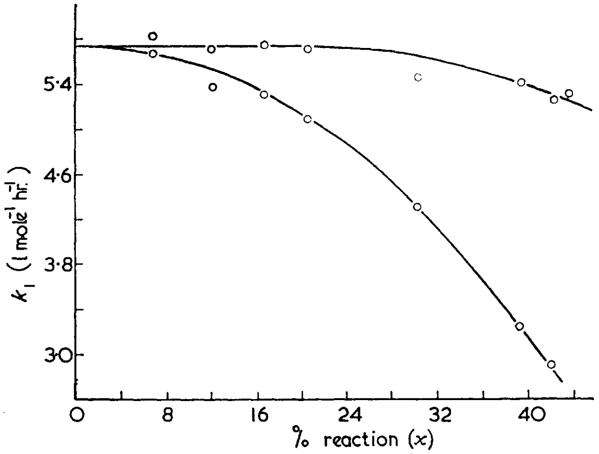

Fig. 1. Rate constants for the reaction of methyl iodide with *N*-ethyl-*N*-methyl-aniline. The points on the upper curve were calculated from equation (1), those of the lower curve from equation (4).

The quaternisation of dimethylaniline by allyl iodide obeys equation (1), although quaternisation by ethyl, n-propyl, or n-butyl iodide, does not. Allyldimethylanilinium iodide decomposes 30 times faster than trimethylanilinium iodide, probably owing to the differing bond strengths.

In the reactions yielding good rate constants, an accurate value of k_1 was also obtained by plotting x against values of k_3 obtained from the equation,

$$dx/dt = k_3(a - x)^2 \qquad (4)$$

and extrapolating these to zero reaction (cf. lower curve of Fig. 1). Values of k_1 were therefore calculated for the other systems by this means. When the conductivity method was used to measure very slow reactions it was sometimes possible to calculate k_1 from the initial tangents. After correcting for the thermal expansion of the solvent, good Arrhenius plots were obtained.

When it was known that the " exchange " reaction did not take place, equilibrium constants were calculated from a directly measured equilibrium or, when this was impossible, by trial-and-error substitution into equation (3) until good values of k_1 were obtained.

(*b*) *Reactions in mixed solvents.* For solvents containing 0—60% of chlorobenzene the methods outlined above were satisfactory, but not for solvents containing 80% or more of chlorobenzene because of the extremely small equilibrium constants, the " exchange " reaction, and the formation of a solid product. The influence of the solvent was such that in some cases the maximum conversion was less than 1%. In a few cases a secondary product, different from the initial product and formed in an " exchange " reaction, completely obscured the initial reaction. All the reactions studied produced a solid salt in some solvents, and this caused autocatalysis in some cases. In addition, the observed rate was sometimes dependent on the rate of crystallisation, as reported by Edwards.[17]

DISCUSSION

Structural Variations.—Among many studies of quaternary ammonium salt formation,[10-12,15,16,18,19] relatively few [1c,d,9,14,20] have been concerned with the temperature-dependence of reactions of dimethylaniline. This was studied in the present work, which involves a systematic variation of the alkyl groups in both the base and halide, of the halogen, and of ring substituents in the base.

Tables 1—4 give results for reactions in nitrobenzene. Measurements were made at four temperatures at least, and rate constants were corrected for the thermal expansion of the solvent. Activation energies and frequency factors were calculated by the method of

TABLE 1.

Summary of rate constants (10^2k_1, in l. mole^{-1} hr.$^{-1}$) at different temperatures for quaternisation of a base $R\cdot C_6H_4\cdot NR'_2$.

Reaction no.	R	R′	120·1°	100°	80°	60°	40°	25°	6°
With MeI.									
1	H	Me	—	—	985	319	103	39·6	—
2	*p*-CHO	Me	—	—	7·015	1·82	0·362	0·104	—
3	*m*-NO_2	Me	—	—	21·0	5·94	1·945	0·440	0·0979
4	*p*-Br	Me	—	—	197	62·6	16·8	6·27	—
5	*o*-Me	Me	—	—	47·35	11·5	2·98	0·73	0·292 †
6	*m*-Me	Me	—	—	1250	453	134	49·0	10·9
7	H	Me/Et *	—	—	604	192	51·8	22·8	4·74
8	H	Et	—	—	100·5	25·05	6·57	1·71	0·297
With EtI.									
9	H	Et	47·7	30·3	9·02	2·23	0·261	—	—
10	*m*-Me	Et	94·9	37·2	12·6	2·815	0·747	—	—
11	*p*-Me	Et	140	51·6	17·8	4·71	1·195	—	—
12	H	Me/Et *	—	—	54·2	15·7	4·48	1·49	—
13	H	Me	—	—	78·3	25·6	7·31	2·51	0·449
14	*m*-NO_2	Me	—	—	0·653	—	—	—	—
15	*o*-Me	Me	—	—	1·82	—	—	—	—
16	*p*-CHO	Me	—	4·00	0·894	0·192	0·0314	0·00755	—
17	*p*-Br	Me	—	—	17·5	4·36	1·22	0·352	0·0645
18	*m*-Me	Me	—	—	126	39·6	10·4	4·03	0·962
19	*p*-Me	Me	—	—	274	95·5	31·7	11·6	—
20	*p*-MeO	Me	—	—	425	165	51·0	20·5	3·8 †
21	*p*-NO	Me	—	—	176	59·2	16·6	4·40	2·27
With EtBr.									
22	H	Et	4·53	1·54	0·392	0·0780	0·0185	—	—
23	H	Me	—	34·9	7·99	2·22	0·521	—	—
24	*p*-Me	Me	—	—	22·5	6·00	1·45	0·443	—
With Pr^nI.									
25	H	Me	—	—	14·6	5·02	1·13	0·467	—
With Bu^nI.									
26	H	Me	—	33·2	11·8	3·25	0·764	0·211	—
With $CH_2{:}CH\cdot CH_2I$.									
27	H	Me	—	—	2490	940	333	143	46·2

* Ph·NMeEt. † These values were not used in the calculations of E and $\log_{10}A$ (Table 3).

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[17] Edwards, *Trans. Faraday Soc.*, 1937, **33**, 1294.
[18] Long, *J.*, 1911, 2164.
[19] Davis and Lewis, *J.*, 1934, 1599.
[20] Davis, *J.*, 1938, 1865.

TABLE 2.

Summary of equilibrium constants (K in l. mole^{-1}) at different temperatures for quaternisation of a base $R{\cdot}C_6H_4{\cdot}NR'_2$.

Reaction no.	R	R′	120·1°	100°	80°	60°	40°	25°
				With MeI.				
1	H	Me	—	—	17·7	66·7	123 †	—
3	*m*-NO_2	Me	—	—	0·13	0·22	—	0·43
5	*o*-Me	Me	—	—	0·46	0·89	—	—
6	*m*-Me	Me	—	—	8·7	137	406	—
7	H	Me/Et *	—	—	28·9	77·5	291	—
8	H	Et	—	—	13·9	28·0	64·9	—
				With EtI.				
9	H	Et	—	0·56	1·17	—	—	—
10	*m*-Me	Et	0·495	0·875	1·6	—	—	—
11	*p*-Me	Et	0·74	1·5	—	—	—	—
				With EtBr.				
22	H	Et	0·046	0·0795	0·169	0·219	—	—
				With $CH_2{:}CH{\cdot}CH_2I$.				
27	H	Me	—	—	—	7·35	40·6	—

* Ph·NMeEt. † This value was not used in the calculation of ΔH and ΔS (Table 4).

TABLE 3.

Summary of kinetic results.

Reaction no.	R	R′	$\log_{10}k_1^{80}$ (l. mole^{-1} sec.$^{-1}$)	E (kcal. mole^{-1})	$\log_{10}A$ (l. mole^{-1} sec.$^{-1}$)
			With MeI.		
1	H	Me	−2·58	12·15	4·94
2	*p*-CHO	Me	−4·71	16·08	5·25
3	*m*-NO_2	Me	−4·23	14·25	4·60
4	*p*-Br	Me	−3·29	13·16	4·86
5	*o*-Me	Me	−3·89	15·63	5·79
6	*m*-Me	Me	−2·44	12·54	5·32
7	H	Me/Et *	−2·77	12·49	4·97
8	H	Et	−3·56	15·33	5·93
			With EtI.		
9	H	Et	−4·72	16·10	5·24
10	*m*-Me	Et	−4·50	15·64	5·18
11	*p*-Me	Et	−4·33	14·59	4·70
12	H	Me/Et *	−3·835	13·57	4·57
13	H	Me	−3·64	13·55	4·74
14	*m*-NO_2	Me	−5·74	—	—
15	*o*-Me	Me	−5·295	—	—
16	*p*-CHO	Me	−5·58	18·50	5·89
17	*p*-Br	Me	−4·33	14·68	4·755
18	*m*-Me	Me	−3·48	12·86	4·48
19	*p*-Me	Me	−3·12	11·94	4·27
20	*p*-MeO	Me	−2·92	11·58	4·25
21	*p*-NO	Me	−3·36	11·99	4·06
			With EtBr.		
22	H	Et	−5·21	17·10	5·40
23	H	Me	−4·63	15·95	5·24
24	*p*-Me	Me	−4·21	14·89	5·01
			With Pr^nI.		
25	H	Me	−4·37	13·54	4·01
			With Bu^nI.		
26	H	Me	−4·50	14·99	4·78
			With $CH_2{:}CH{\cdot}CH_2I$.		
27	H	Me	−2·18	10·53	4·34

* Ph·NMeEt.

TABLE 4.

Summary of thermodynamic quantities.

Reaction no.	R	R′	$\log_{10}K^{80}$ (l. mole^{-1})	ΔH (kcal. mole^{-1})	ΔS_{80} (cal. mole^{-1} degree^{-1})	ΔS^{*}_{80} (cal. mole^{-1} degree^{-1})
			With MeI.			
1	H	Me	1·25	−15·4	−37·9	−38·25
3	*m*-NO_2	Me	−0·89	−4·7	−17·5	−39·82
5	*o*-Me	Me	−0·34	−7·8	23·65	−34·36
6	*m*-Me	Me	0·94	−18·5	−48·2	−36·54
7	H	Me/Et *	1·45	−12·7	−29·2	−38·13
8	H	Et	1·14	−8·4	−18·8	−33·72
			With EtI.			
9	H	Et	0·07	−8·3	−23·3	−36·87
10	*m*-Me	Et	0·215	−8·1	−22·1	−37·14
11	*p*-Me	Et	−0·13 (120°)	−10·3	−25·6 (120°)	−39·55 (120°)
			With EtBr.			
22	H	Et	−0·835	−8·0	−26·5	−36·15
			With $CH_2{:}CH{\cdot}CH_2I$.			
27	H	Me	0·21	−17·7	−49·1	−41·00

* Ph·NMeEt.

TABLE 5.

Solubilities and melting points.

Iodide	Solubility (mmole l.$^{-1}$)	M. p.*
$Ph{\cdot}NMe_3^+$	24·7	200° (sub.)
p-$Me{\cdot}C_6H_4{\cdot}NMe_3^+$	20·2	210—211° (sub.)
p-$MeO{\cdot}C_6H_4{\cdot}NMe_3^+$	9·07	232° (sub.)
p-$Br{\cdot}C_6H_4{\cdot}NMe_3^+$	4·36	195° (dec.)
m-$Me{\cdot}C_6H_4{\cdot}NMe_3^+$	41·9	184° (sub.)
m-$NO_2{\cdot}C_6H_4{\cdot}NMe_3^+$	1·46	203°
o-$Me{\cdot}C_6H_4{\cdot}NMe_3^+$	28·9	205—206° (sub.)
p-$NO{\cdot}C_6H_4{\cdot}NMe_3^+$	38	~180°

* Sub. = sublimes; dec. = decomposition.

least squares. Where the total thermodynamic entropy of reaction could be calculated from a van't Hoff plot, the entropy of activation at 80° ΔS^{*}_{80} was also calculated. At 80° the relevant equation becomes

$$\Delta S^{*}_{80} = 4{\cdot}576 \log_{10} A - 60{\cdot}86. \qquad (5)$$

Table 5 contains the melting points and solubilities in nitrobenzene at 25°, of the solid salts obtained.

It is convenient to regard the quaternisation of tertiary amines by alkyl halides as an attack on the halide by the nitrogen lone-pair; this displaces the halogen atom which becomes an anion. The rate of quaternisation, which depends on the electron availability at the nitrogen atom, is influenced by the inductive effects of groups attached directly to the nitrogen or to the aromatic ring, and a guide to the electron availability is the basicity of the aniline, the most basic derivatives generally showing the greatest reactivity.[20,21] The rate also depends on the steric strain imposed by groups around the reaction centre, the strengths of the reacting bonds, and the degree of solvent interaction which can facilitate the reaction by stabilising the charges as they develop. In the present work steric and polar effects are the most important, modifying the rate through the activation energy. The frequency factor, however, also varies, and often in such a way that it partly compensates for the changes in the activation energy.

(*a*) *Influence of steric hindrance.* The influence of steric hindrance imposed by the

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[21] Davis and Addis, *J.*, 1937, 1622.

structure of the tertiary amino group is illustrated by changes in both parameters A and E (Table 3). Although dimethyl- is less basic than diethyl-aniline,[22] it reacts faster.

The replacement of one N-methyl group by ethyl lowers the rate only slightly, probably because of a balance between the enhanced basicity and the increased steric retardation. A second ethyl group causes a much greater retardation, in all cases due to a rise in E, though A also rises, in agreement with previous work.[12,19,21] In the reactions of methyl iodide with these three bases lower values of $-\Delta H$, $-\Delta S$, and $-\Delta S^*$ are associated with the ethylanilines, indicating that the solvation sheath is less developed and suggesting that bulky groups near the reaction centre slow the reaction by hindering close approach, not only of the reactants, but also of the stabilising solvent molecules.

Dimethyl-*o*-toluidine shows a decreased reactivity, in contrast to the other toluidines, due to the "*ortho*-effect." Discussion[14,23-26] about this has been centred on the configuration of the nitrogen atom and the possibility of hydrogen-bonding between the nitrogen atom and the *ortho*-group. The steric orientation of the nitrogen lone-pair appears to have been overlooked, however, for models show that when the nitrogen atom is trigonal and planar with the aromatic ring, as proposed by Watson,[24] the orientation of the non-bonding electrons is unsuitable for the formation of the hydrogen bonds proposed by him. The arguments of Brown and Fried[25] are also open to criticism since in the bicyclic compounds studied it is not only impossible for the tertiary amino group to twist out of the plane of the ring but also, because of this, it is unlikely that hydrogen bonds will be formed.

A more likely explanation is that the dialkylamino group is forced out of the plane of the ring, becoming tetrahedral, with the non-bonding electron pair suitably orientated for some form of hydrogen-bonding to the *o*-methyl group. The change in the value of A found in all cases follows from the different steric requirements of the tetrahedral nitrogen atom.

(*b*) *Influence of ring substituents.* Quaternisations with both ethyl and methyl iodide are sensitive to the influence of ring substituents and both series of reactions conform to the Hammett equation, $\log_{10}(k/k_0) = \rho\sigma$, where k_0 is the value of the rate constant k when there is no substituent, and σ is a constant dependent only on the properties of the ring substituent. Values of σ reported by Jaffé[27] were plotted against the smoothed values of $\log_{10}k_1^{80}$ obtained in the present work (Table 3), as shown in Fig. 2. The negative values of ρ, which depends only on the reaction and the experimental conditions, show that the reactions are favoured by an increase in electron availability at the nitrogen atom. In each series the value for the reaction of *p*-dimethylaminobenzaldehyde lies far off the line through the other points, which may be connected with the unique interaction between aldehyde and *p*-amino-groups.[27]

The reactions of ethyl iodide show the most negative value of ρ, revealing a greater sensitivity to the electron availability at the nitrogen atom. If there is more steric hindrance associated with ethyl iodide, an increased electron availability may allow a greater nitrogen–carbon separation in the transition state, reducing the steric strain and thus increasing the effect of variation in the electron availability at the nitrogen atom.

In conformity with previous work[1c,d] it is found that *meta*- and *para*-substituents modify the rate of reaction with methyl iodide through the activation energy alone. This is illustrated in Fig. 3, where the line has the theoretical slope of $-2{\cdot}303\boldsymbol{R}T$.

In Fig. 4 the values of E and $\log_{10}A$ for the reactions of two ethyl halides with various substituted dimethylanilines are shown. The behaviour here differs from that with methyl iodide. There is now a roughly linear relation between E and $\log_{10}A$. The four quaternisations of diethylanilines by ethyl halides also display this behaviour.

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[22] Taylor, *Nature*, 1958, **181**, 265.
[23] Fahim and Galaby, *J.*, 1950, 3529; von Braun, Arkuszewski, and Köhler, *Ber.*, 1918, **51**, 282.
[24] Watson, "Modern Theories of Organic Chemistry," Oxford Univ. Press, 1941, p. 241.
[25] Brown and Fried, *J. Amer. Chem. Soc.*, 1943, **65**, 1841.
[26] Hughes, *Quart. Rev.*, 1948, **2**, 107.
[27] Jaffé, *Chem. Rev.*, 1953, **53**, 191.

Although cases are known where a change of reaction conditions results in such a change of behaviour,[28] no reports have so far appeared in which so small a change of structure as the present leads to so marked a change. An unexpected relation between methyl and ethyl iodide as the aniline is varied, as shown in Fig. 5, appears to be due to the combined influence of the " compensation effect " and of a geometric effect which influences A alone and reflects the presence of preferred orientations in the reactions of ethyl iodide.

In reactions with methyl iodide the base will assume all conformations corresponding to free rotation about the H_3C–N axis, whereas in reactions with ethyl iodide this rotation will be restricted by steric interaction between the groups attached to nitrogen and to C-1 of ethyl iodide, which prevents the molecule from adopting many of the conformations otherwise possible; this decreases A without affecting E. The superimposed " compensation effect " arises because of an increased steric strain produced, with ethyl iodide, when a change of the ring substituent diminishes the electron availability at the nitrogen atom and creates a need for closer approach of the reactants; it probably reflects the oblique approach of reactants and the bending of bonds.

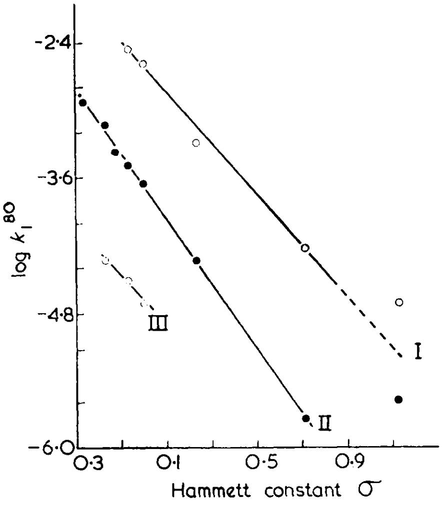

FIG. 2.

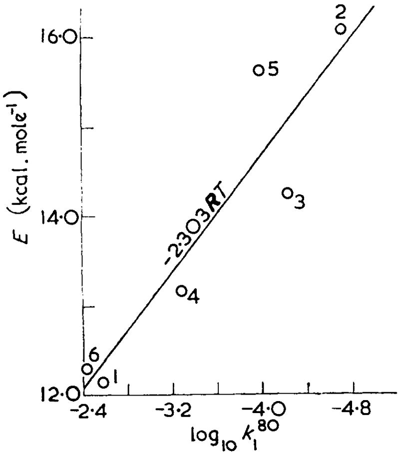

FIG. 3.

FIG. 2. Hammett plot. Curve I; reaction of methyl iodide with *NN*-dimethylanilines, $\rho = -2{\cdot}29$. Curve II; reaction of ethyl iodide with *NN*-dimethylanilines, $\rho = -2{\cdot}85$. Curve III; reaction of ethyl iodide with *NN*-diethylanilines, $\rho \approx -2{\cdot}3$. All rate constants are for 80°.

FIG. 3. The relation between E and $\log_{10}k_1^{80}$ for the reactions of methyl iodide with *NN*-dimethylanilines. The reactions are designated by the numbers given in Table 1.

The variation of A may therefore be represented roughly by the relation,

$$\log_{10}A^{\mathrm{Et}} \approx \log_{10}A^{\mathrm{Me}} - \text{Constant} + 0{\cdot}3(E^{\mathrm{Et}} - E^{\mathrm{Me}}), \qquad (6)$$

in which the factor 0·3 was obtained from the slope of Fig. 4. Superimposed upon this relation will be changes in A caused by different solvation patterns with the two halides. The solvation sheath in the reactions with ethyl iodide is likely to be less compact, and, as suggested by Harris and Weale,[4] most sensitive to the polarity of the complex, thus

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[28] Timm and Hinshelwood, *J.*, 1938, 862.

increasing the factor of proportionality in equation (6). If it were doubled, for example, the relation becomes,

$$\log_{10}A^{\mathrm{Et}} \approx \log_{10}A^{\mathrm{Me}} - \text{Constant} + 0{\cdot}6(E^{\mathrm{Et}} - E^{\mathrm{Me}}). \qquad (7)$$

The values of the constant required to make equation (7) fit in each case are: $Ph{\cdot}NEt_2$ 1·17, *m*-$Me{\cdot}C_6H_4{\cdot}NMe_2$ 1·02, $Ph{\cdot}NMeEt$ 1·04, $Ph{\cdot}NMe_2$ 1·02, *p*-$Br{\cdot}C_6H_4{\cdot}NMe_2$ 1·03, and *p*-$CHO{\cdot}C_6H_4{\cdot}NMe_2$ 0·84. These values give general support to the view that there are preferred orientations associated with the reactions of ethyl iodide, a view conforming to early ideas about the nature of the probability factor.

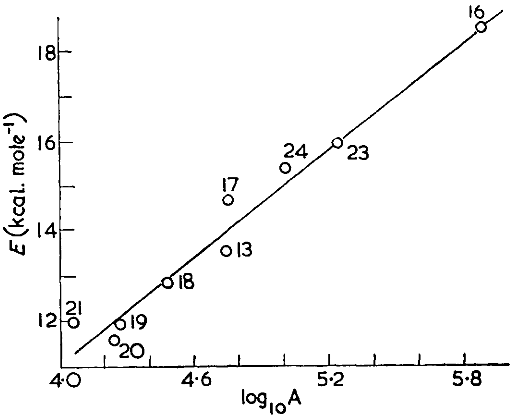


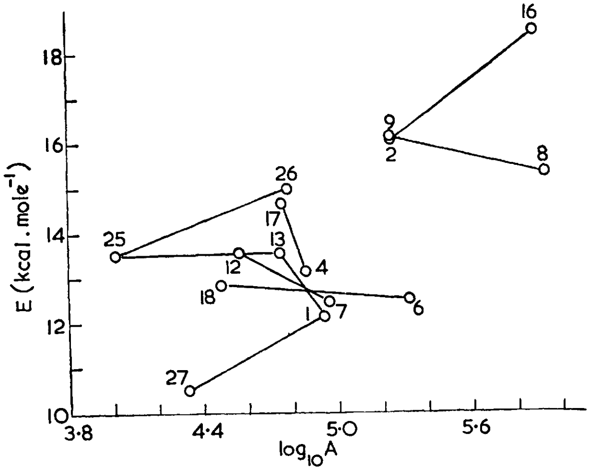
FIG. 4.

FIG. 4. The relation between E and $\log_{10}A$ for the reactions of ethyl halides with *NN*-dimethylanilines. The reactions are designated by the numbers given in Table 1.

FIG. 5. The relation between E and $\log_{10}A$ for the reactions of alkyl iodides with various anilines. The reactions are designated by the numbers given in Table 1.

The lines join points corresponding to the reactions of a single aniline.

FIG. 5.



Models show that this exclusion of conformations is most likely to occur if the nitrogen atom in the transition state has a trigonal planar configurations, similar to that of the carbon atom,[29] a view at variance with one expressed by Glasstone *et al.*[30] Their conclusion was based on the similarity of the values of ΔS^* and ΔS found in the reaction of methyl iodide with dimethylaniline. The similarity has been confirmed in the present work (Table 4, provided the equilibrium constant at 40° is not used in calculation of ΔS), but is the exception rather than the rule. It may be objected that the equilibrium constants, and therefore the calculated entropies of reaction, are known to be unreliable owing to ionisation of the salt, but this is no reason for accepting results for one reaction and

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[29] Hughes, *Quart. Rev.*, 1951, **5**, 245; Ingold, *ibid.*, 1957, **11**, 1.

[30] Glasstone, Laidler, and Eyring, "Theory of Rate Processes," McGraw Hill, New York, 1941, p. 419.

rejecting results for the other ten. Doubt is therefore thrown upon these earlier views of the stereochemistry of the transition complex, and in this respect the early availability [13] of results for a single reaction may have been misleading.

(*c*) *Influence of Alkyl Halide.* The quaternisations are sensitive to variation of the halide and, as previously reported,[16] iodides react faster than bromides. This can be correlated with the respective bond strengths, which are [31] 67·0 kcal. mole^{-1} for Et–Br, and 52·0 kcal. mole^{-1} for Et–I.

The rate is mainly dependent on the activation energy, although the value of A also changes so as to give some " compensation." The variation of A probably arises from a modification of the steric requirements owing to the need for entering and leaving groups to compete equally in the transition state.

The reactions of dimethylaniline with five alkyl halides are represented in Tables 1 and 3 and Fig. 5. The greater reactivity of allyl iodide can be ascribed to the much lower carbon–iodine bond strength (34·4 kcal. mole^{-1}).[31]

The values of A and E for reactions of ethyl, propyl, and butyl iodide show an unusual relation, noted earlier.[32] It has been attributed to the smaller number of conformations available to the propyl group in the transition state.[33] Models show that only if the terminal group in the propyl chain is directed away from the reaction centre are the reacting bonds subjected to a strain similar to that with ethyl iodide. The value of E then remains unchanged, but there is a fall in the value of A. The configuration of minimum steric hindrance has a somewhat lower probability in the reactions of butyl iodide, and it is not surprising that there is a compromise, whereby the maximum product of the energy and entropy terms is associated with higher values of both E and A. The relation between these quantities in the reactions of propyl and butyl iodide, therefore, is a clear example of compensation.

Total Enthalpies and Entropies of Reaction.—Equilibrium constants for the reactions of substituted anilines gave a poor Hammett plot, probably owing to a varying ionisation of the salts. The values, however, are of qualitative interest (Tables 2 and 4).

The fastest reactions are also the most exothermic and involve the largest entropy loss. Variation of the base affects rates and equilibria similarly, in contrast to variations of the alkyl halide.

The entropy of reaction, ΔS, often depends on the change in solvation during a reaction, and the negative entropies here show that products are more solvated than the reactants. If all the reactants are similarly solvated, ΔS will indicate the solvation of the final product. The conclusions drawn on this basis are qualitatively supported by the measured solubilities.

The enthalpy of the reaction varies roughly in parallel with the entropy, indicating that solvation of the product contributes substantially to the total exothermicity. The properties of the solvation sheath are determined by the polarity of the quaternary amino-group, and not by any direct interaction between a ring-substituent and the solvent, since the introduction of a nitro-group into trimethylanilinium iodide lowers its solubility in nitrobenzene although the melting points of the two salts are similar (Table 5).

Influence of Solvent Variations.—(*a*) *The internal structure of the solvent.* The Menschutkin reaction has been studied with a variety of solvent systems,[13,17,34-36] and the rate is sometimes controlled through variations in A alone—with different pure solvents,[2] with mixed solvents,[1*b*] and with reactions at different pressures.[3,4]

A possible cause of this, which seems to have been so far overlooked, is the influence of

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[31] Geller and Skinner, *J.*, 1949, 1145.

[32] Winkler and Hinshelwood, *J.*, 1935, 1147; Dunbar and Hammett, *J. Amer. Chem. Soc.*, 1950, **72**, 109.

[33] Ivanoff and Magat, *Chim. phys.*, 1950, **47**, 914, 922.

[34] Hawkins, *J.*, 1922, 1170.

[35] Fairclough and Hinshelwood, *J.*, 1937, 1573; Raine and Hinshelwood, *J.*, 1939, 1378.

[36] Watanabe and Fuoss, *J. Amer. Chem. Soc.*, 1956, **78**, 527.

the internal order of the pure solvent. In the results of Grimm, Ruf, and Wolf [2] for the reaction of ethyl iodide with triethylamine, E varies only slightly within the series of aromatic solvents, suggesting that the solvated transition complexes may be similar. Solvent molecules have less freedom in the ordered solvation sheath than in the bulk solvent, and the entropy change depends, not only on the degree of order in the solvation sheath, but also on that in the pure solvent.

An indication of the internal order of a solvent at a certain temperature is given by its melting point, since solvents only just above their melting points will have a tendency toward crystallinity. In a series of solvents associated with an almost constant value of E, solvents with higher freezing points may, therefore, be expected to be associated with less negative entropies of activation, or higher values of A. In a plot of $\log_{10}A$ against solvent freezing point for the results of Grimm, Ruf, and Wolf (Fig. 6), there is a trend in the predicted direction. The two sets of results of Pickles and Hinshelwood [2] give similar plots.

An unexpected feature is that the points fall on two roughly parallel lines, and that all the solvents associated with the upper line have marked molecular symmetry. The connection between symmetry and melting point is shown by the fact that most *para*-disubstituted benzene derivatives melt at a higher temperature than their *ortho*- and *meta*-isomers.

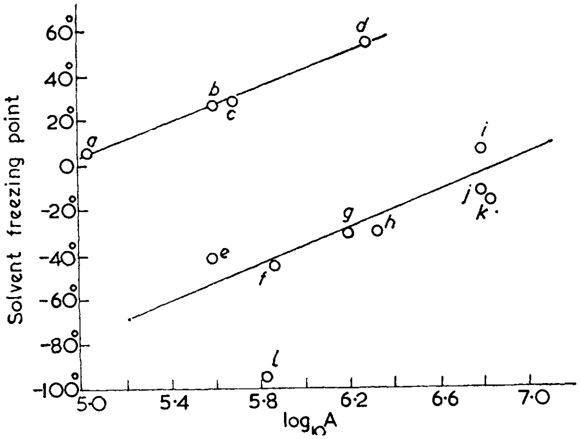

FIG. 6. The relation between $\log_{10}A$ and the freezing point of the solvent used for the reaction.

a, C_6H_6.	*e*, PhF.	*i*, $PhNO_2$.
b, CH_2Ph_2.	*f*, PhCl.	*j*, PhCN.
c, Ph_2O.	*g*, PhI.	*k*, *o*-$C_6H_4Cl_2$.
d, *p*-$C_6H_4Cl_2$.	*h*, PhBr.	*l*, PhMe.

Symmetrical molecules may be able to rotate in their crystals more easily than non-symmetrical molecules, which could lead to the observed behaviour, since it would create increased disorder in the crystal, and therefore in the pure liquid just above the melting point. A larger entropy loss would then be observed on the formation of the solvation sheath.

That this may be the case with carbon tetrachloride, used by Pickles and Hinshelwood [2] and associated with the upper line, is shown by its low entropy of melting. The solvent has two crystal forms, and during the transition between them there is a large entropy change,[37,38] caused by the onset of molecular rotation.[39] On the other hand, no such transitions have been observed with benzene,[38] which is also associated with the upper line in these plots.

Since the internal order of solvents that contract on freezing is increased by pressure, the views outlined above predict an increase of A with increase in pressure, as found experimentally.[3,4] The values of $\log_{10}A$ reported by Harris and Weale [4] were plotted

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[37] Davidson, Argersinger, and Michaelis, *J. Phys. Colloid Chem.*, 1948, **52**, 332.
[38] Ubbelohde, *Quart. Rev.*, 1950, **4**, 356.
[39] Staveley, *Quart. Rev.*, 1949, **3**, 72.

against the calculated freezing point of their solvent (methanol) at the pressures used, giving very slightly curved lines. A plot of smoothed values of $\log_{10}A$ from the results of Venkataraman and Hinshelwood[1b] against the calculated freezing points of the mixed solvents used also reveals a linear relation for solvents containing more than 60% nitrobenzene.

(*b*) *Experimental work.* The present study was undertaken in order to extend the knowledge of dependence on the solvent medium, three reactions being studied in mixtures of nitrobenzene and chlorobenzene. *N*-Ethyl-*N*-methylaniline and dimethyl-*p*-toluidine were quaternised with ethyl iodide, and dimethylaniline with methyl iodide (Tables 6—8) (factors to correct for the thermal expansion of the solvent were estimated by interpolation between those for the pure components). Values for reactions that took place heterogeneously have been excluded from Tables 7 and 8, and those obtained by extrapolation or interpolation are in parentheses.

The parameters for the reaction of methyl iodide with dimethylaniline gave smooth curves when plotted against solvent composition; on extrapolation they gave consistent values for pure chlorobenzene. These refer to a reaction which has not been proved to take place, but are of theoretical interest.

In conformity with published work,[1b,40] the rate increases with increase in the polarity of the solvent. In the present work this is due mainly to variations of E, which follows the same general trend in the three reactions studied. The rate is sensitive to initial additions of either component of the solvent, but there is a region of intermediate composition in which it is less sensitive. Somewhat similar behaviour has been reported for other systems.[35] The similarity, however, does not extend to values of A which in previous cases increased with increase in the polarity of the solvent, whereas in the present work the small variation of A is almost linearly proportional to the larger variation of E.

TABLE 6.

Quaternisations in nitrobenzene–chlorobenzene mixtures.

Methyl iodide with dimethylaniline.

PhNO$_2$ (wt. %)	10^2k_1 (l. mole^{-1} hr.$^{-1}$)					K (l. mole^{-1})	
	80°	60°	40°	25°	6°	60°	80°
80	604	213	63·6	21·7	4·57	25·0	7·1
60	604	214	59·55	21·0	4·29	8·76	2·74
40	463	164	42·2	14·45	2·84	(2·51)	0·87
20	—	104	19·2	7·68	1·61	0·66	(0·35)
10	—	—	~50 *	—	—	—	—
0	3·5 *	20·1 *	6·4 *	0·305 *	—	(0·15)	(0·13)

Ethyl iodide with N-*ethyl*-N-*methylaniline.*

	10^2k_1 (l. mole^{-1} hr.$^{-1}$)			
	80°	60°	40°	25°
60	27·8	9·80	2·53	0·711

Ethyl iodide with dimethyl-p-*toluidine.*

	10^2k_1 (l. mole^{-1} hr.$^{-1}$)						
	140°	120·1°	100°	80°	60°	40°	25°
80	—	—	—	206	72·2	19·1	8·75
60	—	—	—	95·3	32·9	9·20	3·37
40	—	—	—	64·0	22·15	6·99	2·16
20	—	—	—	6·80	29·9 *	6·81 *	2·28 *
10	13·8	7·34	2·82	5·10	8·01, 9·0 *	1·14 *	0·54 *
0	5·62	6·53	2·23	0·819	1·20, 3·4 *	0·58 *	—

* Heterogeneous reactions.

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[40] Archer and Hudson, *J.*, 1950, 3259; Bose and Hinshelwood, *J.*, 1958, 4085.

TABLE 7.

General Summary.

$PhNO_2$ (wt. %)	E (kcal. mole^{-1})	$\log_{10}A$ (l. mole^{-1} sec.$^{-1}$)	$\log_{10}k_1^{80}$ (l. mole^{-1} sec.$^{-1}$)
Methyliodide with dimethylaniline.			
100	12·15	4·94	−2·58
80	12·91	5·24	−2·75
60	13·08	5·35	−2·755
40	13·51	5·50	−2·865
20	13·98	5·48	−3·08
0	(14·5)	(5·62)	(−3·38)
Ethyl iodide with N-*ethyl*-N-*methylaniline.*			
100	13·57	4·57	−3·835
60	13·96	4·57	−4·075
Ethyl iodide with dimethyl-p-*toluidine.*			
100	11·94	4·27	−3·12
80	12·20	4·30	−3·25
60	12·75	4·32	−3·57
40	12·75	4·16	−3·74
20	—	—	−4·72
10	13·6	2·74	−5·68
0	14·0	3·05	−5·66

Equilibrium constants measured for the reaction of methyl iodide with dimethylaniline are contained in Table 6; smoothed values of these were used to calculate the rate of the reverse reaction at 80° (k_2^{80}), and ΔH and ΔS, at each solvent composition, as given in Table 8. The reverse rate is much more sensitive than the forward rate to changes in solvent composition, and, in contrast, is increased by the addition of non-polar solvent. There is also a trend to lower exothermicity and entropy loss in the solvents of lower polarity. Comparison of the changes of ΔH and E shows that the activation energy for the reverse reaction falls appreciably with decrease in solvent polarity. This corresponds to the rapid increase in the reverse reaction rate, and thus to the high sensitivity of the equilibrium constant to solvent polarity.

TABLE 8.

Equilibrium results for reaction of methyl iodide and dimethylaniline in nitrobenzene–chlorobenzene mixtures.

$PhNO_2$ (wt. %)	ΔH (kcal. mole^{-1})	$\log_{10}K^{80}$ (l. mole^{-1})	$\log_{10}k_2^{80}$ (sec.$^{-1}$)	ΔS_{80} (cal. degree^{-1} mole^{-1})	ΔS^{*}_{80} (cal. degree^{-1} mole^{-1})
100	−15·4	1·25	−3·83	−37·9	−38·25
80	−15·4	0·81	−3·575	−39·8	−36·89
60	−14·5	0·37	−3·15	−39·3	−36·40
40	(−11·7)	−0·61	−2·825	(−33·4)	−35·68
20	(−7·5)	(−0·46)	(−2·62)	(−21·4)	−35·79
0	(−0·1)	(−0·89)	(−2·49)	(−4·4)	(−35·15)

An interpretation of these results probably depends on an understanding of the solvation sheath, and the dependence of this on the bulk solvent composition. Molecules of nitrobenzene in the transition-state solvation sheath seem to be replaceable by molecules of chlorobenzene, resulting in reduced stabilisation for the newly formed dipoles, and a rise of E. A random replacement causes the rise in the value of A.

The strongly polar product appears to have a solvation sheath which contains mainly nitrobenzene molecules and is unaffected by small amounts of chlorobenzene, with the result that ΔH does not vary. Since, however, there is less nitrobenzene in the mixed solvents the solvated product has a lower entropy.

At intermediate solvent compositions, where the activation energy is somewhat less sensitive, there may be a compromise between the energy and the entropy term. Transition complexes can be formed with relatively large numbers of chlorobenzene molecules in the solvation sheath. These correspond to higher values of A, but since the charges are less stabilised there is also a high value of E. The complexes which contain a larger proportion of nitrobenzene have lower values of both A and E and give rise to more reaction. It is, therefore, to this route that the experimental results most nearly conform.

The solubility of a salt $Ph{\cdot}NMe_3^+I^-$ was very dependent on solvent composition, demonstrating a lower solvation in the least polar solvents. This also explains the fall in both $-\Delta H$ and $-\Delta S$, being an indication that there is a diminished solvation sheath in the transition state. Solvation results in a loss of entropy, *i.e.*, entropies of reaction and of activation are negative. A diminished solvation sheath would therefore result in a smaller loss of entropy or a higher value of A, and also in less stabilisation of the charges, causing the higher values of E.

The author thanks Professor Sir Cyril Hinshelwood for help and advice, and the Department of Scientific and Industrial Research for a research studentship.

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