Rate of Enhancement of S_N2 Reactions in Dipolar Aprotic Solvents. The Importance of Transition-state Solvation

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THE well known rate increases of nucleophilic[1] and base-catalysed[2] reactions in dipolar aprotic solvents are susceptible of two general explanations. The first, and most common, explanation is that desolvation of the nucleophile or base in the aprotic solvent relative to the protic solvent raises the energy of the reactants, thus diminishing the energy gap between the reactants and the transition state. The second explanation is that the lowering of the activation energy is caused by increased solvation of the transition state in the dipolar aprotic solvent. A combination of both effects is also conceivable. A direct means of distinguishing between these possibilities, as demonstrated in the work of Arnett,[3] is to determine the difference in the enthalpies of activation of a reaction in a pair of solvents, $\delta\Delta H^*$, and compare them to the enthalpies of transfer of the reactants from one solvent to the other, $\delta\Delta H_S$. The difference between the enthalpy of the activated state in the two solvents, δH^*, can then be obtained from the relation: $\delta H^* = \delta\Delta H_S + \delta\Delta H^*$.

TABLE 1

Rate constants and enthalpies of activation for the reaction $p\text{-YC}_6\text{H}_4\cdot\text{CH}_2\cdot\text{Cl} + \text{C}_5\text{H}_5\text{N} \rightarrow p\text{-YC}_6\text{H}_4\cdot\text{CH}_2\cdot\text{NC}_5\text{H}_5^+ + \text{Cl}^-$ *in dimethylformamide and methanol*

Y	NO_2	H	Me
k_2, MeOH, 25°, l.mole^{-1}sec.$^{-1}$ × 10^6	1·22	3·46	8·20
k_2, DMF, 25°, l.mole^{-1}sec.$^{-1}$ × 10^6	2·51	3·74	9·50
k_2, MeOH, 50°, l.mole^{-1}sec.$^{-1}$ × 10^6	31·0	43·9	79·5
k_2 DMF, 50°, l.mole^{-1}sec.$^{-1}$ × 10^6	26·4	23·7	56·2
ΔH^*, MeOH, kcal./mole	24·1	18·8	16·7
ΔH^*, DMF, kcal./mole	17·3	13·5	13·0

We report the first study of an S_N2 reaction by this method. The system chosen was a Menshutkin reaction, the reaction of pyridine with three benzyl chlorides. The solvent pair used was dimethylformamide and methanol.†

As seen in Table 1, unlike the reaction of negatively charged nucleophiles with alkyl halides[4] the Menshutkin reaction does not exhibit large rate enhancements in the dipolar aprotic solvents.‡ However, a substantial lowering of ΔH^* in the dipolar aprotic solvent is observed, which is quite in line with that observed[1,4] for the reactions of negatively charged nucleophiles. As shown in Table 2, this solvent effect on the enthalpies of

TABLE 2

Heats of solution of benzyl chlorides and pyridine in dimethylformamide and methanol

Compound	ΔH_S, DMF (kcal./mole)	ΔH_S, MeOH (kcal./mole)
$p\text{-NO}_2\cdot\text{C}_6\text{H}_4\cdot\text{CH}_2\text{Cl}$ ..	4·16	5·97
$\text{C}_6\text{H}_5\cdot\text{CH}_2\text{Cl}$	−0·39	0·44
$p\text{-MeC}_6\text{H}_4\cdot\text{CH}_2\text{Cl}$ ..	−0·26	0·60
$\text{C}_5\text{H}_5\text{N}$	−0·09	−0·95

TABLE 3

Enthalpies of transfer from methanol to dimethylformamide of reactants and transition states

	$\delta\Delta H_S$, (kcal./mole)	
Reaction	Reactants	Transition state
$p\text{-NO}_2\cdot\text{C}_6\text{H}_4\cdot\text{CH}_2\text{Cl} + \text{C}_5\text{H}_5\text{N}$	−0·95	−7·8
$\text{C}_6\text{H}_5\cdot\text{CH}_2\text{Cl} + \text{C}_5\text{H}_5\text{N}$	0·03	−5·3
$p\text{-MeC}_6\text{H}_4\cdot\text{CH}_2\text{Cl} + \text{C}_5\text{H}_5\text{N}$	0·00	−3·7

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† These two solvents have very similar dielectric constants (dimethylformamide *ca.* 37, methanol *ca.* 33) thus minimizing polarity differences and focussing upon the difference between aprotic and protic solvents.

‡ This was also observed by Parker and his co-workers, ref. 4, in the reaction of butyl halides and pyridine in methanol and dimethylformamide.

activation is not paralleled by corresponding effects on the enthalpies of solution. Therefore, as shown in Table 3, the lower activation enthalpies for this reaction in the dipolar aprotic solvent are caused by greater solvation of the transition state in the dipolar aprotic solvent and not by a solvent effect on the enthalpies of the reactants.§

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§ It is important to note the very gross nature of this effect. Our calorimetric measurements (Table 2) possess an accuracy of about 2—4%. Yet changes in the heats of solution of several hundred percent would scarcely affect the validity of the above conclusion.

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