The Effect of Solvents on S_N2 Substitution under Phase-transfer Catalysis (Liquid/Solid System)

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Substitution in a two-phase system containing a solid ionophore in the present of a phase-transfer catalyst is accelerated by an increase in the Lewis basicity (measured by the donor number DN) and polarizability (*P*) and is inhibited by an increase in the Lewis acidity, measured by the acceptor number (AN) of the solvent.

Despite widespread use of the phase-transfer catalysis (PTC) method in organic chemistry[1] the effect of solvent type on the reaction rate under PTC conditions has not yet been studied systematically. The influence of solvent on the methylation of onium *p*-nitrophenolates with methyl iodide in the liquid/liquid (l/l) system has been studied.[2] For systems with a solid and liquid phase (l/s), similar work is absent.

We have studied the effect of 17 solvents on the rate of substitution of bromide in l-bromohexane by chloride in a solvent system with solid KCl at 70 °C, reaction (1).

$$C_6H_{13}Br(org) + KCl(s) \xrightarrow{QBr} C_6H_{13}Cl(org) + KBr(s) \qquad (1)$$

Tetrabutylammonium bromide (QBr) was used as the PTC catalyst. The main features of this reaction have already been described,[3,4] and experimental methods have been given.[5] The refining and drying of solvents were carried out by regular methods.[6] For an estimate of the solvent effect, the observed pseudo-first order rate constnat (k_1) obtained after minimal reaction progress was used. This rate constant did not change, even at significant reaction progress up to 90%.

The constant value was obtained by the processing of GLC data (the accuracy of the square determination is 5%) and was averaged during the construction of kinetic curves by the decrease of initial RBr and by the appearance of reaction product RCl. A discussion of kinetic peculiarities follows.

All solvents studied can be divided into three groups. The solvents with high Lewis basicity and, respectively, with high donor number DN (nos. 1–4, see Table 1) fall into the first group. In these solvents, the reaction proceeds even in the absence of a PT catalyst, although with a somewhat lesser rate. Two alcohols (nos. 16 and 17), in which the reaction proceeds very slowly, fall into the second group, and the third group is formed from all remaining solvents. The solvents in the latter group do not significantly affect the reaction rate (less than one order of magnitude). Another order of these solvents in the groups can be observed when their polarizability (*P*) is compared with the rate constant. In this case, they fall into two groups, one of which comprises all aromatic solvents and CCl_4 (point no. 17 is not well-founded). Such a distribution makes it possible to draw some conclusions about both the substitution reaction mechanism in the 1/s system and the mechanism of the solvent effect on this reaction.

There is no significant correlation with the solvent permittivity (ε) (Fig. 1), as with the 1/1 system.[2] This points to only a

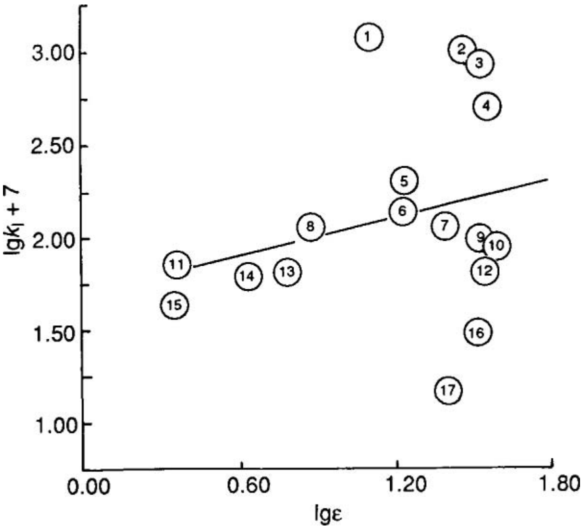

Fig. 1 The absence of a correlation between the substitution free energy (lg k_1) and the relative permittivity (lg ε) for reaction (1)

Table 1 Pseudo first-order rate constants for reaction (1) in various solvents and associated parameters.

No.	Solvent	$k/10^{-5}\,s^{-1}$	AN	DN	log ε	P^a
1	Pyridine	11.22	11.5	43.0	1.09	0.299
2	Hexamethylphosphorus triamide	9.33	12.3	38.1	1.471	0.273
3	1-Methylpyrrolidin-2-one	8.3	14.0	27.3	1.518	0.277
4	*N,N*-Dimethylformamide	4.95	16.1	25.1	1.565	0.257
5	Acetophenone	1.85	12.9	14.1	1.24	0.311
6	Pentan-2-one	1.39	10.3	12.6	1.23	0.231
7	Benzonitrile	1.15	13.8	12.0	1.401	0.308
8	Tetrahydrofuran	1.11	7.8	20.6	0.869	0.246
9	Nitrobenzene	0.91	13.8	3.7	1.541	0.321
10	Acetonitrile	0.876	18.9	13.2	1.574	0.21
11	Toluene	0.709	3.3	3.9	0.376	0.293
12	Nitromethane	0.667	19.3	4.8	1.555	0.232
13	Ethyl acetate	0.657	8.7	10.9	0.779	0.227
14	Anisole	0.61	7.6	7.9	0.635	0.302
15	Carbon tetrachloride	0.44	8.6	0	0.35	0.274
16	Methanol	0.297	41.3	12.0	1.513	0.203
17	Ethanol	0.15	37.1	6.5	1.386	0.221

[a] $P = (n^2 - 1)/(n^2 + 2)$, see ref. 10; for data for AN and DN, see ref. 7.

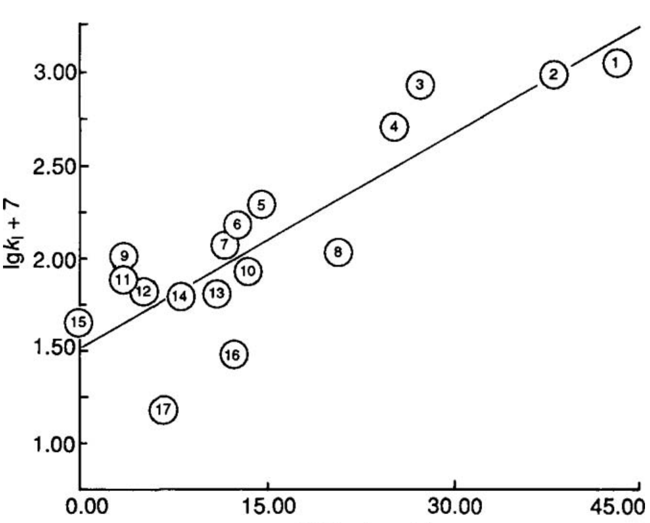

Fig. 2 The relationship between the solvent donor number (DN) and lg k_1 for reaction (1)

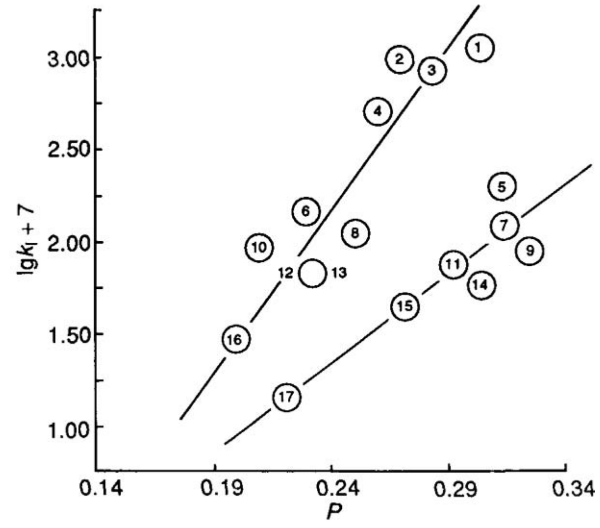

Fig. 3 The effect of the polarizability (P) on lg k_I in reaction (1)

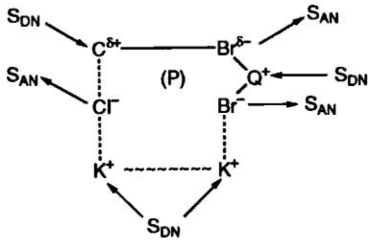

Fig. 4 The interaction of donor (DN) and acceptor (AN) solvent molecules with the adsorption complex at the KCl (solid) surface during the S_N2 reaction (1)

minor contribution of pathways involving ions, or to its complete absence in S_N2 substitution. This conclusion is corroborated for the 1/s system by the fact that there is also no relationship between k_I and AN. If the solvent solvates the leaving group, the reaction rate would increase with increasing AN.

A distinct acceleration of the reaction is observed on moving to solvents with high DN (Fig. 2). As DN values are linear with the solvent Lewis basicity (B),[7] this points to a contribution of the solvent to an increase in incoming Cl^- nucleophilicity (the blocking of charge K^+ at the crystal surfaces) or to the breaking of C–Br bonds in 1-bromohexane. These data suggest the formation of a cyclic adsorption complex[8] on the surface of the solid phase (KCl) inside of which a substitution reaction takes place.

There is satisfactory positive correlation between k_I and the solvent polarizability (P) (or its refractive index) (Fig. 3). In this case, all solvents form two groups with similar slopes and with correlation coefficients $r = 0.934$ (aromatic solvents) and $r = 0.942$ (remaining solvents) on the curves lg k_I *vs.* P.

These facts can be applied to a corroboration of the scheme involving the distribution of the bonds inside an activated complex[9] (Fig. 4).

Although the conclusions obtained are only preliminary, they nevertheless make it possible to choose the reaction conditions in PTC with greater clarity.

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