Symbiotic Effects in Nucleophilic Displacement Reactions at Aliphatic Carbon in Acetonitrile

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Some years ago, it was suggested[1] that as the transition state for an S_N2 reaction may be regarded as an acid-base complex, there should be symbiotic effects[2] on the rates of nucleophilic displacement reactions. When focusing on the entering and leaving groups, experimental data in methanol[2,3] clearly showed that symbiosis was important and governed the so-called leaving-group effect.

Parker[4] has recently claimed that this symbiotic effect is solvent dependent and that the data in methanol and other protic solvents may not be representative for the leaving-group effect in dipolar aprotic solvents. He offered calculations indicating that values for log k_{TsO}/k_I were virtually constant at -1.6 for reactions of both hard and soft bases reacting with methyl iodide and methyl tosylate in dimethylformamide.

We have determined some rate constants for these reactions, I and II, in acetonitrile to get some further information on the leaving-group effect in an aprotic solvent.

$$B + CH_3I \xrightarrow{k_I} CH_3B + I^- \qquad (I)$$

$$B + CH_3OTs \xrightarrow{k_{TsO}} CH_3B + TsO^- \qquad (II)$$
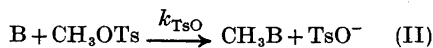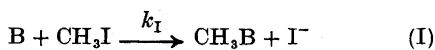
The data are collected in Table 1.

The ratios k_{TsO}/k_I in acetonitrile strikingly parallel the previously obtained ratios in methanol, and the symbiotic effect appears to be even greater in the aprotic solvent than in the protic one, in contrast to Parker's suggestion.[4]

The results obtained in this work are by no means surprising. In recent years several studies on alkylation of ambident bases in various dipolar aprotic solvents have appeared which clearly accord with the idea that the symbiotic effect governs the leaving-group effect. Most significant are the studies on alkylation reactions of ambident anions containing one typical hard and one typical soft nucleophilic

Table 1. Rate constants at 25° in acetonitrile for Reaction II together with calculated values of k_{TsO}/k_I in acetonitrile and methanol.

Nucleophile	k_{TsO}	k_{TsO}/k_I	
B	M^{-1} sec^{-1}	MeCN[a]	MeOH[b]
NCSe$^-$	8.3×10^{-4}	0.0047	0.23
Ph$_3$P	4.4×10^{-5}	0.0077	0.18
NCS$^-$	2.3×10^{-4}	0.0112	0.28
Br$^-$	5.0×10^{-3} [c]	0.025	0.72
N$_3^-$	2.5×10^{-2}	0.102	
Et$_3$N	4.6×10^{-3}	0.131	0.95
OCN$^-$	5.5×10^{-3}	0.32	
Cl$^-$	2.3×10^{-2}	0.33	2.8
AcO$^-$	2.6×10^{-1}	0.54	
CH$_3$O$^-$			4.6
CH$_3$OH			210

[a] Rate constants for reaction I from Ref. 5, except for CH$_3$I + Br$^-$ from Ref. 6. [b] Ref. 1. [c] Ref. 7.

center like the enolate anions,[8,9] imine anions,[10] the benzophenone dianion and alkyl acetoacetate anions,[12-14] the thiocyanate ion,[15] and the indole anion.[16,17] The poor ability of iodide ion to act as nucleophilic catalyst in the synthesis of esters from alkyl chlorides and salts of carboxylic acids in ethyl methyl ketone[18,19] is thus easily understandable. The success of dimethyl sulfate as esterification agent of sterically hindered carboxylic acids[20] is as anticipated. A review on alkylation of ambident bases has recently been published.[21]

Experimental. Tetraphenylarsonium salts were in all cases the sources of the anionic nucleophiles. The purification of these salts, and of acetonitrile, methyl iodide, methyl tosylate and the other nucleophiles was performed as reported.[1,5] The rate constants for the anionic nucleophiles were determined from runs where the initial concentrations of the nucleophiles were lower than 10^{-2} M. The rate constants for the selenocyanate, the thiocyanate, the cyanate, and the azide ions were determined both with the UV and the IR technique.[5] The rate of the reaction between methyl tosylate and tetraphenylarsonium acetate was determined by measuring the formation of methyl acetate by the peak height at 1740 cm^{-1}.

In the cases of triphenyl phosphine, triethyl amine, and the chloride ion, the UV method was applied. The rate constants collected in

Table 1 are supposed to be well within ± 5 %, except the rate constant for the chloride ion which is probably not better than ± 10 % due to the small absorption difference between reactants and products in UV in this reaction. No method was found useful to determine the rate constant for the reaction between methyl tosylate and the cyanide ion.

The UV measurements were performed with a Beckmann DB Spectrophotometer, using 0.1 cm quartz cells. The IR measurements were performed on a Unicam SP 200 Infrared Spectrophotometer using 0.1 cm liquid cells. The temperature during the experiments was $25 \pm 0.2°C$.

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Xanthone Studies
IV.* Hydroxyl Proton Chemical Shifts in the Structural Investigation of Xanthones

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^{1}H NMR-spectroscopy is extensively used in structural investigations of xanthones. Substitution patterns are usually determined on the basis of chemical shift and spin coupling data for the aromatic protons.[1] This paper presents a supplementary method based upon measurement of the chemical shifts in DMSO-d_6 of the hydroxyl protons of oxygenated xanthones.

Contrary to experiences reported for similar studies of flavanoids [2,3] signal detection was not impaired by the small amounts of water invariably present in the solvent and giving rise to a signal at approx. δ 3.5 ppm, nor was excessive signal broadening observed upon keeping the solutions for several hours. In every case investigated the positions and appearances of the hydroxyl signals were not appreciably influenced by the addition of up to 1 % (v/v) of water. There was no evidence for the decomposition of any of the xanthones in DMSO solution.

Xanthones bearing a 1-hydroxyl ** group and one or more methoxyl groups are sparingly soluble in DMSO and their NMR-spectra have, as a result, been recorded in CDCl$_3$ solution. It was expected, however, that the chemical shift of the 1-hydroxyl proton would be determined mainly by its strong intramolecular hydrogen bonding to the carbonyl group and thus that it would be largely solvent-independent. This has been confirmed in some cases for which spectra have been recorded using both solvents.

The hydroxyl protons of the xanthones investigated resonate in the region δ 9.25 – 13.35 ppm (Table 1) and thus, because of the influence of the carbonyl group, they are more or less deshielded relative to the hydroxyl proton of phenol (δ 9.30). As

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** The numbering system is based on 9-xanthenone as the parent compound.