

The Influence of the Solvent on Reaction Velocity

XXV. Dependence of the Substituent Effect on Solvent Composition in the Alkaline Hydrolysis of Benzoic Esters in Dimethyl Sulphoxide-Water Mixtures

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The alkaline hydrolysis of ethyl benzoate, ethyl *p*-aminobenzoate and ethyl *p*-nitrobenzoate in dimethyl sulphoxide-water mixtures containing 400 ml and 200 ml of water per litre has been investigated. The reaction is accelerated by DMSO, but the acceleration is marked only at high DMSO concentrations. The extent to which a substituent influences the reaction velocity is dependent on the solvent. This dependence is closely similar to that occurring for the alkaline hydrolysis in acetone-water and ethanol-water mixtures. The results support the view that the rate enhancement in the presence of DMSO is due to a decreased solvation of the hydroxide ion, which makes it very active.

In two previous investigations^{1,2} of the alkaline hydrolysis of *p*-, *m*-, and *o*-substituted ethyl benzoates in acetone-water and ethanol-water mixtures, it was found that the substituent effect varies to a considerable extent with the solvent. In continuation of these studies we have measured the rates of the alkaline hydrolysis of ethyl benzoate, ethyl *p*-aminobenzoate and ethyl *p*-nitrobenzoate in two mixtures of dimethyl sulphoxide (DMSO) and water at different temperatures. The two substituted esters were chosen so that the substituent effects would be of opposite sign and as pronounced as possible in order that the changes in them caused by variations in the solvent could be measured with the highest accuracy.

EXPERIMENTAL

Ethyl benzoate was distilled at reduced pressure. Ethyl *p*-aminobenzoate and ethyl *p*-nitrobenzoate melted after several crystallizations from ethanol at 90.5–91.5° and 56.5–57.0°, respectively. Dimethyl sulphoxide (Nitroglycerin AB, Gyttorp, Sweden), purified by distillation at reduced pressure and repeated fractional crystallization from the melt, had a melting point of 18.53°. The water used as solvent in the kinetic experiments was freshly distilled.

The solvents for the esters were prepared by diluting a measured volume of water with DMSO to a definite volume in a volumetric flask. The sodium hydroxide solutions were prepared in a similar manner from a stock base solution and DMSO. The method employed in the kinetic experiments was the titration method described previously.³ In each experiment 5 ml of a 0.05 M ester solution and 5 ml of a 0.05 M NaOH solution were measured with a pipette into the two compartments of the reaction vessel, so that after mixing, the initial concentration of each reactant was always 0.025 mole/litre. Seven to ten samples were titrated in each run. The data for all runs conformed well with the second-order rate equation. The esters, especially ethyl *p*-nitrobenzoate, are very sparingly soluble in mixtures of high water content, wherefore experiments with the above-mentioned initial concentrations could not be extended to solvents containing more than 400 ml of water per litre. On the other hand, sodium hydroxide is sparingly soluble in DMSO-water mixtures which contain less than 200 ml of water per litre. Between 7.5° and 50° electrically regulated thermostats constant to within $\pm 0.02^\circ$ were used. Experiments at 0° were carried out in an insulated vessel which contained crushed ice and water. All thermometers were checked against a thermometer calibrated at the National Bureau of Standards (U.S.A.).

RESULTS AND DISCUSSION

Table 1 contains the means of the experimental rate constants corrected for the thermal expansion of the solvent.³ Table 2 gives the activation energies E and the logarithms of the frequency factor A calculated by the method of least squares from the rate constants. The plots of $\log k$ against $1/T$ were linear in all cases. Table 2 contains also the values of the entropy of activation ΔS^* for 25° and the free enthalpy of activation ΔG^* , calculated by the usual formulas.

It has been previously found that the rate of alkaline hydrolysis of ethyl acetate is accelerated by dimethyl sulphoxide,³ the rate increase being especially pronounced at mole fractions of DMSO greater than about 0.28. Table 1 shows that the same is true also for the ethyl benzoates; the rate constant is in every case greater in solvent II (water 200 ml/l) than in solvent I (water 400 ml/l). This increase of reaction velocity has been attributed to an increased

Table 1. The alkaline hydrolysis of esters $\text{XC}_6\text{H}_4\text{COOC}_2\text{H}_5$ in DMSO-water mixtures.

X	Water in the solvent			k l mole ⁻¹ sec ⁻¹						
	ml/l	wt. %	x_w	0.00°	7.50°	15.00°	20.00°	25.00°	40.00°	50.00°
<i>p</i> -NH ₂	400	36.8	0.716			0.000237		0.000612	0.00231	0.00507
»	200	18.1	0.490			0.000330		0.000896	0.00366	0.00883
H	1000 *	100.0	1.000			0.0138		0.0293	0.0800	0.152
»	400	36.8	0.716			0.0141		0.0328	0.0956	0.187
»	200	18.1	0.490	0.0115		0.0437		0.101	0.311	
<i>p</i> -NO ₂	400	36.8	0.716				1.74	2.51	6.30	
»	200	18.1	0.490	1.69	3.20	5.21		9.93		

* Ref.¹

Table 2. The alkaline hydrolysis of esters $\text{XC}_6\text{H}_4\text{COOC}_2\text{H}_5$ in DMSO-water mixtures.

X	Water in the solvent	E cal	$\log A$	ΔS^* E U.	ΔG^* cal
$p\text{-NH}_2$	400 ml/l (solvent I)	16 240	8.692	-20.7	21 820
	200 » (solvent II)	17 380	9.696	-16.2	21 620
H	400 »	13 610	8.482	-21.7	19 490
	200 »	14 040	9.293	-18.0	18 820
$p\text{-NO}_2$	400 »	11 660	8.935	-19.6	16 910
	200 »	11 360	9.323	-17.9	16 100

activity of the hydroxide ion caused by its decreased solvation in presence of DMSO.⁴ The ratios of the rate constants in the two solvents, $k_{\text{II}}/k_{\text{I}}$, increase in the order $p\text{-NH}_2 < \text{H} < p\text{-NO}_2$, as is seen from Table 3. For ethyl p -aminobenzoate and ethyl benzoate $k_{\text{II}}/k_{\text{I}}$ increases, whereas for ethyl p -nitrobenzoate it decreases with rising temperature. On going from solvent I to solvent II, the activation energy (Table 2) increases for ethyl p -aminobenzoate and ethyl benzoate, the increase being particularly large for the former. The increase in the reaction velocity of these esters is entirely due to an increase in the frequency factor, the influence of which more than counteracts the opposite effect of the change in the activation energy. In the case of ethyl p -nitrobenzoate, both the change in E and that in A alter the rate in the same direction.

The ratio $k_{\text{II}}/k_{\text{I}}$ can be written in the form

$$\frac{k_{\text{II}}}{k_{\text{I}}} = \frac{A_{\text{II}}}{A_{\text{I}}} e^{-\Delta E/RT}$$

The values of $A_{\text{II}}/A_{\text{I}}$ and $e^{-\Delta E/RT}$ which reveal the effects of changes in A and E are given in Table 3. The table contains also the values of $\Delta E = E_{\text{II}} - E_{\text{I}}$, $\Delta \Delta S^* = \Delta S^*_{\text{II}} - \Delta S^*_{\text{I}}$ and $\Delta \Delta G^* = \Delta G^*_{\text{II}} - \Delta G^*_{\text{I}}$.

In spite of the fact that the variation of the reaction rate with the water content of the solvent is opposite to that in acetone-water or ethanol-water mixtures, changes in the ratios $k_{\text{X}}/k_{\text{H}}$ follow the same order in DMSO mixtures

Table 3. Comparison of the reactions in solvents I and II.

X	$k_{\text{II}}/k_{\text{I}}$			ΔE	$A_{\text{II}}/A_{\text{I}}$	$\Delta \Delta S^*$	$\Delta \Delta G^*$	$e^{-\Delta E/RT}$ (25°)
	15.00°	25.00°	40.00°					
$p\text{-NH}_2$	1.39	1.46	1.58	+ 1140	10.09	+ 4.5	-200	0.146
H	3.08	3.12	3.22	+ 430	6.46	+ 3.7	-670	0.484
$p\text{-NO}_2$	4.27	4.05	3.92	-300	2.44	+ 1.7	-810	1.166

as in the last-mentioned solvent mixtures, *i.e.* if the substituent X repels electrons (NH_2), k_X/k_H decreases and if the substituent attracts electrons (NO_2), the ratio increases with decreasing water concentration (Table 4). The ratio k_X/k_H increases with rising temperature if X is *p*- NH_2 , and decreases if X is *p*- NO_2 . The lower reaction velocity of ethyl *p*-aminobenzoate compared to that of the unsubstituted ester is due to the higher energy of activation, the ratio of frequency factors having an opposite effect. In the case of ethyl *p*-nitrobenzoate, both A_X/A_H and $E_X - E_H (= \Delta E')$ tend to increase the reaction rate. The values of the two factors, A_X/A_H and $e^{-\Delta E'/RT}$, on which k_X/k_H depends according to the equation

$$\frac{k_X}{k_H} = \frac{A_X}{A_H} e^{-\Delta E'/RT}$$

are given in Table 4. It is seen that $\Delta E'$ is always by far the most important factor.

Table 4 shows also that the substituent effect in each case is considerably greater in solvent II than in solvent I. Also this is in accordance with the variations of the rate in acetone-water and ethanol-water mixtures. The fact that a substituent which increases the negative charge on the carbonyl carbon in the ester molecule reduces and a substituent which makes the carbonyl carbon less negative augments the reaction velocity, and the fact that the substituent effect becomes more pronounced when the dielectric constant of the solvent is decreased indicate that the reaction is governed by the repulsion between the seat of reaction and the attacking hydroxide ion. Since it is reasonable to assume that the electrostatic forces from the substituent to the seat of reaction are always transmitted to the same extent through the molecule itself and because there is no steric effect with *para*-substituted esters, a greater part of the substituent effect is transmitted through solvent II than through solvent I. The absolute percentage of the transmission by the two routes is difficult to estimate, but on the basis of the values of $\Delta \Delta G^{**'}$ in Table 4 it can be concluded that the part of the substituent effect transmitted through solvent II is for ethyl *p*-aminobenzoate greater by 470 cal/mole than that transmitted through solvent I, the total substituent effect in solvent I being 2330 cal/mole. For ethyl *p*-nitrobenzoate the corresponding values are 140 and 2580 cal/mole.

Table 4. Substituent effects in solvents I and II.

X	Solvent	k_X/k_H			$\Delta E'$	A_X/A_H	$\Delta \Delta S^{**'}$	$\Delta \Delta G^{**'}$	$e^{-\Delta E'/RT}$
		15.00°	25.00°	40.00°					
<i>p</i> - NH_2	I	0.0168	0.0187	0.0239	+ 2630	1.62	+ 1.0	+ 2330	0.0118
	II	0.00756	0.00887	0.0118	+ 3340	2.53	+ 1.8	+ 2800	0.00356
<i>p</i> - NO_2	I	86.5	76.6	64.5	- 1950	2.84	+ 1.9	- 2580	26.9
	II	119	98.4	79.4	- 2680	1.07	+ 0.1	- 2720	92.2

The values of the kinetic quantities for the reactions in the acetone-water mixture which contains 400 ml of water per litre are ⁵:

	k_{25}	E	$\log A$
<i>p</i> -NH ₂	0.0000864	16 700	8.23
H	0.00289	14 560	8.18
<i>p</i> -NO ₂	0.246	12 400	8.55

A comparison of these figures with the data in Table 2 shows that the greater reaction velocity in DMSO-water containing the same molar concentration of water is partly due to a lower value of E and partly to a higher value of A , both of which alter the velocity in the same direction. This is interesting since the higher velocity of the alkaline hydrolysis of ethyl acetate in DMSO-water is entirely due to a higher value of the frequency factor, the activation energy being greater in DMSO-water than in acetone-water mixtures. Also these results show how complicated solvent effects can be.

The fact that the substituent effects in alkaline ester hydrolysis are in both direction and order of magnitude similar in DMSO-water and acetone-water mixtures, although the reaction rate increases in the former solvents and decreases in the latter solvents with increasing concentration of the organic component, strongly supports the view that the increased reaction rate in DMSO-water mixtures is due to a higher activity of the hydroxide ion.

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