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ALKALINE HYDROLYSIS OF DICARBOXYLIC ESTERS IN AQUEOUS DIMETHYL SULFOXIDE

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Subsequent to the review article of Parker$^{1)}$ wherein he had pointed out the remarkable rate enhancing ability of dipolar aprotic solvents such as dimethyl sulfoxide on S_N2 reactions involving anions, a number of papers have appeared on the alkaline hydrolysis of monoesters in DMSO - water mixtures$^{2-4)}$. The general expectation of a considerable rate enhancement in solvents containing increasing percentages of DMSO was confirmed and this has been attributed to the diminution of OH^- ion solvation as a result of the competition between this anion and DMSO molecules for the water molecules and to an increase in transition state solvation. It appeared to us of special interest to further investigate the role of DMSO as a solvent in the alkaline hydrolysis of dibasic esters in as much as the effect of the solvent is likely to be discriminating in the hydrolysis of the diester and the half ester anion.

The alkaline hydrolysis of a number of diesters has been investigated in acetone-water and dioxan-water systems and consistantly a ratio of k_1/k_2 greater than 2 has been obtained$^{5-7)}$. This has been attributed to an electrostatic repulsion between the half ester anion and the hydroxide ion in the second step, leading to a lower rate and hence a higher ratio. In view of the varying behaviour of such solvent mixtures in ester hydrolysis, we have now been prompted for the first time to measure the rates of alkaline hydrolysis of diethyl succinate, diethyl phthalate and diethyl adipate in DMSO - water mixtures as also in ethanol - water mixtures and to compare the k_1/k_2 ratios in these solvents.

The rate studies in these solvents were made by titrimetric methods using a screened indicator composed of neutral red and methylene blue. The treatment that has been followed for the evaluation of the rate constants of the I and II steps is that of Frost and Schwemer[8] by which $1/K$ ($= k_1/k_2$) was obtained by a graphical evaluation from different time ratios. Knowing the numerical values of t, B_0 and τ (τ having been evaluated from the $\tau - 1/K$ graphs for various fractions of the total reaction) k_1 was calculated using the relation $\tau = B_0 k_1 t$. From this, k_2 was subsequently obtained as $k_2/k_1 = K$. All the saponification experiments were conducted at the constant ionic strength of 0.02M. This was done essentially to minimise the probability of any medium effects due to changes in ionic strength that will occur as the diacid ion is produced.

Tables I to IV present the kinetic data of this work.

Table I

Alkaline Hydrolysis of Diethyl Succinate
in aqueous DMSO at 35°C

Solvent Composition DMSO - H_2O (v/v)	k_1 ($l.mol^{-1}sec^{-1}$)	k_2 ($l.mol^{-1}sec^{-1}$)	k_1/k_2
50 - 50	0.6902	0.07244	9.54
60 - 40	0.7308	0.08044	9.09
70 - 30	0.9932	0.11752	8.45
80 - 20	1.5986	0.20500	7.76

Table II

Alkaline Hydrolysis of Diethyl Phthalate
in aqueous DMSO at 35°C

Solvent Composition DMSO - H_2O (v/v)	k_1 ($l.mol^{-1}sec^{-1}$)	k_2 ($l.mol^{-1}sec^{-1}$)	k_1/k_2
60 - 40	0.06616	0.006640	9.958
70 - 30	0.13584	0.014928	9.090
80 - 20	0.36720	0.043600	8.426

Table III

Alkaline Hydrolysis of Diethyl Succinate
in aqueous Ethanol at 35°C

Solvent Composition EtOH - H_2O (v/v)	k_1 ($l.mol^{-1}sec^{-1}$)	k_2 ($l.mol^{-1}sec^{-1}$)	k_1/k_2
60 - 40	0.11160	0.02114	5.21
80 - 20	0.05979	0.01652	3.62

Table IV

Alkaline Hydrolysis of Diethyl Phthalate
in aqueous Ethanol at 35°C

Solvent Composition EtOH - H_2O (v/v)	k_1 ($l.mol^{-1}sec^{-1}$)	k_2 ($l.mol^{-1}sec^{-1}$)	k_1/k_2
60 - 40	0.004622	0.0008720	5.29
80 - 20	0.003162	0.0008179	3.84

The following facts emerge from these results:

(a) The rates for both the first and the second steps increase in aqueous dimethyl sulfoxide and decrease in aqueous alcohol with the decrease of water content of these solvent mixtures.

(b) The k_1/k_2 ratios are very large in DMSO - water mixtures compared to alcohol - water mixtures, acetone - water mixtures and dioxan - water mixtures*, but these decrease with increasing proportions of DMSO in the solvent mixtures.

(c) Both k_1 and k_2 increase with increasing percentage of dimethyl sulfoxide, but k_2 increases more rapidly than does k_1.

(d) Diethyl succinate and diethyl phthalate have nearly the same k_1/k_2 ratio, while diethyl adipate has a much lower k_1/k_2 ratio (Table V).

The very large values of k_1/k_2 obtained in DMSO - water mixtures are to be attributed to the differential behaviour of the organic solvent on the two steps of the hydrolytic reaction. While the first step involves an ion and a dipole, the second step is between the hydroxide ion and the half ester ion. The repulsion between this desolvated anion and the half ester anion will be much greater in DMSO - water mixtures leading to a considerable dimunition in the value of k_2. The first step as happens in normal monoester hydrolysis is very much accelerated because of an easier attack by the desolvated hydroxide ion and an increased transition state solvation in DMSO - water mixtures, thereby resulting a large k_1/k_2 ratio. It is also pertinent to point out here that consistent with the general picture that the rate-determining step in $B_{Ac}2$ mechanism is the attack of the OH^- ion on the polarised carbonyl carbon of the ester, the rates of both the steps increase with increase in the percentage of DMSO in spite of the above rate retarding influence in the second step (owing to increase in the desolvated OH^- ion concentration).

Surprising, however, is the effect of increasing the DMSO concentration on the k_1/k_2 ratio. While both the steps increase with increasing proportion of DMSO in the solvent mixtures, the second step gains more than the first

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* The maximum value has never been above 7.12 in the literature for the hydrolysis of diethyl succinate.

step, leading to lower k_1/k_2 ratios in those solvents that contain a larger proportion of DMSO. The larger rate benefit of the second step seems to be due to the decreasing dielectric constant of these solvent mixtures. The large decelerating direct influence of the COO^- ion on the reaction centre in the second step of the reaction is considerably reduced in the solvent of lower dielectric constant. The repulsion between this ion and the OH^- ion would also be much less in these solvents. The fact that k_1/k_2 falls to 4.75 in the hydrolysis of diethyl adipate in 60% DMSO further confirms the operation of such a field effect. It is thus seen that a combination of electrostatic and specific solvation forces are associated with the hydrolysis of dibasic esters.

Table V

Comparison of k_1/k_2 values of various diesters at 35°C

Compound	60% DMSO	70% DMSO
Diethyl succinate	9.090	8.450
Diethyl phthalate	9.954	9.090
Diethyl adipate	4.746	4.295

The data in the present investigations also reveal that k_1 and k_2 for diethyl phthalate are smaller than those for diethyl succinate in both aqueous ethanol and in aqueous DMSO. The reduced reactivity of the aromatic ester is obviously due to the resonance stabilisation of its ground state. But the increase in k_1 (and k_2) for this ester on passing to solvent mixtures containing larger proportions of DMSO is more than for diethyl succinate under similar conditions. This seems to point out to the fact that even closely related substrates have varying sensitivity to the DMSO content in the solvent mixtures and DMSO seems to have a catalysing influence on the benzene ring enhancement of the carbonyl carbon polarizability. Roberts[2c)] has also observed this type of catalysis with ethyl benzoate.

Another notable result that emerges from the present investigations is the near identical values of the k_1/k_2 ratios of diethyl succinate and diethyl phthalate in spite of a large difference in the individual rates. This is in accordance with the work on the configurations of the parent acids where it has been shown that both possess a trans configuration. The lack of any significant hydrogen bonding in phthalic acid has already been pointed out by Westheimer[9]. Radhakrishnamurthi[7] reports values of $r = 5.3 \times 10^{-8}$ cm. and 5.07×10^{-8} cm. for succinic acid and phthalic acid respectively, where r is the distance between the carboxyl groups. The slightly higher k_1/k_2 ratio for the phthalic ester is probably due to the internal polar transmission being called into play in this ester.

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