Solvent Effects on the Kinetics of Alkaline Hydrolysis of Dimethylacetylacetone. Part II.[1] Influence of Dipolar Aprotic Solvent–Water Mixtures

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The influence of a few protic–dipolar aprotic mixtures on the kinetics of alkaline cleavage of dimethylacetylacetone has been studied. The aprotic components used are dimethyl sulphoxide, acetone, dioxan, sulpholan, dimethoxyethane, and hexamethylphosphoramide. In most of these mixtures, the behaviour of the reaction is very analogous with that of alkaline hydrolysis of esters which suggests an identical mechanism for both reactions. Moreover the determination of activation parameters in dimethyl sulphoxide–water mixtures enables one to discuss the part played by the substrate on the reaction rate. Finally, kinetic results which are similar for some media can be explained by their nearly identical basicity.

In Part I[1] the study of the influence of alcohol–water mixtures on the alkaline hydrolysis of dimethylacetylacetone enabled us to confirm that the mechanism established for that reaction was analogous to the $B_{\mathrm{AC}}2$ hydrolysis of esters. After that study for protic media, we thought it worth while to study the influence of protic–dipolar aprotic solvents. In order to compare, as before, the kinetic behaviour with that of alkaline hydrolysis of esters we chose the following mixtures: dioxan–water, acetone–water, dimethyl sulphoxide–water, and sulpholan–water. To complete this series, we examined dimethoxyethane–water and hexamethylphosphoramide–water which as far as we know have not previously been used in the case of esters. Dimethyl sulphoxide–water mixtures, which are frequently used in alkaline hydrolyses, have been specially studied.

Influence of Dimethyl Sulphoxide–Water Mixtures or Rate and Activation Parameters.—We prepared these mixtures by gradually increasing the concentration of dimethyl sulphoxide up to a mol fraction of *ca.* 0·32—0·35 (*ca.* 70% v/v). Beyond such a composition, the reaction is too fast to be examined precisely by the conductivity method. Measurements were made at 25, 20, 15, and 6 °C, and the results[2] are in Tables 1—3. Table 1 gives the parameters used to determine the medium composition, together with the temperature expansion coefficients f which are extrapolated from data from ref. 3. Table 2 gives the values of the rate constants and of k/k_0, k_0 being the rate constant of the reaction in an ethanol–water mixture (*ca.* 2% v/v EtOH) at different temperatures. Table 3 gives values of activation parameters with their standard deviations $\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$, determined by the method of least squares.

Table 1

Temperature expansion coefficients of dimethyl sulphoxide–water mixtures

H_2O % w/w	x_{DMSO}	$[H_2O]$/M	Temperature expansion coefft. f 25 °C	20 °C	15 °C	6 °C
89·1	0·028	50·0	1·002	1·000	0·999	0·997
77·9	0·062	44·4	1·002	1·000	0·998	0·995
67·1	0·102	38·9	1·002	1·000	0·997	0·993
56·6	0·150	33·3	1·003	1·000	0·996	0·991
46·6	0·209	27·9	1·003	1·000	0·996	0·990
40·8	0·251	24·6	1·003	1·000	0·995	0·989
37·0	0·281	22·4	1·003	1·000	0·995	0·988
32·3	0·325	19·7	1·003	1·000	0·995	0·987
27·7	0·376	16·9	1·004	1·000	0·995	0·986

These results may be summarized as follows: addition of dimethyl sulphoxide to the solvent causes an increase in the reaction velocity. The enhancement is gradual at the beginning, then the rise is very steep when the percentage by weight exceeds 50%. When the mol fraction of dimethyl sulphoxide is greater than 0·12, log k is a linear function of the mol fraction of dimethyl sulphoxide and the plot of log k against the logarithm of the molar water concentration is a straight line of negative slope. Supposing that this linearity continues up to water-free solvent we can obtain by extrapolation a rate constant in the anhydrous organic solvent. For the plot log k against x_{DMSO} at 25 °C the equation of the linear part is (1) with $m = 3{\cdot}17 \pm 0{\cdot}09$ and $a = 0{\cdot}71 \pm 0{\cdot}02$, with a correlation coefficient $r = 0{\cdot}998$. For

$$\log k = m x_{\mathrm{DMSO}} + a \qquad (1)$$

$x_{\mathrm{DMSO}} = 1$ k is *ca.* 127 l mol^{-1} s^{-1} and the ratio (2)

$$\frac{k_{\mathrm{DMSO}}}{k_{\mathrm{H_2O}}} = \frac{127}{0{\cdot}133} = 950 \qquad (2)$$

shows the rate-speeding factor of the reaction in aprotic dipolar solvent.

In the range of the temperatures used the solvent effect is independent of the temperature.

The free enthalpy of activation, $\Delta G^\ddagger$ decreases smoothly with increasing dimethyl sulphoxide concentration, thus reflecting the increase in reaction velocity, whereas activation enthalpy and entropy increase: the variation of $\Delta H^\ddagger$ with the medium composition is rapid and linear up to *ca.* $x_{\mathrm{DMSO}} = 0{\cdot}12$ and $\Delta H^\ddagger$ remains constant above that mol fraction. The activation entropy increases continuously in the studied range of mixtures. These changes in $\Delta H^\ddagger$ and $\Delta S^\ddagger$ have opposite influences on reaction rate: the increase in $\Delta S^\ddagger$ governs the rate which thus becomes greater.

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[1] Part I, J. P. Calmon and J. L. Canavy, *J.C.S. Perkin II*, 1972, 706.

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[3] E. Tommila and M. L. Murto, *Acta Chem. Scand.*, 1963, **17**, 1947.

The variation of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ with the solvent composition may be attributed to changes in the solvation of the reactants and the transition state. Addition of dimethyl sulphoxide to the aqueous solvent raises the solubility of the diketone and accordingly its solvation; this grows gradually with increasing sulphoxide concentration in this highly aqueous region [4] ($0 < x_{\mathrm{DMSO}} < 0{\cdot}12$). It follows that the energy of the initial state somewhat decreases with increase of the dimethyl sulphoxide concentration, then becomes greater at higher sulphoxide content owing to the reduced solvation of the hydroxide ion. The decrease of entropy of the initial state can be explained in the same way.

TABLE 2

Rate constants for the reaction in dimethyl sulphoxide–water mixtures

H_2O	25 °C		20 C°		15 °C		6 °C	
% w/w	k/l mol^{-1} s^{-1}	k/k_0	k/l mol^{-1} s^{-1}	k/k_0	k/l mol^{-1} s^{-1}	k/k_0	k/l mol^{-1} s^{-1}	k/k_0
89·1	0·142	1·07	0·116	1·07	0·087	1·05	0·059	1·06
77·9	0·162	1·23	0·125	1·15	0·097	1·17	0·065	1·16
67·1	0·192	1·45	0·145	1·34	0·113	1·36	0·074	1·33
56·6	0·257	1·94	0·212	1·95	0·159	1·92	0·099	1·78
46·6	0·405	3·07	0·322	2·97	0·255	3·07	0·157	2·82
40·3	0·521	3·95	0·445	4·11	0·357	4·30	0·212	3·80
37·0	0·660	5·00	0·560	5·17	0·431	5·40	0·260	4·67
32·3	0·944	7·15	0·735	6·78	0·628	7·57	0·363	6·53
27·7					0·885	10·66	0·527	9·46

TABLE 3

Activation parameters for the reaction in dimethyl sulphoxide–water mixtures

H_2O % w/w	$\Delta H^{\ddagger}$ cal mol^{-1}	$\pm\delta\Delta H^{\ddagger}$ cal mol^{-1}	$\Delta S^{\ddagger}$ cal mol^{-1} K^{-1}	$\pm\delta\Delta S^{\ddagger}$ cal mol^{-1} K^{-1}	$\Delta G^{\ddagger}$ (25 °C) cal mol^{-1}
89·1	7190	360	−38·4	1·3	18,630
77·9	7370	320	−37·4	1·1	18,520
67·1	7620	350	−36·2	1·2	18,410
56·6	7820	300	−35·0	1·1	18,250
46·6	7820	225	−34·1	1·3	17,980
40·8	7870	310	−33·3	1·2	17,790
37·0	7840	280	−33·0	1·1	17,670
32·3	7810	310	−32·4	1·2	17,440

We may assume that the negatively charged dipolar transition state is preferentially solvated by water molecules,[5] and that there is a moderately large initial range of mixtures over which its solvation remains practically unchanged [4] so that the enthalpy and entropy of this state remain constant. Then the solvation continuously decreases, on one hand owing to the increase of the number of water molecules bound to dimethyl sulphoxide, on the other because the pyramidal dimethyl sulphoxide molecules cannot exactly fit around the transition state.[3]

The situation is shown in Figure 1 where H' and S' refer to the initial state and H'' and S'' to the transition state: $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ increase up to *ca.* $x_{\mathrm{DMSO}} = 0{\cdot}12$, this rise being followed by a plateau for $\Delta H^{\ddagger}$ and by a gradual rise for $\Delta S^{\ddagger}$.

The rapid increase in the rate of alkaline hydrolysis of dimethylacetylacetone beyond the value of $x_{\mathrm{DMSO}} = 0{\cdot}12$ may be attributed to the enhancement of the activity of the hydroxide ion,[3,6-10] resulting in a reduction in the anion solvation.

Influence of Some Protic–Dipolar Aprotic Mixtures of the Rate.—We used the following dipolar aprotic solvents: dioxan, acetone, dimethoxyethane, tetrahydrothiophen 1,1-dioxide (sulpholan), and hexamethylphosphoramide. For each dipolar aprotic solvent–water mixture, we

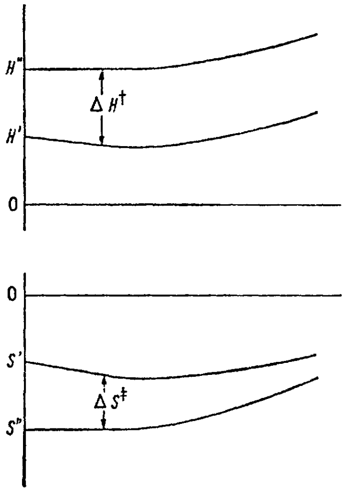

FIGURE 1 Schematic representation of solvation effects in dimethyl sulphoxide–water mixtures

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[6] D. D. Roberts, *J. Org. Chem.*, 1965, **30**, 3516.

[7] E. Tommila and T. P. Pitkänen, *Acta Chem. Scand.*, 1966, **20**, 937.

[8] J. Murto, *Suomen Kem.*, 1961, *B*, **34**, 92.

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gradually decreased the water concentration up to a mol fraction of organic solvent of *ca.* 0·3 (*ca.* 60% v/v organic solvent). So the dielectric constant is always greater than 40 except for dioxan–water. The kinetics were followed at 25 °C for all binary solvents except hexamethylphosphoramide–water for which it was necessary to work at a low temperature (6 °C). The rate constants are in Tables 4—8. The plots of these constants against solvent composition are in Figure 2: in all these protic–dipolar aprotic binary solvents, except dimethyl sulphoxide–water, the rate decreases with increasing aprotic component content of the medium.

TABLE 4

Acetone–water mixtures

H_2O % w/w	x_{acetone}	k/l mol^{-1} s^{-1}
98·5	0·005	0·127
94·4	0·018	0·119
90·0	0·033	0·113
81·2	0·067	0·100
72·2	0·153	0·086
63·2	0·209	0·077
53·9	0·279	0·067
44·5		0·0605

TABLE 5

Sulpholan–water mixtures

H_2O % w/w	$x_{\text{sulpholan}}$	k/l mol^{-1} s^{-1}
91·6	0·014	0·113
85·7	0·024	0·104
74·4	0·049	0·085
63·7	0·079	0·074
53·5	0·115	0·070
43·8	0·161	0·065
34·6	0·271	0·064
25·9	0·385	0·062

TABLE 6

Hexamethylphosphoramide–water mixtures

H_2O % w/w	x_{HMPT}	k/l mol^{-1} s^{-1}
93·1	0·007	0·0553
87·7	0·014	0·0549
77·5	0·028	0·0523
67·3	0·046	0·0501
56·4	0·072	0·0483
47·1	0·120	0·0458
37·8	0·142	0·0428

TABLE 7

Dioxan–water mixtures

H_2O % w/w	x_{dioxan}	k/l mol^{-1} s^{-1}
98	0·004	0·127
93	0·015	0·120
87·7	0·028	0·112
77·5	0·056	0·104
67·6	0·089	0·101
57·8	0·130	0·100
48·3	0·180	0·099
38·9	0·242	0·101

It is not easy to classify the binary solvents dioxan–water, acetone–water, sulpholan–water, and dimethoxyethane–water because of their almost similar behaviour ($0·05 < k$/l mol^{-1} s^{-1} $< 0·13$), but at an identical composition for $x < 0·24$ the reaction rate decreases as follows: dioxan > acetone–dimethoxyethane > sulpholan. In dioxan–water the rate constant increases again beyond $x_{\text{dioxan}} = 0·2$ for which the dielectric constant is lower than 30. This phenomenon can be explained, as for t-butyl alcohol–water, by the appearance of ion pairs.

TABLE 8

Dimethoxyethane–water mixtures

H_2O % w/w	x_{DME}	k/l mol^{-1} s^{-1}
98	0·003	0·127
93·9	0·013	0·122
89·3	0·023	0·116
79·7	0·048	0·105
70·3	0·078	0·096
60·8	0·114	0·087
51·6	0·158	0·076

The results are in all respects similar to those obtained for the alkaline hydrolysis of esters.[11,12]

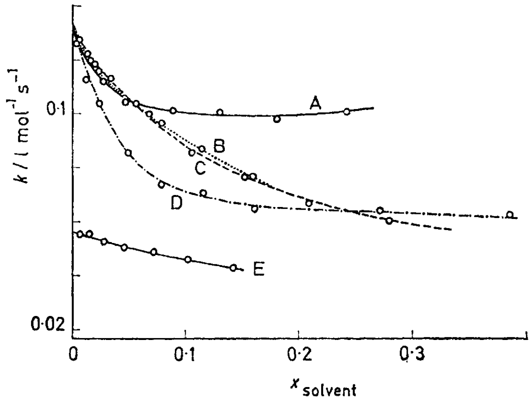

FIGURE 2 Variation of rate constant with solvent composition: A, dioxan–water at 25 °C; B, dimethoxyethane–water at 25 °C; C, acetone–water at 25 °C; D, sulpholan–water at 25 °C; E, hexamethylphosphoramide–water at 6 °C

It seems that the basicity scale Δν [13] may explain the different behaviour of these binary solvents on the reaction rate, except for hexamethylphosphoramide: the closely related results which have been obtained with sulpholan, acetone, dioxan, and dimethoxyethane correspond to basicities of the same order of magnitude. To account for the kinetic behaviour of alkaline hydrolysis of carboxylic esters in dioxan–water and acetone–water on one hand, and dimethyl sulphoxide–water on the other, Tommila [11] argues from the mutual attraction of solvent components, related to their heats of mixing. The hydroxide ions will be less hydrated and consequently the reactions will be faster in it when the

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attraction will be small. This notion seems consistent with the basicity because it is logical to think that intermolecular interactions between water molecules and aprotic solvents of closely related basicity (dioxan, acetone, sulpholan, and dimethoxyethane) will be of similar strength, and thus lead to similar kinetic effects.

Comparative studies of the physical properties of dioxan–water and dimethoxyethane–water[14] indicate that the interaction between dimethoxyethane and water is significantly greater than that between dioxan and water, particularly because of the easy penetration of the dimethoxyethane molecules into the hydrogen-bonded lattices of water.

In agreement with these conclusions about dioxan–water, acetone–water, and dimethoxyethane–water interactions, our results suggest a great structural analogy between acetone–water and dimethoxyethane–water media.

As far as we know, the only reactions studied in the sulpholan–water are alkaline hydrolyses of ethyl benzoates.[15] For ethyl *p*-aminobenzoate for example, this solvent acts in the same way as acetone–water; the plots of k_s/k_u (k_s is the rate constant corresponding to the substituted compound, k_u that of the unsubstituted compound) against solvent composition in both media intersect at *ca.* $x_{\text{solvent}} = 0{\cdot}15$. Beyond that value acetone–water is the more reaction retarding solvent. Aside from the different value of the mol fraction of acetone (0·24 in our case), our results still offer a striking similarity with alkaline hydrolysis of esters.

The most unexpected results have been obtained with hexamethylphosphoramide–water mixtures. This solvent is known to be the most basic and the anion activity is much more enhanced in it than in dimethyl sulphoxide.[16–18] Recent studies have shown a less electrophilic character of this solvent than of dimethyl sulphoxide, essentially because of the great steric hindrance around the phosphorus and the dispersion of the positive charge over all the nitrogen atoms.[19,20] These results suggest the existence of $PO(NMe_2)_3$–H_2O 1 : 1 complexes rather than 2 : 1 as in dimethyl sulphoxide–water mixtures.[3] In accordance with the previous statements about the interactions between water and solvent molecules, hexamethylphosphoramide–water mixtures would be, in highly aqueous solutions, less ' active ' than dimethyl sulphoxide–water. However this effect certainly cannot account by itself for the kinetic behaviour, and a strongly reduced solvation of the transition state by steric hindrance is not excluded.

Conclusion.—The similarity in behaviour between alkaline hydrolysis of dimethylacetylacetone and esters, which has been stressed for alcohol–water solvents,[1] exists for protic–dipolar aprotic solvents, thus bearing out the mechanism suggested by Pearson and Mayerle[21] similar to that of $B_{AC}2$ alkaline hydrolysis of esters. In water–dimethyl sulphoxide mixtures, the only rate-increasing mixtures among those we have studied, the reduction in the degree of hydroxide-ion solvation seems to be the main factor influencing the rate. The similar kinetic effects observed in dioxan–water, acetone–water, sulpholan–water, and dimethoxyethane–water correspond to closely related basicities of the solvents.

EXPERIMENTAL

The method and conditions have been described.[1] The vapour pressure of acetone being high we could not make nitrogen bubble in acetone–water. Therefore we had to work with a stoppered vessel for these mixtures. Hexamethylphosphoramide has a high viscosity and was not a good electrochemical solvent for our purpose. Consequently for this solvent we used the method of Pearson and Mayerle,[21] namely the titration of the acid produced. This technique entails concentrations much higher than the conductivity method, and also required a low temperature (6 °C).

Dioxan (Merck, *pro analysi*) and acetone (Fluka, puriss) were used as received. Dimethyl sulphoxide, dimethoxyethane, sulpholan, and hexamethylphosphoramide were Fluka reagents; they were dried (CaH_2) and distilled through a Vigreux column. Dimethyl sulphoxide was stored over 4 Å molecular sieve.

Calculations were done on an Olivetti Programma 102 computer.

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