Solvent Effects on the Kinetics of Alkaline Hydrolysis of Dimethylacetylacetone. Part I. Influence of Alcohol–Water Mixtures

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The kinetics of the alkaline cleavage of dimethylacetylacetone have been studied conductimetrically in a series of alcohol–water mixtures. The high negative value of the activation entropy in aqueous solutions, and the behaviour of the system in alcohol–water mixtures, shows that the reaction is similar to the alkaline hydrolysis of esters. However the variation of activation enthalpy in a highly aqueous ethanol solution can best be interpreted in terms of a change in solvent structure.

DIMETHYLACETYLACETONE is cleaved by aqueous alkali to give acetate and 1,1-dimethylacetone [reaction (1)]. Pearson and Mayerle [1] studied the rate by titrating the acid produced and found a second-order kinetic law (2),

$$\mathrm{AcCMe_2Ac + OH^- \longrightarrow AcO^- + CHMe_2Ac} \qquad (1)$$

$$v = k[\mathrm{OH^-}][\text{diketone}] \qquad (2)$$

which was explained by a mechanism analogous to that of alkaline hydrolysis [2] of esters ($B_{\mathrm{AC}}2$), as in reactions

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[1] R. G. Pearson and E. A. Mayerle, *J. Amer. Chem. Soc.*, 1951, **73**, 926.

[2] C. K. Ingold, ' Structure and Mechanism in Organic Chemistry,' Cornell Univ. Press, Ithaca, New York, 1953, p. 752.

(3)—(5). For esters the slow step is (3), yet Pearson and

$$\mathrm{AcCMe_2Ac + OH^- \rightleftharpoons {}^-O{\cdot}CMe(OH){\cdot}CMe_2Ac} \qquad (3)$$

$$\mathrm{{}^-O{\cdot}CMe(OH){\cdot}CMe_2Ac \longrightarrow AcOH + {}^-CMe_2Ac} \qquad (4)$$

$$\mathrm{AcOH + {}^-CMe_2Ac \rightleftharpoons AcO^- + CHMe_2Ac} \qquad (5)$$

Mayerle could not define it for the alkaline cleavage of dimethylacetylacetone, because the second-order law did not enable them to distinguish between the first two steps. We have studied the effect of aqueous alcoholic solvents on this alkaline hydrolysis, bearing in mind the apparent analogy with that of esters, which has been studied in alcohol–water mixtures by Tommila and his co-workers.[3] We also attempt to deduce the activation parameters in aqueous solutions.

Determination of the Activation Parameters.—We made several four-temperature kinetic measurements[4] in highly aqueous ethanolic solutions (*ca.* 2% v/v ethanol). Results are in Table 1. By the method of least squares

TABLE 1

Alkaline hydrolysis of dimethylacetylacetone in water

t/°C	25	20	15	6
10^3k_h/l mol^{-1} s^{-1}	132	108	83	55·6

$$\ln\frac{hk_h}{kT} = -\frac{\Delta H^\ddagger}{RT} + \frac{\Delta S^\ddagger}{R} \qquad (6)$$

we obtain, from equation (6) the activation enthalpy $\Delta H^\ddagger = 7030 \pm 250$ cal (correlation coefficient $r = 0{\cdot}999$) and the activation entropy $\Delta S^\ddagger = -39{\cdot}0 \pm 0{\cdot}9$ cal mol^{-1} K^{-1} ($r = 0{\cdot}999$). To explain this value of ΔS, let us try to predict the sign of $\Delta S^\ddagger$ in the different steps of the suggested mechanism.

The addition step (3) has a negative entropy change. In fact the only factor leading to a slight positive increment would result from a decrease in the anion solvation compared with that of the system ' hydroxide ion of small volume–diketone '. It is no doubt largely compensated by the rigidity of the anion and above all by the loss of translational and rotational degrees of freedom. These predictions are confirmed by activation entropies of alkaline hydrolysis of esters. Table 2 shows values of $\Delta S^\ddagger$ as well as those of rate constants of alkaline hydrolysis of a series of aliphatic ethyl esters.[3,5] Roberts[6] obtained similar results, but smaller entropies of activation.

TABLE 2

Alkaline hydrolysis of carboxylic esters in water at 25 °C

Esters	Ref.	$\Delta S^\ddagger$/cal mol^{-1} K^{-1}	10^3k_h/l mol^{-1} s^{-1}
$\mathrm{MeCO_2Et}$	3	−26·7	111
$\mathrm{EtCO_2Et}$	5	−29·5	87
$\mathrm{Pr^nCO_2Et}$	5	−32·4	38·3

The entropy change of the second step is certainly positive or near zero, because the number of translational and rotational degrees of freedom of the cleavage products is far greater than those of the intermediate anion.

Although the activation entropy approaches that of the hydrolysis of esters, it would be difficult to conclude that the first step is rate-determining, especially if the entropy value is near zero in the second step.

Influence of Alcohol–Water Mixtures on the Velocity and the Activation Parameters of the Reaction.—For each type of binary solvent (methanol–water, ethanol–water, and t-butyl alcohol–water) we varied the alcohol concentration gradually, up to a mol fraction of alcohol of *ca.* 0·6. Beyond that value some workers[3,7] have noticed strange kinetic behaviour, namely a great decrease in the rate constant, attributed to the equilibrium (7) and the consequent decrease of the hydroxide ion concentration.

$$\mathrm{OH^- + ROH \rightleftharpoons RO^- + H_2O} \qquad (7)$$

The rate constants were determined at 25 °C in the case of methanol–water and t-butyl alcohol–water mixtures and at 25 and 6 °C for ethanol–water. In the last case a great decrease in reaction velocity led us to use mixtures containing not less than 45% (w/w) water.

RESULTS

The principal experimental results are in Tables 3—5. Table 5 also includes activation parameters for ethanol–water mixtures. The standard deviations ($\delta\Delta H^\ddagger$ and $\delta\Delta S^\ddagger$) cannot be given because the kinetic experiments were only carried out at two temperatures, but which nevertheless did not seriously impair the accuracy of results. Indeed Wiberg[8] suggests that the error made on the slope of

TABLE 3

Methanol–water mixtures

$\mathrm{H_2O}$/% w/w	x_{MeOH}	Expansivity (K^{-1})	$\frac{10^3k_h}{\mathrm{l\ mol^{-1}\ s^{-1}}}$
98·5	0·009	1·001	123
94·5	0·032	1·001	109
90·2	0·058	1·001	88·0
81·5	0·113	1·001	57·0
72·6	0·175	1·002	34·3
63·5	0·244	1·002	21·8
54·3	0·321	1·003	15·4
44·7	0·409	1·003	12·7

TABLE 4

t-Butyl alcohol–water mixtures

$\mathrm{H_2O}$/% w/w	x_{BuOH}	Expansivity (K^{-1})	$\frac{10^3k_h}{\mathrm{l\ mol^{-1}\ s^{-1}}}$
98·5	0·004	1·001	133
94·5	0·014	1·001	129
90·7	0·024	1·001	122
85·8	0·039	1·001	107
82·9	0·048	1·002	102
72·7	0·083	1·003	82·5
63·9	0·120	1·003	68·5
54·8	0·167	1·004	62·1
45·3	0·226	1·004	64·0
35·4	0·306	1·005	69·3
25·0	0·420	1·005	88·8

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[3] E. Tommila, A. Koivisto, J. P. Lyyra, K. Antell, and S. Heimo, *Ann. Acad. Sci. Fennicae.*, 1952, *A*II, 47.

[4] J. L. Canavy, Thesis, Toulouse, 1970.

[5] E. Tommila and S. Hietala, *Acta Chem. Scand.*, 1954, **8**, 257.

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

[7] J. Murto, *Suomen Kem.*, 1962, *B*, **35**, 157.

[8] K. B. Wiberg, ' Physical Organic Chemistry,' John Wiley, New York, 1964, p. 377.

the plot ln k_h/kT against $1/T$ is chiefly controlled by the two extreme temperatures. To compute the error $\delta\Delta H^\ddagger$ in $\Delta H^\ddagger$ Wiberg suggests equation (8), where T and T' are the

$$\delta\Delta H^\ddagger = 2R \cdot \frac{T'T}{T - T'}\alpha \qquad (8)$$

two extreme temperatures and α is the maximum fractional error in the rate constants. If we consider that the accuracy of the determination of the rate constants is 1% we get in that case $\delta\Delta H^\ddagger = 200$ cal mol^{-1}.

TABLE 5

Ethanol–water mixtures

H_2O/% w/w	x_{EtOH}	Expansivity (K^{-1}) 25 °C	Expansivity (K^{-1}) 6 °C	10^3k_h/l mol^{-1} s^{-1} 25 °C	10^3k_h/l mol^{-1} s^{-1} 6 °C	$\Delta H^\ddagger$/cal mol^{-1}	$\Delta S^\ddagger$/cal mol^{-1} K^{-1}	$\Delta G^\ddagger$/cal mol^{-1}
98·5	0·006	1·001	0·999	132	55·7	7030	−39·0	18,650
94·5	0·006	1·001	0·999	124	53·3	6800	−39·9	18,690
90·2	0·040	1·001	0·998	111	48·8	6580	−40·9	18,770
81·4	0·081	1·002	0·996	89·2	40·8	6240	−42·4	18,880
72·4	0·129	1·003	0·992	73·5	28·4	7730	−37·8	18,990
63·4	0·184	1·003	0·990	59·8	18·8	9500	−32·3	19,130
54·2	0·248	1·004	0·989	48·0	1·28	10,920	−28·0	19,260
44·8	0·325	1·005	0·988	43·3	0·97	12,500	−22·9	19,320
35·0	0·420	1·005		38·2				
24·8	0·542	1·005		32·8				

By extrapolation and after numerous measurements made in highly aqueous mixtures, we obtained the rate constant of the reaction at 25 °C in pure water (Figure 1) as $k = 133{\cdot}5 \times 10^3$ l mol^{-1} s^{-1}. A survey of these results, similar to that made by Tommila for alkaline hydrolysis of esters, shows that the rate decreases with increasing alcohol concentration in alcohol–water mixtures.

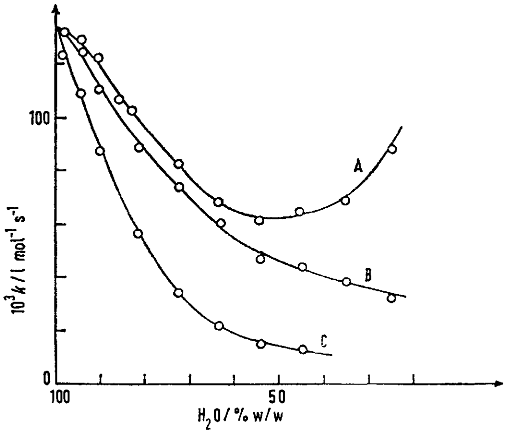

FIGURE 1 Variation of rate constant with proportion of water in the solvent at 25 °C; A, Bu^{t}OH; B, EtOH; C, MeOH

If the solvent composition is given as a percentage by weight, the rate decreases in the sequence Bu^{t}OH > EtOH > MeOH. Beyond 50% ($x_{BuOH} > 0{\cdot}2$) the addition of t-butyl alcohol increases the rate. We think that this inversion of the rate constant is due to a limitation in the chosen physical method; the transition occurs where the dielectric constant falls below 30,[9] and the number of free ions thus falls.

Comparative Study of the Polarity of the Medium.—The Hughes–Ingold theory [10] of solvent effects helps to explain the behaviour in alcohol–water mixtures. Table 6 shows constants for the three pure alcohols [9,11–13] used to determine the medium polarity; they are the physical parameters used by Ingold (dielectric constant ε and dipole moment μ), Kosower's empirical constant Z,[11] and the E_T values of Dimroth and Reichardt.[12] All the parameters are in the sequence MeOH > EtOH > Bu^{t}OH. The theory of Hughes and Ingold predicts that, at a similar composition, the methanol–water solvent gives the maximum decrease in the reaction rate; t-butyl alcohol–water gives the least decrease, in agreement with our results.

TABLE 6

Polarity parameters of alcohols at 25 °C

Solvents	ε [9]	μ/D [13]	Z/kcal mol^{-1} [11]	E_T/kcal mol^{-1} [12]
MeOH	32·6	1·71	83·6	55·5
EtOH	24·3	1·70	79·6	51·9
Bu^{t}OH	9·9	1·67	71·3	43·9

Activation Parameters for the Ethanol–Water Solvent.—Alcohol–water mixtures have been most frequently used in the study of the influence of solvent on activation parameters. Particularly for S_N1 solvolyses, many authors [3,14–19] have noticed an extremum in the activation enthalpies and entropies near the water end of the solvent composition which may be related to the change in the degree of order of the alcohol–water mixtures.[20,21] We see that the free energy of activation varies smoothly with the solvent composition; its gradual increase reflects the decrease in the rate when the water concentration is

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[9] C. Akerlöf, *J. Amer. Chem. Soc.*, 1932, **54**, 4125.

[10] C. K. Ingold, 'Structure and Mechanism in Organic Chemistry,' Cornell Univ. Press, Ithaca, New York, 1953, p. 345.

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[12] K. Dimroth, C. Reichardt, T. Stiepmann, and F. Bohlmann, *Annalen*, 1963, **661**, 1.

[13] Handbook of Chemistry and Physics, 46th edn., 1965—1966, E-57.

[14] A. M. Fainberg and S. Winstein, *J. Amer. Chem. Soc.*, 1957, **79**, 1602.

[15] A. M. Fainberg and S.Winstein, *J. Amer. Chem. Soc.*, 1957, **79**, 5937.

[16] J. B. Hyne and R. E. Robertson, *Canad. J. Chem.*, 1956, **34**, 931.

[17] J. B. Hyne, *J. Amer. Chem. Soc.*, 1960, **82**, 5129.

[18] J. B. Hyne, R. Wills, and R. E. Wonkka, *J. Amer. Chem. Soc.*, 1962, **84**, 2914.

[19] J. B. Hyne and R. Wills, *J. Amer. Chem. Soc.*, 1963, **85**, 3650.

[20] F. Franks and D. J. G. Ives, *Quart. Rev.*, 1966, **20**, 1.

[21] E. M. Arnett, W. G. Bentrude, J. J. Burke, and P. Mc. C. Duggleby, *J. Amer. Chem. Soc.*, 1965, **87**, 1541.

lower in the mixture. On the other hand, the activation enthalpy and entropy pass through a minimum at about $x_{\rm EtOH} = 0{\cdot}08$, then they increase very quickly with increasing alcohol concentration (Figure 2). The enthalpy effect then governs the rate.

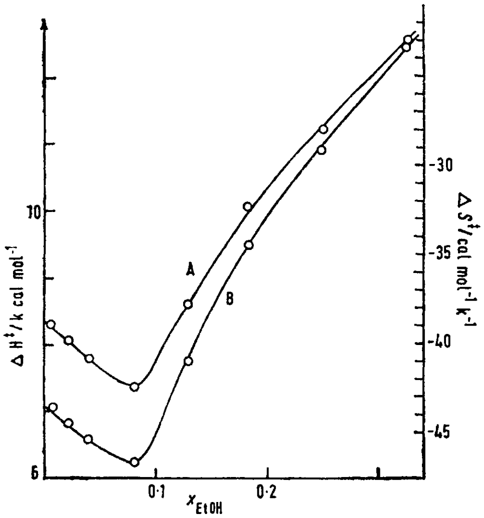

FIGURE 2 Variation of A, $\Delta S^{\ddagger}$; and B, $\Delta H^{\ddagger}$ with mol fraction of ethanol

DISCUSSION

The minimum observed for the activation enthalpy in a highly aqueous composition range is in quite good agreement with the numerous quoted results [3,13,18] so we conclude that the existence of such an extremum is closely connected with the change in the structure of the ethanol–water solvent. However the minimum depth (0·8 kcal mol^{-1}) is about the same as that found for the alkaline hydrolysis of ethyl acetate (1 kcal mol^{-1}).

Beyond the mol fraction of ethanol 0·1, the rapid increase in $\Delta H^{\ddagger}$ may be attributed to changes in the solvation of the transition state. The solvation of the ground state (β-diketone + hydroxide ion + the surrounding solvent molecules) may not be modified in a protic solvent; the hydroxide ion remains solvated by hydrogen-bonding and the β-diketone, in low concentration, has reached beyond $x_{\rm EtOH} = 0{\cdot}1$, its maximum solvation. On the contrary the strongly dipolar anionic transition state whose negative charge is moderately dispersed is not only a hydrogen-bond acceptor [22] but an electrostatic interactor.[3] Consequently an increase in alcohol concentration in the solvent, leading to a decrease in the medium polarity, reduces the solvation of the transition state: thus $\Delta H^{\ddagger}$ increases with increasing water concentration in the solvent. A similar reasoning can be made for the variation in $\Delta S^{\ddagger}$.

Conclusion.—The high negative value of the activation entropy in aqueous solutions and the study of the alkaline cleavage of dimethylacetylacetone in aqueous alcoholic solutions shows the similarity between this reaction and that of the alkaline hydrolysis of esters. On the other hand in alcohol–water mixtures we note a decrease in the reaction rate in the order $\mathrm{Bu^tOH} > \mathrm{EtOH} > \mathrm{MeOH}$ as predicted by the theory of Hughes and Ingold. We notice that the activation enthalpy passes through a minimum at *ca.* $x_{\rm EtOH} = 0{\cdot}08$ and explain this by a variation in the solvent structure.

EXPERIMENTAL

We rejected the u.v. method which is frequently used, because the diketone has only a weak u.v. absorption and monomethylacetylacetone, which may be present, absorbs >50 times as strongly. Earlier work used titration. We preferred the conductivity method. The second-order rate constants are computed from equation (9) in which

$$\log \frac{R_a - R}{R_\infty - R} = k \cdot \frac{t(b-a)}{2{\cdot}303} + \log \frac{R_a - R_0}{R_\infty - R_0} \qquad (9)$$

b is the molar sodium hydroxide concentration, *a* the molar diketone concentration, R_0, R, R_∞, and R_a are the resistances of the solution at times $t = 0, t, t_\infty$, and after titrating the excess of sodium hydroxide with acetic acid. R_∞ can be obtained through an approximate value of R'_∞ corresponding to a sufficiently long time t'_∞. The correction $\varepsilon = R_\infty - R'_\infty$ to be computed can be expressed by equation (10) which includes equation (11) where R_1 is the medium resistance value measured at t_1 which is close to the initial time.

$$\varepsilon = \frac{(R'_\infty - R_0)(R_a - R'_\infty)}{(R_a - R_0)\,u'_\infty} \qquad (10)$$

$$u'_\infty = \exp\left(\frac{t'_\infty\,(R_1 - R_0)(R_a - R_\infty')}{t_1\,2{\cdot}303(R_a - R_0)(R'_\infty - R_0)}\right) \qquad (11)$$

Equipment.—For the resistance measurements we used a WTW precision conductimeter of WBR type fitted with a TAV logarithmic amplifier.

Method. The solvent mixture (50 or 25 cm^3), a standard sodium hydroxide solution (1 or 0·5 cm^3), and a solution of the diketone of known concentration (1 or 0·5 cm^3) in the organic solvent were placed in the reaction vessel which was kept within 0·05 °C of the required temperature. Nitrogen was bubbled continuously to exclude carbon dioxide. We determined each composition of the medium as the percentage weight and mol fraction (*x*) of organic component. When the basic solution and diketone were added to the aqueous mixtures, the volume was corrected at 20 °C to take into account a possible contraction which was measured with a graduated flask. With the ratio of volumes used (1 : 25) the contraction was never very great and could even be neglected (0·5% at most).

Preparation of Dimethylacetylacetone.—3,3-Dimethylpentane-2,4-dione was prepared by stepwise dimethylation of acetylacetone by Bloomfield's method,[23] and purified by low-temperature recrystallisation from light petroleum (−20 °C). Its purity was checked by g.l.c. with a HYFI Varian Aerograph with a Carbowax column and by u.v. spectrophotometry (chromatographic purity 99·5%; u.v. absorption ε = 120). The only impurity is monomethylacetylacetone.

Solvents.—Methanol (Merck, pro analysi) and t-butyl alcohol (Fluka, puriss) were used as supplied. Ethanol was

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[22] R. Alexander, E. C. F. Ko, A. J. Parker, and T. J. Broxton, *J. Amer. Chem. Soc.*, 1968, **90**, 5049.

[23] J. J. Bloomfield, *J. Org. Chem.*, 1961, **26**, 4112.

obtained from absolute alcohol by distillation through a column packed with glass helices to remove benzene.

Computations.—All computations were carried out with an Olivetti Programma 102 computer. The parameters a and b of the equation $y = ax + b$ were calculated by the method of least squares.[24]

We thank Professor V. Gold for reading this paper and for comments.

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[24] R. Lowy and P. Manchon, (*a*) ' Eléments de statistiques appliqués à la Biologie,' vol. 1; (*b*) ' Régression multiple et polynomiale. Application à la statistique des données de mesures,' Olivetti, Paris, 1963.