Acid-catalysed Solvolysis of 2-Diazo-4′-methoxy- and 2-Diazo-2-phenyl-acetophenone in Aqueous–Organic Mixtures

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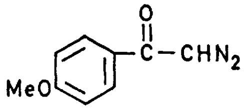
Rate constants for the hydrolysis of 2-diazo-4′-methoxy- and 2-diazo-2-phenyl-acetophenone are reported together with H_0 acidity functions in dimethyl sulphoxide–water, ethanol–water, and methanol–water mixtures containing dilute perchloric acid. The hydrolysis of 2-diazo-2-phenylacetophenone has been studied in ' neutral ' dioxan–water mixtures and in dioxan–water mixtures containing 0.1 M-hydrochloric or -perchloric acid. Results of some kinetic isotope effect studies are reported. Graphs of log (observed rate constant) aqainst H_0 are linear for reactions in perchloric acid solutions of fixed solvent composition. The effects of changing the solvent composition in the presence of 0.1 M-acid are correlated by plotting H_0 + log (observed rate constant) against log (activity of water). 2-Diazo-4′-methoxyacetophenone appears to hydrolyse by an A-1 mechanism in all the solvent mixtures studied. The kinetic behaviour of 2-diazo-2-phenylacetophenone is less consistent: in some conditions an A-2 route seems to be preferred; in others an A–S_E2 route seems more likely; in some cases the reaction is not first order.

In a previous paper [1] the rates of some acid-catalysed reactions in dioxan–water mixtures were correlated by plotting $H_0 + \log k$ against $\log a_W$ where H_0 is the Hammett acidity function, k the apparent first-order rate constant, and a_W the activity of water in the mixture. The expectation of a linear relationship between $H_0 + \log k$ and $\log a_W$ follows if the Bunnett [2] relationship (1) for solvation effects in aqueous solutions is assumed to apply to the results obtained with aqueous–organic solvents. In equation (1) t, s, a, and b represent the

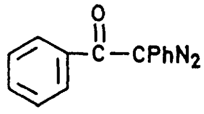
$$H_0 + \log k = \text{constant} + [(t - s) - (a - b)]\log a_W \quad (1)$$

numbers of molecules of water of solvation associated with the transition state, the initial solvated state, the indicator conjugate acid, and the indicator base respectively. The assumption should be valid provided that the activity of water is the only important rate controlling factor apart from the acidity function, and that the values of t, s, a, and b are unaffected by solvent composition.

Earlier results [1] showed that the assumption is probably true for dioxan–water mixtures in that approximately linear correlations were obtained for a number of reactions. In the present work the rates of acid-catalysed hydrolysis of 2-diazo-4′-methoxy- (1) and 2-diazo-2-phenyl-acetophenone (2) have been studied in various aqueous–organic solvents to see if the same correlation as used previously is of value. The solvents used in this work provide a greater test than before of the assumption because the available range of water activity is much greater than in dioxan–water mixtures.



(1)



(2)

EXPERIMENTAL

Materials.—2-Diazo-4′-methoxy- [3] and 2-diazo-2-phenyl-acetophenone [1] were prepared as previously described. The purification of dioxan and *m*-nitroaniline have been described.[3] Dimethyl sulphoxide was purified [4] by fractional distillation from calcium hydride under reduced pressure of nitrogen. Purified dimethyl sulphoxide was stored under nitrogen in a dry box. Ethanol and methanol were AristaR, used without further purification. Stock solutions of acids were prepared by diluting AnalaR acids with distilled water and standardised by titration. Deuterium oxide containing >99.77% ^{2}H for ^{1}H was supplied by Nuclear Magnetic Resonance Limited.

Methods.—The measurement of acidity functions has been described.[1] Reaction rates were measured spectrophotometrically as described in an earlier paper.[1] Reactions were followed to 90% conversion. Reported rate constants which were reproducible to ±3% are the mean of at least two values.

The description of the solvent as 'x% (v/v) organic component' has the same meaning as before.[5]

Results are collected in Tables 1—3.

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[1] C. W. Thomas and L. L. Leveson, *J.C.S. Perkin II*, 1973, 20.

[2] J. F. Bunnett, *J. Amer. Chem. Soc.*, 1961, **83**, 4956.

[3] L. L. Leveson and C. W. Thomas, *J. Chem. Soc.* (*B*), 1967, 680.

[4] C. C. Price and D. D. Cormelite, *J. Amer. Chem. Soc.*, **1966**, **88**, 4039.

[5] L. L. Leveson and C. W. Thomas, *J. Chem. Soc.* (*B*), **1969**, 1051.

TABLE 1

Rate constants (10^2k/min^{-1}) for the hydrolysis of (1) and (2), and H_0 acidity functions in dimethyl sulphoxide–water, ethanol–water, and methanol–water mixtures containing $HClO_4$ at 24.95 °C

[$HClO_4$]/M	50% (v/v) DMSO–water			90% (v/v) ethanol–water *		90% (v/v) methanol–water *	
	(1)	(2)	H_0	(1)	H_0	(1)	H_0
0.025						2.97	2.59
0.05						6.98	2.26
0.065						9.64	2.12
0.08	6.99	4.84	2.23	1.67	2.48	12.6	2.02
0.10	7.37	5.52	2.21	2.25	2.37	17.1	1.92
0.13				3.27	2.22	25.9	1.76
0.14	10.6	8.21	1.98				
0.16	11.8	8.91	1.94	4.58	2.09		
0.18	13.8	10.6	1.84	5.46	2.03		
0.20	16.4	11.5	1.76	6.35	1.94		

* Graphs of the integrated first-order rate equation were non-linear for the hydrolysis of (2) in 90% ethanol- and methanol–water mixtures.

TABLE 2

Rate constants (10^2k/min^{-1}) for the hydrolysis of (1) and (2), and H_0 acidity functions in aqueous-organic solution at 24.95 °C

Volume % organic solvent	DMSO–water 0.1M-$HClO_4$ (1)	(2)	H_0†	Ethanol–water 0.1M-$HClO_4$ (1)	(2)	H_0	Methanol–water 0.1M-$HClO_4$ ‡ (1)	H_0	Dioxan–water Neutral (2)	0.1M-$HClO_4$ (2)	0.1M-HCl (2)
10					*						
15									3.38	17.6	
20					*					16.3	
25									2.25	16.9	7.62
30	12.7	13.8	1.53 (1.63)							11.8	
35									1.24	9.63	
40	11.7	10.3	1.79 (1.82)	6.87	*	1.66		1.50		7.74	6.40
45	10.6		1.87 (1.89)	5.13	7.35	1.84					
50	7.37	5.52	2.21 (2.21)	3.97	6.03	1.97	12.2		0.52	4.49	3.85
55		5.25	2.30 (2.30)	3.30	4.04	2.06					
60	4.48	3.07	2.50 (2.48)		*	2.20	8.89	1.77		2.53	2.76
65						2.30	8.50	1.88			
70					*		7.46	1.97		1.79	3.08
73	2.73	1.42	2.83 (2.77)								
75							7.68	2.03			
80	2.26	1.08	2.93 (2.87)				8.20	2.04		1.51	6.38
82				1.77		2.42					
85							10.6	2.00			
86	2.55	0.91	2.95 (2.88)								
90	3.53	0.98	2.87 (2.85)	2.25	*	2.37	17.1	1.92		2.05	43.9
93				3.38		2.28					
95				4.97		2.17					

* Graphs of the integrated first-order rate equation were curved. † Figures in parentheses are for 0.1M-HCl, computed from the data of Wolford.[7] ‡ For (2) graphs of the integrated first-order rate equation were non-linear or linear with non-reproducible slopes.

DISCUSSION

Acidity Functions.—The variation of the reported Hammett acidity functions with solvent composition is similar to the behaviour of H_0 in dioxan–water mixtures containing 0.1M-perchloric [5] or -hydrochloric [6] acid, the acidity function passing through a maximum as the proportion of non-aqueous component increases. The maxima occur at greater mole fractions of organic solvent than is the case with the dioxan–water system. Acidity function values reported for dimethyl sulphoxide–water mixtures are very close to those calculated for 0.1M-hydrochloric acid using Wolford's data,[7] taking pK_a 2.50 for *m*-nitroaniline (Table 2). For a given mole fraction of organic component the acidity of the 0.1M-perchloric acid solutions is in the order methanol > ethanol > dimethyl sulphoxide.

log k–H_0 Relationships.—The results in Table 1 demonstrate the acidity function dependence of the rate constants. Graphs of log k against H_0 are good straight lines whereas graphs of log k against log C_{H^+} are generally curved.

Results for 2-Diazo-4'-methoxyacetophenone.—Figure 1 shows values of $H_0 + \log k$ plotted against $1 + \log a_W$ for (1) in various solvent systems. Except for the results [5] for dioxan–water mixtures, which have been included for comparison purposes, the correlation curves each consist of two approximately linear portions with an abrupt change of slope in the region, $\log a_w = -0.2$ to -0.1, most probably due to a change in mechanism or to a failure of the assumption of constancy of the degree of hydration.

The similarity of the correlation curves in different solvents suggests that there is no gross change in mechanism from one cosolvent to another. Since (1) almost

TABLE 3

Rate constants for the hydrolysis of (1) and (2) in water, and DMSO–D_2O and dioxan–D_2O mixtures at 24.95 °C

Solvent	Substrate	[$HClO_4$]/M	k/min^{-1}
Water	(1)	0.1	5.31×10^{-1}
40% DMSO–D_2O	(1)	0.1	5.09×10^{-1}
80% DMSO–D_2O	(1)	0.1	8.69×10^{-2}
40% DMSO–D_2O	(2)	0.1	*
80% DMSO–D_2O	(2)	0.1	6.00×10^{-3}
25% Dioxan–D_2O	(2)	0.1	*
25% Dioxan–D_2O	(2)		5.51×10^{-2}

* Graphs of the integrated first-order equation were curved.

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[6] E. A. Braude, *J. Chem. Soc.*, 1948, 1971.

[7] R. K. Wolford, *J. Phys. Chem.*, 1964, **68**, 3392.

certainly[1] hydrolyses by an A-1 route in dioxan–water mixtures Figure 1 suggests that this is the likely mechanism at high water contents in the other solvent systems studied. The kinetic solvent isotope effect for (1) in 40% dimethyl sulphoxide–water (k_H/k_D 0.23) is in agreement with this suggestion[8] and the value, k_H/k_D 0.26 in 80% dimethyl sulphoxide–water, suggests that the mechanism remains A-1 throughout the range of solvent compositions studied. Thus the change of slope of the correlation curves for (1) is due to changes in hydration. The more positive slope of the correlation line at low activity of water is consistent with a decreased hydration of the initial state relative to the transition state, *i.e.* (t — s) is greater than in the highly aqueous solutions. At the same time (a — b) is likely to be smaller than in highly aqueous solutions: the hydration of the indicator conjugate acid will be less and of the neutral indicator about the same (*i.e.* very small).

Using the value of the measured rate constant in pure water together with the value of H_0 for 0.1M-perchloric acid in pure water (0.5—0.7) obtained by extrapolation of the results for dimethyl sulphoxide–water mixtures the value of H_0 + log k is reckoned to be between *ca.* 0.2 and 0.4. All four correlation curves extrapolate to values within this range in pure water. It is difficult to get values of H_0 + log k at high activity of water because acidity functions and rate constants are very sensitive to solvent composition under these conditions. Also reaction rates are becoming relatively fast and the limit of the acidity function range of m-nitroaniline is being reached. Further, the values of a_w used are those for binary solvent mixtures, not for solutions of 0.1M-acid. Considering the relative crudity of the extrapolations the approximate coincidence of the values of H_0 + log k in pure water is encouraging.

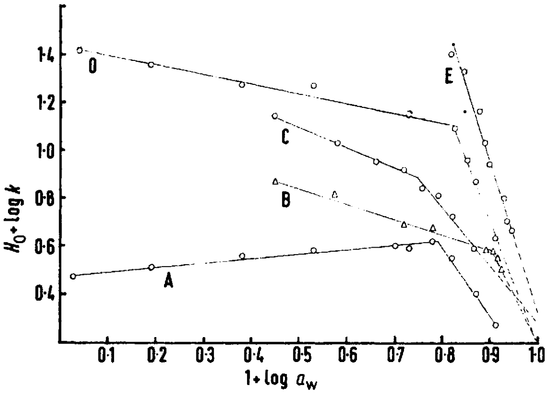

FIGURE 1. H_0 + log k as a function of log (activity of water) for the hydrolysis of (1) and (2) in 0.1M-HClO$_4$ solutions. For convenience 0.40 has been subtracted from the values of H_0 + log k for (2). Values of a_w for methanol–water were computed from J. A. V. Butler, D. W. Thomson, and W. H. Maclennan, *J. Chem. Soc.*, 1933, 674; for ethanol–water from H. W. Foote and S. R. Scholes, *J. Amer. Chem. Soc.*, 1911, **33**, 1309; for dimethyl sulphoxide–water from J. Kenttämaa and J. J. Lindberg, *Suomen Kemi.*, 1960, **B33**, 32. Data for results for dioxan–water mixtures are from ref. 5 and A. L. Vierk, *Z. anorg. Chem.*, 1950, **261**, 283. A, (2) in DMSO–water; B, (1) in ethanol–water; C, (1) in methanol–water; D, (1) in DMSO–water; E, (1) in dioxan–water

Results for 2-Diazo-2-phenylacetophenone.—Earlier work[1] had shown that the graph of H_0 + log k against log a_w for (2) in dioxan–water mixtures has a positive slope in the presence of 0.1M-perchloric acid, and a negative slope in the presence of 0.1M-hydrochloric acid in the range of solvent compositions studied. As the correlation curves ought to extrapolate to roughly the same value at log a_w = 0, and this did not seem to be the case, the work was repeated and the range of activity of water extended as much as possible. The results, together with the earlier ones, are correlated in Figure 2. It can be seen that although the slope of the line is consistently negative for the results with hydrochloric acid solutions, it changes sign for the results with perchloric acid, so that the lines do extrapolate to roughly the same value in water. The point of inflection occurs at log a_w *ca.* 0.07 (*ca.* 50% v/v dioxan). The question again arises as to whether the inflection is a result of a change in mechanism or due to changes in hydration.

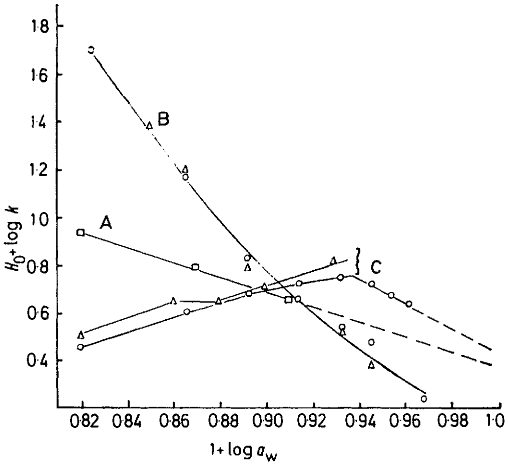

FIGURE 2 H_0 + log k as a function of log (activity of water) for the hydrolysis of (2): □, ○, results of this work; △, previous results.[1] Values of a_w are those for the binary solvent mixture (see Figure 1). A, DMSO–water, 0.1M-HClO$_4$; B, dioxan–water, 0.1M-HCl; C, dioxan–water, 0.1M-HClO$_4$

Previous studies[1,9] on the perchloric acid catalysed hydrolysis of (2) in aqueous dioxan led to the conclusion that the mechanism is A–S_E2 in solutions containing as much as 60% water. Investigations of solvent[1] and kinetic solvent isotope effects[10] showed that the hydrolysis is probably by concomitant A-2 and A–S_E2 routes in the presence of hydrochloric acid, the A-2 route being more important in dioxan-rich mixtures, and the A–S_E2 route predominating in water-rich solvents. It is therefore suggested that 2-diazo-2-phenylacetophenone hydrolyses by an A–S_E2 mechanism in the presence of per-

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[8] J. F. Coetzee and C. D. Ritchie, 'Solute–Solvent Interactions,' Marcel Dekker, Maidenhead, 1969, ch. 7.

[9] J. B. F. N. Engberts, N. F. Bosch, and B. Zwanenberg, *Rec. Trav. chim.*, 1966, **85**, 1068.

[10] L. L. Leveson and C. W. Thomas, *Chem. and Ind.*, 1973, 694.

chloric acid throughout the range of dioxan–water systems studied. The inflection in the correlation curve in Figure 2 is due to changes in hydration in much the same way as has been proposed for (1).

It is interesting that the rate of reaction is significant in 'neutral' dioxan–water mixtures containing < *ca.* 50% v/v dioxan. The 'neutral' reaction is first order in 2-diazo-2-phenylacetophenone.

The correlation curve for the hydrolysis of (2) in dimethyl sulphoxide–water mixtures is included in Figure 1. For (2) the line has a more positive slope than for (1). This suggests that the mechanism of hydrolysis of (2) is A-2 or A–S_E2 at high proportions of dimethyl sulphoxide (the slope of the correlation curve is expected [2] to increase in the order $A\text{-}1 < A\text{-}2 < A\text{–}S_E2$). The observed value k_H/k_D 1.8 for a solution containing 80% dimethyl sulphoxide is in the range expected [8] for an A–S_E2 reaction. Because of the curvature of the graph of the integrated first-order rate equation for the hydrolysis in a solution containing 40% dimethyl sulphoxide–deuterium oxide the ratio k_H/k_D could not be evaluated. However the reaction appears to be A–S_E2 in water-rich dioxan–water mixtures and is likely to be so in water-rich dimethyl sulphoxide–water mixtures. Thus, once again, the change in slope of the correlation curve is due to changes in hydration.

The correlation curves for dioxan–water and dimethyl sulphoxide–water mixtures containing 0.1M-perchloric acid extrapolate to approximately the same value at $\log a_w = 0$ (Figure 2). An experimental value of this intercept could not be obtained because of the insolubility of the substrate in water.

Graphs of the integrated first-order rate equation were curves or non-reproducible straight lines for the perchloric acid catalysed reaction of (2) in methanol–water mixtures, in ethanol–water mixtures containing >60% or <40% ethanol, in 40% dimethyl sulphoxide–deuterium oxide mixture, and in 25% dioxan–deuterium oxide. The mechanism of hydrolysis of 2-diazo-2-phenylacetophenone is obviously very sensitive to solvent composition.

Diagnostic Value of Solvent Effects in Aqueous–Organic Mixtures.—In applying Bunnett's treatment to reactions in aqueous solutions the acidity function and activity of water are changed by altering the acid concentration. With aqueous–organic solutions it is possible to keep the acid concentration constant at a convenient value (thus avoiding variations in the ionic strength), and to change H_0 and a_w by varying the proportion of water in the solvent mixture. This means that substrates that are insoluble in water can be studied. In many aqueous–organic mixtures H_0 passes through a maximum which means that reactions can be studied in solutions having the same acidity function but different activities of water. Although the range of acidity functions is relatively small in aqueous–organic mixtures containing a fixed concentration of acid a resulting advantage is that only one indicator is needed to measure H_0. As has been pointed out [1] it follows that the relative slopes of graphs of $H_0 + \log k$ against $\log a_w$ for different substrates in a given mixture should depend on relative values of $(t - s)$ since the contribution $(a - b)$ of the indicator to the slope is the same in each case. The relative slopes for acid-catalysed reactions should be in the order $A\text{-}1 < A\text{-}2 < A\text{–}S_E2$.

The results reported here show that the correlation is a reasonable one. Graphs for (1) and (2) in different solvent systems are straight lines which for a particular substrate extrapolate to approximately the same value in pure water. The change in slope of the lines can be explained in terms of changes in hydration. The slope of the line for (2) is more positive than that for (1) in dimethyl sulphoxide–water and dioxan–water mixtures [1] as expected if the hydrolysis of (2) is A–S_E2 and of (1) is A-1. Comparisons using the other solvent mixtures are unfortunately not possible due to the erratic kinetic behaviour of (2). It appears that by far the most discriminating solvent mixture is dioxan–water in the composition range 40—90% dioxan, perhaps because of the small degree of interaction of water with the co-solvent. This type of study is probably most useful when comparing the behaviour of a series of substrates of the same structural type, for which solvation effects can be assumed to be similar.

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