

Reactions in Strongly Basic Media. Part 8.¹ Correlation of the Rates of Alkaline Hydrolysis of 2,4-Dinitroanisole and 2-Methoxy-5-nitropyridine in Aqueous Dipolar Aprotic Solvents with Acidity Functions. An Order of Basicity for Aqueous Dipolar Aprotic Solvents

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The rate coefficients for the alkaline hydrolysis of 2,4-dinitroanisole and 2-methoxy-5-nitropyridine have been measured in a series of aqueous dipolar aprotic solvents. These rates have been correlated with the acidity function H_- for aqueous dimethyl sulphoxide, dimethylformamide, sulpholane, and pyridine, which were available, as well as for aqueous acetonitrile, tetramethylurea, and hexamethylphosphoramide, whose acidity function has been constructed. For aqueous dioxane, a satisfactory acidity function could not be constructed. The order of the solvents in increasing the basicity is: hexamethylphosphoramide \gg dimethyl sulphoxide $>$ tetramethylurea $>$ dimethylformamide $>$ pyridine $>$ sulpholane \gg acetonitrile $>$ dioxane. The latter order appears to be related directly to the hydrogen-bonding capacity of the solvent. Except for pyridine, the slopes of the rate-acidity function correlations have been found to be solely a function of the substrate and independent of the dipolar aprotic solvent used. Pyridine catalyses the substitution reactions by direct nucleophilic catalysis.

A number² of investigations have demonstrated the greatly increased activity of anionic nucleophiles in dipolar aprotic solvents. Furthermore, these solvents have been shown to increase the basicity of added base in dipolar aprotic-protic solvent mixtures. Acidity functions have been constructed in dipolar aprotic-protic solvent mixtures containing base using the stepwise indicator method due to Hammett.³⁻⁵ Such scales exist for aqueous dimethyl sulphoxide (DMSO), aqueous sulpholane, aqueous pyridine, and aqueous dimethylformamide (DMF), containing added base, as well as for mixtures containing alcoholic alkoxides. Studies^{1,6,7} have been made of aromatic nucleophilic substitutions in aqueous DMSO containing base and rate-acidity function correlations have been constructed.

In the present study the alkaline hydrolysis of two substrates has been studied and rate-acidity function correlations have been made for an extended series of aqueous dipolar aprotic solvent mixtures containing base. Where the acidity functions measurements were not available, indicator measurements were made and, where possible, scales constructed. The order of basicity of the aqueous dipolar aprotic solvents is discussed.

Experimental

Materials.—2,4-Dinitroanisole, 2-methoxy-5-nitropyridine, aniline indicators, DMSO, and aqueous tetramethylammonium hydroxide (TMAH) were purified as previously described.^{1,4,6-8} The other solvents were purified by standard procedures before standing over 4Å molecular sieves in brown bottles under nitrogen for several days. The solvent was then fractionally distilled under, normally, reduced pressure and stored as above before use. DMF was carefully tested for the presence of dimethylamine with 1,3,5-trinitrobenzene.

Kinetic Measurements.—These were carried out exactly as previously described.^{6,7} Good first-order behaviour was found and the product formed was that expected^{1,7} for aqueous DMSO, sulpholane, pyridine, acetonitrile, tetramethylurea (TMU), dioxane, and hexamethylphosphoramide (HMPA). At

higher mol% dioxane, TMU, and pyridine, the aqueous solvent-base mixtures are immiscible. Aqueous HMPA gave precipitates at higher mol% compositions when base was added; but at lower mol% satisfactory results were obtained. Aqueous acetone gave reproducible kinetic results; but much of the substrate was transformed by a Janovsky-type reaction.⁸ The latter results from substitution by the enolate anion of acetone rather than hydroxide. Aqueous DMF, dimethylacetamide, and *N*-methylpyrrolidone all react fairly rapidly with base to give hydrolysis. For the faster reacting 2,4-dinitroanisole, reproducible results were obtained for aqueous DMF alone and the product was that expected. Rate coefficients were reproducible to $\pm 3\%$, except for aqueous sulpholane and acetonitrile where they were $\pm 5\%$. The solvent compositions are considered to be accurate to $\pm 0.2\%$.

Reaction Products.—These were as expected,^{1,7} i.e. the anions of 2,4-dinitrophenol and 2-hydroxy-5-nitropyridine, except as otherwise noted above when a Janovsky-type reaction occurred. The former products were confirmed by preparative studies giving quantitative yields and identity of kinetic products was confirmed by spectral composition.

Indicator Measurements.—Ionisation studies of a series of overlapping aniline indicators were made in aqueous HMPA, TMU, dioxane, and acetonitrile as described previously.^{4,9} The indicators employed were those used previously⁹ and by others (number 1-6).⁴ Consistent results were obtained for aqueous acetonitrile, HMPA, and TMU and are shown in Table 1. However, for aqueous dioxane, as before,⁹ unsatisfactory agreement of the derived H_- values from different indicators showed that a meaningful scale could not be generated for this system.

Results

The reactions between the two substrates and hydroxide anions were confirmed to be first order in both species. TMAH was always in large excess, thus the reactions approximated to first-order behaviour. The rate coefficients, k_{obs} , were calculated as previously described.⁶ Values of the H_- acidity functions for

aqueous DMSO, sulpholane, pyridine and DMF containing $1.10 \times 10^{-2} \text{M}$ -TMAH were interpolated graphically from the literature.³⁻⁵ The reaction scheme is shown in (i) for 2,4-dinitroanisole, as an example, with k_1 as the rate-determining step.^{1,7}

The acidity functions and the rate coefficients for the

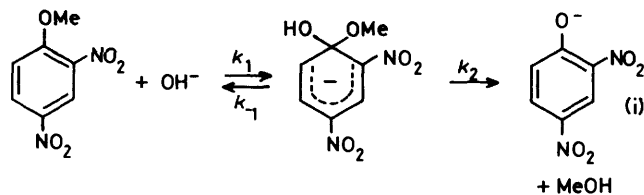


Table 1. Acidity function H_- for aqueous dipolar aprotic solvents containing $1.10 \times 10^{-2} \text{M}$ -TMAH

mol% HMPA	H_- *	mol% TMU	H_- *	mol% acetonitrile	H_- *
13.39	15.16	18.44	14.19	57.93	13.49
17.97	15.81	24.25	14.62	71.68	14.01
24.61	16.89	32.29	15.30	79.86	15.18
29.16	17.60	37.61	15.81	89.21	16.54
35.12	18.31	44.17	16.42		
43.05	19.05	52.50	16.80		
54.24	19.55				

* Deviations are considered to be ± 0.02 .

Table 2. Rate coefficients for the formation of 2,4-dinitrophenoxide anion from 2,4-dinitroanisole in aqueous solvents containing $1.10 \times 10^{-2} \text{M}$ -TMAH at 30.0 °C, together with the values of the acidity functions

		Pyridine					
mol%		33.75	41.63	47.23	54.01	62.29	
H_-		14.51	14.81	14.97	15.16	15.34	
$10^3 k_{\text{obs.}}/s^{-1}$		0.203	0.699	1.24	2.53	5.34	
		Sulpholane					
mol%		28.64	37.43	43.05	49.78	68.48	
H_-		13.64	14.18	14.42	14.84	16.25	
$10^3 k_{\text{obs.}}/s^{-1}$		0.0301	0.0504	0.0743	0.151	0.767	
		Acetonitrile					
mol%		57.93	71.68	79.86	89.21		
H_-		13.49	14.01	15.18	16.54		
$10^3 k_{\text{obs.}}/s^{-1}$		0.0223	0.0455	0.251	1.48		
		TMU					
mol%		18.44	24.25	32.29	37.61	44.17	52.50
H_-		14.19	14.62	15.30	15.81	16.42	16.80
$10^3 k_{\text{obs.}}/s^{-1}$		0.126	0.272	0.813	1.35	3.11	5.59
		HMPA					
mol%		13.39	17.97	24.61	29.16	35.12	43.05
H_-		15.16	15.81	16.89	17.60	18.31	19.05
$10^3 k_{\text{obs.}}/s^{-1}$		0.476	1.36	5.27	11.8	33.4	64.5
		DMF					
mol%		33.10	42.43	48.22	55.00	63.06	72.35
H_-		14.72	14.76	15.04	15.41	16.17	16.24
$10^3 k_{\text{obs.}}/s^{-1}$		1.19	1.51	2.47	5.82	17.6	55.9
		Dioxane					
mol%		12.32	24.02	32.97	45.75		
$[H_-]$		13.0	13.2	13.2	13.4]*		
$10^3 k_{\text{obs.}}/s^{-1}$		0.0187	0.0224	0.0252	0.0318		

* Derived 'kinetic' scale (see text).

hydrolysis reactions are shown in Tables 2 and 3; those for aqueous DMSO were taken from earlier studies.^{1,7} The reaction rates and acidity functions were correlated by a least-squares method. Constants of equation (ii) are given in Table 4.

$$\log k_{\text{obs.}} = IH_- + c \quad (\text{ii})$$

Acidity Functions.—Acidity functions, H_- , are available for a wide range of aqueous dipolar aprotic solvent systems containing base both from the present study and the literature.^{3-5,9} The ordering of the solvents in their ability to increase the basicity of the system at a standard mol% is, in general, consistent and is as follows: HMPA \gg DMSO $>$ TMU $>$ DMF $>$ pyridine $>$ sulpholane \gg acetonitrile $>$ dioxane. The latter solvent does not have a quantitative scale, but can be placed by a consideration of their relative rates of reaction. Only pyridine at high mol% composition changes order significantly to become less effective than sulpholane. Two factors, in the main, cause the increase in basicity. These are the simple replacement of water and the ability of the solvent to complex with water by hydrogen bonding.³ At a constant mol% composition, the effect of replacement of water is the same for all systems. Several studies have been made of hydrogen-bonded complexes with dipolar aprotic solvents. Ting *et al.*¹⁰ made ^1H n.m.r. studies of water as a hydrogen-bond donor to DMF and DMSO. Taft and his co-workers¹¹ have made ^{19}F n.m.r. and i.r. studies of hydrogen-bonded complexes using 5-fluoroindole and have established linear free energy relations for the formation of hydrogen-bonded complexes of various

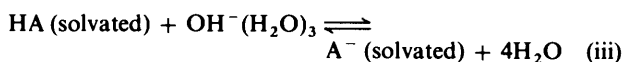
Table 3. Rate coefficients for the formation of 2-hydroxy-5-nitropyridine (5-nitro-2-pyridone) anion from 2-methoxy-5-nitropyridine in aqueous solvents containing 1.10×10^{-2} M-TMAH at 30.0 °C, together with the values of the acidity functions

	Pyridine				Sulpholane		Acetonitrile		TMU		HMPA	
mol%	33.75	41.63	47.23	62.29	58.09	68.48	57.93	71.68	79.86	89.21	52.50	54.24
H_-	14.51	14.81	14.97	15.34	15.44	16.25	13.49	14.01	15.18	16.54	16.80	19.05
$10^3 k_{\text{obs.}}/s^{-1}$	0.0131	0.0325	0.0557	0.160	0.0233	0.0495	0.002 24	0.004 35	0.008 80	0.0468	0.185	4.26
mol%	37.43	43.05	49.78	58.09	68.48							
H_-	14.18	14.42	14.84	15.44	16.25							
$10^3 k_{\text{obs.}}/s^{-1}$	0.005 21	0.007 23	0.0181	0.0233	0.0495							
mol%	57.93	71.68	79.86	89.21								
H_-	13.49	14.01	15.18	16.54								
$10^3 k_{\text{obs.}}/s^{-1}$	0.002 24	0.004 35	0.008 80	0.0468								
mol%	24.25	32.29	37.61	44.17	52.50							
H_-	14.62	15.30	15.81	16.42	16.80							
$10^3 k_{\text{obs.}}/s^{-1}$	0.0177	0.0378	0.0665	0.128	0.185							
mol%	13.39	17.97	24.61	29.16	35.12	43.05	54.24					
H_-	15.16	15.81	16.89	17.60	18.31	19.05	19.55					
$10^3 k_{\text{obs.}}/s^{-1}$	0.0345	0.0735	0.211	0.506	1.19	3.28	4.26					

Table 4. Regression analysis for equation (ii) correlating the alkaline hydrolysis of 2,4-dinitroanisole and 2-methoxy-5-nitropyridine in aqueous dipolar aprotic solvents containing 1.10×10^{-2} M-TMAH at 30.0 °C

Solvent	2,4-Dinitroanisole		Correlation coeff.
	l	c	
DMSO	0.60	-12.39	0.998
DMF	0.66	-13.56	0.989
HMPA	0.55	-12.55	0.997
Sulpholane	0.55	-12.06	0.992
TMU	0.61	-11.59	0.998
Acetonitrile	0.60	-12.74	0.999
Pyridine	1.61	-27.99	0.999
Solvent	2-Methoxy-5-nitropyridine		Correlation coeff.
	l	c	
DMSO	0.46	-11.40	0.997
HMPA	0.49	-11.90	0.998
Sulpholane	0.47	-11.97	0.995
TMU	0.47	-11.61	0.999
Acetonitrile	0.41	-11.23	0.999
Pyridine	1.31	-24.88	0.999

OH reference acids with a wide range of proton acceptors. The proton-accepting ability of the solvents in this study is as follows: HMPA > DMSO > TMU > DMF > pyridine > acetonitrile > dioxane. This is exactly the order found in this study for the ability of the solvents to increase the basicity. This confirms the conclusion that the ability to complex and 'remove' water is the determining factor in increasing the basicity. The 'removal' of water forces the equilibria (iii) to the right as an indicator, HA, is ionised. Finally, it will compete to



desolvate the hydroxide anion to reveal its higher intrinsic basicity.

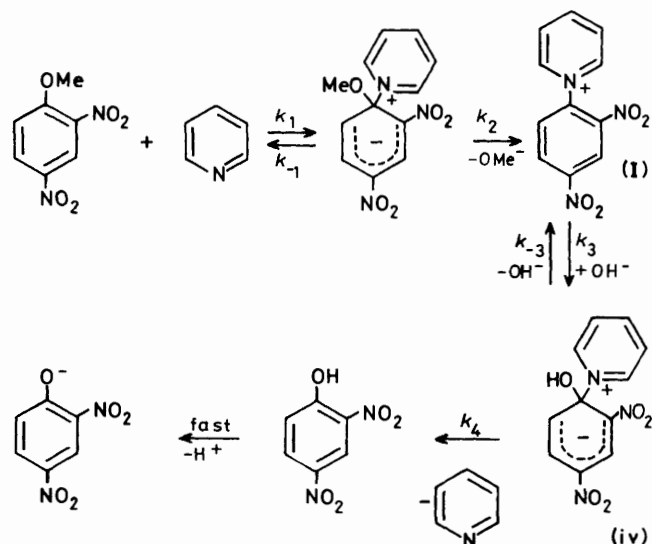
The failure of the generation of an acidity function in aqueous dioxane would appear to be a result of the much lower dielectric constant of dioxane compared with the other dipolar aprotic solvents.¹²

Rate-Acidity Function Correlations.—The rate-acidity function correlations give very good linear relations as shown in Table 4. Correlations have been made with H_- rather than J_- or, in reality, $H_- + \log a_w$ as $\log a_w$ is only available for aqueous DMSO, acetonitrile, HMPA, sulpholane, TMU, and that H_- and $H_- + \log a_w$ for aqueous DMSO are linearly related over a wide range of compositions.⁶

In Table 4 it can be seen that, for each of the substrates, aqueous DMSO, acetonitrile, HMPA, sulpholane, TMU, and DMF give very similar relations. However, the slopes of the correlations in aqueous pyridine are very much greater. It is suggested that, for aqueous pyridine, there is a special factor giving rise to rate accelerations and this is discussed separately below. For both substrates, the slope, l , of the correlation would appear to be a significant function of the particular substrate alone, i.e. ca. 0.59 for 2,4-dinitroanisole and 0.46 for 2-methoxy-5-nitropyridine. The slope appears to be almost independent of the particular dipolar aprotic solvent used.

For aqueous dioxane, H_- values are not available. A 'kinetic' H_- scale can, in principle, be constructed for this system using the rate coefficients for the substrate and the *mean* regression equation from Table 4. Such values can only be considered indicative and, as such, are given in Table 2.

Catalysis by Pyridine.—The reactions in aqueous pyridine are all faster than would be expected from a comparison between H_- for aqueous pyridine and the other results. Furthermore the slopes of the correlations are quite different (see Table 4). The explanation of these results appears to be direct nucleophilic catalysis by pyridine as shown in process (iv). For the normal reaction of the substrate with hydroxide anion as shown in reaction (ii), k_1 , analogous to k_3 in process (iv), is rate determining. In excess of pyridine containing base, k_3 is considered to be rate determining, with the reactive and



positively charged pyridinium cation (I) being formed relatively rapidly. 2,4-Dinitroanisole is very much less reactive towards

base than the pyridinium salt (I).¹³ It is likely that the catalysis of nucleophilic aromatic substitution commonly observed in pyridine solutions operates *via* this pathway.

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Received 27th March 1986; Paper 6/607