Acidities of Some Substituted Ammonium Ions in Dimethyl Sulfoxide†

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pK_a Values in DMSO are reported for ammonium ions derived from amines which have previously been widely used as nucleophiles in nucleophilic aromatic substitution reactions; values are also given for four polynitrodiphenylamines used as indicators.

Dimethyl sulfoxide (DMSO) is a very useful solvent for studying nucleophilic aromatic substitution reactions and several kinetic and mechanistic studies involving reaction with amine nucleophiles have been reported.[1–8] In order to make comparisons of the amines a knowledge of their basicities in DMSO is important. Surprisingly, pK_a values are not available for many ammonium ions derived from amines which have been used in the substitution studies. These amines include piperidine, pyrrolidine, benzylamine and morpholine.

It was shown by Kolthoff and co-workers[9] and by Ritchie and Uschold[10,11] that potentiometric measurements using a glass electrode can be used to determine pK_a values in DMSO. Extensive data have been reported by Bordwell and his group[12,13] using spectrophotometry with overlapping indicators which cover the range 0–32 pK_a units.

We used the spectrophotometric method, taking as our reference point the indicator 2,4-dinitrophenol, **1**, whose pK_a is known[12] to be 5.12 ± 0.04 in DMSO. The other indicators used were 4′,2,4,6-tetranitrodiphenylamine **2**, 2,4,6-trinitrodiphenylamine **3**, *N*-phenyl-2,4-dinitronaphthylamine **4** and 2,4-dinitrodiphenylamine, **5**. These were prepared by reaction of the appropriate chlorodinitro- or chlorotrinitroaromatic with aniline or, in the case of **2**, 4-nitroaniline in ethanol. It is known[14] that the mode of ionisation of these indicators involves proton loss rather than base addition to give σ-adducts. All the indicators showed a pronounced change in their UV–visible spectra on deprotonation. Data are in Table 1.

Table 1 Spectroscopic data for indicators

Indicator	Mp (T/°C)	λ_{max}/nm[a]		δ_H[b]	
		In$^-$	HIn	Amino	Aromatic
1	208 (lit.,[15] 213)	430 (4.31)	—	—	—
2	222 (lit.,[16] 223)	480 (4.53)	403 (4.32)	10.36	9.06 (s), 8.17 (d, *J* 9), 7.26 (d, *J* 9)
3	183 (lit.,[17] 178)	450 (4.37)	386 (4.15)	10.22	8.94 (s), 7.32 (t, *J* 7), 7.17 (t, *J* 7), 7.16 (d, *J* 8)
4	180 (lit.,[18] 180)	515 (4.35)	445 (4.11)	10.12	8.83 (s), 8.67 (d, *J* 8.6), 8.56 (d, *J* 8.7), 7.97 (t, *J* 8.6), 7.76 (t, *J* 8.6), 7.30 (t, *J* 8), 7.09 (t, *J* 8), 7.07 (d, *J* 8)
5	158 (lit.,[19] 157)	435 (4.29)	368 (4.25)	10.17	8.89 (d, *J* 2.7), 8.24 (dd, *J* 9.6, 2.7), 7.10 (d, *J* 9.6), 7.4 (m)

[a] $\log_{10} \varepsilon$ in parentheses. [b] In [$^2H_6$]DMSO. [c] *J* values in Hz.

In a typical experiment spectra were recorded with a constant concentration (4×10^{-5} mol dm^{-3}) of indicator in solutions buffered with an amine and its amine salt. Usually, measurements were made with a salt concentration of 0.01 mol dm^{-3}; if lower salt concentrations were used the ionic strength was maintained at $I = 0.01$ mol dm^{-3} with tetra-*n*-butylammonium chloride. Absorbance measurements yielded the value of the equilibrium constant, *K*, for the equilibrium given in eqn. (1), where HIn is the indicator and In$^-$ its deprotonated form. Representative results for the indicator **2** in solutions containing imidazole and imidazole hydrochloride are shown in Fig. 1 and Table 2. Values for *K* are collected in Table 3 and use of eqn. (2) allowed the calculation of pK_a values for the substituted ammonium ions and also for the indicators **2–5**.

$$\mathrm{HIn} + \mathrm{Am} \rightleftharpoons \mathrm{In}^- + \mathrm{AmH}^+ \qquad (1)$$

$$\log_{10} K = \mathrm{p}K_a(\mathrm{AmH}^+) - \mathrm{p}K_a(\mathrm{HIn}) \qquad (2)$$

Data are collected in Table 4. The results are important in that they allow comparisons of the basicities of the amines in DMSO. However it is useful to make comparisons with pK_a values in water and also with $\Delta G°$ values for proton transfer to ammonia in the gas phase. The latter results show that in the absence of solvent the basicities of aliphatic amines decrease from tertiary to secondary to primary. However this order is inverted in DMSO where *n*-butylamine is the strong-

Table 2 Absorbance data for **2** in DMSO containing imidazole and imidazole hydrochloride at 25 °C

Spectrum number	[Imidazole]/ mol dm^{-3}	[Imidazole H$^+$Cl$^-$]/ mol dm^{-3}	Abs (480 nm)	K[a]
1	0	0.010	0.081	—
2	0.001	0.010	0.275	1.8
3	0.005	0.010	0.685	1.8
4	0.007	0.010	0.808	2.0
5	0.010	0.010	0.919	2.0
6	0.020	0.010	1.096	2.1
7	0.050	0.010	1.236	2.2
8	0.10	0.010	1.276	1.9
9	0.10	0	1.340	—

[a] Calculated as $\dfrac{(\mathrm{Abs} - 0.081)}{(1.340 - \mathrm{Abs})} \cdot \dfrac{[\mathrm{Imidazole\ H^+}]}{[\mathrm{Imidazole}]}$.

Table 3 Values of *K*, defined in eqn. (1), in DMSO at 25 °C and with $I = 0.010$ mol dm^{-3}

Indicator	Amine	K
1	Aniline	0.050 ± 0.002
2	Aniline	0.0056 ± 0.0004
2	Imidazole	2.0 ± 0.2
3	Imidazole	0.023 ± 0.001
3	Dabco	11.3 ± 0.7
3	Triethylamine	11.5 ± 0.7
4	Triethylamine	1.0 ± 0.1
4	Dabco	1.0 ± 0.1
4	Morpholine	1.2 ± 0.1
4	Benzylamine	12.3 ± 0.9
4	Piperidine	60 ± 5
4	*n*-Butylamine	112 ± 10
5	*n*-Butylamine	0.024 ± 0.002
5	Pyrrolidine	0.021 ± 0.003

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Table 4 pK_a Values of substituted ammonium ions and indicators

	DMSO				
Parent amine	pK_a[a]	pK_a[b]	Water pK_a[c]	ΔpK_a (DMSO–water)	ΔG°/kJ mol^{-1} (gas phase)[d]
Aniline	3.82	3.6[9]	4.58	−0.76	28
Imidazole	6.37		7.00	−0.63	—
Dabco	9.06		8.82	0.24	98
Triethylamine	9.07	9.0[9]	10.72	−1.65	115
Morpholine	9.15		8.49	0.66	63
Benzylamine	10.16		9.38	0.78	—
Piperidine	10.85		11.12	−0.27	89
Pyrrolidine	11.06		11.31	−0.25	84
n-Butylamine	11.12	11.1[9] 10.7[11]	10.64	0.48	58
Indicators					
1		5.12[12]			
2	6.07				
3	8.01				
4	9.07				
5	12.74	12.4[10]			

[a]This work. [b]Literature values (with references). [c]From ref. 20. [d]Refers to the process $AmH^+ + NH_3 \rightleftharpoons Am + NH_4^+$ from refs. 21 and 22.

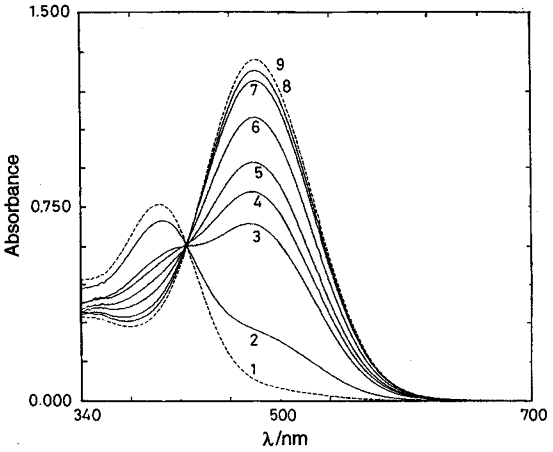

Fig. 1 UV–visible spectra of **2**, 4×10^{-5} mol dm^{-3}, in DMSO containing imidazole and imidazole hydrochloride: scans 1–9 correspond to the conditions given in Table 2.

est base studied and piperidine and pyrrolidine are stronger bases than triethylamine and Dabco.

The results are consistent with the idea, expressed previously, that in solution solvation, involving hydrogen-bonding of NH$^+$ protons, is important in stabilising the acidic cations.[23,24,25] It is known that DMSO is an extremely good hydrogen-bond acceptor,[26] and in this solvent the stabilisation of cationic species will be expected to decrease as the number of NH$^+$ protons available for hydrogen-bonding decreases. The results in Table 4 show that the primary amines *n*-butylamine and benzylamine are stronger bases in DMSO than in water. Pyrrolidine, piperidine and imidazole are slightly weaker bases in DMSO than in water. The tertiary amine triethylamine, where the cation contains a single acidic proton, is a considerably weaker base in DMSO than in water.

The number of acidic hydrogens in the cation available for hydrogen-bonding is not the only factor affecting relative acidities in DMSO and water: dipole–dipole and dipole–ion interactions may also play an important role. Thus the bifunctional amines Dabco and morpholine, where the cations contain respectively one and two acidic protons, are slightly stronger bases in DMSO than in water. This may be due to good solvation of the cations by DMSO involving stabilisation by dipolar interactions. The higher basicity of aniline in water than in DMSO may reflect its poor solvation by water relative to DMSO.

Our results also allow the determination of the pK_a values for acid dissociation of the indicators (Table 4). As expected,[1] increasing the number of nitro groups increases acidity. Comparison of the values for **4** and **3** indicates that annelation of a benzene ring in the naphthylamine derivative, **4**, is almost as effective as addition of an extra nitro group.

It is of interest to compare the acidity of **3** with that of *N*-*n*-butyl-2,4,6-trinitroaniline, **6**. Chamberlin and Crampton[27] showed that reaction of the latter compound with *n*-butylamine in DMSO resulted in competition between anion formation by proton loss and by base addition. They reported a value for K, defined in eqn. (1), of 3.2. This allows the calculation of a pK_a value of 10.61 for **6** in DMSO. This result shows the strongly acidifying effect, by 2.6 pK units, of the *N*-phenyl group relative to the *N*-butyl group. This acidifying effect on the amino proton is sufficient to favour proton loss as the preferred mode of ionisation of the diphenylamines.

Experimental

DMSO and the amines used were the purest available commercial specimens. Hydrochloride salts of imidazole, triethylamine, benzylamine and piperidine were also available commercially. Hydrochlorides of morpholine and *n*-butylamine were prepared by reaction of the amines in diethyl ether with hydrogen chloride; those of aniline, DABCO and pyrrolidine were prepared in solution in DMSO by reaction of equivalent quantities of amine and acid. UV–visible measurements were made at 25 °C using a Shimadzu 2101-PC spectrophotometer.

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