The Temperature Variation of the H_A Acidity Function for Sulphuric Acid and the Thermodyanamics of Protonation of Amides

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The anchoring of the H_A acidity function to 4- and 2-nitroaniline indicators at low acid concentrations has been re-examined and found to be satisfactory. The H_A function has been determined up to 45% sulphuric acid over the temperature range 15—40 °C. As found earlier for the H_0 function, the H_A values become less negative with increasing temperature. The thermodynamic functions of protonation for pyrrole-2-carboxamide, 4-methoxybenzamide, and methacrylamide have been derived. The protonations are slightly endothermic and occur with a decrease in entropy. The thermodynamic functions, $\Delta G°$ and $\Delta H°$, follow the same correlation as those for the protonation of alkylamines and arylamines, and therefore indicate that the predominant form of amide cations in aqueous acid is the *N*-protonated form. The entropy changes, $\Delta S°$, indicate that restricted rotation about the C–N bonds in the amide molecules also makes a contribution.

THE H_A acidity function, first defined for the protonation of amides by Yates *et al.*[1] for sulphuric acid solutions, then measured for hydrochloric acid,[2] and more recently also for perchloric acid solutions,[3] has been found to be followed by other types of compounds in their protonation behaviour (*e.g.* by pyridine oxides [4] and by some carbonyl compounds [5]). The function has also been used to correlate rates of reactions, often taking place at higher temperatures (*e.g.* the hydrolysis of amides [2]). Its variation with temperature has, however, been reported only for perchloric acid solutions so far.[6] In connection with a study of the rates of hydrolysis of methacrylamide in sulphuric acid at higher temperatures, we decided to determine the temperature coefficient of the H_A acidity function for sulphuric acid in order to be able to carry out a more meaningful analysis of the kinetics and, in particular, of the observed activation energy of the reaction.[7] This also gave us an opportunity to look into the question of the validity of an amide acidity function which is based upon 4- and 2-nitroaniline indicators in dilute acid. Doubt upon this question has been cast by the work of Edward and Wong [8] who claim that, if some 2-pyridone indicators (taken as amide analogues) are used in anchoring the scale in dilute acid, a new H_A acidity function, which is less negative by 0.3 units than the original one, is obtained.

A study of the temperature coefficient of the H_A acidity function enables thermodynamic functions for the protonation of amides to be obtained. Very scanty information on this is available in the literature. It has been surmised [9,10] that pK_{AH^+} values of amides are not very temperature dependent, but only the thermodynamic functions have been reported by Attiga and Rochester.[6] They interpreted the ΔH values in terms of hydration change on protonation, but did not comment upon the $\Delta S°$ values. In this work, our object has been to obtain more information on these functions and to compare them with those of structurally related bases.

EXPERIMENTAL

Materials.—Pyrrole-2-carboxamide was synthesized by a known procedure.[11] 4-Methoxybenzamide and methacrylamide were commercial samples (Aldrich) and were recrystallized before use. The nitroaniline indicators, 4- and 2-nitroaniline, were also commercial samples, purified by recrystallization.

Sulphuric acid was AnalaR grade. The acid solutions used were made up by dilution of the concentrated acid with deionised water, and their concentrations were determined by titration with standard alkali. The concentrations are expressed as weight percent, using density data from International Critical Tables.

Spectrophotometric Measurements.—Indicators were added to sulphuric acid solutions in dilute aqueous solution in amounts sufficient to give accurately measurable absorbances (final concentrations *ca.* 10^{-4}M). The sulphuric acid concentrations were corrected for the amount of indicator solution added (usually $<1\%$ by volume).

Full u.v. spectra of methacrylamide in various concentrations of sulphuric acid at room temperature (Figure 1) were recorded on a Unicam SP 800 spectrophotometer. We found that great care was needed in the measurement of solution volumes, if the good isosbestic point shown is to be obtained. Longer drainage times of pipettes are needed as the viscosity of sulphuric acid solutions increases with concentration.

For measurement of ionisation ratios, the instrument used was a Cecil CE 202 u.v.–visible spectrophotometer, which had a thermostatted cell holder. U.v. grade 1 cm spectrophotometric cells were closed with Teflon stoppers during the measurements. The temperature range was from 15 to 40 °C. The temperatures were controlled by a Tecam tempunit to within ± 0.2 °C. Work at 55 °C was attempted, but there was interference from hydrolysis.

RESULTS AND DISCUSSION

Definitions and Overlap Procedure.—The acidity function H_A for the protonation of amides is defined analogously to the original H_0 function of Hammett and Deyrup [12] by equation (1) where a_H is the activity of the

$$H_A = -\log_{10}\left(a_H \frac{f_A}{f_{AH^+}}\right) = pK_{AH^+} - \log_{10}\left(\frac{c_{AH^+}}{c_A}\right) \quad (1)$$

proton, pK_{AH^+} is the negative logarithm of the acid ionisation constant of the conjugate acid of the amide, f_A and f_{AH^+} are the activity coefficients of the amide and

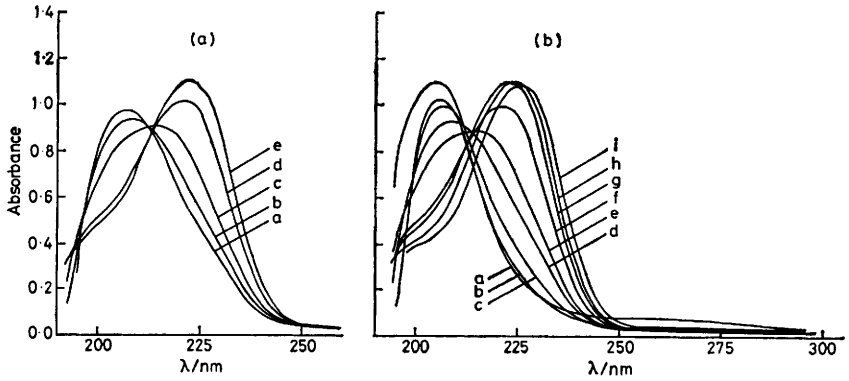

FIGURE 1 U.v. spectra of methacrylamide in sulphuric acid solutions of various concentrations: (a) a, 27.0%; b, 30.8%; c, 36.7%; d, 52.4%; e, 62.6%; (b) a, water; b, 10.0%; c, 20.5%; d, 30.8%; e, 36.7%; f, 52.4%; g, 62.6%; h, 73.5%; i, 98%

its conjugate acid, respectively, and c_A and c_{AH^+} are their concentrations. The evaluation of the H_A acidity function requires the knowledge of the pK_{AH^+} values of amides, which become protonated at progressively higher concentrations of strong acid, and their ionisation ratios, $I = c_{AH^+}/c_A$. The pK_{AH^+} values are determined using Hammett's overlap procedure,[12] since it follows from equation (1) that for two amides (say, A and A'), which become protonated within the same acid concentration range, and for which, because of the identity of the basic groups involved, the ratios of activity coefficients, (f_{AH^+}/f_A) and $(f_{A'H^+}/f_{A'})$, are the same within the acid concentration range in which the protonations occur, equation (2) should hold. This means that there ought

$$pK_{A'H^+} - pK_{AH^+} = \log_{10}\left(\frac{c_{A'H^+}}{c_{A'}}\right) - \log_{10}\left(\frac{c_{AH^+}}{c_A}\right) \quad (2)$$

to be parallel variation of the logarithms of their ionisation ratios within that range. The recognition that parallelism holds only for compounds of closely similar structure led to the need to define other acidity functions in addition to the H_0 function [12] which is now based exclusively on the protonation of variously substituted primary 2- and 4-nitroanilines (Hammett indicators).[13]

Applying equation (2) to ionisation ratios of two amides with overlapping protonation ranges enables the difference between their pK_a values to be found. In order to refer these pK_a values to *the infinitely dilute aqueous standard state*, the most basic compound used must be sufficiently protonated in highly dilute acid for its pK_a to be obtainable using the methods and the theory of dilute aqueous solutions. No primary amide is sufficiently basic for this, and the H_A scale previously obtained by Yates *et al.*[1] for sulphuric acid solutions was based on the protonation of 4- and 2-nitroanilines at the lowest acid concentrations. The first, most basic, indicator in a series is said to ' anchor ' an acidity function scale to the pH scale in highly dilute aqueous acid. It is this ' anchoring ' of the amide acidity function *via* 4- and 2-nitroaniline indicators in dilute acid that we have re-examined in this work.

U.v. Spectra and Isosbestic Points.—The use of equation (2) requires the knowledge of the ionisation ratios of indicators which undergo simple protonation. These are determined by measurement of the u.v. or visible absorption of the indicators over an acid concentration range within which the degree of protonation changes from almost nil to virtually complete, according to equilibrium (3). The proof that spectral changes are

$$A + H^+ \rightleftharpoons AH^+ \quad (3)$$

due to the shift of this simple equilibrium is the observation of a good isosbestic point. In the first paper [1] on the acidity function for the protonation of amides in sulphuric acid, there was no mention of poor isosbestic points, although a recording spectrophotometer was used throughout, but there was a problem of deciding at what acid concentration the amides may be taken to be fully protonated, since spectral changes both in dilute and especially concentrated acid have been observed and have been recognized to have nothing to do with protonation. A successive approximations procedure, based on the inflexion point of the sigmoid protonation curve, led to the conclusion that virtually full protonation may be taken to occur at an acidity function value 1.5 log units more negative than that point. This corresponds to *ca.* 60% acid, or somewhat less, for the most basic amides.

For benzamides, however, it is often claimed that there are no good isosbestic points in sulphuric acid solutions,* apparently on the basis of the spectra published by Edward and Meacock.[14] These authors reported spectra for benzamide between 0 and 97% sulphuric acid which show a reasonable isosbestic point up to 41.4% acid, but a substantial shift in the $\lambda_{max.}$ value and an increase in $\varepsilon_{max.}$ at higher acid concentrations. These were ascribed to a ' medium effect '. A later determination of benzamide spectra [15] makes no reference to a poor isosbestic point in <59% acid. A redetermination of the benzamide spectra in 60—98% sulphuric acid,[16] however, revealed another isosbestic point in that concentration region, which was ascribed to the tautomeric change of the cation from *N*-protonated in *ca.* 60% acid to *O*-

* We thank a referee for drawing our attention to this point.

protonated in anhydrous acid, due to the sharply falling activity of water which is essential for the stabilisation of *N*-protonated cations (see later). Similar changes (including a good isosbestic point) have since been reported in the u.v. spectra of *N*-methyl-*p*-toluohydroxamic acid [17] between 60 and 96% sulphuric acid and have also been ascribed to the tautomeric change in the structure of the cation from *N*-protonated in aqueous acid to *O*-protonated in concentrated acid. The spectra of *p*-methoxybenzamide in 0—97% sulphuric acid, also reported by Edward and Meacock,[14] show a good isosbestic point at 260 nm, with only a slight increase in the $\lambda_{max.}$ value between 41.4 and 97% acid, but with a substantial increase in the $\varepsilon_{max.}$ value over the same range. A good isosbestic point was apparently found for this amide also subsequently,[1,15] since there are no statements to the contrary. The published spectra of *m*-chlorobenzamide [15] also show a good isosbestic point at 234 nm between 26.9 and 46.4% sulphuric acid, which is the region of most rapidly changing ionisation ratios, with a shift to longer wavelengths observed in 60% acid (this almost certainly due to the tautomerism of the cation) and with a smaller shift to shorter wavelengths between pure water and 26.9% acid. The latter is probably due to the changing nature of the unprotonated species owing to hydrogen bonding with the hydronium ion. Evidence for this type of interaction has been found from the effect of very weak organic bases on the conductivity of aqueous acids and from u.v. spectra.[13c,18,19]

In this work we have studied the protonation of methacrylamide using the full u.v. range. The absorption maximum ($\pi \longrightarrow \pi^*$) of the pure amide in water at 205 nm ($\varepsilon_{max.}$ 11 000) shifts to longer wavelengths rapidly up to 62.6% acid, with an excellent isosbestic point at 213 nm between 27.0 and 62.6% acid [Figure 1(a)], *i.e.* in the region of most rapidly changing ionisation ratios. The maximum absorption in 62.6% acid is at 223 nm (ε 11 000). At still higher acid concentrations [Figure 1(b)] this maximum shifts to longer wavelengths and appears at 226 nm in 98% acid (ε 11 000). This shift is quite definite, but because it is so small and because $\varepsilon_{max.}$ values are the same in 62.6 and 98% acid, it is difficult to demonstrate the existence of another isosbestic point. By analogy with the larger spectral changes found for benzamide in the same acid concentration range,[16] we ascribe this spectral change to the tautomeric change of the cation from *N*-protonated in 62.6% acid to *O*-protonated in 98% acid. There is also a slight deviation from the isosbestic point in ≤20% acid, which is similar to that observed for *m*-chlorobenzamide,[15] as mentioned above, and is presumably due to hydrogen bonding (*via* the carbonyl group) to the hydronium ion. In the same acid concentration range there are significant changes in the $n \longrightarrow \pi^*$ (carbonyl) absorption region [Figure 1(b)], which support this suggestion. Here a very flat maximum ($\lambda_{max.}$ *ca.* 260 nm, $\varepsilon_{max.}$ 800) falls to about one third of its value in 10% acid and disappears in 20% acid.

The absorption maximum in 62.6% acid at 223 nm ($\varepsilon_{max.}$ 11 000) is close to the $\pi \longrightarrow \pi^*$ absorption maximum of methyl isopropenyl ketone, which occurs at 218 nm ($\varepsilon_{max.}$ 8 300) in ethanol [20] (which corrected to water [21] would be 226 nm). Similar agreement between amide spectra in *ca.* 60% sulphuric acid and the corresponding ketones in water or 50% sulphuric acid has been found for furamide and benzamide.[15]

Since u.v. spectra of all amides discussed above show changes in ≥60% acid similar to, but less pronounced than, those of benzamide, we have taken the view that their *N*-protonation up to *ca.* 60% acid is followed by conversion to *O*-protonation beyond this acid concentration. In view of the effect of this changeover on the u.v. spectra, we have restricted the present study to three of the most basic amides, for which the acid concentration regions of *N*-protonation and tautomeric change of the cation are sufficiently distinct. N.m.r. chemical shift measurements [22] show the protonation of methacrylamide to be virtually complete in 62.6% sulphuric acid and so the other two more basic amides used in this study are also practically fully protonated at an even lower acid concentration. (Variously substituted benzamides were taken to be fully protonated in 59—69% sulphuric acid.[15])

Other lines of evidence for *N*-protonation of amides in aqueous acids have been reviewed and flaws in some purported evidence against this view pointed out.[23] Rapid NH exchange of amides in dilute aqueous acid, observed by n.m.r.,[24] has always represented strong evidence for *N*-protonation. The unequal rates of exhange of *E*- and *Z*-NH protons, found more recently for primary amides,[25] which could not be explained in terms of the *O*-protonated species, have very recently been examined further by using the n.m.r. saturation-transfer technique and have been interpreted in terms of competition between rapid deprotonation of R–CO–NH_3^+ ions and rapid rotation about the C–N single bond.[26,27] Moreover, no contribution to NH exchange by the *O*-protonated cation could be demonstrated for the most basic primary amides.[26] All n.m.r. evidence obtained in aqueous acids is thus in favour of *N*-protonation of amides, and this, coupled with the u.v. evidence discussed above for a tautomeric change to *O*-protonation in >60% sulphuric acid, justifies us in regarding our results in <60% acid as referring to *N*-protonation. The thermodynamic functions derived (see later) confirm this.

It is well known that solvent has a dramatic effect on tautomeric equilibria in solution.[28] The view that *O*-protonated amides, observed by n.m.r. only in concentrated and anhydrous acid media, persist as dominant species in aqueous acids is based on the assumption that the change of medium by dilution of the acids with water does nothing to change the relative amounts of the two tautomers. This assumption ignores the special solvating properties of water [13c] and conflicts with numerous other lines of evidence,[23] including the results presented in this paper.

Evaluation of Ionisation Ratios.—Following the above conclusions regarding u.v. spectra of amides in sulphuric acid, we have determined the ionisation ratios of three primary amides (pyrrole-2-carboxamide, 4-methoxybenzamide, and methacrylamide) using $\lambda_{max.}$ values in 57.9% acid for the first two and the $\lambda_{max.}$ value in 62.6% acid for the third as the wavelengths for the measurements (see Table 1). The molar absorption coefficients

TABLE 1

The pK_{AH^+} values of amides at various temperatures

Amide	λ/nm	$-pK_{AH^+}$ 15 °C	25 °C	40 °C
Pyrrole-2-carboxamide	290	1.32	1.32	1.31
4-Methoxybenzamide	282	1.58	1.56	1.55
Methacrylamide	223	1.84	1.82	1.79

at these acid concentrations, $\varepsilon_{max.}$, were taken as the values for the conjugate acids (ε_{AH^+}), molar absorption coefficients in water as the values for the unprotonated amides (ε_A), and ε values at intermediate acidities as the values for the equilibrium mixtures of the two forms. The ionisation ratios were calculated from relationship (4).

$$I = \frac{c_{AH^+}}{c_A} = \frac{\varepsilon - \varepsilon_A}{\varepsilon_{AH^+} - \varepsilon} \qquad (4)$$

The ionisation ratios of 4- and 2-nitroaniline have been determined at the $\lambda_{max.}$ values of the free bases (380 and 415 nm, respectively), as is usual.[29]

points corresponding to log I values well within ±1, because of falling accuracy outside these limits.

The pK_{BH^+} value for 4-nitroaniline at 25 °C was taken for granted, since it had been repeatedly established as 1.00 ± 0.03 (see 'best values' tabulated by Paul and Long [30] and two more recent confirmatory determinations [29,31]). We also accepted the values of Johnson *et al.*[29] at other temperatures as our reference. The values decrease with temperature from 1.00 at 25 °C to 0.60 at 90 °C. Our reference value at 15 °C (1.08) was obtained by linear extrapolation of their results by means of a pK_{BH^+} *versus* $1/T$ plot, which is excellent.

The overlap between the log I values for 4- and 2-nitroaniline was satisfactory at all temperatures over the acid concentration range 3—6%, but the resulting pK_{BH^+} values for 2-nitroaniline are more negative than those of Johnson *et al.*[29] by 0.05—0.06 units. The slope of the plot pK_{BH^+} *versus* $1/T$ is the same, however, as that found by Bolton and Hall [32] for this indicator by a direct method, although their values are less negative than ours by 0.11 units. Our measured pK_{BH^+} value at 25 °C (−0.36) agrees with that obtained by overlap with 4-nitroaniline in aqueous trichloroacetic acid by Randles and Tedder.[33] It is also close to the value of −0.33 reported by Ryabova *et al.*[34] in their determination of the H_0 function of sulphuric acid. The overlap procedure itself entails an error of *ca.* ±0.02 in changing from one indicator to the next.

Our results leave no doubt that there is a satisfactory

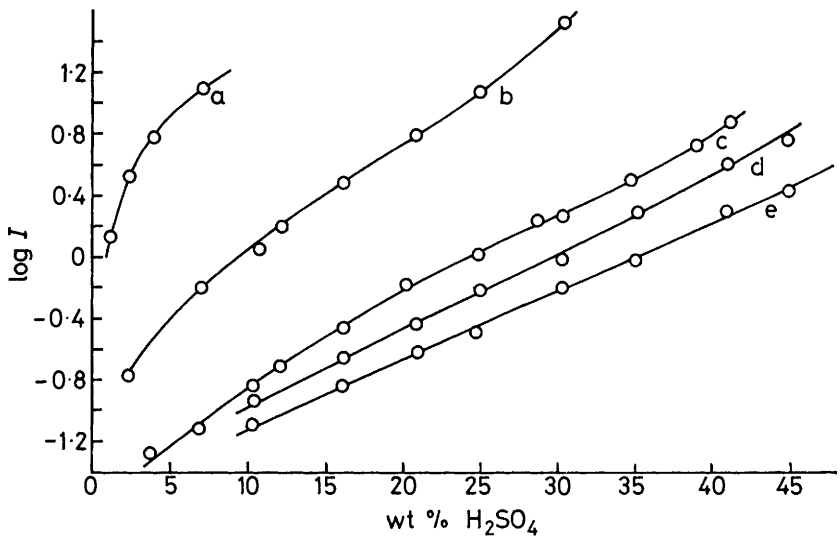

FIGURE 2 Plots of log I *versus* weight percent of sulphuric acid at 25 °C for (a) 4- and (b) 2-nitroaniline and for amides (c) pyrrole-2-carboxamide, (d) 4-methoxybenzamide, and (e) methacrylamide

pK_a *Values and Overlap Regions.*—Plots of log I *versus* weight percent of sulphuric acid were made for all indicators (including methacrylamide) at all experimental temperatures (Figure 2 shows the results for 25 °C), and regions of strict parallelism of lines of adjacent indicators were taken as overlap regions. In applying equation (2), we have been careful to use only overlap region between 2-nitroaniline and pyrrole-2-carboxamide, the most basic amide indicator. The overlap region between these two indicators extends from *ca.* 10 to *ca.* 16% sulphuric acid, with slight differences, depending on temperature. Clear deviation from parallel behaviour is observed only beyond 18% sulphuric acid, where H_0 and H_A functions begin to diverge sig-

nificantly. This is at variance with the figure published by Edward and Wong.[8] We are unable to account for the difference, but feel that our results fully justify the original assumption [1] that the H_A scale can safely be based on primary nitroaniline indicators at the lowest sulphuric acid concentration. The pK_{AH^+} value of −1.32 obtained for pyrrole-2-carboxamide at 25 °C (with a cumulative error of *ca.* ±0.04) is in very good agreement with the value of −1.30 ± 0.05 obtained by Yates *et al.*[3] in perchloric acid, but is more negative by 0.09 units than the values found earlier in sulphuric acid [1] and in hydrochloric acid.[2]

Similarly, satisfactory overlap is found between pyrrole-2-carboxamide and 4-methoxybenzamide over the acid concentration range 21—34%. We have used this latter indicator to extend the H_A scale up to 45% sulphuric acid. Our pK_{AH^+} values for this indicator (accurate to *ca.* ±0.06) agree with the most recently reported values,[3,6] but the earlier reported values for this indicator also are by *ca.* 0.1 unit less negative.[1,2]

log *I* values for methacrylamide show good overlap with this last indicator between 25 and 35% sulphuric acid (*i.e.* a plot of log *I* *versus* $-H_A$ has unit slope) and hence pK_{AH^+} values for this amide were also obtained (accurate to *ca.* ±0.08, allowing for possible cumulative error which would be the same at all temperatures).

A summary of pK_{AH^+} values at various temperatures for the amide indicators and methacrylamide, including the wavelengths at which the spectrophotometric measurements were carried out, is given in Table 1. Good agreement of values for pyrrole-2-carboxamide and 4-methoxybenzamide with values obtained in perchloric acid [3,6] justifies our procedure in calculating the ionisation ratios from u.v. spectra.

The H_A *Acidity Function Values.*—The H_A acidity function values found in this work were plotted and values at round percentages of sulphuric acid were read off the graph, as is usual. They are reported in Table 2. The values at 25 °C are more negative, by *ca.* 0.1 unit on average from *ca.* 15% sulphuric acid onwards, than the earlier published values.[1] The limits of error in the overlap procedure, in changing from one indicator to the next, are ±0.02 and cannot account for the difference of 0.1 unit in the H_A values, but differences of this magnitude between measurements of the H_0 function by various authors have also been found (see comparison of values in Table IX in ref. 29). Since H_0 and H_A values at low acid concentrations should be virtually coincident on theoretical grounds, we find that our H_A values at 25 °C agree most closely up to *ca.* 20% sulphuric acid with the H_0 values of Ryabova *et al.*[34] at the same temperature.

As can be seen from Table 2, differences between H_A values at various temperatures below *ca.* 15% sulphuric acid are small and tend to be random. Therefore, there appears to be no temperature variation in H_A (and H_0) [29] values at these concentrations, which exceeds the limits of error. At higher acid concentrations, like the H_0 values,[29] the H_A values become progressively less negative with increasing temperature. Plots of H_0 at any temperature *versus* H_0 at 25 °C were found to be linear,[29] with slopes $298.15/T$. Analogous plots of H_A values at 15 and 40 °C are also linear, with deviations not exceeding experimental error (the slopes of 1.03_5 and 0.95_2 are close to those predicted from $298.15/T$).

TABLE 2

The values of the acidity function H_A for sulphuric acid over a range of temperature

Wt% H_2SO_4	15 °C	25 °C	40 °C
1.0	0.88	0.89	
2.0	0.55	0.54	0.61
3.0	0.32	0.34	0.38
4.0	0.17	0.19	0.22
5.0	0.04	0.07	0.08
6.0	−0.06	−0.03	−0.02
7.0	−0.17	−0.13	−0.12
8.0	−0.26	−0.23	−0.20
9.0	−0.35	−0.32	−0.30
10.0	−0.42	−0.41	−0.38
11.0	−0.50	−0.50	−0.44
12.0	−0.56	−0.58	−0.54
13.0	−0.64	−0.66	−0.61
14.0	−0.72	−0.73	−0.68
15.0	−0.79	−0.80	−0.75
16.0	−0.87	−0.86	−0.82
17.0	−0.93	−0.93	−0.89
18.0	−1.00	−0.99	−0.95
19.0	−1.06	−1.05	−1.01
20.0	−1.12	−1.11	−1.08
22.0	−1.24	−1.22	−1.19
24.0	−1.34	−1.32	−1.28
26.0	−1.45	−1.41	−1.36
28.0	−1.52	−1.50	−1.45
30.0	−1.61	−1.59	−1.53
32.0	−1.70	−1.68	−1.62
34.0	−1.80	−1.79	−1.73
36.0	−1.92	−1.89	−1.85
38.0	−2.05	−2.02	−1.97
40.0	−2.15	−2.13	−2.10
42.0	−2.26	−2.24	−2.22
45.0	−2.43	−2.38	

Finally, the question of whether the H_A acidity function should differ from the H_0 acidity function by as much as 0.3 units at *ca.* 10% sulphuric acid, as claimed by Edward and Wong,[8] can best be judged by examining the differences between the H_0' and H_0''' acidity functions,[35] which differ on account of a considerable hydration difference between the primary and the tertiary anilinium ions.[35-37] The difference between these two functions is of the order of 0.3 units at *ca.* 18% sulphuric acid, *i.e.* at a much higher acid concentration. A difference of this magnitude at a relatively low sulphuric acid concentration between the H_0 and the H_A acidity functions does not seem reasonable, because differences in hydration changes on protonation between primary amines and primary amides can only be less than those between primary and tertiary amines, and not greater. From our H_A values and the H_0 values of Ryabova *et al.*,[34] which are most consistent with our measurements at low acid concentrations, a difference of 0.3 units between the two functions is found only at *ca.* 32% sulphuric acid. At this acid concentration the difference between H_0' and H_0''' is 0.66 units, which seems reasonable in comparison. Therefore, both on the basis of our measurements and on theoretical grounds, we are

satisfied that the H_A function is soundly based on primary nitroaniline indicators in dilute acid.

Thermodynamic Functions of Proton Ionisation.—The standard enthalpies of proton ionisation from the conjugate acids of the three amides have been obtained from the variation of log K_{AH^+} values from Table 1 with $1/T$ by the method of least squares and are reported in Table 3 with their standard errors. In view of the

TABLE 3

Thermodynamic functions of proton ionisation from protonated amides in water at 298 K

Amide	$-pK_{AH^+}$	ΔG^0_{298} / kJ mol^{-1}	ΔH^0_{298} / kJ mol^{-1}	ΔS^0_{298} / J K^{-1} mol^{-1}
Pyrrole-2-carboxamide	1.32 ±0.04	−7.53 ±0.23	−0.72 ±0.34	22.8 ±1.9
4-Methoxybenzamide	1.56 ±0.06	−8.90 ±0.34	−2.02 ±0.61	23.1 ±3.2
Methacrylamide	1.82 ±0.08	−10.39 ±0.46	−3.46 ±0	23.2 ±1.5

rather narrow temperature range involved, a more realistic estimate of errors in ΔH° is ±1 kJ mol^{-1}. The calculated entropies, with their standard errors, are also given in Table 3 (a more realistic estimate of errors in this quantity is ±4.5 J K^{-1} mol^{-1}). There is a good correlation between ΔG° and ΔH° with a slope of 1.044 ± 0.049, but if the uncertainties in the plotted quantities are taken into account, a variation in slope of ±0.25 is possible. The corresponding functions of Attiga and Rochester [6] show a much poorer correlation with a much higher slope, mainly due to the values for 3-nitrobenzamide. Clearly these slopes cannot be taken to be as meaningful as slopes of analogous correlations for various series of primary ammonium and anilinium ions, which are based on data for many more compounds. We have collected some such slopes from the literature in Table 4. Except for some disagreement in the slopes for *m*- and *p*-anilinium ions between two sets of authors,[32,38] the slopes are very close to 1.2. Such correlations indicate that the free energy changes are governed in a regular manner by the enthalpy component and are expected in terms of Hepler's theory [40] for reactions involving similar compounds and the same charge type. Indications from data in Table 4 being that ionisations of *all* primary ammonium ions (RNH_3^+) may follow the same correlation, we have plotted data for representative aliphatic

TABLE 4

Summary of slopes of ΔG^0_{298} *versus* ΔH^0_{298} correlations for proton ionisations in various series of primary ammonium ions

Compounds	No. in correlation	Slope	Ref.
Primary aliphatic ammonium ions	25	1.217 (r = 0.8716)	*a*
m- and *p*-substituted anilinium ions	21	1.344 (r = 0.9859)	*a*
o-, *m*-, and *p*-substituted anilinium ions	19	1.202 ± 0.011	*b*
Substituted 2- and 4-nitroanilinium ions (Hammett indicators)	14	1.200 ± 0.035	*c*

[a] Ref. 38. [b] Ref. 32. [c] Ref. 39.

primary ammonium ions (R = Me, Et, Pr^n) [41] and aromatic primary ammonium ions (R = Ph, *m*-tolyl) [42] and for a series of 2- and 4-nitroanilinium ions (Hammett indicators) [39] in order to verify this conclusion and in order to see how far the data for amide cations would fit in with those for other primary ammonium ions. The correlation is shown in Figure 3. Its slope, based on all

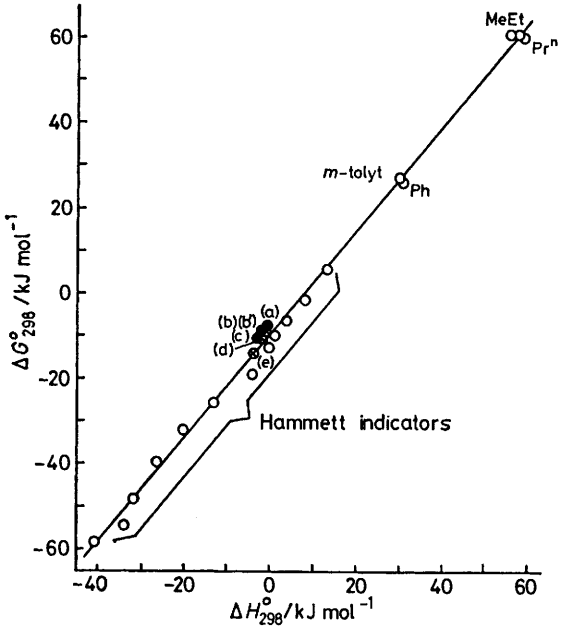

FIGURE 3 The plot of ΔG^0_{298} *versus* ΔH^0_{298} for proton ionisation of variously substituted primary aliphatic ammonium ions, anilinium ions, and amide cations, arising from (a) pyrrole-2-carboxamide; (b,b′) 4-methoxybenzamide; (c) methacrylamide; (d) 3,4,5-trimethoxybenzamide and (e) 3-nitrobenzamide. Full circles—this work; crossed circles—ref. 6; open circles—various sources—see text. (The size of the points is commensurate with the uncertainties in ΔH^0 values for the majority of points in the Figure)

the points shown and obtained by the method of least squares, is 1.220 ± 0.017. All primary ammonium ions thus show a common correlation between ΔG° and ΔH°, and the points for amide cations fall as close to the correlation line as most. In so far as there is a deviation which is outside the limits of error, it is in the direction of more positive ΔG° values, which may arise as a result of less positive entropies in the ionisation of acylammonium ions as compared with primary aryl ammonium ions of similar ΔH° value. [*N.B.* these are all *o*-chloro-(2- or 4-)nitroanilinium ions; [39] *o*-halogenoanilinium ions show more positive entropies of ionisation than expected; [32] hence the deviation of these points in the opposite direction.] The less positive entropies for amide cations can readily be ascribed to restricted rotation in the amide molecules formed by ionisation [equation (5)].

$$RCONH_3^+ + H_2O = RCONH_2 + H_3O^+ \quad (5)$$

The rotational barrier for rotation in acetamide molecules in water [43] is 63 kJ mol^{-1}. This is the chief difference between the ionisation of an *N*-protonated

amide and an anilinium ion, if solvation of the species involved in the reaction is ignored. Acidity function behaviour (the Bunnet and Olsen ϕ value) of amides, however, indicates greater solvation of amide cations as compared with primary nitroanilinium ions of comparable acidity,[13c] and this can most easily be accommodated by an *N*-protonated cation structure in which four water molecules can be hydrogen bonded in the primary solvation shell (one to the carbonyl oxygen and three to NH protons of the ammonium group), as compared with only three that can be bonded to an arylammonium ion. Strong evidence for hydrogen-bonding hydration of primary, secondary, and tertiary aliphatic ammonium ions has been obtained from estimates of their enthalpies of solution relative to that of the ammonium ion,[13c] which increase by *ca.* 7 kcal mol^{-1} (*ca.* 29 kJ mol^{-1}) with substitution of each NH proton by an alkyl group.* The energy of one such hydrogen bond is thus closely comparable with the resonance energy [23] of the amide group (*ca.* 33 kJ mol^{-1}) and therefore solvation energy is responsible for the stability of acylammonium ions in aqueous solution. The effect of greater acylammonium ion solvation on the entropy of the proton ionisation reaction is offset to some extent by the solvation of amide molecules themselves through hydrogen bonding of water to the carbonyl oxygen (evidence for this type of interaction comes from i.r. spectra of amides in polar solvents).[44] In more concentrated acids, *N*-protonated amide cations are ' salted out ' much more than primary nitroanilinium ions (for a recent review of this question see ref. 23) and are converted into *O*-protonated cations which have smaller hydration requirements, both in terms of the number of possible hydrogen bonds (only three) and their strength (because of charge delocalisation within the cation itself).[16] It is generally accepted that, with some exceptions,[45-47] *O*-protonated amide cations exist under anhydrous acid conditions,[23] and almost certainly in the gas phase.[48]

When one tautomer in a tautomeric equilibrium is present in very small amount, it is the major tautomer that determines thermodynamic properties,[23,28] and hence also linear free energy correlations. Thus the correlation of Figure 3 indicates that the dominant form of amide cations in aqueous acid is the *N*-protonated form. Also there is an excellent linear correlation between the free energies of ionisation of compounds of type R–NH_3^+ and R–OH, with R = Et, Ph, and MeCO (*i.e.* including acetamide cation and acetic acid), which involves only accurately known data (see Figure 6 in ref. 23), and leads to the conclusion that *N*-protonated amides are present predominantly in aqueous acid. The same conclusion was reached from the application of the Hammett equation to the pK_a values of substituted benzamides,[15] which follow a correlation with σ constants (and not with σ^+). In view of all this, we do *not* accept as valid the frequently quoted ' thermodynamic ' estimate [49] of the pK_a of *N*-protonated amide cations of *ca.* −8, which is based on two disparate linear free energy correlations (with unknown limits of error) and which specifically takes no account of the solvation of acylammonium ions. The pK_a of the *O*-protonated form of amides can, however, be estimated from a single, very good correlation of the pK_a values of various carbonyl bases with the carbonyl frequency.[50] For benzamide this estimate is −5.85, *i.e.* it is by *ca.* 4 log units more negative than the observed value. This means that the minor *O*-protonated form is present to the extent of *ca.* 1 in 10^4, or 0.01% for primary amides in aqueous acid. A tautomeric equilibrium constant of 10^4 corresponds to a free energy difference between the two forms, in their standard states in water, of only 5.4 kcal mol^{-1} (23 kJ mol^{-1}). That is why the equilibrium shifts readily as the solvating properties of the medium change with increasing acid concentration.[16,23]

* This energy for more acidic ammonium groups ought to be greater.

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