812. *Protonation Equilibria of Amides in Acetic Acid Solutions*

By R. B. HOMER and R. B. MOODIE

The basicities of several amides, and the variation of their ionisation ratios with the concentration of sulphuric acid in anhydrous acetic acid, have been measured. The results are compared with similar figures for aqueous solutions of sulphuric acid. One of the amides (*N*-methyl-2-naphthamide) was used to study the acidity of solutions containing added salts and/or hydrobromic acid in acetic acid.

THE lack of significance of the Hammett and related acidity functions for solutions of strong acids in acetic acid has been discussed by several authors.[1] However, limited correlations between the ionisation ratios of indicator bases and the rates of certain acid-catalysed reactions have been useful in investigations of mechanism.[2] Recent studies of acid catalysis in aqueous solutions [3] suggest that these correlations are most likely to be useful when comparison is made between rates of reaction and the protonation equilibria of indicators which are structurally similar to the substrate in the reaction, particularly with regard to the hydrogen-bonding abilities of the conjugate acids.

For comparison with the rates of acid-catalysed removal of the benzyloxycarbonyl group from benzyloxycarbonylglycine ethyl ester,[4] we have studied the protonation equilibria of several amides in sulphuric acid–acetic acid. One of the amides was selected for further studies of the hydrobromic acid–acetic acid solvent system, and of the effect of added salts in both media.

EXPERIMENTAL

The amides were prepared from the acids by standard methods, and their m. p.s agreed with published values.

Anhydrous acetic acid was prepared from AnalaR glacial acetic acid (after determination of the water content by Karl Fischer titration [5]) by refluxing the latter with the appropriate quantity of acetic anhydride. The amount of residual water, determined by a final Karl Fischer titration, was always less than 0·01%.

Anhydrous sulphuric acid was prepared from the AnalaR material by the addition of oleum until the maximum freezing point was observed.[6] It was found necessary to distil the oleum from potassium persulphate before use in order to remove traces of sulphur dioxide, the absorbance of which interfered with the spectrophotometric measurements.

Anhydrous hydrobromic acid was generated by dropping bromine on to a mixture of naphthalene and tetralin; the gas was bubbled through tetralin to remove bromine and then passed through a cold-trap and over phosphorus pentoxide into anhydrous acetic acid. The saturated solution so obtained (37—40% HBr) was estimated by Volhard titration and diluted as required.

Commercial tetraethylammonium bromide was recrystallised from ethanol–ether.

Tetraethylammonium bromide (10·5 g., 0·05 mole) was shaken with silver oxide (9 g., 0·05 mole) suspended in water (40 ml.). The silver bromide was filtered off. 1M-Sulphuric acid (52 ml.) was added and the water removed by means of a rotatory evaporator. The residue was taken up in ethanol and precipitated with ether; it was then recrystallised once from ethanol–ether and once from ethanol–ethyl acetate to give hygroscopic crystals of tetraethylammonium hydrogen sulphate, m. p. 240° (Acid equiv., 225·5. Calc. for $C_8H_{21}NSO_4$; 227·2).

Both salts, unlike the corresponding tetramethylammonium compounds, were readily soluble in acetic acid.

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[1] S. Bruckenstein, *J. Amer. Chem. Soc.*, 1960, **82**, 307, and references quoted therein.

[2] R. F. Cieciuch and F. H. Westheimer, *J. Amer. Chem. Soc.*, 1963, **85**, 2591; D. Bethell and V. Gold, *J.*, 1958, 1905; D. P. N. Satchell, *J.*, 1958, 1927.

[3] (*a*) R. B. Homer and R. B. Moodie, *J.*, 1963, 4377; (*b*) J. F. Bunnett, *J. Amer. Chem. Soc.*, 1961, **83**, 4956.

[4] R. B. Homer, R. B. Moodie, and H. N. Rydon, *Proc. Chem. Soc.*, 1963, 367, and the following Paper.

[5] M. S. Mitchell and D. M. Smith, "Aquametry," Interscience, New York, 1948.

[6] R. J. Gillespie, E. D. Hughes, and C. K. Ingold, *J.*, 1950, 2473.

Spectra were measured in stoppered 1 cm. silica cells with a Unicam S.P. 500 spectrophotometer, the cell compartment of which was maintained at 50·0° ± 0·2° by means of circulating water from a thermostat. Optical densities were measured at 2-mμ intervals over the absorption bands of interest.

Solutions of tetraethylammonium bromide in sulphuric acid–acetic acid media showed an absorption band, $\lambda_{\text{max.}}$ 272 mμ which increased in intensity with time, and which was believed to be due to traces of the Br_3^- ion. Attempts to avoid the production of this ion by the use of outgassed solutions and darkened vessels were unsuccessful. This limited measurements to acid concentrations of less than 0·1M, below which the absorbing material was produced slowly enough to be effectively blanked out.

RESULTS AND DISCUSSION

The Measurement of the Ionisation Ratio of the Amides.—The amides used were selected because, on protonation, their ultraviolet spectra showed significant changes at longer wavelengths than 265 mμ, where absorption by acetic acid was negligible. The spectrum of the free amide was obtained in pure acetic acid, and that of the conjugate acid of the amide in sulphuric acid–acetic acid of an appropriate concentration (Table 1). The latter spectrum usually shifted to longer wavelengths at higher acidities, and to obtain the ionisation ratio it was necessary, as previously described,[3a, 7] to move the spectrum of the conjugate acid up to 5 mμ toward shorter wavelengths. The spectra for various acidities then all passed through a moderately well defined isosbestic point. These wavelength shifts, and the wavelength used for the calculation of the ionisation ratio, are recorded in Table 1.

TABLE 1

Spectra of the amides in acetic acid at 50°

	Free base *		Conj. acid †			λ (mμ) used for determination of I
	$\lambda_{\text{max.}}$ (mμ)	10^{-3} ε	$\lambda_{\text{max.}}$ (mμ)	10^{-3}ε	Shift (mμ)	
1-Naphthamide	282	5·60	304 ‡	4·55 ‡	2	282
2-Naphthamide	280	5·40	290	7·63	2	298
p-Phenylbenzamide	272	21·96	294	20·60	5	300
N-Methyl-1-naphthamide ...	281	6·00	292	5·15	2	304
N-Methyl-2-naphthamide ...	280	6·54	286	8·38	3	294
N-Methyl-*p*-phenylbenzamide	269	21·02	287	20·70	1 §	290
NN-Dimethyl-1-naphthamide	282	6·51	288	4·80	0	306

* Measured in anhydrous acetic acid. † Measured in 2·15M-H_2SO_4 in acetic acid. ‡ Measured in 4·7M-H_2SO_4 in acetic acid. § Unprotonated peak shifted 1 mμ to the red.

The basicities of the amides in this medium, as measured by the value of log *M* for half-protonation (*M* is the stoicheiometric molar concentration of sulphuric acid) are compared with the H_0 values for half-protonation in aqueous sulphuric acid [3a] in Table 2. It is observed that there is no close correlation between the relative basicities in the two media. The basicities relative to an indicator base of three of these compounds in perchloric acid–acetic acid have been measured.[8]

The Variation of the Ionisation Ratio with Acidity.—In acetic acid, dissociation constants of ion-pairs are very low, and sulphuric acid behaves as a weak monobasic acid.[9] The following equilibria need to be considered:

$$\mathrm{HA} \xrightleftharpoons{K_i^{\mathrm{HA}}} \mathrm{H^+A^-} \xrightleftharpoons{K_d^{\mathrm{HA}}} \mathrm{H^+} + \mathrm{A^-}$$

$$\mathrm{B} + \mathrm{HA} \xrightleftharpoons{K_i^{\mathrm{BHA}}} \mathrm{BH^+A^-} \xrightleftharpoons{K_d^{\mathrm{BHA}}} \mathrm{BH^+} + \mathrm{A^-}$$

The ionisation ratio, *I*, which may be measured spectrophotometrically, is given by:

$$I = (c_{\mathrm{BH^+}} + c_{\mathrm{BH^+A^-}})/c_{\mathrm{B}}$$

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[7] L. A. Flexser, L. P. Hammett, and A. Dingwall, *J. Amer. Chem. Soc.*, 1935, **57**, 2103.

[8] T. Higuchi, C. H. Barnstein, H. Ghassemi, and W. E. Perez, *Analyt. Chem.*, 1962, **34**, 400.

[9] I. M. Kolthoff and S. Bruckenstein, *J. Amer. Chem. Soc.*, 1956, **78**, 1, 10, 2974.

The concentration of the ion-pair between the conjugate acid of the amide and the anion of the added acid, $c_{\mathrm{BH^+A^-}}$, is large compared with $c_{\mathrm{BH^+}}$. It follows that

$$\log I = \log[K_i^{\mathrm{BHA}}\gamma_{\mathrm{B}}\gamma_{\mathrm{HA}}\gamma_{\mathrm{H^+A^-}}/\gamma_{\mathrm{BH^+A^-}}(\gamma_{\mathrm{H^+A^-}} + K_i^{\mathrm{HA}}\gamma_{\mathrm{HA}})] + \log M.$$

HA is the added acid, and M its stoicheiometric molar concentration. At low acid concentrations ($M \sim 10^{-3}$) where activity coefficients (γ) differ little from unity, other workers[10] have observed the expected linear unit-slope correlation between log I and log M. At higher concentrations slopes deviate from unity[11] and curves are not parallel for different indicators.

Plots of log I against log M for the amides, which were measured over the range 10^{-2}—1M-sulphuric acid, are shown in Figure 1. The plots are linear, but the slopes deviate from unity. The slopes are tabulated, together with that of the Hammett indicator 4-chloro-2-nitroaniline,[11] in Table 2. The primary amides show slopes uniformly less than those for the secondary amides. Similar behaviour was observed for these amides in aqueous acid solution,[3a] and was attributed to differences in hydrogen-bonding solvation of the conjugate acids. This explanation is not sufficient to explain the results in sulphuric acid–acetic acid media, because here the trend was not continued with a tertiary amide, *NN*-dimethyl-1-naphthamide, which gave a slope similar to that for the primary amides studied. A similar situation may obtain for aqueous solutions, but the greater basicities of the tertiary amides precluded studies in the range of acidities where meaningful results could be obtained.

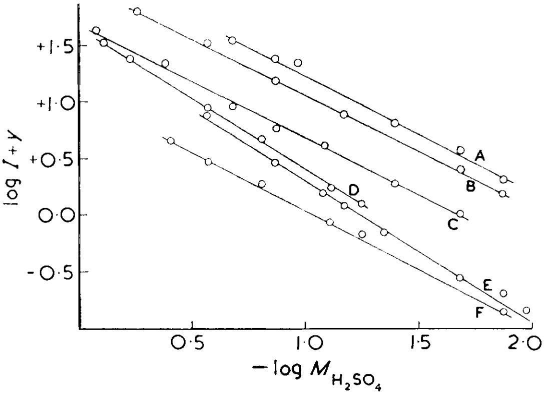

FIGURE 1. Graphs of (log I + y) against −log $M_{\mathrm{H_2SO_4}}$; the constant y is used to adjust the ordinate

(A) *p*-Phenylbenzamide (y = 0·7), (B) 2-naphthamide (y = 0·6), (C) 1-naphthamide (y = 0·6), (D) *N*-methyl-*p*-phenylbenzamide (y = 0·1), (E) *N*-methyl-2-naphthamide (y = 0), (F) *NN*-dimethyl-1-naphthamide (y = −0·3).

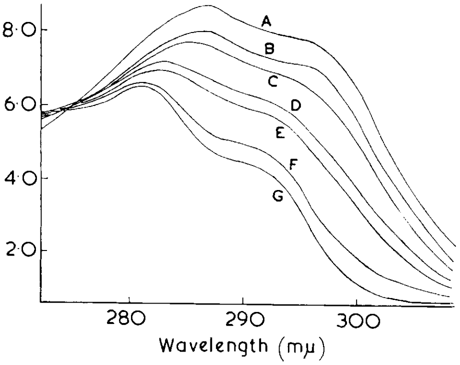

FIGURE 2. Spectrum of *N*-methyl-2-naphthamide in various molarities, M, of sulphuric acid in acetic acid at 50°

(A) 2·15M, (B) 0·71M, (C) 0·24M, (D) 0·07M, (E) 0·05M, (F) 0·01M, (G) 0·00M.

The *N*-methylamides represent the closest model to the substrate of the kinetic study in the following Paper. *N*-Methyl-2-naphthamide, the spectrum of which is shown in Figure 2, was therefore used to investigate the effect of added salts, and of the use of

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[10] T. L. Smith and J. H. Elliot, *J. Amer. Chem. Soc.*, **1953**, **75**, 3566.

[11] N. F. Hall and W. F. Spengeman, *J. Amer. Chem. Soc.*, **1940**, **62**, 2483.

TABLE 2

The basicities of the amides

	d (log I)/d (log M)	$-\log M$ for $I = 1$ in H_2SO_4–AcOH	H_0 for $I = 1$ in H_2SO_4–H_2O
1-Naphthamide	1·04	1·07	−2·73
2-Naphthamide	1·02	1·46	−2·50
p-Phenylbenzamide	1·02	1·50	−2·15
N-Methyl-1-naphthamide	1·23	1·23	−2·20
N-Methyl-2-naphthamide	1·20	1·23	−2·11
N-Methyl-*p*-phenylbenzamide	1·24	1·22	−2·15
NN-Dimethyl-1-naphthamide	1·02	1·32	−1·93
2-Chloro-4-nitroaniline	1·20		

hydrobromic acid instead of sulphuric acid, on the acidity of the medium, as measured by log I.

The Ionisation Ratio of N-*Methyl-2-naphthamide in the Presence of Sulphuric Acid, Hydrobromic Acid, and Added Salts.*—The variation of log I for this compound in various media is shown in Figure 3. Linear variation of log I with log M is observed in each case. Log I values for hydrobromic acid are consistently greater than those for sulphuric acid at the same molar concentration, and the difference, 0·82 log I units, compares well with the difference in H_0 (0·93) observed at lower acid concentrations.[10]

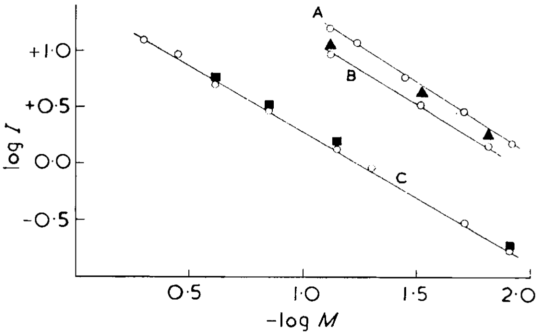

FIGURE 3. Graphs of log I for *N*-methyl-2-naphthamide against $-\log M$, where M is the molar concentration of H_2SO_4 or HBr

Circles: (A) H_2SO_4–AcOH containing 0·091M-$Et_4N^+Br^-$, (B) HBr–AcOH, (C) H_2SO_4–AcOH. Triangles: HBr–AcOH containing 0·045M-$Et_4N^+Br^-$. Squares: H_2SO_4–AcOH. Triangles: HBr–AcOH containing 0·045M-$Et_4N^+Br^-$. Squares: H_2SO_4–AcOH containing 0·091M-$Et_4N^+HSO_4^-$.

Addition of tetraethylammonium hydrogen sulphate to sulphuric acid solutions, and of tetraethylammonium bromide to hydrobromic acid solutions, causes in each case slight increases in acidity, as measured by log I. Quantitatively similar behaviour has been reported when sodium hydrogen sulphate is added to sulphuric acid solutions.[12]

Addition of 0·091M-tetraethylammonium bromide to the sulphuric acid solutions produces a much larger increase in acidity. This suggests that the following equilibrium lies well to the right

$$H_2SO_4 + TEA^+Br^- \rightleftharpoons HBr + TEA^+HSO_4^-$$

In harmony with this is the similarity of log I values for tetraethylammonium bromide in equimolar solutions of sulphuric and hydrobromic acids, as shown in Figure 3.

These results suggest that, when the concentration of sulphuric acid exceeds that of the salt, the increase in acidity should be less marked. Unfortunately, this region was experimentally inaccessible for reasons mentioned in the Experimental section.

The values of log I in the various solutions constitutes a measure of acidity of the solutions towards secondary amides and compounds of similar structure. The application of these results to the kinetics of the removal of the *N*-benzyloxycarbonyl group will be discussed in the next Paper.

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[12] M. A. Paul and L. P. Hammett, *J. Amer. Chem. Soc.*, 1936, **58**, 2182.