Spectrophotometric Determination of Basicity Constants. Part II.[1] Acetanilides

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The basicity constants, K_{BH^+}, of 13 acetanilides have been evaluated in sulphuric acid at 25°. Recent evidence on the site of protonation of amides has been reviewed and a new equation for calculating pK_{BH^+} has been formulated. The values of pK_{BH^+} obtained for the *para*-substituted acetanilides correlate well with Hammett σ values.

Methods of Determining Basicity Constants.—The basicity (or acid dissociation) constant K_{BH^+} is generally evaluated from equation (1) where C_{BH^+} and C_B are the

$$pK_{BH^+} = H_X + \log_{10}C_{BH^+}/C_B \qquad (1)$$

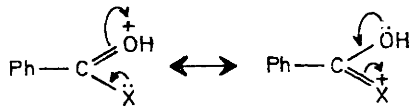
concentrations of conjugate acid and base respectively and H_X is the applicable acidity function, *i.e.* the one for which a plot of ($\log_{10}I = \log_{10}C_{BH^+}/C_B$) against H_X is unity. But since all acidity functions are nearly linear with the original H_0 scale,[2] values of pK_{BH^+} are best quoted using both H_A (for amides)[3] and H_0 plots[4] (refs. 3 and 4 refer to recent values for H_2SO_4).

The strength of a base can also be determined using the linear free energy relationship (l.f.e.r.) (2) defined by Bunnett and Olsen.[5]

$$\log_{10}I + H_0 = \phi(H_0 + \log_{10}C_{H^+}) + pK_{BH^+} \qquad (2)$$

Position of Protonation.—Many arguments have been put forward to support both *O*- and *N*-protonation of amides and these have been reviewed by a number of authors including Liler,[6] Katritzky and Jones,[7] O'Connor,[8] and Homer and Johnson.[9] Some of the more recent evidence on this controversy is presented below.

Liler[10] has used i.r. spectroscopy to support her claims for *N*-protonation. The pK_{BH^+} values of various aromatic aldehydes and ketones have a linear correlation with the carbonyl stretching frequencies, but the frequency for benzamide is widely different from that predicted by this linear plot. Liler therefore considered that the protonation of benzamide occurred on the nitrogen atom. This interpretation may be in error for several reasons, in particular because $\nu_{C=O}$ refers to the free base and no allowance is made for the extra resonance stabilisation possible for *O*-protonated benzamide (I)—(II) compared to compounds such as benzaldehyde and benzyl phenyl ketone. Similar resonance stabilisation, by donation of electrons from a non-



(I) X = NH$_2$ (II) X = NH$_2$
(III) X = OH (IV) X = OH
(V) X = Cl (VI) X = Cl

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[1] Part I, J. W. Barnett and C. J. O'Connor, *J.C.S. Perkin II*, 1973, 1331.

[2] L. P. Hammett and A. J. Deyrup, *J. Amer. Chem. Soc.*, 1932, **54**, 2721.

[3] K. Yates, J. B. Stevens, and A. R. Katritzky, *Canad. J. Chem.*, 1964, **42**, 1957.

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[7] A. R. Katritzky and R. A. Y. Jones, *Chem. and Ind.*, 1961, 722.

[8] C. J. O'Connor, *Quart. Rev.*, 1970, **24**, 553.

[9] R. B. Homer and C. D. Johnson, 'The Chemistry of Amides,' ed. J. Zabicky, Wiley–Interscience, New York, 1970, ch. 3, p. 188.

[10] M. Liler, *Spectrochimica Acta*, 1967, **23A**, 139.

bonding orbital on the atom adjacent to the carbonyl group, may be achieved by O-protonated benzoic acid and benzoyl chloride, and this can be seen by comparing structures (I) and (II) with structures (III) and (IV), and (V) and (VI).

Figure 1 shows the plot of pK_{BH^+} against $\nu_{C=O}$ reported by Liler[10] (solid line); the broken line shows that there is an excellent linear correlation between those compounds which may be stabilised in the same manner as O-protonated benzamide, and such a correlation suggests that the pK_{BH^+} of benzamide measures the degree of O-protonation.

Evidence for O-protonation in very concentrated acid also came from Liler.[11-13] In dilute and moderately concentrated acid solutions n.m.r. spectra have provided conflicting evidence as to the site of protonation.

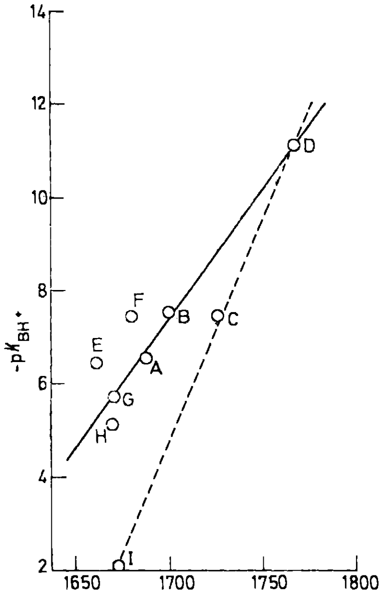

FIGURE 1 Correlations of the basicities of aromatic carbonyl compounds with the carbonyl frequencies:[10] A, acetophenone; B, benzaldehyde; C, benzoic acid; D, benzoyl chloride; E, benzophenone; F, benzyl phenyl ketone; G and H, *cis*- and *trans*-benzylidineacetophenone respectively; I, benzamide

Berger *et al.*[14] and Fraenkel and Franconi[15] concluded that the dominant cation formed even in dilute acid must be the O-protonated amide, with a negligible amount of N-protonated form present.

Liler[11-13,16,17] does not agree with their interpretation and postulates a tautomeric equilibrium in which there is a changeover from the N-protonated cation in dilute and moderately concentrated aqueous acids to the O-protonated cation in highly concentrated and anhydrous acids.

Bruylants *et al.*[18] studied the n.m.r. spectra of a series of anilides in an attempt to show that amides are preferentially protonated on oxygen and weakly on the amide nitrogen. They stated that there exists an equilibrium between the two protonated species, the importance of the N-protonated species depending on the electronic properties of the molecule studied and also on the composition of the solvent.

Benderley and Rosenheck[19] have reported u.v. evidence for predominant O-protonation in dilute acid, but do not completely exclude the existence of some N-protonated cations.

The basicities of *meta*- and *para*-substituted benzamides were applied[20] to the Hammett equation[21] and found to give better correlation with σ[22] than with σ^+.[23] This is in contrast to the dependence of the basicities of benzaldehydes, acetophenones, and benzoic acids on ring substitution where in all cases a better correlation has been found[24,25] by using σ^+ values. It was thus argued that if the proton were attached to the carbonyl group the conjugation with an electron-releasing *para*-substituent would be strong enough to require the use of σ^+ constants. Farlow and Moodie[26] do not believe that this lack of conjugation is due to N-protonation and produced evidence which suggested why such delocalisation of the charge into the ring is unimportant in O-protonated benzamides.

One must conclude on present evidence that in very concentrated acids, amides undoubtedly protonate on the carbonyl oxygen. In dilute and moderately concentrated acid solutions the evidence is also in favour of predominant O-protonation, although there is also a small concentration of N-protonated cation present. The nature of the spectral changes observed for the present set of compounds makes it clear that O-protonation is observed.

RESULTS AND DISCUSSION

Basicity Constants.—The values of the basicity constants, pK_{BH^+}, have been evaluated for the conjugate acids of a number of acetanilides using u.v. spectrophotometry, and sulphuric acid as solvent. For each substrate the value of pK_{BH^+} was obtained from a plot of $\log_{10}I$ against H_A by consideration of equation (3).

$$\log_{10}I = -m_A H_A + pK_{BH^+} \qquad (3)$$

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[11] M. Liler, *Chem. Comm.*, 1971, 115.

[12] M. Liler, *J.C.S. Perkin II*, 1972, 816.

[13] M. Liler, *J.C.S. Perkin II*, 1974, 71.

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[22] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 420.

[23] H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.* (*a*) 1957, **79**, 1913; (*b*) 1958, **80**, 4979.

[24] R. Stewart and K. Yates, *J. Amer. Chem. Soc.*, 1960, **82**, 4059.

[25] R. Stewart and K. Yates, *J. Amer. Chem. Soc.*, 1958, **80**, 6355.

[26] D. W. Farlow and R. B. Moodie, *J. Chem. Soc.* (*B*), 1970, 334.

When $\log_{10}I = 0$, we have (4) where m_A is the slope of the

$$pK_{BH^+} = m_A H_A^{\frac{1}{2}} \qquad (4)$$

plot of $\log_{10}I$ against H_A and $H_A^{\frac{1}{2}}$ is the value of H_A at half-protonation. Only the values of $\log_{10}I$ in the range $\pm1{\cdot}0$ (corresponding to 10—90% protonation) were used since the experimental uncertainty increases rapidly as the ionisation ratio takes on very high or very low values.

The values of $\log_{10}I$ were also plotted against H_0 and, in addition, the basicity constants were calculated using the Bunnett–Olsen l.f.e.r. (2).

For some substituted acetanilides the position of $\lambda_{max.}$ did not shift as the substrate became protonated, while for other acetanilides there was a definite shift in spectrum. The exact method of evaluating pK_{BH^+} was therefore dependent on the behaviour of each particular substrate.

For acetanilide, 4-fluoro-, 4-chloro-, 4-bromo-, 4-iodo-, and 4-methyl-acetanilides there was no lateral shift in spectrum, *i.e.* $\lambda_{max.B} = \lambda_{max.BH^+}$. The absorbances were measured at the one wavelength and the value of pK_{BH^+} evaluated from a plot of $\log_{10}I = \log_{10}(A - A_B)/(A_{BH^+} - A)$ against H_A according to the original method of Hammett and Deyrup.[2] The positions of $\lambda_{max.}$ are given in Table 1.

TABLE 1

Wavelengths at which absorbance values were measured for the calculation of the basicity constants of substituted (X) acetanilides

X	4-OH	4-Me	4-MeO	4-EtO	H	4-F	4-Cl	4-Br	4-I	4-NH_2	4-NO_2
λ_1/nm	242·0	241·2	243·5	244·0	238·0	235·0	244·4	246·5	253·0	240·0	316·5
λ_2/nm										236·4	285·0

X	4-CO_2H		2-Me	
λ_1/nm	(a) 273·4	(b) 268·6	(a) 220·0	(b) 186·5
λ_2/nm		258·7	235·0	196·0

The position of $\lambda_{max.}$ of 4-methoxy-, 4-ethoxy-, and 4-hydroxy-acetanilides remained constant in solutions up to *ca.* 30% (w/w) H_2SO_4, but in more concentrated acid there was a steady bathochromic shift in $\lambda_{max.}$. At the same time, the absorbance at the position of $\lambda_{max.}$ decreased as the solvent was varied from 5 to *ca.* 40% (w/w) H_2SO_4 and then remained constant. For these three substrates pK_{BH^+} was therefore evaluated by considering the absorbances at $\lambda_{max.}$ irrespective of the wavelength at which this maximum occurs.

This same method was used by Noyce and Jorgensen [27] in their work on the basicities of a series of *trans*-substituted chalcones in sulphuric acid. They showed that by taking absorbance values at the wavelength of maximal absorption in each solution, rather than at a fixed wavelength for all solutions of a particular base, one is in effect using the isosbestic point method [28] of correcting for medium effects. This method was also used by Yates and Wai [29] in their calculations of the ionisation ratios of 11 substituted anilines in perchloric acid.

The bathochromic shift in $\lambda_{max.}$ observed for the alkoxy- and hydroxy-substituted acetanilides is most likely due to a strong hydrogen bonding of the alkoxy- and hydroxy-groups with the solvent; this explanation has been previously proposed by Stewart and Yates [30] to explain the deviation of the alkoxy- and hydroxy-groups from a plot of pK_{BH^+} against σ^+ for a series of substituted acetophenones.

For the remaining acetanilides, *i.e.* 4-nitro- and 4-amino-acetanilides, 4-acetamidobenzoic acid and *O*-methylacetanilide, the values of pK_{BH^+} were obtained using the methods of Davis and Geissman [31] and Stewart and Granger.[32] For *p*-nitroacetanilide there was practically no change in the spectrum of the carbonyl peak as the base became protonated and the change was therefore measured over the more substantial shift observed for the nitro-peak.

In the case of 4-acetamidobenzoic acid there was a small peak at 273·4 nm which did not undergo any lateral shift as the base became protonated. The value of pK_{BH^+} was obtained at this one wavelength using the plot of $\log_{10}(A - A_B)/(A_{BH^+} - A)$ against H_A. The pK_{BH^+} of 4-acetamidobenzoic acid was also calculated from absorbance values measured at 268·7 and 258·7 nm; the longer wavelength (268·7 nm) is the position of $\lambda_{max.}$ of the unprotonated base, and 258·7 nm is the wavelength to which this peak shifts on protonation of the substrate. The values of $pK_{BH^+}(m_A H_A^{\frac{1}{2}})$ obtained by the two methods closely resemble each other, as can be seen in Table 2.

When measuring the basicity of 4-aminoacetanilide it was observed that, initially, an aqueous solution had a peak in its spectrum at 244·5 nm. Within *ca.* 1 h, however, this peak had shifted to a new position at 240 nm. We cannot explain this slow spectral change, but have assumed that the substituent subsequently affecting the degree of protonation of the carbonyl group is NH_3^+. In solutions >20% (w/w) sulphuric acid there was a further hypsochromic shift in the position of $\lambda_{max.}$.

The value of pK_{BH^+} for *o*-methylacetanilide has been measured by independently following both the change

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[27] D. S. Noyce and M. J. Jorgensen, *J. Amer. Chem. Soc.*, 1962, **84**, 4312.

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

[29] K. Yates and H. Wai, *J. Amer. Chem. Soc.*, 1964, **86**, 5408.

[30] R. Stewart and K. Yates, *J. Amer. Chem. Soc.*, 1958, **80**, 6355.

[31] C. T. Davis and T. A. Geissman, *J. Amer. Chem. Soc.*, 1954, **76**, 3507.

[32] R. Stewart and M. R. Granger, *Canad. J. Chem.*, 1961, **39**, 2508.

in the n–π^* and π–π^* transitions. The n–π^* transition does not have a well defined peak, but appears as a shoulder on the π–π^* peak and this introduces an arbitrariness when choosing the wavelengths at which to measure the absorbances. The π–π^* peak is, however, well defined but it occurs at a wavelength <200·0 nm and at this level there is an increase in the experimental inaccuracy of the machine used to measure the u.v. spectra. The wavelengths at which the absorbance values were measured are given in Table 1. Ionisation ratios are listed in Supplementary Publication No. SUP 21301 (7 pp.).*

TABLE 2

Comparison of pK_{BH^+} values of substituted (X) acetanilides obtained by acidity function and l.f.e.r. methods

X	Method [a]	m_A	$-H_A^{\frac{1}{2}}$	$-m_AH_A^{\frac{1}{2}}$	m_0	$-H_0^{\frac{1}{2}}$	$-m_0H_0^{\frac{1}{2}}$	ϕ	$-K_{BH^+}$ (l.f.e.r.)	$-c$ [b]	$-(m_0H_0^{\frac{1}{2}} + -m_Ac)$ [c]
4-OH	1	1·14	0·89	1·02	0·97	0·97	0·94	0·11	0·89	0·10	1·06
4-MeO	1	1·10	1·15	1·27	0·94	1·28	1·20	0·10	1·20	0·12	1·33
	2	1·00	1·17	1·16	0·80	1·31	1·05	0·29	1·05		
4-EtO	1	1·05	1·16	1·22	0·88	1·30	1·14	0·18	1·14	0·12	1·27
	2	1·01	1·13	1·14	0·83	1·25	1·04	0·26	1·04		
4-Me	1	1·01	1·27	1·27	0·81	1·44	1·16	0·29	1·16	0·13	1·29
H	1	1·12	1·41	1·58	0·87	1·64	1·42	0·19	1·43	0·15	1·59
	2	1·09	1·47	1·60	0·81	1·69	1·38	0·25	1·41		
4-F	2	1·02	1·67	1·70	0·69	2·01	1·39	0·39	1·47	0·24	1·63
4-Cl	1	0·97	1·95	1·88	0·63	2·38	1·51	0·45	1·63	0·35	1·85
4-Br	1	1·01	2·00	2·01	0·67	2·45	1·64	0·41	1·76	0·41	2·06
	2	1·00	1·85	1·86	0·65	2·26	1·48	0·42	1·59		
4-I	2	0·99	2·09	2·07	0·60	2·64	1·58	0·48	1·74	0·44	2·02
4-NH_2	5	1·26	1·88	2·37	0·85	2·29	1·94	0·19	1·99	0·33	2·36
4-CO_2H	3	1·04	1·96	2·05	0·66	2·44	1·62	0·41	1·73		
	4	1·07	2·05	2·20	0·68	2·59	1·76	0·39	1·87	0·48	2·22
4-NO_2	2	1·06	2·44	2·59	0·61	3·36	1·97	0·46	2·16	0·60	2·61
2-Me	6	0·98	2·65	2·59	0·52	3·64	1·88	0·56	2·13	0·70	2·56
	7	1·84	1·55	2·84	1·31	1·78	2·32	0·40	2·26		

[a] Experimental conditions under which $\log_{10}I$ values were obtained: 1, Cary 14 spectrophotometer and 0·2 cm cells; 2, Cary 14 spectrophotometer and 1·0 cm cells; 3, Techtron Varian spectrophotometer and 1·0 cm cells; $\lambda_B = \lambda_{BH^+} = 273{\cdot}4$ nm; 4, as for method 3, but λ_B 268·7, λ_{BH^+} 258·7 nm; 5, as for method 3, but λ_B 240·0, λ_{BH^+} 236·4 nm; 6, Cary 14 spectrophotometer and 0·2 cm cells; λ_B 220·0, λ_{BH^+} 235·0 nm; 7, Cary 14 spectrophotometer and 1·0 cm cells; λ_B 196·0, λ_{BH^+} 186·5 nm. [b] c Is the intercept in the equation $H_A = mH_0 + c$. [c] See Discussion section, equation (9).

The result obtained from plots of $\log_{10}I$ against H_A and $\log_{10}I$ against H_0, and the values of pK_{BH^+} and results obtained using Bunnett–Olsen's l.f.e.r. are given in Table 2. In all these plots the standard deviations in slope and intercept were in the range $0{\cdot}01 < s < 0{\cdot}11$.

The results obtained for *o*-methylacetanilide are particularly interesting; Table 2 shows that the slopes of the plots of $\log_{10}I$ against H_A evaluated for shifts in each of the transitions are very different, as are the corresponding values of $H_A^{\frac{1}{2}}$. In spite of this difference the values of $m_AH_A^{\frac{1}{2}}$ are in reasonable agreement.

For each acetanilide it is apparent that agreement between the values of $m_0H_0^{\frac{1}{2}}$ and $m_AH_A^{\frac{1}{2}}$ is fair, as is agreement of these values with the pK_{BH^+} values obtained from Bunnett–Olsen's l.f.e.r. The discrepancy between the values of $m_0H_0^{\frac{1}{2}}$, $m_AH_A^{\frac{1}{2}}$, and pK_{BH^+} (l.f.e.r.) increases as the base becomes weaker, *i.e.* as the acidity at which the base is half-protonated increases.

Consider first the differences between the basicity constants measured using the H_A and H_0 acidity scales. The large increase in $m_AH_A^{\frac{1}{2}} - m_0H_0^{\frac{1}{2}}$, from 0·08 units for 4-hydroxyacetamide to 0·62 units for 4-nitroacetanilide, is undoubtedly due to the fact that we have assumed a linear relationship between H_A and H_0 over the entire acid concentration range, with an intercept at the origin. In fact, the plot of H_A against H_0 is curved, as is shown in Figure 2. Up to 16·1% (w/w) sulphuric acid, the H_A and H_0 functions were assumed by Yates *et al.*[3] to coincide, as there was no amide available whose pK_{BH^+} could be determined by ionisation measurements in dilute solution. In solutions more concentrated than 16·1% (w/w) sulphuric acid the slope of H_A against H_0 decreases from a value of 1·00 to *ca.* 0·5.

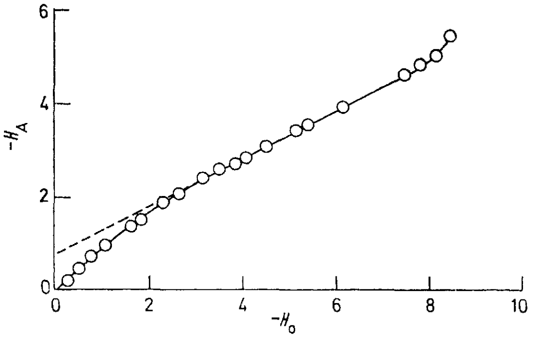

FIGURE 2 Plot of H_A (25°) [3] against H_0 (25°) [4]

Thus, at any point on the graph the relationship between H_A and H_0 can be expressed by equation (5) where for

$$H_A = mH_0 + c \qquad (5)$$

each value of H_0, m and c are, respectively, the slope and intercept of the line drawn tangent to the curve at that point. The range of values of m and c are $0{\cdot}5 \leqslant m \leqslant 1{\cdot}0$ and $0{\cdot}0 \leqslant c \leqslant 0{\cdot}82$.

By making use of equation (5) and also (6) and (7),

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* For details of Supplementary Publications see *J.C.S. Perkin II*, 1974, Index issue. Items less than 10 pp. are supplied as full-size copies.

we can show mathematically that the difference between $m_0H_0^{\frac{1}{2}}$ and $m_AH_A^{\frac{1}{2}}$ is due to a factor involving c, the intercept in equation (9). In equations (6) and (7), K_1

$$\log_{10}I = m_0H_0 + \mathrm{p}K_1 \qquad (6)$$

$$\begin{aligned}\log_{10}I &= m_AH_A + \mathrm{p}K_2 \\ &= m_AmH_0 + m_Ac + \mathrm{p}K_2 \qquad (7)\end{aligned}$$

and K_2 are the values of the basicity constant of the given compound determined using the H_0 and H_A acidity functions respectively.

Thus, by comparison of (6) and (7), equations (8) and (9) obtain.

$$\mathrm{p}K_1 = m_Ac + \mathrm{p}K_2 \qquad (8)$$

$$m_AH_A^{\frac{1}{2}} = m_0H_0^{\frac{1}{2}} + m_Ac \qquad (9)$$

Equation (9) has been applied to our basicity measurements; to do this it was necessary to estimate a value of c from Figure 2. Selected values of $(m_0H_0^{\frac{1}{2}} + m_Ac)$, for each of the substrates studied, are given in the last column of Table 2 and it can be seen that these show a much improved agreement with $m_AH_A^{\frac{1}{2}}$ than do those of uncorrected values of $m_0H_0^{\frac{1}{2}}$.

TABLE 3

Ionisation data obtained from analysis of experiment results of Hashmi and Johnson [37]

Substrate (and method of measurement)	m_0	$-H_0^{\frac{1}{2}}$	$-m_0H_0^{\frac{1}{2}}$	m_A	$-H_A^{\frac{1}{2}}$	$-m_AH_A^{\frac{1}{2}}$
Acetanilide (u.v., 238 nm)	0·30	3·52	1·04	0·60	2·53	1·52
(n.m.r.)	0·36	3·10	1·11	0·66	2·35	1·56
4-Bromo-acetanilide (u.v., 245 nm)	0·40	3·26	1·30	0·72	2·42	1·74
4-Aminoacetanilide (u.v., 245 nm)	0·43	3·12	1·33	0·78	2·36	1·85
(n.m.r.)	0·41	3·37	1·36	0·74	2·50	1·85
3-Aminoacetanilide (n.m.r.)	0·35	3·55	1·23	0·65	2·60	1·68
3-Chloroacetanilide (u.v., 240 nm)	0·43	3·56	1·53	0·78	2·61	2·05
Nicotinamide (u.v., 225 nm)	0·50	5·69	2·85	1·04	3·70	3·86
Isonicotinamide (u.v., 255 nm)	0·50	5·92	2·93	1·02	3·82	3·89
3-Acetylaminopyridinium ion (u.v., 255 nm)	0·35	5·18	1·83	0·69	3·45	2·39
4-Acetylaminopyridinium ion (u.v., 275 nm)	0·43	6·30	2·68	0·83	4·02	3·35

Let us now consider the difference between values of $\mathrm{p}K_{\mathrm{BH^+}}$ measured using the acidity function and l.f.e.r. methods. Bases having a $\mathrm{p}K_{\mathrm{BH^+}} > -1{\cdot}4$ in fact show excellent agreement between $m_0H_0^{\frac{1}{2}}$ and $\mathrm{p}K_{\mathrm{BH^+}}$ (l.f.e.r.). For bases which have a $\mathrm{p}K_{\mathrm{BH^+}} < -1{\cdot}4$, the discrepancy between $m_0H_0^{\frac{1}{2}}$ and $\mathrm{p}K_{\mathrm{BH^+}}$ (l.f.e.r.) increases as the base weakens and this is probably due to the fact that the $\mathrm{p}K_{\mathrm{BH^+}}$ is estimated from the intercept obtained by extrapolation of the graph; the accuracy of $\mathrm{p}K_{\mathrm{BH^+}}$ therefore depends on the slope ϕ remaining constant. Indeed, ϕ is not independent of acid concentration, but rather becomes more positive with increasing acid concentration and this will therefore introduce a larger error in $\mathrm{p}K_{\mathrm{BH^+}}$ as the base being studied gets weaker.

The difference between the values of $\mathrm{p}K_{\mathrm{BH^+}}$ (l.f.e.r.) and $m_AH_A^{\frac{1}{2}}$ are of the same order and direction as was observed by Bunnett and Olsen [5b] for a series of benzamides. It could be suggested that the failure of the Bunnett–Olsen l.f.e.r. is due to the fact that it involves the use of the H_0 scale whereas amides, for example, follow the H_A acidity function. It has been shown,[33] however, that a similar deviation exists between the values of $\mathrm{p}K_{\mathrm{BH^+}}$ (l.f.e.r.) and $\mathrm{p}K_{\mathrm{BH^+}}$ (acidity function) obtained from the data of Johnson *et al.*[4] for a series of nitroaniline indicators whose protonation follows the H_0 scale.

When applying the basicity constants measured to kinetic data the values of $m_AH_A^{\frac{1}{2}}$ should be used, since the use of the H_A acidity scale enables a closer approach to the Hammett requirement of unit slope for the plot of $\log_{10}I$ against H_x.

Literature Values of $\mathrm{p}K_{\mathrm{BH^+}}$.—The $\mathrm{p}K_{\mathrm{BH^+}}$ values of some of the acetanilides have previously been measured; in particular $-\mathrm{p}K_{\mathrm{BH^+}}$ for acetanilide has been quoted as 1·56,[34] 1·5,[35] and 1·53.[36]

Haldna *et al.*[36] studied spectrophotometrically the basicities of three acetanilides. In each case they measured the absorbance values of the peak which is found at 195—215 nm. These peaks do not undergo a lateral shift on protonation and are not generally used in studies of the protonation of bases containing the carbonyl group. It is of interest to note that the slopes of the plots of Haldna *et al.* of $\log_{10}I$ against H_A are in the region 0·59—0·67. Such low values are quite different from the values of *ca.* 1·0 obtained in the present investigation, but could be associated with the fact that the study of Haldna *et al.* involved the measurement of absorbances at a much lower wavelength (of *ca.* 198 nm) compared to the wavelength (of *ca.* 240 nm) used in the present work. A similar difference in slope was observed when the absorbances of *o*-methylacetanilide were measured at *ca.* 190 and *ca.* 230 nm.

Using u.v. and n.m.r. spectrophotometry, Hashmi and Johnson [37] have measured $\mathrm{p}K_{\mathrm{BH^+}}$ for acetanilide, 4-bromo-, 4-amino-, 3-chloro-, and 3-amino-acetanilides, as well as nicotinamide, isonicotinamide, and 3-acetyl- and 4-acetyl-aminopyridinium ions. They reported slopes of between 0·33 and 0·43 units for the plots of $\log_{10}I$ against H_0. We have also plotted their $\log_{10}I$ values against H_A and Table 3 summarises results

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obtained from their data. Since the method of u.v. spectrophotometry used by Hashmi and Johnson to determine values of $\log_{10}I$ appears to be very similar to the method used in this investigation, the reason for the difference in slopes is not apparent. In spite of this, however, the values of $m_{\mathrm{A}}H_{\mathrm{A}}^{\frac{1}{2}}$ for acetanilide and 4-bromoacetanilide are in reasonable agreement.

The basicity constants of a series of *para*-substituted acetanilides were measured by Bruylants *et al.*[38] The substituents (with values of $-\mathrm{p}K_{\mathrm{BH^+}}$ in parentheses) were MeO (1·45), Me (1·51), H (1·74), Cl (1·9), and $\mathrm{NO_2}$ (2·78). For each substrate the value of $\mathrm{p}K_{\mathrm{BH^+}}$ was only calculated at a single wavelength, *i.e.* no allowance was made for a lateral shift in spectrum and, although this does not always occur, we have certainly observed such a shift when 4-nitro- and 4-methoxy-acetanilides become protonated. The results of Bruylants *et al.* showed extremely good agreement between the values of $m_{\mathrm{A}}H_{\mathrm{A}}^{\frac{1}{2}}$ and $m_0H_0^{\frac{1}{2}}$, such agreement being in contrast to the differences observed in the present study and in the work by Haldna *et al.*[36] and Hashmi and Johnson.[37]

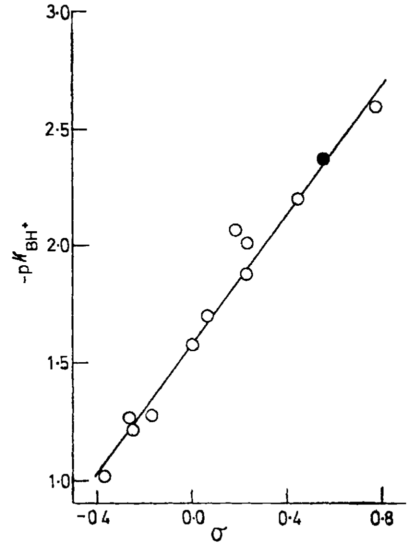

FIGURE 3 Hammett plot of $-\mathrm{p}K_{\mathrm{BH^+}}$ against σ for 4-substituted acetanilides: ○, computed values; ●, value for p-$\overset{+}{\mathrm{N}}\mathrm{H_3C_6H_4NHCOCH_3}$

Moreover their value of $m_{\mathrm{A}}H_{\mathrm{A}}^{\frac{1}{2}}$ (−1·74) for acetanilide differs from all other reported values which lie in the range −1·54 ± 0·04.

The Hammett Equation.—We have recently reported[39] the substituent effects on the n.m.r. spectra (δ_{NH} and $\delta_{\mathrm{CH_3}}$) of *para*-substituted acetanilides and found that the chemical shifts correlate well with Hammett σ values.

The values of $-\mathrm{p}K_{\mathrm{BH^+}} = m_{\mathrm{A}}H_{\mathrm{A}}^{\frac{1}{2}}$ of the *para*-substituted acetanilides measured in this investigation have been plotted against the substituent constants σ[22] and σ^+.[23] Gilbert and Johnson[40] have recently found a much better correlation of $\mathrm{p}K_{\mathrm{a}} = m_0H_0^{\frac{1}{2}}$ against σ^+ (0·985) for protonation equilibrium constants for acetophenones than with plots of $H_0^{\frac{1}{2}}$ against σ^+ (0·931). Figure 3 shows the plot of $-\mathrm{p}K_{\mathrm{BH^+}}$ against σ. The values of ρ are 1·40 ± 0·08 and 0·90 ± 0·08 for plots against σ and σ^+ respectively. The correlation of $-\mathrm{p}K_{\mathrm{BH^+}}$ with σ (0·983) is better than with σ^+ (0·958) and this is only to be expected since interaction of a ring substituent with the carbonyl group is made difficult by the interception of a nitrogen in the resonance chain. The value of ρ = 1·40 is similar to the value 1·31 reported by Bruylants *et al.*[38] for their plot of $\log_{10}K_{\mathrm{BH^+}}$ against σ for a series of substituted acetanilides. The $\mathrm{p}K_{\mathrm{BH}}$ (−2·37) for *p*-aminoacetanilide was not included in the correlation of $\log_{10}K_{\mathrm{BH^+}}$ with σ and σ^+. It is, however, shown in Figure 3 using the value of σ = 0·56 quoted by Clark and Perrin[41] for the p-$\mathrm{NH_3^+}$ substituent. The experimental value of $\mathrm{p}K_{\mathrm{BH^+}}$ is obviously in excellent agreement with the value of $\mathrm{p}K_{\mathrm{BH^+}}$ predicted by this Hammett plot for the substrate *p*-acetamidoanilinium.

For an equilibrium, the size of ρ is indicative of the extent of charge change at the atom of the side chain directly attached to the ring carbon atom in going from one side of the equilibrium to the other. The value of ρ = 1·40 for the plot of $-\mathrm{p}K_{\mathrm{BH^+}}$ against σ for the acetanilides is higher than the value of ρ = 0·92 which has been reported by Yates *et al.*[42] for correlation of $\mathrm{p}K_{\mathrm{BH^+}}$ values of substituted benzamides with σ. This difference is not, however, surprising since in the acetanilide series the benzene ring is directly attached to the nitrogen atom which is involved in resonance stabilisation of the amide and its *O*-protonated conjugate acid.

EXPERIMENTAL

Materials.—AnalaR sulphuric acid was standardised against sodium hydroxide. Solutions of the required percentage composition were prepared by dilution with deionised water by weighing.

4-Acetamidophenol (Koch–Light), 4-acetamidobenzoic acid (Aldrich), 4-fluoroacetanilide (Koch–Light), 4-aminoacetanilide (B.D.H.), 4-nitroacetanilide (B.D.H.), and *o*-methylacetanilide (B.D.H.) were recrystallised from aqueous ethanol and had m.p.s of 169, 260, 152, 162, 216, and 111·5—112·5° respectively. Acetanilide (B.D.H.) was recrystallised from water, m.p. 113·5—114·0°.

4-Methyl-, 4-methoxy-, 4-ethoxy-, 4-chloro-, 4-bromo-, and 4-iodo-acetanilides were prepared by dissolving the substituted aniline in acetic anhydride and, to this solution, adding two drops of concentrated sulphuric acid. The acetanilide precipitated out on standing. The m.p.s of these derivatives were 148, 131, 137, 179, 168, and 184° respectively.

Measurement of Basicity Constants.—Samples (10 ml) of acid solutions of the required concentrations were weighed; the range of acid concentrations generally included at least

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10 samples in the region $-1\cdot0 \leqslant \log_{10}I \leqslant +1\cdot0$, as well as acid solutions in which the substrate is unprotonated and fully protonated. A stock solution of the base was prepared by dissolving substrate ($2\cdot5 \times 10^{-3}$ g) in water (25 ml). Samples (1 ml) of this solution were pipetted into each of the acid samples and the u.v. spectra were measured immediately. Absorbance changes were usually 0·1—0·2 units.

Least squares calculations were made on a Burroughs B6700 computer.

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