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THE HAMMETT ACIDITY FUNCTION AND ITS NON-APPLICABILITY TO AMIDES

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Abstract—Ultraviolet spectral measurements, and a reinvestigation of previous results have shown that many amides are not Hammett bases; the implications to previous work on basicity determinations and kinetic studies are discussed. A simple experimental criterion is described for determining whether a base is of the Hammett type.

THE Hammett acidity function was set up by Hammett and Deyrup[1] to describe the ionization behaviour of weak bases in aqueous sulphuric acid (and has been extended to other acids). It has been assumed to apply to bases of very diverse types, and therein lies its great value. The only well recognized exceptions have been carbinols which form carbonium ions and follow the H_R function,[2] olefins which form carbonium ions and follow the function $H_{R'}$ (where $H_{R'} = H_R - \log a_{H_2O}$)[3] and cation bases which follow an H^+ function.[4]

Recently, we showed[5] that uracil, 5-bromouracil, and some of their N-methyl derivatives are not Hammett bases because graphs of $\log_{10}$ ([Neutral molecule]/[Cation]) against H_0, although straight lines, do not have unit gradient. In view of this surprising result we decided to investigate other amides.

Amides were included by Hammett[6] in the list of compounds completely protonated in 100% sulphuric acid and assumed to obey the H_0 acidity function. Stewart *et al*[7]. measured the pK of several substituted benzamides: they published curves for one compound, *m*-chlorobenzamide, examination of which disclosed[8] that the gradient was 0·65 instead of unity as for a Hammett base. However, this and similar deviations were attributed[9,10] to solvent effects and we therefore investigated benzamide and *p*-nitrobenzamide in detail.

EXPERIMENTAL

p-Nitrobenzamide[11] was repeatedly crystallized from water, and sublimed at 10^{-3} mm; it had m.p. 210·5–202° (lit,[11] m.p. 200°). Benzamide, m.p. 127·5–128·5°, was repeatedly crystallized from water.

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Preparation of sulphuric acid of known concentration

A two litre bottle containing A.R. sulphuric acid and another containing acid diluted to approximately 10N were fitted separately to two sealed burette systems with vacuum filling tubes and automatic zeros. These acids were standardized by dilution of known volumes to approximately 1N and titration against 1·000N sodium hydroxide. The acids were mixed in suitable proportions in 100 cc Pyrex graduated flasks, and 1 hr drainage time was allowed for the burette meniscus. The flasks were cooled at 20° overnight, and the volume made up with distilled water. After again standing at 20° overnight the volume was finally corrected. Calibration of the flasks before and after the acids had been made up in them showed insignificant changes.

All spectra were taken on a Cary 14M-50 recording spectrophotometer, scanning at 1 mμ/sec, with paper rate 4 in/min. The appropriate solvent was used as a blank for each spectrum, and the base-line of the machine was adjusted for each solvent. Experience showed that old samples of sulphuric acid sometimes developed absorption in the 260 mμ region; any sample which required base-line correction of >0·02 optical density units was rejected.

RESULTS

Graphs of the extinction coefficient against H_0 are shown in Figs. 1 and 2 for benzamide and *p*-nitrobenzamide at wavelengths where there is a large change from cation to neutral molecule. It is immediately apparent that the solvent effect on the cation is small, in strongly acid solution, and that on the neutral molecule is small in weakly acid and neutral solution. The solvent effect that would be needed to account for the deviations over the acidity range where both species occur would be so large that this possibility can be eliminated.

A general test of whether a base follows the Hammett acidity function has been devised as follows. Because the arms of the curves of ε against H_0 are reasonably straight, though sometimes sloping, it may be assumed that the solvent effect is linear with H_0. Hence

$$\varepsilon = [B]\{\varepsilon_B + G_B \,.\, H_0\} + [BH^+]\{\varepsilon_{BH^+} + G_{BH^+} \,.\, H_0\} \qquad \text{(i)}$$

$$\therefore \frac{d\varepsilon}{dH_0} = \frac{d[B]}{dH_0}\left\{\varepsilon_B + G_B \,.\, H_0\right\} + [B] \,.\, G_B + \frac{d[BH^+]}{dH_0}\{\varepsilon_{BH^+} + G_{BH^+} \,.\, H_0\} + [BH^+]\, G_{BH^+}$$

where [B] is the mole fraction of the neutral species, and [BH$^+$] that of the conjugate acid.

For a Hammett base we would write

$$\text{p}K = H_0 + \log_{10} \frac{[BH^+]}{[B]}$$

and a plot of $\log_{10}$ ([B]/[BH$^+$]) against H_0 would be a straight line with unit gradient; but because our compounds are not Hammett bases the gradients are not unity. However it is an experimental fact that such plots are straight lines and we write instead

$$\text{p}K = H_0 + n \log_e \frac{[BH^+]}{[B]} \qquad \text{(ii)}$$

For a Hammett base, n would have the value 0·434. Differentiating and rearranging the terms:

$$-[B][BH^+] = n\left\{[B]\frac{d[BH^+]}{dH_0} - [BH^+]\frac{d[B]}{dH_0}\right\}$$

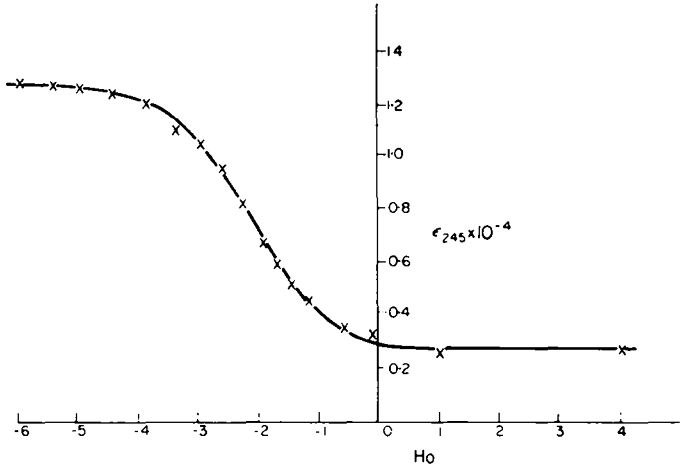

FIG. 1. Benzamide: ϵ at 245 mμ against H_0. Points × are experimental results: line calculated from $pK = H_0 + 1{\cdot}45 \log_{10}$ ([Cation]/[Neutral molecule]).

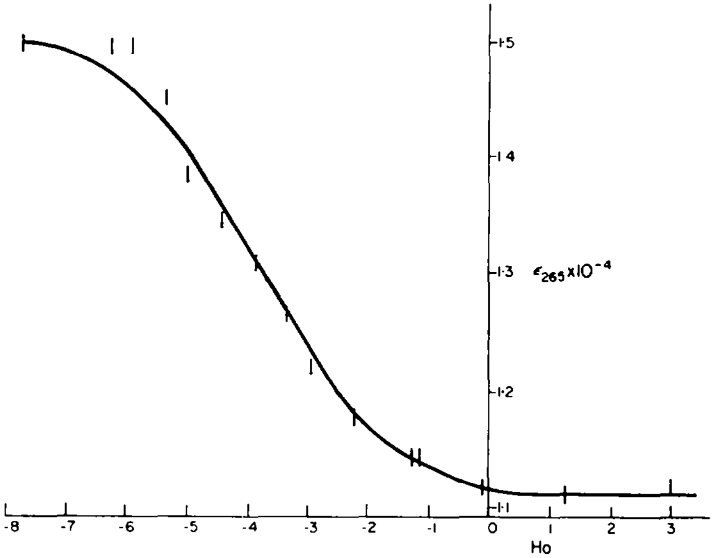

FIG. 2. p-Nitrobenzamide: ϵ at 265 mμ against H_0. Points plotted are experimental results; line calculated from $pK = H_0 + 2{\cdot}5 \log_{10}$ ([Cation]/[Neutral molecule]).

Also

$$[\mathrm{B}] + [\mathrm{BH}^+] = 1 \qquad \text{(iii)}$$

$$\therefore \frac{d[\mathrm{B}]}{d\mathrm{H}_0} = -\frac{d[\mathrm{BH}^+]}{d\mathrm{H}_0}$$

Substituting these expressions into the previous equation:

$$\frac{d[\mathrm{B}]}{d\mathrm{H}_0} = \frac{[\mathrm{B}][\mathrm{BH}^+]}{n}$$

Thus
$$\frac{d\varepsilon}{dH_0} = \frac{[B][BH^+]}{n}\{\varepsilon_B - \varepsilon_{BH^+} + H_0(G_B - G_{BH^+})\}$$
$$+ G_B[B] + G_{BH^+}[BH^+]$$

If the gradient of the curve of ε against H_0 at the point where $[B] = [BH^+] = \frac{1}{2}$ be denoted q, and the H_0 at this point is pK

$$q = \frac{\varepsilon_B - \varepsilon_{BH^+}}{4n} + \tfrac{1}{2}(G_B + G_{BH^+}) + \frac{pK}{4n}(G_B - G_{BH^+})$$

Solving for n:

$$n = \frac{\varepsilon_B - \epsilon_{BH^+} + pK(G_B - G_{BH^+})}{4q - 2(G_B + G_{BH^+})}$$

All the quantities in this expression are readily measured: for the neutral molecule the gradient of the curve is G_B, for the cation it is G_{BH^+}.

For the neutral molecule also, putting $[B] = 1$, $[BH^+] = 0$ in (i)

$$\varepsilon_{neut} = \varepsilon_B + G_B \,.\, H_0$$

For the cation

$$\varepsilon_{cat} = \varepsilon_{BH^+} + G_{BH^+} \,.\, H_0$$

Thus estimates can be made of ε_B and ε_{BH^+}. At the pK,

$$\varepsilon_{pK} = \tfrac{1}{2}\{\varepsilon_B + \varepsilon_{BH^+} + (G_B + G_{BH^+})pK\}$$

Thus the pK is the point at which a straight line

$$\varepsilon = \tfrac{1}{2}\{\varepsilon_B + G_B \,.\, H_0 + \varepsilon_{BH^+} + G_{BH^+} \,.\, H_0\}$$

intersects the experimental curve of ε against H_0.

For a Hammett base $n = 0·434$; Table 1 records values of $0·434/n$ determined for benzamide and *p*-nitrobenzamide. Also included in the Table are values for other amides, which have been calculated for the original data obtained by one of us.[7]

TABLE 1. TESTS OF WHETHER SUBSTITUTED BENZAMIDES ARE HAMMETT BASES

Substituent	From ε plot*		From log plot*		Wavelength for detn, mμ
	0·434/*n*	p*K*†	Gradient	p*K*†	
H	0·62	−2·1	0·66 ± 0·03	−2·1 ± 0·05	245
p-NO$_2$	0·35	−3·8	0·39 ± 0·02	−3·8 ± 0·05	265
m-Br	0·46 ± 0·02	−2·6 ± 0·4	0·52 ± 0·09	−2·5 ± 0·3	247
p-Br	0·55 ± 0·01	−2·15 ± 0·05	0·62	−2·15	261
p-Cl	0·73	−2·3	0·77 ± 0·05	−2·3	256
N-CH$_3$	0·55	−2·0	0·53 ± 0·03	−2·0 ± 0·05	242
o-CH$_3$	0·49	−2·95	0·42 ± 0·05	−2·95 ± 0·05	245
m-CH$_3$	1·00	−1·90	1·00	−1·85	250
p-CH$_3$	0·77 ± 0·07	−1·90 ± 0·05	0·67	−1·90	259
m-OCH$_3$	0·82	−2·45 ± 0·05	0·75 ± 0·05	−2·45 ± 0·15	251
p-OCH$_3$	0·75	−1·65	0·77 ± 0·02	−1·55 ± 0·05	282

* See Text

† Using the H_0 values quoted by Paul and Long, *Chem. Rev.* **57**, 1 (1957).

The accuracy of this work is not as high as for the first two amides mentioned, but it is clear that most of the compounds are not Hammett bases. As a check on the values of $0{\cdot}434/n$, the gradients of the conventional plots of $\log_{10}$ ([Neutral molecule]/[cation]) against H_0 are also tabulated: the two values should be the same.

DISCUSSION

Our work shows that many amides are definitely not Hammett bases. This suggests that the general assumption that weak bases follow the H_0 function may not be justified, and that the protonation of benzoic acids,[9] acetophenones,[12] and benzaldehydes[13] should be further investigated. The discrepancy presumably arises because amides and/or their cations do not have the same activity coefficient behaviour as the nitroanilines for which the Hammett scale was largely derived. It may be that amides follow some other general acidity function, and work to test this point is in hand.

Meanwhile, it is obvious that mechanistic deductions derived from kinetic dependence on H_0 should be applied with caution: this includes the treatment of Bunnett.[14]

Derived pK_{BH^+} values have less significance than was thought: they will be in the correct order in any series, but the numerical increments can be misleading. For example, Stewart *et al.*[7] considered that the dependence of pK_{BH^+} for substituted benzamides on σ rather than σ^+ indicated that amides underwent *N*-protonation. When O-protonation was proved (cf. ref. 15, 16) they offered[16] no alternative explanation for the σ dependence to that in their earlier paper. As the amides are not Hammett bases, arguments based on σ or σ^+ dependence lose their significance.

Recently Edward and Wang[17] have concluded that propionamide is "Probably not a Hammett base". They also discuss the methods available for the determination of p*K* values, and prefer that of Davis and Geissman[18] which has been used extensively by Stewart *et al.*[7,9,12,13]. In our experience however, it is far preferable to plot directly against H_0 the absorption at a suitable wavelength (generally the wavelength maximum of the cation or the neutral molecule): the curves obtained are smoother and it is easier to estimate the absorption of the cation and neutral molecule (cf. detailed discussion in ref. 19).

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