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THE APPLICABILITY OF HAMMETT ACIDITY FUNCTIONS TO SUBSTITUTED PYRIDINES AND PYRIDINE 1-OXIDES

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Abstract—The compounds named in the title have been investigated to determine whether the H_0 value of their solutions in strong sulphuric acid gives the amount of free base present using the H_0 function equation. Innovations in the experimental procedure afford greater accuracy than in previous similar UV spectral measurements. In general, these compounds are Hammett bases.

RECENT work[1–3] has shown that certain amides which undergo O-protonation are not Hammett bases.[4] Previous work had disclosed that the protonation of carbinols,[5] which follow the H_R function, olefins[6] (H_R'), and certain cationic bases,[7] (H^+) are also not Hammett bases. We are currently studying the kinetics of electrophilic substitution of compounds containing the pyridine and pyridine-1-oxide nuclei in strong sulphuric acid.[8,9] Such a study requires knowledge of the relative concentrations of free base and conjugate acid present at known H_0; we therefore investigated, in detail, the protonation behaviour of such compounds.

EXPERIMENTAL

The substituted pyridines were kindly supplied by Professor H. Den Hertog. Where necessary, they were recrystallized. The substituted pyridine-1-oxides were mostly made by oxidizing[10] the corresponding pyridine in peracetic acid. 4-Nitropyridine-1-oxide was prepared by the nitration of pyridine-1-oxide,[10] 3-nitropyridine-1-oxide by oxidation of the 3-aminopyridine with 30% H_2O_2 and trifluoroacetic anhydride,[11] and 2-nitropyridine-1-oxide by oxidation of 2-aminopyridine-1-oxide with 30% H_2O_2 and fuming H_2SO_4.[12] 4-Chloropyridine 1-oxide was prepared by the reaction of acetyl chloride on the 4-nitro compound.[10] M.ps are given in Tables 1 and 2.

Previously,[2] standard H_2SO_4 solutions were made by diluting AR acid to a known volume. In the

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* On study leave from West Regional Laboratories, Lahore, W. Pakistan.

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

[2] A. R. Katritzky and A. J. Waring, *J. Chem. Soc.* 1540 (1962).

[3] A. R. Katritzky, A. J. Waring and K. Yates, *Tetrahedron* **19**, 465 (1963).

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

[5] N. C. Deno, J. J. Jaruzelski and A. Schriesheim, *J. Amer. Chem. Soc.* **77**, 3044 (1955).

[6] N. C. Deno, P. T. Groves and G. Saines, *J. Amer. Chem. Soc.* **81**, 5790 (1959).

[7] J. C. D. Brand, W. C. Horning and M. B. Thornley, *J. Chem. Soc.* 1374 (1952).

[8] A. R. Katritzky and B. J. Ridgewell, *Proc. Chem. Soc.*, 114 (1962) *J. Chem. Soc.* 3753 (1963).

[9] A. R. Katritzky, B. J. Ridgewell and A. M. White, *Chem. & Ind.* 1576 (1964).

[10] E. Ochiai, *J. Org. Chem.* **18**, 534 (1953).

[11] E. C. Taylor and J. S. Driscoll, *J. Org. Chem.* **25**, 1716 (1960).

[12] E. V. Brown, *J. Amer. Chem. Soc.* **79**, 3565 (1957).

present work, two stock solutions of acid were used; one AR acid and the other AR acid diluted to about 50% w/w. Both solutions were standardized by titration of diluted aliquots against standard 0·1 N NaOH. The acids, which were stored in a dry atmosphere (P_2O_5), were mixed (or diluted with water) in appropriate proportions by wt. to give acids of known strength.

Stock solutions of substituted pyridines in dilute acid of known strength, and of the substituted pyridine-1-oxide in water, were made up, and weighed amounts, pipetted into 20 ml Grade A graduated flasks. Acids of known concentrations, prepared as detailed above, were used to make up to the mark, and the H_0 of the subsequent solution obtained by interpolation from the figures of Paul and Long[13] which over the range considered are equiv. to those of Jorgenson and Hartter.[14] For low acid concentrations (<10% w/w), pH = H_0; hence the H_0 values used were determined by pH measurement. This method of making up the solutions differs from that of Katritzky *et al.*[3] in so far as weights instead of volumes are used in the present work.

Complete spectra were recorded on a Perkin-Elmer "Ultracord" model 137 self recording spectrophotometer, and at certain wavelengths (Tables 1 and 2) on a Unicam SP 500 instrument. The appropriate solvent was used as a blank for each determination.

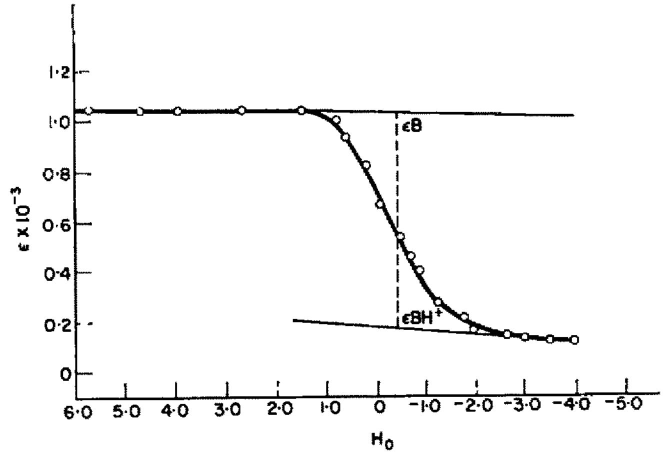

FIG. 1

RESULTS

Graphs of extinction coefficient against H_0 showed the usual sigmoid-type curve (Fig. 1). The values of n and p*Ka* in Equation (i) were obtained by plotting $\log_{10}$ ([cation]/[base]) against H_0 (Fig. 2)

$$H_0 = pKa - n \log_{10} ([\text{cation}]/[\text{base}]) \tag{i}$$

The former quantity was obtained from:

$$\frac{[\text{cation}]}{[\text{base}]} = \frac{\epsilon_B - \epsilon}{\epsilon - \epsilon_{BH^+}} \tag{ii}$$

where ϵ, ϵ_B, ϵ_{BH^+} have their usual significance. For each point on the $\log_{10}$ ([cation]/[base]) against the H_0 plot the values taken for ϵ_B and ϵ_{BH^+} in (ii) were those found from the plot of extinction coefficient against H_0 by producing the linear arms of this latter plot to the required H_0 value, i.e. the assumption made is that the medium effect on ϵ_{BH^+} and ϵ_B remains linear for the short extrapolations involved: the procedure is illustrated in Fig. 1 for one H_0 value.

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[13] M. A. Paul and F. A. Long, *Chem. Rev.* **57**, 1 (1957).

[14] M. J. Jorgenson and D. R. Hartter, *J. Amer. Chem. Soc.* **85**, 878 (1963).

The values of n and p*Ka* found are quoted in Tables 1 and 2. The errors (Tables 1 and 2) quoted were obtained from least squares plots of $\log_{10}$ ([cation]/[base]) against H_0, assuming that the plots are linear for values of $\log_{10}$ ([cation]/[base]) between $-1\cdot1$ to $+1\cdot1$. They take into account errors in the spectral determinations,[15] which are the greatest source of error of all the separate operations involved in this procedure.

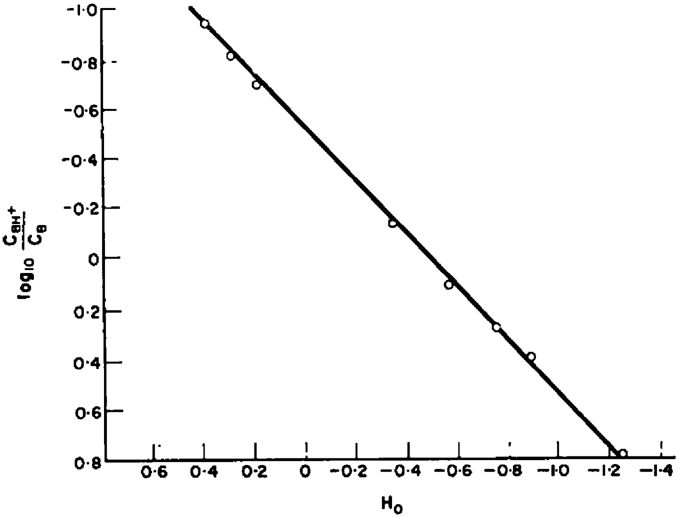

FIG. 2

Results were also calculated using the mathematical method of Katritzky *et al.*[3] This procedure is theoretically equivalent to the one quoted above, and the results agreed well with the values quoted in Tables 1 and 2, but they are not reported, as in this method the gradient of the tangent to the curve of ϵ against H_0 at the point where $[B] = [BH^+]$ has to be estimated by the eye; and no standard errors are available.

Our method becomes equivalent to the Hammett procedure[4] only when the arms of the ϵ against H_0 curve are both parallel to the H_0 axis.

DISCUSSION

All the pyridines and pyridine-1-oxides examined, with the exception of certain 2-substituted pyridine-1-oxides, give values of n close to unity, and so may be regarded as Hammett bases. As Arnett[16] points out, this assumes that the Hammett plot extrapolates to the standard state in water (pH = 7). If this criterion is not obeyed, the observed value of p*Ka* does not refer to the same standard state as that for an ideal Hammett base, and hence the correct value of [cation]/[base] cannot be calculated. Attention should be drawn to the case of benzoic acid, which follows ideal Hammett base behaviour in the observable region of indicator change, but departs sharply from it at lower acidities.[16] This is unlikely to occur for our compounds as they cover a wide range of basicities (pH 1 to H_0 $-6\cdot5$ for pyridines, and pH 0·4 to

[15] G. Svehla, A. Pall and L. Erdey, *Talanta* **10**, 719 (1963).

[16] E. M. Arnett, *Progress in Physical Organic Chemistry* (Edited by Cohen, Streitwiesser and Taft) Vol 1. Interscience (1963).

H_0 −3 for the 1-oxides), and no significant deviations from Hammett base behaviour have been observed (except the anomalous 2-substituted pyridine-1-oxides mentioned above). For any pyridine or pyridine-1-oxide base the ratio [cation]/[base] at any given H_0 value is given by Eq. (i) taking n = 1 and using the measured value of p*Ka*.

TABLE 1. SUBSTITUTED PYRIDINES

Substituent(s)	p*Ka*	n	Wavelength for determination (mμ)	m.p.	m.p. (lit)[17,18]
3,5-Dichloro	0·75 ± 0·03	0·85 ± 0·05	290	65–66	66–67
2,3-Dichloro	−0·85 ± 0·01	0·98 ± 0·03	290	66–67	66·5–67
2,6-Dichloro	−2·86 ± 0·02	1·01 ± 0·03	285	85–87	87–88
2,3,5,6-Tetrachloro	−5·50 ± 0·02	0·82 ± 0·04	317	88–89	90·5–91·5
Pentachloro	−6·02 ± 0·02	0·80 ± 0·04	320	123–124	125–126
3,4,5-Tribromo	0·45 ± 0·01	0·95 ± 0·03	297	103–105	106·5–107·5
2,3,4-Tribromo	−1·07 ± 0·02	0·87 ± 0·03	296	81–83	84–85
2,4,6-Tribromo	−3·36 ± 0·02	0·97 ± 0·03	297	105–107	107·5–108·5
2,3,6-Tribromo	−3·81 ± 0·01	1·03 ± 0·01	313	79·5–80·5	82–83
2,3,4,5-Tetrabromo	−2·47 ± 0·01	1·14 ± 0·03	313	72·5–73·5	74·5–75·5
2,3,5,6-Tetrabromo	−4·90 ± 0·02	0·93 ± 0·03	317	99–101	103·5–104
Pentabromo	−5·23 ± 0·02	0·88 ± 0·04	333	207–208	209·5–210

TABLE 2. SUBSTITUTED PYRIDINE-1-OXIDES

Substituent(s)	p*Ka*	n	Wavelength for determination (mμ)	m.p.	m.p.(lit)
4-Nitro	−1·73 ± 0·05	1·05 ± 0·10	310	158–159	159[10]
3-Nitro	−1·07 ± 0·04	1·00 ± 0·10	280	173–174	172–173[11]
2-Nitro	−2·71 ± 0·02	1·44 ± 0·06	245	86·5–87·5	85–86[12]
4-Chloro	+0·33 ± 0·02	1·10 ± 0·04	265	168–169	169·5[10]
3-Chloro	−0·13 ± 0·03	1·10 ± 0·02	260	55–56[a]	
2-Chloro	−0·77 ± 0·03	1·47 ± 0·07	255	66–67[a]	67–68[19]
4-Acetyl	−0·47 ± 0·01	1·02 ± 0·02	290	131–132	132–135[20]
2-Acetyl	−0·45 ± 0·01	1·01 ± 0·03	265	37–38[b]	
3-Bromo	−0·16 ± 0·02	1·08 ± 0·04	260	45–46[a]	42[21]
2-Cyano	−2·08 ± 0·03	1·23 ± 0·09	268	116–117	
3,5-Dibromo	−0·85 ± 0·05	1·06 ± 0·10	266	141–142	143–144[22]

[a] Deliquescent

[b] Very deliquescent, m.p. determined in an evacuated tube.

A plot (Fig. 3) of p*Ka* against the appropriate substituent constant[23] (σ^- for the 4-acetyl and 4-nitro substituent and σ for the remainder, excluding *ortho* substituents) fits approximately the straight line (ρ = 1·9) obtained by Jaffe[23] for other substituted pyridine-1-oxides. The substituted pyridines show a general trend of decreasing basicity with increasing number of halogen atoms.

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[17] H. J. den Hertog, *Rec. Trav. Chim.* **64**, 85 (1945).

[18] H. J. den Hertog, J. C. M. Schogt, J. de Bruyn, A. de Klerk, *Rec. Trav. Chim.* **69**, 673 (1950).

[19] A. R. Katritzky, *J. Chem. Soc.* 191 (1957).

[20] A. R. Katritzky, *J. Chem. Soc.* 2404 (1956).

[21] J. W. Clark-Lewis and R. P. Singh, *J. Chem. Soc.* 2379 (1962).

[22] H. J. den Hertog, C. H. Henkens and K. Dilz, *Rec. Trav. Chim.* **72**, 296 (1953).

[23] H. H. Jaffé, *J. Org. Chem.* **23**, 1790 (1958).

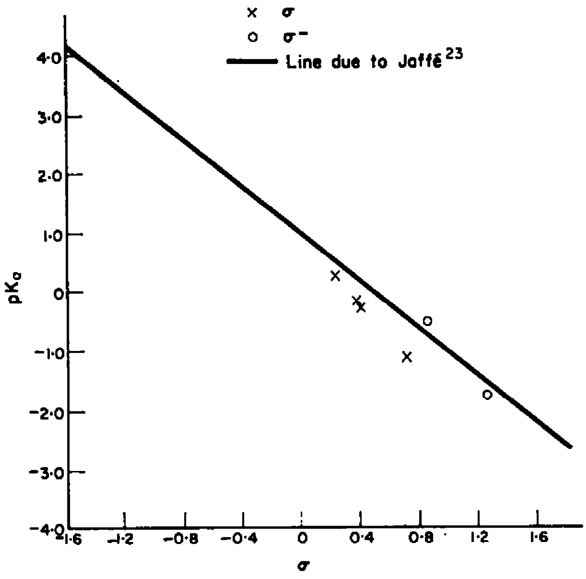

FIG. 3

Arnett and Mach[24] recently found that substituted dimethylanilines do not follow H_0 but generate an acidity function, denoted H_0''' which lies midway between H_0 and the acidity function H_R' for arylcarbonium ions. The compliance of pyridines and pyridine oxides to the H_0 function is rather surprising, and emphasizes the dangers of seemingly simple explanations of acidity function behaviour in terms of specific hydration numbers.

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[24] E. M. Arnett and G. W. Mach, *J. Amer. Chem. Soc.* **86**, 2671 (1964).