THE IONIZATION BEHAVIOR OF AMIDES IN CONCENTRATED SULPHURIC ACIDS

I. A NEW ACIDITY FUNCTION BASED ON A SET OF PRIMARY AMIDE INDICATORS

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ABSTRACT

A set of eight suitably substituted primary amides of progressively weaker basicity have been prepared. Their ionization curves have been determined in sulphuric acids by spectrophotometric methods. These show good overlap and parallelism for successive indicators, enabling the pK values of the indicators to be determined by direct stepwise comparison. Using these pK values and measured ionization ratios, values of a new acidity function, H_A , have been obtained for aqueous solutions up to 82% sulphuric acid. The H_A function decreases much less rapidly than H_0 in this range, being nearly 3 log units less negative at the highest acidity studied. The reasons for this large difference are discussed. The H_A function is shown to be applicable to other amides which have not been employed as indicators.

INTRODUCTION

The acidity function H_0 was originally conceived by Hammett and Deyrup (1) to describe the ionization behavior of weak organic bases in concentrated acid solutions. It has been assumed to be generally applicable to uncharged bases ionizing by simple proton addition, as in

$B + H^+ \rightleftharpoons BH^+$

for which $K_{BH^+} = a_B \cdot a_{H^+} / a_{BH^+}$ is the thermodynamic equilibrium constant defined in terms of molar activities. The acidity function is defined by

$$H_0 = -\log (a_{\rm H^+} \cdot f_{\rm B}/f_{\rm BH^+}) = pK_{\rm BH^+} - \log [\rm BH^+]/[\rm B].$$

The only well recognized exceptions of this charge type have been carbinol and olefin type bases which form carbonium ions on protonation. These have been found to follow the $H_{\rm R}$ (2) and $H_{\rm R}'$ (3) functions respectively.

Recently it has been recognized that the applicability of the H_0 function is considerably more limited than was at one time supposed. This question has been discussed in an excellent and comprehensive review by Arnett (4). The limited generality of the H_0 scale has been clearly demonstrated by the results of two recent investigations. Jorgenson and Hartter (5) have redetermined the H_0 scale using a set of structurally related indicators composed solely of primary anilines, unlike the original Hammett indicators, which although mainly of this type, included an N,N-disubstituted aniline as well as several oxygen type bases. Their new H_0 scale shows considerable divergence from that based on the old set of indicators (1). This demonstrates that acidity functions of the H_0 type are strongly dependent on structural changes in the indicators, even for simple bases of the same charge type. Previously (6) it has been shown that many amides are not Hammett bases, although they ionize by simple proton addition (7). This was shown by the fact that slopes of their log [BH⁺]/[B] values against H_0 were far from unity, as required by the

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defining equation, and that these deviations were too large to be explained by medium effects on the absorption spectra used to obtain ionization ratios.

Thus the results of all previous pK determinations on amides, employing the H_0 scale, do not yield thermodynamic equilibrium constants, but "pK" values in the sense described by Arnett (4). These correspond numerically to the H_0 values of the acids in which the base is half-ionized.

Therefore in general structure pK correlations for weak bases must be interpreted with caution. In addition, rate-acidity function correlations such as those of Bunnett (8), and their interpretation in terms of hydration changes (9), lose much significance in cases where it can be shown that the acidity scale used is not applicable to the type of substrate being considered.

We have therefore investigated the possibility that primary amides are following some other "general" acidity function and wish to report values of a new acidity function, H_{Λ} . This function is based on a set of structurally related primary amide indicators and appears to be generally applicable to the ionization behavior of this class of base. It is considerably different numerically to the H_0 scale even in moderately concentrated acids.

EXPERIMENTAL

Indicators

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The following commercially available indicators were recrystallized to constant melting point: 3,4,5trimethoxybenzamide from methanol-water; m.p. 178.5-179.5 °C (lit. m.p. 176-177 °C (10)); 2,4-dichloro-3,4-dinitrobenzamide from aqueous ethanol; m.p. 262-263 °C. We are unable to find a reported melting point for this compound but analysis gave C, 30.18; H, 1.01; N, 14.96; Cl, 25.59. Calculated for C₇H₃N₃Cl₂O₅: C, 30.0; H, 1.07; N, 15.0; Cl, 25.35. Samples of p-methoxybenzamide, m.p. 166–167 °C (lit. m.p. 163 °C (11)) and m-nitrobenzamide, m.p. 140-141 °C (lit. m.p. 141-143 °C (11)) were kindly supplied to us by Professor J. T. Edward of McGill University. These were also recrystallized to constant melting point before use. The remaining indicators were prepared as follows from the corresponding carboxylic acids, which are all commercially available. The acid chloride was prepared by a standard method (12) and reacted with cold aqueous ammonia to give 3,5-dinitro-4-methylbenzamide, which was recrystallized from aqueous ethanol; m.p. 189.2-190.5 °C (lit. m.p. 187 °C (13)). Calculated for C₈H₇N₃O₅: C, 42.7; H, 3.18; N, 18.7. Found: C, 42.6; H, 3.06; N, 18.6. The same method was used for 2,3,6-trichlorobenzamide. This amide has apparently not been prepared previously; m.p. 170-171 °C. Calculated for C₇H₄Cl₃NO: C, 37.4; H, 1.78; Cl, 47.5; N, 6.24. Found: C, 37.3; H, 1.45; Cl, 47.48; N, 6.09. A modified method (14, 15) was used to prepare 2,4,6-trinitrobenzamide. This was recrystallized from benzene - acetone - petroleum ether; m.p. 267.5-268.5 °C (lit. m.p. 264 °C (15)). Calculated for C₇H₄N₄O₇: C, 32.8; H, 1.56; N, 21.87. Found: C, 32.75; H, 1.50; N, 22.0. Our 2-pyrrolecarboxamide was prepared by the method of Fischer and Van Slyke (16); the product being recrystallized from water; m.p. 174.5–175.5 °C (lit. m.p. 176.5 °C (16)). Calculated for $C_{\delta}H_6N_2O$: C, 54.55; H, 5.45; N, 25.45. Found: C, 54.13; H, 5.85, N, 25.25.

Sulphuric Acids

Sulphuric acid solutions ranging from 0.001 N to 90% by weight were prepared by diluting Fischer C. P. Reagent Grade sulphuric acid (95% min.). Concentrations were determined by titrating weighed samples with standard sodium hydroxide.

Measurement of Ultraviolet Spectra

All spectra were measured on a Bausch and Lomb Spectronic 505 Recording Spectrophotometer using 1 cm quartz cells and a thermostatically controlled cell-block at 25 ± 0.05 °C. Solutions of indicators were prepared as described previously (17). It has been shown (18) that hydrolysis of the amides is negligible during the time required to measure spectra. Periodic checks of solutions of various acid concentrations confirmed this in the present work.

Treatment of Data

Since all compounds gave clearly defined absorption peaks in acid solutions strong enough to convert them essentially to their ionized forms, the wavelengths near this peak, λ_{BH}^{+max} , were used to determine ionization ratios. Absorption spectra of the free base forms obtained in water or dilute acids showed some absorption at this wavelength but the change in ϵ at λ_{BH}^{+max} on going from essentially free base to conjugate acid was in every case large. Plots of ϵ against H_0 were examined for different λ in the region of λ_{BH}^{+max} . Sigmoid type curves were obtained and that wavelength which gave the smoothest curve was chosen to calculate ionization ratios. These were obtained from the relation

$$I = [BH^+]/[B] = (\epsilon - \epsilon_B)/(\epsilon_{BH^+} - \epsilon)$$

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where $\epsilon_{\rm B}$ is the absorption at $\lambda_{\rm BH^{+}max}$ in a solution in which the base is completely un-ionized, $\epsilon_{\rm BH^{+}}$ is the corresponding value in a solution where it is essentially completely ionized and is the value in a solution of intermediate acidity. Values of ϵ_B and ϵ_{BH^+} were obtained for individual compounds as follows. The H_0 value at the inflection point of the above sigmoid curve was assumed to correspond approximately to the point of 50% ionization ([B] = [BH⁺]). Acid solutions having H_0 values 2 log units above and below this value were taken to be acids in which the base was completely unionized and fully ionized respectively, and their ϵ values taken as first approximate ϵ_B and ϵ_{BH^+} values. These were then used to obtain approximate log I values. Plots of these log I values against percent H_2SO_4 showed good parallelism and overlap for successive indicators. These were then used in the standard stepwise procedure to calculate a set of approximate pK values for the indicators and from these a first approximate set of amide acidity function values was obtained. Since this function decreased less steeply than the H_0 function, our original assumptions about the acids corresponding to ϵ_B and ϵ_{BH^+} were in error. This was particularly the case on the strongly acid side of the 50% ionization point. Next, acids of lower and higher acidities than before were chosen to obtain ϵ_B and ϵ_{BH^+} values respectively. These were chosen to correspond (on the first approximate amide acidity scale) to values ± 1.5 log units about the 50% ionization point. Thus it was hoped to minimize medium effects according to the method of Stewart and Granger (19). These new ϵ_B and ϵ_{BH^+} values were then used to obtain a further set of log I values and the whole calculation of pK and amide acidity function values repeated. It was again necessary to make small corrections in the acid concentrations used to obtain $\epsilon_{\rm B}$ and $\epsilon_{\rm BH}$. These were very small in the less concentrated acids used to obtain $\epsilon_{\rm B}$. The whole procedure was reiterated until no further significant changes in the acidity function or pK values were produced and the acids used to obtain ϵ_B and ϵ_{BH^+} were at least 1.5 log units either side of the pK value. By using the method of Stewart and Granger (19) to select the 0% and 100% ionization acids, errors of about 3% in $\epsilon_{\rm B}$ and $\epsilon_{\rm BH^+}$ can be introduced by the arbitrary choice of ± 1.5 log units, if there are no spectral shifts produced by the solvent. However, since the arms of the sigmoid curve are in fact sloping because of spectral shifts, it is felt that introducing a possible error of known magnitude is far less serious than choosing extremely strong acids to obtain ϵ_{BH^+} and thereby introducing errors of unknown magnitude.

Plots of the final log I values against the final acidity function values give straight lines of unit slope. All the individual values of the amide acidity function lie closely on a smooth curve when plotted against acid concentration.

RESULTS AND DISCUSSION

Selection of Indicators and Measurement of Ionization Ratios

Guided by the same general criteria as Jorgenson and Hartter (5), we have prepared a set of structurally related primary amides of progressively weaker base strength. These are principally benzamides substituted in various positions of the benzene ring with methoxy, methyl, halogen, and nitro groups, chosen so that their measurable ionization ranges overlap as much as possible for successive indicators. The overall range of measurable ionization behavior for this set extends from 5-82% aqueous sulphuric acid. Individual indicators were chosen on the following basis. The slopes of plots of log I versus the H_0 function were obtained for 22 primary amides, using previously reported data (6, 17) as well as data obtained in the present study. Except for two widely deviating points (o-toluamide and p-nitrobenzamide) the values of these slopes fall in the range 0.49-0.78. (Redetermination of the slope (0.62) for *m*-toluamide showed that the previously reported (6) value of 1.00 is incorrect.) These values are not randomly scattered within this range but show a general trend, depending on the acidity region in which the amide undergoes extensive ionization. The most strongly basic amides studied have log I versus H_0 slopes of approximately 0.7-0.8, decreasing to slopes of 0.5-0.6 for the most weakly basic. It was this general trend of deviation from H_0 type behavior which suggested the possibility that an amide acidity function could be constructed. Eight amides were then chosen which had the most representative slopes and which gave the best overlap and parallelism of indicator ratio curves spanning the above acidity range.

Ionization ratios $(I = [BH^+]/[B])$ for all indicators were determined by spectrophotometric methods. The amides used have strong absorption maxima in the 215–260 m μ region. On protonation the spectra undergo changes in both λ_{max} and intensity as shown in Table I. In some cases both the neutral molecule and the cation give well-defined peaks

Absor	TA ssorption maxima ar	BLE I Id p <i>K</i> value	s of indicato	ø			
Indicator $\lambda_{\rm B^{mux}}$ log $\epsilon_{\rm B^{mux}}$	$% H_{2}SO_{4}*$ (w/w)	†xnm+H8Λ	log €BH+ ^{max}	$\%_{(w/w)}^{\rm H_2SO_4\ddagger}$	pK (average)	Mean deviation	8u
2-Pyrrolecarboxamide 263 2.92 4-Methoxybenzamide 253 3.21 3,4,5-Trimethoxy- 257 3.41 3.Nitro- 257 3.41 3.5-Dinitro-4-methyl- 215 3.97 23,6-Trichloro- 217 4.21 2,3,6-Trichloro- 233 sh 3.00 2,4.Dichloro- 223 sh 3.00 2,4.Dichloro- 224 dinitro- 236 sh 4.06	24.0 24.0 24.0 27.5 27.0 27.5 27.5 27.5 27.5 27.5 27.0 27.5 27.5 27.5 27.5 27.5 27.5 27.5 27.5	235	4 4 222 2 4 4 232 2 4 4 233 2 4 4 233 2 4 4 5 6 4 2 2 6 6 4 2 2 6 6 4 2 2 6 6 6 7 6 7 6 7 6 7 7 7 6 7 7 7 7 7 7 7	55.6 58.7 751.8 81.5 88.1 88.1	-1.23 -1.42 -2.42 -2.42 -3.30 -2.42 -2.4	日本 1000 11日 11日 11日 11日 11日 11日 11日 11日 11	۵ م م م رو 10 ه ه م رو 10 ه ه م رو

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which are separated by $25-30 \text{ m}\mu$. In other cases this separation is less, notably for the nitro derivatives, and in two cases the absorption of the free base appears as a shoulder on the side of a more intense band occurring below 200 m μ . However, in more strongly acid solutions where protonation has occurred, all compounds give well-defined absorption maxima. In cases where the absorption maxima of the free base ($\lambda_{\rm B}$) and of the conjugate acid (λ_{BH^+}) are well defined and separated, the method of Davis and Geissman (20) has been most frequently employed to obtain log I values. This involves using data obtained at both wavelengths. Since this was not in general the case in the present work, it was decided for uniformity to use data obtained at one wavelength only, namely λ_{BH^+} , to calculate I values. This method gives reliable ionization ratios if there is a large change in intensity at this wavelength in going from the neutral base to the conjugate acid. This was the case with every compound studied. The values obtained give smooth sigmoid curves when plotted against acid concentration. Varying the choice of λ_{BH^+} by 5 m μ resulted in only small changes $(\pm 1\%)$ in the log I values obtained. As a check, the method of Davis and Geissman was used where possible. The ionization curves obtained by each method were identical within the experimental error. In one case only, that of 2,4,6-trinitrobenzamide, the position of the absorption maximum does not shift appreciably with increasing acidity. However, as the acidity is increased, the spectrum undergoes a large increase in intensity and a plot of intensity against acidity does give a titration-type curve. This is considered to be the least reliable of the indicators used. Fortunately it is the weakest indicator base in the set and has therefore not been used to determine any further pK values. Nonetheless its ionization behavior does parallel that of the preceding indicators, and the base strength determined for it on the basis of the I values is in good agreement with what would be predicted from substituent effects, as will be shown in the second part of this series of papers.

The ionization ratios for these amides in various acid concentrations are listed in Table II. The values for each indicator give smooth curves when plotted against percent acid as shown in Fig. 1, with the expected progressive steepening of slopes at higher acidities. These curves are almost linear, although linearity is not necessarily to be expected when log I is plotted against this concentration scale, as is customary (5). The parallelism between overlapping indicator curves is good and shows that Hammett's activity coefficient postulate (4) is valid for this set of structurally related indicators. This means that

$$\log \left(f_{\mathrm{A}_{i}\mathrm{H}^{+}} f_{\mathrm{A}_{j}} / f_{\mathrm{A}_{i}} \cdot f_{\mathrm{A}_{j}\mathrm{H}^{+}} \right) = 0$$

for two amide indicators A_i , A_j in any given solution where their log I values are both measurable. Thus the activity coefficient behavior of this set of amides is reasonably independent of changes in structure. The relationship

$$pK_{A_{i}H^{+}} - pK_{A_{j}H^{+}} = \log [A_{i}H^{+}]/[A_{i}] - \log [A_{j}H^{+}]/[A_{j}] - \log (f_{A_{i}}f_{A_{j}H^{+}}/f_{A_{i}H^{+}}f_{A_{j}})$$

which holds for any two indicators, can therefore be reduced to

1]
$$pK_{A_iH^+} - pK_{A_jH^+} = \log [A_iH^+]/[A_i] - \log [A_jH^+]/[A_j]$$

for use in solutions where the ionization ratios of each are measurable. Hence the pK_{AH^+} value of any of these amides can be determined by direct stepwise comparison providing the pK_{AH^+} value of the preceding indicator is known.

Consideration of Medium Effects on Indicator Curves

The values of ϵ^{\max} and λ^{\max} are both affected by changes in the medium, independently

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% H ₂ SO ₄	$Log I^{\dagger}$	% H ₂ SO ₄	Log I†		
2 Purreless rhove mide		h Mathawahaaa	<i>p</i> -Methoxybenzamide		
2-1 ynoiecarboxannue	1 925	p-intethoxybenza			
4.90	-1.255	10.0	-0.954		
10.09	-0.824	14.0	-0.080		
10.05	-0.400	20.35	-0.455		
20.35	-0.239	23.6	-0.273		
23.87	-0.044	28.8	-0.029		
28.58	+0.225	33.3	+0.191		
34.57	+0.514	33.9	+0.238		
38.95	+0.750	38.3	+0.472		
41.05	+0.898	$\ 39.4$	+0.507		
3.4.5 Trimethowybong	mide	44.6	+0.788		
16 07	0 002	46.2	+0.966		
10.07	-0.995	49.6	+1.072		
20.00	-0.702	NT: 1			
28.08	-0.401	<i>m</i> -Nitrobenzani	de 1 000		
34.07	-0.117	28.58	-1.000		
38.92	+0.103	34.57	-0.697		
41.05	+0.215	38.92	-0.491		
43.20	+0.316	41.05	-0.402		
45.28	+0.469	43.20	-0.287		
49.04	+0.682	45.28	-0.197		
51.69	+0.860	49.04	+0.011		
3.5-Dinitro-4-methylb	enzamide	51.69	+0.148		
34 46	-0.913	55.11	+0.346		
38.80	-0.748	57.5	+0.488		
43.07	-0.575	61.53	+0.800		
48.91	-0.277	9.2.6 Trichlorgh	ana mida		
51 55	0.154	40.04	0.047		
55 09	-0.104	49.04 51.00	-0.947		
55.02	+0.007	51.09	-0.818		
07.0 61.90	+0.200	00.11	-0.500		
01.32	+0.520	07.0	-0.350		
04.10	+0.724	01.53	-0.109		
68.82	+0.983	64.2	+0.051		
2.4-Dichloro-3.5-dinitr	obenzamide	66.48	+0.203		
55.59	-0.857	69.98	+0.449		
58 3	-0.658	73.27	+0.715		
61 53	-0.547	2.4.6-Tuinitrobe	nzamide		
64 21	-0.369	61 53	-1 004		
66 48	-0.235	64 21	-0.749		
60.08	± 0.015	66 49	-0.612		
73.97	± 0.201	60.03	-0.381		
76.11		72 97	-0.001		
77 89	10.501		-0.077		
70.50	+0.001	77 89	+0.195 +0.977		
79.09 01.09	+0.004		+0.277		
81.82	+0.940	(9.59	+0.502		
		1 81.82	+0.713		

TABLE II Ionization ratios* of amide indicators

*Values used to calculate pK and H_A values. †Determined at λ_{BH} +^{max} given in Table I.

of the changes produced by protonation. These medium effects are of uncertain magnitude and extremely difficult to correct for adequately. Since these could substantially affect the slopes of ionization curves on which acidity functions are based, several methods of attempting to correct for these effects have been considered. Apart from the previously mentioned method of Davis and Geissman (20), which leads to a partial cancellation of medium effects on ϵ values, there are two other methods available. One is the well-known isobestic point method, which has been used by Hammett (21), and involves shifting absorption curves laterally until they all intersect at a common point, as they theoretically should in the absence of medium effects. Ionization ratios are then calculated from ϵ values based on these shifted curves. A second method has been described previously (6) VATES ET AL.: IONIZATION BEHAVIOR OF AMIDES. I



FIG. 1. Ionization curves for amide indicators in concentrated sulphuric acids (for indicator numbers see Table III).

and involves the assumption that medium effects are approximately linearly dependent on acidity. Corrected ϵ values are then obtained by an extrapolation procedure. Edward and Meacock (22) have reported substantial medium effects on the spectra of *p*-methoxy-benzamide. We have analyzed our data for this compound by four different methods, using absorption spectra measured in 14 different solutions in the range 0–58% sulphuric acid. The log *I* values obtained have been treated by the method of least squares. The results are shown below.

Method	Slo	pe vs. H_0	"pK"	Slope vs. H	$_{\Lambda}$ p $K_{\rm BH^+}$	Ref.
Davis and Geissman Isobestic point Linear extrapolation Present method	Average	0.67 0.77 0.75 0.70 0.72	$-1.79 \\ -1.77 \\ -1.68 \\ -1.71 \\ -1.74$	$ \begin{array}{r} 0.99 \\ 1.08 \\ \\ 1.00 \\ 1.02 \end{array} $	$-1.50 \\ -1.47 \\ -1.44 \\ -1.47$	(20) (21) (6)

Although there are some large differences in individual log I values, there is reasonable agreement between the slopes and intercepts of the ionization curves obtained by the different methods. Since the differences which result are not large none of these correction methods was applied to the data used to obtain ionization curves in the present study. All of these correction methods are at best inadequate for the following reasons. The Davis and Geissman method only gives good linear plots if $\lambda_{\rm B}^{\rm max}$ and $\lambda_{\rm BH}^{\rm +max}$ are well separated. This was not the case with several of the amides studied. The isobestic point method involves arbitrariness in deciding how to shift experimental absorption curves to produce an approximate isobestic point. Different isobestic points can be chosen, giving different indicator ratios. Further, the procedure is laborious and does not give good linear log I plots. Application of the linear extrapolation method requires knowledge of an acidity scale which itself is not subject to medium effects.

Since medium effects can not be eliminated satisfactorily it was decided to limit their seriousness by using the approach of Stewart and Granger (19) as described previously. It can easily be shown that if medium effects result in errors in individual ϵ values as large as 10%, fortuitous cancellation will result in errors of only about 2–3% in the slopes of indicator curves obtained using the method described in this paper. In addition most

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of the spectral measurements were carried out in only moderately concentrated acids where medium effects are less serious than in the concentrated range (1).

Selection of Primary Indicator

In order to carry out the standard stepwise method of determining pK values, it is necessary to choose a primary indicator base whose ionization behavior can be studied in dilute aqueous solution, where

$$pH = pK_{HIn^+} - \log [HIn^+]/[In]$$

and the activity coefficients of all species involved can be taken to be approximately unity. In this way potentiometric determination of pH and the observable indicator ratio will yield a respectable thermodynamic equilibrium constant. All pK values determined from this by direct comparison will also be thermodynamic equilibrium constants, referred back to ideal dilute aqueous solution as standard state, as will be any acidity function based on these values.

In the present work we are studying ionization equilibria of primary amides. Therefore it is evident that the primary indicator should if possible be an amide. The difficulty is



that amides as a class are considerably weaker bases than amines and it has so far proved impossible to find a primary amide which is strong enough to be measurably ionized in dilute aqueous solution. The strongest bases in this class that we have been able to find are acetamide, propionamide, 2-pyrrolecarboxamide, p-anisamide, and 2-hydroxyphenylurea, in order of decreasing basicity. None of these is measurably ionized in the region accessible to accurate measurements with the glass electrode. While it is true that the introduction of electron-donating substituents would produce stronger bases, it is unlikely that any of the derivatives would be appreciably ionized in dilute aqueous solution either. It is known that the ionization of amides is not very sensitive to substituent effects, particularly resonance effects (23). For example, p-methoxy substitution only changes the half ionization point of benzamide from 36% to 29% sulphuric acid. It is unlikely that even 2,4,6-trimethoxybenzamide would be sufficiently strong to ionize in the pH range. This is illustrated by considering that in the acid dissociation of benzoic acids, which has a similar ρ value to the basic ionization of amides (24), 2,4,6-trimethoxybenzoic acid has a pK_{ρ} only 0.63 log units different from that of benzoic acid itself (25).

We have therefore selected as primary indicator p-nitroaniline, which was used to establish the H_0 scale. In this case we have assumed that the variation of f_{AH^+}/f_A for amide type bases will be very similar to the variation of f_{BH^+}/f_B for the aniline type, over a limited region of acidity extending from 0-2 M sulphuric acid. This assumption is not strictly valid (6), but since the acidity region considered is narrow, it is reasonable that $f_{BH^+}f_A/f_{AH^+}f_B$ will not differ significantly from unity in this range. As a secondary indicator we have selected 2-pyrrolecarboxamide, for the following reasons. It is stable enough in dilute acids and its absorption characteristics are such that consistent and reliable log Ivalues can be obtained. Its measurable ionization range overlaps considerably those of p-nitro- and o-nitro-aniline, as well as those of two of the more strongly basic amides, so that it can be used to bridge the pK gap between dilute solution and those acids where the Can. J. Chem. Downloaded from www.nrcresearchpress.com by George Mason University on 04/21/13 For personal use only.

benzamides are appreciably ionized. The nuclear magnetic resonance (n.m.r.) spectrum of this compound in fluorosulphuric acid at low temperatures shows that it protonates on the carbonyl oxygen like the other amides studied (26).

The log I versus concentration curve for 2-pyrrolecarboxamide is reasonably parallel with those of the two nitroanilines as shown in Fig. 2. Thus the above assumption about



FIG. 2. Ionization curves for (1) p-nitroaniline, (2) o-nitroaniline, (3) 2-pyrrolecarboxamide in dilute sulphuric acid region.

activity coefficient behavior appears to be valid. Its curve is also closely parallel with those of p-methoxy and 3,4,5-trimethoxybenzamide as shown in Fig. 1. We have used the available data for p-nitro- and o-nitro-aniline (27) as well as our own data to establish the pK value for this secondary indicator using Equation [1]. The results are shown in Table I, the average pK value for 2-pyrrolecarboxamide calculated from a large number of measurements in several different acids. The agreement between the values is quite good, giving an average value of -1.23 ± 0.04 for the pK of this indicator. This value has been adopted as a standard for the determination of pK for the remaining amide indicators. It should be noted that any uncertainty introduced by the above treatment as to the absolute value of this pK will be carried through to any pK's or acidity function values determined from it.

Determination of pK Values of Indicators

The pK values of the other seven primary amides have been obtained by direct stepwise comparison using Equation [1] and the above pK of 2-pyrrolecarboxamide as a starting point. We have calculated successive pK values from ionization ratios for each overlapping pair of indicators, taking data directly from the experimental points where possible. In a few cases interpolations have been made from the best smooth curves through the experimental points. Only log I values in the range ± 1.0 (corresponding to 10–90% protonation) were used, since the experimental uncertainty increases rapidly as the ionization ratio takes on very high or very low values. The individual values for a given indicator, obtained in each case from data in several different acids, show good agreement. These have been averaged and are given in Table I. The eight compounds listed constitute a structurally uniform set of amide indicators, suitable for obtaining acidity values for solutions up to 80% sulphuric acid. The H_A Acidity Scale in Sulphuric Acid

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We can now define a function, H_A , in an analogous manner to other acidity functions, such that

$$H_{\rm A} = -\log (a_{\rm H^+}f_{\rm A}/f_{\rm AH^+}) = pK_{\rm AH^+} - \log [\rm AH^+]/[\rm A]$$

where pK_{AH^+} is the thermodynamic dissociation constant for an amide conjugate acid. Values of this function have been determined from the pK values and indicator ratios previously described. The individual $H_{\rm A}$ values for a given acid concentration were obtained using all indicators which were measurably protonated in that acid, again taking only log I values in the range ± 1.0 . These H_{Λ} values are listed in Table III, along

		TABLE	III	
Values of	H_{Λ}	in sulphu	ric acid	solutions

% H ₂ SO ₄ (w/w)	$-H_{\rm A}$ (average)	Mean deviation*	Indicators used†
$16.1\ddagger20.4$	$\begin{array}{c} 0.78 \\ 0.99 \end{array}$	± 0.02	1, 2, 3
$23.9 \\ 28.6 \\ 24.6$	$1.18 \\ 1.43 \\ 1.52$	± 0.01	3, 4, 5
$ 34.6 \\ 38.9 \\ 41.1 $	$1.72 \\ 1.95 \\ 2.03$	$\pm 0.02 \\ \pm 0.03 \\ \pm 0.01$	$\begin{array}{c} 3, 4, 5 \\ 4, 5, 6 \\ 4 5 6 \end{array}$
$43.2 \\ 45.3$	$\begin{array}{c} 2.00\\ 2.14\\ 2.26\end{array}$	$\pm 0.001 \\ \pm 0.005 \\ \pm 0.02$	4, 5, 6 4, 5, 6 4, 5, 6
$49.0 \\ 51.7 \\ 55.1$	$2.47 \\ 2.57 \\ 2.79$	± 0.04	5, 6 6 6 7
57.5 61.5	$2.78 \\ 2.92 \\ 3.20$	± 0.003 0 ± 0.01	6, 7 6, 7 6, 7, 8
$\begin{array}{c} 64.2\\ 66.5\end{array}$	$\begin{array}{c} 3.32\\ 3.50\end{array}$	$\pm 0.05 \pm 0.01$	7, 8, 9 7, 8, 9 7, 8, 9
$70.0 \\ 73.3 \\ 76.1$	$3.74 \\ 4.02 \\ 4.95$	± 0.005 ± 0.005 ± 0.02	7, 8, 9 8, 9 9 10
77.8 79.6	$4.25 \\ 4.35 \\ 4.58$	± 0.02 ± 0.04	9, 10 9, 10 10
81.8	4.79	—	10

*Mean deviation between H_A values obtained using different *Mean deviation between H_A values obtained using different indicators. ${}^{+}H_A$ determined from the following indicators: 1, p-nitroaniline; 2, o-nitroaniline; 3, 2-pyrrolecarboxamide; 4, p-methoxybenzamide; 5, 34,5-trimethoxybenzamide; 6, m-nitrobenzamide; 7, 3,5-dinitro-4-methylbenzamide; 10, 2,4,6-trichlorobenzamide, ${}^{+}H_A$ values for acids more dilute than this are assumed to be the same as the H_0 values of Bascombe and Bell (27).

with the particular indicators used for a given acid. Where more than one indicator was used, the H_{Λ} values were averaged. The agreement between the values obtained using different indicators is good. All values of $H_{\rm A}$ fall on a smooth curve when plotted against percent sulphuric acid. This curve is shown in Fig. 3 with the H_0 scale in the same acid range for comparison.

The difference between the two acidity functions is striking, even at moderate acid concentrations. For example, H_{Λ} is nearly 1 log unit less negative than H_0 even in 50% sulphuric acid, this difference becoming more than 3 log units at the highest acidities studied in the present work. This means that aqueous sulphuric acid can be up to 1000 times less effective in converting a primary amide to its conjugate acid than it is in the corresponding protonation of a primary amine of similar pK value. Thus the protonation behavior of the two types of base, although formally very similar, is considerably different

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quantitatively. This again stresses the fact that acidity functions can be strongly dependent on indicator structure. The actual shape of the H_A curve is roughly similar to that for H_0 but is considerably less steep outside the dilute acid range and is approximately linear in the 10-60% acid region.

Comparison of the H_A and H_0 Functions

The reasons for the large observed differences in the ability of aqueous sulphuric acid to protonate primary amides as against primary amines are not immediately obvious. It is well recognized that the hydration requirements of the indicator species are important factors in determining the rate of rise of indicator acidity. This is especially true of the cations, rather than the neutral bases, as evidenced by the much more rapid rise of $h_{\rm R}$ with increasing acid concentration than that of h_0 , carbonium ions being much less strongly hydrogen bonded to solvent molecules than anilinium ions. Just how this factor operates in the present case is not clear. If the two types of equilibria are written in terms of fully hydrated species, for the amides we have

$$AH^+(H_2O)_m + (a + p - m)H_2O \rightleftharpoons A(H_2O)_a + H^+(H_2O)_p$$

and for the anilines

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$$BH^+(H_2O)_n + (b + p - n)H_2O \rightleftharpoons B(H_2O)_b + H^+(H_2O)_n$$

We can now define the nonlogarithmic acidity functions in terms of fully hydrated species as

$$h_{A} = (a_{H^{+}(H_{2}O)_{p}} \cdot f_{A(H_{2}O)_{a}} / f_{AH^{+}(H_{2}O)_{m}} \cdot a_{H_{2}O}^{(a+p-m)})$$

$$h_{0} = (a_{H^{+}(H_{2}O)_{p}} \cdot f_{B(H_{2}O)_{b}} / f_{BH^{+}(H_{2}O)_{n}} \cdot a_{H_{2}O}^{(b+p-n)})$$

The difference between the two functions can be expressed as the ratio

[2] $h_{\rm A}/h_0 = (f_{\rm BH^+h}.f_{\rm Ah}/f_{\rm Bh}.f_{\rm AH^+h})^{a_{\rm H_2}O^{(m-a)-(n-b)}}$

where the subscripts h refer to hydrated species. The less rapid increase of $h_{\rm A}$ with acidity

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can be attributed to the hydration requirements of the amides in several ways. If the change in hydration on going from a neutral amide to a more strongly hydrated cation is greater than the corresponding hydration change on protonating an aniline, then [(m - a) - (n - b)] will be positive. Hence, as the acid concentration is increased, and the water activity is decreased, h_A/h_0 will decrease, as is observed. If an amide conjugate acid is more strongly hydrated than the corresponding anilinium ion, f_{AH^+} will increase more rapidly with increasing acid than f_{BH^+} . Similarly, if a neutral amide is less strongly hydrated than the corresponding anilinium ion, m_{AH^+} will increase factors will contribute to a less rapid rise of h_A with acid concentration, when compared with h_0 . Any or all of these factors may undergo significant variation with changes in the medium but their relative importance is difficult to predict. Assuming for the moment that the separation of terms in Equation [2] is valid, and that the net variation of the activity coefficient term is less important than that of the term in the water activity, we can write approximately

$$H_0 - H_\Lambda = [(m - a) - (n - b)] \log a_{H_0 O} + \text{constant.}$$

Plotting $(H_0 - H_A)$ against log $a_{\text{Ho}0}$ should then give a curve whose slope at any point can be related to the net hydration changes involved in the two types of equilibria. We have plotted $(H_0 - H_A)$ against available water activity data (28). The relationship is not linear, which is as expected, since even if the above assumptions are valid, the individual hydration numbers can take on different values in different regions of acidity, depending on the amount of "free" water available. The plot shows a steadily decreasing curvature as $\log a_{H_2O}$ is decreased. It is approximately linear over two wide regions, giving a slope of about 1.7 in the 30-60% acid range and about 0.75 in 70-85% range. This suggests that the net increase in hydration on protonation of an amide involves one or two more water molecules than the corresponding increase on protonation of an aniline. Taft (29) has suggested that a hydration number of 3 for an anilinium ion is reasonable in view of the fact that such an ion can hydrogen bond strongly to three water molecules through its acidic protons. However, considering only the numbers of such protons available for hydrogen bonding in the various indicator species, it is difficult to see how [(m-a) - (n-b)] can differ very much from zero. One way around this difficulty is to postulate the following structure for the hydrated amide cation so that its hydration



number can be 5 in solutions where there is sufficient water available. In support of this it is known that [O-H...O] bonds are on the average considerably stronger than the [N-H...O] type (30). Further, aldehydes (31) and ketones (32) whose conjugate acids have only one acidic proton, follow the H_0 function reasonably well. This suggests strongly that a protonated carbonyl group is hydrated by more than one water molecule.

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This simple explanation of the difference between H_{Λ} and H_0 obviously leaves much to be desired except in a qualitative sense, since we have neglected possible variations in the log $(f_{\rm BH^+h}.f_{\Lambda h}/f_{\rm Bh}.f_{\Lambda H^+h})$ term of Equation [2]. However, this term would also have to decrease as the water activity is decreased, to account for the observed differences in h_{Λ} and h_0 , and would require similar kinds of hydration changes on protonation of amides and anilines, i.e. that (m - a) > (n - b).

A knowledge of the activity coefficients of amides and their conjugate acids is clearly desirable in order to be able to assess the importance of the various terms in Equation [2]. We are at present investigating the activity coefficient behavior of some typical amides and their salts. We hope by comparing these results with Boyd's values for typical aniline indicators (33) to be able to assess more quantitatively the importance of the various factors involved.

The Applicability of the H_A Scale

It is evident that the H_A function, like any other acidity function, will be of limited generality. It is, however, important that it be applicable at least to primary amides as a class, in order that it may be used to obtain thermodynamic pK's for other amides and also be useful in studying reaction mechanisms. We have therefore tested the generality of H_A in the following way. Using available experimental data we have plotted log *I* values against H_A for 12 primary amides not used as indicators in the present work. Ten of these gave least mean squares slopes between 0.95 and 1.05 which can be considered as being effectively unity as required by the defining equation for H_A . The mean value and deviation for all 12 was 0.97 ± 0.06 . Thus within the experimental uncertainty caused by medium shifts on the spectra towards the red, which would result in slopes of less than unity, these amides appear to be following H_A reasonably well. It would be interesting to test the generality of the H_0 function in a similar way using representative anilines. This has apparently not been done.

The behavior of the individual amides and the significance of derived pK values will be discussed in detail in Part II of this series.

Estimated Accuracy of the H_A Values

It is impossible to estimate precisely the numerical accuracy of any particular H_A value, since individual errors in determined pK values may be cumulative. Also, as mentioned previously, any uncertainty in the pK of the secondary standard base will be carried through to all subsequently determined pK's, and hence to any H_A values determined from them. The usual estimate of the experimental uncertainty in any pK value obtained by the standard spectrophotometric technique is $\pm 0.05 \log$ unit. Therefore the H_A values should not be considered as known to any better than ± 0.1 units in the lower acidity range and probably ± 0.2 units in the more concentrated region above 60% acid. Nonetheless the following considerations give confidence in the reliability of the values within these limits. The parallelism of the indicator curves is good. These curves are closely spaced enough so that considerable overlap has been achieved. Hence not too much weight has been placed on any one indicator. The several H_A values obtained for any given solution are consistent and all experimental points fall closely on a smooth curve when plotted against concentration.

ACKNOWLEDGMENTS

The financial assistance of the National Research Council of Canada is gratefully acknowledged. We are also grateful for the award of a Province of Ontario Graduate Fellowship to one of us (J. B. S.).

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