The Ionization of Feeble Organic Acids in DMSO–Water Mixtures. Acidity Constants Derived by Extrapolation to the Aqueous State

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Abstract: Using ionization ratio measurements in DMSO–water mixtures containing small fixed amounts of base, the acidity constants of a large number of weak organic acids have been calculated using two extrapolative procedures, both of which involve the use of activity coefficient ratios (log $(f_{A^-}/f_{AH}f_{OH^-})$). The first is based on the Bunnett-Olsen method, developed for acid solutions, and uses a single acidity function; the other is a modified version of the Marziano-Cimino-Passerini method, which was also first used for strong acids. The latter method uses overlapping indicators but does not involve an acidity function. For those compounds whose ionization is closely governed by an acidity function the resulting pK_a's (standard state water) are substantially unchanged from values obtained using the acidity function method. Appreciable differences result for other compounds, however. The different H_- functions available in this medium are examined and discussed in terms of the concept of "excess basicity", the increase in basicity relative to the standard state due to the various species' activity coefficients deviating from unity. Some comments regarding the value of the acidity function concept are also made.

Hitherto inaccessible regions of organic chemistry were opened up for study by Hammett's introduction of the acidity function concept.[1] This technique consists of stepwise and complementary measurements of solution acidity, H_0, and solute basicity, pK_{BH^+}, using eq 1 and starting with

$$H_0 = pK_{BH^+} + \log C_B/C_{BH^+} \qquad (1)$$

$$H_0 = -\log a_{H^+}f_B/f_{BH^+} \qquad (2)$$

known quantities firmly anchored in water as the standard state. The measurements are then extended to more and more feeble solute bases and more and more powerfully acidic solutions.[2] (Throughout this work C represents concentration, a activity (water as standard state), and f activity coefficient, all in *molarity* units.)

The hope that a single acidity function would suffice for different kinds of organic bases, amines, ketones, amides, etc., faded as their ionization behavior was more closely scrutinized.[3] So-called "acidity function failure"[4] is the failure of the activity coefficient ratio in eq 2 to be independent of the structure of the base. Unfortunately, using this term may suggest that the acidity function *concept* has failed. It has done so only to the extent that a single function cannot describe the protonating power of concentrated acid solution toward all bases. It does not invalidate pK_{BH^+} values obtained for a series of compounds whose ionization behavior is sufficiently alike that the activity coefficient ratio is a function only of the medium.[5] By careful checks on the constancy of the term Δ log I (log C_B/C_{BH^+} − log $C_{B'}/C_{B'H^+}$) for the two overlapping indicators B and B′ (the essence of the method) reliable values can often be obtained for the pK_{BH^+} of feeble organic bases. How else, for example, can information be obtained that allows meaningful estimates to be made of the extent of protonation of, say, a ketone or an aldehyde in water at pH 7?[6]

The existence of a multitude of acidity functions for a given acid system does not, in itself, detract from the reliability of the pK values that are obtained, *provided a series of compounds with near-perfect overlap between adjacent indicator bases has been used.* Of course, perfect overlap in the accessible region of measurement does not guarantee that standard state pK values are obtained. It is conceivable that compounds whose ionization ratio plots are perfectly parallel in solutions in which both are measurably ionized diverge in less acidic media. Though such divergence, if substantial, would lead to significant errors in pK[3a] there is no reason to suppose that this is a serious source of error when structurally related compounds are used.[5]

An analogous situation exists in measuring the acidity of feeble acids in powerfully basic media. Most work in this region has been done using a fixed concentration of hydroxide ion and variable amounts of a polar aprotic solvent such as dimethyl sulfoxide (DMSO),[7-11] starting again with pure water as the standard state. Certain aromatic amines have been used to construct an H_- scale that ranges from 12.04 (0.011 M HO$^-$ in water) to over 26 (0.011 M HO$^-$ in 99.6 mol % DMSO, 0.4 mol % water).[7b] The high basicity toward aromatic amines of solutions rich in DMSO is related to the high degree of charge delocalization within the amide anion and it is not surprising that oxygen acids (carboxylic acids and phenols) whose anions have a much smaller degree of charge delocalization do not obey the H_- function constructed using aromatic amines.[7a,10] Indeed, not all aromatic amines give ionization plots that are parallel to those of their neighbors and estimates of the pK values of such compounds are more difficult to make.[7b,12]

In a recent critique of acidity functions, Kreevoy and Baughman[13] state that "the Hammett acidity function concept requires that pK_{HA} for all the acids correlated, in any one of the solvent mixtures involved, be a linear function of pK_{HA_0}, the corresponding quantity in a reference solvent (usually water) *with unit slope*". Strictly speaking, this restriction applies only to those solutions less basic than that in which the anchor compound is 90% ionized (using the usual criteria for making indicator measurements). Perfectly valid standard state pK values may be obtained even if gross deviations from linearity appear in solutions in which some or all of the compounds are highly ionized.[14] (Hallé and Schaal et al.[15] also have questioned the thermodynamic significance of the amine pK values derived during the construction of the H_- scale. Their results, based in part on electrochemical measurements, indicate an increasing spread of pK values for aromatic amines as the DMSO content increases.)

The following is a general statement of the law governing the behavior of a set of valid acidity function indicators,[16] whether they be weak bases or weak acids: the derived pK values of an overlapping Hammett set will only be identical with the standard state pK values when Δ log I for each pair of adjacent compounds is constant in all media that range in composition from that of the standard state to that in which the more basic (acidic) of the pair is 90% ionized.

Recent work in pure DMSO,[17] using both the glass electrode[17a] and indicator[17b] approaches, provides pK values for which DMSO is the standard state. The advantage of referring all acidities and basicities to DMSO is that a very wide range of acidities can be measured in this medium, since its degree of autoprotolysis is so much less than that of water.[19] The advantage of continuing to use water as the standard state, the Hammett approach, is the long familiarity that chemists have had with the system and the pK values determined therein. Furthermore, the shape of the H_- vs. solvent composition curve for aqueous DMSO shows that addition of DMSO to water containing base produces an almost linear change in the basicity of the medium toward aromatic amines from zero to about 85 mol % DMSO. Beyond this point a rapid increase in basicity is noted and the curve approaches the ordinate representing pure DMSO almost asymptotically. In other words, small amounts of water in DMSO cause drastic, and probably nonlinear, changes in the basicity of the medium, owing doubtless to the need of acid anions for hydrogen-bonding-type solvation. Thus measurements in anhydrous DMSO need to be very carefully made in order to obtain absolute pK values in this medium.

In view of the doubts expressed about the value of the acidity function approach in determining pK_{HA} values of feeble organic acids in water, we undertook an indirect study of the problem making use of two new methods of calculation based on those given for acid systems by Bunnett and Olsen[19,20] and by Marziano, Cimino, and Passerini.[21] The former makes use of an acidity function; the latter does not, although it makes use of the same experimental data. We have only recently been able to make use of these two approaches since the necessary data concerning water activity in aqueous DMSO at 25° [22] was hitherto unavailable.

For an organic acid HA we can define K_{HA}:

$$\mathrm{HA} \overset{K_{\mathrm{HA}}}{\rightleftharpoons} \mathrm{H}^+ + \mathrm{A}^-$$

$$K_{\mathrm{HA}} = a_{\mathrm{H}^+}a_{\mathrm{A}^-}/a_{\mathrm{HA}}$$

Similarly,

$$\mathrm{H_2O} \overset{K_{\mathrm{w}}}{\rightleftharpoons} \mathrm{H}^+ + \mathrm{HO}^-$$

$$K_{\mathrm{w}} = a_{\mathrm{H}^+}a_{\mathrm{HO}^-}/a_{\mathrm{H_2O}}$$

In the basic solutions under consideration here, the reaction of interest is more appropriately represented as

$$\mathrm{HA} + \mathrm{HO}^- \overset{K_{\mathrm{b}}}{\rightleftharpoons} \mathrm{A}^- + \mathrm{H_2O}$$

$$K_{\mathrm{b}} = a_{\mathrm{A}^-}a_{\mathrm{H_2O}}/a_{\mathrm{HA}}a_{\mathrm{HO}^-} \quad \text{and} \quad K_{\mathrm{HA}} = K_{\mathrm{b}}K_{\mathrm{w}}$$

Thus we can write

$$K_{\mathrm{HA}}/K_{\mathrm{w}} = (C_{\mathrm{A}^-}/C_{\mathrm{HA}})(a_{\mathrm{H_2O}}/C_{\mathrm{HO}^-})(f_{\mathrm{A}^-}/f_{\mathrm{HA}}f_{\mathrm{HO}^-})$$

Taking logarithms and rearranging gives eq 3 and 4.

$$\mathrm{p}K_{\mathrm{HA}} + \log C_{\mathrm{A}^-}/C_{\mathrm{HA}} = \mathrm{p}K_{\mathrm{w}} + \log C_{\mathrm{HO}^-} - \log a_{\mathrm{H_2O}} - \log f_{\mathrm{A}^-}/f_{\mathrm{HA}}f_{\mathrm{HO}^-} \quad (3)$$

$$\mathrm{p}K_{\mathrm{HA}} + \log C_{\mathrm{A}^-}/C_{\mathrm{HA}} = H_- \quad (4)$$

Applying the Bunnett-Olsen treatment to basic solutions is equivalent to requiring that the term log $(f_{\mathrm{A}_z^-}/f_{\mathrm{HA}_z}f_{\mathrm{HO}^-})$ for a specific acid HA_z be a linear function of the term log $(f_{\mathrm{A}^-}/f_{\mathrm{HA}}f_{\mathrm{HO}^-})$ for a set of acids HA defining an acidity function. (This is less stringent than the Hammett requirement that such terms cancel out.) If the acid HA_z was used in the construction of the scale and if the scale indicators all gave perfect overlap the functions would, of course, be linear and of unit slope; if the ionization of HA_z does not overlap perfectly with the scale indicators the deviation is represented by the term ϕ in eq 5.

$$-\log (f_{\mathrm{A}_z^-}/f_{\mathrm{HA}_z}f_{\mathrm{HO}^-}) = (\phi + 1)[-\log (f_{\mathrm{A}^-}/f_{\mathrm{HA}}f_{\mathrm{HO}^-})] \quad (5)$$

From eq 3, 4, and 5,

$$\mathrm{p}K_{\mathrm{HA}_z} + \log C_{\mathrm{A}_z^-}/C_{\mathrm{HA}_z} - \mathrm{p}K_{\mathrm{w}} - \log C_{\mathrm{HO}^-} + \log a_{\mathrm{H_2O}} = (\phi + 1)(H_- - \mathrm{p}K_{\mathrm{w}} - \log C_{\mathrm{OH}^-} + \log a_{\mathrm{H_2O}})$$

or

$$H_- - \log C_{\mathrm{A}_z^-}/C_{\mathrm{HA}_z} = -\phi(H_- - \mathrm{p}K_{\mathrm{w}} - \log C_{\mathrm{OH}^-} + \log a_{\mathrm{H_2O}}) + \mathrm{p}K_{\mathrm{HA}_z} \quad (6)$$

Plots of $(H_- - \log C_{\mathrm{A}_z^-}/C_{\mathrm{HA}_z})$ against $(H_- - \mathrm{p}K_{\mathrm{w}} - \log C_{\mathrm{OH}^-} + \log a_{\mathrm{H_2O}})$ give $-\phi$ as the slope and pK_{HA_z} as the intercept.

The Marziano–Cimino–Passerini approach, like that of Bunnett and Olsen, depends on there being a linear relationship between values of log $(f_{\mathrm{A}^-}/f_{\mathrm{HA}}f_{\mathrm{OH}^-})$ for different acids. The subsequent treatment, however, makes use of a single reference compound, rather than an acidity function.

Rewriting eq 3 gives eq 7:

$$\mathrm{p}K_{\mathrm{w}} + \log C_{\mathrm{OH}^-} - \log a_{\mathrm{H_2O}} - \log C_{\mathrm{A}^-}/C_{\mathrm{HA}} = \log (f_{\mathrm{A}^-}/f_{\mathrm{HA}}f_{\mathrm{OH}^-}) + \mathrm{p}K_{\mathrm{HA}} \quad (7)$$

For two acids HA_0 (an anchor compound of known pK)[23] and HA_1 with which it overlaps, we can write

$$\mathrm{p}K_{\mathrm{w}} + \log C_{\mathrm{OH}^-} - \log a_{\mathrm{H_2O}} - \log C_{\mathrm{A}_1^-}/C_{\mathrm{HA}_1} = m[\log (f_{\mathrm{A}_0^-}/f_{\mathrm{HA}_0}f_{\mathrm{OH}^-})] + \mathrm{p}K_{\mathrm{HA}_1} = m(\mathrm{p}K_{\mathrm{w}} + \log C_{\mathrm{OH}^-} - \log a_{\mathrm{H_2O}} - \log C_{\mathrm{A}_0^-}/C_{\mathrm{HA}_0} - \mathrm{p}K_{\mathrm{HA}_0}) + \mathrm{p}K_{\mathrm{HA}_1} \quad (8)$$

where $m = \log (f_{\mathrm{A}_1^-}/f_{\mathrm{HA}_1}f_{\mathrm{OH}^-})/\log (f_{\mathrm{A}_0^-}/f_{\mathrm{HA}_0}f_{\mathrm{OH}^-})$.

Graphs plotted according to eq 8 should be (and almost invariably are) linear, giving the value of pK_{HA_1} as the intercept and m as the slope. The process is repeated for a set of overlapping and well-behaved indicators using pK_{HA_1} and the other necessary data to calculate pK_{HA_2}, and so on up the series. Once all the values of m, pK_{HA}, and log $(f_{\mathrm{A}^-}/f_{\mathrm{HA}}f_{\mathrm{OH}^-})$ are known for each member of the set it is convenient to calculate log $(f_{\mathrm{A}_*^-}/f_{\mathrm{HA}_*}f_{\mathrm{OH}^-})$ for a reference indicator HA_* in all solvent mixtures used:

$$\log (f_{\mathrm{A}_*^-}/f_{\mathrm{HA}_*}f_{\mathrm{OH}^-}) = 1/m \log (f_{\mathrm{A}_1^-}/f_{\mathrm{HA}_1}f_{\mathrm{OH}^-}) = 1/mm' \log (f_{\mathrm{A}_2^-}/f_{\mathrm{HA}_2}f_{\mathrm{OH}^-}) = \ldots = 1/\pi m \log (f_{\mathrm{A}_n^-}/f_{\mathrm{HA}_n}f_{\mathrm{OH}^-}) \quad (9)$$

$$\mathrm{p}K_{\mathrm{w}} + \log C_{\mathrm{OH}^-} - \log a_{\mathrm{H_2O}} - \log C_{\mathrm{A}_z}/C_{\mathrm{HA}_z} = m^*[\log (f_{\mathrm{A}_*^-}/f_{\mathrm{HA}_*}f_{\mathrm{OH}^-})] + \mathrm{p}K_{\mathrm{HA}_z} \quad (10)$$

Equation 10 can then be used to estimate pK_{HA} values for *any* acid HA_z for which ionization data are available at any solvent composition.

This method does *not* involve the use of any acidity function, although it does make use of the indicator overlap principle to determine the quantity log $(f_{\mathrm{A}_*^-}/f_{\mathrm{HA}_*}f_{\mathrm{OH}^-})$ for the reference compound.

Data and Calculations

Activity coefficients of water in water–DMSO mixtures at 25° are given by Lam and Benoit;[22] they agree well with the values calculated for 25° by Cox and McTigue[24] from existing 75° data.[25] So that all the concentration units used here may be referred to a common molarity scale, the water activity was also calculated on a molarity basis, using densi-

Table I. Water Activity, H_-, and Associated Data Used in Extrapolative $\mathrm{p}K_{\mathrm{HA}}$ Calculations in Water–DMSO Mixtures at 25°

Mol % DMSO	H_-	$-\log a_{\mathrm{H_2O}}$,[a] M	$\mathrm{p}K_\mathrm{w} + \log C_{\mathrm{OH^-}} - \log a_{\mathrm{H_2O}}$		$H_- - \mathrm{p}K_\mathrm{w} - \log C_{\mathrm{OH^-}} + \log a_{\mathrm{H_2O}}$	$-\log(f_{\mathrm{A*^-}}/f_{\mathrm{HA*}}f_{\mathrm{OH^-}})$
			0.011 M	0.0471 M		
0	(12.04)[b]	0.000	12.04	12.67	0.00	0.00
2	12.21	0 033	12.07	12.70	0.14	0.19
4	12.43	0.065	12.10	12.73	0.33	0.38
6	12.64	0.098	12.14	12.77	0.51	0.57
8	12.84	0.131	12.17	12.80	0.67	0.75
10	13.04	0.164	12.20	12.83	0.84	0.93
12	13.26	0.198	12.24	12.87	1.03	1.11
14	13.49	0.234	12.27	12.90	1.22	1.29
16	13.73	0.272	12.31	12.94	1.42	1.47
18	13.98	0.310	12.35	12.98	1.63	1.65
20	14.24	0.349	12.39	13.02	1.85	1.82
22	14.48	0.389	12.43	13.06	2.05	2.00
24	14.71	0.432	12.47	13.10	2.24	2.17
26	14.92	0.476	12.51	13.14	2.41	2.34
28	15.14	0.520	12.56	13.19	2.58	2.51
30	15.37	0.563	12.60	13.23	2.77	2.67
32	15.58	0.604	12.64	13.27	2.94	2.83
34	15.80	0.644	12.68	13.31	3.12	2.99
36	16.02	0.685	12.72	13.35	3.30	3.15
38	16.22	0.729	12.77	13.40	3.45	3.31
40	16.43	0.775	12.81	13.44	3.62	3.47
42	16.63	0.821	12.86	13.49	3.77	3.62
44	16.84	0.868	12.90	13.54	3.94	3.77
46	17.04	0.913	12.95	13.58	4.09	3.92
48	17.24	0.957	12.99	13.63	4.35	4.07
50	17.44	0.999	13.04	13.67	4.40	4.22
52	17.67	1.043	13.08	13.71	4.59	4.36
54	17.88	1.088	13.13	13.76	4.76	4.51
56	18.08	1.132	13.17	13.80	4.91	4.65
58	18.29	1.176	13.21	13.85	5.08	4.79
60	18.49	1.221	13.26	13.89	5.23	4.93
62	18.69	1.266	13.30	13.94	5.39	5.07
64	18.89	1.311	13.35	13.98	5.54	5.21
66	19.09	1.356	13.39	14.03	5.70	5.35
68	19.30	1.403	13.44	14.07	5.86	5.50
70	19.51	1.450	13.49	14.12	6.02	5.65
72	19.72	1.498	13.54	14.17	6.18	5.80
74	19.93	1.548	13.59	14.22	6.34	5.94
76	20.13	1.600	13.64	14.27	6.49	6.10
78	20.34	1.655	13.69	14.32	6.65	6.26
80	20.58	1.713	13.75	14.38	6.83	6.42
82	20.82	1.775	13.81	14.44	7.01	6.59
84	21.08	1.840	13.88	14.51	7.20	6.76
86	21.35	1.911	13.95	14.58	7.40	6.94
88	21.64	1.988	14.03	14.66	7.61	7.13
90	21.97	2.073	14.11	14.74	7.86	7.34
92	22.35	2.171	14.21	14.84	8.14	7.57
94	22.81	2.293	14.33	14.96	8.48	7.85
95	23.08	2.369	14.41	15.04	8.67	8.01
96	23.41	2.46	14.50	15.13	8.91	8.21
97	23.82	2.58	14.62	15.25	9.20	8.45
98	24.32	2.75	14.79	15.42	9.53	8.77
99	25.12	3.05	15.08	15.72	10.04	9.20
99.61	26.14	3.45	15.49	16.12	10.65	9.69

[a] See text. [b] pH; see text.

ties of water-DMSO mixtures given by Cowie and Toporowski.[26] In order that we may continue using the familiar value of 13.996 for $\mathrm{p}K_\mathrm{w}$ at 25°,[27] the resulting water activities were divided by the molarity of water in pure water, which is 55.347 M at 25°; this gives us a molarity-based water activity scale beginning at 1 in pure water. The resulting molarity-based values of log $a_{\mathrm{H_2O}}$ at 2 mol % intervals in water-DMSO mixtures are given in Table I. Values of $f_{\mathrm{H_2O}}$ are not available between 95 and 100 mol % DMSO;[22] so water activity data in this concentration range are interpolated. Thus the data and associated calculations between 95 and 100 mol % DMSO are probably not wholly reliable.

The two fixed base concentrations habitually used in this work are 0.011 and 0.0471 M; combining the logs of these values with the value 13.996 for $\mathrm{p}K_\mathrm{w}$ at 25° [27] leads to values ($\mathrm{p}K_\mathrm{w}$ + log $C_{\mathrm{OH^-}}$) of 12.037 and 12.669 for these two base concentrations, respectively. This means that the pH of a 0.011 M solution of tetramethylammonium hydroxide in water should be 12.04 at 25°; this was checked by pH-meter measurement several times and found to be correct, provided that CO_2-free water was used and the measurement temperature was correct, or correctly compensated for.

Bunnett–Olsen Method. At present there are six available acidity functions for DMSO-water mixtures. Both the H_- and H_{2-} scales of Stewart et al.[7,10] for primary anilines and diphenylamines and diphenylaminecarboxylic or -sulfonic acids and aminobenzoic acids, respectively, use 0.011 M tetramethylammonium hydroxide (TMAH). The H_-^{q} scale of Katritzky et al.[9] and the H_-^{c} carbon acid scale of Bowden, Cockerill, and Lamper[8] use 0.0471 M TMAH. Two scales, $H_{GC}{}^{0.011}$ and $H_{GC}{}^{0.0471}$, have been determined by Janata and Holtby-Brown[11] using the half-wave reduction potential of cobalticinium ion, relative to a glass electrode. All of these scales were investigated in this work, although for pK_{HA} calculations via eq 6 the H_- scale was preferred. Values of H_- of ($pK_w + \log C_{OH^-} - \log a_{H_2O}$) for both base concentrations, of the Bunnett-Olsen (BO) term ($H_- - pK_w - \log C_{OH^-} + \log a_{H_2O}$), and of the Marziano-Cimeno-Passerini (MCP) term $-\log (f_{A*^-}/f_{HA*}f_{OH^-})$ are listed at intervals of 2 mol % DMSO in Table I.

Marziano–Cimino–Passerini Method. Ionization ratios for some of the diphenylamine and aniline indicators,[28] those originally used in setting up the H_- function for aromatic amines,[7] were used in plots according to eq 8 to give the indicator pK_{HA} values. (The indicators used are labeled (H) in Table II.) With these numbers available, eq 9 was used to give $\log (f_{A*^-}/f_{HA*}f_{OH^-})$ values for a reference indicator over the whole basicity range. Although there is no pressing need to choose one particular indicator as HA* over any other,[29] it was found convenient to use the low pK_{HA} acid 2,4,4′-trinitrodiphenylamine; the values listed in Table I are for this compound. The values for the other H_- indicators are very close to those for this one in any case, as can be seen from the slopes in Table II. The Table I data and eq 10 were then used in all subsequent pK_{HA} calculations using this method.

Calculations. Acidity constant calculations using eq 6 and 10 were carried out using all available ionization ratio data,[8,28] by means of least-squares line fitting on a calculator. Slopes and intercept pK_{HA} values for the two methods, for all available indicators, are given in Table II.

Results

The two methods described above provide a different perspective for assessing the reliability of pK_{HA} values previously determined using the standard Hammett technique. Those indicators which were used to set up the H_- (aromatic amine) scale would not be expected to give greatly altered values by the new methods since the degree of indicator parallelism during the original scale construction was quite high[7b,c] and since this scale and these indicators were used respectively in calculations using eq 6 and 8. However, if the bases of the modified Bunnett-Olsen and Marziano-Cimeno-Passerini treatments are sound the discrepancies between the newly calculated pK_{HA} values and the original ones can give some idea of the cumulative errors that a lengthy overlap operation produces.

For those feeble acids which are structurally unrelated to aromatic amines or whose ionization curves are not parallel to those of the scale indicators the new techniques provide a reasonable means of estimating the pK_{HA} values in the standard state, water.

The correlation coefficients, slope, and intercept pK_{HA} values, resulting from the application of eq 6 and 10 to all of the ionization ratio data currently available to us,[7,8,28] are given in Table II. Plots illustrating the application of the BO method are shown in Figure 1. The data were plotted as illustrated for convenience, in order to have both graph axes positive. Thus the slopes in Table II are listed either as Bunnett-type ϕ values (see eq 6) or as m^* values (see eq 10) and are obtained by multiplying the Figure 1 slopes by minus one. Correlation coefficients for the BO plots are not listed; they have no meaning if the slope is very close to zero,[30] and thus in many cases the correlation coefficient obtained using this method does not indicate the goodness of fit obtained. On the other hand, the correlation coefficients obtained from the use of the other method are significant, and, as can be seen in Table II, they are uniformly excellent. They are listed there to three places of decimals unless the data justify listing more.

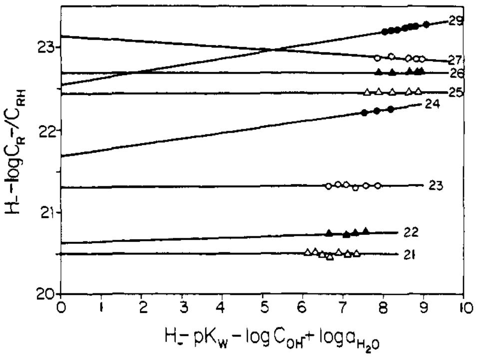

Figure 1. Graph illustrating the use of the BO eq 6 for some H_- indicators. $H_- - \log (C_{A^-}/C_{HA})$ is plotted vertically against $H_- - pK_w - \log C_{OH^-} + \log a_{H_2O}$: pK_{HA} values are y-axis intercepts. Compound numbering as in Table II.

Discussion

Comparison of the AF, BO, and MCP Methods. A good indication of whether or not a series of compounds forms an acidity function set can be obtained from an examination of the eq 10 slopes, m^*. In Table III are listed the average m^* values for several series of compounds, together with the standard deviations for each series; also listed are the standard deviations for pK_{HA} values measured in different ways. For instance, the values for compounds **1–34** measured by the BO method and by the AF method agree with one another to within ±0.19 unit.

We would suggest that a variation in m^* of less than ±0.1 is required to give an acceptable acidity function set. The best set to use for the BO and MCP methods appears to be the aromatic amines used to develop the H_- scale, **1–34;** the set **72–80** (substituted 9-phenylfluorenes) also seems acceptable. Over the range 0–99.6 mol % DMSO pK_{HA}'s measured by the AF, BO, and MCP methods agree with one another to within about 0.5 unit, with most of the error at the high end of the range. Agreement would probably be better if accurate water activity data above 95 mol % DMSO were available. Even so, considering that the acidity range covered extends over 12 log units, between 12 and ~24, this can be regarded as good agreement.

Only compounds which obey the appropriate acidity scale, for instance the H_- set **1–34,** give AF pK_{HA}'s in good agreement with the BO and MCP values. Compounds **35–51,** which do not follow H_- closely,[7b] show considerable divergence between their H_- value at half-deprotonation, and the intercept BO and MCP pK_{HA} values. In all cases except the set **1–34,** the BO and MCP pK_{HA} values agree with one another much better than either value agrees with the AF pK_{HA}, as can be seen clearly from Table III.

Insofar as media containing 0.011 M base may not be directly comparable with those containing 0.0471 M base (see below on this point), conclusions regarding the carbon acids[8] listed in Table II are somewhat more tentative. Nevertheless we may make some statements regarding the numbers obtained.

The phenyl-substituted 9-phenylfluorenes **72–80** appear to form a good acidity function set ($m^* = 1.434 \pm 0.093$), and the BO and MCP pK_{HA} values for these compounds correlate with one another within ±0.43 pK_{HA} units: how-

Table II. Slopes, Correlation Coefficients, and Intercept pK_{HA} Values for Some Weak Organic Acids, According to (6) and (10), from Ionization Ratio Measurements in DMSO–Water Mixtures Containing 0.011 or 0.0471 *M* TMAH

				Eq 6		Eq 10		
No.[a]	Indicator[b]	No. of points	Acidity[c] function pK_{HA}	Slope ϕ	Int pK_{HA}	Corr coeff	Slope m^*	Int pK_{HA}
1	2,4,4'-Tri-NO_2-DPA (H)	5	12.30	0.096	12.38	0.997	1.000	12.39
2	2,4,3'-Tri-NO_2-DPA	4	12.59	0.021	12.64	0.999	0.954	12.66
3	2,4-Di-NO_2-4'-CF_3-DPA	3	12.87	−0.028	12.84	0.99999	0.970	12.90
4	2,4-Di-NO_2-3'-CF_3-DPA	3	13.06	−0.052	13.01	0.996	0.942	13.06
5	2,4-Di-NO_2-3'-Cl-DPA	3	13.17	−0.029	13.13	0.99998	0.969	13.19
6	2,4-Di-NO_2-DPA (H)	4	13.85	−0.023	13.81	0.9996	1.126	14.06
7	2,4-Di-NO_2-3'-Me-DPA	3	13.90	−0.029	13.85	0.9998	1.145	14.15
8	2,4-Di-NO_2-4'-NH_2-DPA	3	14.48	0.003	14.48	0.996	1.179	14.77
9	4,3'-Di-NO_2-DPA	3	14.62	−0.077	14.45	0.998	0.982	14.51
10	4-NO_2-3'-CF_3-DPA (H)	4	14.90	−0.021	14.85	0.998	1.039	14.91
11	4-NO_2-3'-Cl-DPA	3	15.00	0.014	15.05	0.9998	1.073	15.10
12	4-NO_2-DPA (H)	4	15.67	−0.037	15.54	0.999	1.010	15.57
13	4-NO_2-3'-Me-DPA	3	15.60	−0.028	15.49	0.999	1.027	15.53
14	4-NO_2-4'-NH_2-DPA	3	16.40	0.014	16.40	0.99996	1.046	16.38
15	4-Cl-2-NO_2AN (H)	7	17.08	−0.068	16.76	0.99999	1.010	16.90
16	2-NO_2-DPA (H)	6	17.91	0.005	17.92	0.99999	1.148	18.32
17	4-CH_3SO_2-DPA (H)	6	18.80	−0.004	18.77	0.99999	1.093	18.94
18	2,3,5,6-Tetra-Cl-AN	5	19.22	0.044	19.47	0.999	1.150	19.68
19	3-NO_2-DPA	6	19.53	−0.019	19.42	0.999	1.031	19.34
20	4,3'-Di-Cl-DPA (H)	6	19.73	0.003	19.74	0.9998	1.055	19.67
21	3-CF_3-DPA (H)	7	20.48	0.001	20.49	0.9996	1.058	20.44
22	3-Cl-DPA	4	20.73	−0.015	20.63	0.999	1.086	20.88
23	4-Cl-DPA (H)	6	21.33	−0.001	21.31	0.9995	1.110	21.61
24	3-CH_3O-DPA	3	22.22	−0.070	21.67	0.9999	1.129	22.65
25	DPA (H)	5	22.44	−0.001	22.44	0.99995	1.200	23.39
26	4-CN-AN (H)	5	22.68	0.0003	22.69	0.99998	1.202	23.64
27	3,4,5-Tri-Cl-AN	5	22.86	0.032	23.13	0.9996	1.240	24.11
28	4-CH_3-DPA	7	22.95	−0.025	22.74	0.9995	1.180	23.73
29	4-CH_3O-DPA	7	23.22	−0.080	22.54	0.9996	1.108	23.44
30	3,5-Di-Cl-AN (H)	7	23.59	0.008	23.67	0.9996	1.140	24.05
31	3,4-Di-Cl-AN	5	24.60	−0.001	24.58	0.994	1.143	25.07
32	3-CN-AN (H)	5	24.64	−0.034	24.31	0.998	1.107	24.80
33	3-CF_3-AN (H)	4	25.40	0.0001	25.40	0.99998	1.233	26.70
34	3-Cl-AN (H)	3	25.63	−0.012	25.50	0.9999	1.216	26.77
35	4-NO_2-2,6-di-*t*-Bu-AN	3	17.40	−0.080	17.00	0.9999	0.943	16.93
36	4-NO_2-N-trityl-AN	5	17.98	−0.084	17.56	0.9998	1.039	17.90
37	4-NO_2-N-CH_3-AN	5	18.49	−0.109	17.90	0.999	1.014	18.24
38	4-NO_2-N,2-di-CH_3-AN	4	18.58	−0.061	18.24	0.9999	1.049	18.51
39	4-NO_2-N-Et-AN	4	18.58	−0.099	18.04	0.9999	1.007	18.30
40	4-NO_2-N-*i*-Pr-AN	5	18.66	−0.100	18.11	0.9999	1.003	18.35
41	4-NO_2-2,6-di-CH_3-AN	4	18.71	−0.155	17.89	0.9999	0.933	18.07
42	4-NO_2-2-CH_3-AN	4	18.83	−0.135	18.10	0.9997	0.955	18.29
43	4-NO_2-AN	4	18.91	−0.143	18.11	0.99997	0.958	18.35
44	4-NO_2-N-*t*-Bu-AN	4	19.64	−0.021	19.52	0.9997	1.064	19.63
45	2,2'-Dipyridylamine	8	19.91	−0.213	18.56	0.9995	0.834	18.53
46	4-NO_2-3,5-di-CH_3-AN	6	21.16	0.103	21.90	0.998	1.225	22.23
47	2,6-Di-Cl-AN	4	22.40	0.026	22.61	0.999	1.239	23.64
48	4-NO_2-2,3,5,6-tetra-Me-AN	5	22.66	0.259	24.84	0.9996	1.514	26.05
49	2,5-Di-Cl-AN	7	22.71	0.017	22.84	0.998	1.207	23.71
50	2,3-Di-Cl-AN	4	23.14	−0.126	22.03	0.992	0.960	22.13
51	2,4-Di-Cl-AN	5	23.46	−0.094	22.64	0.995	0.995	22.74
52	2-NO_2-FL	3	17.96	−0.086	17.17	0.993	1.015	17.41
53	9-Biphenyl-4-yl-FL	4	18.21	0.354	19.26	0.996	1.438	19.36
54	2-CN-FL	4	18.96	0.393	20.36	0.999	1.605	20.98
55	7H-Benzo[*c*]-FL	4	19.62	0.093	19.56	0.996	1.225	19.88
56	2-Br-FL	4	20.56	0.044	20.21	0.9997	1.080	20.07
57	2-Cl-FL	4	20.59	−0.175	18.97	0.9996	0.889	19.03
58	9-Benzyl-FL	5	21.20	−0.019	20.55	0.993	1.039	20.51
59	9-Me-FL	6	21.80	0.137	22.17	0.995	1.214	22.20
60	4H-Cyclopenta[*def*]-phenanthrene	4	21.79	−0.064	20.80	0.974	1.009	20.88
61	FL	6	22.10	0.092	22.15	0.997	1.194	22.35
62	9-Et-FL	5	22.22	0.051	21.99	0.988	1.168	22.31
63	2-OMe-FL	4	22.36	−0.132	20.78	0.998	0.971	21.09
64	9-*i*-Pr-FL	5	22.70	0.164	23.25	0.951	1.304	23.68
65	9-*t*-Bu-FL	4	23.41	0.107	23.58	0.998	1.339	24.71
66	Phenalene	2	19.45	0.080	19.30	(1)	1.215	19.64
67	4-Cl-2-NO_2-AN	3	(17.08)[d]	−0.097	16.62	0.997	0.936	16.60
68	4-NO_2-AN	4	(18.91)[e]	−0.159	17.97	0.999	0.964	18.32
69	2-NO_2-AN	5	*f*	−0.179	17.54	0.999	0.953	17.94
70	4-CN-9-Ph-FL	5	15.40	0.879	18.27	0.991	2.024	18.47
71	9-Ph-3,4-benzo-FL	4	16.60	0.344	17.75	0.997	1.404	17.76
72	9-(*m*-Cl-Ph)-FL	4	17.66	0.427	19.12	0.993	1.515	19.22
73	9-(*m*-CF_3-Ph)-FL	3	17.69	0.213	18.32	0.994	1.259	18.30
74	9-(p-Cl-Ph)-FL	6	18.10	0.263	18.91	0.992	1.368	19.10

Table II (*Continued*)

		No. of	Acidity[c]	Eq 6		Eq 10		
No.[a]	Indicator[b]	points	function pK_{HA}	Slope ϕ	Int pK_{HA}	Corr coeff	Slope m^*	Int pK_{HA}
75	9-(*m*-OMe-Ph)-FL	4	18.47	0.289	19.35	0.992	1.456	19.80
76	9-(*n*-Me-Ph)-Fl	4	18.96	0.293	19.90	0.993	1.475	20.40
77	9-Ph-FL	12	18.59	0.333	19.67	0.995	1.529	20.24
78	9-(*m*-Me-Ph)-FL	4	18.84	0.215	19.38	0.998	1.405	19.96
79	9-(*p*-OMe-Ph)-FL	3	19.01	0.344	20.19	0.9998	1.558	20.83
80	9-(*p*-NMe$_2$-Ph)-FL	5	19.61	0.194	20.02	0.994	1.341	20.38

[a] Numbers 1–14, ref 7a, 28b; 15–51, ref 7b, 28a; 52–69 and 77, ref 8b; 70–80, ref 8a. [b] DPA = diphenylamine; AN = aniline; FL = fluorene. (H) = indicator used for MCP method. [c] Numbers 1–34, H_-;[7] 35–51, H_- at half-deprotonation;[7b] 52–66 and 70–80, H_-^c;[8] 67 and 68, H_-, see no. 15 and 43. [d] Value obtained using H_-, given in ref 8b. [e] H_- at half-deprotonation. [f] Not listed.

Table III. Average m^* Values and Standard Deviation between pK_{HA}'s Measured in Different Ways, for the Compounds in Table II

No. and type of indicator[a]	Acidity function	Av m^* value	BO/AF[b]	MCP/AF[b]	BO/MCP[b]
1–34, aromatic amines	H_-	1.091 ± 0.083	±0.19	±0.50	±0.55
35–51, aromatic amines[c]	H_-	1.055 ± 0.156	±0.85	±1.09	±0.48
52–65, 70, 71, aromatic hydrocarbons	H_-^c	1.245 ± 0.274	±1.13	±1.25	±0.38
72–80, 9-phenylfluorenes	H_-^c	1.434 ± 0.093	±0.93	±1.31	±0.43

[a] From Table II. [b] AF = acidity function method. BO = Bunnett–Olsen method, eq 6. MCP = Marziano–Cimino–Passerini method, eq 10. Standard deviation between pK_{HA} values measured in the two ways shown in the column heading. [c] AF pK taken as H_- at half-deprotonation.

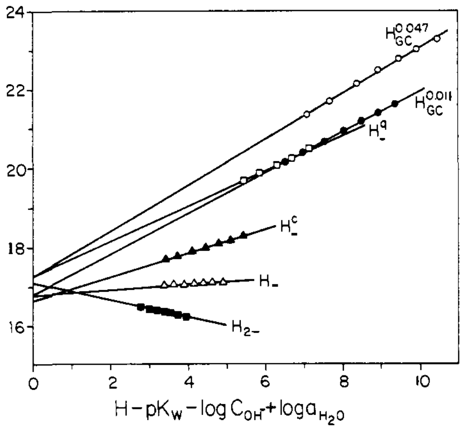

Figure 2. BO plots for **15** using six different acidity functions, illustrating convergence on a common pK_{HA} value.

ever, the AF values are about one pK unit lower. This is the case for all the carbon acids **52–66** and **70–80** in Table II. It is possible that anchoring difficulties encountered in setting up the H_-^c scale account for these discrepancies.[8,31,32]

It is rather difficult to estimate errors in pK_{HA} values, whether obtained by the MCP or BO methods, or by the AF method. In some cases the extrapolations are very long; obviously the better the ionization ratio data the better the intercept pK_{HA} value. We estimate that for reasonably good data the error in all three methods should be approximately: 0-25 mol % DMSO, ±0.05 units; 25-50%, ±0.1 unit: 50-80%, ±0.2 unit; 80-95%, ±0.5 unit; 95-100%, ±1-2 units.[33]

Use of the H₋ Scale in the BO Method. Although we have used the H_- scale in developing the Bunnett-Olsen eq 6, primarily because we feel that H_- is the most accurately known acidity function in DMSO and because it encompasses almost the whole 0-100 mol % DMSO range, we could reasonably have used any other acidity function. We have checked this in a number of cases; a typical example, compound 15, is shown in Figure 2. It is apparent that all of the extrapolations converge on more or less the same point; in this case the average extrapolated pK_{HA} is 17.04 ± 0.31. Considering that the AF values for the solution in which this compound is half-ionized differ by as much as 4.2 units this can be considered good agreement. Thus one can justify using the H_- scale in the BO approach, even for compounds that do not follow it.

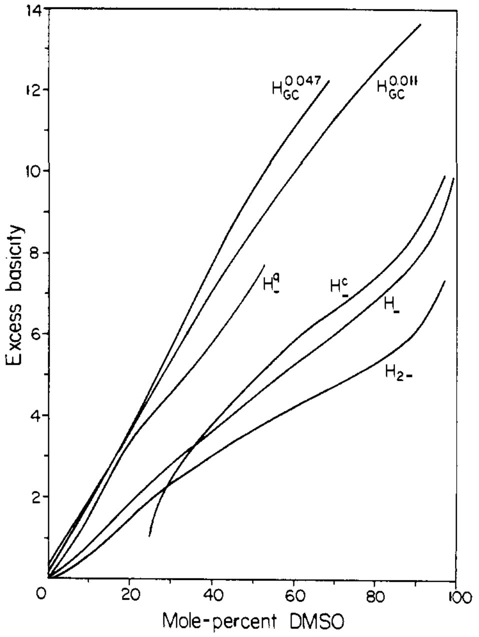

Figure 3. Excess basicities ($H - pK_w - \log C_{OH^-} + \log a_{H_2O}$) for different acidity functions in DMSO-water mixtures as a function of medium composition.

Excess Basicity. The excess basicity of a medium, $H - pK_w - \log C_{OH^-} + \log a_{H_2O}$, represents the increase in basicity relative to the standard state that is due to the various species' activity coefficients deviating from unity, and can be used to compare acidity functions set up using different concentrations of base.[34] Figure 3 shows a plot of excess basicity against solvent composition for the six acidity functions used herein. Apart from the clearly anomalous behavior of the H_-^c scale at the lower end and the possibly anomalous behavior of the $H_{GC}^{0.011}$ scale at the upper end, the various acidity functions tend to be affected in the same way as the solvent composition changes. Indeed, one can show that the acidity functions are linear in one another over a considerable range, and this applies also to the excess basicities.

It is apparent from Figure 3 that the excess basicities derived from the $H_{GC}{}^{0.011}$ and $H_{GC}{}^{0.0471}$ scales are not the same. We may conclude from this that water–DMSO mixtures containing 0.011 or 0.0471 *M* base are sufficiently different media to produce significantly different medium activity coefficients for species dissolved in them. Apart from the already-mentioned anomalies, the important features of Figure 3 appear to be a change in slope at 25–35 mol % DMSO, which is not unreasonable as many physical properties of water–DMSO mixtures change at about this value,[22,26] and a sharp upward turn at ~85 mol % DMSO, which probably means that f_{OH^-} starts to increase rapidly at about this point.

Conclusions

1. Equations have been derived that allow the Bunnett–Olsen and Marziano–Cimino–Passerini methods to be applied to ionization of feeble acids in basic aqueous DMSO.

2. Using these methods, estimates have been made of the pK_{HA} values of 80 nitrogen and carbon acids. The values obtained are as reliable as those obtained by the acidity function method, for compounds that follow the appropriate function closely. For other compounds the extrapolative pK_{HA} appears to be better, insofar as the extrapolation goes directly back to the standard state, water. Use of these extrapolative techniques obviates the necessity for setting up new acidity functions.

3. The MCP technique does not use an acidity function directly and correlations obtained using it are slightly better, since the BO approach tends to magnify errors by accumulating those present in the ionization data and those in the acidity function used.

4. The MCP technique shows great promise in the analysis of kinetic data, since the activity coefficient ratio for the individual compound whose kinetics are being studied can be readily calculated. A simple extension should permit estimates of quantities such as $\log f_{A^-}/f_{\ddagger}$, and the amount of charge present at the transition state.

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