mixtures consisted of varying ratios of $R_1H:R_2H:Br_2$ from 1:1:5 to 1:1:100 with Freon 112 as the internal standard in sealed, degassed tubes. The tubes were irradiated at 40.0 ± 0.1° until at least 10% of each substrate had reacted. The excess bromine was destroyed with ice-cold aqueous sodium bisulfite. The organic substrates were extracted with a suitable solvent (Freon 113 or *o*-dichlorobenzene), washed once with cold water, and dried over anhydrous sodium sulfate.

The stability of the substrates in excess bromine in the dark was checked both with and without added hydrogen bromide. Bromocyclohexane and *cis*-4-bromo-*tert*-butylcyclohexane were found to be unstable in a 100-fold mole excess of bromine but over at least 10 half-lives they were stable in a 30-fold mole excess of bromine, with equivalent amounts of added hydrogen bromide. The other substrates were stable to equivalent amounts of hydrogen bromide and 100-fold excess of molecular bromine.

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Ionization of Nitrogen and Oxygen Acids in Strongly Basic Systems

A. Albagli, A. Buckley, A. M. Last, and Ross Stewart*

Contribution from the Department of Chemistry,
University of British Columbia, Vancouver 8, British Columbia, Canada.
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Abstract: The ionization of three types of weak acid (neutral nitrogen and oxygen acids and anionic nitrogen acids) has been compared in aqueous and methanolic dimethyl sulfoxide (DMSO) solutions. The H_- scales for the nitrogen acids (aromatic amines) and the oxygen acids (any of several hindered phenols) diverge as the DMSO concentration increases, with the medium's basicity being much greater toward the nitrogen acids. The pK values of the latter tend to be larger in methanolic than in aqueous DMSO. A unique scale for phenols cannot be constructed over the whole range of solvent compositions because the compound's ionization curves are not all parallel. Indeed, addition of DMSO to aqueous hydroxide, up to about 20 mol %, *reduces* the basicity of the system toward hindered phenols. This does not occur when DMSO is added to methanolic methoxide, nor with nitrogen acids in either medium.

In the last decade, there has been considerable interest in strongly basic systems, and a number of groups have used the general Hammett technique to construct acidity scales in the region beyond pH 14.[1] In some cases bases have simply been added in larger and larger amounts to water, methanol, or like solvent. In others a fixed amount of base (*e.g.*, 0.01 M $(CH_3)_4N^+ \cdot OH^-$) is used and a polar aprotic solvent such as dimethyl sulfoxide (DMSO) is added in larger and larger amounts. The H_- function, which is defined as

$$H_- = \mathrm{p}K_{HA} - \log [HA]/[A^-] = -\log \frac{a_{H^+}f_{A^-}}{f_{HA}}$$

governs the ionization of a neutral acid ($HA \rightleftharpoons H^+ + A^-$) and its generality depends on the activity coefficient ratio f_{A^-}/f_{HA} being dependent only on the composition of the medium and not on the identity of the various indicators used to construct the scale.

Other papers in this series[1e,f] have shown that the H_- function for a 0.01 M solution of tetramethylammonium hydroxide changes from 12 in water (H_- = pH in pure water) to 26 in 99.6 mol % DMSO. The organic acids used to construct this scale were a series of anilines and diphenylamines, and a number of tests have been applied to demonstrate the general validity of the pK and H_- values thus obtained. Carbon acids are less well behaved, however, and numerous cases are known of relative pK values being transposed when the medium is changed.[1d] We shall see from the subsequent discussion that oxygen acids, too, behave rather badly in this regard.

Anionic nitrogen acids generate a somewhat different scale,[1h] designated H_{2-}, because the activity coefficient ratio is affected by the charge type of the acid and conjugate base.

The present work was undertaken to determine the degree of divergence of acidity function behavior caused by variations in structure and charge in the indicators. The latter were either neutral nitrogen acids, monoanionic nitrogen acids, or neutral oxygen acids.

The nitrogen acids were all diphenylamines. The only oxygen acids sufficiently weak to be but partially ionized in strongly basic media are alcohols and certain hindered phenols. The former do not undergo a measurable spectral shift on ionization and hence are unsuitable for this study. Bulky ortho groups cause a considerable reduction in the acidity of phenols, presumably because of steric hindrance to the solvation of the phenoxide ion.[2]

Experimental Section

Those diphenylamines not previously prepared[1e,f,h] are described below. Their pK_{HA} values refer to water as the standard state; the

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(1) (a) K. Bowden, *Chem. Rev.*, **66**, 119 (1966); (b) C. H. Rochester, "Acidity Functions," Academic Press, London, 1970; (c) J. R. Jones, *Quart Rev., Chem. Soc.*, 365 (1971); (d) C. D. Ritchie in "Solute-Solvent Interactions," J. F. Coetzee and C. D. Ritchie, Ed., Marcel Dekker, New York, N. Y., 1969, Chapter 4; (e) D. Dolman and R. Stewart, *Can. J. Chem.*, **45**, 911 (1967); (f) R. Stewart and J. P. O'Donnell, *ibid.*, **42**, 1681 (1964); *J. Amer. Chem. Soc.*, **84**, 493 (1962); (g) J.-C. Halle, R. Gaboriaud, and R. Schaal, *Bull. Soc. Chim. Fr.*, 1851 (1969), and references therein; (h) K. Bowden, A. Buckley, and R. Stewart, *J. Amer. Chem. Soc.*, **88**, 947 (1966).

(2) C. H. Rochester and B. Rossall, *J. Chem. Soc. B*, 743 (1967).

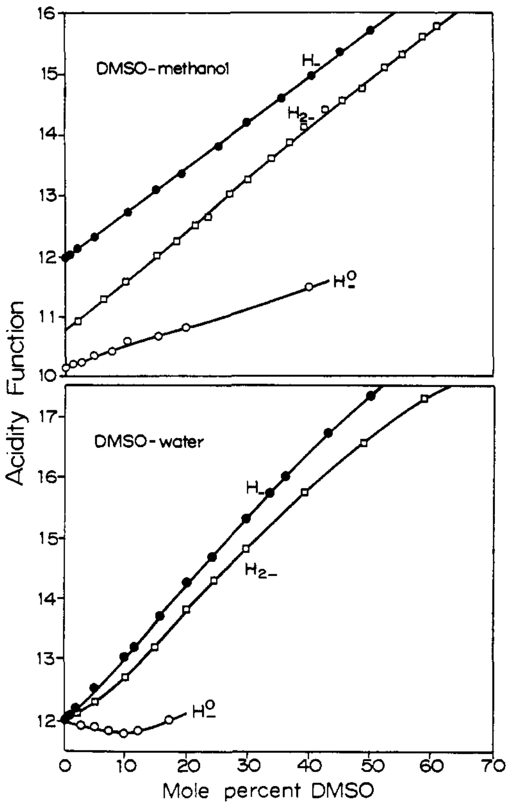

Figure 1. Acidity functions for various types of acid as a function of the mol % DMSO in the system: (●) neutral nitrogen acids, (□) anionic nitrogen acids, (○) 2,6-diisopropylphenol. Upper curves, DMSO–methanol containing 0.010 M sodium methoxide; lower curves, DMSO–water containing 0.011 M tetramethylammonium hydroxide.

ultraviolet data refer to ethanol in the case of neutral amines and ethanol–DMSO mixtures containing sodium ethoxide in the case of amide ions; λ_{max} is given in units of nm with extinction coefficients in parentheses.

2,4-Dinitro-4′-trifluoromethyldiphenylamine (**3**) was synthesized by the reaction of 2,4-dinitrochlorobenzene with *p*-trifluoromethylaniline: mp 125–126.5°; pK_{HA} = 12.87; amine λ_{max} 354 (17,900); amide ion λ_{max} 435 (20,400), 474 (19,500).

Anal. Calcd for $C_{13}H_8N_3O_4F_3$: C, 47.71; H, 2.46; N, 12.84; F, 17.42. Found: C, 47.57; H, 2.62; N, 12.01; F, 17.16.

2,4-Dinitro-3′-trifluoromethyldiphenylamine (**4**) was prepared in the same way as its isomer above: mp 123–125°; pK_{HA} = 13.06; amine λ_{max} 354 (17,500); amide ion λ_{max} 435 (20,000), 474 (18,900).

Anal. Calcd for $C_{13}H_8N_3O_4F_3$: C, 47.71; H, 2.46; N, 12.84; F, 17.42. Found: C, 47.79; H, 2.98; N, 13.05; F, 17.27.

2,4-Dinitro-3′-chlorodiphenylamine (**5**) had mp 182–183°;[3] pK_{HA} = 13.17; amine λ_{max} 356 (17,900); amide ion λ_{max} 432 (20,400), 475 (18,100).

4-Nitro-3′-chlorodiphenylamine (**11**) was prepared by the method of Ullmann and Dahmen;[4] mp 129–130° (lit.[5] 129°); pK_{HA} = 15.00; amine λ_{max} 396 (20,500); amide ion λ_{max} 504 (41,800).

4-Nitro-3′-methyldiphenylamine (**12**) was prepared by the reaction of 4-nitrobenzenesulfonic acid with *m*-toluidine:[4] mp 127–138°; pK_{HA} = 15.60; amine λ_{max} 410 (24,000); amide ion λ_{max} 510 (36,200).

Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.40; H, 5.30; N, 12.28. Found: C, 68.24; H, 5.29; N, 12.12.

4-Nitro-4′-aminodiphenylamine (**14**) was prepared in an analogous manner to the previous compound: mp 206–207° (lit. 207–208°);[4] pK_{HA} = 16.40; amine λ_{max} 420 (19,100); amide ion λ_{max} 518 (29,800).

2,4-Dinitro-4′-aminodiphenylamine (**8**) had been previously prepared but our physical constants differ slightly from those reported earlier.[1f,6] Column chromatography of a commercial sample gave a compound of mp 183–184° (lit.[6] 189–189.5°); amine λ_{max} 378 (14,400); amide ion λ_{max} 496 (17,400).

Anal. Calcd for $C_{12}H_{10}N_4O_4$: C, 52.55; H, 3.65; N, 20.44. Found: C, 52.76; H, 3.75; N, 20.20.

All the phenols were commercially available. The solids were recrystallized from ethanol and sublimed before a final recrystallization; the liquids were distilled under nitrogen.

The techniques used to purify solvents, prepare solutions, and determine pK values have been described elsewhere.[1e,f] The anchor compounds, whose pK values were determined in water using dilute buffers and a glass electrode, were 2,4,4′-trinitrodiphenylamine (pK = 12.30), 2,4,6-trinitro-4′-chlorodiphenylamine-2′-carboxylic acid (pK = 11.78), used for the H_2- scale in water and methanol,[1h] and 2,6-diisopropylphenol (pK = 10.88). In the case of the phenols, there was a considerable solvent effect on the absorption of the phenolate anions. It was therefore necessary to adopt the iterative procedure of Hine and Hine[7] to determine the extinction coefficients of the anions in the various solvent mixtures that were used. (For example 2-*tert*-butylphenolate anion has an absorption maximum at 289 nm with an extinction coefficient of 3350 in water, which shifts to 297 nm and an extinction coefficient of 4077 in 25 mol % aqueous DMSO.[8])

Results and Discussion

Acidity functions for aqueous and methanolic DMSO solutions containing 0.011 M base are plotted in Figure 1. The symbols H_- and H_{2-} are used, as before[1e,h] for the functions that govern respectively the ionization of neutral and anionic aromatic amines. Although a unique scale cannot be constructed over the whole range of DMSO–water compositions using all the phenols studied (see below), a function based on the ionization of a single phenol, 2,6-diisopropylphenol, is included in Figure 1 for purposes of illustration. The shallow function (designated H_-°) is consistent with the much higher degree of charge localization in the anions of oxygen than of nitrogen (and carbon) acids.

The lack of convergence of the three scales in methanolic DMSO as the DMSO concentration approaches zero is clearly shown in Figure 1. In this system convergence need not occur since the pK values used for the anchor compounds (those used to determine the acidity function in 100% alcohol) refer to water as the standard state. However, in aqueous DMSO containing 0.01 M hydroxide ion convergence must occur in water, where H_- = pH = 12.

Nitrogen Acids. The values of H_- for methanolic and ethanolic DMSO systems are reported elsewhere.[9] The values for aqueous DMSO were reported earlier,[1e] but in order to improve the degree of indicator overlap a number of additional indicators were prepared and the H_- scale in aqueous DMSO redetermined (Table I). Both the scale in aqueous DMSO and the pK values of the indicators used earlier were found to agree closely with those previously reported.[1e,f] However, small but significant differences begin to appear

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[3] F. Reverdin and P. Crepieux, *Bull. Soc. Chim. Fr.*, [3] **29**, 235 (1903).

[4] F. Ullmann and R. Dahmen, *Chem. Ber.*, **41**, 3744 (1908).

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[6] A. M. Simonov, *J. Gen. Chem. USSR*, 10, 1220 (1940); *Chem. Abstr.*, 35, 2868 (1941).

[7] J. Hine and M. Hine, *J. Amer. Chem. Soc.*, 74, 5266 (1952).

[8] See Tables III–V, which will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JACS-73-4711. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

[9] A. Albagli, R. Stewart, and J. R. Jones, *J. Chem. Soc. B*, 1509 (1970).

Table I. H_- Values for the DMSO–Water System Containing 0.011 M $(CH_3)_4NOH$[a]

Mol % DMSO	H_-	Indicator[b]
0.4	11.95	**1**
2.0	12.20	**1, 2**
5.0	12.54	**1–5**
11.3	13.19	**2–6**
16.0	13.73	**3–8**
20.3	14.29	**6–10**
24.1	14.72	**6–13**
29.7	15.34	**9–13**
33.6	15.75	**10–14**
36.2	16.01	**12, 14**
43.2	16.74	**14**

[a] See also ref 1e. [b] Indicators used and their pK values (in parentheses) are: **1**, 2,4,4′-trinitrodiphenylamine (12.30); **2**, 2,4,3′-trinitrodiphenylamine (12.59); **3**, 2,4-dinitro-4′-trifluoromethyldiphenylamine (12.87); **4**, 2,4-dinitro-3′-trifluoromethyldiphenylamine (13.06); **5**, 2,4-dinitro-3′-chlorodiphenylamine (13.17); **6**, 2,4-dinitrodiphenylamine (13.85); **7**, 2,4-dinitro-3′-methyldiphenylamine (13.90); **8**, 2,4-dinitro-4′-aminodiphenylamine (14.48); **9**, 3,4′-dinitrodiphenylamine (14.62); **10**, 4-nitro-3′-trifluoromethyldiphenylamine (14.90); **11**, 4-nitro-3′-chlorodiphenylamine (15.00); **12**, 4-nitro-3′-methyldiphenylamine (15.60); **13**, 4-nitrodiphenylamine (15.67); **14**, 4-nitro-4′-aminodiphenylamine (16.40).

Table II. H_-, H_{2-}, and $H_-{}^\circ$ Values[a] for the DMSO-Methanol System Containing 0.01 M $NaOCH_3$

Mol % DMSO	H_-	H_{2-}	$H_-{}^\circ$
2	12.15		10.20
5	12.36	11.11	10.32
10	12.72	11.54	10.50
15	13.13	11.95	10.64
20	13.50	12.33	10.80
25	13.86	12.74	10.96
30	14.28	13.24	11.12
35	14.65	13.87	11.27
40	15.05	14.08	
50	15.83	14.88	
60	16.61	15.73	
70	17.41	16.59	
80		17.50	

[a] Indicators used and their pK values (in parentheses) are: H_-, 4,4′-dinitrodiphenylamine (14.47), and the indicators listed under Table I; **1** (12.30), **2** (12.70), **3** (12.90), **4** (13.08), **5** (13.25), **6** (14.10), **7** (14.15), **8** (15.00), **9** (15.31), **10** (15.74), **11** (15.90), **12** (16.55), **13** (16.64), **14** (17.40); $H_-{}^\circ$, 2,6-diisopropylphenol; H_{2-}, **15**, 2,4,6-trinitro-4′-chlorodiphenylamine-2′-carboxylic acid (11.78); **16**, 2,4,6-trinitrodiphenylamine-2′-carboxylic acid (12.27); **17**, 2,4-dinitrodiphenylamine-4′-carboxylic acid (13.06); **18**, 2,6-dinitrodiphenylamine-4-carboxylic acid (13.91); **19**, 2,4-dinitrodiphenylamine-3′-carboxylic acid (13.60); **20**, 4-chloro-2′,4′-dinitrodiphenylamine-6′-carboxylic acid (15.88); **21**, 2,4-dinitrodiphenylamine-6-carboxylic acid (16.68); **22**, 3,5-dinitro-4-aminobenzoic acid (16.11); **23**, 2,4-dinitrodiphenylamine-2′-carboxylic acid (15.31); **24**, 2-nitrodiphenylamine-4′-carboxylic acid (18.05).

between these pK values and those obtained in the alcoholic systems as the DMSO content is increased.[8] (The methanolic and ethanolic scales were anchored with indicators whose pK values are referred to water as the standard state.)[10] Thus, 4-nitro-4′-aminodiphenylamine, which has a pK_{HA} of 16.4 in aqueous DMSO, appears to be 1 pK unit weaker in methanolic DMSO. This somewhat greater spread in pK values corresponds to a larger ρ value for aromatic amine ionization in alcoholic than in aqueous systems. This is a well-known situation with carboxylic acids where the ρ value rises sharply as one moves from water to methanol or ethanol, and then to DMSO.[11,12] With aromatic amines, however, variations in ΔpK on going from one solvent to another are often quite small.[12–14] Variations of ΔpK with solvent should be manifest in lack of parallelism of ionization plots (log $[A^-]/[HA]$ against a solvent parameter) for a series of indicators. Anilines and diphenylamines give, for the most part, highly parallel plots in all systems studied, indicating that the pK difference, between neighboring indicators at least, is essentially independent of solvent composition. Very small discrepancies may accumulate, however, and produce significant effects when amines that are very much weaker than the anchor compound are compared in different solvents. Such effects have been attributed largely to dispersion forces.[15,16]

The importance of ionic charge, in this connection, can be seen by comparing the H_- and H_{2-} scales in Figure 1a and Table II. There is a difference of more than a unit in the intercepts, and this means that two amine indicators, one neutral and one anionic, can have the same strength in water but differ by more than a unit in methanol. The trend to higher pK values in methanolic DMSO than in aqueous DMSO, observed with the neutral acids, is also apparent with the anionic acids, but here some exceptions were noted. For example, indicator **23**, Table II, whose pK in aqueous DMSO was reported to be 15.45, appears to be actually stronger in methanolic DMSO. In view of the concentration of charge in the conjugate bases of anionic acids, it is perhaps not surprising that these acids show a more erratic solvent effect on pK than do the neutral acids.

Carbon Acids. H_- scales in ethanolic DMSO[17] do not differ greatly for nitrogen and carbon acids.[18,19] A close comparison cannot be made because of difficulties in accurately measuring pK_{HA} values of carbon acids. The ions of most carbon acids that are suitable for constructing a scale between $H_- = 12$ and, *e.g.*, $H_- = 17$ undergo unusual spectral shifts as the degree of ionization changes. This is due, at least in part, to the formation of radical anions.[20] Furthermore, carbon acids are insoluble in water and this further complicates the derivation of valid scales anchored in water. Carbon acids and their conjugate bases, carbanions, occupy a more important position in organic chemistry than do nitrogen acids and amide ions and it is ironic that it is the latter that are relatively well behaved.

Ionization of Hindered Phenols. The pK values in water of 2-*tert*-butylphenol and 2,4-di-*tert*-butylphenol have previously been determined by Rochester[21] and

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(12) C. D. Ritchie and R. E. Uschold, *J. Amer. Chem. Soc.*, **90**, 2821 (1968).

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(15) E. Grunwald and E. Price, *J. Amer. Chem. Soc.*, **86**, 4517 (1964).

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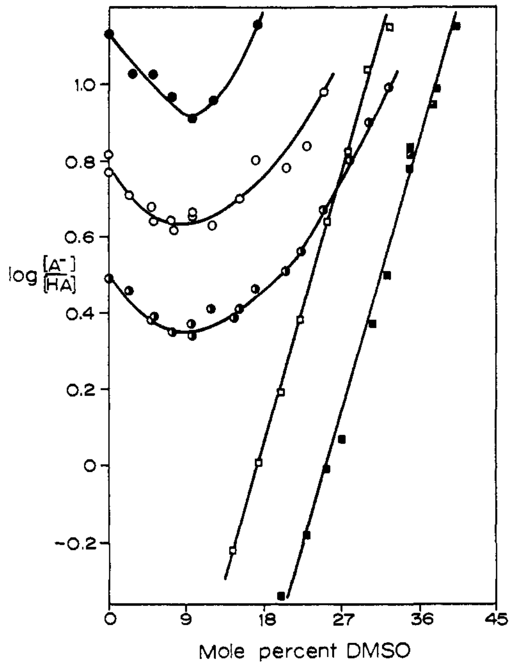

Figure 2. Degree of ionization of various phenols in aqueous DMSO as a function of solvent composition: (●) 2,6-diisopropylphenol, (○) 2-*tert*-butylphenol, (half-shaded circle) 2,4-di-*tert*-butylphenol, (□) 2,6-di-*tert*-butylphenol, (■) 2,6-di-*tert*-butyl-4-methylphenol, (half-shaded square) 2,4,6-tri-*tert*-butylphenol.

our values are in good agreement with his. He was unable to study the ionization of more highly hindered phenols in water because of their very low solubility, but he did show that a number of these compounds could be used to generate a scale in methanol containing varying amounts of sodium methoxide.

In view of the monotonic increase in basicity toward nitrogen and carbon acids that accompanies the addition of DMSO to aqueous solutions of hydroxide ion, we were unprepared for the behavior shown in Figure 2.[8] Addition of DMSO *reduces* the basicity of aqueous hydroxide (but not methanolic methoxide) toward 2,6-diisopropylphenol, 2-*tert*-butylphenol, and 2,4-di-*tert*-butylphenol. Minima in the ionization curves occur near 10 mol % DMSO, and it is only beyond 20 mol % DMSO that all phenols are ionized to a greater extent than they are in water. The more highly hindered compounds, 2,6-*di-tert*-butylphenol and its 4-methyl derivative, are too insoluble to be examined in the solvent range of interest. However, if Cohen and Jones' estimates of the p*K* values of these compounds[22] are even approximately correct, then they too must possess minima. It is also clear from Figure 2 that the ionization curves generated by these compounds are not parallel to those for the other three phenols. Nonparallel plots are also found for phenols in methanolic DMSO but in this case no minima appear. (Nitrogen acids show no minima in their ionization curves, as was demonstrated by a careful examination of the ionization of 2,4,4′-trinitrodiphenylamine in the region 1–10 mol % DMSO. The degree of ionization increased monotonically with increasing DMSO concentration.)

The relatively flat acidity function generated by phenols, that is apparent from the curves in Figure 1, finds ready explanation in the greater degree of charge localization in the case of oxygen acids compared to nitrogen and carbon acids. Indeed, virtually the only nitrogen and carbon acids strong enough to examine are those with extensive charge delocalization. The causes of the anomalous ionization behavior shown in Figure 2 are less obvious. Bulky groups adjacent to the hydroxyl function undoubtedly affect the solvation of both the hydroxyl group and its oxy anion, as has been discussed by Rochester and Rossall,[2] and this may cause the lack of parallelism in the ionization curves for the phenols with one ortho *tert*-butyl group compared to those with two. Whether these effects cause the decrease in basicity that accompanies the addition of DMSO to aqueous hydroxide is uncertain.

Some hydroxylic compounds, *e.g.*, ketone hydrates, are very much better solvated by aqueous DMSO than by pure water[23] and this provides an attractive explanation for the shift of the equilibrium toward the neutral phenol when DMSO is added to aqueous base. Aqueous sulfolane, however, does not solvate ketone hydrates effectively and yet it too represses the ionization of hindered phenols. Indeed, deeper minima occur with aqueous sulfolane than with aqueous DMSO. Further work is required to determine if the effects shown in Figure 2 arise principally because of the phenolic character of the indicators or because of the presence of bulky groups adjacent to the site of dissociation.

Acknowledgment. The financial support of the National Research Council of Canada is gratefully acknowledged.

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