J. Am. Chem. Soc. **1988**, *110*, 4577–4582

Acid–Base Properties of Organic Solvents

Alessandro Bagno and Gianfranco Scorrano*

Contribution from the Centro CNR Meccanismi di Reazioni Organiche, Università di Padova, via Marzolo 1, I-35131 Padova, Italy.

Received August 4, 1987.
Revised Manuscript Received February 9, 1988

Abstract: The protonation equilibria of organic compounds commonly employed as dipolar nonhydroxylic solvents (including amides, nitriles, sulfones, and nitro compounds) have been measured at 25 °C in aqueous sulfuric acid with an NMR technique. The definition of the protonation parameters pK_{BH^+} and m^* allows comparison of the relative basicities in water and in concentrated acids. An inversion of relative basicities is observed between dimethylformamide and hexamethylphosphoric triamide on going from dilute to concentrated solutions. The relative basicity scale for dipolar nonhydroxylic solvents in aqueous sulfuric acid is amides > dimethyl sulfoxide > acetone ≫ acetonitrile > sulfones > nitromethane. The last three functional groups are only 20–50% protonated in 100% sulfuric acid. Hexamethylphosphoric triamide is oxygen-protonated in aqueous acids, and in oleum mixtures it is largely diprotonated; diprotonation also occurs (to a lesser extent) for tetramethylurea.

The acid–base properties of a substance are important parameters, especially when it is used as reaction solvent, for investigation of acid- and base-catalyzed reactions,[1] the building of acidity and basicity scales in nonaqueous media,[2] and the conversion of protonation and deprotonation constants between different solvents.[3] More generally, basicity data of organic solvents may contribute to further clarifying solute–solvent interactions and, by correlation of protonation constants with related data (hydrogen-bonding equilibrium constants, heats of reaction with Lewis acids, etc.), give a more complete picture of its solvating power.[4]

Apart from the nonbasic hydrocarbons, most organic solvents behave as Brønsted bases. Among these, amines, pyridines, and related compounds are strong bases, and their properties are very well-known.[5] All the other functional groups contained in common solvents are weakly basic and require nonideal, concentrated aqueous acid mixtures to undergo protonation. This is one of the reasons for confusing reports in the literature, where for the same compound different pK_{BH^+} values are often quoted. By definition, thermodynamic pK_{BH^+}'s are those obtained in dilute aqueous solutions, directly measured or extrapolated in a suitable way from the concentrated solutions, where measurements are made, to the reference standard state (usually an ideal 1 M solution). The choice of a common standard state is useful to make comparisons among different compounds. It must be pointed out, however, that for weak bases extrapolation from the standard state to the actual solutions and vice versa requires the knowledge of a second parameter, which we have called the solvation parameter (m^*), to account for the deviations from ideality of the concentrated solutions.[6] It is clear that measurements in totally nonaqueous media, such as titrations in glacial acetic acid, are extrapolated to the aqueous standard state with even more difficulty, so that the reliability of such protonation parameters as meaningful thermodynamic quantities is questionable. We will limit our discussion here to data obtained in aqueous solvents, making only passing references to values in other media.

The basicities of ethers, ketones, esters, and sulfoxides in aqueous acids are now well established,[7–9] while information about the behavior of sulfones, nitro compounds, and nitriles is largely qualitative, the only clear indication being of an extremely low basicity.[10,11] Also, data for the protonation behavior in solution of phosphoric amides (of which hexamethylphosphoric triamide is a widely used representative) are rather confusing and do not even provide clear conclusions about the protonation site, although gas-phase data and theoretical calculations seem to favor the O-protonated form.[12] By contrast, the basicity of amides has been extensively investigated,[6,13] although the results for aliphatic amides (with which we are concerned) are obtained with difficulty (see below).

We report in this paper our results on the basic properties of the functional groups SO_2, NO_2, CN, and $CONR_2$, present in some commonly used solvents (e.g., sulfolane, nitromethane, acetonitrile, *N*,*N*-dimethylformamide), and compare them with data for other compounds of interest for their use as solvents.

Results

We have investigated the protonation equilibrium in aqueous sulfuric acid at 25 °C of the following bases: *N*,*N*-dimethylacetamide (DMAC), *N*-methylpyrrolidone (NMPY), *N*,*N*-dimethylformamide (DMF), tetramethylurea (TMU), hexamethylphosphoric triamide (HMPT), nitromethane, acetonitrile, sulfolane, and dimethyl sulfone. None of these has a UV spectrum useful for this kind of study, so all compounds were studied by NMR spectroscopy. Ionization ratios $I = [BH^+]/[B]$ were calculated by eq 1, where ν is the chemical shift of a substrate

$$I = (\nu_B - \nu)/(\nu - \nu_{BH^+}) \qquad (1)$$

signal at a given acidity and ν_B and ν_{BH^+} are the chemical shifts of the free and protonated bases, respectively. All were measured relative to internal trimethylammonium sulfate in order to minimize medium effects,[6,8] and are collected as supplementary material. Values of I were fitted to eq 2, which describes the

$$\log I - \log c_{H^+} = m^*X + pK_{BH^+} \qquad (2)$$

protonation of any weak base, where $\log c_{H^+}$ and X are quantities depending on the acid concentration and may be calculated as

---

(1) Stewart, R. *The Proton: Applications to Organic Chemistry*; Academic: New York, 1985.

(2) Cox, R. A.; Yates, K. *Can. J. Chem.* **1983**, *61*, 2225–2243.

(3) Benoit, R. L.; Louis, C. In *The Chemistry of Nonaqueous Solvents*; Lagowski, J. J., Ed.; Academic: New York, 1978; Vol. V-A, pp 63–117.

(4) Maria, P. C.; Gal, J.-F.; De Franceschi, J.; Fargin, E. *J. Am. Chem. Soc.* **1987**, *109*, 483–492.

(5) Arnett, E. M.; Scorrano, G. *Adv. Phys. Org. Chem.* **1976**, *13*, 83–153.

(6) Bagno, A.; Scorrano, G.; More O'Ferrall, R. A. *Rev. Chem. Intermed.* **1987**, *7*, 313–352.

(7) Perdoncin, G.; Scorrano, G. *J. Am. Chem. Soc.* **1977**, *99*, 6983–6986.

(8) Bagno, A.; Lucchini, V.; Scorrano, G. *Bull. Soc. Chim. Fr.* **1987**, 563–572.

(9) Bagno, A.; Scorrano, G.; Lucchini, V. *Gazz. Chim. Ital.* **1987**, *117*, 475–480.

(10) (a) Hall, S. K.; Robinson, E. A. *Can. J. Chem.* **1964**, *42*, 1113–1122. (b) Olah, G. A.; Ku, A. T.; Olah, J. A. *J. Org. Chem.* **1970**, *35*, 3904–3908.

(11) Olah, G. A.; White, A. M.; O'Brien, D. H. *Chem. Rev.* **1970**, *70*, 561–591.

(12) (a) Skvortsov, N. K.; Tereshchenko, G. F.; Ionin, B. I.; Petrov, A. A. *J. Gen. Chem. USSR* (*Engl. Transl.*) **1976**, *46*, 518–525. (b) Wada, G.; Nakago, S.; Abe, Y. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1381–1385. (c) Matrosov, E. I.; Kryuchkov, A. A.; Nifantyev, E. E.; Kozachenko, A. G.; Kabachnik, M. I. *Phosphorus Sulfur* **1982**, *13*, 69–78. (b) Bollinger, J. C.; Faure, R.; Yvernault, T. *Can. J. Chem.* **1983**, *61*, 328–333. (e) Bollinger, J. C.; Houriet, R.; Kern, C. W.; Perret, D.; Weber, J.; Yvernault, T. *J. Am. Chem. Soc.* **1985**, *107*, 5352–5358.

(13) (a) Cox, R. A.; Yates, K. *Can. J. Chem.* **1981**, *59*, 1560–1567. (b) Cox, R. A.; Druet, L. M.; Klausner, A. E.; Modro, T. A.; Wan, P.; Yates, K. *Can. J. Chem.* **1981**, *59*, 1568–1573.

0002-7863/88/1510-4577$01.50/0

Table I. Protonation Parameters and Acid Concentrations Required To Attain Various Degrees of Protonation

	chem shifts[a]				H_2SO_4, %		
compd	ν_B[b]	ν_{BH^+}[c]	m^*	pK_{BH^+}	half[d]	full[e]	max,[f] %
DMAC	-161.7	93.1	0.62	-0.21 lit -0.28[g]	9.0	55	
NMPY[h]	-96.6	11.4	0.56	-0.71	19.4	64	
	118.9	176.8	0.56	-0.67			
	-15.2	36.2	0.57	-0.76			
			av 0.56	av -0.71			
			lit 0.68[i]	lit -0.71[i]			
DMF[j]	23.6	79.5	0.64	-1.09	25.3	65	
	-7.6	52.4	0.66	-1.19			
	1007.8	1068.4	0.70	-1.11			
			av 0.67	av -1.13 lit -1.2[g]			
TMU	-17.1	31.0 115.1[k]	0.76	-0.14	7.8	50	
HMPT[l]	-57.5	-6.5	0.46	-0.97	26.7	72	
	-1.9	45.2	0.5	-5.5	96.6		77
MeCN[m]	-164.4	19.8					50
$(CH_2)_4SO_2$[m,n]	49.9	140.4					33
	-136.1	-96.3					35
Me_2SO_2[m]	49.7	122.6					24
$MeNO_2$[o]	298.0	356.7					20
Me_2SO[p]			0.42	-1.54	41.9	87	
Me_2CO[q]			0.35	-3.06	75.3		98
MeCOOMe[r]			0.46	-3.90	77.7		99
Et_2O[p]			0.22	-2.39	76.5		93

[a] In hertz at 200 MHz. Negative values denote upfield shifts from internal trimethylammonium sulfate. [b] Chemical shift of free base (in dilute sulfuric acid). [c] Chemical shift of protonated base. This figure represents either the optimized value from experimental data (for compounds for which complete analysis could be carried out) or the experimental value in oleum. [d] Sulfuric acid percent required for half-protonation. [e] Sulfuric acid percent required for >99% protonation. [f] Maximum percent of protonated form in 100% acid if full protonation is not attained. [g] Reference 38. [h] Values from CH_2CO, CH_2N, and CH_3N signals, respectively. [i] Reference 13b. [j] Values from CH_3N (1), CH_3N (2), and CHO signals, respectively. [k] Partially diprotonated. [l] First and second protonation, respectively. [m] See text for an estimate of m^* and pK_{BH^+}. [n] α and β signals, respectively. [o] Maximum percent BH^+ from ref 11. [p] Reference 6. [q] Reference 8. [r] Reference 9.

previously reported.[6,8] In some cases, measurements in 100% acid and oleum containing 13% free SO_3 were also carried out. However, calculation of X in these media involves an extrapolation from the original data set (which reaches 99%)[14] in the region where X changes most rapidly.[6] Given the equivalence $X = -(H_0 + \log c_{H^+})$,[6,15] to compute X we used the H_0 values reported by Gillespie et al.[16] even though they were obtained at a different temperature (22 °C). Values of $\log c_{H^+}$ for oleum were calculated with the assumption that all "free" SO_3 was present as $H_2S_2O_7$, so that $\log c_{H^+}$ could again be calculated[6,8] from the sum of the molar concentrations of H_2SO_4 and $H_2S_2O_7$. For these reasons, these X values are much less reliable than the others, and so will be the derived protonation parameters. Data heavily relying on measurements in oleum, however, were mainly used for establishing trends rather than for computing pK_{BH^+}'s.

The output of the fitting is the slope parameter m^*, which is related to the solvation of BH^+ on a scale relative to nitroanilines,[6] and the thermodynamic pK_{BH^+} value. Both m^* and pK_{BH^+} affect the extent of protonation on changing the acid concentration, high-m^* bases displaying a steeper increase of I on increasing acidity.[5]

Experimental chemical shifts were then plotted vs the H_0 acidity function (from $-H_0 = X + \log c_{H^+}$)[6,15] together with the calculated sigmoid curve obtained from eq 1 and 2, which reveals systematic errors if present.[8]

Amides. These compounds have long been known to be relatively strong bases and to be quantitatively protonated at the oxygen atom in about 60% sulfuric acid.[6,13] However, there has been considerable concern about precise evaluations of their basicity, as the UV and NMR spectra of these compounds are affected by strong medium effects that prevent accurate determinations of ionization ratios.

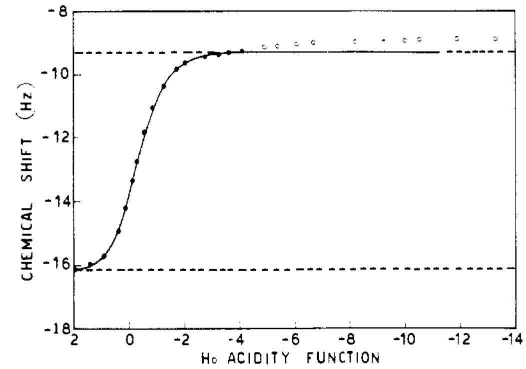


Figure 1. Protonation equilibrium of *N*,*N*-dimethylacetamide. Experimental points marked as open circles were not used in eq 2.

The sigmoid curves for the simple amides DMF, DMAC, and NMPY are well-defined up to ~60% acid, with a chemical shift change of 50–100 Hz at 200 MHz (see Table I). Above 60%, the measured chemical shift is further shifted downfield to an extent between 5 and 20% of the regular change, and no constant value is reached (see for example DMAC, Figure 1). An exception is the signal of the formyl proton of DMF, which is shifted upfield in concentrated acid. This medium effect does not permit an accurate determination of the chemical shift of the protonated base and hence of ionization ratios. Two methods have recently been used to correct for medium effects: one fits the deviations to a solute–solvent interaction model (excess acidity analysis),[13] while the other approaches the solution by statistical means, i.e., principal component analysis (PCA), and its adaptations to the problem.[17] Both require a matrix of experimental responses (chemical shifts or absorbances) sampled at different frequencies and different experimental conditions (acidities); the former method can also treat responses at a single frequency.

---

(14) Johnson, C. D.; Katritzky, A. R.; Shapiro, S. A. *J. Am. Chem. Soc.* **1969**, *91*, 6654–6662.

(15) Lucchini, V.; Modena, G.; Scorrano, G.; Cox, R. A.; Yates, K. *J. Am. Chem. Soc.* **1982**, *104*, 1958–1959.

(16) Gillespie, R. J.; Peel, T. E.; Robinson, E. A. *J. Am. Chem. Soc.* **1971**, *93*, 5083–5087.

(17) (a) Haldna, U.; Murshak, A. *Comput. Chem.* **1984**, *8*, 201–204. (b) Ebber, A.; Haldna, U.; Murshak, A. *Org. React. (Tartu)* **1986**, *23*, 40–50.

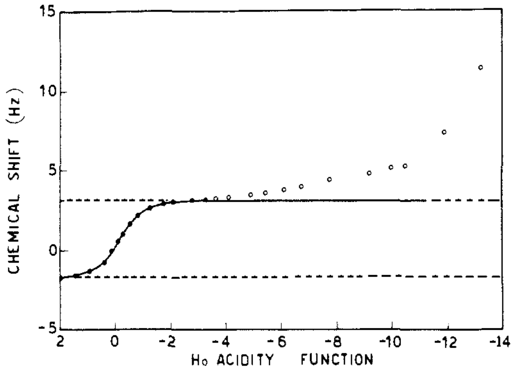


Figure 2. Protonation equilibrium of tetramethylurea (experimental points marked as in Figure 1).

These methods, though powerful, are not well suited for NMR measurements, where often only a single chemical shift is available. PCA is inapplicable in this case, while excess acidity analysis is admittedly of limited precision.[13a] This approach, which relates medium effects to the existence of differently hydrated states, also has a drawback in the case of NMR measurements. Chemical shifts must in fact be measured relative to a standard. The difference between two signals (possibly within the same molecule) will contribute to compensating for the medium effect, giving an empirical correction that can hardly be ascribed to a definite solute–solvent interaction (reflected in the Δm^*_A parameter of ref 13a).

While these two approaches certainly constitute an important contribution to this problem as a whole (also given the remarkable agreement between their results),[17b] it is clear that in this particular case little accuracy will be gained by their use. Therefore, we treated our data by simply eliminating points above ca. 60% acid. This approximation rests on the experimental evidence that most rejected points refer to ionization ratios too large to be accurate and, hence, that the medium affects most exclusively the protonated base.[13] The sigmoid curves obtained in this way are free from systematic errors that were observed if all points were taken into account, thus giving confidence that the remaining data still properly describe the protonation equilibrium.

The m^* and pK_{BH^+} values are collected in Table I. In general, a good agreement was found among the values obtained from different signals. In the case of DMF, the curve of the formyl signal is the worst defined, as overlap with the solvent peak did not allow measurement of its chemical shift between 52 and 55% H_2SO_4. The *N*-methyl protons of DMAC and DMF underwent NMR exchange in the range 0.3–50% H_2SO_4, but those of DMAC collapsed at 5% acid, while those of DMF were only broadened.[18] Since the DMAC chemical shifts would obviously contain contributions from the exchange phenomenon, only the CH_3CO signal was used. On the other hand, DMAC was the least affected by medium effects, with a drift of only 4 Hz up to oleum solutions.

Both TMU and HMPT are largely diprotonated above 100% acid. The protonation curves behave much like the other ones in the initial part, but above 90–98% acid there is a dramatic increase in slope, which can hardly be attributed to medium effects (see Figures 2 and 3). In fact, although no data are available for phosphoramides, ureas are known[11,19] to be diprotonated in FSO_3H-SbF_5. The second sigmoid curve for HMPT is practically complete, and the data could be treated to yield parameters for a second protonation (Table I).

Other Weak Bases. Nitromethane, sulfolane, and acetonitrile are all known to be very weak bases.[10,11] Actually, all these compounds undergo rather small chemical shift changes up to 98% acid. In the oleum solution, all curves show a large additional change, giving chemical shift changes that are comparable to, or higher than, those for amides (Table I). However, the absolute value of the chemical shift change gives little information about the extent of protonation. Rather, the shape of the sigmoid curve should be considered, and this qualitatively shows that these compounds are probably below half-protonation in oleum, as can be seen from Figure 4 for nitromethane. As shown in Figure 4, the curves also suffer from several distortions, probably due to medium effects on the free base. Due to the incompleteness of the curve, and hence to the difficulty in estimating ν_{BH^+}, the equilibrium parameters could be approximately determined for acetonitrile ($m^* = 0.9$, $pK_{BH^+} = -10$) and the two sulfones ($m^* = 0.2$, $pK_{BH^+} = -3.5$) but not for nitromethane.

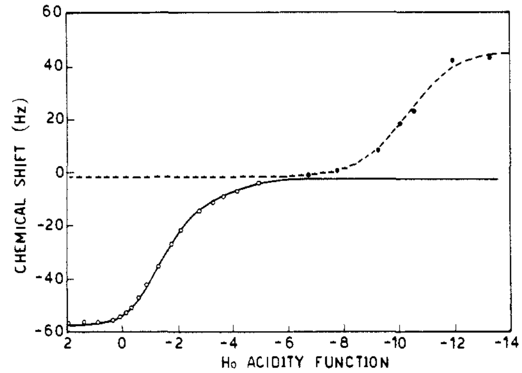


Figure 3. Protonation equilibrium of hexamethylphosphoric triamide. The lower and upper curves correspond to the first and second protonations, respectively.

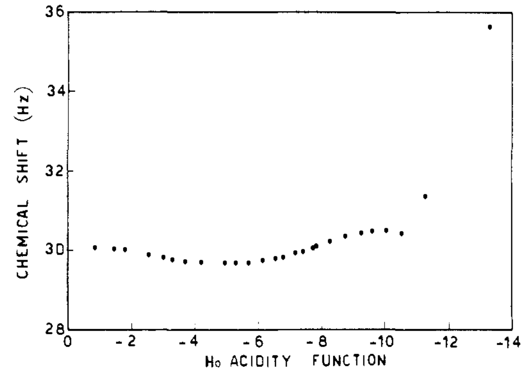


Figure 4. Protonation equilibrium of nitromethane (experimental points only).

Discussion

The most widely quoted reference source for pK_{BH^+}'s has been the 1963 review by Arnett.[20] Many of the data reported therein, and in other tabulations,[21] were, in the words of Arnett and Scorrano, "largely based on the assumption, *now known to be erroneous*, that all weak bases follow the original Hammett acidity function".[5] This, and some other unwarranted extrapolations, make many of the reported pK_{BH^+}'s of little meaning.

The basicity of the organic solvents here discussed appears, for the same reasons, to have been ill-defined so far. Indeed it is not unusual to see some old values of little significance quoted as pK_{BH^+}'s,[22] or a list of different values for the same compound, with discouraging comments.[23] We will first comment, therefore, on the reasons for the differences among the previously reported data, taking dimethyl sulfoxide and *N*-methylpyrrolidone as examples.

Nylen[24] reported $pK_{BH^+} = 0$ for DMSO, on the basis of qualitative experiments in which both dimethyl and diethyl sul-

---

(18) (a) Liler, M. *J. Chem. Soc. B* **1971**, 334–338. (b) McClelland, R. A.; Reynolds, W. F. *J. Chem. Soc., Chem. Commun.* **1974**, 824–825.

(19) Olah, G. A.; White, A. M. *J. Am. Chem. Soc.* **1968**, *90*, 6087–6091.

(20) Arnett, E. M. *Prog. Phys. Org. Chem.* **1963**, *1*, 223–403.

(21) (a) Collumeau, A. *Bull. Soc. Chim. Fr.* **1968**, 5087–5112; (b) Rochester, C. H. *Acidity Functions*; Academic: New York, 1970. (b) Liler, M. *Reaction Mechanisms in Sulfuric Acid*; Academic: New York, 1971.

(22) Pearson, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 6109–6114.

(23) (a) Bordwell, F. G.; Branca, J. C.; Hughes, D. L.; Olmstead, W. N. *J. Org. Chem.* **1980**, *45*, 3305–3313. (b) Bordwell, F. G.; Hughes, D. L. *J. Am. Chem. Soc.* **1986**, *108*, 7300–7309.

(24) Nylen, P. *Z. Anorg. Allg. Chem.* **1941**, *246*, 227–242.

foxide showed no measurable basicity in aqueous solutions. The same value is quoted in Arnett's review.[20] Later, Streuli[25] and Andersen et al.[26] derived aqueous $\mathrm{p}K_{\mathrm{BH}^+}$'s of sulfoxides from titration in nonaqueous media. In this method, a series of amines, whose $\mathrm{p}K_{\mathrm{BH}^+}$'s in water are known, are titrated in acetic anhydride with perchloric acid in glacial acetic acid. The straight line obtained by plotting $\mathrm{p}K_{\mathrm{BH}^+}$'s vs HNP (half-neutralization potentials) might be used, according to these authors, to evaluate $\mathrm{p}K_{\mathrm{BH}^+}$'s for all bases that may be titrated in the same solvent. They reported values of 1.0[25] and 0.91[26] for DMSO. It has been shown, however, that the plot of $\mathrm{p}K_{\mathrm{BH}^+}$ (in water) vs HNP (in acetic anhydride) defines, in the case of sulfoxides, a line with a very different slope from that of amines.[27] This is no surprise, since we now know that water is a highly differentiating solvent for cations, as shown by the energetics of transfer from gas phase to water of different onium ions.[28] Since the equilibrium constant depends upon the relative stabilization of the charged species through solvation,[5,6] we should not expect that the relative basicity remains unchanged when the solvent is changed. A striking example of this behavior is offered by the plots of enthalpy of ionization in $\mathrm{FSO_3H}$ vs $\mathrm{p}K_{\mathrm{BH}^+}$(water).[5] Different families of bases give different correlation lines, the similarity of the two media notwithstanding.

Wada[29] reported $\mathrm{p}K_{\mathrm{BH}^+} = -1.04$, estimated by the changes in the UV spectra of thymol blue and 2-nitroaniline in dilute aqueous $\mathrm{HClO_4}$ upon addition of DMSO. The acid range studied was below 0.5 M, in which DMSO should not be protonated to a significant extent. Indeed, the changes in absorbance caused by addition of DMSO were very small, and we believe that the reported $\mathrm{p}K_{\mathrm{BH}^+}$ refers to equilibria other than protonation.

Direct measurements in aqueous acids were carried out by Haake and Cook,[30] Landini et al.,[27] and Perdoncin and Scorrano.[7] The values reported differ because they were computed in a different way. Haake and Cook plotted log I values vs $-H_0$, and although the line had a slope of 0.62, they quoted as $\mathrm{p}K_{\mathrm{BH}^+}$ the intercept at $H_0 = 0$, i.e., -2.78. If the sulfoxide does not obey the H_0 function (slope different from unity), one cannot get thermodynamic $\mathrm{p}K_{\mathrm{BH}^+}$'s from plots of log I vs $-H_0$. Haake and Cook partially overcame this problem by using the equation $\log I = m(H_0 + \mathrm{p}K_{\mathrm{BH}^+})$ and deriving in this way a $\mathrm{p}K_{\mathrm{BH}^+}$ of -1.72. To solve the problem of finding the correct acidity scale to extrapolate data from the acid solutions to the aqueous standard state, we used the Bunnett–Olsen method,[31] in its first version, using $H_0 + \log c_{\mathrm{H}^+}$ as reference acidity scale[7,27] to define $\mathrm{p}K_{\mathrm{BH}^+}$ and the ϕ parameter, or, more recently,[6] in the equivalent formulation using the X scale, which yields $\mathrm{p}K_{\mathrm{BH}^+}$ and m^* ($=1 - \phi$). The very accurate NMR measurements[7] and the newly defined reference scale give the final values for DMSO at 25 °C: $\mathrm{p}K_{\mathrm{BH}^+} = -1.54$, $m^* = 0.42$.

The values reported for the protonation parameters in aqueous acids have therefore changed (slightly) with time only because the way of computing them from the experimental data has changed with a better understanding of the solvation phenomena that accompany protonation equilibria. There is now a general agreement on the choice of a single reference scale,[2,6,31-33] on the way of building it,[2,6,15,33] and on the meaning to be attributed to both $\mathrm{p}K_{\mathrm{BH}^+}$ and m^*.[6,33]

The case of N-methylpyrrolidone is rather similar. Values of 0.20,[34] -0.2,[35] and -0.3[25] were obtained by titration in nitromethane[34,35] or in acetic anhydride[25] and extrapolated to water as described for DMSO. Studies of changes in the UV spectra of the indicator Metanil Yellow (Acid Yellow) in the presence of NMPY in dilute aqueous acids led[36] to a value of -0.17, with the same shortcomings described for the analogous measurements on DMSO. Virtanen et al.[37] reported $\mathrm{p}K_{\mathrm{BH}^+} = -0.92$ by UV measurements in aqueous sulfuric acid. Treatment of $^{13}\mathrm{C}$ data in aqueous $\mathrm{H_2SO_4}$ according to modern methods finally led Cox et al.[13b] to define the protonation parameters for NMPY as $\mathrm{p}K_{\mathrm{BH}^+} = -0.71$, $m^* = 0.68$, in good agreement with data from this work (see Table I) by $^1\mathrm{H}$ NMR. This shows that good data correctly treated give consistent results even using different experimental techniques in different laboratories.

There is no need to repeat this discussion for all other compounds examined here, and we can now proceed to comment on the results reported in the preceding section.

The structure of O-protonated amides has often been supposed to involve a large delocalization of the positive charge to the N atom.[21c] As a consequence, the number and kind of N substituents is expected to be an important factor affecting the stability and type of solvation of protonated amides, which in turn is semiquantitatively probed by the m^* values.[6]

All the amides dealt with in this paper have a quite similar substitution pattern at nitrogen. Consistently, the m^* values for the simple amides DMF, DMAC, and NMPY are closely similar and in the typical range 0.5–0.6 (cf. also N,N-dimethylbenzamide, which has $m^* = 0.58$).[13b] In contrast, m^* for TMU is substantially higher. This is indicative of diminished solvation, and in fact, the presence of two equivalent resonance contributors in which the positive charge is localized on the two nitrogen atoms accounts for the decrease of interactions with the solvent. In any event, the N atoms remain sufficiently basic to undergo a partial protonation above 98% sulfuric acid. The parameters for this equilibrium, however, could not be determined.

In the case of HMPT, the present data allow one to establish the site of protonation unambiguously. In fact, the first protonation follows a pattern roughly similar to that for common amides, with $m^* = 0.46$. However, this m^* is somewhat lower than values seen before for amides and actually is closer to those for phosphine oxides:[6] Certainly it is rather distant from the typical values for N protonation (usually ≥ 1.0).[6] The large solvation implied by the m^* value confirms that protonation indeed occurs at oxygen[12] and also indicates a minor involvment of the nitrogen atom in delocalizing the charge (i.e., a less efficient interaction $\mathrm{N{-}P{=}OH^+}$ than $\mathrm{N{-}C{=}OH^+}$ in amides). The m^* value (0.47) for the second protonation is also decidedly lower than expected for N protonation, and this is consistent with the increased solvation requirement of the process $\mathrm{BH^+ + H^+ \rightleftharpoons BH_2^{2+}}$ relative to monoprotonation, as might be expected.[6] It must be remarked, however, that the figures for the second protonation depend on the acidity parameters for oleum mixtures and may be somewhat uncertain.

In an extensive study made by Cox et al.[13b] on the protonation of amides, the only compound common to this study is NMPY, whose protonation parameters are, as already noted, within experimental errors of those reported in Table I. Also, if we assume the effect of changing from $\mathrm{CONH_2}$ to $\mathrm{CONMe_2}$ is the same for benzamide and acetamide, we may calculate for DMAC values of $\mathrm{p}K_{\mathrm{BH}^+}$ (-0.19) and m^* (0.59) again within experimental errors of the ones determined in this work.

It is also noticeable that measurements by a conductimetric method[38] in dilute acid solutions on DMAC and DMF have led

---

(25) Streuli, C. A. *Anal. Chem.* **1958**, *30*, 997–1000.

(26) Andersen, K. K.; Edmonds, W. H.; Biasotti, J. B.; Strecker, R. A. *J. Org. Chem.* **1966**, *31*, 2859–2862.

(27) Landini, D.; Modena, G.; Scorrano, G.; Taddei, F. *J. Am. Chem. Soc.* **1969**, *91*, 6703–6707.

(28) Taft, R. W.; Wolf, J. F.; Beauchamp, J. L.; Scorrano, G.; Arnett, E. M. *J. Am. Chem. Soc.* **1978**, *100*, 1240–1249.

(29) Wada, G. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 890–893.

(30) Haake, P.; Cook, R. D. *Tetrahedron Lett.* **1968**, 427–430.

(31) Bunnett, J. F.; Olsen, F. P. *Can. J. Chem.* **1966**, *44*, 1899–1916.

(32) (a) Marziano, N. C.; Cimino, G. M.; Passerini, R. C. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1915–1922. (b) Marziano, N. C.; Traverso, P. G.; Tomasin, A.; Passerini, R. C *J. Chem. Soc., Perkin Trans. 2* **1977**, 306–309. (c) Marziano, N. C.; Traverso, P. G.; Tomasin, A.; Passerini, R. C. *J. Chem. Soc., Perkin Trans. 2* **1977**, 309–313. (d) Passerini, R. C.; Marziano, N. C.; Traverso, P. G. *Gazz. Chim. Ital.* **1975**, *105*, 901–906.

(33) Cox, R. A. *Acc. Chem. Res.* **1987**, *20*, 27–31.

(34) Adelman, R. L. *J. Org. Chem.* **1964**, *29*, 1837–1844.

(35) Streuli, C. A. *Anal. Chem.* **1959**, *31*, 1652–1654.

(36) Breant, M.; Dupin, M. *C. R. Seances Acad. Sci., Ser. C* **1969**, *269*, 306–308.

(37) Olavi, P.; Virtanen, I.; Sodervall, T. *Suom. Kemistil. B.* **1967**, *40*, 337–340.

(38) Grant, H. M.; McTigue, P.; Ward, D. G. *Aust. J. Chem.* **1983**, *36*, 2211–2218.

to pK_{BH^+} values close to ours (see Table I).

Nitriles, sulfones, and nitro compounds are protonated to a rather small extent in our acid system, thus preventing the evaluation of protonation parameters with the usual accuracy. Nevertheless, the estimated $m^* = 0.9$ for acetonitrile is close to the range expected for nitrogen bases ($m^* = 1.0$–1.3).[6] The maximum calculated ionization in 100% acid (ca. 50%) and the estimated pK_{BH^+} of −10 also confirm earlier data.[11]

Sulfones are oxygen bases,[10b] and hence a low m^* value is expected and found (ca. 0.2). This low value, compared to that for sulfoxides (0.42),[6] suggests that the sulfur atom plays a minor role in delocalizing the positive charge in protonated sulfones.

For nitromethane, a low m^* value can be qualitatively inferred from the flatness of the protonation curve, again consistent with oxygen protonation.[11] This compound has been estimated to be 20% protonated in 100% sulfuric acid,[11] which also confirms our results. This extent of protonation, however, is not enough for even a rough pK_{BH^+} estimate.

The data in Table I may be used to establish the relative basicity of organic solvents. Before doing so, however, we must specify the solvent in which we want to compare base strengths. In fact, pK_{BH^+} values refer to the position of equilibrium 3 in water. Going

$$BH^+_w + H_2O_w \rightleftharpoons H_3O^+_w + B_w \qquad (3)$$

from water to H_2SO_4, the degree of protonation increases at different rates depending on the structure of B, as indicated by the different m^* values. We now know that this is due to solvation effects,[6] which obviously depend on the onium ion structure[28,39] and hence on the strength of hydrogen bonding with water.[5,6,28] The consequence of different m^* values can be appreciated by comparing the relative basicities in water and in concentrated acid. To this purpose, we have collected in Table I the sulfuric acid concentration (weight percent) required to attain (a) half-protonation and (b) full protonation (>99%), as well as the maximum percentage of protonated base in 100% acid for those compounds whose protonation is still incomplete in such a solution.

Let us compare the amides, which represent a family of closely related compounds in which, as expected, m^* changes relatively little. We can see that the basicity in water (pK_{BH^+}) follows the order TMU > DMAC > NMPY > HMPT > DMF, whereas above 50% sulfuric acid we have TMU > DMAC > NMPY > DMF > HMPT. The inversion occurs only between HMPT and DMF but is a clear indication of what would happen when comparing compounds with wider changes in structure and m^*'s. One such example can be found in Table I, which shows the relative basicity in water as DMSO > diethyl ether > acetone > methyl acetate; above 80% sulfuric acid this becomes DMSO > methyl acetate ≃ acetone > diethyl ether. We have discussed elsewhere[5,6,40] inversions of relative base strengths for other compounds.

It is obvious that, if an inversion of basicity can occur even on going from water to sulfuric acid, we must take great care in extrapolating data from protonation equilibria studied in water to nonaqueous solvents such as DMSO.[41] In fact, knowing that DMSO in water is more basic (p$K_{BH^+} = -1.54$) than water itself (p$K_{BH^+} = -1.74$)[1,28,42,43] does not help to define equilibrium 4 in

$$BH^+_{DMSO} + DMSO_{DMSO} \rightleftharpoons DMSOH^+_{DMSO} + B_{DMSO} \qquad (4)$$

DMSO, since we still lack the energetics of transfer, for the species involved, from water to DMSO. These data are available for few compounds and indeed show large negative values for the heat of transferring a series of ammonium ions from water to DMSO.[41] If this is due, as suggested,[41] to the formation of stronger hydrogen bonds between BH^+ and DMSO, compared to what happens in water, we can safely predict that the relative strength of bases in water and in DMSO will strongly depend on the structure of BH^+. It comes therefore as no surprise that the relative strength of primary, secondary, and tertiary amines changes on going from water to DMSO.[41]

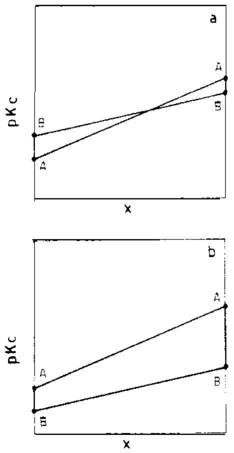


Figure 5. Inversion of relative basicity for compounds A and B having different m^* values ($m^*_A > m^*_B$): (a) B more basic in water; (b) B less basic in water. pK_c = log I − log c_{H^+}.

Although further studies are needed before quantitative estimates can be made, we can already predict, qualitatively, whether an inversion of basicity would occur on going from water to solvents with different solvating power. This is illustrated in Figure 5 for two bases, A and B. The lower solvation requirement for the protonation equilibrium of base A ($m^*_A > m^*_B$; see slopes in Figure 5) makes its protonated form more stable than the corresponding form for base B, in less solvating media (higher X), so that for a fixed X value A becomes more basic than B (Figure 5a). Obviously, if A is more basic than B even in water (Figure 5b), no inversion of basicity is expected on going to higher X, although in principle it might occur in better solvating media than water.

Finally, recalling the above words of caution, we may establish the following basicity scale in aqueous sulfuric acid for dipolar nonhydroxylic organic solvents: amides > DMSO > acetone ≫ acetonitrile > sulfones > nitromethane.

Experimental Section

All compounds studied were commercially available and were purified by distillation if necessary. Sulfuric acid–water solutions and oleum mixtures containing trimethylammonium sulfate were prepared and handled as previously described.[8] NMR spectra were run on a Bruker WP 200 SY spectrometer with 32K data points in acquisition, which yield an accuracy of ca. 0.2 Hz in the measured chemical shift. The solvent band was suppressed by gated decoupling, and the internal temperature was checked by a sample of neat ethylene glycol.

Values of the X function and of log c_{H^+} as a function of acid percent were computed,[6,8] and data processing was carried out[8,9] as previously reported, with the exception of 100% acid and oleum, which exceed the range for which a very accurate H_0 function was determined.[14] For 100% sulfuric acid and oleum mixtures, the H_0 values given by Gillespie et al.[16] as a function of the molar concentration of SO_3 were polynomially interpolated after conversion of the abscissa scale to the more convenient equivalent percent by weight in H_2SO_4, which is the output of titrations. Values of log c_{H^+} were calculated from the sum of the molar concentrations of H_2SO_4 and $H_2S_2O_7$. Molarities were obtained from percent by weight values by means of published density values.[44]

Acknowledgment. Part of this work was written during the tenure of G.S. of a Visiting Professorship at the Université Pierre

---

[39] Bromilow, J.; Abboud, J. L. M.; Lebrilla, C. B.; Taft, R. W.; Scorrano, G.; Lucchini, V. *J. Am. Chem. Soc.* **1981**, *103*, 5448-5453.

[40] Bonvicini, P.; Levi, A.; Lucchini, V.; Modena, G.; Scorrano, G. *J. Am. Chem. Soc.* **1973**, *95*, 5960-5964.

[41] (a) Mucci, A.; Domain, R.; Benoit, R. L. *Can. J. Chem.* **1980**, *58*, 953-958. (b) Benoit, R. L.; McKinnon, M. J.; Bergeron, L. *Can. J. Chem.* **1981**, *59*, 1501-1504. (c) Benoit, R. L.; Boulet, D.; Seguin, L.; Frechette, M. *Can. J. Chem.* **1985**, *63*, 1228-1232.

[42] Bell, R. P. *The Proton in Chemistry*, 2nd ed.; Methuen: London, 1973.

[43] Starkey, R.; Norman, J.; Hintze, M. *J. Chem. Educ.* **1986**, *63*, 473-474.

[44] *CRC Handbook of Chemistry and Physics*, 64th ed.; CRC: Boca Raton, FL, 1983-1984; p F-8.

et Marie Curie, Paris 6, France. The warm hospitality offered by Prof. R. Schaal and his group at ENSCP is acknowledged.

Registry No. DMAC, 127-19-5; TMU, 632-22-4; HMPT, 680-31-9; DMSOO, 67-71-0; SULF, 126-33-0; NMT, 75-52-5; AN, 75-05-8; *N*-methylpyrrolidone, 872-50-4; *N,N*-dimethylformamide, 68-12-2.

Supplementary Material Available: Tables of chemical shift data as a function of sulfuric acid percent by weight (5 pages). Ordering information is given on any current masthead page.

Borderline between E1cB and E2 Mechanisms. Elimination of HCl from Fluorene Derivatives

Alf Thibblin

Contribution from the Institute of Chemistry, University of Uppsala, P.O. Box 531, S-751 21 Uppsala, Sweden. *Received September 2, 1987.*
Revised Manuscript Received February 17, 1988

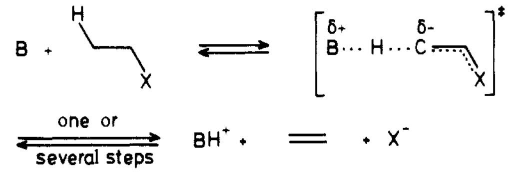
Abstract: The base-promoted elimination of HCl from 9-(2-chloro-2-propyl)fluorene (**2**-Cl) exhibits a kinetic deuterium isotope effect that varies with base strength and solvent character, from a maximum of $k^H/k^D = 8.1$ with HO^- in 25 vol % acetonitrile in water to ~3 in pyridine (neat) at 25 °C. The Brønsted parameter was measured in methanol with substituted quinuclidine bases as $\beta = 0.5$. The large variation in isotope effect could be the result of a varying degree of internal return from a tightly hydrogen-bonded carbanion. However, analysis of β as a function of substrate acidity, leaving group, and α-substituents suggests that the elimination of HCl from the fluorene derivatives is of E2 type. For example, a change in leaving group from AcO^- to Cl^- corresponds to a decrease in β from 0.73 to 0.56 for the 9-(X-methyl)fluorene (**3**-X) series. It is concluded that the reaction coordinate has a relatively large horizontal component corresponding to proton transfer.

There has for a long time been controversy about the position of the mechanistic borderline between stepwise elimination reactions proceeding via a carbanionic intermediate (E1cB) and concerted one-step reactions (E2). What is the dependence of mechanism on structure? For example, is a stepwise mechanism possible for efficient leaving groups? Is there a switch of mechanism on crossing the borderline, i.e., do the mechanisms merge at the borderline, or are both reaction paths employed simultaneously?

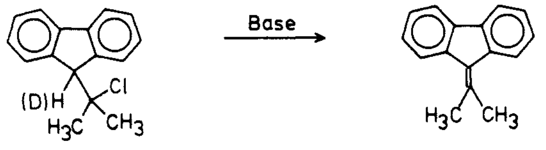
Attempts have been made to distinguish between E2 and irreversible E1cB reactions ($\mathrm{E1cB_I}$) by comparing elimination rates with estimated ionization rates,[1-8] derived, for example, from linear free-energy relationships of Taft type.[4,6] A positive deviation from such a plot has been considered as an indication in favor of the E2 mechanism. This is in accord with the traditional view that E1cB reactions do not involve significant weakening of the bond to the leaving group in the initial proton-abstracting step.[9] Only "inductive" interaction between the leaving group and the carbanionic reaction center is assumed.

We have expressed a different view.[10-13] Thus, the substituent and leaving-group effects are discussed in terms of varying degree of cleavage of the bond to the leaving group in the transition state.

Scheme I

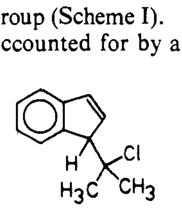


Scheme II

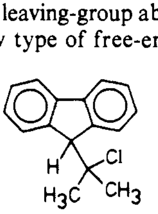


2-Cl **4**

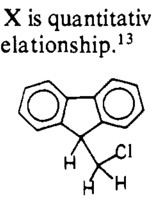
This assistance to proton removal from the electron-withdrawing group X (potential leaving group) results in a unifying view of E2 and E1cB reactions. The hyperconjugative interaction is largest when the base is in a periplanar position relative to the leaving group (Scheme I). The leaving-group ability of X is quantitatively accounted for by a new type of free-energy relationship.[13]



1-Cl



2-Cl



3-Cl

Strong evidence has been presented that the elimination of HCl from **1**-Cl in methanol is a stepwise reaction; the intermediate is a carbanion hydrogen bonded to the conjugate acid of the proton-abstracting base.[11,14,15] It has been concluded that the

---

(1) Hine, J.; Ramsay, O. B. *J. Am. Chem. Soc.* **1962**, *84*, 973–976.

(2) Bordwell, F. G. *Acc. Chem. Res.* **1970**, *3*, 281–290; **1972**, *5*, 374–381.

(3) Cann, P. F.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans. 2* **1974**, *2*, 820–823.

(4) More O'Ferrall, R. A.; Warren, P. J. *J. Chem. Soc., Chem. Commun.* **1975**, 483–484.

(5) Saunders, W. H., Jr. *Acc. Chem. Res.* **1976**, *9*, 19–25.

(6) More O'Ferrall, R. A.; Warren, P. J.; Ward, P. M. *Acta Univ. Ups., Symp. Univ. Ups.* **1978**, *12*, 209–218.

(7) Marshall, D. R.; Thomas, P. J.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1914–1919.

(8) Cavestri, R. C.; Fedor, L. R. *J. Am. Chem. Soc.* **1970**, *92*, 4610–4613. Fedor, L. R.; Glave, W. R. *J. Am. Chem. Soc.* **1971**, *93*, 985–989.

(9) Saunders, W. H., Jr.; Cockerill, A. F. *Mechanisms of Elimination Reactions*; Wiley-Interscience: New York, 1973.

(10) Ahlberg, P. *Chem. Scr.* **1973**, *3*, 183–189.

(11) Thibblin, A.; Ahlberg, P. *J. Am. Chem. Soc.* **1977**, *99*, 7926–7930.

(12) Thibblin, A.; Ahlberg, P. *J. Am. Chem. Soc.* **1979**, *101*, 7311–7317.

(13) Thibblin, A. *Chem. Scr.* **1980**, *15*, 121–127.

(14) Ölwegård, M.; McEwen, I.; Thibblin, A.; Ahlberg, P. *J. Am. Chem. Soc.* **1985**, *107*, 7494–7499.

0002-7863/88/1510-4582$01.50/0