Deprotonation of the *N,N*-Dimethylanilinium Ion. Search for Slow Proton Transfer to Nitrogen[1]

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Abstract: Rates of NH proton exchange in the *N,N*-dimethylanilinium ion in moderately concentrated aqueous perchloric acid at 25° were determined by total line-shape analysis of the methyl group NMR signal. These data give a linear log *k* vs. H_0''' correlation with unit slope and lead to a specific rate of recombination of *N,N*-dimethylaniline with the proton of $(4 \pm 2) \times 10^{10}\ M^{-1}\ \mathrm{sec}^{-1}$. This implies that this reaction is a diffusion-controlled process, and that conjugation of the amine electron pair with the benzene ring has not slowed proton transfer appreciably.

It is an axiom of long standing in mechanistic chemistry that proton transfers to carbon are slow, whereas those involving only nitrogen or oxygen acids and bases are very fast. Quite recently, an important exception to this generally applicable rule was uncovered when it was found that proton transfer to carbon can be very fast provided that the electron pair which receives the proton is localized on a single carbon atom, as in the trichloromethyl anion[2] or the phenylacetylide ion.[3] These substances are rather similar to most nitrogen and oxygen bases where the basic electron pair is also localized on a single atom; they are quite different, on the other hand, from ordinary carbon bases where extensive delocalization of the basic electrons usually takes place.

The observation that electron localization can make proton transfer to carbon fast suggests that delocalization of an unshared pair on nitrogen or oxygen might retard proton transfer to an atom such as this. In order to test this hypothesis, we have begun examining the protonation of amines in which the basic electron pair can conjugate with an adjacent π-electron system. In this initial report of our work, we describe the effects of an adjacent, otherwise unsubstituted benzene ring.

Results

Rates of proton exchange were measured by the NMR line-broadening method. It is convenient for this purpose to use *N,N*-dimethylaniline rather than aniline itself and to observe the methyl group signal under conditions where the amine is essentially completely protonated. As the acidity of the medium, and the rate of exchange of the added proton, is varied, a range will be reached over which the methyl group signal undergoes the familiar transformation from singlet to doublet. Exchange rate constants can be extracted from the detailed shape of the signal in this transition region; this was accomplished in the present work by total line-shape analyis, i.e., by computer fitting of empirical frequency and intensity data to a theoretical function which has the specific rate of exchange as one of its disposable parameters. The results so obtained are listed in Table I.

With *N,N*-dimethylaniline in aqueous solution, this change in shape of the methyl group signal occurs well beyond the pH range in fairly concentrated acid solutions. Acidity functions rather than acid concentrations must therefore be used to analyze the experimental data. Fortunately, an acidity function uniquely appropriate to the present system is available; the H_0''' scale is in fact determined with *N,N*-dimethylanilines and other tertiary amines as the indicator bases.

Table I. Rates of Deprotonation of *N,N*-Dimethylanilinium Ion in Aqueous Perchloric Acid at 25°

Wt % stock acid	$-H_0'''$ Stock	Corr	k, sec^{-1}	η, cP
38.06	3.25	3.06	285	1.155
39.90	3.46	3.31	167, 168, 176	1.202
41.94	3.72	3.52	77.9, 78.5, 80.4	1.260
44.09	4.01	3.82	31.1, 31.3, 31.4	1.338
45.20	4.18	3.95	21.6, 22.1, 22.2	1.391
46.09	4.31	4.12	14.6, 14.6, 14.7	1.420
47.13	4.48	4.26	10.1, 10.2, 10.2	1.481
48.07	4.64	4.40	7.41, 7.45, 7.59, 7.62	1.514
49.10	4.83	4.60	4.44, 4.46, 4.47, 4.48	1.585
50.05	5.00	4.79	2.87, 3.01, 3.07	1.638
52.06	5.41	5.17	1.39, 1.40, 1.42	1.769
54.04	5.84	5.59	0.438, 0.465, 0.543, 0.742	1.917

A minor difficulty still remains, inasmuch as acidity functions are determined using indicators at low concentration, typically 10^{-3} to 10^{-4} *M*, whereas amine concentrations of the order of 0.3 *M* had to be employed in the present work in order to obtain NMR signals sufficiently intense to allow accurate analysis. It is likely that these higher amine concentrations affected the acidity of the solutions, but it is difficult to put a quantitative estimate on the effect. The additional base will, on one hand, reduce the acidity of the medium simply by neutralizing an equivalent amount of acid. The amine salt thus formed, however, may restore part of the acid strength lost through its effect on the activity of water; such behavior is commonly observed for inorganic salts,[4] but little is known about ammonium ions such as that formed here.

Two different estimates of the actual H_0''' values of the kinetic solutions were therefore made. One of these is simply the literature value[5] appropriate to the stock acid solution before any amine is added; this is listed as "Stock" in Table I. The other estimate, labeled "Corr" in this table, is the H_0''' value of the stock solution with an amount of acid removed exactly equivalent to the quantity of amine added. It is likely, on the basis of the reasons presented above, that these two estimates represent the extremes of the effect of the added base. Fortunately, the difference between them is small (ca. 0.2 H_0''' unit), too small to have any material effect on the arguments presented below.

Discussion

The specific rates of NH proton exchange in the *N,N*-dimethylanilinium ion measured here are shown plotted logarithmically against $-H_0'''$ in Figure 1. It may be seen that this acidity function does correlate these rate data quite well. It makes little difference, moreover, whether or not the H_0''' values are corrected for the rather high amine

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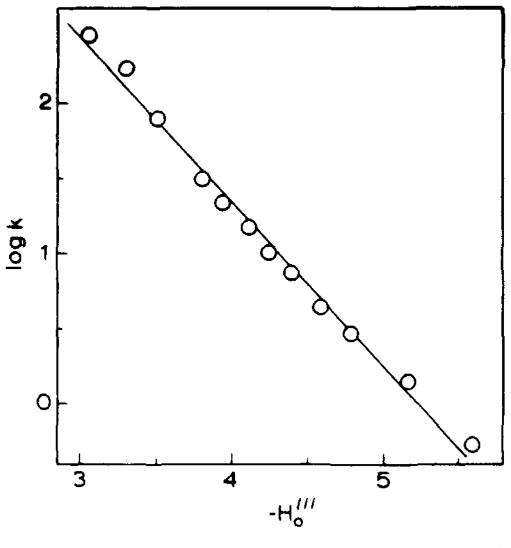
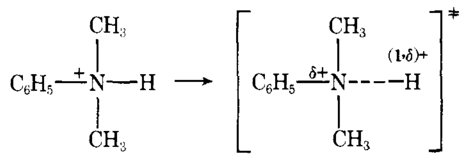


Figure 1. Correlation of specific rates of deprotonation of *N,N*-dimethylanilinium ion with H_0''' using H_0''' values corrected as described in the text.

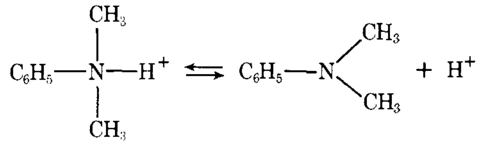
concentrations (0.3 *M*) used in the kinetic measurements; with uncorrected values, log $k = (5.81 \pm 0.13) + (1.06 \pm 0.03)H_0'''$, r (correlation coefficient) = 0.997; and, making corrections as outlined above, log $k = (5.72 \pm 0.13) + (1.09 \pm 0.03)\ H_0'''$, $r = 0.996$. The differences between the parameters in these two sets are less than their experimental uncertainty.

More significant than the goodness of this correlation, however, is the fact that the slope of the relationship is approximately unity. This implies that the medium effect on the kinetic process, eq 1, is equal to the medium effect on



$$\mathrm{C_6H_5{-}\overset{+}{N}(CH_3)_2{-}H} \longrightarrow \left[\mathrm{C_6H_5{-}\overset{\delta+}{N}(CH_3)_2{-}{-}{-}{-}\overset{(1\text{-}\delta)+}{H}}\right]^{\ddagger} \qquad (1)$$

the equilibrium reaction, eq 2. Since the initial states of the



$$\mathrm{C_6H_5{-}N(CH_3)_2{-}H^+} \rightleftharpoons \mathrm{C_6H_5{-}N(CH_3)_2} + \mathrm{H^+} \qquad (2)$$

two processes are the same, this requires the transition state of the kinetic process to be similar to the final state of the equilibrium reaction. The proton is of course fully removed from the aniline molecule in the final state of the equilibrium reaction, and it must therefore also be fully removed in the transition state of the kinetic process (i.e., $\delta = 0$ in eq 1). In other words, proton transfer is complete by the time the slow step of the kinetic process is reached. This implies that proton transfer is rapid, and the subsequent separation of proton-transfer products, which must take place in order for exchange to occur, is slow; i.e., that the process is diffusion controlled. This mechanism is similar to that which applies to the deprotonation of ammonium ions derived from purely aliphatic amines in much less concentrated acids.[6]

Additional evidence supporting this conclusion may be obtained by extrapolating the kinetic data down to dilute acid solution. When this is done using the log k-H_0''' correlation, $k = (6 \pm 2) \times 10^5\ \mathrm{sec^{-1}}$ is obtained. This, when combined with the acidity constant of the *N,N*-dimethylanilinium ion, $\mathrm{p}K_\mathrm{a} = 5.07$,[7] gives $(7 \pm 2) \times 10^{10}\ M^{-1}\ \mathrm{sec^{-1}}$ as the specific rate of protonation of *N,N*-dimethylaniline. This is the approximate value expected for a diffusion-controlled process in aqueous solution at 25°.

Diffusion-controlled reactions should, of course, be sensitive to changes in the viscosity of the medium in which they occur. In the present case, the viscosity increases by a factor of nearly 2 over the range of perchloric acid solutions used (Table I), and it is of interest to see what effect this has on the results obtained. This may be done by multiplying observed rate constants by the factor η/η_0, where η is the viscosity of the solution in which the rate measurement was made and η_0 is the viscosity of pure water at 25°. With this correction, the correlations with H_0''' become much improved in that their slopes are now exactly unity: log $k(\eta/\eta_0) = (5.65 \pm 0.12) + (0.97 \pm 0.03)\ H_0'''$, $r = 0.996$ using uncorrected H_0''' values; and, with corrections to H_0''' made as before, log $k\ (\eta/\eta_0) = (5.57 \pm 0.13) + (1.00 \pm 0.03)\ H_0'''$, $r = 0.996$. These viscosity corrections have no material effect on the rate constant for recombination of *N,N*-dimethylaniline with a proton; the value now is $4 \pm 2 \times 10^{10}\ M^{-1}\ \mathrm{sec^{-1}}$, which is still well within the range expected for a diffusion-controlled process in aqueous solution at 25°.

Thus, it seems clear that the protonation of *N,N*-dimethylaniline is a diffusion-controlled process, and that the proton-transfer step is a very fast reaction. This is similar to the situation for ordinary aliphatic amines whose basic electron pairs cannot be delocalized into a benzene ring. This result, in retrospect, is not altogether surprising, for the amine electron pair in aniline is not very strongly delocalized; this is evident, for example, from the fact that the nitrogen atom of aniline is pyramidal,[8] and that the resonance energy of the molecule, over and above that of an unsubstituted benzene ring, is only of the order of 5 kcal/mol.[9] We are currently engaged in determining whether the introduction of additional conjugating groups, such as nitro, into the para position of *N,N*-dimethylaniline can alter the situation sufficiently to make proton transfer to nitrogen here slow.

Experimental Section

Materials. *N,N*-Dimethylaniline (Matheson Coleman and Bell, free from monomethyl) was distilled at reduced pressure, bp 76–77° (13 mm); it was then immediately frozen and was stored in that state until just before use. Stock acid solutions were prepared from reagent grade perchloric acid (J. T. Baker and Co.) and distilled water; they were made to approximate strength by weight, and the exact concentrations were then determined by titrating weighed aliquots with standard base.

Solutions for kinetic measurements were prepared by weight, using approximately 1.0 g of stock acid to 0.03 g of *N,N*-dimethylaniline.

Kinetics. Spectra were taken with a Varian A-60 spectrometer whose probe temperature was maintained at 25°, as measured by the Van Geet methanol method.[10] Scans were recorded at a sweep rate of 0.1 Hz/sec using an rf power no greater than 0.08 mG. Standard Varian chart paper was employed, with frequency calibrations supplied by the side-band oscillator method. At least three scans were made for each sample; the range covered varied from 10 Hz for singlets to 20 Hz for doublets.

Pairs of intensity and frequency values (43 for singlets and 48 for doublets) were read from these spectra by eye; readings were spaced more closely together along the steeper portions of the curves. These data were then fitted by computer, using nonlinear least-squares analysis, to the Gutowsky-Holm line-shape equation.[11] This equation relates the signal intensity to its frequency in terms of six parameters: the baseline, an intensity scale factor, the midpoint of the signal, the natural line width, the coupling constant, and the specific rate of exchange. Our least-squares routine would not converge if all six of these parameters were left disposable, and two, the coupling constant and the natural line width, were therefore supplied as known constants. A value of the coupling constant, $J = 5.30$ Hz, was obtained by direct measurement on solutions sufficiently acidic to give limiting slow-exchange NMR spectra, and this was then applied directly to the less concentrated solutions. The natural line width, on the other hand, can be expected to vary with acid concentration through its dependence on the viscosity of the medium, which changes appreciably over the range of acidities used. A relationship between natural line width, W, and viscosity, η, of the form $W = a + b\eta/T$,[12] where T is absolute temperature, and a and b are constants, was therefore set up using data (line widths) measured over a range of temperature and viscosity in solutions giving limiting fast and slow-exchange NMR spectra. This expression, $W = (0.35 \pm 0.03) + (34 \pm 2)\eta/\mathrm{T}$, was then used to calculate values of W appropriate to the solutions used for the kinetic measurements. Viscosities were interpolated for this purpose by fitting literature data[13] to a polynomial expression in wt % acid and then using this function to calculate the required values.

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Extension of the H_A Acidity Function into Oleum Mixtures[1]

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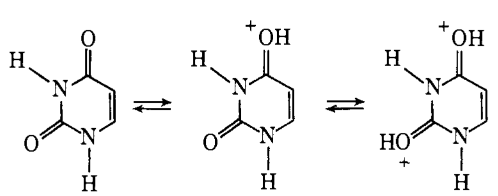
Abstract: The H_A acidity function has been extended from 93% aqueous sulfuric acid to 17% fuming sulfuric acid using weakly basic pyrimidine monocations as indicators. Ionization ratios were determined from ^{1}H NMR chemical shifts at 25°. The H_A and H_0 acidity functions are briefly compared. The effects of methyl substitution at nitrogen and oxygen are discussed.

Compounds containing -C(=O)N< functional groups (amides, ureas, pyrimidines, purines, etc.) constitute several classes of biologically important compounds. Yates and coworkers[3] developed the amide acidity function, H_A, in order to relate basicities of amide moieties in aqueous sulfuric acid. It was later found that other functional groups follow H_A during protonation. Included are the first protonation of some 2,4-dioxopyrimidines,[4] urea[5] (at the oxygen atom), and N-oxides.[6] In fact, the latter class of compounds has been used to extend H_A from 80 to 93% H_2SO_4.[6] Although amides and N-oxides are quite different structurally, they apparently form a valid set of H_A indicators when judged by the criterion that the ratio of activity coefficients is unity ($\gamma_{NO}\gamma_{HA^+}/\gamma_{NOH^+}\gamma_A$) in the region of overlap.

In connection with our work on the protonation of uracil and related derivatives, it became necessary to extend H_A into the oleum region. In general, 2,4-dioxopyrimidines protonate sequentially at the 4-oxo and 2-oxo moieties.[7,8] The strength of the acid required for the first protonation can vary considerably, depending on substitution,[4] and the second protonation requires an acid stronger than 90% H_2SO_4. The only acidity function, H_0, which has been extended far beyond 90% H_2SO_4[9] is unsatisfactory for 2,4-dioxopyrimidines.



In searching for a series of indicators with which to extend H_A, the second protonation of 2,4-dioxopyrimidines appeared to be a feasible choice. Both oxo groups are "urea-like" and should be weakly basic since the pyrimidine is already charged as a result of the first protonation. In this paper, we report an extension of the H_A acidity function from 93% H_2SO_4 to 17% (by weight) fuming H_2SO_4. The five pyrimidines used in this study form a valid set of indicators when judged by normal overlap behavior. Although there is always concern when different functional groups are used to construct an acidity function, the overlap of indicators whose structures involve amides, N-oxides, and monoprotonated pyrimidines appears to be satisfactory. Our results for H_A are compared with those recently obtained for H_0 by Gillespie and coworkers.[9]

Experimental Section

Indicators. Uracil and thymine are commercially available from Aldrich and were used without further purification. 2-Methoxy-4-oxopyrimidine,[10] 4-methoxy-2-oxopyrimidine,[11] and 1,3-dimethyluracil[12] were available from a previous study.[13] The ^{1}H NMR spectra of the pyrimidines were similar to published spectra.[10]

Acid Solutions. The 9.5-96 wt % solutions were prepared by dilution of Baker Analyzed Reagent Grade sulfuric acid (~96%). Concentrations of H_2SO_4 (±0.2%) were calculated by averaging the values derived from 4 to 5 density measurements. For acids stronger than 50 wt % H_2SO_4, the samples for density measurements were diluted by a known amount (approximately 50 wt % H_2SO_4) before the density determinations were made. The weight percent of H_2SO_4 was determined from the density-composition data in the International Critical Tables.[14]

Solutions of 96 wt % H_2SO_4 to 17 wt % fuming H_2SO_4 were