Base-Catalyzed Proton Transfer from an Intramolecularly Hydrogen-Bonded Naphthylammonium Ion in 70% Me₂SO–H₂O (v/v)

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Abstract: Chemical relaxation of the proton transfer equilibrium involving 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene and substituted phenol buffers in 70% Me₂SO–H₂O (v/v) is exceptionally slow with relaxation times in the millisecond range. The dependence of reciprocal relaxation time on buffer concentration is linear at low buffer concentration but at high concentration becomes curved. The curvature is explained quantitatively in terms of an association between the acidic and basic components of the buffer using association constants derived from a study of the phenolate ion catalyzed hydrolyses of *p*-nitrophenyl benzoate and *p*-nitrophenyl *p*-methoxybenzoate under the same conditions. The variation of the first-order rate coefficient for hydrolysis of the esters with buffer concentration is similar to the variation of the reciprocal relaxation time for the proton transfer reaction. From the values of the relaxation times at low buffer concentration where association is less important, catalytic coefficients for proton transfer between 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene and four substituted phenols have been calculated. The variation of the catalytic coefficients with the acid strength of the phenols identifies the mechanism of removal of the intramolecularly hydrogen-bonded proton from protonated 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene as consisting of a rapid equilibrium to give a low concentration of a nonintramolecularly hydrogen-bonded form of the protonated amine followed by attack of phenolate ion on this species. The overall proton transfer occurs slowly because of the strong intramolecular hydrogen bond in the protonated amine.
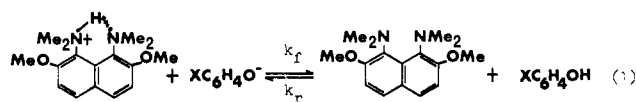
Previously we have studied[1] general base-catalyzed proton transfer from a substituted salicylate ion in aqueous solution using the temperature-jump method. From the variation of the rate coefficient for proton transfer with the strength of the attacking base it was concluded that proton removal from the intramolecularly hydrogen-bonded acid occurs by a two-step process. The first step involves a rapid equilibrium between hydrogen-bonded and non-hydrogen-bonded forms of the acid and the second step consists of base attack on the non-hydrogen-bonded species. This latter step is rate limiting and the non-hydrogen-bonded species is present in low concentration. A single-step attack by base on the hydrogen-bonded proton was not compatible with the results. The object of the present work was to apply the same mechanistic test to the base-catalyzed ionization of protonated 1,8-diaminonaphthalenes.

In water and dioxane–water mixtures containing buffers, general base catalysis was not detected in the ionization of the protonated forms of 1,8-bis(dimethylamino)naphthalene (**1**) and 1,8-bis(diethylamino)naphthalene (**2**).[2] The hydroxide
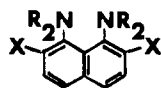
1	R = Me, X = H
2	R = Et, X = H
3	R = Me, X = OMe
4	R = Et, X = OMe

ion catalyzed reaction was predominant. Reaction of the protonated forms of **1** and **2** with hydroxide ion is thermodynamically favorable but occurs with rate coefficients which are several orders of magnitude below the diffusion limit. The presence of a strong intramolecular hydrogen bond in the protonated amines could account for this and may also explain the exceptionally high basicity of the amines[3] (and low acidity of the conjugate acids), pK_a = 12.3[3] and 13.3[2] for **1** and **2**, respectively. Introduction of methoxy groups into the 2 and 7 positions brings about a large increase in base strength (pK_a = ca. 16.3 and 16.6 for **3** and **4**, respectively) and considerably reduces the rates of proton transfer from the ammonium ions

to hydroxide ion.[4] We have now studied general base catalyzed proton transfer from the protonated forms of **2** and **3** in 70% Me₂SO–H₂O (v/v) containing substituted phenol buffers. The choice of solvent and buffer was made on the basis of a recent temperature-jump study by Bernasconi[5] under these conditions. Evidence was presented to show that buffer association was not significant. In our work we have found that buffer association in 70% Me₂SO–H₂O (v/v) cannot be neglected. From an analysis of results at low buffer concentrations the mechanism of proton removal from the protonated forms of 1,8-diaminonaphthalenes has been identified.

Results

Kinetics of Proton Transfer. Chemical relaxation times for equilibrium 1 were measured in 70% Me₂SO–H₂O (v/v) at 25.0 °C using the temperature-jump method. Experiments
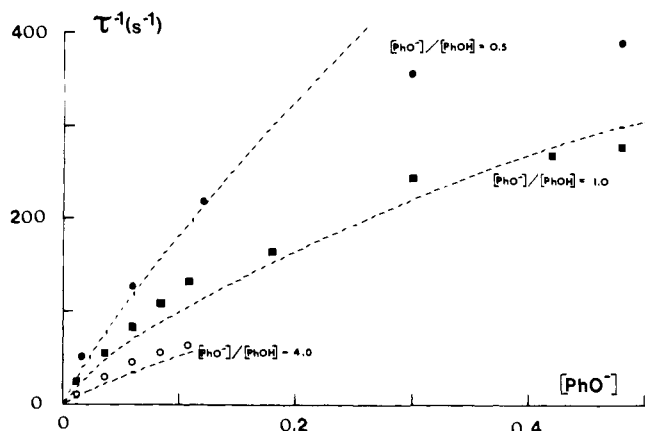
were carried out at different buffer concentrations (0.01–0.5 M) and the ionic strength was maintained at 0.5 M by addition of tetramethylammonium chloride. The concentration of 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene was ca. 2×10^{-4} M. The dependence of reciprocal relaxation time on buffer concentration for phenol–phenolate buffers at three buffer ratios is shown in Figure 1. The points are experimental values and the dashed lines are theoretical plots which are derived in the Discussion Section. A strongly curved dependence of reciprocal relaxation time on concentration was also observed in 2-methylphenol, 4-chlorophenol, and 2-chlorophenol buffers. Measurements were made at several buffer ratios which were chosen so that the amplitudes of the chemical relaxations were large. Figure 2 shows the results obtained with 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene and 1,8-bis(diethylamino)naphthalene in 2-chlorophenol buffers. The relaxations observed in this study are exceptionally slow; the most rapid relaxation occurred with a relaxation time greater than 2×10^{-3} s. Proton transfers between oxygen and nitrogen acids and bases normally occur much more rapidly than this; for example,[6] the equilibrium involving propylamine
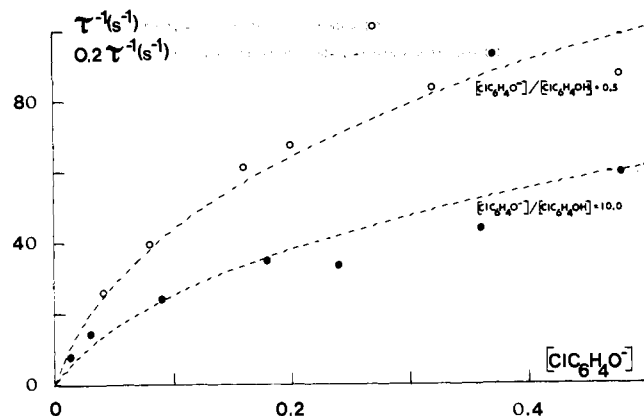
Figure 1. Dependence of reciprocal relaxation time on buffer concentration for equilibration of 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene in 70% Me_2SO-H_2O (v/v) containing phenol buffers.

Figure 2. Dependence of reciprocal relaxation time on buffer concentration for equilibration of 1,8-bis(diethylamino)naphthalene (O) and 1,8-bis-(dimethylamino)-2,7-dimethoxynaphthalene (●) in 70% Me_2SO-H_2O (v/v) containing 2-chlorophenol buffers.

Table I. Kinetic and Equilibrium Results in 70% Me_2SO-H_2O (v/v)

	$pK_a{}^a$	$pK_a{}^b$	K^c	$k_f,{}^c$ M^{-1} s^{-1}	$k_r,{}^c$ M^{-1} s^{-1}
	1,8-Bis(dimethylamino)-2,7-dimethoxynaphthalene				
2-methylphenol	10.28		0.50 ± 0.03	160 ± 30	320 ± 50
phenol	9.99	12.49	0.23 ± 0.02	250 ± 100	1100 ± 300
4-chlorophenol	9.38	11.47	0.09 ± 0.03	300 ± 50	3300 ± 500
2-chlorophenol	8.48		0.018 ± 0.005	350 ± 100	19000 ± 4000
	1,8-Bis(diethylamino)naphthalene				
2-chlorophenol	8.48		11 ± 1	860 ± 100	75 ± 20

^{a} Aqueous solution at infinite dilution, 25.0 °C (ref 8). ^{b} 70% Me_2SO-H_2O (v/v), ionic strength 0.5 M, 20.0 °C (ref 5 and 7). ^{c} 70% Me_2SO-H_2O (v/v), ionic strength 0.5 M, 25.0 °C (this work).

and phenol at concentrations similar to those used here occurs with a relaxation time of ca. 2×10^{-9} s in water.

Previously, for proton transfer involving 1,8-bis(dimethylamino)- and 1,8-bis(diethylamino)naphthalene, buffer catalysis was unobservable[2a] in water and 20% dioxane-water (v/v) containing phosphate or trifluoroethanol buffers. In these solutions the concentration of hydroxide ion is high and the observed chemical relaxation is due to reaction with hydroxide ion. The hydroxide ion concentration in 70% Me_2SO-H_2O (v/v) containing phenol buffers is very low[5,7] and general base catalysis is easily observed.

Equilibrium Studies. Equilibrium constants for reaction 1 were obtained by spectrophotometric measurements under conditions which were similar to those used in the kinetic work. However, lower buffer concentrations were used, usually in the range 0.01-0.10 M. For each substituted phenol the equilibrium constant K was determined at several buffer ratios and the mean values are given in Table I. A value for the equilibrium constant between 1,8-bis(diethylamino)naphthalene and 2-chlorophenol is also shown in Table I.

A pK_a of 16.3 has been estimated for the protonated form of 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene in aqueous solution.[4] This extremely low acidity means that a chemical relaxation in aqueous solution containing phenol buffers would not be observable since the amplitude of the chemical relaxation for an equilibrium of the type shown in (1) is small except when the acid is about half-dissociated. In aqueous solution suitable buffers with pK_a around 16 are not available and in any case it is unlikely that under these conditions general base catalysis would be observable since the largest contribution to the rate would be made by the hydroxide ion catalyzed reaction. In 70% Me_2SO-H_2O (v/v) containing phenol buffers, conditions are more favorable. The pK_a values of substituted phenols are ca. 2 units higher in 70% Me_2SO-H_2O (v/v) than in aqueous solution (see Table I). Since the

pK_a value of 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene is lowered in going from H_2O to 70% Me_2SO-H_2O (v/v),[9] dissociation is about half-complete in 70% Me_2SO-H_2O (v/v) containing phenol buffers with suitable buffer ratios and the amplitude of the chemical relaxation after a temperature-jump is large. The difference in equilibrium constants for reaction of 1,8-bis(diethylamino)naphthalene and 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene with 2-chlorophenol is compatible with the pK_a values of the amines measured in the absence of buffers.[4]

Hydrolysis of Esters in 70% Me_2SO-H_2O (v/v). To determine whether buffer association or some medium effect is important in 70% Me_2SO-H_2O (v/v) containing high concentrations of phenol buffers, the base-catalyzed hydrolysis of several p-nitrophenyl esters was investigated under these conditions. The reactions of p-nitrophenyl benzoate and p-nitrophenyl p-methoxybenzoate occurred at convenient rates and were followed by observing the increase in absorbance at 417 nm due to the liberation of p-nitrophenolate ion. The concentration of esters was initially ca. 5×10^{-5} M in the presence of excess phenol buffer (0.01-0.5 M) and under these conditions formation of p-nitrophenolate ion was accurately first order. The reactions were expected to be first order in the basic component of the buffer but this was not observed. Results for the hydrolysis of p-nitrophenyl p-methoxybenzoate in phenol buffers and for p-nitrophenyl benzoate in 2-chlorophenol buffers are shown in Figures 3 and 4, respectively, in which the points are experimental values. The curvature of the plots can be explained assuming that the basic form of the buffer is partly complexed in a form which is ineffective in catalyzing the hydrolysis reaction. The dotted lines in Figures 3 and 4 are constructed assuming a 1:1 association between substituted phenol and phenolate ion and this will be described in the Discussion Section. In the absence of buffer association or other medium effect the rate coefficients for base-catalyzed
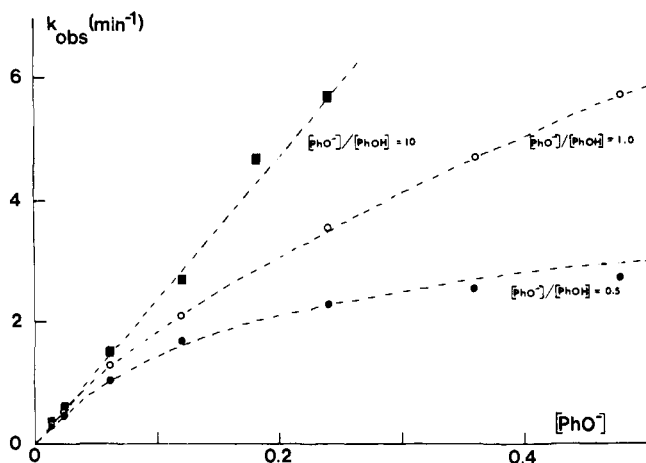
Figure 3. Variation of rate coefficient with buffer concentration for the hydrolysis of p-nitrophenyl p-methoxybenzoate in 70% Me_2SO-H_2O (v/v) containing phenol buffers.

Figure 4. Variation of rate coefficient with buffer concentration for the hydrolysis of p-nitrophenyl benzoate in 70% Me_2SO-H_2O (v/v) containing 2-chlorophenol buffers.

ester hydrolysis would be expected to lie on the same straight line in Figures 3 or 4 irrespective of buffer ratio. This is not observed except at buffer concentrations below ca. 0.05 M. At high ratios of buffer base to buffer acid, where only small amounts of buffer base are removed by complexation, a linear plot is obtained. However, as the buffer ratio is lowered the observed rate coefficients at a fixed stoichiometric concentration of buffer base progressively decrease. Also at low buffer ratios the plots of rate coefficient against buffer concentration are strongly curved.
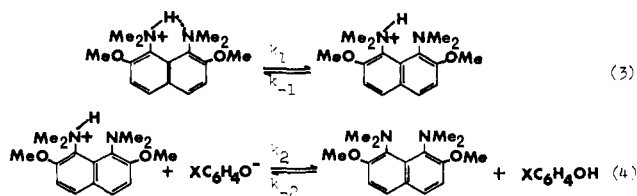
Discussion

Base-Catalyzed Proton Transfer. The purpose of this section is to provide an explanation for the curved plots of reciprocal relaxation time against buffer concentration. For equilibrium 1 with buffer in excess and at fixed buffer ratio the reciprocal relaxation time would be expected to increase linearly with buffer concentration. This is shown in eq 2 in which x is the buffer ratio $(x = [XC_6H_4O^-]/[XC_6H_4OH])$.

$$1/\tau = (k_f + k_r/x)[XC_6H_4O^-] \qquad (2)$$

The hydroxide ion concentration in these solutions is very low[7] and hydroxide ion makes a negligible contribution to the rate. Two explanations for the curvature in Figures 1 and 2 will be put forward and evidence will be presented favoring one of the explanations.

Two-Step Proton Transfer. We have previously shown that proton transfer from an intramolecularly hydrogen-bonded salicylate ion occurs by a two-step process.[1] The same mechanism is shown for proton transfer from the protonated form of 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene in eq 3 and 4. For this mechanism in which the non-hydrogen-

bonded species is present in low concentration the relaxation time under our conditions is given by eq 5 which predicts that at low buffer concentration $(k_2[XC_6H_4O^-] < k_{-1})$ the reciprocal relaxation time will be linearly dependent on buffer concentration but will become independent of buffer at high
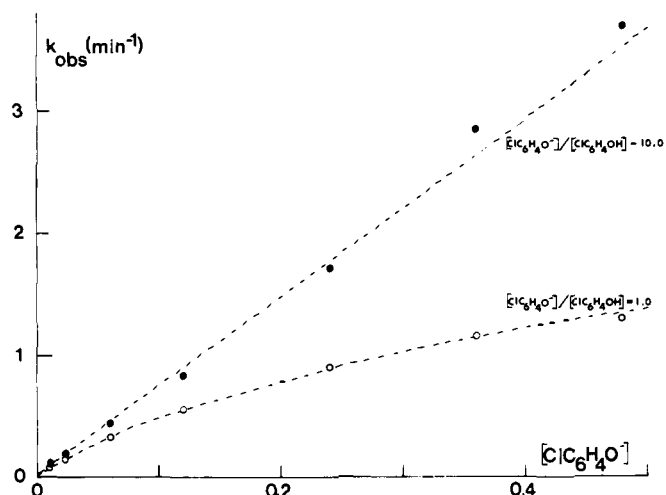
concentrations $(k_2[XC_6H_4O^-] > k_{-1}$.

$$1/\tau = (k_1k_2 + k_{-1}k_{-2}/x)[XC_6H_4O^-]/(k_{-1} + k_2[XC_6H_4O^-]) \qquad (5)$$

This occurs because the rate-determining step changes from step 4 to step 3 as the buffer concentration is increased. Hence the mechanism shown in eq 3 and 4 will explain the observed kinetic behavior. For each of the buffers at different buffer ratios a reasonable fit of eq 5 to the experimental results was obtained. In order to evaluate all the rate coefficients in eq 5 from the fit to the experimental results a measured value for the equilibrium constant for reaction 1 was needed and it was necessary to assume a value for k_2. If the non-hydrogen-bonded form of protonated 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene behaves like a normal protonated amine,[6] the rate coefficient for the thermodynamically favorable proton transfer from this species to each of the phenolate ions will have the same diffusion-limited value $(k_2 = 1 \times 10^{10} M^{-1} s^{-1})$. A different choice for the value of k_2 does not affect the fit of eq 5 to the experimental results, but the choice for k_2 does change the result obtained for k_{-1}. From the fitting procedure it was found that quite similar values for k_1 and k_{-1} were obtained from results in the different buffers and this is expected since step 3 does not involve buffer. The values obtained were $k_1 = 60 \pm 20 s^{-1}$ and $k_{-1} = 2.1 \pm 0.3 \times 10^9 s^{-1}$. The reverse step of reaction 4 involves thermodynamically unfavorable protonation of the amine and the rate coefficient (k_{-2}) is expected to increase linearly with the acid strength of the phenol. This is the result we observe; the overall equilibrium constant for reaction 1 which is inversely related to the acid strength of the phenol decreases along the series X = 2-Me > H > 4-Cl > 2-Cl as the value of k_{-2} increases (see Table I).

Although the mechanism in eq 3 and 4 will explain the dependence of reciprocal relaxation time on buffer concentration, the value of the rate coefficient k_{-1} which results from the fit of eq 5 to the experimental results seems unusually low for the formation of an intramolecular hydrogen bond. A lower value than this has been claimed[10] for hydrogen-bond formation in a salicylate ion but the interpretation of the experimental results has been questioned.[11] An alternative explanation of our results involves a concentration-dependent medium effect or association involving the base catalyst.

Buffer Association. Our choice of solvent and buffer system for study of these proton-transfer reactions was suggested by a recent temperature-jump study made under these conditions.[5] Evidence based on pH measurements and on an analysis

of kinetic results was presented to show that buffer association was not significant. However, a possible explanation of the curvature in Figures 1 and 2 is that association occurs between buffer acid and base species and at high buffer concentrations a large fraction of the buffer base is present in an unreactive and complexed form. Our initial aim was to find a simple proton transfer (for example, the ionization of a carbon acid) which could be studied under these conditions to test for buffer association but a suitable reaction could not be found. However, the results of the hydrolysis of *p*-nitrophenyl benzoate and *p*-nitrophenyl *p*-methoxybenzoate given in Figures 3 and 4 show that buffer association does occur and it is the purpose of this section to decide whether buffer association can account for the curvature in Figures 1 and 2.

For the hydrolysis of *p*-nitrophenyl *p*-methoxybenzoate in phenol/phenolate buffers, it is assumed that rate expression (eq 6) applies where k_{obsd} is the measured first-order rate coefficient for hydrolysis and the concentration term refers to the concentration of noncomplexed phenolate ion. It is also assumed that phenolate ions and phenol molecules are associated according to eq 7 and 8 and that the associated species shows negligible catalytic effect. The assumption is also made that no other medium effect arises when high concentrations of phenol buffer are introduced into 70% Me_2SO-H_2O (v/v).

$$-d[ester]/dt = k_{obsd}[ester] = k_{cat.}[ester][XC_6H_4O^-] \quad (6)$$

$$XC_6H_4O^- + XC_6H_4OH \rightleftharpoons XC_6H_4O^- \ldots HOC_6H_4X \quad (7)$$
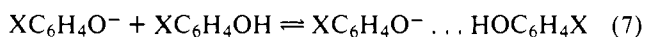
$$K_{assoc} = [XC_6H_4O^- \ldots HOC_6H_4X]/ \\ [XC_6H_4O^-][XC_6H_4OH] \quad (8)$$

A value of $k_{cat.}$ = 25.0 M^{-1} min^{-1} was calculated for the phenolate ion catalyzed hydrolysis of *p*-nitrophenyl *p*-methoxybenzoate from the results at high buffer ratio ($[C_6H_5O^-]/[C_6H_5OH]$ = 10). Under these conditions, since phenolate ion is present in vast excess over phenol, only a small fraction of the base will be removed by complexation. The experimental results at buffer ratios 1.0 and 0.5 were then fitted using this value for $k_{cat.}$ and a chosen best-fit value K_{assoc} = 4.9 M^{-1}. The dashed lines in Figure 3 were calculated using these values and good agreement with the experimental results is obtained at both buffer ratios. Similar calculations were carried out with the data obtained for the hydrolysis of *p*-nitrophenyl benzoate in 2-chlorophenol buffers. The dashed lines in Figure 4 were constructed using $k_{cat.}$ = 8.0 M^{-1} min^{-1} and K_{assoc} = 11.0 M^{-1}.

To test whether buffer association is responsible for the curved dependence of reciprocal relaxation time against buffer concentration for proton transfers involving **2** and **3** we have attempted to fit the experimental results in Figures 1 and 2 with eq 2 corrected to allow for buffer association. The concentration term in eq 2 refers to the concentration of noncomplexed phenolate ion and the concentration of noncomplexed phenol also enters into eq 2 through the buffer ratio. These were calculated for phenol and 2-chlorophenol buffers from the stoichiometric concentrations using the association constants derived from the results of ester hydrolysis. Values for k_f and k_r were obtained from the slopes of the plots in Figures 1 and 2 at low buffer concentration. The results of these calculations are shown as dashed lines in Figures 1 and 2. For proton transfer involving 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene in 2-methylphenol and 4-chlorophenol buffers the curvature in the plots of reciprocal relaxation time against buffer concentration can be accounted for using association constants ca. 5.0 M^{-1}. The proton transfer data for 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene and 1,8-bis(diethylamino)naphthalene in 2-chlorophenol buffers (Figure 2) are fitted quite well using the association

constant derived from the hydrolysis of *p*-nitrophenyl benzoate in this buffer. However, for proton transfer with 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene in phenol buffers, although good agreement is obtained at a buffer ratio of 1.0, the association constant derived from results for the hydrolysis of *p*-nitrophenyl *p*-methoxybenzoate does not reproduce the proton-transfer results at buffer ratios of 0.5 and 4.0 (Figure 1). This may mean that the assumptions involved in calculating buffer association are not entirely valid. In the absence of further evidence we conclude that buffer association is significant under our conditions and that the curvature of the plots in Figures 1 and 2 does not provide evidence for the mechanism shown in eq 3 and 4, but it can be explained by buffer association.

Spectrophotometric equilibrium measurements were also made to investigate the importance of buffer association. If association occurs between the acid and base components of the buffer, at stoichiometric buffer ratios other than unity, the actual buffer ratio will vary as the solution is diluted. The degree of dissociation of 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene was measured in phenol buffers (X = 2-Me, 4-Cl, and 2-Cl, see Table I) at fixed stoichiometric buffer ratio but at different buffer concentrations. However, the results were not sufficiently accurate to permit any conclusions to be drawn since the buffer species absorb quite strongly at the same wavelength as 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene.

Our conclusions on buffer association derived from the results of ester hydrolysis differ from the conclusions of other studies. Measurements of pH failed to detect buffer association in 70% Me_2SO-H_2O (v/v)[5] but the buffer concentrations were not specified. A similar conclusion was reached from further pH measurements[7,12] in 70% Me_2SO-H_2O (v/v) using hydrogen and calomel electrodes with buffer concentrations (ca. 0.01 M) which were much lower than those used in the present work. In 80% Me_2SO-H_2O (v/v) buffer association was detected[7,12] and association constants of ca. 10, 20, and 20 M^{-1} respectively were measured for phenol, 2-bromophenol, and 4-chlorophenol. In the present work at buffer concentrations up to 0.5 M an equilibrium constant of 4.9 was estimated for association between phenol and phenolate ion in 70% Me_2SO-H_2O (v/v) and it is likely that had the pH measurements been made at these concentrations association would have been detected. Association between phenolate ion and phenol was detected from pH measurements in 85–95% Me_2SO-H_2O (v/v) and the association constant increased as the volume percent of Me_2SO was increased.[13] In kinetic work on the formation of Meisenheimer complexes[5] curved plots of reciprocal relaxation time against buffer concentration were obtained under similar conditions to those used here. However, the curvature was much stronger than in our study and was attributed to a change in the rate-limiting step, from rate-limiting proton transfer at low buffer concentration to rate-limiting nucleophilic attack at high buffer concentration. Buffer association was assumed to have a negligible effect. Based on our results for buffer association it is now thought[14] that although such association would have to be taken into account in calculating the exact rate coefficients derived for the various steps in the formation of the Meisenheimer complexes, the correction would be minor and the original explanation[5] for the curved plots in terms of a change in the rate-limiting step with buffer concentration is still valid.

Mechanism of Proton Transfer. The data of plots like those shown in Figures 1 and 2 were analyzed at low buffer concentrations according to eq 2. For each buffer the value of the slope of the plot of reciprocal relaxation time against buffer concentration at fixed buffer ratio was combined with the equilibrium constant of the reaction to give values for k_f and k_r. The values obtained at each buffer ratio were averaged and

the results are given in Table I. These are only approximate since the kinetic and equilibrium measurements were made at concentrations at which some buffer association occurs.

The values of the rate coefficients for proton transfer from the protonated form of 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene to the various phenolate ions are almost constant even though the basicity of the substituted phenolate ions varies by a factor of ca. 25 (as shown by the value of the equilibrium constant K). A similar conclusion can be reached from an estimated value of the rate coefficient for proton transfer from the protonated form of 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene to hydroxide ion. In 70% Me_2SO-H_2O (v/v) containing 0.001 M hydroxide ion, 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene is almost fully in the base form so that kinetic and equilibrium measurements cannot be made. However, measurements have been made[4] in 60% Me_2SO-H_2O (v/v) and by comparison with the results obtained for 1,8-bis(diethylamino)-2,7-dimethoxynaphthalene in 60%[4] and 70%[15] Me_2SO-H_2O (v/v) assuming the change in solvent has a similar effect on both reactions, we can predict that for 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene in 70% Me_2SO-H_2O (v/v) k_{OH^-} = ca. 800 M^{-1} s^{-1} and $K >$ ca. 10^4. By comparison of these values with the data shown in Table I it is seen that although the equilibrium constants for reaction of protonated 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene with hydroxide ion and phenolate ions differ by a factor of at least 10^4, the rate coefficients are within a factor of 3. The most simple mechanism for proton transfer eq 1 involves direct attack of phenolate ion on the intramolecularly hydrogen-bonded proton to give products in a single step. In this case it would be expected that when the protonated amine and the conjugate acid of the attacking base have similar pK_a values, the proton in the transition state will be about half-transferred. The Bronsted exponent should then have a value of ca. 0.5 and for a change in K_a of the attacking base of a factor of 25 the rate coefficient should vary ca. fivefold. This is clearly not the case and this mechanism can therefore be eliminated. However, the mechanism shown in eq 3 and 4 gives a satisfactory explanation of the kinetic results. The dependence of reciprocal relaxation time on buffer concentration predicted for this mechanism is given in eq 5. If the intramolecular process 3 is fast compared with the proton transfer 4, i.e., $k_{-1} > k_2[XC_6H_4O^-]$, eq 5 reduces to

$$1/\tau = (k_2 k_1/k_{-1} + k_{-2}/x)[XC_6H_4O^-] \qquad (9)$$

Equation 9 is of the same form as eq 2 in which $k_f = k_2 k_1/k_{-1}$ and $k_r = k_{-2}$. In this case the mechanism shown in eq 3 and 4 will predict the same linear dependence of reciprocal relaxation time on buffer concentration as the single-step mechanism, and the curvature of the plots of reciprocal relaxation time against buffer concentration is explained in terms of eq 2 or 9 modified to take account of buffer association. The mechanism in eq 3 and 4 will also account for the observation that the rate coefficient for proton transfer from protonated 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene is practically independent of the basicity of the attacking phenolate ion. This mechanism explains the low values of the observed rate coefficient ($k_f = k_2 k_1/k_{-1}$) as arising from an unfavorable equilibrium 3, which corresponds to a strong intramolecular hydrogen bond ($k_1/k_{-1} \ll 1$). Since step 3 is strongly thermodynamically unfavorable in the forward direction, step 4 is thermodynamically favorable for proton transfer to all the phenolate ions and therefore since this is a reaction between an oxygen base and a protonated amine (with no intramolecular hydrogen bond) the rate coefficient (k_2) should be diffusion limited. It follows that the value of k_2 and the observed rate coefficient k_f will be the same for all the phenolate ions and for hydroxide ion.[16] The higher rate coefficient estimated

for hydroxide ion may reflect the difference in diffusion limits for reaction of hydroxide ion and phenolate ions with a protonated amine.[6] The observed reverse rate coefficient k_r is identified with the rate coefficient (k_{-2}) for thermodynamically favorable protonation of 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene by phenol (eq 4). The values of k_{-2} and k_r are expected to increase linearly with the acid dissociation constant of the phenol. Our results are compatible with this expectation since the overall equilibrium constant (K) for reaction 1 is inversely related to the acid strength of the phenol and the value of K decreases along the series 2-Me > H > 4-Cl > 2-Cl as k_{-2} increases (see Table I).

Our conclusion that removal of the intramolecularly hydrogen-bonded proton from the protonated form of 1,8-bis-(dimethylamino)-2,7-dimethoxynaphthalene occurs through the two-step mechanism shown in eq 3 and 4 is similar to our previous observation[1] for proton removal from an intramolecularly hydrogen-bonded salicylate ion in aqueous solution.

Experimental Section

Materials. Details of the preparation of 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene have been published.[4] A method[2] described to us by Dr. R. W. Alder was used for the preparation of 1,8-bis(diethylamino)naphthalene. Samples of *p*-nitrophenyl benzoate and *p*-nitrophenyl *p*-methoxybenzoate were obtained by reaction of the acid chlorides with *p*-nitrophenol. In the preparation of *p*-nitrophenyl *p*-methoxybenzoate the acid chloride was generated in situ from *p*-methoxybenzoic acid and phosphorus oxychloride.[17] Phenols were purified by recrystallization or distillation. Buffer solutions were made up from a weighed amount of the phenol and standard tetramethylammonium hydroxide solution.

Kinetic and Equilibrium Measurements. Proton transfers involving 1,8-bis(diethylamino)naphthalene and 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene were observed spectrophotometrically at ca. 350 nm where the basic forms of the amines absorb strongly. The equilibrium between the amine and its protonated form in a phenol buffer was disturbed by a rapid increase in temperature of 3.7 °C brought about by a discharge of 30 000 V from a 0.01 μF capacitor through the reaction solution. The final temperature was 25.0 °C. For each solution at least five determinations of the chemical relaxation time following a temperature jump were made and the results were reproducible to within ±10% of the average. Chemical reaction to the new equilibrium position occurred slowly with relaxation times greater than 2 ms, which is much longer than the heating time of the solution under these conditions (<0.1 ms).

References and Notes

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(16) In recent years it has proved useful to analyze the rate coefficients for proton-transfer reactions into work terms and intrinsic energy barriers (for a review, see A. J. Kresge, *Chem. Soc. Rev.*, **2**, 475–503 (1973)). The data presented here could be explained in terms of a single-step proton transfer with an exceptionally large work term resulting from solvation changes accompanying the proton transfer. The mechanism shown in eq 3 and 4 identifies the work term as the energy required to break the intramolecular hydrogen bond and this occurs as a separate reaction step before the proton transfer. This seems to us to be a more reasonable explanation of our data than the assumption of unspecified solvation changes accompanying a single-step proton transfer.
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Aromatic Sulfonation. 67.[1] Sulfonation of the 1,6-Methano[10]annulene System. Evidence for Ipso Attack with the 2,7-Dimethyl Derivative

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Abstract: Sulfonation of 1,6-methano[10]annulene (1) with 0.9 equiv of SO_3 in dioxane yields exclusively the 2-sulfonic acid, and with 4 equiv of SO_3 only the 2,7-disulfonic acid. The primary kinetic isotope effect for the monosulfonation of 1 was determined to be $k_H/k_D = 3.8 \pm 0.3$. Sulfonation of 2-methyl-1 yielded the 5-sulfonic acid. The reaction of 2,7-dimethyl-1 with SO_3 in dioxane resulted in peri (65%) and ipso (35%) substitution, with formation of 2,7-dimethyl-1-5-sulfonic acid and 2-methyl-1-7-sulfonic acid, respectively.

Aromaticity is an intriguing phenomenon in organic chemistry. Since the formulation of Hückel's rule there has been a dramatic search for compounds exhibiting aromaticity. Recently the monocyclic compounds containing $(4n + 2)\pi$ electrons have attracted much attention. In 1964 Vogel synthesized 1,6-methano[10]annulene (1), a stable 10π-electron system,[2] which was subjected to various criteria developed to test for aromaticity.[3] The electrophilic aromatic reactivity of 1 was also investigated.[4] In the course of our study on bicyclic 10π-electron systems we thought it of interest to study the sulfonation of the 1,6-methano[10]annulene system.

Results and Discussion

The sulfonation reactions of the investigated compounds are presented in Scheme I. The ^1H NMR characteristics of the isolated potassium sulfonates are listed in Table I. Reaction of 1 with 0.9 equiv of SO_3 in dioxane resulted in the exclusive formation of 1,6-methano[10]annulene-2-sulfonic acid (2).

In order to test whether the α-substitution encounters steric hindrance from the peri hydrogen and possibly also from the methylene bridge the primary kinetic isotope effect was determined.[5] From the ratio of the mono- and dideuteriomonosulfonic acids obtained upon sulfonation of 1-*2,7-d₂* with 0.9 equiv of SO_3 in dioxane, the k_H/k_D was calculated to be 3.8 $\pm$ 0.3. The k_H/k_D for the α-sulfonation of naphthalene-*1,4-d₂* with SO_3 was found to be smaller, viz., 1.9 $\pm$ 0.2 for nitromethane and 2.0 $\pm$ 0.2 for trichlorofluoromethane as solvent.[6] The larger kinetic isotope effect of 1 indicates a relative retardation of the proton removal from the σ complex.[7] This may be rationalized in terms of SO_3 attack from the bottom side of the molecule (trans to C_{11}), as the subsequent proton abstraction from C_2 of the resulting σ complex will be sterically hindered by the adjacent methylene bridge.[10]

The sulfonation of 1 is highly specific in contrast to that of naphthalene where the α:β ratio for monosubstitution with SO_3 in nitromethane at 0 °C was found to be 7.3. The high specificity for the sulfonation of 1 is in agreement with the very high

partial rate factor reported for the protiodetritiation at the 2 position.[4d] For the 3 position this datum is, however, unknown. 11,11-Difluoro-1,6-methano[10]annulene,[11] which is geometrically comparable with 1, has an α:β partial rate factor ratio for protiodetritiation of 23.3,[4d] compared with a value of 7.7 for naphthalene.[12] For the protiodetritiation the steric hindrance is thought to be "small or nonexisting"[13] in contrast to sulfonation. Thus, in spite of the absence of properly determined partial rate factors of 1, the α:β reactivity ratio of 1 appears to be much higher than that of naphthalene and this indicates a much higher selectivity of 1 toward electrophilic substitution. The difference in α:β reactivity between 1 and naphthalene is apparently large enough to overcome the enhanced steric repulsion for α-sulfonation of 1, as compared with naphthalene, which is apparent from the higher kinetic isotope effect of hydrogen (see before).

It is of interest to note that the isomer ratio for 9- and 1-sulfonation of anthracene is still 2.5,[14] despite the maximum kinetic isotope effect for the 9 substitution.[9] The very high reactivity of the 9 position is indicated by the high 9:1 partial rate factor ratio for protiodetritiation,[12b] which is 7.9 × 10^4. In this context it should be pointed out that the (stated) electrophilic bromination and nitration of 1 have been explained in terms of initial formation of addition compounds followed by elimination.[4a,15] This is of special interest for the nitration at the 3 position of 1.[4a]

Upon reaction of 1 with 4 equiv of SO_3 in dioxane the 2,7-disulfonic acid (3) was formed in a yield of more than 90%. Compound 1 is the first aromatic hydrocarbon to undergo disulfonation with SO_3 in dioxane, which is a relatively mild sulfonating reagent,[16] indicating the high reactivity of 1. Reaction of 2-methyl-1,6-methano[10]annulene (4) with both 0.9 and 4 equiv of SO_3 in dioxane resulted in the exclusive formation of the 5-sulfonic acid (5). In contrast the bromination of 4 yields not only the 5- but also the 7-monobromo compound.[4b] As no disulfonation could be accomplished this again confirms the very high α:β reactivity ratio. The high