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Extremely Strong but Sluggish Amine Bases

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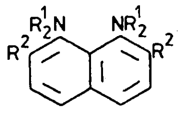
Summary 1,8-Bis(dimethylamino)- (**3**) and 1,8-bis(diethylamino)-2,7-dimethoxynaphthalene (**4**) are extremely strong bases with $pK_a > ca.\ 16$, but proton transfers to and from these amines are exceptionally slow; the reaction involving the protonated form of (**4**) and hydroxide ion in 60% Me_2SO–H_2O (v/v) can be followed with a conventional spectrophotometer ($t_{\frac{1}{2}}$ *ca.* 15 s).

1,8-Bis(dimethylamino)naphthalene (**1**), pK_a 12·3, is a strong base.[1] Its C_2 structure[2,3] suggests the possibility of more extreme properties if the two nitrogen lone pairs of electrons could be forced to rotate into closer proximity (towards a C_{2v} structure). 2,7-Disubstitution in the naphthalene rings should be particularly effective in this respect. At the same time, the rate of the already slow[4] proton transfer to and from the inter-nitrogen position in (**1**) might be reduced further. We find that these expectations are realised but in a most dramatic fashion.



(**1**); $R^1 = Me, R^2 = H$
(**2**); $R^1 = R^2 = Me$
(**3**); $R^1 = Me, R^2 = OMe$
(**4**); $R^1 = Et, R^2 = OMe$

2,7-Dimethyl-[5] and the more readily available[6] 2,7-dimethoxy-1,8-diaminonaphthalenes were alkylated by adding an excess of an alkylating agent (iodomethane or bromoethane) to refluxing solutions of the amines in tetrahydrofuran containing an excess of potassium hydride. In this way (**2**), HBF_4 salt m.p. 239—242 °C;† (**3**), m.p. 67—69·5 °C,† HBF_4 salt m.p. 227—230 °C; and (**4**), m.p. 50—52·5 °C, CF_3CO_2H salt m.p. 77—78 °C† were obtained. As with (**1**)[7], $CDCl_3$ solutions of (**2**), (**3**), or (**4**) plus the corresponding amine salt showed n.m.r. spectra characteristic of slow proton exchange to and from nitrogen. Addition of an equimolar quantity of (**2**) to (**1**) $H^+BF_4^-$ in $CDCl_3$ caused complete conversion (by n.m.r.) into (**1**) and (**2**) $H^+BF_4^-$, $\log_{10}K$ for the equilibrium being $>3·25$. More surprisingly, $\log_{10}K$ was also large ($>2·7$) for $(\mathbf{2})H^+ + (\mathbf{3}) \rightleftharpoons (\mathbf{2}) + (\mathbf{3})H^+$, while $\log_{10}K$ for $(\mathbf{3})H^+ + (\mathbf{4}) \rightleftharpoons (\mathbf{3}) + (\mathbf{4})H^+$ was *ca.* 0·5. Deprotonation of $(\mathbf{3})H^+$ in 1 M aqueous NaOH is undetectable, though 1 M NaOMe in MeOH does cause some deprotonation (u.v. spectra). These results show that the aqueous pK_a values of (**3**) and (**4**) are $>$ *ca.* 16. This was confirmed by spectrophotometric measurements in Me_2SO–H_2O mixtures containing NaOH. In 35% Me_2SO–H_2O (v/v) the values of the equilibrium constants for reaction (1) with B = (**1**), (**3**), and (**4**) are *ca.* 4100, 0·4, and 0·2 l mol^{-1}, respectively. When combined with the aqueous pK_a of

$$BH^+ + OH^- \underset{k_{H_2O}}{\overset{k_{OH^-}}{\rightleftharpoons}} B + H_2O \qquad (1)$$

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† Satisfactory spectroscopic data have been obtained for all new compounds and satisfactory analytical data were obtained on the materials indicated; (**2**) is a low-melting solid.

(**1**), pK_a values of *ca.* 16·3 and 16·6 are calculated for (**3**) and (**4**), respectively.

Rate coefficients for reaction (1) involving 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene were determined using the temperature-jump method. In 60% Me_2SO-H_2O (v/v) at 20·1 °C the results $k_{OH^-} = 440 \pm 50$ l mol^{-1} s^{-1} and $k_{H_2O} = 1·6 \pm 0·3$ s^{-1} were obtained. The ratio of rate coefficients is in good agreement with the equilibrium constant determined spectrophotometrically. The rate coefficient for deprotonation is *ca.* 400-fold lower than the value found for 1,8-bis(dimethylamino)naphthalene.[4] For 1,8-bis(diethylamino)-2,7-dimethoxynaphthalene the reactions are sufficiently slow that a conventional spectrophotometer was used to study the kinetics. Measurements were carried out by following the slow increase in absorbance at 350 nm accompanying formation of the free amine when a small amount of sodium hydroxide solution was introduced into a solution of the protonated amine in 60% Me_2SO-H_2O (v/v) at 20·1 °C. The equilibrium was disturbed in the opposite direction by diluting an equilibrium mixture of the amine and its protonated form in 60% Me_2SO-H_2O (v/v) containing sodium hydroxide. A slow decrease in absorbance at 350 nm was then observed showing that the equilibrium is cleanly reversible. The reactions occurred with half-lives in the range 8—23 s depending upon the hydroxide ion concentration (0·001—0·016 mol l^{-1}). The values $k_{OH^-} = 3·3 \pm 0·4$ l mol^{-1} s^{-1} and $k_{H_2O} = 0·030 \pm 0·003$ s^{-1} were calculated and the ratio is compatible with the equilibrium results obtained spectrophotometrically. Measurements in various mixtures between 0 and 60% Me_2SO-H_2O showed that the rates of proton transfer are not very sensitive to a change in solvent composition in this range. For 1,8-bis(dimethylamino)naphthalene k_{OH^-} is increased *ca.* 2-fold in going from 0 to 35% Me_2SO-H_2O (v/v) and for 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene k_{OH^-} is *ca.* 4-fold higher in 60% compared with 35% Me_2SO-H_2O (v/v).

1,8-Bis(diethylamino)-2,7-dimethoxynaphthalene is a most unusual aromatic amine. With pK 16—17 it is the strongest known neutral base and thermodynamically favourable ionisation of the protonated amine is exceptionally slow. In this latter property the protonated amine resembles proton cryptates[8] in which the proton is held in a molecular cavity. The cryptands are probably less unusual in their thermodynamic basicity but even lower proton transfer rates are observed than for 1,8-bis(diethylamino)-2,7-dimethoxynaphthalene. The low proton transfer rates for (**3**) and (**4**) will make them ineffective bases for carbon deprotonations (as in $E2$ elimination) despite the appealing combination of high basicity and probable low nucleophilicity.‡

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‡ Even for (**1**) this is a severe limitation. Good yields of olefins may be obtained by heating alkyl tosylates *etc.* with (**1**) in dimethylformamide but (**1**) is never the kinetically active base, even with $Me_3N^+CH_2CH_2CN$ (R. W. Alder and D. Edley, unpublished results).

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