Kinetic and Equilibrium Protonation of Some Alkylated 1,8-Diaminonaphthalene Monocations to form Dications: Carbon *versus* Nitrogen Protonation

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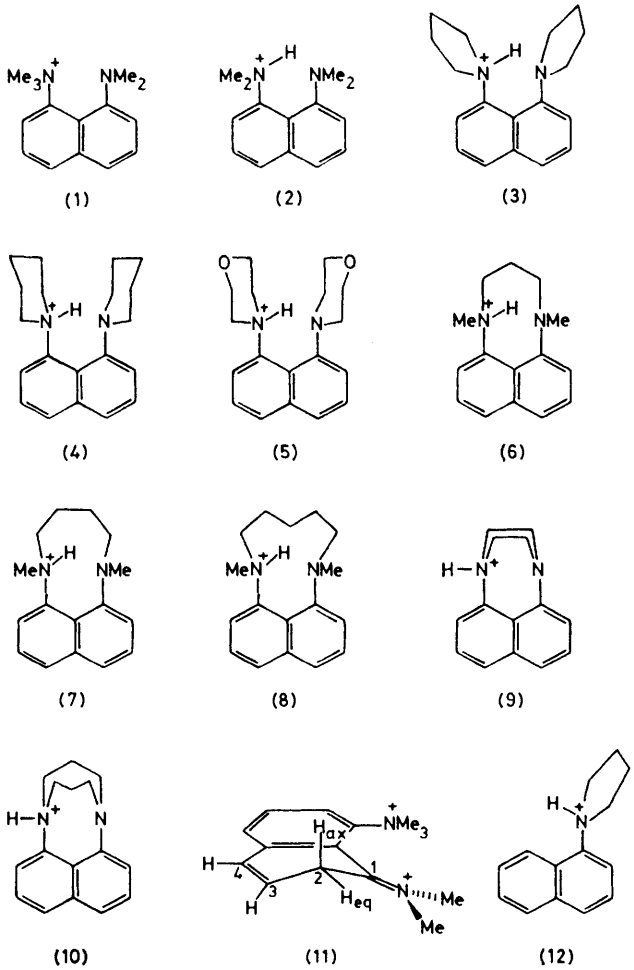
1-Dimethylamino-8-trimethylammoniumnaphthalene tetrafluoroborate (1) is protonated at equilibrium at N, C-2, and C-4 in the ratio 1 : 15 : 4, but kinetically controlled protonation is exclusively at nitrogen. Deuteriation occurs more rapidly at C-4 than C-2, and probably involves rate-limiting ring inversion in the non-planar C-protonated ions. At equilibrium, diprotonation of *NNN'N'*-tetra-alkylated 1,8-diaminonaphthalenes (2)—(10) can occur predominately at N,N or N,*p*-C, depending on the alkyl groups. Kinetically controlled protonation of 1,8-bis(dimethylamino)naphthalene (2) and of 1,8-dipyrrolidinylnaphthalene (3) is exclusively on nitrogen.

C-Protonation of aromatic amines in solution is very uncommon, the best known case being 1,3,5-triaminobenzene and its derivatives.[1] In the gas phase, however, the equilibrium between N- and C-protonation is apparently much more finely balanced. While aniline itself is N-protonated,[2] 3-methyl- and 3-methoxy-aniline are C-protonated.[3] It seems clear that the charge-localised N-protonated ions have much higher solvation energies than the delocalised C-protonated ions, especially in solvents which can act as hydrogen-bond acceptors. At the same time the N-/C-protonation equilibrium should be tipped more in favour of C-protonation in amino-derivatives of aromatic hydrocarbons with smaller localisation energies than benzene. 1-Naphthylamine is probably C-protonated in the gas phase.[4] In solution, however, simple naphthylamines are apparently exclusively N-protonated. In view of this background, we were surprised to discover that, in certain acids (*e.g.* CF_3COOH), 1-dimethylamino-8-trimethylammoniumnaphthalene tetrafluoroborate (1) was protonated on carbon.[5] Our curiosity was further aroused when we found (i) that in very strong acids (*e.g.* CF_3SO_3H) (1) was N-protonated, (ii) that protonation on nitrogen was the result of kinetically controlled reaction, C-protonation being favoured at equilibrium and (iii) that (1) was a *stronger* base than the monoprotonated ion of 1,8-bis(dimethylamino)naphthalene (2).[6] In this paper we describe our study of the kinetic and equilibrium protonation of the alkylated 1,8-diaminonaphthalene monocations (1)—(10); ^{13}C n.m.r. spectra have been particularly useful in elucidating these reactions.



EXPERIMENTAL

1-Dimethylamino-8-trimethylammoniumnaphthalene Tetrafluoroborate (1).—Freshly distilled methyl fluorosulphate (2 molar excess) was added to 1,8-bis(dimethylamino)-naphthalene under nitrogen. After 24 h, the excess methyl fluorosulphate was removed from the reaction mixture under vacuum (1 mmHg) at room temperature. The oily product contained some crystalline hydrogen fluorosulphate salt of 1,8-bis(dimethylamino)naphthalene which was removed by filtration after cooling to 0° on a sintered disc under vacuum. The oily fluorosulphate salt of 1-dimethylamino-8-trimethylammoniumnaphthalene (which could not be induced to crystallise) was dissolved in the minimum of water and a concentrated aqueous solution of sodium tetrafluoroborate added (slight excess). The solution was left at 0° for several hours and the tetrafluoroborate salt of 1-dimethylamino-8-trimethylammoniumnaphthalene (1) slowly crystallised out. After drying, the product was recrystallised twice from ethanol–ethyl acetate, m.p. 127—129° (Found: C, 57.0; H, 6.65; N, 8.85. $C_{15}H_{21}N_2BF_4$ requires C, 57.0; H, 6.7; N,

8.85%). The ^1H n.m.r. spectrum always showed the presence of a little (*ca.* 1%) of the protonated rather than methylated salt (doublet, J 2 Hz, at δ 3.21 for the NMe_2 groups).

The ammonium ions (2)—(10)· as $CF_3CO_2^-$ or BF_4^- salts and their corresponding amines were prepared as previously described.[7]

1-(1-*Naphthyl*)*pyrrolidinium Trifluoromethanesulphonate* (12).—1-Naphthlamine (14.3 g, 0.1 mol), 1,4-dibromobutane (15 ml, 0.126 mol), powdered potassium carbonate (20 g), and bis-2-methoxyethyl ether (100 ml) were refluxed together for 4.25 h under nitrogen. The solution was cooled and acetic anhydride (10 ml) and more potassium carbonate (10 g) added before refluxing for a further 15 min. The reaction mixture was cooled and filtered and the bis-2-methoxyethyl ether was removed at 0.1 mmHg. The residue was mixed with ether (100 ml) and extracted into the minimum volume of 6N-HCl. The acidic extract was made basic and extracted with light petroleum (b.p. 40—60°), interfacial material being removed by filtration. The light petroleum extract yielded crude product (9 g) which was distilled, b.p. 115—116° at 0.1 mmHg (Reppe [8] reports b.p. 137° at 0.4 mmHg), to give 1-(1-naphthyl)pyrrolidine as an oil (6.4 g, 32%), δ_C ($CDCl_3$) 24.7 (β-CH_2), 52.6 (α-CH_2), 111.4, 121.2, 124.2, 124.8, 125.4, 125.8, 128.2 (aromatic CH), 134.9, and 147.7 p.p.m. (quaternary C, one peak not observed).

A dichloromethane solution of the amine was mixed with a dichloromethane solution of trifluoromethanesulphonic acid and ether was added to precipitate the product. Recrystallisation of the product from dichloromethane–ether gave 1-(1-*naphthyl*)*pyrrolidinium trifluoromethanesulphonate* as crystals, m.p. 132—133° (Found: C, 51.9; H, 4.7; N, 3.8. $C_{15}H_{16}F_3NO_3S$ requires C, 51.85; H, 4.65; N, 4.05%), δ_C ($CDCl_3$) 24.1 (β-CH_2), 59.2 (α-CH_2), 118.7, 120.1, 125.3, 127.6, 128.7, 129.4, 131.2 (aromatic CH), 134.5, and 135.8 p.p.m. (quaternary C, one peak not observed).

RESULTS

When dissolved in CF_3SO_3H, FSO_3H, or 98% aqueous H_2SO_4, 1-dimethylamino-8-trimethylammoniumnaphthalene tetrafluoroborate (1) produces a ^{13}C n.m.r. spectrum with 10 lines between 116.0 and 140.7 p.p.m. (aromatic carbons) and lines at 51.7 and 61.5 p.p.m. for the NMe_2 and NMe_3 groups (see Table 1). The ^1H n.m.r. spectrum shows a doublet (J 5 Hz) for NMe_2 at δ 3.75 coupled to the N-H signal at δ 7.3, a singlet at δ 4.01 for NMe_3, and absorptions for two AMX systems in the region δ 7.8—8.6. These spectra are easily assigned as due to the N-protonated ion, (1)H_N^+. Absorptions due to C-protonated species are absent and the solutions in CF_3SO_3H and FSO_3H are unchanged after weeks at room temperature.

In CF_3COOH, (1) is only *ca.* 50% protonated, but (1)H_N^+ is a minor component. The major species is a C-protonated ion, easily recognised from the deshielded (193.1 p.p.m.) and shielded (36.4 p.p.m.) ^{13}C absorptions due to $>C=\overset{+}{N}$ and $>CH_2$ respectively and absorptions in the ^1H n.m.r. at δ 6.90 (1 H, dt, J 9, 1.5 Hz), 6.63 (1 H, m, see later), and 4.35 (2 H, m) which can be assigned to a $-CH=CH-CH_2-$ grouping. Addition of *ca.* 10% CF_3SO_3H to the CF_3COOH solution completes the protonation of (1) and gives a solution whose complex, but clean ^{13}C spectrum can be completely assigned on the basis that the three plausible protonated ions from (1) namely (1) H_N^+, (1)H_{C-2}^+, and (1)H_{C-4}^+ are present in an equilibrium ratio of 1 : 15 : 4. The ^{13}C n.m.r. spectroscopic assignments for (1)H_{C-2}^+ and other ions protonated at the *ortho*-carbon are given in Table 2 and those for (1)H_{C-4}^+ and other *para*-protonated ions in Table 3. It will be seen that the immonium ion carbons of ions in Table 2 are always downfield of those in Table 3. This forms the principal reason for assigning the ions in Table 2 as the *ortho*-protonated ones, by analogy with the greater downfield shifts observed for saturated than for αβ-unsaturated carbonyl carbons. Other evidence in favour of the assignment given is the small chemical shift difference between the vinylic protons observed for the major C-protonated ion from (1) which we assign as (1)H_{C-2}^+ where they form part of a styrene system rather than a vinyl group conjugated with $>C=N^+<$, and the observation of a ^{13}C peak for (1)H_{C-4}^+ and other *para*-protonated ions in the region of 147—154 p.p.m. downfield of any aromatic resonance in *ortho*-protonated species, assigned to C-3 which should bear appreciable positive charge.

TABLE 1

^{13}C N.m.r. data for N-protonated ions

Ion	Alkyl carbons	Aromatic carbons
(1) H_N^+	51.7 ($NHMe_2$), 61.5 (NMe_3)	116.0 (probably C-9), 125.3, 126.2, 127.8, 127.9, 135.6, 136.3, 136.7, 139.6, 140.7
(2) H_N^+	51.5 ($NHMe_2$)	117.3 (C-9),[a] 135.5 (C-1),[a] 138.7 (C-10),[a] 124.9, 128.5, 136.2 (protonated carbons)
(3) H_N^+	25.0 (β-CH_2), 65.3 (α-CH_2)	119.0 (C-9), 135.4 (C-1), 138.2 (C-10), 125.5, 128.0, 135.4 (protonated carbons)
(4) H_N^+	21.5 (γ-CH_2), 26.2 (β-CH_2), 63.1 (α-CH_2)	117.8 (C-9), 135.8 or 134.5 (C-1), 138.9 (C-10), 125.5, 128.4, 134.5 or 135.8 (protonated carbons)
(6) H_N^+	22.7 (β-CH_2), 47.6 (CH_3), 63.5 (α-CH_2)	124.1 (C-9), 136.2 (C-1), 137.4 (C-10), 124.5, 128.7, 131.3 (protonated carbons)
(9) H_N^+	51.5	119.3 (C-9), 134.4 (C-1), 138.1 (C-10), 124.1, 129.0, 134.6 (protonated carbons)
(10) H_N^+	19.0 (β-CH_2), 58.0 (α-CH_2)	122.0 (C-9), 136.1 (C-1), 137.7 (C-10), 127.8, 128.0, 128.8 (protonated carbons)

[a] Identified as a quaternary carbon by low power noise decoupling.

TABLE 2

^{13}C N.m.r. data for ions protonated at C-2

Ions	C-1	C-2	Alkyl carbons	Aromatic and vinyl carbons
(1) H_{C-2}^+	193.1	36.4	46.3, 48.2, 59.6 (Me_3N^+)	119.1, 124.1, 128.5, 129.9, 131.6, 137.2, 142.3, 144.2
(2) H_{C-2}^+	188.2 [a]	*b*	*c*	*c*
(3) H_{C-2}^+	183.6	36.2	β-CH_2 at 24.2 (others obscured) α-CH_2 at 58.4, 61.6 and 69.5 (one obscured)	120.1, 122.4, 127.1, 128.5, 131.0, 139.0, 139.6 and 142.4
(4) H_{C-2}^+	186.1	35.3	*c*	*c*
(7) H_{C-2}^+	188.5 [a]	36.5	*d*	*d*
(8) H_{C-2}^+	189.4 [a]	36.1	*d*	*d*

[a] Identified as a quaternary carbon by low power noise decoupling. [b] Not observed. [c] Present in too low a concentration for analysis. [d] Not analysed.

Conversion of the solutions of (1) in very strong acids, and containing only (1)H_N^+, to the equilibrium mixture of ions is a base-catalysed process *via* free (1). Thus solutions in CF_3SO_3H were stable indefinitely at room temperature, but the equilibrium mixture of ions was formed on refluxing (162°) the solution for 15 min. In aqueous H_2SO_4 or $HClO_4$ solutions the rate of attainment of equilibrium increases with increasing dilution, the half-life being *ca.* 5 min in 85% H_2SO_4 or 72% $HClO_4$ (H_0 − 8).

the case of ions (9) and (10), where no intramolecular $\rangle N^+–H\!:\!N\langle$ bond has to be broken, diprotonation was more or less complete in CF_3COOH, and was *exclusively on nitrogen.*

Because of their weaker basicity it is expected to be more difficult to observed kinetically controlled protonation of ions (2)—(8) than (1). However, when (2) and (3) were dissolved in CF_3SO_3H at −30 °C, only N-protonated ions were observed [see Figure (a)]. Raising the temperature to ambient resulted in the appearance of the C-protonated ions. Actually, attainment of equilibrium is very slow, at least for (3) where a careful study was made. After 4 days at 0 °C, very little C-protonation was apparent [Figure (b)], and attainment of the final equilibrium [Figure (c)] required 5 days at 20 °C.

TABLE 3

^{13}C N.m.r. data for ions protonated at C-4

Ion	C-1	C-3	C-4	Alkyl carbons	Other aromatic and vinyl carbons
(1) H_{C-4}^+	175.3	147.1	35.2	45.4, 47.5 60.0 (Me_3N^+)	121.7, 124.4, 127.9, 130.7, 132.4, 135.2, 143.6
(2) H_{C-4}^+	170.5 [a]	151.5 [d]	35.4	45.5, 47.3, 47.8, 54.8	119.0 (C-9),[a] 146.6 (C-10),[a] C-8 not observed, 121.4, 123.5, 133.3, 137.1 (protonated carbons)
(3) H_{C-4}^+	166.4	150.2	35.2	β-CH_2 at 24.0, 25.6 and 26.2 (one obscured) α-CH_2 at 56.8, 58.0, 62.1, and 70.4	121.1, 122.4, 123.7, 132.2, 136.7, and 139.8
(4) H_{C-4}^+	168.7	150.6	35.0	*b*	*b*
(7) H_{C-4}^+	174.0 [a]	154.0 [d]	35.9	*c*	*c*
(8) H_{C-4}^+	171.4 [a]	151.2 [d]	35.4	*c*	*c*

[a] Identified as a quaternary carbon by low power noise decoupling. [b] Present in too low a concentration for analysis. [c] Not analysed. [d] C–H carbon by low power noise decoupling.

The ions (2)—(8) are considerably weaker bases than (1), and their protonation was studied in mixtures of CF_3COOH and CF_3SO_3H containing large proportions of the latter. In order to ensure that the equilibrium ratio of protonated ions (see Table 4) was obtained, solutions of (2)—(8) in the weaker acid (CF_3COOH) were 'diluted' with the stronger acid (CF_3SO_3H) until diprotonation was complete. Even so, neat CF_3SO_3H was needed for complete protonation of (4), and the spectrum of (7), and perhaps (8), in pure CF_3SO_3H shows the presence of unchanged (7) [or (8)]. The only major shift in the ^{13}C spectrum of (5) in CF_3SO_3H compared with that in CF_3COOH was for the CH_2 carbons next to oxygen (69.0 from 65.3 p.p.m.), and we conclude that (5) merely undergoes (some) O-protonation in CF_3SO_3H. In

TABLE 4

Equilibrium percentages of naphthalenediamine dications in CF_3SO_3H or CF_3COOH–CF_3SO_3H solutions

Compound	N-Protonation	*ortho*-Protonation	*para*-Protonation
(1)	5	75	20
(2)	75	6	19
(3)	20	20	60
(4)	91	4	5
(6)	100	0	0
(7)	0 [a]	25	75
(8)	0 [b]	25	75
(9)	100	0	0
(10)	100	0	0

[a] Lines due to (7), not further protonated, are present in the ^{13}C n.m.r. spectrum in neat CF_3SO_3H. [b] The ^{13}C n.m.r. spectrum of (8) in CF_3SO_3H contains a set of lines which differ only slightly in chemical shift from those of (8) in CF_3COOH; they may be due to (8) or to N-protonated (8).

Deuteriation of (1) CF_3COOD.—When (1) was dissolved in CF_3COOD, the ^1H n.m.r. spectrum showed the presence of (1) and (1)D_{C-2}^+. Separate and sharp absorptions were seen for each species, indicating that addition and loss of D^+ is slow on the n.m.r. time scale. More strikingly, there is no exchange of 2- and 4-H already present in (1) and (1)D_{C-2}^+. H-3 is a double doublet (J 9 and 6 Hz). Very slowly, over several days at room temperature, the absorption for H-3 changes to a doublet (J 6 Hz) and eventually to a singlet when exchange at C-2 and C-4 is complete. Although deuteriation was a clean reaction according to ^1H n.m.r. crystalline deuteriated (1) could not be isolated by evaporation of CF_3COOH under vacuum; it seems possible that the BF_4^- counterion was solvolysed under these conditions. Crystalline deuteriated (1) was prepared by exchange in 50% D_2SO_4–D_2O solution, followed by addition of more D_2O and excess $NaBF_4$ and extraction of (1) into CH_2Cl_2 solution. Redissolving dideuteriated (1) in CF_3COOH led to a ^1H n.m.r. spectrum in which H-3 of (1)H_{C-2}^+ appeared as a doublet with J 1.5 Hz.

N- versus C-*Protonation of* 1-(1-*Naphthyl*)*pyrrolidine in* $CDCl_3$.—The ^{13}C n.m.r. spectrum of (12) in $CDCl_3$ was recorded under conditions of high signal : noise ratio [JEOL FX200, 35 000 pulses on a solution of salt (300 mg) in $CDCl_3$ (1 ml) held in a 10 mm microcell] and the regions of the spectrum where the $\rangle C{=}\overset{+}{N}\langle$ and CH_2 carbons of C-

protonated ions were expected were scrutinised under high amplification. No signals for these carbons could be found. We estimate that 1 part in 250 of C-protonated ion could have been easily detected under these conditions.

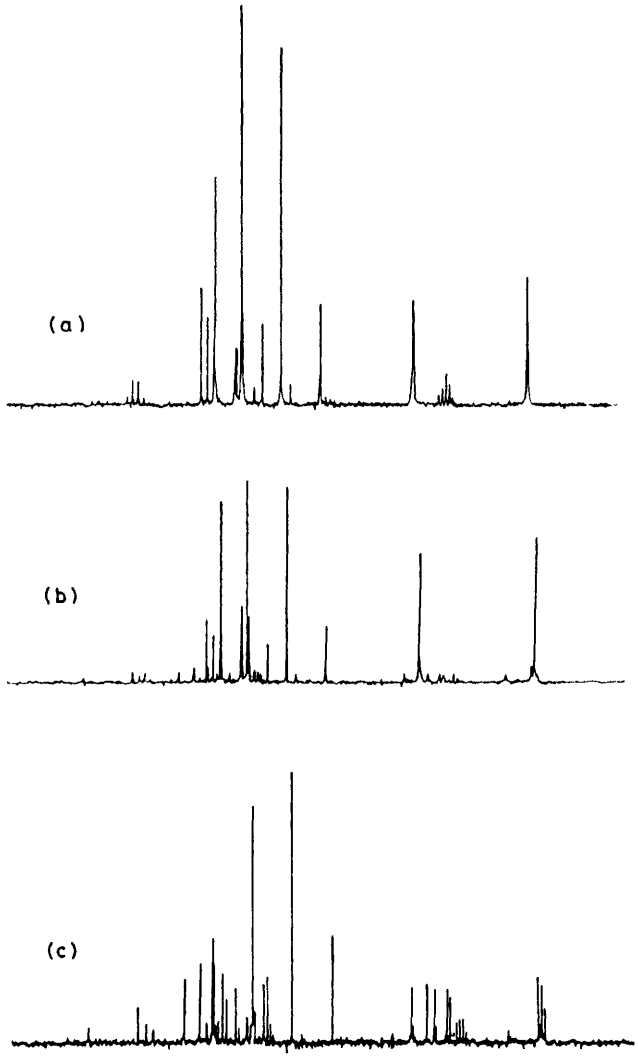


FIGURE ^{13}C N.m.r. spectra of (3) in CF_3SO_3H; (a) at −30 °C immediately after sample preparation: (b) after 4 days at 0 °C; (c) after 5 days at 20 °C. All spectra show lines due to CF_3SO_3H, CD_2Cl_2, and CF_3COOH [from the counterion to (3) used]

DISCUSSION

Equilibrium Protonation.—The primary question must be why C-protonation is relatively favourable for these 8-substituted 1-naphthylamines. It is instructive to compare the protonation of (3) with the N-/C-equilibrium for the 1-(1-naphthyl)pyrrolidinium ion (12). It is apparent that the 8-pyrrolidinium substituent in (3) makes C-protonation more favourable by $\Delta\Delta G \geqslant 4$ kcal mol^{-1}. Of course the media involved are very different, but $CDCl_3$ is a poor hydrogen-bond acceptor and should hardly favour N-protonation. The effect of the 8-substituent could be inductive or steric. The ammonium ion substituents should have a powerful inductive (field) effect but it is hard to see how this can favour C-protonation strongly, since even in the C-protonated ions, the charge is undoubtedly largely on the immonium nitrogen and so cannot be much further from the 8-substituent than in the N-protonated ion. We believe the major effect is a steric one. None of the dications studied here can have planar naphthalene structures. Steric repulsion between the *peri*-substituents will be accommodated by both in-plane and out-of-plane distortions. Models show that the C-protonated ions can readily adopt strongly non-planar geometries [see formula (11)] without inducing too much angle strain. In models, dihedral angles of 50—70° between the C-2–C-1=N^+ plane and that of the non-protonated aromatic ring are quite easily achieved, and this gives very substantial relief from steric interference between the *peri*-groups. Spectroscopic evidence for non-planarity and slow interconversion on the n.m.r. time scale comes from the observation of non-equivalent $\overset{+}{N}HMe_aMe_b$ carbons in the spectra of $(2)H_{C\text{-}2}^+$ and $(2)H_{C\text{-}4}^+$ and similar non-equivalences in the spectra of $(3)H_{C\text{-}2}^+$ and $(3)H_{C\text{-}4}^+$ (see Tables 2 and 3). The CH_2 protons in $(1)H_{C\text{-}2}^+$ are also non-equivalent in their coupling to H-3, although their chemical shifts are accidently equivalent; similar non-equivalent CH_2 protons are seen in other C-protonated ions. As discussed later, we believe interconversion of the non-planar forms is the rate-limiting step in the deuteriation of (1).

In the compounds we have examined there is a delicate balance between N- and C-protonation and between *ortho*- and *para*-protonation. The latter is also initially surprising since naphthalene and its derivatives generally prefer α-protonation (equivalent to *para*-protonation here) which provides greater conjugative stabilisation, in the absence of powerful perturbation from substituents.[9] In fact Lammertsma [9h] recently reported the first case (hexahydropyrene) of preferred β-protonation of an alkylated naphthalene; he advanced sound reasons for the preference in this case. Olah *et al.*[9a] reported increasing amounts of β-protonation for both 1- and 2-halogenonaphthalenes in the order Cl < Br < I; however the evidence (from ^1H n.m.r.) does not seem to exclude the possibility that the supposed β-protonated species are in fact ions formed by α-protonation in the other ring (*i.e.* at C-5 and C-8). This explanation is, we feel, more in accord with the increasingly positive σ^+ values of the substituents along the series. The basicity of the two rings should become more equal in the iodonaphthalenes, but there is no obvious way in which iodine can stabilise the β-protonated ion. In contrast to this case, in the examples we have studied, there is no doubt that the major stabilisation of the ion is expressed in the immonium ion structure, so that the extra conjugative stabilisation possible for the C-4 (*i.e.* α) protonated ion becomes of secondary importance. Ions $(1)H_{C\text{-}2}^+$ and $(1)H_{C\text{-}4}^+$ are certainly not planar species, and non-planarity will further reduce the conjugative advantage, if any, of the C-4 protonated species. In practice,

ortho-protonation is (slightly) preferred for (1) and *para*-protonation is (slightly) preferred for (2)—(4), (7), and (8) (Table 4). Models suggest that it may be possible to achieve greater distortion from planarity for *ortho*-protonated species and this could explain the preference for this site in protonation of the most hindered compound (1); detailed discussion is however not warranted in the absence of force field calculations.

There are interesting variations in the N-/C-protonation ratios of the compounds we have studied. The preference for C-protonation of (3) compared with (2) or (4) is in accord with the theory of *I* strain;[10] in the five-membered pyrrolidine ring, sp^2 hybridised nitrogen (immonium ion, C-protonation) is favoured. It was on this basis, backed up by previous experimental evidence concerning 1,3,5-tripiperidino- and 1,3,5-tripyrrolidinyl-benzene,[1d] that we chose compound (12) as the best case for observing C-protonation in a simple 1-naphthylamine. In practice the *I* strain effect seems to work by stabilising the C-protonated ions from (3); although we made no quantitative study, (3) is undoubtedly a stronger base than (4) which required neat CF_3SO_3H for complete protonation. The dimorpholinonaphthalene ion (5) is apparently even weaker and does not N- or C-protonate in CF_3SO_3H (see Results section). It is worth noting here the very low basicity of these compounds; they possess among the most weakly basic amino nitrogens known; compared with (4) and (5), 2,4,6-trinitroaniline (picramide)[11a] is a strong base! Steric effects and the need to break a strong $\rangle N^+-H\!:\!N\langle$ bond in the second protonation are obviously both important, and it is interesting to compare these compounds with the inside-protonated 1,6-diazabicyclo[4.4.4]tetradecane ion, which does not accept a second proton in neat FSO_3H, but requires magic acid for diprotonation.[12]

Compounds (9) and (10) are much stronger bases and are not C-protonated. Addition of the second proton in these cases is not hindered and does not require the breaking of hydrogen bonds, though it may involve some increase in strain in the bicyclo[3.3.3]undecane system of (10), a feature which may be reflected in the ^{13}C shifts of the aromatic carbons of $(10)H_N^+$, which are distinctly different from those of (9) and other N protonated ions. The reason for the lack of C-protonation of (9) and (10) is plain; C-protonated ions from these species cannot be immonium ions, since the N lone pairs and the ring π-orbitals are orthogonal in (9) and (10).[13]

The results for the medium ring compounds (6)—(8) are difficult to explain in the absence of detailed conformational knowledge. There is a general preference for maximising the number of sp^2 atoms within a medium ring (thus favouring C-protonation). On the other hand models of C-protonated (6) do seem quite strained. It is worth noting that *cis*- and *trans*-isomers of N-protonated (6)—(8) are possible and, with (8) at least, an isomer with the immonium double bond *trans* within the medium ring is possible. We have no experimental evidence bearing on these points. It would have been interesting to study the kinetic protonation of these species, but our studies were hampered by lack of material.

Kinetically Controlled Protonations.—As we pointed out in our preliminary report[5] there are surprisingly few known examples of kinetically controlled protonations in strong acids. At about the time our paper appeared, Koptyug and his co-workers[14] reported several examples which are particularly relevant. On warming from low temperature O-protonated pentamethylanisole rearranges first to the *para*-protonated ion and eventually to the *ortho*-protonated ion,[14a] while with 4-bromo-2,3,5,6-tetramethylanisole the sequence is O- ⟶ *o*-C- ⟶ *p*-C-protonated ion.[14b] In another example 4-bromo-1-naphthol initially protonated at C-2 in FSO_3H at low temperatures, and then rearranged to the C-4 protonated species at −50°.[14c]

We investigated the kinetically-controlled protonation of (1)—(3), which in all cases was exclusively on nitrogen. Since conversion to the equilibrium mixture of ions is a base-catalysed process, the rate of equilibration is a function of the basicity of (1)—(3) and of the strength of the acid used (see the Results section). In practice, dissolving (2) in the strongest acid at ambient temperature always gave the equilibrium mixture of protonated ions, but for (3), partial equilibration was observed and some of this probably resulted from local overheating during the dissolution of (3) in the acid. In none of the cases we examined could we see evidence for more rapid isomerisation to one of the C-protonated ions; both forms were produced in their equilibrium ratio as isomerisation proceeded.

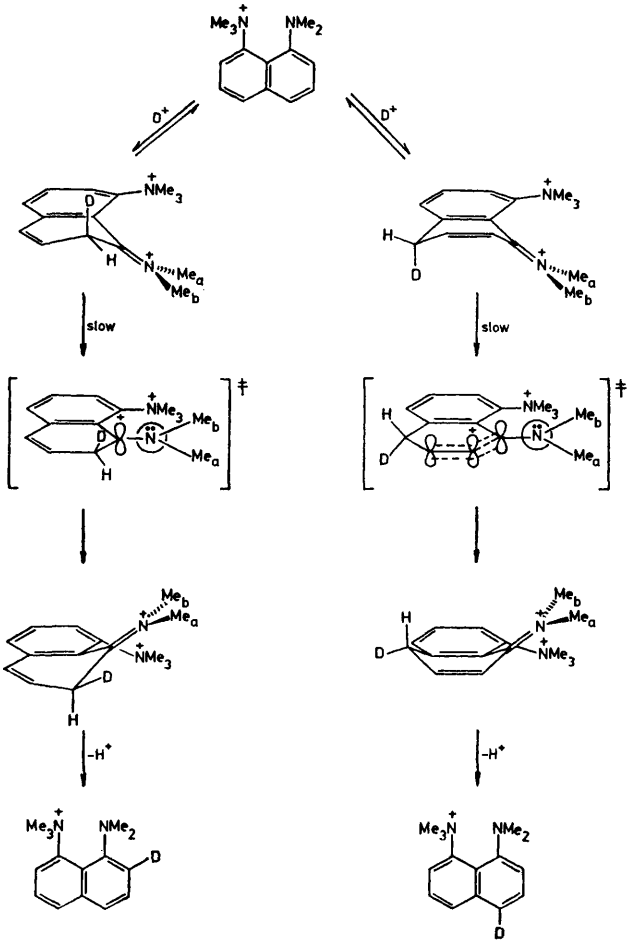
Several observations indicate that not only C-protonation of these species but N-protonation also, is associated with a remarkably high energy barrier. Interconversion of (1), (2), *etc.* and their C-protonated ions is always slow on the n.m.r. time scale at room temperature (separate, sharp spectra observed), even in solutions where $H_0 \approx pK_a$ (the point at which rates should be highest). For reaction (1) log k_2 is *ca.* −0.4 at room temperature in

$$(1)H_N^+ + H_2O \longrightarrow (1) + H_3O^+ \qquad (1)$$

72% $HClO_4$(H_0 −8 [11a,b]), corresponding to $\Delta G^{\ddagger}$ *ca.* 18 kcal mol^{-1}. From the fact that protonation of (1) is *ca.* 50% complete in CF_3COOH (H_0 −3 [11c]) and that $(1)H_N^+$ constitutes *ca.* 5% of the equilibrium mixture of protonated ions, one can estimate a pK_a of *ca.* −5 for N-protonation of (1). Thus in the 72% $HClO_4$, ΔG° for deprotonation of (1) is only ' uphill ' by *ca.* 4 kcal mol^{-1}. With these data one can estimate, using the Marcus–Agmon–Levine[15a-c] or Rehm–Weller[15d] equations that the intrinsic barrier $\Delta G^{\ddagger}$ (0) for N-protonation of (1) is *ca.* 15 kcal mol^{-1}. Protonation of most nitrogen and oxygen functions is near the diffusion-controlled limit, associated with an intrinsic barrier of 2—3 kcal mol^{-1}. It is likely that the lone pair of the NMe_2 group of (1) is buried in amongst the hydrogens of the NMe_3 group and substantial, energetically unfavourable geo-

metrical changes are required before acid can donate a proton to nitrogen.

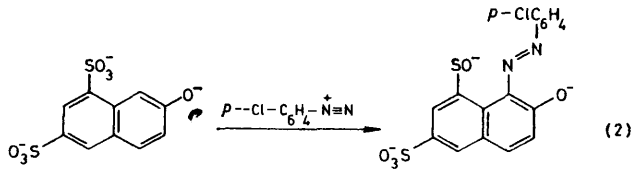
Deuterium Exchange in (1).—When dissolved in CF_3COOD, (1) forms $(1)D_{C-2}^+$ as the major ion, but exchange of the proton already present at C-2 is exceptionally slow, taking days at room temperature. The



SCHEME

^1H n.m.r. spectra observed during this exchange (see Results section) can be interpreted as due to various deuteriated species derived from the $-CH{=}CH{-}CH_{ax}H_{eq}$ unit shown in (11) with $\nu_{H-2ax} = \nu_{H-2eq} = \delta$ 4.35, ν_{H-3} δ 6.63, ν_{H-4} δ 6.90, $J_{2ax,3}$ 1.5 Hz, $J_{2eq,3}$ 6 Hz, $J_{2ax,4} = J_{2eq,4} = 1.5$ Hz, $J_{3,4}$ 9 Hz. Addition and loss of a proton (or deuteron) at C-2 is stereoelectronically controlled and occurs from an axial direction, so that addition and loss of H-2ax is rapid on the laboratory time scale, resulting in the (1) $\rightleftharpoons$ $(1)H_{C-2}^+$ equilibrium, but not in exchange at C-2. Exchange requires interconversion of the equivalent non-planar forms of $(1)H_{C-2}^+$, resulting in interchange of H-2ax and H-2eq. From models, it is likely that the NMe_2 group can only pass the NMe_3 group if it simultaneously rotates, so that, at the transition state, the nitrogen lone pair is orthogonal to the ring π-orbitals (loss of immonium ion conjugation) (see Scheme). This is clearly likely to be associated with a high barrier and we observe by ^1H n.m.r. that in 75% H_2SO_4 the signals for the immonium methyls in $(1)H_{C-2}^+$ remain sharp and distinct at 100°.

In practice, the sequence of changes in the ^1H n.m.r. spectrum of $(1)H_{C-2}^+$ indicate that deuterium exchange occurs somewhat more rapidly at C-4 ($t_{\frac{1}{2}}$ *ca.* 15 h) in (1) than at C-2 ($t_{\frac{1}{2}}$ *ca.* 100 h), despite the fact that deuterium addition occurs more readily at C-2. This fact is indeed in accord with the notion that the rate-limiting step in these exchanges is the conformational process described above and shown in the Scheme. In the transition state where immonium ion conjugation is lost, the C-4 protonated ion should be the more stable since it is an α-protonated naphthalene. If this description of the exchange process is acceptable it represents the first example, to the best of our knowledge, of an electrophilic aromatic substitution in which a conformation process is rate limiting. In the diazo-coupling studied by Zollinger [16] [equation (2)] the rate-limiting



(2)

stage is proton (deuteron) loss, as shown by the observation of a primary isotope effect, but the fact that proton loss is rate limiting is clearly due in part to steric effects and it may well be that there is a non-planar intermediate which can exist in two conformations with either a proton (or deuteron) or the phenylazo group in the reactive and unhindered axial position; proton (deuteron) loss can then only occur from the less stable conformer.

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