Brief Communications

A method for determination of the structure of the intramolecular hydrogen bond in the cations of unsymmetrically substituted 1,8-bis(dimethylamino)naphthalenes in solution

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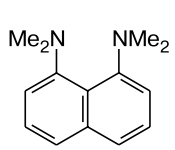
Alkylation of 8-dimethylamino-1-methylamino-4-nitronaphthalene in the CD_3I/KOH/DMSO system afforded a 4-nitro derivative containing the $N(CD_3)Me$ group in position 1. Direct proof of the structure of the intramolecular hydrogen bond in solutions of monoprotonated 4-R-1,8-bis(dimethylamino)naphthalenes was obtained for the first time. ^1H NMR study revealed that the chelated NH proton is shifted to the N(8) atom for R = NO_2 and NH_3^+ and to the N(1) atom for R = NH_2.

Key words: intramolecular hydrogen bond, N-alkylation, "proton sponge", nitro- and aminonaphthalenes.

Sustained attention to 1,8-bis(dimethylamino)naphthalene ("proton sponge", **1**) and its derivatives is due to not only their high basicities but also possibilities provided by their cationic forms (*e.g.*, compound **2**) in the study of the properties of low-barrier intramolecular hydrogen bonds (IHB) (see reviews[1,2] and original papers[3,4]). In particular, the symmetry of such a bond in proton sponge cations is a key and most disputable problem.



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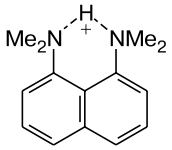

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On the time scale of the NMR experiment, cation **2** is symmetrical; *i.e.*, the chelated proton is exactly in the plane of symmetry bisecting the molecule.[2,3] However, this is merely an apparent pattern. More accurate methods[3,5—7] have shown that the NH proton rapidly vibrates about this plane and the cation structure can be represented more correctly as an equilibrium between two degenerate tautomers (Scheme 1, R = H). In unsymmetrical cations, this equilibrium is disturbed[3,6,8] and its posi-

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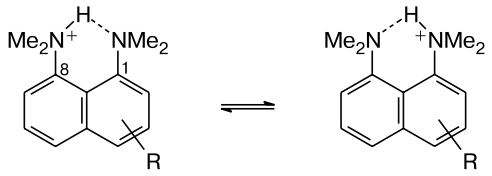
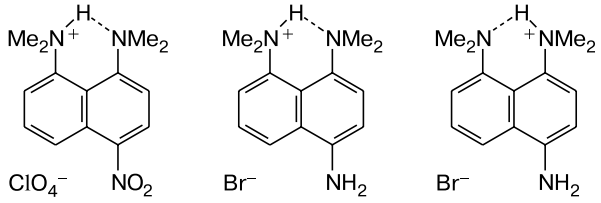
tion can be determined from the $^3J(NH,CH_3)$[8] and $^1J(N,H)$ constants.[9] It is quite a natural assumption that electron-withdrawing substituents R (in position 2, 3, or 4 of the naphthalene ring; see Scheme 1) shift the equilibrium to the left (the proton is localized at the N(8) atom), while the electron-donating ones, to the right (the N(1) atom is more "protonated").[6,8]

Scheme 1



For instance, the consistent data obtained for perchlorate **3** in solutions (NMR)[6,8] and in the solid state (X-ray diffraction analysis)[10] confirm the withdrawing effect of the NO_2 group and locate the proton at the N(8) atom to a 60—70% degree. An X-ray diffraction study of hydrobromide **4** also revealed an asymmetric IHB polarized toward the N(8) atom, which suggests structure **4a** rather than the expected structure **4b** (see Ref. 11). This can be explained by the effects of the crystal packing and the electrostatic field of the counterion. Based on the X-ray diffraction data, one can assume that in all unsymmetrical cations of the types **3** and **4**, the NH proton is shifted to the NMe_2 group that is more distant from the substituent in position 4. Thus, it was important to obtain data on the structure of cation **4** in solution. In the present work, we developed a method of achieving this goal.



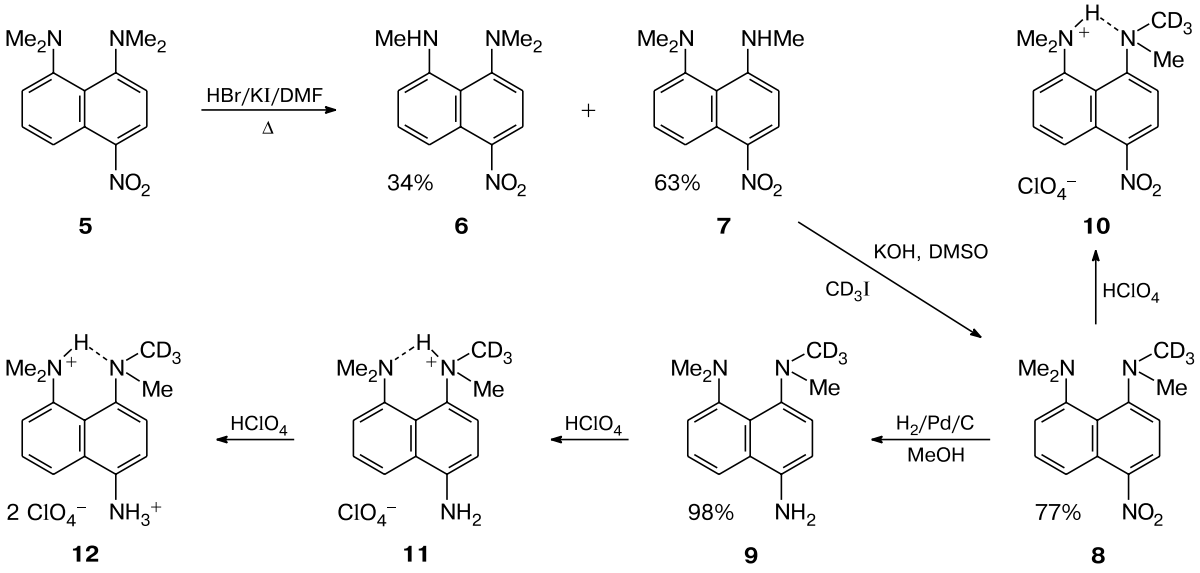
The approach we proposed is based on ^1H NMR study proton sponge cations in which one *N*-methyl group is replaced by a CD_3 group. It is known[2] that an acid proton is coordinated with the *peri*-NMe_2 groups to form classic (for proton sponges) cation **2** with IHB. The signals for the dimethylamino groups are shifted downfield by 0.4 to 0.5 ppm and appear as doublets because of a spin-spin coupling with the NH proton; the latter in turn is manifested in the ^1H NMR spectrum as a broadened singlet or a multiplet (depending on the cation symmetry) at δ 18—20 (see Ref. 8). The constancy of the sum of both constants $^3J_{NH,Me}$ (~5.2 Hz) and their inequality in unsymmetrical derivatives, on the one hand,[8] and their low sensitivities to isotopic substitution,[6] the concentration, the solvent, and the temperature, on the other hand,[9] have been proposed for estimation of the IHB asymmetry degree and the constants of tautomeric equilibrium.[6,8]

Before our research, introduction of the CD_3 group into proton sponges has been described in three studies, all of them dealing with naphthalene derivatives of the type **1**. One of those studies was concerned with preparation of a random mixture of all possible isotopomers by treating 1,8-diaminonaphthalene or its 2,7-dimethoxy derivative with a 1 : 1 mixture of Me_2SO_4 and Me_2SO_4-d_6 in order to discover tautomeric equilibrium in solution (see Scheme 1).[3] The two other were devoted to the synthesis of 1,8-bis(dimethylamino)naphthalene-d_{12} (all the four *N*-methyl groups are isotope-substituted) for kinetic investigations of the hydride reduction of some transition metal complexes[12] or for ^{13}C and ^{15}N NMR studies of proton dynamics in acid complexes **2** (see Ref. 7). Here we selectively introduced for the first time one CD_3 group and obtained proton complexes **10**—**12** (Scheme 2). To do this, diamine **5** was monodealkylated; the structures of the resulting nitro derivatives **6** and **7** were determined by X-ray diffraction analysis (see Ref. 13). Since nitronaphthalene **6** proved to be inert toward MeI in the presence of KOH in both acetone and DMSO, subsequent experiments were carried out with its reactive and more accessible isomer **7**. Alkylation of the latter with CD_3I gave a labeled sample of "nitro sponge" **8** with the known arrangement of the NMe_2 and $N(CD_3)Me$ groups in high yield. Catalytic hydrogenation of nitro compound **8** afforded amine **9**, while protonation of *peri*-diamines **8** and **9** with $HClO_4$ yielded deuterated salts **10**—**12**.

The resonance range for the dialkylamino groups in model salts **10**—**12** and the constants $^3J_{NH,Me}$ are given in Fig. 1.

It can be seen that the integral intensities of the doublets indicate localization of the chelated proton. Indeed, since the integral intensity of the 1-$N(CD_3)Me$ group is half that of the 8-NMe_2 group, it can be easily identified in the ^1H NMR spectrum without having recourse to D, ^{13}C, and ^{14}N NMR spectroscopy. Obviously, the dialkylamino group that is closer to the chelated proton will have a greater chemical shift and a higher constant $^3J_{NH,Me}$ (see Ref. 8). An analysis of the data obtained (see Fig. 1) revealed that the IHB asymmetry in a solution of labeled monoprotonated amine **11** (and hence its analog **4** as well) is just the same as shown in Scheme 2 and correlates completely with the electron-donating nature of the amino group. This conclusion is also true for solutions of complexes **10** and **12** with the electron-withdrawing NO_2 and NH_3^+ groups. Thus, the localization of the NH proton at the N(8) atom in the crystal of compound **4a** is an anomaly most likely associated with peculiar crystal packing or other factors.

Scheme 2



Experimental

^{1}H NMR spectra were recorded on Varian Unity-300 (300 MHz) and Bruker DPX-250 instruments (250 MHz) in acetonitrile-d_3 with $SiMe_4$ as the internal standard. Compounds **6** and **7** were prepared as described earlier;[13] CD_3I was prepared by treating CD_3OD (isotopic purity ≥98%) with phosphorus and iodine according to a standard procedure (the yield of CD_3I was 86%). Alkylation of nitronaphthalene **7** was carried out as described earlier.[14] The properties of isotopomers **8**—**11** (color, solubility, melting point, and ^{1}H NMR spectra) are identical with those of nondeuterated samples.[8,10,11] Diperchlorate **12** was *in situ* generated in CD_3CN by treating salt **11** with an equivalent of 70% $HClO_4$.

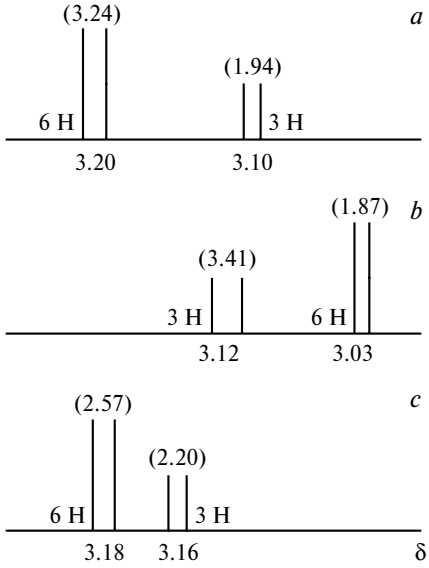


Fig. 1. The range of dialkylamino groups in the ^{1}H NMR spectra (in CD_3CN) of proton sponge salts **10** (*a*), **11** (*b*), and **12** (*c*) (shown on equal scales; the ^3J values (Hz) are given in parentheses).

8-Dimethylamino-1-(*N*-methyl-*N*-trideuteromethylamino)-4-nitronaphthalene (8). Found (%): C, 64.15; H+D, 7.32. $C_{14}H_{14}D_3N_3O_2$. Calculated (%): C, 64.10; H+D, 7.68. ^{1}H NMR ($CDCl_3$), δ: 2.77 (s, 6 H, 8-NMe_2); 2.99 (s, 3 H, 1-N(CD_3)Me); 6.69 (d, 1 H, H(2)); 6.94 (br.d, 1 H, H(7)); 7.48 (t, 1 H, H(6)); 8.30 (d, 1 H, H(3)); 8.43 (br.d, 1 H, H(5)); $J_{2,3}$ = 9.02 Hz, $J_{5,6}$ = 8.64 Hz, $J_{6,7}$ = 7.76 Hz.

8-Dimethylammonio-1-(*N*-methyl-*N*-trideuteromethylamino)-4-nitronaphthalene perchlorate (10). Found (%): C, 46.44; H+D, 5.92; Cl, 9.51. $C_{14}H_{15}D_3ClN_3O_6$. Calculated (%): C, 46.35; H+D, 5.84; Cl, 9.77. ^{1}H NMR, δ: 3.10 (d, 3 H, 1-N(CD_3)Me); 3.20 (d, 6 H, 8-NMe_2); 7.95 (t, 1 H, H(6)); 8.04 (d, 1 H, H(2)); 8.12 (br.d, 1 H, H(7)); 8.32 (d, 1 H, H(3)); 8.43 (dd, 1 H, H(5)); 18.77 (br.s, 1 H, NH); $J_{NH,1\text{-}NMe}$ = 1.94 Hz, $J_{NH,8\text{-}NMe}$ = 3.24 Hz, $J_{2,3}$ = 8.41 Hz, $J_{5,6}$ = 8.74 Hz, $J_{6,7}$ = 7.44 Hz, $J_{5,7}$ = 0.97 Hz.

4-Amino-8-dimethylamino-1-(*N*-methyl-*N*-trideuteromethylammonio)naphthalene perchlorate (11). Found (%): C, 50.41; H+D, 7.16; Cl, 10.51. $C_{14}H_{17}D_3ClN_3O_4$. Calculated (%): C, 50.53; H+D, 6.97; Cl, 10.65. ^{1}H NMR, δ: 3.03 (d, 6 H, 8-NMe_2); 3.12 (d, 3 H, 1-N(CD_3)Me); 5.15 (br.s, 2 H, NH_2); 6.91 (d, 1 H, H(3)); 7.64 (m, 2 H, H(6), H(2)); 7.85 (br.d, 1 H, H(7)); 8.02 (br.d, 1 H, H(5)); 18.64 (br.s, 1 H, NH); $J_{NH,1\text{-}NMe}$ = 3.41 Hz, $J_{NH,8\text{-}NMe}$ = 1.87 Hz, $J_{2,3}$ = $J_{5,6}$ = 8.43 Hz, $J_{6,7}$ = 7.33 Hz.

4-Ammonio-8-dimethylammonio-1-(*N*-methyl-*N*-trideuteromethylamino)naphthalene diperchlorate (12). ^{1}H NMR, δ: 3.16 (d, 3 H, 1-N(CD_3)Me); 3.18 (d, 6 H, 8-NMe_2); 4.20 (br.s, H_2O + NH_3^+); 7.83 (d, 1 H, H(3)); 7.97 (m, 2 H, H(6), H(2)); 8.07 (br.d, 1 H, H(7)); 8.12 (br.d, 1 H, H(5)); 18.79 (br.s, 1 H, NH); $J_{NH,1\text{-}NMe}$ = 2.20 Hz, $J_{NH,8\text{-}NMe}$ = 2.57 Hz, $J_{2,3}$ = 8.06 Hz, $J_{5,6}$ = 8.43 Hz, $J_{6,7}$ = 7.69 Hz.

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