peri-Naphthylenediamines 30.* 1,2,8-Tris(dimethylamino)naphthalene and some other 2-amino derivatives of "proton sponge"

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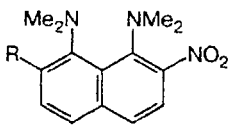
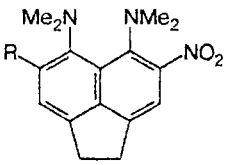
Catalytic hydrogenation of 1,8-bis(dimethylamino)-2-nitronaphthalene afforded previously unknown 2-amino-1,8-bis(dimethylamino)naphthalene. Its *N*-acetyl derivative and 1,2,8-tris(dimethylamino)naphthalene were prepared. The pK_a[1] values of the 2-NH_2-, 2-NHAc-, and 2-NMe_2-substituted "proton sponges" determined by a competition method in DMSO are equal to 10.3, 7.5, and 9.0, respectively.

Key words: naphthylamines, proton sponge, catalytic hydrogenation, methylation, basicity, "supporting effect."

Recently,[2] we have successfully isolated *ortho*-nitro derivatives of 1,8-bis(dimethylamino)naphthalene ("proton sponge") **1** and **2** and their acenaphthene analogs **3** and **4**. These compounds could serve as synthetic precursors of "proton sponges" with *ortho*-dialkylamino groups, for example, **5** and **6**.



1: R = H
2: R = NO_2



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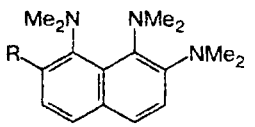
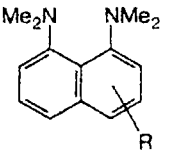


5: R = H
6: R = NMe_2

As in the case of *ortho*-alkoxy derivatives of 1,8-bis(dimethylamino)naphthalene,[3,4] "proton sponges" **5** and **6** are expected to possess a very high basicity, owing to the so-called "supporting effect."[5] In the present work, we studied the possibility and ease of transformation of an *ortho*-nitro group into an *ortho*-dialkylamino group in relation to the **1**→**5** transition, which was chosen because compound **1** is rather readily available.[2]

By analogy with a previous publication,[6] we carried out catalytic hydrogenation of nitro derivative **1**, which gave 2-amino-1,8-bis(dimethylamino)naphthalene (**7**), relatively stable in air. It should be noted that hydrogenation of "nitro sponge" **1** proceeds approximately three times as fast as that of *para*-isomer **8**. The yield of *ortho*-amine **7** can be as high as 100%, while deamination products are not formed at all (*cf.* Ref. 6). Apparently, the driving force for the easy reduction of compound **1** is its higher steric strain, which is markedly relieved when the NO_2 is replaced by the smaller NH_2 group.



7: R = 2-NH_2
8: R = 4-NO_2
9: R = 4-NH_2
10: R = 2-NHAc
11: R = 4-NMe_2

Amine **9** is known[6] to possess very high reactivity: it is rapidly oxidized in air and is readily acylated and alkylated. The substantially lower reactivity of *ortho*-amine **7** is apparently due to steric factors caused by the presence of the neighboring 1-NMe_2 group. This hampers conjugation of the amino group with the aromatic π-system, which results in a decrease in the energy of the higher occupied π-orbital and an increase in the first ionization potential and, hence, it hampers oxidation. Evidently, steric factors are also responsible for the lower reactivity of the 2-NH_2 group in compound **7** toward electrophiles. Indeed, the reactivity of amine **7** is lower than that of *para*-isomer **9** under similar conditions. Thus the latter compound readily

* For Part 29, see Ref. 1.

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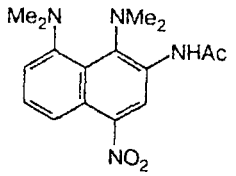
reacts with Ac_2O at room temperature, whereas the *ortho*-amine does not react with acetic anhydride. To prepare amide **10**, heating with a 10-fold excess of Ac_2O is required.

1,2,8-Tris(dimethylamino)naphthalene (**5**) is formed under the same conditions as compound **11** (MeI—KOH—DMF), but this requires a greater excess of MeI and heating for a longer period.

We attempted to use the acetylamino-substituted compound **10** for direct *meta*-substitution into the naphthalene nucleus in its reaction with electrophiles.[1] However, on treatment with nitric and sulfuric acids, amide **10** is converted into a mixture of isomers **12** and **13** in 1 : 3 ratio. No substitution in position 3 was observed. It is noteworthy that the aromatic ring bearing the acetamide group is somewhat deactivated.



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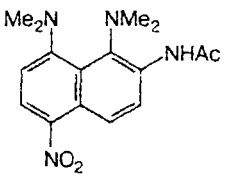

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The first ionization constants pK_a' of compounds **5**, **7**, and **10** in DMSO were estimated by the competition method using ^1H NMR spectroscopy.[6] These measurements gave basicity values of 9.0, 10.3, and 7.5, respectively. The pK_a' value for 1,8-bis(dimethylamino)naphthalene in DMSO amounts to 7.5[7]; this value for, *e.g.*, 1,4,5-tris(dimethylamino)naphthalene (**11**) is 8.0.[6]

Thus, migration of the dimethylamino group from the *para*-position (compound **11**) to the *ortho*-position (compound **5**) increases the basicity by an order of magnitude. This fact, in combination with other experimental data, points to the existence of a "supporting effect" in the *ortho*-amino derivatives of the "proton sponge." Apparently, this effect is largely determined by the activity of the lone electron pair of the *ortho*-substituent rather than by the substituent bulk, *i.e.*, the nature of the effect is mainly electrostatic rather than steric.[5] The +M effects of the NMe_2, NH_2, and NHAc groups decrease in the sequence $NMe_2 > NH_2 > NHAc$, which does not fully coincide with the series of basicity of these derivatives: $NH_2 > NMe_2 > NHAc$. This deviation seems to be due to the fact that the 2-NMe_2 group and the naphthalene ring are noncoplanar to even a greater extent than the amino group and the naphthalene ring, which additionally confirms (*cf.* Ref. 5) the conclusion that the contribution of the steric component to the "supporting effect" is less pronounced than that of electrostatic factors.

Experimental

Preparative and analytical chromatography was performed on Al_2O_3 (the activity grade is indicated). The other experimental details were described previously.[6]

2-Amino-1,8-bis(dimethylamino)naphthalene (7). The catalyst (2% Pd/C; 0.05 g) was added to a solution of compound **1** (0.052 g, 0.2 mmol) in 40 mL of MeOH and hydrogenation was carried out at ~20 °C and atmospheric pressure of H_2. The reaction was completed in 80—100 min. The catalyst was filtered off, methanol was distilled off, and the residue was evacuated to give 0.046 g (100%) of a light-violet oil, relatively stable in air. Found (%): C, 73.02; H, 8.20; N, 18.37. $C_{14}H_{19}N_3$. Calculated (%): C, 73.33; H, 8.35; N, 18.32. ^1H NMR ($CDCl_3$), δ: 2.70, 2.94 (both s, each 6 H, 1- and 8-NMe_2); 3.80 (br.s, 2 H, NH_2); 6.98 (d, 1 H, H(3), $J_{3,4}$ = 8.5 Hz); 7.09 (t, 1 H, H(6), $J_{6,7}$ = 7.3 Hz); 7.16, 7.38 (both dd, each 1 H, H(7), H(5), $J_{5,6}$ = 7.9 Hz, $J_{5,7}$ = 1.5 Hz). IR (Vaseline oil), ν/cm^{-1}: 1570, 1620 (ring); 3335, 3445 (NH_2).

2-Acetamido-1,8-bis(dimethylamino)naphthalene (10). Acetic anhydride (0.19 mL, 2 mmol) was added to a solution of amine **7** (0.046 g, 0.2 mmol) in 3 mL of chloroform and the mixture was refluxed for 2 h. After cooling, the mixture was concentrated to dryness, treated with 3 mL of concentrated KOH, and extracted with benzene (4×3 mL). The solvent was evaporated, the residue was chromatographed (V, elution with $CHCl_3$), and the colorless fraction with R_f 0.71 was collected (TLC monitoring). Yield 0.045 g (83%). Amide **10** is formed as light lilac crystals, m.p. 130—132 °C (from *n*-heptane). Found (%): C, 71.03; H, 7.92; N, 15.42. $C_{16}H_{21}N_3O$. Calculated (%): C, 70.82; H, 7.80; N, 15.48. ^1H NMR ($CDCl_3$), δ: 2.25 (s, 3 H, $COCH_3$); 2.68, 2.94 (both s, each 6 H, 1- and 8-NMe_2); 7.24 (m, 2 H, H(5), H(7)); 7.46 (m, 1 H, H(6), $J_{6,7}$ = 7.5 Hz); 7.54, 8.32 (both d, each 1 H, H(3), H(4), $J_{3,4}$ = 8.8 Hz); 8.42 (br.s, 1 H, NH). IR (Vaseline oil), ν/cm^{-1}: 1520, 1580 (ring); 1650 (C=O); 3240 (NH).

Nitration of 2-acetamido-1,8-bis(dimethylamino)naphthalene (10). A mixture of HNO_3 (d = 1.41 g cm^{-3}) (0.005 mL, 0.07 mmol) and 1 mL of concentrated H_2SO_4 was added dropwise with vigorous stirring to a solution of amide **10** (0.020 g, 0.07 mmol) in 1 mL of concentrated H_2SO_4 cooled to −15 °C. The light-brown mixture was stirred for 10 min at the same temperature, poured onto 20 g of ground ice, and neutralized with concentrated ammonia (12 mL). The products were extracted with $CHCl_3$ and chromatographed (III, elution with chloroform); the red fraction with R_f 0.37 was collected to give 21.2 mg (92%) of a dark-red crystalline mixture of **2-acetamido-(12)** and **7-acetamido-4-nitro-1,8-bis(dimethylamino)naphthalenes (13)** in 1 : 3 ratio (based on the ^1H NMR data), which was not separated. Found (%): C, 61.10; H, 6.47; N, 17.60. $C_{16}H_{20}N_4O_3$. Calculated (%): C, 60.75; H, 6.37; N, 17.71. ^1H NMR ($CDCl_3$), δ of compound **12** (mixed with **13**): 2.26 (s, 3 H, $COCH_3$); 2.67, 2.98 (both s, each 6 H, 8- and 1-NMe_2); 7.17 (dd, 1 H, H(7)); 7.41 (dd, 1 H, H(6), $J_{5,6}$ = 8.2 Hz, $J_{6,7}$ = 7.5 Hz, $J_{5,7}$ = 0.7 Hz); 7.75 (br.s, 1 H, NH); 8.85 (s, 1 H, H(3)); the signal of H(5) overlaps with the signals of isomer **13**. Compound **13** (mixed with **12**): 2.26 (s, 3 H, $COCH_3$); 2.79, 2.93 (both s, each 6 H, 8- and 1-NMe_2); 6.92, 8.09, 8.20, 8.40 (all d, each 1 H, H(2), H(3), H(6), H(5), $J_{2,3}$ = 8.7 Hz, $J_{5,6}$ = 9.4 Hz); 7.58 (br.s, 1 H, NH).

1,2,8-Tris(dimethylamino)naphthalene (5). The synthesis and isolation of the product were carried out by analogy with compound **11**,[6] except that MeI was taken in a 25-fold excess, the reaction mixture was stirred at 100 °C for 2 h (rather than 1 h), and a concentrated solution of KOH was used instead of

concentrated ammonia. The reaction of amine **7** (0.046 g) gave 0.042 g (81%) of dimethylamino derivative **5** as a reddish oil with R_f 0.70 (V, EtOAc—C_6H_6, 1 : 3) or 0.20 ($CHCl_3$). Found (%): C, 74.75; H, 8.93; N, 16.37. $C_{16}H_{23}N_3$. Calculated (%): C, 74.66; H, 9.01; N, 16.33. ^{1}H NMR ($CDCl_3$), δ: 2.64, 2.79, 3.00 (all s, each 6 H, 2-, 1-, and 8-NMe_2); 6.99 (d, 1 H, H(7)); 7.18 (t, 1 H, H(6), $J_{6,7}$ = 7.3 Hz); 7.27, 7.34, 7.44 (all d, each 1 H, H(3), H(5), H(4), $J_{3,4}$ = 8.5 Hz, $J_{5,6}$ = 7.9 Hz).

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