peri-Naphthylenediamines

19.* Acid-catalyzed transformations of 4,5-bis(dialkylamino)-1-hydroxymethylnaphthalenes

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The action of concentrated HCl on 4,5-bis(diethylamino)-1-hydroxymethylnaphthalene resulted in its cyclodimerization of the "head-to-head" type to form a spiro-compound, but, unlike its 4,5-bis(dimethylamino)-analog, cyclodimerization products did not occur on Al_2O_3. The transformation of 4,5-bis(dimethylamino)-1-hydroxymethylnaphthalene on Al_2O_3, TiO_2, and SiO_2 afforded the previously unknown di[4,5-bis(dimethylamino)naphthyl-4]methane, a spiro-compound of the "head-to-tail" type. 4,5-Bis(diethylamino)-1-hydroxymethylnaphthalene and 4,5-bis(diethylamino)naphthalene-1-carbaldehyde were synthesized.

Key words: naphthylmethyl carbocations, cyclodimerization, spiro-compounds; acid catalysis.

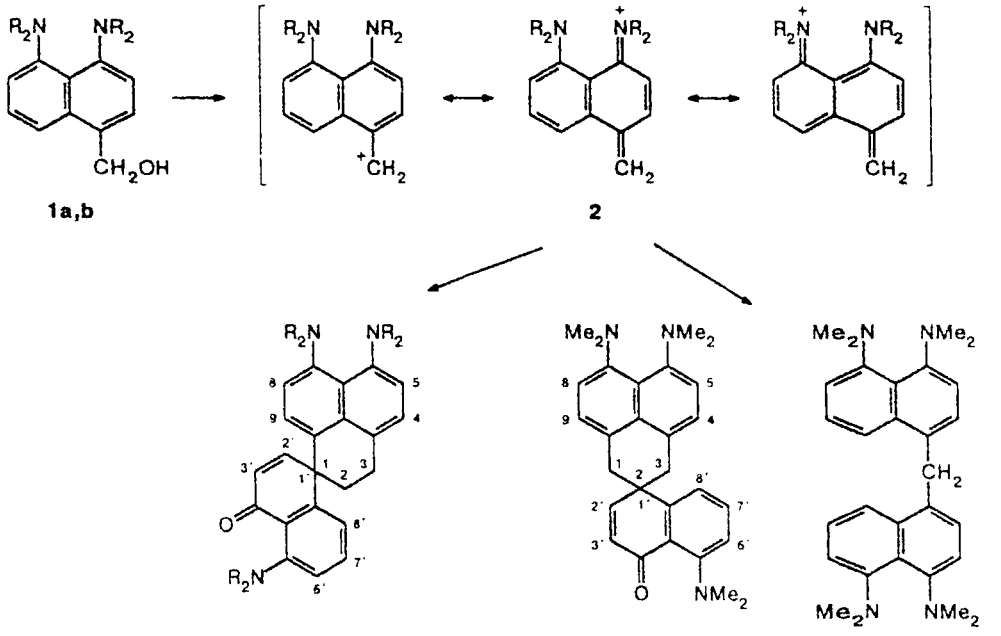
Previously we have discovered HCl- and H_3PO_4-catalyzed[2,3] and Al_2O_3-catalyzed[4,5] transformations of 4,5-bis(dimethylamino)-1-hydroxymethylnaphthalene (**1a**) in which the resonance-stabilized carbocation **2** generated *in situ* undergoes "head-to-head" type (during protonation) or "head-to-tail" type (on Al_2O_3) cyclodimerization to form spiro-compounds **3a** or **4**, respectively (Scheme 1).

Cyclodimerization of 4,5-bis(diethylamino)-1-hydroxymethylnaphthalene (**1b**) under the same conditions and also on SiO_2 and TiO_2 was studied in the present work.

The previously unknown alcohol **1b** was obtained by Vilsmeier formylation of 1,8-bis(diethylamino)naphtha-

* For Part 18, see Ref. 1.

Scheme 1



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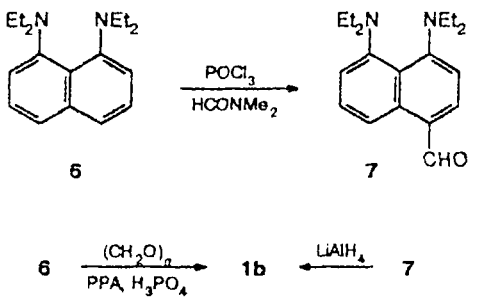
lene (**6**) followed by reduction of aldehyde **7** with $LiAlH_4$ in Et_2O (in a 41.7% overall yield), and also by hydroxymethylation of compound **6** with paraform in a mixture of polyphosphoric acid (PPA) and H_3PO_4 (in a 53% yield) (Scheme 2).

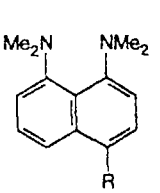
Scheme 2



Treatment of the hydroxymethyl derivative **1b** with concentrated HCl at 40 °C followed by alkalinization of the mixture afforded a nonsymmetrical spiro-compound **3b** in low yield. Multiple repetition of this process increases the yield of the spiro-compound to 22%. The lower yield of compound **3b** as compared with that of **3a** may result from the fact that carbocation **2b** is less stable due to the noncoplanarity of the bulky diethylamino groups and the naphthalene π-system. Therefore, along with "head-to-head" type cyclodimerization,[2,3] competitive transformation of carbocation **2b** into the original compound **1b** is observed upon alkalinization.

Unlike **1a**,[4,5] alcohol **1b** does not undergo cyclodimerization on anhydrous Al_2O_3 in C_6H_6 (3 h at 80 °C). Strong resinification is observed in this case, and aldehyde **7** is the only isolated product (yield 50%). Dehydration of alcohol **1b** with carbocation **2b** or oxidation of alcohol **1b** with atmospheric oxygen are the conceivable mechanisms of its formation.

Compound **1b** does not undergo cyclodimerization on SiO_2 and TiO_2, whereas its lower homolog **1a** forms the expected symmetrical spiro-compound **4** on SiO_2, Al_2O_3, and TiO_2[4,5] in 55, 37, and 23% yields, respectively. The main product of the transformation on TiO_2 is the known[6] aldehyde **8** (in 51% yield), which is absent on SiO_2 completely. The reactions of compound **1a** on SiO_2, Al_2O_3, and TiO_2 afford also di[4,5-bis(dimethylamino)naphthyl-1]methane (**5**) in 27, 25, and 11% yields, respectively. This compound may be formed *via ipso*-substitution of the CH_2OH group with carbocation **2**. We have observed similar *ipso*-substitution for other napthylmethyl carbocations.[4,5] Compound **5** is a new representative of a "double proton sponge" (*cf.* Ref. 7).



8: R = CHO
9: R = Me_2NCH_2

It is surprising that amine **9**, which is always formed on Al_2O_3 and hinders the purification of spiro-compound **4**,[5] is absent among the reaction products on SiO_2 and TiO_2.

Experimental

^1H NMR spectra were recorded on a Unity-300 spectrometer (300 MHz) with $SiMe_4$ as the internal standard. IR spectra were obtained on a UR-20 instrument, and UV spectra were recorded on a Specord M40 spectrophotometer. Mass spectra were recorded on an MX-1321 A spectrometer with direct inlet of the sample into the ionizing chamber at 50—100 °C and a 70 eV ionizing voltage. TiO_2—rutyl ("pure" grade, 98% purity), silica gel L 40/100 (Chemapol), and Al_2O_3 for chromatography (Brockmann activity II, calcined 20 min at 250 °C) were used as cyclodimerization catalysts.

4,5-Bis(diethylamino)naphthalene-1-carbaldehyde (7). A Vilsmeier reagent (prepared by dropwise addition of freshly distilled $POCl_3$ (0.51 mL, 5.5 mmol) to dry DMF (5.5 mL) at −15 °C) was added dropwise to a solution of 1,8-bis(diethylamino)naphthalene (**6**)[8] (2.9 g, 11 mmol) in dry toluene (20 mL) for 30 min with stirring and cooling. The mixture was kept for 1 h and warmed to 0 °C, then cold water (70 mL) and a 10% NaOH solution (2 mL) were added. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (4×15 mL). The toluene and chloroform extracts were concentrated and the combined residues were chromatographed on a column with Al_2O_3 (4×1.5 cm). Elution with hexane afforded a light-yellow fraction of the original compound **6** (yield 0.29%). After that, elution with chloroform was carried out to give 0.40 g (13%) of bright-yellow aldehyde **7** (R_f 0.56 (Al_2O_3, $CHCl_3$)). Found (%): C, 76.25; H, 8.50; N, 9.25. $C_{19}H_{26}N_2O$. Calculated (%): C, 76.47; H, 8.78; N, 9.39. IR (in thin layer), ν/cm^{-1}: 1680 (C=O), 1574 (C=C arom.). UV (MeOH), λ_{max}/nm (log ε): 223.5 (4.34), 267.5 (4.29), 353.7 (3.72) sh, 400 (4.12). ^1H NMR ($CDCl_3$), δ: 0.95 (t, 6 H, 5-$\underline{Me}CH_2N$); 1.00 (t, 6 H, 4-$\underline{Me}CH_2N$); 3.08—3.28 (m, 4 H, 5-Me$\underline{CH_2}N$); 3.35—3.45 (m, 4 H, 4-Me$\underline{CH_2}N$); 6.95 (d, 1 H, H(3), $J_{3,2}$ = 8.13 Hz); 7.01 (dd, 1 H, H(6), $J_{6,7}$ = 7.61, $J_{6,8}$ = 1.1 Hz); 7.46 (t, 1 H, H(7), $J_{7,8}$ = 8.39 Hz, $J_{7,6}$ = 7.69 Hz); 7.72 (d, 1 H, H(2), $J_{2,3}$ = 8.13 Hz); 8.96 (dd, 1 H, H(8), $J_{7,8}$ = 8.40 Hz, $J_{8,6}$ = 1.1 Hz); 10.09 (s, 1 H, CHO).

The pH of the aqueous layer was then adjusted to 14, and the solution was extracted with $CHCl_3$ (5×15 mL) to give 1.77 g of the initial compound **6** suitable for repeated formylation without additional purification.

4,5-Bis(diethylamino)-1-hydroxymethylnaphthalene (1b). *A.* $LiAlH_4$ (45 mg, 1.18 mmol) was added with stirring to a solution of aldehyde **7** (350 mg, 1.17 mmol) in dry Et_2O (20 mL), and the mixture was stirred until decoloration. Then water (5 mL) was added, and the ethereal layer was separated and concentrated. The residue was chromatographed on a column with Al_2O_3 (2.5×8 cm) in $CHCl_3$ to give 342 mg (97%) of alcohol **1b**. Found (%): C, 75.39; H, 9.21; N, 9.20. $C_{19}H_{28}N_2O$. Calculated (%): C, 75.96; H, 9.39; N, 9.32. ^1H NMR ($CDCl_3$), δ: 0.98 (t, 12 H, 4-, 5-$\underline{Me}CH_2N$); 2.80 (s, 1 H, OH); 3.18—3.30 (m, 8 H, 4-, 5-Me$\underline{CH_2}N$); 5.03 (s, 2 H, CH_2); 6.91* (br.d, 1 H, H(3)); 7.01* (br.d, 1 H, H(6)); 7.32 (d, 1 H, H(2), $J_{2,3}$ = 7.69 Hz); 7.37* (br.dd, 1 H, H(7)); 7.73* (br.dd, 1 H, H(8)).

* The signals marked were significantly broadened due to dynamic processes, which made difficult an accurate determination of the spin-spin coupling constants.

B. Compound **6** (2.70 g, 10 mmol)[8] and PPA (5 g) were dissolved with stirring in 75% H_3PO_4 (8 mL). Paraform (0.75 g, 25 mmol) was added to the solution at 45 °C, and the mixture was stirred at 45 °C for 40 h until the original compound **6** disappeared (TLC). The mixture was diluted with water (120 mL) and alkalized with 20% NaOH to pH 14. The oil formed was extracted with $CHCl_3$ (4×25 mL), and the extract was concentrated *in vacuo*. The products were isolated by chromatography on a column with Al_2O_3 (4×2.5 cm) with a hexane—$CHCl_3$ gradient to give 1.58 g (53%) of compound **1b** identical to that obtained by method *A*.

Spiro[6,7-bis(diethylamino)-2,3-dihydrophenalene-1,1′-(5′-diethylamino-1′,4′-dihydronaphthalen-4′-one)] (3b). A solution of compound **1b** (70 mg, 0.23 mmol) in 35% HCl (3 mL) was kept at 40 °C for 5 min, diluted with equal volume of water, and poured into 20% NaOH (10 mL). The suspension was shaken with $CHCl_3$ (3×5 mL), and the extract was concentrated *in vacuo*. The residue obtained was treated 10 times as described above. The product was purified by chromatography on a column with Al_2O_3 (2×20 cm, eluent $CHCl_3$—AcOEt (2 : 1)) to give 13 mg (22%) of compound **3b**. Found (%): C, 80.06; H, 8.43; N, 8.21. $C_{34}H_{43}N_3O$. Calculated (%): C, 80.11; H, 8.50; N, 8.24. IR, CCl_4, ν/cm^{-1}: 1669 (C=O); 1590 (C=C arom.). UV (MeOH), λ_{max}/nm (log ε): 229.5 (4.02), 263.9 (3.52) sh, 302.0 (3.38), 416.5 (3.15). ^1H NMR ($CDCl_3$), δ: 0.92—1.06 (m, 12 H, 6-, 7-$\underline{Me}CH_2N$); 1.15 (t, 6 H, 5′-$\underline{Me}CH_2N$); 2.18 (m, 2 H, 2-CH_2); 3.09—3.38 (m, 14 H, 6-, 7-, 5′-Me$\underline{CH_2}N$, 3-CH_2); 6.27 (d, 1 H, H(3′), $J_{3',2'}$ = 10.04 Hz); 6.40 (dd, 1 H, H(6′), $J_{6',7'}$ = 6.96 Hz, $J_{6',8'}$ = 0.81 Hz); 6.82 (br.s, 2 H, H(8), H(9)); 6.93 (dd, 1 H, H(8′), $J_{8',7'}$ = 7.88 Hz, $J_{8',6'}$ = 0.81 Hz); 6.98 (d, 1 H, H(5), $J_{5,4}$ = 7.04 Hz); 7.01 (d, 1 H, H(2′), $J_{2',3'}$ = 9.96 Hz); 7.15 (t, 1 H, H(7′), $J_{7',6'}$ = 7.91 Hz, $J_{7',8'}$ = 7.98 Hz); 7.19 (d, 1 H, H(4), $J_{4,5}$ = 6.87 Hz). MS, *m/z* (I_{rel} (%)): 509 $[M]^+$ (55), 495 (20), 480 $[M-Et]^+$ (100), 463 (26), 435 (33).

Transformations of 4,5-bis(dimethylamino)-1-hydroxymethylnaphthalene (1a). *A.* *On TiO_2.* A mixture of 4,5-bis(dimethylamino)-1-hydroxymethylnaphthalene (**1a**)[3] (85 mg, 0.35 mmol) and TiO_2 (2 g) in C_6H_6 (15 mL) was kept at 80 °C for 25 h (TLC control). The TiO_2 was then filtered off and washed with $CHCl_3$ (3×10 mL). The benzene and chloroform solutions were concentrated and the residues were combined and chromatographed on a column with Al_2O_3 (2×25 cm) in $CHCl_3$ to isolate 43 mg (51%) of aldehyde **8** (the product was identified by comparison with an authentic sample),[6] 27 mg (23%) of spiro[6,7-bis(dimethylamino)-1,3-dihydrophenalene-2,1′-(5′-dimethylamino-1′,4′-dihydronaphthalen-4′-one)] (**4**) (the ^1H NMR spectrum of product **4** corresponded to that described previously),[2,3] and 19 mg (25%) of di[4,5-bis(dimethylamino)naphthyl-1]methane (**5**) as fine colorless crystals, m.p. 166—167 °C (*n*-C_7H_{16}). Found (%): C, 78.93; H, 8.20; N, 12.70. $C_{29}H_{36}N_4$. Calculated (%): C, 79.05; H, 8.23. ^1H NMR ($CDCl_3$), δ: 2.77 (s, 6 H, 1-Me_2N); 2.83 (s, 6 H, 8-Me_2N); 4.62 (s, 2 H, CH_2); 6.80 (d, 1 H, H(2), $J_{2,3}$ = 7.81 Hz); 6.90 (d, 1 H, H(3), $J_{3,2}$ = 7.79 Hz); 6.96 (dd, 1 H, H(7), $J_{7,6}$ = 7.51 Hz, $J_{7,5}$ < 1 Hz); 7.31 (t, 1 H, H(6), $J_{6,7}$ = 7.62 Hz, $J_{6,5}$ = 8.17 Hz); 7.57 (dd, 1 H, H(5), $J_{5,6}$ = 8.10 Hz, $J_{5,7}$ < 1 Hz).

B. *On silica gel.* A mixture of compound **3a**[3] (230 mg, 0.94 mmol) and silica gel (5 g) in C_6H_6 (60 mL) was kept at 80 °C for 15 h (TLC control). The silica gel was filtered off and washed with $CHCl_3$ (3×20 mL). The benzene and chloroform solutions were concentrated, and the residues were combined and chromatographed on a column with Al_2O_3 (4×1.5 cm) in heptane to give 57 mg (27%) of compound **5**, m.p. 166—167 °C.

The column was then washed with ethyl acetate to give 110 mg (55%) of spiro-compound **4**.

Transformations of 4,5-bis(diethylamino)-1-hydroxymethylnaphthalene (1a). *A.* *On Al_2O_3.* A mixture of compound **1b** (50 mg, 0.17 mmol) and anhydrous Al_2O_3 (3 g) in C_6H_6 (15 mL) was kept at 80 °C for 3 h (TLC control). Extensive resinification was observed. The mixture was cooled, and the Al_2O_3 was filtered off and washed with $CHCl_3$ (3×10 mL). The benzene and chloroform solutions were concentrated, and the residues were combined and chromatographed on a column with Al_2O_3 (1×10 cm) in $CHCl_3$ to give 25 mg (50%) of product **7** and 7 mg (14 %) of the original alcohol **1b**.

B. *On TiO_2.* A mixture of compound **1b** (150 mg, 0.5 mmol) and TiO_2 (3 g) in C_6H_6 (25 mL) was kept at 80 °C for 40 h (TLC control). The TiO_2 was filtered off and washed with $CHCl_3$ (3×10 mL). The benzene and chloroform solutions were concentrated, and the residues were combined and chromatographed on a column with Al_2O_3 (1×10 cm) in $CHCl_3$ to give 13 mg (9%) of aldehyde **7** and 104 mg (69%) of the original alcohol **1b**.

C. *On silica gel.* A mixture of compound **1b** (400 mg, 1.33 mmol) and SiO_2 (8 g) in C_6H_6 (45 mL) was kept at 80 °C for 40 h (TLC control) to give 336 mg (84%) of the original compound **1b**.

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References

1. N. V. Vistorobskii and A. F. Pozharskii, *Izv. Akad. Nauk, Ser. Khim.*, 1996, 2297 [*Russ. Chem. Bull.*, 1996, **45**, 2181 (Engl. Transl.)].
2. N. V. Vistorobskii, A. F. Pozharskii, S. V. Shorshnev, and A. I. Chernyshev, *Mendeleev Commun.*, 1991, 10.
3. N. V. Vistorobskii, A. F. Pozharskii, A. I. Chernyshev, and S. V. Shorshnev, *Zh. Org. Khim.*, 1991, **27**, 1036 [*J. Org. Chem. USSR*, 1991, 27 (Engl. Transl.)].
4. A. F. Pozharskii, N. V. Vistorobskii, M. I. Rudnev, and A. I. Chernyshev, *Izv. Akad. Nauk, Ser. Khim.*, 1996, 2032 [*Russ. Chem. Bull.*, 1996, **45**, 1934 (Engl. Transl.)].
5. A. F. Pozharskii and N. V. Vistorobskii, *Izv. Akad. Nauk, Ser. Khim.*, 1996, 1016 [*Russ. Chem. Bull.*, 1996, **45**, 971 (Engl. Transl.)].
6. N. V. Vistorobskii and A. F. Pozharskii, *Zh. Org. Khim.*, 1989, **25**, 2154 [*J. Org. Chem. USSR*, 1989, **25** (Engl. Transl.)].
7. Th. Bart, C. Krieger, F. A. Neugebauer, and H. Staab, *Angew. Chem., Intern. Ed. Engl.*, 1991, **30**, 1028.
8. L. A. Kurasov, A. F. Pozharskii, and V. V. Kuz'menko, *Zh. Org. Khim.*, 1981, **17**, 1947 [*J. Org. Chem. USSR*, 1981, **17** (Engl. Transl.)].

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