Alumina-catalyzed cyclodimerization of 4-hydroxymethyl derivatives of 1,8-bis(dimethylamino)- and 1,8-dimethoxynaphthalenes to symmetrical spiro compounds

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4-Hydroxymethyl derivatives of 1,8-bis(dimethylamino)- and 1,8-dimethoxynaphthalenes undergo cyclodimerization on alumina to form symmetrical spiro compounds of the "head-to-tail" type. The reaction is considered to be a two-step electrophilic substitution with the participation of naphthylmethyl carbocations.

Key words: naphthylmethyl carbocations, electrophilic substitution, spiro compounds.

We have recently established that 4-hydroxymethyl-1,8-bis(dimethylamino)naphthalene (**1a**) when treated with concentrated HCl gives nonsymmetrical spiro compound **4** (Scheme 1).[1] The *in situ* formation of the resonance-stabilized carbocation **2a** was supposed, which enters the Diels—Alder reaction simultaneously as a reactive diene and dienophile.

In the present work, we have made an attempt to extend this reaction to 4-hydroxymethyl-1,8-dimethoxynaphthalene (**1b**). However, according to the ^{1}H NMR data, even the brief treatment of alcohol **1b** with concentrated HCl or CF_3CO_2H resulted in the formation of a mixture of oligomers probably corresponding to the structure **9**. It is evident that under these conditions two types of particles co-exist: a neutral molecule **1b** and carbenium cation **2b** whose interaction results in oligomerization.

To prevent oligomerization, carbocations were generated in a medium of lower acidity. In one of the experiments, alcohol **1b** was kept for 3 days on a chromatographic column with Al_2O_3. Subsequent elution with chloroform gave oligomers of the type **9**, the initial compound, and a compound with molecular weight 386, testifying to the dimerization of the fragments of the initial compound. The spectral parameters of the product obtained agree with the structure **8b** (the hitherto unknown type of symmetrical spiro compounds). It contains the conjugated carbonyl group (ν(C=O) 1655 cm^{-1}, δ ^{13}C 184.6), three MeO groups, two of which are equivalent, and two separate methylene groups bound with the sp^2-hybridized carbon atoms. The carbon atoms of these groups are equivalent, according to the ^{13}C NMR spectrum, and the protons are nonequivalent in pairs (the ^{1}H NMR spectrum of the AB type with δ 2.96 and 3.75).

Under similar conditions, alcohol **1a** also gives symmetrical spiro compound **8a** in ~23 % yield, and compounds **8a** and **8b** have similar spectral parameters. Two other products isolated were identified as aldehyde (**10**) (19 %)[2] and 4-dimethylaminomethyl-1,8-bis(dimethylamino)naphthalene (**11**) (22 %). Their formation can be considered as indirect proof of the participation of the carbenium ion **2a** in the corresponding transformations. Aldehyde **10** is likely obtained due to the dehydrogenation of alcohol **1a** with carbenium ion **2a**, and the reaction of the latter with dimethylamine (liberated upon hydrolysis of immonium salt **7a**) results in the formation of compound **11**.

The change in the direction of cyclodimerization of compound **1a** on going from protic acids to the Lewis catalyst (Al_2O_3) can be explained as follows. Alcohol **1a** transforms[1] rapidly into spiro compound **4** even at pH < 1. Taking into account the high basicity of the "proton sponge," [3] it is clear that the concentration of nonprotonated base **1a** in the strongly acidic medium should be minimum. Therefore, carbocation **2a** does not form oligomers and other by-products under these conditions. In fact, the $(4\pi+2\pi)$-cycloaddition with the formation of compound **4** is the only possible channel of its reaction. By contrast, a small equilibrium amount of carbenium ion **2a** is unambiguously generated on Al_2O_3, while the initial alcohol exists predominantly in the nonprotonated form. As a result, the latter is attacked by cation **2a** to form aldehyde **10** and a mixture of oligomers. The primary stage of the oligomerization likely gives dinaphthylmethane **5a** from which carbocation **6** is generated. The subsequent intramolecular *ipso*-attack of the methylene group on the ring carbon atom of the other naphthalene fragment results in the final product **8a** *via* inter-

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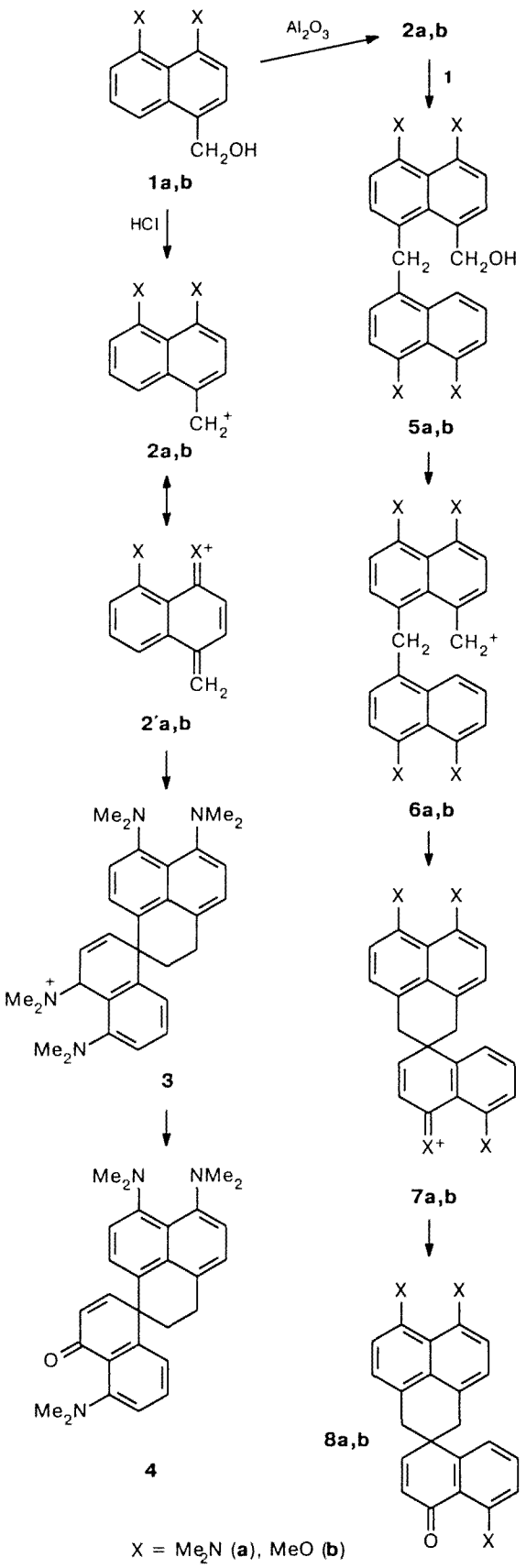
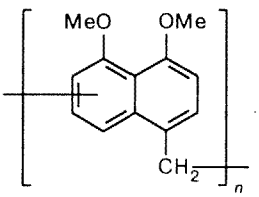
Scheme 1





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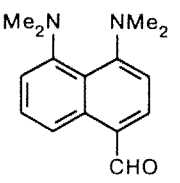

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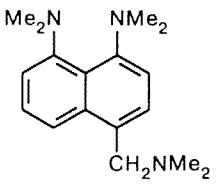

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mediate salt **7a**. Thus, the whole process is the two-step electrophilic substitution, but it is not the $(4\pi+2\pi)$-cycloaddition.

It should be mentioned in conclusion that compounds **8** belong to the rare class of spiro compounds of the "head-to-tail" type that are difficult to obtain. It has been mentioned previously that the cyclodimerization of methylenequinones,[4,5] and that of methylenequinoneimine **2a**, results in the formation of only spiro products of the "head-to-tail" type similar to compound **4**.

Experimental

^{1}H NMR and IR spectra were recorded on Unity-300 (^{1}H, 300 MHz, ^{13}C, 75.4 MHz) and UR-20 spectrometers, respectively. UV spectra were recorded on a Specord M-40 spectrophotometer. Mass spectra were recorded on an MKh-1321 spectrometer with the direct inlet of a sample at 100—150 °C and accelerating voltage of 70 eV.

4-Hydroxymethyl-1,8-dimethoxynaphthalene (1b). $NaAlH_4$ (0.081 g) was added to a solution of 4-formyl-1,8-dimethoxynaphthalene[6] (1.13 g) in anhydrous THF (10 mL), and the mixture was stirred for 15 min at 40 °C. After cooling, H_2O (0.2 mL) was added dropwise, and the organic layer was decanted. THF was distilled off, and the crystalline residue was recrystallized from benzene with addition of Al_2O_3 (0.2 g). White crystals with m.p. 99—100 °C were obtained (yield 1.08 g, 95 %). R_f 0.38 (Al_2O_3, $CHCl_3$). Found (%): C, 69.89; H, 5.94. $C_{13}H_{14}O_3$. Calculated (%): C, 70.02; H, 5.88. IR (CCl_4), ν/cm^{-1}: 3620 (OH, free); 3514 (OH, bound); 1578 (C—C aryl). ^{1}H NMR ($CDCl_3$), δ: 3.96 (s, 6 H, 1,8-$(OMe)_2$); 4.97 (s, 2 H, CH_2); 6.76 (d, 1 H, 2-H, $J_{2,3}$ = 7.91 Hz); 6.92 (d, 1 H, 7-H, $J_{7,6}$ = 7.92 Hz); 7.43 (d, 1 H, 3-H); 7.50 (dd, 1 H, 6-H, $J_{6,5}$ = 8.21 Hz); 7.68 (dd, 1 H, 5-H, $J_{5,7}$ = 0.58 Hz).

Spiro[6,7-dimethoxy-2,3-dihydrophenalene-2,1′-5′-methoxy-1′,4′-dihydronaphthalen-4-one] (8b). A solution of 4-hydroxymethyl-1,8-dimethoxynaphthalene (**1b**) (0.4 g) in $CHCl_3$ (3 mL) was applied onto a column with Al_2O_3 (Brockmann activity II, 4×15 cm) filled in benzene. $CHCl_3$ (50 mL) was passed, and then the column was allowed to stand for 72 h at ~20 °C. Three fractions were eluted with $CHCl_3$.

The first fraction with R_f 0.84 contained a mixture of oligomers (**9**). A yellowish amorphous powder with m.p. 87—95 °C (CCl_4—hexane, 1 : 1) was obtained in 0.12 g (31 %) yield. IR (CCl_4), ν/cm^{-1}: 3020—2940, 2842 (C—H); 1578 (C—C aryl); 1277 (C—O). ^1H NMR (DMSO-d_6), δ: 3.78—3.96 (m, 6 H, 2 OMe); 4.42, 4.56, 4.64, 4.73 and 4.84 (s, ~1.5 H, CH_2); 6.75—6.95 (m, ~2 H, H-2, and H-7); 7.38—7.55 (m, ~2 H, H-3, H-5, and H-6).

The second fraction with R_f 0.52 contained spiro compound **8b**. A slightly creamish amorphous powder with m.p. 234—236 °C (decomp., CCl_4) was obtained in the yield of 0.11 g (31 %). Found (%): C, 77.34; H, 5.80. $C_{25}H_{22}O_4$. Calculated (%): C, 77.70; H, 5.34. UV (MeOH), λ_{max}/nm (logε): 316 (4.21), 331 (4.20). IR (CCl_4), ν/cm^{-1}: 3030, 2967, 2944 (C—H); 1655 (C=O); 1579, 1543 (C—C aryl); 1265, 1219 (C—O). ^1H NMR ($CDCl_3$), δ: 2.96 (d, 2 H, 1-$H^{(a)}$ and 3-$H^{(a)}$, J_{gem} = 15.24 Hz); 3.75 (d, 2 H, 1-$H^{(b)}$, and 3-$H^{(b)}$); 4.00 (s, 9 H, 6,7-$(OMe)_2$, and 5′-OMe); 6.21 (d, 1 H, 3′-H); 6.67 (d, 1 H, 2′-H, $J_{2',3'}$ = 10.25 Hz); 6.85 (d, 2 H, 5-H and 8-H, $J_{5,4} = J_{8,9}$ = 7.91 Hz); 6.98 (d, 1H, 6′-H, $J_{6',7'}$ = 8.20 Hz); 7.18 (d, 2 H, H-4 and H-9); 7.25 (d, 1 H, 8′-H, $J_{8',7'}$ = 7.91 Hz); 7.58 (dd, 1-H, 7′-H). ^{13}C NMR (75.4 MHz, $CDCl_3$), δ: 39.27 (C-2); 43.81 (C-1 and C-3); 56.22, 56.61 (MeO); 106.46 (C-5 and C-8); 110.25 (C-6′); 117.43 (C-6a); 118.41 (C-3a and C-9a); 121.40 (C-4′a); 124.63 (C-4 and C-9); 128.27 (C-3′); 129.65 (C-8′); 131.55 (C-9b); 133.44 (C-7′); 148.91 (C-2′); 151.58 (C-8′a); 156.36 (C-6 and C-7); 160.56 (C-5′); 184.55 (C=O). MS, *m/z* (*I* (%)): 386 [M^+] (100), 371 (5), 355 (6), 213 (9), 171 (4), 129 (9), 101 (6).

The initial alcohol **1b** (yield 0.14 g, 35 %) was isolated from the third fraction with R_f 0.38.

Spiro[6,7-bis(dimethylamino)-2,3-dihydrophenalene-2,1′-5′-dimethylamino-1′,4′-dihydronaphthalen-4-one] (8a). A solution of compound **1a** (0.3 g, 1.2 mmol) in $CHCl_3$ (3 mL) was applied onto a column filled with Al_2O_3 in benzene (2×25 cm) and $CHCl_3$ (5 mL) was passed. Then the column was kept for 78 h. A yellow fraction with R_f 0.61 was collected first upon elution with $CHCl_3$. Its repeated purification on a column (2×15 cm) gave almost pure aldehyde **10** (55 mg, 19 %) identified with the known sample by ^1H NMR and other physicochemical parameters.[2]

The yellow zone with R_f 0.12 containing a mixture of spiro compound **8a** and amine **11** in the ratio ~1 : 1 was eluted as the second fraction. It was also repeatedly chromatographed on a column with calcined Al_2O_3 (~I activity, 1.5×20 cm, eluent $CHCl_3$). The yellow fraction was eluted, $CHCl_3$ was distilled off, and spiro product **8a** (59 mg, 23 %) as a lemon-yellow powder with m.p. 158—160 °C (decomp.) was obtained after recrystallization from an EtOH—H_2O (5 : 1) mixture. Found (%): C, 79.03; H, 7.20; N, 10.04. $C_{28}H_{31}N_3O$. Calculated (%): C, 79.06; H, 7.30; N, 9.88. UV (MeOH), λ_{max}/nm (logε): 230 (4.51), 291 (3.75), 301 (3.77), 317 sh (3.63), 418 (3.29). IR (CCl_4), ν/cm^{-1}: 1647 (C=O); 1610 (C—C aryl). ^1H NMR ($CDCl_3$), δ: 2.81 (s, 12 H, 6,7-NMe_2); 2.94 (s, 6 H, 5′-NMe_2); 2.97 (d, 2 H, 1-$H^{(a)}$ and 3-$H^{(a)}$, J_{gem} = 14.65 Hz); 3.75 (d, 2 H, 1-$H^{(b)}$ and 3-$H^{(b)}$); 6.19 (d, 1 H, 3′-H, $J_{3',2'}$ = 10.26 Hz); 6.67 (d, 1 H, 2′-H); 6.91 (d, 2 H, 5-H, and 8-H, $J_{5,4} = J_{8,9}$ = 7.62 Hz); 6.97 (d, 1 H, 6′-H, $J_{6',7'}$ = 8.20 Hz); 7.02 (d, 1 H, 8′-H, $J_{8',7'}$ = 7.62 Hz); 7.10 (dd, 2 H, 4-H, and 9-H, $^4J_{4(9),CH_2}$ = 0.59 Hz); 7.46 (dd, 1 H, 7′-H). ^{13}C NMR (75.4 MHz, $CDCl_3$), δ: 38.85 (C-1 and C-3); 39.97 (C-2); 44.33, 44.43 (6-, 7- and 5′-NMe_2); 112.60 (C-5 and C-8); 114.51 (C-6′); 116.46 (C-3a and C-9a); 120.25 (C-6a); 121.05 (C-4′a); 125.49 (C-4 and C-9); 128.81 (C-8′); 129.31 (C-3′); 130.83 (C-9b); 132.30 (C-7′); 148.75 (C-6 and C-7); 149.92 (C-2′); 152.11 (C-8′a); 153.32 (C-5′); 184.56 (C=O). MS, *m/z* (*I* (%)): 425 [M^+] (73), 410 (24), 379 (14), 271 (5), 227 (7), 211 (11), 149 (29), 84 (25), 68 (47), 57 (100).

After the spiro compound, a colorless fraction was eluted, from which $CHCl_3$ was distilled off, and amine **11** (52 mg, 16 %) as a thick colorless oil was obtained. ^1H NMR ($CDCl_3$), δ: 2.28 (s, 6 H, $CH_2N\underline{Me}_2$); 2.78 (s, 12 H, 1- and 8-NMe_2); 3.67 (s, 2 H, $C\underline{H}_2NMe_2$); 6.83 (d, 1 H, 2-H, $J_{2,3}$ = 7.67 Hz); 6.93 (dd, 1 H, 7-H, $J_{7,6}$ = 7.95, $J_{7,5}$ = 1.02 Hz); 7.20 (d, 1 H, 3-H); 7.35 (dd, 1 H, 6-H, $J_{6,5}$ = 8.35); 7.74 (dd, 1 H, 5-H). MS, *m/z* (*I* (%)): 271 [M^+] (53), 227 (53), 197 (8), 182 (15), 168 (6), 114 (12), 57 (100).

The last fraction eluted gave initial alcohol **1a** (15 mg, 5 %) after removal of $CHCl_3$.

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