A New Procedure for Fusion of a Five-Membered Ring. Building up of the Naphtho[1,8-*bc*]furan System

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Abstract—Reactions of 2,6-di-*tert*-butylnaphthalene-1,5-diol with aminals derived from aromatic aldehydes afforded 2-aryl-4,8-di-*tert*-butyl-2*H*-naphtho[1,8-*bc*]furan-5-ols and 2-aryl-4,8-di-*tert*-butylnaphtho[1,8-*bc*]-furan-5-ones.

Naphtho[1,8-*bc*]furans belong to *peri*-fused heterocycles which are systematically studied in our laboratory [1, 2]. The known methods for the synthesis of naphtho[1,8-*bc*]furan derivatives are based on transformations of substituents in positions 1 and 8 of the naphthalene ring or acid-catalyzed carbonylation at the *peri* position with respect to already existing hydroxy group [3].

In the present communication, we propose a novel procedure for fusion of a five-membered heteroring via reaction of aminals with naphthalene-1,5-diol derivatives in which positions 2 and 6 are occupied by substituents preventing ortho substitution. As initial compound we selected 2,6-di-tert-butylnaphthalene-1,5-diol which was described in patent [4]. The reaction occurred on fusion of the reactants at 160-170°C without a solvent. After heating for a short time under the conditions ensuring a limited contact with atmospheric oxygen, the major products were 4,8-di-tertbutyl-2*H*-naphtho[1,8-*bc*]furan-5-ols **IIa**–**IIc**. The second isolated product was methylenequinone III which was formed by oxidation of 2H-naphtho[1,8-bc]furan II. The transformation of compounds II into III was confirmed by oxidation of the former with potassium hexacyanoferrate(III).

As follows from Scheme 1, the first reaction step $(\mathbf{A} \rightarrow \mathbf{B})$ requires base catalysis. Aryldimorpholinomethane ArCH(NR₂)₂ abstracts proton from the naphthalene hydroxy group with liberation of morpholine molecule. The resulting iminium ion ArCH=N⁺R₂) attacks *para* position (C⁴) of ambident naphtholate ion **A**. The next step is heterocyclization ($\mathbf{B} \rightarrow \mathbf{II}$) with closure of five-membered ring and elimination of one more morpholine molecule. Had this process been preceded by deprotonation of the second hydroxy group $(\mathbf{B} \rightarrow \mathbf{C})$, the final product would be naphtho-[1,8-bc:4,5-cb]difuran **E** (Scheme 1) which was not detected in the reaction mixture.

In fact, both compounds **II** and **III** were always formed; their ratio depended primarily on the nature and position of substituents in the aryl group of the aminal, as well as on the reaction conditions (temperature, contact with atmospheric oxygen, etc.). 2*H*-Naphtho[1,8-*bc*]furans **II** having electron-donor substituents in the aryl group are more stable. This suggests homolytic rather than ionic (hydride) mechanism of the oxidation of compounds **II**.

The structure of compounds II and III was confirmed by the spectral data and elemental analyses. The IR spectra of **II** contained absorption bands due to stretching vibrations of the hydroxy group at 3480-3510 cm⁻¹. The position of that band in combination with the presence in the ¹H NMR spectrum of a signal at δ 5.3–6.5 ppm (which disappears upon deuteration) indicates the absence of intramolecular hydrogen bond. The carbonyl absorption band in the IR spectra of methylenequinones III is characterized by a reduced frequency (1630–1640 cm⁻¹) due to electron-donor effect of the oxygen atom in the five-membered heteroring and high degree of conjugation between the naphthalene system and aryl substituent. In the ¹H NMR spectra of 2*H*-naphtho[1,8-*bc*]furans II we observed a signal from the 2-H proton ($\delta \sim 6.6$ ppm); no such signal was present in the spectra of methylenequinones III.



Ar = Ph (a), 4-MeOC₆H₄ (b), 3,4-(MeO)₂C₆H₃ (c), 4-BrC₆H₄ (d); R₂N = morpholino.

EXPERIMENTAL

The IR spectra were recorded on a Specord IR-71 instrument from samples dispersed in mineral oil. The ¹H NMR spectra were measured on Varian Unity-300 and Bruker Avance DPX-250 spectrometers using HMDS as internal reference and CDCl₃ or CD₃CN as solvent. The purity of the products was checked by thin-layer chromatography on aluminum oxide with chloroform as eluent.

Reaction of 2,6-di-*tert*-butylnaphthalene-1,5-diol (I) with aryldimorpholinomethanes. *a. With dimorpholino(phenyl)methane*. A mixture of 0.136 g (0.5 mmol) of compound I and 0.4 g of dimorpholino-(phenyl)methane was heated for 10 min at 160–170°C, cooled, and recrystallized from 2 ml of ethanol. Yield of 4,8-di-*tert*-butyl-2-phenyl-5*H*-naphtho[1,8-*bc*]-furan-5-one (IIIa) 0.09 g (51%); bright yellow substance, mp 193–194°C (from alcohol). IR spectrum, v, cm⁻¹: 1633 (C=O). ¹H NMR spectrum (CDCl₃), δ , ppm: 1.4 s (9H, *t*-Bu), 1.6 s (9H, *t*-Bu), 7.42–7.46 d (1H, H_{naphth}, *J* = 8.02 Hz), 7.46–7.52 t (1H, H_{benz}, *J* = 7.15 Hz), 7.54–7.6 t (2H, H_{benz}, *J* = 7.91 Hz), 7.9 s

(1H, H_{naphth}), 7.93–7.96 d (1H, H_{naphth}, J = 7.91 Hz), 8.0–8.4 d (2H, H_{benz}, J = 7.14 Hz). Found, %: C 83.65; H 7.03. C₂₅H₂₆O₂. Calculated, %: C 83.8; H 7.26. The mother liquor was evaporated, and the residue was recrystallized from acetonitrile. Yield of 4,8-di-*tert*butyl-2-phenyl-2*H*-naphtho[1,8-*bc*]furan-5-ol (**IIa**) 0.04 g (22 %); colorless substance, mp 165–166°C. IR spectrum, v cm⁻¹: 3510 (OH). Found, %: C 83.56; H 7.77. C₂₆H₃₀O₃. Calculated, %: C 83.3; H 7.78.

b. With 4-methoxyphenyldimorpholinomethane. A mixture of 0.068 g (0.25 mmol) of compound I and 0.109 g (0.375 mmol) of 4-methoxyphenyldimorpholinomethane was heated for 10 min at 160–170°C, cooled, and recrystallized from 2 ml of ethanol. Yield of 4,8-di-*tert*-butyl-2-(4-methoxyphenyl)-5*H*-naphtho-[1,8-*bc*]furan-5-one (IIIb) 0.02 g (20.6%); bright yellow substance, mp 262–263°C. IR spectrum, v, cm⁻¹: 1633 (C=O). ¹H NMR spectrum (CD₃CN), δ , ppm: 1.28 s (9H, *t*-Bu), 1.62 s (9H, *t*-Bu), 3.88 s (3H, OCH₃), 7.0–7.96 m (4H, H_{benz}), 7.42–7.86 m (3H, H_{naphth}). Found, %: C 80.21; H 7.43. C₂₆H₂₈O₃. Calculated, %: C 80.41; H 7.22. The mother liquor was evaporated, and the residue was recrystallized from acetonitrile. Yield of 4,8-di-tert-butyl-2-(4-methoxyphenyl)-2H-naphtho[1,8-bc]furan-5-ol (IIb) 0.045 g (46.2%); colorless substance, mp 185–186°C. IR spectrum, v, cm⁻¹: 3487 (OH). ¹H NMR spectrum (CD₃CN), δ, ppm: 1.42 s (9H, *t*-Bu), 1.44 s (9H, *t*-Bu), 3.75 s (3H, OCH₃), 6,51 s (1H, OH), 6.64 s (1H, CH_{furan} , J = 1.11 Hz), 6.68–6.74 d (2H, H_{benz}, J =8.8 Hz), 6.97–7.01 d (1H, H_{naphth} , J = 8.72 Hz), 7.16 s (1H, H_{naphth} , J = 1.41 Hz), 7.21–7.25 d (2H, H_{benz} , J = 8.6 Hz), 7.26–7.3 d (1H, H_{naphth}, J = 8.75 Hz). Found, %: C 79.46; H 7.52. C₂₆H₃₀O₃. Calculated, %: C 80.0; H 7.69.

c. With 3,4-dimethoxyphenyldimorpholinomethane. A mixture of 3 g (11 mmol) of compound I and 7.1 g (22 mmol) of 3,4-dimethoxyphenyldimorpholinomethane was heated for 10 min at 160–170°C, cooled, and recrystallized from ethanol. Yield of 4,8-di-tertbutyl-2-(3,4-dimethoxyphenyl)-2H-naphtho[1,8-bc]furan-5-ol (IIc) 3.75 g (81%), mp 221-222°C. IR spectrum, v, cm⁻¹: 3499 (OH). ¹H NMR spectrum (CDCl₃), δ, ppm: 1.43 s (9H, *t*-Bu), 1.45 s (9H, *t*-Bu), 3.77 s (3H, OCH₃), 3.87 s (3H, OCH₃), 5,3 s (1H, OH), 6.76 s (1H, CH_{furan}, J = 1.36 Hz), 6.85 s (1H, H_{benz}, J =1.15 Hz), 6.84–6.88 d (1H, H_{benz} , J = 8.37 Hz), 7.16 d (1H, H_{benz}, J = 8,24 Hz), 7.07 s (1H, H_{naphth}, J =1.53 Hz), 7.11–7.15 d (1H, H_{naphth} , J = 8.63 Hz), 7.4– 7.44 d (1H, H_{naphth} , J = 8.64 Hz). Found, %: C 77.42; H 7.78. C₂₇H₃₂O₄. Calculated, %: C 77.14; H 7.62.

d. With 4-bromophenyldimorpholinomethane. A mixture of 0.136 g (0.5 mmol) of compound I and 0.341 g (1 mmol) of 4-bromophenyldimorpholinomethane was heated for 10 min at 160–170°C, cooled, and recrystallized from 2 ml of ethanol. Yield of 2-(4bromophenyl)-4,8-di-tert-butyl-5H-naphtho[1,8-bc]furan-5-one (IIId) 0.08 g (36.6%); bright yellow substance, mp 166–167°C. IR spectrum, v. cm⁻¹: 1647 (C=O). Found, %: C 68.93; H 5.86. C₂₅H₂₅BrO₂. Calculated, %: C 68.65; H 5,72.

Oxidation of 4,8-di-tert-butyl-2-(3,4-dimethoxyphenyl)-2H-naphtho[1,8-bc]furan-5-ol (IIc). A solution of 0.418 g (1.6 mmol) of K_3 [Fe(CN)₆] and 0.075 g (1.6 mmol) of NaOH in water was added to a solution of 0.07 g (0.167 mmol) of compound IIc in 2 ml of benzene, and the mixture was stirred for 1 h. The organic layer was separated, the solvent was distilled off under reduced pressure, and the residue was recrystallized from ethanol. Yield of 4,8-di-tert-butyl-2-(3,4dimethoxyphenyl)-5H-naphtho[1,8-bc]furan-5-one (IIIc) 0.066 g (95%); bright yellow substance, mp 160–161°C. IR spectrum, v, cm⁻¹: 1633 (C=O). ¹H NMR spectrum (CDCl₃), δ , ppm: 1.44 s (9H, *t*-Bu), 1.57 s (9H, t-Bu), 3.95 s (3H, OCH₃), 4.1 s (3H, OCH₃), 7.02–7.06 d (1H, H_{benz}, J = 8.45 Hz), 7.39– 7.43 d (1H, H_{naphth}, J = 8.03 Hz), 7.52 s (1H, H_{benz}, J =1.79 Hz), 7.62–7.66 d (1H, H_{benz}, J = 8.48 Hz), 7.87 s (1H, H_{naphth}), 7.91–7.96 d (1H, H_{naphth} , J = 8.01 Hz). Found, %: C 77.31; H 7.56. C₂₆H₂₈O₃. Calculated, %: C 77.51; H 7.18.

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