

Cyclic Tautomer of 1,5-Diacetyl-4,8-dihydroxynaphthalene and Its Reaction with Hydrazine

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Abstract—Demethylation of 1,5-diacetyl-4,8-dimethoxynaphthalene by the action of anhydrous aluminum chloride gave 6-acetyl-2,5-dihydroxy-2-methylnaphtho[1,8-*bc*]furan which reacted with hydrazine to produce 3,8-dimethyl-1,2,6,7-tetraazapyrene.

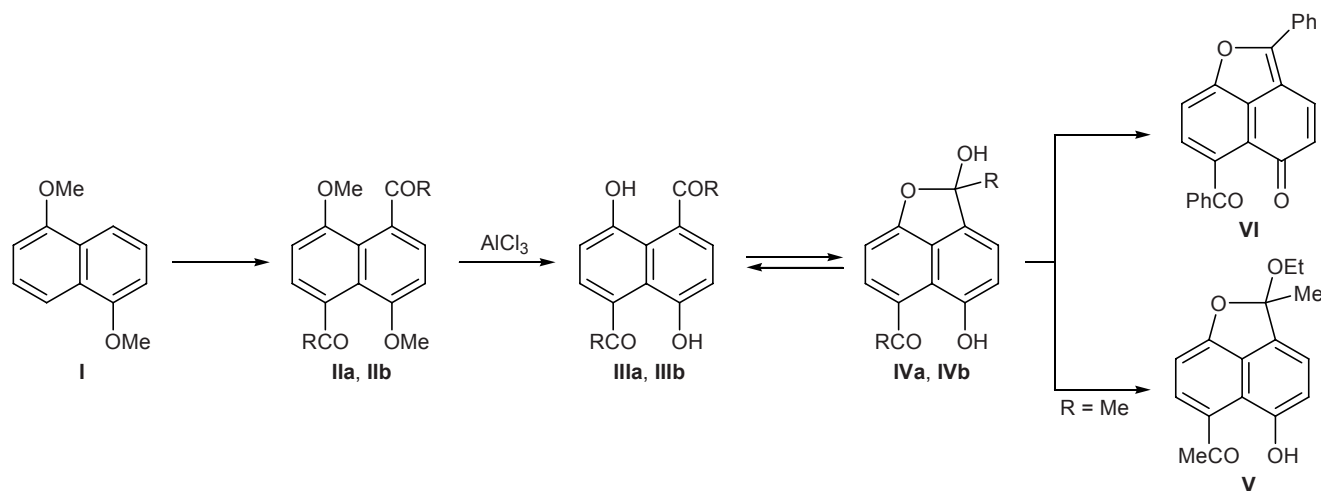
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peri-Hydroxynaphthyl ketones are universal building blocks for the synthesis of various *peri*-fused heterocyclic compounds of the naphthalene series [1]. It may be supposed that naphthalene derivatives having two ketone moieties in the *peri* positions could be potential precursors of bis-*peri*-fused heterocyclic system. In the present work 1,5-dimethoxynaphthalene (**I**) was acylated with acetic anhydride in the presence of perchloric acid, and 1,5-diacetyl-4,8-dimethoxynaphthalene (**IIa**) thus obtained was heated with anhydrous aluminum chloride. As a result, we isolated target compound **IIIa** (Scheme 1).

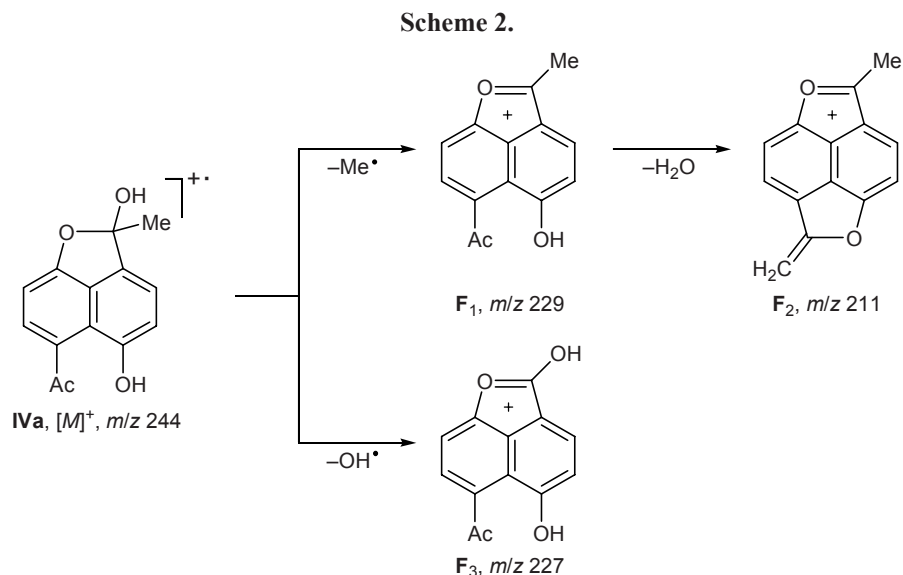
Bis-*peri*-hydroxy diketone **IIIa** in solution gives rise to equilibrium with cyclic hemiacetal isomer **IVa**.

The presence of the latter was confirmed by the formation of 2-ethoxynaphtho[1,8-*bc*]furan **V** when dihydroxy diketone **IIIa** was heated in ethanol. The ring-chain tautomeric equilibrium of compound **IIIa** is displaced toward cyclic structure **IVa**, as follows from the presence in the ¹H NMR spectrum of upfield (δ 4.10 ppm, 2-OH) and downfield (δ 12.78 ppm, 5-OH) one-proton signals from magnetically non-equivalent protons in the two chemically different hydroxy groups, two three-proton signals from the methyl groups, and four one-proton doublets from aromatic protons. The hemiacetal structure of **IVa** was also confirmed by the fragmentation pattern of its molecular ion, observed in the electron-impact mass

Scheme 1.



R = Me (a), Ph (b).



spectrum. The main fragmentation pathways involve elimination of hydroxyl and methyl radicals from the molecular ion with formation of ions **F**₁ and **F**₃ having naphtho[1,8-*bc*]furylium structure (Scheme 2).

Presumably, bis-*peri*-hydroxy benzoyl derivative **IIIb** synthesized by us previously is also capable of being converted into cyclic tautomer **IVb**. However, the latter readily loses water molecule to give the corresponding naphtho[1,8-*bc*]furan-5-one **VI** having quinoid structure [2]. Thus, bis-*peri*-hydroxy diketones **IIIa** and **IIIb** cannot be isolated as individual substances, and their presence in trace amounts among demethylation products of compounds **IIa** and **IIb** may be judged only by the presence of a characteristic spot remaining at the start upon chromatography in a thin layer of aluminum oxide.

Transformation of hemiacetal **IVb** into methylenequinone structure **VI** allows intermediate **A** to be formed as a tight ion pair of naphtho[1,8-*bc*]furylium cation and hydroxide anion and its subsequent dehydration. Obviously, analogous intermediate **B** is not formed from acetyl derivative **IVa** because of weaker

ability of methyl group (as compared to phenyl) to delocalize positive charge (Scheme 3).

We can presume with a high probability that the structure of naphtho[1,8-*bc*]furan derivatives **IVa** and **V** is similar to the structure of another derivative of the same heterocyclic system (compound **VII**), which was synthesized by us previously [3] and identified by X-ray analysis. An indirect support is provided by similarity in the chemical shifts of methyl and hydroxy protons and protons in the naphthalene ring in the ¹H NMR spectra of these compounds (Table 1). The downfield position of the hydroxy proton signal (δ 12.8 ppm) indicates formation of approximately equally strong intramolecular hydrogen bonds in compounds **IVa**, **V**, and **VII** (seven-membered H-ring). According to the X-ray diffraction data, the H-ring and the naphtho[1,8-*bc*]furan fragment in molecule **VII** lie in one plane, and hydrogen atom in the hydroxy group on C¹ appears in the vicinity of the straight line connecting the hydroxy and carbonyl oxygen atoms ($\angle\text{OHO} \approx 170^\circ$). It is known [4] that hydrogen bond is characterized by the maximal strength when the proton is located at the straight line connecting the two elec-

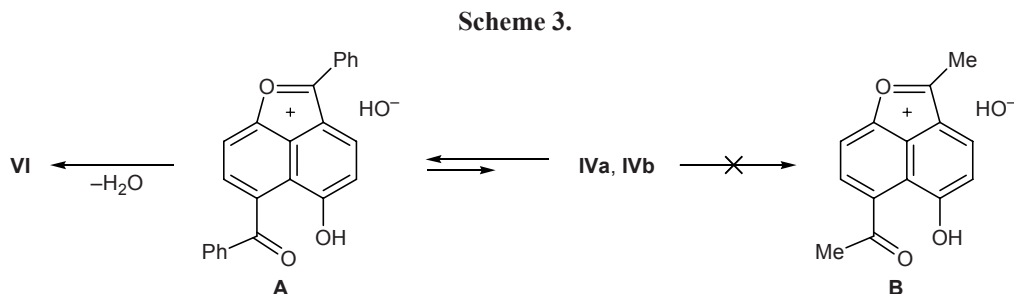
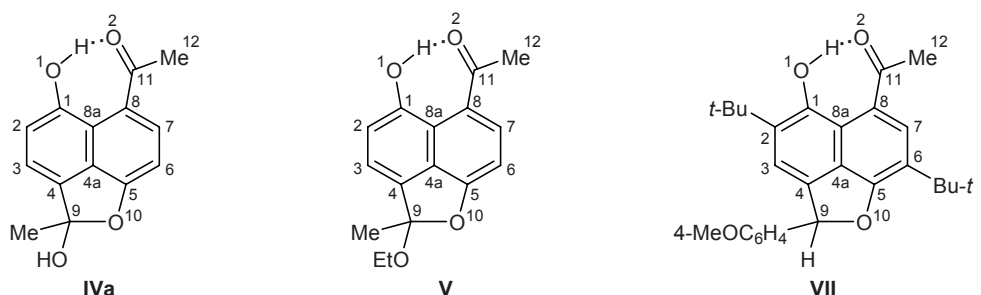


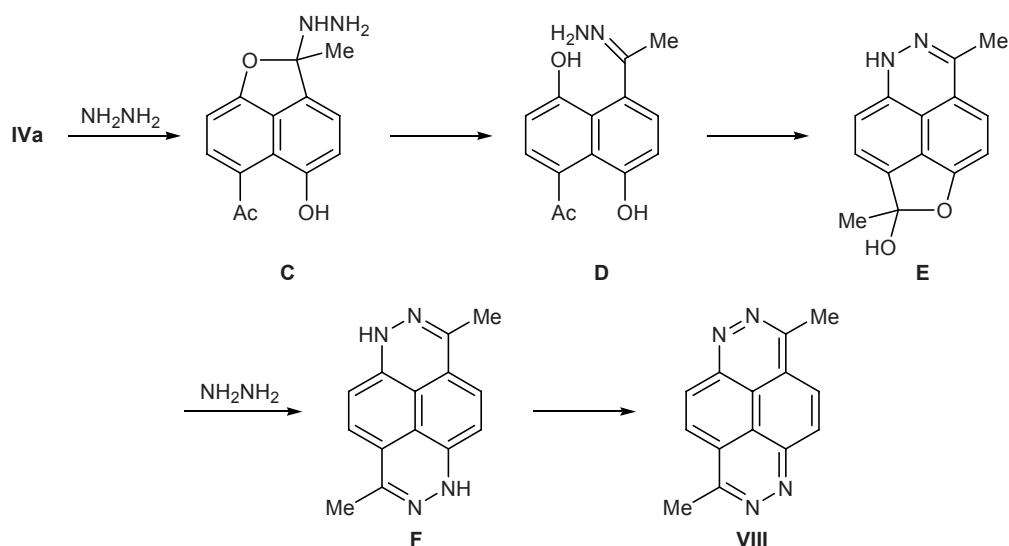
Table 1. Chemical shifts of some protons in the ^1H NMR spectra of compounds **IVa**, **V**, and **VII**, δ , ppm (J , Hz)


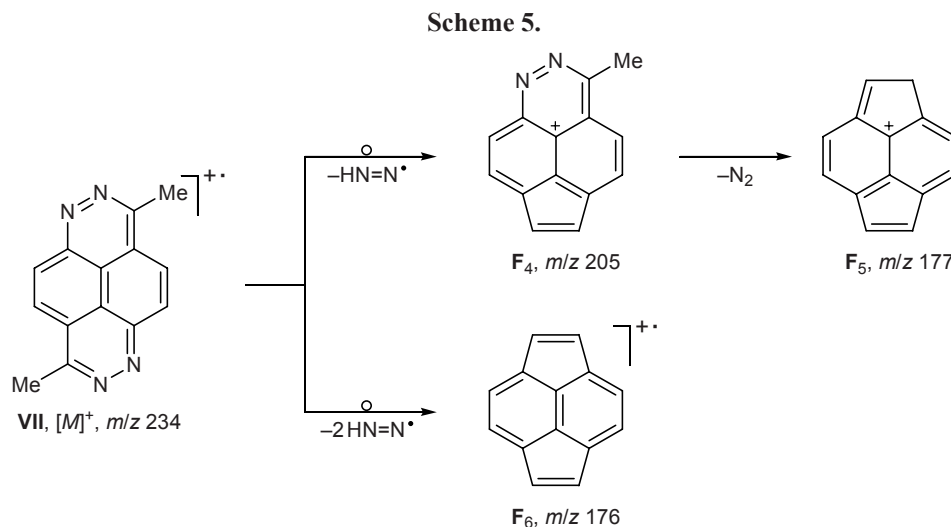
Compound no.	C^{12}H_3	2-H	3-H	6-H	7-H	1-OH
IVa	2.52 s	7.04 d (7.77)	7.35 d (7.77)	6.63 d (8.09)	8.18 d (8.09)	12.77 s
V	2.80 s	7.13 d (7.67)	7.32 d (7.67)	6.65 d (8.13)	8.30 d (8.13)	12.80 s
VII	2.80 s		7.20 s		8.25 s	12.80 s

tronegative atoms. Assuming identical conformations of the seven-membered H-ring in **IVa**, **V**, and **VII**, we can conclude that the intramolecular hydrogen bond in these structures is very strong. Considerable difference in the bond angles formed by carbon atoms of the naphthalene ring in the seven-membered H-ring ($\text{C}^1\text{C}^{8a}\text{C}^8$) and five-membered heteroring ($\text{C}^4\text{C}^{4a}\text{C}^5$) in molecule **VII** should be noted ($\sim 23^\circ$); the difference in the distances between the *peri*-carbon atoms in these rings ($\text{C}^1\cdots\text{C}^8$ and $\text{C}^4\cdots\text{C}^5$) is also large (0.37 Å; Table 2). These data indicate strong in-plane distortion of the naphthalene fragment. Such distortion of molecules **IVa**, **V**, and **VII**, induced by the presence of *peri*-fused five-membered heteroring, favors formation of stable seven-membered H-ring via compensation of repulsion between the oxygen atoms of the hydroxy

and carbonyl groups involved in intramolecular hydrogen bond.

By heating hemiacetal **IVa** with hydrazine hydrate in ethanol we obtained 1,2,6,7-tetraazapyrene **VIII** (Scheme 4) as the first representative of a new *peri*-fused heterocyclic system. On the basis of the results of our studies and concepts developed in [5, 6], a probable reaction scheme includes cascade heterocyclization **IVa** \rightarrow **C** \rightarrow **D** \rightarrow **E** \rightarrow **F** (Scheme 4); the subsequent oxidation of 1*H*,6*H*-1,2,6,7-tetraazapyrene **F** with atmospheric oxygen yields compound **VIII**. The ^1H NMR spectrum of tetraazapyrene **VIII** contained two two-proton doublets in the aromatic region and a six-proton singlet from the two methyl groups. The structure of **VIII** was also confirmed by mass spectrometry (Scheme 5). The main fragmentation pathways of

Scheme 4.



the molecular ion of **VIII** were elimination of one or two $N=NH\cdot$ radicals with formation of rearrangement ions **F₄** and **F₆**.

EXPERIMENTAL

The IR spectra were recorded on a Specord 71IR spectrometer from samples dispersed in mineral oil. The ^1H NMR spectra were measured on a Bruker Avance DPX-250 instrument from solutions in CDCl_3 . The mass spectra (electron impact, 70 eV) were obtained on a Kratos mass spectrometer with direct sample admission into the ion source (accelerating voltage 1.75 kV).

1,1'-(4,8-Dimethoxynaphthalene-1,5-diyl)diethanone (IIa). 1,5-Dimethoxynaphthalene (**Ia**), 806 mg (4.3 mmol), was dissolved in 3 ml of acetic anhydride, 4 drops of 70% perchloric acid were added under stirring, and the mixture was left to stand for 15 min at room temperature. After cooling, the precipitate was filtered off, washed with alcohol, and dried in air. Yield 680 mg (58%), colorless crystals, mp 187–188°C; published data [7]: mp 187–188°C.

1-(2,5-Dihydroxy-2-methylnaphtho[1,8-*bc*]furan-6-yl)ethanone (IVa). Anhydrous aluminum chloride, 500 mg (3.7 mmol), was added in portions under stirring to a solution of 200 mg (0.74 mmol) of compound **IIa** in 2 ml of tetrachloroethane. The resulting suspension was stirred for 10 min at room temperature until a thick oily material separated, and the mixture was then heated for 1.25 h on a water bath. The oily layer gradually dissolved, the solution was cooled and poured into ice water, and the mixture was extracted with chloroform (2×10 ml). The extract was evaporated in air, and the glassy residue was ground first with

methanol and then with diethyl ether. Yield 130 mg (73%), yellow crystals, mp 141–145°C (from methanol). ^1H NMR spectrum, δ , ppm: 1.90 s (3H, 2- CH_3), 2.52 s (3H, 6- COCH_3), 4.08 br.s (1H, 2-OH), 6.63 d (1H, 8-H, $J_{8,7} = 8.09$ Hz), 7.04 d (1H, 4-H, $J_{4,3} = 7.77$ Hz), 7.35 d (1H, 3-H, $J_{3,4} = 7.77$ Hz), 8.18 d (1H, 7-H, $J_{7,8} = 8.09$ Hz), 12.77 s (1H, 5-OH). Mass spectrum, m/z (I_{rel} , %): 244 (46) $[M]^+$, 229 (100) **F₁**, 227 (22) **F₃**, 211 (23) **F₂**, 187 (11), 183 (16), 155 (13), 127 (18), 43 (58).

1-(2-Ethoxy-5-hydroxy-2-methylnaphtho[1,8-*bc*]furan-6-yl)ethanone (V). A solution of 122 mg (0.5 mmol) of compound **IVa** in chloroform was subjected to chromatography on aluminum oxide of activity grade II according to Brockmann using ethanol as eluent. Yield 100 mg (74%), pale yellow crystals, mp 125–127°C. ^1H NMR spectrum, δ , ppm: 1.10 t (3H, CH_2CH_3 , $J = 7.50$ Hz), 1.90 s (3H, 2- CH_3), 2.80 s (3H, 6- COCH_3), 3.05 q (1H, OCH_2 , $J = 7.50$ Hz), 3.22 q

Table 2. Selected bond angles ω and bond lengths d in the molecule of 1-[4,8-di-*tert*-butyl-5-hydroxy-2-(4-methoxyphenyl)-2H-naphtho[1,8-*bc*]furan-6-yl)ethanone (**VII**) according to the X-ray diffraction data [3]^a

Angle	ω , deg	Bond	d , Å
$\text{O}^1\text{C}^1\text{C}^{8a}$	121.34	$\text{O}^1\text{—H}$	1.098
$\text{C}^1\text{C}^{8a}\text{C}^8$	132.50	$\text{O}^2 \cdots \text{H}$	1.402
$\text{C}^{8a}\text{C}^8\text{C}^{11}$	126.15	$\text{O}^1\text{—O}^2$	2.492
$\text{C}^9\text{C}^4\text{C}^{4a}$	107.31	$\text{O}^1\text{—C}^{11}$	3.148
$\text{C}^4\text{C}^{4a}\text{C}^5$	109.77	$\text{C}^1\text{—C}^8$	2.650
$\text{C}^{4a}\text{C}^5\text{O}^{10}$	110.51	$\text{C}^4\text{—C}^5$	2.284

^a For atom numbering, see structures **IVa**, **V**, and **VII** [3] shown above.

(1H, OCH₂, $J = 7.50$ Hz), 6.65 d (1H, 8-H, $J_{8,7} = 8.13$ Hz), 7.13 d (1H, 4-H, $J_{4,3} = 7.67$ Hz), 7.32 d (1H, 3-H, $J_{3,4} = 7.67$ Hz), 8.30 d (1H, 7-H, $J_{7,8} = 8.13$ Hz), 12.80 s (1H, 5-OH). Found, %: C 70.21; H 6.17. C₁₆H₁₆O₄. Calculated, %: C 70.58; H 5.92.

3,8-Dimethyl-1,2,6,7-tetraazapyrene (VIII). Hydrazine hydrate, 0.04 ml (1.25 mmol), was added to a solution 70 mg (0.29 mmol) of compound **IVa** in 2 ml of ethanol, the mixture was heated for 1 h under reflux, one drop of acetic acid was added, and the mixture was heated under reflux for 10 min. After cooling, the precipitate was filtered off and washed with ethanol. Yield 30 mg (68%), red-brown powder, mp 175–180°C. IR spectrum, ν , cm⁻¹: 1620, 1600, 1590. ¹H NMR spectrum, δ , ppm: 3.45 s (6H, 3-CH₃, 8-CH₃), 8.49 d (2H, 4-H, 9-H, $J = 9.30$ Hz), 8.94 d (2H, 5-H, 10-H, $J = 9.30$ Hz). Mass spectrum, m/z (I_{rel} , %): 234 (100) [M]⁺, 205 (7) F₄, 177 (43) F₅, 176 (61) F₆, 151 (32), 87 (31), 76 (28), 43 (22).

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