SYNTHESIS OF DERIVATIVES OF NAPHTHO[2,3-b]FURAN-4,9-DIONE

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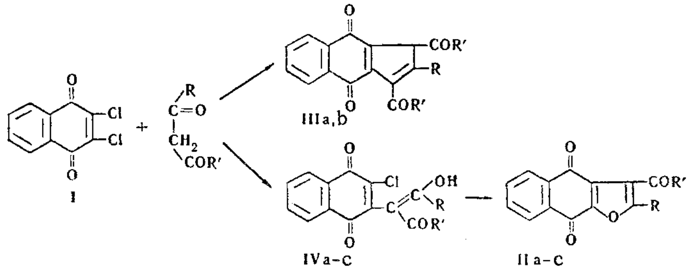
The reaction of 2,3-dichloro-1,4-naphthoquinone with ketoenols has been studied. A series of substituted naphtho[2,3-b]furan-4,9-quinones has been synthesized and some of their reactions have been studied.

We have found that the reaction of 2,3-dichloro-1,4-naphthoquinone (I) with acetoacetic ester forms not 3-ethoxycarbonyl-2-methylnaphtho[2,3-b]furan-4,9-quinone (IIa), as stated earlier [1], but 1,3-diethoxycarbonyl-2-methylnaphtho[2,3-b]cyclopent-1-ene-4,9-quinone (IIIa). Similarly, the condensation of I with benzoylacetic ester leads to 1,3-diethoxycarbonyl-2-phenylnaphtho[2,3-b]cyclopent-1-ene-4,9-quinone (IIIb).

According to the literature [1, 2], IIa can be synthesized by the reaction of sodioacetoacetic ester with I followed by the cyclization of the chloro-1,4-naphthoquinone derivative formed (IVa) by treatment with piperidine. The condensations of I with benzoylacetic ester and acetylacetone were carried out similarly. The cyclization of IVb and IIb was performed by the action of piperidine, and IIc was obtained with a yield of 47% when tetramethylammonium hydroxide was used as catalyst.



a $R=CH_3$, $R'=OC_2H_5$; b $R=C_6H_5$, $R'=OC_2H_5$; c $R=CH_3$, $R'=CH_3$

With other ketoenols – formylacetone, γ-phenylacetoacetic ester, formylsuccinic ester, and oxaloacetic ester – I forms only resinous products.

We have studied some reactions of the naphtho[2,3-b]furan-4,9-quinone derivatives. The acid V was obtained from 3-ethoxycarbonyl-2-phenylnaphtho[2,3-b]furan-4,9-quinone, and this was converted by decarboxylation into 2-phenylnaphtho[2,3-b]furan-4,9-quinone (VI), which had been synthesized previously by another method [3]. The reductive acetylation of VI led to the diacetyl derivative VII. From the acid chlorides, 2-phenyl- and 2-methyl-4,9-dioxonaphtho[2,3-b]furan-3-carboxamides (VIIIa and b), and also the dimethylamide of 2-methyl-4,9-dioxonaphtho[2,3-b]furan-3-carboxylic acid (VIIIc) were obtained. Under the conditions of reductive acetylation, VIIIb was converted into the 4,9-diacetoxynaphthofuran derivative IX.

The Friedel–Crafts acylation of benzene with 4,9-dioxo-2-phenylnaphtho[2,3-b]furan-3-carbonyl chloride gave 3-benzoyl-2-phenylnaphtho[2,3-b]furan-4,9-quinone (X), obtained previously [2] from I and dibenzoylmethane. The bromination of IIb led to the bromoacetyl derivative XIa or the dibromoacetyl derivative (IXb).

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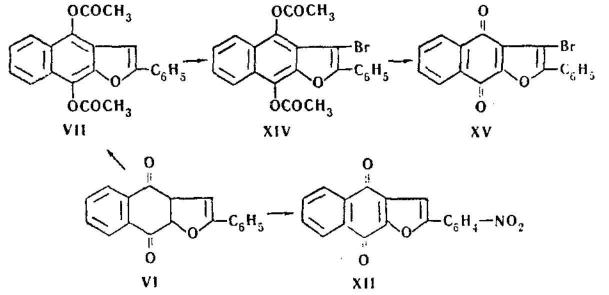
Some electrophilic substitution reactions have been studied using 2-phenylnaphtho[2,3-b]furan-4,9-quinone (VI) as example.

Compound VI does not undergo Friedel–Crafts acylation when aluminum chloride is used as catalyst and does not undergo bromination; on nitration it forms 2-p-nitrophenylnaphtho[2,3-b]furan-4,9-quinone (XII), the reductive acetylation of which gives 2-p-diacetylaminophenylnaphtho[2,3-b]furan-4,9-quinone (XIII).

It was possible to introduce a bromine atom into the β position of the furan nucleus indirectly. The bromination of 4,9-diacetoxy-2-phenylnaphtho[2,3-b]furan (VII) gave the 3-bromo derivative (XIV), which, after deacetylation and oxidation with oxygen, was converted into 3-bromo-2-phenylnaphtho[2,3-b]furan-4,9-quinone (XV).

The positions of the nitro group and the bromine atom were shown by NMR spectroscopy. The spectrum of VI has a singlet with a chemical shift of 7.04 ppm, which is ascribed to the proton at C_3. The aromatic protons of the phenyl substituent give a multiplet signal in the 7.6 ppm region. In the spectrum of XV the singlet signal due to the proton at C_3 disappears. The spectrum of XII retains the signal of the proton at C_3 (δ 7.28 ppm), and the aromatic protons of the phenyl substituent form a quartet with the chemical shifts δ_1 7.46 ppm and δ_2 8.13 ppm and the SSCC J = 9 Hz. The shape of the signals shows that the nitro group is present in the para position. The spectra were recorded on a JNM-4H-100 spectrometer with CF_3COOH as solvent and TMS as standard, using the δ scale.



EXPERIMENTAL

Ethyl α-(3-chloro-1,4-dioxo-2-naphthyl)acetoacetate (IVa). A solution of 0.76 g (5 mmoles) of the sodium derivative of acetoacetic ester in 5 ml of absolute ethanol was added to a suspension of 1.1 g (0.005 mole) of 2,3-dichloro-1,4-naphthoquinone in 5 ml of absolute ethanol. The mixture was stirred at room temperature for 5 min, and the unchanged I was separated off. The filtrate was acidified with dilute acetic acid, and the precipitate was filtered off. Yield 74%, mp 105-106°C (mp 106-107°C [4]).

Diacetyl(3-chloro-1,4-dioxo-2-naphthyl)methane (IVc) was obtained similarly with a yield of 89%, mp 138-139°C (from 75% acetic acid) (mp 131-132°C [4]). Found %: C 62.04; H 3.94; Cl 12.56%. $C_{15}H_{11}ClO_4$. Calculated %: C 61.97; H 3.81; Cl 12.20.

Ethyl α-(3-chloro-1,4-dioxo-2-naphthyl)benzoylacetate (IVb) was also obtained similarly with a yield of 70%.*

3-Ethoxycarbonyl-2-phenylnaphtho[2,3-b]furan-4,9-quinone (IIb). A solution of 0.59 g of IVb in 10 ml of absolute ethanol and 0.6 ml of piperidine was boiled for 1 h and cooled, and the precipitate was filtered off. Yield 94%, mp 182-183°C (from ethanol). Found %: C 72.81; H 4.08. $C_{21}H_{14}O_5$. Calculated %: C 72.83; H 4.07.

3-Acetyl-2-methylnaphtho[2,3-b]furan-4,9-quinone (IIc). A mixture of 0.35 g (5.1 mmoles) of sodium ethoxide in 10 ml of absolute ethanol and 0.93 g (6.1 mmoles) of tetramethylammonium bromide was boiled for 5 min and was then cooled, and 1.45 g (5 mmoles) of IVc was added. The reaction mixture was boiled for 1 h and cooled, and the precipitate was filtered off. Yield 48%, mp 208-209°C (from acetic acid) (mp 202°C [2]). Found %: C 70.68; H 4.28. $C_{15}H_{10}O_4$. Calculated %: C 70.86; H 3.96.

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*The yield is given for the liquid technical product, which was used for further reactions without additional purification.

1,3-Diethoxycarbonyl-2-phenylnaphtho[2,3-b]cyclopent-1-ene-4,9-quinone (IIIb). A mixture of 1.1 g (5 mmoles) of I and 2.13 g (10 mmoles) of the sodium derivative of benzoylacetic ester in 10 ml of absolute ethanol was boiled for 1 h. After cooling, the precipitate was separated off and crystallized from glacial acetic acid. Yield 78%, mp 152-153°C. Found %: C 72.29; H 4.77. $C_{25}H_{20}O_6$. Calculated %: C 72.10; H 4.84.

1,3-Diethoxycarbonyl-2-methylnaphtho[2,3-b]cyclopent-1-ene-4,9-quinone (IIIa) was obtained similarly with a yield of 85%; mp 153°C (mp 152°C [1]).

4,9-Dioxo-2-phenylnaphtho[2,3-b]furan-3-carboxylic acid (V). A solution of 0.5 g (1.5 mmole) of IIb in 4.5 ml of glacial acetic acid and 0.5 ml of concentrated sulfuric acid was boiled for 3 h. The reaction mixture was cooled and the precipitate was filtered off. Yield 65%, mp 214°C (from ethanol). Found %: C 71.80; H 3.40. $C_{19}H_{10}O_5$. Calculated %: C 71.70; H 3.17.

2-Phenylnaphtho[2,3-b]furan-4,9-quinone (VI). A mixture of 1 g (3.1 mmole) of V and 10 ml of 85% orthophosphoric acid was heated at 209°C for 2-3 h. The reaction mixture was poured onto ice, and the precipitate was filtered off. Yield 70%, mp 253-254°C (from acetic acid) (mp 246.5-247.5°C [3]). Found %: C 79.06; H 3.83. $C_{18}H_{10}O_3$. Calculated %: C 78.82; H 3.67.

4,9-Diacetoxy-2-phenylnaphtho[2,3-b]furan (VII). Over 1 h, 2 g of zinc dust was added to a boiling solution of 0.45 g (1.6 mmole) of VI in a mixture of 20 ml of pyridine and 20 ml of acetic anhydride. The reaction mixture was boiled for 1 h and was poured into 400 ml of cold water. On the following day the precipitate was filtered off. Yield 85%, mp 217-218°C (from acetic acid). Found %: C 73.23; H 4.43. $C_{22}H_{16}O_5$. Calculated %: C 73.32; H 4.47.

4,9-Dioxo-2-phenylnaphtho[2,3-b]furan-3-carboxamide (VIIIa) was obtained by the action of aqueous ammonia on the chloride of the acid V with a yield of 75%, mp 304°C (from ethanol). Found %: C 71.57; H 4.80; N 4.51. $C_{19}H_{11}NO_4$. Calculated %: C 71.92; H 3.49; N 4.42.

2-Methyl-4,9-dioxonaphtho[2,3-b]furan-3-carboxamide (VIIIb) was obtained similarly. Yield 60%, mp 320°C (from acetic acid). Found %: C 65.73; H 3.88. $C_{14}H_9NO_4$. Calculated %: C 65.88; H 3.55.

The dimethylamide of 2-methyl-4,9-dioxonaphtho[2,3-b]furan-3-carboxylic acid (VIIIc) was obtained by the action of an aqueous solution of dimethylamine on the acid chloride with ice cooling. Yield 81%, mp 219°C (from ethanol). Found %: C 68.16; H 4.45; N 5.01. $C_{16}H_{13}NO_4$. Calculated %: C 67.84; H 4.63; N 4.94.

Under the conditions of reductive acetylation, VIIIb was converted into 4,9-diacetoxy-2-methylnaphtho[2,3-b]furan-3-carboxamide (IX) in a yield of 88%, mp 228°C (from acetic acid). Found %: C 63.13; H 4.20; N 3.86. $C_{18}H_{15}NO_6$. Calculated %: C 63.34; H 4.43; N 4.10.

3-Benzoyl-2-phenylnaphtho[2,3-b]furan-4,9-quinone (X). In portions, 0.75 g of aluminum chloride was added to a solution of 4,9-dioxo-2-phenylnaphtho[2,3-b]furan-3-carbonyl chloride [obtained from 1.59 g (5 mmoles) of V] in 75 ml of dry benzene. The reaction mixture was boiled for 6 h. The complex was decomposed with dilute hydrochloric acid, the layers were separated, and the benzene was distilled off in vacuum. Yield 74%, mp 233-234°C (from ethanol) (mp 231°C [2]).

3-Bromoacetyl-2-methylnaphtho[2,3-b]furan-4,9-quinone (XIa). With stirring, a solution of 0.96 g (6 mmoles) of bromine in 15 ml of dioxane was gradually added to a suspension of 1.27 g (5 mmoles) of IIc in 15 ml of dioxane at 10-15°C. After the end of the addition, the solution was stirred for another 30 min at room temperature. Then the solvent was distilled off in vacuum. Yield 97%, mp 215°C (from acetic acid). Found %: C 53.75; H 2.78; Br 24.29. $C_{19}H_9BrO_4$. Calculated %: C 54.08; H 2.72; Br 23.99.

3-Dibromoacetyl-2-methylnaphtho[2,3-b]furan-4,9-quinone (XIb). A suspension of 0.87 g (3.4 mmoles) of IIb in 20 ml of carbon tetrachloride was treated with 1.1 g (6.9 mmoles) of bromine, and the reaction mixture was left at room temperature for two days. Then the precipitate was filtered off, yield 85%, mp 225°C (from acetic acid). Found %: Br 38.40. $C_{15}H_8Br_2O_2$. Calculated %: Br 38.78.

2-p-Nitrophenylnaphtho[2,3-b]furan-4,9-quinone (XII). With ice cooling, 0.2 ml of nitric acid (d 1.343) was added to a solution of 0.55 g (2 mmoles) of VI in 4 ml of concentrated sulfuric acid. The reaction mixture was stirred at room temperature for 3 h and poured onto ice, and the precipitate was filtered off. Yield 39%, mp 339°C (from acetic acid). Found %: C 67.43; H 2.82; N 4.35. $C_{18}H_9NO_5$. Calculated %: C 67.71; H 2.84; N 4.39.

4,9-Diacetoxy-2-p-diacetylaminophenylnaphtho[2,3-b]furan (XIII) was obtained from XII under the conditions of reductive acetylation. Yield 52%, mp 190-191°C (from ethanol). Found %: C 67.59; H 4.50. $C_{26}H_{21}NO_7$. Calculated %: C 67.96; H 4.60.

4,9-Diacetoxy-3-bromo-2-phenylnaphtho[2,3-b]furan (XIV). At room temperature, 0.36 g (2 mmoles) of bromine in 5 ml of glacial acetic acid was slowly added to a suspension of 0.72 g (2 mmoles) of VII in 30 ml of glacial acetic acid. Stirring was continued for another 3 h, and the precipitate was filtered off. Yield 80%, mp 219-220°C (from acetic acid). Found %: C 59.76; H 3.38; Br 18.51. $C_{22}H_{15}BrO_5$. Calculated %: C 60.15; H 3.44; Br 18.19.

3-Bromo-2-phenylnaphtho[2,3-b]furan-4,9-quinone (XV). 0.4 g (0.9 mmole) of XIV in 5 ml of absolute ethanol was heated with a catalytic amount of sodium ethoxide for 2-3 min. Then the reaction mixture was cooled, and oxygen was passed through it at room temperature. The precipitate was filtered off. Yield 56%, mp 207-208°C (from acetic acid). Found %: C 61.30; H 2.67; Br 22.80. $C_{18}H_9BrO_3$. Calculated %: C 61.22; H 2.57; Br 22.62.

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