NEW SYNTHESIS OF NAPHTHO[2,1-b]FURAN DERIVATIVES FROM 1,2-DIHYDROXY-4-NAPHTHYL-β-DICARBONYL COMPOUNDS

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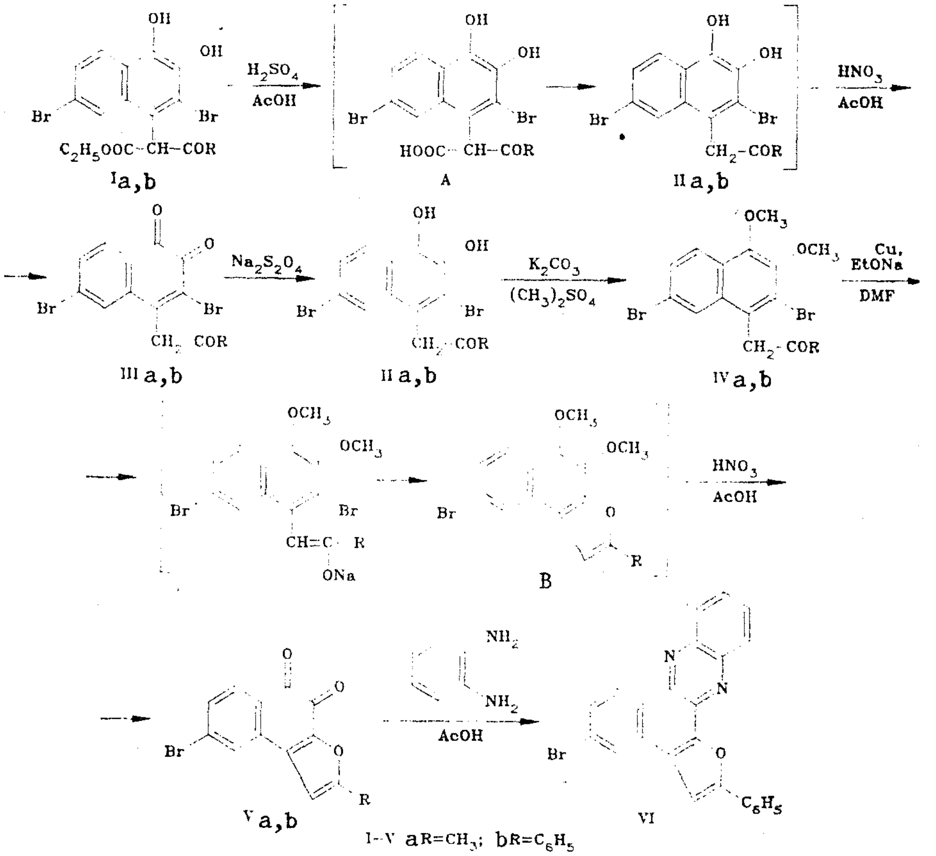
A method for obtaining 4-acetonyl (4-phenacyl) derivatives of 1,2-dioxo- and 1,2-dihydroxynaphthalenes is proposed. The previously unknown naphtho[2,1-b]furan o-quinones were synthesized from the latter derivatives.

The aim of the present research was to study the possibility of using the previously obtained [1] β-keto esters Ia,b, substituted with a dihydroxynaphthyl residue, in the synthesis of naphtho[2,1-b]furan derivatives that contain an o-quinone fragment.

The first stage of this research was the study of the possibility of obtaining 4-acetonyl(4-phenacyl)-1,2-dihydroxynaphthalenes IIa,b from keto esters Ia,b. It was found that the best way to carry out the decarboxylation is to heat esters Ia,b in acetic acid in the presence of catalytic amounts of H_2SO_4; esterification of the acetic acid with subsequent spontaneous decarboxylation of the resulting acetoacetic (benzoylacetic) acid A evidently occurs in this case [2].



I–V aR=CH_3; bR=C_6H_5

Certain difficulties were encountered in isolating IIa,b, and their oxidation to the corresponding o-quinones IIIa,b with purification of the latter and reduction to the desired IIa,b was found to be preparatively most convenient for obtaining them in pure form.

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The IR spectra of IIa,b contain intense bands of hydroxy groups at 3160-3500 cm^{-1}; they are absent in the spectra of 1,2-naphthoquinones IIIa,b, but bands of carbonyl groups appear at 1670-1710 cm^{-1}.

Compounds IIa,b contain a ketomethyl (ketophenyl) grouping and a bromine atom in adjacent positions of the naphthalene ring. It is known that an aromatic halogen atom can be replaced by a phenol residue via the Ullmann reaction in the presence of copper and an alkaline agent:

$$\mathrm{ArHal} + \mathrm{ArOH} \xrightarrow{\mathrm{Cu,\ NaOH}} \mathrm{Ar} \quad \mathrm{O-Ar}$$

From this it seemed expedient to investigate the possibility of carrying out, under these conditions, intramolecular cyclization with the participation of the β-carbon atom of the naphthalene ring bonded to the bromine atom and the enolate anion formed due to the CH_2CO fragment in the 4 position of the molecule. It was found that cyclization occurs when solutions of dimethoxy derivatives IVa,b are heated in DMF in the presence of an equimolar amount of EtONa and a catalytic amount of copper. According to TLC data, the process goes to completion quite rapidly; however, the isolation of dimethoxy derivatives B presencts considerable difficulties, and the best variant is their oxidation (without isolation from the reaction mixtures) to the desired o-quinones Va,b.

Signals of an AB system of 6-H protons at 7.89 ppm (d, J_{67} = 8.3 Hz) and 7.95 ppm (d, J_{67} = 8.1 Hz) and 7-H protons at 7.53 ppm (dd, J_{76} = 8.3 Hz, J_{79} = 1.7 Hz) and 7.58 ppm (dd, J_{76} = 8.1 Hz, J_{79} = 1.9 Hz), respectively, and a doublet of a 9-H proton (8.17 and 8.26 ppm, respectively) are characteristic for the PMR spectra of Va,b. The formation of a furan ring is confirmed by the characteristic multiplicity of the signals of 3-H protons at 7.23 ppm (q, J = 0.9 Hz) and the 2-CH_3 group (d, J = 0.9 Hz) in the spectrum of Va. A multiplet of protons of a phenyl substitutent in the 2 position (7.6 ppm) is observed in the spectrum of Vb, while the signal of the 3-H proton (8.13 ppm) is shifted to weak field under the influence of the adjacent benzo substituent.

The existence of the o-quinoid structure in Vb was confirmed by reaction with o-phenylenediamine. The classification of Va,b as o-quinones is also confirmed by the presence in the IR spectra of absorption bands at 1690-1650 cm^{-1}, which usually characterize the carbonyl groups of quinones, while these bands are absent in the IR spectrum of phenazine derivative VI. The experimentally found mass numbers of the molecular ions in the mass spectra of VA,b correspond to the calculated molecular masses.

EXPERIMENTAL

The IR spectra of suspensions of the compounds in mineral oil were recorded with a UR-10 spectrometer. The UV spectra of solutions in alcohol were obtained with a Perkin—Elmer 575 spectrophotometer. The mass spectra were recorded with a Varian MAT-112 mass spectrometer (70 eV) with direct introduction of the samples into the ion source. The PMR spectra were obtained iwth a Varian XL-200 spectrometer with tetramethylsilane (TMS) as the internal standard. The individuality of the substances was monitored on Silufol-254 plates in chloroform with development in UV light.

The results of elementary analysis for C, H, and Hal were in agreement with the calculated values.

3,6-Dibromo-4-acetonyl-1,2-naphthoquinone (IIIa, $C_{13}H_8Br_2O_3$). A 22.6-g (0.05 mole) sample of 1,2-dihydroxy-3,6-dibromo-4-(1-ethoxycarbonyl-2-oxopropyl)naphthalene (Ia) was dissolved in 150 ml of glacial acetic acid, and the solution was refluxed in the presence of a catalytic amount (0.5 ml) of concentrated H_2SO_4 for 6 h. The reaction solution was cooled to 20°C, 5.0 ml of HNO_3 (d 1.35) was added, and the mixture was stirred for 5 min and cooled. The resulting orange crystals were removed by filtration, washed with acetic acid, and dried to give a product with mp 163-165°C (from acetic acid) in 70% yield.

A similar method was used to obtain **3,6-dibromo-4-phenacyl-1,2-naphthoquinone (IIIb, $C_{18}H_{10}Br_2O_3$)**, with mp 179-180°C (from acetic acid), in 71% yield.

1,2-Dihydroxy-3,6-dibromo-4-acetonylnaphthalene (IIa, $C_{13}H_{10}Br_2O_3$). A solution of 6.94 g (0.04 mole) of sodium dithionite in 20 ml of water was added with stirring at 40°C to a solution of 3.72 g (0.01 mole) of 1,2-naphthoquinone IIIa in a mixture of dioxane (20 ml) and alcohol (60 ml), and the decolorized reaction mixture was diluted with water and extracted with benzene. The benzene was evaporated until the volume of the mixture was small, and the resulting crystals were removed by filtration and dried to give a product with mp 160-161°C (from benzene) in 90% yield.

A similar method was used to obtain **1,2-dihydroxy-3,6-dibromo-4-phenacylnaphthalene (IIb, $C_{18}H_{12}BrO_3$)**, with mp 190-191°C (from methanol), in 96% yield.

1,2-Dimethoxy-3,6-dibromo-4-acetonylnaphthalene (IV, $C_{15}H_{14}Br_2O_3$). A mixture of 3.74 g (0.01 mole) of 1,2-dihydroxynaphthalene IIa, 5.04 g (0.04 mole) of dimethyl sulfate, 5.52 g (0.04 mole) of anhydrous potassium carbonate, and 100 ml of dry acetone was refluxed for 6 h, after which it was filtered, and the precipitate was washed with acetone. The solvent was evaporated, 100 ml of water was added to the residue (an oil), and the mixture was allowed to stand in a refrigerator overnight. The crystallized precipitate was removed by filtration, washed with water, and dried to give a product with mp 78-80°C (from isopropyl alcohol) in 74% yield.

A similar procedure was used to obtain **1,2-dimethoxy-3,6-dibromo-4-phenacylnaphthalene (IVb, $C_{20}H_{16}Br_2O_3$)**, with mp 154-155°C (from isopropyl alcohol), in 63% yield.

2-Methyl-8-bromo-4,5-naphtho[2,1-b]furanquinone (Va, $C_{13}H_7BrO_3$). A 0.2-g sample of copper and 1.0 g (5 mmole) of a 26.5 solution of sodium methoxide were added to a solution of 2.0 g (5 mmole) of 1,2-dimethoxynaphthalene IVa in 25 ml of DMF, and the mixture was relfuxed for 2 h, allowed to stand overnight at room temperature, and filtered. Acetic acid (10 ml) was added to the filtrate, and the mixture was diluted with water and extracted with chloroform. The chloroform was evaporated, and the residue was dissolved in 15 ml of acetic acid. A 0.5-ml (0.01 mole) sample of HNO_3 (d 1.35) was added to the resulting solution at 20-25°C, and the mixture was stirred for 15 min and cooled. The resulting precipitate was removed by filtration, washed with water, and dried to give 0.32 g (22%) of Va with mp 225-226°C (from acetone—dioxane (1:2)). IR spectrum: 1690, 1650 cm^{-1} (C=O). M^+ 290 (^{79}Br).

2-Phenyl-8-bromo-4,5-naphtho[2,1-b]furanquinone (Vb, $C_{18}H_9BrO_3$). This compound was obtained in 37% yield by the method described above for Va and had mp > 300°C (from acetone—dioxane (1:2)). IR spectrum: 1690, 1650 cm^{-1} (C=O). UV spectrum, λ_{max}, nm (log ε): 234 (3.81), 280 (4.30), 360 (4.30), 460 (3.07). M^+ 462 (^{79}Br).

2-Phenyl-5-bromofurano[2,3-a]benzo[c]phenazine (VI, $C_{24}H_{13}BrN_2O_3$). A solution of 0.22 g (2 mmole) of o-phenylenediamine in 15 ml of acetic acid was added to a solution of 0.35 g (1 mmole) of furanquinone Vb in 130 ml of acetic acid, and the reaction solution was refluxed for 10 min and cooled. The resulting precipitate was removed by filtration and washed with methanol to give 0.26 g (61%) of VI with mp 280-281°C (from DMF). UV spectrum, λ_{max}, nm (log ε): 270 (4.68), 330 (4.54), 383 (3.65), 445 (3.00), 530 (2.98).

LITERATURE CITED

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