SYNTHESIS OF o-QUINONES OF 3H-BENZ[e]INDOLE

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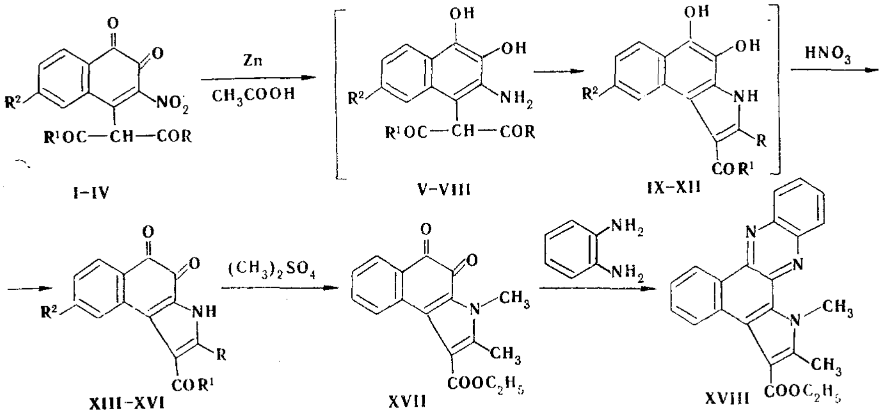
4,5-Dioxo-4,5-dihydro-3H-benz[e]indole derivatives were synthesized from 3-nitro-o-naphthoquinones with keto enol residues in the 4 position. One of these products was methylated at the nitrogen atom of the pyrrole ring. The N-methyl derivative was used for the synthesis of a phenazine.

We have previously proposed a new preparative method for the synthesis of dioxonaphthyl keto enols [1]. The heretofore inaccessible 3-nitro-o-naphthoquinones (I-IV) with keto enol residues in the 4 position were obtained in high yields by this method.

Intramolecular cyclization with the participation of the resulting amino group and the keto enol residue occurs in the reduction of 3-nitro derivatives I-IV with zinc in acetic acid. It is apparent that reduction of the o-quinone to 1,2-dihydroxy-3-aminonaphthalenes V-VIII also takes place simultaneously with reduction of the nitro group, since we observed complete decolorization of the reaction solution during the reaction. 1,2-Dihydroxy derivatives (IX-XII) of 3H-benz[e]indole cannot be isolated because of the fact that they are readily oxidized by air oxygen.

4,5-Dioxo-4,5-dihydro-3H-benz[e]indoles (XIII-XVI) were obtained by oxidation of IX-XII with nitric acid.



I, XIII R=CH_3, R^1=OC_2H_5, R^2=H; II, XIV R=CH_3, R^1=CH_3, R^2=H; III, XV R=C_6H_5, R^1=OC_2H_5, R^2=Br; IV, XVI R=CH_3, R^1=OC_2H_5, R^2=Br

The methylation of 1-ethoxycarbonyl-2-methyl-4,5-dioxo-4,5-dihydro-3H-benz[e]indole (XIII) with dimethyl sulfate gave N-methyl derivative XVII, which, upon reaction with o-phenylenediamine, gave phenazine derivative XVIII in high yield.

Intense absorption bands that are characteristic for the NH groups are observed at 3180-3260 cm^{-1} in the IR spectra of XIII-XVI, whereas this band is absent in the spectrum of N-methyl derivative XVII. The classification of XIII-XVII as o-quinones is confirmed by the presence in the IR spectra of absorption bands at 1590-1650 cm^{-1}, which usually characterize the carbonyl groups of quinones, whereas these bands are absent in the IR spectrum of phenazine derivative XVIII.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with UR-10 and Perkin-Elmer spectrometers. The UV spectra of solutions in alcohol were obtained with

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TABLE 1. 4,5-Dioxo-4,5-dihydro-3H-benz[e]indole Derivatives (XIII-XVI)

Compound	mp, °C	Found, %			Empirical formula	Calc., %			Yield, %
		C	H	N		C	H	N	
XIII	265—266[a]	67,8	4,4	4,9	$C_{16}H_{13}NO_4$	67,8	4,6	4,9	88
XIV	239—240[b]	71,3	3,9	5,4	$C_{15}H_{11}NO_3$	71,1	4,4	5,5	64
XV	229—230[a]	59,4	3,4	3,3	$C_{21}H_{14}BrNO_4$[c]	59,4	3,3	3,3	70
XVI	280—282[d]	52,9	2,9	4,0	$C_{16}H_{12}BrNO_4$[e]	53,1	3,3	3,9	82

[a] From acetone. [b] From acetic acid. [c] Found: Br 19.0%. Calculated: Br 18.8%. [d] From dimethylformamide (with decomposition). [e] Found: Br 22.3%. Calculated: Br 22.1%.

TABLE 2. Spectral Characteristics of XIII-XVI

Compound	IR spectrum, ν, cm^{-1}		UV spectrum, λ_{max}, nm (log ε)
	C=O	NH	
XIII	1630, 1700	3200	210 (4,42), 265 (4,40), 360 sh (3,75)
XIV	1590, 1670, 1690	3200	220 (4,31), 265 (4,28), 380 sh (3,72)
XV	1650, 1710	3260	205 (4,47), 282 (4,59), 355 (3,92)
XVI	1640, 1700	3190	208 (4.39), 235 (4,24), 281 (4,39), 350 (3,92)

Hitachi EPS-3T and Perkin-Elmer 575 spectrophotometers. 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 individuality of the substances was monitored on Silufol-254 plates in chloroform; the plates were developed in UV light.

1,2-Dioxo-1,2-dihydro-3-nitro-4-(2,4-dioxo-3-amyl)naphthalene (II). This compound was obtained in 77% yield by the method in [1] by condensation of 3-nitro-1,2-naphthoquinone with acetylacetone and had mp 199-200°C [from isopropyl alcohol—acetone (2:1)]. IR spectrum: 1610, 1690, and 1710 cm^{-1} (C=O). UV spectrum, λ_{max} (log ε): 258 (3.87) and 350 nm (shoulder) (3.20). Found: C 59.7; H 3.5; N 4.5%; M^+ 301. $C_{15}H_{11}NO_6$. Calculated: C 59.8; H 3.7; N 4.6%; M 301.

1-Ethoxycarbonyl-2-methyl-4,5-dioxo-4,5-dihydro-3H-benz[e]indole (XIII). A 14-g sample of zinc dust was added in portions in the course of 20 min to a refluxing solution of 6.62 g (0.02 mole) of 1,2-dioxo-1,2-dihydro-3-nitro-4-(1-ethoxycarbonyl-2-oxopropyl)naphthalene (I) in 300 ml of acetic acid, and the mixture was refluxed until the reaction mixture became completely colorless. The hot solution was filtered, 1.5 ml of nitric acid (sp. gr. 1.35) was added to the filtrate, and the mixture was stirred for 2-3 min. The resulting dark-red mixture was diluted with 300 ml of water, and the precipitate was removed by filtration, washed with water, and dried to give 5 g (88%) of XIII. A similar method was used to obtain XIV-XVI (Table 1).

1-Ethoxycarbonyl-2,3-dimethyl-4,5-dioxo-4,5-dihydro-3H-benz[e]indole (XVII). A 5.04-g (0.04 mole) sample of dimethyl sulfate and 5.56 g (0.04 mole) of anhydrous potassium carbonate were added to a refluxing solution of 2.83 g (0.01 mole) of 1-ethoxycarbonyl-2-methyl-4,5-dioxo-4,5-dihydro-3H-benz[e]indole (XIII) in a mixture of dioxane (20 ml) with acetone (50 ml), after which the hot solution was filtered, and the solvent was evaporated to a small volume. Methanol (10 ml) was added to the residue, and the precipitated orange crystals were removed by filtration, washed with isopropyl alcohol, and dried to give 2.1 g (71%) of XVII with mp 176-177°C (from methanol). IR spectrum: 1650 and 1700 cm^{-1} (C=O). UV spectrum, λ_{max} (log ε): 210 (4.41), 266 (4.37), and 380 nm (3.80). Found: C 69.0; H 5.3; N 4.6%; M^+ 297. $C_{17}H_{15}NO_4$. Calculated: C 68.7; H 5.1; N 4.7%; M 297.

1-Benzo[a]-1,2-dimethyl-3-ethoxycarbonylpyrrolo[4,5-c]phenazine (XVIII). A 2.97-g (0.01 mole) sample of 1-ethoxycarbonyl-2,3-dimethyl-4,5-dioxo-4,5-dihydro-3H-benz[e]indole (XVII) was dissolved in 50 ml of acetic acid, 1.6 g (0.015 mole) of o-phenylenediamine was added to the resulting solution, and the mixture was refluxed for 5-10 min. It was then diluted with water, and the resulting yellow crystals were removed by filtration, washed with water, and dried to give 3.24 g (88%) of XVIII with mp 183-184°C (from acetic acid). IR spectrum: 1690 cm^{-1} (C=O). UV spectrum, λ_{max} (log ε): 210 (4.49), 264 (4.69), 310 (4.49), 385 (3.96), and 430 nm (3.90). Found: C 74.8; H 5.0; N 11.4%; M^+ 369. $C_{23}H_{19}N_3O_2$. Calculated: C 74.8; H 5.2; N 11.4%; M 369.

LITERATURE CITED

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SYNTHESIS AND TRANSFORMATIONS OF 1-METHYL-4-ARYL-7-R-ISOQUINOLINES

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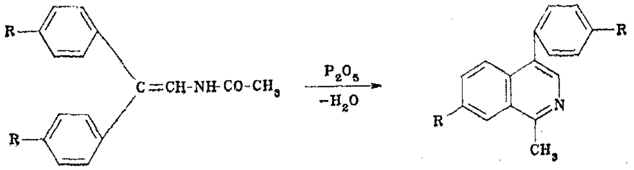
1-Methyl-4-aryl-7-R-isoquinolines were obtained by cyclization of 1,1-diaryl-2-acetamidoethylenes in the presence of phosphorus pentoxide. The condensation of the products with diethyl oxalate leads to the formation of ethyl 1-(4-aryl-7-R-isoquinolyl)pyruvates, which react with o-phenylenediamine to give 1-(4-aryl-7-R-isoquinolyl)-2-[3-(4H)-oxo-2-quinoxalyl]methanes.

We have previously obtained a number of aminoethanols that contain diarylmethylol and primary amino groups, and we also studied the acetylation of the products and synthesized 1,1-diaryl-2-acetamidoethylenes from the acetyl derivatives [1]. Continuing our synthetic studies to obtain physiologically active substances, we attempted to cyclize ethylenes I under the conditions of the Bischler—Napieralski reaction [2] with vinylamides Ia-d as the starting compounds. This made it possible to synthesize not only isoquinolines that contain electron-donor substituents in the aromatic ring but also isoquinolines that contain halogen atoms. Halo derivatives of isoquinoline of this type have previously been obtained only indirectly [3].



Ia-d IIa-d

The most characteristic absorption bands in the IR spectra of isoquinolines II are the bands at ~1640 and 2980-2990 cm^{-1}, which were assigned, respectively, to the azomethine bond of the isoquinoline ring and to the C—H bond of a methyl group in the 1 position.

Signals of protons of a CH_3 group are found at 2.85-2.95 ppm in the PMR spectra of solutions of these compounds in $CDCl_3$. The PMR spectrum of isoquinoline IIb in this region also contains another two singlet signals (2.35 and 2.47 ppm), which are related, respectively, to the p-CH_3 and 7-CH_3 groups. Of the signals of the aromatic protons (7.15-8.1 ppm), the most distinguishable is the signal of the proton in the 3 position of the isoquinoline ring (8.2-8.3 ppm). On passing to the hydrochlorides the corresponding signals are shifted 0.2-0.3 ppm to weak field (in d_6-DMSO).

It is known that a methyl group in the ortho position relative to the ring nitrogen atom in aromatic nitrogen-containing heterocycles is characterized by increased reactivity [4]. Taking this into account, we carried out the condensation of isoquinolines II with diethyl oxalate (III) in the presence of potassium ethoxide, as a result of which we obtained ethyl isoquinolylpyruvates (IV), which, according to the IR and PMR spectral data, exist primarily in the enol form.

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