9. V. A. Bolotin and L. I. Mazhilis, Litovsk. Fiz. Sbornik, 27, 113 (1987).
10. L. I. Mazhilis and V. A. Bolotin, 7th All-Union Conference on "The use of computers in chemical investigations and molecular spectroscopy," Abstracts, Riga (1986), p. 107.
11. S. Saidac, P. Gheorghe, A. Savulescu, and M. Zaharia, Rev. Chim. Bucur., 33, 816 (1982).
12. V. N. Garalene, A. P. Stankyavichyus, and L. I. Mazhilis, Khim.-farm. Zh., No. 11, 1305 (1986).
13. L. I. Mazhilis and P. B. Terent'ev, Khim.-farm. Zh., No. 5, 580 (1987).
14. A. Gordon and R. Ford, The Chemist's Companion, Wiley-Interscience (1973).
15. A. Etienne and A. Staehelin, Bull. Soc. Chim. Fr., No. 6, 743 (1954).
16. P. B. Terent'ev, L. I. Mazhilis, A. G. Kalandarishvili, and A. P. Stankyavichyus, Khim. Geterotsikl. Soedin., No. 8, 1052 (1986).
17. N. P. Peet and R. J. Barbuch, Org. Mass. Spectrom., 19, 171 (1984).
18. T. Kaiya and Y. Kawazoe, Tetrahedron, 41, 511 (1983).

SYNTHESIS OF ortho- AND para-QUINONES OF THE BENZINDOLE SERIES

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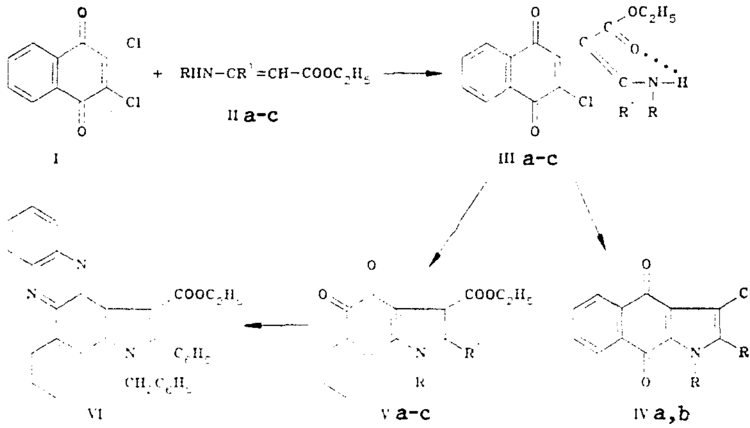
Ethyl esters of α-(3-chloro-1,4-naphthoquinon-3-yl)crotonic or cinnamic acids were obtained by the reaction of 2,3-dichloro-1,4-naphthoquinone with ethyl esters of N-substituted β-aminocrotonic or β-aminocinnamic acids. These esters were converted by alkaline fusion into benz[f]indole-4,9-dione-3-carboxylic acids, and into ethyl esters of benz[g]indole-4,5-dione-3-carboxylic acid by the action of acetic acid.

Linear benzindoles are of interest as compounds with possible biological activity, but are presently difficult to obtain [1, 2]. The aim of the present work was to study a new approach to the synthesis of benz[f]- and benz[g]indoles, containing an o-quinoid type fragment in their structure. In contrast with the previously described [3] method of synthesis of compounds of this type, we chose as the starting compounds 2,3-dichloro-1,4-naphthoquinone (I) and esters of N-substituted β-aminocrotonic (IIa, c) and β-aminocinnamic (IIb) acids. The reaction of quinone I with esters IIa-c leads at the first stage to α-naphthoquinonyl-3-enamino esters IIIa-c, in which the presence of an intramolecular hydrogen bond (IMHB) be-



II—V a $R=C_6H_5$, $R^1=CH_3$; b $R=CH_2C_6H_5$, $R^1=C_6H_5$; c $R=R^1=CH_3$

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*Deceased.

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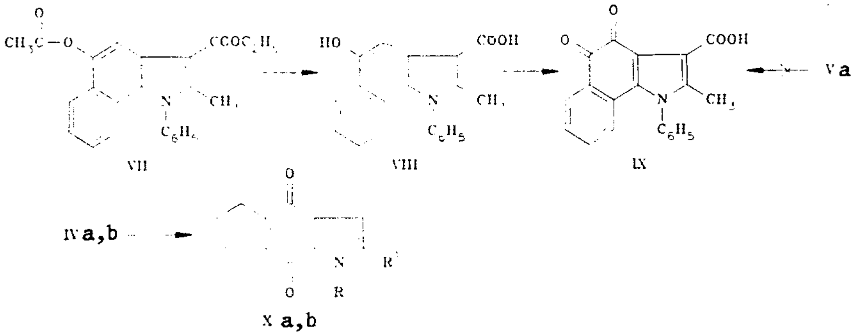
tween the enamine NH group and the β-ethoxycarbonyl group is characteristic. The presence of a strong IMHB is indicated by the fact that bands of the NH group are present in the 3240-3260 cm^{-1} region of the IR spectra of solutions of compounds IIIa-c, which do not change their strength on dilution to a concentration of 5-0.02% ($CHCl_3$).

Alkaline fusion of enamino esters IIIa, b leads to linear benzindoles IVa, b. The cyclization is accompanied by saponification of the ethoxycarbonyl groups, as a result of which the derivatives of benz[f]indole-4,9-dione-3-carboxylic acid IVa, b are obtained. A similar cyclization product of IIIc could not be obtained because of strong resinification of the reaction mixture. The use of acetic acid as the cyclizing agent results in a different path of pyrrole ring closure — the previously described [4] derivatives of benz[g]indole-4,5-dione Va-c are formed. The presence of the o-quinoid structure for these compounds is confirmed by the formation of quinoxalino[2,3-e]benz[g]indole VI on heating quinone IVb with o-phenylenediamine. It can thus be seen that the saponification of the ethoxycarbonyl group in compounds IVa, b already occurs during the indole cyclization. However, the corresponding carboxylic acid cannot be obtained by saponification of the ester group in compound Va. In all cases (in both acid and alkaline media) strong resinification of the reaction medium is observed. The corresponding carboxylic acid was synthesized by a different scheme: by the alkaline saponification of 1-phenyl-2-methyl-3-ethoxycarbonyl-5-acetoxybenz[g]indole (VII), acid VIII was obtained, the oxidation of which by nitric acid resulted in 1-phenyl-2-methylbenz[g]indole-4,5-dione-3-carboxylic acid (IX). However, the latter could not be decarboxylated. In contrast to this, when heated to 230°C in the presence of copper, acids IVa, b undergo decarboxylation with the formation of benz[f]indoles Xa, b.



EXPERIMENTAL

The IR spectra were recorded on a Perkin—Elmer 599 spectrophotometer in mineral oil in chloroform solution at a concentration of 5-0.02%. The PMR spectra were run on a Varian XL-200 spectrometer (in $CDCl_3$), using TMS as internal standard. The course of the reaction was monitored chromatographically on Silufol UV-254 plates in benzene—acetone, 9:1, chloroform systems with development in UV light.

The characteristics and yields of the compounds obtained are given in Table 1. The data of the elemental analysis for C, H, Cl, and N correspond to the calculated values.

Ethyl Ester of β-Phenylamino-α-(3-chloro-1,4-naphthoquinone)crotonic Acid (IIIa), Ethyl Ester of β-Methylamino-α-(3-chloro-1,4-naphthoquinone)crotonic Acid (IIIc), and Ethyl Ester of β-Benzylamino-α-(3-chloro-1,4-naphthoquinone)cinnamic Acid (IIIb). A 20-mmole portion of sodium acetate and 10 mmoles of dichloronaphthoquinone I are added with stirring to a suspension of 10 mmoles of compounds IIa-c in 30 ml of absolute alcohol. The reaction mixture is boiled for 2 h, cooled, the precipitate is filtered, and the filtrate is evaporated in vacuo. The residue is recrystallized from a 1:1 ethyl acetate—petroleum ether mixture.

1-Phenyl-2-methylbenz[f]indole-4,9-dione-3-carboxylic Acid (IVa), 1-Benzyl-2-phenylbenz[f]indole-4,9-dione-3-carboxylic Acid (IVb), and 1-Phenyl-2-methyl-5-hydroxybenz[g]indole-3-carboxylic Acid (VIII). Two drops of water are added to 30 mmoles of sodium hydroxide, and the mixture is heated to 150°C. A 10-mmole portion of compounds IIIa, b or 5-acetoxybenz[g]indole VII [5] is added at 170-175°C to the melt formed, and the mixture is stirred for 5 min. It is then cooled, and after adding 15 ml of water, is acidified with dilute hydrochloric acid to pH 5. The precipitate is filtered, and recrystallized from dioxane.

TABLE 1. Characteristics of Synthesized Compounds

Compound*	Empirical formula	mp, °C	IR spectrum, ν, cm⁻¹			PMR spectrum, δ, ppm	Yield, %
			C=O	NH	OH		
IIIa	$C_{22}H_{18}ClNO_4$	142...143	1640, 1680	3240	—	1,14 (3H, t, $CH_2\mathbf{CH_3}$); 1,87 (3H, s, CH_3); 4,11 (2H, q, $\mathbf{CH_2}CH_3$); 7,81 ... ...7,19 (m, CH arom.); 9,89 (1H, s, NHC_6H_5)	31
IIIb	$C_{28}H_{22}ClNO_4$	161...162	1650, 1675	3260			36
IIIc	$C_{17}H_{16}ClNO_4$	101...102	1650, 1675	3260		1,12 (3H, t, $CH_2\mathbf{CH_3}$); 1,84 (3H, s, CH_3); 3,02 (3H, d, $NH\mathbf{CH_3}$); 4,11 (2H, q, $\mathbf{CH_2}CH_3$); 8,02 ... ...7,27 (m, CH arom.); 9,66 (1H, s, $NHCH_3$)	30
IVa	$C_{20}H_{13}NO_4$	282**	1670, 1700	—	2660	2,50 (3H, s, CH_3): 7,70 ... ...7,27 (m, CH arom.);	50
IVb	$C_{26}H_{17}NO_4$	289**	1670, 1710	—	2700		34
Vb	$C_{28}H_{21}NO_4$	204...205					60
VI	$C_{34}H_{25}N_3O_2$	254...256					98
VIII	$C_{20}H_{15}NO_3$	260...261					34
IX	$C_{20}H_{13}NO_4$	298					55
Xa	$C_{19}H_{13}NO_2$	217...218	1670				30
Xb	$C_{25}H_{17}NO_2$	253...254					25

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*Compounds Va, c were obtained in a yield of 83 and 75%, respectively.

**Decomposition.

1-Phenyl-2-methyl-3-ethoxycarbonylbenz[g]indole-4,5-dione (Va), 1-Benzyl-2-phenyl-3-ethoxycarbonylbenz[g]indole-4,5-dione (Vb), and 1,2-Dimethyl-3-ethoxycarbonylbenz[g]indole-4,5-dione (Vc). A mixture of 1 mmole of compounds IIIa-c, 2 mmoles of sodium acetate, and 20 ml of glacial acetic acid is boiled for 1 h. A 20-ml portion of water is added, the precipitate is filtered and recrystallized from methanol.

1-Benzyl-2-phenyl-3-ethoxycarbonylquinoxaline[2,3e]benz[g]indole (VI). A mixture of 0.45 g (1 mmole) of compound Vb, 0.2 g (2 mmoles) of o-phenylenediamine, and 7 ml of glacial acetic acid is boiled for 5 min. The mixture is cooled, and the precipitate formed is filtered, washed with water, methanol, and dried to yield 0.49 g of compound VI.

1-Phenyl-2-methylbenz[g]indole-4,5-dione-3-carboxylic Acid (IX). A 0.3-ml portion of nitric acid (d 1.35) is added with stirring to a suspension of 1 g (3 mmoles) of 5-hydroxybenz[g]indole VIII in 10 ml of glacial acetic acid. The mixture is boiled for 5 min, cooled, and 20 ml of water are added. The precipitate is filtered and recrystallized from DMFA to yield 0.6 g of compound IX.

1-Phenyl-2-methylbenz[f]indole-4,9-dione (Xa) and 1-Benzyl-2-phenylbenz[f]indole-4,9-dione (Xb). A mixture of 3 mmoles of acid IVa, b and 1.1 g of copper powder is held for 3 min at 250°C. The reaction mxiture is cooled, 20 ml of dichloroethane are added, the precipitate is filtered, and the filtrate is dried in vacuo. The residue is recrystallized from ethanol.

LITERATURE CITED

1. N. N. Suvorov, V. A. Porotikova, and V. N. Eraksina, Khim. Geterotsikl. Soedin., No. 1, 24 (1970).
2. P. Germeraad and H. W. More, J. Org. Chem., 39, 774 (1974).
3. U. Kucklander, Arch. Pharm., 312, 431 (1979).
4. A. N. Grinev, Hun-Shiczjun, and A. P. Terent'ev, Zh. Obshch. Khim., 30, 3668 (1960).
5. A. N. Grinev, Hun-Shiczjun, and A. P. Terent'ev, Zh. Obshch. Khim., 32, 1951 (1962).