of colorless crystals of 1-acetyl-5-methoxy-4-nitro-3-(2-phthalimidoethyl)indole (XII). Further elution gave 1.78 g (34%) of colorless crystals of 4-acetylamino-5-methoxy-3-(2-phthalimidoethyl) indole (XI).

B. To a solution of 4 g (12 mmole) of phthalic derivative X in 40 ml of pyridine was added 2.82 ml (28 mmole) acetic anhydride and mixed for 6 h at 40°. The precipitated material was filtered off, washed with ether, and dried under vacuum over solid KOH to give 3.74 g (83%) of compound XI.

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REACTIONS OF DERIVATIVES OF N-ARYL-2-METHYL-3-ETHOXYCARBONYL-4,5-DIHYDROXY-6-BROMOINDOLES

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Some 4,5-dihydroxyindoles, with an acetoacetic ester substituent at the 7 position were used to synthesize 7-acetonyl-4,5-dihydroxyindoles. Methylation of these compounds gave 4-hydroxy-5-methoxy- and 4,5-dimethoxyindoles. On reaction with hydroxylamine, these compounds were converted to the oximes. Oxidation of 4,5-dihydroxyindoles with nitric acid gave 4,5-indolequinones.

The o-quinones of the benzofuran and indole series react with ketoenols in the presence of zinc chloride to give 4,5-dihydroxyfurans (and indoles), substituted at the 7 position with a ketoenol group [1]. The resulting o-dihydroxy derivatives of benzofuran and indole can be used as starting compounds in the synthesis of heterocyclic analogs of some biologically active catechol derivatives [2, 3], and they are therefore of interest in the search for new drugs.

The present work is devoted to a study of 4,5-dihydroxyindoles. Acid hydrolysis of N-aryl-4,5-dihydroxyindoles (Ia-c) [1] with an acetoacetic ester group at position 7, gave N-aryl-7-acetonyl-4,5-dihydroxyindoles (IIIa-c) in 36-59% yield. The reaction was carried out by heating compounds Ia-c in acetic acid in the presence of a catalytic amount of orthophosphoric acid. In addition, the intermediate reaction products — indolylacetoacetic acids IIa-c — were isolated in 16-21% yield. Under similar reaction conditions the ketonic splitting of 4,5-dihydroxybenzofurans [1, 4] was accompanied by tarring. On increasing the reaction time, the yield of the substances decreased sharply.

o-Dihydroxyderivatives of indole are unstable in both acid and strongly alkaline media. In the preparation of 4,5-dimethoxyderivatives of 4,5-dihydroxyindoles, IIIb and c were first converted to the more alkali-stable 4-hydroxy-5-methoxyindoles (IVa and b); in the case of

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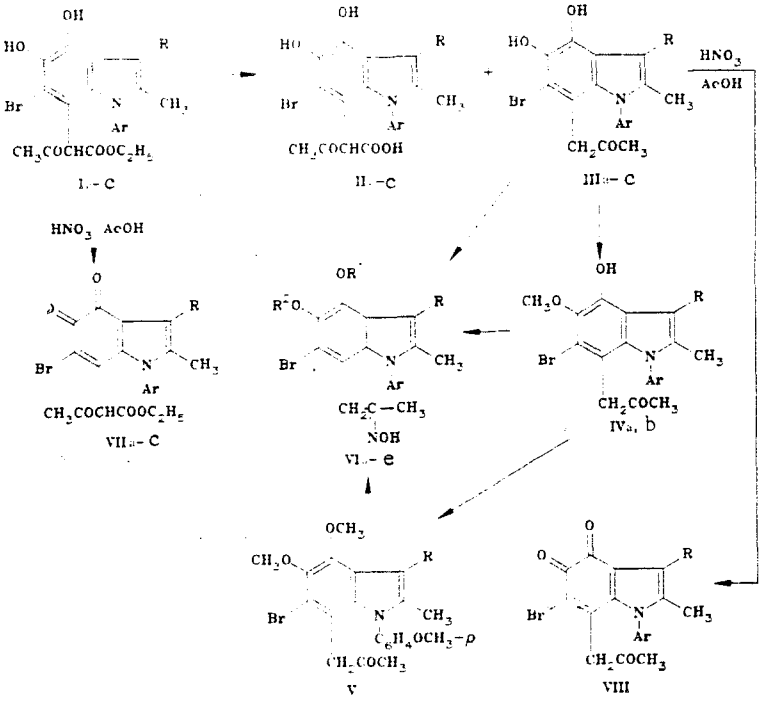


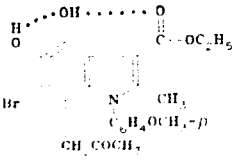
I—VIII R=$COOC_2H_5$, I—III, VII a Ar=C_6H_5, b Ar=$C_6H_4CH_3$-*p*, c Ar=$C_6H_4OCH_3$-*p*; IV a Ar=$C_6H_4CH_3$-*p*, b Ar=$C_6H_4OCH_3$-*p*; VI a—d R^1=H, e R^1=CH_3; a, b R^2=H, c—e R^2=CH_3; a, c Ar=$C_6H_4CH_3$-*p*, b,d,e Ar=$C_6H_4OCH_3$-*p*; VIII Ar=$C_6H_4CH_3$-*p*

compounds IVb, this was then converted to V. The first stage of the alkylation with dimethyl sulfate was carried out in the presence of potassium carbonate, and the second with sodium hydroxide.

The oximes of the 4,5-dihydroxy-, 4-hydroxy-5-methoxy-, and 4,5-dimethoxy-7-acetonylindoles (VIa-e) were obtained from the 7-acetonylindoles IIIa-c, IVa, b, and V by reaction with hydroxylamine hydrochloride in the presence of sodium acetate in alcohol. Catalytic hydrogenation of the oximes VIa-e gave a complex mixture of compounds from which the individual compounds could not be isolated.

The dihydroxy derivatives of the indoles Ia-c and IIIb were readily oxidized by nitric acid in acetic acid to the corresponding 4,5-indolequinones. The time of the oxidation reaction should not exceed 5-7 min; the acetoacetic ester group of compounds Ia-c is unchanged.

The IR spectra of the 4,5-dihydroxyindoles IIa-c and IIIa-c were characterized by sharp or somewhat broadened absorption bands due to the hydroxyl group at 3520-3470 cm^{-1}. It should be noted that changing the concentration of the dihydroxyindoles in an inert solvent does not change the character of the spectra, indicating that there are no intermolecular hydrogen bonds [5]. Thus, in the IR spectra of the 4,5-dihydroxyindole IIIc (1% solution in $CHCl_3$ and 0.02% solution in CCl_4) the OH group gives rise to two absorption bands: at 3520 (slightly broadened) and 2950 cm^{-1} (broad). These bands were assigned respectively to the hydroxyl at position 5, which participates in intramolecular hydrogen bonds with the 4-OH group (as in the case of 1,2-dioles), and to the hydroxyl group at position 4, which participates in chelate-type intramolecular hydrogen bonding with the $COOC_2H_5$ at position 3.



The intramolecular character of the association of ther 4-OH group is confirmed by the IR spectrum of 4,5-dimethoxyindole V where the carbonyl ester group absorbs at 1690 cm^{-1} in comparison with the IR spectra of compounds IIIc and IVb in which it absorbs at ~1640 cm^{-1}.

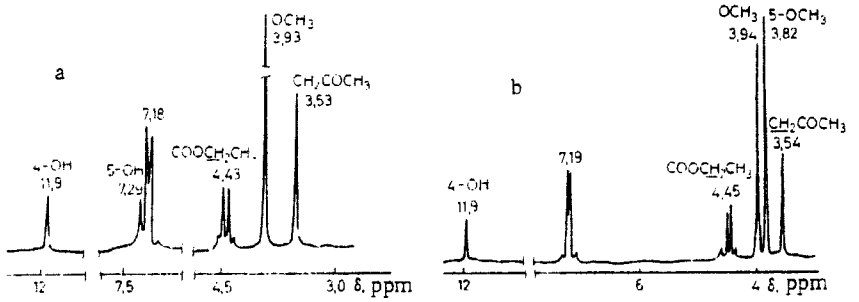


Fig. 1. PMR spectra. a) 1-(p-Methoxyphenyl)-2-methyl-3-ethoxycarbonyl-4,5-dihydroxy-6-bromo-7-acetonylindole (IIIc); b) 1-(p-methoxyphenyl)-2-methyl-3-ethoxycarbonyl-4-hydroxy-5-methoxy-6-bromo-7-acetonylindole (IVb).

TABLE 1. Derivatives of 4,5-Dihydroxyindoles IIa-c and IIIa-c

Compound	mp, °C	IR spectrum, ν, cm^{-1}			Found, %				Empirical formula	Calculated, %				Yield, %
		C=O	COOH	OH	C	H	Br	N		C	H	Br	N	
IIa	219—220	1590, 1710	2600—2750	3490	53.7	4.2	16.3	2.8	$C_{22}H_{20}BrNO_7$	53.9	4.1	16.3	2.9	16
IIb	238—240	1590, 1635	2550—2660	3465, 3540	54.8	4.5	16.0	2.7	$C_{23}H_{22}BrNO_7$	54.8	4.4	15.8	2.8	20
IIc	224—225	1590, 1630	2520—2700	3470	52.8	4.2	15.4	2.6	$C_{23}H_{22}BrNO_8$	53.1	4.3	15.3	2.7	21
IIIa	249—250	1630, 1730	—	3470	56.3	4.5	17.6	3.1	$C_{21}H_{20}BrNO_5$	56.5	4.5	17.9	3.1	36
IIIb	223—225	1610, 1730	—	3470, 3520	57.5	4.5	17.1	3.0	$C_{22}H_{22}BrNO_5$	57.4	4.8	17.4	3.0	59
IIIc*	231—233	1590, 1640	—	3460	55.4	4.5	17.1	2.9	$C_{22}H_{22}BrNO_6$	55.5	4.7	16.8	2.9	54

*PMR spectrum (acetone-D_6): 1.41 (t, $COOCH_2\underline{CH_3}$); 1.7 (s, $CH_2CO\underline{CH_3}$); 2.34 (s, 2-CH_3); 3.53 (s, $\underline{CH_2}COCH_3$); 3.93 (s, $C_6H_4O\underline{CH_3}$-p); 4.43 (q, $COO\underline{CH_2}CH_3$); 7.18 (m, protons of the aromatic ring of the aryl substituent); 7.29 (s, 5-OH); 11.9 ppm (s, 4-OH).

The position of the methyl group in the products of monomethylation was established from comparisons of IR and PMR data of the starting dihydroxyindole IIIc and the monomethoxyindole IVb. In the IR spectrum of the monomethoxy derivative IVb, the 5-OH absorption band is absent, while the broad 4-OH band at 2950 cm^{-1} is preserved. The PMR spectra of compounds IIIc and IVb contain singlets due to the 4-OH group proton in the weak-field region at 11.9 ppm (see Fig. 1), and in the spectrum of compound IVb there is a singlet from the 5-OCH_3 group protons at 3.82 ppm. Thus, methylation of 4,5-dihydroxyindoles with dimethyl sulfate in the presence of potassium carbonate gives the 4-hydroxy-5-methoxyindoles. The IR spectra of the indolylacetic acids IIa-c were characterized by broad bands at 2750-2520 cm^{-1}, which are typical of the carboxyl hydroxyl group. In the IR spectra of the 4,5-indolequinones VIIa-c and VIII there are bands at 1720-1680 cm^{-1}, characteristic of quinones.

EXPERIMENTAL

IR spectra were taken on UR-10 and Perkin-Elmer spectrometers. PMR spectra on a Varian XL-100 (internal standard — TMS). The purity of the compounds was checked by chromatography on Silufol-254 plates in chloroform; spots were visualized in UV light.

1-Phenyl-2-methyl-3-ethoxycarbonyl-4,5-dihydroxy-6-bromo-7-(1-carboxy-2-oxopropyl)-indole (IIa) and 1-Phenyl-2-methyl-3-ethoxycarbonyl-4,5-dihydroxy-6-bromo-7-acetonylindole (IIIa). To a solution of 2.7 g (5 mmole) of 1-phenyl-2-methyl-3-ethoxycarbonyl-4,5-dihydroxy-6-bromo-7-(1-ethoxycarbonyl-2-oxopropyl)indole (Ia) in 50 ml of acetic acid was added 0.5 ml of orthophosphoric acid. The reaction mixture was refluxed for 12 h, and an equal volume of water added. The precipitated material was filtered off, washed with water, and dried to give 0.8 g (36%) of compound IIIa. The acetone filtrate was evaporated, the residue recrystallized from chloroform to give 0.4 g (16%) of compound IIa.

Compounds IIb, c and IIIb, c were prepared by the same method (Table 1).

1-(p-Tolyl)-2-methyl-3-ethoxycarbonyl-4-hydroxy-5-methoxy-6-bromo-7-acetonylindole (IVa). To a solution of 2.3 g (5 mmole) of 4,5-dihydroxyindole IIIb in 100 ml of dry acetone was added 2.52 g (20 mmole) of dimethyl sulfate and 2.8 g (20 mmole) of anhydrous potassium car-

TABLE 2. Oximes of the 7-Acetonylindoles VIa-e and 4,5-Indolequinones VIIa-c

Compound	mp, °C*	Found, %				Empirical formula	Calculated, %				Yield, %
		C	H	Br	N		C	H	Br	N	
VIa	255—256	55.3	4.8	16.9	5.9	$C_{22}H_{23}BrN_2O_5$	55.6	4.9	16.8	5.9	84
VIb	228—230	53.8	4.8	16.1	5.8	$C_{22}H_{23}BrN_2O_6$	53.8	4.7	16.3	5.7	89
VIc	235—236	56.3	5.3	16.2	6.0	$C_{23}H_{25}BrN_2O_5$	56.5	5.2	16.3	5.7	97
VId	234—235	54.7	5.0	15.8	5.5	$C_{23}H_{25}BrN_2O_6$	54.7	5.0	15.8	5.5	92
VIe	165—167 †	55.6	5.3	15.3	5.2	$C_{24}H_{27}BrN_2O_6$	55.5	5.2	15.4	5.4	85
VIIa	132—134 †	55.8	4.3	15.5	2.7	$C_{24}H_{22}BrNO_7$	55.8	4.3	15.5	2.7	38
VIIb	167—168 †	56.8	4.5	15.0	2.5	$C_{25}H_{24}BrNO_7$	56.6	4.6	15.1	2.6	87
VIIc	202—204 †	54.9	4.3	14.7	2.3	$C_{25}H_{24}BrNO_6$	54.9	4.4	14.6	2.5	94

*Compounds VIa,b were recrystallized from a 1:1 mixture of alcohol and dioxane; VIc from a 1:1 mixture of methanol and dioxane; VId,e from alcohol.
†Melts without decomposition.

bonate. The reaction mixture was refluxed for 5-7 h. At the end of the reaction the inorganic salt was filtered off and washed with acetone. The acetone solution was evaporated to a small volume and cooled. The precipitate which formed was filtered off and washed with acetone to give 2.0 g (84%) of compound IVa, mp 205-206° (from acetone). Found, %: C 58.4, H 5.2, Br 16.8, N 2.7. $C_{23}H_{24}BrNO_5$. Calculated, %: C 58.2, H 5.1, Br 16.8, N 2.9.

Using the same method, compound IVb mp 215-216° (from acetone) was obtained in 92% yield. IR spectrum (0.02% solution in CCl_4): 2950 (OH), 1720, 1640 cm^{-1} (C=O). PMR spectrum (acetone-D_6): 1.42 (t, $COOCH_2\underline{CH_3}$), 1.75 (s, $CH_2CO\underline{CH_3}$), 2.33 (s, 2-CH_3), 3.54 (s, $\underline{CH_2}COCH_3$), 3.82 and 3.94 (two s, $C_6H_4O\underline{CH_3}$, 5-$O\underline{CH_3}$), 4.45 (q, $COO\underline{CH_2}CH_3$), 7.19 (q, aromatic ring protons, A_2B_2 type), 11.9 ppm (s, 4-OH). Found, %: C 56.0, H 4.9, Br 16.3, N 2.9. $C_{23}H_{24}BrNO_6$. Calculated, %: C 56.3, H 4.9, Br 16.3, N 2.9.

1-(p-Methoxyphenyl)-2-methyl-3-ethoxycarbonyl-4,5-dimethoxy-6-bromoindole (V). To a suspension of 2.5 g (5 mmole) of 4-hydroxy-5-methoxyindole IVb in 60 ml of dioxane with mixing was added 10 ml (20 mmole) of 2N NaOH. The reaction mixture was mixed for 2-3 min, and then 1.26 g (10 mmole) of dimethyl sulfate was added, after which mixing was continued at 70-80° for 2 h and 30 min. At the end of the reaction, the mixture was diluted with water and neutralized with hydrochloric acid to pH 5. The precipitated material was filtered off, washed with water, dried, and extracted with petroleum ether. The petroleum extract was evaporated to a small volume and cooled to give 1.7 g (67%) of compound V, mp 113-114° (from petroleum ether). IR spectrum: 1720, 1690 cm^{-1} (C=O). Found, %: C 57.3, H 5.3, Br 16.0, N 2.8. $C_{24}H_{26}BrNO_6$. Calculated, %: C 57.2, H 5.2, Br 15.8, N 2.8.

Oxime of 1-(p-Tolyl)-2-methyl-3-ethoxycarbonyl-4,5-dihydroxy-6-bromo-7-acetonylindole (VIa). To a solution of 2.3 g (5 mmole) of 4,5-dihydroxy-7-acetonylindole IIIb in 250 ml of absolute alcohol was added 0.7 g (10 mmole) of hydroxylamine hydrochloride and 0.82 g (10 mmole) of anhydrous sodium acetate. The reaction mixture was refluxed for 3 h and diluted with water. The precipitated material was filtered off, washed with water, and dried to give 2.0 g (84%) of compound VIa.

Compounds VIb-e were prepared by the same method, using the amount of solvent needed to dissolve the starting compounds (Table 2).

1-Phenyl-2-methyl-3-ethoxycarbonyl-6-bromo-7-(1-ethoxycarbonyl-2-oxopropyl)-4,5-indolequinone (VIIa). To a suspension of 2.6 g (5 mmole) of 4,5-dihydroxyindole Ia in 30 ml of acetic acid at 20° was added 0.63 ml (7 mmole) of nitric acid (d 1.35) in 6 ml of acetic acid. The reaction mixture was mixed for 5-7 min, diluted with an equal quantity of water, and extracted with benzene. The benzene extract was washed with water, dried, and passed through a column of silica gel in benzene, the benzene evaporated, and the residue dissolved in 30 ml of methanol. The violet precipitate was filtered off and dried to give 1.0 g (38%) of compound VIIa. IR spectra: 1720, 1670, 1630, 1610, 1600 cm^{-1} (C=O).

Compounds VIIb,c (Table 2) were prepared in the same way.

1-(p-Tolyl)-2-methyl-3-ethoxycarbonyl-6-bromo-7-acetonyl-4,5-indolequinone (VIII). To a suspension of 2.3 g (5 mmole) of 4,5-dihydroxyindole IIIb in 30 ml of acetic acid at 20°

was added 0.63 ml (7 mmole) of nitric acid (d 1.35). The reaction mixture was stirred for 5 min and diluted with water. The violet precipitate was filtered off, washed with water, and dried to give 1.9 g (82%) of compound VIII, mp 172-173° (from alcohol). Found, %: C 57.4, H 4.6, Br 17.2, N 2.9. $C_{22}H_{20}BrNO_5$. Calculated, %: C 57.6, H 4.4, Br 17.4, N 3.0.

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SYNTHESIS OF 3-METHYLPYRIDO[3,2,1-j,k]CARBAZOLIUM SALTS AND DERIVED CYANINE DYES

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When carbazole is heated with formaldehyde and acetone (or with methyl vinyl ketone) in the presence of mineral acid, 3-methylpyrido[3,2-j,k]carbazolium salts form. These react with p-dimethylaminobenzaldehyde, triethyl orthoformate, Michler's ketone, 1-ethylquinolinium iodide, or 1,3,3-trimethyl-2-formylmethyleneindolinium iodide to give the respective cyanine dyes. Deviations of the unsymmetrical dyes and Hückel molecular orbital calculations show that the Brooker basicity of the pyrido[3,2,1-j,k]carbazolium series is lower than that of the 1-phenylquinolinium series.

It has previously been shown that diphenylamine and other secondary aromatic amines undergo heterocyclization with the condensation products of formaldehyde with acetone, to form N-aryl(alkyl)-substituted lepidinium salts [1, 2]. It was of interest to extend this reaction to heterocycles containing a diarylamine segment, in order to obtain condensed systems with a nitrogen bridge atom and cyanine dyes with those terminal groups. The present communication presents a study of cyclization with the above-mentioned carbonyl components in the presence of mineral acid, of the heterocyclic analog of diphenylamine, viz., carbazole; pyrido[3,2,1-j,k]carbazolium salts (Ia, b) were obtained. Formation of analogous salts has been noted only in the patent literature [3-5]. Salt Ic (X = I) was separated in very low yield (3.6%) in the condensation of carbazole with methyl vinyl ketone in ethanol solution in the presence of zinc chloride, orthonitrophenol, and sulfuric acid. In patents [3-5] no physical constants are given either for salt Ic or for cyanine dyes prepared from it, although valuable sensitizing properties of the latter in silver halide emulsions are noted.

We were able to increase the yield of pyrido[3,2,1-j,k]carbazolium salt severalfold by changing the solvent and condensing agent, and by using the more available formaldehyde and acetone instead of methyl vinyl ketone. In view of the fact that carbazole undergoes polycondensation with formaldehyde to give resin [6], we modified the condensation procedure previously used for diphenylamine [2]. To obtain salts Ia, b formaldehyde was first condensed with acetone, and the resulting mixture of 4-hydroxybutanone and 3-butenone was reacted with carbazole in the presence of mineral acid and nitrobenzene (the latter is required for oxidation of the intermediate product). The reaction was also carried out under the same condi-

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