EXPERIMENTAL

The UV spectra were recorded on a Specord instrument in ethanol. The IR spectra were obtained on an SP-1000 instrument for tablets with potassium bromide. The PMR spectra were obtained on an FX-900 instrument. The mass-spectral investigations were conducted on a JMS-DX 300 instrument at 70 eV. The reactions and the purities of the obtained compounds were monitored by TLC on Silufol UV-254 plates in benzene with development in iodine vapor. The elemental analyses for C and H correspond to the calculated compositions.

The initial p- and m-nitrophenyl-2-formylpyrroles were obtained by the method in [10].

General Procedure for the Production of Compounds (III, IV). In a 250-ml flask fitted with a Soxhlet extractor, in which there was 10 g of anhydrous sodium sulfate, we placed 0.5 g (23 mmoles) of 1-nitrophenyl-2-formylpyrrole and 23 mmoles of the respective amine, dissolved in 100-200 ml of dry benzene. The mixture was boiled for 20 h, the solvent was evaporated, and the solid residue was recrystallized from alcohol. The properties of the obtained compounds (III, IV) are given Table 1.

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SYNTHESIS OF DERIVATIVES OF 1,3-DIHYDROSPIRO[2H-INDOLE-2,2'-PYRROLIDINE]

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UDC 547.759.5'753'743.1.07

Derivatives of 1,3-dihydrospiro[2H-indole-2,2'-pyrrolidine] were synthesized by the reaction of 2-methylene-2,3-dihydro-1H-indoles with α-iodoacetamide. Treatment of the products with alkyl iodides in the presence of potassium hydroxide gave 1'-substituted spiroindole-2,2'-pyrrolidines. The 1,3-dihydrospiro[2H-indole-2,2'-pyrrolidines] were converted by the action of perchloric acid into 2-(2-carbamoylethyl)-3H-indolium perchlorates.

The alkylation of heterocyclic enamines containing an exocyclic carbon—carbon double bond and derivatives of 2-methylene-2,3-dihydro-1H-indole, in particular, has so far been studied little [1, 2]. According to data in [3], the alkylation of 2-methylene-1,3,3-trimethyl-2,3-dihydro-1H-indole with methyl iodide takes place at the β-carbon atom of the enamine group, and the corresponding 2-isopropylidene base is formed. The reaction of the above-mentioned indoline enamine with 2-halogenoalkanols or oxiranes is also accompanied by initial C-alkylation and leads finally to derivatives of spiro[indole-2,2'-furan] [4, 5]. The spiroannellation of the pyrroline ring to the indole ring by the action of 2-methylene-2,3-dihydro-1H-indole with tetracyanoethylene was described earlier [6]. It is known that

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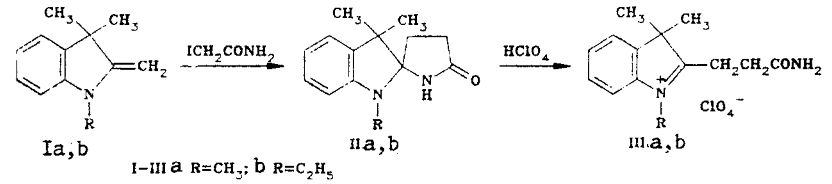
the alkylation of enamines of the pyrrolidine series, obtained from cycloalkanones, by α-bromoacetamides takes place at the nitrogen atom of the enamine group with the formation of 1-carbamoylmethylpyrrolidines [7].

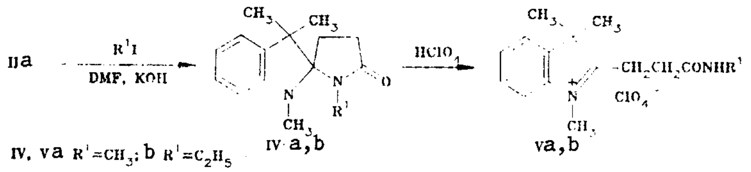
The aim of the present work was to investigate the products from the reaction of 2-methylene-2,3-dihydro-1H-indoles (Ia, b) with α-iodoacetamide.

In the reaction of indolineenamines (Ia, b) with α-iodoacetamide in dioxane alkylation takes place at the β-carbon atom of the enamino group, and the final reaction products are derivatives of 1,3-dihydrospiro[2H-indole-2,2'-pyrrolidine] (IIa, b). In the course of the reaction a certain part of the initial bases (Ia, b) is converted by the action of the released hydrogen iodide into 1,2,3,3-tetramethyl- and 2,3,3-trimethyl-1-ethyl-3H-indolium iodides, respectively.



The IR spectra of (IIa, b) contained absorption bands at 3170 (N–H) and 1695 cm^{-1} (C=O), characteristic of five-membered lactams [8]. In the ^{13}C NMR spectrum of (IIa) the signal for the carbon atom of the carbonyl group appears at 170.4 ppm (γ-lactam) [9], while the signal of the sp^3-hybridized α-carbon atom of the indole ring appears at 92.3 ppm.

The action of perchloric acid on the spiroindole-2,2'-pyrrolidines (IIa, b) leads to opening of the pyrrolidine ring with the formation of 2-(2-carbamoylethyl)-3H-indolium perchlorates (IIIa, b). 1'-Substituted 1,3-dihydrospiro[2H-indole-2,2'-pyrrolidines] (IVa, b) were obtained by the reaction of (IIa) with methyl iodide and ethyl iodide in DMFA in the presence of potassium hydroxide. Treatment of (IVa, b) with perchloric acid gave the 3H-indolium perchlorates (Va, b).



The IR spectrum of the perchlorate (Va) contains absorption bands for the secondary amide at 3395 (N–H), 1670 (C=O), and 1545 cm^{-1} (amide II) [8]. In the ^{13}C NMR spectrum of the perchlorate the signal of the sp^2-hybridized α-carbon atom of the indole ring lies at 198.0 ppm, which is typical of 3H-indolium salts [10, 11].

EXPERIMENTAL

The IR spectra were recorded on a Perkin–Elmer 325 instrument for tablets with potassium bromide. The ^1H NMR spectra were obtained on a Tesla BS-487C spectrometer at 80 MHz with HMDS as internal standard. The ^{13}C NMR spectra were obtained on a Tesla BS-567A spectrometer at 25.14 MHz. The mass spectra were recorded on an LKB-9000 instrument with direct injection into the ion source at 160-180°C and 40 eV. The reaction and the individualities of the compounds were monitored by TLC on aluminum oxide of II activity in the 3:5 acetone–hexane system with development in iodine vapor. The elemental analyses agreed with the calculated compositions.

5'-Oxo-1,3,3-trimethyl-1,3-dihydrospiro[2H-indole-2,2'-pyrrolidine] (IIa, $C_{14}H_{18}N_2O$). A mixture of 12.13 g (70 mmoles) of 2-methylene-1,3,3-trimethyl-2,3-dihydro-1H-indole (Ia) and 18.5 g (100 mmoles) of α-iodoacetamide in 25 ml of dioxane was heated at 95-100°C for 5 h. The 1,2,3,3-tetramethyl-3H-indolium iodide (6.20 g) was filtered off, the filtrate was evaporated, and the residue was crystallized twice from alcohol. The yield was 4.2 g (26%); mp 205-206°C. ^1H NMR spectrum (deuterochloroform): 1.17 (3H, s, 3-CH_3); 1.20 (3H, s, 3-CH_3); 1.93-2.63 (4H, m, CH_2CH_2), 2.69 (3H, s, 1-CH_3), 6.22 (1H br.s NH); 6.33-7.26 ppm (4H, m, ArH). ^{13}C NMR spectrum (deuterochloroform): 20.8 (3-CH_3), 23.8 ($C_{(3')}$), 24.7 (3-CH_3), 28.2 (1-CH_3), 30.2 ($C_{(4')}$), 46.1 ($C_{(3)}$), 92.3 ($C_{(2)}$), 107.5 ($C_{(7)}$), 119.1, 121.7 ($C_{(4),(5)}$), 128.0 ($C_{(6)}$), 136.6 ($C_{(3a)}$), 148.5 ($C_{(7a)}$), 176.4 ppm (C=O). M^+ 230.

3,3-Dimethyl-5'-oxo-1-ethyl-1,3-dihydrospiro[2H-indole-2,2'-pyrrolidine] (IIb, $C_{15}H_{20}N_2O$). A mixture of 4.68 g (25 mmoles) of 3,3-dimethyl-2-methylene-1-ethyl-2,3-dihydro-1H-indole (Ib) and 6.47 g (35 mmoles) of α-iodoacetamide in 10 ml of dioxane was heated at 95-100°C for 5.5 h. The 2,3,3-trimethyl-1-ethyl-3H-indolium iodide (1.80 g) was filtered off, the filtrate was evaporated, and the residue was chromatographed on a column (600 × 30 mm) with aluminum oxide (R_f 0.55, eluant 3:5 methyl ethyl ketone—hexane). The yield was 1.10 g (18%); mp 116-117°C (from acetone). ^1H NMR spectrum (deuterochloroform): 1.17 (3H, s, 3-CH_3), 1.22 (3H, s, 3-CH_3), 1.22 (3H, t, J = 7.0 Hz, CH_2CH_3), 1.93-2.67 (4H, m, CH_2CH_2), 2.85 (2H, q, J = 7.0 Hz, CH_2CH_3), 6.29 (1H, br.s, NH), 6.36-7.18 ppm (4H, m, ArH).

2-(2-Carbamoylethyl)-1,3,3-trimethyl-3H-indolium Perchlorate (IIIa, $C_{14}H_{19}ClN_2O_5$). To a solution of 1.15 g (5 mmoles) of (IIa) in 7 ml of alcohol we added 0.85 g of 60% perchloric acid. The crystalline substance was filtered off and recrystallized from alcohol. Yield 1.32 g (80%); mp 178-179°C. IR spectrum: 3450 (N—H), 3345 (N—H), 1695 (C=O), 1150-1040, 960-940, 630-620 cm^{-1} (ClO_4^-). ^1H NMR spectrum (trifluoroacetic acid): 1.35 (6H, s, 3.3-CH_3), 2.79 (2H, t, J = 7.5 Hz, CH_2), 3.24 (2H, t, J = 7.5 Hz, CH_2), 3.87 (3H, s, 1-CH_3), 7.27-7.48 ppm (4H, m, ArH).

3,3-Dimethyl-2-(2-carbamoylethyl)-1-ethyl-3H-indolium Perchlorate (IIIb, $C_{15}H_{21}ClN_2O_5$). The compound was obtained from 0.49 g (2 mmoles) of (IIb) by analogy with the perchlorate (IIIa). Yield 0.60 g (87%); mp 172-173°C (from alcohol). ^1H NMR spectrum (trifluoroacetic acid): 1.32 (6H, s, 3.3-CH_3), 1.32 (3H, t, J = 7.0 Hz, CH_2CH_3), 2.78 (2H, t, J = 7.0 Hz, CH_2CO), 3.19 (2H, t, J = 7.0 Hz, CH_2CH_2CO), 4.31 (2H, q, J = 7.0 Hz, CH_2CH_3), 7.26-7.44 ppm (4H, m, ArH).

5'-Oxo-1,1',3,3-tetramethyl-1,3-dihydrospiro[2H-indole-2,2'-pyrrolidine] (IVa, $C_{15}H_{20}N_2O$). To a solution of 2.30 g (10 mmoles) of (IIa) in 20 ml of DMFA we added 1.40 g (25 mmoles) of finely ground potassium hydroxide, and we then added dropwise 2.84 g (1.25 ml, 20 mmoles) of methyl iodide. The mixture was kept at 20°C for 1 h, poured into 150 ml of water, and extracted with ether (3 × 15 ml). The extract was washed with water (2 × 20 ml) and dried with calcium chloride. The solvent was distilled, and the residue was crystallized from petroleum ether. Yield 1.0 g (41%); mp 87-88°C. IR spectrum: 1695 cm^{-1} (C=O). ^1H NMR spectrum (deuterochloroform): 1.17 (3H, s, 3-CH_3), 1.22 (3H, s, 3-CH_3), 1.96-2.58 (4H, m, CH_2CH_2), 2.28 (3H, s, 1'-CH_3), 2.64 (3H, s, 1-CH_3), 6.32-7.26 ppm (4H, m, ArH). M^+ 244.

5'-Oxo-1,3,3-trimethyl-1'-ethyl-1,3-dihydrospiro-[2H-indole-2,2'-pyrrolidine] (IVb, $C_{16}H_{22}N_2O$). The compound was obtained from 2.30 g (10 mmoles) of (IIa) and 3.12 g (1.61 ml, 20 mmoles) of ethyl iodide by analogy with (IVa). Yield 0.90 g (35%); mp 112-113°C (from a mixture of acetone and petroleum ether). IR spectrum: 1690 cm^{-1} (C=O). ^1H NMR spectrum (deuterochloroform): 0.84 (3H, t, J = 7.3 Hz, CH_2CH_3), 1.14 (3H, s, 3-CH_3), 1.20 (3H, s, 3-CH_3), 1.82-2.77 (4H, m, CH_2CH_2), 2.71 (3H, s, 1-CH_3), 3.14 (2H, q, J = 7.3 Hz, CH_2CH_3), 6.27-7.19 ppm (4H, m, ArH).

2-[2-(N-Methylcarbamoyl)ethyl]-1,3,3-trimethyl-3H-indolium Perchlorate (Va, $C_{15}H_{21}ClN_2O_5$). A solution of 0.73 g (3 mmoles) of (IVa) in 4 ml of alcohol was neutralized with 60% perchloric acid. The mixture was kept at —5°C for 12 h, and the crystalline substance was filtered off and recrystallized from alcohol. Yield 0.53 g (51%), mp 135-136°C. ^1H NMR spectrum (deuteroacetonitrile): 1.60 (6H, s, 3.3-CH_3), 2.71 (3H, d, J = 4.9 Hz, $NHCH_3$), 2.74 (2H, t, J = 7.5 Hz, CH_2), 3.34 (2H, t, J = 7.6 Hz, CH_2), 4.01 (3H, s, 1-CH_3), 6.63 (1H, br.s, NH), 7.56-7.81 ppm (4H, m, ArH). ^{13}C NMR spectrum (deuteroacetonitrile): 22.0 (3.3-CH_3), 23.3 (CH_2), 26.0 ($NHCH_3$), 31.6 (CH_2), 35.3 (1-CH_3), 55.3 ($C_{(3)}$), 115.5 ($C_{(7)}$), 123.4 ($C_{(4)}$), 129.5, 130.3 ($C_{(5)}$, $C_{(6)}$), 142.3, 142.4 ($C_{(3a)}$, $C_{(7a)}$), 170.4 (CO), 198.0 ppm ($C_{(2)}$).

1,3,3-Trimethyl-2-[2-(N-ethylcarbamoyl)ethyl]-3H-indolium Perchlorate (Vb, $C_{16}H_{23}ClN_2O_5$). The compound was obtained from 0.78 g (3 mmoles) of (IVb) by analogy with the perchlorate (Va). Yield 0.47 g (44%); mp 159-160°C (from alcohol). IR spectrum: 3440 (N—H), 1670 (C=O), 1540 (amide II), 1150-1040, 960-940, and 630-620 cm^{-1} (ClO_4^-). ^1H NMR spectrum (trifluoroacetic acid): 0.84 (3H, t, J = 7 Hz, CH_2CH_3), 1.30 (6H, s, 3.3-CH_3), 2.51-3.37 (6H, m, 3 × CH_2), 3.82 (3H, s, 1-CH_3), 7.22-7.43 ppm (4H, m, Ar).

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MONONITRATION OF DERIVATIVES OF BENZISATINS

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.1:543.422.25

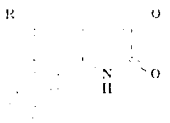
The mononitration of benz[e]-, benz[f]-, and benz[g]isatins and their tetrahydro derivatives was realized. It was established on the basis of an analysis of the ^{1}H NMR and mass spectra that substitution takes place at position 5 in the derivatives of the [g] series and at the position adjacent to the NH group in derivatives of the [f] series and in the case of 6,7,8,9-tetrahydrobenz[e]isatin. This reaction path corresponds to the maximum electron density in the HOMO, calculated by the CNDO method. In benz[e]isatin, contrary to the general relationship and to the quantum-chemical prediction, the nitro group initially enters the ring annellated with the indole ring.

Published data on the introduction of a nitro group into the aromatic part of the benzindole system mostly concern compounds containing alkyl groups in the pyrrole ring [1-4]. Thus, it was shown, on the basis of data from the PMR spectra of nitro derivatives [3] and the corresponding amines [4], that mixtures of compounds are formed during the nitration of angular dimethylbenzindoles, but the nitro group always enters the ring which is annellated to the indole ring.

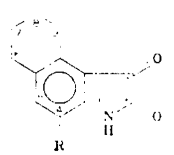
We studied the direction of the mononitration of benz[e]-, benz[f]-, and benz[g]isatins (Ia-IIIa) and their tetrahydro derivatives (IVa-VIa).

I a,b

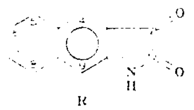
II a,b



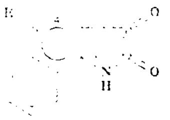
III a, b



IV a, b



V a, b



VI a, b

Ia – VIa $R=H$; Ib – VIb $R=NO_2$

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