form, dried, and recrystallized from water to give 1.65 g (53%) of a product with mp 253-254°C (dec., in a sealed capillary) and R_f 0.70. Found:C 32.8; H 1.6; Br 36.5%; neutralization equivalent 218; M^+ 219. $C_6H_3BrO_4$. Calculated: C 32.9; H 1.4; Br 36.5%; neutralization equivalent 219; M^+ 219. IR spectrum: 2450-2570 (OH from COOH), 1731 (C=O from COOH), 1623 (C=O), 1600, 1555 cm^{-1} (C=C).

3,5-Dibromocomanic Acid (VII). This acid was similarly obtained from 1.5 g of ester VI in 2.3 ml of concentrated H_2SO_4. Recrystallization of the crude product from anhydrous alcohol gave 1 g (70%) of a product with mp 219-220°C (dec., in a sealed capillary) and R_f 0.66. Found: C 24.0; H 0.9; Br 54.0%; neutralization equivalent 296; M^+ 298. $C_6H_2Br_2O_4$. Calculated: C 24.2; H 0.7; Br 53.7%; neutralization equivalent 298; M^+ 298. IR spectrum: 2400-2570 (OH from COOH), 1730 (C=O from COOH), 1605-1580 cm^{-1} (C=O from C=C).

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BENZOXAZOLE IN THE HETARYLATION REACTION*

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N-Acylbenzoxazolium salts formed in situ in the reaction of benzoxazole with acylating agents react with indoles with opening of the oxazole ring to give tri(3-indolyl)methanes. Hetarylation products are formed in the reaction of N-acylbenzoxazolium salts in situ with oxindole and pyrazolone.

Up until now hetarylation with N-acyl heteroaromatic cationic salts in situ has been extended only to two types of azoles – imidazoles [2] and perimidine [3]. Pyrazoles could not be used in this reaction. In the present research we decided to investigate the behavior of benzoxazole under the conditions of the hetarylation reaction [4] upon reaction with nucleophilic aromatic and heteroaromatic compounds in the presence of acylating agents.

We found that N,N'-dialkylanilines do not undergo hetarylation in the case of the reaction of benzoxazole with N,N'-dialkylanilines in the presence of acylating agents in an inert solvent; however, the oxazole ring in the intermediately formed N-acylbenzoxazolium salt I opens to give N-acyl-o-aminophenols II, and the unchanged N,N'-dialkylanilines are recovered in quantitative yield. However, in the case of the reaction with indoles under similar conditions tri(3-indolyl)methanes (V) are formed in addition to II, regardless of the nature of the acyl halide used. When the reaction is carried out in acetic anhydride, V undergoes partial acylation to give bis(1-acyl-3-indolyl)(3-indolyl)methane (Vd). The formation of V can be represented as the result of succesive addition of indole molecules to the intermediately formed N-acylbenzoxazolium cations of I and III and the existence of intermediate IV in equilibrium with open form IVa and successive alkylation of a gramine fragment of a third molecule of indole, which leads to final products V. Similar processes have also been previously noted for N,N'-diacylbenzimidazolium salts [5].

We also were unable to introduce the benzoxazole residue into the indole ring by means of protic benzoxazole salts formed in the reaction of o-aminophenol and tri(3-indolyl)methane with indole.

*See [1] for our preliminary communication.

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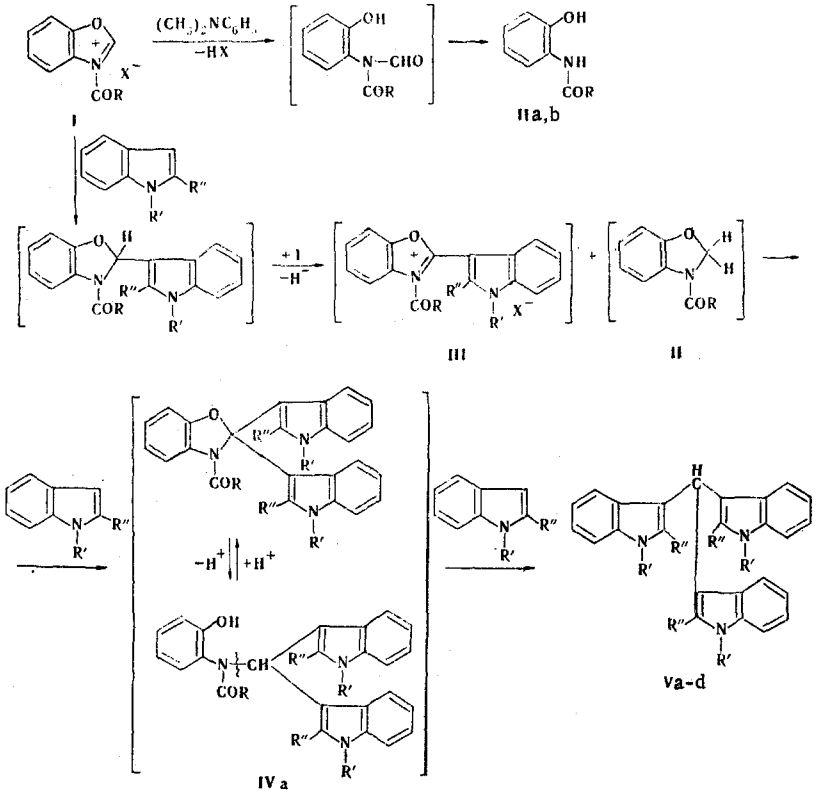
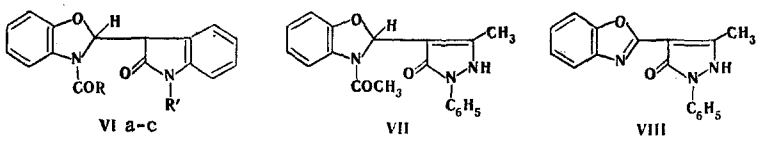


II a R = CH_3; b R = C_6H_5; X = Cl^-, CH_3COO^-; V a R′ = R″ = H; b R′ = CH_3, R″ = H; c R′ = H, R″ = CH_3; d 2R′ = $COCH_3$, R′ = R″ = H

Of all of the investigated nucleophilic organic compounds, only oxindole and 1-phenyl-3-methyl-5-pyrazolone formed the usual hetarylation products (VI-VIII) under the described conditions. When the reaction was carried out in acetic anhydride, oxindole underwent acetylation at the nitrogen atom to give 1-acetyl-2-substituted benzoxazolines (VIc and VII) in all cases:



VI a R = C_6H_5, R′ = H; b R =  , R′ = H; c R = CH_3, R′ = $COCH_3$

When the reaction was carried out in an inert aprotic solvent with equimolar amounts of acyl halides, we obtained substituted 1-acylbenzoxazolines VI in the case of hetarylation of oxindole and always only 1-phenyl-3-methyl-4-(2-benzoxazolyl)pyrazol-5-one (VIII) in the reaction with pyrazolone, regardless of the nature of the acyl halide used in the reaction, and o-acylaminophenols (II). Hydride shift from the intermediately formed derivative of the VII type to the N-acylbenzoxazolium cation evidently takes place in these cases, as shown in the scheme presented above, as in the previously proved mechanism of cationotropic hetarylation [4].

Compound VIII is also formed in the reaction of benzoxazole hydrochloride with pyrazolone; o-aminophenol was isolated as a side product.

The tris(3-indolyl)methane (V) structure is confirmed by the high-resolution mass spectra. Thus elimination of a hydrogen atom by the molecular ion and successive cleavage of initially one and then a second exocyclic C–C bond are observed in the fragmentation of Va, as a result of which the following ions are observed in addition to the molecular ion in the spectrum: $[M-H]^+$, $[M-\text{indole}]^+$, $[\text{indole}]^+$, and $[CH-\text{indole}]^+$. The fragmentation of the molecular ions of Vb and Vc proceeds similarly. Thus $[M-H]^+$, $[M-1\text{-methylindole}]^+$, $[1\text{-methylindole}]^+$, and $[CH-1\text{-methylindole}]^+$ ions are recorded in the spectrum of Vb, and $[M-H]^+$, $[M-2\text{-methylindole}]^+$, and $[CH_2-2\text{-methylindole}]^+$ ions are recorded in the spectrum of Vc. In the case of Vd the molecular ion successively eliminates two molecules of ketene; this is characteristic for N-acetyl deriva-

tives. Three types of ions are formed as a result of cleavage of one or two exocyclic C–C bonds in succession: $[M-N\text{-acylindole}]^+$, $[CH-\text{indole}]^+$, and $[\text{indole}]^+$.

The structures of VI-VIII were also confirmed by the high-resolution mass spectra. The interannular C–C bond undergoes cleavage to give two ions – $[M-\text{oxindole}]^+$ and $[\text{oxindole}]^+$ – in the fragmentation of the molecular ion of IVa,b. In addition, the amide C–N bond undergoes cleavage with the elimination of a [COR'] fragment and the formation of an $[M-COR]^+$ ion. The fragmentation of the molecular ions of VIc and VII proceeds similarly, except that two molecules of ketene are eliminated in the step involving cleavage of the amide bond in the case of VIc, and one molecule of ketene is eliminated in the case of VII; this is characteristic for N-acetyl derivatives. We recorded $[M-C_2H_2O]^+$, $[M-\text{oxindole}]^+$, and $[\text{oxindole}]^+$ ions in the spectrom of VIc, $[M-C_2H_2O]^+$, $[M-\text{pyrazolone}]^+$, $[\text{pyrazolone}]^+$ ions in the spectrum of VII, and $[M-H]^+$, $[M-\text{pyrazolone}]^+$, and $[\text{pyrazolone}]^+$ ions in the spectrum of VIII. The elementary compositions of all of the molecular and fragment ions were determined by means of the high-resolution mass spectra, and the mass-spectral data confirmed the structures of the synthesized compounds in all cases.

EXPERIMENTAL

The IR spectra of chloroform solutions of the compounds were recorded with a UR-20 spectrometer. The mass spectra were obtained with Varian CH-6 and MAT-311 spectrometers at an accelerating voltage of 3 kV, ion-source temperatures of 80 and 115-130°C, a cathode emission current of 300 mA, and an ionizing voltage of 70 V. The PMR spectra of solutions of the compounds in d_6-DMSO were recorded at room temperature with a Varian XL-100 spectrometer and tetramethylsilane as the internal standard. Chromatography was accomplished with a loose thin layer of Al_2O_3 (activity II on the Brockmann scale) with elution with chloroform–benzene–hexane (30:6:1) (A) and chloroform–benzene–hexane–methanol (30:6:1:1) (B) and development with iodine vapors and in UV light.

N-Benzoyl-o-aminophenol (II). A mixture of 1.2 g (0.01 mole) of benzoxazole, 1.2 g (0.01 mole) of dimethylaniline, 1.4 g (0.01 mole) of benzoyl chloride, and 10 ml of dry benzene was refluxed for 2 h, after which it was subjected to steam distillation, and the residue in the distilling flask was separated and recrystallized from n-butanol to give 1.5 g (72%) of a product with mp 166-167°C (mp 167-168°C [6]).

Tris(1-methyl-3-indolyl)methane (Vb). A) A mixture of 1.2 g (0.01 mole) of benzoxazole, 1.3 g (0.01 mole) of 1-methylindole, and 15 ml of acetic anhydride was heated at 125°C for 4 h, after which the precipitate was removed by filtration, washed with methanol, and recrystallized from dimethylacetamide (DMF) to give 0.9 g (75%) of a product with mp **291-292°C** and R_f 0.9 (A). IR spectrum: 1500, 1600, and 1620 cm^{-1} (indole ring). PMR spectrum, δ: 6.43-8.60 (aromatic protons), 5.9 (CH), and 3.8 ppm (CH_3). Mass spectrum, m/e (relative intensity in percent): 403 (75.5); 402 (33.0); 273 (15.6); 272 (8.9); 271 (17.3); 270 (100); 143 (5.2); 142 (10.1); 130 (6.8); 129 (6.2); 128 (5.1); 77 (7.1). Found: C 83.7; H 6.2; N 10.3%. $C_{28}H_{25}N_3$. Calculated: C 83.6; H 6.4; N 10.6%. Workup of the filtrate gave 1 g (63%) of N-acetyl-o-aminophenol with mp 201-202° (from methanol) and R_f 0.2 (A) (mp 201-202°C [6]).

B) A mixture of 1.5 g (0.01 mole) of benzoxazole hydrochloride, 1.3 g (0.01 mole) of 1-methylindole, and 20 ml of dry DMF was maintained at room temperature for 6 h, after which it was worked up as described above to give 0.5 g (42%) of a product with mp 291-292°C (from DMF) and R_f 0.9 (A). No melting-point depression was observed for a mixture of a sample of this product with a sample of the product obtained by method A.

Bis(1-acetyl-3-indolyl)(3-indolyl)methane (Vd). This compound, with mp 168-169°C (from n-butanol) and R_f 0.2 (A), was similarly obtained in 25% yield. IR spectrum: 1690 (C=O) and 3490 cm^{-1} (NH). PMR spectrum, δ: 6.43-8.74 (aromatic protons), 10.4 (NH), 5.9 (CH), and 2.2 ppm. ($COCH_3$). Mass spectrum, m/e (relative intensity in percent): 445 (14.8); 404 (26.0); 403 (68.8); 402 (15.7); 361 (23.7); 360 (52.4); 288 (20.0); 246 (29.2); 245 (68.5); 244 (59.4); 243 (100); 218 (12.0); 217 (18.1); 216 (25.5); 118 (10.2); 117 (68.9); 91 (17.7); 90 (29.5); 89 (25.7); 64 (19.4). Found: C 79.6; H 5.1; N 10.2%. $C_{27}H_{31}N_3O$. Calculated: C 80.4; H 5.3; N 10.4%.

Tris(3-indolyl)methane (Va). This compound, with mp 245-246°C (from n-butanol) and R_f 0.2 (A), was similarly obtained in 73% yield. IR spectrum: 3480 (NH); 1500, 1600, and 1610 cm^{-1} (indole ring). PMR spectrum, δ: 10.5 (NH), 5.9 (CH), and 6.45-8.70 ppm (aromatic protons). Found: C 82.1; H 6.1; N 11.5%. $C_{25}H_{22}N_3$. Calculated: C 82.4; H 6.0; N 11.5%.

Tris(2-methyl-3-indolyl)methane (Vc). This compound, with mp > 300°C (from DMF) and R_f 0.2 (A), was obtained in 58% yield. Found: C 82.5; H 6.9; N 10.3%. $C_{28}H_{25}N_3$. Calculated: C 82.7; H 6.9; N 10.3%.

1-Phenyl-3-methyl-4-(3-acetyl-2-benzoxazolinyl)pyrazol-5-one (VII). A mixture of 1.2 g (0.01 mole) of benzoxazole, 0.7 g (0.01 mole) of 1-phenyl-3-methylpyrazol-5-one, and 10 ml of acetic anhydride was heated at 125°C for 5 h, after which it was cooled, and the precipitate was removed by filtration, washed with water, dried, and recrystallized from n-butanol to give 2 g (61%) of a product with mp 168-169°C and R_f 0.2 (A). IR spectrum: 1650, 1695 (C=O) and 3422 cm^{-1} (NH). PMR spectrum, δ: 2.25 (CH_3), 2.45 ($COCH_3$), and 7.15-8.05 ppm (aromatic protons). Mass spectrum, m/e (relative intensity in percent): 335 (38.9); 294 (13.3); 293 (62.6); 292 (5.0); 276 (6.4); 186 (15.2); 185 (100); 174 (6.9); 148 (6.8); 145 (5.9); 120 (13.8); 109 (9.6); 105 (5.0); 104 (13.3); 103 (5.1); 93 (6.9); 91 (11.7); 77 (21.0); 71 (5.2); 65 (8.2); 57 (8.2); 55 (6.1); 51 (7.5); 44 (15.9); 43 (17.1); 42 (7.3); 39 (5.14). Found: C 67.9; H 5.1; N 12.8%. $C_{19}H_{16}N_3O_3$. Calculated: C 68.1; H 4.8; N 12.5%.

1-Acetyl-3-(3-acetyl-2-benzoxazolinyl)-2-oxindole (VIc). This compound, with mp 226-228°C (from n-butanol) and R_f 0.5 (B), was similarly obtained in 21% yield. IR spectrum: 1690, and 1710 cm^{-1} (C=O). Found: C 68.2; H 5.0; N 8.5%. $C_{19}H_{16}N_2O_4$. Calculated: C 67.9; H 4.8; N 8.3%.

1-Phenyl-3-methyl-4-(2-benzoxazolyl)pyrazol-5-one (VIII). A) A mixture of 1.2 g (0.01 mole) of benzoxazole, 0.8 g (0.005 mole) of 1-phenyl-3-methylpyrazol-5-one, 0.7 g (0.005 mole) of benzoyl chloride, and 25 ml of dry benzene was refluxed for 3 h, after which water was added, and the organic layer was separated and dried. The benzene was removed by distillation, and the residue was recrystallized from n-butanol to give 0.9 g (60%) of a product with mp 183-184°C and R_f 0.4 (B). IR spectrum: 3422 (NH) and 1700 cm^{-1} (C=O). Found: C 69.8; H 5.4; N 14.7%. $C_{24}H_{18}N_3O_3$. Calculated: C 70.1; H 5.1; N 14.4%. Workup of the filtrate gave 0.5 g (50%) of N-benzoyl-o-aminophenol with mp 167-168°C (from n-butanol). No melting-point depression was observed for a mixture of a sample of this product with a genuine sample.

B) A mixture of 1.5 g (0.01 mole) of benzoxazole hydrochloride, 1.7 g (0.01 mole) of 1-phenyl-3-methyl-pyrazol-5-one, and 20 ml of dry DMF was heated at 100°C for 2 h, after which water was added, and the resulting precipitate was separated, washed with methanol, and recrystallized from n-butanol to give 1.2 g (80%) of a product with mp 184-185°C and R_f 0.4 (B). No melting-point depression was observed for a mixture of a sample of this product with a sample of the compound prepared by the above method. The IR spectra of the two samples were identical.

3-(3-Benzoyl-2-benzoxazolyl)-2-oxindole (VIa). This compound, with mp 210-212°C (from n-butanol) and R_f 0.5 (B), was similarly obtained in 23% yield. IR spectrum: 1650, 1710 (C=O); 3430 cm^{-1} (NH). Mass spectrum, m/e (relative intensity in percent): 357 (6.3); 356 (24.5); 132 (3.3); 106 (8.9); 105 (100); 77 (29.0); 51 (3.2). Found: C 74.2; H 4.5; N 7.9%. $C_{22}H_{16}N_2O_3$. Calculated: C 74.0; H 4.3; N 7.6%.

3-[3-(2-Thenoyl)benzoxazolin-2-yl]-2-oxindole (VIb). This compound, with mp 252-253°C (fron n-butanol) and R_f 0.4 (B), was similarly obtained in 22% yield. IR spectrum: 1665, 1707 (C=O); 3425 cm^{-1} (NH). Mass spectrum, m/e (relative intensity in percent): 362 (4.3); 361 (29.3); 360 (100); 359 (33.8); 358 (14.9); 357 (12.0); 356 (3.0); 354 (3.1); 223 (3.3); 116 (5.2); 113 (5.1); 112 (6.3); 111 (100); 83 (3.5); 39 (7.4). Found: C 66.0; H 3.9; N 7.4; S 9.0%. $C_{20}H_{14}N_2O_3S$. Calculated: C 66.3; H 3.9; N 7.7; S. 8.9%.

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