solution, and the mixture was refluxed for 8 h. The solvent was evaporated, and the reaction mass was diluted with 100 ml of 10% aqueous KOH. The precipitate was removed by filtration and washed to neutrality with water. The precipitate after filtration was dissolved in isopropyl alcohol saturated with HCl, after which the solvent was evaporated. The hydrochloride of δ-carboline X was extracted from the residue by refluxing with 250 ml of water. The solution was cooled and filtered, and the filtrate was made alkaline to pH 10-11 with 10% aqueous KOH solution. The resulting precipitate was removed by filtration, washed with water, and recrystallized. The yield of carboline X was 0.5 g (30%) (Table 2).

4-Methyl-δ-carboline (XI). A 1-ml (0.01 mole) sample of aldehyde III was added to a heated (to 35°C) solution of 1.8 g (0.01 mole) of indolinone I and 1 ml of triethylamine in 50 ml of alcohol, after which the mixture was allowed to stand at room temperature for 10-12 h. The solvent was then evaporated, and the reaction mixture was worked up and δ-carboline XI was isolated as in the synthesis of X. The yield of carboline XI was 0.4 g (22%) (Table 2).

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INDOLE DERIVATIVES.

123.* EFFECT OF THE SUBSTITUENT IN THE 2 POSITION ON THE CARBOMETHOXYLATION OF 2-SUBSTITUTED 3-INDOLYLACETONITRILES

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It is shown that the size rather than the electronegativity of the substituent in the 2 position of the indole ring has an effect on the Claisen condensation of 2-substituted 3-indolylacetonitriles with dimethyl carbonate. Carbomethoxylation of the side chain is generally accompanied by methylation of the nitrogen atom of the indole ring.

It was recently established that the C-carbomethoxylation of 3-indolylacetonitrile is accompanied by N-carbomethoxylation and leads to the formation of N-carbomethoxy-3-indolylcyanoacetic ester [2]. In the present research we studied carbomethoxylation under the conditions of the Claisen condensation of 3-indolylacetonitriles that contain various substituents in the 2 position of the indole ring. It seemed of interest to ascertain the effect of both the electronic and steric properties of the substituents.

The necessary 3-indolylacetonitriles I-IV with CH_3, C_6H_5, tert-Bu, and $COOCH_3$ substituents were obtained by known methods [3-5]. 2-Cyano-3-indolylacetonitrile (V) was obtained from 2-cyano-3-methylindole [6] by the method described for 2-carbomethoxy-3-cyanomethylfuran [7].

The introduction of the substituents listed above in the 2 position of 3-indolylacetonitrole hinders carbomethyoxylation. In contrast to 3-indolylacetonitrile, its 2-substi-

*See [1] for Communication 122.

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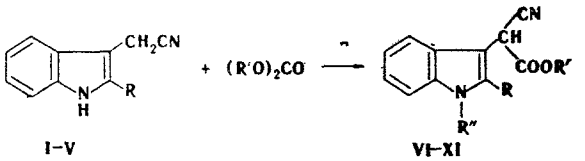
tuted derivatives do not undergo carbomethoxylation in refluxing ether. The C-carbomethoxylation of 2-substituted 3-indolylacetonitrile in the side chain can be realized in diglyme in the presence of sodium hydride at 75-80°C; N-methylation of the nitrogen atom of the indole ring is observed in this case.

The alkylation of the nitrogen atom of the indole ring with dimethyl carbonate under the conditions of the Claisen condensation probably proceeds via a $B_{al}2$ mechanism, which is a special case of an S_N2 reaction. This is also confirmed by the fact that carbethoxylation of the side chain is not accompanied by ethylation of the nitrogen atom in the reaction of 2-methyl-3-indolylacetonitrile with diethyl carbonate under the same conditions; this is readily explained by the greater steric hindrance in the reaction of the N-indole anion with the ethyl residue than with the methyl residue in S_N2 reactions [8]:



I–V VI–XI

I R=CH_3; II R=C_6H_5; III R=*t*-Bu; IV R=$COOCH_3$; V R=CN; VI R=R′=R″=CH_3; VII R=CH_3, R′=C_2H_5, R″=H; VIII R=C_6H_5, R′=R″=CH_3; IX R=*t*-Bu, R′=R″=CH_3; X R=$COOCH_3$, R′=CH_3, R″=H; XI R=CN, R′=R″=CH_3

The unfavorable effect of the substituent in the 2 position on C-acylation can be equalized if a less sterically hindered acylating agent, viz., methyl formate, is used in place of dimethyl carbonate. The side chain in this case undergoes formylation in refluxing ether, and the products are obtained in high yields.

XII XIII

However, a very bulky substituent (tert-Bu) in the 2 position also hinders C-formylation.

Thus the influence of a substituent in the 2 position of 3-indolylacetonitrile is exerted, first, in hindering C-acylation and, second, in N-alkylation of the nitrogen atom of the indole ring. Since both electron-donor (CH_3) and electron-acceptor (CN) substituents have an identical effect on the reactivity of 3-indolylacetonitrile in carbomethoxylation, the effect of a substituent in the 2 position is explained by a steric factor.

2-Carbomethoxy-3-indolylacetonitrile behaves somewhat differently — the 2-carbomethoxy group hinders C-acylation in the side chain but does not lead to N-alkylation. The absence of N-alkylation cannot be explained by a decrease in the nucleophilicity of the nitrogen atom of the indole ring due to the —I and —M effects of the carbomethoxy group, since the electron-acceptor cyano group does not hinder N-alkylation. On the basis of the literature data [9] we assume that the absence of N-alkylation in the case of 2-carbomethoxy-3-indolylacetonitrile is explained by the ability of the substituent and the nucleophilic reaction center to form an N-chelate with the cation.

During an analysis of the PMR spectra of the 2-substituted 3-indolylcyanoacetic esters obtained we noted an anomalously high value of the chemical shift of the signal of the α-H proton for 2-tert-butyl-3-indolylcyanoacetic ester. We assumed that the chemical shift of this proton is anomalously high because of the van der Waals interaction of its electron shells and the adjacent bulky substituent, viz., the tert-butyl group, the possibility of which was noted in [10]. For this we also recorded the PMR spectrum of the specially obtained dimethyl N-methyl-2-tert-butyl-3-indolylmalonate (XIV). The signal of the α-H proton in the PMR spectrum of this compound was found to be located at weaker field (by 0.7 ppm) relative to the chemical shift of the α-H proton of unsubstituted N-carbomethoxy-3-indolylmalonic ester.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The UV spectra of solutions of the compounds in ethanol were obtained with a Specord UV-vis spectrophotometer. The PMR spectra of solutions of the compounds in deutero-

chloroform were recorded with JNM-4H-100 and HFT-80 spectrometers with tetramethylsilane as the internal standard. The mass spectra were obtained with an MKh-1303 spectrometer with direct introduction of the samples into the ion source.

1-Acetyl-2-cyano-3-methylindole. A mixture of 11 g (0.07 mole) of 2-cyano-3-methylindole, 30 g (0.35 mole) of anhydrous sodium acetate, and 250 ml of acetic anhydride was refluxed for 5 h, after which the acetic anhydride was removed almost completely by distillation, and the residue was cooled and poured into water. The aqueous mixture was allowed to stand overnight, after which the reaction product was removed by filtration, washed on the filter with water, and air dried at room temperature to give 19.5 g (97%) of a product with mp 119-120°C (from methanol). IR spectrum: 1720 (C=O) and 2240 cm^{-1} (C≡N). UV spectrum, λ_{max} (log ε): 205 (4.42), 238 (4.33), and 315 nm (shoulder) (4.00). PMR spectrum: 246 (s, 3-CH_3), 2.80 (s, N-CO-CH_3), 7.30-7.60 (m, 4-, 5-, 6-H), and 8.25 ppm (t, 7-CH). Found: C 72.6; H 5.3; N 13.7%; M^+ 198. $C_{12}H_{10}N_2O$. Calculated: C 72.7; H 5.0; N 14.1%; M 198.

1-Acetyl-2-cyano-3-bromomethylindole. A mixture of 9 g (0.0045 mole) of 1-acetyl-2-cyano-3-methylindole, 8.5 g (0.048 mole) of N-bromosuccinimide (NBS), and a catalytic amount of benzoyl peroxide in 150 ml of dry carbon tetrachloride was refluxed for 5 h, after which the resulting succinimide was removed by filtration with a heated funnel, and the residue on the filter was washed with 300 ml of hot carbon tetrachloride. The solution was evaporated to a volume of 120 ml, and the concentrate was allowed to stand for crystallization. The precipitate was removed by filtration and stored in a vacuum desiccator over activated charcoal. This procedure gave 10 g (80%) of a product with mp 152-153,C (from ethanol). IR spectrum: 1700 (C=O) and 2220 cm^{-1} (C≡N). UV spectrum, λ_{max} (log ε): 208 (4.46), 230 (4.31), 290 (4.31), and 320 nm (shoulder) (4.03). PMR spectrum: 2.84 (s, $COCH_3$), 4.75 (s, CH_2), and 7.15-7.83 ppm (m, aromatic protons). Found: C 52.3; H 3.3; N 10.4%; M^+ 276 (50.5%), 278 (49.5%). $C_{12}H_9BrN_2O$. Calculated: C 51.8; H 3.2; N 10.0%; M 276.

2-Cyano-3-indolylacetonitrile (V). A mixture of 18 g (0.065 mole) of 1-acetyl-2-cyano-3-bromomethylindole in 250 ml of chloroform, 6 g (0.093 mole) of potassium cyanide, and 1 g of tetrabutylammonium bromide in 100 ml of water was stirred at 20°C for 8 h, after which the chloroform layer was separated, and the aqueous layer was extracted with chloroform (three 100-ml portions). The organic layer was washed with water (three 200-ml portions) and dried with $MgSO_4$. The chloroform was removed by distillation to a volume of 30 ml, and the concentrated solution was chromatographed with a column filled with Al_2O_3 (elution with chloroform). A substance precipitated from chloroform in the form of pale-yellow fine crystals, which were removed by filtration and dried to give 6 g (50%) of a product with mp 136-138°C (from ether). IR spectrum: 2230 (strong) (C≡N); 2265 (weak) (C≡N); 3340, 3410 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 207 (shoulder) (4.29), 225 (4.55), and 285 nm (4.29). PMR spectrum: 4.00 (s, CH_2) 7.20-7.80 (m, aromatic protons), and 8.80 ppm (s, NH). Found: C 72.6; H 4.0; N 22.9%; M^+ 181. $C_{11}H_7N_3$. Calculated: C 72.9; H 3.9; N 23.2%; M 181.

Methyl 1,2-Dimethyl-3-indolylcyanoacetate (VI). A solution of 3.4 g (0.02 mole) of 2-methyl-3-indolylacetonitrile in 30 ml of dimethyl carbonate was added dropwise at 50-60°C to a stirred suspension of 2.4 g (0.1 mole) of sodium hydride in 25 ml of diglyme, during which the temperature was simultaneously raised to 80°C. At the end of the addition, the mixture was allowed to cool slowly and was maintained at room temperature for 24 h. The excess sodium hydride was then decomposed by the addition of 10 ml of methanol, and the reaction product was isolated from its salt by the addition of 50 ml of 50% acetic acid. The precipitate was removed by filtration and washed with water, methanol, and ether to give 4.67 g (82%) of a product with mp 153-154°C (from methanol). IR spectrum: 1745 (C=O) and 2265 cm^{-1} (C≡N). UV spectrum, λ_{max} (log ε): 222 (4.56), 282 (3.92), and 292 nm (3.86). PMR spectrum: 2.43 (s, CH_3), 3.62 (s, $COOCH_3$), 3.73 (s, N-CH_3), 5.00 (s, α-CH), and 7.2-7.7 ppm (m, aromatic protons). Found: C 69.6; H 5.8; N 11.2%; M^+ 242. $C_{14}H_{14}N_2O_2$. Calculated: C 69.5; H 5.8; N 11.6%; M 242.

Ethyl 2-Methyl-3-indolylcyanoacetate (VII). A solution of 3.4 g (0.02 mole) of 2-methyl-3-indolylacetonitrile in 40 ml of diethyl carbonate was added dropwise at 50-60°C to a stirred suspension of 2.4 g (0.1 mole) of sodium hydride in 25 ml of diglyme, during which the temperature was raised simultaneously to 90°C. At the end of the addition, the mixture was heated at 100°C for 1 h, after which it was allowed to stand at room temperature for 24 h. Methanol (10 ml) and 50 ml of 50% acetic acid were added successively, and the mixture was poured into 100 ml of water. The aqueous mixture was extracted with ether (three 50-ml portions), and the extract was washed with water and sodium bicarbonate and dried with $MgSO_4$.

The ether was removed completely by distillation, 5 ml of chloroform was added to the residue, and the mixture was chromatographed with a column filled with Al_2O_3 (elution with chloroform). The chloroform was removed by distillation, the residue was dissolved in ether, and petroleum ether was added to the solution until crystllization commenced. The precipitate was removed by filtration to give 2.9 g (60%) of a product with mp 110-112°C. IR spectrum: 1730 (C=O), 2260 (C≡N), and 3380 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 220 (4.43), 270 (3.74), 280 (3.74), and 288 nm(3.66). PMR spectrum: 1.30 (t, CH_2CH_3), 2.40 (s, 2-CH_3), 4.30 (q, $-OCH_2CH_3$), 4.95 (s, α-CH), 7.2-7.7 (m, aromatic protons), and 9.30 ppm (s, NH). Found: C 69.9; H 5.9; N 11.4%; M^+ 242. $C_{14}H_{14}N_2O_2$. Calculated: C 69.5; H 5.8; N 11.6%; M 242.

Methyl 1-Methyl-2-phenyl-3-indolylcyanoacetate (VIII). This compound was obtained from 2.4 g (0.1 mole) of sodium hydride in 25 ml of diglyme and 4.2 g (0.018 mole) of 2-phenyl-3-indolylacetonitrile in 30 ml of dimethyl carbonate, as in the preparation of VI. Workup gave 3 g (59%) of a product with mp 164-165°C (from methanol). IR spectrum: 1750, 1760 (C=O); 2260 cm^{-1} (C≡N). UV spectrum, λ_{max} (log ε): 212 (shoulder) (4.85), 220 (4.85), 235 (shoulder) (4.68), and 293 nm (4.53). PMR spectrum: 3.50 (s, N–CH_3), 3.7 (s, $COOCH_3$), 4.8 (s, α-CH), and 7.2-7.7 ppm (aromatic protons). Found: C 75.0; H 5.4; N 9.6%; M^+ 304. $C_{19}H_{16}N_2O_2$. Calculated: C 75.0; H 5.3; N 9.2%; M 304.

Methyl 1-Methyl-2-tert-butyl-3-indolylcyanoacetate (IX). A solution of 4 g (0.019 mole) of 2-tert-butyl-3-indolylacetonitrile in 30 ml of dimethyl carbonate was added dropwise at 50-60°C to a stirred suspension of 2.4 g (0.1 mole) of sodium hydride in 25 ml of diglyme, during which the temperature was raised simultaneously to 80°C. At the end of the addition, the mixture was heated at 80°C for 1 h and allowed to stand for 24 h. The excess sodium hydride was decomposed by the addition of 10 ml of methanol, and the reaction product was liberated from its Na salt by the addition of 50 ml of 50% acetic acid. The mixture was poured into 100 ml of water, and the aqueous mixture was extracted with ether (three 50-ml portions). The extract was washed with water and sodium bicarbonate and dried with $MgSO_4$. The ether was removed by distillation to a volume of 20 ml, and petroleum ether was added to the concentrate until crystallization commenced. The precipitate was removed by filtration and air dried to give 2.5 g (47%) of a product with mp 125-126°C (from methanol). IR spectrum: 1755 (C=O) and 2260 cm^{-1} (C≡N). UV spectrum, λ_{max} (log ε): 210 (shoulder) (4.01), 223 (4.50), 285 (3.87), and 290 nm (3.75). PMR spectrum: 1.60 [s, $C(CH_3)_3$], 3.7 (s, $COOCH_3$), 3.80 (s, N–CH_3), 5.80 (s, α-CH), and 7.2-7.7 ppm (m, aromatic protons). Found: C 72.4; H 7.3; N 9.8%; M^+ 284. $C_{17}H_{20}N_2O_2$. Calculated: C 71.9; H 7.1; N 9.9%; M 284.

Methyl 2-Carbomethoxy-3-indolylcyanoacetate (X). A solution of 4 g (0.02 mole) of 2-carbomethoxy-3-indolylacetonitrile in 25 ml of dimethyl carbonate was added dropwise at 60°C to a stirred suspension of 2.4 g (0.1 mole) of sodium hydride in 25 ml of diglyme, after which the mixture was heated at 100°C for 2 h and allowed to stand at room temperature for 24 h. The excess sodium hydride was decomposed with 10 ml of methanol, and the reaction product was liberated from its Na salt by the addition of 50 ml of 50% acetic acid. The mixture was poured into 150 ml of water, and the aqueous mixture was extracted with chloroform (three 100-ml portions). The extract was washed with water and sodium bicarbonate and dried with $MgSO_4$. The chloroform was removed by distillation to a volume of 20 ml, ether was added to the concentrate, and the mixture was allowed to stand for crystallization. The precipitate was removed by filtration and washed with ether to give 2.2 g (45%) of a product with mp 137-138°C. IR spectrum: 1705 (C=O), 1755 (C=O), 2260 (weak) (C≡N), and 3375 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 208 (4.33) and 295 nm (4.24). PMR spectrum: 3.82 (s, α-$COOCH_3$), 3.95 (s, 2-$COOCH_3$), 6.15 (s, CH), and 9.40 ppm (s, NH). Found: C 61.8; H 4.6; N 10.2%; M^+ 272. $C_{14}H_{12}N_2O_4$. Calculated: C 61.8; H 4.4; N 10.3%; M 272.

Methyl 1-Methyl-2-cyano-3-indolylcyanoacetate (XI). This compound was obtained from 0.6 g (0.025 mole) of sodium hydride in 10 ml of diglyme and 0.9 g (0.005 mole) of 2-cyano-3-indolylacetonitrile in 10 ml of dimethyl carbonate, as in the preparation of IX. Workup gave 0.3 g (25%) of a product with mp 165-167°C (from methanol). IR spectrum: 1750 (C=O), 2230 (strong) (2-C≡N), and 2265 cm^{-1} (weak) (α-C≡N). UV spectrum, λ_{max}(log ε): 210 (shoulder) (4.35), 230 (4.43), 255 (4.11), and 290 nm (4.15). PMR spectrum: 3.84 (s, $COOCH_3$), 3.94 (s, N–CH_3), 5.12 (s, α-CH), and 7.2-7.8 ppm (m, aromatic protons). Found: C 66.0; H 4.5; N 16.4%; M^+ 253. $C_{14}H_{11}N_3O_2$. Calculated: C 66.4; H 4.4; N 16.6%; M 253.

Methyl 2-Methyl-3-indolylacetate (XII). Dry hydrogen chloride was passed through a solution of 4.1 g (0.03 mole) of 2-methyl-3-indolylacetonitrile in 50 ml of methanol while cooling the flask with water in such a way that the temperature of the reaction mixture did not ex-

ceed 60-70°C. As soon as hydrogen chloride absorption was complete, the gas flow was discontinued, and the reaction mixture was maintained at 60°C for 2 h. The methanol was removed by vacuum distillation, 100 ml of water was added, and the mixture was extracted with ether (three 100-ml portions). The extract was washed with water and sodium bicarbonate and dried with $MgSO_4$. The ether was removed by distillation; and the residue was distilled *in vacuo* to give 3 g (50%) of a product with bp 220-230°C (5 mm) and mp 66-68°C (from aqueous methanol). IR spectrum: 1735 (C=O) and 3390 cm^{-1} (NH). UV spectrum, λ_{max}(log ε): 203 (shoulder) (4.28), 222 (4.58), 280 (3.97), and 288 nm (3.39). PMR spectrum: 2.39 (s, 2-CH_3), 3.65 (s, $COOCH_3$), 3.68 (s, CH_2), and 7.60 ppm (s, NH). Found: C 70.9; H 6.6; N 6.9%; M^+ 203. $C_{12}H_{13}NO_2$. Calculated: C 70.9; H 6.4; N 6.9%; M 203.

Methyl 2-Methyl-3-indolylformylacetate (XIII). A solution of 2 g (0.01 mole) of methyl 2-methyl-3-indolylacetate in 20 ml of methyl formate was added at 35°C to a suspension of 1.2 g (0.05 mole) of sodium hydride in 25 ml of absolute ether, after which the mixture was allowed to stand at room temperature for 24 h. The excess sodium hydride was decomposed with 5 ml of methanol, and the reaction product was liberated from the salt by the addition of 25 ml of 50% acetic acid. The mixture was poured into 100 ml of water, and the aqueous mixture was extracted with ether. The extract was washed with water and sodium bicarbonate and dried with $MgSO_4$. The ether was removed by distillation to a volume of 5 ml, and the precipitated crystals were removed by filtration to give 1.4 g (60%) of a product with mp 154-155°C (from aqueous methanol). IR spectrum: 1620, 1650, 1685 (C=C–C=O); 3200 (broad) (OH); 3385 cm^{-1} (NH). UV spectrum, λ_{max}(log ε): 203 (shoulder) (4.29), 225 (4.59), 280 (4.07), and 287 nm (4.01). PMR spectrum: 2.40 (s, 2-CH_3), 3.76 (s, $COOCH_3$), 7.20 (d, =CH–OH), 8.10 (s, NH), 7.00-7.60 (m, aromatic protons), and 12.05 ppm (d, =CH–OH, J = 12.7 Hz). Found: C 68.0; H 6.0; N 6.0%; M^+ 231. $C_{13}H_{13}NO_3$. Calculated: C 67.5; H 5.6; N 6.0%; M 231.

2-tert-Butyl-3-indolylacetic Acid. A mixture of 5 g (0.025 mole) of 2-tert-butyl-3-indolylacetonitrile, 5 g (0.125 mole) of NaOH, and 35 ml of ethylene glycol was refluxed for 4 h, after which it was cooled and poured into 200 ml of water. The aqueous mixture was extracted with ether, acidified with dilute hydrochloric acid, and extracted with ether. The ether extracts were washed with water and dried with $MgSO_4$, and the ether was removed by distillation to a volume of 15 ml. The precipitated crystals were removed by filtration and air dried to give 4.5 g (78%) of a product with mp 140-141°C. IR spectrum: 1720 (C=O), 2500-2800 (OH), and 3400 cm^{-1} (NH). UV spectrum, λ_{max}(log ε): 205 (shoulder) (4.46), 227 (4.66), 282 (3.99), and 290 nm (3.94). PMR spectrum: 1.36 [s, $C(CH_3)_3$], 3.88 (s, CH_2), 7.90 (s, NH), and 10.80 ppm (s, OH). Found: C 73.1; H 7.8; N 6.1%; M^+ 231. $C_{14}H_{17}NO_2$. Calculated: C 72.7; H 7.4; N 6.1%; M 231.

Methyl 2-tert-Butyl-3-indolylacetate. A 3.7-g (0.016 mole) sample of 2-tert-butyl-3-indolylacetic acid was treated with an ether solution of diazomethane obtained from 10 g of nitrosomethylurea. After 2 h, the ether was removed by distillation, and the residue was crystallized from aqueous methanol to give 3.5 g (90%) of a product with mp 74-75°C (from ether–petroleum ether). IR spectrum: 1740 (C=O) and 3400 cm^{-1} (NH). UV spectrum, λ_{max}(log ε): 207 (shoulder) (4.26), 222 (4.54), 282 (3.91), and 290 nm (3.84). PMR spectrum: 1.38 [s, $C(CH_3)_3$], 3.35 (s, $COOCH_3$), 3.86 (s, CH_2), 7.05-7.45 (m, aromatic protons), and 8.08 ppm (s, NH). Found: C 73.5; H 8.0; N 5.6%; M^+ 245. $C_{15}H_{19}NO_2$. Calculated: C 73.5; H 7.8; N 5.7%; M 245.

Dimethyl 1-Methyl-2-tert-butyl-3-indolylmalonate (XIV). This compound was obtained from 2.45 g (0.01 mole) of methyl 2-tert-butyl-3-indolylacetate, 1.2 g (0.05 mole) of sodium hydride, and 20 ml of dimethyl carbonate in 15 ml of diglyme at 100°C, as in the preparation of IX. Workup gave 1.3 g (40%) of a product with mp 133-134°C (from methanol). IR spectrum: 1740 and 1760 cm^{-1} (C=O). UV spectrum, λ_{max}(log ε): 207 (shoulder) (4.34), 223 (4.56), 278 (4.00), and 295 nm (4.00). PMR spectrum: 1.58 [s, $C(CH_3)_3$], 3.70 (s, $COOCH_3$), 3.80 (s, N–CH_3), and 5.60 (s, α-CH). Found: C 6.81; H 7.6; N 4.2%; M^+ 317. $C_{18}H_{23}NO_4$. Calculated: C 68.1; H 7.3; N 4.4%; M 317.

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SYNTHESIS AND SOME REACTIONS OF 3-CYANOPYRIDINE-2-THIONES

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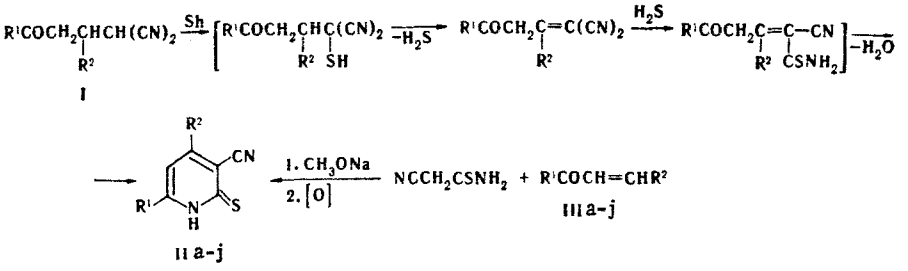
New methods for the synthesis of 3-cyanopyridine-2-thiones by the reaction of δ-keto nitroles with sulfur and by condensation of chalcones or benzylideneacetone with cyanothioacetamide are given. The compounds obtained were used in various reactions for the preparation of alkylated products, disulfides, and condensed heterocycles, viz., thieno[2,3-b]pyridines and pyrido[2',3':2,3]thieno[4,5-d]-pyrimidines.

3-Cyanopyridine-2-thiones are of interest as physiologically active substances [1, 2], as well as intermediates in the synthesis of new condensed heterocyclic systems [3] that are difficult to obtain by other methods. Up until now, the principal methods for their preparation have been the reaction of 2-chloro-3-cyanopyridines with alkali metal sulfides or thiourea [4, 5] and the condensation of β-dicarbonyl compounds with cyanothioacetamide [6].

We have developed two new methods for the preparation of 3-cyanopyridine-2-thione derivatives (II). The first method consists in the thiolation of δ-keto nitriles I, which are readily formed in the reaction of chalcones with malononitrile. In contrast to the data in [7], the use of organic bases such as morpholine gives better results in the synthesis of nitriles I. In the second method 3-cyanopyridine-2-thiones (II) are formed by the reaction of chalcones IIIa-c,g-i or benzylideneacetone (IIIj) with cyanothioacetamide in the presence of sodium methoxide. The reactions under consideration supplement one another satisfactorily and can be recommended for preparative purposes.



I, II, IIIa $R^1=R^2=C_6H_5$; b $R^1=C_6H_5$, $R^2=p$-ClC_6H_4; c $R^1=C_6H_5$, $R^2=p$-$CH_3OC_6H_4$; I, IId $R^1=p$-$CH_3OC_6H_4$, $R^2=C_6H_5$; e $R^1=p$-$CH_3C_6H_4$, $R^2=C_6H_5$; f $R^1=p$-FC_6H_4, $R^2=C_6H_5$; II, III g $R^1=C_6H_5$, $R^2=p$-$NO_2C_6H_4$; h $R^1=C_6H_5$, $R^2=p$-$(CH_3)_2NC_6H_4$; i $R^1=C_6H_5$, $R^2=o$-$F_2CHOC_6H_4$; j $R^1=CH_3$, $R^2=C_6H_5$

To confirm the structure of the isolated pyridine-2-thiones II we obtained 3-cyano-4,6-

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