AZAINDOLE DERIVATIVES.

60.* NUCLEOPHILIC SUBSTITUTION REACTIONS IN 6-CHLORO-5-AZAINDOLINES

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Reactions involving nucleophilic substitution of the halogen atoms in 1-benzyl-6-chloro-7-cyano-5-azaindoline by alkoxy groups and residues of various amines were investigated. The effect of electron-acceptor substituents on the saponification of the alkoxy groups to give hydroxy groups is demonstrated. The effect of the character of the fusion of the pyridine and pyrrole rings on the ease of nucleophilic substitution is examined.

The investigation of the reactions of 6-chloro-5-azaindolines with nucleophilic agents is of interest from the point of view of a study of the mutual effect of five- and six-membered nitrogen-containing heterocycles in the two-ring system.

In the case of 6-chloro-7-azaindolines we have previously demonstrated the substantial hindrance to nucleophilic substitution of the chlorine atom in the 6 position [2]. However, the 6-chloro-5-azaindolines examined in this research are characterized by the same overall geometry of the molecule and identical distances of the chlorine atoms from the pyrroline ring and, in addition, are distinguished by a significantly smaller degree of inductive interaction of the nitrogen heteroatoms.

The preparative interest in the reactions described above is due to the recently discovered central antiserotonin activity of some 6-amino-substituted 5-azaindolines [3].

We have established that nucleophilic substitution of the chlorine atom in 6-chloro-5-azaindoline (Ia) [4] by a methoxy group can be realized under considerably milder conditions (100°C for 6 h) as compared with the analogous reaction in 6-chloro-7-azaindolines (190°C for 6 h) [5]. The same reaction takes place even more readily in the case of 1-benzyl-6-chloro-7-cyano-5-azaindoline (II) [4], in which the chlorine atom is activated by the adjacent electron-acceptor cyano group and is relatively easily replaced by methoxy and allyloxy groups to give IIIa, b.

As in the case of other 5-azaindoline compounds [1], the oxidation of methoxy derivative IV with activated γ-manganese dioxide makes it possible to obtain the corresponding 5-azaindole product (V).

In contrast to 6-methoxy-5-azaindoline (IV), for which saponification of the methoxy group to give 6-hydroxy-5-azaindoline, which exists primarily in the lactam form (VI), takes place under rather severe conditions, a similar process in the case of 1-benzyl-6-alkoxy-7-cyano-5-azaindolines (IIIa, b) takes place during an attempt to carry out the alcoholysis of the nitrile group by refluxing with a methanol solution of hydrogen chloride. 1-Benzyl-6-allyloxy-7-cyano-5-azaindoline (IIIb) is converted to 1-benzyl-6-hydroxy-7-cyano-5-azaindoline (VII) under the influence of hydrogen chloride in a mixture of dioxane and water even at room temperature.

Saponification of the nitrile group in IIIa to an amide group tc give 1-benzyl-6-methoxy-7-carboxamido-5-azaindoline (VIII) can be realized in low yield only in the case of prolonged refluxing with a solution of sodium hydroxide. When IIIa is treated with sodium in liquid ammonia, one observes the unusual reduction of the 5-azaindoline ring at

*See [1] for Communication 59.

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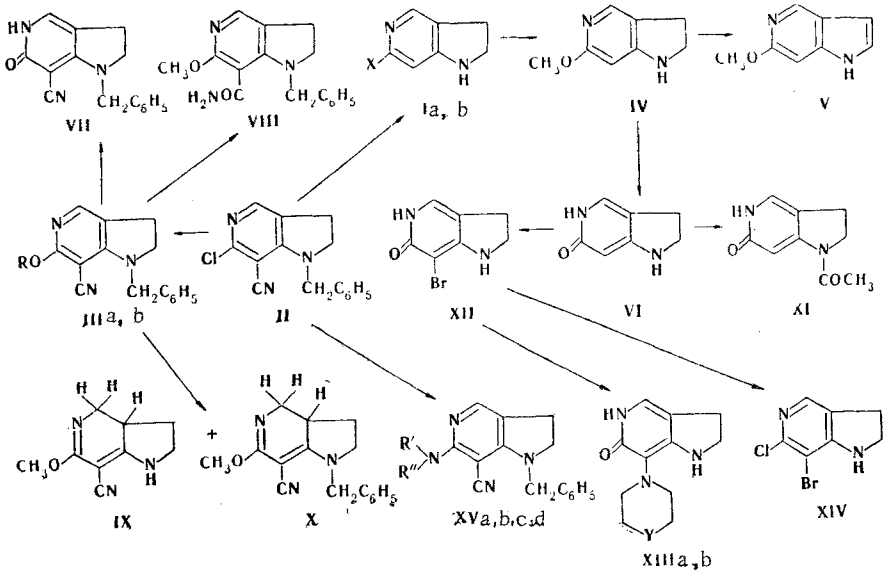
the double bond in the 3a and 4 positions, which is accompanied by partial N-debenzylation to give 3a,4-dihydro-6-methoxy-7-cyano-5-azaindoline (IX) and its N-benzyl derivative (X). The position of the multiple bonds in dihydro product IX was established unambiguously by PMR and IR spectroscopy.

When 6-hydroxy-5-azaindoline (VI) is refluxed with acetic anhydride, it readily forms an N-acetyl derivative at the pyrroline nitrogen atom (XI), and it is converted smoothly to 6-hydroxy-7-bromo-5-azaindoline (XII) by the action of bromine in concentrated hydrobromic acid. Nucleophilic substitution of the bromine atom in XII by residues of various amines can be realized only under very severe conditions (at 190-200°C for 11-15 h). The reactions are accompanied by pronounced resinification (aniline, benzylamine, and diethylamine), and the corresponding 6-hydroxy-7-amino-5-azaindolines (XIIIa, b) can be obtained in good yields only in the case of cyclic amines (piperidine and morpholine). The replacement of the hydroxy group of XII by chlorine by means of phosphorus oxychloride takes place with a great deal of difficulty and ambiguously. 6-Chloro-7-bromo-5-azaindoline (XIV) can be isolated in less than 10% yield.



I a X=Cl, b X=Br; III a R=CH_3, b R=$CH_2CH{=}CH_2$; XIII a Y=CH; b Y=O; XV a R′=R″=H; b R′=H, R″=CH_2CH_2OH; c R′=CH_3, R″=$CH_2CH_2C_6H_3(OCH_3)_2$; d R′=R″=CH_3

Nucleophilic substitution of the chlorine atom in the 6 position of the 5-azaindoline system by bromine by refluxing II with concentrated hydrobromic acid was accompanied by N-debenzylation and decyanation and led to 6-bromo-5-azaindoline (Ib).

As in the case of replacement of chlorine by an alkoxy group, but under relatively milder conditions than in the case of 6-chloro-7-cyano-5-azaindoline (II), the chlorine atom in 1-benzyl-6-chloro-7-cyano-5-azaindoline (II) is replaced by residues of various amines. The best results were obtained when the reaction was carried out in dimethylformamide (DMF) in an open system. We were able to accomplish similar reactions with amines and alcoholates for 6-chloro-7-azaindoline compounds only in a bomb under considerably more severe conditions [6].

Thus our research showed that the transition from 6-chloro-7-azaindoline compounds to the corresponding 6-chloro-5-azaindoline derivatives, which entails an increase in the distance between the nitrogen atoms in the two-ring azaindoline system and thereby weakening of their mutual influence with respect to the inductive effect, actually leads to facilitation of nucleophilic substitution processes. The additional introduction of a 7-cyano group promotes the indicated nucleophilic reactions to an even greater extent.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a Perkin-Elmer 457 spectrometer. The UV spectra of solutions of the compounds in ethanol were recorded with a Perkin-Elmer 402 spectrophotometer. The PMR spectra were recorded

with a JNM-4H-100 spectrometer with tetramethylsilane as the internal standard. The mass spectra were recorded with an MAT-112 spectrometer (direct introduction of the samples) at 70 eV.* The synthesis of 1-benzyl-6-methoxy-7-cyano-5-azaindoline (IIIa) was described in [1]. The compounds obtained were quite soluble in DMF and alcohols but only slightly soluble in water and hexane.

6-Methoxy-5-azaindoline (IV). A mixture of dry sodium methoxide, [obtained from 2 g (87 mmole) of sodium], 1 g (6.5 mmole) of chloroazaindoline Ia, and 50 ml of anhydrous DMF was stirred at 100° for 6 h, after which it was evaporated *in vacuo*, and 50 ml of water and 50 ml of chloroform were added. The chloroform extract was dried with magnesium sulfate and evaporated, and the residue was crystallized from cyclohexane to give 0.45 g (46.3%) of light-pink crystals of IV with mp 105-106°C. UV spectrum, λ_{max} (log ε): 211 (4.4), 249 (3.8), and 285 nm (3.5). Found: C 64.0; H 6.7; N 18.8%; M^+ 150. $C_8H_{10}N_2O$. Calculated: C 64.0; H 6.7; N 18.7%; M 150.

6-Methoxy-5-azaindole (V). A 10-g sample of activated γ-manganese dioxide was added to a solution of 1 g (6.7 mmole) of IV in 200 ml of benzene, and the mixture was stirred until the starting IV vanished according to thin-layer chromatography (TLC) (on Silufol UV-254 in methanol, detection by UV). The manganese dioxide was removed by filtration and washed with 100 ml of benzene. The benzene solution was evaporated *in vacuo*, and the residue was crystallized from benzene with added activated charcoal to give 0.4 g (40.7%) of colorless crystals of V with mp 127.5-128.5°C. The product was quite soluble in chloroform, acetone, and alcohols but less soluble in benzene. UV spectrum, λ_{max} (log ε): 228 (4.6), 256 (3.5), and 294 nm (3.5). Found: C 64.5; H 5.3; N 19.0%; M^+ 148. $C_8H_8N_2O$. Calculated: C 64.8; H 5.4; N 18.9%; M 148.

1-Benzyl-6-allyloxy-7-cyano-5-azaindoline (IIIb). A solution of 6.51 g (24 mmole) of chloroazaindoline II in 53 ml of anhydrous DMF was added to a freshly prepared solution of sodium allylate [from 1.38 g (60 mmole) of sodium and 60 ml of allyl alcohol], and the mixture was stirred at 105°C for 5 h. It was then evaporated *in vacuo*, 100 ml of water and 100 ml of chloroform were added, and the aqueous layer was separated and extracted with chloroform. The chloroform extract was dried with magnesium sulfate and evaporated. The residue was crystallized from heptane to give 6.50 g (93.1%) of colorless crystals of IIIb with mp 110-111°C. The product was quite soluble in ether and ethyl acetate. IR spectrum: 2210 cm^{-1} (C≡N). PMR spectrum (CD_3OD): 3.00 (2H, t, 3-CH_2), 3.70 (2H, t, 2-CH_2), 4.85 (2H, m, CH_2O); 5.20, 5.50 (2H, m, CH_2=); 5.90, 6.30 (1H, m, CH=); 4.96 (2H, s, $CH_2C_6H_5$); 7.40 (5H, C_6H_5); 7.6 ppm (1H, m, 4-CH). Found: C 74.5; H 5.5; N 14.6%; M^+ 291. $C_{18}H_{17}N_3O$. Calculated: C 74.2; H 5.9; N 14.4%; M 291.

1-Benzyl-6-hydroxy-7-cyano-5-azaindoline (VII). Hydrogen chloride was passed into a refluxing solution of 1 g (4 mmole) of methoxyazaindoline IIIa in 100 ml of methanol for 15 h, after which the methanol was removed by vacuum distillation. Water (20 ml) and 100 ml of chloroform were added to the residue, and the mixture was neutralized with potassium carbonate. The aqueous layer was separated and extracted with chloroform (two 50-ml portions). The chloroform extracts were dried with magnesium sulfate and evaporated *in vacuo* to give 0.55 g (58%) of VII. IR spectrum: 1670 (C=O) and 2220 cm^{-1} (C≡N). No melting-point depression was observed for a mixture of this product with a genuine sample, and the IR spectra of the two substances were identical.

1-Benzyl-6-methoxy-7-carboxamido-5-azaindoline (VIII). A 3-g (11 mmole) sample of azaindoline IIIa was refluxed for 119 h with 50 ml of a 7% aqueous solution of sodium hydroxide, after which it was extracted with chloroform (two 100-ml portions). The chloroform extracts were dried with magnesium sulfate and evaporated *in vacuo*, and the residue was triturated with acetone to give 0.71 g (22%) of VIII as colorless crystals with mp 180-182°C. The product was quite soluble in hot benzene. IR spectrum: 1620 (C=N); 1680 (C=O); 3200, 3300, 3400 cm^{-1} (NH_2). PMR spectrum (d_6-DMSO): 2.93 (2H, t, 3-CH_2), 3.58 (2H, t, 2-CH_2), 3.90 (3H, s, CH_3O), 4.57 (2H, s, $CH_2C_6H_5$), 7.26 (5H, s, C_6H_5), and 7.56 ppm (1H, t, 4-CH). Found: C 67.8; H 5.7; N 14.6%; M^+ 283. $C_{16}H_{17}N_3O_2$. Calculated: C 67.8; H 6.1; N 14.8%; M 283.

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6-Methoxy-7-cyano-3a,4-dihydro-5-azaindoline (IX). A 150-ml sample of liquid ammonia and 0.94 g (40 mmole) of sodium were added to 0.5 g (2 mmole) of azaindoline IIIa, and the mixture was stirred for 3 h. The ammonia was evaporated, and the residue was decomposed with methanol. Chloroform (100 ml) was added, and the precipitate was removed by filtration and extracted with 100 ml of acetone. The acetone extract was evaporated to give 0.13 g of a mixture of products, to which 50 ml of water and 50 ml of ethyl acetate were added. The undissolved substance was removed by filtration to give 0.04 g (8%) of dihydroazaindoline IX as colorless crystals with mp 220-222°C. The substance was soluble in hot acetone but only slightly soluble in ethyl acetate. IR spectrum: 2210 cm^{-1} (C≡N). PMR spectrum (in $CDCl_3$): 1.50 (2H, m, 3-CH_2), 2.20 (2H, m, 2-CH_2), 2.91 (2H, m, 4-CH_2), 3.55 (4H, m, CH_3O + 3a-CH), and 6.6 ppm (1H, s, NH). Found: C 60.8; H 6.2; N 23.8%; M^+ 177. $C_9H_{11}N_3O$. Calculated: C 61.0; H 6.3; N 23.7%; M 177. The ethyl acetate extract was evaporated to dryness to give 0.03 g of a mixture of IX and X (according to the mass-spectrometric data). Evaporation of the chloroform solution obtained in the initial treatment of the reaction mixture gave 0.13 g of a mixture of substances, which, according to the results of TLC [on Silufol UV-254, elution with ethyl acetate–benzene (1:2), detection with iodine vapors], contained, in addition to IX and X, four other unidentified reaction products. Compounds IX and X were not isolated from this mixture.

1-Acetyl-6-hydroxy-5-azaindoline (XI). A 0.5-g (4 mmole) sample of azaindoline VI was refluxed with 50 ml of acetic anhydride, the mixture was evaporated *in vacuo*, and the residue was recrystallized from ethanol to give 0.65 g (91.2%) of XI as colorless crystals with mp 323-325°C. IR spectrum: 1650 (6-CO) and 1680 cm^{-1} (1-$COCH_3$). Found: C 60.5; H 5.7; N 15.7%; M^+ 178. $C_9H_{10}N_2O_2$. Calculated: C 60.7; H 5.7; N 15.7%; M 178.

6-Hydroxy-7-bromo-5-azaindoline (XII). A 3.1-g (19 mmole) sample of bromine was added to a solution of 2.5 g (18 mmole) of VI in 70 ml of concentrated hydrobromic acid, and the mixture was stirred for 4 h. The precipitate was removed by filtration and washed with acetone (three 50-ml portions) to give 3.92 g of the hydrobromide of XII, treatment of which with 50% aqueous potassium carbonate gave 2.80 g (73.8%) of XII as colorless crystals with mp 221-222°C (dec., from methanol). The substance was only slightly soluble in methanol and DMF. UV spectrum, λ_{max} (log ε): 226 (5.1) and 280 nm (4.8). IR spectrum: 1660 cm^{-1} (C=O). PMR spectrum (in CD_3OD): 2.95 (2H, t, 3-CH_2), 3.65 (2H, t, 2-CH_2), and 6.91 (1H, m, 4-CH). Found: C 38.9; H 3.4; N 12.9%; M^+ 214. $C_7H_7BrN_2O$. Calculated: C 39.1; H 3.3; N 13.0%; M 215.

6-Hydroxy-7-piperidino-5-azaindoline (XIIIa). A mixture of 0.5 g (2 mmole) of XII and 25 ml (0.25 mole) of piperidine was heated in a 120-ml bomb at 190-200°C for 11 h, after which it was treated with water, made alkaline with potassium carbonate, and extracted with chloroform. The chloroform extract was dried with magnesium sulfate and evaporated *in vacuo* and the residual amine was removed by distillation with xylene. The product was recrystallized from isopropyl alcohol to give 0.25 g (57%) of XIIIa as colorless crystals with mp 220-222°C. The product was only slightly soluble in chloroform, ethyl acetate, and acetone and insoluble in ether and water. Found: C 65.8; H 8.0; N 19.1%. $C_{12}H_{17}N_3O$. Calculated: C 65.7; H 7.8; N 19.2%. The hydrochloride had mp 272-274°C (dec.). Found: C 56.0; H 7.2; Cl 13.8; N 16.0%. $C_{12}H_{17}N_3O \cdot HCl$. Calculated: C 56.4; H 7.1; Cl 13.8; N 16.4%.

6-Hydroxy-7-morpholino-5-azaindoline (XIIIb). A mixture of 0.5 g (2 mmole) of XII and 15 ml (0.19 mole) of morpholine was heated in a 55-ml bomb at 190-200°C for 15 h, after which it was treated with water and excess potassium carbonate and extracted with chloroform. The chloroform extract was dried with magnesium sulfate and evaporated *in vacuo*, and the excess amine was removed by distillation with xylene. The substance was recrystallized from ethanol to give 0.4 g (90.5%) of XIIIb as colorless crystals with mp 293-295°C. UV spectrum, λ_{max} (log ε): 226 (4.7) and 280 nm (4.1). IR spectrum: 3100, 3240, 3320, and 3420 cm^{-1} (N–H). PMR spectrum (in CF_3COOD): 2.97 (2H, t, 3-CH_2), 3.70 (2H, t, 2-CH_2), 3.79, 3.95 ppm (8H, m, OCH_2CH_2N). Found: C 59.7; H 6.8; N 19.2%; M^+ 221. $C_{11}H_{15}N_3O_2$. Calculated: C 59.7; H 6.8; N 19.0%; M 221.

6-Chloro-7-bromo-5-azaindoline (XIV). A 3.92-g (13 mmole) sample of the hydrobromide of XII was refluxed for 22 h with 70 ml of phosphorus oxychloride, after which the mixture was evaporated *in vacuo*, 20 ml of water and 100 ml of chloroform were added to the residue, and the mixture was neutralized with potassium carbonate. The aqueous layer was separated and extracted with chloroform (two 100-ml portions), and the chloroform extracts were dried

with magnesium sulfate and evaporated *in vacuo*, The residue was refluxed with 100 ml of ethyl acetate, and the hot ethyl acetate solution was separated and evaporated to give 0.26 g (8.6%) of XIV as colorless crystals with mp 175-177°C (from ethanol). The product was only slightly soluble in chloroform, ethyl acetate, and ether. UV spectrum, λ_{max} (log ε): 212 (4.4) and 267 nm (4.3). IR spectrum: 3100 cm^{-1} (N–H). PMR spectrum (in CD_3OD): 3.10 (2H, t, 3-CH_2), 3.70 (2H, t, 2-CH_2), and 7.76 ppm (1H, s, 4-CH). Found: C 36.2; H 2.9; N 12.1%; M^+ 232. $C_7H_6BrClN_2$. Calculated: C 36.0; H 2.7; N 12.0%; M 233.5.

6-Bromo-5-azaindoline (Ib). A 315-ml sample of concentrated HBr was added to 2.63 g (9.8 mmole) of II, and the mixture was refluxed for 40 h with simultaneous removal of the hydrobromic acid by distillation. The reaction mixture was evaporated *in vacuo*, and the residue was mixed with 20 ml of water and 100 ml of chloroform. The mixture was made alkaline with potassium carbonate, the chloroform layer was separated, and the aqueous layer was extracted with chloroform (two 100-ml portions). The combined chloroform extracts were dried with magnesium sulfate and evaporated *in vacuo*. The residue was recrystallized from benzene to give 0.63 g (32.6%) of crystals of Ib with mp 130-132°C. UV spectrum, λ_{max} (log ε): 212 (4.3) and 261 nm (4.3). IR spectrum: 3110 cm^{-1} (N–H). PMR spectrum (in $CDCl_3$): 2.90 (2H, t, 3-CH_2), 3.60 (2H, t, 2-CH_2), 6.55 (1H, s, 7-CH), and 7.82 ppm (1H, s, 4-CH). Found: C 42.5; H 3.6; N 14.3%; M^+ 199. $C_7H_7BrN_2$. Calculated: C 42.2; H 3.6; N 14.1%; M 199.

1-Benzyl-6-amino-7-cyano-5-azaindoline (XVa). A mixture of 3.16 g (11.7 mmole) of II, 5.72 g (31 mmole) of potassium phthalimide, and 3.02 g (20.5 mmole) of phthalimide was heated at 240-265°C (bath temperature) for 1.5 h. The products were refluxed for 2 h with a 5% aqueous solution of potassium hydroxide, after which the mixture was cooled and extracted with chloroform. The chloroform extract was dried with magnesium sulfate and evaporated *in vacuo* to give 1.83 g (62.3%) of XVa as light-yellow crystals with mp 212-213°C (from alcohol). The substance was quite soluble in chloroform, less soluble in alcohols and acetone, and only slightly soluble in water. IR spectrum: 2195 (C≡N); 1642, 3300, 3410, 3460 cm^{-1} (NH_2). Found: C 72.1; H 5.4; N 22.5%; M^+ 250. $C_{15}H_{14}N_4$. Calculated: C 72.0; H 5.6; N 22.4%; M 250.

1-Benzyl-6-(β-hydroxyethylamino)-7-cyano-5-azaindoline (XVb). A mixture of 5 g (18.6 mmole) of II and 52 g (0.85 mmole) of ethanolamine was heated at 180°C for 12 h, after which it was evaporated *in vacuo*, and the residue was treated with 50 ml of water, made alkaline with potassium carbonate, and extracted with chloroform (three 50-ml portions). The extract was washed with 50 ml of water, dried with magnesium sulfate, and evaporated to give 4.24 g (78%) of XVb as colorless crystals with mp 126-127°C (from benzene). The substance was quite soluble in benzene, chloroform, and acetone. Found: C 69.4; H 6.2; N 19.3%. $C_{17}H_{18}N_4O$. Calculated: C 69.4; H 6.2; N 19.0%. The hydrochloride, with mp 194-195°C, was a white crystalline substance that was soluble in alcohols and water but only slightly soluble in acetone. Found: C 61.7; H 5.7; Cl 10.8; N 17.1%. $C_{17}H_{18}N_4O \cdot HCl$. Calculated: C 61.7; H 5.8; Cl 10.7; N 17.0%.

1-Benzyl-6-(N-methylhomoveratrylamino)-7-cyano-5-azaindoline (XVc). A mixture of 0.62 g (2.3 mmole) of II, 4 g (20 mmole) of N-methylhomoveratrylamine, and 11.3 g of DMF was refluxed for 5 h, after which it was evaporated *in vacuo*, and the residue was treated with 50 ml of water, made alkaline with potassium carbonate, and extracted with benzene. The benzene was removed, and the residue was converted to the hydrochloride, which was triturated with ethyl acetate and recrystallized twice from isopropyl alcohol with added charcoal to give 0.3 g (28%) of the hydrochloride of XVc as colorless crystals with mp 199-200°C. Found: C 67.2; H 6.3; Cl 7.2; N 11.7%. $C_{26}H_{28}N_4O_2 \cdot HCl$. Calculated: C 67.2; H 6.3; Cl 7.6; N 12.0%. Pronounced resinification of the reaction mixture occurred when the reaction was carried out at 180°C (for 6 h) without DMF.

1-Benzyl-6-dimethylamino-7-cyano-5-azaindoline (XVd). Anhydrous dimethylamine was passed through a refluxing solution of 2.43 g (9 mmole) of II in 80 ml of DMF for 6.5 h, after which the mixture was evaporated *in vacuo*, and the residue was mixed with 50 ml of water and 100 ml of chloroform. The mixture was neutralized with potassium carbonate, and the organic layer was separated, washed with 50 ml of water, dried with magnesium sulfate, and evaporated *in vacuo* to give 2.5 g (100%) of XVd in the form of a light-yellow oil, which crystallized slowly to give a product with mp 89-90°C. The substance was only slightly soluble in benzene but was quite soluble in acetone and chloroform. Found: C 73.3; H 6.4; N 20.1%. $C_{17}H_{18}N_4$. Calculated: C 73.4; H 6.5; N 20.1%. The hydrochloride

had mp 162-163°C (from isopropyl alcohol). Found: Cl 11.1%. $C_{17}H_{18}N_4 \cdot HCl$. Calculated: Cl 11.3%.

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ACIDITIES OF 1-INDOLYLACETIC AND CARBAZOLYLACETIC ACIDS. INDUCTIVE CONSTANTS OF INDOLYL AND CARBAZOLYL GROUPS

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The pK_a values of 1-indolylacetic, 3-(9-ethyl)carbazolylacetic, and a number of 3,6-disubstituted 9-carbazolylacetic acids in aqueous ethanol solutions were determined by potentiometry. The inductive constants of the corresponding heterocyclic fragments were calculated from the values obtained. It is shown that annelation of the benzene ring with the pyrrole ring of indole gives rise to a decrease in the negative inductive effect of the heteroring. A linear relationship between the acidic properties of carbazoles and the corresponding 9-carbazolylacetic acids was established.

We have previously shown [1, 2] that the terminal sp^2-hybridized atom in the 9-alkenylcarbazole series is appreciably less shielded in the ^{13}C NMR spectra as compared with N-vinyl derivatives of pyrrole [3]. This fact indicates the smaller effect of p—π conjugation of the p electrons of the nitrogen atom of the carbazolyl ring with the π electrons of the C=C bond. However, the possibility that deshielding of the terminal vinyl atom on passing from 1-vinylpyrrole (chemical shift 95.89 ppm [4]) and 1-vinylindole (96.0 ppm [5]) to 9-vinylcarbazole (101.18 ppm [1]) may be determined by (in addition to steric reasons) an increase in the negative inductive effect of the heterorings in the same order is not excluded; whereas in ordinary enamines the effects of conjugation prevail over the negative inductive effects of the aminoalkyl or aminocycloalkyl groups [6], in the N-vinylamines under discussion, in addition to p—π conjugation, one observes the competitive and conjugation-weakening delocalization of the p electrons in the heterocyclic fragments, which may appreciably increase the role of inductive effects in the distribution of the electron densities of the C=C groups and their contribution to the reactivity. It is only natural that quantitative data on the σ_I constants of the indicated heterocycles not only are necessary for a solution of the problem noted above but are also of fundamental importance for an understanding of the chemistry of heterocycles of the pyrrole series.

In the present research to determine the inductive constants of 1-indolyl and carbazolyl groups we determined the pK_a values in aqueous ethanol of a number of acetic acids that contain a heterocyclic fragment, viz., 1-indolylacetic (I), 9-carbazolylacetic (IIa-e), and 3-(9-ethylcarbazolyl)acetic (III) acids.

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