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INDOLOPYRIDINES WITH A HETERO ATOM AT A POSITION OF FUSION. 6.* ELECTROPHILIC SUBSTITUTION IN INDOLO[2,1-a]ISOQUINOLINE

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Nitration, halogenation, azo coupling, aminomethylation, hydroxymethylation, and acylation reactions of indolo[2,1-a]isoquinoline in a neutral or weakly acid medium gave derivatives at the $C_{(11)}$ position (the pyrrole ring). Using nitrosation as an example, it was shown that electrophilic substitution at the benzene ring of the indole fragment can occur in a strongly acid medium.

Chemical reactions of indolo[2,1-a]isoquinoline (I) have been studied insufficiently: only its reduction to 5,6,11,11a-tetrahydro [2] and 5,6-dihydro derivatives [3] and also conversion to the disulfide at the $C_{(11)}$ position in the presence os sulfur [4] have been described. In the present paper, we consider electrophilic substitution reactions of this indole for the case of its nitrosation, nitration, halogenation, azo coupling, aminomethylation, hydroxymethylation, and acylation.

A comparison of the PMR spectra of polycycle I in $CDCl_3$ and CF_3COOH (we obtained its spectra in DMSO-d_6 [5]) indicated that electrophilic addition of a proton H^+ occurred at the free $C_{(11)}$ position of the π-excess pyrrole ring. Protons of the CH_2 group that formed during recording of the spectrum in the acid were manifested by a singlet peak in two proton units in the region of 5.1 ppm, which was accompanied by disappearance of the peak of proton 11-H at 7.38 ppm ($CDCl_3$). Formation of quaternary salt IA in an acid medium was indicated by shift of peaks of protons 5-H and 6-H of the pyridinium ring by approximately 1 ppm to a weaker field (in comparison with the starting base) and a decrease of approximately 0.6 Hz of the spin–spin coupling constant (SSCC). Thus, attack of the indoloisoquinoline by electrophilic agents should occur at the unsubstituted position of the pyrrole ring, but functionalization of polycycle I at the $C_{(11)}$ position should be carried out in neutral or weakly acid media. In acid media, preliminary protonation of this position is possible, which leads to a change of the orientation of electrophilic substitution. This was confirmed during nitrosation of compound I by sodium nitrite in concentrated hydrochloric acid, giving a high yield of 9-nitroisoindoloisoquinoline (IIa). Mononitrosation was confirmed by elemental analysis and the mass spectrum, in which there was a peak of molecular ion $M^{+\cdot}$ with m/z 246 of maximum intensity and also a peak of fragment $[M-NO]^{+\cdot}$ with m/z 216 (60%). The introduction of a nitroso group into the benzene ring of the indole fragment was indicated by the PMR spectrum, which contained a double peak of pyrrole proton 11-H (8.21 ppm, J ~ 1 Hz) and a peak of proton 1-H (9.32 ppm) with unchanged multiplet nature in comparison with the spectrum of the starting indole I. The appearance of a broadened doublet peak at 8.55 ppm (J = 7.0 Hz) with an integrated intensity of two proton units, a peak assigned to protons 7-H and 8-H, indicated the presence of a NO group in the $C_{(9)}$ position. Proton 10-H resonated at 8.33 ppm in the form of a broadened peak with a SSCC of 2.5 Hz (at the half-height). In addition, it should be noted that intermediately formed cation IA should orient the introduction of the nitroso group in the para position with respect to nitrogen, where the mobility of the hydrogen atom is greatest, as established for aromatic N,N-dialkylamines and 2-methylindoles [6]. The shift, in the PMR spectrum of nitroso derivative IIa, of the peaks of all 10 protons by 0.5-1.2 ppm to

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[*] For Communication 5 see [1].

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TABLE 1. Characteristics of Compounds II-VII

Compound	Empirical formula	M^+	Mp, °C	R_f (heptane–ether 1 : 1)	IR spectrum, ν, cm^{-1}	Yield, %
IIa	$C_{16}H_{10}N_2O$	246	204...206	0,58	—	77
IIb	$C_{16}H_{10}N_2O_2$	262	188...190	0,31	1546, 1370	67
IIIa	$C_{16}H_{10}BrN$	297	219...221	0,56 (3 : 1)	—	39
IIIb	$C_{16}H_9Br_2N$	377	188...190	0,4 (2 : 1)	—	52
IIIc	$C_{16}H_{10}IN$	343	123...125	0,35 (2 : 1)	—	46
IVa	$C_{22}H_{15}N_3$	321	102...104	0,33	—	94
IVb	$C_{22}H_{14}N_4O_2$	366	126...128	0,3	1520, 1330	92
V	$C_{21}H_{23}ClN_2$	338,5	223...225	—	—	80
VIa	$C_{17}H_{11}NO$	245	163...165	0,41	1660 sh, 1650 sh, 1645	93
Oxime VIa	$C_{17}H_{12}N_2O$	260	160...162	0,40	3400, 1642	52
VIb	$C_{18}H_{13}NO$	259	132...134	0,33	1660 sh, 1640 sh, 1635	38...68
VIc	$C_{23}H_{15}NO$	321	141...142	0,5	1645	42
VId	$C_{23}H_{14}ClNO$	355	178...180	0,53	1660 sh, 1650 sh, 1635	79
VIIa	$C_{17}H_{13}NO$	247	173...175	0,4	3300, 3180, 2945, 2870	58...89
VIIb	$C_{23}H_{17}NO$	323*	138...140	0,5	3480, 3300, 3180, 3070, 2940, 2870	59

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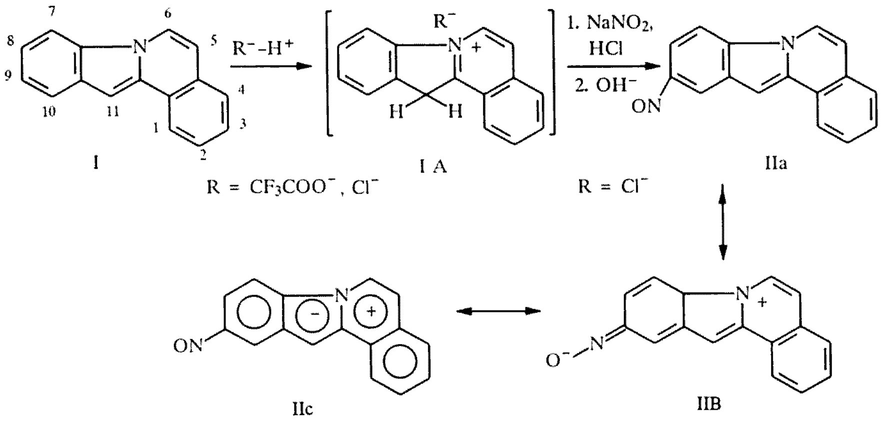
*In the mass spectrum of compound VIIb, the peak of molecular ion M^+ was absent. There were peaks of the following ions: $[M - RRCO]^{+\cdot}$ 219 (26%); 218 (18); $[PhCOH]^{+\cdot}$ 106 (53); $[PhCO]^{+\cdot}$, 105 (100).

weak fields in comparison with the peaks of the corresponding protons in the spectrum of starting compound I (see [5] and Table 2) and the deep (dark-green) color of compound IIa were probably due to the great contribution of polar forms IIB and IIC.



Nitration of indole I was carried out by nitric acid in acetic anhydride at −10°C. Under these conditions, we obtained in good yield 11-nitroindoloisoquinoline (IIb), the formation of which was indicated by disappearance of the proton peak of the pyrrole ring and retention of peaks of two complex systems ABCD in the PMR spectrum of this compound. The mass spectrum of compound IIb contained not only a peak of a molecular ion of medium intensity with m/z 262, but also high-

TABLE 2. Parameters of PMR Spectra of Compounds I-VII

Compound	Chemical shift, δ, ppm (multiplet nature, SSCC, J, Hz)					
	1-H	5-H	6-H	7-H	10-H	Other protons
I	8,15 (m)	6,68 (d)	8,05 (d, 7,5)	7,84 (m)	7,76 (m)	7,38 (s, 11-H); 7,55...7,28 (5H)
I*	8,4 (m)	7,85 (d)	9,05 (d, 6,9)	8,56 (m)	—	5,1 (s, CH_2); 7,7...8,3 (6H)
II*2	9,32 (m)	7,81 (d)	9,60 (d, 7,0)	8,55 (br.d, 7,0)	8,33 (br.m, $J_{1/2}$=2,5)	8,55 (br.m, 8-H); 7,7...8,47 (m, 4H); 8,21 (1H, d, J = 1,9 Hz, 11-H)
IIb	9,83 (m)	7,38 (d)	8,28 (d, 7,0)	8,59 (m)	—	7,4...7,88 (6H)
IIIa	9,25 (m)	6,75 (d)	8,03 (d, 7,5)	7,81 (m)	7,75 (m)	7,35...7,5 (4H); 7,55 (1H)
IVa*2	9,45 (m)	7,25 (d)	8,75 (d, 7,5)	8,23 (m)	—	7,1...8,0 (11H)
V	8,4 (m)	6,86 (d)	8,58 (d, 7,5)	8,13 (m)	7,71 (m)	7,0...7,6 (5H); 5,4 (N^+H); 3,92 (q, CH_2, 4H); 2,66 (s, CH_2); 1,28 (t, 6H)
VIa	9,35 (m)	7,16 (d)	8,32 (d, 7,6)	8,61 (m)	7,89 (m)	10,94 (s, CHO); 7,8...7,45 (5H)
oxime VIa	8,45 (m)	6,83 (d)	8,15 (d, 7,5)	8,45 (m)	7,8 (m)	9,23 (OH); 7,68...7,38 (5H); 7,25 (CH=N)
VIb	9,23 (m)	6,98 (d)	8,18 (d, 7,5)	8,06 (m)	7,81 (m)	2,88 (s, CH_3); 7,3...7,66 (6H)
VIc	8,57 (dd, 8,0)	6,97 (d)	8,17 (d, 7,5)	7,95 (m)	7,95 (m)	7,9...7,2 (10H)
VId*3	8,57 (ddd, 8,0; 1,8; 0,8)	7,25 (d)	8,75 (d, 7,3)	7,85 (m)	8,20 (m)	7,95 and 7,55 (4H, two ddd, 8,5; 2,1 , 1,7 Hz 2′,6′- and 3′,5′-H)
VIIa	8,42 (dd)	6,7 (d)	8,1 (d, 7,5)	7,53 (m)	7,8 (d, 8,0)	5,34 and 1,62 (s, and br.s, CH_2OH); 7,4...6,95 (5H)
VIIb	8,16 (m)	6,67 (d)	8,08 (d, 7,5)	7,9 (m)	7,9 (m)	10,0 and 1,6 ppm (s and br.s, CHOH)

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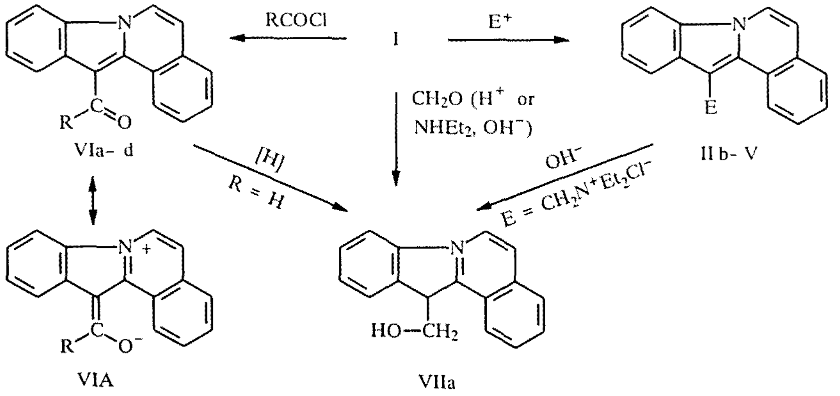
*In trifluoroacetic acid.

*2In DMSO-d_6.

*3In deuteroacetone.

intensity peaks of the $[M-NO]^{+\cdot}$ and $[M-NO_2]^{+\cdot}$ with m/z 232 and 216, respectively. A peak of maximum intensity was assigned to the fragment $[M-OH]^{+\cdot}$, which could be formed because of the closeness of protons 1-H and 10-H to the oxygen of the nitro group.



IIb E = NO_2; IIIa E = Br; IIIc E = I; IVa E = N=NPh, b E = N=$NC_6H_4NO_2$-*p*; V E = $CH_2NH(Et)_2Cl$;
VIa R = H, b R = CH_3, c R = Ph, dR = C_6H_4Cl-*p*

Halogenation of indoloisoquinoline I was carried out by the reaction of bromine water (to bromo derivatives IIIa and IIIb) and with an aqueous solution KI_3 (to monoiodo derivative IIIc). The structure of monobromo derivative IIIa was confirmed by the PMR spectrum, which was similar to the spectrum of 11-nitro derivative IIb (Table 2). The formation of dibromo derivative IIIb and II-iodo derivative IIIc was confirmed by elemental analysis and mass spectrometrically. The PMR spectra of these compounds could not be recorded in satisfactory form because of their poor solubility. Most probably, the second bromine atom in compound IIIb occupied the 9 position (similarly to bromination of 2-bromo-3-methylindole [6]).

The azo coupling reaction of indole I with diazonium salt obtained from aniline and p-nitroaniline occurred in a neutral medium at the 11 position with formation of azo dyes IVa and IVb in high yield.

In an attempt to aminoethylate indole I by the formaldehyde – secondary amine system in acetic acid, after neutralization of the reaction mixture, in all cases, instead of alkylaminomethyl derivatives, we obtained 11-hydroxymethylindoloisoquinoline (VIIa). The resulting aminomethylindoles are probably unstable and facilely hydrolyze during water – alkali treatment. For confirmation of this assumption, we carried out the Mannich reaction with diethylamine in a strongly acid medium (HCl) and obtained diethylaminomethylindoloisoquinoline hydrochloride (V). During alkalization of the solution of this salt, we actually observed abstraction of the diethylamino group and formation of alcohol VIIa. The latter was also back – synthesized by direct hydroxymethylation of indole I by formaldehyde in acetic acid and, moreover, by reduction of formyl derivative VIa by sodium borohydride. In the IR spectrum of alcohol VIIa, the CH_2OH group gave two bands of hydroxyl absorption at 3300 and 3180 cm^{-1}. The mass spectrum contained an intense peak of a molecular ion with m/z 247. The PMR spectrum of this compound contained two singlet peaks of CH_2OH group protons at 5.34 and 1.62 ppm.

Acylation of indoloisoquinoline I also occurred at the pyrrole ring similarly to acylation of indolo[1,2-a]pyridine [5]. As a result of formylation, acetylation, and aroylation, monoacyl derivatives VIa-d were obtained. Acetylation by acetic anhydride in acid was more preparative (70% yield) than by the Schotten – Baumann reaction (38% yield), which is probably due to the homogeneity of the system in the first case. The PMR spectra of acyl – substituted indoles VIa-d contained no peak of proton 11-H, and there was a shift of the peaks of protons 1-H and 10-H to weak fields in comparison with the starting indole I. In the IR spectra, the absorption band of stretching vibrations of the C═O group, which was in strong bonding with the indolizine fragment, was manifested not in the region of 1720-1680 cm^{-1}, which is usual for it, but at 1660-1635 cm^{-1}, which is probably due to the great contribution of the bipolar structure VIA of these compounds. Such bipolarity was observed previously [7] in the case of acylated indolizines during their investigation by x-ray diffraction analysis. In 3-benzoylindolizine, one N – C bond was found to be shortened (1.25 Å instead of 1.45 Å), and the C – O bond was longer than in the unbonded carbonyl (1.32 Å and 1.22 Å, respectively). Therefore, it becomes understandable that 11-formylindoloisoquinoline VIa (unlike its simpler analog, indolo[1,2-a]pyridine) does not react with nitromethane during heating in acetic acid (the reaction was carried out by the method described in [5]).

Benzoyl derivative VIc was reduced to 11-(α-hydroxy)benzylindoloisoquinoline VIIb, in whose PMR spectrum the methine proton of the alcohol group resonated in an anomalously weak field (at 10 ppm), which correlates with the similar strong shift to weak fields of the peak of methylene protons in the case of 11-hydroxymethyl derivative VIIa.

EXPERIMENTAL

The PMR spectra were recorded on a Bruker WP-80 spectrometer, and the mass spectra were recorded on an MKh-1303 instrument with electron ionization energy 70 eV. The substances were purified and recovered on chromatographic columns with silica gel L 40/100, and the eluent was hexane – ether. The characteristics of the synthesized substances are given in Tables 1 and 2.

The data of elemental analysis corresponded to the calculated values.

9-Nitrosoindolo[2,1-a]isoquinoline (IIa). To a mixture of 0.8 g (3.7 mmoles) of indoloisoquinoline I with 2 ml of concentrated hydrochloric acid cooled to 0°C was added 10 g of finely crushed ice and then, with stirring and cooling with ice, a solution of 0.6 g of $NaNO_2$ in 2 ml of water. The mixture was stirred for another 0.5 h, and the yellow precipitate was separated and transferred portionwise to 5 ml of a concentrated soda solution. The whole was extracted with ether (3 × 15 ml). We obtained 0.7 g of dark-green crystals of nitroso product IIa. Mass spectrum of IIa, m/z (%): M^+ 246 (100), 232 (60), 231 (50), $[M - HCN]^+$, 219 (31), $[M - CO]^+$ (31), $[M - CO]^+$ 218 (19), $[M - HCO]^+$ 219 (31), $[M - CO]^+$ 218 (19), $[M - NO]^+$ 216 (60).

11-Nitroindolo[2,1-a]isoquinoline (IIb). With stirring, a solution of 0.3 ml of concentrated nitric acid in 1.5 ml of acetic anhydride was added to a solution of 0.5 g (2.3 mmoles) of indoloisoqinoline I in 14 ml of acetic anhydride cooled to –10°C. The mixture was held for 0.5 h and then worked up with ice water (27 ml), neutralized with a saturated soda solution, and extracted with chloroform. The extract was washed with water and dried, the solvent was evaporated, and the residue was purified on a column with 20 g of silica gel and recrystallized from ethanol. We obtained 0.4 g (66.6%) of mononitro derivative IIb as a brown powder. Mass spectrum of IIb, m/z (%): M^+ 262 (46), $[M - OH]^+$ 245 (100), 233 (64), $[M - NO]^+$ 232 (86), 217 (57), $[M - NO_2]^+$ 216 (71), 209 (54).

11-Bromoindolo[2,2-a]isoquinoline (IIIa). With stirring, bromine water was added portionwise to a solution of 0.15 g (0.69 mmole) of indolizine I in 15 ml of chloroform until disappearance of the starting compound I (monitored by thin-layer chromatography). The mixture was worked up with sodium bicarbonate to pH 8, and the organic layer was separated, evaporated, and purified chromatographically on a column with silica gel using an ether eluent. We obtained 0.08 g of compound IIIa as yellow crystals. Mass spectrum, m/z (%): M^+ 297 (100), $[M - Br]^+$ 217 (71), $[M - HBr]^+$ 216 (14).

9,11-Dibromoindolo[2,1-a]isoquinoline (IIIb). This compound was obtained similarly from 0.012 g (0.55 mmole) of indolizine I using excess bromine. We recovered 0.11 g of the compound (0.05 g as a precipitate from the reaction mixture and 0.06 g after chromatographic separation) as dark-brown crystals. Mass spectrum, m/z (%): M^+ 377 (2), 375 (3), 373 (2), $[M - Br]^+$ 297 (8), 295 (7), $[M - 2Br]^+$ 217 (11), 182 (22), 150 (31), $[HBr]^+$ 82 (100), $[Br]^+$ 81 (89), 80 (99).

11-Iodoindolino[2,1-a]isoquinoline (IIIc). With stirring, a 0.1 N solution of I_2 and KI in water and a 0.1 N solution of KOH were added dropwise to a solution of 0.15 g (0.69 mmole) of indolizine I in 40 ml of ether, maintaining the pH at 8-9. The ether layer was separated, dried with magnesium sulfate, and passed through a layer (~5 cm) of silica gel. After the ether was driven off, 0.11 g of black crystals of IIIc was recovered. Mass spectrum, m/z (%): M^+ 343 (4), $[M - C_7H_5]^+$ 254 (62), $[M - I+H]^+$ 217 (100), $[HI]^+$ 128 (74), 127 (57).

11-Phenylazo- (IVa) and 4-Nitrophenylazoindolo[2,1-a]isoquinoline (IVb). With stirring and cooling (20°C), a solution of 8 mmoles of phenyldiazonium chloride was added to a solution of 0.6 g (2.8 mmoles) of polycycle I in a mixture of 60 ml of dioxane and 15 ml of water, maintaining the pH at about 7 with a saturated aqueous potash solution. The mixture was held under these conditions for 3 h, poured into 300 ml of water, and extracted with chloroform (3 × 50 ml). The extract was washed with water (3 × 50 ml) and dried with sodium sulfate. After removal of the solvent, 0.9 g of red-brown crystals of IVa was obtained. Similarly, from 1.0 g (4.6 mmoles) of I and 10 mmoles of p-nitrophenyldiazonium chloride, 1.54 g of azo product IVb was obtained as a brown powder. Because of the poor solubility of dyes IVa and IVb, their UV spectra was recorded without quantitative evaluation of the extinction coefficient (ethanol), IVa: 265, 294, 435, 470 nm; IVb: 222, 320, 405, 520 nm.

Mannich Aminomethylation. A. 11-(Diethylaminomethyl)indolo-[2,1-a]isoquinoline Hydrochloride (V). With stirring, 0.3 g (1.4 mmoles) of indole I was added to a mixture consisting of 1.0 ml of diethylamine, 0.9 ml of a 40% formaldehyde solution, and 0.5 ml of acetic acid cooled to 5°C. The mixture was heated to 70°C, and, after 0.5 h, 1 ml of concentrated hydrochloric acid was added. The whole was held for 9 h at the indicated temperature. The resulting precipitate was separated (hot filtration). We obtained 0.37 g of salt V, green crystals.

B. Similarly, with addition (or without addition) of concentrated hydrochloric acid, condensation was carried out with diethylamine (dimethylamine, piperidine, and morpholine). The reaction mixture was neutralized with a 10% KOH solution to pH 8-10 and held for 3 h, and the precipitate was separated, washed with water, and dried. In all cases, instead of the allylaminomethyl derivative, the hydroxymethyl derivative of indoloisoquinoline VIIa was obtained.

11-Formylindolo[2,1-a]isoquinoline (VIa). With cooling with ice and stirring, 10.8 ml (0.13 mmole) of dry dimethylformamide (DMF) was slowly added to 9 ml (0.13 mole) of freshly distilled thionyl chloride. After 30 min, the resulting sulfur dioxide was removed by scavenging with nitrogen, and a solution of 1.80 g (8.3 mmoles) of indole I in 42 ml of DMFA was slowly added to the mixture, maintaining the temperature not higher than 20°C. The mixture was stirred for 1 h at 20°C. It was poured onto ice, neutralized with an aqueous KOH solution, and brought to pH 10. The resulting precipitate was filtered and washed with water, alcohol, and ether. We obtained 1.89 g of formyl derivative VIa, green crystals. Mass spectrum, m/z (%): M^+ 245 (31), 209 (36), 169 (43), 109 (100).

11-Formylindolo[2,1-aa]isoquinoline Oxime. With stirring at 60°C for 30 min, a solution of 0.4 g (1.63 mmoles) of formylindole VIa in 40 ml of ethanol was added to a solution of 0.57 g (4.1 mmoles) of $NH_2OH \cdot HCl$ and 1 g (12.2 mmoles) of sodium acetate in 2 ml of water, and the whole was held at this temperature for 3 h. Then the mixture was cooled with ice (1 h), and the precipitate was separated and stirred with water, alcohol, and ether. We obtained 0.22 g of the oxime as yellow crystals. Mass spectrum, m/z (%): M^+ 260 (35), $[M - OH]^+$ 243 (21), $[M - H_2O]^+$ 242 (50), 219 (65), 218 (100), 217 (38).

11-(Hydroxymethyl)indolo[2,1-a]isoquinoline (VIIa). A. A solution of 0.22 g (0.65 mmole) of quaternary salt V in 50 ml of water was alkalized with a 10% NaOH solution to pH 11 and held for 5 h, and the precipitate was separated, washed with water (100 ml), cold alcohol, and ether, and dried. We obtained 93 mg (58%) of the hydroxymethyl derivative.

B. A mixture of 0.5 g of paraform and 0.3 g (3.4 mmoles) of indole I in 5 ml of CH_3COOH was heated for 3 h at 50°C and 0.5 h at 70°C and poured into 50 ml of cold water. The precipitate was separated and washed with water, alcohol, and ether. The whole was dried, and 0.22 g (63%) of compound VIIa was obtained, with mp and PMR spectrum identical to those of the alcohol previously obtained by method A.

C. With stirring for 2 h, 0.5 g of sodium borohydride was added to a solution of 0.28 g (1.1 mmoles) of formylindole VIa in 50 ml of methanol. The mixture was held for 2 h and then poured into water (50 ml), and the precipitate was separated, washed with water, alcohol, and ether, and dried. We obtained 0.25 g of compound VIIa, colorless crystals, with mp and PMR spectrum identical to those of samples obtained by methods A and B.

11-Acetylindolo[2,1-a]isoquinoline (VIb). A solution of 0.5 g (2.3 mmoles) of indole I in a mixture of 4.5 ml of acetic anhydride and 0.5 ml of CH_3COOH was boiled for 48 h and then poured onto ice (50 g) and alkalized to pH 9. The resulting oily layer was separated, dissolved in chloroform, and washed with water (3 × 10 ml) and dried, the solvent was driven off, and the residue was crystallized from heptane. We obtained 0.4 g (68%) of acetylindole VIb as yellow crystals. Mass spectrum, m/z (%): M^+ 259 (25), $[M - CH_3]^+$ 244 (50), 105 (8), 104 (52), 103 (100).

11-Benzoylindolo[2,1-a]isoquinoline (VIc). With vigorous stirring, 1 ml of benzoyl chloride was added dropwise to a mixture of 0.8 g (3.7 mmoles) of indole I with 10 ml of a 10% KOH solution, and the whole was heated for 3 h at 50°C. The precipitate was filtered and washed with water, alcohol, and ether. We obtained 0.81 g of green crystals, which were purified on a short column with aluminum oxide (the eluent was a 1:1 ether–hexane mixture). We recovered 0.5 g of 11-benzoylindole VIc, yellow crystals.

Similarly, 0.36 g (38%) of acetyl derivative VIb was obtained from 0.5 g (6.7 mmoles) and 0.8 g (3.7 mmoles) of indole I.

11-(4-Chlorobenzoyl)indolo[2,1-a]isoquinoline (VId). A mixture of 0.2 g (0.92 mmole) of indole I, 0.45 g (2.62 mmoles) of 4-chlorobenzoyl chloride, and 0.19 g (1.97 mmoles) of triethylamine in 25 ml of dry benzene was boiled for 17 and cooled to 20°C. After separation of the precipitate of triethylamine hydrochloride, benzene and excess triethylamine were driven off under vacuum. The residue (1.3 g) was purified on a column; the adsorbent was aluminum oxide (20 × 2 cm), and the eluent was 1:1 ether–hexane. We recovered 0.45 g of a yellow–brown powder. We obtained 0.26 g of yellow crystals. Mass spectrum, m/z (%): M^+ 355 (100), $[M - Cl]^+$ 321 (4), $[M - C_6H_4Cl]^+$ 244 (42); $[M - COC_6H_4Cl]^+$ 217 (33).

α-Hydroxybenzylindolo[2,1-a]isoquinoline (VIIb). This compound was obtained similarly to hydroxymethylindole VIIa from 0.17 g (0.53 mmole) of VI in 30 ml of ethanol and 0.5 g of sodium borohydride, and 0.1 g (59%) of light-yellow crystals was recovered.

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