DRUG SYNTHESIS METHODS AND MANUFACTURING TECHNOLOGY

3-ARYLAMINOINDOLES IN THE SYNTHESIS OF INDOLO[3,2-b]QUINOLINE DERIVATIVES

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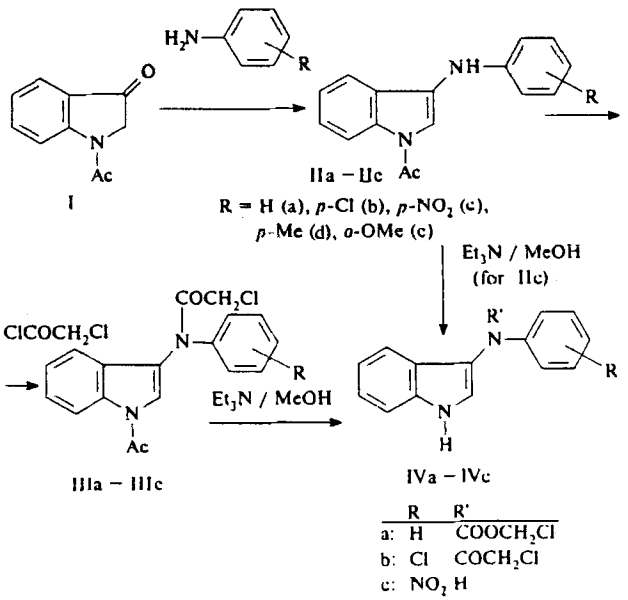
As is known [1], N-acetylindoxyl (I) is capable of forming 3-arylaminoindoles (II) on heating with substituted anilines in acetic acid. Recently [2] we have reported that N-acetyl-3-*p*-nitrophenylaminoindole (IIc) can be used as an initial compound for the synthesis of new derivatives of 1,2- and 1,4-dihydro-δ-carboline.

In this work we have studied some properties of 3-arylaminoindoles IIa – IIe and developed a new method for the synthesis of related indolo[3,2-b]quinolines.

N-Acetyl-3-arylaminoindoles IIa – IIe were obtained by the known method [1]. As for the individual compounds, it was possible to isolate only N-acetyl-3-*p*-chlorophenylaminoindole IIb in addition to compounds IIc and IId described in [1]. We failed to isolate the derivatives of aniline (IIa) and o-anisidine (IIe), but treatment of the reaction mass with chloroacetyl chloride led to readily separated and stable N-acetyl-N′-chloroacetylarylaminoindoles IIIa and IIId (yields, 73 and 60%, respectively). N,N′-Diacyl derivatives IIIb – IIId were obtained by heating monoacetyl-3-arylaminoindoles IIb – IId in chloroacetyl chloride. Note that the N′-chloroacetyl derivative IIIc (R = *p*-NO_2) forms readily in good yield (64%), whereas a similar N′-acetyl derivative was not obtained at all [1].

Interaction of IIIa and IIIb with triethylamine in methanol leads to detachment of the N-acetyl group with the formation of N′-chloroacetyl derivatives of 3-arylaminoindole (IVa, IVb). A similar treatment of IIIc leads to a completely deacylated 3-*p*-nitrophenylaminoindole IVc. The latter compound is also necessary for deacylation of IIc [2]. We failed to perform the N′-chloroacetylation of IVc. The structures of 3-arylaminoindoles IIb, IIc, and IVc at the indole derivatives were confirmed by ^{1}H NMR spectra measured in DMSO-d_6. The spectra show 1H singlets in the region of 7.89 – 7.42 ppm, which are indicative of a proton at position 2 of the indole cycle.



Derivatives of 3-arylaminoindole can be considered as new cyclic enamines with the electron density in position 2 increased due to the presence of the 3-amino group. This assumption was confirmed by the results of ^{1}H NMR study of the deuteron exchange in compounds IIb, IIc, IIIc, and IVc. The maximum exchange rate was observed in compound IIb (R = *p*-Cl), where the ^{1}H NMR spectrum, measured in CD_3COOD immediately after dissolution of the compound, contained no signal due to proton in position 2 of the indole molecule. At the same time, this signal was observed in the

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spectra of IIc, IIIc, and IVc measured under the same conditions. The content of C_2-nondeuterated molecules was 33 and 35% in compounds IIc and IVc, respectively, and 100% in compound IIIc. The lower deuteron exchange in compound IIc (R = *p*-NO_2) as compared to that in compound IIb (R = *p*-Cl) can be explained by the electron-acceptor action of the NO_2 group reducing the electron-donor effect of the *exo*-NH fragment. The ^{1}H NMR spectra of 3-arylaminoindoles IIc, IIIc, and IVc were measured again after heating the ampules with solutions for 1 h on a boiling water bath. The spectrum of IIc (with N-acyl group) had no signals due to a proton at C_2, thus showing that the deuteron exchange was complete. The exchange in compound IVc (with a free NH group) proceeds at a markedly slower rate than in compound IIc, as indicated by a signal of the proton at C_2. The intensity of this signal amounts to 11% of the initial level, from which we infer that the deuteron exchange rate depends not only on the substituent in the 3-aminoaryl core, but on the substituent (here, the $COCH_3$ group) at the indole nitrogen atom as well. Finally, the introduction of one more electron-acceptor N'-acyl group in compound IIIc excluded the possibility of deuteron exchange under these conditions, as indicated by the unchanged ^{1}H NMR spectrum of this compound.

These results led us to the following conclusion: compounds of the types II and IV must, while compounds such as III must not, enter into reactions of electrophilic exchange at the position 2.

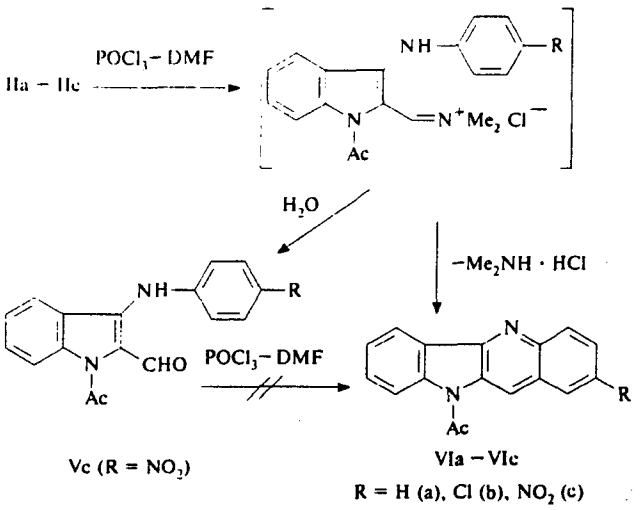
Indeed, it was found that formylation of N,N'-diacylarylaminoindle IIIc under the action of Vilsmeier reagent did not take place in the temperature range from 0 to 130°C, and only the initial compound IIIc was isolated from the reaction mixture.

The formylation of N-acetyl-3-arylaminoindoles II was studied for the nitro derivative IIc. The electrophilic attack of the Vilsmeier reagent at position 2 of the indole cycle was accompanied by closing the pyridine ring and the formation of an indolo[3,2-b]quinoline VIc in addition to the formyl derivative Vc. It is important to note that the ratio of products depends on the process duration. For example, the main reaction product (yield, 74%) after interaction for 2 h at 20°C was aldehyde Vc, although the ^{1}H NMR spectrum of the compound showed that it also contained about 11% of tetracycle VIc. Indeed, the ^{1}H NMR spectrum in DMSO-d_6 exhibited signals due to tetracycle Vc (see Table 1) in addition to the signals of 2-formyl derivative Vc at 2.72 ppm (s, 3H, CH_3), 7.34 and 7.62 ppm (2m, 4H, C_6H_4 of indole ring), 7.14 – 8.13 ppm (A_2B_2 system, 4H, $C_6H_4NO_2$), 10.00 ppm (bs, 1H, NH), 10.03 ppm (bs, 1H, CHO). Reaction under the same conditions for 20 h led to approximately equal amounts of Vc and VIc, and tetracycle VIc was dominating (yield, 67%) after the interaction for 70 h. A special experiment demonstrated that aldehyde Vc does not convert into indoloquinoline VIc under the conditions studied. Therefore, heterocyclization is likely to occur at the stage of immonium salt formation by the scheme

TABLE 1. Yields and Physicochemical Characteristics of 3-Arylaminoindole and Indolo[3,2-b]quinoline Derivatives

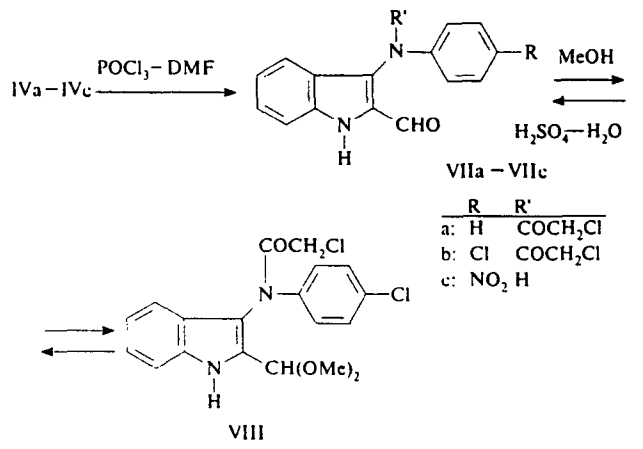
Compound	Yield, %	M.p., °C, solvent	Mol. weight	Empirical formula	M^+	IR spectrum (ν_{max}, cm^{-1})
IIb	35	102 – 104; *i*-PrOH	284	$C_{16}H_{13}N_2ClO \cdot H_2O$	284	3600, 3500, 3400, 1680, 1600
IIIa	73	146 – 147; MeOH	326	$C_{18}H_{15}N_2Cl_2O_2$	326	1715, 1665, 1600
IIIb	81	167 – 168; MeOH	361	$C_{18}H_{14}N_2Cl_2O_2$	361	1775, 1705, 1500
IIIc	64	157 – 158; MeOH – DMF, 10 : 1	371	$C_{18}H_{14}N_3ClO_4$	371	1720, 1590
IIId	78	145 – 147; *i*-PrOH	340	$C_{18}H_{17}N_2ClO_2$	340	1720, 1690, 1610
IIIe	60	178 – 179; MeOH	356	$C_{18}H_{17}N_2ClO_3$	356	3100, 1710 – 1680, 1590
IVa	81	203 – 204 (decomp.); dioxane	284	$C_{16}H_{13}N_2ClO$	284	3300, 3120, 3060, 1680, 1600
IVb	75	227 – 228 (decomp.); dioxane	319	$C_{16}H_{12}N_2Cl_2O$	320	3300, 3100, 1680
IVc*	92 and 79	220 – 222; MeOH	253	$C_{14}H_{11}N_3O_2$	253	3350, 1590
Vc	74	189 – 190; MeOH – dioxane, 1 : 1	323	$C_{17}H_{13}N_3O_4$	323	3200, 1690, 1625, 1610, 1595
VIa**	14	179 – 180; MeOH – DMF, 1 : 1	260	$C_{17}H_{12}N_2O_2$	260	1700, 1620, 1580
VIb	22	189 – 190; DMF	294	$C_{17}H_{11}N_2ClO$	294	1690, 1620, 1610
VIc	67	247 – 247; DMF	305	$C_{17}H_{11}N_3O_3$	305	1680, 1610, 1585
VIIa	70	177 – 178 (decomp.); MeOH	312	$C_{17}H_{13}N_2ClO_2$	312	3440 – 3260, 1670 – 1650, 1620, 1590
VIIb	31	185 – 186 (decomp.); *i*-PrOH	347	$C_{17}H_{12}N_2Cl_2O_2$	347	3300, 3220, 1690, 1670 – 1650, 1620, 1580
VIIc	98	237 – 238 (decomp.); DMF – H_2O, 2 : 1	281	$C_{15}H_{11}N_3O_3$	281	3290, 1640, 1600, 1575
VIII	29	183 – 184; MeOH	392	$C_{18}H_{18}N_2Cl_2O_3$	393	3440, 1680, 1580
IXa*	48 and 94	330; (subl.) DMF	263	$C_{15}H_9N_3O_2$	263	3300 – 3080, 1620, 1590
IXb	26	275 – 277; DMF	291	$C_{16}H_9N_3O_3$	291	1710, 1630, 1615

* Yields for compounds IVc and IXa are indicated for the methods 1 and 2, respectively.
** Ref. [3]: compound VIa, m.p., 178°C.



By the same token, we converted 3-arylaminoindoles IIa and IIb into tetracyclic compounds VIa and VIb (without isolating IIa). The structure of indolo[3,2-b]quinolines was confirmed by data of ^{1}H NMR spectroscopy (Table 3). Note that the physical properties and ^{1}H NMR spectrum of VIa agree with the published data (earlier, this compound was synthesized by a different method [3]).

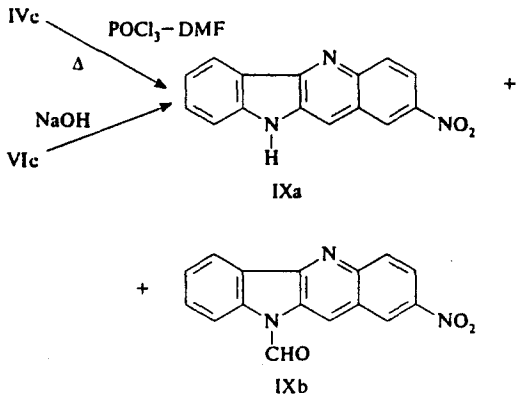
Formylation of compounds IVa – IVc under the same conditions leads to the appearance of only the 2-formylindole derivatives VIIa – VIIc. No pyridine cyclization in IVa and IVb was observed, since the benzene ring was deactivated by the presence of N′-chloroacetyl substituent.



After the formylation of IVb (R = Cl), we have isolated 2-formylindole dimethylacetal (VIII). This compound was obtained, in addition to 2-formylindole VIIb, as a result of washing the reaction products with hot methanol (this was done for purification purposes). The structure of VIII was confirmed by the ^{1}H NMR spectrum, in which a signal due to the acetal proton is observed at 5.69 ppm in the form of a broad singlet (Table 2). Additional evidence is provided by hydrolysis of acetal VIII under the action of sulfuric acid in aqueous dioxane, which leads to a quantitative yield of 2-formylindole (VIIb).

Nor did cyclization take place in the case of formylation of IVc (having no N-*exo*-acyl group), apparently because of the strong electron acceptor effect of the nitro group and insufficient activation of the intermediate immonium cation (since no electron-acceptor acetyl group is present in position 1).

Nevertheless, quinoline cyclization was observed upon the interaction of 3-(*p*-nitrophenyl)aminoindole (IVb) with the Vilsmeier reagent under much more rigid conditions (100°C), which allowed us to isolate two compounds: 2-nitro-10H-indolo[3,2-b]quinoline (IXa) and 2-nitro-10-formylindolo[3,2-b]quinoline (IXb). The N-unsubstituted indoloquinoline (IXa) was also obtained by alkaline hydrolysis of the corresponding 10-acetyl derivative VIc.



The ^{1}H NMR spectrum of compound IXa contained the following signals (δ, ppm): 7.35 (t, 1H, H-C^7), 7.35 (d, 1H, H-C^9), 7.68 (t, 1H, H-C^8), 8.33 (spl. s, 2H, H-C^3) and H-C^4), 8.40 (d, 1H, H-C^6), 8.65 (s, 1H, H-C^{11}), 9.23 (spl. s, 1H, H-C^1). In the region of low fields, there are signals due to the NH proton at 11.70 ppm (1H), having the shape of a broad singlet.

We have also measured the ^{1}H NMR spectrum of a freshly prepared solution of N-formyl compound IXb (because of the limited solubility of this compound, the solution was prepared by heating the system to 90 – 100°C for 15 – 20 min). The spectrum exhibited some signals with strictly defined multiplicity, such as the triplets at 7.58 and 7.81 ppm (1H, NH-C^7 and 1H, H-C^8, respectively), a multiplet centered at 8.32 ppm (3H, H-C^3, H-C^4, and H-C^6), and a narrow singlet at 9.90 ppm (1H, HC=O). In addition, the spectrum contained strongly broadened signals at 8.20, 9.22, and 9.41 ppm, which could be assigned to H-C^9, H-C^{10}, and H-C^{11}, respectively. The appearance of smeared signals is indicative of a chemical reaction proceeding at a sufficiently high rate in the sample solution. We naturally assumed that it was residual water (a certain amount of which is always present in DMSO) leading to hydrolysis of the formamide groups with the formation of formic acid, thereby converting tetracycles Xb into an N-unsubstituted product IXa. In order to verify this hypothesis, we heated the solution for a prolonged time (about 3 h) at 90 – 100°C. The main signals in

the ^{1}H NMR spectrum measured after the treatment were those of tetracycle IXa described above (experiment with a mixed sample containing tetracycle IXa showed complete coincidence of the signals). The spectrum also displayed well identifiable intense signals at 8.20 and 11.70 ppm corresponding to formic acid. According to the spectrum, tetracycle IXb with a formyl group at the indole nitrogen atom was present in solution in a very small amount.

It should be recalled that indoloquinolines (quindolines) were earlier obtained by condensation of the substituted N-acetylineindoxyls with isatin in an alkaline medium [4]. Another possible pathway of quindoline synthesis is based on the interaction of I and its 5-methoxy derivative with o-aminobenzaldehyde [3]. Sevodin et al. [5, 6] described a method to obtain quindolines with alkyl and aryl groups in the quinoline part of the molecule.

Thus, the results of the investigation described above led to the development of a new method for the synthesis of previously unreported derivatives of indolo[3,2-b]quinoline. These compounds possess a planar structure and can be considered as promising intercalating agents. It would also be reasonable to perform screening of the new compounds with respect to their antiviral and antitumor activity.

EXPERIMENTAL PART

The IR spectra of synthesized compounds were measured on a Perkin-Elmer Model 457 spectrophotometer using samples prepared as Nujol mulls. The mass spectra were obtained on a Varian MAT-112 mass spectrometer with direct introduction of the sample into the ion source. The ionizing electron energy was 70 eV, and the temperature in the ionization chamber was 180°C. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian XL-200 instrument using TMS as an internal standard. The course of the reactions was monitored and the samples were identified by thin-layer chromatography on Silufol UV-254 plates (eluted in the chloroform – methanol system, 10 : 1, and developed under UV irradiation).

The results of elemental analyses (C, H, N, Cl) coincided with the calculated values.

N-Acetyl-3-*p*-nitrophenyl- (IIc) and N-acetyl-3-*p*-methylphenyl- (IId) aminoindoles were obtained by the method described in [1].

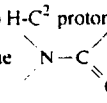
N-Acetyl-3-*p*-chlorophenylaminoindole (IIb). A mixture of 8.75 g (50 mmole) of N-acetylindoxyl, 6.4 g (50 mmole) *p*-chloraniline, and 25 ml acetic acid was boiled for 1 h. Then the reaction mixture was concentrated by evaporation, mixed with ethanol, and cooled. The residue was

TABLE 2. ^{1}H NMR Spectra of Compounds IIb, IIc, IIIa – IIIe, IVa – IVc, VIIa – VIIc, and VIII

Compound	Solvent	Chemical shifts (δ, ppm)						
		$COCH_3$	$COCH_2Cl$	NH	N'H	H-C^2	H-$C^{4\,5\,6,7}$*	C_6H_4R'
IIb	DMSO-d_6	2.62 s	–	–	8.20 s	7.57 s	7.29, 7.37, 7.73, 8.37	7.14, 7.24 (A_2B_2)
	CD_3COOD	2.61 s	–	–	–	–	7.25, 7.35, 7.56, 8.40	7.03, 7.18 (A_2B_2)
IIc	DMSO-d_6	2.67 s	–	–	9.21 s	7.89 s	7.31, 7.40, 7.62, 8.39	7.12, 8.09 (A_2B_2)
	CD_3COOD	2.66 s	–	–	–	7.64 s 33%	7.28, 7.39, 7.54, 8.44	7.04, 8.10 (A_2B_2)
IIIa	DMSO-d_6	2.67 s	4.41 s	–	–	***	7.26, 7.33, 7.39, 8.37 (2H)	7.44 (m, 5H)
IIIb	DMSO-d_6	2.67 s	4.41 s	–	–	***	7.26, 7.38, 7.54, 8.38 (2H)	7.47 (m, 4H)
IIIc	DMSO-d_6	2.69 s	4.50 s	–	–	8.47 s	7.27 – 7.39 (3H), 8.45 (1H)	7.74, 8.24 (A_2B_2)
	CD_3COOD	2.70 s	4.32 s	–	–	8.09 s 100 %	7.21 – 7.60 (3H), 8.47 (1H)	7.69, 8.20 (A_2B_2)
IIId	DMSO-d_6	2.66 s	4.39 s	–	–	***	7.18 – 7.49 (7H), 8.35 (2H), 2.27 (s, CH_3-C_4')	
IIIe	DMSO-d_6	2.65 s	4.27 s	–	–	***	6.87 – 8.07 (7H), 8.35 (2H), 3.87 (s, OCH_3)	
IVa	DMSO-d_6	–	4.24 s	11.23 bs	–	7.73 bs	7.03, 7.14, 7.34, 7.42 (9H),	
IVb	DMSO-d_6	–	4.25 s	11.47 bs	–	7.75 s	7.05 (1H), 7.16 (1H), 7.43 (6H),	
IVc	DMSO-d_6	–	–	11.14 bs	8.93 s	7.42 s	6.99, 7.13, 7.32, 7.41	6.76, 8.01 (A_2B_2)
IVc	CD_3COOD	–	–	–	–	7.28 c 35 % **	7.03 (1H), 7.14 (1H), 7.38 (2H)	6.75, 8.00 (A_2B_2)
VIIa	DMSO-d_6	–	4.40 bs	12.30 bs	–	10.07 (s, CHO)	7.10 – 8.80 (9H)	
VIIb	DMSO-d_6	–	4.20 bs	12.36 bs	–	10.04 (s, CHO)	7.19 – 7.69 (8H)	
VIIc	DMSO-d_6	–	–	11.85 bs	9.41 bs	9.88 (s, CHO)	6.95 – 7.59 (4H)	6.88, 8.08 (A_2B_2)
VIII	DMSO-d_6	–	4.05 bs 4.25 bs	11.64 bs	–	5.68 bs [$CH(OMe)_2$]	7.08 (1H), 7.18 (1H), 7.39 – 7.49 (6H), 3.20, 3.35 (bs, 6H, $(OCH_3)_2$	

* Proton signals have the form of triplets and doublets (J_{ortho} ~ 8 – 9 Hz) composed of additionally split components (J_{meta} ~ 3 Hz, J_{para} < 1 Hz);

** Integral intensity of the signal due to protons partly exchanged with deuterons;

*** The signals due to H-C^2 protons fall within the region of aromatic protons; individual signals are strongly broadened, apparently because of the amide isomerism with respect to the  bond (substituent in position 3).

filtered and washed with ethanol and ethyl ether. Yield of compound IIb, 5 g.

N-Acetyl-3-(N-chloroacetyl-N-aryl)aminoindoles (IIIb – IIId). A mixture of 15 mmole of the corresponding 1-acetyl-3-arylaminoindoline (IIb – IId) and 20 ml chloracetyl chloride was boiled for 15 min. Then the reaction mixture was concentrated by evaporation, mixed with 10 – 15 ml of isopropanol, and boiled for another 10 min. The mixture was cooled, filtered, and washed with isopropanol and ethyl ether.

N-Acetyl-3-(N'-chloroacetyl-N'-aryl)aminoindoles (IIIa, IIIe). A mixture of 10 mmole N-acetylindoxyl, 15 mmole aniline or *o*-anisidine, and 5 ml acetic acid was boiled for 15 min. The reaction mixture was concentrated by evaporation, mixed with 3 ml chloracetyl chloride, and boiled for another 15 min. Then 4 ml of isopropanol was added in drops and the mixture was boiled again for 15 min, concentrated by evaporation, cooled, and mixed with 20 – 30 ml of methanol. The residue was filtered and washed with methanol and ethyl ether.

3-(N'-Chloroacetyl-N'-aryl)aminoindoles (IVa, IVb). To a solution of 10 mmole of the corresponding compound IIIa or IIIb in 50 ml of methanol was added 3 ml (20 mmole) triethylamine. The mixture was boiled for 1 h while the target compound gradually precipitated. On cooling, the precipitate was filtered and washed with methanol.

3-(*p*-Nitrophenyl)aminoindole (IVc).

Method 1. Compound IVc is obtained from IIIa by analogy with the synthesis of compounds IVa and IVb.

Method 2. A suspension of 5.8 g (20 mmole) of compound IIc, 270 ml of methanol, and 9 ml (60 mmole) triethylamine was boiled for 2 h and cooled. The precipitate was filtered and washed with methanol. The mother liquor was concentrated to 3/4 of the initial volume by evaporation and the residue was filtered and washed with methanol. Total yield of compound IVc, 3.95 g. No depression was observed for the melting temperature of a mixture of samples obtained by methods 1.

10-Acetylindolo[3,2-b]quinoline (VIa). A mixture of 17.5 g (100 mmole) N-acetylindoxyl, 9.5 mmole aniline, and 50 ml acetic acid was boiled for 15 min. Then the reaction mass was evaporated to dryness and dissolved in 30 ml of distilled DMF. The solution was cooled to 5°C and added in drops to the Vilsmeier complex (prepared by a conventional method using 60 ml DMF and 28 ml $POCl_3$), maintaining the temperature within 10 – 15°C. The reaction mass was allowed to stand for 16 h at 20°C, poured into water with ice (~ 800 g), and stirred for 2 h. Then the solution was neutralized by 20% NaOH. The resinous deposit was filtered, transferred into 100 ml of methanol, and heated. The solution was cooled and the deposit filtered to yield 8.4 g of a technical-grade VIa, which was purified by boiling with 70 ml of methanol. The deposit was filtered hot and washed by hot methanol to obtain 3.6 g of indoloquinoline VIa.

2-Chloro-10-acetylindolo[3,2-b]quinoline (VIb). A solution of 12 g (42 mmole) of compound IIb in 85 ml DMF was added in drops to the Vilsmeier complex (prepared by a conventional method using 85 ml DMF and 12 ml $POCl_3$), maintaining the temperature within 10 – 15°C. Then the reaction mixture was stirred for 5 h at 20°C. The deposit was filtered and washed with DMF and methanol to obtain 2.7 g of indoloquinoline VIb.

2-Nitro-10-acetylindolo[3,2-b]quinoline (VIc). A solution of 2.9 g (10 mmole) of compound IIc in 29 ml DMF was added at 10 – 15°C to the Vilsmeier complex (6 ml DMF; 2.9 ml $POCl_3$), and the mixture was allowed to stand for 70 h at 20°C. Then the reaction mixture was stirred for 1 h at 50°C and cooled. The deposit was filtered and washed with DMF, water, and methanol to obtain 2 g of indoloquinoline VIc.

1-Acetyl-2-formyl-3-(*p*-nitrophenyl)aminoindole (Vc). Obtained from 0.75 g (2.5 mmole) of compound IIc by a procedure similar to that used for the synthesis of compound VIc. A difference consists in that the reaction mass is stirred for 2 h at 20°C and poured into water with ice. In 2 h the deposit was filtered and washed with water, isopropanol, and ethyl ether to obtain 0.6 g of aldehyde Vc.

2-Formyl-3-(N'-chloroacetyl-N'-phenyl)-, N'-(*p*-chlorophenyl)aminoindoles (VIIa, VIIb) and 2-formyl-3-(*p*-nitrophenyl)aminoindole (VIIc). Obtained from the corresponding compounds IVa – IVc by a procedure similar to that used for the synthesis of compound VIc. A difference consists in that the reaction mass is allowed to stand for 20 h at 20°C and then a threefold excess of ice-cold water is added. The precipitate is filtered and washed with water and isopropanol (VIIa, VIIc) or hot methanol (VIIb) to obtain the corresponding 2-formylindoles VIIa – VIIc.

2-Formyl-3-(N'-chloroacetyl-N-*p*-chlorophenyl)amin oindole acetal (VIII). The deposit formed during 20 h in the methanol mother liquor, obtained after washing the technical-grade VIIb, was filtered and washed with methanol to obtain compound VIII.

TABLE 3. ^1H NMR Spectra of Compounds VIa – VIc in DMSO-d_6

Compound	Chemical shifts (δ, ppm)					
	$COCH_3$	H-C^1	H-C^3	H-C^4	H-$C^{6\,7\,8}$ *	H-C^{11}
VIa	2.95 s	7.54, 7.64, 7.73, 7.78 (t, H-$C^{2,3,7,8}$), 8.18, 8.19 (d, J 8 Hz, H-$C^{4,6}$), 8.36, 8.37, (d, J 8 Hz, H-$C^{1,9}$)				9.03 s
VIb	2.93 s	8.35 (d, J 2.9 Hz)	7.74 (dd, J_1 2.9 Hz, J_2 8.9 Hz)	8.16 (d, J 8.9 Hz)	7.54 (1H), 7.74 (1H), 8.34 (2H)	9.01 s
VIc	3.00 s	9.35 (d, J 2.6 Hz)	8.48 (dd, J_1 2.9 Hz, J_2 8.9 Hz)	8.36 (d, J 9.2 Hz)	7.61 (1H), 7.83 (1H), 8.45 (2H)	9.42 s

* Proton signals have the form of triplets and doublets (J_{ortho} ~ 8 – 9 Hz) composed of additionally split components (J_{meta} ~ 3 Hz, J_{para} < 1 Hz).

Hydrolysis of dimethylacetal (VIII). To a suspension of 0.5 g (1.3 mmole) of compound VIII in 20 ml of water was added 0.2 ml concentrated H_2SO_4 and the mixture was heated to boiling. Then dioxane was added until a solution was obtained. The solution was boiled for 1 h and cooled. The precipitate was filtered and washed with water and isopropanol. Yield of aldehyde VIIb, 0.45 g (100%). The melting temperature of a mixture of this product with compound VIIb obtained as described above showed no evidence of depression.

2-Nitro-10H-indolo[3,2-b]quinoline (IXa).

Method 1. Mother (DMF) liquor obtained after the filtration of 10-formylindoloquinoline IXb (see below) was poured into water. The precipitate was filtered and washed with water and methanol. Yield of compound IXa, 0.25 g.

Method 2. To a suspension of 6.2 g (20 mmole) of 10-acetylindoloquinone VIc in 160 ml of dioxane was added 30 ml of 1 N NaOH solution. The mixture was boiled on stirring for 3 h. The precipitate was filtered and washed with water. Yield of compound IXa, 5.1 g. The melting temperature of a mixture of this product with compound IXa obtained by method 1 showed no evidence of depression.

2-Nitro-10-formylindolo[3,2-b]quinoline (IXb). Synthesized from 0.5 g (2 mmole) of compound IVc under conditions analogous to those used for obtaining aldehyde VIIc. The difference consists in that the reaction mass obtained after standing for 20 h at 20°C is additionally stirred for 1 h at 120°C. During this, the initial deposit dissolves and a new precipitate appears. On cooling the mixture, the precipitate is filtered and washed with DMF, water, and methanol to obtain 0.15 g of the 10-formyl derivative IXb.

Yields and physicochemical characteristics of the synthesized compounds are presented in Table 2.

Parameters of the ^{1}H NMR spectra of compounds IIb, IIc, IIIa – IIIe, IVa – IVc, VIIa – VIIc, and VIII are listed in Table 3.

Parameters of the ^{1}H NMR spectra of compounds VIa – VIc are given in Table 3.

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