REACTION OF AROMATIC o-DIAMINES WITH ISATINS.

3.* 4-NITRO- AND 4,5-DINITRO-o-PHENYLENEDIAMINES

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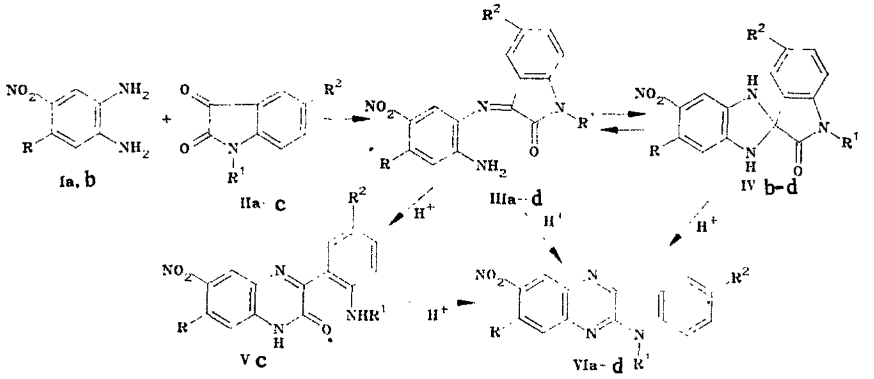
The interaction of nitro-o-phenylenediamines with isatins yielded nitroindolo[2,3-b]quinoxalines, 3-(2-aminophenyl)-2(1H)-nitroquinoxalines, nitrospiro[2H-benzimidazolin-2,3'-indolin]-2'-ones, and Schiff bases. The position of the nitro group in the compounds obtained was demonstrated.

We showed in [1, 2] that the interaction of o-phenylenediamine and 2,3-diaminonaphthalene with isatins in general leads to the formation of three types of products: indolo[2,3-b]quinoxalines, 3-(2-aminophenyl)-2(1H)-quinoxalines, and spiro [2H-benzimidazolin-2,3'-indolin]-2'-ones.

In this work we investigated the influence of a decrease in the basicity of the o-diamine on the corresponding products of this reaction, on the example of 4-nitro- and 4,5-dinitro-o-phenylenediamines.

In the interaction of 4-nitro-o-phenylenediamine with isatin in acetic acid, a 2- or 3-nitro derivative of indoloquinoxaline is formed, but its structure was not discussed in [3]. The authors of [4] suggested that this is 2-nitroindoloquinoxaline, since in 4-nitro-o-phenylenediamine, primarily the more basic amino group in the 2-position reacts with the β-carbonyl of isatin.

In the condensation of 4-nitro-o-phenylenediamine Ia with isatins IIa-c, we obtained 2-nitroindoloquinoxalines VIa-c (Table 1). The constants of 2-nitroindoloquinoxaline VIa coincide with the data of [3].



I a $R=H$; b $R=NO_2$; II a $R^1=R^2=H$; b $R^1=CH_3$, $R^2=H$; c $R^1=CH_3$, $R^2=NO_2$; III—VI a $R=R^1=R^2=H$; b $R=R^2=H$, $R^1=CH_3$; c $R=H$, $R^1=CH_3$, $R^2=NO_2$; d $R=NO_2$, $R^1=CH_3$, $R^2=H$

3-Nitroindoloquinoxaline IX was produced according to the scheme on the following page. Condensation of 4-nitro-o-phenylenediamine Ia with N-acetylisatin IId, both in ethanol and in acetic acid, leads to the acetylaminophenylquinoxalinone VII, since N-acetylisatin reacts with bases at the carbon atom of the α-carbonyl with opening of the ring [5]. Hydrolysis of compound VII in hydrochloric acid led to 7-nitro-3-(2-aminophenyl)-2(1H)-quinoxalinone (VIII), which, when boiled in acetic acid, forms 3-nitroindoloquinoxaline X. Its spectral character-

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*For communication 2, see [1].

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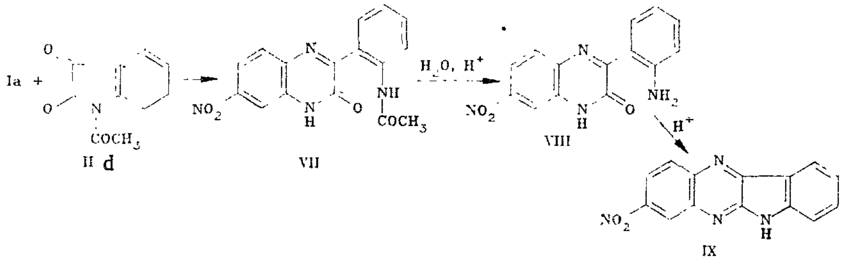
TABLE 1. Yields of the Products of the Reaction of o-Diamines with Isatins

Starting materials		Reaction product	Yield, %		
diamine	isatin		alcohol	0.1 N soln. of HCl in alcohol	CH_3COOH
Ia [7]	IIa	IIIa	54	—	—
		VIa	4	57	72
Ia	IIb	IVb	75	1,5	9
		VIb	Traces	65	56
Ia	IIc	IIIc	27	—	—
		IVc	41	4	—
		Vc	Traces	46	64
		VIc	Traces	17	24
Ia	IId	VII	33	—	98
Ib [8]	IIb	IVd	—	89	86
		VId	—	Traces	2,5



istics are very similar to the corresponding characteristics for 2-nitroindoloquinoxaline VIa, but the IR spectra differ in the region of 700-900 cm^{-1}, and the short-wave absorption band of 3-nitroindoloquinoxaline IX in the electronic spectrum is somewhat bathochromically shifted (Table 2).

In ethanol, in the condensation of 4-nitro-o-phenylenediamine Ia with isatin IIa, chiefly the Schiff base IIIa is formed, with N-methylisatin IIb the spiro-compound IVb, while in the case of N-methyl-5-nitroisatin IIc, both compounds were isolated (IIIc and IVc, respectively). Indoloquinoxalines VIa-c and aminophenylquinoxalinone Vc, in contrast to condensation with o-phenylenediamine [2], were present only as traces (Table 1). The reaction proceeds with intermediate formation of Schiff bases IIIa-c, which we observed in chromatographic monitoring of the course of the reaction (thin-layer chromatography). In contrast to the corresponding Schiff bases from o-phenylenediamine, the less basic amino group in these compounds reacts chiefly at the β-carbon atom, forming spiro-compounds IVb, c. Acid hydrolysis facilitates attack at the carbon atom of the α-carbonyl. Thus, the Schiff base IIIc, when boiled in acetic acid for 1 h, is converted to a mixture of aminophenylquinoxallinone Vc, indoloquinoxaline VIc, and the spiro-compound IVc. The spiro-compound IVc, when boiled in acetic acid for 3 h, is also converted to a mixture of compounds Vc and VIc; moreover, the Schiff base IIIc is formed as an intermediate (thin-layer chromatography). Consequently, indoloquinoxalines VIa-d are obtained chiefly from Schiff bases, since cyclization, for example, of 6-nitroaminophenylquinoxalinone Vc to 2,9-dinitroindoloquinoxaline VIc requires substantially more rigorous conditions — boiling in acetic acid containing 1% HCl for 30 h. Moreover, the direct reaction of the diamine Ia with the isatin IIc, just as in the case of N-acetylisatin IId, would lead to 7-nitroaminophenylquinoxalinone.

In 4,5-dinitro-o-phenylenediamine Ib, the basicity of both of the amino groups is greatly lowered, and in ethanol the reaction practically does not occur. In acid catalysis the indoloquinoxaline VId was isolated only with a small yield, and the spiro-compound IVd was chiefly formed (Table 1); it was converted to the indoloquinoxaline VId only when boiled in acetic acid with an addition of HCl for 25 h.

In the electronic spectra of nitrocompounds IVb, c, in comparison with unsubstituted spiro-compounds [2], a new band appears at 440 nm (Table 2), related to charge transfer from the amino groups of the benzimidazoline fragment to the nitro group. The appearance of a second nitro group in the benzimidazoline fragment (compound IVd) shifts this band bathochromically by 20 nm. The electronic spectra of aminophenylnitroquinoxalinones Vc, VII, and

TABLE 2. Characteristics of the Reaction Products of Nitro-o-phenylenediamines with Isatins

Compound	Mp*, °C	R_f†	UV spectrum, λ_{max}, nm (log ε)	IR spectrum, cm^{-1}		Found, %			Gross formula	Calculated, %		
				C=O	N–H	C	H	N		C	H	N
IIIa	210 (разл.)	0,09	210 (4,20), 249 (4,22), 312 (3,76), 388 (4,00), 490 (3,68)	1720	3490, 3380, 3200	59,7	3,4	19,5	$C_{14}H_{10}N_4O_3$	59,6	3,5	19,3
IIIc	227—229	0,21	215 (4,23), 250 (4,20), 318 (4,08), 520 (3,59)	1715	3485, 3380, 3150	52,7	3,0	20,8	$C_{15}H_{11}N_5O_5$	52,7	3,2	20,6
IVb	210—211	0,26	212 (4,52), 283 (4,20), 445 (3,98)	1730	3420	60,6	4,0	19,1	$C_{15}H_{12}N_4O_3$	60,8	4,1	18,9
IVc	229—231	0,13	213 (4,42), 282 (4,26), 333 (4,19), 437 (3,98)	1730	3360	52,5	3,3	20,8	$C_{15}H_{11}N_5O_5$	52,7	3,2	20,6
IVd	234	0,20	213 (4,62), 284 (4,34), 465 (3,71)	1710	3430, 3260	52,8	3,2	20,7	$C_{15}H_{11}N_5O_5$	52,7	3,2	20,6
Vc	287—288	0,39	213 (4,42), 310 (4,26), 369 (4,29), 458 (4,08)	1675	3150	52,9	3,3	20,7	$C_{15}H_{11}N_5O_5$	52,7	3,2	20,6
VII	290—292	0,10	226 (4,23), 308 (3,95), 375 (3,84)	1685 1660	3300, 3100	59,3	3,6	17,5	$C_{16}H_{12}N_4O_4$	59,2	3,7	17,3
VIII	263—265	0,31	209 (4,53), 310 (4,03), 370 (4,00), 465 (3,67)	1670	3480, 3370, 3200	59,3	3,6	19,2	$C_{14}H_{10}N_4O_3$	59,6	3,5	19,3
VIa	338—340 [3]	0,48	213 (4,40), 275 (4,41), 313 (4,29), 405 (3,57)	—	3180	63,5	2,9	21,0	$C_{14}H_8N_4O_2$	63,6	3,0	21,2
VIb	235—237	0,88	215 (4,46), 280 (4,50), 320 (4,37), 422 (3,54)	—	—	64,5	3,7	20,4	$C_{15}H_{10}N_4O_2$	64,7	3,6	20,2
VIc	274—275	0,84	208 (4,13), 260 (4,31), 326 (4,65), 405 (3,59)	—	—	56,0	2,9	21,4	$C_{15}H_9N_5O_4$	55,8	2,8	21,6
VId	232—234	0,92	215 (4,51), 266 (4,34), 325 (4,53), 415 (3,58)	—	—	55,9	2,8	21,5	$C_{15}H_9N_5O_4$	55,8	2,8	21,6
IX	363—365	0,48	230 (4,39), 275 (4,42), 317 (4,31), 405 (3,56)	—	3180	63,6	3,0	21,4	$C_{14}H_8N_4O_2$	63,6	3,0	21,2

*Compounds IIIa, c, VIII were crystallized from ethanol, IVb, c, VId from chloroform, IVd, VII, VIa, b, IX from a mixture of ethanol and DMFA, Vc, VIc from DMFA.

†Chloroform–acetone, 10:1.

VIII are similar to the spectra of unsubstituted analogs [2]. The long-wave band of charge transfer from the amino group of the phenyl substituent to the quinoxaline fragment disappears in acetaminophenylnitroquinoxalinone VII, just as in acetaminophenylquinoxalinone. The presence of a nitro group in the quinoxalinone fragment in compounds VIc and VIII leads to a substantial (60 nm) bathochromic shift of the long-wave band in comparison with unsubstituted compounds. The presence of a nitro group in the quinoxaline portion of the nitroindoloquinoxalines VIa-c leads to a certain (up to 10 nm) bathochromic shift of the long-wave band in comparison with unsubstituted analogs [2]. The position of the nitro group (compound IX), as well as the introduction of a second nitro group into the quinoxaline fragment (compound VId), only slightly changes the shape of the spectrum (Table 2). The electronic spectra of Schiff bases IIIa, c are characterized by absorption in the region of 500 nm, which confirms their structure [6].

EXPERIMENTAL

The individuality of the compounds synthesized was monitored by the method of thin-layer chromatography on plates of Silufol UV-254. The electronic absorption spectra of the compounds in ethanol (10^{-4} M) were recorded on a Specord UV-vis spectrophotometer. The IR spectra (in tablets of KBr) were recorded on a UR-20 spectrophotometer.

Interaction of o-Diamines with Isatins. A. To a heated solution of 3 mmoles of the o-diamine Ia [7] in a minimum amount of ethanol, a saturated solution of 3 mmoles of isatin IIa-d in ethanol was added, and the mixture boiled until the starting materials disappeared (thin-layer chromatography). The reaction mass was cooled, and the precipitate, representing the Schiff bases IIIa, c (from isatins IIa, c), the spiro-compound IVb (from isatin IIb), or acetaminophenylquinoxalinone VII (from isatin IId), were filtered off. The filtrate was evaporated and separated by column chromatography on silica gel L40/100 (Chemapol), eluting with a 1:10 mixture of acetone and chloroform.

B. To a heated solution of 3 mmoles of the hydrochloride of the o-diamine Ia in a minimum amount of ethanol or the o-diamine Ib [8] in a 0.1 N solution of HCl in ethanol, or to a solution of the o-diamines Ia, b in acetic acid, a heated solution of 3 mmoles of the isatin IIa-d in the corresponding solvent was added, and the mixture boiled until the starting materials disappeared (thin-layer chromatography). The reaction mass was cooled, diluted with an equal volume of water, and the precipitate filtered off. If it was an individual substance, it was recrystallized from a suitable solvent (Table 2), while the mixture of indoloquinoxaline VIc and aminophenylquinoxalinone Vc was separated by column chromatography on aluminum oxide (pH of the aqueous extract 9-10), eluting with DMFA. The filtrate was neutralized with aqueous ammonia to pH 5-7, extracted with chloroform, the extract evaporated and separated on silica gel L40/100 (Chemapol), eluting with a 1:10 mixture of acetone and chloroform. The yields and characteristics of the compounds obtained are cited in Tables 1 and 2.

3-(2-Aminophenyl)-2(1H)-7-nitroquinoxalinone (VIII). We boiled 0.32 g (1 mmole) of acetaminophenylquinoxalinone VII in 10 ml of a 6 N aqueous solution of HCl for 1 h. The hydrochloride of aminophenylquinoxalinone VIII was filtered off, neutralized with aqueous ammonia to pH 5-7, and the base VIII was obtained. Yield 0.26 g (93%).

3-Nitroindolo[2,3-b]quinoxaline (IX). A solution of 0.14 g (0.5 mmole) aminophenylquinoxalinone VIII in 10 ml of acetic acid was boiled for 6 h. Upon cooling it was diluted with water, alkalinized to pH 9 with aqueous ammonia, the precipitate filtered off, and recrystallized from 10 ml of a 1:1 mixture of ethanol and DMFA. Yield of compound IX 0.06 g (46%).

2,9-Dinitroindolo[2,3-b]quinoxaline (VIc). A solution of 0.16 g (0.5 mmole) aminophenylquinoxalinone Vc in 20 ml of acetic acid with an addition of 0.4 ml of a 6 N aqueous solution of HCl was boiled for 30 h. After cooling it was diluted with water, neutralized to pH 7 with ammonia, the precipitate filtered off and recrystallized from 5 ml of DMFA. Yield of indoloquinoxaline VIc 0.12 g (80%). According to the spectral characteristics and a mixed melting point test, the substance is analogous to the indoloquinoxaline VIc obtained from o-diamine Ia and isatin IIc.

2,3-Dinitroindolo[2,3-b]quinoxaline (VId). We boiled 0.16 g (0.5 mmole) of the spiro-compound IVd in 12 ml of acetic acid with an addition of 0.3 ml of a 6 N aqueous solution of HCl for 25 h. After cooling it was diluted with water, neutralized to pH 7 with aqueous ammonia, and extracted with chloroform. The extract was evaporated and separated by column chromatography on silica gel L40/100 (Chemapol), eluent chloroformacetone, 3:1. Yield of compound VId 0.07 g (43%). According to the spectral characteristics and a mixed melting point test, the substance was analogous to the indoloquinoxaline VId obtained from the o-diamine Ib and N-methylisatin IIb in acetic acid.

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