PRODUCTS OF THE CONDENSATION OF 5-NITRO- AND 5,6-DINITRO-1,2,3-TRIMETHYLBENZIMIDAZOLIUM SALTS WITH o-HYDROXYALDEHYDES

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UDC 547.785.5'814.1:542.953

The corresponding 2-(o-hydroxystyryl)benzimidazoles were obtained by the condensation of aromatic o-hydroxyaldehydes with 5-nitro- and 5,6-dinitro-1,2,3-trimethylbenzimidazolium salts. It was established that derivatives of salicylaldehyde and 5-methoxysalicylaldehyde are capable of intramolecular cyclization in absolute, aprotic solvents to form spiro(benzimidazoline-2,2'-[2H]chromene) derivatives.

In [1] we recently demonstrated that the anhydro bases of 2-(o-hydroxystyryl)-1,3-dimethylbenzimidazolium salts, in contrast to the analogous benzoxazolium [2] and benzothiazolium [3] derivatives, exist in the open form. Assuming that this difference is caused by the low electrophilicity of the meso carbon atom of the imidazole rings, we decided to increase it by the introduction of acceptor groups into the benzene ring of benzimidazole. For this, we undertook the synthesis of 2-(o-hydroxystyryl) derivatives of benzimidazolium salts based on 5-nitro- and 5,6-dinitro-1,2,3-trimethylbenzimidazolium salts. The latter were obtained as the methosulfates (I and II) by alkylation of the corresponding nitro-1,2-dimethylbenzimidazoles with dimethyl sulfate. In alcohol in the presence of piperidine, compound I readily condenses with salicylaldehyde and its derivatives (5-nitro and 3,5-dibromo) and also with 2-hydroxynaphthaldehyde. In the case of II, however, the condensation in basic media is apparently accompanied by hydrolytic cleavage of the imidazole ring. This does not interfere with the preparation of merocyanines with 3,5-dibromosalicylaldehyde and 2-hydroxynaphthaldehyde (VIII and IX), which are only slightly soluble and crystallize from the reaction mass during the reaction. However, if the condensation proceeds comparatively slowly and the mero-

TABLE 1. Solvatochromism of Anhydros Bases (III, V, VI, and IX) in Aqueous Acetone Solutions*

Amt. of water in the acetone, vol.%	z, kcal/mole	λ_{max}, nm				E_t, kcal/mole			
		III	V	VI	IX	III	V	VI	IX
0,0	67,0	—	—	500	—	—	—	57,2	—
1,0	68,1	550	543	—	560	52,0	52,6	—	50,9
2,5	70,0	540	—	—	—	52,8	—	—	—
5,0	72,9	520	530	—	546	54,9	53,9	—	52,1
7,5	75,0	515	—	—	—	55,4	—	—	—
10,0	76,6	510	514	472	536	56,0	55,6	60,6	53,1
15,0	78,7	505	—	—	—	56,5	—	—	—
20,0	80,7	500	504	460	527	57,0	56,7	62,2	54,0
25,0	82,1	490	—	458	—	58,3	—	62,4	—
30,0	83,2	—	496	454	519	—	57,4	63,0	55,0
Constants in the equation $E_t = aZ + b$		a				0,44	0,36	0,36	0,27
		b, kcal/mole				48,4	49,2	54,4	49,5

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*The concentration of III and VI was $0.5 \cdot 10^{-4}$ M, and the concentration of V and IX was $0.25 \cdot 10^{-4}$ M.

Lensovet Leningrad Technological Institute. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 961-966, July, 1971. Original article submitted December 10, 1970.

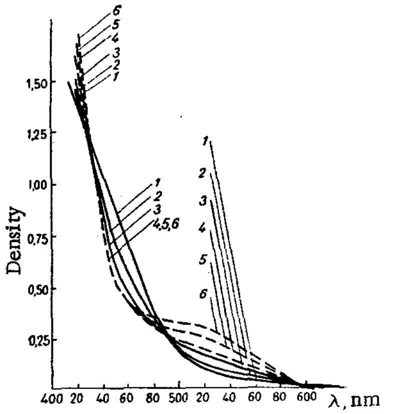


Fig. 1

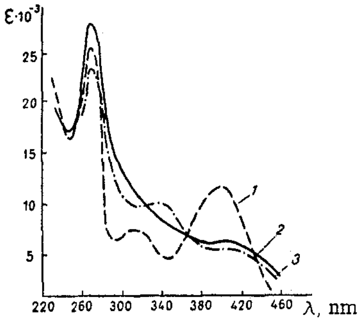
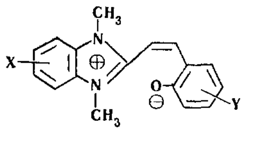


Fig. 2

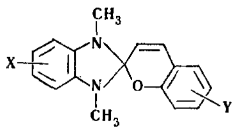
Fig. 1. Absorption spectra of 5,6-dinitro-2-(o-hydroxystyryl)-1,3-dimethyl benzimidazolium (VII, c 0.5 · 10^{-4} M) in aqueous acetone solutions at the following water concentrations: 1) 5; 2) 10; 3) 15; 4) 20; 5) 25; 6) 30 vol.%.

Fig. 2. Absorption spectra of 5-nitro- and 5,6-dinitro-1,3-dimethylspiro(benzimidazoline-2,2'-[2H]chromenes) in dioxane: 1) IIIa; 2) VIIa; 3) Xa (c 0.5 · 10^{-4} M).

cyanines formed remain in solution, the products of the opening of the heteroring hinder the isolation of the merocyanine in pure form. The products of the condensation of II with the appropriate aldehydes were obtained as salts by refluxing in acetic anhydride, and the anhydro bases (VII and X) were isolated from them by the action of ammonia.



III–X



IIIa, VIIa, Xa

III–VI X = 5(6)-NO_2; VII–X X = 5,6-$(NO_2)_2$; III–VII Y = H;
IV, VIII Y = 5',6'-benzo; V, IX Y = 3',5'-Br_2; VI, V Y = 5'-NO_2;
X Y = 5'-OCH_3

The hydrolytic character of the cleavage of the imidazole ring of I and II in the presence of piperidine in alcohol was confirmed in the case of II and 5-nitro-1,3-dimethyl-2-ethylbenzimidazolium perchlorate (XI). Only a mixture of isomeric 4- and 5-nitro-2-methylpropionylamino-N-methylanilines (XII) was isolated, instead of the product of the condensation of XI with salicylaldehyde, in the presence of piperidine. The structures of XII (without separation of the mixture) were proved by their preparation from XI in water by the action of alkali, as well as by the IR, UV, and PMR spectra (in KBr, ν_{NH} 3330 cm^{-1}, ν_{CO} 1660 cm^{-1}; in alcohol λ_{max} 380 nm, log ε 4.25). The following signals are present in the PMR spectrum of a chloroform solution of the mixture of isomers: two triplets from the protons of the methyl groups of the propionyl grouping (1.07 and 1.7 ppm), two adjacent quartets from the protons of the CH_2CO groups (about 2 ppm), a doublet from the three protons of the $NH-CH_3$ group (3.07 ppm), a three-hydrogen singlet from the H_3C-NCO group (3.23 ppm), and a quartet from the proton of the $H-NCH_3$ group (3.78 ppm).

The anhydro bases of the o-hydroxystyryl derivatives of the nitro- and dinitrobenzimidazolium salts (III-X) are intensely colored, crystalline substances with indistinct melting points (with decomposition) of ~280°. Some of them (III, IV, and VII) form crystalline hydrates. The presence of water of hydration was detected from the intense absorption at ~3600 cm^{-1} in the IR spectra of solutions in acetonitrile and was confirmed by elementary analysis. Compounds III-X are moderately soluble in polar organic solvents, and slightly soluble or insoluble in water and nonpolar organic solvents. Absorption in the region of the vibrations of the carbonyl group is absent in the IR spectra of crystalline samples (in KBr) of III-X, which attests to considerable polarization of the conjugated system and proximity to a dipolar limiting structure.

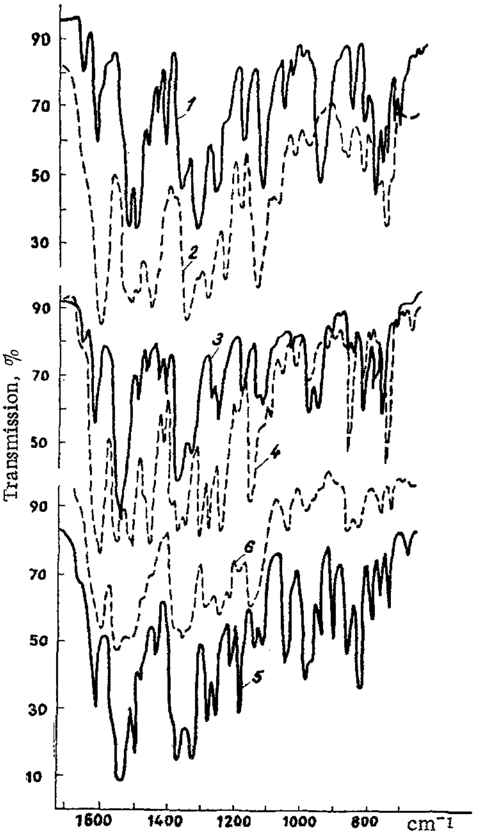


Fig. 3. IR spectra of 2-(2-hydroxystyryl)-benzimidazoliums and the corresponding spiro(benzimidazolinechromenes) (in KBr): 1) IIIa; 2) III; 3) VIIa; 4) VII; 5) Xa; 6) X.

Also in accord with this sort of structure is the dependence of the electronic absorption spectra of III-VI, VIII, and IX on the nature of the solvent. These compounds have the clearly expressed negative solvatochromism (Table 1) that is characteristic for intraionoid compounds [4]. It should be noted that a solution of III in anhydrous acetone (in contrast to a solution in alcohol) has λ_{max} 380 nm. When water (~1%) is added, the color of the acetone solution deepens sharply, and an absorption band with a maximum of ~545 nm appears in the spectrum. A linear dependence of the energy of transition of the long-wave absorption band (E_t) from the Z value of the solvent [5] ($E_t = aZ + b$) is observed for III, V, VI, and IX in aqueous acetone solutions. As seen from the data in Table 1, the degree of shifting of λ_{max} from Z, i.e., the polarizability of the conjugated system, depends on the nature of the substituents in both parts of the molecule. As expected, simultaneous reinforcement of the acceptor properties of the substituents in both portions of the molecule leads to a decrease in the shift; two bromine atoms in the meta position relative to the conjugation chain, in accordance with the σ_1 value for bromine, have the same effect as one meta nitro group [6]. At the same time, the presence of a nitro group in the para position relative to the phenolic oxygen of the aldehyde component results (in contrast to the bromine atoms in the ortho and para positions relative to it) in a significant decrease in the conjugation of the phenoxide oxygen with the acceptor in the heterocyclic portion of the molecule ($b^{IV} - b^{III} = 6$ kcal/mole, and $b^{V} - b^{III} = 0.8$ kcal/mole).

A different pattern is observed for VII and X. Although VII and X are intensely colored in the crystalline state, their alcohol solutions do not give an absorption band with a maximum above 400 nm. These compounds and, as noted above, III behave anomalously in acetone solution. A comparison of the spectra of VII in aqueous acetone solutions (Fig. 1) shows that there is an equilibrium between the two forms of VII (VII and VIIa). An intensely colored compound with λ_{max} ~ 510 nm (30% H_2O) appears as the percentage of water increases. A small hypsochromic shift of the absorption curves relative to the isopiestic point as the percentage of water increases (above 15%) is apparently induced by the negative solvatochromism of the colored form of VII. We assumed that the most probable reason for the sharp increase in the color of III (see above), VII, and X in anhydrous acetone is intramolecular cyclization with the formation of compounds of the spiropyran type (IIIa, VIIa, and Xa). This cyclization could most likely have been expected precisely for these compounds as a consequence of the increased nucleophilicity of the oxygen atom.

To verify this assumption, we attempted to isolate the indicated highly colored forms. For this, III, VII, and X were dissolved by heating in anhydrous acetone, the solutions were evaporated in vacuo to a small volume, and the dissolved substances were precipitated by the addition of petroleum ether and then reprecipitated from benzene by the addition of petroleum ether. Compounds IIIa, VIIa, and Xa obtained in this way dissolved readily in organic solvents of low polarity (the solubility of VIIa in benzene was 0.8% at 20° compared with 5% in dioxane) and melted at much lower temperatures than the starting III, VII, and X. These properties attest to the relatively low polarity of IIIa, VIIa, and Xa. Dioxane solutions of them are yellow (Fig. 2), which does not contradict a cyclic structure including a fragment of the p-nitroaniline type. The absorption spectra of these solutions are monotypic. In addition, the spectra of dioxane solutions of III and IIIa, VII and VIIa, and X and Xa are identical, which attests to intramolecular cyclization of III, VII, and X in absolute dioxane.

A comparison of the IR spectra of IIIa, VIIa, and Xa with those of the corresponding merocyanine forms (III, VII, and X, Fig. 3) also confirms the spiropyran structure of the former [7, 8]. The IR spectra of IIIa,

TABLE 2. 2-(o-Hydroxyarylvinyl)benzimidazoliums (III-X)

Comp.	X	Y	Absorption spectrum (alcohol)		R_f*	Empirical formula	Found %			Calc. %			Yield, %
			$c \cdot 10^5$ m	λ_{max}, nm (lg ε)			C	H	N	C	H	N	
III	5-NO_2	H	3,7	350, 495 (4,14; 4,06)	0,65 (E : EA, 4 : 1)	$C_{17}H_{15}N_3O_3 \cdot 1/2H_2O$	64,0	5,5	13,1	64,1	5,0	13,2	53
IV	5-NO_2	5′,6′-Benzo	1,0	260, 535 (5,33; 4,25)	0,72 (E : EA, 3 : 2)	$C_{21}H_{17}N_3O_3 \cdot H_2O$	67,6	5,6	11,4	66,9	5,0	11,1	72
V	5-NO_2	3′,5′-Br_2	0,33	255, 345, 494 (4,4; 4,26; 4,22)	0,66 (E : EA, 1 : 4)	$C_{17}H_{13}Br_2N_3O_3$	Br	34,4	9,2	Br	34,2	9,0	71
VI	5-NO_2	5′-NO_2	0,33	310, 400, 452 (4,18; 4,22; 4,28)	0,45 (E : EA, 1 : 4)	$C_{17}H_{14}N_4O_5$	—	—	15,9	—	—	15,8	91
VII	5,6-$(NO_2)_2$	H	4,7	277, 340, 380 (4,23; 4,08; 4,0)	0,67 (E : EA, 1 : 3)	$C_{17}H_{14}N_4O_5 \cdot 1/2H_2O$	56,3	4,5	15,9	56,2	4,1	15,4	34
VIII	5,6-$(NO_2)_2$	5′,6′-Benzo	1,0	237, 278, 555 (4,56; 4,26; 4,04)	0,53 (E : EA, 1 : 9)	$C_{21}H_{16}N_4O_5$	62,0	4,4	13,2	62,5	4,0	13,8	67
IX	5,6-$(NO_2)_2$	3′,5′-Br_2	1,0	250, 352, 515 (4,33; 4,13; 4,13)	0,78 (EA)	$C_{17}H_{12}Br_2N_4O_5$	Br	31,6	10,8	Br	31,2	10,9	69
X	5,6-$(NO_2)_2$	5′-OCH_3	—		0,8 (E : D, 1 : 3)	$C_{18}H_{16}N_4O_6$	55,9	4,6	14,6	56,2	4,2	14,6	38

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* From chromatography on activity II aluminum oxide; E is ethanol, EA is ethyl acetate; D is dioxane.

† Compounds IV-VI, VIII, and IX were crystallized from alcohol (~1 : 100), and III, VII, and X were crystallized from 60% alcohol (~1 : 35).

TABLE 3. 5-Nitro- and 5,6-Dinitro-1,3-dimethylspiro(benzimidazoline-2,2′-[2H]chromenes) (IIIa, VIIa, and Xa)

Comp.	X	Y	mp	Empirical formula	Found %			Calc. %			Yield, %
					C	H	N	C	H	N	
IIIa	5-NO_2	H	136	$C_{17}H_{15}N_3O_3$	66,5	5,2	13,7	66,1	4,9	13,6	20
VIIa	5,6-$(NO_2)_2$	H	208	$C_{17}H_{14}N_4O_5$	57,1	4,8	15,9	57,6	4,0	15,8	43
Xa	5,6-$(NO_2)_2$	5-OCH_3	161	$C_{18}H_{16}N_4O_6$	55,6	4,5	14,3	56,2	4,3	14,6	32

VIIa, and Xa contain absorption bands at 1640-1650 cm^{-1} ($\nu_{C=C}$ of the pyran ring) and at 940-960 cm^{-1} (a band characteristic for spiropyrans, but its assignment is not unambiguous), which are absent in the spectra of merocyanine, and the bands at about 1420-1435 cm^{-1} and 1210-1220 cm^{-1} that are found in the spectra of III, VII, and X are absent. In addition, the spectra differ markedly at 1500-1600 cm^{-1}: for the spirans, the intensity of the band of the aromatic ring at 1610 cm^{-1} is about one-half the intensity of the $\nu_{NO_2\text{-as}}$ band, while the intensities are about the same for the merocyanines.

EXPERIMENTAL

5-Nitro-1,2,3-trimethylbenzimidazolium Methosulfate (I). A 3.8 g (0.02 mole) sample of a mixture of 5- and 6-nitro-1,2-dimethylbenzimidazoles (obtained by the action of dimethyl sulfate on 2-methyl-5-nitrobenzimidazole in potassium hydroxide) and 2.35 ml (0.025 mole) of dimethyl sulfate was heated at 140° until everything dissolved. The reaction was considered to be complete when a sample of the mass dissolved completely in water (after about 30 min). The melt was triturated with 30 ml of acetone, and the colorless crystals were removed by filtration. Crystallization from acetone (1 : 70) gave 2.7 g (43%) of I with mp 175°. Compound I dissolved readily in water and alcohol and had R_f 0.45 [Al_2O_3 with elution by chloroform–ethyl acetate (1 : 9)]. Found %: N 13.4; S 10.2. $C_{11}H_{15}N_3O_6S$. Calculated %: N 13.2; S 10.1.

5,6-Dinitro-1,2,3-trimethylbenzimidazolium Methosulfate (II). A mixture of 8 g (0.034 mole) of 5,6-dinitro-1,2-dimethylbenzimidazole [9] and 6.6 ml (0.068 mole) of dimethyl sulfate was heated at 140° until the reaction mass dissolved completely in water (after about 30 min). The viscous mass was triturated with 40 ml of acetone, and the solid was filtered and washed with acetone to give 9.8 g (80%) of II. Crystallization from alcohol gave a product with mp 242° and R_f 0.3 [Al_2O_3 with elution by alcohol–ethyl acetate (1 : 3)]. Found %: N 15.7; S 9.1. $C_{11}H_{14}N_4O_8S$. Calculated %: N 15.5; S 8.8.

5-Nitro- and 5,6-Dinitro-1,3-dimethyl-2-(2-hydroxyarylvinyl)benzimidazoliums (III-X, Table 2). The appropriate aldehyde (2 mmole) and 1.2 ml (12 mmole) of piperidine were added to a hot solution of 2 mmole of I or II in 15 ml of alcohol. The solution acquired an intense color after the addition of piperidine. The mixture was stirred with refluxing for about 30 min until a precipitate developed (IV-VI, VIII, and IX), or (in the preparation of III) until I was no longer present in the reaction mass (as monitored by chromatography on Al_2O_3). The precipitate was filtered (III was isolated after the addition of a twofold amount of water), washed with water, and crystallized; the purity of the compounds was monitored chromatographically.

Compounds VII and X were obtained after refluxing a solution of 1.5 mmole of II and 1.5 mmole of salicylaldehyde or 5-methoxysalicylaldehyde in 3 ml of acetic anhydride for 12-15 h. The mixture was cooled, 7 ml of water was added, 1 ml of concentrated HCl was added, and the mixture was refluxed for 20 min with activated charcoal. The crystals of the hydrochlorides of VII or X that precipitated after cooling were separated by filtration and crystallized from water. (They dissolved on heating in 150 ml portions of water followed by evaporation to one-half the original volume.) The thus purified salt was dissolved in hot water (1 : 150), the solution was cooled, and 25% ammonium hydroxide was added until the mixture had pH 9-10. The resulting deeply colored, finely crystalline precipitates of VII or X were filtered, washed with water, and crystallized from aqueous alcohol.

5-Nitro- and 5,6-Dinitro-1,3-dimethylspiro(benzimidazoline-2,2'-[2H]chromenes) (IIIa, VIIa, and Xa, Table 3). A 0.1 g sample of III, VII, or X was refluxed for 30 min with 120 ml of anhydrous acetone. The solution was filtered, evaporated to 30 ml in vacuo, and 60 ml of petroleum ether was added. The resulting precipitate was filtered and dissolved by heating in 100 ml of absolute benzene. The solution was filtered, evaporated in vacuo to 10 ml, and 50-70 ml of petroleum ether was added. The resulting precipitate was filtered, washed with petroleum ether, and dried in a vacuum desiccator.

5-Nitro-1,3-dimethyl-2-ethylbenzimidazolium Perchlorate (XI). Like I, this was similarly obtained in 30% yield from 5(6)-nitro-2-ethylbenzimidazole [10]. The melt was dissolved in alcohol, and XI was precipitated by the addition of magnesium perchlorate to this solution to give a product with mp 225° (alcohol) and R_f 0.3 (Al_2O_3 with elution by chloroform). Found %: Cl 11.1. $C_{11}H_{14}ClN_3O_6$. Calculated %: Cl 11.1.

4- and 5-Nitro-2-methylpropionylamino-N-methylanilines (XII). A total of 2 ml (3.5 mmole) of 10% potassium hydroxide was added with stirring to a solution of 0.6 g (2 mmole) of XI in 10 ml of water, and the resulting flocculent yellow precipitate was washed with water until it gave a neutral reaction to give 0.38 g (64%) of XII with mp 175° [from benzene (1 : 30)] and R_f 0.8 (Al_2O_3 and elution with chloroform). Found %: C 55.4; H 6.6. $C_{11}H_{15}N_3O_3$. Calculated %: C 55.6; H 6.3.

The UV spectra were recorded with SFD-2, (Fig. 2 and Table 2), and SF-10 spectrometers (Fig. 1 and Table 1). The IR spectra were recorded with an IKS-22 spectrometer, and the PMR spectrum was obtained at a frequency of 100 MHz.

LITERATURE CITED

1. L. S. Éfros, É. R. Zakhs, and N. K. Beresneva, Khim. Geterotsikl. Soedin., 1004 (1970).
2. Australian Patent No. 62,296 (1960); British Patent No. 889,196 (1962).
3. R. Guglielmetti and J. Metzger, Bull. Soc. Chim. France, 3329 (1969).
4. A. I. Kipriyanov, Usp. Khim., 29, 1337 (1960).
5. E. Kosower, J. Am. Chem. Soc., 80, 3253 (1958).
6. Handbook of Chemistry, Vol. 3 [in Russian], Khimiya (1964), pp. 959, 962.
7. I. Ya. Pavlenishvili, Author's Abstract of Dissertation [in Russian], Tbilisi (1970).
8. G. Arnold and G. Paal, Tetrahedron., 25, 5995 (1969).
9. K. Fries, E. Modrow, B. Racke, and K. Weber, Ann., 454, 216 (1927).
10. T. Momai, H. Higurashi, M. Abe, and D. Mizuno, Yakugaku Zasshi, 78, 242 (1958); Chem. Abstr., 52, 11,822b (1958).