SYNTHESIS OF BIS(o-HYDROXYPHENYL)-1,3,5-TRIAZINES, 1,2,4-TRIAZOLES, AND OXADIAZOLE BY RECYCLIZATION OF THE o-HYDROXYPHENYL-4-OXO-1,3-BENZOXAZINIUM CATION

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The acidic cyclization of disalicylamide gave 2-(o-hydroxyphenyl)- and 2-(oacetoxyphenyl)-4-oxo-1,3-benzoxazinium perchlorates, by reaction of which with hydroxylamine, hydrazines, benzamidine, guanidines, and S-methylisothiourea bis(o-hydroxyphenyl)-1,2,4-oxadiazole, triazoles, and sym-triazines were synthesized. Mono- and bis(o-acetoxyphenyl)triazoles were obtained.

Bis(o-hydroxyphenyl)-sym-triazines have recently found application as highly effective light stabilizers for polymers [1, 2]. The aim of the present research was to develop a general method for the synthesis of derivatives of this series of compounds, as well as their azole analogs — a special group of heterocyclic luminophores with improved (owing to intramolecular phototransfer of a proton) luminescence properties [3].

We have previously shown the possibility of the preparation of o-hydroxyphenyl-1,2,4oxadiazoles and triazoles by the reaction of 4-oxo-1,3-benzoxazinium salts (I) with hydroxylamine, hydrazine hydrate, and monosubstituted hydrazines [4, 5]. In a continuation of these studies the recyclization of the oxazinone ring was used for the preparative synthesis of previously unknown bis(o-hydroxyphenyl)-1,2,4-oxadiazole (VI) and triazoles VII on the basis of the newly synthesized o-hydroxyphenyl-4-oxo-1,3-benzoxazinium perchlorate (II) and was extended for the first time to the preparation of bis(o-hydroxyphenyl)-sym-triazines (IX) by the reaction of perchlorate II with amidines (benzamidine, guanidine, methylguanidine, and Smethylisothiourea).

The synthesis of the indicated heterocyclic compounds (method A) is realized by the addition of a 1,2- or 1,3-bifunctional amine in alcohol or glacial acetic acid to perchlorate II with subsequent refluxing of the mixture for 2-5 min. The recyclization is also realized at room temperature (see the scheme at top of page after Table 1), but the products are obtained in lower yields. The resulting heterocycles are isolated from the reaction mixtures in the form of colorless or light-yellow crystalline substances that are virtually insoluble in water.

Data on the yields and properties of the synthesized substances are presented in Table 1. Their structures and compositions were confirmed by the results of elementary analysis, data from PMR and IR spectroscopy, and, in the case of triazines, synthesis of previously known compounds (IXa,b) [6].

The IR spectra of the compounds obtained by recyclization of perchlorate II do not contain the bands of carbonyl absorption that are characteristic for products of cleavage and ring opening and most derivatives of benzoxazinium salts I [7], and this confirms their structure. A group of bands of medium intensity of heteroatomatic absorption at 1505-1635 cm⁻¹ and two absorption bands that are characteristic for the vibrations of Ar-O-H bonds at 1210-1265 cm⁻¹ are present in the spectra of these compounds (see Table 1).

The absorption of the phenolic OH groups in the oxadiazole shows up in the form of two bands of medium intensity at 3320 and 3200 cm^{-1} , which are shifted to the low-frequency region as a consequence of the formation by the hydroxy groups of strong intramolecular hydrogen bonds (IHB) with the heteroring nitrogen atoms.

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	н	3,9 4,3	4,9 4,6 8,8	4,2 4,9	4,6	roton 10.3%
	<u>ں</u>	66,1 65,6	69,9 65,7 65,3	61,7 66,0	69,7	f OH p
Empirical formula		C14H16N2O3 C14H11N3O2	C ₁₅ H ₁₅ N ₃ O ₂ C ₂₀ H ₁₅ N ₃ O ₂ C ₁₆ H ₁₄ N ₄ O ₂	C ₁₆ H ₁₃ N ₃ O ₂ S C ₁₇ H ₁₅ N ₃ O ₃	C24H19N3O4	om (singlets o 1% falsnalate
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	н	4,5 5,2	4,8 4,6 7,7	5,4 4,5	4,5	and 1.
	υ	66,6 65,3	70,1 65,5 65,6	61,9 65,6	669,9	1 9.71
IR spectrum, cm ⁻¹	Ar-0-H	1235, 1220 1250, 1235	1245, 1220 1260, 1250 1265, 1230	1240, 1225 1210, 1200	1230, 1210	ArH), and
	aromatic C ≈ N and C = C	1610, 1585, 1557 1605, 1595 (sh.), 1560,	1625, 1585, 1510 1635, 1600, 1505 1635, 1615, 1595 (sh),	1615, 1587, 1540 1675 (sh.), 1600, 1555,	1703, 1610, 1595, 1580, 1535	5.85-8.09 (8H, m,
	ococH ₃			1700	1745	сн _э), (
	ни & но	3320, 3200 2695, 1835	3190 3280 3285, 2641			(3H, s, N
mp, °C tion sol- vent		167—168 PrOH 309—310 Aqueous DMF	137-138 Aqu. PrOH 150-151 The same 244 Aqu. DMF	151—152 PrOH 196—197 C ₆ H ₆	118	pectrum: 4.12
Com- pound		VII a	VIIb ^a VIIc IXc	qIIIV	x	aPMR si

Synthesized Bis(o-hydroxyphenyl)heterocycles (VI, VII, IX) and Triazole Acetates (VIIIb, X) TABLE 1.



II, IV, VII $R^1=H$; III, V, VIII $R^1=Ac$; VII, VIII a R=H, b R=Me, c R=Ph; IX a R=Ph, b $R=NH_2$, c R=NHMe, d R=SMe

The presence in the spectra of triazoles VIIb,c of only one weak absorption band at 3190 and 3280 cm⁻¹, respectively, indicates further (as compared with oxadizole) strengthening of the IHB and the formation of stronger quasi-aromatic rings, particularly those formed by 3-(o-hydroxyphenyl) substituents; this is also confirmed by the shift of the signals of the pro-tons of the OH group in the PMR spectra to the weak-field region (to 11.3 ppm).

The absorption bands of the phenolic groups in the spectrum of triazole VIIa are overlapped by the absorption of the stretching and deformation vibrations of the NH groups, which show up in the form of broad bands at 2205-3185 and $1720-1903 \text{ cm}^{-1}$, respectively.

Absorption bands of OH groups at $3115-3600 \text{ cm}^{-1}$ are not observed in the case of the triazines, probably because of the formation of strong IHB and, in the case of triazines IXb,c, because of possible masking by the broad absorption of the amino groups.

Starting o-hydroxyphenyl-enzoxazinium perchlorate II was obtained by acidic cyclization [8] of disalicylamide [9] in the presence of acetic anhydride as the dehydrating agent. However, in carrying out the synthesis one should take into account the possibility, when excess acetic anhydride is present, of obtaining, in addition to perchlorate II, its 0-acetate, viz., 2-(o-acetoxyphenyl)-4-oxo-1,3-benzoxazinium perchlorate (III), and, as a consequence, the formation in the recyclization of uncrystallized perchlorate II of bis(o-hydroxyphenyl)heterocycles containing their monoacetates as impurities. The weak bands of ester absorption at 1700 cm⁻¹ in the IR spectra and the different integral intensities of the signals of the protons of the OH groups in the PMR spectra, as well as the low-intensity signal of the methyl protons of the acetate grouping at 1.23 ppm, constitute evidence for partial acetylation of the 3-(o-hydroxyphenyl) substituents of the triazoles corresponding (according to the previously proposed [5] recyclization scheme) to the o-hydroxyphenyl substituent of starting cation II. When the triazoles are recrystallized, the intensities of the bands of ester absorption in the IR spectra decrease, and the decrease in the intensity of the acetate signal in the PMR spectra is accompanied by an increase in the intensity of the weak-field signal of the OH proton, which indicates a decrease in the percentage of acetylated heterorings during recrystallization.

When the synthesis of the triazoles is carried out in alcohol, their monoacetates are not formed even on the basis of a genuine sample of acetate III, i.e., deacylation possibly does not accompany but rather precedes recyclization of the oxazinone ring, since acetate III is readily converted to perchlorate II during recrystallization in acetic acid with added DMF (to increase the solubility). Despite this, we were able to realize the recyclization of perchlorate III in acetic acid with retention of the acetate group and obtained 3-(o-acetoxyphenyl)triazole VIIIb in 40% yield.

However, the instability of perchlorate III with respect to deacylation under the influ-

ence of bases (hydrazines, DMF, etc.) indicates that the production of partially acetylated bis(o-hydroxyphenyl)triazoles is probably not associated with the possible formation of its acetate during the synthesis of perchlorate II but rather occurs directly under the conditions of recyclization of perchlorate II with the participation of the acetates or acetylhydrazines that are readily formed under these conditions [10].

In the preparation of triazole X we showed the possibility of the preparative synthesis of the diacetates of the synthesized heterocycles VI, VII, and IX by their acid-catalyzed acetylation.

Recyclization under the influence of hydroxylamine, hydrazines, and amidines to give oxadiazole, triazoles, and triazines is also readily accomplished with o-hydroxyphenyl-4- oxo-1,3-benzoxazine (IV) (method B), which was obtained by deprotonation of perchlorate II, and by the method in [6].

The synthesized bis(o-hydroxyphenyl)heterocycles can also be obtained by direct condensation of disalicylamide with 1,2- and 1,3-bifunctional amines; however, the yields in this case are low and, in the case of triazines, are generally insignificant [6].

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a Specord 71 IR spectrometer. The PMR spectra of solutions of the triazoles in tetrachloroethane with deuteration and of a solution of triazine IXd in CF_3COOH were recorded with a Tesla BS-467 spectrometer at 20°C with hexamethyldisiloxane as the internal standard.

2-(o-Hydroxyphenyl)-4-oxo-1,3-benzoxazinium Perchlorate (II). A solution (obtained by cooling) of 1 ml (0.01 mole) of 70% HClO₄ in 3 ml of acetic anhydride was added to a suspension of 2.55 g (0.01 mole) of disalicylamide [9] in 15 ml of glacial acetic acid, and the reaction mixture was refluxed until crystals were liberated. It was then cooled, diluted with a threefold excess of ether, and filtered to give 2.42 g (74%) of yellow crystals with mp 208-211°C (dec.) (from glacial acetic acid with the addition of DMF until the solid dissolved). IR spectrum: 3030 (sh), 2930 (sh), 1740, 1600, 1550, 1505, 1490, 1130, and 1050 cm⁻¹. Found: C 49.9; H 3.2; Cl 10.0; N 4.4%. C₁₄H₉NO₃·HClO₄. Calculated: C 49.5; H 3.0; Cl 10.4; N 4.1%.

2-(o-Hydroxypheny1)-4-oxo-1,3-benzoxazine (IV), with mp 200-201°C (from propanol) [6], or the starting disalicylamide, with mp 197-198°C (dec., from aqueous alcohol) [9], was formed in quantitative yield when perchlorate II was treated with excess triethylamine or water, respectively.

 $\frac{2-(o-Acetoxypheny1)-4-oxo-1, 3-benzoxazinium Perchlorate (III) or Perchlorate (II). These compounds were obtained in quantitative yield by treatment of a suspension of benzoxazinone IV in acetic anhydride or in glacial AcOH with an equimolar amount of 70% HClO₄. Perchlorate III was obtained in the form of light-yellow crystals with mp 237°C (dec.). IR spectrum 3185 (sh), 1780 (OCOCH₃), 1740 (C=O), 1620, 1595, 1565, 1510, 1170, and 1105 cm⁻¹. Found: C 50.3; H 2.8; N 3.7; Cl 9.3%. C16H11NO4.HClO₄. Calculated: C 50.6; H 3.0; N 3.4; Cl 9.0%.$

 $\frac{2-(o-Acetoxypheny1)-4-oxo-1,3-benzoxazine (V).}{One drop of HClO_4 was added to a suspension of 1.15 g (5 mmole) of benzoxazine IV in 3 ml of acetic anhydride, and the mixture was heated to the boiling point, cooled, and filtered to give 1.1 g (87%) of light-yellow crystals with mp 203-204°C (from aqueous alcohol). IR spectrum: 1740 (OCOCH_3), 1690 (C=O), 1610, 1560, and 1200 cm⁻¹. Found: C 68.6; H 3.7; N 4.8%. C16H11NO4. Calculated: C 68.3; H 3.9; N 5.0%.$

Benzoxazinone V was also obtained in quantitative yield by treatment of perchlorate III with excess triethylamine.

<u>3,5-Bis(o-hydroxyphenyl)-1,2,4-oxadiazole (VI).</u> A 0.69-g (0.01 mole) sample of hydroxylamine hydrochloride and 1.70 g (5 mmole) of perchlorate II or 1.20 g (5 mmole) of benzoxazinone IV were added successively to a suspension of 0.82 g (0.01 mole) of anhydrous AcONa in glacial AcOH, and the reaction mixture was heated to the boiling point, cooled, diluted with water, and filtered to give colorless crystals with mp 167-168°C (from propanol).

3,5-Bis(o-hydroxyphenyl)-1,2,4-triazoles (VIIa,c). A 1.7-g (5 mmole) sample of perchlorate II was added to an alcohol solution of 0.6 ml (0.01 mole) of hydrazine hydrate or 1.0 ml (0.01 mmole) of phenylhydrazine, and the reaction mixture was refluxed for 30 min, cooled, and diluted with water to give, respectively, colorless or light-brown crystals. Triazoles VIIa, c were similarly obtained from benzoxazine IV.

<u>1-Methyl-3,5-bis(o-hydroxyphenyl)-1,2,4-triazole (VIIb).</u> A 0.98-g (5 mmole) sample of methylhydrazine sulfate and 1.70 g (5 mmole) of perchlorate II were added successively to an alcohol solution of 0.5 g of Na in 19 ml of propanol, and the reaction mixture was heated rapidly to the boiling point. After 30 min, the mixture was cooled, diluted with water, and extracted with ether. The ether was evaporated to give 1.02 g (80%) of a light-brown product with mp 134-135°C (from aqueous propanol).

<u>l-Methyl-3-(o-hydroxyphenyl)-5-(acetoxyphenyl)-1,2,4-triazole (VIIIb).</u> A 0.47-g (5 mmole) sample of methylhydrazine sulfate and 0.98 g (25 mmole) of perchlorate III were added successively to a suspension of 0.41 g (5 mmole) of AcONa in 7 ml of AcOH, and the reaction mixture was refluxed for 5 min, cooled, diluted with water, and extracted with ether. The extract was dried, and the ether was evaporated. The oily residue was dissolved by heating in benzene, and the solution was worked up to give 0.28 g (40%) of colorless crystals with mp 196-197°C (from benzene).

<u>1-Phenyl-3,5-bis(o-acetoxyphenyl)-1,2,4-triazole (X)</u>. Two drops of 70% HClO₄ were added to a suspension of 1.64 g (5 mmole) of triazole VIIc in acetic anhydride, and the mixture was heated to the boiling point, cooled, and treated with water. The resulting oil crystallized on standing to give 2.02 g (96%) of colorless crystals with mp 118-119°C (from aqueous alcohol).

2,6-Bis(o-hydroxyphenyl)-1,3,5-triazines (IXa,c,d). A 1.36-g (10 mmole) sample of methylguanidine nitrate or 1.39 g (5 mmole) of S-methylisothiourea sulfate and 1.70 g (5 mmole) of perchlorate were added successively to an alcohol solution of 0.5 g of Na in 19 ml of propanol, and the reaction mixture was heated rapidly, refluxed for 3 min, cooled, and diluted with water. The light-yellow reaction products were removed by filtration.

Triazines IXb,c, were similarly obtained from benzoxazinone IV in 46 and 43% yields, respectively.

Triazine IXc and NH triazole VIIA were slightly soluble in polar organic solvents at room temperature but were more soluble in the hot solvents. Benzoxazinone IV, oxadiazole VI, triazines IXa,b,c, and n-substituted triazoles VIIb,c and X were quite soluble. In contrast to acetates V and X, o-hydroxyphenylbenzoxazinone IV, oxadiazole VI, triazoles VIIa-c and VIIIb, and triazines IXa-d gave a brown or violet coloration with an alcohol solution of ferric chloride.

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