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SYNTHESIS AND PROPERTIES OF CONDENSED DERIVATIVES OF RESORUFIN

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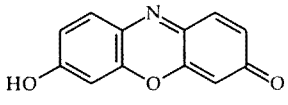
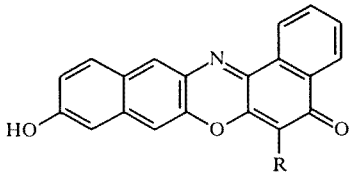
10-Hydroxy-5H-dibenzo[a,i]phenoxazin-5-one and its 6-chloro derivative — condensed derivatives of resorufin, simultaneously containing in the molecule linearly and angularly condensed benzene rings — were synthesized. Their spectral–luminescent properties were investigated.

The hydroxy derivatives of phenoxazinones, and in particular resorufin (7-hydroxy-3H-phenoxazin-3-one), are effective luminophores of red luminescence and are widely used as generating compounds in returned lasers of the visible range of the spectrum [1, 2]. Since the extension of the π-electronic system of the luminophores often leads to a substantial change in their spectral–luminescent properties, it was of interest to study the condensed analogs of resorufin, in particular the linear-annelated ones, containing an extended oxazine chromophore system.

In the present article, the synthesis and the spectral–luminescent properties are described of 10-hydroxy-5H-dibenzo[*a*,i]phenoxazin-5-one (I) and its 6-chloro derivative (II) simultaneously containing in the molecule the linearly and angularly condensed benzene rings.



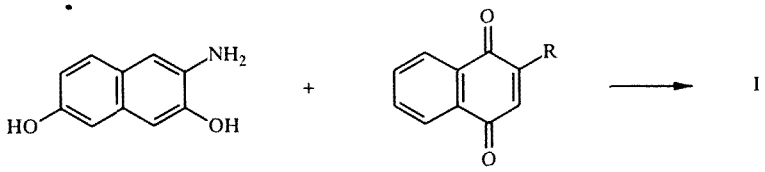
Resorufin



I R = H; II R = Cl

As known, phenoxazinones condensed at the quinoid moiety are formed in the reaction of o-aminophenols with 2-hydroxy-1,4-naphthoquinone [3]. The characteristic feature of this reaction is the fact that formation of the phenoxazine system occurs in it as a result of the reaction of the corresponding 2-(2′-hydroxyanilino)-1,4-naphthoquinone, the primary condensation product, with a second molecule of o-aminophenol, and therefore the ratio of the reagents substantially influences the yield of the reaction products.

Compound I was obtained in the present work by two methods, in analogy with [3]: by a condensation of 2,7-dihydroxy-3-aminonaphthalene (III) with 2-hydroxy-1,4-naphthoquinone (method A) or with 2-(2′-hydroxyanilino)-1,4-naphthoquinone (method B), but its yield did not exceed 7% in both cases.



R = OH (method A), *o*-OHC_6H_4NH (method B)

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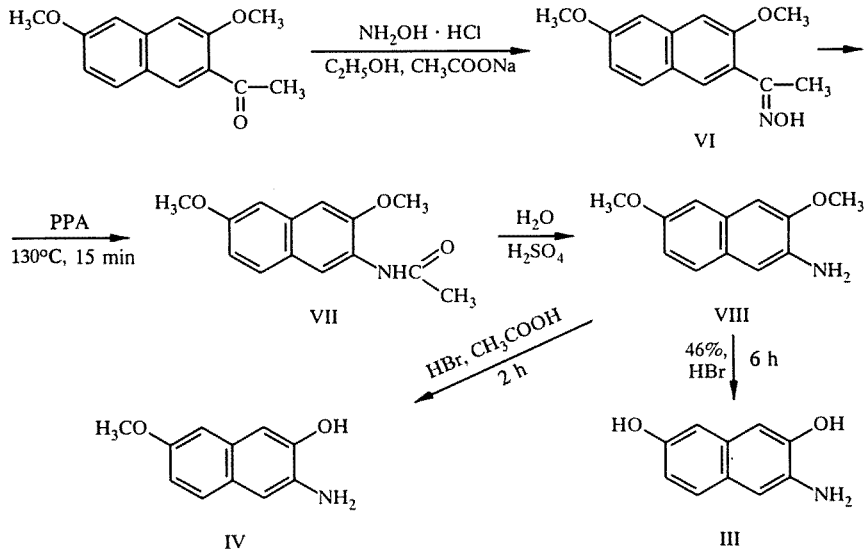
TABLE 1. PMR Spectra of Compounds I and II in DMSO-d_6

Compound	Chemical shifts, δ, ppm (J, Hz) aromatic protons									
	1-H	2-H	3-H	4-H	6-H	8-H	9-H	11-H	12-H	13-H
I	8,14 d (8,12)	7,82 t (8,40, 7,33)	7,90 t (7,27, 7,0)	8,65 d (7,32)	6,44 s	8,36 s	7,20 d (1,94)	7,12 d. d (9,0, 2,18; 9,0, 2,11)	8,0 d (9,0)	7,68 s
II	8,21 d (7,76)	7,85 t over-laps s 13-H	7,95 t (8,11, 6,89)	8,68 d (7,95)		8,43 s	7,26 s	7,16 d. d (9,0, 6,84)	8,04 d (8,93)	7,68 s over-laps s 2-H

On the other hand, during the condensation of 2-hydroxy-7-methoxy-3-aminonaphthalene (IV) with 2-hydroxy-1,4-naphthoquinone, instead of the corresponding phonoxazinone, 2-(2′-hydroxy-7-methoxynaphthyl-3′-amino)-1,4-naphthoquinone (V) is formed in an almost quantitative yield. In an attempt to carry out the reaction of compound V with compounds III and IV by method B, the closure of the phenoxazine ring did not take place.

In the reaction of substituted o-aminophenols with 2,3-dichloro-1,4-naphthoquinone in an alcoholic medium in the presence of potassium acetate, as shown in [4], the corresponding 6-chlorophenoxazin-5-ones are formed. Thus, 6-chloro-5H-dibenzo[*a*,i]phenoxazin-5-one was obtained rom 3-amino-2-naphthol by this method in a yield of 18%. Condensation of compound III with 2,3-dichloro-1,4-naphthoquinone under these conditions gave compound II in a yield of only 3%.

The starting compounds III and IV were obtained by the following scheme: the Beckmann rearrangement of 2-acetyl-3,6-dimethoxynaphthalene (VI) oxime in the presence of polyphosphoric acid (PPA) gave 2-acetylamino-3,6-dimethoxynaphthalene (VII), which was converted in dilute sulfuric acid into the corresponding amine (VIII), forming compound III in a yield of 53% on boiling in hydrobromic acid, and compound IV in a 79% yield with hydrobromic acid in acetic acid.



The structure of all the synthesized compounds I-VIII was confirmed by the elemental analysis data, by PMR spectra (Tables 1 and 2) and by mass spectra. Table 1 shows the PMR spectra of compounds I and II in DMSO-d_6. The absence of a singlet signal of a proton at 6.44 ppm in compound II, in contrast to compound I, indicates the presence of a substituent therein in position 6. In compound V, in contrast to compound I, there are proton signals of the NH group at the C_3 atom, which confirms its structure with an opened oxazine ring.

The spectral-luminescent characteristics of compounds I, II, and V are given in Table 3, which shows that the long-wave absorption band of compound I displays a certain hypsochromic shift (about 15 nm) in comparison with resorufin [5]. This agrees

TABLE 2. PMR Spectra of Substituted Naphthalenes III, IV-VIII

Compound (solvent)	R^1	R2	R^3	Chemical shifts, δ, ppm									
				aromatic protons, J, Hz					protons of substituents in the ring				
				1-H	4-H	5-H	6-H	8-H	NH_2	OCH_3 (2)	OCH_3 (7)	$CH_3C{=}NOH$	$NHCOCH_3$
III (DMFA-D_7)	OH	NH_2	OH	6,97 s	6,99 s	7,39 d (8,7)	6,85 d.d (9,6, 2,5)	6,92 d (2,5)					
IV (DMFA-D_7)	OH	NH_2	OCH_3	7,00 s	6,95 s	7,38 d (8,8)	6,88 d.d (8,8; 2,5)	7,07 d (2,5)	NH_2+OH 4,17 s (3H)		3,94		
VI ($CDCl_3$)	OCH_3	$C(=NOH)CH_3$	OCH_3	7,00* br.s	7,77 s	7,67 d (9,5)	6,93 d.d (9,5, 2,5)	7,00* br.s	—	3,90 s	3,92 s	10,6 br.s (N—OH) 2,20 s (CH_3)	
VII ($CDCl_3$)	OCH_3	$NHC(=O)CH_3$	OCH_3	6,91 br.s	7,90 br.s	7,65 d (9,5)	6,90 d.d (9,5, 2,5)	6,94 br.s	—	3,88 s	3,98 s	—	8,75 s (NH) 2,20 s (CH_3)
VIII*[2] ($CDCl_3$)	OCH_3	NH_2	OCH_3	7,10 s	6,90 br. s	7,50 d	6,88 d.d	6,98 d	3,30 br.s	3,88 s	3,98 s	—	—
VIII*[2] (DMFA-D_7)	OCH_3	NH_2	OCH_3	7,16* s	7,00 s	7,39 d (8,8)	6,89 d.d (8,8, 2,5)	7,14* (2,5)	4,17*[3] s	3,85 s	3,96 s	—	—

*The 1-H and 8-H signals overlap.

*[2]The 4-H, 6-H, and 8-H signals partly overlap.

*[3]If DMFA is not anhydrous the NH_2 signal is masked by H_2O proton signals.

TABLE 3. Spectral-Luminescent Characteristics of Compounds I, II, V

Compound	Solvent	Absorption, λ_{max}, nm (log ε)	Luminescence λ_{max}, nm (φ_{dl})
I	Ethanol	232 (4,30), 264 (4,23), 458 (4,40)	535mp, 590 (about 0.05)
	0.1 N solution of KOH in ethanol	245 (4,37), 273 (4,27), 340 mp(3,48), 593 (4,22)	Absent
	Toluene	295 mp(3,48), 340 mp(3,48), 430 (4,24)	525 (about 0.05)
II	Ethanol	236 (4,46), 269 (4,37), 470 (4,32)	550, 595mp (about 0.05)
	0.1 N solution of KOH in ethanol	244 (4,56), 275 (4,41), 340 mp (3,93), 600 (4,26)	Absent
	Toluene	295 mp 3,48), 340 mp(3,48), 450 (4,26)	530 (0,10)
V	Ethanol	228 (4,42), 270 (4,26), 325 mp(3,90), 513 (3,40)	Absent
	0.1 N solution of KOH in ethanol	238 (4,70), 273 (4,53), 335 mp(3,90), 603 (3,85)	Absent

well qualitatively with the literature data stating that the angular annelation of phenoxazinones at the quinoid moiety of the molecule causes a substantial hypsochromic shift of the absorption bands, while the linear annelation at the benzene ring results in only a weak bathochromic shift [6], which results in the observed overall hypsochromic shift of compound I in comparison with resorufin. The presence of a chlorine atom in the molecule of compound II leads to a certain bathochromic shift of the absorption bands in comparison with compound I. Addition of an acid to the alcoholic solutions of compounds I and II does not change the absorption spectrum, while upon addition of an alkali, their long wave band, as in resorufin, undergoes a considerable bathochromic shift ($\Delta\lambda$ of about 130 nm, in resorufin — 97 nm). It should be noted that in contrast to resorufin, compounds I and II in alcoholic solutions have only a weak luminescence with a considerable Stokes shift, which practically disappears on alkalization. In nonpolar solvents their absorption and luminescence spectra are shifted to the short-wave region, while the luminescence intensifies in comparison with the alcoholic solutions.

Compound V does not luminesce, while its absorption spectrum is sensitive to the addition of alkali. Acidification does not change its absorption spectrum, in contrast to 2-(2′-hydroxyanilino)-1,4-naphthoquinone [3], which in an ethanolic solution forms a cyclic structure by the action of an acid, which leads to a shift of the absorption maximum from 480 to 400 nm.

Thus, a structural modification of the resorufin molecule by the addition of additional condensed benzene rings makes it possible to produce new luminophores, but their spectral-luminescent characteristics were found to be not much different from the characteristics of resorufin itself.

EXPERIMENTAL

The PMR spectra were recorded on a WM-250 Bruker spectrometer (250 MHz) in DMSO-d_6 and $CDCl_3$, using TMS as internal standard. The absorption spectra were run on Hitachi-356 spectrophotometer and the luminescence spectra on Hitachi MPF-2A and SDL-1 spectrophotometers using an DKSSh-1000 xenon lamp as the excitation source. The luminescence quantum yields were measured relative to standards — rhodamine 6Zh (φ_{fl} = 0.94) and cresyl violet (φ_{fl} = 0.56) in ethanol [7]. The mass spectra were obtained on an LKB-9000 mass spectrometer at an ionizing voltage of 70 eV.

The elemental analysis data for C, H, and N of compounds I-VIII correspond to the calculated values.

2-Acetyl-3,6-dimethoxynaphthalene Oxime (VI, $C_{14}H_{15}NO_3$). A mixture of 3.5 g (0.015 mole) of 2-acetyl-3,6-dimethoxynaphthalene [8], 1.6 g (0.23 mole) of hydroxylamine hydrochloride and 1.5 g of sodium acetate in 75 ml of ethanol was boiled for 1 h. After cooling the precipitate was filtered off, dried, and recrystallized from benzene. Yield 3 g (80%), mp 197°C. UV spectrum (in ethanol), λ_{max}, nm (log ε): 241 (4.80), 329 (3.47). Luminescence, λ_{max}, nm: 360. M^+ 245.

2-Acetylamino-3,6-dimethoxynaphthalene (VII, $C_{14}H_{15}NO_3$). A solution of 3.5 g (0.014 mole) of compound VI in 90 g of PPA was stirred for 30 min at 130°C and then poured into water. The precipitate was filtered off, washed with water, and dried. Yield 2.8 g (80%), mp 181°C (from a 1:1 chloroform–heptane mixture). UV spectrum (in ethanol), λ_{max}, nm (log ε): 244 (4.69), 321 (3.60), 336 (3.69), M^+ 245.

2-Amino-3,6-dimethoxynaphthalene (VIII, $C_{12}H_{13}NO_2$). A solution of 7.7 g (0.028 mole) of compound VII in a mixture of 1.5 liter of water and 70 ml of a conc. H_2SO_4 was heated on a water bath with stirring for 5 h, then cooled, neutralized with a sodium carbonate solution, and the precipitate was filtered off and dried. Yield 3.9 g (61%), mp 142°C. UV spectrum (in ethanol), λ_{max}, nm (log ε): 237 (4.79), 340 (3.69). Luminescence, λ_{max}, nm (φ_{fl}): 400 (0.26). M^+ 203.

3-Amino-2-hydroxy-7-methoxynaphthalene (IV, $C_{11}H_{11}NO_2$). A mixture of 2.2 g (0.010 mole) of compound VIII, 20 ml of HBr, and 20 ml of CH_3COOH was boiled for 2 h, then cooled, neutralized with a 5% solution of NaOH, and the precipitate was filtered off, washed with water, and dried. Yield 1.6 g (79%), mp 206°C (from ethanol, with decomposition). UV spectrum (in ethanol), λ_{max}, nm (log ε): 236 (4.75), 342 (3.69). Luminescence, λ_{max}, nm (φ_{fl}): 400 (0.35). UV spectrum (in a 0.1 N solution of KOH in ethanol), λ_{max}, nm (log ε): 242 (4.70), 355 (4.20). Luminescence, λ_{max}, nm (φ_{fl}) 431 nm (0.38).

2,7-Dihydroxy-3-aminonaphthalene (III, $C_{10}H_9NO_2$). A solution of 4 g (0.02 moles) of compound VIII in 150 ml of HBr was boiled for 6 h, then cooled, neutralized with 25% solution of NaOH, and the precipitate was filtered off, washed with water, and dried. Yield 2.9 g (79%), mp 229°C (from water). UV spectrum (in ethanol), λ_{max}, nm (log ε): 236 (4.76), 342 (3.95). Luminescence, λ_{max}, nm (φ_{fl}): 405, (0.25). UV spectrum (in a 0.1 N solution of KOH in ethanol); λ_{max}, nm (log ε): 249 (4.70), 290 sh (3.74), 347 (3.70). Luminescence, λ_{max}, nm (φ_{fl}): 400 (about 0.05), M^+ 175.

10-Hydroxy-5H-dibenzo[*a*,i]phenoxazin-5-one (I, $C_{20}H_{11}NO_3$). A. A mixture of 0.8 g (4.5 mmoles) of compound III and 0.4 g (2.2 mmoles) of 2-hydroxy-1,4-naphthoquinone [9] in 20 ml of CH_3COOH was boiled for 3 h. The dark-brown solution was diluted with water, the precipitate was filtered off, dried, and chromatographed on silica gel with benzene. Yield 20 mg (3.0%) mp 308-310°C, M^+ 313.

B. A mixture of 0.32 g (1.8 mmoles) of compound III and 0.48 g (1.8 mmoles) of 2-(2′-hydroxyanilino)-1,4-naphthoquinone was heated on a water bath for 5 h in 70 ml of CH_3COOH. The dark-brown solution was diluted with water, the precipitate was filtered off, dried (0.22 g) and chromatographed on silica gel with benzene. The first yellow fraction (50 mg) of the product was collected and chromatographed by a benzene–acetone mixture. Yield 40 mg (7.0%).

6-Chloro-10-hydroxy-5H-dibenzo[*a*,i]phenoxazin-5-one (II, $C_{20}H_{10}ClNO_3$). A mixture of 0.5 g (2.8 mmoles) of compound III, 0.65 g (2.8 mmoles) of 2,3-dichloro-1,4-naphthoquinone and 0.51 g (6.4 mmoles) of anhydrous CH_3COOH in 80 ml of ethanol was boiled for 2 h. The dark-brown solution was diluted with water, the precipitate was filtered off, and dried and chromatographed twice (benzene–acetone). Yield 30 mg (3.0%), mp 282°C.

2-(2′-Hydroxy-7′-methoxynaphthyl-3′-amino)-1,4-naphthoquinone (V, $C_{21}H_{14}NO_4$). A mixture of 0.4 g (2 mmoles) of compound IV and 0.18 g (1 mmole) of 2-hydroxy-1,4-naphthoquinone was heated for 6 h in 15 ml of CH_3COOH. The solution was diluted with water, the precipitate was filtered off and dried. Yield 0.33 g (92%), mp 285°C. PMR spectrum (DMSO-d_6): 8.6 (3-H, s); 8.1 (5-H, d.d, J = 8.0; 2.0 Hz); 7.9 (6-H, t, J = 7.5; 1.5 Hz); 7.8 (7-H, d.d, J = 7.5; 1.5 Hz); 8.0 (8-H, d.d, J = 8.0; 2.0 Hz); 7.2 (4′-H, d, J = 3.0 Hz); 6.9 (5′-H, d.d, J = 8.5; 3.0 Hz); 7.75 (6′-H, d, J = 8.5 Hz, the proton signal overlaps with the 8-H signal); 7.77 (8′-H, s); 7.3 (1′-H, s); 4.0 (3-H, s, CH_3); 9.55 (N–H, s).

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