

Synthesis and Properties of 4,4'-Bis[5-alkyl(aryl)benzoxazol-2-yl]-2-hydroxy(alkoxy)biphenyls

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Abstract—Synthesis of 2-hydroxy(methoxy)-4,4'-biphenyldicarboxylic acids was developed. Based on their reactions with *o*-aminophenols we prepared for the first time 4,4'-bis[5-alkyl(aryl)benzoxazol-2-yl]-2-hydroxy(alkoxy)biphenyls, which might be of interest as luminescent dyes. Hydroxy compounds in a salt form possess abnormally high Stokes shift.

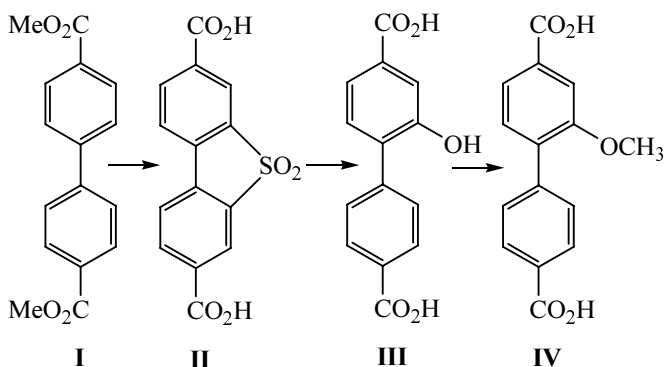
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Biphenyl derivatives are widely used as dyes, liquid-crystalline materials, biologically active and medicinal preparations [1–5]. Luminescent dyes with benzazole moieties directly attached to a biphenyl fragment possess a high practical potential. However the studies of their synthesis are relatively few [6–9] and concern only unsubstituted biphenyls. The presence of electron-donor or electron-acceptor substituents in the biphenyl fragment of the molecule essentially affects the electron density distribution in the molecule and consequently its spectral and luminescent characteristics.

We report here on the results of the synthesis of 2-hydroxy(methoxy)-4,4'-biphenyldicarboxylic acids (**III** and **IV**) and 4,4'-bis[5-alkyl(aryl)benzoxazol-2-yl]-2-hydroxy(alkoxy)biphenyls prepared therefrom. Our interest to this type compounds was attracted both by the prospect to apply them as luminescent dyes and by the accessibility of the initial raw material, namely, dimethyl 4,4'-biphenyldicarboxylate.

We developed a simple and efficient procedure for introduction of a hydroxy group into the position 2 of dimethyl 4,4'-biphenyldicarboxylate (**I**) providing the target compound **III** in a 97% yield. The boiling of diester **I** with excess chlorosulfonic acid led to the formation in a quantitative yield of dibenzothiophene-5,5'-dioxide-3,7-dicarboxylic acid (**II**), which on treatment with sodium hydroxide at 300°C transformed into 2-hydroxy-4,4'-biphenyldicarboxylic acid (**III**) [10]. 2-Methoxy-4,4'-biphenyldicarboxylic acid (**IV**) was obtained in a 94%

yield by alkylation of phenol **III** with methyl iodide in alkaline medium.

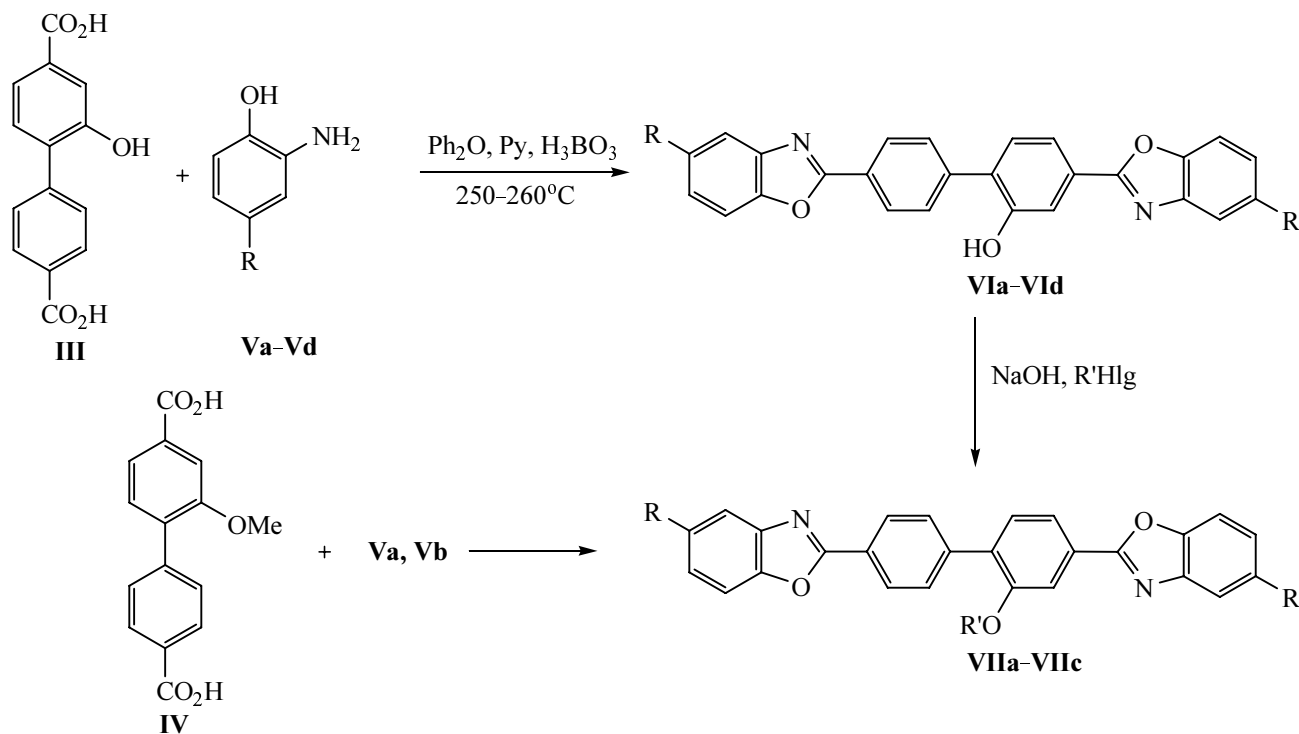


The synthesis of bisbenzoxazole derivatives **VIa–VIId**, **VIIa**, and **VIIIb** was performed by condensation of 2-hydroxy(methoxy)-4,4'-biphenyldicarboxylic acids (**III** and **IV**) with alkyl(phenyl)aminophenols **Va–Vd** in a mixture of diphenyl ether and pyridine, 4:1, at 250–260°C in the presence of boric acid [9]. The yields of bisbenzoxazoles **VIa–VIId** and **VIIa–VIIIc** reached 73–96%.

Alkoxy derivatives **VIIa** and **VIIIb** were also prepared by another procedure, a direct O-alkylation of 4,4'-bis(benzoxazol-2-yl)-2-hydroxybiphenyls **VIa** and **VIb** with alkyl halides or the corresponding dialkyl sulfates in a solution of lower aliphatic alcohols.

The composition of compounds **II–IV** and also of bisbenzoxazoles **VIa–VIId** and **VIIa–VIIIc** was confirmed by elemental analyses; their structure was consistent with

[†] Deceased.

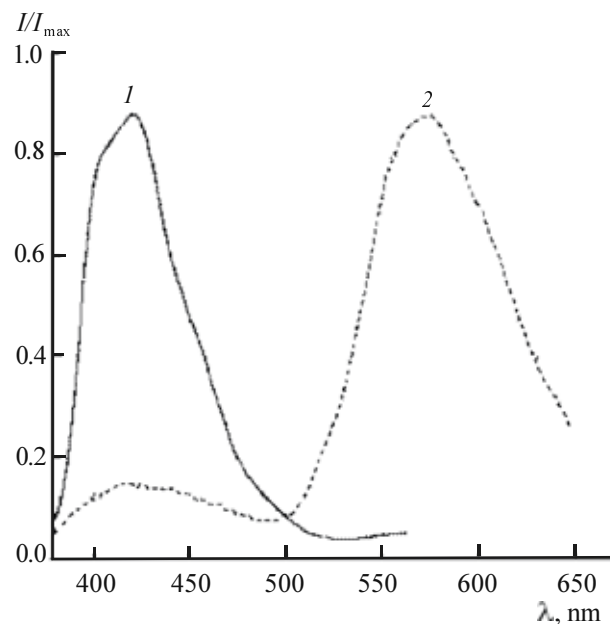


V, VI, R = H (a), Me (b), Ph (c), *t*-Bu (d); VII, R = H, R' = Me (a); R = R' = Me (b); R = H, R' = Et (c).

the IR and ^1H NMR spectra. The absorption bands in the IR spectra are in agreement with the assumed structures. Comparing the spectra of the initial diacids **III** and **IV** with those of 4,4'-bis[5-alkyl(aryl)benzoxazol-2-yl]-2-hydroxy(alkoxy)biphenyls **VIa-VIc** and **VIIa-VIIc** synthesized it should be noted that the absorption bands belonging to the aromatic structures were retained, the strong band of the ester group at 1730 cm^{-1} disappeared, and appeared a strong absorption band at $1565\text{--}1580\text{ cm}^{-1}$ corresponding to the bending vibrations of -N=C-O- fragment in the ring [11]. The strong absorption band in the region $1470\text{--}1480\text{ cm}^{-1}$ is apparently due to the conjugation of the biphenyl fragment with the benzoxazole structure in the molecule. The stretching vibrations of the aromatic C-H bonds give rise to the bands in the region $3060\text{--}3020\text{ cm}^{-1}$, and the bands of the stretching vibrations of the O-H bond of the hydroxy group are observed in the region $3460\text{--}3520\text{ cm}^{-1}$.

In the ^1H NMR spectra of compounds **VIa-VIc** and **VIIa-VIIc** the signals from the protons at C3' and C6', C3' and C5' of the biphenyl moiety appear as doublets at 8.15–8.25 ppm (4H) with a coupling constant 8.3 Hz. The proton signals from the benzoxazolyl and the other biphenyl protons are observed as a rule as multiplets in the region 7.15–7.60 ppm. The singlets of the methyl group of the benzoxazole fragment appear at 2.25–2.44 ppm

(**VIb**, **VIIb**), of the *tert*-butyl group $\text{C-C}(\text{CH}_3)_3$ in compound **VIc**, at 1.18 ppm, multiplet of the phenyl in compound **VIc** is observed at 6.95–7.35 ppm. The methoxy group protons in the spectra of compounds **VIIa** and **VIIb** give rise to a singlet at 3.95 ppm, and the ethoxy



Fluorescence spectra of compound **VIb**. 1, DMSO, 2, DMSO + NaOH.

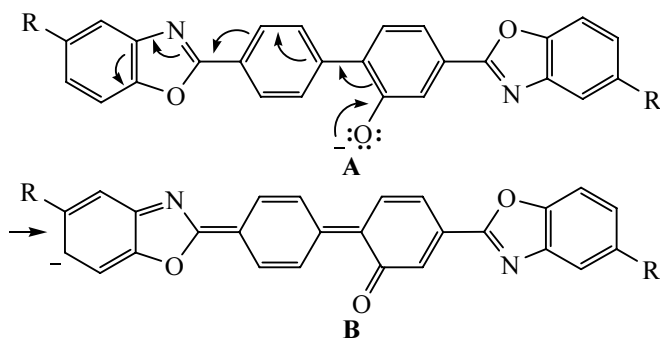
Absorption and fluorescence spectra of compounds **VIa–VIa**, **VIIa**, and **VIIb** in the salt and protonated forms

Compd.no.	Protonated form. Solvent DMSO			Salt form. Solvent DMSO + NaOH		
	Absorption λ_{\max} , nm	Fluorescence λ_{\max} , nm	Stokes shift, nm	Absorption λ_{\max} , nm	Fluorescence λ_{\max} , nm	Stokes shift, nm
VIa	315	415	100	330	572	242
VIb	350	420	70	330	575	245
VIc	350	425	75	335	577	242
VIId	345	420	75	330	570	240
VIIa	345	418	73	330	416	86
VIIb	352	420	68			

group in compound **VIIc** forms a characteristic triplet at 1.36 ppm and a quartet at 4.23 ppm.

The electron absorption spectra of bisbenzoxazoles **VIa–VIId**, **VIIa**, and **VIIb** contain a longwave band at 315–350 nm. These compounds are characterized by strong fluorescence with a maximum in a range 415–425 nm and can be applied as optical bleaching agents. Compounds **VIa–VIId** containing a free hydroxy group in the position 2 exhibit the properties of fluorescent pH-indicators, and in the salt forms their fluorescence maxima shift to the yellow-green region (λ 570–580 nm) at virtually the same absorption frequency; thus the compounds demonstrate an abnormally large Stokes shift (\approx 240 nm). The spectral characteristics of compounds **VIa–VIId**, **VIIa**, and **VIIb** are given in the table.

This fact apparently originates from the large contribution of the canonical form **A** and alterations in the structure of the excited state of the molecule. In this case probably plays the role the increased coplanarity in the tautomer form **B** resulting in the elongation of the conjugation chain and consequently in the change in the electron density distribution in the molecule.



EXPERIMENTAL

Melting points were measured on a Koeffler heating block. ^1H and ^{13}C NMR spectra were registered on

spectrometers Bruker Avance-400 (400 MHz), and Tesla BS-587A and BS-567A with operating frequencies 80 and 100 MHz respectively using TMS as internal reference. IR spectra were recorded on a spectrophotometer Specord M-80 in a range 400–4000 cm^{-1} from samples pelletized with KBr. The purification and drying of solvents and reagents was performed by common procedures. The reaction progress was monitored by TLC on plastic plated with silica gel 60 F₂₅₄ (Merck Art. 7734).

Dibenzothiophene-5,5'-dioxide-3,7-dicarboxylic acid (II). To 81 g (0.3 mol) of dimethyl 4,4'-biphenyldicarboxylate (**I**) was added 116.5 g (1 mol) of chlorosulfonic acid, and the mixture was heated for 3 h at 130–155°C till the end of hydrogen chloride liberation. The excess acid was evaporated at a reduced pressure, and the residue was treated with ice water. The separated precipitate was filtered off, washed with a large volume of water, and dried in a drying cabinet at 50°C. Yield 90 g (99%), mp >300°C (decomp.). ^1H NMR spectrum (DMSO-*d*₆), δ , ppm: 8.4 s (6H_{arom}). Found, %: C 55.11; H 2.52. C₁₄H₈O₆S. Calculated, %: C 55.26; H 2.64. *M* 304.27.

2-Hydroxy-4,4'-biphenyldicarboxylic acid (III). In a steel cylinder 400 g of NaOH was melted and heated to 300°C. Sulfone **II** (90 g, 0.29 mol) was added thereto by small portions at stirring, the mixture was then stirred for 15 min at 315–320°C. The reaction mixture was cooled to room temperature and treated with 1 N hydrochloric acid. The precipitate formed was filtered off, washed with water, and dried in a drying cabinet at 50°C. Yield 77 g (97%), mp >300°C (decomp.). ^1H NMR spectrum (DMSO-*d*₆), δ , ppm: 7.45 m (2H, H⁵, H⁶), 7.61 s (1H, H³), 7.71 d (2H, H^{2'} and H⁶, *J* 8.3 Hz), 7.99 d (2H, H^{3'} and H⁵, *J* 8.3 Hz), 10.2 br.s (1H, OH). Found, %: C 65.14; H 3.93. C₁₄H₁₀O₅. Calculated, %: C 65.10; H 3.91. *M* 258.22.

2-Methoxy-4,4'-biphenyldicarboxylic acid (IV). Into a round-bottom flask was charged 100 ml of CH₃OH,

10 ml of H₂O, 4.0 g of KOH, 2.58 g of phenol **III**, and 5 ml of methyl iodide. The reaction mixture was boiled for 14 h. On completion of the reaction the mixture was diluted with 100 ml of 20% HCl solution. The separated precipitate was filtered off and recrystallized from a mixture CH₃OH–H₂O, 10:1. Yield 2.6 g (94.5%), mp 330–332°C (subl.). ¹H NMR spectrum (DMSO-*d*₆), δ, ppm: 3.83 s (3H, OMe), 7.44–7.75 m (5H_{arom}), 7.99 d (2H, H^{3'} and H^{5'}, *J* 8.3 Hz). Found, %: C 65.03; H 3.87. C₁₅H₁₃O₅. Calculated, %: C 65.12; H 3.90. *M* 273.25.

4,4'-Bis(benzoxazol-2-yl)-2-hydroxybiphenyl (VIa). General procedure. In a flask equipped with a mechanical agitator, reflux condenser, and a thermometer was heated at 160–170°C while constant stirring for 2 h a mixture of 2.72 g (0.01 mol) of compound **III**, 2.18 g (0.02 mol) of *o*-aminophenol, 40 ml of diphenyl ether, 10 ml of pyridine, and 0.15 g (0.025 mol) of boric acid. After 2 h the temperature was raised to 250–260°C, and heating at this temperature continued for 6 h. Then the reaction mixture was cooled, diluted with 50 ml of acetic acid, and boiled for 30 min. The precipitated crystals were filtered off and dried. Yield 3.9 g (95%), mp >300°C (decomp.). ¹H NMR spectrum (DMSO-*d*₆), δ, ppm: 7.25–8.00 m (13H_{arom}), 8.25 d (2H, H^{3'} and H^{5'} of biphenyl, *J* 8.3 Hz). Found, %: C 77.20; H 3.98; N 6.90. C₂₆H₁₆N₂O₃. Calculated, %: C 77.22; H 3.99; N 6.93. *M* 404.42.

Likewise were prepared compounds **VIb–VIId**.

4,4'-Bis(5-methylbenzoxazol-2-yl)-2-hydroxybiphenyl (VIb). The reaction mixture was heated for 4 h at 160–170°C and 5 h at 250–260°C. Yield 96%, mp 345–346°C. ¹H NMR spectrum (CF₃CO₂D), δ, ppm: 2.25 s (6H, 2CH₃), 7.2–8.3 m (13H_{arom}). Found, %: C 77.74; H 4.68; N 6.47. C₂₈H₂₀N₂O₃. Calculated, %: C 77.76; H 4.66; N 6.48. *M* 432.48.

4,4'-Bis(5-phenylbenzoxazol-2-yl)-2-hydroxybiphenyl (VIc) was obtained from 0.64 g (0.0025 mol) of compound **III** and 0.93 g (0.005 mol) of 2-amino-4-phenylphenol (**Ve**). Yield 1.2 g (87%), mp >365°C (decomp.). ¹H NMR spectrum (CF₃CO₂D), δ, ppm: 6.95–7.35 m (10H, 5-Ph-H in benzoxazol-2-yl), 7.45 d (2H, H^{2'} and H^{6'}, *J* 8.3 Hz), 7.65–7.85 m (9H_{arom}), 8.15 d (2H, H^{3'} and H^{5'} of biphenyl, *J* 8.3 Hz). Found, %: C 82.04; H 4.39; N 5.11. C₃₈H₂₄N₂O₃. Calculated, %: C 82.00; H 4.35; N 5.03. *M* 556.62.

4,4'-Bis(5-*tert*-butylbenzoxazol-2-yl)-2-hydroxybiphenyl (VIId) was obtained from 0.516 g (0.002 mol) of acid **III** and 0.67 g (0.004 mol) of 2-amino-4-*tert*-butylphenol (**Vd**). Yield 0.82 g (78%), mp >300°C

(decomp.). ¹H NMR spectrum (CF₃CO₂D), δ, ppm: 1.18 s [18H, C–(CH₃)₃], 7.2–8.3 m (13H_{arom}). Found, %: C 79.01; H 6.25; N 5.43. C₃₄H₃₂N₂O₃. Calculated, %: C 79.04; H 6.24; N 5.42. *M* 516.64.

4,4'-Bis(benzoxazol-2-yl)-2-methoxybiphenyl (VIIa). *a.* Analogously to the synthesis of compound **VIa** 0.67 g (0.0025 mol) of acid **IV** and 0.55 g (0.005 mol) of *o*-aminophenol **Va** in a mixture of 20 ml of diphenyl ether, 3 ml of pyridine, and 0.15 g (0.025 mol) of boric acid was heated at 160–170°C for 1 h and at 250–260°C for 3 h. After an appropriate workup we obtained compound **VIIa** in an yield 0.87 g (84%).

b. To a solution of 0.4 g (0.01 mol) of compound **VIa** in 20 ml of ethanol was added 0.48 g (0.12 mol) of NaOH, and 0.1 ml (0.01 mol) of dimethyl sulfate. The reaction mixture was boiled at reflux for 1 h, then it was cooled and diluted with 100 ml of water. The precipitate was filtered off and recrystallized from acetic acid. Yield 370 mg (88.7%).

c. To a solution of 0.2 g (0.005 mol) of compound **VIa** in 100 ml of ethanol containing 0.24 g (0.05 mol) of NaOH was added 0.4 ml of methyl iodide, and the mixture was boiled for 30 h. Then the reaction mixture was poured into 100 ml of 5% hydrochloric acid, the precipitate was filtered off and recrystallized from acetic acid. Yield 175 mg (84%), mp 193–195°C. ¹H NMR spectrum (CF₃CO₂D), δ, ppm: 3.95 s (3H, OMe), 7.30–7.95 m (13H_{arom}), 8.25 d (2H, H^{3'} and H^{5'} of biphenyl, *J* 8.2 Hz). Found, %: C 77.52; H 4.34; N 6.70. C₂₇H₁₈N₂O₃. Calculated, %: C 77.49; H 4.34; N 6.69. *M* 418.45.

4,4'-Bis(5-methylbenzoxazol-2-yl)-2-methoxybiphenyl (VIIb) was prepared as described in method *a.* Yield 0.8 g (73%), mp 310–312°C. ¹H NMR spectrum (CF₃CO₂D), δ, ppm: 2.44 s (6H, 2CH₃), 3.95 s (3H, OCH₃), 7.23 d (2H, H^{2'} and H^{6'} of biphenyl, *J* 8.12 Hz), 7.5–7.95 m (9H_{arom}), 8.22 d (2H, H^{3'} and H^{5'} of biphenyl, *J* 8.12 Hz). Found, %: C 78.00; H 4.93; N 6.28. C₂₉H₂₂N₂O₃. Calculated, %: C 77.76; H 4.97; N 6.27. *M* 446.50.

4,4'-Bis(benzoxazol-2-yl)-2-ethoxybiphenyl (VIIc). To a solution of 0.4 g (0.01 mol) of compound **VIa** in 100 ml of ethanol containing 0.48 g (0.12 mol) of NaOH was added 1 ml of ethyl bromide, and the mixture was boiled for 30 min. Then the reaction mixture was poured into 100 ml of 5% hydrochloric acid, the precipitate was filtered off and recrystallized from acetic acid. Yield 0.32 g (73.5%), mp 154°C. ¹H NMR spectrum (CF₃CO₂D), δ, ppm: 1.36 t (3H, OCH₂CH₃, *J* 6 Hz), 4.23 q (2H, OCH₂CH₃, *J* 6 Hz), 7.30–7.95 m (13H_{arom}), 8.25 d (2H,

H^{3'} and H^{5'} of biphenyl, J 8.2 Hz). Found, %: C 77.72; H 4.65; N 6.45. C₂₈H₂₀N₂O₃. Calculated, %: C 77.76; H 4.66; N 6.48. M 432.48.

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