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Synthesis and Fluorescent Properties of Some New Unsymmetric *bis*-Benzothiazolyl Furans and Thiophenes

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Summary. Some new *mono-* and *bis*-benzothiazolyl compounds with furan or thiophene nuclei were synthesized by multistep reactions from the corresponding furan and thiophene aldehydes. The data obtained from emission spectra show a large influence of the benzothiazole rings on the relative quantum efficiency of the compounds under investigation.

Keywords. Benzothiazole; Fluorescence; Relative quantum efficiency.

Synthese und Fluoreszenzeigenschaften von neuen unsymmetrischen *bis*-Benzothiazolylfuranen und thiophenen

Zusammenfassung. Einige neue *bis*-Benzothiazolylverbindungen mit einem Furan- bzw. Thiophenenring wurden in einer mehrstufigen Reaktion dargestellt. Die Fluoreszenzdaten der untersuchten Verbindungen zeigen einen großen Einfluß der Benzothiazolringe auf die relative Fluoreszenzquantenausbeute.

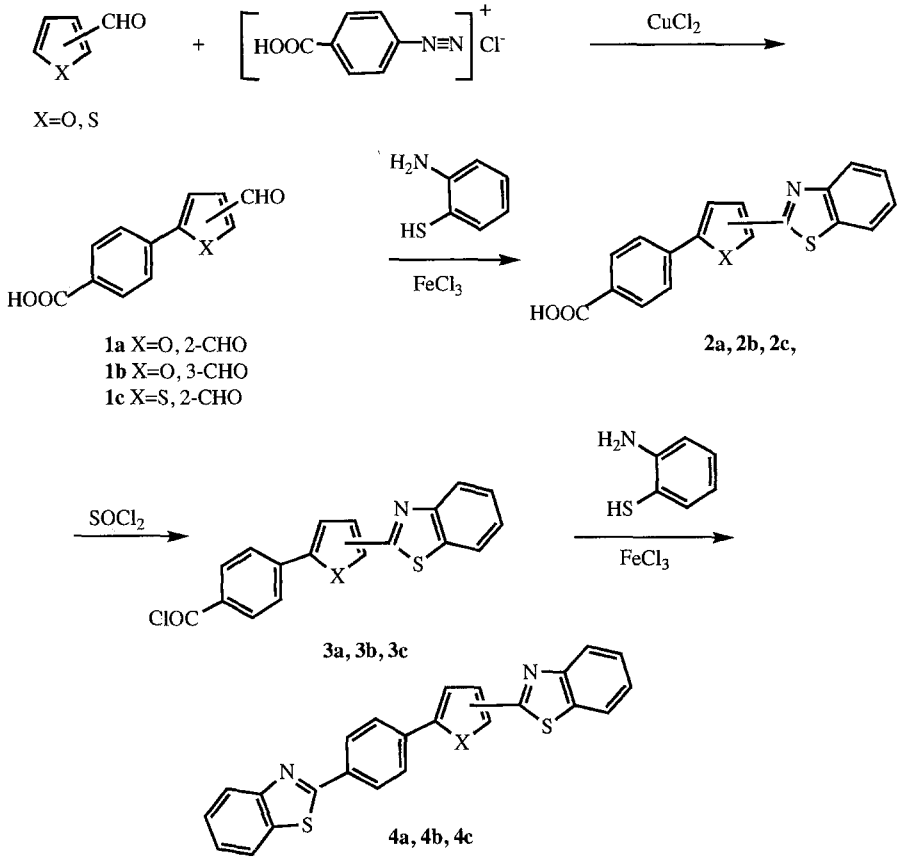
Introduction

In continuation of our studies on the synthesis and fluorescent properties of 2-substituted benzothiazoles [1, 2, 3, 4], we have prepared some new *bis*-benzothiazolyl compounds containing furan or thiophene nuclei.

The importance of benzothiazole derivatives – due to their biological activity and their use as pesticides [5], growth-regulating substances [6], and intermediates for dyes, plant protectants, and pharmaceuticals [7] – has led to extensive studies of these molecules. Derivatives of benzothiazole are frequently fluorescent, and some of them are used as optical brighteners [8] and substances for fluorometric measurements [9]. However, so far a systematic study on the synthesis and spectral characteristics of *bis*-benzothiazolyl derivatives is lacking. There are only a few data describing compounds containing two benzothiazole rings attached *via* a heterocyclic system, such as 2,5-*bis*-benzothiazolyl furan [10], 2,5-*bis*-benzothiazolyl-thiophene [11], its derivatives [12, 13] and vinylogues thereof [14].

Results and Discussion

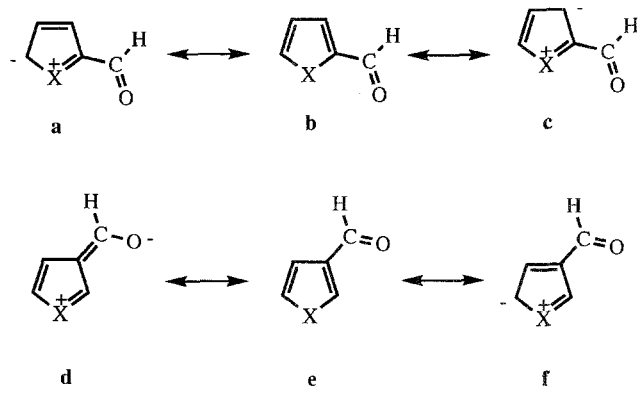
Starting with furan and thiophene aldehydes, we have synthesized the *bis*-benzothiazolyl compounds **4a–c** according to Scheme 1. Our attempts to obtain the corresponding thienyl compound **4d** were unsuccessful. Beside these three substances prepared as the aim of our investigations, all intermediates obtained in these multistep reactions expect **1a** and **2a** are also new.



Scheme 1

In the first step, we tried to arylate 3-furanaldehyde as well as 2- and 3-thiophenealdehyde with the diazonium salt of *p*-aminobenzoic acid using the well known procedure for 2-furanaldehyde [15]. We found that this reaction depends on the position of the aldehyde group attached to the furan or thiophene nucleus with respect to the heteroatom. Comparing the arylation of 3-furanaldehyde with that of 2-furanaldehyde, we found that 3-furanaldehyde yields only 36% of 5-(*p*-carboxyphenyl)-3-furanaldehyde (**1b**), whereas the corresponding 2-isomer (**1a**) was obtained in 59% yield. The difference between the reactivities of the two isomeric thiophene aldehydes is even more remarkable. This behavior can be explained by different electron delocalization and mesomeric polar structures of 2- and 3-substituted heterocyclic aldehydes according to Scheme 2.

We suppose that the prefered structures are **a** and **d**, respectively. As a result, 3-thiophene aldehyde couldn't be arylated at all. Because of this lack of reactivity



Scheme 2

using the pathway in Scheme 1, we couldn't obtain 2-(*p*-(2-benzothiazolylphenyl)-4-(2-benzothiazolyl)-thiophene (**4d**). Therefore, starting with 3-thiophenealdehyde, we prepared the corresponding 2-(3-thienyl)-benzothiazole (**5**); however, our attempt to arylate **5** was also unsuccessful. It is also evident from the arylations that the furan derivatives are more reactive than the corresponding thiophene derivatives. This behavior is in agreement with the greater aromaticity of thiophenes with respect to furans. 2-Furanaldehyde yields 59% of **1a** upon arylation; 2-thiophenealdehyde yields only 10% of **1b**. 3-Furanaldehyde yields 36% of **1b**, and 3-thiophenealdehyde does not react at all.

All other reaction steps were carried out in the same way, starting with arylated aldehydes. Benzothiazolyl compounds **2a–c**, synthesized from appropriate aldehydes and *o*-aminothiophenol according to a modified method of condensation [16] with yields of about 40%, have been converted to the corresponding chlorocarbonyl derivatives **3a–c**. In the last step, the chlorocarbonyl compounds were condensed with *o*-aminothiophenol [17] to obtain the *bis*-benzothiazolyl compounds **4a–c** in good yields.

The absorption and fluorescence spectroscopic data of benzothiazolyl compounds (**2a–c**) and *bis*-benzothiazolyl compounds (**4a–c**) are given in Table 1.

Substitution of the carboxy group in compounds **2a–c** with the benzothiazole ring causes a slight bathochromic shift (18–29 nm) of the longwave absorption as well as of the fluorescence maxima (10–25 nm). Comparing the emission properties of compounds **2a**, **2c**, **4a**, and **4c** with the emission properties of 2-(2-furyl)- and 2-(2-thienyl)-benzothiazole, which exhibit a very low fluorescence [3], a significant difference is observed. Compounds **2a** and **2c**, obtained by introduction of a carboxy group in position 5 of 2-(2-furyl)-benzothiazole and 2-(2-thienyl)-benzothiazole, exhibit large values of relative quantum efficiencies (0.39 and 0.32). Upon converting compounds **2a** and **2c** into **4a** and **4c**, these values become even greater (0.81 and 0.51). In the 3-furyl series, the parent compound (2-(3-furyl)-benzothiazole) is not fluorescent at all; its *p*-carboxyphenyl derivative (**2b**) is slightly fluorescent, and the corresponding *bis*-benzothiazolyl compound (**4b**) exhibits a strong fluorescence. From these observations we can conclude that the investigated *bis*-benzothiazolyl compounds may be used as luminophores.

Table 1. Absorption and fluorescence emission spectroscopic data of benzothiazolyl compounds **2a–c** and **4a–c**

	Absorption		Emission		
	λ_{max} (nm)	lgε	λ_{ex} (nm)	λ_{em} (nm)	Φ_r
2a	280	4.25	358	400	0.39
	362	4.73		420	
	382 sh				
2b	225	5.43	325	420	0.06
	271	5.15			
	326	5.20			
2c	265	4.83	370	415	0.32
	370	5.59		435	
4a	315	5.38	385	420	0.81
	383	4.72		445	
	404 sh				
4b	291	5.30	355	430	0.35
	355	5.52			
4c	388	5.34	385	430	0.51
				455	

Experimental

Melting points were obtained with a Kofler block and are uncorrected. UV/Vis spectra were taken on a Hitachi Perkin-Elmer 124 spectrophotometer with freshly prepared 10^{-5} *M* ethanolic solutions. Fluorescence spectra, obtained at room temperature on a fluorescence spectrometer Perkin-Elmer 3000 with 10^{-7}–10^{-8} *M* concentrations of freshly prepared ethanolic solutions, were corrected using quinine sulfate in perchloric acid as a standard [18]. Relative fluorescence quantum efficiencies (Φ_r) were calculated relative to quinine sulfate in 0.5 *M* sulfuric acid ($\Phi = 0.588$) or 3-aminophthalimide in ethanolic solution [19] according to the equation given below [20].

$$\Phi_r = \Phi_s \cdot \frac{A_r}{A_r} \cdot \frac{d_s}{d_r}$$

Φ_r and Φ_s are the fluorescence quantum efficiences of examined compound and standard, respectively; A_r and A_s represent the integrated area under the corrected fluorescence spectrum of examined compound and standard, respectively; and d_r and d_s are the optical densities of examined compound and standard, respectively.

The IR spectra were recorded on a Perkin-Elmer 297 spectrophotometer (KBr discs); the ^{1}H NMR spectra were recorded on a Joel JMM-FX-100 FT spectrometer with *TMS* as the internal reference in *DMSO*-d_6 solutions.

2-(p-(2-benzothiazolyl)-phenyl)-5-(2-benzothiazolyl)-furan (**4a**)

2.0 g (6.2 mmol) 2-(5-*p*-carboxyphenyl-2-furyl)-benzothiazole [4] was heated with 10 ml (137 mmol) thionylchloride during 4 h on an oil bath at 85 °C; the corresponding 2-(5-*p*-chlorocarbonylphenyl-2-furyl)-benzothiazole (**3a**) was obtained. Yield: 1.02 g (48%); m.p.: 292–296 °C (benzene); IR (KBr): $\nu = 1765\,cm^{-1}$ (COCl); ^{1}H NMR (*DMSO*-d_6): $\delta = 7.48$–7.61 (m, 4H, 2H fur. + 2H aromat.), 7.98–8.19 (m, 6H aromat.) ppm.

A solution of 0.7 g (2.1 mmol) of 2-(5-*p*-chlorocarbonylphenyl-2-furyl)-benzothiazole (**3a**) in 50 ml of chlorobenzene was heated to reflux. To the stirred solution, 0.5 g (4 mmol) of *o*-aminothiophenole dissolved in chlorobenzene were added. The reaction mixture was heated under reflux for one hour. After cooling, a crystalline product (**4a**) was obtained.

Yield: 0.5 g (59%); m.p.: 233–236 °C (mixture of ethanol and *DMF*); IR (KBr): $\nu = 1470$, 910 cm^{-1} (benzothiazole); ^1H NMR (*DMSO*-d_6): $\delta = 7.50–7.62$ (m, 6H, fur. + aromat.), 8.07–8.28 (m, 8H, aromat.) ppm; $C_{24}H_{14}N_2OS_2$ (410.52); calcd.: C 70.22, H 3.44, N 6.82; found: C 70.45, H 3.61, N 7.11.

2-(p-(2-benzothiazolyl)-phenyl)-4-(2-benzothiazolyl)furan (**4b**)

By arylation of 6.8 g (80 mmol) of 3-furanaldehyde with a freshly prepared solution of diazotated *p*-aminobenzoic acid, 5-(*p*-carboxyphenyl)-3-furanaldehyde (**1b**) was obtained.

Yield: 6.36 g (36%); m.p.: 230–235 °C (ethanol); IR (KBr): $\nu = 1670\ cm^{-1}$ (COOH, CHO); ^1H NMR (*DMSO*-d_6): $\delta = 7.01$ (s, 1H, H_4 fur.), 7.99–8.09 (m 5H, H_2 fur, 3H aromat.), 10.13 (s, 1H, CHO), 13.12 (s, 1H, COOH) ppm; $C_{12}H_8O_4$ (216.38); calcd.: C 66.70, H 3.72; found: C 66.58, H 3.93.

To a boiling solution of 3.2 g (15 mmol) of 5-(*p*-carboxyphenyl)-3-furanaldehyde (**1b**) in 35 ml of pyridine a solution of 1.9 g (15 mmol) of *o*-aminothiophenol in 15 ml of pyridin was added dropwise; the stirred reaction mixture was refluxed for 0.5 h. The mixture was then poured into 350 ml of 2 *M* hydrochloric acid, and after cooling overnight the obtained crystalline product was oxidized with an ethanolic solution of $FeCl_3$ to obtain 2-(2-*p*-carboxyphenyl-4-furyl)- benzothiazole (**2b**).

Yield: 1.75 g (36%); m.p.: 258–262 °C (mixture of *DMF*, ethanol, and water); IR (KBr): $\nu = 1680$ (COOH), 910 (benzoth.) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 7.19$ (d, $J = 1.9$ Hz, 1H, fur.), 7.46–7.59 (m, 2H, aromat.), 8.02–8.16 (m, 7H, aromat.), 13.15 (s, 1H, COOH) ppm; $C_{18}H_{11}NO_3S$ (321.4); calcd.: C 67.27, H. 3.45, N. 4.36; found: C 66.98, H 3.71, N 4.61.

Heating of 1.6 g (5.0 mmol) 2-(*p*-carboxyphenyl-4-(2-benzothiazolyl)-furan (**2b**) with 10 ml (137 mmol) thionylchloride for 4 h on an oil bath at 85° afforded the corresponding 2-(5-*p*-chlorocarbonylphenyl-3-furyl)-benzothiazole (**3b**).

Yield: 0.69 g (40.8%); m.p.: 133–136 °C; IR (KBr): $\nu = 1760$ (COCl), 910 (benzoth.) cm^{-1}.

A solution of 0.7 g (2.0 mmol) of 2-(2-*p*-chlorocarbonylphenyl-4-furyl)-benzothiazole (**3b**) in 50 ml of chlorobenzene was heated under reflux. To the stirred solution, 0.3 g (2 mmol) of *o*-aminothiophenole dissolved in 10 ml chlorobenzene were added. The reaction mixture was heated under reflux for one hour. After cooling, a crystalline product (**4b**) was obtained.

Yield: 0.266 g (32.4%); m.p.: 151–154 °C (*DMF*/ethanol); IR (KBr): $\nu = 1470$, 910 cm^{-1} (benzoth.); ^1H NMR (*DMSO*-d_6): $\delta = 7.19$ (s, 1H, fur.), 7.46–7.62 (m, 4H, aromat.), 8.08–8.21 (m, 8H, aromat.) ppm; $C_{24}H_{14}N_2OS_2$ (410.52); calcd.: C 70.22, H 3.44, N 6.82; found: C 70.48, H 3.64, N 7.21.

2-(p-(2-benzothiazolyl)-phenyl)-5-(2-benzothiazolyl)-thiophene (**4c**)

By arylation of 7.4 g (65 mmol) of 2-thiophenealdehyde with a freshly prepared solution of 9.0 g (65 mmol) diazotated *p*-aminobenzoic acid, 5-(*p*-carboxyphenyl)-2-thiophenealdehyde (**1c**) was obtained.

Yield: 1.6 g (10.5%); m.p.: 280–288 °C (ethanol); IR (KBr): $\nu = 1670\ cm^{-1}$ (COOH; CHO); ^1H NMR (*DMSO*-d_6): $\delta = 7.89$ (d, $J = 3.92$ Hz, 1H, thioph.), 7.95–8.03 (m, 4H, aromat.), 8.10 (d, $J = 3.95$ Hz, 1H, thioph.), 9.95 (s, 1H, CHO), 13.15 (s, 1H, COOH) ppm; $C_{12}H_8O_3S$ (232.25); calcd.: C 62.08, H 3.47; found: C 63.89, H 3.48.

To a boiling solution of 3.1 g (14 mmol) of 5-(*p*-carboxyphenyl)-2-thiophenealdehyde (**1c**) in 50 ml of pyridine, a solution of 1.7 g (14 mmol) of *o*-aminothiophenole in 15 ml of pyridine was added dropwise, and the stirred reaction mixture was refluxed 0.5 h. The mixture was then poured into 430 ml of 2 *M*

hydrochloric acid, and after cooling overnight the obtained crystalline product was oxidized with an ethanolic solution of $FeCl_3$ to obtain 2-(*p*-carboxyphenyl-2-thienyl)-benzothiazole (**2c**).

Yield: 1.18 g (40%); m.p.: above 300 °C (*DMF* ethanol water); IR (KBr): $\nu = 1680$ (COOH), 905 (benzoth.) cm^{-1} ^1H NMR (*DMSO*-d_6): $\delta = 7.46–7.59$ (m, 2H, aromat.), 7.82 (d, $J = 3.77$ Hz, 1H, thioph.), 7.89–8.17 (m, 7H, aromat. + thioph.), 13.11 (s, 1H, COOH) ppm; $C_{18}H_{11}NO_2S_2$ (337.33); calcd.: C 64.09, H 3.29, N 4.15; found: C 63.82, H 3.62, N 3.89.

Upon heating of 1.0 g (2.9 mmol) 2-(*p*-carboxyphenyl)-5-(2-benzothiazolyl)-thiophene (**3b**) with 10 ml (137 mmol) thionylchloride during 4 h on an oil bath at 85 °C, the corresponding 2-(5-*p*-chlorocarbonylphenyl-2-thienyl)-benzothiazole (**3c**) was obtained in 0.85 g (82%) yield.

A solution of 0.8 g (2.4 mmol) of 2-(5-*p*-chlorocarbonylphenyl-2-thienyl)-benzothiazole(**3c**) in 40 ml of chlorobenzene was heated under reflux. To the stirred solution, 0.5 g (4 mmol) of *o*-aminothiophenole dissolved in chlorobenzene were added. The reaction mixture was heated under reflux for one hour. After cooling, a crystalline product (**4c**) was obtained.

Yield: 0.82 g (80%); m.p.: 259–260 °C (*DMF*/ethanol); IR (KBr): $\nu = 1475$, 900 cm^{-1} (benzoth.); ^1H NMR: unsoluble in *DMSO*-d_6; $C_{24}H_{14}N_2S_3$ (426.57); calcd.: C 67.58, H 3.31, N 6.57; found: C 67.87, H 3.13, N 6.89.

2-(3-thienyl)-benzothiazole (**5**)

To a boiling solution of 5.7 g (50 mmol) of 3-thiophenealdehyde in 20 ml of pyridine, a solution of 6.3 g (50 mmol) of *o*-aminothiophenole in 15 ml pyridine was added dropwise. The stirred reaction mixture was refluxed for 0.5 h and then poured into 430 ml of 2 *M* hydrochloric acid. After cooling overnight, the obtained crystalline product was dissolved in ethanol and oxidized with a solution of $FeCl_3$ to obtain 2-(3-thienyl)-benzothiazole (**5**).

Yield: 7.25 g (66.1%); m.p.: 107–110 °C (dil. ethanol); IR (KBr): $\nu = 1470$, 890 cm^{-1} (benzoth.); ^1H NMR (*DMSO*-d_6): $\delta = 7.43–8.15$ (m, 6H, aromat. + thioph.), 8.40 (s, 1H, H_2 thioph.); $C_{11}H_7NS_2$ (217.13); calcd.: C 60.80, H 3.25, N 6.45; found: C 60.51, H 3.41, N 6.82.

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