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Synthesis and Some Transformations of *trans*-1-Methyl-2-[β-(2'-thienyl)vinylene]-1*H*-benzimidazole

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Abstract—The condensation of 1,2-dimethylbenzimidazole with thiophene-2-aldehyde in the presence of fused zinc chloride results in 1-methyl-2-[β-(2-thienyl)vinylene]-1*H*-benzimidazole. Its electrophilic substitution reactions (nitration, bromination, sulfonation, formylation, acylation) were studied. All the reactions occur in the 5-position of the thiophene ring. Only in the case of bromination in dichloroethane 5',5(6)-dibromo-derivative was obtained. Data of the quantum-chemical calculations of the total positive charge on the carbon atoms of the protonated molecules of thienylbenzimidazoles including the vinylene group and without it are reported.

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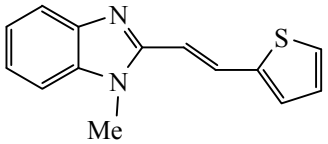
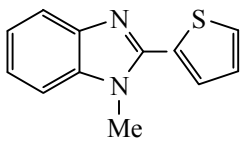
The mutual influence of heterocyclic rings in bihetaryls is an interesting and as yet poorly studied problem. The scarcest data are on the reactivity of compounds in which benzothiazole and π-excessive thiophene rings are linked to each other. Previously the reactivity of furylvinylbenzimidazole was studied [1]. Introducing the substituents containing a π-system into the benzimidazole molecule increases the fluorescence quantum yield. To this type belong, for example, benzimidazolylstilbenes containing benzene and pyridine rings used as the optical bleaching agents [2, 3].

The goal of our study was to develop or to choose a convenient synthesis method and to examine the relative reactivity of 1-methyl-2-[β-(2-thienyl)vinylene]benzimidazole **I** and to compare it with that of the benzimidazole analog **II** lacking the vinylene group [4].



I



II

Compound **I** we synthesized in ~75% yield by heating of a mixture of 1,2-dimethylbenzimidazole with thiophene-2-aldehyde at 160°C in the presence of fused zinc chloride. Further compound **I** was brought into reactions with the electrophilic reagents: acetyl nitrate, bromine in dichloroethane, a mixture of sulfuric acid and polyphosphoric acids, hexamethylenetetramine and carboxylic acids in polyphosphoric acid (PPA) (Table 1).

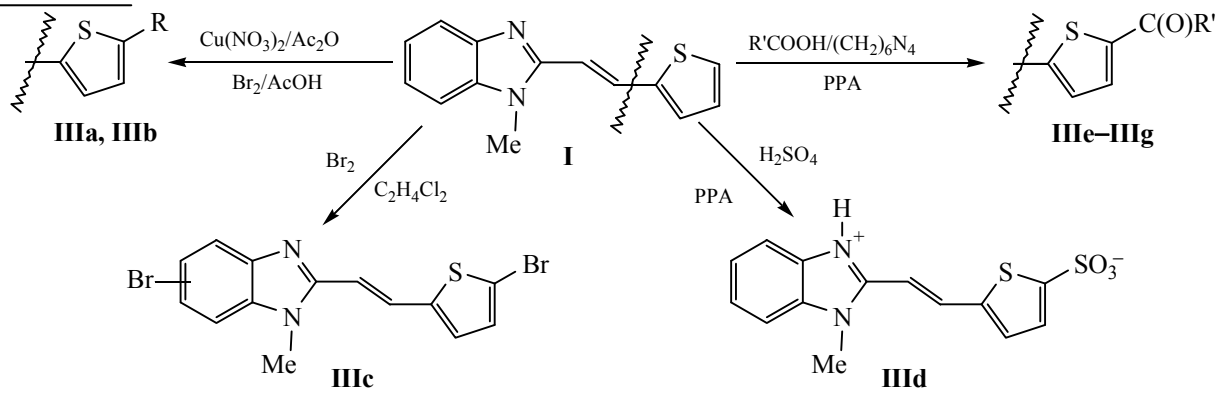
A comparison of the chemical shifts of the $H^{3'}$ protons (7.22 and 7.51 ppm) of the 2-thienyl group in the ^{1}H NMR spectra of compounds **I** and **II** shows that in these compounds the proton of **I** is the most strongly shielded. This is primarily due to the inductive effect and the deshielding (electron-acceptor) effect of the benzimidazole substituents, which is less in the first case. Therefore, we can expect a high reactivity of the thiophene ring in compound **I**.

Our studies confirm this assumption. Thus, the nitration of 1-methyl-2-[β-(2-thienyl)vinylene]-1*H*-benz-imidazole **I** proceeds under mild conditions by the action of $Cu(NO_3)_2$ and acetic anhydride at 10°C (yield of 5-nitro-derivative **III** was 75%), while compound **II** is nitrated with a mixture of fuming nitric acid (*d* 1.51 g cm^{-3}) and acetic anhydride at 0°C [4]. We failed in similar to carry out the selective nitration of compound **I**. Unlike benzimidazole **II**, the bromination of **I** with bromine in acetic acid at 20°C results also in the 5-substitution of the thiophene ring. The bromination of compound **I** in refluxing dichloroethane proceeds interestingly: not only thiophene ring, but also benzene moiety undergoes an electrophilic attack. This is apparently explained by the electron-donor effect of vinylene group in the neutral molecule of compound **I**. In contrast, in an acid

Table 1. Yields, melting points, and elemental analysis data for compounds **I, IIIa–IIIg**

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
I	75	86–87	70.29	4.88	11.72	$C_{14}H_{12}N_2S$	69.97	5.03	11.66
IIIa	76	215–216	59.33	4.11	15.04	$C_{14}H_{11}N_3O_2S$	58.93	3.89	14.72
IIIb	66	123–124	52.97	3.59	25.40 Br	$C_{14}H_{11}BrN_2S$	52.68	3.47	25.03Br
IIIc	57	144–145	41.89	2.76	40.51 Br	$C_{14}H_{10}Br_2N_2S$	42.24	2.53	40.14Br
IIId	63	295–296	52.76	3.93	9.03	$C_{14}H_{12}N_2O_3S_2$	52.48	3.78	8.74
IIIe	89	176–177	66.79	4.33	10.79	$C_{15}H_{12}N_2OS$	67.14	4.51	10.4
IIIf	79	220–221	67.73	4.93	10.22	$C_{16}H_{14}N_2OS$	68.06	5.00	9.92
IIIg	83	174–175	73.49	4.87	7.73	$C_{21}H_{16}N_2OS$	73.23	4.68	8.13

medium (AcOH) the transformation of the substrate into the cationic form is passivated by the benzimidazole fragment. As a result, the reaction involves exclusively the thiophene moiety.



R = NO_2 (**a**), Br (**b**), R' = H (**e**), Me (**f**), Ph (**g**).

Previously, the sulfonation of 1-methyl-2-(2'-thienyl)benzimidazole **II** was performed by the action of concentrated sulfuric acid and polyphosphoric acid at 120°C [4]. In these conditions a strong tarring was observed. Therefore the synthesis of sulfonic acid **IIId** (in 63% yield) was performed at 60°C. Similar to sulfonic acid of compound **II**, the acid **IIId** also exists in the betaine form. In the ^{1}H NMR spectrum the signal of the sulfo group proton was observed at 12.32 ppm only in trifluoroacetic acid solution (Table 2).

Since the formylation of compound **II** with the Vilsmeier reagent was unsuccessful, in this work for the formylation of **III** we used hexamethylenetetramine in polyphosphoric acid at 60°C. The reaction occurs in 0.5 h to give aldehyde **IIIe** in 89% yield. For comparison, the formylation of compound **II** proceeded over 10 h [5].

The acylation of compound **I** by the action of carboxylic acids in the presence of polyphosphoric acid also occurs under mild conditions (50–60°C, 1–2 h) to afford the 5'-acyl derivatives **IIIf** and **IIIg**, whereas in the case of compound **II** the acyl derivatives were obtained at 110–150°C within 20 h in 22–51% yields.

The comparison of the behavior of thienylbenzimidazole **II** and thienylvinylenebenzimidazole **I** in the electrophilic substitution reactions shows that they form a 5'-substituted thiophene derivatives. However, the reactions of compound **I** occur much faster and under milder conditions than those of **II**. The presence of the vinylene group between the rings weakens the deshielding effect of the benzimidazole substituent on the thiophene ring. The quantum-chemical calculations by the B3LYP/6-31G(d, p) method confirm this assumption. Thus, a net positive charge on the carbon atoms of the thiophene ring in the protonated molecules of compounds **I** and **II** (since the reactions proceed in the acidic medium) equals (+0.065) and (+0.113), respectively. In addition, unlike

Table 2. Spectral parameters of compounds **I, IIIa–IIIg**

Comp. no.	IR spectrum, ν, cm^{-1}	^1H NMR spectrum, δ, ppm (*J*, Hz, $CDCl_3$)
I	–	3.87 s (3H, NCH_3), 6.89 d (1H, H_{vinyl}, *J* 15.8), 7.05 t (1H, $H^{4'}$, *J* 5.0), 7.12 d (1H, $H^{3'}$, *J* 3.9), 7.25–7.29 m (3H, 5,6,7-H_{Ar}), 7.37 d (1H, $H^{5'}$, *J* 5.5), 7.70–7.73 m (1H, 4-H_{Ar}), 8.03 d (1H, H_{vinyl}, *J* 15.8)
IIIa	1370 s (NO_2) 1530, 1550 as (NO_2)	3.88 s (3H, NCH_3), 7.09 d (1H, H_{vinyl}, *J* 15.5), 7.13 d (1H, $H^{3'}$, *J* 4.3), 7.29–7.36 m (3H, 5,6,7-H_{Ar}), 7.73–7.76 m (1H, 4-H_{Ar}), 7.85 d (1H, $H^{4'}$, *J* 4.3), 7.99 d (1H, H_{vinyl}, *J* 15.5)
IIIb	–	3.88 s (3H, NCH_3), 7.07 d (1H, $H^{4'}$, *J* 3.7), 7.15 d (1H, H_{vinyl}, *J* 15.8), 7.17 d (1H, $H^{3'}$, *J* 3.7), 7.27–7.31 m (3H, 5,6,7-H_{Ar}), 7.69–7.72 m (1H, 4-H_{Ar}), 8.02 d (1H, H_{vinyl}, *J* 15.8)
IIIc	–	3.89 s (3H, NCH_3), 7.08 d (1H, $H^{4'}$, *J* 3.8), 7.17 d (1H, H_{vinyl}, *J* 15.9), 7.17 d (1H, $H^{3'}$, *J* 3.8), 7.31 d (2H, 6,7-H_{Ar}, *J* 7.9), 7.75 s (1H, 4-H_{Ar}), 8.00 d (1H, H_{vinyl}, *J* 15.9)
IIId[a]	1260 (SO_2)	3.80 s (3H, NCH_3), 6.85 d (1H, H_{vinyl}, *J* 16.0), 7.10 d (1H, $H^{3'}$, *J* 4.0), 7.28 s (4H, 4,5,6,7-H_{Ar}), 7.52 d (1H, $H^{4'}$, *J* 4.0), 7.68 d (1H, H_{vinyl}, *J* 16.0), 11.95 s (1H, SO_2OH)
IIIe	1680 (C=O)	3.87 s (3H, NCH_3), 7.09 d (1H, H_{vinyl}, *J* 15.5), 7.30 d (1H, $H^{3'}$, *J* 3.9), 7.29–7.34 m (3H, 5,6,7-H_{Ar}), 7.69 d (1H, $H^{4'}$, *J* 3.9), 7.73–7.76 m (1H, 4-H_{Ar}), 8.07 d (1H, H_{vinyl}, *J* 15.5), 9.89 s (1H, CHO)
IIIf	1650 (C=O)	2.55 s (3H, CH_3), 3.88 s (3H, NCH_3), 7.09 d (1H, H_{vinyl}, *J* 15.8), 7.28 d (1H, $H^{3'}$, *J* 4.0), 7.30–7.34 m (3H, 5,6,7-H_{Ar}), 7.67 d (1H, $H^{4'}$, *J* 4.0), 7.73–7.77 m (1H, 4-H_{Ar}), 8.05 d (1H, H_{vinyl}, *J* 15.8)
IIIg	1670 (C=O)	3.88 s (3H, NCH_3), 7.10 d (1H, H_{vinyl}, *J* 16.0), 7.28 d (1H, $H^{3'}$, *J* 4.1), 7.30–7.34 m (3H, 5,6,7-H_{Ar}), 7.53 t (3H, 3,4,5-H_{Ar}, *J* 7.5), 7.69 d (1H, $H^{4'}$, *J* 4.1), 7.73–7.77 m (1H, 4-H_{Ar}), 7.91 d (2H, 2,6-H_{Ar}, *J* 7.2), 8.03 d (1H, H_{vinyl}, *J* 16.0)

[a] ^1H NMR spectrum is removed in trifluoroacetic acid.

the previously studied furan analogs [1], compounds **IIIe**–**IIIg** were found to undergo no changes in the *trans*-orientation of the substituents at the double bond. The toluene and acetonitrile solutions of compounds **IIIe**–**IIIg** fluoresce strongly when irradiated with UV light, which suggests their photoluminescent properties.

EXPERIMENTAL

The IR spectra were recorded on a Specord 75 IR spectrometer for the samples in chloroform. The ^1H NMR spectra were taken on a Varian Unity 300 instrument (300 MHz) in the pulsed Fourier mode relative to the residual proton signals of $CDCl_3$ and DMSO-d_6 (δ 7.26 and 2.50 ppm, respectively). The elemental analysis was carried out on a Perkin-Elmer 2400 instrument. The melting points were determined by the capillary method. The reaction progress and individuality of the synthesized compounds were monitored by TLC using the plates coated with Al_2O_3 of **II** degree of the Brockman activity (detecting with iodine vapor) or Silufol UV-254 plates.

1-Methyl-2-[β-(thien-2-yl)vinylene]-1*H*-benzimidazole (I). A mixture of 4.48 g (40 mmol) of thiophene-2-aldehyde, 5.84 g (40 mmol) of 1,2-dimethylbenzimidazole and 0.9 g (0.07 mol) of fused zinc chloride was heated for 3 h at 160°C. The reaction mixture was cooled and triturated with acetone and water. The precipitate was separated and crystallized from heptane. The yield, melting point, and elemental analysis data of **I** are given in Table 1.

1-Methyl-2-[β-(5-nitrothien-2-yl)vinylene]-1*H*-benzimidazole (IIIa). Preparation of the nitrating mixture: to 16.9 g (70 mmol) of $Cu(NO_3)_2 \cdot 3H_2O$ was added in small portions 40 ml of acetic anhydride with cooling, making sure that the temperature of the reaction mixture does not rise above 30–40°C. When the exothermic reaction completed, the mixture was kept at room temperature for 24 h. After the precipitate of copper(II) acetate was filtered off, the resulting mixture was stored no more than 10 days at 5–10°C.

To a solution of 1.20 g (5 mmol) of compound **I** in 5 ml of acetic anhydride was added dropwise 1.4 ml of the nitrating mixture under vigorous stirring at room temperature over 330–40 min. The mixture was diluted with 25 ml of cold water and neutralized with 25% solution of ammonia. The precipitate was separated, washed thoroughly with water, and crystallized from a benzene–heptane mixture (1:1).

1-Methyl-2-[β-(5-bromothien-2-yl)vinylene]-1*H*-benzimidazole (IIIb). To a solution of 1.20 g (5 mmol) of compound **I** in 20 ml of acetic acid was slowly added 1.6 g (10 mmol) of bromine in 10 ml of acetic acid under vigorous stirring at 50°C. The

reaction mixture was kept at this temperature for 1 h. The precipitated hydrobromide **IIIb** was separated. The free base was obtained by the action of 50 ml of 10% aqueous ammonia solution followed by recrystallization from heptane.

1-Methyl-5(6)-bromo-2-[β-(5-bromothien-2-yl)-vinylene]-1*H*-benzimidazole (IIIc). To a solution of 1.20 g (5 mmol) of compound **I** in 10 ml of dichloroethane at 80°C was gradually added a solution of 2.4 g (15 mmol) of bromine in 10 ml of dichloroethane. After heating at the same temperature for 2 h the reaction mixture was cooled and concentrated. The residue was neutralized with aqueous ammonia and extracted with 2×25 ml of chloroform. The extract was dried, concentrated, and chromatographed on a column (*h* 20 cm, *d* 2.5 cm) filled with alumina eluting with chloroform. After chloroform removal, the residue was recrystallized from n-octane.

1-Methyl-2-[β-(5-sulfothien-2-yl)vinylene]-1*H*-benzimidazole (IIId). A mixture of 1.20 g (5 mmol) of compound **I**, 0.59 g (6 mmol) of sulfuric acid (*d* 1.84 g cm^{-3}), and 15 g of polyphosphoric acid was heated at 60°C for 1 h. Then the reaction mixture was cooled and diluted with 50 ml of water. The precipitate was separated and recrystallized from water.

1-Methyl-2-[β-(5-formylthien-2-yl)vinylene]-1*H*-benzimidazole (IIIe). A mixture of 1.20 g (5 mmol) of compound **I** and 1.40 g (10 mmol) of hexamethylenetetramine in 15 g of polyphosphoric acid was stirred at 60°C for 0.5 h. Then the reaction mixture was diluted with 50 ml of water and carefully neutralized with concentrated ammonia solution to pH 7–8. The reaction product was extracted with 50 ml of chloroform and chromatographed on a column (*h* 20 cm, *d* 2.5 cm) filled with alumina, eluting with chloroform. The target compound was recrystallized from aqueous alcohol.

1-Methyl-2-[β-(5-acetylthien-2-yl)vinylene]-1*H*-benzimidazole (IIIf). A mixture of 1.20 g (5 mmol) of compound **I** and 0.6 g (10 mmol) of glacial acetic acid in 20 g of polyphosphoric acid was stirred at 50°C for 1 h. Then the reaction mixture was diluted with 75 ml of water and neutralized with ammonia. Further isolation of the reaction product was carried out similarly to compound **IIIe**.

1-Methyl-2-[β-(5-benzoylthien-2-yl)vinylene]-1*H*-benzimidazole (IIIg). A mixture of 1.20 g (5 mmol) of compound **I** and 1.22 g (10 mmol) of benzoic acid in 20 g of polyphosphoric acid was stirred at 60°C for 2 h. Then the benzoylation product was isolated and purified similarly to compounds **IIIe**, **IIIf**.

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