A NOVEL SYNTHESIS OF [1]BENZOTHIENO[3,2-*b*][1]BENZOFURAN

Kateřina ČERNOVSKÁ[1], Miloslav NIČ, Pavel PIHERA and Jiří SVOBODA[2,*]

Department of Organic Chemistry, Institute of Chemical Technology, Prague, 166 28 Prague 6, Czech Republic; e-mail: [1] katerina.cernovska@vscht.cz, [2] jiri.svoboda@vscht.cz

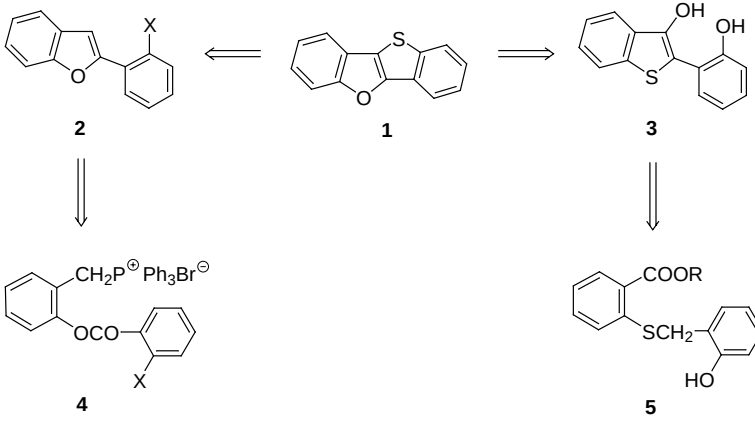
Received October 25, 2000
Accepted December 14, 2000

A new synthesis of the title compound based on the formation of the furan ring in the key step was elaborated. Methyl 2-methoxy[1]benzothieno[3,2-*b*][1]benzofuran-7-carboxylate (**15**) was prepared by this methodology as a new type of a core for liquid crystal synthesis.
Key words: [1]Benzothieno[3,2-*b*][1]benzofuran; Benzofurans; Benzothiophenes; Fused heterocycles; Heteropentalenes; Liquid crystals.

Synthesis and reactivity of [1]benzothieno[3,2-*b*]furan and thieno[3,2-*b*]-[1]benzofuran has been extensively investigated in the last years[1–3]. It was shown that [1]benzothieno[3,2-*b*]furan and its vinyl derivatives can be used[4,5] in Diels–Alder reactions for construction of a new benzofused heterocyclic system – [1]benzothieno[3,2-*b*][1]benzofuran (**1**), the reactivity of which was also reported[6]. General disadvantages of the studied cycloadditions involve high reaction temperatures, long reaction times, lower yields and the necessity to use the sealed-tube technique. Side reactions as a result of consecutive cycloaddition reactions also complicated syntheses of the ring system **1** and its derivatives. The design and synthesis of new types of liquid crystalline materials is an important area, as it can supply target molecules for the mesophase behaviour investigation. Recently, we introduced[7,8] the thieno[3,2-*b*]furan skeleton as a new type of heteroaromatic core for construction of new ferroelectric liquid crystals. That is why an effective synthesis of dibenzofused system **1** for creating a core of new liquid crystals was the aim of our following studies. In this paper, we wish to report the results of development of a general synthesis of **1** as well as its unsymmetrically disubstituted derivative **15**.

Retrosynthetic disconnection (Scheme 1) of the parent heterocyclic system of **1** led to a key intermediate: a 2-(2-sulfanylphenyl)[1]benzofuran **2**, possessing a thiol group (X = SH) or a precursor group in position 2 of the phenyl ring. Formation of the thiophene ring could be achieved[9–13] by an

electrophilic or radical transformation of the corresponding sulfenyl halide. The structure **2** should be accessible by an intramolecular cycloaddition reaction of the Wittig type[14–18] from phosphonium salt **4**. The second concept is based on disconnection of the furan ring of **1** leading to dihydroxy derivative **3**. Cyclization of analogous diols has been applied[19] in the dibenzofuran synthesis. Opening of the thiophene ring of **3** leads to an open-chain 2-sulfanylbenzoate derivative **5**.

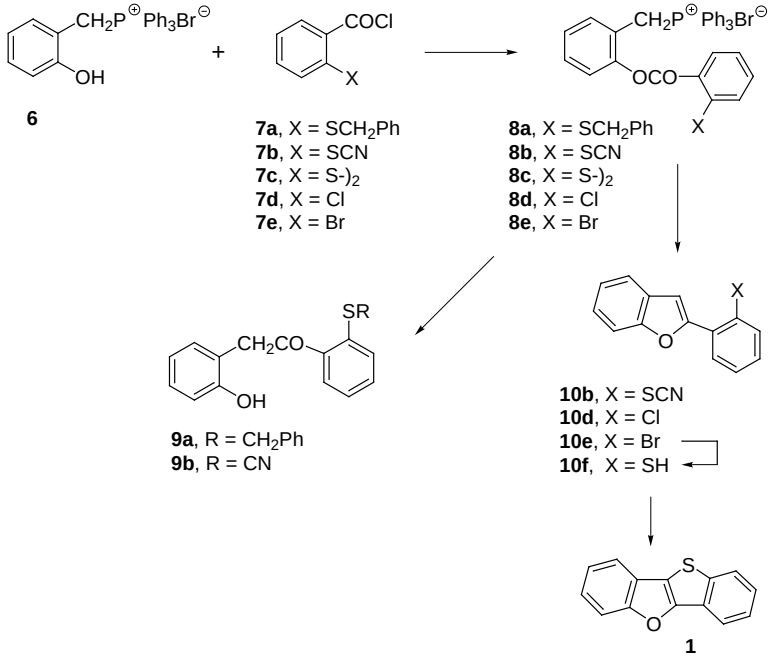


SCHEME 1

2-(2-Substituted phenyl)[1]benzofurans are available by various procedures in moderate yields[16,20–22], but most of the used methods are not compatible with the presence of a free thiol group. Although many protective groups for the thiol functionality are known[23], deprotection usually needs strong agents, which could at the same time attack the furan ring in **2**. We attempted to mask the thiol group in **2** as an *S*-benzyl derivative, thiocyanate or disulfide, the latter two being able to cyclize directly[24] (Scheme 2). Another chance of introducing the thiol group in the molecule **2** is a transformation of the corresponding halobenzene precursors.

However, acylation of phosphonium salt **6** (ref.[15]) with 2-(benzylsulfanyl)benzoyl chloride (**7a**) did not result in the formation of the corresponding acylated derivative **8a** but compound **9a**, which was probably formed by subsequent cyclization and furan ring opening, was obtained instead. Neither strong anhydrous conditions nor lowering the reaction temperature to 0 °C led to isolation of **8a**. 2-Thiocyanatobenzoyl chloride (**7b**), on the other hand, furnished smoothly and in a good yield phosphonium salt **8b**. Its subsequent intramolecular cyclization using triethylamine in toluene did not afford the desired [1]benzofuran **10b** either, but the open de-

rivative **9b** was isolated as the sole product. No trace of compound **10b** could be detected by TLC and HLPC analyses in the course of the reaction. From these results it can be concluded, that intramolecular Wittig reaction of this type with sulfur-containing compounds proceeds in a different course from that postulated earlier[14]. A different course showed also the attempted reaction with disulfide **7c**. In the acylation step, we indeed ob-



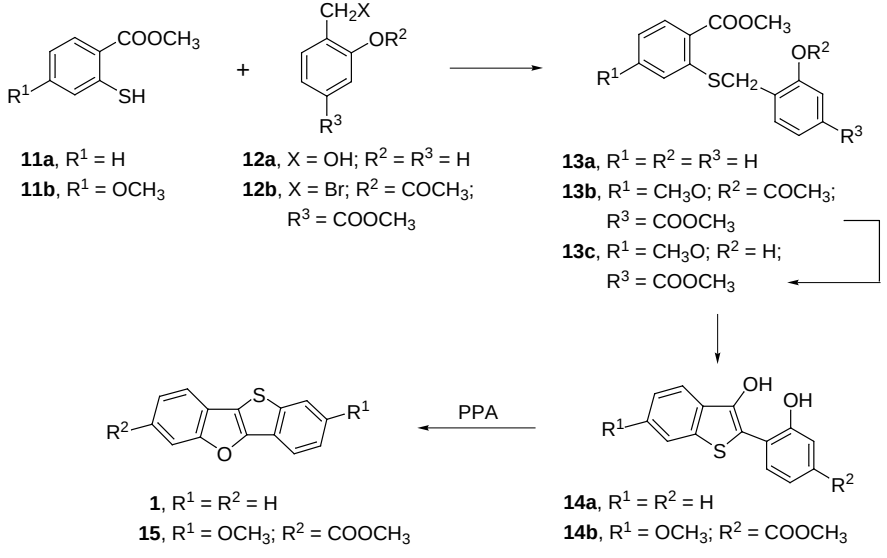
SCHEME 2

tained the required bisphosphonium salt **8c**, though not in analytical purity, but its structure was confirmed by spectral measurements. Cyclization of salt **8c** with triethylamine in toluene led to the formation of a complex mixture of products from which, surprisingly, compound **1** was isolated in a low yield of 5%. Although its occurrence in the reaction mixture confirms the assumed course of the reaction sequence, its low yield suggests that some decomposition reactions are preferred. This can also be supported by the fact that triphenylphosphine was isolated from the reaction mixture in 22% yield. The same results were obtained when phosphonium salt **6** was treated with **7c** in a one-pot reaction.

That is why we tried to introduce the thiol functionality by transformation of halo derivatives **10d** and **10e**. These 2-(2-halophenyl)[1]benzofurans

were easily obtained by using the above mentioned concept – acylation of phosphonium salt **6** with 2-chloro- (**7d**) or 2-bromobenzoyl chloride (**7e**) proceeded smoothly as well as the subsequent base-catalyzed cyclization to **10d** and **10e**, respectively. Lithiation[16,25,26] of bromo derivative **10e** was performed with butyllithium in THF at –78 °C and the formed lithium salt was trapped by sulfur to afford thiol **10f** in 68% yield. Cyclization of analogous thiols was accomplished with various agents[9–13]. In our case, the reactions of **10f** with bromine and *N*-bromosuccinimide (NBS) in various solvents (dioxane, acetic acid, tetrachloromethane) failed. Even after long-term heating with iodine in 1,4-dioxane, compound **1** was isolated only in a low yield of 21%. A good yield of **1** was obtained by heating **10d** and **10e** with elemental sulfur in a sealed tube at high temperature. Optimization of this reaction with bromo derivative **10e** showed that cyclization does not take place below 230 °C. The best yield of **1** (58%) was obtained by heating both components at 300 °C for 2 h. Analogously, chloro derivative **10d** afforded **1** under the same conditions in a 68% yield. Because this high-temperature process was not more advantageous than the older procedures[4], we tried to exploit the second concept based on the furan ring disconnection.

Due to instability of hydroxybenzyl halides[27], a standard base-catalyzed alkylation of 2-sulfanylbenzoate ester **11a** was impossible (Scheme 3). Thus, a Lewis-acid-catalyzed[28] alkylation with salicyl alcohol (**12a**) was chosen.



11a, R^1 = H
11b, R^1 = OCH_3

12a, X = OH; R^2 = R^3 = H
12b, X = Br; R^2 = $COCH_3$; R^3 = $COOCH_3$

13a, R^1 = R^2 = R^3 = H
13b, R^1 = CH_3O; R^2 = $COCH_3$; R^3 = $COOCH_3$
13c, R^1 = CH_3O; R^2 = H; R^3 = $COOCH_3$

14a, R^1 = R^2 = H
14b, R^1 = OCH_3; R^2 = $COOCH_3$

1, R^1 = R^2 = H
15, R^1 = OCH_3; R^2 = $COOCH_3$

SCHEME 3

Alkylation of **11a** was effected with freshly prepared zinc iodide in dichloromethane and compound **13a** was obtained in 65% yield. We investigated the base-catalyzed cyclization of **13a** with various bases: application of potassium *tert*-butoxide, sodium hydride and dimsyl sodium led only to recovery of the starting compound. Only lithium diisopropylamide (LDA) was effective in the deprotonation of the slightly acid hydrogen atoms of the methylene group. Cyclization in THF at room temperature then afforded the desired dihydroxy-2-phenyl[1]benzothiophene **14a** in 90% yield. Subsequent cyclodehydration of **14a** was accomplished successfully by heating with polyphosphoric acid (PPA) to 90 °C giving **1** in a moderate yield of 47%.

This synthetic sequence was successfully used for synthesis of a difficultly accessible, unsymmetrically disubstituted [1]benzothieno[3,2-*b*][1]benzothiophene derivative **15** possessing both substituents on the long axis of the molecule. Its synthesis (Scheme 3) started with 4-methoxy-2-sulfanylbenzoate ester **11b** (ref.[29]). Preparation of such a properly substituted salicyl alcohol is not an easy task, therefore alkylation was performed rather with bromo compound **12b** (refs[30,31]), while the hydroxyl group was protected as an acetate. Under basic conditions, ester **13b** was obtained in 86% yield. The protecting group in **13b** was removed by transesterification with methanol under sodium methoxide catalysis to afford **13c** in 97% yield. Subsequent cyclization was accomplished with potassium *tert*-butoxide under analogous conditions and **14b** was isolated in 58% yield. It was found that compound **14b** exists in solution (deuteriochloroform) as a mixture of keto and enol forms in approximately 90 : 10 ratio. Cyclodehydration of **14b** to the desired ester **15** was performed with PPA in toluene at 80 °C with 52% yield.

A new synthetic procedure based on the formation of the furan ring in the key step was elaborated for preparation of [1]benzothieno-[3,2-*b*][1]benzofuran and its derivatives. Application of compound **15** in synthesis and physical studies of new ferroelectric liquid crystals will be the subject of further research.

EXPERIMENTAL

Melting points were determined on a Boetius block and are uncorrected. ^{1}H NMR spectra were taken on a Varian–Gemini 300 HC spectrometer. Deuteriochloroform and DMSO-d_6 (compounds **8b**–**8d**) were used as solvents, their signals serving as internal standards. Chemical shifts are given in the δ-scale (ppm), coupling constants ^3J(H,H) in Hz. IR spectra were recorded on a Nicolet FTIR 740 spectrometer in chloroform or KBr (compounds **8b**–**8d**).

Triphenyl{2-[(2-thiocyanatobenzoyl)oxy]benzyl}phosphonium Bromide (**8b**)

To a stirred mixture of phosphonium bromide **6** (ref.[14]) (1.75 g, 3.89 mmol), 2-thiocyanatobenzoyl chloride[32] (1.01 g, 5.11 mmol) and chloroform (4 ml), dry pyridine (0.65 g, 8.05 mmol) was added dropwise under cooling to 0 °C. Stirring was continued for 45 min, the solution was diluted with chloroform (50 ml), washed with water and dried with anhydrous magnesium sulfate. Evaporation of the filtrate and trituration of the residue with ether (10 ml) afforded 2.0 g (84%) of phosphonium bromide **9b**, m.p. 162–166 °C. ^{1}H NMR (DMSO-d_6): 5.23 d, 2 H, J = 15.4 (CH_2-P^+); 7.00–7.90 m, 23 H (Ar-H). IR (KBr): 2 154 (SCN); 1 711 (C=O). For $C_{33}H_{25}BrNO_2PS$ (610.5) calculated: 64.92% C, 4.13% H, 2.29% N; found: 65.22% C, 4.33% H, 2.01% N.

In an analogous manner, the following phosphonium bromides were obtained:

P,P,P,P′,P′,P′-Hexaphenyl-P,P′-{disulfanediylbis[(1,2-phenylene)carbonyloxy(1,2-phenylene)methylene]}bisphosphonium bromide (**8c**). Yield 97%, m.p. 148–152 °C. ^{1}H NMR (DMSO-d_6): 5.26 d, 2 H, J = 15.4 (CH_2-P^+); 7.05–7.95 m, 23 H (Ar-H). IR (KBr): 1 717 (C=O).

{2-[(2-Chlorobenzoyl)oxy]benzyl}triphenylphosphonium bromide (**8d**). Yield 90%, m.p. 173–175 °C. ^{1}H NMR (DMSO-d_6): 5.13 d, 2 H, J = 14.8 (CH_2-P^+); 7.05–7.85 m, 23 H. IR (KBr): 1 736 (C=O). For $C_{32}H_{25}BrClO_2P$ (587.9) calculated: 65.38% C, 4.29% H, 13.59% Br, 6.03% Cl; found: 65.52% C, 4.50% H, 11.10% Br, 6.78% Cl.

{2-[(2-Bromobenzoyl)oxy]benzyl}triphenylphosphonium bromide (**8e**). Yield 92%, m.p. 188–190 °C; ref.[16], m.p. 189–192 °C.

1-[(2-Benzylsulfanyl)phenyl]-2-(2-hydroxyphenyl)ethan-1-one (**9a**)

A solution of 2-(benzylsulfanyl)benzoyl chloride[33] (1.30 g, 4.94 mmol) in chloroform (10 ml) was added dropwise to a stirred mixture of phosphonium bromide **6** (1.73 g, 3.85 mmol), pyridine (0.78 g, 9.9 mmol) and chloroform (15 ml) at 0 °C. Stirring was continued at room temperature for 1 h and the reaction mixture was worked up as for **8b**. The crude product was purified by column chromatography (silica gel, elution with a hexane–toluene, 1 : 1) to afford 0.93 g (72%) of ethanone **9a,** m.p. 115.5–117 °C (toluene–hexane). ^{1}H NMR: 4.16 s, 2 H (CH_2S); 5.37 s, 2 H (CH_2CO); 7.14 t, 1 H, J = 7.6; 7.25–7.48 m, 12 H; 8.01 d, 1 H, J = 7.7. IR: 1 708 (C=O). For $C_{21}H_{18}O_2S$ (334.4) calculated: 75.42% C, 5.43% H, 9.59% S; found: 75.32% C, 5.54% H, 9.84% S.

2-(2-Hydroxyphenyl)-1-(2-thiocyanatophenyl)ethan-1-one (**9b**)

To a slurry of phosphonium bromide **8b** (1.88 g, 3.88 ml) in dry 1,2-dimethoxyethane, triethylamine (0.65 ml, 4.66 mmol) was added and the mixture was stirred at room temperature for 1 h. Triethylammonium bromide was filtered off and the filtrate was evaporated to dryness. Column chromatography (silica gel, toluene–*tert*-butyl methyl ether, 10 : 1) afforded 0.52 g (63%) of compound **9b**, m.p. 159–162 °C (ethyl acetate). ^{1}H NMR: 4.33 s, 2 H (CH_2CO); 5.90 s, 1 H (OH); 6.90 m, 2 H; 7.18 m, 2 H; 7.50 dd, 1 H, J_1 = 7.7, J_2 = 7.1; 7.68 dd, 1 H, J_1 = 7.7, J_2 = 6.6; 7.99 d, 1 H, J = 8.2; 8.27 d, 1 H, J = 7.7. ^{13}C NMR (one quaternary carbon was not detected): 41.0 (CH_2), 112.9, 117.4 (C-H), 121.0, 122.0 (C-H), 128.3 (C-H), 129.5 (C-H), 129.9 (C-H), 131.9 (C-H), 132.1, 132.4 (C-H), 135.2 (C-H), 154.9 (C-OH), 200.4 (C=O). IR: 3 453 (OH); 2 146 (SCN); 1 666 (CO). MS, *m/z* (%): 242 (30) [M^+ – HCN], 226 (50) [M^+ – HCN – O], 162 (100) [$C_8H_4NOS]^+$, 134 (20) [$C_7H_4NS]^+$, 107 (70), 77 (20), 57 (20). For

$C_{15}H_{11}NO_2S$ (269.3) calculated: 66.90% C, 4.12% H, 5.20% N, 11.90% S; found: 67.40% C, 4.25% H, 5.20% N, 11.68% S.

2-(2-Chlorophenyl)[1]benzofuran (**10d**)

A mixture of phosphonium salt **8d** (1.5 g, 2.55 mmol), triethylamine (0.54 ml, 3.9 mmol) and dry toluene (15 ml) was stirred and refluxed in nitrogen atmosphere for 1.5 h, the solid was filtered off, the filtrate was evaporated and the crude product was extracted with pentane (5 × 15 ml) to remove triphenylphosphine oxide. The pentane solution was evaporated and the residue was purified by column chromatography (silica gel, hexane) and 0.494 g (85%) of **10d** was obtained, m.p. 45–46 °C; ref.[22], m.p. 47–48 °C.

2-(2-Bromophenyl)[1]benzofuran (**10e**)

In an analogous manner to **10d**, bromo derivative **10e** was obtained, yield 58%, m.p. 35–37 °C; ref.[16], m.p. 36–37 °C.

2-[1]Benzofuran-2-yl)benzene-1-thiol (**10f**)

Butyllithium (1.50 ml of 2.2 M solution in hexanes, 3.30 mmol) was added dropwise to a solution of bromo derivative **10e** (0.75 g, 2.74 mmol) in dry tetrahydrofuran (10 ml) at –78 °C in nitrogen atmosphere, the mixture was stirred at the temperature for 2 h and subsequently sulfur (90 mg, 2.81 mmol) was added in two portions. Stirring was continued at room temperature for 16 h and then lithium aluminum hydride (0.40 g, 10.8 mmol) was added. After 4 h at room temperature, excess of the hydride was decomposed with a saturated aqueous ammonium chloride solution (5 ml) and the product was extracted with ether (3 × 10 ml). The combined organic layers were washed with water (10 ml) and dried with anhydrous magnesium sulfate. The crude product was purified by column chromatography (silica gel, hexane) and 0.42 g (68%) of oily **10f** was obtained. ^{1}H NMR: 7.23–7.35 m, 4 H; 7.42 s, 1 H (H-3); 7.44 dd, 1 H, J_1 = 7.8, J_2 = 2.2; 7.54 d, 1 H, J = 8.8; 7.65 d, 1 H, J = 8.8; 7.93 dd, 1 H, J_1 = 7.7, J_2 = 2.2. IR: 2 552 (SH). For $C_{14}H_{10}OS$ (226.3) calculated: 74.31% C, 4.45% H, 14.16% S; found: 74.24% C, 4.25% H, 14.01% S.

[1]Benzothieno[3,2-*b*][1]benzofuran (**1**)

Method A. To phosphonium salt **6** (3.0 g, 6.68 mmol) in dry toluene (40 ml), 2,2′-disulfanediyldi(benzoyl chloride)[34] (**7c**) (1.27 g, 3.70 mmol) and triethylamine (2.8 ml, 20.1 mmol) were successively added. The mixture was stirred and heated to reflux for 6 h, cooled to room temperature and worked up as for **10d**. Column chromatography (silica gel, hexane) afforded 76 mg (5%) of **1**, m.p. 129–132 °C; ref.[4], m.p. 130–132 °C, and 240 mg (14%) of triphenylphosphine, m.p. 78–80 °C, identical with a standard.

Method B. In an analogous reaction of phosphonium bromide **8c** (1.10 g, 094 mmol), triethylamine (0.40 ml, 2.87 mmol) and toluene (9 ml), 45 mg (11%) of **1** was obtained along with 110 mg (22%) of triphenylphosphine.

Method C. A solution of thiol **10f** (0.26 g, 1.15 mmol) and iodine (0.87 g, 3.45 mmol) in 1,4-dioxane (10 ml) was refluxed under nitrogen for 72 h, diluted with water (100 ml) and washed with chloroform (4 × 25 ml). The combined organic layers were washed with a 5% sodium thiosulfate solution (3 × 30 ml), water (25 ml) and dried with anhydrous magnesium

sulfate. The filtrate was evaporated and the residue chromatographed (silica gel, hexane); 54 mg (21%) of **1** was obtained.

Method D. A mixture of bromo derivative **10e** (100 mg, 0.37 mmol) and sulfur (20 mg, 0.62 mmol) was heated in a sealed tube at 300 °C for 3 h. After cooling, the content of the tube was dissolved in chloroform (30 ml), the solution was filtered and evaporated. Purification by column chromatography (silica gel, hexane) afforded 50 mg (58%) of **1**. In a similar manner, chloro derivative **10d** (0.76 g, 3.32 mmol) and sulfur (0.177 g, 5.52 mmol) afforded compound **1** in 68% yield.

Method E. A mixture of diol **14a** (0.600 g, 2.48 mmol) and polyphosphoric acid (20 g) was heated under stirring at 90 °C in nitrogen atmosphere, and, after cooling, decomposed with water (200 ml) and washed with ethyl acetate (3 × 50 ml). Combined organic solutions were washed with water (30 ml), brine (30 ml) and dried with anhydrous magnesium sulfate. After removing the solvent, the residue was purified by column chromatography (silica gel, hexane) to afford 260 mg (47%) of **1**.

Methyl 4-(Bromomethyl)-3-acetoxybenzoate (**12b**)

A stirred mixture of methyl 3-acetoxy-4-methylbenzoate[30,31] (5.0 g, 24.0 mmol), *N*-bromosuccinimide (5.35 g, 30 mmol), dibenzoyl peroxide (0.2 g) and tetrachloromethane (60 ml) was heated to reflux for 6 h, cooled to room temperature and filtered. The filtrate was evaporated and the residue crystallized to afford 4.58 g (66%) of bromo derivative **12b**, m.p. 116–118 °C (diethyl ether–hexane). ^{1}H NMR: 2.39 s, 3 H (CH_3CO); 3,91 s, 3 H (OCH_3); 4.42 s, 2 H (CH_2Br); 7.49 d, 1 H, J = 7.6 (H-5); 7.46 d, 1 H, J = 2.1 (H-2); 7.89 dd, 1 H (H-6). IR: 1 721 (C=O). For $C_{11}H_{11}BrO_4$ (287.1) calculated: 46.02% C, 3.86% H, 27.83% Br; found: 45.97% C, 3.74% H, 27.58% Br.

Methyl 2-[(2-Hydroxybenzyl)sulfanyl]benzoate (**13a**)

A mixture of methyl thiosalicylate (**11a**) (2.0 g, 11.9 mmol), 2-hydroxybenzyl alcohol (**12a**) (1.47 g, 11.9 mmol) and freshly prepared zinc iodide (3.79 g, 12 mmol) in dry dichloromethane (30 ml) was stirred at room temperature in nitrogen atmosphere for 14 h, poured into cold water (150 ml), washed with chloroform (3 × 30 ml) and dried with anhydrous magnesium sulfate. The solvent was evaporated and after crystallization from toluene, 2.10 g (65%) of ester **13a** was obtained, m.p. 95–97 °C. ^{1}H NMR: 3.93 s, 3 H (OCH_3); 4.22 s, 2 H (CH_2S); 6.09 s, 1 H (OH); 6.87 m, 2 H; 7.22 m, 3 H; 7.46 m, 2 H; 7.95 dd, 1 H, J_1 = 7.7, J_2 = 1.7. IR: 3 421 (OH); 1 711 (CO). For $C_{15}H_{14}O_3S$ (274.3) calculated: 65.68% C, 5.15% H, 11.67% S; found: 66.08% C, 5.57% H, 11.39% S.

Methyl 2-{[2-Acetoxy-4-(methoxycarbonyl)benzyl]sulfanyl}-4-methoxybenzoate (**13b**)

A mixture of ester **11b** (ref.[29]) (2.63 g, 13.3 mmol), bromo derivative **12b** (4.0 g, 13.9 mmol), freshly fused potassium carbonate (5.3 g, 38.3 mmol) and dry acetone (100 ml) was stirred at room temperature for 2 h, then filtered and the solvent was evaporated. After crystallization from methanol, 4.84 g (86%) of **13b** was obtained, m.p. 81–83 °C. ^{1}H NMR: 2.37 s, 3 H (CH_3CO); 3.74 s, 3 H (OCH_3); 3.89 s, 3 H (OCH_3); 3.91 s, 3 H (OCH_3); 4.09 s, 2 H (CH_2); 6.64 d, 1 H, J = 1.6; 6.67 d, 1 H, J = 2.0; 7.61 d, 1 H, J = 8.0; 7.77 d, 1 H, J = 1.6; 7.85 dd, 1 H; 7.96 dd, 1 H. IR: 1 769, 1 720 (C=O). For $C_{20}H_{20}O_7S$ (404.4) calculated: 59.40% C, 4.98% H, 7.93% S; found: 59.36% C, 4.85% H, 7.69% S.

Methyl 2-{[2-Hydroxy-4-(methoxycarbonyl)benzyl]sulfanyl}-4-methoxybenzoate (**13c**)

To a solution of ester **13b** (4.40 g, 10.9 mmol) in dry methanol (50 ml), sodium methoxide (54 mg, 1 mmol) was added and the mixture was stirred at room temperature for 30 min. Then it was acidified with a methanolic HCl solution and evaporated to dryness. The residue was taken into chloroform (150 ml), washed successively with water (30 ml) and saturated sodium chloride solution, and dried with anhydrous magnesium sulfate. Evaporation of the solvent was followed by crystallization from toluene to afford 3.82 g (97%) of **13c**, m.p. 147–149 °C. ^{1}H NMR: 3.82 s, 3 H (OCH_3); 3.91 s, 6 H (2 × OCH_3); 4.24, 2 H (CH_2); 6.33 d, 1 H, J = 2.0; 6.74 dd, 1 H, J_1 = 8.8, J_2 = 2.4; 7.38 d, 1 H, J = 7.9; 7.55 dd, 1 H; 7.98 d, 1 H. IR: 3 591, 3 410 (OH); 1 707 (C=O). For $C_{18}H_{18}O_6S$ (362.4) calculated: 59.66% C, 5.01% H, 8.85% S; found: 59.44% C, 5.06% H, 8.88% S.

2-(2-Hydroxyphenyl)[1]benzothiophen-3-ol (**14a**)

A solution of diisopropylamine (16.2 ml, 120 mmol) in tetrahydrofuran (175 ml) was treated with a 1.6 M solution of butyllithium in hexanes (41.7 ml, 87 mmol) at –78 °C, the mixture was stirred at 0 °C for 0.5 h and cooled back to –78 °C. At this temperature, ester **13a** (8.35 g, 29 mmol) in tetrahydrofuran (40 ml) was added dropwise and stirring was continued at room temperature for 1 h. The reaction was quenched with water (200 ml), the mixture was acidified with dilute hydrochloric acid (1 : 1) and washed with chloroform (3 × 100 ml). The combined organic layers were washed successively with water and brine and dried with anhydrous magnesium sulfate. After evaporation of the solvent, the residue was purified by column chromatography (silica gel, hexane) and 4.29 g (62%) of **14a** was obtained as an yellowish oil. ^{1}H NMR: 6.98 t, 1 H, J = 8.2; 7.08 t, 1 H, J = 7.8; 7.38 m, 2 H; 7.51 m, 2 H; 7.74 d, 1 H, J = 8.2; 7.81 d, 1 H, J = 8.1. IR: 3 575, 3 241, 3 069, 2 927, 1 676, 1 576, 1 450, 1 287, 1 178, 1 160, 1 093, 1 060. For $C_{14}H_{10}O_2S$ (242.3) calculated: 69.40% C, 4.16% H, 13.23% S; found: 69.11% C, 4.44% H, 13.06% S.

Methyl 2-Hydroxy-4-(3-hydroxy-6-methoxy[1]benzothiophen-2-yl)benzoate (**14b**)

To a solution of ester **13c** (0.50 g, 1.38 mmol) in dry tetrahydrofuran (10 ml), a solution of potassium *tert*-butoxide (0.46 g, 4.12 mmol) in tetrahydrofuran (5 ml) was added dropwise at room temperature in nitrogen atmosphere. The mixture was stirred for 5 h, acidified with methanolic hydrogen chloride to pH 3, diluted with water (20 ml) and washed with dichloromethane (2 × 30 ml). The organic solution was washed with water (30 ml), saturated sodium chloride solution (30 ml) and dried with anhydrous magnesium sulfate. Evaporation left a residue which was chromatographed (silica gel, chloroform–methanol 97 : 3) and afforded 263 mg (58%) of **14b**, m.p. 141–145 °C. In a deuteriochloroform solution, both keto and enol forms were detected in ^{1}H NMR in approximately 10 : 90 ratio. Only the ^{1}H NMR spectrum of the enol form could be assigned: 3.86 s, 3 H (OCH_3); 3.94 s, 3 H (OCH_3); 6.74 dd, 2 H; 7.02 d, 1 H, J = 8.3; 7.44 d, 1 H, J = 8.3; 7.48 d, 1 H, J = 2.0; 7.70 d, 1 H, J = 8.8. IR: 3 460 (OH); 1 718 (C=O). For $C_{17}H_{14}O_5S$ (330.4) calculated: 61.81% C, 4.27% H, 9.71% S; found: 61.55% C, 4.50% H, 9.48% S.

Methyl 2-Methoxy[1]benzothieno[3,2-*b*][1]benzofuran-7-carboxylate (**15**)

A toluene solution (10 ml) of **14b** (0.45 g, 1.36 mmol) was added to polyphosphoric acid (10 g) and the mixture was vigorously stirred at 80 °C for 1 h. After decomposition with cold water (200 ml) and washing with chloroform (3 × 10 ml), the combined organic layers were washed with water (2 × 30 ml), saturated sodium hydrogencarbonate solution (20 ml) and dried with anhydrous magnesium sulfate. After evaporation of the solvent, crude **2** was purified by column chromatography (silica gel, dichloromethane–hexane 1 : 1) to afford 0.22 g (52%) of ester **2**, m.p. 168–170 °C. ^{1}H NMR: 3.71 s, 3 H (OCH_3); 3.97 s, 3 H (OCH_3); 7.11 d, 1 H, *J* = 8.2; 7.35 d, 1 H, *J* = 2.0; 7.67 d, 1 H, *J* = 8.3; 7.90 d, 1 H, *J* = 8.8; 8.03 d, 1 H, *J* = 8.2; 8.27 d, 1 H, *J* = 2.1. IR: 1 714 (C=O). For $C_{17}H_{12}O_4S$ (312.3) calculated: 65.38% C, 3.87% H, 10.27% S; found: 65.11% C, 3.84% H, 10.08% S.

The authors are indebted to the corresponding departments of the Central Laboratories of the Institute of Chemical Technology, Prague, for elemental analyses and spectral measurements. Financial support from the Grant Agency of the Czech Republic is gratefully acknowledged (project No. 106/00/0580).

REFERENCES

1. Svoboda J., Nič M., Paleček J.: *Collect. Czech. Chem. Commun.* **1993**, *58*, 2983.
2. Svoboda J., Pihera P., Sedmera P., Paleček J.: *Collect. Czech. Chem. Commun.* **1996**, *61*, 888.
3. Váchal P., Pihera P., Svoboda J.: *Collect. Czech. Chem. Commun.* **1997**, *62*, 1468.
4. Pihera P., Paleček J., Svoboda J.: *Collect. Czech. Chem. Commun.* **1998**, *63*, 681.
5. Pihera P., Dvořáková H., Svoboda J.: *Collect. Czech. Chem. Commun.* **1999**, *64*, 389.
6. Pihera P., Svoboda J.: *Collect. Czech. Chem. Commun.* **2000**, *65*, 58.
7. Váchal P., Svoboda J., Glogarová M., Stibor I.: *Mol. Cryst. Liq. Cryst. Sci. Technol., Sect. A* **1999**, *328*, 367.
8. Černovská K., Svoboda J., Stibor I., Glogarová M., Vaněk P., Novotná V.: *Ferroelectrics* **2000**, *241*, 231.
9. Campaigne E., Ergener L., Heaton B. G.: *J. Org. Chem.* **1962**, *27*, 4111.
10. Tedjamulia M. L., Tominaga Y., Castle R. N., Lee M. L.: *J. Heterocycl. Chem.* **1983**, *20*, 1143.
11. Jackson J. L.: *J. Heterocycl. Chem.* **1991**, *28*, 109.
12. Zherdeva S. Yu., Zheltov A. Ya., Kozik T. A., Stepanov B. I.: *Zh. Org. Khim.* **1980**, *16*, 425.
13. Chapman N. B., Hughes C. G., Scrowston R. M.: *J. Chem. Soc. C* **1970**, 2431.
14. Hercouet A., Le Corre M.: *Tetrahedron* **1981**, *37*, 2867.
15. Guillaumel J., Royer R.: *Eur. J. Med. Chem. - Chim. Ther.* **1983**, *18*, 431.
16. Guillamel J., Boccara N., Demerseman P.: *J. Heterocycl. Chem.* **1990**, *27*, 1047.
17. Capuano L., Ahlhelm A., Hartmann H.: *Chem. Ber.* **1986**, *119*, 2069.
18. Twyman L. J., Allsop D.: *Tetrahedron Lett.* **1999**, *40*, 9383.
19. Sargent M. V., Stransky P. O.: *Adv. Heterocycl. Chem.* **1984**, *35*, 1.
20. Hellwinkel D., Göke K.: *Synthesis* **1995**, 1135.
21. LaForge F. B.: *J. Am. Chem. Soc.* **1933**, *55*, 3040.
22. Sahm W., Schinzel E., Jürges P.: *Justus Liebigs Ann. Chem.* **1974**, 523.

23. Greene T. W., Wuts P. G. M.: *Protective Groups in Organic Synthesis*. Wiley, New York 1991.
24. Ashby J., Cook C. C.: *Adv. Heterocycl. Chem.* **1974**, *16*, 181.
25. Gilman H., Fullhart L.: *J. Am. Chem. Soc.* **1949**, *71*, 1478.
26. Ruhlandt-Serge K., Power P. P.: *Bull Soc. Chim. Fr.* **1992**, *6*, 594.
27. Chauhan M. S., Dean F. M., McDonald S., Robinson M. S.: *J. Chem. Soc., Perkin Trans. 1* **1973**, 359.
28. Guindon Y., Frenette R., Fortin R., Rokach J.: *J. Org. Chem.* **1983**, *48*, 1357.
29. Connor D. T., Cetenko W. A., Unangst P. C., Johnson E. A.: Eur. Pat. Appl. 187,487 (1986); *Chem. Abstr.* **1986**, *105*, 226335.
30. Thomas A. F.: *Helv. Chim. Acta* **1965**, *48*, 1057.
31. Oseledchik V. S., Karpejskii M. Y., Florentyev V. L.: *Izv. Akad. Nauk SSSR, Ser. Khim.* **1973**, 1315.
32. Simchen G.: *Angew. Chem.* **1966**, *78*, 674.
33. Rajšner M., Protiva M.: *Cesk. Farm.* **1962**, *11*, 404.
34. Douglass I. B., Farah B. S.: *J. Org. Chem.* **1961**, *26*, 351.