ELECTROPHILIC SUBSTITUTION REACTIONS OF [1]BENZOTHIENO[3,2-*b*]FURAN

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In chlorination, bromination, iodination, nitration, sulfonation, formylation, and trifluoroacetylation of [1]benzothieno[3,2-*b*]furan (**1**) the substituent enters the 2-position. The said halogenations go by the addition–elimination mechanism. When the substitution is continued, the second substituent enters the 6-position of heterocycle **1**. The ^{1}H and ^{13}C NMR spectra have been completely assigned. Substituent effects on NMR parameters are discussed.

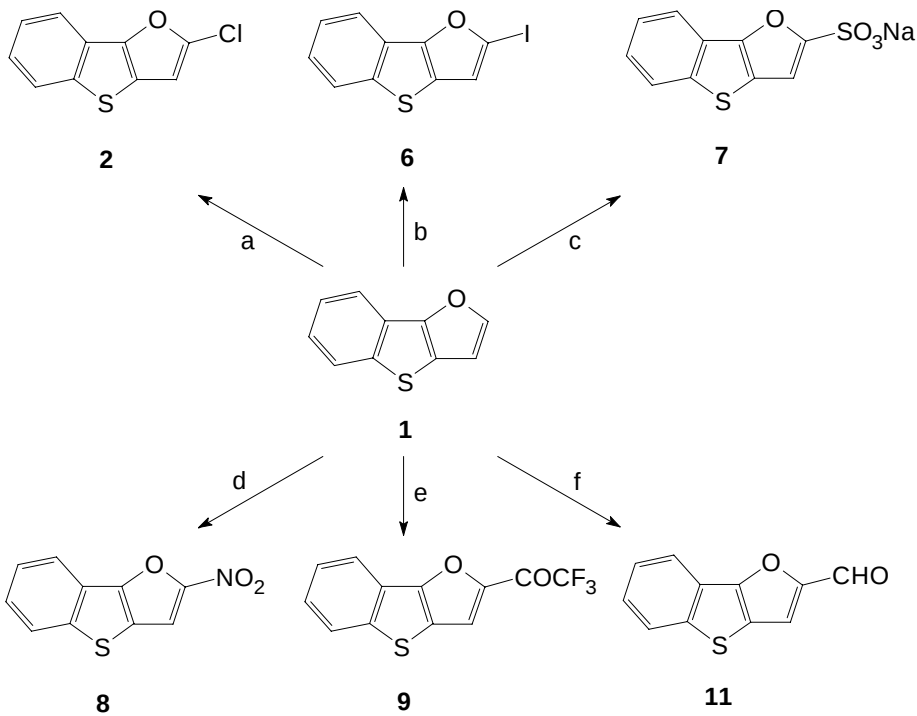
Key words: [1]Benzothieno[3,2-*b*]furan; Electrophilic substitution.

In our previous paper[1] we described the synthesis of the then unknown basic heterocyclic system – [1]benzothieno[3,2-*b*]furan (**1**). Studies of electrophilic substitution reactions of analogous heterocyclic compounds – [1]benzothieno[3,2-*b*]thiophene[2,3], [1]benzothieno[3,2-*b*]pyrrole[4], furo[3,2-*b*]indole[5,6] and thieno[3,2-*b*]benzofuran[7] – showed that the electrophilic particle usually[8] enters the 2-position. In these cases the stability of both the starting heterocycle and product with regard to acid reagents represents the limiting factor for successful reaction course and good yield of reaction product. In the context of these findings we decided to explore the reactivity of heterocycle **1** to a variety of electrophiles at various conditions.

Due to polymerization side reactions, the chlorination of compound **1** with the unstable complex of dioxane dichloride in dioxane as well as with nonstoichiometric pyridine hydrochloride–chlorine complex[9] in pyridine gave only low yields (26% and 11%, respectively) of 2-chloro[1]benzothieno[3,2-*b*]furan (**2**) (Scheme 1). Only the application of neutral complex benzyltriethylammonium tetrachloroiodate[10] gave the chloro derivative **2** in the yield of 65%.

When monitoring the course of bromination of compound **1** with dioxane dibromide[11] with the help of TLC we found that the R_F value of the isolated product, i.e. 2-bromo[1]benzothieno[3,2-*b*]furan (**3**) (Scheme 2), differs from that of the substance detected in the reaction mixture. With the aim of verification of structure of this un-

known substance, we carried out the reaction at –40 °C and measured the ^{1}H NMR spectrum of the reaction mixture at this temperature. In this way it was possible to prove the existence of an unstable intermediate, *trans*-2,3-dibromo-2,3-dihydro[1]benzothieno[3,2-*b*]furan (**4**), which results from addition of bromine to the double bond of heterocycle **1**. The *trans* configuration of compound **4** was assigned on the basis of similarity with ^{1}H NMR spectrum of *trans*-2,3-dibromo-2,3-dihydro[1]benzofuran[12]. This fact indicates that the bromination (and obviously the chlorination too) of compound **1** proceeds by the addition–elimination mechanism with a regioselective elimination of hydrogen halide. This mechanism was confirmed earlier for benzo[*b*]furan[12,13]. With the application of pyridine hydrotribromide complex[11] the bromo derivative **3** was obtained in a lower yield of 36%. On the other hand, the bromi-



a) $C_6H_5CH_2N^+(CH_2CH_3)_3\ ICl_4^-$; b) I_2, $Hg(OCOCH_3)_2$; c) pyridine-SO_3, then NaOH;
d) *N*-nitro-(2-methylpyridinium)tetrafluoroborate; e) $(CF_3CO)_2O$, CH_3COONa;
f) $POCl_3$, $HCON(CH_3)_2$

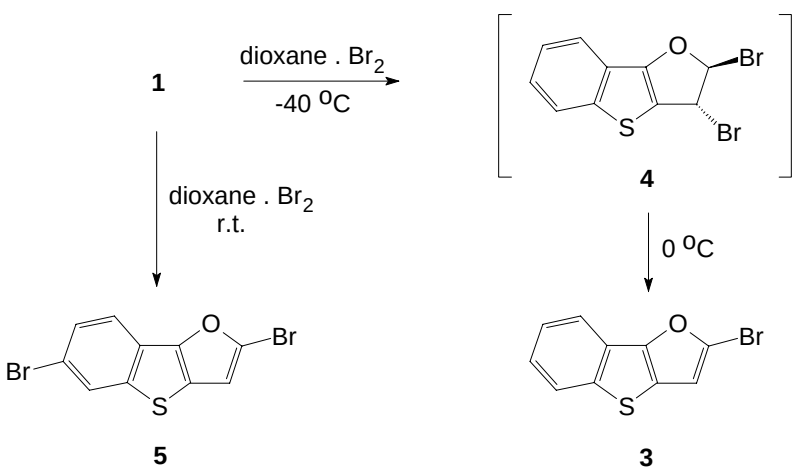
SCHEME 1

nation of compound **1** with an excess of dioxane dibromide in dioxane at room temperature gave smoothly 2,6-dibromo[1]benzothieno[3,2-*b*]furan (**5**).

The mild iodination method with a mixture of iodine and silver sulfate[14] failed to give successful results with compound **1**. However, 2-iodo[1]benzothieno[3,2-*b*]furan (**6**) was obtained with an average yield of 45% by action of the complex of iodine monochloride with benzyltriethylammonium chloride in acetic acid[15] (Scheme 1). The best results were obtained with the use of iodine and mercuric acetate[16] (66%) or mercuric oxide[17] (54%).

The sulfonation of compound **1** was carried out with the use of well-known complexes dioxane–sulfur trioxide and pyridine–sulfur trioxide[18]. Whereas application of the former reagent resulted in degradation of heterocycle **1**, the long-term heating with the latter in 1,2-dichloroethane gave [1]benzothieno[3,2-*b*]furan-2-sulfonic acid which was isolated as sodium salt (**7**).

Attempts at nitration of heterocycle **1** with a mixture of acetic anhydride and nitric acid[19] led to polymeric products only, the same being true of the applications of nitronium fluoroborate in sulfolane[20] or nitromethane. Only after the nitration with *N*-nitro(2-methylpyridinium) fluoroborate[21] we could detect 2-nitro[1]benzothieno[3,2-*b*]furan (**8**) in the reaction mixture. However, all attempts at its isolation in an analytically pure form failed due to its instability. Hence the structure of compound **8** was only confirmed spectroscopically. An attempt at nitration of compound **1** with a mixture of ammonium nitrate and trifluoroacetic anhydride[22] gave no nitro derivative **8**, but it was possible to isolate 2-trifluoroacetyl[1]benzothieno[3,2-*b*]furan (**9**) in low yield (about 5%) from the reaction mixture by column chromatography. Although trifluoroacetylation of five-membered heterocycles proceeds without catalysis by Lewis acids[23], in our case the trifluoroacetic acid set free in the reaction course catalyzed the subsequent destruction of compound **1** accompanied by formation of polymers. Therefore we chose a procedure in which the



SCHEME 2

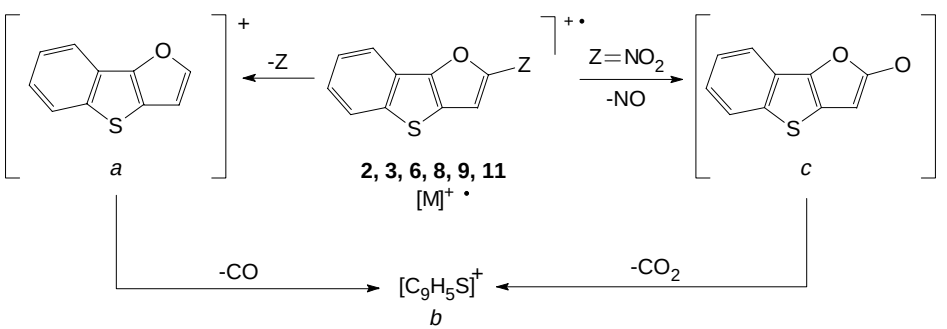
trifluorocetic acid formed was neutralized by the base present in the reaction mixture – triethylamine or a mixture of acetic acid and sodium acetate. Better results, however, were obtained in the presence of 4-dimethylaminopyridine (27% yield of compound **9**) or sodium acetate alone (freshly remelted) in dichloromethane (33% yield).

In spite of the fact that the Friedel–Crafts reactions of furan derivatives have been thoroughly investigated[24,25], we did not succeed in preparing 2-acetyl[1]benzothieno[3,2-*b*]furan (**10**). The application of acetic anhydride in the presence of various Lewis acids – $HgCl_2$, $ZnCl_2$, $TiCl_4$, $AlCl_3$ – was unsuccessful: at low temperatures (–20 °C) the reaction did not take place, and any increase in temperature only resulted in degradation of the starting compound **1**. With more reactive acetyl chloride, compound **1** was decomposed immediately. The modified formylation reaction[26] using *N*,*N*-dimethylacetamide and $POCl_3$ was unsuccessful too.

On the other hand, the Vilsmeier–Haack reaction[5,27] proceeded smoothly, giving [1]benzothieno[3,2-*b*]furan-2-carboxaldehyde (**11**) in the yield of 76%.

All the newly synthesized substances (except for the nitro derivative **8**) gave satisfactory results of elemental analyses. The mass spectra of compounds **2**, **3**, **5**, **6**, **9**, **11** exhibit the same fragmentation patterns which can be considered characteristic. The molecular cation-radical ion eliminates the 2-substituent to give the ion *m/z* 173 ($C_{10}H_5SO$, *a*, $[M - X]^+$) which, on expulsion of carbon monoxide, produces an intensive ion *m/z* 145 (C_9H_5S, *b*, rel. intensity 45–100%). The fragmentation of 2-nitro derivative **8** takes a different course: nitrogen oxide is split off at first, and the cation-radical *c* formed subsequently splits off carbon dioxide to give ion *b* (Scheme 3). This behaviour, at the same time, confirms the suggested structure of nitro derivative **8**.

The one-proton singlet in the ^1H NMR spectra of all the derivatives studied shows that the substitution takes place at the furan nucleus. A change in multiplicity (from doublet to singlet) as compared with the parent substance **1** is always observed with the carbon atom signal at lower field which was assigned to C-2 on the basis of its chemical shift. This means that all the monosubstituted derivatives have their substituent at 2-position. The signal pattern in dibromo derivative **5** agrees with substitution in both



SCHEME 3

6- and 7-positions. This problem was solved by experimental assignment of all the protons with the help of heteronuclear correlations and proton-coupled spectra. The starting point is the above-mentioned assignment of C-2 and C-3 and the assignments of H-2 and H-3 derived from them. Hence the quaternary carbon with the highest chemical shift exhibiting couplings with H-2 and H-3 (in compound **1**) belongs to C-8b atom. The quaternary carbon which also interacts with H-2 and H-3 is then C-3a. The H-8 and H-5 protons can be mutually differentiated on the basis of the ^3J coupling with C-8b which is only possible for the former. As H-8 in compound **5** gives a doublet at 7.703 ppm with J_{ortho} = 8.5 Hz, the second substituent must be at 6-position. Other pieces of evidence are provided by the multiplicity of C-6 signal in this compound (see Table III) and by the coupling of this carbon with H-8 proved by heteronuclear correlation.

The furan protons H-2 and H-3 in compound **1** differ from the benzene protons by their multiplicity (doublet) and low vicinal constant (Table II). For their differentiation it is sufficient to use the heteronuclear correlation (the proton interacting with C-2, whose resonance is shifted downfield due to the adjacent oxygen, is H-2). The protons H-5 and H-8 of the ABCD system of benzene ring can be differentiated on the basis of the ^3J coupling of H-8 with C-8b which in turn is determined by the coupling with H-3 (see above). With the help of the proton assignment carried out (Table I) it is then easy to find the carbons corresponding to them. The quaternary C-4a is the one showing couplings with H-6 and H-8, and C-8a with H-5 and H-7. The substituent-carrying carbon (C-2, and in compound **5** also C-6) was determined on the basis of the correlations with H-3 using the fine structure of proton-coupled spectra. The iodo derivative **6** also showed a very characteristic upfield shift, in compound **9** – in addition – the interaction of C-2 with fluorine atoms was made use of (Table III). The said assignments are summarized in Tables I–III the latter also containing the data on the H,C couplings obtained from the proton-coupled spectra.

The effect of 2-substituent makes itself felt primarily at the neighbouring H-3 proton which, depending on the substituent nature, is shifted either upfield (in compounds **2**, **3**, and **5** by 0.187, 0.064, and 0.068 ppm, respectively) or downfield (in compounds **6**, **7**, **8**, **9**, and **11** by 0.126, 0.421, 0.964, 1.040, and 0.768 ppm, respectively). An observable transmission of this effect can be traced at H-8 in compounds **2**, **3**, **5**, and **7** (upfield shifts by 0.054, 0.045, 0.042, and 0.054 ppm, respectively), whereas in compounds **8**, **9**, and **11** the H-6 through H-8 protons show distinct downfield shifts (by 0.060 to 0.206 ppm). The magnitudes of proton–proton couplings (Table II) are practically uniform throughout the whole series. Also in the ^{13}C NMR spectra the maximum influence on the chemical shift is seen in C-2 (**2**: –6.59, **3**: –20.92, **5**: –20.3, **6**: –54.96, **8**: 7.29, **9**: 3.30, **11**: 9.37) again depending on the nature of substituent. Also distinct is the effect on C-3, especially so with R = I (9.79 ppm), $COCF_3$ (13.02 ppm), or CHO (10.24 ppm). It is also manifested at the quaternary carbons C-3a and C-8a of furan ring, being stronger at the latter. The transmission of substituent effect to the benzene

TABLE I
Proton chemical shifts (ppm) and signal multiplicities[a] in compounds **1–11**

Compound	Proton					
	H-2 d	H-3 s	H-5 ddd	H-6 ddd	H-7 ddd	H-8 ddd
1	7.672	6.836[b]	7.822	7.316	7.429	7.901
2	–	6.651	7.806	7.316	7.426	7.847
3	–	6.772	7.800	7.319	7.425	7.856
5	–	6.768	7.935[b]	–	7.527[c]	7.703[b]
6	–	6.962	7.796	7.309	7.424	7.859
7[d]	–	7.257	7.838	7.361	7.426	7.847
8	–	7.800	7.892[e]	7.522[f]	7.546[f]	8.086[e]
9	–	7.876	7.865	7.500	7.525	8.105
11[g]	–	7.604	7.843	7.459	7.489	8.047

[a] Abbreviations used: s singlet, d doublet, t triplet, m multiplet. [b] Doublet. [c] Doublet of doublets. [d] Measured in D_2O. [e] Multiplet. [f] Triplet. [g] Additional signal: 9.743 s (CH=O).

TABLE II
Proton–proton interaction constants *J* in compounds **1–7**, **9** and **11**

Compound	*J*(H,H), Hz					
	(5,6)	(5,7)	(5,8)	(6,7)	(6,8)	(7,8)
1[a]	8.1	1.1	0.7	7.2	1.3	7.9
2	8.1	1.1	0.7	7.2	1.3	8.0
3	8.1	1.1	0.7	7.2	1.3	7.9
5	–	1.7	–	–	–	8.5
6	8.1	1.0	0.8	7.2	1.3	8.0
7	8.1	1.2	0.7	7.2	1.4	7.9
9[b]	n	n	n	n	n	n
11	7.4	1.5	0.7	7.3	1.3	7.9

[a] $J(2,3)$ = 2.0 Hz. [b] Second-order spectrum, not determined.

TABLE III
^{13}C NMR data on compounds **1–7**, **9** and **11** (capital letters denote direct coupling, small letters denote long range coupling)

Compound		C-2	C-3	C-3a	C-4a	C-5	C-6	C-7	C-8	C-8a	C-8b
1	δ	146.07	106.85	122.56	141.65	124.18	123.79	124.64	118.66	125.08	151.98
	Multy	Dd	Dd	dd	ddd	Ddddd	Ddd	Ddd	Dddd	ddd	ddd
	^1J	204.7	179.9	–	–	162.2	161.5	160.7	162.6	–	–
	^nJ	10.9	13.9	8.1,1.8	10.0,7.9,1.1	8.1,1.5,1.5,0.6	7.9,1.3	7.5,1.0	8.2,1.5,1.5	7.4,7.4,1.5,0.9	9.0,9.0,1.2
2	δ	139.48	103.91	123.28	140.21	124.01	124.01	124.96	118.48	124.74	149.74
	Multy	d	D	dd	ddd	Ddd	Ddd	Ddd	Dddd	ddd	dd
	^1J		185.6			161.9	161.9	160.6	163.1		
	^nJ	6.1		2.2,2.2	10.1,7.8,1.0	7.8,1.3	7.8,1.3	7.4,0.9	8.2,1.6,1.4	8.1,8.1,1.5	7.4,3.1
3	δ	125.15	108.55	123.65	140.34	124.04	124.10	124.94	118.58	124.61	152.05
	Multy	d	D	d	ddd	Dddd	Ddd	Dd	Dddd	dddd	dd
	^1J	–	185.9	–	–	162.6	161.8	160.9	163.1		
	^nJ	6.8		1.7	9.0,9.0,1.3	5.9,1.4,1.4	4.1,1.1	7.3	8.1,1.3,1.3	7.7,7.7,0.9,0.9	6.6,4.5
5	δ	125.77	108.55	124.12	141.68	126.54	117.45	128.32	119.51	123.34	151.36
	Multy	d	D	d	d	Ddd	ddd	Dd	D	ddd	dd
	^1J	–	186.4	–	–	168.7	–	168.3	166.9	–	–
	^nJ	6.9	–	1.7	8.9	5.8,1.3	11.3,4.5,2.7	5.3	–	8.5,6.2,1.3	6.4,4.0

TABLE III
(*Continued*)

Compound		C-2	C-3	C-3a	C-4a	C-5	C-6	C-7	C-8	C-8a	C-8b
6	δ	91.11	116.63	124.03	140.71	124.07	124.25	124.86	118.80	124.41	155.57
	Multy	d	D	m	dd	Ddd	Ddd	Dd	Ddd	m	m
	^1J	–	185.2	–	–	164.2	161.9	161.0	163.0	–	–
	^nJ	8.4	–	–	10.1,9.8	8.2,1.5	8.1,1.3	7.8	10.0,1.4	–	–
7[a]	δ	153.36	109.72	123.69	143.35	125.50	126.47	126.33	120.35	125.08	155.20
	Multy	d	D	dd	dd	Dd	Dd	Dd	Ddd	ddd	dd
	^1J	–	185.8	–	–	164.2	161.9	162.7	164.9	–	–
	^nJ	6.6		1.5,1.5	10.0,8.6	8.1	7.6	7.8	6.9,1.2	7.5,7.5,1.2	6.9,2.0
9[b,c,d]	δ	149.37	119.86	123.28	145.36	124.55	125.74	127.70	121.41	123.28	158.16
	Multy	S	Dq	S	S	D	D	D	D	D	D
	^1J	–	–	–	–	–	–	–	–	–	–
	^nJ	–	3.2	–	–	–	–	–	–	–	–
11[e]	δ	155.44	117.08	124.03	144.36	124.39	126.70	125.44	120.74	123.81	156.32
	Multy	d	Ddd	S	dd	Ddd	Ddd	Dd	Ddd	ddd	dd
	^1J	–	185.1	–	–	162.3	162.1	162.7	164.5	–	–
	^nJ	9.8	6.7,3.4	–	8.0,8.0	7.7,1.8	7.9,1.3	7.6	6.2,1.3	7.9,7.9,1.2	9.8,9.8

[a] In D_2O. [b] Additional signals: 116.43 Sq, J(C,F) = 289.4; 168.47 Sq, J(C,F) = 37.7 ($COCF_3$). [c] Small letter denotes fluorine-caused multiplicity. [d] C–F coupling. [e] Additional signal: 177.62 D, J = 180.1 (CH=O).

ring is documented by the changes in chemical shifts of C-4a as compared with compound **1**, and for compounds **7**, **9**, and **11** at carbons C-6, C-7, and C-8. Hence it can be stated that [1]benzothieno[3,2-*b*]furan behaves as a true heteroaromatic system.

The direct coupling constants ^1J(C,H) of furan carbons C-2 and C-3 in compound **1** (Table III) are close to the analogous values[28] in furan (201 and 175 Hz) or benzofuran (202 and 177 Hz). The magnitude of ^1J(C-3, H-3) in the polysubstituted derivatives (185.1–186.4 Hz) is nearer to the values for C-3, which again confirms the correctness of our assignment. However, they reflect also the influence of electronegativity of 2-substituent. Generally it is $|^3J(C,H)| > |^2J(C,H)| \approx |^4J(C,H)|$ (ref.[29]). The magnitude of ^2J(C,H) is strongly affected by the electronegativity of neighbouring atoms. This causes the high values observed with J(C-2,H-3), J(C-6,H-5), and J(C-6,H-7) (Table III). In several cases (Table III, C-3a, C-5, C-8, and C-8a) even interactions through four bonds were observed. Although they are considered unusual, literature gives examples of their occurrence[30–35], particularly in aromatic and heteroaromatic systems.

EXPERIMENTAL

The melting points were determined with a Boetius apparatus and are not corrected. The infrared spectra were measured with a Nicolet 740 apparatus and the wavenumbers are given in cm^{-1}. The ^1H NMR spectra of compounds **4** and **8** were measured with a Varian Gemini-300 apparatus (300 MHz). The other substances were studied on a Varian VXR-400 spectrometer (400 MHz for ^1H and 100 MHz for ^{13}C) at 25 °C. The solvent was deuteriochloroform except for compound **7** which was measured in D_2O. The chemical shifts are given in δ scale (ppm), the coupling constants in Hz. TMS or the solvent signal (δ(C) 77.0) was used as the internal standard. The multiplicity of signals in ^{13}C NMR spectra was determined in the APT experiment. The proton-coupled spectra were measured by the method of gated decoupling (decoupler off during acquisition). The 2D NMR experiments – COSY, delay-COSY, HETCOR and HETCOR optimized for detection of small constants (J = 3, 5, and 10 Hz) – were realized by means of pulse sequences and programs delivered by the manufacturer.

The mass spectra of positive ions obtained by electron impact were measured on a JEOL DX 300 and ZAB-EQ apparatus with the electron ionizing energy of 70 eV. The thin layer chromatography was performed on 2.5 × 7.5 cm plates (Kieselgel G, Fluka), and the detection was carried out with a solution of cerium(IV) ammonium nitrate in 10% sulfuric acid or with iodine. The procedures described in literature were adopted for preparation of the complexes of chlorine with pyridine hydrochloride[9], pyridine hydrotribromide[11], benzyltriethylammonium dichloroiodate[15], benzyltriethylammonium tetrachloroiodate[10] and *N*-nitro(2-methylpyridinium) fluoroborate[36].

2-Chloro[1]benzothieno[3,2-*b*]furan (**2**)

A solution of compound **1** (0.157 g, 0.901 mmol) in acetone (13 ml) was cooled with ice to 0–5 °C and treated with benzyltriethylammonium tetrachloroiodate (1.524 g, 3.31 mmol). The mixture was cooled and stirred 1 h, diluted with chloroform (15 ml), washed with 5% aqueous sodium thiosulfate (2 × 20 ml), water, saturated sodium chloride solution, and dried with anhydrous magnesium sulfate. After filtration and evaporation of the solvent, the residue was purified by column chromatography (silica gel, hexane as eluent). Yield 0.123 g (65%) compound **2**, m.p. 59–60.5 °C (hexane). For $C_{10}H_5ClOS$ (208.7) calculated: 57.56% C, 2.42% H, 16.99% Cl, 15.36% S; found: 57.60% C, 2.54% H, 17.54% Cl, 15.79% S. IR spectrum ($CHCl_3$): 3 144, 3 065, 3 012 (C–H), 1 529, 1 505, 1 459, 1 426,

1 396, 1 342, 1 184, 1 069, 1 017, 929. Mass spectrum (*m/z*, % rel. int.): 210 (35), 209 (15), 208 (100, M^+), 180 (25, $M^+ - CO$), 173 (15, $M^+ - Cl$), 145 (80, $M^+ - Cl - CO$), 104 (15), 69 (15).

2-Bromo[1]benzothieno[3,2-*b*]furan (**3**)

A. A solution of dioxane dibromide (1.57 g, 6.33 mmol) in a dioxane–dichloromethane mixture 1 : 1 (10 ml) was added drop by drop to a solution of compound **1** (1 g, 5.74 mmol) in the same solvent mixture (6 ml) with exclusion of air moisture and with external cooling with ice water to 0–5 °C. The mixture was stirred with constant cooling 75 min, neutralized with solid sodium hydrogencarbonate, after 20 min filtered, the solvent was evaporated, and the residue was purified by column chromatography (silica gel, hexane as eluent). Yield 0.840 g (3.32 mmol, 58%) compound **3**, m.p. 89–91 °C (hexane). For $C_{10}H_5BrOS$ (253.1) calculated: 47.45% C, 1.99% H, 31.57% Br, 12.67% S; found: 47.81% C, 2.23% H, 30.74% Br, 13.11% S. IR spectrum ($CHCl_3$): 3 142, 3 064, 3 012 (C–H), 1 496, 1 454, 1 393, 1 340, 1 180, 1 063, 1 016, 917, 727, 665. Mass spectrum (*m/z*, % rel. int.): 254 (75, M^+), 252 (70, M^+), 173 (25, $M^+ - Br$), 145 (100, $M^+ - Br - CO$), 69 (30), 57 (20), 55 (20), 43 (20).

B. After heating the reaction mixture from preparation of compound **4** from –40 °C to 0 °C, it was possible to detect evolution of hydrogen bromide. The subsequent column chromatography of the evaporation residue (silica gel, hexane as eluent) gave compound **3** (129 mg, 35%) whose physicochemical and spectral data agreed with those sub *A*.

trans-2,3-Dibromo-2,3-dihydro[1]benzothieno[3,2-*b*]furan (**4**)

A solution of dioxane dibromide (365 mg, 1.48 mmol) in deuteriochloroform (2 ml) was added drop by drop to a solution of compound **1** (254 mg, 1.46 mmol) in deuteriochloroform (2 ml) at –60 °C. The mixture was stirred with constant cooling 12 min, diluted with deuteriochloroform (2 ml), and its ^1H NMR spectrum was measured at –40 °C. ^1H NMR spectrum of compound **4** ($CDCl_3$): 5.33 s, 1 H (H-3); 6.47 s, 1 H (H-2); 7.29 t, 1 H (H-6); 7.41 t, 1 H (H-7); 7.84 m, 2 H (H-5 and H-8).

2,6-Dibromo[1]benzothieno[3,2-*b*]furan (**5**)

A solution of compound **1** (1.00 g, 5.74 mmol) in dioxane (5 ml) was added dropwise to a mixture of dioxane dibromide (1.56 g, 6.32 mmol) in dioxane (10 ml). Two other portions of dioxane dibromide (2 × 0.5 g, 2.02 mmol) were added after 1.5 and 2.5 h stirring, respectively. The reaction mixture was stirred with constant cooling 4 h, then it was washed with 5% aqueous sodium carbonate solution, diluted with benzene (20 ml), the organic portion was washed with 5% sodium thiosulfate solution (2 × 20 ml), with saturated sodium chloride solution (20 ml), and dried with anhydrous magnesium sulfate. The evaporation residue was purified by column chromatography (silica gel, hexane as eluent) to give 0.910 g (48%) compound **5**, m.p. 127–129 °C (hexane–benzene 10 : 1). For $C_{10}H_4Br_2OS$ (332.0) calculated: 36.18% C, 1.21% H, 48.13% Br, 9.66% S; found: 35.89% C, 1.31% H, 47.98% Br, 9.88% S. IR spectrum ($CHCl_3$): 3 012, 1 518, 1 482, 1 452, 1 336, 1 252, 1 060, 1 042, 917, 810. Mass spectrum (*m/z*, % rel. int.): 334 (55, M^+), 332 (100, M^+), 330 (50, M^+), 251 (10, $M^+ - HBr$), 225 (55, $M^+ - HBr - CO$), 223 (55, $M^+ - HBr - CO$), 149 (15), 144 (40), 97 (10), 83 (15), 69 (40), 57 (20).

2-Iodo[1]benzothieno[3,2-*b*]furan (**6**)

A solution of compound **1** (87 mg, 0.50 mmol) in dichloromethane (5 ml) was added dropwise to a suspension of mercuric acetate (160 mg, 0.503 mmol) in dichloromethane (5 ml) with stirring. After 15 min, a 94 mM solution of iodine in dichloromethane (6 ml, 0.57 mmol) was added drop by drop,

and the mixture was stirred 30 min, diluted with chloroform (10 ml), and filtered. The filtrate was washed with 5% aqueous sodium thiosulfate (2 × 20 ml), water, saturated sodium chloride solution, and dried with anhydrous magnesium sulfate. The solvent was evaporated and the residue was purified by column chromatography (silica gel, hexane as eluent) to give 99 mg (66%) compound **6**, m.p. 120–121.5 °C (hexane). For $C_{10}H_5IOS$ (300.1) calculated: 40.02% C, 1.68% H, 42.29% I, 10.68% S; found: 39.92% C, 1.72% H, 42.36% I, 10.24% S. IR spectrum ($CHCl_3$): 3 138, 3 062, 3 011 (C–H), 1 446, 1 387, 1 336, 1 168, 1 058, 1 041, 961, 908, 798. Mass spectrum (*m/z*, % rel. int.): 301 (15), 300 (100, M^+), 173 (30, $M^+ - I$), 145 (50, $M^+ - I - CO$), 101 (10), 69 (15).

Sodium [1]Benzothieno[3,2-*b*]furan-2-sulfonate (**7**)

Pyridine–sulfur trioxide complex (461 mg, 2.90 mmol) was added to a solution of compound **1** (494 mg, 2.84 mmol) in 1,2-dichloroethane (10 ml), and the suspension formed was heated to boiling with exclusion of air moisture 34 h. After cooling, a solution of sodium hydroxide (265 mg, 6.63 mmol) in distilled water (10 ml) was added drop by drop, the organic layer was separated and dried with anhydrous magnesium sulfate. Evaporation of the solvent gave 283 mg (1.62 mmol) of starting compound **1**. The aqueous phase was evaporated, the residue was dissolved in hot distilled water (10 ml) and neutralized to pH ca 6 with 1.5 M HCl (0.95 ml). The solution was evaporated and the solid residue was extracted with ethanol (2 × 25 ml). Evaporation of the solvent gave 187 mg (56%, calculated on the substance recovered) sodium salt **7**, which on recrystallization from absolute ethanol gave pale pink glossy plates, m.p. above 360 °C. For $C_{10}H_5NaO_4S_2$ (276.3) calculated: 43.48% C, 1.82% H, 23.21% S; found. 43.03% C, 1.73% H, 22.40% S. IR spectrum (KBr): 3 130, 3 079, 3 061 (C–H), 1 628, 1 456, 1 244, 1 209 (SO_3^-), 1 109, 1 080, 1 040 (SO_3^-), 927, 835.

2-Nitro[1]benzothieno[3,2-*b*]furan (**8**)

A 0.0438 M solution of *N*-nitro-(2-methylpyridinium) tetrafluoroborate in dry acetonitrile (3 ml, 0.131 mmol) was added drop by drop to a solution of compound **1** (21.6 mg, 0.124 mmol) in dry acetonitrile (2 ml) under nitrogen at –10 °C. The reaction mixture was stirred at –10 °C 1 h, at 0–5 °C 3 h, and at 40 °C 4 h, whereupon it was diluted with dichloromethane (20 ml), and washed with water, saturated solution of sodium hydrogencarbonate, and saturated solution of sodium chloride. The organic phase was dried with anhydrous magnesium sulfate, the solvent was evaporated, and the residue was separated by column chromatography (silica gel, hexane–toluene 4 : 1 as eluent) to give 2 mg of starting compound **1** and 12 mg of impure product **8** which was characterized spectroscopically. ^{1}H NMR spectrum ($CDCl_3$): 7.53 m, 2 H (H-6 and H-7); 7.79 s, 1 H (H-3); 7.89 m, 1 H (H-5); 8.08 m, 1 H (H-8). Mass spectrum (*m/z*, % rel. int.): 220 (15), 219 (85, M^+), 189 (30, $M^+ - NO$), 145 (50, $M^+ - NO - CO_2$), 123 (30), 111 (45), 97 (70), 83 (65), 69 (85), 57 (100), 43 (85).

2-Trifluoroacetyl[1]benzothieno[3,2-*b*]furan (**9**)

Trifluoroacetic anhydride (1.0 ml, 7.2 mmol) was added drop by drop to a mixture of compound **1** (0.169 g, 0.970 mmol), freshly remelted sodium acetate (1.17 g, 14.3 mmol) and dry dichloromethane (12 ml) under nitrogen at 0–5 °C. The reaction mixture was stirred with cooling 30 min, at room temperature 22 h, and at 35 °C 3 h, whereupon the second portion of trifluoroacetic anhydride (0.9 ml, 6.5 mmol) was added and stirring was continued for another 30 h. The mixture was diluted with dichloromethane (20 ml) and the unreacted reagent was decomposed by adding 30 ml 5% sodium hydrogencarbonate; the organic layer was washed with saturated sodium chloride solution and dried with anhydrous magnesium sulfate. The solvent was evaporated and the residue was separated by TLC (preparative plates Merck, hexane–toluene 4 : 1 as eluent) to give 0.089 g starting compound **1**

and 0.070 g (56% calculated on the substance recovered) 2-trifluoroacetyl derivative **9**, m.p. 123–125 °C (hexane). For $C_{12}H_5F_3O_2S$ (270.2) calculated: 53.34% C, 1.86% H, 11.86% S; found: 53.10% C, 1.95% H, 11.69% S. IR spectrum ($CHCl_3$): 3 015 (C–H), 1 693 (C=O), 1 538, 1 505, 1 452, 1 425, 1 245, 1 201, 1 158, 1 127, 977, 900. Mass spectrum (*m/z*, % rel. int.): 271 (15), 270 (95, M^+), 206 (20), 201 (100, $M^+ - CF_3$), 173 (10, $M^+ - CF_3 - CO$), 145 (65, $M^+ - CF_3 - CO - CO$), 101 (20), 91 (15), 69 (30).

[1]Benzothieno[3,2-*b*]furan-2-carboxaldehyde (**11**)

Freshly distilled phosphoryl trichloride (0.6 ml, 6.55 mmol) was added dropwise to *N*,*N*-dimethylformamide (1.8 ml) with external cooling with ice. After 20 min stirring, a solution of compound **1** (1.0 g, 5.74 mmol) in *N*,*N*-dimethylformamide (1.8 ml) was added, and the mixture was stirred at 0–5 °C 2 h and at room temperature 45 min, whereupon it was decomposed by pouring it into 2.5% sodium carbonate solution (150 ml). The solid was collected by filtration and recrystallized from ethanol–chloroform 2 : 1 to give 0.882 g (76%) aldehyde **11**, m.p. 163–165 °C. For $C_{11}H_6O_2S$ (202.2) calculated: 63.35% C, 2.97% H, 15.84% S; found: 62.27% C, 3.10% H, 15.47% S. IR spectrum ($CHCl_3$): 1 676 (CHO). Mass spectrum (*m/z*, % rel. int.): 203 (10), 202 (100, M^+), 201 (10), 174 (10, $M^+ - CO$), 145 (30, $M^+ -$ CHO – CO), 102 (15), 83 (15), 69 (25), 57 (30), 55 (20), 43 (30), 41 (20).

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