Synthesis of 4-(trifluoromethyl)thiocoumarins*

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A convenient method for the synthesis of poorly studied 4-(trifluoromethyl)thiocoumarins from 1-[2-(*tert*-butylthio)phenyl]-2,2,2-trifluoroethanones was developed. Thiopyranone core of 4-(trifluoromethyl)thiocoumarins was constructed by S-acylation of 1-[2-(*tert*-butylthio)phenyl]-2,2,2-trifluoroethanones with bromoacetyl bromide followed by treatment with triphenylphosphine to give the phosphonium salt and subsequent intramolecular Wittig reaction. S-Acylation of these substrates with acetyl chlorides bearing active methylene group and subsequent intramolecular Knövenagel condensation gave 3-substituted 4-(trifluoromethyl)thiocoumarins.

Key words: 4-(trifluoromethyl)thiocoumarins, 3-substituted 4-(trifluoromethyl)thiocoumarins, S-acylation, intramolecular Wittig reaction, intramolecular Knövenagel condensation.

Thiocoumarins (2*H*-thiochromen-2-ones)[1] are the structural analogs of coumarins, in which the pyran oxygen atom is replaced with the sulfur atom. Sometimes, the term thiocoumarins is applied to two other structural analogs of coumarins, namely, to 2-thioxocoumarins (or 2*H*-chromene-2-thiones with the S atom in the thione moiety) and dithiocoumarins (or 2*H*-thiochromene-2-thiones with the S atoms in both the chromene scaffold and the thione moiety). In general, 2*H*-thiochromen-2-ones received much less attention from the researchers than coumarins. Recently, the interest of the synthetic chemists and pharmacologists on thiocoumarins significantly increased.[2,3] It should be noted that chemistry of 4-hydroxy-2*H*-thiochromen-2-one (or 4-hydroxy-1-thiocoumarin),[4—10] which can be synthesized by several simple methods,[11] is relatively well studied. At the same time, the synthetic approaches to 4-alkyl(aryl)thiocoumarins are not so simple,[12—15] because the Pechmann condensation widely used to synthesize coumarins has limited applications for thiocoumarins.[16,17] Therefore, it is not surprising that 4-(trifluoromethyl)thiocoumarins remain virtually unstudied. Patent[18] claims the Pechmann synthesis of the only representative of this class of compounds, *viz.*, 1,2-dihydro-6-trifluoromethyl-2,2,4-trimethyl-9-thiopyran-8-ono[5,6-*g*]quinoline, in 3% yield. In contrast, 4-trifluoromethyl-substituted coumarins, *e.g.*, 7-amino- and 7-hydroxy-4-(trifluoromethyl)coumarins, as well as their derivatives have found wide practical applications as fluorescent probes for different biological, analytical, photochemical, and medicinal studies.[19,20] Taking into account structural similarity of coumarins and their thio analogs, the development of the syntheses of 4-(trifluoromethyl)thiocoumarins, further evaluation of their biological activity, and examination of their possible application in technical fields are challenging.

The aim of the present work is the development of a versatile synthetic procedure to access 4-(trifluoromethyl)thiocoumarins (4-trifluoromethyl-2*H*-thiochromen-2-ones) **1** bearing substituents both in the benzene ring and at position 3.

Our idea was to use 1-[2-(*tert*-butylthio)phenyl]-2,2,2-trifluoroethanones **2** as the starting material in

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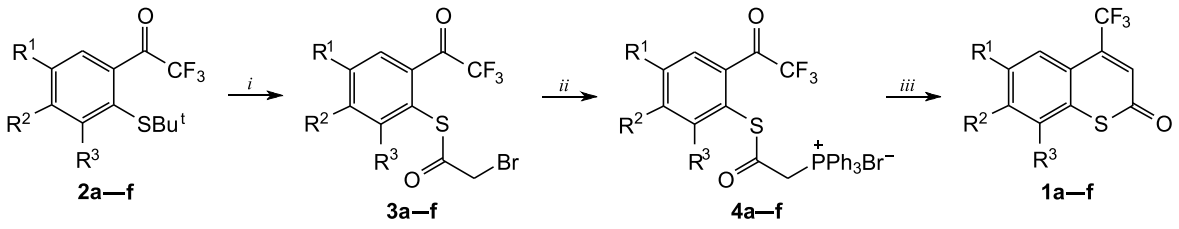
the synthesis of thiocoumarins **1** (Scheme 1). It was shown earlier[21] that *tert*-butyl thioethers in the presence of $TiCl_4$ readily transformed to thioacetates. Taking into account this fact, we believed that the key transformation of compounds **2** to bromoacetyl derivatives **3** can be accomplished in a good yield using bromoacetyl bromide. Next, the reaction of compounds **3** with Ph_3P will produce phosphonium salts **4**, and the synthesis will be finalized by the base-induced intramolecular Wittig cyclization to give the target 4-(trifluoromethyl)-2*H*-thiochromen-2-ones **1**. Successful transformation of bromoacetyl derivatives of salicylic aldehydes to coumarins by the intramolecular Wittig reaction was described by Khazi and coworkers.[22]

Ketones **2a—f** reacted with bromoacetyl bromide (1.1 equiv.) in the presence of $TiCl_4$ (1.1 equiv.) in CH_2Cl_2 at 0 °C to give *S*-phenyl 2-bromothioacetates **3a—f**. The key factor for the successful synthesis of compounds **3** is the absence of traces of water and acids (HCl and HBr) in the reaction mixture. Under these conditions, noticeable decomposition of compounds **2a—f** is avoided and products **3a—f** are formed sufficiently pure (the NMR spectroscopy data) and can be used in the next reaction step. Compound **3a** was isolated pure by vacuum distillation, no additional purification of *S*-phenyl 2-bromothioacetates **3b—f** was carried out due to their hydrolytic instability. Attempted purification of compounds **3b—f** by silica gel or alumina column chromatography resulted in the noticeable hydrolysis of their OC—S bond. Phosphonium salts **4a—f** were synthesized by the reaction of compounds **3a—f** with PPh_3 in toluene at room temperature for 24 h. The intramolecular Wittig cyclization of phosphonium salts **4a—f** in the presence of Et_3N in CH_2Cl_2 gave the target 4-(trifluoromethyl)-2*H*-thiochromen-2-ones **1a—f**. In all cases, isolation of hydrolytically unstable phosphonium salts **4a—f** is not required. The reaction mixture obtained by the reaction of **3a—f** with Ph_3P, which was a toluene solution with a precipitate, was homogenized by addition of CH_2Cl_2 and then treated with an excess of Et_3N. The developed approach allowed us to synthesize different 4-(trifluoromethyl)thiocoumarins **1b—f** bearing substituents at the benzene ring, including halogen-substituted thiocoumarins **1b**,**d**,**e**, coumarin **1c** with the electron-withdrawing nitro group, and coumarins **1f** with electron-donating methoxy group. The yields of thiocoumarins **1a—f** over three steps varied from moderate to good (see Scheme 1).

For the synthesis of 3-substituted 4-(trifluoromethyl)thiocoumarins we also used S-acylation of the sulfur atom of the *tert*-butylthio group in compound **2a** (Scheme 2).

In this case, the acylating agents were acetyl chlorides with active methylene group. Subsequent intramolecular Knövenagel condensation of the phenylacetic acid derivative **3g** carried out at heating in Et_3N as a solvent gave hydroxy-substituted derivative **5**. Compound **5** was found very stable to elimination of the water molecule. Dehydration of compound **5** to afford thiocoumarin **1g** was accomplished by treatment of the solution of **5** in pyridine with $SOCl_2$. In contrast, the reaction of ketone **2a** with 2-cyanoacetyl chloride directly resulted in

Scheme 1

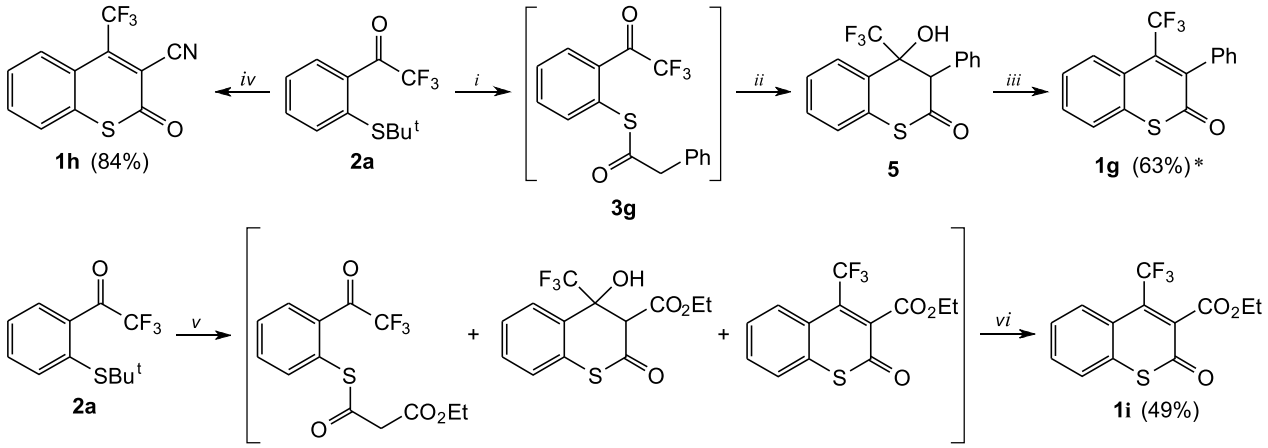


Compounds **1—4**	R^1	R^2	R^3	Yield of **1** (%)*	Compounds **1—4**	R^1	R^2	R^3	Yield of **1** (%)*
a	H	H	H	55	**d**	H	H	Cl	76
b	Cl	H	H	59	**e**	H	H	Br	52
c	NO_2	H	H	44	**f**	OMe	OMe	H	54

* Yields are given over three steps.

Reagents and conditions: *i.* $BrCH_2C(O)Br$, $TiCl_4$, CH_2Cl_2, 0 °C; *ii.* PPh_3, toluene; *iii.* Et_3N, CH_2Cl_2.

Scheme 2



* Over three steps.

Reagents and conditions: *i*. $PhCH_2C(O)Cl$, $TiCl_4$, CH_2Cl_2, −10 °C; *ii*. Et_3N, 60 °C; *iii*. $SOCl_2$, pyridine, −5 °C; *iv*. $NCCH_2C(O)Cl$, $TiCl_4$, CH_2Cl_2, −10 °C; *v*. $EtO_2CCH_2C(O)Cl$, $TiCl_4$, CH_2Cl_2, −10 °C; *vi*. Et_3N, THF.

thiocoumarins **1h**. In the case of $EtO_2CCH_2C(O)Cl$, the reaction mixture contained both intermediates along with the target coumarin **1i**. The intermediates were converted to coumarin **1i** by treatment with Et_3N in refluxing THF.

The structures of compounds **1a—i** were confirmed by ^1H, ^{19}F, and ^{13}C NMR spectroscopy, mass spectrometry, and elemental analysis. Thus, the ^1H NMR spectra of compounds **1a—f** exhibited the broadened singlets of the C(3)H proton at δ_H 6.91—7.15. In the ^1H NMR spectrum of thiocoumarin **1a**, the characteristic signal of the C(5)H proton is observed at δ_H 8.02 as a low field broadened doublet with spin-spin coupling constant of J = 8.3 Hz. It is of interest that the ^1H NMR spectrum of isomeric 2-(trifluoromethyl)-4*H*-thiochromen-4-one showed a quartet of the C(3)H proton at δ_H 7.33 (J = 0.8 Hz) and a doublet of doublets of doublets of the C(5)H proton that significantly shifted downfield to δ_H 8.52 (J = 8.1 Hz, J = 1.4 Hz, J = 0.7 Hz).[23] In the ^{13}C NMR spectra of compounds **1a—i**, the C(2) carbonyl carbon signals are observed in the δ_C 180—185 range. Such downfield shift of the carbonyl carbon signal is characteristic of thiocoumarins; while the carbonyl carbon signal of 4-trifluoromethylcoumarins is observed at δ_C ~160.[24] In the ^{19}F NMR spectra, the singlet signals of the fluorine atoms are observed at about δ_F −62 for compounds **1a—f** and in the δ_F −51÷−56 range for compounds **1g—i**. The chemical shift values observed in the ^{19}F NMR spectra of compounds **1a—i** agree well with the expected chemical shifts of the CF_3 group at the double bond. Mass spectra of compounds **1a—i** revealed the molecular ion peaks (except for compound **1g**) as well as the peaks of benzo[*b*]thiophene cation resulting from the loss of CO from molecular ion.[1] In the mass spectra of compounds **1a,b,d—h**, the peaks of benzo[*b*]thiophene cation are the most abundant thus being one of the proofs of the presence of the thiocoumarin scaffold but not the thiochromone one.[25]

The structure of compound **1a** was unambiguously established by X-ray diffraction analysis. The general view of molecule **1a** is shown in Fig. 1. All atoms of the bicyclic system in thiocoumarin **1a** are in one plane that is in a good agreement with X-ray diffraction data for thiocoumarins.[26—28]

For the synthesis of the starting ketones **2a—f**, we used different approaches (Scheme 3). Thus, compounds **2a,e** were synthesized by the reaction of 1-(2-fluorophenyl)-2,2,2-trifluoroethanones **6a,e** with *tert*-butylthiol in the presence of K_2CO_3 in DMF at 80 °C, whereas ketone **2b** was prepared from 1-(2,5-dichlorophenyl)-2,2,2-trifluoroethanone **6b** in the presence of Cs_2CO_3. Ketones **2c,d,f** were synthesized from 2-(*tert*-butylthio)-5-nitrobenzaldehyde (**7**), 2-(*tert*-butylthio)-3-chlorobenzaldehyde (**8**), and 2-(*tert*-butylthio)-4,5-dimethoxybenzaldehyde (**9**), respectively, using the Ruppert—Prakash reagent followed by the Swern oxidation of

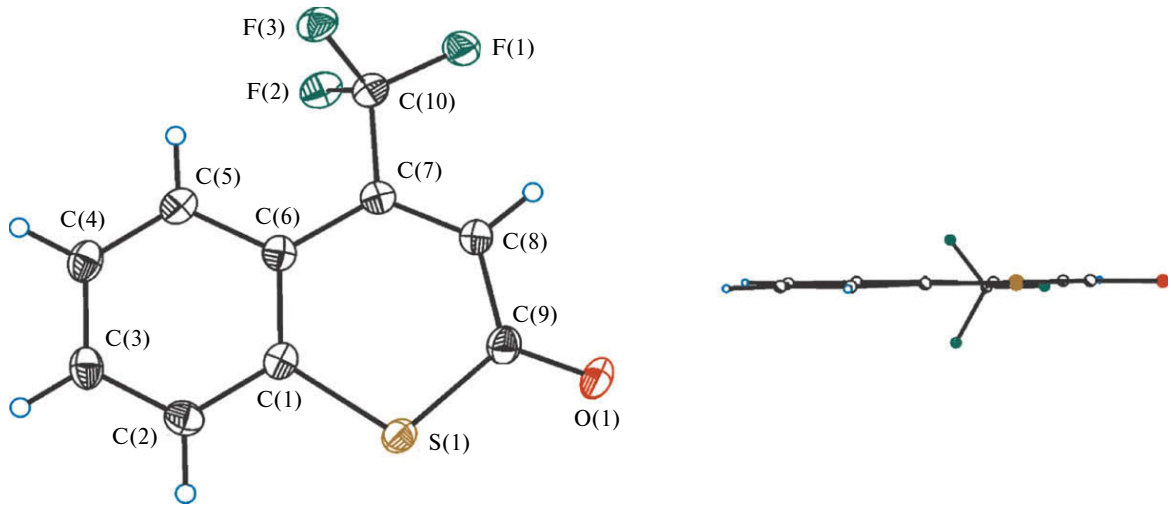
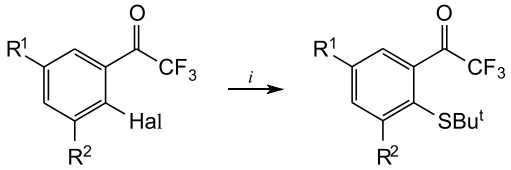


Fig. 1. General view of the molecule **1a** (two projections). Thermal ellipsoids are drawn at 50% probability level.

the resulting trifluoromethylcarbinols **6c,d,f**. 6-Nitroveratraldehyde was found to be a convenient precursor for benzaldehyde **9** (see Experimental).

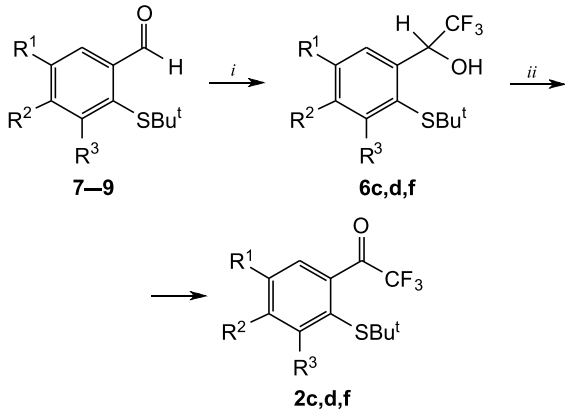
Scheme 3



6a,b,e **2a,b,e**

$R^1 = R^2 = H$; Hal = F (**2a**, **6a**);
R^1 = Cl, R^2 = H; Hal = Cl (**2b**, **6b**);
R^1 = H, R^2 = Br; Hal = F (**2e**, **6e**)

Reagents and conditions: $HSBu^t$, K_2CO_3, DMF, 80 °C.



7—9 **6c,d,f** **2c,d,f**

$R^1 = NO_2$, $R^2 = R^3 = H$ (**2c**, **6c**, **7**);
$R^1 = R^2 = H$, R^3 = Cl (**2d**, **6d**, **8**);
$R^1 = R^2$ = OMe, $R^3 = H$ (**2f**, **6f**, **9**)

Reagents and conditions: *i*. CF_3SiMe_3, Bu_4NF, THF; *ii*. $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, –70 °C.

In summary, we developed a convenient synthesis of 4-(trifluoromethyl)thiocoumarins that involved S-acylation of 1-[2-(*tert*-butylthio)phenyl]-2,2,2-trifluoroethanones with bromoacetyl bromide, subsequent preparation of phosphonium salts upon treatment with triphenylphosphine, and the final intramolecular Wittig reaction. We succeeded in making 3-substituted 4-(trifluoromethyl)thiocoumarins accessible by the S-acylation of 1-[2-(*tert*-butylthio)phenyl]-2,2,2-trifluoroethanones with acetyl chlorides bearing the active methylene group and subsequent Knövenagel condensation. The preparative procedures for the synthesis of new 1-[2-(*tert*-butylthio)phenyl]-2,2,2-trifluoroethanones were developed.

Experimental

^1H, ^{19}F-{^1H}, and ^{31}P-{^1H} NMR spectra were recorded on a Bruker Avance^{TM} 300 spectrometer (operating frequencies of 300 (^1H), 282.38 (^{19}F), and 121.495 MHz (^{31}P)). The ^{19}F NMR chemical shifts were measured relative to CF_3CO_2H as an internal standard and referred to $CFCl_3$. The ^{31}P NMR chemical shifts are reported relative to 85% H_3PO_4 as an internal standard. ^{13}C-{^1H} NMR spectra were recorded on a Bruker Avance^{TM} 400 instrument (operating frequency of 101 MHz (^{13}C)). The ^{13}C NMR shifts were measured relative to $CDCl_3$ (δ_C 77.0) and referred to $SiMe_4$. NMR spectra were recorded in $CDCl_3$ unless specified otherwise.

Electron impact mass spectra were recorded on a Shimadzu GCQP-2020 single quadrupole gas chromatograph-mass spectrometer. High resolution electrospray ionization mass spectrometry (HRMS (ESI)) was per-

formed on a Shimadzu LCMS-9030 tandem quadrupole time-of-flight LC/MS system. IR spectra were recorded for the KBr pellets on a Bruker Tensor 37 FT-IR in the range of 4000—400 cm^{-1}.

Elemental analysis was carried out in the Laboratory for microanalysis of A. N. Nesmeyanov Institute of Organoelement Compounds of the Russian Academy of Sciences. Automatic determination of C, H, and N contents was carried out on an Elementar vario MICRO cube elemental analyzer (Germany). Classical elemental microanalysis determination of carbon and hydrogen was carried out by express gravimetric analysis.

N,*N*-Dimethylformamide and DMSO were distilled over CaH_2. Dichloromethane and tetrahydrofuran were refluxed over CaH_2 and distilled. Toluene was refluxed over sodium metal and distilled. Bromoacetyl bromide and triethylamine were distilled prior to use. Reactions with $TiCl_4$ were carried out under dry nitrogen. Petroleum ether (PE; b.p. 40—70 °C) and ethyl acetate were refluxed over $CaCl_2$ and distilled.

(Trifluoromethyl)trimethylsilane (the Ruppert—Prakash reagent) was purchased from P&M. 2,2,2-Trifluoro-1-(2-fluorophenyl)ethanone (**6a**), 1-(2,5-dichlorophenyl)-2,2,2-trifluoroethanone (**6b**), and 1-(3-bromo-2-fluorophenyl)-2,2,2-trifluoroethanone (**6e**) were synthesized as earlier described.[29] 2-(*tert*-Butylthio)-5-nitrobenzaldehyde (**7**) and 2-(*tert*-butylthio)-3-chlorobenazaldehyde (**8**) were synthesized following the known procedure.[30]

4-(Trifluoromethyl)-2*H*-thiochromen-2-one (1a). To a solution of 1-[2-(*tert*-butylthio)phenyl]-2,2,2-trifluoroethanone (**2a**) (1.57 g, 6 mmol) and bromoacetyl bromide (1.33 g, 6.6 mmol) in CH_2Cl_2 (20 mL) cooled to 0 °C, a solution of $TiCl_4$ (1.25 g, 6.6 mmol) in CH_2Cl_2 (3 mL) was added dropwise. A mixture was stirred at 0 °C for 1 h, then slowly heated to 20 °C, stirred for 1 h, cooled to 0 °C, and treated with water. The organic layer was separated, washed with 5% aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and the drying agent was filtered off. The filtrate was concentrated *in vacuo*. Vacuum distillation of the residue afforded 1.76 g (90%) of *S*-(2-[2,2,2-trifluoroacetyl)phenyl]-2-bromothioacetate (**3a**). To a solution of compound **3a** (1.76 g, 5.4 mmol) in toluene (15 mL), a solution of PPh_3 (1.42 g, 5.4 mmol) in toluene (5 mL) was added. The mixture was stirred for 24 h, during this period of time a thick precipitate of (2-oxo-2-{[2-(2,2,2-trifluoroacetyl)]thio}ethyl)triphenylphosphonium bromide (**4a**) was formed. Dichloromethane (20 mL) was added to the reaction mixture, which resulted in complete dissolution of the precipitate. The resulting solution was cooled with an ice-water bath and treated with Et_3N (1.52 g, 15 mol). The obtained mixture was stirred for 24 h and concentrated *in vacuo*. Product **1a** was isolated by silica gel column chromatography (elution with PE—AcOEt, 9 : 1). Yield 0.76 g (55% over three steps).

Compound **3a**, Yellowish liquid, b.p. 130—135 °C (1 Torr). ^{1}H NMR (300 MHz), δ: 7.94 (d, 1 H, CH_{arom}, J = 7.5 Hz); 7.78—7.54 (m, 3 H, CH_{arom}); 4.15 (s, 2 H, CH_2Br). ^{13}C NMR (101 MHz), δ: 189.7, 181.6 (q, J = 35.8 Hz), 137.2, 133.9, 133.8, 130.0, 129.9 (q, J = 3.0 Hz), 128.4, 116.0 (q, J = 292.1 Hz), 33.0. ^{19}F NMR (282 MHz), δ: –71.83 (s). Found (%): C, 36.76; H, 2.00. $C_{10}H_6BrF_3O_2S$. Calculated (%): C, 36.72; H, 1.85.

Compound **4a**. An aliquot of phosphonium salt **4a** precipitated from toluene upon the reaction of compound **3a** with Ph_3P was collected by filtration and analyzed by NMR spectroscopy. White crystals. ^{1}H NMR (300 MHz), δ: 8.02—7.52 (m, 19 H, 15 CH_{Ph} and 4 CH_{arom}); 6.23 (d, 2 H, CH_2P, J = 13.0 Hz). ^{19}F NMR (282 MHz), δ: –71.76 (s). ^{31}P NMR (122 MHz), δ: 20.98 (s).

Compound **1a**. Yellowish crystals, m.p. 76—77 °C (from PE). IR (KBr), ν/cm^{-1}: 3063, 1644, 1606, 1596, 1547, 1431, 1294, 1183, 1164, 1149, 1116, 940, 912, 769, 726, 697, 543. ^{1}H NMR (400 MHz), δ: 8.02 (d, 1 H, C(5)H, J = 8.3 Hz); 7.65—7.55 (m, 2 H, CH_{arom}); 7.52 (dd, 1 H, CH_{arom}, J = 10.9 Hz, J = 4.1 Hz); 7.02 (s, 1 H, C(3)H). ^{13}C NMR (101 MHz), δ: 184.0, 140.2 (q, J = 30.0 Hz), 137.9, 130.6, 128.4 (q, J = 3.4 Hz), 127.2, 126.7, 123.6 (q, J = 6.2 Hz), 122.7 (q, J = 276.8 Hz), 121.1. ^{19}F NMR (376 MHz), δ: –62.47 (s). MS (EI, 70 eV), m/z (I_{rel} (%)): 230 $[M]^+$ (12), 202 $[M - CO]^+$ (100), 183 $[M - F - CO]^+$ (47), 152 $[M - CF_2 - CO]^+$ (75). Found (%): C, 52.36; H, 2.29. $C_{10}H_5F_3OS$. Calculated (%): C, 52.18; H, 2.19.

6-Chloro-4-(trifluoromethyl)-2*H*-thiochromen-2-one (1b) was synthesized similarly to compound **1a** from 1-[2-(*tert*-butylthio)-5-chlorophenyl]-2,2,2-trifluoroethanone (**2b**) (1.78 g, 6 mmol). *S*-[4-Chloro-2-(2,2,2-trifluoroacetyl)phenyl] 2-bromothioacetate (**3b**) obtained in the first reaction step was used further without additional purification.

Compound **3b**. Yellowish liquid. ^{1}H NMR (300 MHz), δ: 7.86 (br.s, 1 H, CH_{arom}); 7.67 (dd, 1 H, CH_{arom}, J = 8.4 Hz, J = 2.0 Hz); 7.60 (d, 1 H, CH_{arom}, J = 8.4 Hz); 4.14 (s, 2 H, CH_2Br). ^{19}F NMR (282 MHz), δ: –72.08 (s).

Compound **4b**. An aliquot of phosphonium salt **4b** precipitated from toluene upon the reaction of compound **3b** with Ph_3P was collected by filtration and analyzed by NMR spectroscopy. White crystals. ^{1}H NMR (300 MHz), δ: 7.99—7.52 (m, 18 H, 15 CH_{Ph} and 3 CH_{arom}); 6.19 (d, 2 H, CH_2P, J = 12.9 Hz). ^{19}F NMR (282 MHz), δ: –72.02 (s). ^{31}P NMR (122 MHz), δ: 20.92 (s).

Compound **1b** was isolated by silica gel column chromatography (elution with PE—AcOEt, 8 : 1). Yield 0.93 g (59%). Yellowish crystals, m.p. 118—119 °C (from PE—AcOEt, 30 : 1). IR (KBr), ν/cm^{-1}: 3114, 1643, 1606, 1536, 1402, 1293, 1277, 1197, 1175, 1155, 1126, 954, 916, 824, 731, 684, 517. ^{1}H NMR (300 MHz), δ: 8.04—7.91 (m, 1 H, C(5)H); 7.59 (dd, 1 H, CH_{arom}, J = 8.6 Hz, J = 1.9 Hz);

7.50 (d, 1 H, CH_{arom}, J = 8.6 Hz); 7.05 (s, 1 H, C(3)H). ^{13}C NMR (126 MHz), δ: 183.2, 139.3 (q, J = 30.3 Hz), 136.1, 133.4, 130.9, 128.0 (q, J = 3.7 Hz), 127.8, 124.5 (q, J = 6.1 Hz), 122.4 (q, J = 277.2 Hz), 122.3. ^{19}F NMR (282 MHz), δ: –62.62 (s). MS (EI, 70 eV), m/z (I_{rel} (%)): 264 $[M]^+$ (32), 236 $[M - CO]^+$ (100), 217 $[M - F - CO]^+$ (35), 186 $[M - CF_2 - CO]^+$ (25). Found (%): C, 45.09; H, 1.67. $C_{10}H_4ClF_3OS$. Calculated (%): C, 45.38; H, 1.52.

6-Nitro-4-(trifluoromethyl)-2*H*-thiochromen-2-one (1c) was synthesized similarly to compound **1a** from 1-[2-(*tert*-butylthio)-5-nitrophenyl]-2,2,2-trifluoroethanone (**2c**) (1.84 g, 6 mmol). *S*-[4-Nitro-2-(2,2,2-trifluoroacetyl)phenyl] 2-bromothioacetate (**3c**) obtained in the first reaction step was used further without additional purification.

Compound **3c**. Yellowish liquid. ^{1}H NMR (300 MHz), δ: 8.73 (br.s, 1 H, CH_{arom}); 8.52 (dd, 1 H, CH_{arom}, J = 8.6 Hz, J = 2.4 Hz); 7.92 (d, 1 H, CH_{arom}, J = 8.6 Hz); 4.18 (s, 2 H, CH_2Br). ^{19}F NMR (282 MHz), δ: –71.97 (s).

Compound **1c** was isolated by silica gel column chromatography (elution with PE—AcOEt, 8 : 1). Yield 0.72 g (44%). Yellowish crystals, m.p. 125—126 °C (PE—AcOEt, 30 : 1). IR (KBr), ν/cm^{-1}: 3119, 3064, 1664, 1622, 1599, 1560, 1519, 1342, 1289, 1203, 1181, 1148, 1136, 888, 843, 733, 512. ^{1}H NMR (300 MHz), δ: 8.98—8.79 (m, 1 H, C(5)H); 8.44 (dd, 1 H, CH_{arom}, J = 8.9 Hz, J = 2.2 Hz); 7.75 (d, 1 H, CH_{arom}, J = 8.9 Hz); 7.14 (s, 1 H, C(3)H). ^{13}C NMR (101 MHz), δ: 181.9, 146.4, 144.8, 139.6 (q, J = 30.8 Hz), 127.9, 125.2 (q, J = 6.0 Hz), 124.6, 123.6 (q, J = 3.8 Hz), 122.5 (q, J = 277.2 Hz), 121.5. ^{19}F NMR (282 MHz), δ: –62.61 (s). MS (EI, 70 eV), m/z (I_{rel} (%)): 275 $[M]^+$ (28), 247 $[M - CO]^+$ (72), 217 $[M - CO - NO]^+$ (72), 201 $[M - CO - NO_2]^+$ (100). Found (%): C, 43.51; H, 1.54; N, 5.11. $C_{10}H_4F_3NO_3S$. Calculated (%): C, 43.64; H, 1.47; N, 5.09.

8-Chloro-4-(trifluoromethyl)-2*H*-thiochromen-2-one (1d) was synthesized similarly to compound **1a** from 1-(2-*tert*-butylthio-3-chlorophenyl)-2,2,2-trifluoroethanone (**2d**) (1.78 g, 6 mmol). *S*-[2-Chloro-6-(2,2,2-trifluoroacetyl)phenyl] 2-bromothioacetate **(3d)** obtained in the first reaction step was used further without additional purification.

Compound **3d**. Yellowish liquid. ^{1}H NMR (300 MHz), δ: 7.84 (dd, 1 H, CH_{arom}, J = 8.0 Hz, J = 1.3 Hz); 7.75 (dm, 1 H, CH_{arom}, J = 7.8 Hz); 7.62 (t, 1 H, CH_{arom}, J = 7.9 Hz); 4.20 (s, 2 H, CH_2Br). ^{19}F NMR (282 MHz), δ: –72.76 (s).

Compound **1d** was isolated by silica gel column chromatography (elution with PE—AcOEt, 10 : 1). Yield 1.20 g (76%). Yellowish crystals, m.p. 118—119 °C (from PE—AcOEt, 30 : 1). IR (KBr), ν/cm^{-1}: 3062, 1648, 1608, 1581, 1466, 1382, 1289, 1242, 1185, 1166, 1138, 1116, 912, 883, 804, 798, 727, 617. ^{1}H NMR (300 MHz), δ: 7.97 (d, 1 H, C(5)H, J = 8.3 Hz); 7.70 (d, 1 H, CH_{arom}, J = 7.9 Hz); 7.48 (t, 1 H, CH_{arom}, J = 8.1 Hz); 7.05 (s, 1 H, C(3)H). ^{13}C NMR (101 MHz), δ: 183.6, 140.1 (q, J = 30.1 Hz), 136.4, 131.31, 131.0, 127.3, 126.9 (q, J = 3.5 Hz), 124.1 (q, J = 6.1 Hz), 123.0, 122.6 (q, J = 276.8 Hz). ^{19}F NMR (282 MHz), δ: –61.91 (s). MS (EI, 70 eV), m/z (I_{rel} (%)): 264 $[M]^+$ (28), 236 $[M - CO]^+$ (100), 217 $[M - F - CO]^+$ (32), 186 $[M - CF_2 - CO]^+$ (25). Found (%): C, 45.31; H, 1.64. $C_{10}H_4ClF_3OS$. Calculated (%): C, 45.38; H, 1.52.

8-Bromo-4-(trifluoromethyl)-2*H*-thiochromen-2-one (1e) was synthesized similarly to compound **1a** from 1-[3-bromo-2-(*tert*-butylthio)phenyl]-2,2,2-trifluoroethanone (**2e**) (2.05 g, 6 mmol). *S*-[2-Bromo-6-(2,2,2-trifluoroacetyl)phenyl] 2-bromothioacetate (**3e**) obtained in the first reaction step was used further without additional purification.

Compound **3e**. Yellowish liquid. ^{1}H NMR (300 MHz), δ: 7.98 (dd, 1 H, CH_{arom}, J = 8.1 Hz, J = 1.2 Hz); 7.84—7.66 (m, 1 H, CH_{arom}); 7.49 (t, 1 H, CH_{arom}, J = 7.9 Hz); 4.15 (s, 2 H, CH_2Br). ^{19}F NMR (282 MHz), δ: –72.75 (s).

Compound **1e** was isolated by silica gel column chromatography (elution with PE—AcOEt, 10 : 1). Yield 0.96 g (52%). Yellowish crystals, m.p. 113—114 °C (from PE—AcOEt, 30 : 1). IR (KBr), ν/cm^{-1}: 3063, 1647, 1612, 1580, 1537, 1461, 1379, 1290, 1239, 1181, 1157, 1127, 1063, 919, 793, 729, 613. ^{1}H NMR (300 MHz), δ: 8.02 (d, 1 H, C(5)H, J = 8.3 Hz); 7.88 (d, 1 H, CH_{arom}, J = 7.9 Hz); 7.41 (t, 1 H, CH_{arom}, J = 8.1 Hz); 7.02 (s, 1 H, C(3)H). ^{13}C NMR (126 MHz), δ: 184.2, 140.3 (q, J = 30.0 Hz), 138.2, 134.8, 127.6, 127.5 (q, J = 3.7 Hz), 124.2 (q, J = 6.2 Hz), 123.4, 122.5 (q, J = 277.2 Hz), 120.9. ^{19}F NMR (282 MHz), δ: –61.76 (s). MS (EI, 70 eV), m/z (I_{rel} (%)): 308 $[M]^+$ (28), 280 $[M - CO]^+$ (100), 201 $[M - CO - Br]^+$ (79), 181 $[M - HF - CO - Br]^+$ (25). Found (%): C, 38.81; H, 1.37. $C_{10}H_4BrF_3OS$. Calculated (%): C, 38.86; H, 1.30.

6,7-Dimethyloxy-4-(trifluoromethyl)-2*H*-thiochromen-2-one (1f) was synthesized similarly to compound **1a** from 1-[2-(*tert*-butylthio)-4,5-dimethoxyphenyl]-2,2,2-trifluoroethanone (**2f**) (1.93 g, 6 mmol). A solution of $TiCl_4$ in CH_2Cl_2 was added at –10 °C, the reaction mixture was stirred at –10 °C for 1 h, then heated to 20 °C and stirred for 1 h. *S*-[4,5-Dimethoxy-2-(2,2,2-trifluoroacetyl)phenyl] 2-bromothioacetate (**3f**) obtained in the first reaction step was used further without additional purification.

Compound **3f**. Yellowish crystals. ^{1}H NMR (300 MHz), δ: 7.44 (d, 1 H, CH_{arom}, J = 1.2 Hz); 7.16 (s, 1 H, CH_{arom}); 4.17 (s, 2 H, CH_2Br); 4.00 (s, 3 H, OMe); 3.98 (s, 3H, OMe). ^{19}F NMR (282 MHz), δ: –70.98 (s).

Compound **1f** was isolated by silica gel column chromatography (elution with PE—AcOEt, 3 : 1). Yield 0.94 g (54%). Lemon yellow crystals, m.p. 162—163 °C (from PE—AcOEt, 30 : 1). IR (KBr), ν/cm^{-1}: 3094, 1642, 1607, 1532, 1518, 1464, 1413, 1356, 1285, 1263, 1231, 1201, 1182, 1155, 1120, 1066, 914, 872, 848, 732, 527. ^{1}H NMR (300 MHz), δ: 7.38 (s, 1 H, CH_{arom}); 6.96 (s, 1 H, CH_{arom}); 6.91 (s, 1 H, C(3)H); 4.01 (s, 3 H, OMe); 3.98 (s, 3 H, OMe). ^{13}C NMR (101 MHz), δ: 184.0, 152.0,

148.4, 139.8 (q, J = 29.6 Hz), 132.6, 122.9 (q, J = 276.7 Hz), 120.9 (q, J = 6.2 Hz), 114.5, 109.4 (q, J = 3.5 Hz), 108.0, 56.4, 56.1. ^{19}F NMR (282 MHz), δ: −62.74 (s). MS (EI, 70 eV), m/z (I_{rel} (%)): 290 $[M]^+$ (62), 262 $[M - CO]^+$ (100), 247 $[M - CH_3 - CO]^+$ (55), 219 $[M - CO - COCH_3]^+$ (36), 199 $[M - HF - CO - COCH_3]^+$ (41). HRMS (ESI): found m/z 291.0298 $[M + H]^+$; calculated for $C_{12}H_{10}F_3O_3S^+$ 291.0297. Found (%): C, 49.54; H, 3.18. $C_{12}H_9F_3O_3S$. Calculated (%): C, 49.66; H, 3.13.

3-Phenyl-4-(trifluoromethyl)-2*H*-thiochromen-2-one (1g). To a solution of compound **2a** (2.62 g, 10 mmol) and phenylacetyl chloride (1.70 g, 11 mmol) in CH_2Cl_2 (30 mL) cooled to −10 °C, a solution of $TiCl_4$ (2.09 g, 11 mmol) in CH_2Cl_2 (5 mL) was added. The mixture was stirred at −10 °C for 1 h, then heated to 20 °C, stirred for 1 h, treated with water, the organic layer was separated, and washed with 10% aqueous K_2CO_3 to obtain 2.72 g (84%) of *S*-[2-(2,2,2-trifluoroacetyl)phenyl] 2-phenylthioacetate (**3g**) as a yellowish liquid. Compound **3g** was used further without additional purification. A solution of compound **3g** (1.2 g, 3.7 mmol) in Et_3N (10 mL) was heated at 60 °C for 4 h. The volatiles were removed *in vacuo*. 4-Hydroxy-3-phenyl-4-(trifluoromethyl)thiochroman-2-one (**5**) was isolated by silica gel column chromatography (elution with PE—AcOEt, 4 : 1). Yield 1.1 g (91%). To a solution of compound **5** (0.32 g, 1 mmol) in anhydrous pyridine (5 mL) cooled to −5 °C, a solution of thionyl chloride (0.18 g, 1.5 mmol) in diethyl ether (1 mL) was added dropwise. The reaction mixture was warmed to 20 °C, stirred at this temperature for 16 h, and poured into ice-water (50 mL). Product **1g** was extracted with diethyl ether (3×20 mL), the combined organic layers were successively washed with 5% aqueous HCl and brine, and dried with $MgSO_4$. The drying agent was filtered off and the filtrate was concentrated *in vacuo*. Compound **1g** was isolated by silica gel column chromatography (elution with PE—AcOEt, 4 : 1). Yield 0.25 g (83%). Yellowish crystals.

Compound **3g**. ^{1}H NMR (300 MHz), δ: 7.86 (d, 1 H, CH_{arom}, J = 7.4 Hz); 7.70—7.51 (m, 3 H, CH_{arom}); 7.48—7.30 (m, 5 H, CH_{arom}); 3.94 (s, 2 H, $C\underline{H}_2Ph$). ^{19}F NMR (282 MHz), δ: −71.97 (s).

Compound **5**. White crystals, m.p. 108—109 °C (from PE—AcOEt, 30 : 1). ^{1}H NMR (300 MHz), δ: 7.91 (d, 1 H, CH_{arom}, J = 7.7 Hz); 7.54 (td, 1 H, CH_{arom}, J = 7.5 Hz, J = 1.5 Hz); 7.48—7.41 (m, 1 H, CH_{arom}); 7.38—7.31 (m, 4 H, CH_{arom}); 7.25—7.22 (m, 2 H, CH_{arom}); 4.47 (s, 1 H, C(3)H); 2.33 (s, 1 H, OH). ^{19}F NMR (376 MHz), δ: −79.49 (s). Found (%): C, 59.25; H, 3.51. $C_{16}H_{11}F_3O_2S$. Calculated (%): C, 59.26; H, 3.42.

Compound **1g**. M.p. 154—156 °C (from PE—AcOEt, 30 : 1). IR (KBr), ν/cm^{-1}: 3060, 1619, 1606, 1594, 1542, 1428, 1343, 1297, 1206, 1167, 1117, 1101, 1083, 944, 834, 746, 732, 695, 599. ^{1}H NMR (300 MHz), δ: 8.07 (d.q, 1 H, C(5)H, J = 8.2 Hz, J = 2.8 Hz); 7.61—7.41 (m, 6 H, CH_{arom}); 7.23 (m, 2 H, CH_{arom}). ^{13}C NMR (101 MHz), δ: 185.2, 138.3, 136.8 (q, J = 28.1 Hz), 135.8, 133.9, 129.8, 129.3 (q, J = 4.8 Hz), 129.0 (q, J = 1.5 Hz), 128.7, 128.1, 126.9, 126.3, 123.4 (q, J = 280.3 Hz), 122.9. ^{19}F NMR (282 MHz), δ: −51.73 (s). MS (EI, 70 eV), m/z (I_{rel} (%)): 280 $[M + 2 H - CO]^+$ (18), 278 $[M - CO]^+$ (100), 257 $[M - HF - H]^+$ (20), 228 $[M - CF_2 - CO]^+$ (12). HRMS (ESI): found m/z 307.0400 $[M + H]^+$; calculated for $C_{16}H_{10}F_3OS^+$ 307.0399. Found (%): C, 62.64; H, 3.11. $C_{16}H_9F_3OS$. Calculated (%): C, 62.74; H, 2.96.

2-Oxo-4-(trifluoromethyl)-2*H*-thiochromene-3-carbonitrile (1h). To a solution of compound **2a** (2.62 g, 10 mmol) and cyanoacetyl chloride (1.14 g, 11 mmol) in CH_2Cl_2 (30 mL) cooled to −10 °C, a solution of $TiCl_4$ (2.09 g, 11 mmol) in CH_2Cl_2 (5 mL) was added dropwise. The mixture was stirred at −10 °C for 1 h, warmed to 20 °C, and stirred for 1 h. After the standard aqueous workup described for the synthesis of compound **1a**, product **1h** was obtained in the yield of 2.14 g (84%). Red brown crystals, m.p. 161—162 °C (from PE—AcOEt, 10 : 1). IR (KBr), ν/cm^{-1}: 2232, 1629, 1597, 1582, 1536, 1434, 1360, 1298, 1211, 1199, 1183, 1169, 1150, 958, 784, 741, 700, 639. ^{1}H NMR (300 MHz), δ: 8.15 (dq, 1 H, C(5)H, J = 8.6 Hz, J = 2.8 Hz); 7.74 (t, 1 H, CH_{arom}, J = 7.5 Hz); 7.66—7.53 (m, 2 H, CH_{arom}). ^{13}C NMR (101 MHz, $CDCl_3$—DMSO-d_6 (10 : 1), δ: 179.7, 145.6 (q, J = 29.9 Hz), 137.3, 133.6, 130.2 (q, J = 4.8 Hz), 128.5, 127.5, 121.7 (q, J = 280.3 Hz), 120.6, 111.2, 110.7. ^{19}F NMR (282 MHz), δ: −56.19 (s). MS (EI, 70 eV), m/z (I_{rel} (%)): 255 $[M]^+$ (30), 227 $[M - CO]^+$ (100), 208 $[M - HF - CO]^+$ (31), 177 $[M - CF_2 - CO]^+$ (47). Found (%): C, 51.78; H, 1.71; N, 5.61. $C_{11}H_4F_3NOS$. Calculated (%): C, 51.77; H, 1.58; N, 5.49.

Ethyl 2-oxo-4-trifluoromethyl-2*H*-thiochromene-3-carboxylate (1i). To a solution of ketone **2a** (0.53 g, 2 mmol) and $EtO_2CCH_2C(O)Cl$ (0.39 g, 2.6 mmol) in CH_2Cl_2 (20 mL) cooled to −10 °C, a solution of $TiCl_4$ (0.42 g, 2.2 mmol) in CH_2Cl_2 (3 mL) was added dropwise. The mixture was stirred at −10 °C for 1 h, warmed to 20 °C, and stirred for 1 h. The product mixture obtained after the workup described for the synthesis of compound **1a** was dissolved in THF (15 mL) and Et_3N (1 mL) was added. The mixture was refluxed for 1 h and concentrated *in vacuo*. Product **1i** was isolated by silica gel column chromatography (elution with PE—AcOEt, 5 : 1). Yield 0.30 g (49%). Yellow crystals, m.p. 58—59 °C (from PE—AcOEt, 30 : 1). IR (KBr), ν/cm^{-1}: 2980, 1736, 1636, 1589, 1550, 1432, 1355, 1294, 1260, 1214, 1184, 1172, 1148, 1086, 1021, 959, 774, 735, 664. ^{1}H NMR (300 MHz), δ: 8.10 (d, 1 H, C(5)H, J = 8.0 Hz); 7.75—7.48 (m, 3 H, CH_{arom}); 4.49 (q, 2 H, OCH_2, J = 7.1 Hz); 1.44 (t, 3 H, Me, J = 7.1 Hz). ^{13}C NMR (101 MHz), δ: 182.1, 163.3, 136.4, 135.5 (q, J = 30.4 Hz), 131.0, 130.7, 129.4 (q, J = 4.4 Hz), 127.5, 126.6, 122.4 (q, J = 278.8 Hz), 120.6, 62.8, 13.8. ^{19}F NMR (282 MHz), δ: −56.19 (s). MS (EI, 70 eV), m/z (I_{rel} (%)): 302 $[M]^+$ (15), 274 $[M - CO]^+$ (61), 246 $[M - 2 CO]^+$ (52), 229 $[M - CO_2C_2H_5]^+$ (100), 201

$[M - CO_2C_2H_5 - CO]^+$ (48). Found (%): C, 51.67; H, 3.21. $C_{13}H_9F_3O_3S$. Calculated (%): C, 51.66; H, 3.00.

1-[2-(*tert*-Butylthio)phenyl]-2,2,2-trifluoroethanone (2a). To a suspension of finely grounded K_2CO_3 (9.67 g, 70 mmol) in DMF (80 mL), a solution of 1-(2-fluorophenyl)-2,2,2-trifluoroethanone (**6a**) (9.54 g, 49.7 mmol) and *tert*-butyl mercaptan (5.82 g, 64.6 mmol) in DMF (20 mL) was added. The reaction mixture was heated at 70—80 °C for 8 h, cooled to 20 °C, poured into ice-water (300 mL), and extracted with diethyl ether (3×60 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, and the drying agent was filtered off. The filtrate was concentrated *in vacuo*. Product **2a** was isolated by vacuum distillation Yield 9.23 g (71%). Yellowish liquid, b.p. 85—90 °C (1 Torr). ^{1}H NMR (400 MHz), δ: 7.70 (d, 1 H, CH_{arom}, J = 7.7 Hz); 7.61—7.53 (m, 1 H, CH_{arom}); 7.53—7.48 (m, 2 H, CH_{arom}); 1.29 (s, 9 H, SBu^t). ^{13}C NMR (101 MHz), δ: 186.4 (q, J = 36.3 Hz), 140.0, 138.3, 132.6, 131.7, 128.7, 127.9, 115.7 (q, J = 291.6 Hz), 48.1, 30.9. ^{19}F NMR (376 MHz), δ: −73.88 (s). Found (%): C, 55.00; H, 5.05. $C_{12}H_{13}F_3OS$. Calculated (%): C, 54.95; H, 5.00.

1-[5-Chlorophenyl-2-(*tert*-butylthio)]-2,2,2-trifluoroethanone (2b) was synthesized similarly to compound **2a** from 1-(2,5-dichlorophenyl)-2,2,2-trifluoroethanone (**6b**) (4.54 g, 18.7 mmol) and *tert*-butyl mercaptan (2.20 g, 24.3 mmol) in the presence of Cs_2CO_3 (7.90 g, 24.2 mmol) in DMF (60 mL). Reaction temperature was 70 °C, reaction time was 3 h. Compound **2b** was isolated by vacuum distillation. Yield 2.72 g (54%). Light yellow liquid, b.p. 100—101 °C (2 Torr). ^{1}H NMR (400 MHz), δ: 7.62 (d, 1 H, CH_{arom}, J = 8.3 Hz); 7.53 (dd, 1 H, CH_{arom}, J = 8.3 Hz, J = 2.2 Hz); 7.46 (s, 1 H, CH_{arom}); 1.28 (s, 9 H, SBu^t). ^{13}C NMR (101 MHz), δ: 185.2 (q, J = 37.2 Hz), 141.5, 139.6, 135.3, 131.7, 130.9, 127.7 (q, J = 1.2 Hz), 115.4 (q, J = 291.4 Hz), 48.6, 30.9. ^{19}F NMR (282 MHz), δ: −74.02 (s). Found (%): C, 48.59; H, 4.26. $C_{12}H_{12}ClF_3OS$. Calculated (%): C, 48.57; H, 4.08.

1-[3-Bromo-2-(*tert*-butylthio)phenyl]-2,2,2-trifluoroethanone (2e) was synthesized similarly to compound **2a** from 1-(3-bromo-2-fluorophenyl)-2,2,2-trifluoroethanone (**6e**) (3.7 g, 13.6 mmol) and *tert*-butyl mercaptan (1.60 g, 17.7 mmol) in the presence of K_2CO_3 (2.63 g, 19 mmol) in DMF (50 mL). Reaction temperature was 80 °C, reaction time was 8 h. Compound **2e** was isolated by vacuum distillation. Yield 2.72 g (59%). Light yellow liquid, b.p. 95—100 °C (1 Torr). ^{1}H NMR (400 MHz), δ: 7.92 (dd, 1 H, CH_{arom}, J = 7.4 Hz, J = 2.0 Hz); 7.42—7.30 (m, 2 H, CH_{arom}); 1.30 (s, 9 H, SBu^t). ^{13}C NMR (101 MHz), δ: 186.5 (q, J = 36.9 Hz), 144.1, 136.6, 134.9, 132.4, 130.9, 126.7, 115.3 (q, J = 291.2 Hz), 52.1, 31.5. ^{19}F NMR (282 MHz), δ: −74.76 (s). Found (%): C, 42.32; H, 3.68. $C_{12}H_{12}BrF_3OS$. Calculated (%): C, 42.24; H, 3.55.

1-[2-(*tert*-Butylthio)-5-nitrophenyl]-2,2,2-trifluoroethanone (2c). To a solution of oxalyl chloride (2.6 g, 20 mmol) in CH_2Cl_2 (65 mL) cooled to −75 °C, a solution of DMSO (3.14 g, 40 mmol) in CH_2Cl_2 (5 mL) was added and after 15 min a solution of 1-(2-*tert*-butylthio-5-nitrophenyl)-2,2,2-trifluoroethanol (**6c**) (3.09 g, 10 mmol) in CH_2Cl_2 (10 mL) was added. The obtained mixture was stirred for 30 min and a solution of Et_3N (6.1 g, 60 mmol) in CH_2Cl_2 (10 mL) was added. The mixture was warmed to 20 °C and treated with water. The organic layer was separated, successively washed with 3% aqueous HCl and brine, dried with $MgSO_4$, and concentrated *in vacuo*. Compound **2c** was isolated by silica gel column chromatography (elution with PE—CH_2Cl_2, 1 : 1). Yield 2.5 g (81%). Yellow crystals, m.p. 35—36 °C. ^{1}H NMR (300 MHz), δ: 8.43 (br.s, 1 H, CH_{arom}); 8.38 (dd, 1 H, CH_{arom}, J = 8.6 Hz, J = 2.5 Hz); 7.89 (d, 1 H, CH_{arom}, J = 8.6 Hz); 1.43 (s, 9 H, SBu^t). ^{13}C NMR (101 MHz), δ: 183.2 (q, J = 37.2 Hz), 146.3, 144.5, 137.6, 136.1, 126.0, 123.6 (q, J = 1.9 Hz), 115.5 (q, J = 291.3 Hz), 49.8, 31.1. ^{19}F NMR (376 MHz), δ: −73.33 (s). Found (%): C, 46.81; H, 3.99; N, 4.69. $C_{12}H_{12}F_3NO_3S$. Calculated (%): C, 46.90; H, 3.94; N, 4.56.

1-[2-(*tert*-Butylthio)-3-chlorophenyl]-2,2,2-trifluoroethanone (2d) was synthesized similarly to compound **2c** from 1-(2-*tert*-butylthio-3-chlorophenyl)-2,2,2-trifluoroethanol (**6d**) (3.49 g, 12 mmol), oxalyl chloride (4.57 g, 36 mmol), DMSO (5.65 g, 72 mmol), and Et_3N (10.9 g, 108 mmol). Compound **2d** was isolated by vacuum distillation. Yield 2.72 g (81%). Yellow liquid, b.p. 89—93 °C (2 Torr). ^{1}H NMR (300 MHz), δ: 7.73 (d, 1 H, CH_{arom}, J = 8.0 Hz); 7.46 (t, 1 H, CH_{arom}, J = 7.8 Hz); 7.30 (d, 1 H, CH_{arom}, J = 8.0 Hz); 1.30 (s, 9 H, SBu^t). ^{13}C NMR (101 MHz), δ: 186.5 (q, J = 37.0 Hz), 144.2, 143.0, 133.2, 130.9, 130.3, 125.9, 115.4 (q, J = 291.2 Hz), 51.8, 31.4. ^{19}F NMR (282 MHz), δ: −70.83 (s). Found (%): C, 48.51; H, 4.11. $C_{12}H_{12}ClF_3OS$. Calculated (%): C, 48.57; H, 4.08.

1-[2-(*tert*-Butylthio)-4,5-dimethoxyphenyl]-2,2,2-trifluoroethanone (2f) was synthesized similarly to compound **2c** from 1-(2-*tert*-butylthio-4,5-dimethoxyphenyl)-2,2,2-trifluoroethanol (**6f**) (5.60 g, 17.3 mmol), oxalyl chloride (5.47 g, 43.2 mmol), DMSO (5.43 g, 69.2 mmol), and Et_3N (10.50 g, 104 mmol). Compound **2f** was isolated by silica gel column chromatography (elution with PE—AcOEt, 3 : 1). Yield 5.06 g (91%). Yellow crystals, m.p. 47—49 °C. ^{1}H NMR (300 MHz), δ: 7.14 (s, 1 H, CH_{arom}); 7.04 (s, 1 H, CH_{arom},); 3.97 (s, 3 H, OMe); 3.95 (s, 3 H, OMe); 1.27 (s, 9 H, SBu^t). ^{13}C NMR (101 MHz), δ: 184.8 (q, J = 35.7 Hz), 151.2, 149.2, 132.0, 126.0, 121.1, 115.9 (q, J = 292.0 Hz), 111.0 (q, J = 2.1 Hz), 56.2, 56.1, 48.0, 30.8. ^{19}F NMR (282 MHz), δ: −72.50 (s). Found (%): C, 51.90; H, 5.31. $C_{14}H_{17}F_3O_3S$. Calculated (%): C, 52.17; H, 5.32.

1-(2-*tert*-Butylthio-5-nitrophenyl)-2,2,2-trifluoroethanol (6c). To a solution of 2-(*tert*-butylthio)-5-nitrobenzaldehyde (**7**) (7.18 g, 30 mmol) in THF (80 mL), CF_3SiMe_3 (5.12 g, 36 mmol) was added. The mixture was cooled to 5 °C and 1 *M* Bu_4NF (1 mL) in THF was added. The resulting mixture was stirred at 20 °C for 16 h, treated with 3% aqueous HCl (30 mL), and stirred for 16 h. The or-

ganic layer was separated, the aqueous layer was extracted with diethyl ether (2×30 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was crystallized from PE—AcOEt (30 : 1) to afford 8.07 g (87%) of product **6c**, yellow crystals. M.p. 55—56 °C (from PE—AcOEt, 30 : 1). ^{1}H NMR (300 MHz), δ: 8.61 (s, 1 H, CH_{arom}); 8.22 (dd, 1 H, CH_{arom}, J = 8.6 Hz, J = 2.5 Hz); 7.83 (d, 1 H, CH_{arom}, J = 8.6 Hz); 6.28—5.84 (m, 1 H, $CHCF_3$); 3.16 (s, 1 H, OH); 1.38 (s, 9 H, SBu^t). ^{13}C NMR (101 MHz), δ: 147.9, 141.9, 140.3, 138.2, 124.1 (q, J = 283.2 Hz), 123.5, 123.2, 69.3 (q, J = 32.0 Hz), 49.5, 31.1. ^{19}F NMR (282 MHz), δ: −77.3 (s). Found (%): C, 46.56; H, 4.65; N, 4.44. $C_{12}H_{14}F_3NO_3S$. Calculated (%): C, 46.60; H, 4.65; N, 4.53.

1-(2-*tert*-Butylthio-3-chlorophenyl)-2,2,2-trifluoroethanol (6d) was synthesized similarly to compound **6c** from 2-(*tert*-butylthio)-3-chlorobenzaldehyde (**8**) (3.66 g, 16 mmol) and CF_3SiMe_3 (2.73 g, 19.2 mmol). Compound **6d** was isolated by silica gel column chromatography (elution with PE—AcOEt, 10 : 1). Yield 4.28 g (89%). White crystals, m.p. 102—103 °C. ^{1}H NMR (300 MHz), δ: 7.21 (d, 1 H, CH_{arom}, J = 7.7 Hz); 7.14 (dd, 1 H, CH_{arom}, J = 8.0 Hz, J = 1.4 Hz); 6.95 (t, 1 H, CH_{arom}, J = 7.9 Hz); 6.05—5.59 (m, 1 H, $CHCF_3$); 2.24 (d, 1 H, OH, J = 4.7 Hz); 0.90 (s, 9 H, SBu^t). ^{13}C NMR (101 MHz), δ: 142.9, 142.1, 132.2, 131.2, 130.3, 126.6 (q, J = 2.2 Hz), 124.4 (q, J = 283.1 Hz), 70.9 (q, J = 31.5 Hz), 50.8, 31.2. ^{19}F NMR (282 MHz), δ: −77.11 (s). Found (%): C, 48.24; H, 4.77. $C_{12}H_{14}ClF_3OS$. Calculated (%): C, 48.24; H, 4.72.

1-(2-*tert*-Butylthio-4,5-dimethoxyphenyl)-2,2,2-trifluoroethanol (6f) was synthesized similarly to compound **6c** from 2-(*tert*-butylthio)-4,5-dimethoxybenzaldehyde (**9**) (4.6 g, 18 mmol) and CF_3SiMe_3 (3.07 g, 21.6 mmol). Compound **6f** was isolated by silica gel column chromatography (elution with PE—AcOEt, 3 : 1). Yield 5.68 g (97%). Light yellow crystals, m.p. 68—69 °C. ^{1}H NMR (300 MHz), δ: 7.25—7.15 (br.s, 1 H, CH_{arom}); 7.10 (s, 1 H, CH_{arom}); 6.00 (q, 1 H, $CHCF_3$, J = 6.8 Hz); 3.95 (s, 3 H, OMe); 3.92 (s, 3 H, OMe); 2.06 (s, 1 H, OH); 1.32 (s, 9 H, SBu^t). ^{13}C NMR (101 MHz), δ: 150.0, 148.6, 132.1, 124.8 (q, J = 283.0 Hz), 124.0, 120.6, 110.3, 69.8 (q, J = 31.4 Hz), 55.9, 55.9, 47.3, 30.8. ^{19}F NMR (282 MHz), δ: −77.09 (s). Found (%): C, 51.85; H, 5.97. $C_{14}H_{19}F_3O_3S$. Calculated (%): C, 51.84; H, 5.90.

2-(*tert*-Butylthio)-4,5-dimethoxybenzaldehyde (9). To a solution of 6-nitroveratraldehyde (5.27 g, 25 mmol) and *tert*-butyl mercaptan (4.5 g, 50 mmol) in DMSO (80 mL), Cs_2CO_3 (9.77 g, 30 mmol) was added. The resulting red-brown solution was heated at 45—50 °C for 30 min, cooled to 20 °C, and poured into ice-water. The product was extracted with EtOAc (3×60 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, and the drying agent was filtered off. The filtrate was concentrated *in vacuo*. Compound **9** was isolated by silica gel column chromatography (elution with PE—AcOEt, 4 : 1). Yield 5.08 g (80%). Light yellow crystals, m.p. 72—73 °C. ^{1}H NMR (300 MHz), δ: 10.61 (s, 1 H, CHO); 7.52 (s, 1 H, CH_{arom}); 7.06 (s, 1 H, CH_{arom}); 3.98 (s, 3 H, OMe); 3.97 (s, 3 H, OMe); 1.31 (s, 9 H, SBu^t). ^{13}C NMR (101 MHz), δ: 192.5, 152.9, 150.1, 133.2, 130.4, 121.2, 109.3, 56.3, 56.1, 47.4, 30.9. Found (%): C, 61.34; H, 6.99. $C_{13}H_{18}O_3S$. Calculated (%): C, 61.39; H, 7.13.

Table 1. Crystallographic parameters and refinement statistics for compound **1a**

Parameter	Value
Molecular formula	$C_{10}F_3OSH_5$
Molecular weight	230.20
Crystal system	Monoclinic
Space group	$P2_1/n$
a/Å	4.5647(7)
b/Å	11.3412(17)
c/Å	17.504(2)
β/deg	96.806(4)
V/Å^3	899.8(2)
Z	4
d_{calc}/g cm^{-3}	1.699
μ/mm^{-1}	0.372
F(000)	464
Scan range, θ/deg	2.14—26.04
Number of unique reflactions	1769
R_{int}	0.0423
Number of refined parameters	136
Number of reflections with $I \geqslant 2\sigma(I)$	1487
Completeness of diffraction data (%)	99.4
GOOF	1.096
Convergence of refinement ($R_1(F)$)[a] against the reflections with $I \geqslant 2\sigma(I)$	0.0426
Convergence of refinement against all reflections ($wR_2(F^2)$[b]	0.1172
Residual electron density, ρ_{min}/ρ_{max}, e Å^{-3}	0.475/−0.381

[a] $R_1 = \Sigma||F_o| - |F_c||/\Sigma(F_o)$.
[b] $wR_2 = (\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]^{1/2}$.

X-ray diffraction analysis of compound 1a was carried out on an APEX II CCD diffractometer (λ(Mo-$K\alpha$) = = 0.71073 Å, graphite monochromator, ω scan mode) at 100 K. The structure was solved by a direct method and refined by the full-matrix least square method in an anisotropic approximation for non-hydrogen atoms against F^2_{hkl}. Hydrogen atoms were placed geometrically. The data were processed, decoded, and the structure was refined using APEX2[31] and SHELXL[32] software. The main crystallographic parameters of compound **1a** are summarized in Table 1. The structure was deposited with the Cambridge Crystallographic Data Center (CCDC 2347681).

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Animal Testing and Ethics

No human or animal subjects were used in this research.

Conflict of Interest

The authors declare no competing interests.

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