A Novel Synthesis of Deactivated Benzylic Triflones

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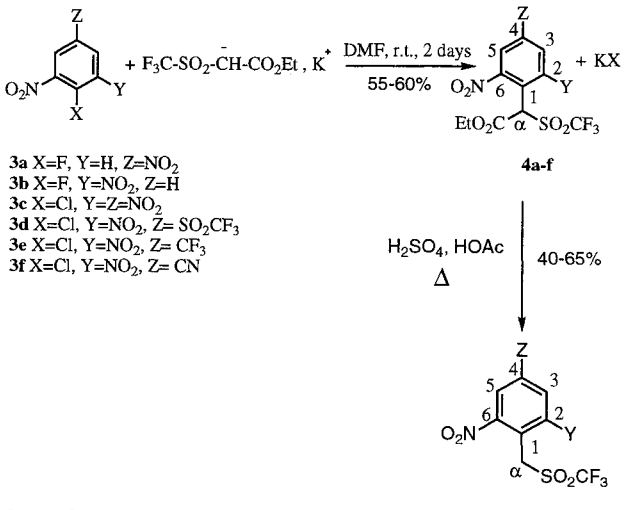
A two-step synthesis of benzylic triflones, based on the reaction of 2,4,6-trisubstituted phenyl halides **3a–f** with the anion of ethyl (trifluoromethanesulfonyl)acetate **1** followed by a decarboxylation reaction, is reported. The structural assignments are supported by spectroscopic data.

The trifluoromethanesulfonyl group (SO_2CF_3) is one of the strongest neutral electron-withdrawing[1] groups known. In particular, it increases to a large extent the acidity of hydrogen atoms in α positions. In fact, the conjugated bases are stabilized and NMR studies give information on the ability of the SO_2CF_3 group to delocalize a negative charge.[2,3] Moreover, trifluoromethanesulfonyl substituted aromatic compounds are of potential interest as intermediates for the preparation of pharmaceuticals, agrochemicals and dyes.[4–8]

We report here the synthesis of new deactivated benzylic triflones starting from ethyl (trifluoromethanesulfonyl)-acetate **(1)** (Method A) or sodium trifluoromethanesulfinate (triflinate) $NaSO_2CF_3$ **(2)** (Method B).

Method A is based on the ability of electron deficient phenyl halides **3a–f** to react readily by nucleophilic aromatic substitution (S_NAr)[9,10] with a weak nucleophilic carbon center like the anion of the ethyl (trifluoromethanesulfonyl)acetate **(1)** (Scheme 1).[1,3]

The phenyl halide **3a–f** was added to a DMF solution of the anion prepared by the addition of one equivalent of potassium *tert*-butoxide to one equivalent of **1**. After two days, the solvent was evaporated under reduced pressure and the ester compound **4** was isolated as a red product and used without further purification. Structures **4a–f** were consistent with most data obtained from ^1H and ^{13}C NMR spectroscopy (Tables 1 and 2). However, these spectra showed special features (see NMR characteristics discussed later).



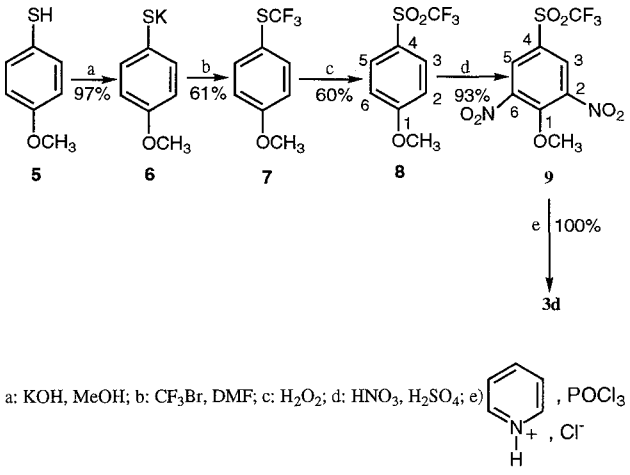
3a X=F, Y=H, Z=NO_2
3b X=F, Y=NO_2, Z=H
3c X=Cl, Y=Z=NO_2
3d X=Cl, Y=NO_2, Z= SO_2CF_3
3e X=Cl, Y=NO_2, Z= CF_3
3f X=Cl, Y=NO_2, Z= CN

Scheme 1

Table 1. Esters **4**

Compound	Yield (%)	mp (°C)
4a	60	204
4b	55	red oil
4c	60	216
4d	58	red oil
4e	56	red oil
4f	55	red oil

The starting halide **3b** was prepared by refluxing a solution of 1-chloro-2,6-dinitrobenzene in THF with KF in the presence of 18-crown-6 ether. Compound **3d** was obtained by a multistep procedure from the corresponding anisole **7**,[11] itself prepared from 4-methoxythiophenol[12] **(5)** (Scheme 2). The potassium 4-methoxythiophenoxide **(6)** reacted with CF_3Br[12] to give **7** and then oxidation of **7** with hydrogen peroxide[13] led to the corresponding sulfone **8**. Nitration of this sulfone provided the anisole **9**. Compound **9** was warmed with anhydrous pyridine hydrochloride; when no evolution of gas was observed, $POCl_3$ was added, and the product **3d** was obtained as pale yellow crystals after an additional reflux.[11]



Scheme 2

The S_NAr process involved in the synthesis of compounds **4** has been supported by a kinetic study;[10] the measured rate constant was faster for the aryl fluoride than for the corresponding aryl iodide. In this case, the rate-determining step is controlled by the electronegativity and the steric hindrance of the halogen atom and not by its polarisability.[9] Formation of the anionic intermediate σ-complex is rate-determining.[9]

Table 2. Spectroscopic Data for Esters **4**

Compound	IR (CH_3CN) ν (cm^{-1})	^1H NMR (CD_3CN/TMS) δ, J (Hz)	^{13}C NMR (CD_3CN/TMS) δ	^{19}F NMR (CD_3CN/$CFCl_3$) δ
4a	2631, 2073, 1843, 1670, 1644, 1601, 1237, 1199	8.39 (d, $J_{3,5}$ = 2.6, 1H, H_3), 8.20 (dd, $J_{5,6}$ = 8.9, $J_{5,3}$ = 2.6, 1H, H_5), 7.67 (d, $J_{6,5}$ = 8.9, 1H, H_6), 3.77 (q, J = 7.1, 2H, OCH_2), 0.97 (t, J = 7.1, 3H, CH_3)	164.26 (CO), 148.11 (C_2), 142.77 (C_1), 139.64 (C_4), 135.36 (C_3), 124.73 (C_5), 121.84 (SO_2CF_3), 119.36 (C_6), 71.19 (C_α), 57.76 (OCH_2), 14.36 (CH_3)	−77.63 (s, SO_2CF_3)
4b	2639, 2078, 1830, 1681, 1639, 1188	7.99 (d, $J_{3,4}$ = $J_{5,4}$ = 8.1, 2H, $H_{3,5}$), 7.54 (t, $J_{4,3}$ = $J_{4,5}$ = 8.1, 1H, H_4), 3.81 (m, 2H, OCH_2), 1.00 (m, 3H, CH_3)	166.86 (CO), 153.53 ($C_{2,6}$), 128.32 ($C_{3,5}$), 126.80 (C_4), 126.16 (C_α), 123.37 (C_1), 122.70 (SO_2CF_3), 59.15 (OCH_2), 14.68 (CH_3)	−76.79 (s, SO_2CF_3)
4c	2644, 2075, 1829, 1683, 1639, 1617, 1241, 1194, [1670, 1600, 1255, 1202, 1174][a]	8.74 (s, 2H, $H_{3,5}$), 4.05 (m, 2H, OCH_2), 1.19 (m, 3H, CH_3)	165.23 (CO), 151.52 ($C_{2,6}$), 144.59 (C_4), 132.99 (C_α), 126.34 (C_1), 122.94 ($C_{3,5}$), 121.93 (SO_2CF_3), 59.74 (OCH_2), 14.52 (CH_3)	−77.91 (s, SO_2CF_3)
4d	No IR data	8.47 (s, 2H, $H_{3,5}$), 3.94 (m, 2H, OCH_2), 1.10 (m, 3H, CH_3)	No ^{13}C NMR data	−72.1 (s, SO_2CF_3) −72.7 (s, SO_2CF_3)
4e	2631, 2074, 1827, 1685, 1253, 1194	8.15 (s, 2H, $H_{3,5}$), 3.85 (m, 2H, OCH_2), 0.98 (m, 3H, CH_3)	166.13 (CO), 152.98 ($C_{2,6}$), 130.89 (C_α), 128.67 (C_4, C_1), 125.5 ($C_{3,5}$), 123.36 ($ArCF_3$), 122.58 (SO_2CF_3), 59.45 (OCH_2), 14.51 (CH_3)	−77.78 (s, SO_2CF_3) −62.18 (s, Ar-CF_3)
4f	2626, 2079, 1832, 1682, 1650, 1617, 1258, 1188	8.26 (s, 2H, $H_{3,5}$), 3.90 (m, 2H, OCH_2), 1.07 (m, 3H, CH_3)	165.79 (CO), 152.50 ($C_{2,6}$), 134.63 (C_α), 129.55 (C_1), 132.00 ($C_{3,5}$), 122.55 (SO_2CF_3), 115.96 (CN), 110.49 (C_4), 59.43 (OCH_2), 14.54 (CH_3)	−77.58 (s, SO_2CF_3)

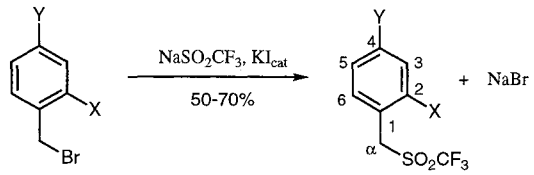
[a] IR measured in KBr.

When the esters **4a–e** were heated in an aqueous mixture of sulfuric and acetic acids, a decarboxylation occurred leading to the deactivated benzylic triflones **10a–e** (Scheme 1, Tables 3 and 4).

However, the triflone **10f** could not be obtained from **4f** by this procedure. Indeed, in these conditions, the cyano group in the para position was also hydrolyzed to a carboxylic acid function. In smooth acid or in basic conditions, the compound **10f** has not yet been prepared.

Another route for the synthesis of these deactivated benzylic triflones was investigated (Method B). The substitution of deactivated benzylic bromides with triflinate ion (in the presence of iodide ion as catalyst) was found to give very poor yields. For example, compound **10a** was isolated in a 10% yield after warming in CH_3CN for one month. In fact, the method described by Hendrickson[1] is not efficient when the aromatic ring is highly deactivated. Nevertheless, this method was used to prepare some intermediates **12a–c** for the synthesis of new benzylic triflones **17a–b**.

Treatment of compounds **11a–c** with one equivalent of sodium triflinate[14] **2** gave the sulfones **12a–c** in fair to good yields (Scheme 3, Tables 3 and 4).



11a X= H, Y=CF_3
11b X= H, Y=SO_2CF_3
11c X=NO_2, Y= H

12a
12b
12c

Scheme 3

Table 3. Compounds **10**, **12** and **17**.

Compound	Yield (%)/Method	mp (°C)	MS (70 ev) m/z
10a	63/A 10/B	98	314 ($M^{+\cdot}$)
10b	40/A	115	268 (M-NO_2)$^+$, 245 (M-CF_3)$^+$, 181 (M-SO_2CF_3)$^+$
10c	65/A	88	358 (M-H)$^+$
10d	50/A	133	377 (M-CF_3)$^+$, 313 (M-SO_2CF_3)$^+$
10e	45/A	85	363 (M-F)$^+$, 313 (M-CF_3)$^+$, 249 (M-SO_2CF_3)$^+$
12a	52/A	95	292 ($M^{+\cdot}$)
12b	50/A	120	356 ($M^{+\cdot}$), 223 (M-SO_2CF_3)$^+$
12c	70/A	66	269 ($M^{+\cdot}$)
17a	58/A	80	318 (M-F)$^+$, 268 (M-CF_3)$^+$
17b	60/A	72	332 (M-CF_3)$^+$, 268 (M-SO_2CF_3)$^+$

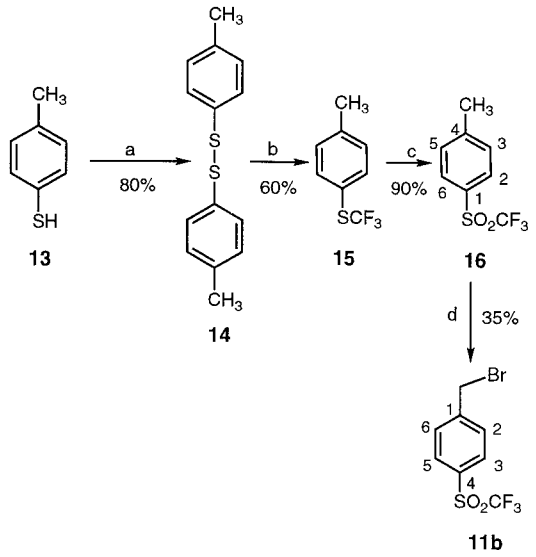
Table 4. Spectroscopic Data of Compounds **10**, **12** and **17**

Compound	IR (CH_3CN) ν (cm^{-1})	^1H NMR (DMSO-d_6/TMS) δ, J (Hz)	^{13}C NMR (DMSO-d_6/TMS) δ	^{19}F NMR (DMSO-d_6/$CFCl_3$), δ
10a	2634, 2072, 1961, 1740, 1612, 1199, 1159, 1130	8.89 (d, $J_{3,5}$ = 2.4, 1 H, H_3), 8.72 (dd, $J_{5,6}$ = 8.5, $J_{5,3}$ = 2.4, 1 H, H_5), 8.08 (d, $J_{5,6}$ = 8.5, 1 H, H_6), 5.87 (s, 2 H, CH_2)	148.79 (C_2), 148.42 (C_4), 136.05 (C_6), 128.39 (C_5), 126.64 (C_1), 121.05 (C_3), 119.12 (SO_2CF_3), 51.99 (C_α)	−78.2 (s, SO_2CF_3)
10b	2628, 2078, 1739, 1617, 1205, 1131	8.55 (d, $J_{3,4}$ = $J_{5,4}$ = 8.2, 2 H, $H_{3,5}$), 8.07 (t, $J_{4,3}$ = $J_{4,5}$ = 8.2, 1 H, H_4), 5.74 (s, 2 H, CH_2)	150.25 ($C_{2,6}$), 132.93 (C_4), 130.59 ($C_{3,5}$), 118.95 (SO_2CF_3), 114.05 (C_1), 47.53 (C_α)	−77.1 (s, SO_2CF_3)
10c	2636, 2075, 1825, 1615, 1200	9.16 (s, 2 H, $H_{3,5}$), 5.85 (s, 2 H, CH_2)	151.37 ($C_{2,6}$), 149.27 (C_4), 126.00 ($C_{3,5}$), 121.03 (C_1), 119.90 (SO_2CF_3), 48.96 (C_α)	−76.7 (s, SO_2CF_3)
10d	2639, 2078, 1830, 1620, 1204	9.10 (s, 2 H, $H_{3,5}$), 5.84 (s, 2 H, CH_2)	151.37 ($C_{2,6}$), 133.32 (C_4), 131.68 ($C_{3,5}$), 123.17 (C_1), 119.04 ($ArSO_2CF_3$), 119.04 ($CH_2SO_2CF_3$), 48.13 (C_α)	−72.1 (s, SO_2CF_3) −72.7 (s, SO_2CF_3)
10e	2637, 2067, 1829, 1639, 1205	8.94 (s, 2 H, $H_{3,5}$), 5.79 (s, 2 H, CH_2)	150.60 ($C_{2,6}$), 132.00 (C_4), 127.53 ($C_{3,5}$), 118.70 (C_1), 121.50 ($ArCF_3$), 118.80 ($CH_2SO_2CF_3$), 47.70 (C_α)	−76.8 (s, SO_2CF_3) −61.4 (s, $ArCF_3$)
12a	2628, 2078, 1946, 1829, 1623, 1204	7.85 (d, $J_{3,5}$ = $J_{2,6}$ = 8.2, 2 H, $H_{3,5}$), 7.72 (d, $J_{2,6}$ = $J_{3,5}$ = 8.2, 2 H, $H_{2,6}$), 5.44 (s, 2 H, CH_2)	159.52 (C_1), 132.37 ($C_{2,6}$), 130.02 (C_4), 125.67 ($C_{3,5}$), 123.96 ($ArCF_3$), 119.36 (SO_2CF_3), 54.02 (C_α)	−57.0 (s, $ArCF_3$) −72.0 (s, SO_2CF_3)
12b	2631, 2073, 1940, 1830, 1610, 1204	8.22 (d, $J_{3,5}$ = $J_{2,6}$ = 8.4, 2 H, $H_{3,5}$), 7.90 (d, $J_{2,6}$ = $J_{3,5}$ = 8.4, 2 H, $H_{2,6}$), 5.56 (s, 2 H, CH_2)	135.20 (C_1), 133.57 ($C_{2,6}$), 131.16 ($C_{3,5}$), 130.48 (C_4), 119.26, 119.16 (SO_2CF_3), 53.82 (C_α)	−71.9 (s, SO_2CF_3) −74.0 (s, SO_2CF_3)
12c	2631, 2074, 1828, 1614, 1202, 1133	8.17 (dd, $J_{3,4}$ = 8.5, 1 H, H_3), 7.88 (td, $J_{5,6}$ = 7.5, $J_{5,3}$ = 1.65, 1 H, H_5), 7.80 (m, 1 H, H_6), 7.77 (m, 1 H, H_4), 5.63 (s, 2 H, CH_2)	148.87 (C_2), 134.69 (C_6), 134.30 (C_5), 131.54 (C_4), 125.90 (C_3), 119.95 (C_1), 119.27 ($CH_2SO_2CF_3$), 52.41 (C_α)	−73.1 (s, SO_2CF_3)
17a	2637, 2062, 1967, 1625, 1199	8.54 (d, $J_{3,5}$ = 1.4, 1 H, H_3), 8.31 (dd, $J_{5,6}$ = 8.1, $J_{5,3}$ = 1.4, 1 H, H_5), 8.06 (d, $J_{6,5}$ = 8.1, 1 H, H_6), 5.80 (s, 2 H, CH_2)	149.16 (C_2), 135.98 (C_6), 131.54 (C_4), 130.86 (C_5), 125.73 (C_1), 123.05 (C_3), 122.60 ($ArCF_3$), 119.13 ($CH_2SO_2CF_3$), 51.97 (C_α)	−57.6 (s, $ArCF_3$) −73.1 (s, SO_2CF_3)
17b	2634, 2078, 1615, 1215, 1157, 1125	8.77 (s, 1 H, H_3), 8.70 (d, $J_{5,6}$ = 7.9, 1 H, H_5), 8.26 (d, $J_{5,6}$ = 8.1, 1 H, H_6), 5.80 (s, 2 H, CH_2)	149.53 (C_2), 137.06 (C_6), 135.46 (C_5), 132.16 (C_4), 129.72 (C_1), 127.79 (C_3), 119.06 ($ArSO_2CF_3$, $CH_2SO_2CF_3$), 52.03 (C_α)	−73.0 (s, SO_2CF_3) −73.3 (s, SO_2CF_3)

The starting benzylic bromide **11b** was obtained from the 4-methylthiophenol **13** (Scheme 4). This thiophenol was oxidized to the disulfide **14** by hydrogen peroxide.[15] A further alkylation of **14** by CF_3Br in the presence of sodium hydroxymethanesulfinate (Rongalite)[15] provided compound **15** in a 60% yield. Oxidation of **15** with hydrogen peroxide led to compound **16**. A benzylic bromination of **16** was performed with *N*-bromosuccinimide (NBS) under irradiation with a 250W halogen lamp at reflux in a CCl_4 medium under an argon atmosphere. The mixture of mono and dibromo derivatives was separated by chromatography to give **11b** in a 35% yield.

Then, the triflones **17a–b** were obtained from **12a** and **12b**, respectively, in a 60% yield by nitration in a mixture of sulfuric and nitric acids (Scheme 5, Tables 3 and 4).

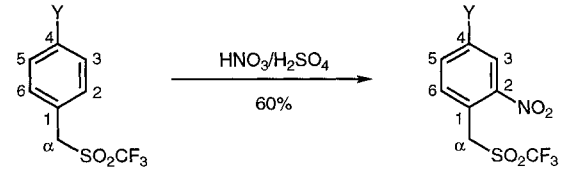
The NMR spectra of compounds **4b–f** show some specific features. On the one hand, the ^1H NMR spectrum was devoid of the signal corresponding to the H_α proton and showed two broad signals for the ethyl group instead of the expected triplet and quadruplet typical of an A_2X_3 system. On the other hand, the ^{13}C NMR spectrum exhibited a signal at low field (δ = 130) for the C_α carbon characteristic of an unsaturated carbon. This observation was not consistent with a classical sp^3 carbon.



a: H_2O_2; b: $CF_3Br_{(g)}$, DMF, Rongalite; c: H_2O_2, H^+; d: NBS, CCl_4, hv

Scheme 4

To understand the broadening of the signals of the ethyl group on the ^1H NMR spectrum, a low temperature NMR experiment was conducted for compound **4f**.



12a Y=CF_3
12b Y=SO_2CF_3

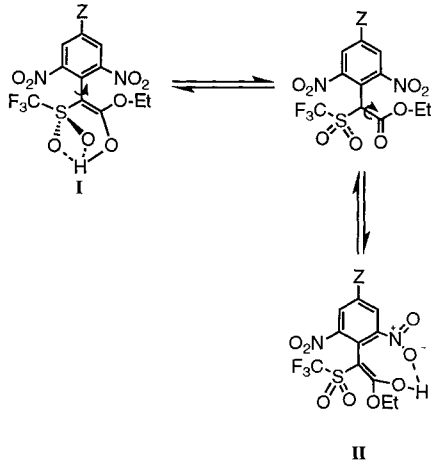
17a Y=CF_3
17b Y=SO_2CF_3

Scheme 5

When the temperature of the probe was decreased (from 293K to 223K in CD_3CN), the broad A_2X_3 system was gradually split into two ABX_3 systems in an 80/20 ratio and similarly the singlet of the aromatic protons ($H_{3,5}$) split into two AB systems in the same proportions. A similar result was obtained in ^{19}F NMR, the singlet at $\delta = -77.58$ typical of a SO_2CF_3 group was divided into two other singlets. At 223K, the chemical shifts were $\delta = -77.12$ and -77.68. However, when the temperature of the probe was increased (from 293K to 340K in CD_3CN), sharp signals typical for an A_2X_3 system were again observed ($^3J_{OCH_2-CH_3} = 9.6$ Hz) in the ^1H NMR spectrum of **4f**.

The analysis of all these spectroscopic results is consistent with the presence of two enol forms **I** and **II** (Scheme 6) stabilized by an intramolecular hydrogen bond. These enol structures account for the chemical shift ($\delta = 130$) of the C_α carbon typical of a sp^2 hybridization and with IR data (ν (CO), 1670 cm^{-1} in KBr or 1680 cm^{-1} in CH_3CN). This value was lower than expected for the carbonyl of an ester group.

This temperature-dependent phenomenon may be explained by an equilibrium between the two forms **I** and **II** because of an energy barrier to rotation around the C_α–C–O bond (Scheme 6).



4b Z=H, **4c** Z=NO_2, **4d** Z= SO_2CF_3,
4e Z= CF_3, **4f** Z= CN

Scheme 6

In the case of compounds **10a–e**, **12a–c**, and **17a–b** spectroscopic data were consistent with the structure of classical benzylic triflones. Both the ^1H NMR and ^{13}C NMR spectra exhibited, besides aromatic signals, other signals corresponding to the methylene group (H_α, from $\delta = 5.74$ to 5.87 and C_α, from $\delta = 47.53$ to 51.99). The ^{19}F NMR spectra indicated the presence of the trifluoromethanesulfonyl group (SO_2CF_3, from $\delta = -72.6$ to -78.2).

In conclusion, simple benzylic triflones are shown to be readily available by alkylation of a triflinate anion[1] (Method B). Functionalization of the aromatic ring can occur but did not allow the preparation of highly deactivated benzylic triflones. However, these compounds were accessible by the use of ethyl (trifluoromethanesulfonyl)acetate **(1)** (Method A). This building block was itself prepared easily from triflinate anion.[1,3] Method A appears to complement Method B and to be of much broader scope.

Melting points were determinated on a C. Reichert microscope (hot stage type) and were uncorrected. ^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a BRUCKER AC300 (300 MHz) instrument with tetramethylsilane (TMS) as internal standard for ^1H NMR, ^{13}C NMR and with $CFCl_3$ for ^{19}F NMR operating, respectively, at 300 MHz, 75.5 MHz and 282.4 MHz. Chemical shifts are reported in parts per million (ppm) and coupling constants J in Hertz (Hz). The peaks are characterized by s (singlet), d (doublet), t (triplet). Mass spectra (EI, 70 eV) were obtained using a NERMAG R10-10C apparatus. IR spectra were recorded on a NICOLET 400D spectrometer. Elemental analyses were determined by the Microanalytical laboratory of the University of Rouen and satisfactory analyses were obtained (C ± 0.25, H ± 0.25 and N ± 0.30%). Column chromatography was performed with Merck silica gel (70–230 mesh) using various ratios of EtOAc : pentane or Et_2O : pentane. TLC was carried out on Merck 60F-254 precoated silica gel plates (0.25 mm). All reagents were obtained from various commercial sources and used as received. Ethyl (trifluoromethanesulfonyl)acetate[3] **(1)**, sodium trifluoromethanesulfinate $NaSO_2CF_3$[14] **(2)**, 4-trifluoromethanethioanisole[12] **(7)** and 4-trifluoromethanethiotoluene[15] **(15)** were prepared according to standard procedures. When needed, reactions were carried out under Ar. Tetrahydrofuran (THF) and Et_2O were distilled from Na/benzophenone under Ar. CH_3CN was distilled from CaH_2 under Ar.

General Procedures:

Method A: A mixture of ethyl (trifluoromethanesulfonyl) acetate **(1)** (4.5 mmol) and *t*-BuOK (4.5 mmol) in freshly distilled DMF was stirred under Ar. After 10 min, the phenyl halide **4** (4.5 mmol) was added and the red solution was stirred for 48 h more at r.t. The solvent was removed under reduced pressure and the product **4** was isolated as a red product without further purification. Decarboxylation occured when a mixture of 98% H_2SO_4 (5 mL) and HOAc (10 mL) in H_2O (10 mL), was added to the previous residue. The mixture was stirred at 100 °C for 8 h, cooled and poured into an ice and water mixture. A pale yellow solid was filtered. Compounds **10** were purified by column chromatography followed by recrystallization from EtOAc/pentane.

Method B: A solution of substituted BnBr (20 mmol) **11** and sodium triflinate (3.6 g, 21 mmol) **(2)** in CH_3CN (50 mL) was heated in the presence of iodide ion (2 mmol) as catalyst. Monitoring the disappearance of the starting bromide by TLC, the mixture was cooled, the salts were filtered and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography using a linear EtOAc gradient in hexane to give **12** as a solid. An analytical sample was obtained by recrystallization from EtOAc/pentane.

Halide 3b:
A mixture of 1-chloro-2,6-dinitrobenzene (5 g, 24.6 mmol), KF (2 g, 49.2 mmol) and 18-crown-6 (6.5 g, 24.6 mmol) in freshly distilled THF (50 mL) was refluxed for 36 h. After cooling, the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography using a mixture of Et_2O/pentane (25%) as eluent to give compound **3b** in an 81% yield (3.8 g); mp = 51 °C.

^{19}F NMR (CD_3CN): $\delta = -126.78$ (td, 1 F, $J_{FH3,5} = 6.5$; $J_{FH4} = 1.41$).

^{1}H NMR (CD_3CN): $\delta = 8.38$ (dd, 2 H, $J_{H3,5H4} = 8.5$; $J_{H3,5F} = 6.6$; $H_{3,5}$); 7.57 (dt, 1 H, $J_{H4H3,5} = 8.5$; $J_{H4F} = 1.4$; H_4).

Halide 3d:
Compound **7** (12.25 g, 59 mmol) was heated with 35% H_2O_2 (50.5 mL, 0.59 mol) in glacial HOAc (100 mL) to 80 °C. After a few minutes, the mixture was kept at 50 °C for 48 h. Then, the yellow solution was poured into H_2O (150 mL), extracted with Et_2O (3 × 50 mL), washed with a 10% $NaHCO_3$ solution and dried ($MgSO_4$). After evaporation of the solvent under reduced pressure, the (4-methoxyphenyl)trifluoromethanesulfone **(8)** was obtained in a 60% yield (8.5 g, 35 mmol) as a yellow oil.

^{19}F NMR (DMSO-d_6): $\delta = -74.5$ (s, SO_2CF_3).

^{1}H NMR (DMSO-d_6): $\delta = 8.04$ (d, 2 H, $J = 8.9$, $H_{3,5}$), 7.34 (d, 2 H, $J = 8.9$, $H_{2,6}$), 3.95 (3 H, s, OCH_3).

The sulfone **8** (8.3 g, 34.5 mmol) was warmed at 100 °C for an hour with 98% H_2SO_4 (4.5 mL, 2.3 equiv). After cooling, 100% HNO_3 (14.3 mL) was added slowly by cooling with an ice-water bath. The red solution was then warmed at 100 °C for 8 h; after cooling, the mixture was poured into water and a yellow solid was formed. After filtration and drying, the 2,6-dinitro-4-trifluoromethanesulfonylanisole **(9)** was obtained as a pale yellow powder in a 93% yield (10.6 g, 32 mmol); mp = 56 °C.

^{19}F NMR (DMSO-d_6): $\delta = -72.8$ (s, SO_2CF_3).

^{1}H NMR (DMSO-d_6): $\delta = 8.98$ (s, 2 H, $H_{2,6}$), 4.09 (s, 3 H, OCH_3).

Compound **9** (10.6 g, 32 mmol) was heated with anhyd pyridine hydrochloride (26.5 g, 0.23 mol) on an oil bath to 115–120 °C until gaseous products were no longer released. Then the mixture was cooled to 50 °C and $POCl_3$ (30 mL) was added. The solution was refluxed for 30 min, cooled and carefully poured into H_2O. The precipated product was filtered and dried to give 10.7 g (100%) of compound **3d**; mp = 94 °C (Lit.[8]: 97–98 °C).

^{19}F NMR (DMSO-d_6): $\delta = -74.5$ (s, SO_2CF_3).

^{1}H NMR (DMSO-d_6): $\delta = 8.20$ (s, 2 H, $H_{3,5}$).

Halide 11b:
Compound **15** (4.9 g, 21.6 mmol) was heated with 35% H_2O_2 (20.8 mL) in glacial HOAc (33 mL) to 80 °C. After a few minutes, the mixture was kept at 50 °C for 48 h. Then, the solution was poured into H_2O (100 mL), extracted with Et_2O (3 × 50 mL), washed with a 10% $NaHCO_3$ solution and dried ($MgSO_4$). Evaporation of the solvent under reduced pressure gave the 4-tolyltrifluoromethanesulfone **(16)** in a 90% yield (4.9 g, 20 mmol) as an oil.

^{19}F NMR ($CDCl_3$): $\delta = -79.1$ (s, SO_2CF_3).

^{1}H NMR ($CDCl_3$): $\delta = 7.85$ (d, 2 H, $J = 8.3$, $H_{2,6}$), 7.39 (d, 2 H, $J = 8.3$, $H_{3,5}$), 2.44 (s, 3 H, CH_3).

A mixture of **16** (2 g, 7.8 mmol) and NBS (1.39 g, 7.8 mmol), freshly recrystallized in hot H_2O, was refluxed for 10 h under irradiation (250 W halogen lamp) in CCl_4 (20 mL). The mixture rapidly became orange and then progressively turned white. After cooling, the solid was filtered and the solvent was removed under reduced pressure. The yellow residue was chromatographed through a short column to separate the starting material (pentane as eluent), the dibromo derivative (elution with 1–1.5% of Et_2O in pentane) and the 4-trifluoromethanesulfonylbenzyl bromide **(11b)** (elution with 2–2.5% of Et_2O in pentane) as a white solid in a 35% yield; mp = 46 °C.

^{19}F NMR ($CDCl_3$): $\delta = -78.65$ (s, SO_2CF_3).

^{1}H NMR ($CDCl_3$): $\delta = 8.07$ (d, 2 H, $J = 8.3$, $H_{2,6}$), 7.70 (d, 2 H, $J = 8.3$, $H_{3,5}$), 4.54 (s, 2 H, CH_2).

Nitration of Compounds 12:
A solution of the sulfone **12** (3.5 mmol) in 98% H_2SO_4 (40 mmol, 2.25 mL) was cooled at 0 °C and then 100% nitric acid (78 mmol, 3.2 mL) was added. The mixture was allowed to warm at 100 °C for 16 h and after cooling, the mixture was poured into an ice and water mixture (50 mL). The yellow solid was filtered and an analytical sample was obtained by recrystallization from EtOAc/pentane in a 60% yield.

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