Supporting Information

Electrophilic aromatic trifluoromethylthiolation with the second generation of trifluoromethanesulfenamide

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General Information

Dry ACN and dry DCE were purchased from Sigma Aldrich. Commercial reagents were used as supplied. NMR spectra were recorded on a Bruker AV 400 spectrometer at 400 MHz ($^1$H NMR), 100 MHz ($^{13}$C NMR), 376 MHZ ($^{19}$F NMR). All coupling constants were reported in Hz. Melting points were determined using a Köfler bench apparatus (calibration substances were specified).

General Procedure A:

A 10mL sealed tube equipped with a magnetic stirrer was charged with arene (0.50 mmol, 1.0 equiv.) and TsNMeSCF$_3$ (1a) or TsNMeSCF$_2$CF$_3$ (1b) (1.2eq) in dry DCE. Reaction was stirred at room temperature 1min. and triflic acid was added slowly (0.2 equiv) and the reaction was stirred at 80°C for 18h. Conversion was checked by $^{19}$F NMR with PhOCF$_3$ as internal standard. After completion, the reaction was warmed at room temperature and the solvent was removed under vacuum and the residue was purified by flash chromatography (100% cyclohexane to 95/5 cyclohexane/EtOAc – 90/10 cyclohexane/EtOAc for bisphenol) to give the desired product.

General Procedure B:

A 10mL sealed tube equipped with a magnetic stirrer was charged with arene (0.50 mmol, 1.0 equiv.) and TsNMeSCF$_3$ (1a) or TsNMeSCF$_2$CF$_3$ (1b) (1.2eq) in dry DCE. Reaction was stirred at room temperature 1min. and triflic acid was added slowly (1.0 equiv) and the reaction was stirred at 80°C for 18h. Conversion was checked by $^{19}$F NMR with PhOCF$_3$ as internal standard. After completion, the reaction was warmed at room temperature and DCM (5 mL) was added and the organic phase was washed three times with distilled water and with NaCl saured solution. Organic phase was dried over MgSO$_4$, filtered and concentrated. The residue was purified by flash chromatography (100% cyclohexane to 95/5 cyclohexane/EtOAc) to give the desired product.

General Procedure C:

A 10mL sealed tube equipped with a magnetic stirrer was charged with arene (0.50 mmol, 1.0 equiv.) and TsNMeSCF$_3$ (1a) (1.2eq) in dry ACN. Reaction was stirred at room temperature 1min. and TMSCl was added slowly (0.2 equiv or 1.0 equiv.) and the reaction was stirred at 80°C for 18h. Conversion was checked by $^{19}$F NMR with PhOCF$_3$ as internal standard. After completion, the reaction was warmed at room temperature and the solvent was removed under vacuum and the residue was purified by flash chromatography (100% cyclohexane to 95/5 cyclohexane/EtOAc) to give the desired product.

Synthesis of 2,4-dimethoxy-1-[(trifluoromethyl)sulfanyl]benzene (3a)

![O
\(\text{SCF}_3\)]

Procedure : A

$^1$H NMR: $\delta = 7.53$ (m, 1H), 6.54-6.50 (massif, 2H), 3.88 (s, 3H), 3.83 (s, 3H).
$^{19}$F NMR: $\delta = -44.13$ (s, 3F). (in accordance with literature [1])
Synthesis of 4-[(trifluoromethyl)sulfanyl]benzene-1,3-diol (3b)

![Chemical Structure]

Procedure: A
Brown solid. Melting point: under 50°C.
$^1$H NMR: $\delta = 7.41$ (d, $^3$J(H,H) = 8.6 Hz, 1H), 6.56 (d, $^3$J(H,H) = 2.7 Hz, 1H), 6.85 (dd, $^3$J(H,H) = 8.6 Hz, 2.7 Hz, 1H), 6.10-4.50 (br, 2H).
$^{19}$F NMR: $\delta = -44.52$ (s, 3F).
$^{13}$C NMR: $\delta = 161.1, 159.5, 139.6, 128.8$ (q, $^1$J(C,F) = 315 Hz), 109.9, 103.0, 99.62 (q, $^3$J(C,F) = 1.7 Hz).
Elemental analysis calcd (%) for C$_7$H$_5$F$_3$O$_2$S: C 40.00, H 2.40, S 15.26. Found: C 40.12, H 2.29, S 15.47.

Synthesis of 1-methoxy-4-[(trifluoromethyl)sulfanyl]benzene (3c)

![Chemical Structure]

Procedure: A
$^1$H NMR: $\delta = 7.58$ (d, $^3$J(H,H) = 8.7 Hz, 2H), 6.93 (d, $^3$J(H,H) = 8.7 Hz, 2H), 3.84 (s, 3H).
$^{19}$F NMR: $\delta = -44.41$ (s, 3F). (in accordance with literature [2])

Synthesis of 4-[(trifluoromethyl)sulfanyl]phenol (3d)

![Chemical Structure]

Procedure: A
$^1$H NMR: $\delta = 7.47$ (d, $^3$J(H,H) = 8.4 Hz, 2H), 6.88 (d, $^3$J(H,H) = 8.7 Hz, 2H), 5.80 (br, 1H).
$^{19}$F NMR: $\delta = -44.48$ (s, 3F). (in accordance with literature [3])
Synthesis of 4-methoxy-2-[(trifluoromethyl)sulfanyl]phenol (3e)

Procedure : A

1H NMR: $\delta = 7.08$ (m, 1H), 7.01 (m, 2H), 6.02 (br, 1H), 3.78 (s, 3H).

13C NMR: $\delta = 153.7$, 152.6, 129.0 (q, $^3J(C,F) = 311$ Hz), 121.6 (2C), 117.1, 108.3 (q, $^3J(C,F)=1.5$ Hz), 56.2.

19F NMR: $\delta = -43.22$ (s, 3F). (in accordance with literature [3])

Synthesis of 2-[(trifluoromethyl)sulfanyl]naphthalen-1-ol (3f)

Procedure : A

Brown solid. Melting point: 75°C (calibration substance: Benzil at 95°C)

1H NMR: $\delta = 8.51$ (d, $^3J(H,H) = 8.6$ Hz, 1H), 8.27 (d, $^3J(H,H) = 8.5$ Hz, 1H), 7.82 (d, $^3J(H,H) = 7.9$ Hz, 1H), 7.68 (ddd, $^3J(H,H) = 8.3$, 6.8, 1.5Hz, 1H), 7.58 (ddd, $^3J(H,H) = 8.5$, 6.6, 1.5Hz, 1H), 6.83 (d, $^3J(H,H) = 7.9$ Hz, 1H), 1.9 Hz, 1H), 6.83 (d, $^3J(H,H) = 7.9$ Hz, 1H),

19F NMR: $\delta = -43.72$ (s, 3F).

13C NMR: $\delta = 155.0$, 138.7, 136.7, 129.5 (q, $^3J(C,F) = 317$ Hz), 128.3, 126.0, 125.9, 125.1, 122.3, 112.6 (q, $^3J(C,F)=1.9$ Hz), 108.5.

Elemental analysis calcd (%) for C_{11}H_{7}F_{3}OS: C 54.10, H 2.89, S 13.13. Found: C 54.21, H 3.17, S 13.29.

Synthesis of 1,3,5-trimethyl-2-[(trifluoromethyl)sulfanyl]benzene (3g)

Procedure : A

1H NMR: $\delta = 7.00$ (s, 2H), 2.52 (s, 3H), 2.29 (s, 3H).

19F NMR: $\delta = -42.46$ (s, 3F). (in accordance with literature [4])

Synthesis of 4-methyl-[(trifluoromethyl)sulfanyl]benzene (3h)

19F NMR: $\delta = -43.70$ (s, 3F). (in accordance with literature [5])
Synthesis of 3-bromo-4-[(trifluoromethyl)sulfanyl]phenol (3i)

Procedure : B

\[ \delta = 7.58 \ (d, \ J(H,H) = 8.2 \ Hz, \ 1H), \ 7.24 \ (d, \ J(H,H) = 2.9 \ Hz, \ 1H), \ 6.85 \ (dd, \ J(H,H) = 8.4 \ Hz, \ 2.7 \ Hz, \ 1H), \ 5.92 \ (br, \ 1H). \]

\[ \delta = -43.77 \ (s, \ 3F). \] (in accordance with literature [3])

Synthesis of 4-bromo-2-[(trifluoromethyl)sulfanyl]phenol (3j)

Procedure : B

\[ \delta = 7.69 \ (d, \ J(H,H) = 2.5 \ Hz, \ 1H), \ 7.52 \ (dd, \ J(H,H) = 8.9, \ 2.5 \ Hz, \ 1H), \ 6.97 \ (d, \ J(H,H) = 8.9 \ Hz, \ 1H). \]

\[ \delta = -43.00 \ (s, \ 3F). \]

Synthesis of 2-iodo-4-methoxy-1-[(trifluoromethyl)sulfanyl]benzene (3k)

Procedure : B

Yellow oil.

\[ \delta = 7.70 \ (d, \ J(H,H) = 8.7 \ Hz, \ 1H), \ 7.51 \ (d, \ J(H,H) = 2.8 \ Hz, \ 1H), \ 6.93 \ (dd, \ J(H,H) = 8.7, \ 2.8 \ Hz, \ 1H), \ 3.82 \ (s, \ 3H). \]

\[ \delta = -43.85 \ (s, \ 3F). \]

Elemental analysis calcd (%) for C₈H₆F₃IOS: C 28.76, H 1.81, S 9.60. Found: C 28.57, H 1.74, S 9.5.
Synthesis of 2-nitro-4-[(trifluoromethyl)sulfanyl]benzene-1,3-diol (3l)

Procedure: B
$^1$H NMR: $\delta = 11.39$ (br, 1H), 10.90 (br, 1H), 7.72 (d, $^3J(H,H) = 8.9$ Hz, 1H), 6.63 (d, $^3J(H,H) = 8.9$ Hz, 1H).
$^{13}$C NMR: $\delta = 159.3$, 158.7, 148.9, 130.8 (q, $^1J(C,F) = 307$ Hz), 124.5, 110.6, 103.5 (q, $^3J(C,F) = 1.9$ Hz).
$^{19}$F NMR: $\delta = -43.46$ (s, 3F).

Synthesis of 3-bromo-2-[(trifluoromethyl)sulfanyl]-1-benzothiophene (3m)

Procedure: B
$^1$H NMR: $\delta = 7.90-7.87$ (m, 1H), 7.81-7.78 (m, 1H), 7.52-7.48 (m, 1H).
$^{19}$F NMR: $\delta = -43.77$ (s, 3F). (in accordance with literature [5])

Synthesis of 3-[(trifluoromethyl)sulfanyl]-1H-indole (3n)

Procedure: C
$^1$H NMR: $\delta = 8.56$ (br, 1H), 7.80 (m, 1H), 7.53 (d, $^3J(H,H) = 2.6$ Hz, 1H), 7.42 (m, 1H), 7.32-7.24 (massif, 2H).
$^{19}$F NMR: $\delta = -45.36$ (s, 3F). (in accordance with literature [1])

Synthesis of 3-methyl-2-[(trifluoromethyl)sulfanyl]-1H-indole (3o)

Procedure: C
$^1$H NMR: $\delta = 8.20$ (br, 1H), 7.70 (m, 1H), 7.44-7.37 (massif, 2H), 7.26 (m, 1H), 2.54 (s, 3H).
$^{19}$F NMR: $\delta = -43.65$ (s, 3F). (in accordance with literature [1])
Synthesis of N,N-dimethyl-4-[(trifluoromethyl)sulfanyl]aniline (3p)

![Chemical structure](image)

Procedure : C

$^1$H NMR: $\delta = 7.46$ (d, $^{3}J(H,H) = 8.6$ Hz, 2H), 6.67 (d, $^{3}J(H,H) = 8.6$ Hz, 2H), 3.01 (s, 3H).

$^{19}$F NMR: $\delta = -42.65$ (s, 3F). (in accordance with literature [3])

Synthesis of 2,4-dimethoxy-1-[(pentafluoroethyl)sulfanyl]benzene (4a)

![Chemical structure](image)

Procedure : A

$^1$H NMR: $\delta = 7.51$ (d, $^{3}J(H,H) = 8.5$ Hz, 1H), 6.52-6.50 (massif, 2H), 3.87 (s, 3H), 3.83 (s, 3H).

$^{19}$F NMR: $\delta = -82.94$ (t, $^{3}J(F,F) = 3.4$ Hz, 3F), -93.06 (q, $^{3}J(F,F) = 3.5$ Hz, 2F).

$^{13}$C{ $^{19}$F} NMR: $\delta = 164.3$, 162.7, 141.0, 120.0 (CF2), 118.9 (CF3), 105.7, 101.7 (t, $^{3}J(C,F)= 2$ Hz), 99.3, 56.1, 55.62.

Elemental analysis calcd (%) for C$_{10}$H$_9$F$_5$O$_2$S: C 41.67, H 3.15, S 11.12. Found: C 41.79, H 2.91, S 11.4.

Synthesis of 4-[(pentafluoroethyl)sulfanyl]phenol (4d)

![Chemical structure](image)

Procedure : A

$^1$H NMR: $\delta = 7.51$ (m, 2H), 6.88 (m, 2H), 5.85 (br, 1H).

$^{19}$F NMR: $\delta = -82.94$ (t, $^{3}J(F,F) = 3.4$ Hz, 3F), -93.06 (q, $^{3}J(F,F) = 3.5$ Hz, 2F).

$^{13}$C NMR: $\delta = 158.5$, 139.4, 116.7, 120.1 (tq, $^{1}J(C,F) = 248$ Hz, $^{2}J(C,F) = 43$ Hz, CF2), 118.9 (qt, $^{1}J(C,F) = 291$ Hz, $^{2}J(C,F) = 36$ Hz, CF3), 113.3 (t, $^{3}J(C,F)= 2$ Hz).

Synthesis of N,4-dimethyl-N-[(pentafluoroethyl)sulfanyl]benzene-1-sulfonamide (1b)

![Chemical structure](image)

A flame-dried vessel was successively charged, under nitrogen, with diisopropylethylamine (1.0 equiv.) and anhydrous dichloromethane. The resulting mixture was cooled to -20°C before addition of DAST (1.1 equiv.) followed by the addition of TMSCF2CF$_3$ (1.0 equiv.)
in 20 min interval. After 2 hours under stirring at -20°C and a solution of TsNH2 (1.5 equiv.) (in dry EtOAc 50ml) was added dropwise at -20°C and the reaction was stirred at 25°C overnight. The reaction medium was washed with distilled water twice. The organic phase was dried over Na2SO4 and evaporated in vacuo. The crude residue was purified by chromatography over silica (Cyclohexane/EtOAC: 90/10 to 80/20) to afford the corresponding N,N-diethyl-1,1,2,2,2-pentafluoro-N-(4-methylbenzenesulfonyl)ethene-1-sulfinimidamide (71% yield). This last compound was dissolved in dry DCM and sulfuric acid (3.5 equiv.) was added dropwise and the mixture was refluxed overnight. After total completion, the reaction medium was washed with distilled water four times. The organic phase was dried over Na2SO4 and evaporated in vacuo. The crude was titurated with cyclohexane. The beige solid was filtered and dried over pressure to obtain the expected 4-methyl-N-[(pentafluoroethyl)sulfanyl]benzene-1-sulfonamide (89% yield). A flame-dried flask was charged with the previous sulfonamide in dry DCM under nitrogen and DIPEA (1.1 equiv.) was added at 0°C. MeOTf (1.2 equiv.) was added slowly and the reaction was stirred at 0°C for 30 min. The organic phase was washed with HCl 0.5M and NaCl aqueous saturated solution. Organic layer was dried over MgSO4, concentrated and the crude product was purified by flash chromatography (Cylohexane/EtOAc : 9/1) to give the N,4-dimethyl-N-[(pentafluoroethyl)sulfanyl]benzene-1-sulfonamide (1b, 95% yield).

Pale yellow liquid.

1H NMR: δ = 7.77 (d, 3J(H,H) = 8.5 Hz, 1H), 7.35 (d, 3J(H,H) = 8.5 Hz, 1H), 3.28 (s, 3H), 2.45 (s, 3H).

19F NMR: δ = -82.62 (t, 3J(F,F) = 3.0 Hz, 3F), -99.71 (s, 2F).

13C{19F} NMR: δ = 145.2, 134.1, 130.1, 127.91, 119.5 (CF2), 118.3 (CF3), 44.0, 21.6. 

Elemental analysis calcd (%) for C10H10F5NO2S2: C 35.82, H 3.01, N 4.18, S 19.12. Found: C 35.88, H 3.19, N 4.45, S 19.05.

Reference: