Supporting Information

Difluoromethylation of *N*-arylsulfonyl hydrazones with difluorocarbene leading to difluoromethyl aryl sulfones

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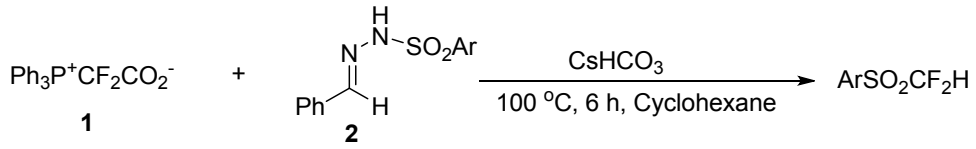
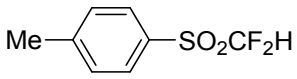
1. General information

Solvents and reagents were purchased from commercial sources and used as received unless otherwise noted. ^{1}H, ^{13}C and ^{19}F NMR spectra were detected on a 500 MHz, 400 MHz or 300 MHz NMR spectrometer. Data for ^{1}H NMR, ^{13}C NMR and ^{19}F NMR were recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, coupling constant (s) in Hz). Mass spectra were obtained on a GC-MS. High resolution mass data were recorded on a high resolution mass spectrometer in the EI or ESI mode.

2. General procedure for Difluoromethylation.



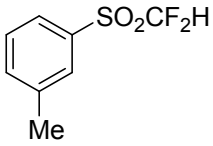
A dried Sealed tube was charged with **2** (0.1 mmol), $Ph_3P^+CF_2CO_2^-$ (71.2 mg, 0.3 mmol)，$CsHCO_3$ (155 mg) and cyclohexane (2 mL) under N_2. The resulting mixture was stirred at 100 °C for 6h. After being cooled to room temperature, the mixture was subjected to flash column chromatography to afford the pure product.



2a

1-((difluoromethyl)sulfonyl)-4-methylbenzene (2a)[1]

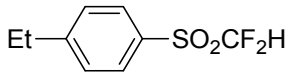
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.1 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 6.15 (t, *J* = 53.5 Hz, 1H), 2.48 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.78 (d, *J* = 53.5 Hz, 2F).



2b

1-((difluoromethyl)sulfonyl)-3-methylbenzene (2b)[1]

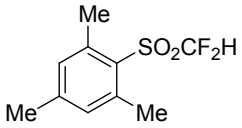
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.76 (m, 2H), 7.58 (d, *J* = 7.7 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 6.16 (t, *J* = 53.4 Hz, 1H), 2.47 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.75 (d, *J* = 53.4 Hz, 2F).



2c

1-((difluoromethyl)sulfonyl)-4-ethylbenzene (2c)

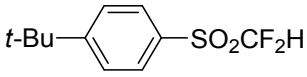
Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 2H), 6.15 (t, *J* = 53.5 Hz, 1H), 2.77 (q, *J* = 7.6 Hz, 2H), 1.28 (t, *J* = 7.6 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.80 (d, *J* = 53.5 Hz, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.37 (s), 130.74 (s), 129.12 (s), 128.75 (s), 114.61 (t, *J* = 285.4 Hz), 29.07 (s), 14.90 (s). IR (neat) ν = 501, 531, 551, 602, 668, 836, 1080, 1115, 1168, 1189, 1305, 1347, 1412, 1596, 2927, 2971 cm^{-1}; HRMS (EI) Calcd for $C_9H_{10}O_2F_2S$ $[M]^+$: 220.2363, Found: 220.0370.



2d

2-((difluoromethyl)sulfonyl)-1,3,5-trimethylbenzene (2d)

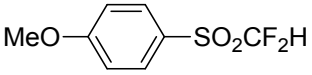
Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (s, 2H), 6.14 (t, *J* = 53.7 Hz, 1H), 2.65 (s, 6H), 2.32 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -122.64 (d, *J* = 53.7 Hz, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.81 (s), 143.45 (s), 132.70 (s), 126.28 (s), 115.78 (t, *J* = 285.9 Hz), 23.19 (s), 21.22 (s). IR (neat) ν = 486, 522, 560, 604, 622, 669, 693, 755, 811, 855, 1036, 1108, 1158, 1170, 1187, 1285, 1307, 1342, 1449, 1602 cm^{-1}; HRMS (EI) Calcd for $C_{10}H_{12}O_2F_2S$ $[M]^+$: 234. 2629, Found: 234.0526.



2e

1-(tert-butyl)-4-((difluoromethyl)sulfonyl)benzene (2e)

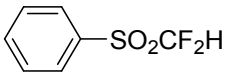
Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.6 Hz, 2H), 7.63 (d, *J* = 8.7 Hz, 2H), 6.16 (t, *J* = 53.5 Hz, 1 H), 1.35 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.80 (d, *J* = 53.4 Hz, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.17 (s), 130.51 (s), 128.51 (s), 126.67 (s), 114.63 (t, *J* = 285.5 Hz), 35.53 (s), 30.95 (s). IR (neat) ν = 501, 540, 561, 588, 610, 646, 693, 753, 842, 1078, 1105, 1171, 1300, 1593, 2966 cm^{-1}; HRMS (EI) Calcd for $C_{11}H_{14}O_2F_2S$ $[M]^+$: 248.2895, Found: 248.0683.



2f

1-((difluoromethyl)sulfonyl)-4-methoxybenzene (2f)[2]

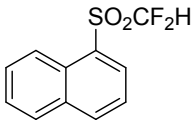
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.9 Hz, 2H), 7.07 (d, *J* = 8.9 Hz, 2H), 6.14 (t, *J* = 53.7 Hz, 1H), 3.90 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.78 (d, *J* = 53.7 Hz, 2F).



2g

((difluoromethyl)sulfonyl)benzene (2g)[3]

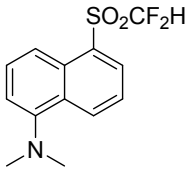
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.7 Hz, 2H), 7.79 (t, *J* = 7.5 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 2H), 6.17 (t, *J* = 53.4 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.64 (d, *J* = 53.4 Hz, 2F).



2h

1-((difluoromethyl)sulfonyl)naphthalene (2h)[4]

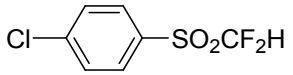
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 8.7 Hz, 1H), 8.39 (d, *J* = 7.4 Hz, 1H), 8.24 (d, *J* = 8.1 Hz, 1H), 7.97 (d, *J* = 8.1 Hz, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 7.65 (td, *J* = 7.7, 4.0 Hz, 2H), 6.30 (t, *J* = 53.5 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.61 (d, *J* = 53.5 Hz, 2F).



2i

5-((difluoromethyl)sulfonyl)-N,N-dimethylnaphthalen-1-amine (2i)

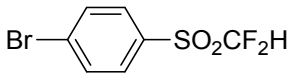
Yellow solid. M.P. 102-103 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 8.5 Hz, 1H), 8.43 (d, *J* = 8.7 Hz, 1H), 8.37 (d, *J* = 7.4 Hz, 1H), 7.65-7.59 (m, 2H), 7.22 (t, J = 7.7 Hz, 1H), 6.31 (t, *J* = 53.6 Hz, 1H), 2.88 (s, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.71 (d, *J* = 53.7 Hz, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.03 (s), 134.26 (s), 133.74 (s), 131.69 (s), 129.91 (s), 129.34 (s), 127.89 (s), 123.43 (s), 118.74 (s), 115.76 (s), 115.15 (t, *J* = 286.8 Hz), 45.39 (s). IR (neat) ν = 446, 522, 554, 640, 791, 1058, 1111, 1149, 1168, 1200, 1303, 1343, 1570 cm^{-1}; HRMS (EI) Calcd for $C_{13}H_{13}O_2F_2S$ $[M]^+$: 285.3096, Found: 285.0635.



2j

1-chloro-4-((difluoromethyl)sulfonyl)benzene (2j)[1]

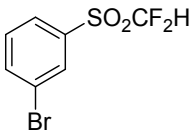
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.6 Hz, 2H), 7.62 (d, *J* = 8.6 Hz, 2H), 6.18 (t, *J* = 53.4 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.30 (d, *J* = 53.3 Hz, 2F).



2k

1-bromo-4-((difluoromethyl)sulfonyl)benzene (2k)[5]

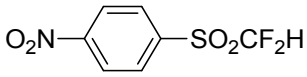
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.7 Hz, 2H), 7.78 (d, *J* = 8.6 Hz, 2H), 6.17 (t, *J* = 53.3 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.29 (d, *J* = 53.4 Hz, 2F).



2l

1-bromo-3-((difluoromethyl)sulfonyl)benzene (2l)[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.93-7.89 (m, 2H), 7.52 (t, *J* = 8.0 Hz, 1H), 6.19 (t, *J* = 53.3 Hz, 1H). ^{19}F NMR (376 MHz,$CDCl_3$) δ -121.16 (d, *J* = 53.2 Hz, 2F).

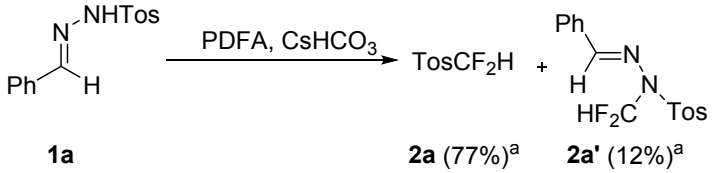


2m

1-((difluoromethyl)sulfonyl)-4-nitrobenzene (2m)[6]

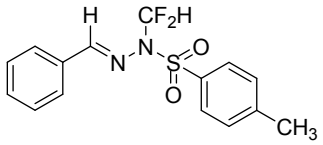
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 8.3 Hz, 2H), 8.20 (d, *J* = 8.3 Hz, 2H), 6.25 (t, *J* = 53.1 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.61 (d, *J* = 53.1 Hz, 2F).

3. The determination of the side difluoromethylation product



1a **2a** (77%)[a] **2a'** (12%)[a]

A side difluoromethylation product was always detected by ^{19}F NMR spectrometry (about -102 ppm) in the reaction mixtures. The byproduct for the conversion of substrate **1a** was isolated and its structure was determined (**2a'**).



2a'

(E)-N'-benzylidene-N-(difluoromethyl)-4-methylbenzenesulfonohydrazide (2a')

Yellow solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.69 (d, *J* = 7.0 Hz, 2H), 7.47 – 7.37 (m, 3H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.18 (t, *J* = 58.8 Hz, 1H), 2.42 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.27 (d, *J* = 58.7 Hz, 2F). ^{13}C NMR (101 MHz,$CDCl_3$) δ 161.90 (d, *J* = 1.9 Hz), 145.38 (s), 133.68 (s), 132.91 (s), 131.91 (s), 129.77 (s), 128.78 (s), 128.58 (s), 128.50 (s), 111.67 (t, *J* = 253.1 Hz), 21.69 (s). IR (neat) ν = 535, 565, 602, 671, 692, 757, 813, 837, 864, 887, 1004, 1047, 1111, 1175, 1189, 1224, 1364, 1450, 1574, 1598, 1609 cm^{-1}; HRMS (ESI) Calcd for $C_{15}H_{15}O_2N_2F_2S$ $[M+H]^+$: 325.0822, Found: 325.0817.

4. References

[1] C.-A. De, P. -R.Van, R. Pollet, *Bull. Soc. Chim. Belg.* 1965, **74**, 270-280.

[2] Boiko, Yagupol'skii, *J. Org. Chem. USSR* 1971, **7**, 784- 788.

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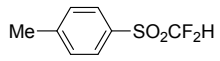
[4] J. Hine, J.-J. Porter, *J. Am. Chem. Soc.* 1960, **82**, 6178-6181.

[5] E.-S. Endel'man., V.-S. Danilenko, F.-P. Trinus, P.-A. Yufa, A.-G. Fadeicheva, I.-I. Muravov, Y.-A. Fialkov, L.-M. Yagupol'skii, *Pharm. Chem. J.* 1973, **7**, 755-759.

[6] G.-K. Prakash, C.-F.Ni, F. Wang, J.-B. Hu, G.-A. Olah, *Angew. Chem. Int. Edit.* 2011, **50**, 2559-2563.

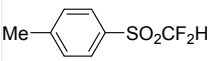
5. Copies of ^{1}H NMR, ^{19}F NMR and ^{13}C NMR Spectra of 2a-2m and 2a'.

^{19}F NMR



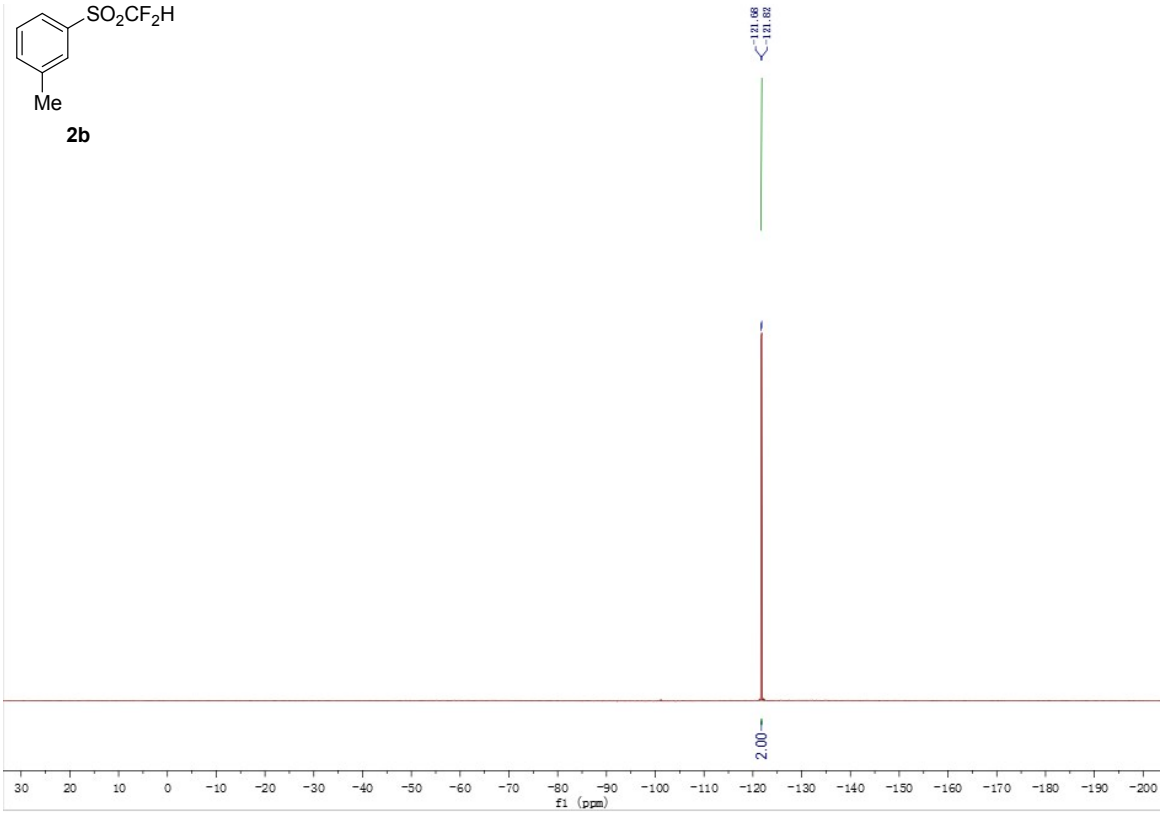
2a

^{1}H NMR

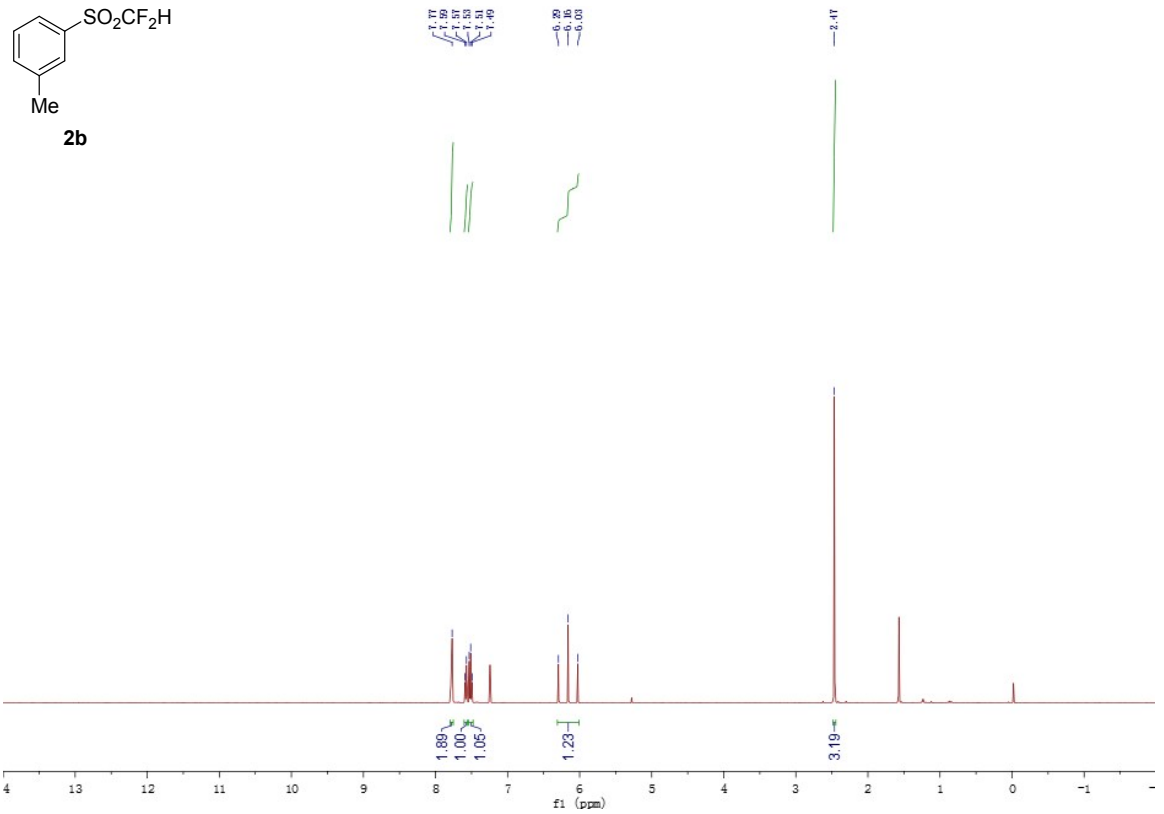


2a

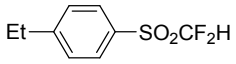
^{19}F NMR



^{1}H NMR

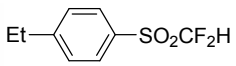


^{19}F NMR



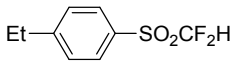
2c

^{1}H NMR



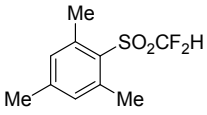
2c

^{13}C NMR



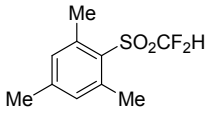
2c

^{19}F NMR



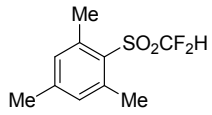
2d

^{1}H NMR



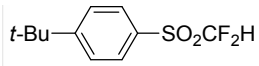
2d

^{13}C NMR



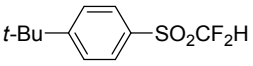
2d

^{19}F NMR

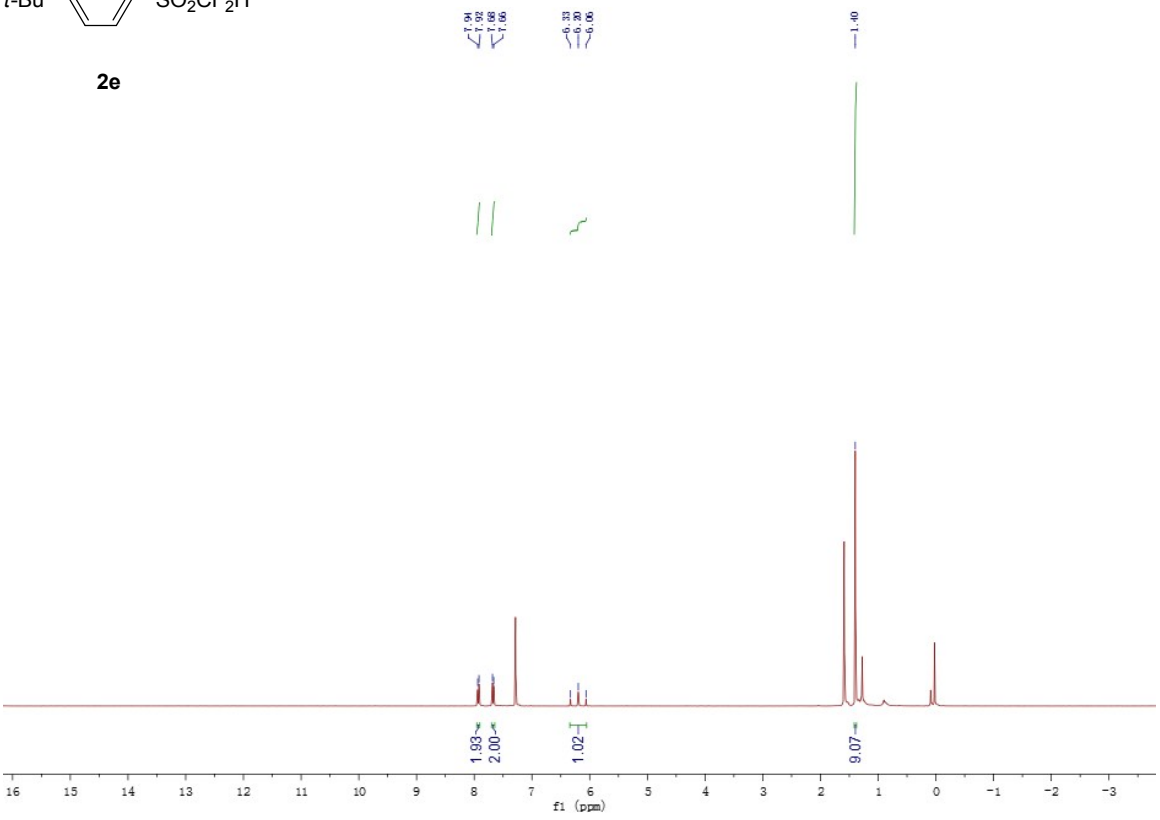


2e

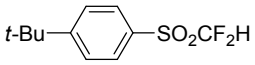
^{1}H NMR



2e

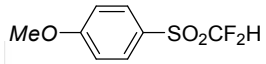


^{13}C NMR

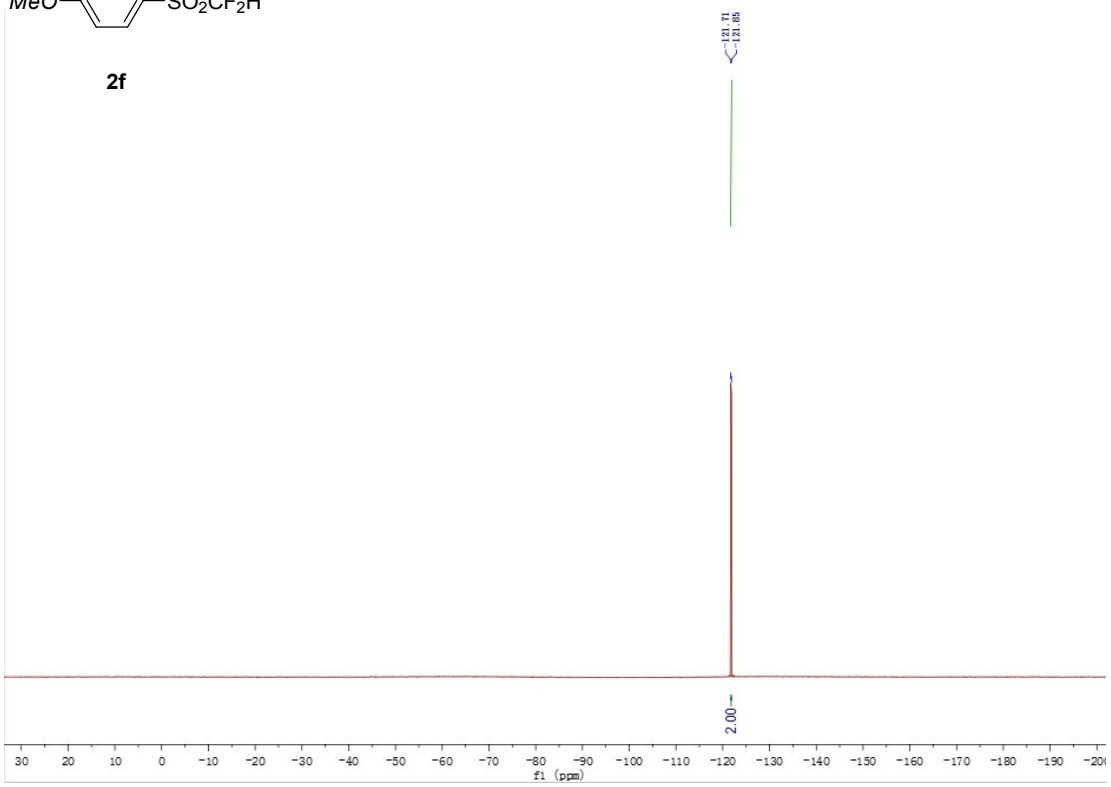


2e

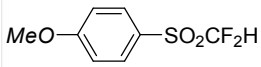
^{19}F NMR



2f

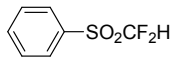


^{1}H NMR



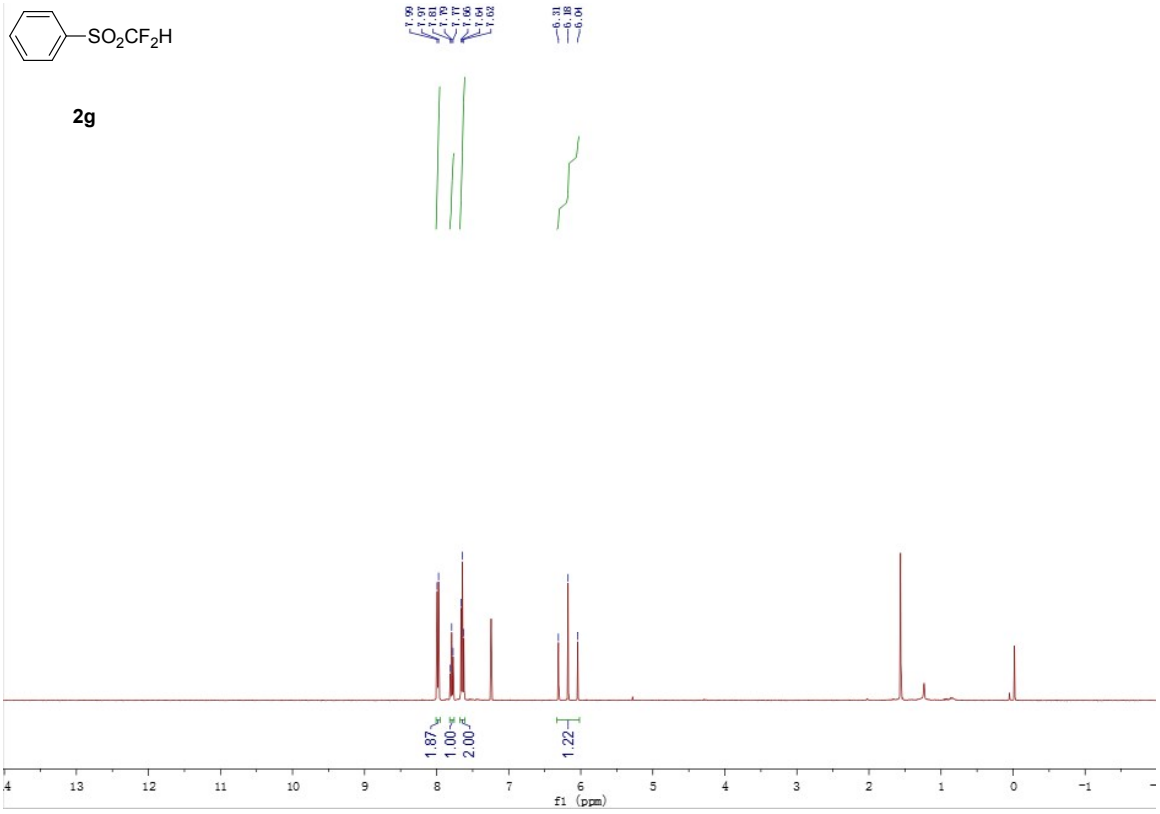
2f

^{19}F NMR

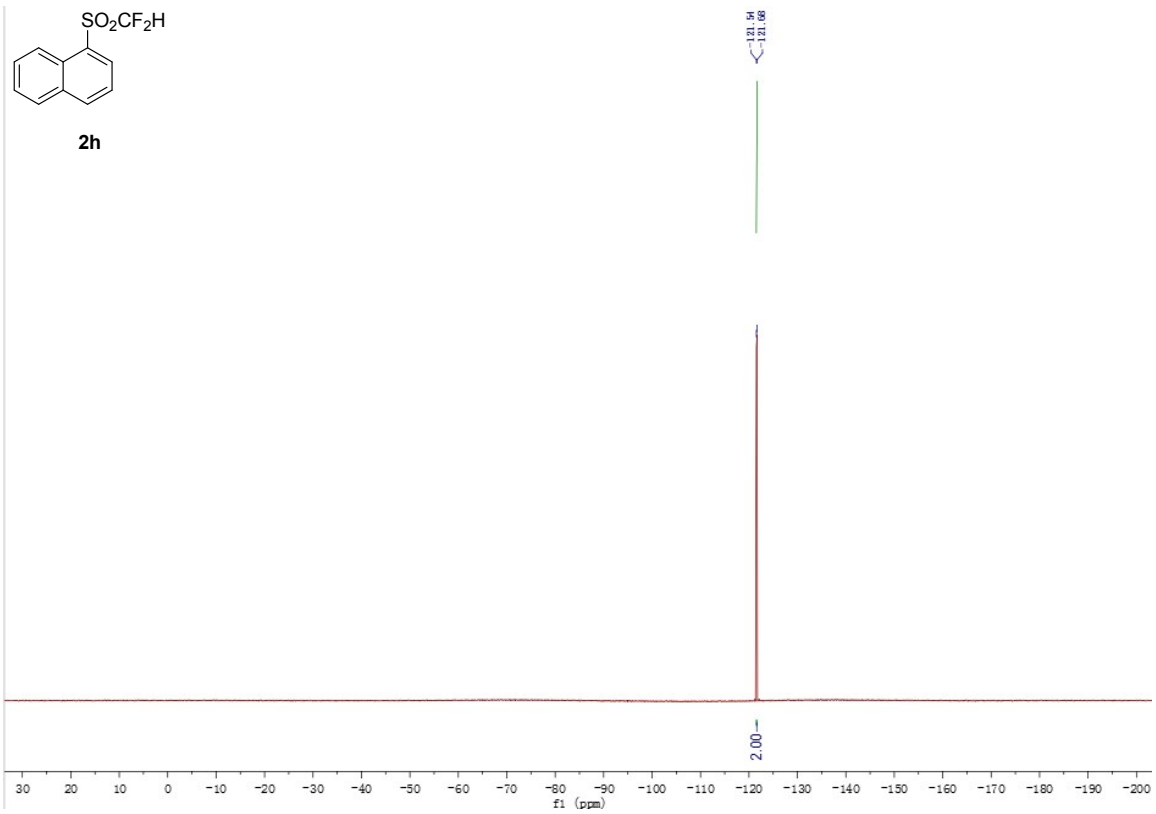


2g

^{1}H NMR



^{19}F NMR



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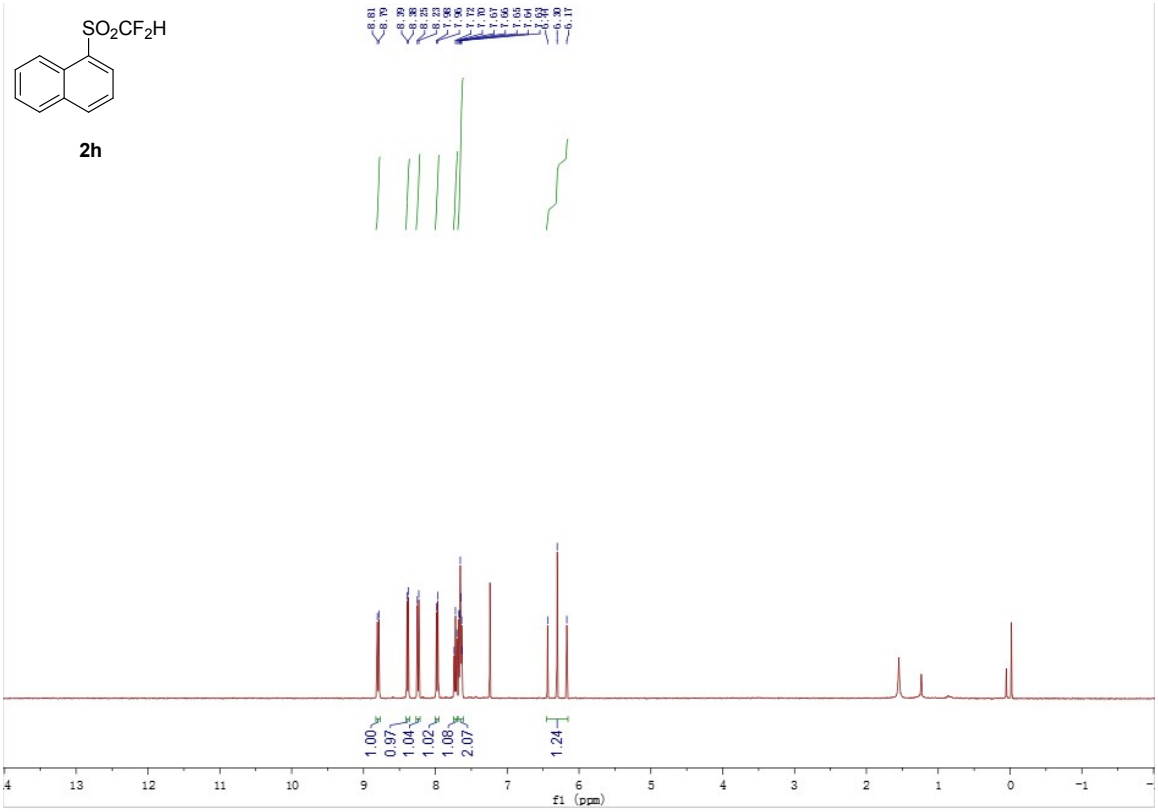

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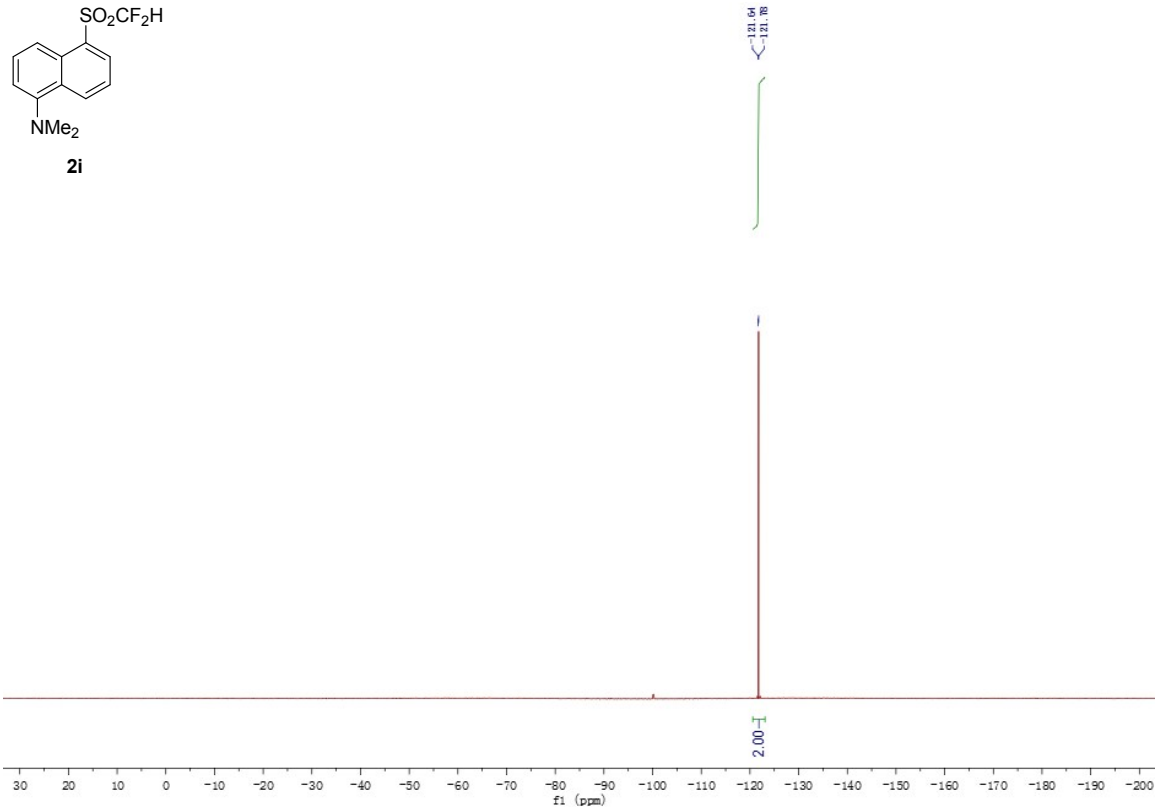
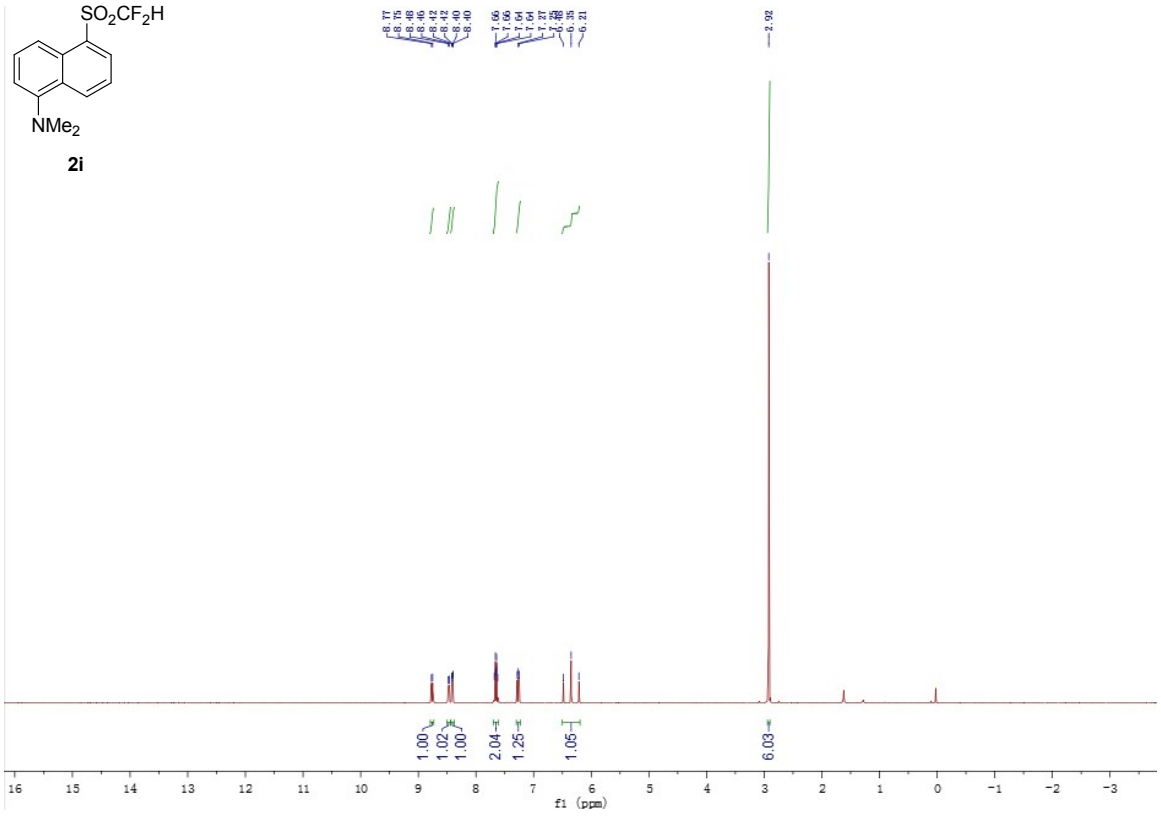
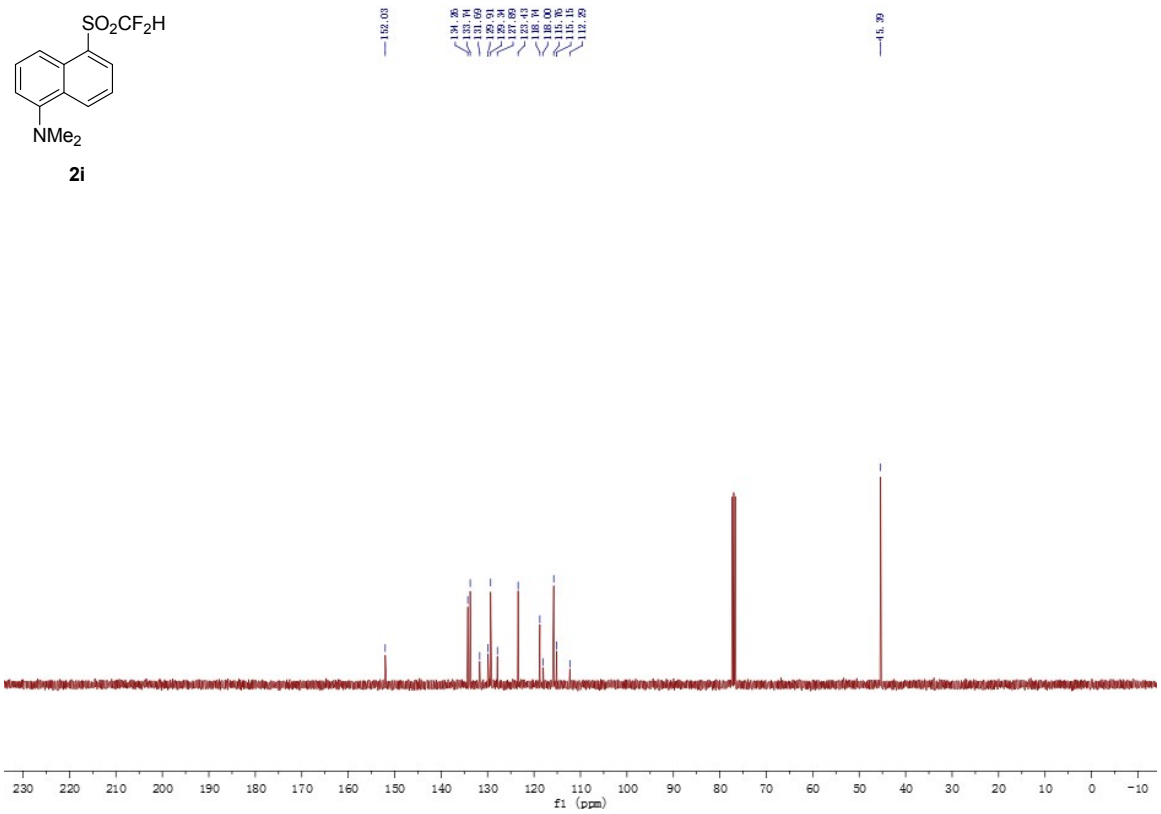


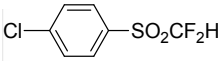
^{1}H NMR



^{13}C NMR

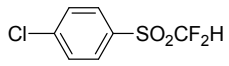


^{19}F NMR

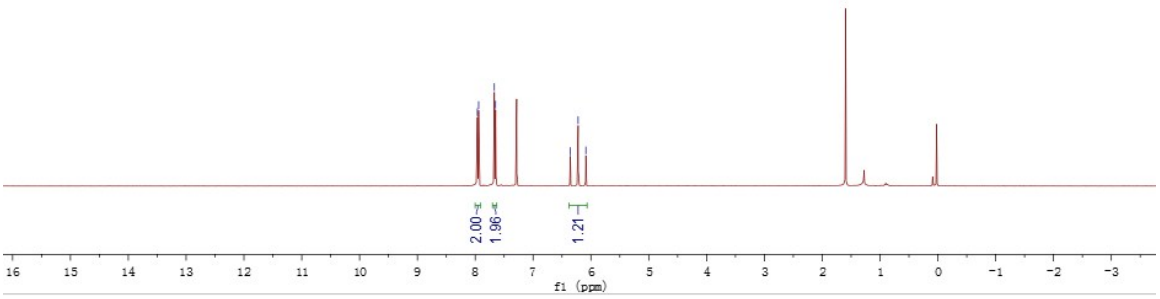


2j

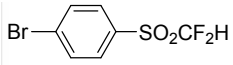
^{1}H NMR



2j

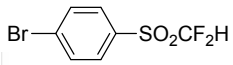


^{19}F NMR



2k

^{1}H NMR



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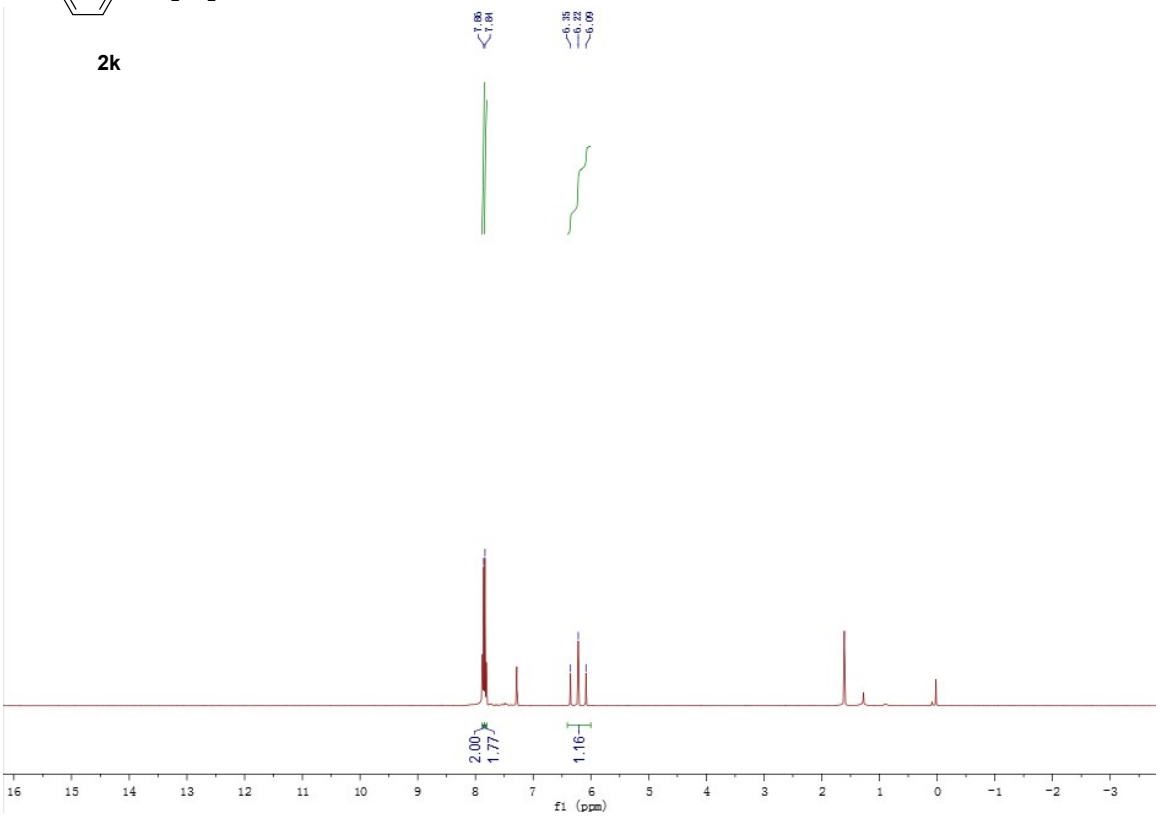
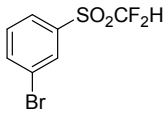
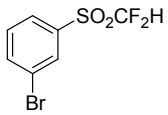


^{19}F NMR



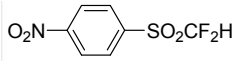
2l

^{1}H NMR



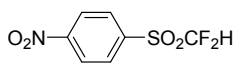
2l

^{19}F NMR



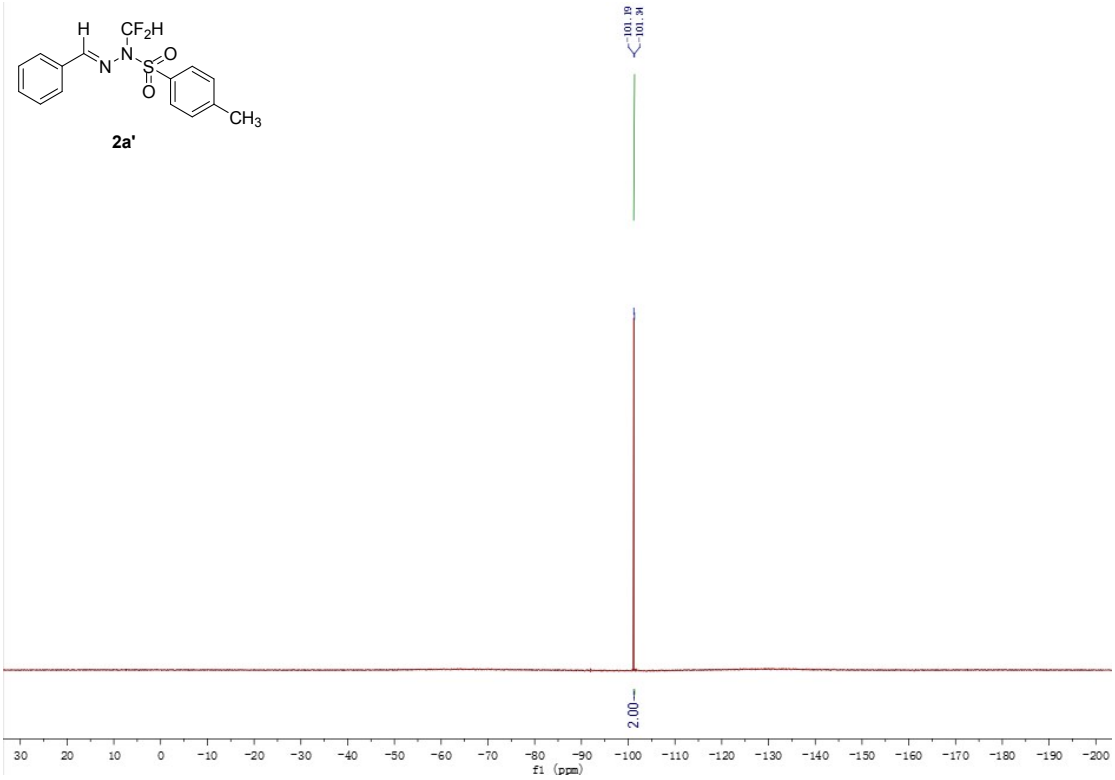
2m

^{1}H NMR

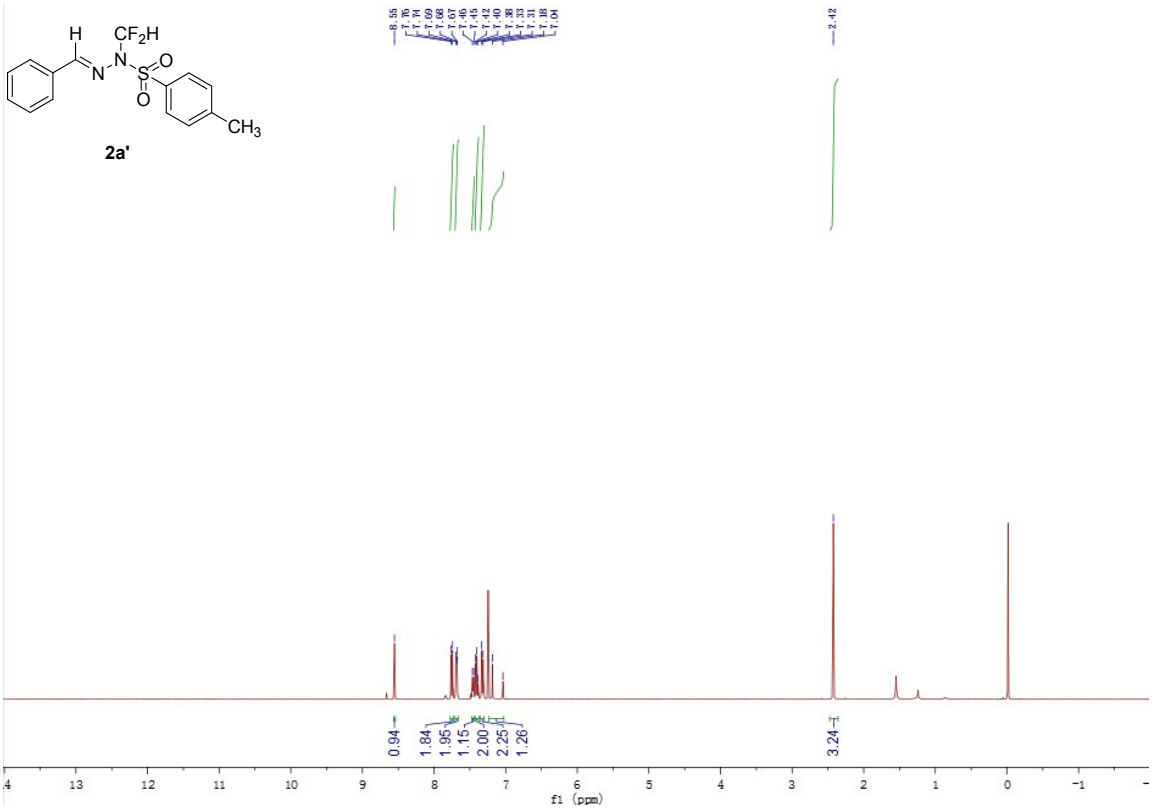


2m

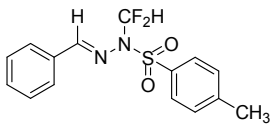
^{19}F NMR



^{1}H NMR



^{13}C NMR



2a'

161.90
161.89
145.38
133.66
132.91
131.91
129.77
128.78
128.58
128.50
114.19
111.67
109.16
21.69
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)