Electronic Supplementary Material (ESI) for RSC Advances.


# Combinatorial synthesis and biological evaluations of (*E*)-*β*-trifluoromethyl vinylsulfones as antitumor agents

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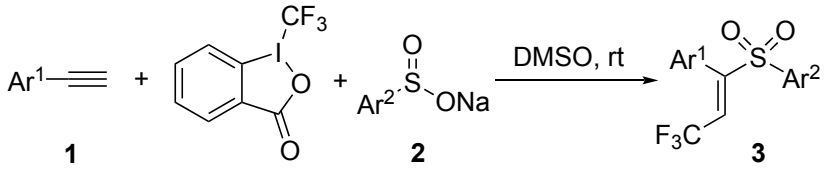
## Supporting Information

**General experimental methods:**

Unless otherwise stated, all commercial reagents were used as received. All solvents were dried and distilled according to standard procedures. Flash column chromatography was performed using silica gel (60-Å pore size, 32–63µm, standard grade). Analytical thin–layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated on rotary evaporators at ~20 Torr at 25–35°C. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale. $^{1}H$ and $^{13}C$ NMR spectra were recorded in $CDCl_3$ on a Bruker DRX-400 spectrometer operating at 400 MHz and 100 MHz, respectively. All chemical shift values are quoted in ppm and coupling constants quoted in Hz. High resolution mass spectrometry (HRMS) spectra were obtained on Bruker micrOTOF II Instrument (ESI source, Ion polarity).

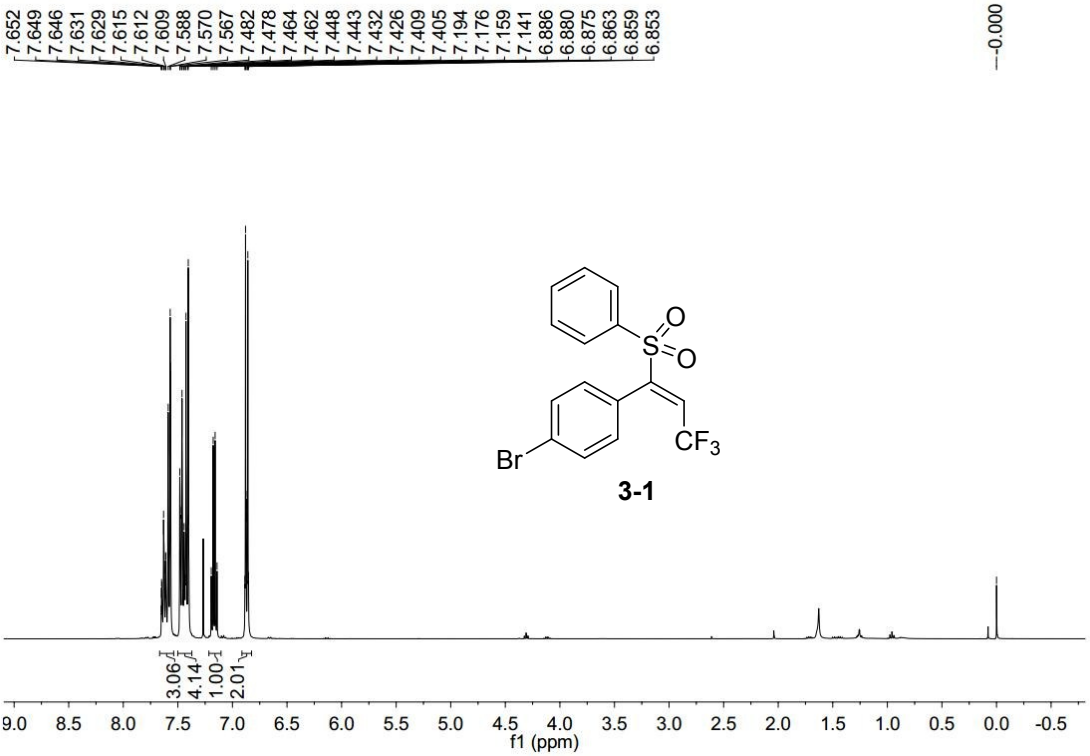
*General experimental procedure for the combinatorial synthesis of* (*E)-β-trifluoromethyl vinylsulfones:*

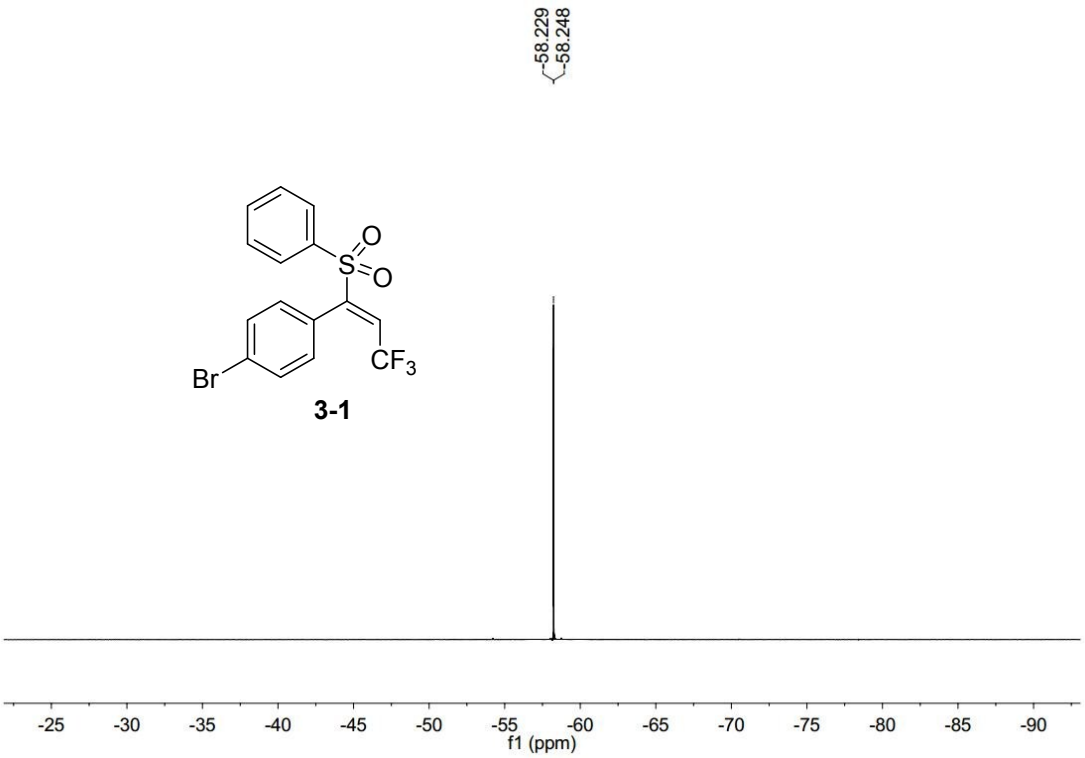



A mixture of alkyne **1** (0.2 mmol) and Togni reagent (0.22 mmol) in DMSO (1.0 mL) was stirred for several minutes. Then sodium benzenesulfinate **2** (0.4 mmol) in DMSO (2.0 mL) was added to the solution. The mixture was stirred overnight at room temperature. After completion of reaction as indicated by TLC, water (10 mL) was added and the mixture was extracted by EtOAc (3 x 10 mL). The solvent was evaporated and the residue was purified by flash column chromatography (EtOAc/*n*-hexane, 1:8) to give the desired product **3**.

*Experimental procedure for the synthesis of* (*E*)-*β*-*trifluoromethyl vinylsulfone* ***3-1*** *on 10 mmol scale:*

A mixture of alkyne **1a** (10 mmol) and Togni reagent (11 mmol) in DMSO (50.0 mL) was stirred for several minutes. Then sodium benzenesulfinate **2a** (20 mmol) in DMSO (100.0 mL) was added to the solution. The mixture was stirred overnight at room temperature. After completion of reaction as indicated by TLC, water (300 mL) was added and the mixture was extracted by EtOAc (3 x 200 mL). The solvent was evaporated and the residue was purified by flash column chromatography (EtOAc/*n*-hexane, 1:8) to give the desired (*E*)-1-Bromo-4-(3,3,3-trifluoro-1-(phenylsulfonyl)prop-1-en-1-yl)benzene **3-1** in 72.1% yield.

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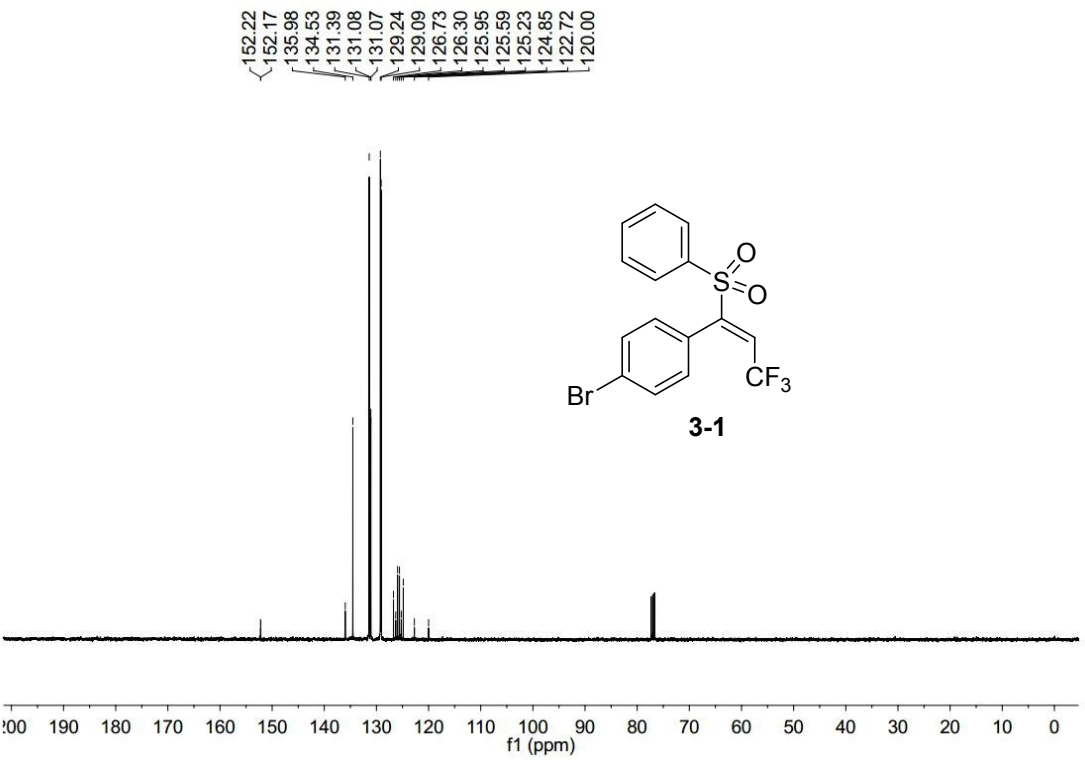
O
S
O
Br
CF3
3-1
-25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90
f1 (ppm)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135.98
134.53
131.39
131.08
131.07
129.24
129.09
126.73
126.30
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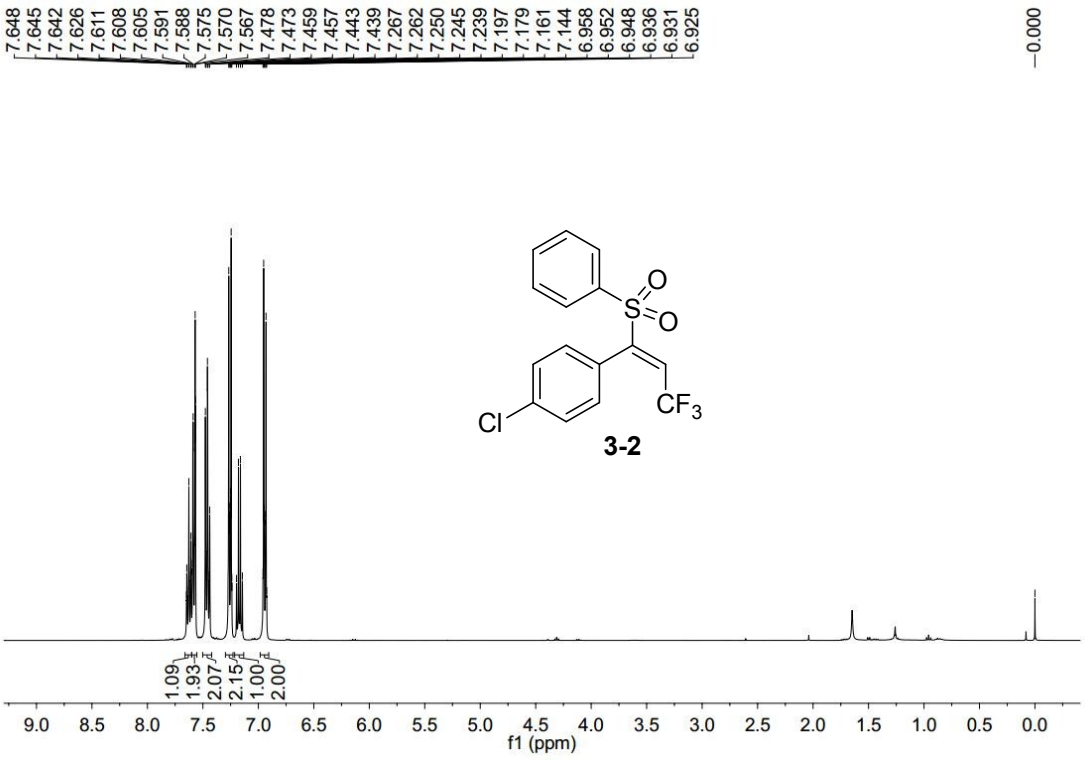
125.59
125.23
124.85
122.72
120.00
O
S
O
Br
CF3
3-1
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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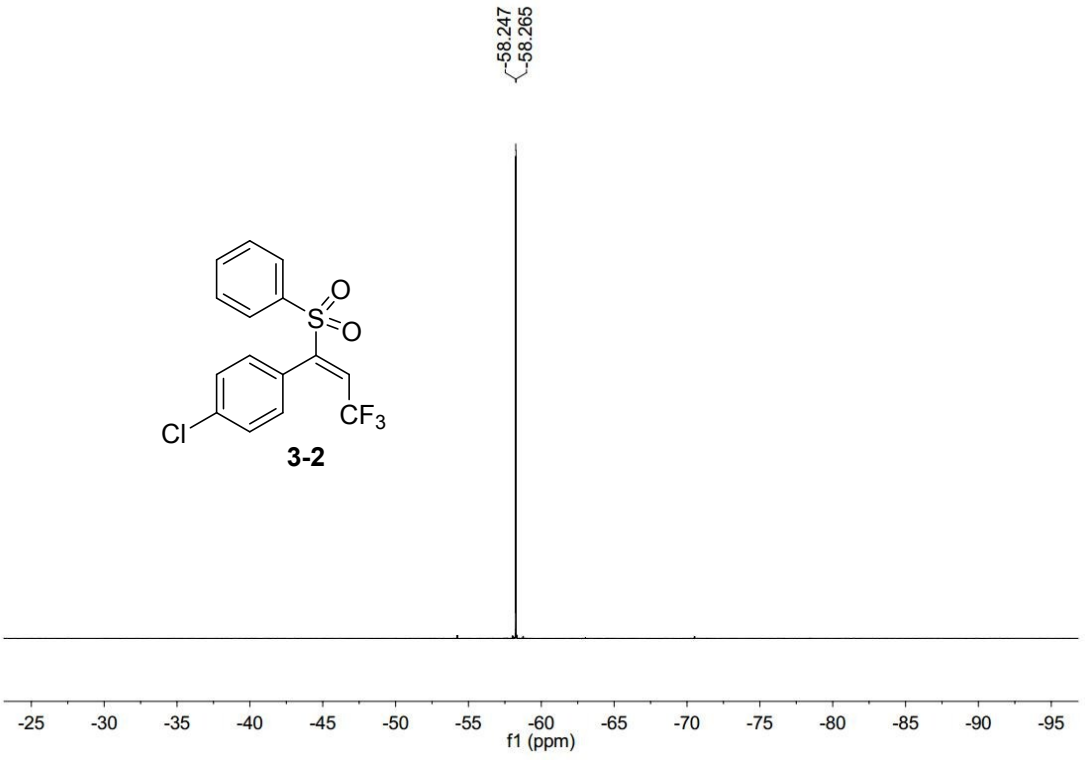
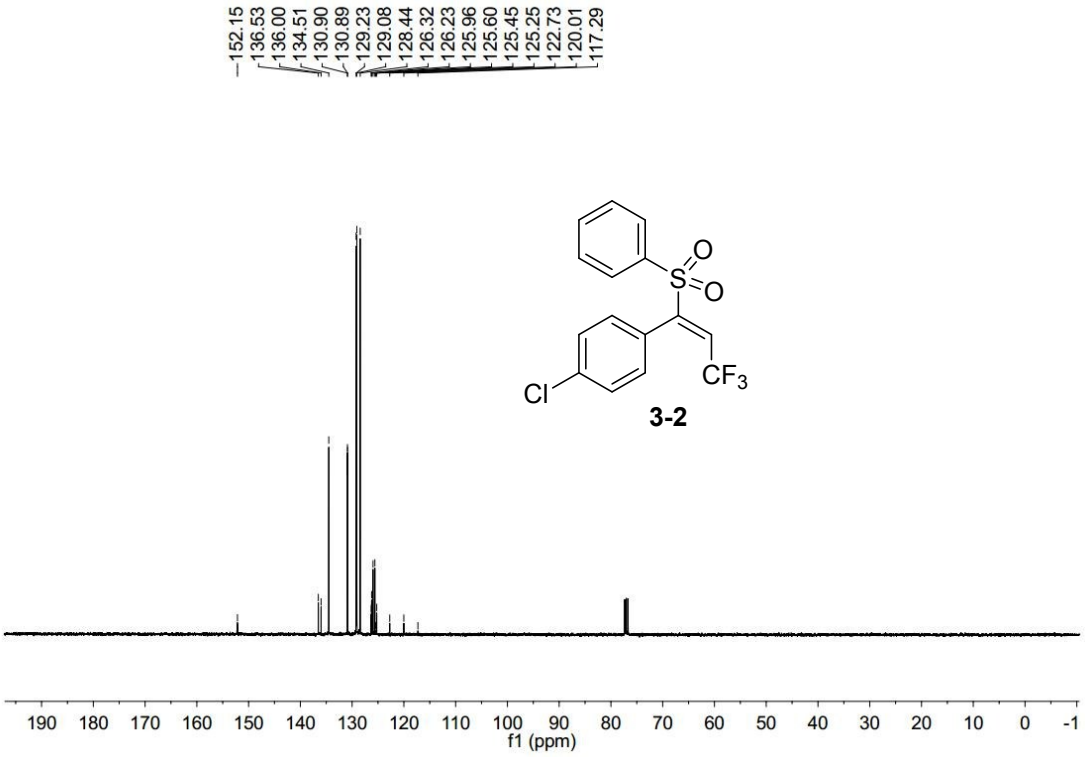
7.473
7.459
7.457
7.443
7.439
7.267
7.262
7.250
7.245
7.239
7.197
7.179
7.161
7.144
6.958
6.952
6.948
6.936
6.931
6.925
0.000
O
S
O
Cl
CF3
3-2
1.09
1.93
2.07
2.15
1.00
2.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


-58.247
-58.265
O
S
O
Cl
CF3
3-2
-25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95
f1 (ppm)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129.08
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126.23
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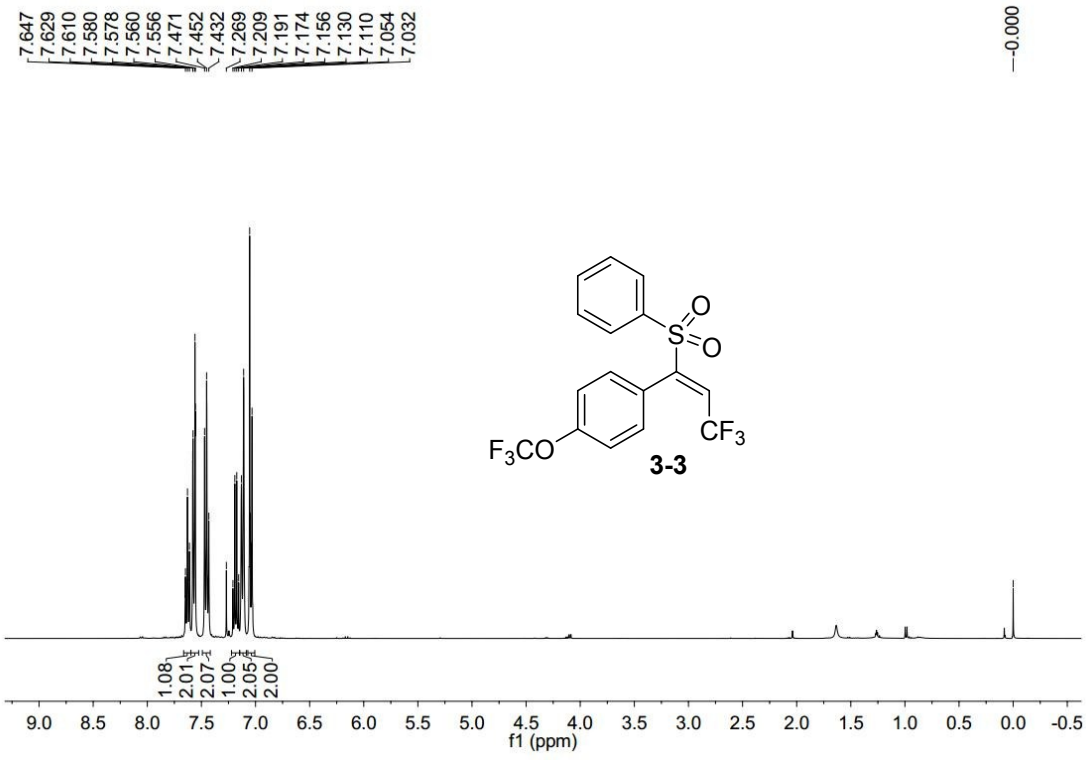
125.60
125.45
125.25
122.73
120.01
117.29
O
S
O
Cl
CF3
3-2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)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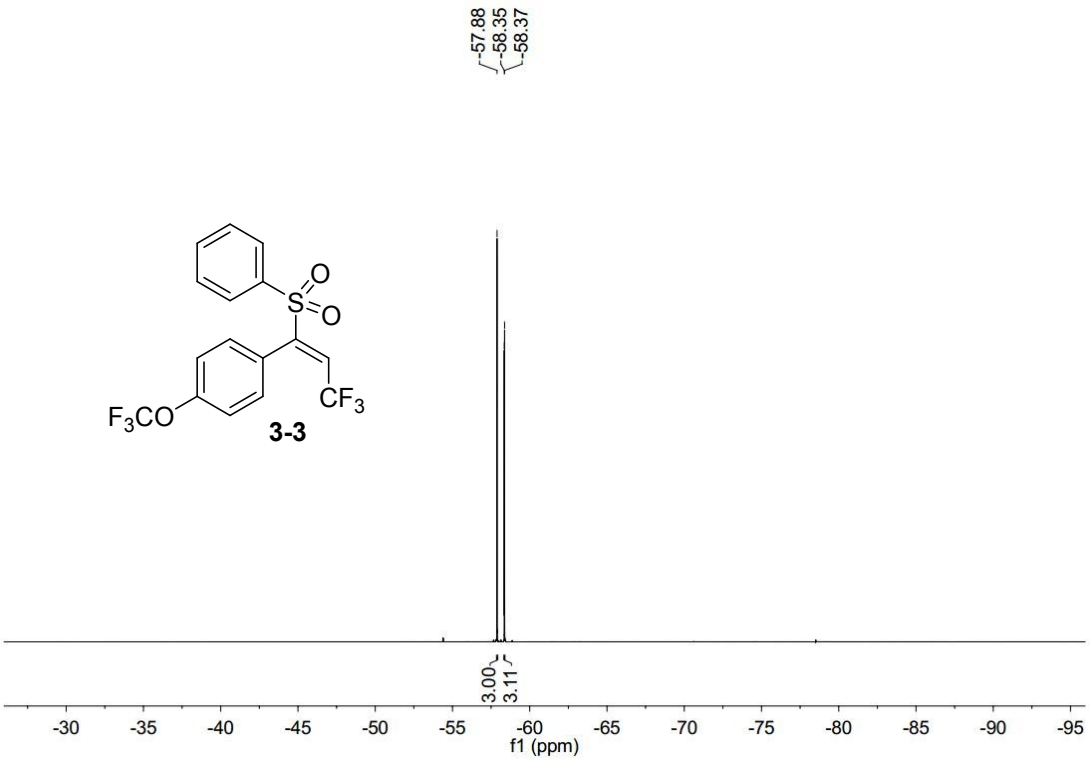
7.191
7.174
7.156
7.130
7.110
7.054
7.032
-0.000
O
S
O
F3CO
CF3
3-3
1.08
2.01
2.07
1.00
2.05
2.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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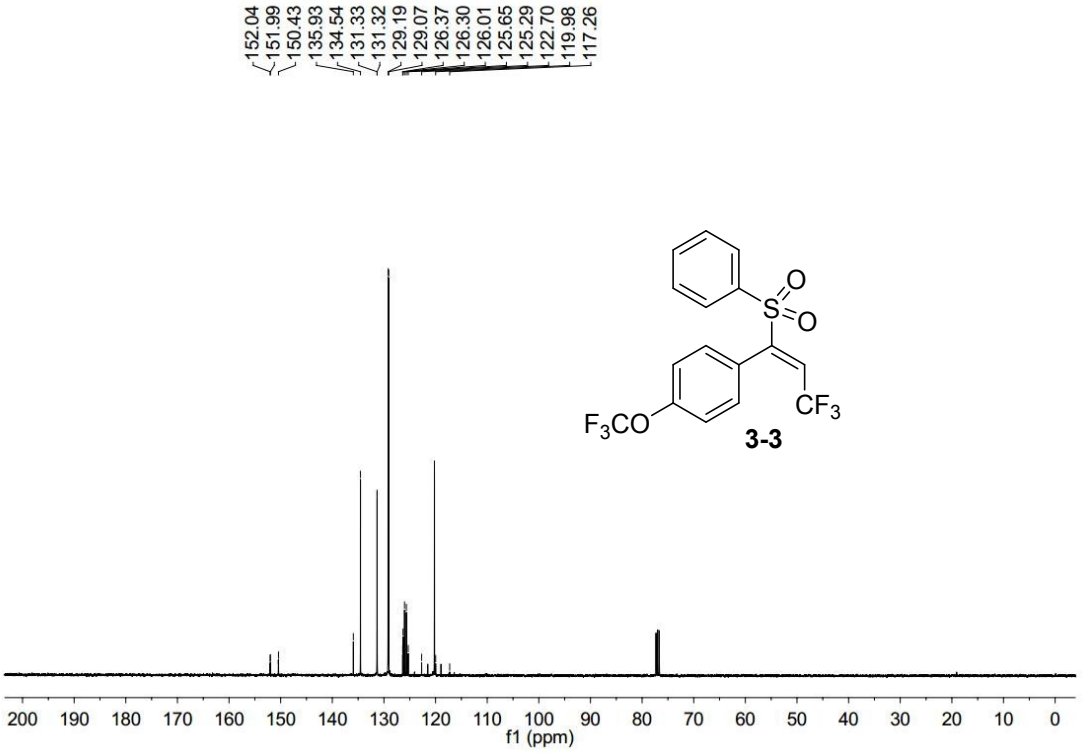
-58.35
-58.37
O
S
O
F3CO
CF3
3-3
3.00
3.11
-30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95
f1 (ppm)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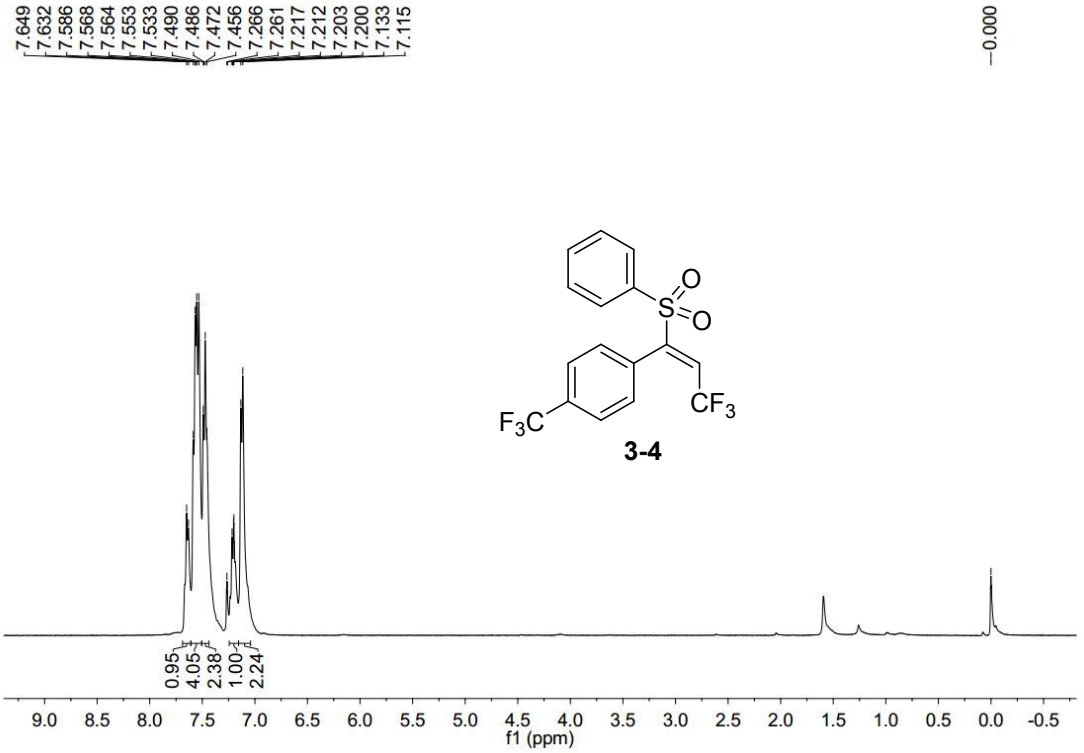
135.93
134.54
131.33
131.32
129.19
129.07
126.37
126.30
126.01
125.65
125.29
122.70
119.98
117.26
O
S
O
F3CO
CF3
3-3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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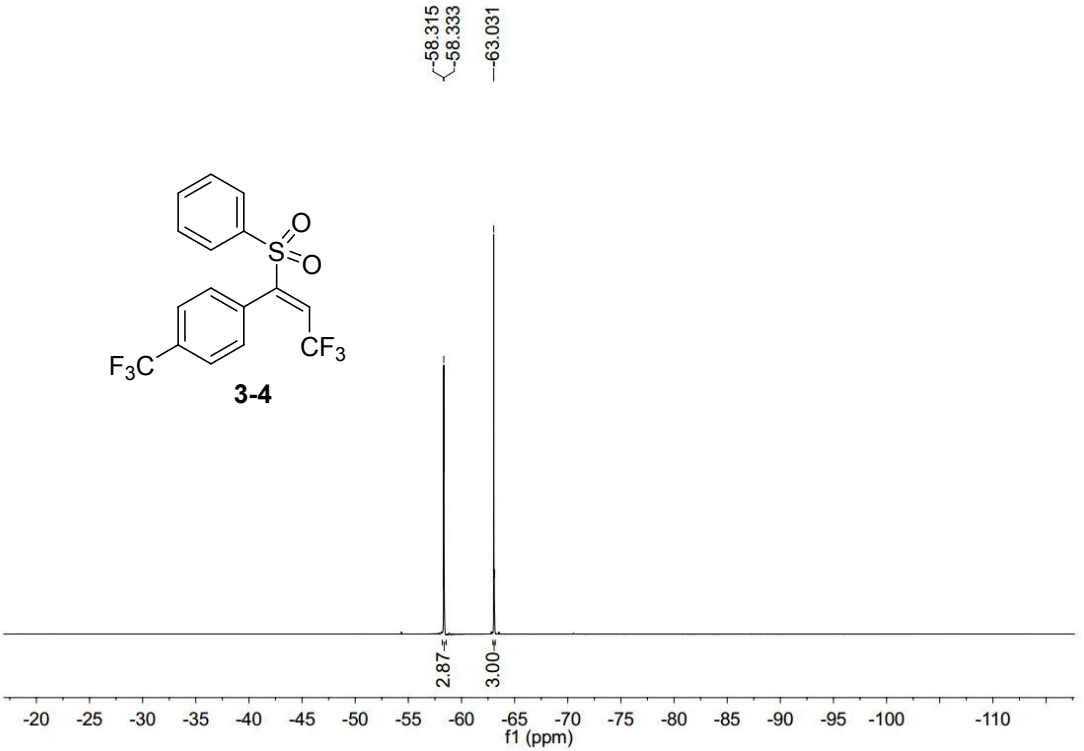
7.217
7.212
7.203
7.200
7.133
7.115
0.000
O
S
O
F3C
CF3
3-4
0.95
4.05
2.38
1.00
2.24
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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S
O
F3C
CF3
3-4
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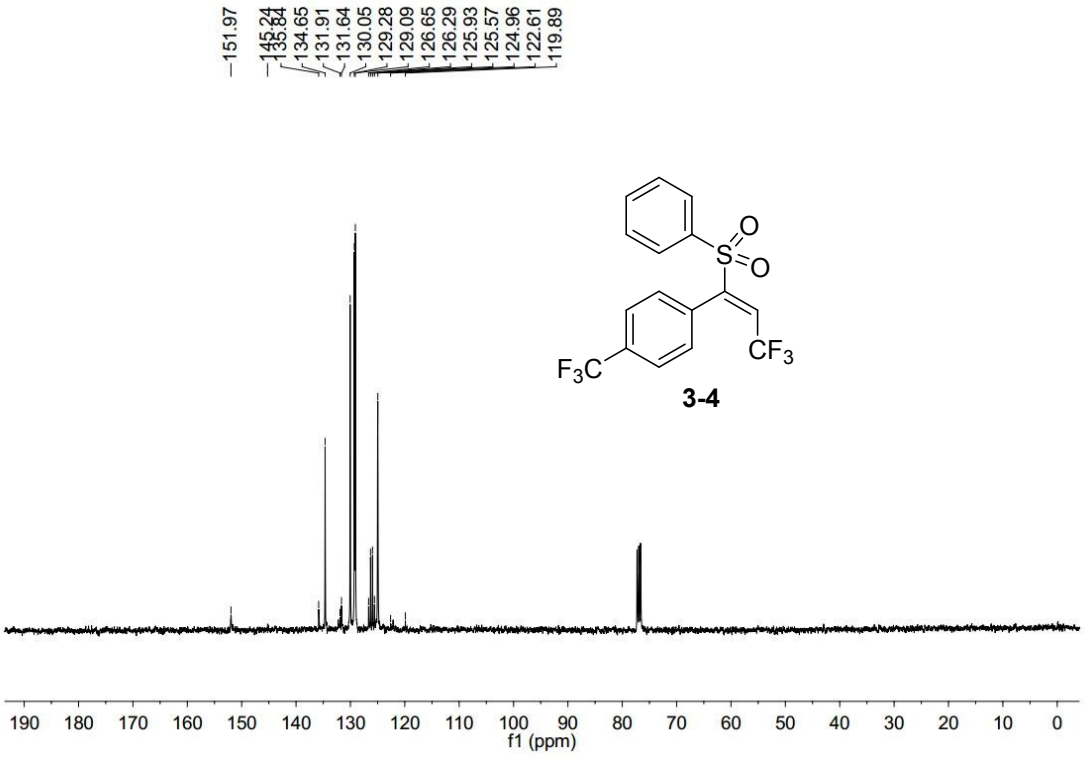
3.00
-20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -110
f1 (ppm)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126.29
125.93
125.57
124.96
122.61
119.89
O
S
O
F3C
CF3
3-4
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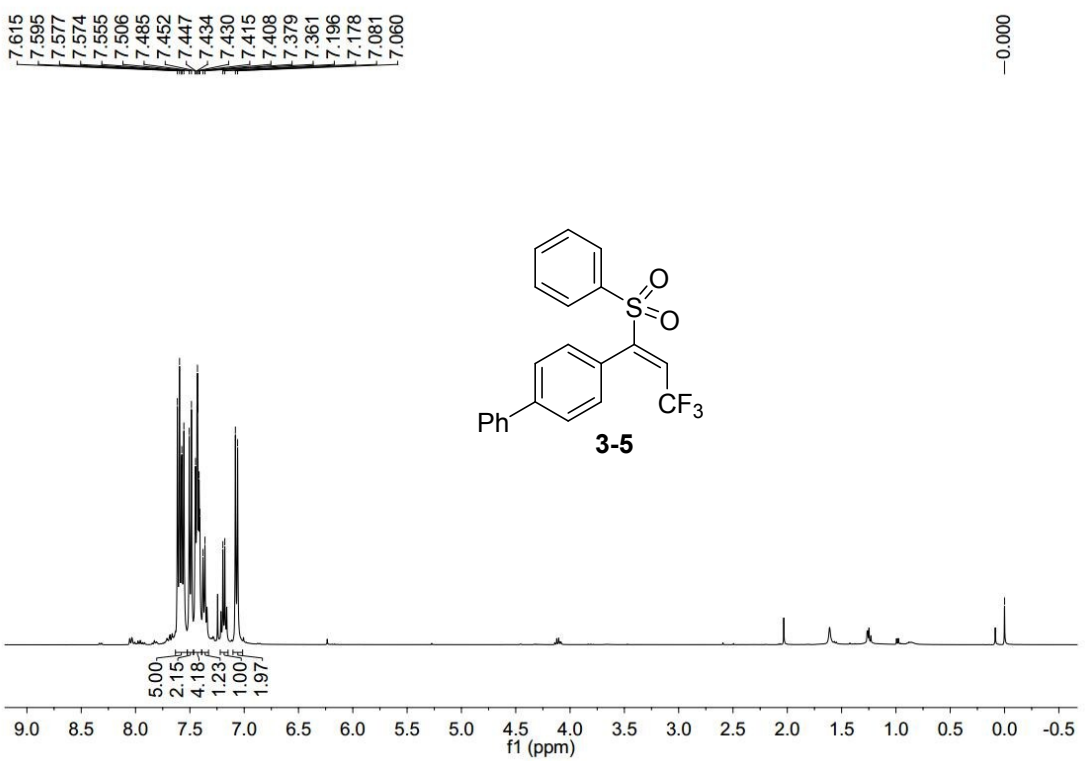
f1 (ppm)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7.452
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7.434
7.430
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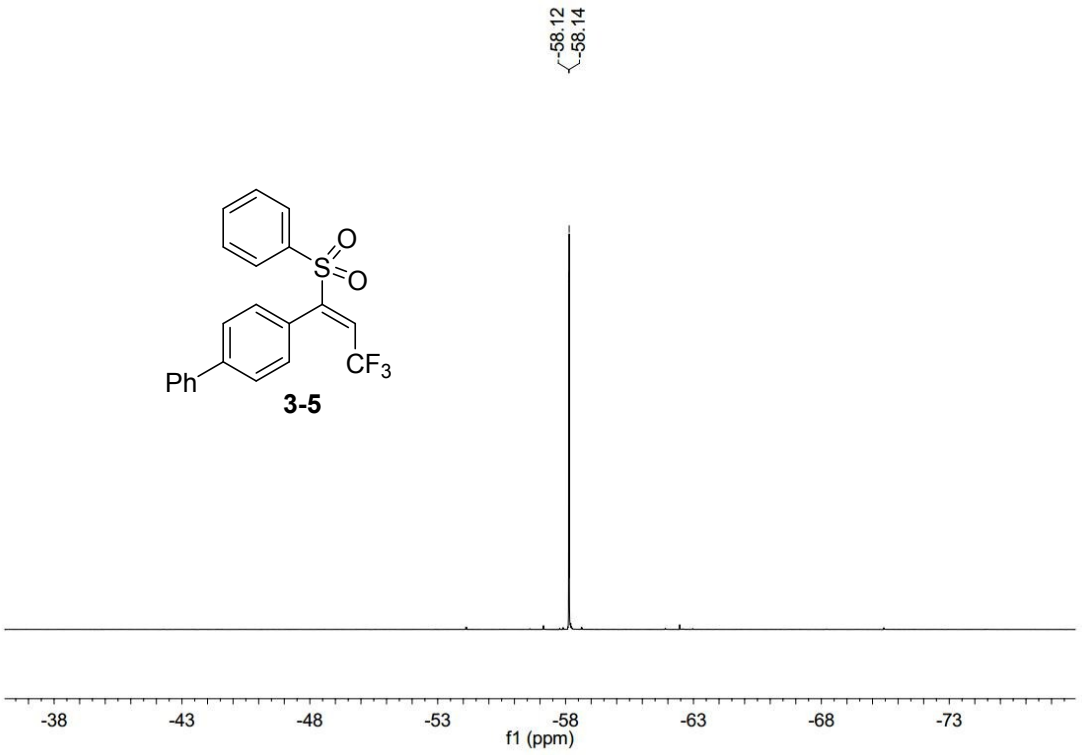
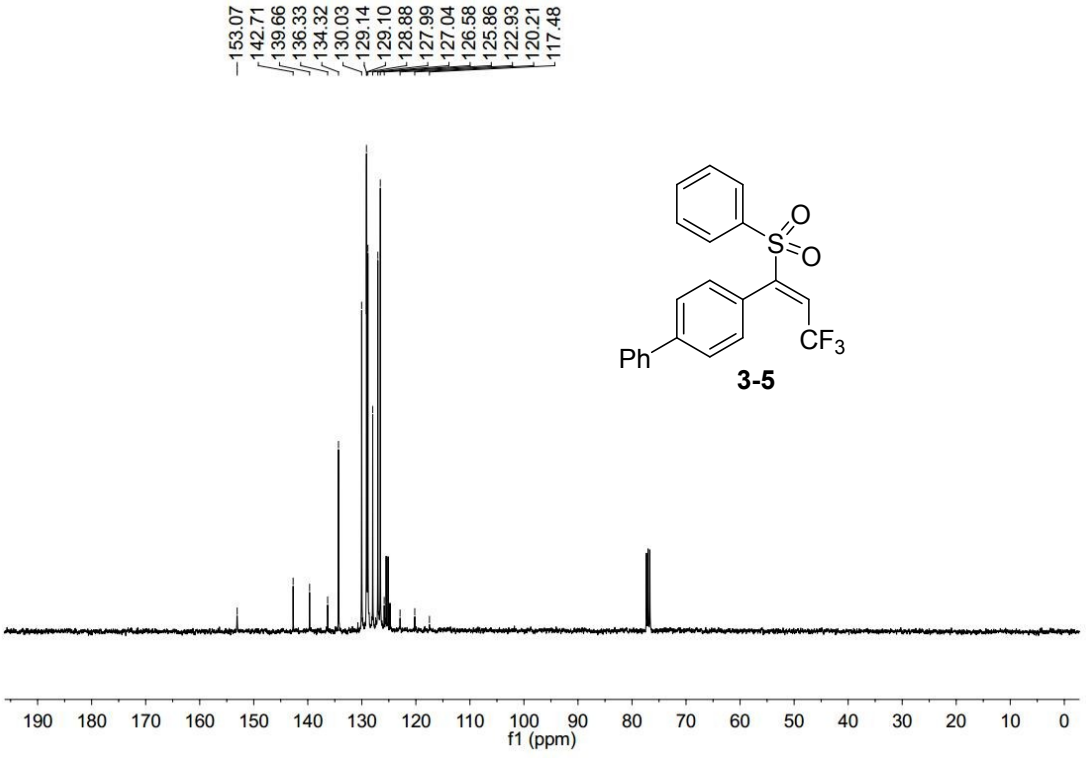
7.408
7.379
7.361
7.196
7.178
7.081
7.060
0.000
O
S
O
Ph
CF3
3-5
5.00
2.15
4.18
1.23
1.00
1.97
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


-58.12
-58.14
O
S
O
Ph
CF3
3-5
-38
-43
-48
-53
-58
-63
-68
-73
f1 (ppm)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134.32
130.03
129.14
129.10
128.88
127.99
127.04
126.58
125.86
122.93
120.21
117.48
O
S
O
Ph
CF3
3-5
190
180
170
160
150
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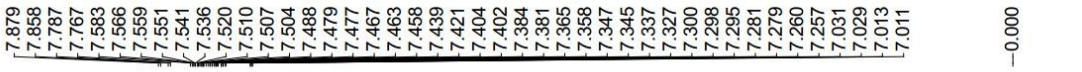
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.510
7.507
7.504
7.488
7.479
7.477
7.467
7.463
7.458
7.439
7.421
7.404
7.402
7.384
7.381
7.365
7.358
7.347
7.345
7.337
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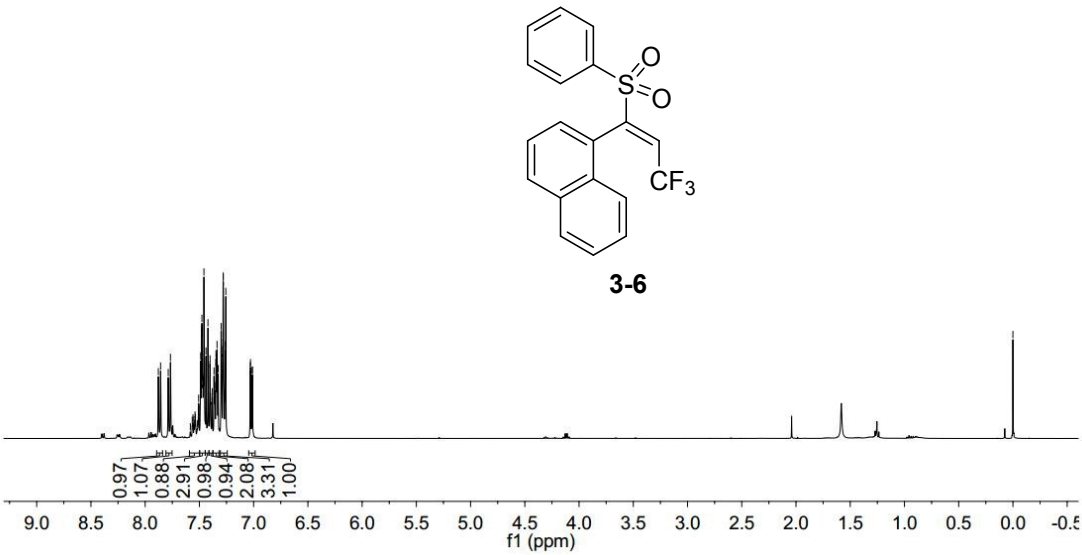
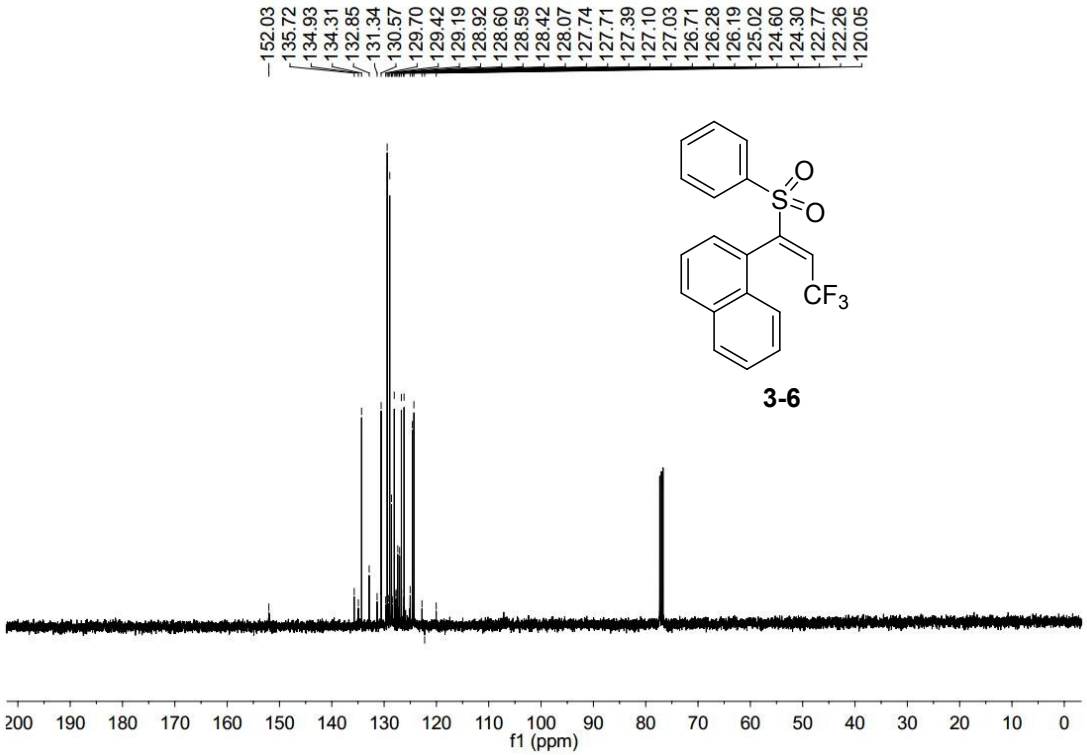

O
S
O
CF3
0.97
1.07
0.88
2.91
0.98
0.94
2.08
3.31
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

**3-6**


60.074
60.093
O
S
O
CF3
-25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95
f1 (ppm)

**3-6**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128.42
128.07
127.74
127.71
127.39
127.10
127.03
126.71
126.28
126.19
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124.30
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122.26
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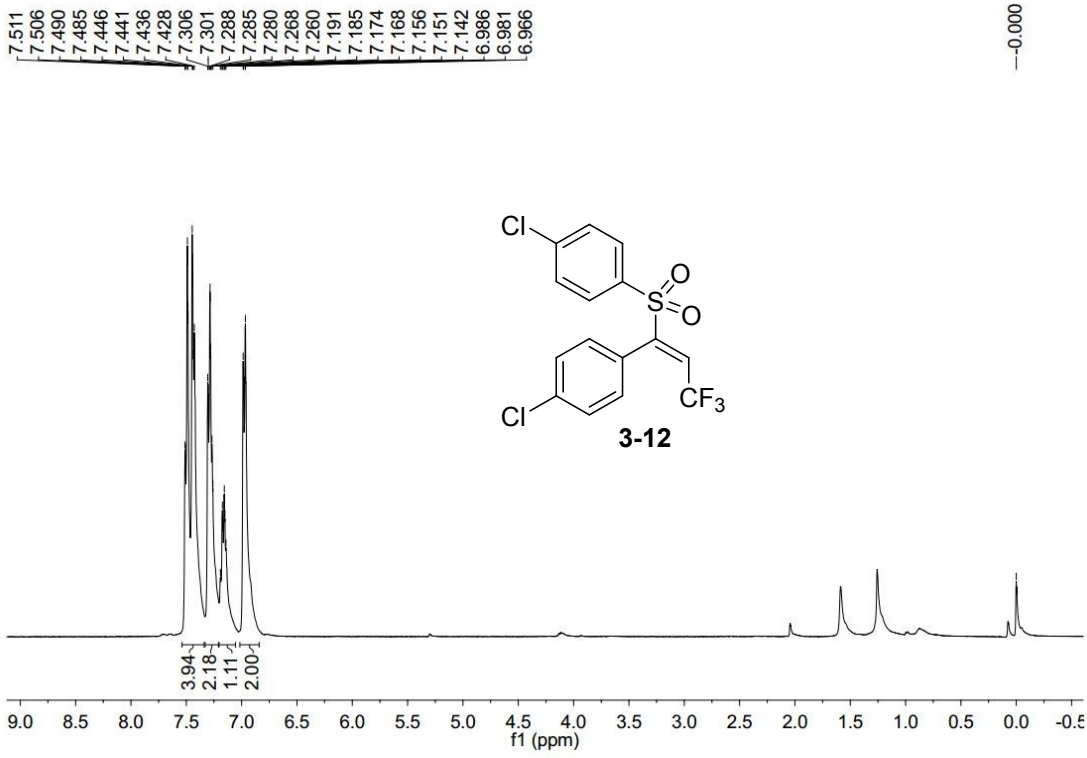
O
S
O
CF3
f1 (ppm)

**3-6**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7.268
7.260
7.191
7.185
7.174
7.168
7.156
7.151
7.142
6.986
6.981
6.966
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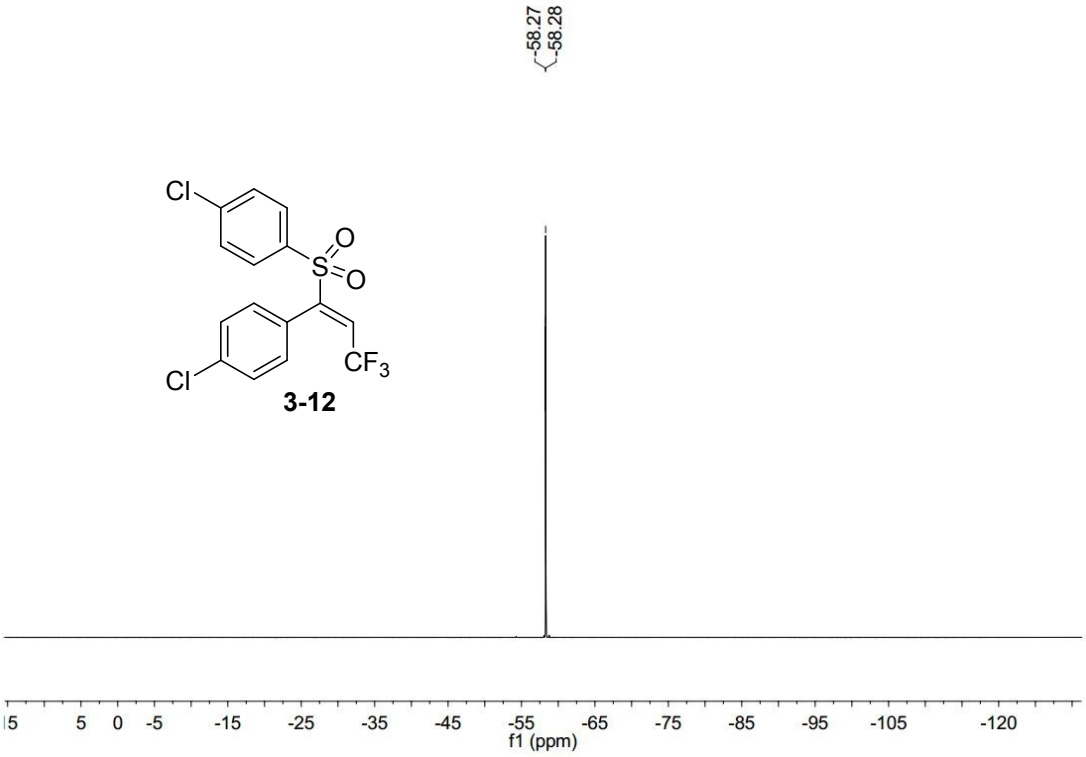
O
S
O
CF3
Cl
3.94
2.18
1.11
2.00
f1 (ppm)

**3-12**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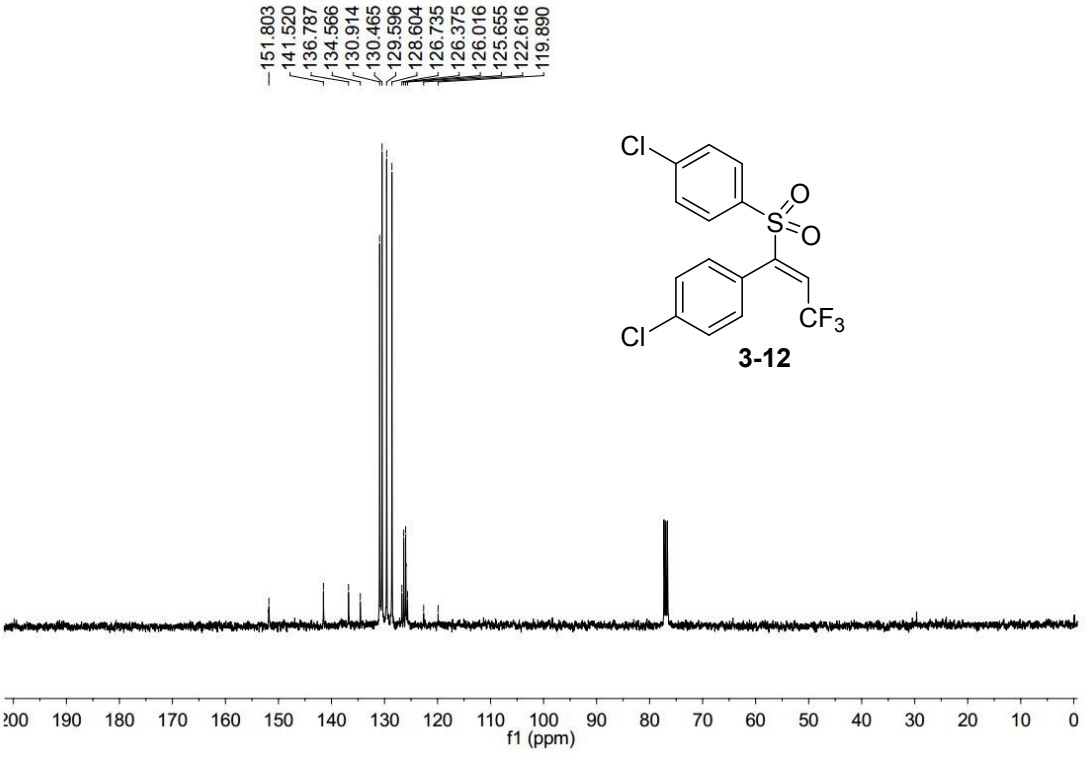
O
S
O
CF3
Cl
3-12
f1 (ppm)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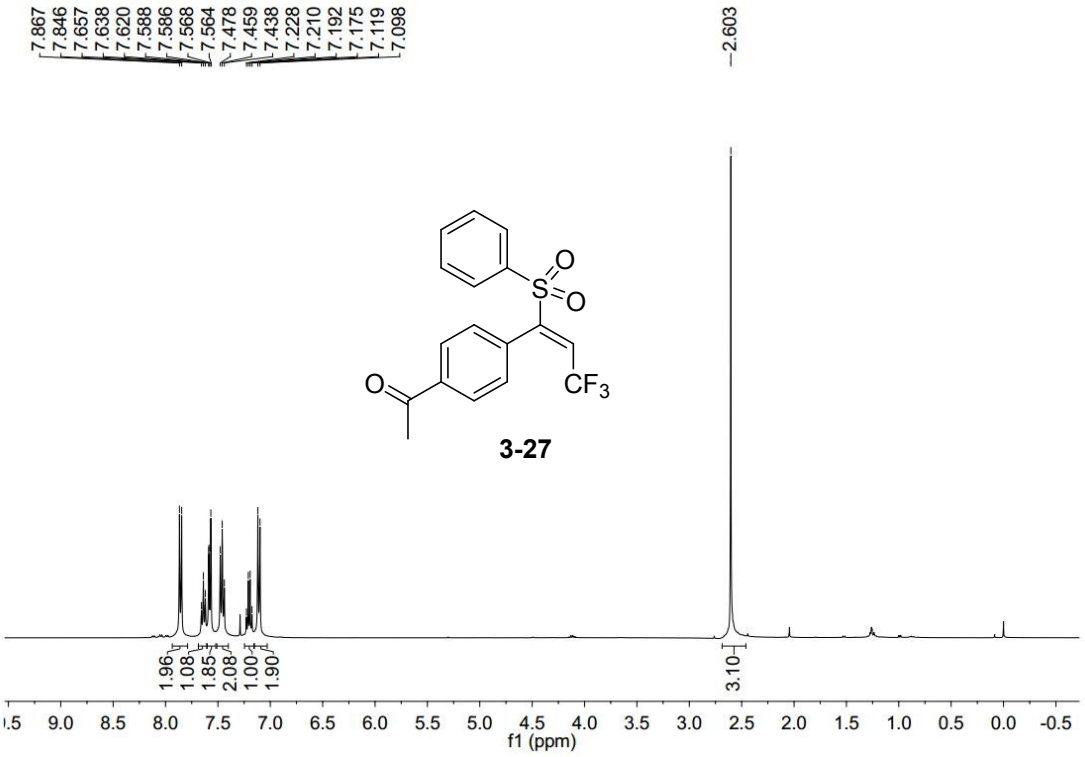
S
O
CF3
Cl
3-12
f1 (ppm)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7.459
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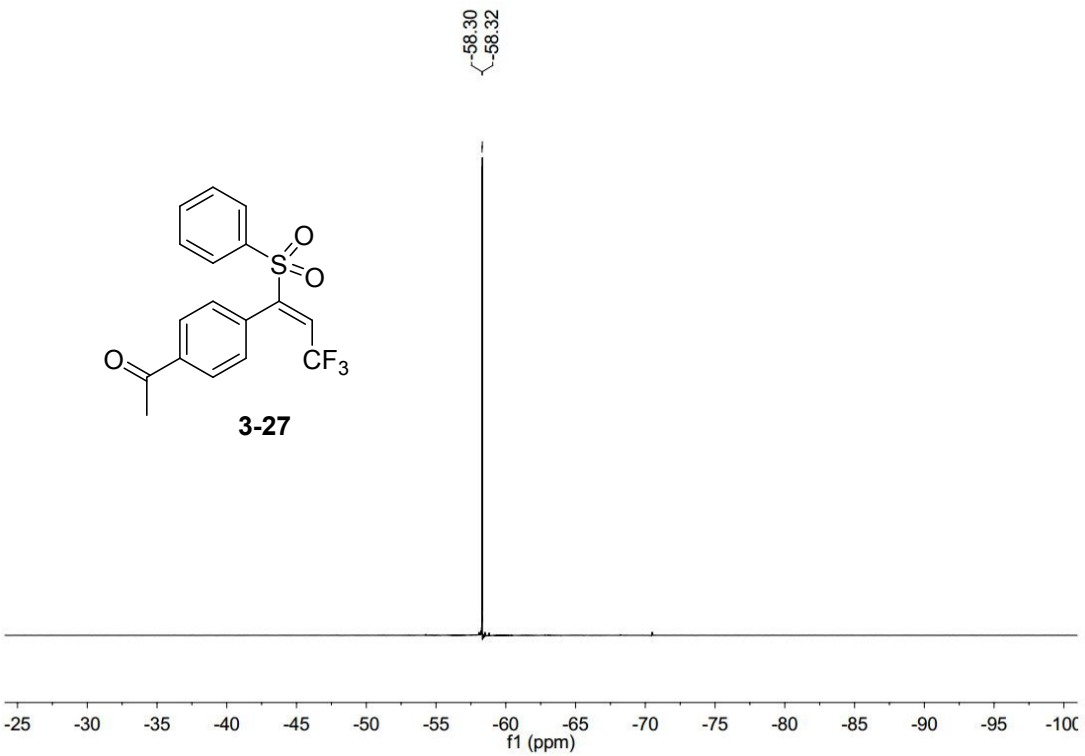
7.228
7.210
7.192
7.175
7.119
7.098
2.603
O
S
O
O
CF3
1.96
1.08
1.85
2.08
1.00
1.90
3.10
f1 (ppm)

**3-27**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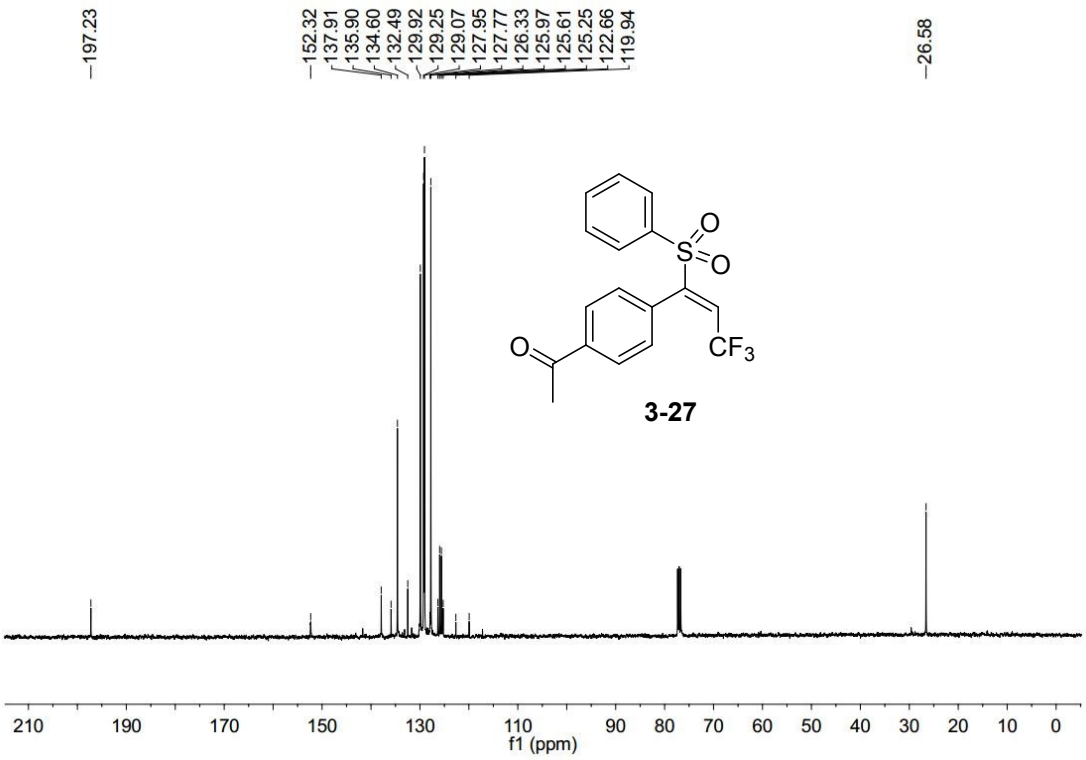
-58.32
O
S
O
O
CF3
f1 (ppm)

**3-27**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152.32
137.91
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134.60
132.49
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129.25
129.07
127.95
127.77
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125.97
125.61
125.25
122.66
119.94
26.58
O
S
O
O
CF3
3-27
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)