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Direct fluoroalkylthiolation of indoles with iodofluoroethane enabled by $Na_2S_2O_4$

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General information

Unless otherwise mentioned, solvents and reagents were purchased from commercial sources and used as received. All manipulations were carried out in glass reaction tube equipped with a magnetic stir bar. ^{1}H NMR, ^{19}F-NMR and ^{13}C NMR spectra were recorded on a Bruker AM500/300 spectrometer using d^{6}-DMSO or $CDCl_3$ as solvent, TMS as internal standard substance. Chemical shifts (δ) are reported in ppm, and coupling constants (J) are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. The Mass spectrum was received via Agilent (7000C) GC-MS/Waters (Quattro Micro).

General procedure

Synthesis of fluoroethylthiolated indoles[1, 2]

Indoles(0.3mmol) 1a, $Na_2S_2O_4$(0.5-2.7mmol), additives and 3 ml solvent were added to a Schlenk sealed tube, following iodofluoroethane 2 (0.9 mmol) was added to the mixture solution. After addition, the mixture was allowed for string 4 h under set temperature. Then, 10ml water was added, and the reaction mixture was extracted by ethyl acetate 3 times. The organic layer was combined, washed with brine for once and dried over Na_2SO_4. The solvent was removed by reduce pressure rotary evaporation and purified by column chromatography on silica gel with petroleum ether/ethyl acetate to give 3/4/5.

Synthesis of perfluoroalkylated indoles

Indoles(0.3mmol) 1a, $Na_2S_2O_4$(2.7mmol), DMSO/CH_3CN/H_2O(1/2/1) 3 ml solvent were added to a Schlenk sealed tube, following iodofluoroalkane 2 (0.9 mmol) was added to the mixture solution. After addition, the mixture was allowed for string 4-8 h under 70 ℃. Then, 10ml water was added, and the reaction mixture was extracted by ethyl acetate 3 times. The organic layer was combined, washed with brine for once and dried over Na_2SO_4. The solvent was removed by reduce pressure rotary evaporation and purified by column chromatography on silica gel with petroleum ether/ ethyl acetate to give 5c and 5d.

Control experiments of 2-methyl-3-((2,2,2-trifluoroethyl)thio)-1H-indole

2-methyl-3-((2,2,2-trifluoroethyl)thio)-1H-indole (0.3 mmol), $Na_2S_2O_4$(2.7 mmol), and 3 mL DMSO/CH_3CN/H_2O(1/2/1) solvent were added to a Schlenk sealed tube, following iodofluoroethane 2a (0.9 mmol) was added to the mixture solution and then the resulting mixture was string for 10 min. After addition, the mixture was allowed for string under 80 ℃. Then, the reaction mixture was checked by F^{19} NMR at 1h, 2h, 3h, 4h.

Optimization of reaction condition

S-Table 1 Solvent effect[a]

Entry	Solvent	Yield (%)
1	1,4-dioxane	n.d.
2	H_2O	n.d.
4	CH_3CN	trace
5	DMF	trace
6	DMSO/H_2O(1/2)	trace
7	DMSO/CH_3CN/H_2O(1/1/1)	45
8	DMSO/CH_3CN/H_2O(1/0/1)	14
9	DMSO/CH_3CN/H_2O(0/1/1)	0
10	DMSO/CH_3CN/H_2O(1/2/0.75)	47
11	DMSO/CH_3CN/H_2O(1/2/0.25)	23

[a]Reaction conditions: **1a** (0.3 mmol, 1.0 eq), **CF_3CH_2I** (0.9 mmol, 3.0 eq), $Na_2S_2O_4$ (2.7 mmol 9 eq), solvent (3.0 mL), 80℃, 4h, ^{19}F NMR yields using $PhCF_3$ as an internal standard.

S-Table 2 Additives effect[a]

Entry	additives	Yield (%)
1	$Na_2S_2O_4$/$NaHCO_3$	26
2	$Na_2S_2O_4$/Cs_2CO_3	27
3	$Na_2S_2O_4$/$NaHSO_4$	23
6	$Na_2S_2O_4$(6.0 equiv)	76
8	$Na_2S_2O_4$(8.0 equiv)	88

[a]Reaction conditions: **1a** (0.3 mmol, 1.0 eq), **CF_3CH_2I** (0.9 mmol, 3.0 eq), $Na_2S_2O_4$ (2.7 mmol 9 eq), DMSO/CH_3CN/H_2O(1/2/1) (3.0 mL), 80℃, 4h, ^{19}F NMR yields using $PhCF_3$ as an internal standard.

S-Table 3 Reaction ratio[a]

Entry	**1**(mmol)	**2**(mmol)	$Na_2S_2O_4$(mmol)	Yield (%)
1	1	1.5	3.0	24
2	1	1.5	9.0	29
3	1	6	3.0	44

[a]Reaction conditions: **1a**, **CF_3CH_2I**, $Na_2S_2O_4$, DMSO/CH_3CN/H_2O(1/2/1) solvent (3.0 mL), 80℃, 4h, ^{19}F NMR yields using $PhCF_3$ as an internal standard.

S-Table 4 Temperature effect[a]

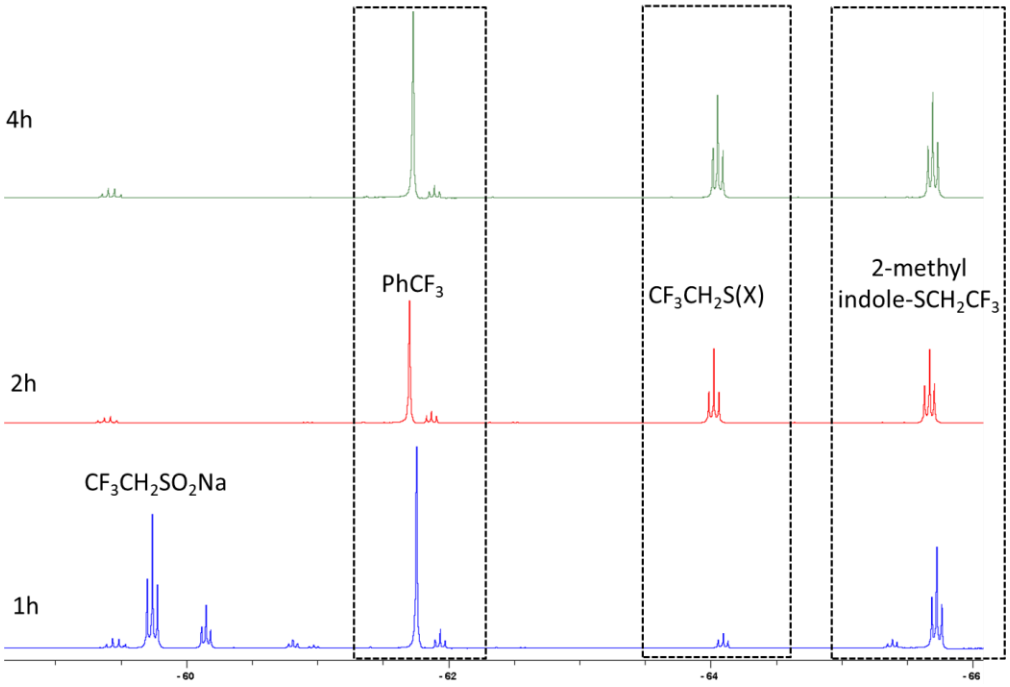
Entry	Temperature(℃)	Yield (%)
1	25	n.d
2	60	trace
3	70	77
4	80	99
9	$Na_2S_2O_4$(9.0 equiv)	99

[a]Reaction conditions: **1a** (0.3 mmol, 1.0 eq), **CF_3CH_2I** (0.9 mmol, 3.0 eq), $Na_2S_2O_4$ (2.7 mmol 9 eq), DMSO/CH_3CN/H_2O(1/2/1) (3.0 mL), 4h, ^{19}F NMR yields using $PhCF_3$ as an internal standard.

S-Table 5 Reaction time[a]

Entry	Time(h)	Yield (%)
1	1	76
2	2	87
3	3	97
4	4	99

[a]Reaction conditions: **1a** (0.3 mmol, 1.0 eq), **CF_3CH_2I** (0.9 mmol, 3.0 eq), $Na_2S_2O_4$ (2.7 mmol 9 eq), DMSO/CH_3CN/H_2O(1/2/1) (3.0 mL), 80℃, ^{19}F NMR yields using $PhCF_3$ as an internal standard.



S-Figure 1. F^{19}-NMR of Control experiments 3a[2]

Characterization data of Compounds

2-methyl-3-((2,2,2-trifluoroethyl)thio)-1H-indole 3a,[3] ^{1}H-NMR (500 MHz, DMSO-d, 293K, TMS): δ ppm 11.45 (s, 1H), 7.51 (d, *J* = 7.35 Hz, 1H), 7.33 (d, *J* = 7.50Hz, 1H), 7.12-7.02 (m, 2H), 3.40(q, *J* = 10.55 Hz, 2H). ^{13}C-NMR (125 MHz, DMSO-d): δ ppm 142.37, 135.73, 130.00, 126.67 (q, *J* = 275.03 Hz), 121.67, 120.20, 118.01, 111.64, 98.36, 38.23 (q, *J* = 29.69 Hz). ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -65.11 (t, *J* = 10.43 Hz). Calculated MS: 231.0, GC-MS(EI): 230.9.

5-methoxy-2-methyl-3-((2,2,2-trifluoroethyl)thio)-1H-indole 3b,[1] ^{1}H-NMR (500 MHz, DMSO-d, 293K, TMS): δ ppm 11.27 (s, 1H), 7.18 (d, *J* = 8.50 Hz, 1H), 6.96 (s, 1H), 6.69 (d, *J* = 8.50 Hz, 1H), 3.75 (s, 3H), 3.40 (q, *J* = 10.50 Hz, 2H), 2.42 (s, 3H). ^{13}C-NMR (125 MHz, DMSO-d): δ ppm 154.53, 142.83, 130.70, 126.73 (q, *J* = 275.13 Hz), 112.34, 111.23, 100.27, 97.96, 55.73, 37.56 (q, *J* = 29.50 Hz). ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.88 (t, *J* = 10.72 Hz). Calculated MS: 275.1, GC-MS(EI): 275.0.

5-fluoro-2-methyl-3-((2,2,2-trifluoroethyl)thio)-1H-indole 3c, ^{1}H-NMR (500 MHz, DMSO-d, 293K, TMS): δ ppm 11.56 (s, 1H), 7.34-7.27 (m, 1H), 7.18 (d, *J* = 9.00 Hz, 1H), 6.94-6.86 (m, 1H), 3.42 (q, *J* = 10.55 Hz, 2H), 2.45 (s, 3H). ^{13}C-NMR (125 MHz, DMSO-d): δ ppm 157.16, 144.56, 132.24, 130.24, 130.85 (d, *J* = 9.89 Hz), 126.67 (q, *J* = 274.71 Hz), 112.67 (d, *J* = 9.49 Hz), 109.54 (d, *J* = 25.75 Hz), 103.02 (d, *J* = 23.80 Hz), 98.61 (d, *J* = 4.38 Hz), 37.59 (q, *J* = 29.78 Hz), 12.13. ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -65.11 (t, *J* = 10.53 Hz), 123.85-123.97(m, 1F). HRMS (EI-TOF) m/z: [M+]+ Calculated for 263.0392, Found 263.0397.

2-methyl-5-nitro-3-((2,2,2-trifluoroethyl)thio)-1H-indole 3d, ^{1}H-NMR (500 MHz, DMSO-d, 293K, TMS): δ ppm 11.17 (s, 1H), 8.35 (s, 1H), 7.96 (d, *J* = 8.90 Hz, 1H), 7.46 (d, *J* = 9.00 Hz, 1H), 3.51 (q, *J* = 10.50 Hz, 2H), 2.48 (s, 3H). ^{13}C-NMR (125 MHz, DMSO-d): δ ppm 146.86, 141.81, 139.07, 129.70, 126.60 (q, *J* = 274.98 Hz), 117.27, 114.69, 112.13, 101.32, 37.60 (q, *J* = 29.88 Hz), 12.20. ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -65.13 (t, *J* = 10.49 Hz). HRMS (EI-TOF) m/z: [M+]+ Calculated for 290.0337, Found 290.0346.

2-(4-fluorophenyl)-3-((2,2,2-trifluoroethyl)thio)-1H-indole 3e, ^{1}H-NMR (500 MHz, DMSO-d, 293K, TMS): δ ppm 11.90 (s, 1H), 7.98-7.93 (m, 2H), 7.66 (d, *J* = 7.60 Hz, 1H), 7.44 (d, *J* = 8.00 Hz, 1H), 7.39-7.33-7.93 (m, 2H), 7.22-7.12 (m, 2H), 3.50 (q, *J* = 10.51 Hz, 2H). ^{13}C-NMR (125 MHz, DMSO-d): δ ppm 163.52, 161.57, 141.18, 136.24, 131.10(d, *J* = 8.23 Hz), 130.67, 128.36, 126.44 (q, *J* = 274.69 Hz), 123.06, 120.82, 119.06, 115.99, 115.81, 112.35, 98.88, 37.78 (q, *J* = 30.10 Hz). ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.76 (t, *J* = 10.46 Hz). HRMS (EI-TOF) m/z: [M+]+ Calculated for 325.0548, Found 325.0553.

1-methyl-2-phenyl-3-((2,2,2-trifluoroethyl)thio)-1H-indole 3f,[3] ^{1}H-NMR (300 MHz, DMSO-d, 293K, TMS): δ ppm 7.71 (d, *J* = 7.56 Hz, 1H), 7.63-7.49(m, 6H), 7.35-7.18(m, 2H), 3.63(s, 3H), 3.42 (q, *J* = 10.61 Hz, 2H). ^{13}C-NMR (75 MHz, DMSO-d): 145.85, 137.17, 131.21, 130.55, 129.31, 129.24, 128.71, 126.37 (q, *J* = 274.88Hz), 122.91, 121.07, 119.06, 111.13, 100.06, 38.05(q, *J* = 30.11Hz), 31.86. ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.87 (t, *J* =

10.74 Hz), Calculated MS: 321.1, GC-MS(EI): 320.8.

4-methyl-3-((2,2,2-trifluoroethyl)thio)-1H-indole 3g,[2] ^{1}H-NMR (300 MHz, DMSO-d, 293K, TMS): δ ppm 11.50 (s, 1H) , 7.56 (d, *J* = 2.67 Hz, 1H) , 7.24 (d, *J* = 8.08 Hz, 1H), 7.03 (t, *J* = 7.95 Hz, 1H), 6.81 (d, *J* = 7.08 Hz, 1H), 3.55 (q, *J* = 10.59 Hz, 2H). ^{13}C-NMR (75 MHz, DMSO-d): 136.58, 132.80, 129.99, 126.34 (q, *J* = 275.03 Hz), 126.12, 121.92, 121.65, 110.15, 101.14, 39.97(covered), 18.83. ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.36 (t, *J* = 10.50 Hz), Calculated MS: 231.0, GC-MS(EI): 230.9.

7-methyl-3-((2,2,2-trifluoroethyl)thio)-1H-indole 3h,[2] ^{1}H-NMR (300 MHz, DMSO-d, 293K, TMS): δ ppm 11.52(s, 1H) , 7.61 (d, *J* = 2.73Hz, 1H) , 7.44 (d, *J* = 7.68 Hz, 1H), 7.11-7.68(m, 2H), 3.52(q, *J* = 10.56Hz, 2H), 2.49(s, 3H). ^{13}C-NMR (75 MHz, DMSO-d): 135.71, 131.51, 128.32, 126.23 (q, *J* = 274.77Hz), 122.46, 121.47, 120.15, 115.79, 105.38, 37.98(q, *J* = 29.69Hz), 16.58. ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.93 (t, *J* = 10.41 Hz), Calculated MS: 245.0, GC-MS(EI): 244.8.

3-((2,2,2-trifluoroethyl)thio)-1H-indole 3i,[2] ^{1}H-NMR (300 MHz, DMSO-d, 293K, TMS): δ ppm 11.54 (s, 1H), 7.66-7.60 (m, 2H), 7.48-7.38 (m, 1H), 7.23-7.04 (m, 2H) 3.53(q, *J* =10.56 Hz, 2H). ^{13}C-NMR (75 MHz, DMSO-d): δ ppm 136.25, 131.92, 128.60, 126.24 (q, *J* = 274.63 Hz), 121.99, 119.97, 118.22, 112.22, 101.06, 38.00 (q, *J* = 29.78 Hz). ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.96 (t, *J* = 10.02 Hz), Calculated MS: 231.0, GC-MS(EI): 230.9.

5-methoxy-3-((2,2,2-trifluoroethyl)thio)-1H-indole 3j,[2] ^{1}H-NMR (300 MHz, DMSO-d, 293K, TMS): δ ppm 11.38 (s, 1H) , 7.55 (d, *J* = 2.71 Hz, 1H), 7.33 (d, *J* = 8.76 Hz, 1H), 7.06(d, *J* = 2.22 Hz, 1H), 6.82 (dd, J_1= 2.40Hz, J_2= 8.76Hz , 1H), 3.79(s, 3H), 3.51(q, *J* = 10.59 Hz, 2H). ^{13}C-NMR (75 MHz, DMSO-d): 154.24, 132.41, 131.17, 129.29, 126.30(q, *J* = 274.63Hz), 113.04, 112.22, 100.55, 99.77, 55.29, 37.92(q, *J* = 29.56Hz). ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.88 (t, *J* = 10.74 Hz), Calculated MS: 261.0, GC-MS(EI): 260.8.

7-methoxy-3-((2,2,2-trifluoroethyl)thio)-1H-indole 3k,[3] ^{1}H-NMR (300 MHz, DMSO-d, 293K, TMS): δ ppm 11.67 (s, 1H) , 7.48 (d, *J* = 2.70 Hz, 1H), 7.19 (d, *J* = 7.95 Hz, 1H), 7.06(t, *J* = 7.86 Hz, 1H), 6.72 (d, *J* = 7.59Hz, 1H), 3.90(s, 3H), 3.51(q, *J* = 10.56 Hz, 2H). ^{13}C-NMR (75 MHz, DMSO-d): 146.53, 131.30, 130.21, 126.30, 126.24(q, *J* = 274.65Hz), 120.77, 110.91, 102.47, 101.91, 55.26, 37.99(q, *J* = 29.89Hz). ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.94 (t, *J* = 10.54 Hz), Calculated MS: 261.0, GC-MS(EI): 260.8.

3-((2,2,2-trifluoroethyl)thio)-1H-indole-5-carbonitrile 3l,[2] ^{1}H-NMR (300 MHz, DMSO-d, 293K, TMS): δ ppm 12.06(s, 1H), 8.06(s, 1H), 7.85(d, *J* = 2.58 Hz, 1H), 7.60(d, *J* = 8.31 Hz, 1H), 7.53(dd, J_1=1.44Hz, J_2=8.49Hz , 2H), 3.62(q, *J* = 10.35 Hz, 2H). ^{13}C-NMR (75 MHz, DMSO-d): 138.14, 134.58, 128.50, 126.06(q, *J* = 275.27 Hz), 124.79, 123.88, 120.38, 114.22, 102.55, 102.25, 37.97(q, *J* = 29.44Hz). ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.88 (t, *J* = Hz), Calculated MS: 256.0, GC-MS(EI): 255.8.

fluoro-3-((2,2,2-trifluoroethyl)thio)-1H-indole 3m,[3] ^{1}H-NMR (300 MHz, DMSO-d, 293K,

TMS): δ ppm 11.64(s, 1H), 7.69-7.45(d, *J* = 2.67Hz, 2H), 7.43(dd, J_1= 4.55 Hz, J_2 = 8.76Hz , 1H), 7.30 (dd, J_1=2.40Hz, J_2= 9.60Hz , 1H), 3.53(q, *J* = 10.56 Hz, 2H). ^{13}C-NMR (75 MHz, DMSO-d): 158.08(d, *J* = 231.81Hz), 134.44, 133.26, 129.77(d, *J* = 9.89Hz), 126.64(q, *J* = 274.79Hz), 125.79(s), 113.87(d, *J* = 9.53Hz), 110.70(d, *J* = 26.02Hz), 103.46(d, *J* = 23.73Hz), 101.61(d, *J* = 4.75Hz), 38.30(q, *J* = 29.74Hz). ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.93 (t, *J* = 10.59 Hz, 3F), -123.44~-123.56(m, 1F) Calculated MS: 249.0, GC-MS(EI): 248.8.

5-chloro-3-((2,2,2-trifluoroethyl)thio)-1H-indole 3n,[2] ^{1}H-NMR (300 MHz, DMSO-d, 293K, TMS): δ ppm 11.74(s, 1H), 7.72(d, *J* = 2.64 Hz, 1H), 7.61(d, *J* = 1.83 Hz, 1H), 7.47(d, *J* = 8.58Hz, 1H), 7.18(dd, J_1 = 2.01 Hz, J_2 = 8.58 Hz , 1H), 3.57(q, *J* = 10.56 Hz, 2H). ^{13}C-NMR (75 MHz, DMSO-d): 134.73, 133.80, 129.99, 126.21(q, *J* = 274.74Hz), 124.91, 122.07, 117.51, 113.89, 100.98, 37.93(q, *J* = 29.83Hz). ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.96 (t, *J* = 10.36 Hz), Calculated MS: 265.0, GC-MS(EI): 264.8.

5-bromo-3-((2,2,2-trifluoroethyl)thio)-1H-indole 3o,[2] ^{1}H-NMR (300 MHz, DMSO-d, 293K, TMS): δ ppm 11.74(s, 1H), 7.75(d, *J* = 1.56 Hz, 1H), 7.71(d, *J* = 2.64 Hz, 1H), 7.43(d, *J* = 8.58Hz, 1H), 7.30(dd, J_1=1.86Hz, J_2=8.55Hz , 1H), 3.57(q, *J* = 10.56 Hz, 2H). ^{13}C-NMR (75 MHz, DMSO-d): 134.98, 133.63, 130.61, 126.21(q, *J* = 274.50Hz), 124.59, 120.55, 114.33, 112.74, 100.77, 37.92(q, *J* = 29.67Hz). ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.93 (t, *J* = Hz), Calculated MS: 308.9, GC-MS(EI): 308.9.

5,5'-difluoro-3-((2,2,2-trifluoroethyl)thio)-1H,1'H-2,3'-biindole 4m, ^{1}H-NMR (500 MHz, DMSO-d, 293K, TMS): δ ppm 11.82 (s, 1H), 11.22 (s, 1H), 7.89 (s, 1H), 7.49-7.45 (m, 1H), 7.24-7.17 (m, 3H), 7.03-6.97 (m, 1H), 6.91-6.86 (m, 1H), 3.55 (q, *J* = 10.50 Hz, 2H). ^{13}C-NMR (125 MHz, DMSO-d): δ ppm 158.19 (d, *J* = 232.36 Hz), 158.14 (d, *J* = 232.46 Hz) 140.97, 135.04, 133.61, 133.40, 130.98 (d, *J* = 10.15 Hz), 129.75 (d, *J* = 10.01 Hz), 126.55 (q, *J* = 274.88 Hz), 114.06 (d, *J* = 9.68 Hz), 110.92 (d, *J* = 23.99 Hz), 110.37 (d, *J* = 25.83 Hz), 103.40 (d, *J* = 23.86 Hz), 102.96 (d, *J* = 23.99Hz), 101.24 (d, *J* = 4.24 Hz), 98.42 (d, *J* = 4.61 Hz), 37.542 (q, *J* = 30.09 Hz), 12.13. ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.84 (t, *J* = 10.49 Hz, -CF_3), -122.92~-123.00 (m, Ph-F), -123.11~-123.22(m, Ph-F). HRMS (EI-TOF) m/z: [M+]+ Calculated for 382.0563, Found 382.0575.

5,5'-dichloro-3-((2,2,2-trifluoroethyl)thio)-1H,1'H-2,3'-biindole 4n, ^{1}H-NMR (500 MHz, DMSO-d, 293K, TMS): δ ppm 11.92 (s, 1H), 11.29 (s, 1H), 7.92 (s, 1H), 7.53-7.45 (m, 3H), 7.23 (d, *J* = 8.55 Hz, 1H), 7.16 (d, *J* = 8.77 Hz, 1H), 7.05 (d, *J* = 8.60 Hz, 1H), 3.59 (q, *J* = 10.45 Hz, 2H). ^{13}C-NMR (125 MHz, DMSO-d): δ ppm 140.97, 135.55, 135.34, 134.95, 131.56, 130.40, 126.54 (q, *J* = 274.66 Hz), 125.64, 125.51, 122.73, 122.28, 117.80, 117.20, 114.49, 113.56, 100.74, 97.87, 37.43 (q, *J* = 30.38 Hz). ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.83 (t, *J* = 10.66 Hz). HRMS (EI-TOF) m/z: [M+]+ Calculated for 413.9972, Found 413.9981.

5,5'-dibromo-3-((2,2,2-trifluoroethyl)thio)-1H, 1'H-2,3'-biindole 4o, ^{1}H-NMR (500 MHz, DMSO-d, 293K, TMS): δ ppm 11.92 (s, 1H), 11.27 (s, 1H), 7.89 (s, 1H), 7.61-7.57 (m, 2H),

7.27 (d, *J* = 8.60 Hz, 1H), 7.19-7.14 (m, 2H), 3.58 (q, *J* = 10.50 Hz, 2H). ^{13}C-NMR (125 MHz, DMSO-d): δ ppm 140.80, 135.79, 135.59, 134.82, 132.14, 131.01, 126.54 (q, *J* = 274.54 Hz), 125.26, 124.84, 120.80, 114.93, 113.98, 113.54, 113.40, 100.55, 97.65, 37.38 (q, *J* = 30.48 Hz). ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -64.83 (t, *J* = 10.35 Hz). HRMS (EI-TOF) m/z: [M+]+ Calculated for 501.8962, Found 501.8970.

3-((2,2-difluoroethyl)thio)-2-methyl-1H-indole 5a,[3] ^{1}H-NMR (300 MHz, $CDCl_3$, 293K, TMS): δ ppm 11.44 (s, 1H), 7.59-7.44 (m, 1H), 7.40-7.30 (m, 1H),7.16-7.00 (m, 2H), 5.97 (tt, J_1 = 4.38Hz, J_2 = 56.43Hz , 1H), 3.02 (td, J_1 = 4.38Hz, J_2 = 16.20Hz , 2H), 2.50 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ ppm 141.44, 135.20, 129.77, 121.16, 117.47, 116.17 (t, *J* = 239.21Hz), 111.15, 98.17, 38.14 (q, *J* = 22.20 Hz), 11.65. ^{19}F-NMR (282 MHz, $CDCl_3$) δ ppm -114.80(dt, J_1=16.11Hz, J_2=56.53Hz), Calculated MS: 227.1, GC-MS(EI): 227.0.

3-((2-fluoroethyl)thio)-2-methyl-1H-indole 5b,[3] ^{1}H-NMR (300 MHz, $CDCl_3$, 293K, TMS): δ ppm 11.39 (s, 1H), 7.54-7.44 (m, 1H), 7.36-7.24 (m, 1H), 7.13-7.00(m, 2H), 4.37(dt, J_1=6.31Hz, J_2=47.42Hz, 2H), 2.86(dt, J_1=6.35Hz, J_2=20.42Hz, 2H), 2.46 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ ppm 141.33, 135.28, 130.12, 121.06, 120.57, 117.56, 111.07, 98.43, 81.63 (d, *J* = 167.37 Hz), 35.33(d, *J* = 19.61Hz), 11.63. ^{19}F-NMR (282 MHz, $CDCl_3$) δ ppm -212.90 (tt, J_1=20.41Hz, J_2=47.32Hz), Calculated MS: 209.1, GC-MS(EI): 208.9.

2-methyl-3-(trifluoromethyl)-1H-indole 5c,[4] ^{1}H-NMR (500 MHz, DMSO-d, 293K, TMS): δ ppm 11.75 (s, 1H), 7.50 (d, *J* = 12.40 Hz, 1H), 7.39 (d, *J* = 12.5 Hz, 1H), 7.18-7.06 (m, 2H), 2.50 (s, 3H). ^{13}C-NMR (125 MHz, DMSO-d): δ ppm 137.61(q, *J* = 4.08 Hz), 135.06, 126.18 (q, *J* = 264.34 Hz), 125.04, 122.25, 121.08, 118.12, 111.91, 100.66 (q, *J* = 34.48 Hz), 12.57. ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -52.68 (s, $-CF_3$). Calculated MS: 199.1, GC-MS(EI): 199.0.

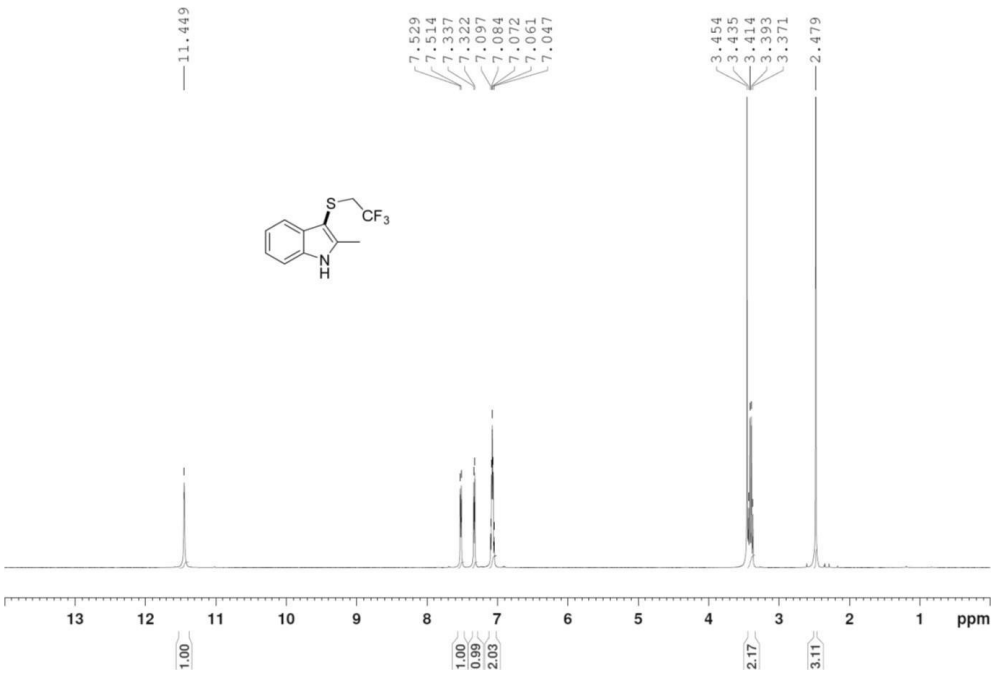
2- methyl-3-(perfluorobutyl)-1H-indole 5d,[4] ^{1}H-NMR (500 MHz, DMSO-d, 293K, TMS): δ ppm 11.85 (s, 1H), 7.42 (d, *J* = 7.89 Hz, 1H), 7.37 (d, *J* = 8.25 Hz, 1H), 7.14-7.01 (m, 2H), 2.44 (s, 3H). ^{13}C-NMR (125 MHz, DMSO-d): δ ppm 139.22 (q, *J* = 4.96 Hz), 135.33, 126.10, 122.18, 121.09, 118.63, 111.92, 98.09 (q, *J* = 26.78 Hz), 12.68, 122.00-110.00 (m, C_4F_9). ^{19}F-NMR (282 MHz, DMSO-d) δ ppm -80.79~-80.89 (m, $-CF_3$), -123.48 (q, *J* = 11.89 Hz, $-CF_2$-), 122.89 (q, *J* = 8.72 Hz, $-CF_2$-), -125.72~-125.83 (m, $-CF_2$-). Calculated MS: 349.1, GC-MS(EI): 348.9.

Reference

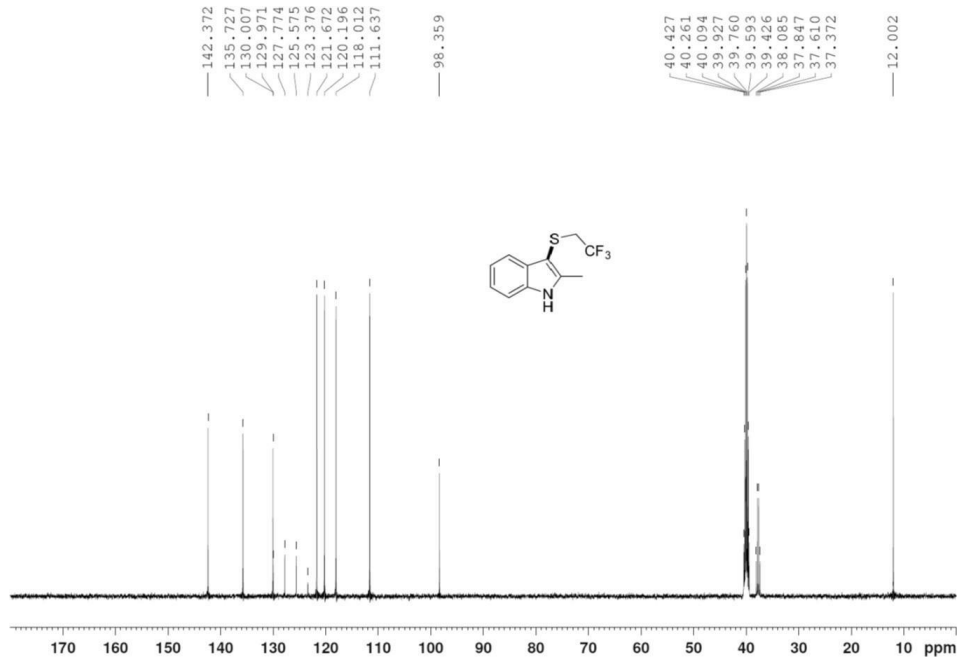
1. Q. Yan, L. Jiang, W. Yi, Q. Liu and W. Zhang, *Advanced Synthesis & Catalysis*, 2017, **359**, 2471-2480.
2. R. Wang, L. Jiang and W. Yi, *The Journal of Organic Chemistry*, 2018, **83**, 7789-7798.
3. F. Leng, J. Huang, N. Yu and G. Wang, *Tetrahedron Letters*, 2021, **85**, 153488.
4. A. Ghosh, M. Lecomte, S.-H. Kim-Lee and A. T. Radosevich, *Angewandte Chemie International Edition*, 2019, **58**, 2864-2869.

Copies of NMR spectra

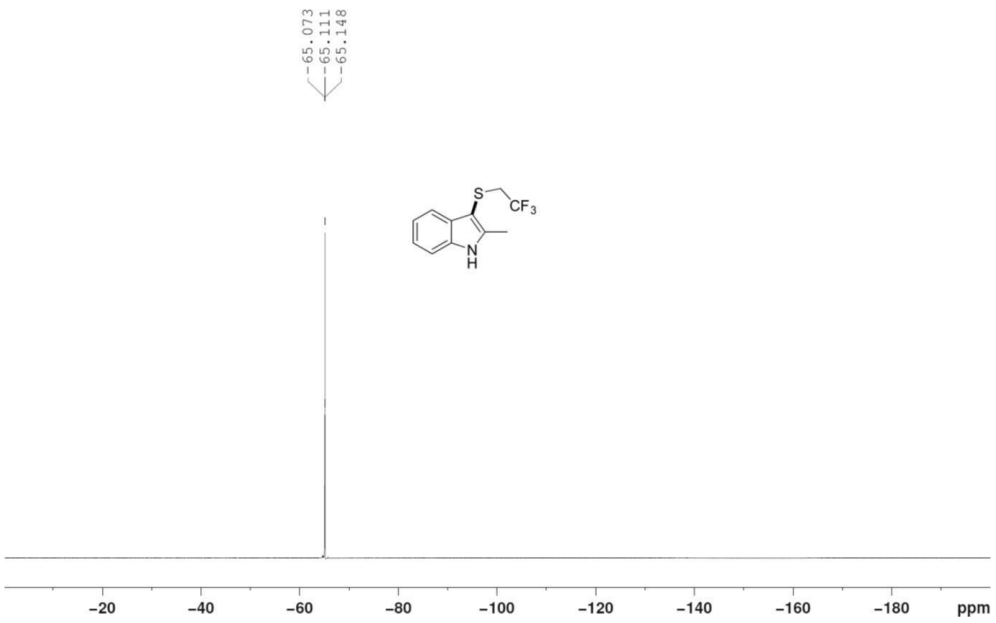
^{1}H-NMR(d-DMSO, 500MHz) of 3a



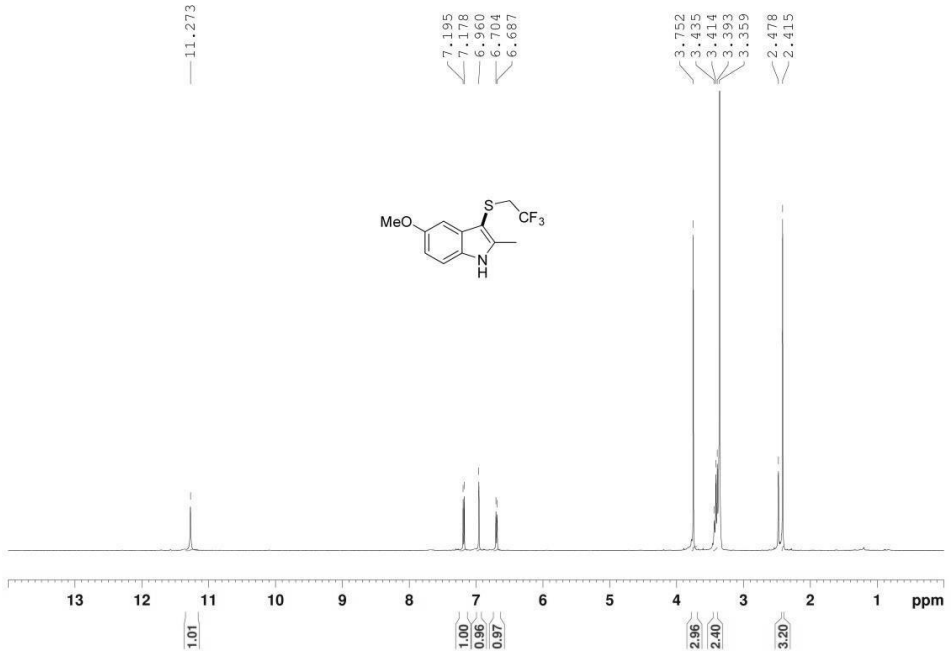
^{13}C-NMR(d-DMSO, 125MHz) of 3a



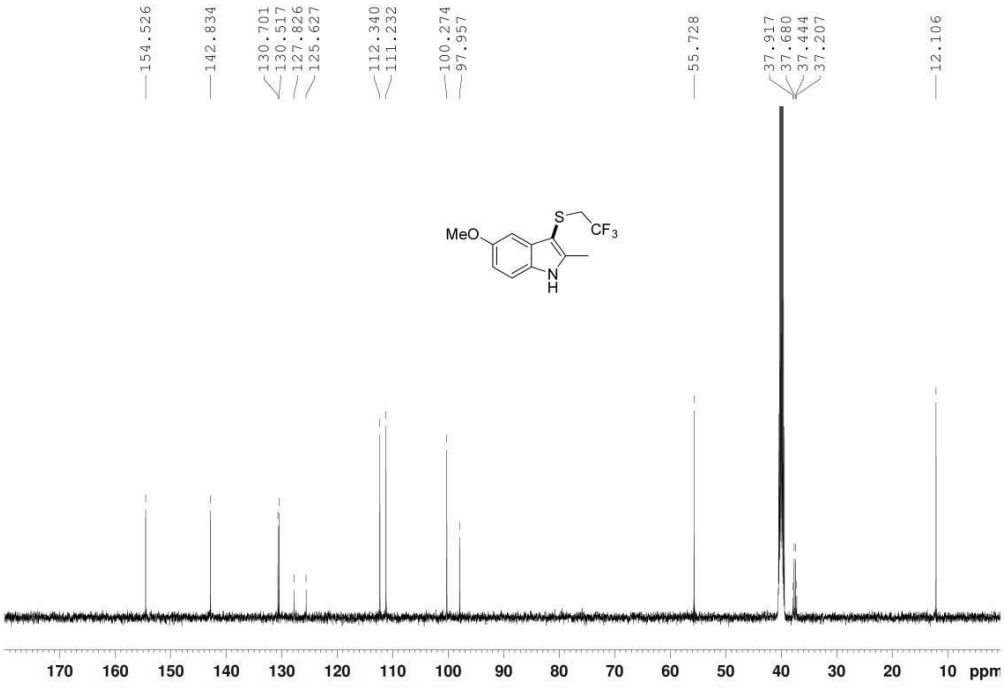
^{19}F-NMR(d-DMSO, 282MHz) of 3a



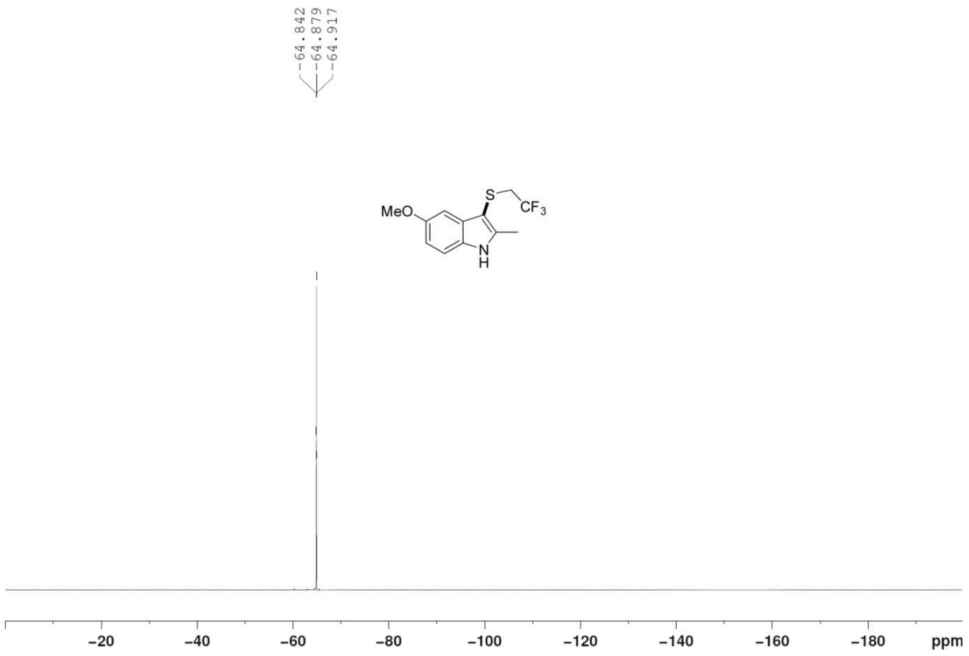
^{1}H-NMR(d-DMSO, 500MHz) of 3b



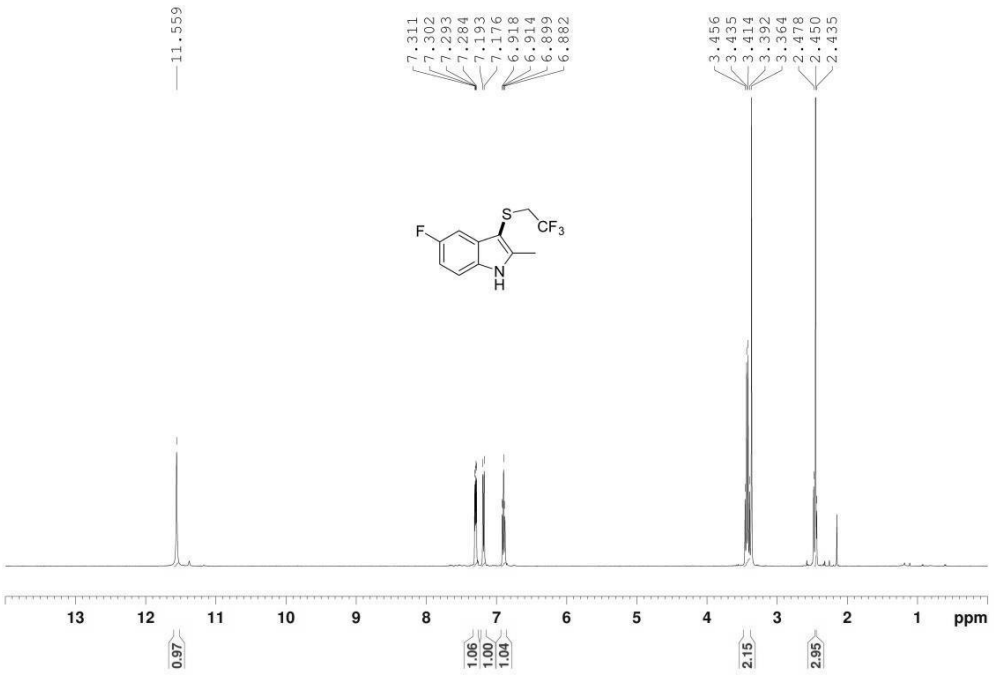
^{13}C-NMR(d-DMSO, 125MHz) of 3b



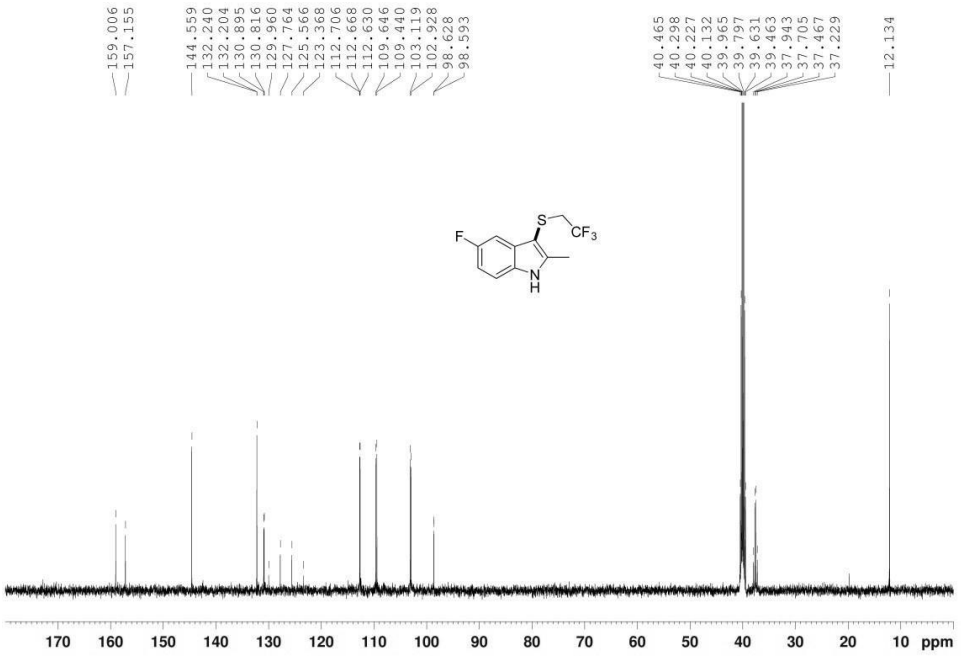
^{19}F-NMR(d-DMSO, 282MHz) of 3b



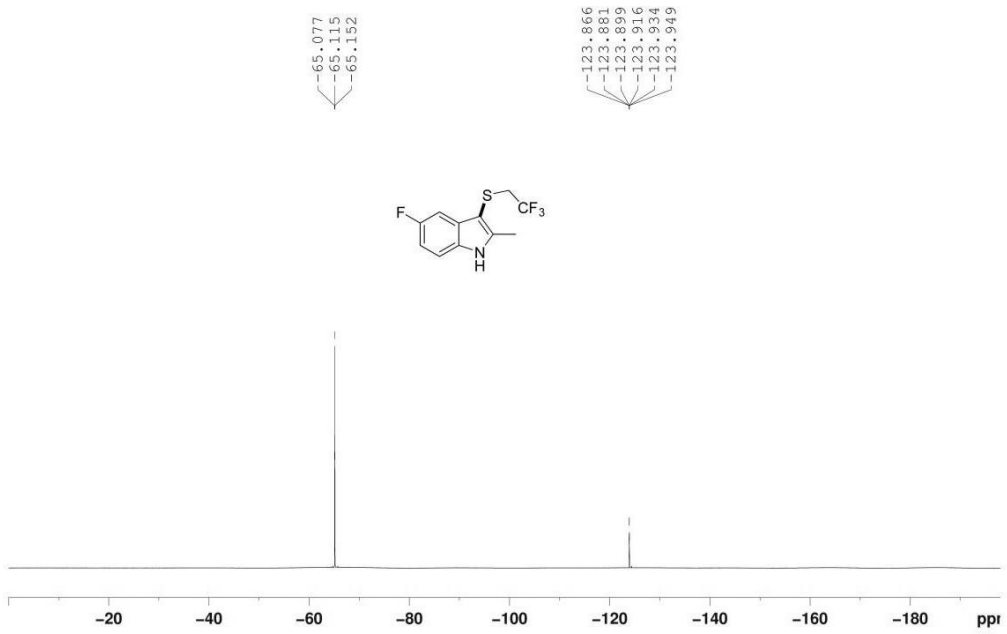
[1]H-NMR(d-DMSO, 500MHz) of 3c



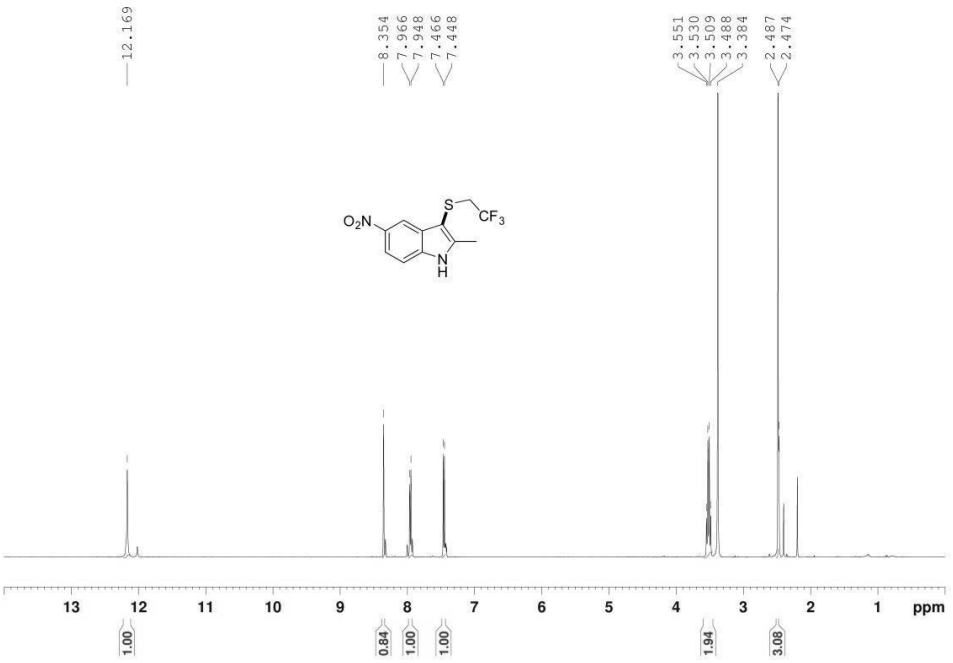
[13]C-NMR(d-DMSO, 125MHz) of 3c



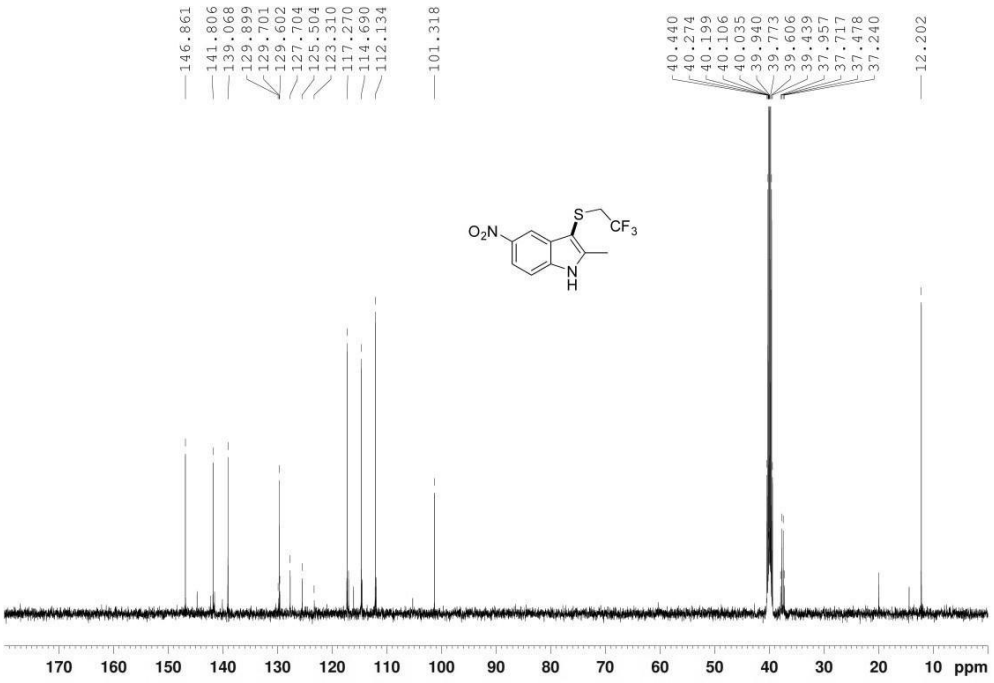
^{19}F-NMR(d-DMSO, 282MHz) of 3c



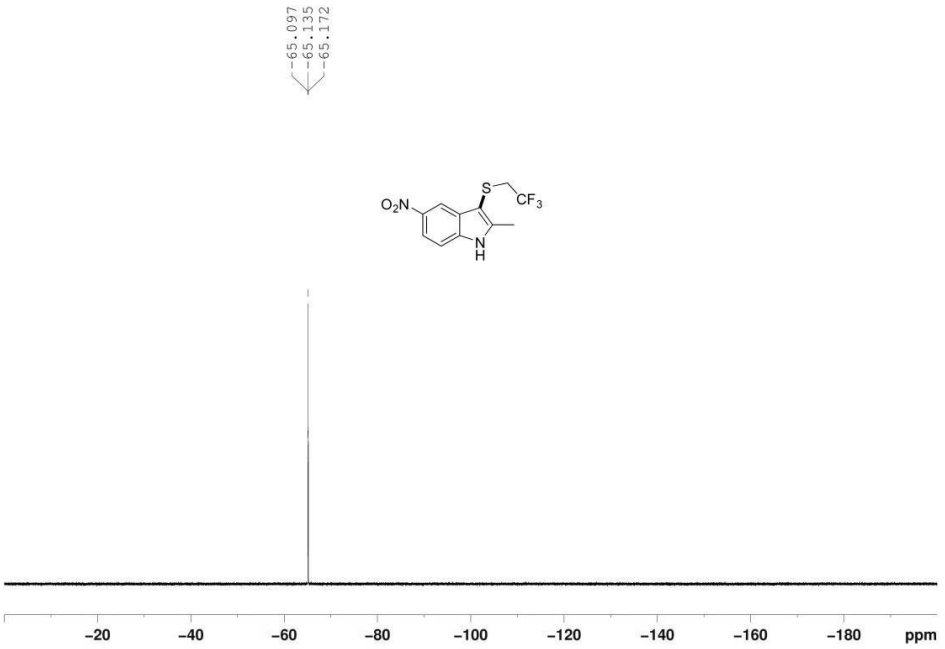
^{1}H-NMR(d-DMSO, 500MHz) of 3d



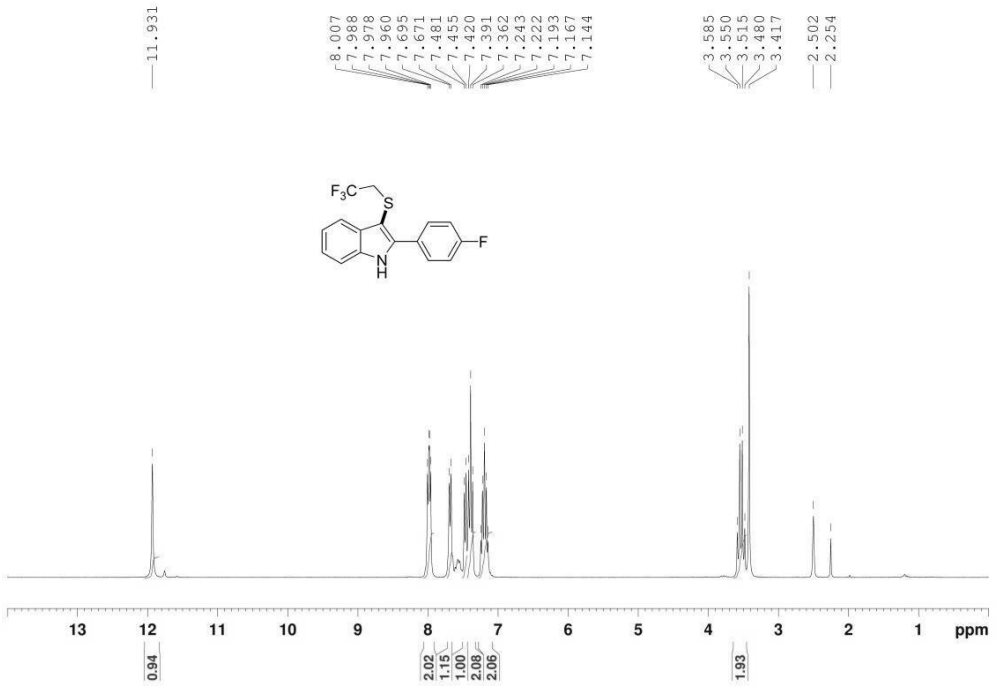
^{13}C-NMR(d-DMSO, 125MHz) of 3d



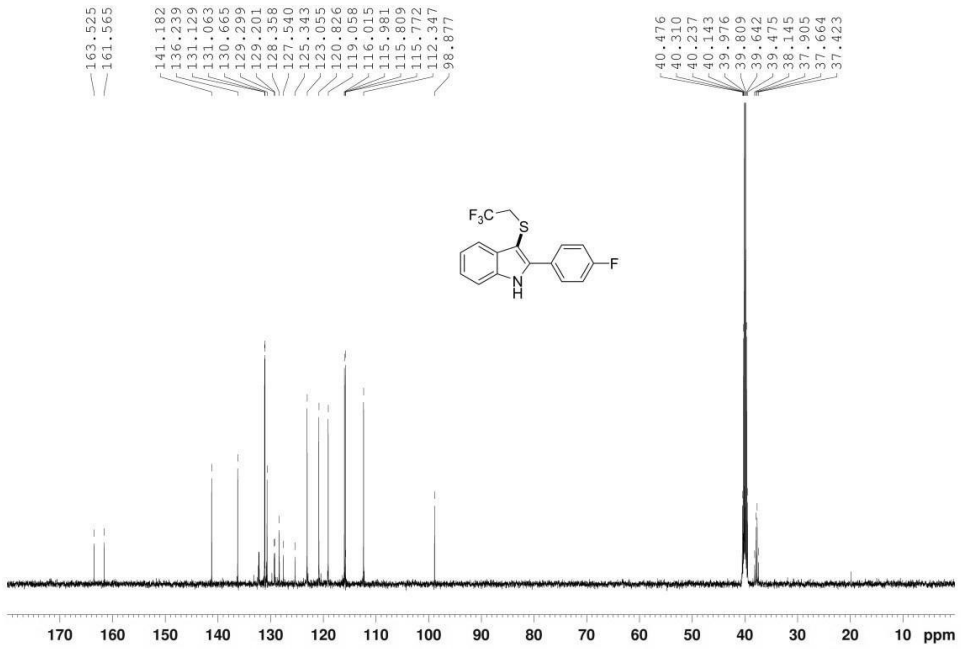
^{19}F-NMR(d-DMSO, 282MHz) of 3d



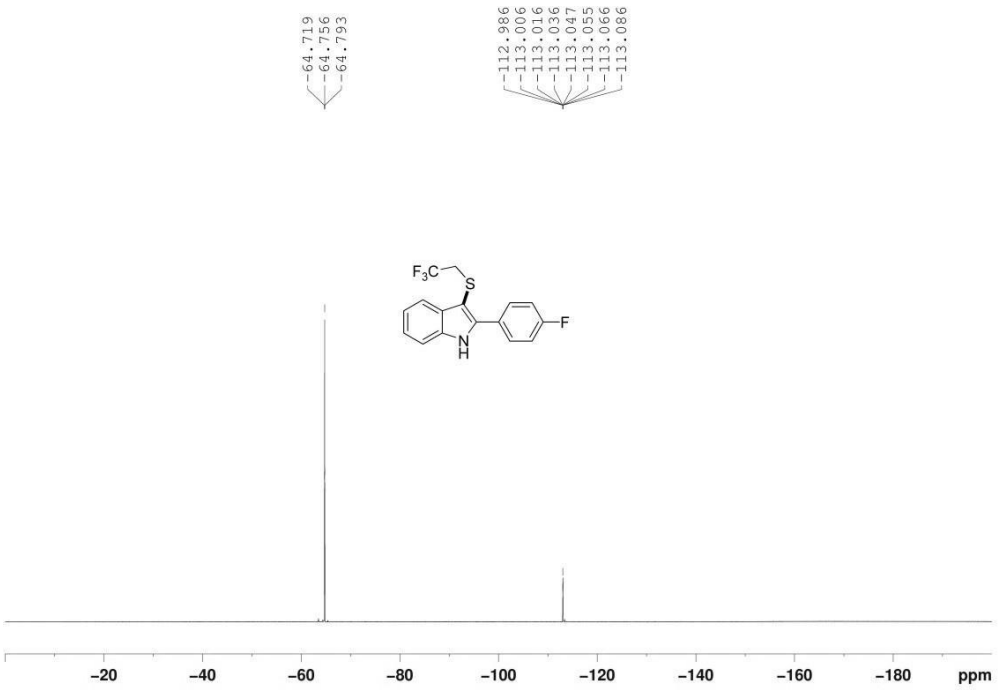
^{1}H-NMR(d-DMSO, 500MHz) of 3e



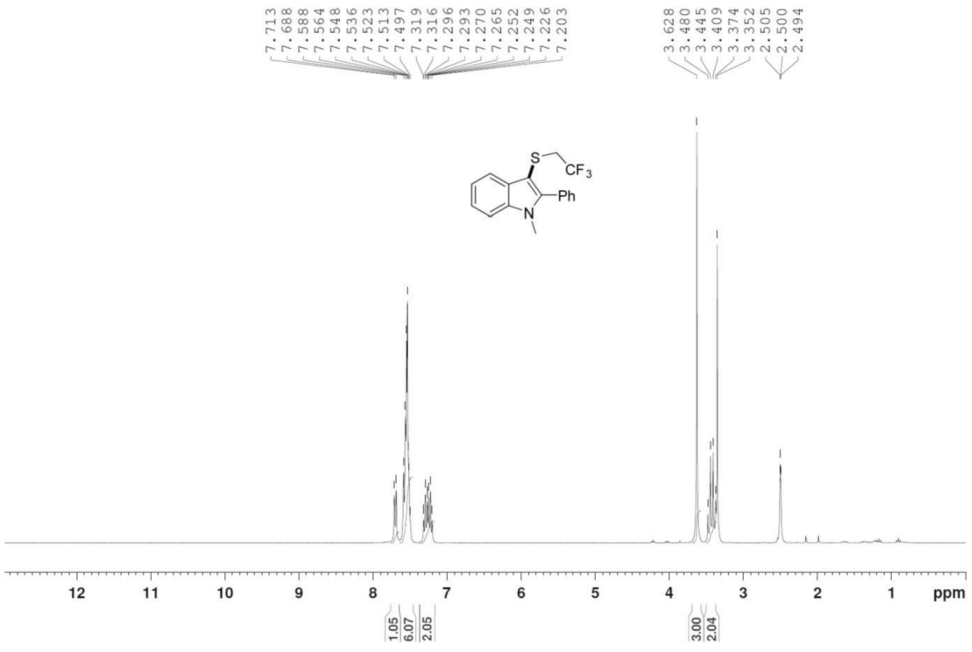
^{13}C-NMR(d-DMSO, 125MHz) of 3e



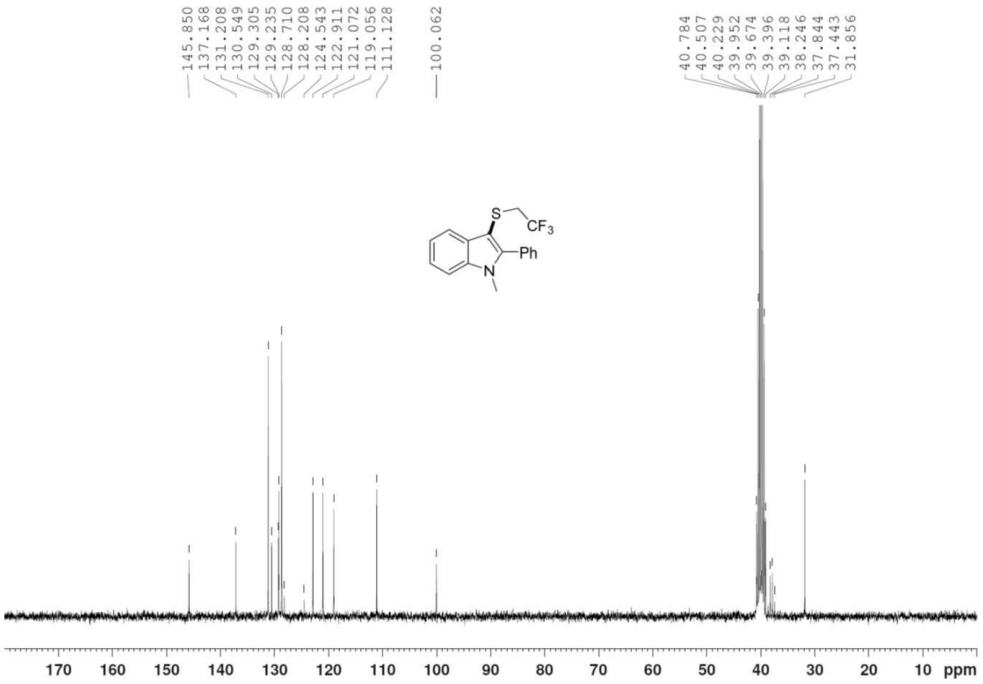
^{19}F-NMR(d-DMSO, 282MHz) of 3e



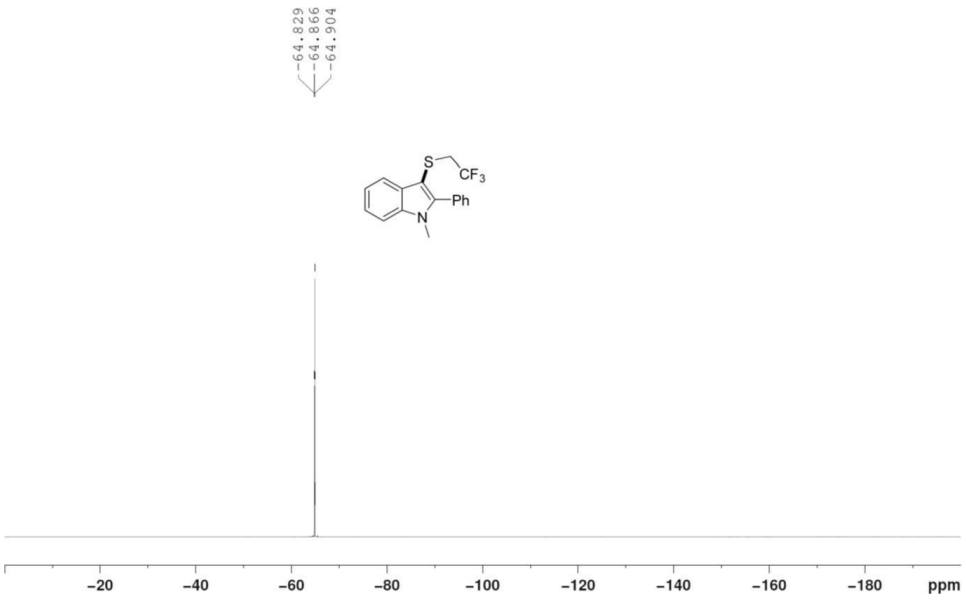
^{1}H-NMR(d-DMSO, 300MHz) of 3f



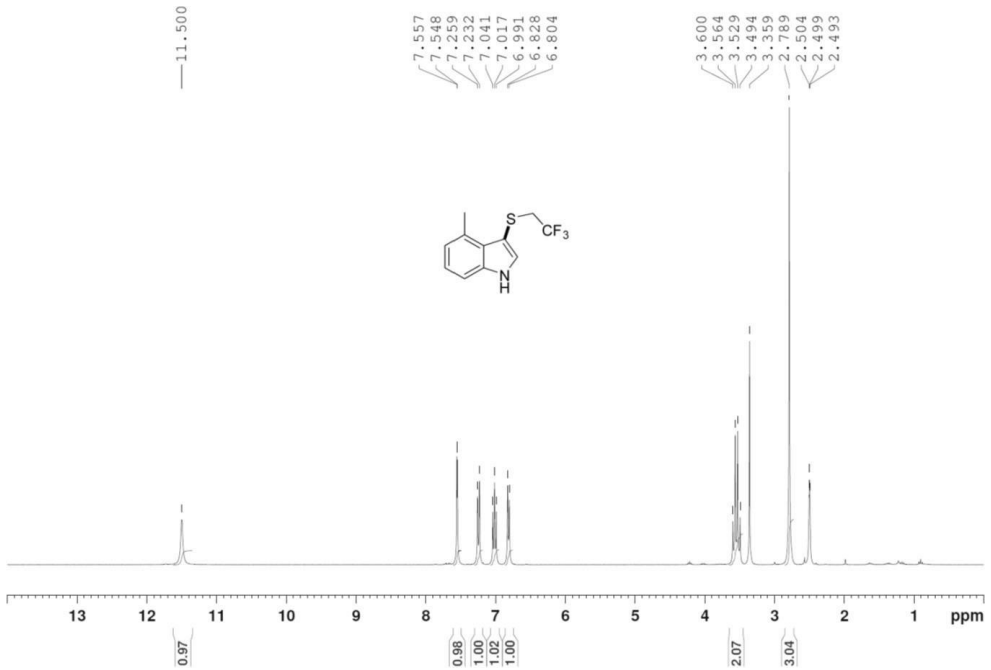
^{13}C-NMR(d-DMSO, 75MHz) of 3f



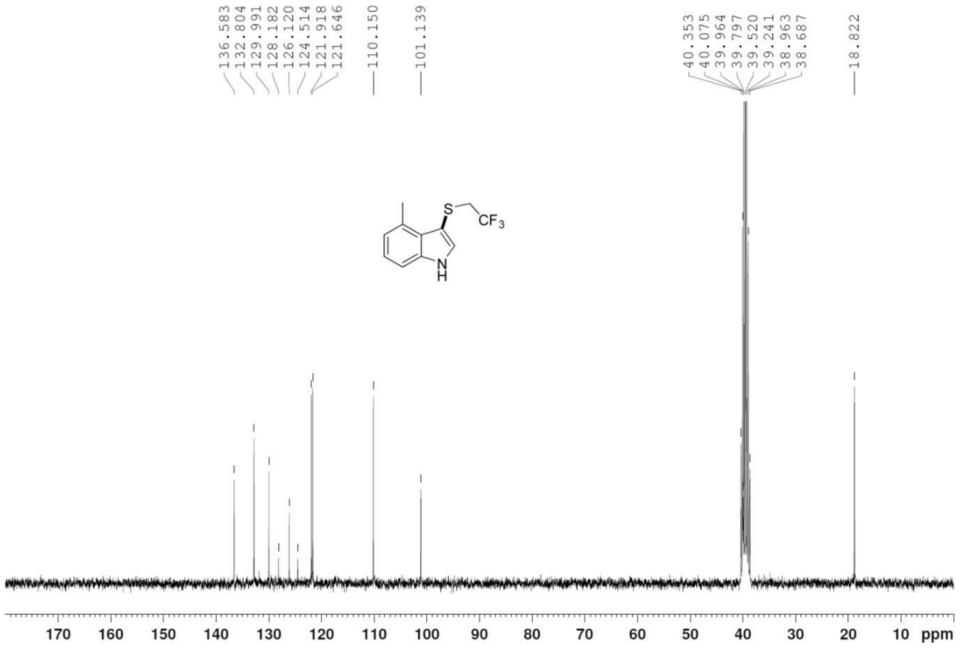
^{19}F-NMR(d-DMSO, 282MHz) of 3f



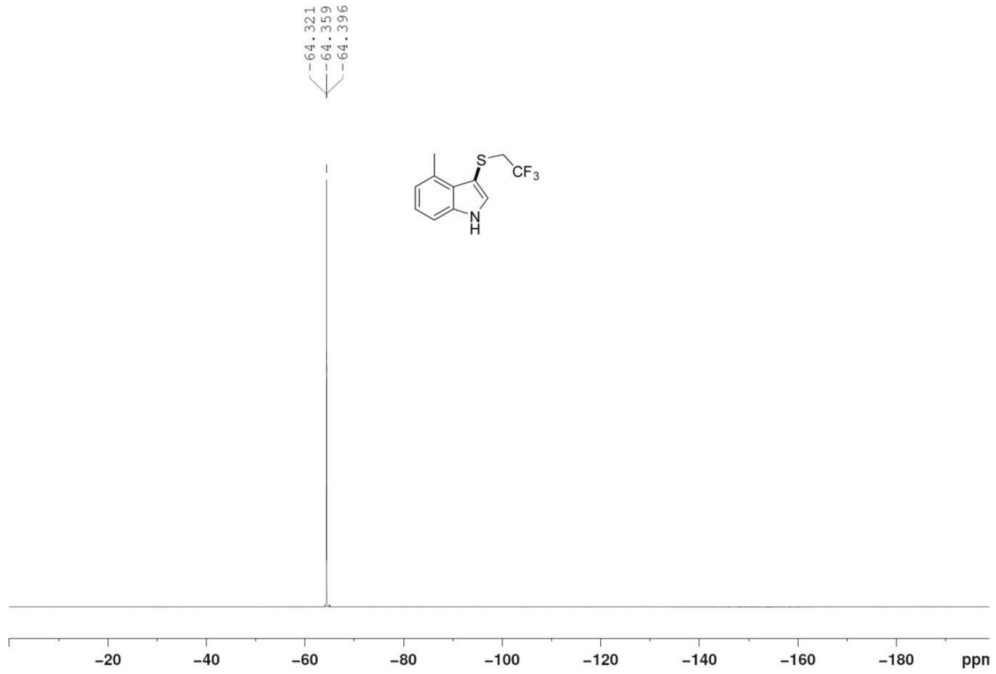
^{1}H-NMR(d-DMSO, 300MHz) of 3g



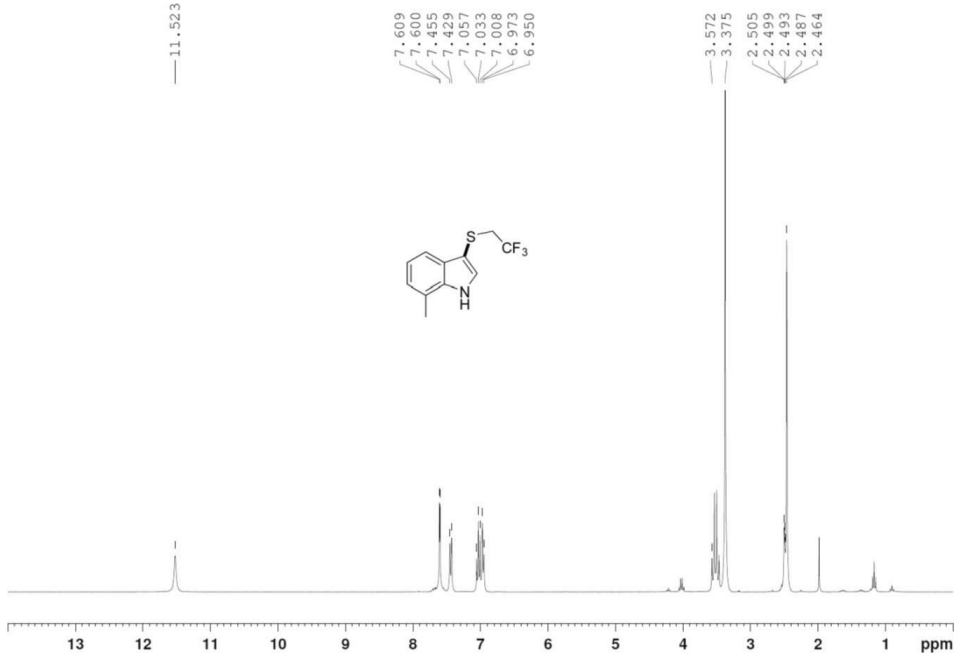
^{13}C-NMR(d-DMSO, 75MHz) of 3g



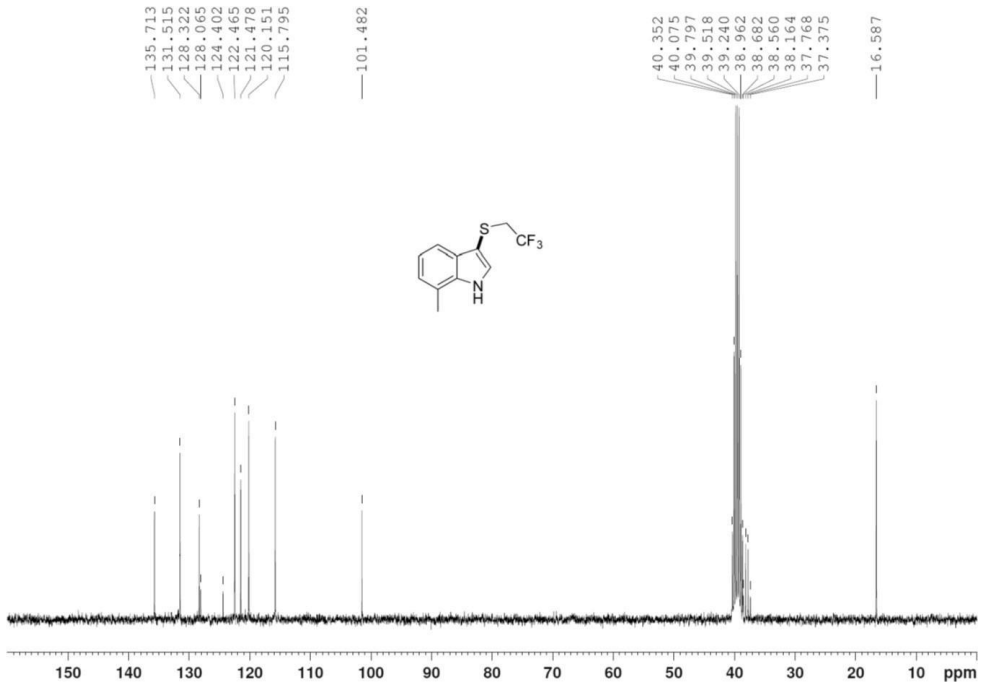
^{19}F-NMR(d-DMSO, 282MHz) of 3g



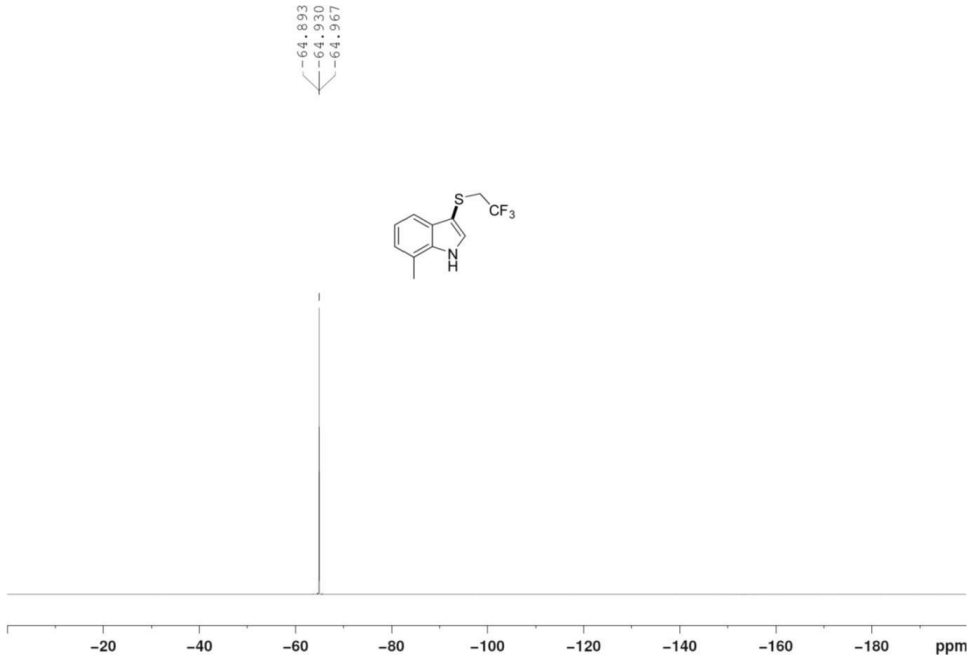
^{1}H-NMR(d-DMSO, 300MHz) of 3h



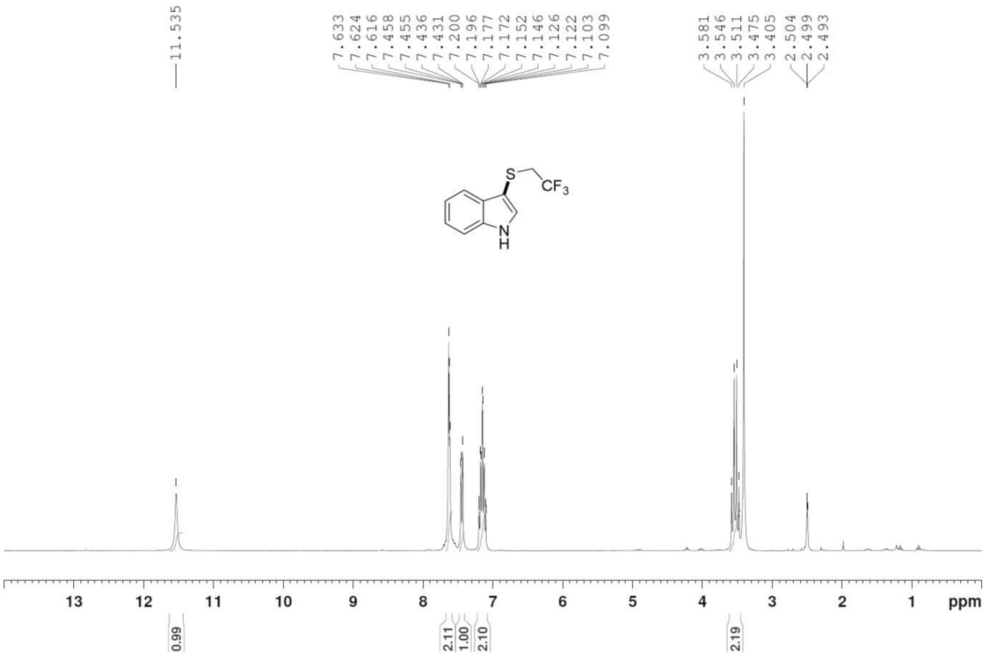
^{13}C-NMR(d-DMSO, 75MHz) of 3h



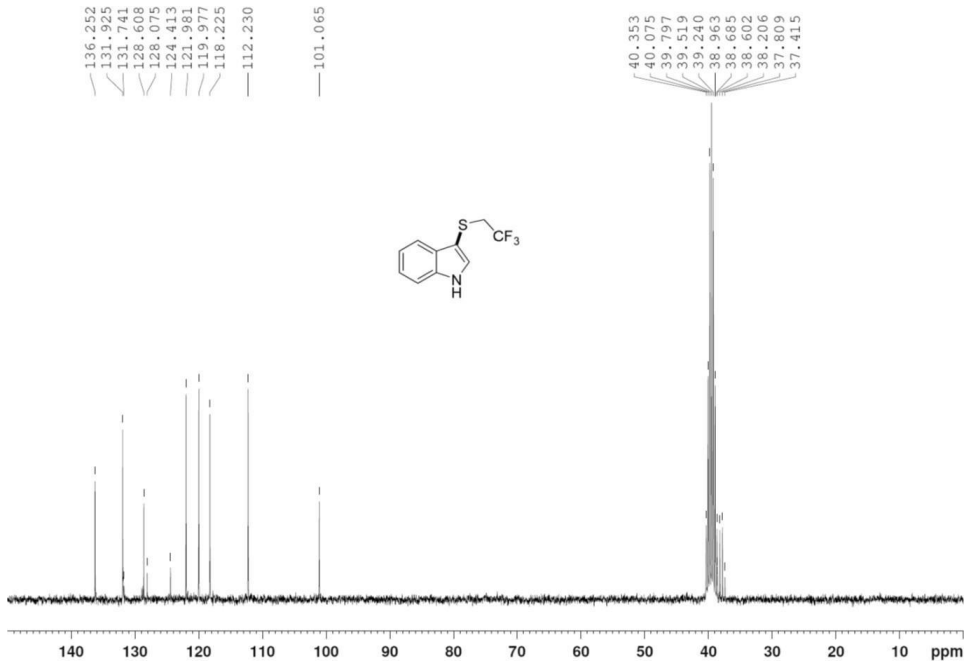
^{19}F-NMR(d-DMSO, 282MHz) of 3h



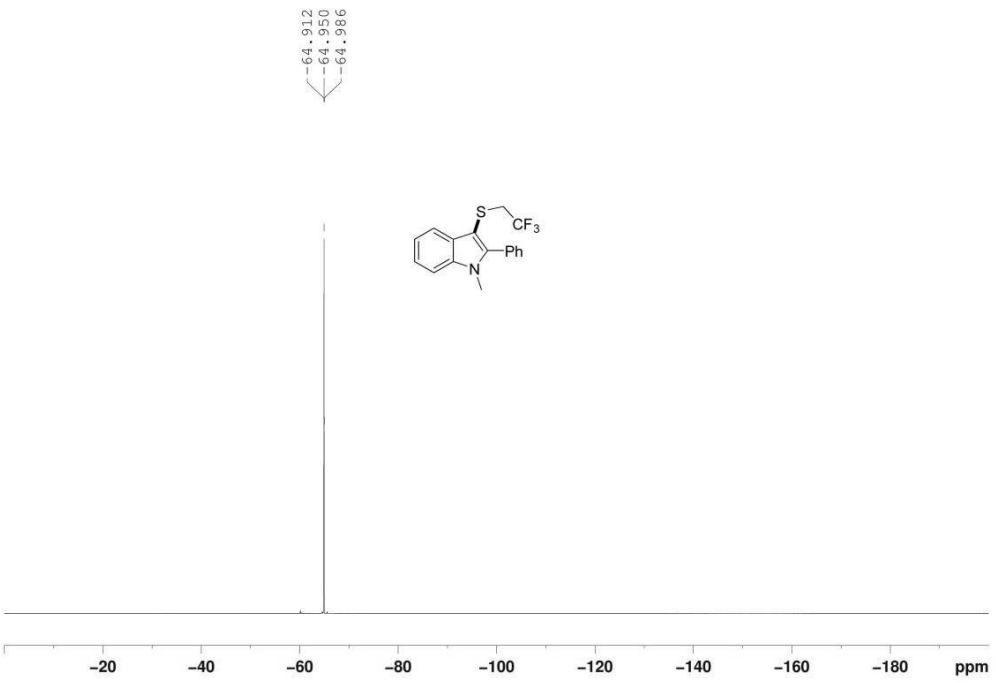
^{1}H-NMR(d-DMSO, 300MHz) of 3i



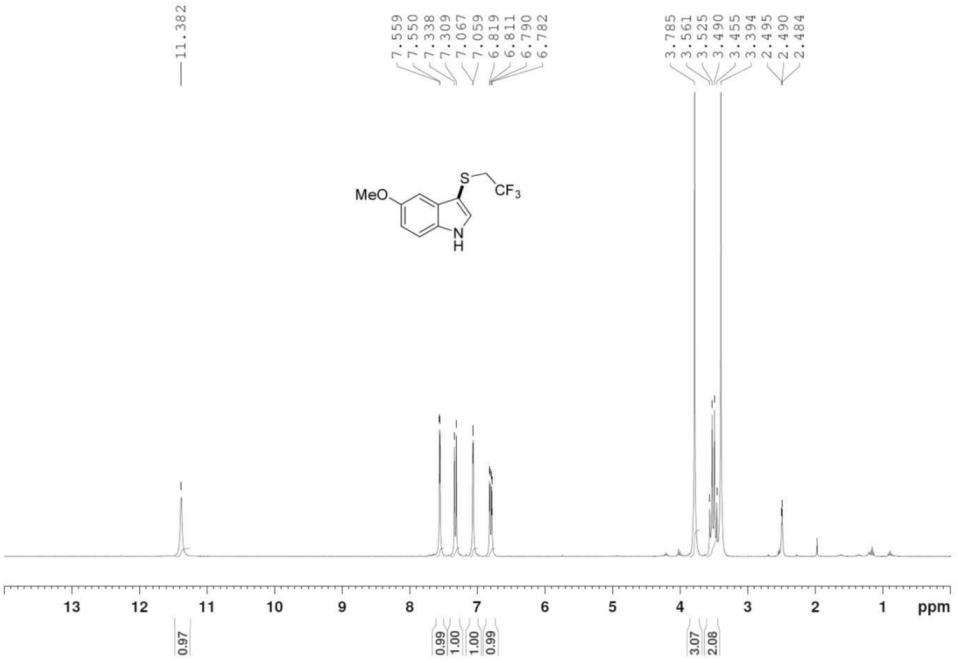
^{13}C-NMR(d-DMSO, 75MHz) of 3i



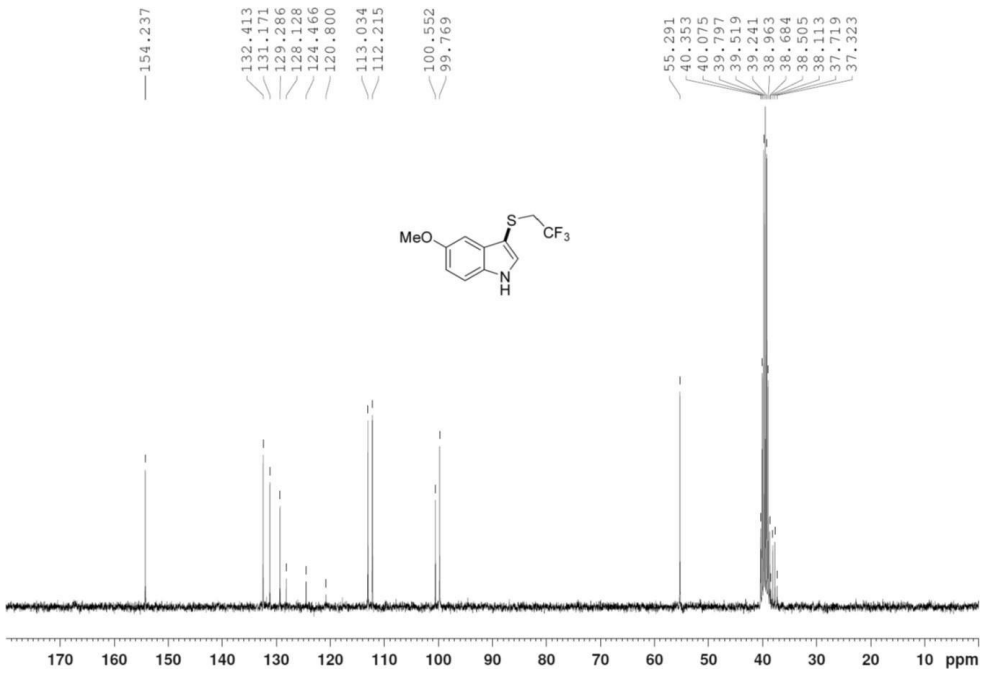
^{19}F-NMR(d-DMSO, 282MHz) of 3i



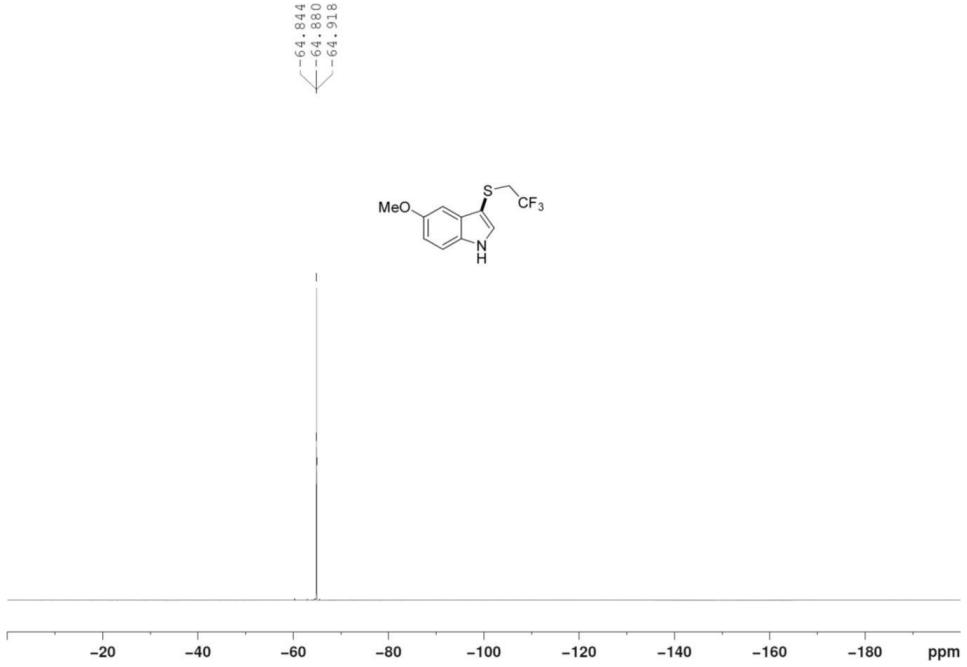
^{1}H-NMR(d-DMSO, 300MHz) of 3j



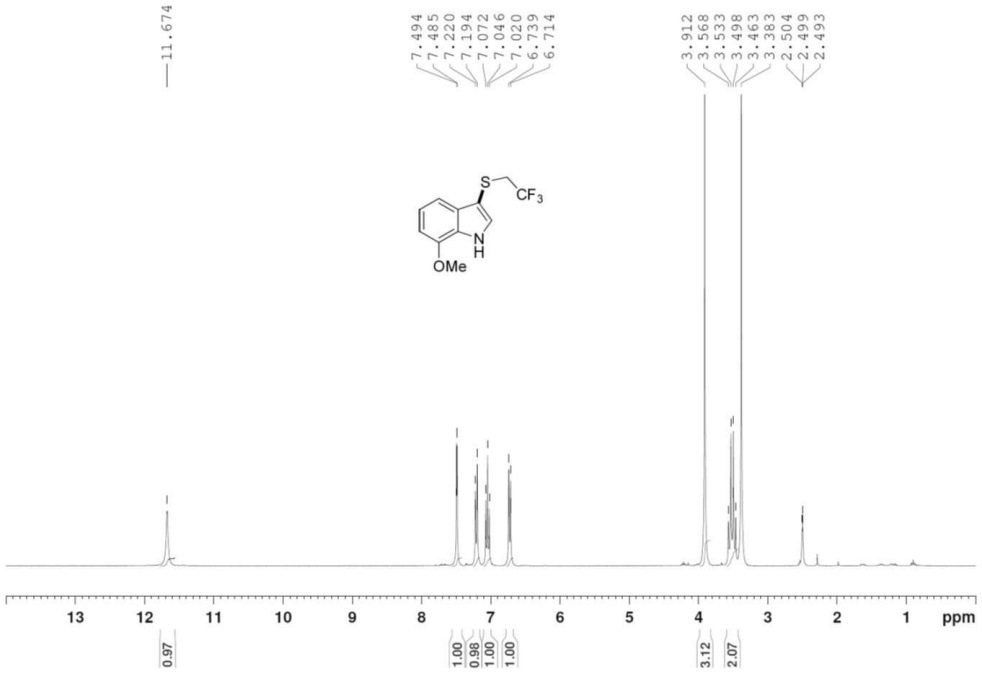
^{13}C-NMR(d-DMSO, 75MHz) of 3j



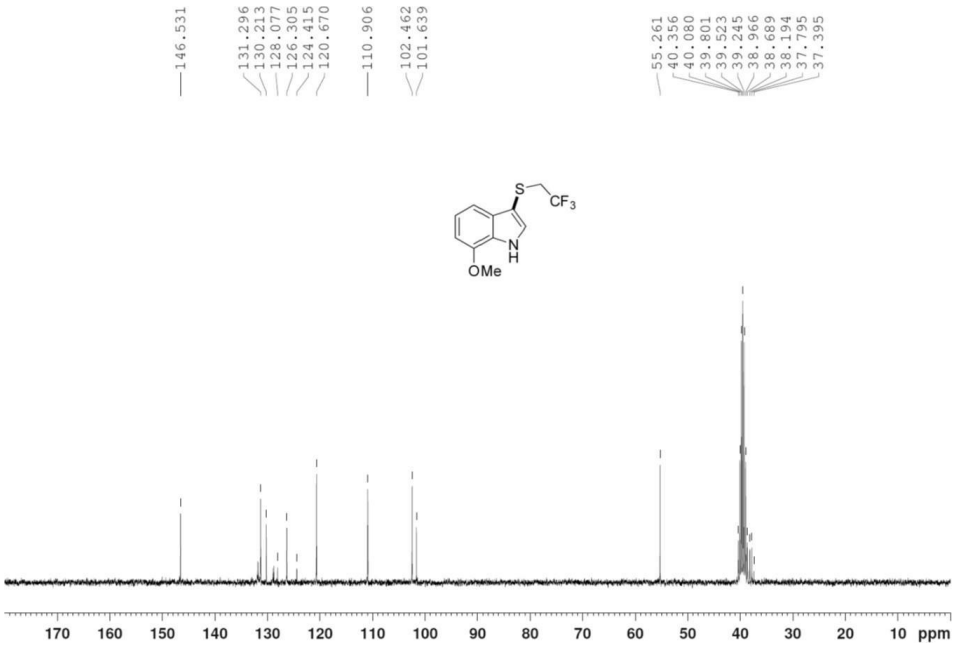
^{19}F-NMR(d-DMSO, 282MHz) of 3j



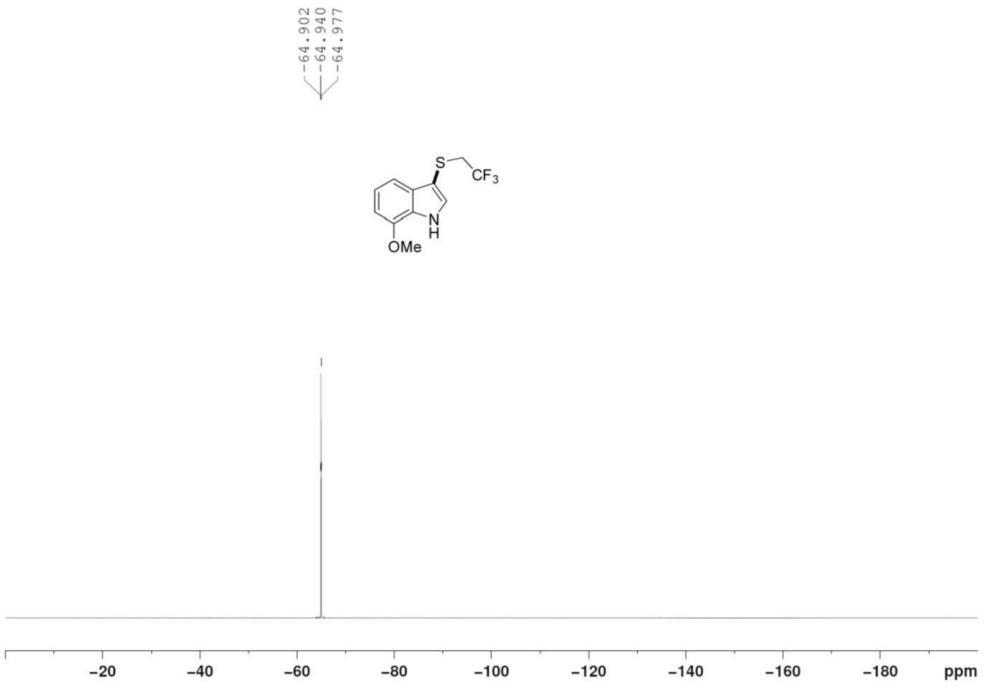
^{1}H-NMR(d-DMSO, 300MHz) of 3k



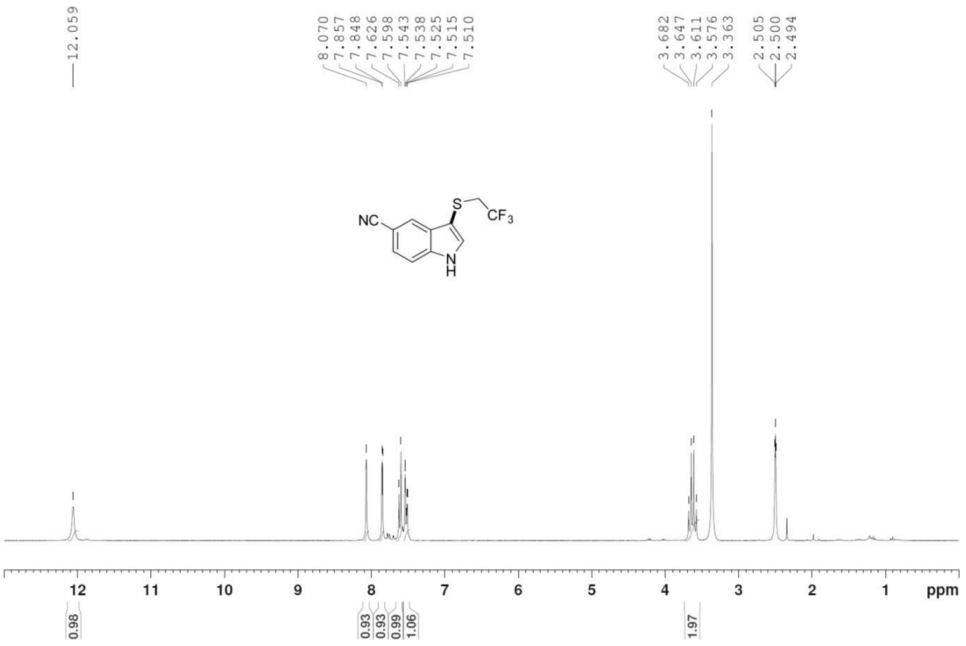
^{13}C-NMR(d-DMSO, 75MHz) of 3k



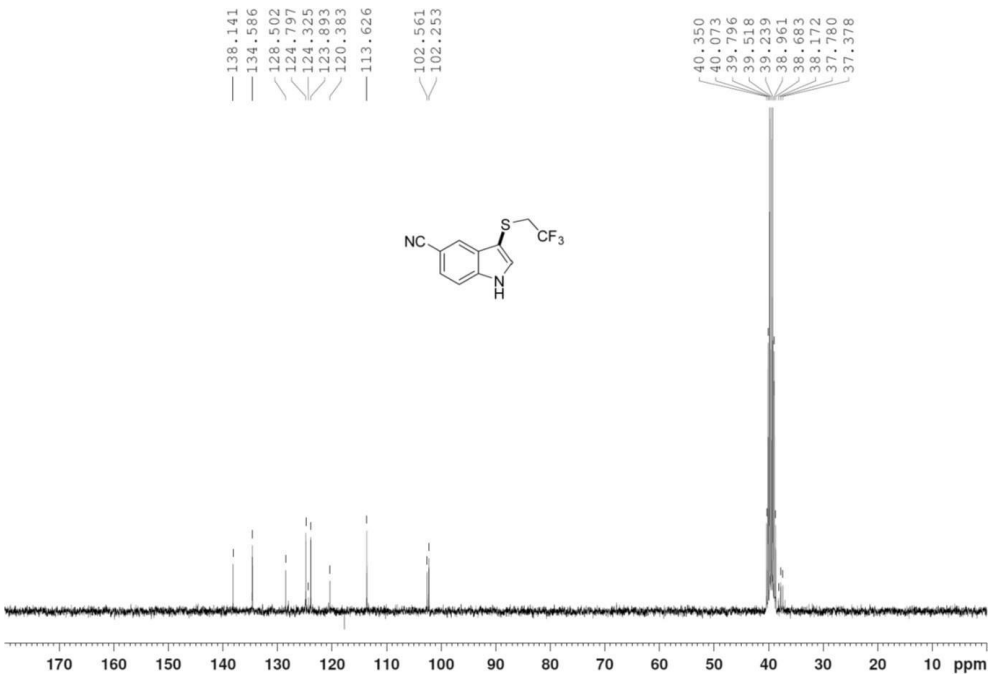
^{19}F-NMR(d-DMSO, 282MHz) of 3k



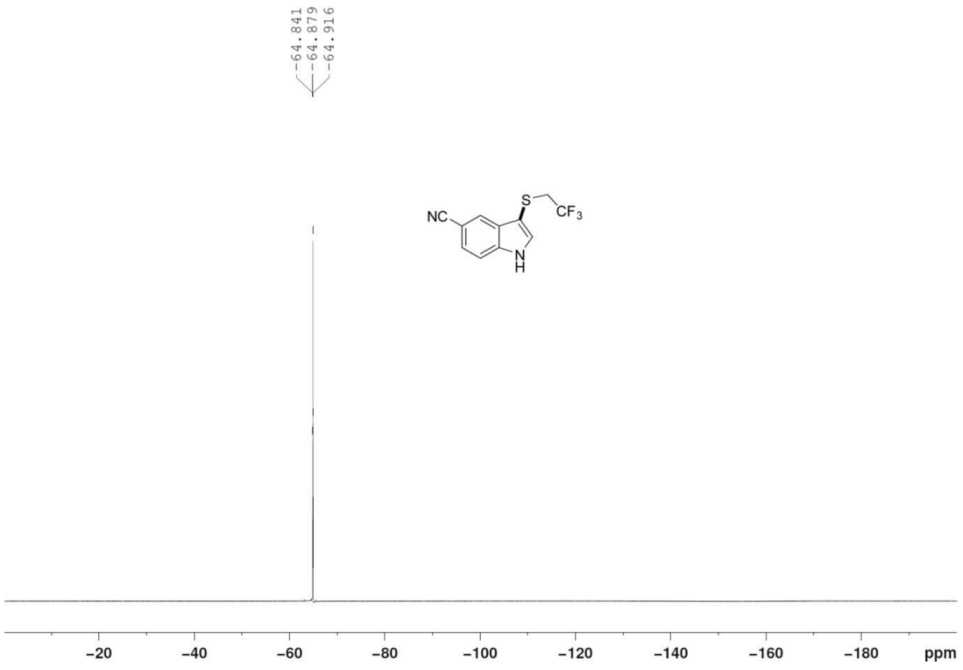
^{1}H-NMR(d-DMSO, 300MHz) of 3l



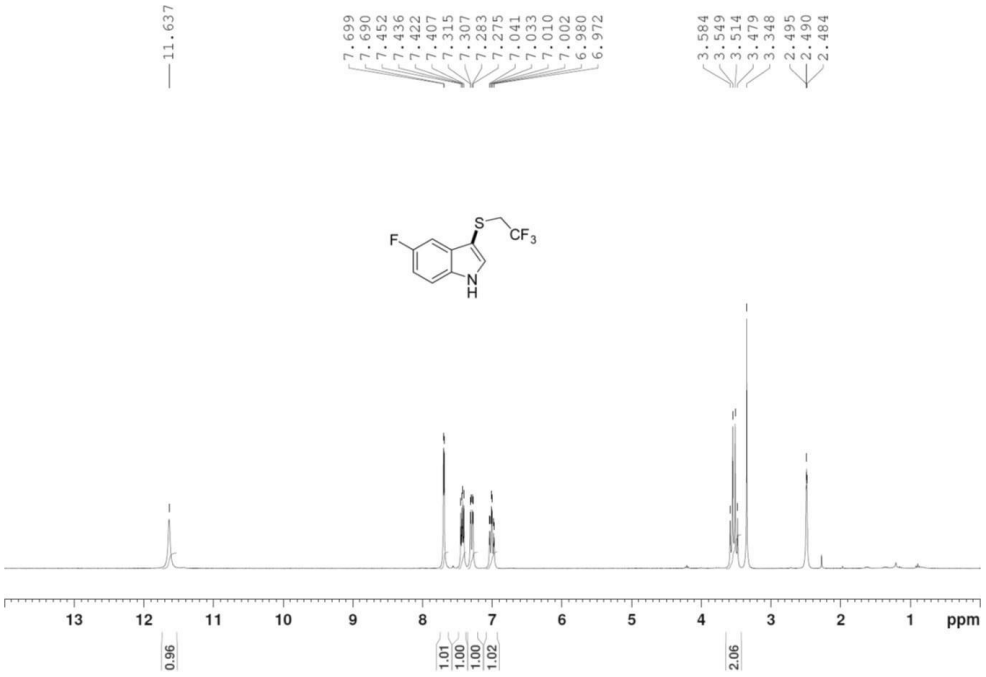
^{13}C-NMR(d-DMSO, 75MHz) of 3l



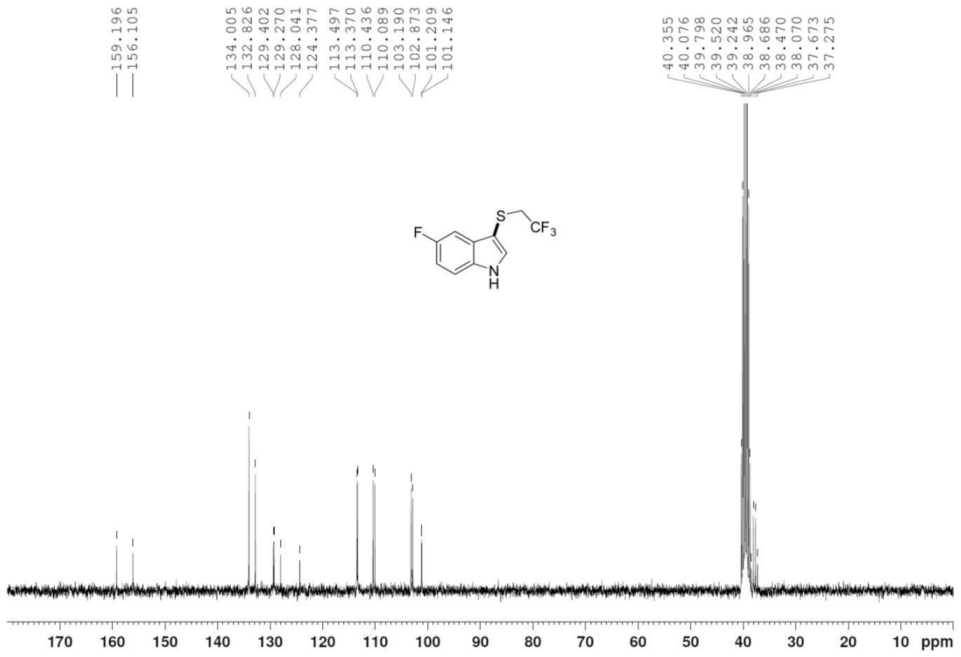
^{19}F-NMR(d-DMSO, 282MHz) of 3l



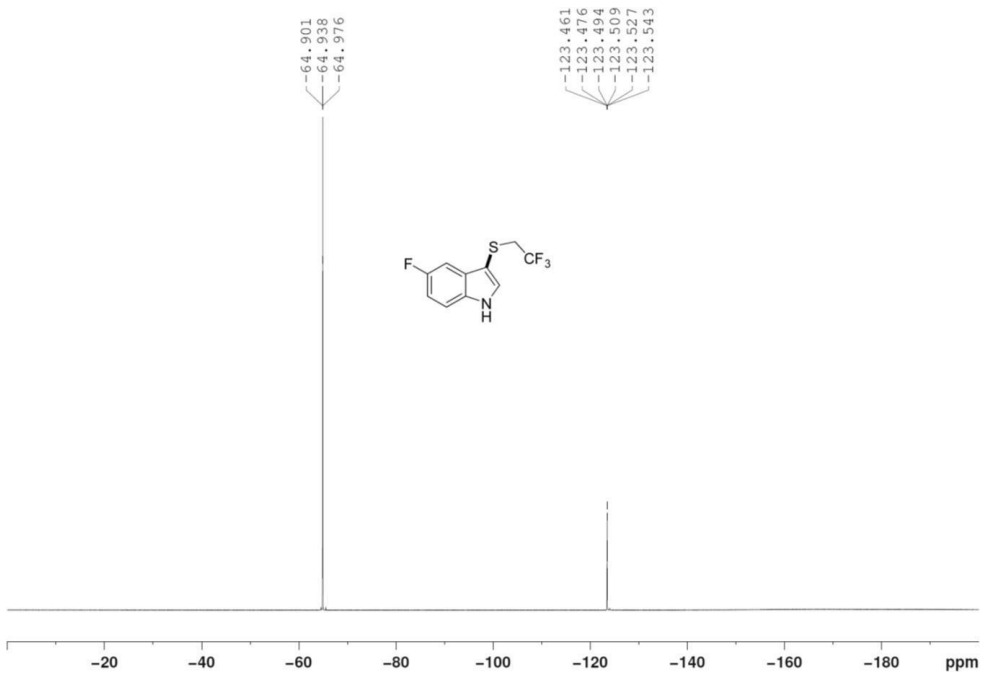
^{1}H-NMR(d-DMSO, 300MHz) of 3m



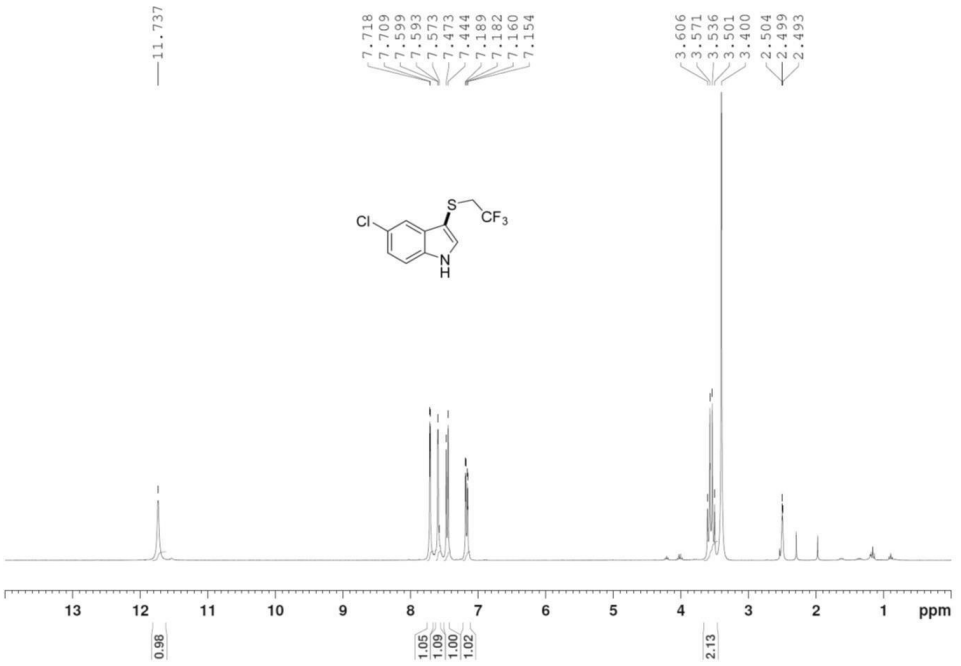
^{13}C-NMR(d-DMSO, 75MHz) of 3m



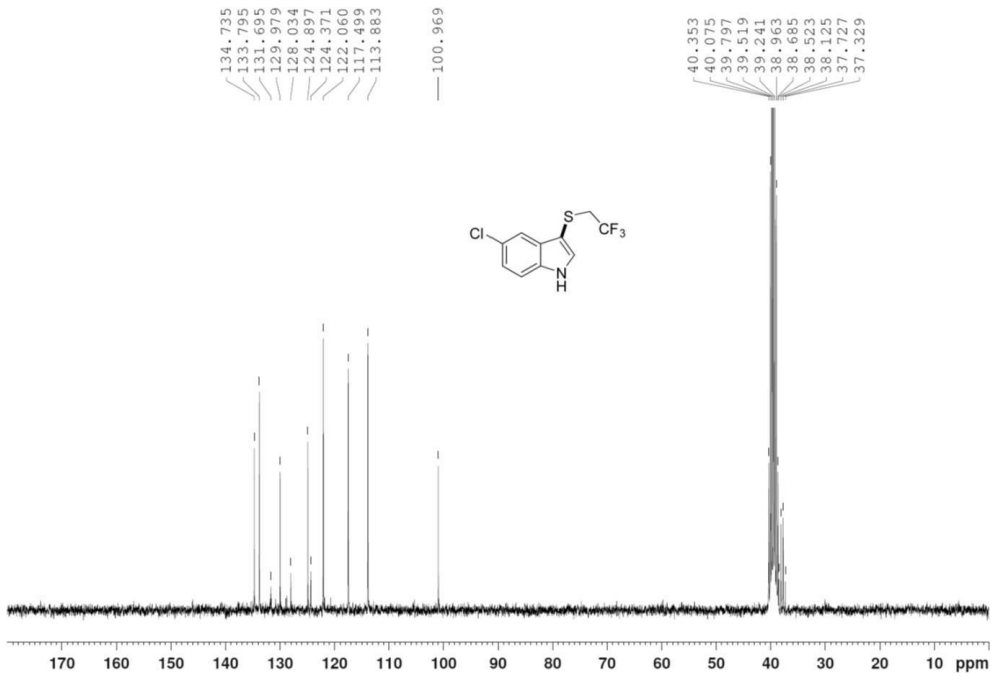
^{19}F-NMR(d-DMSO, 282MHz) of 3m



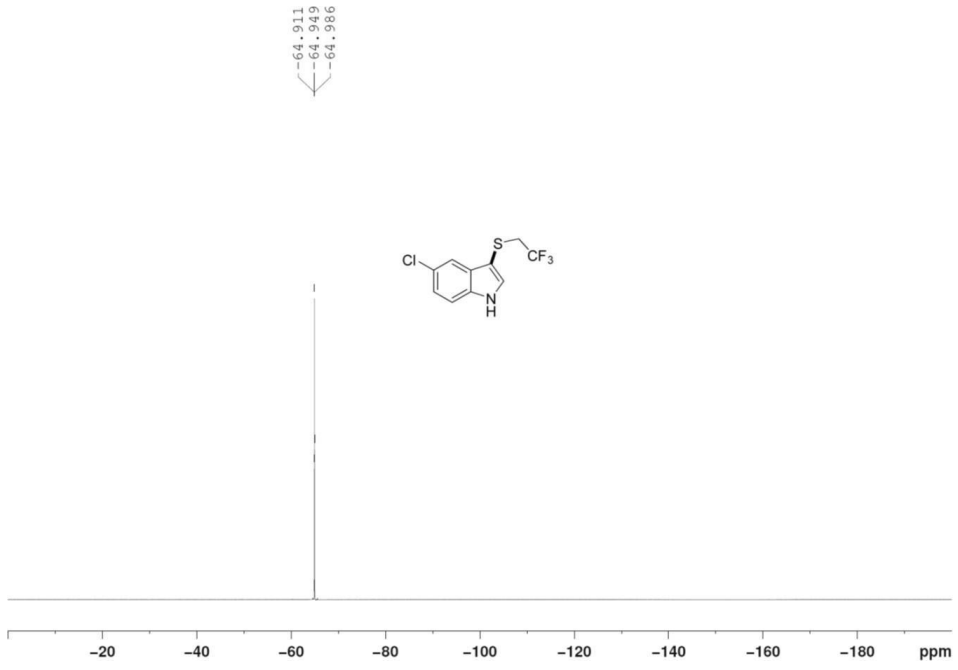
^{1}H-NMR(d-DMSO, 300MHz) of 3n



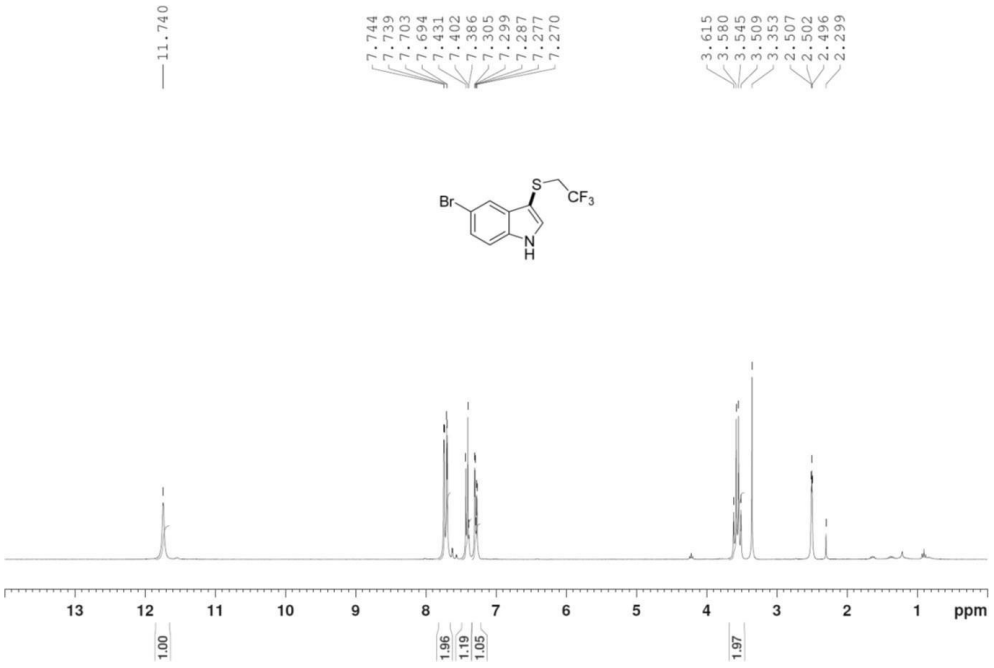
^{13}C-NMR(d-DMSO, 75MHz) of 3n



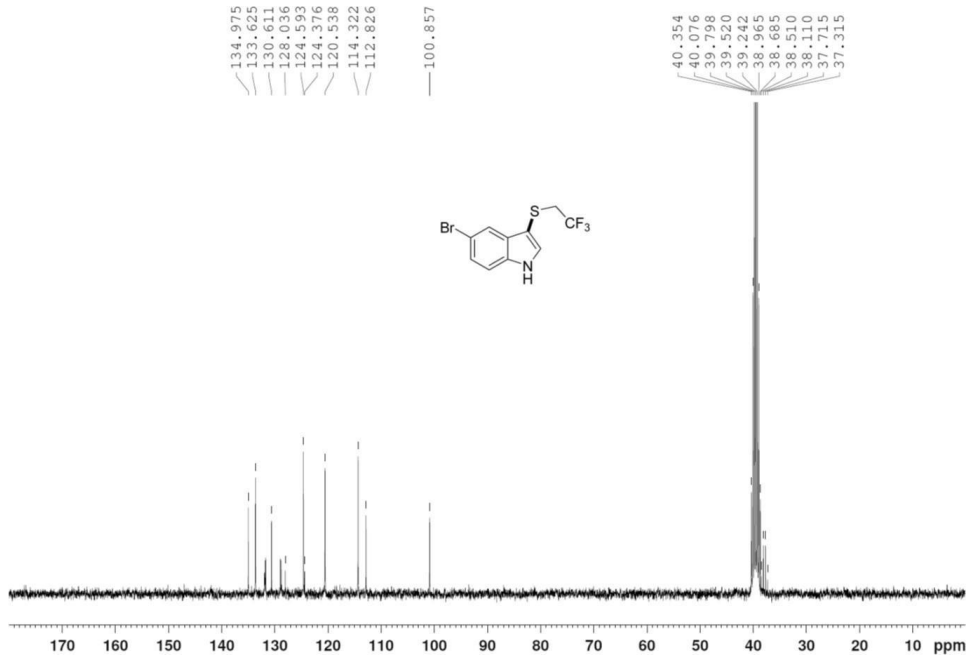
^{19}F-NMR(d-DMSO, 282MHz) of 3n



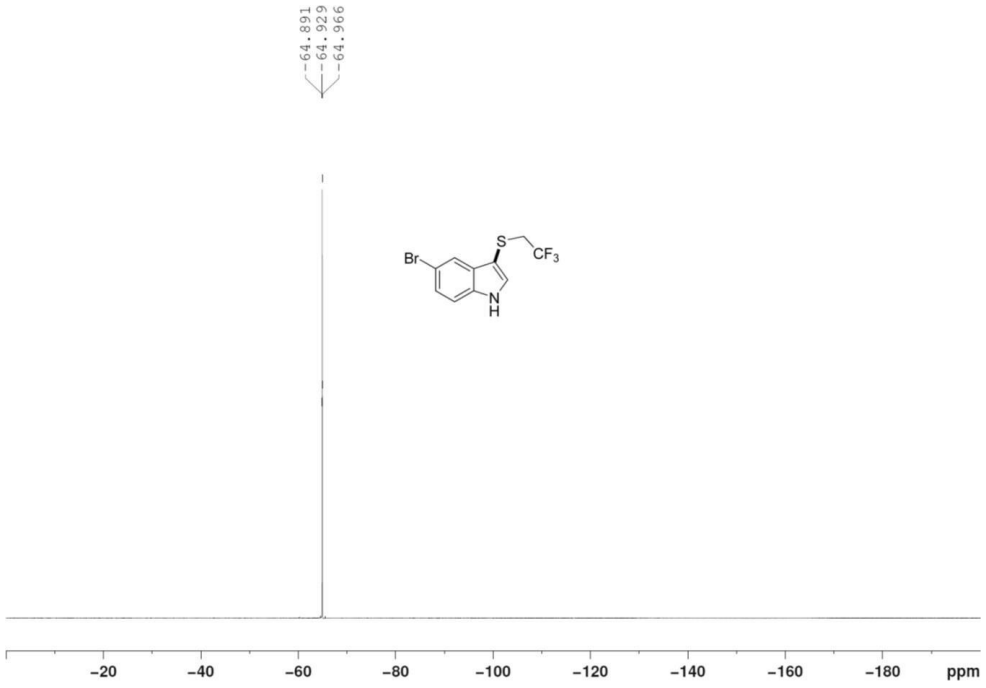
^{1}H-NMR(d-DMSO, 300MHz) of 3o



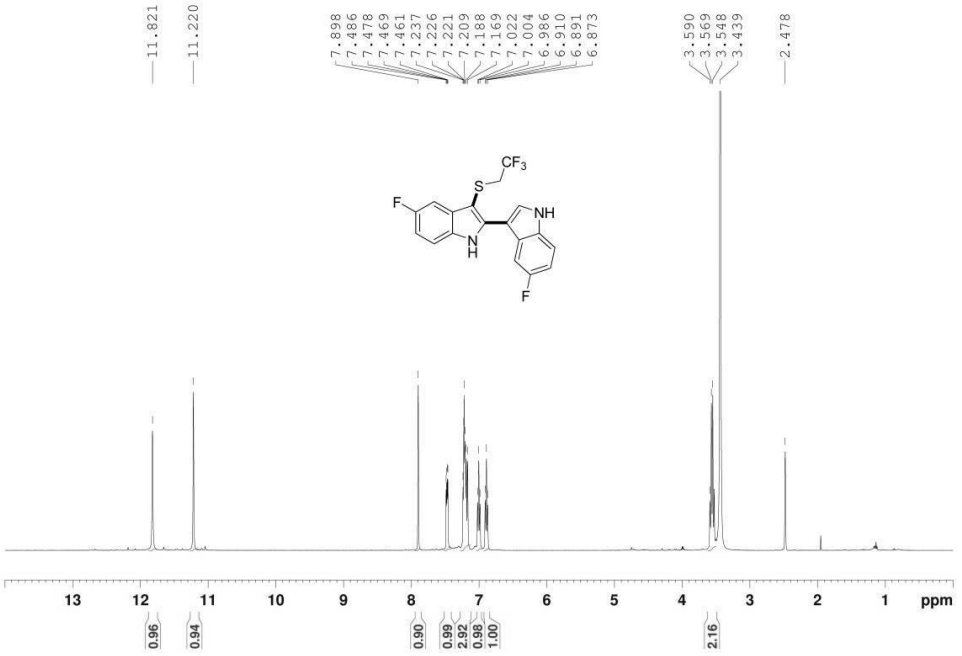
^{13}C-NMR(d-DMSO, 75MHz) of 3o



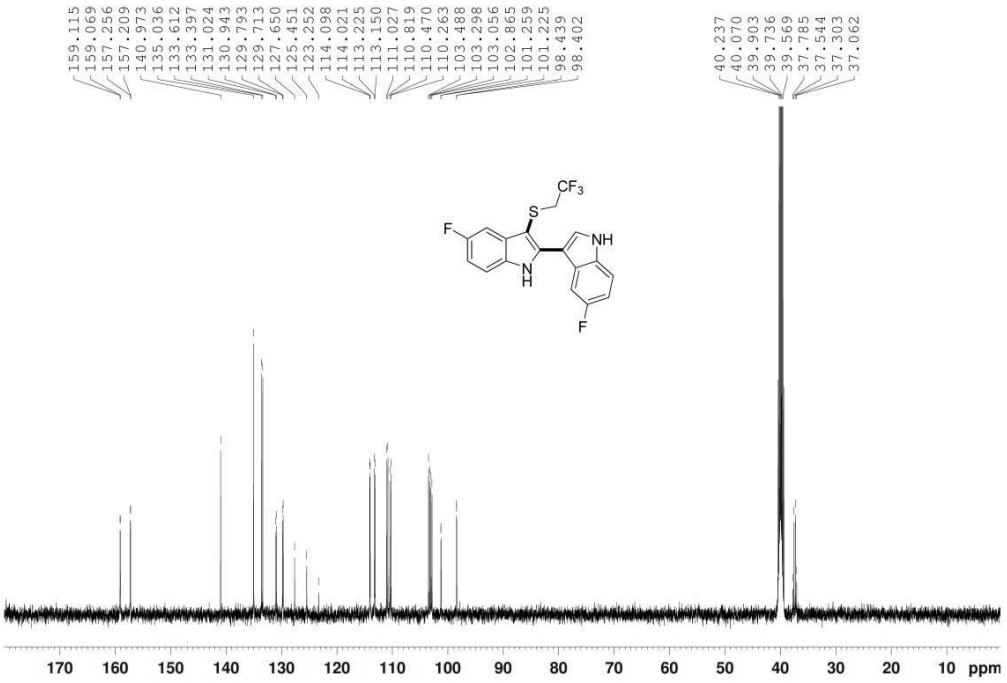
^{19}F-NMR(d-DMSO, 282MHz) of 3o



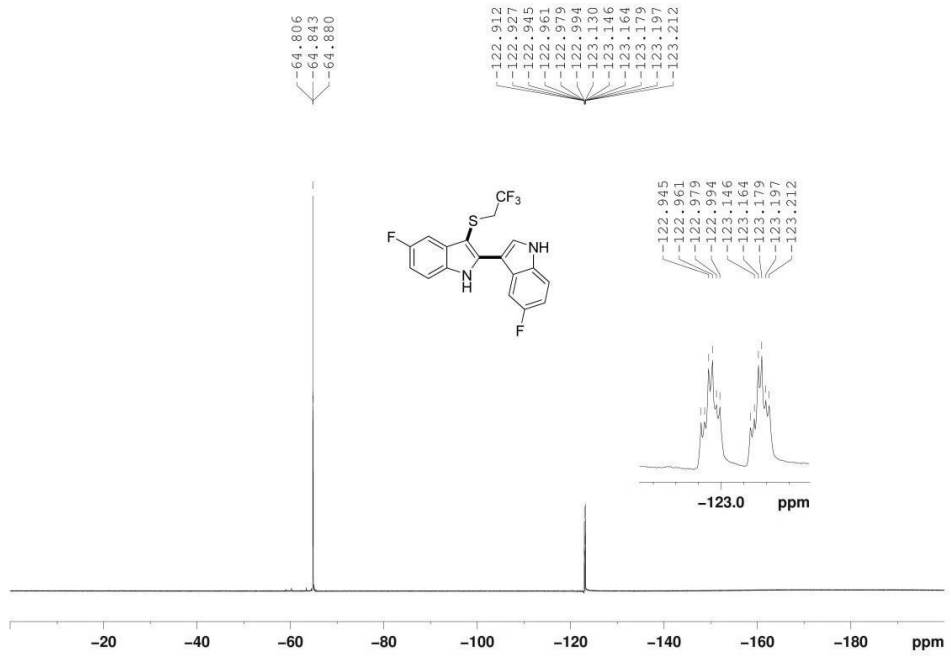
^{1}H-NMR(d-DMSO, 500MHz) of 4m



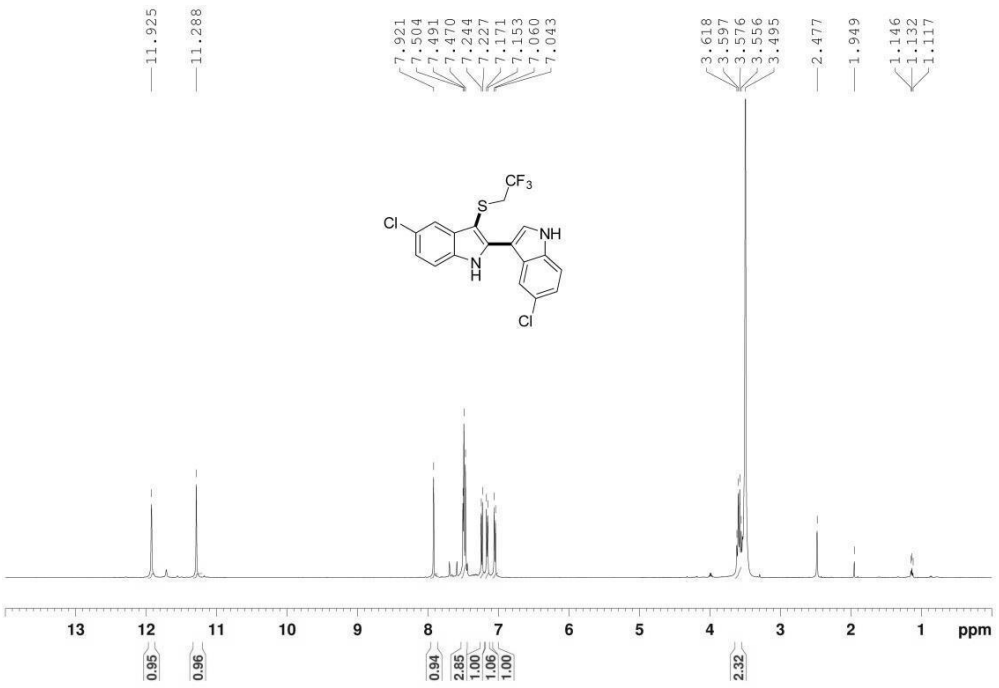
^{13}C-NMR(d-DMSO, 125MHz) of 4m



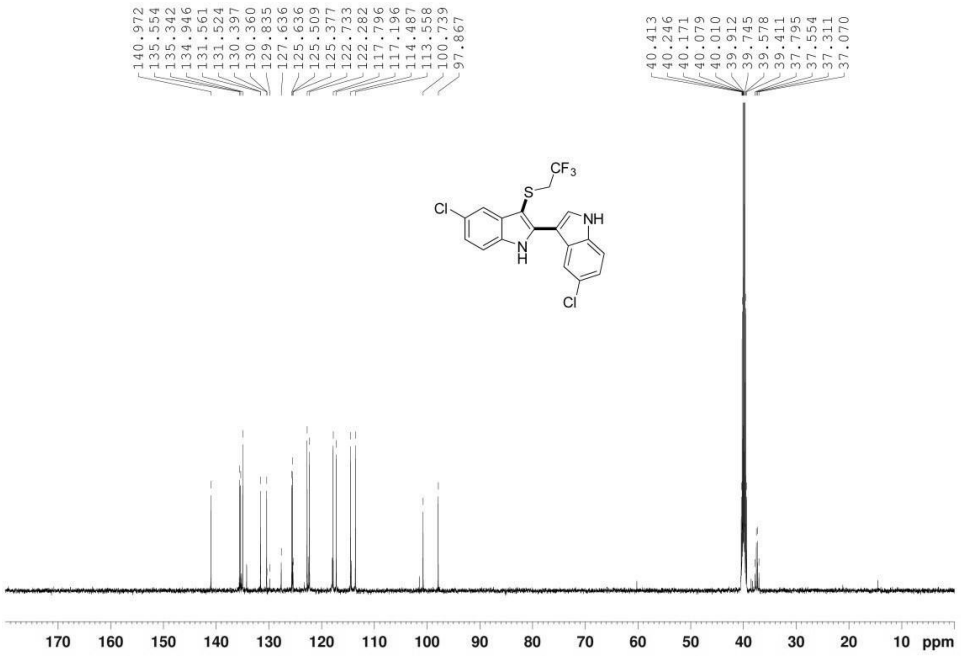
^{19}F-NMR(d-DMSO, 282MHz) of 4m



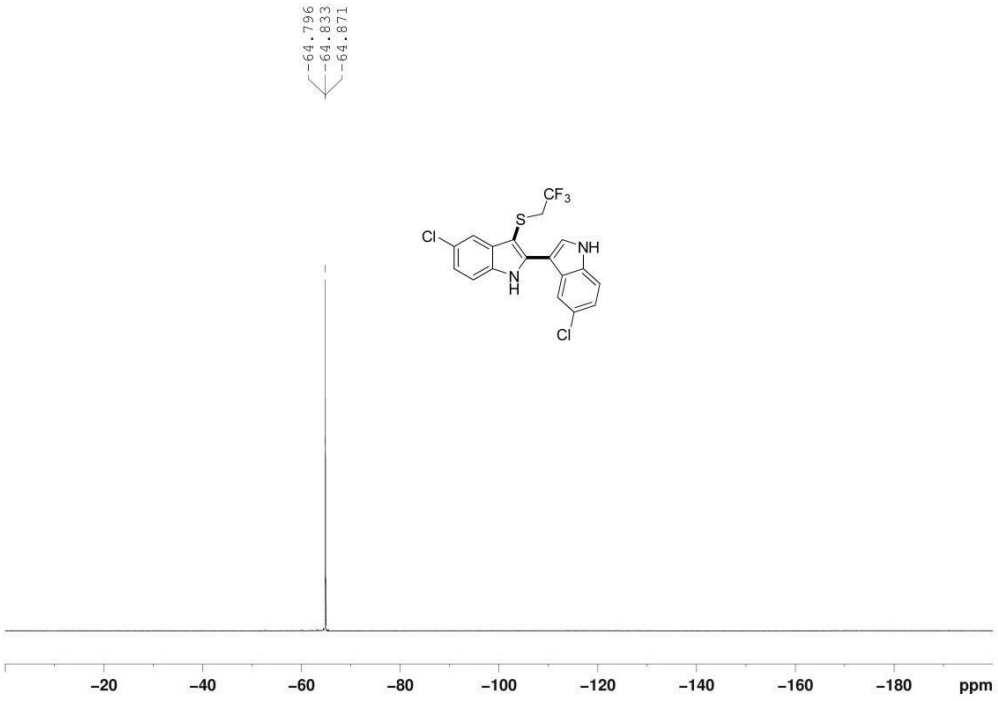
^{1}H-NMR(d-DMSO, 500MHz) of 4n



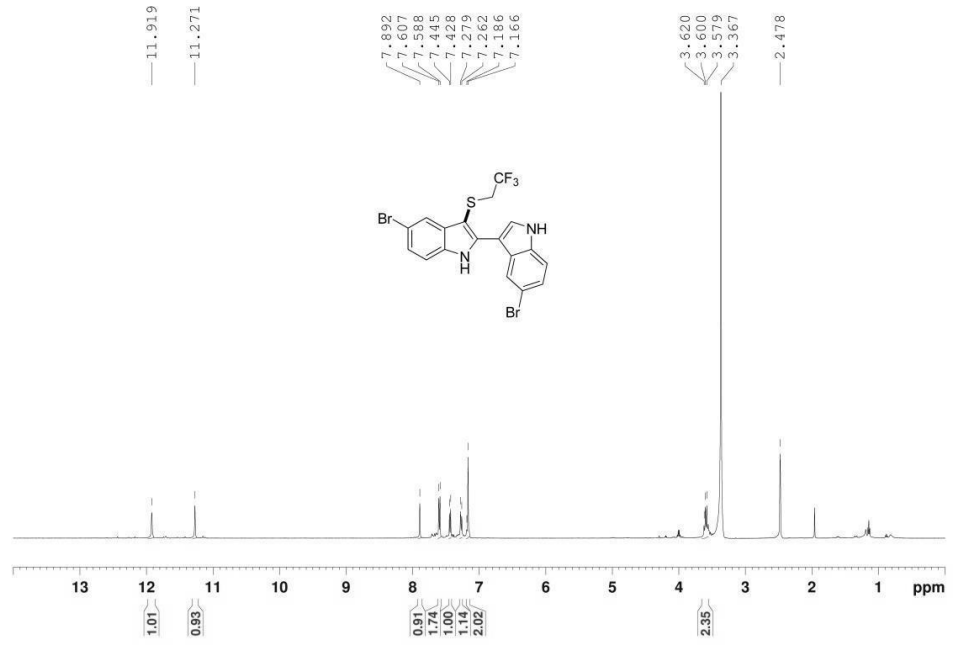
^{13}C-NMR(d-DMSO, 125MHz) of 4n



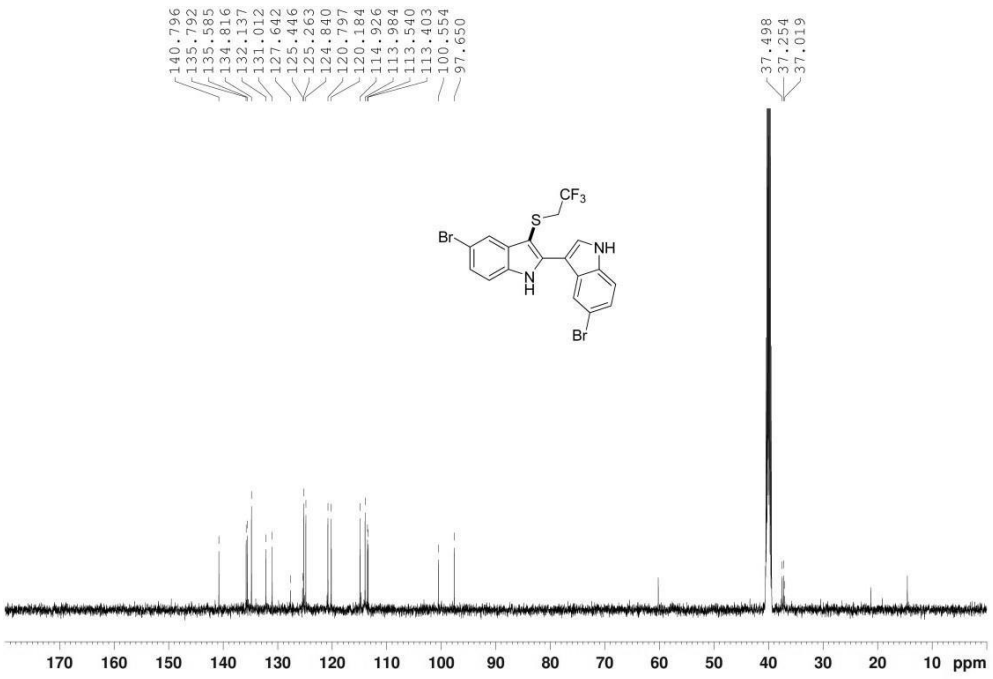
^{19}F-NMR(d-DMSO, 282MHz) of 4n



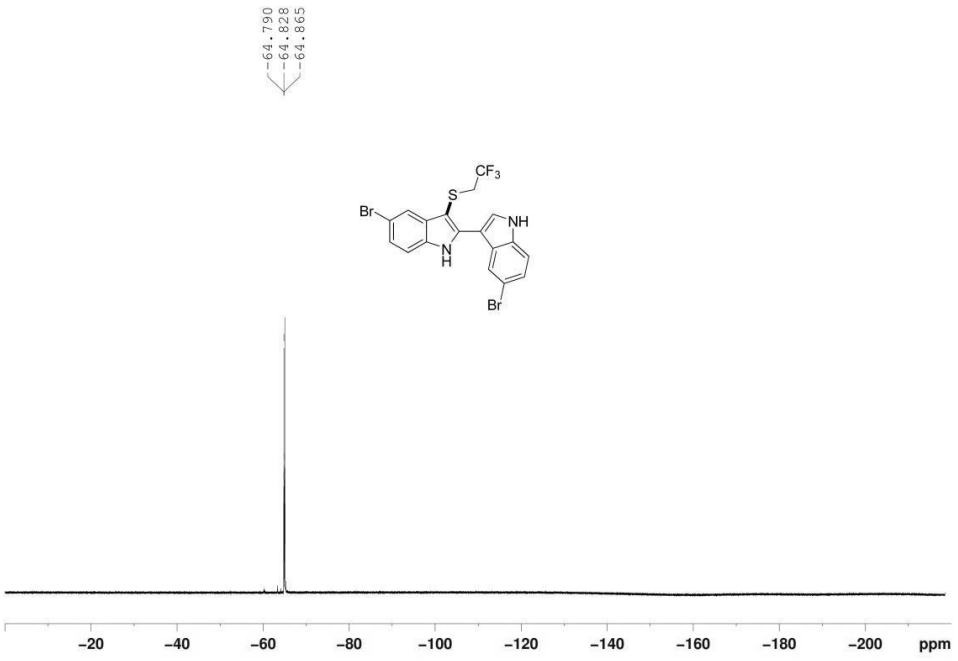
^{1}H-NMR(d-DMSO, 500MHz) of 4o



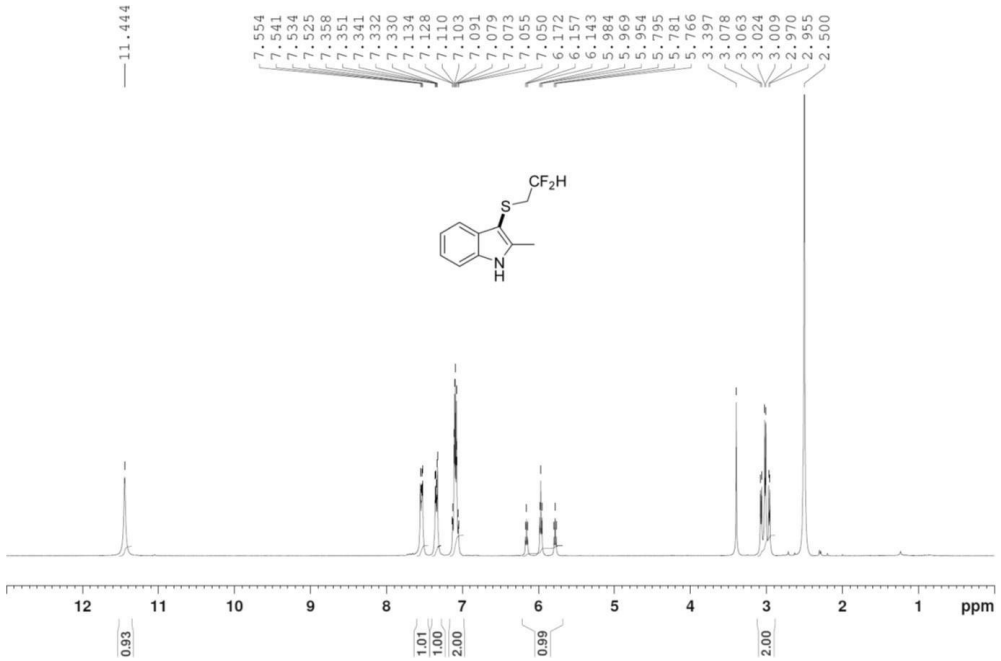
^{13}C-NMR(d-DMSO, 125MHz) of 4o



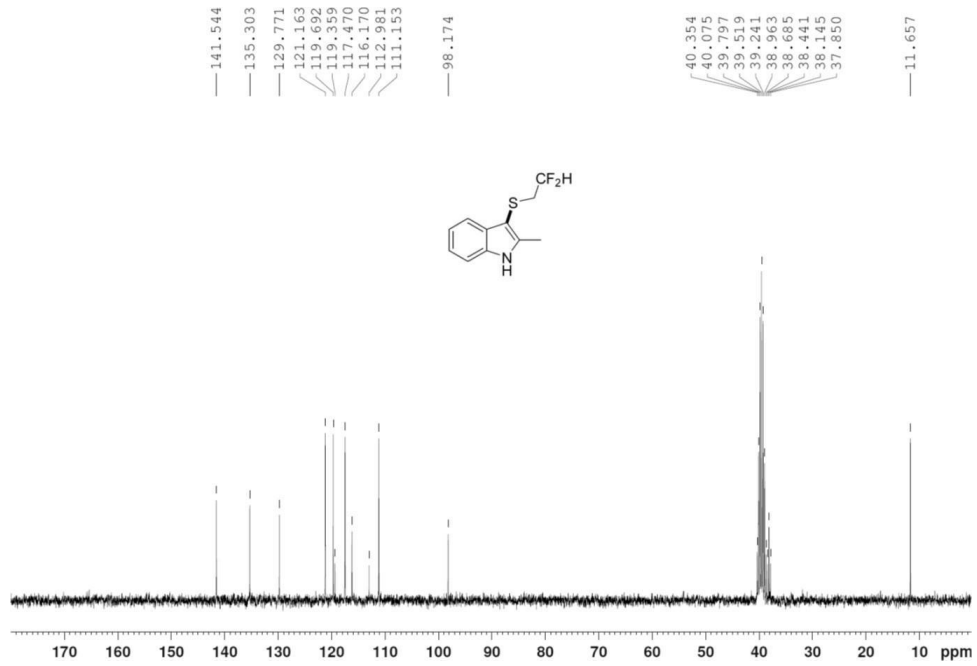
^{19}F-NMR(d-DMSO, 282MHz) of 4o



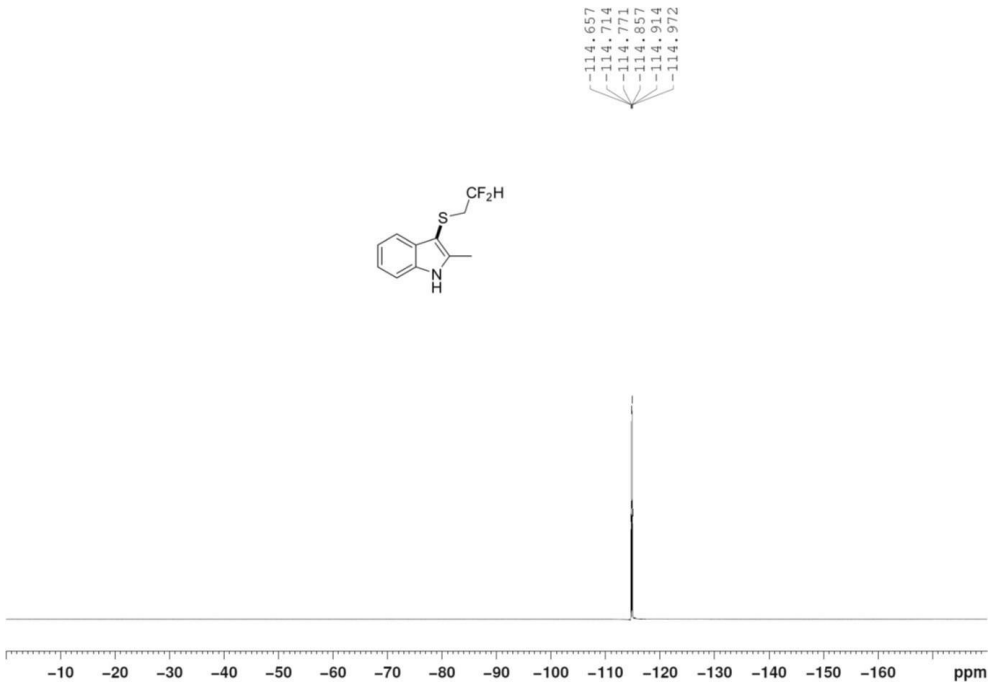
^{1}H-NMR(d-DMSO, 300MHz) of 5a



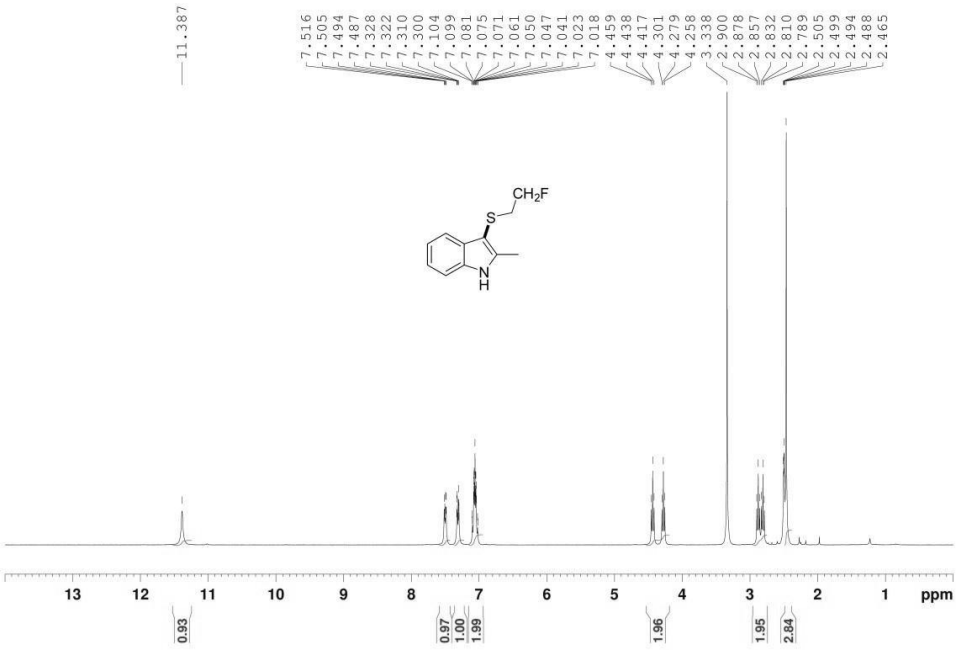
^{13}C-NMR(d-DMSO, 75MHz) of 5a



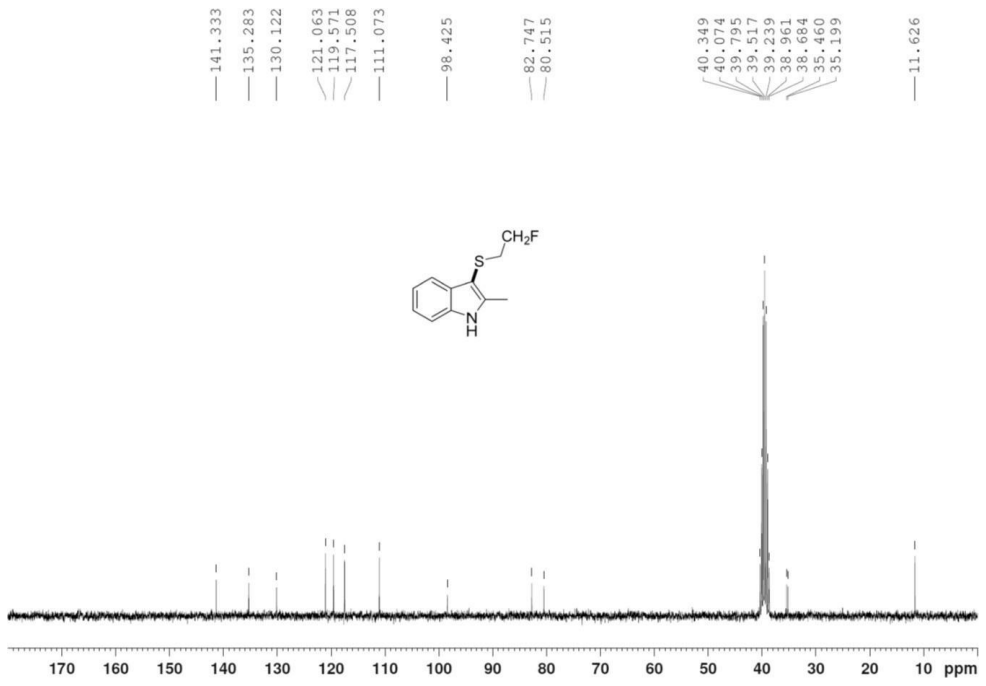
^{19}F-NMR(d-DMSO, 282MHz) of 5a



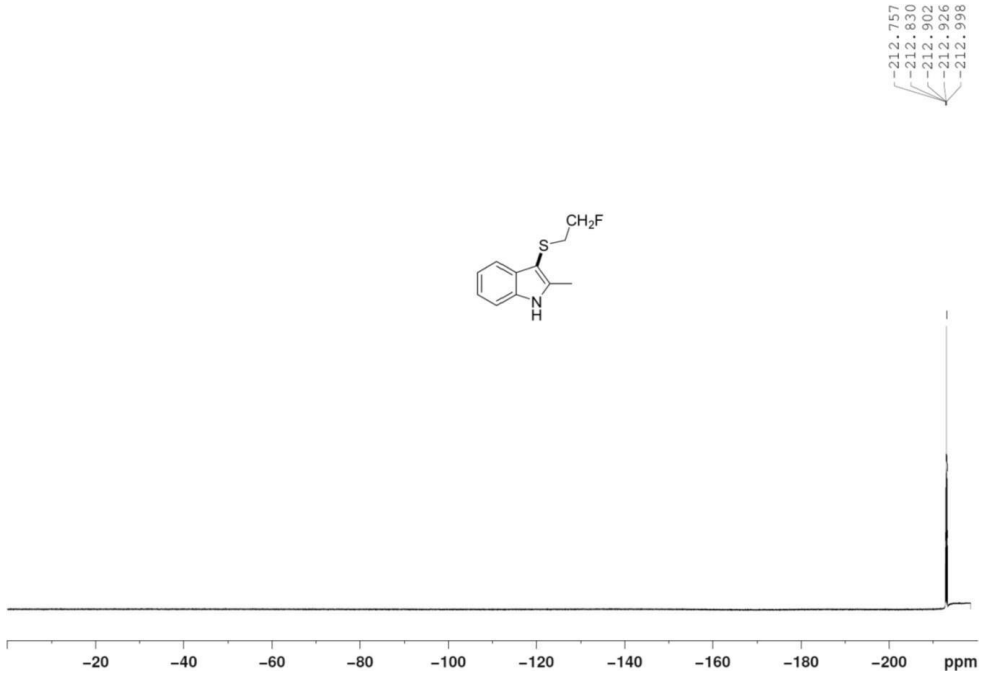
^{1}H-NMR(d-DMSO, 300MHz) of 5b



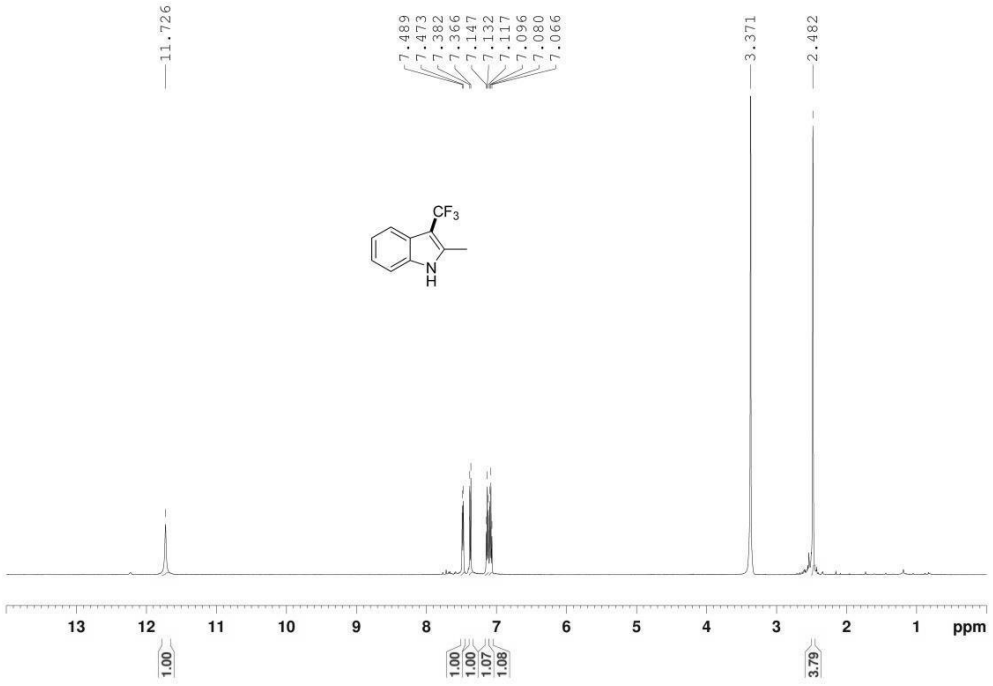
^{13}C-NMR(d-DMSO, 75MHz) of 5b



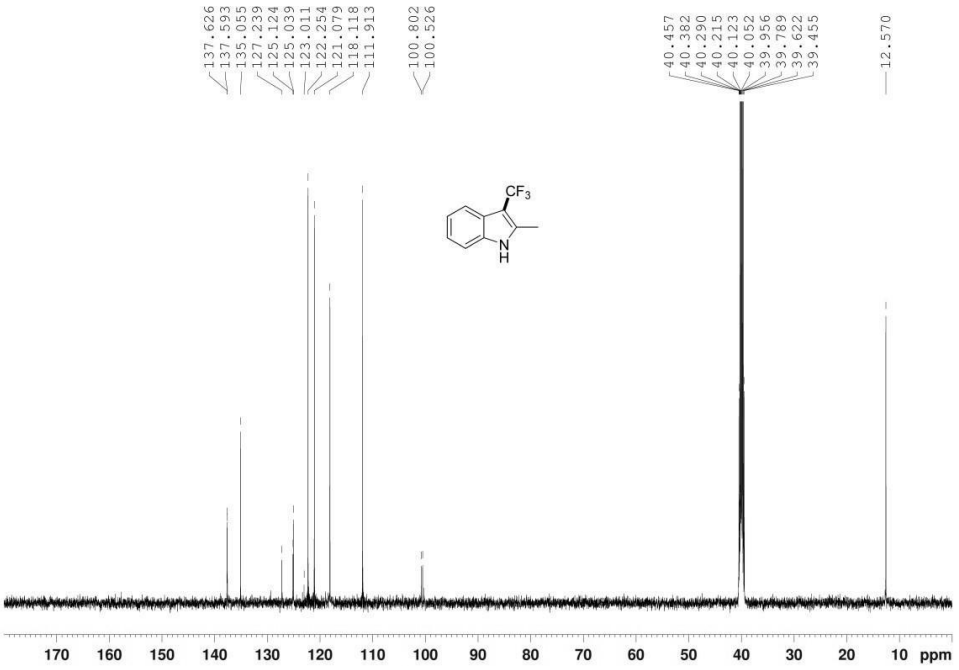
^{19}F-NMR(d-DMSO, 282MHz) of 5b



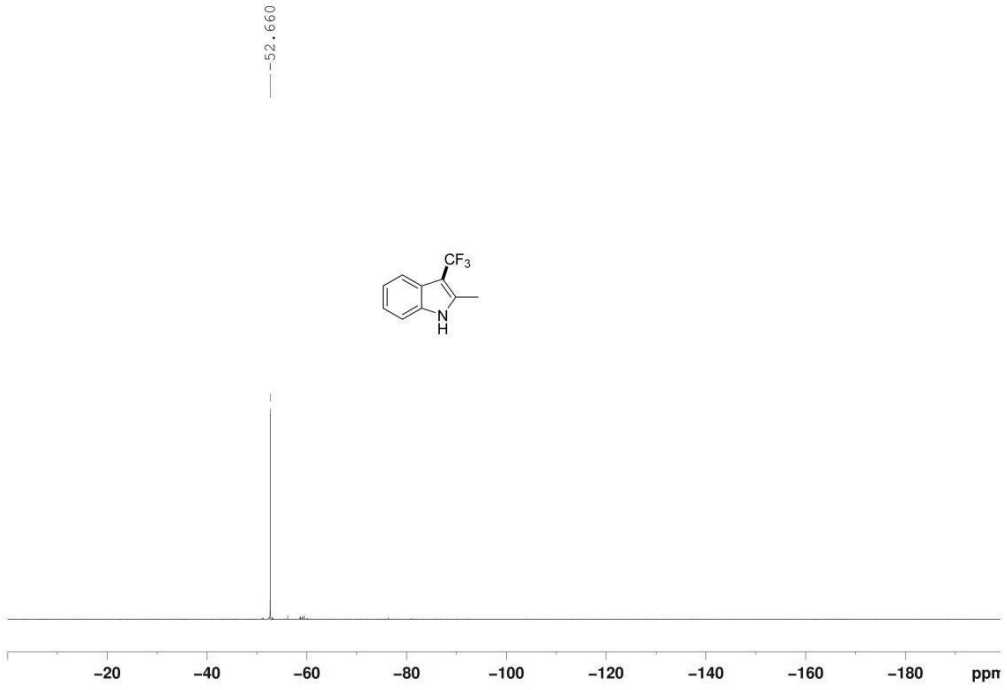
^{1}H-NMR(d-DMSO, 500MHz) of 5c



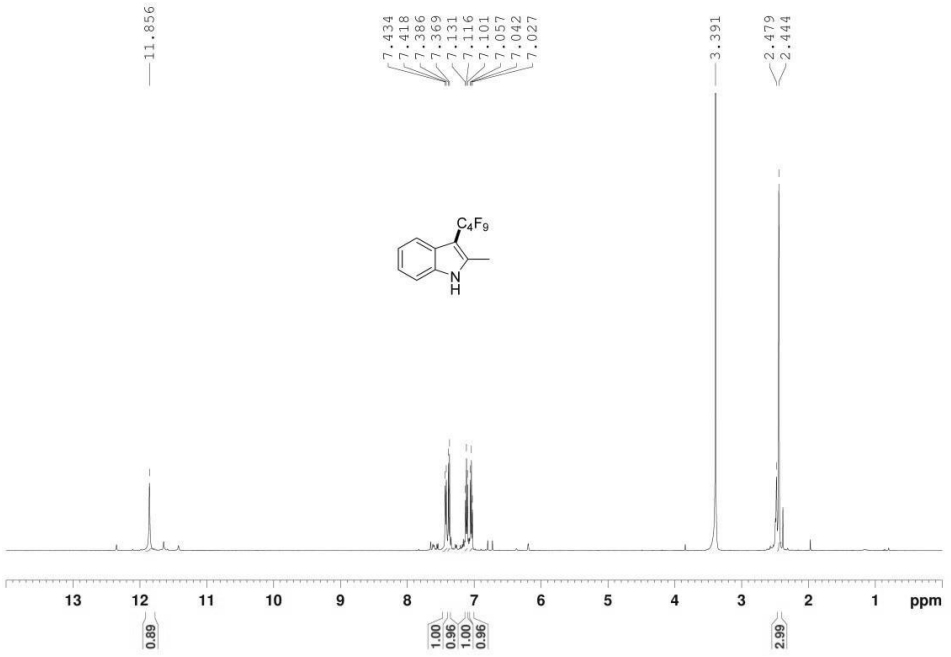
^{13}C-NMR(d-DMSO, 125MHz) of 5c



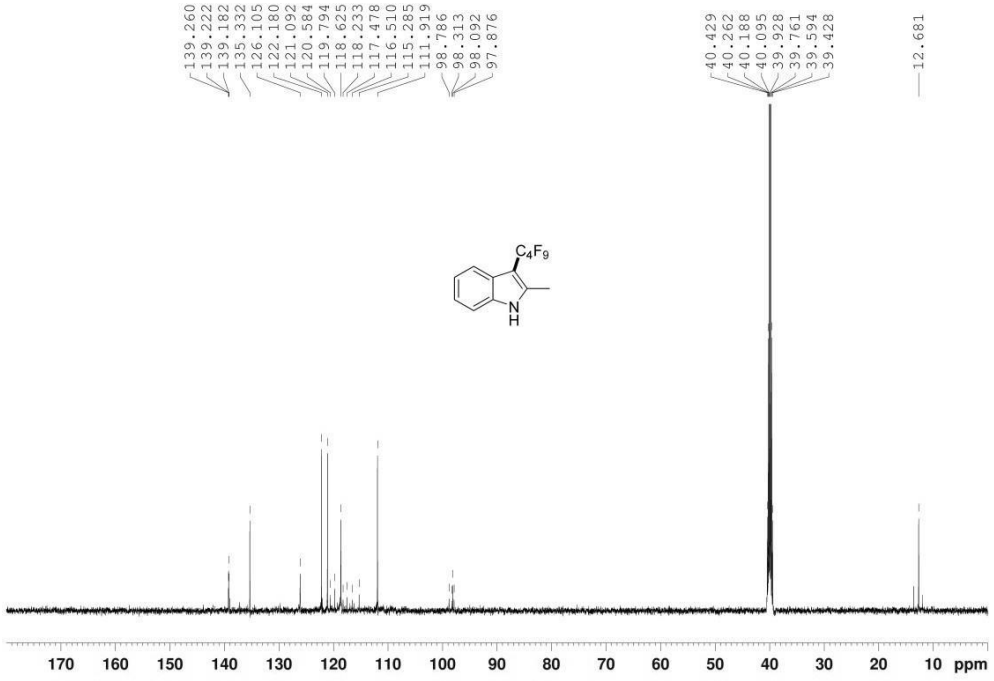
^{19}F-NMR(d-DMSO, 282MHz) of 5c



^{1}H-NMR(d-DMSO, 500MHz) of 5d



^{13}C-NMR(d-DMSO, 125MHz) of 5d



^{19}F-NMR(d-DMSO, 282MHz) of 5d