Supporting Information

Novel Use of 2-$BTSO_2CF_2H$ for the Metal-Free Electrophilic Difluoroalkanethiolation of Indoles

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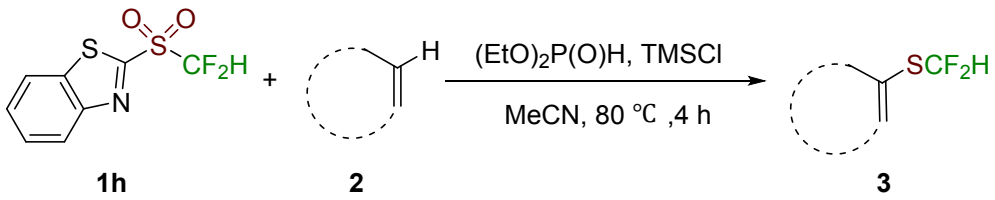
1. General information

Unless otherwise mentioned, all manipulations were conducted with a standard Schlenk tube under N_2 atmosphere, and reagents were purchased from commercial sources and used without further purification. Flash chromatography was performed using 300-400 mesh silica gel. NMR spectra were obtained on a Bruker AV400，Agilent MR400 (400 MHz for ^{1}H; 376 MHz for ^{19}F; 100 MHz for ^{13}C) or Bruker AV500 (500 MHz for ^{1}H; 472 MHz for ^{19}F; 126 MHz for ^{13}C). ^{1}H NMR and ^{13}C NMR chemical shifts were determined relative to internal $(CH_3)_4Si$ (TMS) at δ 0.0. High Resolution MS (HRMS) were performed on an Agilent 6224 TOF LC/MS spectrometer.

2. General procedure for the synthesis of 3a-3s.

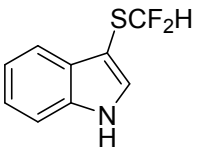


1h **2** **3**

A mixture of 2-((difluoromethyl)sulfonyl)benzo[*d*]thiazole **1h** (1.5 mmol, 1.5 equiv) and (het)arene (1.0 mmol, 1.0 equiv) were added to a dry Schlenk tube. The tube was evacuated and backfilled with pure N_2 for 3 times. Then $(EtO)_2P(O)H$ (0.4 mL, 3.0 mmol, 3.0 equiv), TMSCl (0.4 mL, 3.0 mmol, 3.0 equiv) and dry MeCN (5 mL) were added with syringe under N_2 atmosphere. Then the mixture was stirred at 80 °C for 4 h. After the reaction was complete, the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel by using a mixture of petroleum ether/EtOAc as an eluent to provide the desired products **3**.

3. Characterization data of 3a-3s.

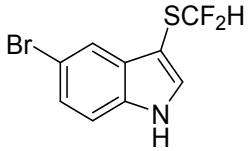
3-((difluoromethyl)thio)-1*H*-indole (3a)[1]



General procedure was followed using indole (117.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate =20/1) to afford product **3a** as a yellow oil (141.3 mg, 71%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.83 –7.81 (m, 1H), 7.45 (d, J = 2.5 Hz, 1H), 7.42 – 7.40 (m, 1H), 7.32 – 7.27 (m, 2H), 6.82 (t, J = 57.5 Hz, 1H). ^{19}F NMR (376

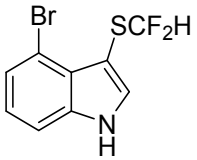
MHz, $CDCl_3$) δ -92.09 (d, *J* = 57.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.2, 132.0, 129.8, 123.9 (t, *J* = 274.0 Hz), 123.2, 121.3, 119.3, 111.7, 96.5.

5-bromo-3-((difluoromethyl)thio)-1*H*-indole (3b)[2]



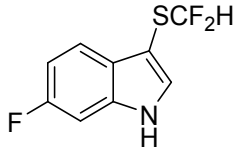
General procedure was followed using 5-bromo-1*H*-indole (195.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 20/1) to afford product **3b** as a yellow oil (175.0 mg, 63%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.89 (d, *J* = 1.5 Hz, 1H), 7.44 (d, *J* = 3.0 Hz, 1H), 7.34 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.24 (d, *J* = 2.5 Hz, 1H), 6.77 (t, *J* = 57.5 Hz, 1H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -92.21 (d, *J* = 57.5 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.8, 133.1, 131.7, 126.4, 122.8 (t, *J* = 276.7 Hz), 122.2, 114.9, 113.2, 96.3 (t, *J* = 3.7 Hz).

4-bromo-3-((difluoromethyl)thio)-1*H*-indole (3c)[3]



General procedure was followed using 5-bromo-1*H*-indole (195.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 20/1) to afford product **3c** as a white solid (185.6 mg, 67%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.52 (d, *J* = 2.8 Hz, 1H), 7.41 (dd, *J* = 10.0, 8.4 Hz, 1H), 7.12 (t, *J* = 8.0 Hz, 1H), 6.98 (t, *J* = 58.0 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -95.36 (d, *J* = 58.3 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.3, 134.4, 126.3, 126.1, 121.3 (t, *J* = 276.0 Hz), 114.3, 111.4, 97.7.

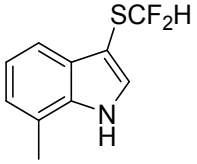
3-((difluoromethyl)thio)-6-fluoro-1*H*-indole (3d)[4]



General procedure was followed using 6-fluoro-1*H*-indole (135.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 20/1) to afford product **3d** as a yellow oil (163.0 mg, 75%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.70 (dd, *J* = 8.8, 5.2 Hz, 1H), 7.44 (d, *J* = 2.4 Hz, 1H), 7.09 (dd, *J* = 9.2, 2.0 Hz, 1H), 7.02 (td, *J* = 9.6, 2.4 Hz, 1H), 6.83

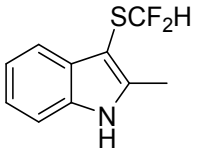
(t, J = 57.2 Hz, 1H).^{19}F NMR (376 MHz, $CDCl_3$) δ -92.01 (d, J = 56.4 Hz), -119.43 – -119.50 (m).^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7 (d, J = 239.0 Hz), 136.1 (d, J = 13.0 Hz), 132.2, 126.2, 123.6 (t, J = 275.0 Hz), 120.4 (d, J = 11.0 Hz), 110.3 (d, J = 24.0 Hz), 98.1 (d, J = 26.0 Hz), 96.9.

3-((difluoromethyl)thio)-7-methyl-1*H*-indole (3e)[2]



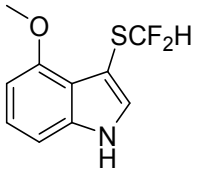
General procedure was followed using 7-methyl-1*H*-indole (131.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 20/1) to afford product **3e** as a yellow oil (140.6 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.68 (d, J = 7.2 Hz, 1H), 7.44 (s, 1H), 7.23 (t, J = 9.2 Hz, 1H), 7.12 (d, J = 6.0 Hz, 1H), 6.85 (t, J = 57.6 Hz, 1H), 2.50 (s, 3H).^{19}F NMR (376 MHz, $CDCl_3$) δ -91.94 (d, J = 56.4 Hz). ^{19}F NMR (376 MHz, $cdcl_3$) δ -91.94 (d, J = 56.4 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 131.6, 129.3, 123.9 (t, J = 274.0 Hz), 123.8, 121.5, 120.9, 117.0, 97.0, 16.3.

3-((difluoromethyl)thio)-2-methyl-1*H*-indole (3f)[5]



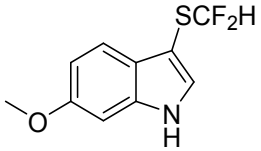
General procedure was followed using 2-methyl-1*H*-indole (131.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 20/1) to afford product **3f** as a yellow oil (134.0 mg, 63%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.71 – 7.70 (m, 1H), 7.32 – 7.30 (m, 1H), 7.23 – 7.20 (m, 2H), 6.75 (t, J = 57.5 Hz, 1H), 2.55 (s, 3H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -92.02 (d, J = 57.3 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.0, 135.5, 131.2, 123.8 (t, J = 277.2 Hz), 122.8, 121.4, 119.0, 111.1, 93.9 (t, J = 3.7 Hz), 12.5.

3-((difluoromethyl)thio)-4-methoxy-1*H*-indole (3g)[6]



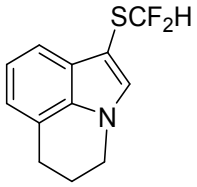
General procedure was followed using 4- methoxy-1*H*-indole (147.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 20/1) to afford product **3g** as a yellow oil (115.0 mg, 50%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.31 (d, *J* = 2.5 Hz, 1H), 7.20 (t, *J* = 8.0 Hz, 1H), 7.07 (t, *J* = 58.5 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.62 (d, *J* = 8.0 Hz, 1H), 3.98 (s, 3H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -95.34 (d, *J* = 58.8 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.7, 138.5, 130.8, 124.9 (t, *J* = 275.3 Hz), 124.6, 118.6, 105.3, 101.8, 97.2, 55.9.

3-((difluoromethyl)thio)-6-methoxy-1*H*-indole (3h)[3]



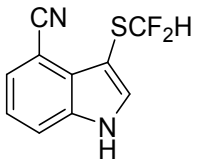
General procedure was followed using 6-methoxy-1*H*-indole (147.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 20/1) to afford product **3h** as a yellow oil (153.0 mg, 67%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.43 (d, *J* = 2.5 Hz, 1H), 7.30 (d, *J* = 9.0 Hz, 1H), 7.22 (d, *J* = 2.5 Hz, 1H), 6.93 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.79 (t, *J* = 57.5 Hz, 1H), 3.90 (s, 3H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -91.99 (d, *J* = 56.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.4, 132.3, 131.0, 130.5, 121.2 (t, *J* = 276.3 Hz), 113.9, 112.5, 100.6, 96.2, 55.8.

1-((difluoromethyl)thio)-5,6-dihydro-4*H*-pyrrolo[3,2,1-ij]quinoline (3i)[4]



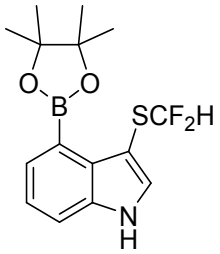
General procedure was followed using 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline (157.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 20/1) to afford product **3i** as a yellow oil (127.0 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.6 Hz, 1H), 7.33 (s, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 6.8 Hz, 1H), 6.82 (t, *J* = 57.6 Hz, 1H), 4.20 (t, *J* = 5.6 Hz, 2H), 3.03 (t, *J* = 5.6 Hz, 2H), 2.28 - 2.24 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -92.27 (d, *J* = 56.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.6, 133.3, 128.3, 124.0 (t, *J* = 274.0 Hz), 122.3, 121.3, 119.7, 116.8, 94.0, 44.5, 24.5, 22.7.

3-((difluoromethyl)thio)-1*H*-indole-4-carbonitrile (3j)



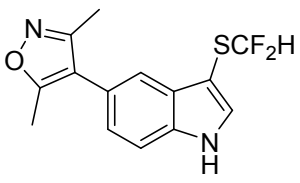
General procedure was followed using 4-carbonitrile-1*H*-indole (142.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 20/1) to afford product **3j** as a yellow solid (74.0 mg, 33%). ^{1}H NMR (400 MHz, DMSO) δ 12.31 (s, 1H), 8.03 (d, *J* = 2.8 Hz, 1H), 7.99 (s, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.22 (t, *J* = 56.0 Hz, 1H). ^{19}F NMR (376 MHz, DMSO) δ -92.80 (d, *J* = 56.4 Hz).^{13}C NMR (100 MHz, DMSO) δ 138.2, 135.7, 133.4, 123.9 (t, *J* = 274.0 Hz), 123.6, 120.6, 120.1, 117.8, 104.3, 94.8. HRMS (ESI): m/z calcd. for $C_{10}H_6F_2N_2S$ $[M+H]^+$ 225.0293, found: 225.0292.

3-((difluoromethyl)thio)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (3k)



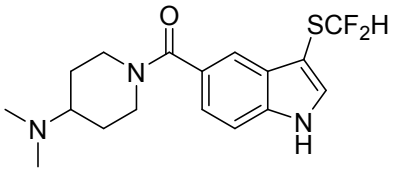
General procedure was followed using 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (243.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 20/1) to afford product **3k** as a white solid (208.1 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 7.57 (dd, *J* = 6.8, 0.8 Hz, 1H), 7.47 – 7.43 (m, 2H), 7.30 (d, *J* = 7.2, 1H), 7.09 (t, *J* = 59.6 Hz, 1H), 1.49 (s, 12H).^{19}F NMR (376 MHz, $CDCl_3$) δ -96.22 (d, *J* = 60.2 Hz).^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 133.6, 131.6, 127.9, 124.2 (t, *J* = 273.0 Hz), 122.4, 113.8, 98.0, 84.4, 24.9. HRMS (ESI): m/z calcd. for $C_{15}H_{18}BF_2NO_2S$ $[M+H]^+$ 326.1192, found: 326.1201.

4-(3-((difluoromethyl)thio)-1*H*-indol-5-yl)-3,5-dimethylisoxazole (3l)



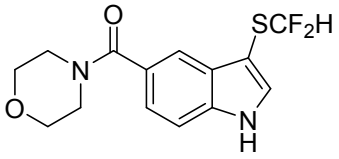
General procedure was followed using 4-(1*H*-indol-4-yl)-3,5-dimethylisoxazole (212.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 20/1) to afford product **3l** as a yellow solid (217.5 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03 (s, 1H), 7.67 (s, 1H), 7.56 (d, *J* = 2.0 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 1H), 7.17 (dd, *J* = 8.5, 1.5 Hz, 1H), 6.70 (t, *J* = 57.5 Hz, 1H), 2.45 (s, 3H), 2.32 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -91.84 (d, *J* = 57.3 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.2, 159.1, 135.5, 132.8, 130.3, 124.4, 123.2, 121.9 (t, *J* = 276.0 Hz), 120.1, 117.3, 112.1, 96.4, 11.6, 10.9. HRMS (ESI): m/z calcd. for $C_{14}H_{12}F_2N_2OS$ $[M+H]^+$ 295.0711, found: 295.0728.

(3-((difluoromethyl)thio)-1*H*-indol-5-yl)(4-(dimethylamino)piperidin-1-yl)methanone (3m)



General procedure was followed using (4-(dimethylamino)piperidin-1-yl)(1*H*-indol-5-yl)methanone (271.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 20/1) to afford product **3m** as a yellow oil (254.2 mg, 74%). ^{1}H NMR (500 MHz, DMSO) δ 12.21 (s, 1H), 7.83 (d, *J* = 2.5 Hz, 1H), 7.65 (s, 1H), 7.55 (d, *J* = 8.5 Hz, 1H), 7.32 (t, *J* = 56.0 Hz, 1H), 7.27 (dd, *J* = 8.5, 1.0 Hz, 1H), 3.41 – 3.36 (m, 3H), 3.11 – 2.82 (m, 2H), 2.68 (s, 6H), 2.06 (s, 2H), 1.64 – 1.62 (m, 2H). ^{19}F NMR (376 MHz, DMSO) δ -92.11 (d, *J* = 56.3 Hz). ^{13}C NMR (126 MHz, DMSO) δ 170.6, 137.4, 135.4, 129.6, 128.2, 121.9, 121.5 (t, *J* = 273.8 Hz), 118.2, 112.7, 94.1, 62.5, 60.2, 21.2, 14.5. HRMS (ESI): m/z calcd. for $C_{17}H_{21}F_2N_3OS$ $[M+H]^+$ 354.1446, found: 354.1791.

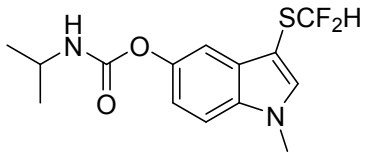
(3-((difluoromethyl)thio)-1H-indol-5-yl)(morpholino)methanone (3n)



General procedure was followed using (1*H*-indol-5-yl)(morpholino)methanone (230.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 20/1) to afford product **3n** as a yellow solid (200.0 mg, 64%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.07 (s, 1H), 7.79 (s, 1H), 7.39 (d, *J* = 2.5 Hz, 1H), 7.22 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.13 (dd, *J* = 8.5, 1.0 Hz, 1H), 6.68 (d, *J* = 57.0 Hz, 1H), 3.78 – 3.57 (m, 8H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -

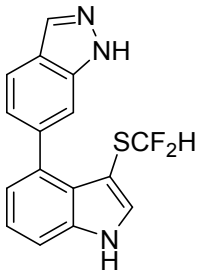
92.46 (d, J = 57.2 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.29, 137.43, 134.18, 129.7, 127.74, 122.44, 123.33 (t, J = 276.4 Hz), 118.90, 112.69, 96.66 (d, J = 3.9 Hz), 67.30. HRMS (ESI): m/z calcd. for $C_{14}H_{14}F_2N_2O_2S$ $[M+H]^+$ 313.0817, found: 313.0838.

3-((difluoromethyl)thio)-1-methyl-1*H*-indol-5-yl isopropylcarbamate (3o)



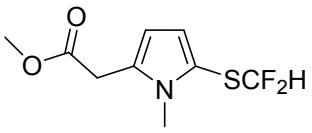
General procedure was followed using 1*H*-indol-5-yl isopropylcarbamate (218.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 10/1) to afford product **3o** as a yellow solid (201.0 mg, 67%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, J = 2.0 Hz, 1H), 7.31 (s, 1H), 7.28 (d, J = 9.0 Hz, 1H), 7.09 (dd, J = 9.0, 2.5 Hz, 1H), 6.63 (t, J = 57.5 Hz, 1H), 4.96 (s, 1H), 3.95 – 3.88 (m, 1H), 3.76 (s, 3H), 1.25 (d, J = 6.5 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -92.45 (dd, J = 57.7, 2.5 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.4, 145.9, 137.1, 134.8, 130.8, 122.0 (t, J = 276.0 Hz), 117.6, 111.7, 110.2, 94.2, 43.4, 33.4, 23.0. HRMS (ESI): m/z calcd. for $C_{14}H_{16}F_2N_2O_2S$ $[M+H]^+$ 315.0973, found: 315.0985.

6-(3-((difluoromethyl)thio)-1*H*-indol-4-yl)-1*H*-indazole (3p)



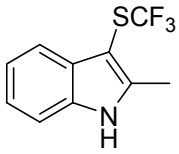
General procedure was followed using 6-(1*H*-indol-4-yl)-1H-indazole (233.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 20/1) to afford product **3p** as a yellow solid (138.6 mg, 44%). ^{1}H NMR (500 MHz, DMSO) δ 13.06 (s, 1H), 11.98 (s, 1H), 8.11 (s, 1H), 7.76 – 7.72 (m, 2H), 7.54 – 7.51 (m, 2H), 7.27 (t, J = 7.5 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 7.03 (d, J = 7.0 Hz, 1H), 6.76 (t, J = 57.5 Hz, 1H). ^{19}F NMR (376 MHz, DMSO) δ -93.65 (d, J = 57.2 Hz). ^{13}C NMR (126 MHz, DMSO) δ 140.2, 138.3, 137.6, 135.4, 135.1, 133.8, 126.1, 123.9, 122.9, 122.4, 122.4, 121.4 (t, J = 273.4 Hz), 119.5, 112.2, 111.3, 93.5. HRMS (ESI): m/z calcd. for $C_{16}H_{11}F_2N_3S$ $[M+H]^+$ 316.0715, found: 316.0819.

methyl 2-(5-((difluoromethyl)thio)-1-methyl-1*H*-pyrrol-2-yl)acetate (3q)



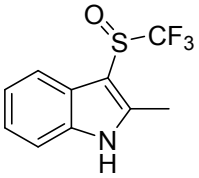
General procedure was followed using methyl 2-(4-methyl-1*H*-pyrrol-2-yl)acetate (153.0 mg, 1.0 mmol). The crude product was pmethyl 2-(5-((difluoromethyl)thio)-1-methyl-1H-pyrrol-2-yl)acetateurified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 40/1) to afford product 3q as a yellow oil (136.0 mg, 58%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.69 (d, J = 57.5 Hz, 1H), 6.58 (d, J = 4.0 Hz, 1H), 6.15 (d, J = 3.5 Hz, 1H), 3.74 (s, 3H), 3.70 (s, 2H), 3.65 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -92.99 (d, J = 57.0 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.3, 130.7, 122.0 (t, J = 277.7 Hz), 120.6, 111.6 (t, J = 4.1 Hz), 109.6, 52.3, 33.5, 31.3. HRMS (ESI): m/z calcd. for $C_9H_{11}F_2NO_2S$ $[M+H]^+$ 236.0551, found: 236.0568.

2-methyl-3-((trifluoromethyl)thio)-1*H*-indole (3r)[7]



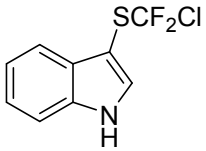
General procedure was followed using 2-$BTSO_2CF_3$ (1.5 mmol) and 2-methyl-1*H*-indole (131.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 40/1) to afford product **3r** as a yellow oil (76.2 mg, 33%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.94 (s, 1H), 7.54 – 7.52 (m, 1H), 7.41 – 7.39 (m, 1H), 7.18 – 7.12 (m, 2H), 2.52 (s, 3H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -44.17. ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.4, 135.8, 133.9 (q, J = 310.9 Hz), 130.5, 122.4, 121.2, 117.8, 112.1, 89.0, 12.0.

2-methyl-3-((trifluoromethyl)sulfinyl)-1*H*-indole (3r′)



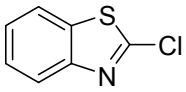
The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 7/1) to afford product **3r′**as a white solid (106.0 mg, 43%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 1H), 7.95 (d, J = 7.2 Hz, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.26 – 7.20 (m, 2H), 2.57 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -72.26. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.1, 135.5, 126.6 (q, J = 243.6 Hz), 124.4, 123.7, 122.5, 120.2, 111.4, 104.3, 12.4. HRMS (ESI): m/z calcd. For $C_{10}H_8F_3NOS$ $[M+H]^+$ 248.0351, found: 248.0390.

3-((chlorodifluoromethyl)thio)-1*H*-indole (3s)



General procedure was followed using 2-$BTSO_2CF_2Cl$ (1.5 mmol) and 1*H*-indole (131.0 mg, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 40/1) to afford product **3s** as a yellow oil (53.9 mg, 23%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.86 – 7.84 (m, 1H), 7.54 (d, *J* = 3.0 Hz, 1H), 7.44 – 7.42 (m, 1H), 7.34 – 7.29 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -29.65. ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.0, 133.1, 130.8 (t, *J* = 325.8 Hz), 129.5, 123.4, 121.7, 119.5, 111.8, 98.2. HRMS (ESI): m/z calcd. for $C_9H_6ClF_2NS$ $[M-H]^-$ 231.9805, found: 231.9815.

2-chlorobenzo[*d*]thiazole

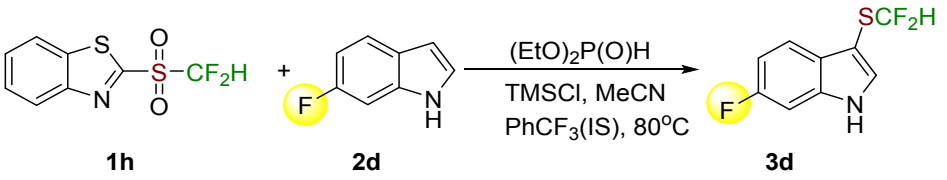


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dq, J = 6.4, 0.4 Hz, 1H), 7.78 (dq, J = 6.4, 0.4 Hz, 1H), 7.50 – 7.46 (m, 1H), 7.42 – 7.39 (m, 1H).

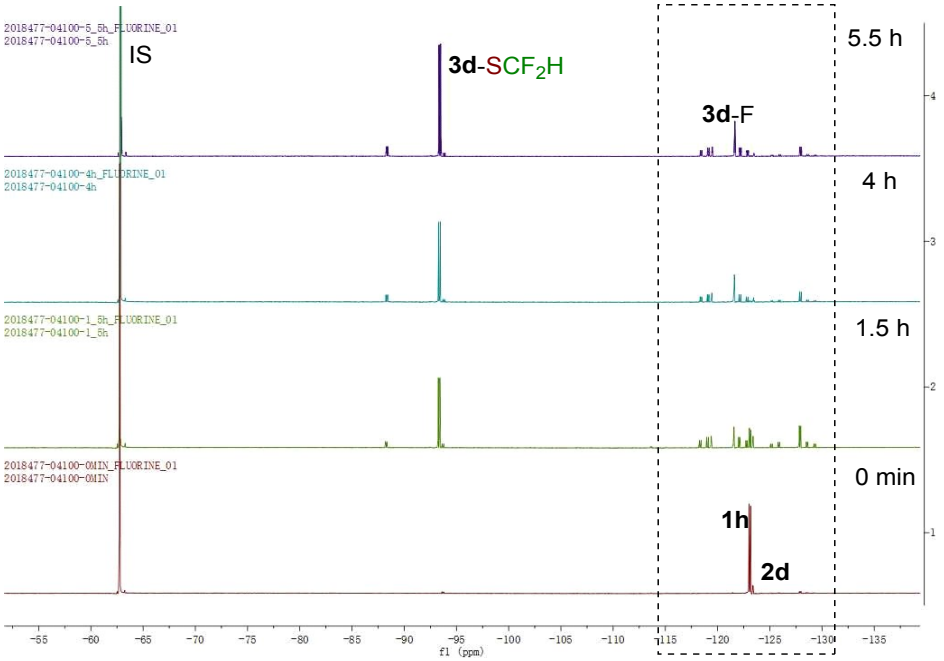
4. Mechanistic Studies

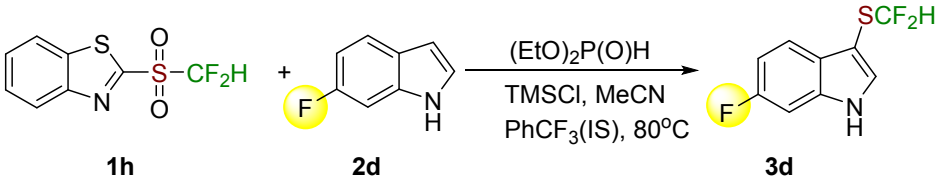
4.1 In suit ^{19}F NMR analysis.

To detect the key intermediates of $(EtO)_2P(O)H$/TMSCl mediated direct difluoromethylthiolation, the experiment was conducted and monitored by the in suit ^{19}F NMR. The reagent **1h** (−123.3 ppm) promptly disappeared within 1.5 h at 80℃, and small friable signals appeared between −118.5 and −123.0 ppm, which is believed to be $HCF_2S(O)H$ according to previous report.

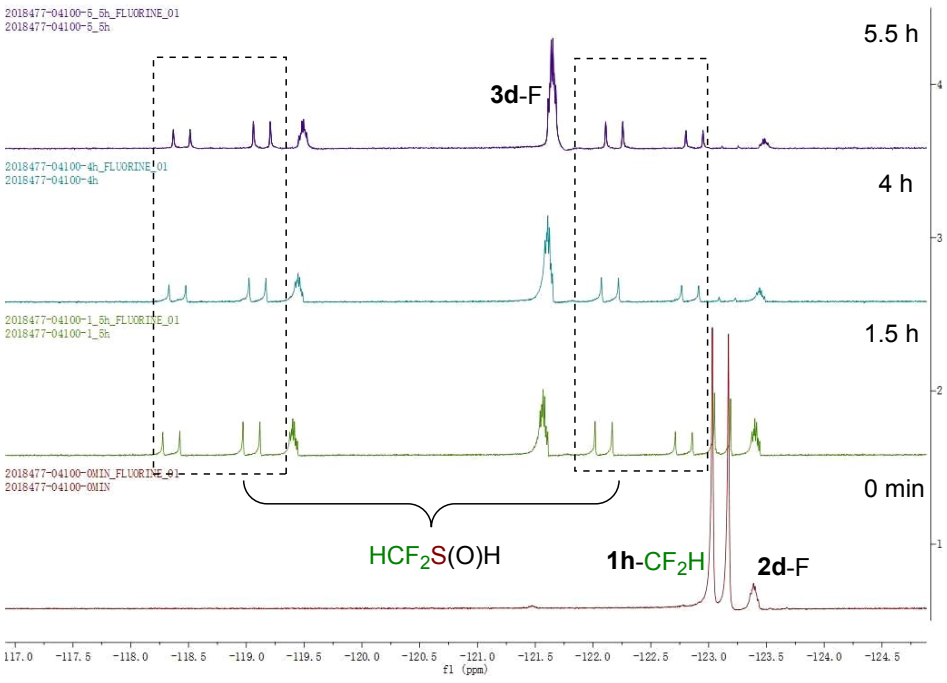


1h **2d** **3d**

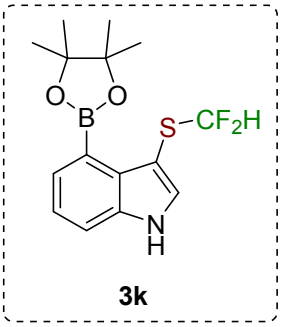




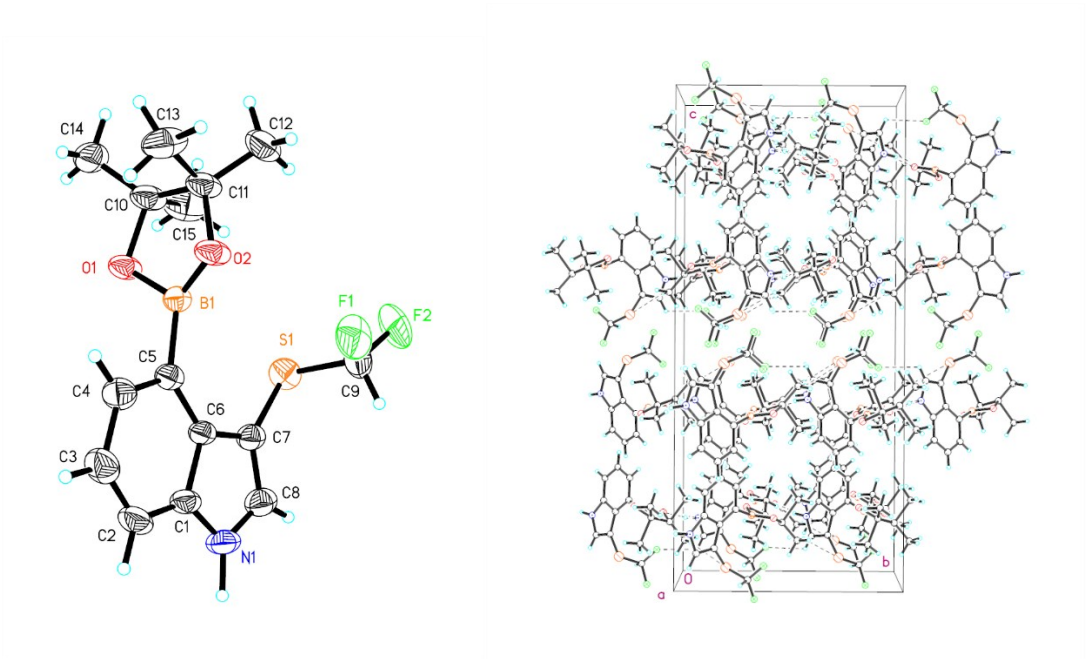
1h **2d** **3d**



5. X-ray crystal structure analysis of 3k:



3k



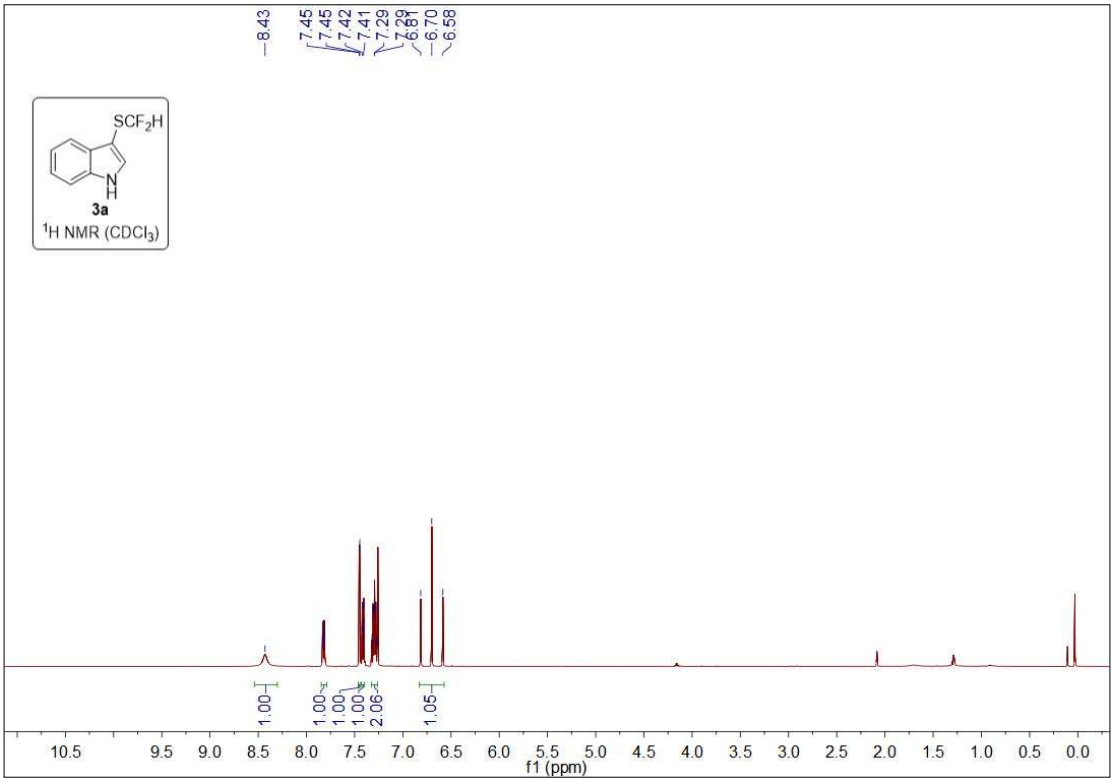
Crystal data and structure refinement for mo_d8v19075_0m.

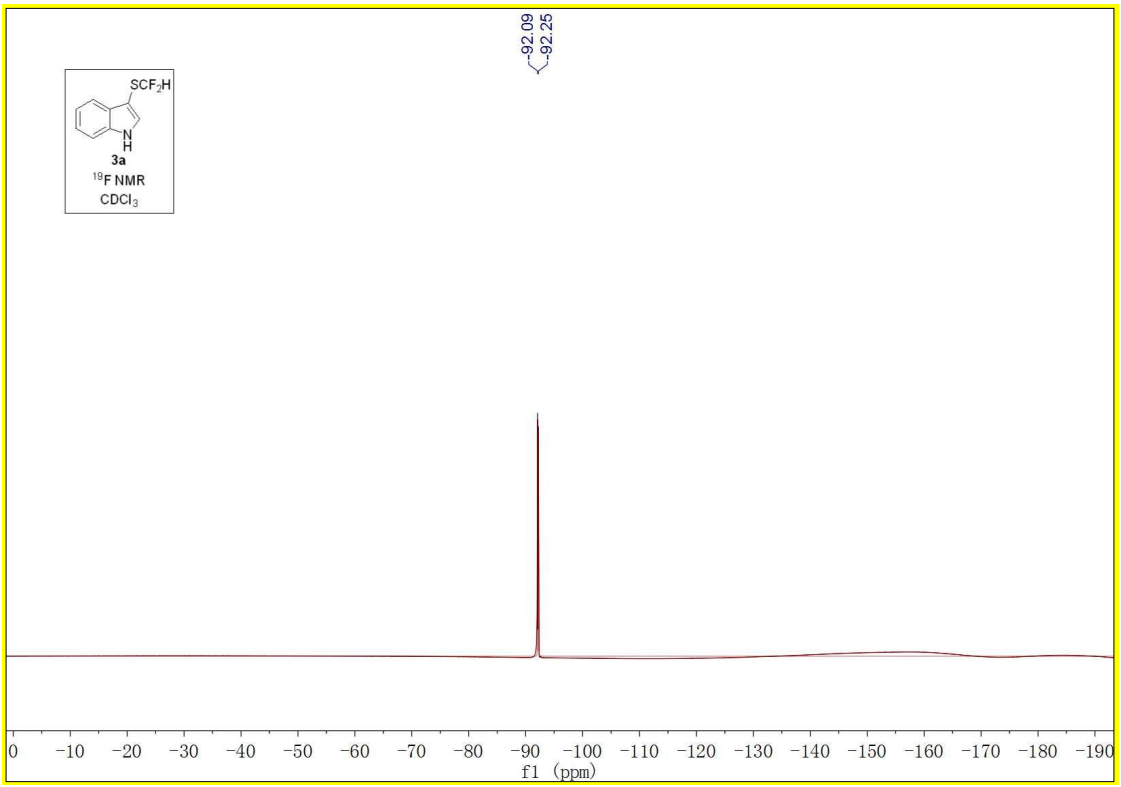
Identification code	mo_d8v19075_0m
Empirical formula	$C_{15}H_{18}F_2NO_2S$
Formula weight	325.17
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P b c a
Unit cell dimensions	a = 7.0875(4) Å α = 90°
	b = 10.6127(5) Å β = 90°.
	c = 14.5537(7) Å γ = 90°.
Volume	3327.5 (2) $Å^3$
Z	8

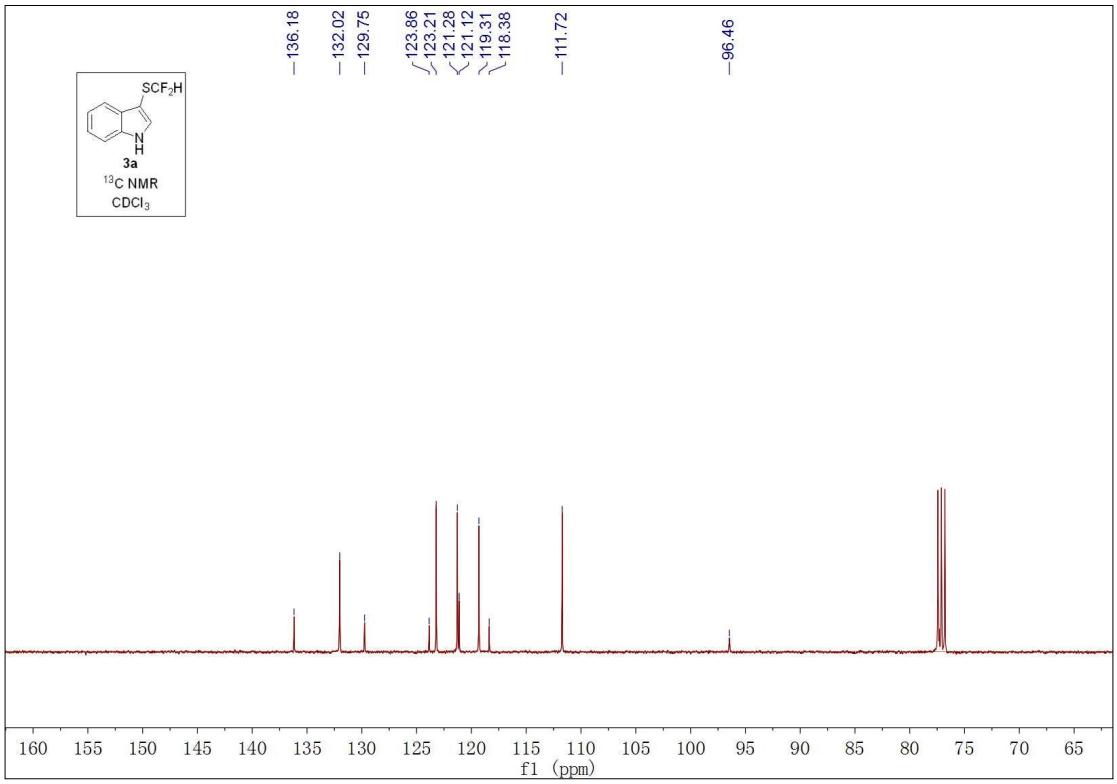
Density (calculated)	1.298 Mg/m^3
Absorption coefficient	0.219 mm^{-1}
F(000)	1360
Crystal size	0.180 x 0.150 x 0.120 mm^3
Theta range for data collection	2.816 to 25.999°.
Index ranges	-10<=h<=10, -16<=k<=16, -36<=l<=36
Reflections collected	27898
Independent reflections	3260 [R(int) = 0.0728]
Completeness to theta = 25.242°	99.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.4612
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3260 / 135 / 311
Goodness-of-fit on F^2	1.024
Final R indices [I>2sigma(I)]	R1 = 0.0674, wR2 = 0.1840
R indices (all data)	R1 = 0.0869, wR2 = 0.2059
Absolute structure parameter	0.014(4)
Largest diff. peak and hole	0.309 and -0.284 $e.Å^{-3}$

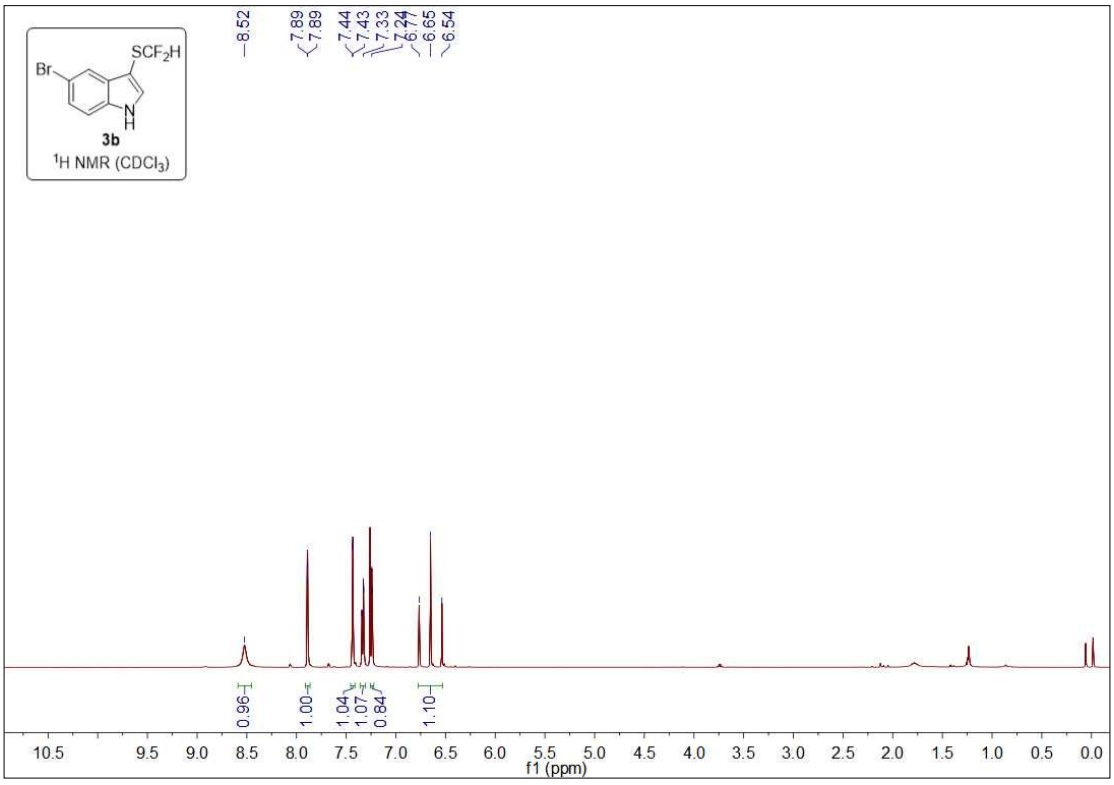
[1] Z. Huang, O. Matsubara, S. Jia, E. Tokunaga and N. Shibata, *Org. Lett.,* 2017, **19**, 934–937.
[2] Q. Yan, L.Jiang, W. Yi, Q. Liu and W. Zhang, *Adv. Synth. Catal.,* 2017, **359**, 2471–2480.
[3] X. Zhao, A. Wei, T. Li, Z. Su, J. Chen and K. Lu, *Org. Chem. Front.,* 2017, **4**, 232–235.
[4] T. Ding, L. Jiang and W. Yi, *Org. Lett.,* 2018, **20**, 170−173.
[5] L. Jiang, W. Yi and Q. Liu, *Adv. Synth. Catal.,* 2016, **358**, 3700−3705.
[6] J. Li, D. Zhu, L. Lv and C.-J. Li, *Chem. Sci.,* 2018, **9**, 5781–5786.
[7] H. Chachignon, M. Maeno, H. Kondo, N. Shibata and D. Cahard, *Org. Lett.,* 2016, **18**, 2467−2470.

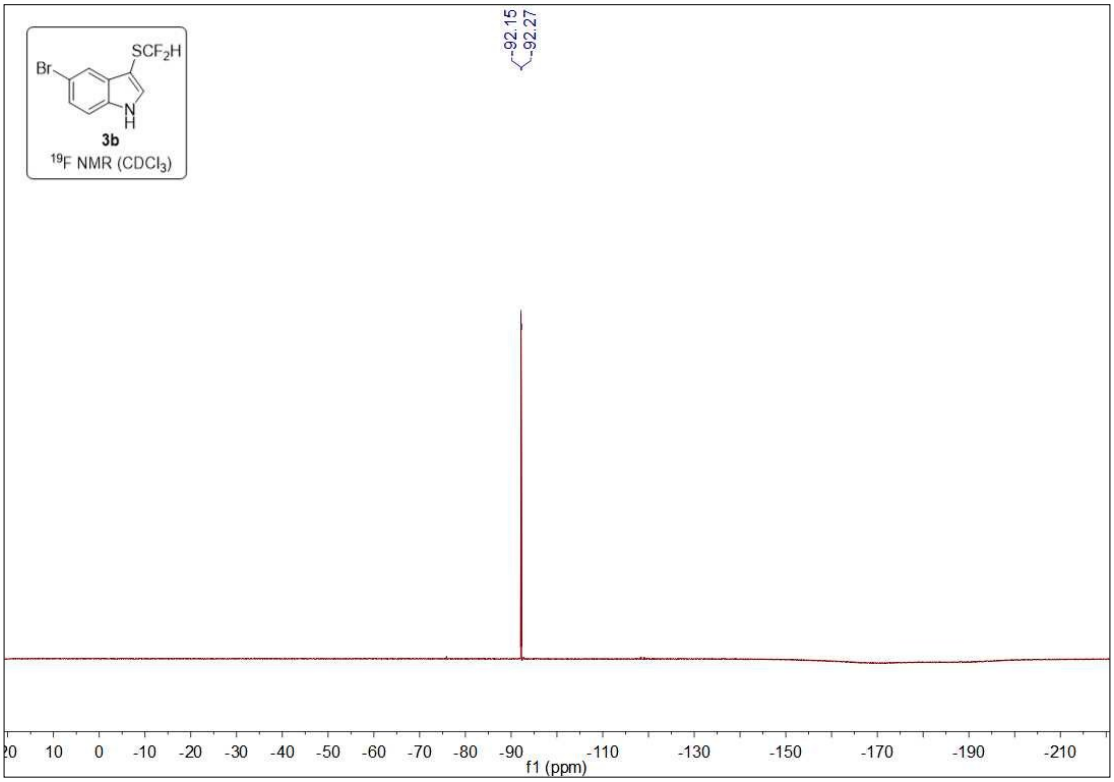
6. Copies of NMR Spectra

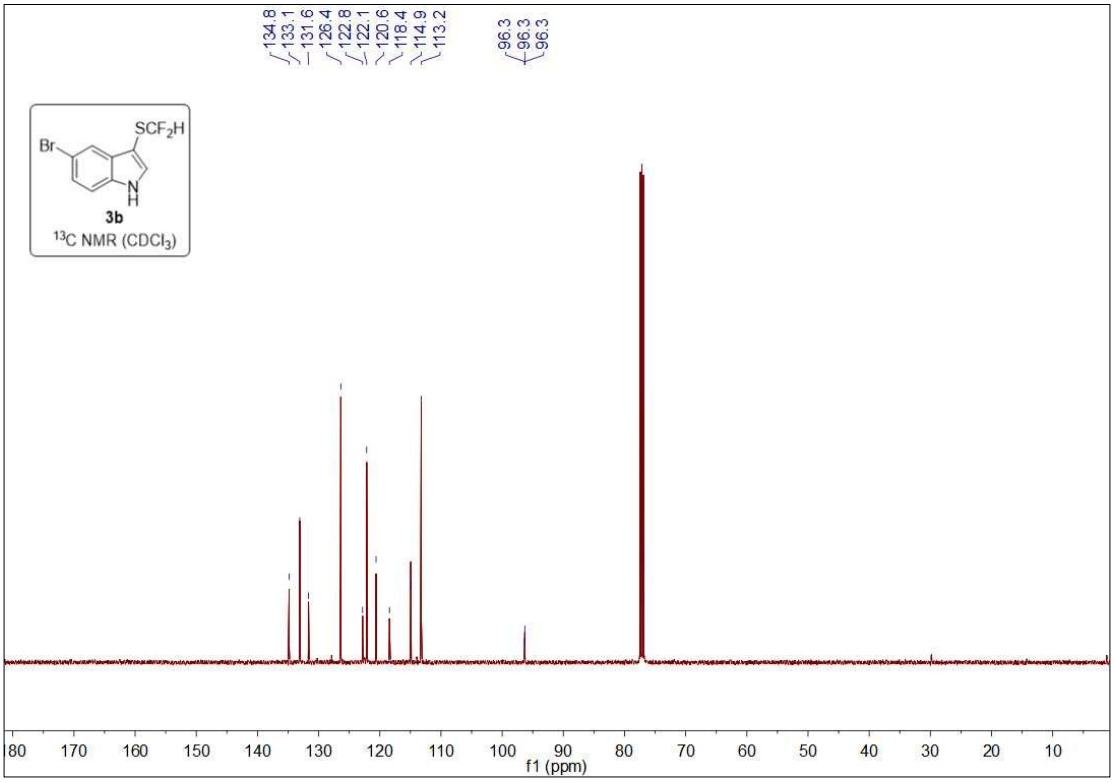


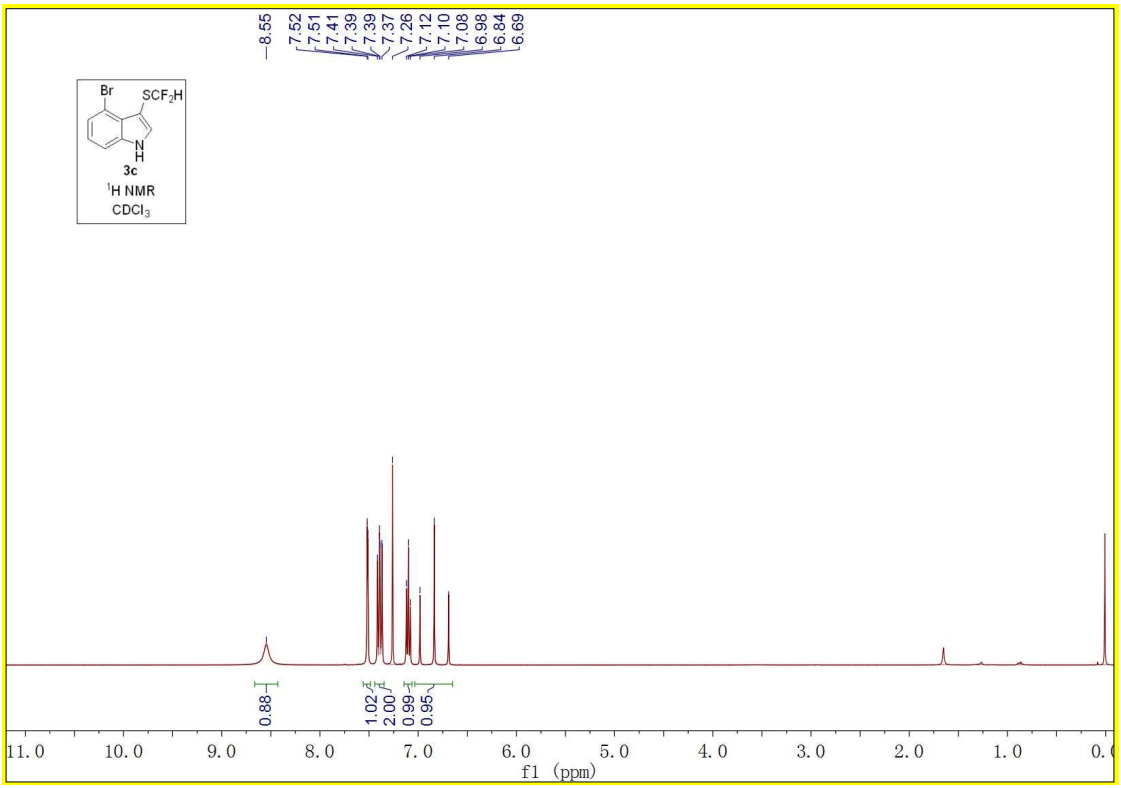


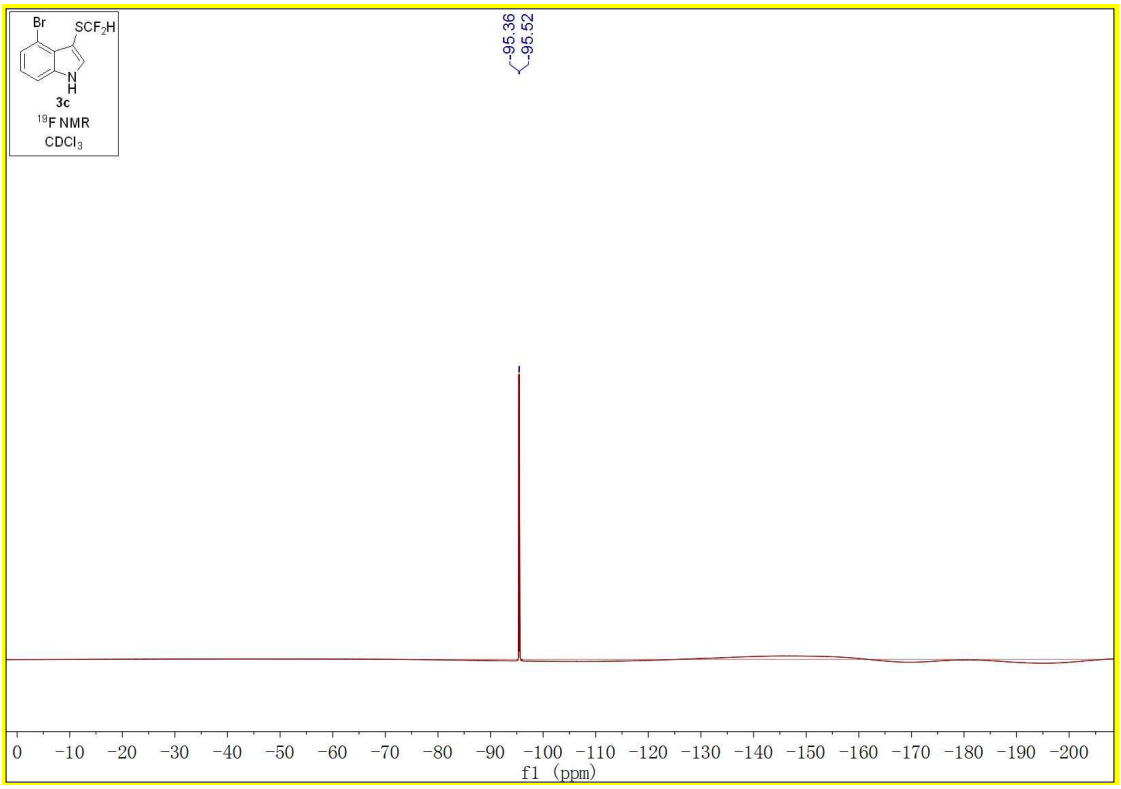

136.18
132.02
129.75
123.86
123.21
121.28
121.12
119.31
118.38
111.72
96.46
SCF2H
3a
13C NMR
CDCl3
160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65
f1 (ppm)


8.52
7.89
7.89
7.44
7.43
7.33
7.24
6.77
6.65
6.54
SCF2H
Br
3b
1H NMR (CDCl3)
0.96
1.00
1.04
1.07
0.84
1.10
10.5 9.5 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)


-92.15
-92.27
Br
SCF2H
N
H
3b
19F NMR (CDCl3)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190 -210
f1 (ppm)


134.8
133.1
131.6
126.4
122.8
122.1
120.6
118.4
114.9
113.2
96.3
96.3
96.3
Br
SCF2H
N
H
3b
13C NMR (CDCl3)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


8.55
7.52
7.51
7.41
7.39
7.39
7.37
7.26
7.12
7.10
7.08
6.98
6.84
6.69
Br
SCF2H
N
H
3c
1H NMR
CDCl3
0.88
1.02
2.00
0.99
0.95
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
f1 (ppm)


Br
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N
H
3c
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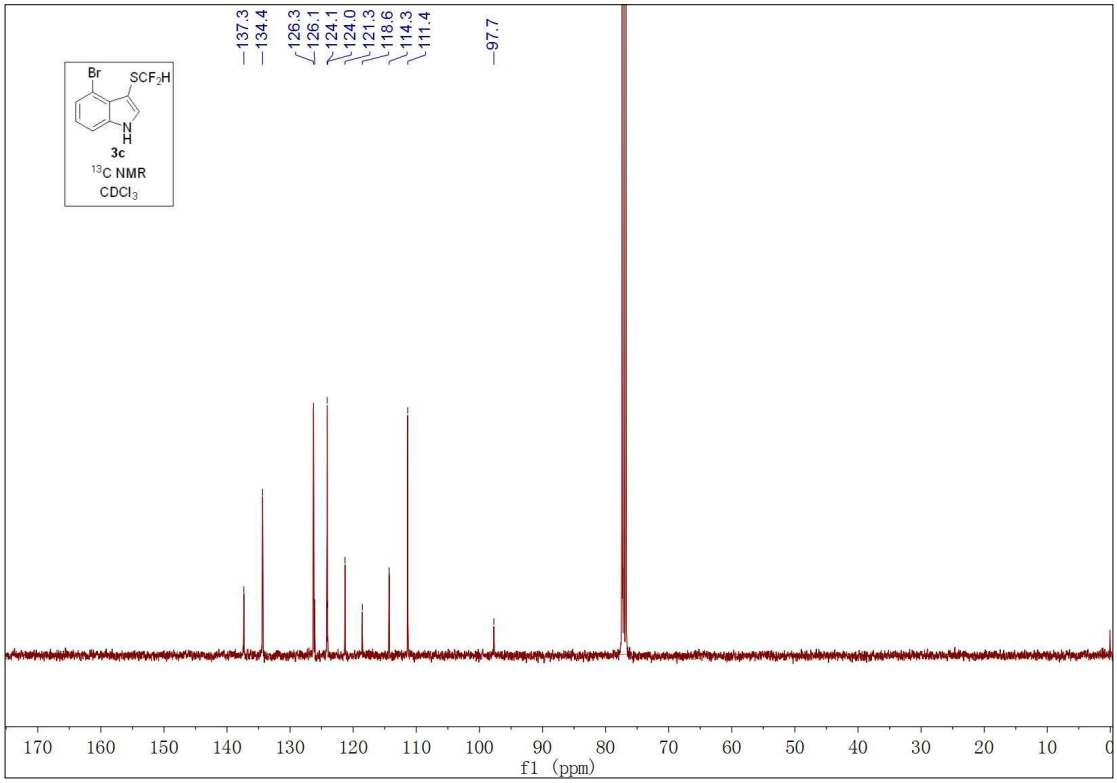
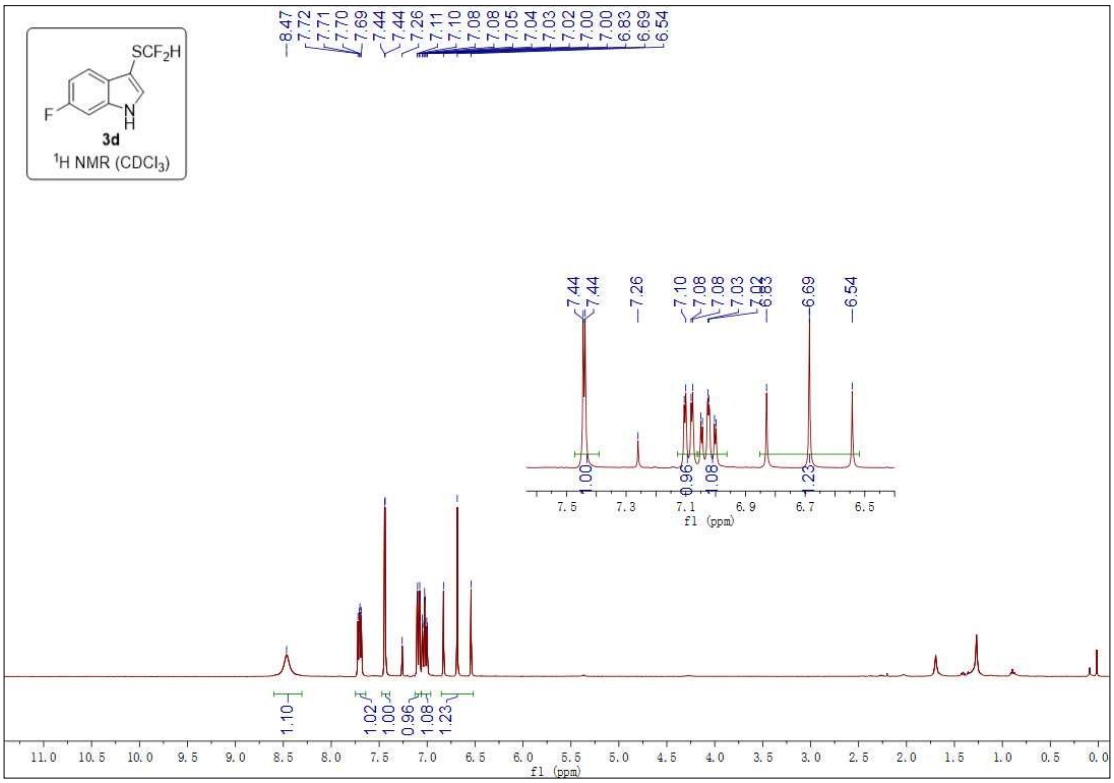
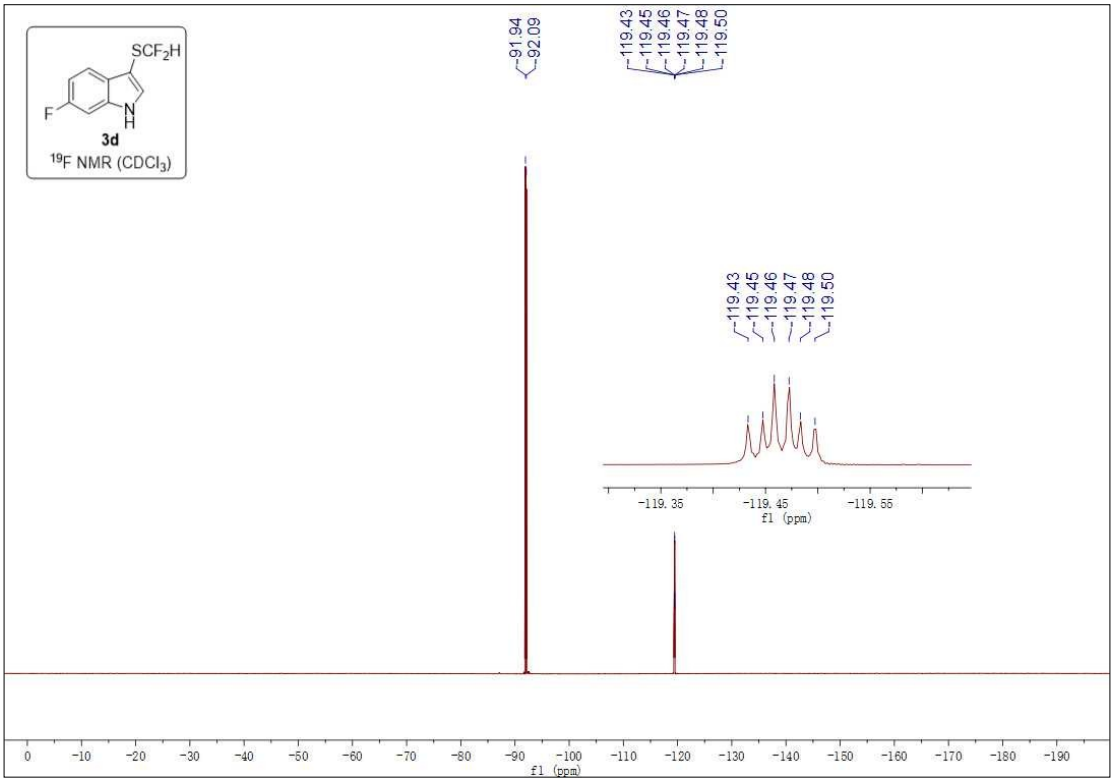
-95.52
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)


137.3
134.4
126.3
126.1
124.1
124.0
121.3
118.6
114.3
111.4
97.7
Br
SCF2H
N
H
3c
13C NMR
CDCl3
f1 (ppm)


8.47
7.72
7.71
7.70
7.69
7.44
7.44
7.26
7.11
7.10
7.08
7.08
7.05
7.04
7.03
7.02
7.00
7.00
6.83
6.69
6.54
SCF2H
F
N
H
3d
1H NMR (CDCl3)
1.10
1.02
1.00
0.96
1.08
1.23
f1 (ppm)


SCF2H
F
N
H
3d
19F NMR (CDCl3)
91.94
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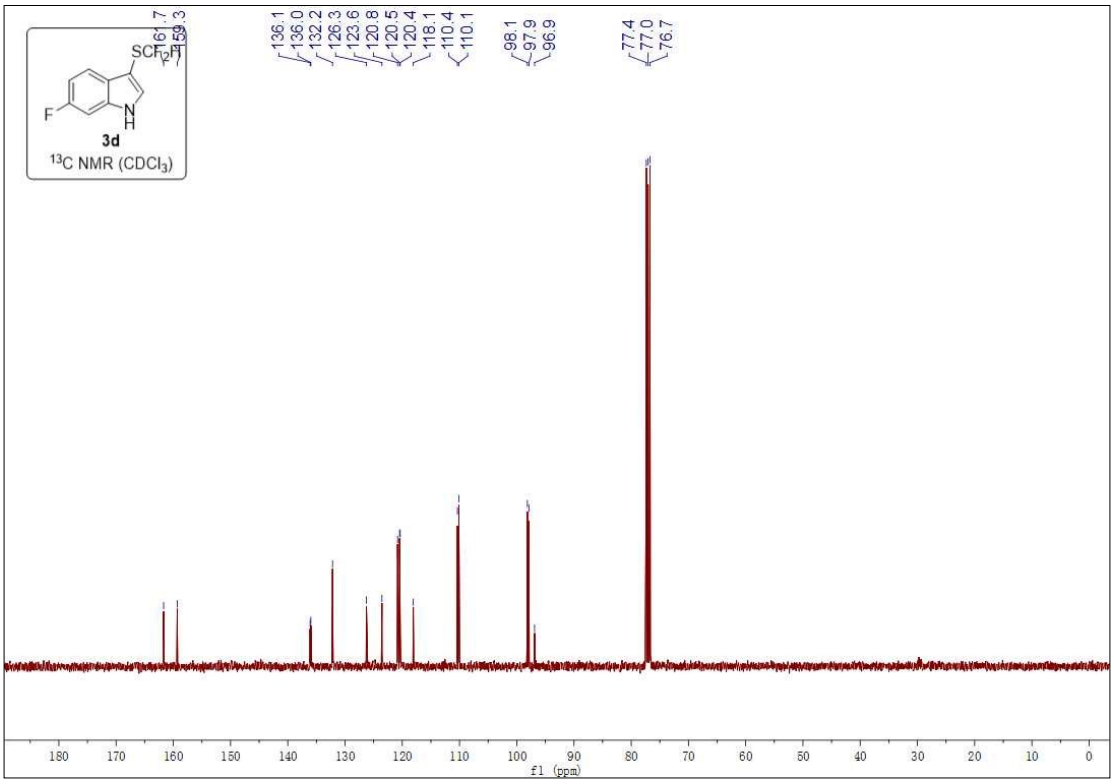
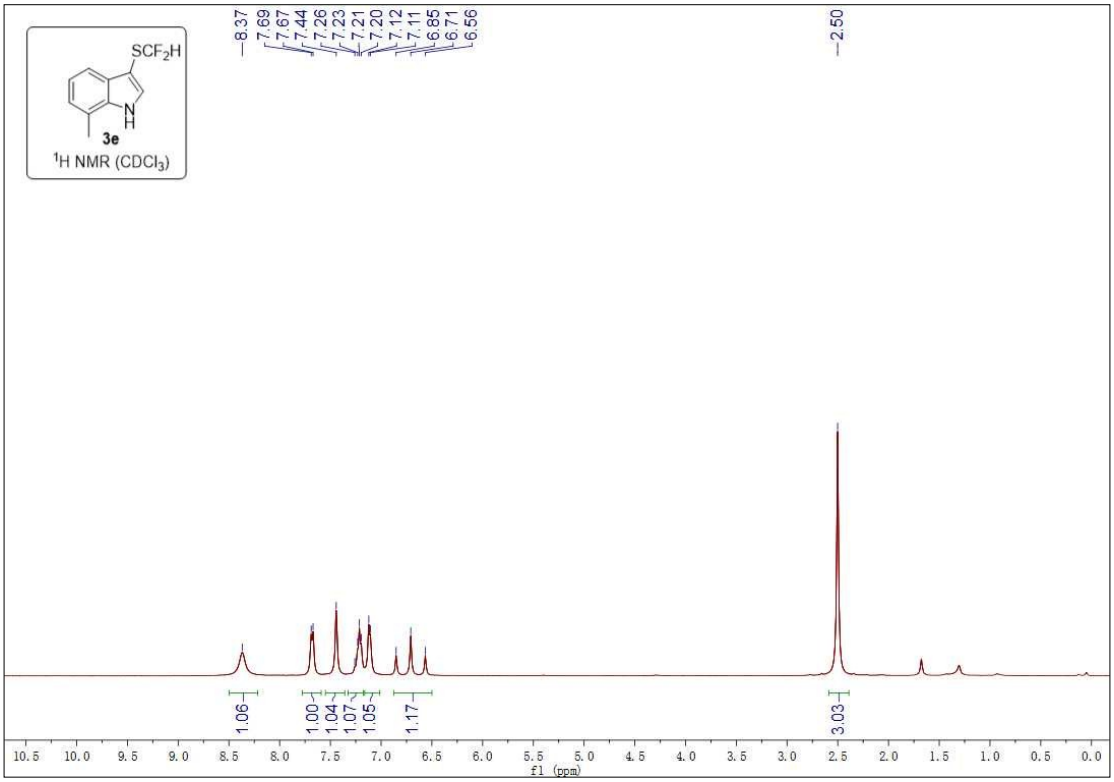
119.43
119.45
119.46
119.47
119.48
119.50
-119.35
-119.45
-119.55
f1 (ppm)


SCF2H
F
N
H
3d
13C NMR (CDCl3)
161.7
159.3
136.1
136.0
132.2
126.3
123.6
120.8
120.5
120.4
118.1
110.4
110.1
98.1
97.9
96.9
77.4
77.0
76.7
f1 (ppm)


SCF2H
N
H
3e
1H NMR (CDCl3)
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7.69
7.67
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7.26
7.23
7.21
7.20
7.12
7.11
6.85
6.71
6.56
2.50
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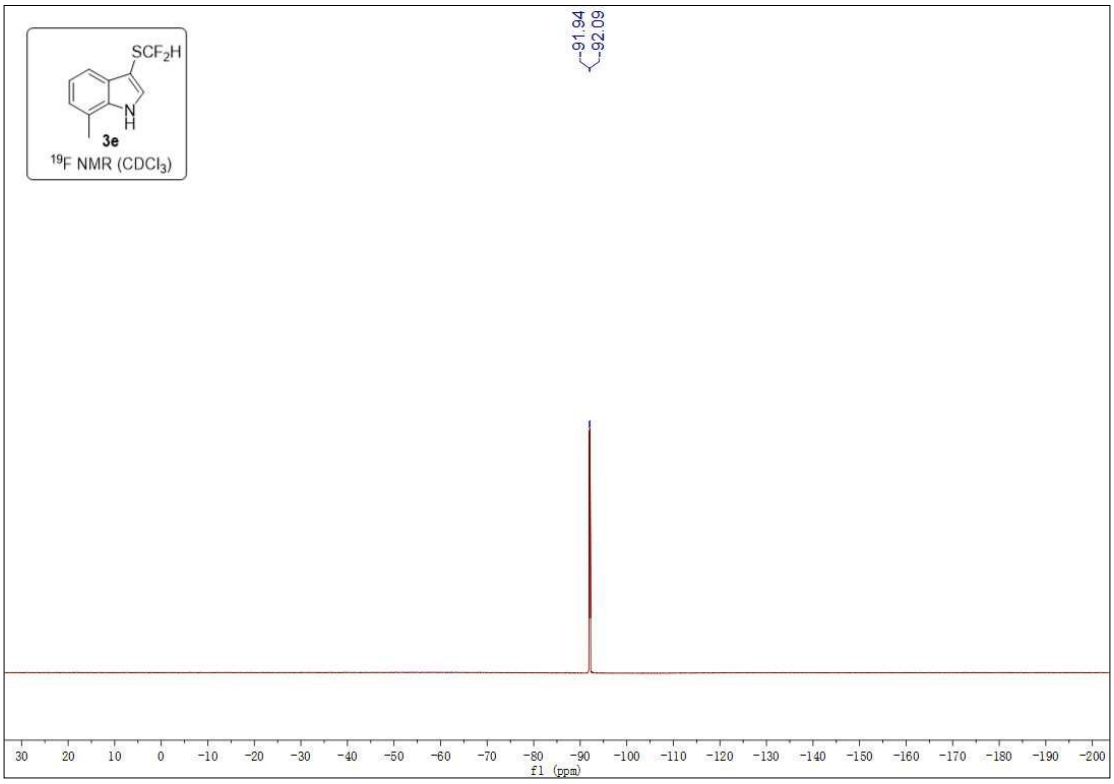
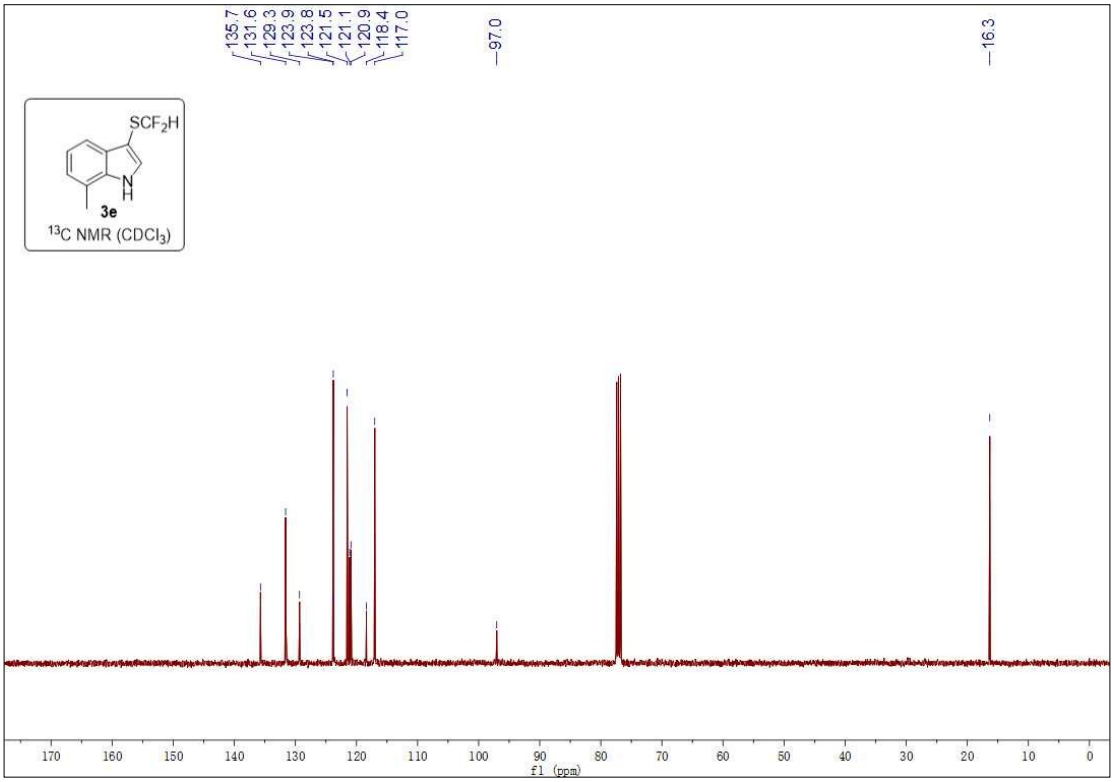
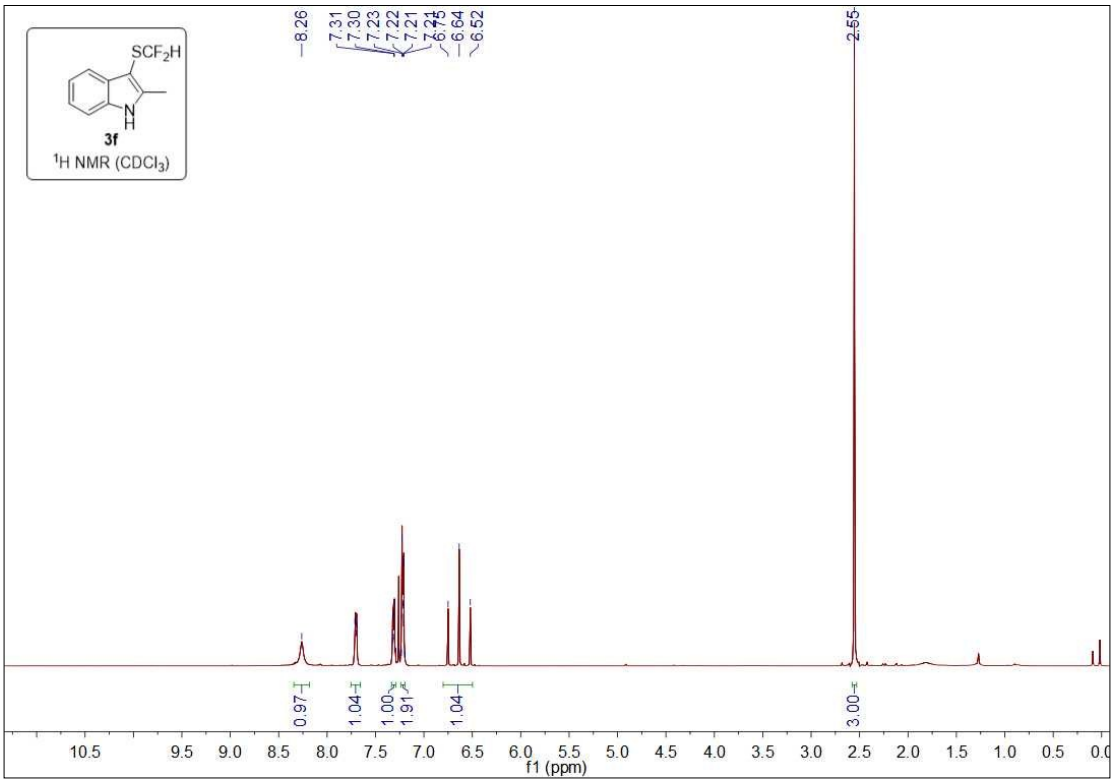
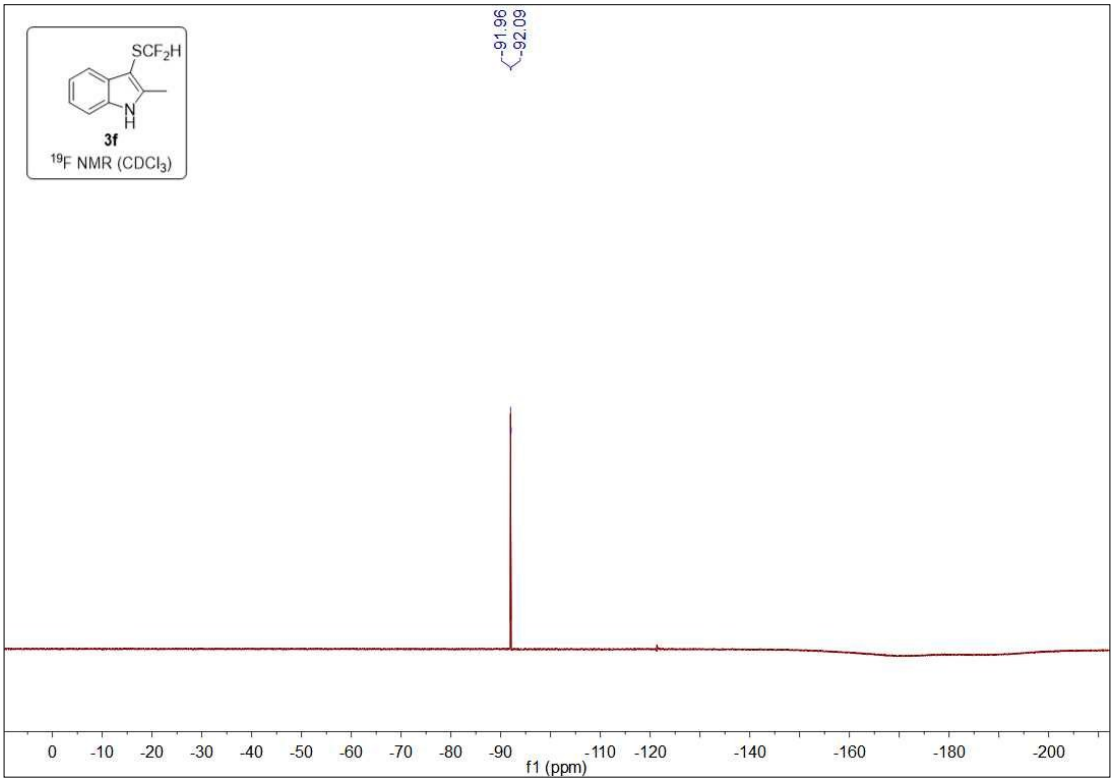
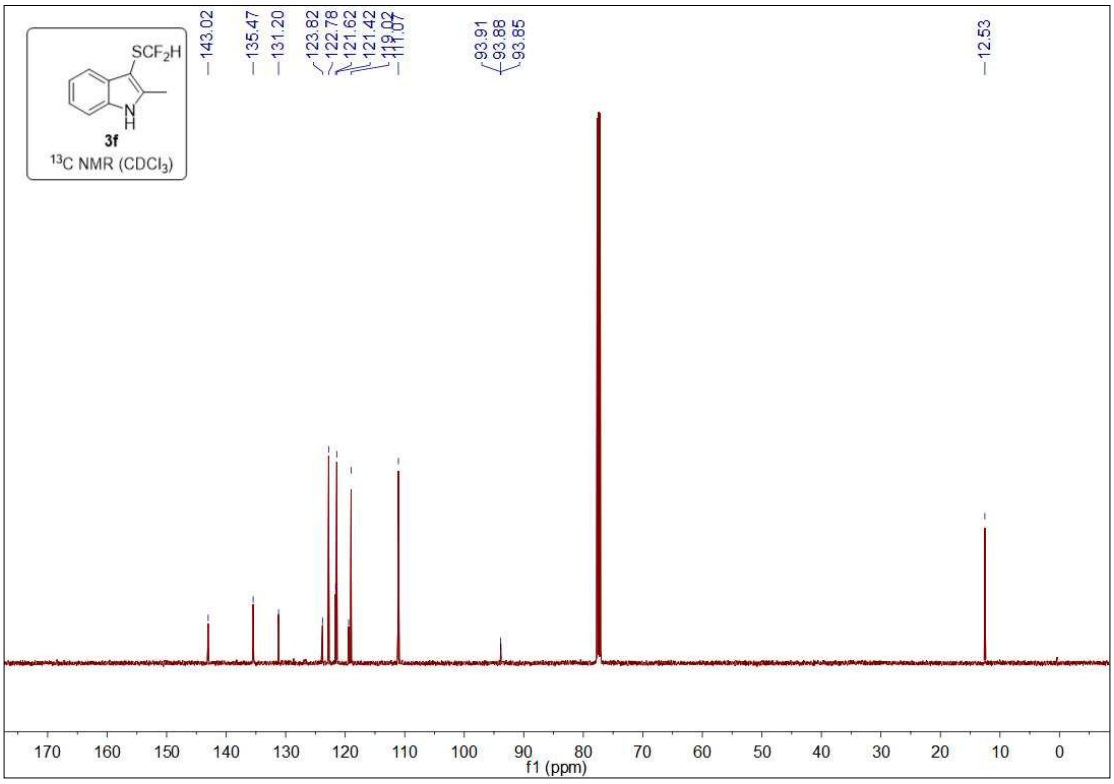
1.00
1.04
1.07
1.05
1.17
3.03
f1 (ppm)

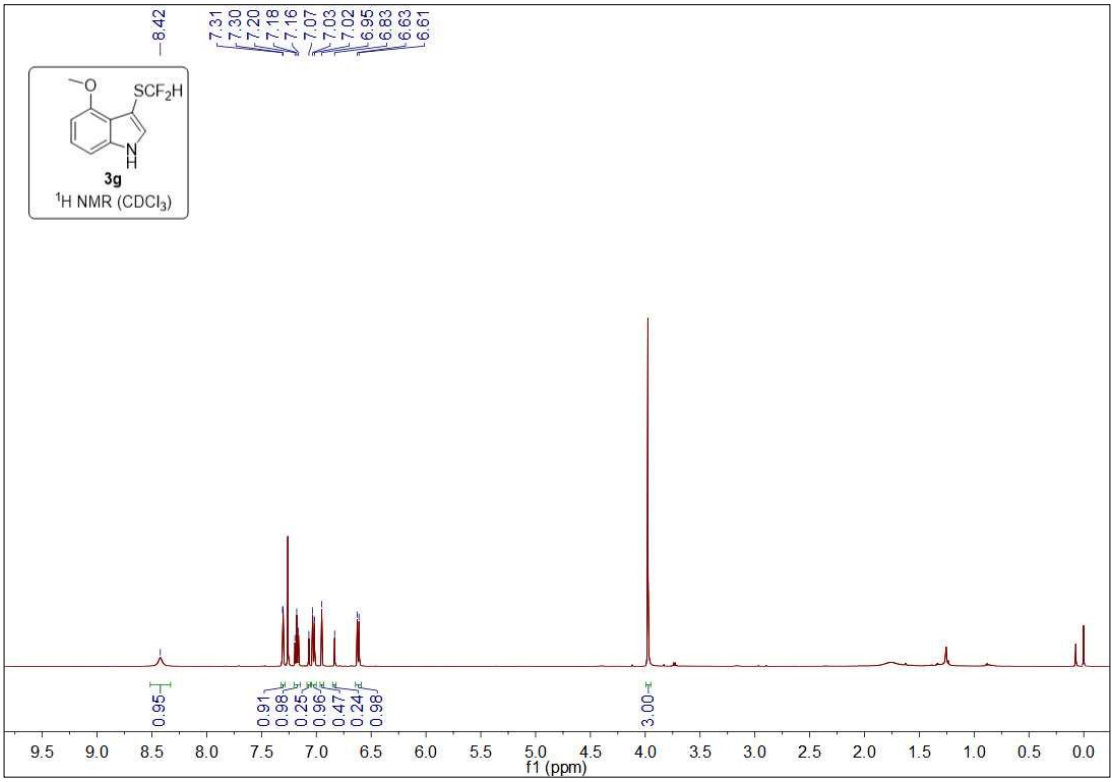

SCF2H
N
H
3e
19F NMR (CDCl3)
-91.94
-92.09
f1 (ppm)

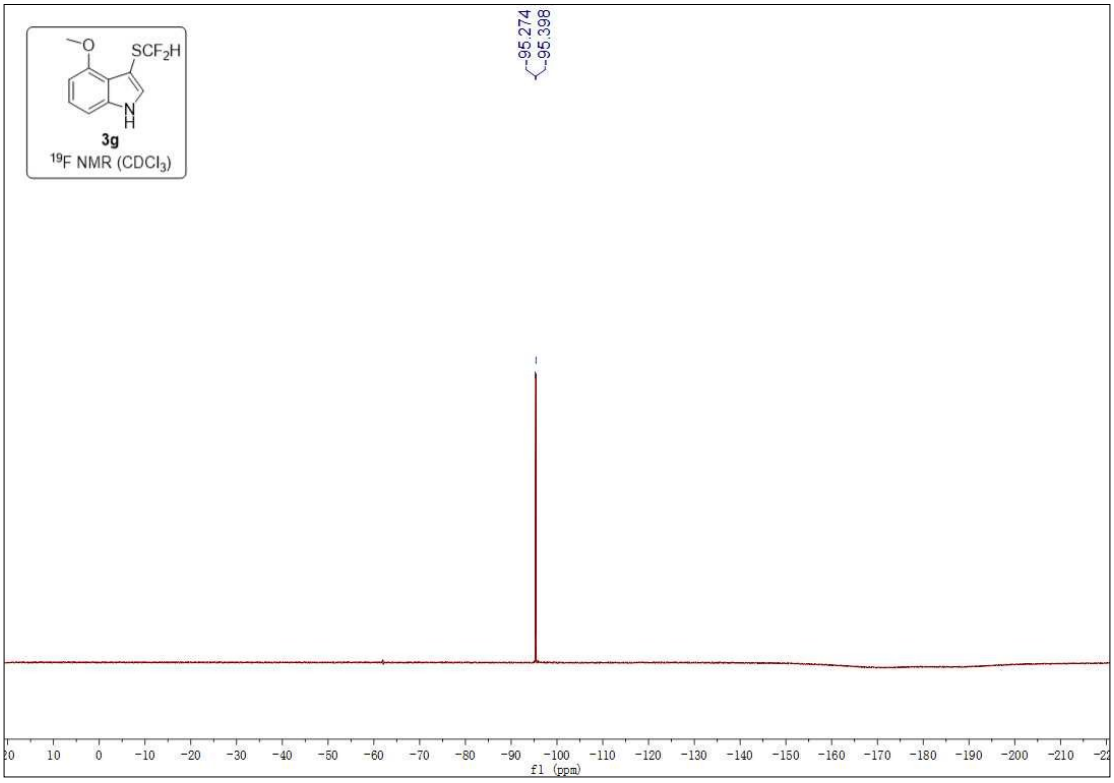

135.7
131.6
129.3
123.9
123.8
121.5
121.1
120.9
118.4
117.0
97.0
16.3
SCF2H
3e
13C NMR (CDCl3)
f1 (ppm)

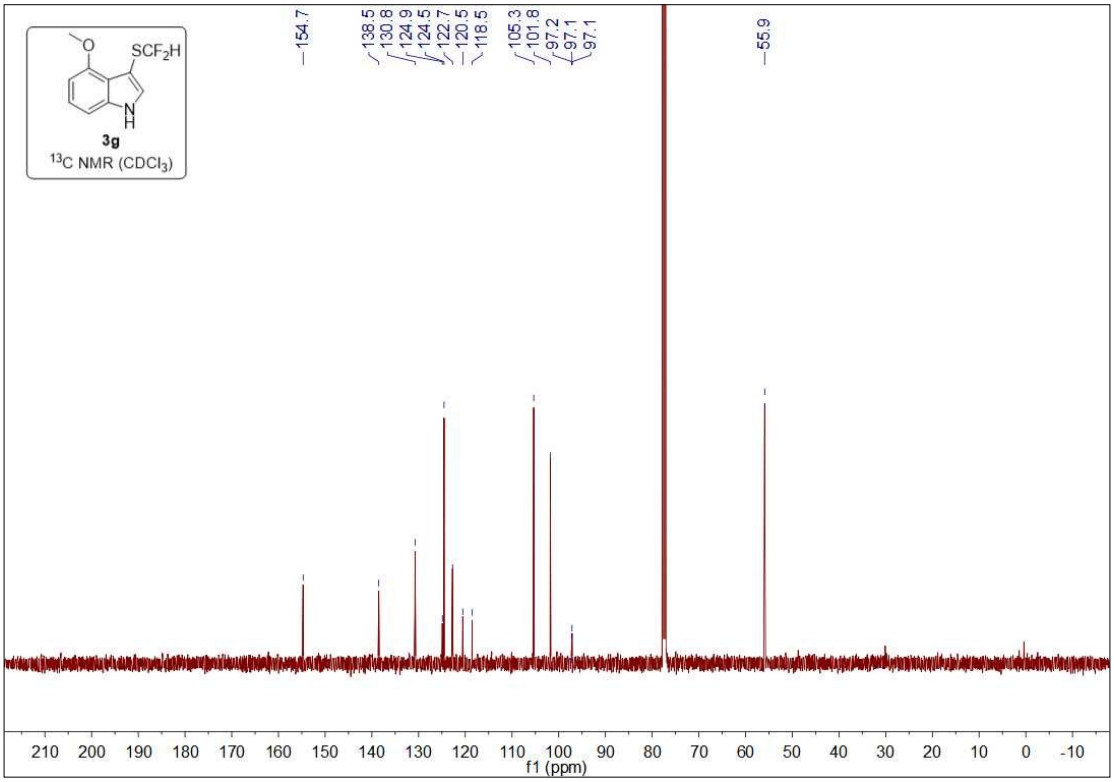

8.26
7.31
7.30
7.23
7.22
7.21
6.64
6.52
2.55
SCF2H
3f
1H NMR (CDCl3)
0.97
1.04
1.00
1.91
1.04
3.00
f1 (ppm)

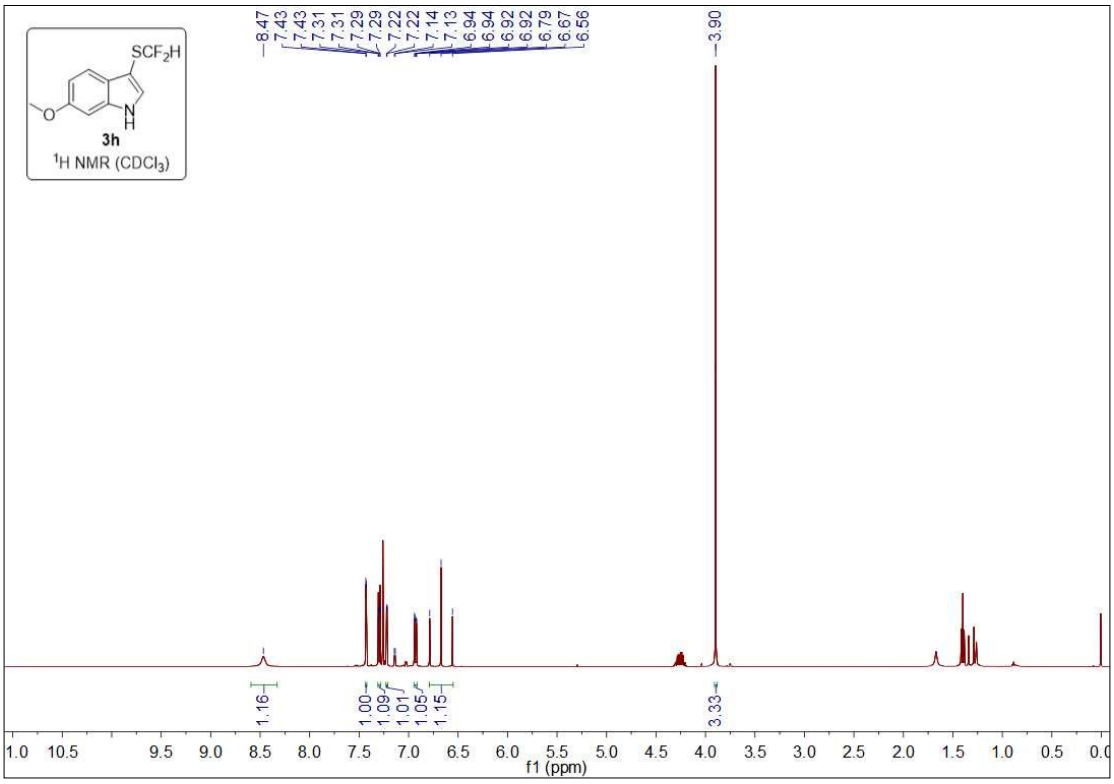

SCF2H
N
H
3f
19F NMR (CDCl3)
-91.96
-92.09
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-120
-140
-160
-180
-200
f1 (ppm)

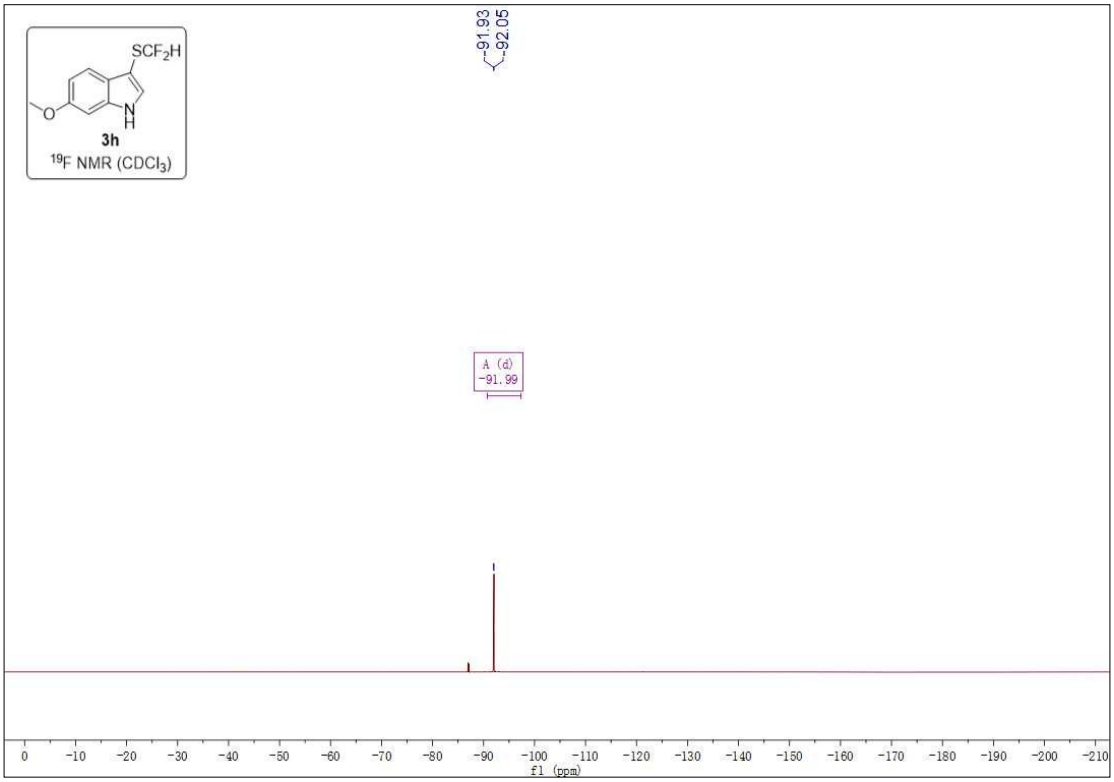

SCF2H
N
H
3f
13C NMR (CDCl3)
143.02
135.47
131.20
123.82
122.78
121.62
121.42
119.02
111.07
93.91
93.88
93.85
12.53
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

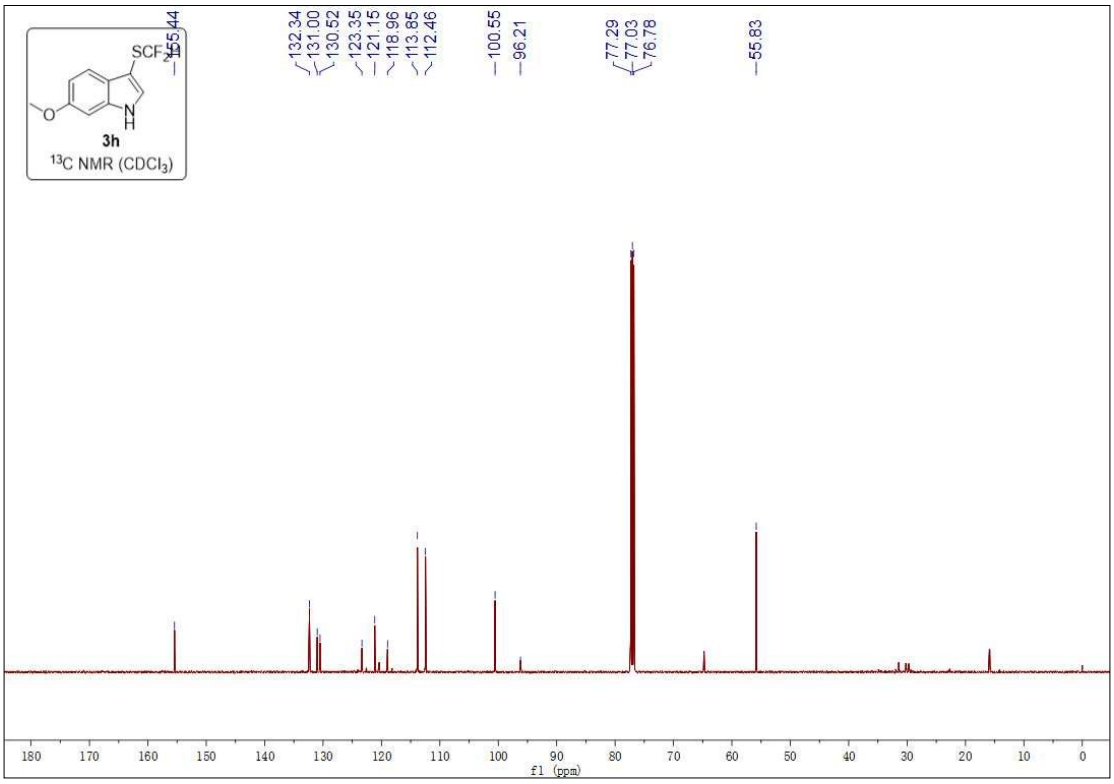

8.42
7.31
7.30
7.20
7.18
7.16
7.07
7.03
7.02
6.95
6.83
6.63
6.61
SCF2H
3g
1H NMR (CDCl3)
0.95
0.91
0.98
0.25
0.96
0.47
0.24
0.98
3.00
f1 (ppm)

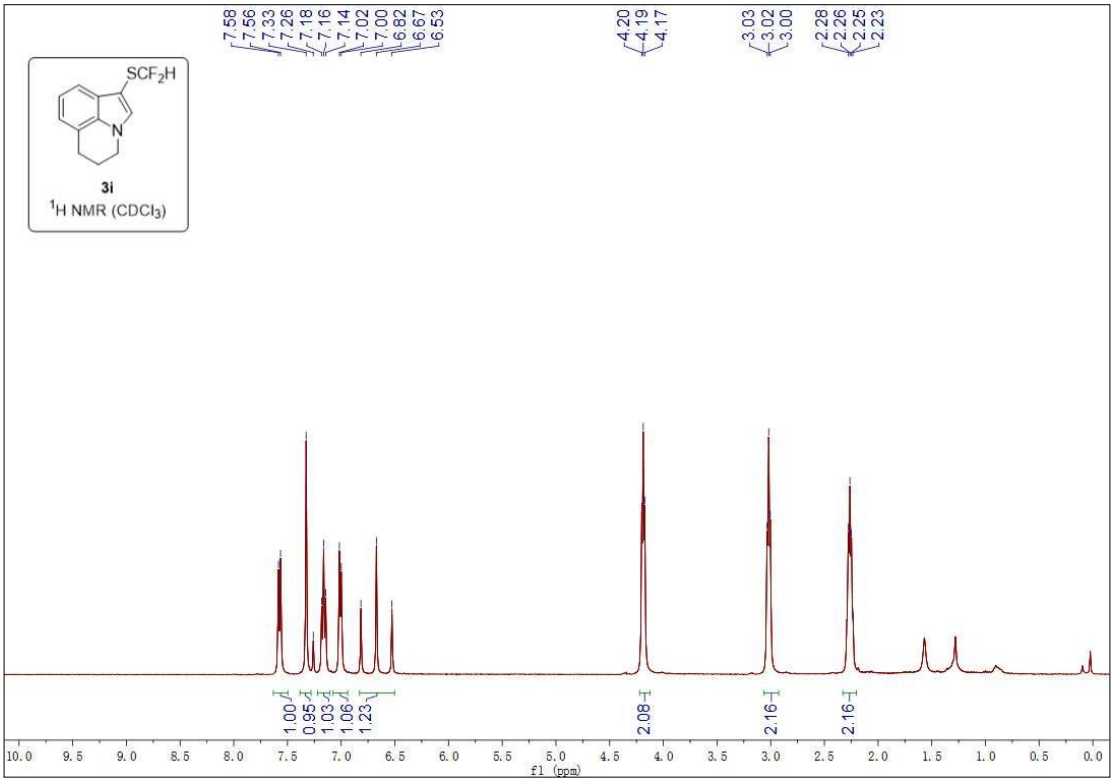

95.274
95.398
SCF2H
3g
19F NMR (CDCl3)
f1 (ppm)

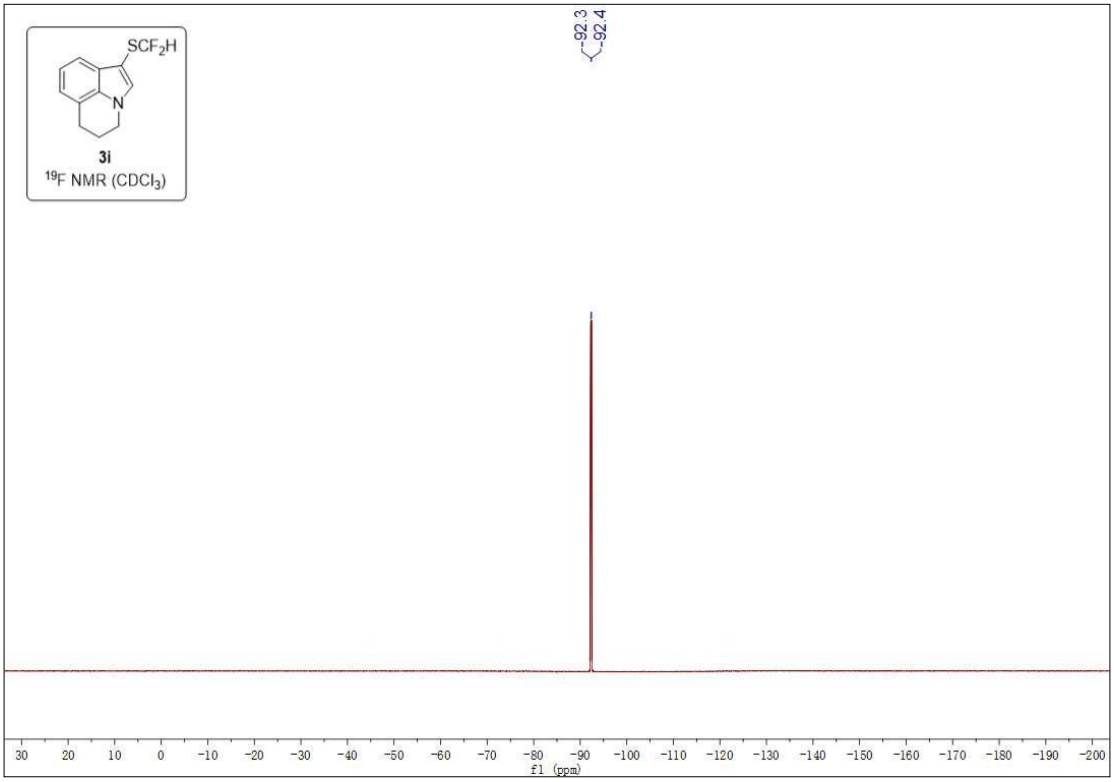

SCF2H
O
N
H
3g
13C NMR (CDCl3)
154.7
138.5
130.8
124.9
124.5
122.7
120.5
118.5
105.3
101.8
97.2
97.1
97.1
55.9
f1 (ppm)

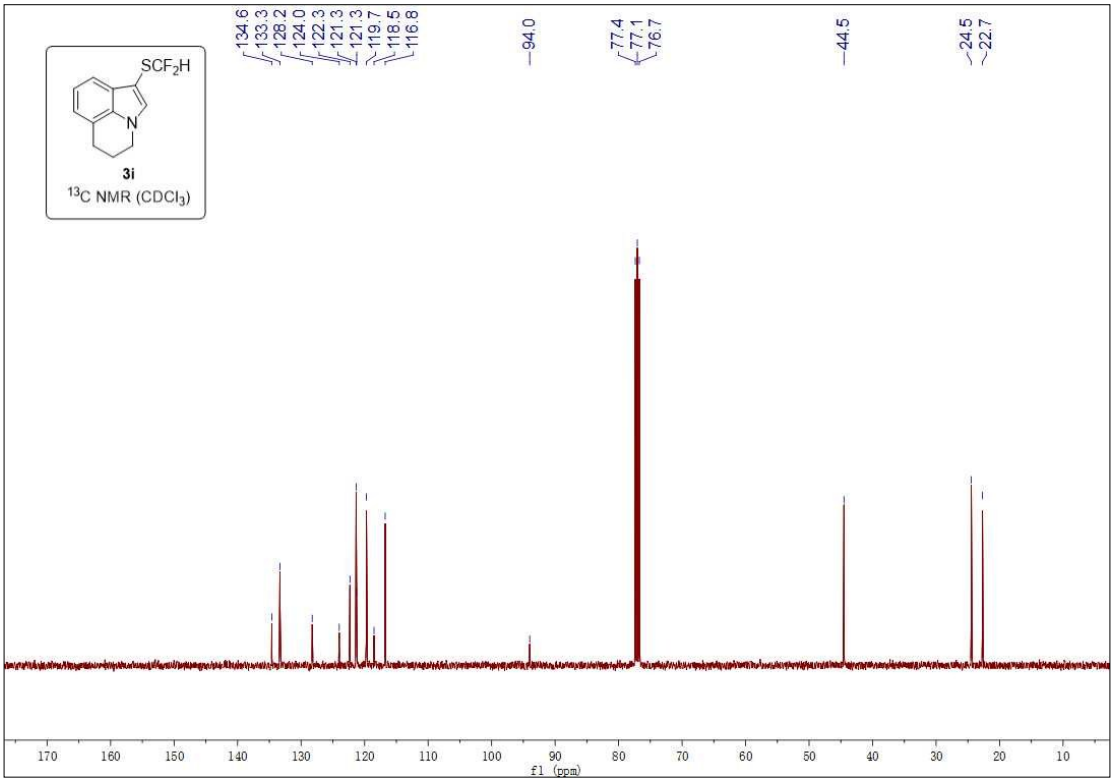

SCF2H
O
N
H
3h
1H NMR (CDCl3)
8.47
7.43
7.43
7.31
7.31
7.29
7.29
7.22
7.22
7.14
7.13
6.94
6.94
6.92
6.92
6.79
6.67
6.56
3.90
1.16
1.00
1.09
1.01
1.05
1.15
3.33
f1 (ppm)

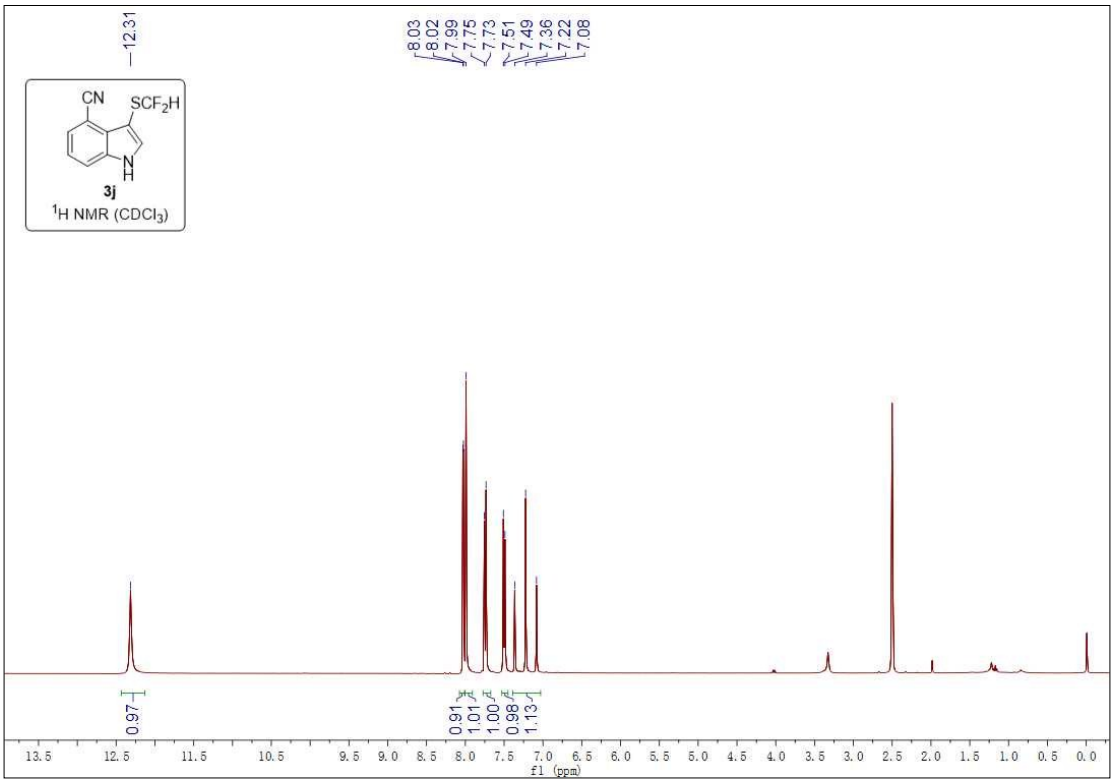

SCF2H
3h
19F NMR (CDCl3)
-91.93
-92.05
A (d)
-91.99
f1 (ppm)

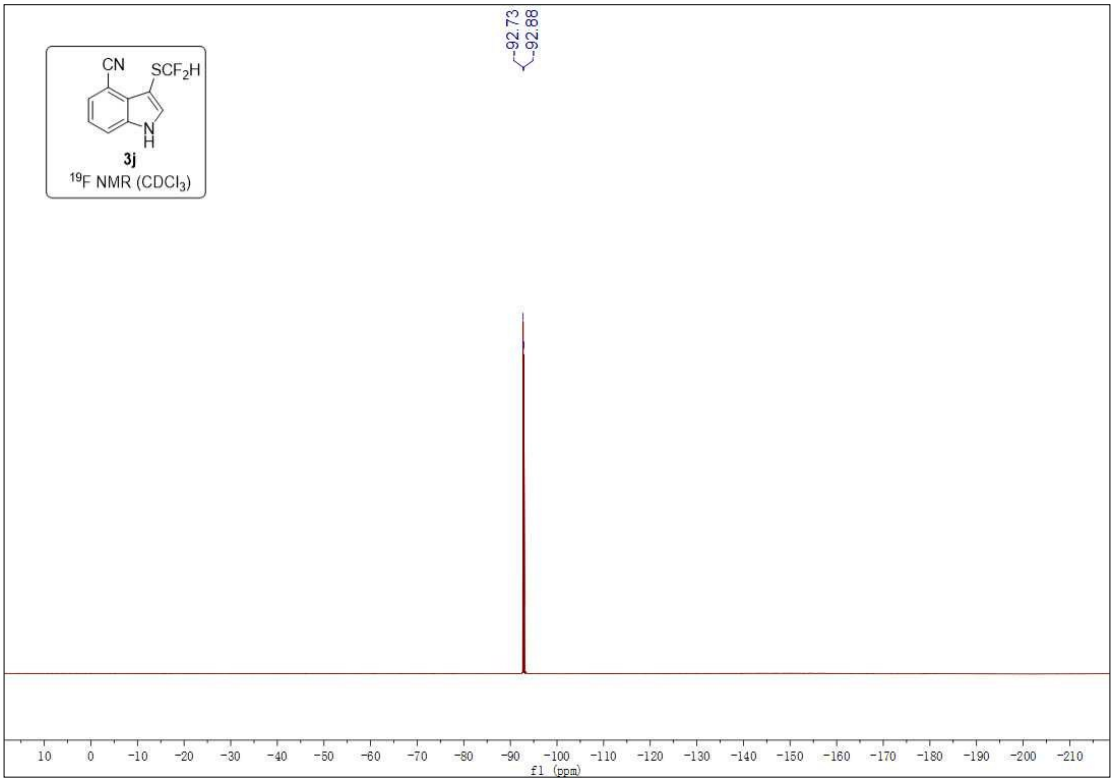

SCF2H
3h
13C NMR (CDCl3)
155.44
132.34
131.00
130.52
123.35
121.15
118.96
113.85
112.46
100.55
96.21
77.29
77.03
76.78
55.83
f1 (ppm)

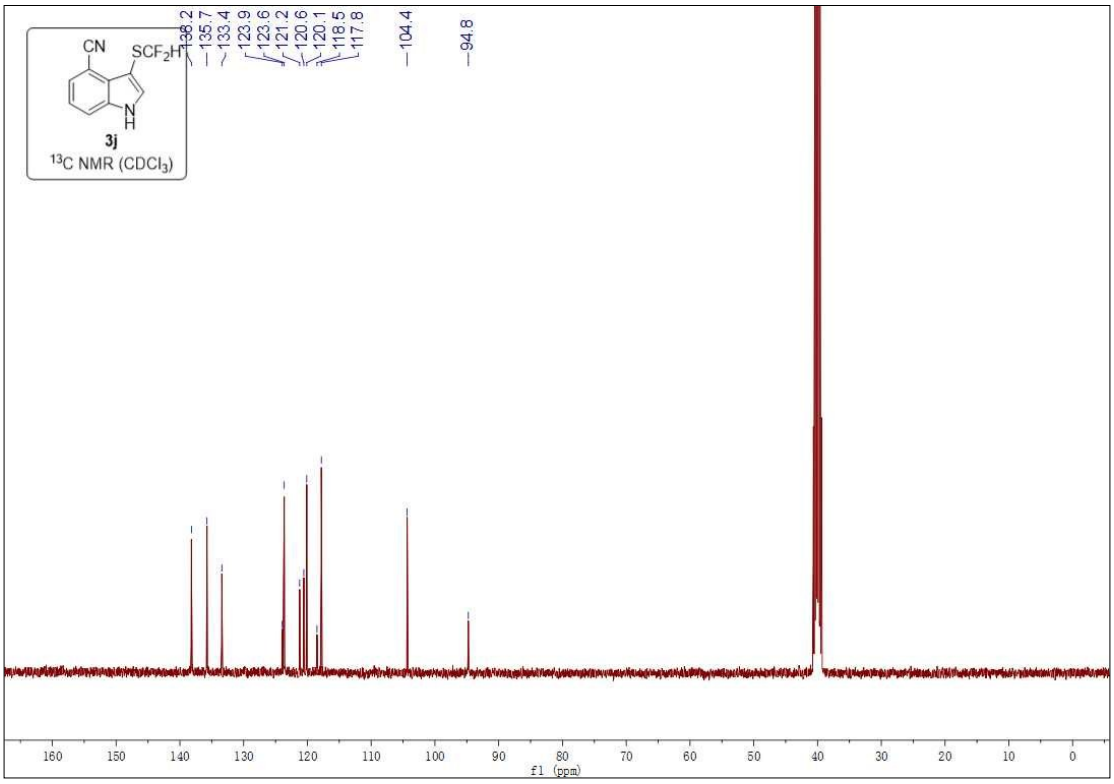

7.58
7.56
7.33
7.26
7.18
7.16
7.14
7.02
7.00
6.82
6.67
6.53
4.20
4.19
4.17
3.03
3.02
3.00
2.28
2.26
2.25
2.23
SCF2H
N
3i
1H NMR (CDCl3)
1.00
0.95
1.03
1.06
1.23
2.08
2.16
2.16
f1 (ppm)

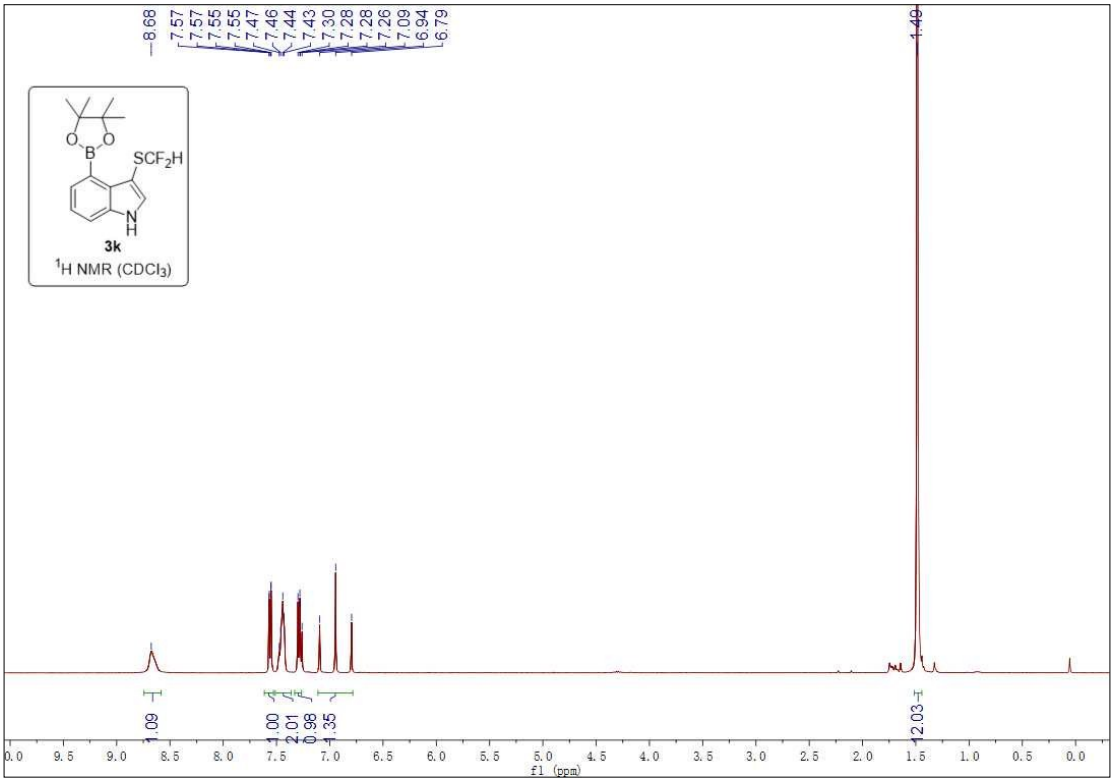

-92.3
-92.4
SCF2H
N
3i
19F NMR (CDCl3)
f1 (ppm)

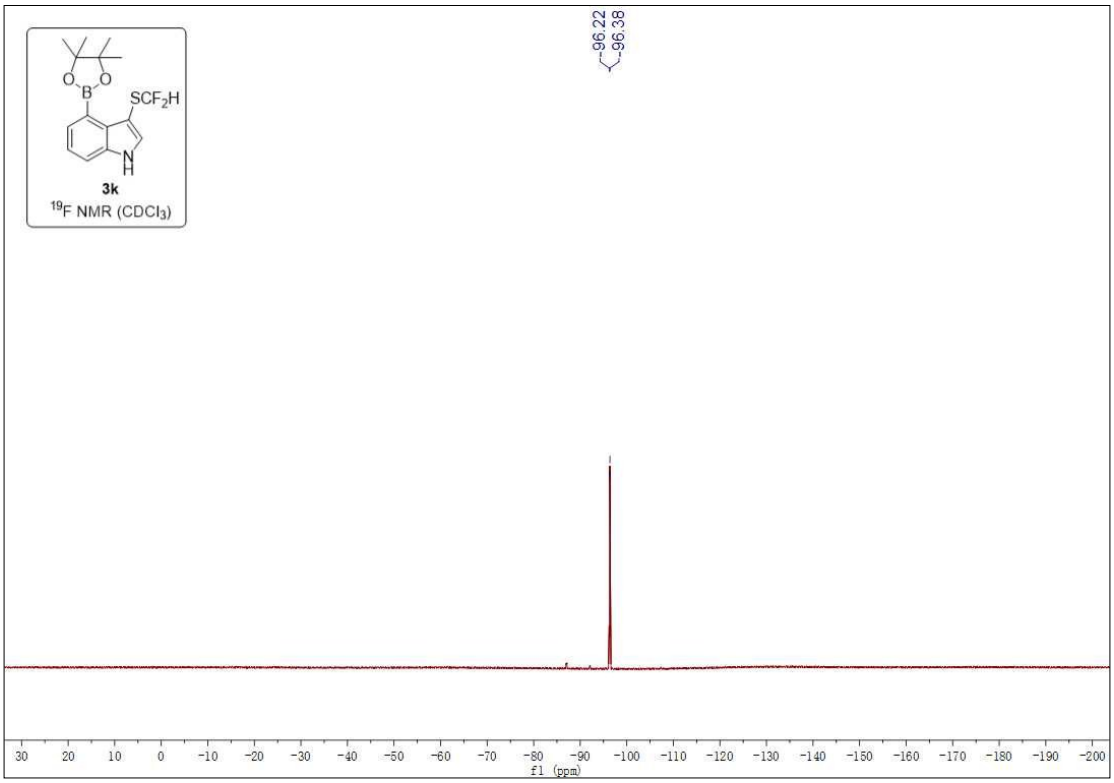

134.6
133.3
128.2
124.0
122.3
121.3
121.3
119.7
118.5
116.8
94.0
77.4
77.1
76.7
44.5
24.5
22.7
SCF2H
N
3i
13C NMR (CDCl3)
f1 (ppm)

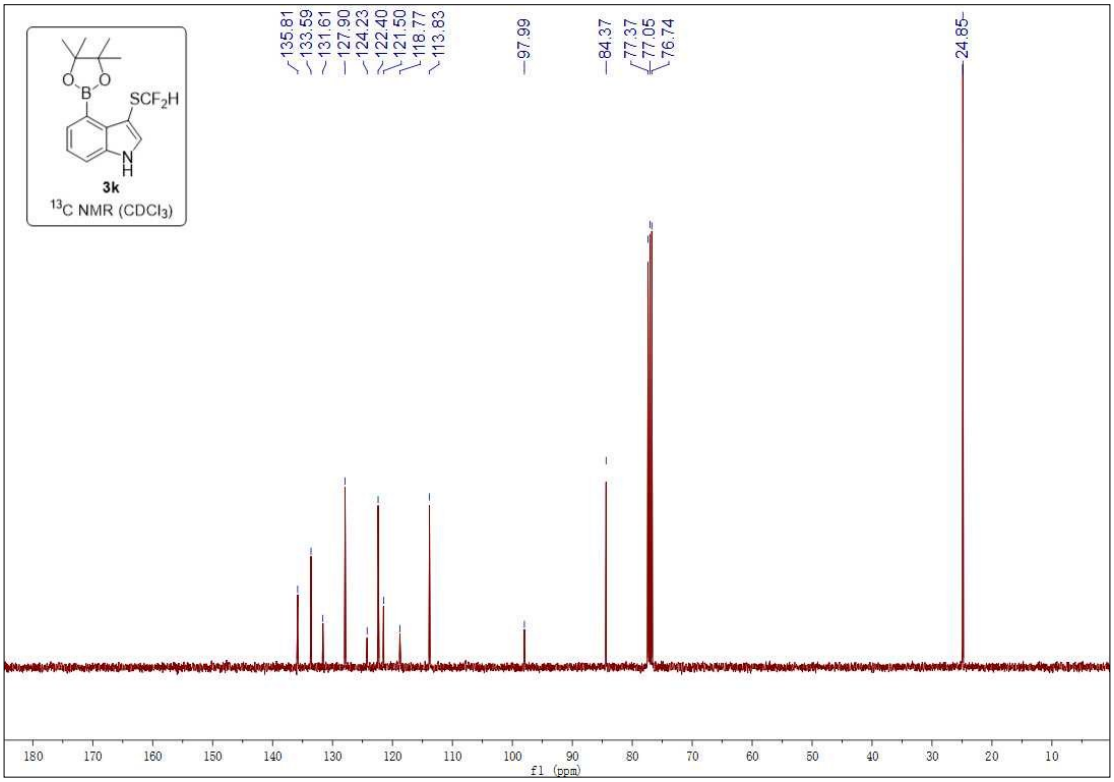

12.31
8.03
8.02
7.99
7.75
7.73
7.51
7.49
7.36
7.22
7.08
CN
SCF2H
N
H
3j
1H NMR (CDCl3)
0.97
0.91
1.01
1.00
0.98
1.13
f1 (ppm)

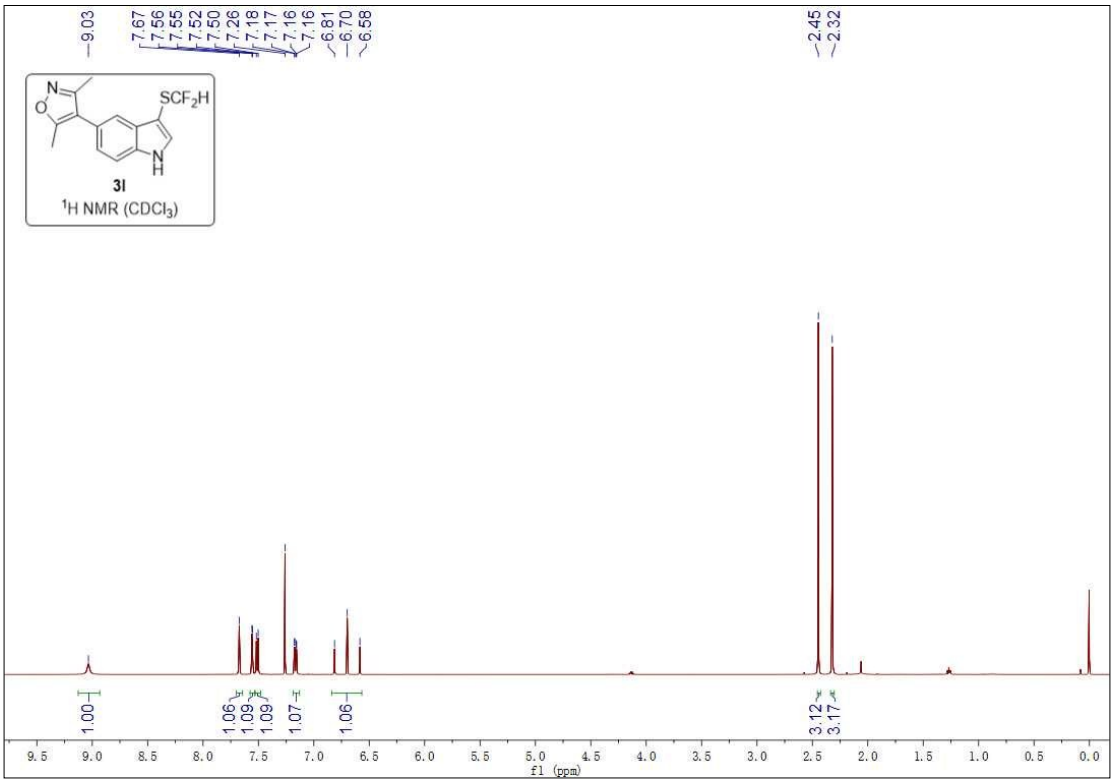

CN
SCF2H
N
H
3j
19F NMR (CDCl3)
-92.73
-92.88
f1 (ppm)

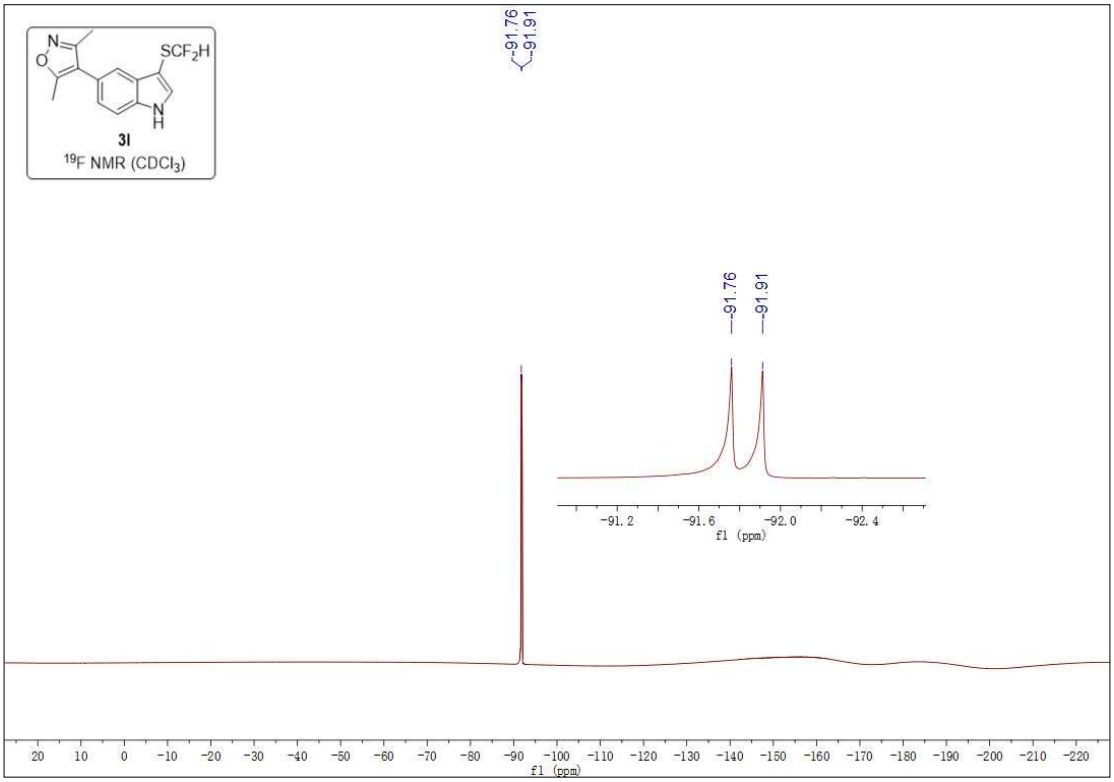

CN
SCF2H
N
H
3j
13C NMR (CDCl3)
138.2
135.7
133.4
123.9
123.6
121.2
120.6
120.1
118.5
117.8
104.4
94.8
f1 (ppm)

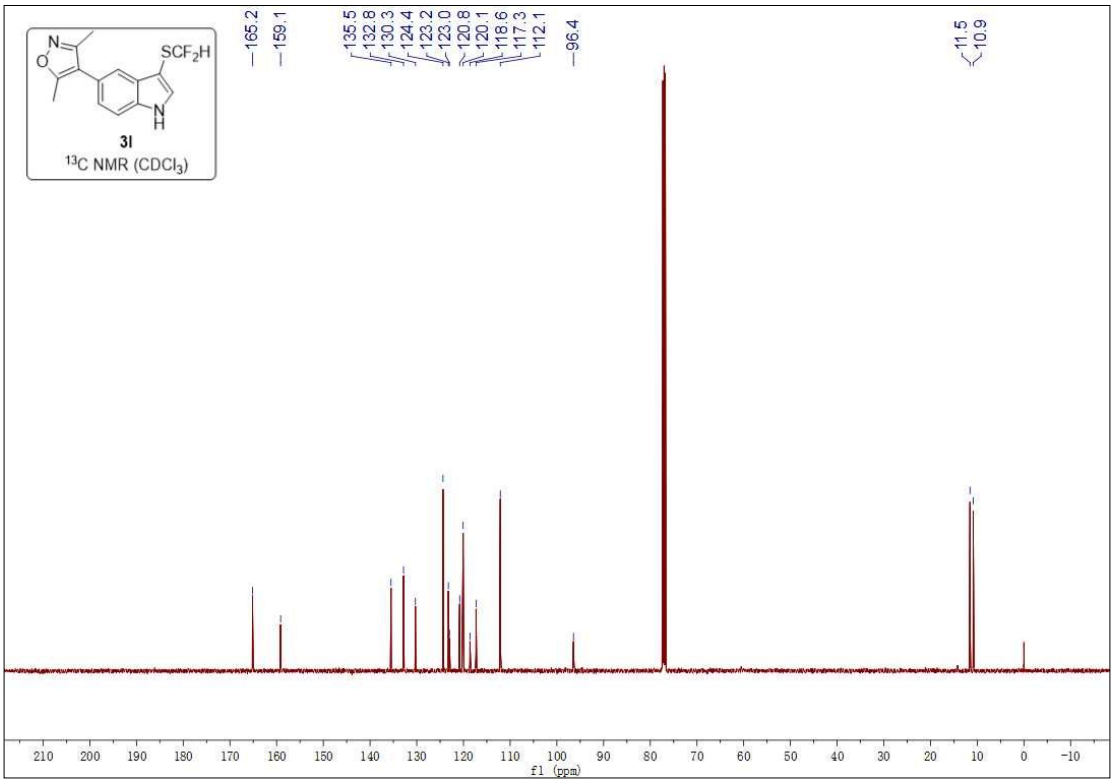

8.68
7.57
7.57
7.55
7.55
7.47
7.46
7.44
7.43
7.30
7.28
7.28
7.26
7.09
6.94
6.79
1.40
SCF2H
3k
1H NMR (CDCl3)
1.09
1.00
2.01
0.98
1.35
12.03
f1 (ppm)

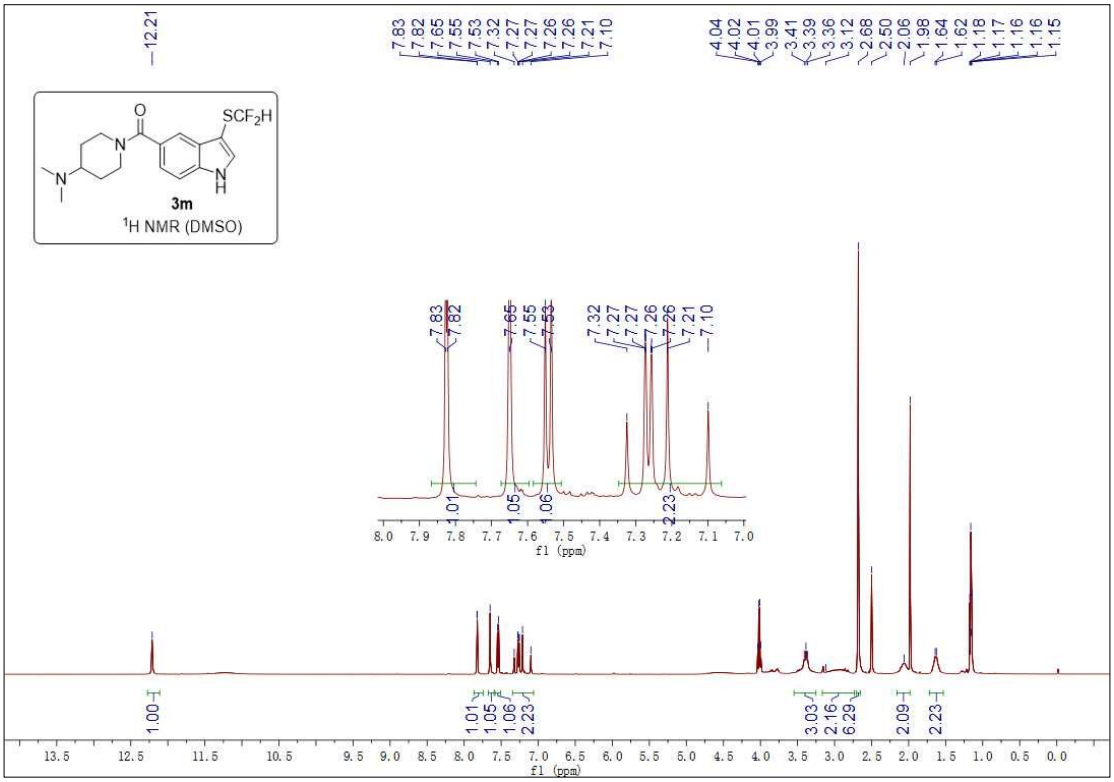

96.22
96.38
SCF2H
3k
19F NMR (CDCl3)
f1 (ppm)

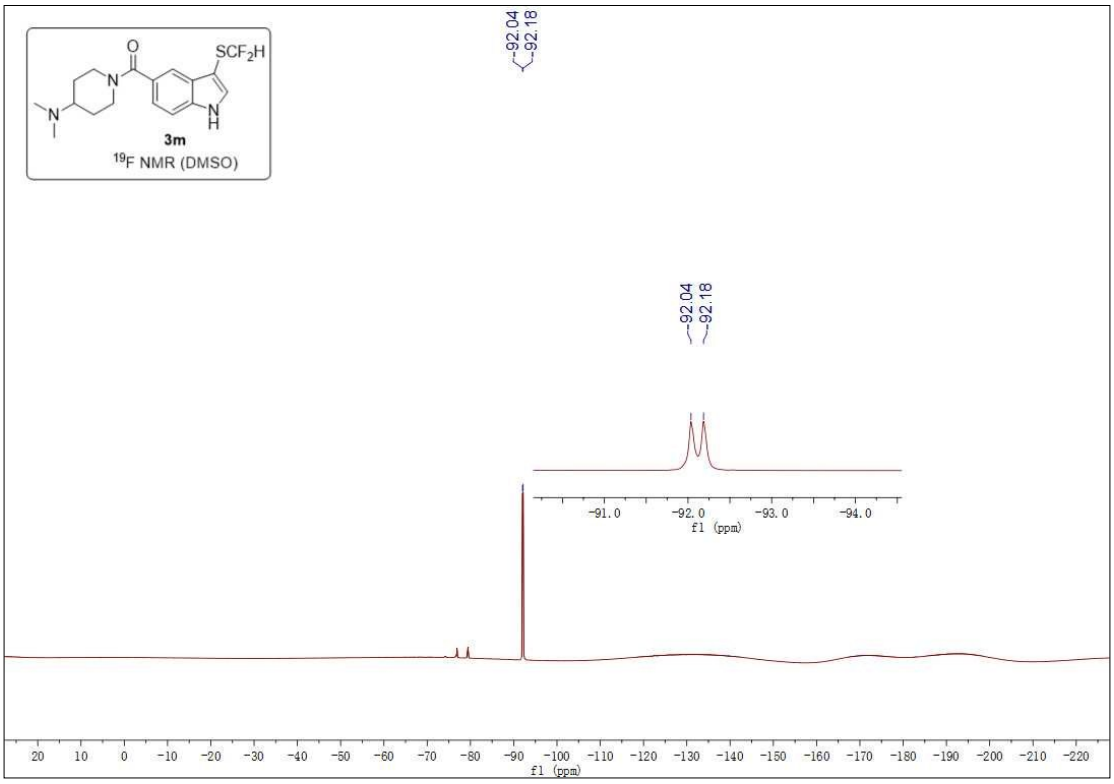

135.81
133.59
131.61
127.90
124.23
122.40
121.50
118.77
113.83
97.99
84.37
77.37
77.05
76.74
24.85
SCF2H
3k
13C NMR (CDCl3)
f1 (ppm)

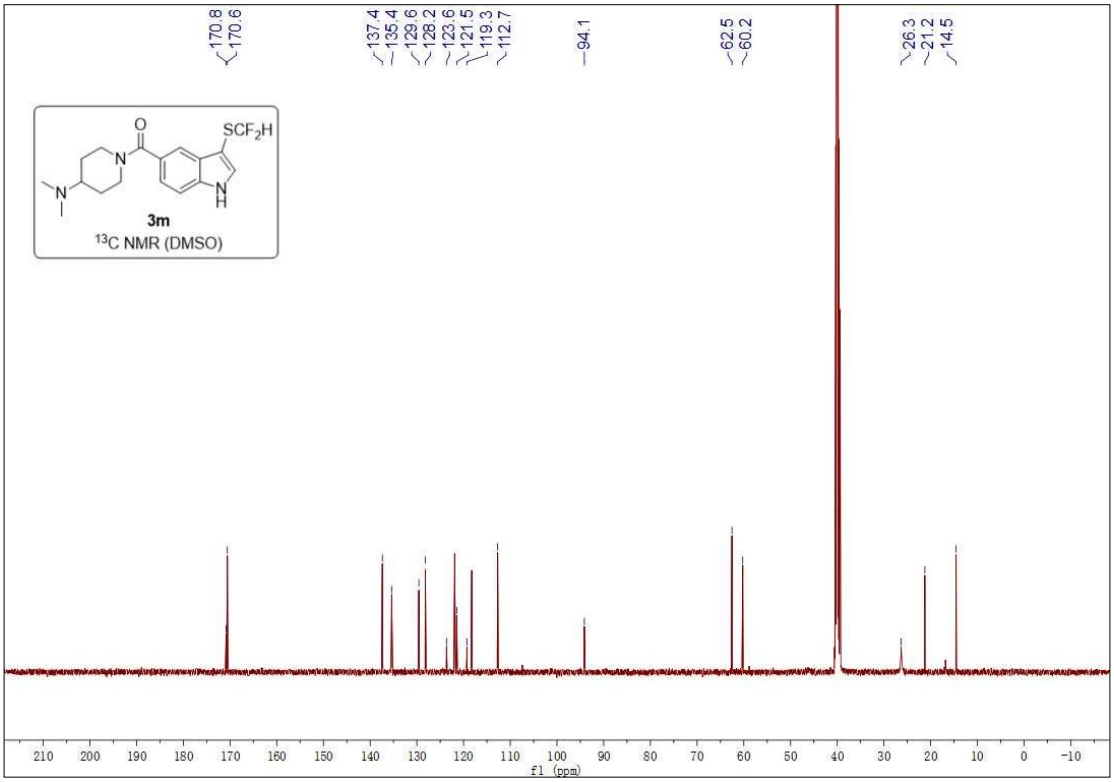

9.03
7.67
7.56
7.55
7.52
7.50
7.26
7.18
7.17
7.16
7.16
6.81
6.70
6.58
2.45
2.32
SCF2H
3l
1H NMR (CDCl3)
1.00
1.06
1.09
1.09
1.07
1.06
3.12
3.17
f1 (ppm)

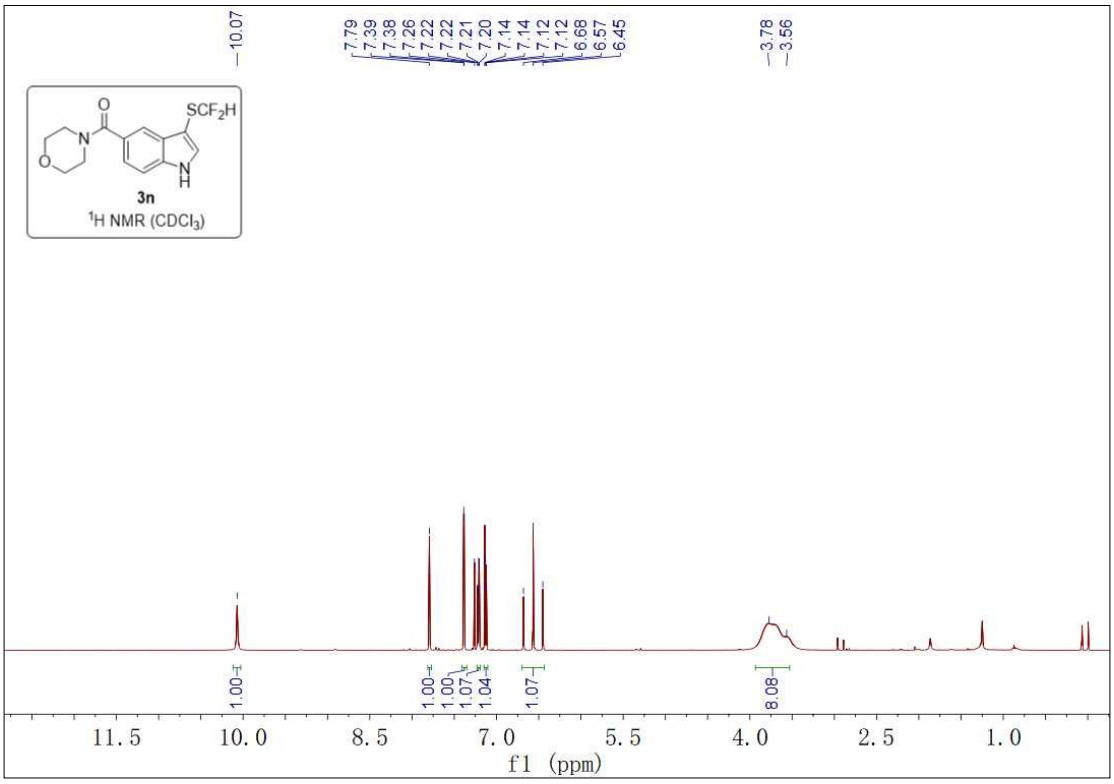

-91.76
-91.91
3l
19F NMR (CDCl3)
-91.76
-91.91
-91.2
-91.6
-92.0
-92.4
f1 (ppm)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

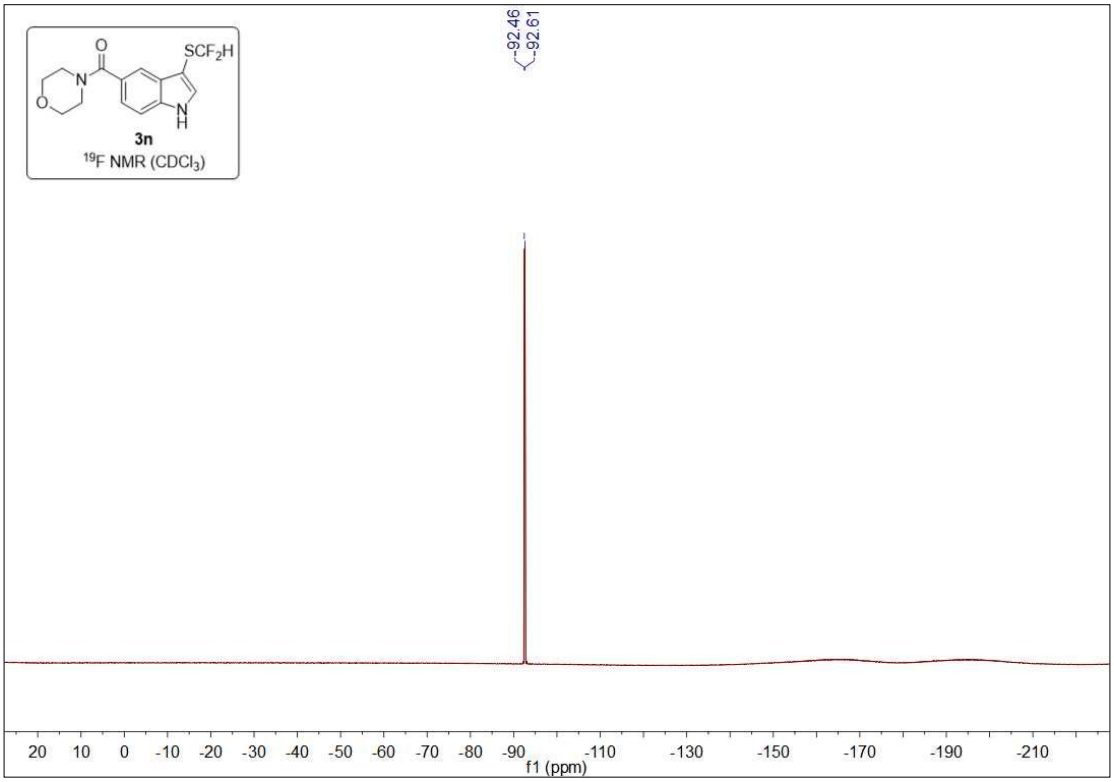

165.2
159.1
135.5
132.8
130.3
124.4
123.2
123.0
120.8
120.1
118.6
117.3
112.1
96.4
11.5
10.9
3l
13C NMR (CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

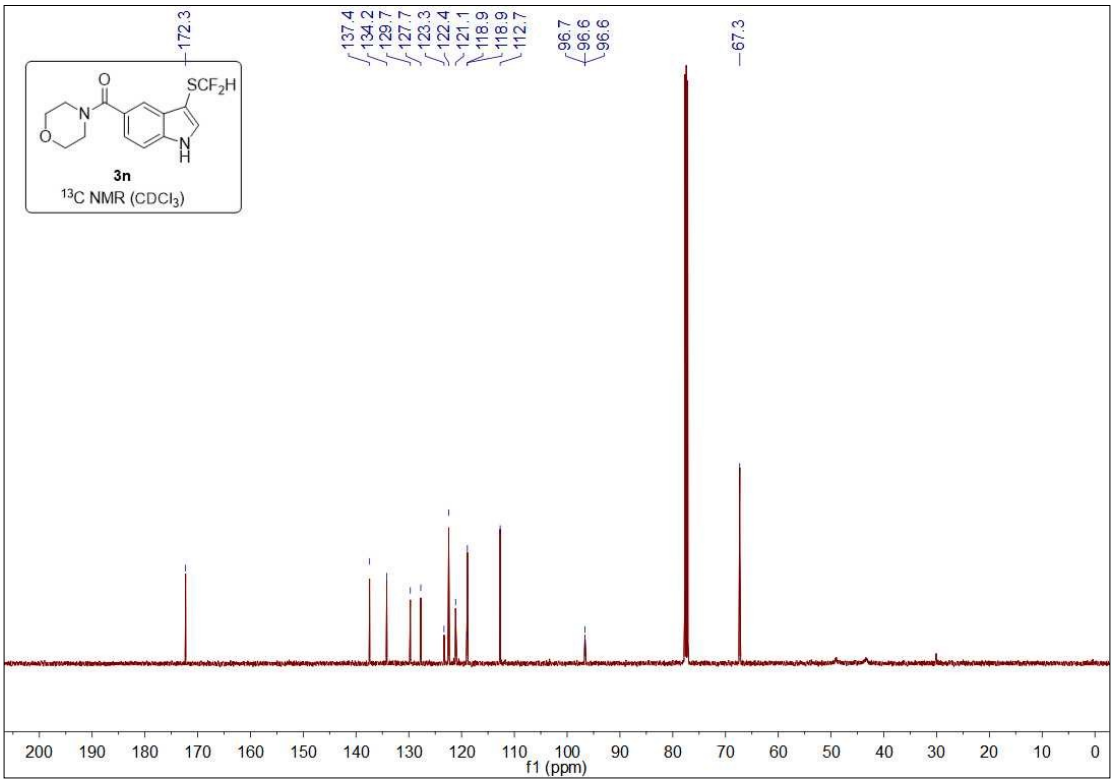

12.21
7.83
7.82
7.65
7.55
7.53
7.32
7.27
7.27
7.26
7.26
7.21
7.10
4.04
4.02
4.01
3.99
3.41
3.39
3.36
3.12
2.68
2.50
2.06
1.98
1.64
1.62
1.18
1.17
1.16
1.16
1.15
SCF2H
3m
1H NMR (DMSO)
1.00
1.01
1.05
1.06
2.23
3.03
2.16
6.29
2.09
2.23
f1 (ppm)

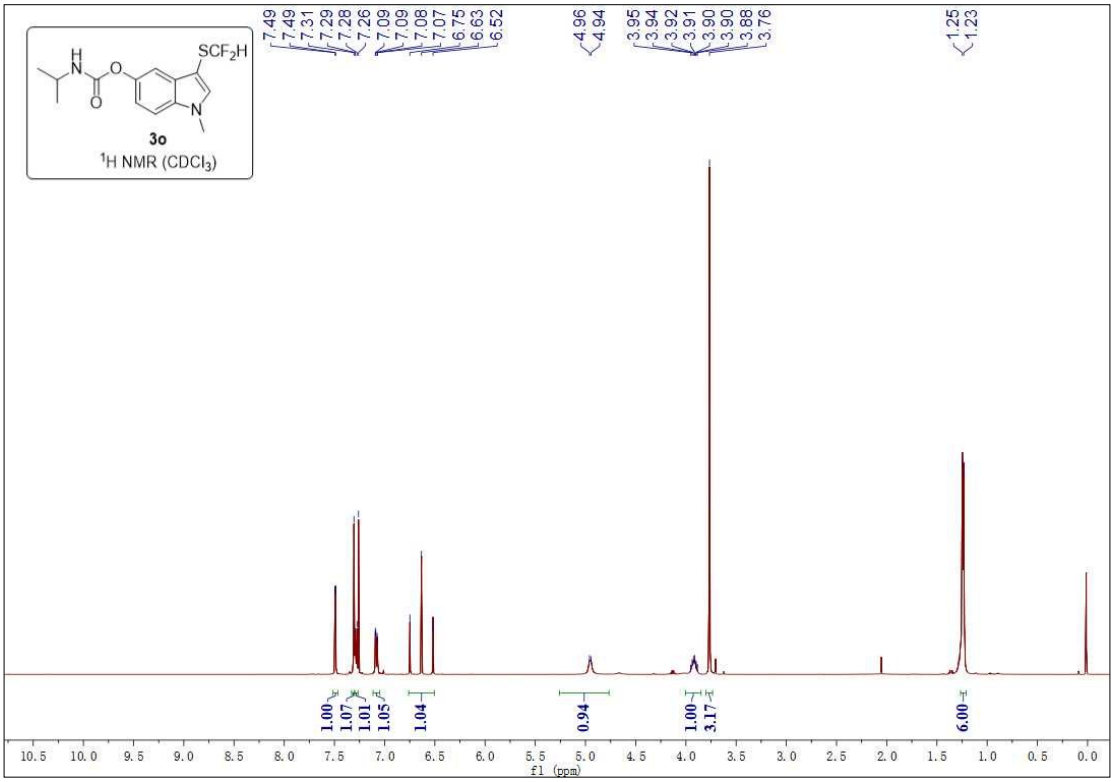

92.04
92.18
SCF2H
3m
19F NMR (DMSO)
f1 (ppm)

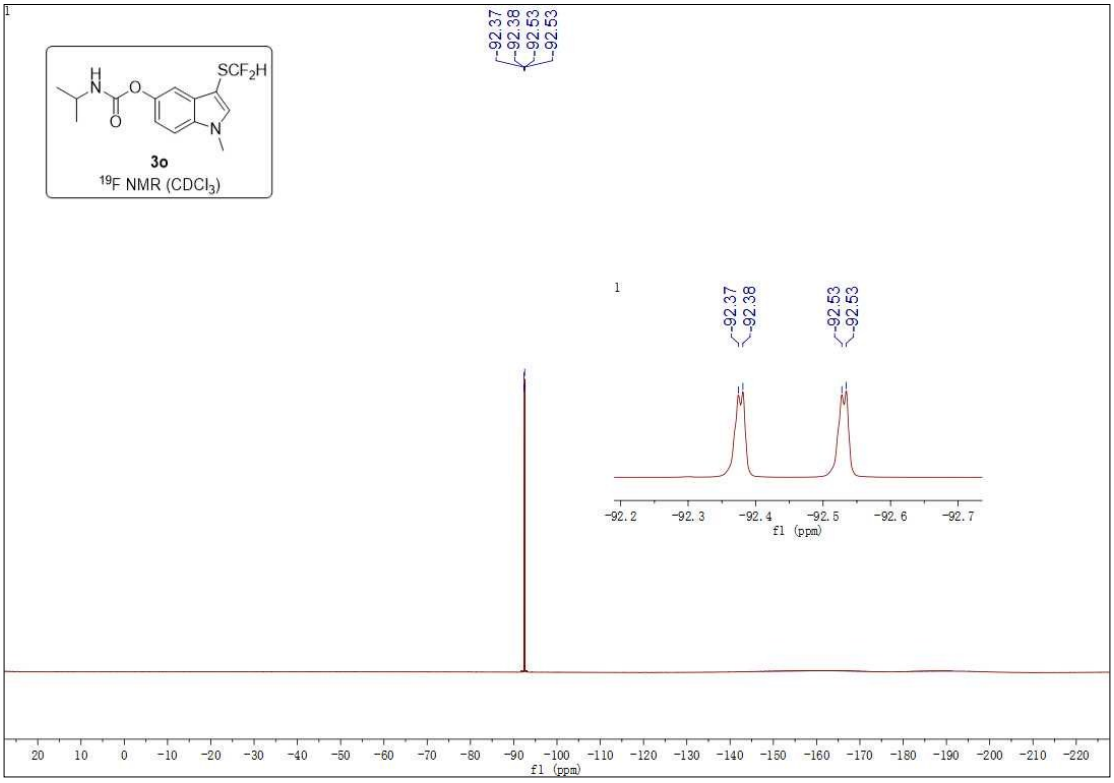

170.8
170.6
137.4
135.4
129.6
128.2
123.6
121.5
119.3
112.7
94.1
62.5
60.2
26.3
21.2
14.5
SCF2H
3m
13C NMR (DMSO)
f1 (ppm)

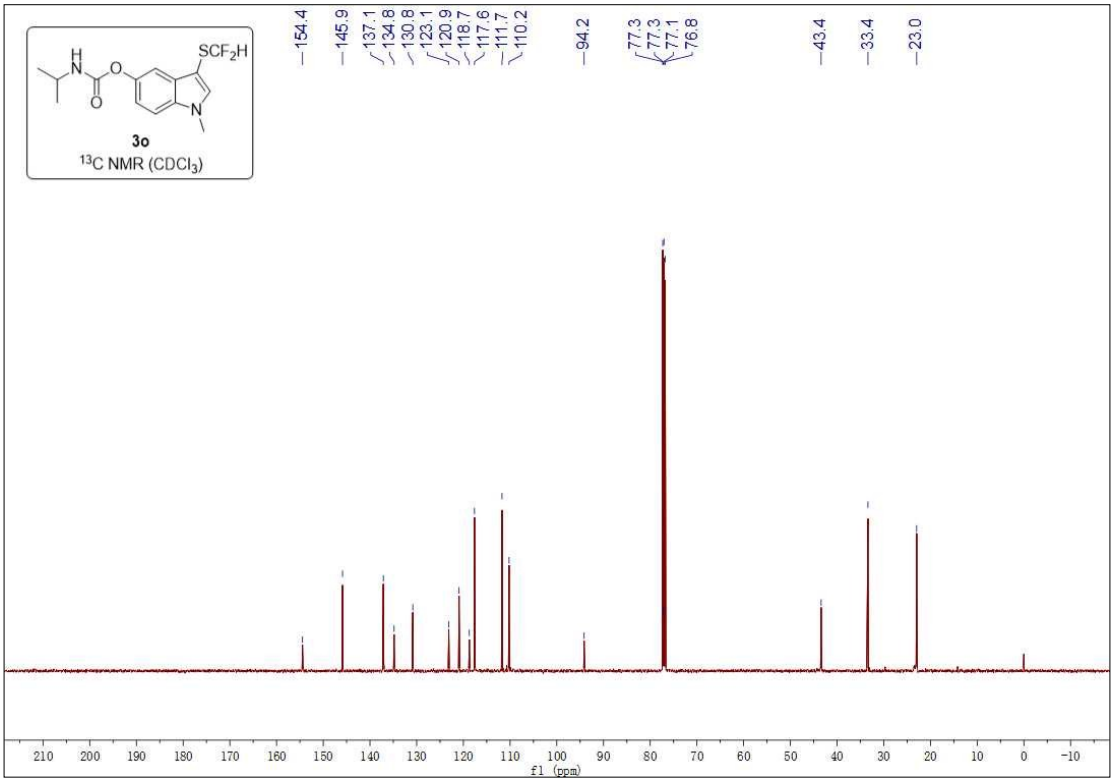

10.07
7.79
7.39
7.38
7.26
7.22
7.22
7.21
7.20
7.14
7.14
7.12
7.12
6.68
6.57
6.45
3.78
3.56
SCF2H
3n
1H NMR (CDCl3)
1.00
1.00
1.00
1.07
1.04
1.07
8.08
f1 (ppm)

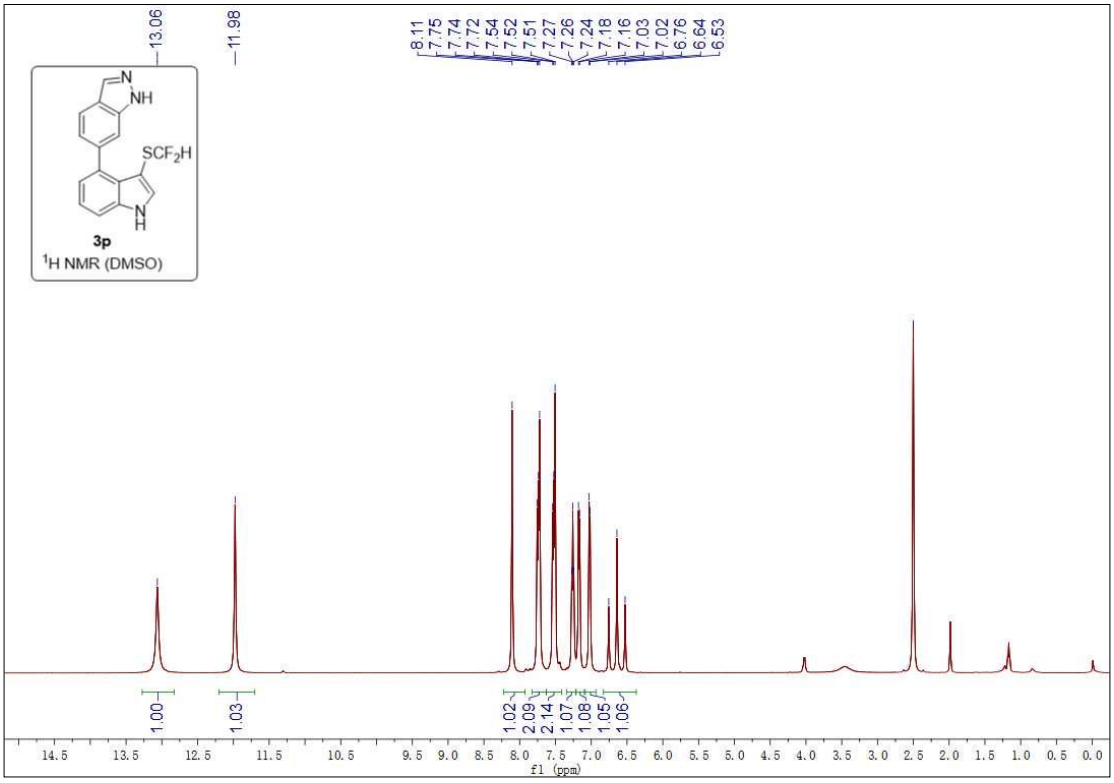

-92.46
-92.61
3n
19F NMR (CDCl3)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190 -210
f1 (ppm)

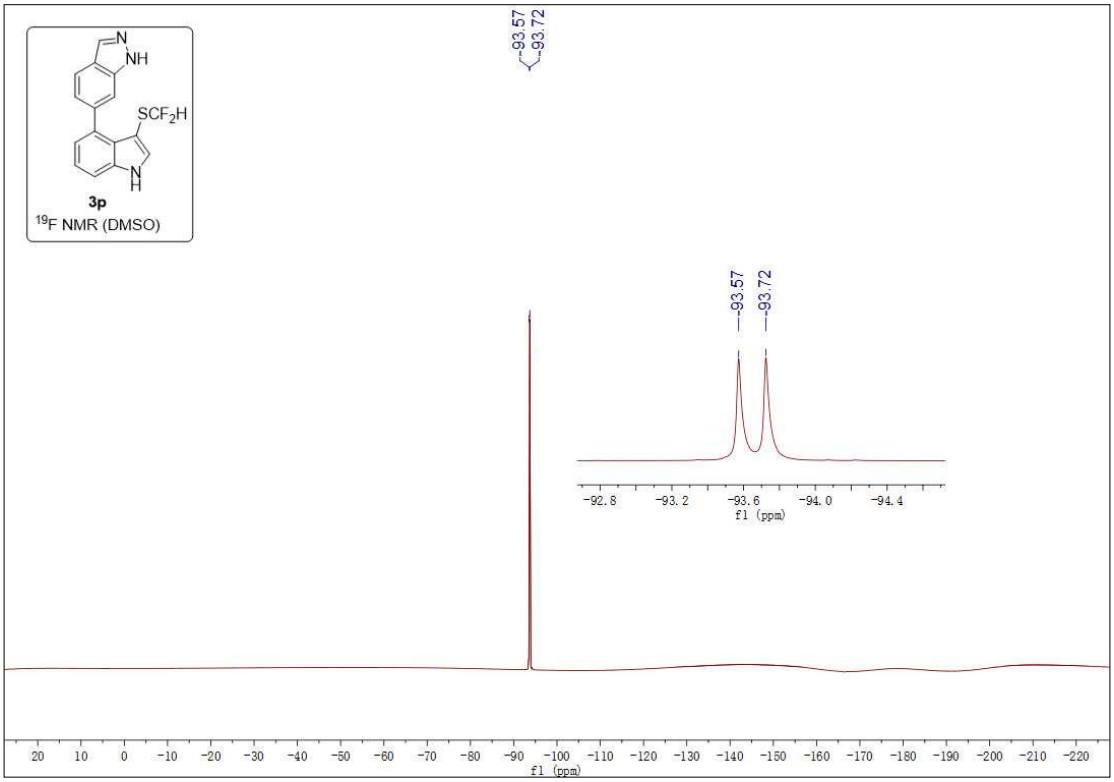

172.3
137.4
134.2
129.7
127.7
123.3
122.4
121.1
118.9
118.9
112.7
96.7
96.6
96.6
67.3
3n
13C NMR (CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

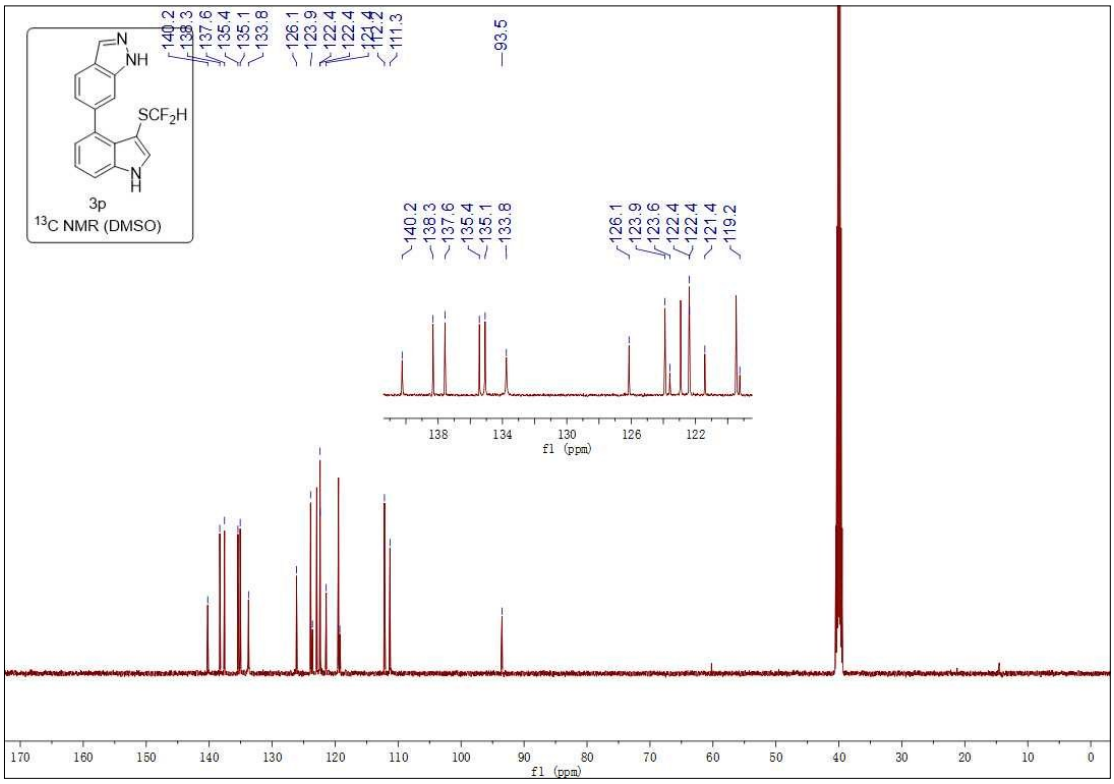

7.49
7.49
7.31
7.29
7.28
7.26
7.09
7.09
7.08
7.07
6.75
6.63
6.52
4.96
4.94
3.95
3.94
3.92
3.91
3.90
3.90
3.88
3.76
1.25
1.23
SCF2H
3o
1H NMR (CDCl3)
1.00
1.07
1.01
1.05
1.04
0.94
1.00
3.17
6.00
f1 (ppm)

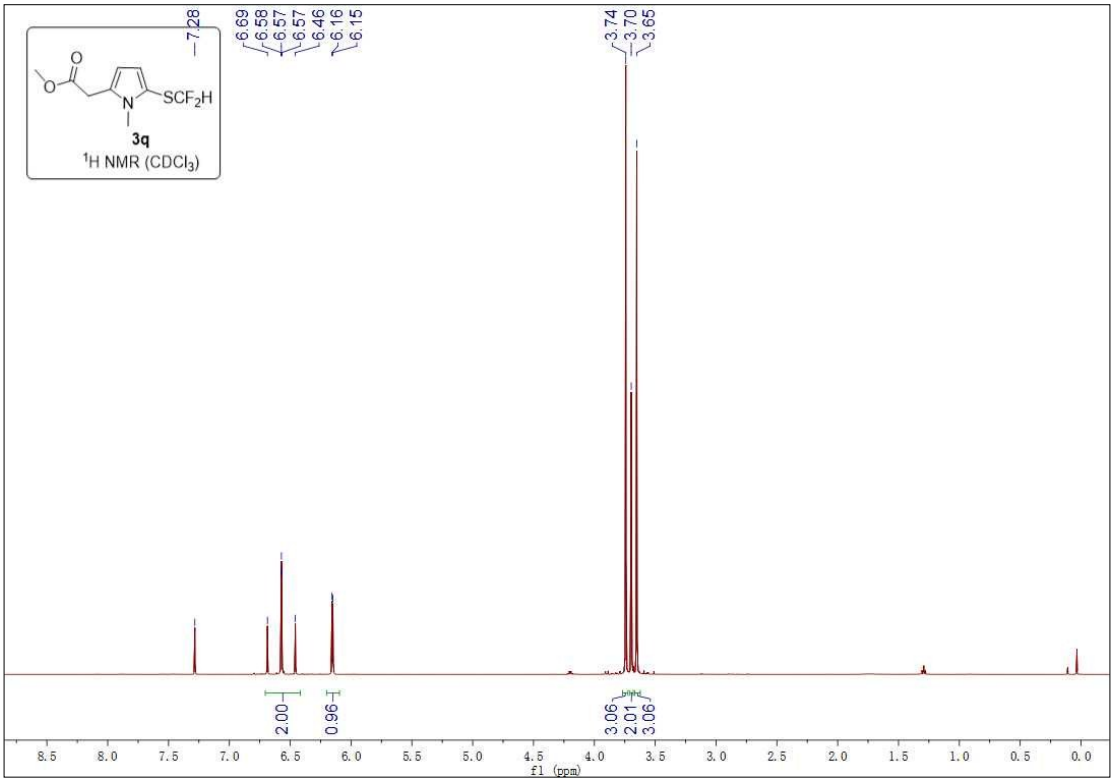

-92.37
-92.38
-92.53
-92.53
SCF2H
3o
19F NMR (CDCl3)
-92.37
-92.38
-92.53
-92.53
f1 (ppm)
f1 (ppm)

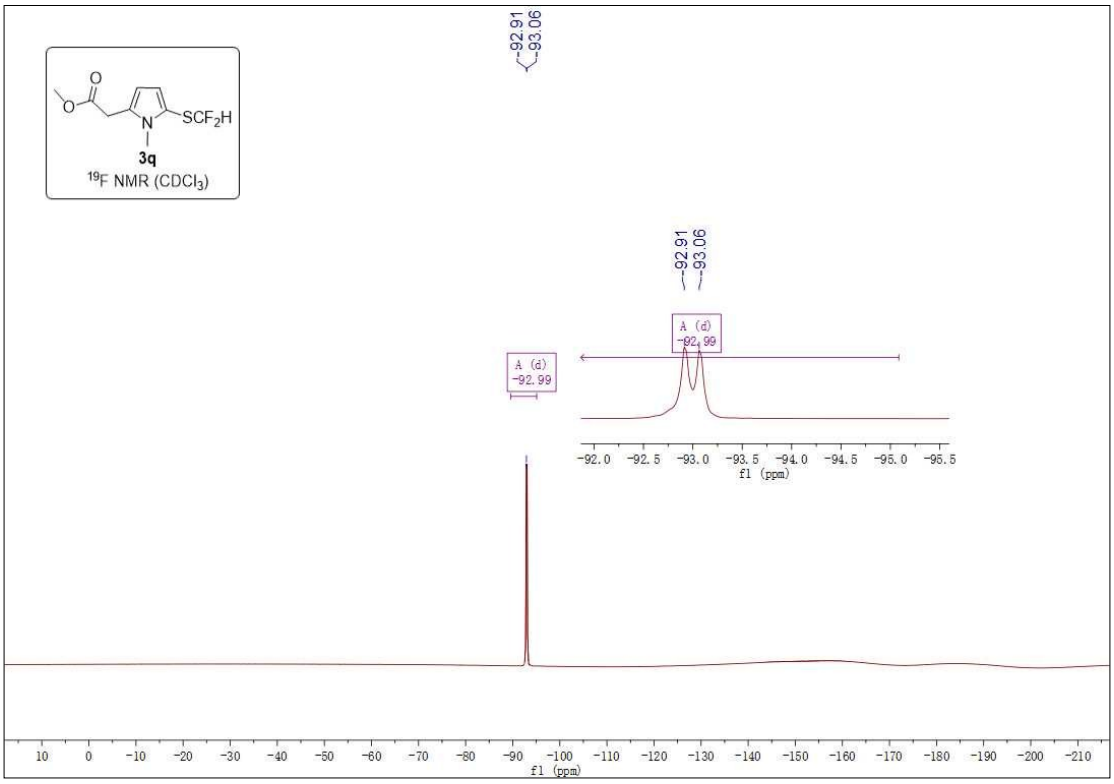

154.4
145.9
137.1
134.8
130.8
123.1
120.9
118.7
117.6
111.7
110.2
94.2
77.3
77.3
77.1
76.8
43.4
33.4
23.0
SCF2H
3o
13C NMR (CDCl3)
f1 (ppm)

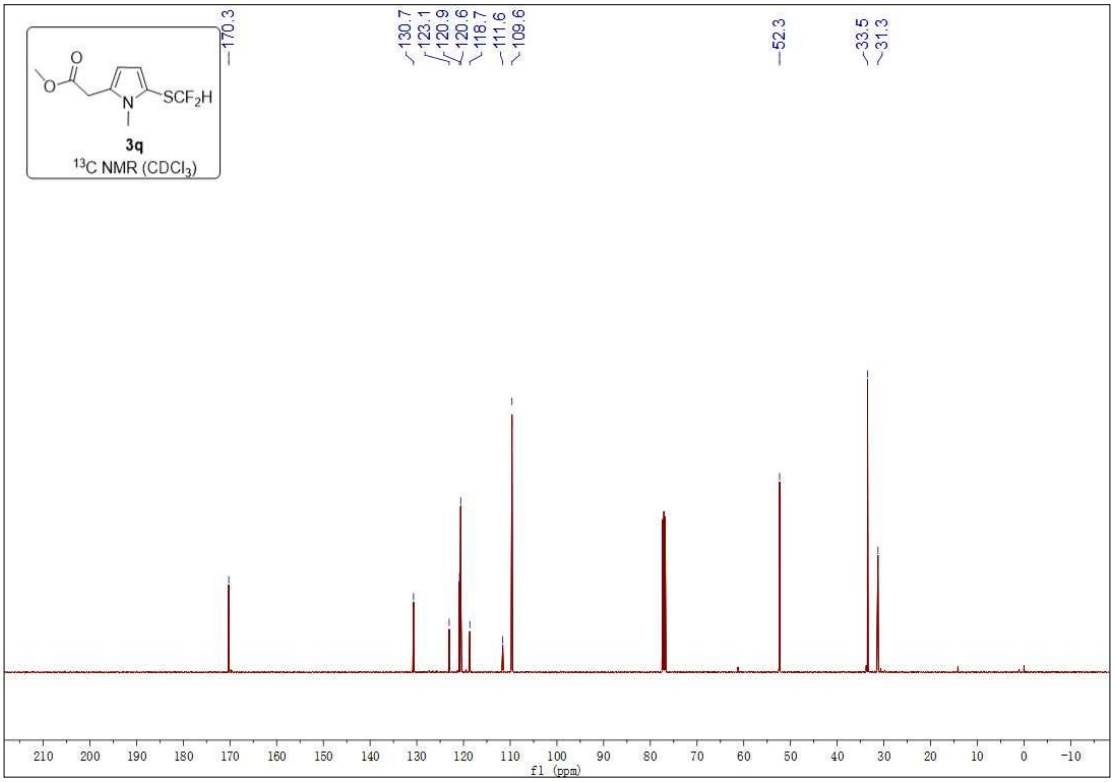

13.06
11.98
8.11
7.75
7.74
7.72
7.54
7.52
7.51
7.27
7.26
7.24
7.18
7.16
7.03
7.02
6.76
6.64
6.53
SCF2H
3p
1H NMR (DMSO)
1.00
1.03
1.02
2.09
2.14
1.07
1.08
1.05
1.06
f1 (ppm)

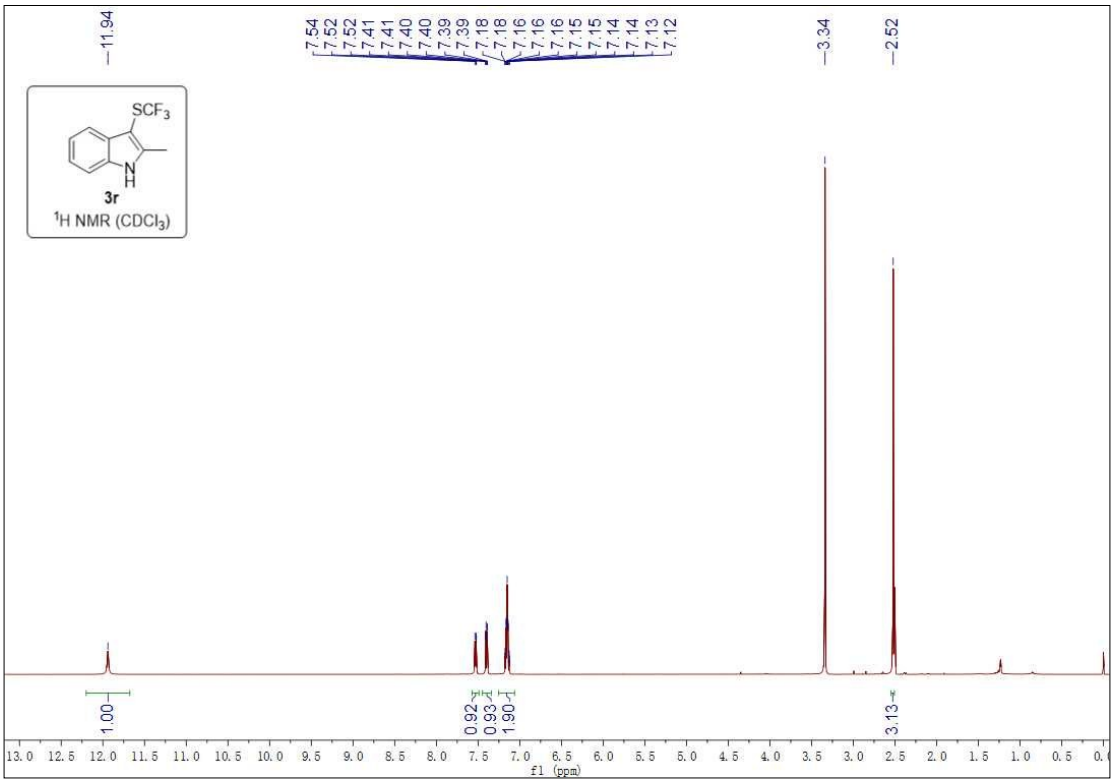

3p
19F NMR (DMSO)
-93.57
-93.72
f1 (ppm)

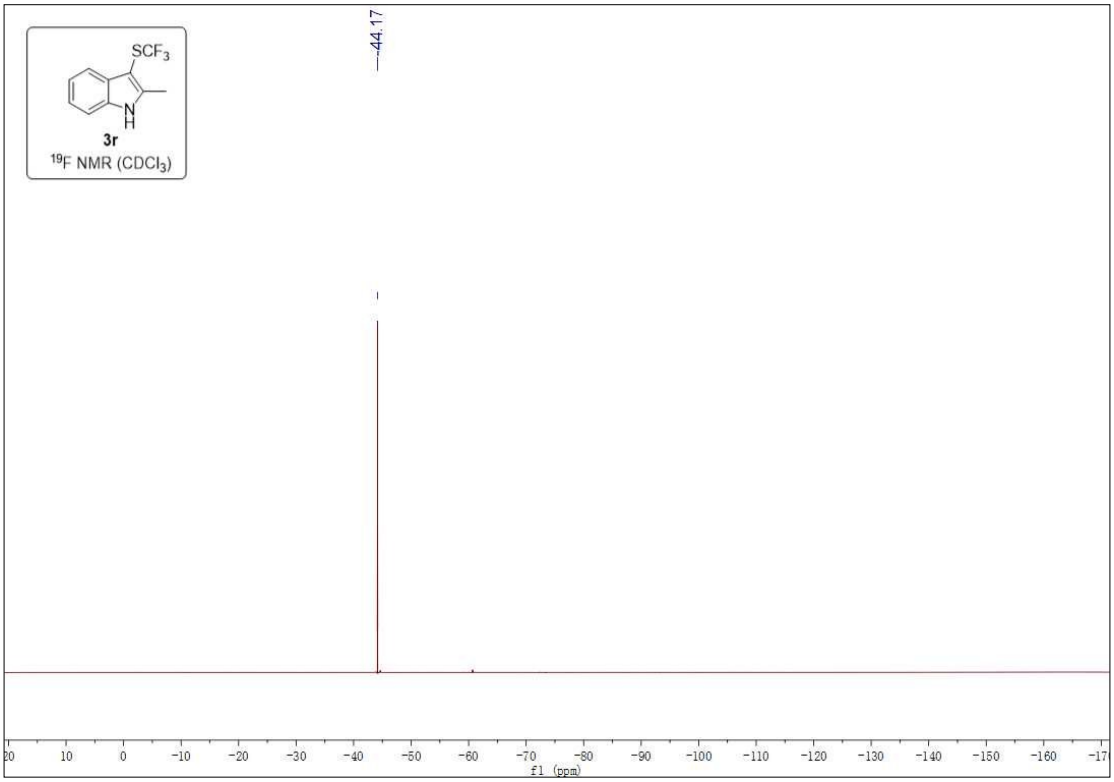

3p
13C NMR (DMSO)
140.2
138.3
137.6
135.4
135.1
133.8
126.1
123.9
122.4
122.4
121.4
111.3
93.5
f1 (ppm)

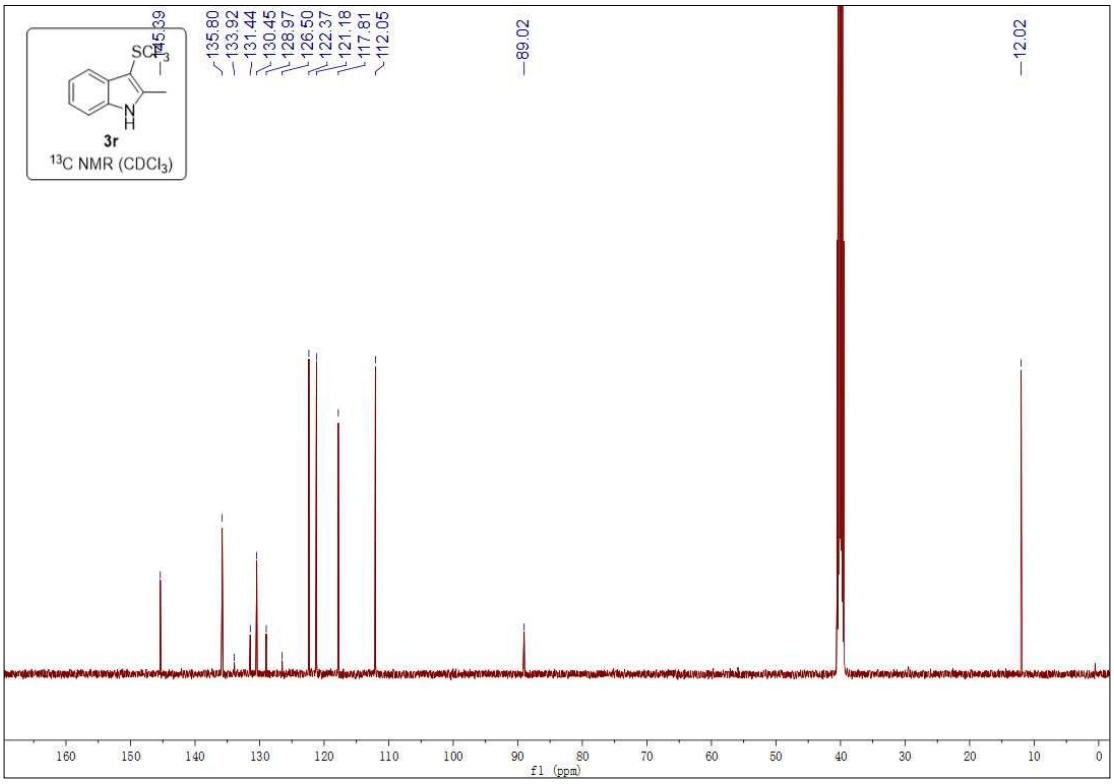

7.28
6.69
6.58
6.57
6.57
6.46
6.16
6.15
3.74
3.70
3.65
SCF2H
3q
1H NMR (CDCl3)
2.00
0.96
3.06
2.01
3.06
f1 (ppm)

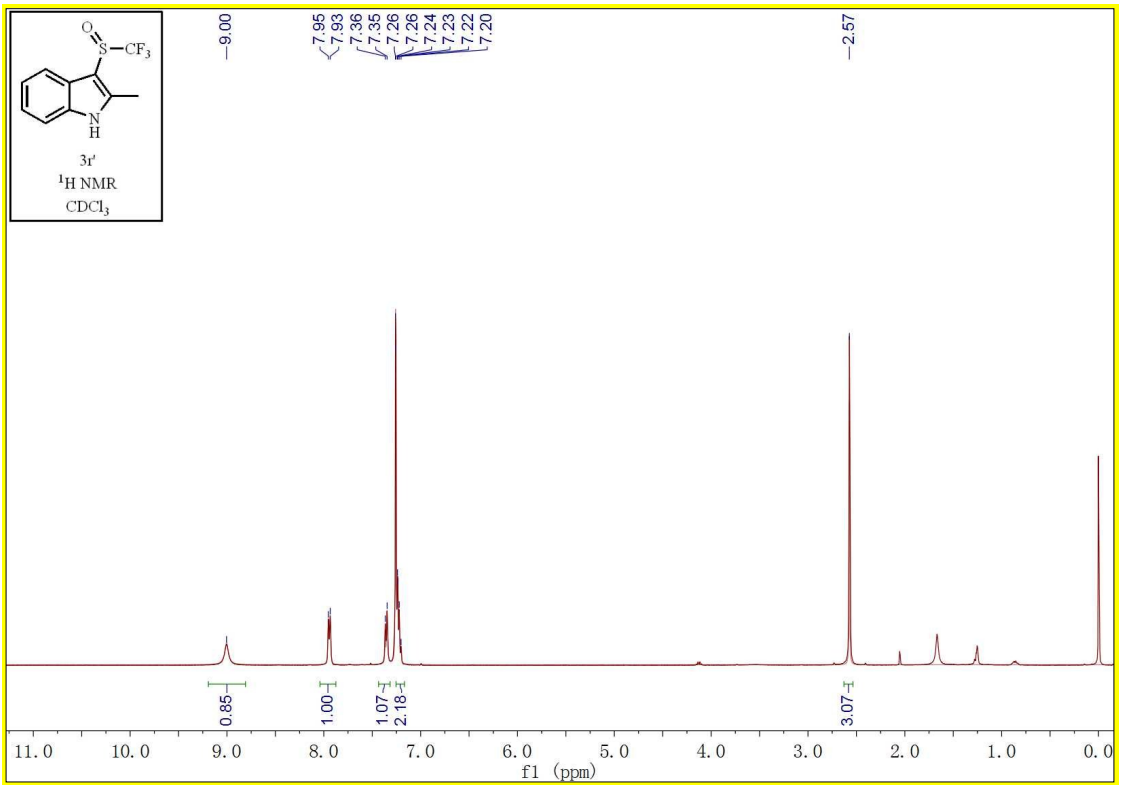

92.91
93.06
SCF2H
3q
19F NMR (CDCl3)
A (d)
-92.99
f1 (ppm)

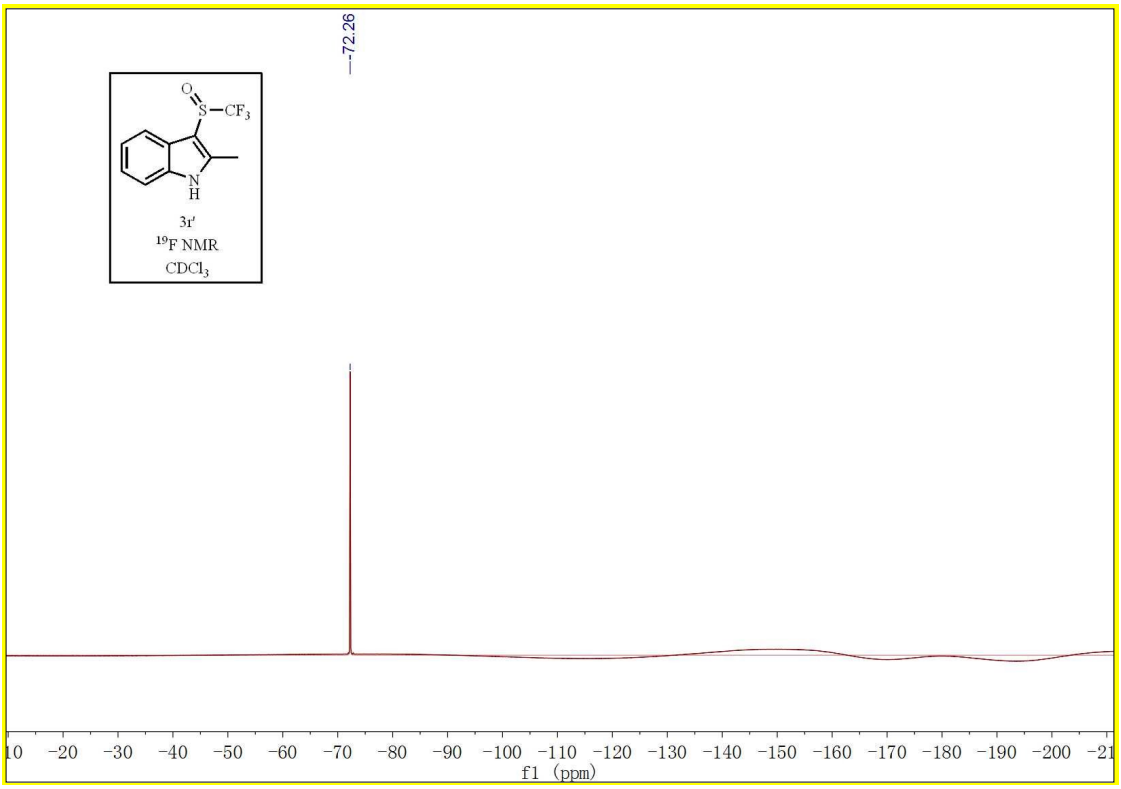

170.3
130.7
123.1
120.9
120.6
118.7
111.6
109.6
52.3
33.5
31.3
3q
13C NMR (CDCl3)
f1 (ppm)

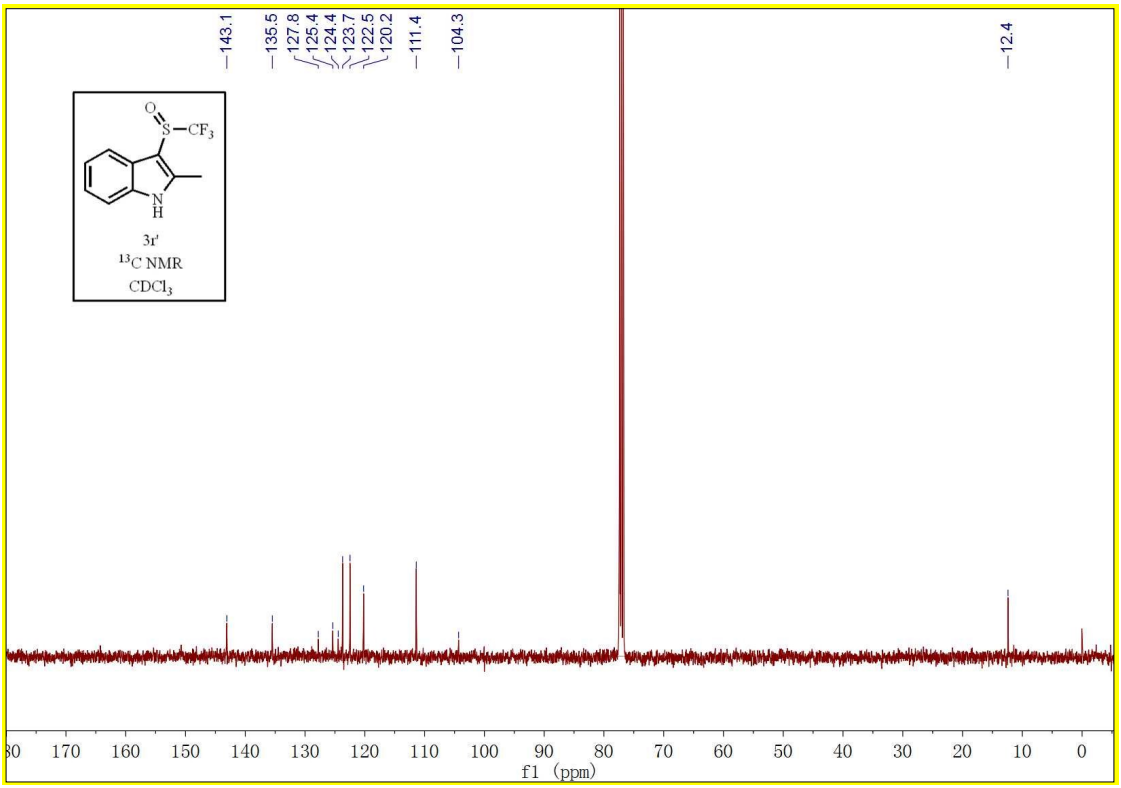

11.94
7.54
7.52
7.52
7.41
7.41
7.40
7.40
7.39
7.39
7.18
7.18
7.16
7.16
7.16
7.15
7.15
7.14
7.14
7.13
7.12
3.34
2.52
3r
1H NMR (CDCl3)
1.00
0.92
0.93
1.90
3.13
f1 (ppm)

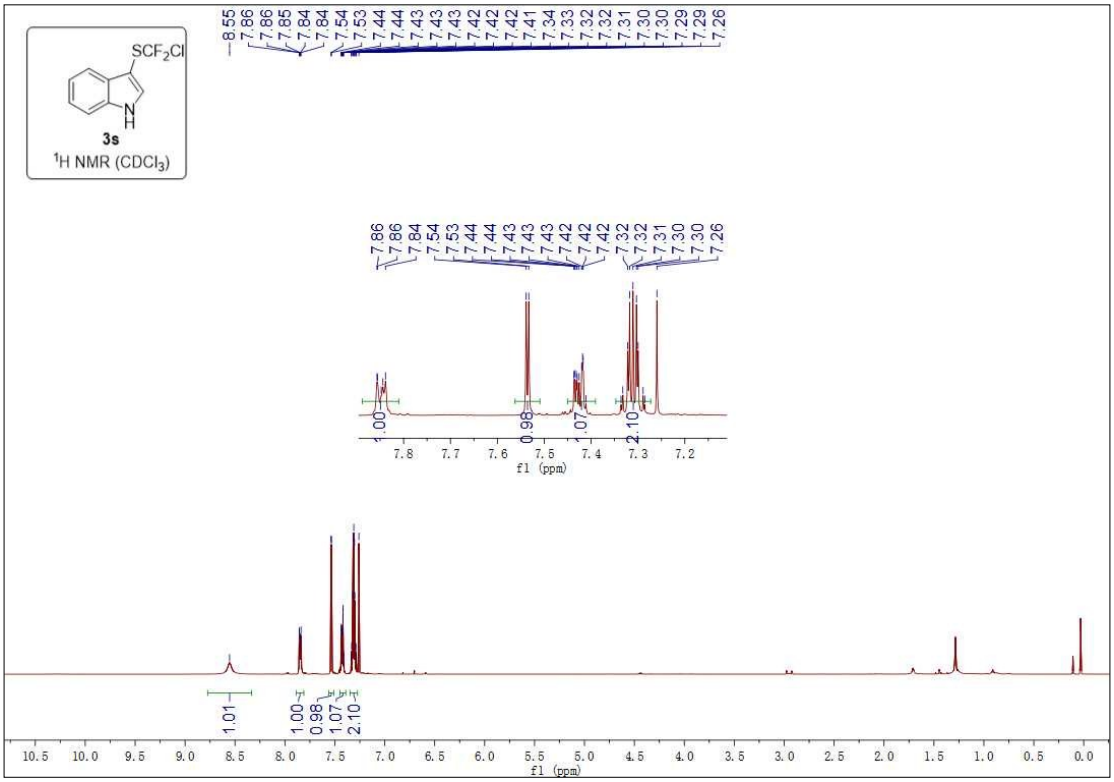

SCF3
3r
19F NMR (CDCl3)
-44.17
f1 (ppm)

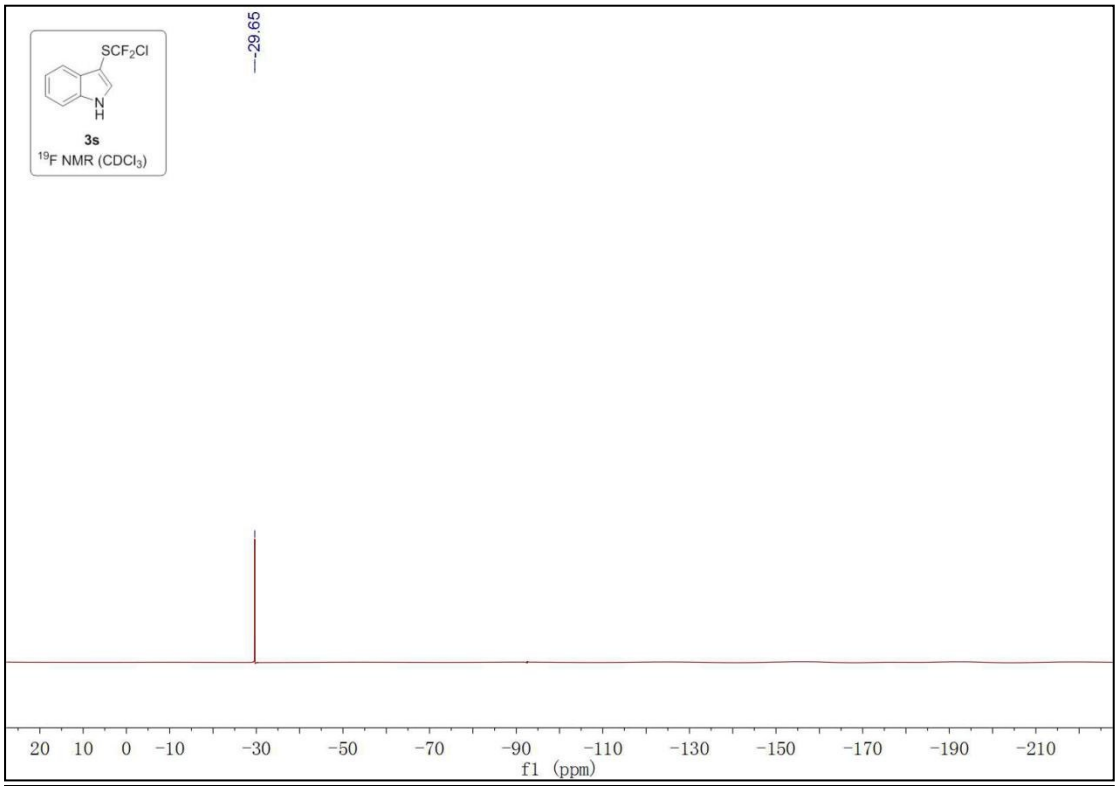

SCF3
3r
13C NMR (CDCl3)
145.39
135.80
133.92
131.44
130.45
128.97
126.50
122.37
121.18
117.81
112.05
89.02
12.02
f1 (ppm)

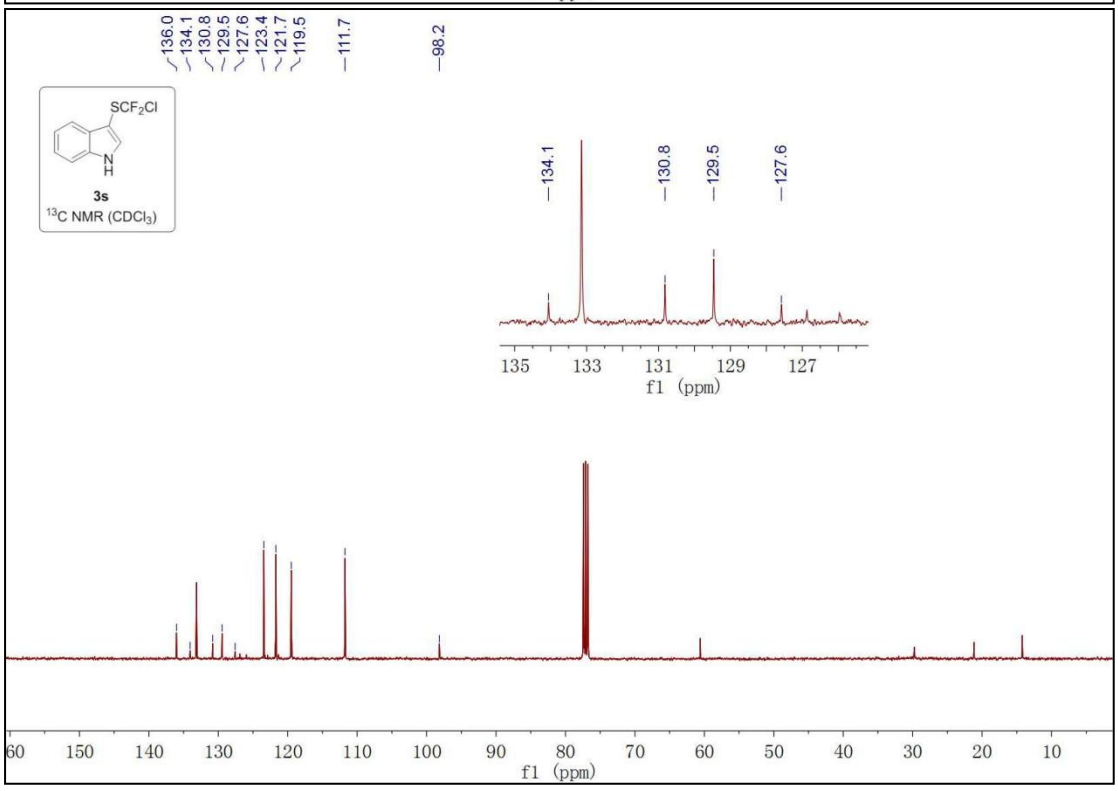

3r'
^{1}H NMR
$CDCl_3$
9.00
7.95
7.93
7.36
7.35
7.26
7.26
7.24
7.23
7.22
7.20
2.57
0.85
1.00
1.07
2.18
3.07
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

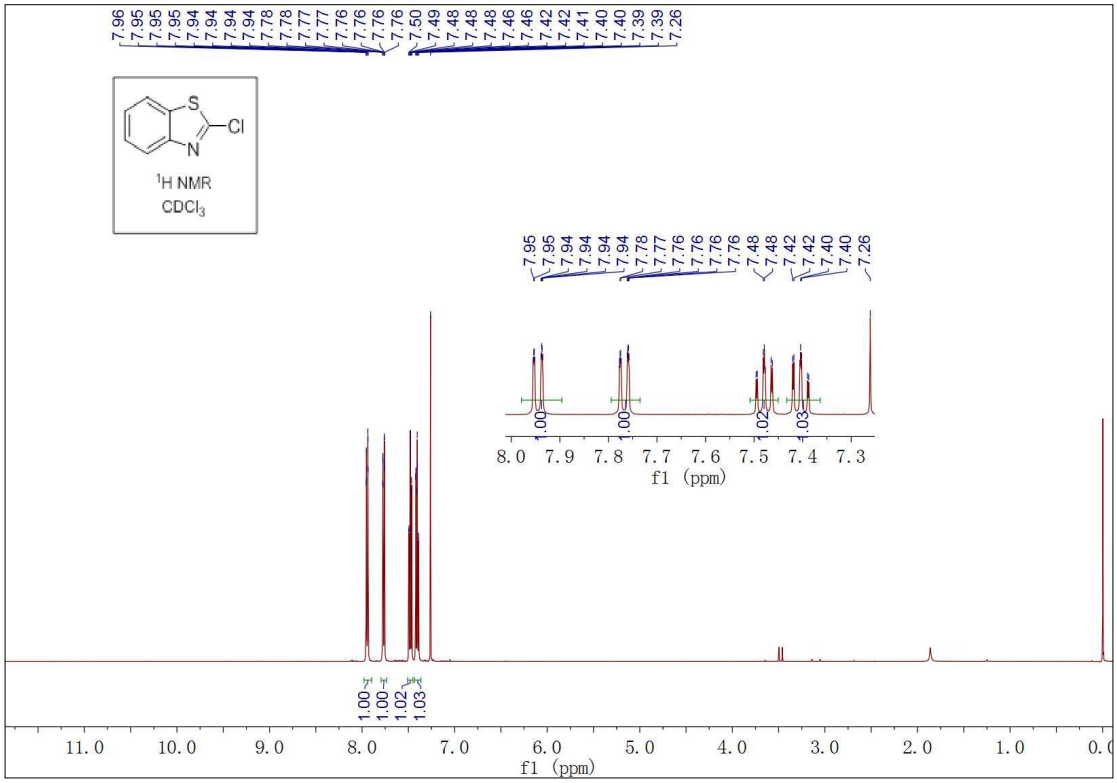

3r'
^{19}F NMR
$CDCl_3$
-72.26
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-21
f1 (ppm)


143.1
135.5
127.8
125.4
124.4
123.7
122.5
120.2
111.4
104.3
12.4
3r'
13C NMR
CDCl3
f1 (ppm)


3s
1H NMR (CDCl3)
f1 (ppm)


SCF2Cl
3s
19F NMR (CDCl3)
-29.65
20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210
f1 (ppm)


136.0
134.1
130.8
129.5
127.6
123.4
121.7
119.5
111.7
98.2
SCF2Cl
3s
13C NMR (CDCl3)
134.1
130.8
129.5
127.6
135 133 131 129 127
f1 (ppm)
60 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


7.96 7.95 7.95 7.95 7.94 7.94 7.94 7.78 7.78 7.77 7.77 7.76 7.76 7.76 7.76 7.50 7.49 7.48 7.48 7.48 7.46 7.46 7.42 7.42 7.41 7.40 7.40 7.39 7.26
S
Cl
N
1H NMR
CDCl3
7.95 7.95 7.94 7.94 7.94 7.78 7.77 7.76 7.76 7.76 7.48 7.48 7.42 7.42 7.40 7.40 7.26
1.00 1.00 1.02 1.03
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3
f1 (ppm)
1.00 1.00 1.02 1.03
11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
f1 (ppm)