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Supporting Information

For

Synthesis of trifluoromethyl-containing isoindolinones from tertiary enamides via cascade radical addition and cyclization process

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(A) General Methods

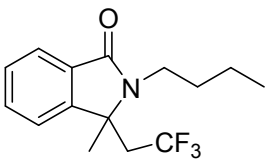
Commercially available reagents were used as received without further purification unless otherwise indicated. Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) using Silica Gel 60 F254 plates and were visualized by fluorescence quenching at 254 nm. For chromatographic purifications, analytically pure solvents were used and the silica gel 300-400 mesh was used as the solid support. ^{1}H NMR and ^{13}C NMR chemical shifts were reported in δ units, parts per million (ppm) relative to the chemical shift of residual solvent. Reference peaks for chloroform in ^{1}H NMR and ^{13}C NMR spectra were set at 7.26 ppm and 77.0 ppm, respectively.

(B) Analytical data for the products

Typical experimental procedure for the synthesis of trifluoromethyl-containing isoindolinones 2 and 4

In a 25 mL sealed tube, a mixture of *N*-butyl-*N*-(prop-1-en-2-yl)benzamide **1a** (43.4mg, 0.2 mmol), KHF_2 (12.4 mg, 1.0 equiv), $TMSCF_3$ (113.8 mg, 4 equiv), $PhI(OAc)_2$ (257.7mg, 4 equiv), EtOAc (2mL) was stirred at 80℃ under N_2 for 12h. The reaction mixture was quenched with saturate brine, dried over anhydrous Na_2SO_4, and evaporated in vacuum. The residue was purified by flash chromatography on silica gel by gradient elution (ethyl acetate in petroleum ether, 4:1) to obtain the corresponding product **2a**.

2-butyl-3-methyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



2a

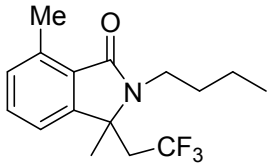
Yellow liquid , 75 % yield ; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.84 (d, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 3.67-3.69 (m, 1H), 3.21-3.07 (m, 1H), 2.76 (q, *J* = 10.1 Hz, 2H), 1.96-1.79 (m, 1H), 1.59 (d, *J* = 10.9 Hz, 4H), 1.43 (dd, *J* = 13.4, 8.8 Hz, 2H), 0.98 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 167.77, 147.62, 131.62, 131.35, 128.70, 124.23(q, J_{CF} = 278.4Hz), 123.72, 121.21, 61.87, 40.36 (q, J_{CF} = 27.3 Hz), 40.08, 31.18, 26.43, 20.71, 13.82.

^{19}F NMR (377 MHz, $CDCl_3$) δ = -61.60 (s).

HRMS (ESI-TOF) m/z = 308.1233 [M + Na] $^+$, calcd for $C_{15}H_{18}F_3NNaO$: 308.1238

2-butyl-3, 7-dimethyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



2b

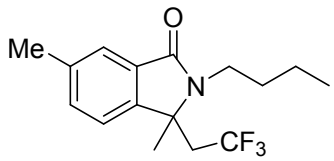
Yellow solid , 72 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.40 (t, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 8.0 Hz, 2H), 3.64-3.66 (m, 1H), 3.10-3.12 (m, 1H), 2.81-2.67 (m, 5H), 1.91-1.80 (m, 1H), 1.63-1.56 (m, 1H), 1.55 (d, *J* = 6.7 Hz, 3H), 1.45-1.39 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 167.57, 147.20, 136.70, 129.97, 129.63, 127.26, 123.54 (q, J_{CF} = 278.4 Hz), 117.54, 59.90, 39.60 (q, J_{CF} = 27.1 Hz), 38.93, 30.18, 25.71, 19.75, 16.24, 12.79.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -61.60 (s).

HRMS (ESI-TOF) m/z =322.1377 [M + Na] $^+$, calcd for $C_{16}H_{20}F_3NNaO$:322.1395

2-butyl-3, 6-dimethyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



2c

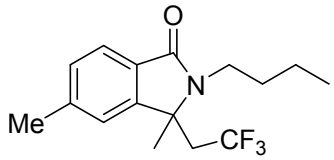
Yellow liquid , 66 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.64 (s, 1H), 7.36 (d, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 7.7 Hz, 1H), 3.72-3.61 (m, 1H), 3.20-3.08 (m, 1H), 2.73 (q, *J* = 10.1 Hz, 2H), 2.43 (d, *J* = 13.7 Hz, 3H), 1.90-1.79 (m, 1H), 1.65-1.53 (m, 4H), 1.46-1.38 (m, 2H), 0.97 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 167.89, 144.87, 138.77, 132.53, 131.43, 124.56 (q, J_{CF} = 278.4 Hz), 123.92, 120.96, 61.68, 40.56 (q, J_{CF} = 27.2 Hz), 40.05, 31.17, 26.49, 21.32, 20.70, 13.83.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -61.59 (s).

HRMS (ESI-TOF) m/z =322.1389 [M + Na] $^+$, calcd for $C_{16}H_{20}F_3NNaO$: 322.1395

2-butyl-3, 5-dimethyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



2d

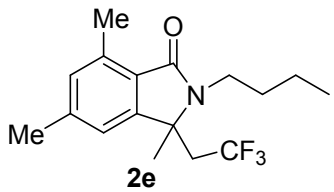
White solid , 73 % yield ; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.71 (d, *J* = 7.7 Hz, 1H), 7.29-7.25 (m, 1H), 7.20 (s, 1H), 3.65-3.67 (m, 1H), 3.18-3.06 (m, 1H), 2.81-2.67 (m, 2H), 2.46 (s, 3H), 1.90-1.80 (m, 1H), 1.57 (d, *J* = 13.3 Hz, 4H), 1.46-1.38 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.85, 148.01, 142.23, 129.65, 128.79, 124.53 (q, J_{CF} = 278.4 Hz), 123.47, 121.63, 61.64, 40.55 (q, J_{CF} = 27.3 Hz),40.02, 31.22, 26.49, 21.99, 20.70, 13.84.

^{19}F NMR (377 MHz, $CDCl_3$) δ = -61.58 (s).

HRMS (ESI-TOF) m/z = 322.1389 $[M + Na]^+$, calcd for $C_{16}H_{20}F_3NNaO$: 322.1395

2-butyl-3, 5, 7-trimethyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



2e

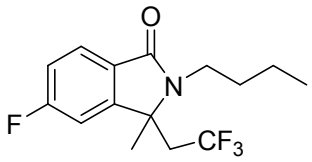
Yellow liquid , 68 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.50 (s, 1H), 7.12 (s, 1H), 3.61 (ddd, *J* = 14.3, 11.1, 5.3 Hz, 1H), 3.14-3.16 (m, 1H), 2.92-2.94 (m, 1H), 2.80-2.82 (m, 1H), 2.44 (s, 3H), 2.39 (s, 3H), 1.90-1.83 (m, 1H), 1.65-1.56 (m, 4H), 1.45-1.39 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.92, 141.48, 138.77, 135.09, 132.19, 131.61,124.46 (q, J_{CF} = 278.5 Hz), 121.75, 62.33, 39.68, 38.03 (q, J_{CF} = 27.1 Hz),31.06, 24.48, 21.05, 20.75, 18.67, 13.82.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -62.69 (s).

HRMS (ESI-TOF) m/z =336.1546 $[M + Na]^+$, calcd for $C_{17}H_{22}F_3NNaO$: 336.1551

2-butyl-5-fluoro-3-methyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



2f

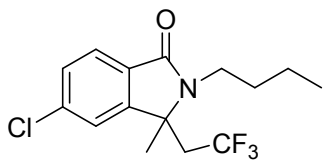
Yellow solid , 67 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.82 (dd, *J* = 8.3, 5.0 Hz, 1H), 7.17 (td, *J* = 8.8, 2.0 Hz, 1H), 7.10 (dd, *J* = 8.1, 1.8 Hz, 1H), 3.65-3.67 (m, 1H), 3.16-3.09 (m, 1H), 2.82-2.67 (m, 2H), 1.89-1.80 (m, 1H), 1.64-1.55 (m, 4H), 1.46-1.38 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.68, 165.95, 164.28, 150.04, 125.76, 124.36 (q, J_{CF} = 278.3 Hz),116.53, 108.88, 61.55,40.47 (q, J_{CF} = 27.5 Hz), 40.18, 31.17, 26.39, 20.67, 13.81.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -61.65 (s), -106.97 (s).

HRMS (ESI-TOF) m/z = 326.1119 [M + Na] $^+$, calcd for $C_{15}H_{17}F_4NNaO$: 326.1144

2-butyl-5-chloro-3-methyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



2g

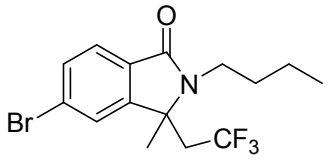
White solid , 60 % yield ; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.77 (d, *J* = 8.1 Hz, 1H), 7.48-7.37 (m, 2H), 3.66-3.68 (m, 1H), 3.10-3.12 (n, 1H), 2.87-2.65 (m, 2H), 1.91-1.78 (m, 1H), 1.59 (d, *J* = 11.5 Hz, 4H), 1.48-1.35 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.71, 149.21, 137.97, 129.82, 129.36, 125.03,δ 124.33 (q, J_{CF} = 278.2 Hz), 121.76, 61.65, 40.43 (q, J_{CF} = 27.4 Hz),40.20, 31.09, 26.37, 20.68, 13.81.

^{19}F NMR (377 MHz, $CDCl_3$) δ = -61.61 (s).

HRMS (ESI-TOF) m/z = 342.0877 [M + Na] $^+$, calcd for $C_{15}H_{17}ClF_3NNaO$: 342.0848

5-bromo-2-butyl-3-methyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



2h

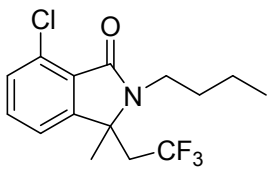
Yellow solid , 71 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.70 (t, *J* = 6.7 Hz, 1H), 7.63-7.59 (m, 1H), 7.57 (s, 1H), 3.66-3.68 (m, 1H), 3.15-3.08 (m, 1H), 2.83-2.68 (m, 2H), 1.89-1.80 (m, 1H), 1.62-1.54 (m, 4H), 1.45-1.38 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.77, 149.41, 132.20, 130.30, 126.24, 125.21, 124.70, 124.32 (q, J_{CF} = 278.4 Hz), 61.63, 40.41 (q, J_{CF} = 27.5 Hz),40.18, 31.07, 26.37, 20.67, 13.81.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -61.62 (s).

HRMS (ESI-TOF) m/z = 386.0336 [M + Na] $^{+}$, calcd for $C_{15}H_{17}BrF_3NNaO$: 386.0343

2-butyl-7-chloro-3-methyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



2i

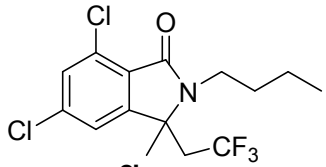
White solid , 70 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.47 (t, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.32 (d, *J* = 7.5 Hz, 1H), 3.73-3.61 (m, 1H), 3.21-3.05 (m, 1H), 2.88-2.68 (m, 2H), 1.92-1.81 (m, 1H), 1.64-1.54 (m, 4H), 1.46-1.38 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 165.36, 150.12, 132.30, 131.48, 130.38,127.33,124.36 (q, J_{CF} = 278.4 Hz), 119.79, 60.79, 40.47 (q, J_{CF} = 27.4 Hz)， 40.21, 30.95, 26.64, 20.70, 13.77.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -61.58 (s).

HRMS (ESI-TOF) m/z =342.0829 [M + Na] $^{+}$, calcd for $C_{15}H_{17}ClF_3NNaO$: 342.0848

2-butyl-5,7-dichloro-3-methyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



2j

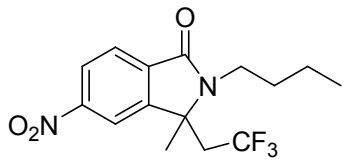
Yellow solid , 36 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.43 (d, *J* = 1.5 Hz, 1H), 7.30 (d, *J* = 1.5 Hz, 1H), 3.64-3.66 (m, 1H), 3.08-3.10 (m, 1H), 2.81-2.68 (m, 2H), 1.90-1.82 (m, 1H), 1.58 (s, 1H), 1.56 (s, 3H), 1.40-1.42 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 164.44, 151.20, 138.05, 132.43, 130.54, 126.04, 124.28 (q, J_{CF} = 278.7 Hz), 120.42, 60.73, 40.45 (q, J_{CF} = 27.6 Hz), 40.32, 30.92, 26.57, 20.69, 13.77.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -61.55 (s).

HRMS (ESI-TOF) m/z =376.0453 $[M + Na]^+$, calcd for $C_{15}H_{16}Cl_2F_3NNaO$: 376.0459

2-butyl-3-methyl-5-nitro-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



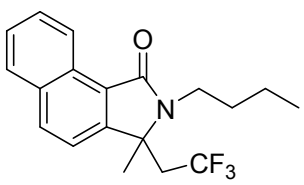
2k

White solid , 67 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.38 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.31 (d, *J* = 1.0 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 3.71-3.73 (m, 1H), 3.22-3.13 (m, 1H), 2.92-2.82 (m, 2H), 1.94-1.81 (m, 1H), 1.65 (d, *J* = 13.3 Hz, 3H), 1.63-1.57 (m, 1H), 1.49-1.39 (m, 2H), 0.99 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 165.38, 150.20, 148.59, 136.68, 124.91, 124.57, 124.17 (q, J_{CF} = 278.5 Hz),117.03, 62.10, 40.55,40.27 (d, J_{CF} = 27.6 Hz), 30.90, 26.34, 20.66, 13.76.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -61.65 (s).

2-butyl-3-methyl-3-(2, 2, 2-trifluoroethyl)-2,3-dihydro-1H-benzo[e]isoindol-1-one



2l

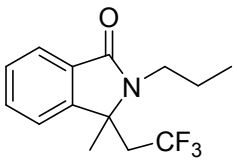
Yellow liquid , 60 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.25 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.67 (t, *J* = 8.0 Hz, 1H), 7.58 (t, *J* = 7.9 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 3.74-3.76 (m, 1H), 3.20-3.22 (m, 1H), 2.84 (q, *J* = 10.1 Hz, 2H), 1.94-1.90 (m, 1H), 1.69-1.64 (m, 1H), 1.62 (d, *J* = 9.8 Hz, 3H), 1.49-1.42 (m, 2H), 1.00 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 168.73, 147.72, 133.31, 132.54, 129.27, 128.14, 128.11, 126.81,125.80 (q, J_{CF} = 278.4Hz), 125.25, 124.22, 118.20, 61.22, 40.17 (q, J_{CF} = 27.2 Hz),40.08, 31.25, 26.28, 20.80, 13.87.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -61.69 (s).

HRMS (ESI-TOF) m/z =358.1392 $[M + Na]^+$, calcd for $C_{19}H_{20}F_3NNaO$: 358.1395

3-methyl-2-propyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



2m

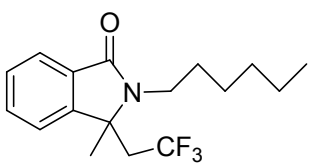
White solid , 64 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.84 (d, *J* = 7.5 Hz, 1H), 7.56 (td, *J* = 7.5, 1.1 Hz, 1H), 7.47 (td, *J* = 7.5, 0.9 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 3.64-3.66 (m, 1H), 3.09-3.11 (m, 1H), 2.82-2.70 (m, 2H), 1.94-1.85 (m, 1H), 1.71-1.63 (m, 1H), 1.58 (s, 3H), 1.00 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.76, 147.57, 131.61, 131.31, 128.68, 124.50 (q, J_{CF} = 278.4 Hz), 123.70, 121.20, 41.91,40.52 (q, J_{CF} = 27.3 Hz), 26.45, 22.31, 11.81.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -61.64 (s).

HRMS (ESI-TOF) m/z =294.1067 $[M + Na]^+$, calcd for $C_{14}H_{16}F_3NNaO$: 294.1082

2-hexyl-3-methyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



2n

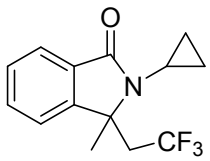
Yellow liquid , 55 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.84 (d, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 3.66-3.68 (m, 1H), 3.12-3.14 (m, 1H), 2.83-2.69 (m, 2H), 1.94-1.82 (m, 1H), 1.67-1.54 (m, 4H), 1.39 (dd, *J* = 14.1, 7.9 Hz, 2H), 1.33 (d, *J* = 3.4 Hz, 4H), 0.90 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.71, 147.57, 131.59, 131.33, 128.67, 124.39(q, J_{CF} = 277.8 Hz), 123.69, 121.18, 61.83, 40.51 (q, J_{CF} = 27.2 Hz), 40.30, 31.52, 29.00, 27.14, 26.45, 22.61, 14.05.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -61.62 (s).

HRMS (ESI-TOF) m/z =336.1537 $[M + Na]^+$, calcd for $C_{17}H_{22}F_3NNaO$: 336.1551

2-cyclopropyl-3-methyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



2o

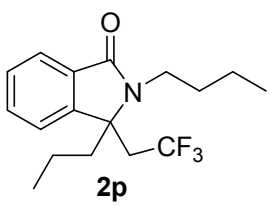
White solid , 65 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.82 (d, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.41 (d, *J* = 7.7 Hz, 1H), 3.00 (dq, *J* = 15.7, 10.1 Hz, 1H), 2.79 (dq, *J* = 15.7, 10.0 Hz, 1H), 2.50-2.43 (m, 1H), 1.63 (s, 3H), 1.16-1.11 (m, 1H), 1.07-1.03 (m, 1H), 1.00-0.92 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.90, 147.14, 131.83, 131.28, 128.68, 124.63 (q, J_{CF} = 278.4 Hz), 123.88, 121.35, 63.15, 40.52 (q, J_{CF} = 27.1 Hz), 26.90, 21.99, 5.07, 4.70.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -61.24 (s).

HRMS (ESI-TOF) m/z =292.0902 $[M + Na]^+$, calcd for $C_{14}H_{14}F_3NNaO$: 292.0925

2-butyl-3-propyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



2p

Yellow liquid , 57 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.83 (d, *J* = 7.4 Hz, 1H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.3 Hz, 1H), 7.35 (d, *J* = 7.5 Hz, 1H), 3.52-3.43 (m, 1H), 3.27-3.18 (m, 1H), 2.83-2.70

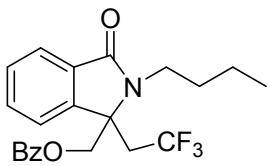
(m, 2H), 1.96-1.85 (m, 2H), 1.83-1.76 (m, 1H), 1.60-1.62 (m, 1H), 1.43-1.45 (m, 2H), 0.99 (t, J = 7.2 Hz, 3H), 0.94-0.86 (m, 1H), 0.76 (t, J = 7.2 Hz, 3H), 0.54 (dd, J = 14.6, 7.9 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 168.57, 145.63, 132.26, 131.52, 128.57, 124.52 (q, J_{CF} = 278.2 Hz), 123.59, 121.25, 65.07, 40.47 (q, J_{CF} = 27.2 Hz), 40.16, 39.93, 30.71, 20.84, 15.48, 13.85, 13.57.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -60.85 (s).

HRMS (ESI-TOF) m/z =336.1556 $[M + Na]^+$, calcd for $C_{17}H_{22}F_3NNaO$: 336.1551

(2-butyl-3-oxo-1-(2, 2, 2-trifluoroethyl)isoindolin-1-yl)methyl benzoate



2q

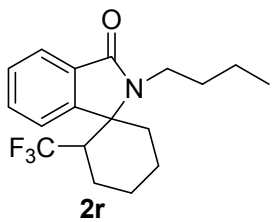
Yellow liquid , 42 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.88 (t, J = 6.4 Hz, 3H), 7.59 (dd, J = 16.3, 7.2 Hz, 2H), 7.55-7.48 (m, 2H), 7.45 (t, J = 7.8 Hz, 2H), 4.53 (s, 2H), 3.77-3.79 (m, 1H), 3.24-3.26 (m, 1H), 2.95-2.97 (m, 2H), 1.95-1.85 (m, 1H), 1.60-1.53 (m, 1H), 1.46-1.35 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.24, 165.60, 143.35, 133.72, 132.08, 131.78, 129.51, 129.46, 128.80, 128.69, 124.51 (q, J_{CF} = 278.8Hz), 123.89, 121.94, 67.66, 63.86, 40.94, 36.17 (q, J_{CF} = 24.2 Hz) , 31.01, 20.67, 13.72.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -60.71 (s).

HRMS (ESI-TOF) m/z =428.1444 $[M + Na]^+$, calcd for $C_{22}H_{22}F_3NNaO_3$: 428.1449

2'-butyl-2-(trifluoromethyl)spiro[cyclohexane-1,1'-isoindolin]-3'-one



2r

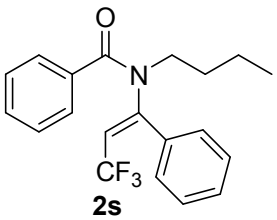
Yellow liquid , 57 % yield ; The major isomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.88 (dd, *J* = 6.0, 2.6 Hz, 1H), 7.73 (dd, *J* = 6.1, 2.0 Hz, 1H), 7.55-7.46 (m, 2H), 3.62-3.64 (m, 1H), 3.11-3.13 (m, 1H), 2.71-2.73 (m, 1H), 2.23-1.83 (m, 8H), 1.60-1.54 (m, 2H), 1.46-1.39 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 167.65, 145.96, 132.28, 130.55, 128.46, 125.77 (q, J_{CF} = 281.9 Hz), 124.09, 123.82, 64.44, 45.48 (q, J_{CF} = 24.2 Hz), 40.12, 36.36, 31.14, 24.05, 22.83, 22.04, 20.80, 13.81.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -67.20 (s).

HRMS (ESI-TOF) m/z =348.1546 $[M + Na]^+$, calcd for $C_{18}H_{22}F_3NNaO$: 348.1551

(E)-*N*-butyl-*N*-(3, 3, 3-trifluoro-1-phenylprop-1-enyl)benzamide



2s

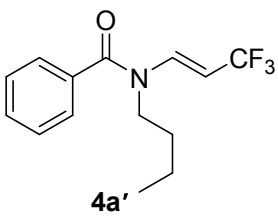
Yellow liquid , 66 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.45 (d, *J* = 7.3 Hz, 2H), 7.39 (dd, *J* = 10.5, 4.2 Hz, 2H), 7.35 (d, *J* = 5.9 Hz, 4H), 7.28 (t, *J* = 7.6 Hz, 2H), 5.33 (q, *J* = 8.3 Hz, 1H), 3.66-3.54 (m, 2H), 1.64 (dd, *J* = 15.5, 7.5 Hz, 2H), 1.31 (dd, *J* = 15.1, 7.5 Hz, 2H), 0.90 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 171.45, 151.21 (q, J_{CF} = 6.0 Hz), 135.89, 133.76, 130.44, 130.31, 129.05, 129.04, 128.47, 128.20, 127.71, 113.75 (q, J_{CF} = 35.2 Hz), 48.24, 30.06, 20.11, 13.75.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -55.30 (s).

HRMS (ESI-TOF) m/z =370.1384 $[M + Na]^+$, calcd for $C_{20}H_{20}F_3NNaO$: 370.1395

(E)-*N*-butyl-*N*-(3, 3, 3-trifluoroprop-1-enyl)benzamide



4a′

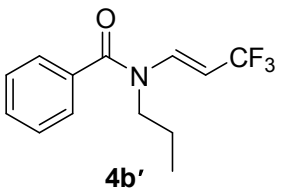
Yellow liquid , 64 % yield ; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.56-7.43 (m, 5H), 7.39 (d, *J* = 13.5 Hz, 1H), 5.09 (dd, *J* = 14.2, 6.2 Hz, 1H), 3.82-3.69 (m, 2H), 1.72-1.61 (m, 2H), 1.40 (dd, *J* = 15.0, 7.4 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 171.10, 136.86, 133.89, 131.21, 128.79, 128.01, 124.36 (q, J_{CF} = 267.4 Hz), 96.52 (d, J_{CF} = 34.3 Hz), 43.81, 28.46, 20.20, 13.76.

^{19}F NMR (377 MHz, $CDCl_3$) δ = -59.97 (s).

HRMS (ESI-TOF) m/z =294.1082 $[M + Na]^+$, calcd for $C_{14}H_{16}F_3NNaO$: 294.1082

(E)-*N*-propyl-*N*-(3, 3, 3-trifluoroprop-1-enyl)benzamide



4b′

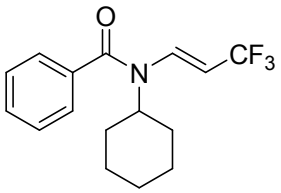
Yellow liquid , 72 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.52 (dd, *J* = 10.8, 4.2 Hz, 1H), 7.50-7.44 (m, 4H), 7.39 (d, *J* = 7.5 Hz, 1H), 5.08-5.10 (m, 1H), 3.76-3.69 (m, 2H), 1.74-1.67 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 171.12, 136.84, 133.86, 131.20, 128.78, 128.00, 124.33 (q, J_{CF} = 267.4 Hz), 96.54 (q, J_{CF} = 34.7 Hz), 45.49, 19.69, 11.29.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -60.03 (s).

HRMS (ESI-TOF) m/z =280.0922 $[M + Na]^+$, calcd for $C_{13}H_{14}F_3NNaO$: 280.0925

(E)-*N*-cyclohexyl-*N*-(3,3,3-trifluoroprop-1-enyl)benzamide



4c′

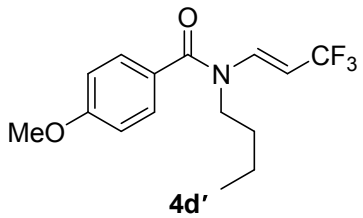
Yellow liquid , 47 % yield ; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.55-7.40 (m, 5H), 7.10 (d, *J* = 14.5 Hz, 1H), 5.40 (m, 1H), 3.97 (m, 1H), 2.06 (m, 2H), 1.88 (d, *J* = 13.3 Hz, 2H), 1.81 (d, *J* = 11.1 Hz, 2H), 1.39-1.19 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 171.92, 136.10, 135.09, 131.11, 128.71, 127.92, 124.40 (q, J_{CF} = 267.8 Hz), 99.48 (q, J_{CF} = 34.3 Hz), 57.66, 29.42, 26.19, 25.27.

^{19}F NMR (377 MHz, $CDCl_3$) δ = -60.50 (s).

HRMS (ESI-TOF) m/z =320.1221 [M + Na] $^+$, calcd for $C_{16}H_{18}F_3NNaO$: 320.1238

(E)-*N*-butyl-4-methoxy-*N*-(3, 3, 3-trifluoroprop-1-enyl)benzamide



4d′

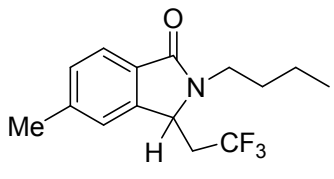
Colorless liquid , 68 % yield ; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.44 (t, *J* = 9.0 Hz, 3H), 6.96 (d, *J* = 8.7 Hz, 2H), 5.06 (m, 1H), 3.87 (s, 3H), 3.80-3.71 (m, 2H), 1.64 (dd, *J* = 14.5, 7.0 Hz, 2H), 1.39 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.85, 162.02, 137.42, 130.45, 125.79, 124.50 (q, J_{CF} = 267.3 Hz), 114.04, 95.85 (q, J_{CF} = 34.3 Hz), 55.46, 43.99, 28.46, 20.23, 13.76.

^{19}F NMR (377 MHz, $CDCl_3$) δ = -59.75 (s).

HRMS (ESI-TOF) m/z =324.1155 [M + Na] $^+$, calcd for $C_{15}H_{18}F_3NNaO_2$: 324.1187

2-butyl-5-methyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



4e

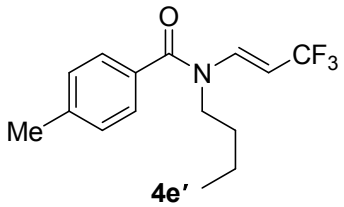
Yellow liquid , 33 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.73 (d, *J* = 8.3 Hz, 1H), 7.30 (d, *J* = 7.1 Hz, 2H), 4.70 (dd, *J* = 6.6, 3.4 Hz, 1H), 4.07-4.09 (m, 1H), 3.11-3.13 (m, 1H), 2.78-2.68 (m, 1H), 2.54-2.56 (m, 1H), 2.47 (s, 3H), 1.64-1.57 (m, 2H), 1.35 (dd, *J* = 15.0, 7.5 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 168.13, 144.37, 142.58, 129.81, 129.37, 125.74 (q, J_{CF} = 277.8 Hz), 123.60, 123.07, 53.42, 39.57, 36.66 (q, J_{CF} = 28.1 Hz), 30.09, 21.99, 20.07, 13.75.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -62.59 (s).

HRMS (ESI-TOF) m/z = 308.1241 $[M + Na]^+$, calcd for $C_{15}H_{18}F_3NNaO$: 308.1238

(E)-N-butyl-4-methyl-N-(3, 3, 3-trifluoroprop-1-enyl)benzamide



4e′

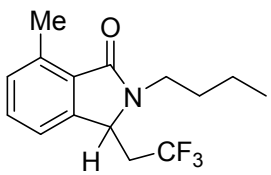
Yellow liquid , 36 % yield ; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41 (d, *J* = 13.9 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 7.9 Hz, 2H), 5.06-5.08 (m, 1H), 3.80-3.69 (m, 2H), 2.41 (s, 3H), 1.67-1.61 (m, 2H), 1.39 (dd, *J* = 15.1, 7.5 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 171.21, 141.75, 137.17, 130.89, 129.38, 128.23, 124.44 (q, J_{CF} = 267.4 Hz), 96.09 (q, J_{CF} = 35.3 Hz), 43.81, 28.45, 21.51, 20.22, 13.76.

^{19}F NMR (376 MHz, $CDCl_3$) δ = -59.84 (s).

HRMS (ESI-TOF) m/z =308.1203 $[M + Na]^+$, calcd for $C_{15}H_{18}F_3NNaO$: 308.1238

2-butyl-7-methyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



4f

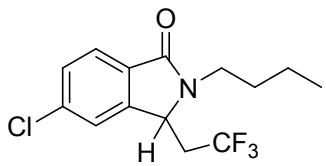
Yellow liquid , 70 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.43 (t, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 4.69 (dd, *J* = 6.3, 3.5 Hz, 1H), 4.04-4.06 (m, 1H), 3.10-3.12 (m, 1H), 2.77-2.65 (m, 4H), 2.63-2.50 (m, 1H), 1.66-1.60 (m, 1H), 1.56-1.58 (m, 1H), 1.40-1.33 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.83, 144.54, 137.85, 131.28, 130.81, 128.89, 125.70 (q, J_{CF} = 277.8 Hz), 119.89, 53.02, 39.54, 36.91 (q, J_{CF} = 28.1 Hz), 30.09, 20.14, 17.25, 13.73.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -62.55 (s).

HRMS (ESI-TOF) m/z = 308.1218 [M + Na] $^+$, calcd for $C_{15}H_{18}F_3NNaO$: 308.1238

2-butyl-5-chloro-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



4g

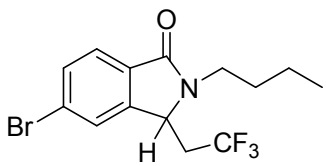
Yellow liquid , 63 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.78 (d, *J* = 8.1 Hz, 1H), 7.52 (s, 1H), 7.49 (dd, *J* = 8.1, 1.6 Hz, 1H), 4.73 (dd, *J* = 6.9, 3.2 Hz, 1H), 4.07-4.09 (m, 1H), 3.17-3.08 (m, 1H), 2.76 (dqd, *J* = 19.0, 11.2, 3.3 Hz, 1H), 2.63-2.52 (m, 1H), 1.66-1.61 (m, 1H), 1.61-1.56 (m, 1H), 1.35 (dd, *J* = 15.0, 7.5 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.95, 145.38, 138.26, 130.46, 129.52, 125.42 (d, J_{CF} = 277.3 Hz), 125.05, 123.19, 53.37, 39.75, 36.27 (q, J_{CF} = 28.4 Hz), 30.01, 20.04, 13.68.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -62.51 (s).

HRMS (ESI-TOF) m/z = 328.0697 [M + Na] $^+$, calcd for $C_{14}H_{15}ClF_3NNaO$: 328.0692

5-bromo-2-butyl-3-(2, 2, 2-trifluoroethyl)isoindolin-1-one



4h

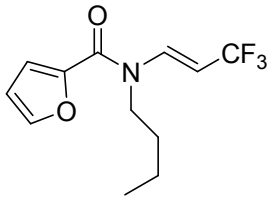
Yellow liquid , 54 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.72 (d, *J* = 8.0 Hz, 1H), 7.68 (s, 1H), 7.65 (dd, *J* = 8.0, 1.5 Hz, 1H), 4.73 (dd, *J* = 6.8, 3.2 Hz, 1H), 4.12-4.03 (m, 1H), 3.15-3.07 (m, 1H), 2.82-2.70 (m, 1H), 2.57-2.59 (m, 1H), 1.66-1.56 (m, 2H), 1.35 (dd, *J* = 15.0, 7.5 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.08, 145.57, 132.41, 130.88, 126.56, 126.14, 125.42 (q, J_{CF} = 277.4 Hz), 125.27, 77.26, 77.05, 76.84, 53.29, 39.71, 36.21 (q, J_{CF} = 28.4 Hz), 29.99, 20.04, 13.72.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -62.51 (s).

HRMS (ESI-TOF) m/z = 372.0169 [M + Na] $^+$, calcd for $C_{14}H_{15}BrF_3NNaO$: 372.0187

(E)-N-butyl-N-(3, 3, 3-trifluoroprop-1-enyl)furan-2-carboxamide



6a

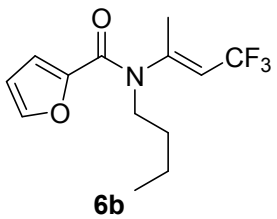
Yellow liquid , 60 % yield ; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.96 (d, *J* = 14.2 Hz, 1H), 7.60 (s, 1H), 7.16 (d, *J* = 3.3 Hz, 1H), 6.62-6.50 (m, 1H), 5.17-5.19 (m, 1H), 3.85-3.63 (m, 2H), 1.73-1.61 (m, 2H), 1.46-1.33 (m, 2H), 0.98 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 159.17, 146.49, 145.57, 136.19, 124.54 (q, J_{CF} = 268.7 Hz), 119.47, 111.96, 97.35 (q, J_{CF} = 34.4 Hz), 44.38, 28.67, 20.16, 13.71.

^{19}F NMR (377 MHz, $CDCl_3$) δ = -59.93 (s).

HRMS (ESI-TOF) m/z =284.0877 [M + Na] $^+$, calcd for $C_{12}H_{14}F_3NNaO_2$: 284.0874

(E)-N-butyl-N-(4,4,4-trifluorobut-2-en-2-yl)furan-2-carboxamide



6b

Yellow liquid , 60 % yield ; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.44 (s, 1H), 7.05 (d, *J* = 3.5 Hz, 1H), 6.46 (dd, *J* = 3.4, 1.7 Hz, 1H), 5.40 (q, *J* = 7.9 Hz, 1H), 3.63-3.56 (m, 2H), 2.16 (s, 3H), 1.59 (dd, *J* = 15.5, 7.8 Hz, 2H), 1.38 (dd, *J* = 15.1, 7.5 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H).

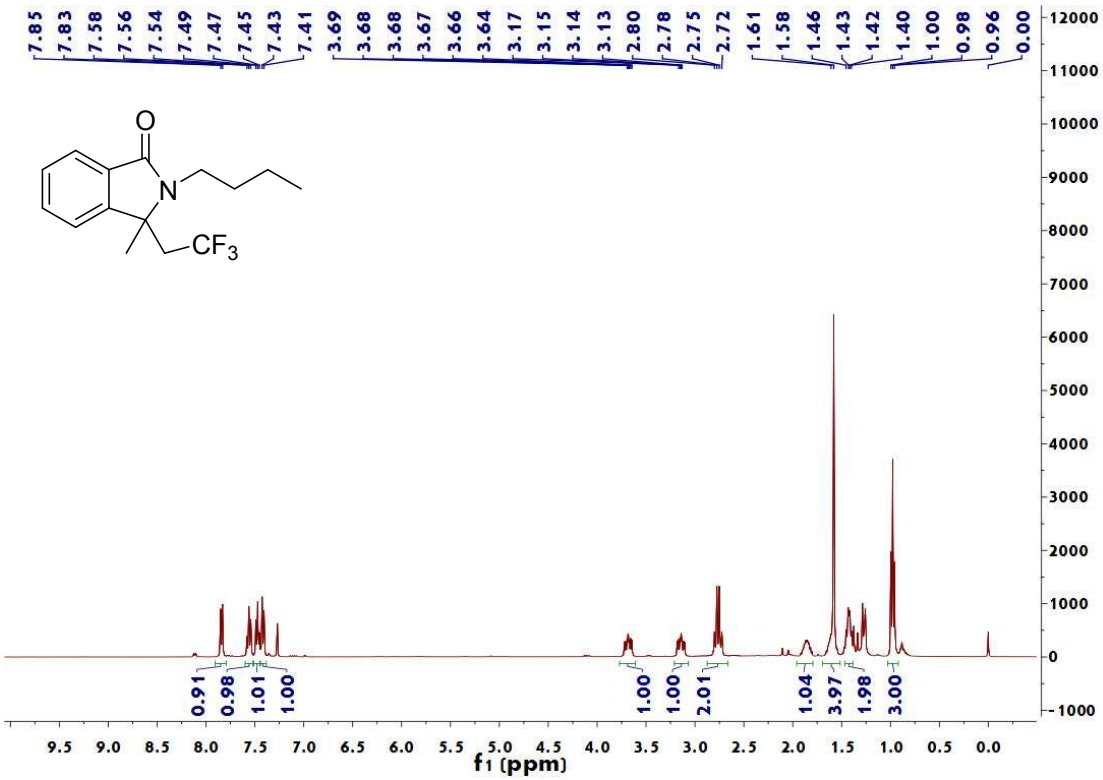
^{13}C NMR (151 MHz, $CDCl_3$) δ = 158.57, 149.51 (q, J_{CF} = 6.0 Hz), 147.52, 144.26, 122.87 (q, J_{CF} = 270.1 Hz), 117.05 (q, J_{CF} = 34.7 Hz), 117.10, 111.60, 46.77, 29.87, 20.08, 18.24, 13.77.

^{19}F NMR (565 MHz, $CDCl_3$) δ = -58.22 (s).

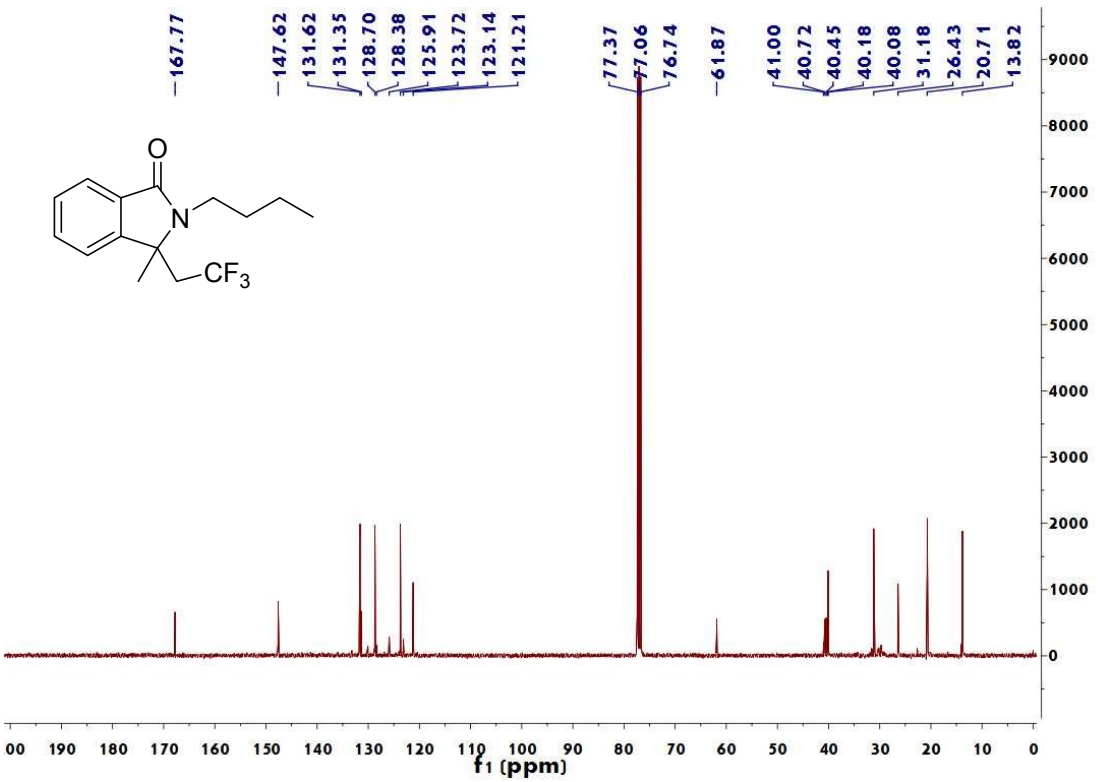
HRMS (ESI-TOF) m/z =298.1055 [M + Na] $^+$, calcd for $C_{13}H_{16}F_3NNaO_2$: 298.1031

(C) **Spectra**

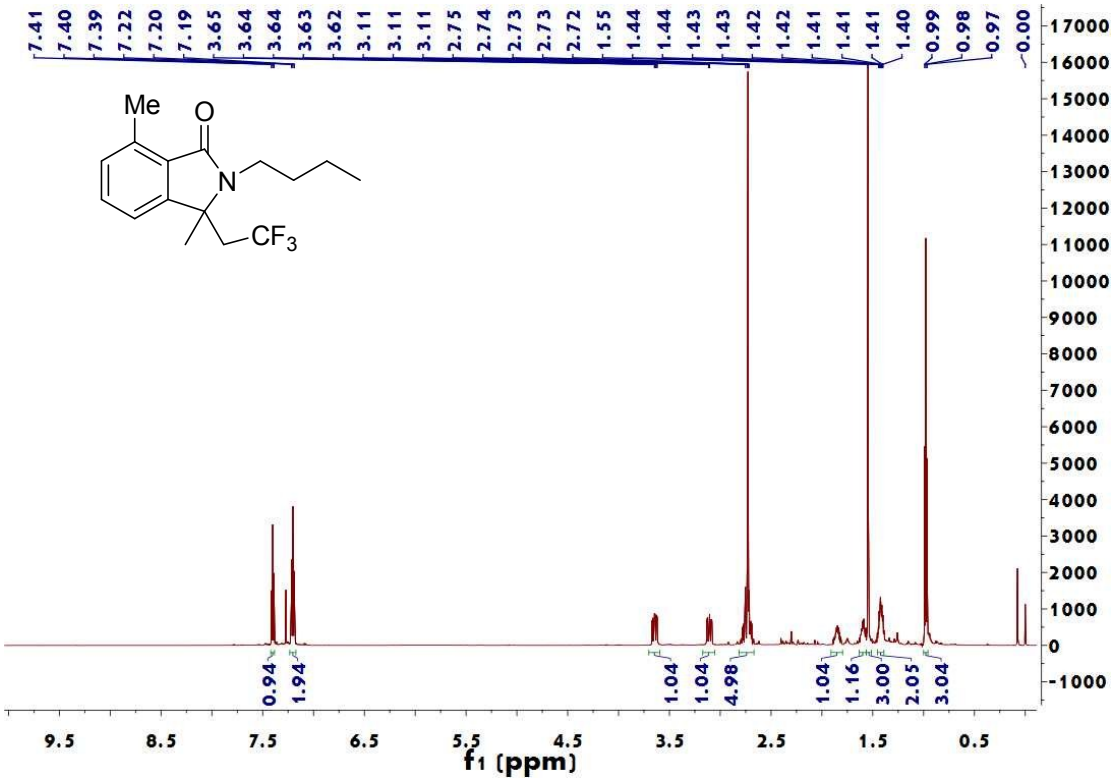
2a. ^{1}H NMR



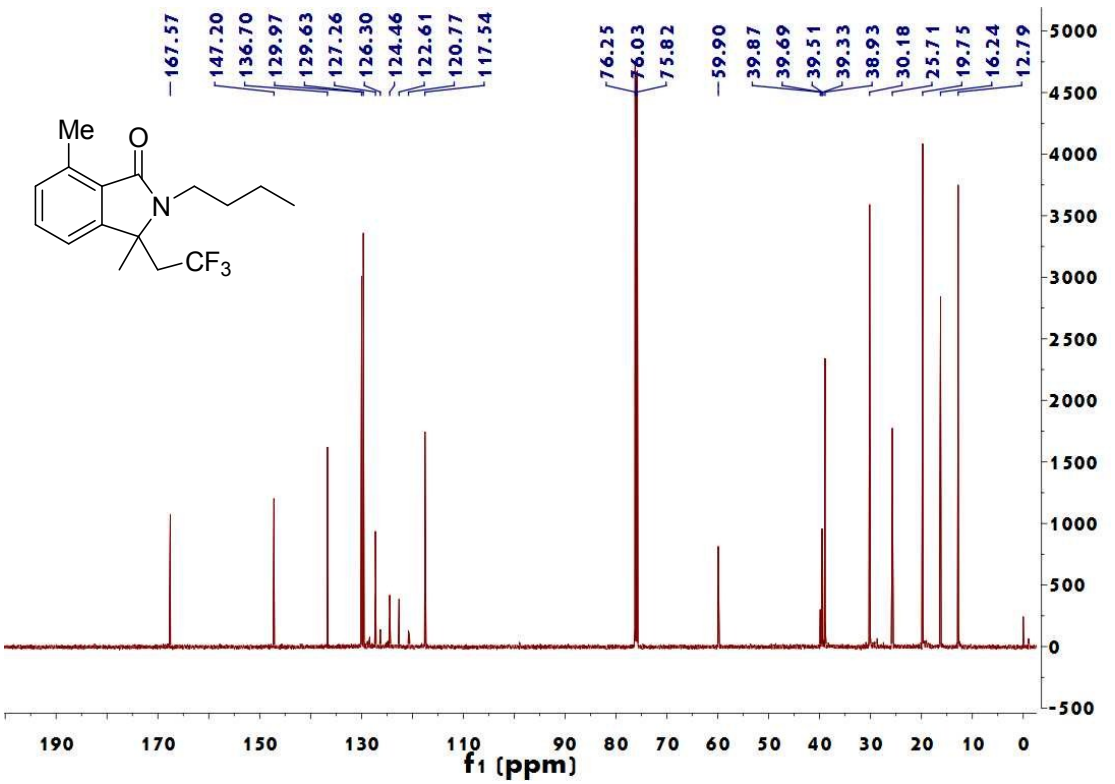
2a.^{13}C NMR



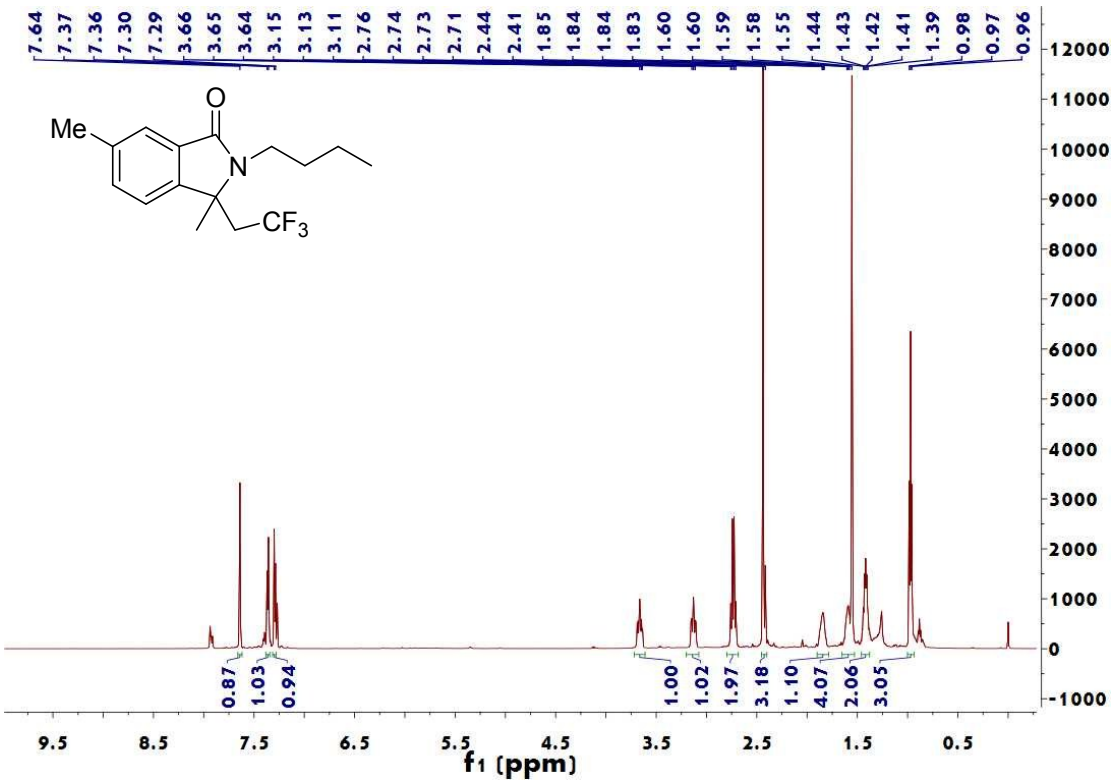
2b. ^{1}H NMR



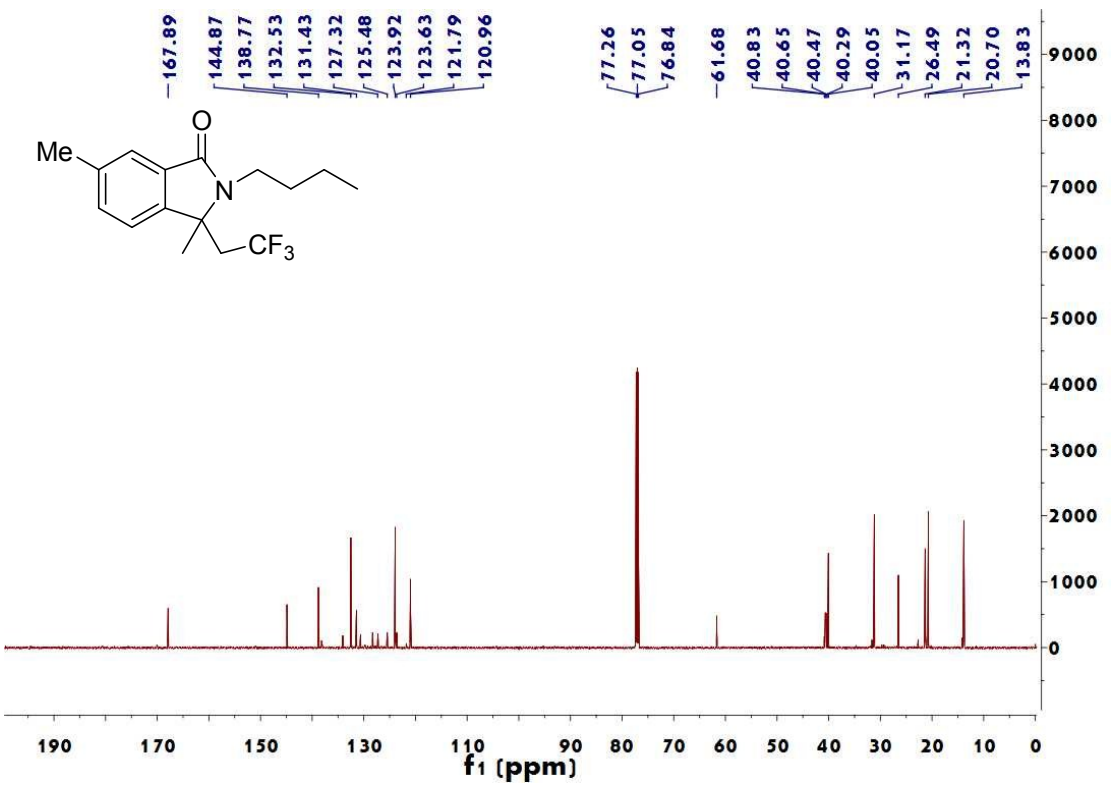
2b.^{13}C NMR



2c. ^{1}H NMR



2c.^{13}C NMR



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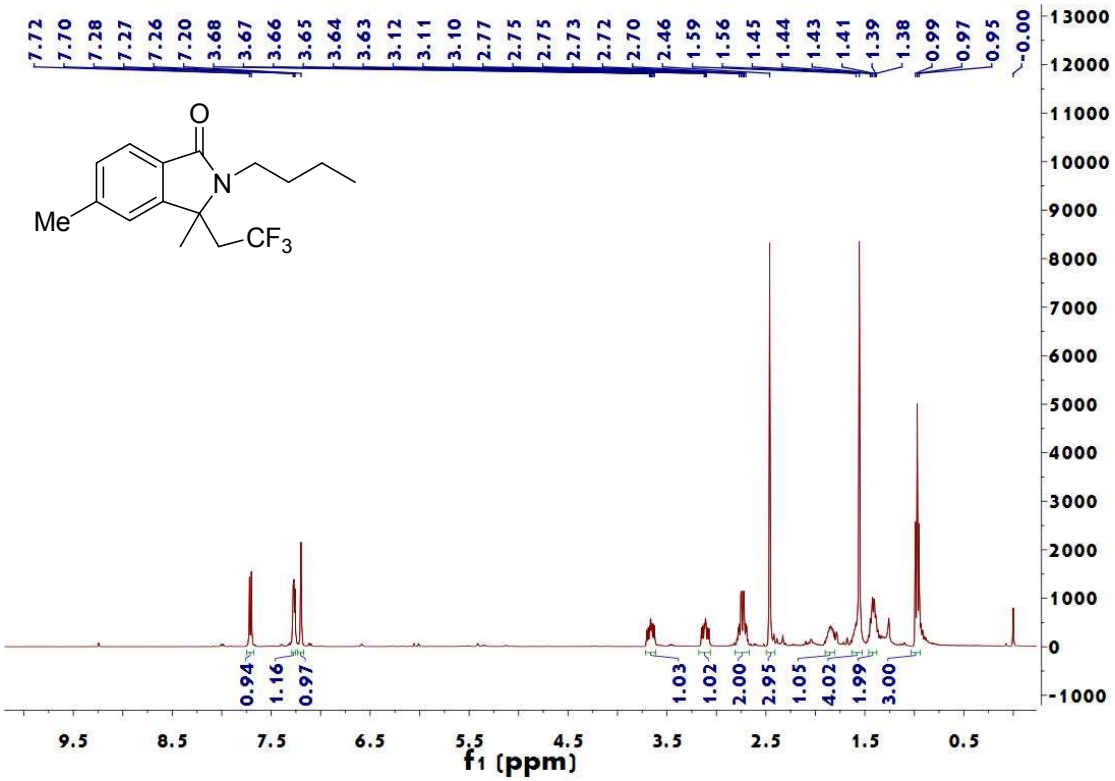
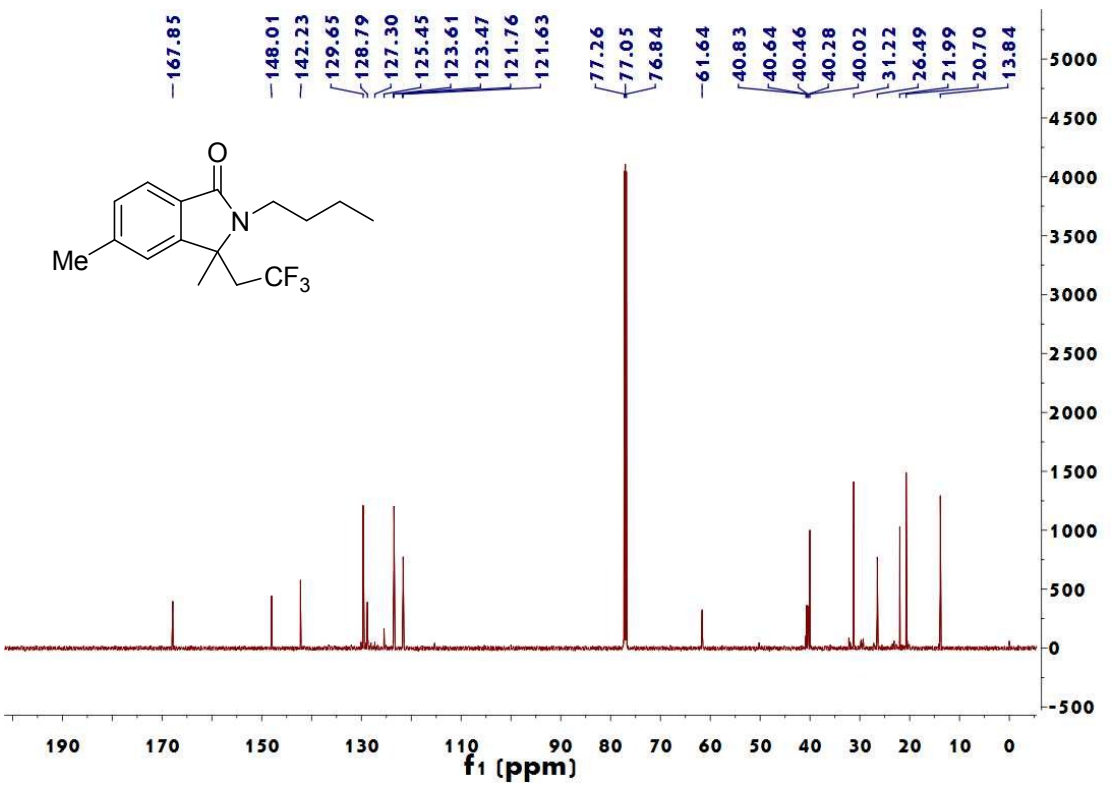
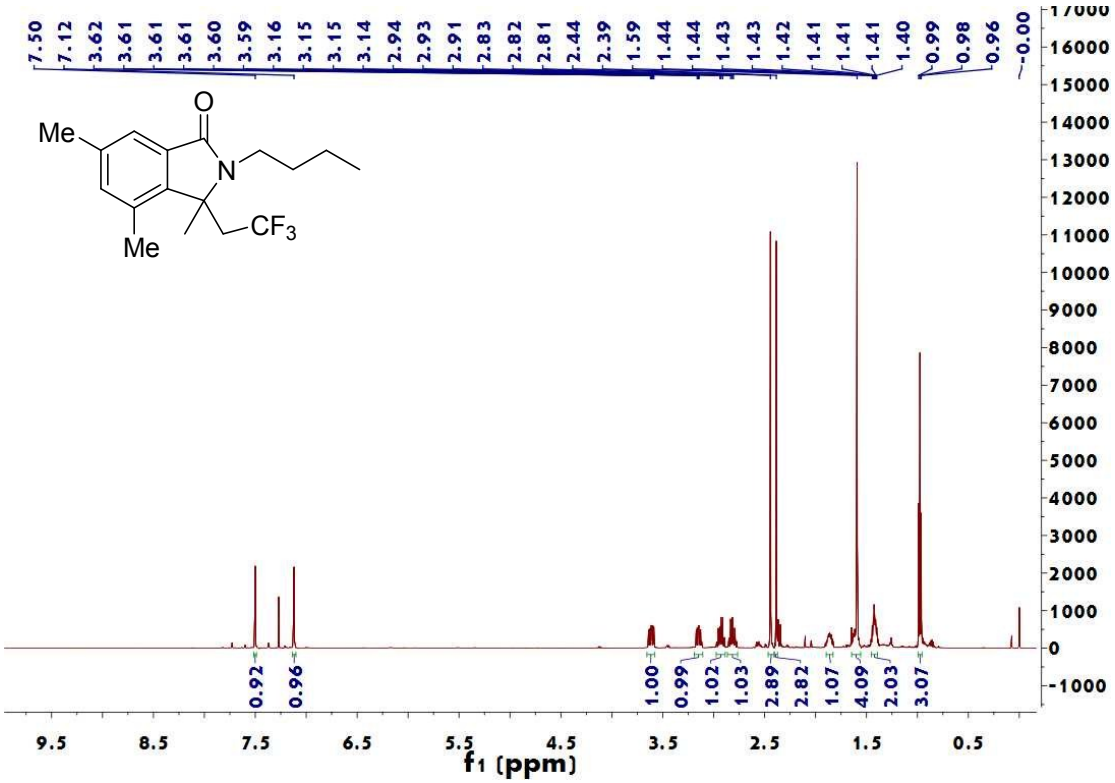


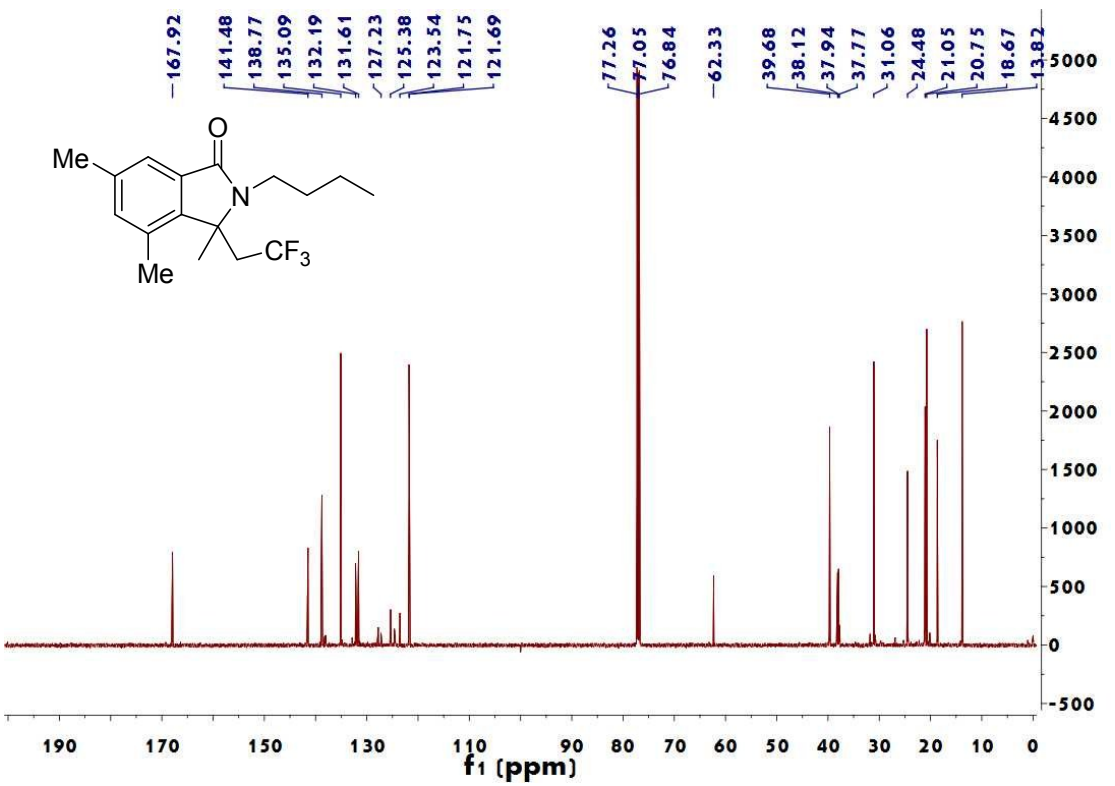
2d.^{13}C NMR



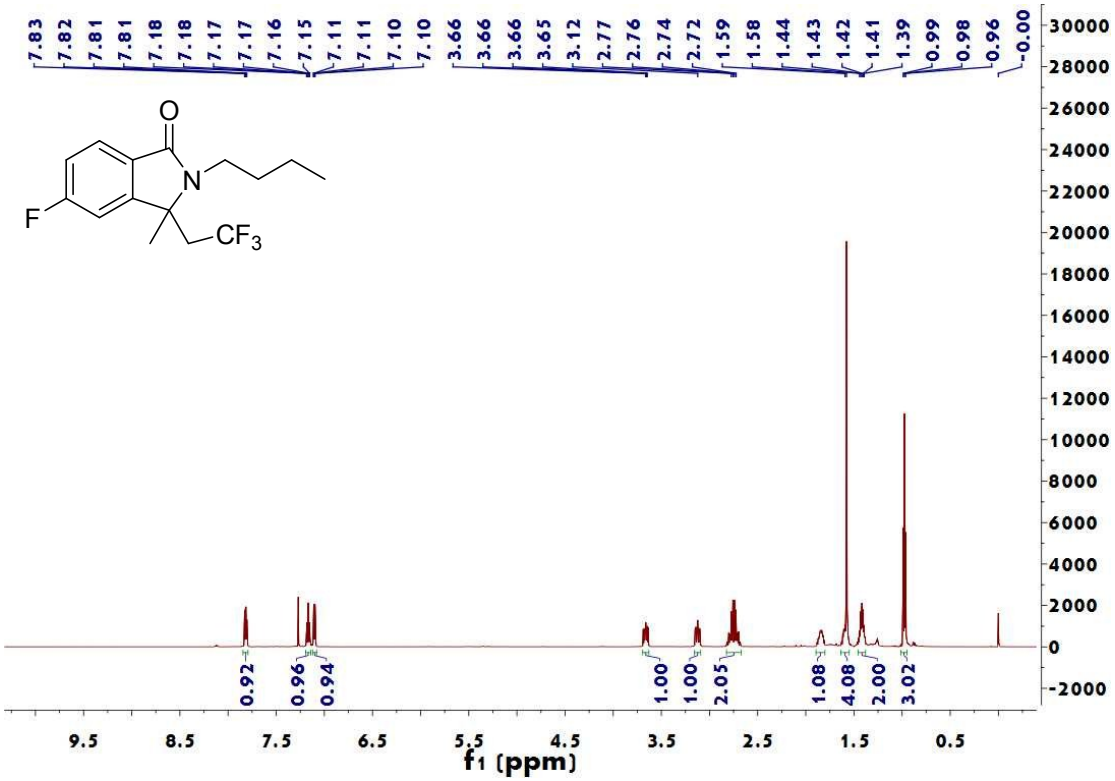
2e. ^{1}H NMR



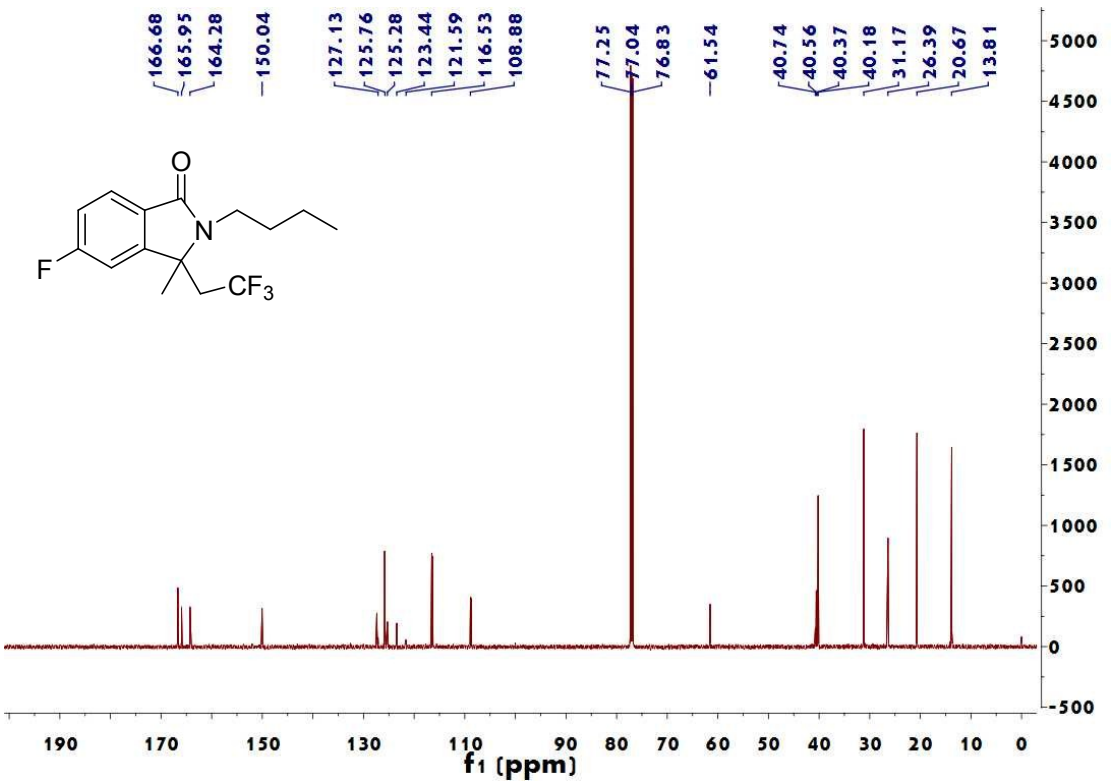
2e.^{13}C NMR



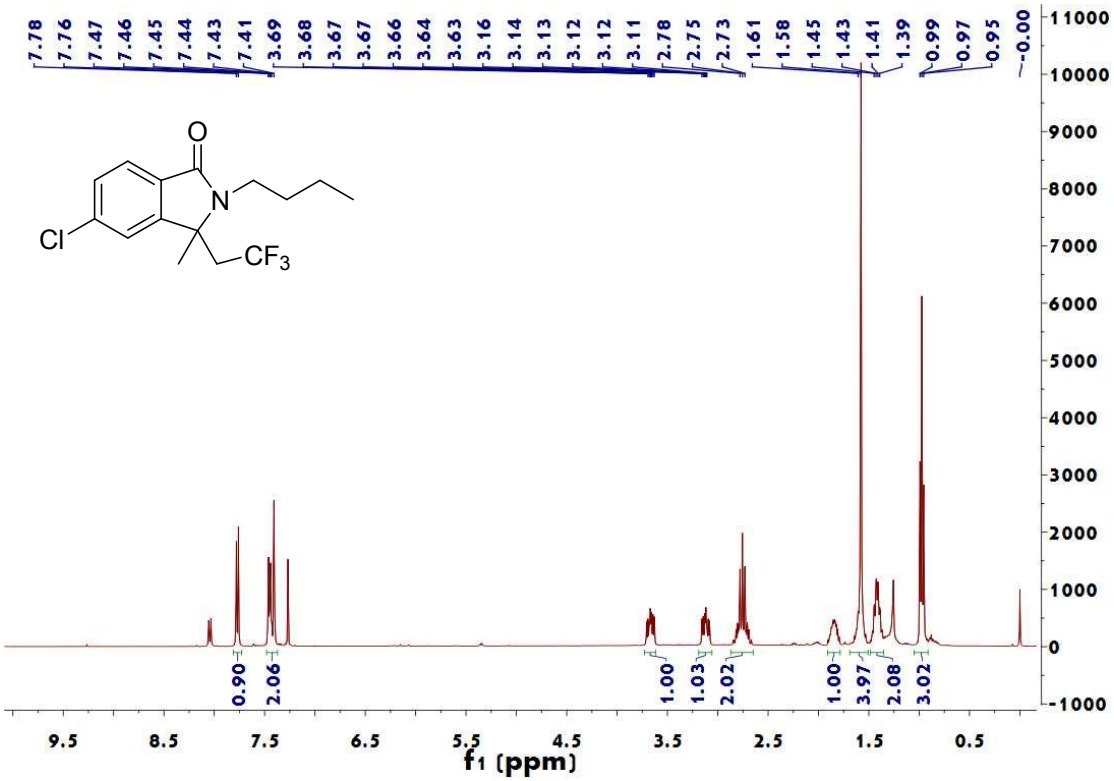
2f. ^{1}H NMR



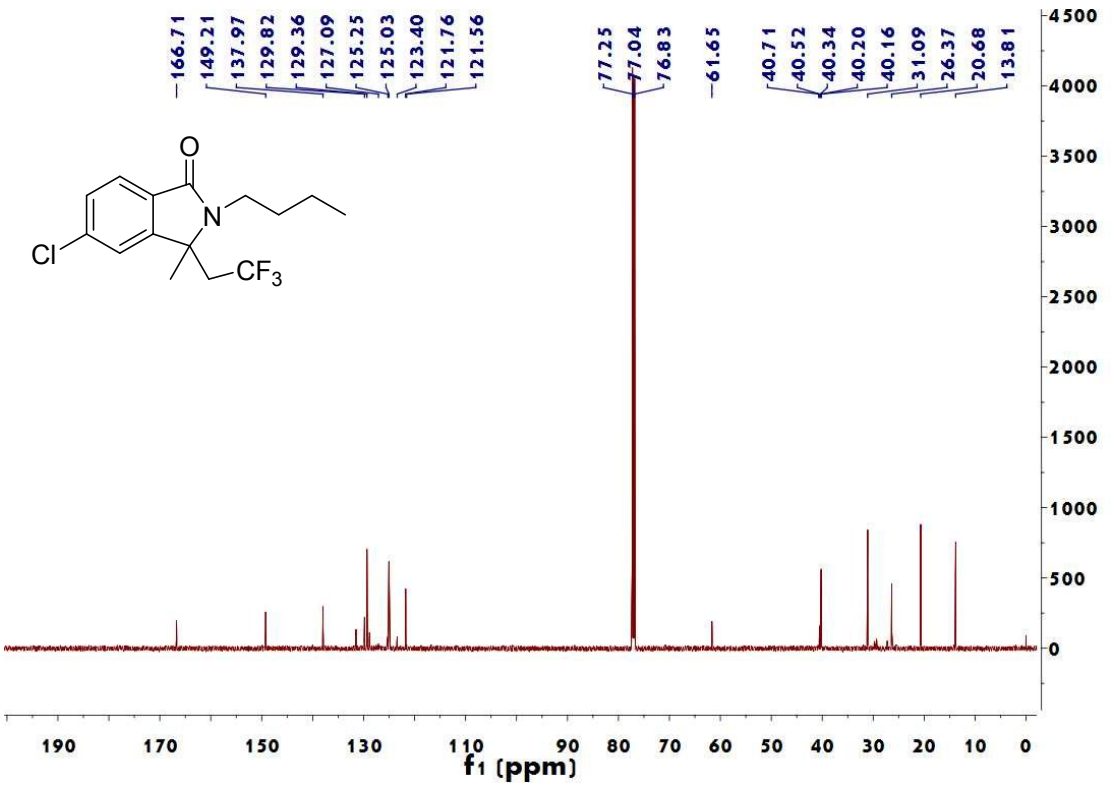
2f.^{13}C NMR



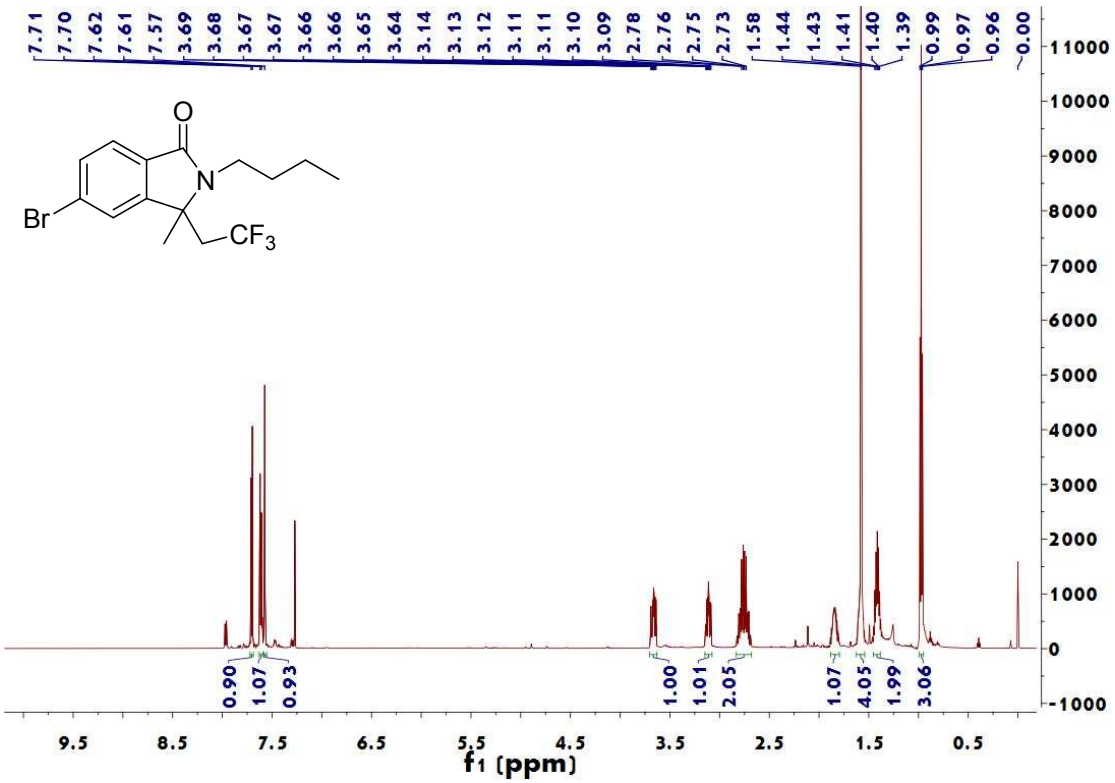
2g. ^{1}H NMR



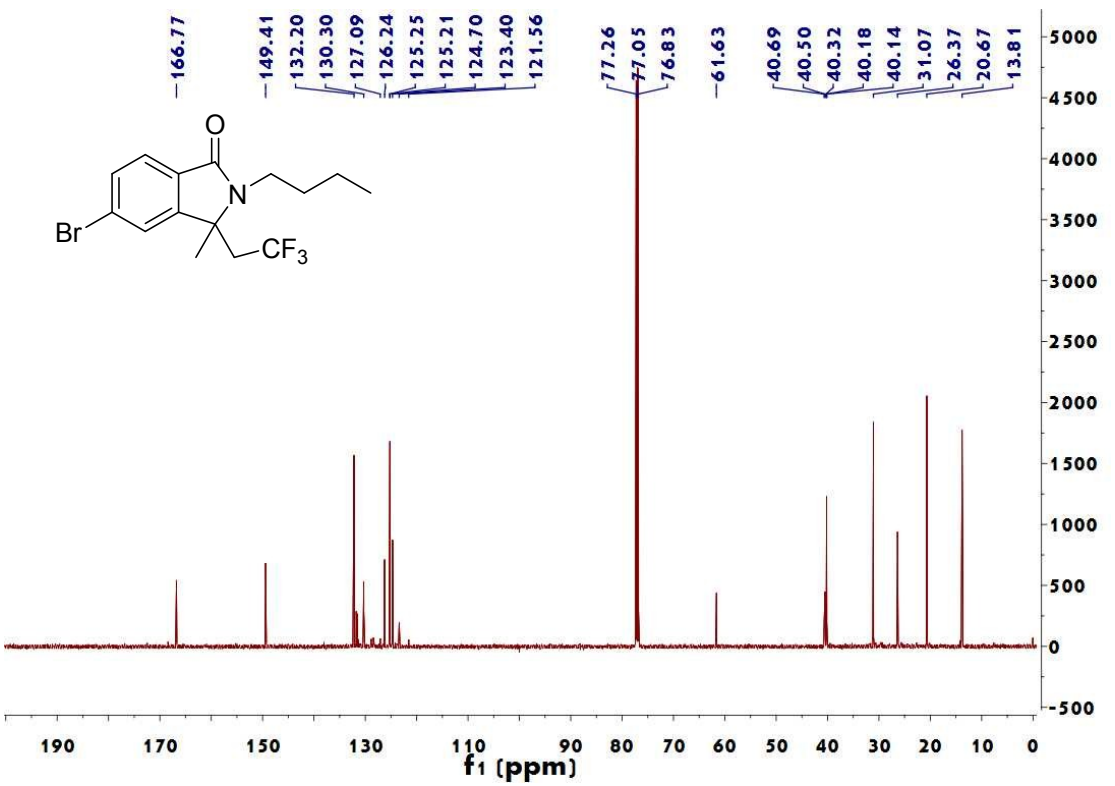
2g.^{13}C NMR



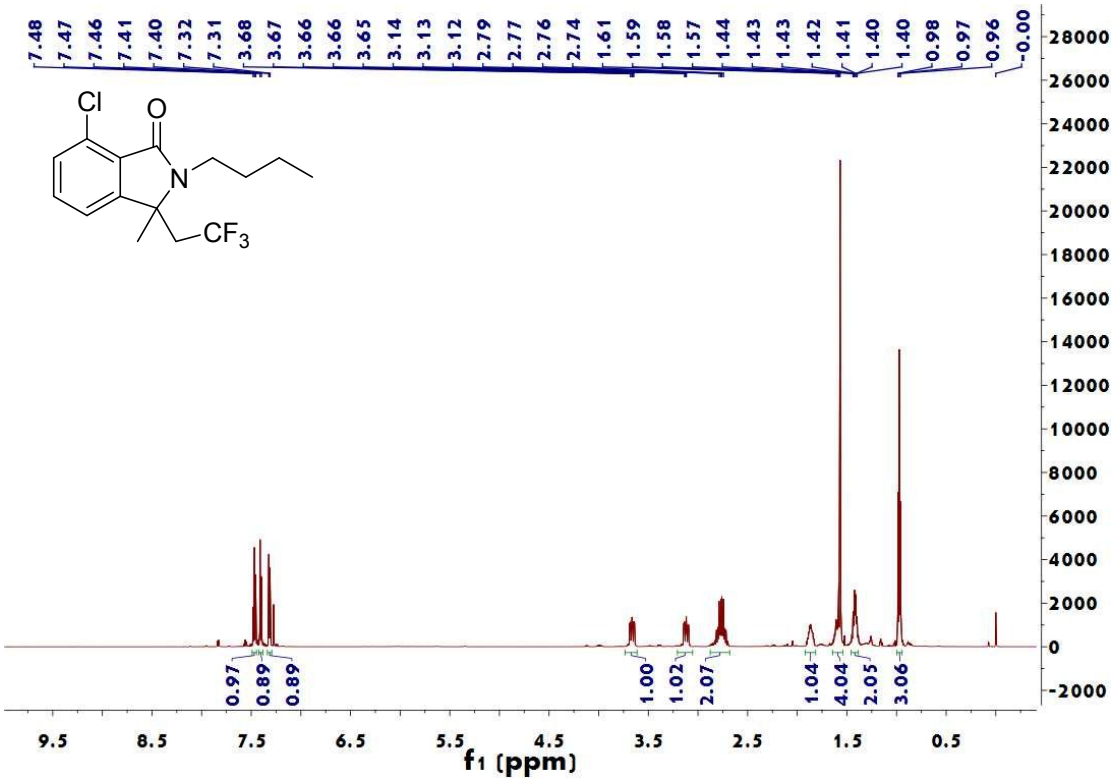
2h. ^{1}H NMR



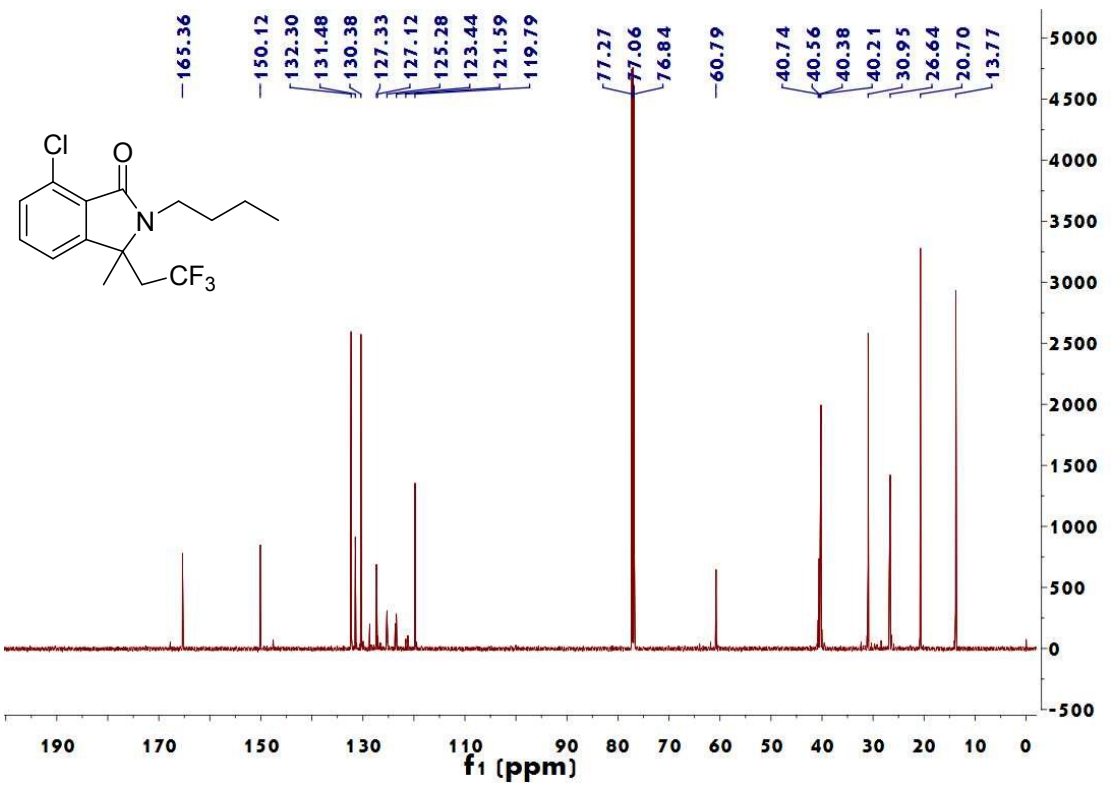
2h.^{13}C NMR



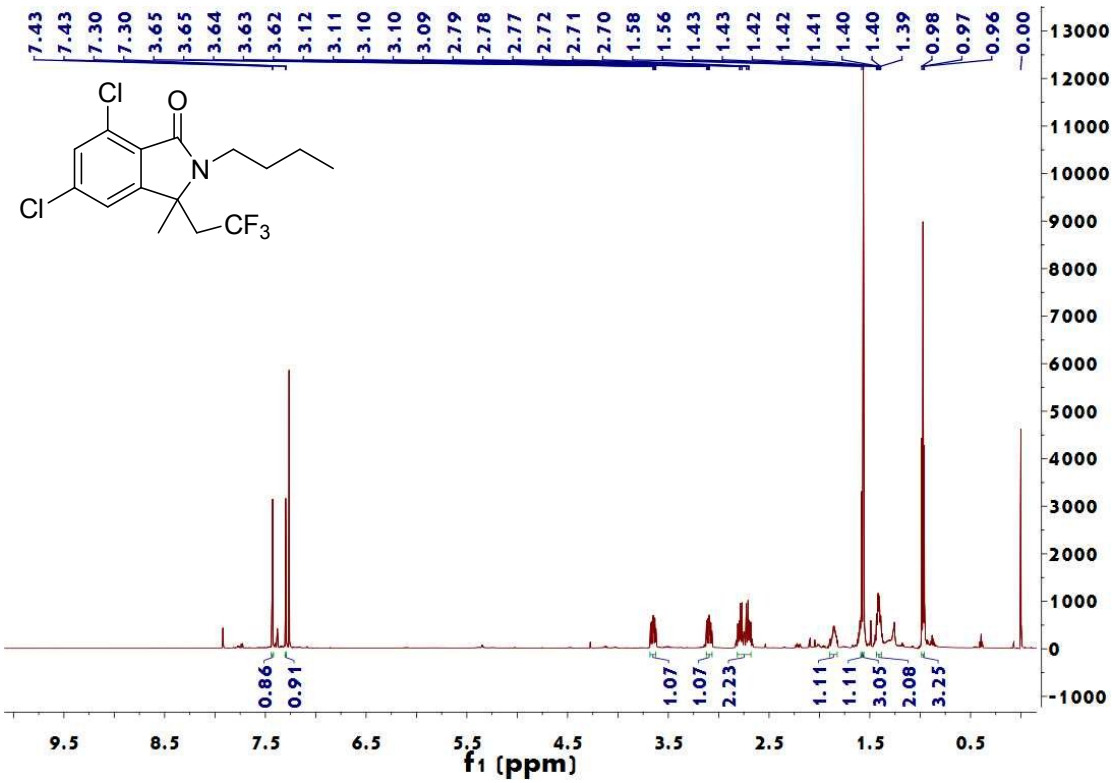
2i. ^{1}H NMR



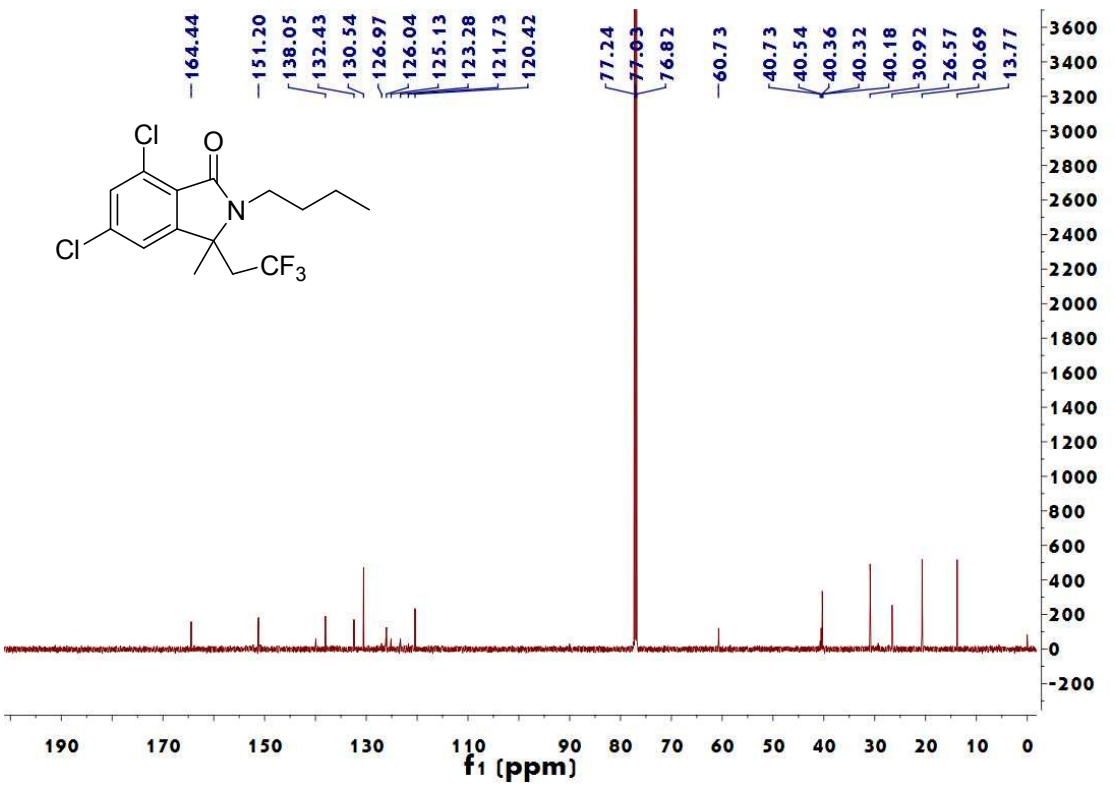
2i.^{13}C NMR



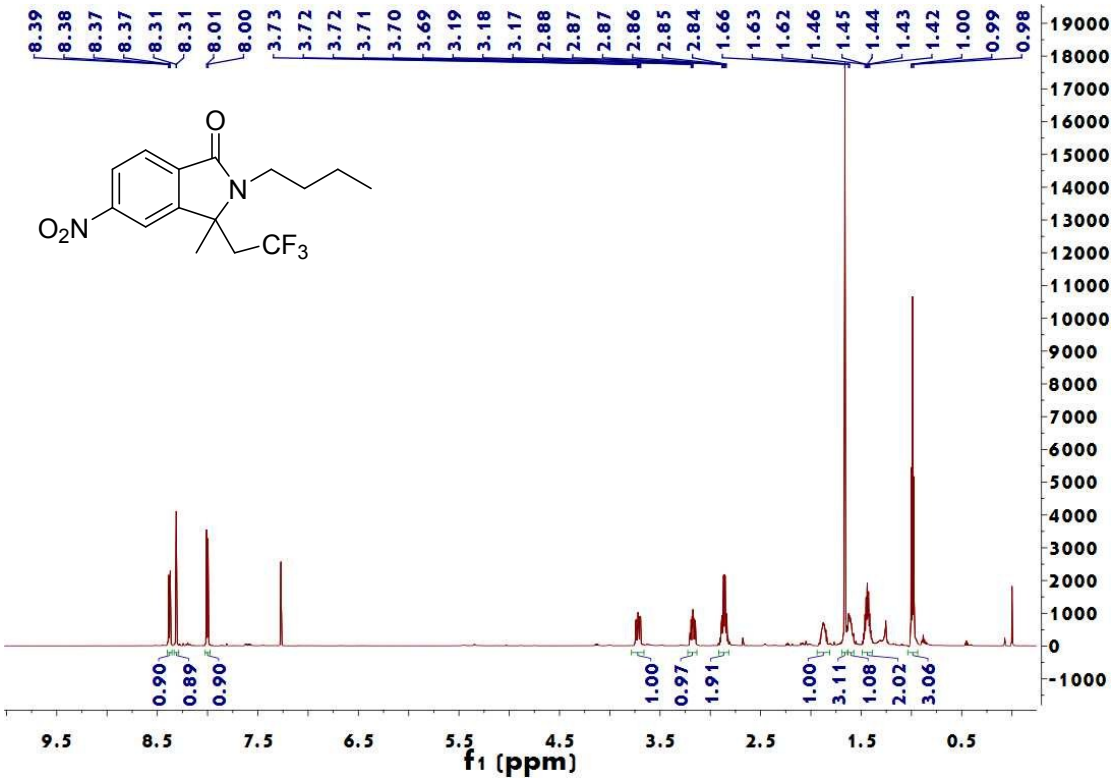
2j. ^{1}H NMR



2j.^{13}C NMR



2k. ^{1}H NMR



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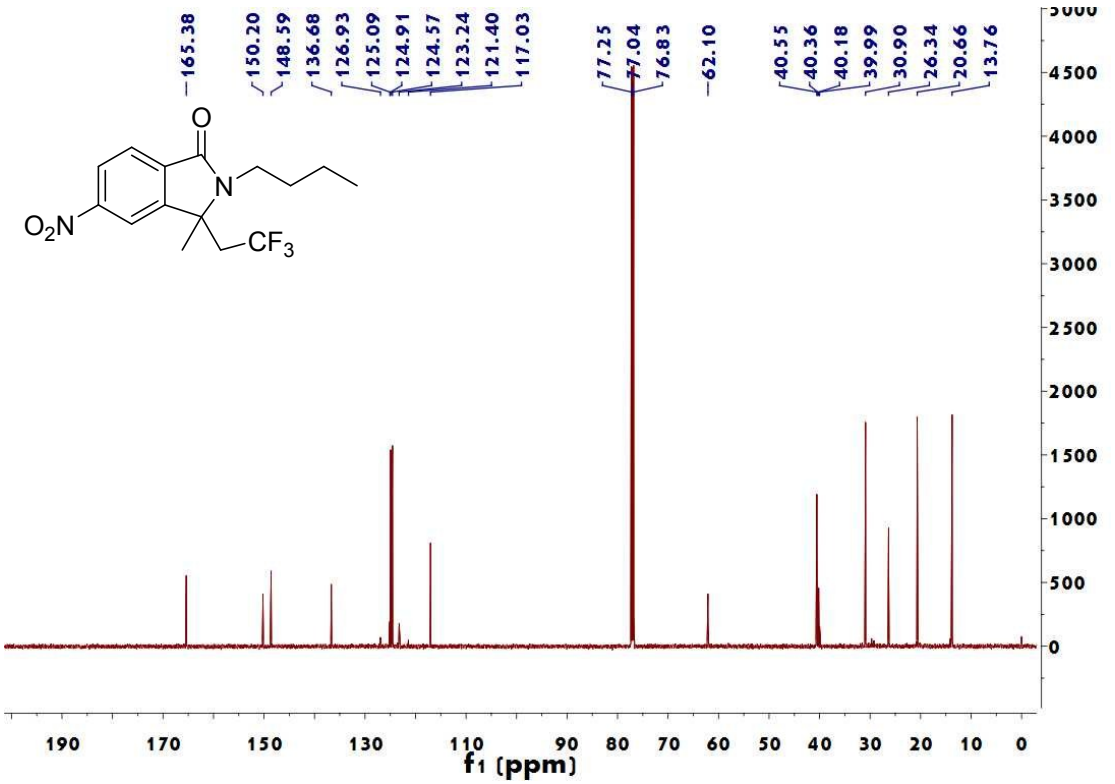
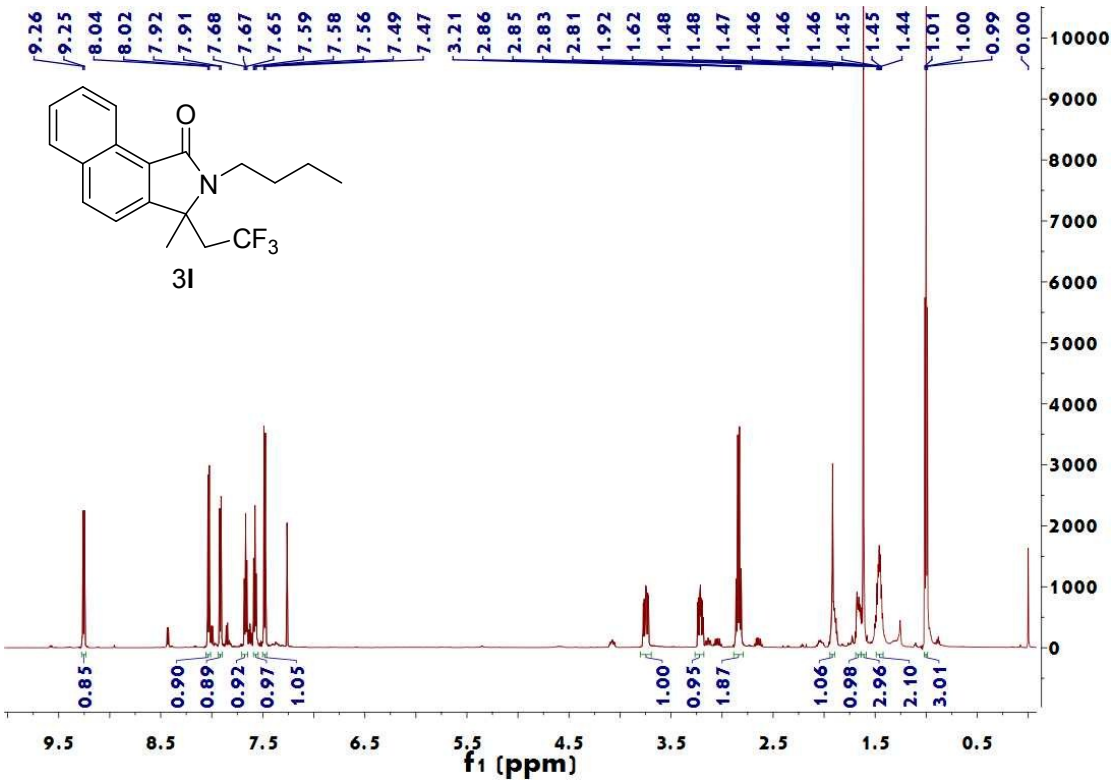
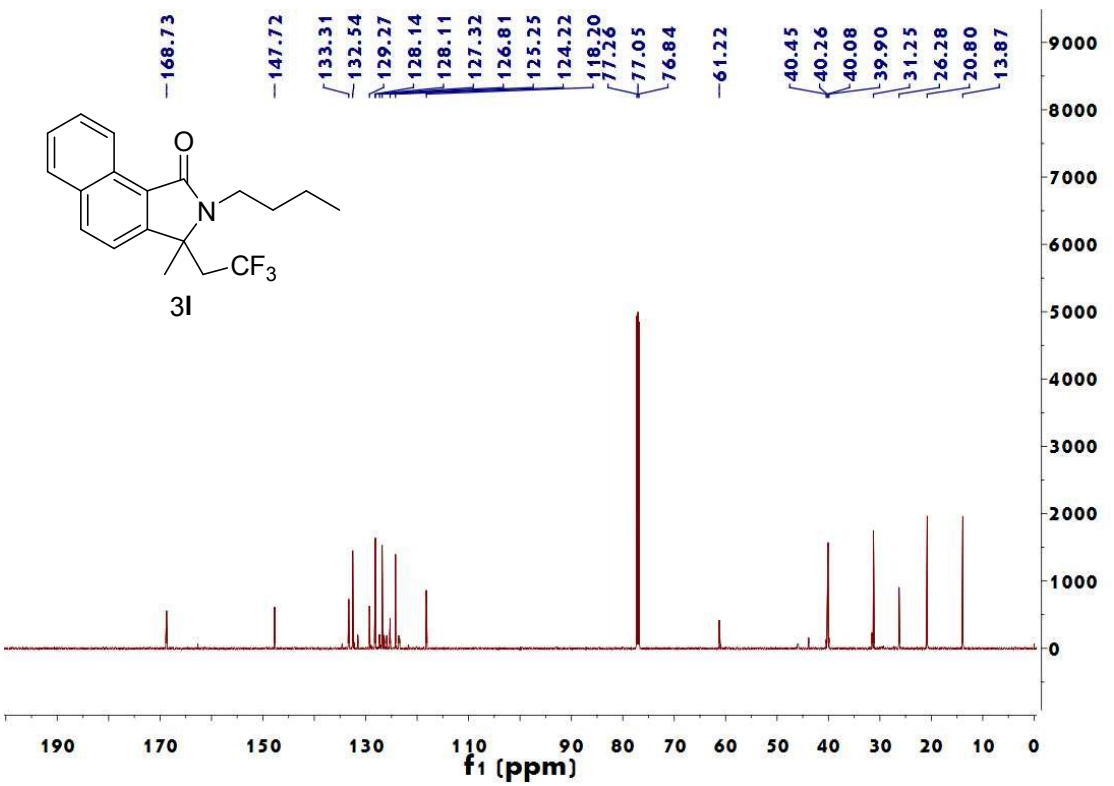


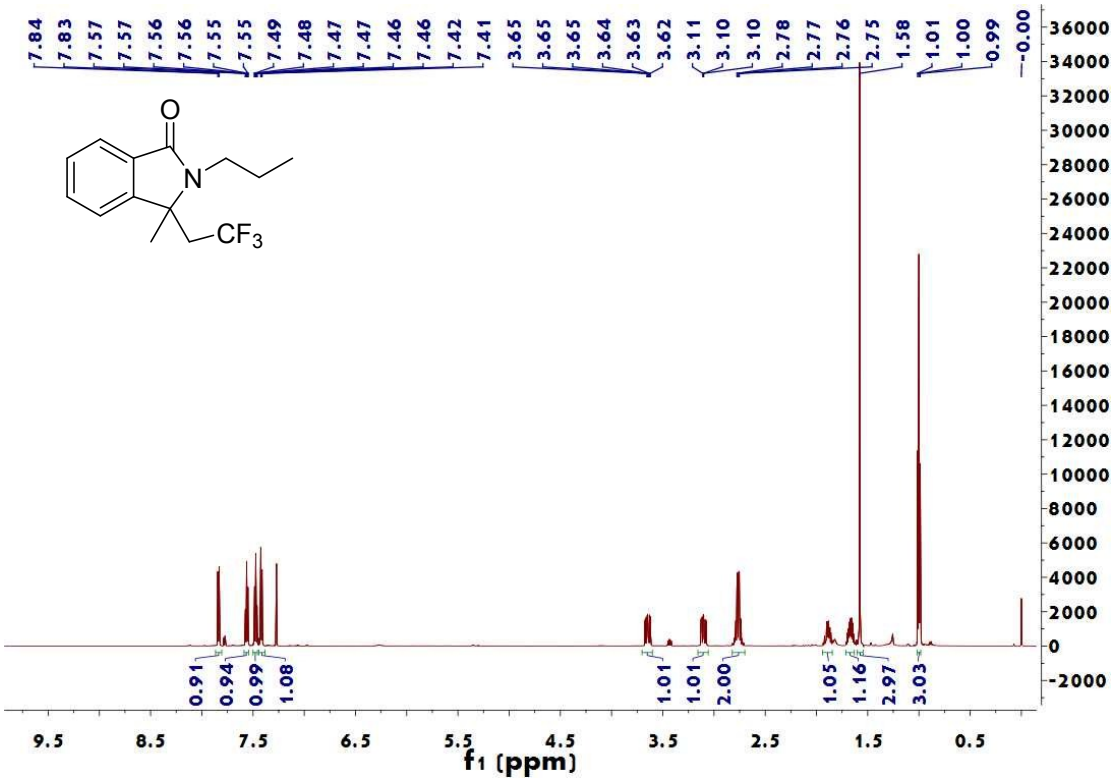
2l. ^{1}H NMR



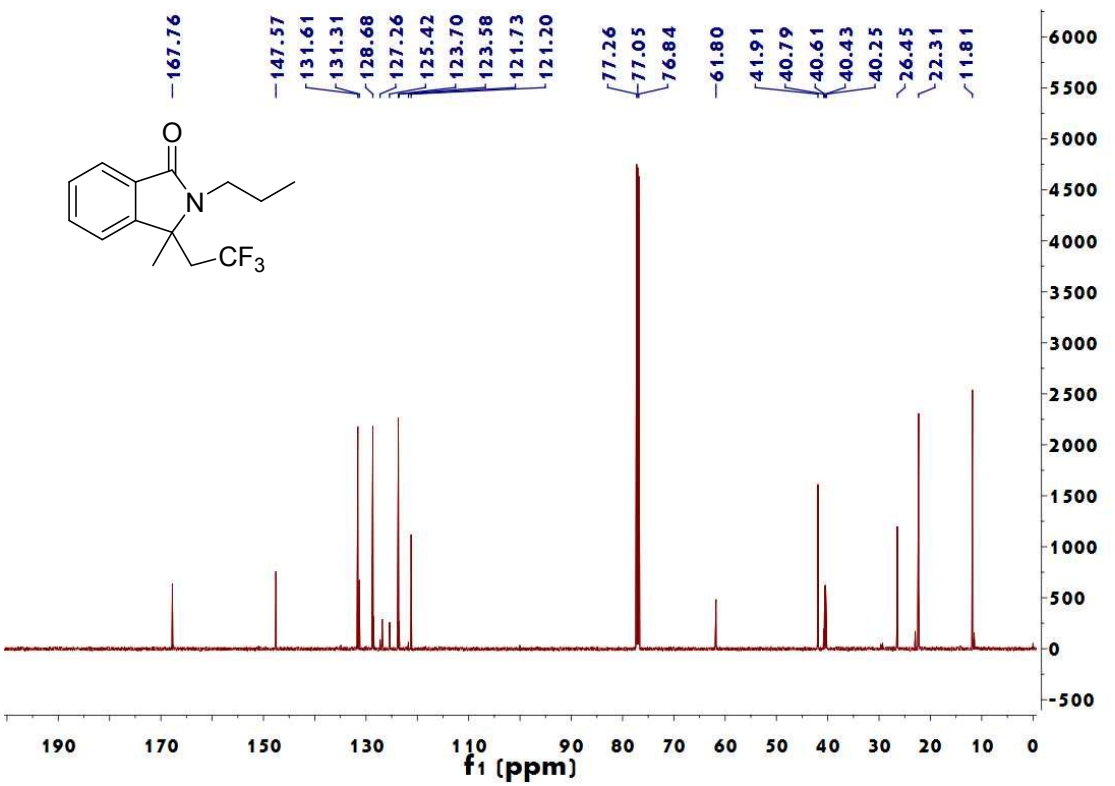
2l. ^{13}C NMR



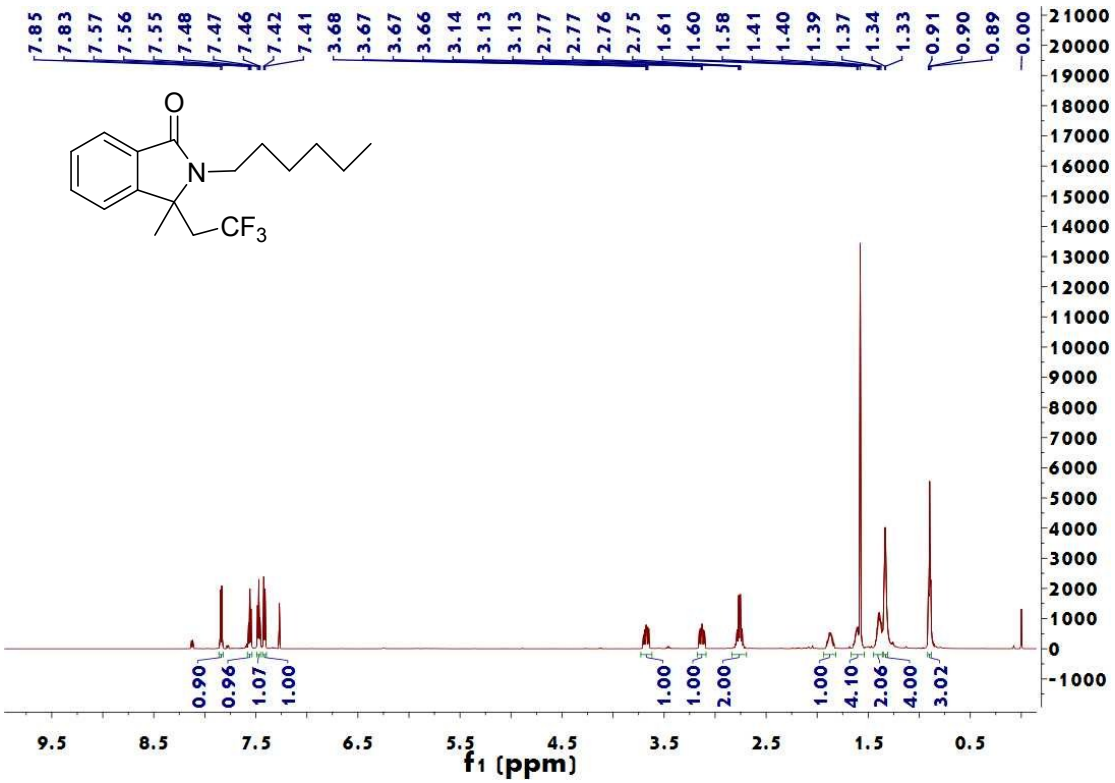
2m. ^{1}H NMR



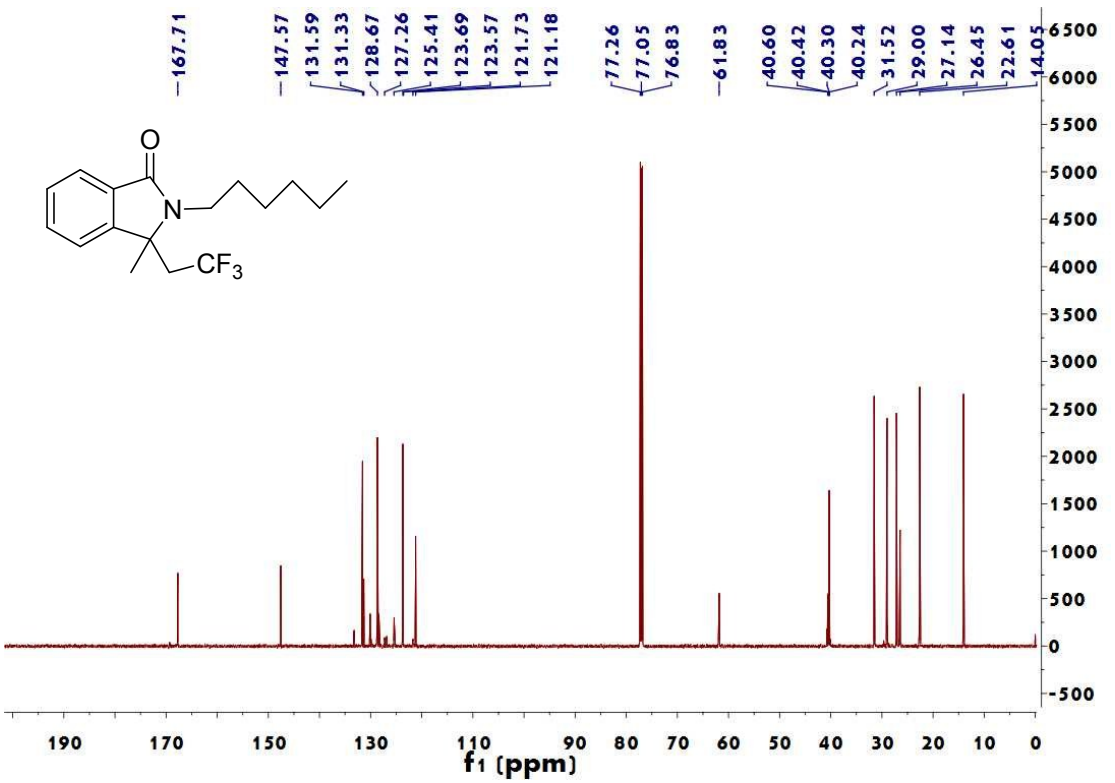
2m.^{13}C NMR



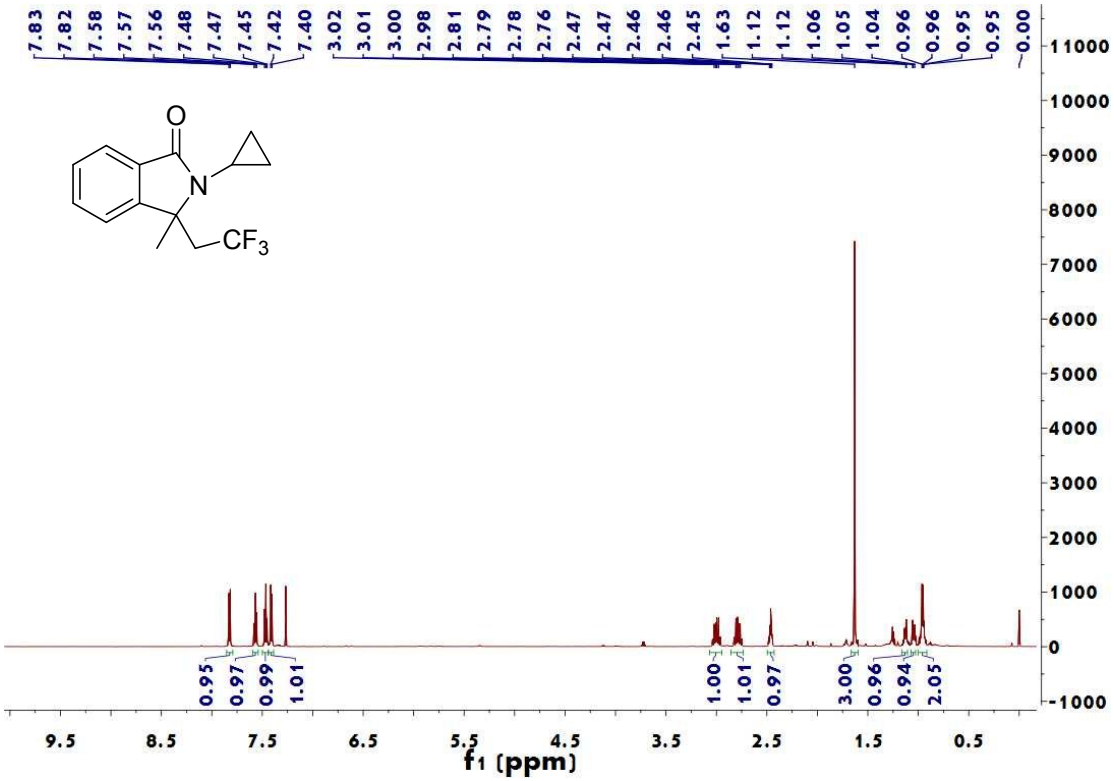
2n. ^{1}H NMR



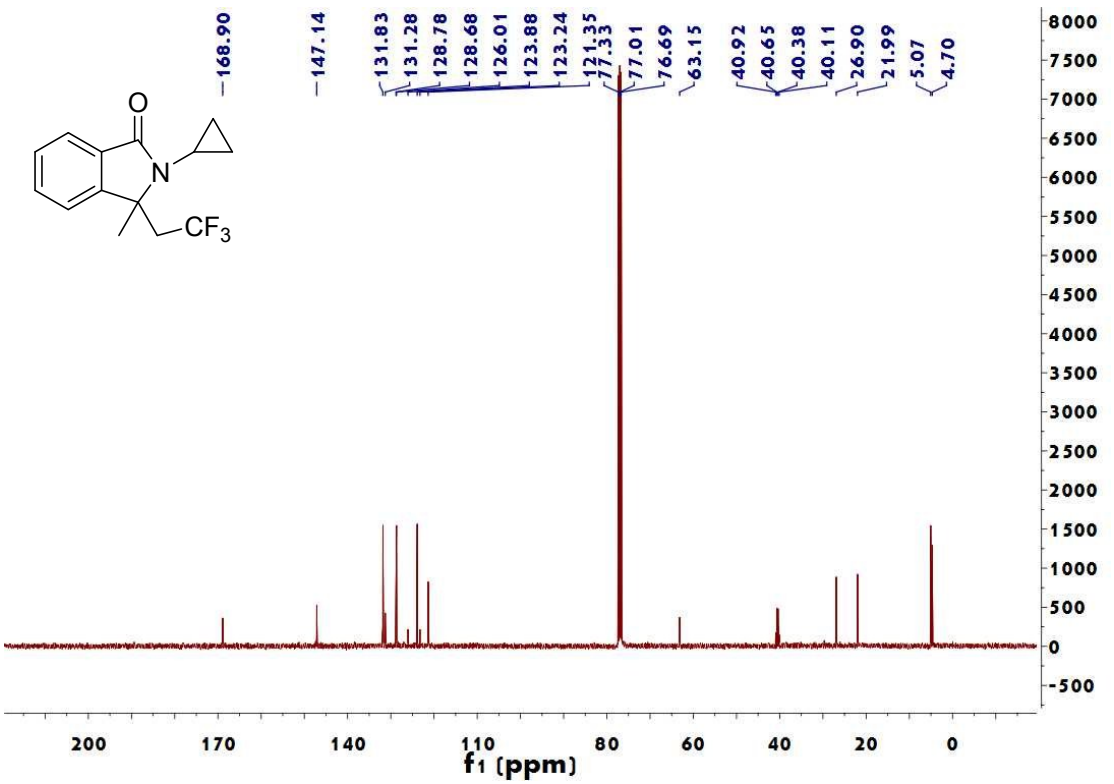
2n.^{13}C NMR



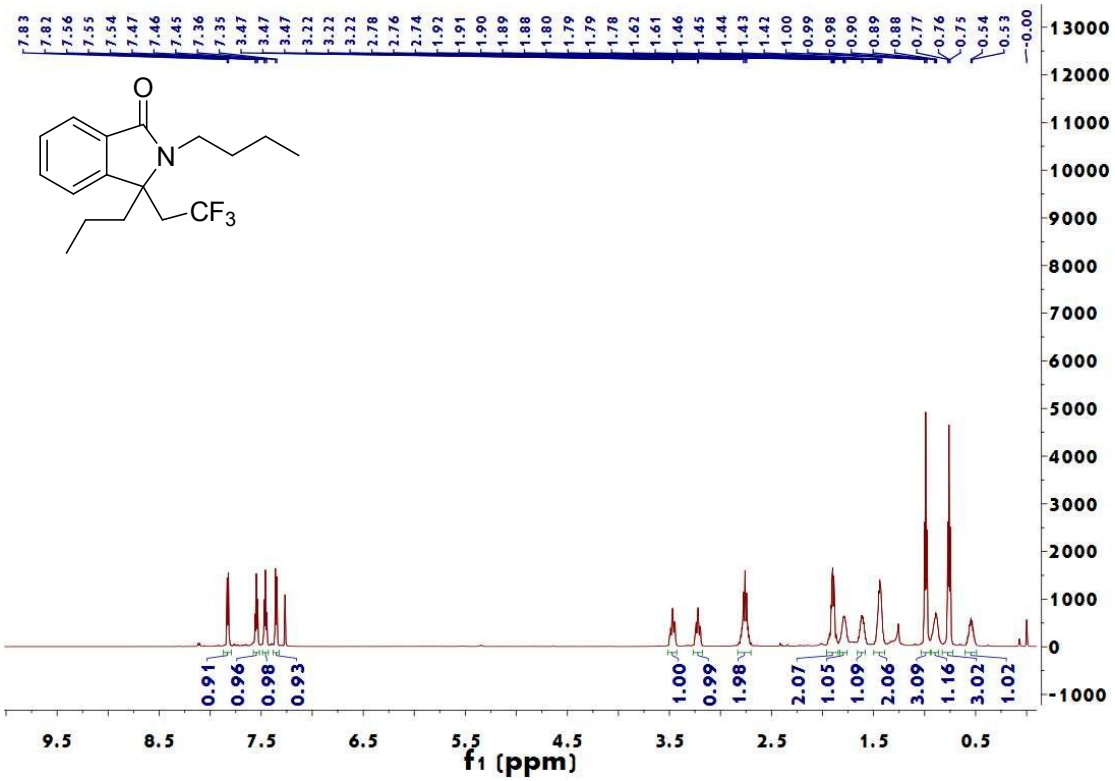
2o. ^{1}H NMR



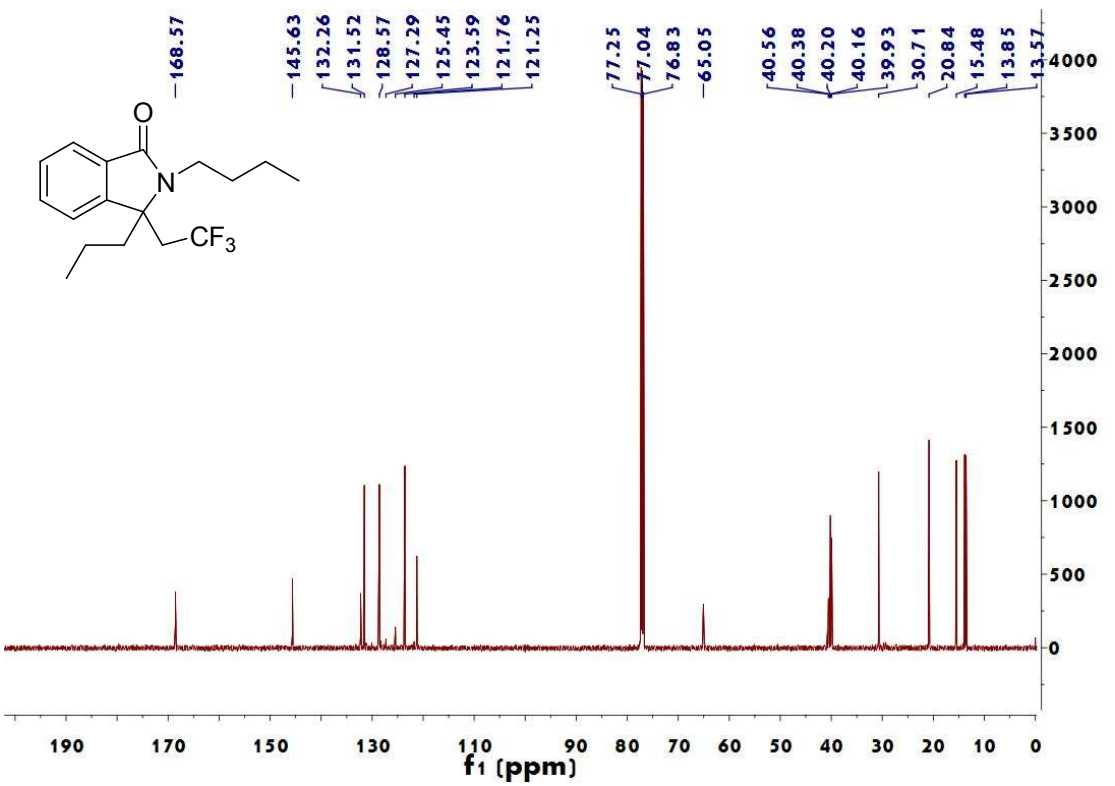
2o.^{13}C NMR



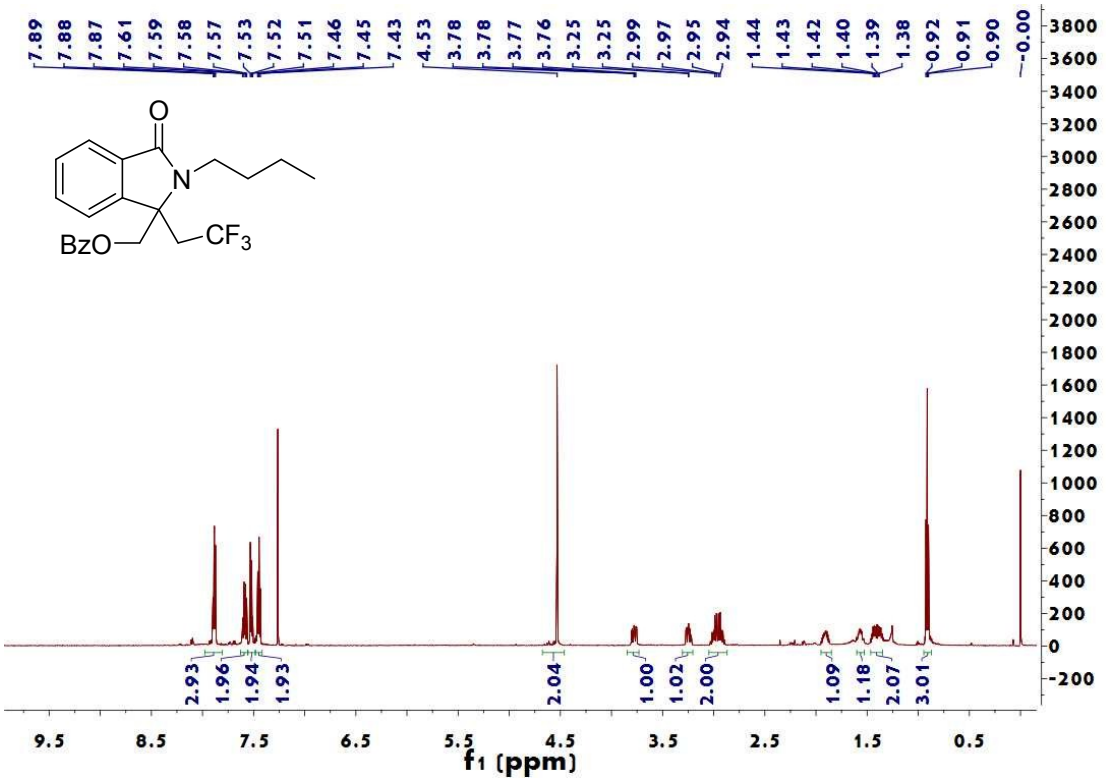
2p. ^{1}H NMR



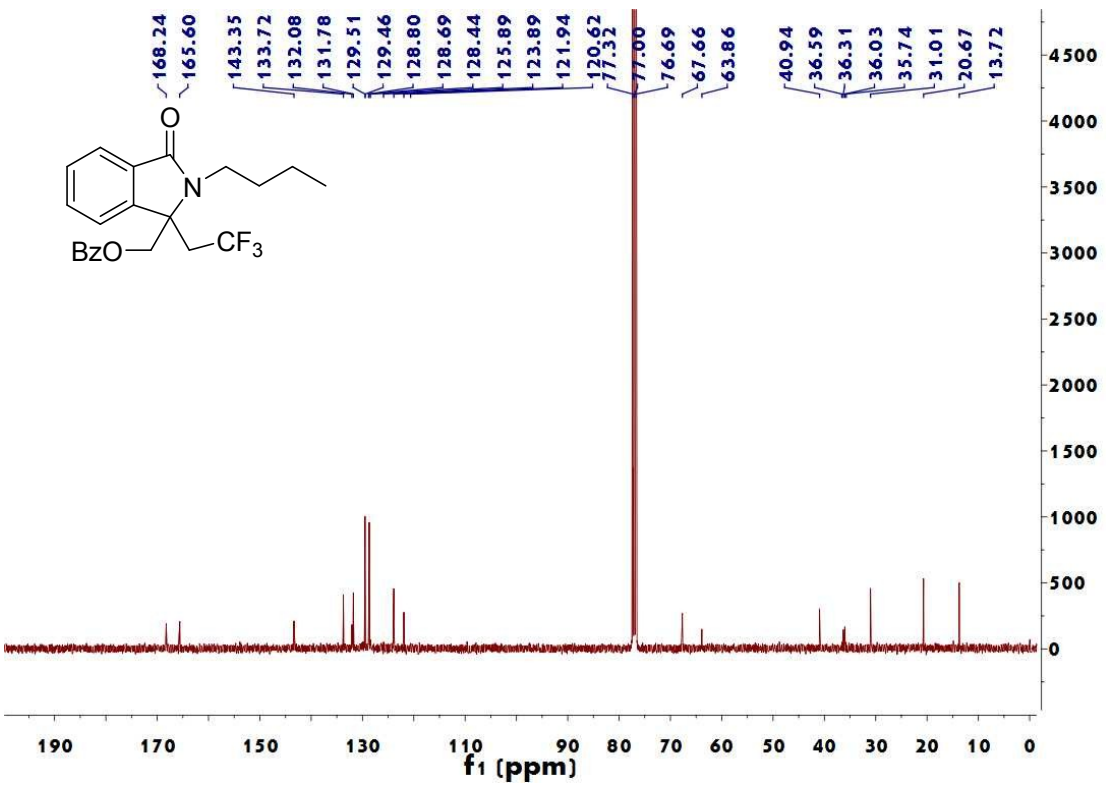
2p.^{13}C NMR



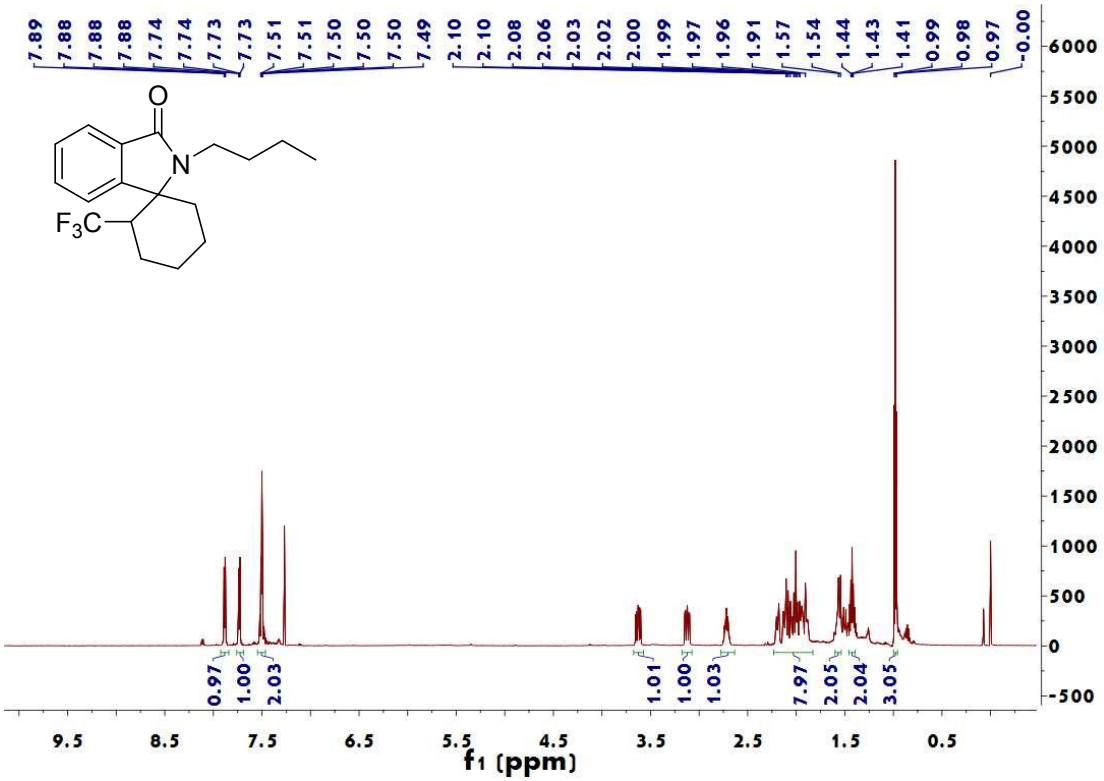
2q. ^{1}H NMR



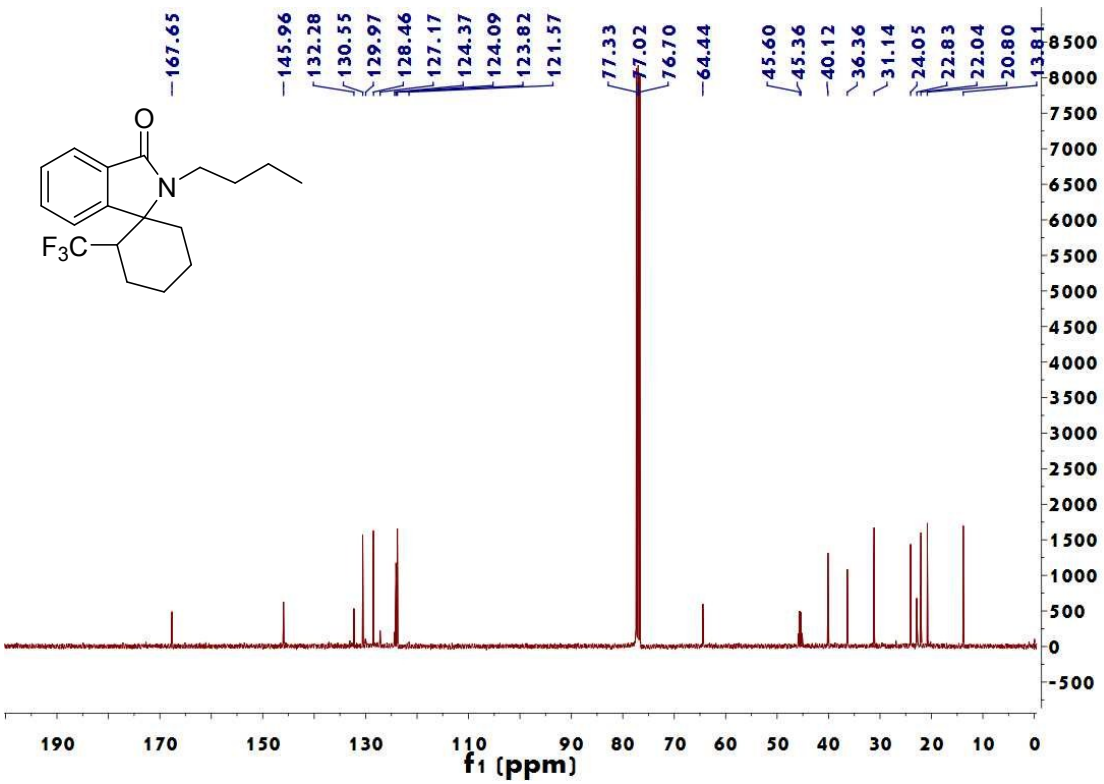
2q.^{13}C NMR



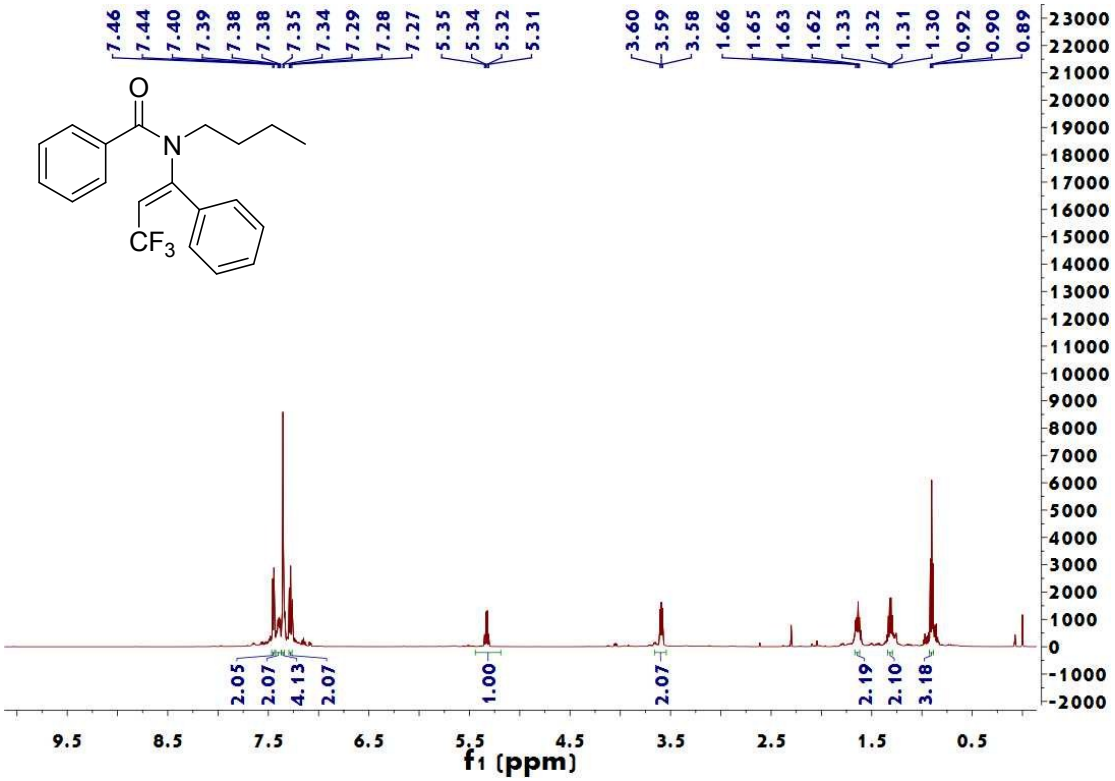
2r. ^{1}H NMR



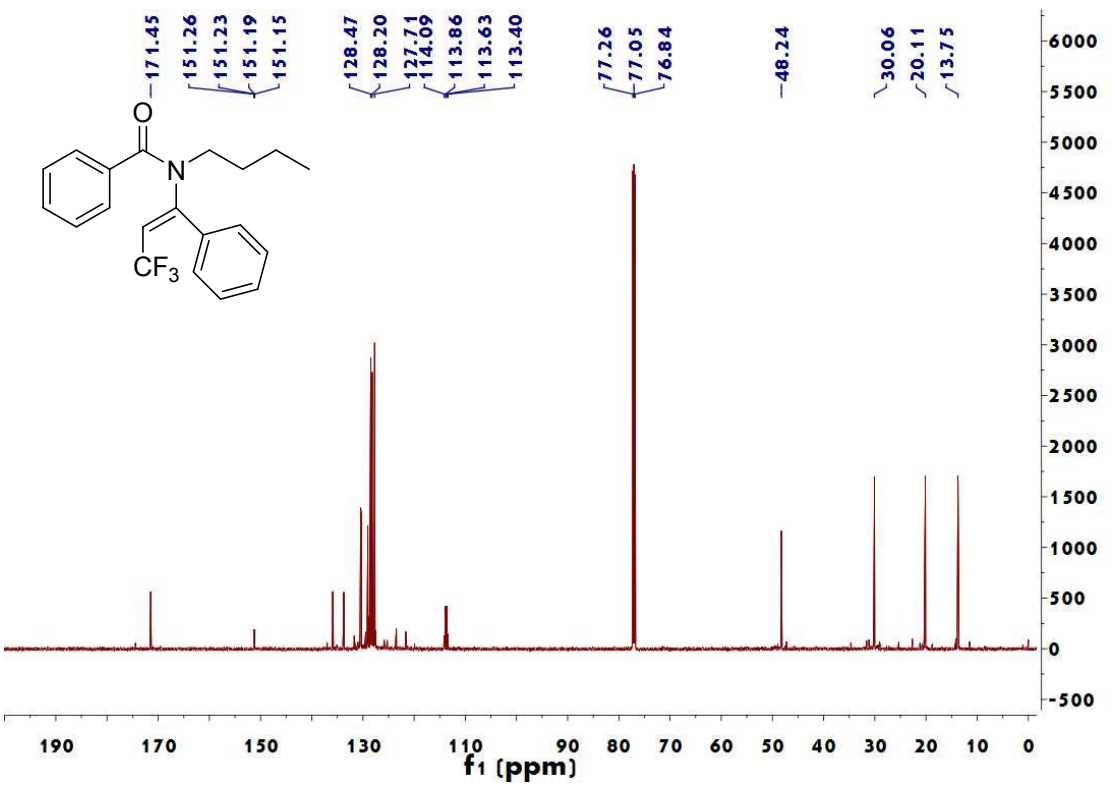
2r.^{13}C NMR



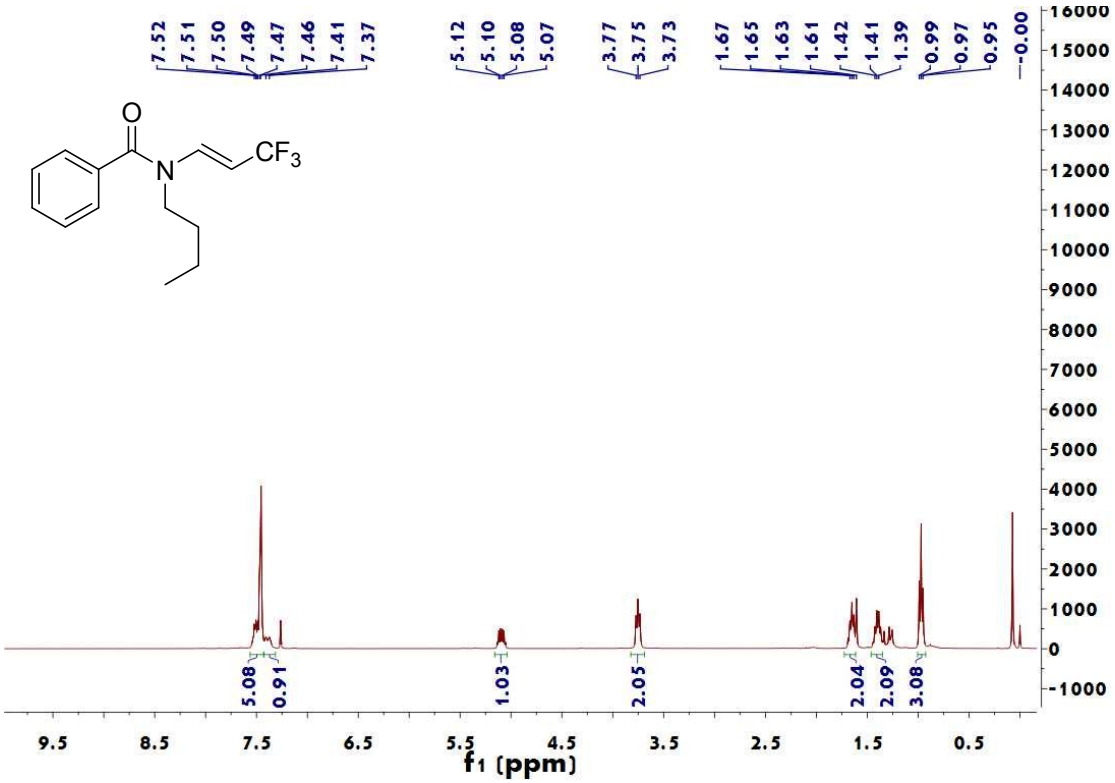
2s. ^{1}H NMR



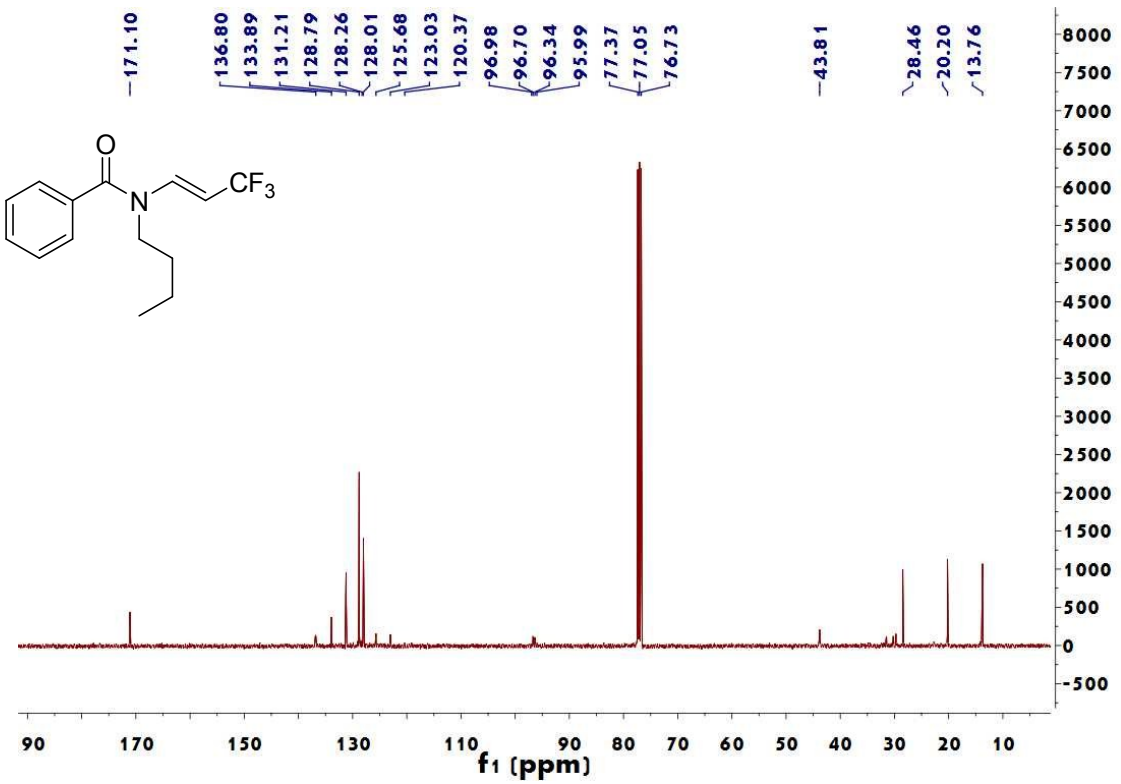
2s.^{13}C NMR



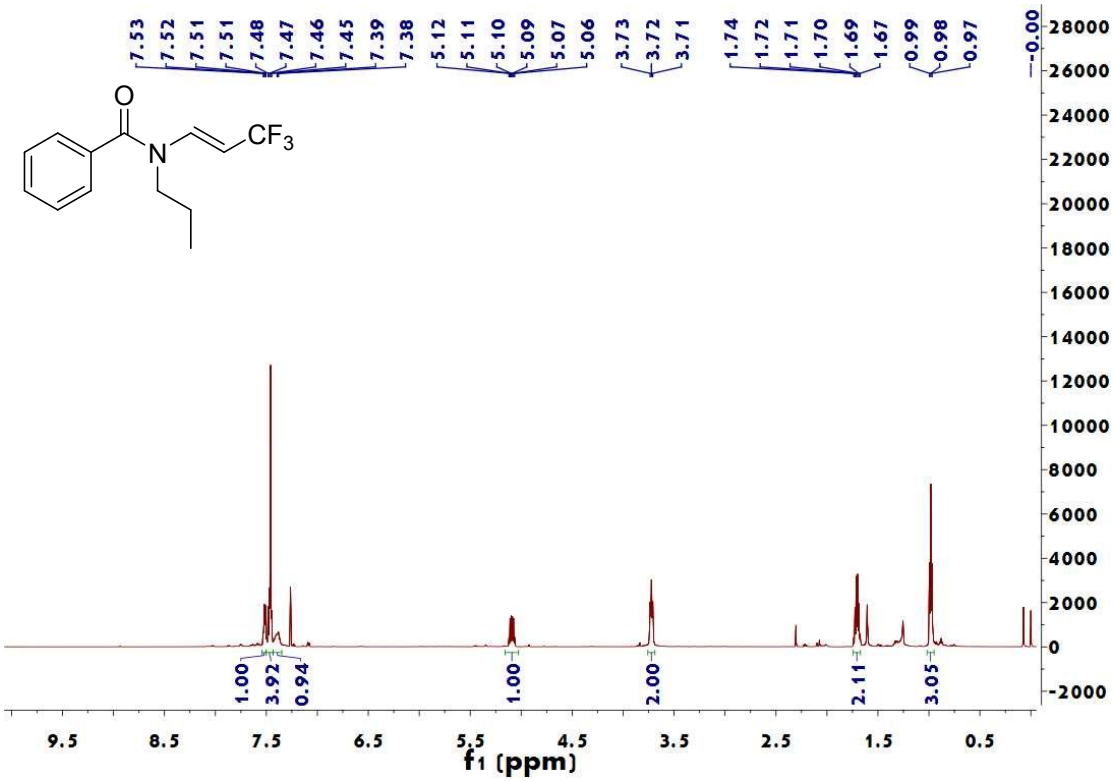
4a′. ^{1}H NMR



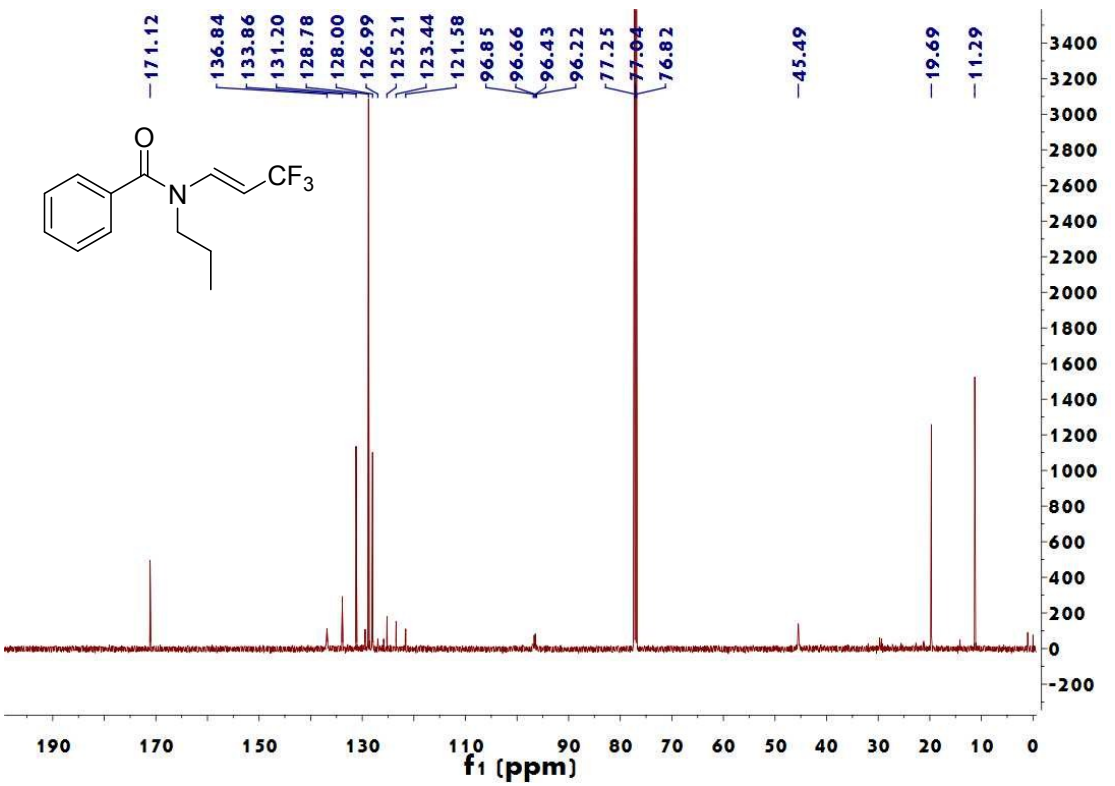
4a′.^{13}C NMR



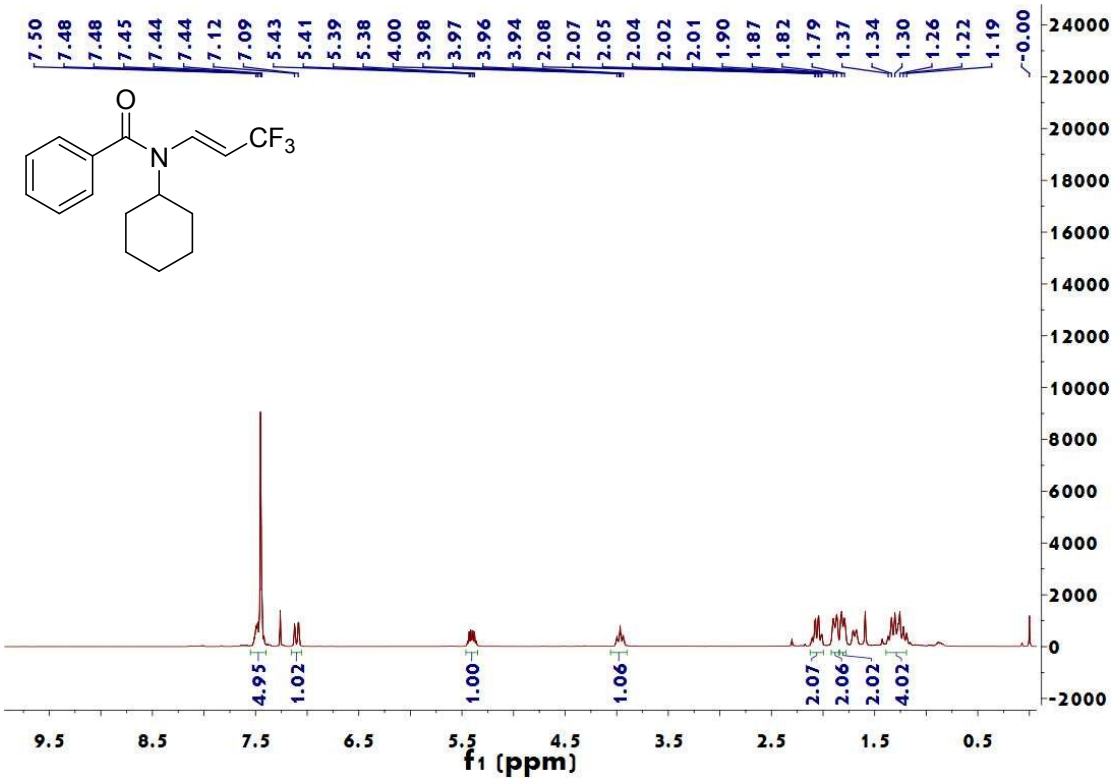
4b′. ^{1}H NMR



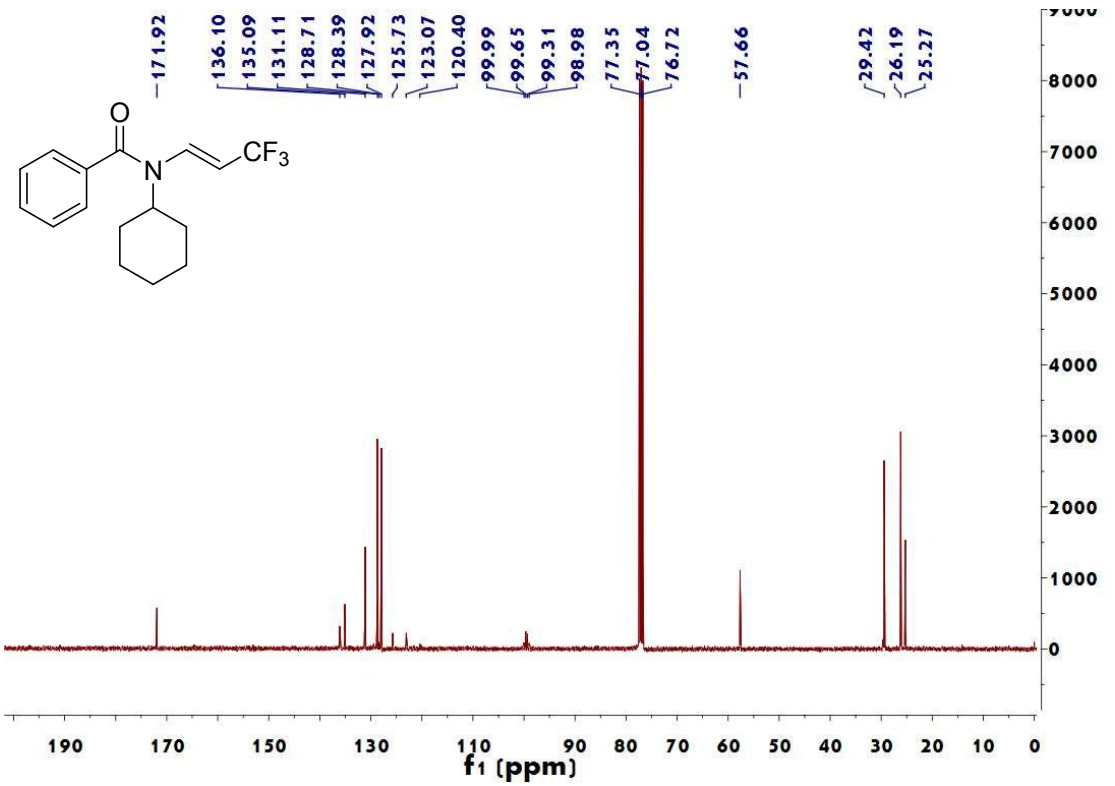
4b′.^{13}C NMR



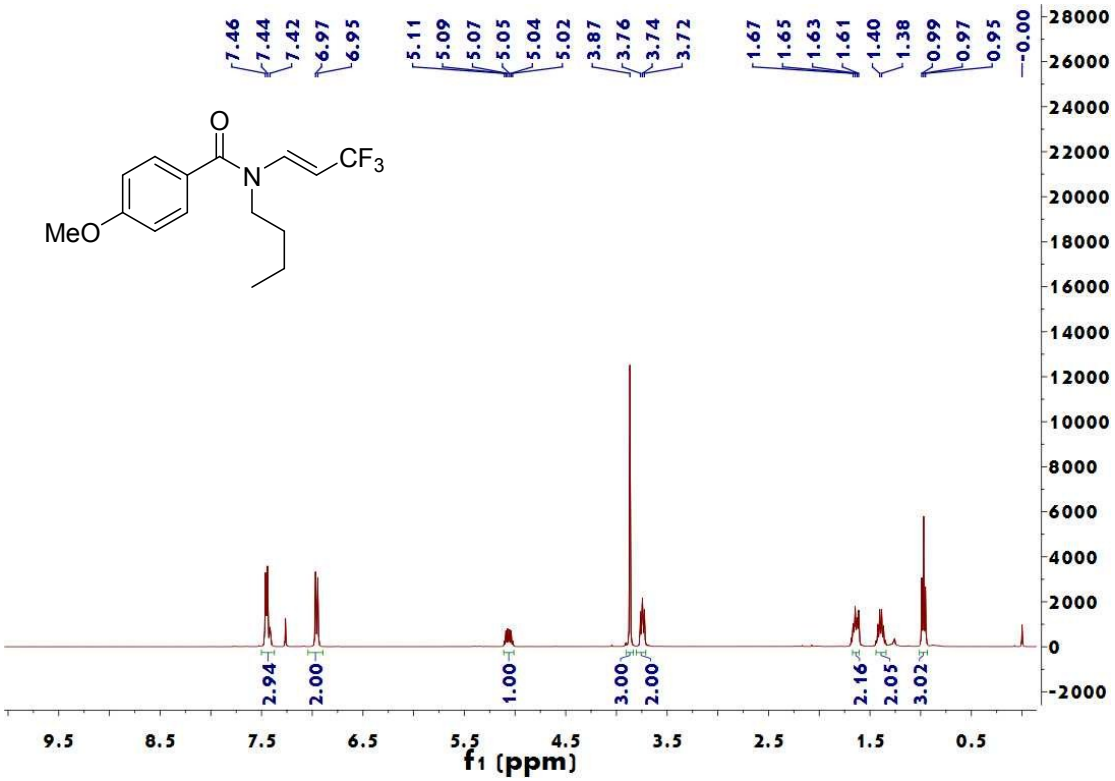
4c′. ^{1}H NMR



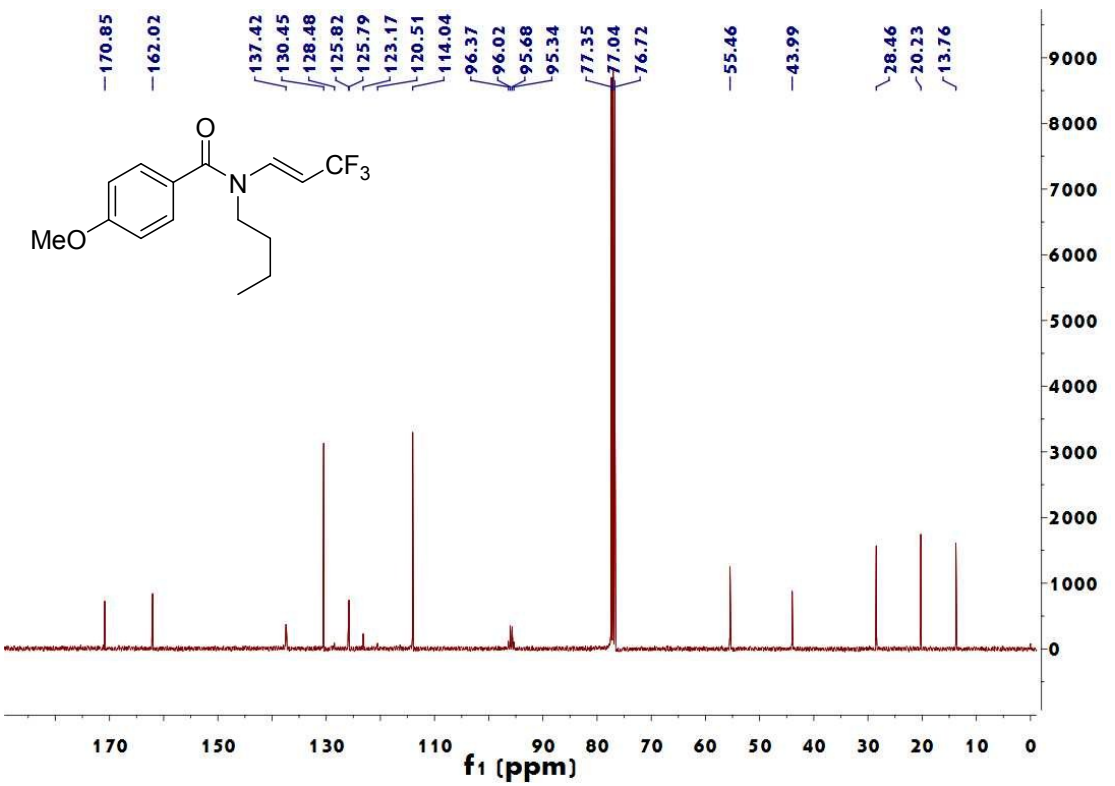
4c′.^{13}C NMR



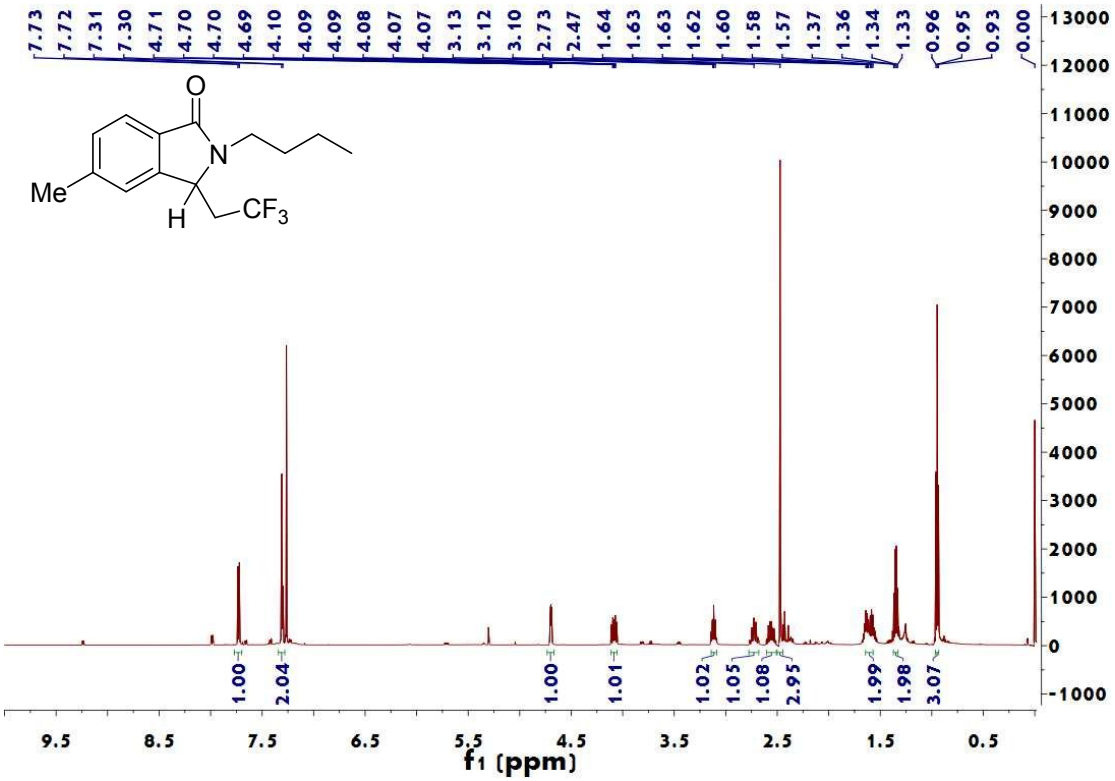
4d′. ^{1}H NMR



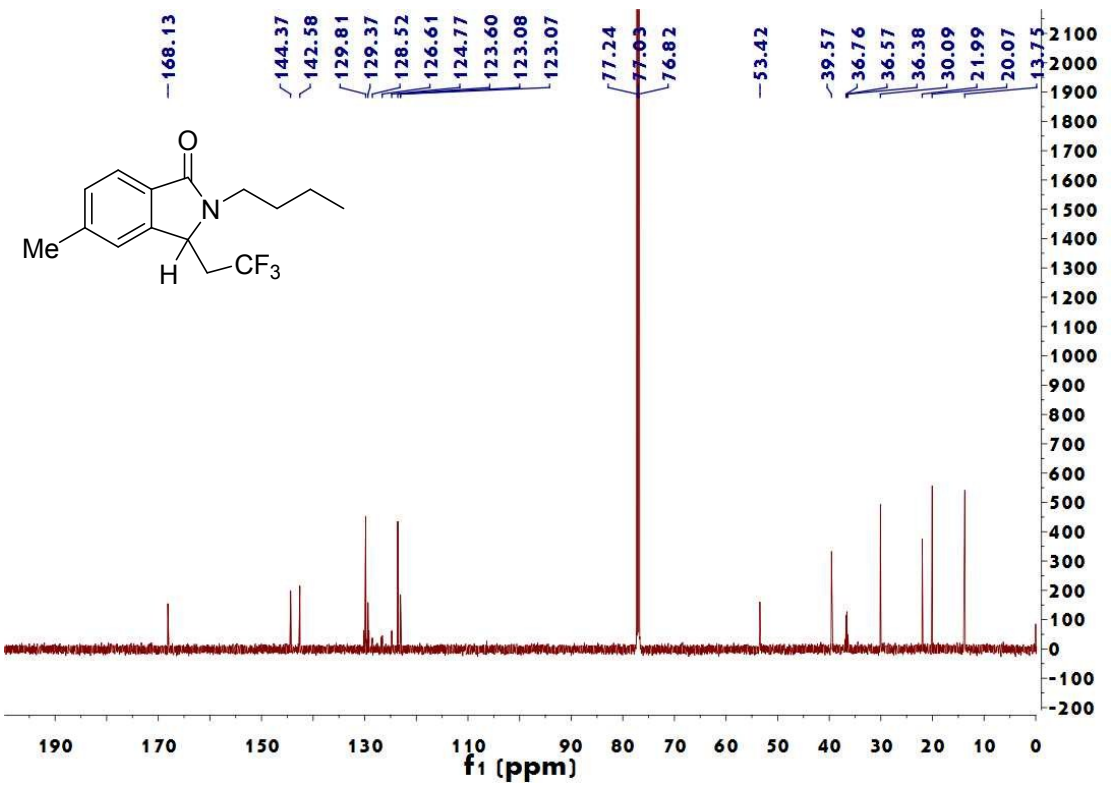
4d′.^{13}C NMR



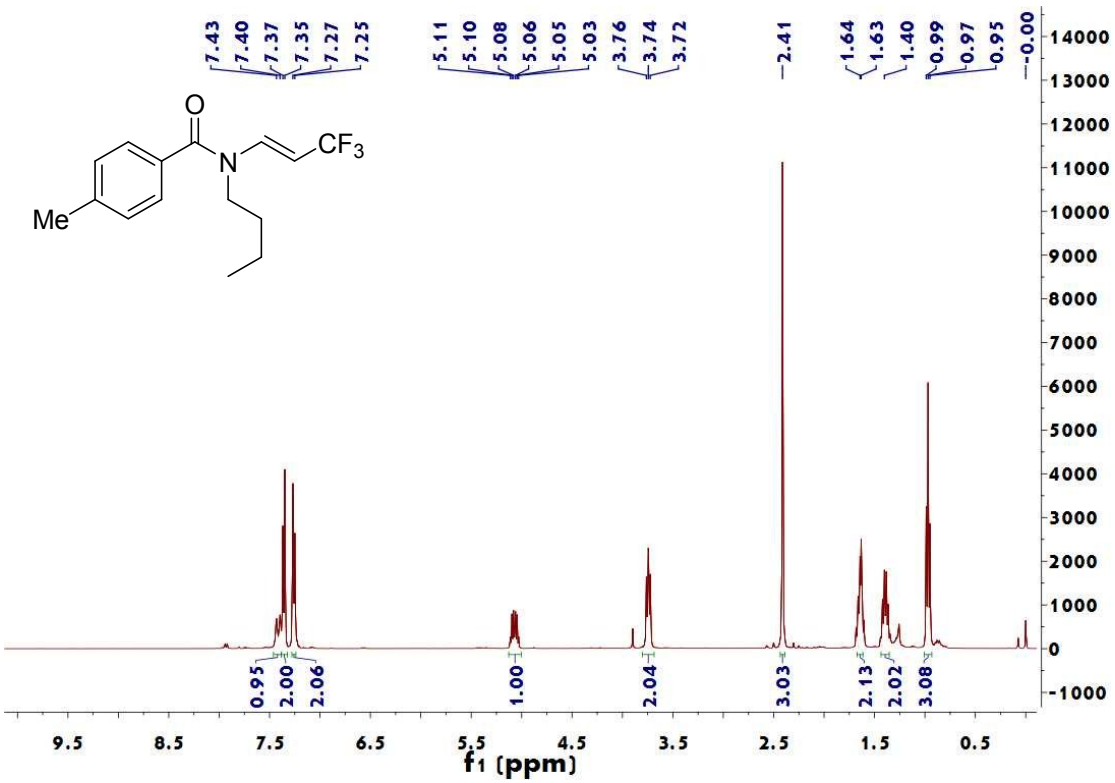
4e. ^{1}H NMR



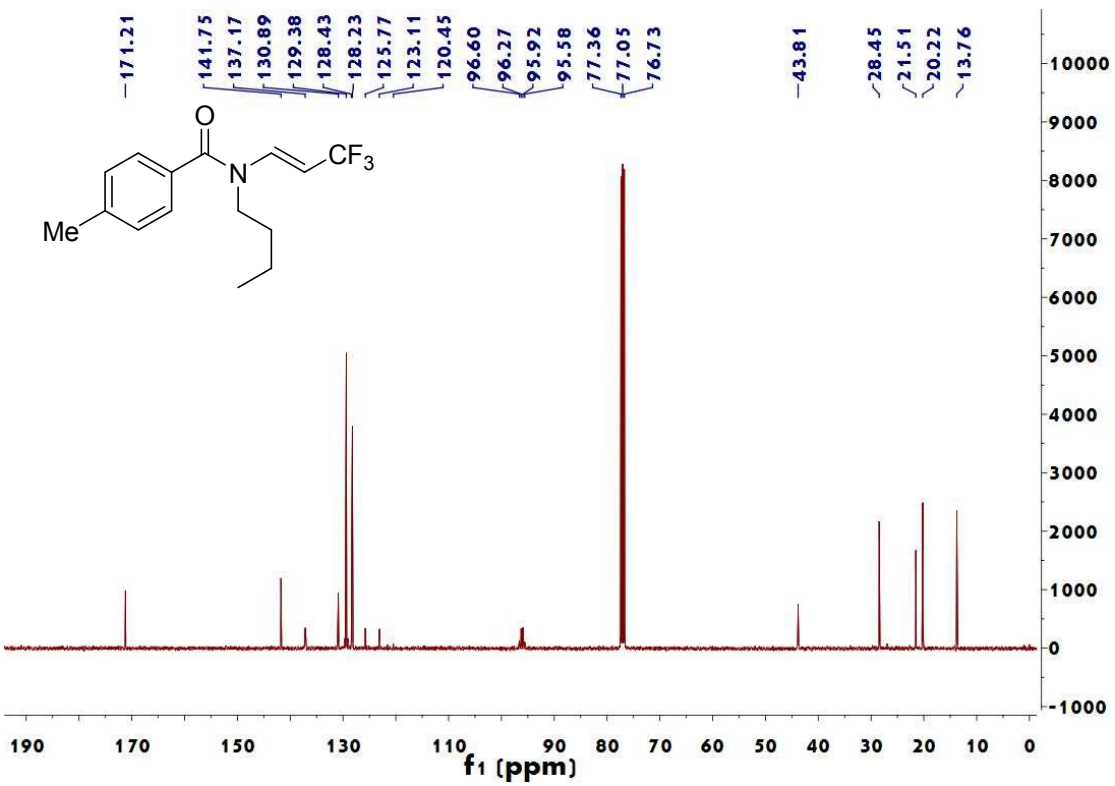
4e.^{13}C NMR



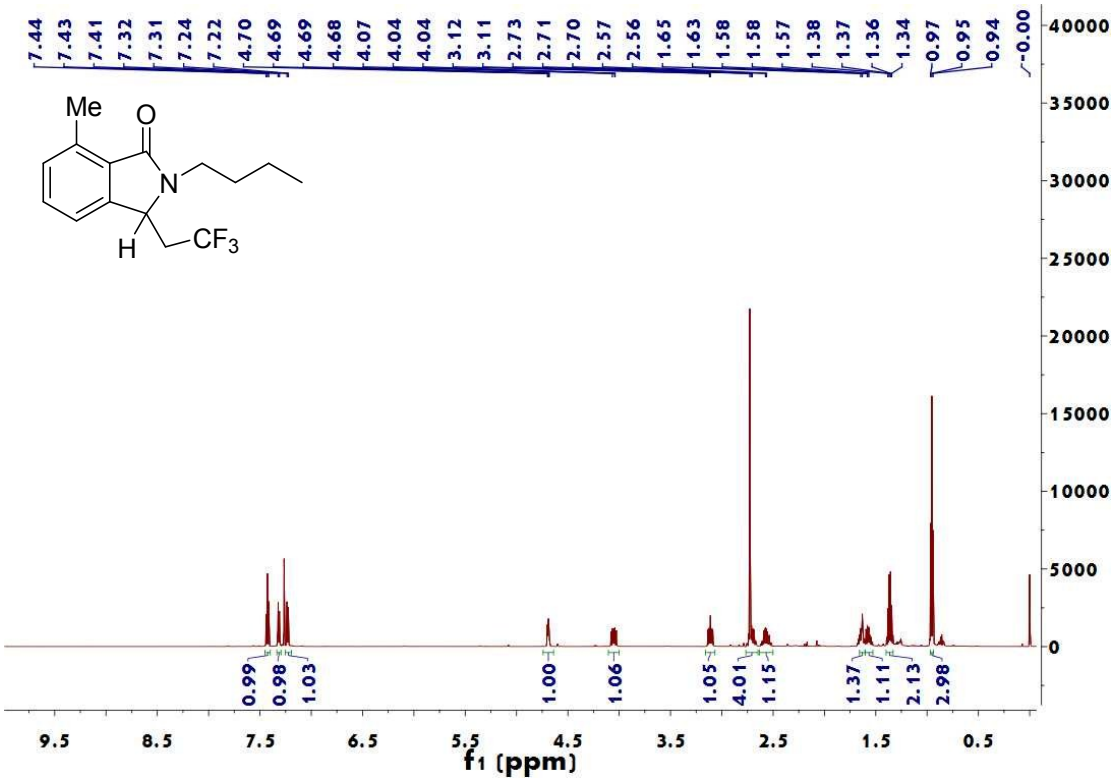
4e′. ^{1}H NMR



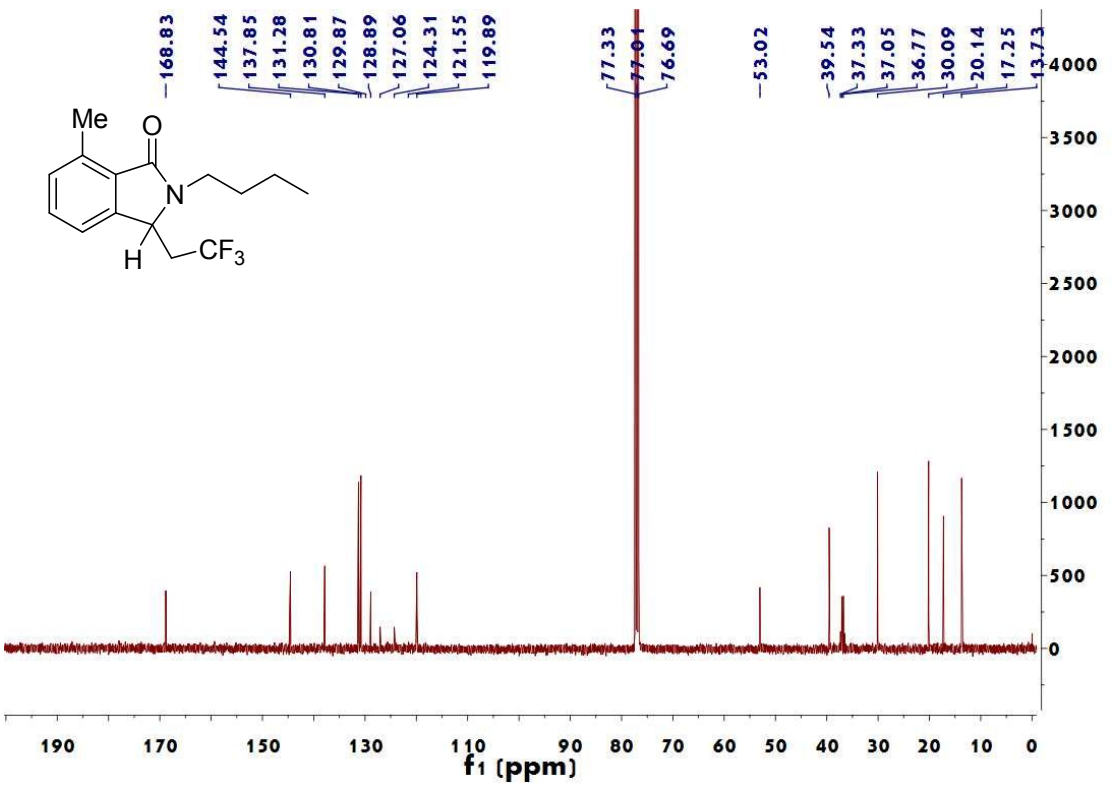
4e′.^{13}C NMR



4f. ^{1}H NMR



4f.^{13}C NMR



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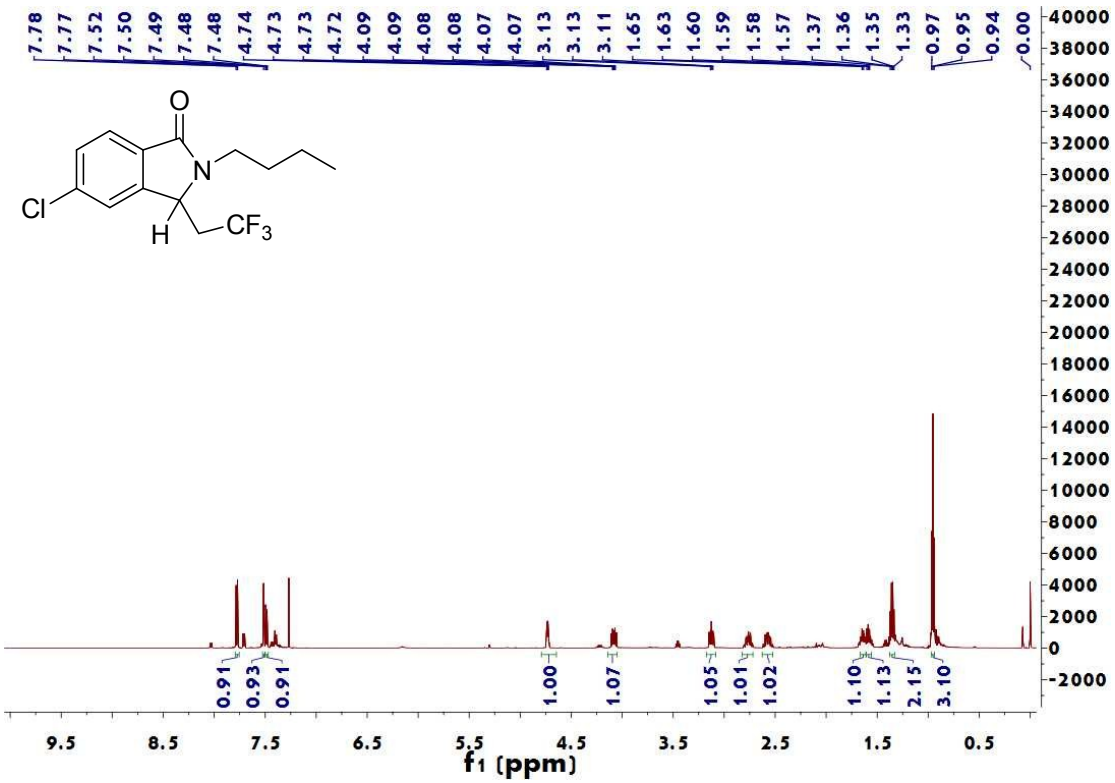
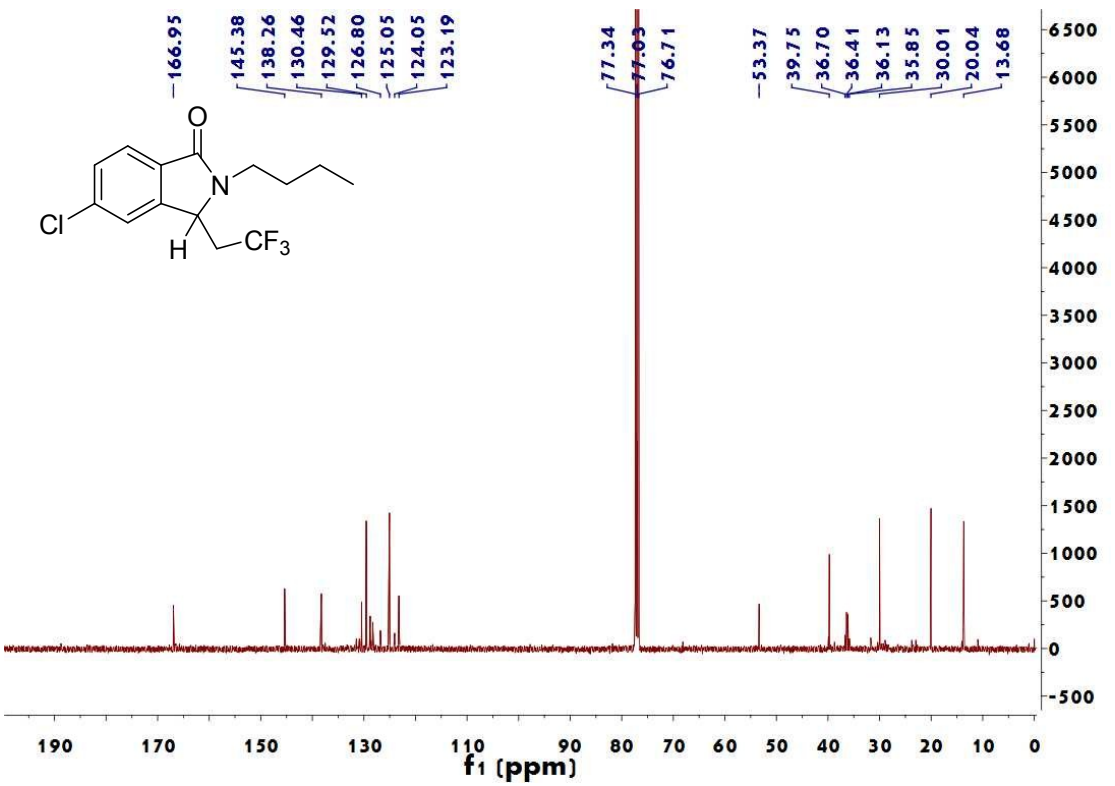
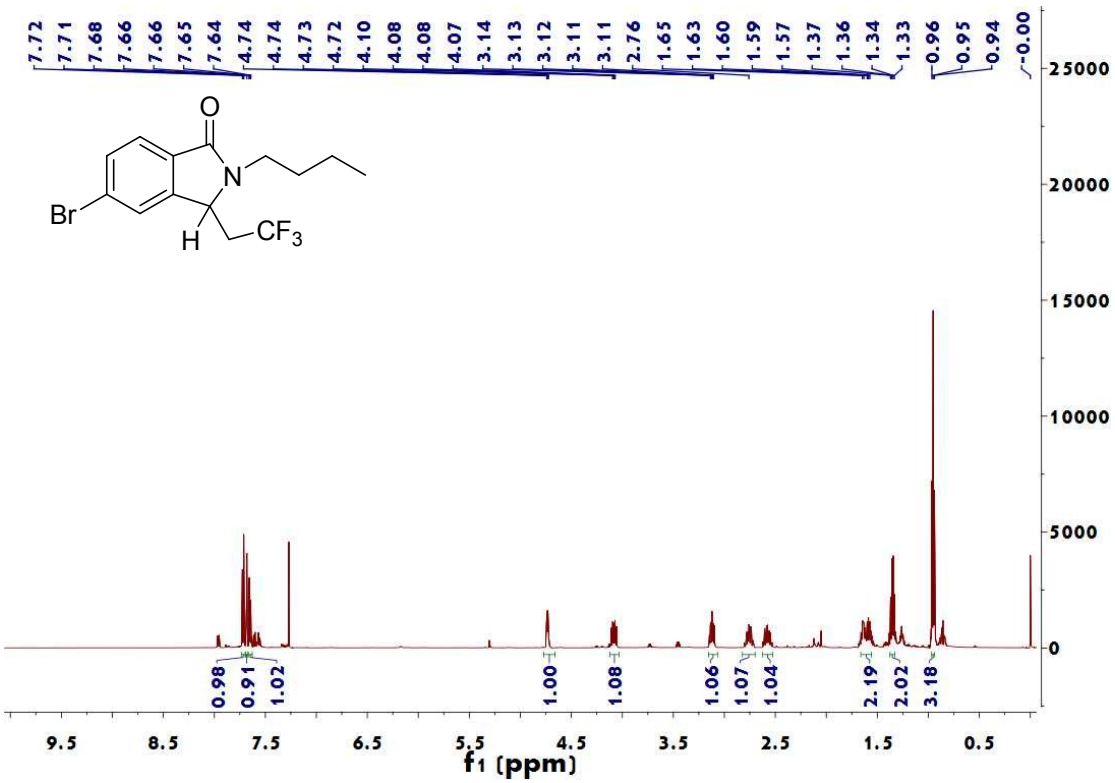


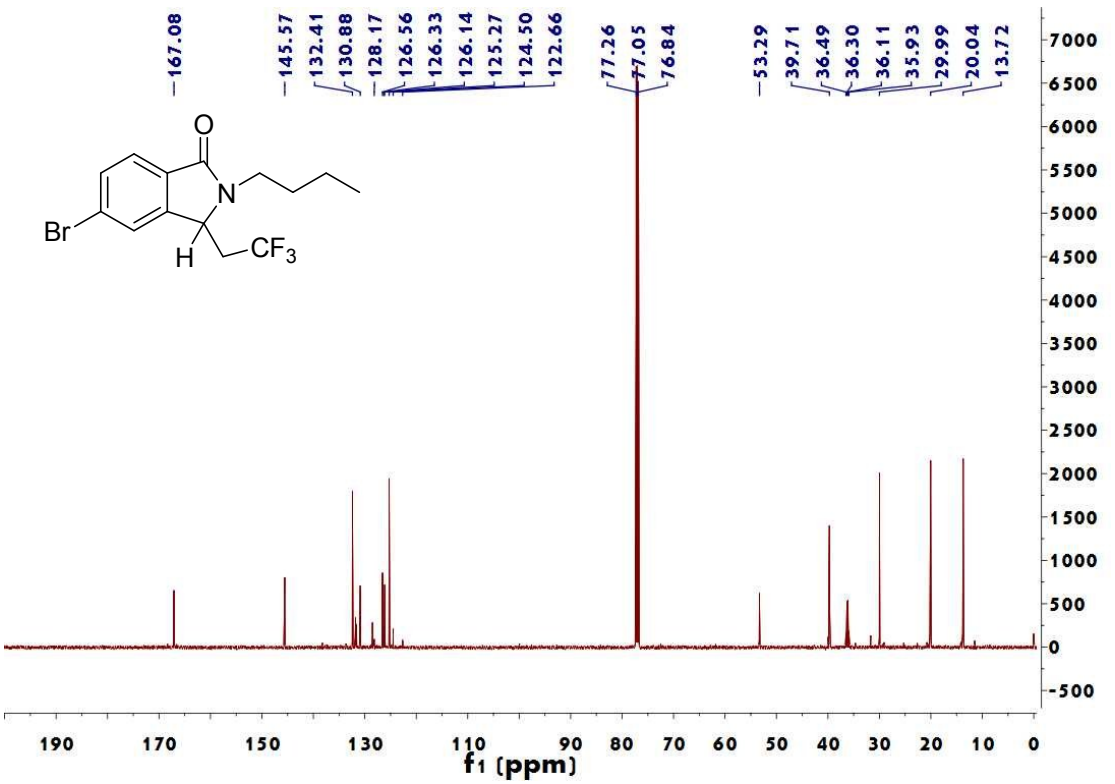
4g.^{13}C NMR



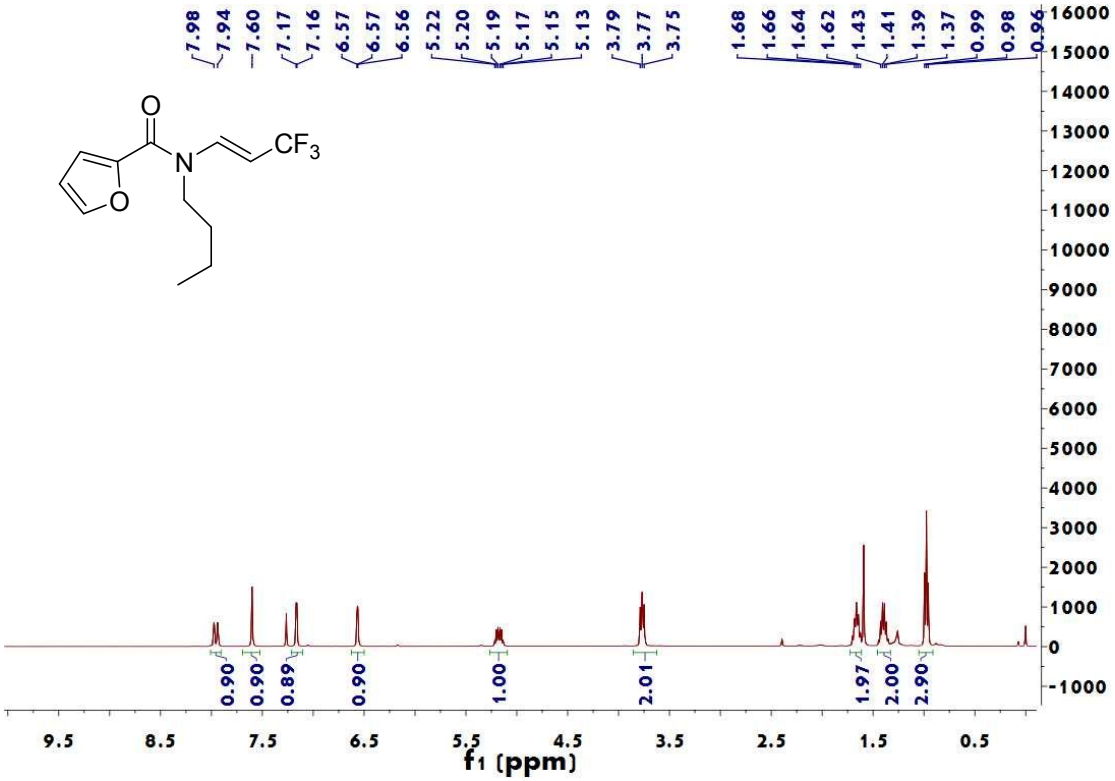
4h. ^{1}H NMR



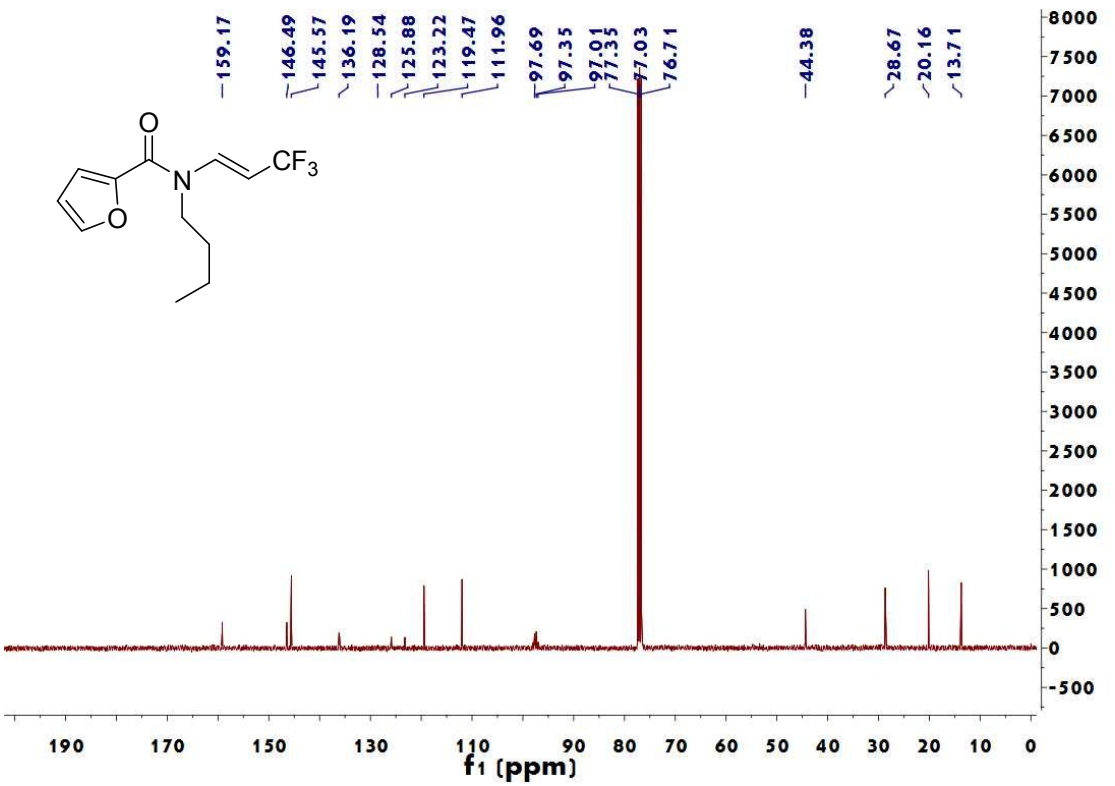
4h.^{13}C NMR



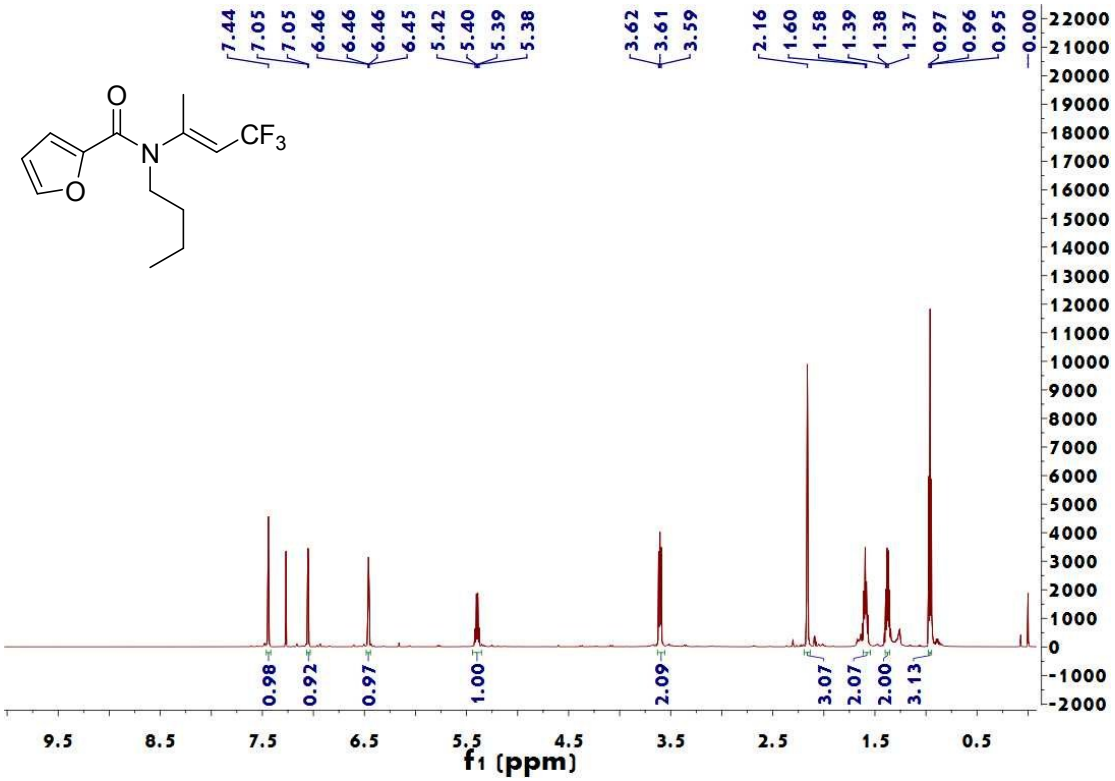
6a. ^{1}H NMR



6a.^{13}C NMR



6b. ^{1}H NMR



6b.^{13}C NMR