Supplementary Information

Photo-Induced Selective α/γ-Functionalization of Aliphatic Amines via Intramolecular Hydrogen Atom Transfer

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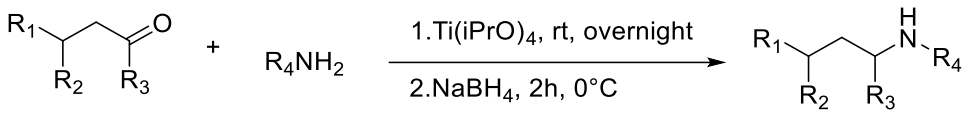
1. General Information

All reactions were carried out under an atmosphere of dry and deoxygenated argon in a glovebox (H_2O and O_2 < 0.1 ppm). ^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz), ^{19}F NMR (376 MHz) and ^{31}P NMR (162 MHz) spectra were recorded on a 400 MHz Quantum-I Plus 400 in $CDCl_3$ as a solvent and recorded in parts per million relative to the internal standard tetramethylsilane. The NMR spectra were referenced to tetramethylsilane (TMS, 0.0 ppm), $CDCl_3$ (7.26 ppm or 77.0 ppm for ^{1}H and ^{13}C respectively). The ^{1}H NMR spectra are reported as follows: δ, chemical shift; coupling constants (J are given in hertz, Hz); integration. Coupling constants are reported as follows: s = singlet, br. s = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, etc. High-resolution mass spectroscopy (HRMS) data of the products were collected on a Waters Xevo G2QTOF/UPLC mass spectrometer using electrospray ionization. Analytical thin-layer chromatography (TLC) was performed on silicycle 250 mm silica gel F-254 plates. Products were purified by flash chromatography on 200-300 meshsilica gels, SiO_2. The photoreaction instrument (WPP-TEC-1020SL) was purchased from WATTCAS, China.

2. Synthesis of Starting Materials

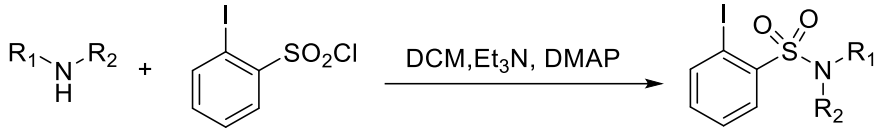
2.1 General procedure: Synthesis of amines:



Titanium(IV) isopropoxide (2 mL, 6.6 mmol) was added to a commercially available solution of methylamine in methanol (2 M, 7.5 mL) followed by the addition of the starting aldehyde (5 mmol). The reaction mixture was stirred at ambient temperature overnight, after which sodium borohydride (0.2 g, 5 mmol) was added and the resulting mixture was further stirred for another period of 2 h. The reaction was then quenched by the addition of water (1 mL), the resulting inorganic precipitate was filtered and washed with diethyl ether (20 mL). The organic layer was separated and the aqueous part was further extracted with diethyl ether (20 mL 2). The combined ether extracts were dried (K_2CO_3) and concentrated in vacuo to give N-methyl secondary amines in high purity.[1]

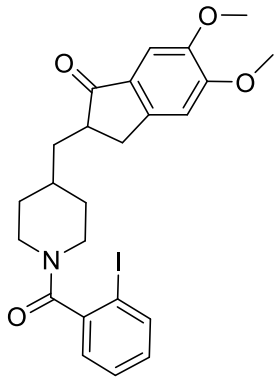
2.2 General procedure: Synthesis of tethered amines:

An oven dried 5 mL Wheaton V-vial containing a stirring bar was charged with amine (10 mmol), trimethylamine (20 mmol) in dichloromethane (30 mL) and capped under N2 atmosphere (glovebox) with an open-top cap with septum. Then, iodobenzoyl chloride (12 mmol, Dissolved in 20 ml of DCM) was added and the reaction was stirred at room temperature for 2-12 h (monitored by GC/MS). After reaction, the solvent was removed by rotary evaporation and purified by column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent.[2]



An oven dried 5 mL Wheaton V-vial containing a stirring bar was charged with amine (10 mmol), trimethylamine (20 mmol) and DMAP(1 mmol) in dichloromethane (30 mL) and capped under N2 atmosphere (glovebox) with an open-top cap with septum. Then, o-iodobenzene sulfonyl chloride (12 mmol, Dissolved in 20 ml of DCM) was added and the reaction was stirred at room temperature for 2-12 h (monitored by GC/MS). After reaction, the solvent was removed by rotary evaporation and purified by column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent.[2]

2.3 Tethered amine analytics:

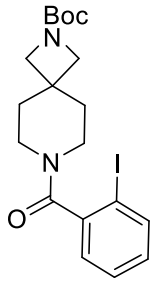


2-((1-(2-iodobenzoyl)piperidin-4-yl)methyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (1.1)

Physical State: white solid

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (dd, *J* = 11.6, 8.4 Hz, 1H), 7.40 – 7.27 (m, 1H), 7.16 (d, *J* = 31.8 Hz, 2H), 7.02 (t, *J* = 7.3 Hz, 1H), 6.83 (s, 1H), 4.73 (dd, *J* = 22.5, 10.5 Hz, 1H), 3.92 (s, 3H), 3.86 (s, 3H), 3.45 – 3.28 (m, 1H), 3.22 (dd, *J* = 17.0, 7.5 Hz, 1H), 3.00 (dt, *J* = 56.9, 12.8 Hz, 1H), 2.85 – 2.73 (m, 1H), 2.67 (d, *J* = 15.3 Hz, 2H), 1.85 (dd, *J* = 24.6, 11.0 Hz, 3H), 1.72 – 1.17 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.47, 207.39, 169.26, 169.08, 155.59, 149.48, 148.74, 142.69, 139.37, 139.03, 130.11, 130.07, 129.12, 129.09, 128.48, 128.30, 126.95, 126.74, 107.43, 104.33, 92.60, 92.39, 60.41, 56.30, 56.12, 47.58, 46.85, 45.11, 45.06, 44.96, 44.91, 41.94, 41.91, 41.75, 41.71, 38.61, 38.44, 38.31, 34.71, 34.58, 34.48, 34.37, 33.45, 33.41, 33.25, 33.09, 33.01, 32.49, 32.33, 32.08, 32.02, 31.39, 31.02, 21.10, 14.24.

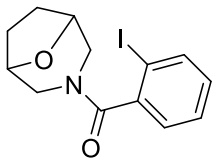


Tert-butyl 7-(2-iodobenzoyl)-2,7-diazaspiro[3.5]nonane-2-carboxylate (1.2)

Physical State: white solid

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 8.0 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 1H), 7.07 (d, *J* = 7.4 Hz, 1H), 6.98 (t, *J* = 7.7 Hz, 1H), 3.59 (dt, *J* = 25.0, 8.3 Hz, 6H), 3.17 – 2.94 (m, 2H), 1.87 – 1.68 (m, 3H), 1.54 (ddd, *J* = 20.6, 9.6, 6.0 Hz, 1H), 1.34 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.20, 156.27, 142.22, 139.18, 130.26, 128.44, 126.82, 92.41, 79.49, 44.03, 38.60, 35.50, 34.67, 33.66, 28.40.

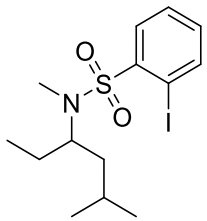


(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)(2-iodophenyl)methanone (1.3)

Physical State: white solid

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dt, *J* = 26.8, 7.2 Hz, 1H), 7.45 – 7.18 (m, 2H), 7.08 (d, *J* = 5.8 Hz, 1H), 4.48 (s, 1H), 4.35 (t, *J* = 14.6 Hz, 1H), 4.23 (d, *J* = 5.1 Hz, 1H), 3.52 (dd, *J* = 12.6, 4.9 Hz, 1H), 3.32 (dd, *J* = 12.5, 4.4 Hz, 1H), 3.16 (dd, *J* = 13.1, 4.6 Hz, 1H), 2.96 (dd, *J* = 12.5, 6.2 Hz, 1H), 1.97 (dd, *J* = 16.1, 10.1 Hz, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.17, 170.44, 142.14, 141.75, 139.77, 139.16, 130.39, 130.35, 128.60, 128.17, 127.22, 126.86, 92.87, 92.11, 73.95, 73.73, 73.42, 73.19, 53.24, 52.09, 47.64, 47.58, 28.23, 27.71, 27.51, 27.33.



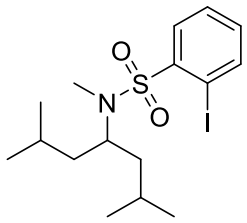
2-iodo-N-methyl-N-(5-methylhexan-3-yl)benzenesulfonamide (1.4)

Physical State: colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 7.9 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 3.60 – 3.48 (m, 1H), 2.94 (s, 3H), 1.53 (dt, *J* = 14.4, 7.1 Hz, 1H), 1.45 (dd, *J* = 14.6, 7.3 Hz, 2H), 1.36 – 1.24 (m, 3H), 0.80 (t, *J* = 7.6 Hz, 6H), 0.74 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.98, 132.94, 131.88, 128.17, 92.33, 56.99, 41.11, 29.01, 25.27, 24.68, 22.64, 22.51, 11.17.

HRMS (ESI) calcd $C_{14}H_{23}INO_2S^+$ $[M + H]^+$: 396.0489, found: 396.0490.



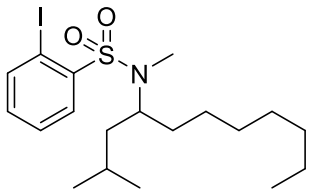
N-(2,6-dimethylheptan-4-yl)-2-iodo-N-methylbenzenesulfonamide (1.5)

Physical State: colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (dd, *J* = 7.9, 1.6 Hz, 1H), 8.10 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.49 (td, *J* = 7.9, 1.2 Hz, 1H), 7.17 (td, *J* = 7.6, 1.6 Hz, 1H), 3.59 (p, *J* = 7.0 Hz, 1H), 2.98 (s, 3H), 1.53 (dp, *J* = 13.2, 6.6 Hz, 2H), 1.42 – 1.16 (m, 5H), 0.81 (d, *J* = 6.6 Hz, 6H), 0.72 (d, *J* = 6.5 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.95, 142.79, 133.01, 132.09, 128.20, 92.67, 53.21, 41.21, 29.10, 24.64, 22.52, 22.48.

HRMS (ESI) calcd $C_{16}H_{27}INO_2S^+$ $[M + H]^+$: 424.0802, found: 424.0801.



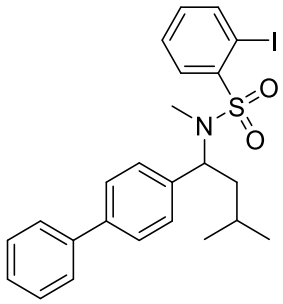
2-iodo-N-methyl-N-(2-methylundecan-4-yl)benzenesulfonamide (1.6)

Physical State: colorless oil

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.20 – 8.12 (m, 1H), 8.08 (dd, *J* = 7.7, 2.8 Hz, 1H), 7.52 – 7.43 (m, 1H), 7.15 (td, *J* = 7.6, 2.6 Hz, 1H), 3.56 (dd, *J* = 8.6, 4.7 Hz, 1H), 3.02 – 2.79 (s, 3H), 1.60 – 1.48 (m, 1H), 1.42 – 1.32 (m, 3H), 1.30 – 1.24 (m, 3H), 1.18 (m, 7H), 0.94 – 0.69 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.96, 132.94, 131.94, 128.19, 92.46, 55.43, 41.43, 32.35, 31.78, 29.45, 29.19, 29.09, 26.49, 24.70, 22.69, 22.64, 22.54, 14.18.

HRMS (ESI) calcd $C_{19}H_{33}INO_2S^+$ $[M + H]^+$: 466.1271, found: 466.1262.



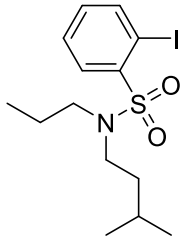
N-(1-([1,1'-biphenyl]-4-yl)-3-methylbutyl)-2-iodo-N-methylbenzenesulfonamide (1.7)

Physical State: colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 – 8.04 (m, 2H), 7.60 (dd, *J* = 18.7, 7.8 Hz, 4H), 7.47 (t, *J* = 7.6 Hz, 3H), 7.36 (dd, *J* = 15.8, 7.8 Hz, 3H), 7.19 (td, *J* = 7.7, 1.4 Hz, 1H), 5.00 (dd, *J* = 9.9, 5.6 Hz, 1H), 2.94 (s, 3H), 2.15 – 2.09 (m, 1H), 1.76 – 1.62 (m, 1H), 1.55 – 1.41 (m, 1H), 0.88 (dd, *J* = 26.9, 6.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.03, 142.64, 140.76, 140.53, 136.44, 133.25, 131.84, 128.98, 128.91, 128.30, 127.52, 127.12, 127.11, 92.93, 60.45, 57.87, 39.48, 30.15, 24.84, 23.31, 21.85, 21.14, 14.33.

HRMS (ESI) calcd $C_{24}H_{27}INO_2S^+$ $[M + H]^+$: 520.0802, found: 520.0796.



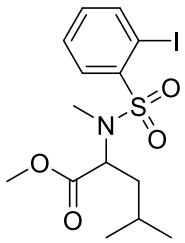
2-iodo-N-isopentyl-N-propylbenzenesulfonamide (1.8)

Physical State: colorless oil

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (dd, *J* = 19.9, 7.4 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 3.36 – 3.23 (m, 4H), 1.55 (dh, *J* = 19.7, 7.0, 6.5 Hz, 3H), 1.39 (dt, *J* = 15.4, 7.9 Hz, 2H), 0.86 (dd, *J* = 19.5, 7.0 Hz, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.92, 142.43, 133.07, 131.62, 128.16, 92.77, 48.76, 45.26, 36.52, 25.84, 22.39, 21.18, 11.26, 1.06.

HRMS (ESI) calcd $C_{14}H_{23}INO_2S^+$ $[M + H]^+$: 396.0489, found: 396.0488.



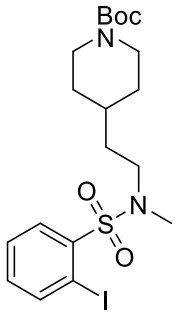
Methyl N-((2-iodophenyl)sulfonyl)-N-methylleucinate (1.9)

Physical State: light yellow oil

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.21 – 8.05 (m, 2H), 7.51 (t, *J* = 7.3 Hz, 1H), 7.20 (td, *J* = 7.6, 1.5 Hz, 1H), 4.52 (dd, *J* = 9.7, 5.0 Hz, 1H), 3.63 (s, 3H), 3.07 (s, 3H), 1.75 – 1.61 (m, 3H), 0.94 (d, *J* = 5.7 Hz, 3H), 0.83 (d, *J* = 6.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.98, 143.00, 141.79, 133.29, 131.83, 128.22, 92.26, 77.43, 77.11, 76.79, 57.22, 56.09, 52.61, 52.11, 38.44, 36.66, 30.89, 24.88, 24.52, 23.19, 22.99, 21.34, 21.24, 1.06.

HRMS (ESI) calcd $C_{14}H_{21}INO_4S^+$ $[M + H]^+$: 426.0230, found: 426.0235.



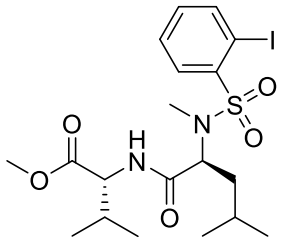
Tert-butyl 4-(2-((2-iodo-N-methylphenyl)sulfonamido)ethyl)piperidine-1-carboxylate (2.0)

Physical State: colorless oil

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.19 – 8.06 (m, 2H), 7.61 – 7.47 (m, 1H), 7.22 (td, *J* = 7.6, 1.7 Hz, 1H), 4.05 (s, 2H), 3.29 (t, *J* = 7.1 Hz, 2H), 2.91 (s, 3H), 2.65 (s, 2H), 1.54 (t, *J* = 6.9 Hz, 3H), 1.47 (s, 10H), 1.33 – 1.24 (m, 2H), 1.06 (qd, *J* = 12.6, 4.3 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.84, 143.08, 141.38, 133.36, 131.74, 128.30, 92.63, 92.59, 79.35, 47.62, 34.06, 33.97, 33.11, 28.49.

HRMS (ESI) calcd $C_{19}H_{30}IN_2O_4S^+$ $[M + H]^+$: 509.0965, found: 509.0968.



Methyl N-((2-iodophenyl)sulfonyl)-N-methyl-L-leucyl-D-valinate (2.1)

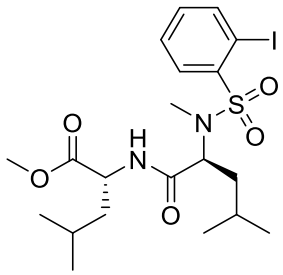
Physical State: light yellow oil

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.26 (dd, *J* = 7.9, 1.5 Hz, 1H), 8.13 (d, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 8.2 Hz, 1H), 7.24 (td, *J* = 7.7, 1.4 Hz, 1H), 7.11 (d, *J* = 8.5 Hz, 1H), 4.53 (dd, *J* = 8.6, 4.7 Hz, 1H), 4.17 (dd, *J* = 8.6, 5.6 Hz, 1H), 3.76 (s, 3H), 3.02 (s, 3H), 2.25 (ddd, *J* = 13.7, 6.9, 4.9 Hz, 1H), 1.94 (ddd, *J* = 13.6, 8.7, 6.1 Hz, 1H), 1.40

(dt, *J* = 13.1, 6.7 Hz, 1H), 1.29 (ddd, *J* = 13.2, 7.3, 5.7 Hz, 1H), 1.00 (dd, *J* = 13.8, 6.9 Hz, 6H), 0.67 (dd, *J* = 6.5, 3.3 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.14, 169.33, 143.12, 141.40, 133.72, 132.40, 128.43, 92.63, 57.46, 52.21, 36.97, 31.19, 31.01, 24.76, 22.44, 22.11, 19.19, 17.67.

HRMS (ESI) calcd $C_{19}H_{30}IN_2O_5S^+$ $[M + H]^+$: 525.0915, found: 525.0920.



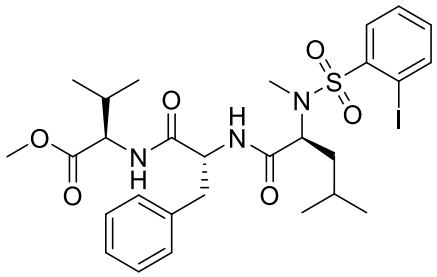
Methyl N-((2-iodophenyl)sulfonyl)-N-methyl-L-leucyl-D-leucinate (2.2)

Physical State: light yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (dd, *J* = 7.9, 1.5 Hz, 1H), 8.12 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.52 (td, *J* = 7.9, 1.0 Hz, 1H), 7.22 (td, *J* = 7.6, 1.5 Hz, 1H), 6.92 (d, *J* = 7.8 Hz, 1H), 4.62 – 4.47 (m, 1H), 4.13 (dt, *J* = 14.2, 6.6 Hz, 2H), 3.73 (s, 3H), 2.99 (s, 3H), 1.92 (ddd, *J* = 13.7, 8.5, 6.2 Hz, 1H), 1.78 – 1.36 (m, 5H), 1.35 – 1.20 (m, 5H), 0.95 (t, *J* = 6.1 Hz, 6H), 0.91 – 0.80 (m, 2H), 0.68 (dd, *J* = 6.6, 1.1 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.08, 169.28, 143.13, 141.38, 133.71, 132.31, 128.44, 92.58, 60.42, 57.29, 52.31, 50.94, 41.06, 36.98, 31.12, 29.71, 24.82, 24.72, 22.90, 22.42, 22.11, 21.67, 21.08, 14.22.

HRMS (ESI) calcd $C_{20}H_{32}IN_2O_5S^+$ $[M + H]^+$: 539.1071, found: 539.1070.



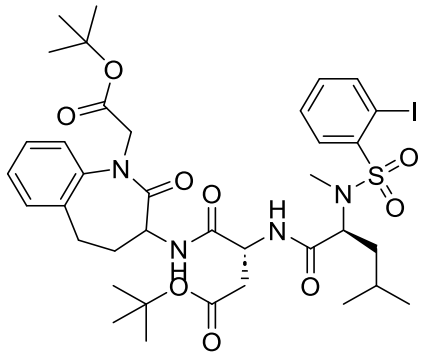
Methyl N-((2-iodophenyl)sulfonyl)-N-methyl-L-leucyl-D-phenylalanyl-D-valinate (2.3)

Physical State: light yellow solid

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.24 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.15 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.55 (td, *J* = 7.9, 1.2 Hz, 1H), 7.35 – 7.18 (m, 8H), 6.57 (d, *J* = 8.6 Hz, 1H), 4.87 – 4.39 (m, 2H), 4.08 (dd, *J* = 8.1, 6.1 Hz, 1H), 3.74 (s, 3H), 3.25 (dd, *J* = 14.1, 6.3 Hz, 1H), 3.07 (dd, *J* = 14.1, 8.8 Hz, 1H), 2.62 (s, 3H), 2.18 – 2.09 (m, 1H), 1.93 – 1.78 (m, 2H), 1.41 (dt, *J* = 13.3, 6.6 Hz, 1H), 1.17 (dt, *J* = 13.4, 6.6 Hz, 1H), 0.97 – 0.76 (m, 7H), 0.64 (dd, *J* = 6.5, 5.3 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.01, 170.65, 169.93, 143.16, 141.24, 136.67, 133.77, 132.56, 129.31, 128.89, 128.72, 128.44, 127.05, 92.75, 57.31, 55.01, 52.18, 37.58, 36.88, 31.04, 30.88, 24.71, 22.22, 22.04, 18.87, 17.63.

HRMS (ESI) calcd $C_{28}H_{39}IN_3O_6S^+$ $[M + H]^+$: 672.1599, found: 672.1608.



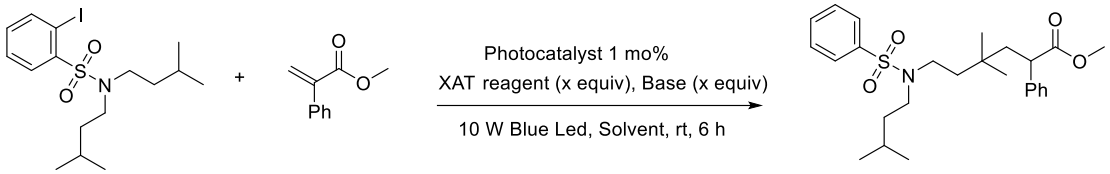
Tert-butyl (3R)-4-((1-(2-(tert-butoxy)-2-oxoethyl)-2-oxo-2,3,4,5-tetrahydro-1H-benzo[b]azepin-3-yl)amino)-3-((S)-2-((2-iodo-N-methylphenyl)sulfonamido)-4-methylpentanamido)-4-oxobutanoate (2.4)

Physical State: light yellow solid

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.33 (dd, *J* = 7.9, 1.5 Hz, 1H), 8.12 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.59 – 7.38 (m, 3H), 7.36 – 7.30 (m, 1H), 7.28 – 7.20 (m, 3H), 7.16 (d, *J* = 7.9 Hz, 1H), 4.85 (dt, *J* = 8.4, 5.9 Hz, 1H), 4.55 (dt, *J* = 11.2, 7.6 Hz, 1H), 4.28 (d, *J* = 17.0 Hz, 1H), 4.03 (t, *J* = 7.1 Hz, 1H), 3.35 (td, *J* = 12.9, 7.9 Hz, 4H), 3.17 (s, 3H), 2.84 – 2.46 (m, 4H), 2.15 (td, *J* = 11.7, 7.7 Hz, 1H), 1.89 – 1.71 (m, 1H), 1.62 – 1.47 (m, 3H), 1.44 (d, *J* = 6.0 Hz, 18H), 0.71 (dd, *J* = 52.0, 6.2 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.28, 170.58, 170.23, 169.52, 167.61, 143.05, 141.01, 140.49, 135.58, 133.67, 132.80, 129.68, 128.39, 127.99, 127.26, 122.63, 82.28, 81.70, 60.50, 57.36, 51.29, 49.99, 49.35, 37.88, 37.19, 35.55, 31.28, 28.01, 24.65, 22.34, 21.88. **HRMS (ESI)** calcd $C_{37}H_{52}IN_4O_9S^+$ $[M + H]^+$: 855.2494, found: 855.2490.

3. Optimization of the Reaction Parameters

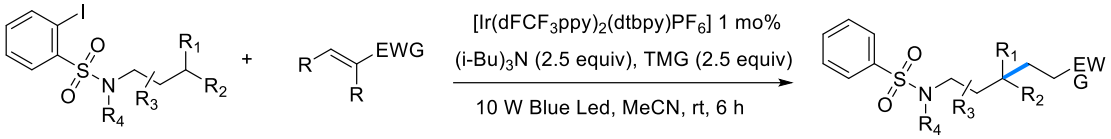


序号	Catalyst	Solvent	XAT reagent	Base	结果
1	4-CZIPN	DMF	Et_3N	-	trace
2	4-CZIPN	DMSO	Et_3N	-	15 %
3	4-CZIPN	MeCN	Et_3N	-	19 %
4	4-CZIPN	DCM	Et_3N	-	12 %
5	4-CZIPN	MeCN	Et_3N	Na_2CO_3	23 %
6	4-CZIPN	MeCN	Et_3N	Cs_2CO_3	26 %
7	4-CZIPN	MeCN	Et_3N	TMG	31%
8	4-CZIPN	MeCN	Bn_3N	TMG	21 %
9	4-CZIPN	MeCN	Bn_3N	-	trace
10	4-CZIPN	MeCN	$(i\text{-}Bu)_3N$	TMG	42 %
11	4-CZIPN	MeCN	$(i\text{-}Bu)_3N$	-	trace
12	4-CZIPN	MeCN	$(TMS)_3SiOH$	Na_2CO_3	trace
13	$Ir(dFCF_3ppy)_2(dtbpy)PF_6$	MeCN	$(i\text{-}Bu)_3N$	TMG	83 %
14	$Ir(dFFppy)_2(dtbpy)PF_6$	MeCN	$(i\text{-}Bu)_3N$	TMG	76 %
15	$Ir(ppy)_2(dtbpy)PF_6$	MeCN	$(i\text{-}Bu)_3N$	TMG	67%
16	$Ir(ppy)_3$	MeCN	$(i\text{-}Bu)_3N$	TMG	trace
17	$Ru(bpy)_3Cl$	MeCN	$(i\text{-}Bu)_3N$	TMG	trace

Table S1: Optimization of the reaction parameters.

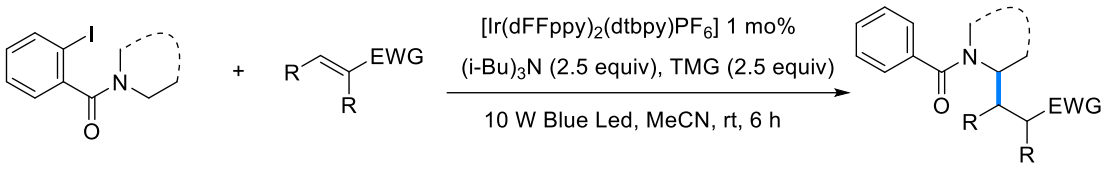
4. α、β、γ-C(sp^3)−H functionalization of amines

4.1 General procedure A:



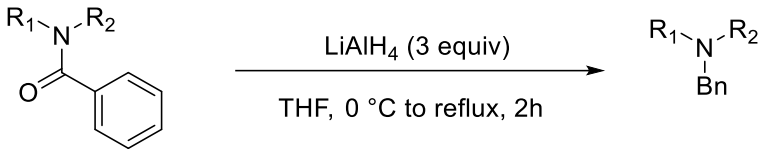
The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a Teflon-coated magnetic stir bar was added [Ir(dFCF$_3$ppy)$_2$(dtbpy)PF$_6$] 1 mo%, the corresponding imide (0.2 mmol), TMG (70 μL), MeCN (1 mL) and (i-Bu)$_3$N（140 μL） was added via pipette. The reaction mixture was stirred and irradiated using a 10 W 450 nm LED lamp for 6 hours and control the temperature at about 20 °C until the reaction was complete (monitored by TLC). After reaction, the solvent was removed by rotary evaporation and purified by preparative thin layer chromatography using petroleum ether/ethyl acetate as the eluent.

4.2 General procedure B:



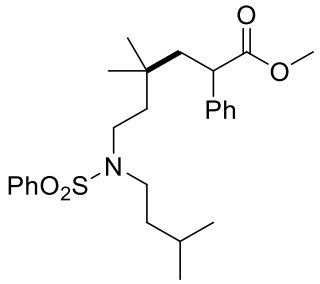
The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a Teflon-coated magnetic stir bar was added [Ir(dFCF$_3$ppy)$_2$(dtbpy)PF6] 1 mo%, the corresponding imide (0.2 mmol), TMG (70 μL), MeCN (1 mL) and (i-Bu)$_3$N（140 μL） was added via pipette. The reaction mixture was stirred and irradiated using a 10 W 450 nm LED lamp for 6 hours and control the temperature at about 20 °C until the reaction was complete (monitored by TLC). After reaction, the solvent was removed by rotary evaporation and purified by preparative thin layer chromatography using petroleum ether/ethyl acetate as the eluent.

4.3 General procedure C:



Dissolve the product with THF and place it at 0 °C, lithium aluminum hydride (1M in THF, 3 ml) was added dropwise to the reaction solution and then continue stirring for 30 minutes. The reaction mixture was allowed to warm to room temperature, stirred for 3 h and then treated successively with H_2O, 15% aq NaOH. The reaction mixture was extracted with ethyl acetate and the combined organic extracts were dried by Na_2SO_4, filtered and concentrated in vacuo. The solvent was removed by rotary evaporation and purified by column chromatography on silica gel column to afford product.[3]

4.4 Data for product:



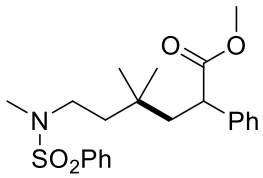
Methyl 6-(N-isopentylphenylsulfonamido)-4,4-dimethyl-2-phenylhexanoate (1c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 76.4 mg of the title compound **1c** (light yellow oil; 83% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.3 Hz, 2H), 7.62 – 7.47 (m, 3H), 7.34 (d, *J* = 4.9 Hz, 4H), 7.30 – 7.25 (m, 1H), 3.67 (d, *J* = 6.7 Hz, 4H), 3.20 – 2.91 (m, 4H), 2.31 (dd, *J* = 14.2, 9.1 Hz, 1H), 1.66 – 1.46 (m, 4H), 1.44 – 1.35 (m, 2H), 0.90 (dd, *J* = 10.6, 6.9 Hz, 11H), 0.86 – 0.79 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 140.6, 140.1, 132.3, 129.1, 128.8, 127.8, 127.27, 127.1, 52.2, 47.3, 46.5, 45.3, 43.9, 40.4, 37.4, 32.9, 26.8, 26.8, 25.7, 22.4.

HRMS (ESI) calcd $C_{26}H_{38}NO_4S^+$ $[M + H]^+$: 460.2516, found: 460.2515



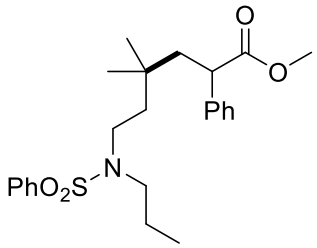
Methyl 4,4-dimethyl-6-(N-methylphenylsulfonamido)-2-phenylhexanoate (2c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 54.9 mg of the title compound **2c** (colorless oil; 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.4 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 2H), 7.33 (d, *J* = 3.8 Hz, 4H), 7.28 (dd, *J* = 7.3, 3.9 Hz, 1H), 3.70 – 3.67 (m, 1H), 3.66 (s, 3H), 3.10 – 2.96 (m, 2H), 2.72 (s, 3H), 2.31 (dd, *J* = 14.2, 8.9 Hz, 1H), 1.59 (dd, *J* = 14.2, 3.8 Hz, 1H), 1.54 – 1.46 (m, 2H), 0.91 (d, *J* = 5.2 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 140.5, 137.8, 132.5, 129.1, 128.7, 127.8, 127.33, 127.2, 52.2, 47.4, 46.3, 45.3, 39.3, 34.7, 32.8, 26.9.

HRMS (ESI) calcd $C_{22}H_{30}NO_4S+$ $[M + H]^+$: 404.1890, found: 404.1891



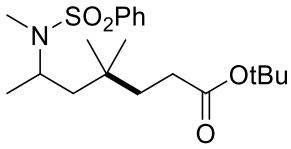
Methyl 4,4-dimethyl-2-phenyl-6-(N-propylphenylsulfonamido)hexanoate (3c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 75.2 mg of the title compound **3c** (colorless oil; 87% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 – 7.78 (m, 2H), 7.63 – 7.49 (m, 3H), 7.34 (d, *J* = 4.4 Hz, 4H), 7.27 (dd, *J* = 8.8, 4.5 Hz, 1H), 3.68 (d, *J* = 9.1 Hz, 4H), 3.18 – 2.90 (m, 4H), 2.30 (dd, *J* = 14.2, 9.0 Hz, 1H), 1.55 (m, 5H), 1.02 – 0.81 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 140.6, 140.1, 132.3, 129.1, 128.7, 127.8, 127.2, 127.1, 52.2, 50.1, 47.3, 45.2, 44.1, 40.4, 32.9, 26.8, 26.8, 22.1, 11.2.

HRMS (ESI) calcd $C_{24}H_{34}NO_4S^+$ $[M + H]^+$: 432.2203, found: 432.2202



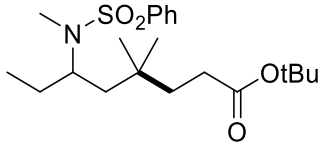
Tert-butyl 4,4-dimethyl-6-(N-methylphenylsulfonamido)heptanoate (4c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 36.9 mg of the title compound **4c** (light yellow oil; 48% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.5 Hz, 2H), 7.62 – 7.47 (m, 3H), 4.35 – 4.13 (m, 1H), 2.70 (s, 3H), 2.22 – 2.13 (m, 2H), 1.64 – 1.55 (m, 2H), 1.47 (s, 9H), 1.45 (s, 2H), 0.97 (d, *J* = 6.3 Hz, 6H), 0.79 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 139.7, 132.3, 129.1, 127.25, 8.1, 49.7, 46.1, 37.4, 32.7, 30.8, 28.1, 27.7, 26.5, 26.3, 18.89.

HRMS (ESI) calcd $C_{20}H_{34}NO_4S^+$ $[M + H]^+$: 384.2203, found: 384.2209



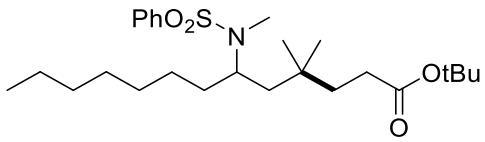
Tert-butyl 4,4-dimethyl-6-(N-methylphenylsulfonamido)octanoate (5c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 38.9 mg of the title compound **5c** (light yellow oil; 49% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (t, *J* = 7.6 Hz, 2H), 7.62 – 7.41 (m, 3H), 3.94 (dd, *J* = 13.1, 6.4 Hz, 1H), 2.72 – 2.60 (m, 3H), 2.21 – 2.07 (m, 2H), 1.56 (dd, *J* = 16.2, 8.2 Hz, 3H), 1.49 – 1.41 (m, 9H), 1.34 – 1.21 (m, 4H), 0.94 (dd, *J* = 7.9, 4.8 Hz, 6H), 0.78 (dd, *J* = 15.5, 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 140.2, 132.2, 128.9, 127.1, 80.1, 56.1, 43.4, 37.6, 32.4, 30.7, 28.1, 27.9, 26.6, 26.5, 26.5, 11.5.

HRMS (ESI) calcd $C_{21}H_{36}NO_4S^+$ $[M + H]^+$: 398.2360, found: 398.2351



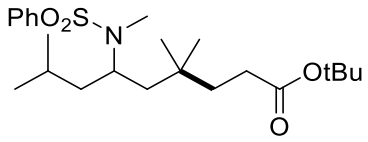
Tert-butyl 4,4-dimethyl-6-(N-methylphenylsulfonamido)tridecanoate (6c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 51.5 mg of the title compound **6c** (light yellow oil; 55% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (t, *J* = 8.9 Hz, 2H), 7.54 (td, *J* = 13.9, 7.7 Hz, 3H), 4.05 – 3.91 (m, 1H), 2.68 (d, *J* = 11.1 Hz, 3H), 2.24 – 2.07 (m, 2H), 1.57 (m, 3H), 1.46 (d, *J* = 11.1 Hz, 9H), 1.29 (m, 4H), 1.18 (m, 9H), 0.94 (d, *J* = 7.8 Hz, 6H), 0.90 – 0.83 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 140.1, 132.2, 128.9, 127.2, 80.1, 54.6, 43.5, 37.6, 33.5, 32.5, 31.7, 30.8, 29.3, 29.1, 28.1, 27.0, 26.6, 26.5, 22.6, 14.1.

HRMS (ESI) calcd $C_{26}H_{46}NO_4S^+$ $[M + H]^+$: 468.3142, found: 468.3133



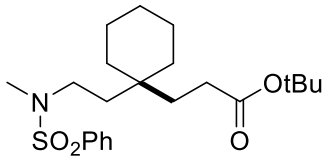
Tert-butyl 4,4,8-trimethyl-6-(N-methylphenylsulfonamido)nonanoate (7c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 52.1 mg of the title compound **7c** (colorless oil; 61% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.76 (m, 2H), 7.62 – 7.45 (m, 3H), 4.20 – 4.11 (m, 1H), 2.70 (s, 3H), 2.22 – 2.10 (m, 2H), 1.58 (t, *J* = 8.3 Hz, 2H), 1.47 (s, 9H), 1.16 (ddd, *J* = 21.6, 11.8, 5.6 Hz, 2H), 0.96 (d, *J* = 3.6 Hz, 6H), 0.85 (dd, *J* = 10.2, 6.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 140.1, 132.3, 128.9, 127.3, 80.1, 52.3, 43.2, 42.4, 37.8, 32.5, 30.8, 28.1, 26.6, 24.9, 22.8, 22.4.

HRMS (ESI) calcd $C_{23}H_{40}NO_4S^+$ $[M + H]^+$: 426.2673, found: 426.2671



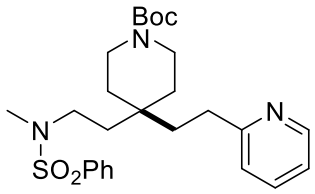
Tert-butyl 3-(1-(2-(N-methylphenylsulfonamido)ethyl)cyclohexyl)propanoate (8c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 39.4 mg of the title compound **8c** (colorless oil; 48% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (ddt, *J* = 6.4, 4.5, 2.6 Hz, 2H), 7.49 (dtt, *J* = 14.9, 9.2, 7.1, 3.3 Hz, 3H), 3.00 – 2.79 (m, 2H), 2.72 – 2.58 (m, 3H), 2.21 – 2.00 (m, 2H), 1.72 – 1.57 (m, 2H), 1.44 (dq, *J* = 12.8, 4.1 Hz, 4H), 1.37 (q, *J* = 2.5 Hz, 9H), 1.34 – 1.25 (m, 3H), 1.21 – 1.15 (m, 4H), 1.10 – 0.89 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 173.0, 137.9, 137.1, 132.5, 132.5, 129.1, 127.51, 127.3, 80.2, 80.1, 51.7, 45.6, 40.6, 38.2, 35.4, 35.1, 35.0, 34.3, 34.1, 33.7, 31.9, 31.8, 30.0, 29.7, 29.6, 28.5, 28.1, 26.8, 26.7, 26.2, 23.9, 21.4.

HRMS (ESI) calcd $C_{22}H_{36}NO_4S^+$ $[M + H]^+$: 410.2360, found: 410.2355



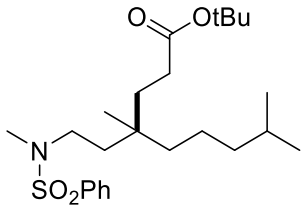
Tert-butyl 4-(2-(N-methylphenylsulfonamido)ethyl)-4-(2-(pyridin-2-yl)ethyl)piperidine-1-carboxylate (9c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~4:1) afforded 34.2 mg of the title compound **9c** (white solid; 35% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 – 8.47 (m, 1H), 7.81 (t, *J* = 8.6 Hz, 2H), 7.69 – 7.49 (m, 4H), 7.25 – 7.07 (m, 2H), 3.52 – 3.32 (m, 3H), 3.11 (s, 1H), 3.08 – 2.95 (m, 1H), 2.89 – 2.78 (m, 3H), 2.75 (m, 2H), 2.68 (s, 1H), 1.91 – 2.05 (m, 1H)1.81 – 1.61 (m, 4H), 1.46 (m, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 161.6, 155.0, 154.8, 149.2, 149.1, 137.7, 136.9, 136.6, 136.6, 132.6, 132.6, 129.1, 127.4, 127.3, 122.9, 121.2, 121.2, 79.4, 79.3, 51.4, 51.4, 45.5, 45.5, 40.1, 36.4, 36.1, 35.2, 35.0, 34.8, 33.9, 33.4, 31.9, 28.4.

HRMS (ESI) calcd $C_{26}H_{38}N_3O_4S^+$ $[M + H]^+$: 488.2578, found: 488.2572



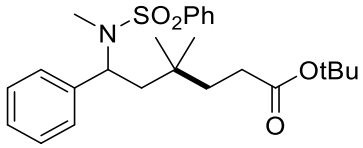
Tert-butyl 4,8-dimethyl-4-(2-(N-methylphenylsulfonamido)ethyl)nonanoate (10c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 36.9 mg of the title compound **10c** (colorless oil; 42% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.9 Hz, 2H), 7.67 – 7.50 (m, 3H), 3.03 (dd, *J* = 10.0, 6.2 Hz, 2H), 2.78 (d, *J* = 2.1 Hz, 3H), 2.22 – 2.08 (m, 2H), 1.59 – 1.44 (m, 14H), 1.26 – 1.09 (m, 6H), 0.96 – 0.80 (m, 10H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 137.9, 132.5, 129.1, 127.3, 80.2, 46.1, 39.7, 39.3, 36.6, 34.8, 34.2, 34.1, 30.2, 28.1, 27.8, 24.4, 22.6, 21.1.

HRMS (ESI) calcd $C_{24}H_{42}NO_4S^+$ $[M + H]^+$: 440.2829, found: 440.2828



Tert-butyl 4,4-dimethyl-6-(N-methylphenylsulfonamido)-6-phenylhexanoate (11c)

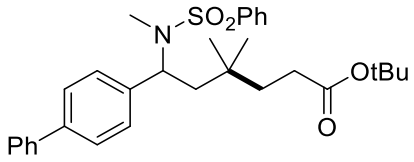
Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 47.3 mg of the title compound **11c** (light yellow oil; 53% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.1, 2.9 Hz, 2H), 7.56 – 7.47 (m, 1H), 7.47 – 7.36 (m, 2H), 7.23 (d, *J* = 1.8 Hz, 5H), 5.25 (dt, *J* = 8.5, 4.3 Hz, 1H), 2.75 (d, *J* = 4.4 Hz, 3H), 2.24 – 2.05 (m, 2H), 2.05 – 1.93 (m, 1H), 1.61 (dt, *J* = 14.1, 4.4 Hz, 1H),

1.53 – 1.47 (m, 2H), 1.44 (d, *J* = 4.4 Hz, 9H), 0.87 (d, *J* = 4.1 Hz, 3H), 0.77 (d, *J* = 4.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 140.1, 138.9, 132.2, 128.8, 128.3, 128.3, 127.8, 127.3, 80.1, 57.3, 42.5, 37.7, 32.7, 30.7, 29.2, 28.1, 26.9, 26.8

HRMS (ESI) calcd $C_{25}H_{36}NO_4S+$ $[M + H]^+$: 446.2360, found: 446.2361



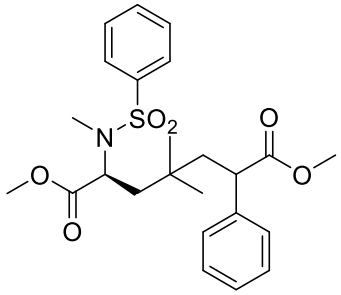
Tert-butyl 6-([1,1'-biphenyl]-4-yl)-4,4-dimethyl-6-(N-methylphenylsulfonamido)hexanoate (12c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~4:1) afforded 45.9 mg of the title compound **12c** (light yellow oil; 44% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.62 (m, 2H), 7.49 – 7.44 (m, 2H), 7.43 – 7.32 (m, 7H), 7.29 (dd, *J* = 12.4, 6.5 Hz, 1H), 7.20 – 7.17 (m, 2H), 5.19 (dd, *J* = 8.5, 4.7 Hz, 1H), 2.69 (s, 3H), 2.14 – 1.99 (m, 2H), 1.99 – 1.89 (m, 1H), 1.58 – 1.53 (m, 1H), 1.42 (t, *J* = 8.3 Hz, 2H), 1.34 (s, 9H), 0.80 (s, 3H), 0.71 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 140.6, 140.5, 140.1, 138.0, 132.3, 128.9, 128.8, 128.7, 127.5, 127.3, 127.0, 126.9, 80.2, 57.1, 42.5, 37.8, 32.8, 30.7, 29.3, 28.1, 27.0, 26.9

HRMS (ESI) calcd $C_{31}H_{40}NO_4S^+$ $[M + H]^+$: 522.2673, found: 522.2677



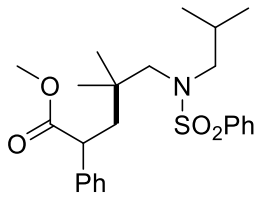
Dimethyl (2S)-4,4-dimethyl-2-(N-methylphenylsulfonamido)-6-phenylheptanedioate (13c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (8:1~4:1) afforded 38.8 mg of the title compound **13c** (colorless oil; 42% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 – 7.75 (m, 2H), 7.64 – 7.56 (m, 1H), 7.56 – 7.47 (m, 2H), 7.38 – 7.31 (m, 4H), 7.30 – 7.22 (m, 1H), 4.80 – 4.66 (m, 1H), 3.73 – 3.62 (m, 4H), 3.38 (d, *J* = 16.4 Hz, 3H), 2.87 (d, *J* = 3.0 Hz, 3H), 2.39 (ddd, *J* = 23.6, 14.2, 8.9 Hz, 1H), 1.89 – 1.74 (m, 2H), 1.74 – 1.64 (m, 1H), 1.55 (ddd, *J* = 14.5, 7.1, 3.3 Hz, 1H), 1.00 (d, *J* = 2.1 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9, 171.1, 140.4, 138.6, 132.5, 128.7, 128.7, 128.7, 127.8, 127.8, 127.4, 127.4, 127.2, 55.8, 55.7, 52.2, 51.8, 47.4, 47.3, 45.9, 45.7, 40.9, 40.8, 33.6, 33.6, 30.3, 26.3, 26.3, 26.0.

HRMS (ESI) calcd $C_{24}H_{32}NO_6S^+$ $[M + H]^+$: 462.1945, found: 462.1942



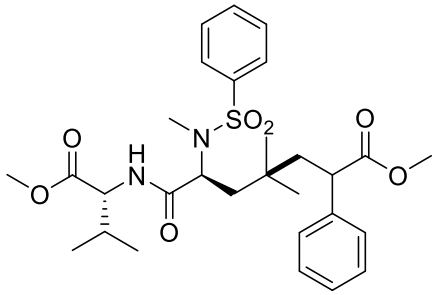
Methyl 5-(N-isobutylphenylsulfonamido)-4,4-dimethyl-2-phenylpentanoate (14c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~4:1) afforded 27.6 mg of the title compound **14c** (colorless oil; 32% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.1 Hz, 2H), 7.61 – 7.54 (m, 1H), 7.51 (t, *J* = 7.5 Hz, 2H), 7.35 (d, *J* = 4.3 Hz, 4H), 7.31 – 7.27 (m, 1H), 3.74 (dd, *J* = 8.4, 3.4 Hz, 1H), 3.67 (d, *J* = 1.2 Hz, 3H), 3.12 – 2.99 (m, 2H), 2.96 (d, *J* = 7.5 Hz, 2H), 2.38 (dd, *J* = 13.5, 9.2 Hz, 1H), 2.08 (dp, *J* = 13.4, 6.6 Hz, 1H), 1.72 (dd, *J* = 14.3, 3.1 Hz, 1H), 1.01 (d, *J* = 2.7 Hz, 6H), 0.75 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 140.4, 139.9, 132.3, 128.9, 128.7, 127.9, 127.5, 127.3, 58.7, 57.9, 52.2, 47.4, 44.4, 36.4, 26.4, 25.9, 25.6, 20.1.

HRMS (ESI) calcd $C_{24}H_{34}NO_4S^+$ $[M + H]^+$: 432.2203, found: 432.2211



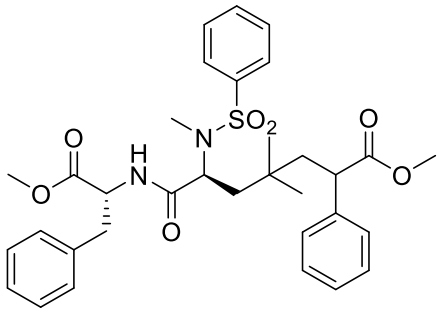
Methyl (6S)-7-(((R)-1-methoxy-3-methyl-1-oxobutan-2-yl)amino)-4,4-dimethyl-6-(N-methylphenylsulfonamido)-7-oxo-2-phenylheptanoate (16c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~3:1) afforded 70.7 mg of the title compound **16c** (white solid; 63% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.75 (m, 2H), 7.55 (ddq, *J* = 34.9, 21.4, 7.2, 6.7 Hz, 3.5H), 7.31 (d, *J* = 8.5 Hz, 1H), 7.25 (td, *J* = 9.3, 8.5, 4.2 Hz, 3H), 6.67 (dd, *J* = 43.4, 8.3 Hz, 1H), 4.55 – 4.37 (m, 1.5H), 4.30 (d, *J* = 9.4 Hz, 0.5H), 3.74 – 3.78 (m, 0.5H), 3.73 (d, *J* = 1.7 Hz, 1.5H), 3.70 (d, *J* = 1.7 Hz, 1.5H), 3.62 (d, *J* = 1.7 Hz, 1.5H), 3.61 (d, *J* = 1.7 Hz, 2H), 3.58 – 3.53 (m, 0.5H), 2.82 (dd, *J* = 20.9, 1.8 Hz, 3H), 2.36 – 2.01 (m, 4H), 1.57 – 1.48 (m, 0.5H), 1.47 – 1.37 (m, 0.5H), 1.03 – 0.92 (m, 7H), 0.73 (s, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 174.9, 171.9, 171.8, 169.6, 169.1, 140.4, 140.3, 139.6, 139.5, 132.9, 132.8, 129.2, 129.2, 128.6, 128.5, 127.8, 127.1, 127.1, 126.9, 57.3, 57.2, 55.7, 52.2, 52.1, 47.4, 47.3, 45.9, 45.6, 39.3, 39.1, 32.9, 32.9, 31.1, 30.9, 30.0, 29.8, 26.4, 26.4, 26.2, 19.1, 18.9, 17.5, 17.4.

HRMS (ESI) calcd $C_{29}H_{41}N_2O_7S^+$ $[M + H]^+$: 561.2629, found: 561.2624



Methyl (6S)-7-(((R)-1-methoxy-1-oxo-3-phenylpropan-2-yl)amino)-4,4-dimethyl-

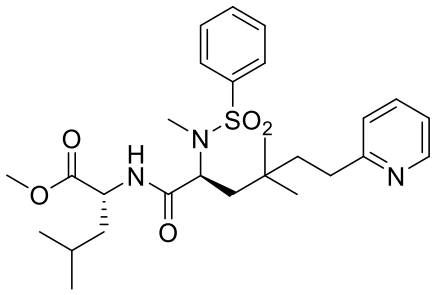
6-(N-methylphenylsulfonamido)-7-oxo-2-phenylheptanoate (17c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~3:1) afforded 68.2 mg of the title compound **17c** (light yellow solid; 56% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 10.8, 7.9 Hz, 2H), 7.67 – 7.50 (m, 2H), 7.45 (t, *J* = 7.7 Hz, 1H), 7.41 – 7.30 (m, 4H), 7.29 (s, 1H), 7.19-7.28 (m, 5H), 6.61 (dd, *J* = 61.8, 8.3 Hz, 1H), 4.78 (tt, *J* = 8.5, 4.8 Hz, 1H), 4.41 (dd, *J* = 8.5, 3.6 Hz, 0.5 H), 4.22 (d, *J* = 9.4 Hz, 0.5 H), 3.71 (s, 3 H), 3.61 (d, *J* = 1.9 Hz, 3H), 3.57-3.60 (m, 0.5H), 3.54 (dd, *J* = 8.7, 3.9 Hz, 0.5 H), 3.19 (dt, *J* = 13.6, 4.4 Hz, 1H), 2.99 (dt, *J* = 14.2, 7.4 Hz, 1H), 2.63 (d, *J* = 29.1 Hz, 3H), 2.30 (dd, *J* = 14.3, 8.7 Hz, 0.5H), 2.09 – 2.15 (d, *J* = 8.5 Hz, 0.5H), 2.02 – 2.05 (m, 0.5H), 1.51 (dd, *J* = 14.2, 3.9 Hz, 0.5H), 1.39 (dd, *J* = 14.2, 4.0 Hz, 0.5H), 1.29 (t, *J* = 7.1 Hz, 0.5H), 0.75-1.05 (m, 3H)), 0.74 – 0.60 (m, 4.5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 174.9, 171.6, 171.4, 169.2, 168.6, 140.4, 140.36, 139.6, 139.3, 135.8, 135.7, 132.9, 132.8, 129.4, 129.2, 129.1, 128.7, 128.7, 128.7, 128.6, 127.8, 127.8, 127.1, 127.1, 127.1, 127.1, 127.1, 60.4, 55.6, 53.5, 53.2, 52.3, 52.2, 52.1, 47.4, 47.2, 45.9, 45.7, 38.9, 38.7, 38.1, 38.1, 32.9, 32.8, 29.9, 29.7, 26.5, 26.5, 26.4, 26.2.

HRMS (ESI) calcd $C_{33}H_{41}N_2O_7S^+$ $[M + H]^+$: 609.2629, found: 609.2628



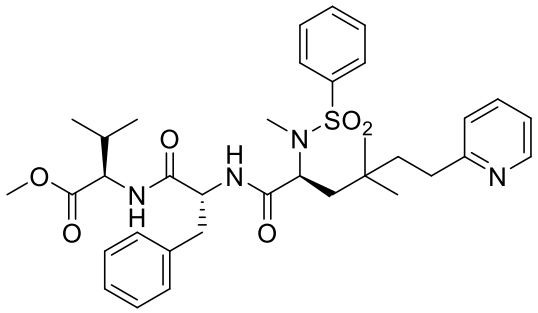
Methyl ((S)-4,4-dimethyl-2-(N-methylphenylsulfonamido)-6-(pyridin-2-yl)hexanoyl)-D-leucinate (18c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~3:1) afforded 48.7 mg of the title compound **18c** (light yellow oil; 47% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 4.4 Hz, 1H), 7.82 (d, *J* = 7.5 Hz, 2H), 7.67 – 7.51 (m, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.15 (dd, *J* = 10.9, 6.2 Hz, 3H), 4.55 (dd, *J* = 7.4, 4.5 Hz, 1H), 4.48 (td, *J* = 9.1, 5.3 Hz, 1H), 3.68 (s, 3H), 2.96 (s, 3H), 2.79 – 2.64 (m, 2H), 2.19 (dd, *J* = 14.2, 7.5 Hz, 1H), 1.76 – 1.46 (m, 6H), 1.00 – 0.92 (m, 10H), 0.89 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 170.1, 162.7, 148.9, 139.5, 136.7, 132.7, 129.1, 127.0, 122.9, 121.1, 55.5, 52.2, 50.8, 42.1, 40.8, 38.6, 32.7, 30.2, 27.1, 26.9, 24.7, 22.9, 21.7.

HRMS (ESI) calcd $C_{27}H_{40}N_3O_5S^+$ $[M + H]^+$: 518.2683, found: 518.2690



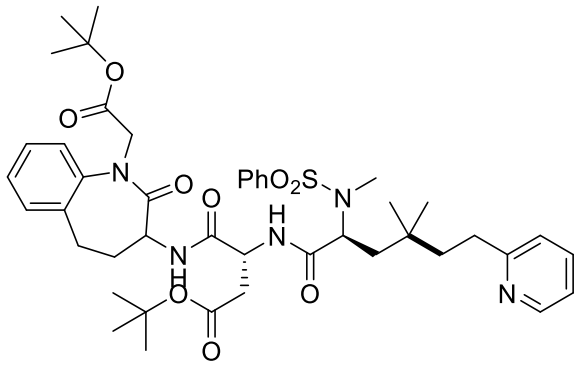
Methyl ((S)-4,4-dimethyl-2-(N-methylphenylsulfonamido)-6-(pyridin-2-yl)hexanoyl)-D-phenylalanyl-D-valinate (19c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~1:1) afforded 74.3 mg of the title compound **19c** (light yellow solid; 57% yield).

^{1}H NMR (400 MHz, CD_3COCD_3) δ 8.51 (dd, *J* = 4.9, 0.8 Hz, 1H), 7.90 – 7.80 (m, 2H), 7.71 – 7.63 (m, 3H), 7.56 (t, *J* = 7.6 Hz, 2H), 7.42 (s, 1H), 7.32 – 7.27 (m, 4H), 7.27 – 7.22 (m, 2H), 7.18 (dd, *J* = 7.0, 5.4 Hz, 1H), 4.73 – 4.59 (m, 2H), 4.31 (dd, *J* = 8.5, 5.7 Hz, 1H), 3.67 (s, 3H), 2.92 – 2.81 (m, 2H), 2.80 (s, 3H), 2.73 – 2.64 (m, 2H), 2.08 (dt, *J* = 4.4, 2.2 Hz, 2H), 2.06 – 2.01 (m, 1H), 1.66 – 1.59 (m, 1H), 1.57 – 1.51 (m, 1H), 0.93 (d, *J* = 5.7 Hz, 7H), 0.81 (d, *J* = 6.7 Hz, 7H).

^{13}C NMR (101 MHz, CD_3COCD_3) δ 171.6, 170.6, 169.7, 162.7, 149.1, 139.7, 137.4, 136.3, 132.6, 129.4, 129.2, 128.3, 127.2, 126.4, 122.6, 120.9, 57.4, 55.8, 54.4, 51.3, 42.5, 39.0, 38.2, 32.4, 30.6, 26.4, 18.4, 17.5.

HRMS (ESI) calcd $C_{35}H_{47}N_4O_6S^+$ $[M + H]^+$: 651.3211, found: 651.3202



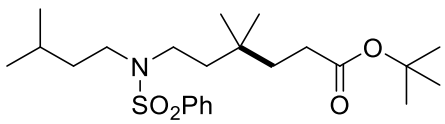
Tert-butyl (3R)-4-((1-(2-(tert-butoxy)-2-oxoethyl)-2-oxo-2,3,4,5-tetrahydro-1H-benzo[b]azepin-3-yl)amino)-3-((S)-4,4-dimethyl-2-(N-methylphenylsulfonamido)-6-(pyridin-2-yl)hexanamido)-4-oxobutanoate (20c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~1:3) afforded 88.4 mg of the title compound **20c** (grey solid; 53% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 – 8.54 (m, 1H), 8.29 – 8.10 (m, 1H), 8.04 – 7.83 (m, 2H), 7.70 (qd, *J* = 7.8, 1.8 Hz, 1H), 7.59 – 7.48 (m, 2H), 7.45 (ddd, *J* = 12.6, 7.5, 3.9 Hz, 3H), 7.42 – 7.36 (m, 2H), 7.29 (ddd, *J* = 7.8, 5.6, 2.6 Hz, 2H), 7.24 – 7.19 (m, 1H), 4.71 – 4.67 (m, 1H), 4.67 – 4.63 (m, 2H), 4.46 – 4.32 (m, 2H), 3.49 – 3.31 (m, 2H), 3.02 (s, 3H), 2.77 – 2.72 (m, 2H), 2.72 – 2.67 (m, 2H), 2.63 – 2.51 (m, 1H), 2.47 (dd, *J* = 16.3, 7.3 Hz, 1H), 2.13 – 1.97 (m, 6H), 1.70 – 1.53 (m, 4H), 1.44 (d, *J* = 4.0 Hz, 9H), 1.43 (q, *J* = 2.0 Hz, 4H), 1.41 (s, 9H), 1.37 – 1.27 (m, 2H), 1.01 – 0.96 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 169.5, 169.1, 167.9, 162.7, 149.3, 141.2, 139.3, 136.5, 135.8, 132.5, 129.4, 129.0, 127.9, 127.4, 126.9, 122.8, 122.6, 121.0, 81.2, 80.2, 55.5, 50.7, 49.6, 49.5, 41.5, 39.3, 36.9, 35.6, 32.8, 32.5, 30.0, 27.7, 27.3, 26.9, 26.6.

HRMS (ESI) calcd $C_{44}H_{60}N_5O_9S^+$ $[M + H]^+$: 834.4106, found: 834.4115



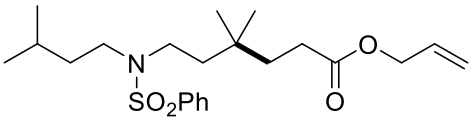
Tert-butyl 6-(N-isopentylphenylsulfonamido)-4,4-dimethylhexanoate (21c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 52.9 mg of the title compound **21c** (colorless oil; 62% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.1 Hz, 2H), 7.54 – 7.37 (m, 3H), 3.05 (ddd, *J* = 12.3, 9.2, 6.2 Hz, 4H), 2.13 – 2.01 (m, 2H), 1.50 (dt, *J* = 20.1, 6.7 Hz, 1H), 1.40 (dd, *J* = 6.7, 4.0 Hz, 2H), 1.37 (d, *J* = 3.2 Hz, 9H), 1.36 – 1.30 (m, 4H), 0.85 – 0.75 (m, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 140.0, 132.3, 129.1, 127.1, 80.2, 46.5, 43.8, 39.9, 37.3, 36.4, 31.9, 30.6, 28.1, 26.6, 25.7, 22.4.

HRMS (ESI) calcd $C_{23}H_{40}NO_4S^+$ $[M + H]^+$: 426.2673, found: 426.2677



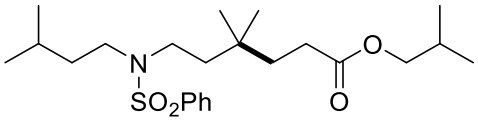
Allyl 6-(N-isopentylphenylsulfonamido)-4,4-dimethylhexanoate (22c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 48.4 mg of the title compound **22c** (colorless oil; 59% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.5 Hz, 2H), 7.63 – 7.48 (m, 3H), 5.94 (ddt, *J* = 16.5, 11.1, 5.7 Hz, 1H), 5.30 (dd, *J* = 31.3, 13.8 Hz, 2H), 4.60 (d, *J* = 5.6 Hz, 2H), 3.25 – 3.04 (m, 4H), 2.36 – 2.23 (m, 2H), 1.66 – 1.51 (m, 3H), 1.51 – 1.32 (m, 4H), 0.93 – 0.85 (m, 12H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 140.0, 132.3, 132.2, 129.1, 127.1, 118.3, 65.1, 46.5, 43.8, 39.8, 37.3, 36.3, 31.9, 29.3, 26.5, 25.7, 22.4.

HRMS (ESI) calcd $C_{22}H_{36}NO_4S^+$ $[M + H]^+$: 410.2360, found: 410.2366



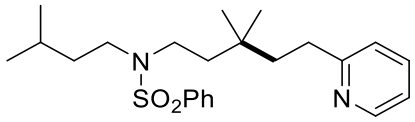
Isobutyl 6-(N-isopentylphenylsulfonamido)-4,4-dimethylhexanoate (23c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 48.6 mg of the title compound **23c** (colorless oil; 57% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.9 Hz, 2H), 7.66 – 7.47 (m, 3H), 3.88 (d, *J* = 6.7 Hz, 2H), 3.30 – 3.05 (m, 4H), 2.28 (dd, *J* = 10.0, 6.9 Hz, 2H), 2.05 – 1.85 (m, 1H), 1.62 (dd, *J* = 13.3, 6.7 Hz, 1H), 1.55 (dd, *J* = 9.6, 7.4 Hz, 2H), 1.51 – 1.44 (m, 2H), 1.44 – 1.34 (m, 2H), 1.01 – 0.89 (m, 18H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.2, 140.0, 132.3, 129.1, 127.1, 70.6, 46.5, 43.8, 39.9, 37.3, 36.4, 31.9, 29.4, 27.7, 26.5, 25.7, 22.4, 19.1.

HRMS (ESI) calcd $C_{23}H_{40}NO_4S^+$ $[M + H]^+$: 426.2673, found: 426.2670



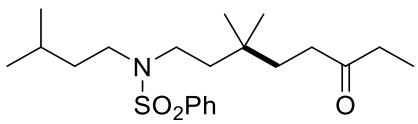
N-(3,3-dimethyl-5-(pyridin-2-yl)pentyl)-N-isopentylbenzenesulfonamide (24c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 55.65 mg of the title compound **24c** (light yellow oil; 69% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (t, *J* = 5.3 Hz, 1H), 7.83 (t, *J* = 6.5 Hz, 2H), 7.65 – 7.55 (m, 2H), 7.51 (t, *J* = 7.4 Hz, 2H), 7.22 – 7.05 (m, 2H), 3.23 – 3.14 (m, 4H), 2.79 – 2.67 (m, 2H), 1.67 – 1.49 (m, 5H), 1.42 (m, 2H), 0.97 (s, 6H), 0.90 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 149.2, 140.1, 136.4, 132.3, 129.0, 127.1, 122.7, 120.9, 46.4, 43.9, 42.0, 39.9, 37.3, 33.1, 32.4, 26.9, 25.7, 22.4.

HRMS (ESI) calcd $C_{23}H_{35}N_2O_2S^+$ $[M + H]^+$: 403.2414, found: 403.2409



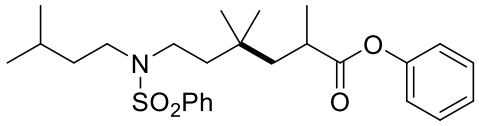
N-(3,3-dimethyl-6-oxooctyl)-N-isopentylbenzenesulfonamide (25c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 48.2 mg of the title compound **25c** (colorless oil; 63% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.4 Hz, 2H), 7.63 – 7.48 (m, 3H), 3.22 – 3.06 (m, 4H), 2.47 (q, *J* = 7.3 Hz, 2H), 2.42 – 2.34 (m, 2H), 1.58 (ddd, *J* = 20.0, 13.3, 6.7 Hz, 1H), 1.52 – 1.44 (m, 4H), 1.40 (dd, *J* = 15.2, 7.1 Hz, 2H), 1.08 (t, *J* = 7.3 Hz, 3H), 0.96 – 0.83 (m, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 211.8, 139.9, 132.3, 129.1, 127.1, 46.6, 44.0, 40.0, 37.4, 37.2, 36.2, 34.9, 31.8, 26.8, 25.7, 22.4.

HRMS (ESI) calcd $C_{21}H_{36}NO_3S^+$ $[M + H]^+$: 382.2410, found: 382.2409



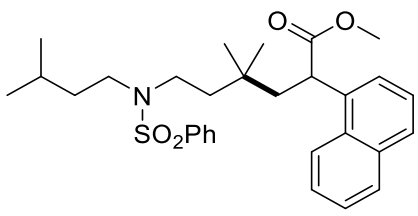
Phenyl 6-(N-isopentylphenylsulfonamido)-2,4,4-trimethylhexanoate (26c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 57.9 mg of the title compound **26c** (colorless oil; 63% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.6 Hz, 2H), 7.62 – 7.56 (m, 1H), 7.53 (dd, *J* = 8.4, 6.6 Hz, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.26 (t, *J* = 7.4 Hz, 1H), 7.13 – 7.04 (m, 2H), 3.32 – 3.09 (m, 4H), 2.75 (ddp, *J* = 11.5, 7.1, 4.4, 3.7 Hz, 1H), 2.02 (dd, *J* = 14.3, 9.2 Hz, 1H), 1.57 (ddd, *J* = 17.3, 11.4, 7.1 Hz, 3H), 1.49 – 1.24 (m, 7H), 0.98 (d, *J* = 5.9 Hz, 6H), 0.90 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.1, 150.8, 140.1, 132.4, 129.4, 129.1, 127.1, 125.8, 46.4, 45.6, 43.8, 40.6, 37.3, 35.8, 32.8, 26.8, 26.6, 25.7, 22.4, 22.4, 20.5.

HRMS (ESI) calcd $C_{26}H_{38}NO_4S^+$ $[M + H]^+$: 460.2516, found: 460.2515



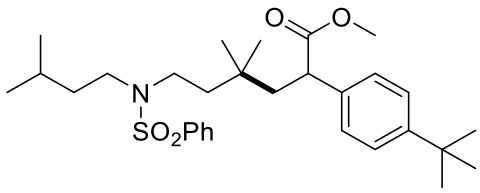
Methyl 6-(N-isopentylphenylsulfonamido)-4,4-dimethyl-2-(naphthalen-1-yl)hexanoate (27c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 45.9 mg of the title compound **27c** (white solid; 45% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.83 – 7.76 (m, 3H), 7.61 – 7.53 (m, 4H), 7.52 – 7.46 (m, 3H), 4.48 (d, *J* = 8.0 Hz, 1H), 3.65 (s, 3H), 3.21 – 3.05 (m, 4H), 2.53 (dd, *J* = 13.8, 8.8 Hz, 1H), 1.66 (d, *J* = 11.0 Hz, 1H), 1.62 – 1.49 (m, 3H), 1.38 (dd, *J* = 14.4, 6.8 Hz, 2H), 0.97 (d, *J* = 14.1 Hz, 6H), 0.90 (d, *J* = 6.5 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.2, 140.0, 136.8, 134.1, 132.3, 130.9, 129.1, 129.0, 127.8, 127.1, 126.5, 125.7, 125.6, 125.4, 123.1, 52.3, 46.5, 45.3, 43.9, 40.6, 37.4, 33.2, 26.7, 26.6, 25.7, 22.4.

HRMS (ESI) calcd $C_{30}H_{40}NO_4S^+$ $[M + H]^+$: 510.2673, found: 510.2669



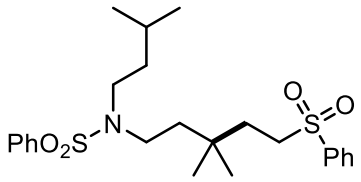
Methyl 2-(4-(tert-butyl)phenyl)-6-(N-isopentylphenylsulfonamido)-4,4-dimethylhexanoate (28c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 74.3 mg of the title compound **28c** (colorless oil; 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.3 Hz, 2H), 7.63 – 7.48 (m, 3H), 7.35 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 8.3 Hz, 2H), 3.70 – 3.62 (m, 4H), 3.15 (tt, *J* = 10.3, 5.4 Hz, 4H), 2.31 (dd, *J* = 14.1, 9.5 Hz, 1H), 1.63 – 1.55 (m, 1H), 1.54 – 1.46 (m, 2H), 1.41 (q, *J* = 6.7 Hz, 2H), 1.33 (s, 9H), 0.93 (s, 3H), 0.91 (d, *J* = 3.4 Hz, 5H), 0.89 (s, 3H), 0.86 – 0.80 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 149.9, 140.0, 137.4, 132.2, 128.9, 127.2, 127.0, 125.5, 52.0, 46.7, 46.4, 45.2, 43.8, 40.2, 37.3, 34.3, 32.7, 31.2, 26.6, 25.6, 22.3.

HRMS (ESI) calcd $C_{19}H_{30}NO_3$+ $[M + H]^+$: 516.3142, found: 516.3151.



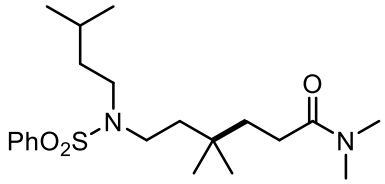
N-(3,3-dimethyl-5-(phenylsulfonyl)pentyl)-N-isopentylbenzenesulfonamide (29c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 45.8 mg of the title compound **29c** (colorless oil; 49% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.89 (m, 2H), 7.86 – 7.74 (m, 2H), 7.72 – 7.63 (m, 1H), 7.62 – 7.47 (m, 5H), 3.20 – 2.92 (m, 6H), 1.72 – 1.32 (m, 7H), 0.88 (d, *J* = 7.1 Hz, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.82, 139.46, 133.85, 132.58, 129.48, 129.26, 128.12, 127.22, 52.22, 47.21, 44.04, 40.27, 37.60, 32.83, 32.07, 27.03, 25.80, 22.54.

HRMS (ESI) calcd $C_{24}H_{36}NO_4S_2^+$ $[M + H]^+$: 466.2080, found: 466.2081.



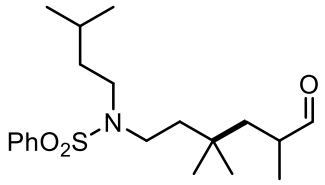
6-(N-isopentylphenylsulfonamido)-N,N,4,4-tetramethylhexanamide (30c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (1:3~1:1) afforded 60.2 mg of the title compound **30c** (colorless oil; 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.64 (m, 2H), 7.57 – 7.36 (m, 3H), 3.11 – 2.79 (m, 10H), 2.27 – 2.10 (m, 2H), 1.53 – 1.38 (m, 5H), 1.31 (q, *J* = 7.0 Hz, 2H), 0.89 – 0.72 (m, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.42, 140.15, 132.44, 129.17, 127.17, 46.86, 44.28, 40.36, 37.57, 37.46, 36.54, 35.66, 32.06, 28.19, 27.00, 25.85, 22.54.

HRMS (ESI) calcd $C_{21}H_{37}N_2O_3S^+$ $[M + H]^+$: 397.2519, found: 397.2522.



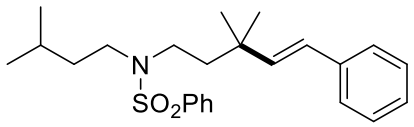
N-isopentyl-N-(3,3,5-trimethyl-6-oxohexyl)benzenesulfonamide (31c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (1:10~1:8) afforded 48.45 mg of the title compound **31c** (colorless oil; 66% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (d, *J* = 2.9 Hz, 1H), 7.82 – 7.62 (m, 2H), 7.58 – 7.37 (m, 3H), 3.19 – 2.90 (m, 4H), 2.44 (dd, *J* = 16.3, 2.7 Hz, 1H), 2.05 (ddd, *J* = 16.4, 10.3, 3.0 Hz, 1H), 1.85 (dqd, *J* = 9.8, 6.8, 2.8 Hz, 1H), 1.53 – 1.28 (m, 5H), 0.91 – 0.69 (m, 16H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 202.94, 140.17, 132.49, 129.19, 127.20, 46.78, 46.57, 43.91, 38.77, 37.55, 35.34, 34.64, 25.83, 24.44, 24.18, 22.57, 22.53, 15.04.

HRMS (ESI) calcd $C_{20}H_{34}NO_3S^+$ $[M + H]^+$: 368.2254, found: 368.2254.



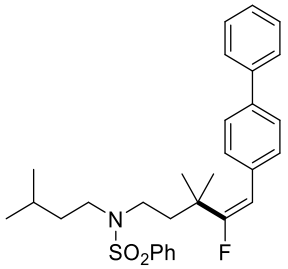
(E)-N-(3,3-dimethyl-5-phenylpent-4-en-1-yl)-N-isopentylbenzenesulfonamide (32c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 52.8 mg of the title compound **32c** (light yellow oil; 66% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 16.8, 7.4 Hz, 2H), 7.64 – 7.50 (m, 2H), 7.50 – 7.31 (m, 4H), 7.29 – 7.12 (m, 2H), 6.64 – 5.39 (m, 2H), 3.23 – 3.02 (m, 4H), 1.73 – 1.66 (m, 2H), 1.62 – 1.53 (m, 2H), 1.42 (d, *J* = 7.1 Hz, 1H), 1.13 (s, 4H), 0.96 – 0.87 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.0, 139.8, 138.9, 137.5, 132.3, 129.0, 128.7, 128.61, 127.7, 127.1, 126.8, 126.5, 126.1, 77.4, 77.1, 76.7, 46.7, 46.4, 44.5, 42.3, 41.4, 37.3, 35.6, 29.7, 29.0, 27.2, 25.7, 22.4, 1.1.

HRMS (ESI) calcd $C_{24}H_{34}NO_2S^+$ $[M + H]^+$: 400.2305, found: 400.2313



(E)-N-(5-([1,1'-biphenyl]-4-yl)-4-fluoro-3,3-dimethylpent-4-en-1-yl)-N-isopentylbenzenesulfonamide (33c)

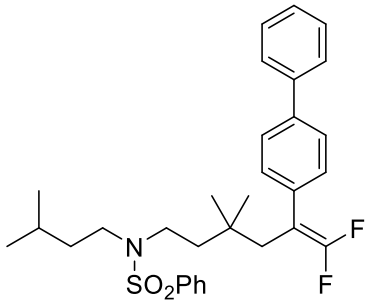
Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 71.2 mg of the title compound **33c** (white solid; 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.9 Hz, 2H), 7.63 (t, *J* = 9.5 Hz, 3H), 7.57 (d, *J* = 7.1 Hz, 4H), 7.49 (t, *J* = 7.3 Hz, 2H), 7.40 (t, *J* = 7.1 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 2H), 6.42 (d, *J* = 27.2 Hz, 1H), 3.28 – 3.16 (m, 4H), 1.76 – 1.68 (m, 2H), 1.62 (m, 1H), 1.45 (dd, *J* = 15.0, 6.9 Hz, 2H), 1.05 (s, 6H), 0.94 (d, *J* = 6.7 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.5, 140.0, 139.8, 132.3, 129.0, 128.8, 127.4, 127.1, 127.0, 126.5, 108.5, 108.2, 46.4, 44.3, 39.2, 38.6, 38.4, 37.2, 26.9, 26.9, 25.7, 22.4, 1.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -101.26, -101.34.

HRMS (ESI) calcd $C_{30}H_{37}FNO_2S^+$ $[M + H]^+$: 494.2524, found: 494.2532



N-(5-([1,1'-biphenyl]-4-yl)-6,6-difluoro-3,3-dimethylhex-5-en-1-yl)-N-isopentylbenzenesulfonamide (34c)

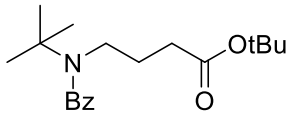
Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (20:1~8:1) afforded 68.2 mg of the title compound **34c** (yellow solid; 65% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.64 (m, 2H), 7.57 – 7.46 (m, 5H), 7.46 – 7.35 (m, 4H), 7.33 – 7.23 (m, 3H), 3.12 – 2.81 (m, 4H), 2.28 (t, *J* = 2.3 Hz, 2H), 1.44 (dh, *J* = 13.6, 6.9 Hz, 1H), 1.39 – 1.28 (m, 2H), 1.26 – 1.20 (m, 2H), 0.87 – 0.63 (m, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.4, 140.4, 140.1, 139.9, 132.3, 129.0, 128.8, 128.7, 127.4, 127.1, 126.9, 77.3, 77.0, 76.7, 46.2, 43.8, 40.3, 40.0, 37.3, 34.6, 26.8, 25.7, 22.4, 1.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ -91.78, -91.90, -91.98, -92.10.

HRMS (ESI) calcd $C_{31}H_{37}F_2NO_2S$ $[M + H]^+$: 525.2513, found: 525.2519



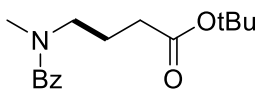
Tert-butyl 4-(N-(tert-butyl)benzamido)butanoate (36c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~3:1) afforded 54.4 mg of the title compound **36c** (colorless oil; 85% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.32 (m, 5H), 3.40 – 3.22 (m, 2H), 1.95 (t, *J* = 7.1 Hz, 2H), 1.78 (p, *J* = 7.2 Hz, 2H), 1.59 (s, 9H), 1.40 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 171.9, 139.6, 128.7, 128.4, 126.1, 80.5, 57.0, 46.9, 32.8, 28.9, 28.0, 27.2.

HRMS (ESI) calcd $C_{19}H_{30}NO_3^+$ $[M + H]^+$: 320.2220, found: 320.2218



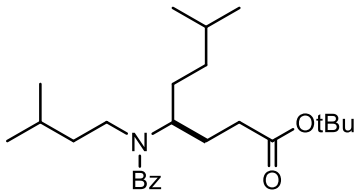
Tert-butyl 4-(N-methylbenzamido)butanoate (37c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~3:1) afforded 41.5 mg of the title compound **37c** (colorless oil; 75% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.35 (m, 5H), 3.75 (s, 1H), 3.14 (t, *J* = 47.9 Hz, 4H), 2.56 (td, *J* = 15.1, 7.4 Hz, 1H), 2.28 (s, 2H), 2.15 (td, *J* = 12.9, 6.1 Hz, 1H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 171.4, 134.5, 130.5, 129.0, 126.5, 81.0, 77.4, 77.3, 77.1, 76.7, 53.8, 51.9, 32.0, 28.0, 24.6.

HRMS (ESI) calcd $C_{16}H_{24}NO_3^+$ $[M + H]^+$: 278.1751, found: 278.1745



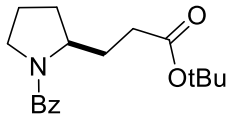
Tert-butyl (S)-4-(N-isopentylbenzamido)-7-methyloctanoate (38c)

Following General Procedure A, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (1:10~1:8) afforded 76.6 mg of the title compound **38c** (colorless oil; 95% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (dqt, *J* = 9.6, 5.9, 3.6 Hz, 5H), 3.63 – 2.91 (m, 3H), 2.32 – 2.08 (m, 2H), 2.08 – 1.77 (m, 2H), 1.74 – 1.43 (m, 6H), 1.38 (d, *J* = 6.0 Hz, 4H), 1.34 (s, 5H), 0.90 (dq, *J* = 6.8, 3.3 Hz, 6H), 0.72 – 0.51 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.46, 172.22, 139.22, 138.21, 137.47, 129.96, 129.16, 129.01, 128.53, 128.45, 128.23, 127.33, 126.81, 126.37, 80.73, 56.90, 43.33, 42.46, 40.04, 39.66, 37.83, 35.99, 32.91, 32.49, 29.83, 28.41, 28.24, 28.22, 27.07, 26.40, 25.36, 24.68, 23.16, 22.69, 22.49, 22.15, 1.15.

HRMS (ESI) calcd $C_{25}H_{42}NO_3^+$ $[M + H]^+$: 404.3159, found: 404.3156.

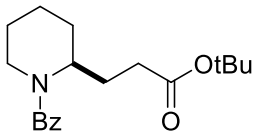


Tert-butyl (S)-3-(1-benzoylpyrrolidin-2-yl)propanoate (39c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (6:1~4:1) afforded 45.6 mg of the title compound **39c** (colorless oil; 75% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.54 (m, 2H), 7.37-7.42 (m, 3H), 4.45 – 4.23 (m, 1H), 3.53 – 3.32 (m, 2H), 2.30-2.45 (m, 2H), 2.15-2.27 (m, 1H), 2.05-2.14 (m, 1H), 1.85-1.97 (m, 1H), 1.81 – 1.62 (m, 3H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 170.3, 137.1, 129.8, 128.1, 127.3, 80.2, 56.6, 50.1, 32.5, 30.2, 29.3, 28.1, 24.9.



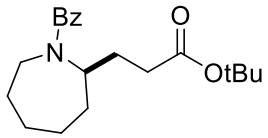
Tert-butyl 3-(1-benzoylpiperidin-2-yl)propanoate (40c)

Following General Procedure B, Purification by flash chromatography on silica gel with etroleum ether/ethyl acetate (6:1~4:1)) afforded 59.5 mg of the title compound **40c** (colorless oil; 94% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (m, 5H), 4.75 (m, 1H), 3.67 (m, 1H), 2.98 (m, 1H), 2.48 – 1.52 (m, 10H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 170.8, 136.8, 129.2, 128.5, 126.5, 80.4, 54.3, 47.9, 43.2, 37.1, 32.3, 28.1, 26.3, 24.9, 19.1.

HRMS (ESI) calcd $C_{19}H_{28}NO_3^+$ $[M + H]^+$: 318.2064, found: 318.2066



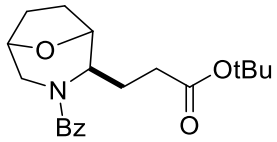
Tert-butyl (R)-3-(1-benzoylazepan-2-yl)propanoate (41c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~4:1) afforded 53.6 mg of the title compound **41c** (colorless oil; 81% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.31 (m, 5H), 4.72 (dq, J = 14.0, 6.9 Hz, 0.45H), 4.31 (dd, J = 13.9, 7.6 Hz, 0.62H), 3.72 (dt, J = 14.3, 7.2 Hz, 0.57H), 3.52 (dd, J = 15.3, 3.9 Hz, 0.47H), 3.00 (dd, J = 14.8, 11.3 Hz, 0.49H), 2.77 (ddd, J = 13.7, 10.4, 3.5 Hz, 0.57H), 2.46 – 2.27 (m, 1H), 2.23 – 1.90 (m, 3.5H), 1.81 (tt, J = 14.7, 7.6 Hz, 4H), 1.69 – 1.61 (m, 0.6H), 1.48 (s, 4H), 1.40 (s, 5H), 1.38 – 1.25 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 172.8, 172.1, 171.2, 137.8, 137.5, 128.7, 128.6, 128.5, 128.4, 126.4, 126.2, 80.5, 80.3, 56.7, 52.8, 43.9, 40.5, 34.6, 33.5, 32.4, 32.1, 30.4, 30.2, 29.7, 29.1, 28.1, 28.1, 27.4, 24.7, 24.6.

HRMS (ESI) calcd $C_{20}H_{30}NO_3^+$ $[M + H]^+$: 332.2220, found: 332.2227



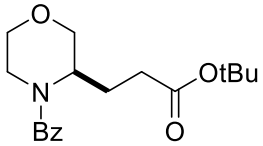
Tert-butyl 3-((2R)-3-benzoyl-8-oxa-3-azabicyclo[3.2.1]octan-2-yl)propanoate (42c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~3:1) afforded 58.8 mg of the title compound **42c** (white solid; 85% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 13.6 Hz, 5H), 4.48 (m, 0.74H), 4.43 (m, 0.27H), 4.32 – 4.25 (m, 0.75H), 4.13 – 4.26 (m, 1.3H), 3.57 (d, *J* = 13.0 Hz, 0.76H), 3.30 – 3.39 (m, 0.27H), 3.24 (d, *J* = 13.6 Hz, 0.27H), 3.18 (d, *J* = 13.0 Hz, 0.74H), 2.47 – 1.81 (m, 8H), 1.64 – 1.54 (m, 1H), 1.50 – 1.41 (s, 7H), 1.37 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 172.1, 171.8, 171.7, 136.0, 135.8, 129.6, 129.5, 128.7, 128.6, 126.7, 126.5, 80.6, 80.3, 77.4, 77.3, 77.1, 76.8, 76.5, 74.8, 74.6, 73.9, 60.0, 54.5, 50.3, 44.3, 32.1, 32.0, 28.1, 28.0, 27.7, 26.5, 25.7, 24.7.

HRMS (ESI) calcd $C_{20}H_{28}NO_4^+$ $[M + H]^+$: 346.2013, found: 346.2014



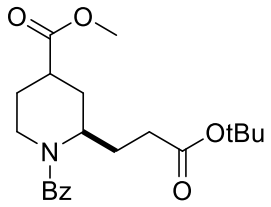
Tert-butyl (R)-3-(4-benzoylmorpholin-3-yl)propanoate (43c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate afforded 60.7 mg of the title compound **43c** (yellow solid; 95% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.32 (m, 5H), 4.86 – 4.18 (m, 1H), 4.09 – 3.08 (m, 6H), 2.13 (m, 4H), 1.43 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 135.6, 129.7, 128.6, 126.8, 80.6, 69.4, 67.1, 32.1, 28.1, 24.2.

HRMS (ESI) calcd $C_{18}H_{26}NO_4^+$ $[M + H]^+$: 320.1856, found: 320.1859.



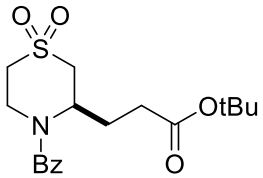
Methyl (2R)-1-benzoyl-2-(3-(tert-butoxy)-3-oxopropyl)piperidine-4-carboxylate (44c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~3:1) afforded 63.7 mg of the title compound **44c** (colorless oil; 85% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 5H), 4.97 (q, *J* = 5.3 Hz, 0.6H), 4.65 (d, *J* = 13.8 Hz, 0.4H), 3.89 (s, 0.4H), 3.66 (m, 3.60H), 3.11 (t, *J* = 13.4 Hz, 0.60H), 2.78 (tt, *J* = 26.9, 14.0 Hz, 1.40H), 2.42 – 2.23 (m, 1H), 2.11 – 1.91 (m, 3H), 1.81 (dt, *J* = 12.0, 6.3 Hz, 3H), 1.73 – 1.49 (m, 2H), 1.47 – 1.35 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9, 172.5, 171.8, 170.9, 170.7, 136.3, 129.5, 128.7, 128.5, 126.6, 126.5, 126.4, 80.5, 53.6, 51.9, 47.3, 41.9, 36.4, 35.9, 32.2, 32.1, 31.7, 31.1, 28.5, 28.1, 25.6, 24.9.

HRMS (ESI) calcd $C_{21}H_{30}NO_5^+$ $[M + H]^+$: 376.2118, found: 376.2112



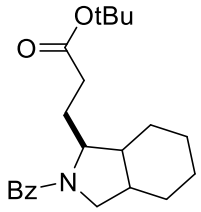
Tert-butyl (R)-3-(4-benzoyl-1,1-dioxidothiomorpholin-3-yl)propanoate (45c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (4:1~2:1) afforded 40.3 mg of the title compound **45c** (colorless oil; 55% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.45 (m, 3H), 7.42 (dd, *J* = 7.6, 1.3 Hz, 2H), 5.74 – 3.53 (m, 3H), 3.15 (t, *J* = 45.7 Hz, 4H), 2.68 – 2.48 (m, 1H), 2.29 (s, 2H), 2.16 (td, *J* = 13.4, 6.7 Hz, 1H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 134.5, 130.6, 129.1, 126.5, 81.1, 53.8, 52.0, 32.1, 28.1, 24.6.

HRMS (ESI) calcd $C_{18}H_{26}NO_5S^+$ $[M + H]^+$: 368.1526, found: 368.1523



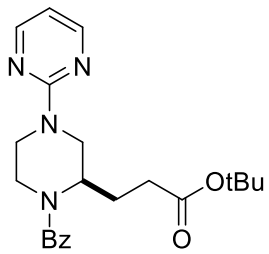
Tert-butyl 3-(2-benzoyloctahydro-1H-isoindol-1-yl)propanoate (46c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~3:1) afforded 59.9 mg of the title compound **46c** (colorless oil; 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 25.2 Hz, 5H), 4.54 – 3.15 (m, 3H), 2.49 (d, *J* = 87.0 Hz, 4H), 2.08 – 1.57 (m, 6H), 1.44 (s, 12H), 1.31 – 1.14 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 169.7, 137.1, 129.7, 128.2, 127.2, 80.2, 62.8, 55.0, 48.2, 42.8, 33.3, 33.0, 32.4, 29.5, 28.1, 26.2.

HRMS (ESI) calcd $C_{22}H_{32}NO_3^+$ $[M + H]^+$: 358.2377, found: 358.2380



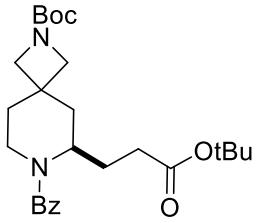
Tert-butyl 3-(1-benzoyl-4-(pyrimidin-2-yl)piperazin-2-yl)propanoate (47c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (3:1~1:1) afforded 61.7 mg of the title compound **47c** (light yellow oil; 79% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 4.7 Hz, 2H), 7.46 (d, *J* = 6.9 Hz, 5H), 6.54 (t, *J* = 4.7 Hz, 1H), 5.14 – 4.49 (m, 3H), 4.02 – 2.81 (m, 4H), 2.59 – 2.10 (m, 2H), 2.06 (d, *J* = 11.1 Hz, 2H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 157.8, 136.1, 129.7, 128.7, 126.8, 110.3, 80.5, 48.9, 46.0, 43.7, 43.1, 32.1, 28.1, 24.4.

HRMS (ESI) calcd $C_{22}H_{29}N_4O_3^+$ $[M + H]^+$: 397.2234, found: 397.2231



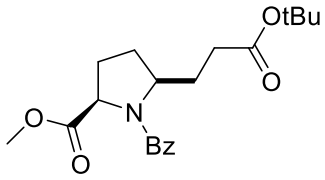
Tert-butyl (R)-7-benzoyl-6-(3-(tert-butoxy)-3-oxopropyl)-2,7-diazaspiro[3.5]nonane-2-carboxylate (48c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~3:1) afforded 83.5 mg of the title compound **48c** (light yellow oil; 91% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.31 (m, 5H), 5.36 – 2.57 (m, 7H), 2.21 (s, 2H), 1.92 (s, 3H), 1.69 (d, *J* = 78.1 Hz, 3H), 1.46 – 1.36 (m, 18H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 156.3, 136.2, 129.6, 128.6, 126.5, 80.7, 79.6, 77.3, 77.2, 37.8, 35.9, 32.6, 32.3, 29.7, 28.4, 28.1, 26.3.

HRMS (ESI) calcd $C_{26}H_{39}N_2O_5^+$ $[M + H]^+$: 459.2853, found: 459.2853



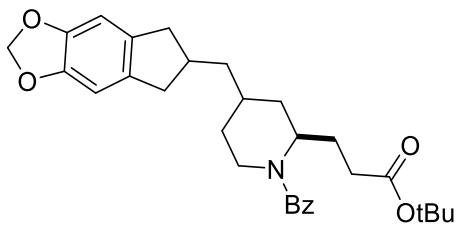
Methyl-(2R,5S)-1-benzoyl-5-(3-(tert-butoxy)-3-oxopropyl)pyrrolidine-2-carboxylate (49c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~3:1) afforded 42.5 mg of the title compound **49c** (colorless oil; 59% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.50 (m, 1H), 7.46 – 7.37 (m, 5H), 4.76 – 4.70 (m, 0.5H), 4.52 (dd, *J* = 17.9, 7.0 Hz, 1H), 4.14 (q, *J* = 7.7, 7.2 Hz, 0.5H), 3.81 (m, 2H), 3.71 (s, 0.5H), 3.43 (s, 1.5H), 2.48 – 2.33 (m, 2H), 2.26 – 2.16 (m, 1H), 2.09 (dt, *J* = 7.4, 4.5 Hz, 1H), 1.92 (dd, *J* = 13.3, 7.2 Hz, 1H), 1.80 (m, 2H), 1.48 (s, 5H), 1.38 (s, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 172.6, 171.7, 170.4, 137.1, 136.8, 129.9, 129.8, 128.5, 128.3, 126.9, 126.6, 80.6, 80.4, 61.9, 59.1, 58.9, 57.5, 52.4, 52.2, 32.8, 32.2, 30.0, 29.6, 29.2, 28.8, 28.1, 28.0, 27.4, 27.0.

HRMS (ESI) calcd $C_{20}H_{28}NO_5^+$ $[M + H]^+$: 362.1962, found: 362.1969



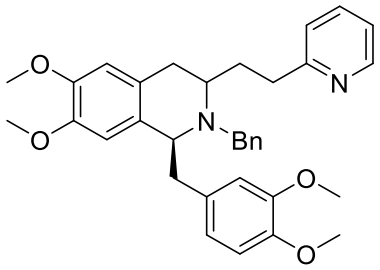
Tert-butyl 3-((2R)-1-benzoyl-4-((6,7-dihydro-5H-indeno[5,6-d][1,3]dioxol-6-yl)methyl)piperidin-2-yl)propanoate (50c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (3:1~1:1) afforded 79.5 mg of the title compound **50c** (white solid; 81% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 5H), 7.15 (s, 1H), 6.86 (s, 1H), 4.96 (s, 0.6H), 4.70 – 4.54 (m, 0.4H), 4.00 – 3.92 (m, 3H), 3.89 (d, *J* = 2.5 Hz, 3.4H), 3.60 (t, *J* = 11.5 Hz, 0.6H), 3.24 (d, *J* = 9.2 Hz, 1H), 3.14 (t, *J* = 13.2 Hz, 0.6H), 2.87 (t, *J* = 13.0 Hz, 0.4H), 2.70 (d, *J* = 15.9 Hz, 2H), 1.93 – 2.46 (m, 5H), 1.93 – 1.49 (m, 5H), 1.45 (s, 6H), 1.38 (s, 3H), 1.19 – 0.95 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.3, 172.8, 172.8, 172.1, 172.1, 171.1, 171.0, 170.95, 170.7, 155.5, 149.4, 148.6, 136.6, 129.3, 129.1, 128.6, 128.4, 126.6, 126.3, 107.3, 104.3, 80.6, 80.4, 77.3, 56.2, 56.1, 54.4, 48.1, 48.1, 45.2, 45.0, 44.9, 44.8, 42.8, 39.1, 39.0, 38.8, 38.7, 36.8, 35.9, 35.0, 33.5, 33.3, 33.1, 33.1, 32.7, 32.4, 32.2, 32.2, 31.6, 29.6, 29.3, 29.2, 29.1, 28.9, 28.1, 28.1, 26.0, 25.5, 25.4.

HRMS (ESI) calcd $C_{30}H_{38}NO_5^+$ [M + H]$^+$: 492.2744, found: 492.2745



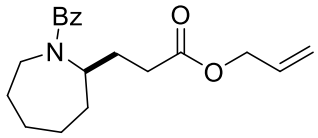
(1S)-2-benzyl-1-(3,4-dimethoxybenzyl)-6,7-dimethoxy-3-(2-(pyridin-2-yl)ethyl)-1,2,3,4-tetrahydroisoquinoline (51c)

Following General Procedure B and C, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (3:1~1:1) afforded 63.4 mg of the title compound **51c** (yellow oil; 59% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (dd, *J* = 5.2, 1.8 Hz, 1H), 7.73 (td, *J* = 7.7, 1.9 Hz, 1H), 7.43 – 7.28 (m, 4H), 7.27 – 7.22 (m, 1H), 7.19 (dd, *J* = 6.6, 3.0 Hz, 2H), 6.88 (d, *J* = 8.1 Hz, 1H), 6.76 (s, 1H), 6.69 (dd, *J* = 8.1, 1.9 Hz, 1H), 6.63 (d, *J* = 1.9 Hz, 1H), 6.36 (s, 1H), 4.27 (q, *J* = 7.1 Hz, 1H), 4.08 (d, *J* = 14.2 Hz, 1H), 4.02 (d, *J* = 2.9 Hz, 6H), 3.87 (dd, *J* = 8.3, 6.1 Hz, 1H), 3.83 (d, *J* = 3.9 Hz, 6H), 3.69 (dq, *J* = 11.3, 6.5, 4.5 Hz, 1H), 3.38 (d, *J* = 14.2 Hz, 1H), 3.24 (dt, *J* = 14.0, 7.9 Hz, 1H), 3.13 (dt, *J* = 14.1, 8.1 Hz, 2H), 2.95 – 2.81 (m, 2H), 2.74 (dd, *J* = 16.6, 4.5 Hz, 1H), 2.22 (q, *J* = 6.5, 5.1 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 149.2, 148.5, 147.3, 147.2, 146.9, 136.5, 133.0, 129.2, 129.1, 128.5, 128.0, 126.5, 126.4, 123.0, 121.8, 121.1, 112.7, 111.4, 111.4, 110.8, 62.4, 56.0, 55.8, 55.8, 55.7, 50.9, 49.1, 43.0, 35.3, 33.3, 29.3.

HRMS (ESI) calcd $C_{34}H_{39}N_2O_4^+$ [M + H]$^+$: 539.2904, found: 539.2901



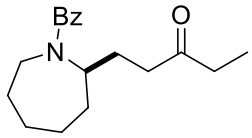
Allyl (R)-3-(1-benzoylazepan-2-yl)propanoate (52c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~3:1) afforded 40.9 mg of the title compound **52c** (colorless oil; 65% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.31 (m, 5H), 5.92 (dddd, *J* = 30.5, 16.6, 11.0, 5.8 Hz, 1H), 5.40 – 5.21 (m, 2H), 4.76 (dq, *J* = 14.0, 7.5 Hz, 0.5H), 4.62 (d, *J* = 5.7 Hz, 1H), 4.49 (h, *J* = 7.4, 6.6 Hz, 1H), 4.31 (d, *J* = 13.6 Hz, 0.5H), 3.79 (dt, *J* = 15.0, 7.2 Hz, 0.5H), 3.54 (d, *J* = 15.6 Hz, 0.5H), 3.00 (dd, *J* = 14.7, 11.1 Hz, 0.5H), 2.76 (ddd, *J* = 13.6, 9.4, 4.6 Hz, 0.5H), 2.51 (td, *J* = 8.6, 3.2 Hz, 1H), 2.16 (ddp, *J* = 22.4, 15.1, 7.9 Hz, 2H), 2.02 – 1.59 (m, 6H), 1.57 – 1.18 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 172.9, 172.3, 171.3, 137.7, 137.3, 132.2, 132.0, 128.8, 128.7, 128.5, 128.4, 126.4, 126.2, 118.4, 118.2, 65.2, 65.2, 56.4, 52.8, 43.9, 40.5, 34.6, 33.6, 31.2, 30.7, 30.3, 30.2, 29.6, 29.1, 27.4, 24.7, 24.7.

HRMS (ESI) calcd $C_{19}H_{26}NO_3^+$ $[M + H]^+$: 316.1907, found: 316.1915



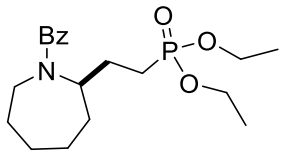
(R)-1-(1-benzoylazepan-2-yl)pentan-3-one (53c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~4:1) afforded 41.3 mg of the title compound **53c** (colorless oil; 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.31 (m, 5H), 4.81 – 4.60 (m, 0.55H), 4.32 (d, *J* = 13.5 Hz, 0.44H), 3.76 (dq, *J* = 14.3, 7.0 Hz, 0.46H), 3.54 (d, *J* = 14.8 Hz, 0.57H), 2.99 (dd, *J* = 14.5, 10.8 Hz, 0.58H), 2.84 – 2.70 (m, 0.47H), 2.58 (tt, *J* = 7.5, 4.2 Hz, 1H), 2.49 (p, *J* = 7.2 Hz, 1H), 2.38 – 2.03 (m, 3H), 2.00 – 1.91 (m, 0.55H), 1.88 (d, *J* = 5.6 Hz, 1H), 1.87 – 1.74 (m, 3.43H), 1.69 (ddt, *J* = 10.7, 8.2, 3.5 Hz, 0.94H), 1.52 – 1.18 (m, 4.62H), 1.08 (t, *J* = 7.3 Hz, 1.65H), 0.98 (t, *J* = 7.3 Hz, 1.30H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 211.4, 210.1, 173.0, 171.2, 137.7, 137.4, 128.7, 128.47, 126.5, 126.1, 56.5, 52.8, 43.6, 40.4, 39.2, 38.5, 36.0, 35.7, 34.7, 34.0, 30.2, 30.1, 29.2, 29.0, 28.3, 27.5, 24.7, 7.8, 7.7.

HRMS (ESI) calcd $C_{18}H_{26}NO_2^+$ [M + H]$^+$: 288.1958, found: 288.1961



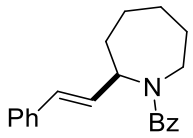
Diethyl (R)-(2-(1-benzoylazepan-2-yl)ethyl)phosphonate (54c)

Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~4:1) afforded 52.3 mg of the title compound **54c** (colorless oil; 71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 6.87 (m, 5H), 4.77 – 4.60 (m, 0.4H), 4.29 (t, *J* = 13.8 Hz, 0.6H), 4.04 (ddq, *J* = 28.4, 14.3, 7.4 Hz, 3.5H), 3.66 (h, *J* = 7.4 Hz, 0.45H), 3.51 (t, *J* = 13.8 Hz, 0.4H), 2.94 (q, *J* = 14.4, 13.7 Hz, 0.5H), 2.70 (tt, *J* = 13.8, 6.1 Hz, 0.5H), 2.21 – 2.40 (m, 0.6H), 2.20 – 1.69 (m, 7H), 1.61 – 1.11 (m, 11H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 171.3, 137.3, 128.8, 128.7, 128.6, 128.4, 126.3, 126.1, 61.6, 57.5, 57.4, 53.7, 53.5, 43.9, 40.4, 34.3, 33.3, 30.2, 29.1, 28.3, 27.5, 27.3, 24.7, 23.3, 21.9, 16.4.

HRMS (ESI) calcd $C_{19}H_{31}NO_4P^+$ [M + H]$^+$: 368.1985, found: 368.1989



(R,E)-phenyl(2-styrylazepan-1-yl)methanone (55c)

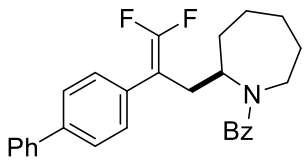
Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (6:1~4:1) afforded 43.5 mg of the title compound **55c** (colorless oil; 71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 6.92 (m, 10H), 6.85 – 6.05 (m, 2H), 6.78 – 6.14 (m, 1H), 4.91 – 3.40 (m, 2H), 3.22 – 2.71 (m, 1H), 2.45 – 1.83 (m, 5H), 1.62 – 1.33 (m, 3H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 172.3, 172.0, 171.8, 137.3, 136.6, 131.3, 129.7, 129.5, 129.2, 129.1, 128.9, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.3, 128.1, 128.1, 127.1, 127.1, 126.5, 126.5, 126.3, 126.2, 126.2, 126.0, 125.9, 59.9, 57.0, 56.0,

55.0, 41.8, 41.1, 40.6, 40.4, 34.9, 34.9, 34.4, 33.6, 30.5, 30.4, 30.3, 30.1, 28.2, 28.1, 27.8, 27.7, 25.1, 24.9, 24.8, 24.8.

HRMS (ESI) calcd $C_{21}H_{24}NO^+$ $[M + H]^+$: 306.1852, found: 306.1850



(R)-(2-(2-([1,1'-biphenyl]-4-yl)-3,3-difluoroallyl)azepan-1-yl)(phenyl)methanone (56c)

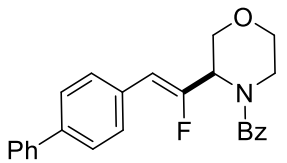
Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~4:1) afforded 71.5 mg of the title compound **56c** (colorless oil; 83% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.54 (m, 4H), 7.53 – 7.45 (m, 2H), 7.43 – 7.31 (m, 5H), 7.28 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.21 – 7.14 (m, 1H), 6.98 – 6.93 (m, 1H), 4.74 (dq, *J* = 12.6, 6.4 Hz, 0.5H), 4.40 (dt, *J* = 13.8, 3.3 Hz, 0.5H), 3.83 (p, *J* = 7.6 Hz, 0.5H), 3.55 – 3.36 (m, 0.5H), 3.13 – 2.97 (m, 0.5H), 2.96 – 2.78 (m, 1H), 2.78 – 2.62 (m, 0.5H), 2.62 – 2.49 (m, 1H), 2.14 (ddd, *J* = 14.3, 8.6, 5.8 Hz, 0.5H), 1.98 (ddd, *J* = 17.2, 12.4, 5.8 Hz, 1H), 1.90 – 1.69 (m, 3.5H), 1.56 – 1.41 (m, 1H), 1.41 – 1.31 (m, 2H), 1.29 – 1.19 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 171.3, 140.7 (dd, J = 292.5, 288.0 Hz), 137.7, 137.2, 132.2, 131.1, 128.9, 128.8, 128.8, 128.6, 128.6, 128.4, 127.9, 127.8, 127.8, 127.5, 127.4, 127.2, 127.1, 127.1, 127.0, 126.2, 126.1, 55.5, 53.0, 44.3, 40.6, 33.2, 32.9, 32.8, 31.7, 30.6, 30.1, 29.1, 28.0, 25.1, 24.8

^{19}F NMR (376 MHz, $CDCl_3$) δ -90.03, -90.14, -90.46, -90.57.

HRMS (ESI) calcd $C_{28}H_{28}F_2NO^+$ $[M + H]^+$: 432.2133, found: 432.2138



(R,Z)-(3-(2-([1,1'-biphenyl]-4-yl)-1-fluorovinyl)morpholino)(phenyl)methanone

(57c)

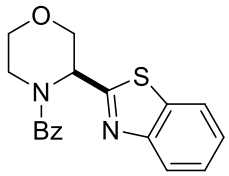
Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~3:1) afforded 61.1 mg of the title compound **57c** (grey solid; 79% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.63 (m, 6H), 7.54 – 7.45 (m, 7H), 7.40 (m, 1H), 6.02 (d, *J* = 40.1 Hz, 1H), 4.42 (dd, *J* = 43.6, 8.3 Hz, 2H), 3.99 (s, 1H), 3.72 (d, *J* = 64.5 Hz, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.7, 140.5, 140.3, 134.9, 131.5, 130.2, 129.3, 129.2, 128.8, 128.7, 127.5, 127.2, 127.0, 126.9, 108.9, 77.3, 67.2, 66.8, 66.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -109.14 (s), -109.25 (s).

HRMS (ESI) calcd $C_{25}H_{23}FNO_2^+$ $[M + H]^+$: 388.1707, found: 388.1709



(3-(benzo[d]thiazol-2-yl)morpholino)(phenyl)methanone (58c)

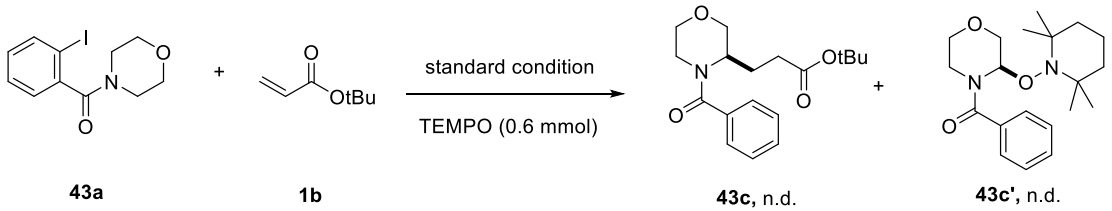
Following General Procedure B, Purification by flash chromatography on silica gel with petroleum ether/ethyl acetate (5:1~3:1) afforded 45.3 mg of the title compound **58c** (yellow solid; 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 7.72 (m, 2H), 7.52 – 7.43 (m, 2H), 7.40 (dt, *J* = 8.8, 4.4 Hz, 3H), 7.30 (td, *J* = 7.8, 3.3 Hz, 2H), 6.06 (s, 1H), 5.16 – 4.35 (m, 2H), 4.10 – 3.12 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 169.4, 153.4, 135.4, 134.6, 130.4, 128.8, 127.2, 126.2, 125.3, 123.5, 121.7, 68.2, 66.9, 51.9, 45.3.

HRMS (ESI) calcd $C_{18}H_{17}N_2O_2S^+$ $[M + H]^+$: 325.1005, found: 325.1007

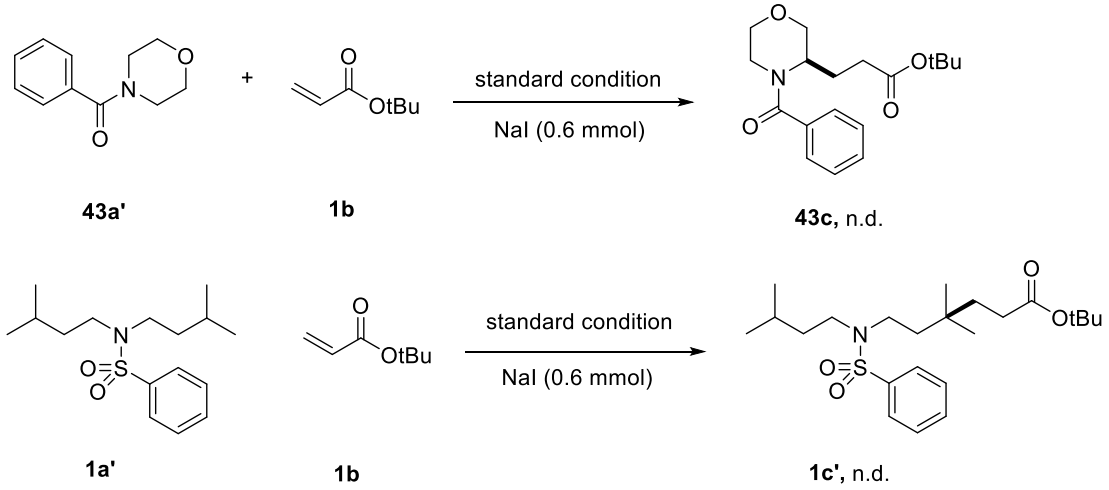
5. Mechanistic Studies



43a **1b** **43c,** n.d. **43c',** n.d.

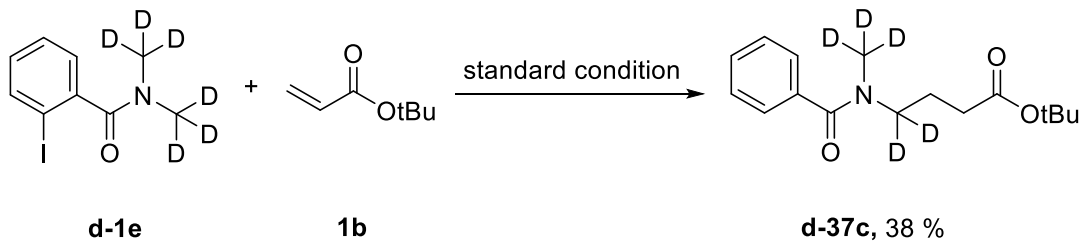
Scheme S1. Free radical inhibition experiment

The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a Teflon-coated magnetic stir bar was added [Ir(dFCF$_3$ppy)$_2$(dtbpy)PF$_6$] 1 mo%, **43a** (0.2 mmol), **1b** (0.4 mmol), TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) (0.6 mmol), TMG (60μL, mmol,), MeCN (1 mL) and (i-Bu)$_3$N（130 μL）was added via pipette. The reaction mixture was stirred and irradiated using a 10 W 450 nm LED lamp for 6 hours and control the temperature at about 20 °C until the reaction was complete (monitored by TLC).



Scheme S2. Controlled experiment

The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a Teflon-coated magnetic stir bar was added [Ir(dFCF$_3$ppy)$_2$(dtbpy)PF$_6$] 1 mo%, **43a'/1a'** (0.2 mmol), **1b** (0.4 mmol), NaI (0.4 mmol), TMG (70 μL, mmol,), MeCN (1 mL) and (i-Bu)$_3$N（140 μL）was added via pipette. The reaction mixture was stirred and irradiated using a 10 W 450 nm LED lamp for 6 hours and control the temperature at about 20 °C until the reaction was complete (monitored by TLC).



Scheme S3. Deuterium-labeling experiments.

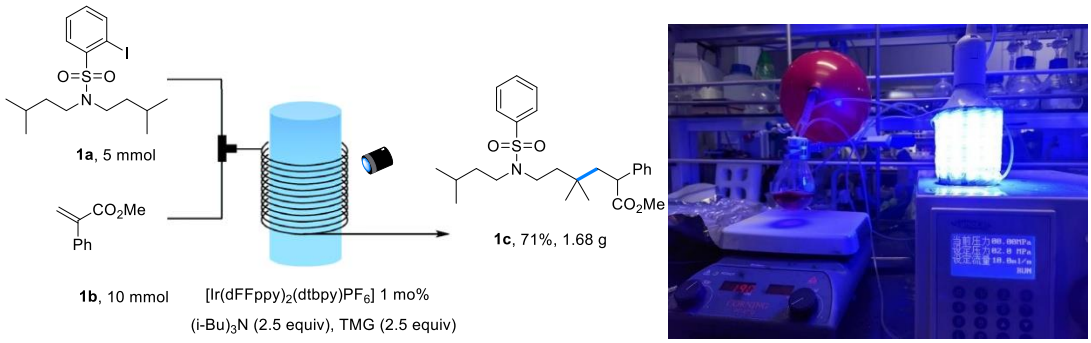
The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a Teflon-coated magnetic stir bar was added [Ir(dFCF$_3$ppy)$_2$(dtbpy)PF6] 1 mo%, **d-1e** (0.2 mmol), **1b** (0.4 mmol), TMG (70 μL, mmol), MeCN (1 mL) and (i-Bu)$_3$N（140 μL） was added via pipette. The reaction mixture was stirred and irradiated using a 10 W 450 nm LED lamp for 2 hours and control the temperature at about 20 °C. After reaction, the solvent was removed by rotary evaporation and purified by column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent to afford **d-37c** in 38%. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.41 (s, 4H), 2.35 (t, *J* = 7.6 Hz, 1H), 2.10 (t, *J* = 7.4 Hz, 1H), 1.94 (q, *J* = 11.3, 9.5 Hz, 2H), 1.38 (d, *J* = 19.2 Hz, 4H).

Scheme S4. KIE experiments.

The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a Teflon-coated magnetic stir bar was added [Ir(dFCF$_3$ppy)$_2$(dtbpy)PF6] 1 mo%, **d-1e** (0.1 mmol), **1e** (0.1 mmol), **1b** (0.4 mmol), TMG (70 μL, mmol,),MeCN (1 mL) and (i-Bu)$_3$N（140 μL） was added via pipette. The reaction mixture was stirred and irradiated using a 10 W 450 nm LED lamp for 1 hours and control the temperature at about 20 °C. After reaction, the solvent was removed by rotary evaporation and purified by column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent to afford product in 40%.

6. Additional Experiments

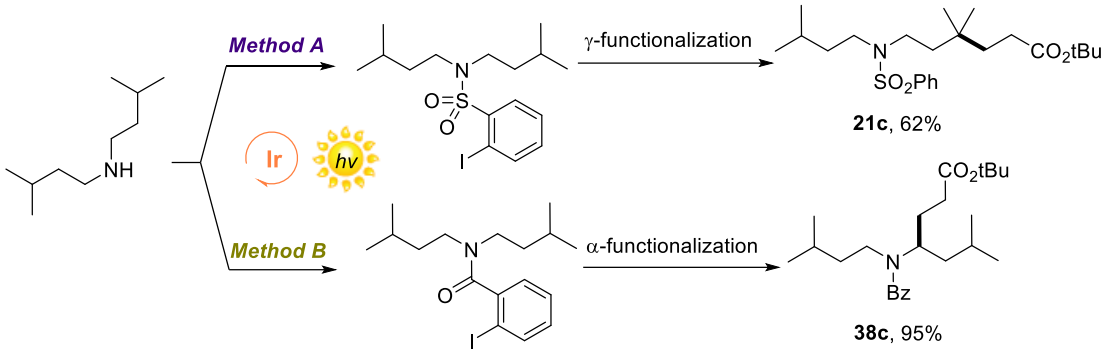
6.1 General procedure for gram-scale continuous-flow reaction



Scheme S5. Gram-scale reaction.

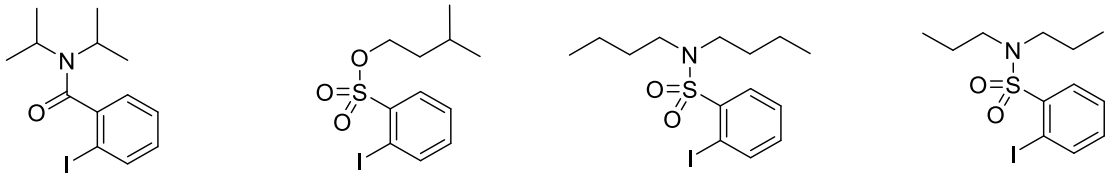
The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a Teflon-coated magnetic stir bar was added [Ir(dFFppy)$_2$(dtbpy)PF$_6$] 1 mo%, **1a** (5 mmol), **1b (**10 mmol**)**, TMG (2.4 mL, mmol,), MeCN (20 mL) and (i-Bu)$_3$N（2.6 mL）was added via pipette. The reaction mixture was stirred and irradiated using a 45 W 450 nm LED lamp for 6 hours and control the temperature at about 35 ˚C until the reaction was complete (monitored by TLC). After reaction, the solvent was removed by rotary evaporation and purified by column chromatography on silica gel (petroleum ether: ethyl acetate = 4:1) afforded **1c** (1.68g, 71% yield) as a colorless oil.

6.2 Protecting-Group Modulation for Site-Selective Modification of Amines



Scheme S6. Protecting-Group Modulation for Site-Selective Modification of Amines

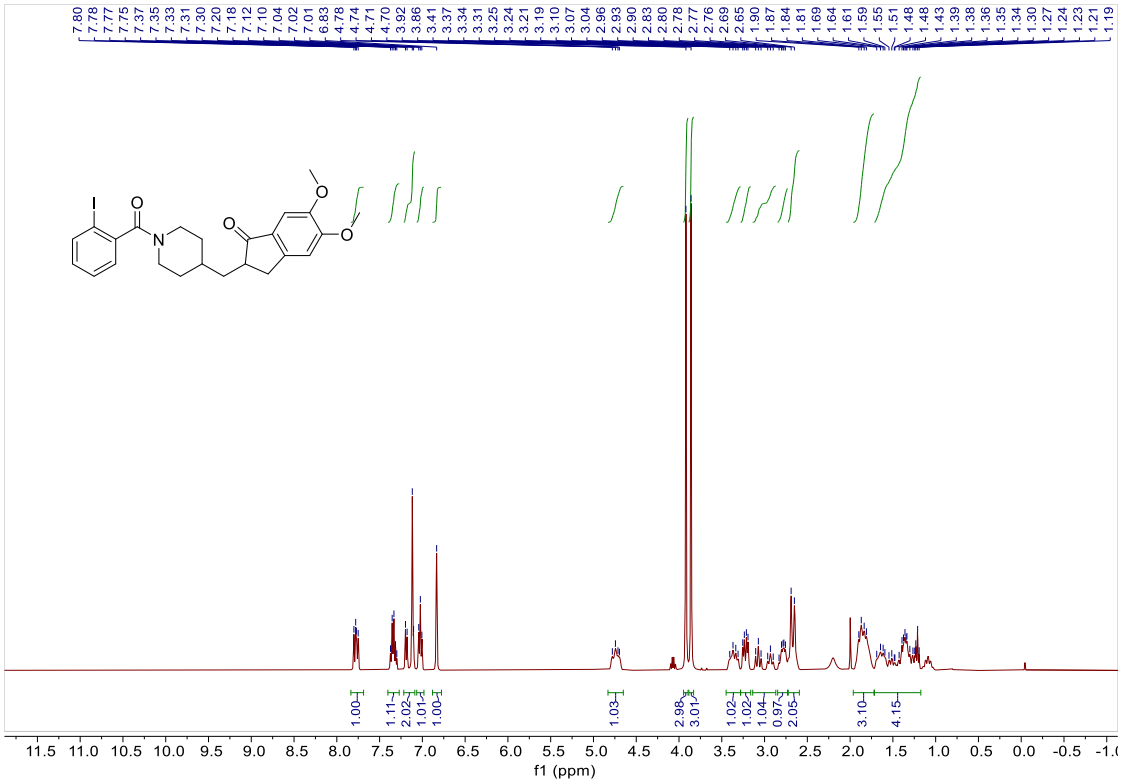
7. Examples of Failed Substrates



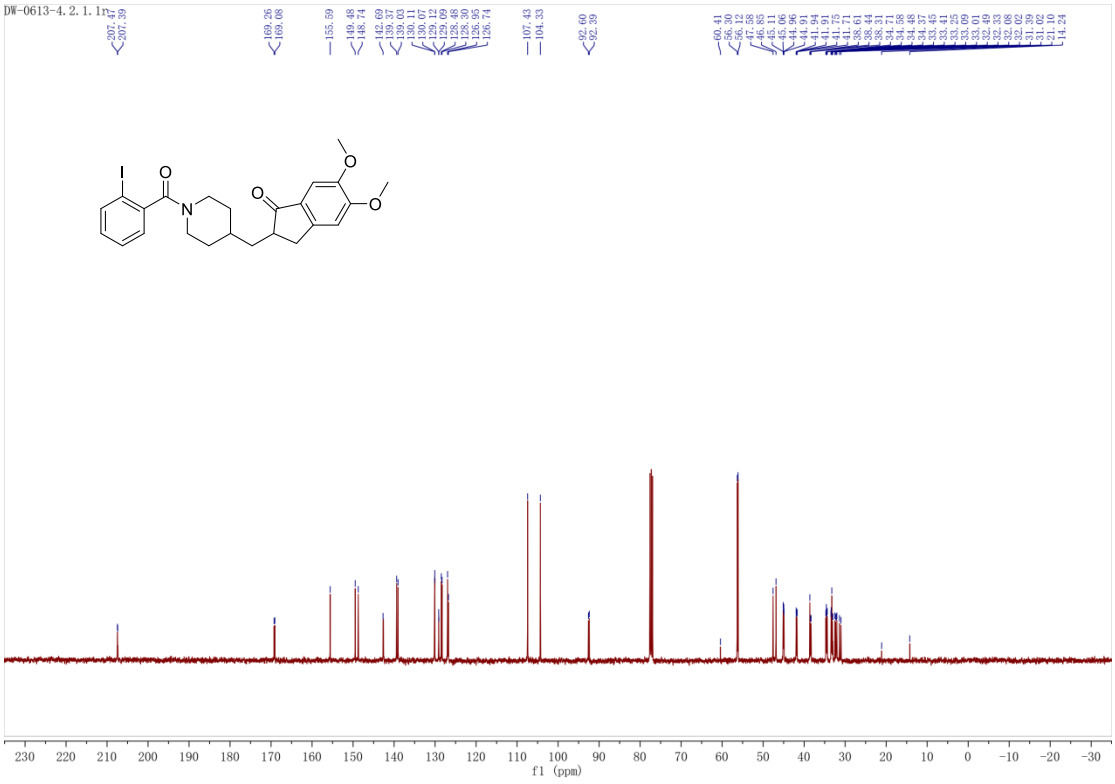
Scheme S7. Examples of failed aubstrates

8. NMR Spectral Data

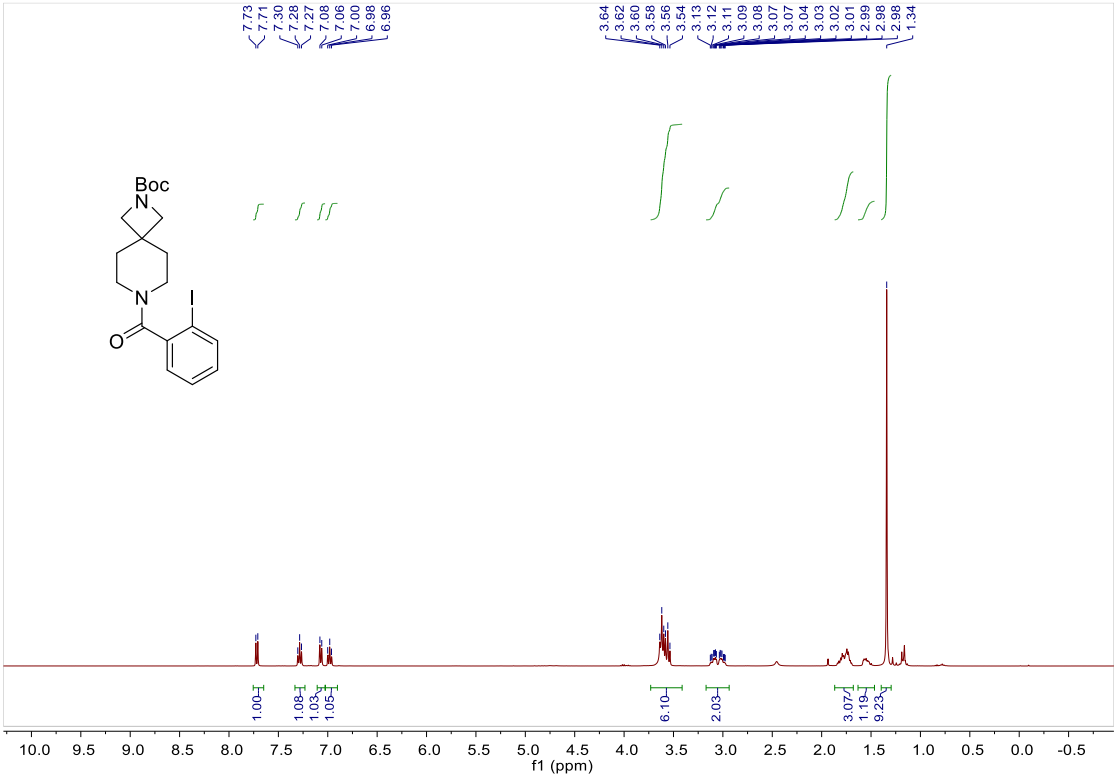
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **1.1**



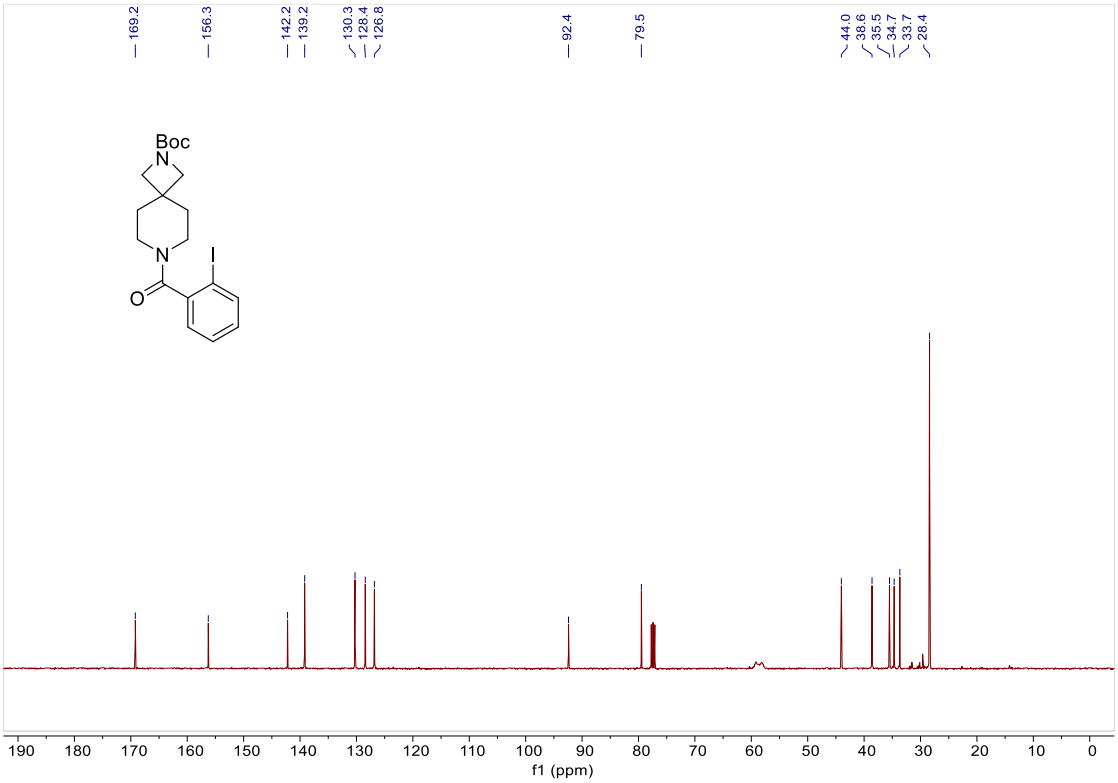
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **1.1**



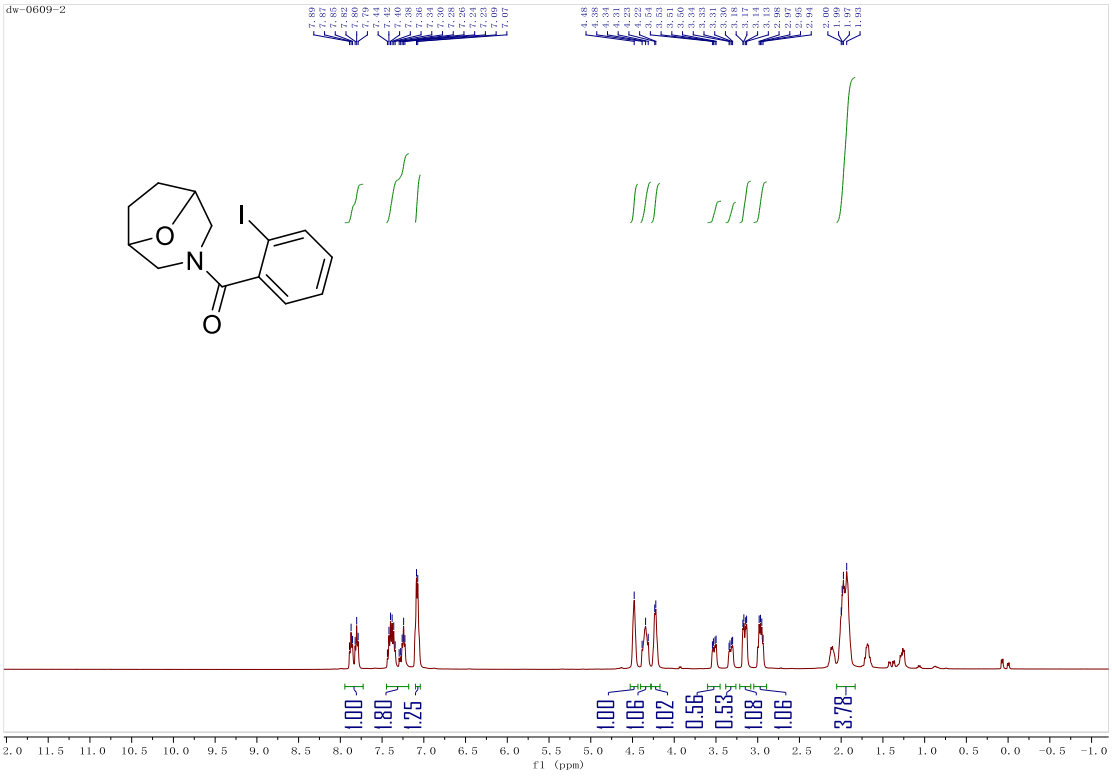
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **1.2**



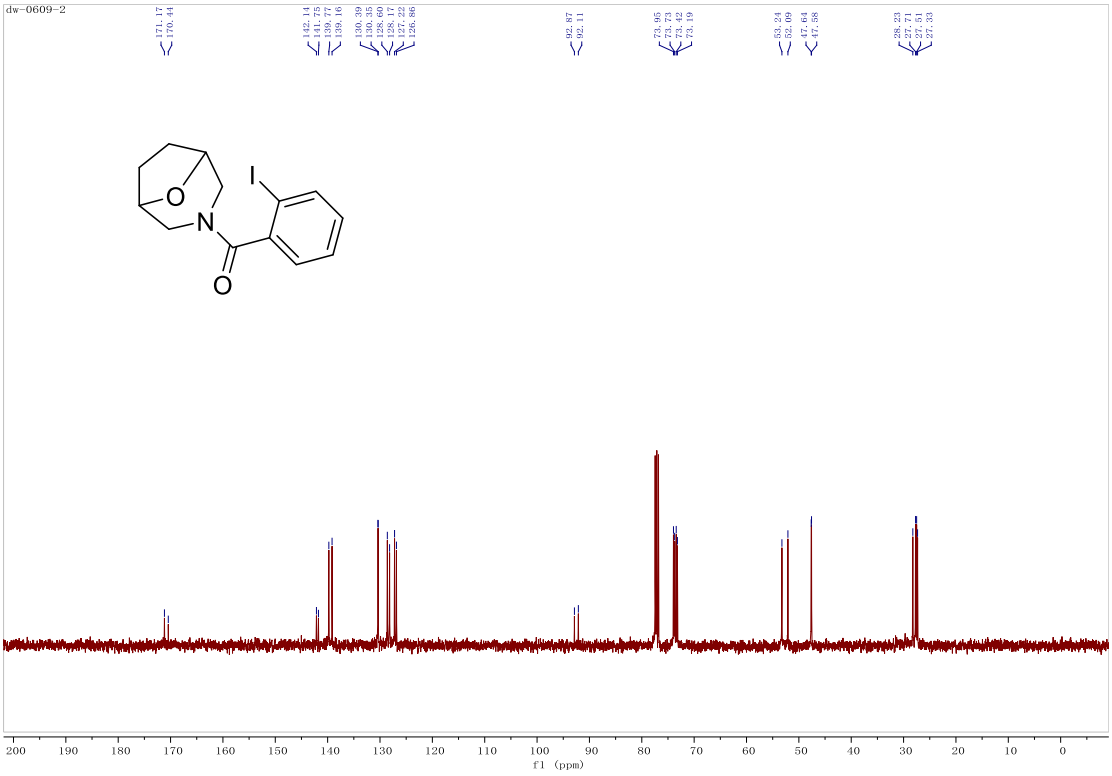
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **1.2**



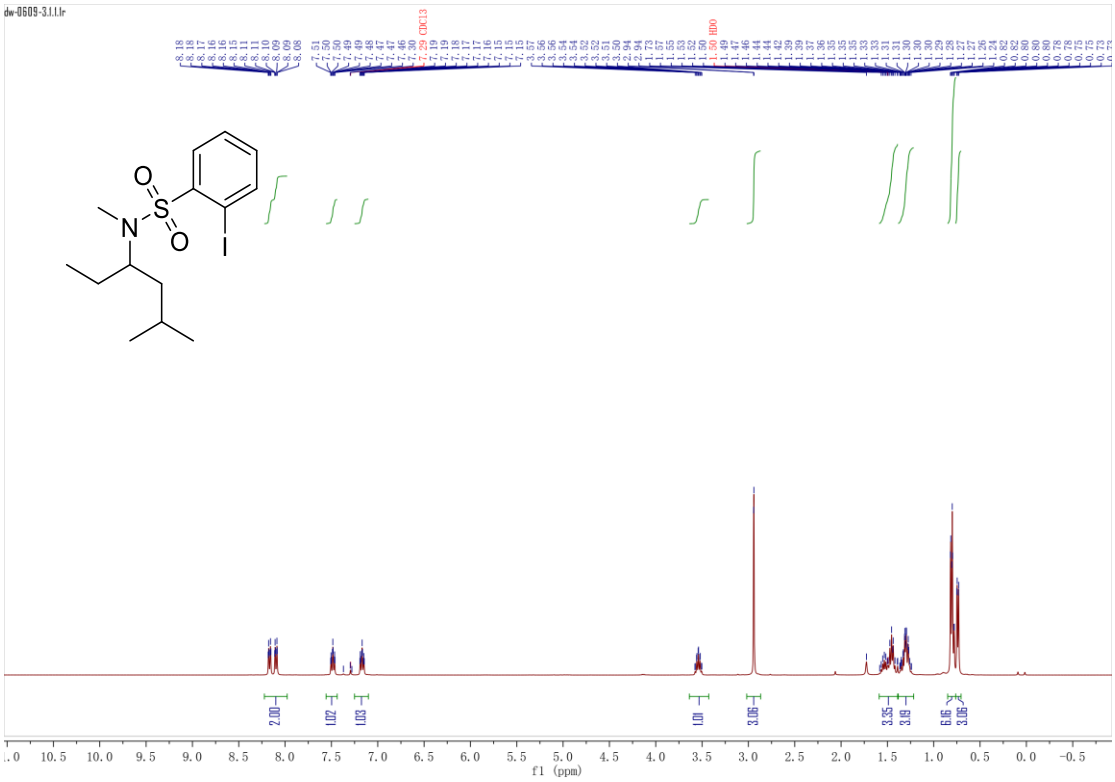
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **1.3**



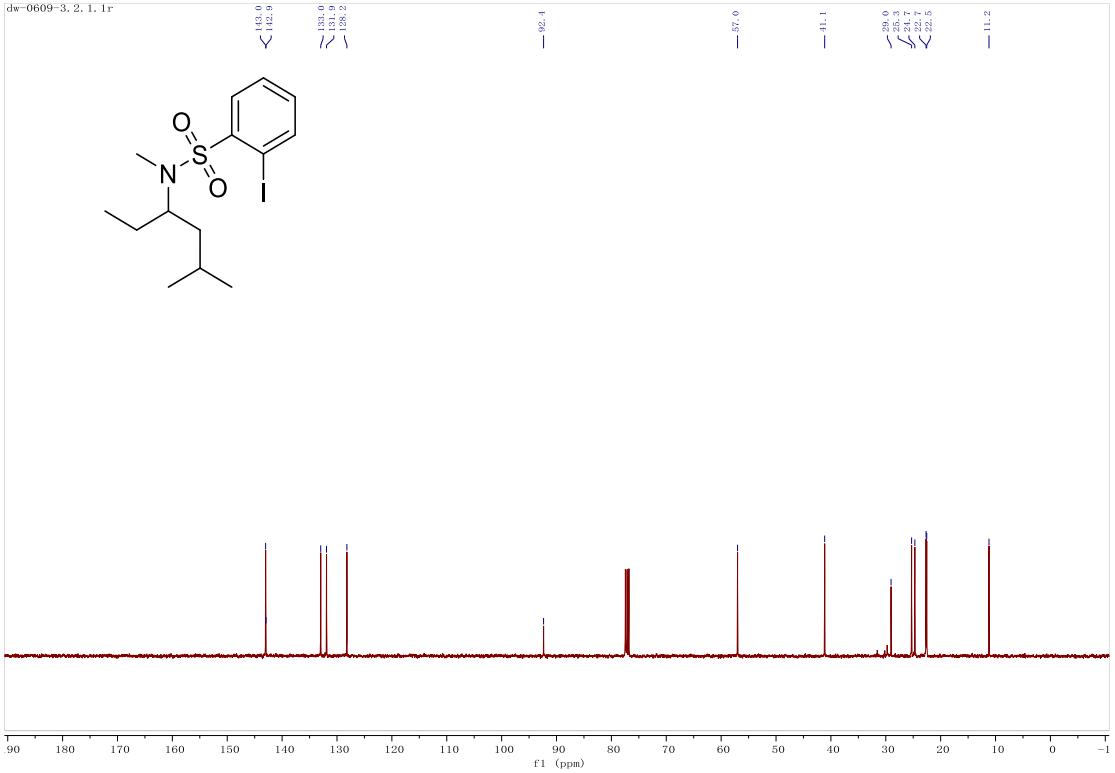
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **1.3**



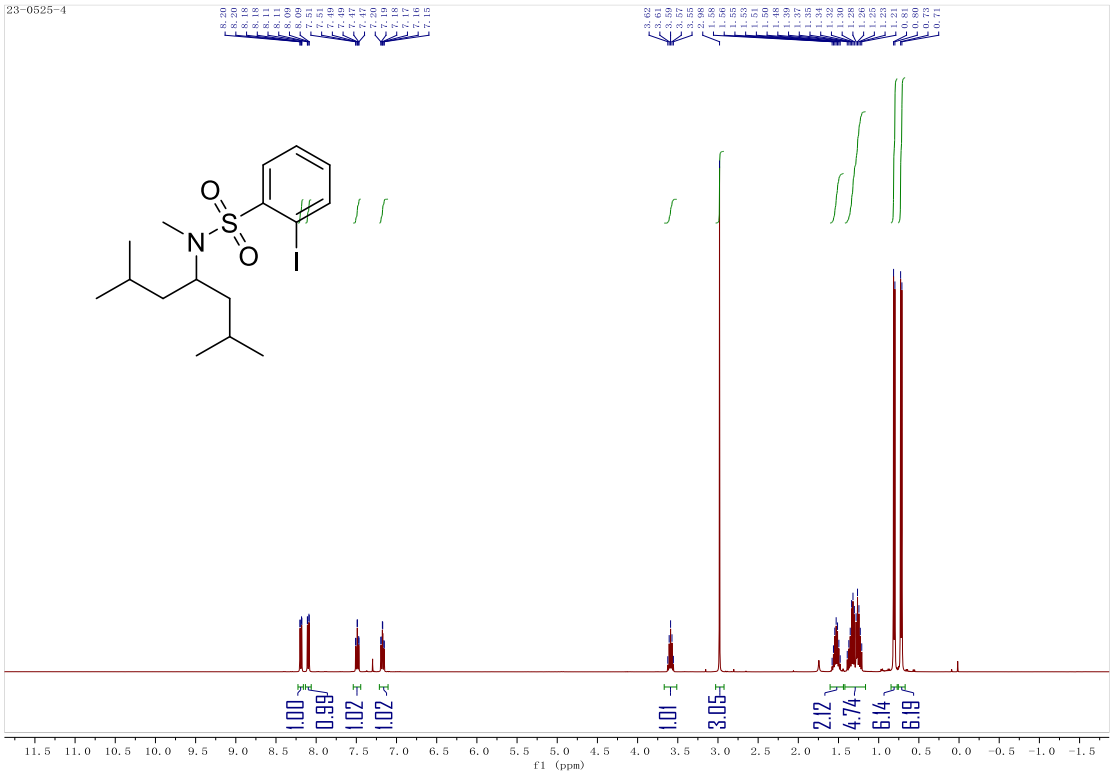
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **1.4**



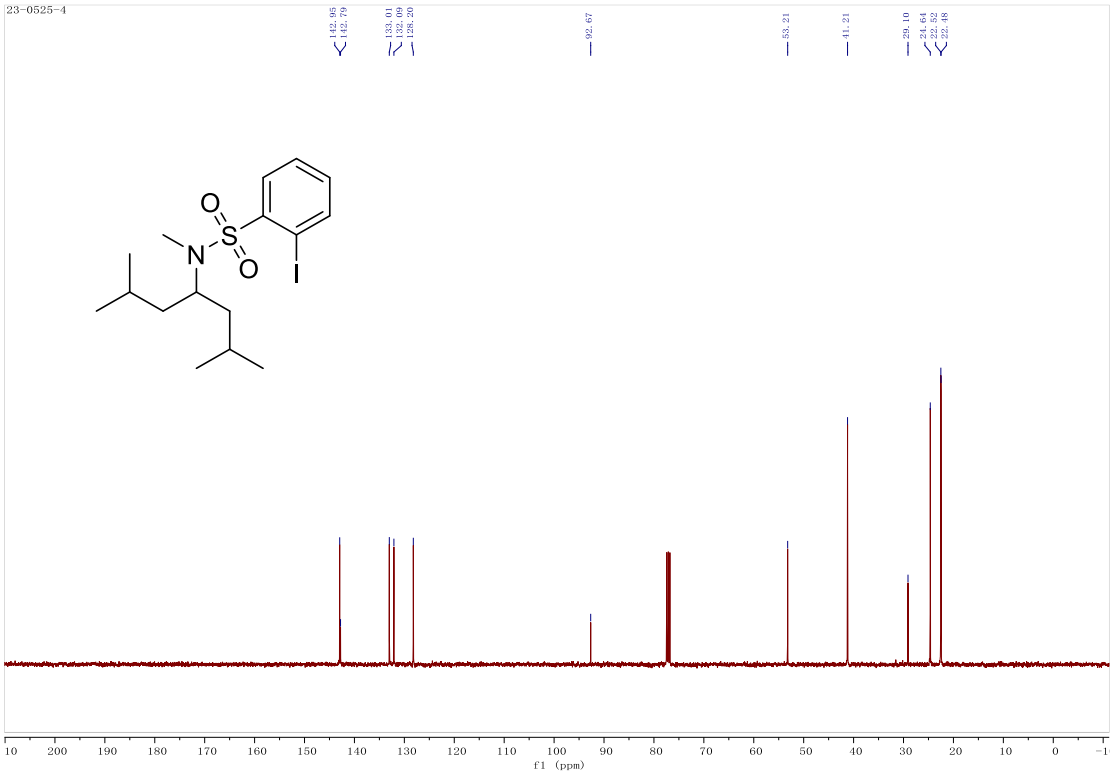
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **1.4**



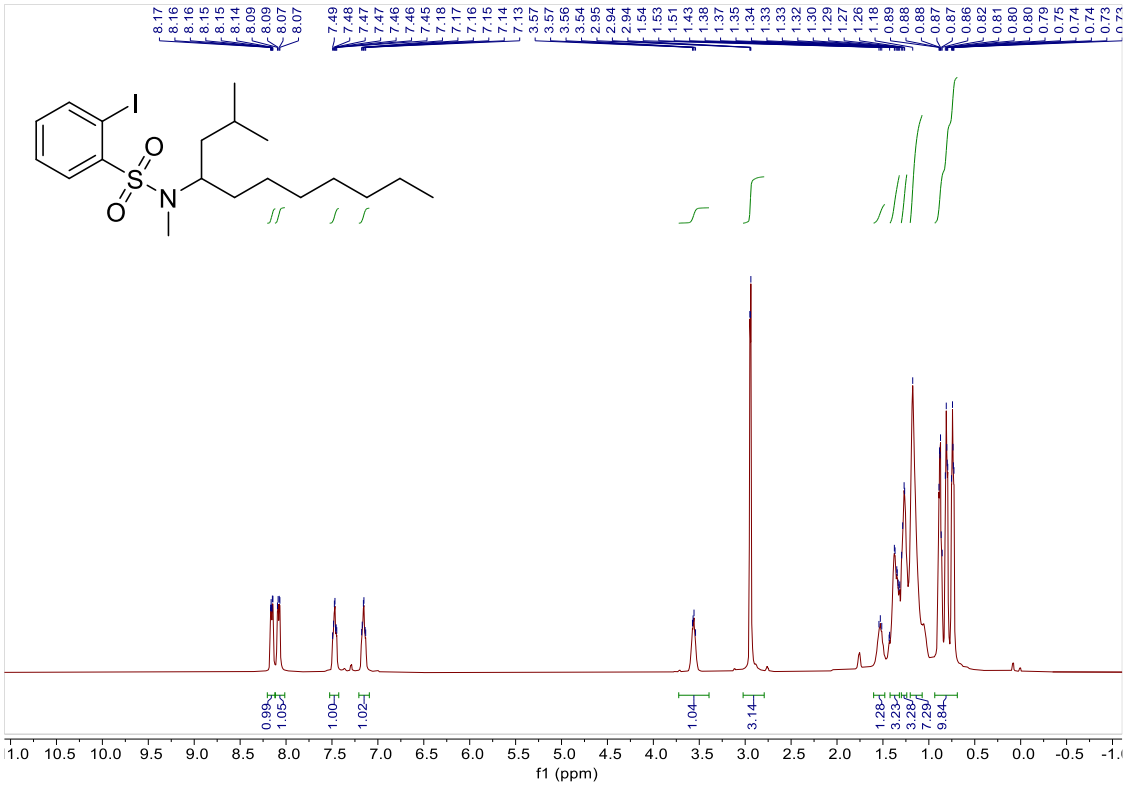
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **1.5**



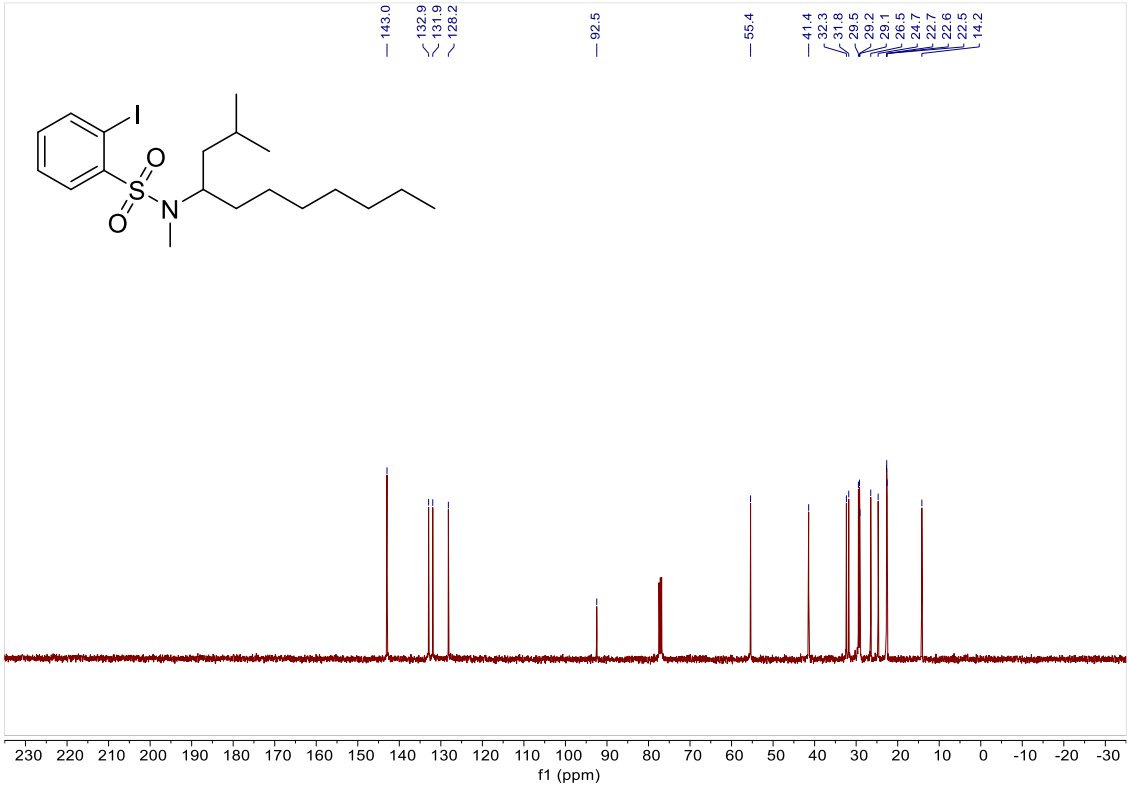
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **1.5**



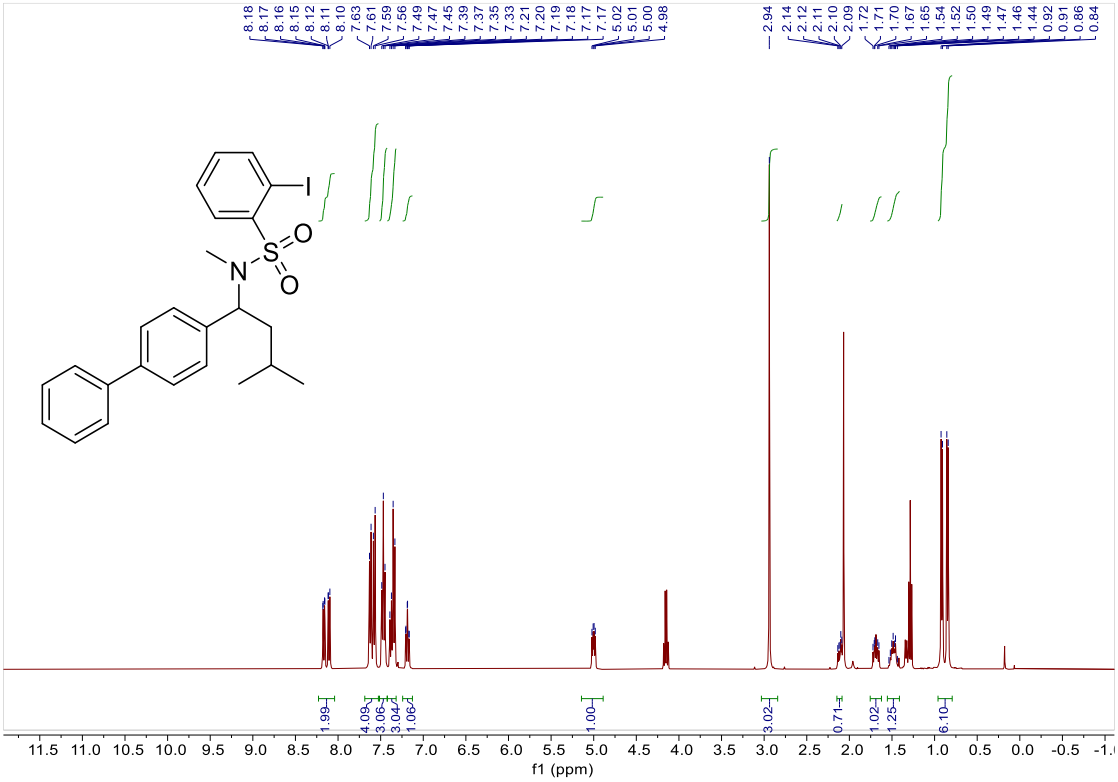
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **1.6**



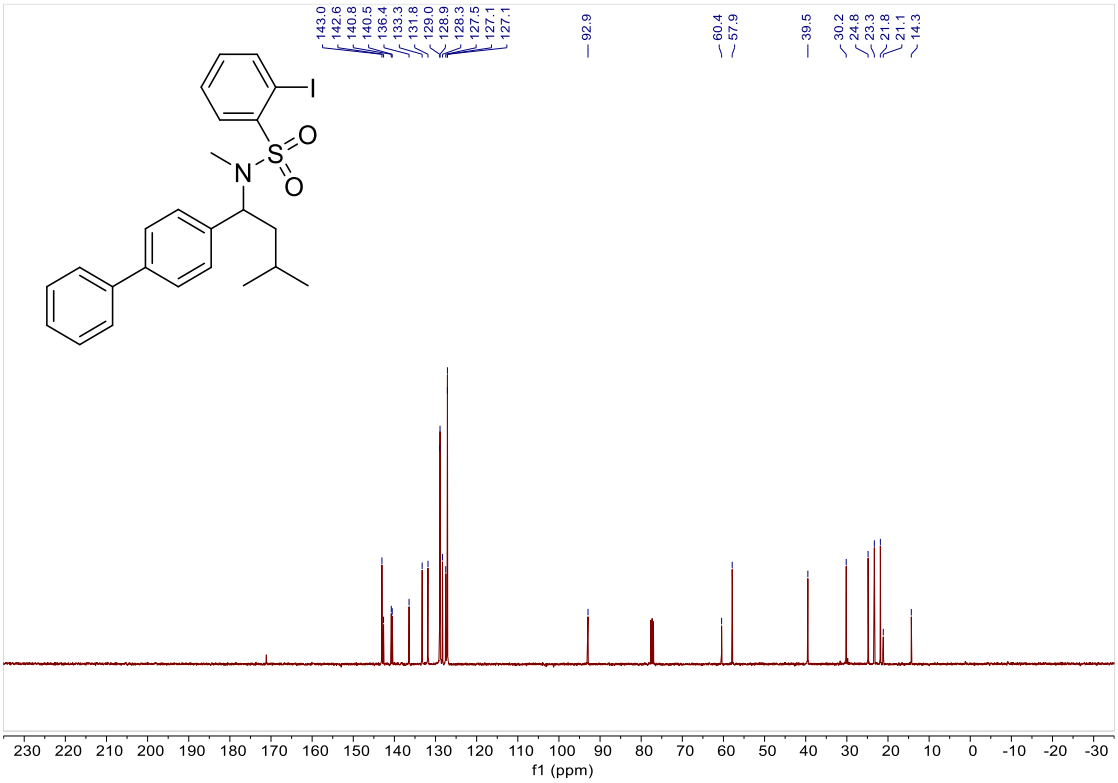
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **1.6**



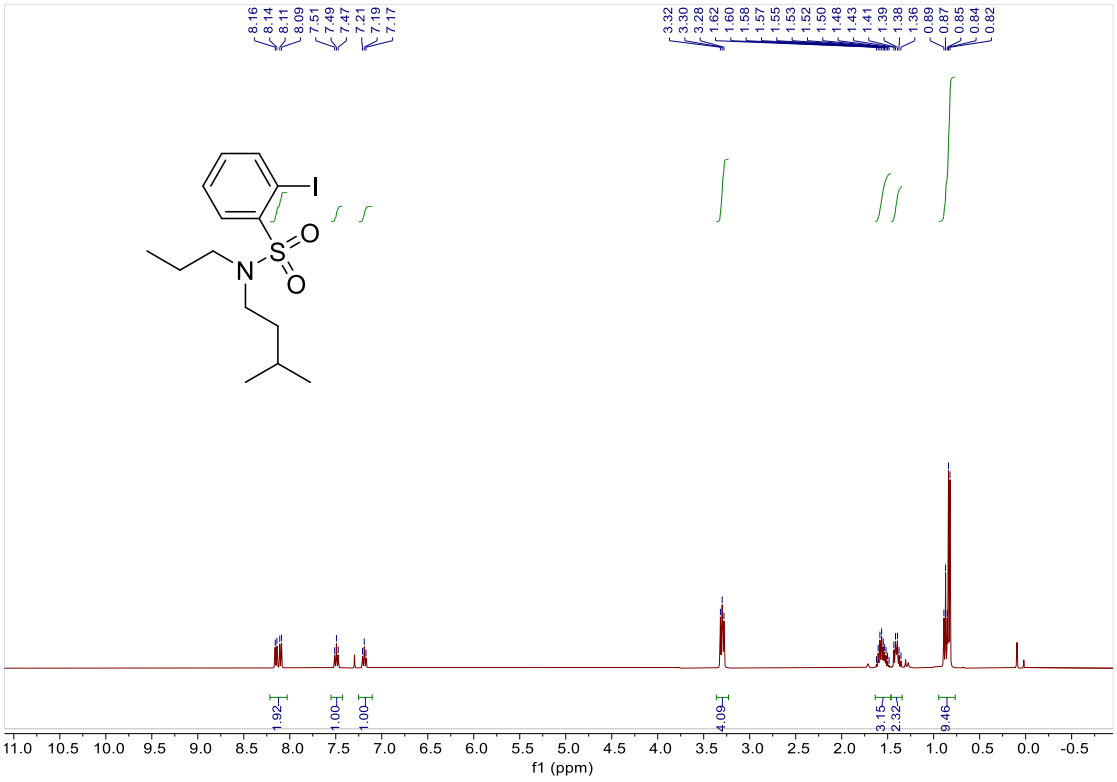
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **1.7**



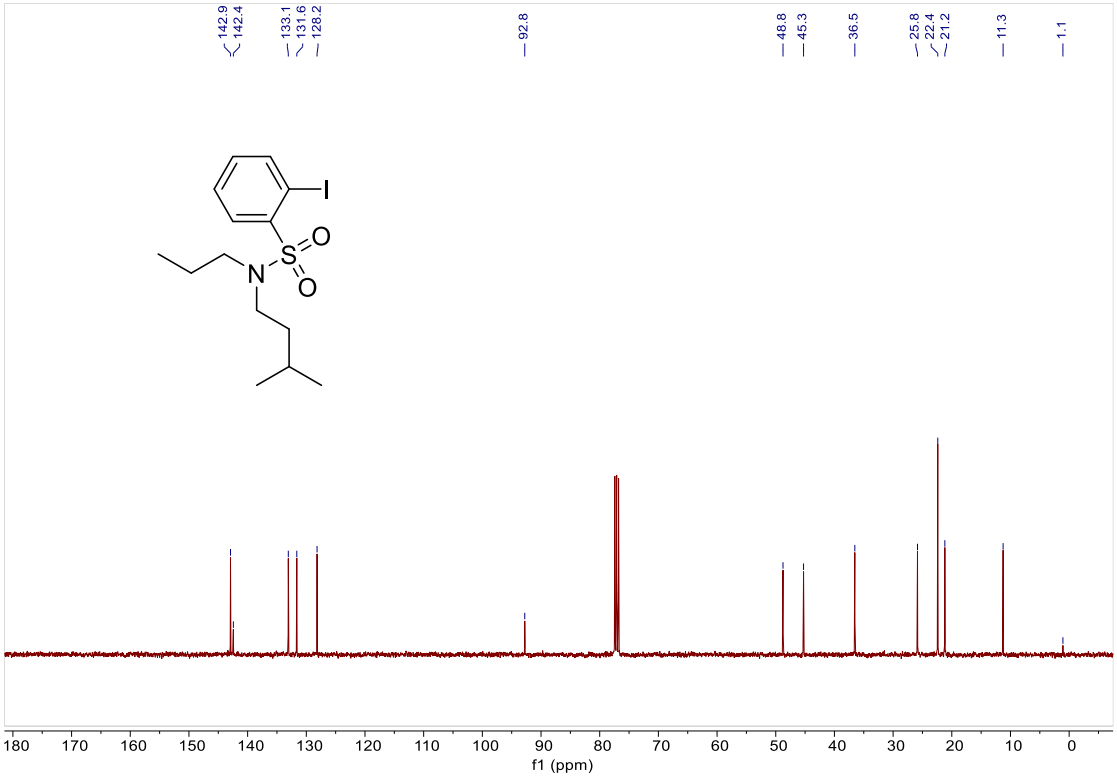
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **1.7**



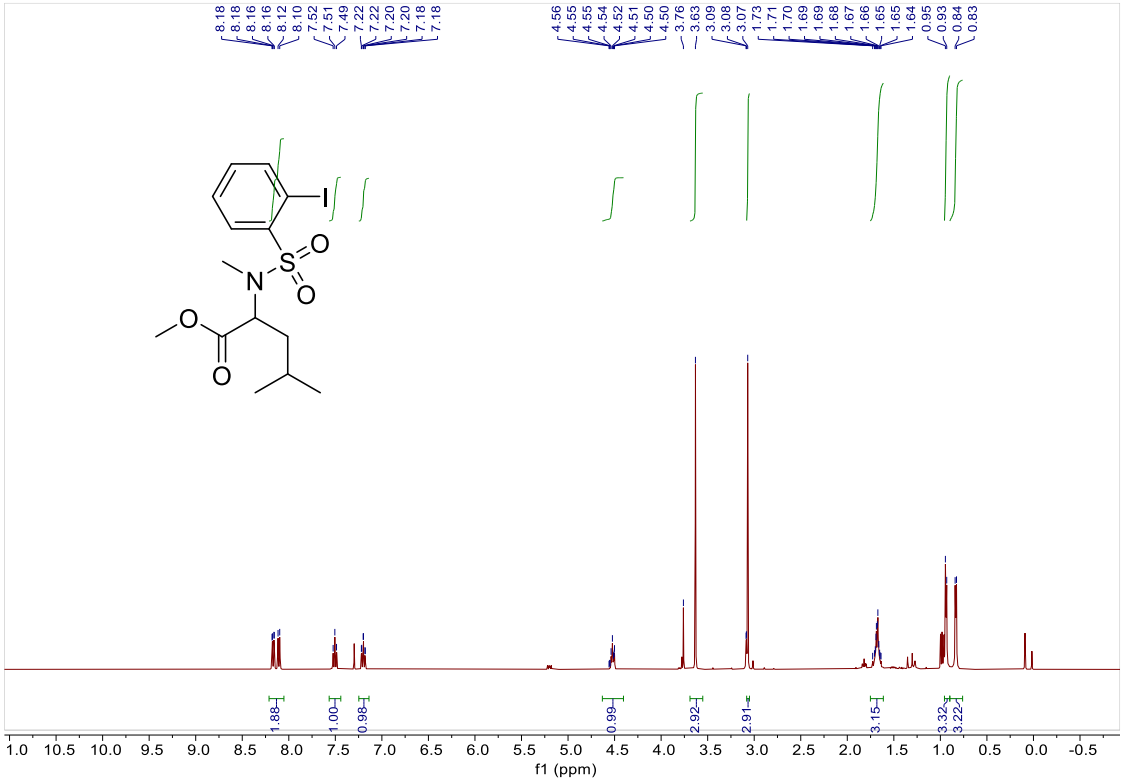
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **1.8**



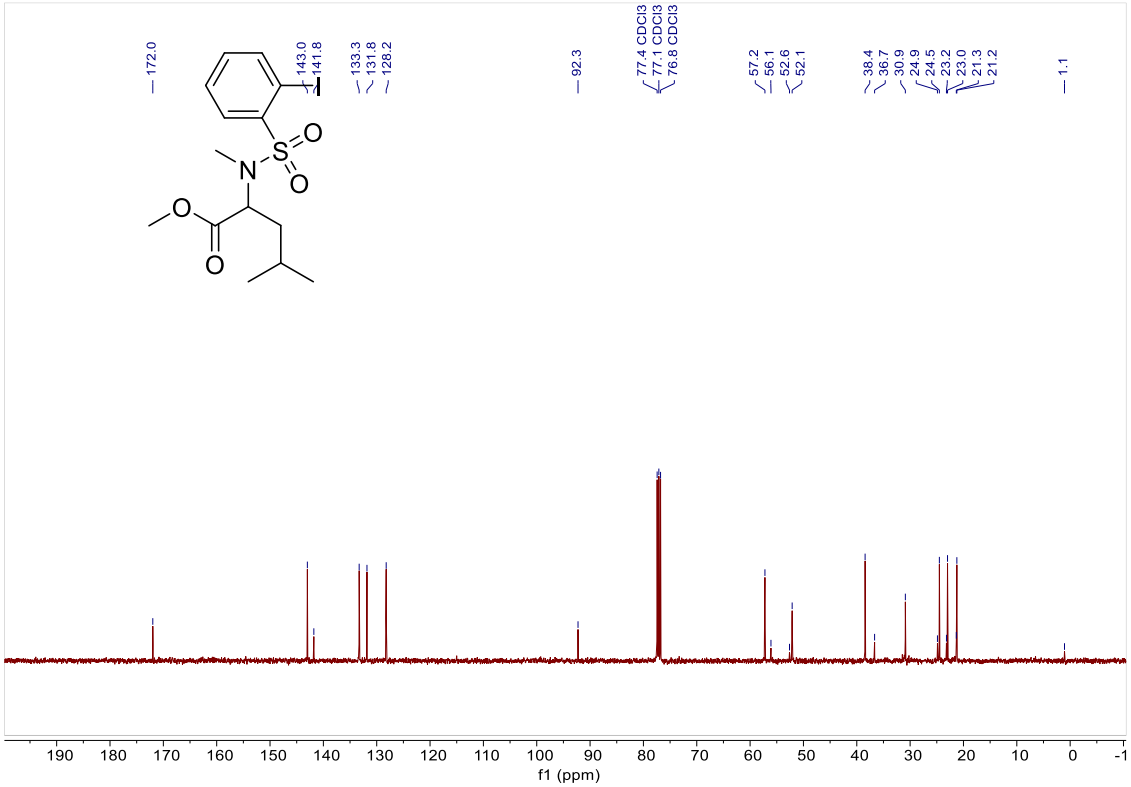
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **1.8**



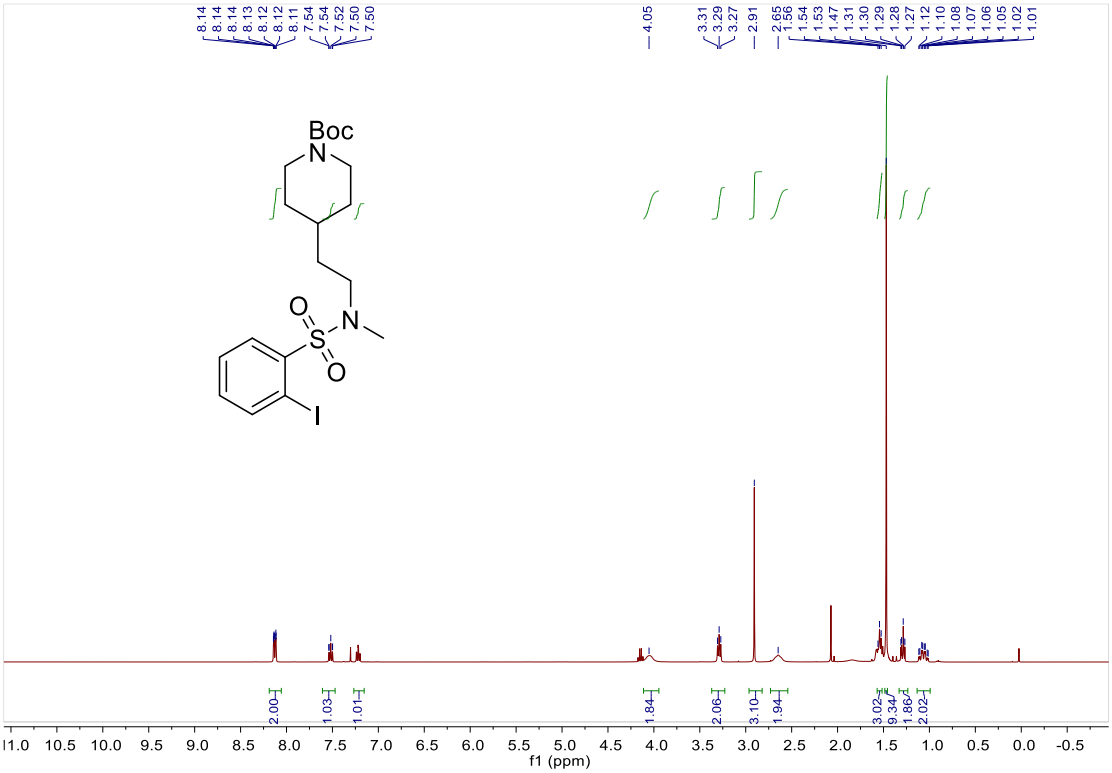
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **1.9**



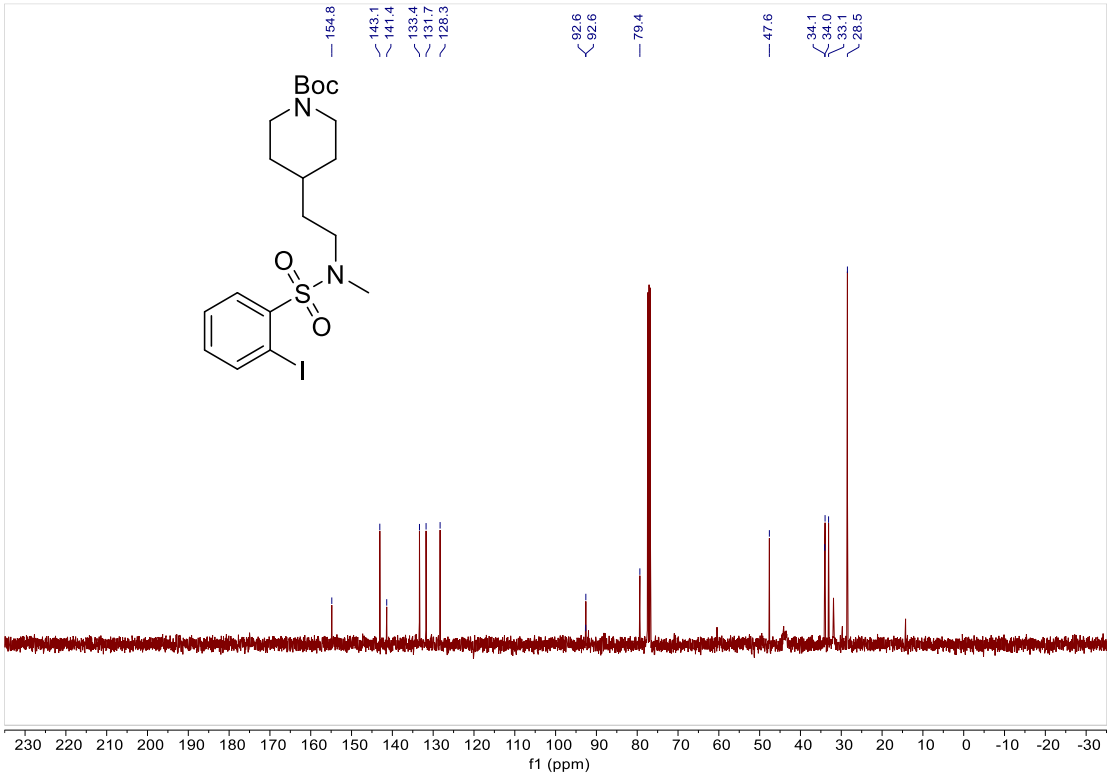
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **1.9**



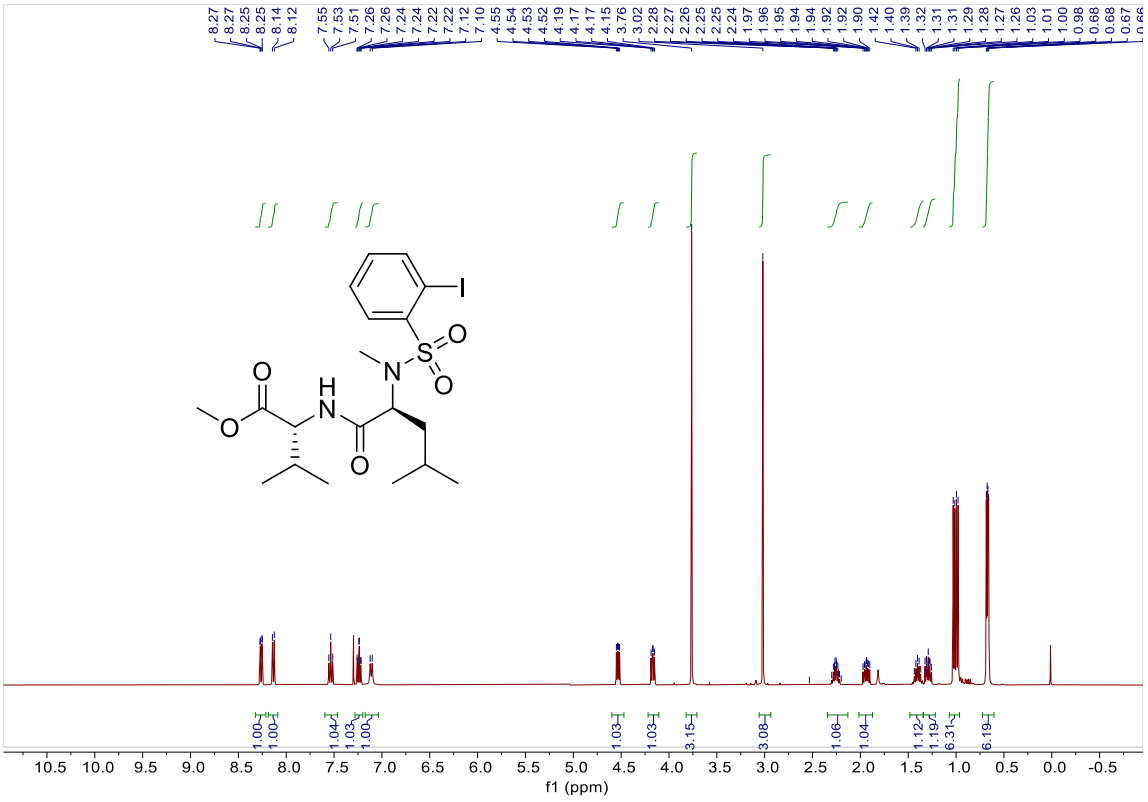
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **2.0**



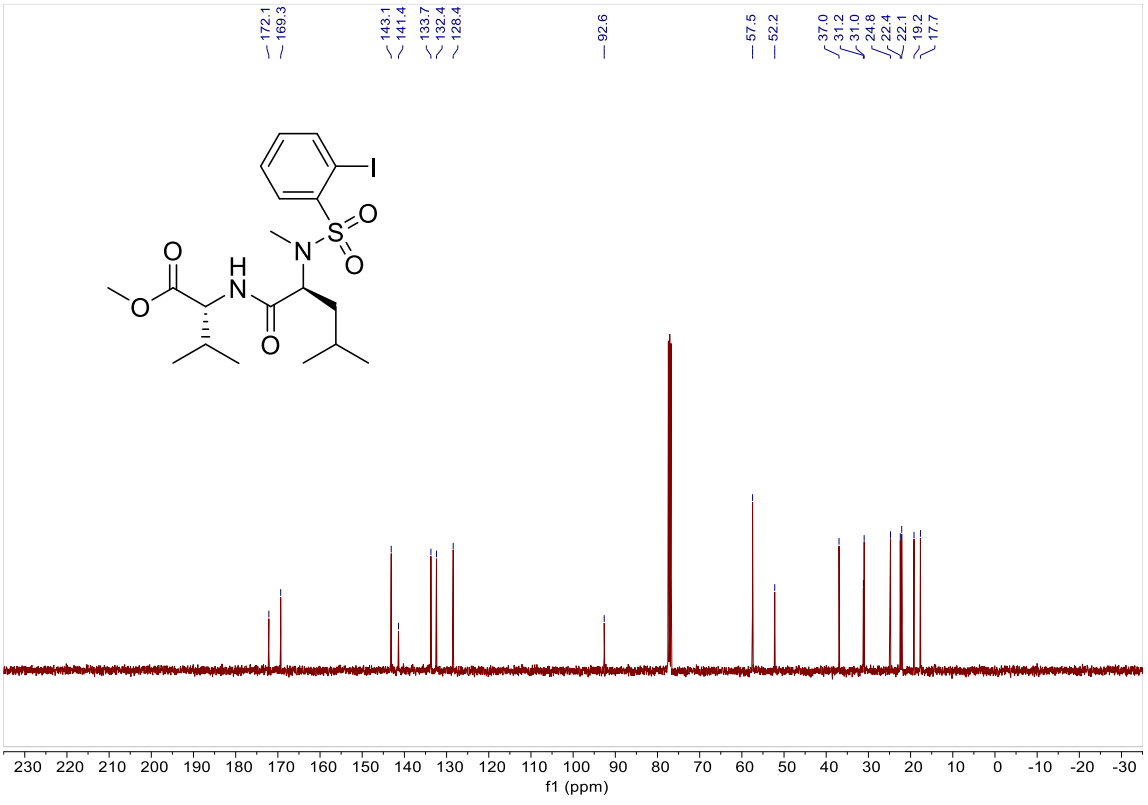
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **2.0**



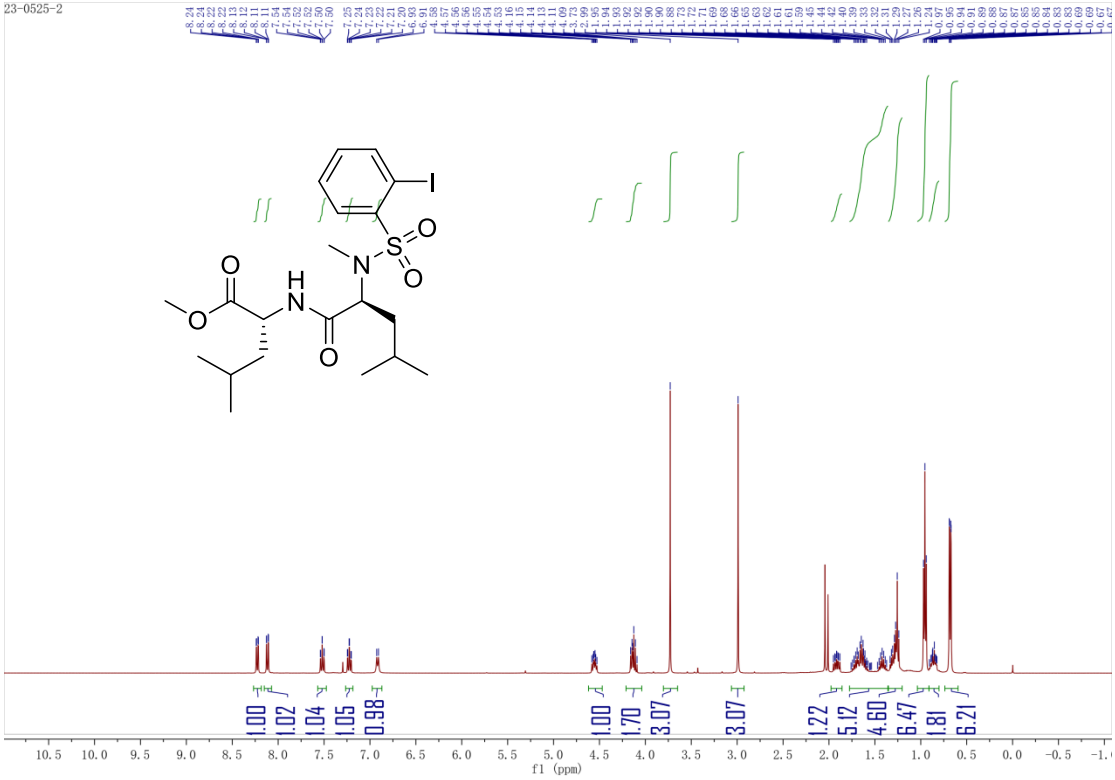
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **2.1**



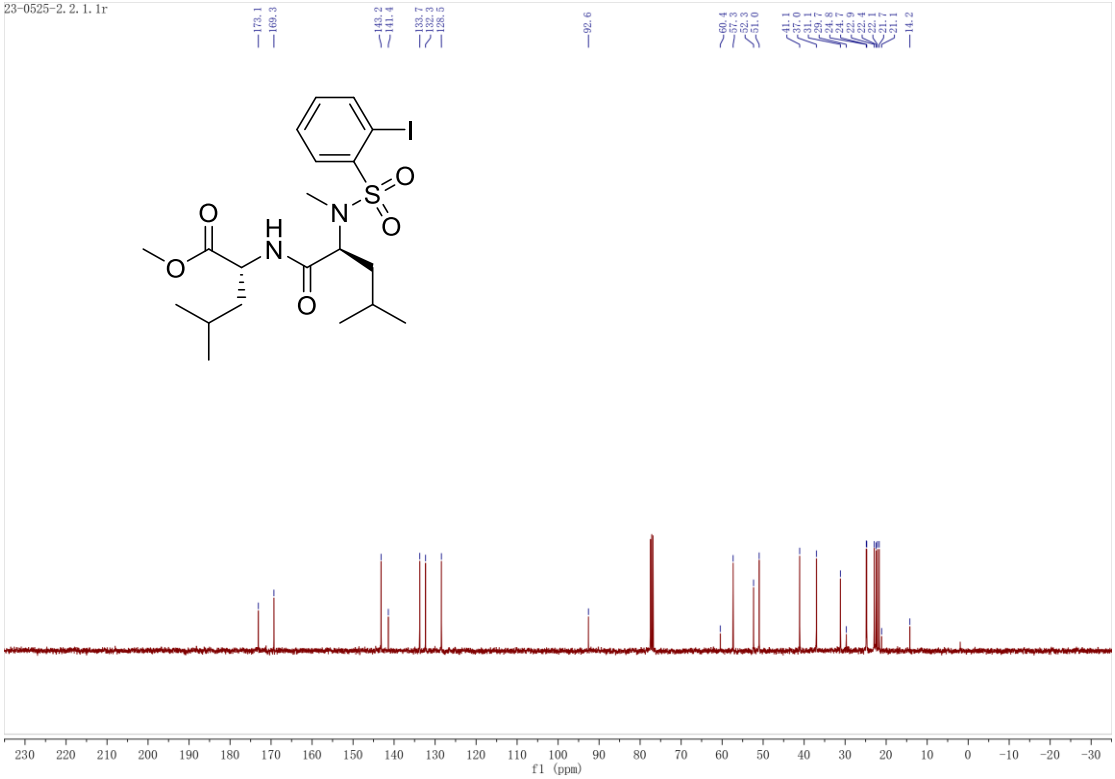
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **2.1**



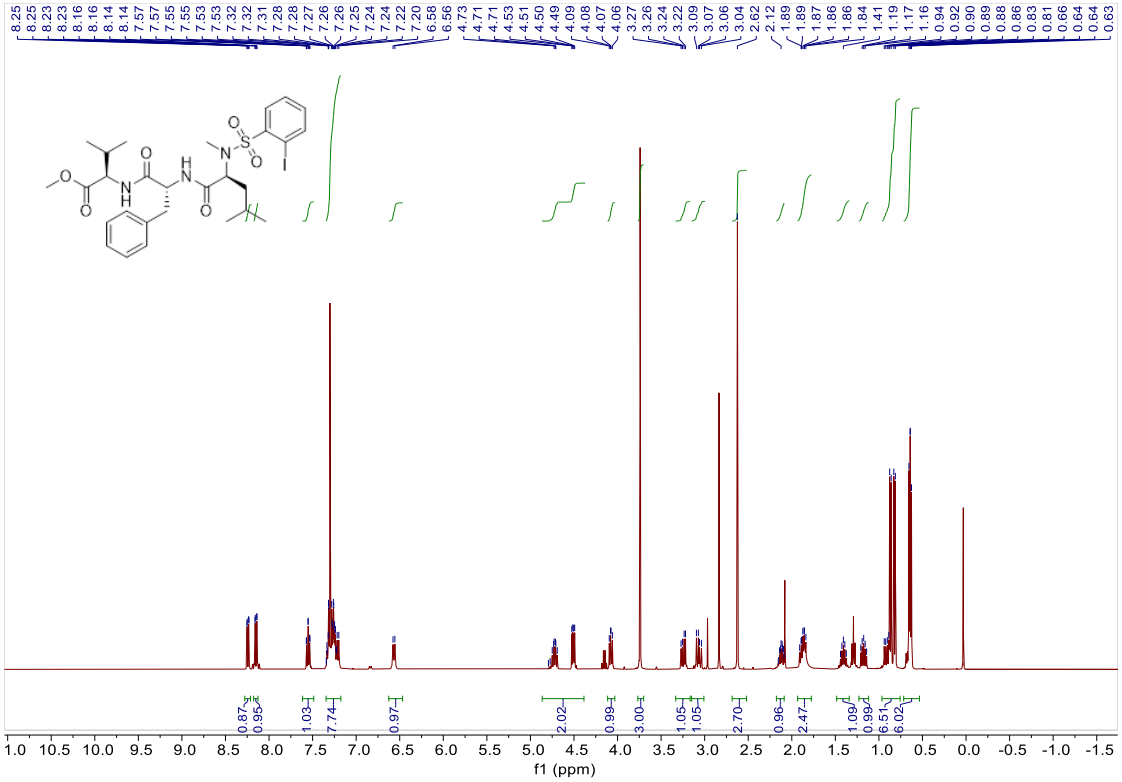
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **2.2**



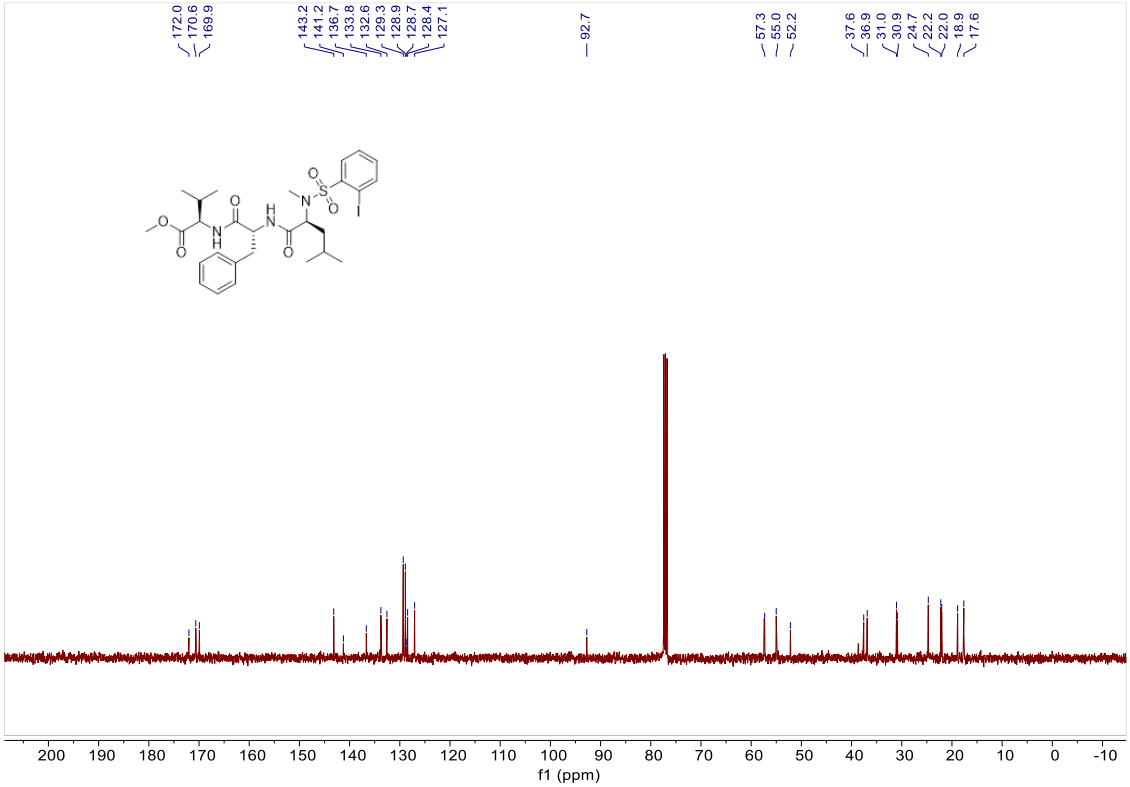
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **2.2**



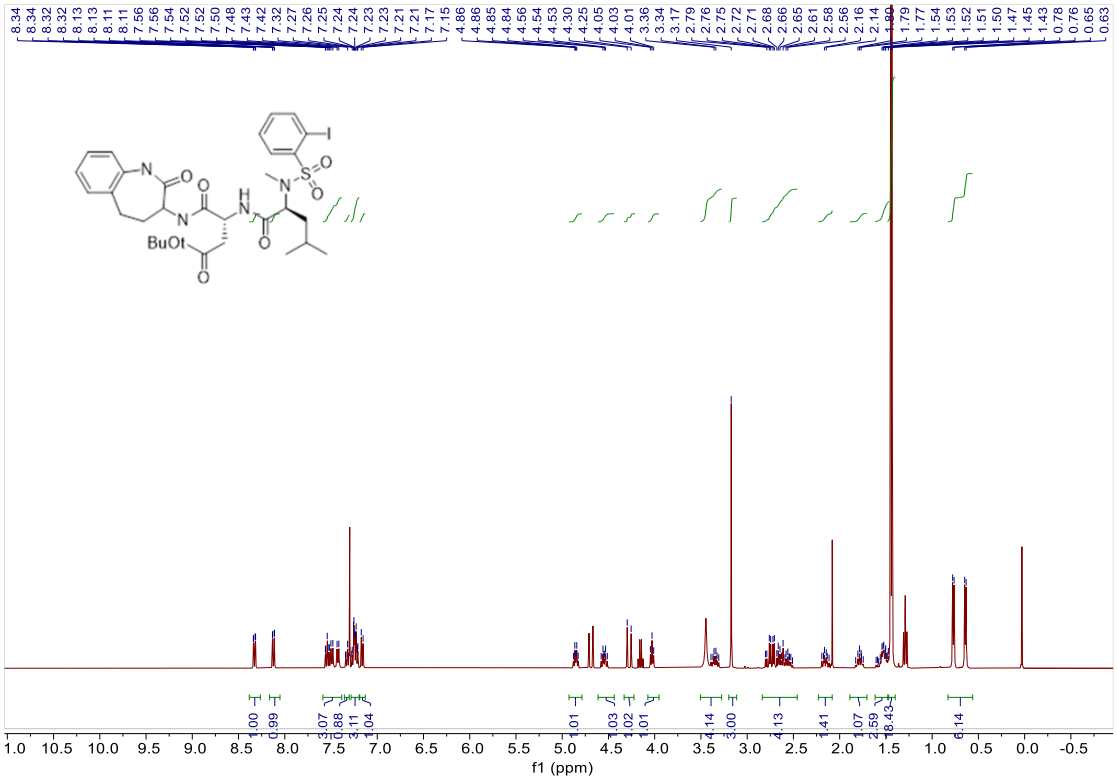
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **2.3**



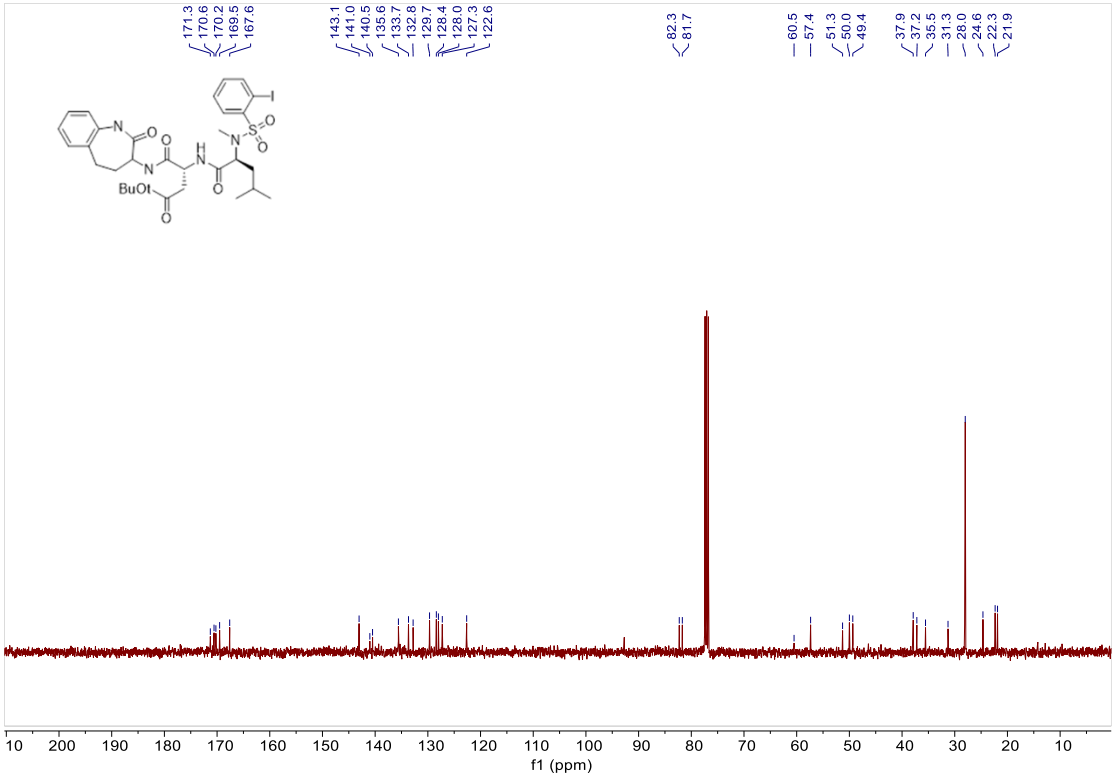
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **2.3**



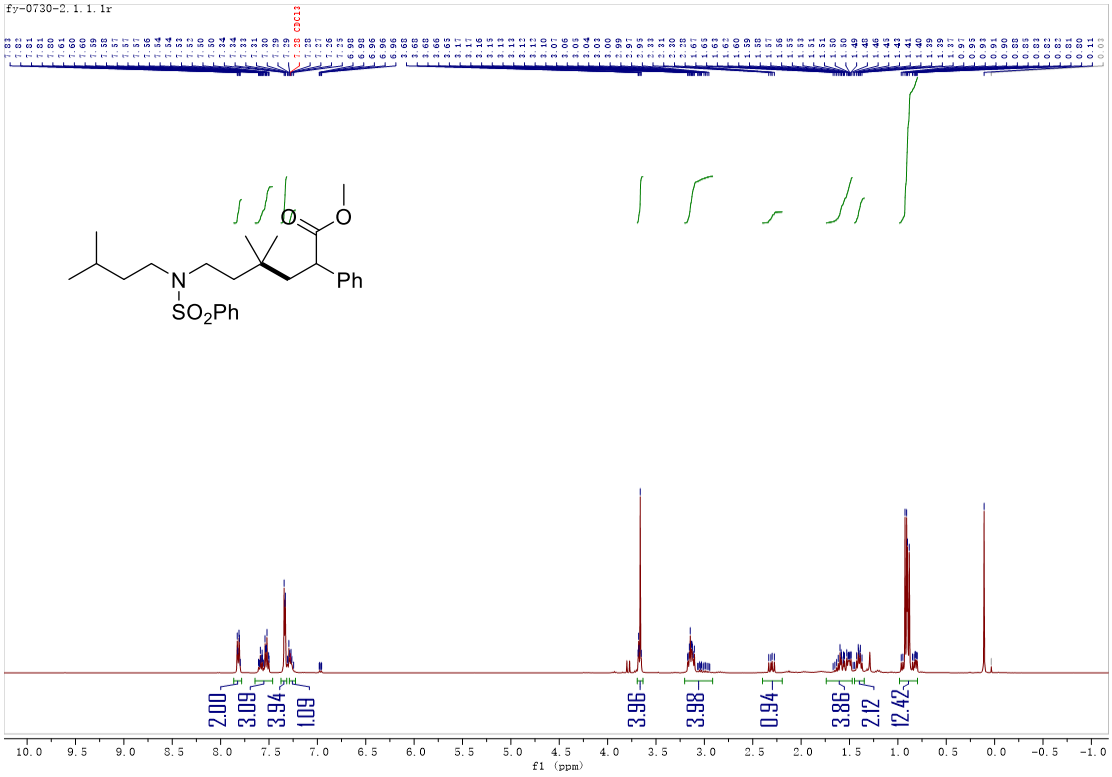
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **2.4**



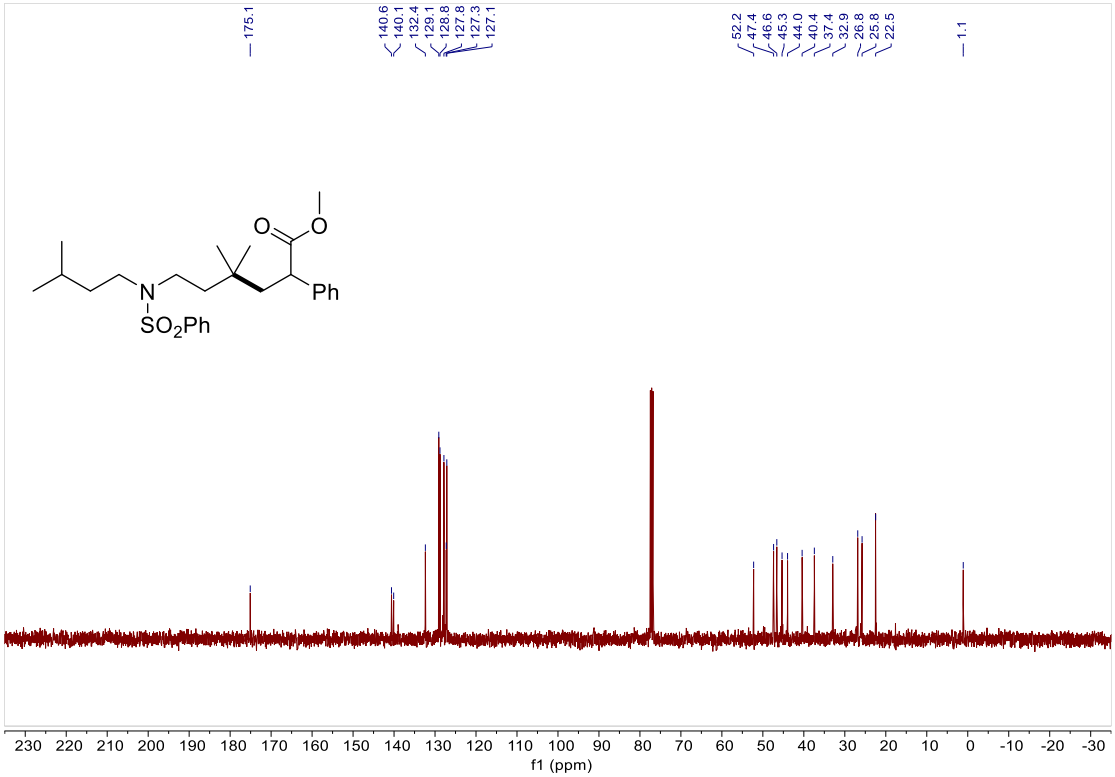
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **2.4**



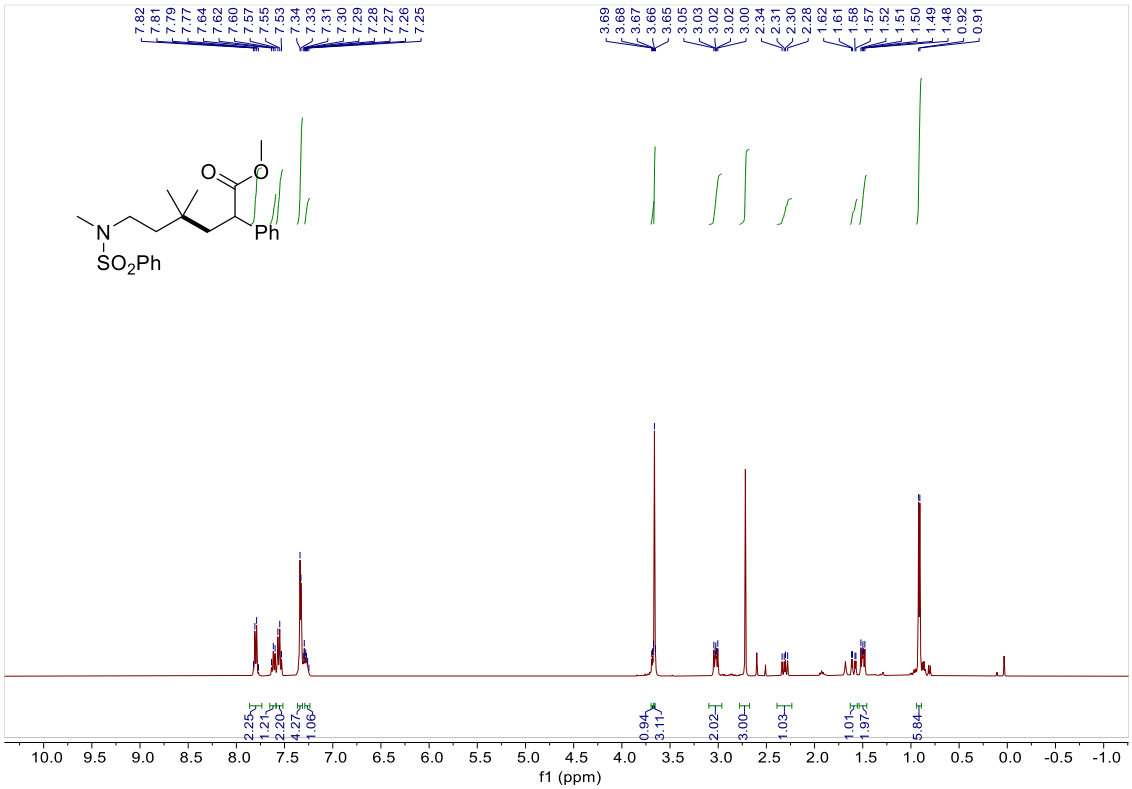
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **1c**



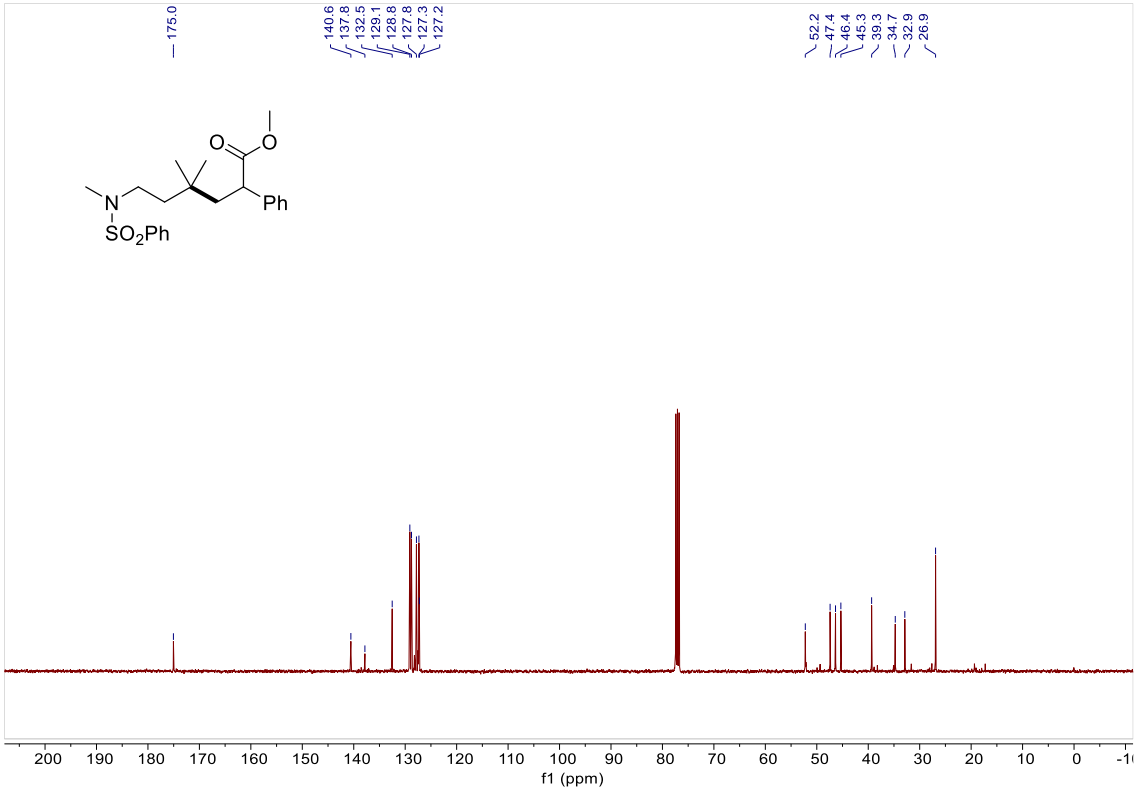
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **1c**



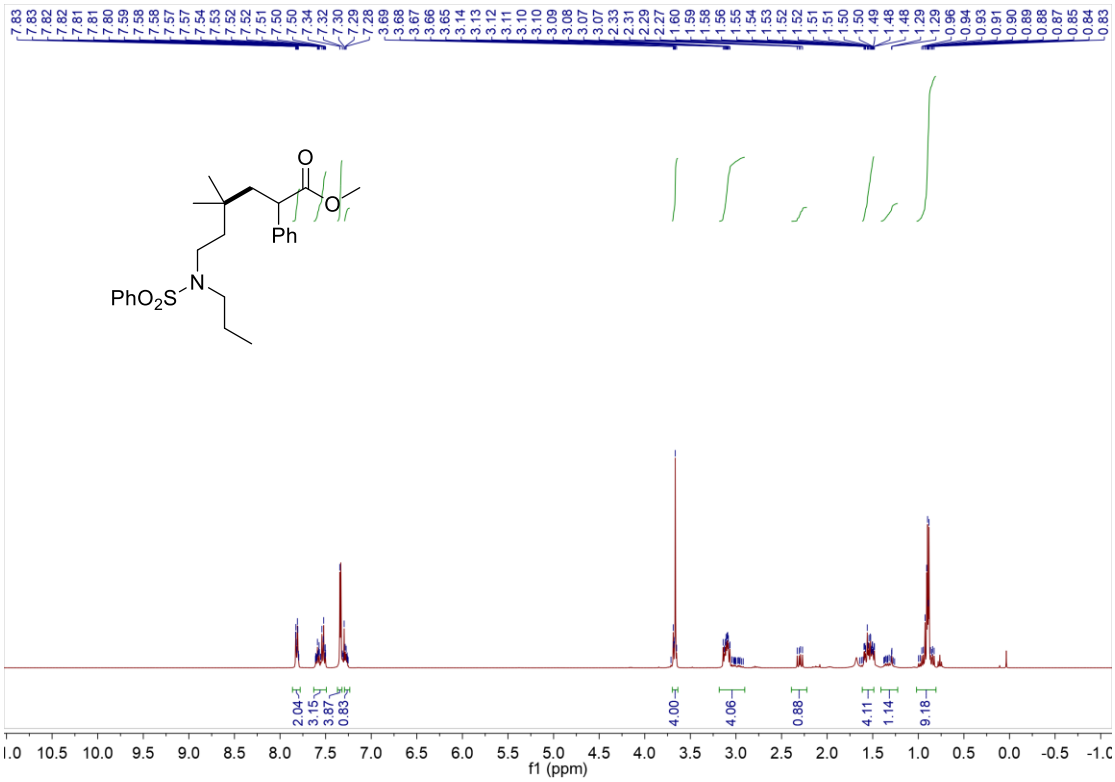
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **2c**



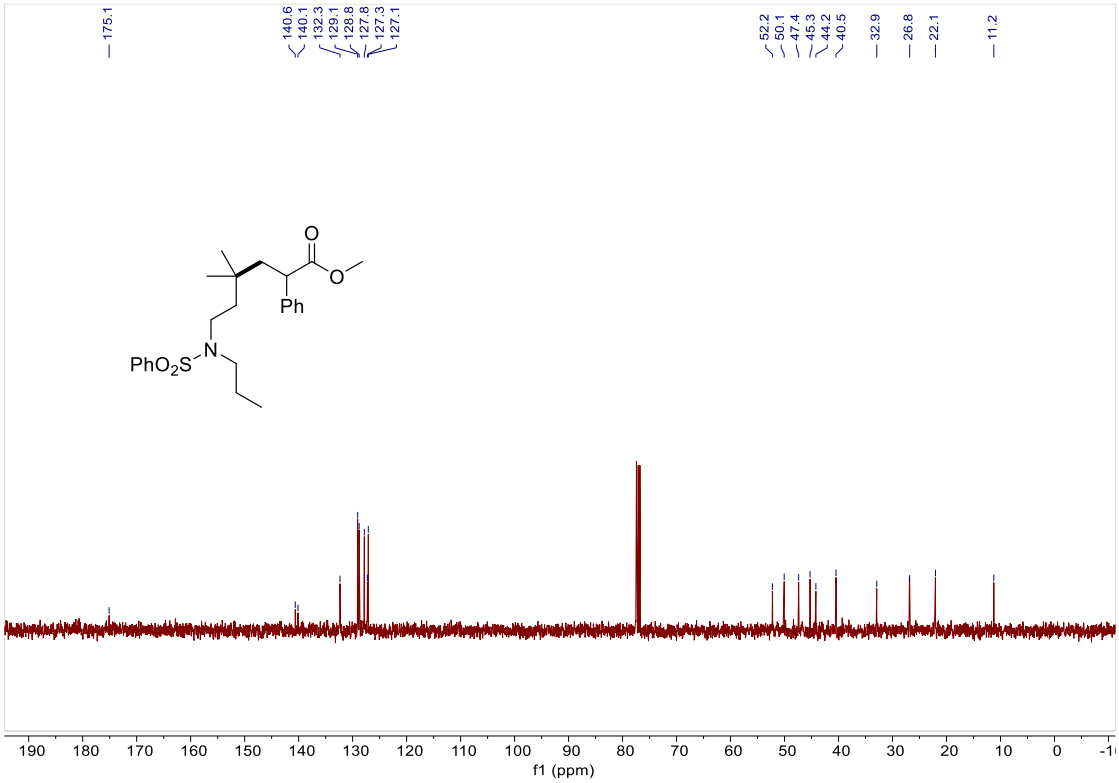
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **2c**



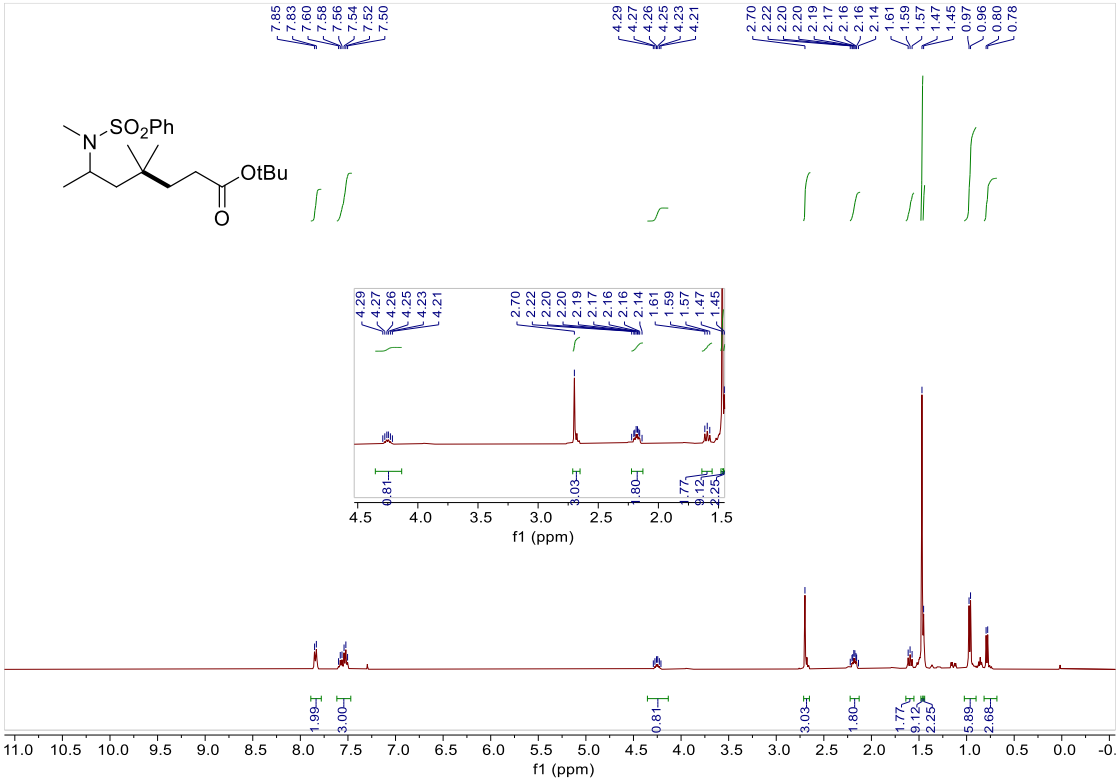
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **3c**



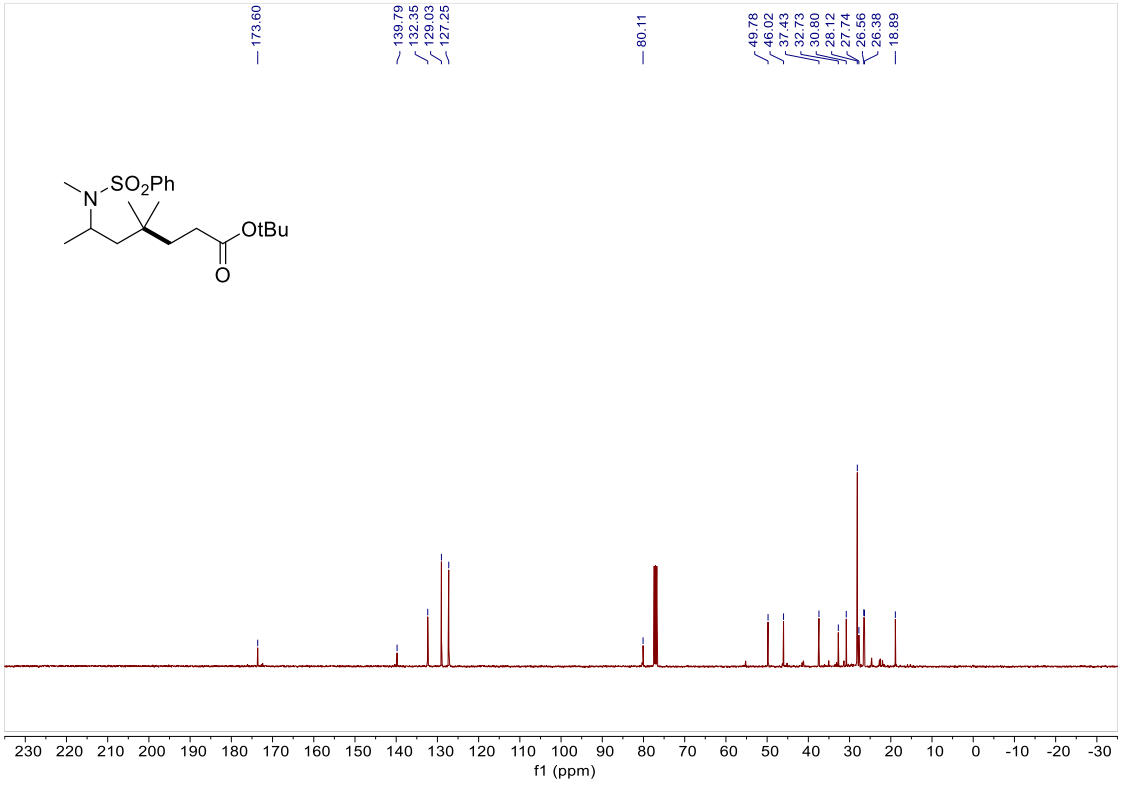
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **3c**



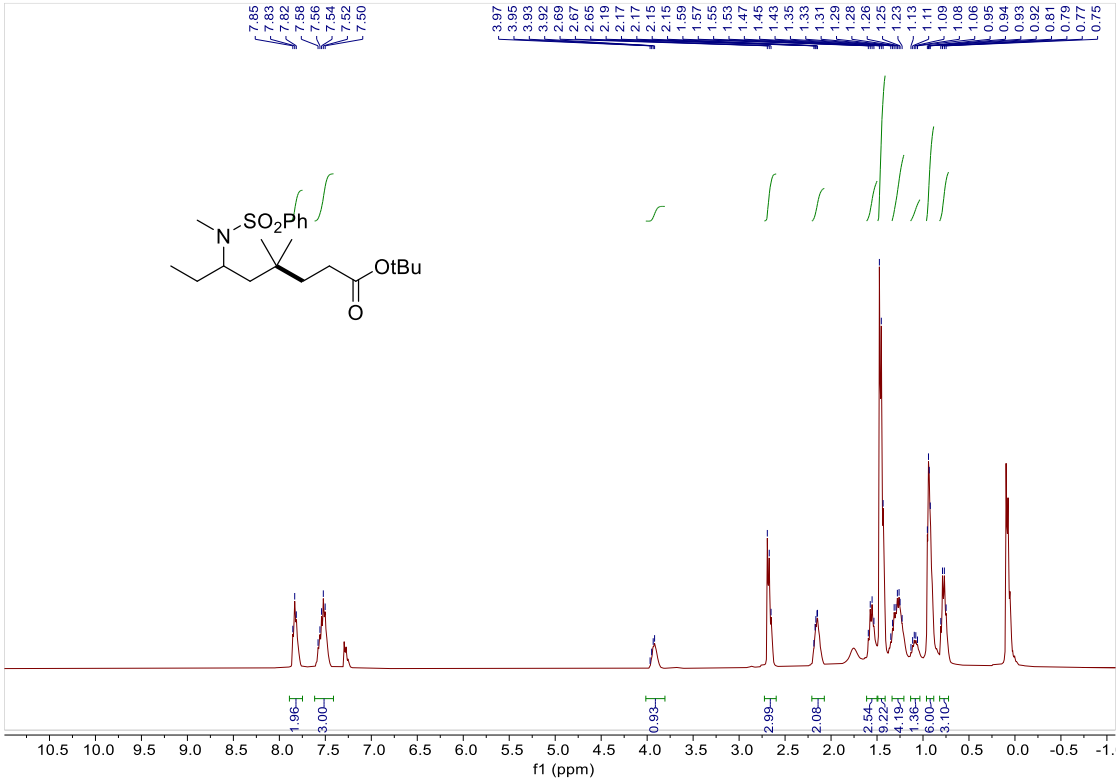
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **4c**



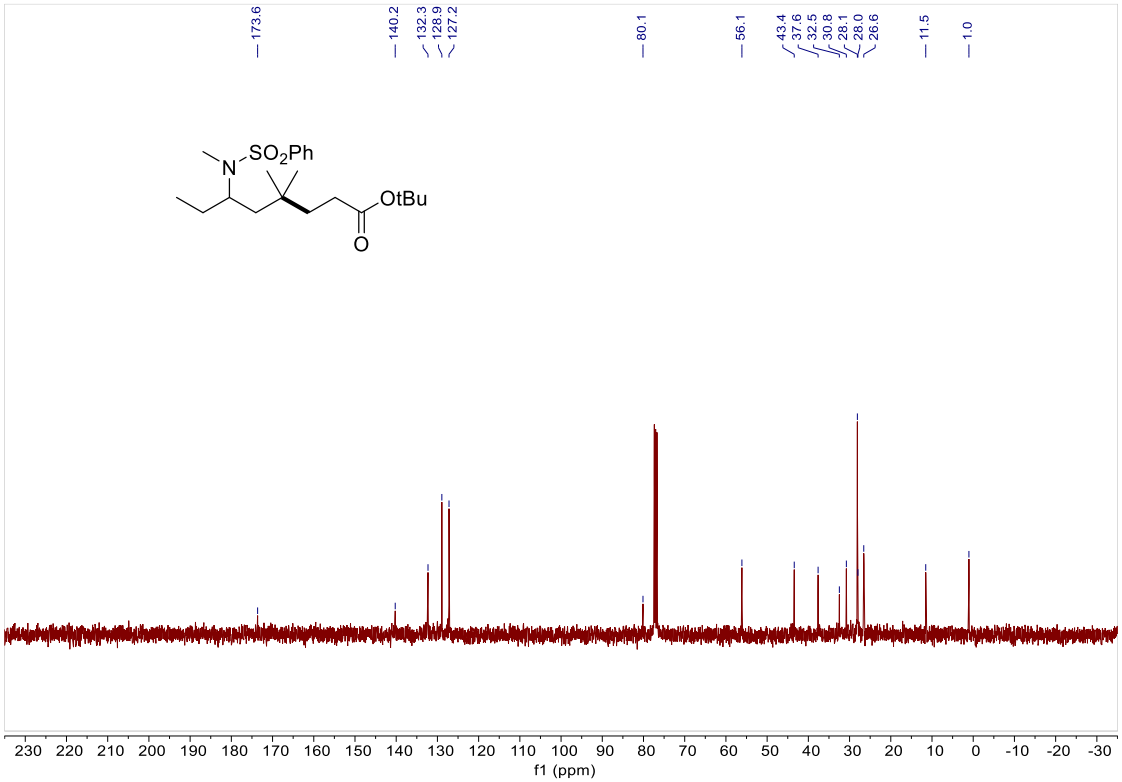
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **4c**



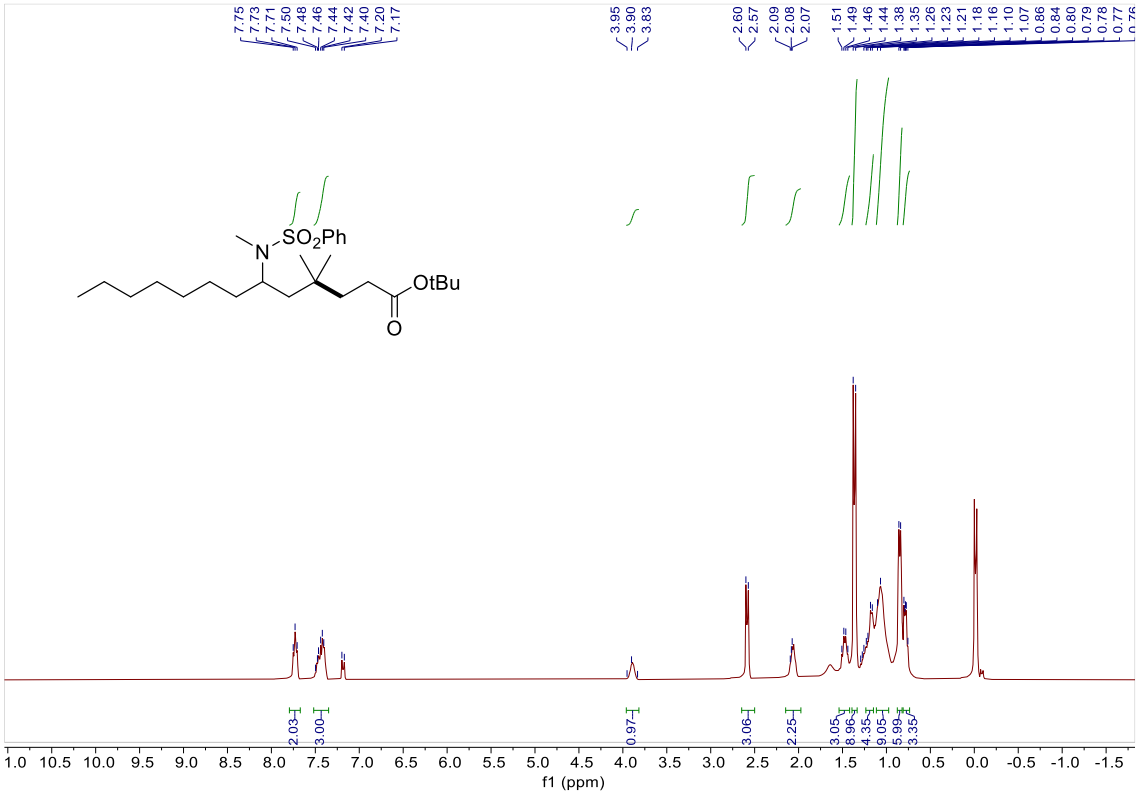
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **5c**



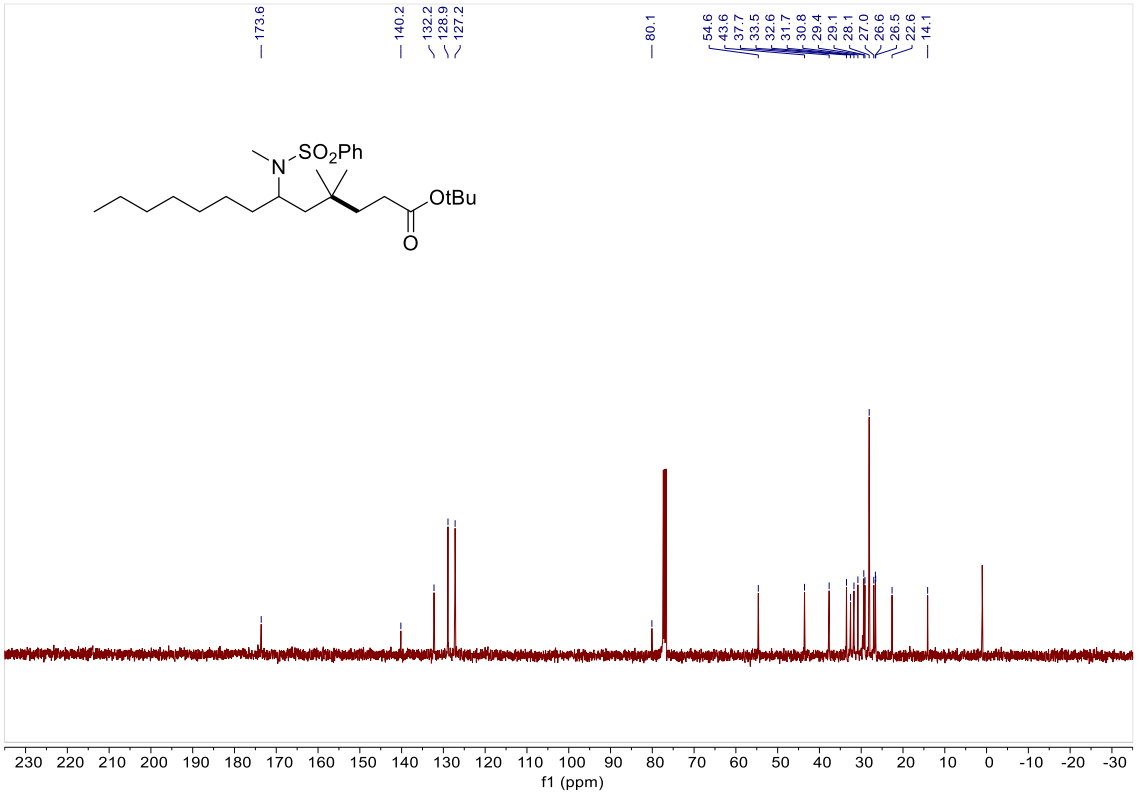
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **5c**



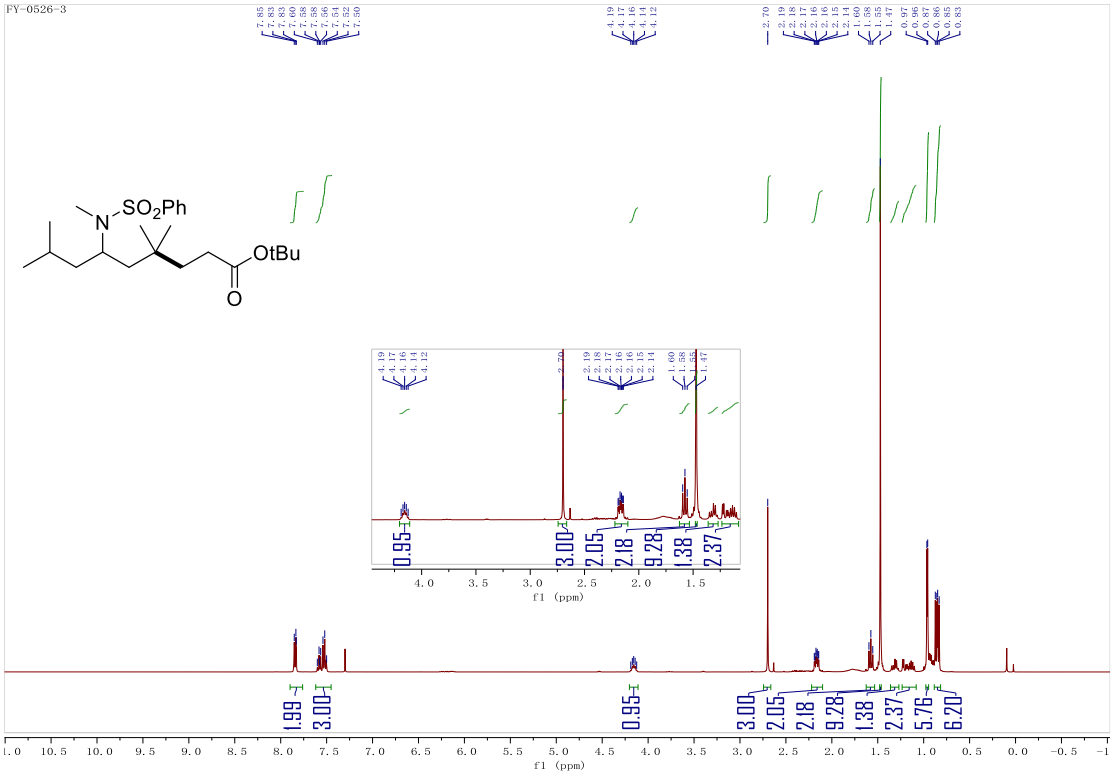
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **6c**



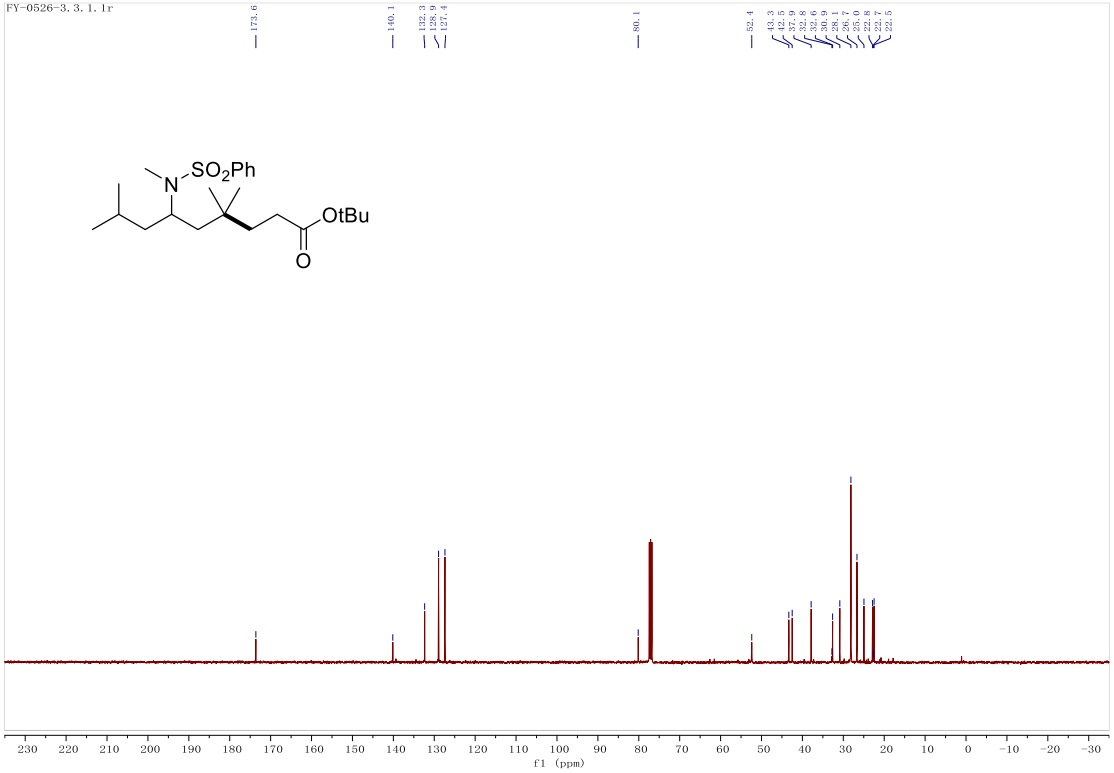
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **6c**



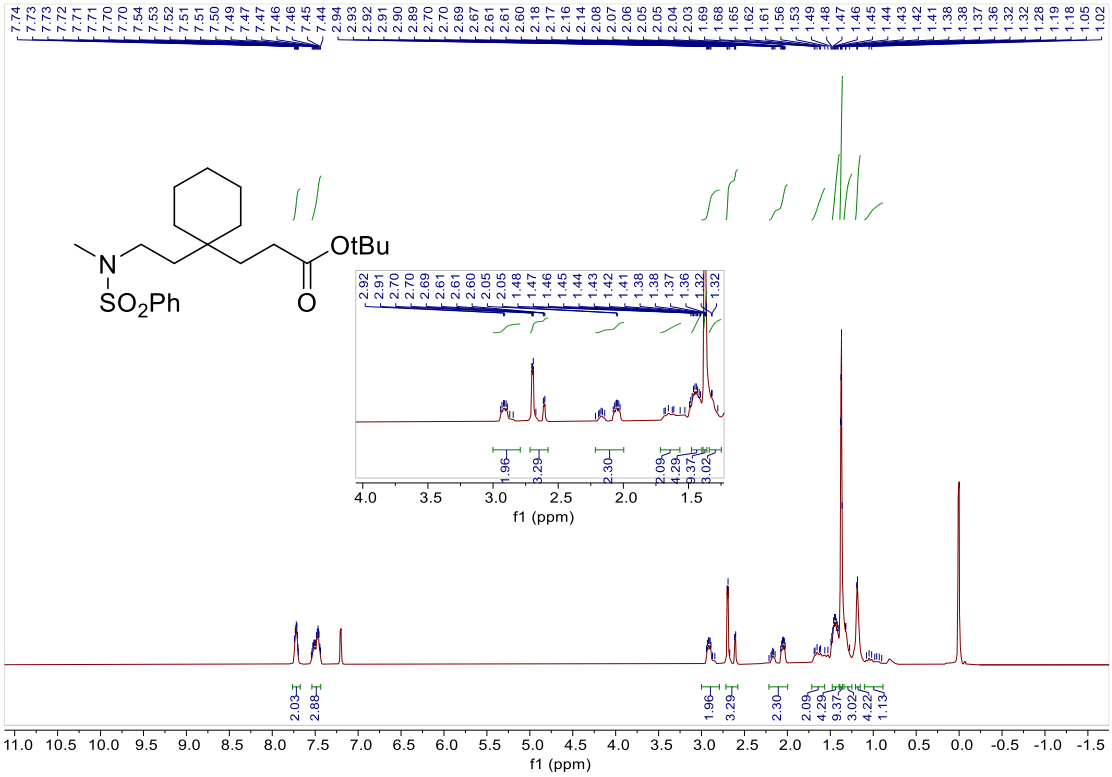
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **7c**



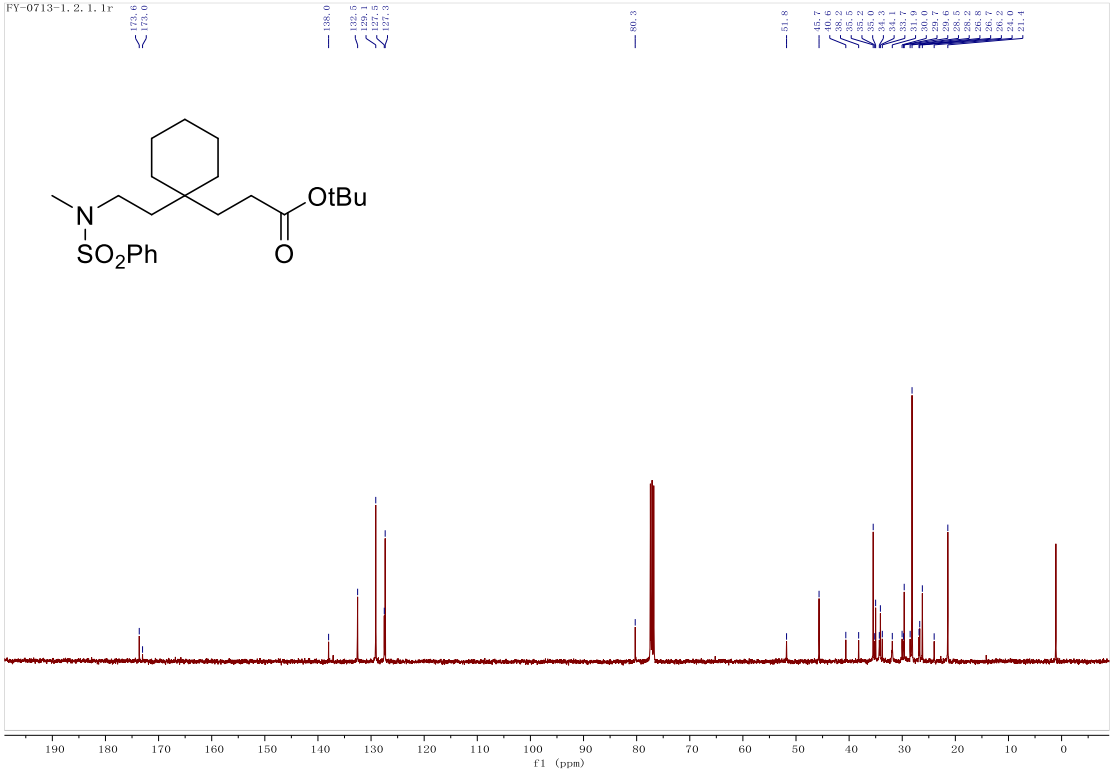
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **7c**



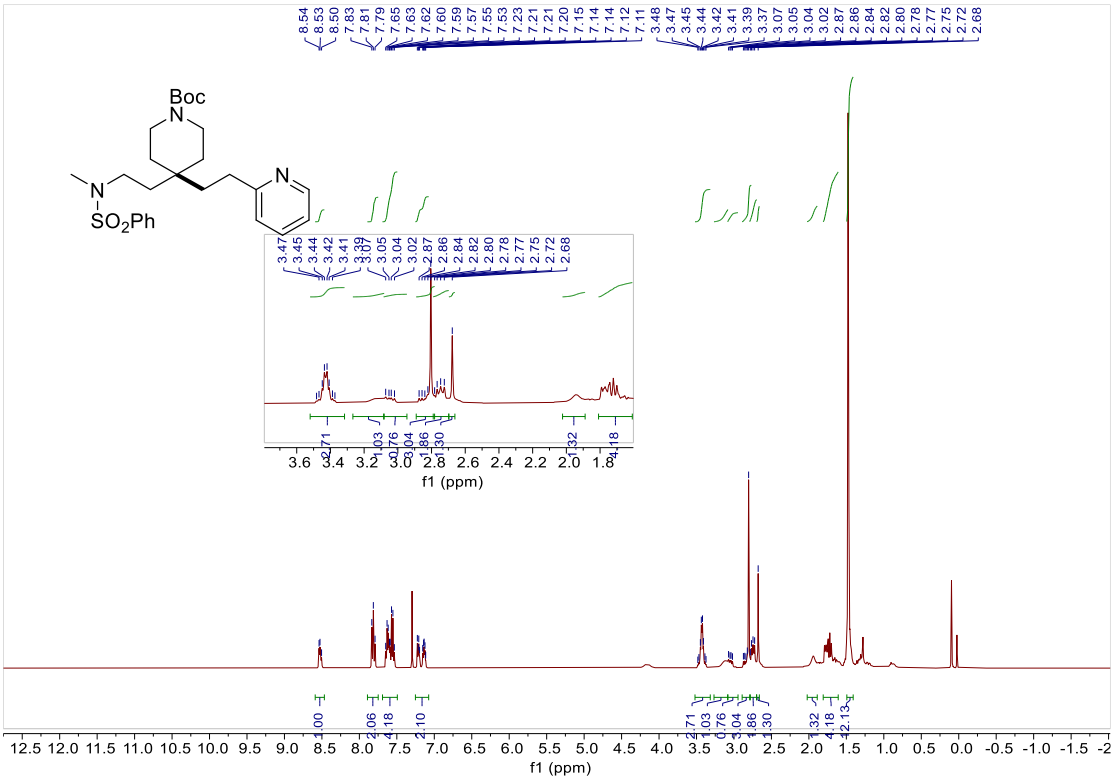
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **8c**



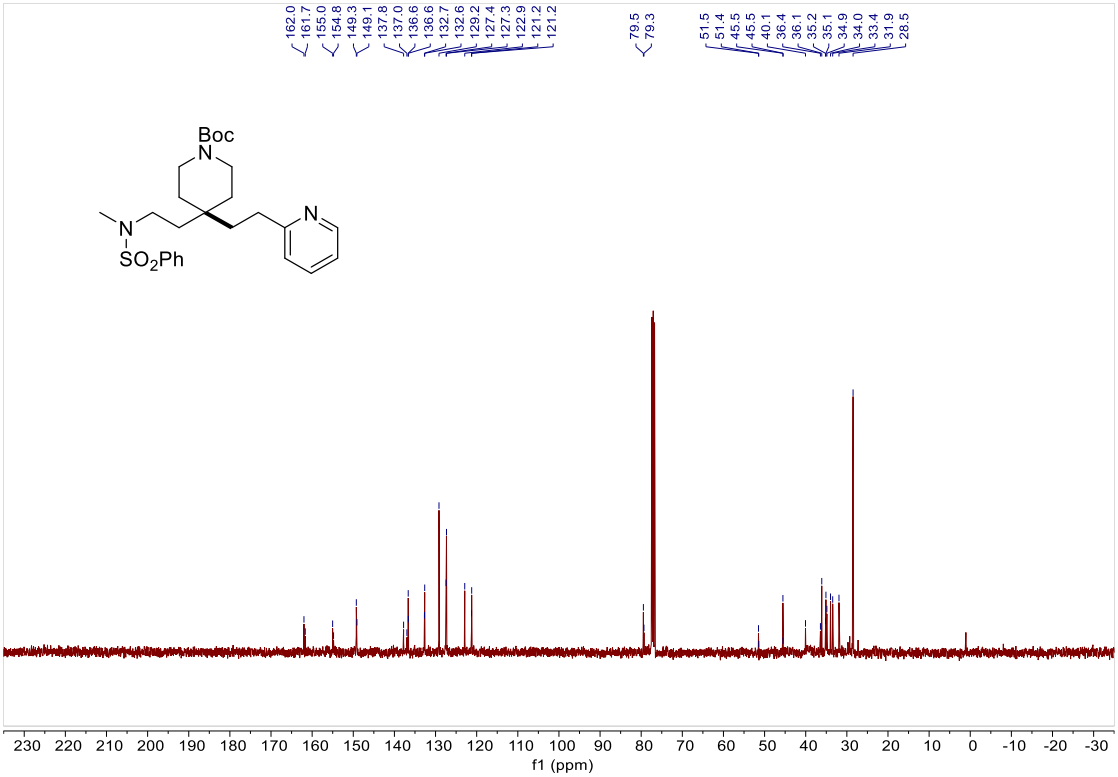
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **8c**



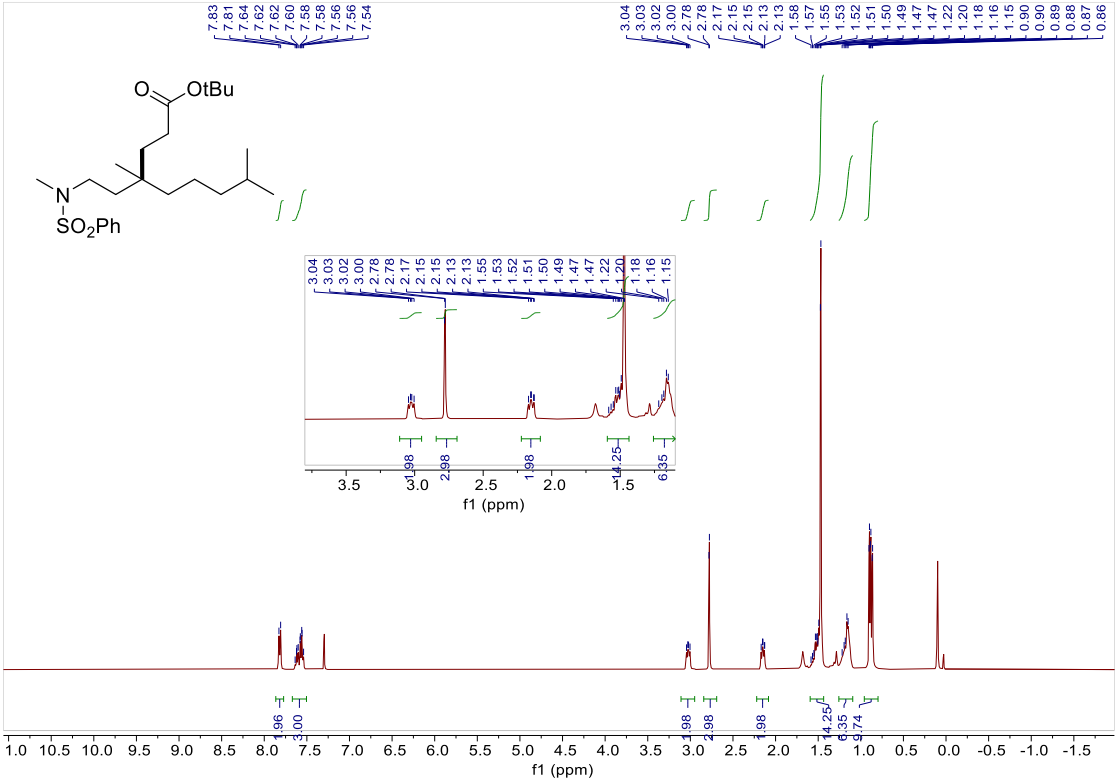
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **9c**



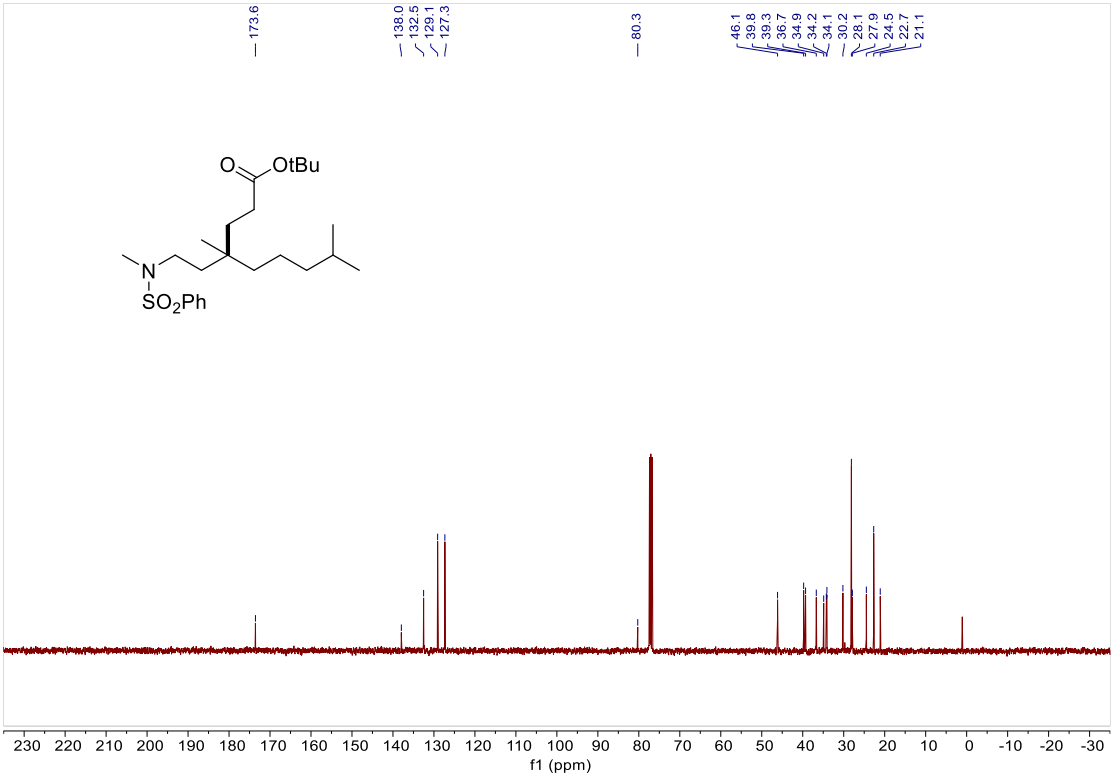
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **9c**



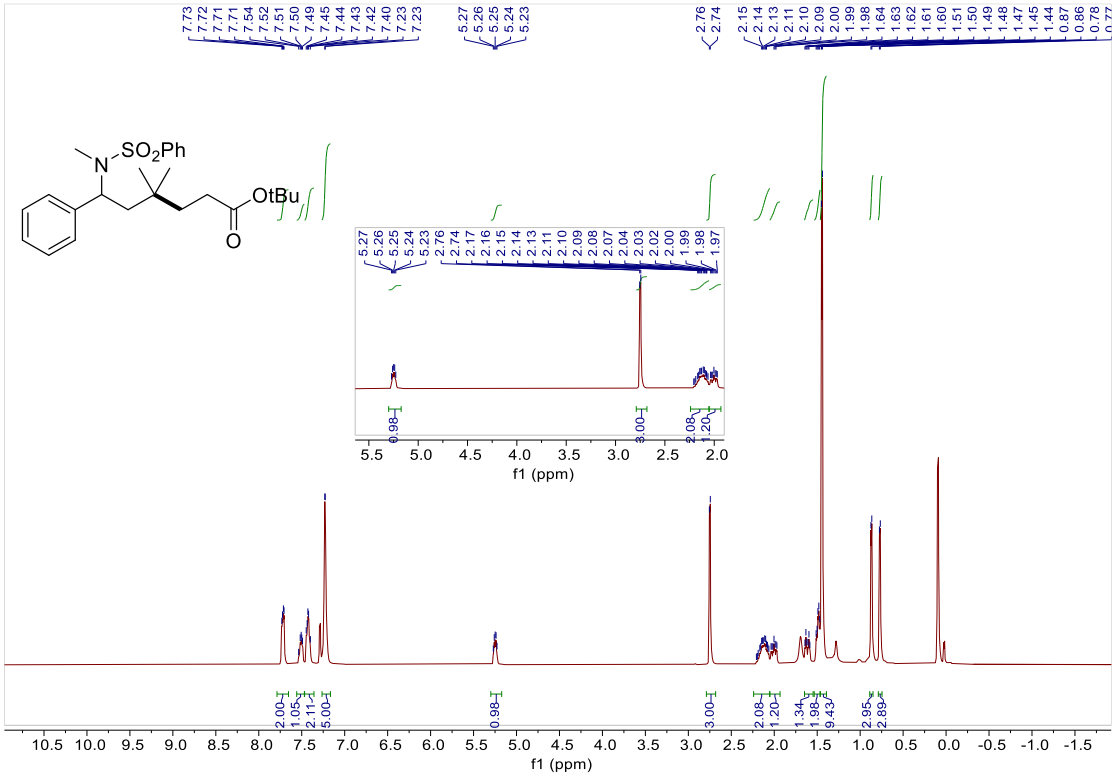
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **10c**



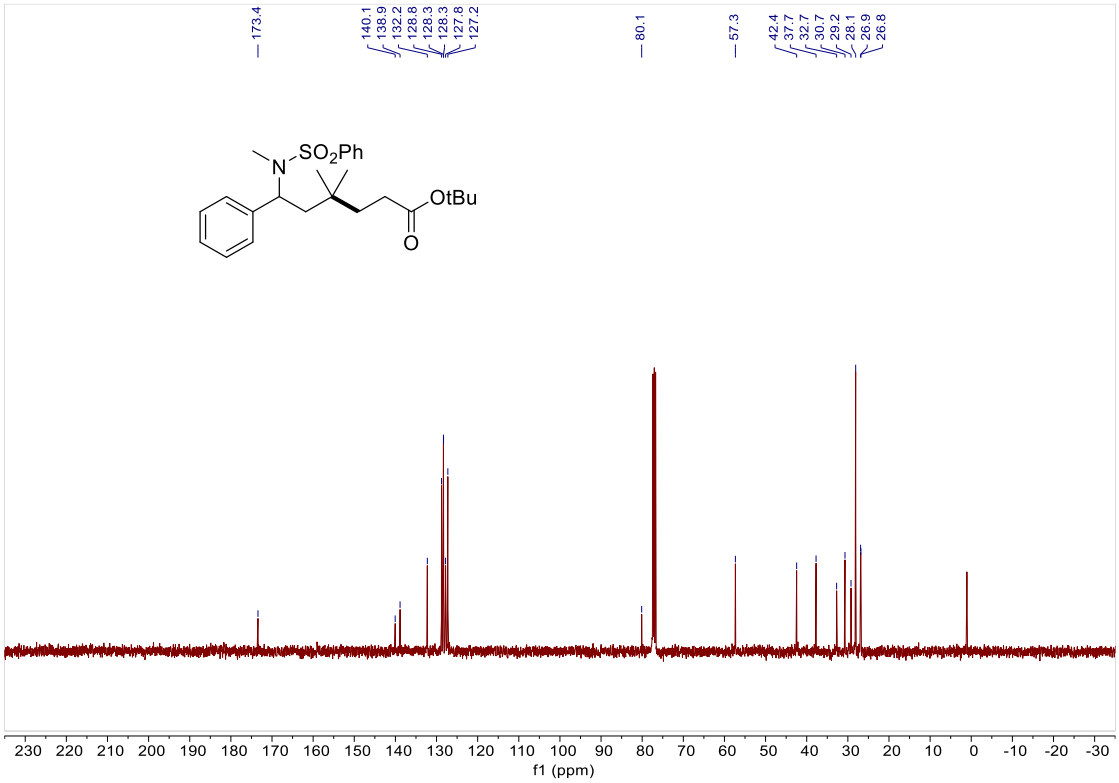
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **10c**



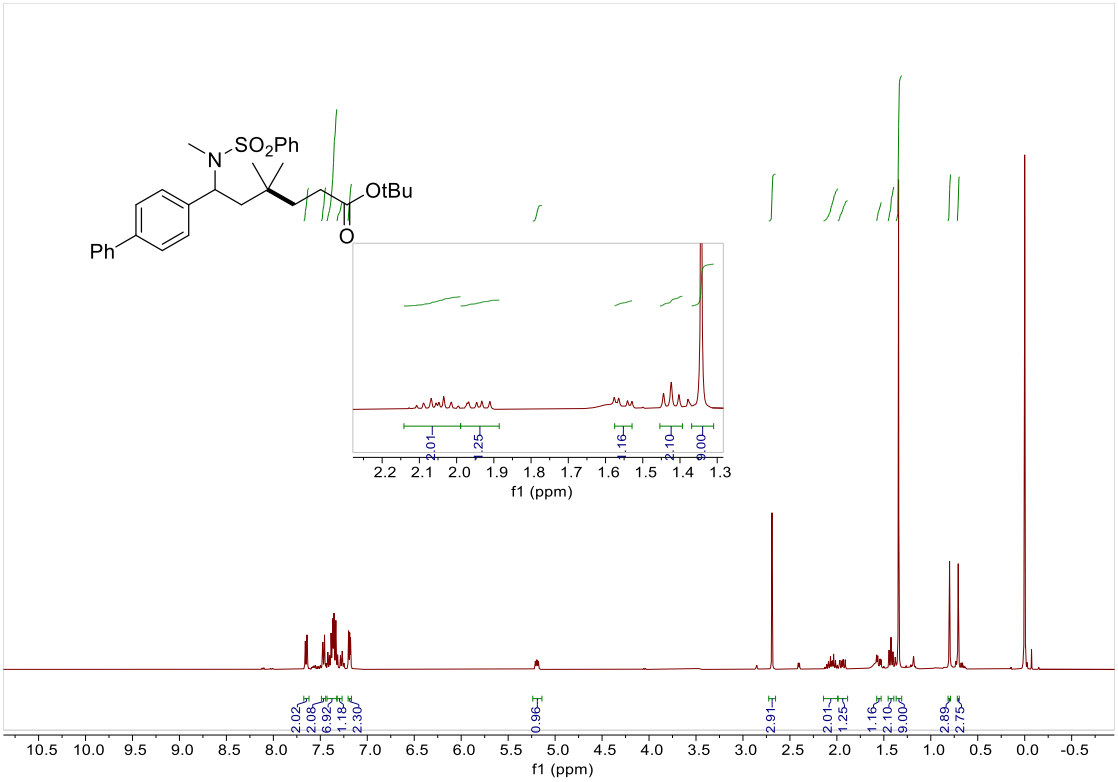
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **11c**



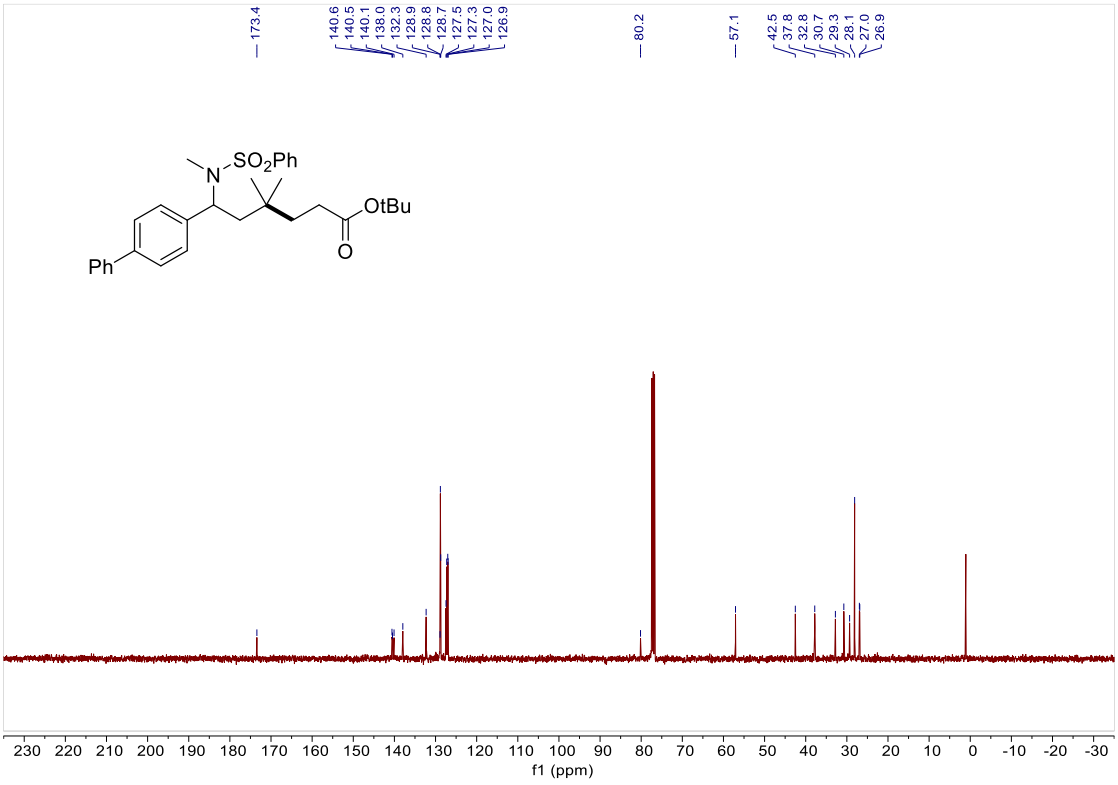
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **11c**



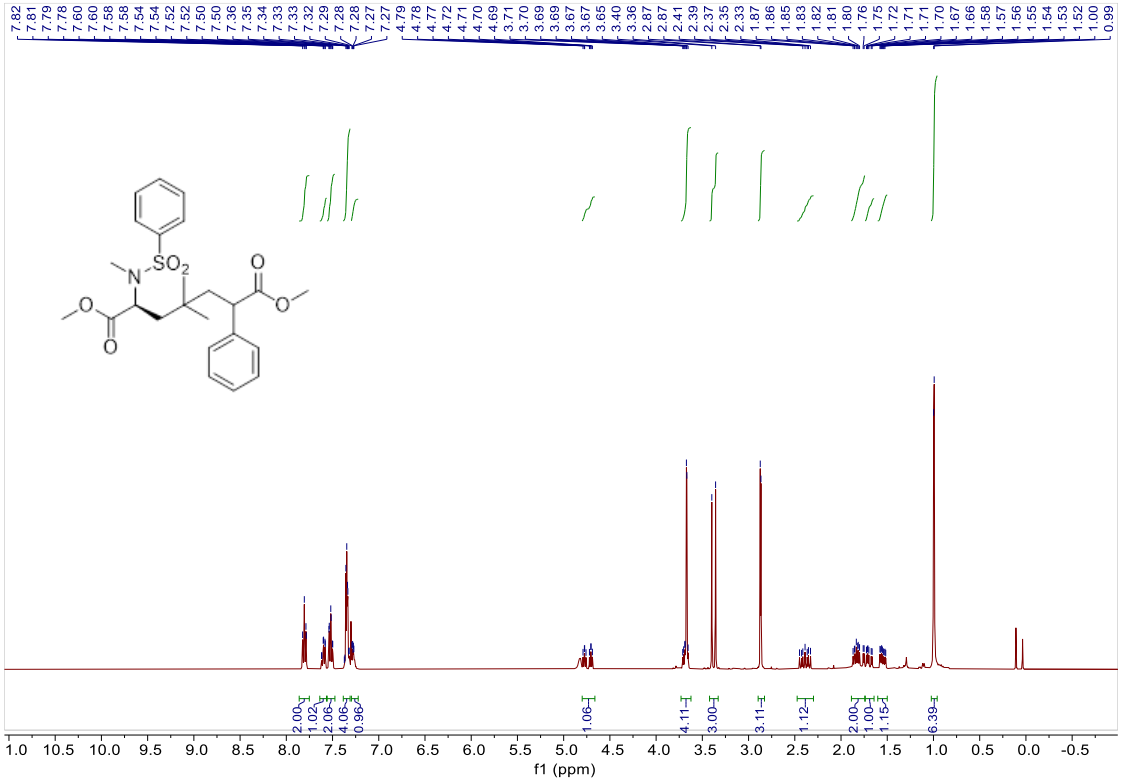
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **12c**



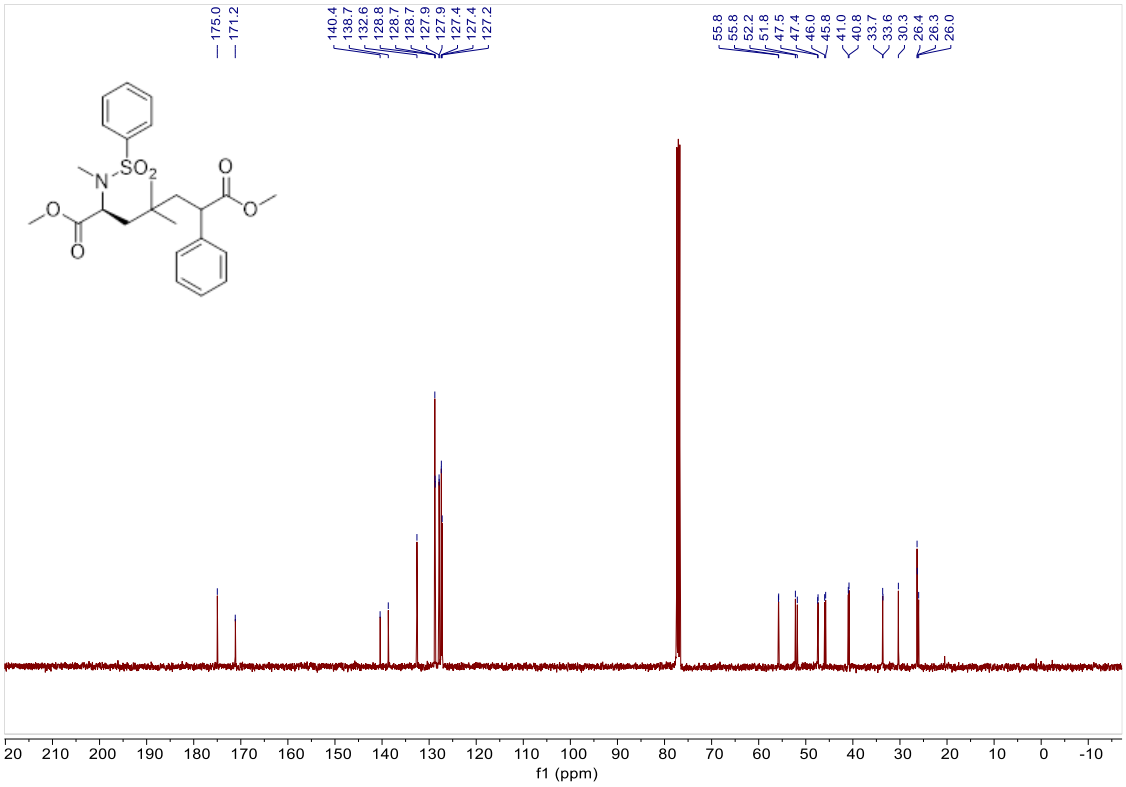
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **12c**



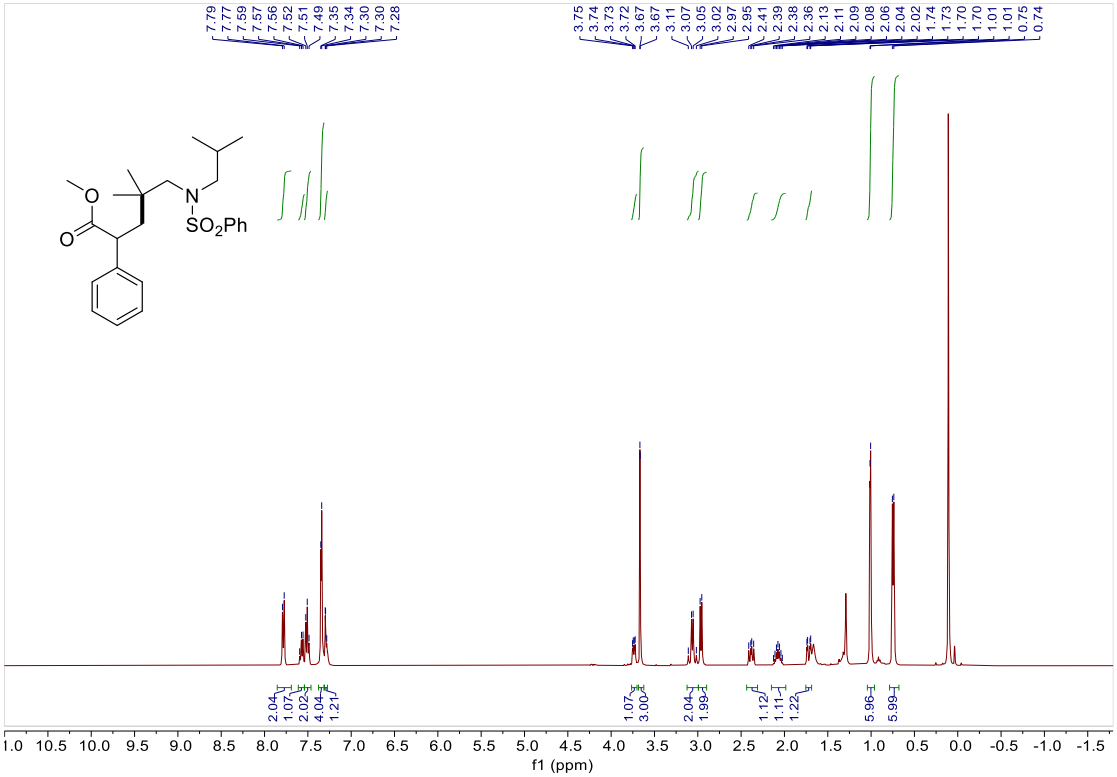
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **13c**



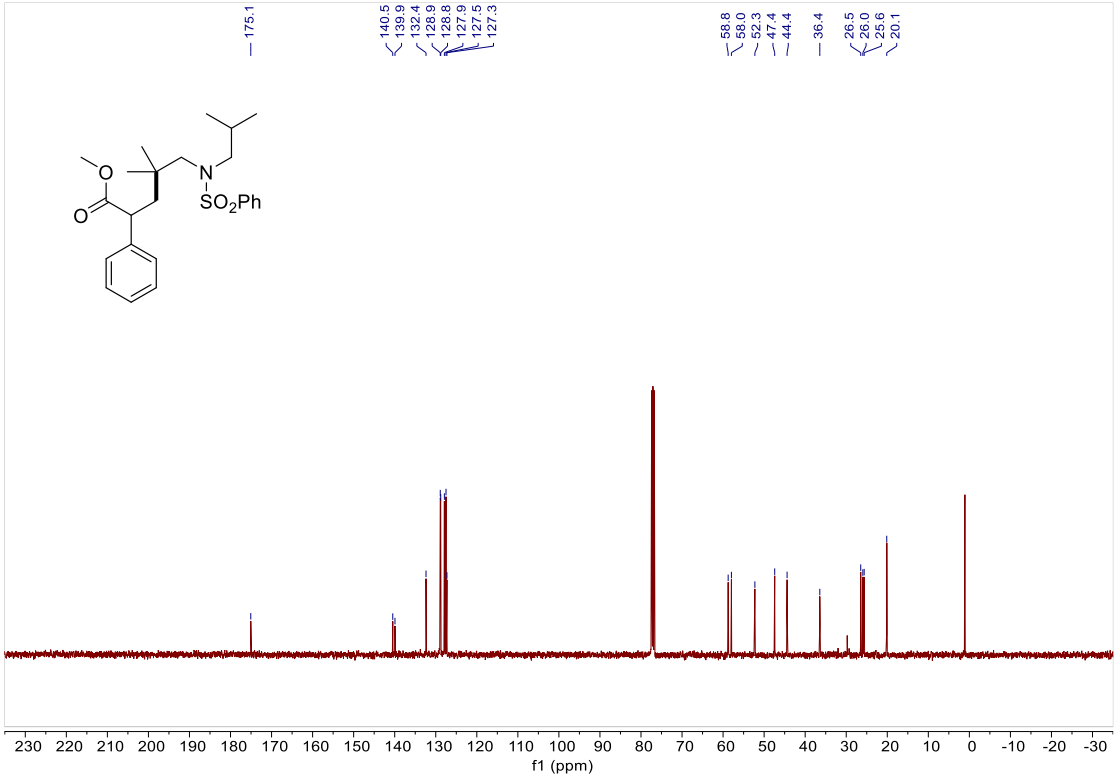
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **13c**



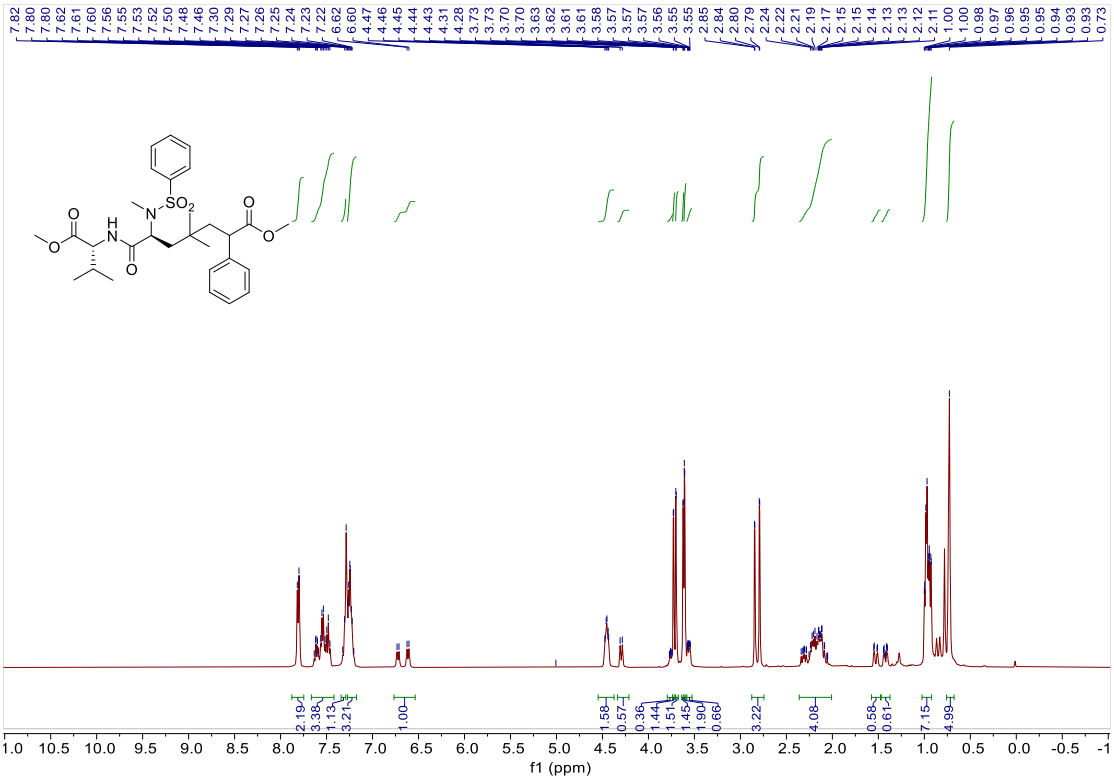
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **14c**



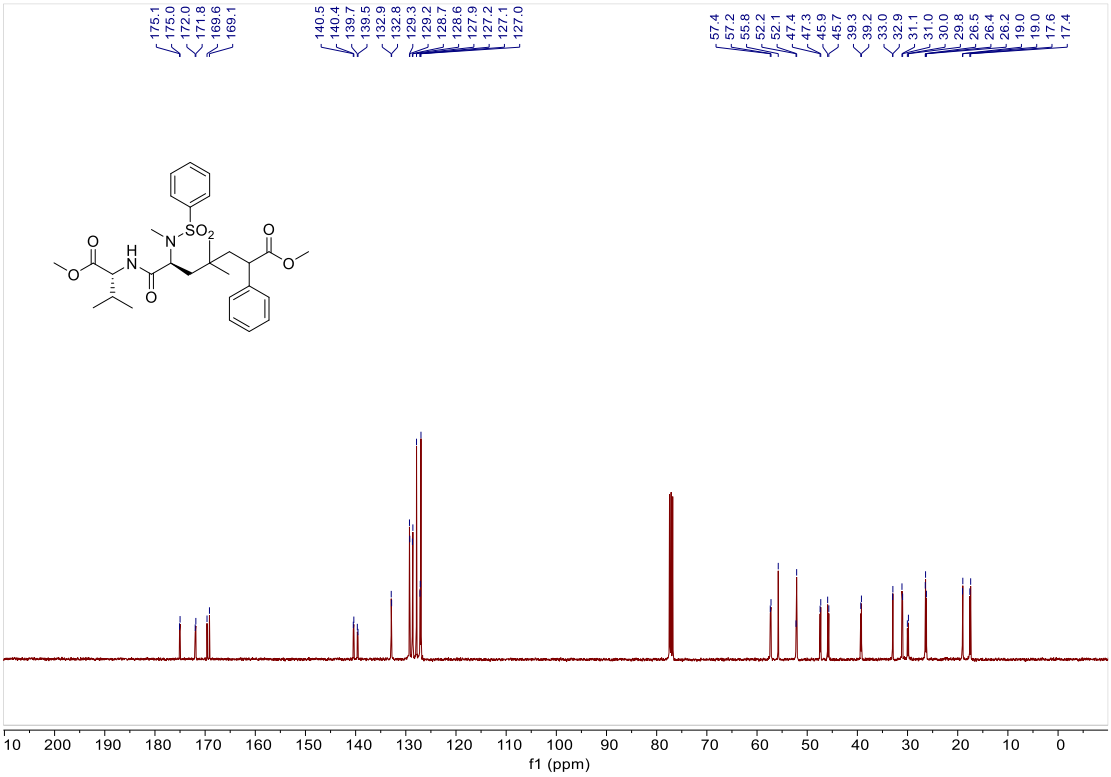
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **14c**



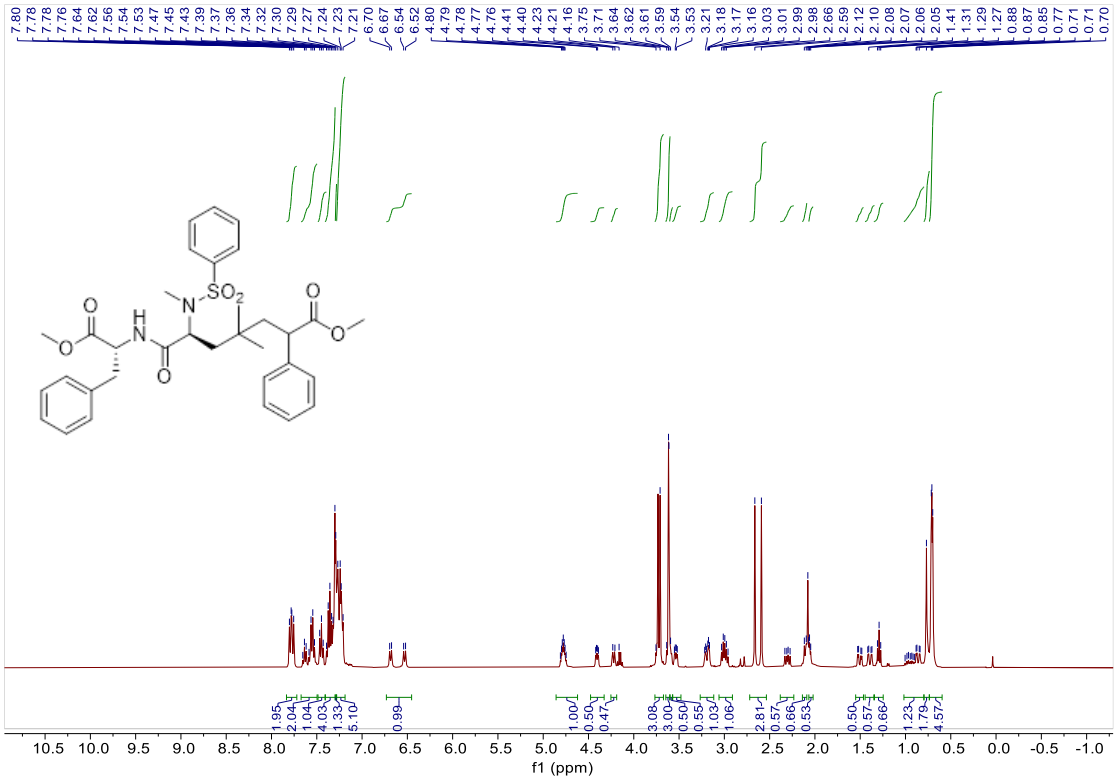
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **16c**



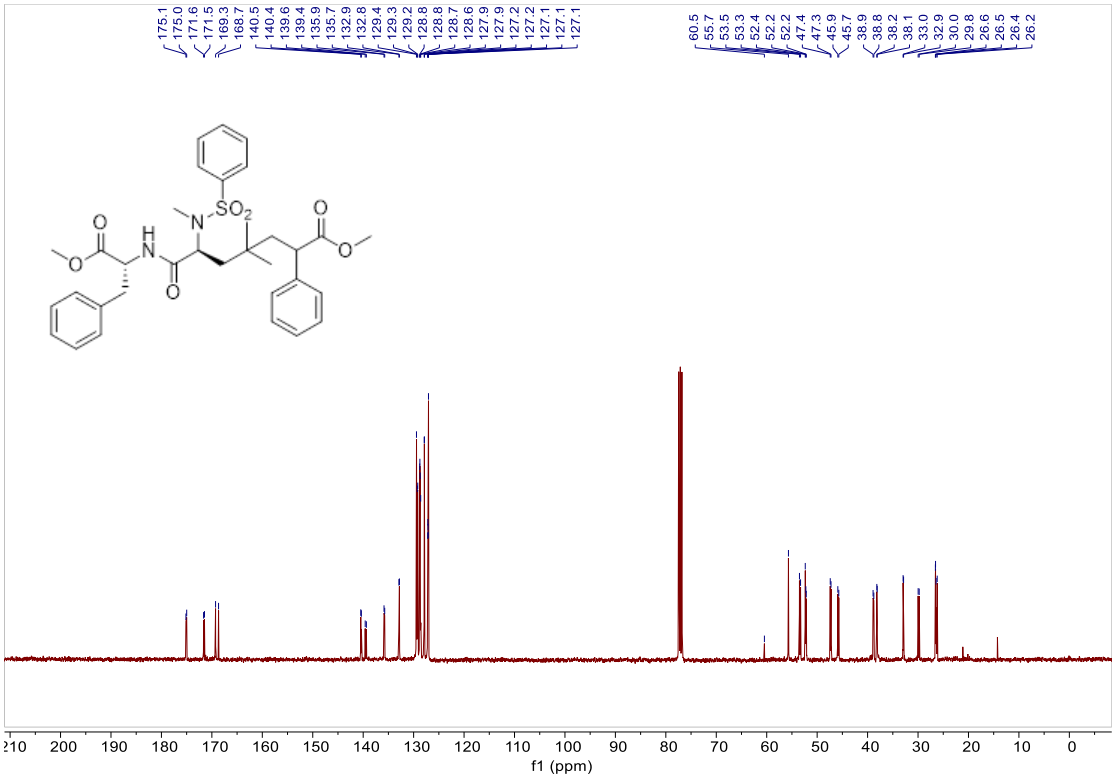
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **16c**



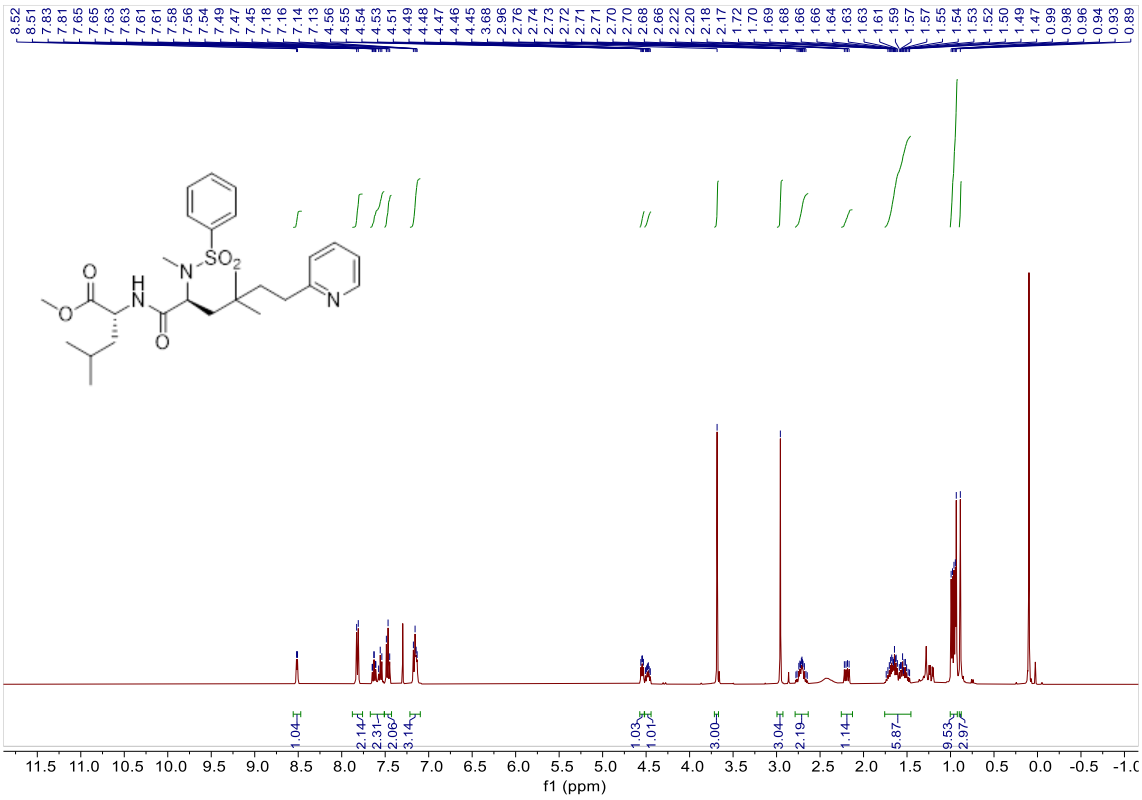
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **17c**



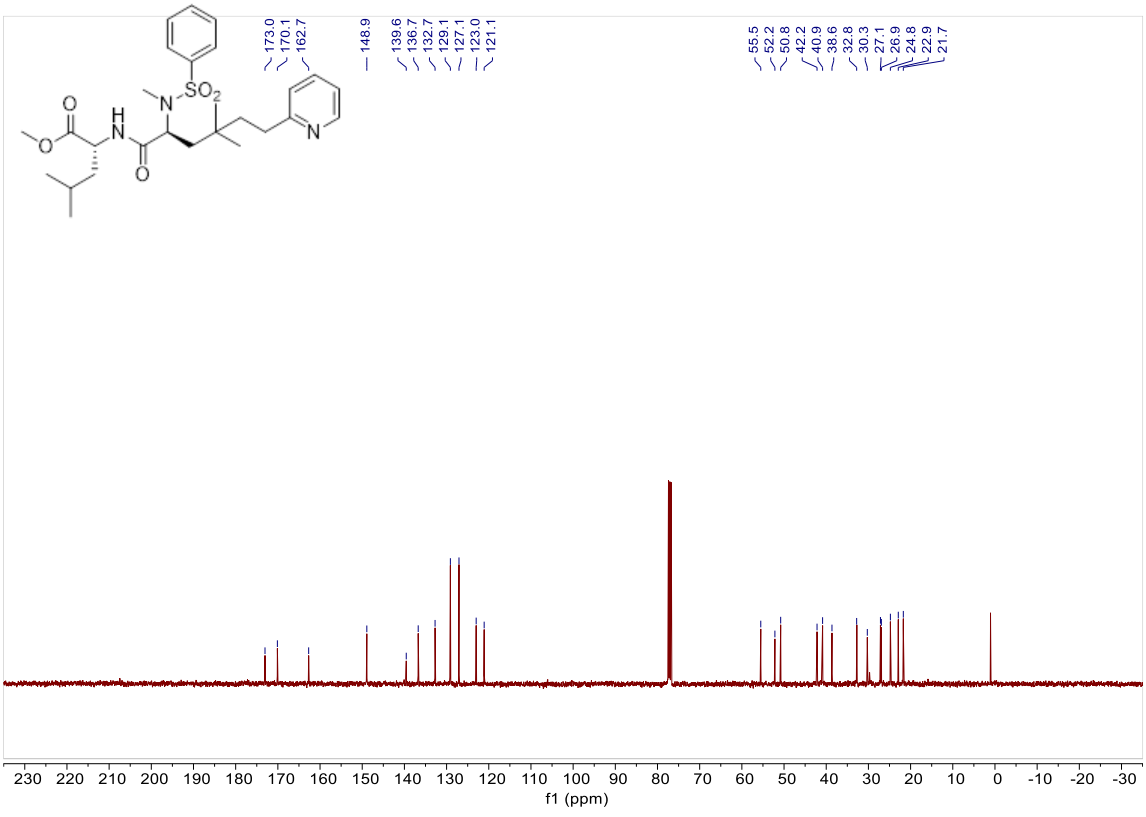
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **17c**



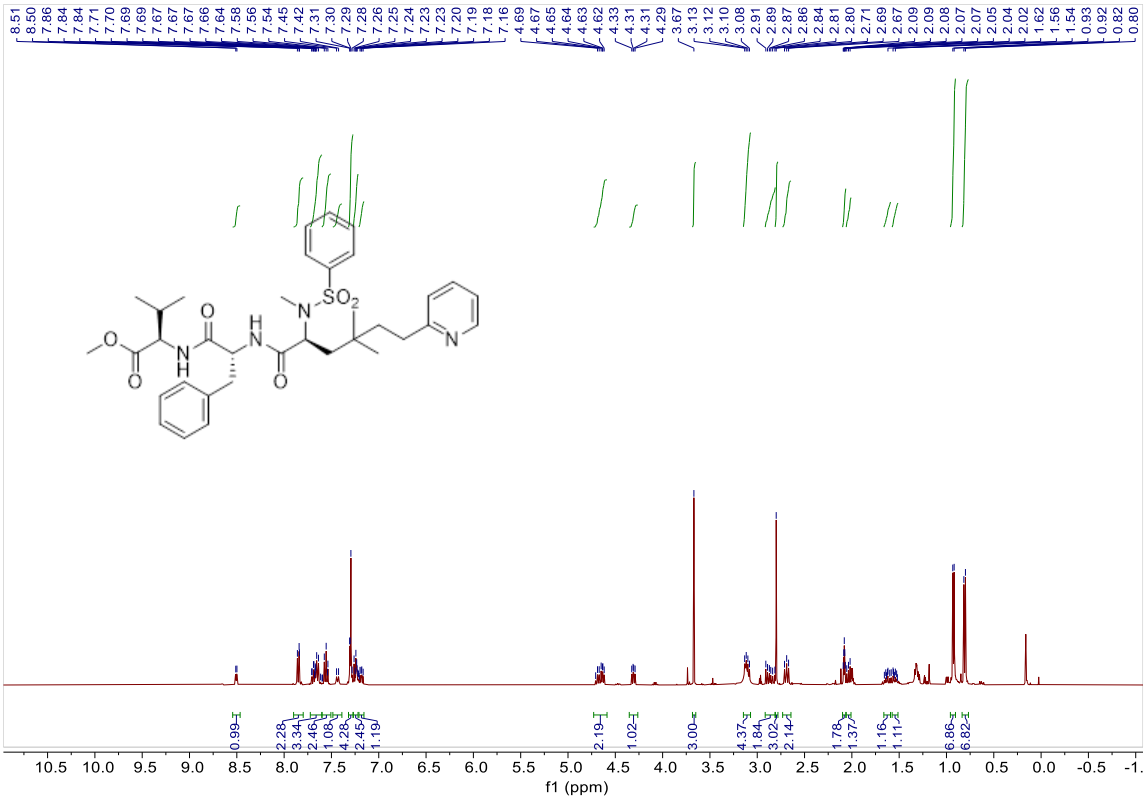
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **18c**



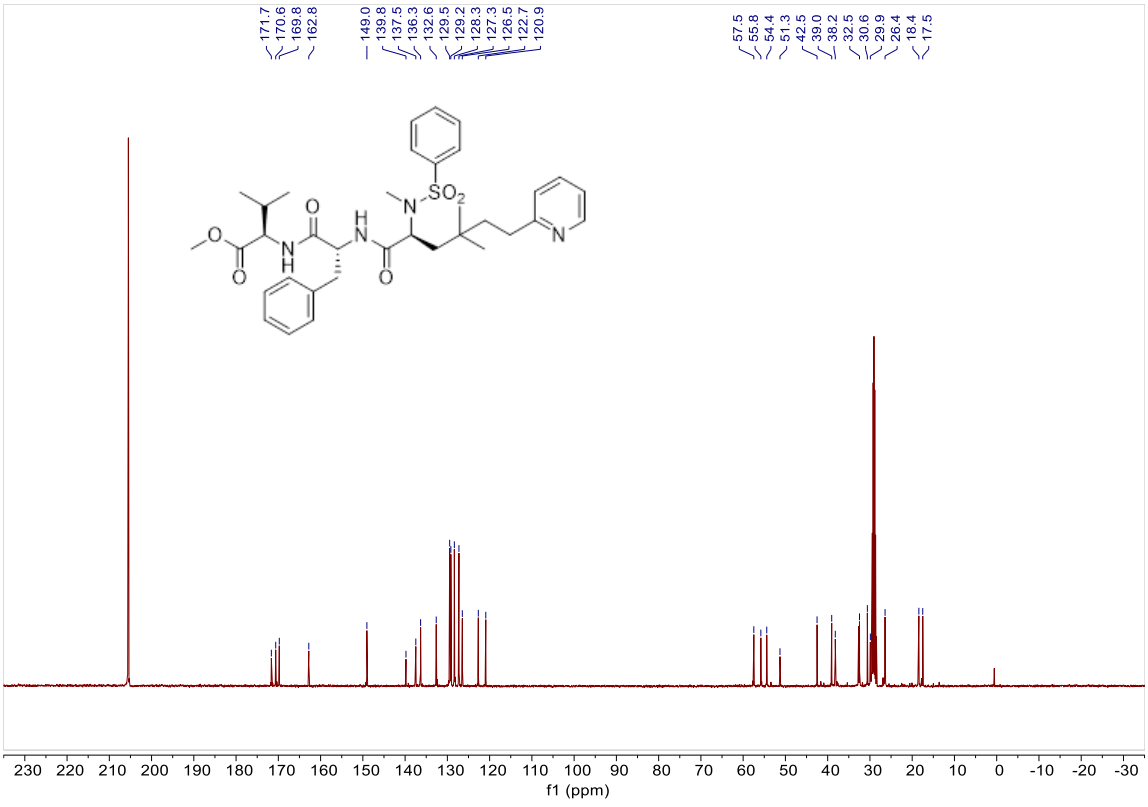
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **18c**



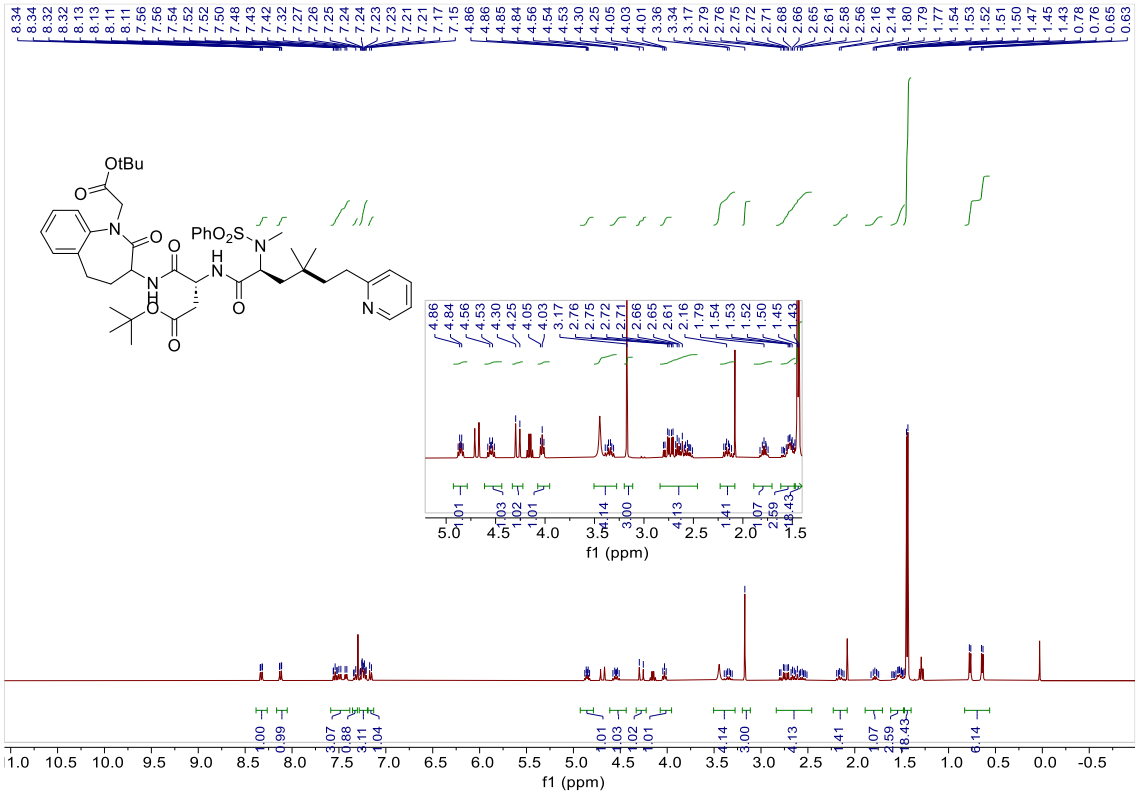
^{1}H NMR spectrum (400 MHz, CD_3COCD_3, 23 ºC) of **19c**



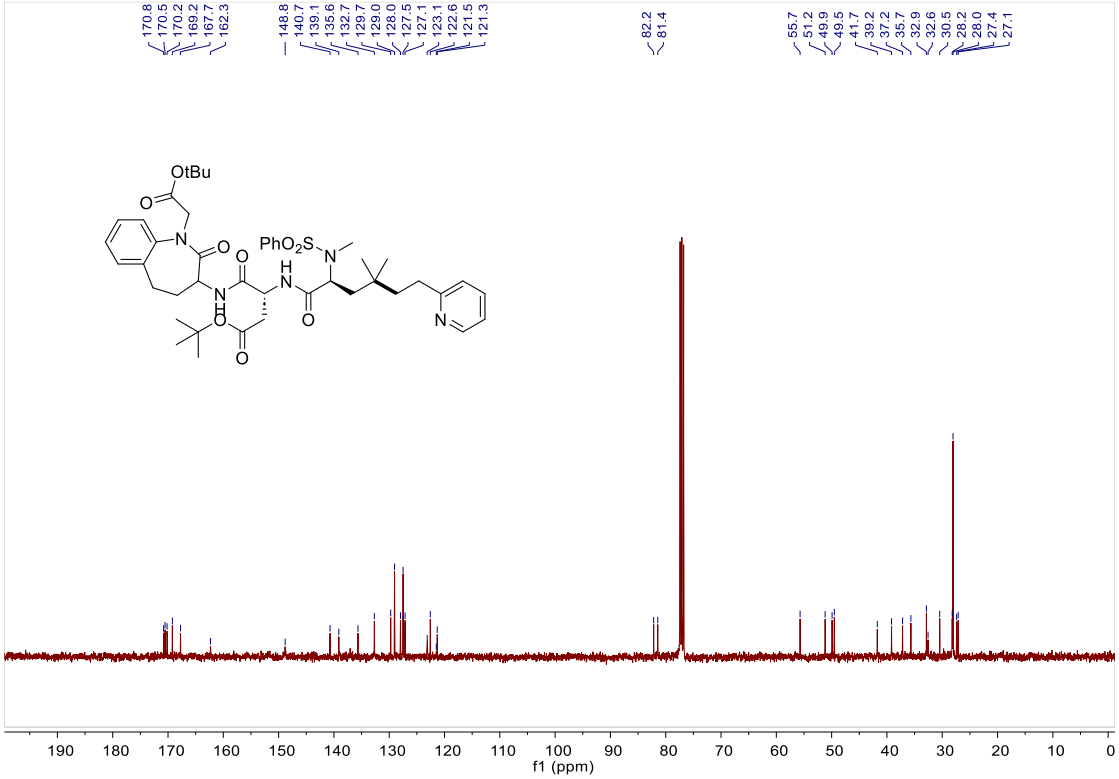
^{13}C NMR spectrum (101 MHz, CD_3COCD_3, 23 ºC) of **19c**



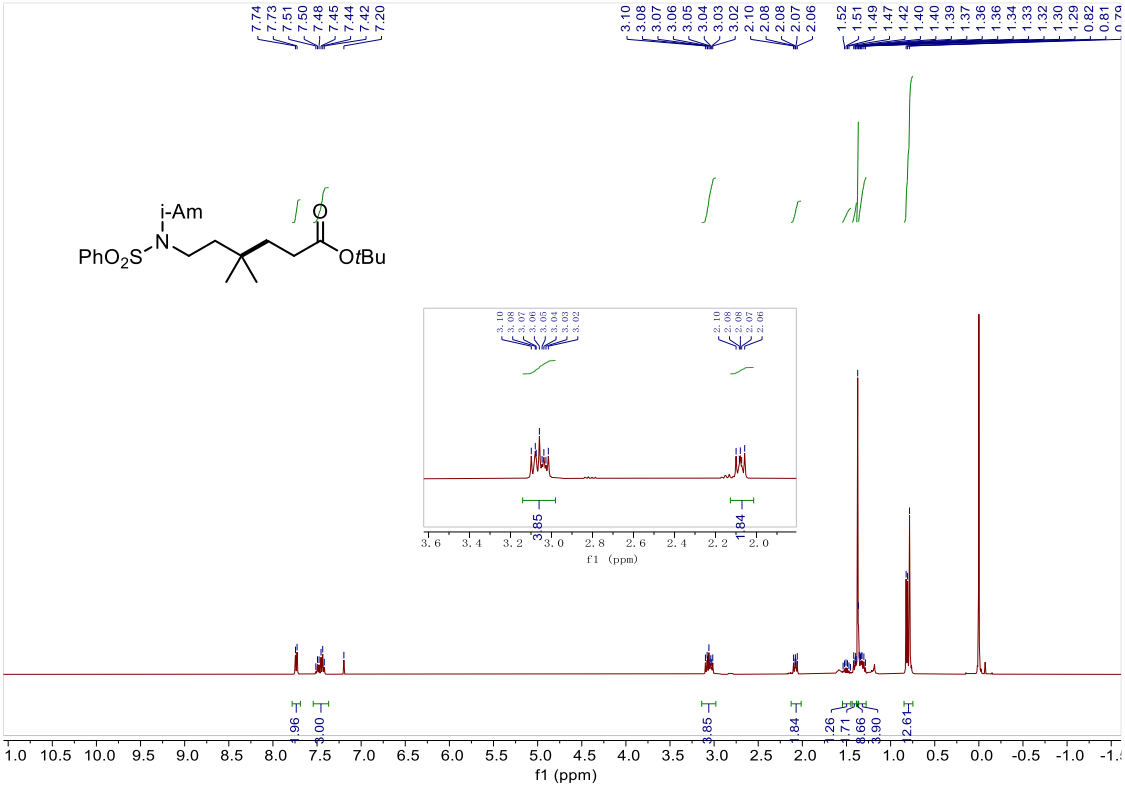
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **20c**



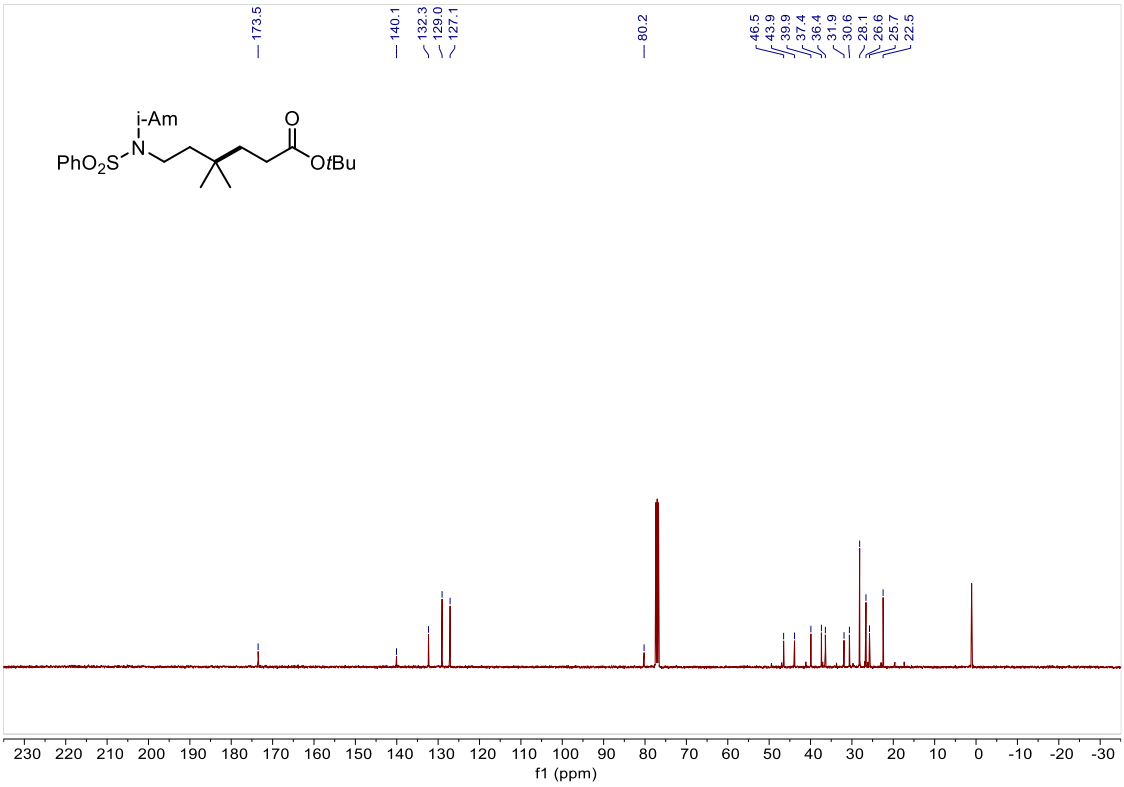
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **20c**



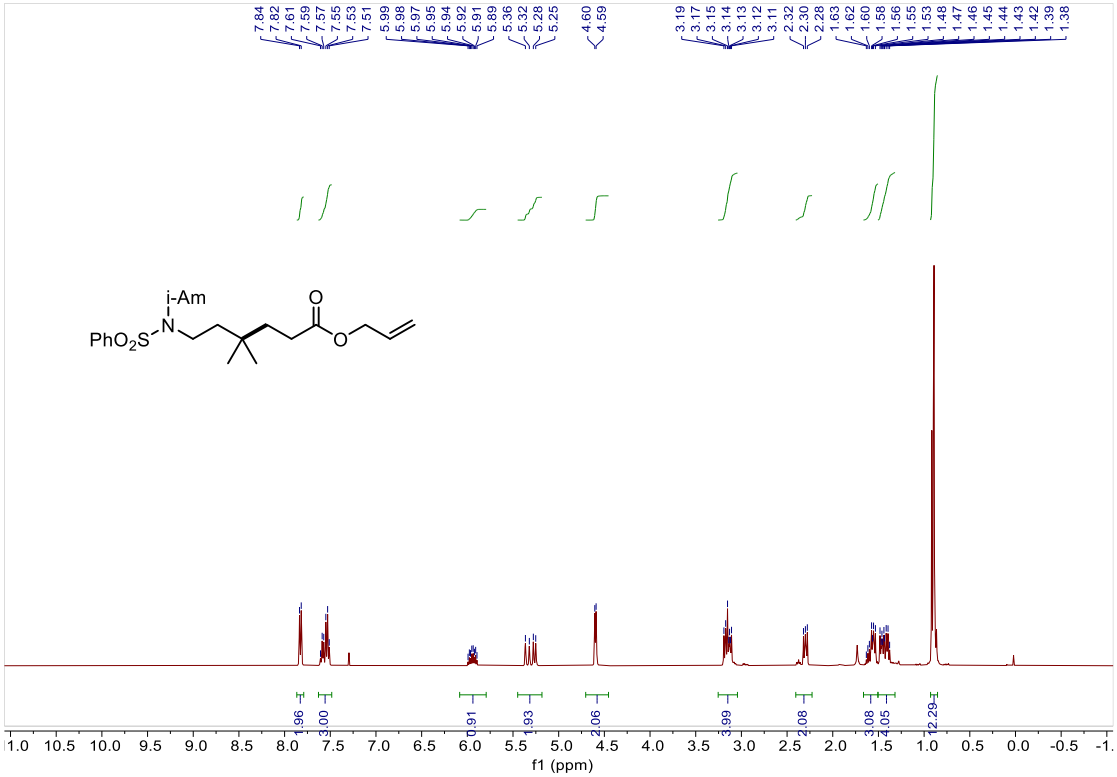
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **21c**



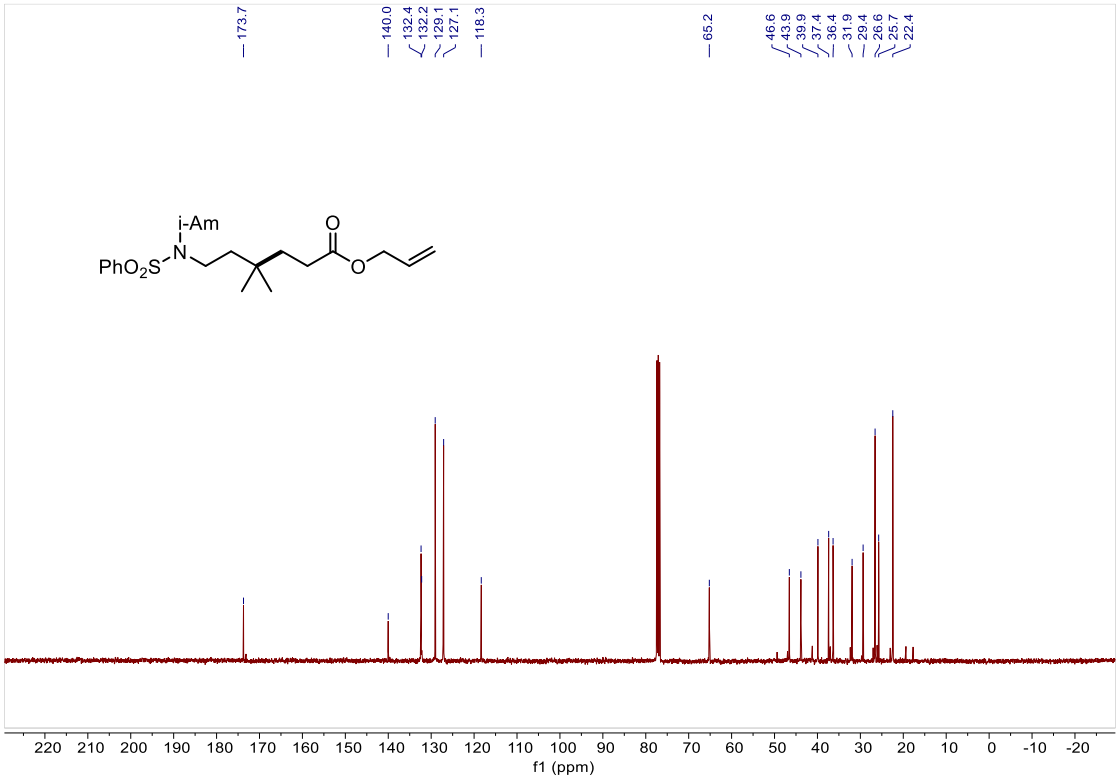
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **21c**



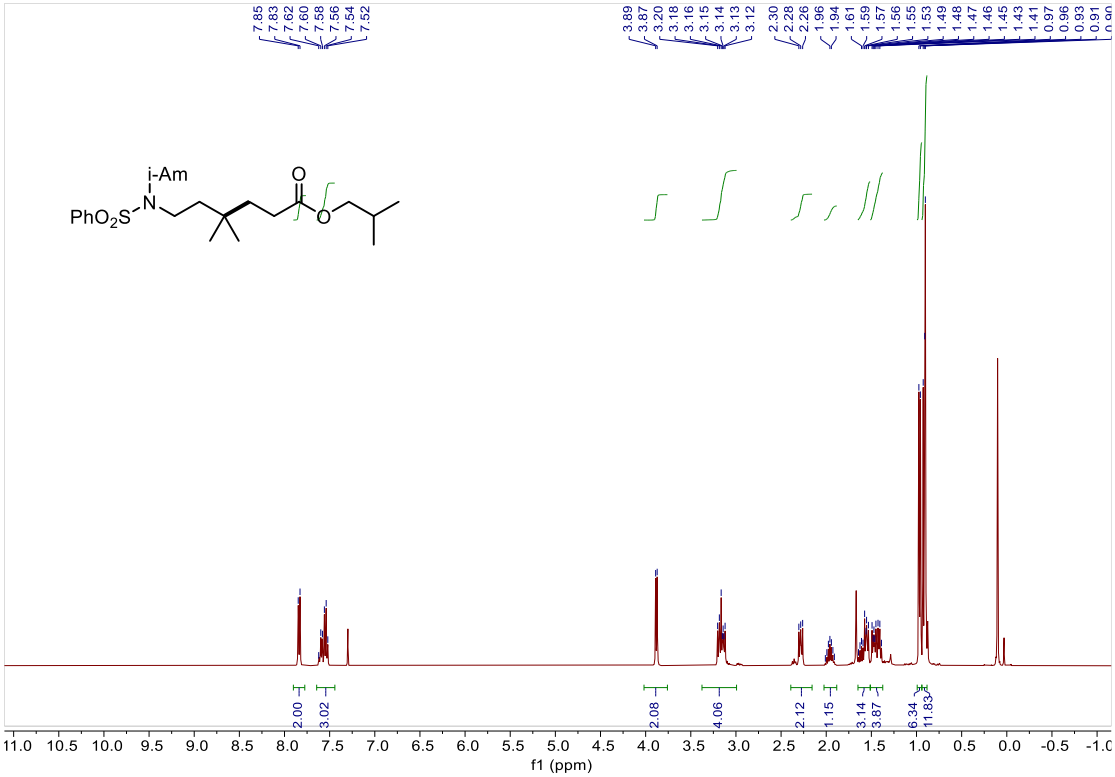
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **22c**



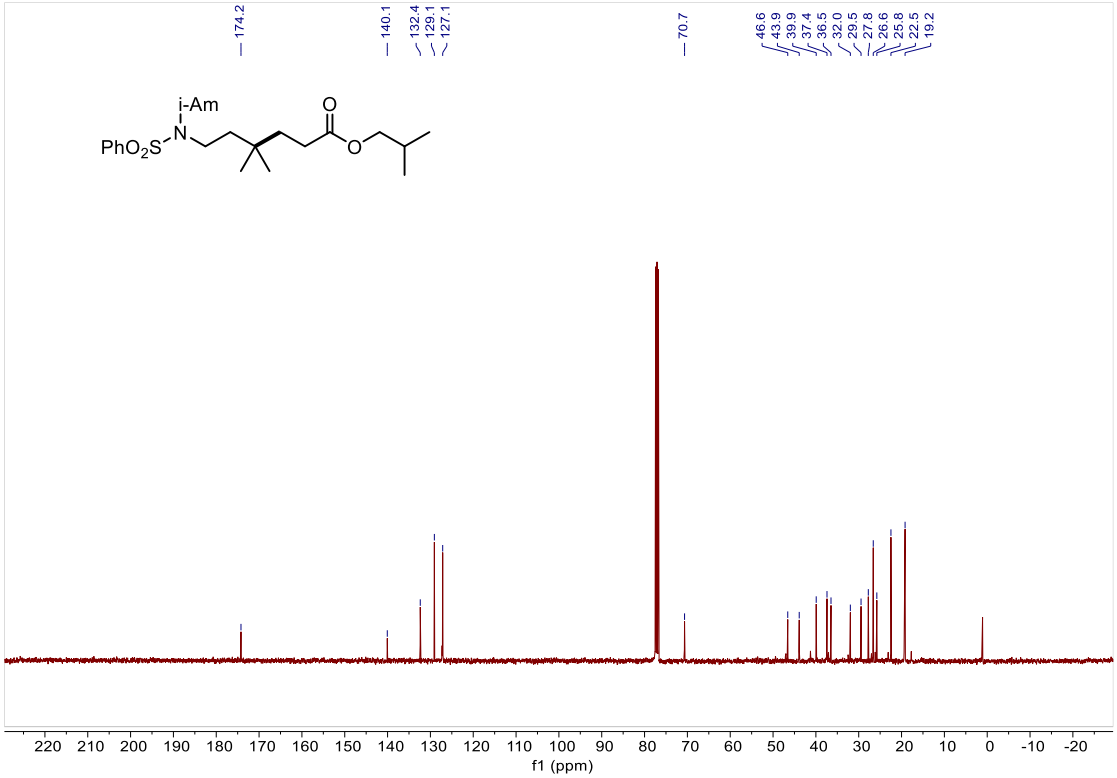
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **22c**



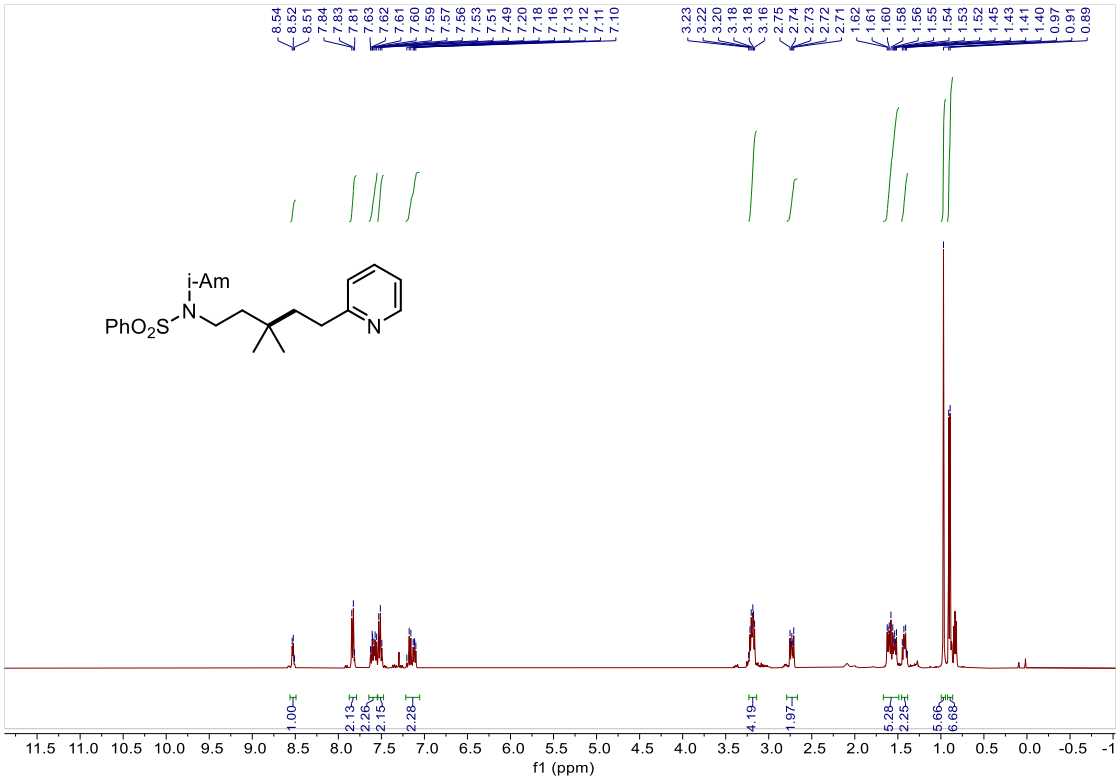
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **23c**



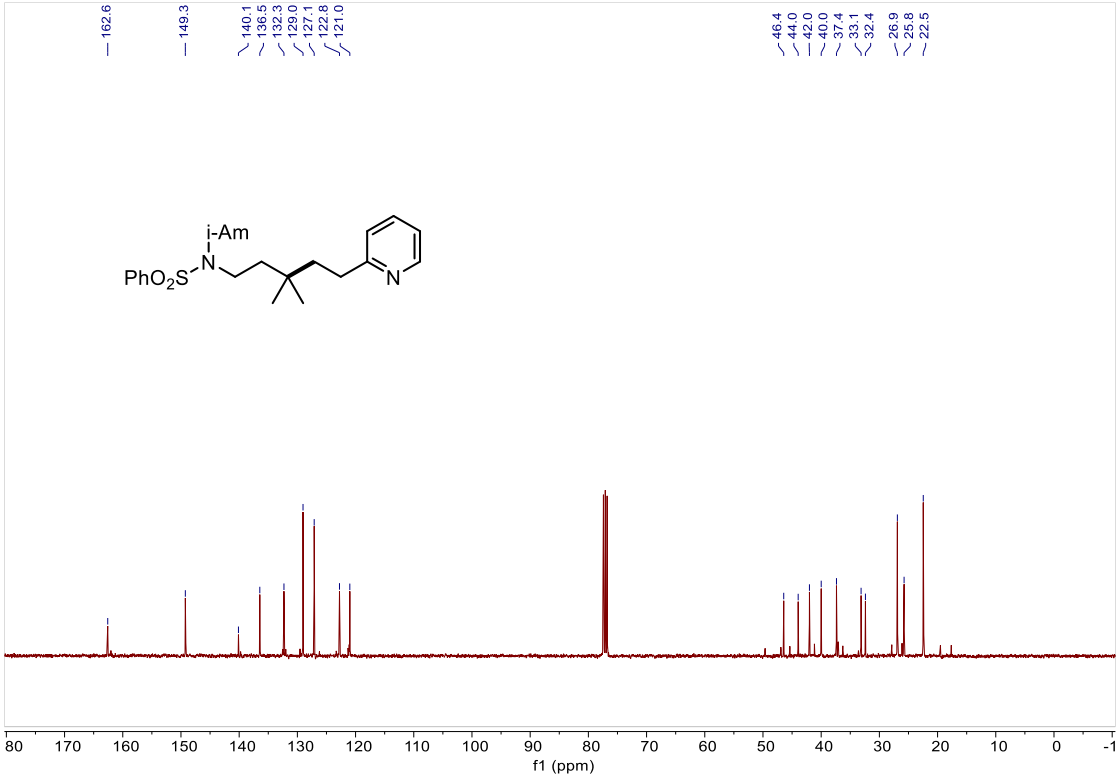
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **23c**



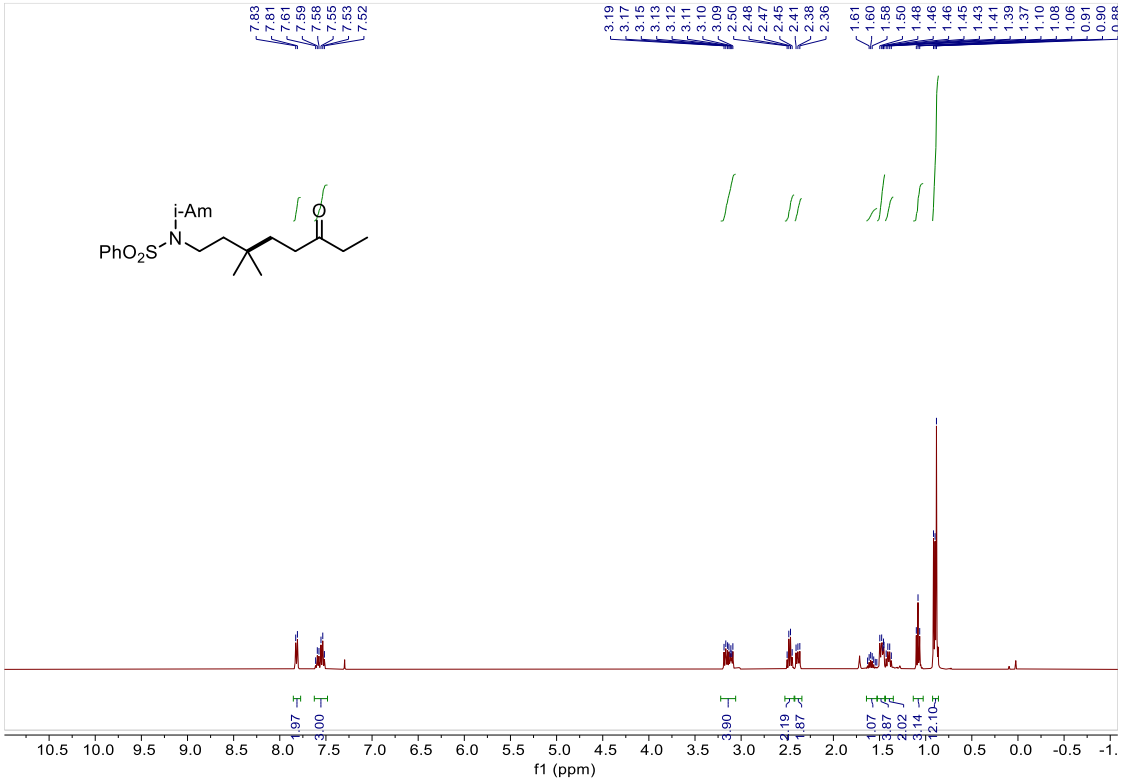
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **24c**



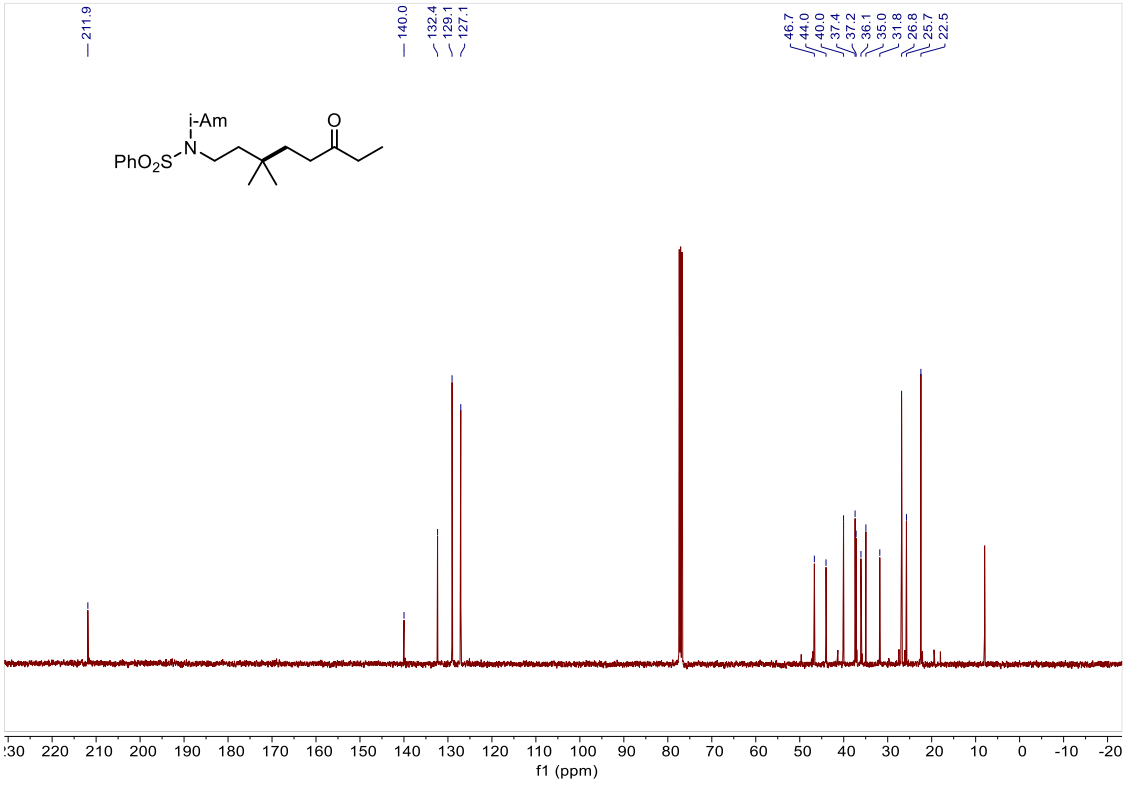
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **24c**



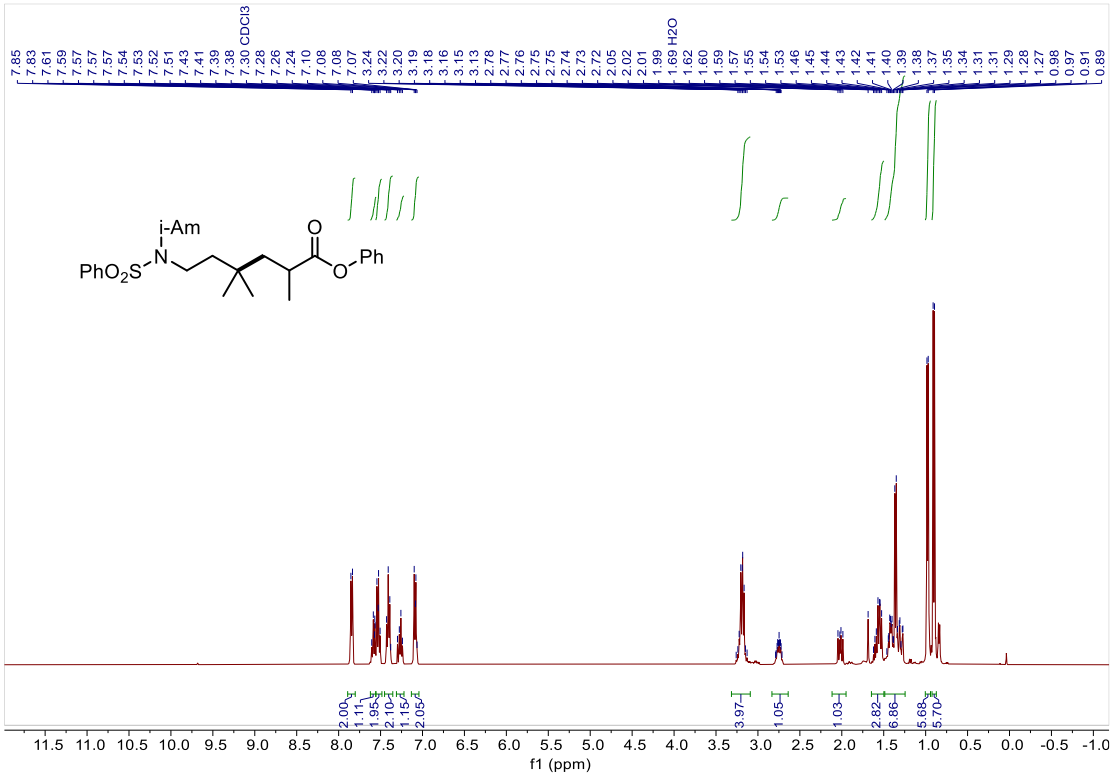
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **25c**



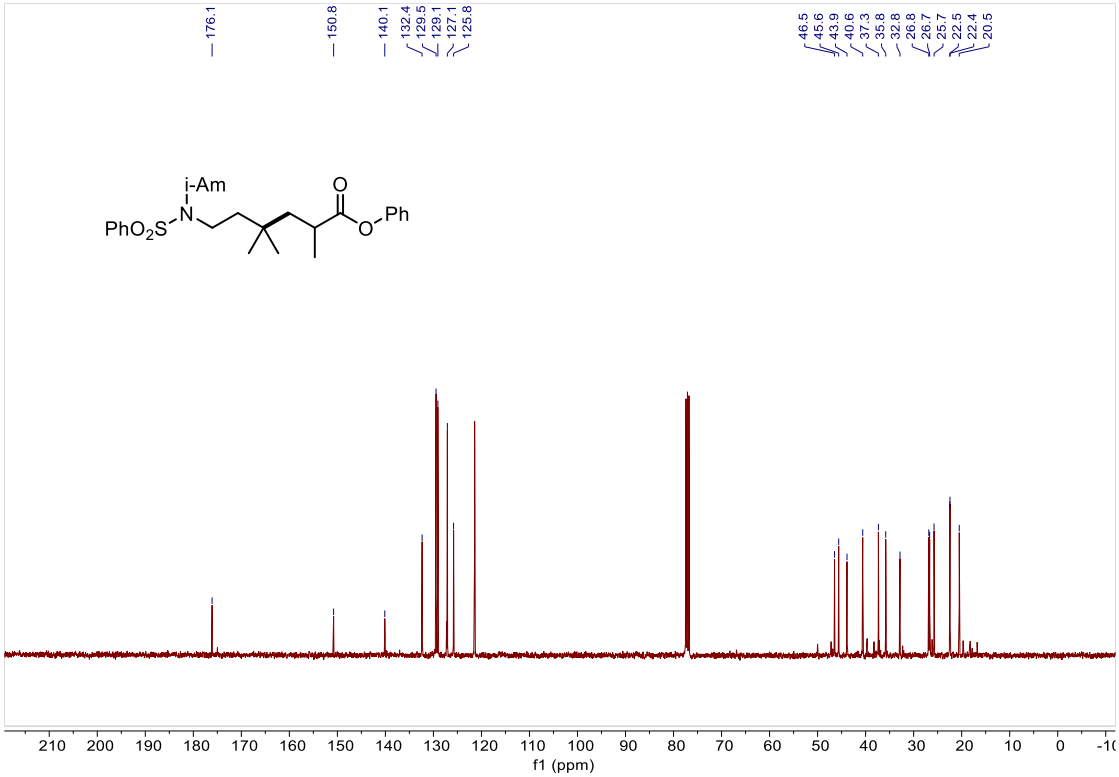
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **25c**



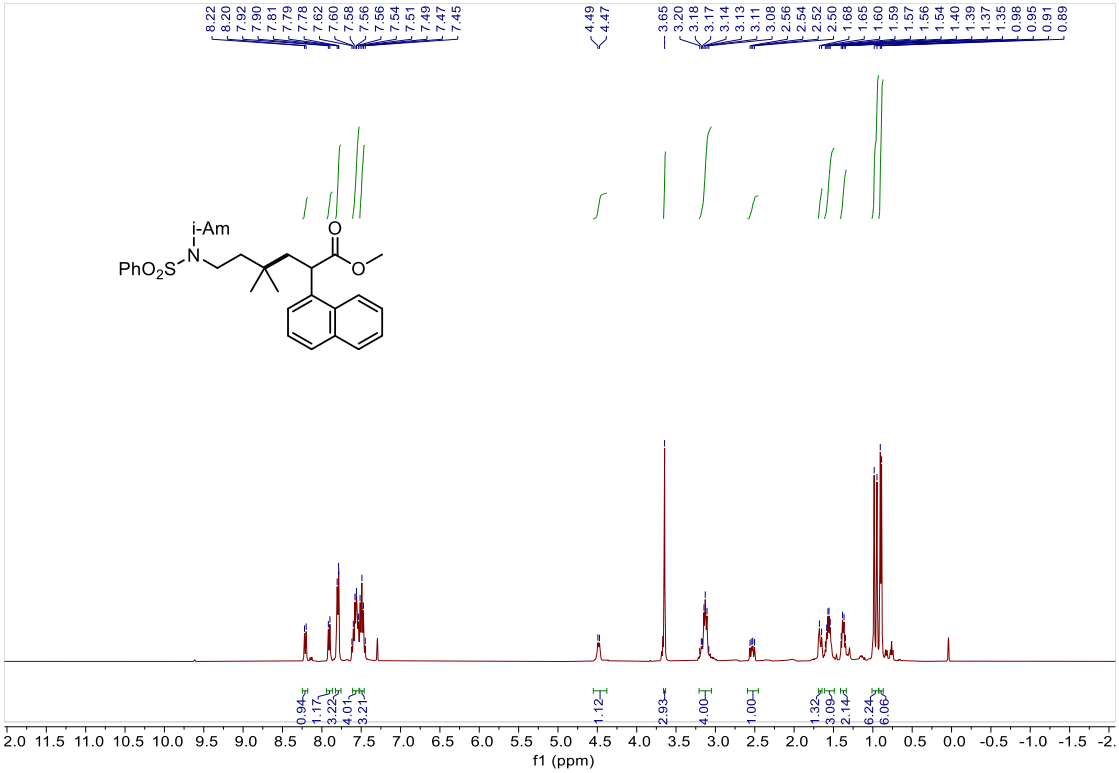
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **26c**



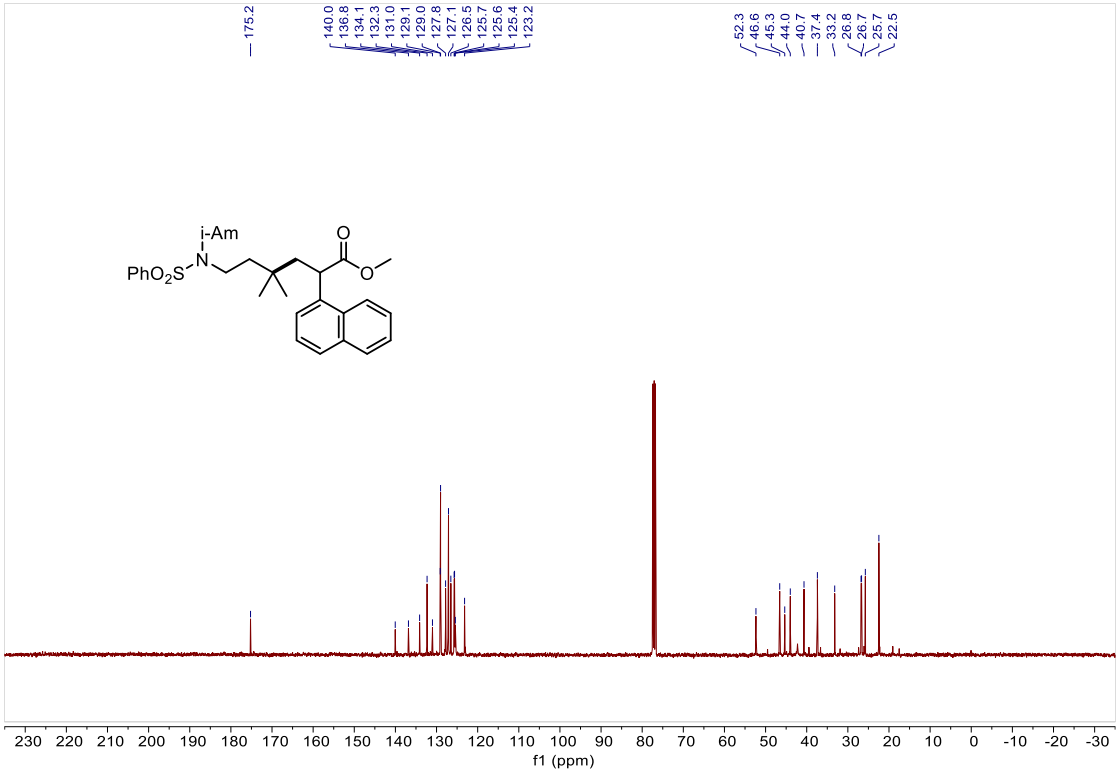
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **26c**



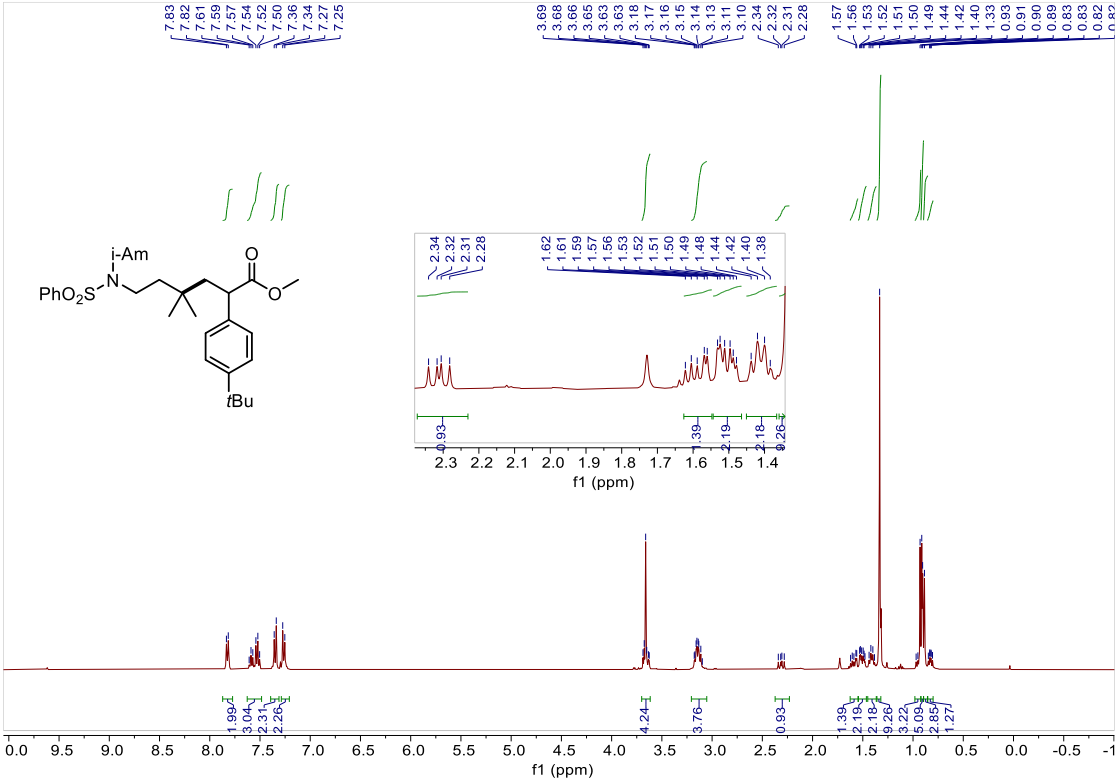
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **27c**



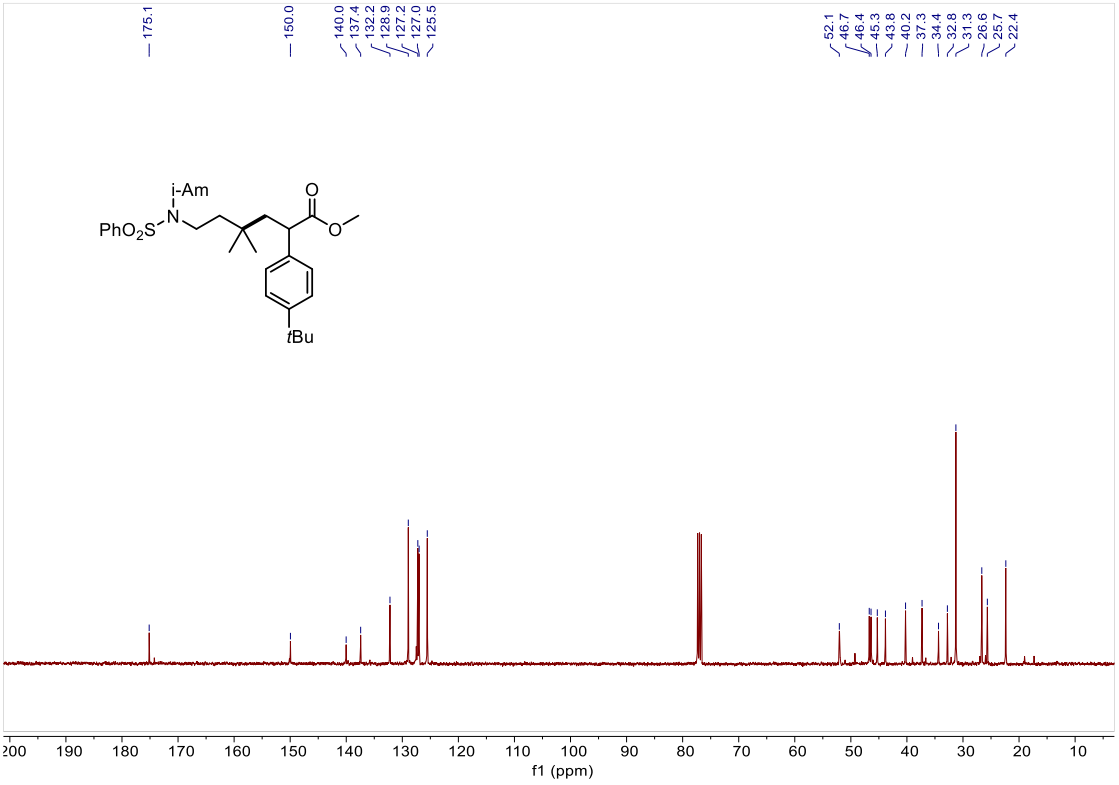
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **27c**



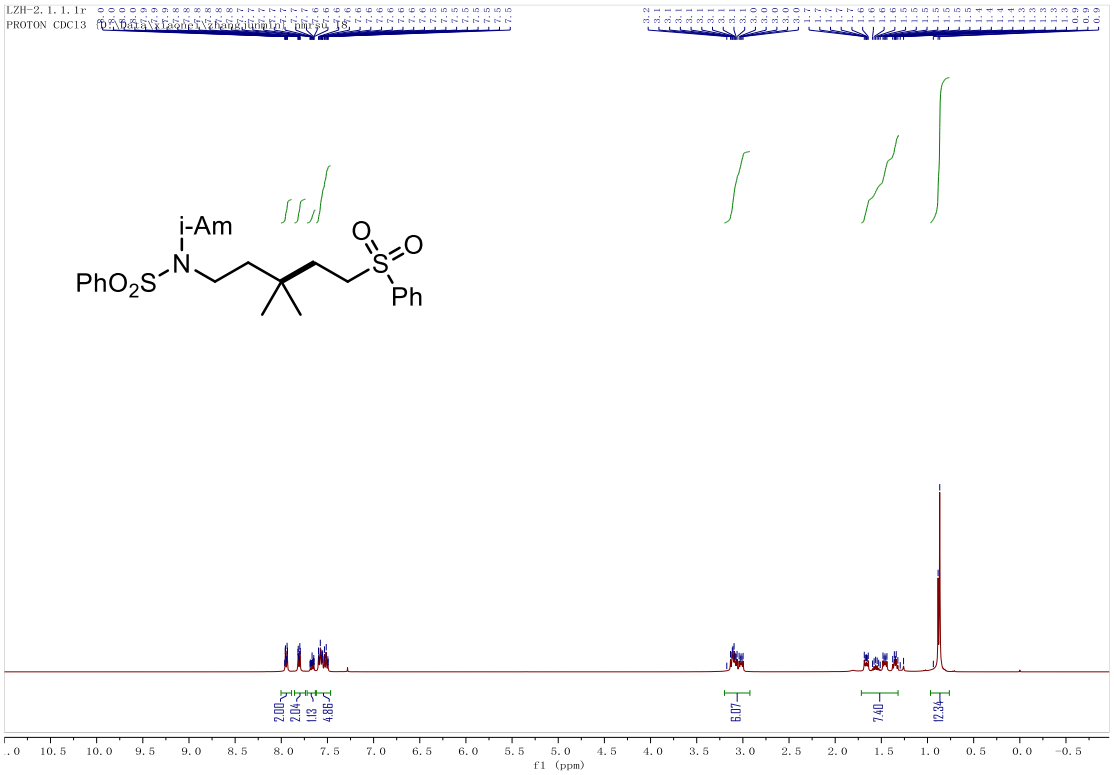
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **28c**



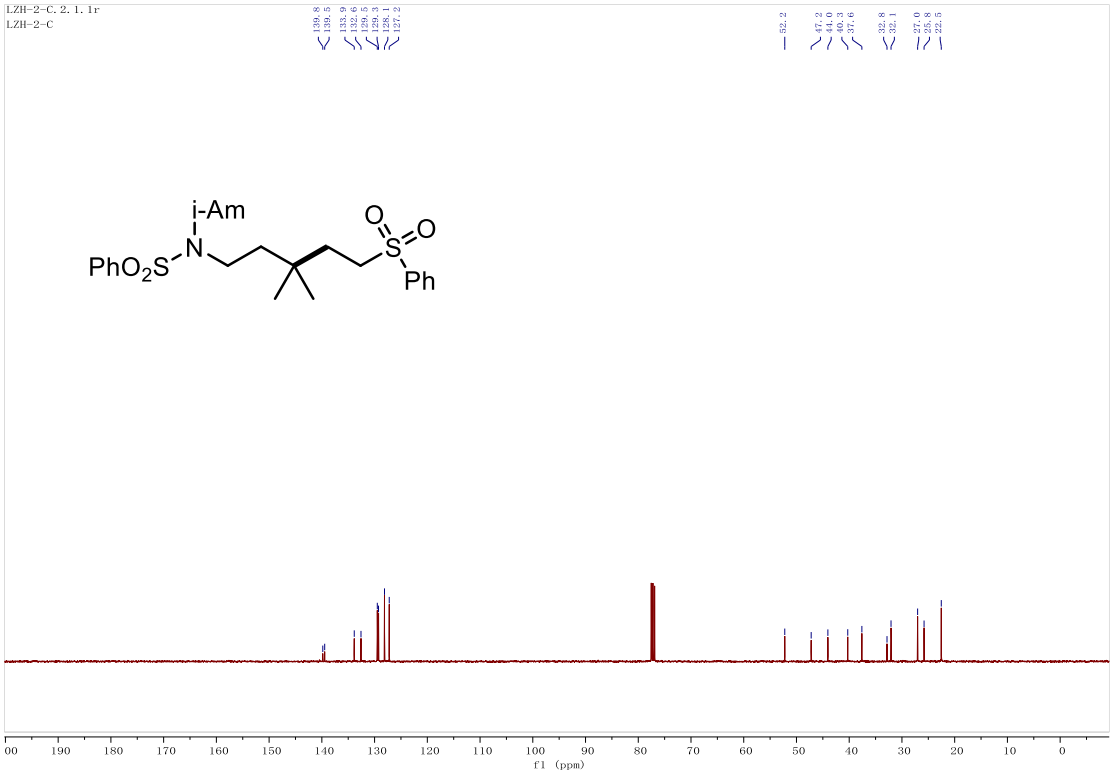
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **28c**



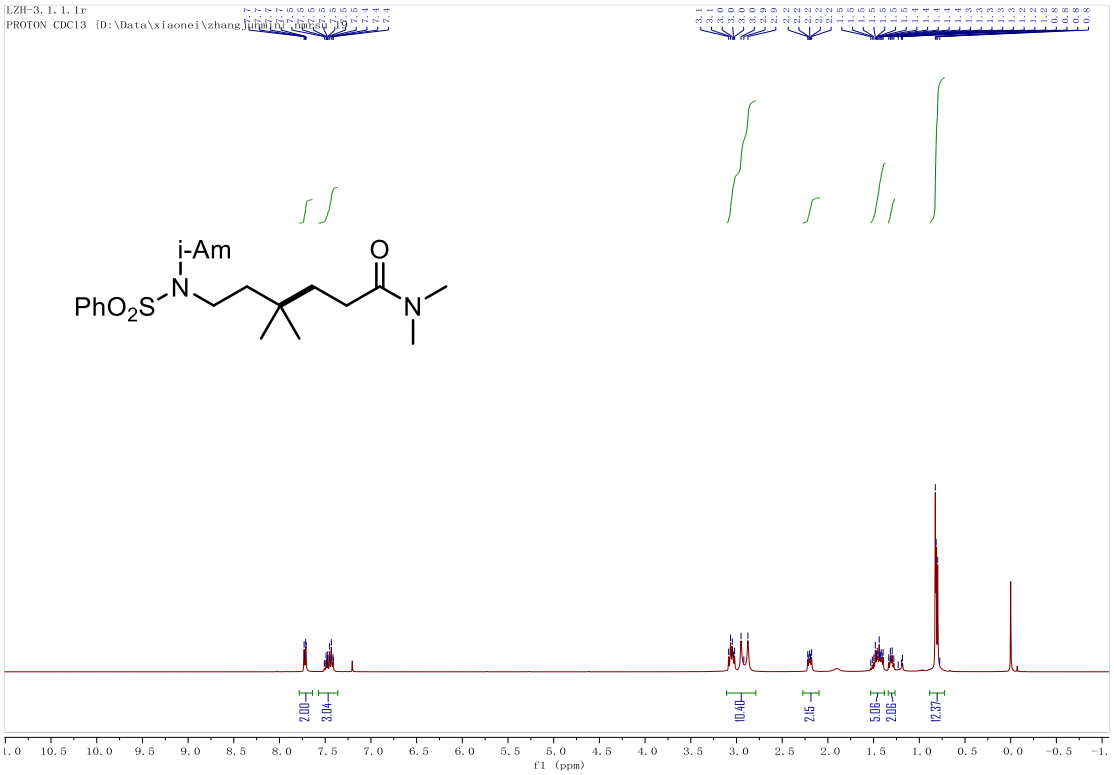
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **29c**



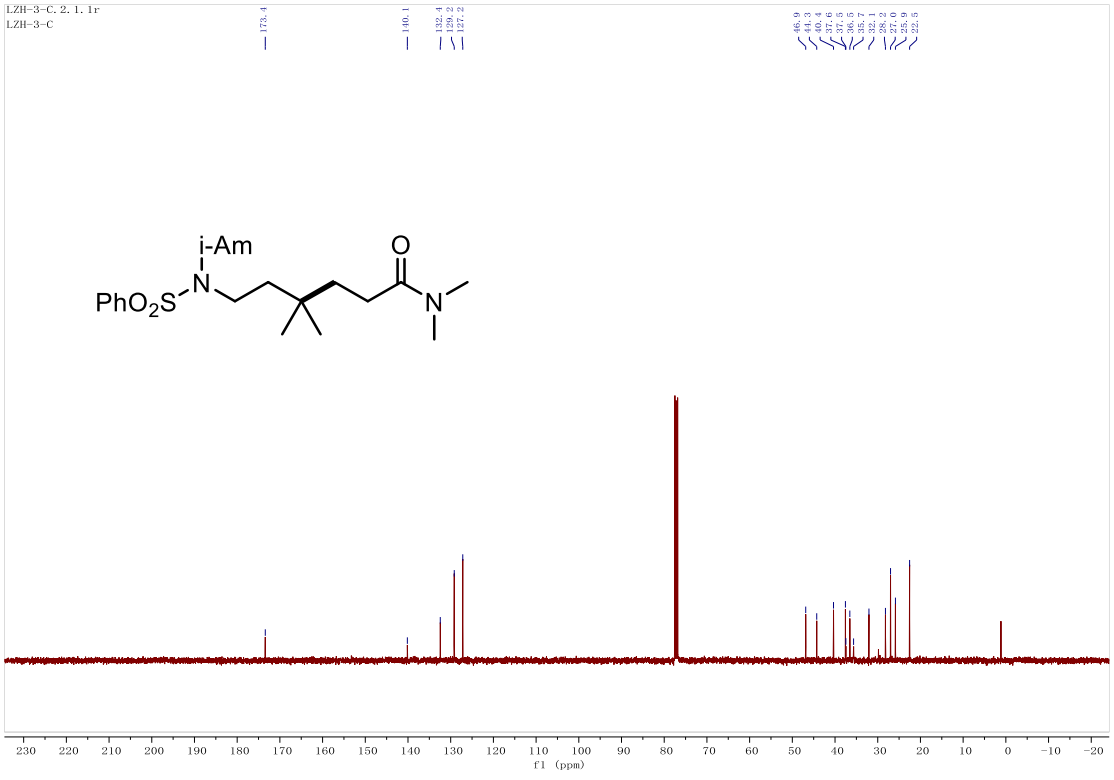
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **29c**



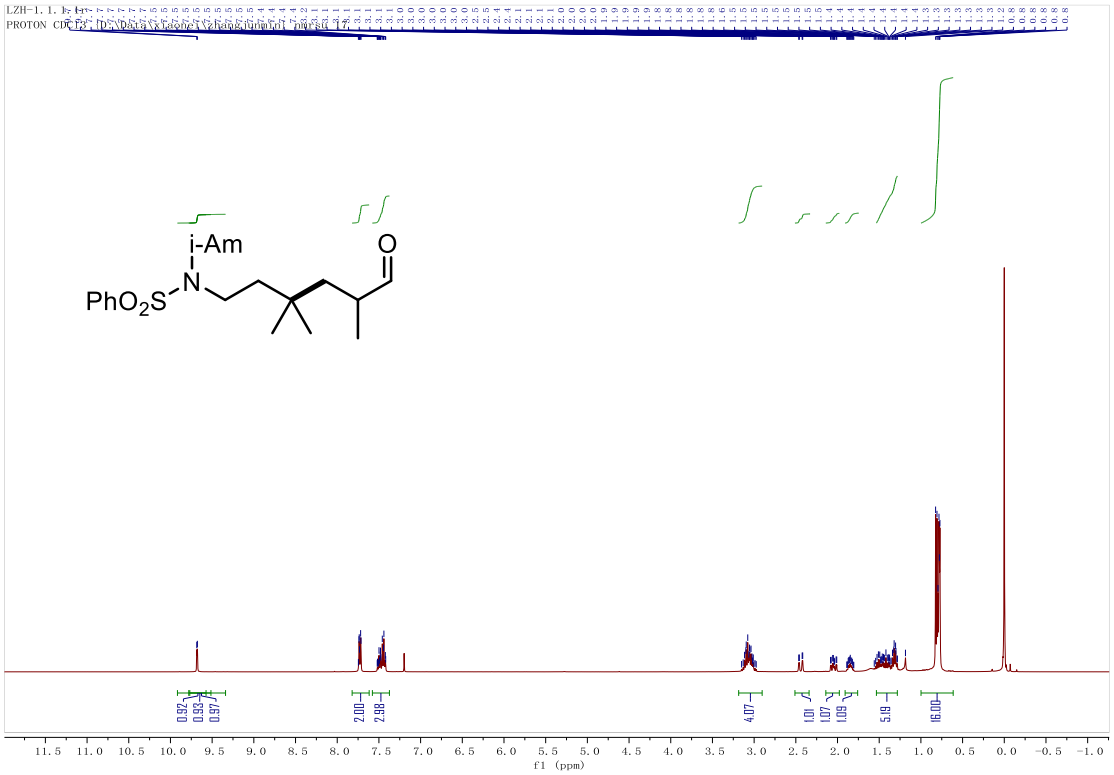
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **30c**



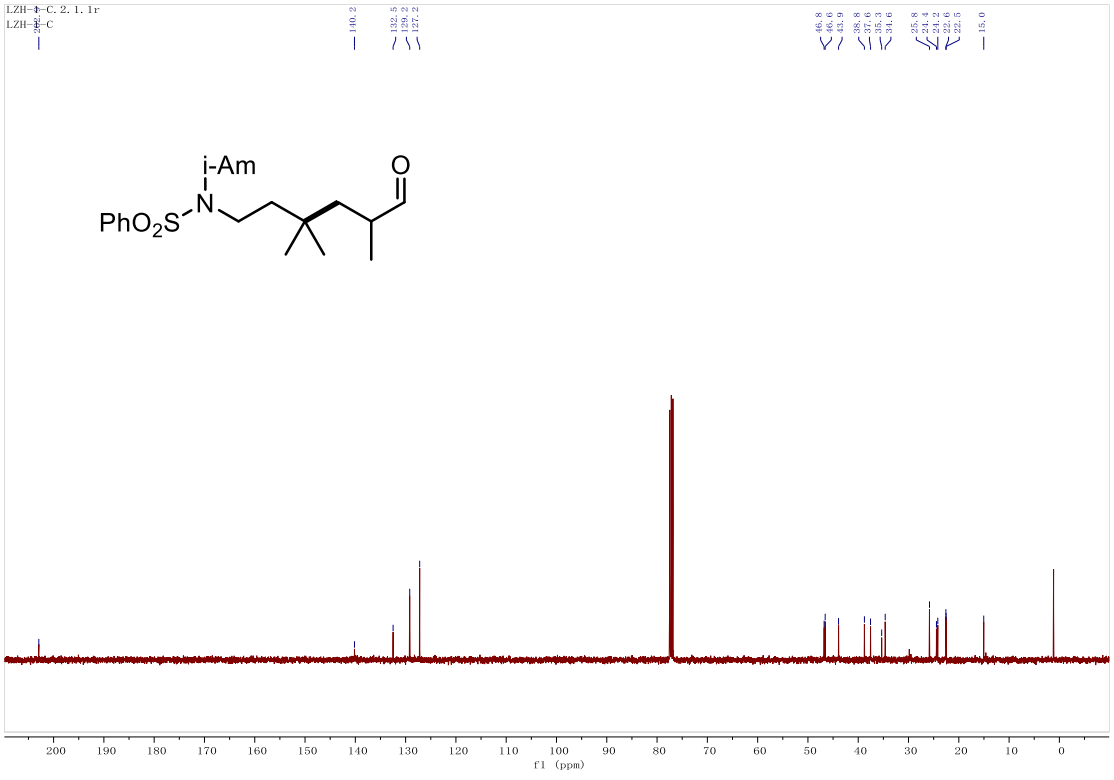
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **30c**



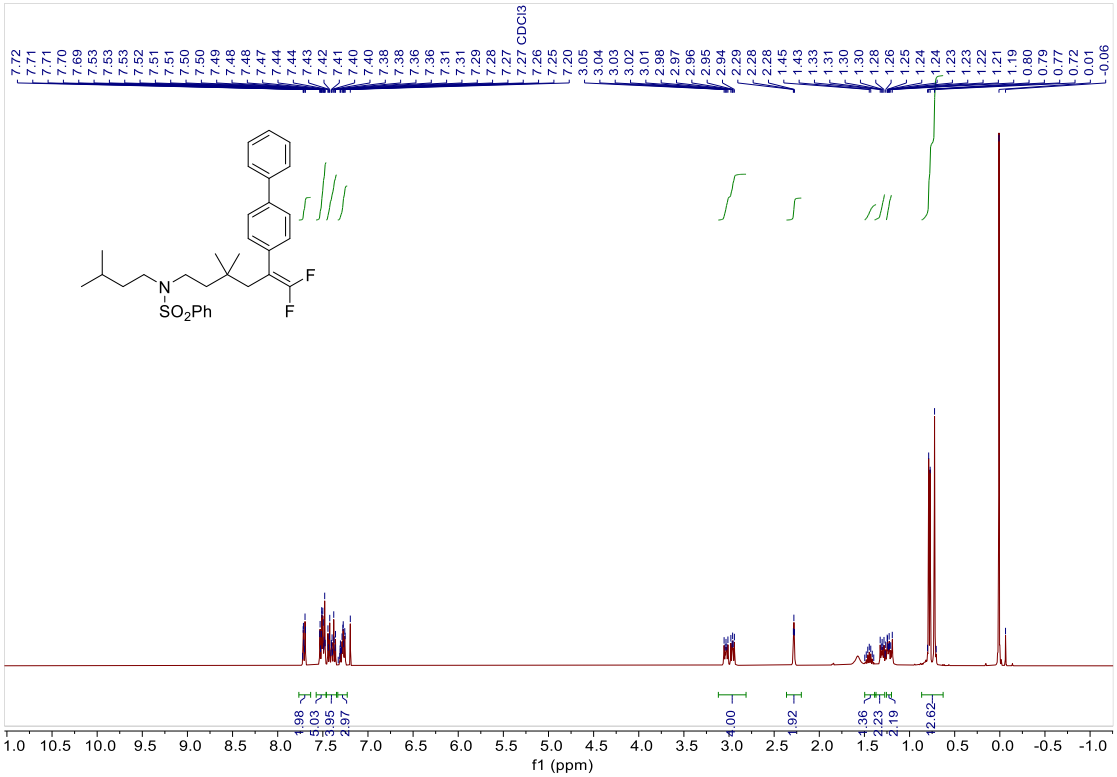
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **31c**



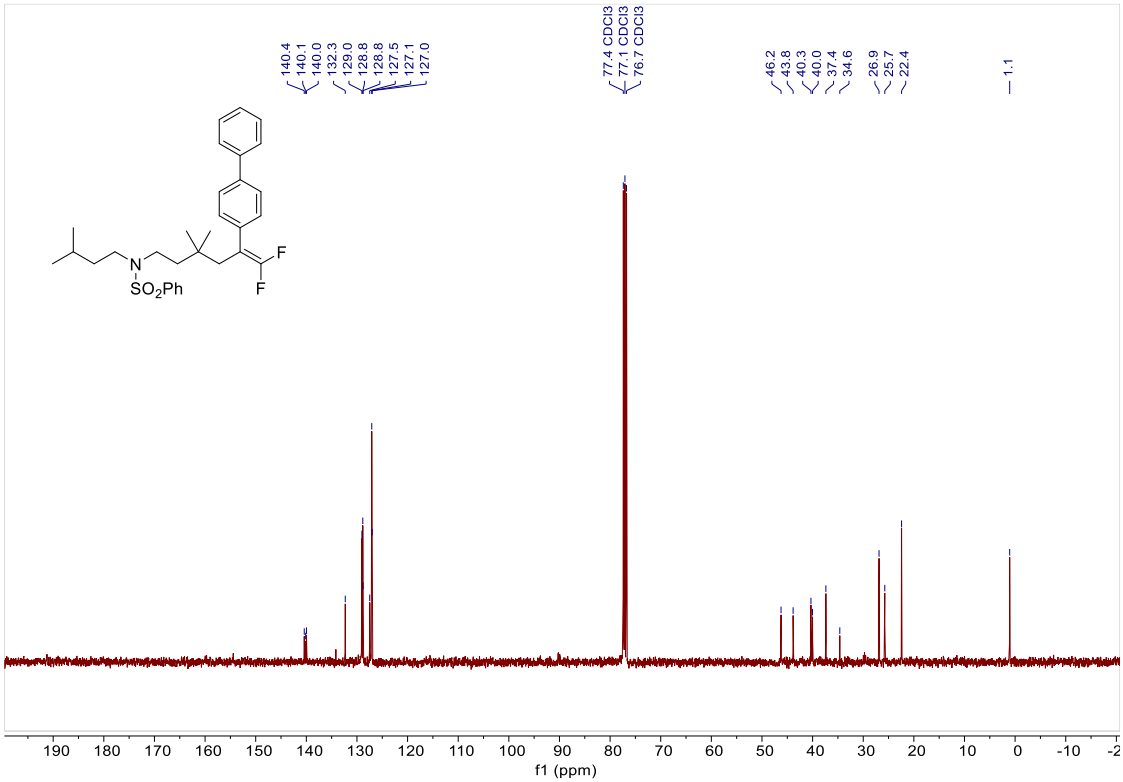
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **31c**



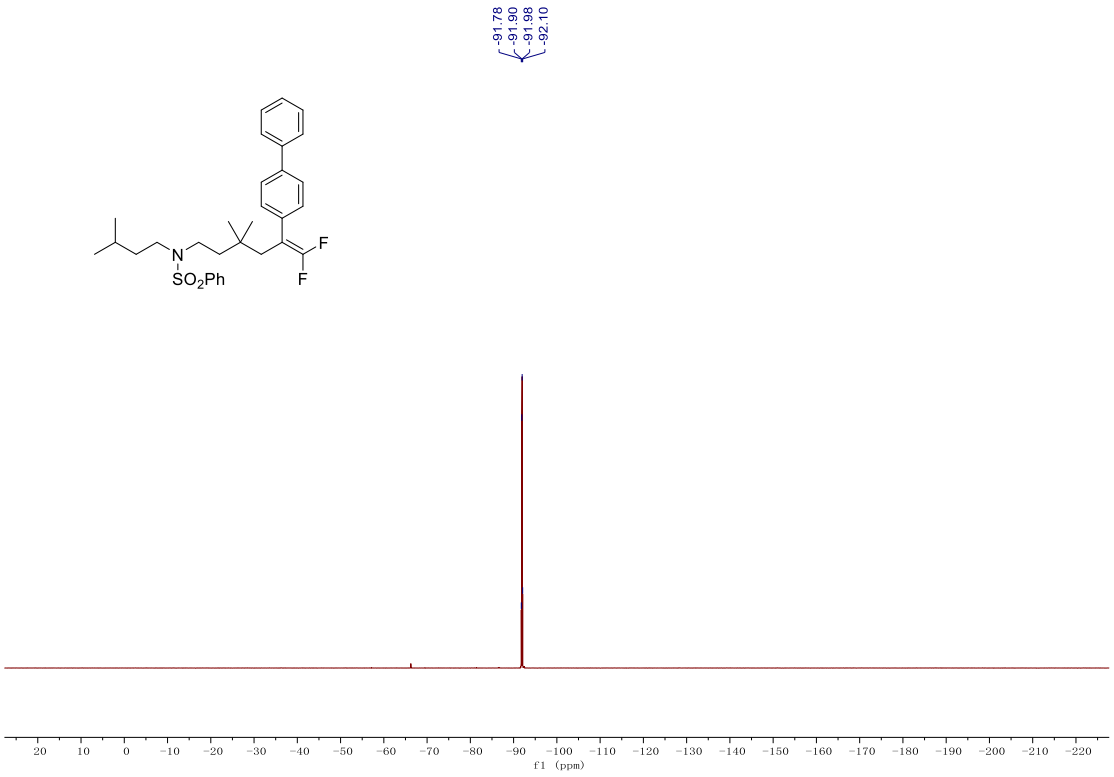
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **32c**



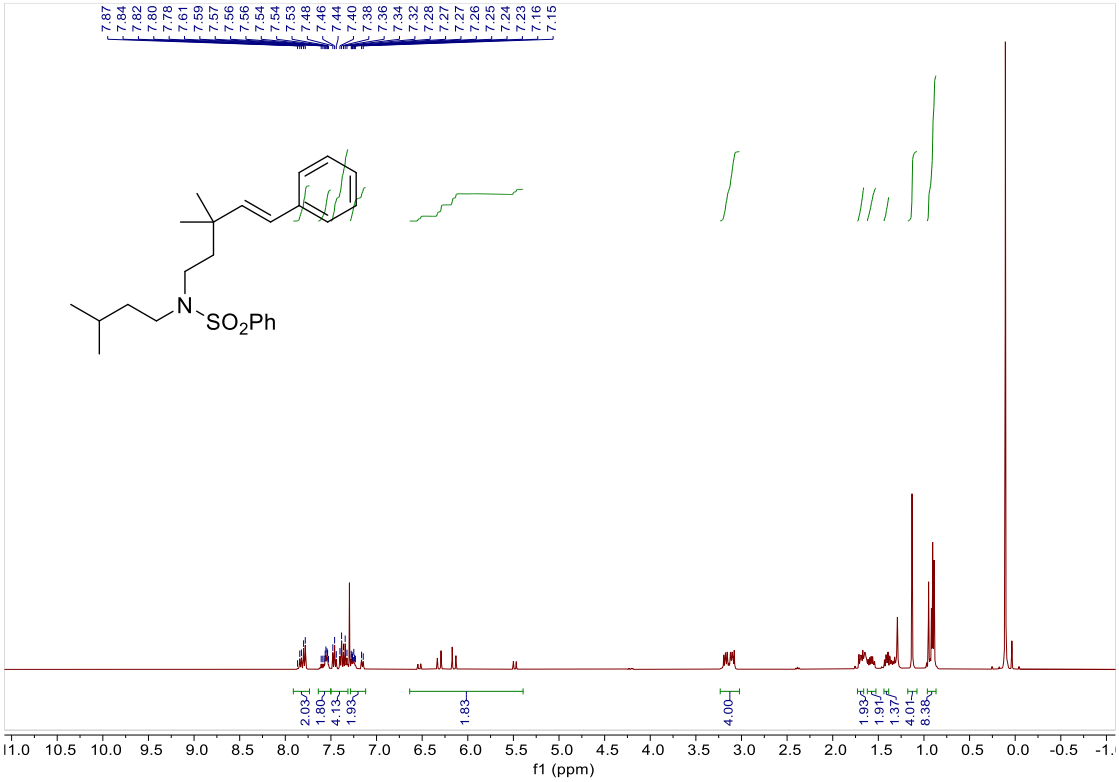
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **32c**



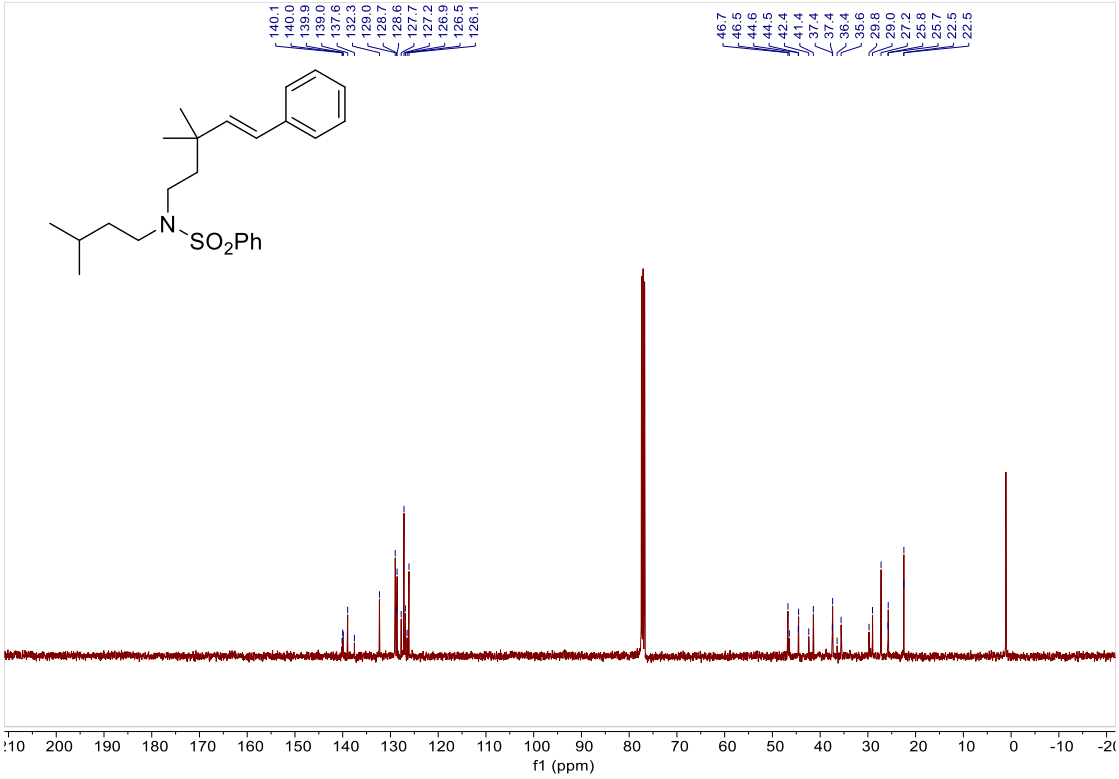
^{19}F NMR spectrum (376 MHz, $CDCl_3$, 23 ºC) of **32c**



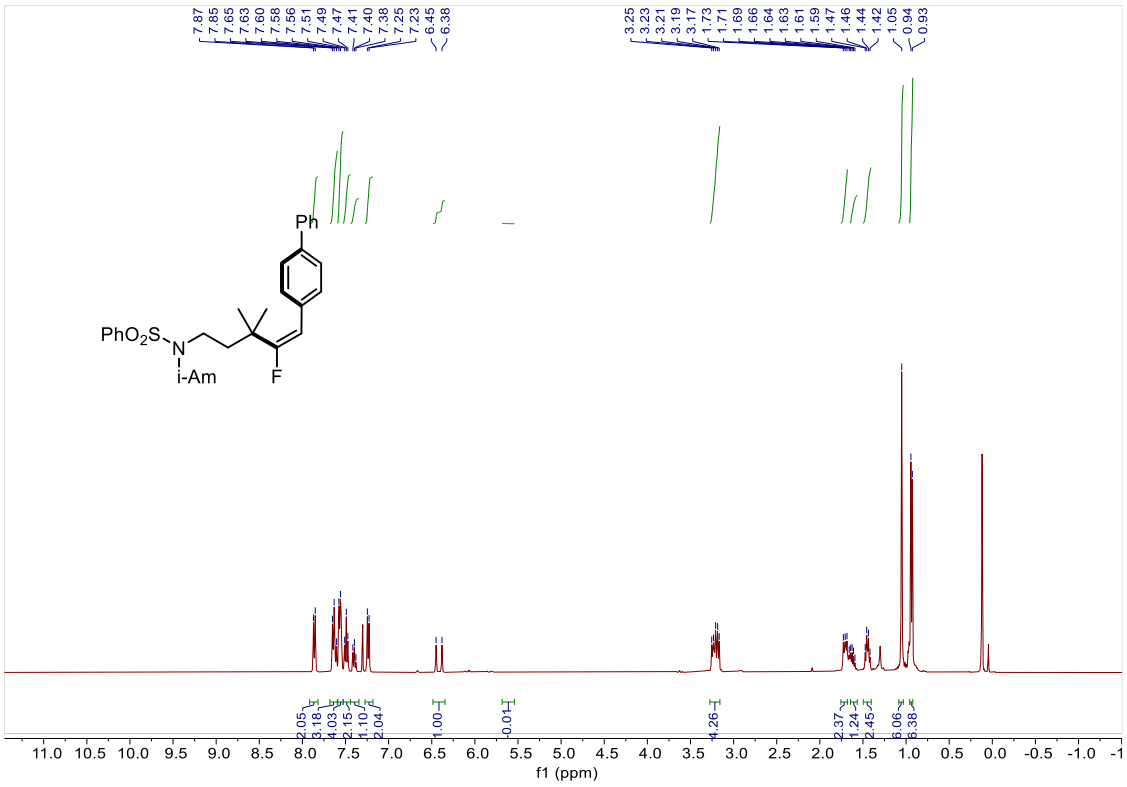
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **33c**



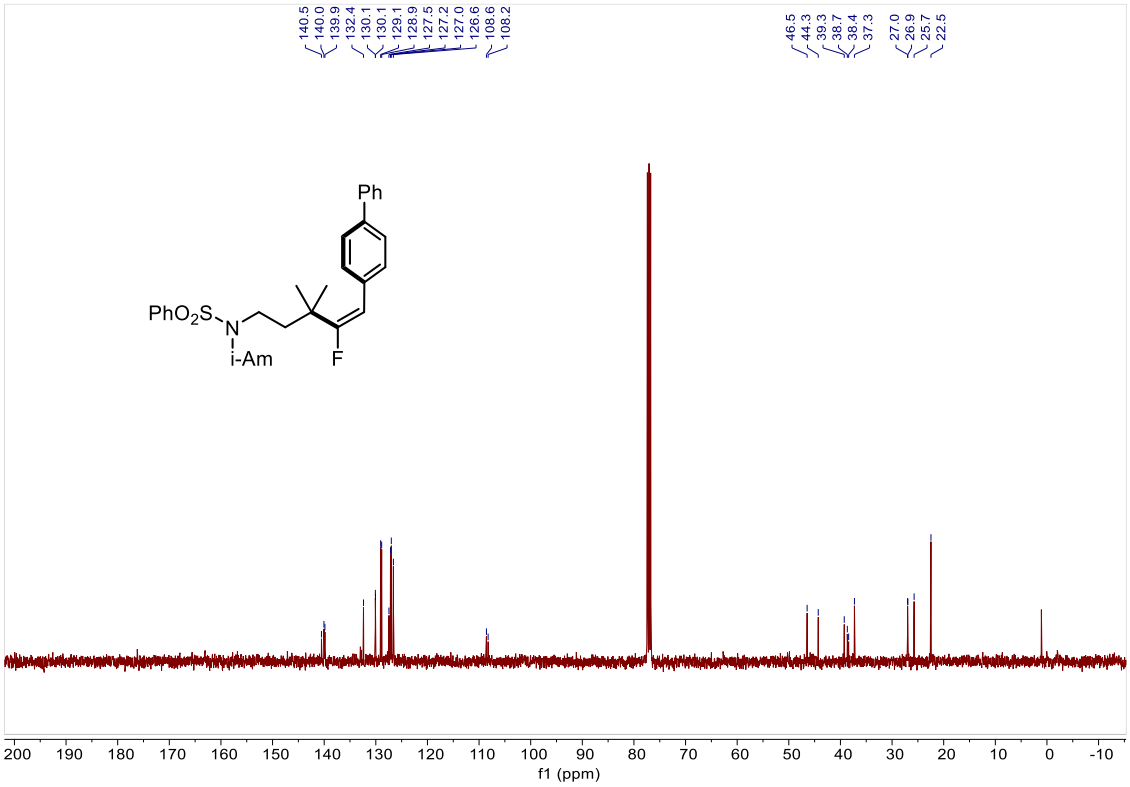
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **33c**



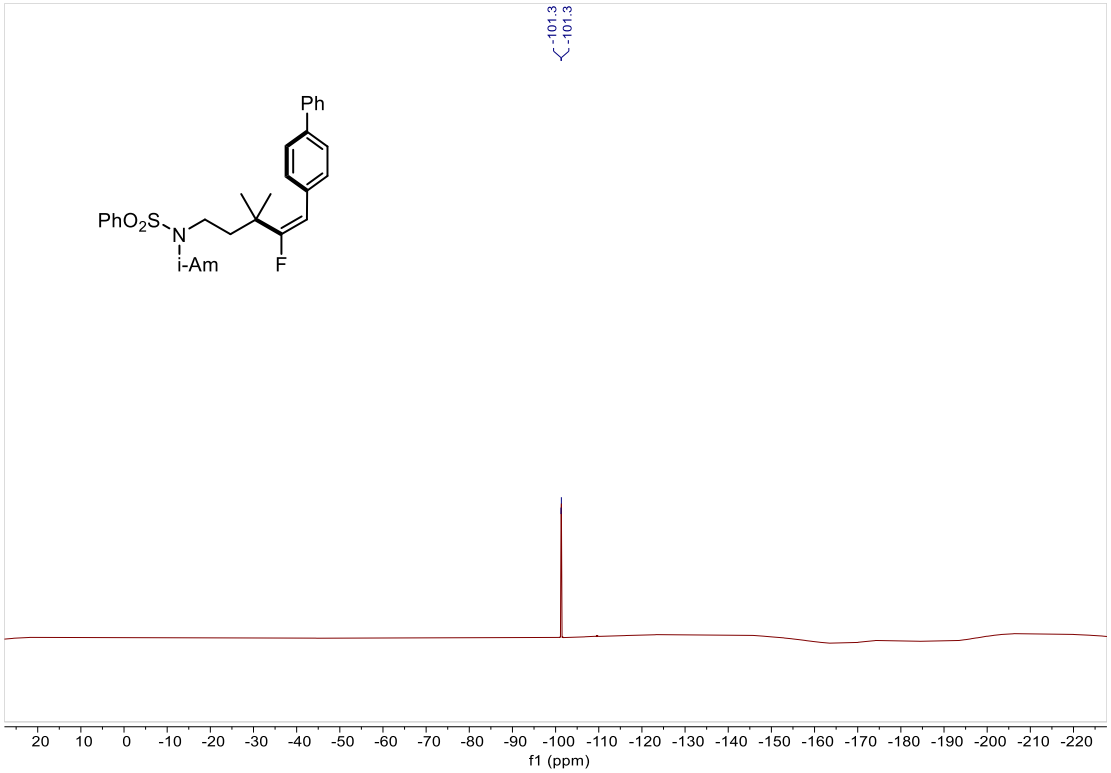
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **34c**



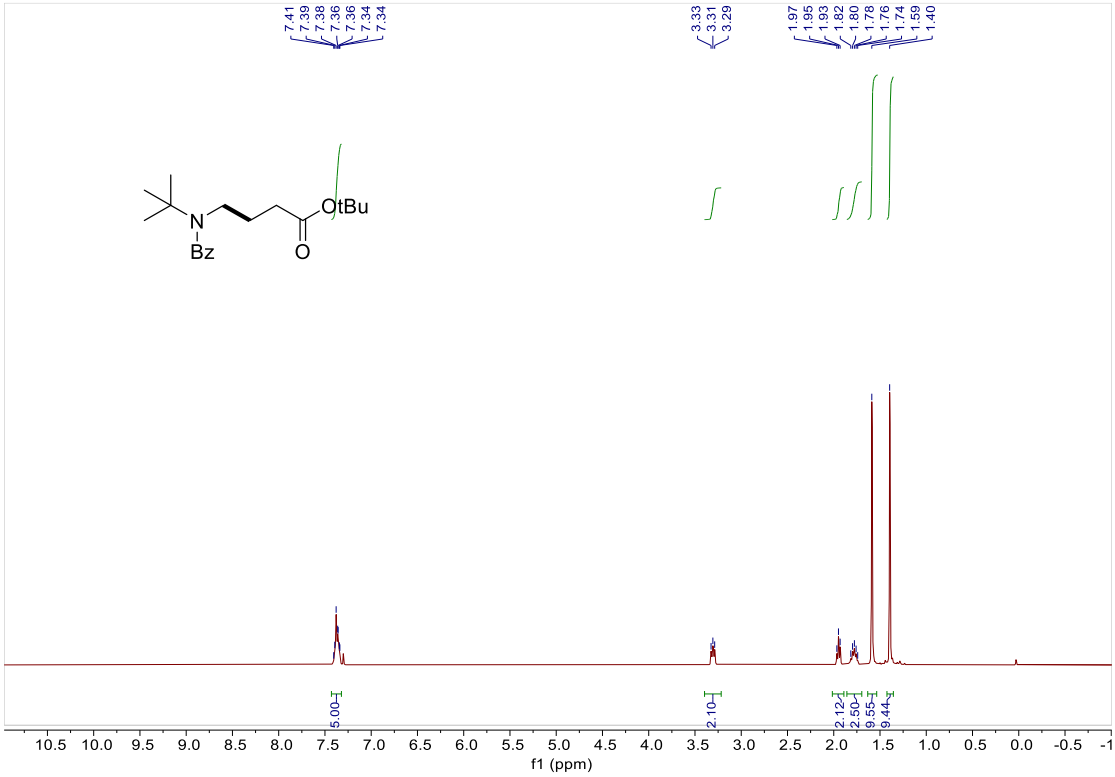
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **34c**



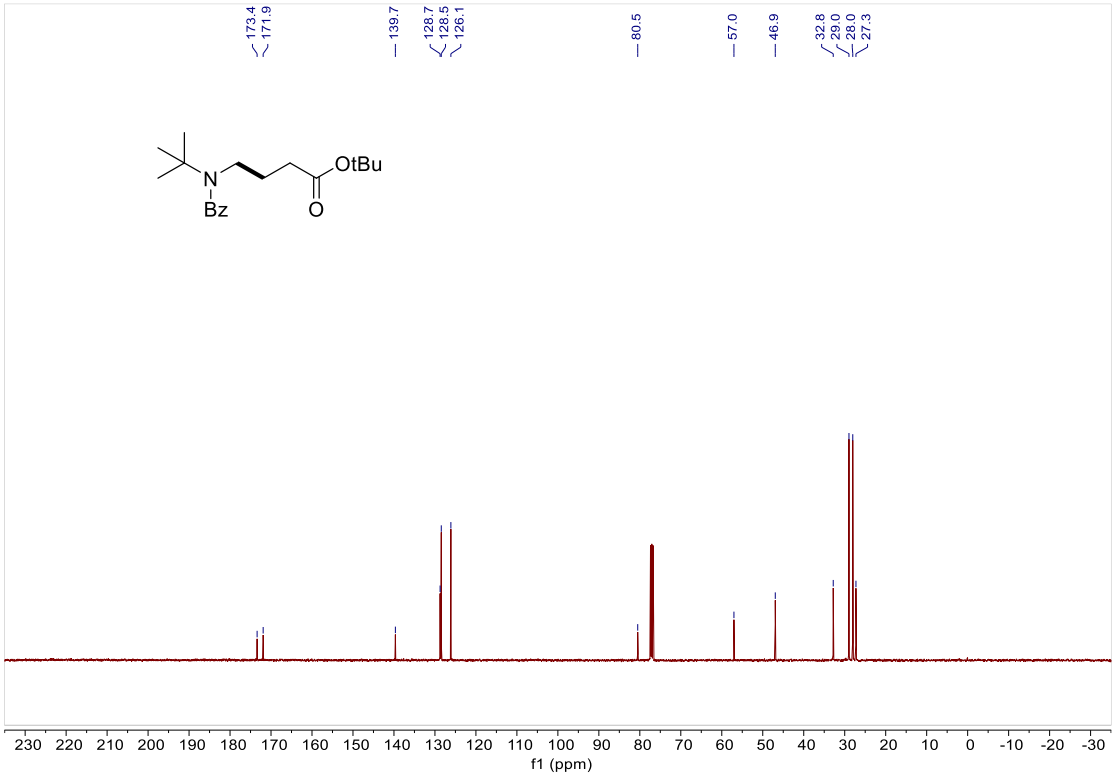
^{19}F NMR spectrum (376 MHz, $CDCl_3$, 23 ºC) of **34c**



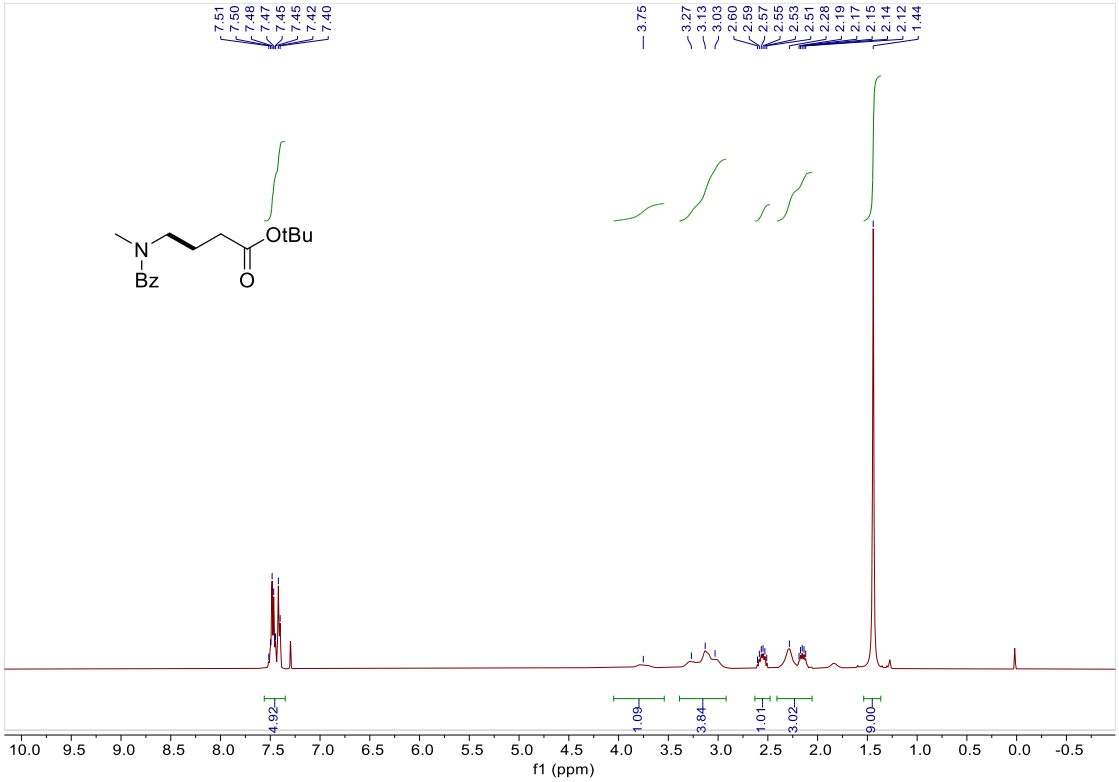
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **36c**



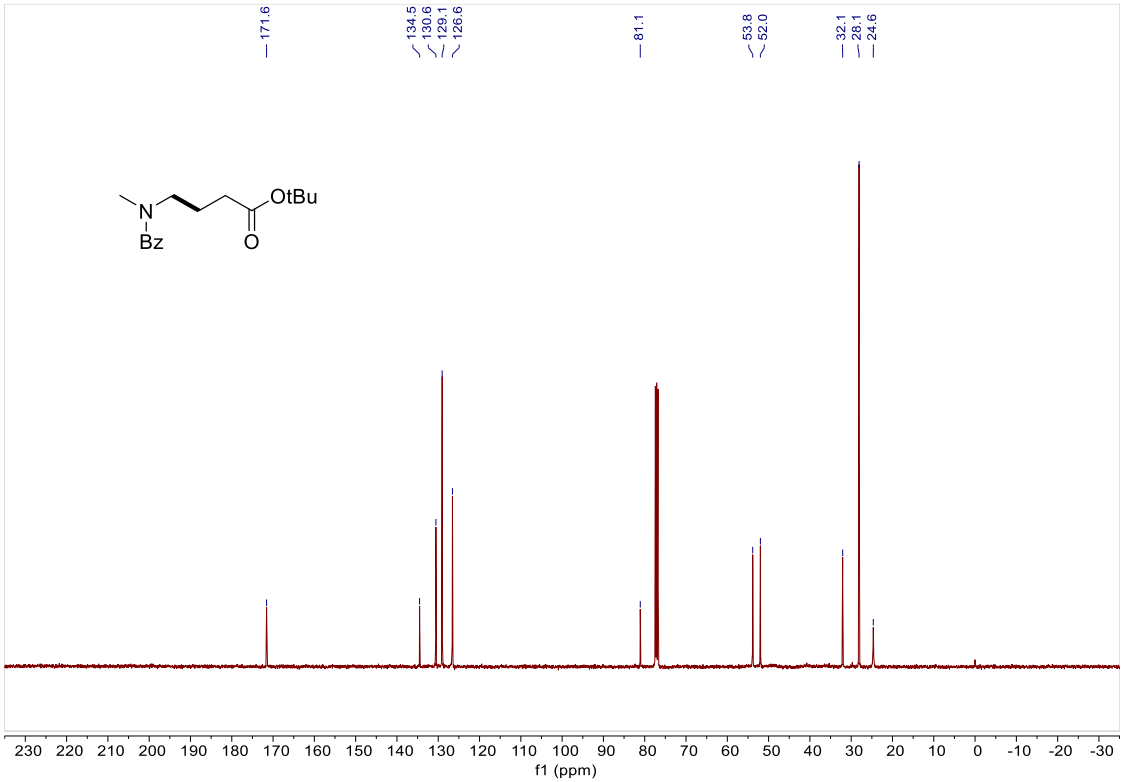
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **36c**



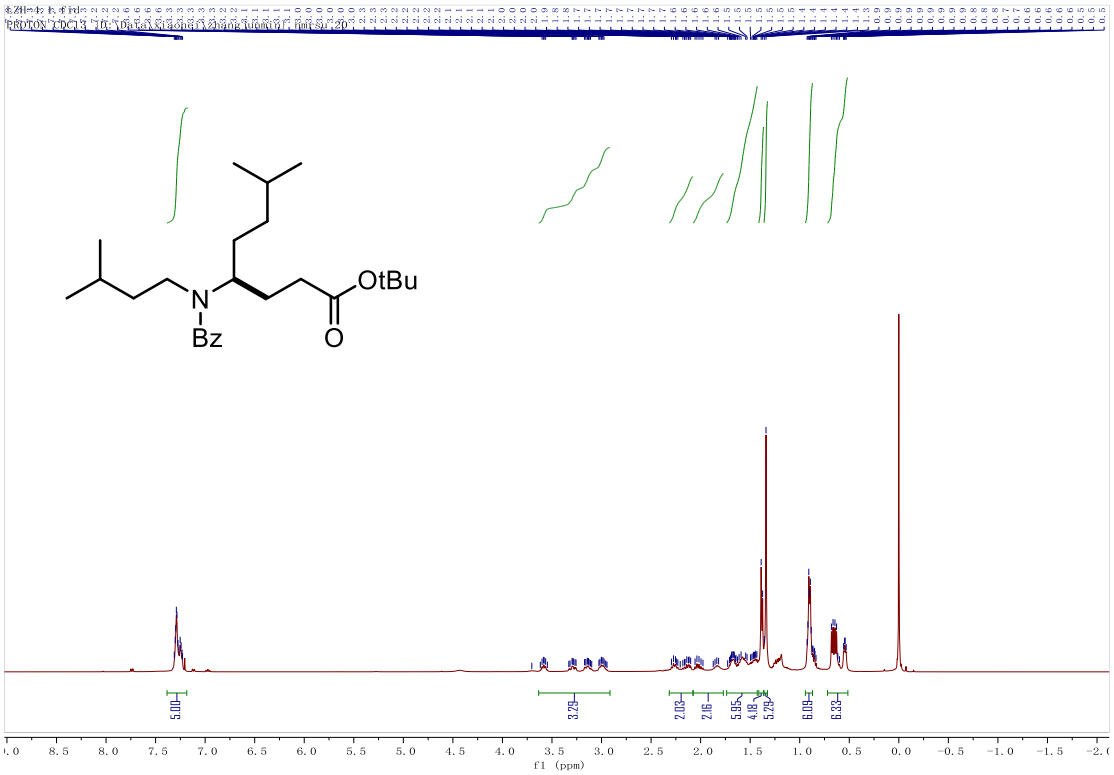
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **37c**



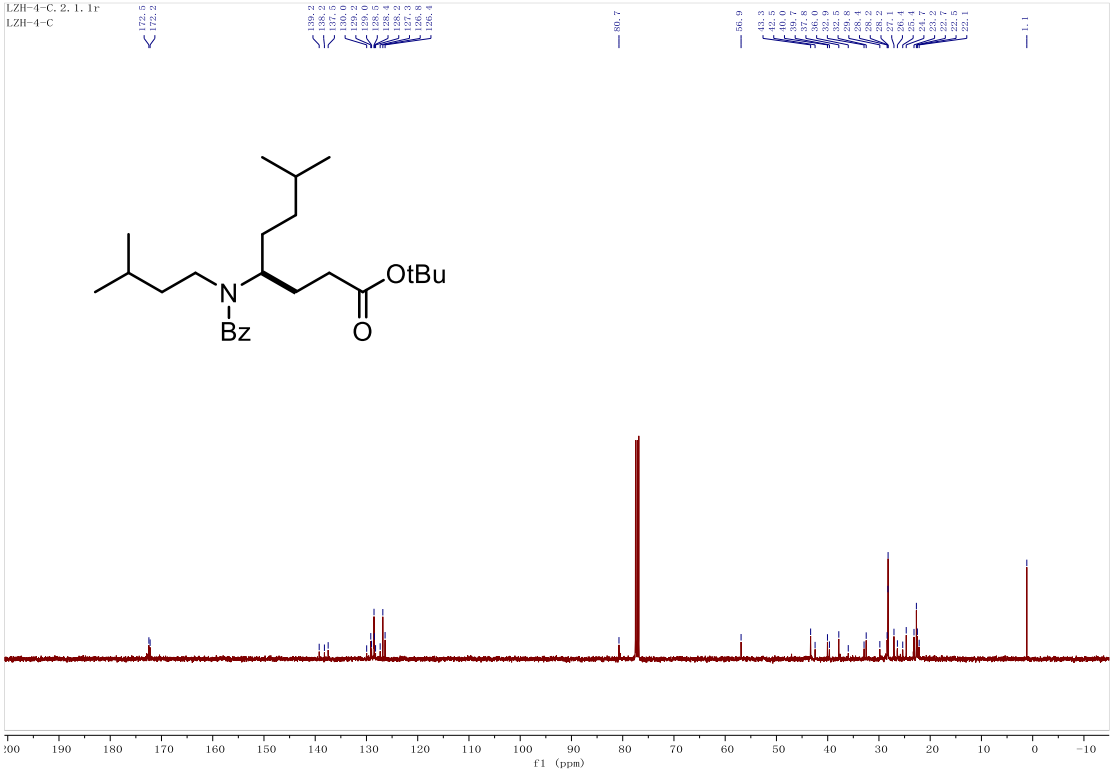
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **37c**



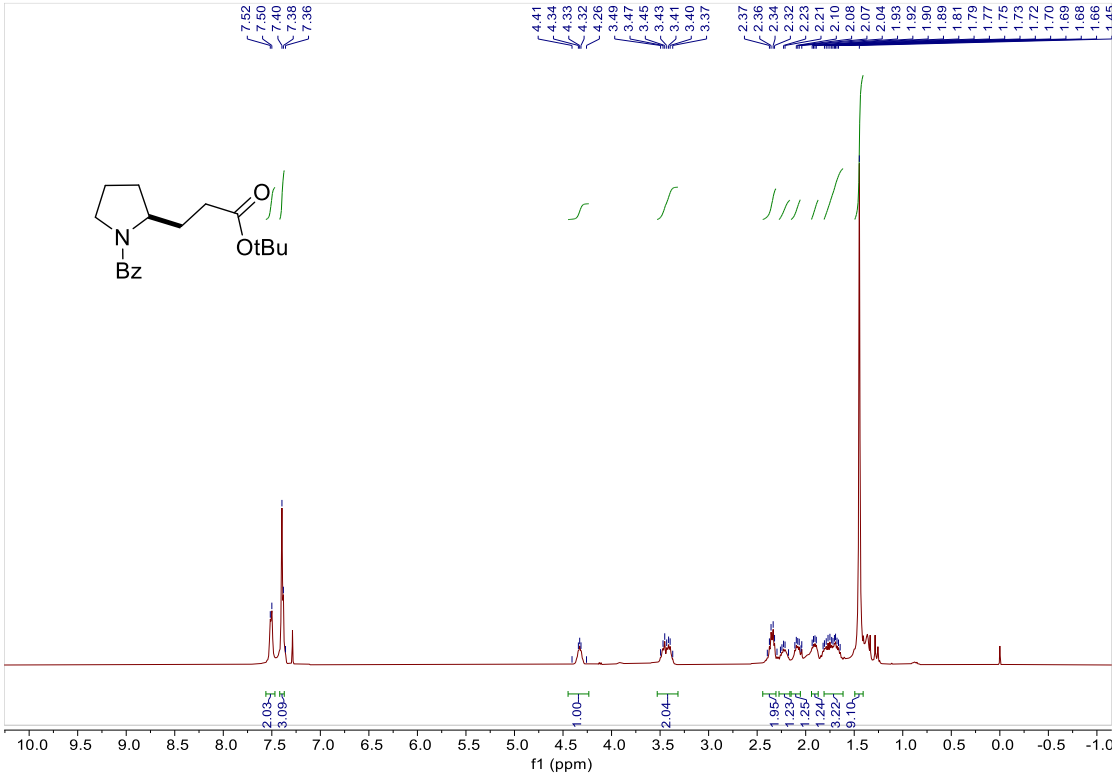
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **38c**



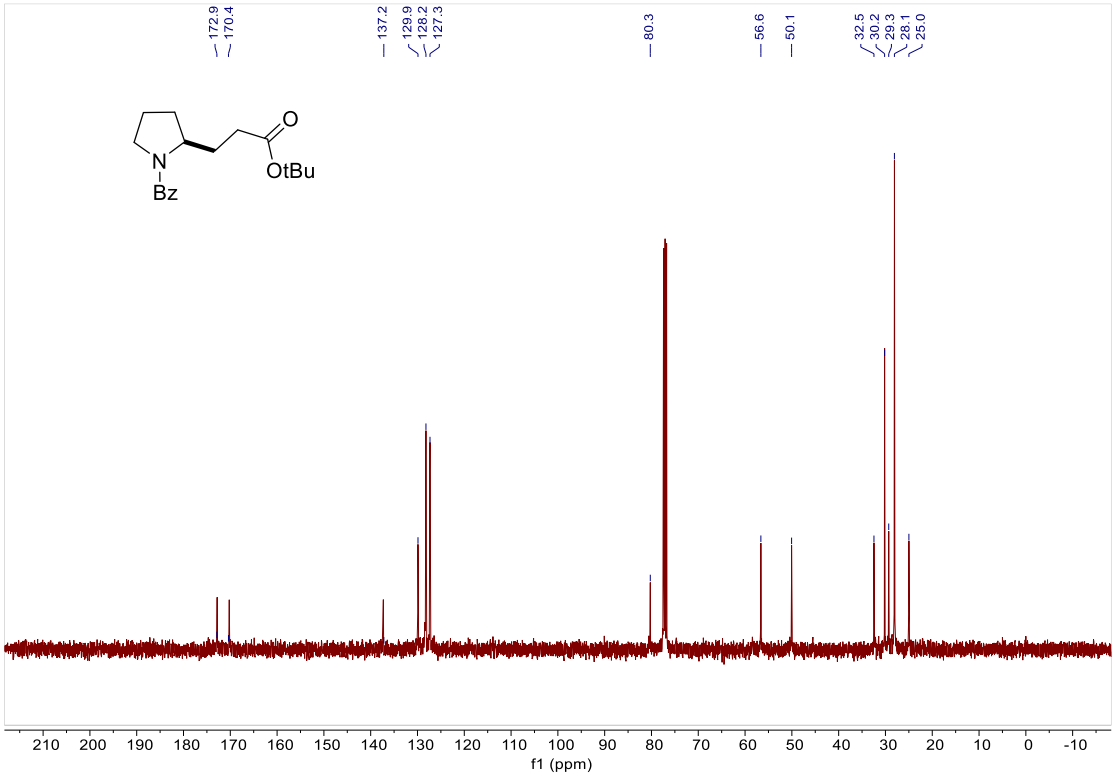
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **38c**



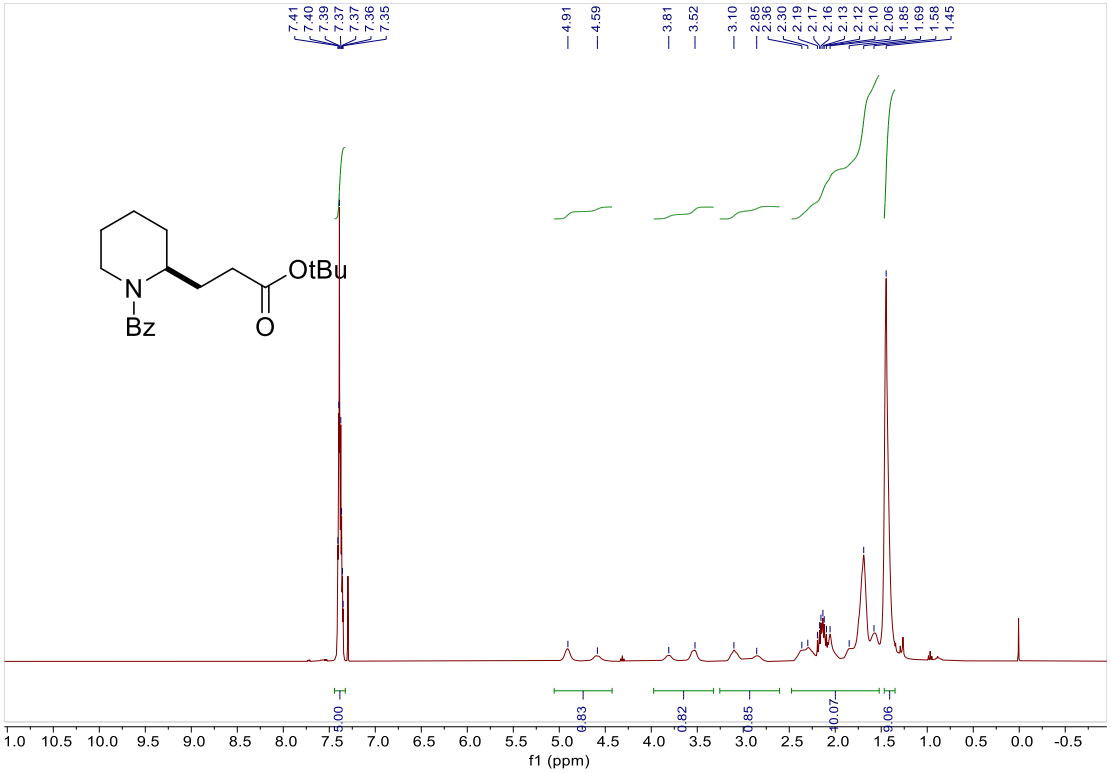
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **39c**



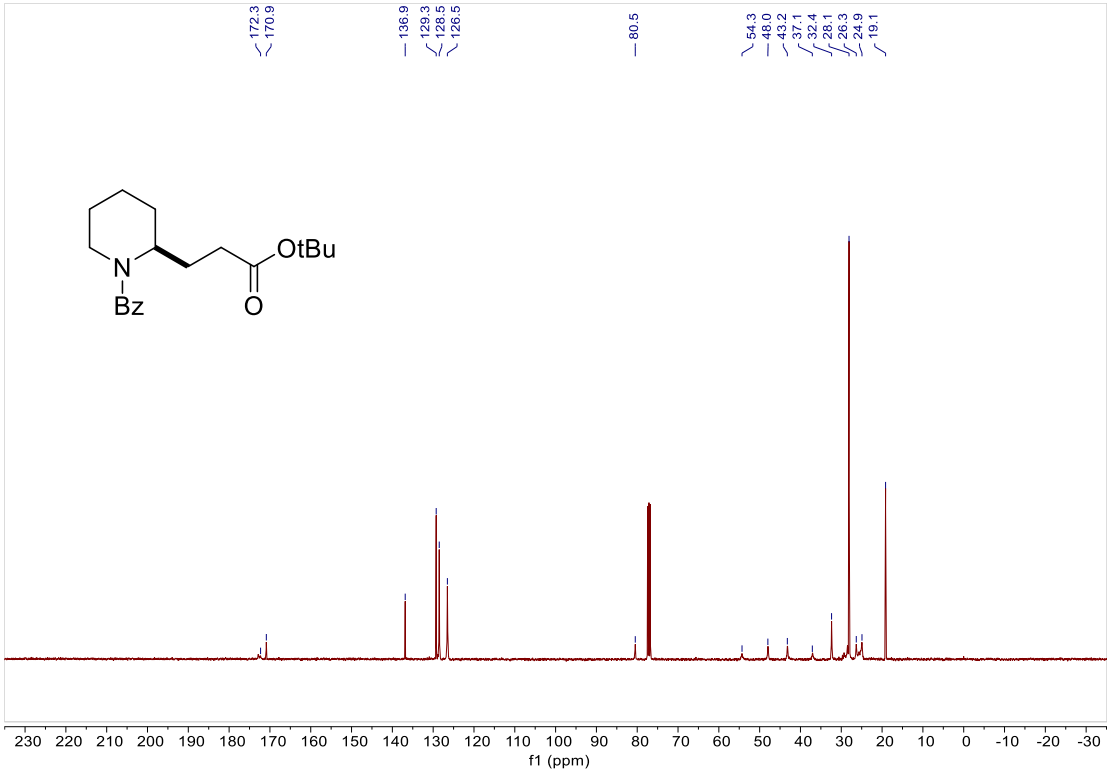
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **39c**



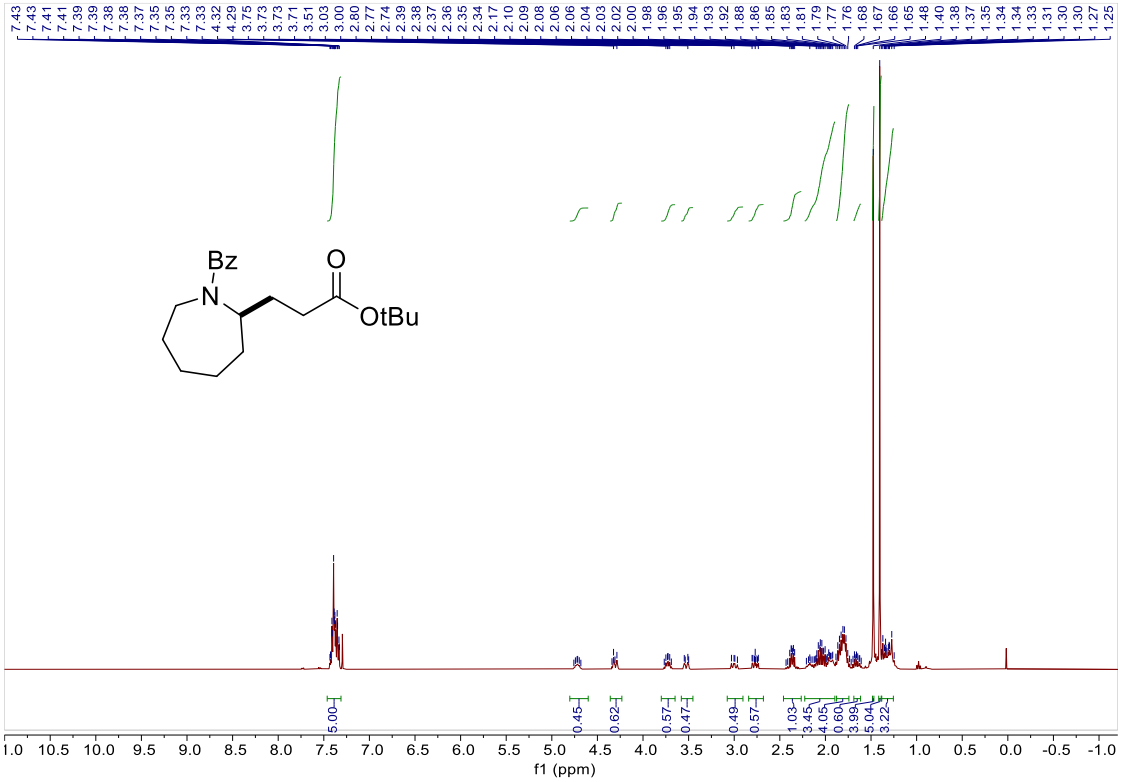
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **40c**



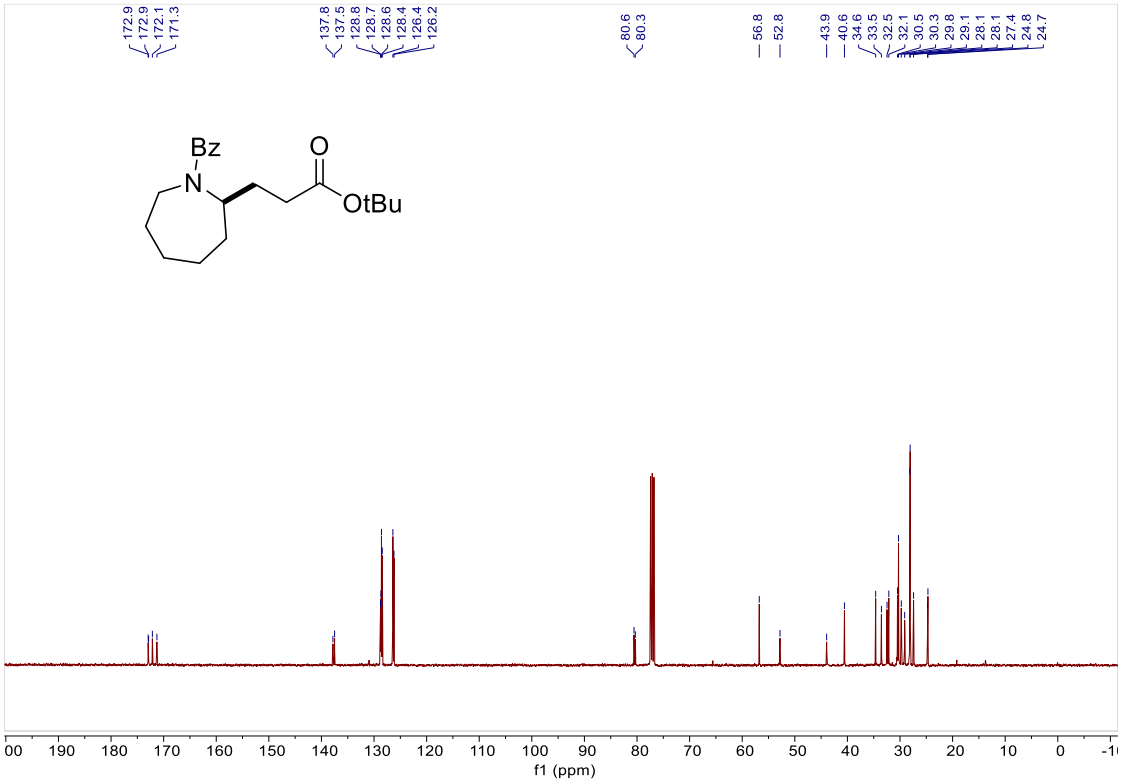
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **40c**



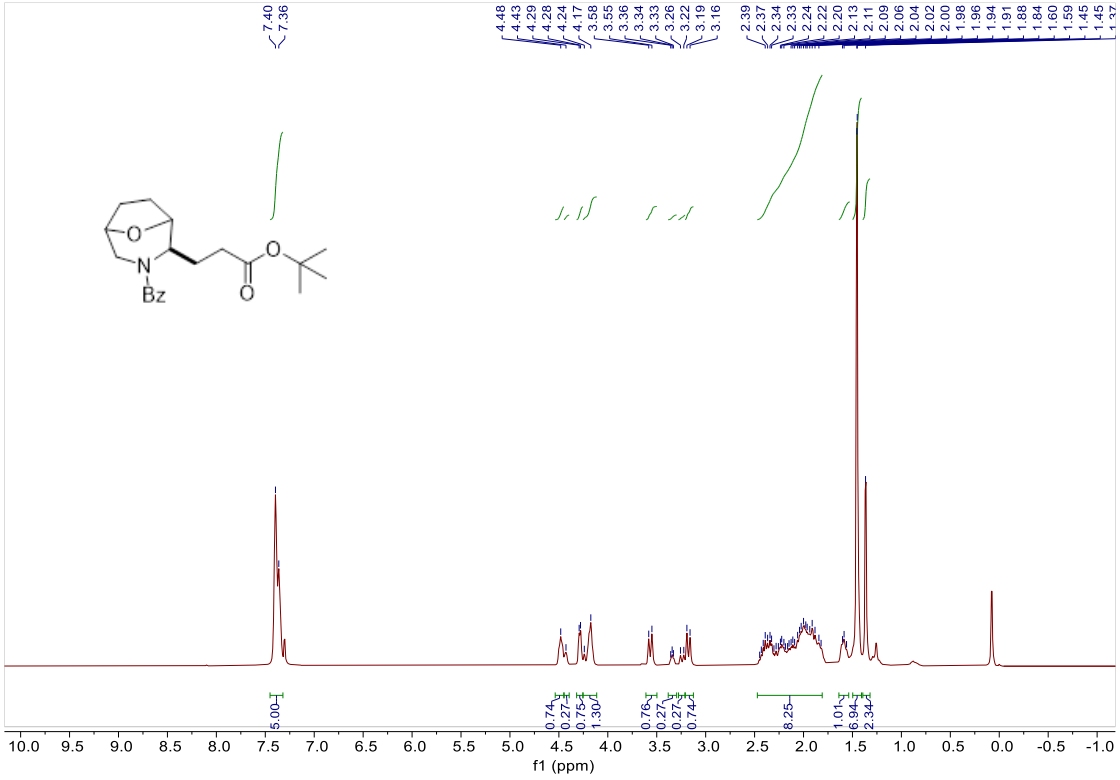
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **41c**



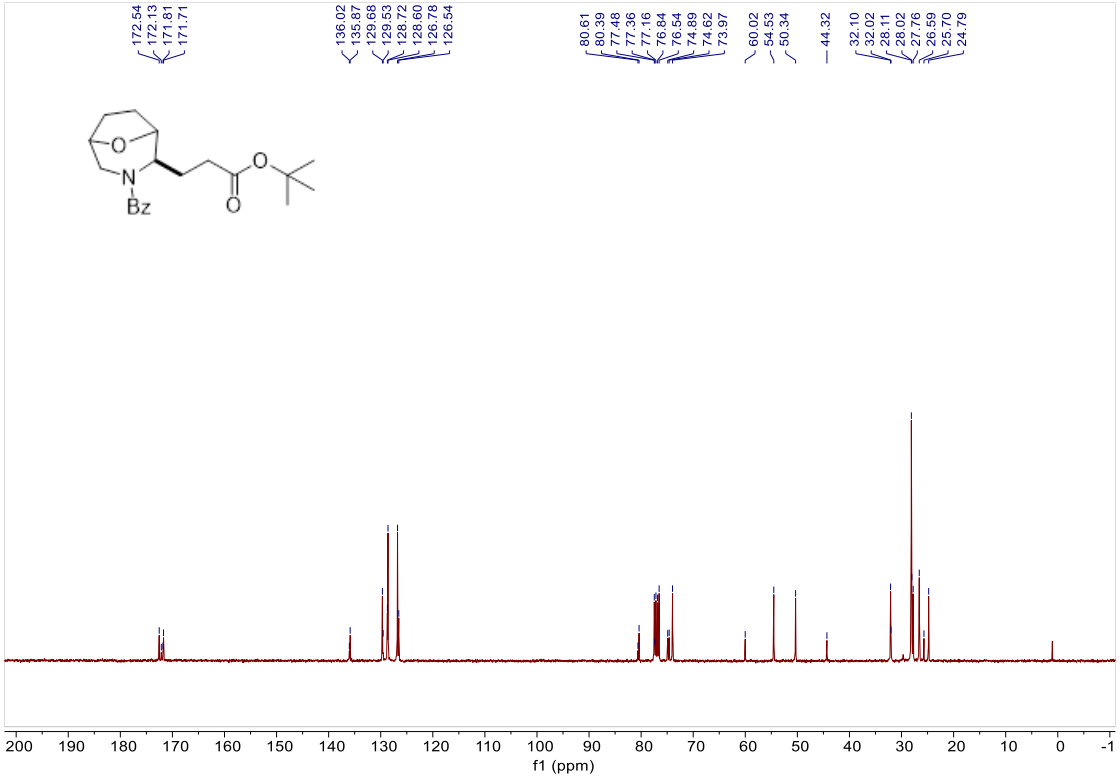
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **41c**



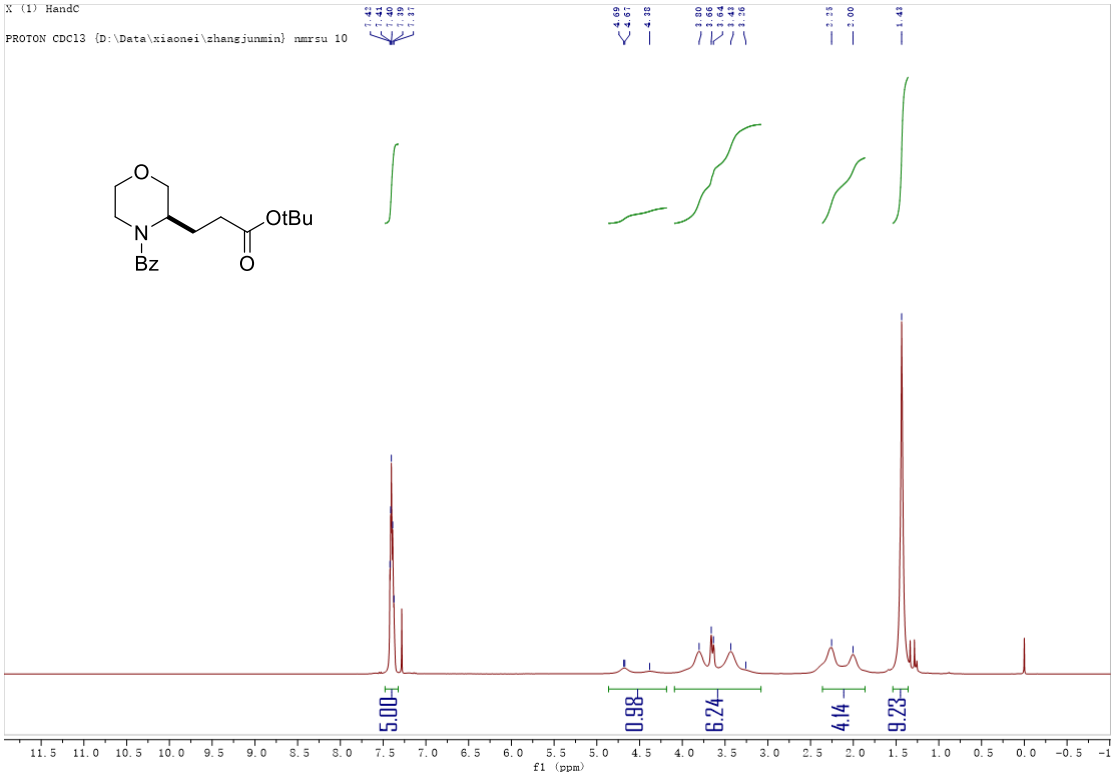
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **42c**



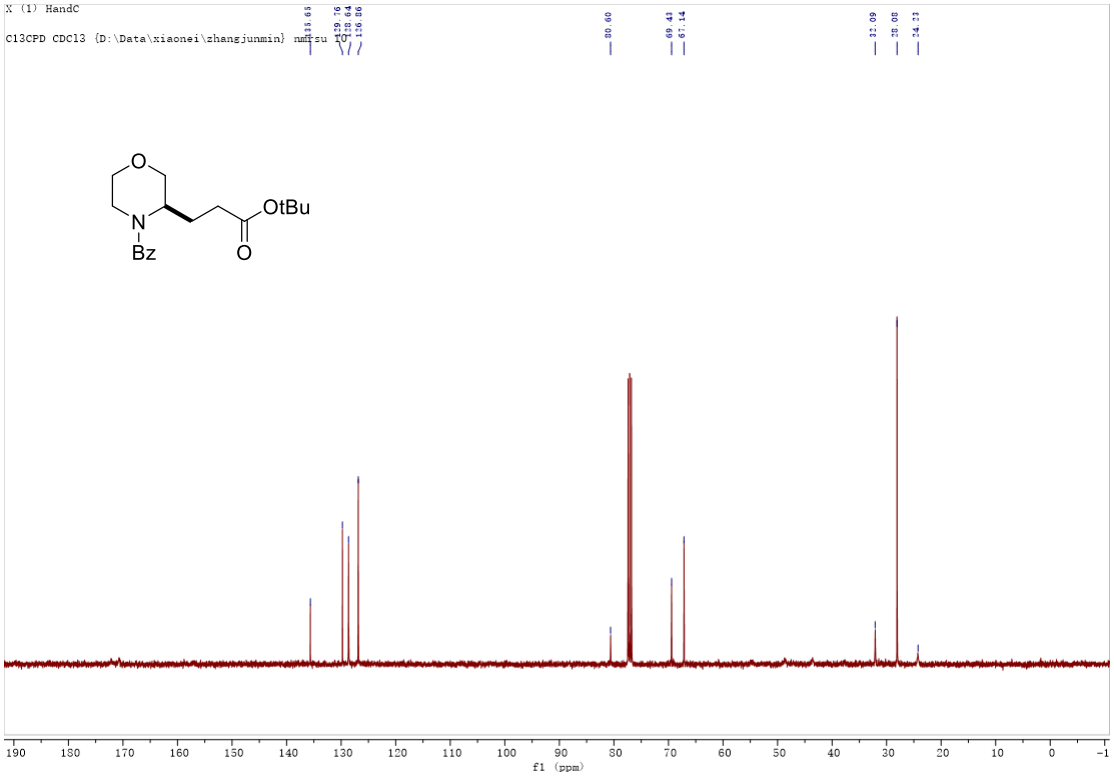
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **42c**



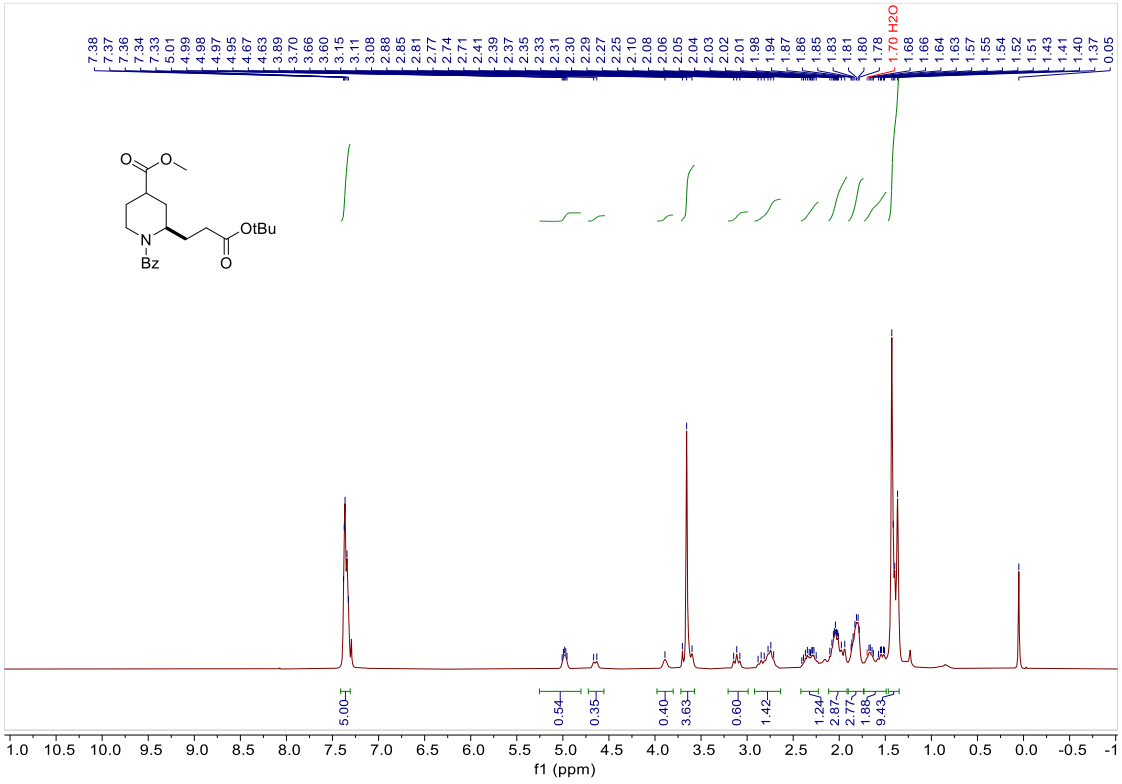
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **43c**



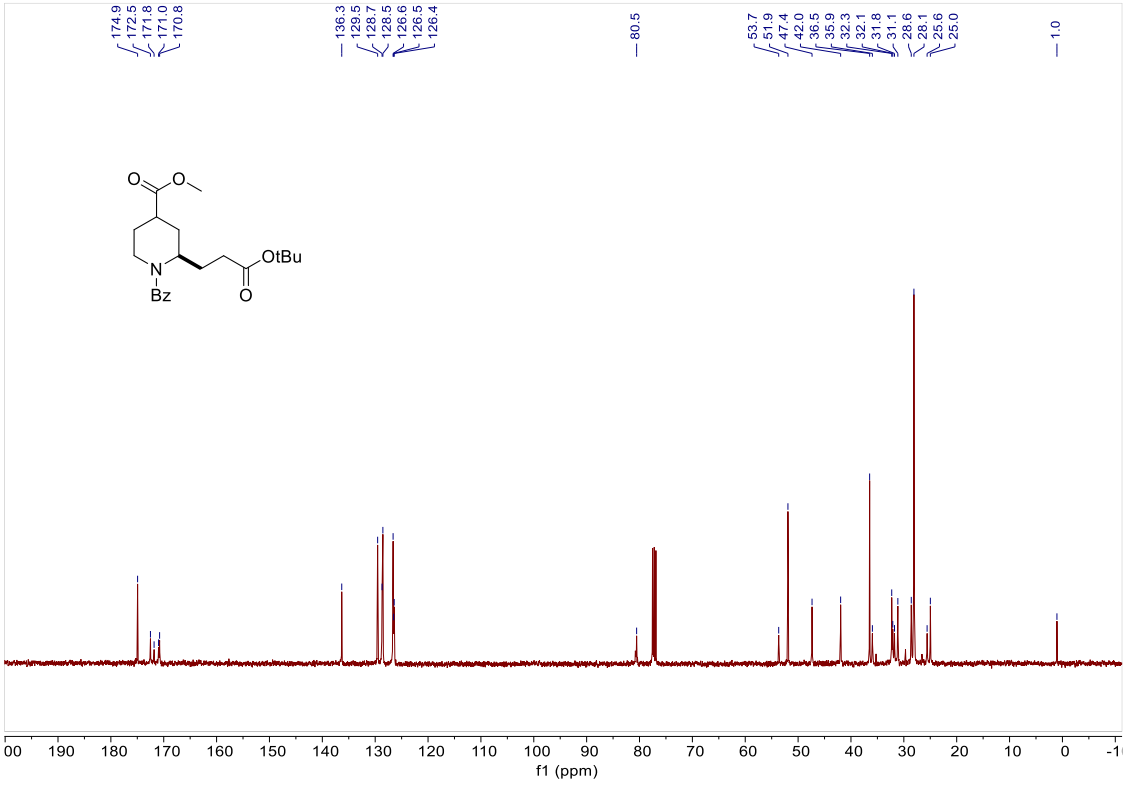
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **43c**



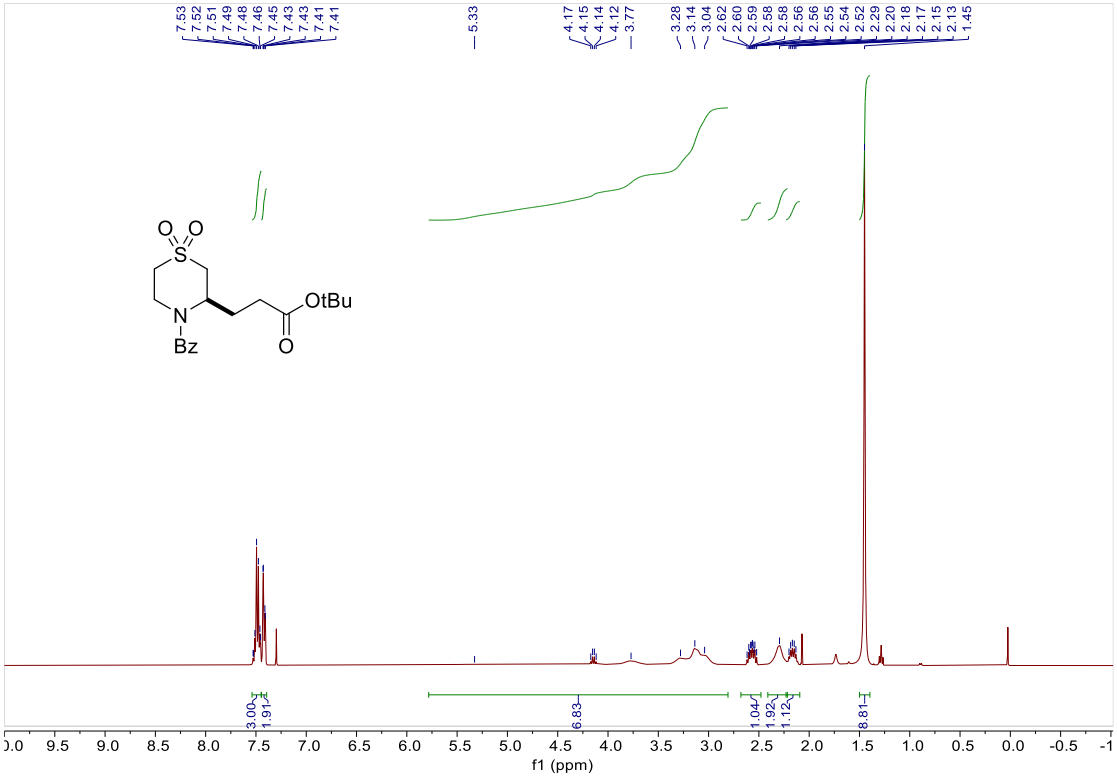
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **44c**



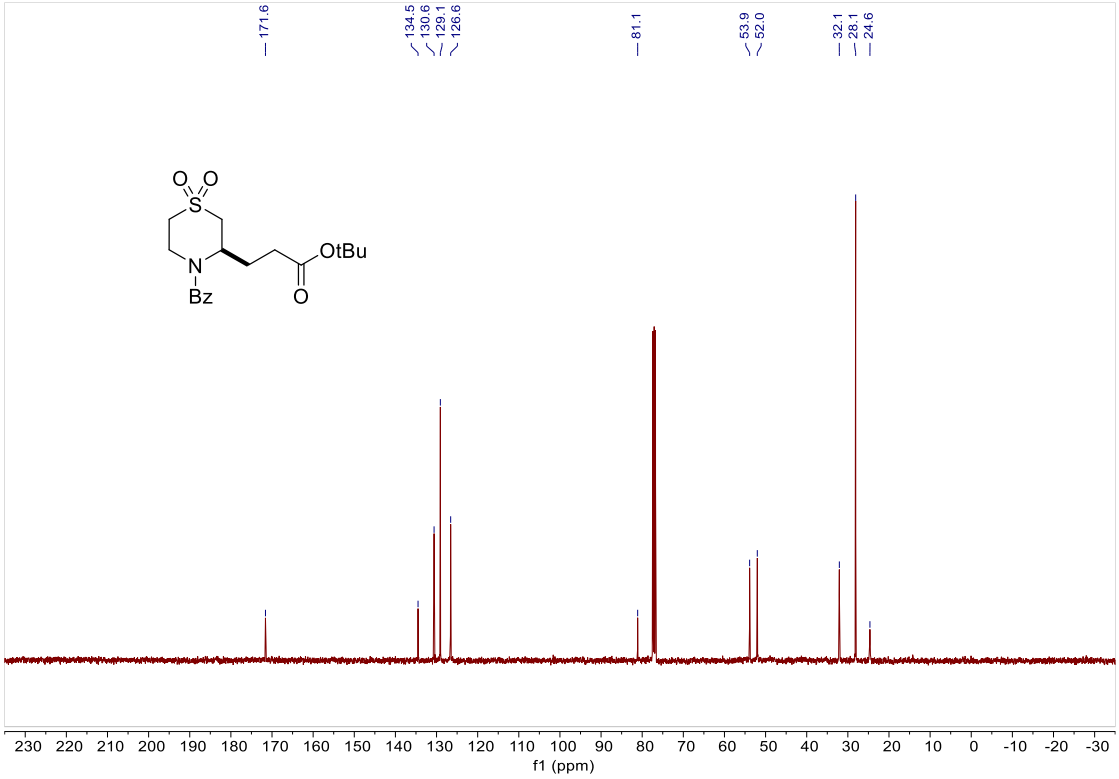
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **44c**



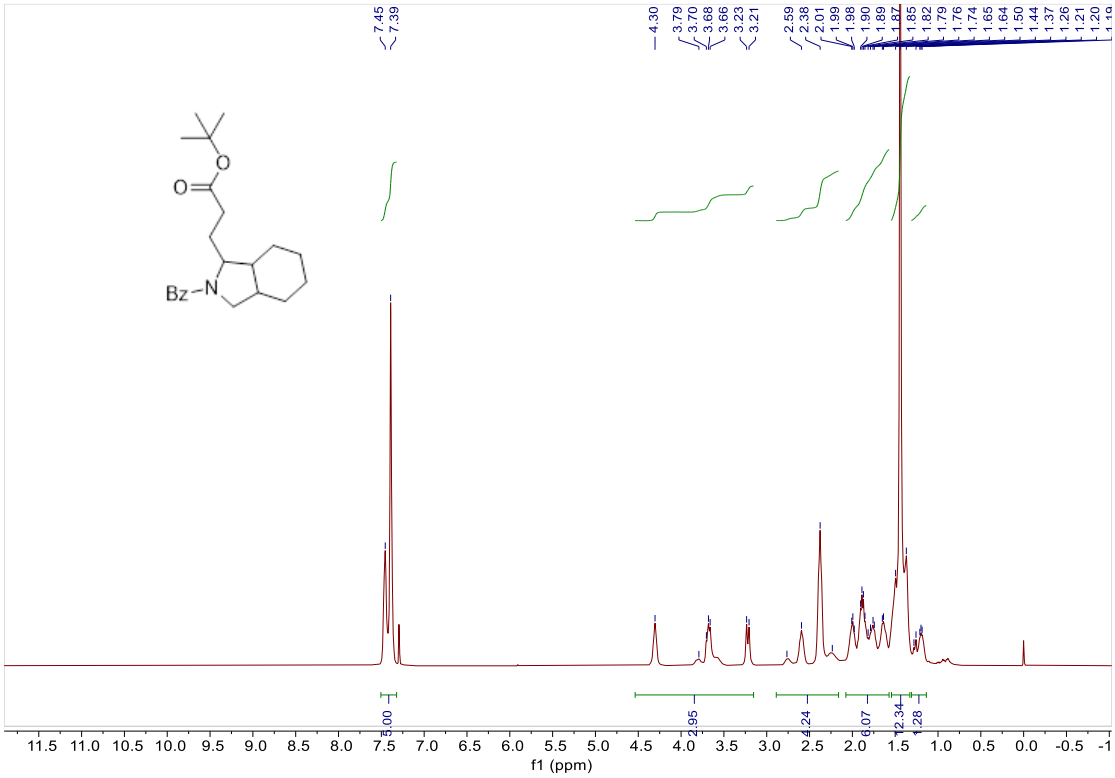
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **45c**



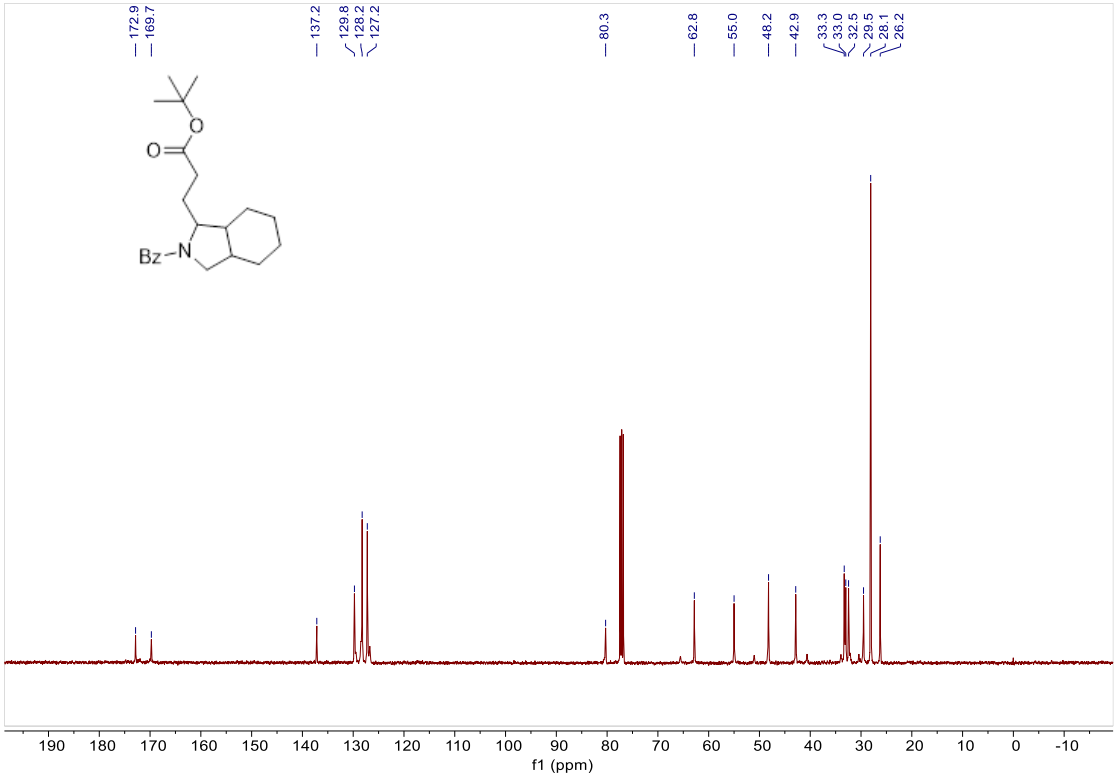
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **45c**



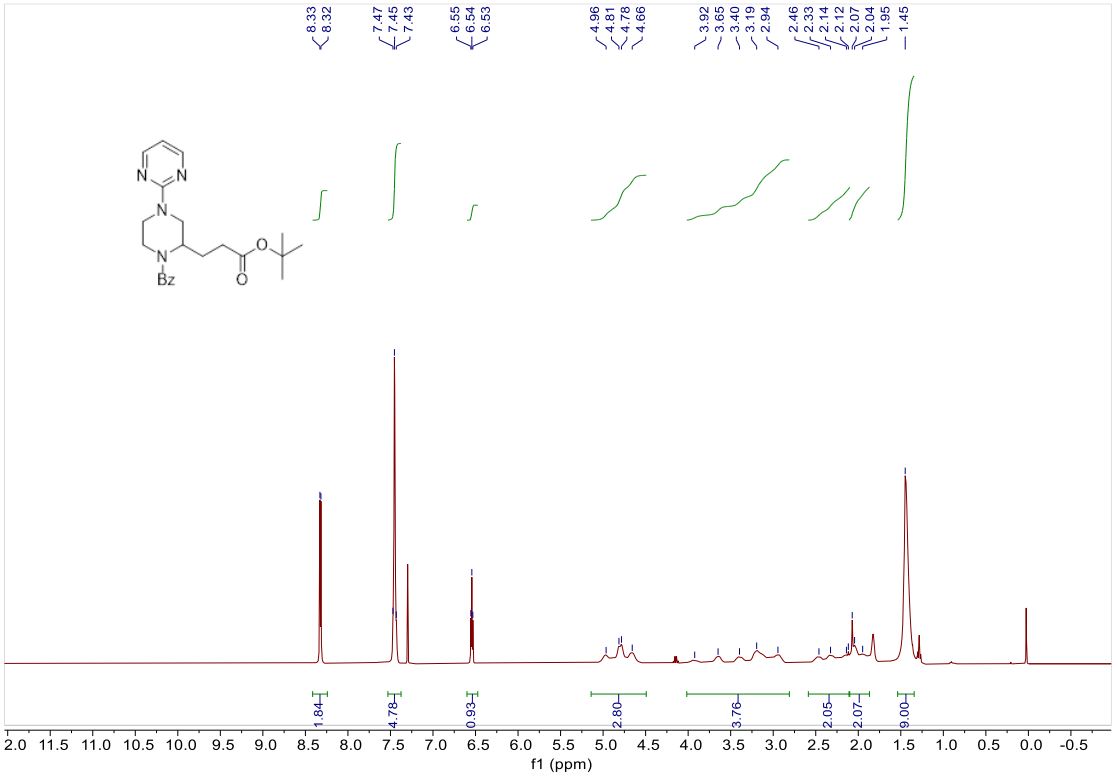
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **46c**



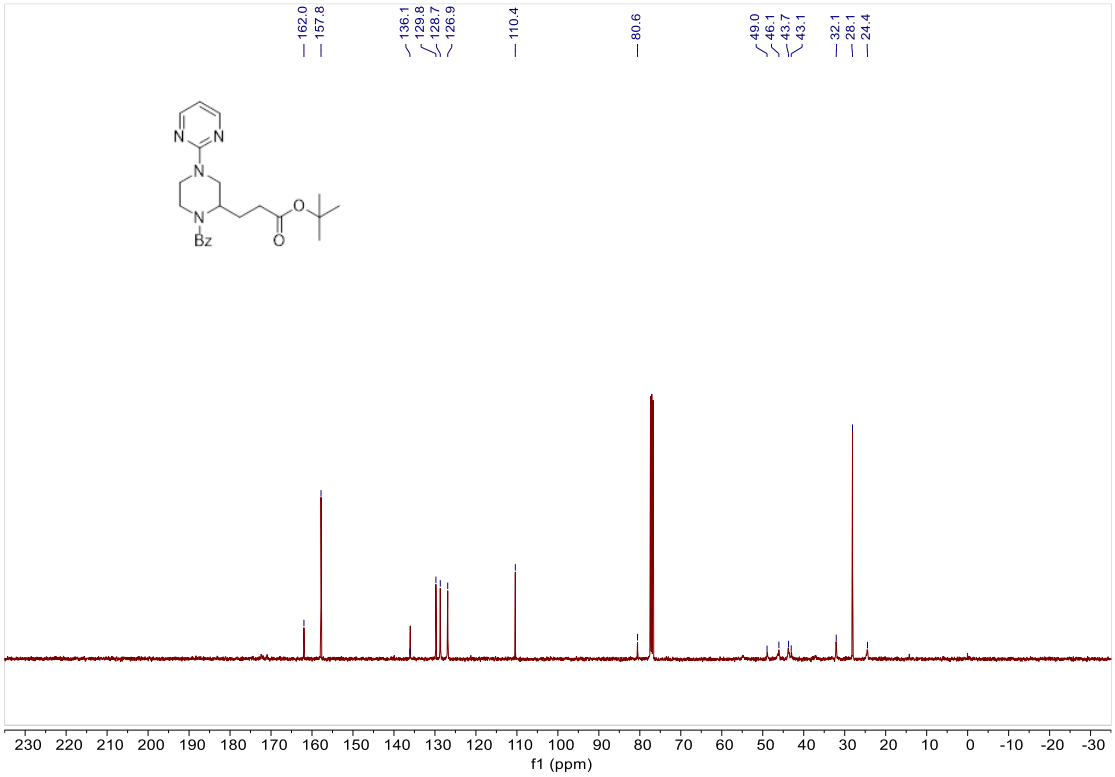
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **46c**



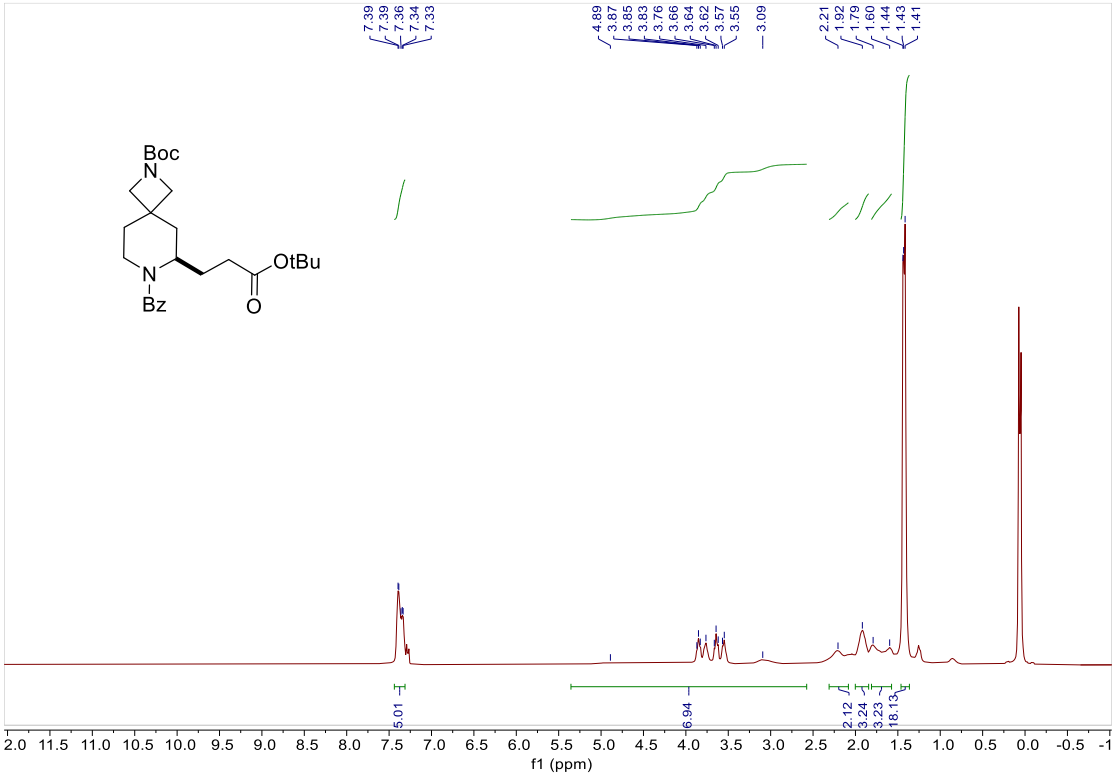
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **47c**



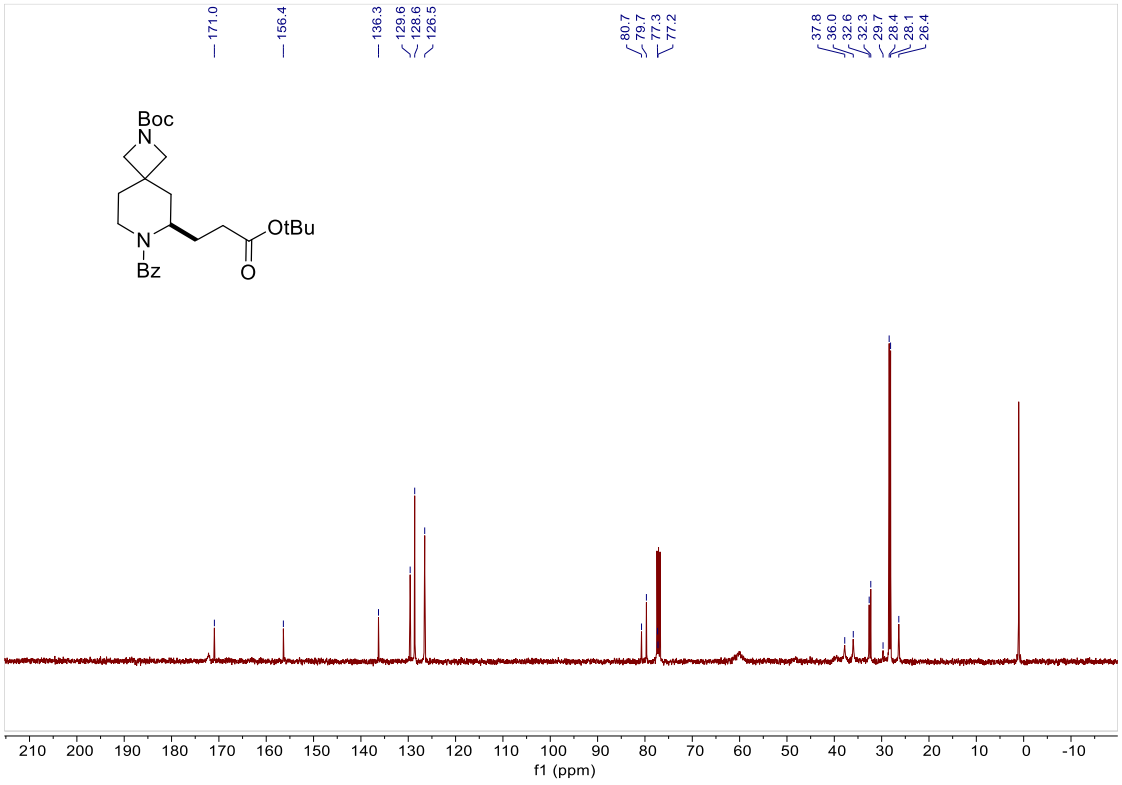
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **47c**



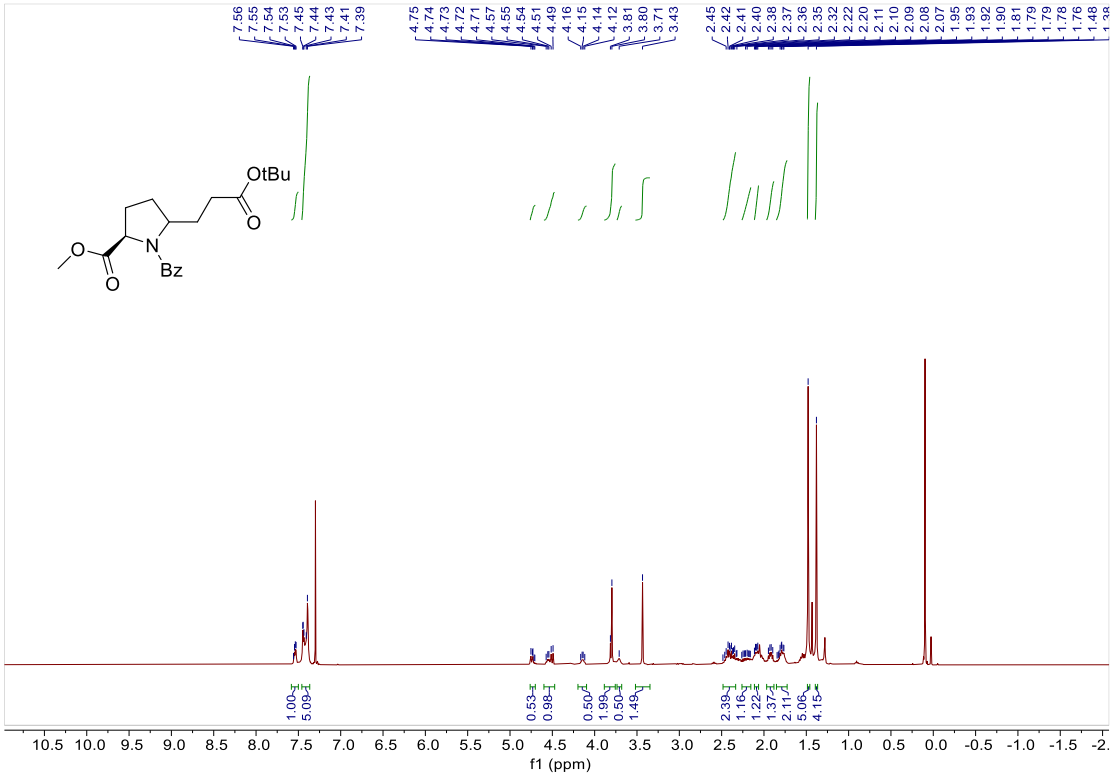
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **48c**



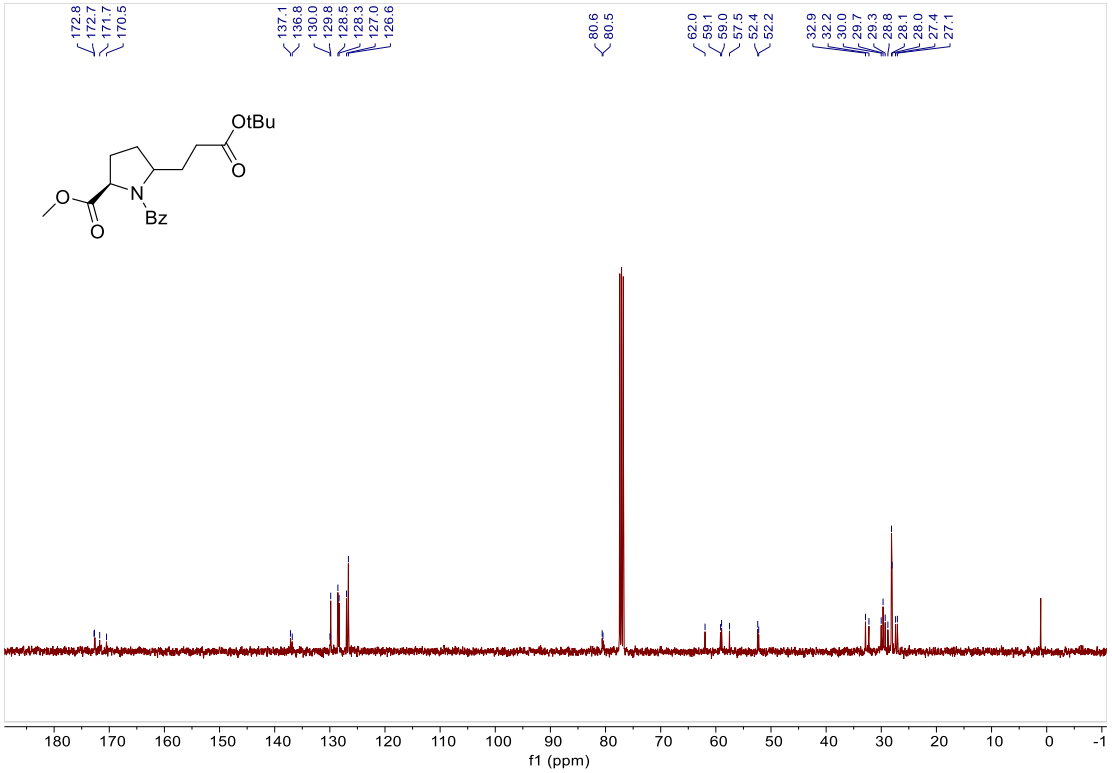
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **48c**



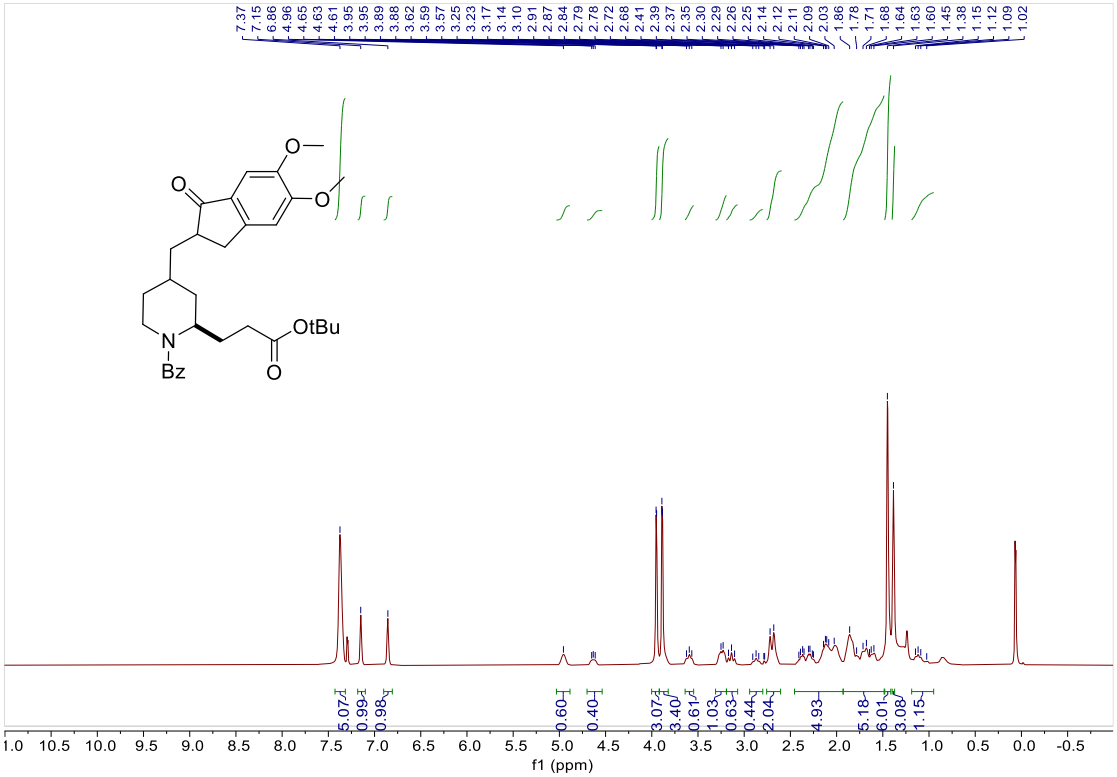
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **49c**



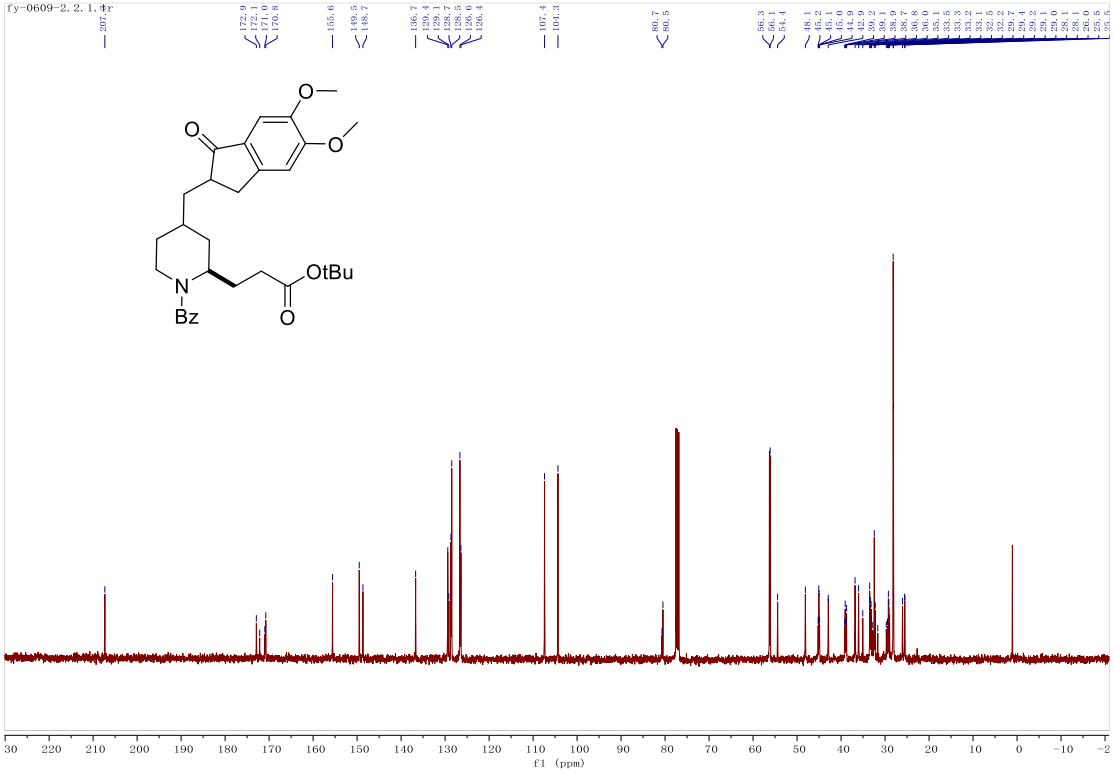
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **49c**



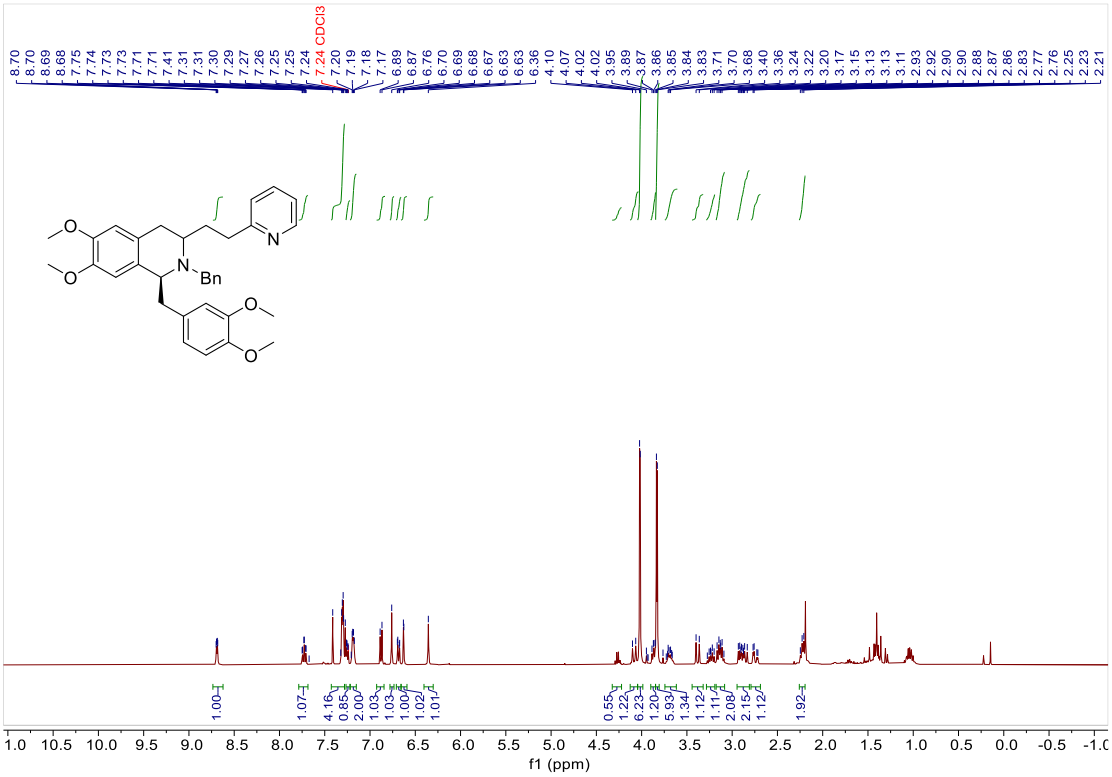
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **50c**



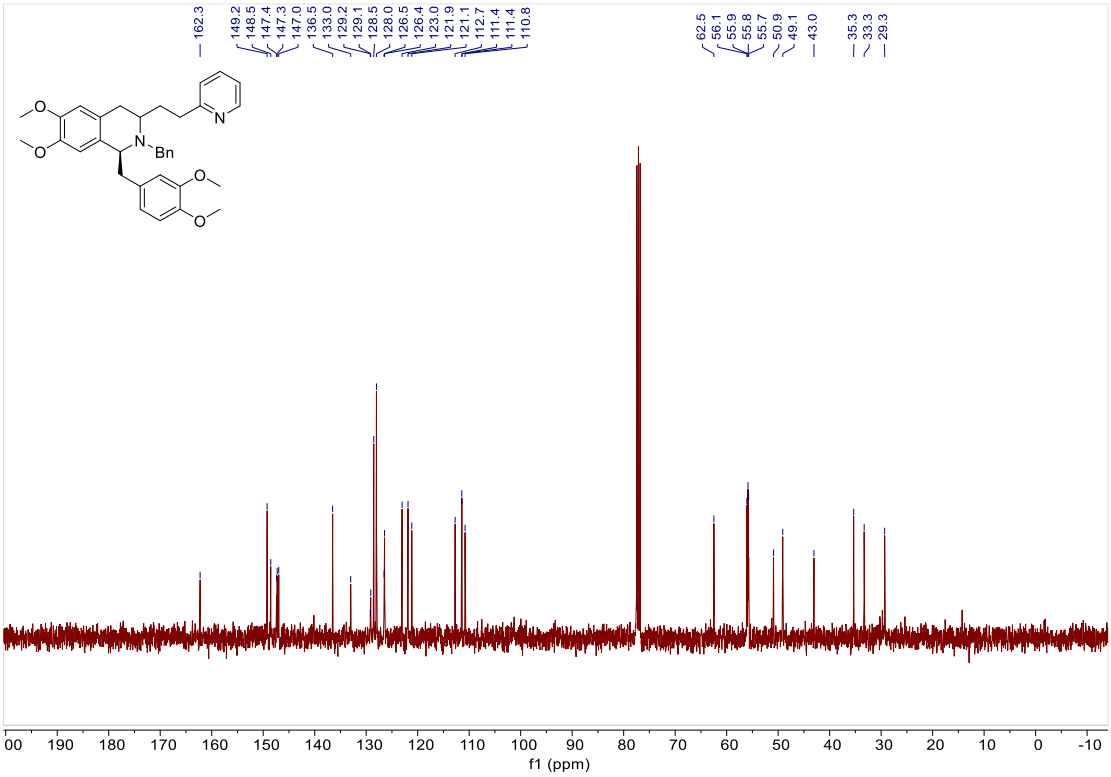
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **50c**



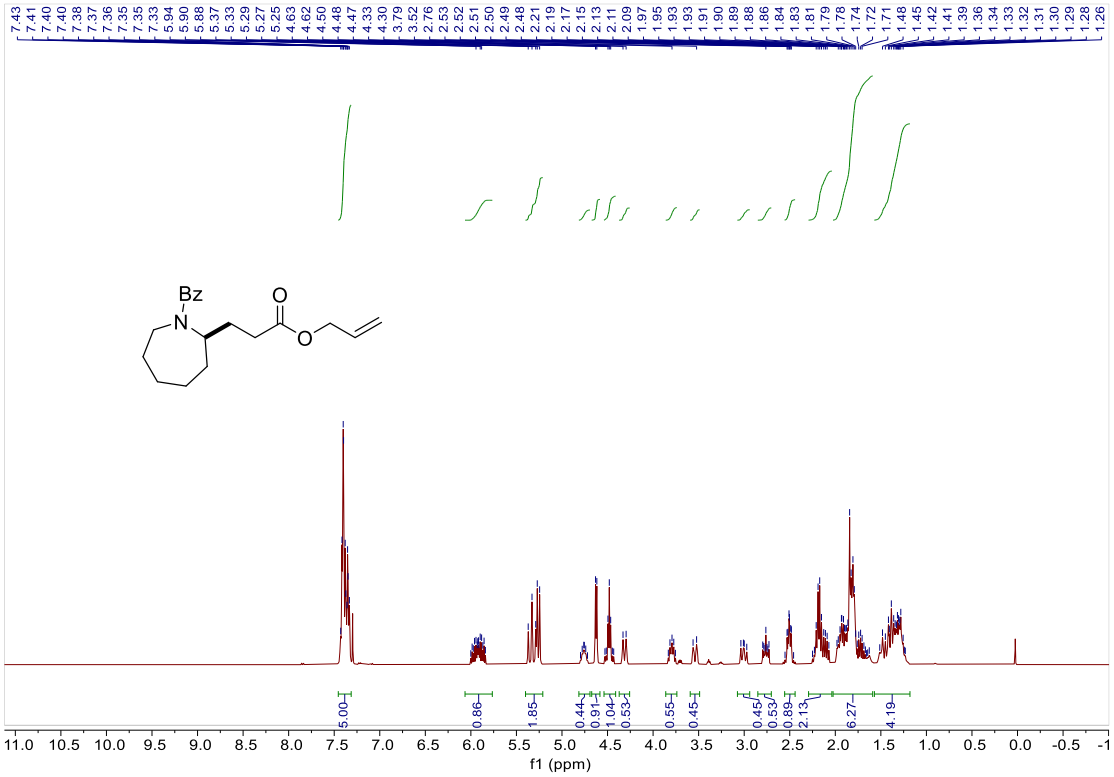
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **51c**



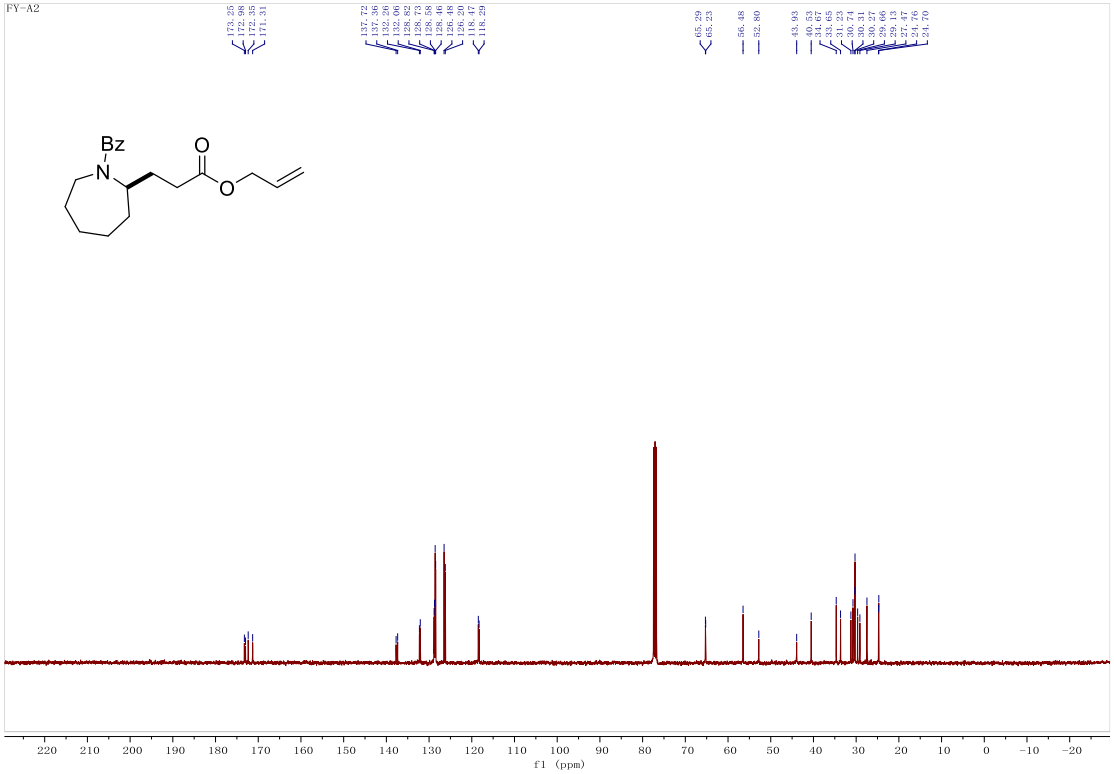
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **51c**



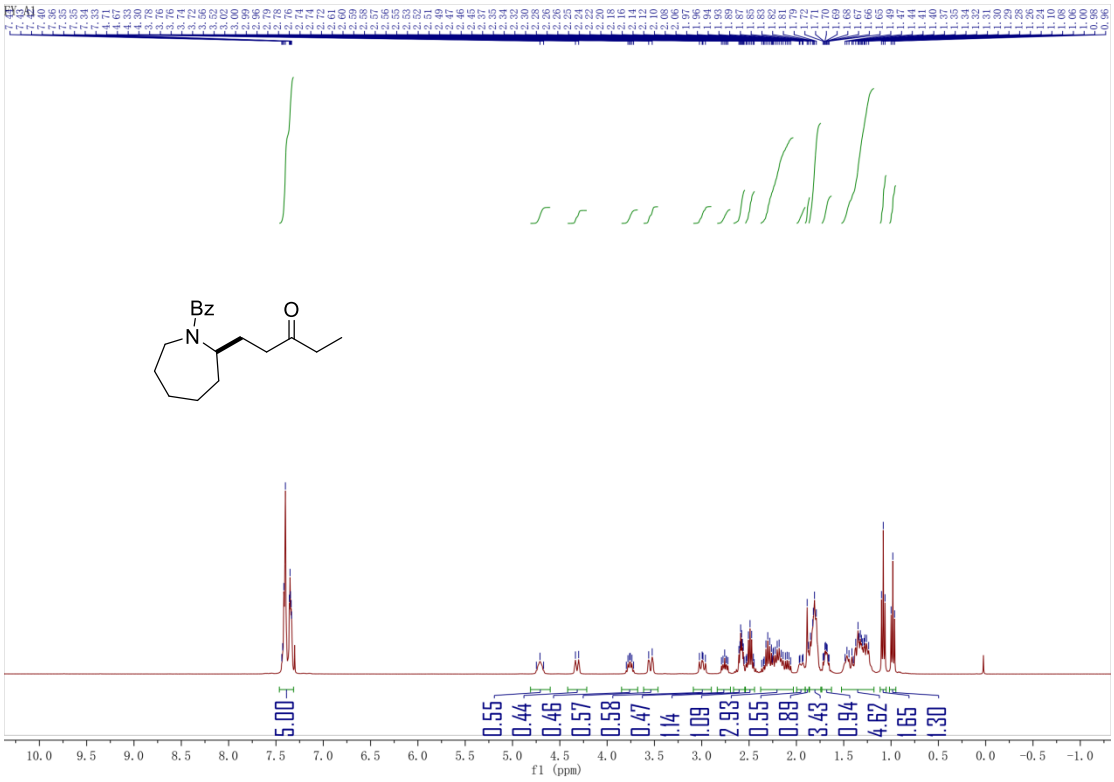
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **52c**



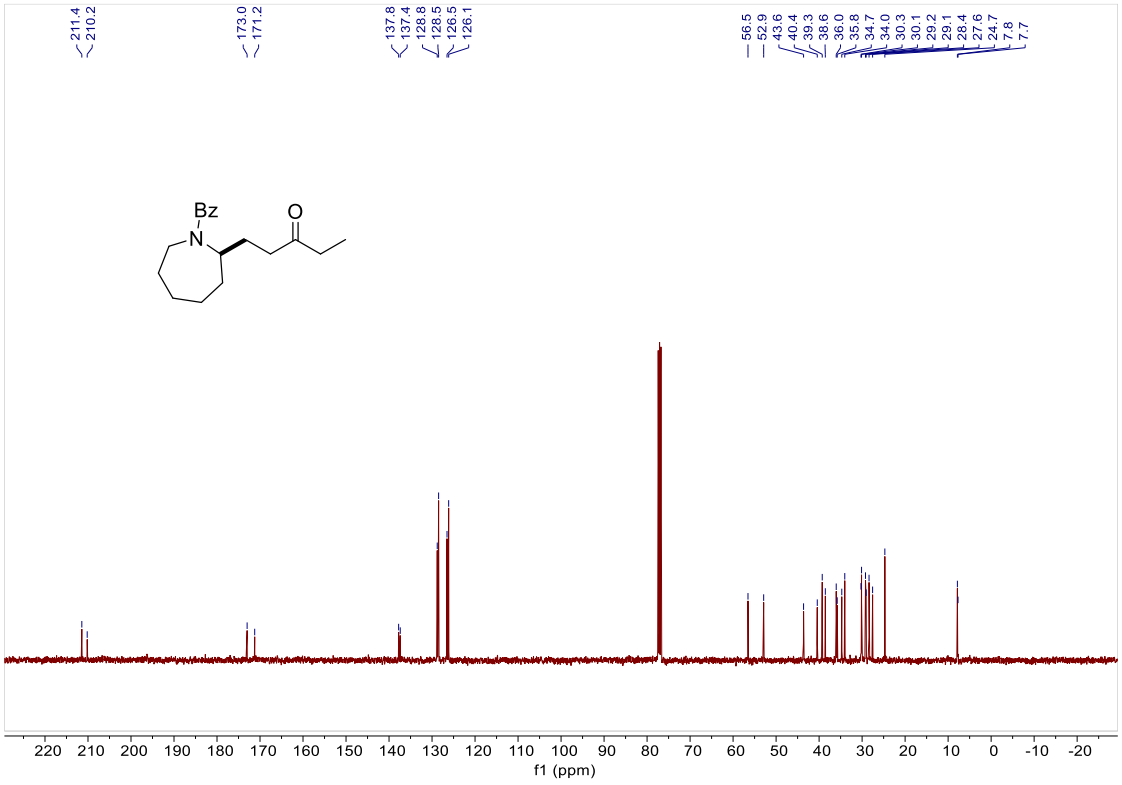
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **52c**



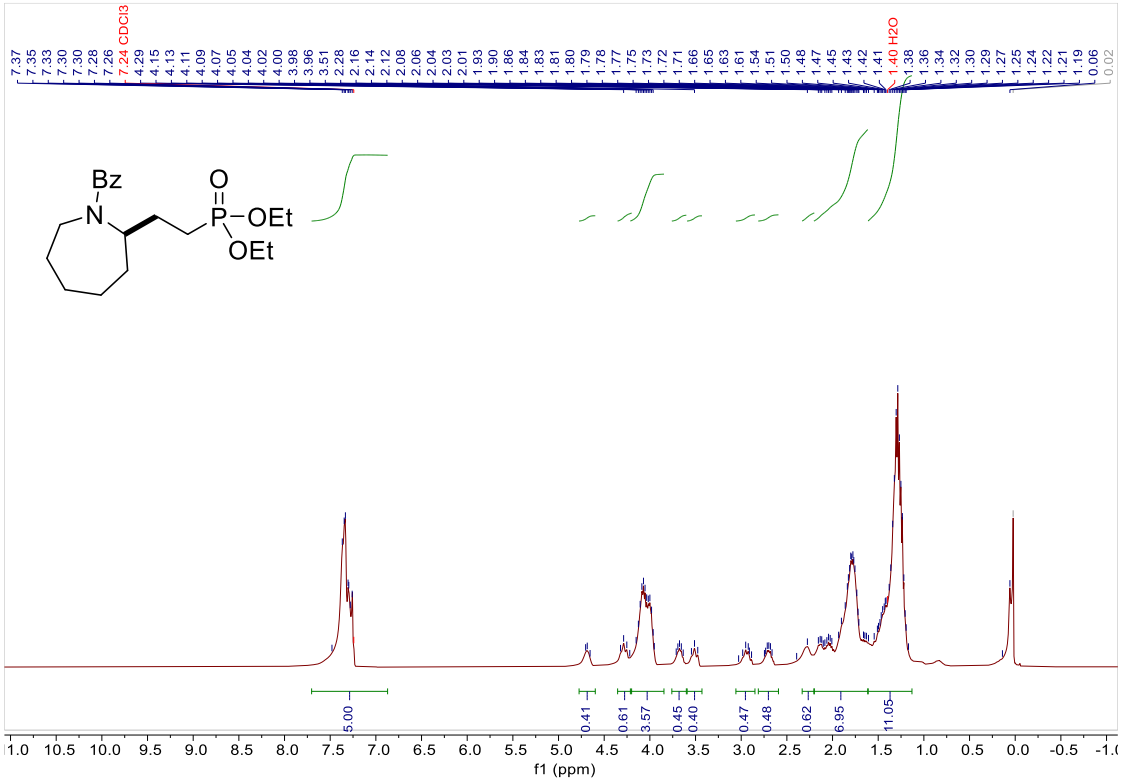
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **53c**



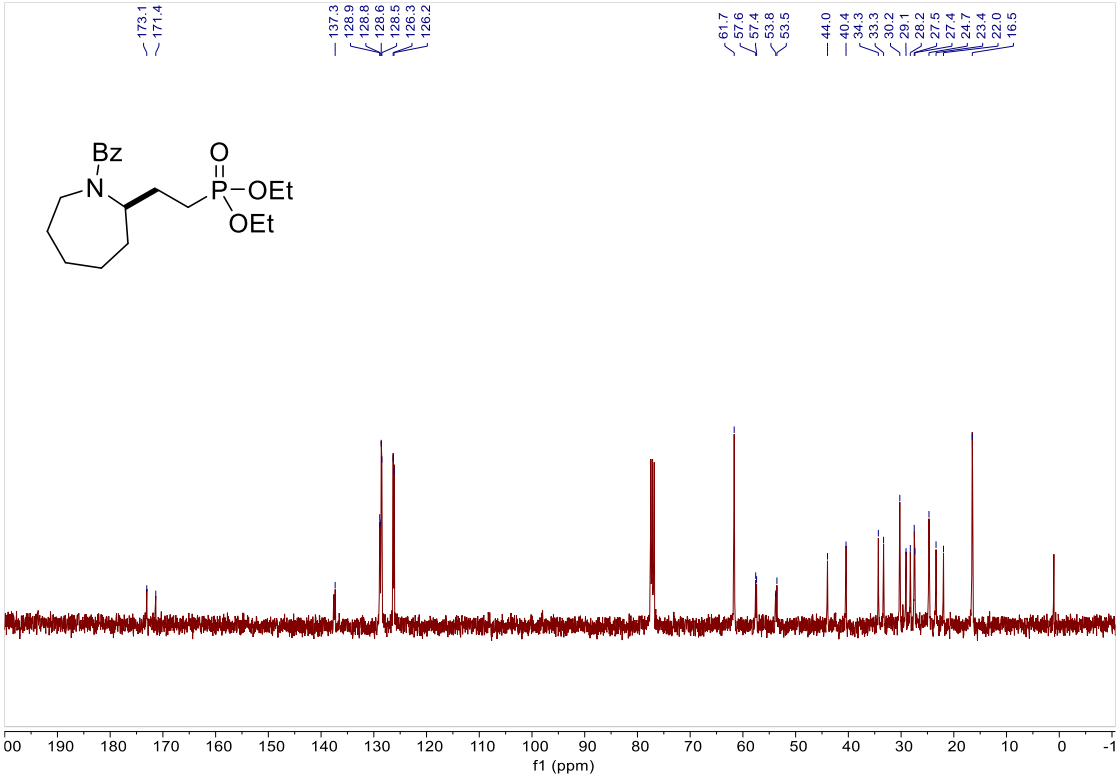
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **53c**



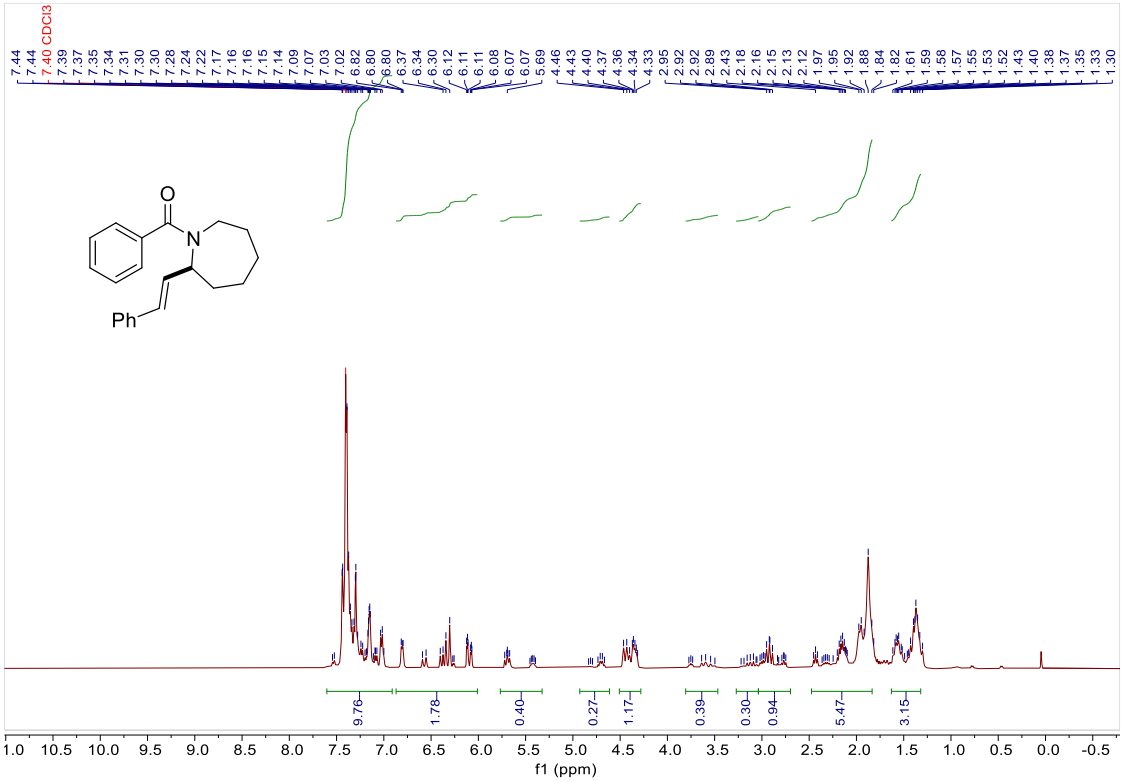
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **54c**



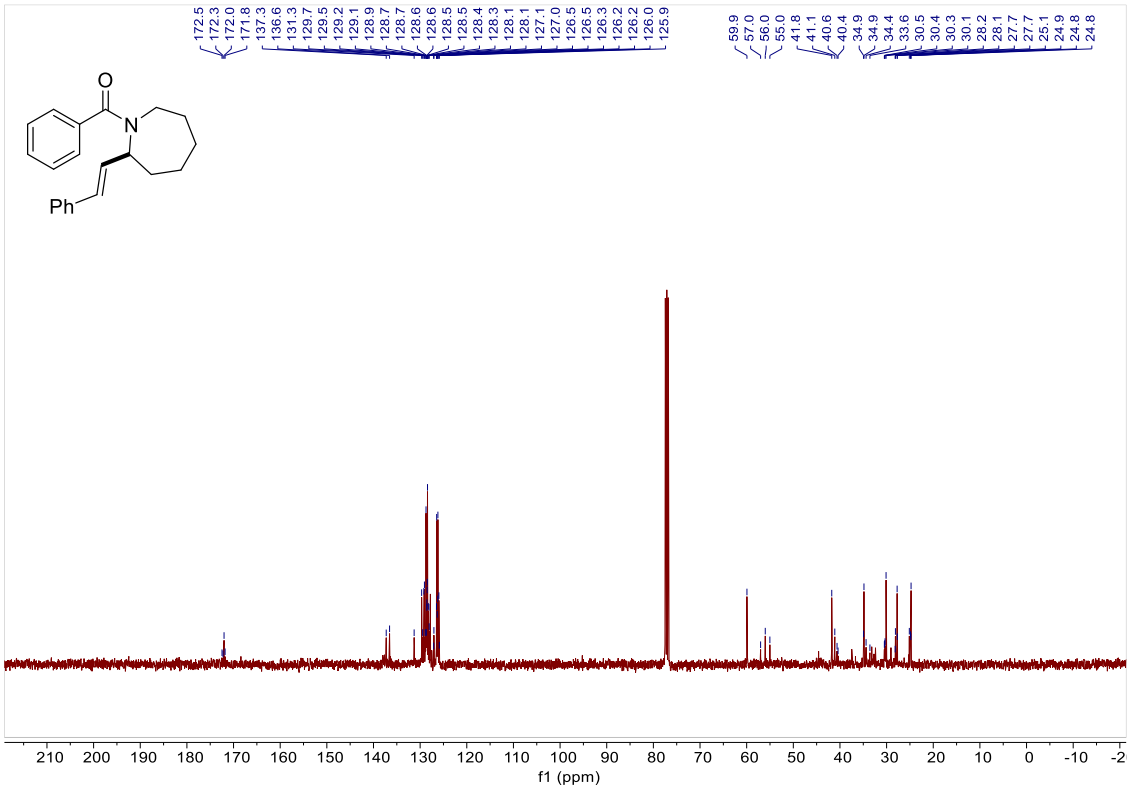
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **54c**



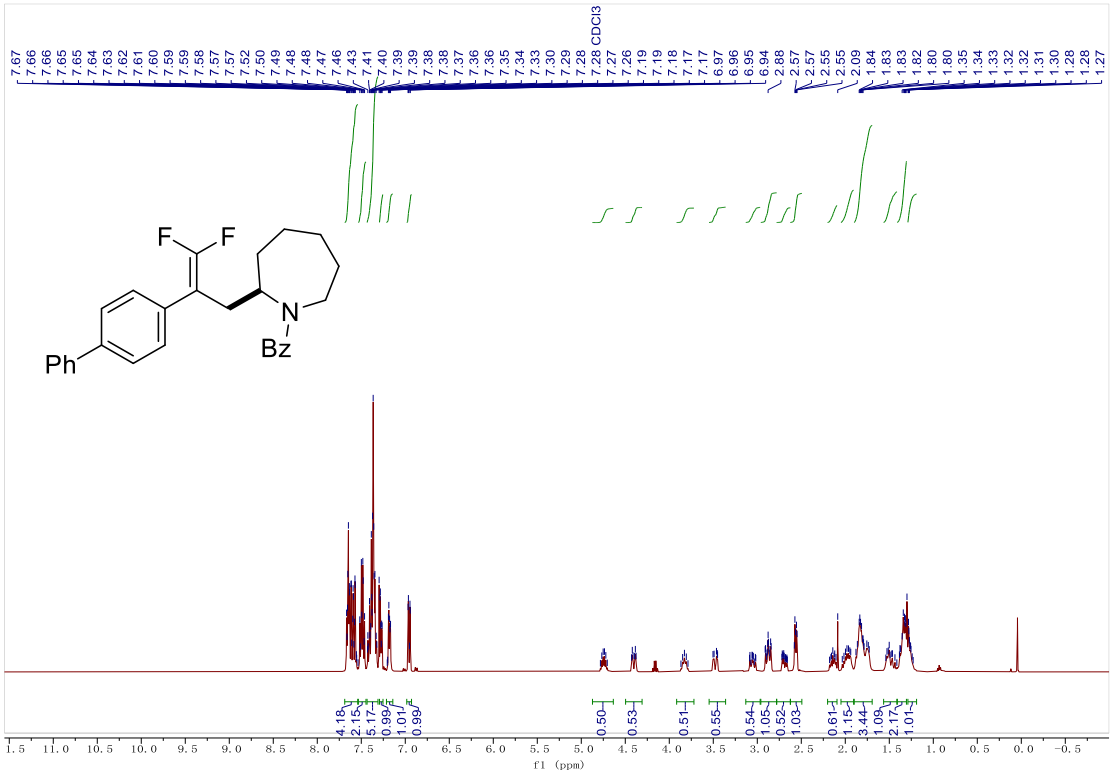
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **55c**



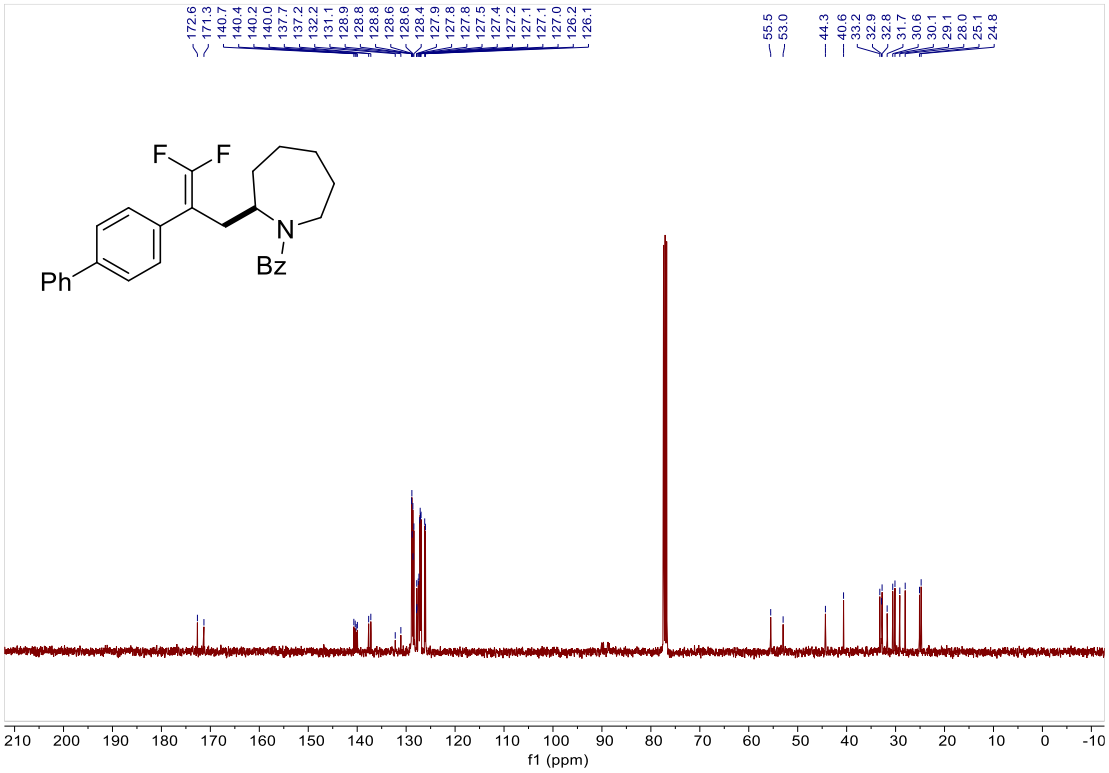
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **55c**



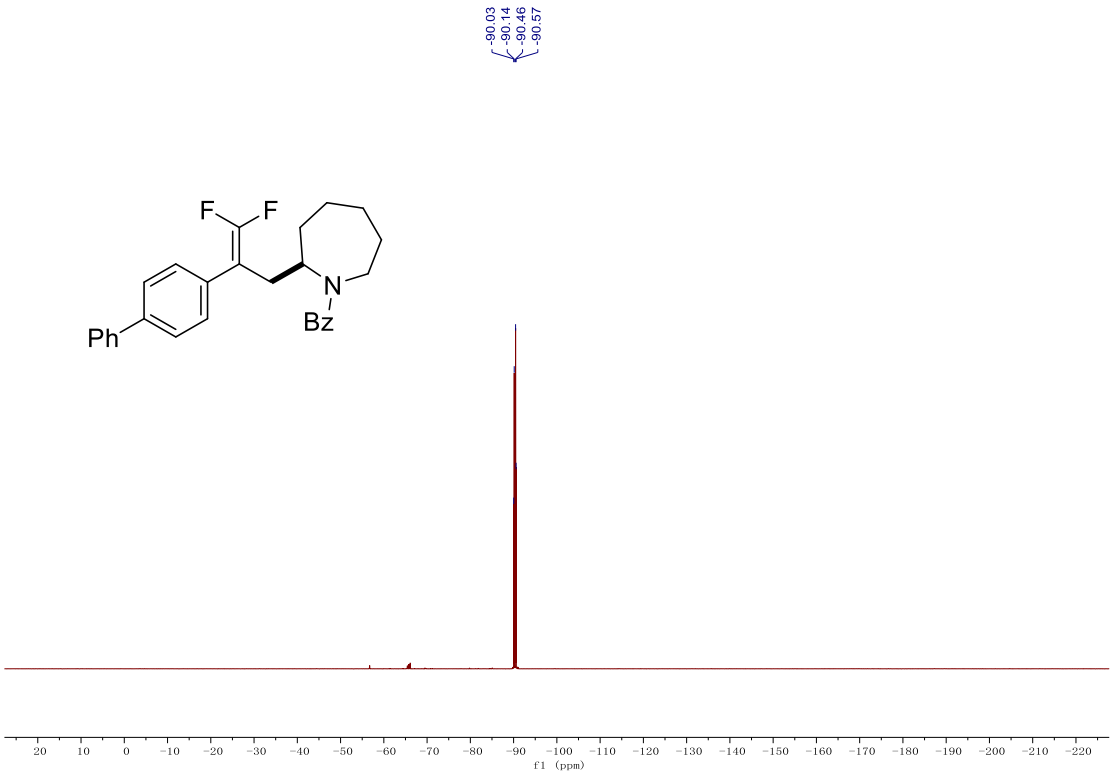
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **56c**



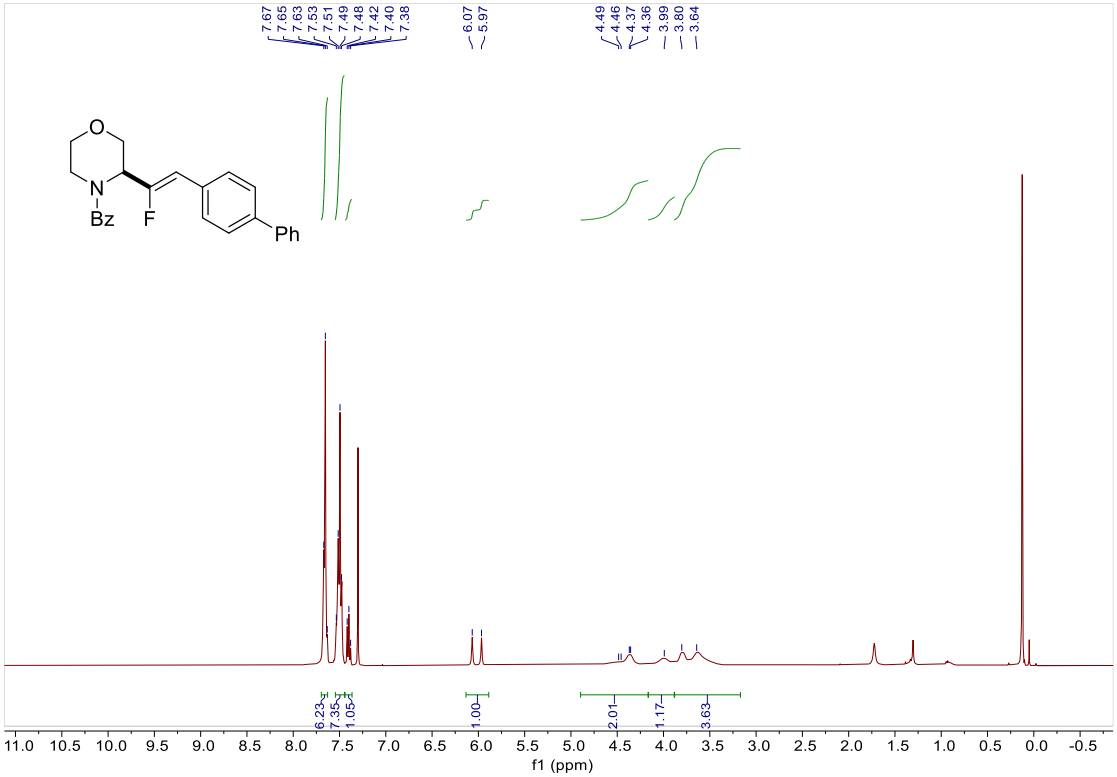
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **56c**



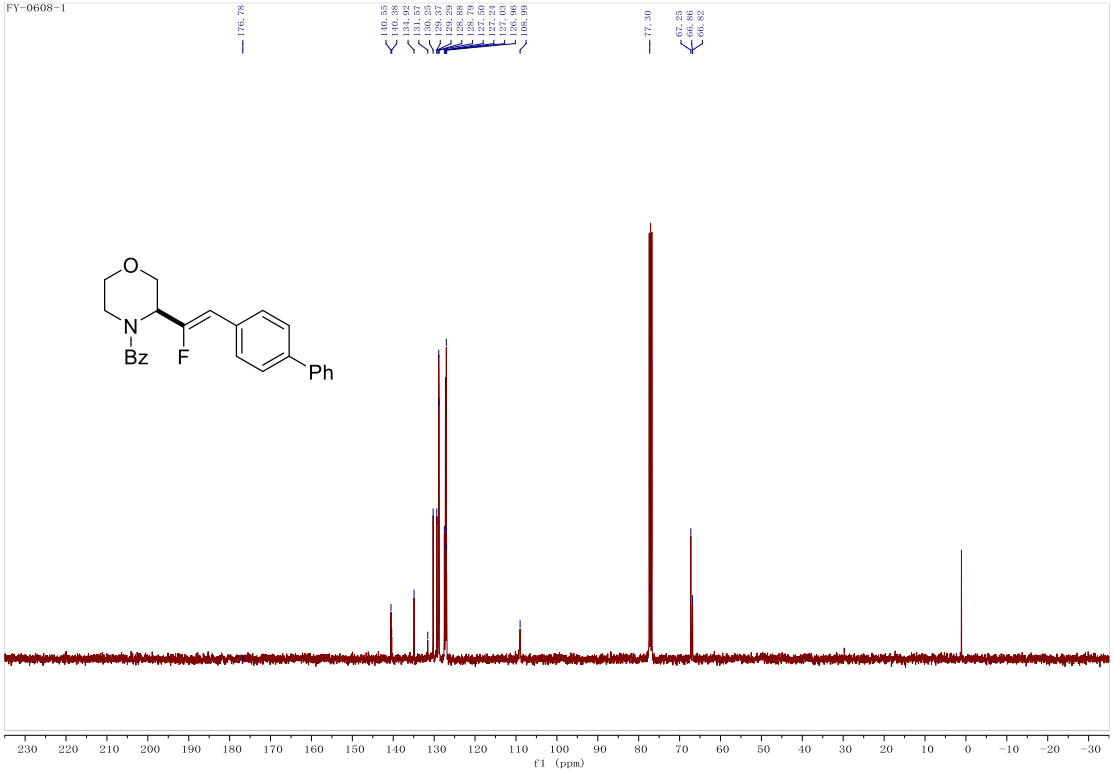
^{19}F NMR spectrum (376 MHz, $CDCl_3$, 23 ºC) of **56c**



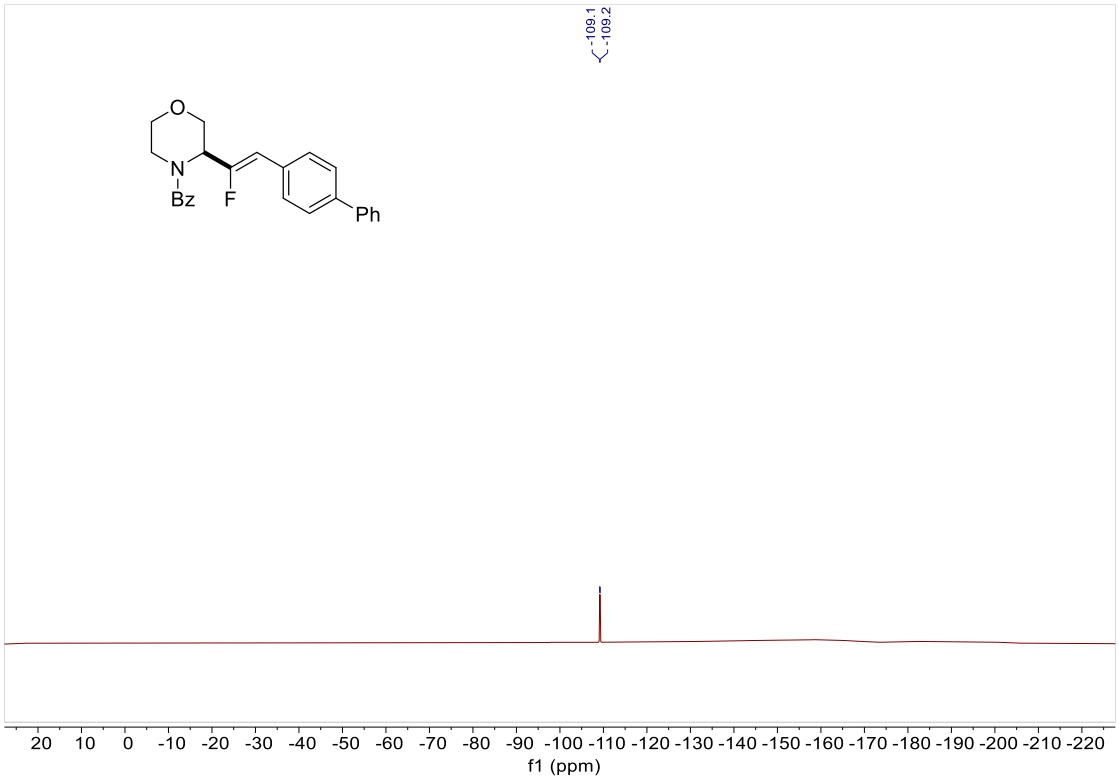
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **57c**



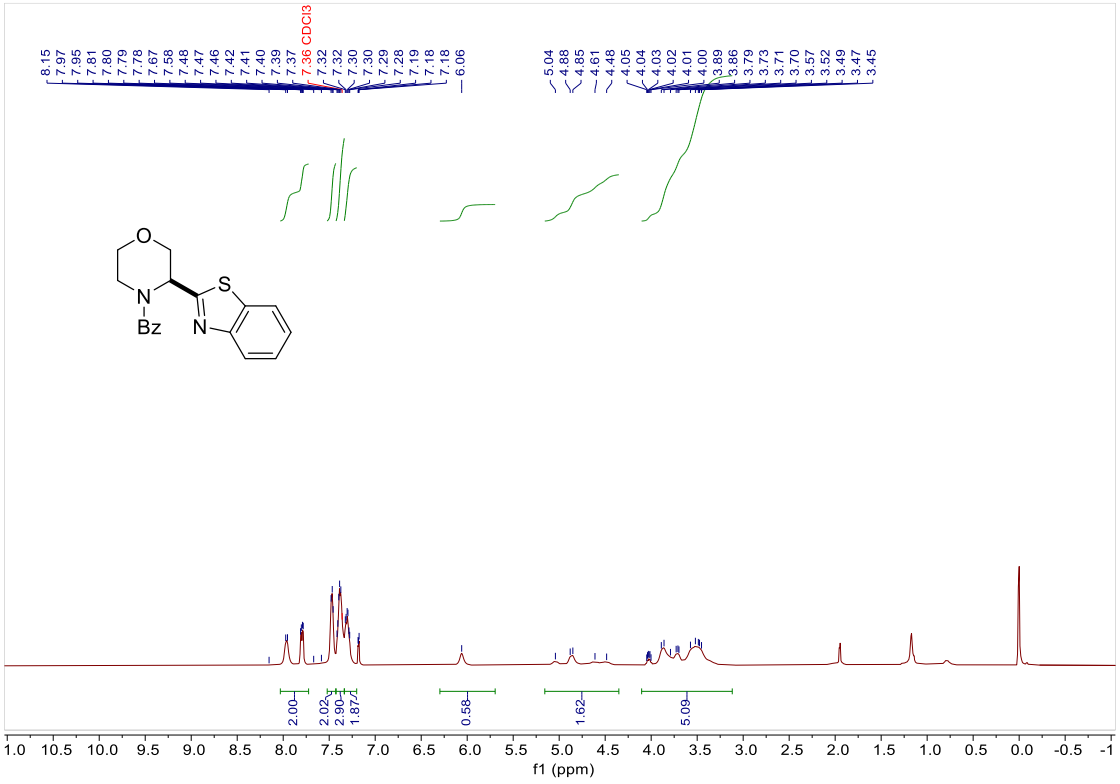
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **57c**



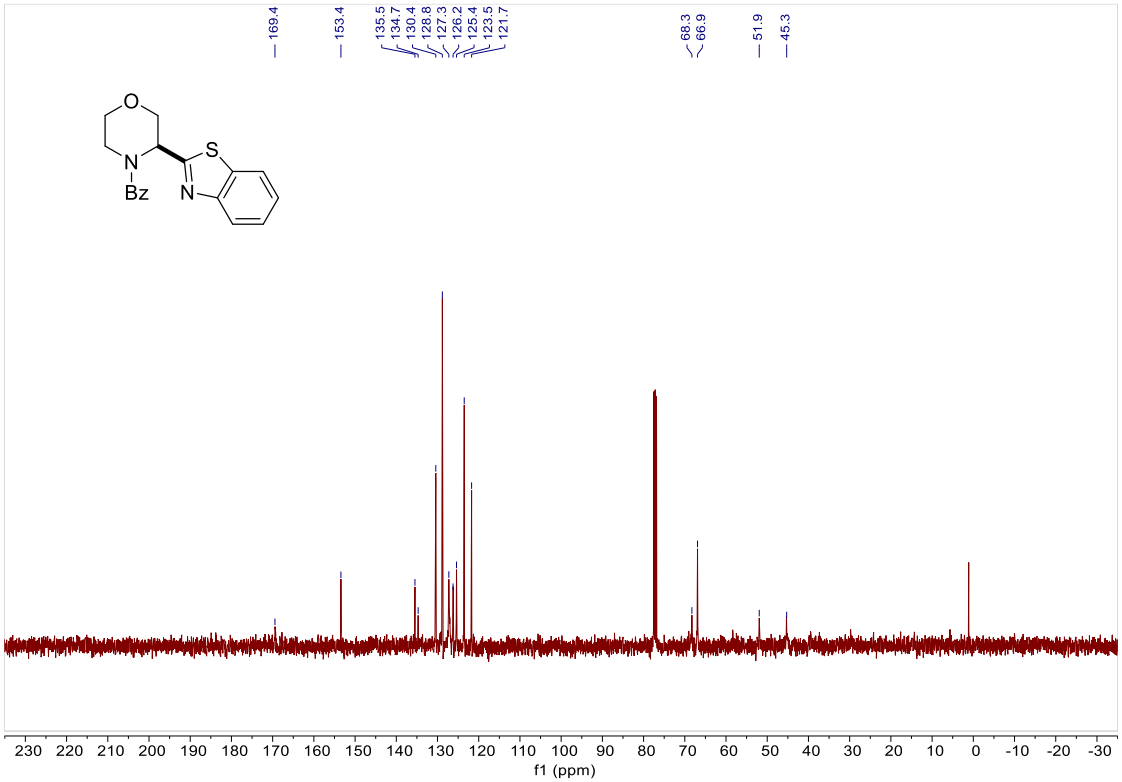
^{19}F NMR spectrum (376 MHz, $CDCl_3$, 23 ºC) of **57c**



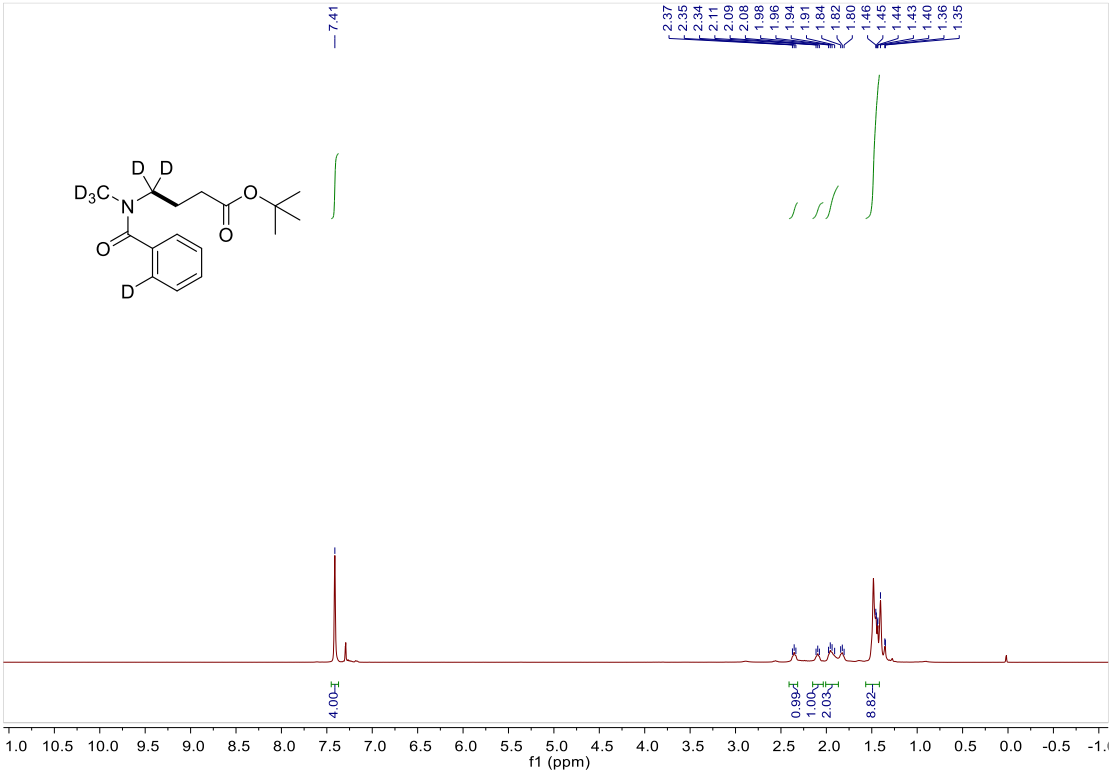
^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **58c**



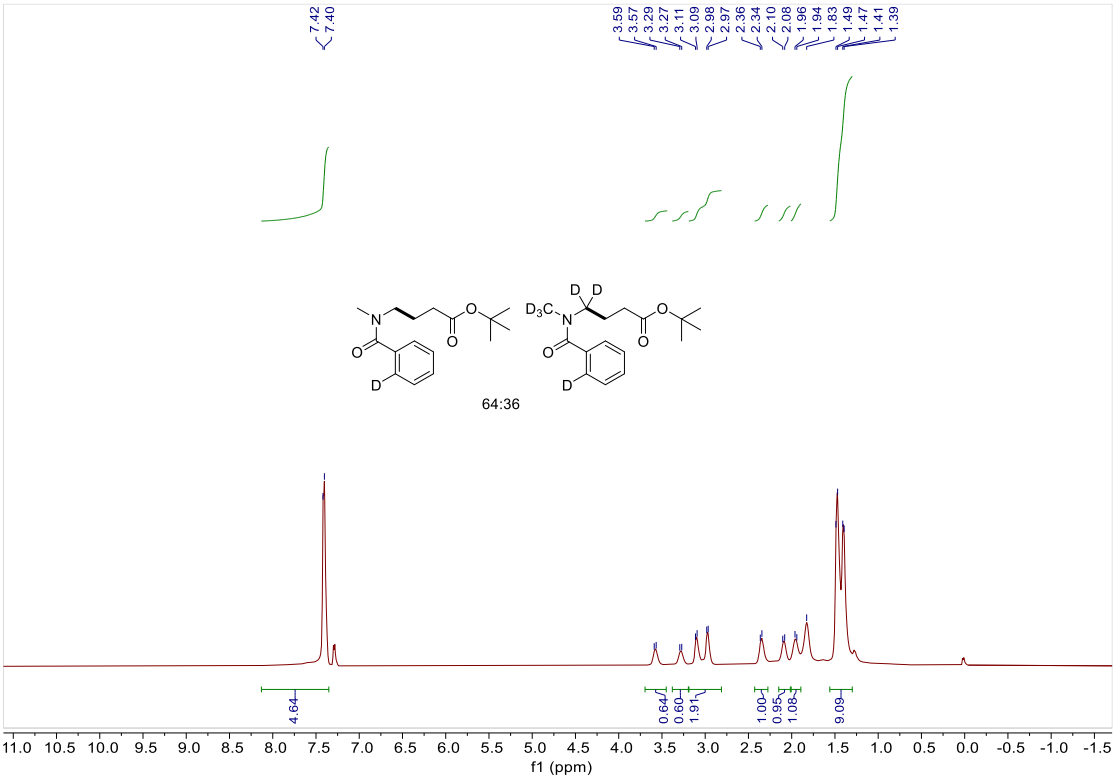
^{13}C NMR spectrum (101 MHz, $CDCl_3$, 23 ºC) of **58c**



^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **d-37c**



^{1}H NMR spectrum (400 MHz, $CDCl_3$, 23 ºC) of **KIE value**



9. References

1. Duhamel, T.; Martínez, M. D.; Sideri, I. K.; Muñiz, K. 1,3-Diamine Formation from an Interrupted Hofmann–Löffler Reaction: Iodine Catalyst Turnover through Ritter-Type Amination. *ACS. Catal.* **2019**, *9*, 7741–7745

2. Parasram, M.; Chuentragool, P.; Wang, Y.; Shi, Y.; Gevorgyan, V. General, Auxiliary-Enabled Photoinduced Pd-Catalyzed Remote Desaturation of Aliphatic Alcohols. *J. Am. Chem. Soc.* **2017**, *139*, 14857–14860

3. Bychek, R. M.; Hutskalova, V.; Bas, Y. P.; Zaporozhets, O. A.; Zozulya, S.; Levterov, V. V.; Mykhailiuk, P. K. Difluoro-Substituted Bicyclo[1.1.1]pentanes for Medicinal Chemistry: Design, Synthesis, and Characterization. *J. Org. Chem.* **2019**, *84*, 15106–15117

4. Nambo, M.; Ghosh, K.; Yim, J. C. H.; Tahara, Y.; Inai, N.; Yanai, T.; Crudden, C. M., Desulfonylative Coupling of Alkylsulfones with gem-Difluoroalkenes by Visible-Light Photoredox Catalysis. *ACS. Catal.* **2022**, *12*, 9526-9532.