Supporting Information

Zn-ProPhenol Catalyzed Enantioselective Mannich Reaction of 2*H*-Azirines with Alkynyl Ketones

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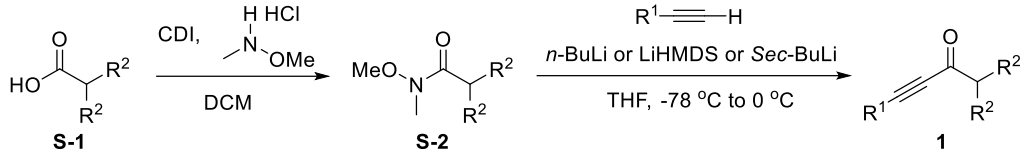
A. General Information

Unless otherwise noted, all reagents were purchased commercially and used as received. Anhydrous tetrahydrofuran (THF) was obtained by distillation from sodium/benzophenone and anhydrous toluene (PhMe) was obtained by distillation from sodium. Anhydrous dichloromethane (CH_2Cl_2) and diethyl ether (Et_2O) were purchased as such from Acros Organics in AcroSeal bottles and were used as received. When performing air-sensitive reactions, reagents and solvents were transferred using either stainless steel cannulae or plastic syringes equipped with stainless steel needles. Air-sensitive reactions were performed under a positive pressure of either nitrogen (N_2) or argon (Ar) in reaction vessels sealed with rubber septa. Analytical thin-layer chromatography (TLC) was performed on glass-backed silica-coated plates (Merck TLC Silica gel 60 F254). Visualization was typically performed using UV light and/or basic potassium permanganate ($KMnO_4$). Purification by flash column chromatography was performed on silica gel (Fisher Scientific, 230–400 mesh, grade 60) using bulk solvents. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 400 MHz using a Varian Mercury 400 spectrometer. All ^{1}H chemical shifts are reported in ppm relative to tetramethylsilane (0.00 ppm) or the residual solvent peak (7.264 ppm for $CDCl_3$). Multiplets were assigned with the assistance of the multiplet tool in Mestrenova, and are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad, app. = apparent. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 101 MHz using a Varian Mercury 400 spectrometer. All ^{13}C chemical shifts are reported in ppm relative to the center of the residual solvent peak (77.16 ppm for $CDCl_3$). Infrared (IR) spectra were recorded on NaCl plates using a Perkin Elmer Paragon 500 FT-IR spectrometer. Enantiomeric excess (ee) were determined by high performance liquid chromatography (HPLC) using an Agilent 1200 series HPLC system using the specified separation conditions. Optical rotations were measured on a Jasco DIP-1000 digital polarimeter using 5 cm glass cells with a Na 589 nm filter. High resolution mass spectrometry (HRMS) was performed at University of Illinois at Urbana-Champaign on a high-resolution mass spectrometer (TOF). Crystal structure determination was performed at University of Notre Dame on a Bruker APEX-II diffractometer using a combination of ω- and φ-scans of 0.5°. For reactions that require heating, all the report reaction temperature are oil bath temperature.

B. General Procedure for the Synthesis of Alkynyl Ketones



Method A: To a flame-dried flask (propane torch for 5 seconds under vacuum) was charged with *N*,*N*-carbonyldiimidazole (1.0 eq.), sealed with a septum, and evacuated and backfilled with argon (balloon) three times. Anhydrous CH_2Cl_2 (total 0.5 M) was added and the resulting suspension was cooled to 0 °C before carboxylic acid **S-1** (1.0 eq.) in CH_2Cl_2 was added dropwise via a syringe, leading to CO_2 evolution. After 30 min, *N*,*O*-dimethylhydroxylamine hydrochloride (2.5 eq.) was quickly added. The reaction was resealed, allowed to warm to room temperature as the ice bath expired, and stirred overnight. After partitioning between CH_2Cl_2 and water, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were washed with 0.1 M H_2SO_4 and saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and concentrated in vacuo to give **S-2**, which was used without purification.

To a flame-dried vial under Argon was charged with alkyne (1.2 equiv) and THF (total 0.4 M). The resulting solution was cooled to -78 ^oC, then *n*-BuLi (2.5 M in hexane, 1.1 equiv) or LiHMDS (1.0 M in THF, 1.1 equiv) or *Sec*-BuLi (1.4 M in hexane, 1.1 equiv) was added dropwise via a syringe. After stirring for 20 minutes at -78 ^oC, the cooling bath was removed, and the reaction was stirred for an additional 10 minutes before it was added dropwise via a syringe to a solution of **S-2** (1.0 equiv) in freshly distilled THF at -78 ^oC. After stirring for 25 minutes at -78 ^oC, the reaction was transferred to a 0 ^oC bath and stirred for 1 hour, at which point it was diluted with Et_2O and poured into aqueous HCl (0.5 M) solution or a buffer (at PH=5) solution with vigorously stirring. After the layers were separated, the aqueous layer was extracted with Et_2O, and the combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give the crude product, which was purified by silica gel column chromatography (petroleum ether/ethyl acetate) to afford alkynyl ketones **1**.

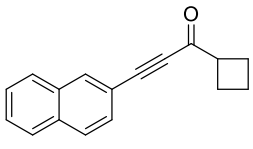
Method B: To a flame-dried flask (propane torch for 5 seconds under vacuum) was charged with *N*,*N*-carbonyldiimidazole (1.1 eq.), sealed with a septum, and evacuated and backfilled with argon (balloon) three times. Anhydrous CH_2Cl_2 (total 0.5 M) was added and the resulting suspension was

cooled to 0 °C before carboxylic acid **S-1** (1.1 eq.) in CH_2Cl_2 was added dropwise via a syringe, leading to CO_2 evolution. After 30 min, *N*,*O*-dimethylhydroxylamine hydrochloride (2.75 eq.) was quickly added. The reaction was resealed, allowed to warm to room temperature as the ice bath expired, and stirred overnight. After partitioning between CH_2Cl_2 and water, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were washed with 0.1 M H_2SO_4 and saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and concentrated in vacuo to give **S-2**, which was used without purification.

To a flame-dried vial under Argon was charged with alkyne (1.0 equiv) and THF (total 0.4 M). The resulting solution was cooled to -78 ^oC, then *n*-BuLi (2.5 M in hexane, 1.1 equiv) or LiHMDS (1.0 M in THF, 1.1 equiv) or *Sec*-BuLi (1.4 M in hexane, 1.1 equiv) was added dropwise via a syringe. After stirring for 20 minutes at -78 ^oC, the cooling bath was removed, and the reaction was stirred for an additional 10 minutes before it was added dropwise via a syringe to a solution of **S-2** (1.1 equiv) in freshly distilled THF at -78 ^oC. After stirring for 25 minutes at -78 ^oC, the reaction was transferred to a 0 ^oC bath and stirred for 1 hour, at which point it was diluted with Et_2O and poured into aqueous HCl (0.5 M) solution or a buffer (at PH=5) solution with vigorously stirring. After the layers were separated, the aqueous layer was extracted with Et_2O, and the combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give the crude product, which was purified by silica gel column chromatography (petroleum ether/ethyl acetate) to afford alkynyl ketones **1**.

For compounds **1a**, **1j**, and **1q**, all these alkynyl ketones were known compounds.[1-3] Some new alkynyl ketones were shown below.

1-Cyclobutyl-3-Phenylprop-2-yn-1-One (1b)



1b

The reaction was performed according **method B**: with cyclobutylcarboxylic acid (550 mg, 5.5 mmol, 1.1 eq.), 2-ethynylnaphthalene (726 mg, 5 mmol, 1 eq.), *n*-BuLi (5.5 mmol, 1.1 eq.), and poured into a mixture of 0.5 M HCl (10 mL) and Et_2O (20 mL). The crude mixture was subjected

to flash silica column chromatography (petroleum ether/EtOAc 30:1) to yield the title compound (**1b**, 737.1 mg, 63%) as light yellow solid.

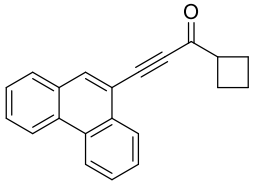
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (s, 1H), 7.80–7.83 (m, 3H), 7.52–7.56 (m, 3H), 3.42–3.51 (m, 1H), 2.41–2.51 (m, 2H), 2.27–2.34 (m, 2H), 1.90–2.10 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 190.0, 134.5, 134.1, 132.9, 128.7, 128.4, 128.2, 128.1, 127.2, 117.5, 92.6, 87.2, 47.9, 25.0, 18.2.

IR (cm^{-1}): 3058, 2943, 2193, 1600, 1347, 1266.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{17}H_{15}O$, 235.1123; found, 235.1123.

1-Cyclobutyl-3-(Phenanthren-9-yl)prop-2-yn-1-One (1c)



1c

The reaction was performed according **method B**: with cyclobutylcarboxylic acid (330 mg, 3.3 mmol, 1.1 eq.), 9-ethynylphenanthrene (660 mg, 3.0 mmol, 1.0 eq.), *n*-BuLi (3.3 mmol, 1.1 eq.), and poured into a mixture of 0.5 M HCl (10 mL) and Et_2O (20 mL). The crude mixture was subjected to flash silica column chromatography (petroleum ether/EtOAc 30:1) to yield the title compound (**1c**, 682.6 mg, 80%) as light yellow solid.

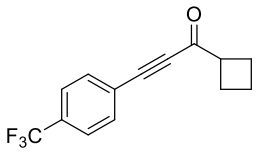
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58–8.64 (m, 2H), 8.37–8.38 (m, 1H), 8.12 (s, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.67–7.70 (m, 3H), 7.58–7.61 (m, 1H), 3.53–3.61 (m, 1H), 2.50–2.60 (m, 2H), 2.34–2.42 (m, 2H), 1.95–2.16 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 189.8, 135.8, 131.4, 130.8, 130.2, 129.3, 129.0, 127.7 127.7, 127.4, 126.7, 123.1, 122.9, 116.8, 91.3, 90.6, 48.0, 25.1, 18.2.

IR (cm^{-1}): 3060, 2984, 2864, 2187, 1661, 1450, 1336, 1238.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{17}O$, 285.1279; found, 285.1277.

1-Cyclobutyl-3-(4-(Trifluoromethyl)phenyl)prop-2-yn-1-One (1d)



1d

The reaction was performed according **method B**: with cyclobutylcarboxylic acid (330 mg, 3.3 mmol, 1.1 eq.), 1-ethynyl-4-(trifluoromethyl)benzene (510 mg, 3.0 mmol, 1.0 eq.), *n*-BuLi (3.3 mmol, 1.1 eq.), and poured into a mixture of 0.5 M HCl (10 mL) and Et_2O (20 mL). The crude mixture was subjected to flash silica column chromatography (petroleum ether/EtOAc 30:1) to yield the title compound (**1d**, 537.0 mg, 71%) as light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60–7.66 (m, 4H), 3.38–3.47 (m, 1H), 2.35–2.45 (m, 2H), 2.22–2.30 (m, 2H), 1.88–2.08 (m, 2H).

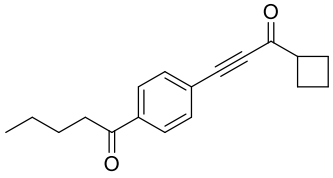
^{13}C NMR (101 MHz, $CDCl_3$): δ 189.4, 133.3, 132.2 (q, $^2J_{F\text{-}C}$ = 32.8 Hz), 125.7 (q, $^3J_{F\text{-}C}$ = 3.6 Hz), 124.2, 123.7 (q, $^1J_{F\text{-}C}$ = 270.8 Hz), 89.3, 88.1, 47.8, 24.8, 18.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ -63.6 (s, 3F).

IR (cm^{-1}): 2948, 2869, 2206, 1670, 1324, 1258, 1170, 1130.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{14}H_{12}F_3O$, 253.0840; found, 253.0842.

1-(4-(3-Cyclobutyl-3-Oxoprop-1-yn-1-yl)phenyl)pentan-1-One (1e)



1e

The reaction was performed according **method A**: with cyclobutylcarboxylic acid (500 mg, 5.0 mmol, 1 eq.), 4-ethynylbenzonitrile (762 mg, 6.0 mmol, 1.2 eq.), *n*-BuLi (5.5 mmol, 1.1 eq.), and poured into a mixture of 0.5 M HCl (10 mL) and Et_2O (20 mL). The crude mixture was subjected to flash silica column chromatography (petroleum ether/EtOAc 20:1) to yield the title compound (**1e**, 495.3 mg, 37%) as white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.0 Hz, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 3.39–3.47 (m, 1H), 2.95 (t, *J* = 7.6 Hz, 2H), 2.36–2.45 (m, 2H), 2.22–2.30 (m, 2H), 1.87–2.09 (m, 2H), 1.66–1.74 (m, 2H), 1.35–1.44 (m, 2H), 0.94 (t, *J* = 7.6 Hz, 3H).

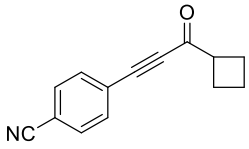
^{13}C NMR (101 MHz, $CDCl_3$): δ 199.7, 189.6, 138.2, 133.2, 128.3, 124.7, 90.2, 88.7, 47.8, 38.7,

26.5, 24.8, 22.6, 18.1, 14.1.

IR (cm^{-1}): 2956, 2867, 2204, 1665, 1404, 1206.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{21}O_2$, 269.1542; found, 269.1541.

4-(3-Cyclobutyl-3-Oxoprop-1-yn-1-yl)benzonitrile (1f)



1f

The reaction was performed according **method B**: with cyclobutylcarboxylic acid (550 mg, 5.5 mmol, 1.1 eq.), 4-ethynylbenzonitrile (635 mg, 5.0 mmol, 1.0 eq.), LiHMDS (1.0 M in THF, 5.5 mmol, 1.1 eq.), and poured into a mixture of 0.5 M HCl (10 mL) and Et_2O (20 mL). The crude mixture was subjected to flash silica column chromatography (petroleum ether/EtOAc 10:1) to yield the title compound (**1f**, 763.0 mg, 73%) as white solid.

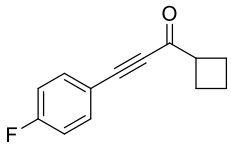
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62–7.67 (m, 4H), 3.38–3.46 (m, 1H), 2.33–2.43 (m, 2H), 2.22–2.30 (m, 2H), 1.85–2.08 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 189.2, 133.5, 132.4, 125.1, 118.1, 114.1, 89.5, 88.6, 47.8, 24.8, 18.1.

IR (cm^{-1}): 2988, 2952, 2227, 2204, 1661, 1499, 1404, 1264, 1123.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{14}H_{12}NO$, 210.0919; found, 210.0921.

1-Cyclobutyl-3-(4-Fluorophenyl)prop-2-yn-1-One (1g)



1g

The reaction was performed according **method B**: with cyclobutylcarboxylic acid (165 mg, 1.65 mmol, 1.1 eq.), 1-ethynyl-4-fluorobenzene (180 mg, 1.5 mmol, 1.0 eq.), *n*-BuLi (1.65 mmol, 1.1 eq.), and poured into a mixture of 0.5 M HCl (10 mL) and Et_2O (20 mL). The crude mixture was subjected to flash silica column chromatography (petroleum ether/EtOAc 30:1) to yield the title compound (**1g**, 227.3 mg, 75%) as light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51–7.54 (m, 2H), 7.01–7.06 (m, 2H), 3.33–3.42 (m, 1H), 2.32–

2.41 (m, 2H), 2.18–2.27 (m, 2H), 1.82–2.05 (m, 2H).

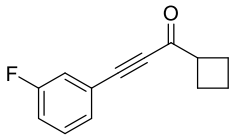
^{13}C NMR (101 MHz, $CDCl_3$): δ 189.7, 164.1 (d, $^1J_{F-C}$ = 241.9 Hz), 135.5 (d, $^3J_{F-C}$ = 8.8 Hz), 116.4, 116.3 (d, $^2J_{F-C}$ = 22.2 Hz), 90.0, 86.8, 47.7, 24.8, 18.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ -106.8 – -106.8 (m, 1F).

IR (cm^{-1}): 2985, 2946, 2866, 2201, 1664, 1505, 1233

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{13}H_{12}FO$, 203.0872; found, 203.0872.

1-Cyclobutyl-3-(3-Fluorophenyl)prop-2-yn-1-One (1h)



1h

The reaction was performed according **method A**: with cyclobutylcarboxylic acid (500 mg, 5.0 mmol, 1 eq.), 1-ethynyl-3-fluorobenzene (762 mg, 6.0 mmol, 1.2 eq.), *n*-BuLi (5.5 mmol, 1.1 eq.), and poured into a mixture of 0.5 M HCl (10 mL) and Et_2O (20 mL). The crude mixture was subjected to flash silica column chromatography (petroleum ether/EtOAc 20:1) to yield the title compound (**1e**, 717.0 mg, 71%) as light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.33 (m, 2H), 7.19–7.22 (m, 1H), 7.09–7.14 (m, 1H), 3.34–3.43 (m, 1H), 2.31–2.41 (m, 2H), 2.19–2.27 (m, 2H), 1.82–2.05 (m, 2H).

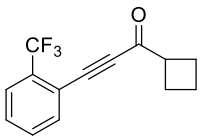
^{13}C NMR (101 MHz, $CDCl_3$): δ 189.5, 162.4 (d, $^1J_{F-C}$ = 246.5 Hz), 130.6 (d, $^3J_{F-C}$ = 8.4 Hz), 129.1 (d, $^4J_{F-C}$ = 3.2 Hz), 122.1 (d, $^3J_{F-C}$ = 9.3 Hz), 119.8 (d, $^2J_{F-C}$ = 23.0 Hz), 118.2 (d, $^2J_{F-C}$ = 21.0 Hz), 90.0 (d, $^4J_{F-C}$ = 3.3 Hz), 87.2, 47.8, 24.8, 18.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ -112.2 – -112.2 (m, 1F).

IR (cm^{-1}): 2986, 2946, 2867, 1667, 1607, 1580, 1432, 1341, 1284, 1266.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{13}H_{12}FO$, 203.0872; found, 203.0876.

1-Cyclobutyl-3-(2-(Trifluoromethyl)phenyl)prop-2-yn-1-One (1i)



1i

The reaction was performed according **method B**: with cyclobutylcarboxylic acid (220 mg, 2.2

mmol, 1.1 eq.), 1-ethynyl-2-(trifluoromethyl)benzene (340 mg, 2.0 mmol, 1.0 eq.), *n*-BuLi (2.2 mmol, 1.1 eq.), and poured into a mixture of 0.5 M HCl (10 mL) and Et_2O (20 mL). The crude mixture was subjected to flash silica column chromatography (petroleum ether/EtOAc 30:1) to yield the title compound (**1i**, 267.1 mg, 53%) as light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68–7.71 (m, 2H), 7.51–7.57 (m, 2H), 3.37–3.46 (m, 1H), 2.36–2.46 (m, 2H), 2.20–2.28 (m, 2H), 1.84–2.08 (m, 2H).

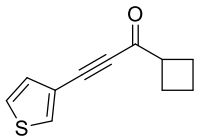
^{13}C NMR (101 MHz, $CDCl_3$): δ 189.5, 135.6, 132.9 (q, $^2J_{F\text{-}C}$ = 29.9 Hz), 131.9, 130.6, 126.3 (q, $^3J_{F\text{-}C}$ = 5.0 Hz), 123.3 (q, $^1J_{F\text{-}C}$ = 271.9 Hz), 118.5, 91.0, 86.8, 47.9, 24.6, 18.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -62.4 (s, 3F).

IR (cm^{-1}): 2988, 2949, 2869, 2206, 1602, 1491

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{14}H_{12}F_3O$, 253.0840; found, 253.0841.

1-Cyclobutyl-3-(Thiophen-3-yl)prop-2-yn-1-One (1k)



1k

The reaction was performed according **method A**: with cyclobutylcarboxylic acid (300 mg, 3.0 mmol, 1 eq.), 3-ethynylthiophene (388.8 mg, 3.6 mmol, 1.2 eq.), *n*-BuLi (3.3 mmol, 1.1 eq.), and poured into a mixture of 0.5 M HCl (10 mL) and Et_2O (20 mL). The crude mixture was subjected to flash silica column chromatography (petroleum ether/EtOAc 20:1) to yield the title compound (**1k**, 359.1 mg, 63%) as light yellow oil.

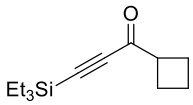
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (dd, *J* = 0.8 Hz, *J* = 1.2 Hz, 1H), 7.31 (dd, *J* = 2.8 Hz, *J* = 2.8 Hz, 1H), 7.20 (dd, *J* = 0.8 Hz, *J* = 1.2 Hz, 1H), 3.34–3.43 (m, 1H), 2.33–2.43 (m, 2H), 2.19–2.28 (m, 2H), 1.83–2.06 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 189.9, 133.9, 130.5, 126.4, 119.6, 87.4, 87.2, 47.7, 24.9, 18.1.

IR (cm^{-1}): 3017, 2984, 2865, 2196, 1660, 1359, 1247.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{11}H_{11}OS$, 191.0531; found, 191.0532.

1-Cyclobutyl-3-(Triethylsilyl)prop-2-yn-1-One (1l)



1l

The reaction was performed according **method A**: with cyclobutylcarboxylic acid (500 mg, 5.0 mmol, 1 eq.), triethyl(ethynyl)silane (840.0 mg, 6.0 mmol, 1.2 eq.), *n*-BuLi (5.5 mmol, 1.1 eq.), and poured into a mixture of 0.5 M HCl (10 mL) and Et_2O (20 mL). The crude mixture was subjected to flash silica column chromatography (petroleum ether/EtOAc 20:1) to yield the title compound (**1l**, 677.0 mg, 61%) as yellow oil.

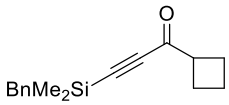
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.24–3.33 (m, 1H), 2.28–2.38 (m, 2H), 2.15–2.23 (m, 2H), 1.81–2.03 (m, 2H), 0.97–1.01 (m, 9H), 0.62–0.67 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 189.7, 102.3, 97.6, 47.7, 24.8, 18.0, 7.5, 4.1.

IR (cm^{-1}): 2957, 2877, 2149, 1672, 1461, 1239.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{13}H_{23}OSi$, 223.1518; found, 223.1516.

3-(Benzyldimethylsilyl)-1-Cyclobutylprop-2-yn-1-One (1m)



1m

The reaction was performed according **method B**: with cyclobutylcarboxylic acid (550 mg, 5.5 mmol, 1.1 eq.), benzyl(ethynyl)dimethylsilane (870 mg, 5.0 mmol, 1.0 eq.), *Sec*-BuLi (5.5 mmol, 1.1 eq.), and poured into a mixture of buffer (PH=5, 10 mL) and Et_2O (20 mL). The crude mixture was subjected to flash silica column chromatography (petroleum ether/EtOAc 30:1) to yield the title compound (**1m**, 474.1 mg, 37%) as light yellow oil.

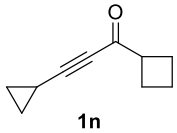
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (t, *J* = 7.6 Hz, 2H), 7.07–7.14 (m, 3H), 3.24–3.34 (m, 1H), 2.28–2.37 (m, 2H), 2.27 (s, 2H), 2.15–2.23 (m, 2H), 1.81–2.05 (m, 2H), 0.21 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 189.5, 138.1, 128.6, 128.6, 125.0, 102.2 97.6, 47.6, 25.6, 24.7, 18.1, -2.4.

IR (cm^{-1}): 3025, 2948, 2151, 1669, 1493, 1337, 1251

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{16}H_{21}OSi$, 257.1362; found, 257.1363.

1-Cyclobutyl-3-Cyclopropylprop-2-yn-1-One (1n)



1n

The reaction was performed according **method A**: with cyclobutylcarboxylic acid (500 mg, 5.0 mmol, 1 eq.), ethynylcyclopropane (396.0 mg, 6.0 mmol, 1.2 eq.), *n*-BuLi (5.5 mmol, 1.1 eq.), and poured into a mixture of 0.5 M HCl (10 mL) and Et_2O (20 mL). The crude mixture was subjected to flash silica column chromatography (petroleum ether/EtOAc 20:1) to yield the title compound (**1n**, 540.0 mg, 73%) as yellow oil.

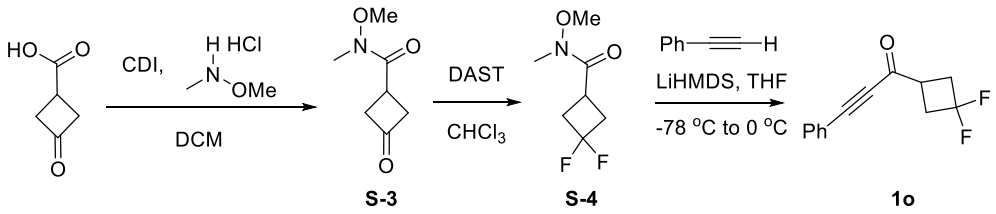
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.19–3.20 (m, 1H), 2.12–2.24 (m, 4H), 1.79–1.91 (m, 2H), 1.35 (s, 1H), 0.85–0.93 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 189.9, 100.1, 75.6, 47.6, 24.8, 18.0, 10.0, -0.1.

IR (cm^{-1}): 2985, 2946, 2867, 2204, 1662, 1360, 1245.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{10}H_{13}O$, 149.0966; found, 149.0966.

1-(3,3-Difluorocyclobutyl)-3-Phenylprop-2-yn-1-One (1o)



To a flame-dried flask (propane torch for 5 seconds under vacuum) was charged with *N*,*N*-carbonyldiimidazole (10 mmol, 1.0 eq.), sealed with a septum, and evacuated and backfilled with argon (balloon) three times. Anhydrous CH_2Cl_2 (16 mL) was added and the resulting suspension was cooled to 0 °C before 3-oxocyclobutane-1-carboxylic acid (1140 mg, 10 mmol, 1.0 eq.) in CH_2Cl_2 (4 mL) was added dropwise via a syringe, leading to CO_2 evolution. After 30 min, *N*,*O*-dimethylhydroxylamine hydrochloride (25 mmol, 2.5 eq.) was quickly added. The reaction was resealed, allowed to warm to room temperature as the ice bath expired, and stirred overnight. After partitioning between CH_2Cl_2 and water, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were washed with 0.1 M H_2SO_4 and saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and concentrated in vacuo to give **S-3** (1.57 g, 10 mmol), which was used without

purification.

To a round-bottom flask equipped with a stirrer bar, **S-3** (1.57 g, 10 mmol), and $CHCl_3$ (70 mL) was added dropwise via a syringe of (diethylamino)sulfur trifluoride (DAST) (3.22 g, 20 mmol). After the addition, the reaction mixture was heated to 40 ^oC and reacted for 72 h. Then, the reaction mixture was cooled down to room temperature, added saturated aq. $NaHCO_3$ (70 mL). The resulting mixture was vigorously stirred for 15 minutes. After partitioning between $CHCl_3$ and water, the aqueous layer was extracted with $CHCl_3$, and the combined organic layers were dried over Na_2SO_4, and concentrated in vacuo to give **S-4** (1.79 g), which was used without purification.

To a flame-dried vial under Argon was charged with ethynylbenzene (1.01 g, 10 mmol) and THF (20 mL). The resulting solution was cooled to -78 ^oC, then LiHMDS (1.0 M in THF, 10 mL, 10 mmol) was added dropwise via a syringe. After stirring for 20 minutes at -78 ^oC, the cooling bath was removed, and the reaction was stirred for an additional 10 minutes before it was added dropwise via a syringe to a solution of **S-4** (1.79 g) in freshly distilled THF (10 mL) at -78 ^oC. After stirring for 25 minutes at -78 ^oC, the reaction was transferred to a 0 ^oC bath and stirred for 1 hour, at which point it was diluted with Et_2O (40 mL) and poured into aqueous HCl (0.5 M, 20 mL) solution with vigorously stirring. After the layers were separated, the aqueous layer was extracted with Et_2O, and the combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give the crude product, which was purified by silica gel column chromatography (petroleum ether/ethyl acetate=30:1) to afford alkynyl ketone **1o** (1.14 g, 52% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56–7.58 (m, 2H), 7.45–7.49 (m, 1H), 7.37–7.40 (m, 2H), 3.19–3.29 (m, 1H), 2.78–3.03 (m, 4H).

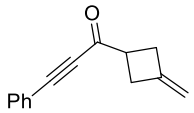
^{13}C NMR (101 MHz, $CDCl_3$): δ 186.3, 133.4, 131.4, 129.0, 119.6, 118.6 (dd, $^1J_{F\text{-}C}$ = 282.7 Hz, $^1J_{F\text{-}C}$ = 282.6 Hz), 93.9, 86.3, 38.3 (t, $^2J_{F\text{-}C}$ = 24.4 Hz), 35.6 (dd, $^3J_{F\text{-}C}$ = 6.0 Hz, $^1J_{F\text{-}C}$ = 6.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ -83.3 – -83.9 (m, 1F), -95.6 – -96.2 (m, 1F).

IR (cm^{-1}): 2961, 2197, 1669, 1489, 1441, 1297, 1163

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{13}H_{11}F_2O$, 221.0778; found, 221.0777.

1-(3-Methylenecyclobutyl)-3-Phenylprop-2-yn-1-One (1p)



1p

The reaction was performed according **method B**: with 3-methylenecyclobutane-1-carboxylic acid (616 mg, 5.5 mmol, 1.1 eq.), ethynylbenzene (505 mg, 5.0 mmol, 1.0 eq.), *n*-BuLi (5.5 mmol, 1.1 eq.), and poured into a mixture of 0.5 M HCl (10 mL) and Et_2O (20 mL). The crude mixture was subjected to flash silica column chromatography (petroleum ether/EtOAc 30:1) to yield the title compound (**1p**, 627.3 mg, 64%) as light yellow oil.

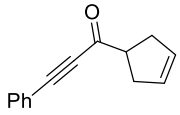
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.57 (m, 2H), 7.42–7.46 (m, 1H), 7.34–7.38 (m, 2H), 4.84–4.86 (m, 2H), 3.35–3.43 (m, 1H), 3.08–3.15 (m, 2H), 2.92–2.99 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 189.0, 143.6, 133.3, 131.0, 128.9, 120.1, 107.6, 92.6, 86.7, 42.7, 35.0.

IR (cm^{-1}): 3074, 2966, 2921 2198, 1665, 1489, 1334, 1260

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{14}H_{13}O$, 197.0966; found, 197.0966.

1-(Cyclopent-3-en-1-yl)-3-Phenylprop-2-yn-1-One (1r)



1r

The reaction was performed according **method B**: with cyclopent-3-ene-1-carboxylic acid (616 mg, 5.5 mmol, 1.1 eq.), ethynylbenzene (505 mg, 5.0 mmol, 1.0 eq.), *n*-BuLi (5.5 mmol, 1.1 eq.), and poured into a mixture of 0.5 M HCl (10 mL) and Et_2O (20 mL). The crude mixture was subjected to flash silica column chromatography (petroleum ether/EtOAc 30:1) to yield the title compound (**1r**, 715.4 mg, 73%) as light yellow oil.

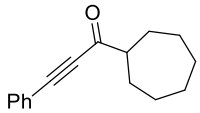
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53–7.56 (m, 2H), 7.41–7.45 (m, 1H), 7.34–7.38 (m, 2H), 5.66–5.70 (m, 2H), 3.37–3.41 (m, 1H), 2.82–2.89 (m, 2H), 2.64–2.71 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 190.0, 133.3, 130.9, 129.1, 128.8, 120.3, 91.8, 87.3, 51.4, 35.5.

IR (cm^{-1}):3059, 2922, 2852, 2201, 1665, 1443, 1286

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{14}H_{13}O$, 197.0966; found, 197.0967.

1-Cycloheptyl-3-Phenylprop-2-yn-1-One (1s)



1s

The reaction was performed according **method B**: with cycloheptanecarboxylic acid (781 mg, 5.5 mmol, 1.1 eq.), ethynylbenzene (505 mg, 5.0 mmol, 1.0 eq.), *n*-BuLi (5.5 mmol, 1.1 eq.), and poured into a mixture of 0.5 M HCl (10 mL) and Et_2O (20 mL). The crude mixture was subjected to flash silica column chromatography (petroleum ether/EtOAc 30:1) to yield the title compound (**1r**, 813.6 mg, 72%) as light yellow oil.

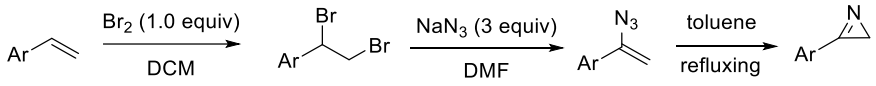
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55–7.57 (m, 2H), 7.41–7.45 (m, 1H), 7.34–7.38 (m, 2H), 2.65–2.71 (m, 1H), 2.03–2.09 (m, 2H), 1.70–1.79 (m, 4H), 1.51–1.61 (m, 6H).

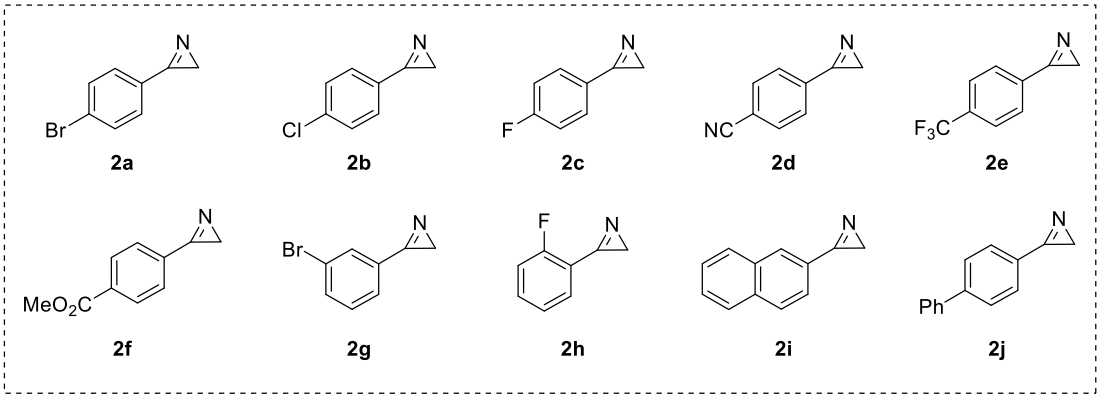
^{13}C NMR (101 MHz, $CDCl_3$): δ 192.0, 133.2 130.8, 128.8, 120.4, 91.3, 87.6, 54.3, 30.0, 28.7, 26.6.

IR (cm^{-1}): 2926, 2856, 2199, 1665, 1489, 1445, 1274

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{16}H_{19}O$, 227.1436; found, 227.1437.

C. General Procedure for the Synthesis of 2*H*-Azirines



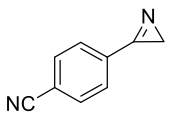


To a solution of alkene (5 mmol) in DCM (10 mL) cooled to 0 °C was added bromine (5 mmol) dropwise. The resulting solution was stirred at room temperature for 5 minutes. Upon completion as indicated by TLC, the reaction was quenched with saturated aqueous Na_2SO_3 and stirred vigorously. The organic phase was separated and the aqueous phase was extracted with DCM (20 mL ×2). The organic extracts were dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give the crude product which was used in next step without further purification.

To a solution of dibromide in DMF (10mL) was added NaN_3 (3.0 equiv). The mixture was stirred overnight at room temperature, then diluted with water and extracted with diethyl ether (20 mL ×3). The combined organic layers were washed for three times with water, and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give the crude product which was used in next step without further purification.

The crude vinyl azide was refluxed in toluene (0.1 M) for 2 hours. The reaction mixture was cooled to room temperature and concentrated under reduced pressure to give the crude product, which was purified by silica gel column chromatography (petroleum ether/ethyl acetate) to afford 2*H*-azirine.

For compounds **2a**-**2c** and **2e**-**2j**, all these 2*H*-azirines were known compounds.[4-7] A new 2*H*-azirine was shown below.



2d

518.6 mg, 73% yield, light yellow solid. Eluting with petroleum ether/EtOAc = 30:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99–8.01 (m, 2H), 7.84–7.86 (m, 2H), 1.87 (s, 2H);

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.9, 133.1, 130.1, 129.6, 118.1, 116.5, 20.9;

IR (cm^{-1}): 3047, 2229, 2098, 1624, 1502

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_9H_7N_2$, 143.0609; found, 143.0610.

D. References

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4) Chen, L.; Li, H.; Li, P.; Wang, L. *Org. Lett.* **2016**, *18*, 3646-3649.

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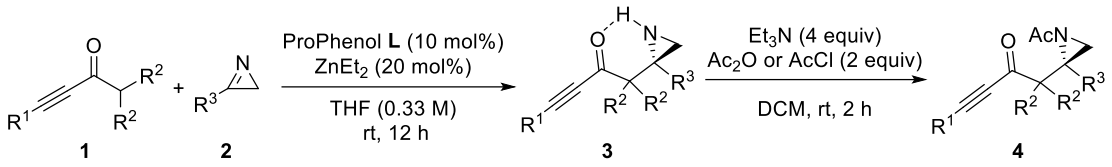
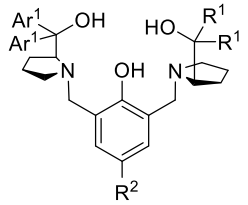
E. General Procedure for the Mannich Reaction of 2*H*-Azirines with Alkynyl Ketones





(*S*, *S*)-ProPhenol

L1, $Ar^1 = R^1$ = Ph, R^2 = Me

L4, Ar^1 = Ph, R^1 = 3,5-$(CF_3)_2$-C_6H_3, R^2 = Me

A 5 mL thick-wall microwave vial was flame-dried (propane torch for 5 seconds under vacuum) with a magnetic stir bar inside. (*S*,*S*)-ProPhenol ligand **L1** or **L4** (10 mol %) was added and the system was placed under an atmosphere of argon (balloon). The ligand was then dissolved in freshly distilled THF (0.1 mL). Et_2Zn (1.0 M in hexane, 20 mol %) was added and the suspension was stirred at room temperature for 30 min. A second flame-dried vial (propane torch for 5 seconds under vacuum) was charged with alkynyl ketone **1** (0.1 mmol) and 2*H*-azirine **2** (0.15 mmol), and the system was placed under an atmosphere of argon (balloon). Freshly distilled THF (0.2 mL) was added and the prepared substrate solution was introduced to the stirred catalyst solution at room temperature. The combined reaction mixture was then sealed and stirred for 12 h at room temperature. Filtration through a plug of Celite and florisil gave the crude reaction mixture, which was concentrated in vacuo and purified by silica gel column chromatography (petroleum ether/ethyl acetate) to give the Mannich adduct **3**.

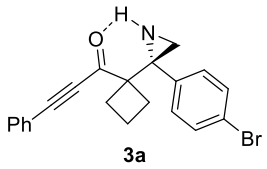
To a 10 mL vial placed with all the obtained Mannich adduct **3** (1 eq.) and a magnetic stir bar was added anhydrous CH_2Cl_2 (1 mL), Et_3N (4 eq.), and Ac_2O or AcCl (2 eq.). The resulting mixture was stirred at room temperature for 2 h. Then mixture was then direct purified by flash silica gel column chromatography (petroleum ether/ethyl acetate) to give the product **4**.

Unless otherwise noted, **L1** was used as the Ligand, Ac_2O was used as the acetylation reagent.

For the racemic products, the same conditions were applied with a 1:1 mixture of the (*S*,*S*)- and (*R*,*R*)-ProPhenol ligands (**L1**) as the catalytic system.

F. Analysis Data for the Obtained Products

(*R*)-1-(1-(2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-Phenylprop-2-yn-1-One (3a)



3a

31.9 mg, 84% yield, 95% ee (determined by acetylation), yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.56 (m, 2H), 7.45–7.49 (m, 1H), 7.36–7.42 (m, 4H), 7.21–7.23 (m, 2H), 2.49–2.55 (m, 1H), 2.17–2.28 (m, 5H), 1.78–1.88 (m, 2H), 1.08 (brs, 1H).

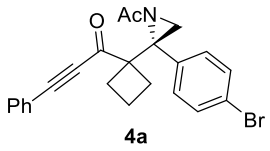
^{13}C NMR (101 MHz, $CDCl_3$): δ 189.3, 139.1, 133.2, 131.7, 131.1, 130.2, 129.0, 122.1, 120.1, 93.4, 87.1, 59.4, 42.9, 30.0, 26.8, 25.9, 15.1.

IR (cm^{-1}): 2946, 2198, 1658, 1488, 1287.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{19}BrNO$, 380.0650; found, 380.0641.

$[\alpha]_D^{25}$: +2.34 (*c* = 1.0, $CHCl_3$)

(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-Phenylprop-2-yn-1-One (4a)



4a

35.0 mg, 83% yield, 95% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.50 (m, 3H), 7.36–7.40 (m, 4H), 7.10–7.13 (m, 2H), 3.13 (s, 1H), 3.01–3.07 (m, 1H), 2.76 (s, 1H), 2.51–2.59 (m, 1H), 2.35–2.43 (m, 1H), 2.07–2.14 (m, 1H), 1.95–2.04 (m, 1H), 1.93 (s, 3H), 1.84–1.92 (m, 1H).

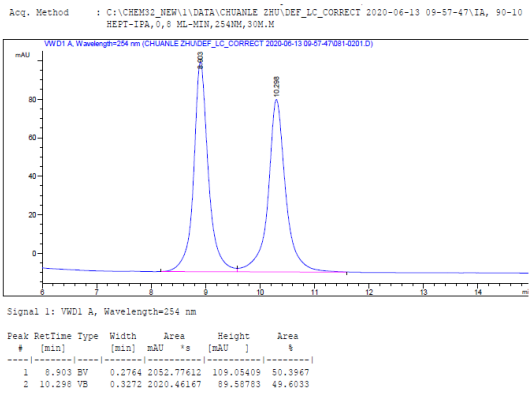
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.7, 179.9, 133.7, 133.1, 132.2, 131.3, 129.7, 129.0, 123.2, 119.8, 93.6, 86.5, 59.4, 50.5, 33.2, 27.8, 27.3, 25.0 15.6.

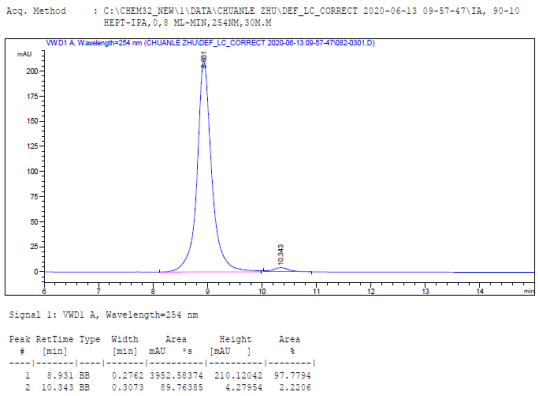
IR (cm^{-1}): 2992, 2942, 2197, 1693, 1662, 1490, 1368, 1258.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{21}BrNO_2$, 422.0756; found, 422.0754.

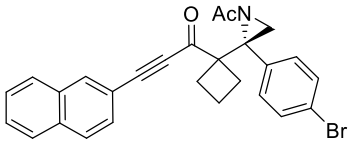
HPLC: 95% ee, (Daicel CHIRALPAK IA, 90:10 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 8.9 min, T_{minor} = 10.3 min)

[α]$_D^{25}$: -42.87 (*c* = 0.5, $CHCl_3$)





(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-(naphthalen-2-yl)prop-2-yn-1-One (4b)



4b

32.0 mg, 68% yield, 98% ee, light yellow oil. **L4** was used as the Ligand. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.82–7.85 (m, 3H), 7.52–7.59 (m, 2H), 7.45–7.48 (m, 1H), 7.39–7.41 (m, 2H), 7.14–7.16 (m, 2H), 3.19 (s, 1H), 3.05–3.12 (m, 1H), 2.84 (s, 1H), 2.54–2.62 (m, 1H), 2.39–2.46 (m, 1H), 2.12–2.18 (m, 1H), 1.89–2.07 (m, 5H).

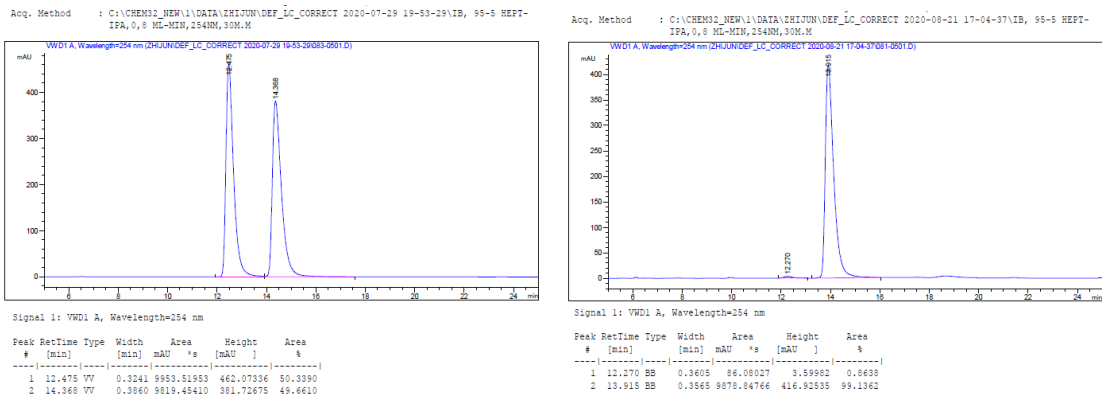
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.7, 180.0, 134.5, 134.2, 133.8, 12.8, 132.2, 129.8, 128.5, 128.4, 128.3, 128.2, 127.5, 123.2, 116.9, 94.2, 86.8, 59.5, 50.5, 33.3, 27.8, 27.4, 25.0, 15.6.

IR (cm^{-1}): 2942, 2194, 1692, 1660, 1368, 1227

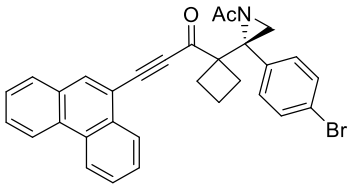
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{27}H_{23}BrNO_2$, 472.0912; found, 472.0919.

HPLC: 95% ee, (Daicel CHIRALPAK IA, 90:10 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 8.9 min, T_{minor} = 10.3 min)

[α]$_D^{25}$: +7.13 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-(Phenanthren-9-yl)prop-2-yn-1-One (4c)



4c

37.6 mg, 72% yield, 95% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62–8.67 (m, 2H), 8.17 (d, *J* = 8.4 Hz, 1H), 8.06 (s, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.61–7.74 (m, 4H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 1H), 3.13–3.20 (m, 2H), 2.89 (s, 1H), 2.60–2.67 (m, 1H), 2.45–2.52 (m, 1H), 2.23–2.28 (m, 1H), 2.04–2.12 (m, 1H), 1.91–1.99 (m, 4H).

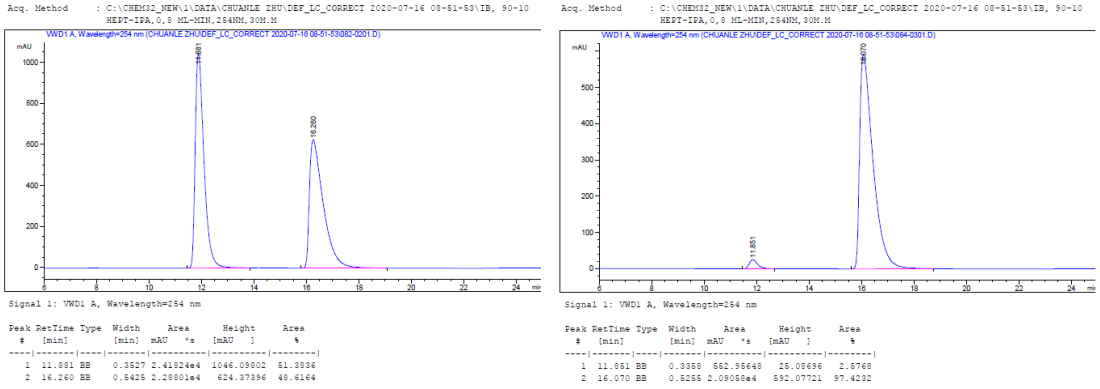
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.8, 180.0, 135.7, 133.8, 132.2, 131.5, 130.7, 130.6, 130.2, 129.8, 129.4, 129.3, 127.9, 127.8, 127.6, 126.5, 123.3, 123.0, 116.4, 92.2, 90.7, 59.5, 50.5, 33.3, 28.0, 27.5, 25.0, 15.7.

IR (cm^{-1}): 2942, 2183, 1691, 1658, 1370, 1233

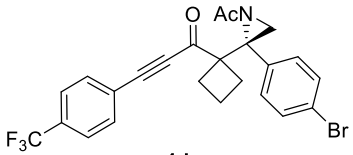
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{31}H_{25}BrNO_2$, 522.1069; found, 522.1069.

HPLC: 95% ee, (Daicel CHIRALPAK IB, 90:10 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 16.0 min, T_{minor} = 11.8 min)

$[\alpha]_D^{25}$: -19.08 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-(4-(Trifluoromethyl)phenyl)prop-2-yn-1-One (4d)



4d

38.8 mg, 79% yield, 96% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63–7.65 (m, 2H), 7.57–7.59 (m, 2H), 7.39–7.41 (m, 2H), 7.10–7.13 (m, 2H), 3.11 (s, 1H), 3.00–3.02 (m, 1H), 2.73 (s, 1H), 2.53–2.60 (m, 1H), 2.35–2.43 (m, 1H), 2.08–2.10 (m, 1H), 1.88–2.03 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 187.6, 179.8, 133.6, 133.3, 132.7 (q, $^{2}J_{F\text{-}C}$ = 32.8 Hz), 132.2, 129.7, 125.9 (q, $^{3}J_{F\text{-}C}$ = 3.6 Hz), 123.7 (q, $^{1}J_{F\text{-}C}$ = 268.1 Hz), 123.6, 123.3, 90.9, 87.6, 59.5, 50.3, 33.0, 27.8, 27.2, 24.9, 15.6.

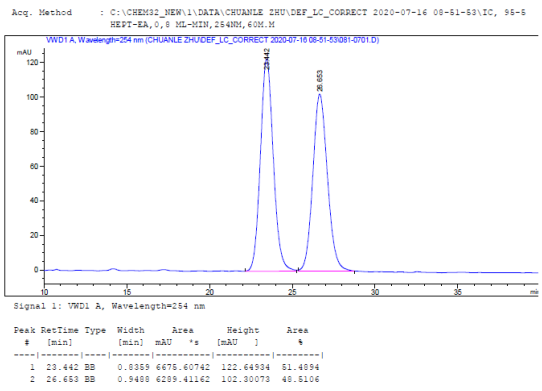
^{19}F NMR (376 MHz, $CDCl_3$): δ -63.6 (s, 3F).

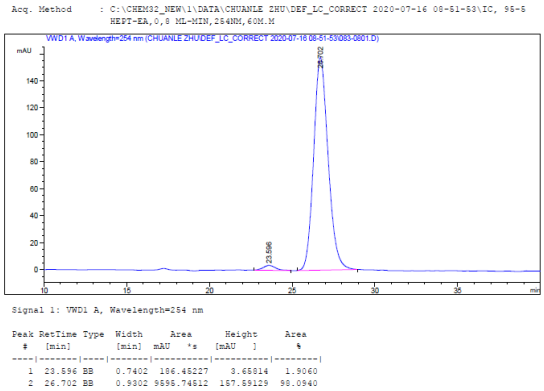
IR (cm^{-1}): 2945, 2203, 1694, 1447, 1323

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{24}H_{20}BrF_3NO_2$, 490.0630; found, 490.0634.

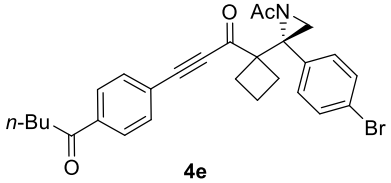
HPLC: 96% ee, (Daicel CHIRALPAK IC, 95:5 heptane/Ethyl Acetate, 0.8 mL/min, λ = 254 nm; T_{major} = 26.7 min, T_{minor} = 23.6 min)

$[\alpha]_D^{25}$: -59.36 (*c* = 1.0, $CHCl_3$)





(*R*)-1-(4-(3-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-oxoprop-1-yn-1-yl)phenyl)pentan-1-One (4e)



4e

32.4 mg, 64% yield, 96% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.0 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.8 Hz, 2H), 2.93–3.11 (m, 4H), 2.73 (s, 1H), 2.52–2.59 (m, 1H), 2.35–2.42 (m, 1H), 1.89–2.12 (m, 6H), 1.70 (hept, *J* = 7.6 Hz, 2H), 1.34–1.44 (m, 2H), 0.93 (t, *J* = 7.2 Hz, 3H).

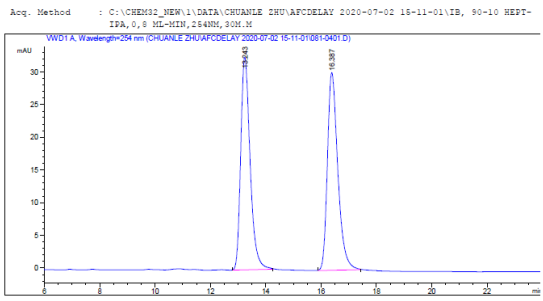
^{13}C NMR (101 MHz, $CDCl_3$): δ 199.6, 187.6, 179.8, 138.5, 133.6, 133.2, 132.2, 129.7, 128.4, 124.0, 123.3, 91.7, 88.2, 59.5, 50.3, 38.7, 33.1, 27.8, 27.2, 26.5, 25.0, 22.6, 15.6, 14.2.

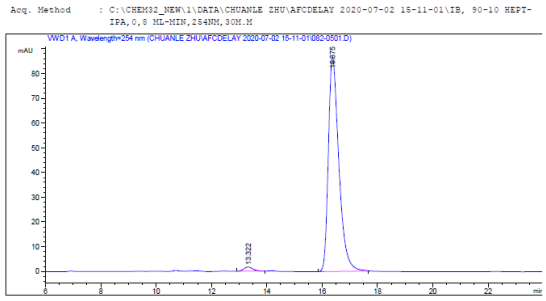
IR (cm^{-1}): 2955, 2199, 1688, 1367.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{28}H_{29}BrNO_3$, 506.1331; found, 506.1339.

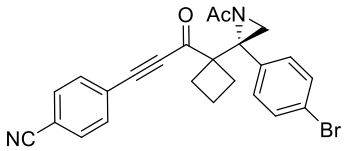
HPLC: 96% ee, (Daicel CHIRALPAK IB, 90:10 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 16.3 min, T_{minor} = 13.3 min)

$[\alpha]_D^{25}$: -12.41 (*c* = 1.0, $CHCl_3$)





(*R*)-4-(3-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-oxoprop-1-yn-1-yl)benzonitrile (4f)



4f

31.7 mg, 71% yield, 86% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66–7.68 (m, 2H), 7.54–7.56 (m, 2H), 7.37–7.40 (m, 2H), 7.08–7.12 (m, 2H), 3.08 (s, 1H), 2.96–3.02 (m, 1H), 2.70 (s, 1H), 2.52–2.60 (m, 1H), 2.34–2.41 (m, 1H), 2.06–2.13 (m, 1H), 1.86–2.00 (m, 5H).

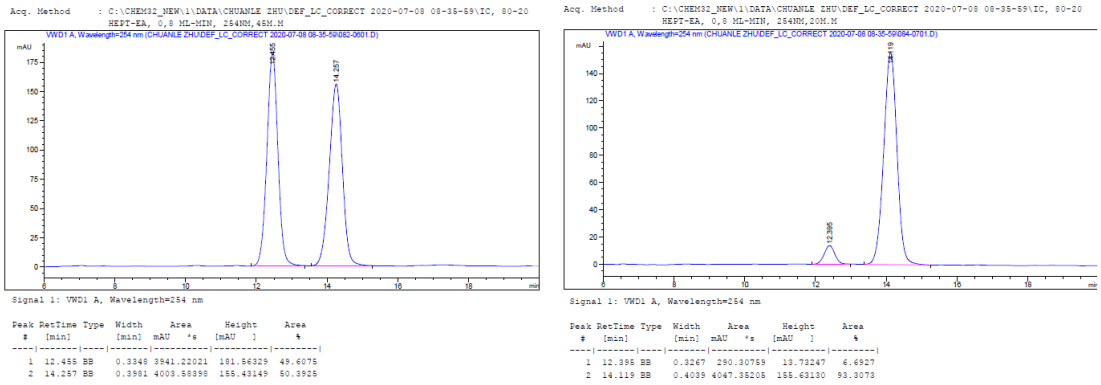
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.5, 179.7, 133.5, 133.4, 132.6, 132.2, 129.8, 124.5, 123.4, 118.0, 114.5, 90.1, 88.9, 59.5, 50.2, 32.9, 27.8, 27.2, 24.9, 15.6.

IR (cm^{-1}): 2945, 2230, 2203, 1667, 1497, 1370.

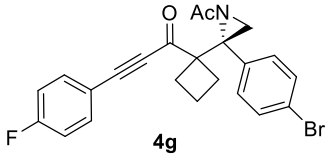
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{24}H_{20}BrN_2O_2$, 447.0708; found, 447.0710.

HPLC: 86% ee, (Daicel CHIRALPAK IC, 80:20 heptane/ethyl acetate, 0.8 mL/min, λ = 254 nm; T_{major} = 14.1 min, T_{minor} = 12.4 min)

$[\alpha]_D^{25}$: -23.98 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-(4-Fluorophenyl)prop-2-yn-1-One (4g)



4g

30.3 mg, 69% yield, 86% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–7.50 (m, 2H), 7.38–7.41 (m, 2H), 7.06–7.12 (m, 4H), 3.11 (s, 1H), 3.00–3.06 (m, 1H), 2.74 (s, 1H), 2.51–2.58 (m, 1H), 2.34–2.42 (m, 1H), 2.06–2.13 (m, 1H), 1.87–2.04 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 187.7, 179.9, 164.3 (d, $^{1}J_{F\text{-}C}$ = 252.9 Hz), 135.5 (d, $^{3}J_{F\text{-}C}$ = 8.9 Hz), 133.7, 132.2, 129.8, 123.2, 116.6 (d, $^{2}J_{F\text{-}C}$ = 22.2 Hz), 115.9 (d, $^{4}J_{F\text{-}C}$ = 3.6 Hz), 92.5, 86.5, 59.3, 50.4, 33.1, 27.8, 27.3, 25.0, 15.6.

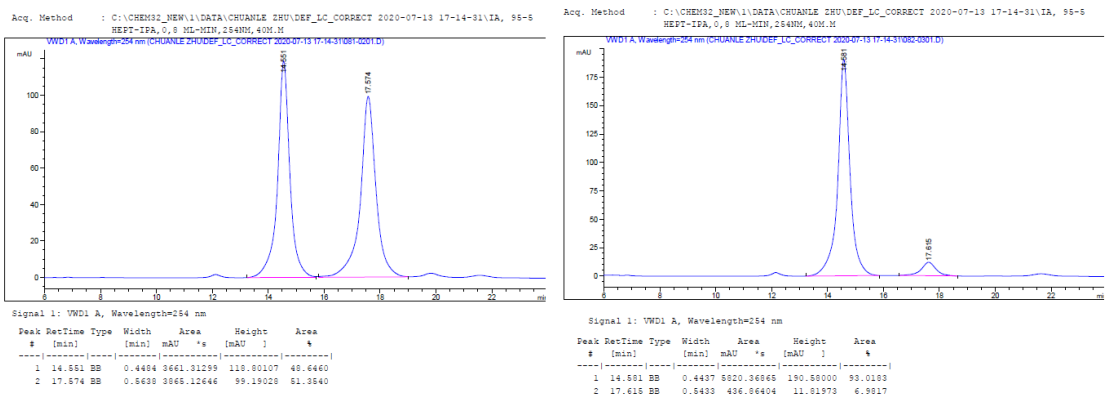
^{19}F NMR (376 MHz, $CDCl_3$): δ -105.7 – -105.8 (m, 1F).

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{20}BrFNO_2$, 440.0661; found, 440.0665.

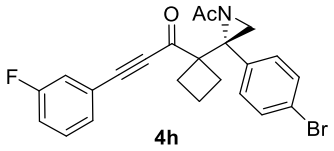
IR (cm^{-1}): 2944, 2199, 1693, 1662, 1505, 1230.

HPLC: 86% ee, (Daicel CHIRALPAK IA, 95:5 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 14.6 min, T_{minor} = 17.6 min)

$[\alpha]_D^{25}$: -34.84 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-(3-Fluorophenyl)prop-2-yn-1-One (4h)



4h

31.3 mg, 71% yield, 83% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.41 (m, 3H), 7.26–7.28 (m, 1H), 7.15–7.20 (m, 2H), 7.10–7.12 (m, 2H), 3.11 (s, 1H), 2.99–3.05 (m, 1H), 2.73 (s, 1H), 2.52–2.59 (m, 1H), 2.35–2.42 (m, 1H), 2.06–2.12 (m, 1H), 1.87–1.99 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 187.6, 179.9, 162.5 (d, $^{1}J_{F\text{-}C}$ = 246.2 Hz), 133.6, 132.2, 130.8 (d, $^{3}J_{F\text{-}C}$ = 8.5 Hz), 129.7, 129.0 (d, $^{4}J_{F\text{-}C}$ = 3.2 Hz), 123.3, 121.5 (d, $^{3}J_{F\text{-}C}$ = 9.0 Hz), 119.7 (d, $^{2}J_{F\text{-}C}$ = 23.1 Hz), 118.7 (d, $^{2}J_{F\text{-}C}$ = 21.1 Hz), 91.5, 86.7, 59.5, 50.3, 33.1, 27.8, 27.2, 25.0, 15.5.

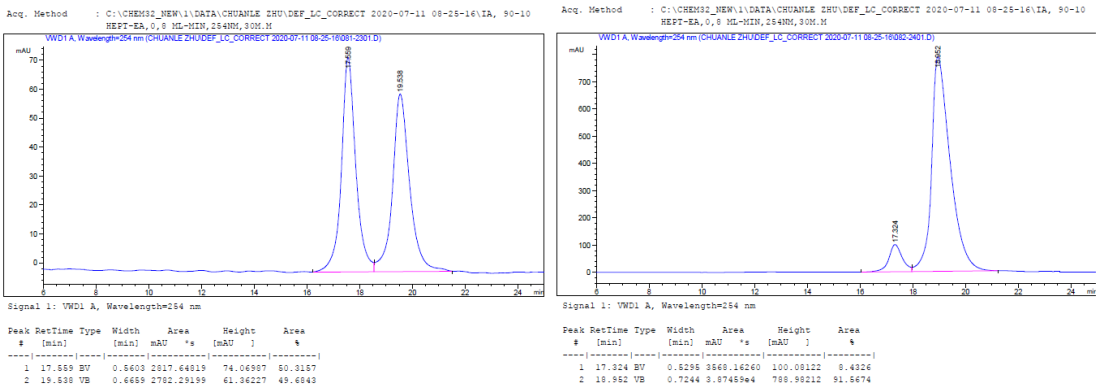
^{19}F NMR (376 MHz, $CDCl_3$): δ -111.6 – -111.6 (m, 1F).

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{20}BrFNO_2$, 440.0661; found, 440.0664.

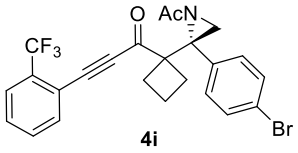
IR (cm^{-1}): 2944, 2197, 1693, 1665, 1484, 1369, 1269.

HPLC: 83% ee, (Daicel CHIRALPAK IA, 90:10 heptane/ethyl acetate, 0.8 mL/min, λ = 254 nm; T_{major} = 18.9 min, T_{minor} = 17.3 min)

$[\alpha]_D^{25}$: -48.42(*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-(2-(Trifluoromethyl)phenyl)prop-2-yn-1-One (4d)



4i

34.4 mg, 70% yield, 91% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67–7.73 (m, 2H), 7.55–7.59 (m, 2H), 7.38–7.40 (m, 2H), 7.12–7.15 (m, 2H), 3.08 (s, 1H), 3.00–3.06 (m, 1H), 2.75 (s, 1H), 2.54–2.61 (m, 1H), 2.34–2.41 (m, 1H), 2.09–2.13 (m, 1H), 1.82–2.00 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 187.4, 179.9, 136.2, 133.5, 132.2 (q, $^{2}J_{F\text{-}C}$ = 31.0 Hz), 132.1, 130.9, 129.9, 126.4 (q, $^{3}J_{F\text{-}C}$ = 5.0 Hz), 123.3 (q, $^{1}J_{F\text{-}C}$ = 270.9 Hz), 123.2, 118.1, 90.6, 87.9, 59.6, 50.2, 32.8, 27.8, 27.0, 24.9, 15.6.

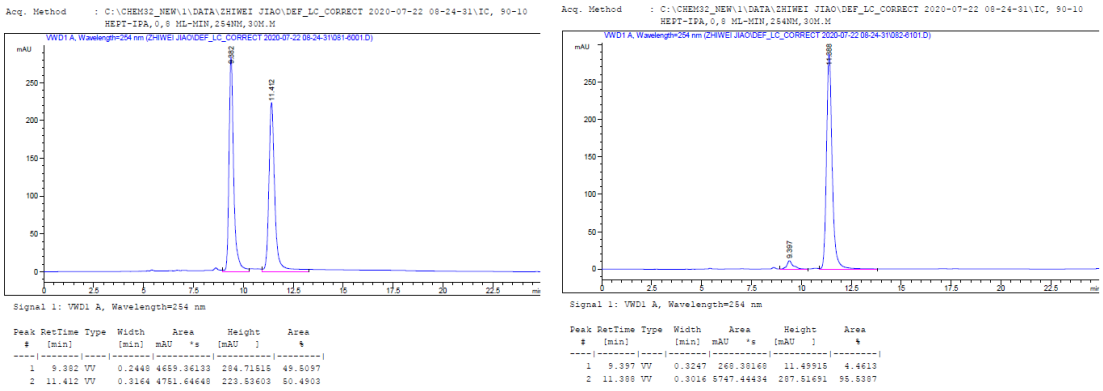
^{19}F NMR (376 MHz, $CDCl_3$): δ -62.0 (s, 3F).

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{24}H_{20}BrF_3NO_2$, 490.0630; found, 490.0639.

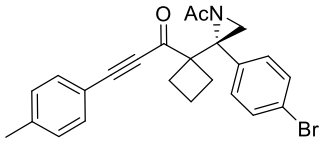
IR (cm^{-1}): 2945, 2203, 1694, 1667, 1492, 1320, 1172.

HPLC: 91% ee, (Daicel CHIRALPAK IA, 90:10 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 11.3 min, T_{minor} = 9.3 min)

$[\alpha]_D^{25}$: -85.17 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-(*p*-Tolyl)prop-2-yn-1-One (4j)



4j

21.0 mg, 48% yield, 90% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.40 (m, 4H), 7.19–7.20 (m, 2H), 7.10–7.12 (m, 2H), 3.14 (s, 1H), 3.02–3.07 (m, 1H), 2.77 (s, 1H), 2.50–2.58 (m, 1H), 2.35–2.42 (m, 4H), 2.07–2.12 (m, 1H), 1.84–2.04 (m, 5H).

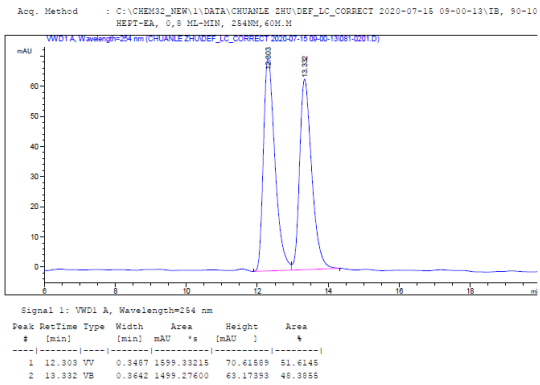
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.8, 180.0, 142.2, 133.8, 133.2, 132.1, 129.8, 129.7, 123.2, 116.7, 94.3, 86.5, 59.4, 50.5, 33.2, 27.8, 27.3, 25.0, 22.0, 15.6.

IR (cm^{-1}): 2943, 2194, 1693, 1659, 1369, 1260.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{24}H_{23}BrNO_2$, 436.0912; found, 436.0916.

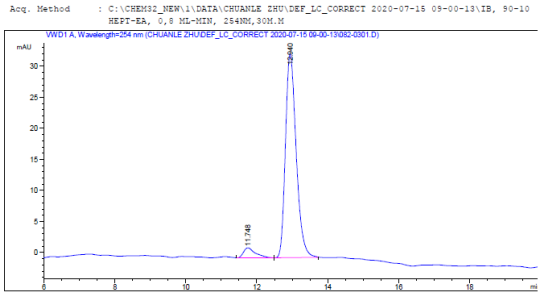
HPLC: 90% ee, (Daicel CHIRALPAK IC, 90:10 heptane/ethyl acetate, 0.8 mL/min, λ = 254 nm; T_{major} = 12.9 min, T_{minor} = 11.7 min)

$[\alpha]_D^{25}$: -47.77 (*c* = 1.0, $CHCl_3$)



Signal 1: VWD1 A, Wavelength=254 nm

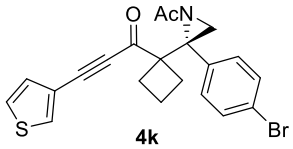
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.303	VV	0.3487	1599.33215	70.61589	51.6145
2	13.332	VB	0.3642	1499.27600	63.17393	48.3855



Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.748	BV	0.3376	37.08505	1.60741	5.1196
2	12.940	VB	0.3230	687.42438	32.81448	94.8814

(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-(Thiophen-3-yl)prop-2-yn-1-One (4k)



4k

34.7 mg, 81% yield, 98% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68–7.69 (m, 1H), 7.33–7.39 (m, 3H), 7.09–7.14 (m, 3H), 3.10 (s, 1H), 2.96–3.02 (m, 1H), 2.74 (s, 1H), 2.49–2.57 (m, 1H), 2.33–2.41 (m, 1H), 2.05–2.11 (m, 1H), 1.85–2.12 (m, 5H).

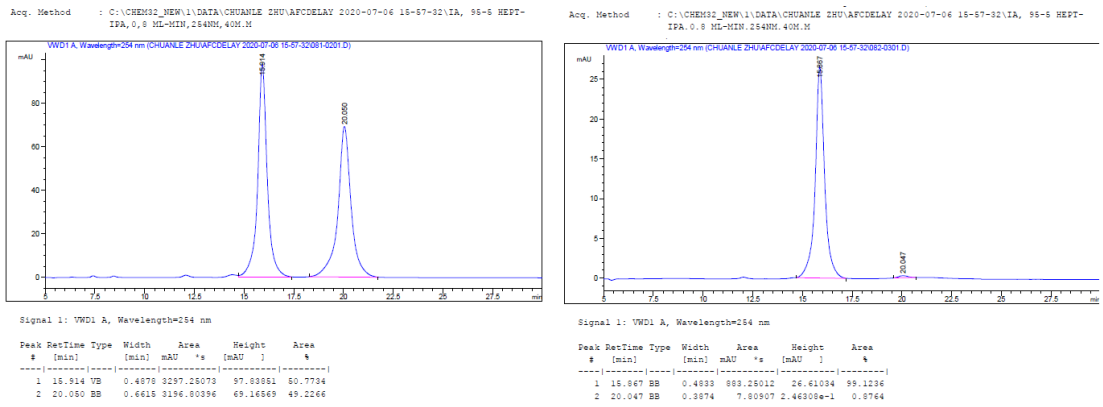
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.7, 179.9, 134.4, 133.7, 132.1, 130.2, 129.7, 126.8, 123.2, 119.1, 89.0, 86.8, 59.3, 50.4, 33.2, 27.7, 27.3, 25.0, 15.6.

IR (cm^{-1}): 2932, 2192, 1658, 1363.

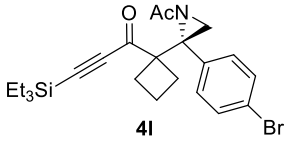
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{19}BrNO_2S$, 428.0320; found, 428.0313.

HPLC: 98% ee, (Daicel CHIRALPAK IA, 95:5 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 15.8 min, T_{minor} = 20.0 min)

$[\alpha]_D^{25}$: -21.75 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-(Triethylsilyl)prop-2-yn-1-One (4l)



4l

37.6 mg, 82% yield, 95% ee, light yellow oil. AcCl was used as the acetylation reagent. Eluting with petroleum ether/EtOAc = 5:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.42 (m, 2H), 7.05–7.09 (m, 2H), 2.99–3.06 (m, 2H), 2.66 (d, *J* = 5.2 Hz, 1H), 2.45–2.50 (m, 1H), 2.30–2.35 (m, 1H), 1.86–2.02 (m, 6H), 0.94–0.99 (m, 9H), 0.61–0.68 (m, 6H).

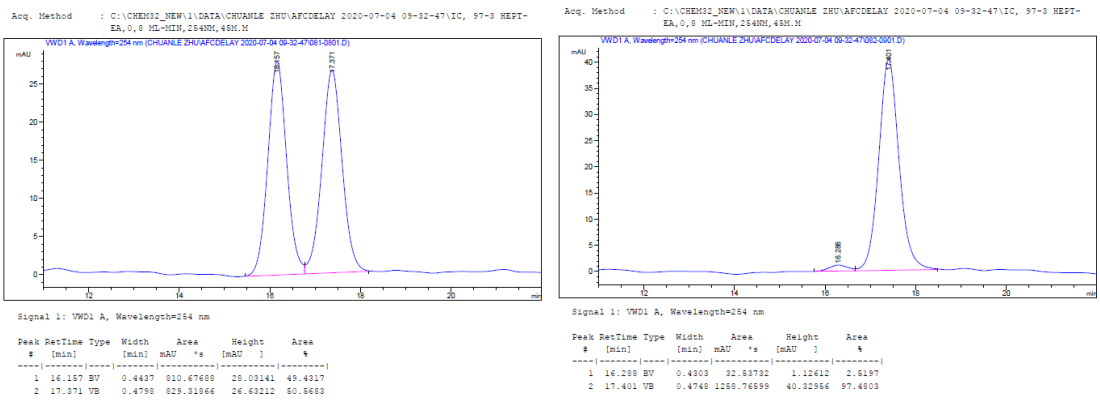
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.4, 180.0, 133.6, 132.1, 129.7, 123.2, 101.7, 99.6, 59.2, 50.3, 33.3, 27.7, 27.2, 25.0, 15.5, 7.5, 4.0.

IR (cm^{-1}): 2955, 2876, 2147, 1698, 1669, 1369.

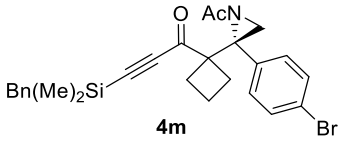
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{31}BrNO_2Si$, 460.1307; found, 460.1306.

HPLC: 95% ee, (Daicel CHIRALPAK IC, 97:3 heptane/ethyl acetate, 0.8 mL/min, λ = 254 nm; T_{major} = 17.4 min, T_{minor} = 16.2 min)

$[\alpha]_D^{25}$: -58.65 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-(Benzyldimethylsilyl)prop-2-yn-1-One (4m)



4m

39.0 mg, 79% yield, 86% ee, light yellow oil. AcCl was used as the acetylation reagent. Eluting with petroleum ether/EtOAc = 5:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.40 (m, 2H), 7.20–7.24 (m, 2H), 7.11–7.14 (m, 1H), 7.00–7.03 (m, 4H), 2.91–2.98 (m, 1H), 2.89 (s, 1H), 2.44–2.51 (m, 2H), 2.25–2.32 (m, 1H), 2.21 (s, 2H), 1.80–2.00 (m, 6H), 0.19 (s, 3H), 0.18 (s, 3H).

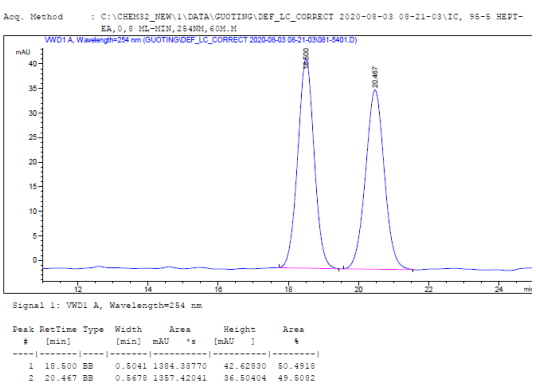
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.3, 179.8, 137.8, 133.6, 132.1, 129.7, 128.7, 128.5, 125.2, 123.2, 101.6, 99.6, 59.2, 50.1, 33.1, 27.6, 27.1, 25.4, 24.9, 15.4, -2.4, -2.5.

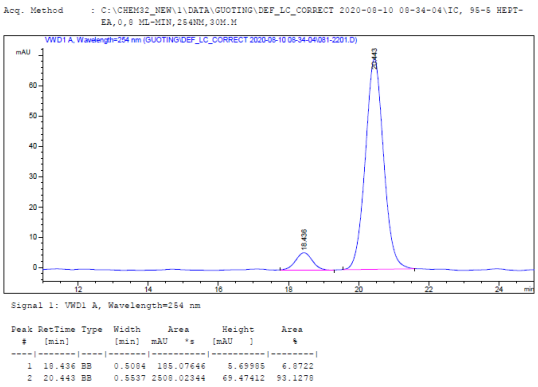
IR (cm^{-1}): 2953, 2149, 1695, 1668, 1492, 1367

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{26}H_{29}BrNO_2Si$, 494.1151; found, 494.1148.

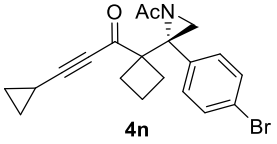
HPLC: 86% ee, (Daicel CHIRALPAK IC, 95:5 heptane/ethyl acetate, 0.8 mL/min, λ = 254 nm; T_{major} = 20.4 min, T_{minor} = 18.4 min)

$[\alpha]_D^{25}$: -61.63 (*c* = 1.0, $CHCl_3$)





(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-Cyclopropylprop-2-yn-1-One (4n)



4n

15.5 mg, 40% yield, 94% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8.8 Hz, 2H), 7.06 (d, *J* = 8.8 Hz, 2H), 3.01 (s, 1H), 2.92–2.97 (m, 1H), 2.61 (s, 1H), 2.42–2.50 (m, 1H), 2.25–2.33 (m, 1H), 1.80–2.04 (m, 6H), 1.32–1.38 (m, 6H), 0.97–0.99 (m, 2H), 0.80–0.84 (m, 2H).

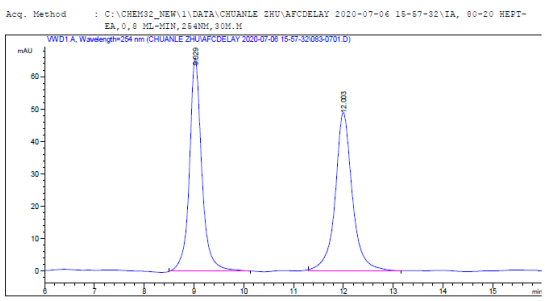
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.8, 179.9, 133.9, 132.1, 129.6, 123.0, 101.7, 75.2, 59.0, 50.4, 33.2, 27.8, 27.3, 25.0, 15.5, 10.1, 0.0.

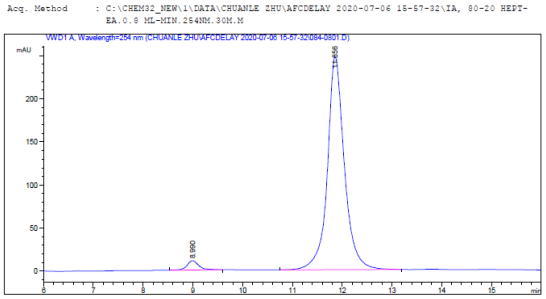
IR (cm^{-1}): 2943, 2204, 1692, 1659, 1365

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{20}H_{21}BrNO_2$, 386.0756; found, 386.0753.

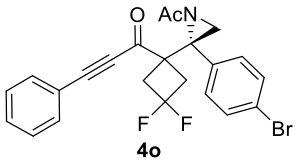
HPLC: 94% ee, (Daicel CHIRALPAK IA, 80:20 heptane/ethyl acetate, 0.8 mL/min, λ = 254 nm; T_{major} = 11.8 min, T_{minor} = 9.0 min)

$[\alpha]_D^{25}$: -53.26 (*c* = 1.0, $CHCl_3$)





(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)-3,3-Difluorocyclobutyl)-3-Phenylprop-2-yn-1-One (4o)



4o

33.6 mg, 73% yield, 88% ee, light yellow oil. AcCl was used as the acetylation reagent. Eluting with petroleum ether/EtOAc = 2:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.51 (m, 3H), 7.39–7.42 (m, 4H), 7.13–7.15 (m, 2H), 3.63–3.72 (m, 1H), 3.01–3.14 (m, 2H), 2.73–2.87 (m, 3H), 1.97 (d, J = 2.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 184.8 (d, $^{4}J_{F\text{-}C}$ = 4.0 Hz), 179.3, 133.3, 132.4, 132.3, 131.8, 130.1, 129.1, 123.8, 119.2, 117.1 (dd, $^{1}J_{F\text{-}C}$ = 270.6 Hz, $^{1}J_{F\text{-}C}$ = 270.4 Hz), 95.8, 85.9, 49.5 (d, $^{4}J_{F\text{-}C}$ = 2.7 Hz), 48.9 (dd, $^{3}J_{F\text{-}C}$ = 6.9 Hz, $^{3}J_{F\text{-}C}$ = 7.0 Hz), 41.3 (t, $^{2}J_{F\text{-}C}$ = 24.8 Hz), 40.9 (t, $^{2}J_{F\text{-}C}$ = 25.1 Hz), 33.7, 24.9.

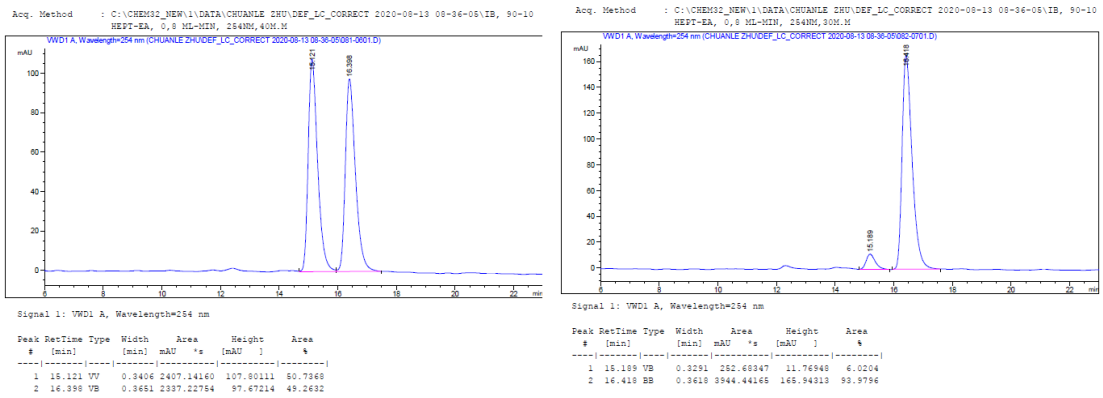
^{19}F NMR (376 MHz, $CDCl_3$): δ -86.4 – -86.9 (m, 1F), -94.5 – -95.1 (m, 1F).

IR (cm^{-1}): 2956, 2196, 1697, 1669, 1490, 1303

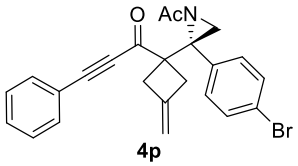
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{19}BrF_2NO_2$, 458.0567; found, 458.0567.

HPLC: 88% ee, (Daicel CHIRALPAK IB, 90:10 heptane/ethyl acetate, 0.8 mL/min, λ = 254 nm; T_{major} = 16.4 min, T_{minor} = 15.1 min)

$[\alpha]_D^{25}$: -35.64 (c = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)-3-Methylenecyclobutyl)-3-Phenylprop-2-yn-1-One (4p)



4p

35.2 mg, 81% yield, 95% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.51 (m, 3H), 7.37–7.42 (m, 4H), 7.11–7.13 (m, 2H), 4.96 (t, *J* = 2.4 Hz, 1H), 4.88 (t, *J* = 2.4 Hz, 1H), 3.67–3.73 (m, 1H), 3.16–3.21 (m, 1H), 3.12 (s, 1H), 3.00–3.06 (m, 1H), 2.83–2.88 (m, 1H), 2.77–2.79 (m, 1H), 1.93 (s, 3H).

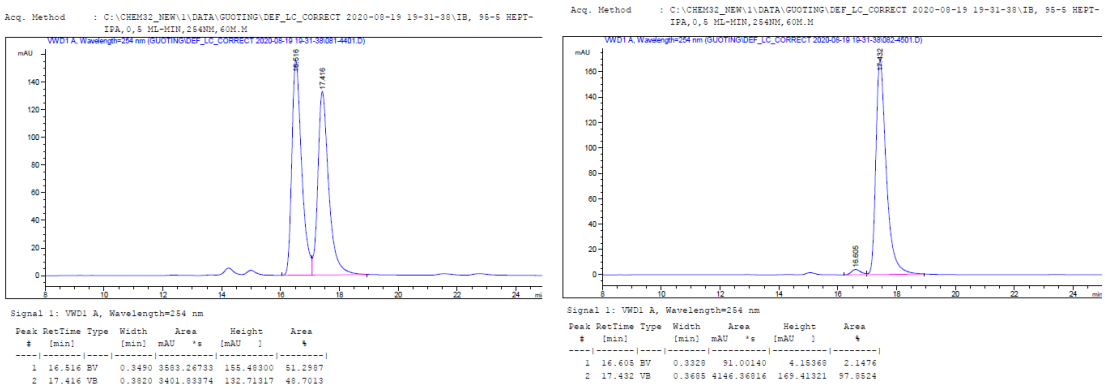
^{13}C NMR (101 MHz, $CDCl_3$): δ 186.9, 179.6, 140.1, 133.7, 133.2, 132.2, 131.4, 129.6, 129.0, 123.2, 119.7, 108.6, 94.2, 86.4, 55.0, 49.7, 38.2, 38.0, 33.9, 24.9.

IR (cm^{-1}): 2920, 2197, 1691, 1663, 1399, 1277

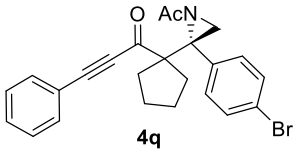
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{24}H_{21}BrNO_2$, 434.0756; found, 434.0746.

HPLC: 95% ee, (Daicel CHIRALPAK IB, 95:5 heptane/iPrOH, 0.5 mL/min, λ = 254 nm; T_{major} = 17.4 min, T_{minor} = 16.6 min)

$[\alpha]_D^{25}$: -135.33 (*c* = 1.0, $CHCl_3$)



(R)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclopentyl)-3-Phenylprop-2-yn-1-One (4q)



4q

21.8 mg, 50% yield, 95% ee, light yellow oil. Using **L4** as the ligand. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–7.54 (m, 3H), 7.34–7.43 (m, 6H), 2.88 (s, 1H), 2.81 (s, 1H), 2.51–2.58 (m, 1H), 2.04–2.13 (m, 5H), 1.68–1.76 (m, 4H), 1.51–1.55 (m, 1H).

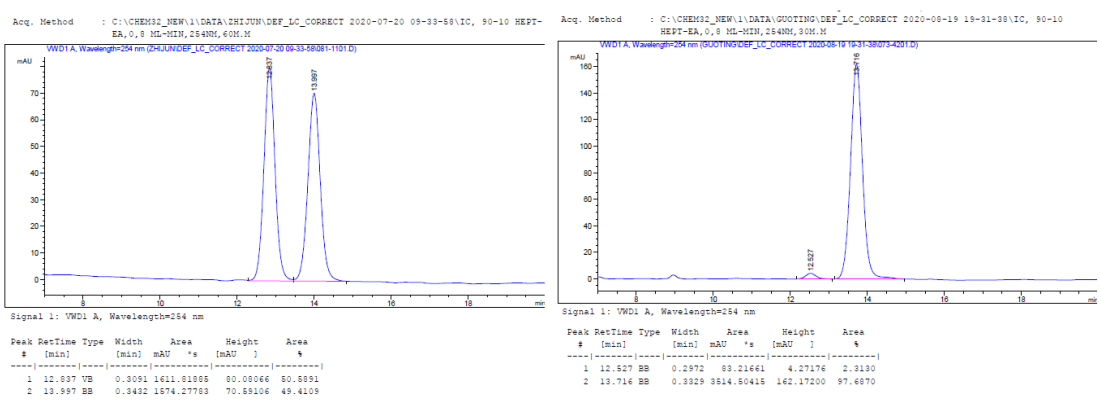
^{13}C NMR (101 MHz, $CDCl_3$): δ 189.6, 178.4, 135.2, 133.2, 131.6, 131.5, 131.2, 129.0, 123.1, 119.9, 93.2, 87.2, 65.5, 52.5, 34.4, 32.6, 32.5, 25.0, 24.7, 24.4.

IR (cm^{-1}): 2957, 2872, 2195, 1664, 1489, 1267

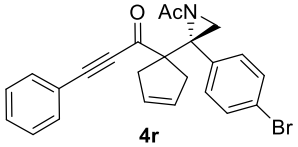
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{24}H_{23}BrNO_2$, 436.0912; found, 436.0910.

HPLC: 95% ee, (Daicel CHIRALPAK IC, 90:10 heptane/ethyl acetate, 0.8 mL/min, λ = 254 nm; T_{major} = 13.7 min, T_{minor} = 12.5 min)

$[\alpha]_D^{25}$: -12.20 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cyclopent-3-en-1-yl)-3-Phenylprop-2-yn-1-One (4r)



4r

36.7 mg, 73% yield, 82% ee, light yellow oil. Using **L4** as the ligand. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53–7.55 (m, 2H), 7.46–7.50 (m, 1H), 7.34–7.42 (m, 6H), 5.68–5.70 (m, 1H), 5.56–5.58 (m, 1H), 3.14–3.19 (m, 1H), 2.83–2.96 (m, 1H), 2.78 (s, 1H), 2.54–2.59 (m, 1H), 2.11 (s, 3H).

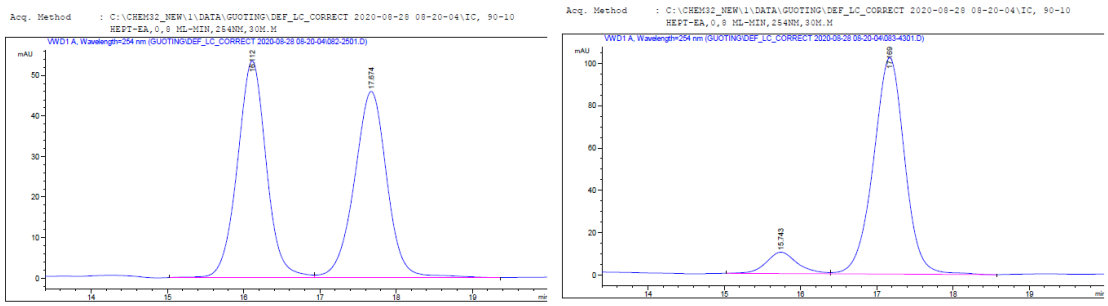
^{13}C NMR (101 MHz, $CDCl_3$): δ 188.6, 178.4, 135.0, 133.3, 131.6, 131.6, 131.3, 129.5, 129.0, 127.6, 123.1, 119.8, 93.7, 87.2, 64.6, 51.7, 39.2, 38.9, 34.0, 24.7.

IR (cm^{-1}): 2922, 2195, 1669, 1488, 1271

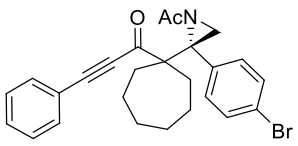
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{24}H_{21}BrNO_2$, 434.0756; found, 434.0749.

HPLC: 82% ee, (Daicel CHIRALPAK IC, 90:10 heptane/ethyl acetate, 0.8 mL/min, λ = 254 nm; T_{major} = 17.1 min, T_{minor} = 15.7 min)

$[\alpha]_D^{25}$: -6.82 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(4-Bromophenyl)aziridin-2-yl)cycloheptyl)-3-Phenylprop-2-yn-1-One (4s)



4s

24.6 mg, 53% yield, 87% ee, light yellow oil. Using **L4** as the ligand. Eluting with petroleum

ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56–7.58 (m, 2H), 7.45–7.49 (m, 2H), 7.38–7.42 (m, 5H), 2.80 (s, 1H), 2.56 (s, 1H), 2.19–2.25 (m, 2H), 2.08 (s, 3H), 1.87–1.93 (m, 1H), 1.71–1.82 (m, 1H), 1.39–1.59 (m, 8H).

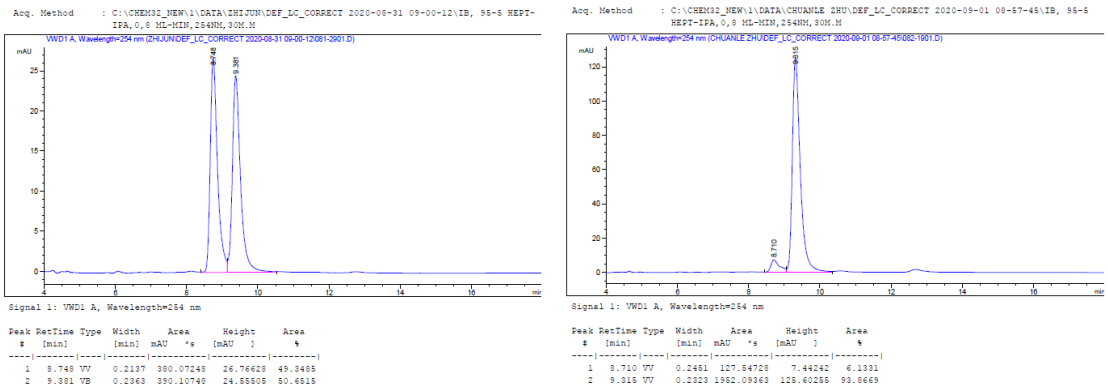
^{13}C NMR (101 MHz, $CDCl_3$): δ 190.8, 177.7, 134.9, 133.3, 132.9, 131.1, 131.1, 128.9, 123.0, 120.2, 93.6, 88.2, 58.6, 54.6, 33.1, 32.4, 32.1, 30.2, 30.1, 24.8, 23.7, 23.7.

IR (cm^{-1}): 2926, 2855, 2197, 1658, 1460, 1388, 1270

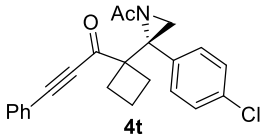
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{26}H_{27}BrNO_2$, 464.1225; found, 464.1221.

HPLC: 87% ee, (Daicel CHIRALPAK IB, 95:5 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 9.3 min, T_{minor} = 8.7 min)

$[\alpha]_D^{25}$: -61.73 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(4-Chlorophenyl)aziridin-2-yl)cyclobutyl)-3-Phenylprop-2-yn-1-One (4t)



4t

33.6 mg, 89% yield, 95% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.50 (m, 3H), 7.36–7.40 (m, 2H), 7.17–7.24 (m, 4H), 3.14 (s, 1H), 3.01–3.08 (m, 1H), 2.77 (s, 1H), 2.51–2.59 (m, 1H), 2.35–2.43 (m, 1H), 2.06–2.13 (m, 1H), 1.85–2.02 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 187.7, 180.0, 134.9, 133.2, 133.1, 131.3, 129.4, 129.2, 129.0, 119.8,

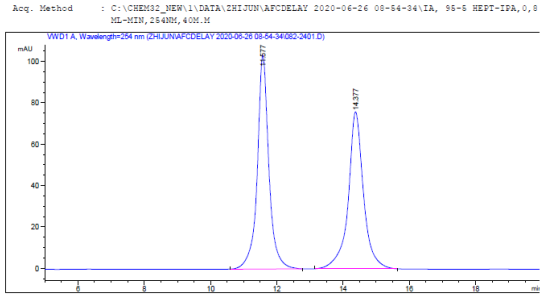
93.5, 86.5, 59.5, 50.4, 33.2, 27.8, 27.3, 25.0, 15.6.

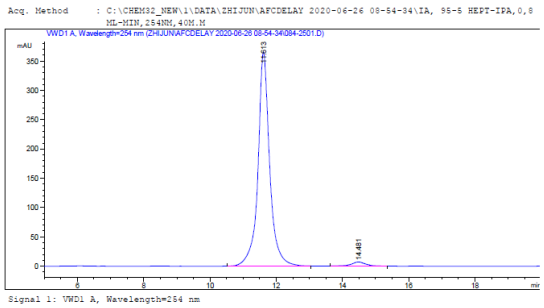
IR (cm^{-1}): 2942, 2197, 1693, 1661, 1492, 1258.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{21}ClNO_2$, 378.1261; found, 378.1261.

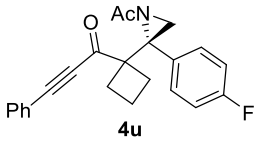
HPLC: 95% ee, (Daicel CHIRALPAK IA, 95:5 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 11.6 min, T_{minor} = 14.4 min)

$[\alpha]_D^{25}$: -108.25 (c = 1.0, $CHCl_3$)





(*R*)-1-(1-(1-Acetyl-2-(4-Fluorophenyl)aziridin-2-yl)cyclobutyl)-3-Phenylprop-2-yn-1-One (4u)



4u

31.7 mg, 88% yield, 95% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.51 (m, 3H), 7.36–7.41 (m, 2H), 7.22–7.25 (m, 2H), 6.93–6.97 (m, 2H), 3.15 (s, 1H), 3.01–3.08 (m, 1H), 2.76 (s, 1H), 2.53–2.61 (m, 1H), 2.35–2.43 (m, 1H), 2.06–2.13 (m, 1H), 1.85–2.01 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 187.8, 180.1, 162.8 (d, $^1J_{F\text{-}C}$ = 247.6 Hz), 133.1, 131.3, 130.5 (d, $^4J_{F\text{-}C}$ = 4.5 Hz), 130.0 (d, $^3J_{F\text{-}C}$ = 8.2 Hz), 129.0, 119.8, 116.0 (d, $^2J_{F\text{-}C}$ = 21.4 Hz), 93.4, 86.6, 59.7, 50.5, 33.1, 27.8, 27.3, 25.0, 15.5.

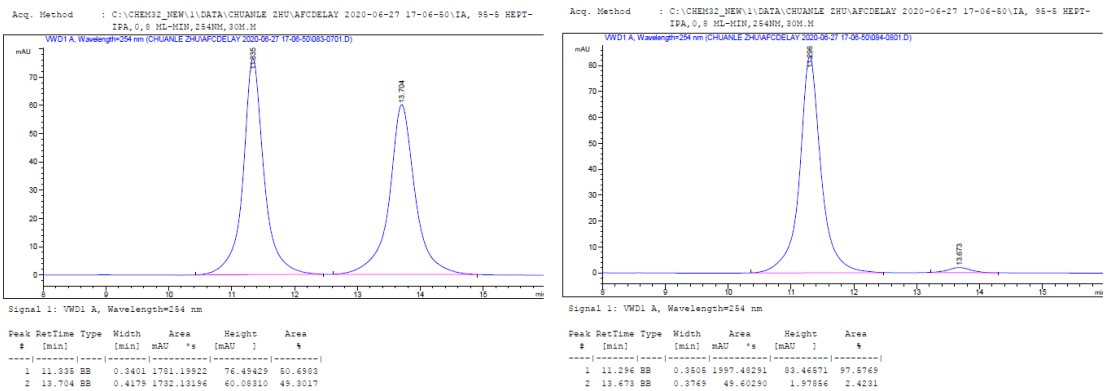
^{19}F NMR (376 MHz, $CDCl_3$): δ -112.7 – -112.8 (m, 1F)

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{21}FNO_2$, 362.1556; found, 362.1555.

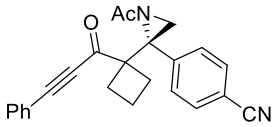
IR (cm^{-1}): 2941, 2198, 1693, 1662, 1513, 1369, 1256

HPLC: 95% ee, (Daicel CHIRALPAK IA, 95:5 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 11.3 min, T_{minor} = 13.7 min)

[α]$_D^{25}$: -79.46 (*c* = 1.0, $CHCl_3$)



(R)-4-(1-Acetyl-2-(1-(3-Phenylpropioloyl)cyclobutyl)aziridin-2-yl)benzonitrile (4v)



4v

26.1 mg, 71% yield, 96% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55–7.57 (m, 2H), 7.46–7.50 (m, 3H), 7.36–7.41 (m, 4H), 3.11 (s, 1H), 2.98–3.04 (m, 1H), 2.84 (s, 1H), 2.52–2.60 (m, 1H), 2.35–2.43 (m, 1H), 2.12–2.18 (m, 1H), 1.89–2.05 (m, 5H).

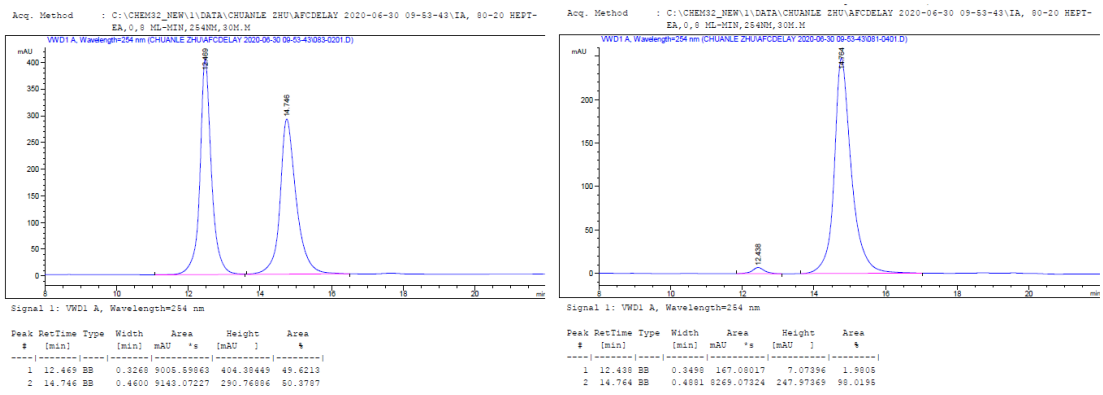
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.6, 179.0, 140.1, 133.2, 132.6, 131.5, 129.1, 129.0, 119.6, 118.3, 112.7, 94.0, 86.4, 59.1, 50.4, 33.6, 27.7, 27.3, 24.8, 15.6.

IR (cm^{-1}): 2942, 2229, 2197, 1693, 1661, 1370, 1288.

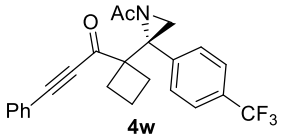
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{24}H_{21}N_2O_2$, 369.1603; found, 369.1600.

HPLC: 96% ee, (Daicel CHIRALPAK IA, 80:20 heptane/ethyl acetate, 0.8 mL/min, λ = 254 nm; T_{major} = 14.7 min, T_{minor} = 12.4 min)

[α]$_D^{25}$: -48.45 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(4-(Trifluoromethyl)phenyl)aziridin-2-yl)cyclobutyl)-3-Phenylprop-2-yn-1-One (4w)



4w

28.4 mg, 69% yield, 90% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.54 (m, 5H), 7.37–7.41 (m, 4H), 3.16 (s, 1H), 3.02–3.08 (m, 1H), 2.83 (s, 1H), 2.55–2.62 (m, 1H), 2.38–2.45 (m, 1H), 2.11–2.18 (m, 1H), 1.87–2.05 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 187.7, 179.5, 138.7, 133.2, 131.4, 130.9 (q, $^{2}J_{F\text{-}C}$ = 32.6 Hz), 129.0, 128.5, 125.9 (q, $^{3}J_{F\text{-}C}$ = 3.7 Hz), 123.9 (q, $^{1}J_{F\text{-}C}$ = 270.6 Hz), 119.7, 93.8, 86.5, 59.3, 50.4, 33.4, 27.7, 27.3, 24.9, 15.6.

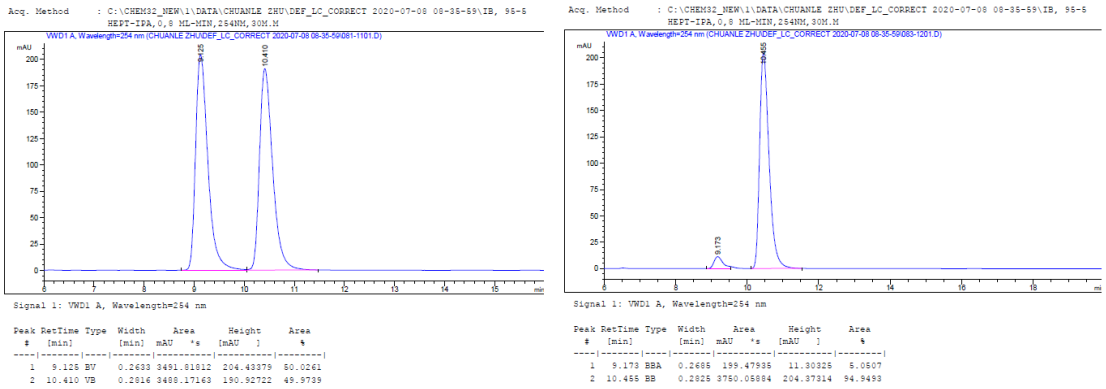
^{19}F NMR (376 MHz, $CDCl_3$): δ -63.3 (s, 3F)

IR (cm^{-1}): 2942, 2198, 1694, 1662, 1327, 1170

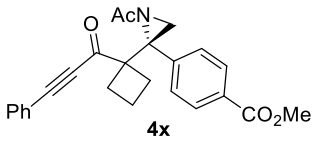
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{24}H_{21}F_3NO_2$, 412.1524; found, 412.1521.

HPLC: 90% ee, (Daicel CHIRALPAK IB, 95:5 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 10.4 min, T_{minor} = 9.1 min)

$[\alpha]_D^{25}$: -98.07 (*c* = 1.0, $CHCl_3$)



Methyl (*R*)-4-(1-Acetyl-2-(1-(3-Phenylpropioloyl)cyclobutyl)aziridin-2-yl)benzoate (4x)



4x

33.3 mg, 83% yield, 83% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91–7.93 (m, 2H), 7.43–7.48 (m, 3H), 7.34–7.38 (m, 2H), 7.28–7.30 (m, 2H), 3.85 (s, 3H), 3.20 (s, 1H), 3.04–3.11 (m, 1H), 2.80 (s, 1H), 2.52–2.59 (m, 1H), 2.36–2.44 (m, 1H), 1.97–2.14 (m, 2H), 1.84–1.89 (m, 4H).

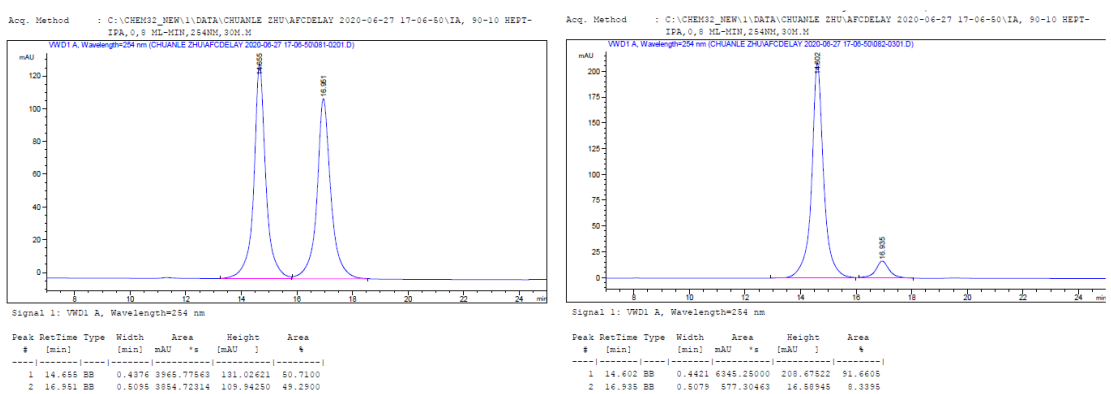
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.7, 179.7, 166.5, 139.7, 133.1, 131.3, 130.5, 130.2, 129.0, 127.9, 119.7, 93.6, 86.5, 59.3, 52.4, 50.4, 33.6, 27.8, 27.4, 24.9, 15.6.

IR (cm^{-1}): 2994, 2949, 2198, 1723, 1662, 1612, 1437, 1284

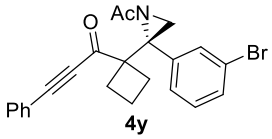
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{25}H_{24}NO_4$, 402.1705; found, 402.1704.

HPLC: 96% ee, (Daicel CHIRALPAK IA, 80:20 heptane/ethyl acetate, 0.8 mL/min, λ = 254 nm; T_{major} = 14.6 min, T_{minor} = 16.9 min)

$[\alpha]_D^{25}$: -82.93 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(3-Bromophenyl)aziridin-2-yl)cyclobutyl)-3-Phenylprop-2-yn-1-One (4y)



4y

31.9 mg, 76% yield, 86% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.52 (m, 3H), 7.37–7.41 (m, 4H), 7.12–7.22 (m, 2H), 3.12 (s, 1H), 3.01–3.07 (m, 1H), 2.75 (s, 1H), 2.53–2.61 (m, 1H), 2.35–2.42 (m, 1H), 2.07–2.14 (m, 1H), 1.84–2.05 (m, 5H).

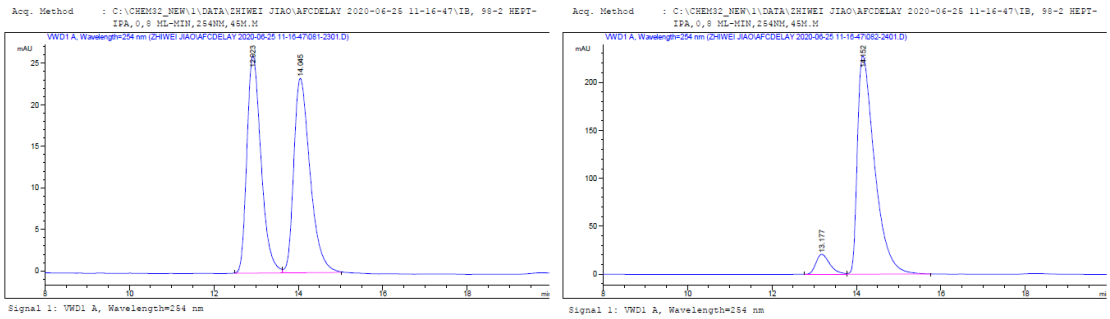
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.7, 179.7, 137.0, 133.1, 132.1, 131.3, 131.2, 130.4, 129.0, 126.9, 123.0, 119.8, 93.7, 86.5, 59.4, 50.5, 33.1, 27.8, 27.4, 25.0, 15.6.

IR (cm^{-1}): 2941, 2197, 1694, 1661, 1486, 1369.

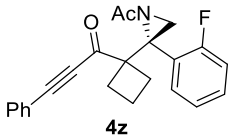
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{21}BrNO_2$, 422.0756; found, 422.0757.

HPLC: 86% ee, (Daicel CHIRALPAK IB, 98:2 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 14.1 min, T_{minor} = 13.1 min)

$[\alpha]_D^{25}$: -104.42 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(2-Fluorophenyl)aziridin-2-yl)cyclobutyl)-3-Phenylprop-2-yn-1-One (4z)



4z

20.9 mg, 58% yield, 97% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.55 (m, 6H), 7.21–7.25 (m, 1H), 7.04–7.08 (m, 1H), 6.94–7.00 (m, 1H), 3.05 (s, 1H), 2.77–2.83 (m, 2H), 2.58–2.66 (m, 1H), 2.31–2.38 (m, 1H), 2.17–2.24 (m, 4H), 1.78–1.88 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 188.3, 179.3, 160.5 (d, $^{1}J_{F\text{-}C}$ = 247.5 Hz), 133.2, 132.6 (d, $^{4}J_{F\text{-}C}$ = 3.2 Hz), 131.1, 131.0 (d, $^{3}J_{F\text{-}C}$ = 8.7 Hz), 128.9, 124.3 (d, $^{4}J_{F\text{-}C}$ = 3.5 Hz), 122.0 (d, $^{2}J_{F\text{-}C}$ = 13.3 Hz), 120.1, 116.5 (d, $^{2}J_{F\text{-}C}$ = 23.2 Hz), 93.5, 86.7, 60.3, 48.3, 32.5 (d, $^{3}J_{F\text{-}C}$ = 5.7 Hz), 28.1 (d, $^{4}J_{F\text{-}C}$ = 3.3 Hz), 27.5, 24.5 (d, $^{5}J_{F\text{-}C}$ = 2.4 Hz), 15.5.

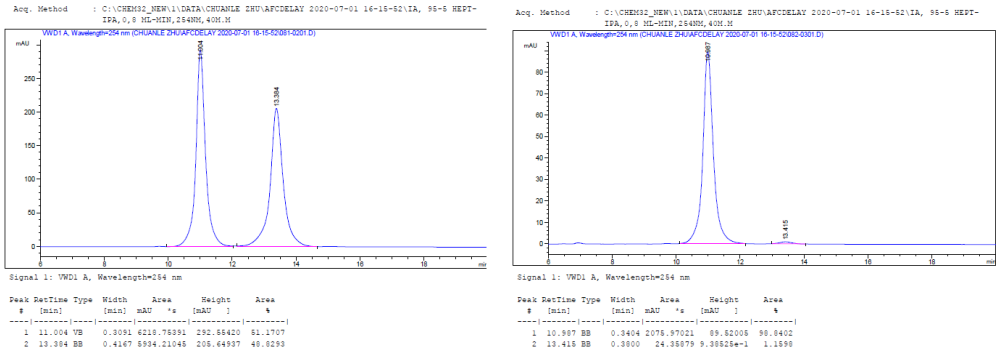
^{19}F NMR (376 MHz, $CDCl_3$): δ -109.1 – -109.2 (m, 1F).

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{21}FNO_2$, 362.1556; found, 362.1556.

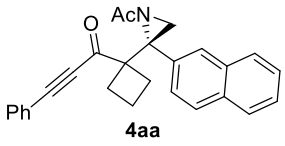
IR (cm^{-1}): 2949, 2198, 1662, 1490, 1370

HPLC: 95% ee, (Daicel CHIRALPAK IA, 95:5 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 11.0 min, T_{minor} = 13.4 min)

$[\alpha]_D^{25}$: -39.68 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(1-Acetyl-2-(Naphthalen-2-yl)aziridin-2-yl)cyclobutyl)-3-Phenylprop-2-yn-1-One (4aa)



4aa

33.4 mg, 85% yield, 95% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73–7.76 (m, 4H), 7.43–7.47 (m, 5H), 7.34–7.38 (m, 2H), 7.25–7.28 (m, 1H), 3.37 (s, 1H), 3.21–3.26 (m, 1H), 2.87 (s, 1H), 2.53–2.71 (m, 1H), 2.45–2.52 (m, 1H), 2.02–2.18 (m, 2H), 1.90–1.95 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 188.0, 180.3, 133.2, 133.1, 133.1, 132.2, 131.2, 129.0, 128.9, 128.5,

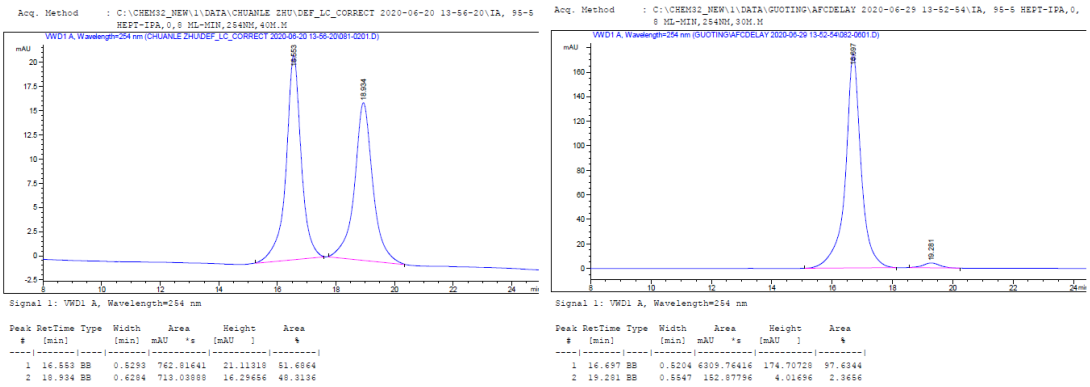
128.1, 127.7, 127.0, 126.8, 124.3, 119.9, 93.4, 86.7, 59.6, 50.8, 33.7, 28.0, 27.6, 25.0, 15.7.

IR (cm^{-1}): 2941, 2197, 1691, 1661, 1369, 1284.

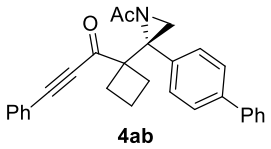
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{27}H_{24}NO_2$, 394.1807; found, 394.1801.

HPLC: 95% ee, (Daicel CHIRALPAK IA, 95:5 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 16.7 min, T_{minor} = 19.3 min)

$[\alpha]_D^{25}$: -23.80 (*c* = 1.0, $CHCl_3$)



(*R*)-1-(1-(2-([1,1'-Biphenyl]-4-yl)-1-Acetylaziridin-2-yl)cyclobutyl)-3-Phenylprop-2-yn-1-One (4ab)



4ab

33.2 mg, 79% yield, 87% ee, light yellow oil. Eluting with petroleum ether/EtOAc = 3:1 for column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.52 (m, 6H), 7.42–7.46 (m, 2H), 7.38–7.41 (m, 3H), 7.33–7.36 (m, 1H), 7.28–7.30 (m, 2H), 3.27 (s, 1H), 3.13–3.18 (m, 1H), 2.81 (s, 1H), 2.57–2.65 (m, 1H), 2.41–2.48 (m, 1H), 2.01–2.15 (m, 2H), 1.90–1.95 (m, 4H).

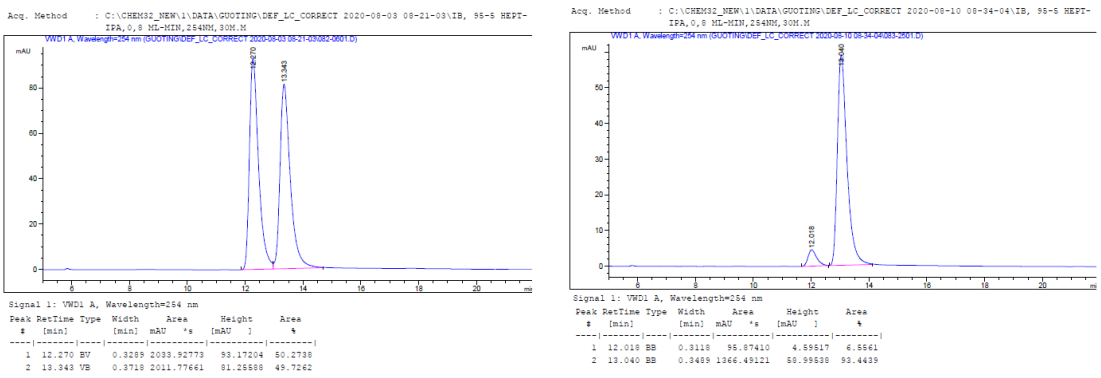
^{13}C NMR (101 MHz, $CDCl_3$): δ 188.0, 180.5, 141.5, 140.2, 133.5, 133.2, 131.2, 129.0, 129.0, 128.2, 127.9, 127.6, 127.2, 120.0, 93.4, 86.7, 59.6, 50.6, 33.4, 27.9, 27.4, 25.1, 15.7.

IR (cm^{-1}): 2940, 2198, 1691, 1661, 1487, 1368.

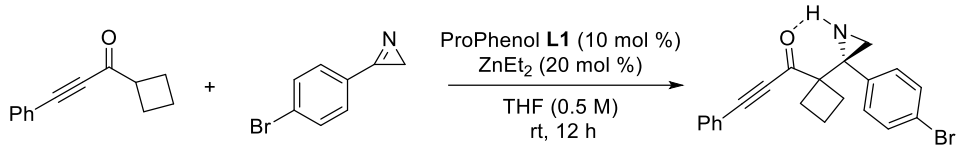
HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{29}H_{26}NO_2$, 420.1964; found, 420.1959.

HPLC: 87% ee, (Daicel CHIRALPAK IB, 95:5 heptane/iPrOH, 0.8 mL/min, λ = 254 nm; T_{major} = 13.0 min, T_{minor} = 12.0 min)

$[\alpha]_D^{25}$: -9.76 (*c* = 1.0, $CHCl_3$)



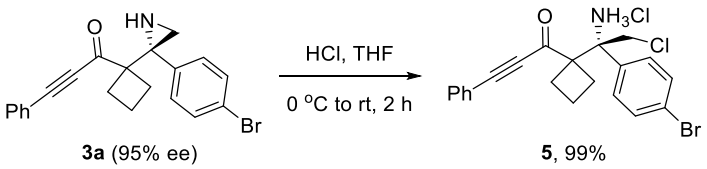
G. Procedure for the Scale-Up Synthesis and Transformation of 3a



1a (368 mg, 2 mmol) **2a** (588 mg, 3 mmol) **3a** 0.621 g, 78% yield, 95% ee

A 10 mL thick-wall microwave vial was flame-dried (propane torch for 5 seconds under vacuum) with a magnetic stir bar inside. (*S*,*S*)-ProPhenol ligand **L1** (127.6 mg, 0.2 mmol) was added and the system was placed under an atmosphere of argon (balloon). The ligand was then dissolved in freshly distilled THF (2 mL). Et_2Zn (1.0 M in hexane, 0.4 mL, 0.4 mmol) was added dropwise and the suspension was stirred at room temperature for 30 min. A second flame-dried vial (propane torch for 5 seconds under vacuum) was charged with alkynyl ketone **1a** (368.0 mg, 2 mmol) and 2*H*-azirine **2a** (588.0 mg, 3 mmol), and the system was placed under an atmosphere of argon (balloon). Freshly distilled THF (2 mL) was added and the prepared substrate solution was introduced to the stirred catalyst solution at room temperature. The combined reaction mixture was then sealed and stirred for 12 h at room temperature. Filtration through a plug of Celite and florisil gave the crude reaction mixture, which was concentrated in vacuo and purified by silica gel column chromatography (petroleum ether/ethyl acetate=3:1) to give the Mannich adduct **3a** (0.621 g, 78% yield, 95% ee).

The Applications of 3a



3a (95% ee) **5**, 99%

A 10 mL thick-wall microwave vial was flame-dried (propane torch for 5 seconds under vacuum) with a magnetic stir bar inside. To a solution of **3a** (76 mg, 0.2 mmol) in anhydrous THF (4 mL) was added HCl (2.0 M in Et_2O, 0.3 mL, 0.6 mmol) at 0 °C under N_2. The resulting mixture was allowed to warm up to room temperature, and stirred for 2 hours. Removal of the solvent under reduced pressure to give product **5** as a grey solid.

(*R*)-1-(1-(1-Amino-1-(4-Bromophenyl)-2-Chloroethyl)cyclobutyl)-3-Phenylprop-2-yn-1-One· Hydrogen Chloride (5)

90.0 mg, 99% yield. Grey solid.

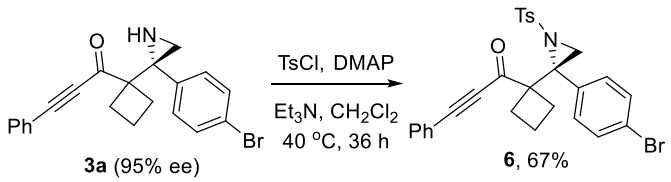
^{1}H NMR (400 MHz, d_6-DMSO): δ 9.44 (brs, 3H), 7.60–7.62 (m, 2H), 7.51–7.54 (m, 3H), 7.40–7.47 (m, 4H), 4.63 (d, *J* = 12.4 Hz, 1H), 4.25 (d, *J* = 12.8 Hz, 1H), 3.10–3.23 (m, 1H), 2.85–2.93 (m, 1H), 2.31–2.41 (m, 2H), 1.53–1.62 (m, 2H).

^{13}C NMR (101 MHz, d_6-DMSO): δ 190.0, 133.8, 133.7, 132.3, 131.9, 131.2, 130.3, 129.7, 123.5, 119.0, 96.0, 86.9, 65.1, 61.1, 28.3, 28.1, 25.8, 15.6.

IR (cm^{-1}): 3402, 2978, 2194, 1648, 1518, 1493

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{21}BrCl_2NO$, 452.0184; found, 452.0187.

$[\alpha]_D^{25}$: +69.34 (*c* = 1.0, THF)



3a (95% ee) **6**, 67%

A 10 mL thick-wall microwave vial was flame-dried (propane torch for 5 seconds under vacuum) with a magnetic stir bar inside was added DMAP (1.2 mg, 0.01 mmol), TsCl (38.0 mg, 0.2 mmol). Then a solution of **3a** (38.0 mg, 0.1 mmol), Et_3N (40.4 mg, 0.4 mmol) in anhydrous CH_2Cl_2 (1.5 mL) was added at room temperature under N_2. The resulting mixture was stirred at 40 °C for 36 h. After this time, the reaction was extracted three times with dichloromethane (10 mL each) and H_2O. The organic layers were combined, washed with brine and dried over magnesium sulfate. Solvent

was removed by rotary evaporation. The crude material was further purified by silica gel chromatography (hexanes/EtOAc = 10:1) to yield **6** as a white solid.

(*R*)-1-(1-(2-(4-Bromophenyl)-1-Tosylaziridin-2-yl)cyclobutyl)-3-Phenylprop-2-yn-1-One (6)

35.8 mg, 67% yield. White solid.

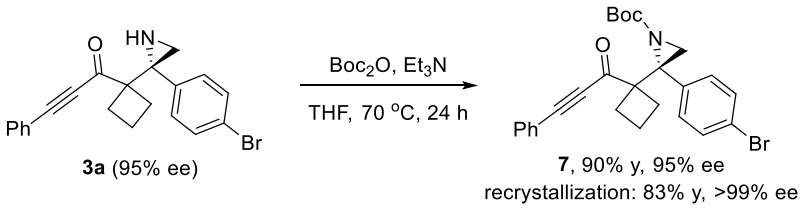
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69–7.71 (m, 2H), 7.47–7.52 (m, 3H), 7.38–7.42 (m, 4H), 7.27–7.32 (m, 4H), 3.26 (s, 1H), 2.81–2.85 (m, 1H), 2.77 (s, 1H), 2.63–2.71 (m, 1H), 2.44 (s, 3H), 2.35–2.40 (m, 1H), 1.94–2.01 (m, 1H), 1.80–1.88 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 187.0, 144.6, 136.3, 133.1, 131.8, 131.7, 131.5, 131.3, 129.7, 129.1, 128.1, 123.9, 119.8, 93.4, 86.6, 60.8, 55.5, 36.3, 27.6, 26.6, 21.9, 15.2.

IR (cm^{-1}): 2949, 2197, 1664, 1489, 1326, 1160.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{28}H_{25}BrNO_3S$, 534.0739; found, 534.0732.

$[\alpha]_D^{25}$: -136.32 (*c* = 1.0, $CHCl_3$)



A 10 mL thick-wall microwave vial was flame-dried (propane torch for 5 seconds under vacuum) with a magnetic stir bar inside was added Boc_2O (87.2 mg, 0.4 mmol). Then a solution of **3a** (38.0 mg, 0.1 mmol), Et_3N (80.8 mg, 0.8 mmol) in anhydrous THF (1 mL) was added at room temperature under N_2. The resulting mixture was stirred at 70 °C for 24 h. After this time, the reaction was extracted three times with ethyl acetate (10 mL each) and H_2O (10 mL). The organic layers were combined, washed with brine and dried over magnesium sulfate. Solvent was removed by rotary evaporation. The crude material was further purified by silica gel chromatography (hexanes/EtOAc = 20:1) to yield **7** as a white solid.

***tert*-Butyl (*R*)-2-(4-Bromophenyl)-2-(1-(3-Phenylpropioloyl)cyclobutyl)aziridine-1-Carboxyl ate (7)**

43.2 mg, 90% yield, 95% ee, white solid. After recrystallization, 83% yield, >99% ee

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–7.53 (m, 3H), 7.37–7.42 (m, 4H), 7.20–7.22 (m, 2H), 3.07 (s, 1H), 2.88–2.94 (m, 1H), 2.63–2.71 (m, 2H), 2.36–2.44 (m, 1H), 1.79–2.04 (m, 3H), 1.19 (s, 9H).

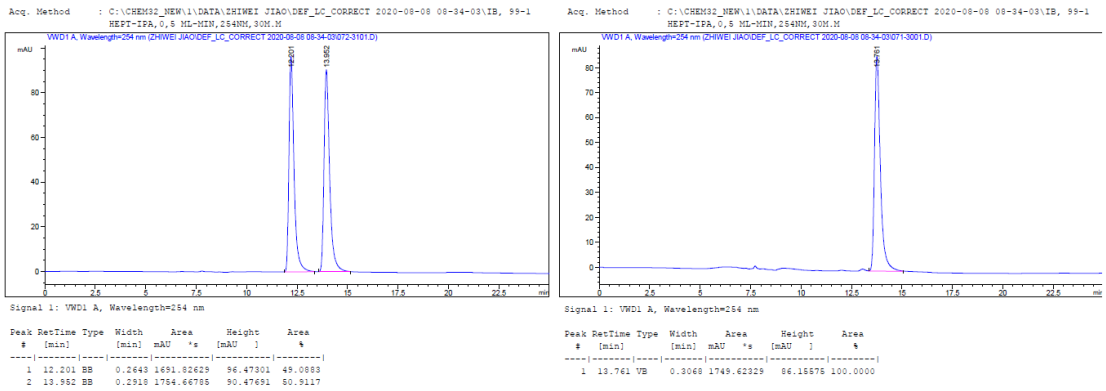
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.8, 160.1, 133.4, 133.1, 131.5, 131.3, 131.2, 129.0, 123.2, 120.0, 93.1, 86.7, 81.8, 60.2, 50.5, 33.0, 27.8, 27.4, 26.9, 15.6.

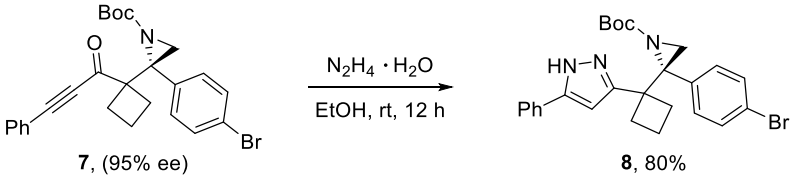
IR (cm^{-1}): 2979, 2939, 2198, 1718, 1663, 1367, 1255

HRMS (ESI-TOF, m/z): $[M+Na]^+$ Calcd. for $C_{26}H_{26}BrNO_3Na$, 502.0994; found, 502.0994.

HPLC: >99% ee, (Daicel CHIRALPAK IB, 99:1 heptane/iPrOH, 0.5 mL/min, λ = 254 nm; T_{major} = 13.7 min,)

$[\alpha]_D^{25}$: -14.24 (*c* = 0.5, $CHCl_3$)





A 5 mL vial, equipped with a stir bar, was charged with **7** (48 mg, 0.1 mmol) and EtOH (1 mL). Hydrazine monohydrate (10 mg, 0.2 mmol) was added to the solution at rt. The resulting solution was stirred at rt for 12 h before concentrating in vacuo. Flash silica column chromatography (petroleum ether/EtOAc = 3:1) gave the title compound **8** as colorless oil.

***tert*-Butyl (*R*)-2-(4-Bromophenyl)-2-(1-(5-Phenyl-1*H*-Pyrazol-3-yl)cyclobutyl)aziridine-1-Carboxylate (8)**

39.4 mg, 80% yield, colorless oil.

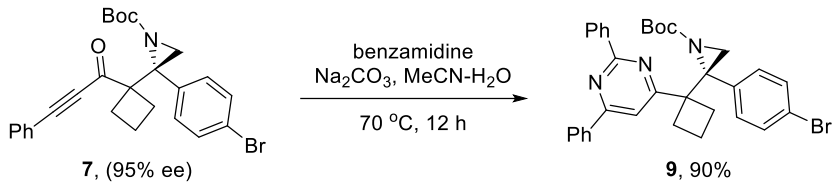
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.26–7.30 (m, 1H), 7.24–7.26 (m, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 6.27 (s, 1H), 2.82 (s, 1H), 2.61 (s, 1H), 2.32–2.50 (m, 3H), 2.04–2.12 (m, 2H), 1.83–1.90 (m, 1H), 1.40 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 160.7, 135.6, 131.1, 130.6, 128.8, 127.8, 125.7, 122.3, 101.4, 82.6, 54.4, 45.4, 34.0, 31.6, 30.6, 28.0, 16.2.

IR (cm^{-1}): 2979, 1713, 1490, 1460, 1368, 1339, 1250.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{26}H_{29}BrN_3O_2$, 494.1443; found, 494.1434.

$[\alpha]_D^{25}$: +120.78 (*c* = 0.5, $CHCl_3$)



7, (95% ee) **9**, 90%

To a solution of **7** (24 mg, 0.05 mmol) in acetonitrile/H_2O (0.5/0.2 mL) was added Na_2CO_3 (26.5 mg, 0.25 mmol) and benzamidine (8.4 mg, 0.07 mmol), respectively. The mixture was stirred at 70 °C for overnight before cooling down to rt. EtOAc (10 mL) and H_2O (10 mL) were added, and the layers were separated. The aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was subjected to flash column chromatography on silica gel (Petroleum ether: EtOAc = 20: 1) to yield **9** as colorless oil.

***tert*-Butyl (*R*)-2-(4-Bromophenyl)-2-(1-(2,6-Diphenylpyrimidin-4-yl)cyclobutyl)aziridine-1-C arboxylate (9)**

26.2 mg, 90% yield, colorless oil.

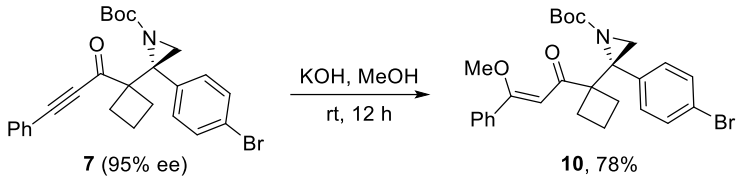
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54–8.56 (m, 2H), 8.03–8.05 (m, 2H), 7.50–7.53 (m, 6H), 7.23–7.26 (m, 3H), 7.07 (d, *J* = 8.8 Hz, 2H), 2.79–3.01 (m, 3H), 2.79 (s, 1H), 2.56–2.63 (m, 1H), 2.24–2.31 (m, 1H), 1.91–1.95 (m, 2H), 1.24 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 173.4, 164.1, 163.9, 160.5, 138.3, 137.7, 134.2, 131.8, 131.0, 130.9, 130.8, 129.1, 128.7, 128.5, 127.5, 122.6, 112.5, 81.6, 53.8, 53.6, 33.2, 20.2, 29.0, 27.9, 16.0.

IR (cm^{-1}): 2977, 1716, 1567 1365, 1282, 1247.

HRMS (ESI-TOF, m/z): $[M+H]^+$ Calcd. for $C_{32}H_{33}BrN_3O_2$, 582.1756; found, 582.1749.

$[\alpha]_D^{25}$: -18.13 (*c* = 0.5, $CHCl_3$)



To a solution of **7** (24 mg, 0.05 mmol) in MeOH (0.5 mL) was added KOH (85%, 6.6 mg, 0.1 mmol). The mixture was stirred at room temperature for 12 h. EtOAc (10 mL) and H_2O (10 mL) were added, and the layers were separated. The aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was subjected to flash column chromatography on silica gel (Petroleum ether: EtOAc = 4: 1) to yield **10** as white solid.

***tert*-Butyl (*R, Z*)-2-(4-Bromophenyl)-2-(1-(3-Methoxy-3-Phenylacryloyl)cyclobutyl)aziridine-1-Carboxylate (10)**

20.0 mg, 78% yield, white solid.

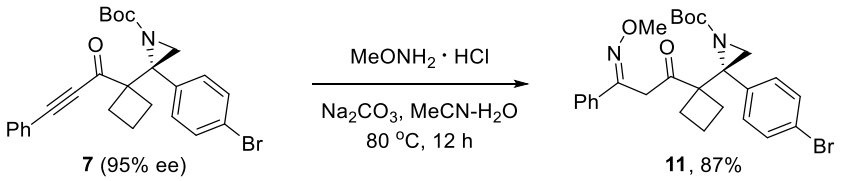
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44–7.46 (m, 2H), 7.26–7.30 (m, 1H), 7.16–7.23 (m, 4H), 7.09–7.12 (m, 2H), 4.01 (d, *J* = 17.6 Hz, 1H), 3.86 (s, 3H), 3.53 (d, *J* = 17.2 Hz, 1H), 3.11 (s, 1H), 2.88–2.95 (m, 1H), 2.58–2.65 (m, 2H), 2.27–2.35 (m, 1H), 1.79–2.08 (m, 3H), 1.15 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 197.4, 171.6, 160.3, 135.2, 134.0, 131.5, 131.4, 130.0, 128.5, 128.0, 123.0, 97.5, 81.7, 58.6, 56.5, 51.5, 32.9, 27.8, 26.8, 15.7.

IR (cm^{-1}): 2934, 1715, 1681, 1586, 1567, 1368, 1283

HRMS (ESI-TOF, m/z): $[M+Na]^+$ Calcd. for $C_{27}H_{30}BrNO_4Na$, 534.1256; found, 534.1252.

$[\alpha]_D^{25}$: -104.58 (*c* = 1.0, $CHCl_3$)



To a solution of **7** (36 mg, 0.075 mmol) in acetonitrile/H_2O (0.8/0.2 mL) was added Na_2CO_3 (23.9 mg, 0.225 mmol) and *O*-methoxylamine hydrogen chloride (12.5 mg, 0.15 mmol), respectively. The mixture was stirred at 80 °C for overnight before cooling down to rt. EtOAc (10 mL) and H_2O (10 mL) were added, and the layers were separated. The aqueous phase was extracted with EtOAc (3 x

10 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was subjected to flash column chromatography on silica gel (Petroleum ether: EtOAc = 20: 1) to yield **11** as colorless oil.

***tert*-Butyl (*R, E*)-2-(4-Bromophenyl)-2-(1-(3-(Methoxyimino)-3-Phenylpropanoyl)cyclobutyl) aziridine-1-Carboxylate (11)**

34.3 mg, 87% yield, colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.36 (m, 1H), 7.19–7.26 (m, 4H), 6.91 (d, *J* = 7.6 Hz, 2H), 5.67 (s, 1H), 3.76 (s, 3H), 3.02 (s, 1H), 2.69–2.76 (m, 1H), 2.61 (s, 1H), 2.46–2.54 (m, 1H), 2.17–2.24 (m, 1H), 1.99–2.04 (m, 1H), 1.75–1.84 (m, 2H), 1.19 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 204.1, 160.0, 152.2, 135.7, 133.7, 131.9, 130.7, 129.3, 128.6, 126.0, 123.2, 81.9, 62.3, 59.2, 50.1, 37.2, 32.9, 28.3, 27.7, 27.0, 15.9.

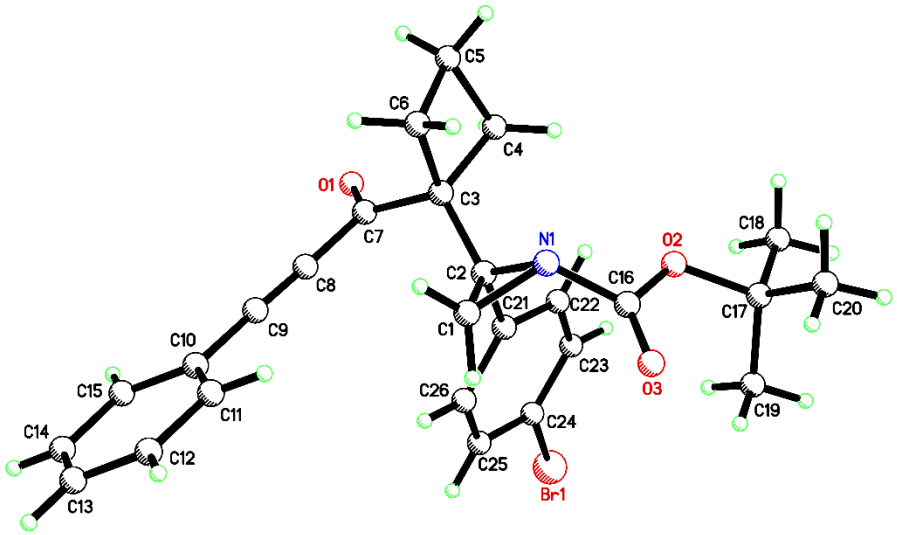
IR (cm^{-1}): 2997, 2938, 1714, 1492, 1397, 1367, 1276.

HRMS (ESI-TOF, m/z): $[M+Na]^+$ Calcd. for $C_{27}H_{31}BrN_2O_4Na$, 549.1365; found, 549.1362.

$[\alpha]_D^{25}$: -72.90 (*c* = 1.0, $CHCl_3$)

H. X-Ray Crystallographic Data

The obtained compound **7** (43.2 mg, 95% ee) was dissolved in CH_2Cl_2 (0.2 mL) in a 20 mL vial, then petroleum ether (15 mL) was added slowly. The resulted two-phase mixture was allowed to open to air to volatilize the solvent and stand overnight. Separated the white solid and the solvent. Concentrated the solvent under reduced pressure to give compound **7**. The obtained compound **7** (> 99% ee) was heated to reflux in petroleum ether (10 mL) till the dissolve of the solid. Then the resulting solvent was allowed to open to air to volatilize the solvent and cool down to room temperature naturally. Then the colorless crystal of **7** was formed. The X-ray crystallographic structures for **7**. ORTEP representation with 50% probability thermal ellipsoids. Solvent are omitted for clarity. Crystal data have been deposited to CCDC, number 2027241.

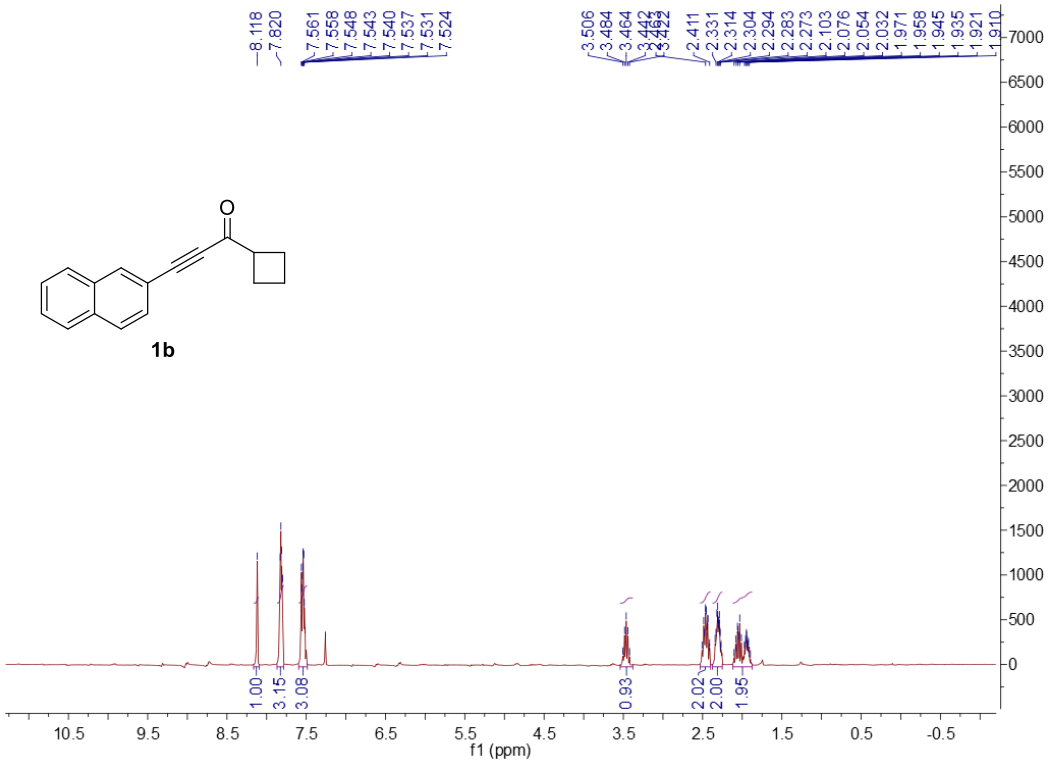


Empirical formula	$C_{26}H_{26}BrNO_3$
Formula weight	480.39
Temperature	120 (2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, $P2_12_12$
Unit cell dimensions	a = 17.3328(19) Å alpha = 90 deg. b = 10.8849(12) Å beta = 90 deg. c = 12.6609(14) Å gamma = 90 deg.
Volume	2388.7(5)Å^3
Z, Calculated density	4, 1.336 Mg/m^3
Absorption coefficient	1.747 mm^{-1}
F(000)	992
Crystal size	0.209×0.193×0.133 mm^3
Theta range for data collection	1.608 to 28.297 deg.
Limiting indices	-22 ≤ h ≤ 23,–14≤ k ≤ 14,–16 ≤ l ≤ 16
Reflections collected / unique	36821 / 5951 [R(int) = 0.0377]
Completeness to theta = 25.242	100.0 %
Refinement method	Full-matrix least-squares on F^2

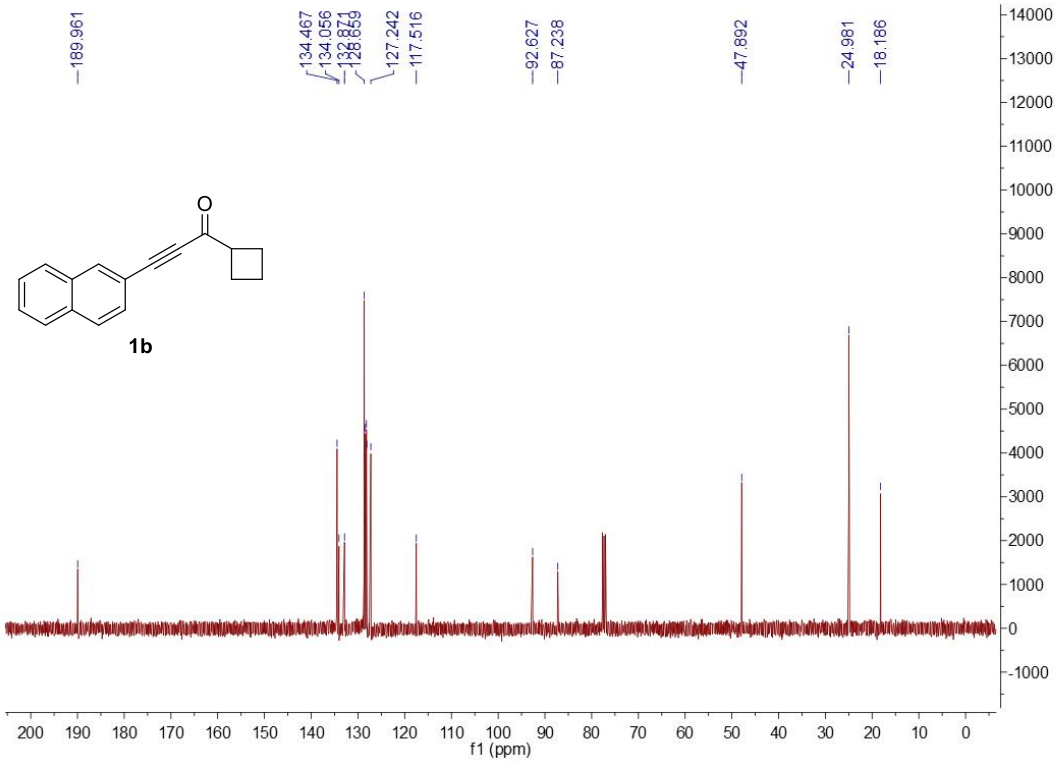
Data / restraints / parameters	5951 / 0 / 283
Goodness-of-fit on F^2	1.040
Final R indices [I>2sigma(I)]	R1 = 0.0322, wR2 = 0.0662
R indices (all data)	R1 = 0.436, wR2 = 0.0698
Absolute structure parameter	0.002(3)
Extinction coefficient	n/a
Largest diff. peak and hole	0.473 and -0.578 $e^{-}.Å^{-3}$

I. NMR Spectra of New Compounds

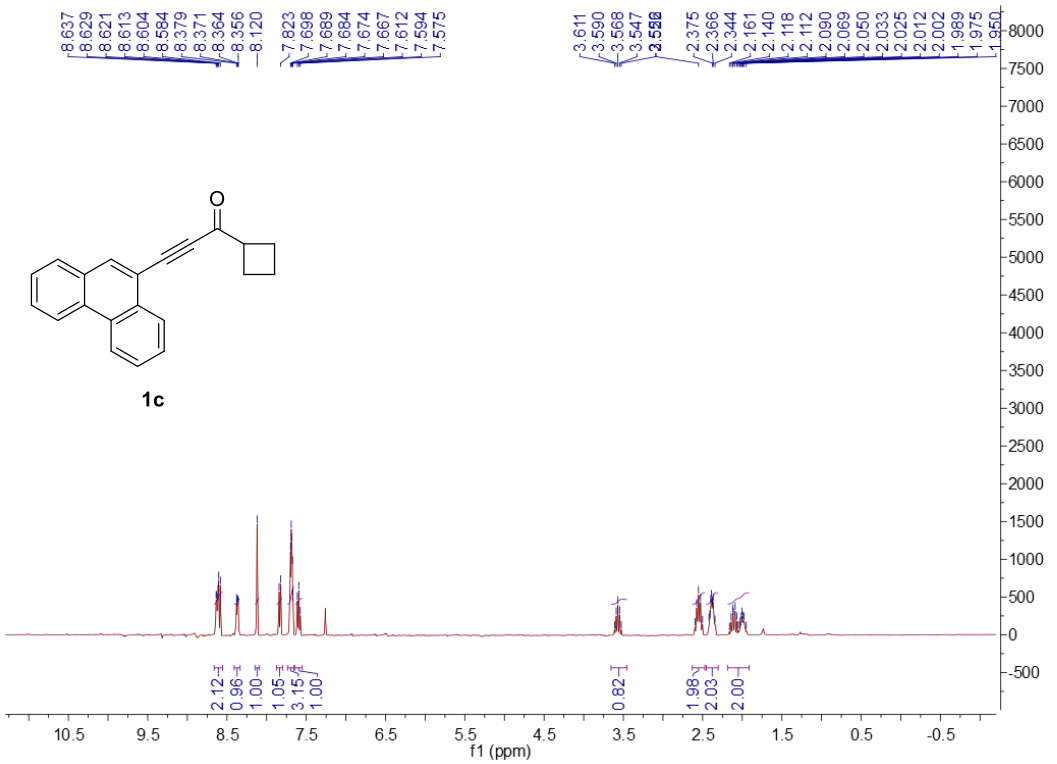
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1b



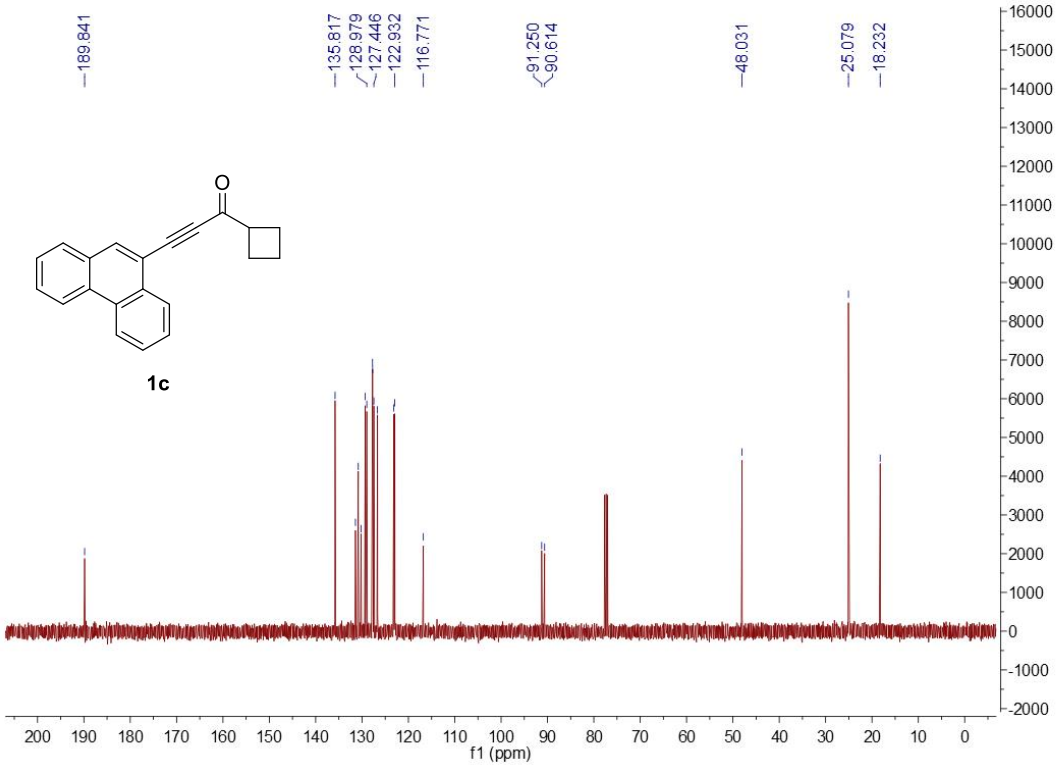
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1b



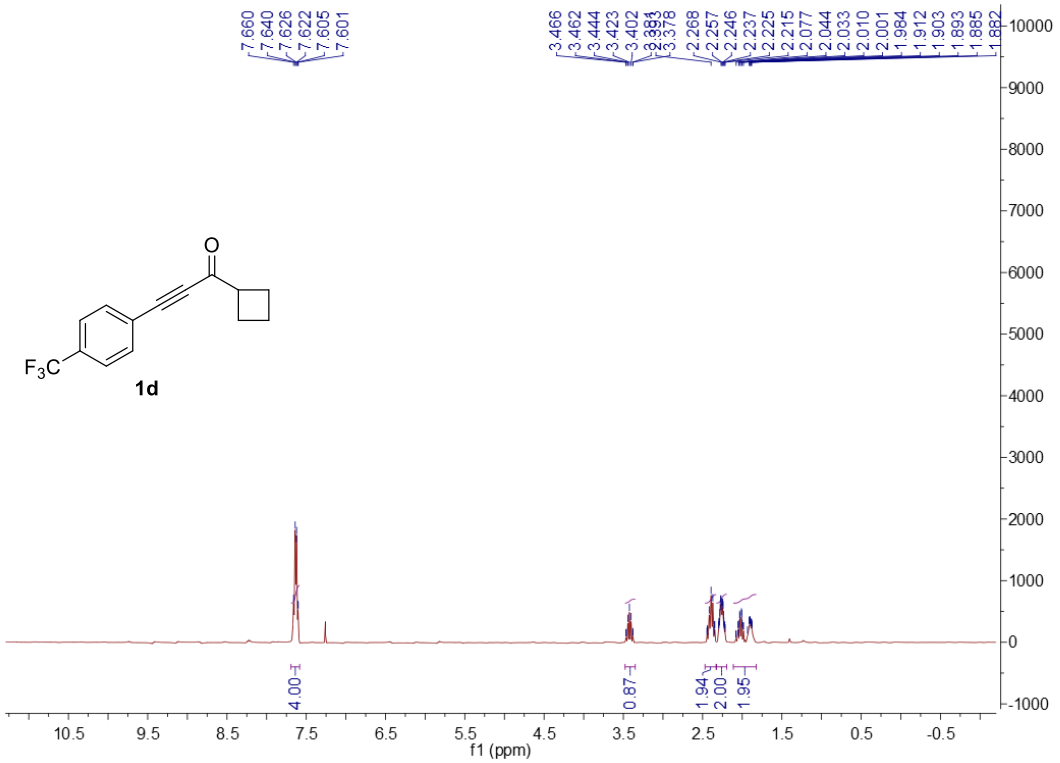
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1c



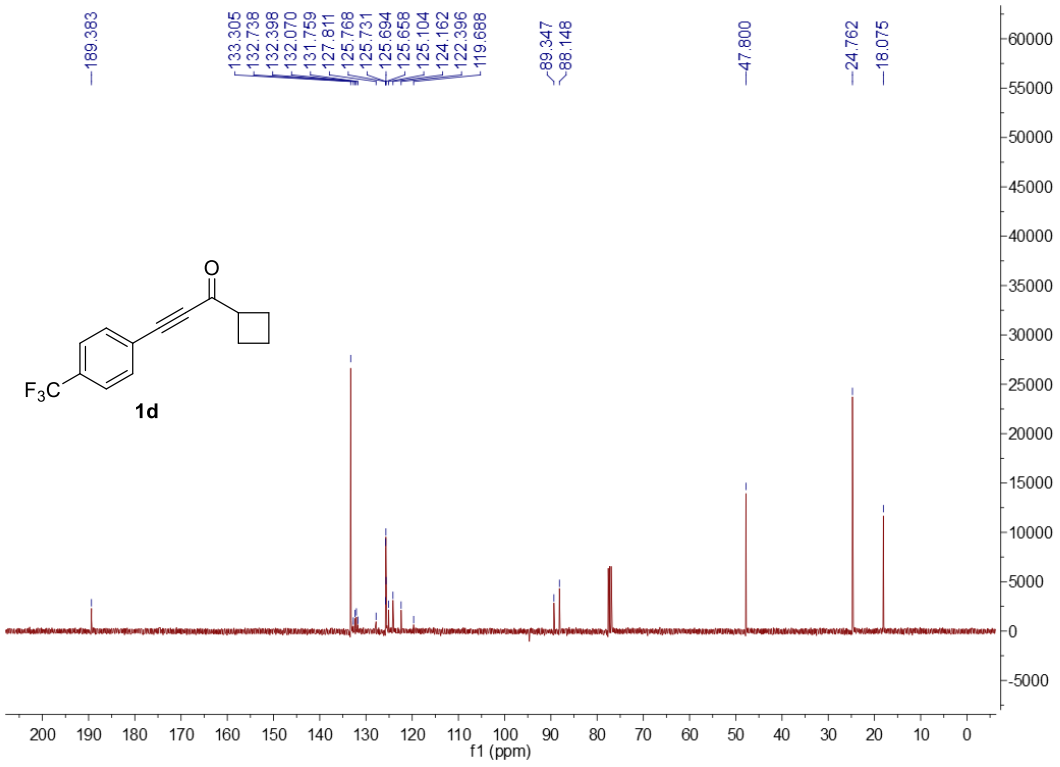
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1c



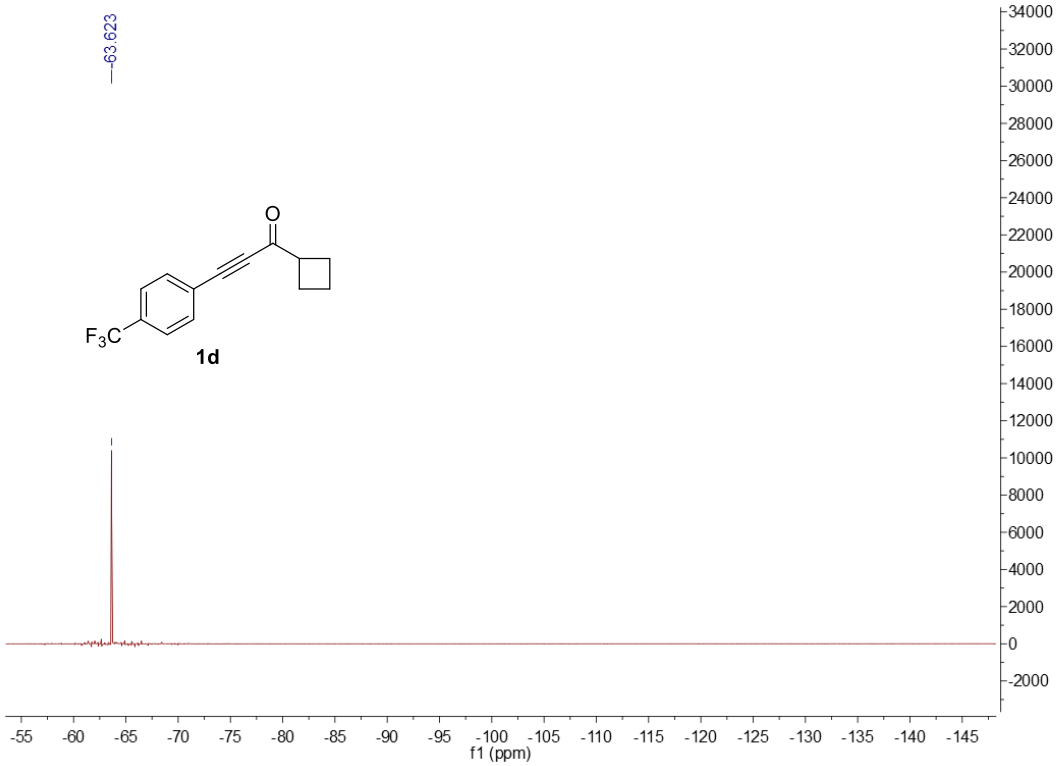
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1d



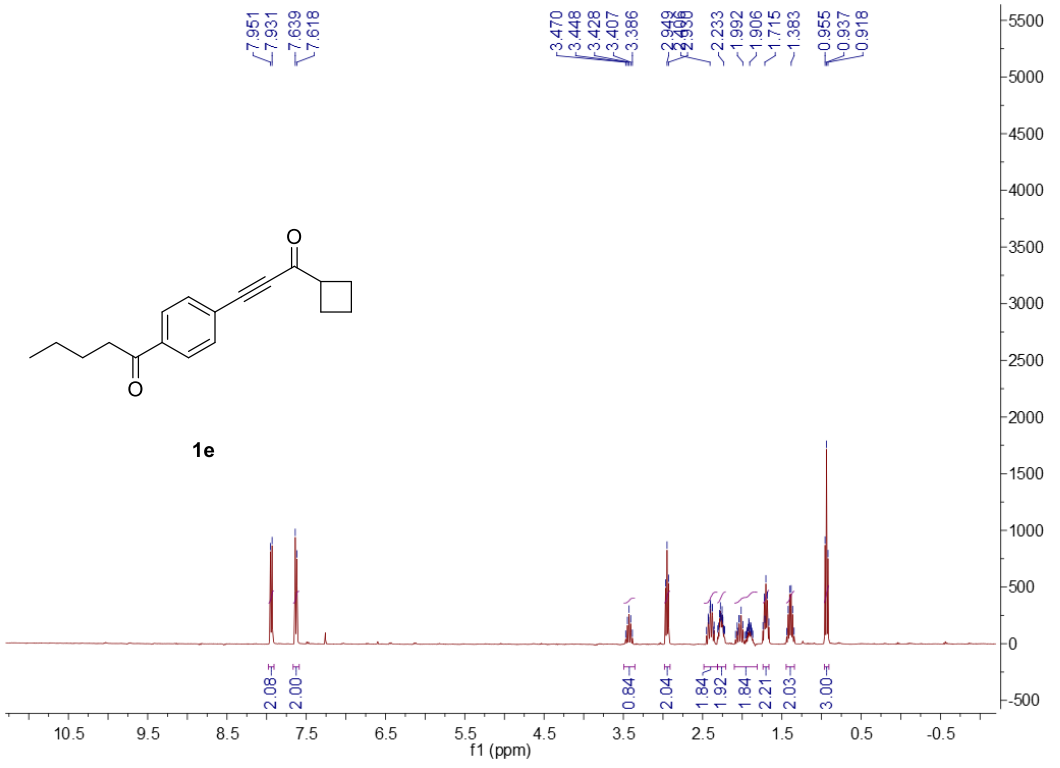
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1d



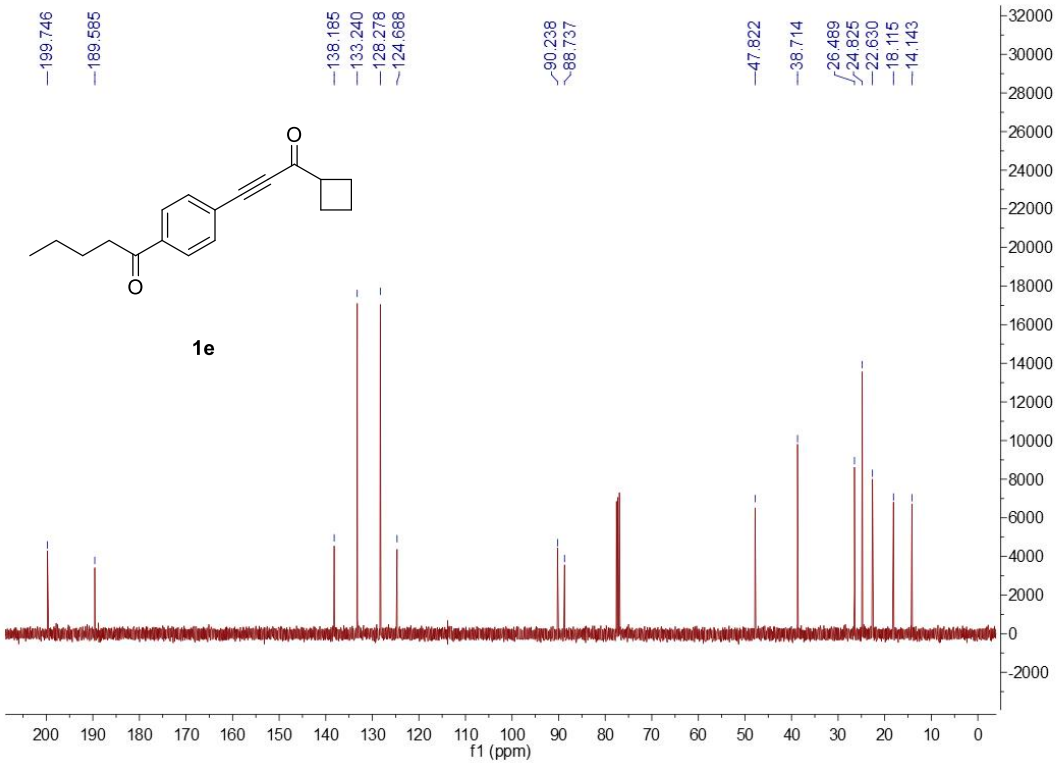
^{19}F NMR (376 MHz, $CDCl_3$) spectrum for 1d



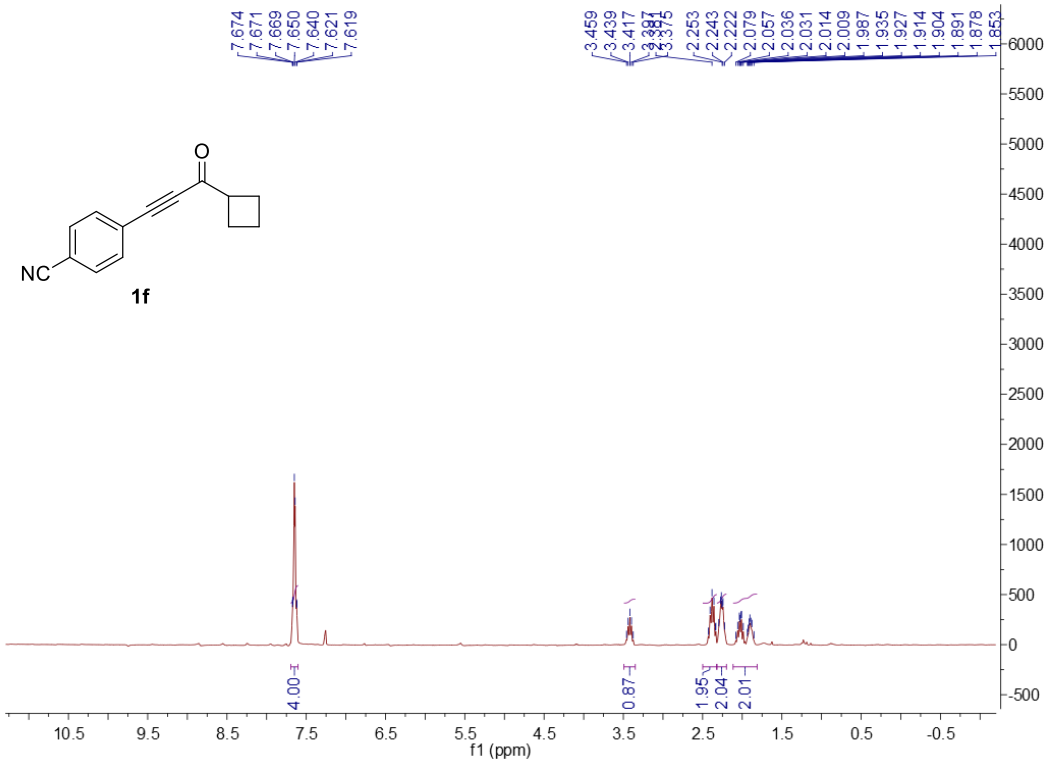
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1e



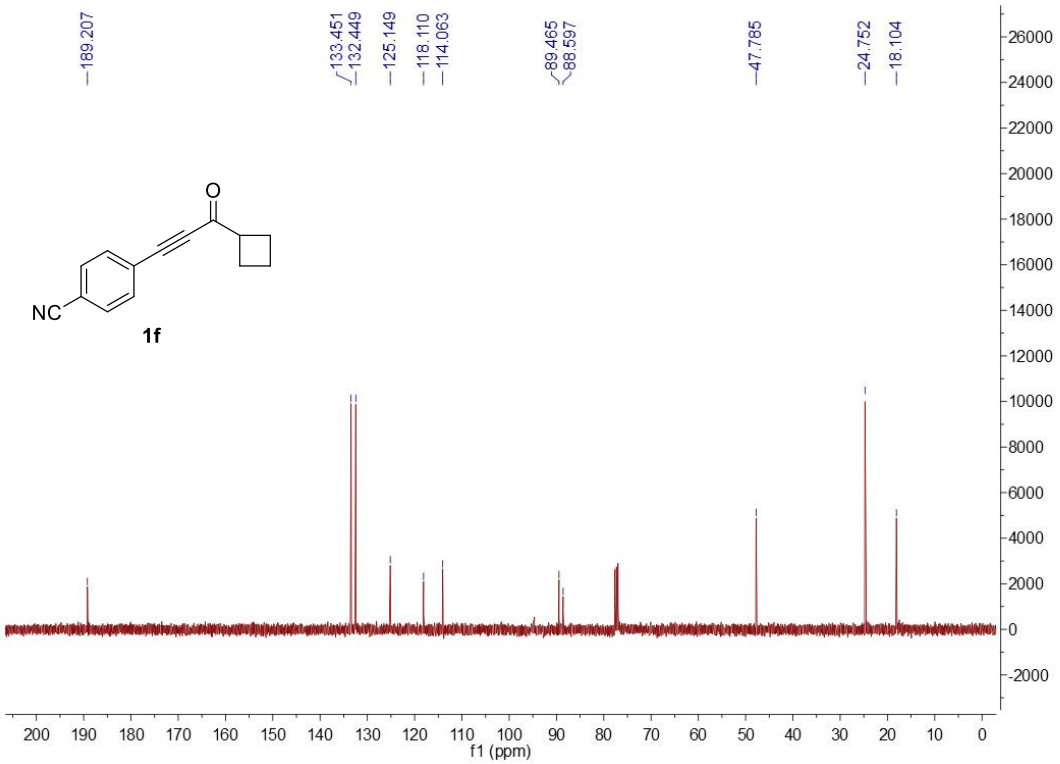
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1e



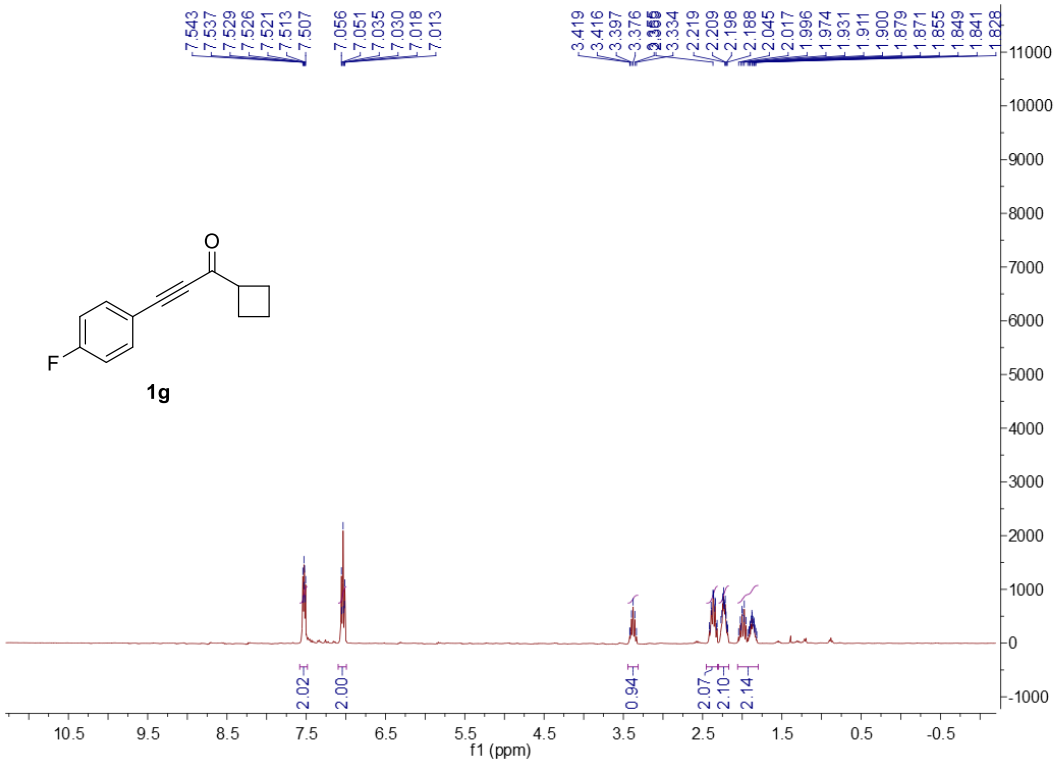
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1f



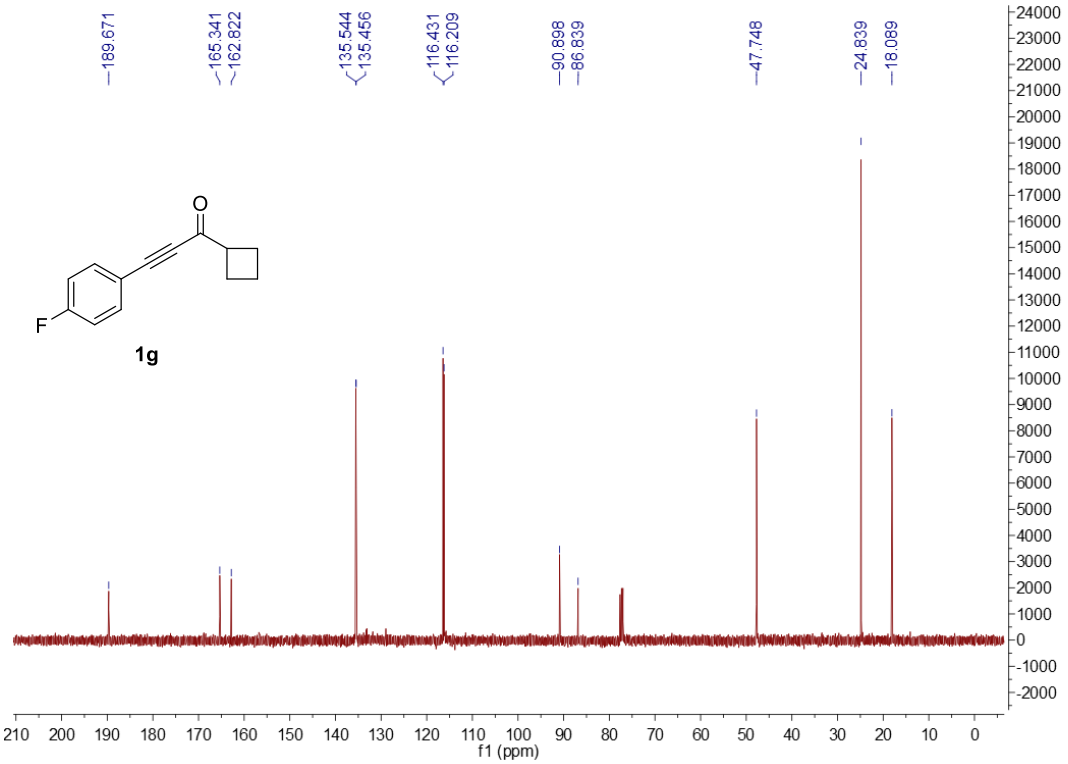
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1f



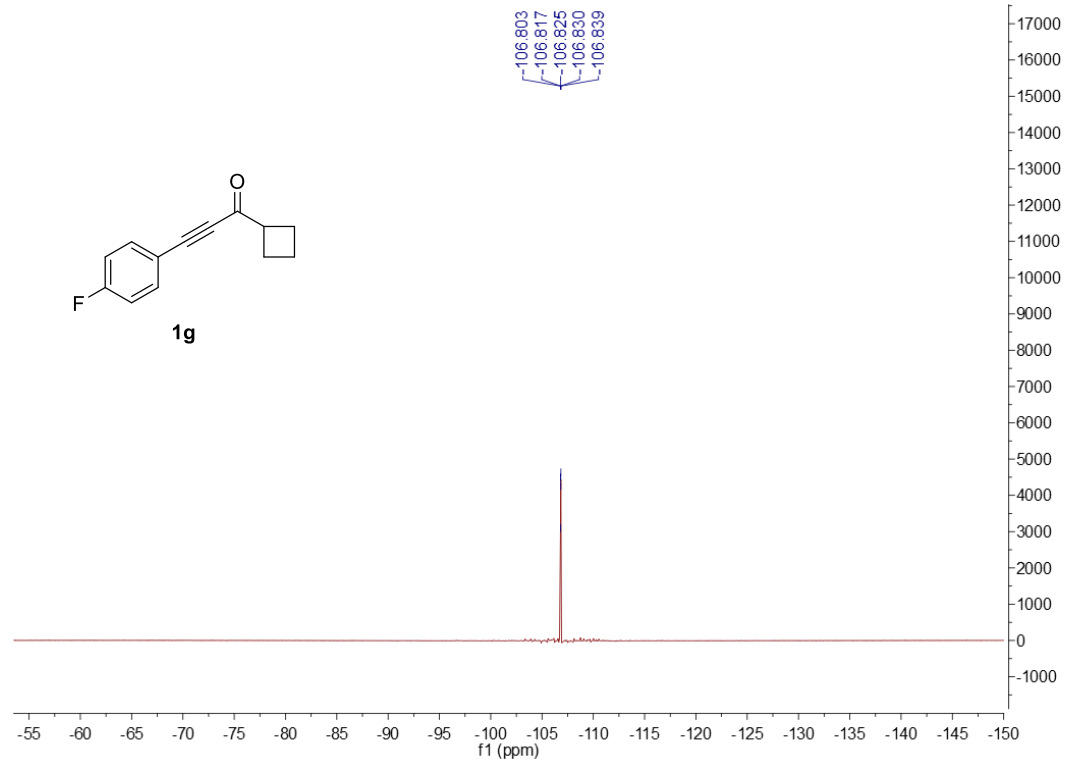
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1g



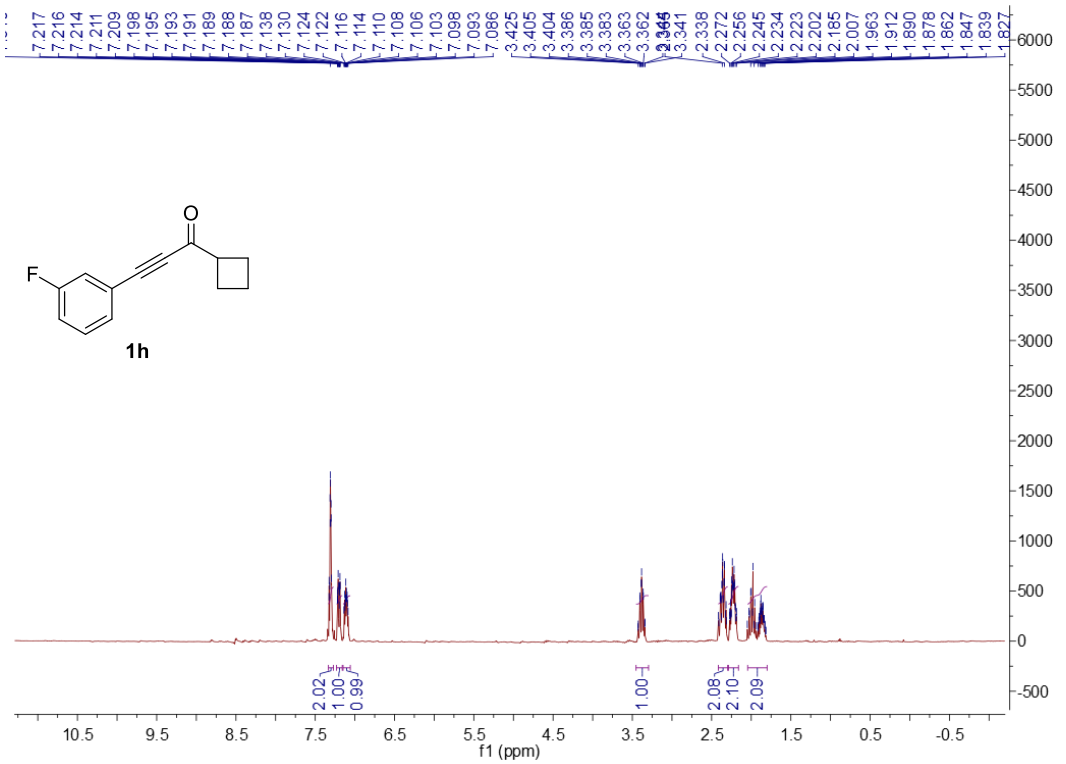
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1g



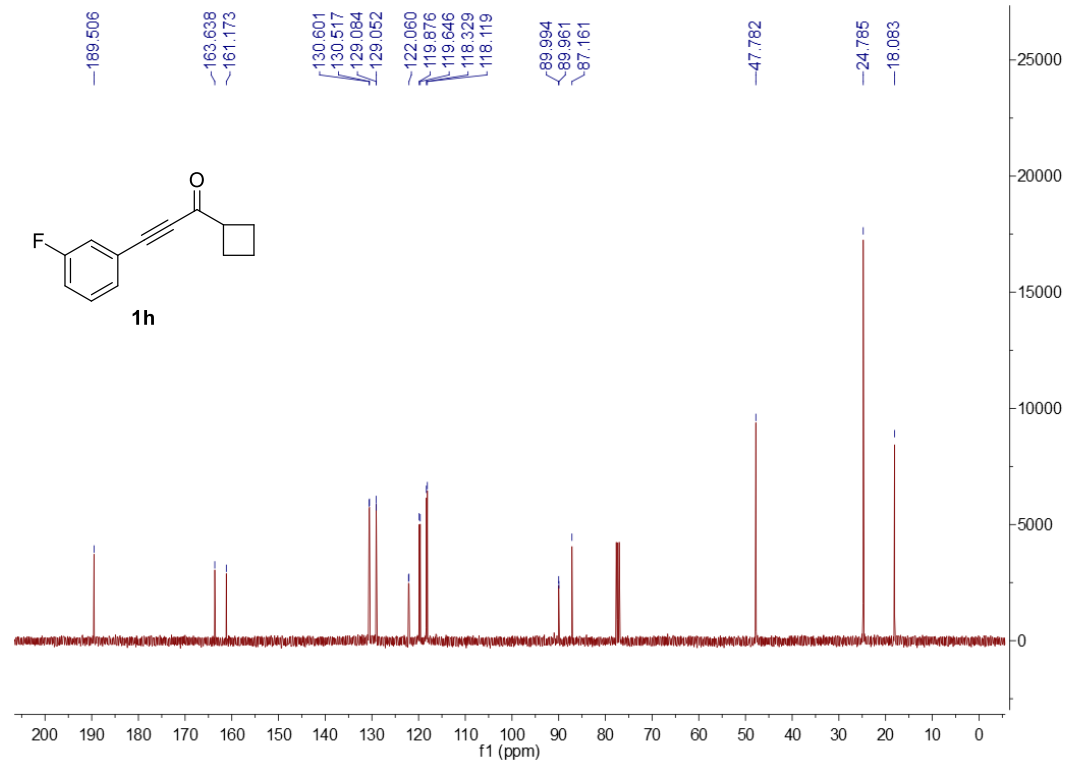
^{19}F NMR (376 MHz, $CDCl_3$) spectrum for 1g



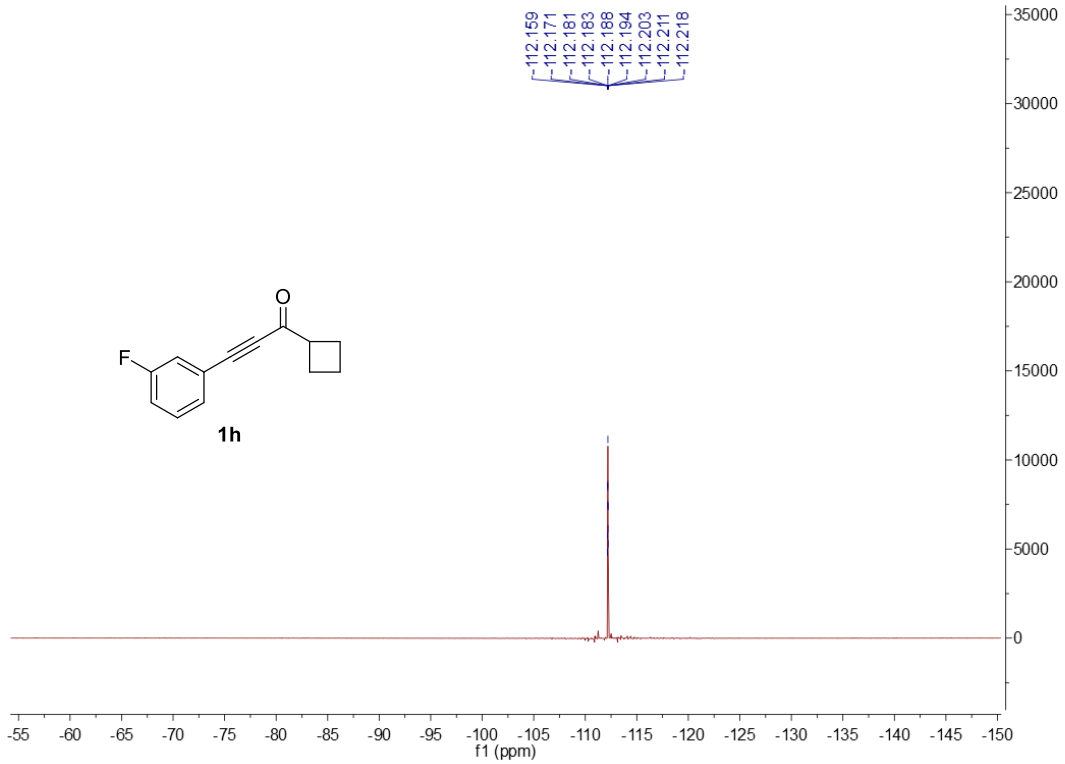
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1h



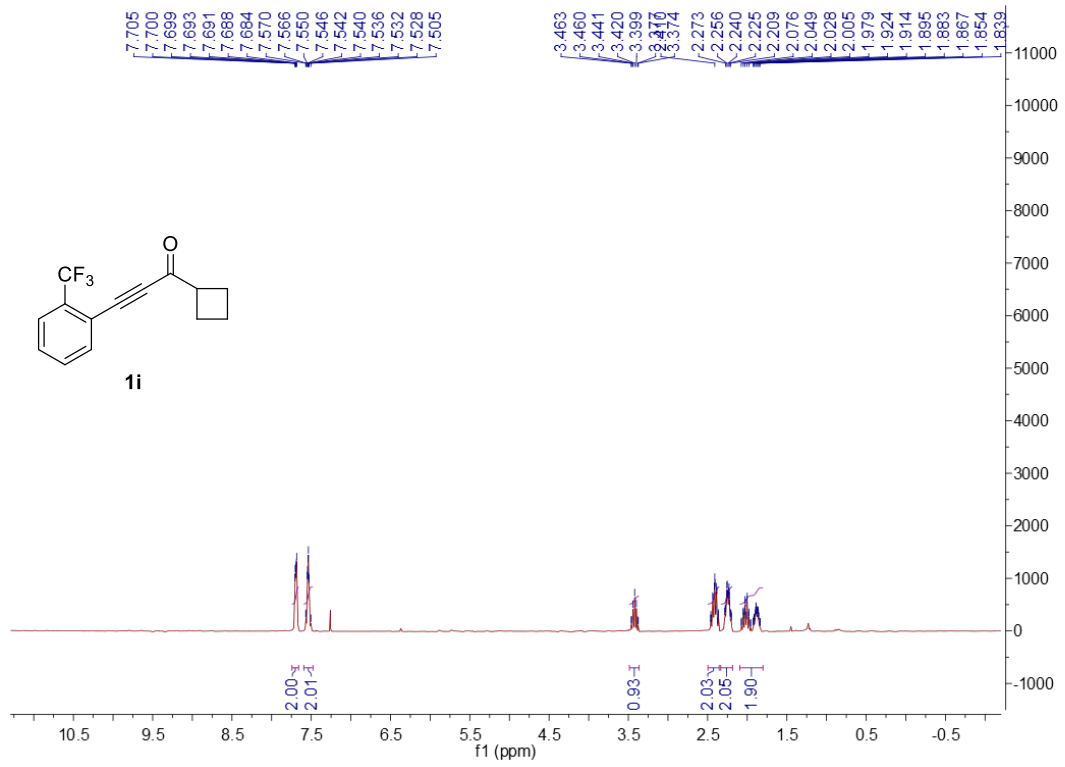
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1h



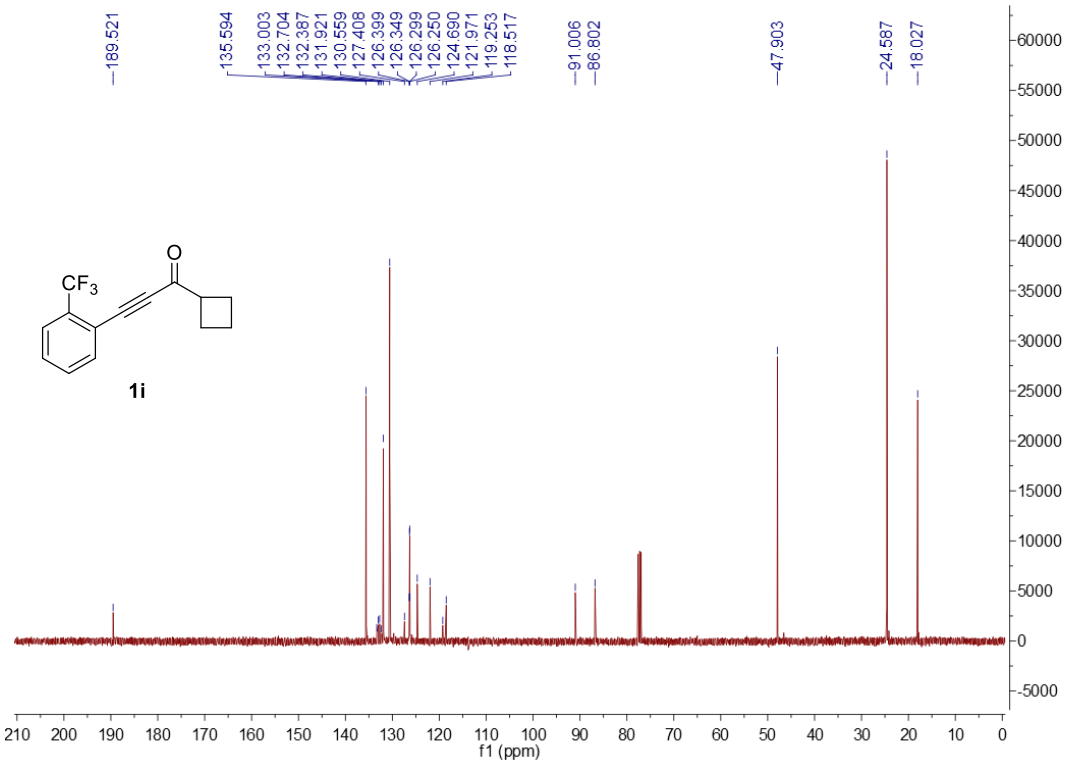
^{19}F NMR (376 MHz, $CDCl_3$) spectrum for 1h



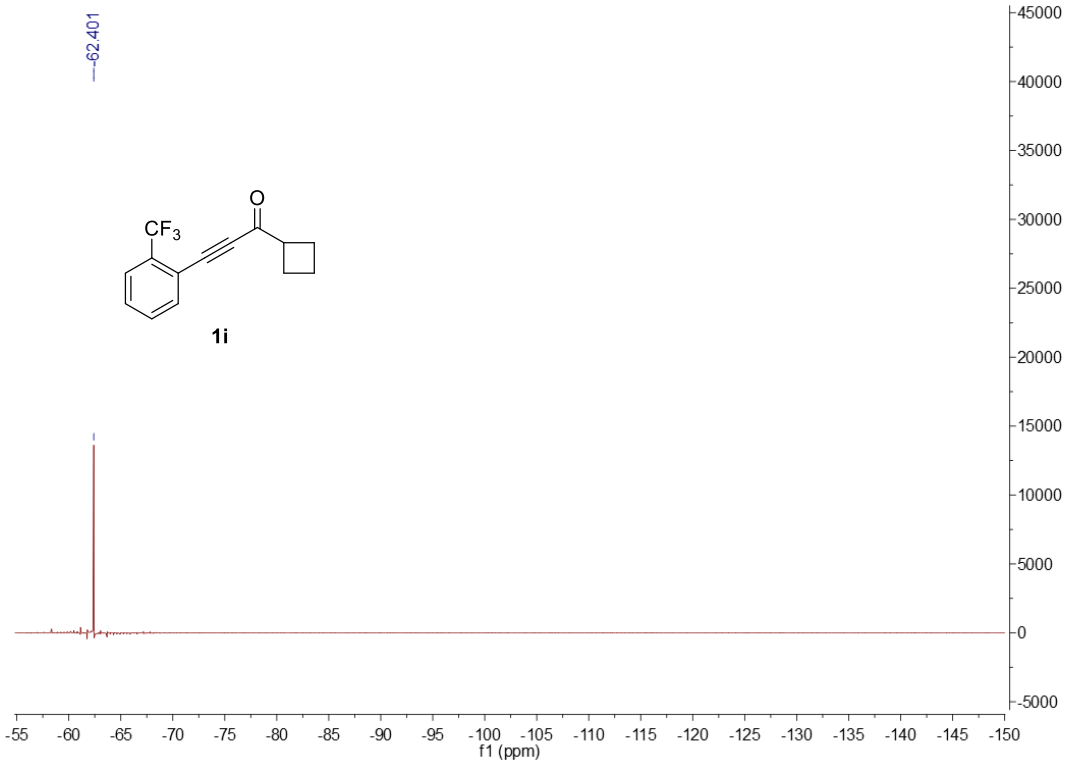
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1i



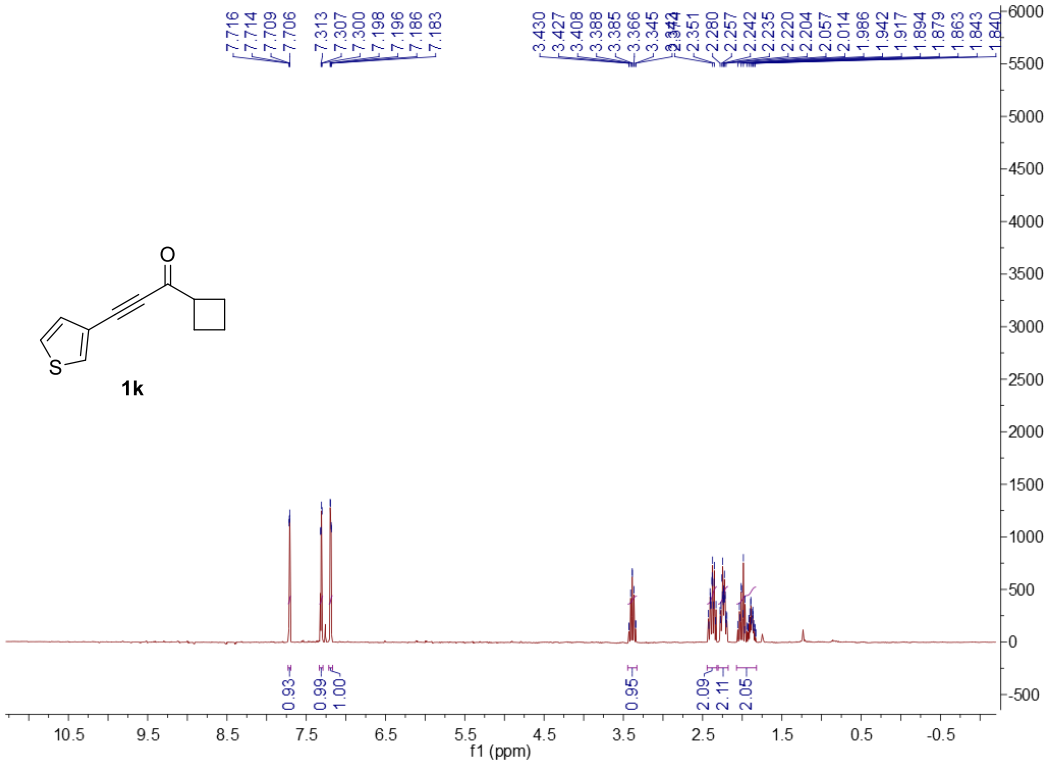
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1i



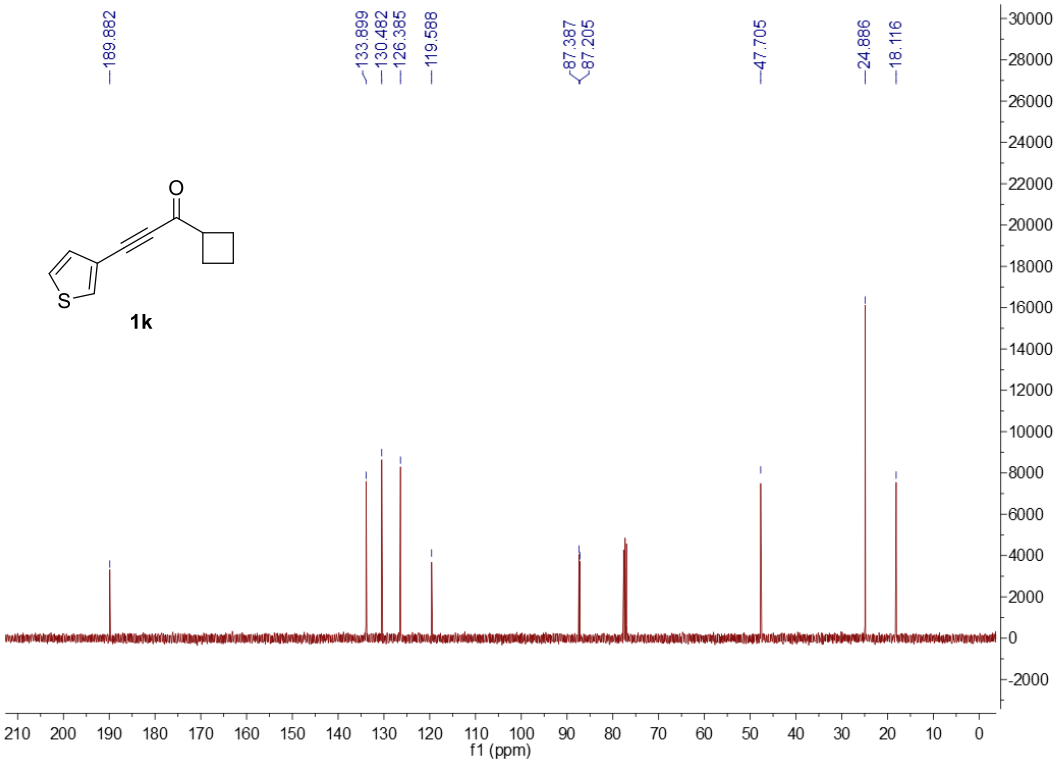
^{19}F NMR (376 MHz, $CDCl_3$) spectrum for 1i



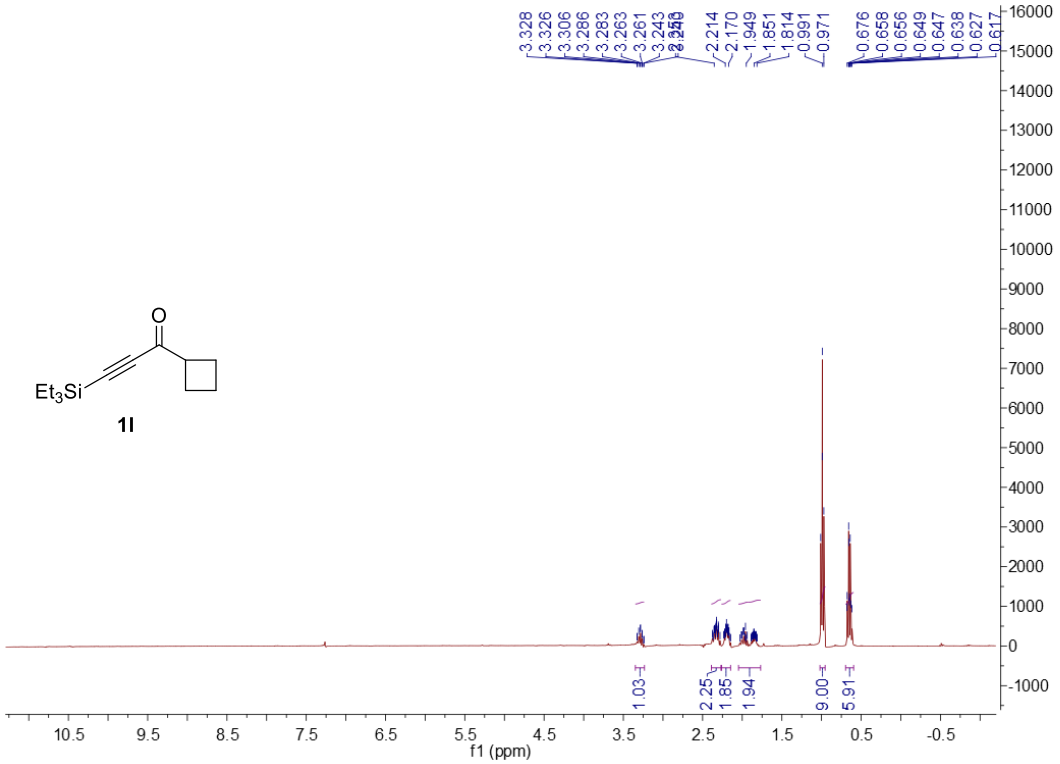
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1k



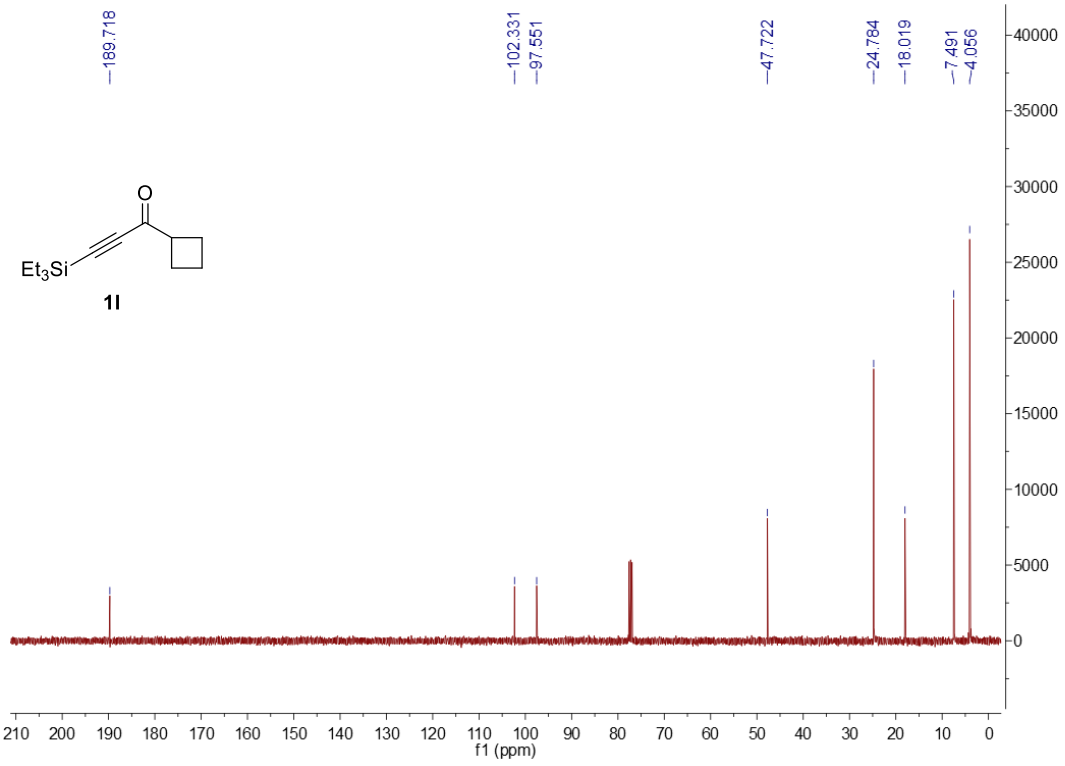
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1k



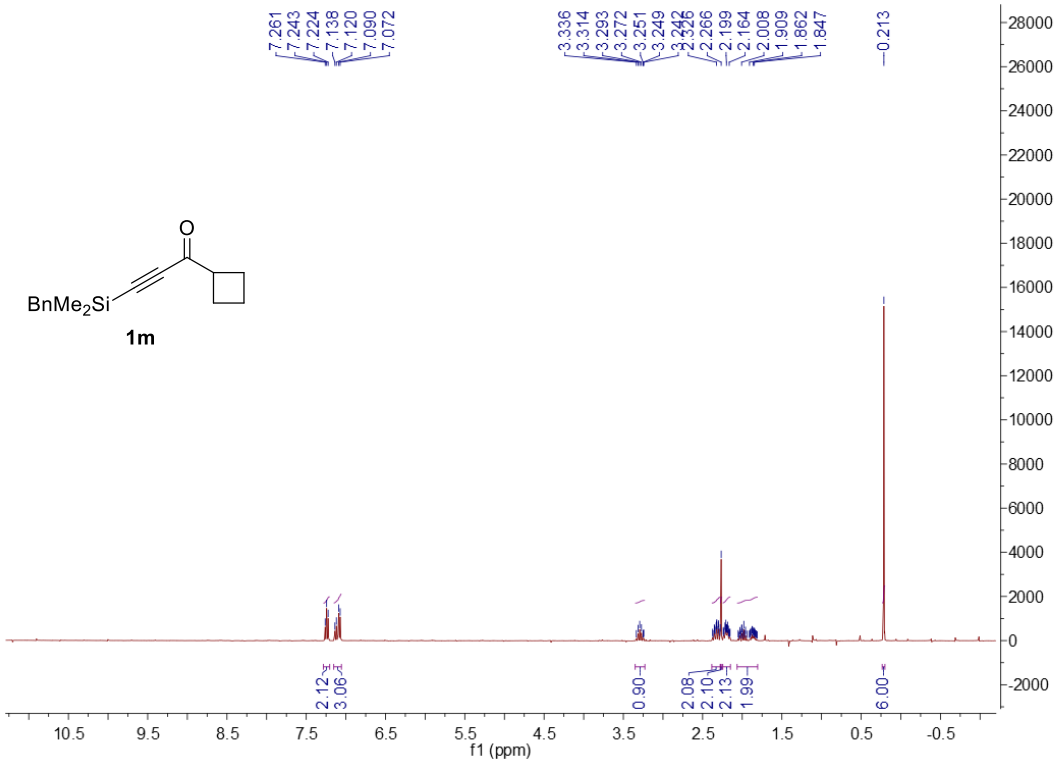
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1l



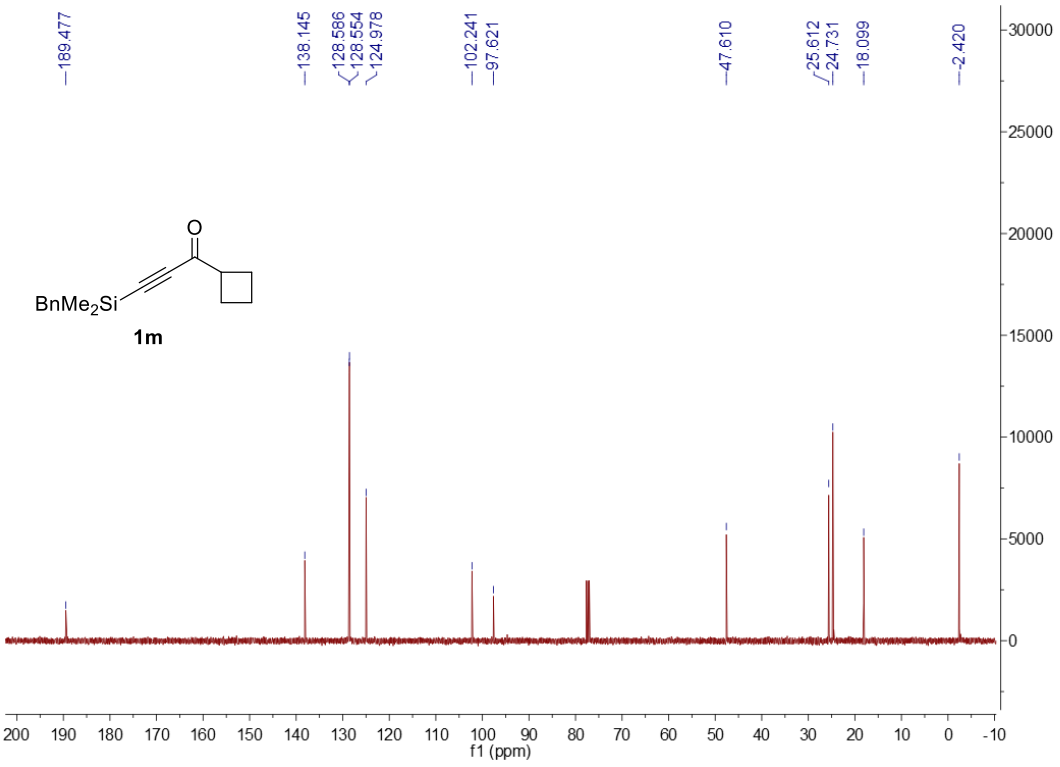
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1l



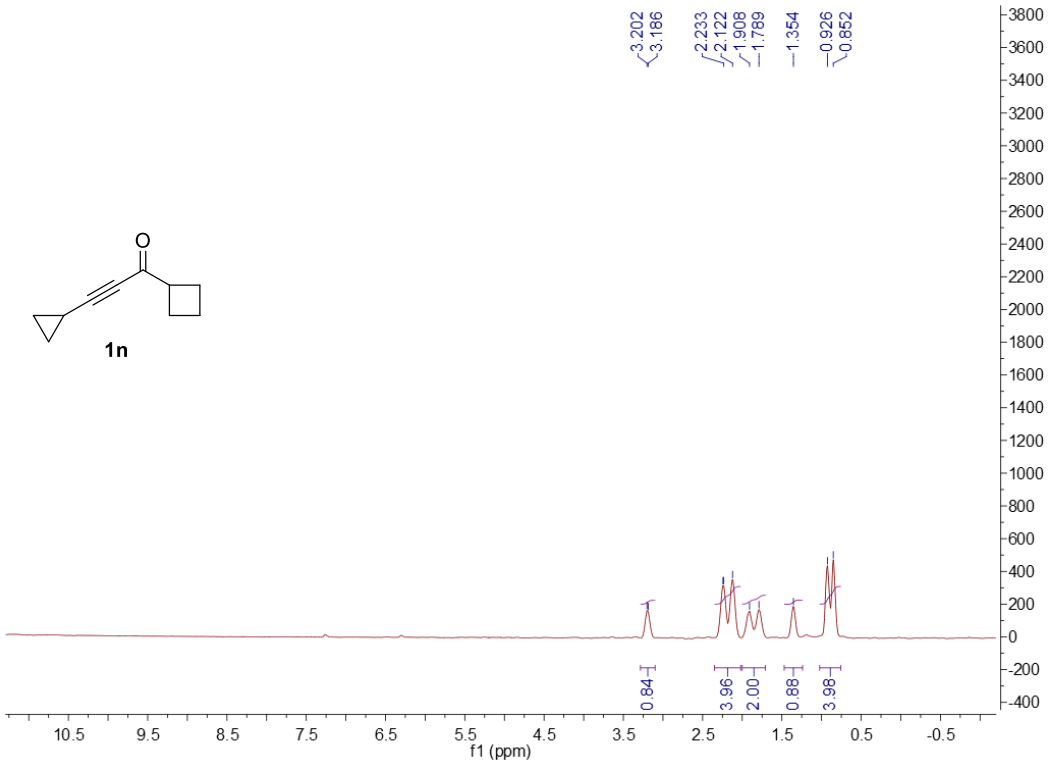
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1m



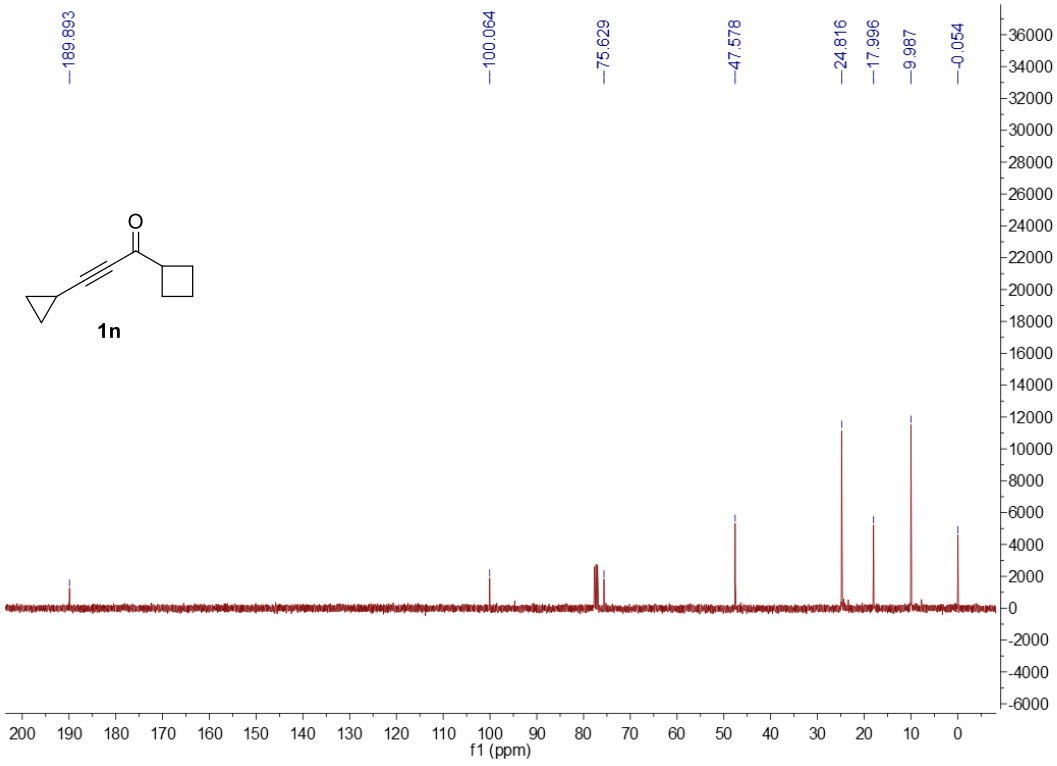
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1m



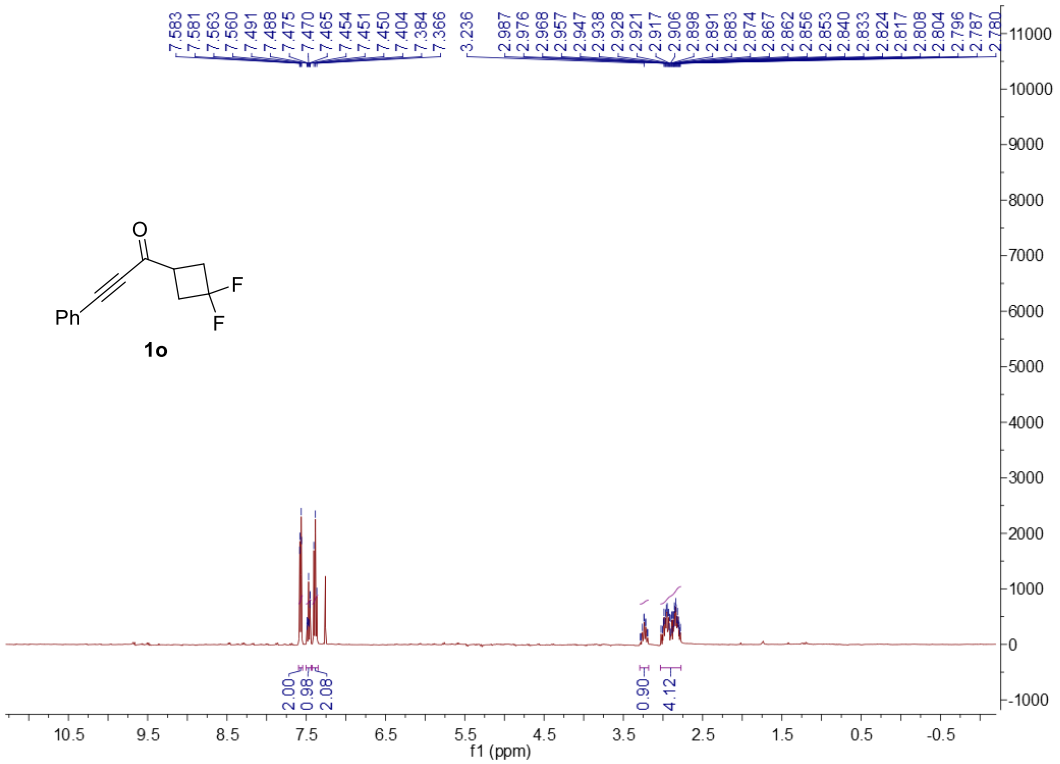
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1n



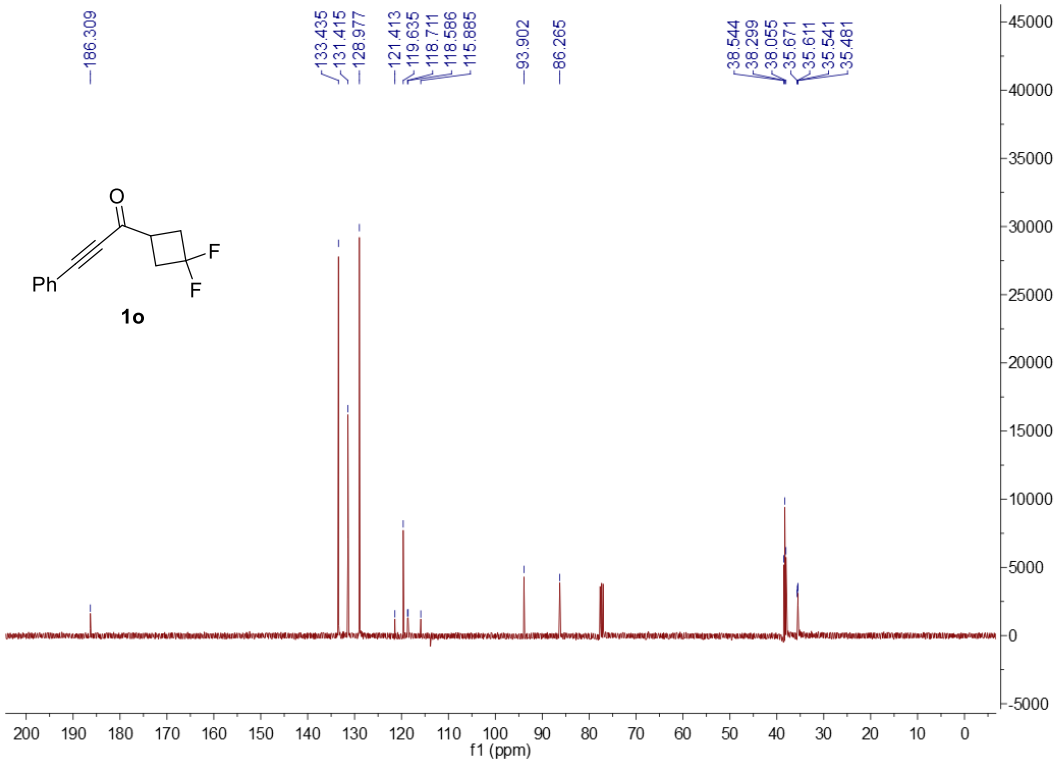
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1n



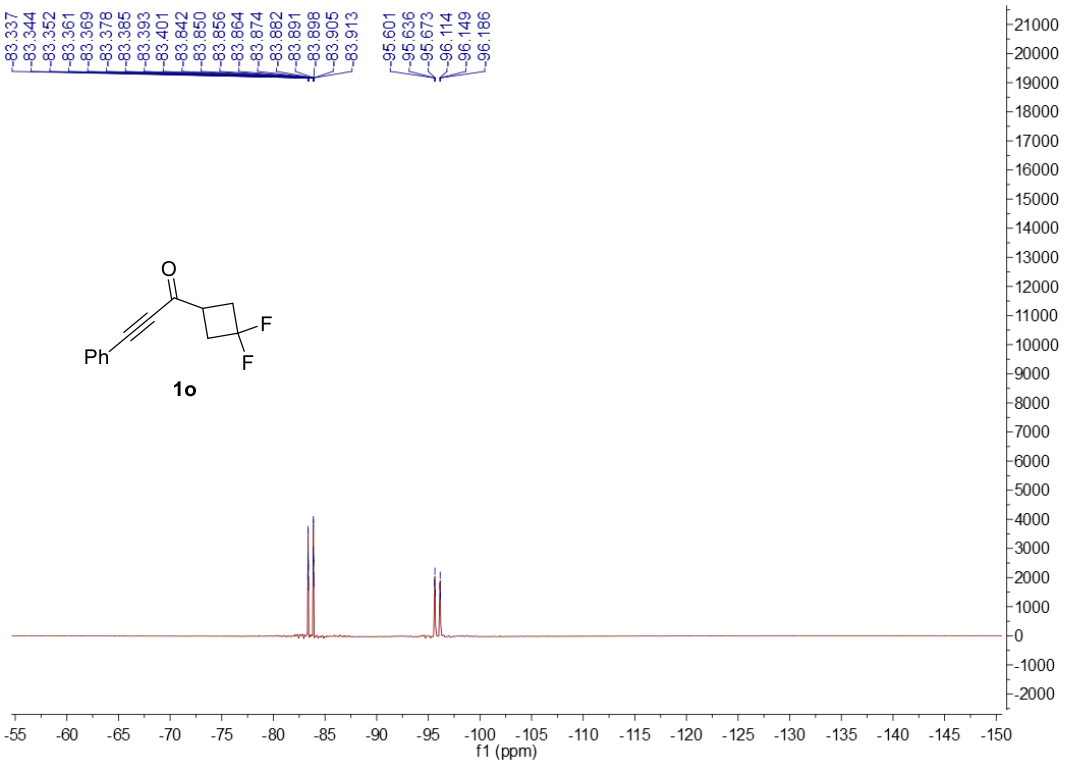
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1o



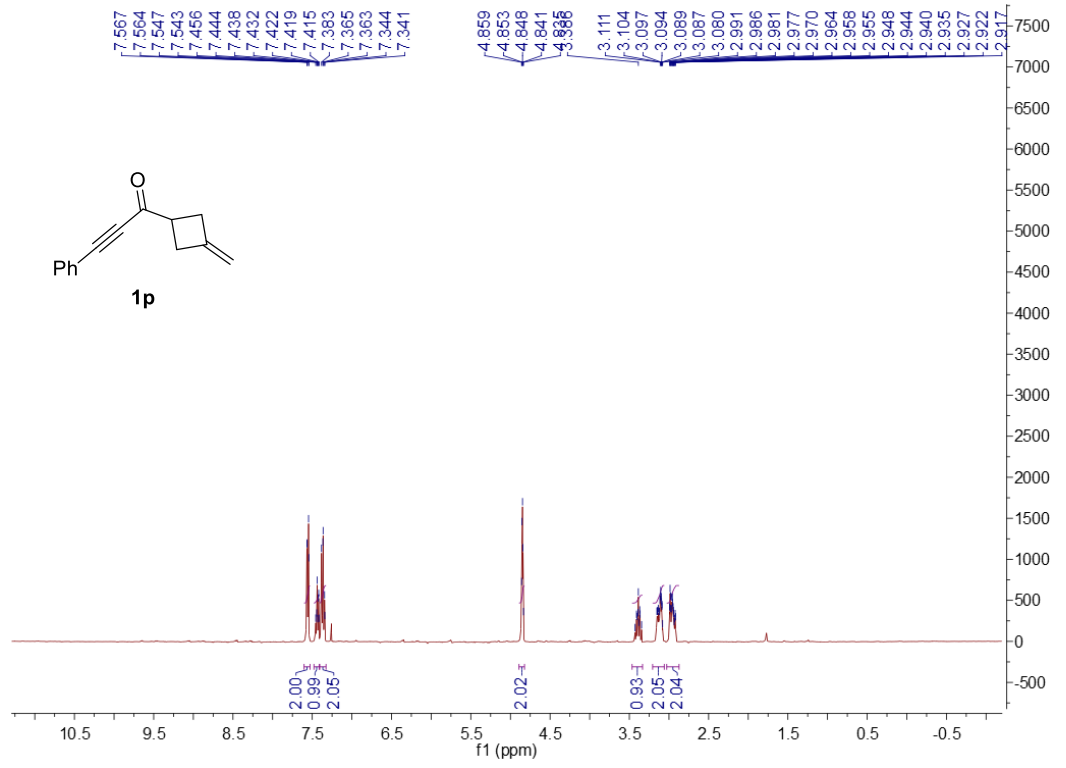
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1o



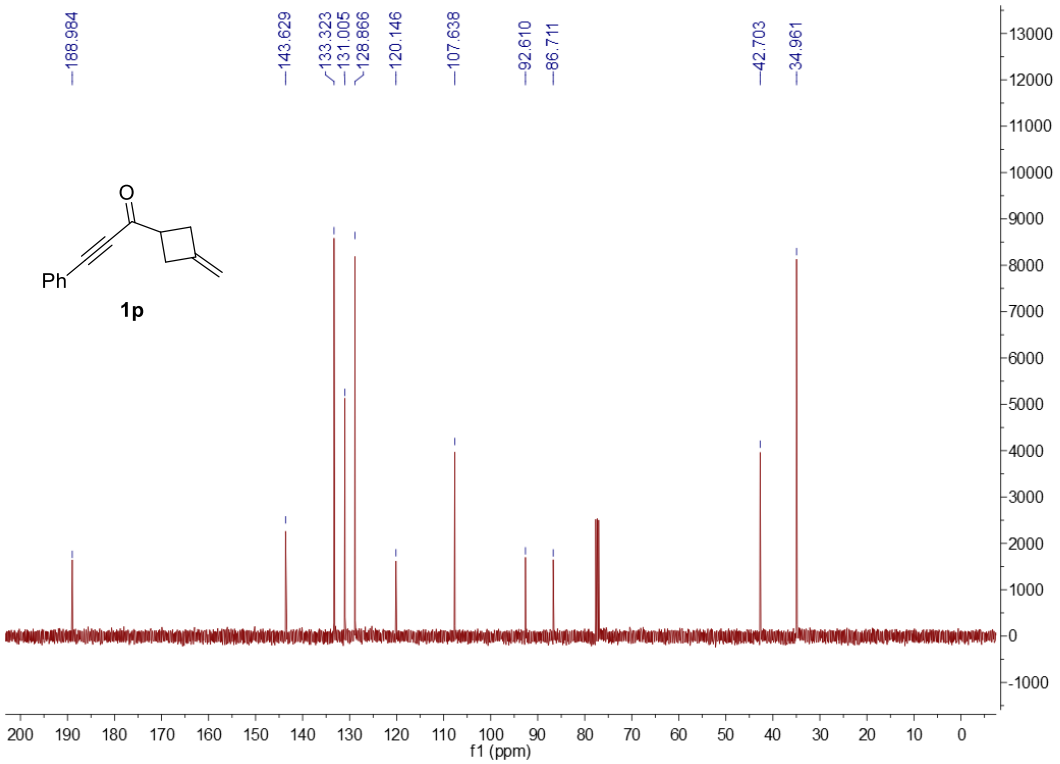
^{19}F NMR (376 MHz, $CDCl_3$) spectrum for 1o



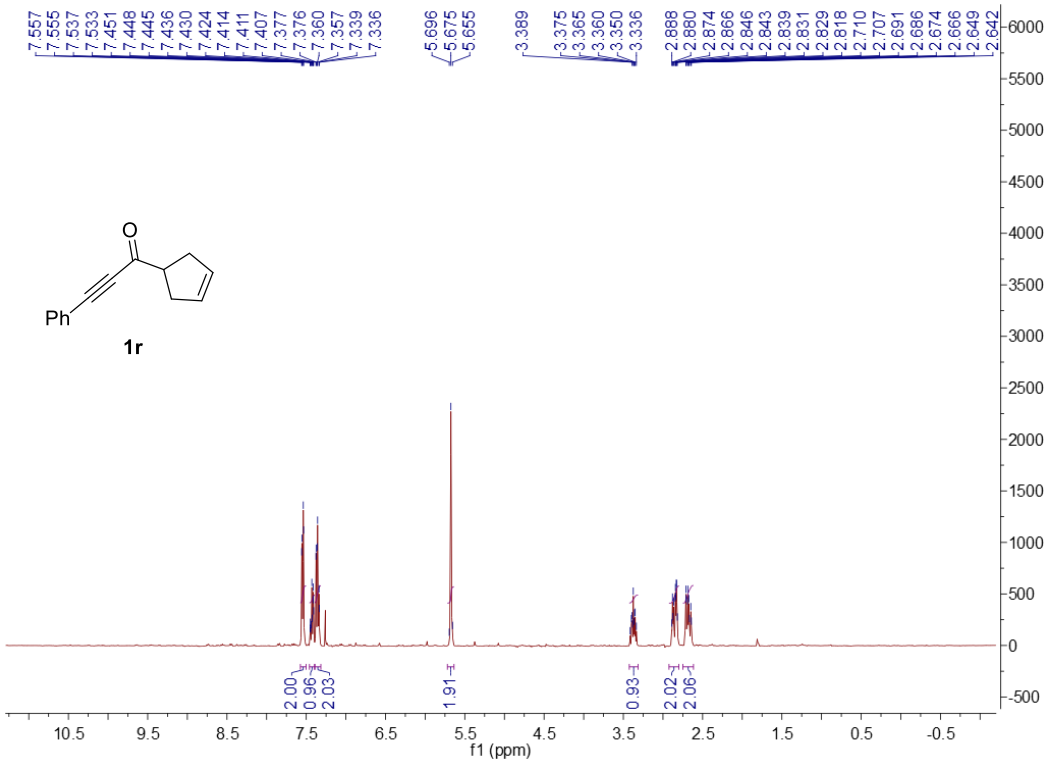
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1p



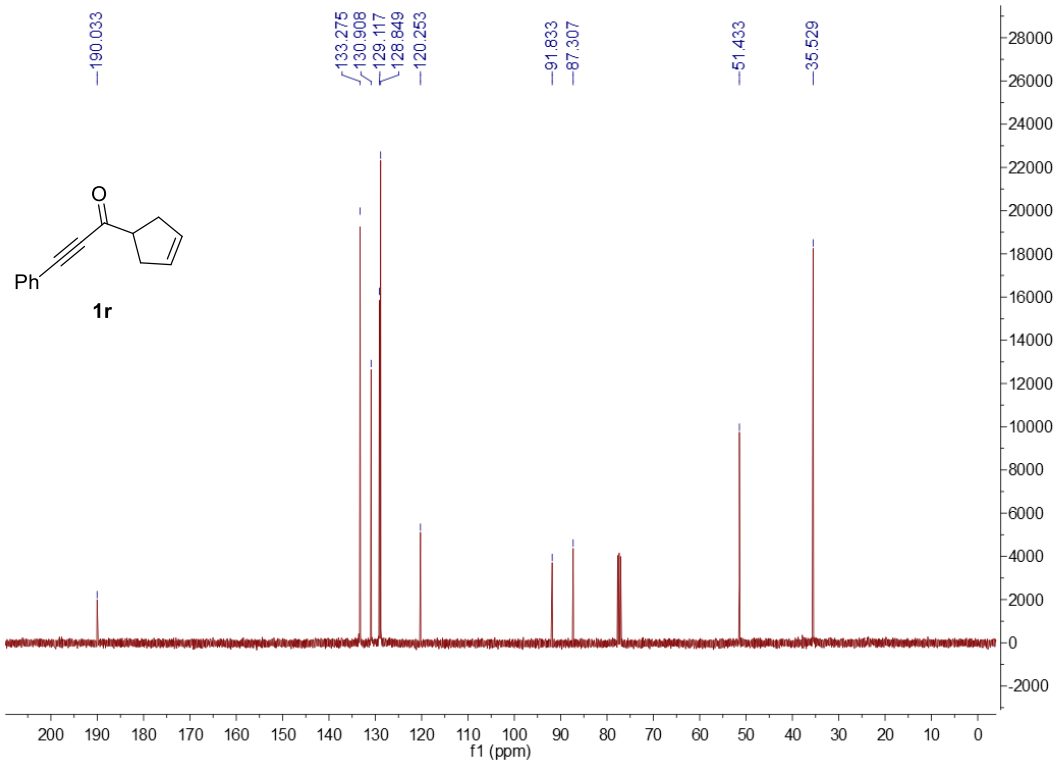
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1p



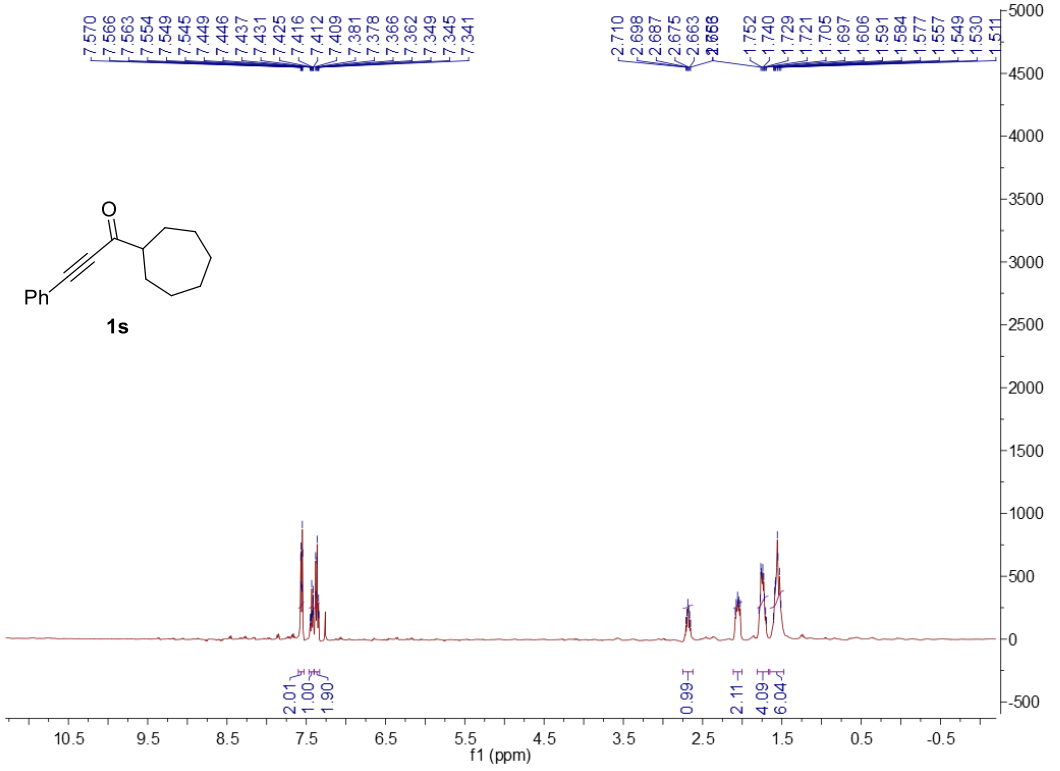
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1r



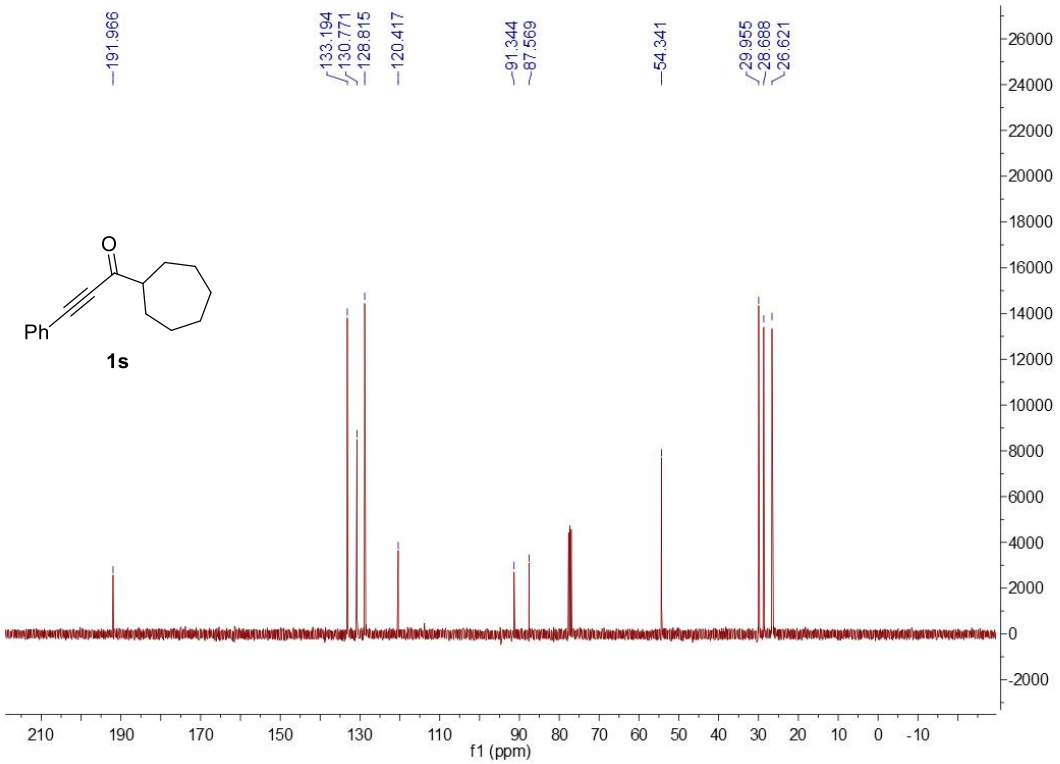
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1r



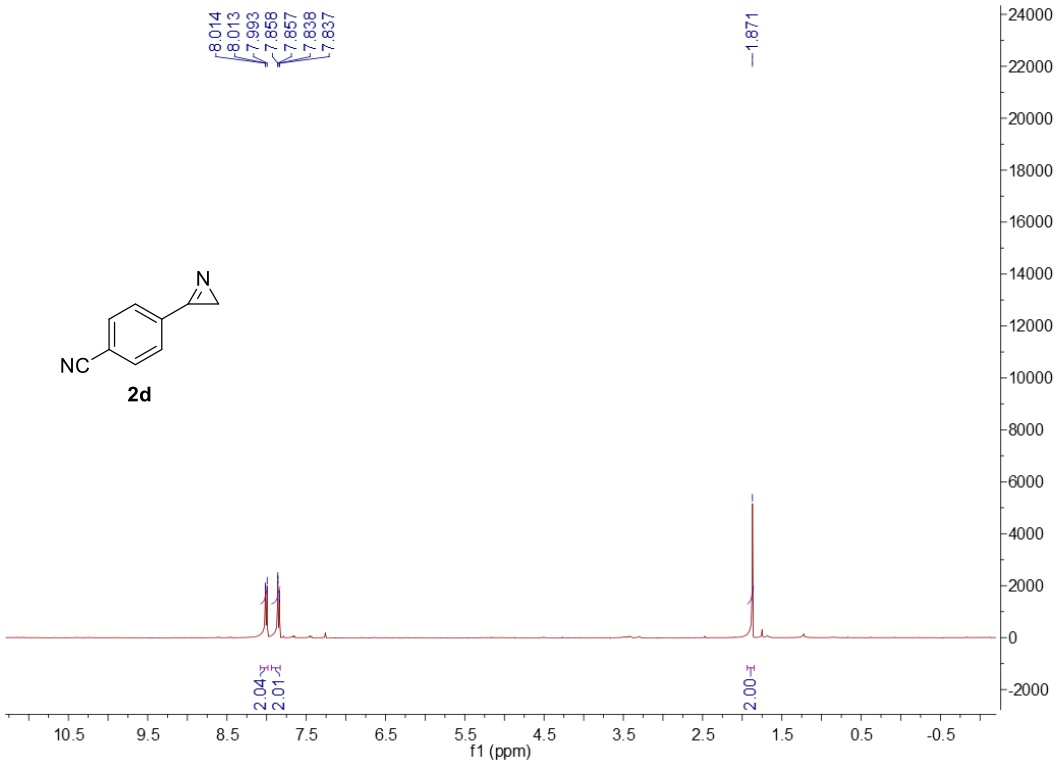
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 1s



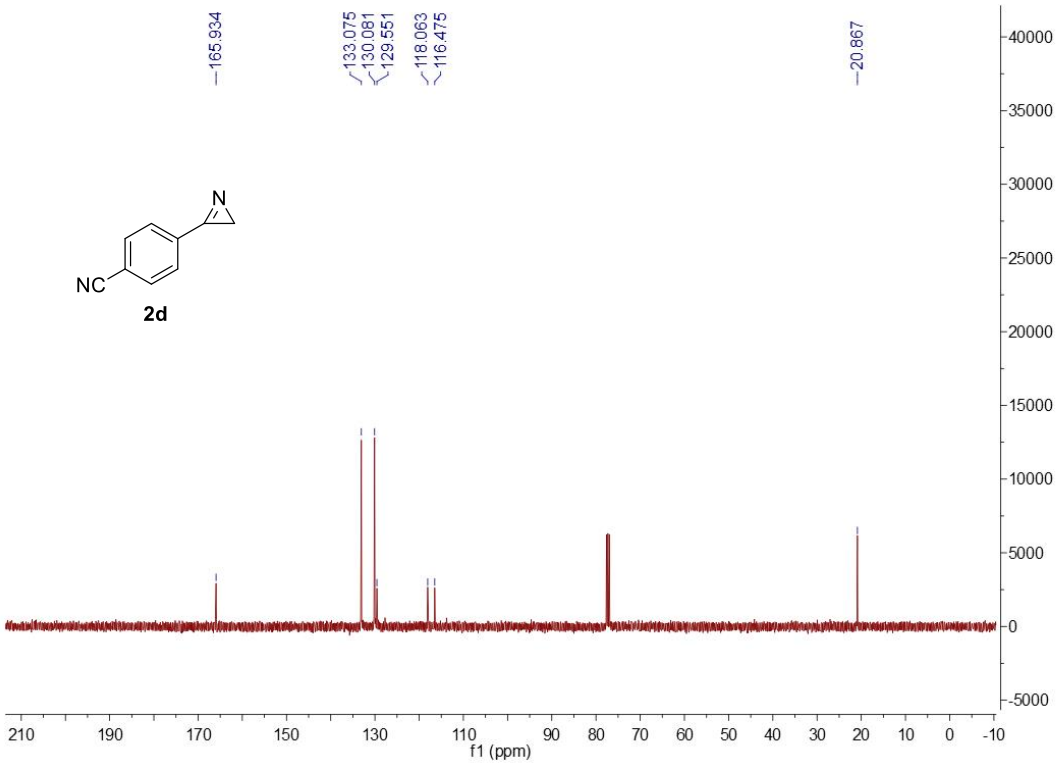
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 1s



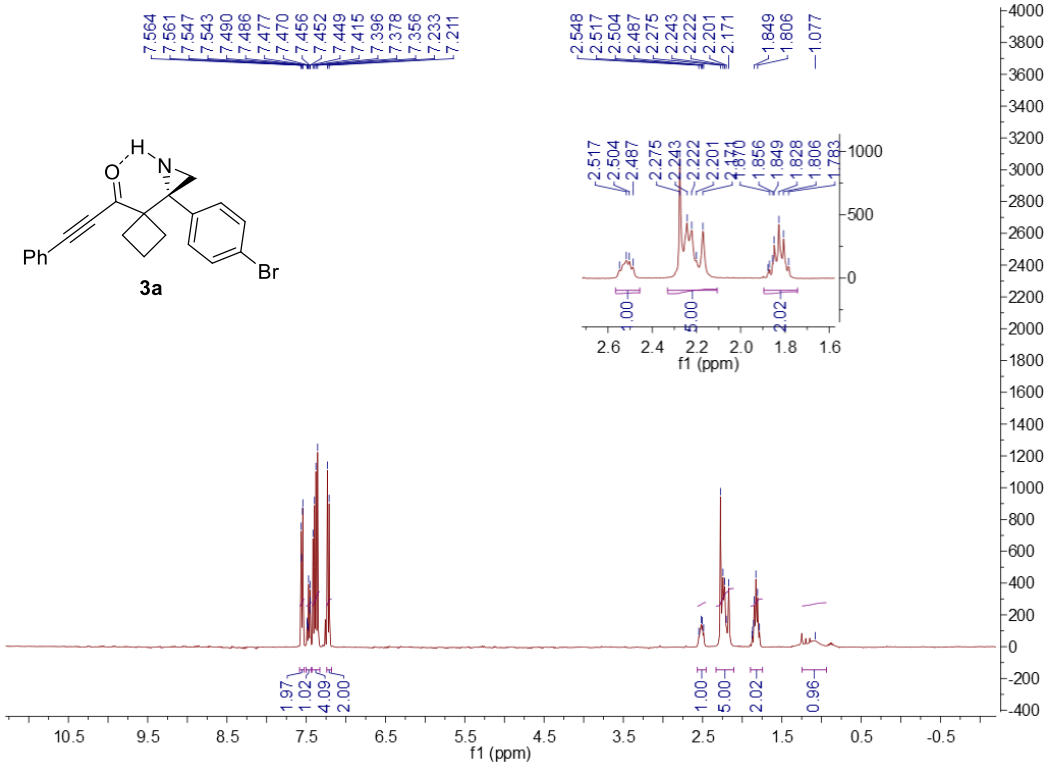
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 2d



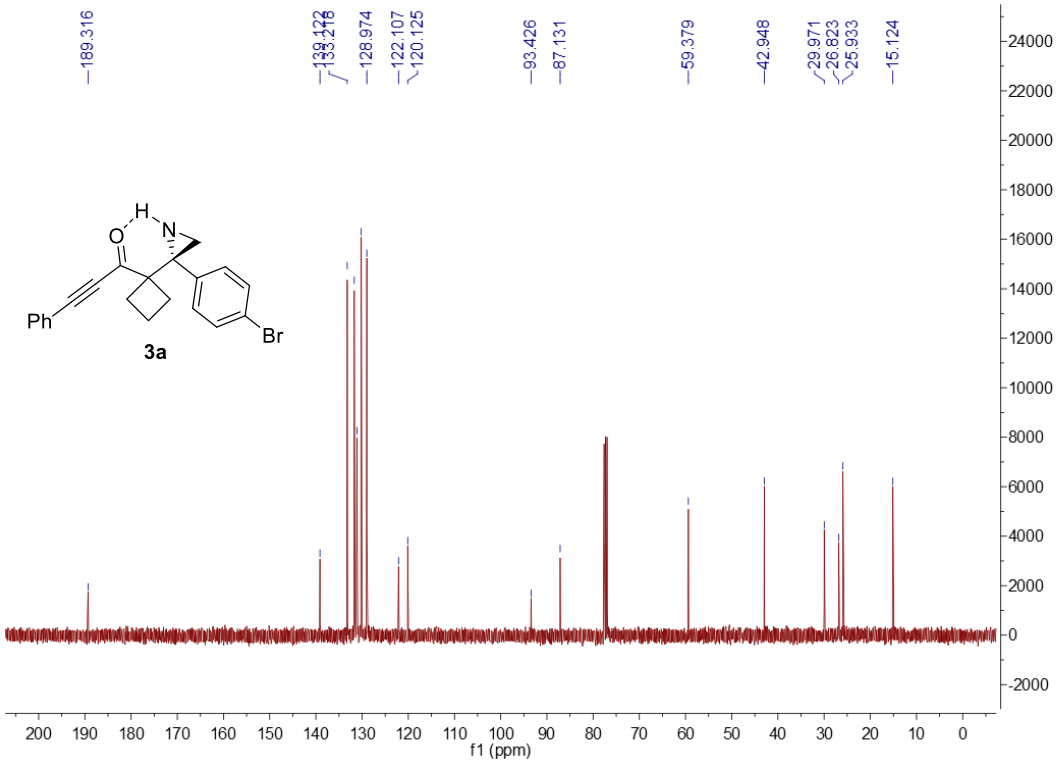
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 2d



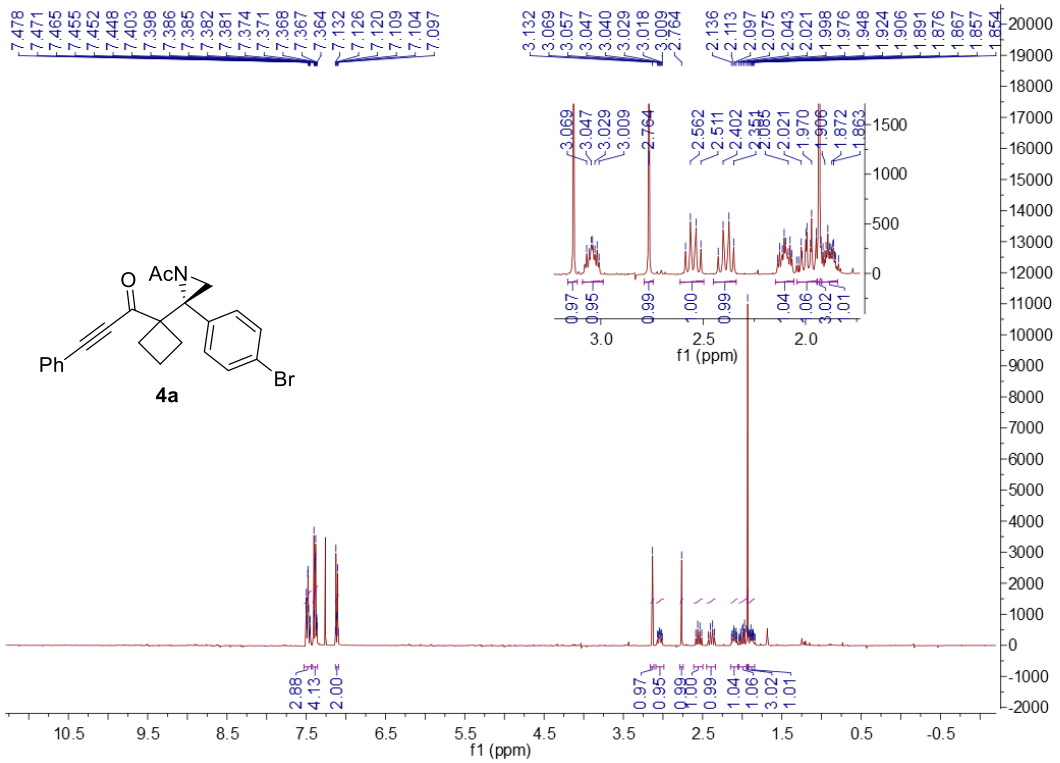
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3a



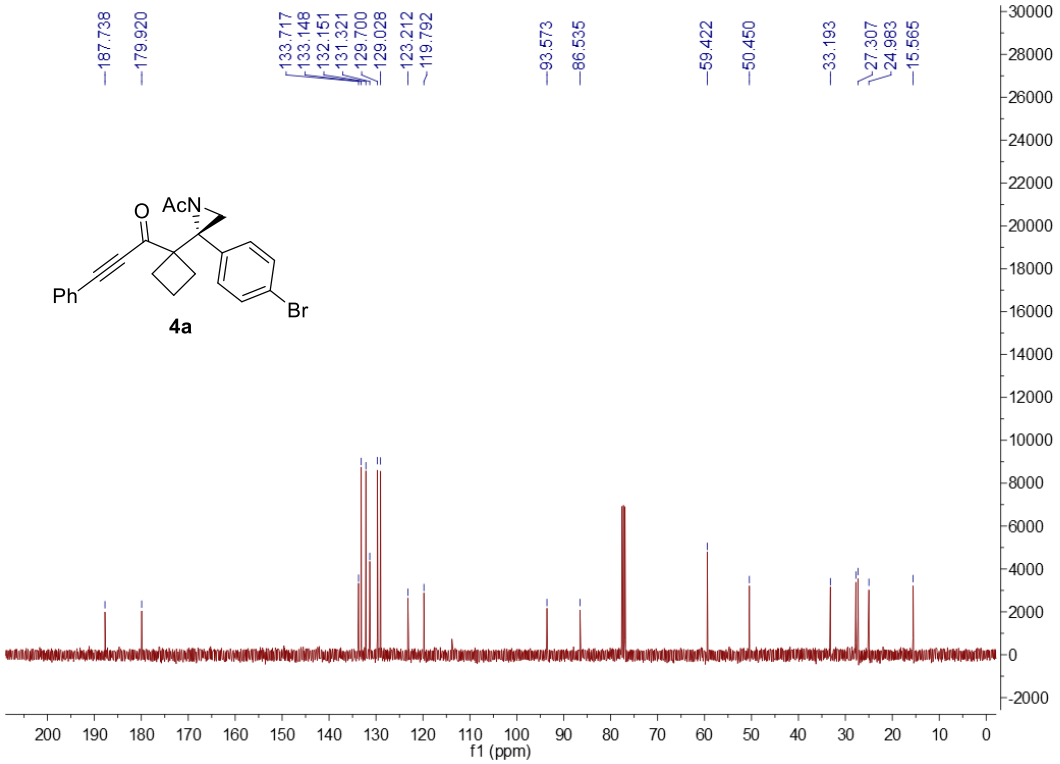
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 3a



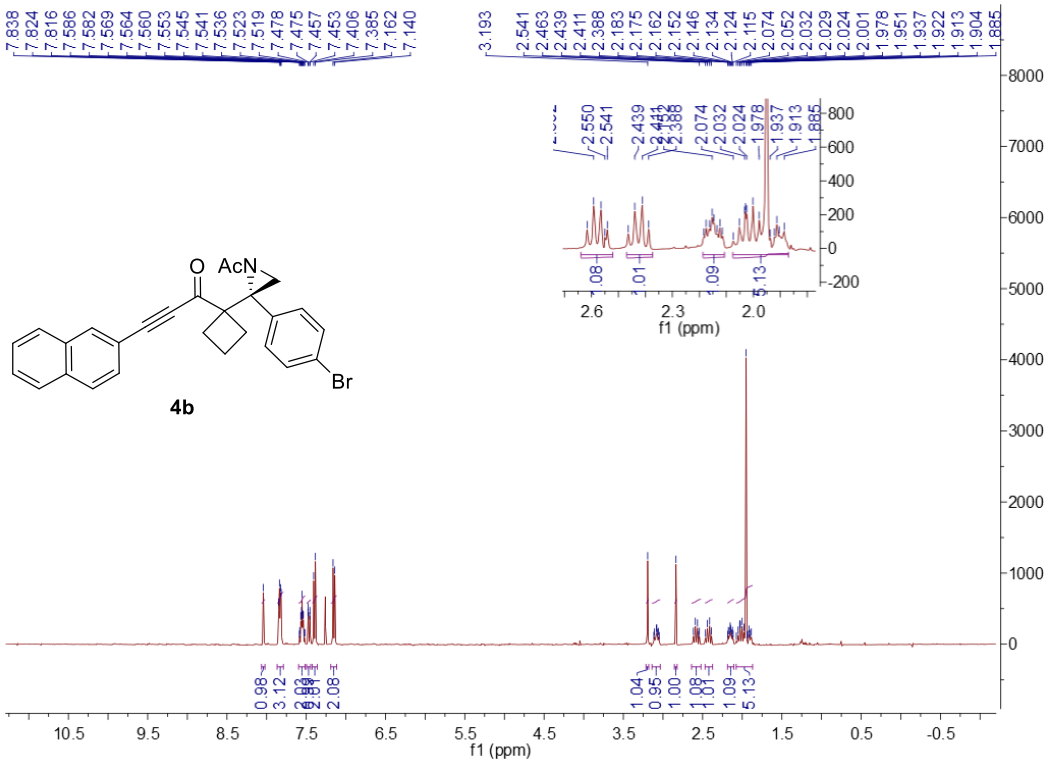
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4a



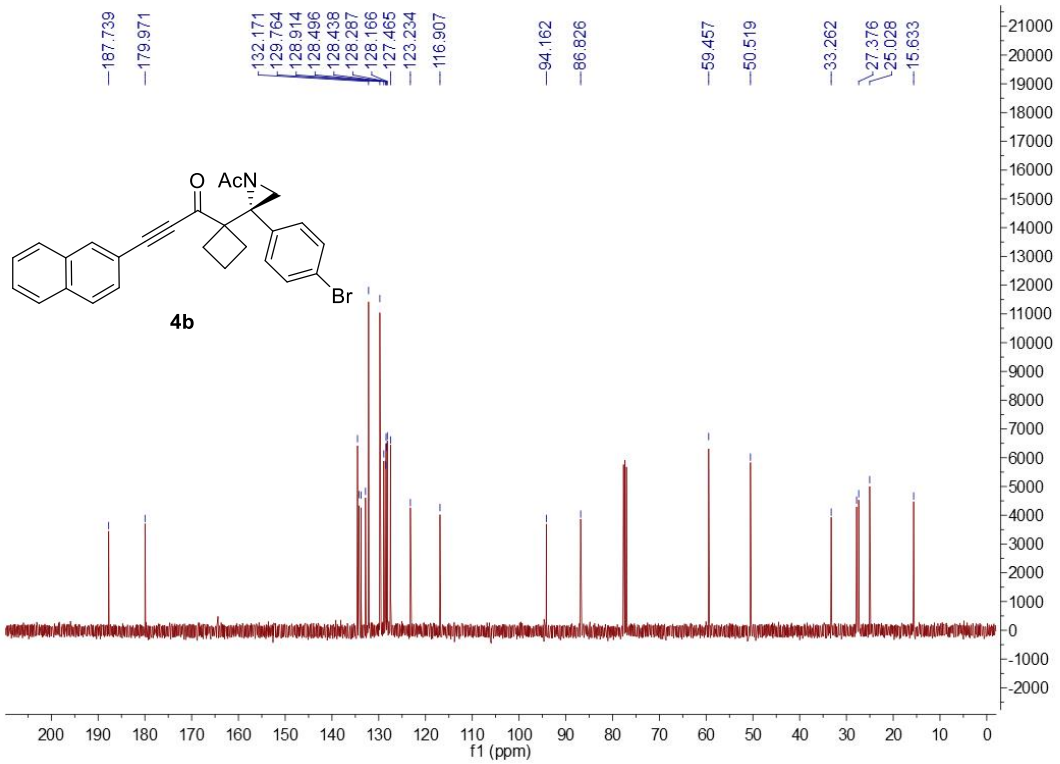
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4a



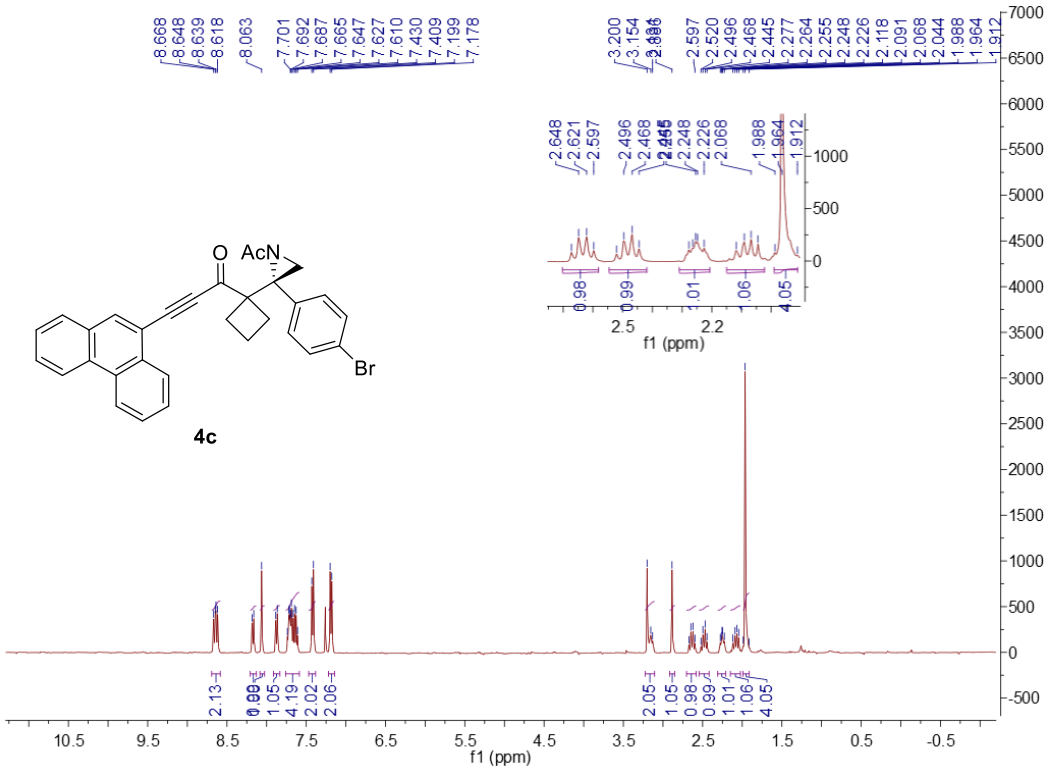
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4b



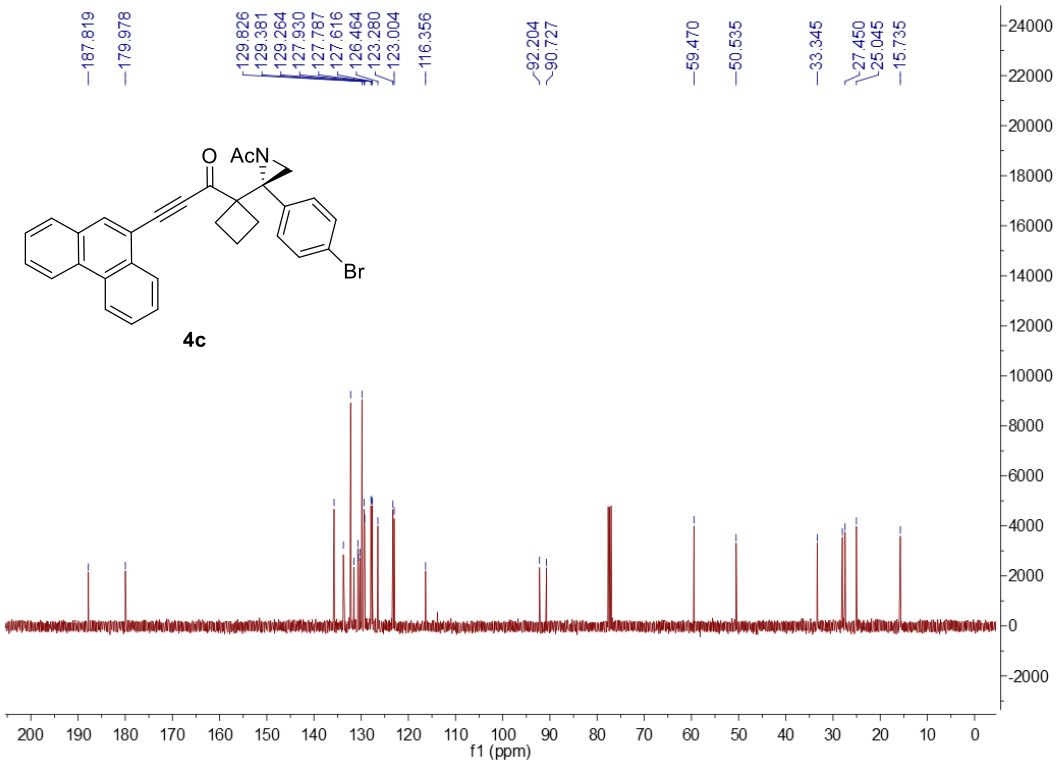
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4b



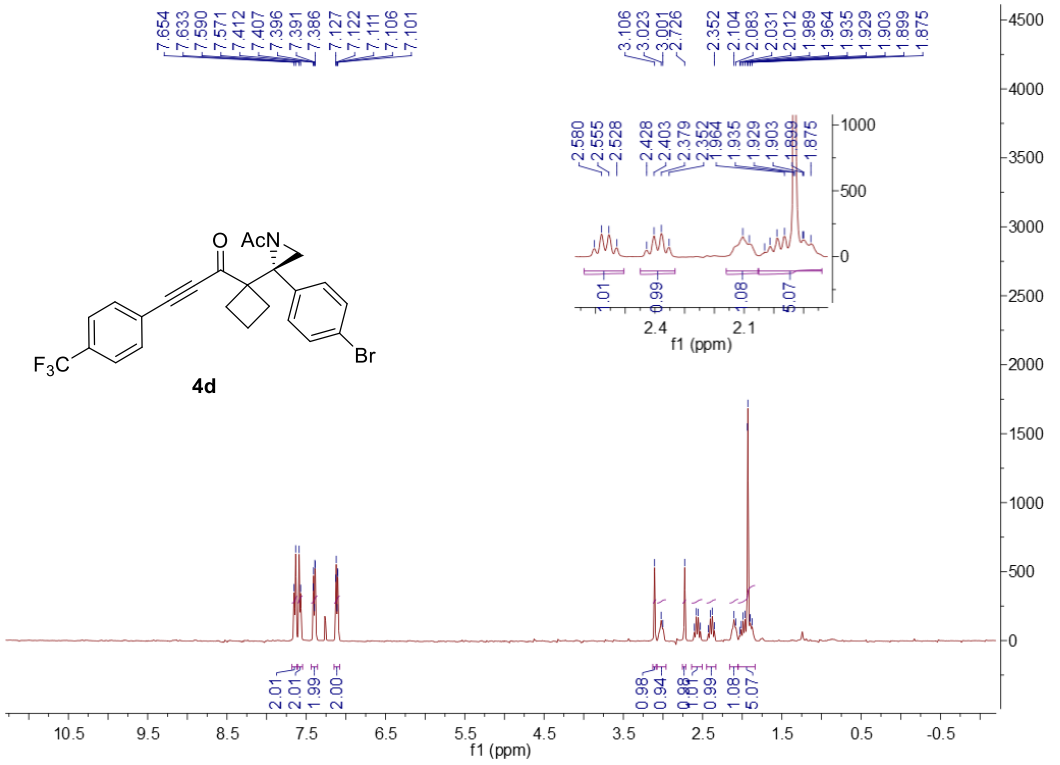
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4c



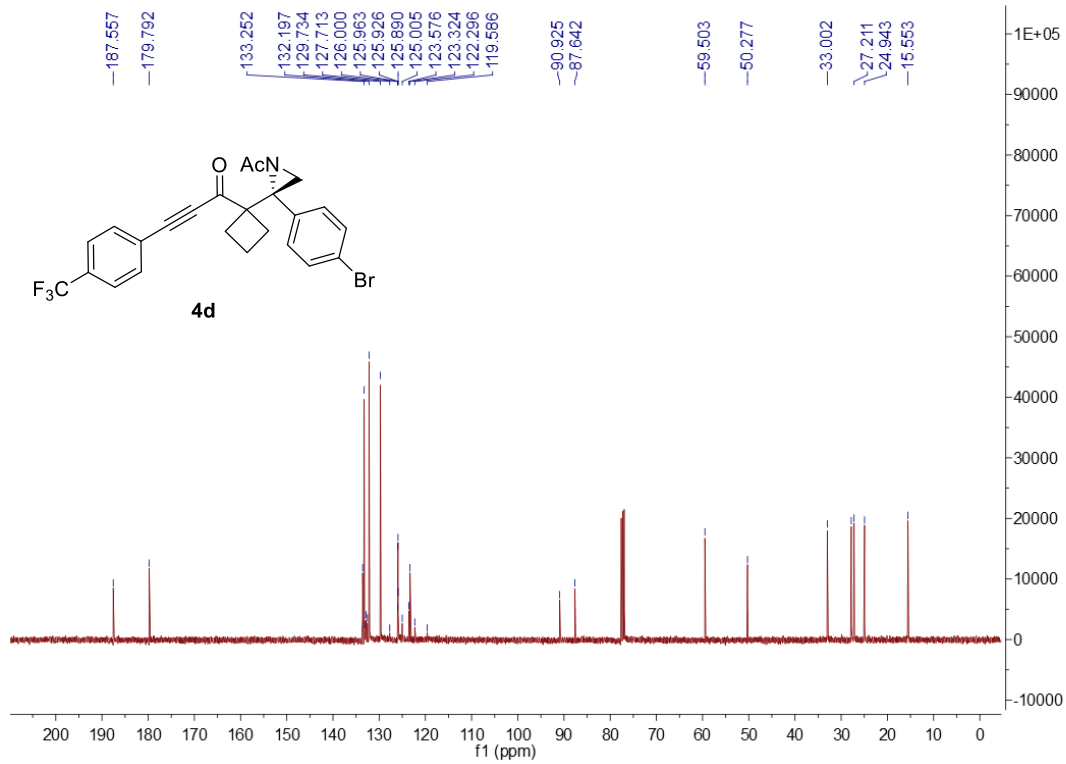
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4c



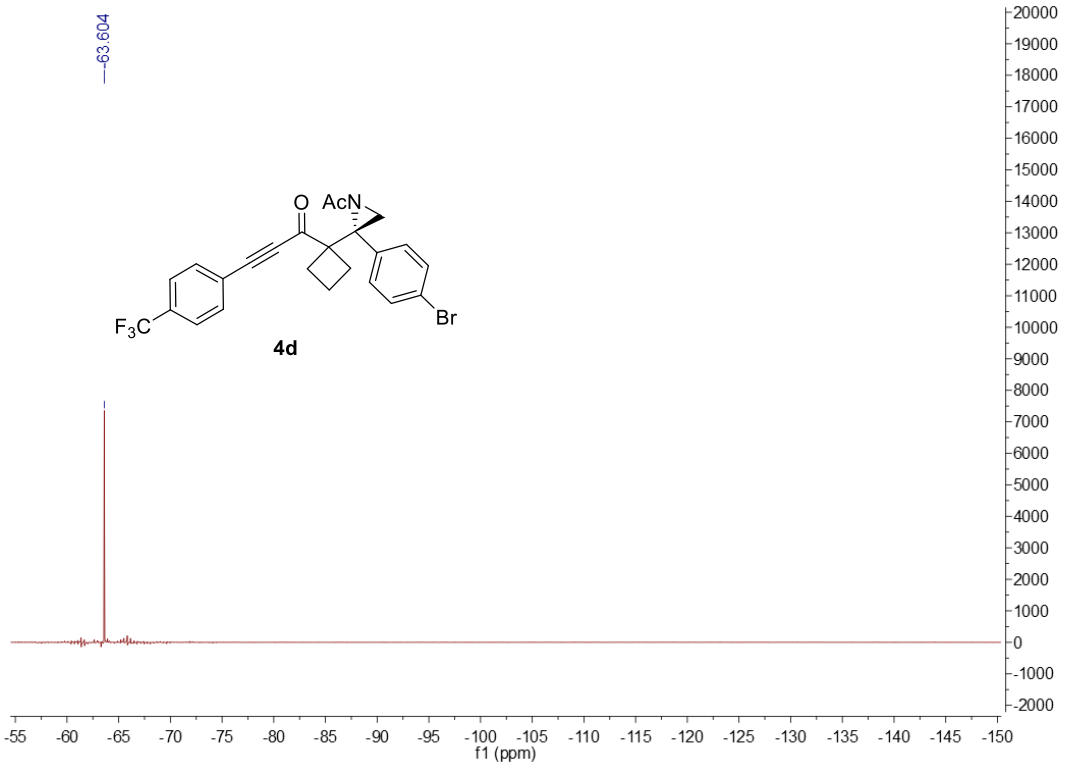
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4d



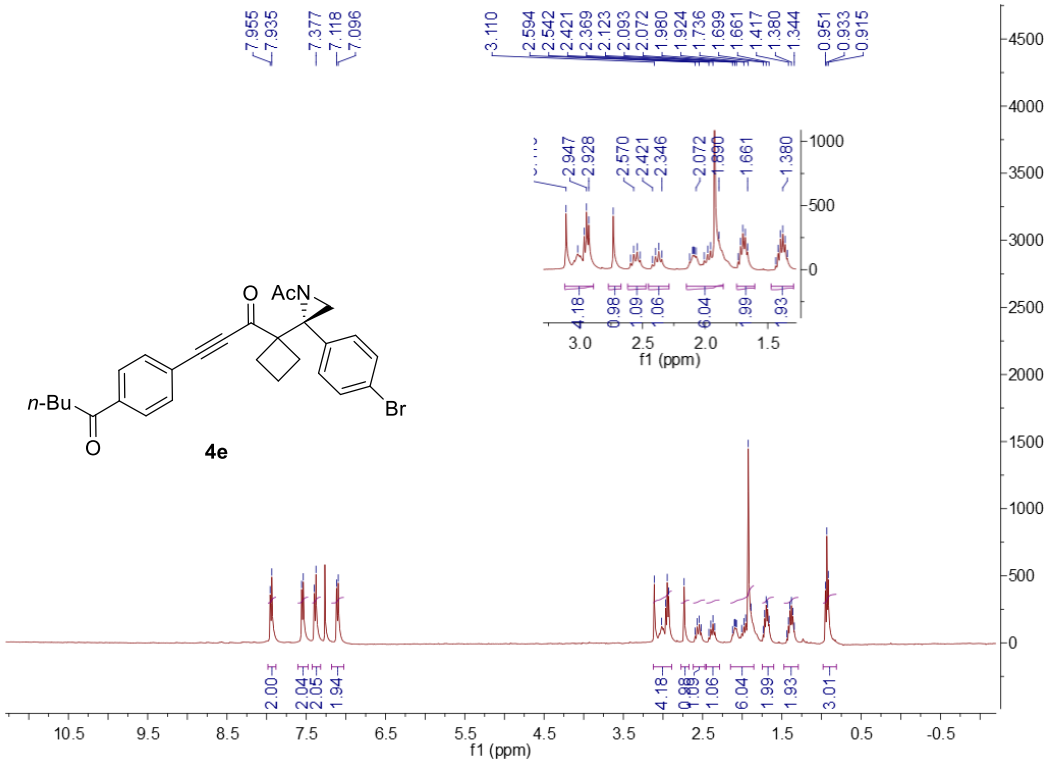
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4d



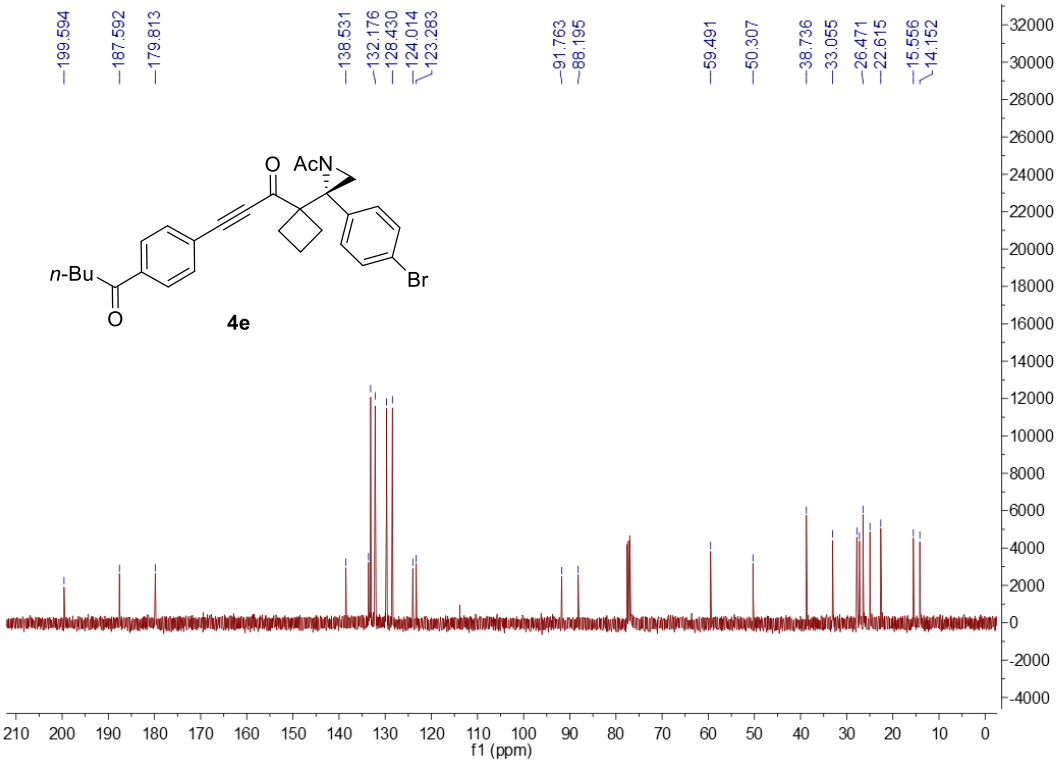
^{19}F NMR (376 MHz, $CDCl_3$) spectrum for 4d



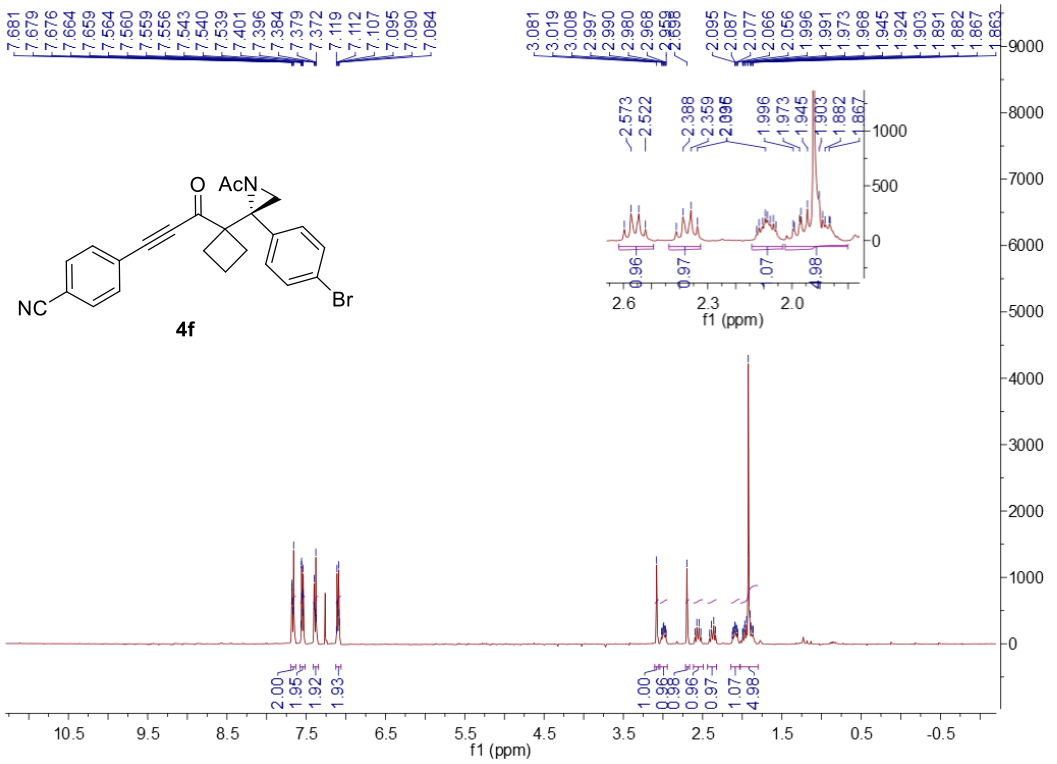
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4e



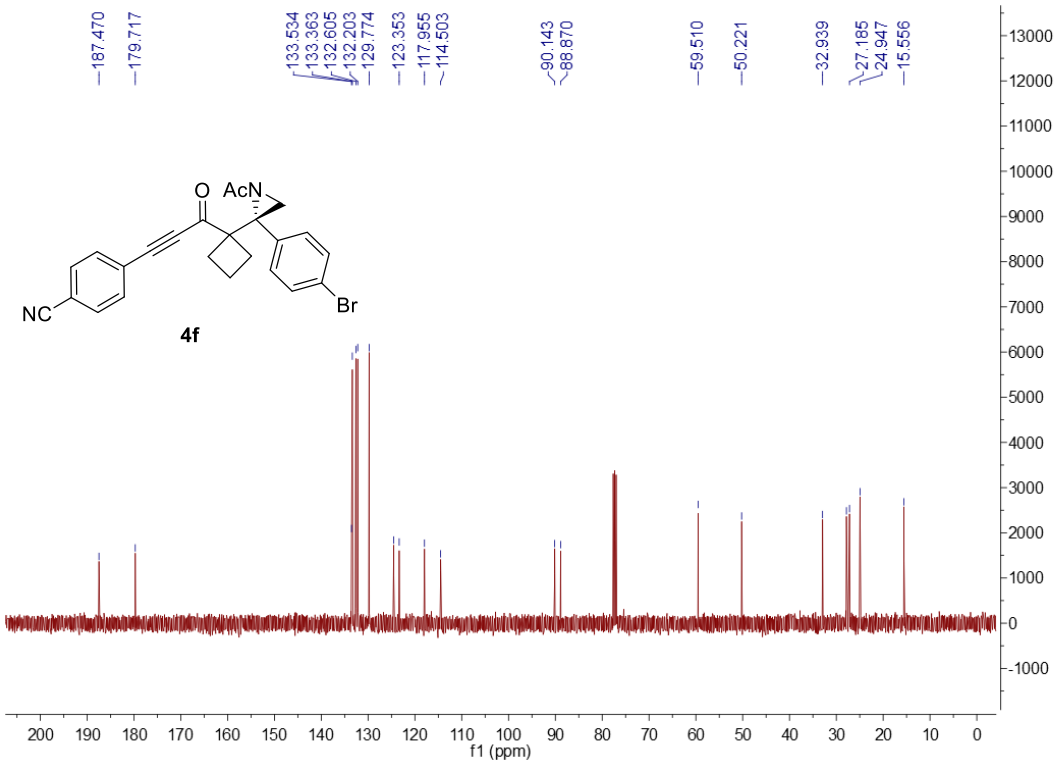
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4e



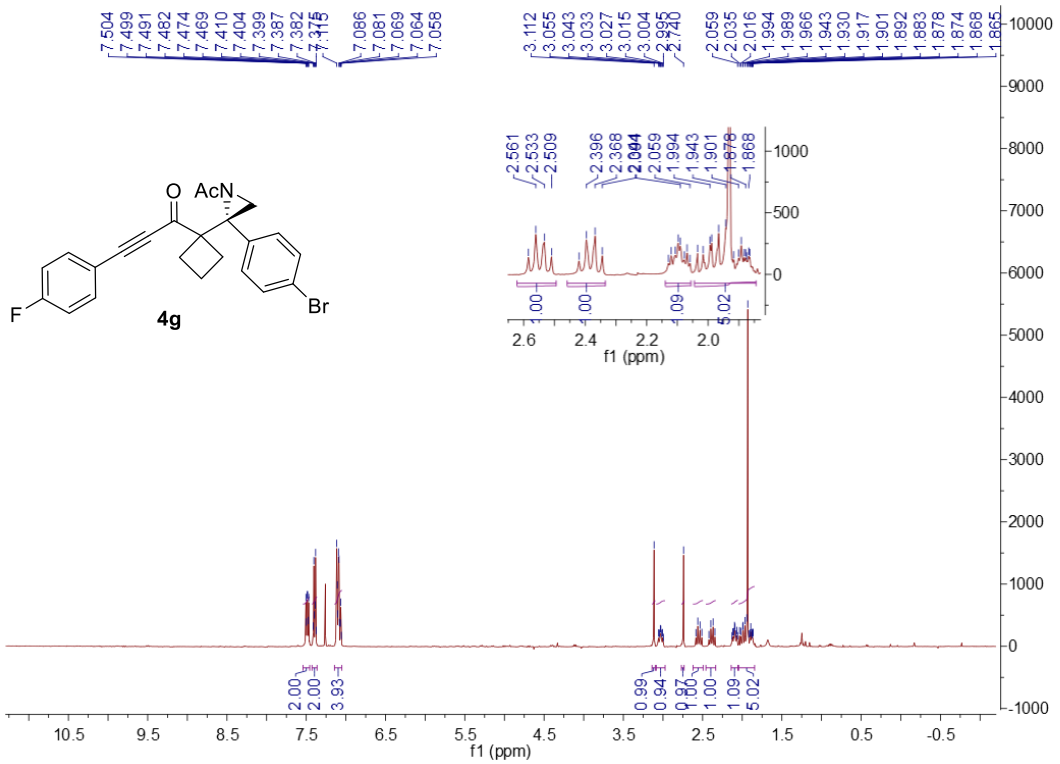
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4f



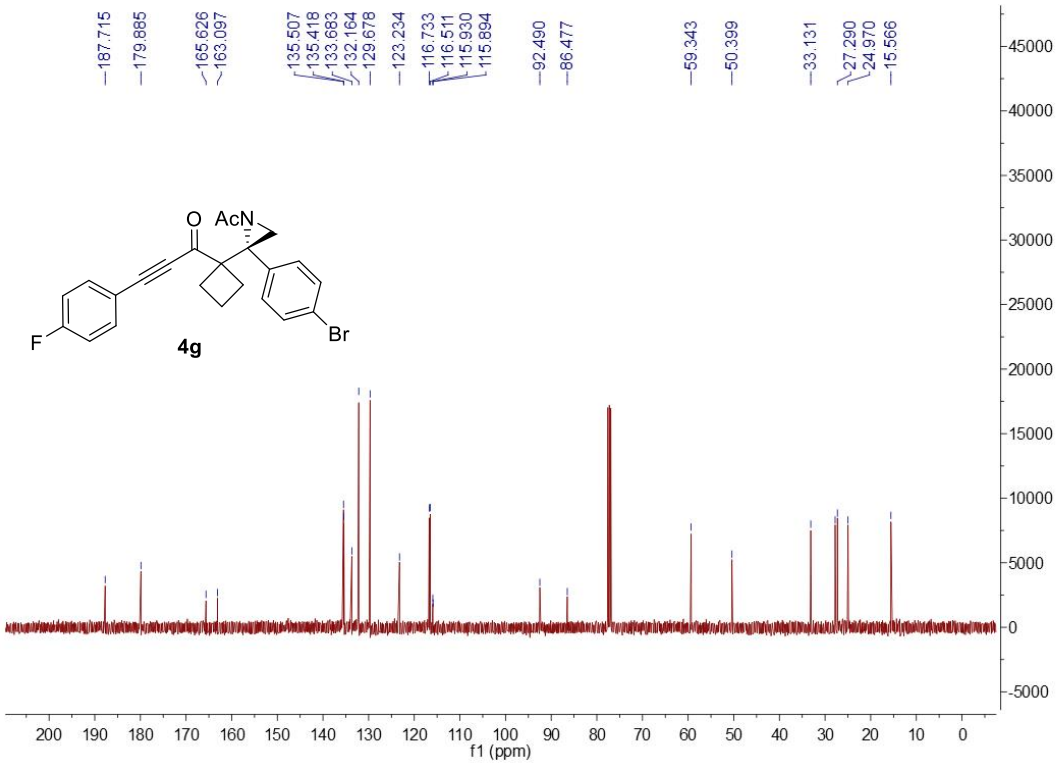
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4f



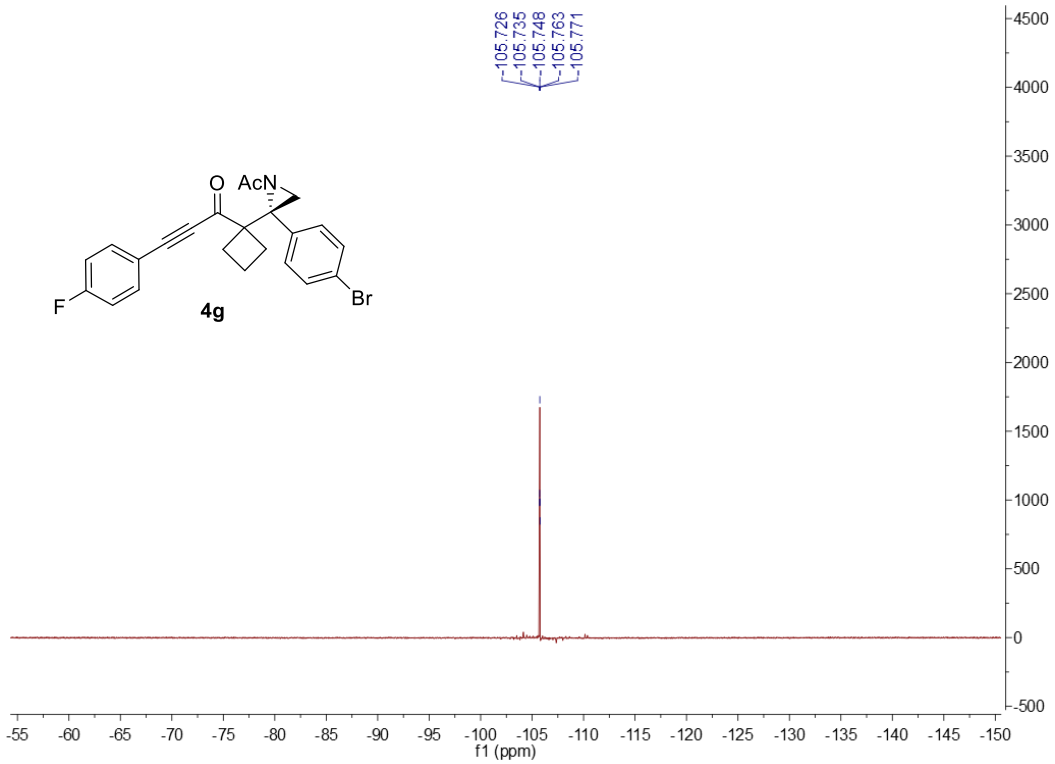
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4g



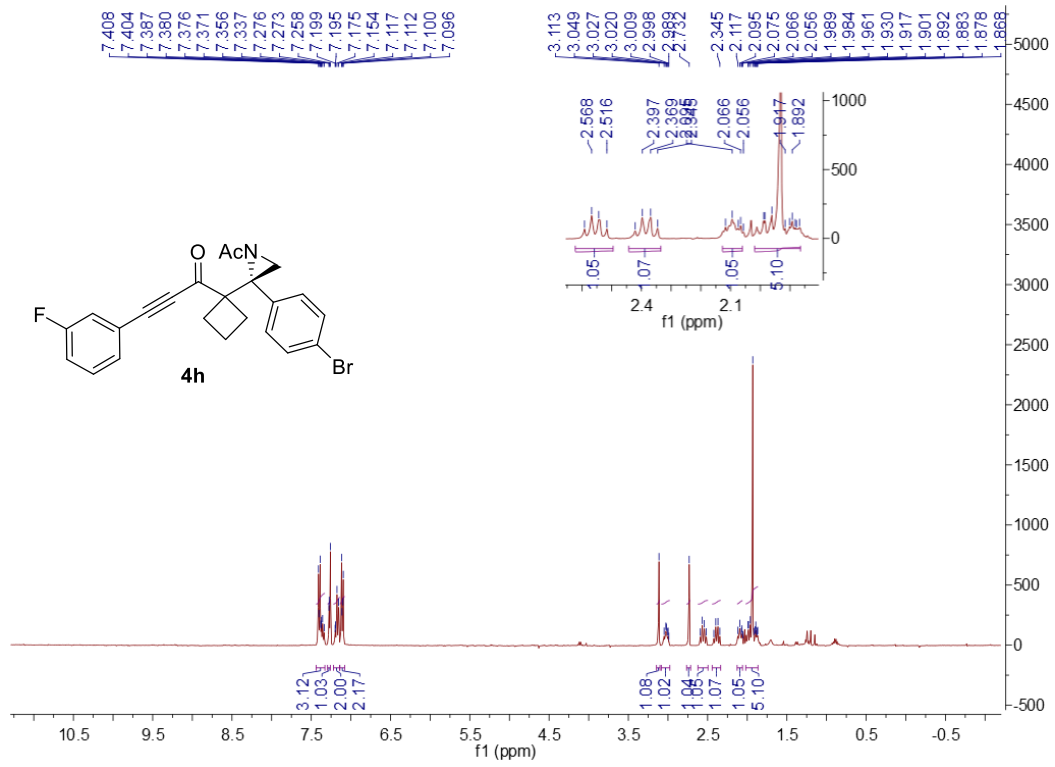
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4g



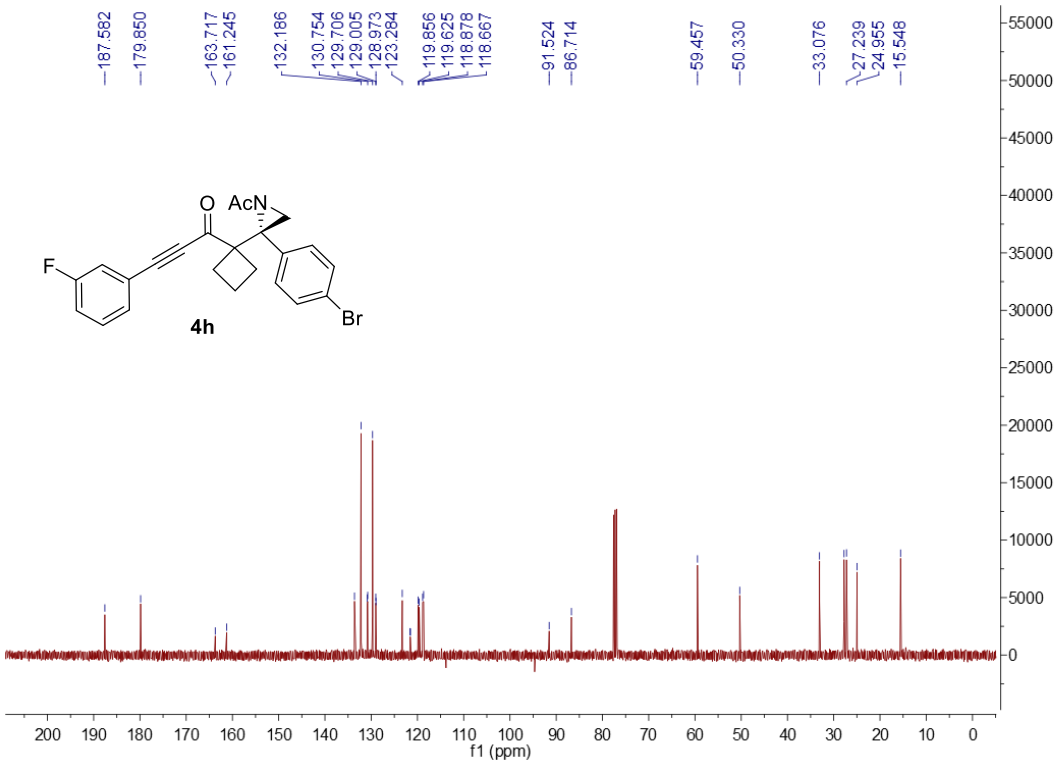
^{19}F NMR (376 MHz, $CDCl_3$) spectrum for 4g



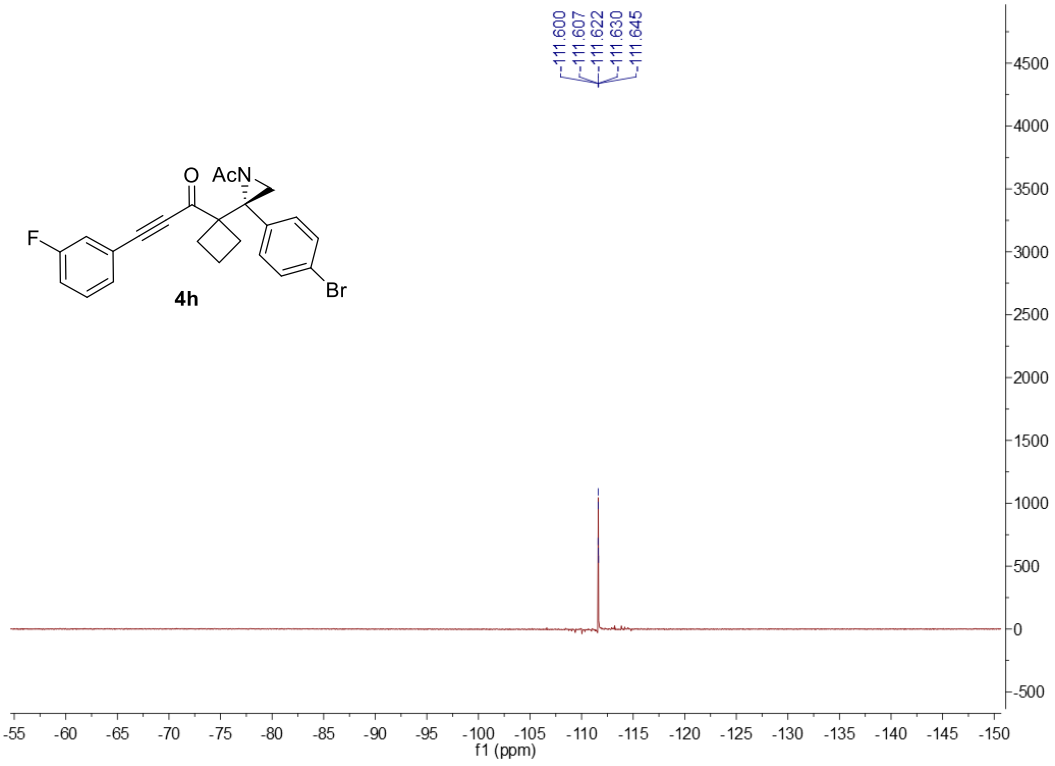
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4h



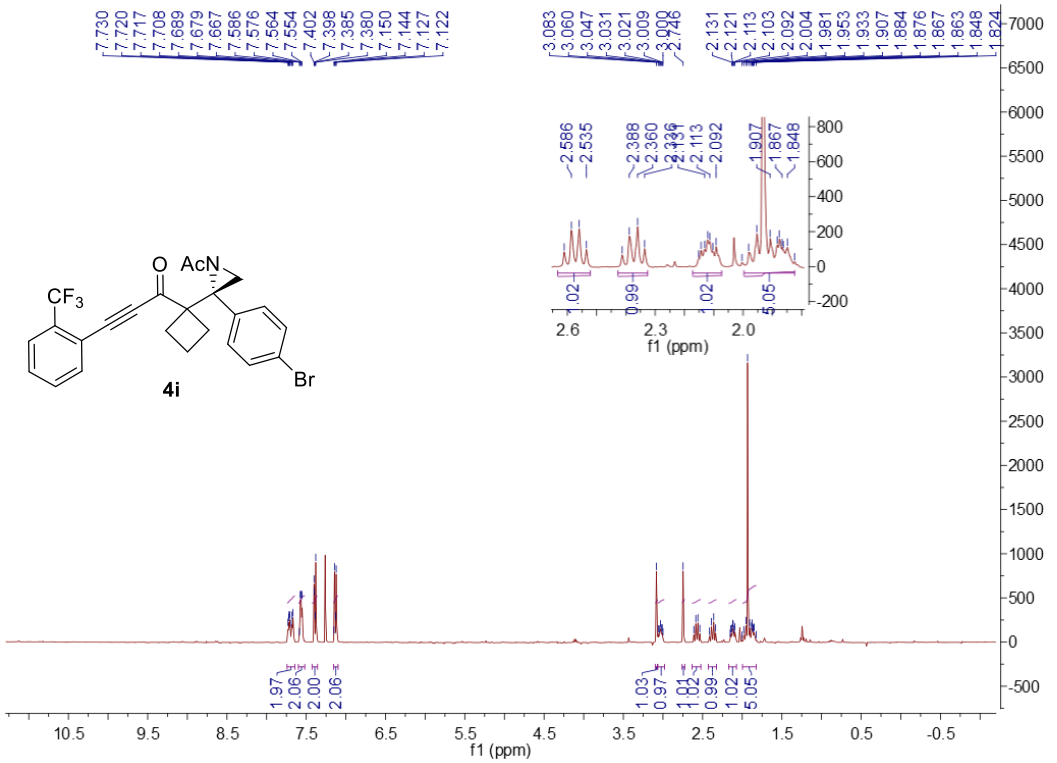
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4h



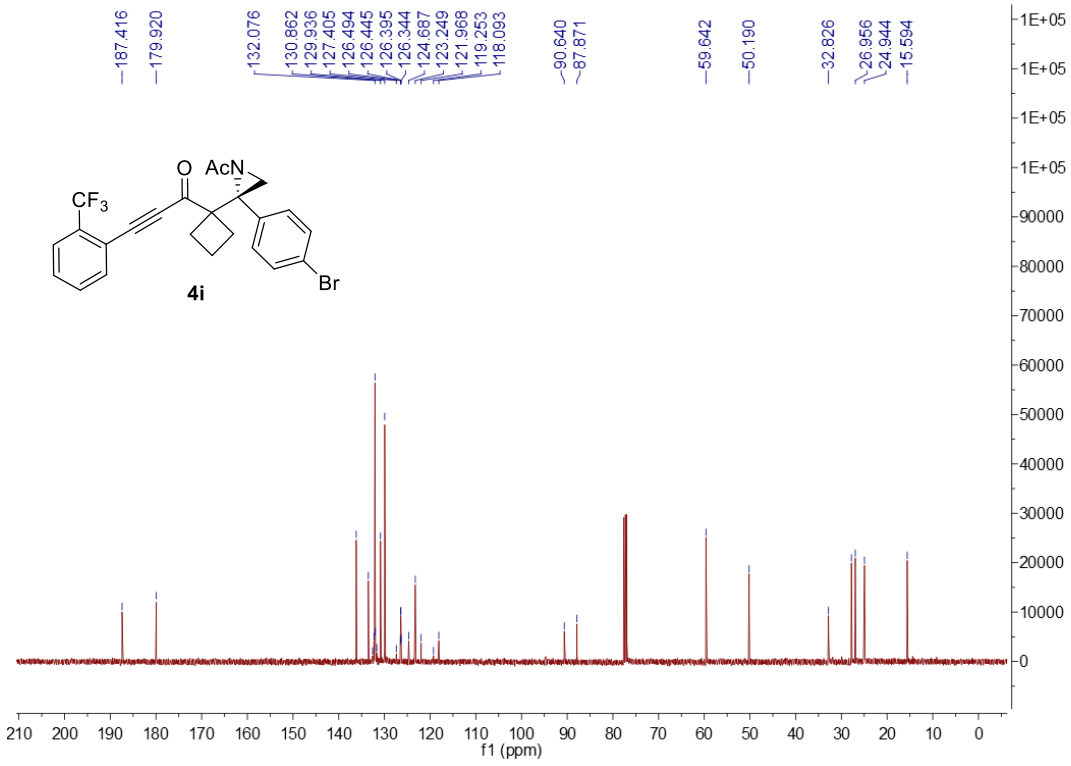
^{19}F NMR (376 MHz, $CDCl_3$) spectrum for 4h



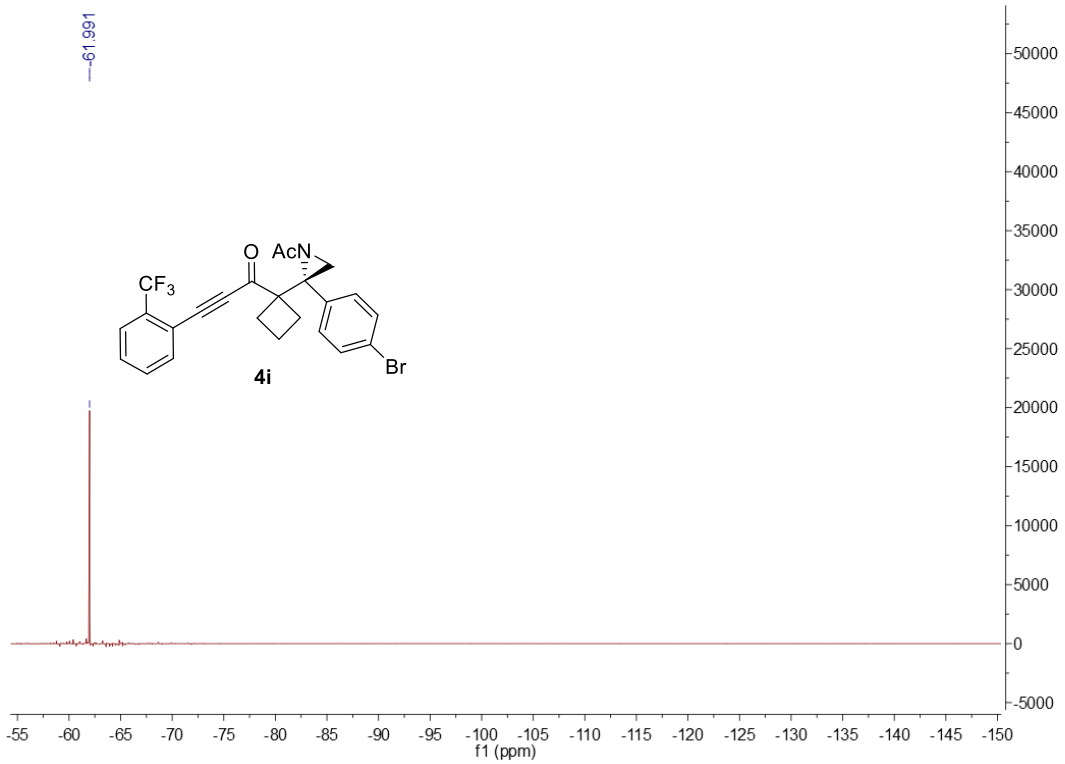
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4i



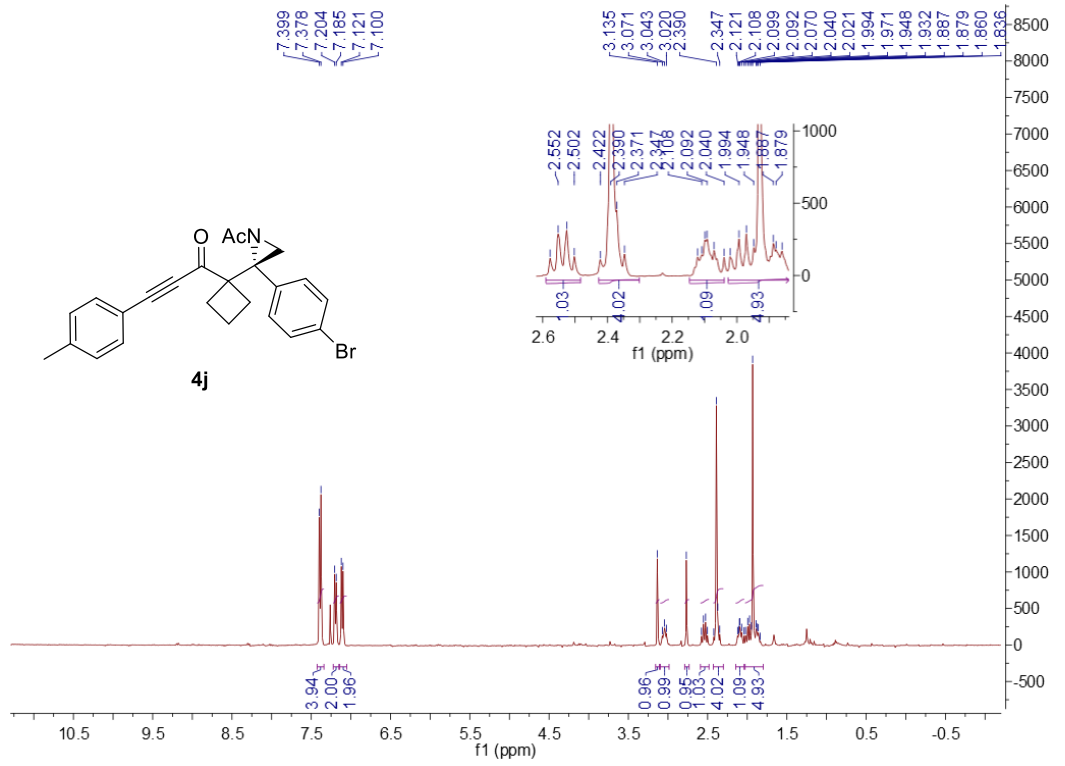
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4i



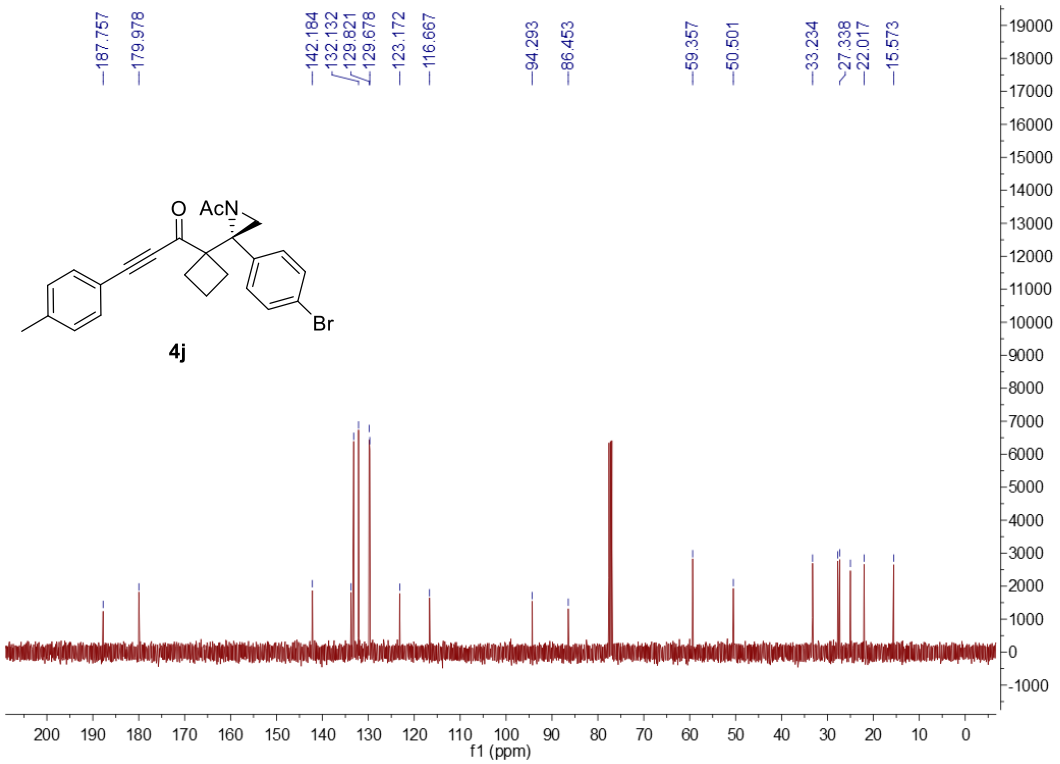
^{19}F NMR (376 MHz, $CDCl_3$) spectrum for 4i



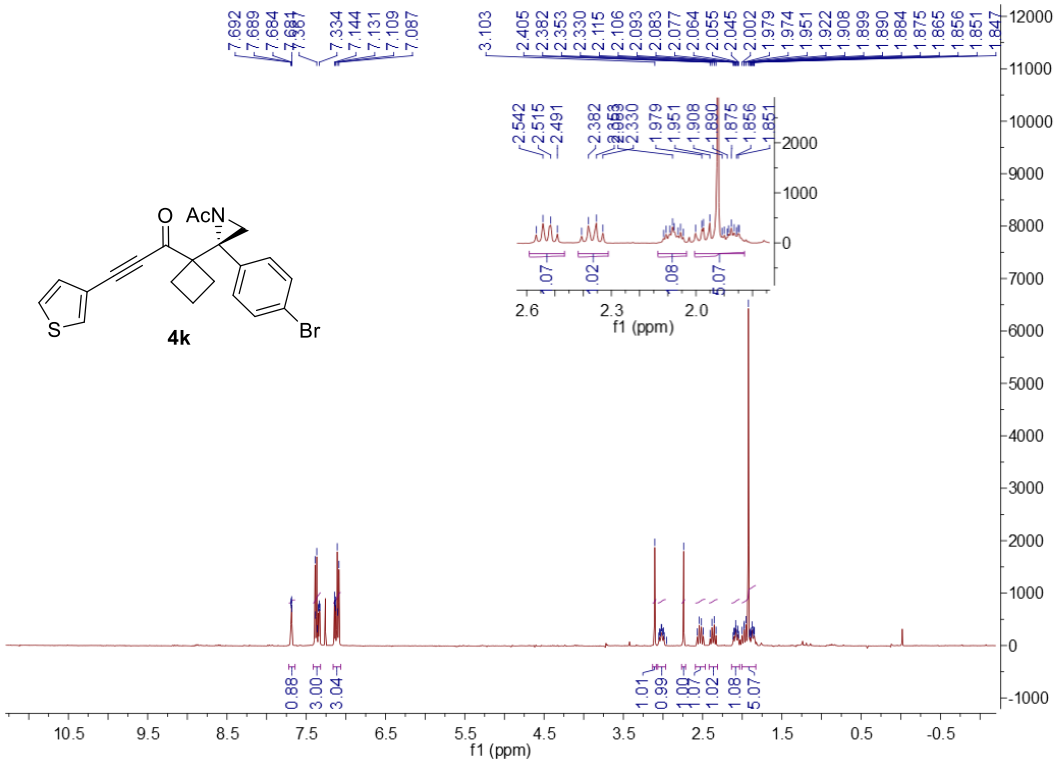
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4j



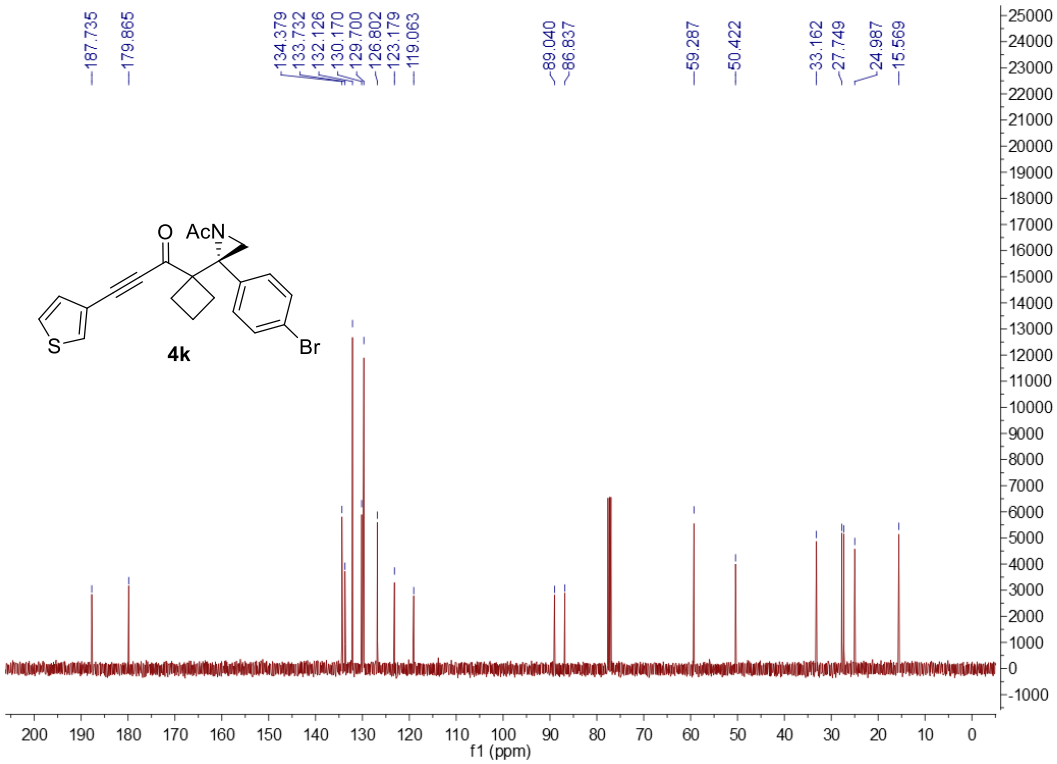
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4j



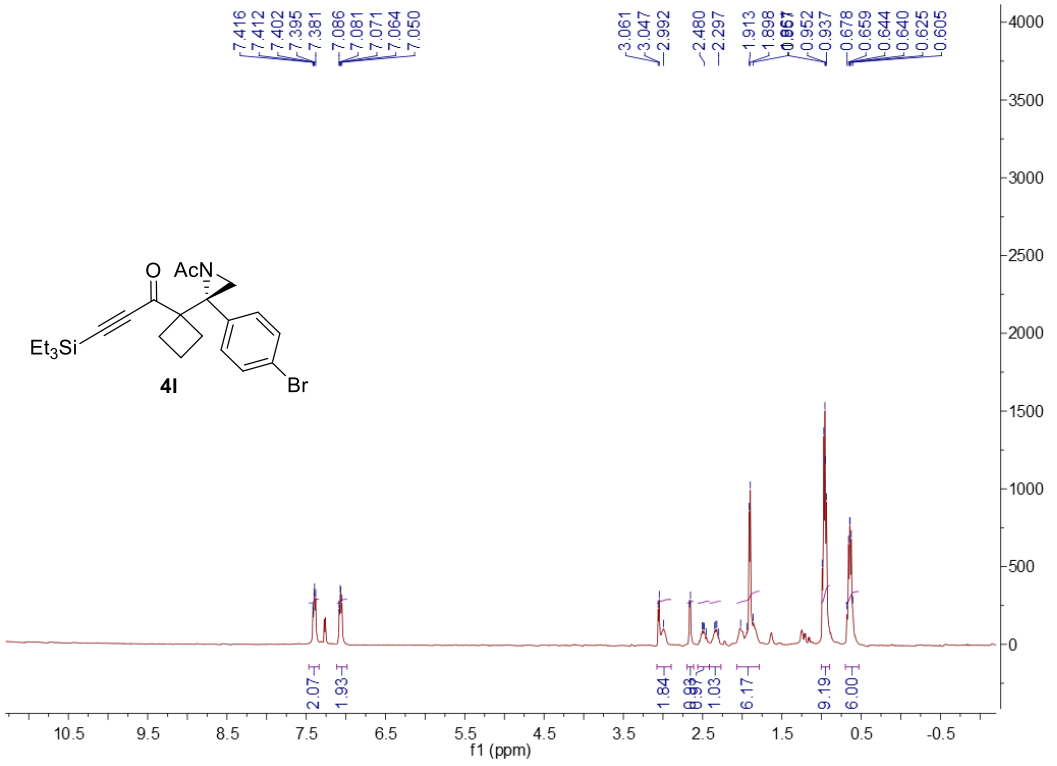
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4k



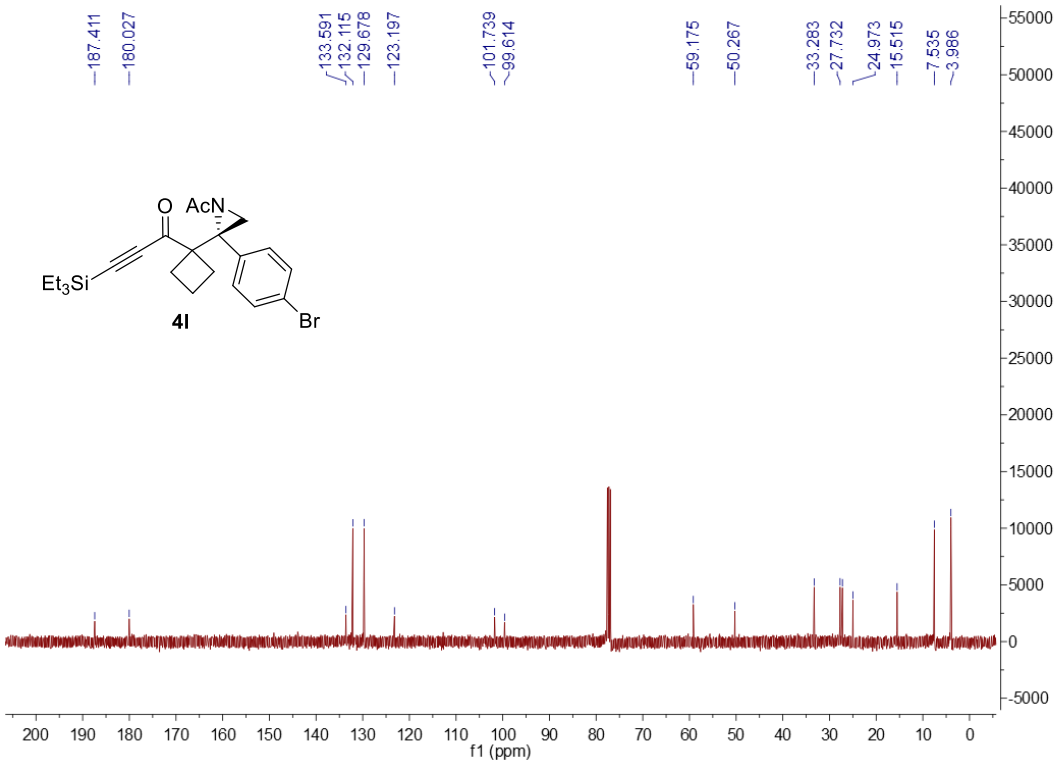
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4k



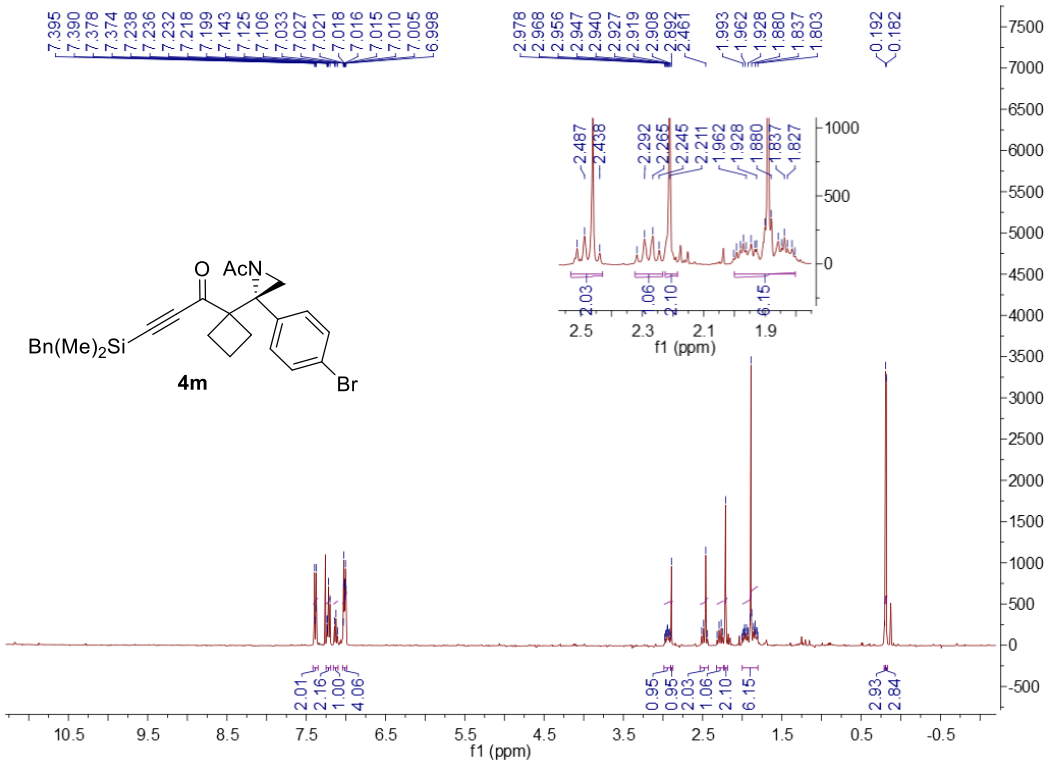
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4l



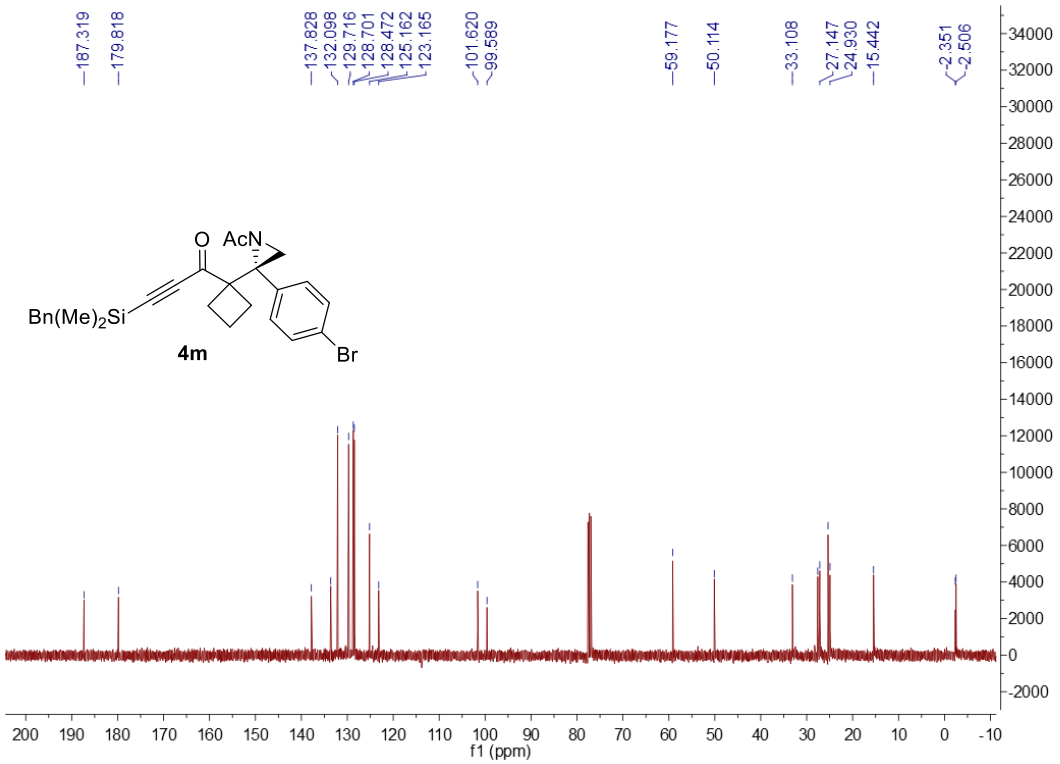
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4l



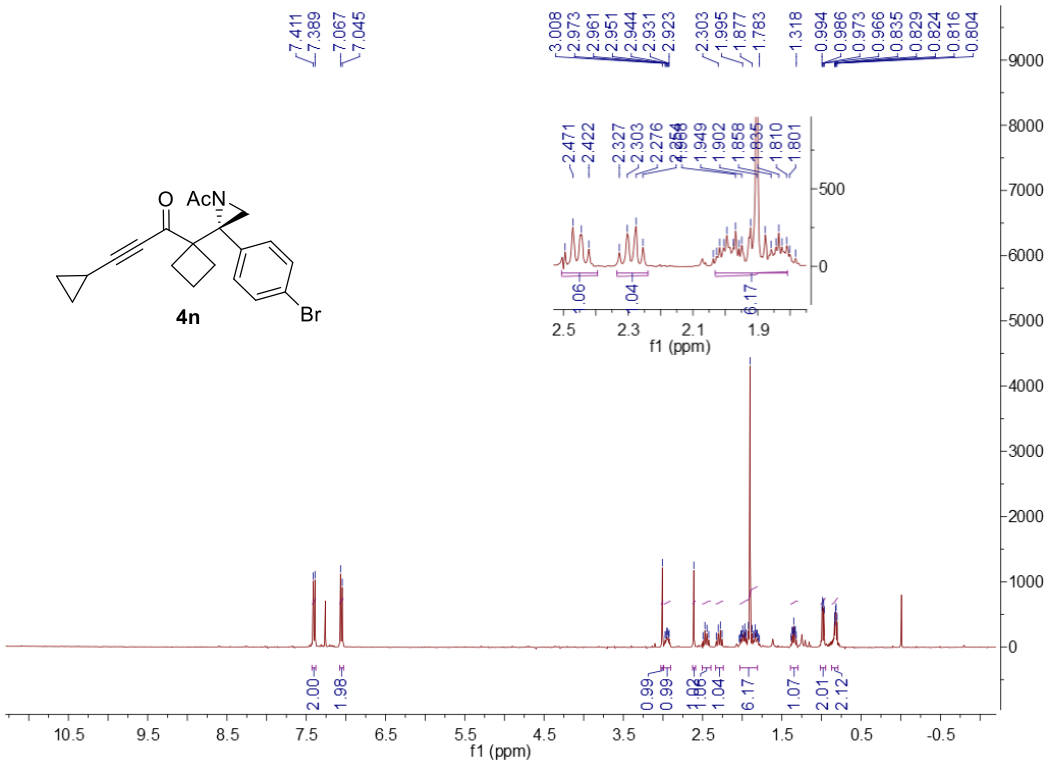
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4m



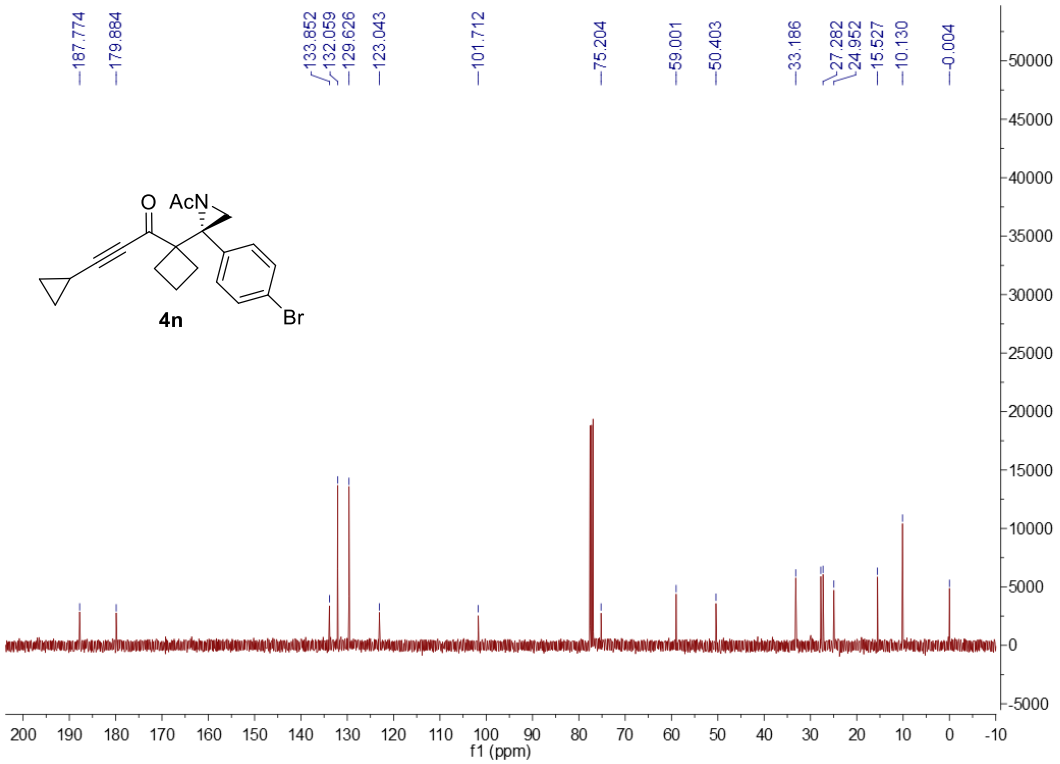
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4m



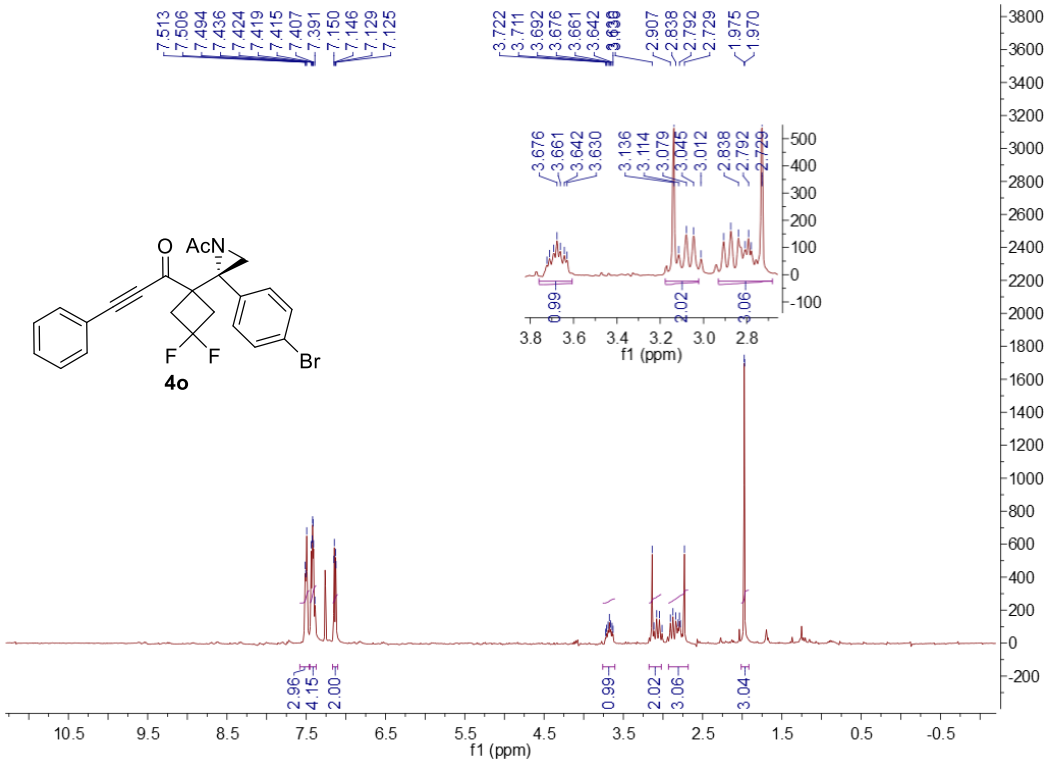
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4n



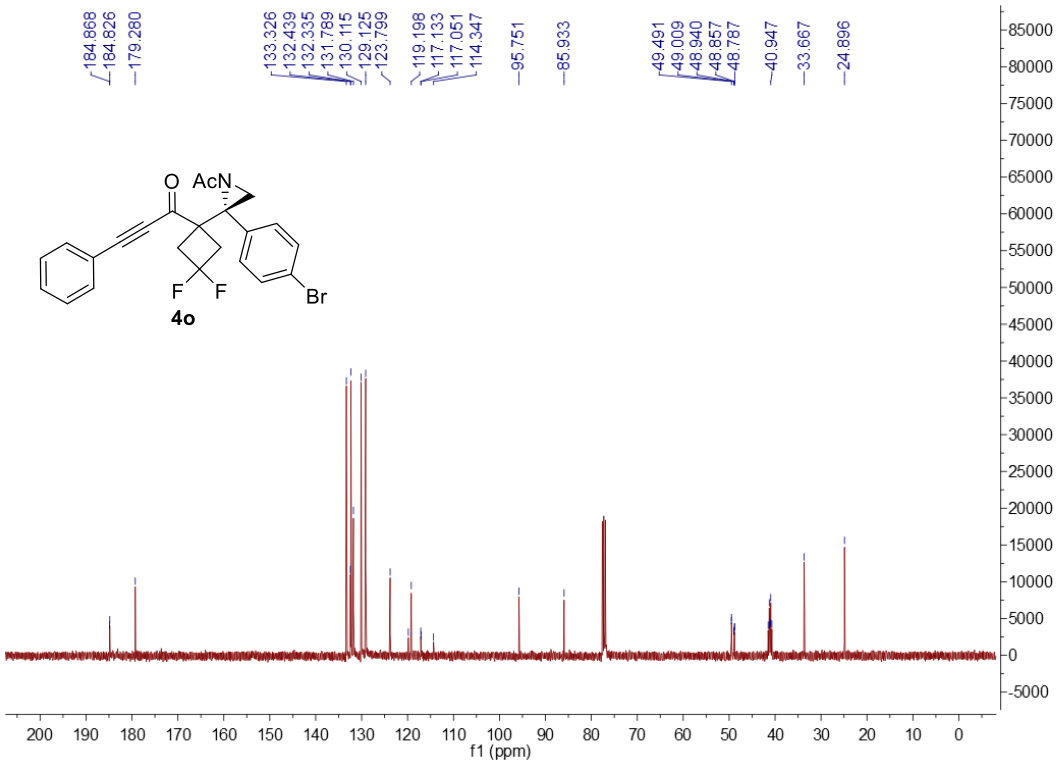
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4n



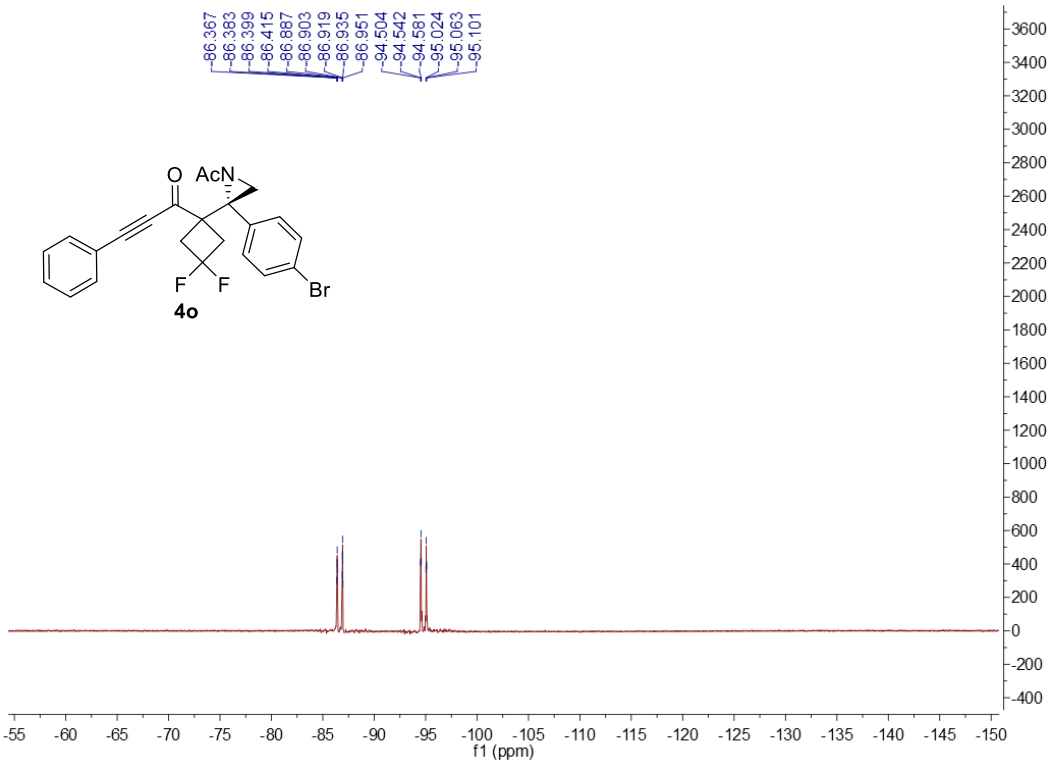
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4o



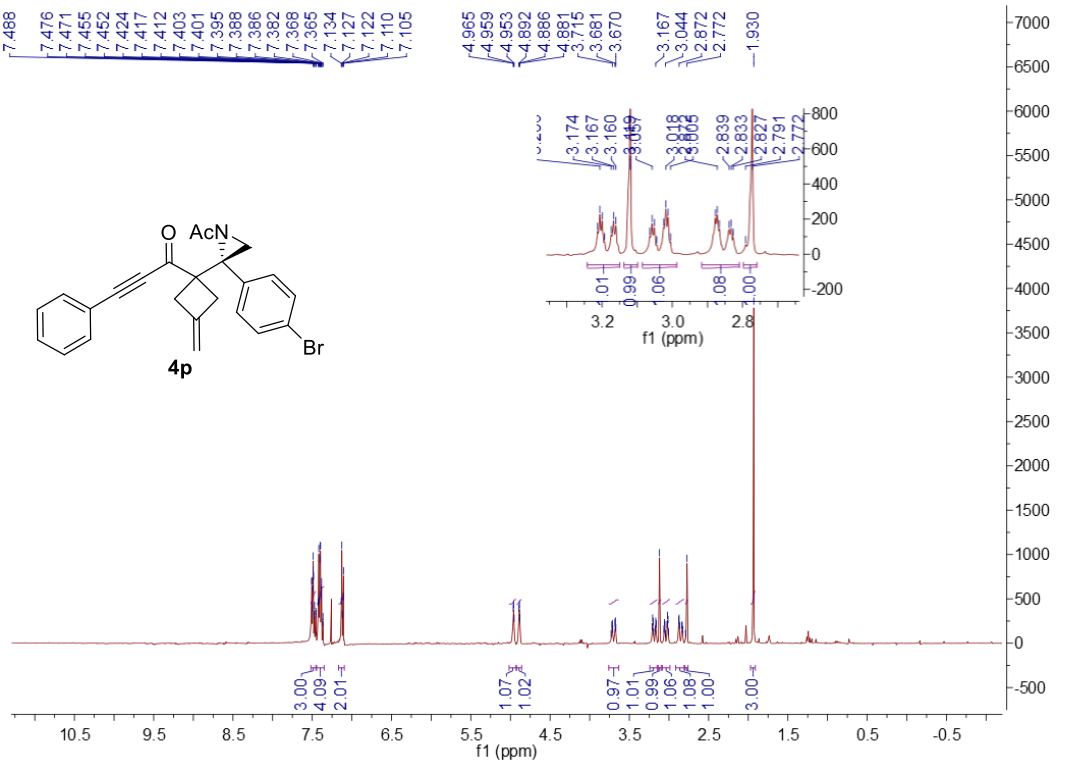
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4o



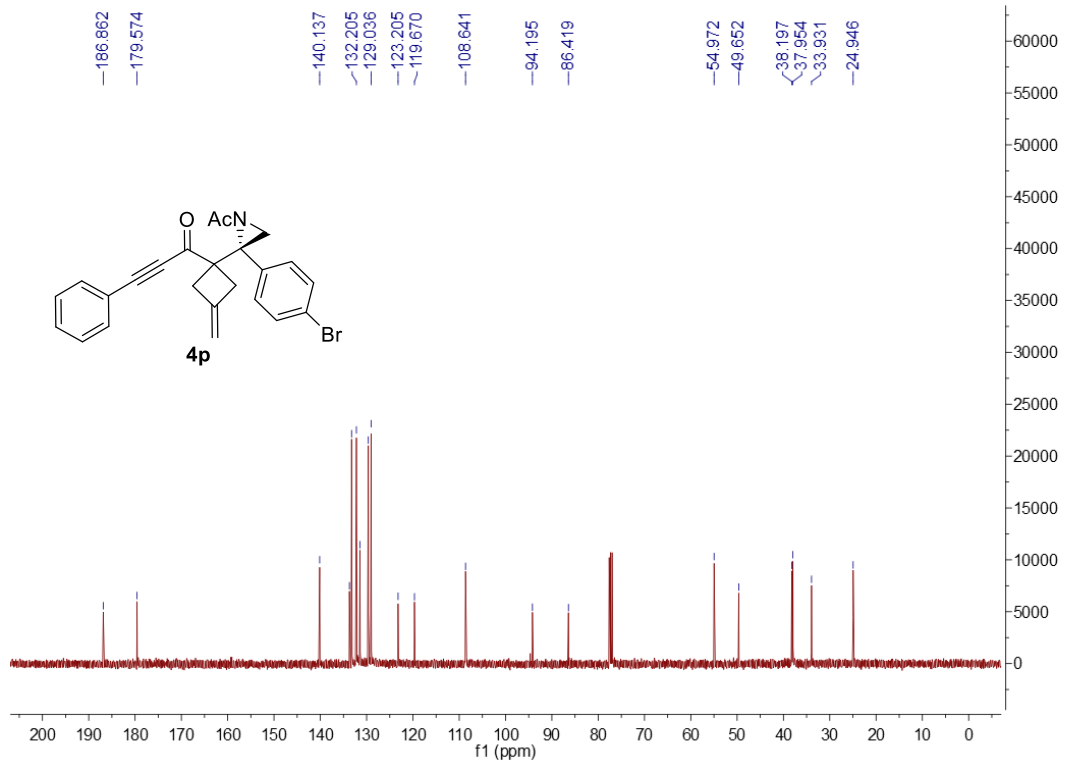
^{19}F NMR (376 MHz, $CDCl_3$) spectrum for 4o



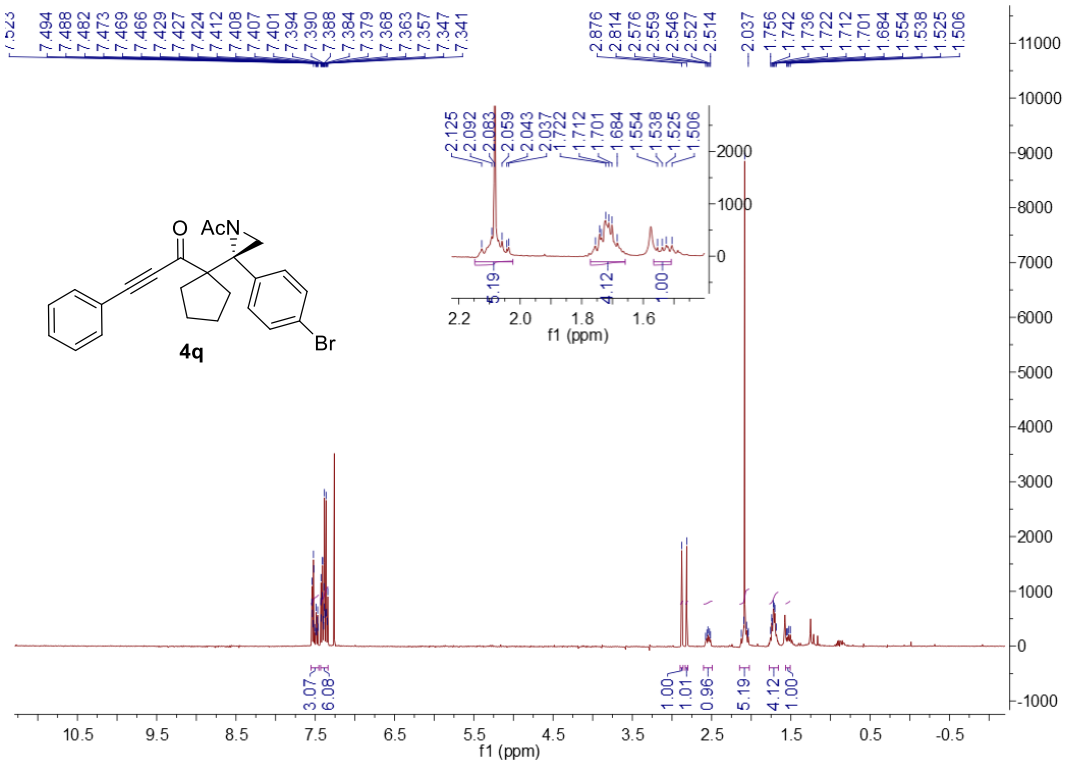
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4p



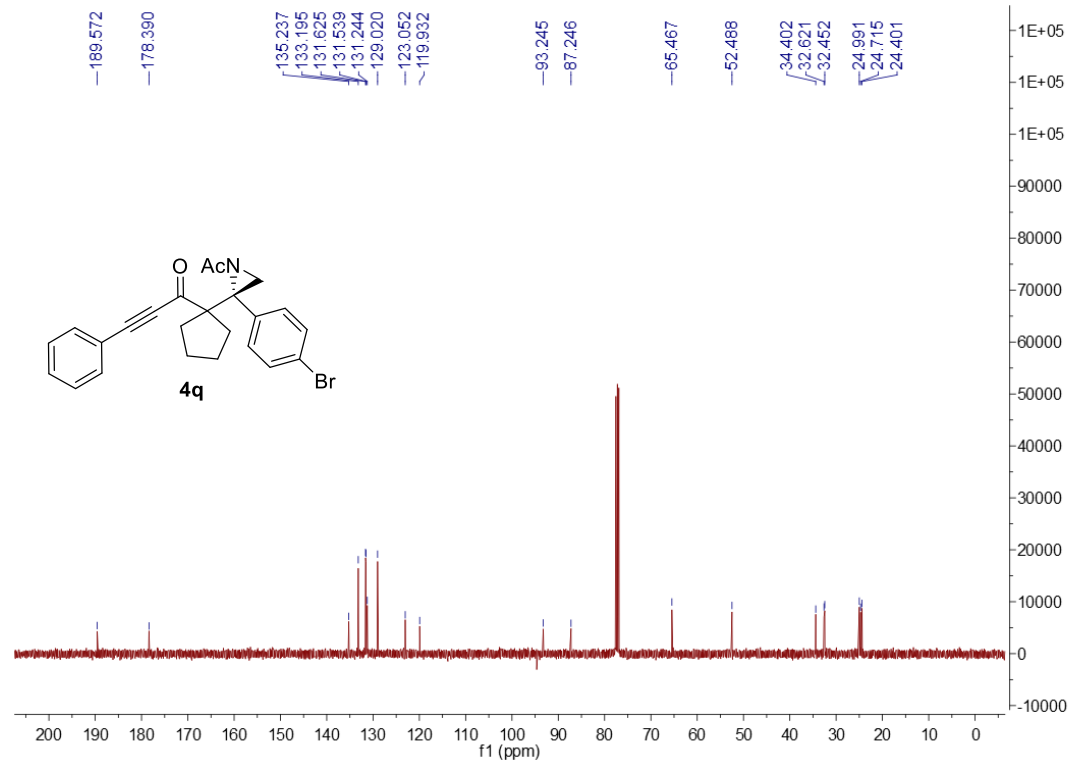
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4p



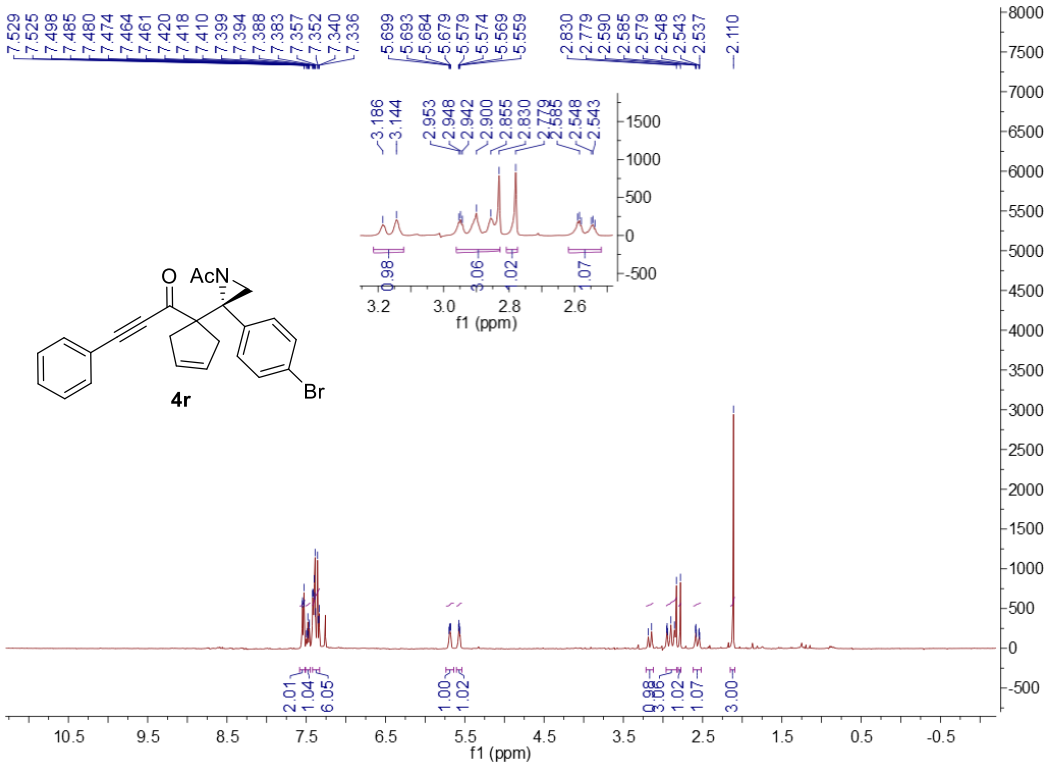
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4q



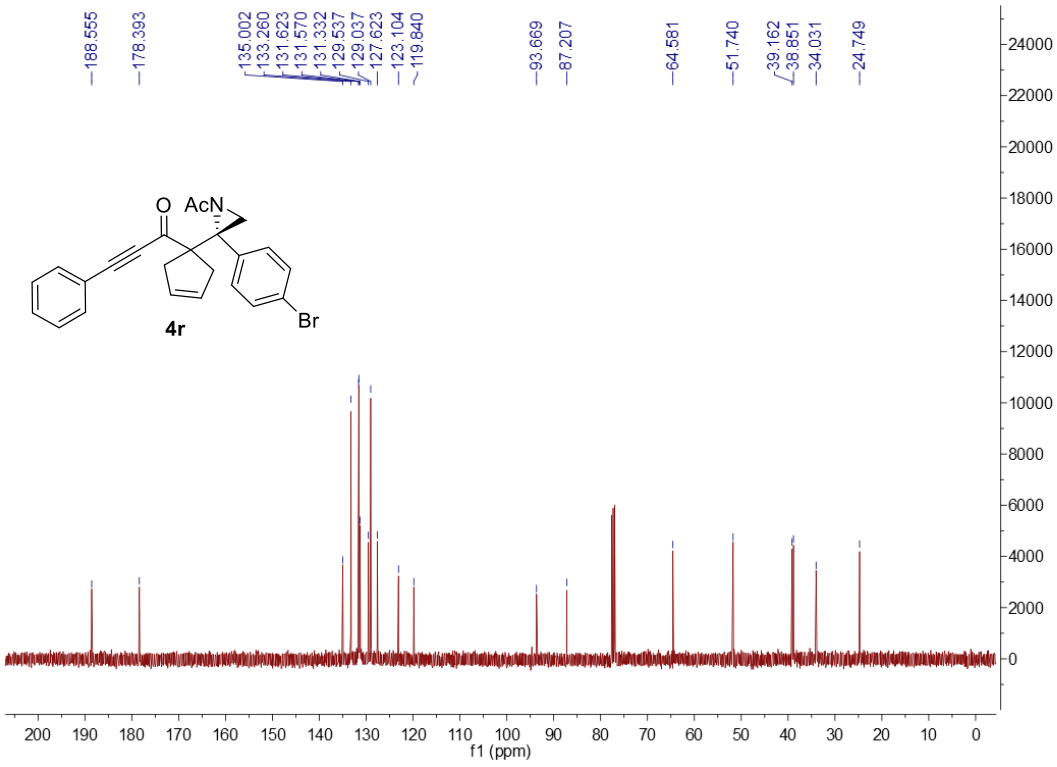
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4q



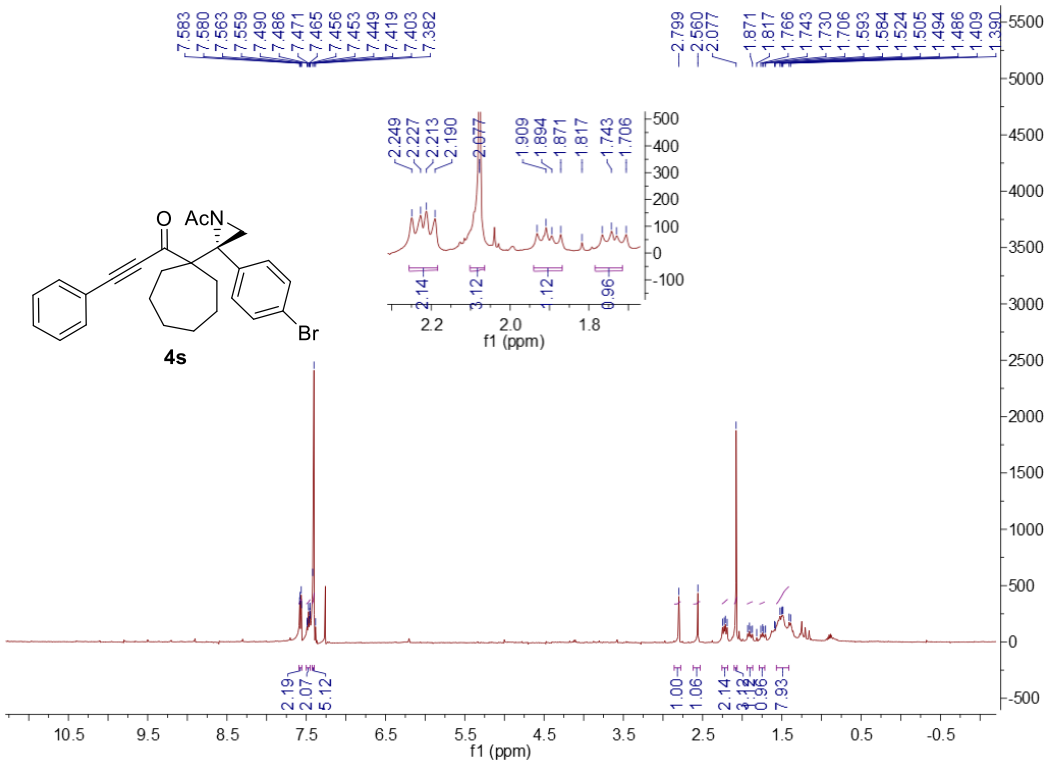
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4r



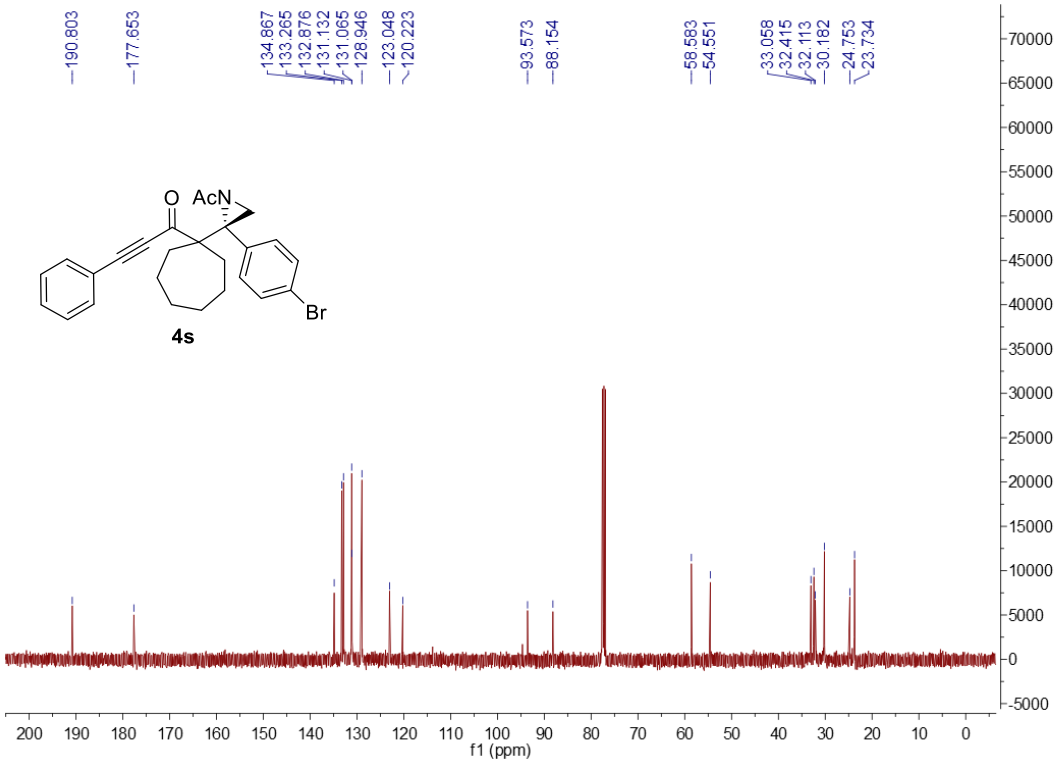
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4r



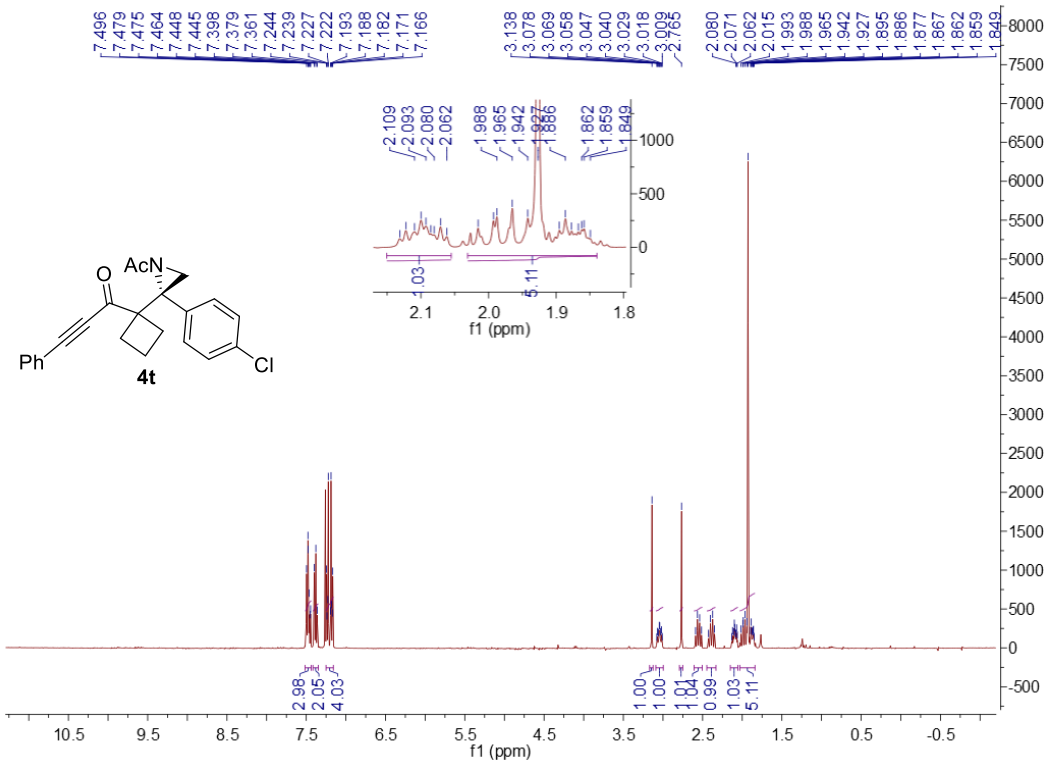
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4s



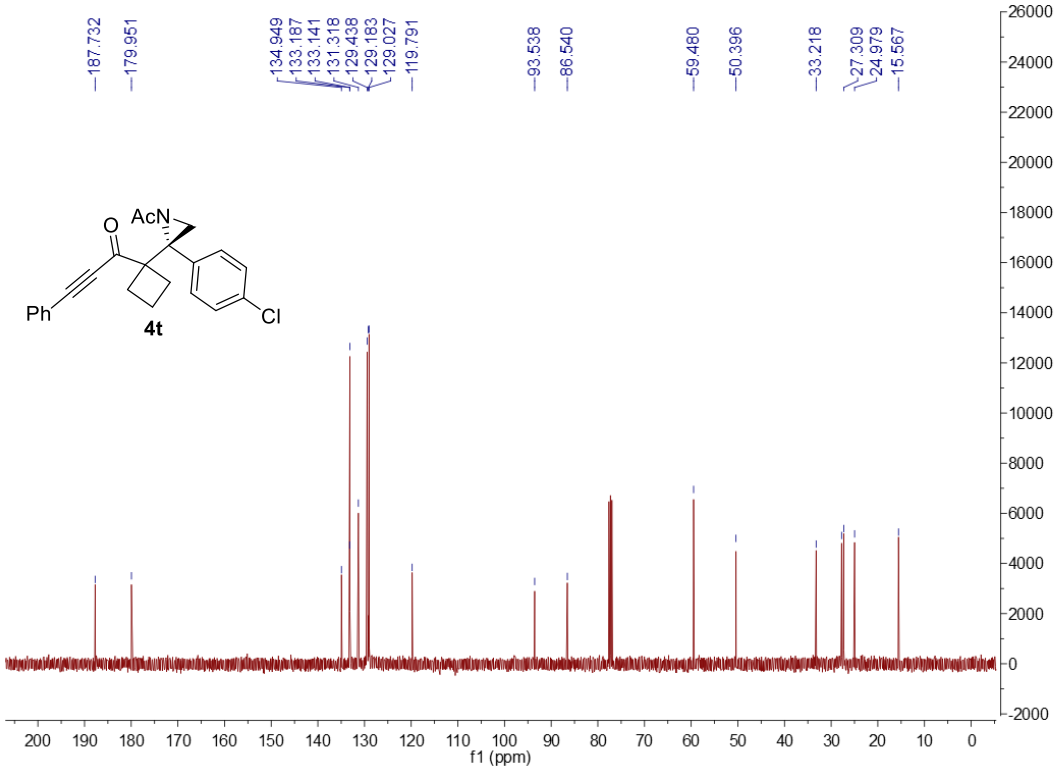
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4s



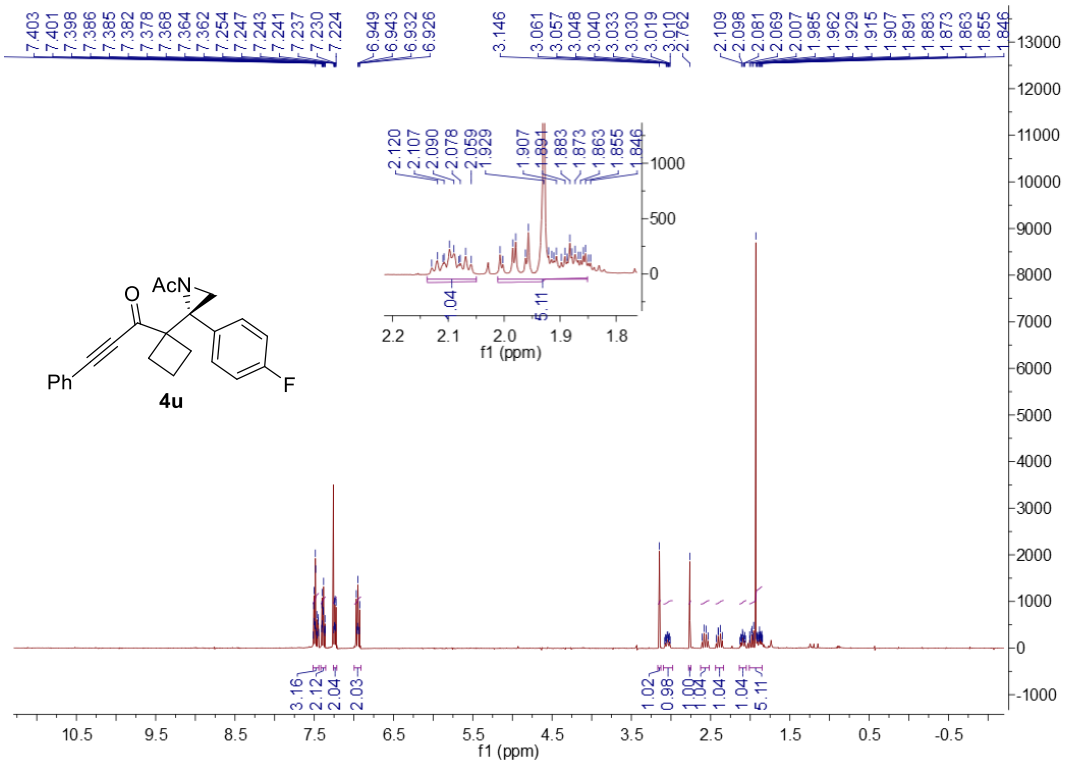
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4t



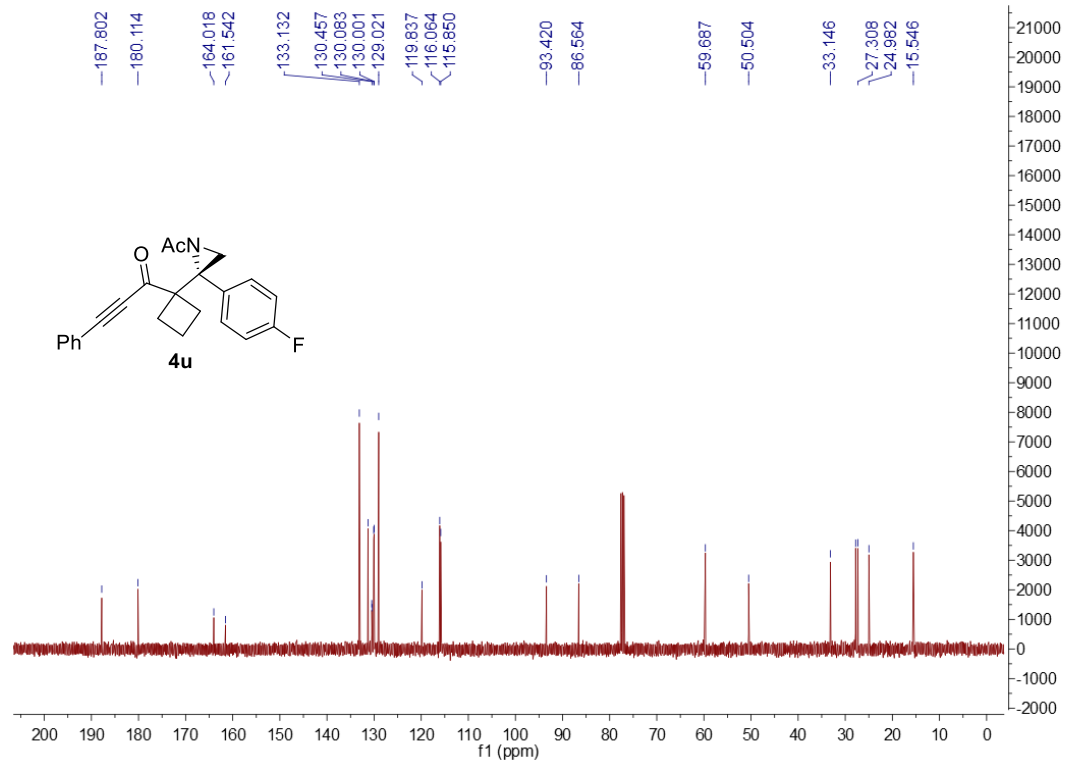
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4t



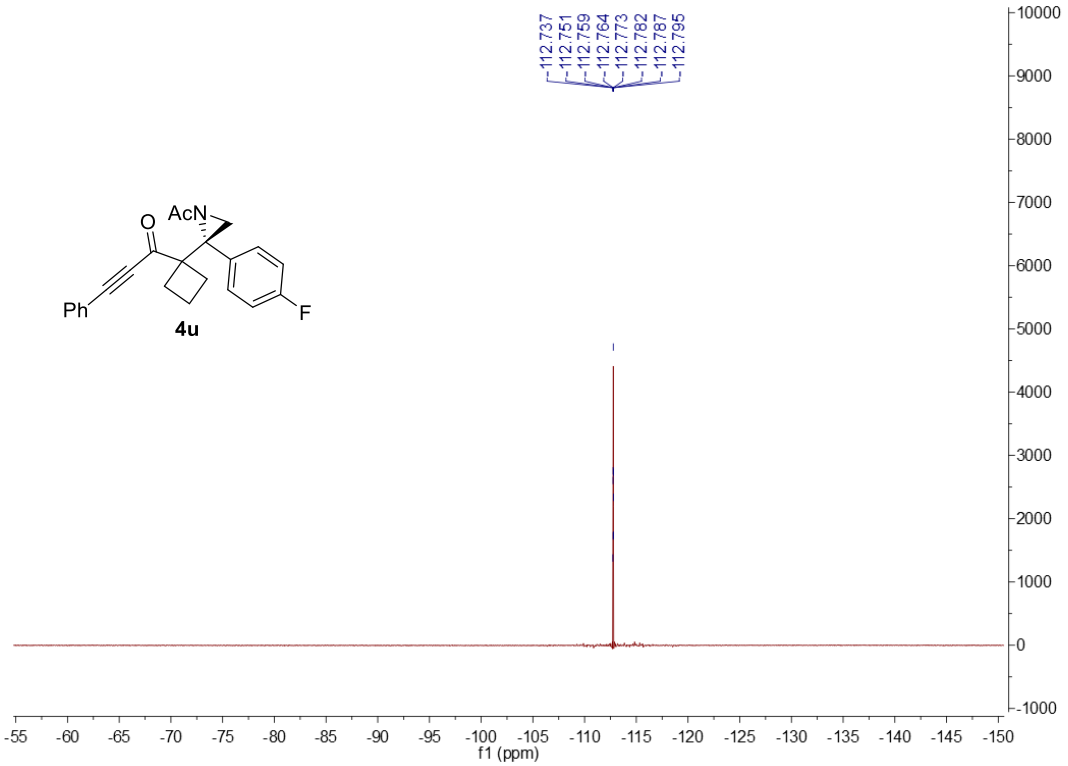
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4u



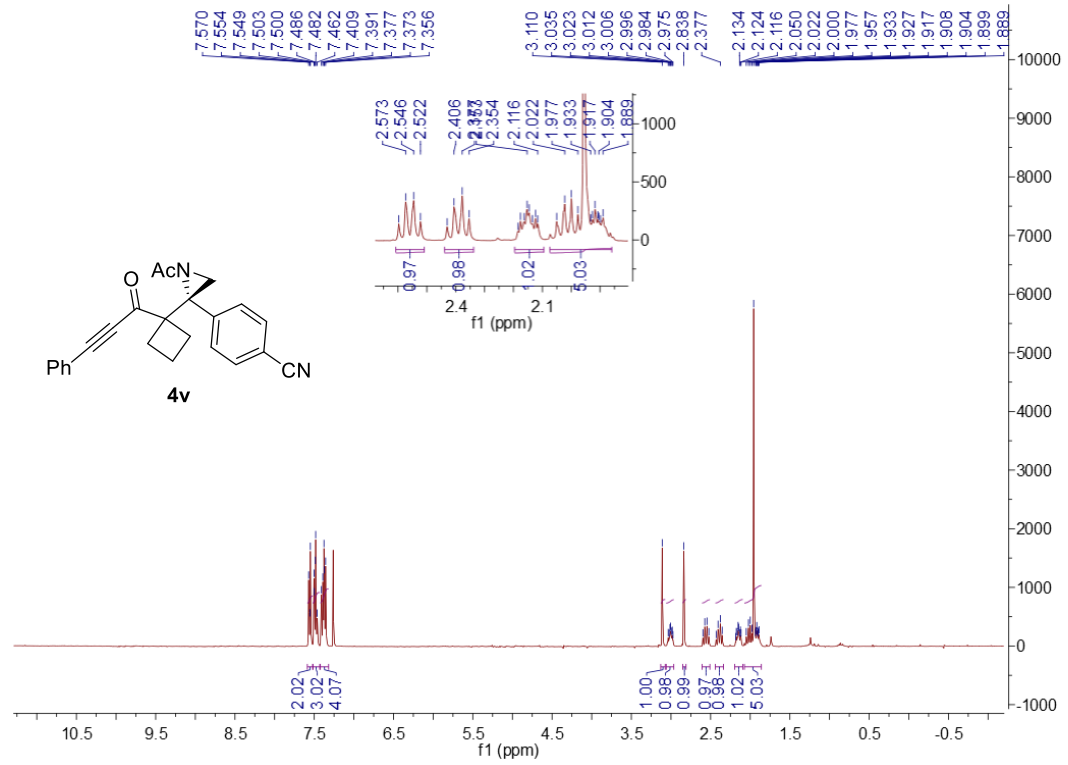
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4u



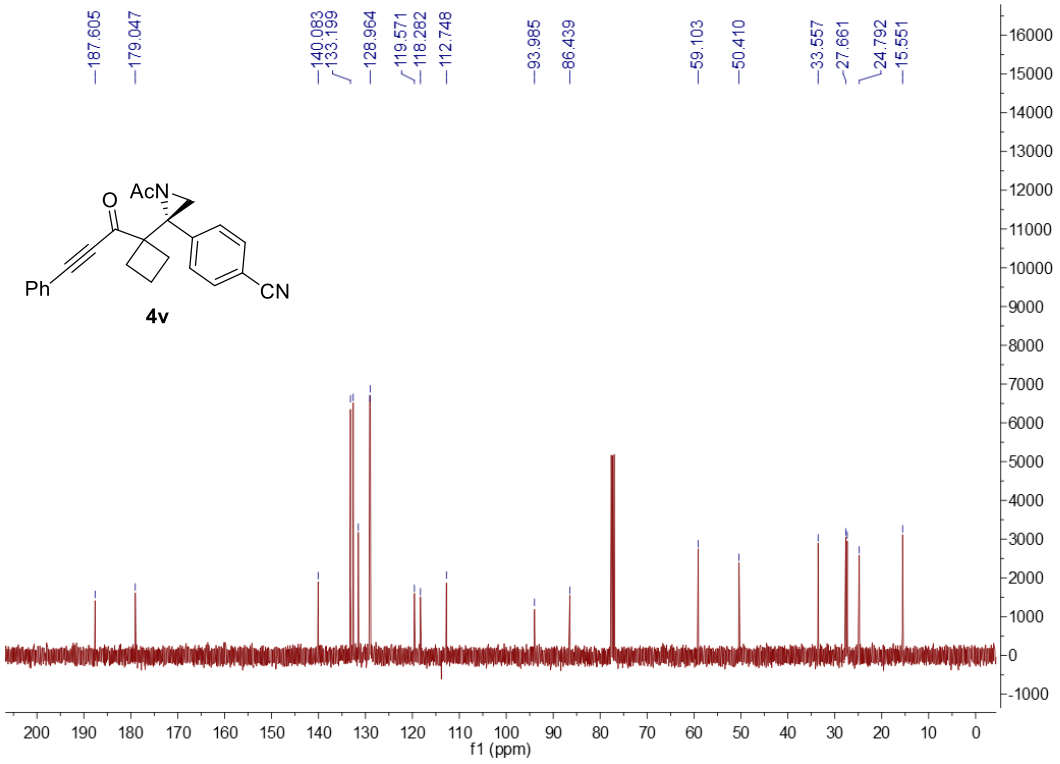
^{19}F NMR (376 MHz, $CDCl_3$) spectrum for 4u



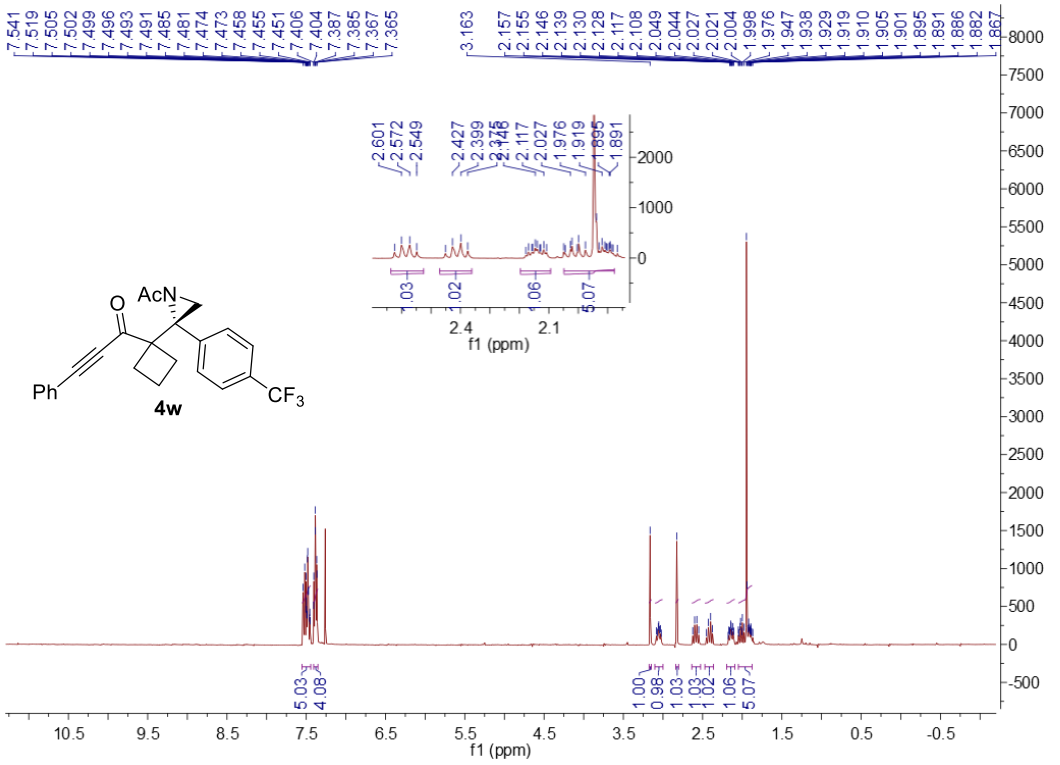
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4v



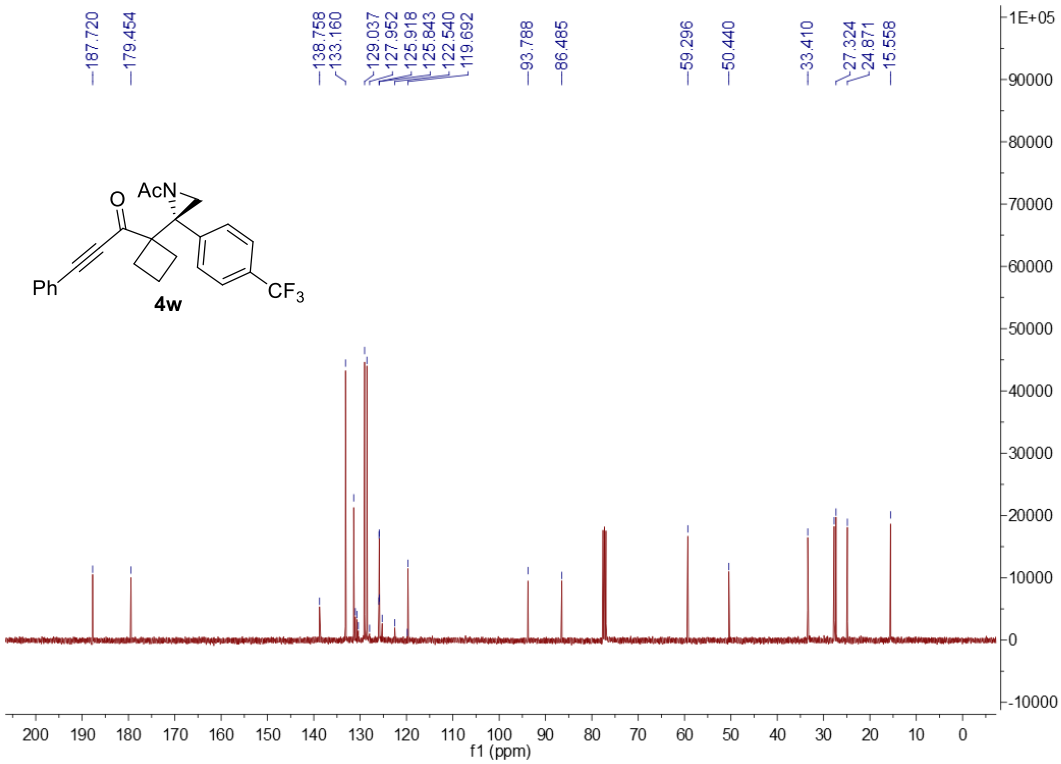
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4v



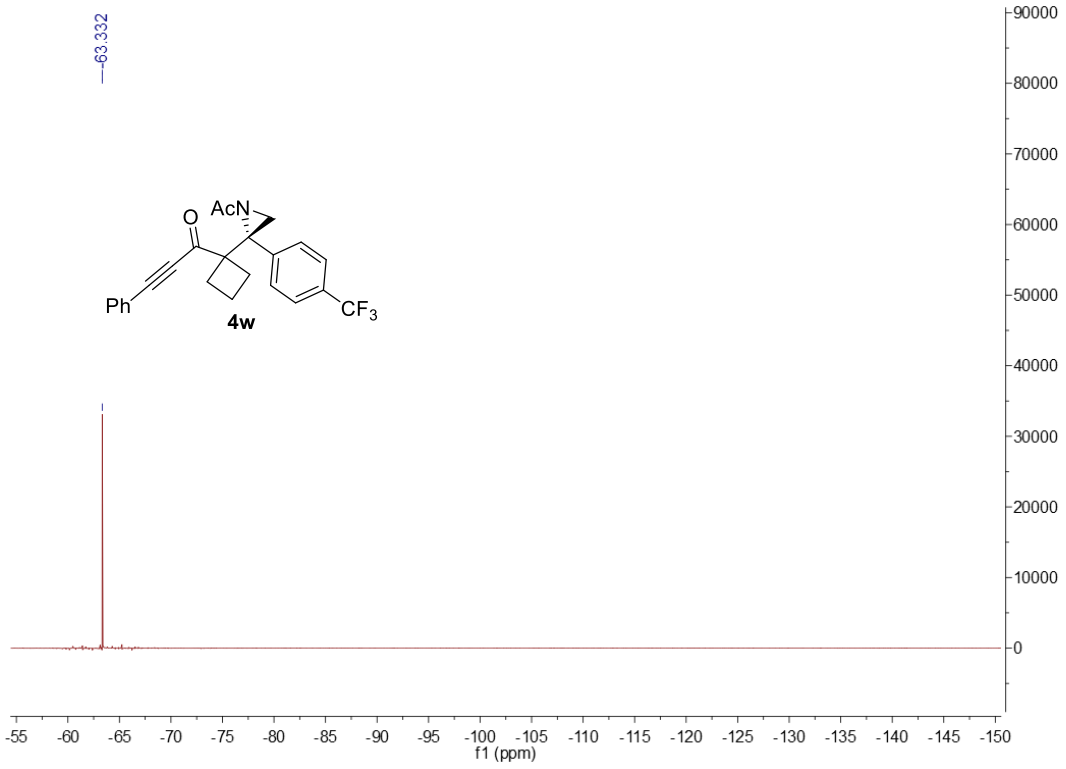
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4w



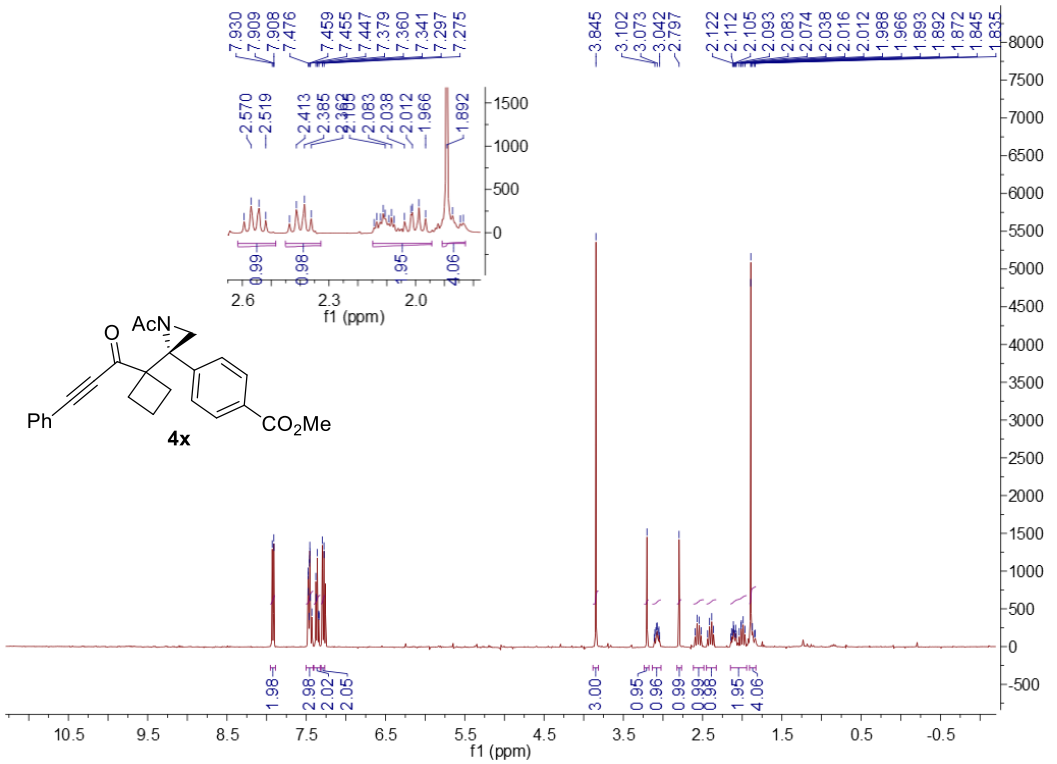
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4w



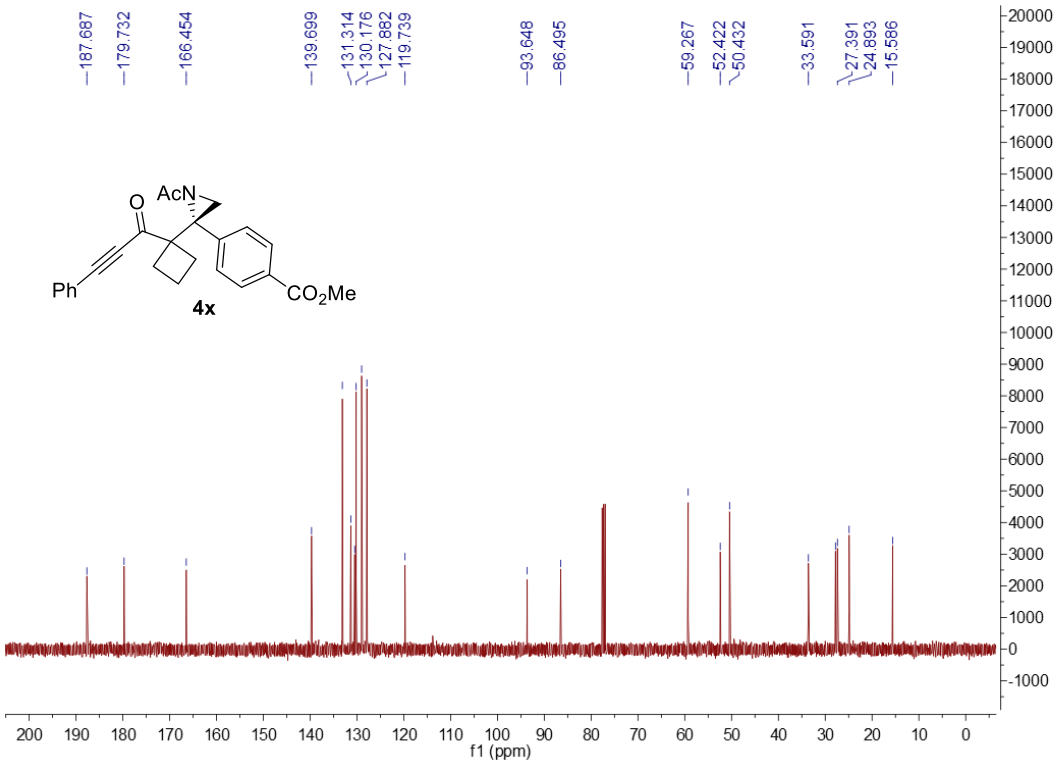
^{19}F NMR (376 MHz, $CDCl_3$) spectrum for 4w



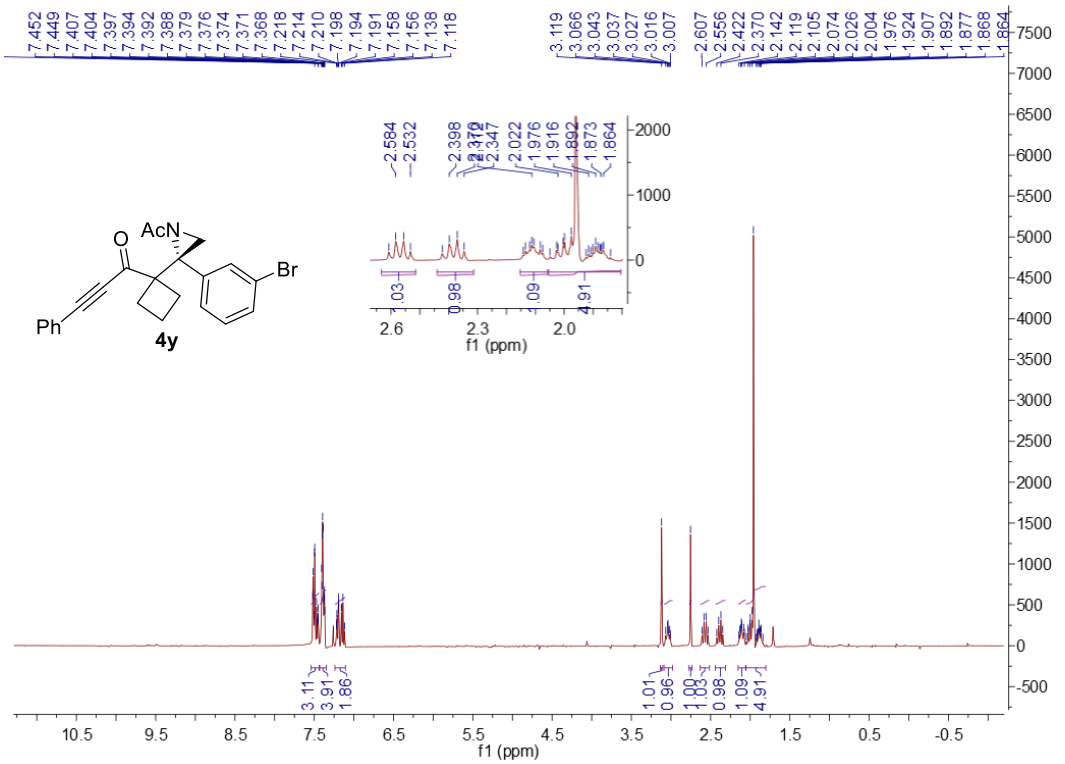
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4x



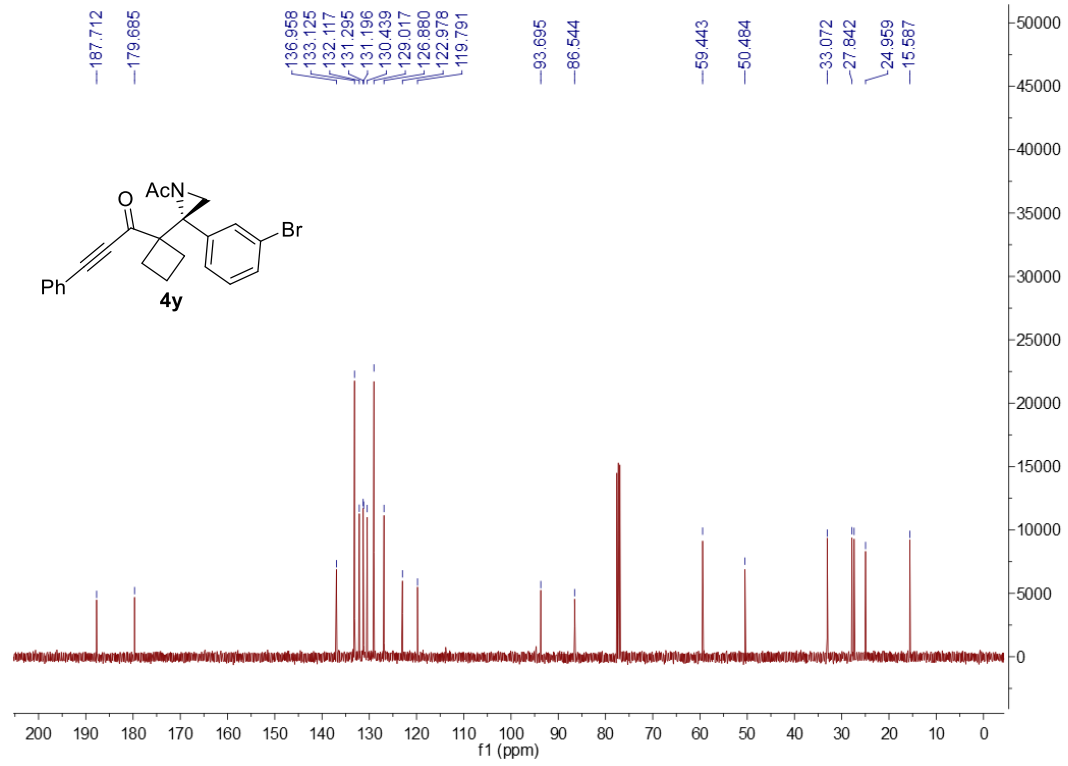
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4x



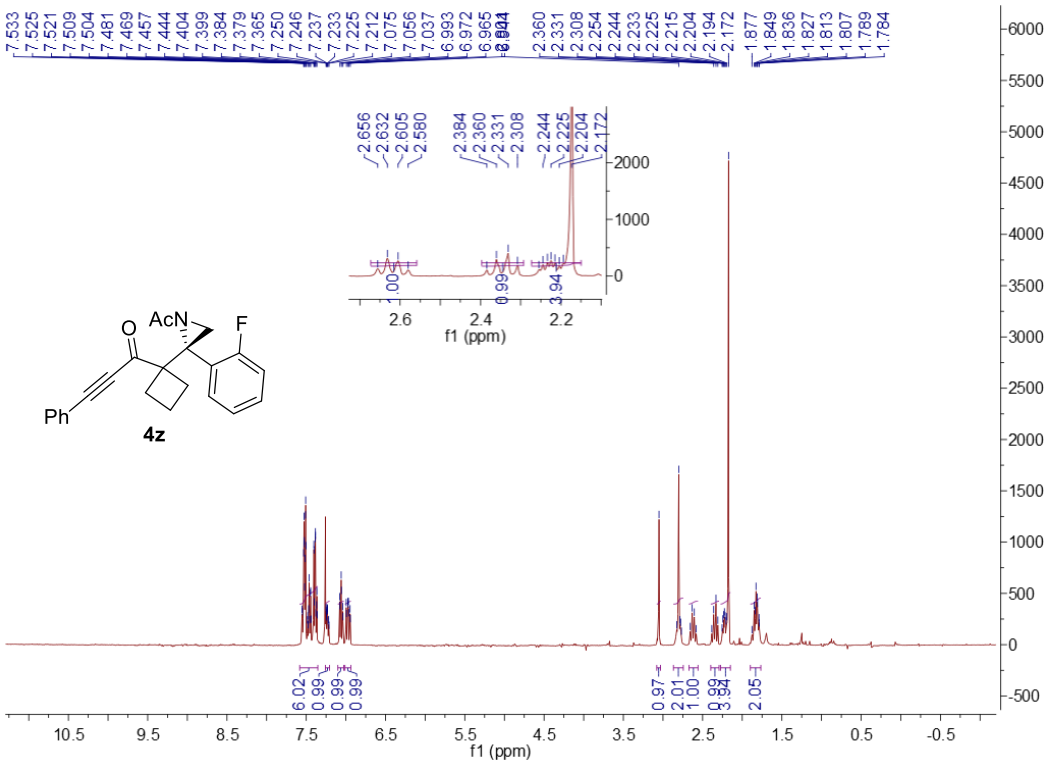
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4y



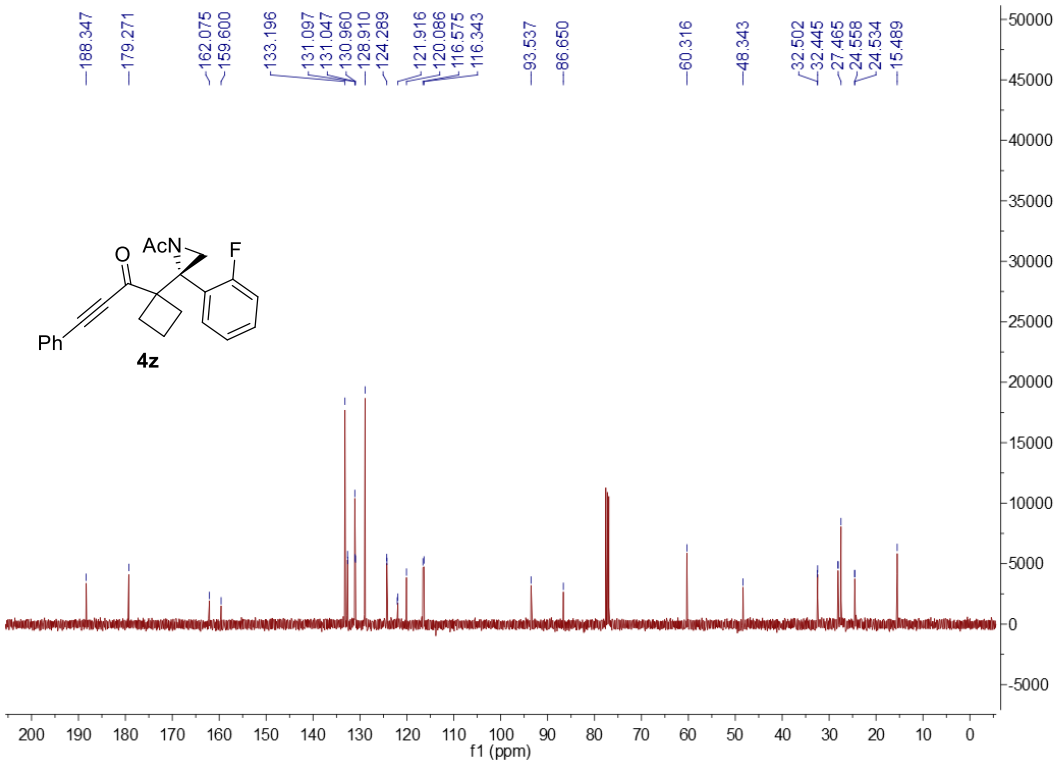
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4y



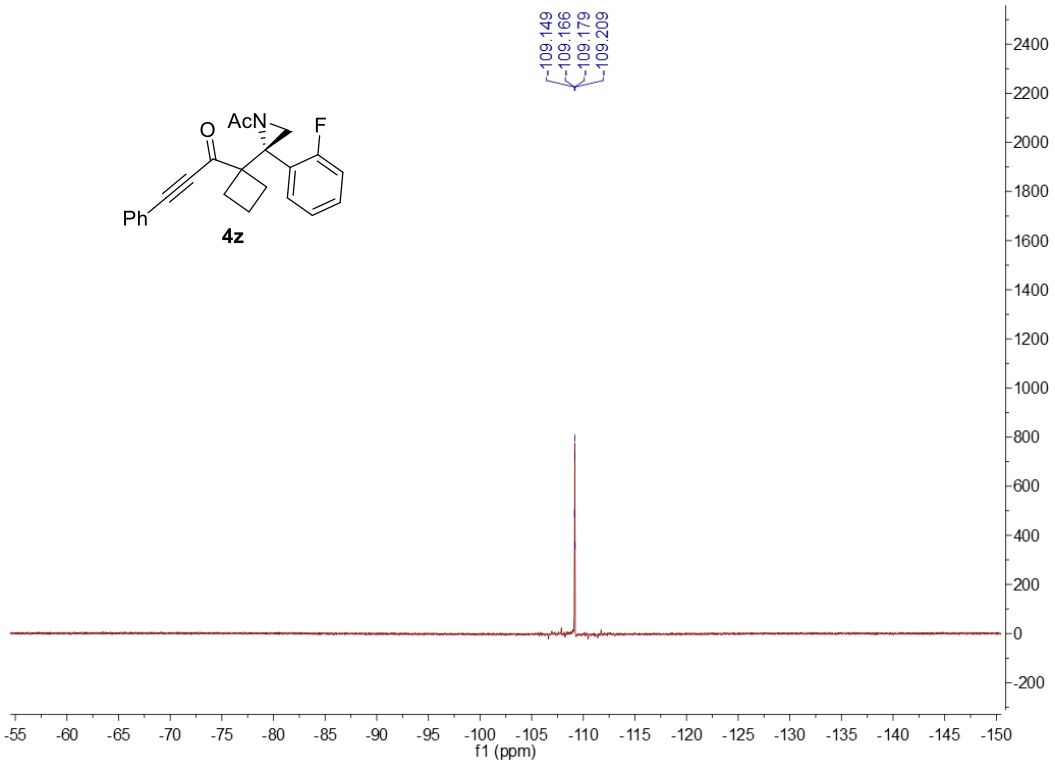
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4z



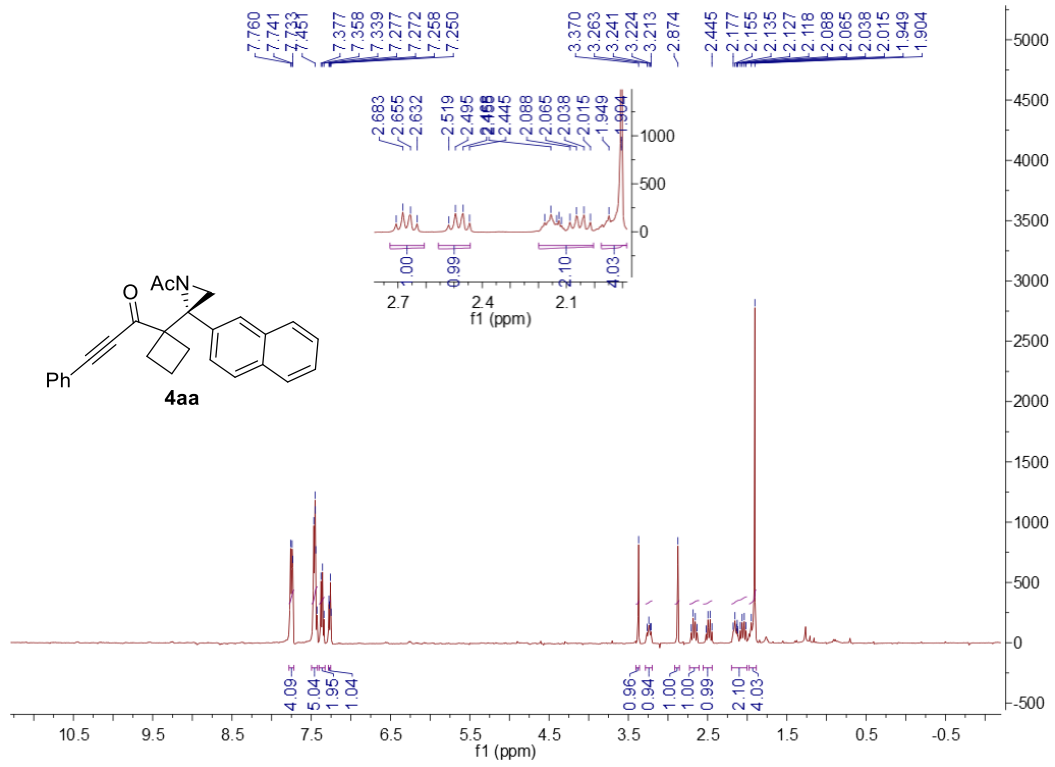
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4z



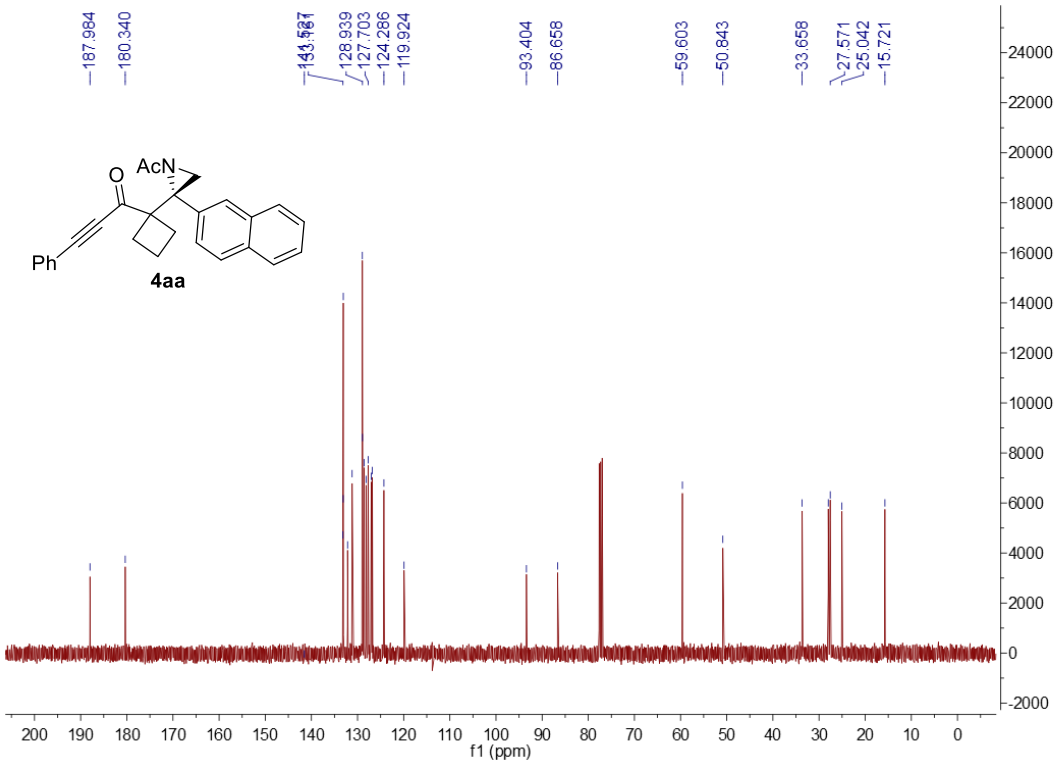
^{19}F NMR (101 MHz, $CDCl_3$) spectrum for 4z



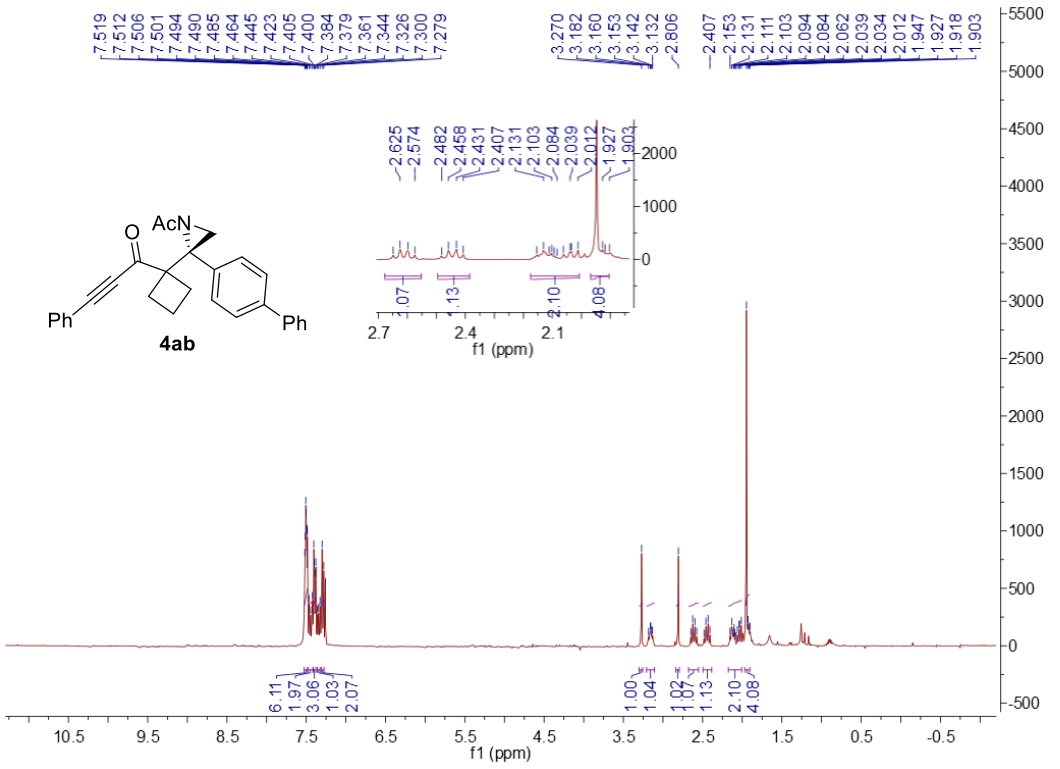
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4aa



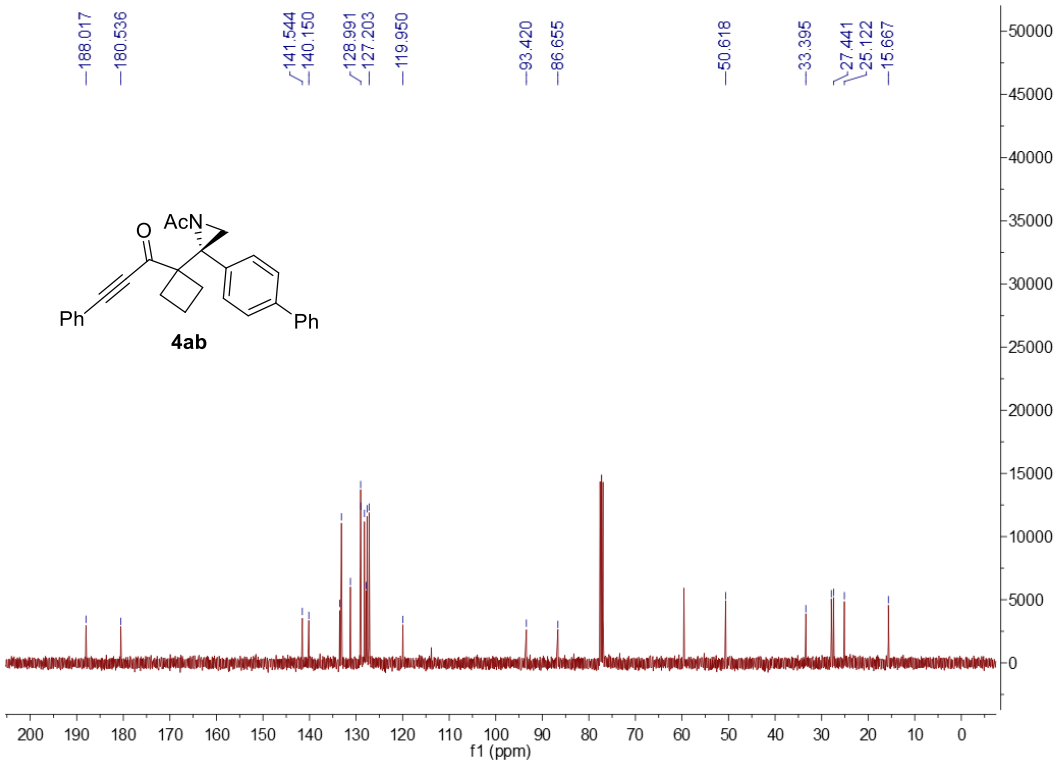
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4aa



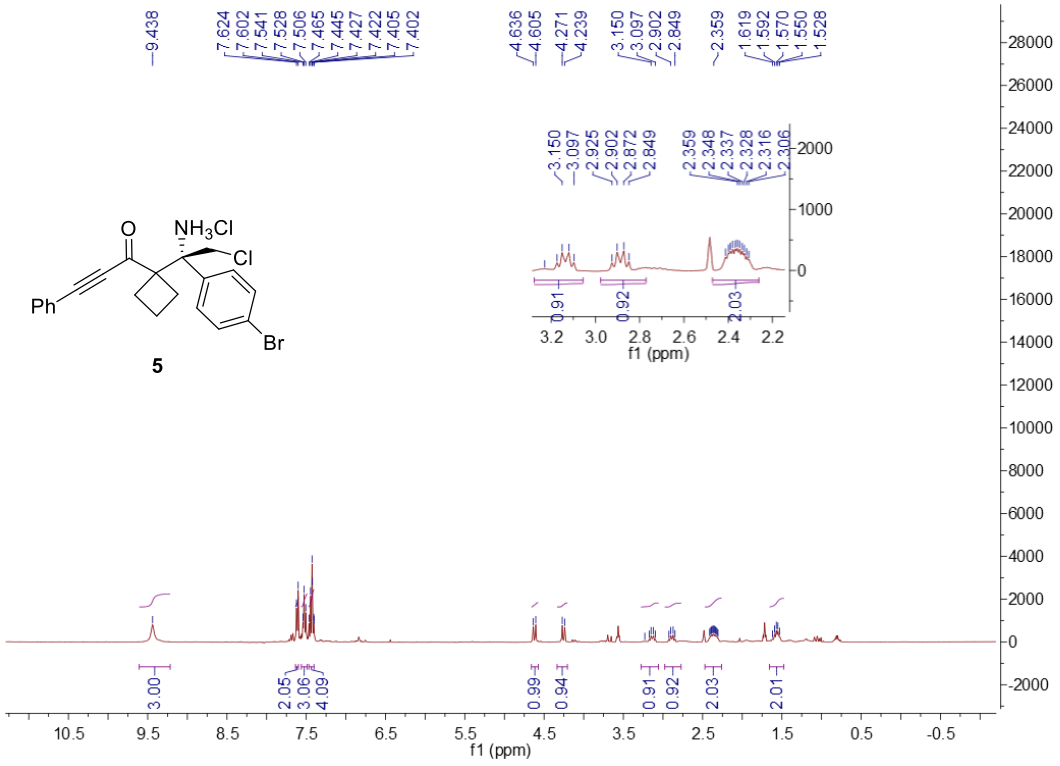
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4ab



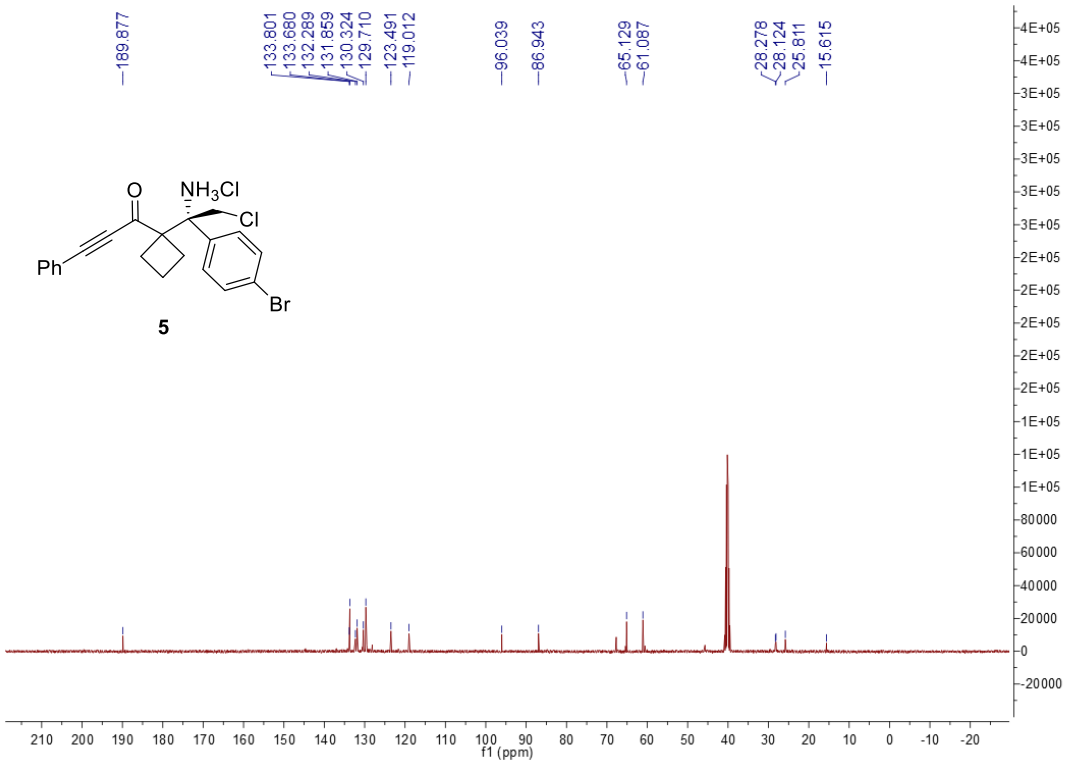
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4ab



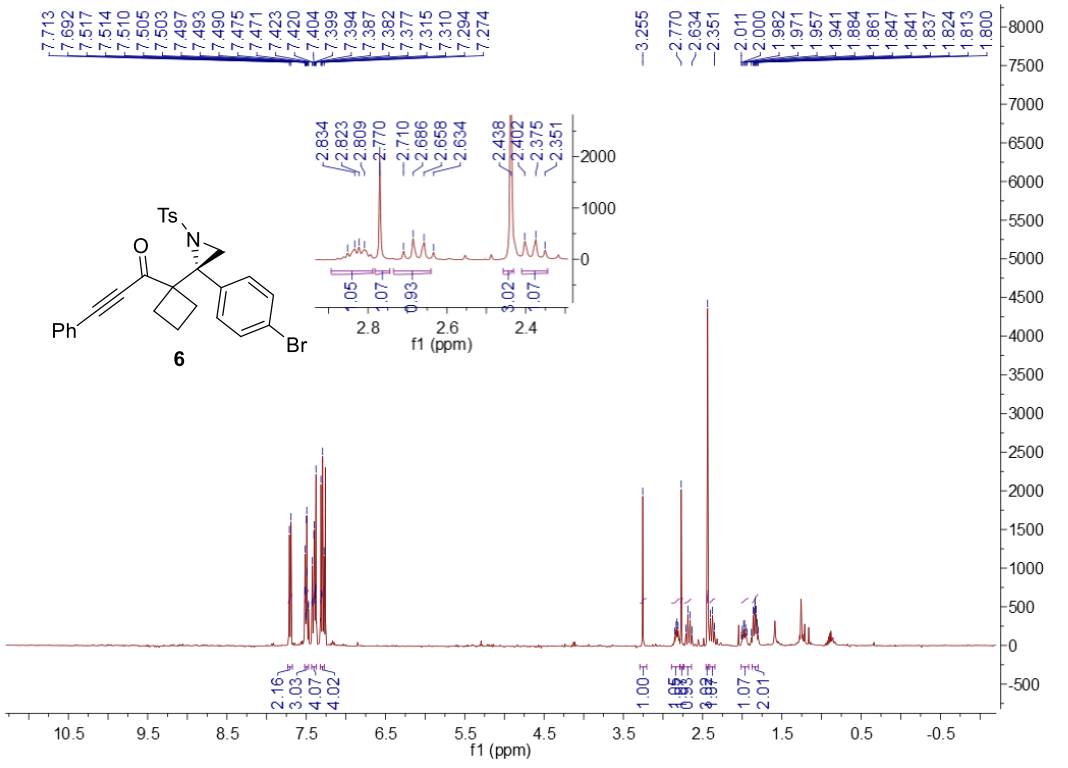
^{1}H NMR (400 MHz, d_6-DMSO) spectrum for 5



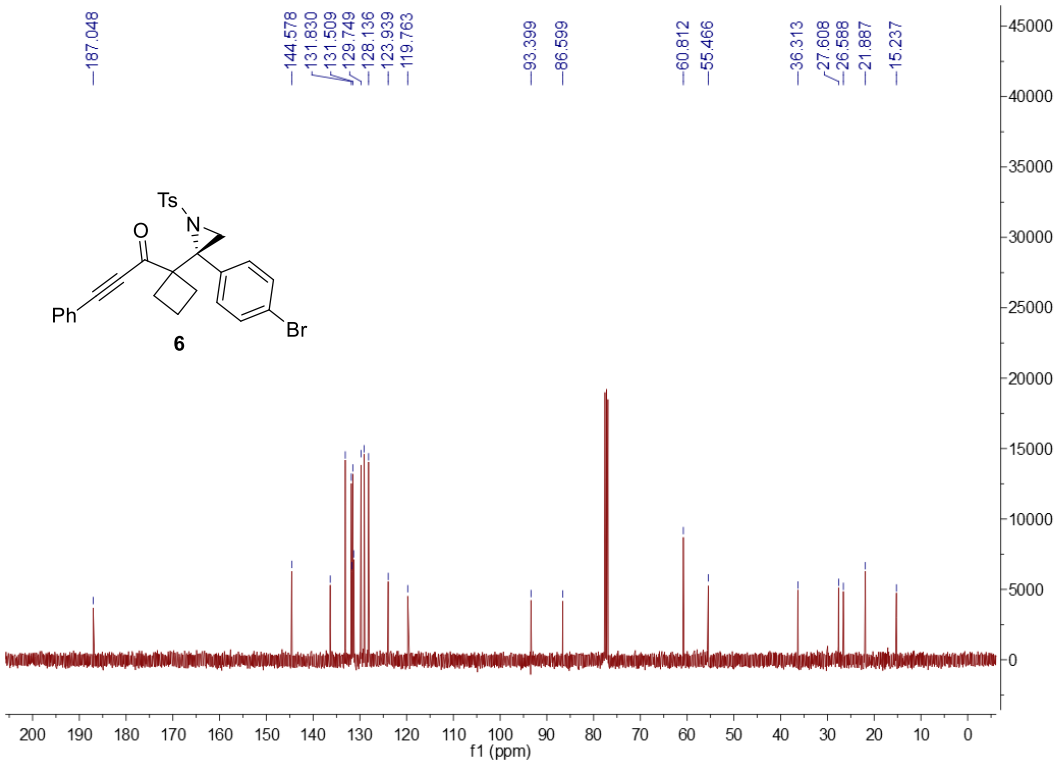
^{13}C NMR (101 MHz, d_6-DMSO) spectrum for 5



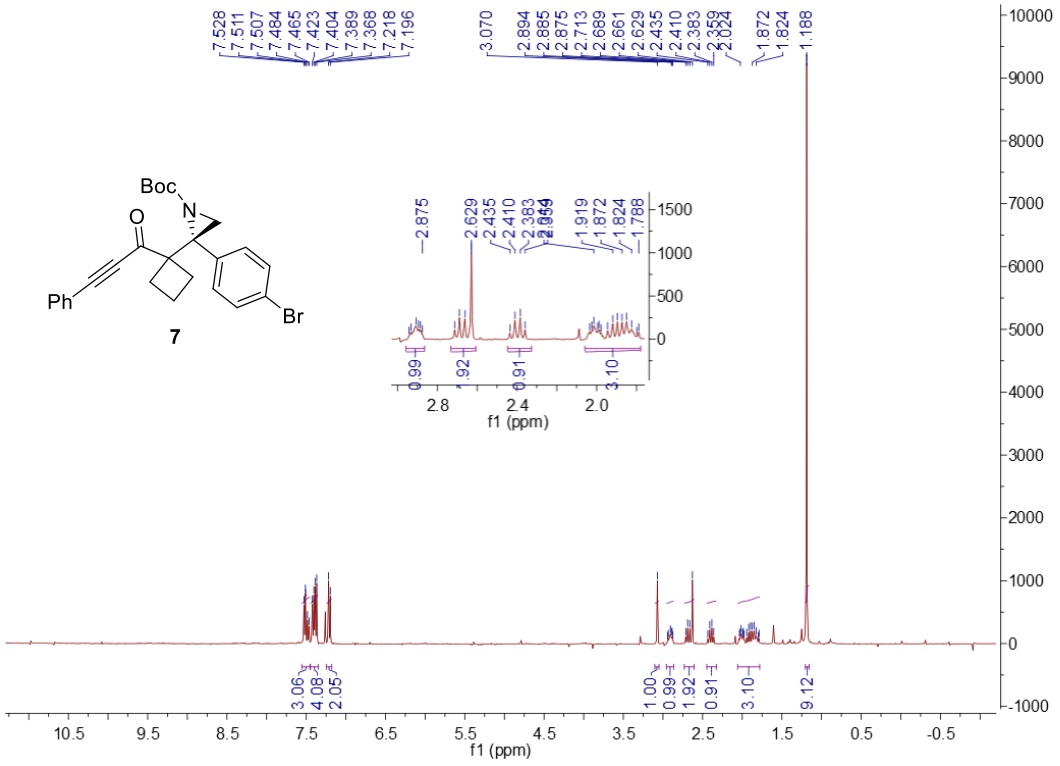
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 6



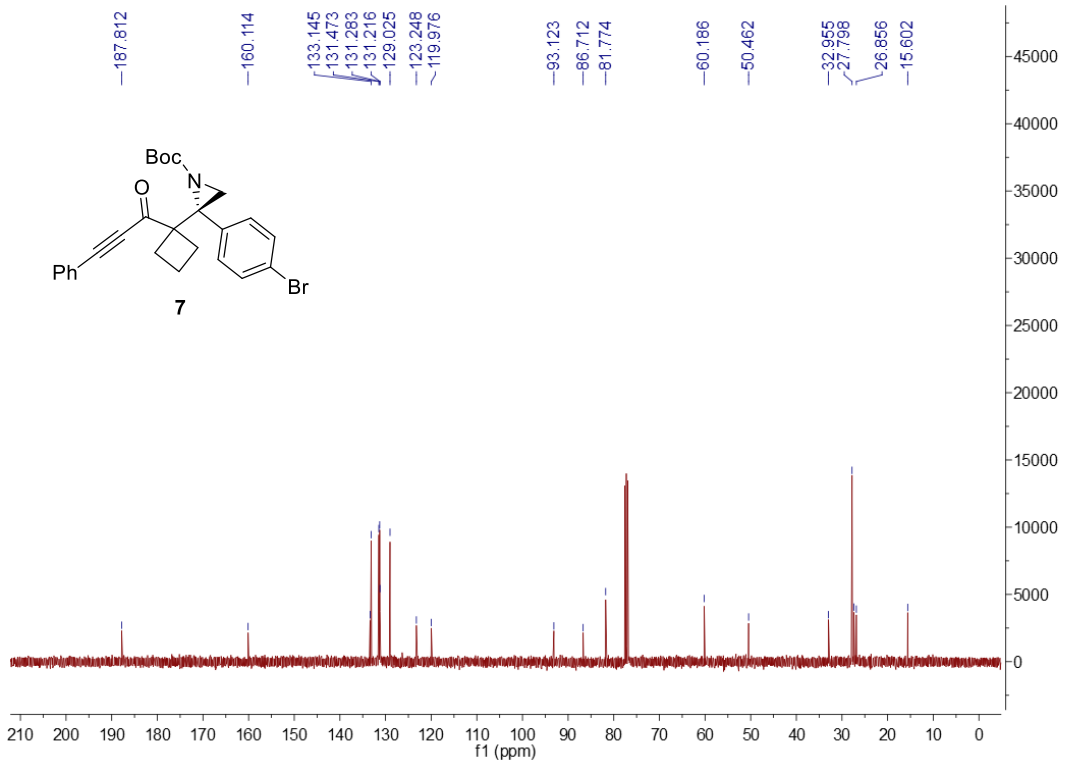
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 6



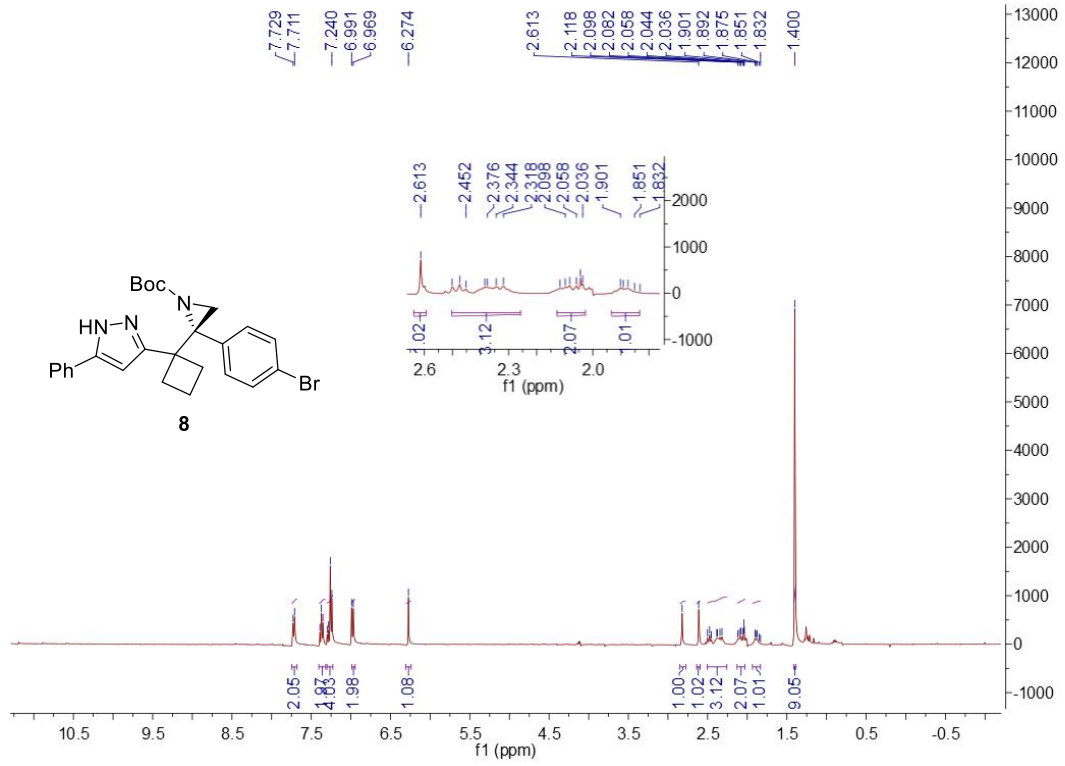
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 7



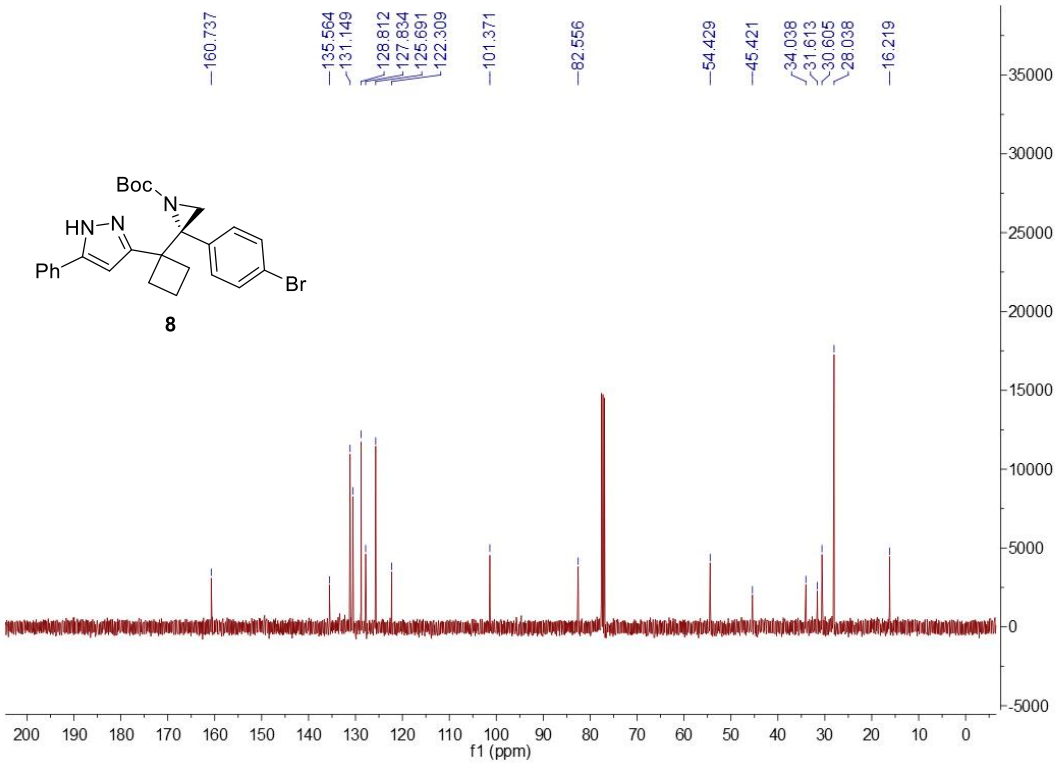
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 7



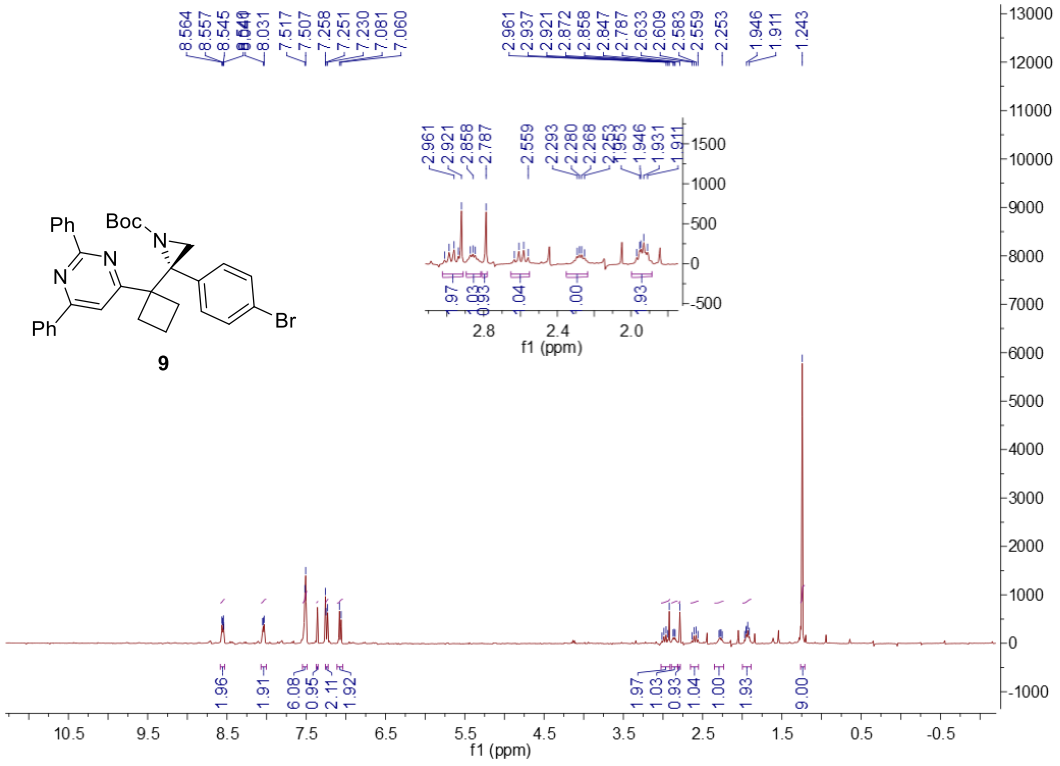
^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 8



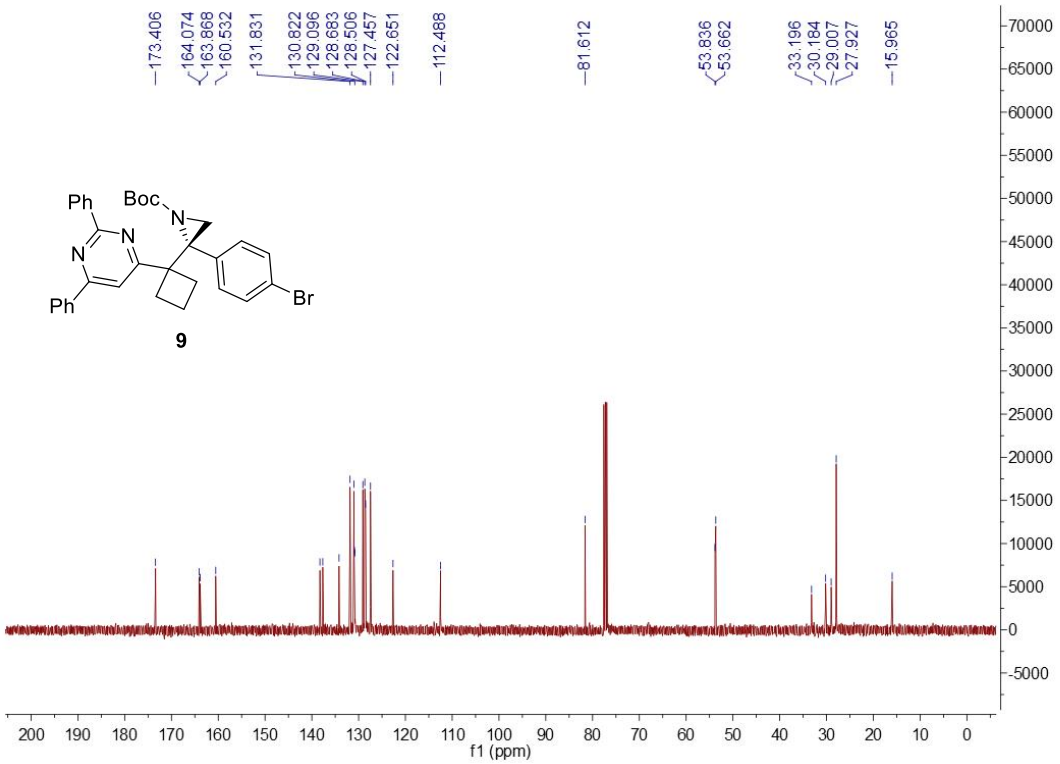
^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 8



^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 9

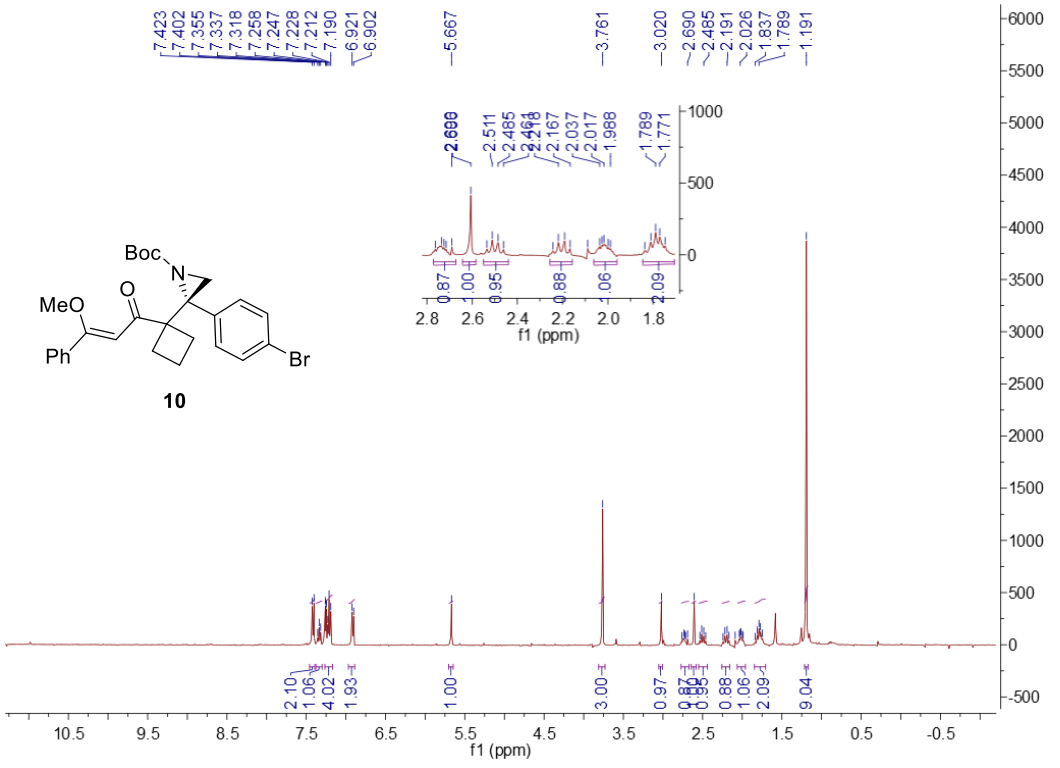


^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 9



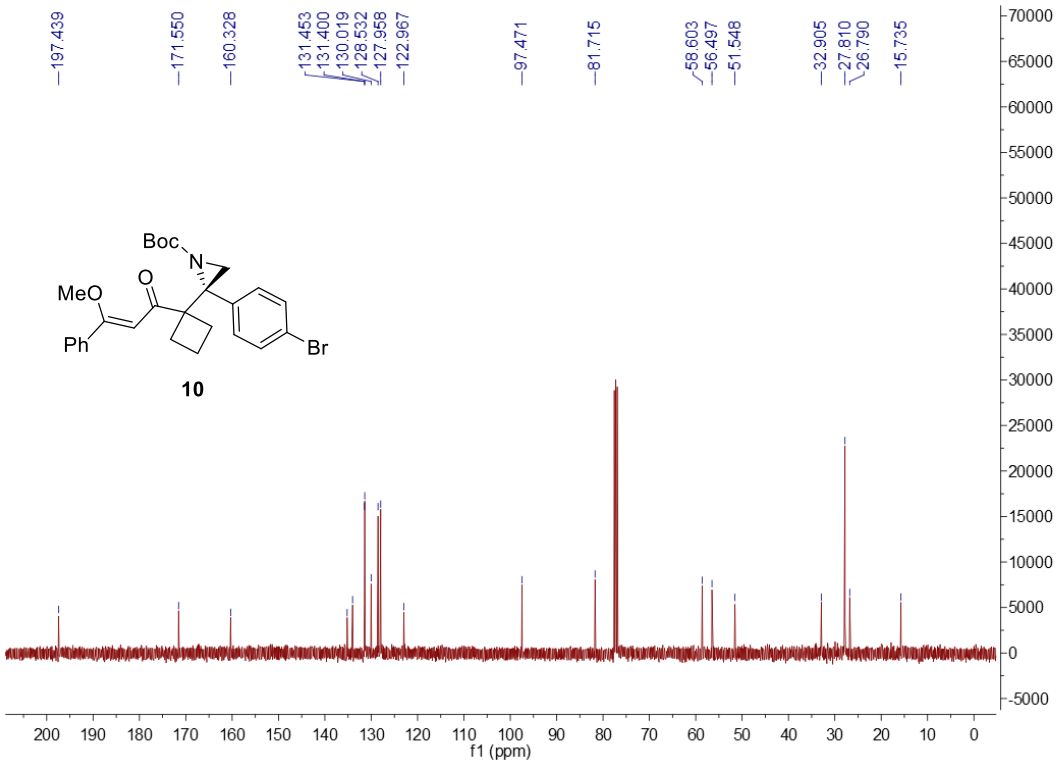
9

^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 10

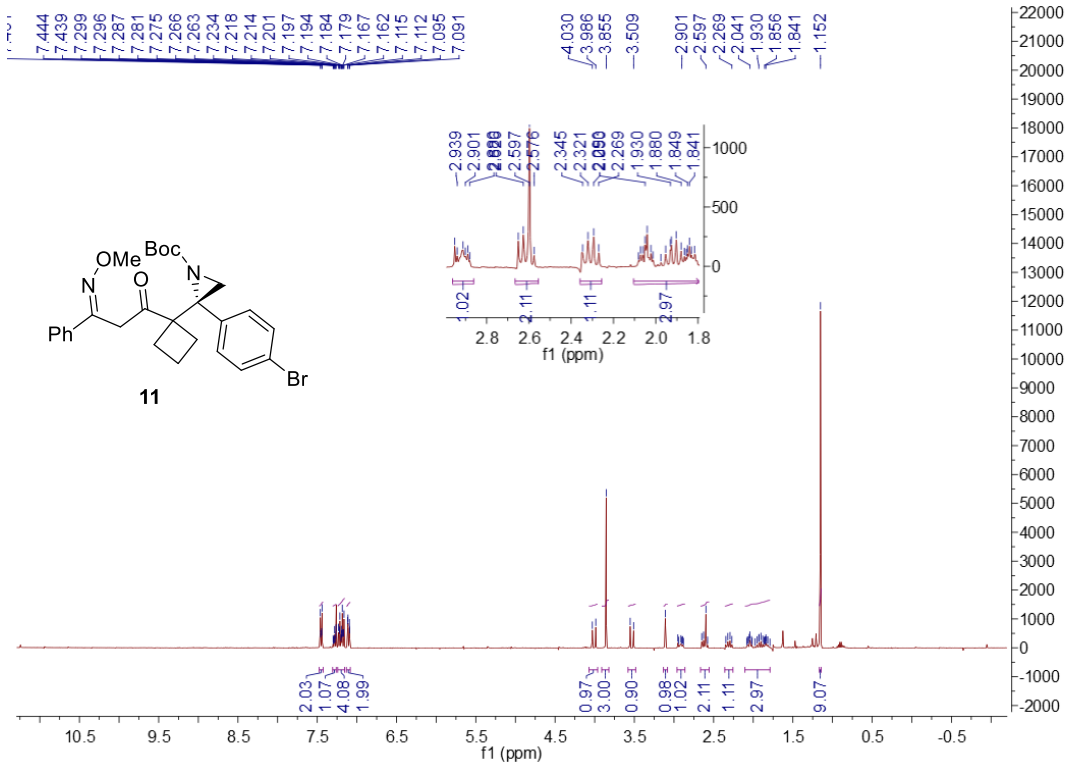


10

^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 10



^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 11



^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 11