# Concise Synthesis of (−)-Cycloclavine and (−)-5-*epi*-Cycloclavine via Asymmetric C–C Activation

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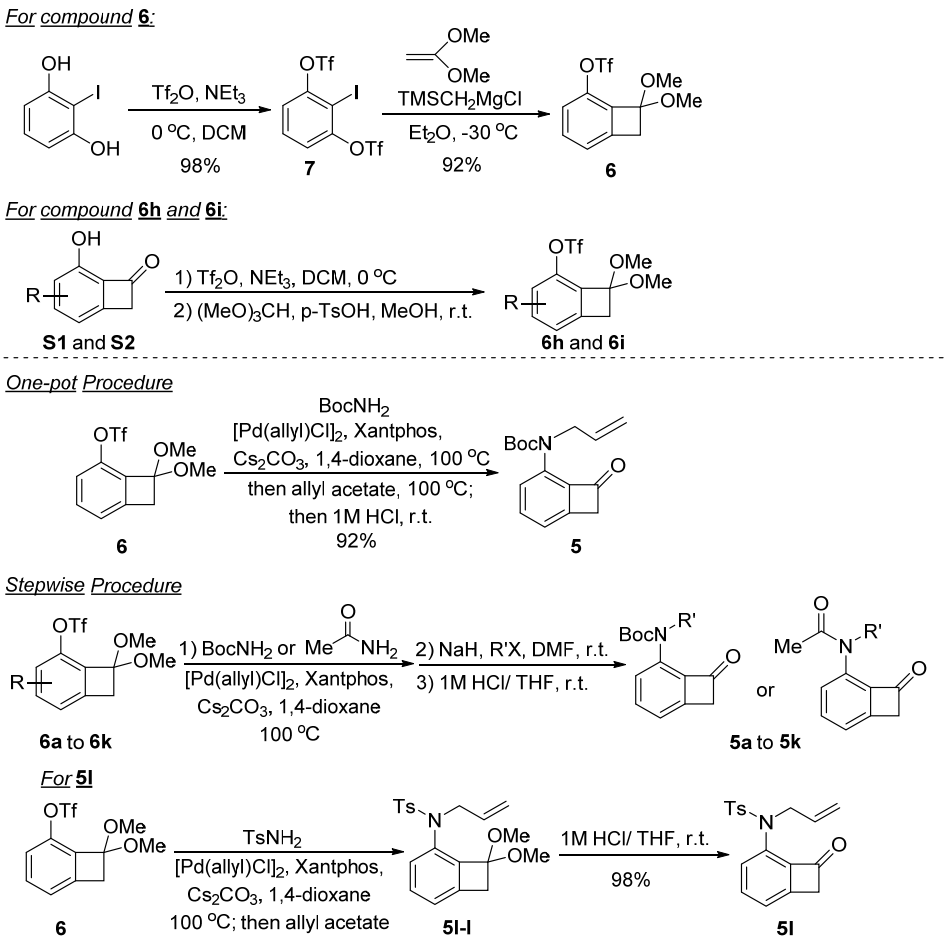
## 1. General information

Unless otherwise noted, all screening reactions were carried out in 4-mL vial sealed with PTFE lined caps. Solvents for the rhodium catalyzed C–C bond activation reaction were distilled over corresponding drying agents then freeze-pump-thawed three times before use. Methyl acetate was distilled over phosphorus pentoxide and freeze-pump-thawed three times before use. Rhodium precatalysts were purchased from Strem. All commercially available substrates were used without further purification. Thin layer chromatography (TLC) analysis was run on silica gel plates purchased from EMD Chemical (silica gel 60, F254). Infrared spectra were recorded on a Nicolet iS5 FT-IR Spectrometer using neat thin film technique. High-resolution mass spectra (HRMS) were obtained on an Agilent 6224 TOF-MS spectrometer and are reported as *m*/*z*. Nuclear magnetic resonance spectra ($^{1}$H NMR and $^{13}$C NMR) were recorded with a Bruker Model DMX 400 (400 MHz, $^{1}$H at 400 MHz, $^{13}$C at 101 MHz). For $CDCl_3$ solutions, the chemical shifts were reported as parts per million (ppm) referenced to residual protium or carbon of the solvents: $CHCl_3$ δ H (7.26 ppm) and $CDCl_3$ δ C (77.00 ppm). Coupling constants were reported in Hertz (Hz). Data for $^{1}$H NMR spectra were reported as following: chemical shift (δ, ppm), multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, ddd = doublet of doublet of doublets, m = multiplet), coupling constant (Hz), and integration. Analytical HPLC was carried out on an Angilent 1260 infinity HPLC with DAD, Chiralpak IA-IF, served as columns, and mixtures of *n*-hexane and *i*-PrOH were used for elution.

## 2. Experimental Procedure and Characterization Data

### I. *General information about substrate synthesis*

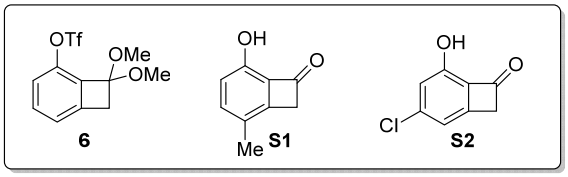
*The substrates for the C−C Activation reactions were synthesized following the route shown below*




Compound **6** was synthesized according to the reported procedure[1]. Compounds **6h** and **6i** were synthesized in two steps from literature known benzocyclobutenone precursors[2] **S1** and **S2**. For the following C–N bond coupling reaction, alkylation and deprotection sequence, substrate **5** was synthesized using a one-pot procedure[3], while substrates **5a**-**5k** and **5m** to **5n** were synthesized following the stepwise procedure. For compound **5l**, because the C–N bond coupling was not efficient enough, we purified the intermediate **5l-I** and subjected it to the following reactions.

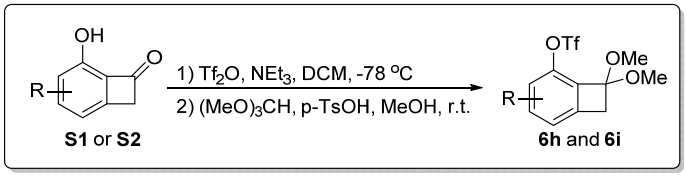
### II. *Synthesis of intermediates and substrates **5** to **5n***

a) *Synthesis of known compounds* **6**, **S1** *and* **S2**:



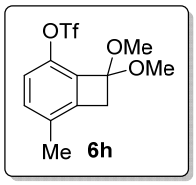

Compounds **6**, **S1** and **S2** were synthesized according to the reported procedure, Their spectroscopic data match those reported in literature[1,2].

b) *Synthesis of compounds* **6h** *and* **6i**:



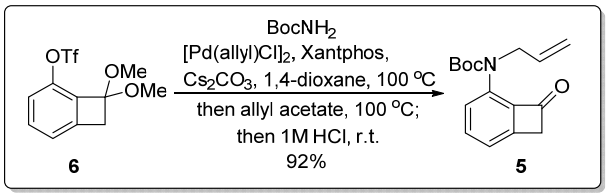

**Representative procedure**:

To a 100 mL flamed-dried Schlenk flask equipped with a stir bar and a nitrogen-filled balloon was added **S1** (843.7 mg, 5.7 mmol, 1.0 equiv.) in dichloromethane (30 mL). The system was cooled to -78 °C with a dry ice-acetone bath before $NEt_3$ (1.58 mL, 11.4 mmol, 2.0 equiv.) and $Tf_2O$ (1.15 mL, 6.84 mmol, 1.2 equiv.) were added dropwisely. Upon completion of the addition, the system was kept at -78 °C and stirred for 1 h under nitrogen atmosphere. After the starting material was fully consumed, the reaction mixture was quenched with saturated aqueous $NH_4Cl$ solution (20 mL) and warmed to room temperature. The mixture was extracted with ethyl acetate (3×20 mL), washed with brine, and dried over $Na_2SO_4$. The combined organic extract was concentrated under reduced pressure and subjected to next step without further purification. The crude product was dissolved in MeOH (20 mL) before $(MeO)_3CH$ (5.61 mL, 51.3 mmol, 9.0 equiv.) and *p*-TsOH (108.4 mg, 0.57 mmol, 0.1 equiv.) were added to the stirring solution. The reaction was stirred at room temperature overnight. The reaction was quenched by saturated aqueous $NaHCO_3$ solution (20 mL) and the mixture was extracted with ethyl acetate (3×20 mL), washed with brine, and dried over $Na_2SO_4$. The crude product was purified by silica gel flash column chromatography (EtOAc/Hexane=1/10) to afford compound **6h** as a colorless oil in 96% yield over two steps (1.78 g).




Compound **6h** was isolated as a colorless oil in 96% yield over two steps (1.78 g). $R_f$ = 0.6 (EtOAc/Hexane=1/5). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.17 (dd, *J* = 8.6, 0.9 Hz, 1H), 7.05 (d, *J* = 8.5 Hz, 1H), 3.45 (s, 6H), 3.31 (s, 2H), 2.23 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 143.1, 138.6, 135.6, 134.6, 132.5, 120.1, 120.0, 117.0, 104.5, 51.8, 42.4, 16.4. **IR:** ν 3446, 2065, 1635, 1423, 1256, 1211, 860, 750, 618 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 349.0328 Found: 349.0323.

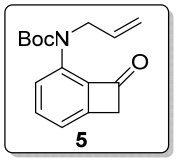
c) *Synthesis of compound* **5**:




**Procedure**:

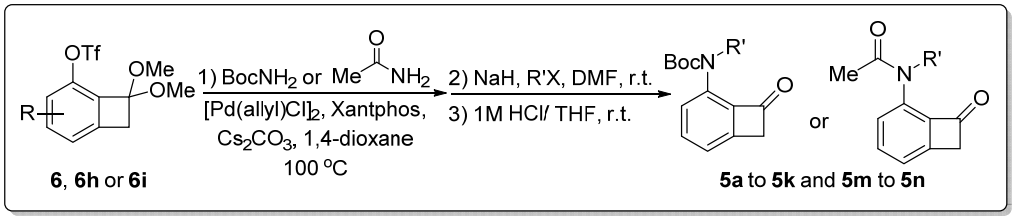
To a 20 mL flamed-dried vial equipped with a stir bar was added **6** (312.3 mg, 1 mmol, 1.0 equiv.), $BocNH_2$ (175.8 mg, 1.5 mmol, 1.5 equiv.), $[Pd(allyl)Cl]_2$ (18.3 mg, 0.05 mmol, 5 mol%), Xantphos (86.8 mg, 0.15 mmol, 15 mol%) and $Cs_2CO_3$ (975 mg, 3.0 mmol, 3.0 equiv.). Then the vial was loosely capped and transferred into a nitrogen-filled glovebox

and 1,4-dioxane (10 mL) was added to the mixture before the vial was tightly capped and transferred out. The system was heated to 100 °C overnight. The reaction was then cooled down to room temperature and allyl acetate (0.54 mL, 5 mmol, 5.0 equiv.) was added to the mixture inside glovebox. The mixture was stirred at 100 °C for another 10 min. After cooling the reaction back to room temperature, 1M HCl (6 mL) was added dropwisely to the vial and the mixture was stirred for 1 h at room temperature. The reaction was then quenched by saturated aqueous $NaHCO_3$ solution (30 mL) and the mixture was extracted with ethyl acetate (3×20 mL), washed with brine, and dried over $Na_2SO_4$. The crude product was purified by silica gel flash column chromatography (EtOAc/Hexane=1/10) to afford compound **5** as a colorless oil in 92% yield (252 mg).



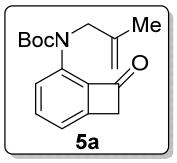

Compound **5** was isolated as a colorless oil in 92% yield in one pot (252 mg). $R_f$ = 0.4 (EtOAc/Hexane=1/5). **$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.52 (d, *J* = 8.4 Hz, 1H), 7.48 – 7.41 (m, 1H), 7.18 (d, *J* = 7.1 Hz, 1H), 5.80 (ddt, *J* = 17.5, 10.4, 5.3 Hz, 1H), 5.13 – 5.01 (m, 2H), 4.57 (d, *J* = 5.1 Hz, 2H), 3.89 (s, 2H), 1.49 (s, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 185.4, 153.1, 150.5, 139.0, 135.9, 135.7, 133.8, 123.4, 118.5, 116.0, 81.7, 51.2, 51.1, 28.1. **IR:** ν 2977, 2929, 1765, 1707, 1599, 1478, 1367, 1239, 1147, 976, 787, 575 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 296.1257. Found: 296.1256.

d) *Synthesis of compounds* **5a** to **5k** and **5m** to **5n**:

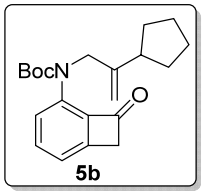



**Procedure** (using **5a** as an example):

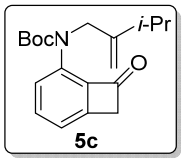
To a 20 mL flamed-dried vial equipped with a stir bar was added **6** (665.2 mg, 2.13 mmol, 1.0 equiv.), $BocNH_2$ (391.9 mg, 3.34 mmol, 1.5 equiv.), $[Pd(allyl)Cl]_2$ (38.9 mg, 0.11 mmol, 5 mol%), Xantphos (184.9 mg, 0.32 mmol, 15 mol%) and $Cs_2CO_3$ (2.08 g, 6.4 mmol, 3.0 equiv.). Then the vial was loosely capped and transferred into a nitrogen-filled glovebox and 1,4-dioxane (10 mL) was added to the mixture before the vial was tightly capped and transferred out. The system was then heated to 100 °C overnight. Upon completion, the reaction was cooled to room temperature and filtered through a pad of celite. The filtrate was concentrated under reduced pressure and the crude product was dissolved in DMF (10 mL). NaH (74.88 mg, 3.12 mmol, 1.5 equiv.) was added to the mixture, followed by 3-chloro-2-methyl-1-propene (0.42 mL, 3.12 mmol, 1.5 equiv.). The mixture was stirred overnight at room temperature. Upon completion, the reaction was quenched with water and extracted with ethyl acetate (3×20 mL), washed with brine, and dried over $Na_2SO_4$. The crude product was dissolved in 6 mL tetrahydrofuran and transferred to a 20 mL vial charged with a stir bar. While stirring, 2 mL of 1M HCl aqueous solution was added to the mixture. After stirring for 1 h at room temperature, saturated $NaHCO_3$ aqueous solution was added dropwisely to quench the reaction. The mixture was extracted with ethyl acetate (3×20 mL), washed with brine, and dried over $Na_2SO_4$. The crude product was purified by silica gel flash column chromatography (EtOAc/Hexane=1/5) to afford compound **5a** as a colorless oil in 94% yield (575 mg) over 3 steps. [All the R'X used in substrate preparation were literature known compounds[4]]



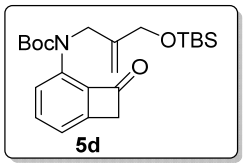

Compound **5a** was isolated as a colorless oil in 94% yield over 3 steps. $R_f$ = 0.5 (EtOAc/Hexane=1/5). **$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.51 (d, *J* = 8.4 Hz, 1H), 7.48 – 7.42 (m, 1H), 7.18 (d, *J* = 7.0 Hz, 1H), 4.76 – 4.73 (m, 1H), 4.70 (s, 1H), 4.51 (s, 2H), 3.88 (s, 2H), 1.68 (s, 3H), 1.49 (s, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 185.4, 153.3, 150.5, 141.3, 139.2, 135.9, 135.7, 123.5, 118.5, 110.7, 81.6, 53.9, 51.1, 28.1, 19.9. **IR:** ν 3080, 2976, 2931, 1766, 1708, 1599, 1478, 1367, 1240, 1159, 975, 788, 576 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 310.1414. Found: 310.1414.




Compound **5b** was isolated as a colorless oil in 86% yield over 3 steps. $R_f$ = 0.6 (EtOAc/Hexane=1/5). **$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.52 (d, *J* = 8.4 Hz, 1H), 7.49 – 7.42 (m, 1H), 7.18 (d, *J* = 7.0 Hz, 1H), 4.78 (s, 1H), 4.68 (s, 1H), 4.55 (s, 2H), 3.89 (s, 2H), 2.35 (p, *J* = 8.5 Hz, 1H), 1.82 (td, *J* = 11.2, 6.8 Hz, 2H), 1.72 – 1.62 (m, 2H), 1.61 – 1.52 (m, 2H), 1.49 (s, 9H), 1.44 – 1.34 (m, 2H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 185.3, 153.2, 150.4, 148.5, 139.1, 136.0, 135.8, 123.3, 118.4, 106.3, 81.5, 52.8, 51.0, 43.6, 31.2, 28.0, 24.8. **IR:** ν 2955, 2869, 1766, 1708, 1599, 1478, 1367, 1243, 1157, 981, 787, 575 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 364.1883. Found: 364.1880.

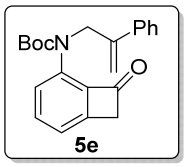



Compound **5c** was isolated as a colorless oil in 97% yield over 3 steps. $R_f$ = 0.6 (EtOAc/Hexane=1/5). **$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.51 (d, *J* = 8.4 Hz, 1H), 7.48 – 7.42 (m, 1H), 7.18 (d, *J* = 7.0 Hz, 1H), 4.76 (s, 1H), 4.67 (s, 1H), 4.56 (s, 2H), 3.88 (s, 2H), 2.23 (hept, *J* = 6.4 Hz, 1H), 1.48 (s, 9H), 1.03 (d, *J* = 7.0 Hz, 6H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 185.4, 153.3, 151.1, 150.5, 139.2, 136.0, 135.9, 123.4, 118.5, 106.6, 81.6, 52.1, 51.1, 31.6, 28.1, 21.6. **IR:** ν 3435, 2965, 2930. 1766, 1708, 1599, 1478, 1367, 1243, 1155, 981, 786 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 316.1907. Found: 316.1906.

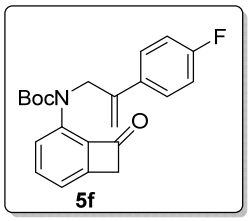



Compound **5d** was isolated as a colorless oil in 91% yield over 3 steps. $R_f$ = 0.7 (EtOAc/Hexane=1/5). **$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.49 (d, *J* = 8.3 Hz, 1H), 7.45 (dd, *J* = 8.3, 6.8 Hz, 1H), 7.18 (d, *J* = 6.8 Hz, 1H), 5.05 (d, *J* = 1.5 Hz, 1H), 4.83 (d, *J* = 1.4 Hz, 1H), 4.58 (s, 2H), 4.09 (s, 2H), 3.88 (s, 2H), 1.48 (s, 9H), 0.87 (s, 9H), 0.02 (s, 6H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 185.4, 153.2, 150.5, 144.3, 139.4, 135.9, 135.6, 123.5, 118.6, 109.7, 81.7, 64.1, 51.2, 50.7, 28.1, 25.8,

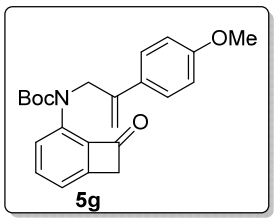
18.3, -5.5. **IR:** v 2929, 2856, 1766, 1711, 1600, 1478, 1367, 1257, 1158, 977, 838, 765 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 418.2408. Found: 418.2410.



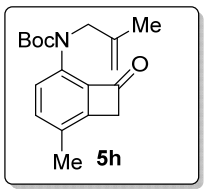

Compound **5e** was isolated as a colorless oil in 30% yield over 3 steps. $R_f$ = 0.5 (EtOAc/Hexane=1/5). **$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.40 (dd, *J* = 8.4, 7.1 Hz, 1H), 7.35 – 7.24 (m, 6H), 7.18 (d, *J* = 7.1 Hz, 1H), 5.25 (s, 1H), 5.05 (s, 1H), 5.02 (s, 2H), 3.90 (s, 2H), 1.47 (s, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 185.5, 153.1, 150.4, 144.5, 139.5, 139.1, 135.8, 135.2, 128.2, 127.7, 126.4, 124.1, 118.7, 112.7, 81.7, 51.9, 51.2, 28.0. **IR:** v 2977, 2926, 1766, 1707, 1599, 1478, 1368, 1241, 1157, 981, 750, 704 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 350.1751. Found: 350.1761.



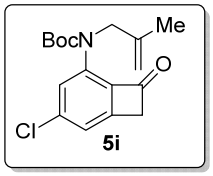

Compound **5f** was isolated as a light yellow solid in 75% yield over 3 steps. Melting Point: 91-92 °C. $R_f$ = 0.4 (EtOAc/Hexane=1/5). **$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.40 (t, *J* = 7.7 Hz, 1H), 7.34 – 7.26 (m, 3H), 7.19 (d, *J* = 7.1 Hz, 1H), 6.97 (t, *J* = 8.5 Hz, 2H), 5.18 (s, 1H), 5.03 (s, 1H), 5.00 (s, 2H), 3.90 (s, 2H), 1.47 (s, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 185.6, 162.4 (d, *J* = 246.7 Hz), 153.1, 150.4, 143.6, 139.4, 135.8, 135.2 (d, *J* = 3.4 Hz), 135.1, 128.1 (d, *J* = 8.0 Hz), 124.2, 118.8, 115.0 (d, *J* = 21.4 Hz), 112.9, 81.8, 51.8, 51.2, 28.0. **$^{19}$F NMR (470 MHz, $CDCl_3$)**: δ -68.4. **IR:** v 3435, 2930, 1764, 1707, 1600, 1510, 1368, 1234, 1157, 981, 841, 750 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 390.1476. Found: 390.1483.



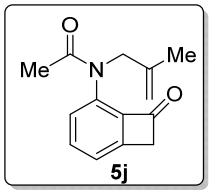

Compound **5g** was isolated as a colorless oil in 37% yield over 3 steps. $R_f$ = 0.4 (EtOAc/Hexane=1/5). **$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.40 (t, *J* = 7.7 Hz, 1H), 7.31 (d, *J* = 8.3 Hz, 1H), 7.29 – 7.25 (m, 2H), 7.18 (d, *J* = 7.1 Hz, 1H), 6.83 (d, *J* = 8.6 Hz, 2H), 5.18 (s, 1H), 4.96 (s, 1H), 4.99 (s, 2H), 3.89 (s, 2H), 3.80 (s, 3H), 1.47 (s, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 185.5, 159.2, 153.2, 150.4, 143.7, 139.5, 135.7, 135.2, 131.6, 127.4, 124.2, 118.7, 113.5, 111.2, 81.7, 55.2, 51.8, 51.2, 28.1. **IR:** v 3454, 2978, 2932, 1763, 1706, 1600, 1513, 1368, 1249, 1156, 1033, 981, 836, 749, 576 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 402.1676 Found: 402.1669.



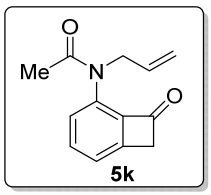

Compound **5h** was isolated as a colorless oil in 87% yield over 3 steps. $R_f$ = 0.6 (EtOAc/Hexane=1/5). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.39 (d, *J* = 8.3 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 1H), 4.74 (s, 1H), 4.70 (s, 1H), 4.49 (s, 2H), 3.82 (s, 2H), 2.30 (s, 3H), 1.67 (s, 3H), 1.48 (s, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 185.3, 153.4, 149.2, 141.4, 138.9, 136.8, 133.2, 128.8, 124.7, 110.8, 81.4, 53.9, 50.0, 28.1, 19.9, 16.9. **IR:** ν 2976, 2922, 1761, 1706, 1577, 1497, 1389, 1366, 1242, 1154, 1088, 979, 764 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 302.1751 Found: 302.1749.




Compound **5i** was isolated as a colorless oil in 60% yield over 3 steps. $R_f$ = 0.4 (EtOAc/Hexane=1/5). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.67 (s, 1H), 7.17 (d, *J* = 1.3 Hz, 1H), 4.80 – 4.71 (m, 1H), 4.67 (s, 1H), 4.53 (s, 2H), 3.86 (s, 2H), 1.69 (s, 3H), 1.50 (s, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 183.6, 152.9, 151.2, 141.8, 141.0, 137.0, 136.7, 123.6, 118.9, 110.6, 82.3, 54.0, 50.7, 28.0, 19.9. **IR:** ν 2977, 2930, 1766, 1713, 1594, 1446, 1366, 1275, 1155, 1071, 980, 764, 749 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 344.1024 Found: 344.1028.

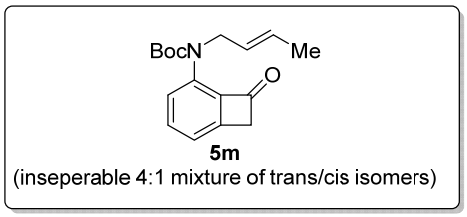



Compound **5j** was isolated as a colorless oil in 78% yield over 3 steps. $R_f$ = 0.4 (acetone/Hexane=1/5). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.53 (dd, *J* = 8.1, 7.3 Hz, 1H), 7.36 (d, *J* = 7.3 Hz, 1H), 7.30 (s, 1H), 4.76 (s, 1H), 4.72 (s, 1H), 4.50 (s, 2H), 3.97 (s, 2H), 2.15 (s, 3H), 1.67 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 185.5, 170.0, 151.4, 140.5, 136.3, 135.1, 125.7, 121.0, 112.2, 53.9, 51.8, 22.5, 20.0. **IR:** ν 3005, 1762, 1665, 1596, 1477, 1377, 1275, 1260, 764, 750 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 230.1176 Found: 230.1179.



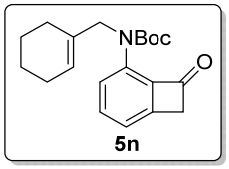

Compound **5k** was isolated as a colorless oil in 85% yield over 3 steps. $R_f$ = 0.4 (acetone/Hexane=1/5). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.54 (dd, *J* = 8.1, 7.3 Hz, 1H), 7.38 (d, *J* = 7.3 Hz, 1H), 7.29 (s, 1H), 5.78 (ddt, *J* = 17.2, 10.6, 5.5 Hz, 1H), 5.18 – 5.03 (m, 2H), 4.53 (d, *J* = 5.5 Hz, 2H), 3.99 (s, 2H), 2.13 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 185.5, 169.8,

151.6, 136.3, 135.1, 133.0, 126.0, 121.3, 117.1, 51.9, 51.3, 22.6. **IR:** v 2922, 1762, 1668, 1596, 1478, 1375, 1275, 1139, 970, 750, 570 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 216.1019 Found: 216.1015.




**5m**
(inseperable 4:1 mixture of trans/cis isomers)

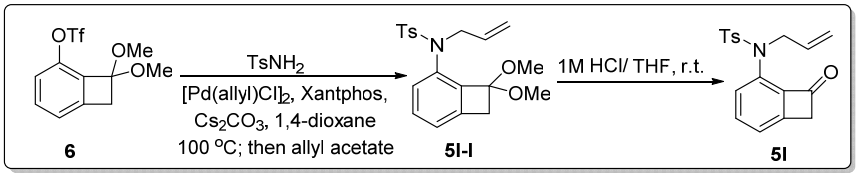
Compound **5m** was isolated as a colorless oil in 88% yield over 3 steps. $R_f$ = 0.6 (EtOAc/Hexane=1/5). **$^1$H NMR (400 MHz, $CDCl_3$):** δ (reported as a E/Z mixture) 7.53 – 7.40 (m, 2H), 7.19 (td, *J* = 7.1, 1.4 Hz, 1H), 5.59 – 5.29 (m, 2H), 4.63 – 4.57 (m, 0.4H), 4.48 (dt, *J* = 5.6, 1.3 Hz, 1.6H), 3.93 – 3.85 (m, 2H), 1.64 – 1.57 (m, 3H), 1.49 (s, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ (reported as a E/Z mixture) 185.52, 185.46, 153.2, 150.6, 150.5, 139.5, 139.1, 135.9, 135.84, 135.82, 135.7, 127.8, 126.6, 126.51, 126.48, 124.1, 123.6, 118.7, 118.4, 81.6, 81.5, 51.2, 51.1, 50.7, 46.2, 28.2, 28.1, 17.7, 13.0. **IR:** v 2975, 2927, 1763, 1704, 1599, 1580, 1477, 1366, 1308, 1232, 1159, 1138, 974 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 288.1594; Found: 288.1591.




**5n**

Compound **5n** was isolated as a colorless oil in 80% yield over 3 steps. $R_f$ = 0.6 (EtOAc/Hexane=1/5). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.45 (d, *J* = 4.4 Hz, 2H), 7.22 – 7.16 (m, 1H), 5.45 – 5.37 (m, 1H), 4.43 (s, 2H), 3.89 (s, 2H), 1.94 – 1.82 (m, 4H), 1.56 – 1.50 (m, 2H), 1.48 (s, 9H), 1.47 – 1.43 (m, 2H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 185.6, 153.5, 150.5, 139.6, 135.8, 135.8, 133.7, 123.8, 122.6, 118.5, 81.4, 54.3, 51.2, 28.1, 26.0, 24.9, 22.5, 22.3. **IR:** v 3450, 2976, 2928, 1764, 1704, 1634, 1478, 1366, 1234, 1157, 1137, 980 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 328.1907; Found: 328.1903.

e) *Synthesis of compound* **5l**:

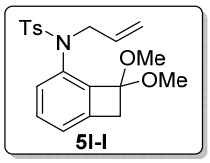



**6** **5l-I** **5l**

**<u>Procedure (step 1)</u>**:

To a 8 mL flamed-dried vial equipped with a stir bar was added **6** (156.2 mg, 1 mmol, 1.0 equiv.), $TsNH_2$ (205.4 mg, 1.2 mmol, 2.4 equiv.), $[Pd(allyl)Cl]_2$ (36.6 mg, 0.10 mmol, 20 mol%), Xantphos (173. mg, 0.30 mmol, 60 mol%) and $Cs_2CO_3$ (488.7 mg, 1.5 mmol, 3.0 equiv.). Then the vial was loosely capped and transferred into a nitrogen-filled glovebox and 1,4-dioxane (4 mL) was added to the mixture before the vial was tightly capped and transferred out. The system was then heated to 100 °C overnight. Upon completion, the reaction was cooled to room temperature and filtered through a pad of celite. The filtrate was concentrated under reduced pressure and the crude product was dissolved in DMF (10 mL). NaH (20.0 mg, 0.5 mmol, 2 equiv.) was added to the mixture, followed by allyl bromide (121.0 mg, 1.0

mmol, 2.0 equiv.). The mixture was stirred overnight at room temperature. Upon completion, the reaction was quenched with water and extracted with ethyl acetate (3×20 mL), washed with brine, and dried over $Na_2SO_4$. The crude product was was purified by silica gel flash column chromatography (EtOAc/Hexane=1/3) to afford compound **5l-I** as a colorless oil in 47% yield (88 mg).

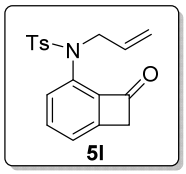


**5l-I**

Compound **5l-I** was isolated as a colorless oil in 47% yield. $R_f$ = 0.4 (EtOAc/Hexane=1/3). **$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.60 (d, *J* = 8.3 Hz, 2H), 7.20 (d, *J* = 7.7 Hz, 2H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 7.3 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 5.41 (t, *J* = 6.7 Hz, 1H), 5.37 (s, 1H), 5.27 (d, *J* = 1.3 Hz, 1H), 4.09 (d, *J* = 6.7 Hz, 2H), 3.33 (s, 6H), 3.32 (s, 2H), 2.41 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 142.8, 142.8, 141.5, 141.2, 137.6, 133.6, 130.5, 129.3, 127.1, 126.4, 123.0, 117.2, 106.1, 52.0, 47.6, 41.5, 21.5. **IR:** v 3278, 2935, 2831, 1639, 1599, 1451, 1328, 1238, 1160, 1104, 1061, 1034, 850, 791, 664, 550 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 374.1421; Found: 374.1417.

**Procedure (step 2)**:

Compound **5l-I** (136 mg, 0.36 mmol, 1.0 equiv.) was dissolved in 6 mL tetrahydrofuran and transferred to a 20 mL vial charged with a stir bar. While stirring, 2 mL of 1M HCl aqueous solution was added to the mixture. After stirring for 1 h at room temperature, saturated $NaHCO_3$ aqueous solution was added dropwisely to quench the reaction. The mixture was extracted with ethyl acetate (3×20 mL), washed with brine, and dried over $Na_2SO_4$. The crude product was purified by silica gel flash column chromatography (EtOAc/Hexane=1/5) to afford compound **5l** as a colorless oil in 98% yield (117.5 mg).



**5l**

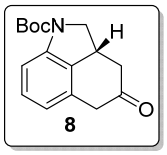
Compound **5l** was isolated as a colorless oil in 98% yield from **5l-I**. $R_f$ = 0.3 (EtOAc/Hexane=1/3). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.64 (dd, *J* = 8.2, 0.8 Hz, 1H), 7.54 (dd, *J* = 8.2, 7.2 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.33 (dd, *J* = 7.2, 0.7 Hz, 1H), 7.21 (d, *J* = 7.8 Hz, 2H), 5.69 (ddt, *J* = 17.1, 10.3, 5.8 Hz, 1H), 5.09 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.00 (dq, *J* = 10.3, 1.4 Hz, 1H), 4.49 (dt, *J* = 5.8, 1.6 Hz, 2H), 3.80 (s, 2H), 2.39 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 184.4, 150.8, 144.0, 141.2, 136.3, 134.4, 132.9, 132.6, 129.5, 128.0, 127.3, 121.1, 118.3, 52.2, 51.2, 21.6. **IR:** v 2924, 1766, 1595, 1473, 1354, 1164, 1090, 973, 814, 748, 662, 545 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 328.1002 Found: 328.1003.

## III. *Procedure for C–C bond activation and characterization of compounds **8** to **8l***

**Procedure:**

In a nitrogen filled glove box, a 4 mL vial was charged with the benzocyclobutenone substrates (**5** to **5l,** 0.1 mmol), $Rh(COD)_2BF_4$ (5 mol%, 0.005 mmol, 2.1 mg) and (*R*)-DTBM-segphos (6 mol%, 0.006 mmol, 7.1 mg). After adding 1 mL 1,4-dioxane, the vial was capped and the solution was maintained at certain temperature (90 $^oC$ or 110 $^oC$) for 12h. Upon completion, it was cooled to room temperature and the solvent was removed by rotavap under reduced pressure.

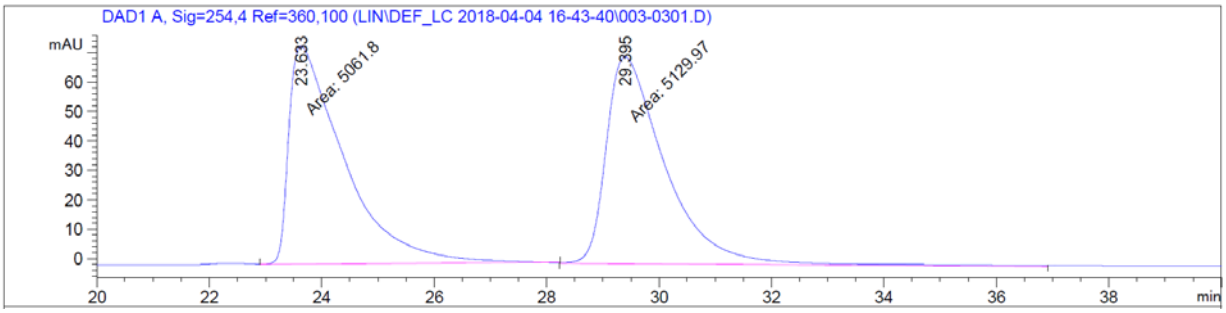
The crude product was directly purified by silica gel flash chromatography to yield **8** to **8l**.




**8** (518.2 mg) was isolated as a white solid in 95% yield**.** Melting Point: 115-116 °C. $Rh(COD)_2BF_4$ (3 mol%, 0.06 mmol, 24.4 mg) and (*R*)-DTBM-segphos (3.6 mol%, 0.072 mmol, 84.9 mg) were used and the reaction was maintained at 90 °C. $R_f$ = 0.4 (EtOAc/Hexane=1/3). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.72 – 7.20 (m, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 4.41 (s, 1H), 3.79 – 3.63 (m, 1H), 3.63 – 3.54 (m, 1H), 3.52 (s, 2H), 2.95 (dd, *J* = 16.2, 5.3 Hz, 1H), 2.30 (dd, *J* = 16.2, 12.3 Hz, 1H), 1.57 (s, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 208.7, 152.4, 130.3, 129.1, 121.0, 112.9, 81.1, 55.3, 44.0, 42.2, 34.0, 28.4. **IR:** v 2975, 1700, 1462, 1389, 1351, 1252, 1161, 1135, 948, 856, 784, 762, 735 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 296.1257. Found: 296.1254.

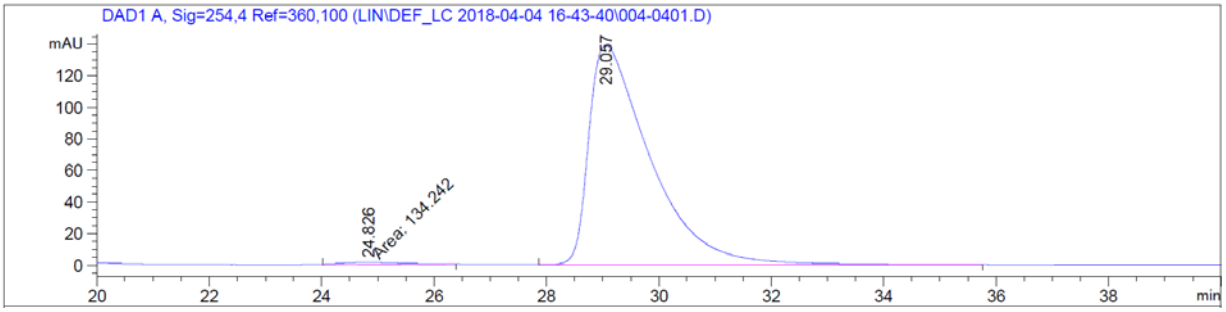
Chiral HPLC (Chiralpak IF, hexane:isopropanol = 98:2, 1 mL/min, 254 nm), $t_{minor}$ = 24.8 min, $t_{major}$= 29.0 min. $[\alpha]_D^{21.5}$ = -139 (c= 2.20, $CHCl_3$) at 97.5 % e.e.

**Racemic Sample 8**

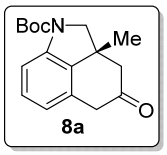



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 23.633 | MM | 1.1375 | 5061.79883 | 74.16519 | 49.6656 |
| 2 | 29.395 | MM | 1.2159 | 5129.96924 | 70.31551 | 50.3344 |

**Enantiomeric Sample 8**



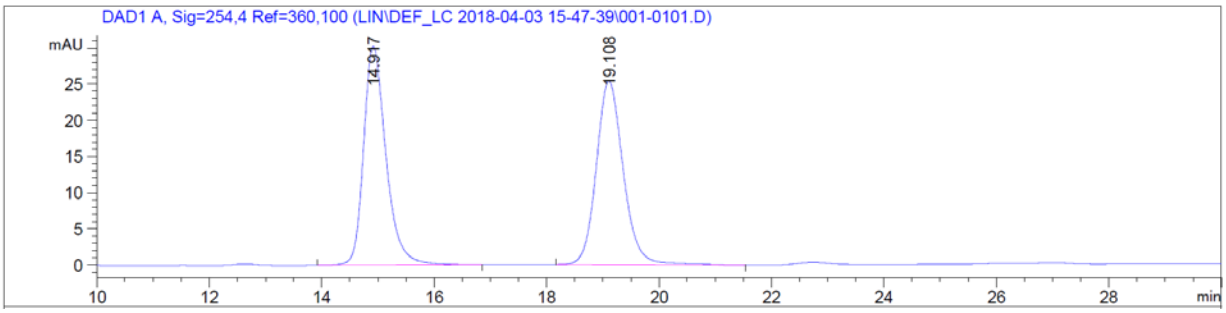
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 24.826 | MM | 1.4330 | 134.24211 | 1.56128 | 1.2608 |
| 2 | 29.057 | BB | 1.1122 | 1.05130e4 | 139.02695 | 98.7392 |




**8a** (25.0 mg) was isolated as a white solid in 88% yield**.** Melting Point: 154-156 °C. $Rh(COD)_2BF_4$ (5 mol%, 0.005 mmol, 2.1 mg) and (*R*)-DTBM-segphos (6 mol%, 0.006 mmol, 7.1 mg) were used and the reaction was maintained at 90 °C. $R_f$ = 0.4 (EtOAc/Hexane=1/3). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.73 – 7.20 (m, 1H), 7.18 (t, *J* = 7.8 Hz, 1H), 6.77 (d, *J* = 7.5 Hz, 1H), 3.99 (s, 1H), 3.71 (d, *J* = 10.8 Hz, 1H), 3.60 (d, *J* = 21.7 Hz, 1H), 3.50 (d, *J* = 21.7 Hz, 1H), 2.80 (d, *J* = 15.6 Hz, 1H), 2.52 (d, *J* = 15.6 Hz, 1H), 1.58 (s, 9H), 1.26 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 208.8, 152.6, 140.5, 129.5, 129.0, 121.3, 113.1, 81.7, 62.3, 50.9, 40.7, 39.7, 28.4, 25.8. **IR:** ν 3444, 2975, 1700, 1621, 1475, 1389, 1337, 1162, 1136, 855, 750 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 310.1414. Found: 310.1415.

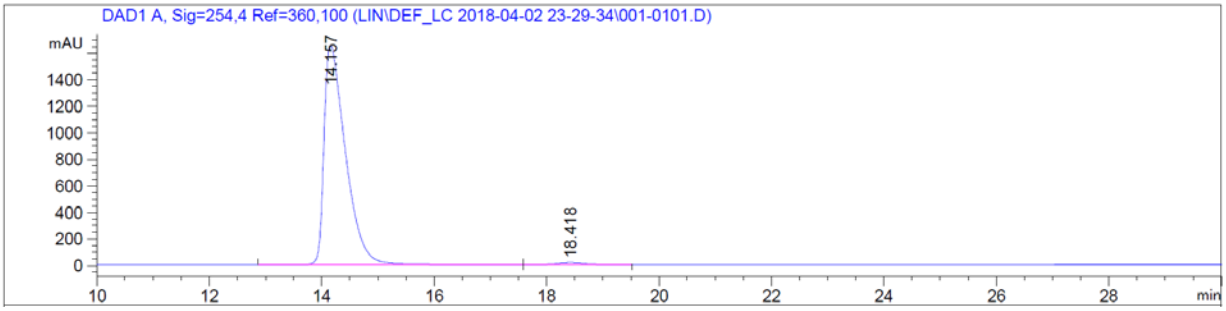
Chiral HPLC (Chiralpak IF, hexane:isopropanol = 98:2, 1 mL/min, 254 nm), $t_{minor}$ = 18.4 min, $t_{major}$= 14.1 min. $[\alpha]_D^{21.5}$ = -91.2 (c= 1.04, $CHCl_3$) at 98 % e.e.

**Racemic Sample 8a**

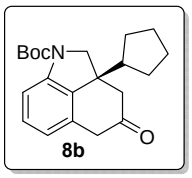



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 14.917 | BB | 0.4215 | 838.23456 | 30.22814 | 49.6893 |
| 2 | 19.108 | BB | 0.5101 | 848.71851 | 25.38437 | 50.3107 |

**Enantiomeric Sample 8a**



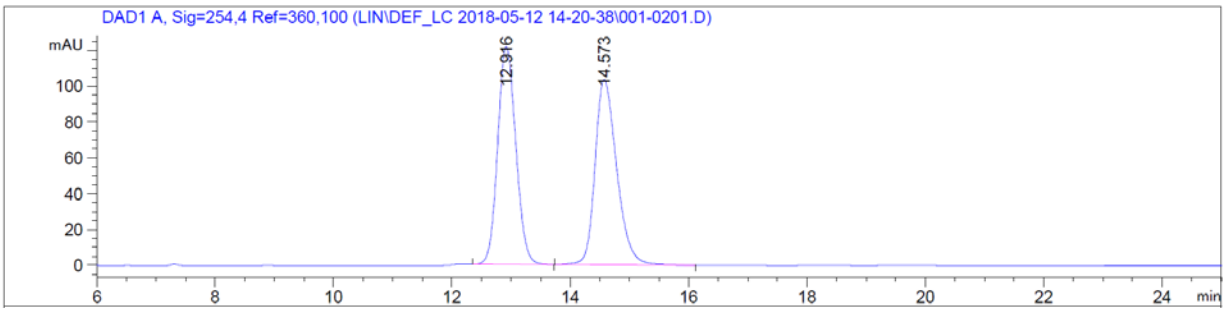

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 14.157 | BB | 0.3958 | 4.36475e4 | 1654.24170 | 98.9617 |
| 2 | 18.418 | BB | 0.4994 | 457.95563 | 14.08207 | 1.0383 |




**8b** (26.6 mg) was isolated as a colorless oil in 78% yield**.** $Rh(COD)_2BF_4$ (5 mol%, 0.005 mmol, 2.1 mg) and (*R*)-DTBM-segphos (6 mol%, 0.006 mmol, 7.1 mg) were used and the reaction was maintained at 90 °C. $R_f$ = 0.4 (EtOAc/Hexane=1/3). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.75 – 7.19 (m, 1H), 7.18 (s, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 4.13 (m, 1H), 3.65 (d, *J* = 21.9 Hz, 1H), 3.57 (d, *J* = 11.4 Hz, 1H), 3.45 (d, *J* = 22.0 Hz, 1H), 2.92 (d, *J* = 15.7 Hz, 1H), 2.46 (d, *J* = 15.7 Hz, 1H), 1.88 (d, *J* = 8.4 Hz, 1H), 1.77 (dtd, *J* = 11.0, 7.3, 3.0 Hz, 1H), 1.66 – 1.49 (m, 12H), 1.44 – 1.29 (m, 2H), 1.28 – 1.10 (m, 2H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 209.4, 152.0, 140.5, 129.9, 129.0, 121.4, 120.9, 113.0, 81.8, 57.0, 50.2, 48.3, 45.5, 41.1, 28.4, 28.4, 27.6, 27.2, 25.1, 24.8. **IR:** v 3442, 2957, 1699, 1618, 1461, 1388, 1275, 1162, 1137, 750, 521 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 342.2064. Found: 342.2062.

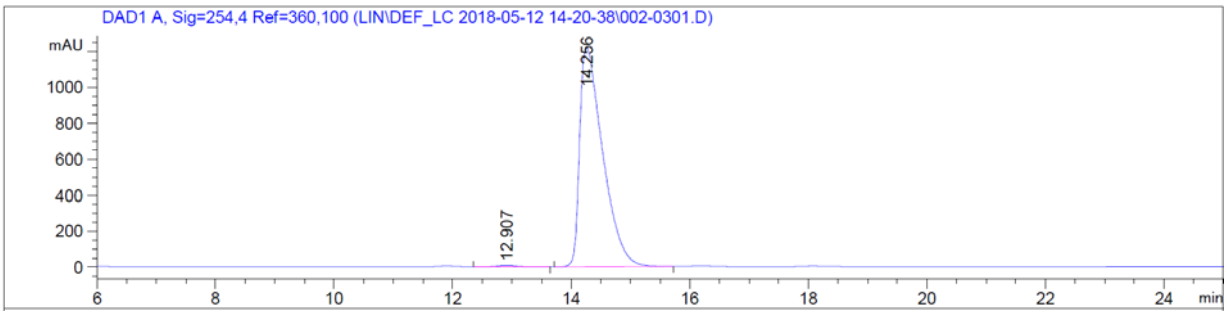
Chiral HPLC (Chiralpak IF, hexane:isopropanol = 98:2, 1 mL/min, 254 nm), $t_{minor}$ = 12.9 min, $t_{major}$= 14.2 min. $[\alpha]_D^{21.5}$ = -68.4 (c= 0.70, $CHCl_3$) at 98% e.e.

**Racemic Sample 8b**

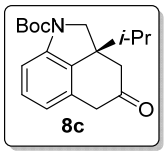


| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 12.916 | BB | 0.3328 | 2595.53271 | 121.70525 | 49.6854 |
| 2 | 14.573 | BB | 0.3905 | 2628.40674 | 103.41245 | 50.3146 |

**Enantiomeric Sample 8b**



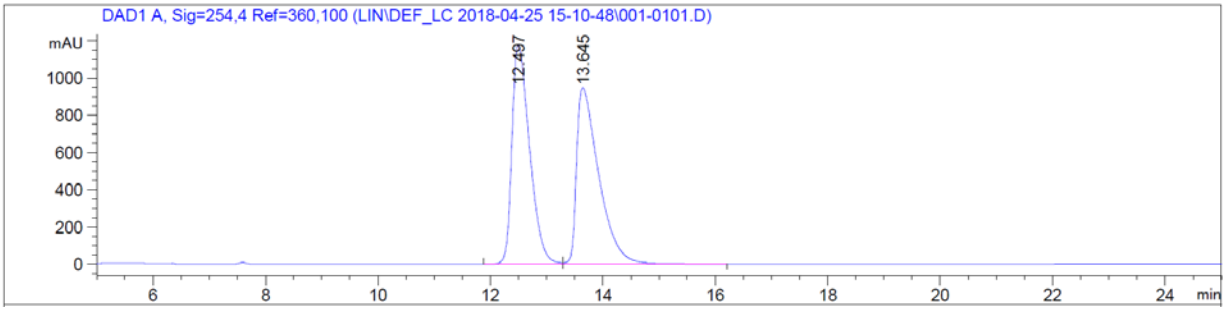

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 12.907 | BB | 0.3278 | 206.30048 | 9.79096 | 0.6215 |
| 2 | 14.256 | BB | 0.4024 | 3.29901e4 | 1224.24268 | 99.3785 |




**8c** (22.0 mg) was isolated as a white solid in 71% yield**.** Melting Point: 122-124 °C. $Rh(COD)_2BF_4$ (5 mol%, 0.005 mmol, 2.1 mg) and (*R*)-DTBM-segphos (6 mol%, 0.006 mmol, 7.1 mg) were used and the reaction was maintained at 90 °C. $R_f$ = 0.4 (EtOAc/Hexane=1/3). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.71 – 7.16 (m, 1H), 7.19 (s, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 4.17 (m, 1H), 3.63 (d, *J* = 22.0 Hz, 1H), 3.54 – 3.38 (m, 2H), 3.03 (d, *J* = 15.7 Hz, 1H), 2.41 (d, *J* = 15.7 Hz, 1H), 1.71 (dq, *J* = 13.6, 6.8 Hz, 1H), 1.59 (m, 9H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.77 (d, *J* = 6.8 Hz, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 209.3, 152.0, 130.1, 129.0, 121.5, 112.9, 80.9, 55.8, 48.8, 46.2, 41.0, 34.4, 28.4, 17.5, 16.8. **IR:** v 3441, 1699, 1635, 1457, 1386, 1275, 1260, 1139, 750 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 338.1727. Found: 338.1716.

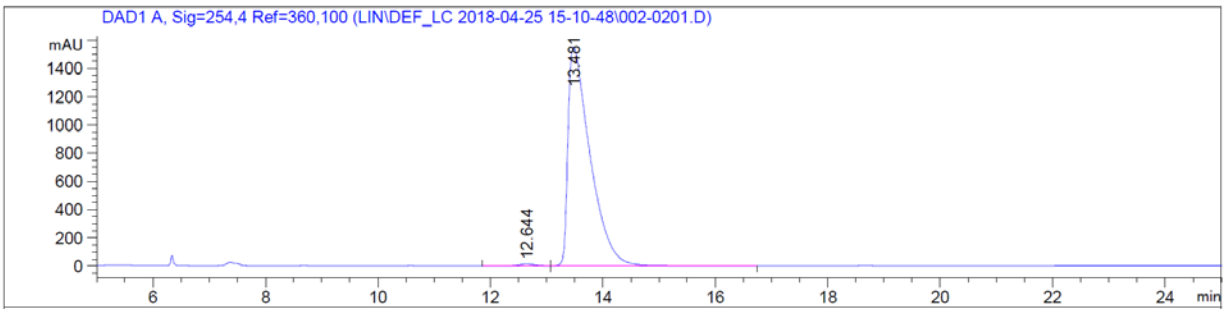
Chiral HPLC (Chiralpak IF, hexane:isopropanol = 99:1, 1 mL/min, 254 nm), $t_{minor}$ = 12.6 min, $t_{major}$= 13.5 min. $[\alpha]_D^{21.5}$ = -63.5 (c= 0.95, $CHCl_3$) at 98% e.e.

**Racemic Sample 8c**

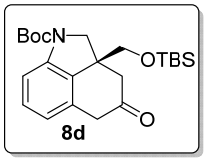



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 12.497 | BV | 0.3366 | 2.57255e4 | 1178.75208 | 49.7820 |
| 2 | 13.645 | VB | 0.4073 | 2.59508e4 | 948.21454 | 50.2180 |

**Enantiomeric Sample 8c**




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 12.644 | BV | 0.3301 | 304.48911 | 14.20492 | 0.7134 |
| 2 | 13.481 | VB | 0.4005 | 4.23781e4 | 1552.24231 | 99.2866 |

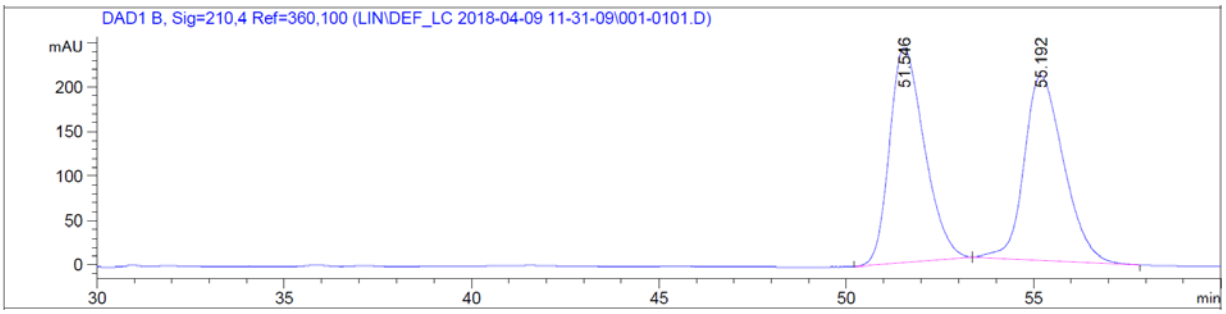



**8d**

**8d** (28.5 mg) was isolated as a white solid in 71% yield**.** Melting Point: 95-97 $^{o}$C. $Rh(COD)_2BF_4$ (5 mol%, 0.005 mmol, 2.1 mg) and (*R*)-DTBM-segphos (6 mol%, 0.006 mmol, 7.1 mg) were used and the reaction was maintained at 90 $^{o}$C. $R_f$ = 0.5 (EtOAc/Hexane=1/3). **$^{1}$H NMR (400 MHz, $CDCl_3$):** δ 7.74 – 7.19 (m, 1H), 7.20 (t, *J* = 7.7 Hz, 1H), 6.76 (d, *J* = 7.6 Hz, 1H), 4.07 (m, 1H), 3.70 – 3.54 (m, 4H), 3.40 (d, *J* = 21.6 Hz, 1H), 2.96 (d, *J* = 16.1 Hz, 1H), 2.40 (d, *J* = 16.1 Hz, 1H), 1.57 (s, 9H), 0.81 (s, 9H), -0.06 (d, *J* = 3.0 Hz, 6H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 208.1, 152.5, 131.5, 129.4, 121.2, 112.9, 80.9, 68.3, 58.3, 46.6, 41.4, 28.4, 25.8, 18.3, -5.7, -5.9. **IR:** ν 2929, 2885, 2856, 1705, 1459, 1388, 1347, 1256, 1163, 1137, 1099, 838, 782 cm$^{-1}$; **HRMS** calcd. For $[M+K]^+$: 456.1967. Found: 456.1980.

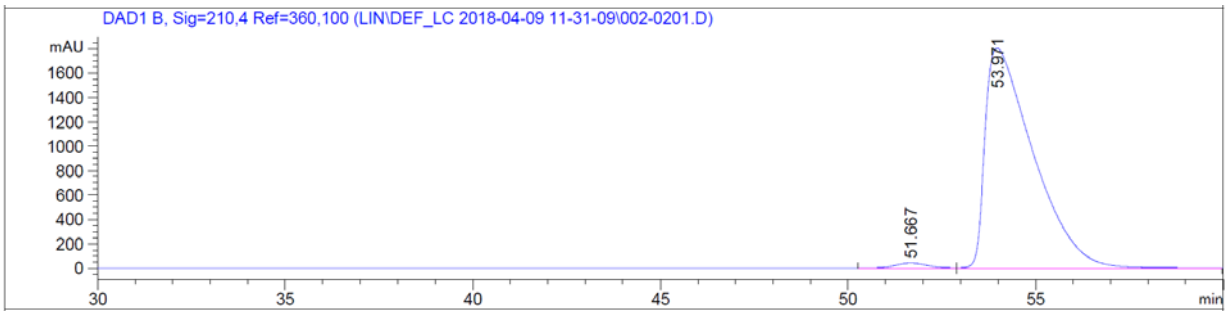
Chiral HPLC (Chiralpak IF, hexane:isopropanol = 99:1, 0.3 mL/min, 210 nm), $t_{minor}$ = 51.7 min, $t_{major}$= 54.0 min. $[\alpha]_D^{21.5}$ = -28.2 (c= 1.31, $CHCl_3$) at 97% e.e.

**Racemic Sample 8d**

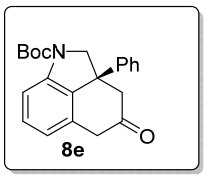



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 51.546 | BB | 1.0015 | 1.55841e4 | 241.28061 | 50.5455 |
| 2 | 55.192 | BB | 1.1354 | 1.52477e4 | 207.47116 | 49.4545 |

**Enantiomeric Sample 8d**




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 51.667 | BB | 0.8834 | 2295.71265 | 40.49353 | 1.4071 |
| 2 | 53.971 | BBA | 1.2752 | 1.60853e5 | 1802.44165 | 98.5929 |



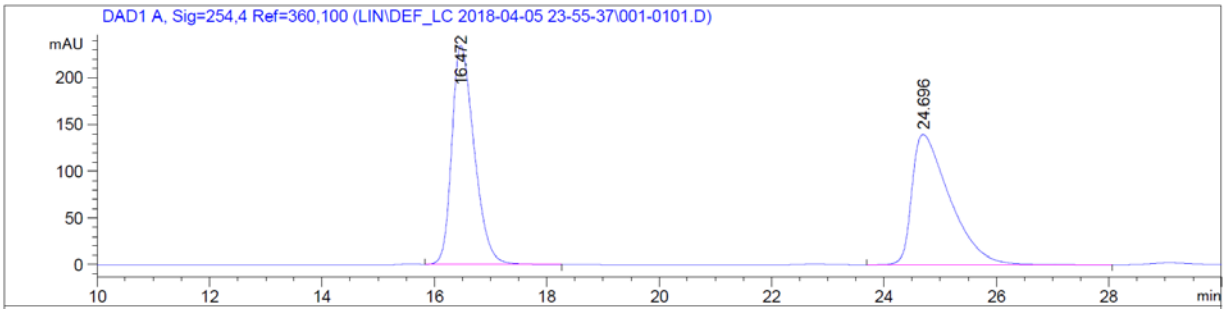
**8e**

**8e** (26.8 mg) was isolated as a colorless oil in 78% yield**.** $Rh(COD)_2BF_4$ (5 mol%, 0.005 mmol, 2.1 mg) and (*R*)-DTBM-segphos (6 mol%, 0.006 mmol, 7.1 mg) were used and the reaction was maintained at 90 °C. $R_f$ = 0.4 (EtOAc/Hexane=1/3). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.88 – 7.30 (m, 1H), 7.34 – 7.24 (m, 3H), 7.24 – 7.16 (m, 1H), 7.03 (d, *J* = 6.3 Hz, 2H), 6.85 (d, *J* = 7.6 Hz, 1H), 4.28 (m, 1H), 4.07 (d, *J* = 10.9 Hz, 1H), 3.48 (d, *J* = 16.2 Hz, 1H), 3.41 (d, *J* = 21.0 Hz, 1H), 3.24 (d, *J* = 21.0 Hz, 1H), 2.75 (d, *J* = 16.2 Hz, 1H), 1.66 – 1.43 (m, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ

208.1, 152.3, 143.3, 140.9, 132.5, 130.8, 129.7, 129.0, 127.3, 126.1, 121.4, 113.2, 81.1, 64.5, 51.0, 47.1, 41.8, 28.4. **IR:** ν 3443, 1699, 1634, 1474, 1385, 1275, 1162, 1137, 750, 701 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 350.1751. Found: 350.1745.

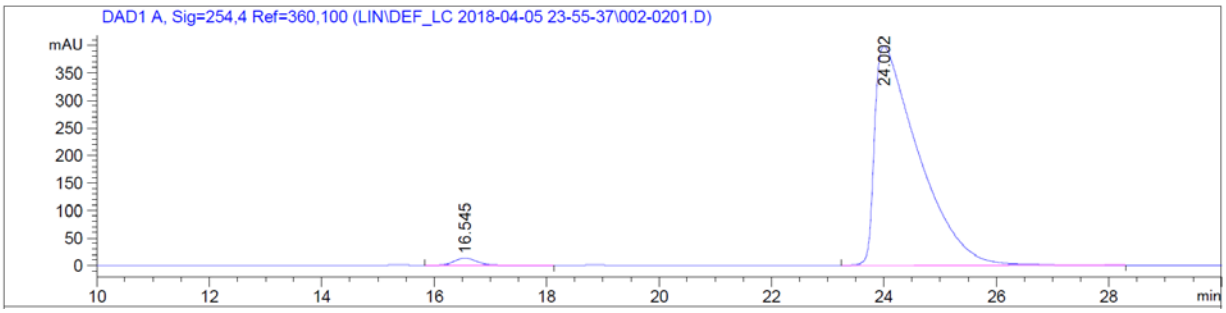
Chiral HPLC (Chiralpak IF, hexane:isopropanol = 98:2, 1 mL/min, 254 nm), $t_{minor}$ = 16.5 min, $t_{major}$= 24.0 min. $[\alpha]_D^{21.5}$ = -118.9 (c= 0.95, $CHCl_3$) at 97% e.e.

**Racemic Sample 8e**

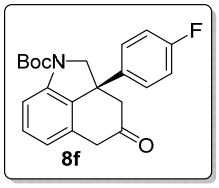



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 16.472 | BB | 0.4282 | 6509.98535 | 234.23973 | 49.8598 |
| 2 | 24.696 | BB | 0.7025 | 6546.60889 | 139.75941 | 50.1402 |

**Enantiomeric Sample 8e**




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 16.545 | BB | 0.4256 | 371.59622 | 13.39684 | 1.6909 |
| 2 | 24.002 | BB | 0.7812 | 2.16053e4 | 398.07251 | 98.3091 |



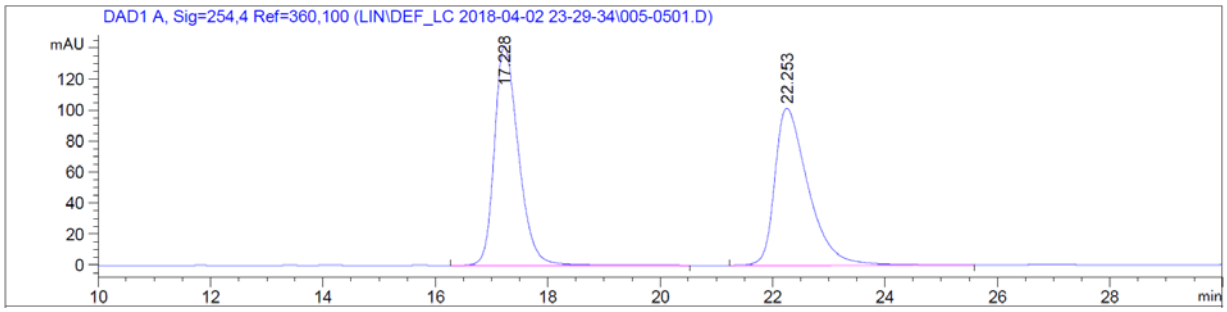
**8f**

**8f** (34.0 mg) was isolated as a colorless oil in 93% yield**.** Melting Point: 97-99 °C. $Rh(COD)_2BF_4$ (5 mol%, 0.005 mmol, 2.1 mg) and (*R*)-DTBM-segphos (6 mol%, 0.006 mmol, 7.1 mg) were used and the reaction was maintained at 90 °C. $R_f$

= 0.3 (EtOAc/Hexane=1/3). **$^{1}$H NMR (400 MHz, $CDCl_3$):** δ 7.90 – 7.25 (m, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.07 – 6.90 (m, 4H), 6.86 (d, *J* = 7.5 Hz, 1H), 4.22 (m, 1H), 4.05 (d, *J* = 10.9 Hz, 1H), 3.45 (s, 1H), 3.40 (d, *J* = 5.7 Hz, 1H), 3.22 (d, *J* = 21.1 Hz, 1H), 2.76 (d, *J* = 16.1 Hz, 1H), 1.64 – 1.42 (m, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 207.8, 161.8 (d, *J* = 247.0 Hz), 152.3, 139.0, 129.9, 127.9 (d, *J* = 8.2 Hz), 121.6, 115.9 (d, *J* = 21.4 Hz), 113.3, 64.2, 51.1, 46.2, 41.7, 28.4. **$^{19}$F NMR (470 MHz, $CDCl_3$)**: δ -68.4. **IR:** ν 3442, 1635, 1507, 1474, 1386, 1337, 1275, 1161, 1138, 750, 516 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 390.1476. Found: 390.1464.

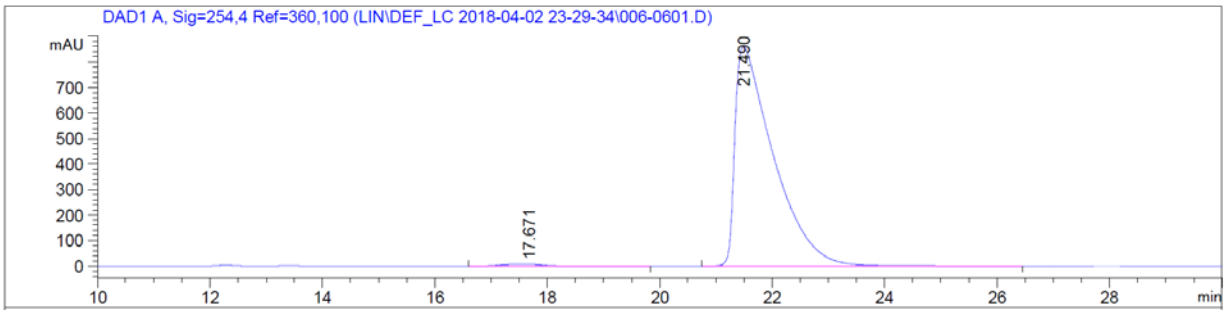
Chiral HPLC (Chiralpak IF, hexane:isopropanol = 98:2, 1 mL/min, 254 nm), $t_{minor}$ = 17.7 min, $t_{major}$= 21.5 min. $[\alpha]_D^{21.5}$ = -89.9 (c= 0.88, $CHCl_3$) at 98% e.e.

**Racemic Sample 8f**

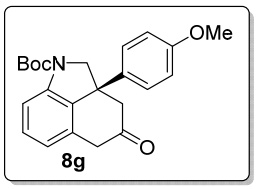



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 17.228 | BB | 0.4557 | 4224.91748 | 141.76109 | 50.1852 |
| 2 | 22.253 | BB | 0.6238 | 4193.74316 | 101.54588 | 49.8148 |

**Enantiomeric Sample 8f**



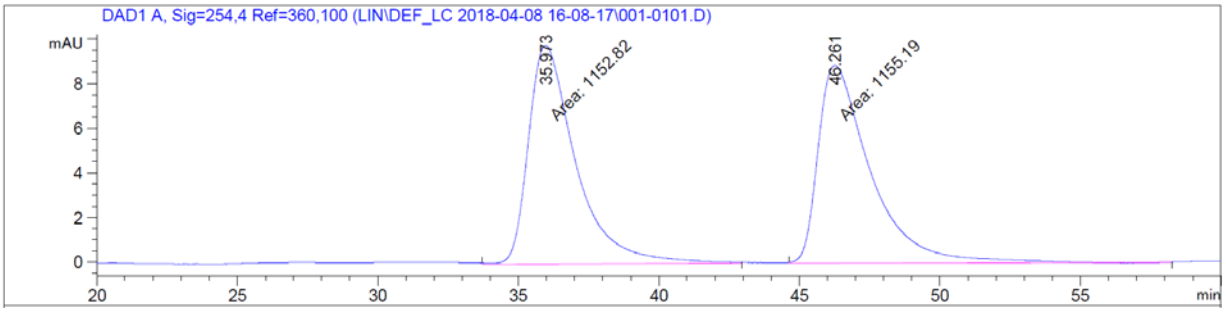

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 17.671 | BB | 0.6837 | 401.00906 | 7.90668 | 0.9663 |
| 2 | 21.490 | BB | 0.6845 | 4.10976e4 | 861.54816 | 99.0337 |




**8g** (31.3 mg) was isolated as a colorless oil in 76% yield**.** $Rh(COD)_2BF_4$ (5 mol%, 0.005 mmol, 2.1 mg) and (*R*)-DTBM-segphos (6 mol%, 0.006 mmol, 7.1 mg) were used and the reaction was maintained at 90 °C. $R_f$ = 0.3 (EtOAc/Hexane=1/3). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.85 – 7.23 (m, 1H), 7.29 (t, *J* = 7.7 Hz, 1H), 6.93 (d, *J* = 8.3 Hz, 2H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.79 (d, *J* = 8.8 Hz, 2H), 4.24 (m, 1H), 4.03 (d, *J* = 10.9 Hz, 1H), 3.75 (s, 3H), 3.53 – 3.33 (m, 2H), 3.24 (d, *J* = 21.0 Hz, 1H), 2.73 (d, *J* = 16.1 Hz, 1H), 1.62 – 1.36 (m, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 208.2, 158.6, 152.3, 141.0, 135.3, 132.8, 130.8, 129.6, 127.3, 121.4, 114.3, 113.2, 81.0, 64.6, 55.2, 51.1, 46.3, 41.8, 28.4. **IR:** ν 3442, 2056, 1699, 1621, 1511, 1474, 1386, 1337, 1275, 1256, 1162, 1137, 1029, 833, 750 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 402.1676. Found: 402.1673.

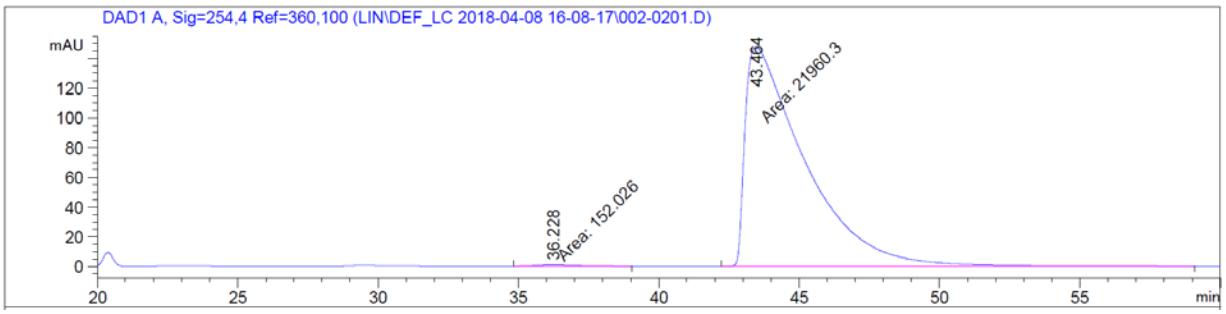
Chiral HPLC (Chiralpak ID, hexane:isopropanol = 98:2, 1 mL/min, 254 nm), $t_{minor}$ = 36.2 min, $t_{major}$= 43.5 min. $[\alpha]_D^{21.5}$ = -104.9 (c= 1.06, $CHCl_3$) at 99% e.e.

**Racemic Sample 8g**

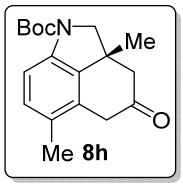



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 35.973 | MM | 1.9547 | 1152.81665 | 9.82926 | 49.9486 |
| 2 | 46.261 | MM | 2.1657 | 1155.18762 | 8.89003 | 50.0514 |

**Enantiomeric Sample 8g**



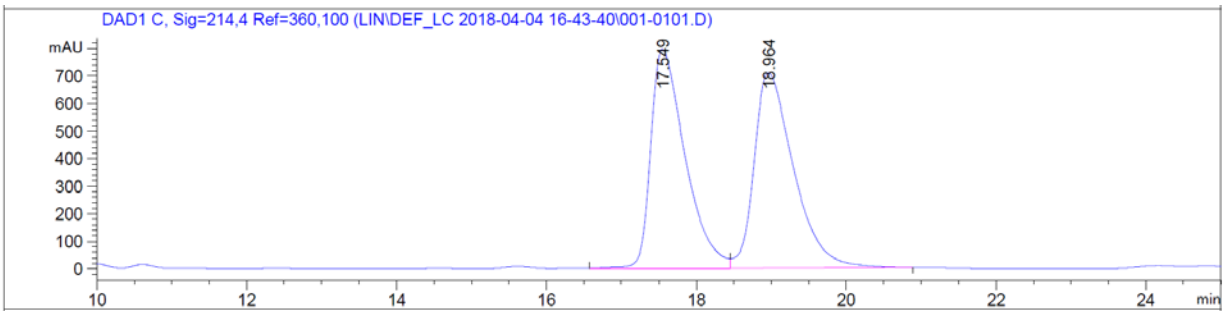
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 36.228 | MM | 2.2703 | 152.02570 | 1.11607 | 0.6875 |
| 2 | 43.464 | MM | 2.4780 | 2.19603e4 | 147.70340 | 99.3125 |




**8h** (28.5 mg) was isolated as a white solid in 95% yield**.** Melting Point: 140-142 °C. $Rh(COD)_2BF_4$ (5 mol%, 0.005 mmol, 2.1 mg) and (*R*)-DTBM-segphos (6 mol%, 0.006 mmol, 7.1 mg) were used and the reaction was maintained at 90 °C. $R_f$ = 0.4 (EtOAc/Hexane=1/3). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.64 – 7.11 (m, 1H), 7.02 (d, *J* = 8.0 Hz, 1H), 3.98 (m, 1H), 3.69 (d, *J* = 10.7 Hz, 1H), 3.48 (d, *J* = 22.0 Hz, 1H), 3.40 (d, *J* = 22.1 Hz, 1H), 2.78 (d, *J* = 15.1 Hz, 1H), 2.54 (d, *J* = 15.1 Hz, 1H), 2.18 (s, 3H), 1.57 (s, 9H), 1.23 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 208.9, 152.6, 129.5, 127.8, 112.8, 80.8, 62.0, 50.8, 39.5, 38.9, 29.7, 28.4, 25.9, 17.7. **IR:** v 3443, 2974, 1699, 1626, 1484, 1387, 1369, 1338, 1257, 1159, 1137, 816, 751 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 324.1570. Found: 324.1568.

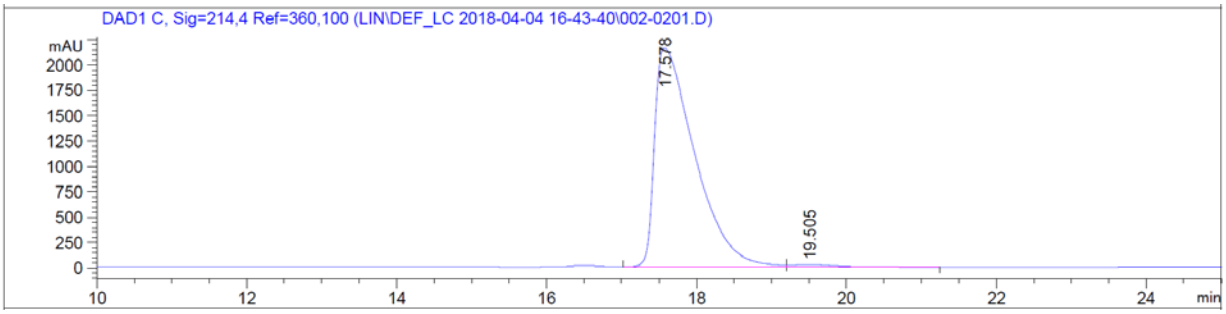
Chiral HPLC (Chiralpak IF, hexane:isopropanol = 99:1, 1 mL/min, 214 nm), $t_{minor}$ = 19.5 min, $t_{major}$= 17.6 min. $[\alpha]_D^{21.5}$ = -88.7 (c= 1.19, $CHCl_3$) at 98% e.e.

**Racemic Sample 8h**

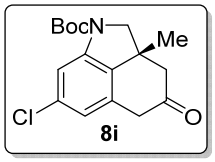



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 17.549 | BV | 0.4790 | 2.51541e4 | 795.31250 | 49.2640 |
| 2 | 18.964 | VB | 0.5527 | 2.59057e4 | 708.27655 | 50.7360 |

**Enantiomeric Sample 8h**



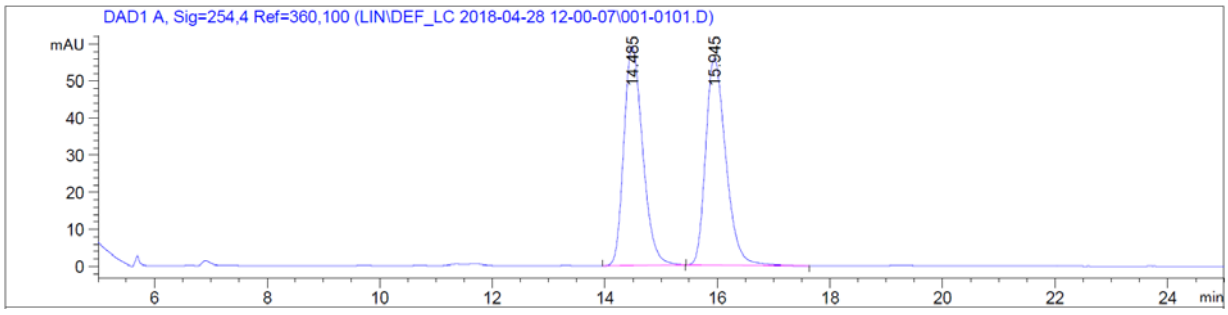

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 17.578 | VV | 0.5570 | 8.04349e4 | 2157.27026 | 98.7408 |
| 2 | 19.505 | VB | 0.6250 | 1025.72388 | 23.88517 | 1.2592 |




**8i** (24.0 mg) was isolated as a colorless oil in 76% yield**.** $Rh(COD)_2BF_4$ (5 mol%, 0.005 mmol, 2.1 mg) and (*R*)-DTBM-segphos (6 mol%, 0.006 mmol, 7.1 mg) were used and the reaction was maintained at 90 °C. $R_f$ = 0.4 (EtOAc/Hexane=1/3). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.80 – 7.19 (m, 1H), 6.78 (d, *J* = 1.2 Hz, 1H), 3.98 (m, 1H), 3.73 (d, *J* = 10.8 Hz, 1H), 3.57 (d, *J* = 21.8 Hz, 1H), 3.45 (d, *J* = 21.8 Hz, 1H), 2.80 (d, *J* = 15.6 Hz, 1H), 2.50 (d, *J* = 15.6 Hz, 1H), 1.58 (s, 9H), 1.25 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 207.7, 166.8, 152.4, 141.6, 121.1, 113.8, 109.6, 50.7, 40.4, 29.7, 28.4, 25.8. **IR:** ν 3400, 2975, 1705, 1618, 1479, 1437, 1371, 1337, 1275, 1157, 1139, 859, 751, 592 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 344.1024. Found: 344.1027.

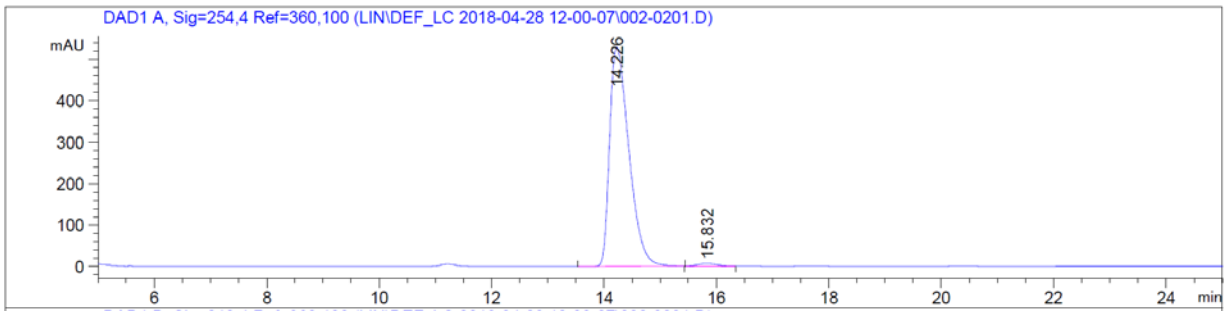
Chiral HPLC (Chiralpak IF, hexane:isopropanol = 99:1, 1 mL/min, 254 nm), $t_{minor}$ = 15.8 min, $t_{major}$= 14.2 min. $[\alpha]_D^{21.5}$ = -69.8 (c= 0.43, $CHCl_3$) at 98% e.e.

**Racemic Sample 8i**

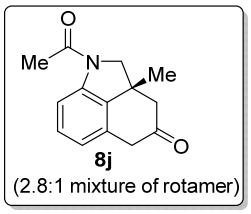


| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 14.485 | BB | 0.3618 | 1377.60852 | 59.13932 | 49.7598 |
| 2 | 15.945 | BB | 0.3870 | 1390.90991 | 55.76566 | 50.2402 |

**Enantiomeric Sample 8i**




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 14.226 | BB | 0.3681 | 1.26037e4 | 528.79913 | 98.8756 |
| 2 | 15.832 | BB | 0.3521 | 143.32492 | 6.38088 | 1.1244 |

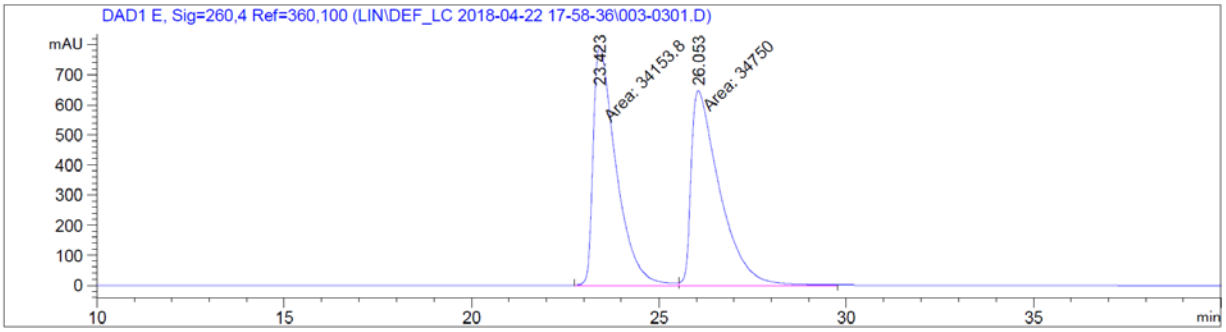



**8j**
(2.8:1 mixture of rotamer)

**8j** (20.7 mg, 2.8:1 mixture of rotamer) was isolated as a colorless oil in 90% yield**.** $Rh(COD)_2BF_4$ (5 mol%, 0.005 mmol, 2.1 mg) and (*R*)-DTBM-segphos (6 mol%, 0.006 mmol, 7.1 mg) were used and the reaction was maintained at 90 °C. $R_f$ = 0.4 (acetone/Hexane=1/3). **$^1$H NMR (400 MHz, $CDCl_3$):** δ (major rotamer) 7.95 (d, *J* = 8.0 Hz, 1H), 7.22 (t, *J* = 7.8 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 3.96 (d, *J* = 9.9 Hz, 1H), 3.90 (d, *J* = 10.0 Hz, 1H), 3.66 – 3.57 (m, 1H), 3.52 (d, *J* = 21.8 Hz, 1H), 2.83 (d, *J* = 15.5 Hz, 1H), 2.55 (d, *J* = 15.6 Hz, 1H), 2.24 (s, 3H), 1.30 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ (all the peaks observed) 208.3, 168.8, 140.3, 134.4, 131.0, 129.32, 129.27, 128.97, 126.7, 122.8, 122.5, 115.4, 112.8, 63.8, 62.5, 50.7, 50.6, 40.7, 40.6, 39.0, 25.9, 25.3, 24.1, 23.9. **IR:** ν 3442, 2064, 1636, 1472, 1399, 1276, 750, 569 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 230.1176. Found: 230.1176.

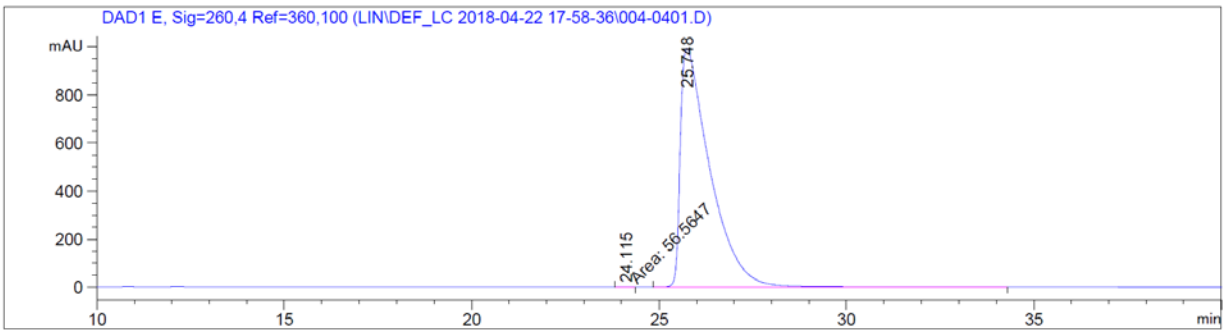
Chiral HPLC (Chiralpak IF, hexane:isopropanol = 85:15, 1 mL/min, 260 nm), $t_{minor}$ = 24.1 min, $t_{major}$= 25.7 min. $[\alpha]_D^{21.5}$ = -135.3 (c= 0.91, $CHCl_3$) at 99% e.e.

**Racemic Sample 8j**

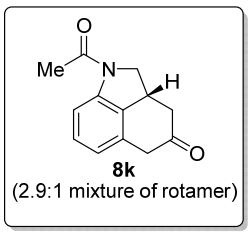



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 23.423 | MF | 0.7142 | 3.41538e4 | 796.97180 | 49.5674 |
| 2 | 26.053 | FM | 0.8927 | 3.47500e4 | 648.80408 | 50.4326 |

**Enantiomeric Sample 8j**




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 24.115 | MM | 0.5411 | 56.56469 | 1.74236 | 0.1032 |
| 2 | 25.748 | BB | 0.7927 | 5.47543e4 | 993.96942 | 99.8968 |



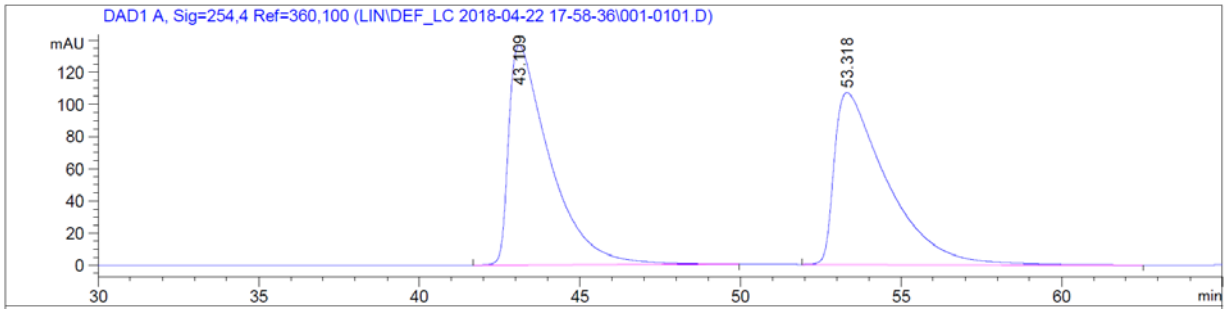

**8k**
(2.9:1 mixture of rotamer)

**8k** (17.2 mg, 2.9:1 mixture of rotamer) was isolated as a white solid in 80% yield**.** Melting Point: 154-156 °C. $Rh(COD)_2BF_4$ (5 mol%, 0.005 mmol, 2.1 mg) and (*R*)-DTBM-segphos (6 mol%, 0.006 mmol, 7.1 mg) were used and the reaction was maintained at 90 °C. $R_f$ = 0.4 (acetone/Hexane=1/3). **$^1$H NMR (400 MHz, $CDCl_3$):** δ (major rotamer) 7.94 (d, *J* = 8.0 Hz, 1H), 7.22 (t, *J* = 7.8 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 4.41 (t, *J* = 9.1 Hz, 1H), 3.88 – 3.78 (m, 1H), 3.74 (t, *J* = 9.6 Hz, 1H), 3.55 (s, 2H), 2.97 (dd, *J* = 16.1, 5.3 Hz, 1H), 2.33 (dd, *J* = 16.1, 12.0 Hz, 1H), 2.24 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ (all the peaks observed) 208.2, 168.5, 141.1, 131.7, 130.4, 130.2, 129.3, 129.0, 122.4, 122.1, 115.2, 112.5,

56.4, 55.6, 43.8, 43.7, 42.1, 35.0, 33.6, 29.7, 24.2, 23.9. **IR:** v 3440, 2050, 1635, 1472, 1416, 1275, 749, 578 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 216.1019. Found: 216.1010.

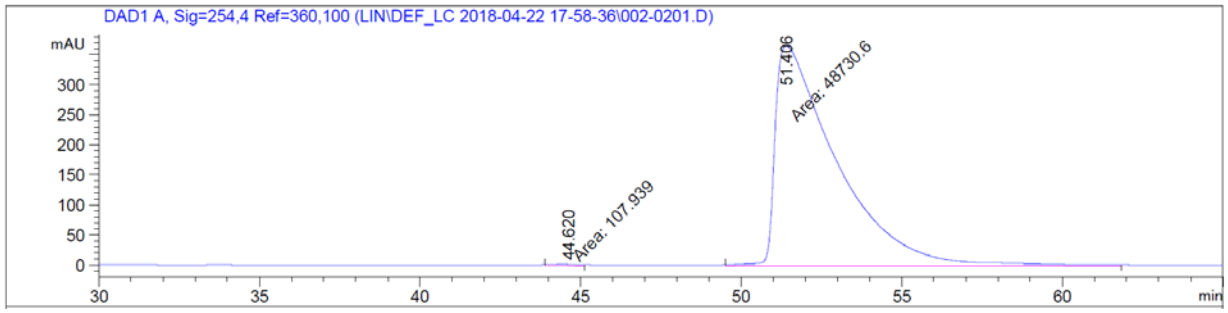
Chiral HPLC (Chiralpak IF, hexane:isopropanol = 85:15, 1 mL/min, 254 nm), $t_{minor}$ = 44.6 min, $t_{major}$= 51.4 min. $[\alpha]_D^{21.5}$ = -177.9 (c= 0.95, $CHCl_3$) at 99% e.e.

**Racemic Sample 8k**

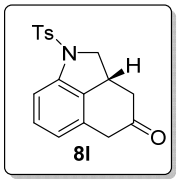



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 43.109 | BB | 1.2759 | 1.21946e4 | 136.54861 | 49.9805 |
| 2 | 53.318 | BB | 1.6252 | 1.22041e4 | 106.79595 | 50.0195 |

**Enantiomeric Sample 8k**




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 44.620 | MM | 1.0347 | 107.93900 | 1.73873 | 0.2210 |
| 2 | 51.406 | MM | 2.2181 | 4.87306e4 | 366.16602 | 99.7790 |



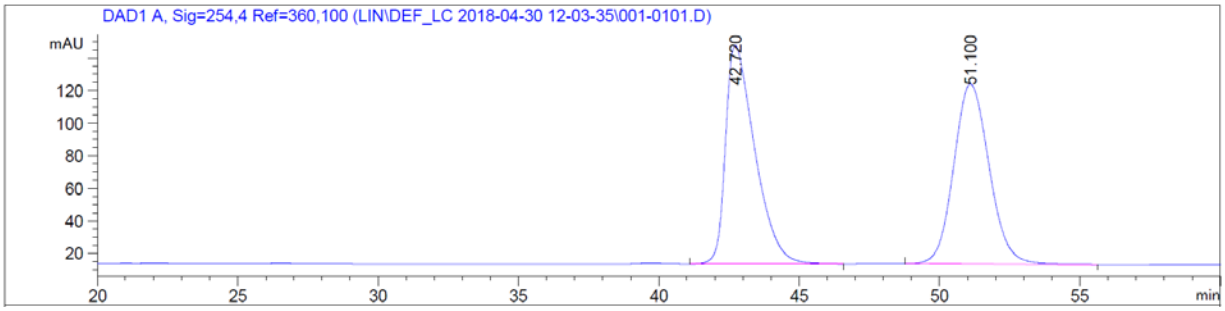

**8l**

**8l** (32.0 mg) was isolated as white solid in 91% yield**.** Melting Point: 127-129 °C. $Rh(COD)_2BF_4$ (10 mol%, 0.01 mmol, 4.2 mg) and (*R*)-DTBM-segphos (12 mol%, 0.012 mmol, 14.2 mg) were used and the reaction was maintained at 90 °C

for 12 h then at 110 °C for 12 h. $R_f$ = 0.2 (EtOAc/Hexane=1/3). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.71 (d, *J* = 8.4 Hz, 2H), 7.47 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.26 (d, *J* = 1.4 Hz, 2H), 7.25 – 7.18 (m, 1H), 6.81 (dd, *J* = 7.6, 0.9 Hz, 1H), 4.40 (dd, *J* = 9.9, 8.4 Hz, 1H), 3.55 – 3.47 (m, 1H), 3.46 – 3.44 (s, 2H), 3.38 (dd, *J* = 10.7, 10.0 Hz, 1H), 2.85 (dd, *J* = 16.1, 5.4 Hz, 1H), 2.38 (s, 3H), 2.11 (dd, *J* = 16.1, 12.1 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 207.7, 144.4, 140.6, 133.7, 130.9, 129.8, 129.4, 127.3, 122.5, 113.3, 57.8, 43.6, 41.8, 34.7, 21.6. **IR:** v 3441, 2064, 1707, 1635, 1456, 1353, 1275, 1165, 1095, 750, 660, 581, 543 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 328.1002. Found: 328.1002.

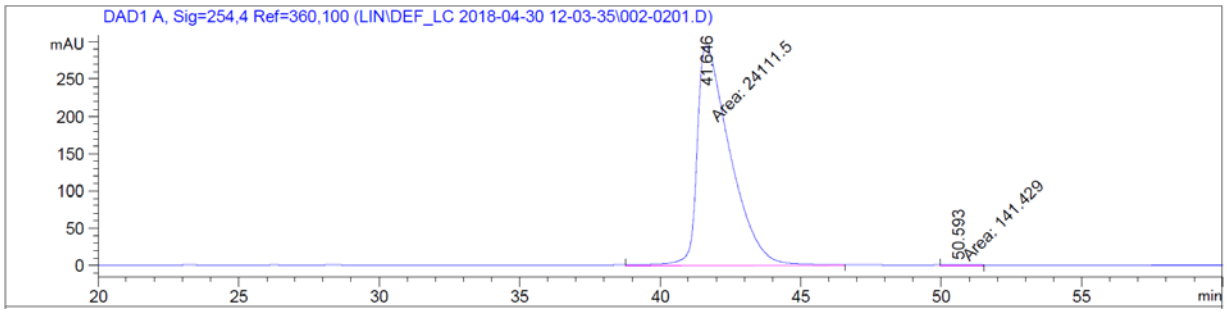
Chiral HPLC (Chiralpak IF, hexane:isopropanol = 85:15, 1 mL/min, 254 nm), $t_{minor}$ = 50.6 min, $t_{major}$= 41.6 min. $[\alpha]_D^{21.5}$ = -134.5 (c= 0.62, $CHCl_3$) at 99% e.e.

**Racemic Sample 8l**

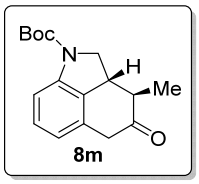



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 42.720 | BB | 1.1037 | 9729.44531 | 134.22519 | 50.1079 |
| 2 | 51.100 | BB | 1.3663 | 9687.53711 | 110.55894 | 49.8921 |

**Enantiomeric Sample 8l**



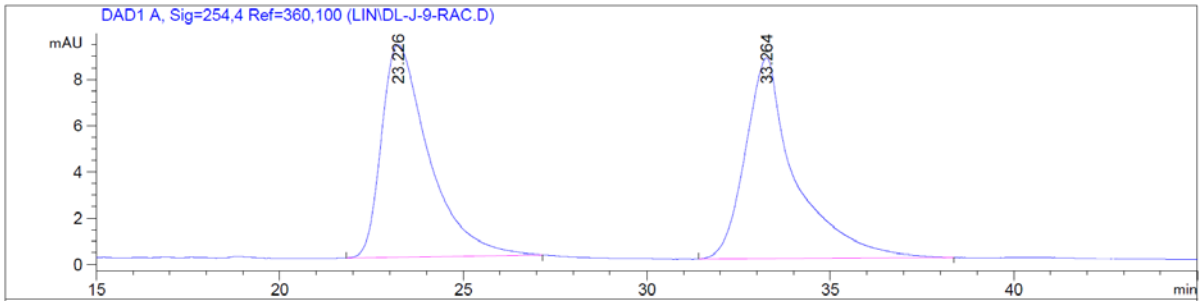

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 41.646 | MM | 1.3625 | 2.41115e4 | 294.94385 | 99.4169 |
| 2 | 50.593 | MM | 1.3283 | 141.42949 | 1.77458 | 0.5831 |




**8m** (17.1 mg) was isolated as a white solid in 75% yield**.** Melting Point: 155-159 °C. $Rh(COD)_2BF_4$ (10 mol%, 0.01 mmol, 4.2 mg) and (*R*)-DTBM-segphos (12 mol%, 0.012 mmol, 14.2 mg) were used and the reaction was maintained at 90 °C for 12 h. $R_f$ = 0.6 (EtOAc/Hexane=1/5). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.76-7.20 (m, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 6.88 – 6.69 (m, 1H), 4.38 (br, 1H), 3.64 (t, *J* = 10.5 Hz, 1H), 3.57 (s, 2H), 3.40 – 3.24 (m, 1H), 2.35 (dq, *J* = 12.0, 6.6 Hz, 1H), 1.58 (s, 9H), 1.23 (d, *J* = 6.7 Hz, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 210.0, 152.4, 130.4, 129.0, 120.9, 112.8, 81.0, 54.7, 48.4, 41.8, 40.6, 28.4, 12.4. **IR:** ν 2966, 2925, 2853, 1702, 1475, 1462, 1389, 1354, 1162, 1136, 776 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 310.1414. Found: 310.1406.

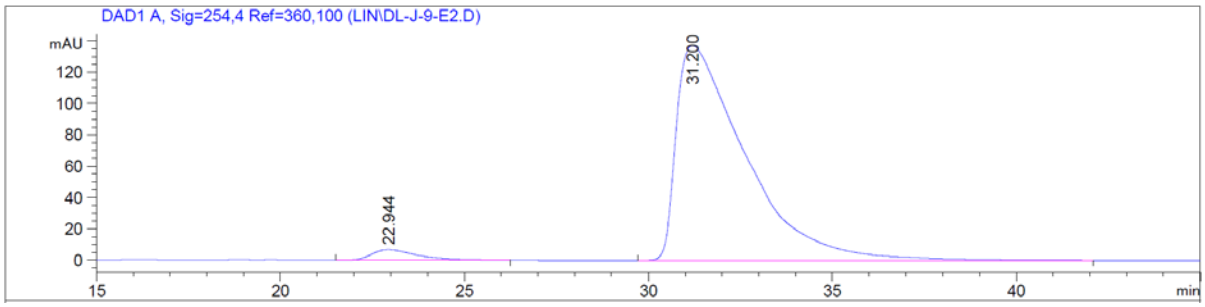
Chiral HPLC (Chiralpak IF, hexane:isopropanol = 98:2, 1 mL/min, 254 nm), $t_{minor}$ = 22.9 min, $t_{major}$= 31.2 min. $[\alpha]_D^{21.5}$ = -114.8 (c= 1.08, $CHCl_3$) at 94% e.e.

**Racemic Sample 8m**

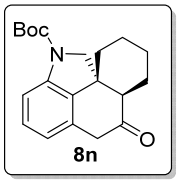



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 23.226 | BB | 1.2728 | 819.87750 | 9.17241 | 49.9569 |
| 2 | 33.264 | BB | 1.2774 | 821.29224 | 8.66851 | 50.0431 |

**Enantiomeric Sample 8m**



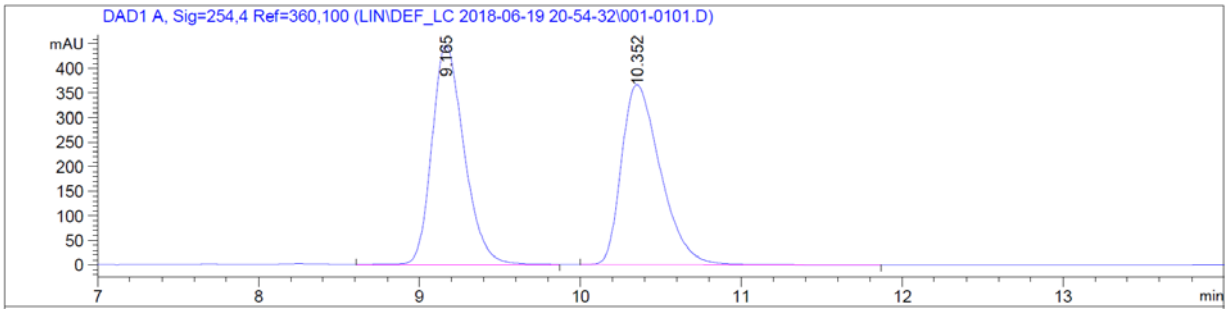
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 22.944 | BB | 1.2073 | 581.18683 | 6.73112 | 3.1409 |
| 2 | 31.200 | BB | 1.8371 | 1.79224e4 | 137.27806 | 96.8591 |




**8n** (26.7 mg) was isolated as a colorless oil in 82% yield**.** $Rh(COD)_2BF_4$ (10 mol%, 0.01 mmol, 4.2 mg) and (*R*)-DTBM-segphos (12 mol%, 0.012 mmol, 14.2 mg) were used and the reaction was maintained at 90 °C for 12 h. $R_f$ = 0.6 (EtOAc/Hexane=1/5). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.76 – 7.21 (m, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 6.76 (d, *J* = 7.6 Hz, 1H), 4.47 – 4.08 (m, 1H), 3.65 – 3.47 (m, 3H), 2.55 – 2.42 (m, 1H), 2.41 – 2.33 (m, 1H), 1.82 – 1.73 (m, 1H), 1.71 – 1.64 (m, 1H), 1.60 (s, 9H), 1.55 – 1.48 (m, 1H), 1.41 – 1.19 (m, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 210.1, 152.6, 139.9, 135.3, 129.8, 128.8, 121.1, 112.9, 80.9, 58.7, 52.9, 42.6, 41.2, 32.4, 28.4, 22.6, 22.0, 21.2. **IR:** ν 2924, 2853, 1705, 1620, 1460, 1387, 1351, 1162, 1138, 1081, 777 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 350.1727. Found: 350.1722.

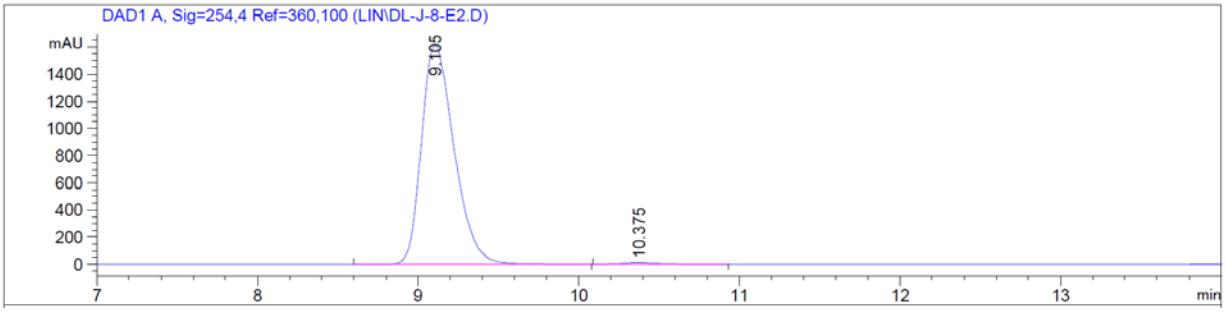
Chiral HPLC (Chiralpak IA, hexane:isopropanol = 99:1, 1 mL/min, 254 nm), $t_{minor}$ = 10.4 min, $t_{major}$= 9.1 min. $[\alpha]_D^{21.5}$ = -97.6 (c= 2.67, $CHCl_3$) at 98% e.e.

**Racemic Sample 8n**



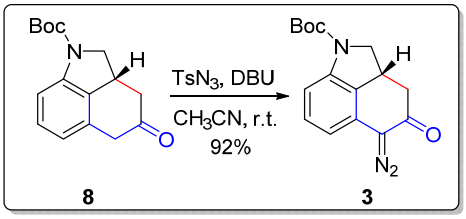

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.165 | BB | 0.2130 | 6234.80469 | 446.14462 | 50.2401 |
| 2 | 10.352 | BB | 0.2606 | 6175.20605 | 366.40610 | 49.7599 |

**Enantiomeric Sample 8n**



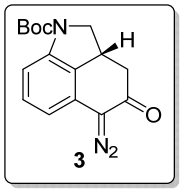

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.105 | BB | 0.2165 | 2.27470e4 | 1613.47888 | 99.2855 |
| 2 | 10.375 | BB | 0.2537 | 163.69363 | 10.06678 | 0.7145 |

IV. *Procedure and characterization data for the total synthesis of (–)-cycloclavine*

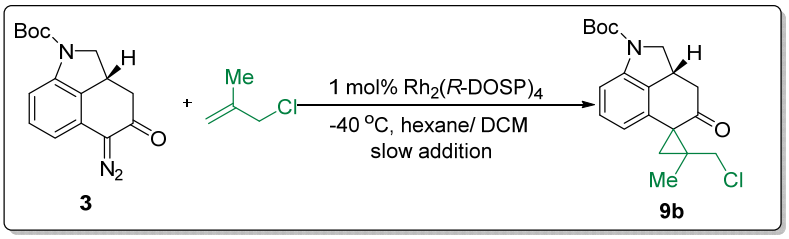



**Procedure:**

A 20 mL vial with a stir bar was charged with **8** (672 mg, 2.46 mmol, 1.0 equiv.) and $TsN_3$ (581.9 mg, 2.95 mmol, 1.2 equiv.) in $CH_3CN$ (10 mL). After adding DBU (441 µL, 2.95 mmol, 1.2 equiv.) at 0 °C, the vial was capped and the mixture was stirred at 0 °C for 2 h. Upon completion, it was warmed up to room temperature and the solvent was removed by rotavap under reduced pressure. The crude product was purified by silica gel flash chromatography (heaxane:ethyl acetate= 10:1) to yield the desired product **3**.

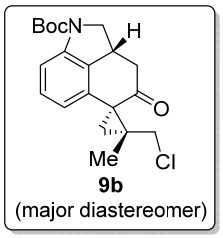



Compound **3** was isolated as a bright yellow solid in 92% yield (670 mg). Melting Point: 148-150 °C (decomposed). $R_f$ = 0.5 (EtOAc/Hexane=1/5). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.64 – 7.02 (m, 1H), 7.23 (t, *J* = 7.9 Hz, 1H), 6.61 (d, *J* = 7.9 Hz, 1H), 4.40 (m, 1H), 3.74 – 3.49 (m, 2H), 2.93 (dd, *J* = 15.6, 5.3 Hz, 1H), 2.50 (dd, *J* = 15.5, 13.1 Hz, 1H), 1.57 (s, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 192.3, 152.3, 130.0, 124.5, 122.0, 113.2, 111.5, 81.2, 70.3, 55.4, 42.1, 34.2, 28.4. **IR:** ν 3453, 2084, 1698, 1651, 1475, 1459, 1391, 1356, 1275, 1261, 1163, 1141, 859, 750 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 300.1343. Found: 300.1339. $[\alpha]_D^{21.5}$ = -167.8 (c= 1.57, $CHCl_3$).

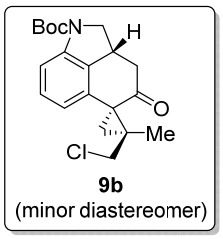



**Procedure[5]:**

To a 50 mL flamed-dried Schlenk flask equipped with a stir bar and a nitrogen-filled balloon was added $Rh_2$(*R*-DOSP)$_4$ (12.7 mg, 0.0068 mmol, 1 mol%) and 3-chloro-2-methyl-1-propene (604.9 mg, 6.68 mmol, 10 equiv.) in hexane (15 mL). The system was cooled to -40 °C before **3** (200 mg, 0.67 mmol, 1.0 equiv.) in hexane/toluene (4 mL/ 2 mL) was added using slow-addition pump with a speed of 2 mL/ h. After the addition of **3** was finished, the system was kept at -40 °C for another 20 min. After the starting material was fully consumed, the reaction solution was directly loaded to a silica gel column while the temperature was still below 0 °C. The crude product was purified by silica gel flash column chromatography (EtOAc/Hexane=1/50) to afford compound **9b** as a white solid in 85% yield. Two diastereomers of compound **9b** were isolated through silica gel chromatography, with a ratio of 5.8:1. The relative stereochemistry of the major isomer was determined by X-ray crystallagraphy.

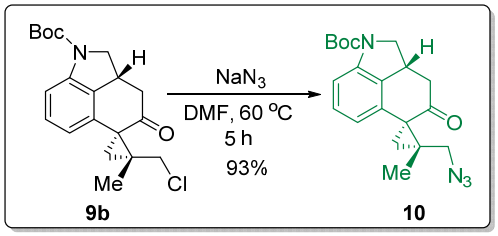



Compound **9b** (major diastereomer) was isolated as a white solid in 73% yield (175.8 mg). Melting Point: 183-184 °C (decomposed). $R_f$ = 0.4 (EtOAc/Hexane=1/5). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.74 – 7.22 (m, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 6.55 (d, *J* = 7.8 Hz, 1H), 4.46 (s, 1H), 3.93 (d, *J* = 8.0 Hz, 1H), 3.75 (d, *J* = 11.4 Hz, 1H), 3.68 – 3.55 (m, 2H), 3.07 (dd, *J* = 17.7, 5.8 Hz, 1H), 2.29 (dd, *J* = 17.7, 11.9 Hz, 1H), 2.12 (d, *J* = 5.4 Hz, 1H), 1.67 (d, *J* = 5.4 Hz, 1H), 1.57 (s, 9H), 1.06 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 206.7, 152.4, 141.1, 133.7, 128.5, 118.9, 113.0, 81.5, 54.9, 48.8, 44.7, 43.0, 39.9, 32.7, 28.4, 22.9, 17.2. **IR**: v 3444, 2977, 2098, 1694, 1617, 1462, 1390, 1350, 1258, 1142, 750 cm$^{-1}$; **HRMS** calcd. For $[M+H]^+$: 362.1517. Found: 362.1513. $[\alpha]_D^{21.5}$ = -132.3 (c= 1.10, $CHCl_3$).




Compound **9b** (minor diastereomer) was isolated as a colorless oil in 12% yield (30.3 mg). The stereochemistry was tentatively assigned based on preliminary experimental results. After subjecting this minor diastereomer to further deprotection and oxidation of the indoline to the indole, we found the compound obtained is likely the diastereomer of compound **2** according to the $^1$H-NMR spectrum. This experiment suggested that the diastereomer observed here should arise from the stereocenter close to the methyl and methylene chloride group. $R_f$ = 0.3 (EtOAc/Hexane=1/5). **$^1$H NMR**

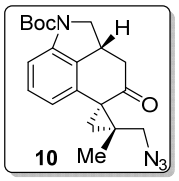
**(400 MHz, $CDCl_3$):** δ 7.77 – 7.25 (m, 1H), 7.20 (t, *J* = 7.8 Hz, 1H), 6.59 (d, *J* = 7.7 Hz, 1H), 4.42 (s, 1H), 3.93 – 3.75 (m, 1H), 3.60 (dd, *J* = 13.9, 10.3 Hz, 2H), 3.21 (d, *J* = 11.3 Hz, 1H), 3.00 (dd, *J* = 17.8, 5.1 Hz, 1H), 2.35 (dd, *J* = 18.1, 11.9 Hz, 1H), 1.99 (d, *J* = 5.6 Hz, 1H), 1.64 (d, *J* = 5.6 Hz, 1H), 1.57 (s, 9H), 1.33 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 206.0, 152.4, 134.1, 131.0, 128.8, 118.4, 113.2, 80.8, 54.8, 50.5, 44.9, 44.1, 37.3, 33.2, 28.4, 21.1, 16.5. **IR**: v 2976, 2930, 1698, 1477, 1462, 1391, 1351, 1322, 1256, 1166, 1143, 736 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 362.1517. Found: 362.1516.



**9b** **10**

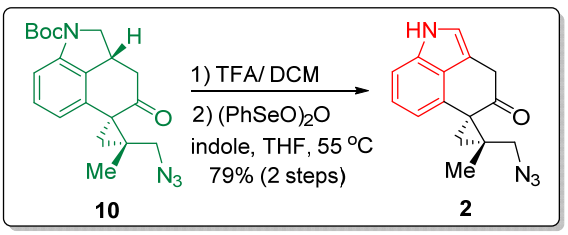
**Procedure:**

A 20 mL vial with a stir bar was charged with **9b** (150 mg, 0.41 mmol, 1.0 equiv. the major diastereomer) and $NaN_3$ (161.7 mg, 2.49 mmol, 6.0 equiv.) in DMF (10 mL). The vial was capped and the mixture was stirring at 60 °C for 5 h. Upon completion, it was cooled down to room temperature and the reaction mixture was quenched with brine (10 mL). The mixture was extracted with ethyl acetate (3×20 mL), washed with brine, and dried over $Na_2SO_4$. The combined organic extract was concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (heaxane:ethyl acetate= 20:1) to yield the desired product **10**.



**10**

Compound **10** was isolated as a white solid in 93% yield (140 mg). Melting Point: 116-118 °C. $R_f$ = 0.6 (EtOAc/Hexane=1/5). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.75 – 7.22 (m, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 6.54 (d, *J* = 7.8 Hz, 1H), 4.47 (s, 1H), 3.96 – 3.76 (m, 1H), 3.63 (dd, *J* = 11.3, 8.9 Hz, 1H), 3.55 (d, *J* = 12.7 Hz, 1H), 3.39 (d, *J* = 12.8 Hz, 1H), 3.04 (dd, *J* = 17.6, 5.3 Hz, 1H), 2.29 (dd, *J* = 17.6, 12.0 Hz, 1H), 2.00 (d, *J* = 5.5 Hz, 1H), 1.58 (d, *J* = 5.6 Hz, 9H), 1.54 (d, *J* = 5.5 Hz, 1H), 0.99 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 206.9, 152.4, 133.5, 131.7, 128.5, 118.9, 112.9, 80.8, 55.1, 44.8, 42.2, 37.8, 32.8, 28.4, 21.1, 17.8. **IR:** v 3439, 2096, 1694, 1635, 1462, 1390, 1259, 1166, 1139, 1079, 749 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 369.1921. Found: 369.1922. $[\alpha]_D^{21.5}$ = -167.8 (c= 0.87, $CHCl_3$).

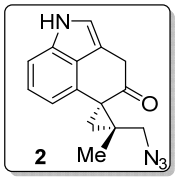


**10** **2**

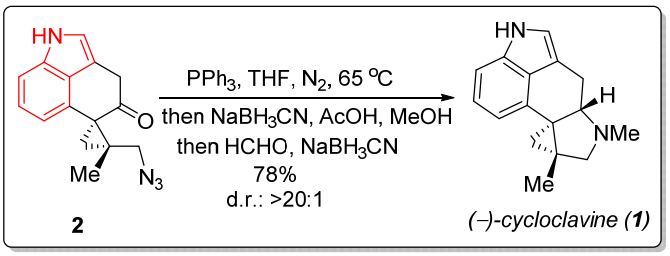
**Procedure[6]:**

A 20 mL vial with a stir bar was charged with **10** (36.8 mg, 0.1 mmol, 1.0 equiv.) in dichloromethane (5 mL). TFA (1 mL) was added dropwisely to the stirring solution and the mixture was stirred at room temperature for 1 h. The reaction

mixture was then quenched with saturated aqueous $NaHCO_3$ solution (10 mL) and extracted with dichloromethane (3×10 mL), washed with brine, and dried over $Na_2SO_4$. The combined organic extract was concentrated under reduced pressure. The crude product was transferred to a flame-dried 8 mL vial and $(PhSeO)_2O$ (18.0 mg, 0.05 mmol, 0.5 equiv.) and indole (23.4 mg, 0.2 mmol, 2.0 equiv.) was added. The vial was loosely capped and transferred into a nitrogen-filled glovebox, where anhydrous THF (2 mL) was used to dissolve the mixture. After stirring at 55 °C for 2 h, the vial was cooled down to room temperature and the solvent was removed under reduced pressure. The crude product was purified by silica gel flash chromatography (dichloromethane:methanol= 100:0 to 100:1) to yield the desired product **2**. Compound **2** is unstable even under nitrogen atmosphere at low temperature, normally directly subjected to the next step right after purification. Here we provide $^1$H-NMR and $^{13}$C-NMR data for compound **2**.

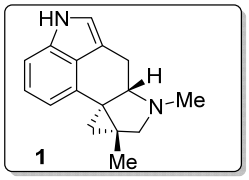



Compound **2** was isolated as a colorless oil in 79% yield over 2 steps (21.2 mg). $R_f$ = 0.5 (DCM/MeOH=20/1). **$^1$H NMR (500 MHz, $CDCl_3$):** δ 8.10 (s, 1H), 7.25 – 7.13 (m, 2H), 6.96 (s, 1H), 6.57 (d, *J* = 6.6 Hz, 1H), 4.03 (d, *J* = 19.5 Hz, 1H), 3.87 (d, *J* = 19.6 Hz, 1H), 3.59 (d, *J* = 12.8 Hz, 1H), 3.30 (d, *J* = 12.7 Hz, 1H), 2.21 – 2.12 (m, 1H), 1.56 – 1.44 (m, 1H), 1.28 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 204.0, 133.4, 128.5, 126.8, 123.0, 118.0, 114.8, 109.4, 108.7, 56.4, 41.8, 39.2, 36.8, 21.6, 16.6.




**Procedure:**

An 8 mL vial was charged with **2** (35.0 mg, 0.13 mmol, 1.0 equiv.) and $PPh_3$ (103.4 mg, 0.39 mmol, 3.0 equiv.). After adding THF (1 mL) inside a nitrogen-filled glovebox, the vial was capped and the mixture was stirred at 65 °C for 2 h. After that, MeOH (5 mL) was added to the solution as well as $NaBH_3CN$ (10.3 mg, 0.16 mmol, 1.3 equiv.) and AcOH (100 µL). The mixture was then stirred for 30 min at room temperature, before HCHO (37 wt% solution in water, 270 µL) and another portion of $NaBH_3CN$ (10.3 mg, 0.16 mmol, 1.3 equiv.) was added. The mixture was further stirred for 30 min. Upon completion, the reaction was quenched by brine (10 mL). The mixture was extracted with dichloromethane (3×10 mL), washed with brine, and dried over $Na_2SO_4$. The crude product was purified by silica gel flash chromatography (dichloromethane:methanol= 100:0 to 50:1) to yield the desired natural product **1**. The characterization data of compound **1** matches the reported data[7].

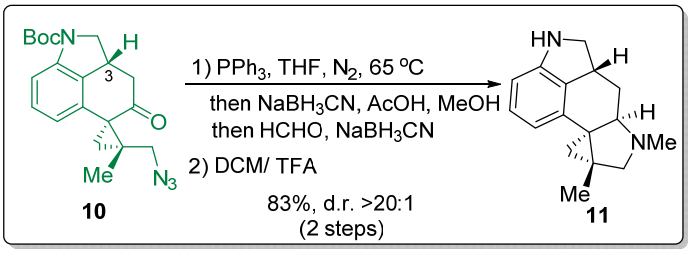



Compound **1** was isolated as a white solid in 78% yield (24.3 mg). Melting Point: 158-160 °C. $R_f$ = 0.4 (DCM/MeOH=20/1). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.92 (br, 1H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.90 (s, 1H), 6.83 (d, *J* = 6.9 Hz, 1H), 3.17 (d, *J* = 9.0 Hz, 1H), 3.14 (dd, *J* = 14.2, 3.2 Hz, 1H), 2.79 (dd, *J* = 11.5, 3.7 Hz, 1H), 2.61 (t, *J* = 12.2 Hz, 1H), 2.41 (d, *J* = 8.6 Hz, 1H), 2.37 (s, 3H), 1.69 (s, 3H), 1.61 (d, *J* = 3.4 Hz, 1H), 0.46 (d, *J* = 3.5 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 135.4, 133.6, 128.7, 122.9, 118.1, 113.2, 110.4, 107.9, 69.6, 65.6, 39.9, 34.4, 27.8, 24.9, 24.2, 16.5. **IR:** ν 3416, 2076, 1634, 1448, 1276, 749, 616 $cm^{-1}$; **HRMS** calcd. For $[M+Na]^+$: 261.1362. Found: 261.1360. $[\alpha]_D^{21.5}$ = -45.3 (c= 0.86, $CHCl_3$). [Reported $[\alpha]_D^{21.5}$ = -58.9 (c= 0.23, $CHCl_3$)][7]

**Comparison of the NMR Data between Synthesized 1 and Reported 1**

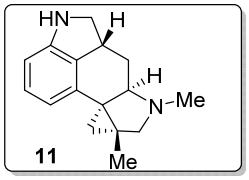
| H-NMR of Synthesized **1** | H-NMR of Reported **1** | $^{13}$C-NMR of Synthesized **1** | $^{13}$C-NMR of Reported **1** |
|---|---|---|---|
| 7.92 (br, 1H) | 7.92 (br, 1 H) | 135.4 | 135.4 |
| 7.14 (d, *J* = 8.0 Hz, 1H) | 7.15 (d, J = 8.4 Hz, 1H) | 133.6 | 133.5 |
| 7.09 (t, *J* = 7.6 Hz, 1H) | 7.10 (app t, J = 7.7 Hz, 1H) | 128.7 | 128.7 |
| 6.90 (s, 1H) | 6.91 (s, 1 H) | 122.9 | 122.9 |
| 6.83 (d, *J* = 6.9 Hz, 1H) | 6.84 (d, J = 7.0 Hz, 1H) | 118.1 | 118.1 |
| 3.17 (d, *J* = 9.0 Hz, 1H) | 3.17 (d, J = 9.1 Hz, 1H) | 113.2 | 113.2 |
| 3.14 (dd, *J* = 14.2, 3.2 Hz, 1H) | 3.15 (dd, J = 14.0, 4.2 Hz, 1H) | 110.4 | 110.3 |
| 2.79 (dd, *J* = 11.5, 3.7 Hz, 1H) | 2.79 (dd, J = 11.2, 3.5 Hz, 1H) | 107.9 | 107.9 |
| 2.61 (t, *J* = 12.2 Hz, 1H) | 2.61 (t, J = 12.6 Hz, 1H) | 69.6 | 69.6 |
| 2.41 (d, *J* = 8.6 Hz, 1H) | 2.42 (d, J = 8.4 Hz, 1H) | 65.6 | 65.6 |
| 2.37 (s, 3H) | 2.37 (s, 3 H) | 39.9 | 39.9 |
| 1.69 (s, 3H) | 1.70 (s, 3 H) | 34.4 | 34.3 |
| 1.61 (d, *J* = 3.4 Hz, 1H) | 1.61 (d, J = 2.8 Hz, 1H) | 27.8 | 27.8 |
| 0.46 (d, *J* = 3.5 Hz, 1H) | 0.46 (d, J = 3.5 Hz, 1H) | 24.9 | 24.9 |
| | | 24.2 | 24.2 |
| | | 16.5 | 16.5 |

## V. *Procedure and characterization data of total synthesis of (–)-5-epi-cycloclavine*

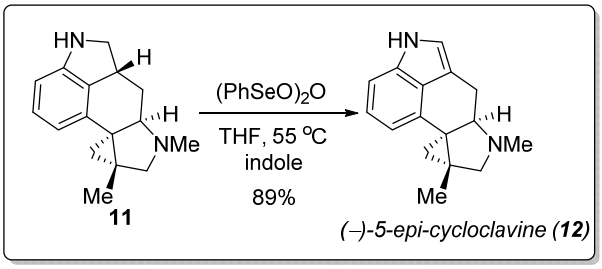


**Procedure:**

An 8 mL vial was charged with **10** (51.4 mg, 0.14 mmol, 1.0 equiv.) and $PPh_3$ (109.8 mg, 0.42 mmol, 3.0 equiv.). After adding THF (1 mL) inside a nitrogen-filled glovebox, the vial was capped and the mixture was stirred at 65 °C for 2 h. After that, MeOH (5 mL) was added to the solution as well as $NaBH_3CN$ (13.2 mg, 0.21 mmol, 1.5 equiv.), AcOH (97 μL, 1.68 mmol, 12 equiv.). The mixture was then stirred for 30 min at room temperature, before HCHO (37 wt% solution in water, 240 μL) and another portion of $NaBH_3CN$ (13.2 mg, 0.21 mmol, 1.5 equiv.) was added. The mixture was further stirred for 30 min. Upon completion, the reaction was quenched by brine (10 mL). The mixture was extracted with dichloromethane (3×10 mL), washed with brine, and dried over $Na_2SO_4$. The crude product was dissolved in 5 mL dichloromethane and 1 mL of trifluoroacetic acid was added dropwisely to the stirring solution. After the mixture was stirred for 1 h, the reaction was quenched by saturated $NaHCO_3$ aqueous solution (10 mL). The mixture was extracted with dichloromethane (3×10 mL), washed with brine, and dried over $Na_2SO_4$. The crude product was purified by silica gel flash chromatography (dichloromethane:methanol= 100:0 to 20:1) to yield the desired product **11**.

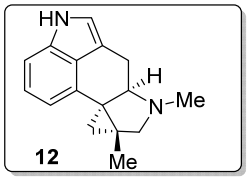



Compound **11** was isolated as a white solid in 83% yield (28.0 mg). Melting Point: 119-120 °C. $R_f$ = 0.2 (DCM/MeOH=20/1). **$^1$H NMR (400 MHz, $CDCl_3$):** δ 6.97 (td, *J* = 7.7, 0.9 Hz, 1H), 6.49 (d, *J* = 7.6 Hz, 1H), 6.24 (d, *J* = 7.7 Hz, 1H), 3.83 (t, *J* = 8.4 Hz, 1H), 3.34 (ddd, *J* = 12.1, 8.5, 4.4 Hz, 1H), 3.23 (dd, *J* = 10.9, 8.4 Hz, 2H), 2.51 (d, *J* = 4.5 Hz, 1H), 2.33 (d, *J* = 9.5 Hz, 1H), 2.29 – 2.23 (m, 4H), 1.58 (d, *J* = 4.8 Hz, 1H), 1.39 (ddd, *J* = 13.2, 11.9, 4.8 Hz, 1H), 1.03 (s, 3H), 0.91 (d, *J* = 4.9 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 149.4, 133.4, 133.3, 127.1, 113.7, 106.1, 72.5, 67.3, 55.1, 39.5, 38.8, 35.2, 34.4, 33.2, 30.7, 17.3. **IR:** ν 3443, 2065, 1635, 1275, 1260, 764, 750, 566 $cm^{-1}$; **HRMS** calcd. For $[M+H]^+$: 241.1699. Found: 241.1704. $[\alpha]_D^{21.5}$ = -138 (c= 0.71, $CHCl_3$).




**Procedure:**

To a flame-dried 8 mL vial charged with **11** (14.4 mg, 0.06 mmol, 1.0 equiv.) was added $(PhSeO)_2O$ (10.8 mg, 0.03 mmol, 0.5 equiv.) and indole (21.1 mg, 0.18 mmol, 3.0 equiv.). The vial was loosely capped and transferred into a nitrogen-filled glovebox, where anhydrous THF (1 mL) was used to dissolve the mixture. After stirring at 55 °C for 2 h, the vial was cooled down to room temperature and the solvent was removed by rotavap under reduced pressure. The crude product was purified by silica gel flash chromatography (dichloromethane:methanol= 100:0 to 20:1) to yield the desired product **12**. The characterization data of compound **12** matches the reported data[7a].




Compound **12** was isolated as a white solid in 89% yield (12.7 mg). Melting Point: 175-176 $^{o}$C (decomposed). $R_f$ = 0.4 (DCM/MeOH=20/1). **$^{1}$H NMR (400 MHz, $CDCl_3$):** δ 7.92 (br, 1H), 7.20 – 7.13 (m, 2H), 6.90 (t, *J* = 1.9 Hz, 1H), 6.62 (dd, *J* = 5.1, 2.7 Hz, 1H), 3.54 (dd, *J* = 11.0, 5.6 Hz, 1H), 3.08 – 2.97 (m, 2H), 2.67 (d, *J* = 8.8 Hz, 1H), 2.62 (ddd, *J* = 14.5, 11.0, 1.8 Hz, 1H), 2.51 (s, 3H), 1.59 (d, *J* = 4.4 Hz, 1H), 1.15 (d, *J* = 6.3 Hz, 4H). ). **$^{1}$H NMR (400 MHz, $CD_2Cl_2$):** δ 8.05 (br, 1H), 7.18 – 7.07 (m, 2H), 6.92 (t, *J* = 1.8 Hz, 1H), 6.58 (dd, *J* = 6.4, 1.4 Hz, 1H), 3.47 (dd, *J* = 10.8, 5.6 Hz, 1H), 3.01 (dd, *J* = 14.6, 5.6 Hz, 1H), 2.98 (d, J = 8.8 Hz, 1H), 2.66 (d, *J* = 8.8 Hz, 1H), 2.60 (ddd, *J* = 14.5, 11.0, 1.8 Hz, 1H), 2.49 (s, 3H), 1.60 – 1.52 (m, 1H), 1.12 (s, 3H), 1.11 (d, *J* = 4.5 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)**: δ 133.3, 130.4, 127.4, 122.9, 118.1, 112.9, 111.6, 107.6, 62.9, 59.7, 35.8, 35.4, 33.2, 20.1, 18.6, 14.9. **IR:** ν 3420, 1635, 1275, 1260, 764, 749, 528 cm$^{-1}$; **HRMS** calcd. For $[M+H]^+$: 239.1543. Found: 239.1550. $[\alpha]_D^{21.5}$ = -42 (c= 0.64, $CHCl_3$).

**Comparison of the NMR Data between Synthesized 12 and Reported 12**[7a]

| H-NMR of Synthesized **12** (in $CD_2Cl_2$) | H-NMR of Reported **12** (in $CD_2Cl_2$) | $^{13}$C-NMR of Synthesized **12** (in $CDCl_3$) | $^{13}$C-NMR of Reported **12** (in $CDCl_3$) |
|---|---|---|---|
| 8.05 (br, 1H) | 8.04 (br s, 1 H) | 133.3 | 133.3 |
| 7.18 – 7.07 (m, 2H) | 7.15-7.10 (m, 2 H) | 130.4 | 130.5 |
| 6.92 (t, *J* = 1.8 Hz, 1H) | 6.92 (dd, J = 1.8 Hz, 1H) | 127.4 | 127.4 |
| 6.58 (dd, *J* = 6.4, 1.4 Hz, 1H) | 6.58 (dd, J = 6.6, 0.6 Hz, 1H) | 122.9 | 122.9 |
| 3.47 (dd, *J* = 10.8, 5.6 Hz, 1H) | 3.47 (dd, J = 10.8, 6.0 Hz, 1H) | 118.1 | 118.1 |
| 3.01 (dd, *J* = 14.6, 5.6 Hz, 1H) | 3.01 (dd, J = 14.4, 6.0 Hz, 1H) | 112.9 | 112.9 |
| 2.98 (d, J = 8.8 Hz, 1H) | 2.98 (d, J = 8.4 Hz, 1H) | 111.6 | 111.7 |
| 2.66 (d, *J* = 8.8 Hz, 1H) | 2.66 (d, J = 9.0 Hz, 1H) | 107.6 | 107.6 |
| 2.60 (ddd, *J* = 14.5, 11.0, 1.8 Hz, 1H) | 2.59 (ddd, J = 16.2, 11.4, 1.8 Hz, 1H) | 62.9 | 62.9 |
| 2.49 (s, 3H) | 2.48 (s, 3 H) | 59.7 | 59.8 |
| 1.60 – 1.52 (m, 1H) | 1.57 (d, J = 3.0 Hz, 1H) | 35.8 | 35.8 |
| 1.12 (s, 3H) | 1.12 (s, 3 H) | 35.4 | 35.4 |
| 1.11 (d, *J* = 4.5 Hz, 1H) | 1.11 (d, J = 4.2 Hz, 1H) | 33.2 | 33.2 |
| | | 20.1 | 20.1 |
| | | 18.6 | 18.6 |
| | | 14.9 | 14.9 |

## 3. References

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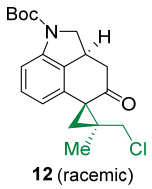
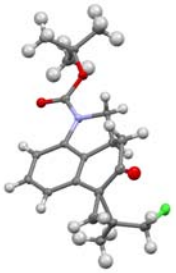
(6) Ninomiya, I.; Kiguchi, T.; Hashimoto, C.; Barton, D. H. R.; Lusinchi, X.; Milliet, P. *Tetrahedron Lett.* **1985**, *26*, 4183.

(7) (a) Petronijevic, F. R.; Wipf, P. *J. Am. Chem. Soc.* **2011**, *133*, 7704. (b) McCabe, S. R.; Wipf, P. *Angew. Chem. Int. Ed.* **2017**, *56*, 324.

## 4. X-Ray Data



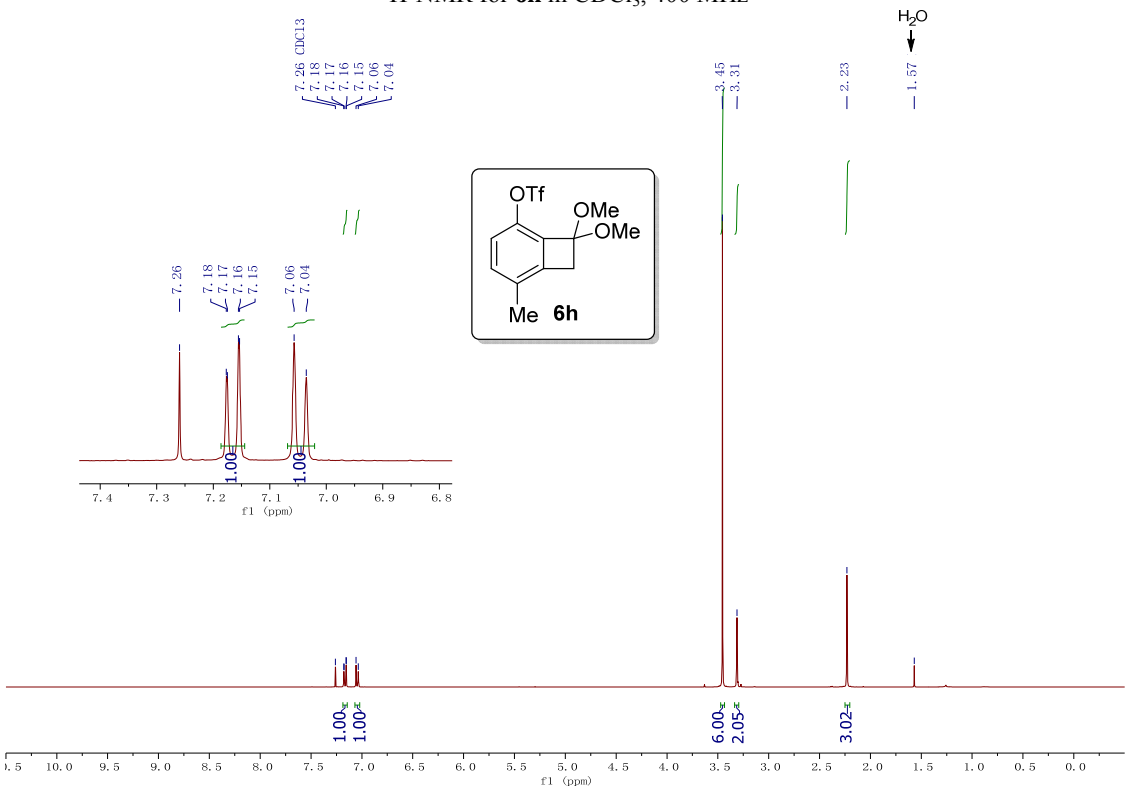
**12** (racemic)



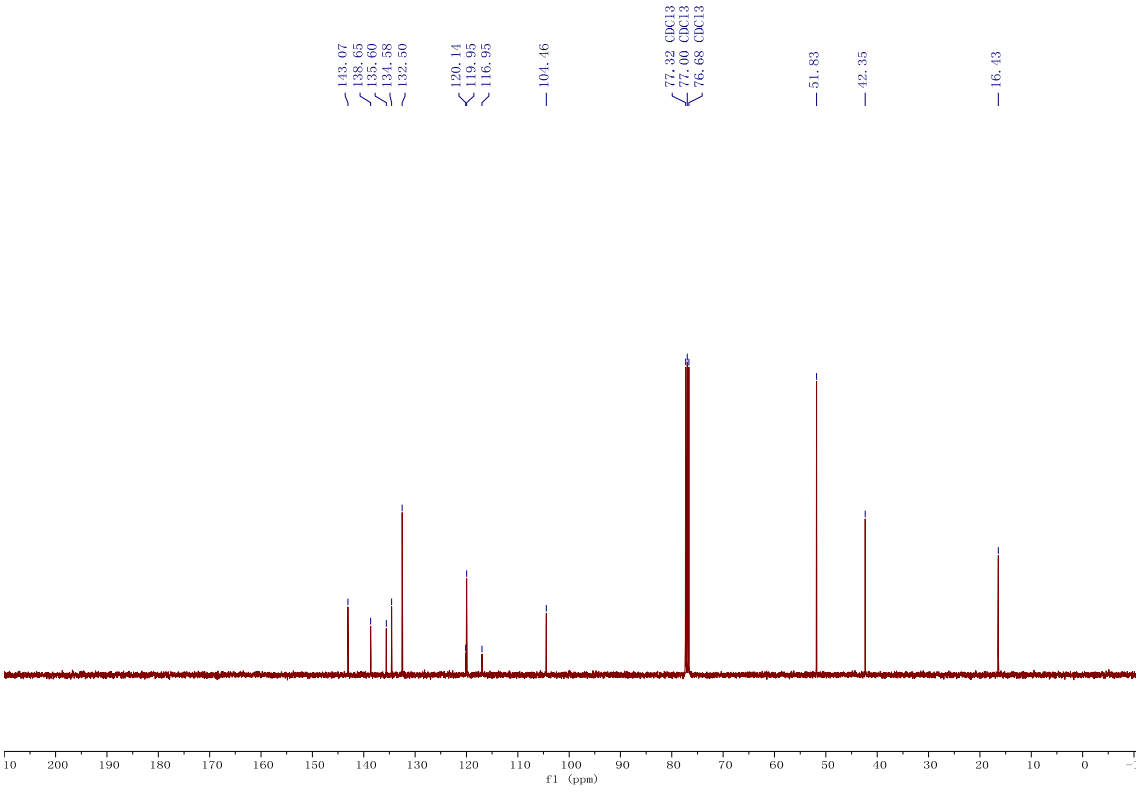
| **Table S1** Crystal data and structure refinement for **12** (racemic). | |
|---|---|
| Empirical formula | $C_{20}H_{24}ClNO_3$ |
| Formula weight | 361.85 |
| Temperature/K | 100(2) |
| Crystal system | orthorhombic |
| Space group | $P2_12_12_1$ |
| a/Å | 9.2522(8) |
| b/Å | 10.3247(9) |
| c/Å | 19.5321(16) |
| α/° | 90 |
| β/° | 90 |
| γ/° | 90 |
| Volume/Å$^3$ | 1865.8(3) |
| Z | 4 |
| $\rho_{calc}$g/cm$^3$ | 1.288 |
| μ/mm$^{-1}$ | 0.223 |
| F(000) | 768.0 |
| Crystal size/mm$^3$ | 0.04 × 0.03 × 0.03 |
| Radiation | MoKα (λ = 0.71073) |
| 2Θ range for data collection/° | 4.17 to 56.626 |
| Index ranges | $-12 \le h \le 8$, $-13 \le k \le 10$, $-26 \le l \le 26$ |
| Reflections collected | 13956 |
| Independent reflections | 4589 [$R_{int}$ = 0.0471, $R_{sigma}$ = 0.0647] |
| Data/restraints/parameters | 4589/0/230 |
| Goodness-of-fit on $F^2$ | 1.041 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0485, $wR_2$ = 0.1097 |
| Final R indexes [all data] | $R_1$ = 0.0689, $wR_2$ = 0.1175 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.36/-0.36 |
| Flack parameter | -0.09(5) |
| | |
| | |

## 5. Spectra

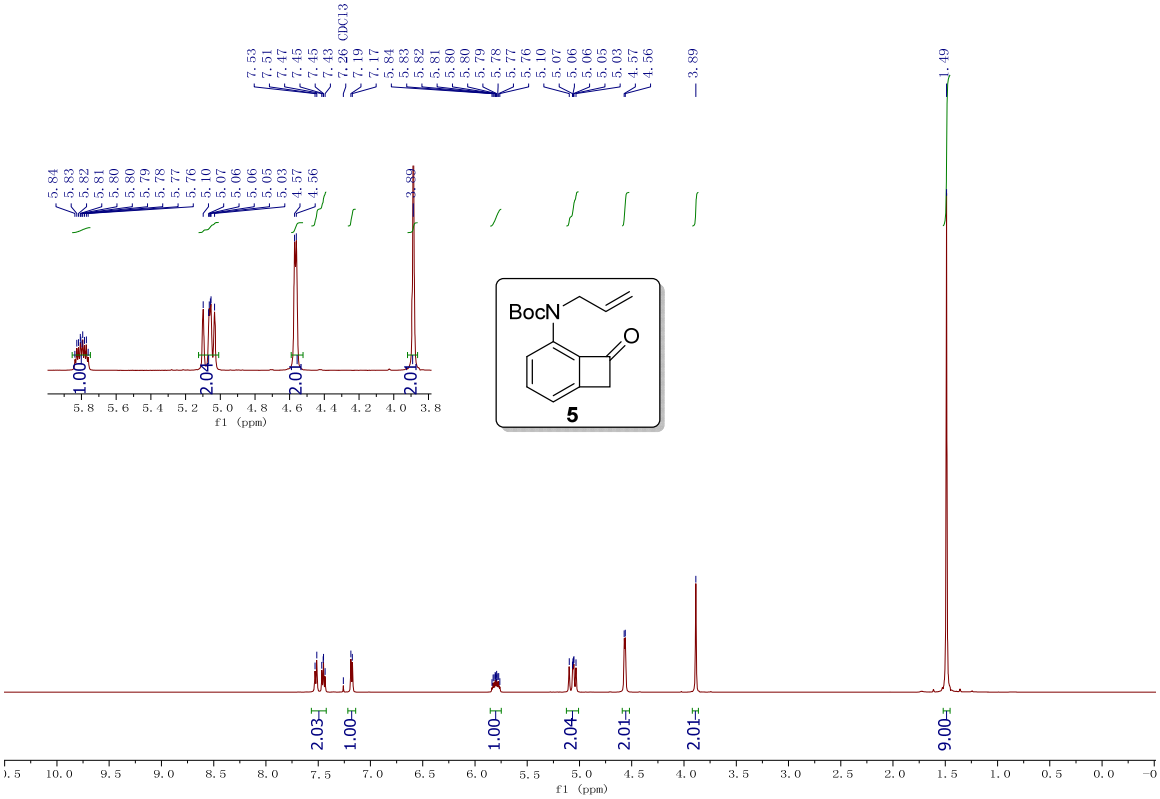
$^{1}$H-NMR for **6h** in $CDCl_3$, 400 MHz



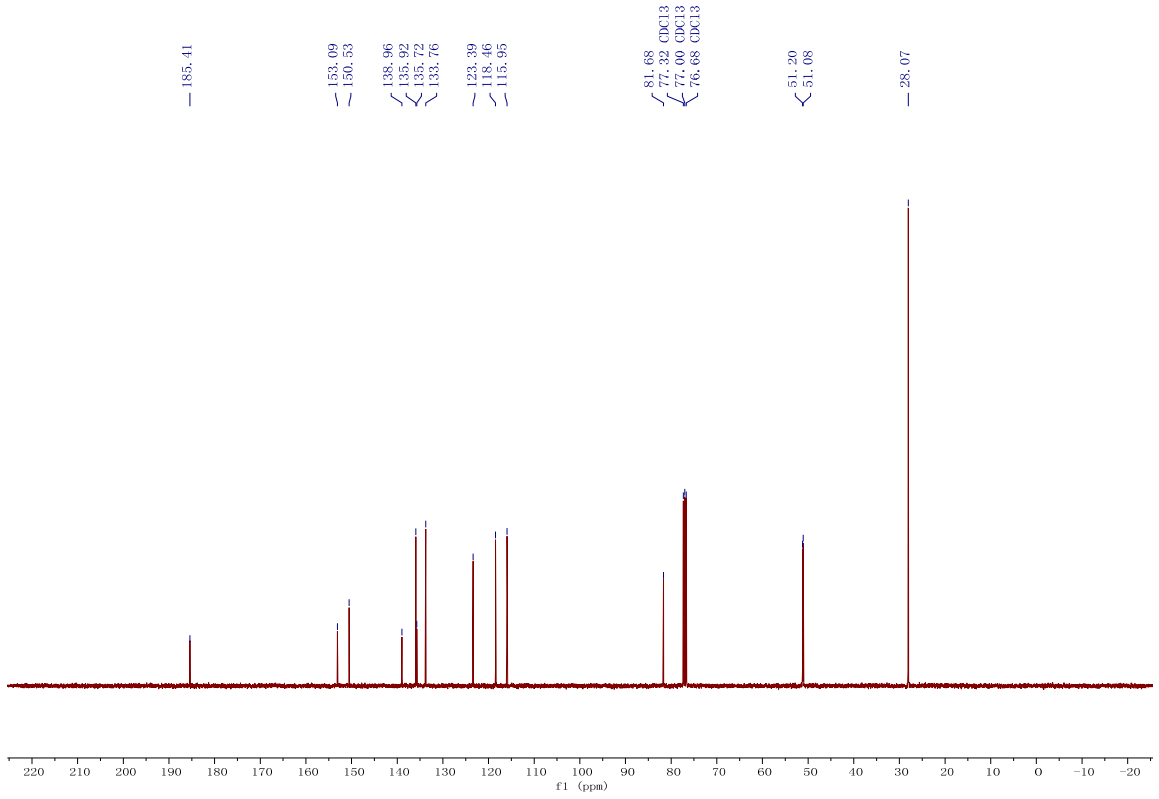

$^{13}$C-NMR for **6h** in $CDCl_3$, 101 MHz



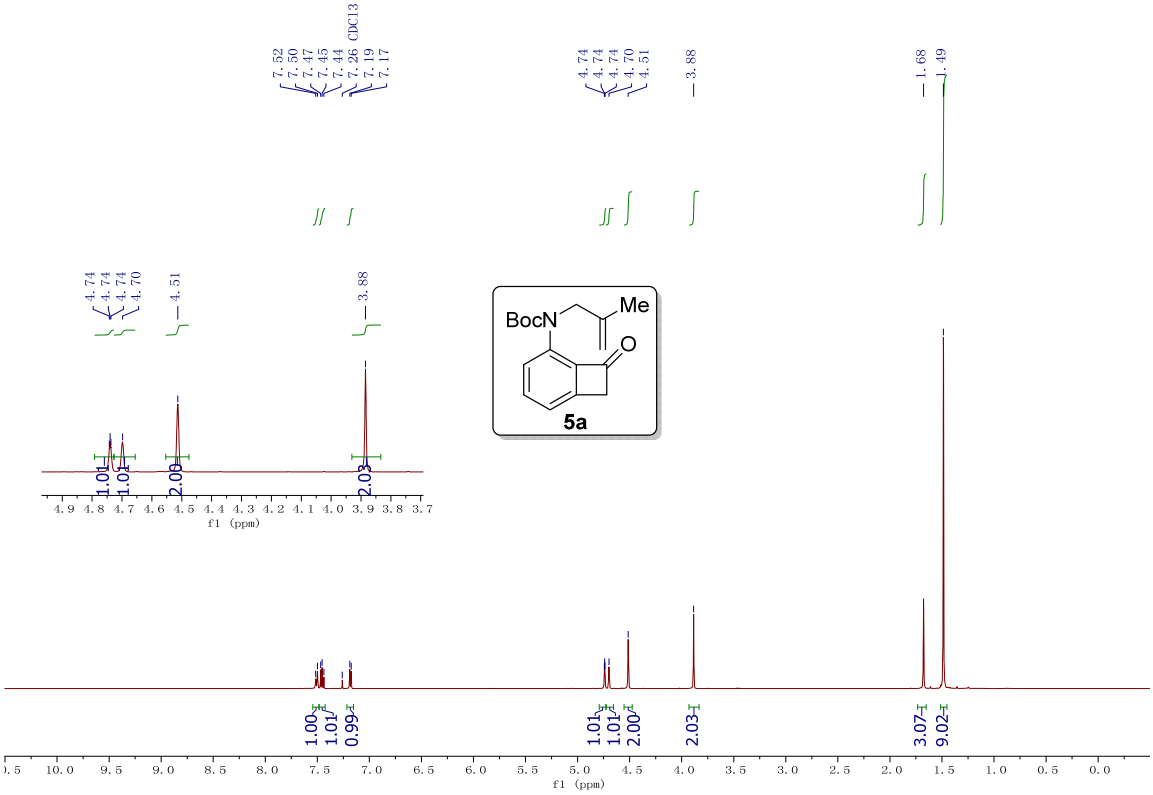
$^{1}$H-NMR for **5** in $CDCl_3$, 500 MHz



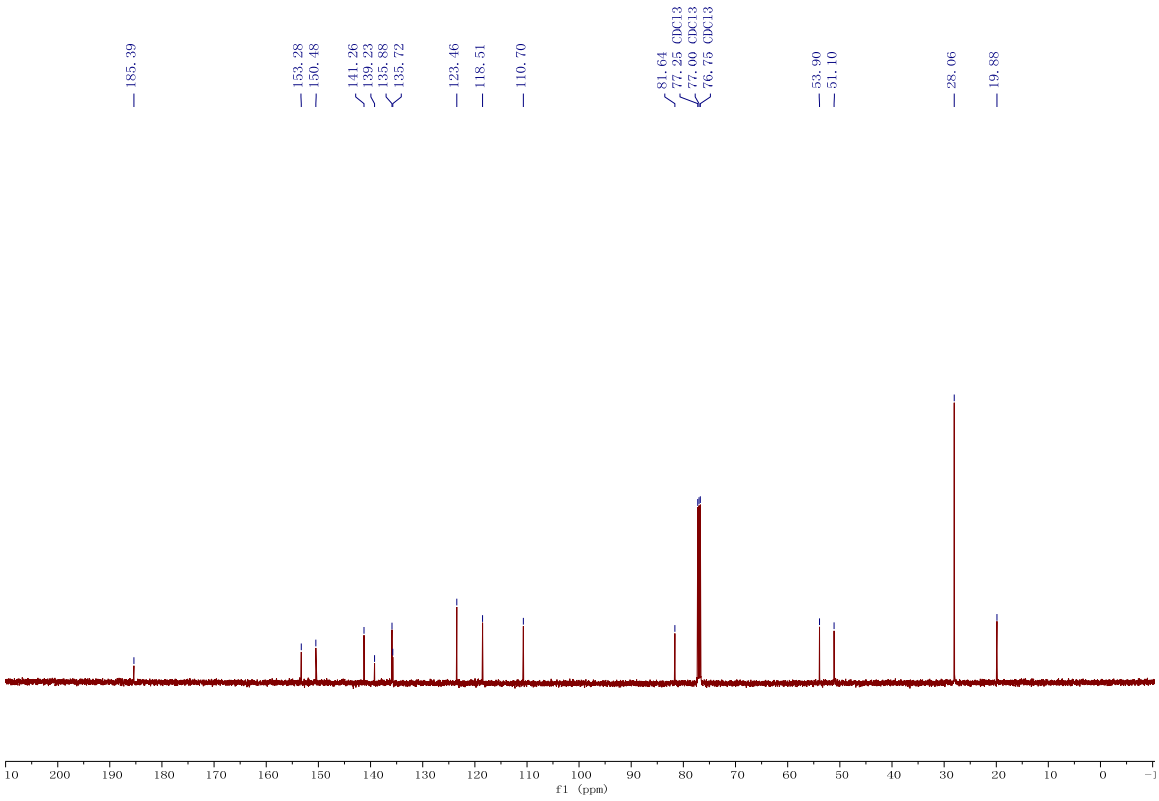

$^{13}$C-NMR for **5** in $CDCl_3$, 101 MHz



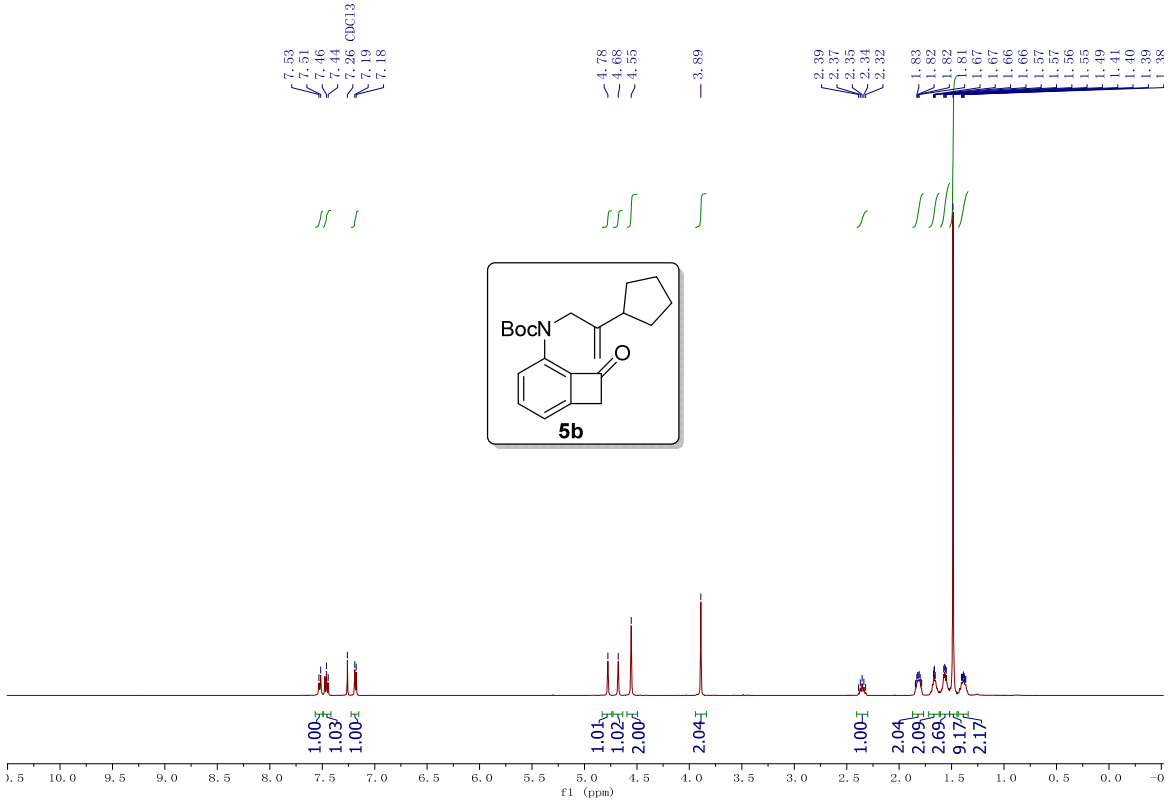
$^{1}$H-NMR for **5a** in $CDCl_3$, 500 MHz



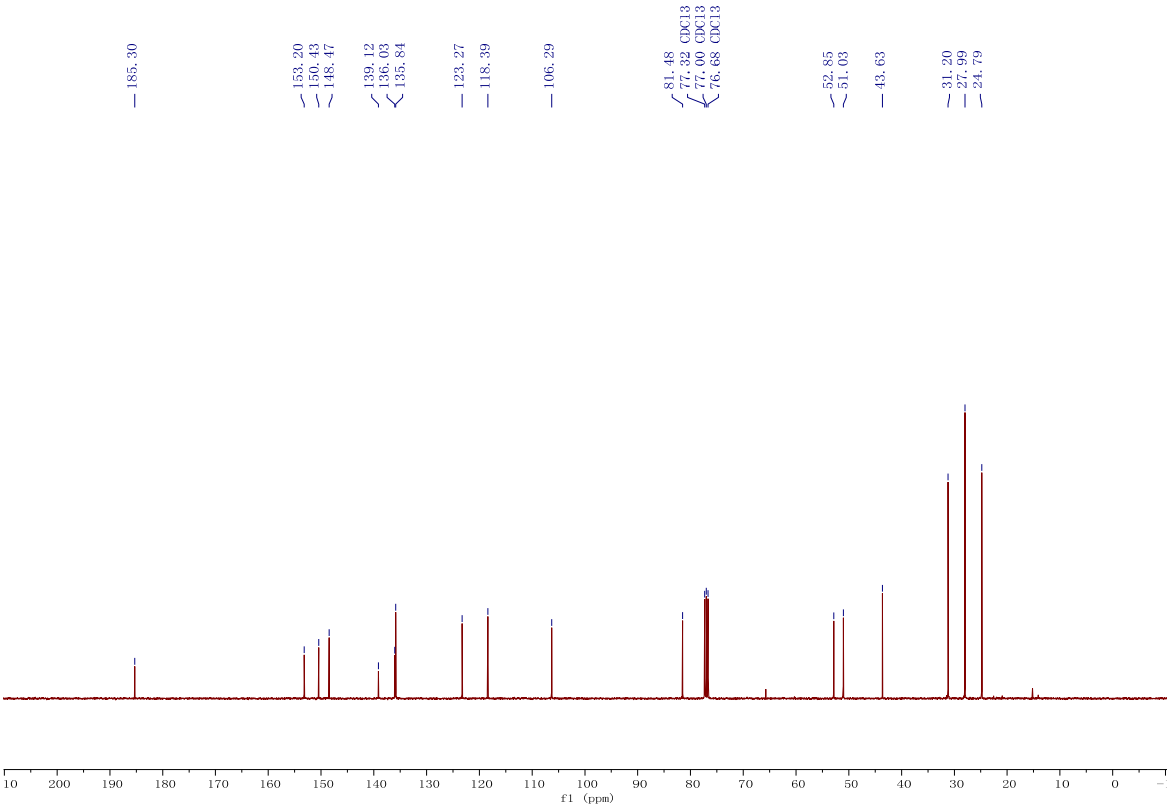

$^{13}$C-NMR for **5a** in $CDCl_3$, 101 MHz



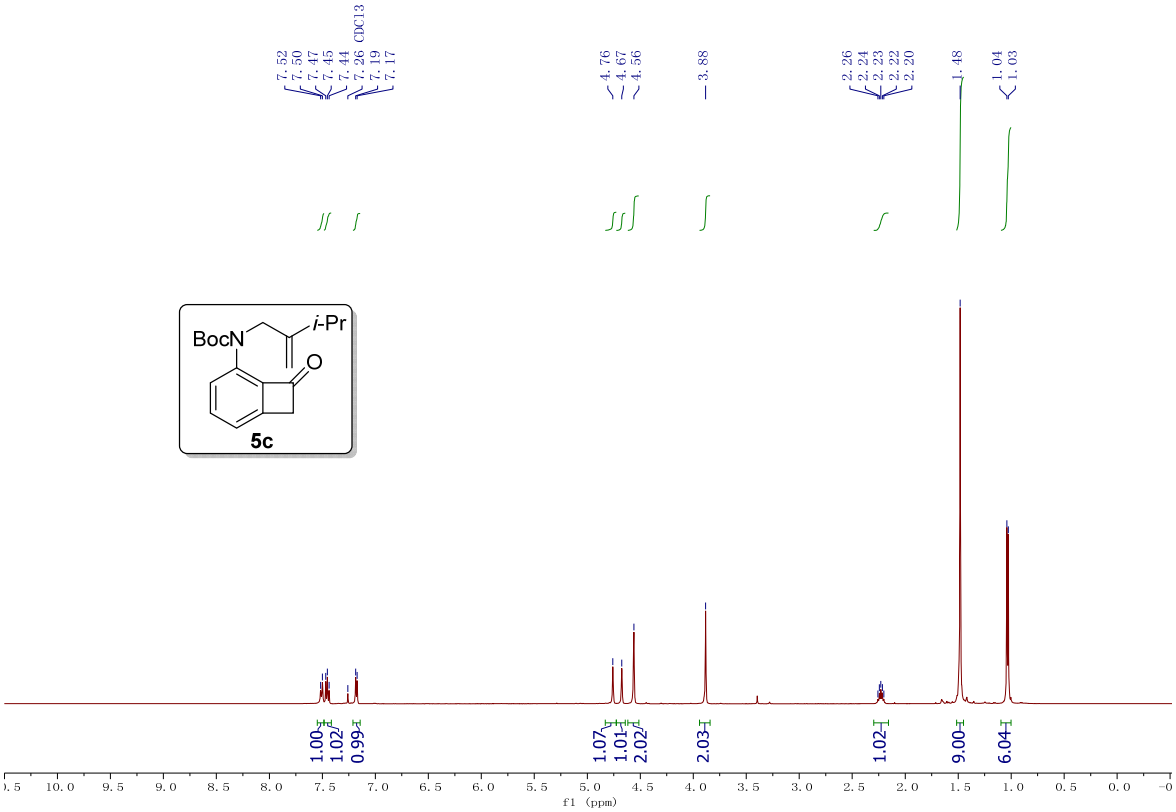
$^{1}$H-NMR for **5b** in $CDCl_3$, 500 MHz



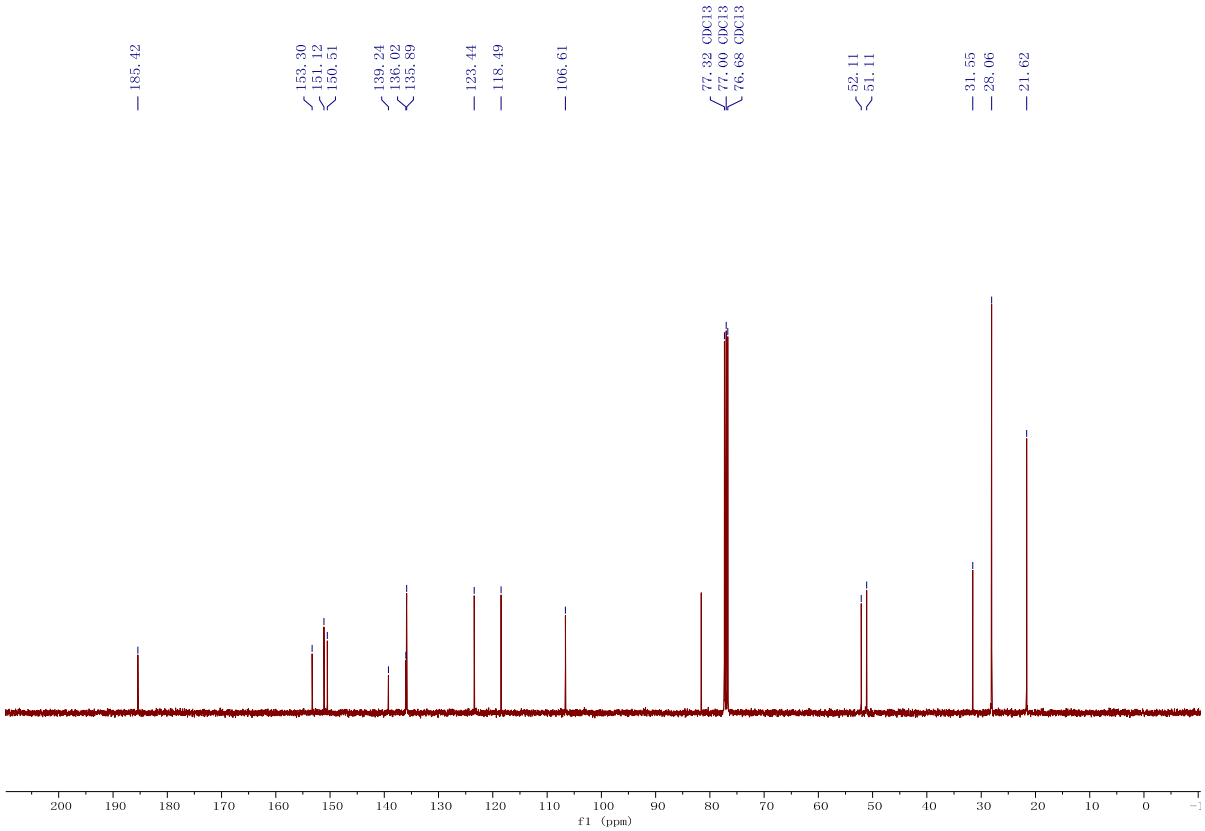

$^{13}$C-NMR for **5b** in $CDCl_3$, 101 MHz



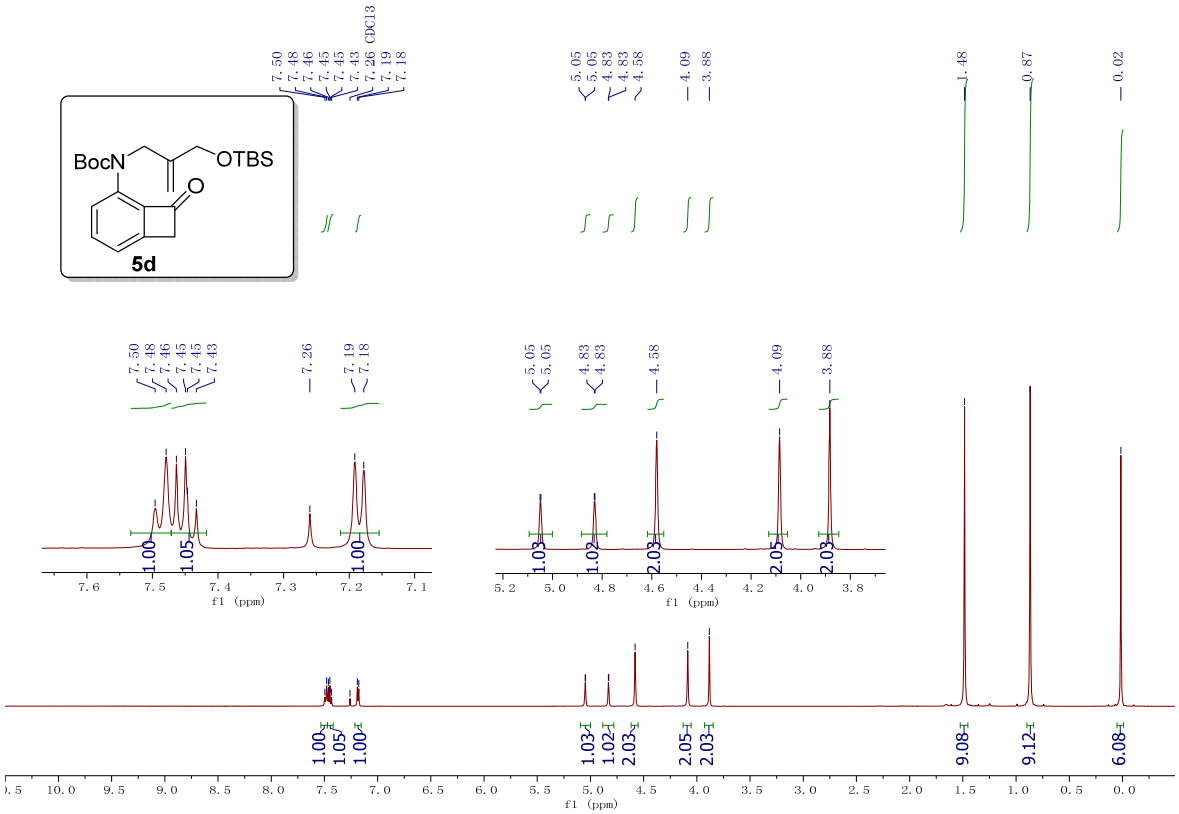
$^{1}$H-NMR for **5c** in $CDCl_3$, 500 MHz



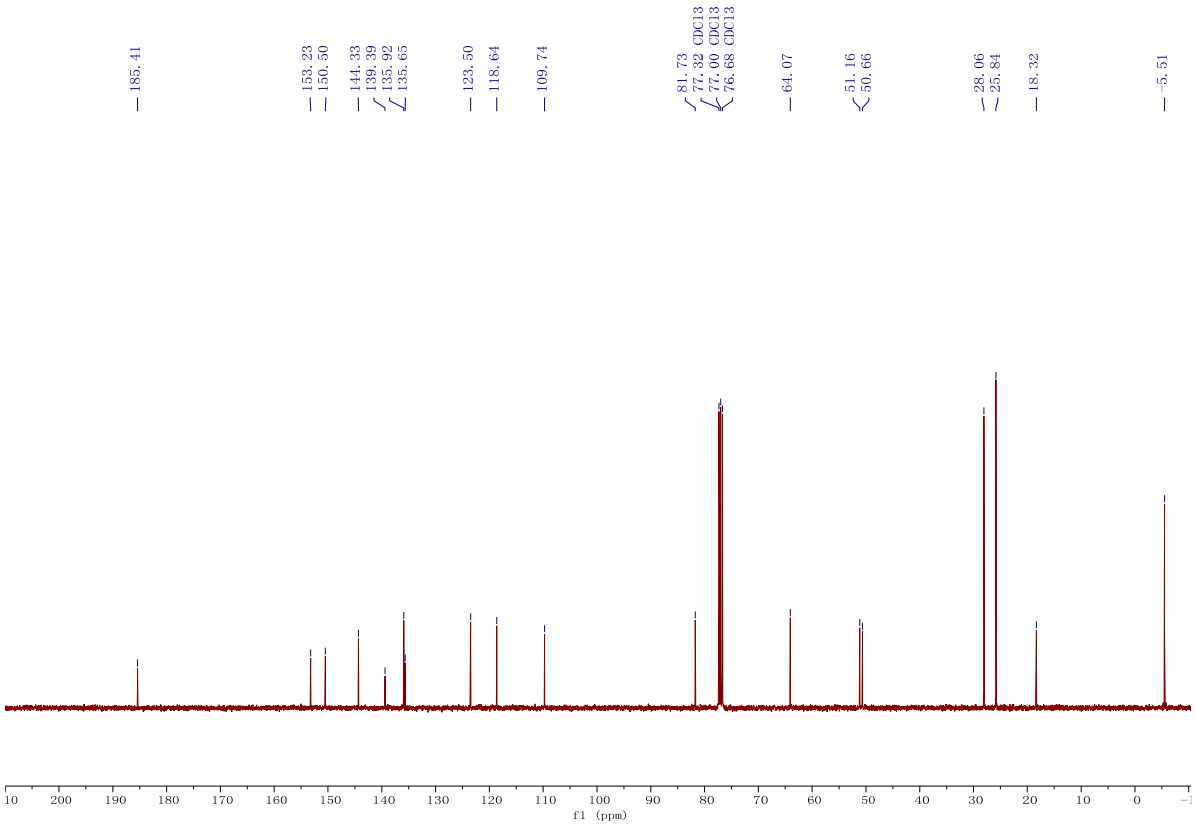

$^{13}$C-NMR for **5c** in $CDCl_3$, 101 MHz



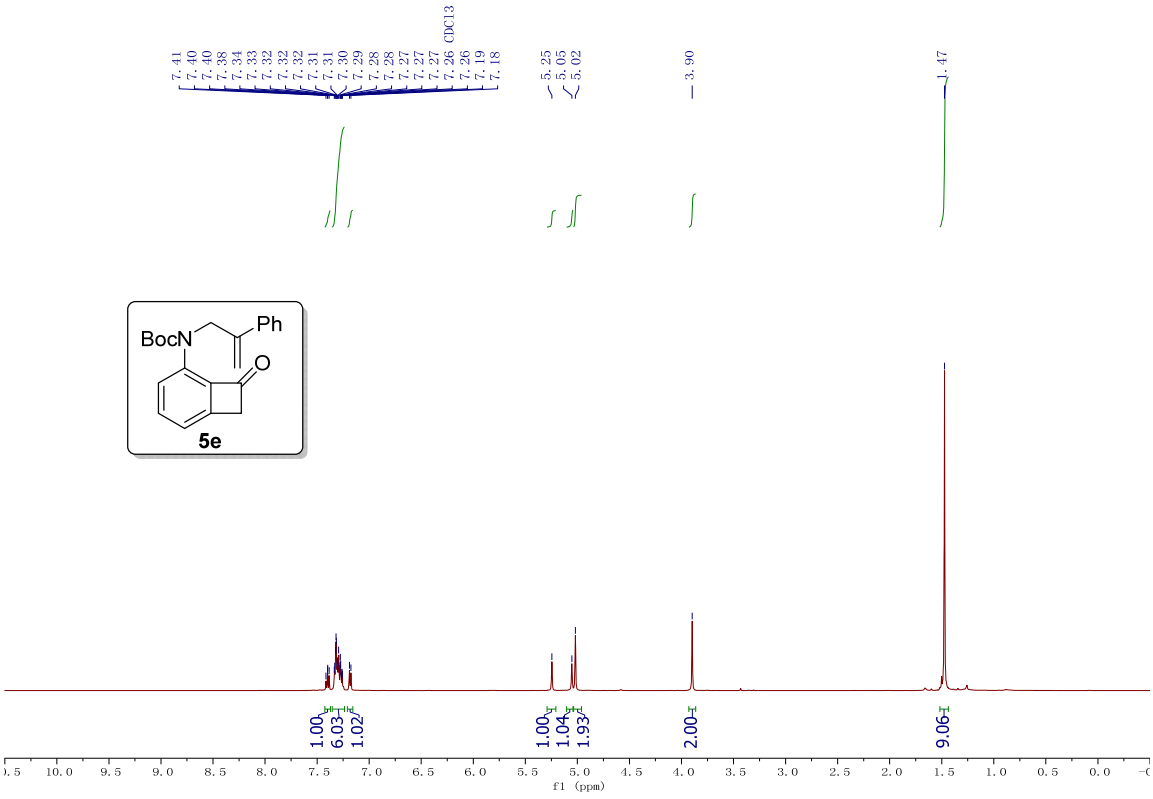
$^{1}$H-NMR for **5d** in $CDCl_3$, 500 MHz



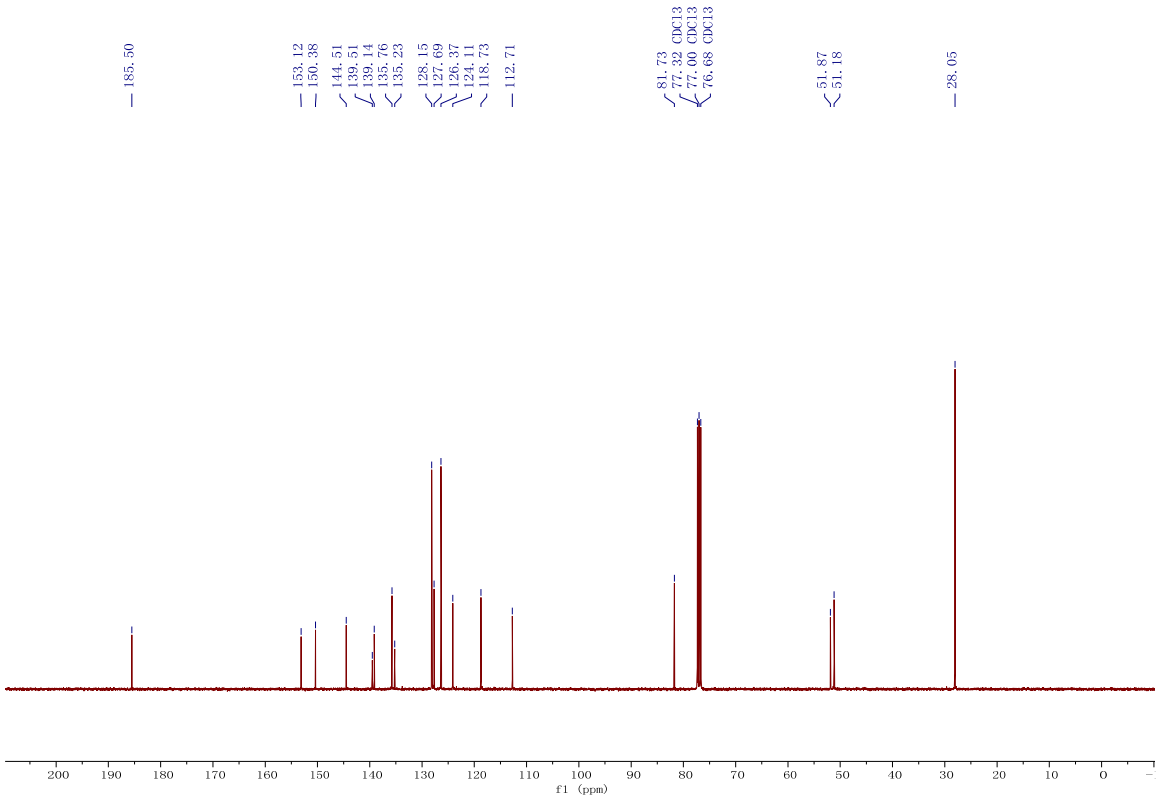

$^{13}$C-NMR for **5d** in $CDCl_3$, 101 MHz



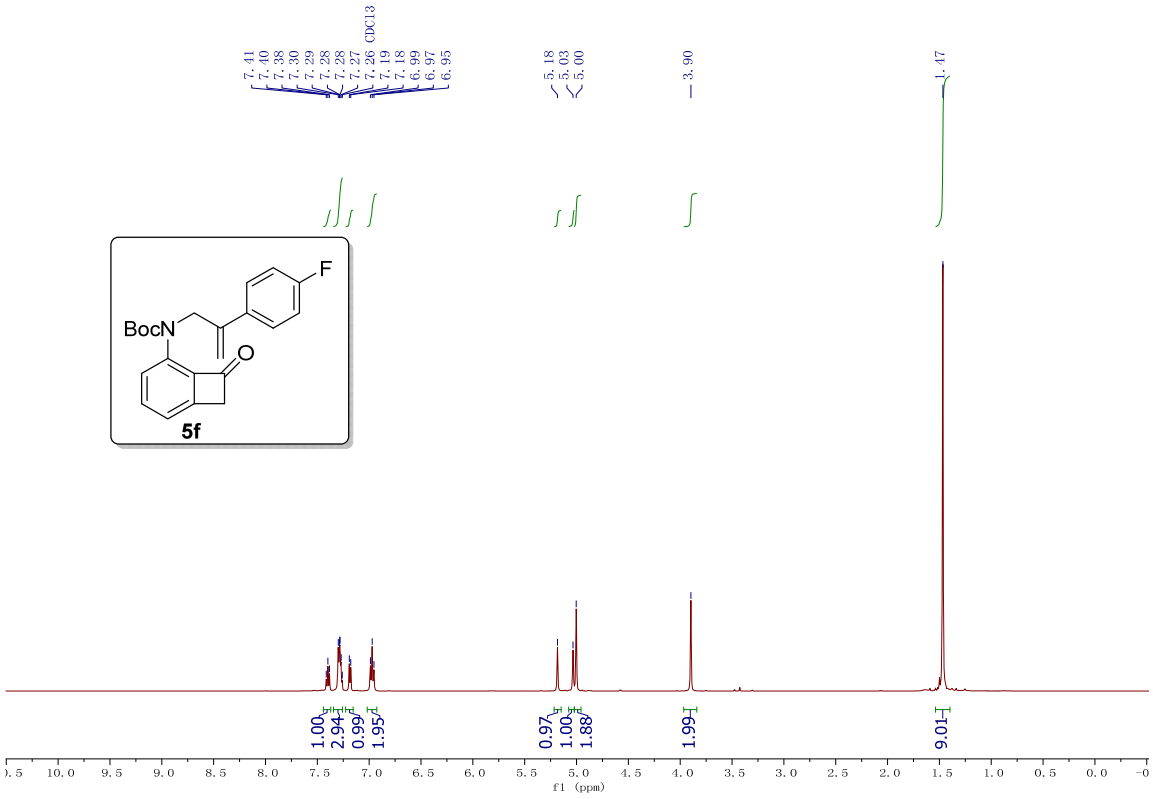
$^{1}$H-NMR for **5e** in $CDCl_3$, 500 MHz



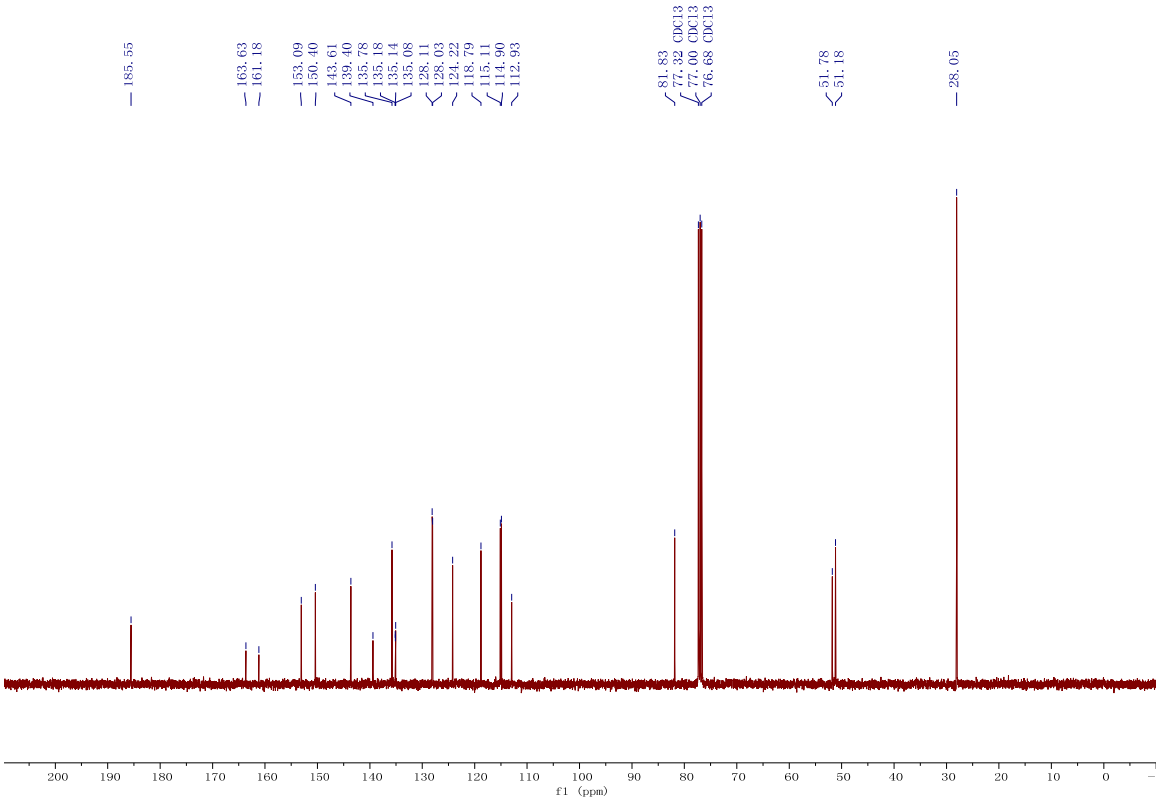

$^{13}$C-NMR for **5e** in $CDCl_3$, 101 MHz



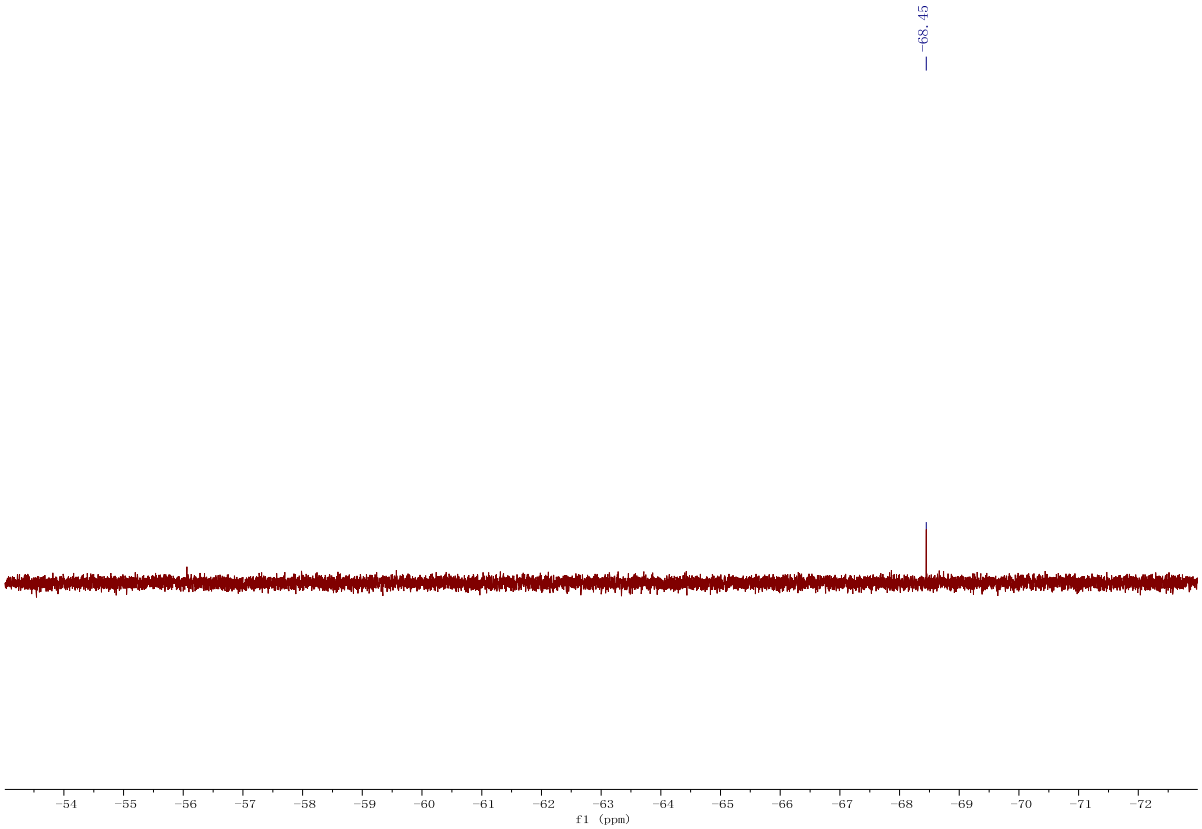
$^{1}$H-NMR for **5f** in $CDCl_3$, 500 MHz



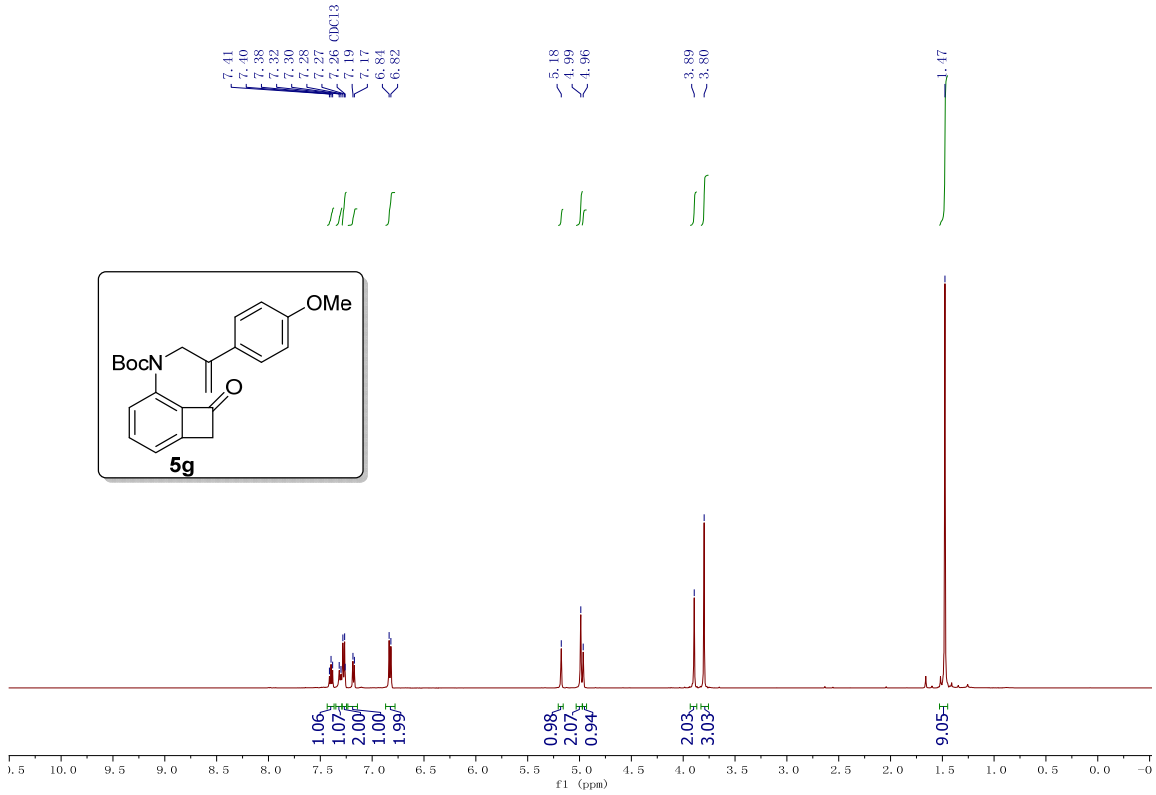

$^{13}$C-NMR for **5f** in $CDCl_3$, 101 MHz



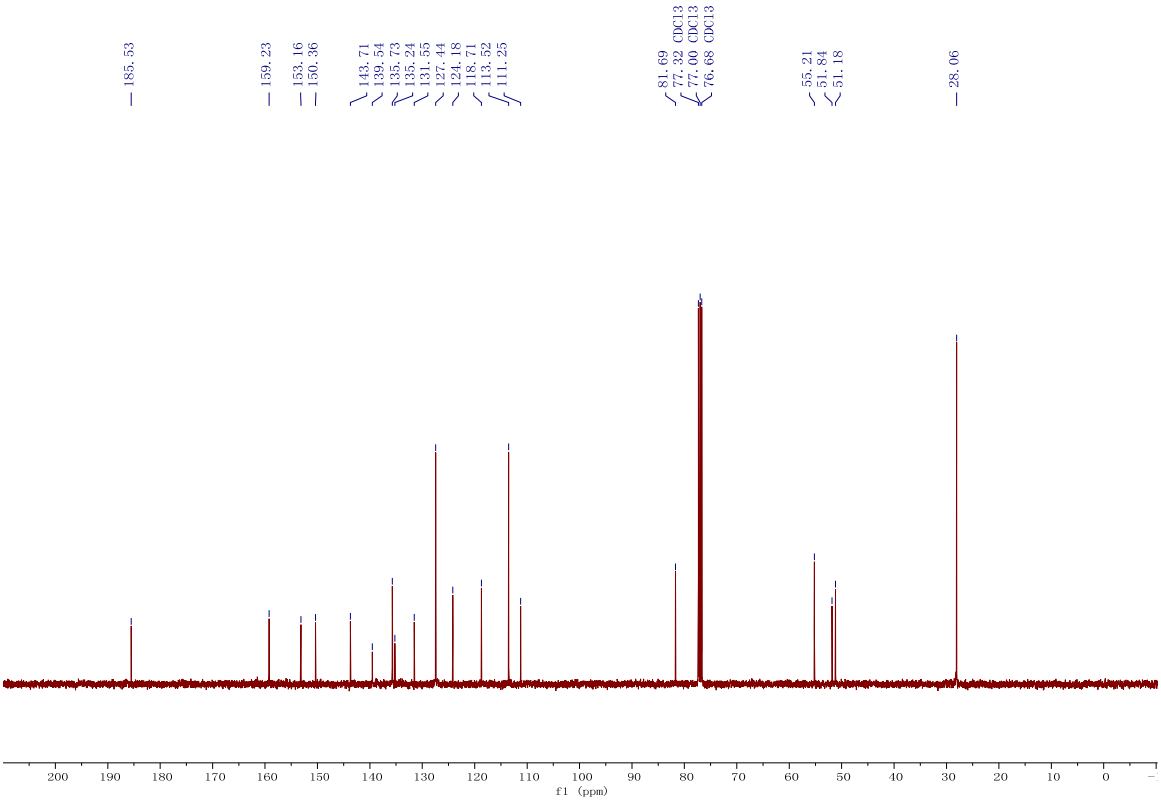
$^{19}$F-NMR for **5f** in $CDCl_3$, 470 MHz



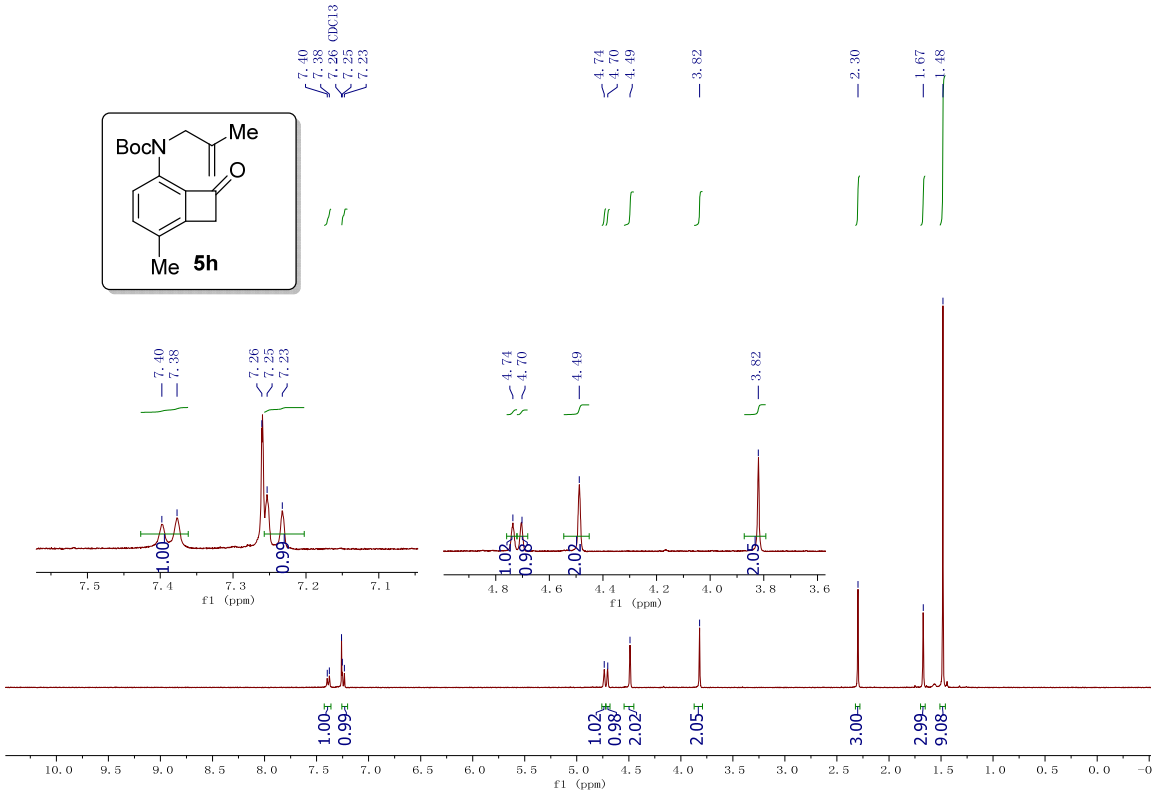
$^{1}$H-NMR for **5g** in $CDCl_3$, 500 MHz



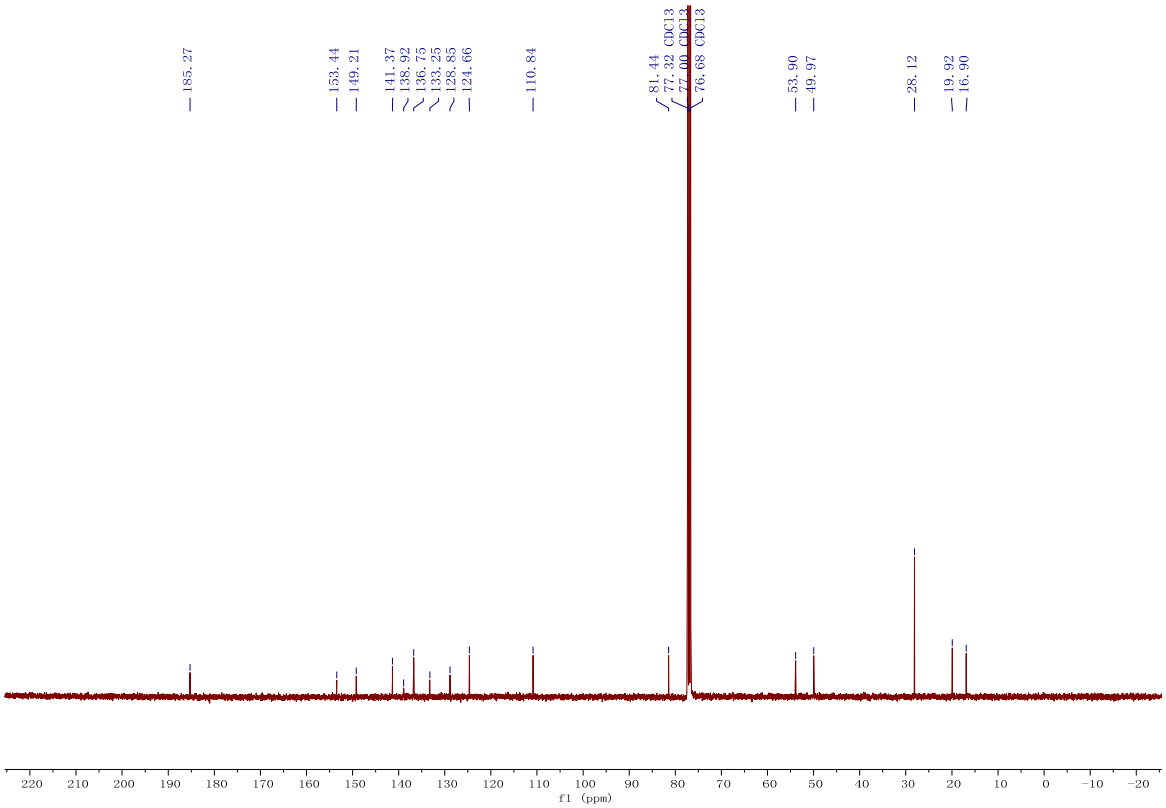

$^{13}$C-NMR for **5g** in $CDCl_3$, 101 MHz



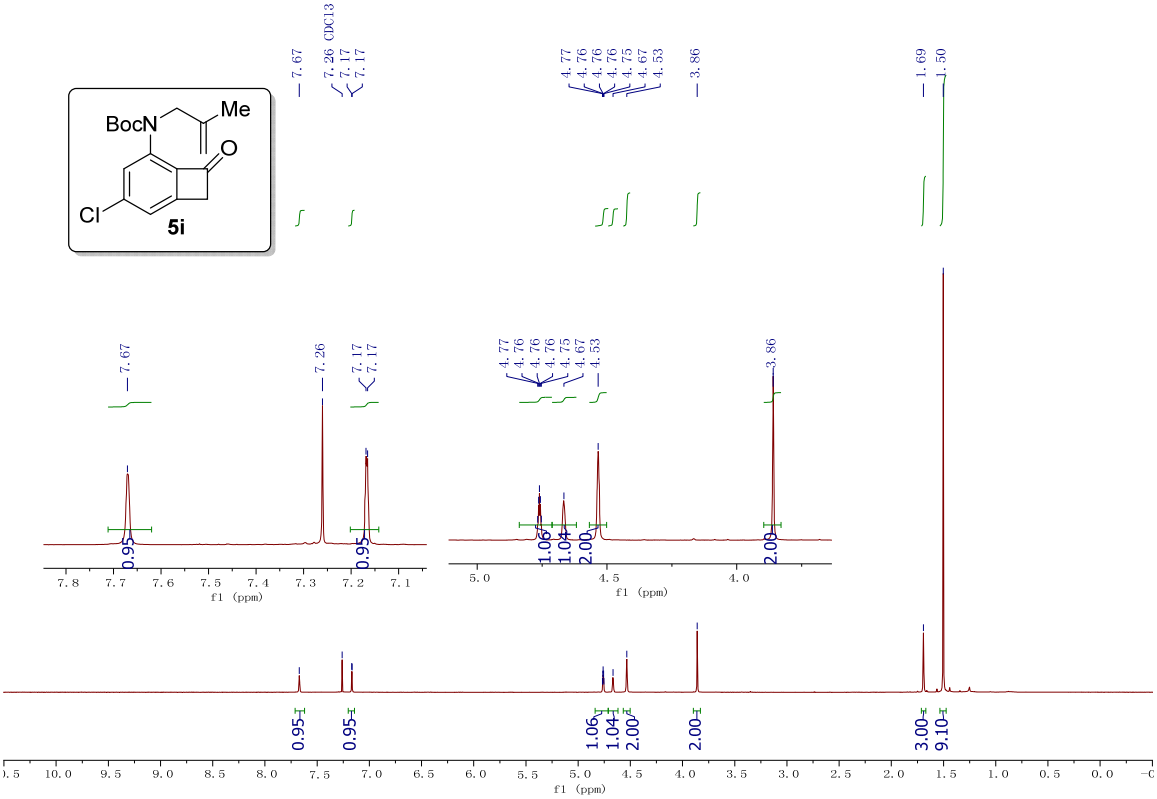
$^{1}$H-NMR for **5h** in $CDCl_3$, 500 MHz



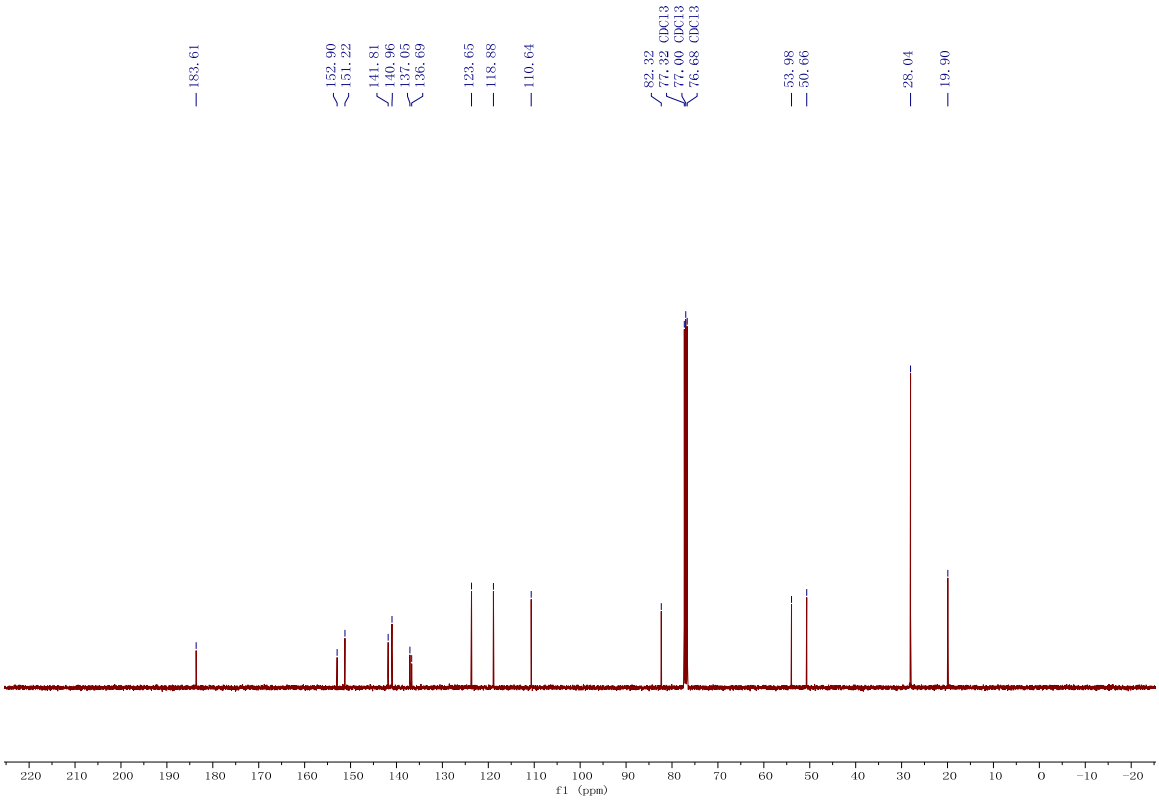

$^{13}$C-NMR for **5h** in $CDCl_3$, 101 MHz



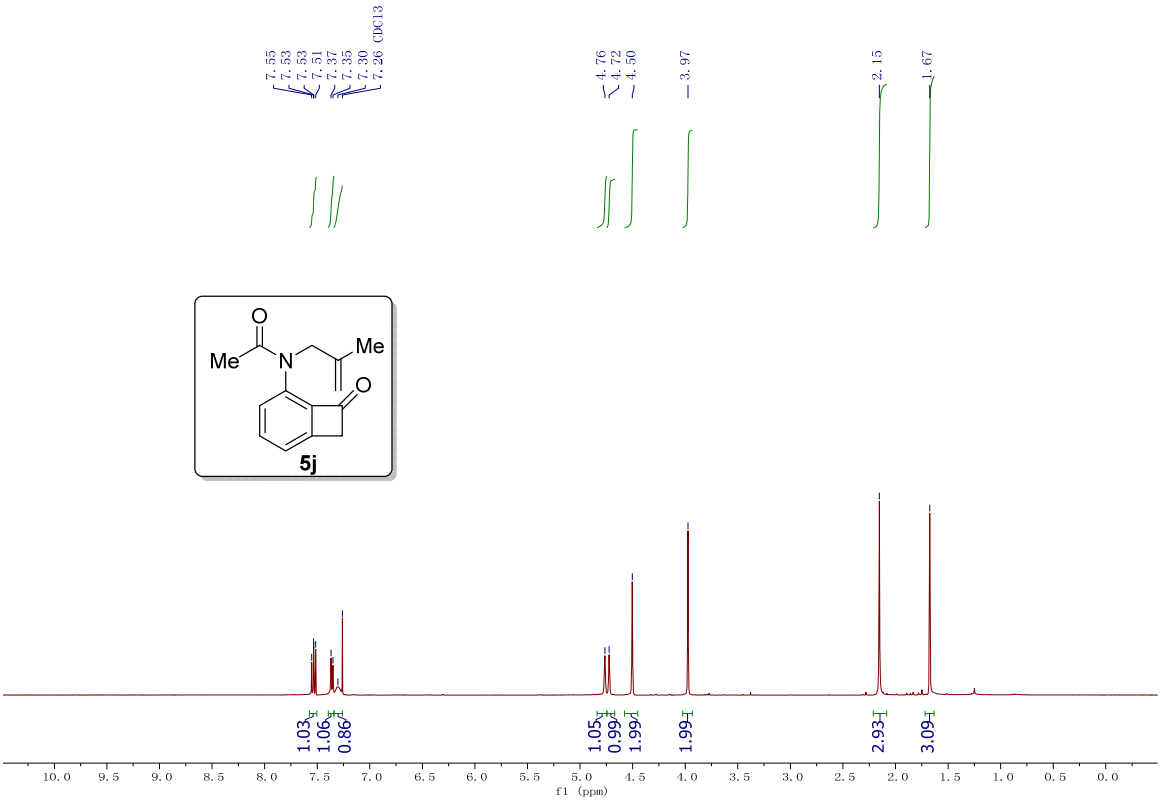
$^{1}$H-NMR for **5i** in $CDCl_3$, 500 MHz



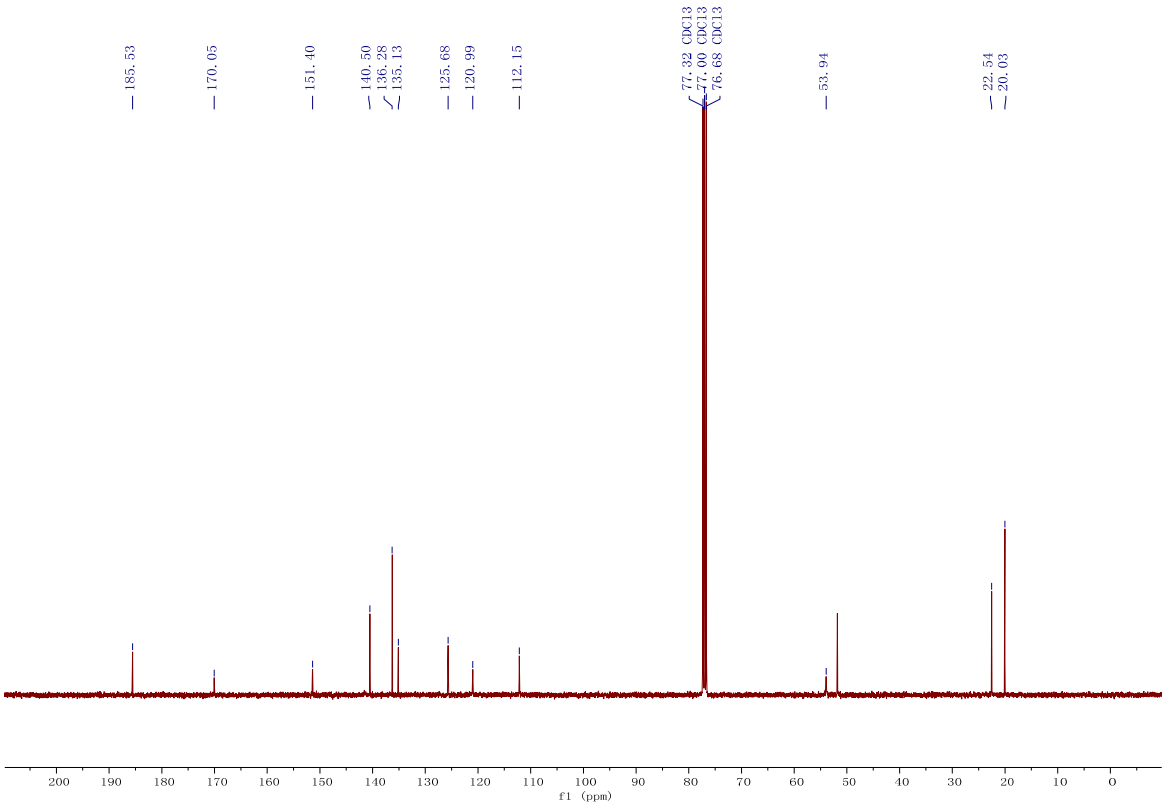

$^{13}$C-NMR for **5i** in $CDCl_3$, 101 MHz



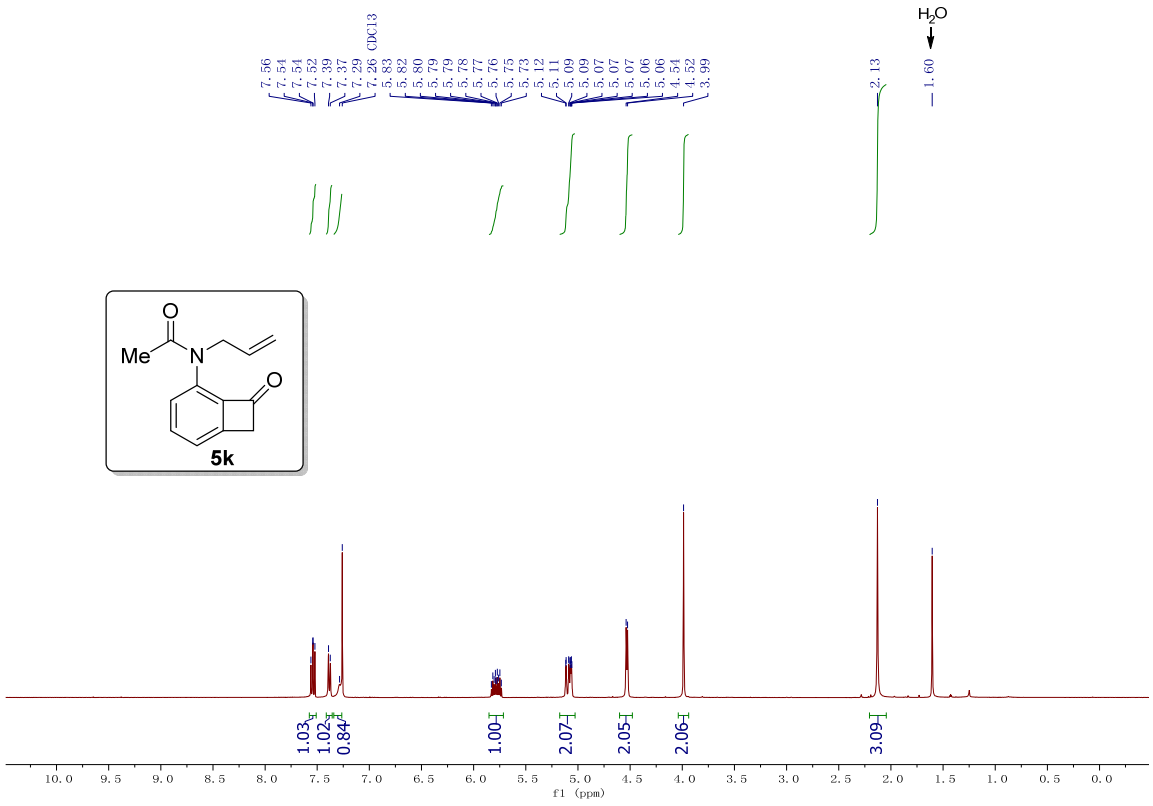
$^{1}$H-NMR for **5j** in $CDCl_3$, 500 MHz



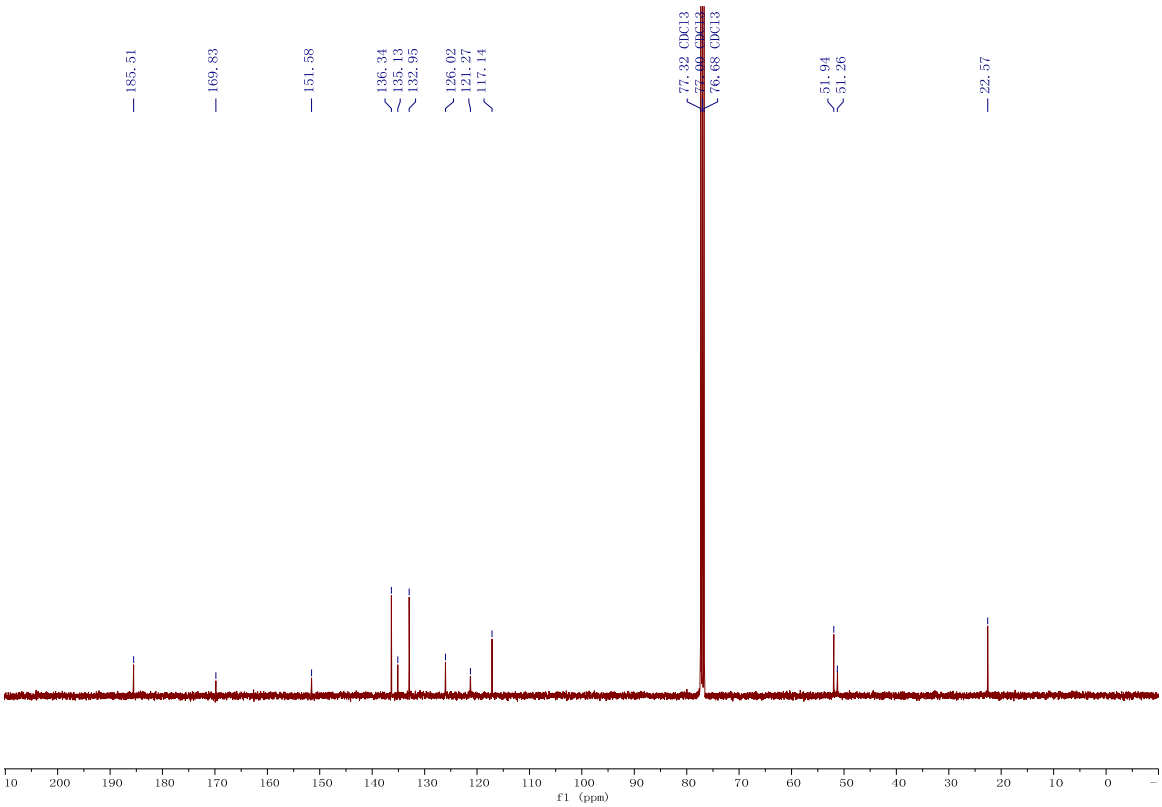

$^{13}$C-NMR for **5j** in $CDCl_3$, 101 MHz



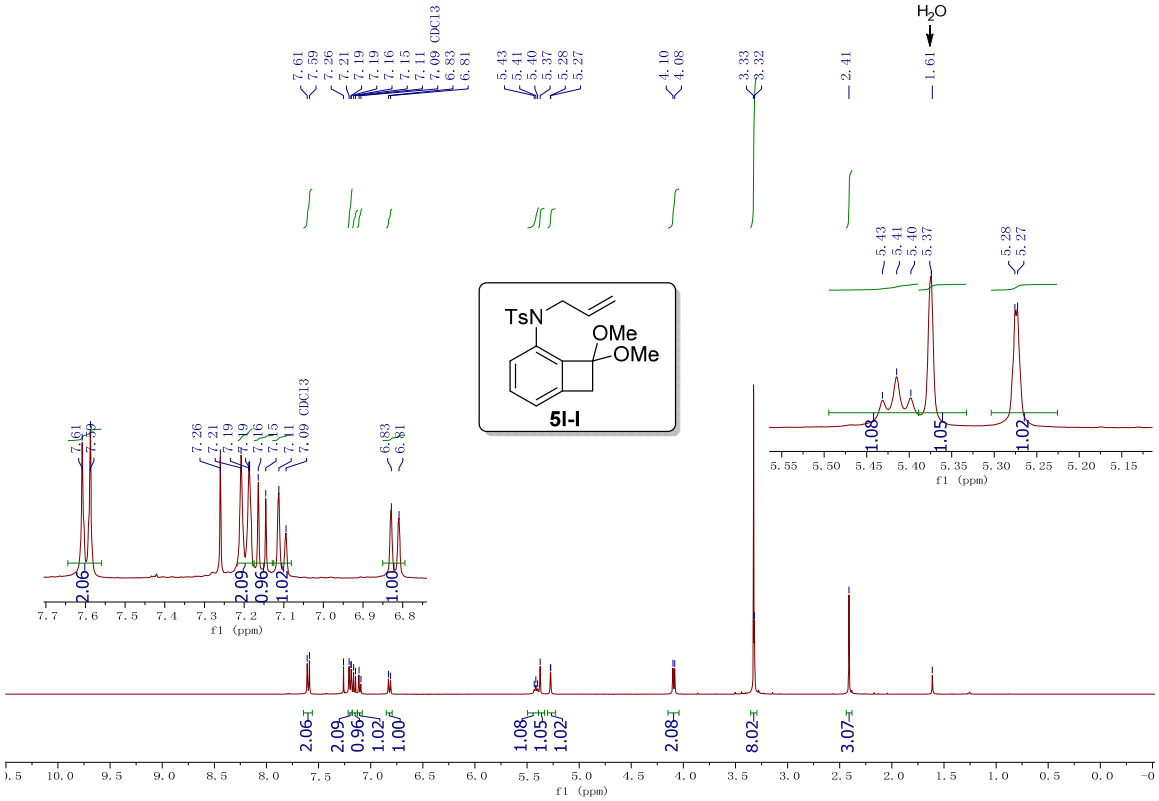
$^{1}$H-NMR for **5k** in $CDCl_3$, 500 MHz



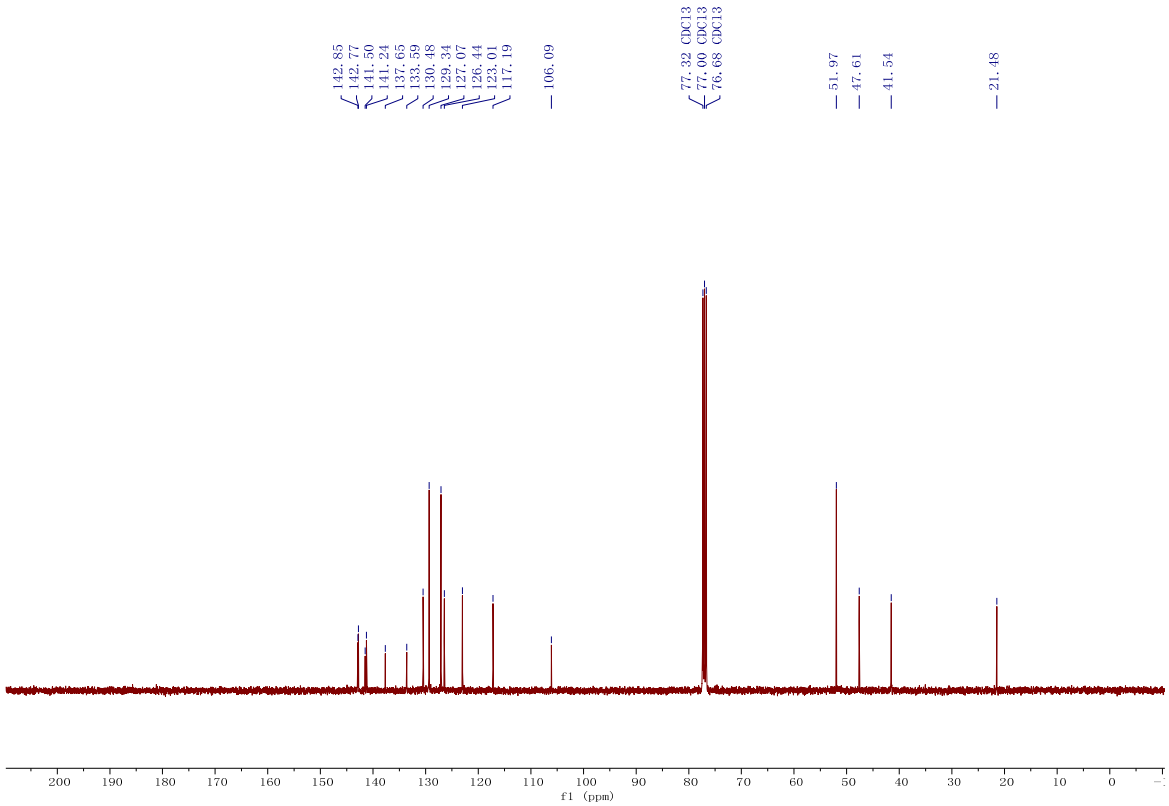

$^{13}$C-NMR for **5k** in $CDCl_3$, 101 MHz



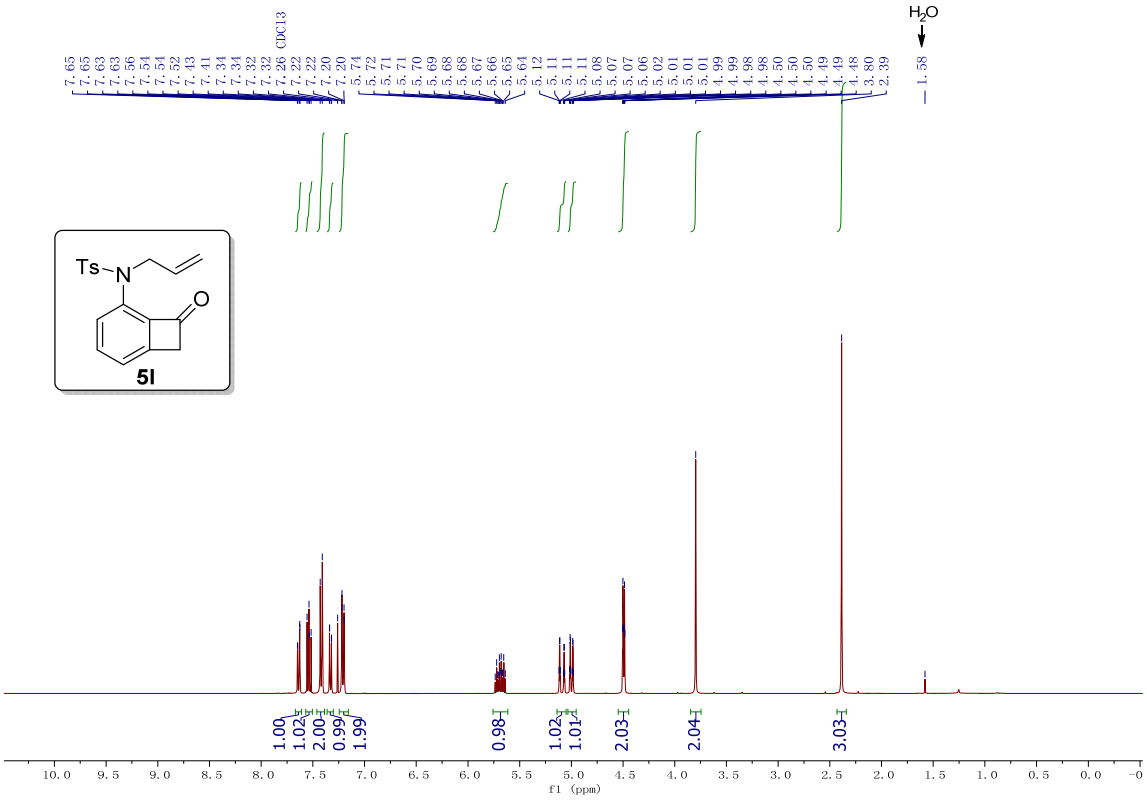
$^{1}$H-NMR for **5l-I** in $CDCl_3$, 400 MHz



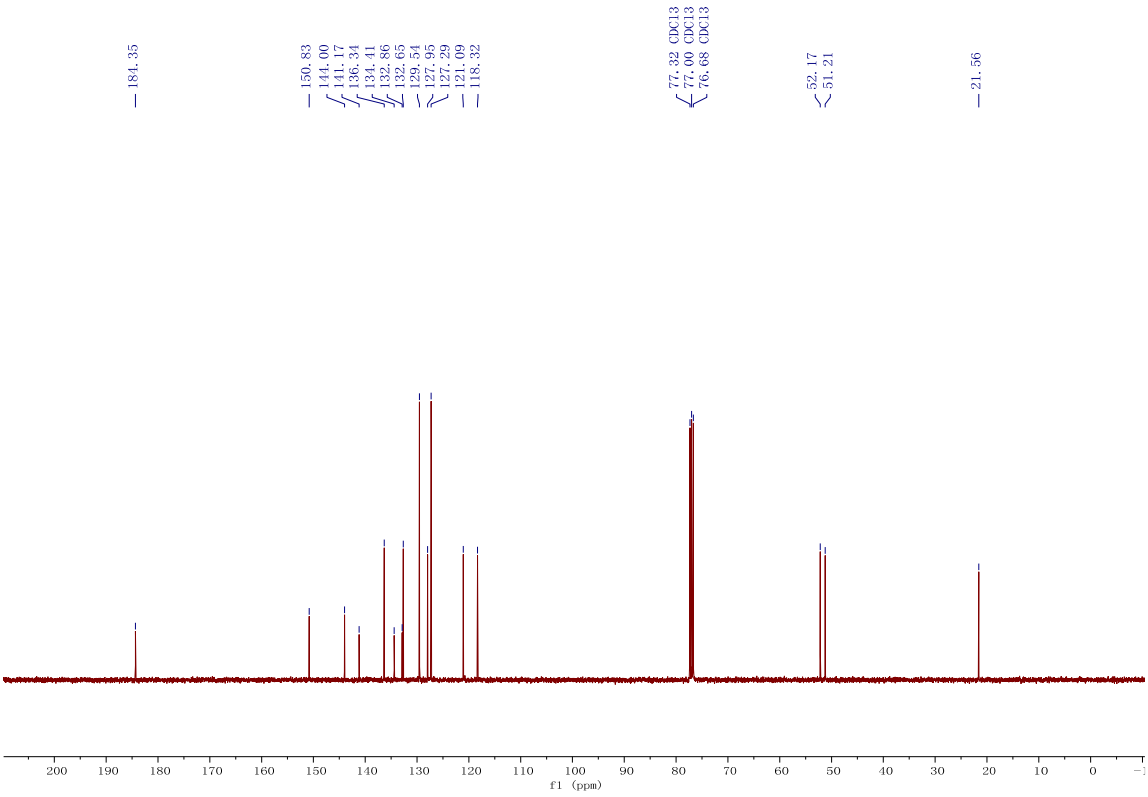

$^{13}$C-NMR for **5l-I** in $CDCl_3$, 101 MHz



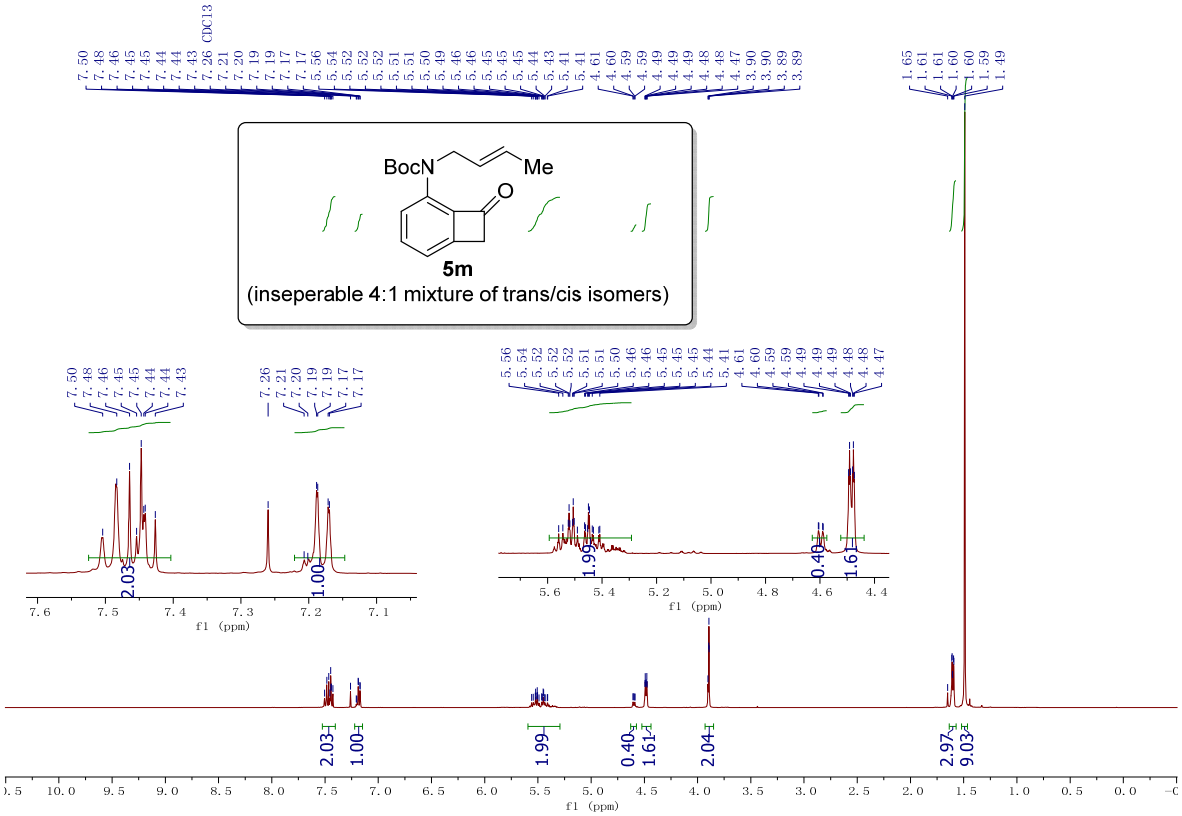
$^{1}$H-NMR for **5l** in $CDCl_3$, 400 MHz




$^{13}$C-NMR for **5l** in $CDCl_3$, 101 MHz

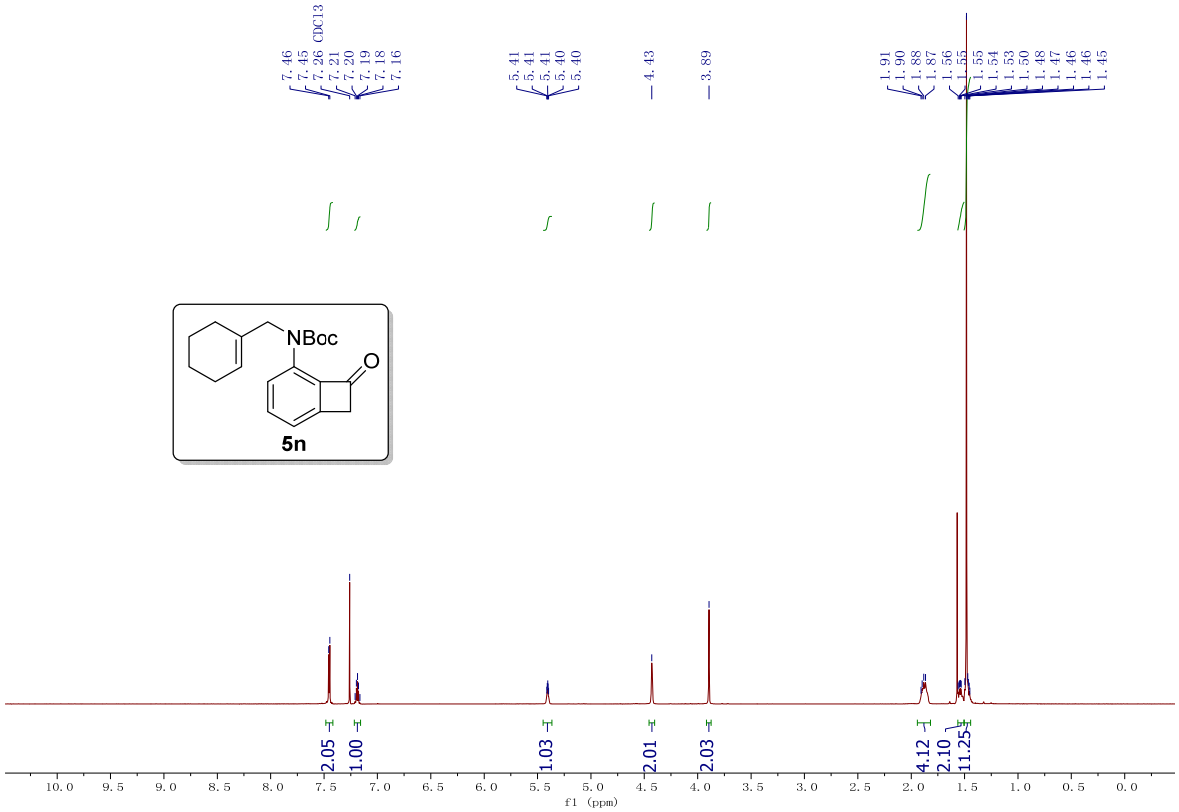


$^{1}$H-NMR for **5m** in $CDCl_3$, 400 MHz

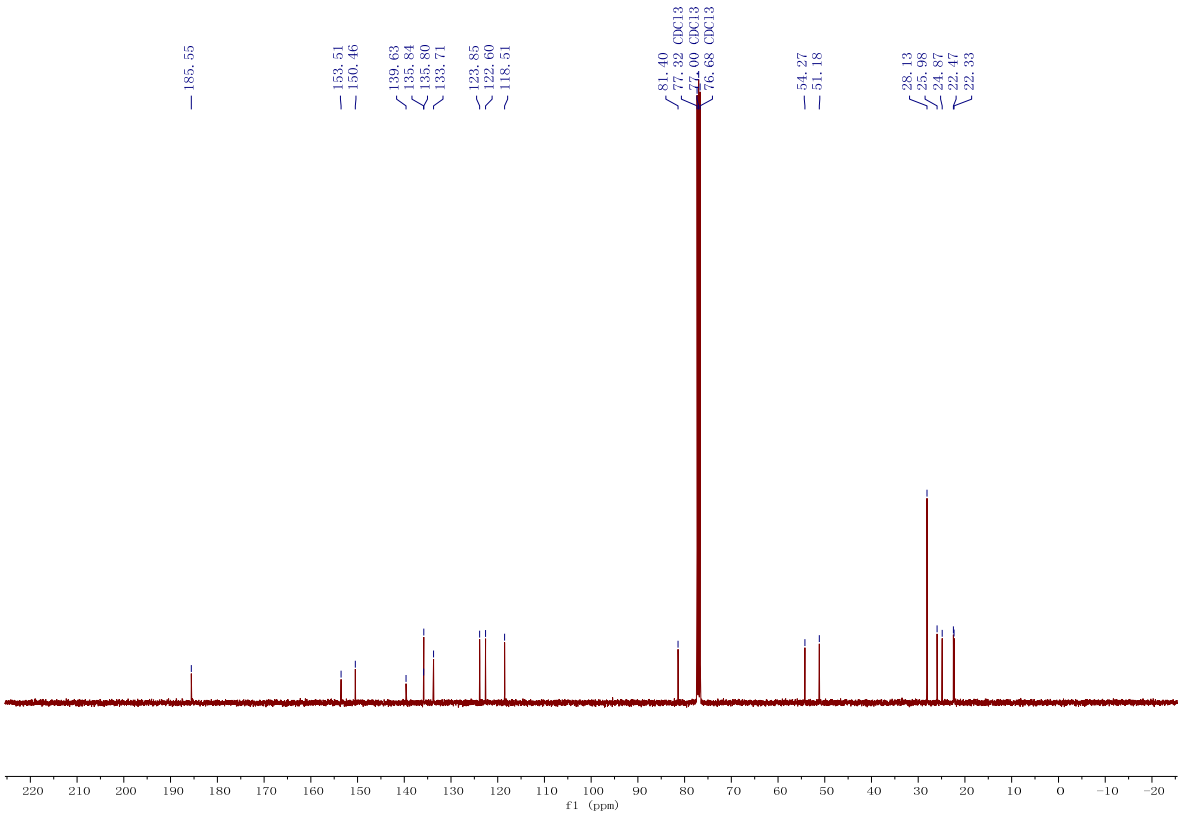



$^{13}$C-NMR for **5m** in $CDCl_3$, 101 MHz

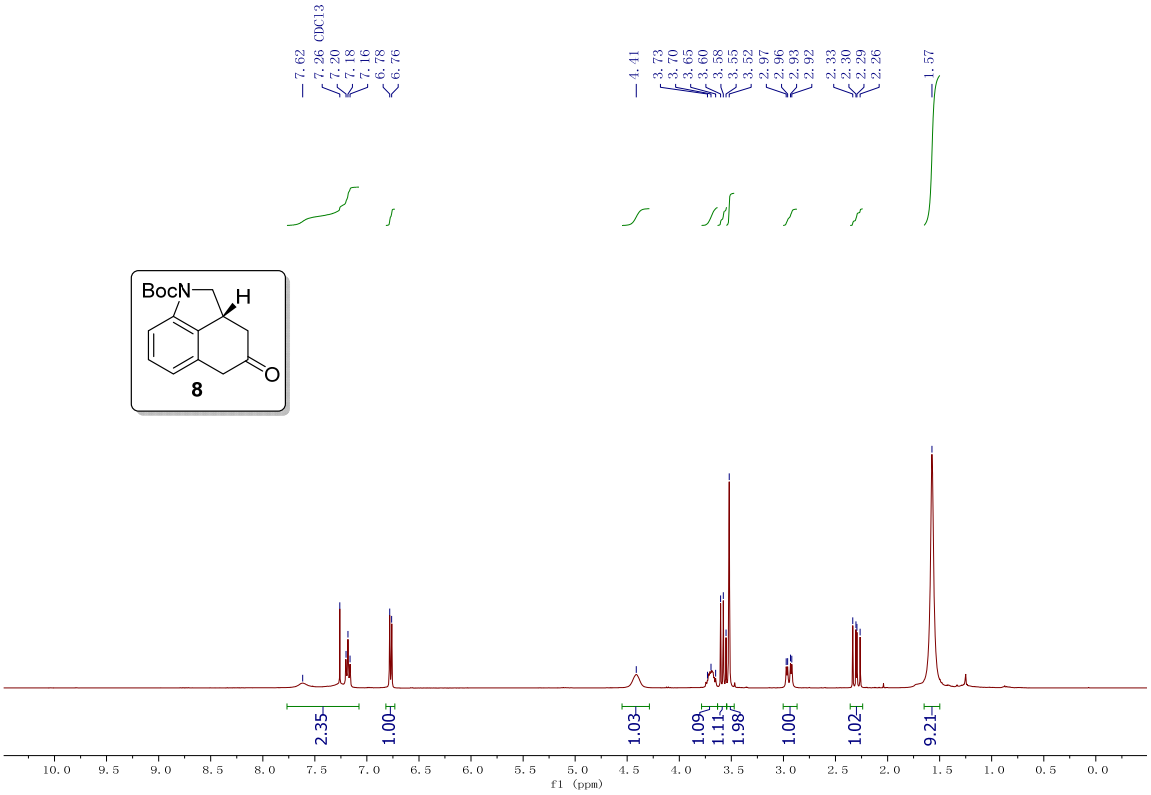
$^{1}$H-NMR for **5n** in $CDCl_3$, 400 MHz



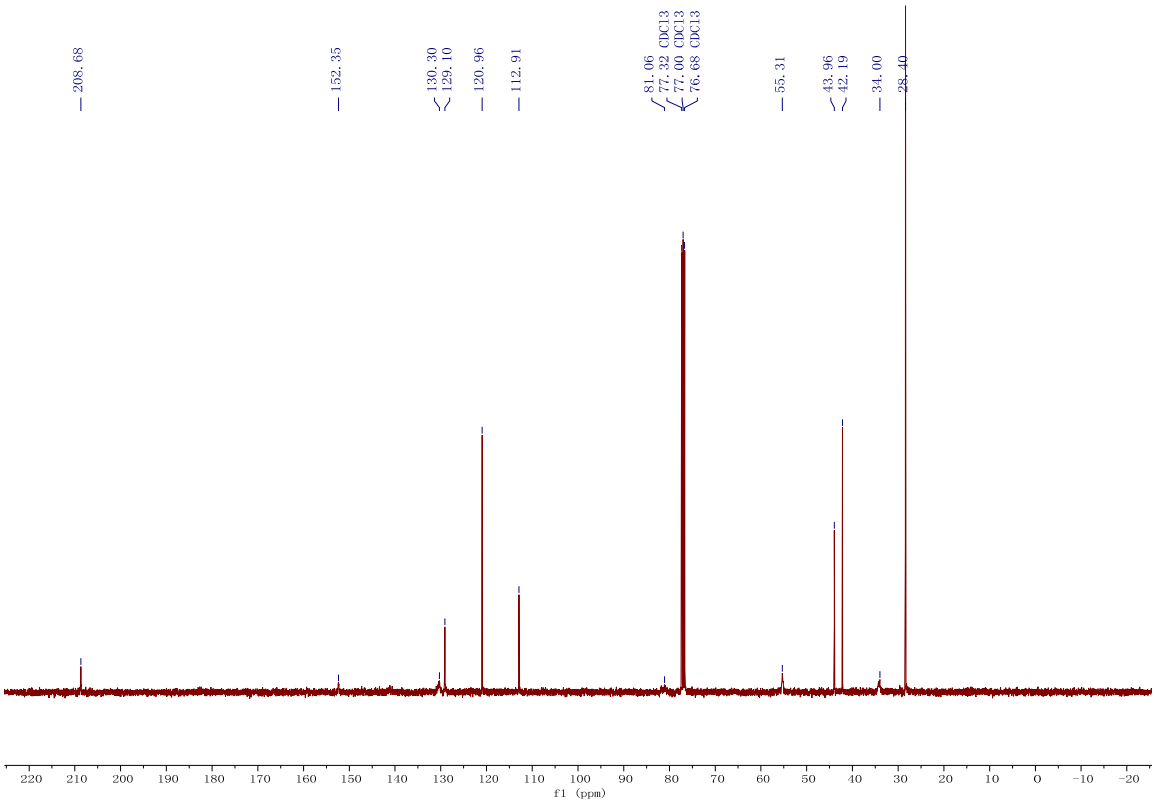

$^{13}$C-NMR for **5n** in $CDCl_3$, 101 MHz



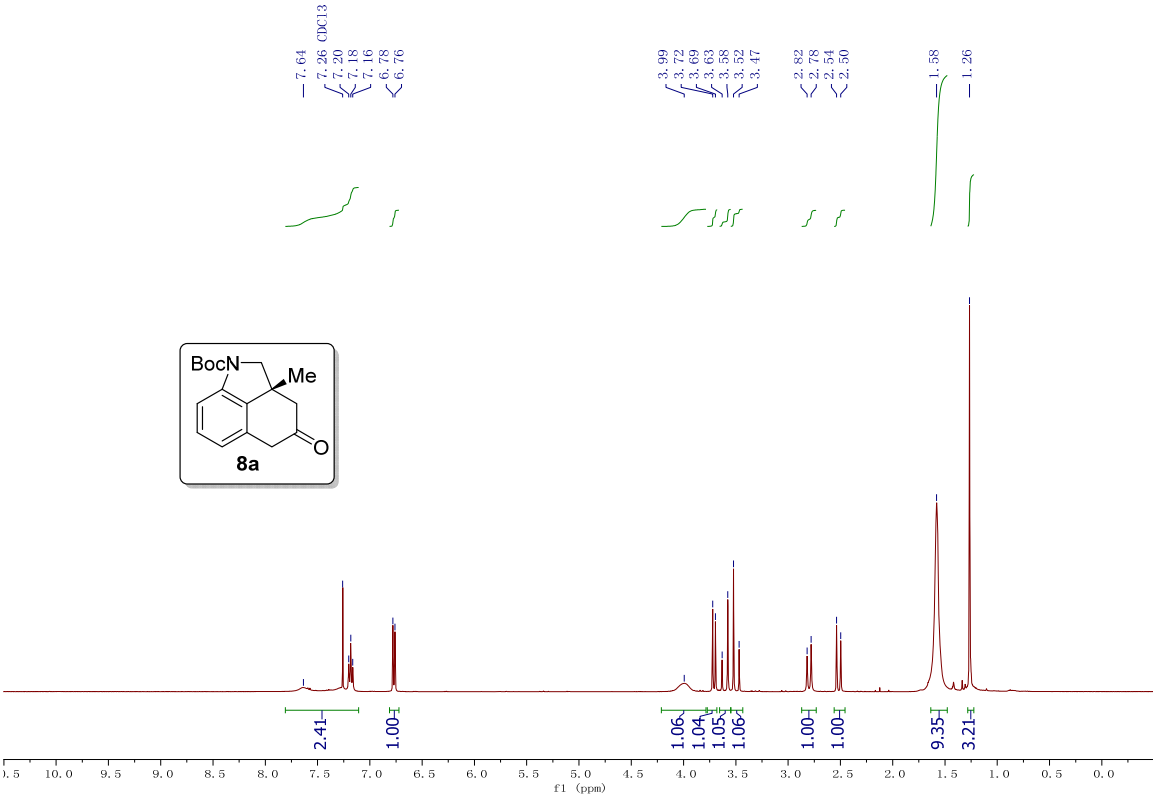
$^{1}$H-NMR for **8** in $CDCl_3$, 400 MHz



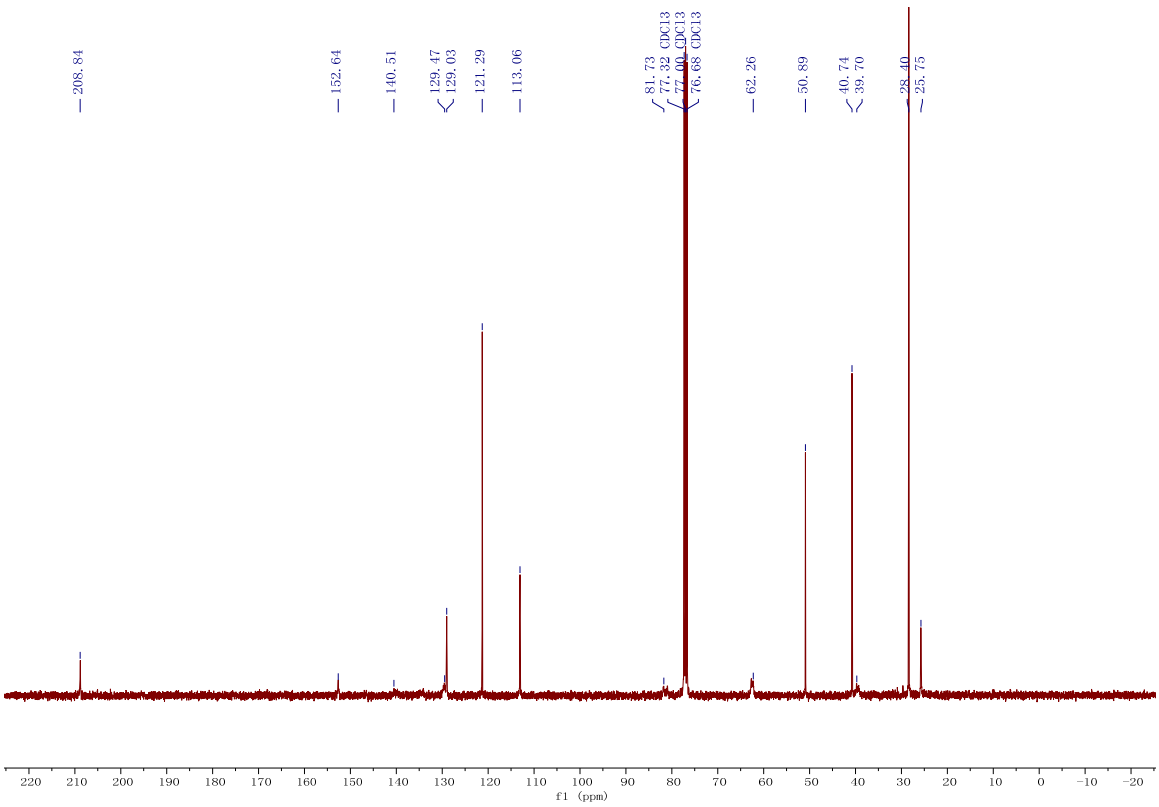

$^{13}$C-NMR for **8** in $CDCl_3$, 101 MHz



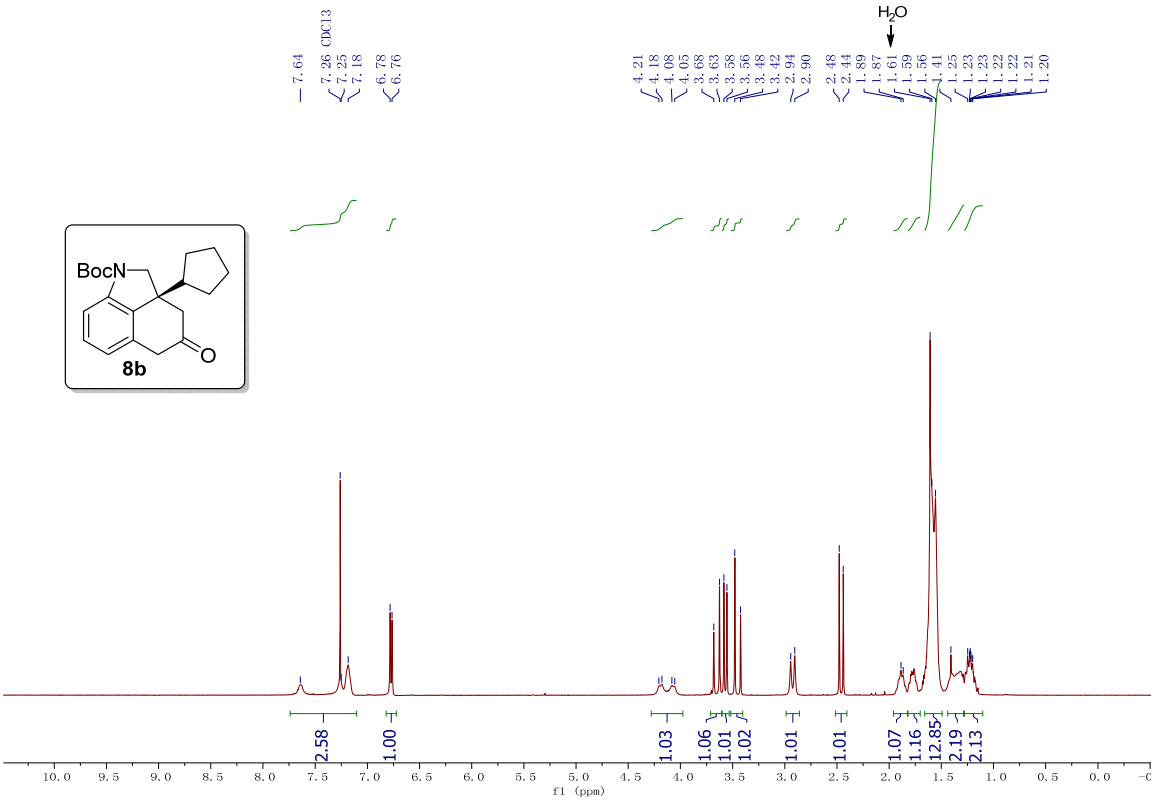
$^{1}$H-NMR for **8a** in $CDCl_3$, 400 MHz



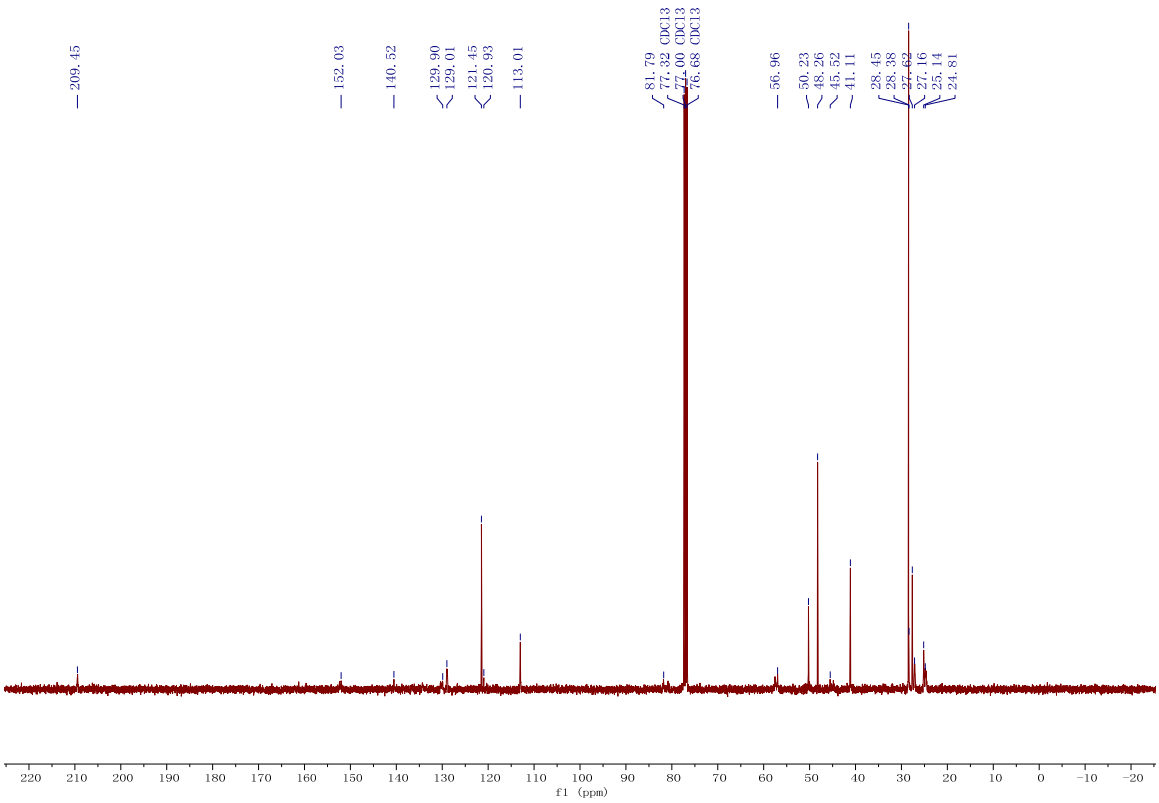

$^{13}$C-NMR for **8a** in $CDCl_3$, 101 MHz



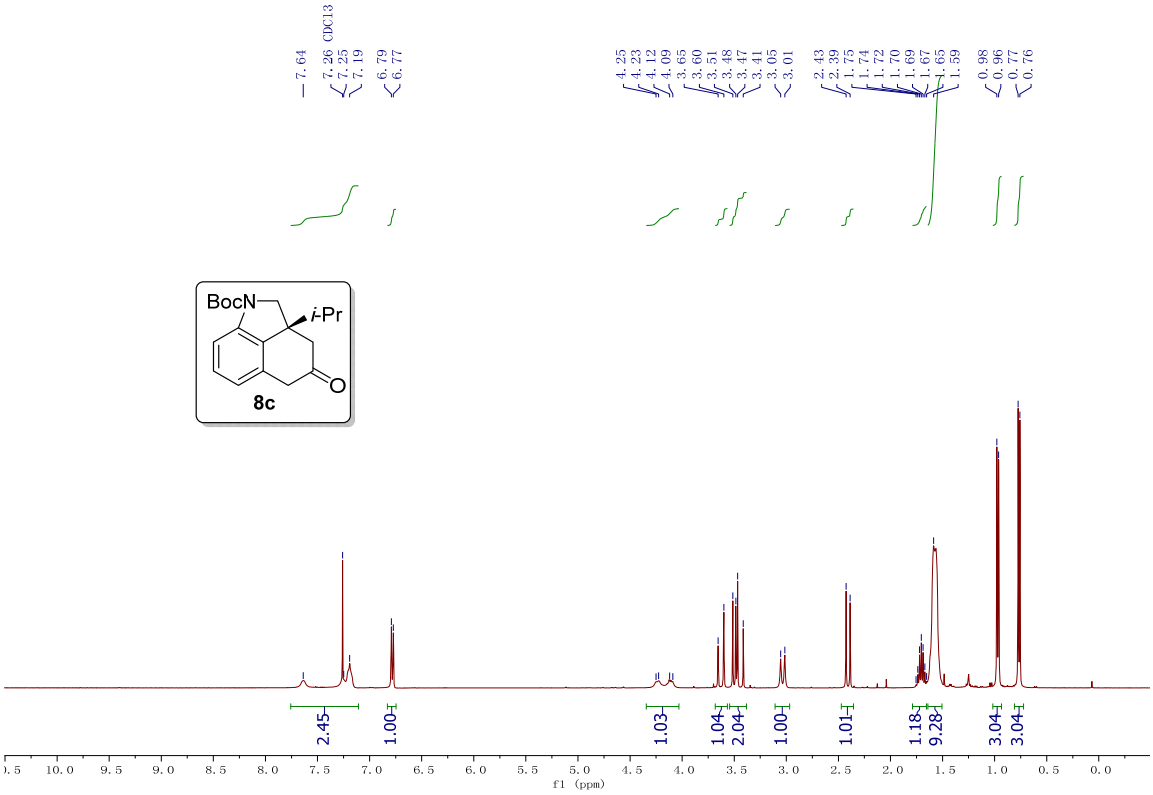
$^{1}$H-NMR for **8b** in $CDCl_3$, 400 MHz



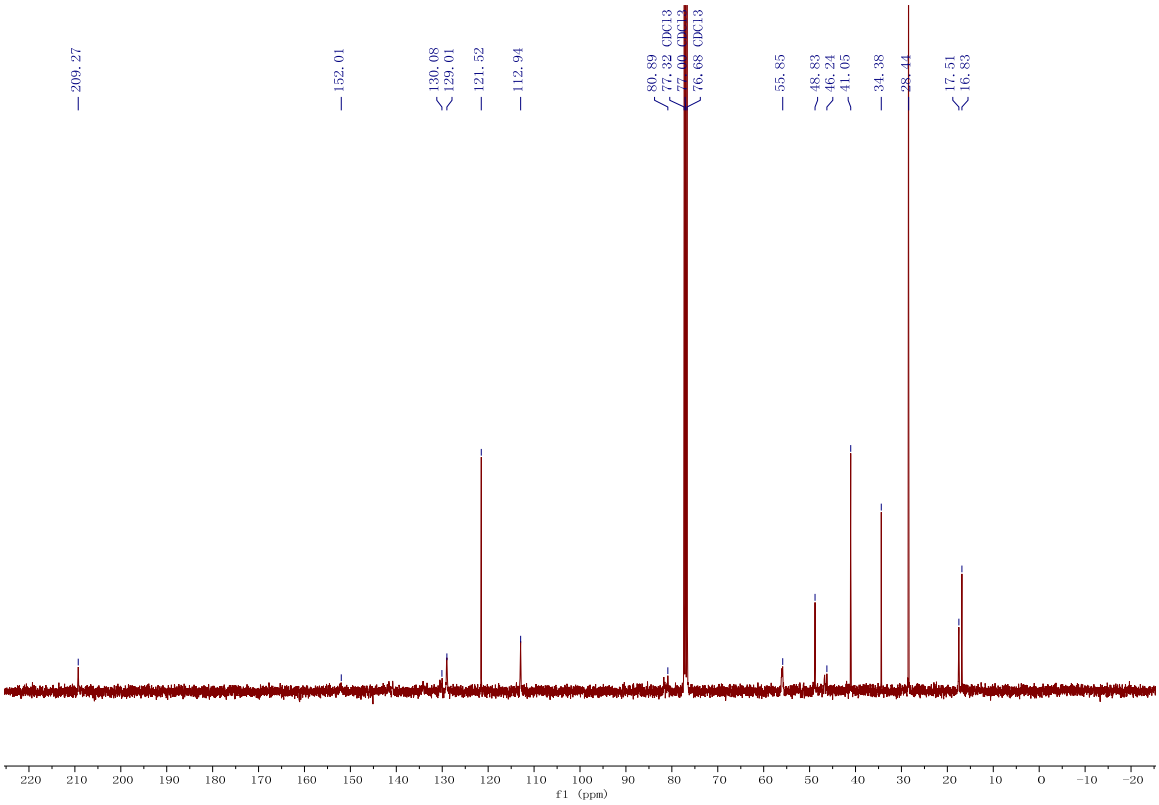

$^{13}$C-NMR for **8b** in $CDCl_3$, 101 MHz



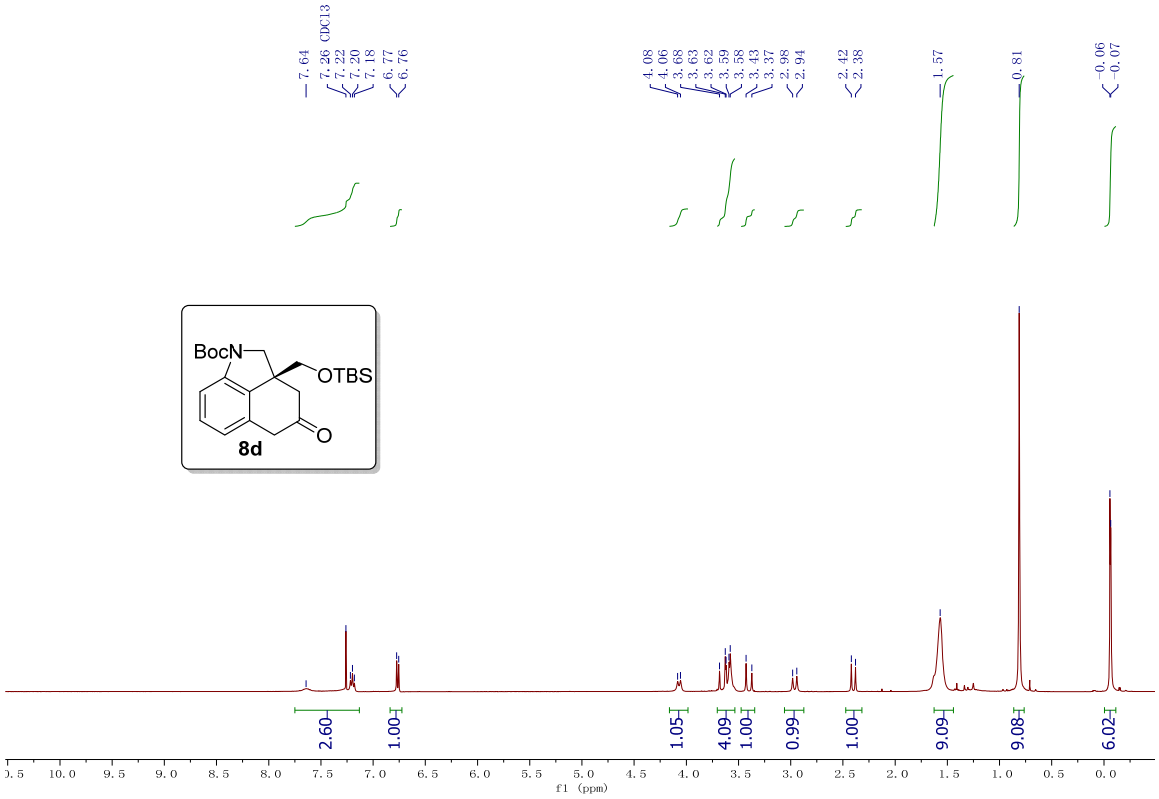
$^{1}$H-NMR for **8c** in $CDCl_3$, 400 MHz



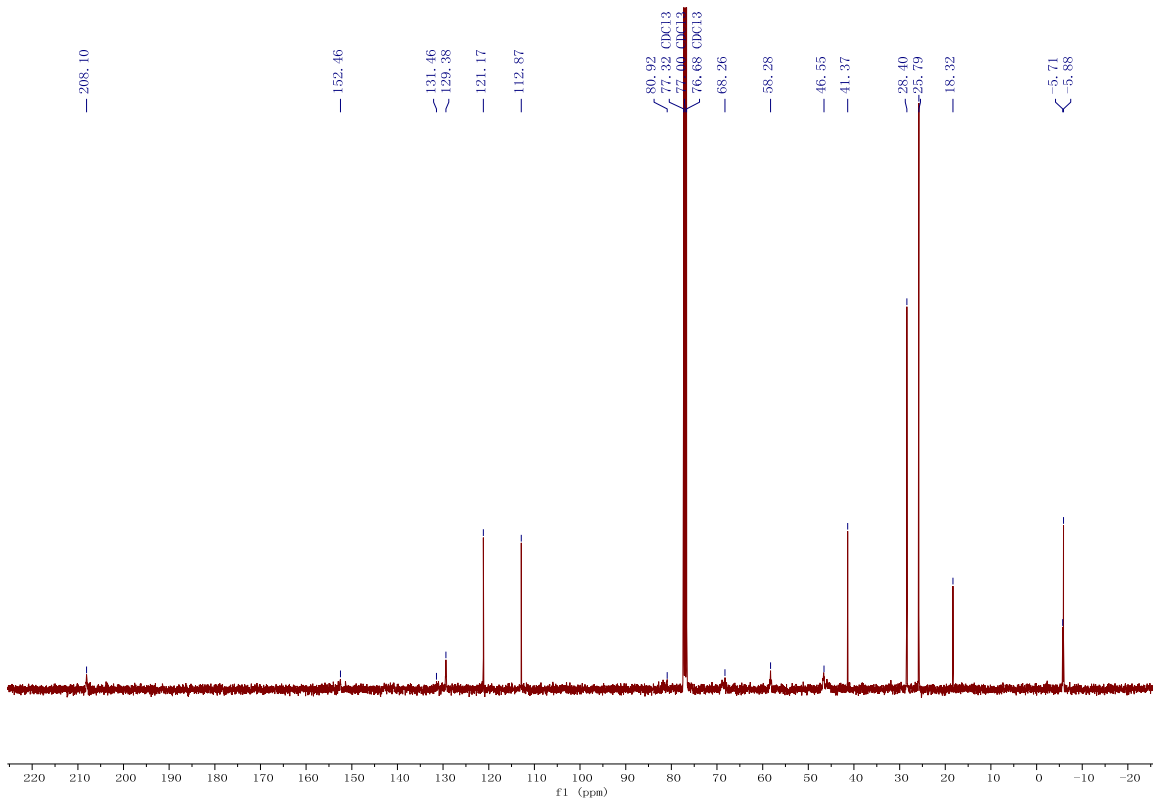

$^{13}$C-NMR for **8c** in $CDCl_3$, 101 MHz



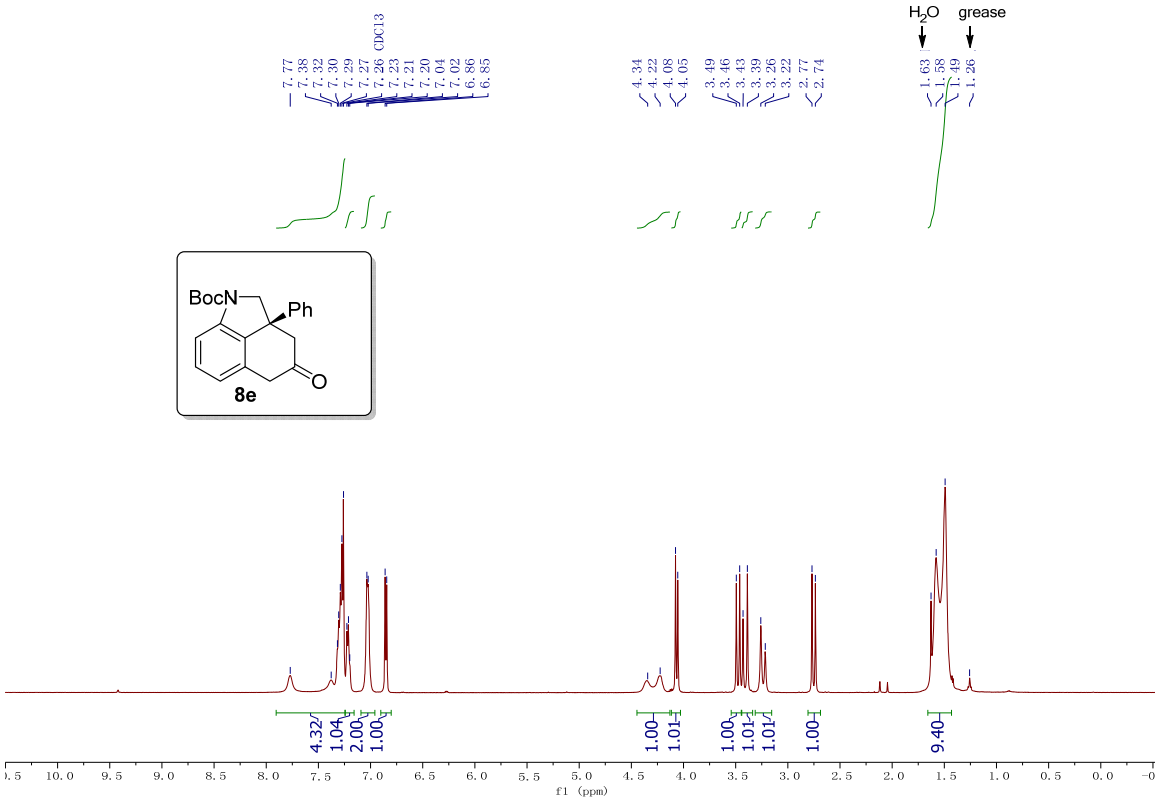
$^{1}$H-NMR for **8d** in $CDCl_3$, 400 MHz



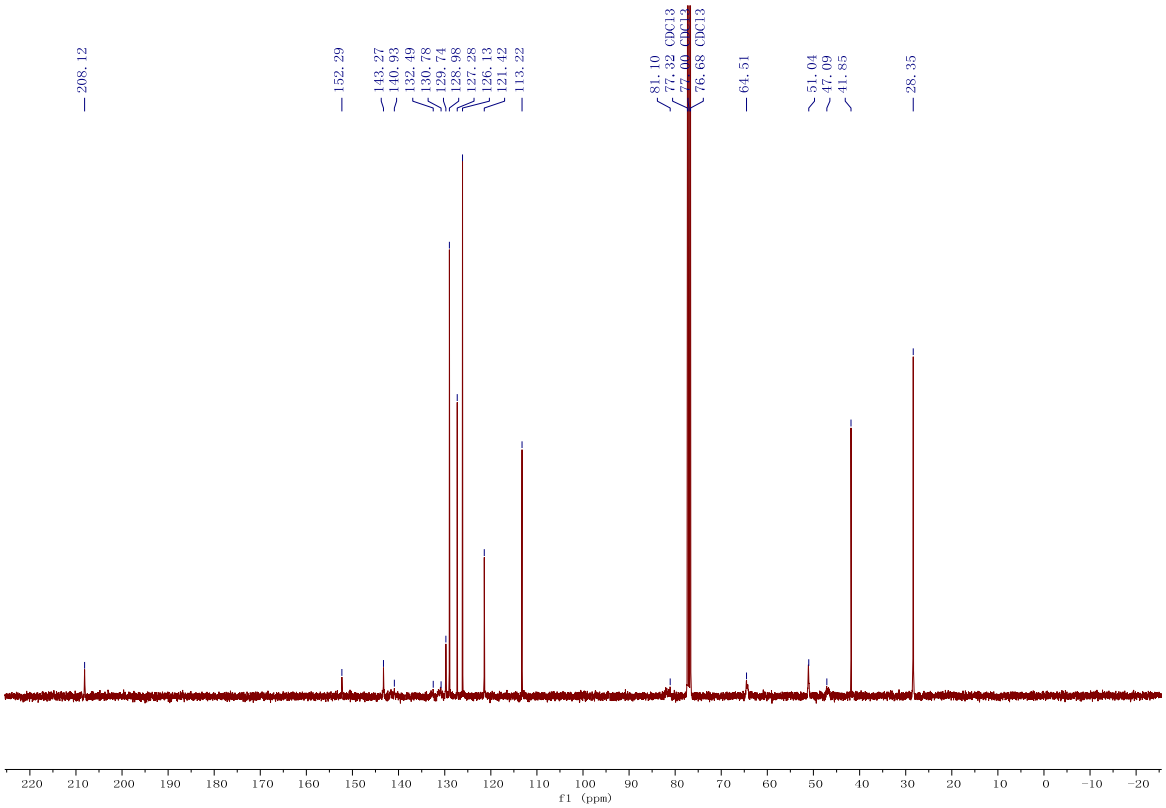

$^{13}$C-NMR for **8d** in $CDCl_3$, 101 MHz



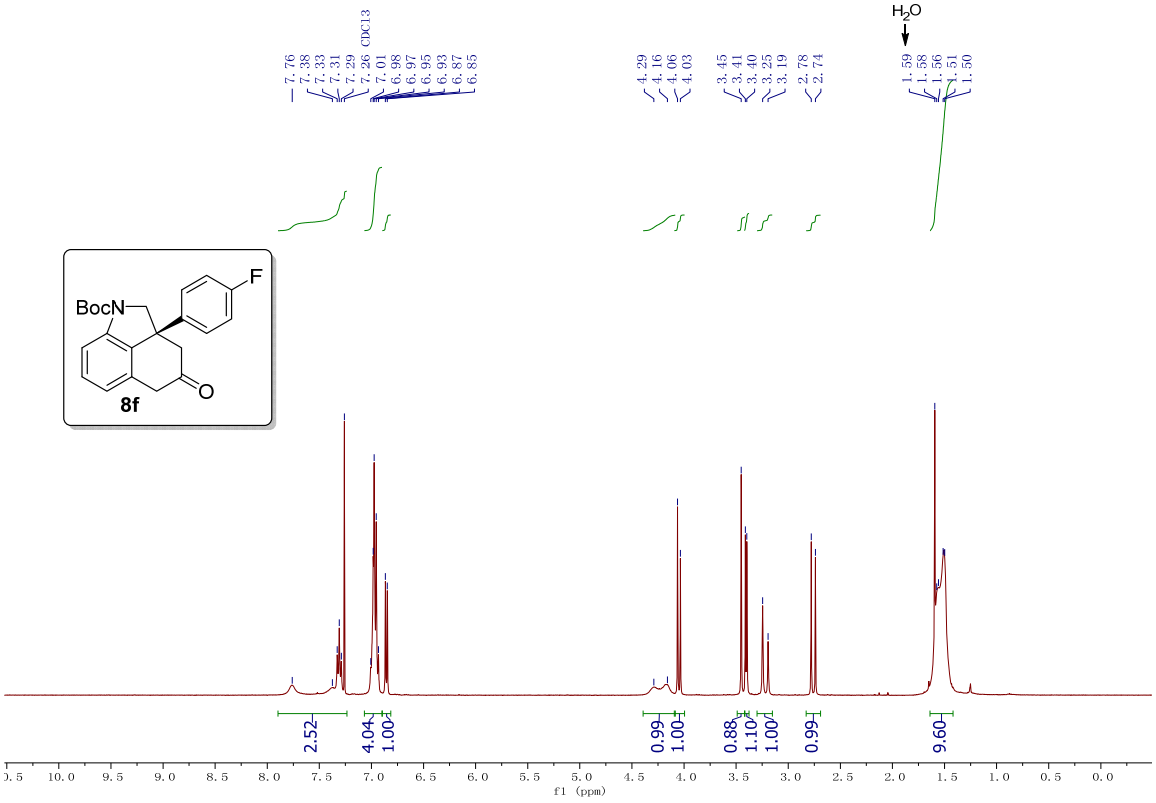
$^{1}$H-NMR for **8e** in $CDCl_3$, 400 MHz



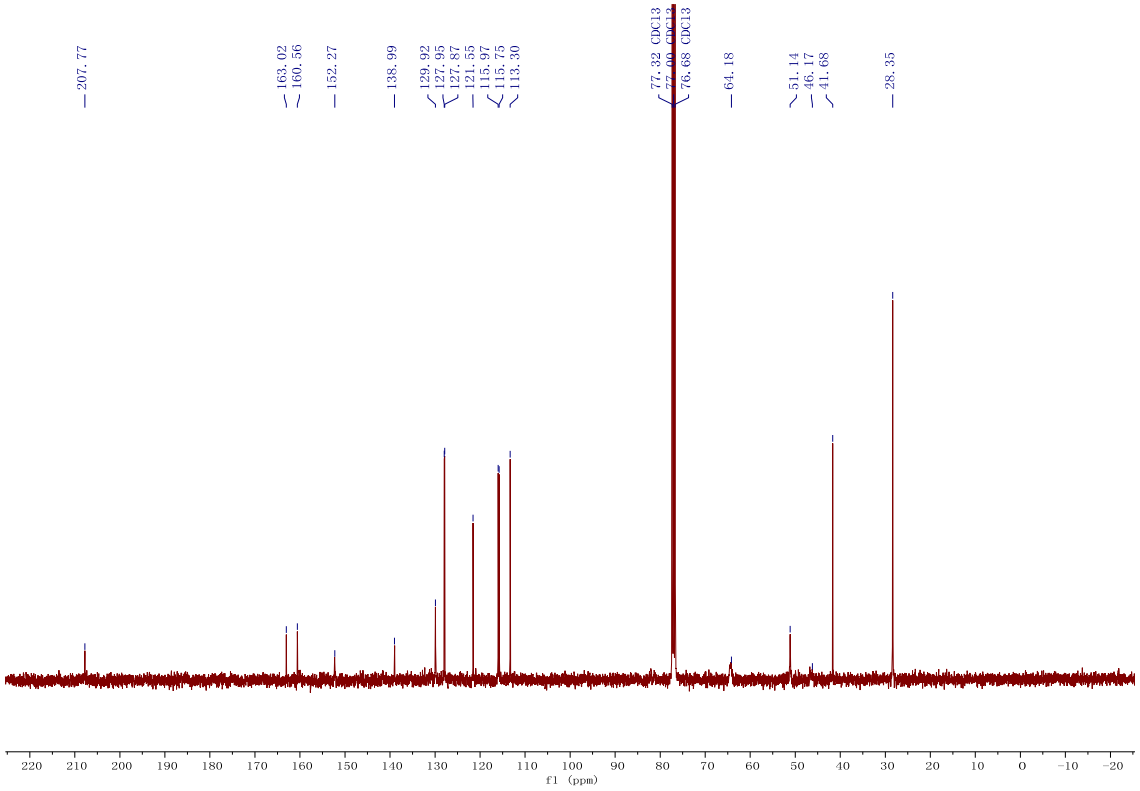

$^{13}$C-NMR for **8e** in $CDCl_3$, 101 MHz



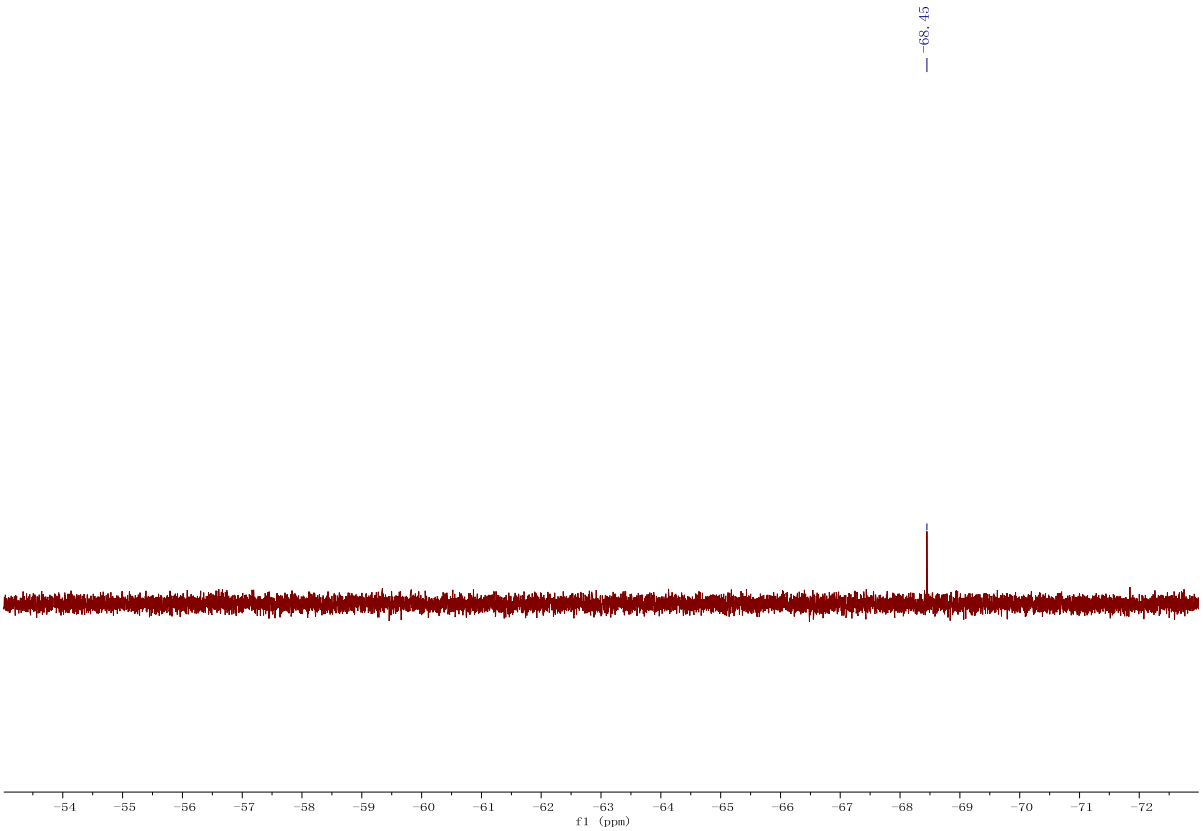
$^{1}$H-NMR for **8f** in $CDCl_3$, 400 MHz



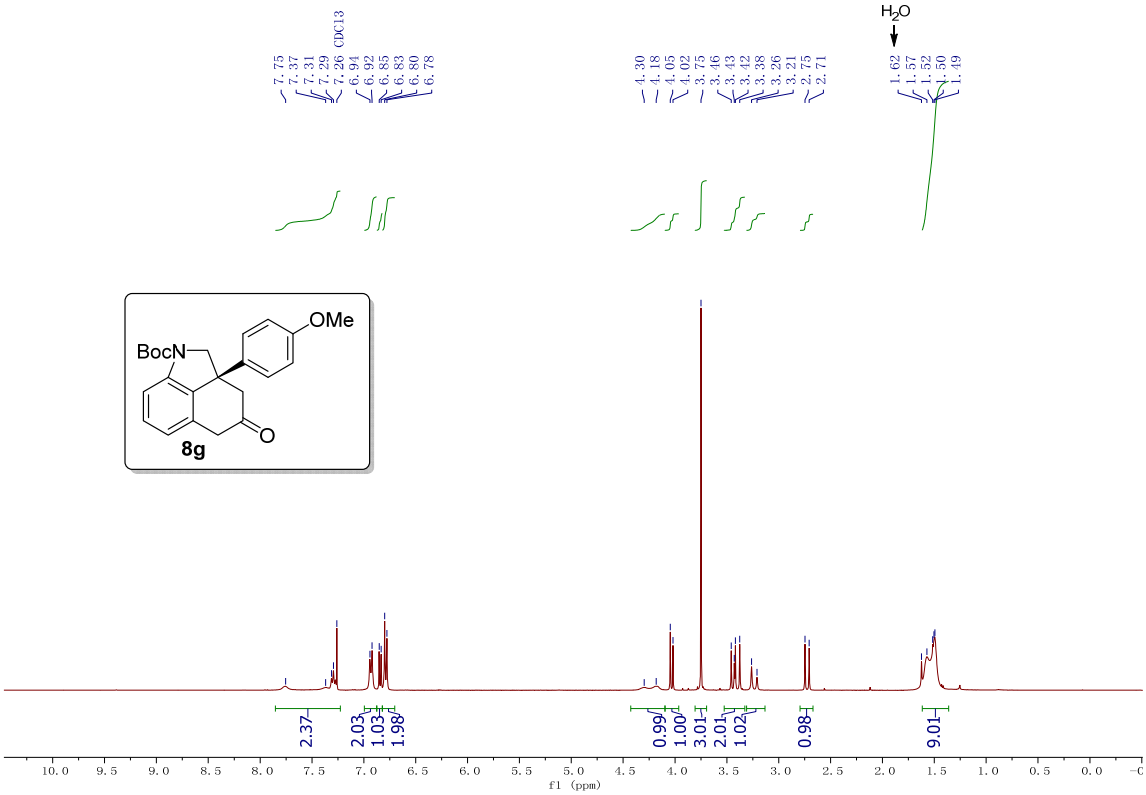

$^{13}$C-NMR for **8f** in $CDCl_3$, 101 MHz



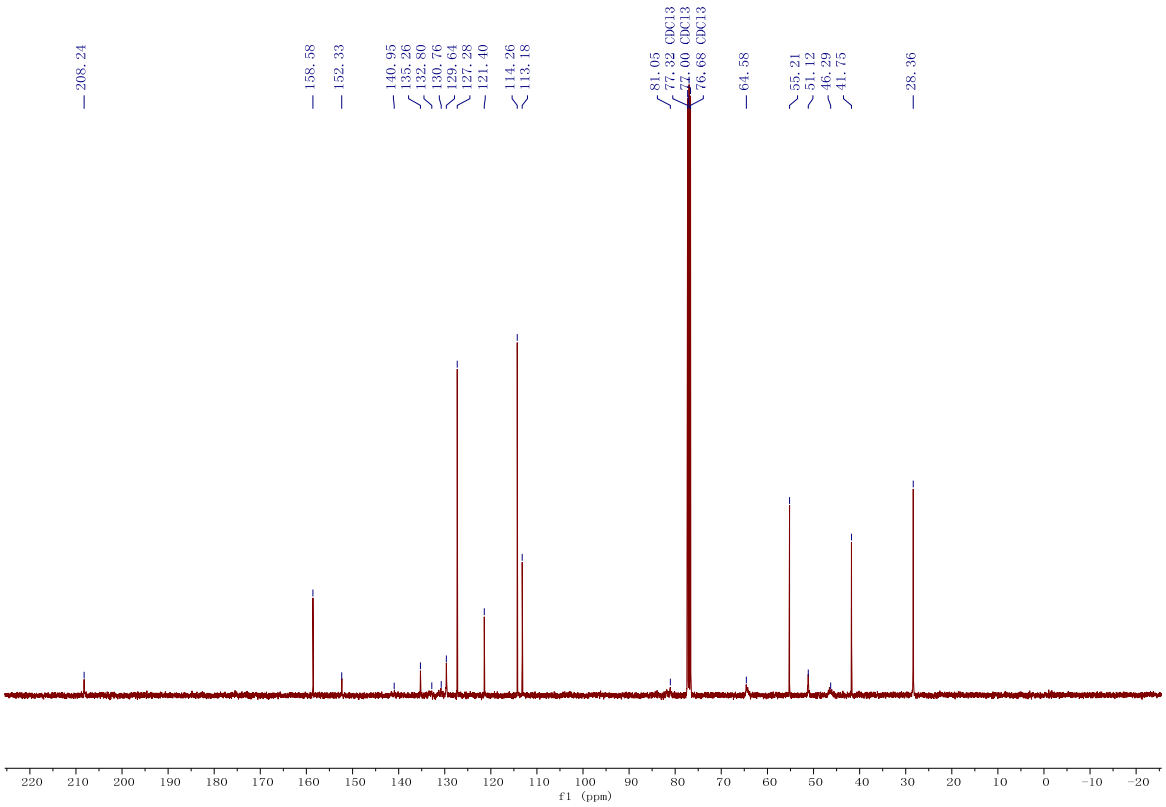
$^{19}$F-NMR for **8f** in $CDCl_3$, 470 MHz



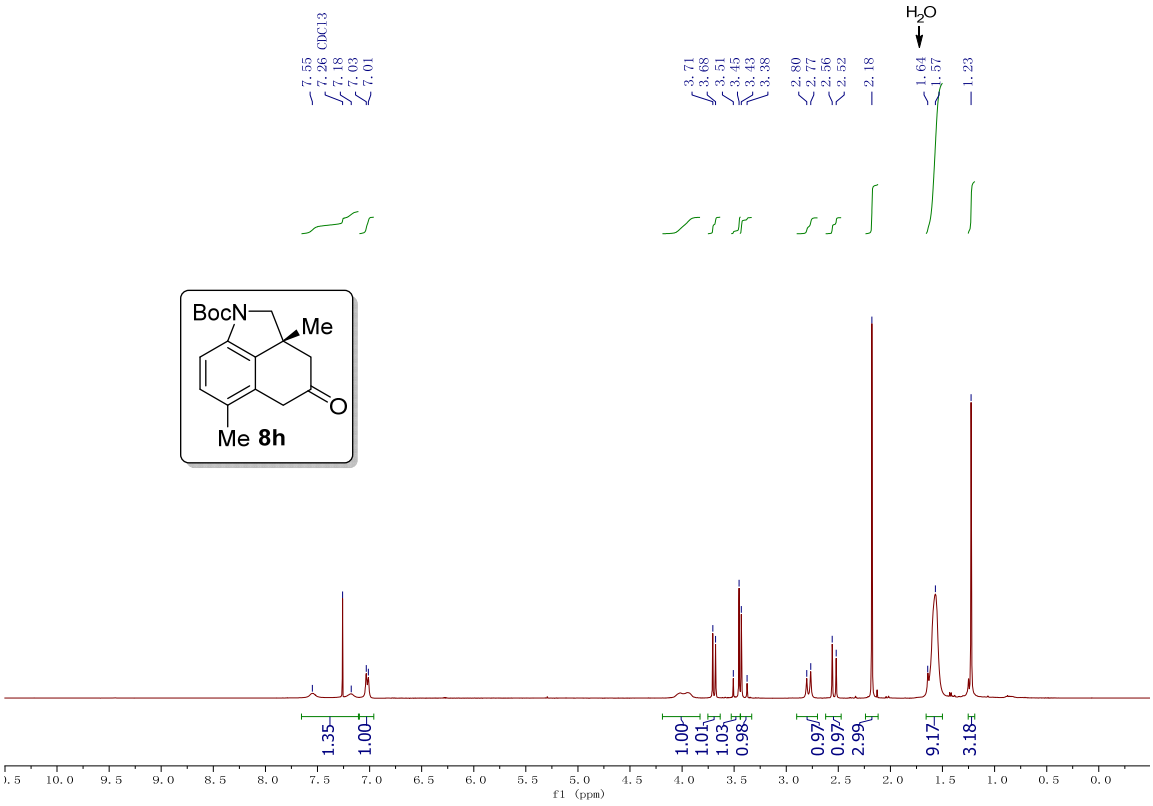
$^{1}$H-NMR for **8g** in $CDCl_3$, 400 MHz



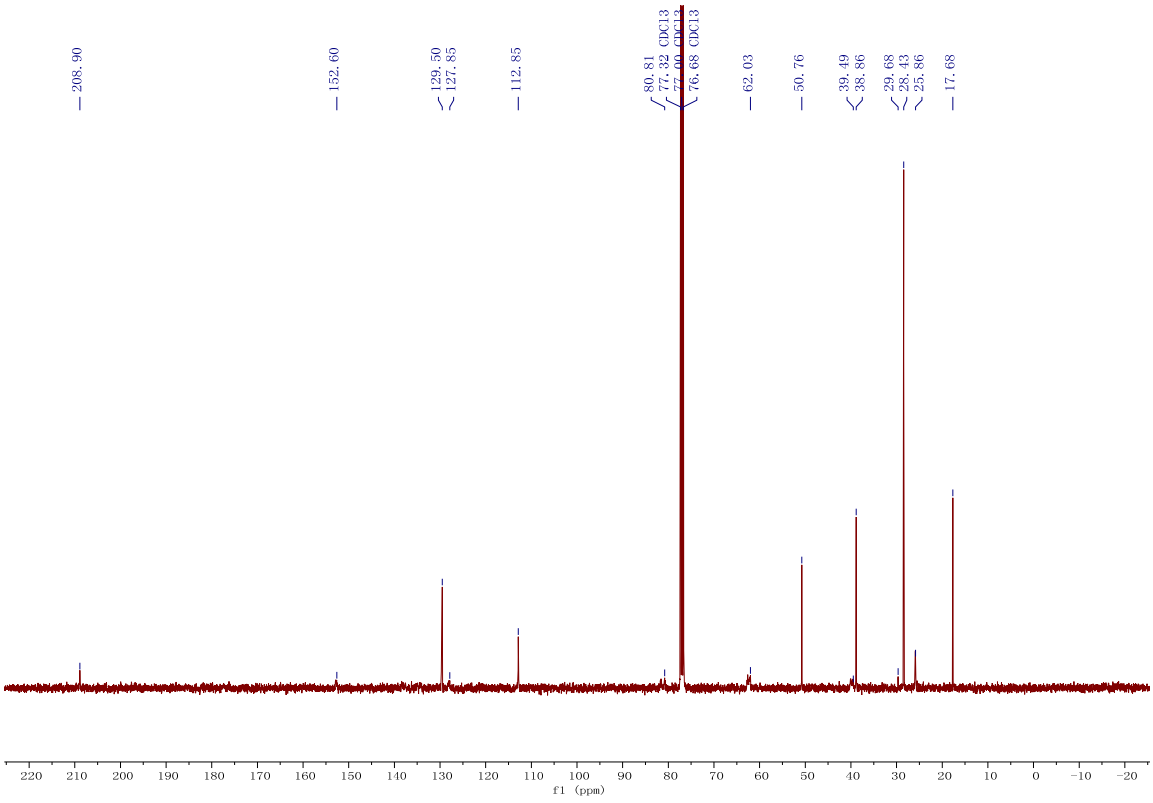

$^{13}$C-NMR for **8g** in $CDCl_3$, 101 MHz



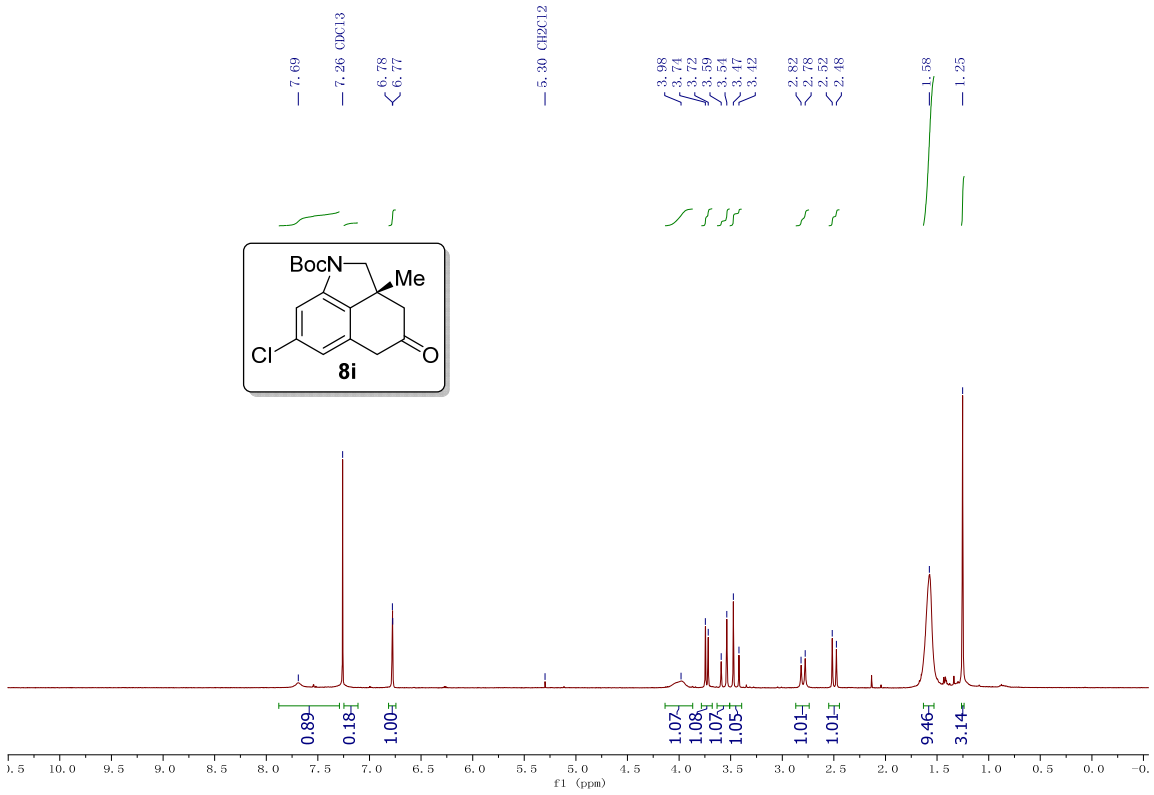
$^{1}$H-NMR for **8h** in $CDCl_3$, 400 MHz



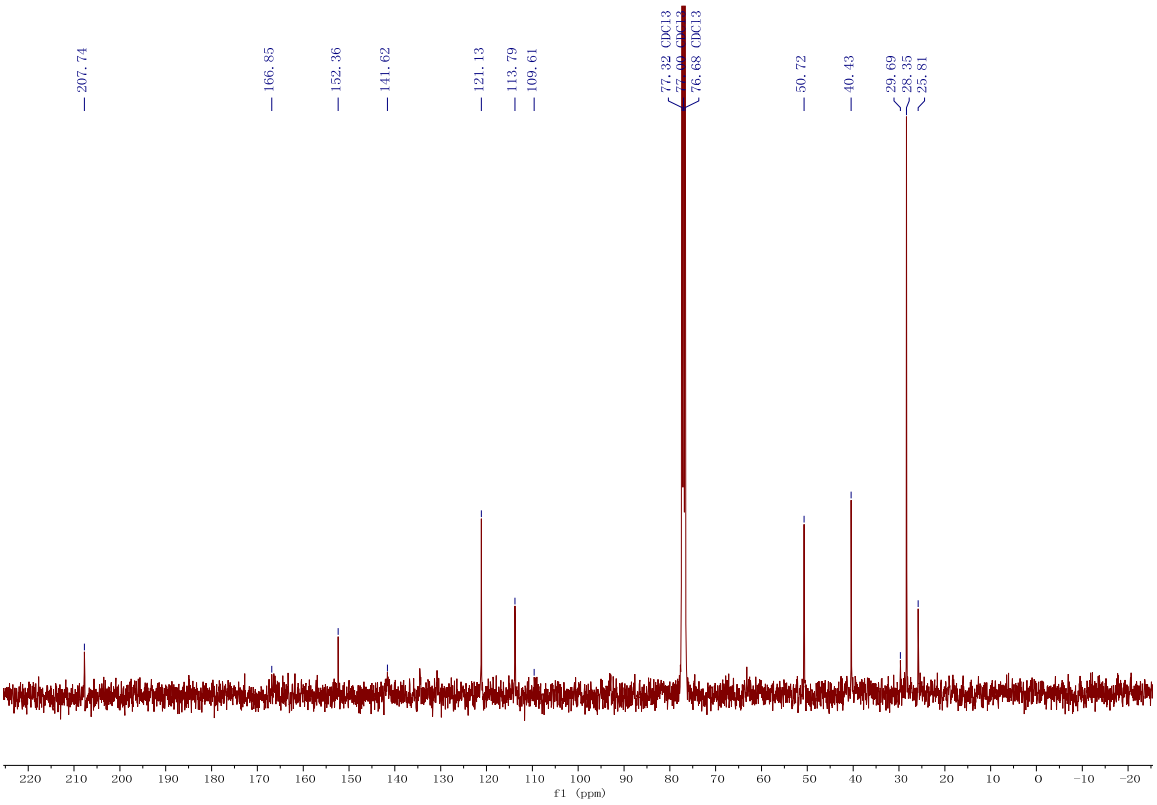

$^{13}$C-NMR for **8h** in $CDCl_3$, 101 MHz



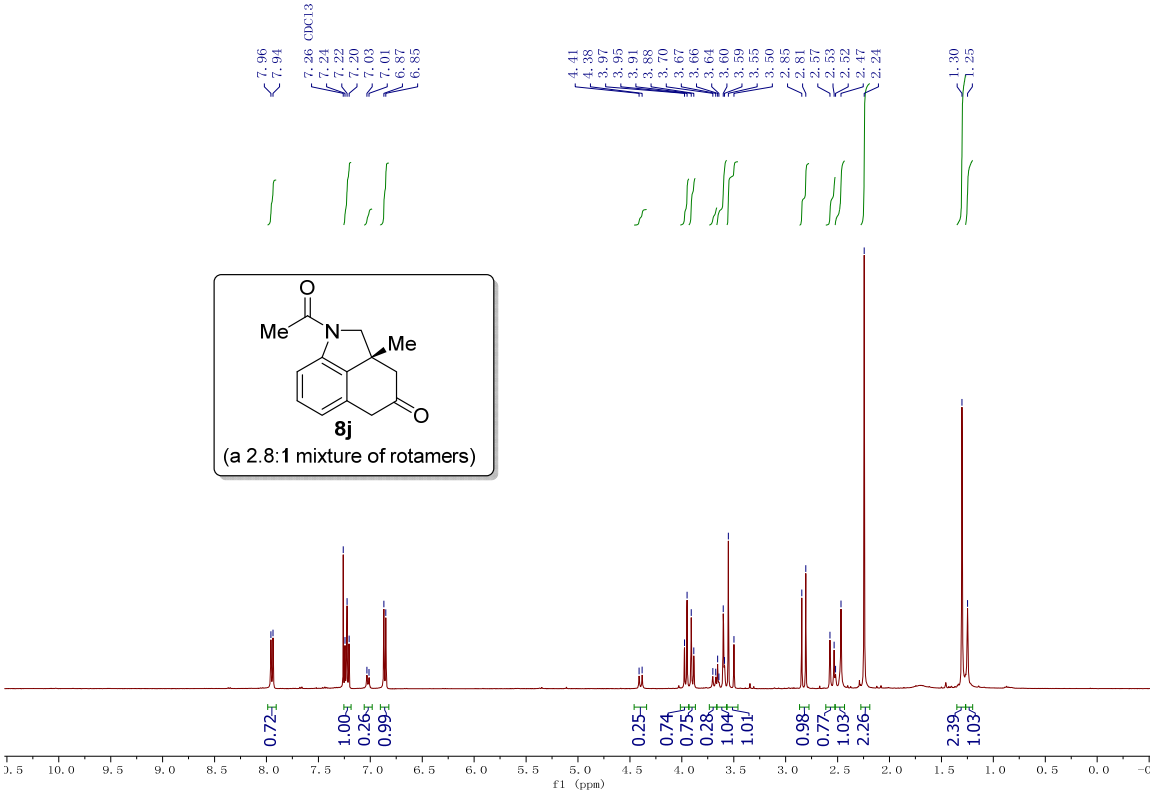
$^{1}$H-NMR for **8i** in $CDCl_3$, 400 MHz



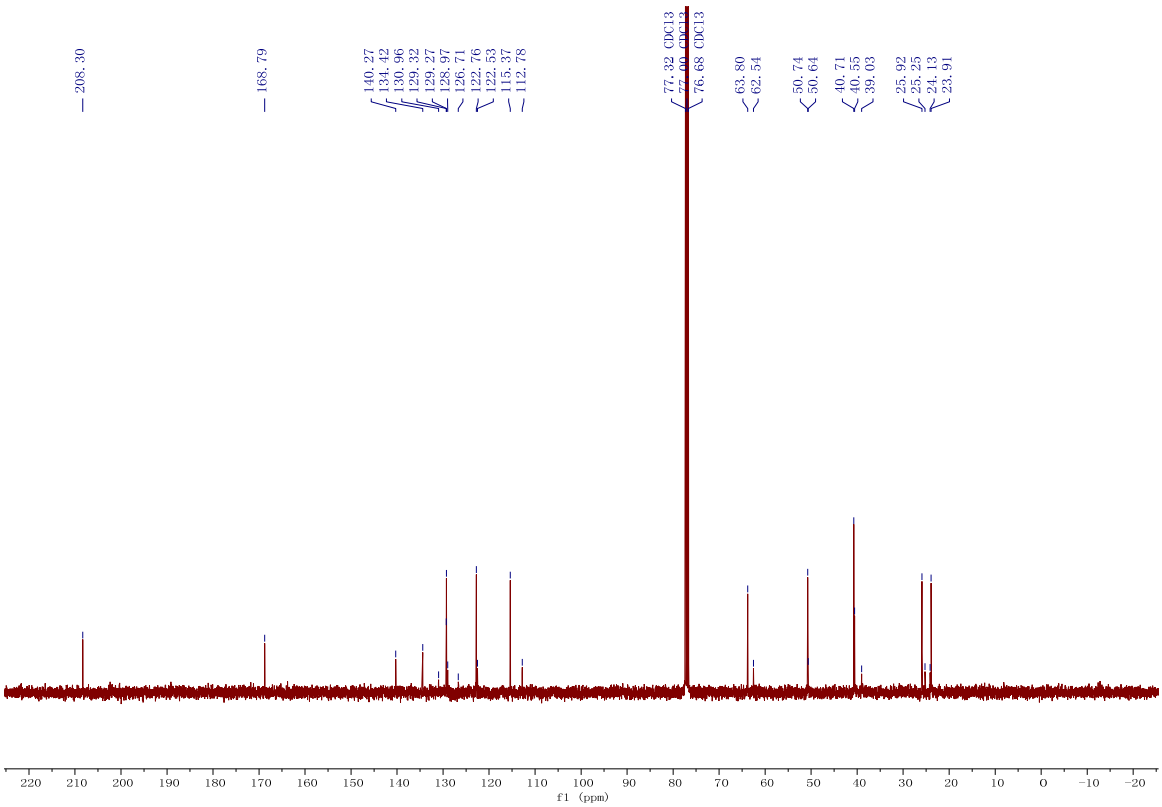

$^{13}$C-NMR for **8i** in $CDCl_3$, 101 MHz



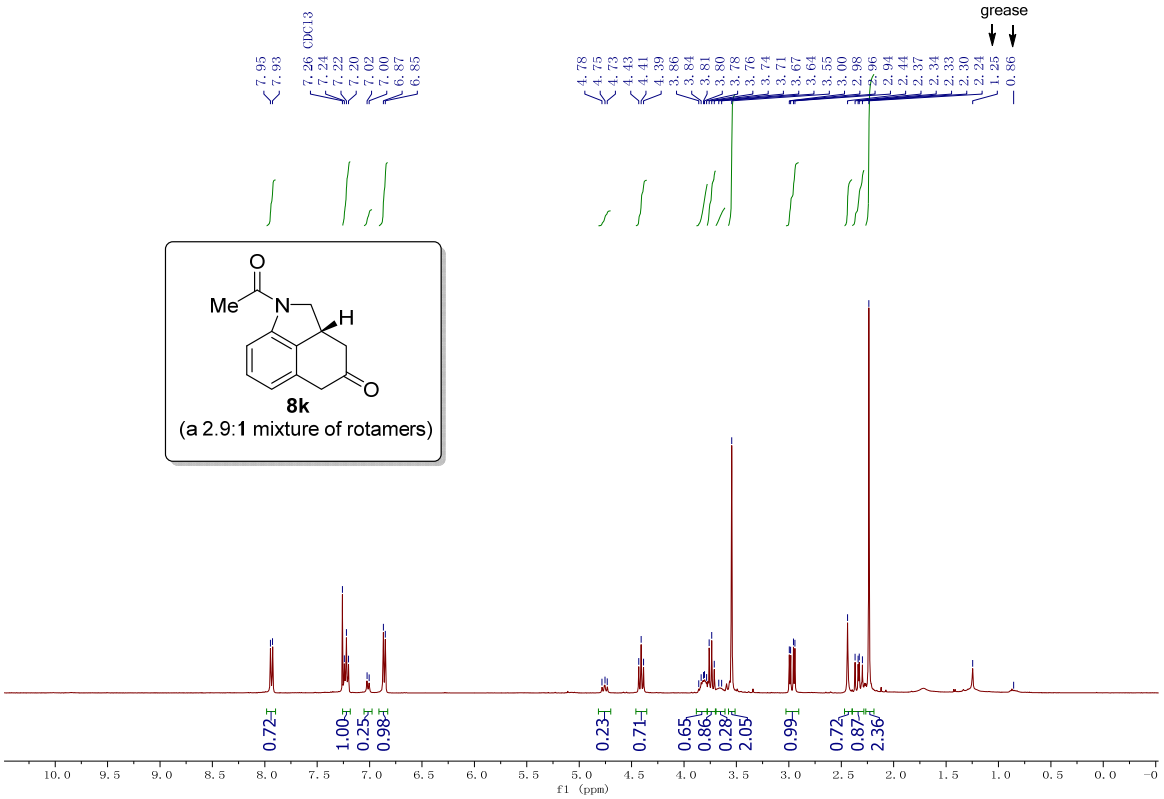
$^{1}$H-NMR for **8j** in $CDCl_3$, 400 MHz



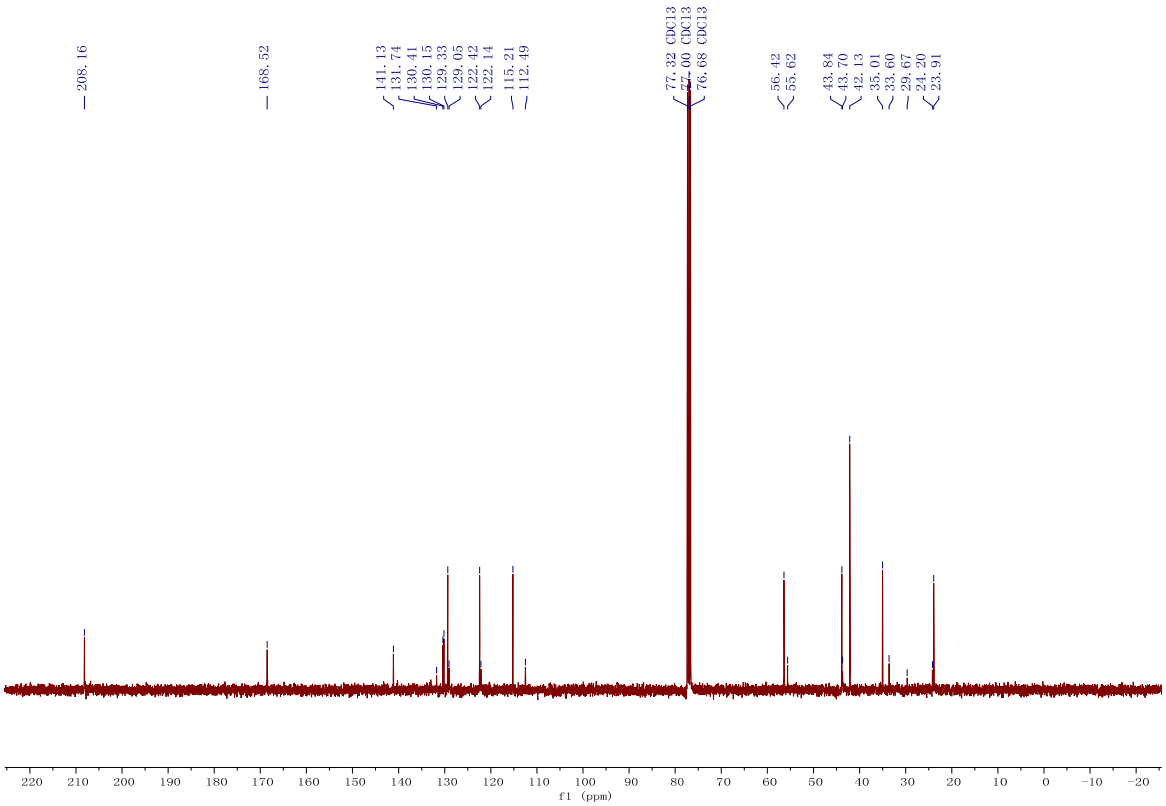

$^{13}$C-NMR for **8j** in $CDCl_3$, 101 MHz



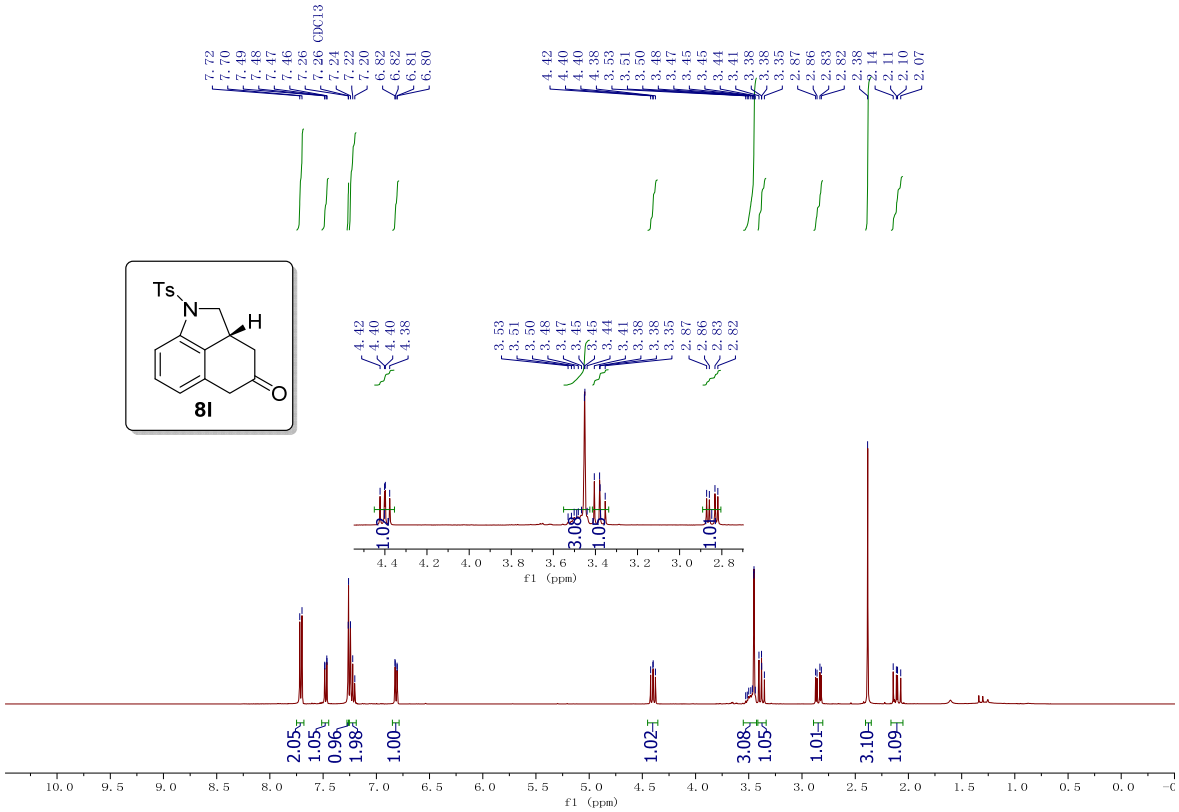
$^{1}$H-NMR for **8k** in $CDCl_3$, 400 MHz



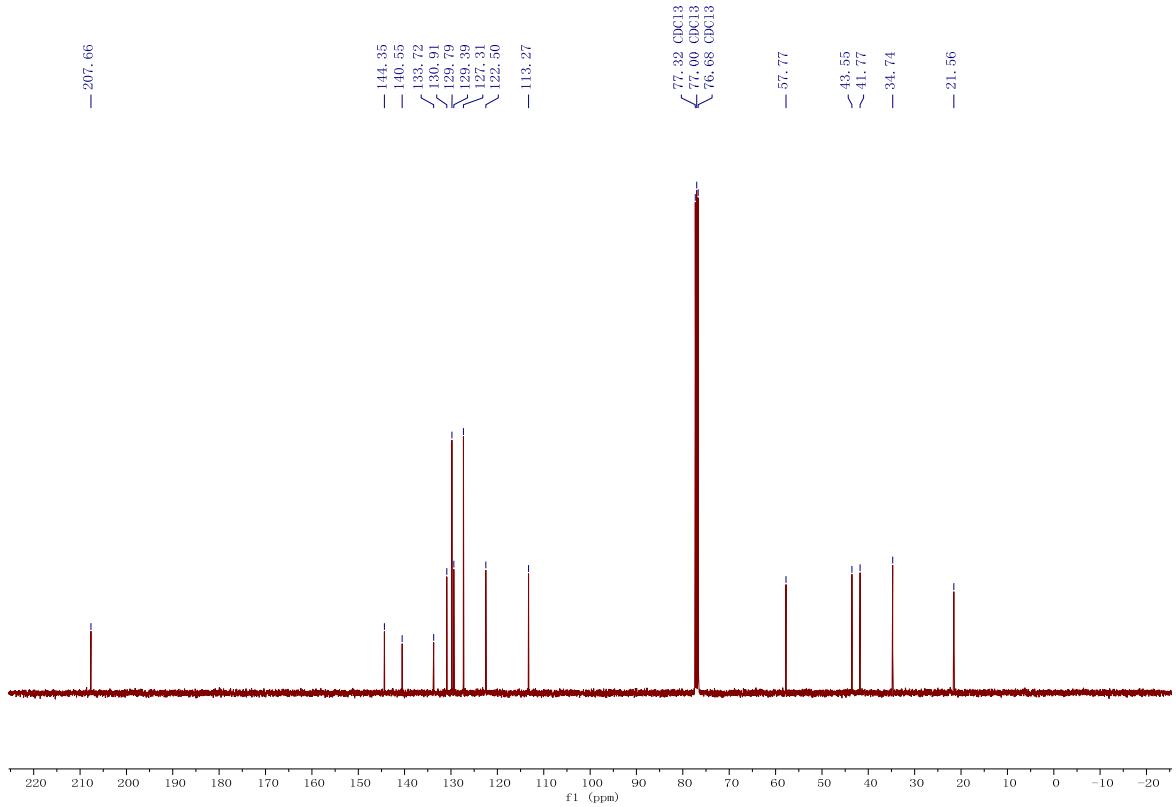

$^{13}$C-NMR for **8k** in $CDCl_3$, 101 MHz



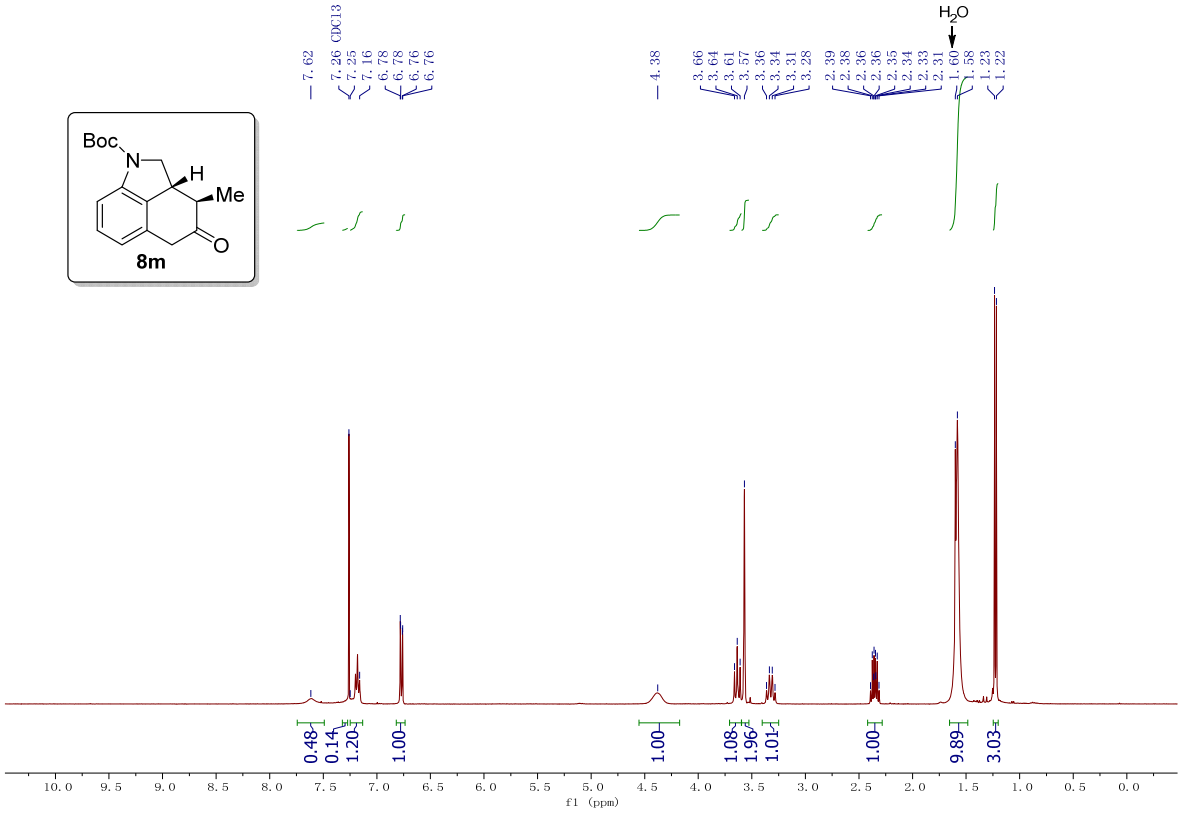
$^{1}$H-NMR for **8l** in $CDCl_3$, 400 MHz



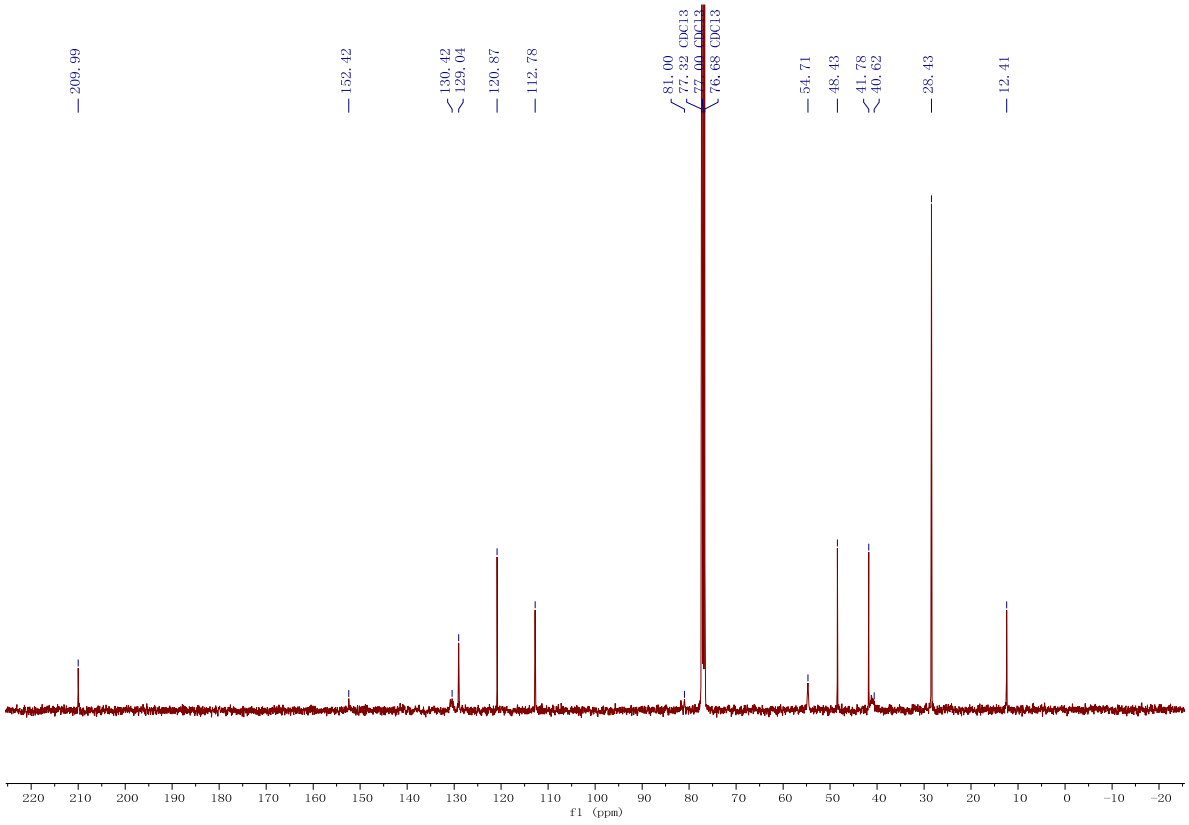

$^{13}$C-NMR for **8l** in $CDCl_3$, 101 MHz



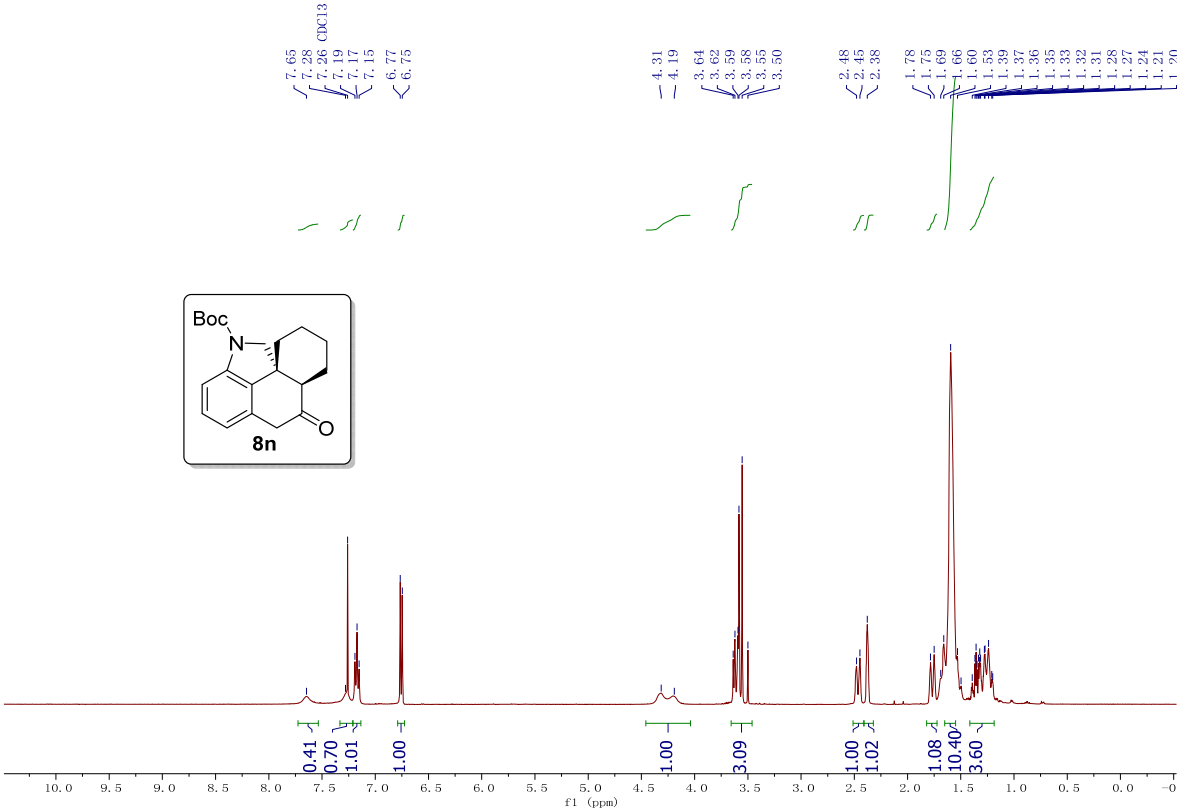
$^{1}$H-NMR for **8m** in $CDCl_3$, 400 MHz



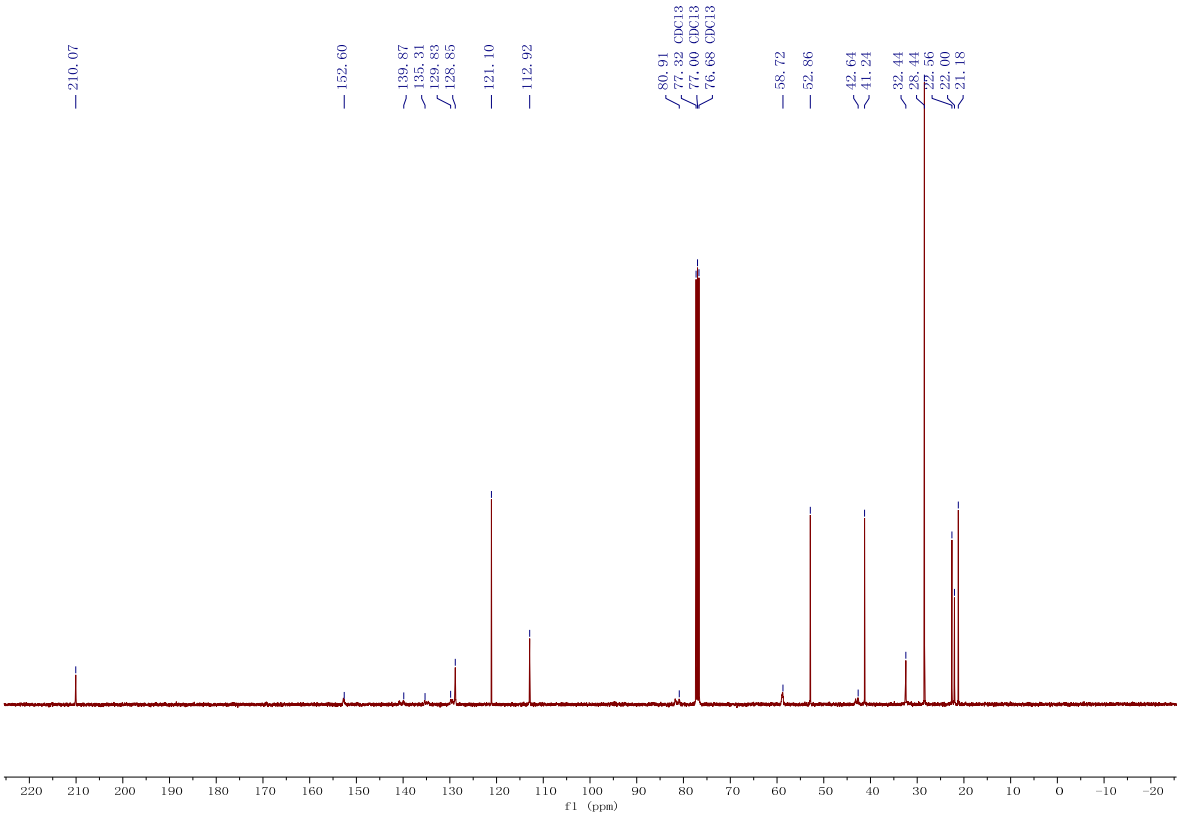

$^{13}$C-NMR for **8m** in $CDCl_3$, 101 MHz



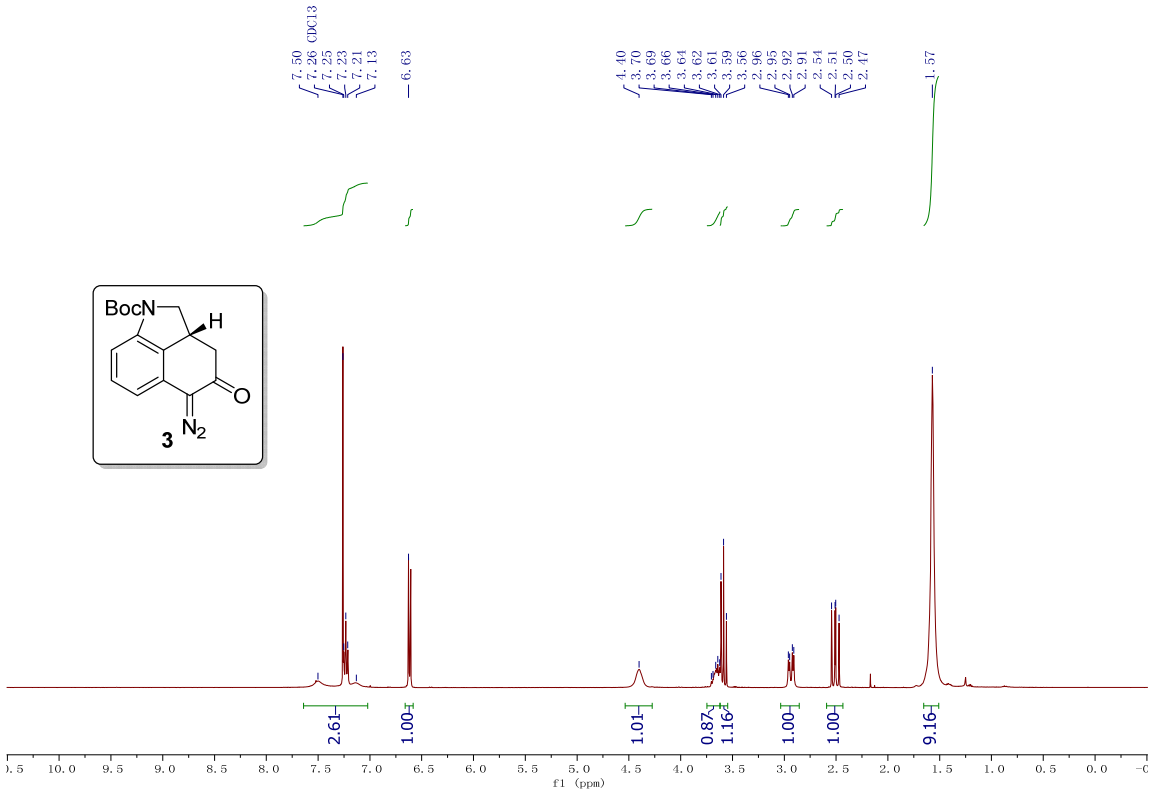
$^{1}$H-NMR for **8n** in $CDCl_3$, 400 MHz



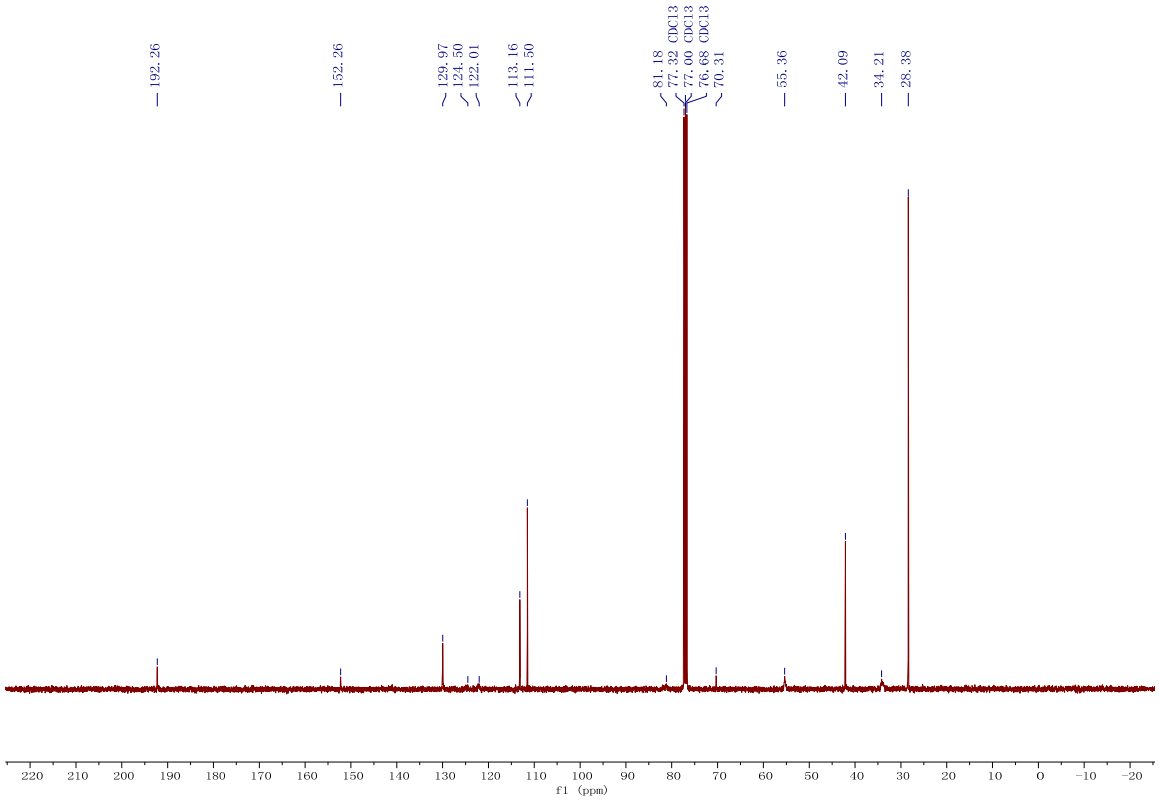

$^{13}$C-NMR for **8n** in $CDCl_3$, 101 MHz



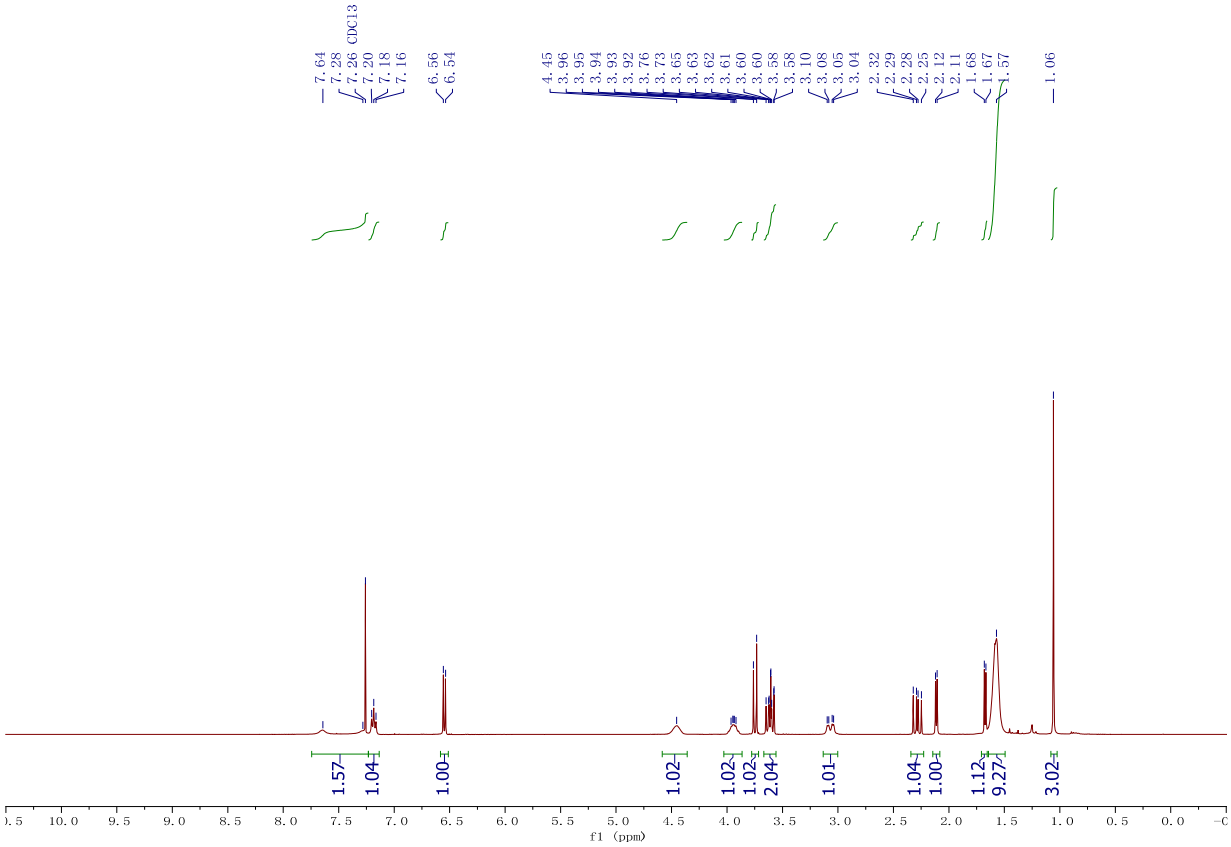
$^{1}$H-NMR for **3** in $CDCl_3$, 400 MHz



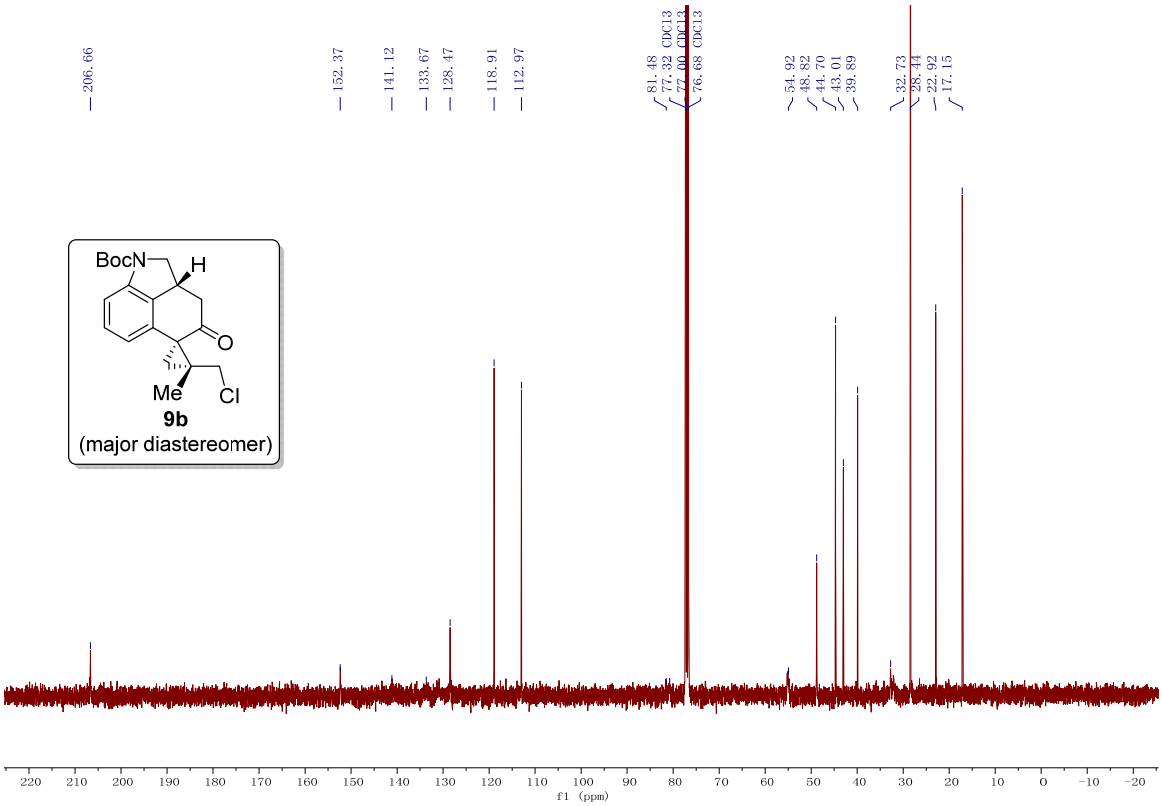

$^{13}$C-NMR for **3** in $CDCl_3$, 101 MHz



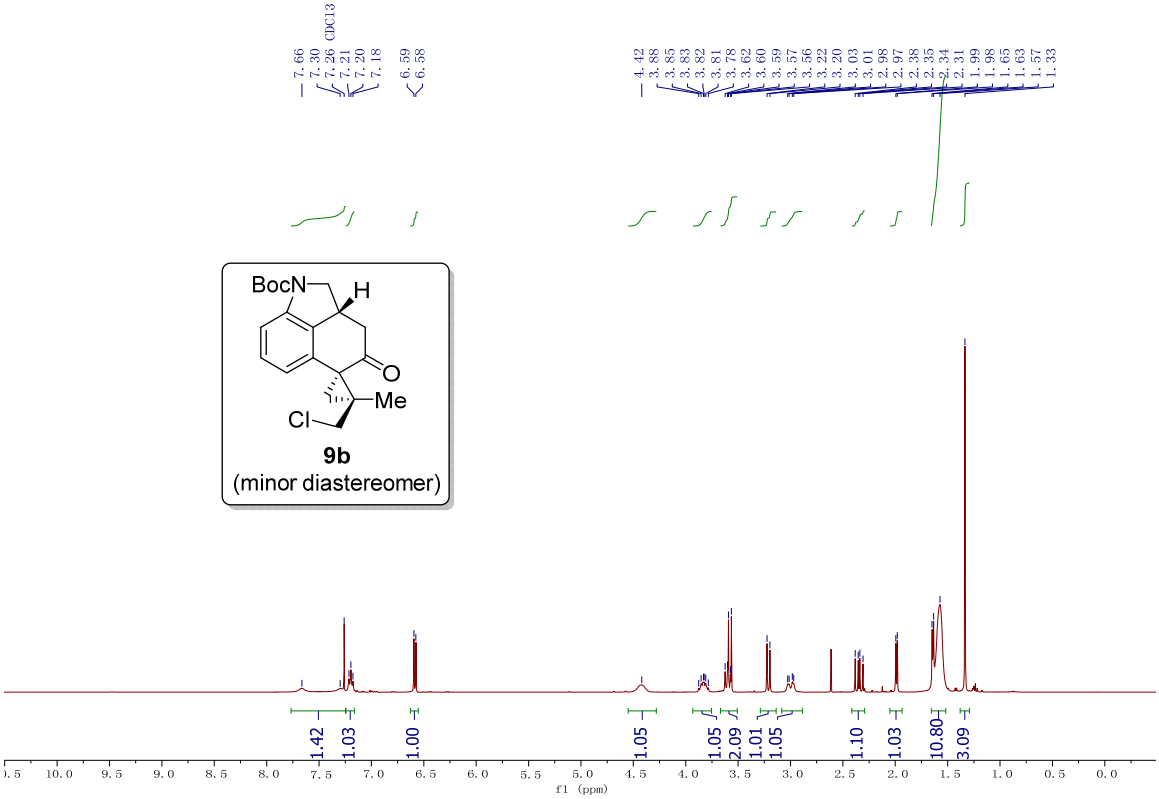
$^{1}$H-NMR for **9b** (major) in $CDCl_3$, 400 MHz



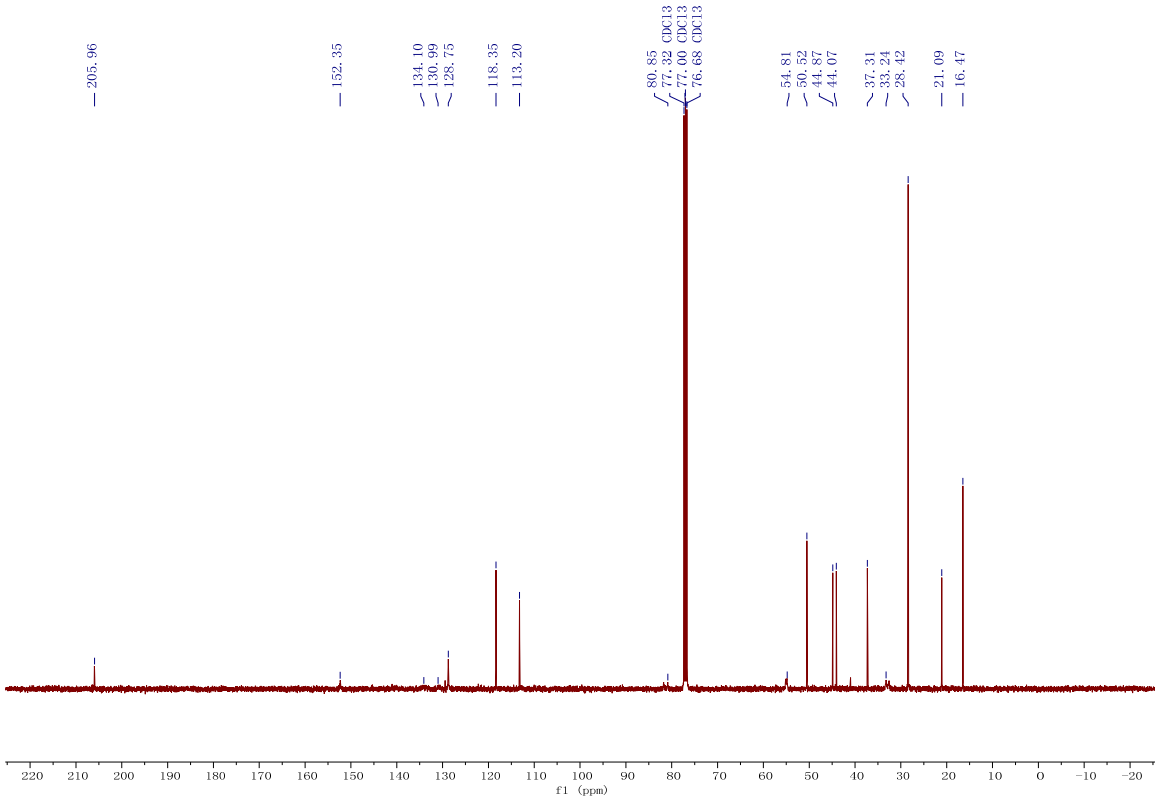

$^{13}$C-NMR for **9b** (major) in $CDCl_3$, 101 MHz



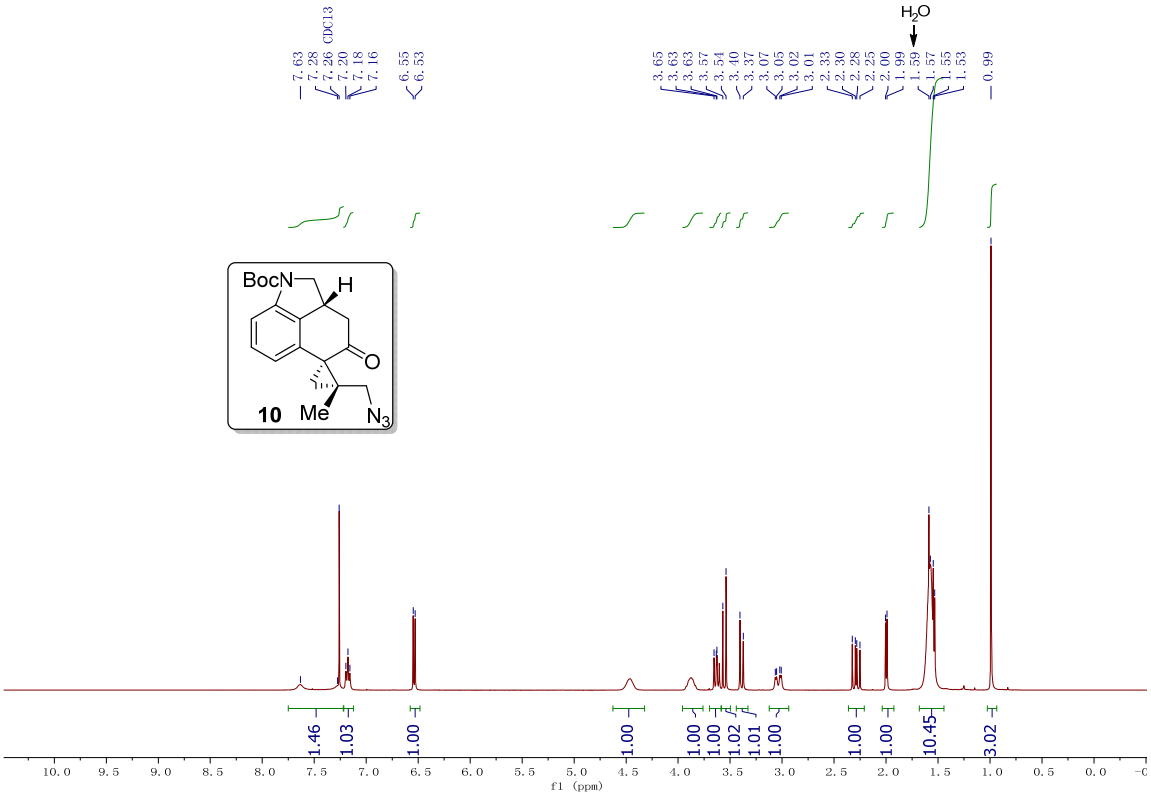
$^{1}$H-NMR for **9b** (minor) in $CDCl_3$, 400 MHz



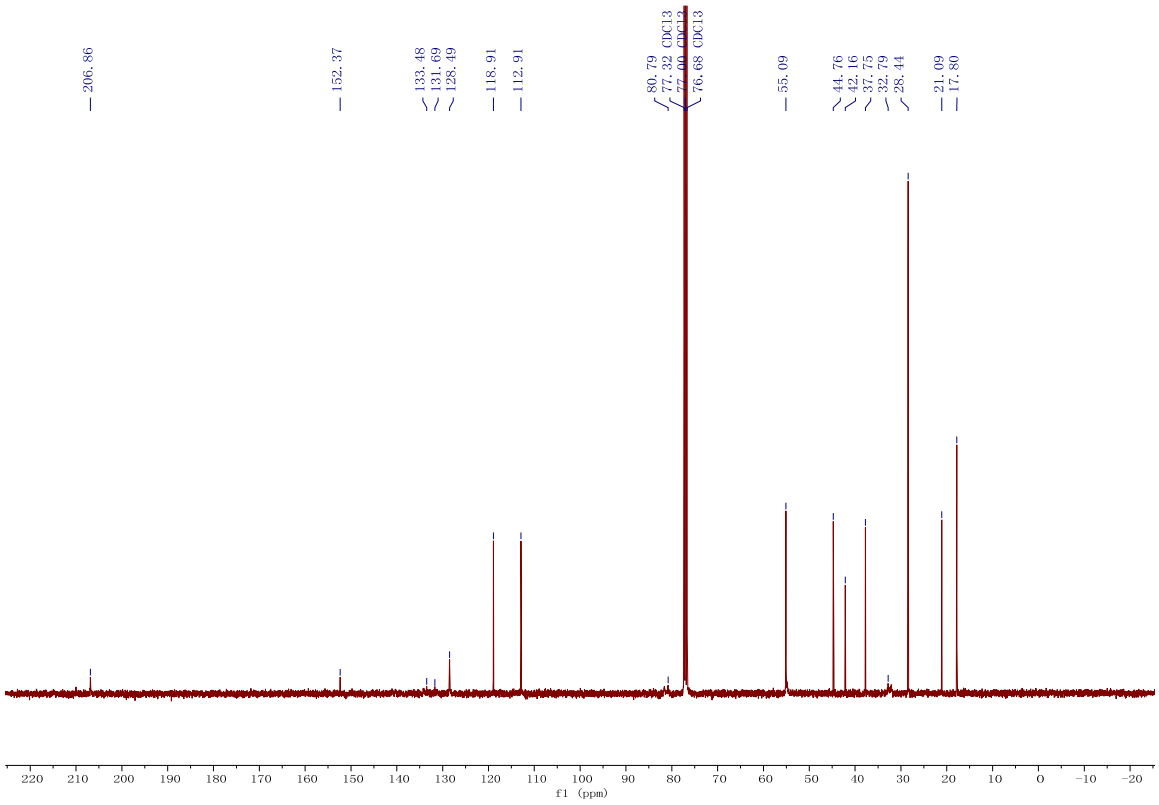

$^{13}$C-NMR for **9b** (minor) in $CDCl_3$, 101 MHz



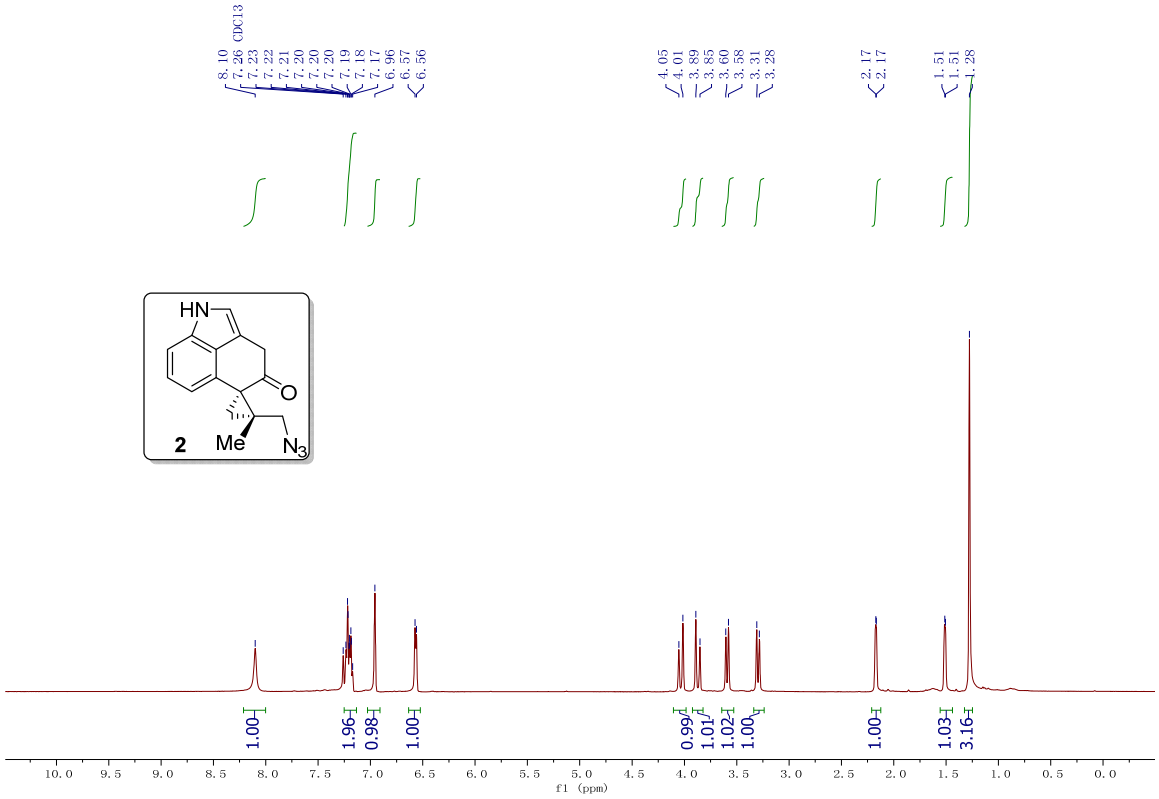
$^{1}$H-NMR for **10** in $CDCl_3$, 400 MHz



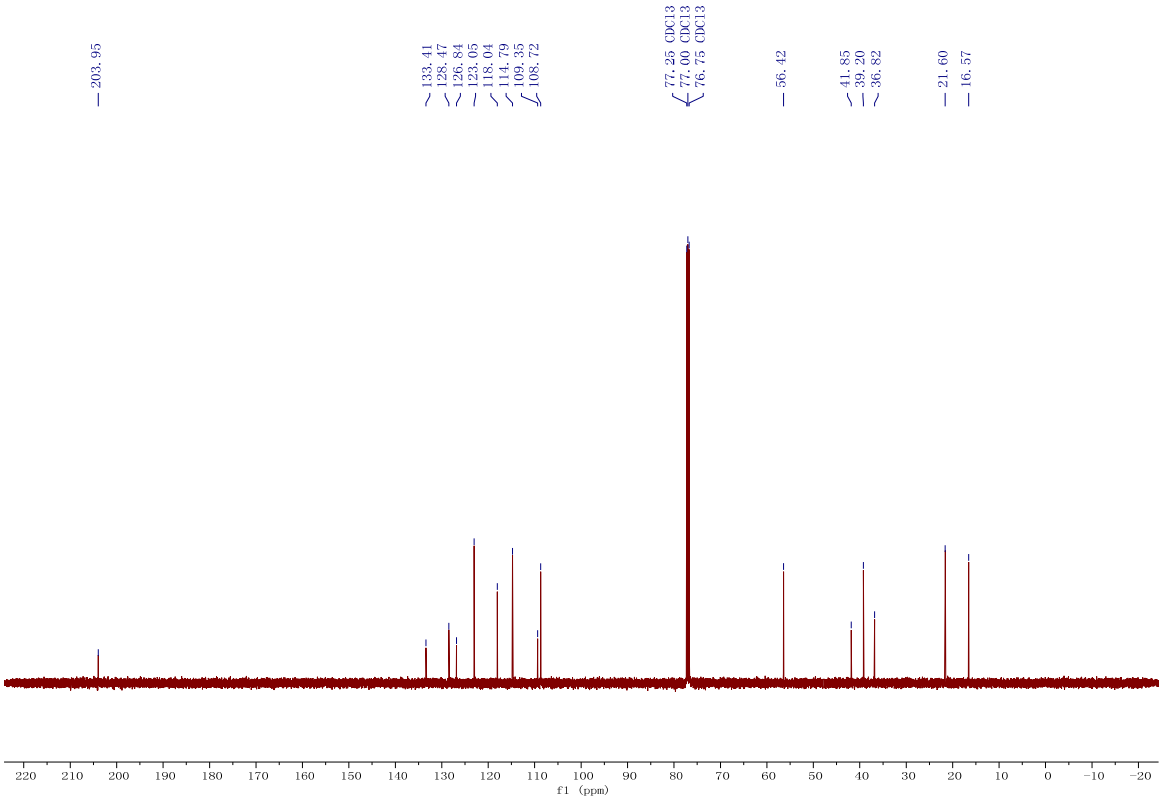

$^{13}$C-NMR for **10** in $CDCl_3$, 101 MHz



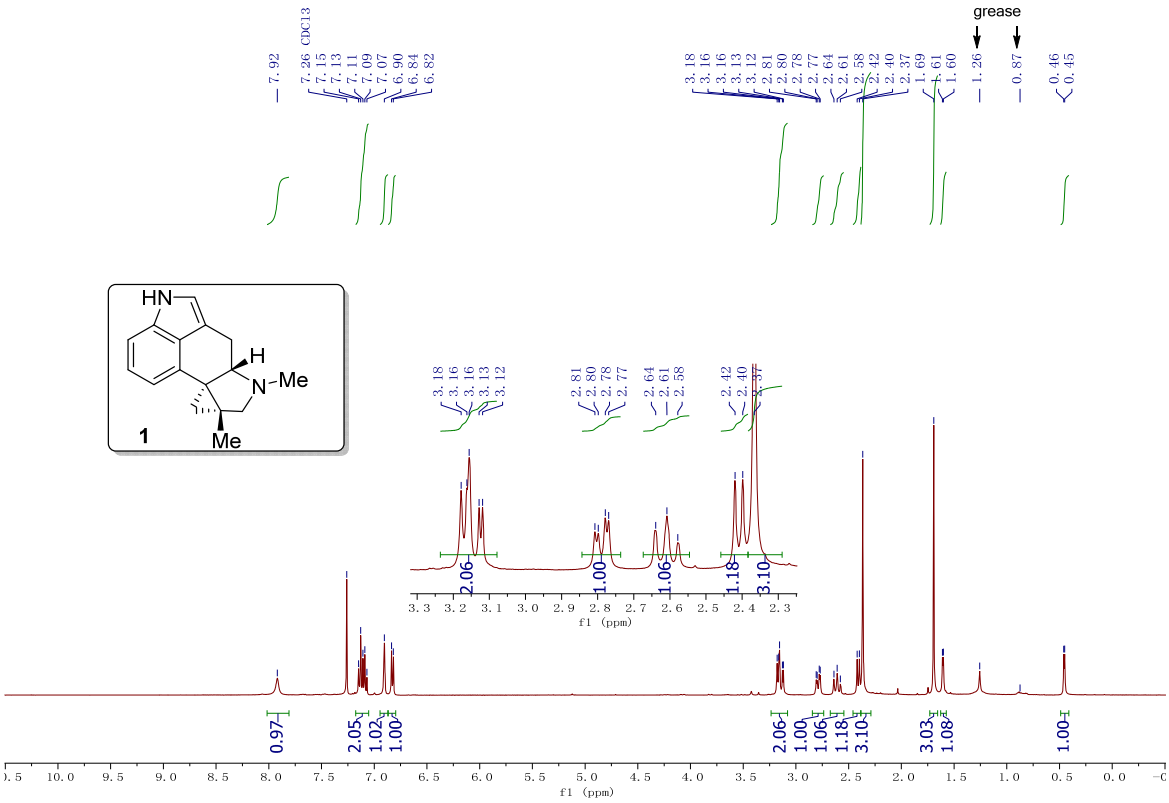
$^{1}$H-NMR for **2** in $CDCl_3$, 400 MHz



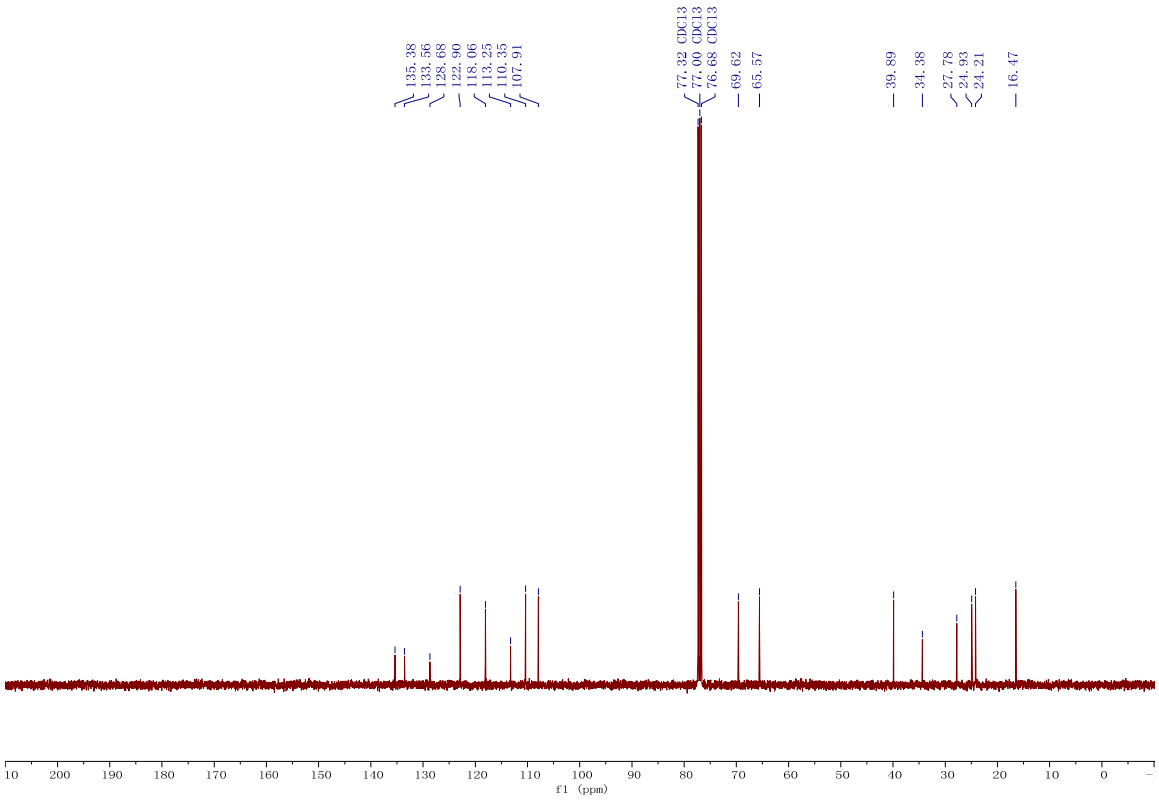

$^{13}$C-NMR for **2** in $CDCl_3$, 101 MHz



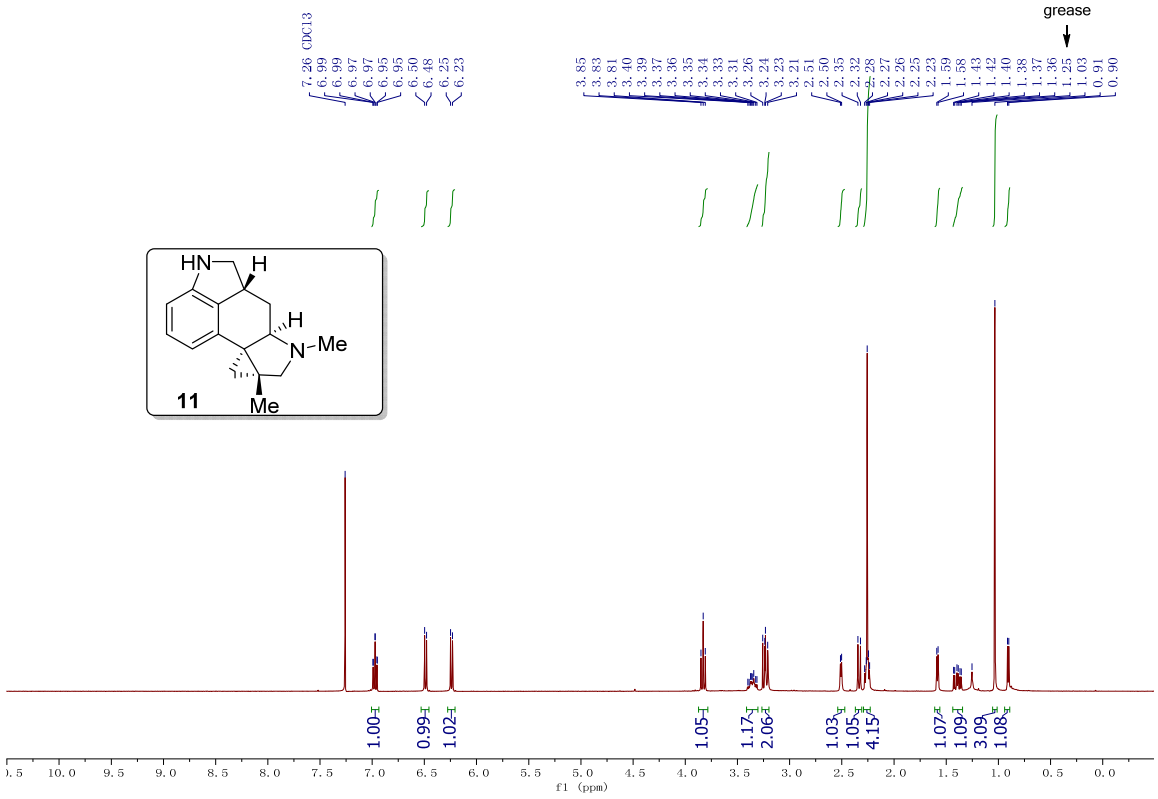
$^{1}$H-NMR for **1** in $CDCl_3$, 400 MHz



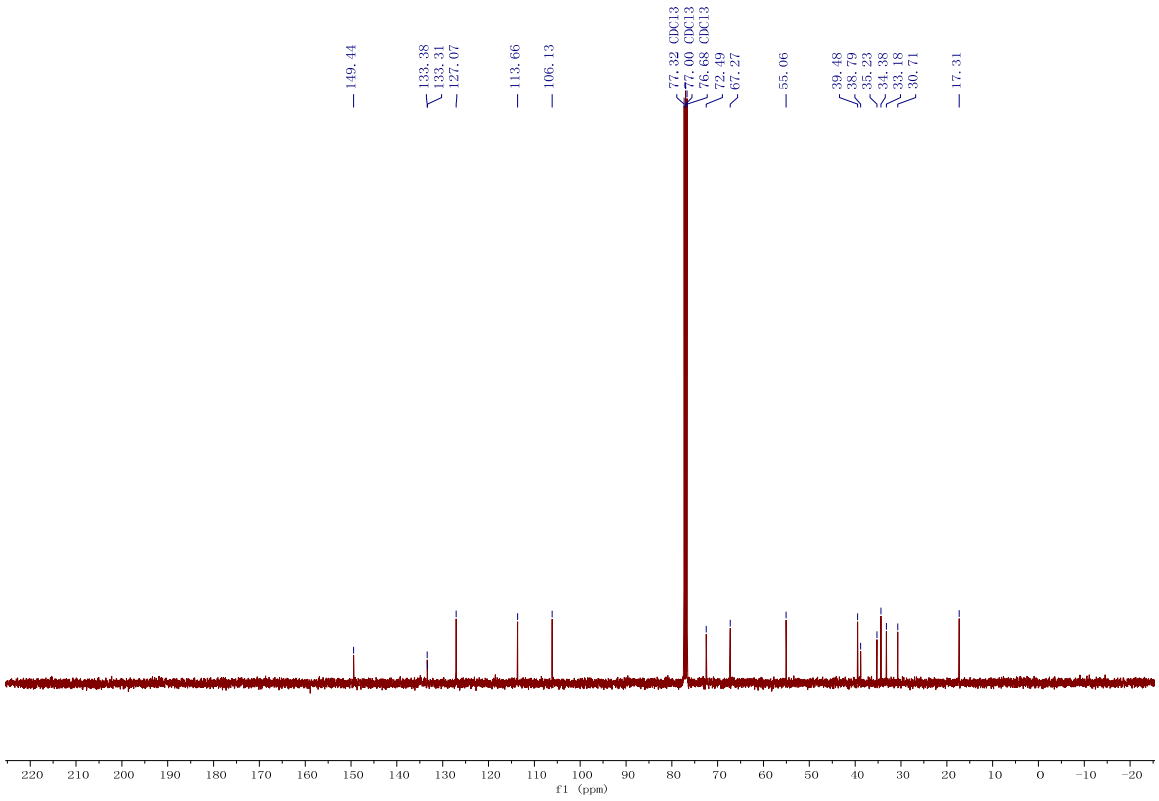

$^{13}$C-NMR for **1** in $CDCl_3$, 101 MHz



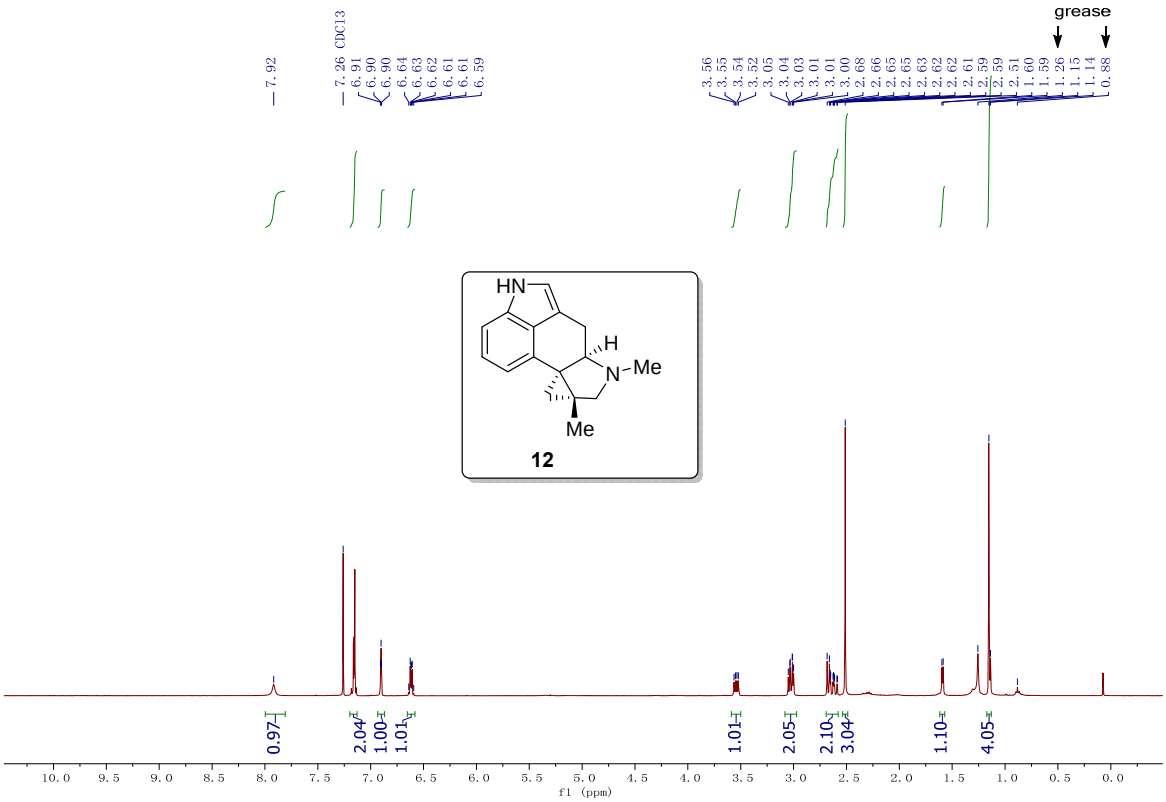
$^{1}$H-NMR for **11** in $CDCl_3$, 400 MHz



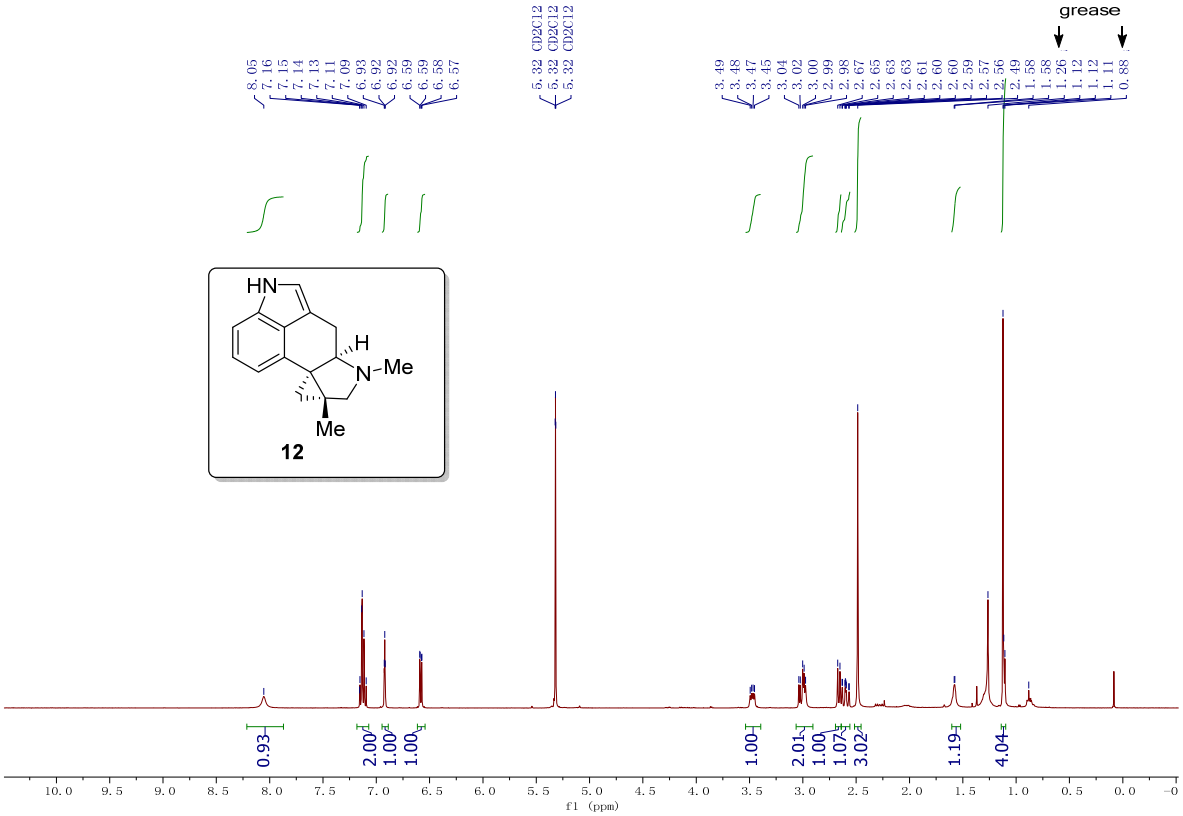

$^{13}$C-NMR for **11** in $CDCl_3$, 101 MHz



$^{1}$H-NMR for **12** in $CDCl_3$, 400 MHz




$^{1}$H-NMR for **12** in $CD_2Cl_2$, 400 MHz



$^{13}$C-NMR for **12** in $CDCl_3$, 101 MHz