Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Information

Synthetic progress toward the marine natural product zamamiphidin A

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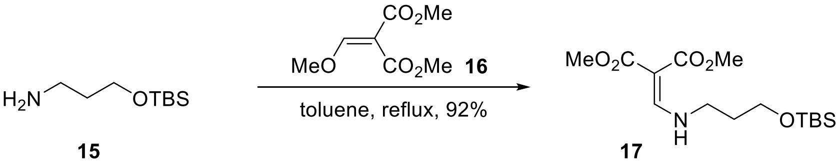
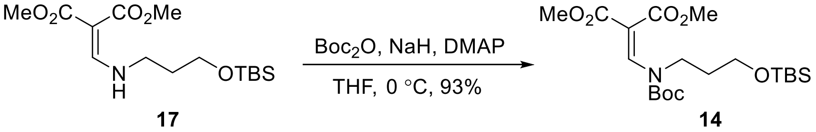
1. General Information

All reactions that require anhydrous conditions were performed in flame-dried glassware under Ar atmosphere and all reagents were purchased from commercial suppliers without further purification. Solvent purification was conducted according to Purification of Laboratory Chemicals 2nd edn (Perrin, D. D., Armarego, W. L. F. and Perrin, D. R., Pergamon Press: Oxford, 1980). Reactions were monitored by thin layer chromatography (TLC, 0.2 mm, HSGF254) supplied by Yantai Chemicals (China). Visualization was accomplished with UV light, exposure to iodine, stained with basic solution of $KMnO_4$. The products were purified by flash column chromatography on silica gel (200 – 300 meshes) from the Anhui Liangchen Silicon Material Company (China). ^1H NMR and ^{13}C NMR spectra were recorded on Varian INOVA-400/54 or Agilent DD2-600/54 instruments and calibrated by using residual undeuterated chloroform (δ, ^1H NMR = 7.260, ^{13}C NMR = 77.0)，undeuterated methanol (δ, ^1H NMR = 3.35, ^{13}C NMR = 49.8). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, br = broad, tt = triple triple, m = multiplet, and coupling constants (J) are reported in Hertz (Hz). Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum Two FT-IR spectrometer. High-resolution mass spectra (HRMS) were recorded on Bruker Apex IV FTMS or Agilent LC-MSD TOF ESI mass spectrometers. The specific optical rotation was obtained from Rudolph Research Analytical Autopol VI automatic polarimeter. LC/MS analysis was performed on HP Agilent 6420 Triple Quad LC/MS.

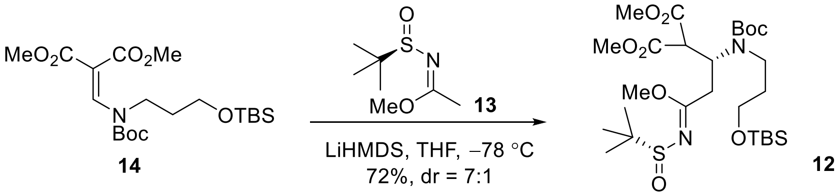
2. Experimental Procedures and Characterization Data



Synthesis of Compound 17: To a solution of **15**[1] (32.8 g, 0.173 mmol, 1.5 equiv) in toluene (500 mL) was added dimethyl methoxymethylenemalonate **16** (20.0 g, 0.115 mmol, 1.0 equiv). The reaction mixture was heated to reflux for 1 h and then evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 5:1, v/v) to yield compound **17** (35.0 g, 92%) as a colorless oil. **TLC**: (petroleum ether/EtOAc = 3:1, v/v) $R_f = 0.5$. **^{1}H NMR** (600 MHz, $CDCl_3$): *δ* 9.23 – 9.22 (m, 1H), 7.99 – 7.97 (d, *J* = 14.4 Hz, 1H), 3.73 (s, 3H), 3.65 (s, 3H), 3.62 (t, *J* = 5.4 Hz, 2H), 3.44 – 3.41 (q, *J* = 6.6 Hz, 2H), 1.76 – 1.72 (p, *J* = 6.0 Hz, 2H), 0.85 (s, 9H), 0.01 (s, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$): *δ* 169.5, 166.2, 160.4, 88.6, 59.1, 51.0, 50.8, 46.5, 33.0, 25.7, 18.1, –5.6. **IR** (neat): ν_{max} = 2950 (m), 2856 (w), 1715 (m), 1655 (s), 1610 (s), 1441 (s), 1201 (vs), 1075 (vs), 833 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{15}H_{30}NO_5Si$ $[M+H]^+$ 332.1888, found 332.1882.



Synthesis of Compound 14: Compound **17** (10.0 g, 30.2 mmol, 1.0 equiv) and DMAP (184 mg, 1.51 mmol, 0.05 equiv) were dissolved in THF (400 mL) at 0 °C under an argon atmosphere. NaH (2.42 g, 60% suspension in mineral oil, 60.4 mmol, 2.0 equiv) was added to the mixture in small portions. After being stirred for 20 min at 0 °C, Boc_2O (9.90 g, 45.3 mmol, 1.5 equiv) was added and the resulting mixture was stirred for 1 h at the same temperature. After the reaction was completed, saturated aqueous $NaHCO_3$ solution (200 mL) was added. The layers were separated, and the aqueous layers was extracted with CH_2Cl_2 (2 × 300 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 20:1, v/v) to yield **14** (12.1 g, 93%) as a colorless oil. **TLC**: (petroleum ether/EtOAc = 15:1, v/v) $R_f = 0.3$. **^{1}H NMR** (600 MHz, $CDCl_3$): *δ* 8.11 (s, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 3.58 – 3.54 (m, 4H), 1.75 – 1.71 (m, 2H), 1.49 (s, 9H), 0.85 (s, 9H), 0.01 (s, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$): *δ* 166.8, 165.9, 152.0, 140.7, 104.7, 83.7, 60.7, 52.4, 52.1, 43.9, 31.0, 27.9, 25.8, 18.2, –5.5. **IR** (neat): ν_{max} = 2952 (m), 2857 (w), 1725 (s), 1619 (s), 1472 (w), 1435 (s), 1232 (s), 1059 (vs), 832 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{20}H_{37}NNaO_7Si$ $[M+Na]^+$ 454.2232, found 454.2228.



Synthesis of Compound 12[2]: Under an argon atmosphere, LiHMDS (1 M in THF, 3.60 mL, 3.60 mmol, 1.6 equiv) was added to a solution of **13** (601 mg, 3.39 mmol, 1.5 equiv) in anhydrous THF (50 mL) at −78 °C and the reaction mixture was stirred at the same temperature for 20 min. Then a solution of **14** (974 mg, 2.26 mmol, 1.0 equiv) in anhydrous THF (5 mL) was added slowly. After being stirred at −78 °C for another 1 h, the reaction mixture was poured into saturated aqueous NH_4Cl solution (50 mL). The layers were separated, and the aqueous layers was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The dr value was determined by LC-MS analysis of the crude mixture (dr = 7:1). The residue was purified by silica gel flash column chromatography petroleum ether/EtOAc = 7:1, v/v) to yield the major isomer **12** (989 mg, 72%, a colorless oil) and the minor isomer **12b** (82 mg, 6%, a colorless oil).

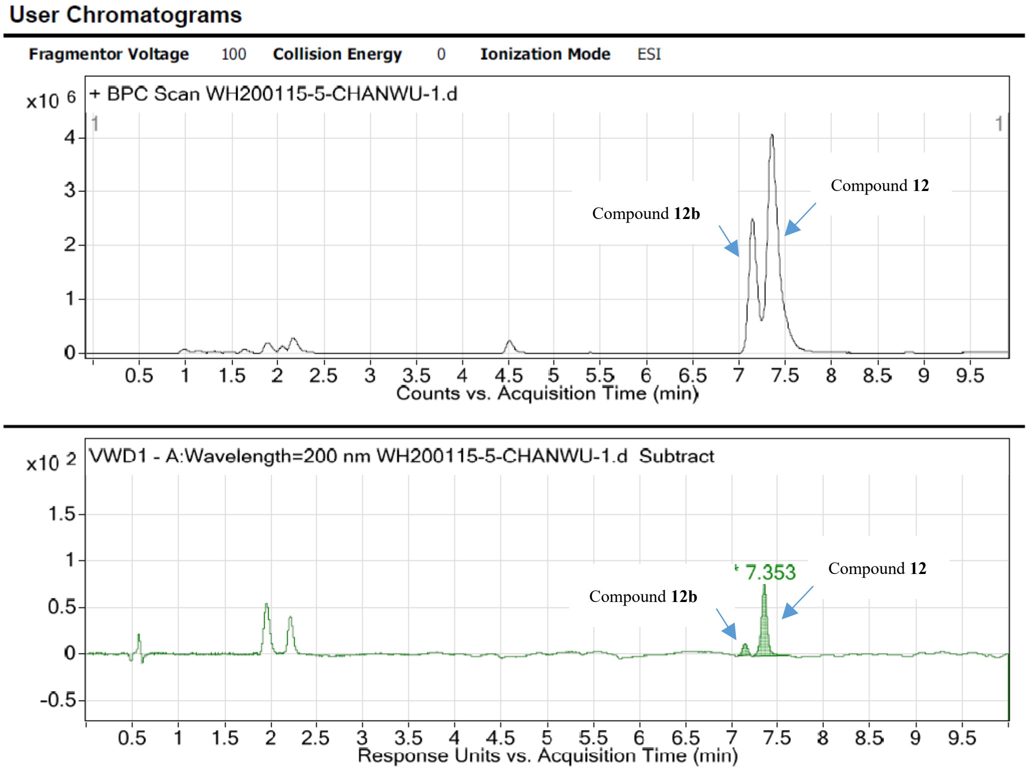
Major isomer 12: **TLC**: (petroleum ether/EtOAc = 6:1, v/v) R_f = 0.2. **Optical rotation**: $[\alpha]_D^{25}$= −77.4 (*c* = 0.34, $CHCl_3$). **^{1}H NMR** (600 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 4.37 – 4.16 (m, 2H), 3.76 – 3.69 (m, 9H), 3.62 – 3.54 (m, 3H), 3.14 – 3.09 (m, 2H), 2.89 – 2.76 (m, 1H), 1.79 – 1.65 (m, 2H), 1.55 (s, 5H), 1.42 (s, 4H), 1.19 (s, 9H), 0.87 (s, 9H), 0.01 (s, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 173.9, 173.6, 167.9, 167.8, 167.3, 154.5, 81.6, 79.9, 61.0/61.0, 57.7, 55.9, 55.7, 55.5, 54.3, 54.2, 52.9, 52.8, 52.6, 49.7, 35.6, 34.2, 32.3, 31.5, 28.3, 25.9, 21.9, 18.2, −5.4. **IR** (neat): ν_{max} = 2953 (m), 2857 (w), 1740 (s), 1697 (s), 1614 (s), 1289 (s), 1161 (vs), 1079 (vs), 834 (vs), 775 (vs) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{27}H_{52}N_2NaO_9SSi$ $[M + Na]^+$ 631.3055, found 631.3049.

Minor isomer 12b: **TLC**: (petroleum ether/EtOAc = 6:1, v/v) R_f = 0.2. **Optical rotation**: $[\alpha]_D^{25}$= −63.3 (*c* = 0.18, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 4.33 – 4.11 (m, 1H), 3.71 – 3.67 (m, 9H), 3.52 – 3.41 (m, 3H), 3.17 – 2.96 (m, 4H), 1.67 – 1.58 (m, 2H), 1.49 (s, 4H), 1.42 (s, 5H), 1.18 – 1.16 (m, 9H), 0.85 (s, 9H), 0.00 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 172.4, 167.9, 167.7, 167.5, 167.2, 154.6, 81.0, 80.0, 61.0, 60.9, 56.9, 56.2, 56.0, 54.4, 54.1, 52.8, 52.7, 52.5, 49.6, 35.6, 33.8, 32.2, 31.5, 28.2, 25.8, 21.8, 18.2, −5.5. **IR** (neat): ν_{max} = 2953 (m), 2857 (w), 1740 (s), 1615 (s), 1434 (s), 1226 (vs), 1161 (vs), 1079 (vs), 970 (s), 834 (vs), 775 (vs), 661 (w) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{27}H_{52}N_2NaO_9SSi$ $[M + Na]^+$ 631.3055, found 631.3050.

Analysis LC-MS of Michael addition of 14 with 13

Run Information:

Analytical HPLC: Aglient LC-MS QQQ 6420A; Column: Ultimate UHPLC XB-C18 (1.8 μm, 2.1*50 mm); Solvent: H_2O/CH_3CN (the gradient of CH_3CN is from 20% to 70% during 0–4.5 min, 70% to 95% during 4.5–9 min, 95% to 20% during 9–10 min); Flow = 0.4 mL/min; Detected by UV at 200 nm; Retention time for major isomer **12** and minor isomer **12b** in LC-MS: 7.353 min (compound **12**, major), 7.144 min (compound **12b**, minor); Base peak chromatogram: 7.388 min (compound **12**, major, $[M+H]^+$ = 608.8), 7.150 min (compound **12b**, minor, $[M+H]^+$ = 608.8)



User Chromatograms

Fragmentor Voltage 100 **Collision Energy** 0 **Ionization Mode** ESI

Integration Peak List

Peak	Start	RT	End	Height	Area	Area %
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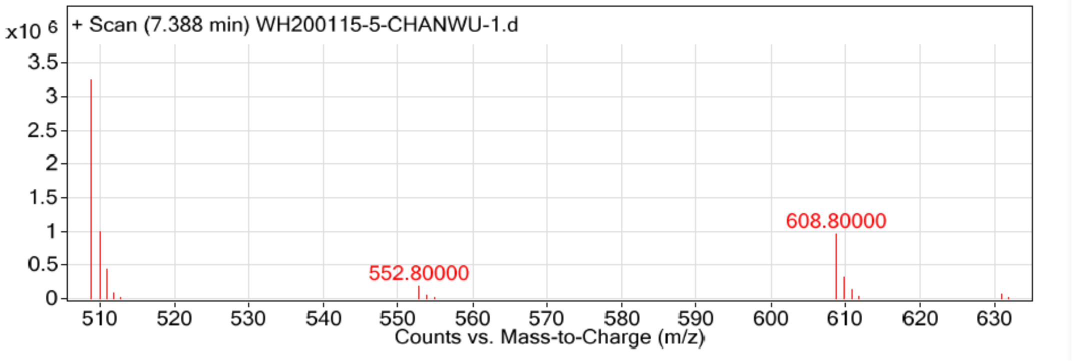
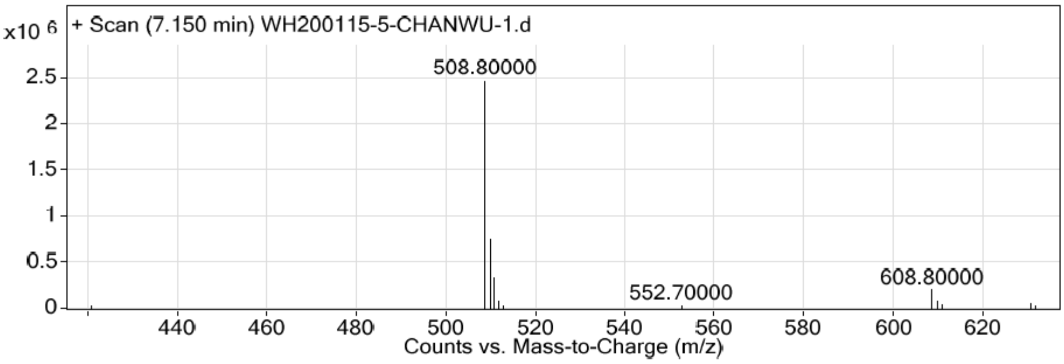
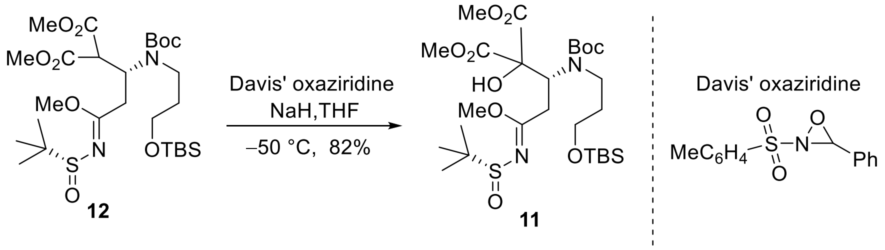
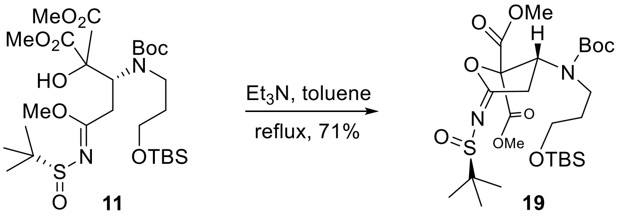




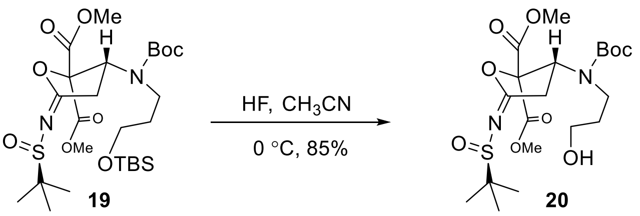


Synthesis of Compound 11: To a solution of compound **12** (10.0 g, 16.4 mmol, 1.0 equiv) in THF (300 mL) at −50 °C, NaH (984 mg, 60% suspension in mineral oil, 24.6 mmol, 1.5 equiv) was added in small portions under a nitrogen atmosphere. After being stirred at the same temperature for 20 minutes, a solution of Davis' oxaziridine (5.42 g, 19.7 mmol, 1.2 equiv) in THF (50 mL) was added slowly over 20 minutes. The resulting mixture was stirred for 12 h at −50 °C before being quenched with saturated aqueous ammonium chloride solution (aq. NH_4Cl, 200 mL). Then the mixture was diluted with CH_2Cl_2 (300 mL), and the layers was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 300 mL). The organic layers were combined and dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc =4:1, v/v) to afford **11** (8.39 g, 82% yield) as a colorless oil. **TLC**: (petroleum ether/EtOAc = 3:1, v/v) R_f = 0.2. **Optical rotation**: [α]

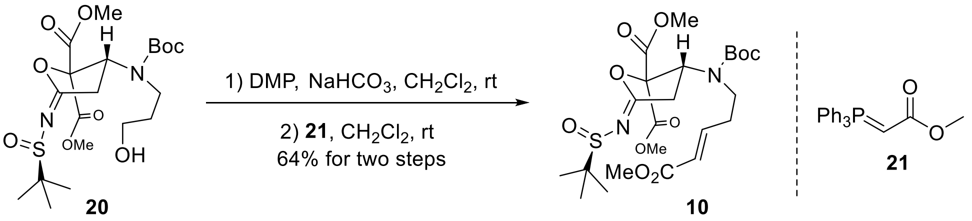
$^{25}_{D}$= −26.0 (*c* = 0.15, $CHCl_3$). **^{1}H NMR** (600 MHz, CD_3OD): *δ* 5.67 – 5.63 (m, 1H), 3.83 (s, 6H), 3.77 – 3.75 (m, 3H), 3.67 – 3.64 (m, 2H), 3.44 (brs, 2H), 3.23 (brs, 1H), 2.87 (brs, 1H), 1.87 (brs, 1H), 1.70 (brs, 1H), 1.50 (s, 9H), 1.26 (s, 9H), 0.96 (s, 9H), 0.11 (s, 6H). **^{13}C NMR** (150 MHz, CD_3OD, some signals exist as a pair due to the presence of amide rotamers): *δ* 177.3, 177.1, 171.6, 171.4, 157.9, 157.6, 84.5, 84.1, 82.3, 82.2, 65.9, 63.5, 62.8, 57.9, 57.7, 56.6, 56.0, 54.5, 54.2, 53.0, 44.1, 43.8, 34.6, 33.7, 32.6, 29.5, 27.3, 22.9, 20.0, −4.4. **IR** (neat): ν_{max} = 2953 (m), 2857 (w), 1747 (s), 1697 (s), 1434 (s), 1251 (vs), 1145 (vs), 1080 (vs), 834 (vs) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{27}H_{52}N_2NaO_{10}SSi$ [M + Na]$^+$ 647.3004, found 647.3000.



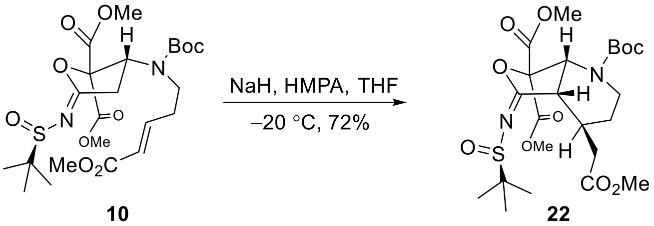
Synthesis of Compound 19: To a solution of **11** (10.0 g, 16.0 mmol, 1.0 equiv) in toluene (500 mL) was added Et_3N (22.2 mL, 160 mmol, 10.0 equiv). The reaction mixture was heated to reflux for 2 h. Then the mixture was concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc =5:1, v/v) to afford **19** (6.73 g, 71% yield) as a colorless oil. **TLC**: (petroleum ether/EtOAc = 1:1, v/v) R_f = 0.6. **Optical rotation**: [α] $^{25}_{D}$= −103.4 (*c* = 0.26, $CHC1_3$). **^{1}H NMR** (400 MHz, CD_3OD): *δ* 4.80 (brs, 1H, overlapped), 3.88 (s, 6H), 3.83 (s, 3H), 3.77 – 3.66 (m, 2H), 3.54 (brs, 1H), 3.39 – 3.22 (m, 3H, overlapped), 1.88 – 1.74 (m, 2H), 1.46 (s, 9H), 1.29 (s, 9H), 0.96 (s, 9H), 0.13 (s, 6H). **^{13}C NMR** (100 MHz, CD_3OD): *δ* 174.3, 168.6, 166.5, 157.1, 94.4, 82.9, 63.8, 62.3, 58.7, 55.5, 54.6, 50.0 (detected by DEPT 135), 38.5, 34.0, 29.4, 27.2, 23.0, 19.9, −4.4. **IR** (neat) ν_{max} = 2954 (m), 2857 (w), 1749 (s), 1668 (s), 1365 (s), 1250 (vs), 1164 (vs), 1068 (vs), 774 (vs) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{26}H_{48}N_2NaO_9SSi$ [M + Na]$^+$ 615.2742, found 615.2746.



Synthesis of Compound 20: To a solution of **19** (5.01 g, 8.45 mmol, 1.0 equiv) in CH_3CN (100 mL) was added HF (40% aq, 3.65 mL, 84.5 mmol, 10.0 equiv) slowly over 1 h at 0 °C. The reaction was stirred for 30 minutes at the same temperature before being quenched with saturated aqueous $NaHCO_3$ solution (50 mL) and diluted with water (50 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 200 mL). The organic layers were combined and dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/acetone =2:1, v/v) to afford compound **20** (3.43 g, 85% yield) as a white foam. **TLC**: (petroleum ether/ acetone = 2:1, v/v) R_f = 0.3. **Optical rotation**: $[\alpha]_D^{25} = -120.8$ (c = 0.24, $CHC1_3$). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 5.29 (brs, 1H), 3.80 (s, 6H), 3.59 – 3.48 (m, 3H), 3.18 (brs, 3H), 1.82 (brs, 1H), 1.67 (brs, 1H), 1.41 (s, 9H), 1.21(s, 9H). **^{13}C NMR** (150 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 175.4, 174.2, 169.1, 166.3, 164.5, 164.1, 154.7, 91.3, 89.3, 88.8, 82.8, 81.0, 61.0, 59.5, 58.8, 57.2, 56.9, 54.0, 53.3, 47.4, 44.3, 35.6, 32.9, 32.4, 32.0, 31.8, 28.1, 21.8. **IR** (neat): ν_{max} = 3416 (br), 2957 (m), 1748 (s), 1655 (vs), 1434 (m), 1366 (s), 1209 (s), 1161 (vs), 1061 (vs), 777 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{20}H_{34}N_2NaO_9S$ $[M + Na]^+$ 501.1877, found 501.1878.

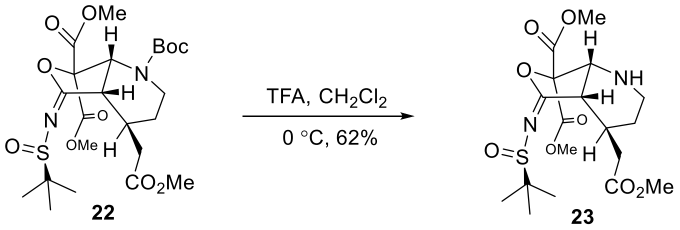


Synthesis of Compound 10: To a solution of compound **20** (2.00 g, 4.18 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) was added Dess-Martin periodinane (2.66 g, 6.27 mmol, 1.5 equiv) and $NaHCO_3$ (702 mg, 8.36 mmol, 2.0 equiv). The mixture was stirred at room temperature for 1 h. After consumption of **20**, saturated aqueous Na_2SO_3 solution (30 mL) was added. The resulting mixture was diluted with water, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was filtered through a short pad of silica gel (eluted with petroleum ether/acetone =2:1, v/v) and concentrated in vacuo. The residue was dissolved in dry CH_2Cl_2 (20 mL) under a nitrogen atmosphere, and **21** (2.24 g, 6.69 mmol, 1.6 equiv) was added at room temperature. After being stirred for 1 h, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/acetone =2.5:1, v/v) to afford **10** (1.42 g, 64% yield) as a colorless oil. **TLC**: (petroleum ether/ acetone = 2:1, v/v) $R_f = 0.4$. **Optical rotation**: $[\alpha]_D^{25} = -114.3$ ($c = 0.28$, CHC1$_3$). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 6.87 – 6.82 (dt, J = 15.6, 7.8 Hz, 1H), 5.87 – 5.84 (d, J = 15.0 Hz, 1H), 5.10 – 4.56 (m, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 3.71 (s, 3H), 3.58 – 3.55 (m, 1H), 3.25 – 3.12 (m, 3H), 2.43 (brs, 2H), 1.40 (s, 9H), 1.23(s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 170.7, 168.7, 166.5, 164.8, 154.3, 145.0, 122.9, 91.0, 87.1, 81.4, 61.0, 57.6, 56.5, 54.1, 53.3, 51.5, 49.2, 47.7, 35.4, 32.2, 28.0, 21.7. **IR** (neat): ν_{max} = 2956 (m), 1748 (s), 1657 (vs), 1435 (s), 1366 (s), 1249 (s), 1157 (vs), 1069 (vs), 773 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{23}H_{36}N_2NaO_{10}S$ $[M + Na]^+$ 555.1983, found 555.1980.

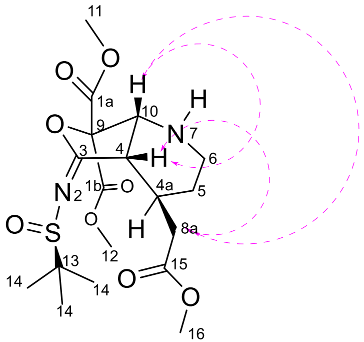


10 **22**

Synthesis of Compound 22: Under a nitrogen atmosphere, HMPA (0.53 mL, 3.00 mmol, 3.0 equiv) was added to a solution of **10** (530 mg, 1.00 mmol, 1.0 equiv) in THF (5 mL) at −20 °C. Then NaH (160 mg, 60% suspension in mineral oil, 4.00 mmol, 4.0 equiv) was added in small portions. The reaction mixture was stirred at this temperature for 1 h before being quenched with saturated aqueous $NaHCO_3$ solution (10 mL) and diluted with CH_2Cl_2 (10 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The organic layers were combined and dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc =1:1, v/v) to afford **22** (382 mg, 72% yield) as a white foam. **TLC**: (petroleum ether/EtOAc = 1:1, v/v) $R_f = 0.2$. **Optical rotation**: $[\alpha]_D^{25} = +27.5$ ($c = 0.32$, CHC1$_3$). **^{1}H NMR** (400 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 5.63 – 5.57 (m, 1H), 4.09 – 4.05 (m, 0.5 H), 3.85 (s, 3H), 3.82 (s, 3H), 3.77 – 3.72 (m, 0.5 H), 3.68 (s, 3H), 3.05 – 2.91 (m, 2H), 2.66 – 2.60 (m, 0.5H), 2.48 – 2.42 (m, 0.5H), 2.36 – 2.21 (m, 2H), 1.88 – 1.84 (m, 1H), 1.45 (s, 9H), 1.33 – 1.29 (m, 1H), 1.24 (s, 9H). **^{13}C NMR** (100 MHz, CDCl$_3$, some signals exist as a pair due to the presence of amide rotamers): δ 171.9, 171.8, 169.4, 165.6, 165.1, 154.7, 154.2, 89.0, 88.8, 81.9, 81.3, 56.7, 56.6, 55.7, 55.5, 54.0, 53.7, 53.4, 51.8, 42.6, 42.5, 39.8, 38.5, 38.4, 38.3, 31.6, 30.5, 28.1, 26.8, 26.7, 21.9. **IR** (neat): $\nu_{\max}$ = 2955 (m), 1739 (s), 1697 (s), 1436 (s), 1365 (s), 1259 (s), 1161 (vs), 1087 (vs), 799 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{23}H_{36}N_2NaO_{10}S$ [M + Na]$^+$ 555.1983, found 555.1987.



Synthesis of Compound 23: To a solution of **22** (53 mg, 0.10 mmol) in CH$_2$Cl$_2$ (5 mL) was added TFA (1 mL) at 0 ºC. After being stirred for 30 minutes at the same temperature, the mixture was diluted with CH$_2$Cl$_2$ (10 mL). The pH of the mixture was adjusted to 10 by adding aqueous saturated NaHCO$_3$ solution. The layers were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 50 mL). The organic layers were combined and dried over Na$_2$SO$_4$, filtered, and evaporated in vacuo. The residue was purified by silica gel flash column chromatography (petroleum ether/acetone =2:1, v/v) to afford **23** (27 mg, 62 % yield) as a colorless oil. **TLC**: (petroleum ether/acetone = 2:1, v/v) R$_f$ = 0.3. **Optical rotation**: $[\alpha]_D^{25}$= +20.7 (*c* = 0.30, CHC1$_3$). **^{1}H NMR** (400 MHz, CDCl$_3$): δ 4.15 – 4.14 (m, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.67 (s, 3H), 3.06 (s, 1H), 2.90 (brs, 1H), 2.77 – 2.75 (m, 2H), 2.49 – 2.48 (m, 2H), 1.75 – 1.70 (m, 1H), 1.44 – 1.41 (m, 1H), 1.25 (s, 9H). **^{13}C NMR** (150 MHz, CDCl$_3$): δ 171.9, 168.7, 165.2, 164.8, 90.9, 56.9, 56.6, 54.0, 53.5, 51.8, 45.5, 38.7, 36.8, 27.4, 25.8, 21.8. **IR** (neat): $\nu_{\max}$ = 3442 (br), 2924 (m), 1737 (s), 1659 (vs), 1437 (s), 1246 (s), 1173 (s), 1064 (vs), 788 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{18}H_{28}N_2NaO_8S$ [M + Na]$^+$ 455.1459, found 455.1455. *NOTE: The structure of* ***23*** *was confirmed by 2D NMR experiments, see Table S1. The relative stereochemistry of* ***23*** *was established by NOE experiments.*

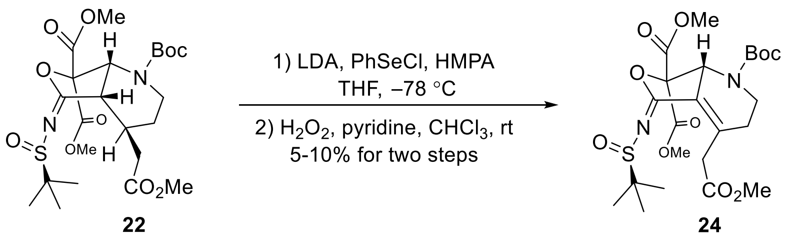


23

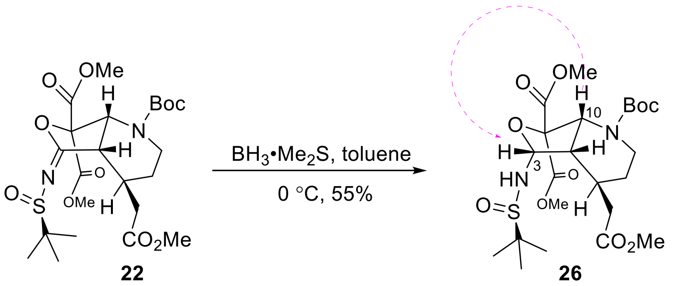
Table S1. 2D NMR Data for Compound 23

Atom	^{1}H Shift (ppm)	^{1}H mult.	*J* Values (Hz)	^{13}C Shift (ppm)	^{13}C mult.[a]	COSY[b]	HMBC[c]
1a	--	--	--	164.8	C	--	--
1b	--	--	--	165.2	C	--	--
3	--	--	--	168.7	C	--	--
4	3.06	s	--	45.5	CH	H-10	C3, C4a, C5, C10, C8a,
4a	2.90	brs	--	27.4	CH	H-8a	--
5	1.75 – 1.70, 1.44 – 1.41	m	--	25.8	CH$_2$	H-6	C4a, C6, C8a
6	2.77 – 2.75	m	--	38.7	CH$_2$	H-5	C4a, C5, C10
8a	2.49 – 2.48	m	--	36.8	CH$_2$	H-4a	C4, C4a, C5, C15
9	--	--	--	90.9	C	--	--
10	4.15 – 4.14	m	--	56.6	CH	H-4	C3, C6, C9
11	3.85	s	--	53.5	CH$_3$	--	C1a
12	3.82	s	--	54.0	CH$_3$	--	C1b
13	--	--	--	56.9	C	--	--
14	1.25	s	--	21.8	CH$_3$	--	C13
15	--	--	--	171.9	C	--	--
16	3.67	s	--	51.8	CH$_3$	--	C15

(a) Determined by HMQC correlation; (b) protons that correlate to protons; (c) carbons that correlate to protons.

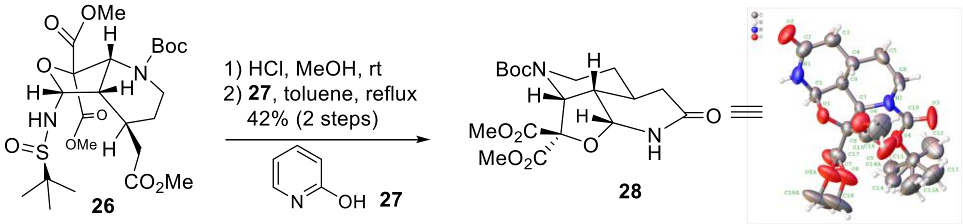


Synthesis of Compound 24: Under a nitrogen atmosphere, LDA (282 μL, 1 M in THF, 0.282 mmol, 1.5 equiv) was added to a solution of **22** (100 mg, 0.188 mmol, 1.0 equiv) and HMPA (100 μL, 0.564 mmol, 3.0 equiv) in anhydrous THF (10 mL) at −78 °C. After the mixture was stirred at −78 °C for 20 min, a solution of phenylselenenyl chloride (47.5 mg, 0.244 mmol, 1.3 equiv) in anhydrous THF (2 mL) was added dropwise. The resulting mixture was stirred at −78 °C for 1 h before being quenched with water. The mixture was warmed to rt and the layers separated. The aqueous layers were extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude product was dissolved in $CHCl_3$ (10 mL). Then pyridine (30 μL, 0.376 mmol, 2.0 equiv) and H_2O_2 (50 μL, 0.50 mmol, 2.6 equiv) was added sequentially at room temperature. After the reaction mixture was stirred for 1 h, saturated aqueous $NaHCO_3$ solution (10 mL) was added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were combined and dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/ EtOAc =2:1, v/v) to afford **24** (5-10 mg, 5-10% yield) as a white foam. *Note: the yield and reproducibility of compound **24** were poor.*

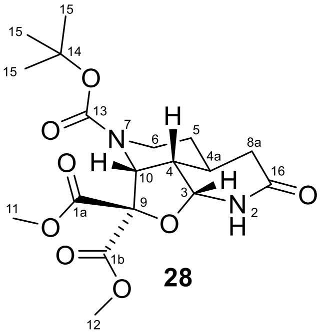


Synthesis of Compound 26: Under an argon atmosphere, $BH_3 \cdot Me_2S$ (12 μL, 0.12 mmol, 1.2 equiv) was added slowly to a solution of **22** (53 mg, 0.10 mmol, 1.0 equiv) in toluene (10 mL) at 0 °C. After being stirred for 30 min, the reaction was quenched with methanol (5 mL) and diluted with water (20 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The organic layers were combined and dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/acetone =2:1, v/v) to afford **26** (29 mg, 55% yield) as a white foam. **TLC**: (petroleum ether/acetone = 2:1, v/v) R_f = 0.2. **Optical rotation**: $[\alpha]_D^{25}$= −23.5 (*c* = 0.26, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 5.83 – 5.76 (m, 1H), 5.35 – 5.31 (m, 1H), 4.60 – 4.57 (m, 0.3H), 4.41 – 4.38 (m, 0.7H), 4.06 – 4.02 (m, 0.7H), 3.89 – 3.87 (m, 0.3H), 3.83 (s, 3H), 3.78 (s, 3H), 3.67 (s, 3H), 2.55 – 2.50 (m, 1H), 2.39 – 2.32 (m, 1H), 2.27 – 2.08 (m, 2H), 2.04 – 1.93 (m, 1H), 1.84 – 1.76 (m, 1H), 1.46 – 1.45 (m, 9H), 1.19 – 1.18 (m, 10H). **^{13}C NMR** (100 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 171.7, 171.6, 169.8, 169.5, 167.8, 167.7, 154.9, 92.2, 84.8, 84.7, 81.2, 80.6, 57.8, 57.5, 56.2, 53.9, 53.8, 53.1, 53.0, 51.7, 48.2, 48.0, 40.3, 39.3, 39.2, 31.6, 31.1, 28.4, 28.3, 28.2, 22.4, 22.3. **IR** (neat): $\nu_{\max}$ = 2955 (m), 1739 (vs), 1697 (s), 1436 (s), 1365 (s), 1259 (s), 1087 (s), 799 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{23}H_{38}N_2NaO_{10}S$ $[M + Na]^+$ 557.2139, found 557.2142. *The relative stereochemistry of **26** was established by NOE experiments.*



Synthesis of Compound 28: To a solution of **26** (54 mg, 0.10 mmol, 1.0 equiv) in dry methanol (10 mL) was added HCl (0.30 mL, 1.2 mmol, 4 M in dioxane, 12.0 equiv) under an argon atmosphere. The reaction mixture was stirred for 3 h at this temperature before being quenched with aqueous saturated $NaHCO_3$ solution, and the pH of the mixture was adjusted to 10. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The organic layers were combined and dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The resulting crude product was dissolved in toluene (20 mL) and 2-hydroxypyridine (**27**) (10 mg, 0.10 mmol, 1.0 equiv) was added. The reaction mixture was heated to reflux for 3 h. Then the mixture was concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/Acetone =2:1, v/v) to afford **28** (17 mg, 42% yield for two steps) as a white solid. **TLC**: (petroleum ether/acetone = 1:1, v/v) R_f = 0.4. **Optical rotation**: $[\alpha]_D^{25}$= +27.6 (*c* = 0.25, $CHCl_3$). **M. p.**: 216 – 218 ºC. **^{1}H NMR** (400 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 6.30 (s, 1H), 5.79 – 5.65 (m, 1H), 5.30 – 5.28 (m, 0.2H), 5.27 – 5.25 (m, 0.8H), 4.10 – 4.05 (m, 0.8H), 3.97 – 3.93 (m, 0.2H), 3.82 – 3.81 (m, 6H), 2.64 – 2.43 (m, 2H), 2.18 – 1.99 (m, 3H), 1.74 – 1.64 (m, 1H), 1.48 – 1.45 (m, 9H), 1.33 – 1.17 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 170.9, 168.3, 167.5, 155.1, 83.8/83.8, 83.5, 81.2, 80.7, 58.2, 57.6, 53.6, 53.4, 53.3, 53.2, 41.4, 41.3/41.3, 40.4, 37.3, 37.2, 28.3, 28.1, 28.0, 27.3, 27.2. **IR** (neat): $\nu_{\max}$ = 2918 (m), 1741 (vs), 1694 (vs), 1406 (s), 1343 (s), 1262 (vs), 1068 (vs), 801 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{18}H_{26}N_2NaO_8$ [M + Na]$^+$ 421.1581, found 421.1581. *NOTE: The structure of **30** was confirmed by 2D NMR experiments, see Table S2. The relative stereochemistry of **30** was established by X-ray crystallographic analysis.* ***X-ray crystallographic data**: see part 5 of supporting information.*

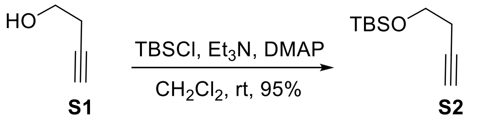


28

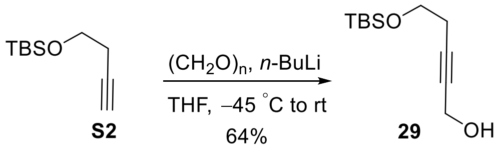
Table S2. 2D NMR Data for Compound 28

Atom	^{1}H Shift (ppm)	^{1}H mult.	*J* Values (Hz)	^{13}C Shift (ppm)	^{13}C mult.^{a}	COSY^b	HMBC^c
1a	--	--	--	168.3	C	--	--
1b	--	--	--	167.5	C	--	--
2	6.30	s	--	--	NH	--	--
3	5.30 – 5.25	m	--	83.5	CH	H-4	C16
4	2.18 – 1.99	m	--	41.4, 41.3	CH	H-10	C3, C10
4a	2.18 – 1.99	m	--	27.3, 27.2	CH	H-5	C8a
5	1.74 – 1.64, 1.33 – 1.17	m	--	28.0	CH_2	H-6, H-4a	C4, C4a, C8a
6	4.10 – 3.93, 2.64 – 2.43	m	--	41.3, 40.4	CH_2	H-5	C4a, C5, C10
8a	2.64 – 2.43, 2.18 – 1.99	m	--	37.3, 37.2	CH_2	H-4a	C4, C4a, C5, C16
9	--	--	--	83.8, 83.8	C	--	--
10	5.79 – 5.65	m	--	58.2, 57.6	CH	H-4	C1a, C1b, C3, C4, C4a, C6, C13,
11	3.82 – 3.81	m	--	53.6, 53.4	CH_3	--	C1a
12	3.82 – 3.81	m	--	53.3, 53.2	CH_3	--	C1b
13	--	--	--	155.1	C	--	--
14	--	--	--	81.2, 80.7	C	--	--
15	1.48 – 1.45	m	--	28.3, 28.1	CH3	--	C14
16	--	--	--	170.9	C	--	--

(a) Determined by HMQC correlation; (b) protons that correlate to protons; (c) carbons that correlate to protons

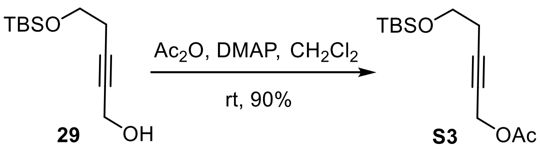


Synthesis of Compound S2[3]: To a solution of but-3-yn-1-ol **S1** (21.6 mL, 0.285 mol, 1.0 equiv), Et_3N (47.5 mL, 0.342 mol, 1.2 equiv), and DMAP (3.48 g, 28.5 mmol, 0.1 equiv) in dry CH_2Cl_2 (500 mL) was added TBSCl (51.5 g, 0.342 mol, 1.2 equiv) in small portions at room temperature. The reaction mixture was stirred for 3 h before being quenched with water (300 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 200 mL). The combined organic layers were dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc =20:1, v/v) to afford **S2** (50.0 g, 95% yield) as a colorless liquid. **TLC**: (petroleum ether/EtOAc = 9:1, v/v) $R_f = 0.9$. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.74 (t, J = 7.2 Hz, 2H), 2.42 – 2.38 (dt, J = 7.2, 2.4 Hz, 2H), 1.95 (t, J = 2.4 Hz, 1H), 0.90 (s, 9H), 0.07 (s, 6H).**^{13}C NMR** (100 MHz, $CDCl_3$): δ 81.5, 69.3, 61.7, 25.9, 22.8, 18.3, –5.3. **IR** (neat): ν_{max} = 3314 (m), 2960 (s), 2930 (s), 1472 (s), 1258 (s), 836 (s), 749 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{10}H_{20}NaOSi$ $[M + Na]^+$ 207.1176, found 207.1181.

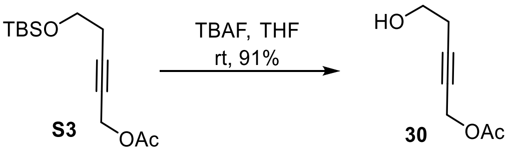


Synthesis of Compound 29[3]: To a solution of **S2** (11.0 g, 0.060 mol, 1.0 equiv) in THF (500 mL) at −45 °C under nitrogen was added dropwise *n*-BuLi (26.5 mL, 0.066 mol, 2.5 M in hexane, 1.1 equiv). After being stirred at −45 °C for 15 min, paraformaldehyde (5.4 g, 0.18 mol, 3.0 equiv) was added. The resulting reaction mixture was warmed to ambient temperature and stirred for 3 h. After the reaction was completed, the reaction was quenched with saturated aqueous $NaHCO_3$ solution (200 mL) and diluted with CH_2Cl_2 (200 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 200 mL). The combined organic layers were dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc =5:1, v/v) to afford **29** (8.2 g, 64% yield) as a colorless oil. **TLC**: (petroleum ether/EtOAc = 5:1, v/v) $R_f = 0.3$. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 4.24 – 4.23 (m, 2H), 3.72 (t, J = 7.2 Hz, 2H), 2.43 (t, J = 7.2 Hz, 2H), 1.65 (t, J = 6.0 Hz, 1H), 0.89 (s, 9H), 0.07 (s, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 83.4, 79.5, 61.8, 51.3, 25.9, 23.1, 18.3, –5.3.

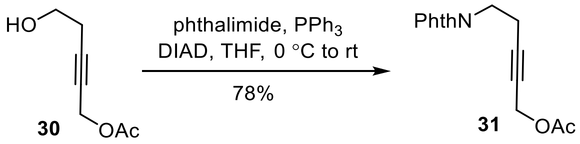
IR (neat): $\nu_{\max}$ = 3339 (br), 2929 (s), 2857 (s), 1472 (m), 1256 (s), 1102 (vs), 836 (vs) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{11}H_{22}NaO_2Si$ [M+Na]$^+$ 237.1281, found 237.1272.



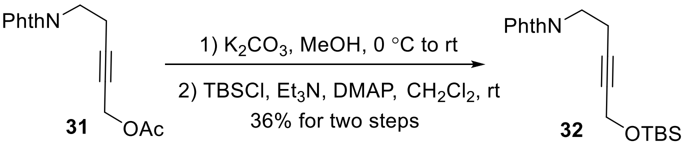
Synthesis of Compound S3: To a solution of alcohol **16** (10.0 g, 46.7 mmol, 1.0 equiv), Et_3N (13.0 mL, 93.4 mmol, 2.0 equiv), and DMAP (0.114 g, 0.934 mmol, 0.02 equiv) in anhydrous CH_2Cl_2 (100 mL) was added dropwise acetic anhydride (5.30 mL, 56.4 mmol, 1.21 equiv) at room temperature under Ar atmosphere. After the mixture was stirred for 2 h at the same temperature, the reaction was quenched with water (100 mL) and diluted with CH_2Cl_2 (100 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 20:1, v/v) to yield compound **S3** (10.8 g, 90% yield) as a colorless oil. **TLC**: (petroleum ether/EtOAc = 10:1, v/v) R_f = 0.5. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 4.62 (s, 2H), 3.69 (t, *J* = 7.2 Hz, 2H), 2.42 – 2.39 (m, 2H), 2.05 (s, 3H), 0.86 (s, 9H), 0.04 (s, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.2, 84.5, 75.0, 61.5, 52.6, 25.8, 23.1, 20.7, 18.2, −5.4. **IR** (neat) $\nu_{\max}$ = 2953 (m), 2930 (m), 2857 (m), 1747 (s), 1219 (vs), 1101 (vs), 1023 (s), 833 (vs), 775 (vs) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{13}H_{24}NaO_3Si$ [M + Na]$^+$ 279.1387, found 279.1382.



Synthesis of Compound 30: TBAF (47.0 mL, 1 M in THF, 47.0 mmol, 1.2 equiv) was added to a solution of compound **S3** (10.0 g, 39.0 mmol, 1.0 equiv) in THF (100 mL) at room temperature. The reaction mixture was stirred at the same temperature for 1 h and quenched with water (100 mL). The layers were separated and the aqueous layers was extracted with EtOAc (3× 200 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 3:2 v/v) to afford alcohol **30** (5.05 g, 91% yield) as a colorless oil. **TLC**: (petroleum ether/EtOAc = 3:2, v/v) R_f = 0.3. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.65 (t, *J* = 2.0 Hz, 2H), 3.73 – 3.68 (q, *J* = 6.0 Hz, 2H), 2.50 – 2.46 (tt, *J* = 2.0, 6.4 Hz, 2H), 2.18 (t, *J* = 6.0 Hz, 1H), 2.07 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.4, 84.1, 75.9, 60.7, 52.6, 23.1, 20.7. **IR** (neat): $\nu_{\max}$ = 3418 (br), 2945 (w), 2237 (w), 1737 (s), 1378 (s), 1220 (vs), 1021 (vs), 966 (s), 847 (w) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_7H_{10}NaO_3$ [M + Na]$^+$ 165.0522, found 165.0521.

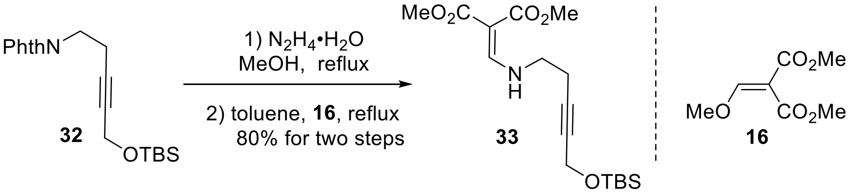


Synthesis of Compound 31: To a solution of compound **30** (6.00 g, 42.2 mmol, 1.0 equiv), phthalimide (7.45 g, 50.6 mmol, 1.2 equiv) and PPh_3 (13.3 g, 50.6 mmol, 1.2 equiv) in fresh distilled THF (100 mL) was added DIAD (10.0 mL, 50.6 mmol, 1.2 equiv) dropwise at 0 °C under Ar atmosphere. The resulting mixture was then warmed to ambient temperature and stirred for 1 h before removal of the solvent under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 4:1, v/v) to afford **31** (8.94 g, 78% yield) as a white solid. **TLC**: (petroleum ether/EtOAc = 2:1, v/v) $R_f = 0.6$. **M. p.**: 76 – 78 ºC. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.86 – 7.82 (m, 2H), 7.74 – 7.69 (m, 2H), 4.58 (t, *J* = 2.0 Hz, 2H), 3.85 (t, *J* = 7.2 Hz, 2H), 2.65 – 2.60 (tt, *J* = 7.2, 2.0 Hz, 2H), 2.04 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.1, 167.9, 134.0, 132.0, 123.3, 83.2, 76.0, 52.4, 36.4, 20.7, 18.7. **IR** (neat): $\nu_{\max}$ = 2945 (w), 1745 (s), 1705 (vs), 1393 (s), 1219 (s), 1113 (s), 1022 (s), 716 (vs) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{15}H_{13}NNaO_4$ [M + Na]$^+$ 294.0737, found 294.0733.

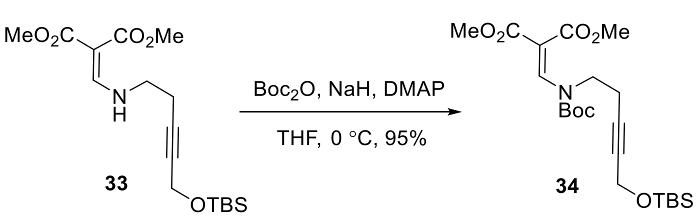


Synthesis of Compound 32: To a solution of compound **31** (10.0 g, 36.9 mmol, 1.0 equiv) in MeOH (200 mL) was added K_2CO_3 (5.10 g, 36.9 mmol, 1.0 equiv) at 0 °C. Then the reaction was warmed to room temperature. After being stirred for 0.5 h, the mixture was diluted with water (200 mL). The aqueous layers was extracted with EtOAc (3× 200 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was directly used in next step without further purification. To a solution of the above residue in CH_2Cl_2 (100 mL), TBSCl (5.56 g, 36.9 mmol, 1.0 equiv), Et_3N (6.20 mL, 44.3 mmol, 1.20 equiv), and DMAP (90.0 mg, 0.738 mmol, 0.02 equiv) were added successively at room temperature. The mixture was stirred for 10 h before being quenched with water (100 mL). After separation of the two layers, the aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc =10:1, v/v) to afford **32** (4.56 g, 36%

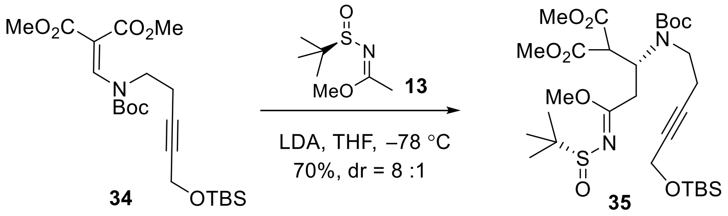
yield over two steps) as a colorless oil. **TLC**: (petroleum ether/EtOAc = 7:1, v/v) R_f = 0.4. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.85 – 7.83 (m, 2H), 7.72 – 7.70 (m, 2H), 4.23 (t, J = 2.0 Hz, 2H), 3.84 (t, J = 7.2 Hz, 2H), 2.64 – 2.60 (m, 2H), 0.85 (s, 9H), 0.05 (s, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 168.0, 134.0, 132.0, 123.3, 80.9, 80.6, 51.8, 36.6, 25.8, 18.7, 18.3, −5.2. **IR** (neat): ν_{max} = 2929 (m), 2856 (m), 1773 (s), 1707 (vs), 1393 (s), 1361 (s), 1073 (vs), 834 (vs), 716 (vs) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{19}H_{25}NNaO_3Si$ $[M + Na]^+$ 366.1496, found 366.1492.



Synthesis of Compound 33: Hydrazine hydrate (aq. 80%, 6.40 mL, 106 mmol, 7.5 equiv) was added to a solution of compound **32** (7.28 g, 21.2 mmol, 1.5 equiv) in MeOH (200 mL). After being refluxed for 3 h, the reaction mixture was diluted with water (200 mL) and CH_2Cl_2 (200 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 400 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was dissolved in toluene (300 mL) and dimethyl methoxymethylenemalonate **16** (2.46 g, 14.1 mmol, 1.0 equiv) was added. The resulting mixture was heated to reflux for 2 h and then evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum eth1er/EtOAc = 4:1, v/v) to yield compound **33** (4.00 g, 80%) as a colorless oil. **TLC**: (petroleum ether/EtOAc = 3:1, v/v) R_f = 0.5. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.33 – 9.30 (m, 1H), 8.06 – 8.02 (d, J = 14.0 Hz, 1H), 4.29 (t, J = 2.0 Hz, 2H), 3.78 (s, 3H), 3.71 (s, 3H), 3.48 – 3.43 (q, J = 6.4 Hz, 2H), 2.52 – 2.49 (m, 2H), 0.89 (s, 9H), 0.10 (s, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 169.5, 166.3, 160.2, 89.6, 81.8, 80.4, 51.7, 51.2, 51.1, 48.4, 25.8, 21.4, 18.3, −5.2. **IR** (neat): ν_{max} =2951 (m), 2857 (m), 1659 (s), 1610 (s), 1441 (s), 1362 (s), 1198 (vs), 834 (vs), 801 (vs) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{17}H_{29}NNaO_5Si$ $[M + Na]^+$ 378.1707, found 378.1704.



Synthesis of Compound 34: Under an argon atmosphere, compound **33** (10.0 g, 28.1 mmol, 1.0 equiv) and DMAP (172 mg, 1.41 mmol, 0.05 equiv) were dissolved in THF (300 mL) at 0 ºC. Subsequently, NaH (2.25 g, 60% suspension in mineral oil, 56.2 mmol, 2.0 equiv) was added to the mixture in small portions. After being stirred for 20 min, Boc_2O (9.20 g, 42.1 mmol, 1.5 equiv) was added, and the resulting mixture was stirred for 1 h at the same temperature. Then saturated aqueous $NaHCO_3$ solution (200 mL) was added to quench the reaction at 0 °C. The layers were separated, and the aqueous layers was extracted with CH_2Cl_2 (2 × 300 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 20:1, v/v) to yield **34** (12.1 g, 95%) as a colorless oil. **TLC**: (petroleum ether/EtOAc = 15:1, v/v) $R_f = 0.3$. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.14 (s, 1H), 4.26 (s, 2H), 3.87 (s, 3H), 3.76 (s, 3H), 3.66 – 3.62 (m, 2H), 2.49 – 2.46 (m, 2H), 1.52 (s, 9H), 0.90 (s, 9H), 0.10 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 166.9, 165.7, 151.7, 139.9, 104.9, 84.3, 80.7, 80.6, 53.0, 52.3, 51.8, 44.5, 27.9, 25.8, 18.2, −5.2. **IR** (neat): ν_{max} = 2953 (m), 2857 (m), 1726 (s), 1621 (s), 1436 (s), 1369 (s), 1196 (s), 1136 (vs), 835 (vs), 775 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{22}H_{37}NNaO_7Si$ $[M + Na]^+$ 478.2232, found 478.2232.



Synthesis of Compound 35: Under an argon atmosphere, to a solution of **13**[2] (583 mg, 3.29 mmol, 1.5 equiv) in anhydrous THF (50 mL) was added LDA (1 M in THF, 3.50 mL, 3.50 mmol, 1.6 equiv) at −78 °C and the resulting solution was stirred at −78 °C for 20 min. Then a solution of **34** (1.00 g, 2.19 mmol, 1.0 equiv) in THF (5 mL) was slowly added. After being stirred at −78 °C for another 1 h, the reaction mixture was poured into saturated aqueous NH_4Cl solution (50 mL). The layers were separated, and the aqueous layers was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The dr value was determined by LC-MS analysis of the crude mixture (dr = 8:1). The residue was purified by silica gel flash column chromatography petroleum ether/EtOAc = 8:1, v/v) to yield the major isomer **35** (970 mg, 70%, a colorless oil) as the main product and the minor isomer **35b** (70 mg, 5%, a colorless oil).

Major isomer 35: **TLC**: (petroleum ether/EtOAc = 6:1, v/v) $R_f = 0.2$. **Optical rotation**: $[\alpha]_D^{25}$= −88.3 (*c* = 0.30, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 4.36 – 4.13 (m, 2H), 4.25 (s, 2H, overlapped), 3.77 – 3.70 (m, 9H), 3.65 – 3.51 (m, 1H), 3.27 – 3.14 (m, 2H), 2.93 – 2.80 (m, 1H), 2.41 – 2.27 (m, 2H), 1.54 (s, 5H), 1.43 (s, 4H), 1.19 (s, 9H), 0.89 (s, 9H), 0.09 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): *δ* 173.5, 173.1, 167.8, 167.6, 167.3, 154.3, 154.2, 81.9, 80.4, 80.0, 58.0, 56.1, 55.8, 55.6, 54.4, 54.2, 52.9, 52.8, 52.6, 51.9, 51.2, 49.9, 35.6, 34.3, 28.3, 25.8, 21.9, 19.2, 18.5, 18.3, −5.1. **IR** (neat): $\nu_{\max}$ = 2953 (m), 2858 (w), 1739 (s), 1699 (s), 1614 (s), 1250 (s), 1157 (s), 1074 (vs), 835 (vs), 776 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{29}H_{52}N_2NaO_9SSi$ [M + Na]$^+$ 655.3055, found 655.3061.

Minor isomer 35b: **TLC**: (petroleum ether/EtOAc = 6:1, v/v) R_f = 0.2. **Optical rotation**: $[\alpha]_D^{25}$= −10.0 (*c* = 0.16, $CHCl_3$). **^{1}H NMR** (600 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): *δ* 4.36 – 4.11 (m, 2H), 4.25 (m, 2H, overlapped), 3.76 – 3.70 (m, 9H), 3.44 – 3.36 (m, 1H), 3.23 – 3.20 (m, 2H), 3.01 – 2.99 (m, 1H), 2.42 – 2.27 (m, 2H), 1.51 (s, 4H), 1.44 (s, 5H), 1.20 (s, 4H), 1.18(s, 5H), 0.89 (s, 9H), 0.09 (s, 6H).**^{13}C NMR** (100 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): *δ* 172.2, 171.6, 167.8, 167.5, 167.3, 154.3, 82.0, 81.6, 80.6, 80.0, 57.3, 56.3, 56.1, 54.5, 54.2, 52.9, 52.8, 52.6, 51.9, 51.2, 49.7, 35.6, 33.9, 28.2, 25.8, 21.9, 19.2, 18.5, 18.3, −5.1. **IR** (neat): $\nu_{\max}$ = 2928 (m), 1741 (s), 1700 (s), 1614 (s), 1462 (s), 1366 (s), 1286 (s), 1158 (vs), 951 (s), 815 (s), 777 (s), 681 (m) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{29}H_{52}N_2NaO_9SSi$ [M + Na]$^+$ 655.3055, found 655.3058.

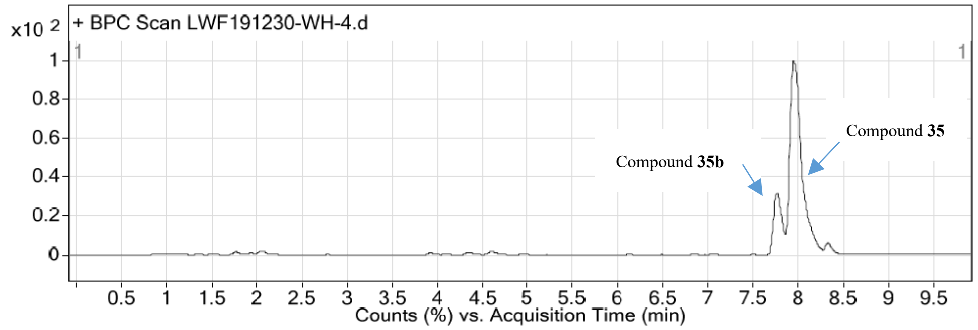
Analysis LC-MS of Michael addition of 34 with 13

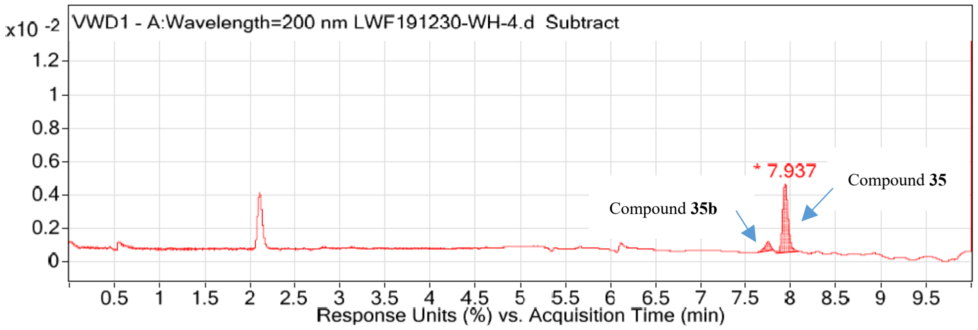
Run information:

Analytical HPLC: Aglient LC-MS QQQ 6420A; Column: Ultimate UHPLC XB-C18 (1.8 μm, 2.1*50mm); Solvent: H_2O/CH_3CN (the gradient of CH_3CN is from 20% to 70% during 0−4.5 min, 70% to 95% during 4.5−9 min, 95% to 20% during 9−10 min); Flow = 0.4 mL/min; Detected by UV at 200 nm; Retention time for major isomer **35** and minor isomer **35b** in LC-MS: 7.937min (compound **35**, major), 7.749 min (compound **35b**, minor); Base peak chromatogram: 7.980 min (compound **35**, major, [M + H]$^+$ = 632.8, [M + Na]$^+$ = 654.8), 7.752 min (compound **35b**, minor, [M+H]$^+$ = 632.8).

User Chromatograms

Fragmentor Voltage 100 **Collision Energy** 0 **Ionization Mode** ESI





Integration Peak List

Peak	Start	RT	End	Height	Area	Area %
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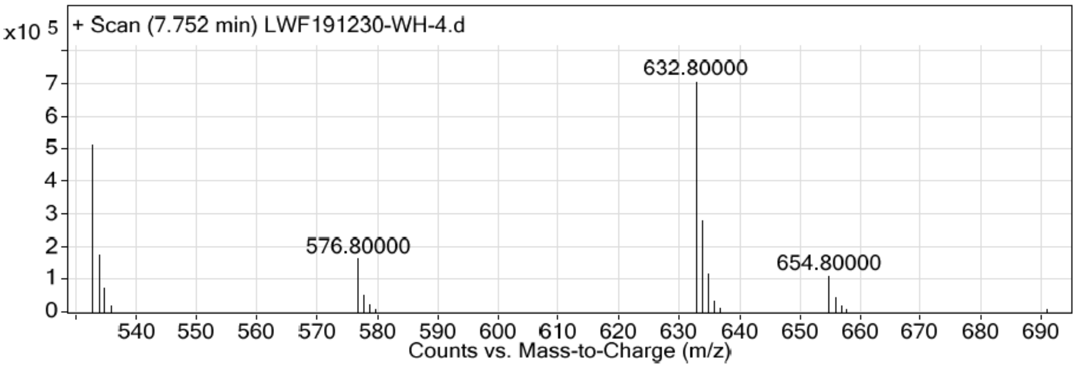
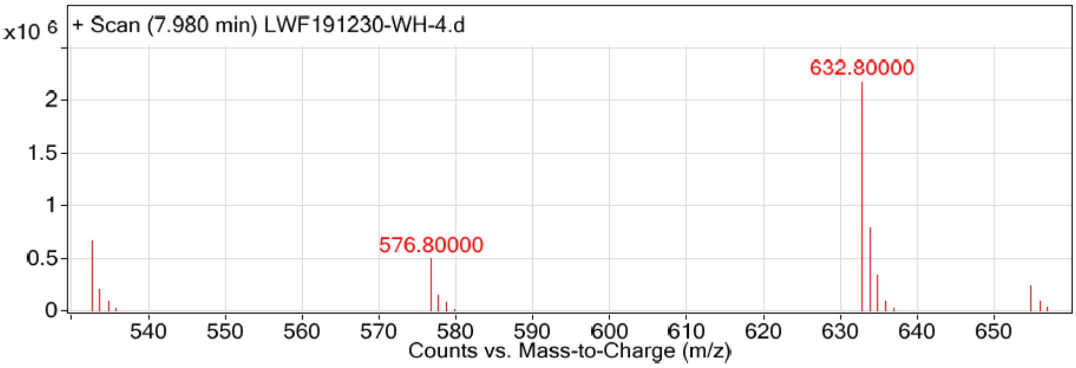
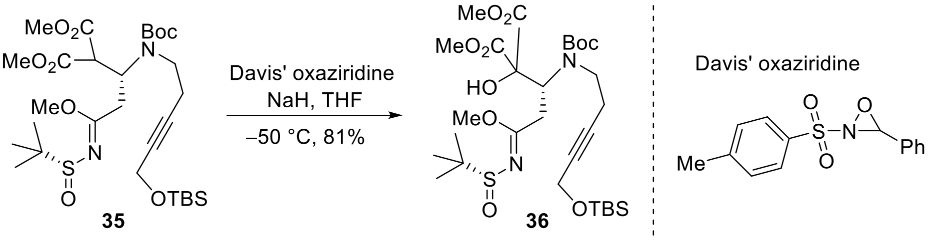
2	7.836	7.937	8.088	96.84	402.45	100

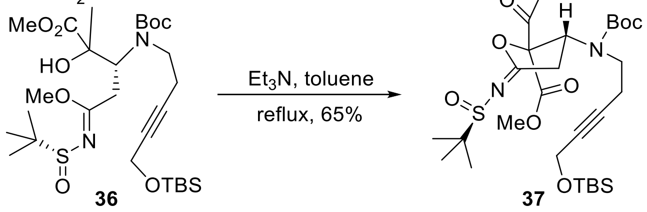
User Spectra





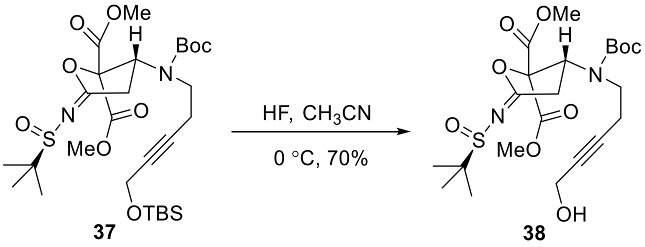


Synthesis of Compound 36: To a solution of compound **35** (10.0 g, 15.8 mmol, 1.0 equiv) in THF (300 mL) at −50 °C under a nitrogen atmosphere, NaH (948 mg, 60% suspension in mineral oil, 23.7 mmol, 1.5 equiv) was added in small portions. After being stirred at the same temperature for 20 minutes, a solution of Davis' oxaziridine (5.23 g, 19.0 mmol, 1.2 equiv) in THF (50 mL) was added slowly over 20 minutes. The resulting mixture was stirred for 12 h at −50 °C before being quenched with saturated aqueous ammonium chloride solution (aq. NH_4Cl, 200 mL). Then the mixture was diluted with CH_2Cl_2 (200 mL), and the layers was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 200 mL). The organic layers were combined and dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc =4:1, v/v) to afford **36** (8.30 g, 81% yield) as a colorless oil. **TLC**: (petroleum ether/EtOAc = 3:1, v/v) R_f = 0.2. **Optical rotation**: $[\alpha]_D^{25}$ = −38.7 (*c* = 0.30, $CHCl_3$). **^{1}H NMR** (400 MHz, CD_3OD): *δ* 5.63 – 5.56 (m, 1H), 4.34 (s, 2H), 3.84 – 3.74 (m, 9H), 3.39 – 3.35 (m, 3H), 2.92 – 2.83 (m, 1H), 2.64 – 2.61 (m, 1H), 2.38 (brs, 1H), 1.51 (s, 9H), 1.27 (s, 9H), 0.96 (s, 9H), 0.17 (s, 6H). **^{13}C NMR** (150 MHz, CD_3OD, some signals exist as a pair due to the presence of amide rotamers): *δ* 176.8, 176.5, 171.4/171.4, 171.2, 157.4, 84.6, 84.4, 84.2, 82.8, 82.7, 82.5, 81.8, 81.6, 58.0, 57.9, 56.8, 56.2, 56.0, 54.6, 54.5, 54.3, 53.5, 45.6, 45.5, 32.5, 32.4, 29.4, 27.1, 23.0, 21.0, 19.9, −4.0. **IR**: (neat): ν_{max} = 2954 (m), 2858 (w), 1747 (s), 1698 (s), 1609 (s), 1435 (s), 1252 (vs), 1158 (vs), 1074 (vs), 835 (vs) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{29}H_{52}N_2NaO_{10}SSi$ $[M + Na]^+$ 671.3004, found 671.3007.

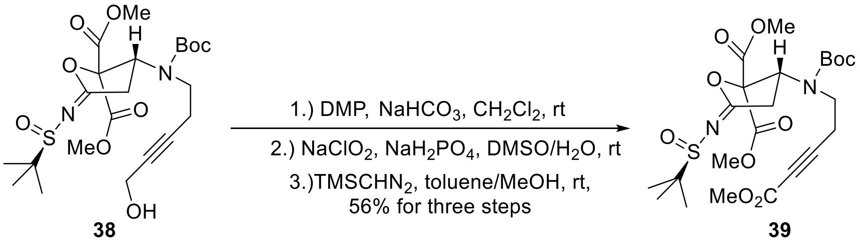


Synthesis of Compound 37: To a solution of **36** (10.0 g, 15.4 mmol, 1.0 equiv) in toluene (500 mL) was added Et_3N (21.4 mL, 154 mmol, 10.0 equiv). The reaction mixture was heated to reflux for 3 h. Then the mixture was concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc =5:1, v/v) to afford **37** (6.17 g, 65% yield) as a colorless oil. **TLC**: (petroleum ether/EtOAc = 1:1, v/v) R_f = 0.6. **Optical rotation**: [α]

$^{25}_{D}$= −116.8 (*c* = 0.40, CHC1$_3$). **^{1}H NMR** (400 MHz, CDCl$_3$): *δ* 5.09 – 4.72 (m, 1H), 4.27 (s, 2H), 3.81 – 3.76 (m, 6H), 3.45 – 3.20 (m, 4H), 2.41 (brs, 2H), 1.39 (s, 9H), 1.23 (s, 9H), 0.88 (s, 9H), 0.08 (s, 6H). **^{13}C NMR** (100 MHz, CDCl$_3$, some signals exist as a pair due to the presence of amide rotamers): *δ* 170.5, 168.9, 166.7, 166.2, 165.0, 164.2, 154.2, 153.5, 91.0, 88.8, 86.8, 83.3, 81.7, 81.2, 80.7, 62.0, 61.0, 57.7, 56.6, 54.0, 53.2, 51.8, 49.5, 48.7, 35.6, 34.5, 32.4, 28.1, 25.8, 22.1, 21.8, 21.7, 19.5, 18.3, −5.2. **IR** (neat): ν_{max} = 2955 (m), 2858 (w), 1747 (s), 1672 (s), 1366 (s), 1241 (s), 1160 (vs), 1072 (vs), 775 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{28}H_{48}N_2NaO_9SSi$ $[M + Na]^+$ 639.2742, found 639.2747.

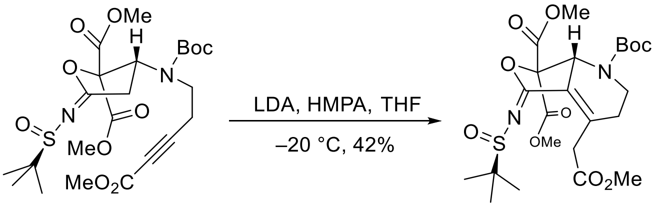


Synthesis of Compound 24: To a solution of **23** (2.00 g, 3.24 mmol, 1.0 equiv) in CH$_3$CN (70 mL) was added HF (aq. 40%, 1.40 mL, 32.4 mmol, 10.0 equiv) slowly over 1 h at 0 °C. The reaction was stirred for 30 minutes at the same temperature before being quenched with saturated aqueous NaHCO$_3$ solution (50 mL) and diluted with water (50 mL). The layers were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 200 mL). The organic layers were combined and dried over Na$_2$SO$_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/acetone =2:1, v/v) to afford **24** (1.14 g, 70% yield) as a white foam. **TLC**: (petroleum ether/ acetone = 2:1, v/v) R_f = 0.3. **Optical rotation**: $[\alpha]^{25}_{D}$= −142.3 (*c* = 0.22, CHC1$_3$).**^{1}H NMR** (400 MHz, CDCl$_3$, some signals exist as a pair due to the presence of amide rotamers): *δ* 5.47 – 5.10 (m, 1H), 4.21 (s, 2H), 4.02 – 3.92 (m, 1H), 3.82 – 3.79 (m, 6H), 3.31 – 3.22 (m, 3H), 2.69 – 2.47 (m, 2H), 1.46 – 1.42 (m, 9H), 1.25 (s, 9H). **^{13}C NMR** (100 MHz, CDCl$_3$, some signals exist as a pair due to the presence of amide rotamers): *δ* 170.6, 166.5, 165.0, 164.5, 154.4, 153.9, 88.6, 87.2, 82.5, 82.1, 81.2, 61.5, 59.8, 58.0, 57.5, 57.2, 54.0, 53.3, 50.8, 47.1, 33.8, 32.9, 28.2, 22.1, 19.3, 18.5. **IR** (neat): ν_{max} = 2957 (m), 1747 (s), 1670 (s), 1434 (s), 1366 (s), 1249 (s), 1158 (vs), 1073 (s), 733 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{22}H_{34}N_2NaO_9S$ $[M + Na]^+$ 525.1877, found 525.1878.



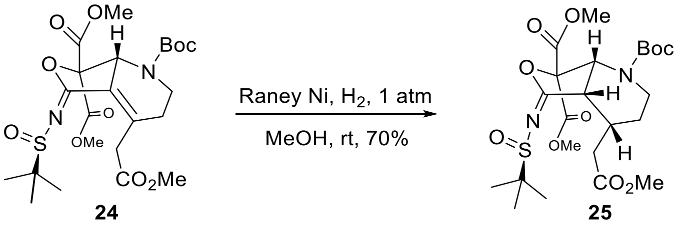
38 **39**

Synthesis of Compound 39: To a solution of compound **38** (2.00 g, 4.00 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added Dess-Martin periodinane (2.54 g, 6.00 mmol, 1.5 equiv) and $NaHCO_3$ (672 mg, 8.00 mmol, 2.0 equiv). The mixture was stirred at room temperature for 1 h. After consumption of **38**, saturated aqueous Na_2SO_3 solution (30 mL) was added. The resulting mixture was diluted with water, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was filtered through a pad of silica gel (eluted with petroleum ether/acetone =2:1, v/v) and concentrated in vacuo. The above crude product was dissolved in a mixture solution of DMSO and H_2O (v/v = 10 mL /10 mL). NaH_2PO_4 (1.44 g, 12.0 mmol, 3.0 equiv) and $NaClO_2$ (1.09 g, 12.0 mmol, 3.0 equiv) were added successively at room temperature. The resulting mixture was stirred for 20 minutes at the same temperature and quenched with saturated aqueous Na_2SO_3 (50 mL) solution. The pH of the mixture was adjusted to 3 with saturated aqueous citric acid solution. Then the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 70 mL). The combined organic phases were dried over Na_2SO_4, filtered, and evaporated in vacuo. The residue was dissolved in a mixture solution of toluene and MeOH (v/v = 10 mL/10 mL) and (trimethylsilyl)diazomethane (2 M in toluene, 3.00 mL, 6.00 mmol, 1.5 equiv) was added at room temperature. After being stirred for 30 minutes, the mixture was concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc =2:1, v/v) to afford **39** (1.19 g, 56% overall yield for three steps) as a colorless oil. **TLC**: (petroleum ether/ acetone = 2:1, v/v) R_f = 0.4. **Optical rotation**: $[\alpha]_D^{25}$= −228.7 (*c* = 0.16, $CHCl_3$).**^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 5.08 – 4.67 (m, 1H), 3.82– 3.74 (m, 9H), 3.63 – 3.28 (m, 4H), 2.60 – 2.49 (m, 2H), 1.40 (s, 9H), 1.23 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): *δ* 175.1, 174.3, 170.5, 168.8, 166.6, 166.3, 165.1, 164.2, 154.0, 153.7, 90.9, 88.7, 86.6, 85.9, 83.7, 81.6, 74.5, 62.3, 61.3, 57.7, 56.8, 56.6, 54.1, 53.3, 52.7, 48.8, 47.8, 35.6, 34.3, 33.2, 32.1, 28.0, 22.0, 21.8, 19.4. **IR** (neat): ν_{max} = 2956 (m), 2239 (m), 1749 (s), 1660 (s), 1434 (s), 1366 (s), 1251 (vs), 1158 (vs), 775 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{23}H_{34}N_2NaO_{10}S$ $[M + Na]^+$ 553.1826, found 553.1826.



39 24

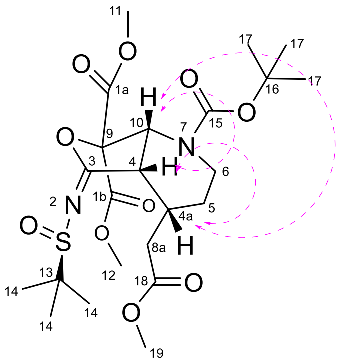
Synthesis of Compound 24: Under a nitrogen atmosphere, *n*-BuLi (1.6 M in hexane, 3.00 mL, 4.80 mmol) was added to a solution of *i*-Pr_2NH (680 μL, 4.85 mmol) in anhydrous THF (6.0 mL) at −20 °C and stirred for 30 min to prepare LDA (0.5 M in THF). To a solution of **39** (500 mg, 0.942 mmol, 1.0 equiv) in anhydrous THF (50 mL), HMPA (413 μL, 2.36 mmol, 2.5 equiv) and the above freshly prepared LDA (0.5 M in THF, 3.80 mL, 1.90 mmol, 2.02 equiv) was added successively at −20 °C. After stirred for 30 min, the reaction was quenched with saturated aqueous NH_4Cl solution (50 mL). The resulting mixture was diluted with water, the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/ EtOAc =2:1, v/v) to afford **24** (210 mg, 42%) as a white foam. **TLC**: (petroleum ether/EtOAc = 1:1, v/v) R_f = 0.2. **Optical rotation**: $[\alpha]_D^{25}$ = +100.5 (*c* = 0.40, $CHCl_3$).**^{1}H NMR** (400 MHz, CD_3OD): δ 5.42 (brs, 1H), 4.41 – 4.37 (m, 1H), 4.15 (brs, 1H), 3.93 (s, 3H), 3.82 (s, 3H), 3.79 – 3.75 (m, 1H), 3.72 (s, 3H), 2.60 – 2.37 (m, 3H), 1.53 (s, 9H), 1.25 (s, 9H). **^{13}C NMR** (100 MHz, CD_3OD): δ 171.9, 167.1, 166.6, 164.9, 156.8, 150.4, 123.4, 88.2, 83.7, 60.9, 58.4, 55.2, 54.7, 53.5, 41.5, 39.0, 33.3, 29.4, 22.8. **IR** (neat): ν_{max} = 2956 (m), 1742 (s), 1700 (s), 1644 (s), 1395 (s), 1230 (s), 1159 (vs), 1084 (vs), 801 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{23}H_{34}N_2NaO_{10}S$ $[M + Na]^+$ 553.1826, found 553.1826.



24 25

Synthesis of Compound 25: To a solution of **24** (200 mg, 0.377 mmol) in 10 mL methanol was added Raney Ni (commercial slurry in water, 1 tsp per mmol of **24,** washed 3 times with methanol). The flask was then charged with a hydrogen atmosphere (1 atm.) and stirred for 1 h. The reaction mixture was filtered through a pad of celite and eluted with methanol (***Caution: the filter cake should not be allowed to become dry***) and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc =1:1, v/v) to afford

25 (141 mg, 70%) as a white foam. **TLC**: (petroleum ether/EtOAc = 1:1, v/v) $R_f = 0.2$. **Optical rotation**: $[\alpha]_D^{25} = +7.5$ (*c* = 0.40, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): *δ* 5.80 – 5.72 (m, 1H), 4.09 – 3.89 (m, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.67 (s, 3H), 3.49 (m, 1H), 3.20 – 3.06 (m, 1H), 2.85 – 2.68 (m, 1H), 2.66 – 2.57 (m, 1H), 2.33 (brs, 1H), 2.10 – 2.00(m, 1H), 1.47 – 1.45 (m, 9H), 1.38 – 1.36 (m, 1H), 1.26 (s, 9H). **^{13}C NMR** (150 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): *δ* 172.6, 172.4, 170.4, 170.3, 165.0, 164.8, 164.4, 164.3, 154.5, 154.0, 91.8, 81.4, 81.1, 58.9, 58.0, 56.1, 56.0, 54.0, 53.5, 53.2, 51.7, 41.3, 41.0, 37.9, 36.4, 35.8, 35.5, 28.1, 28.0, 27.9, 25.1, 24.5, 21.9. **IR** (neat): ν_{max} = 2955 (m), 2925 (m), 1746 (s), 1700 (s), 1655 (s), 1436 (s), 1410 (s), 1159 (vs), 1065 (s), 734 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{23}H_{36}N_2NaO_{10}S$ $[M + Na]^+$ 555.1983, found 555.1985. *NOTE: The structure of **25** was confirmed by 2D NMR experiments, see Table S3. The relative stereochemistry of **25** was established by NOE experiments.*

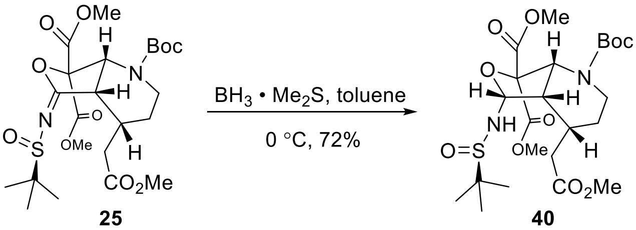


25

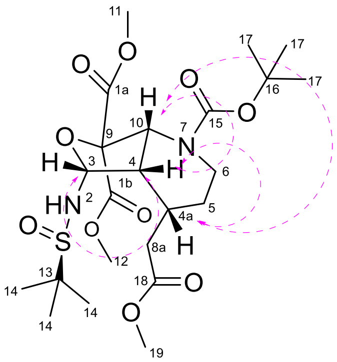
Table S3. 2D NMR Data for Compound 25

Atom	^{1}H Shift (ppm)	^{1}H mult.	*J* Values (Hz)	^{13}C Shift (ppm)	^{13}C mult.^{a}	COSY^b	HMBC^c
1a	--	--	--	165.0, 164.8	C	--	--
1b	--	--	--	164.4, 164.3	C	--	--
3	--	--	--	170.4, 170.3	C	--	--
4	3.49	brs	--	41.3, 41.0	CH	H-10	--
4a	2.33	brs	--	28.0, 27.9	CH	H-5, H-8a	--
5	2.10 – 2.00, 1.38 – 1.36	m	--	25.1, 24.5	CH_2	H-6, H-4a	C4, C4a, C6
6	4.09 – 3.89 2.85 – 2.68	m	--	37.9, 36.4	CH_2	H-5	C15
8a	3.20 – 3.06 2.66 – 2.57	m	--	35.8, 35.5	CH_2	H-4a	C18, C4a, C4, C5
9	--	--	--	91.8	C	--	--
10	5.80 – 5.72	m	--	58.9, 58.0	CH	H-4	C3
11	3.84	s	--	54.0	CH_3	--	C1a
12	3.78	s	--	53.5, 53.2	CH_3	--	C1b
13	--	--	--	56.1, 56.0	C	--	--
14	1.26	s	--	21.9	CH_3	--	C13
15	--	--	--	154.5, 154.0	C	--	--
16	--	--	--	81.4, 81.1	C	--	--
17	1.47 – 1.45	m	--	28.1	CH_3	--	C-16
18	--	--	--	172.6, 172.4	C	--	--
19	3.67	s	--	51.7	CH_3	--	C18

(a) Determined by HMQC correlation; (b) carbons that correlate to protons; (c) protons that correlate to protons.



Synthesis of Compound 40: Under an argon atmosphere, $BH_3 \cdot Me_2S$ (26.0 μL, 0.282 mmol, 3.0 equiv) was added slowly to a solution of **25** (50.0 mg, 0.094 mmol, 1.0 equiv) in toluene (10 mL) at 0 °C. After being stirred for 30 min, the reaction was quenched with methanol (5 mL) and diluted with water (20 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The organic layers were combined and dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/acetone =2:1, v/v) to afford **40** (36.0 mg, 72% yield) as a white foam. **TLC**: (petroleum ether/acetone = 2:1, v/v) R_f = 0.2. **Optical rotation**: $[\alpha]_D^{25}$= −20.0 (*c* = 0.10, $CHCl_3$). **^{1}H NMR** (400 MHz, CD_3OD, some signals exist as a pair due to the presence of amide rotamers): *δ* 5.66 – 5.63 (m, 1H), 5.58 – 5.56 (d, *J* = 7.2 Hz, 1H), 4.00 – 3.85 (m, 1H), 3.82 (s, 3H), 3.75 – 3.73 (m, 3H), 3.71 (s, 3H), 3.09 – 2.94 (m, 1H), 2.89 – 2.78 (m, 1H), 2.55 – 2.39 (m, 2H), 2.26 (brs, 1H), 2.06 (brs, 1H), 1.51 (s, 9H), 1.46 – 1.37 (m, 1H), 1.28 (s, 9H). **^{13}C NMR** (100 MHz, CD_3OD, some signals exist as a pair due to the presence of amide rotamers): *δ* 174.6, 174.5, 170.8, 170.6, 169.9, 169.4, 157.5, 157.3, 92.8, 92.5, 91.9, 91.6, 83.0, 82.8, 63.7, 63.2, 58.2, 54.5, 54.2, 54.0, 52.9, 47.3, 46.7, 40.1, 39.5, 39.4, 38.8, 29.3, 29.2, 26.2, 25.7, 23.6. **IR** (neat): ν_{max} = 3358 (vs), 2922 (s), 1737 (s), 1694 (s), 1644 (s), 1258 (s), 1085 (s), 1059 (s), 1023 (s), 798 (vs) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{23}H_{38}N_2NaO_{10}S$ $[M + Na]^+$ 557.2139, found 557.2144. *NOTE: The structure of **40** was confirmed by 2D NMR experiments, see Table S4. The relative stereochemistry of **40** was established by NOE experiments.*

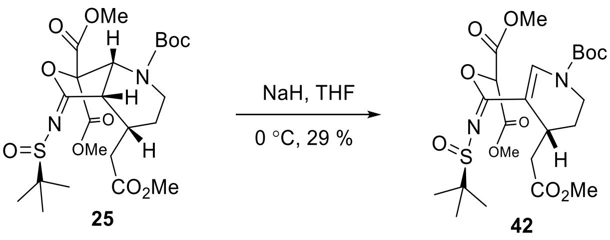


40

Table S4. 2D NMR data for compound 40

Atom	^{1}H Shift (ppm)	^{1}H mult.	*J* Values (Hz)	^{13}C Shift (ppm)	^{13}C mult.[a]	COSY[b]	HMBC[c]
1a	--	--	--	170.8, 170.6	C	--	--
1b	--	--	--	169.9, 169.4	C	--	--
3	5.58 – 5.56	d	7.2	92.8, 92.5	CH	H-4	C4a, C9
4	2.89 – 2.78	m	--	47.3, 46.7	CH	H-3	--
4a	2.26	brs	--	29.2	CH	H-5, H-8a	--
5	2.06, 1.46 – 1.37	brs, m	--	26.2, 25.7	CH_2	H-6, H-4a	C4a
6	4.00 – 3.85, 3.09 – 2.94	m	--	40.1, 38.8	CH_2	H-5	--
8a	2.55 – 2.39	m	--	39.5, 39.4	CH_2	H-4a	C18, C4a, C4, C5
9	--	--	--	91.9, 91.6	C	--	--
10	5.66 – 5.63	m	--	63.7, 63.2	CH	--	--
11	3.82	s	--	54.5	CH_3	--	C1a
12	3.75 – 3.73	m	--	54.2, 54.0	CH_3	--	C1b
13	--	--	--	58.2	C	--	--
14	1.28	s	--	23.6	CH_3	--	C13
15	--	--	--	157.5, 157.3	C	--	--
16	--	--	--	83.0, 82.8	C	--	--
17	1.51	s	--	29.3	CH_3	--	C-16
18	--	--	--	174.6, 174.5	C	--	--
19	3.71	s	--	52.9	CH_3	--	C18

(a) Determined by HMQC correlation; (b) carbons that correlate to protons; (c) protons that correlate to protons.



25 **42**

Synthesis of Compound 42: Under an argon atmosphere, to a solution of **25** (14.0 mg, 0.026 mmol, 1.0 equiv) in dry THF (5 mL) was added NaH (4.0 mg, 60% dispersion in oil, 0.110 mmol, 4.0 equiv) at 0 °C. After stirring for 20 minutes at the same temperature, the reaction mixture was quenched by adding aqueous saturated NH_4Cl solution. The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL), the combined organic phases were dried over Na_2SO_4, filtered, and evaporated in vacuo. The residue was purified by flash column chromatography (petroleum ether/ EtOAc = 2:1, v/v) to afford **42** (4.0 mg, 29 % yield) as a colorless oil. **TLC**: (petroleum ether/EtOAc = 1:1, v/v) $R_f = 0.5$. **Optical rotation**: $[\alpha]_D^{25} = -80.0$ (c = 0.075, $CHC1_3$). ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.08 (s, 1H), 5.73 (s, 1H), 3.92 – 3.86 (m, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 3.67 (s, 3H), 3.37 – 3.29 (m, 2H), 2.79 – 2.75 (m, 1H), 2.29 – 2.22 (m, 1H), 1.98 – 1.84 (m, 2H), 1.52 (s, 9H), 1.17 (s, 9H). ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 172.1, 165.3, 164.7, 151.5, 137.5, 107.9, 83.0, 73.2, 56.0, 53.3, 53.0, 51.6, 38.2, 37.8, 28.7, 28.1, 25.1, 21.9. **IR** (neat) ν_{max} = 2957 (m), 2924 (m), 1721 (s), 1631 (s), 1570 (s), 1258 (s), 1148 (vs), 1076 (s), 1011 (vs), 792 (s) cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{23}H_{36}N_2NaO_{10}S$ $[M+Na]^+$ 555.1983, found 555.1979.

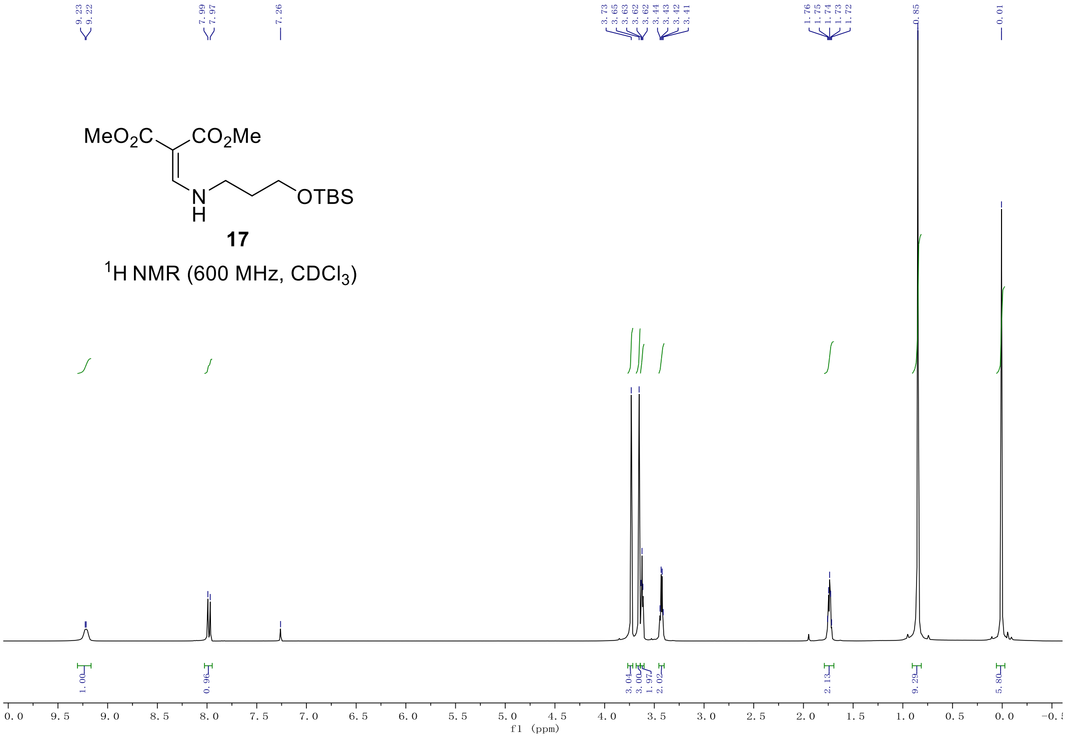
3. References

(1) A. Padwa, P. Rashatasakhon, A. D. Ozdemir and J. Willis, *J. Org. Chem.* 2005, **70**, 519–528.

(2) T. D. Owens, A. J. Souers and J. A. Ellman, *J. Org. Chem.* 2003, **68**, 3−10.

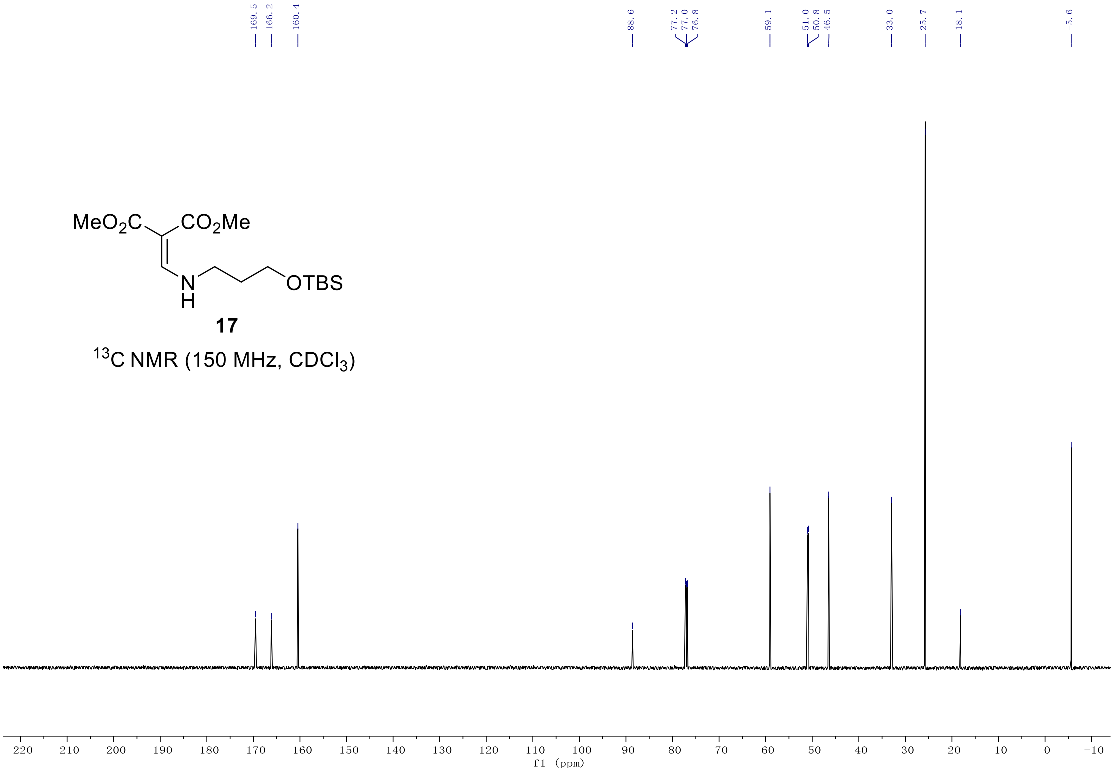
(3) J. Efskind, C. Römming and K. Undheim, *J. Chem. Soc.*, *Perkin Trans. 1*, 2001, 2697–2703.

4. NMR Spectra



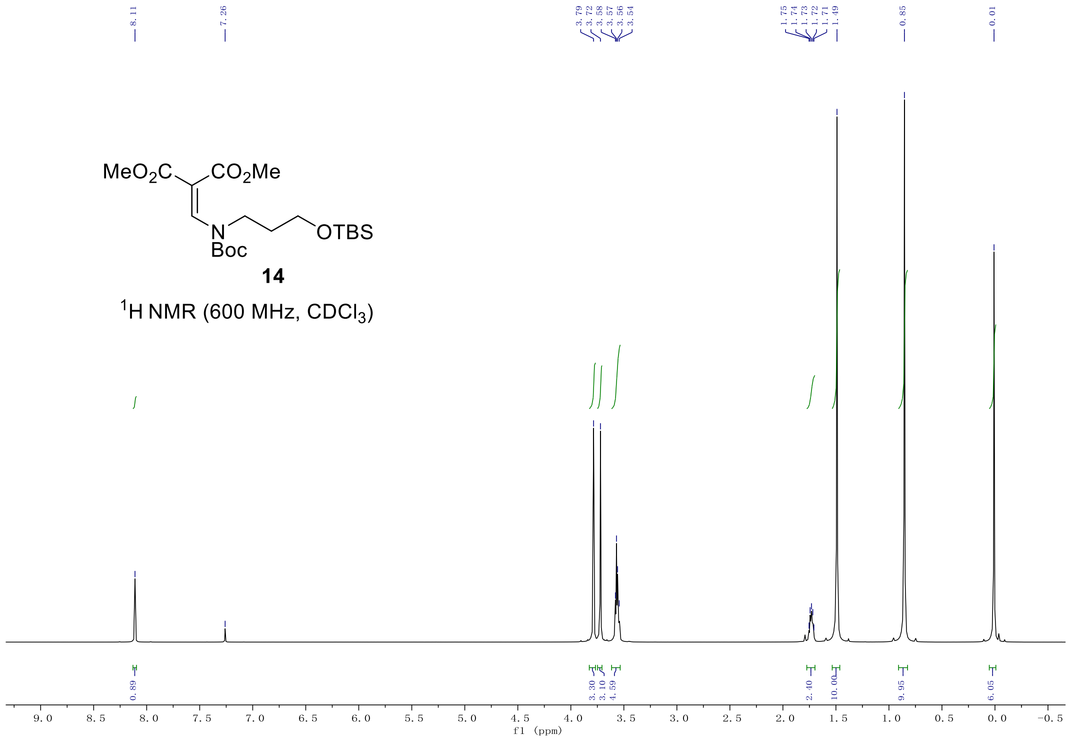
17

^{1}H NMR (600 MHz, $CDCl_3$)



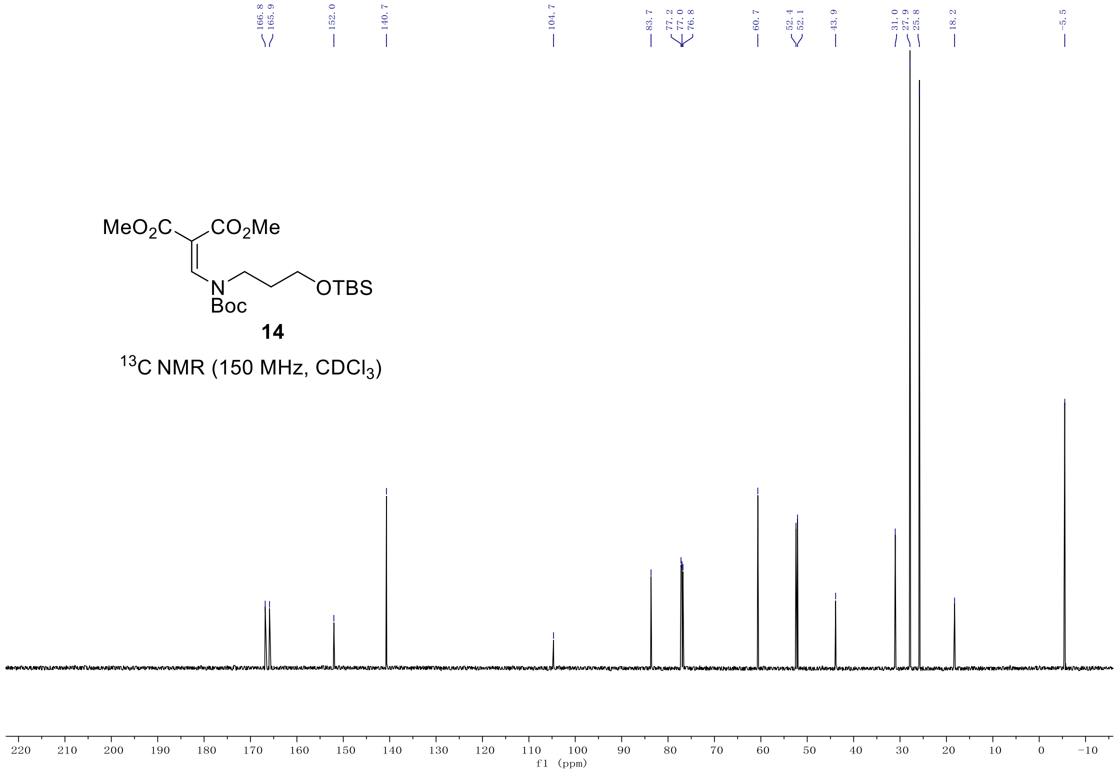
17

^{13}C NMR (150 MHz, $CDCl_3$)



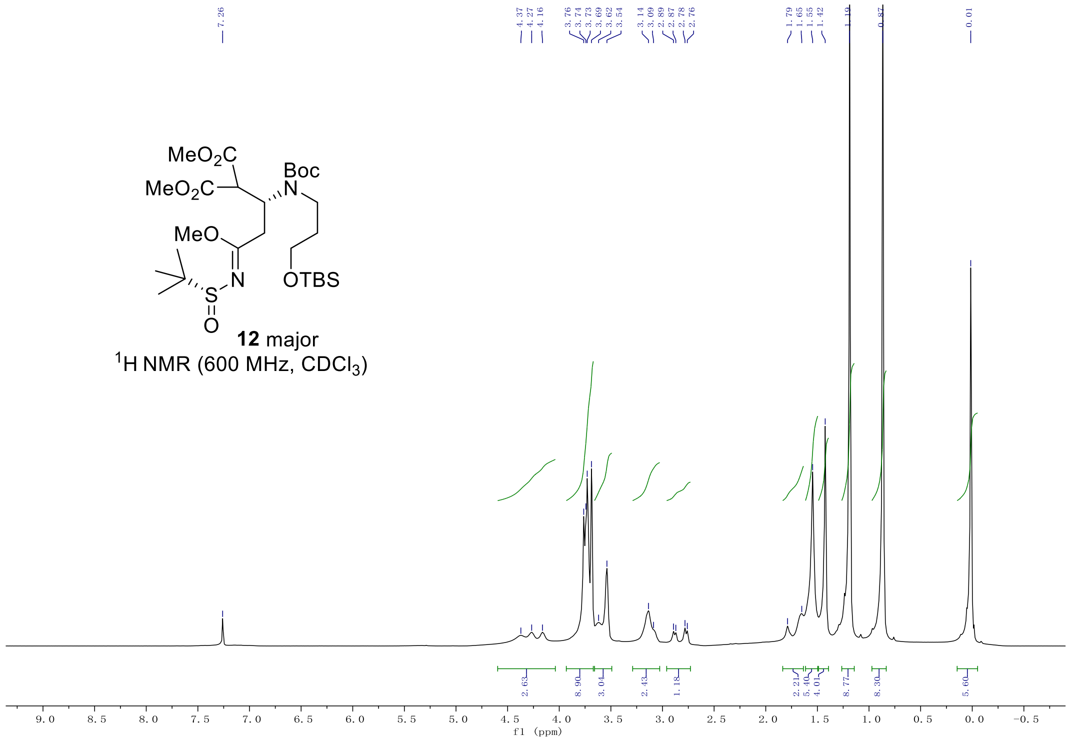
14

^{1}H NMR (600 MHz, CDCl$_3$)



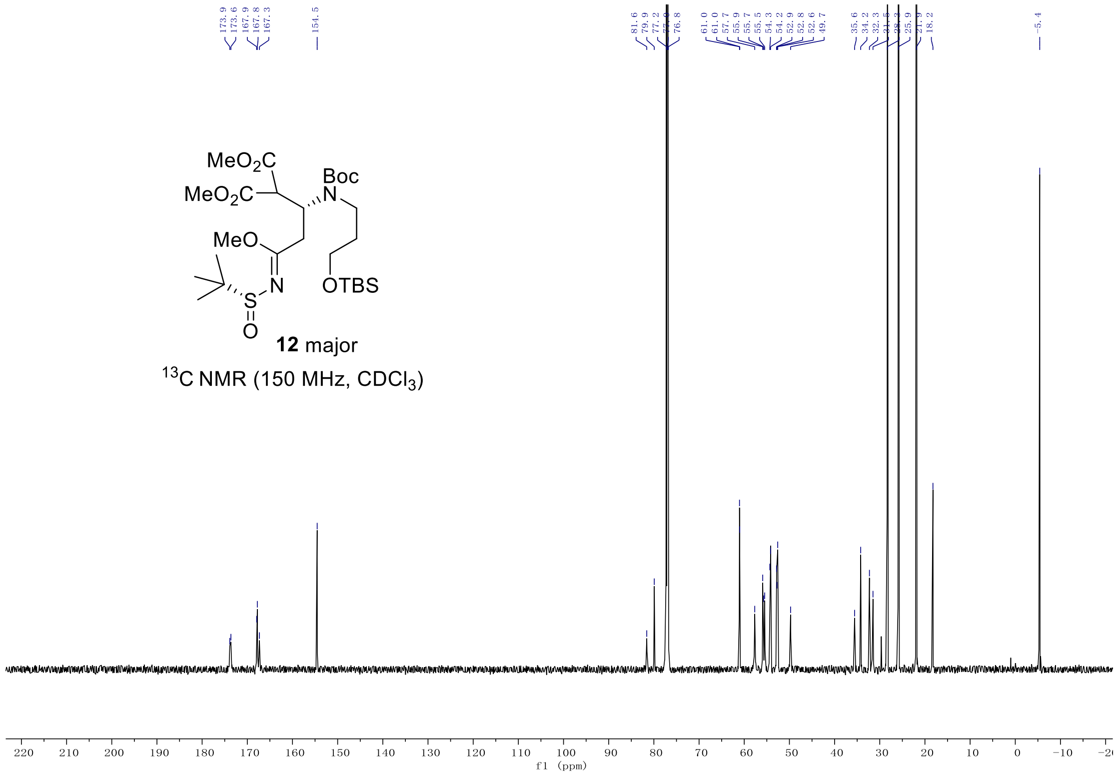
14

^{13}C NMR (150 MHz, CDCl$_3$)



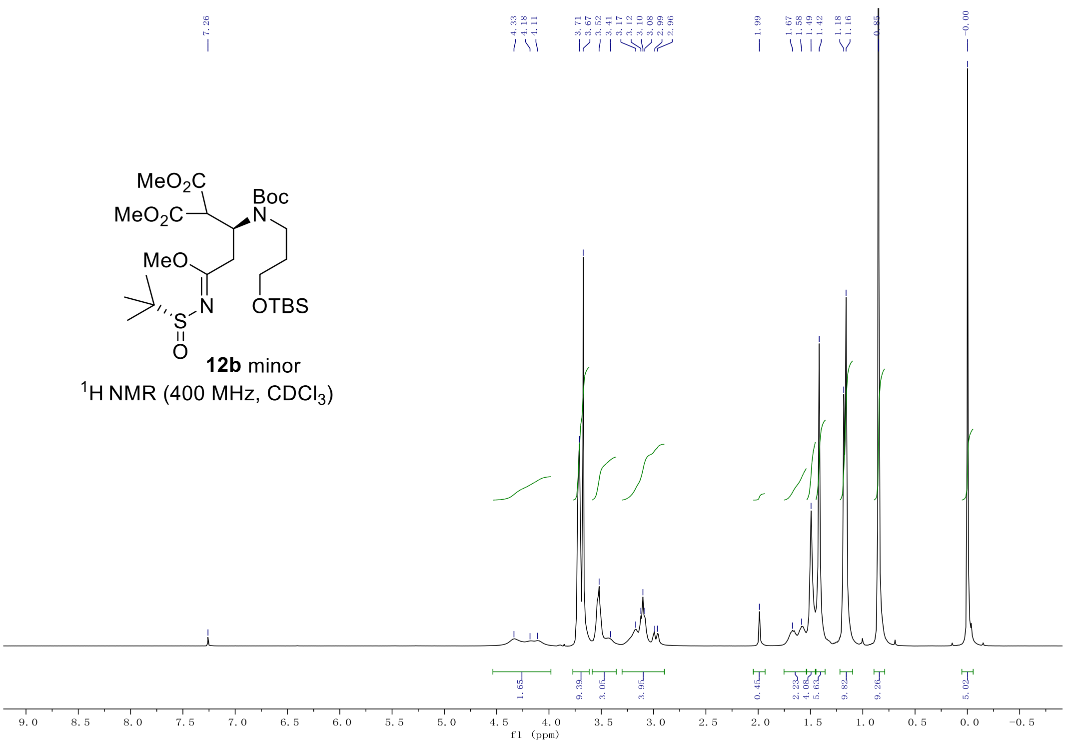
12 major

^{1}H NMR (600 MHz, CDCl$_3$)



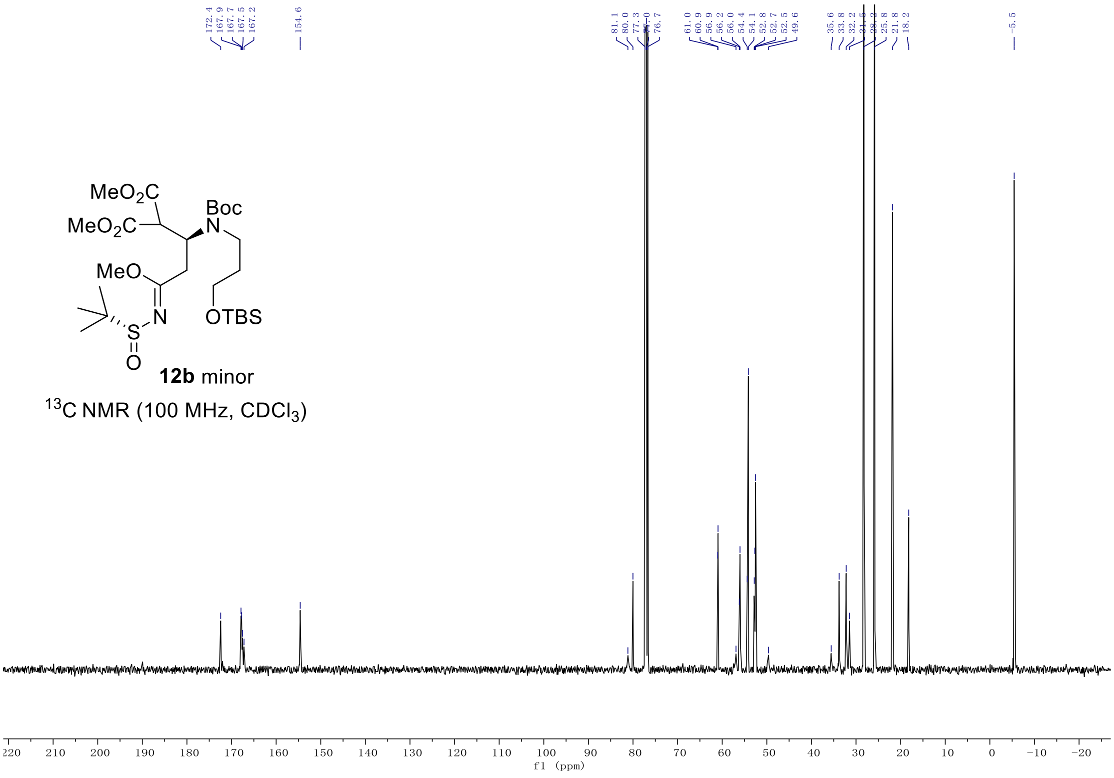
12 major

^{13}C NMR (150 MHz, CDCl$_3$)



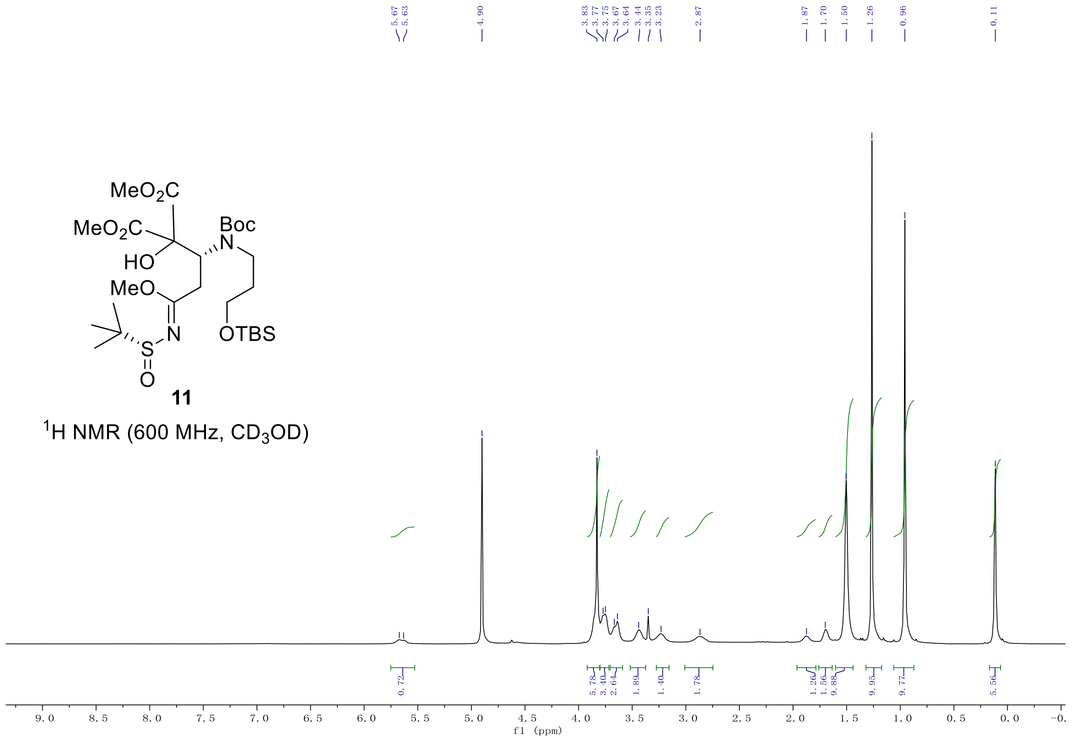
12b minor

^{1}H NMR (400 MHz, CDCl$_3$)



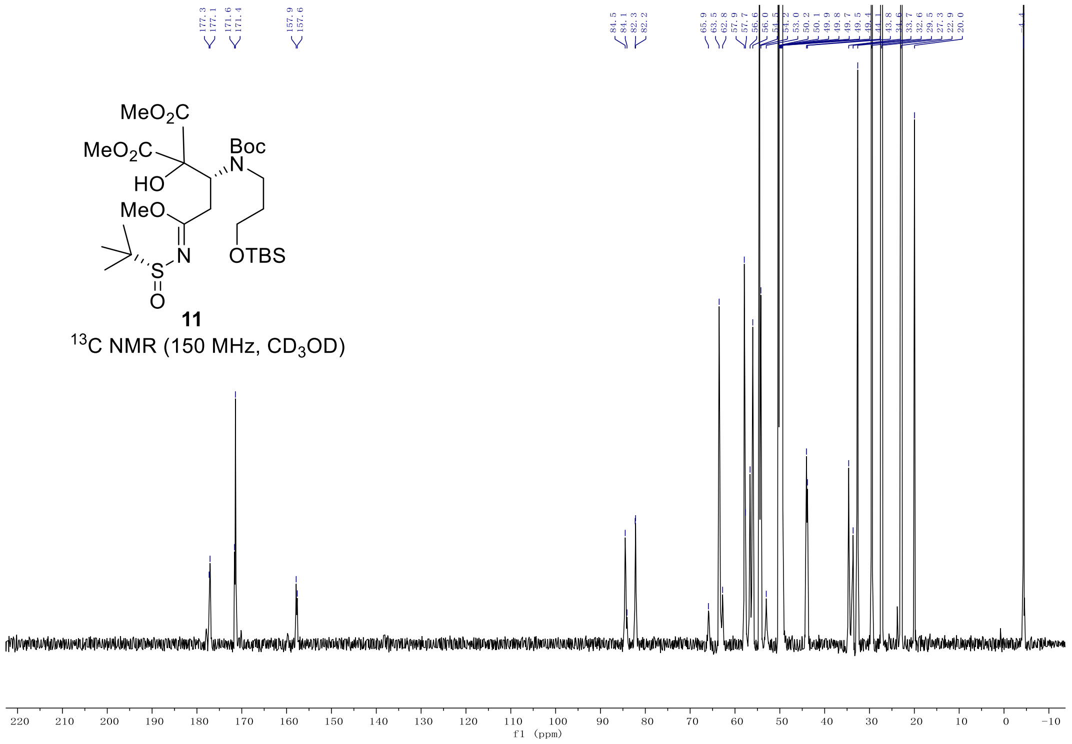
12b minor

^{13}C NMR (100 MHz, CDCl$_3$)



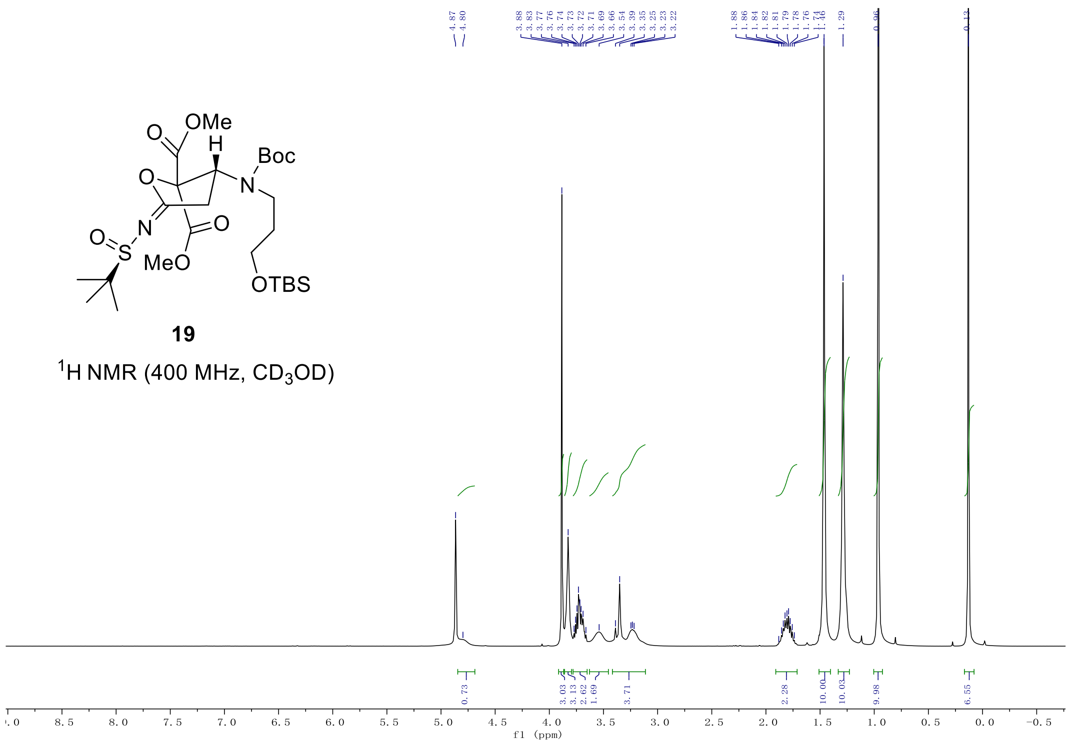
11

^{1}H NMR (600 MHz, CD_3OD)



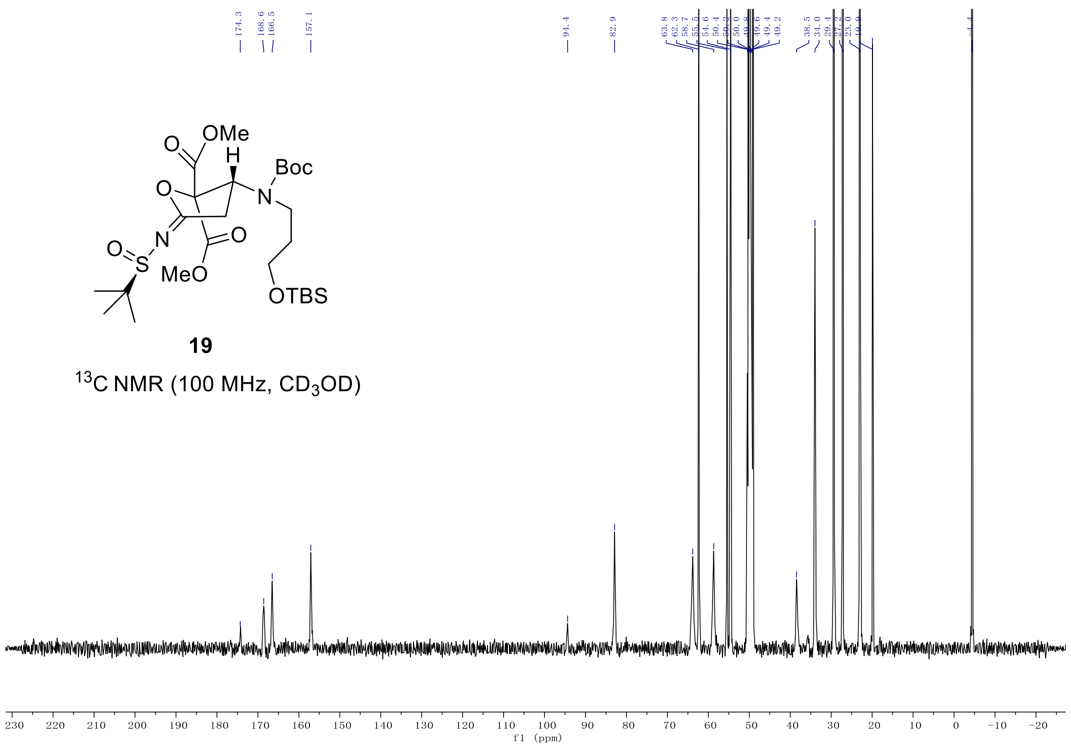
11

^{13}C NMR (150 MHz, CD_3OD)



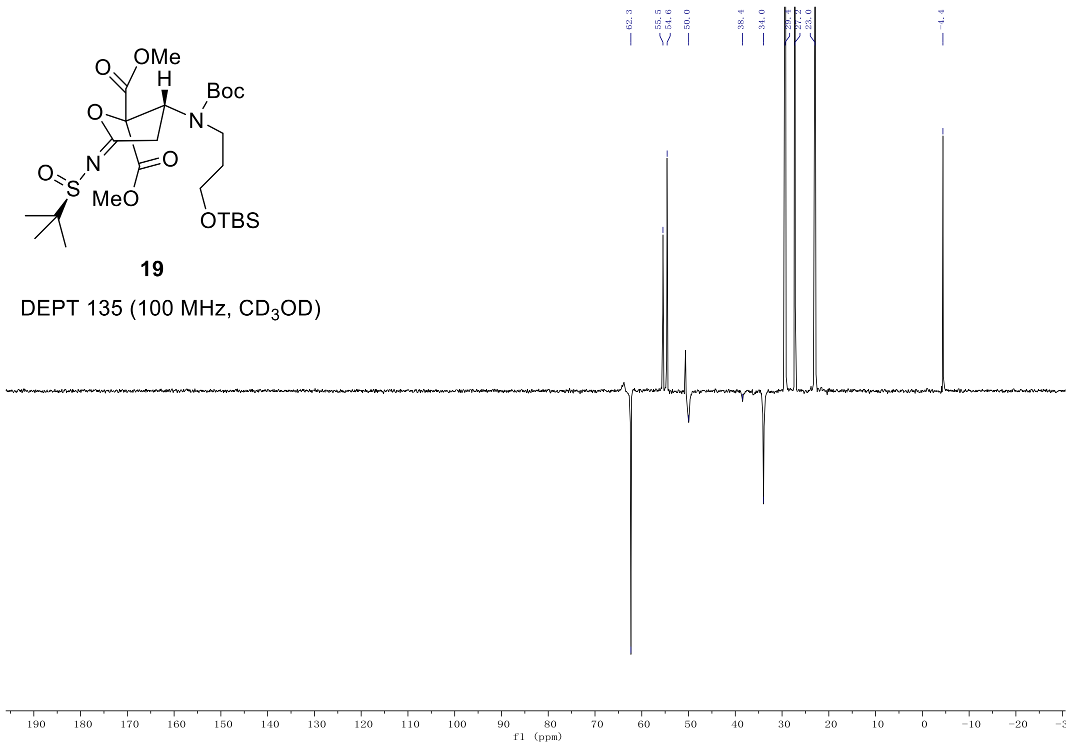
19

^{1}H NMR (400 MHz, CD_3OD)



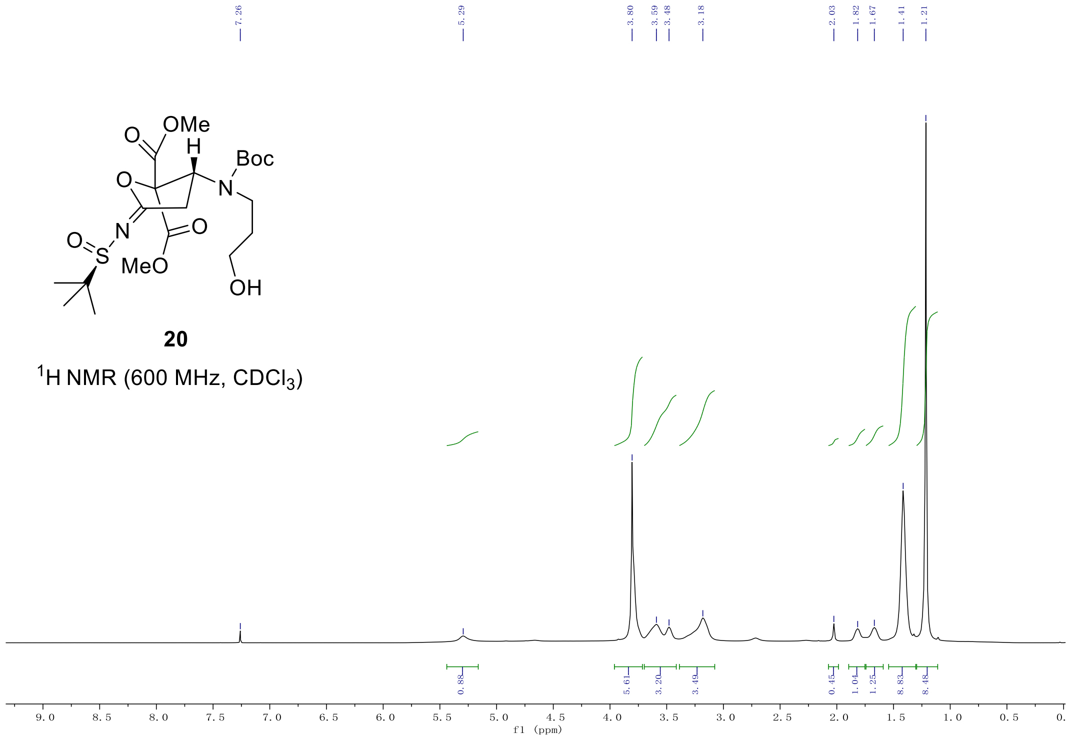
19

^{13}C NMR (100 MHz, CD_3OD)



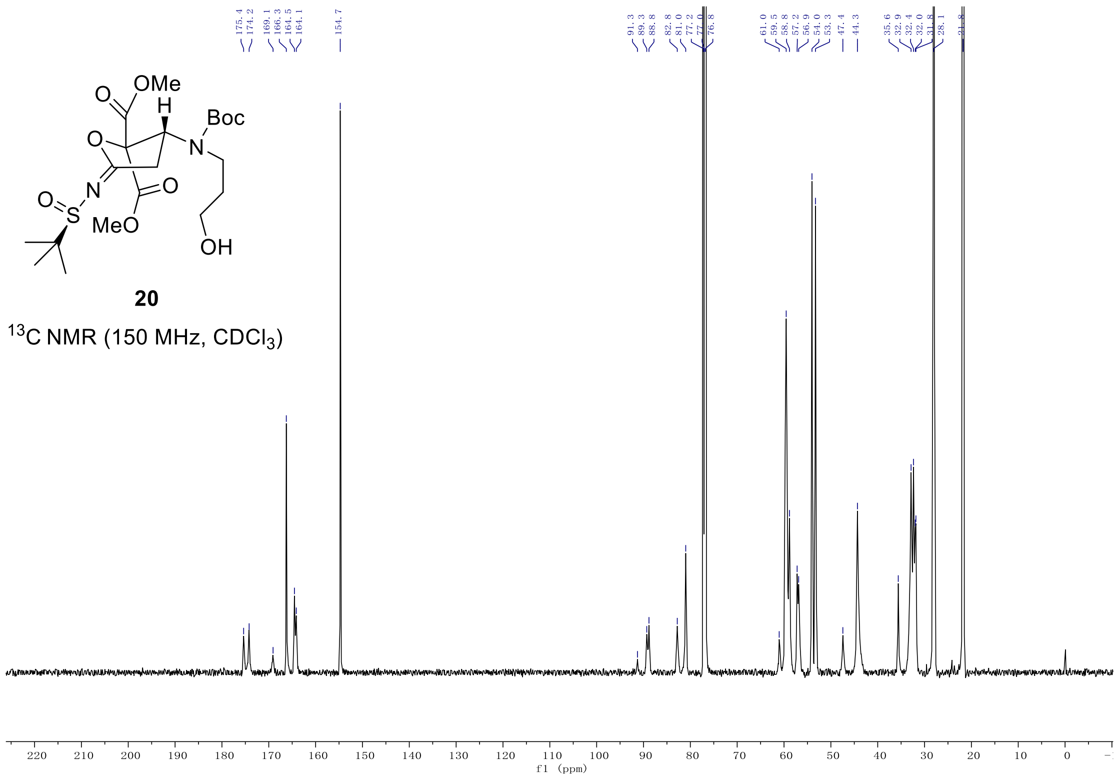
19

DEPT 135 (100 MHz, CD_3OD)



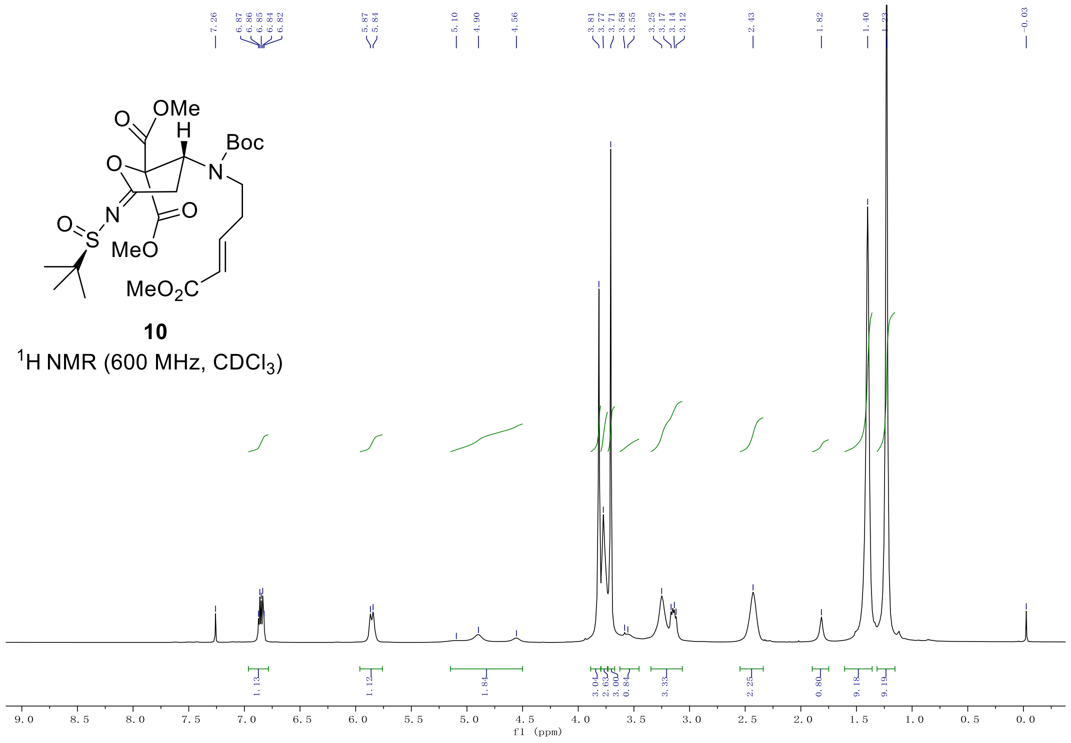
20

^1H NMR (600 MHz, $CDCl_3$)



20

^{13}C NMR (150 MHz, CDCl$_3$)

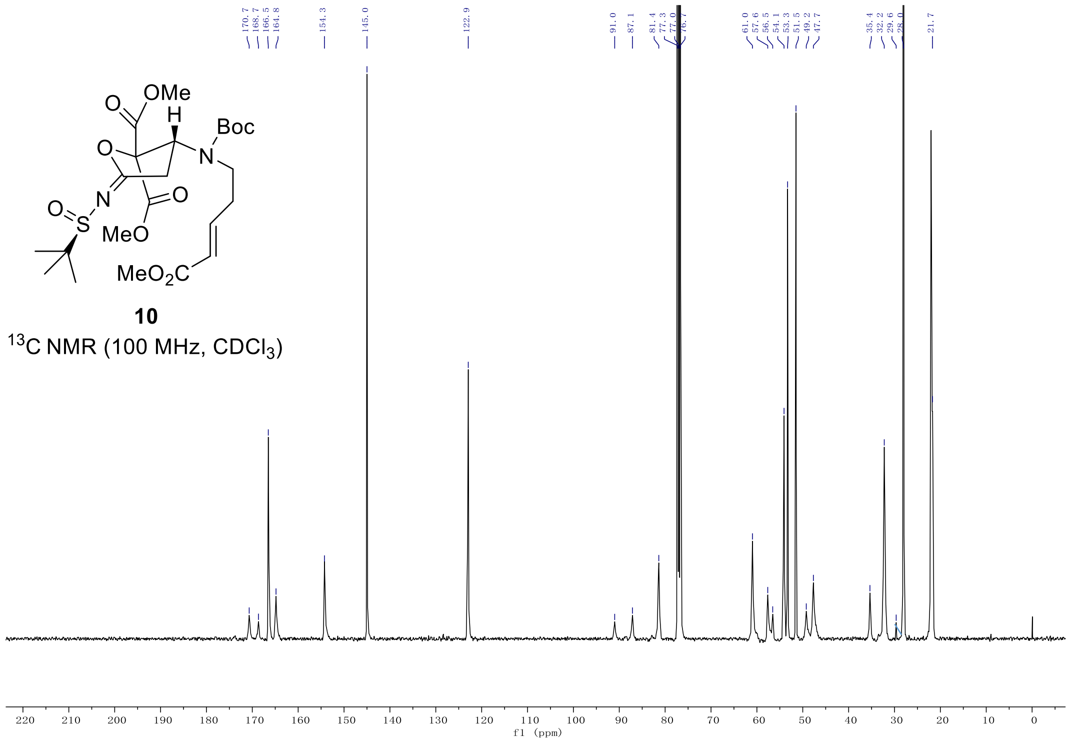


10

^{1}H NMR (600 MHz, CDCl$_3$)

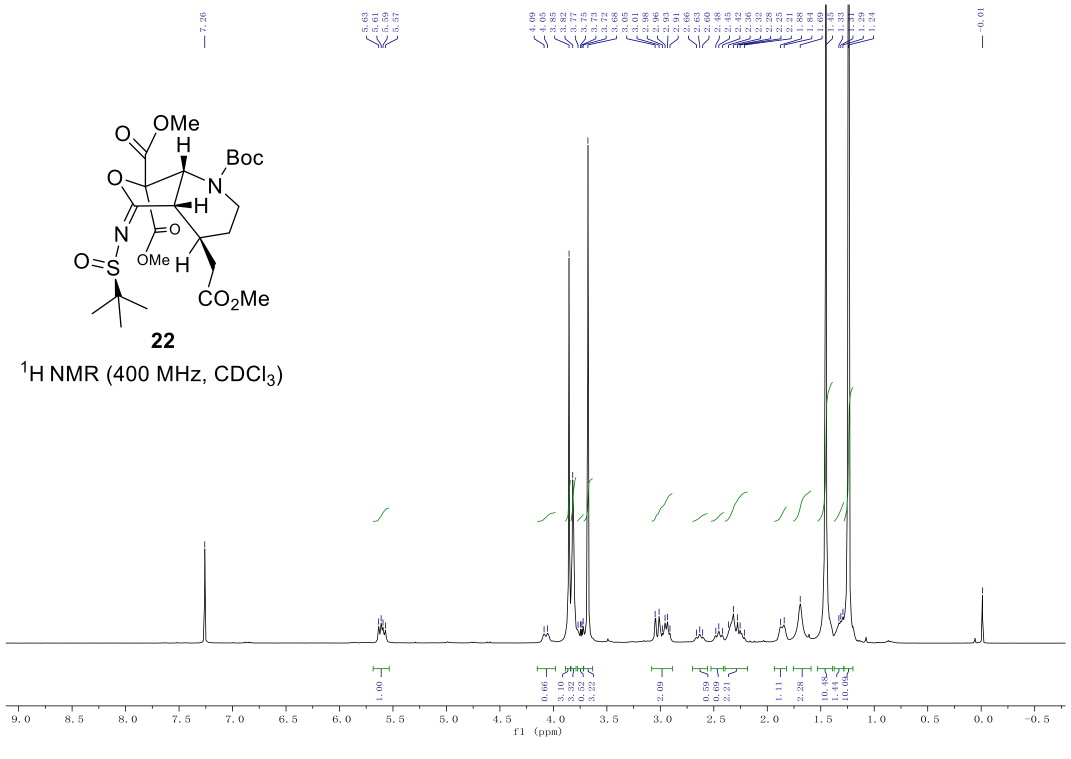
10

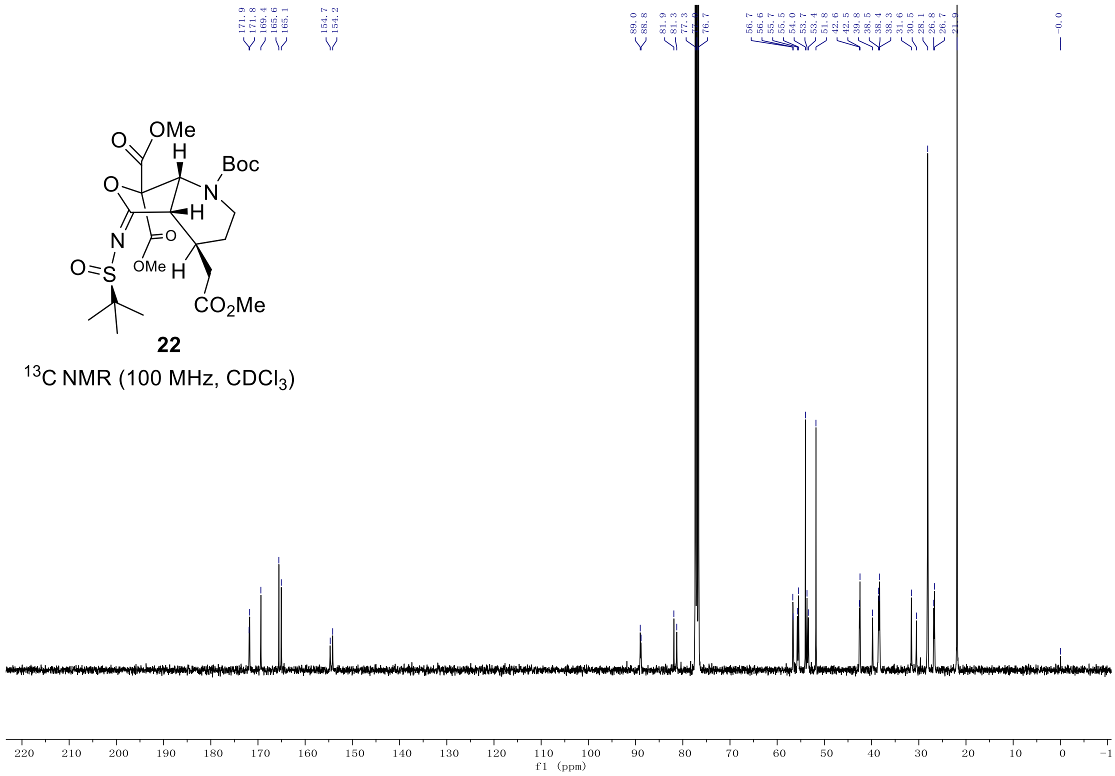
^{13}C NMR (100 MHz, CDCl$_3$)



22

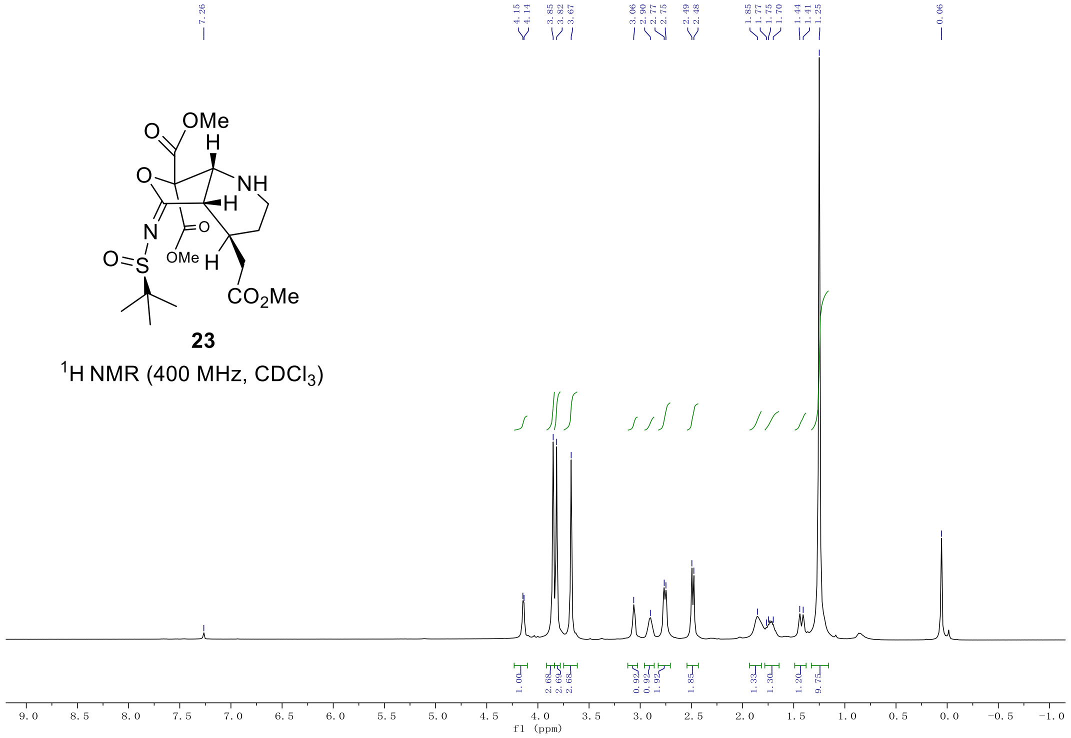
^{1}H NMR (400 MHz, CDCl$_3$)





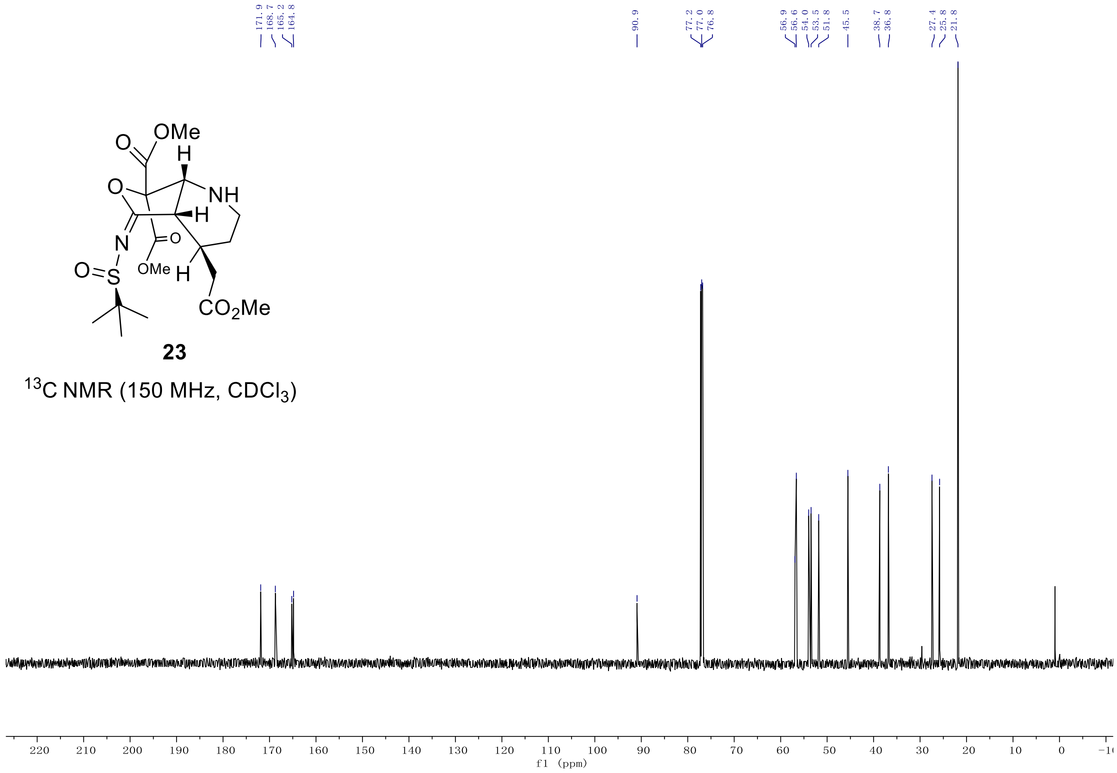
22

^{13}C NMR (100 MHz, CDCl$_3$)



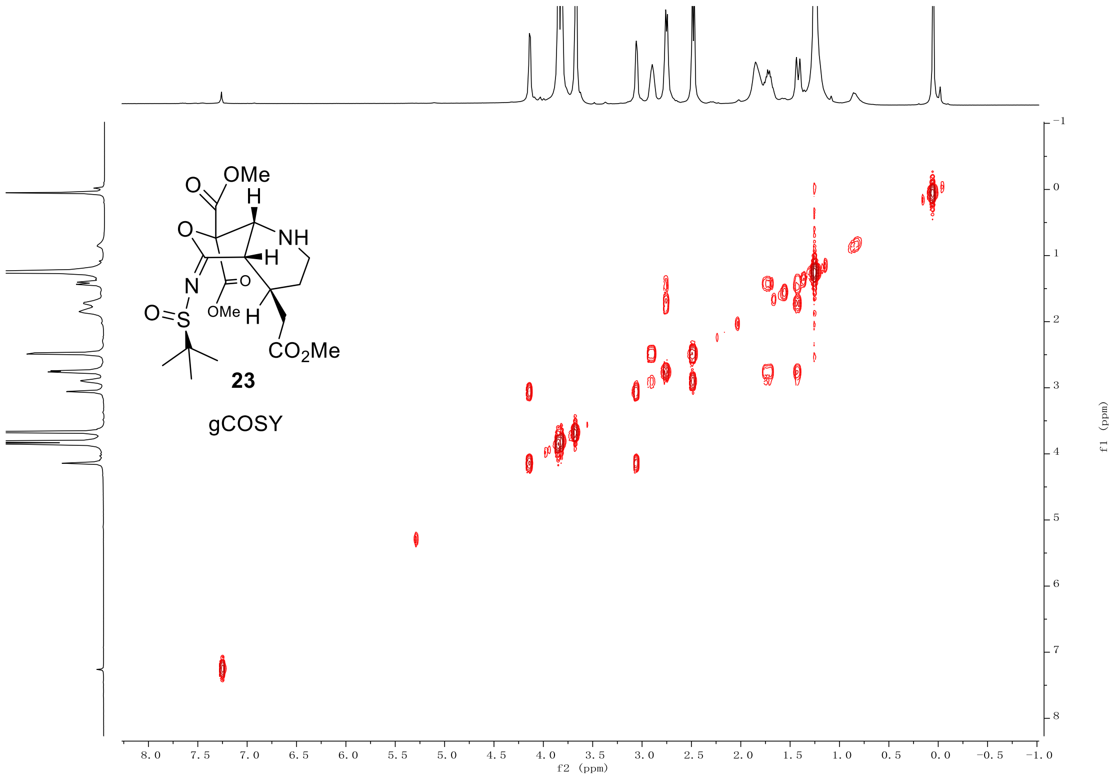
23

^{1}H NMR (400 MHz, CDCl$_3$)



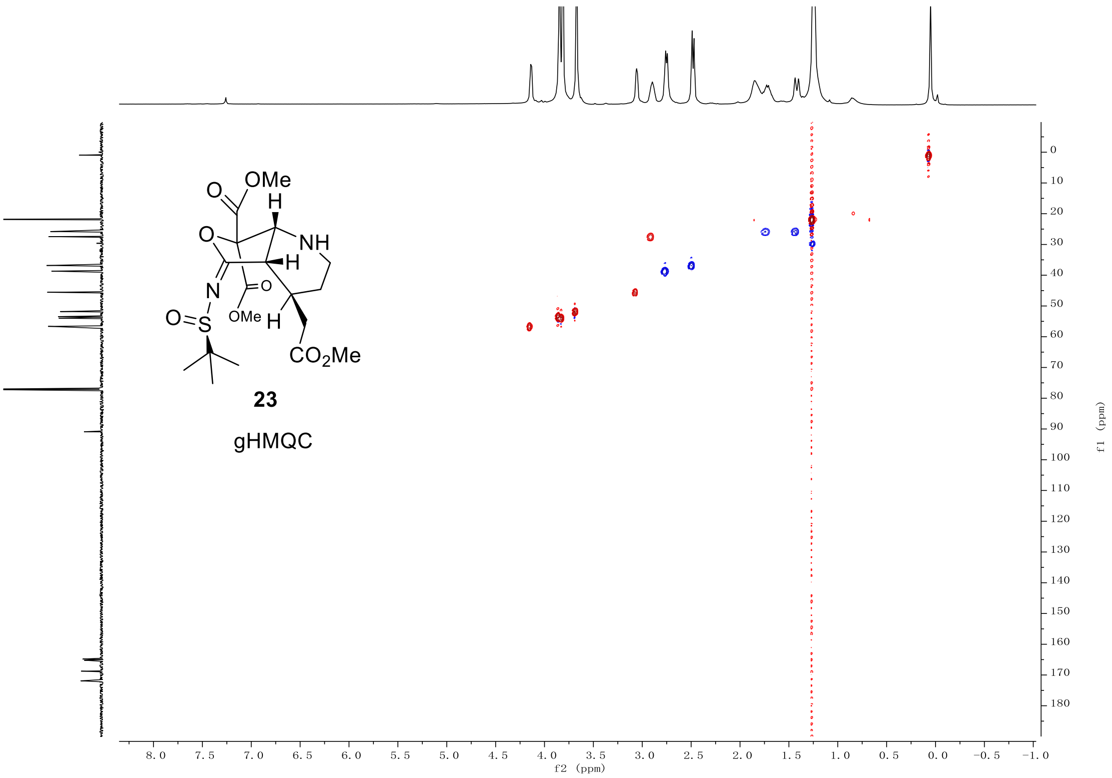
23

^{13}C NMR (150 MHz, CDCl$_3$)



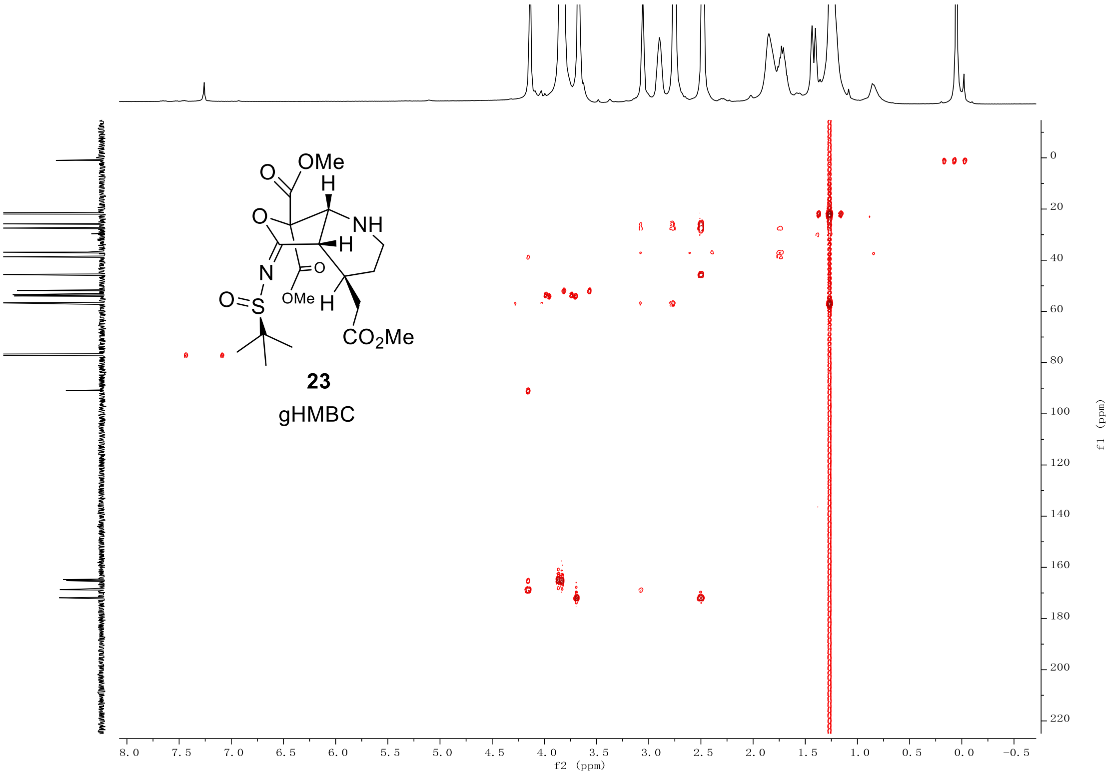
23

gCOSY



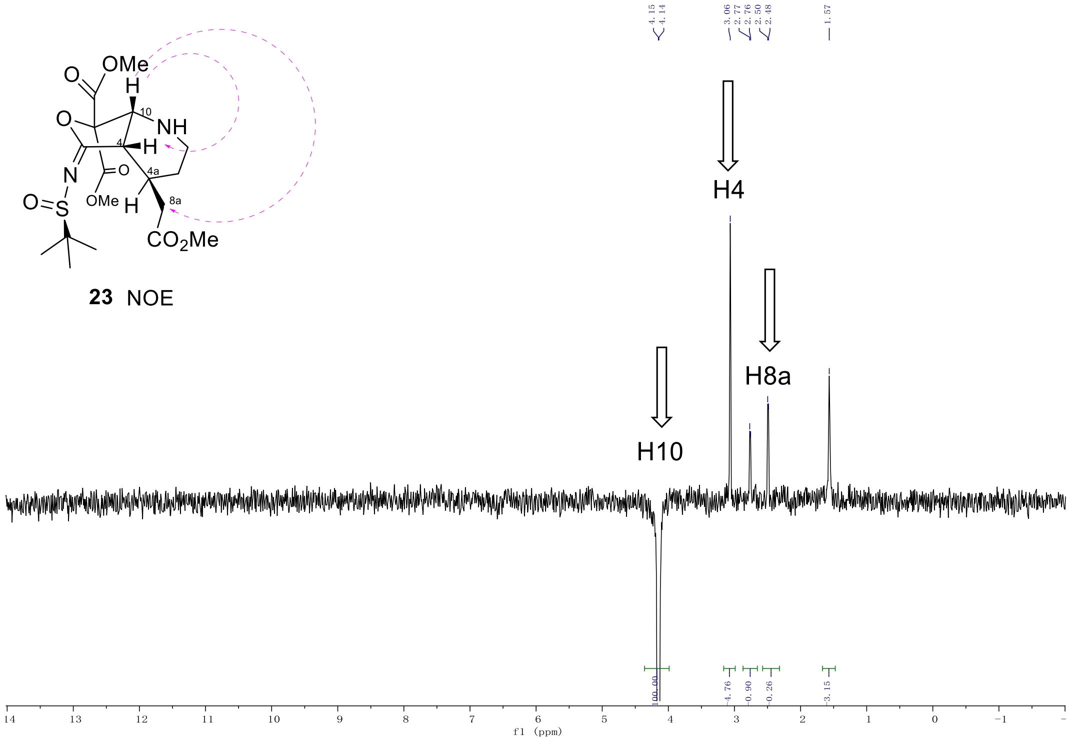
23

gHMQC

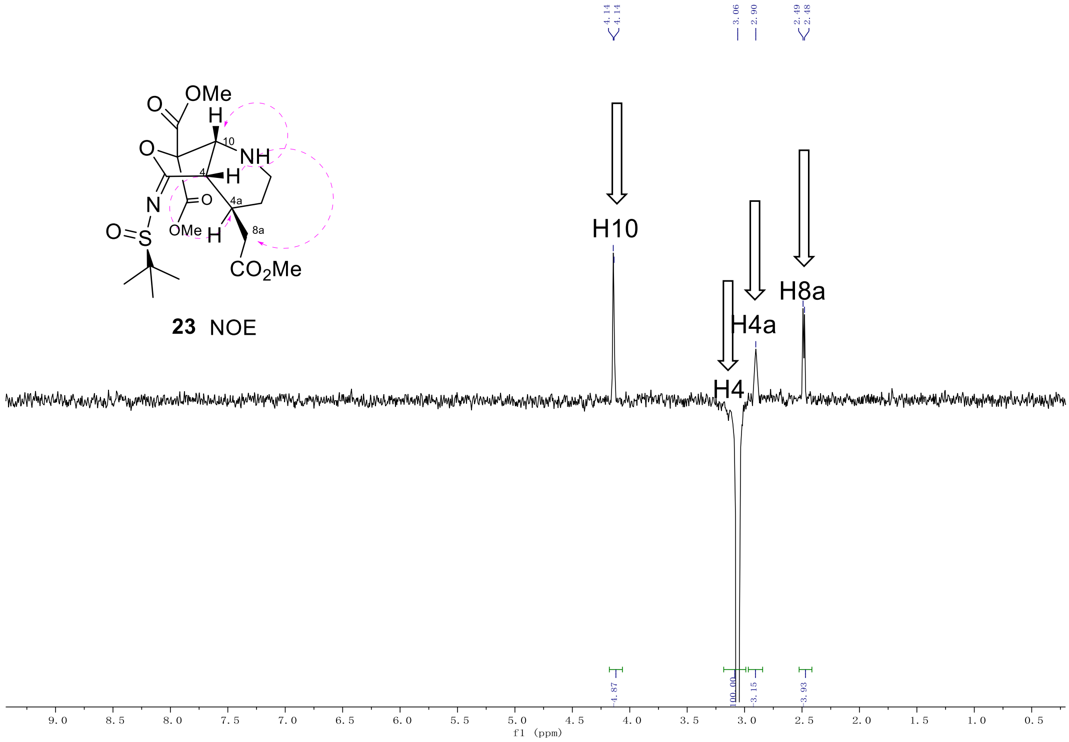


23

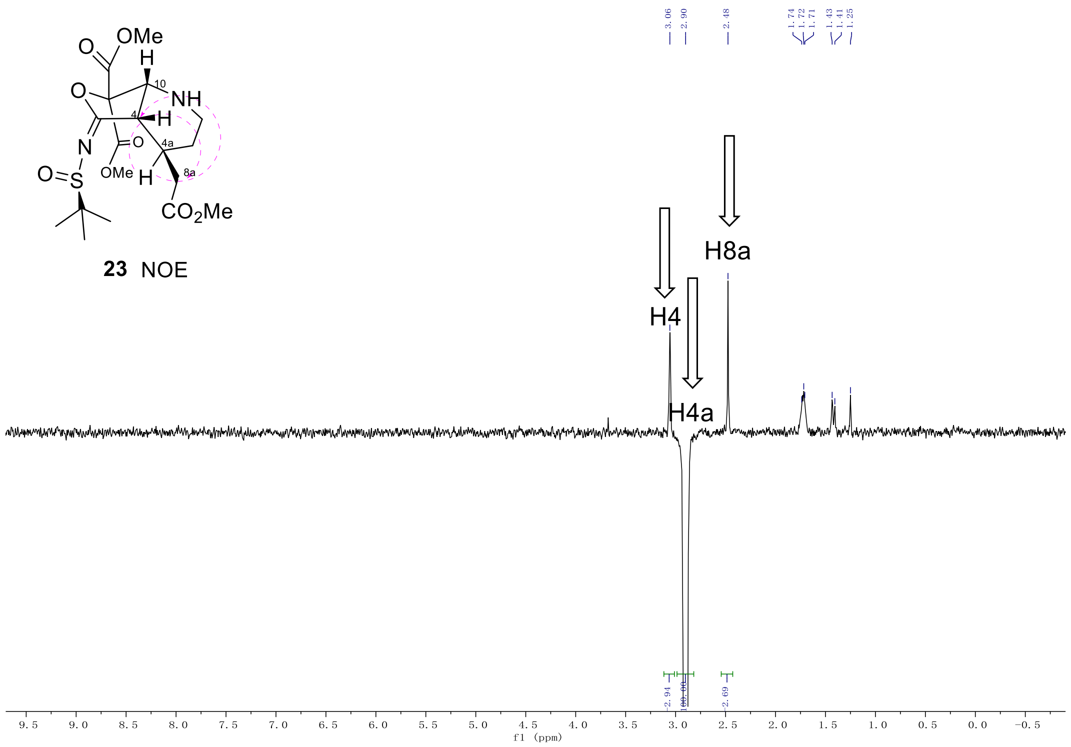
gHMBC

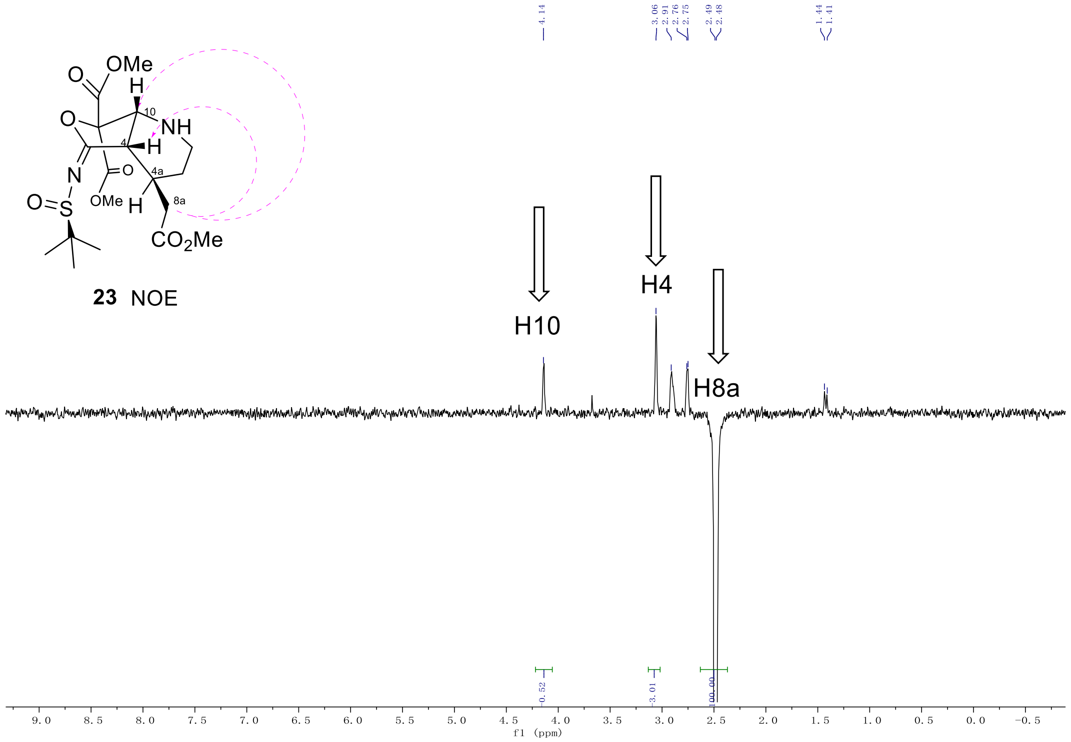

4.15
4.14
3.06
2.77
2.76
2.50
2.48
1.57
OMe
H
10
O
NH
4
H
N
4a
O
O=S
OMe
H
8a
CO2Me
H4
H8a
H10
100.00
-4.76
-0.90
-0.26
-3.15
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

23 NOE


4.14
4.14
3.06
2.90
2.49
2.48
OMe
H
10
O
NH
4
H
N
4a
O
O=S
OMe
H
8a
CO2Me
H10
H4a
H8a
H4
-4.87
100.00
-3.15
-3.93
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

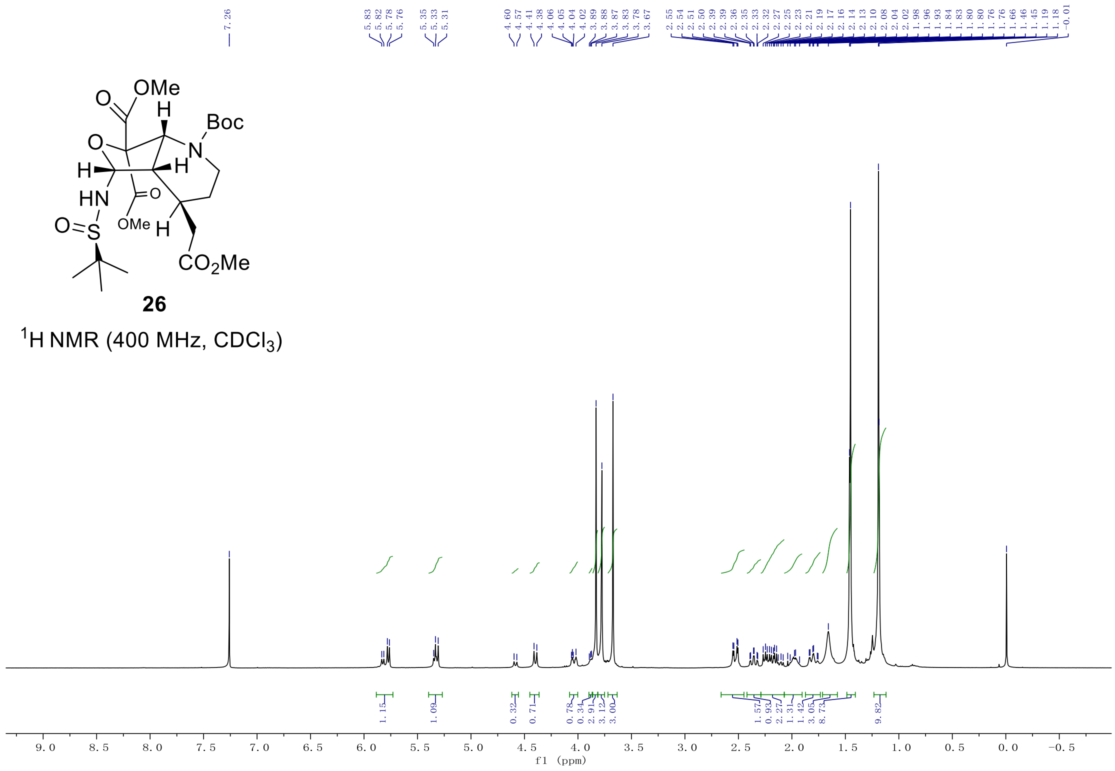
23 NOE


OMe
O
H
10
O
NH
4
H
4a
O
N
O=S
OMe
H
8a
CO2Me
23 NOE
3.06
2.90
2.48
1.74
1.72
1.71
1.43
1.41
1.25
H8a
H4
H4a
2.94
100.00
2.69
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


OMe
O
H
10
O
NH
4
H
4a
O
N
O=S
OMe
H
8a
CO2Me
23 NOE
4.14
3.06
2.91
2.76
2.75
2.49
2.48
1.44
1.41
H10
H4
H8a
0.52
3.01
100.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

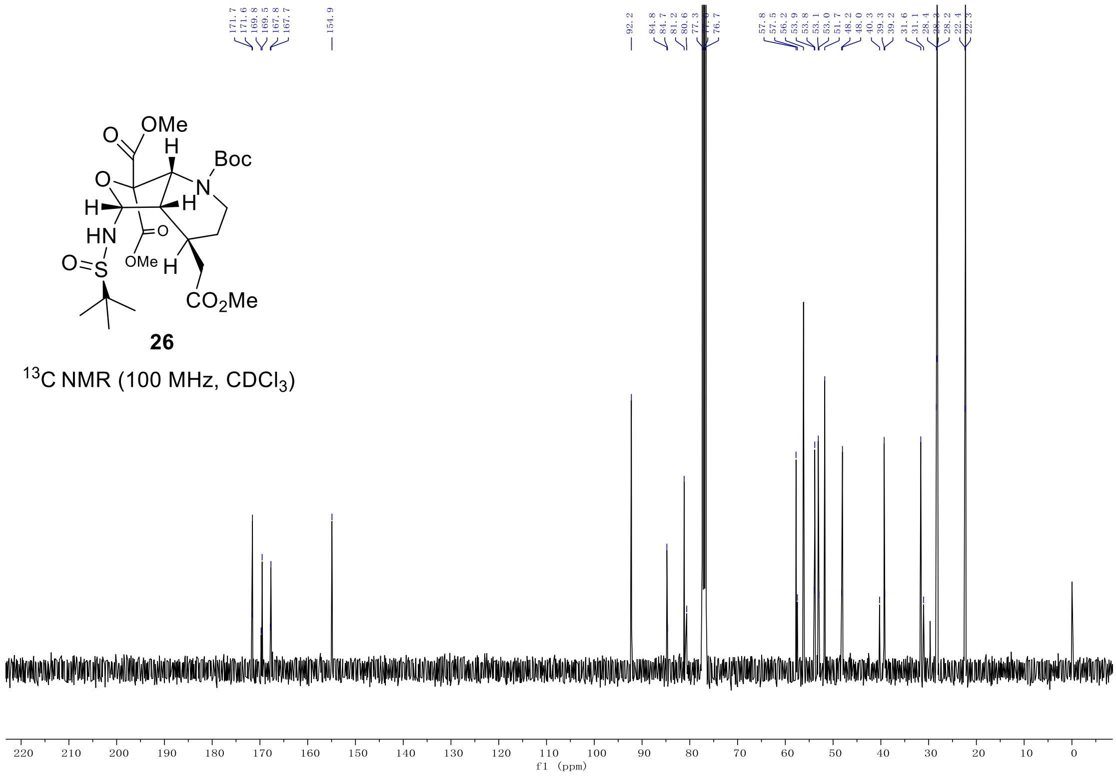
26

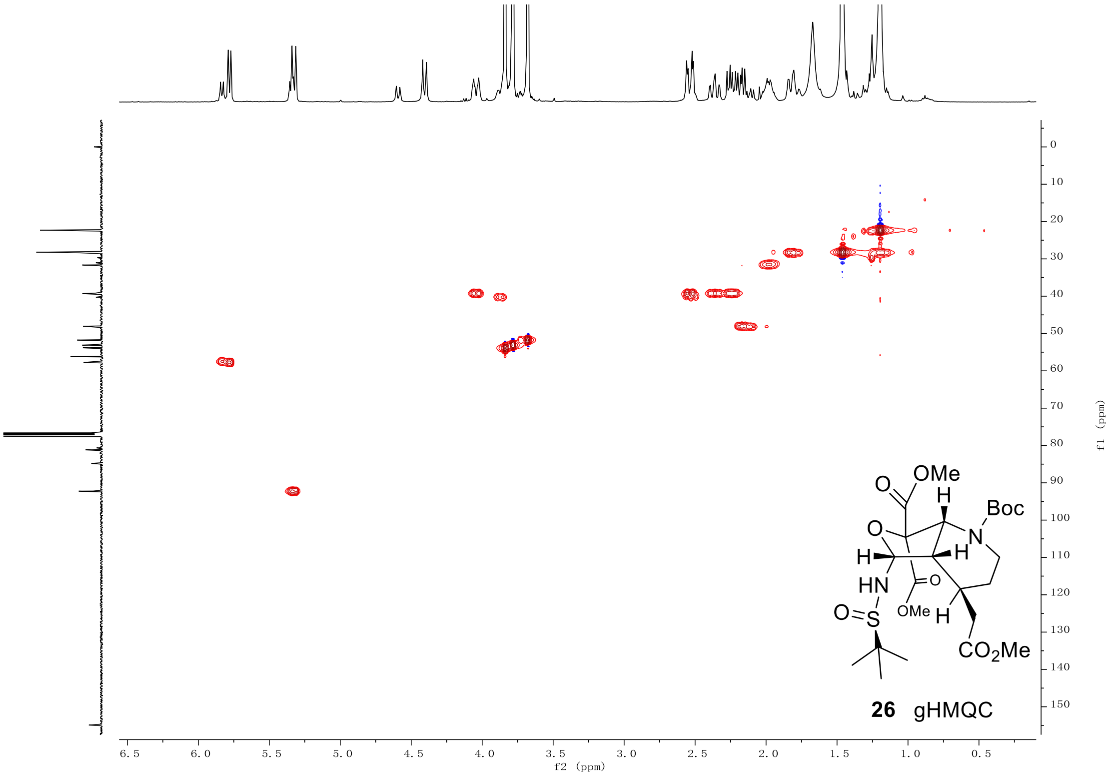
^{1}H NMR (400 MHz, CDCl$_3$)

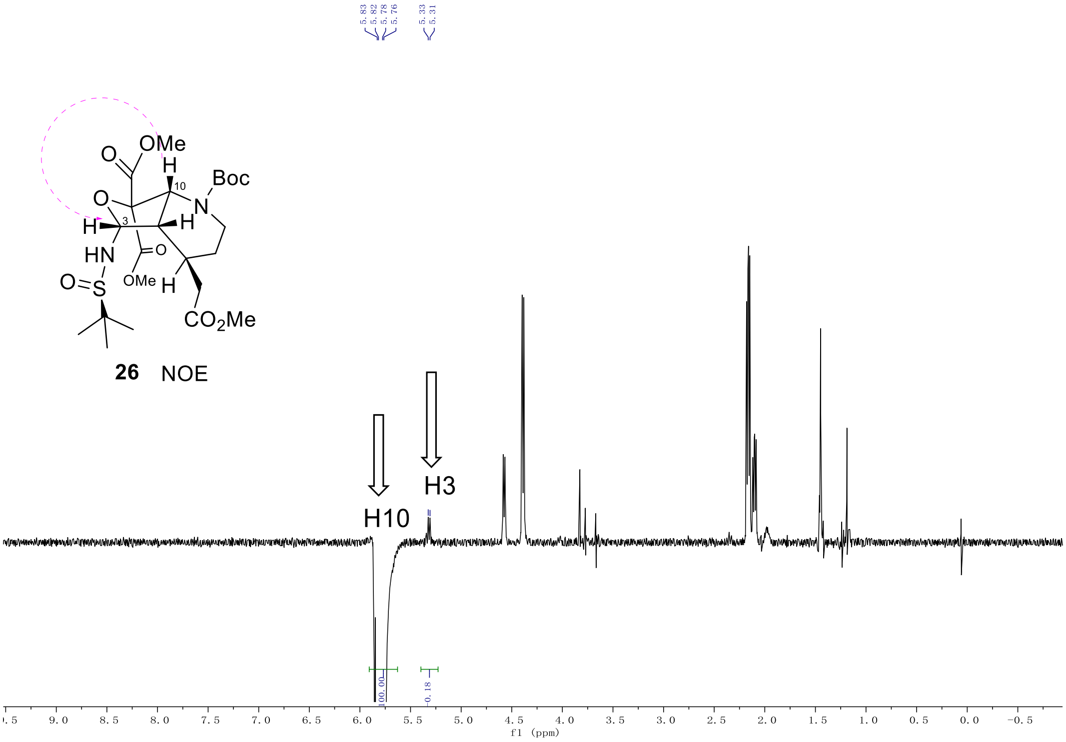


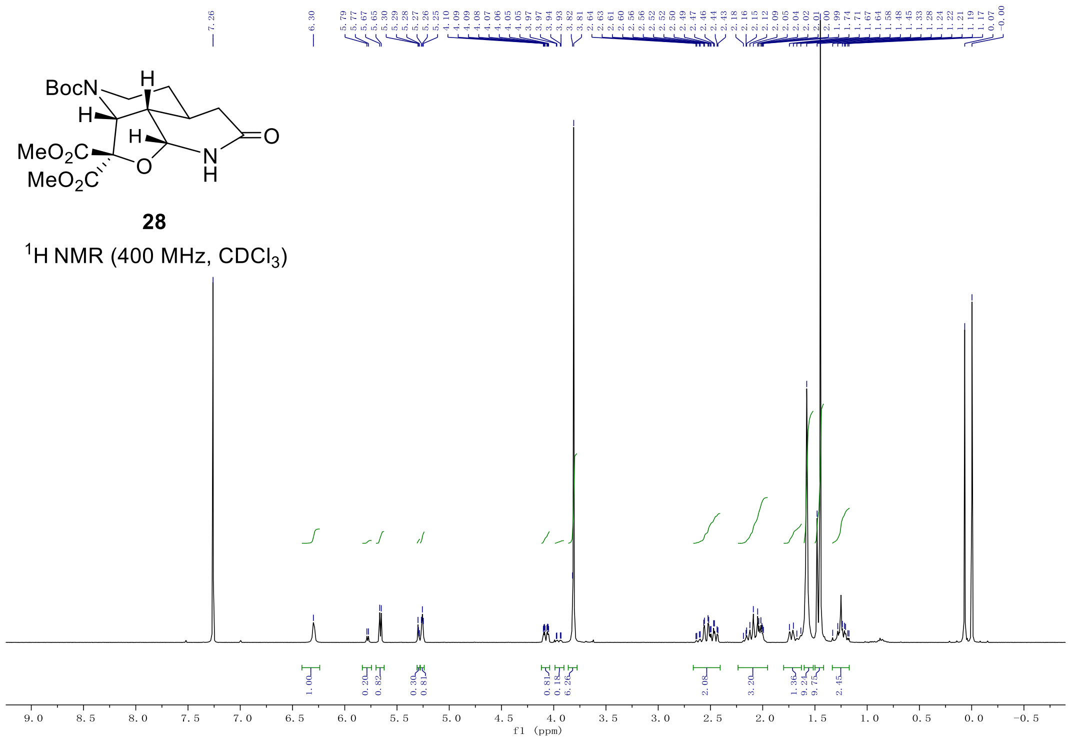
26

^{13}C NMR (100 MHz, CDCl$_3$)



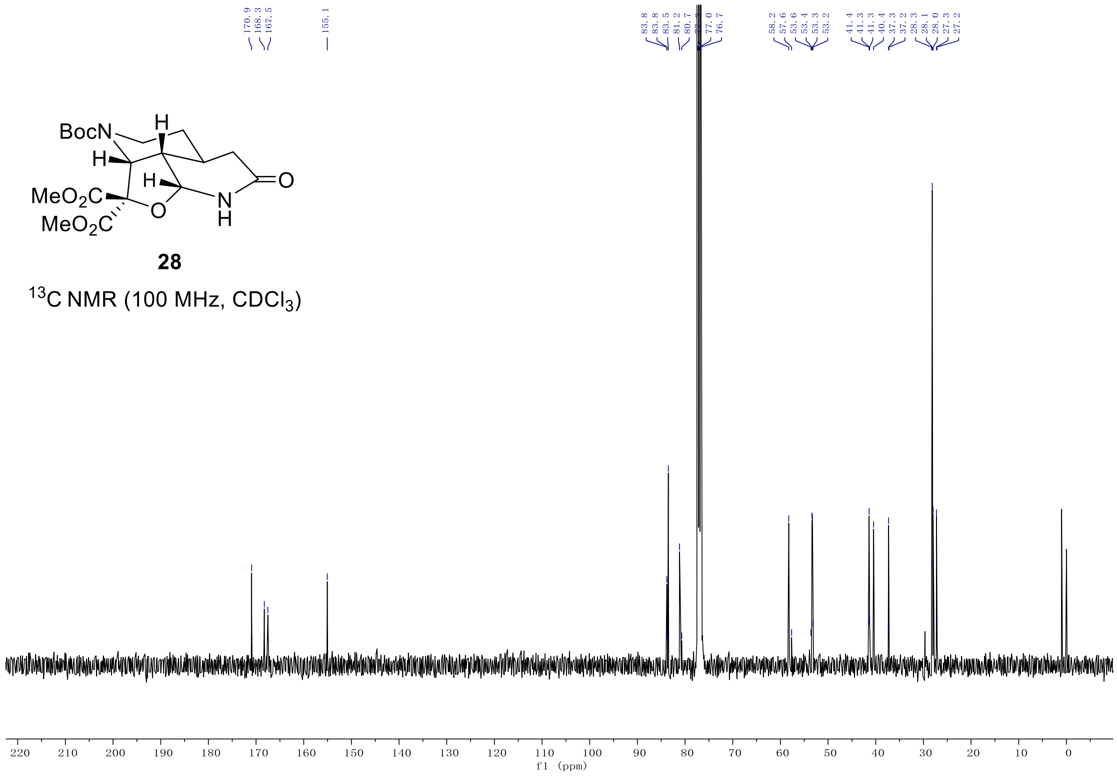

26 gHMQC


26 NOE



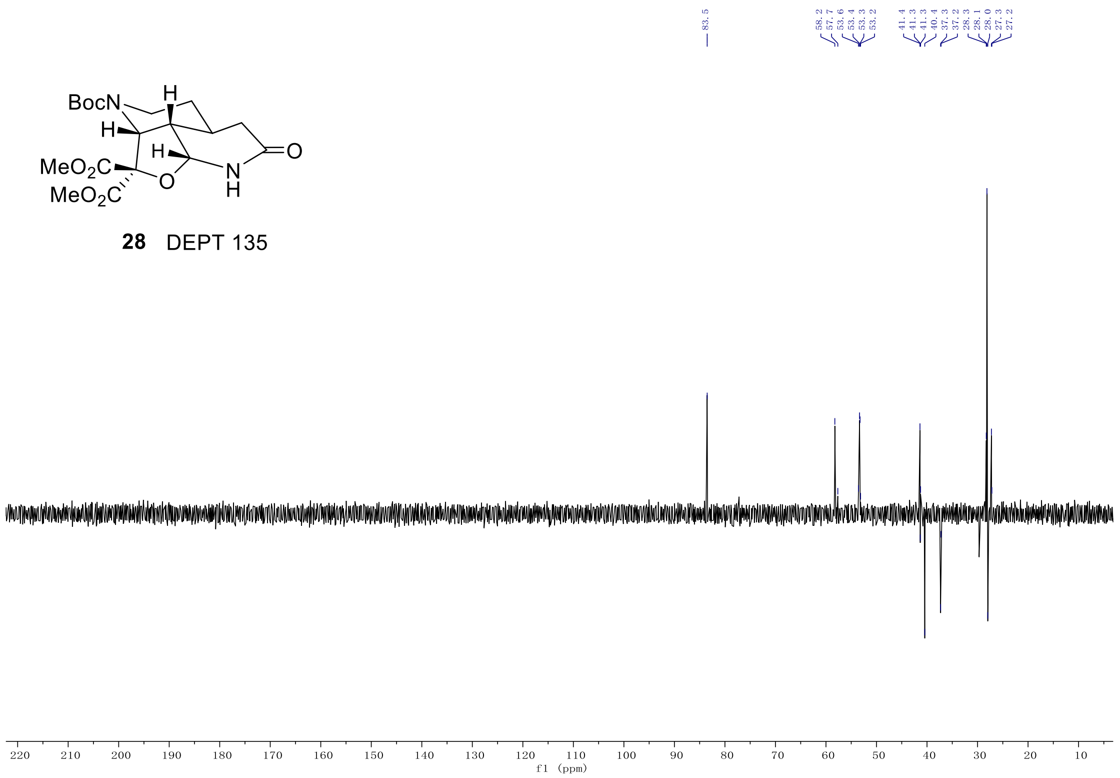
28

^{1}H NMR (400 MHz, CDCl$_3$)

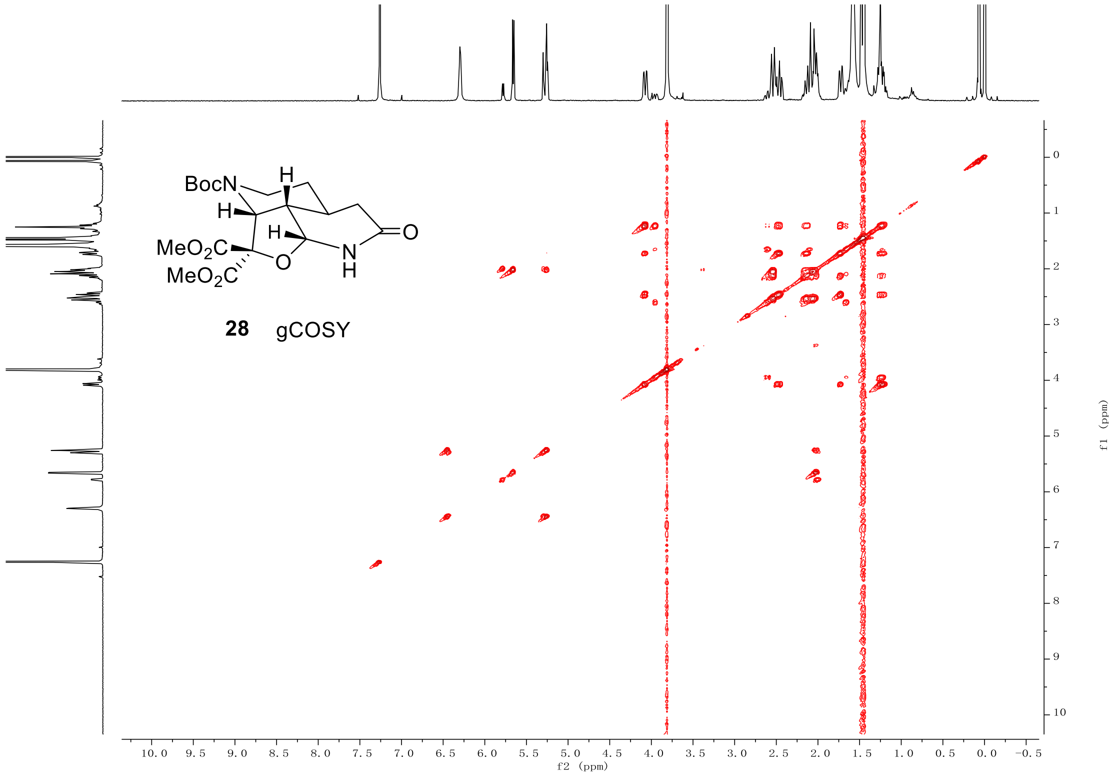


28

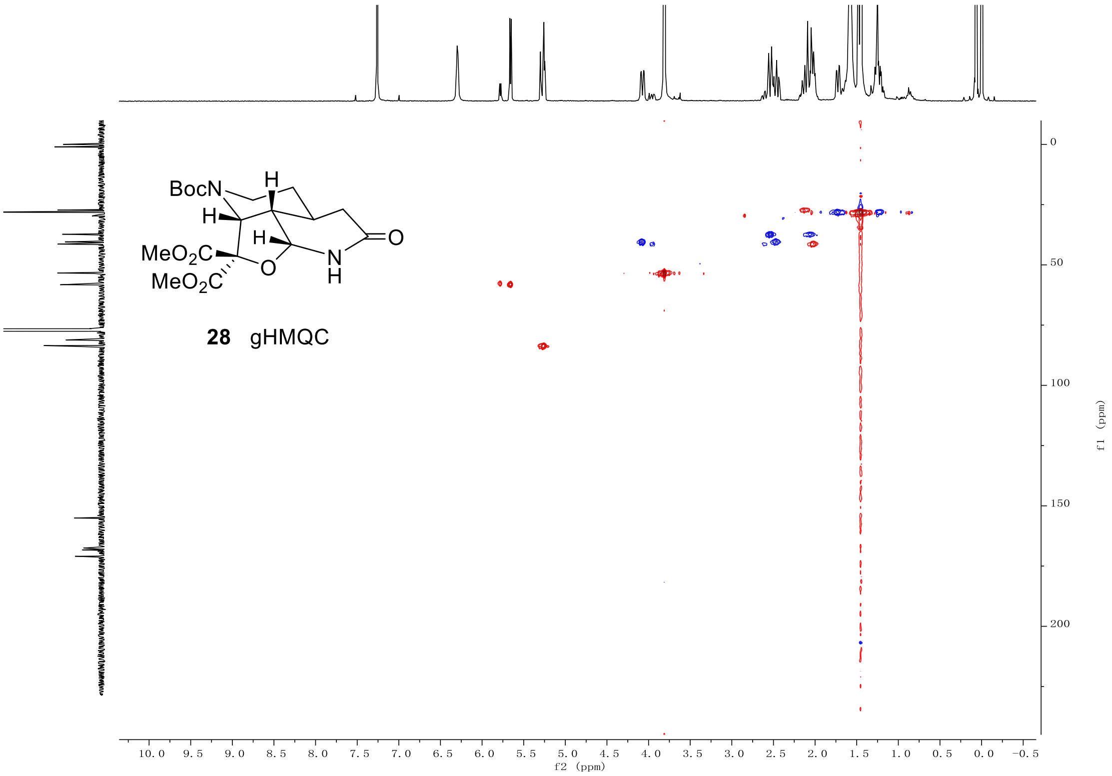
^{13}C NMR (100 MHz, CDCl$_3$)

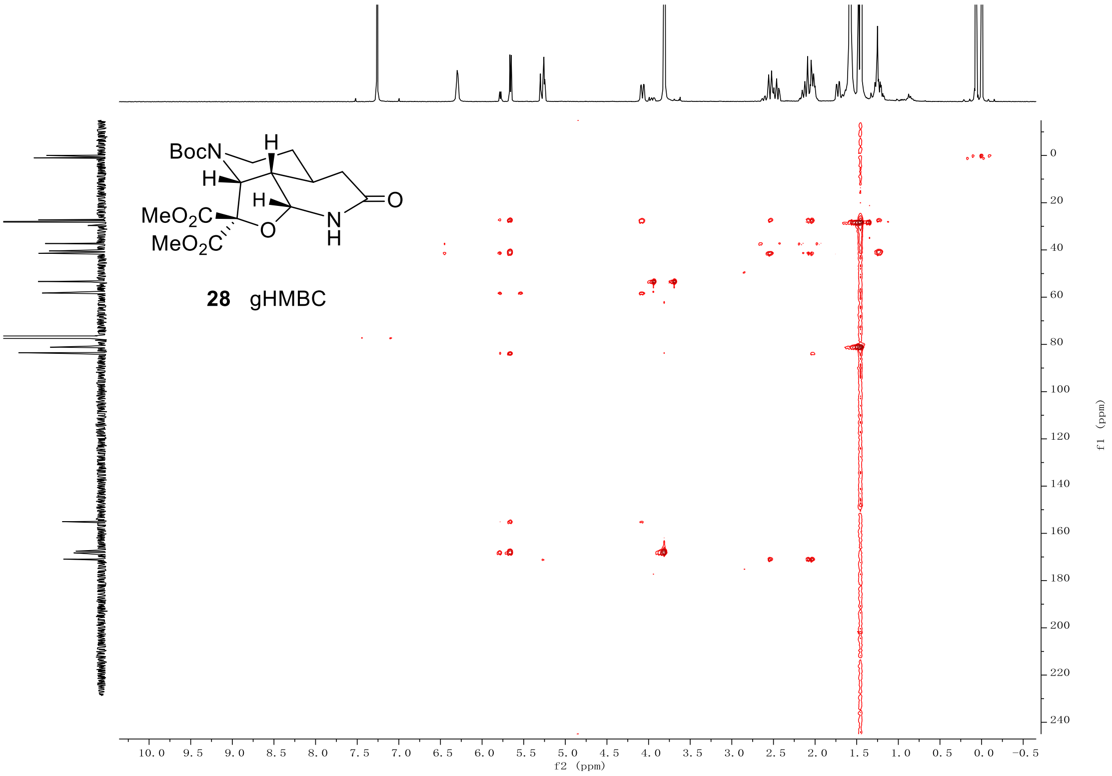


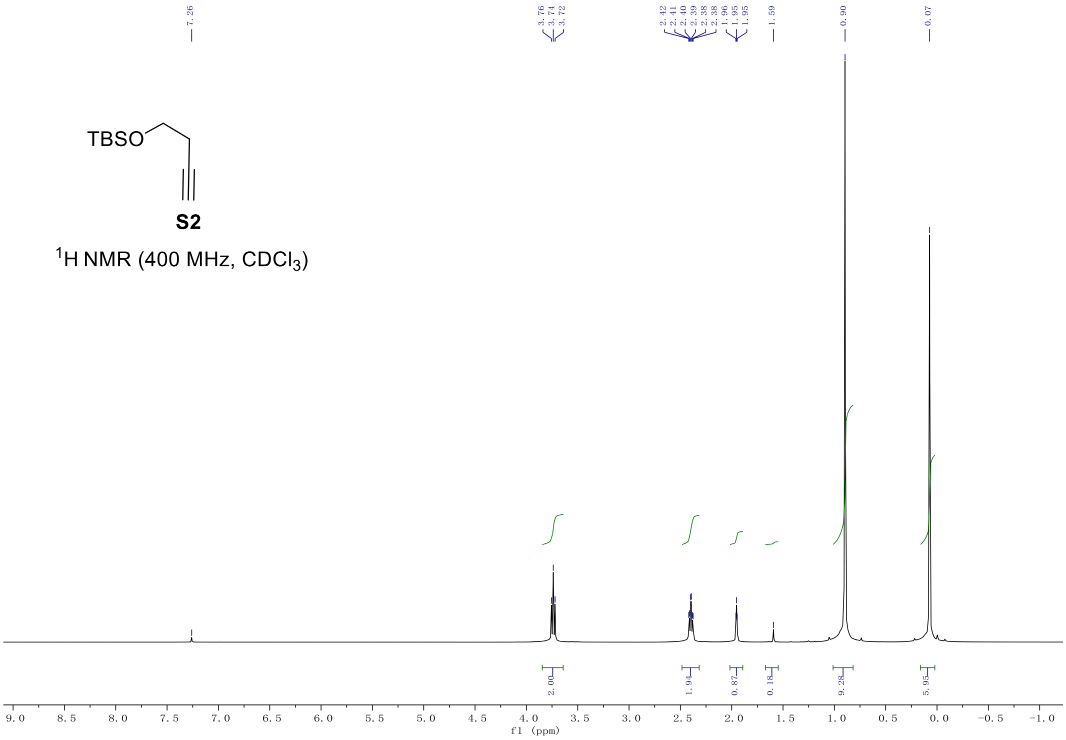
28 DEPT 135



28 gCOSY

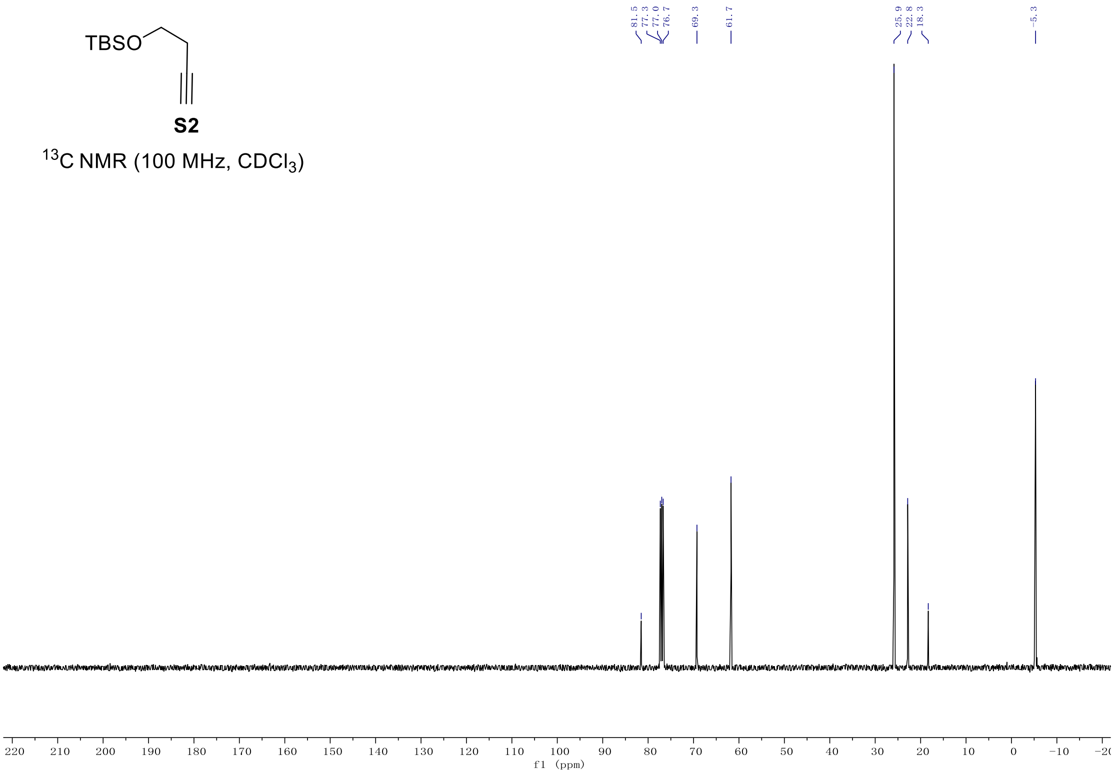

28 gHMQC


28 gHMBC



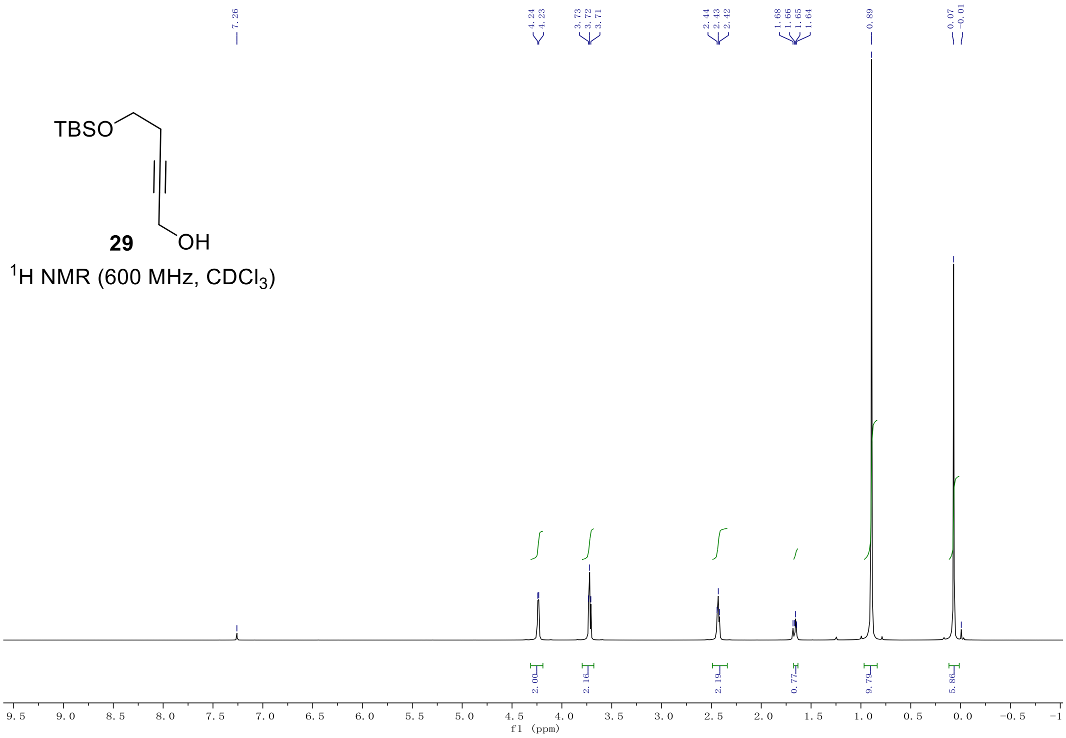
S2

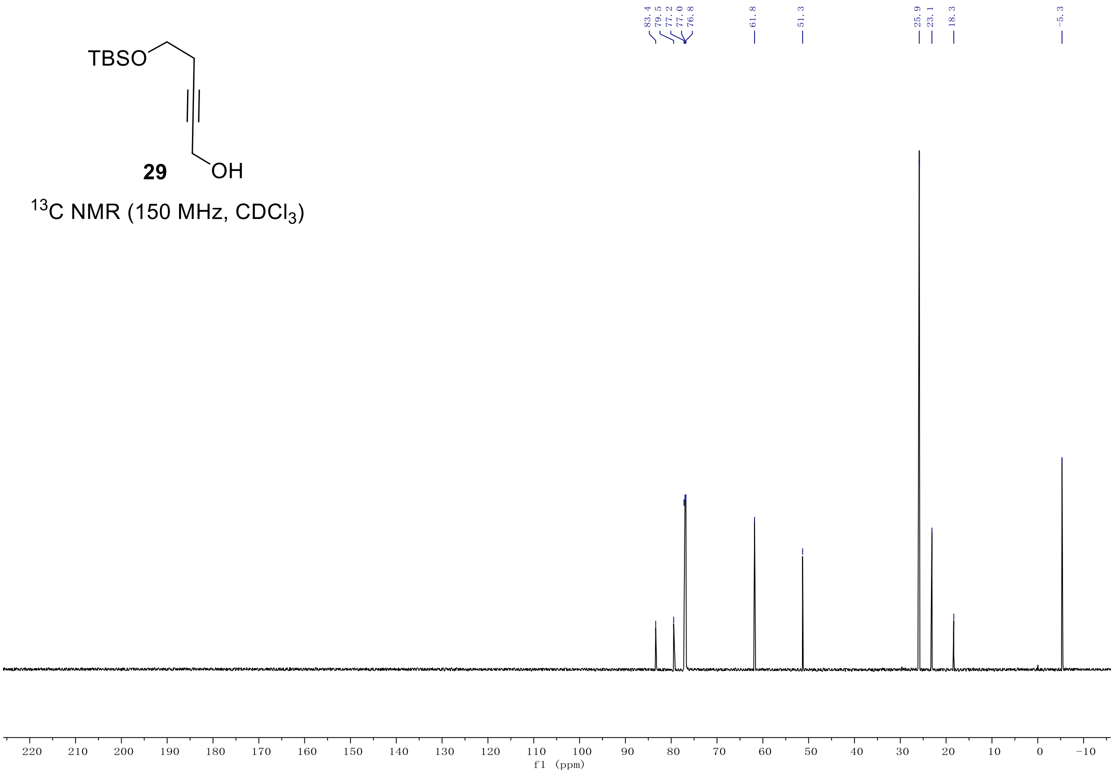
^{1}H NMR (400 MHz, $CDCl_3$)

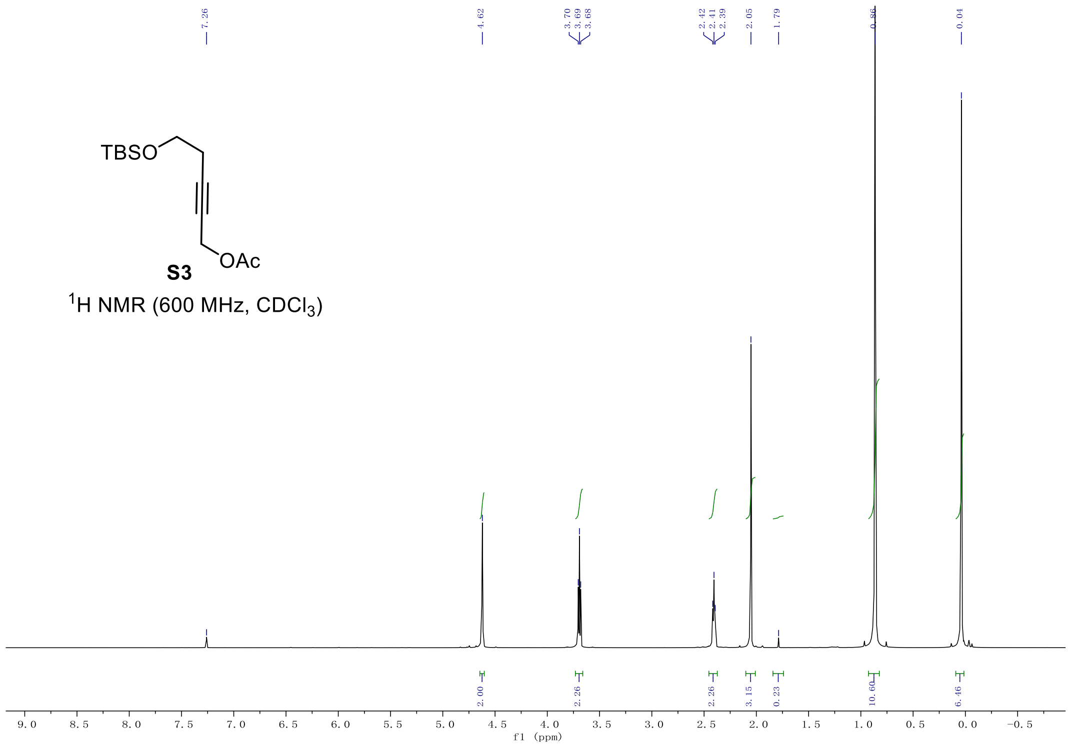


S2

^{13}C NMR (100 MHz, $CDCl_3$)

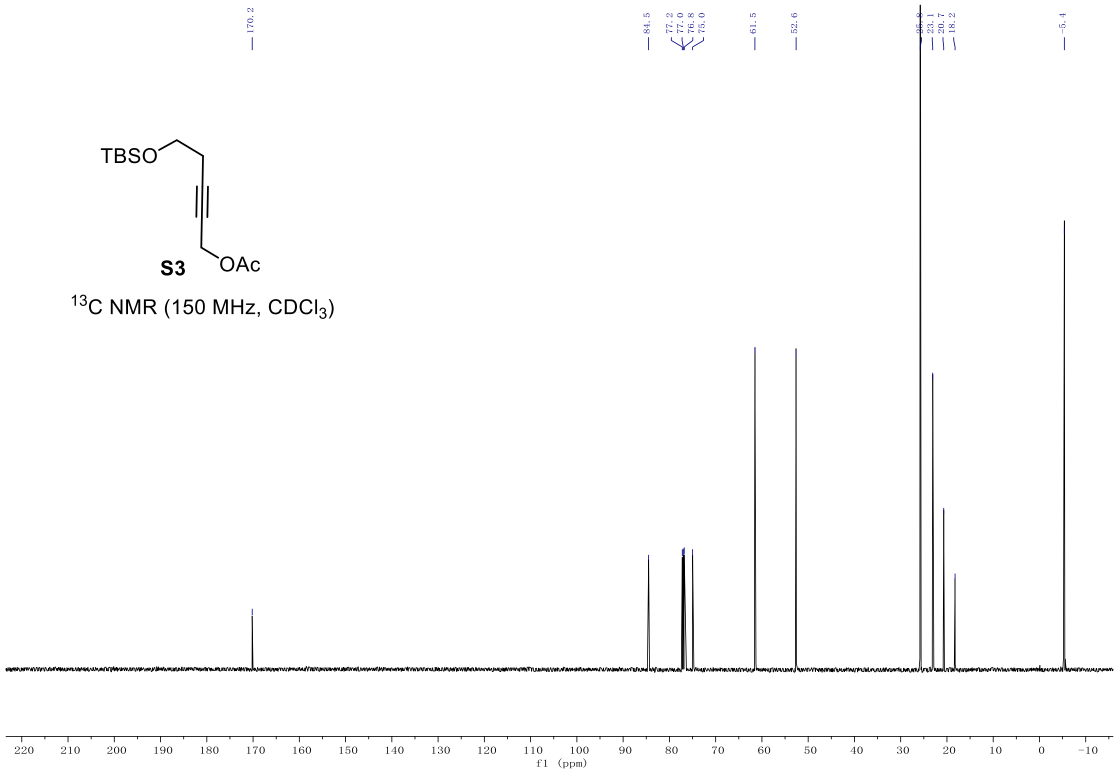

TBSO
OH
29
^{1}H NMR (600 MHz, CDCl$_3$)
7.26
4.24
4.23
3.73
3.72
3.71
2.44
2.43
2.42
1.68
1.66
1.65
1.64
0.89
0.07
-0.01
2.00
2.16
2.19
0.77
9.79
5.86
f1 (ppm)


TBSO
OH
29
^{13}C NMR (150 MHz, CDCl$_3$)
83.4
79.5
77.2
77.0
76.8
61.8
51.3
25.9
23.1
18.3
-5.3
f1 (ppm)



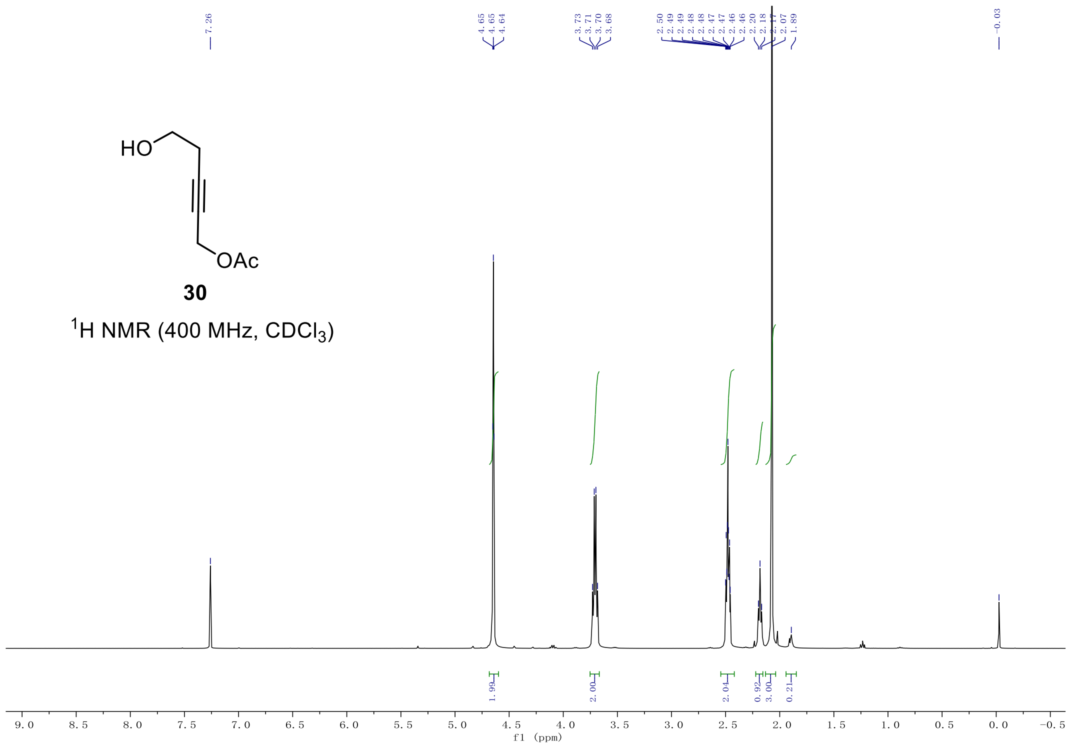
S3

^{1}H NMR (600 MHz, $CDCl_3$)



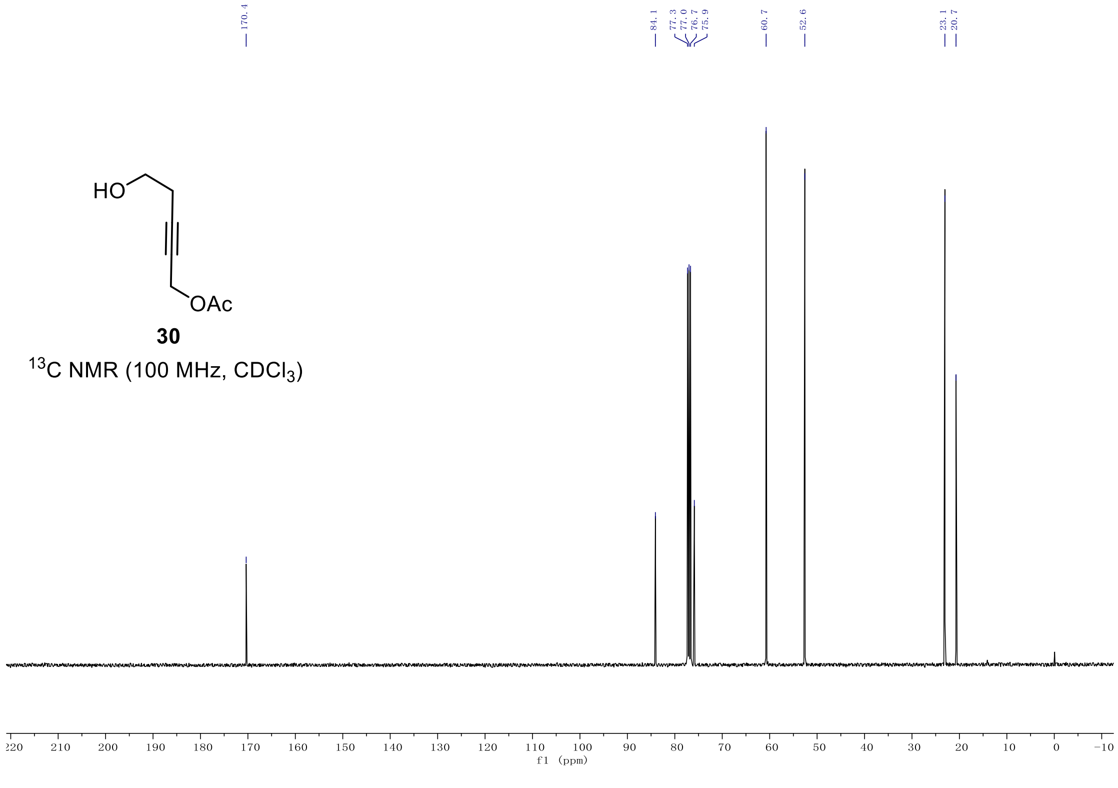
S3

^{13}C NMR (150 MHz, $CDCl_3$)



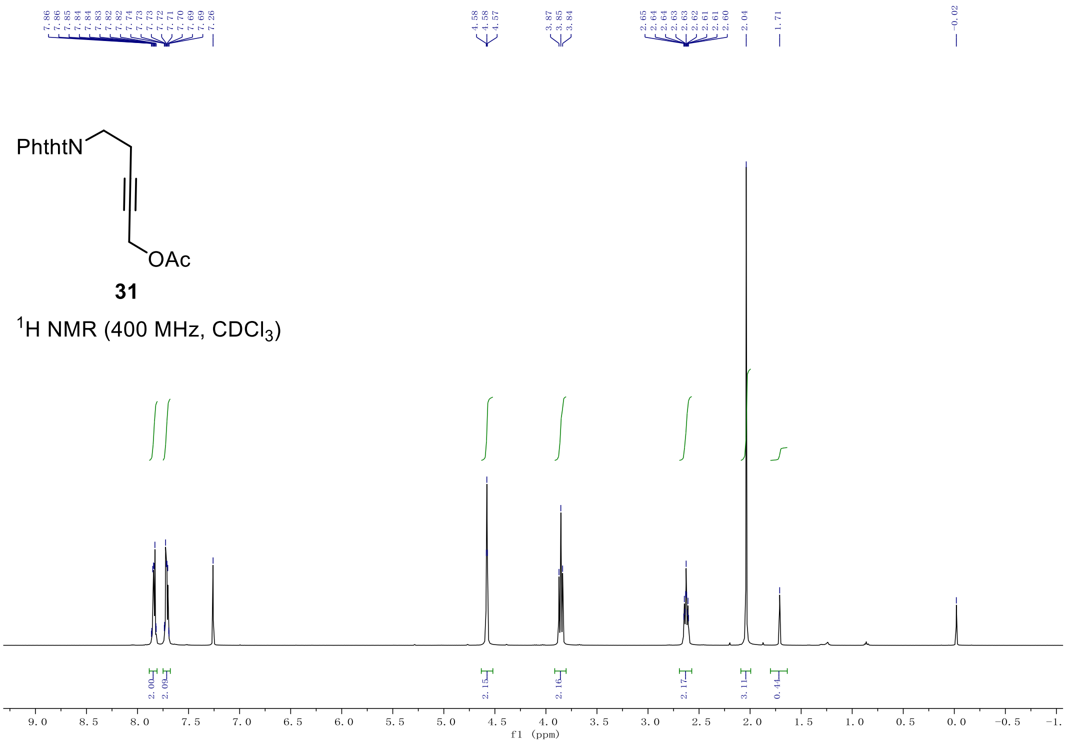
30

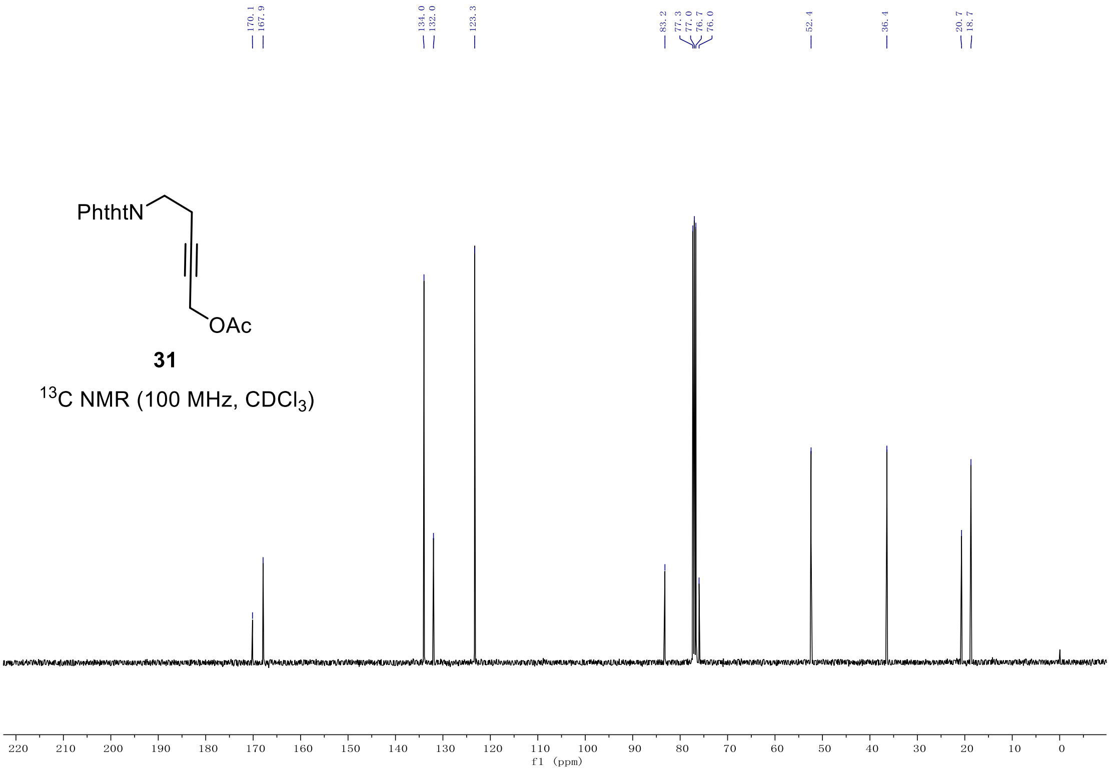
^{1}H NMR (400 MHz, CDCl$_3$)

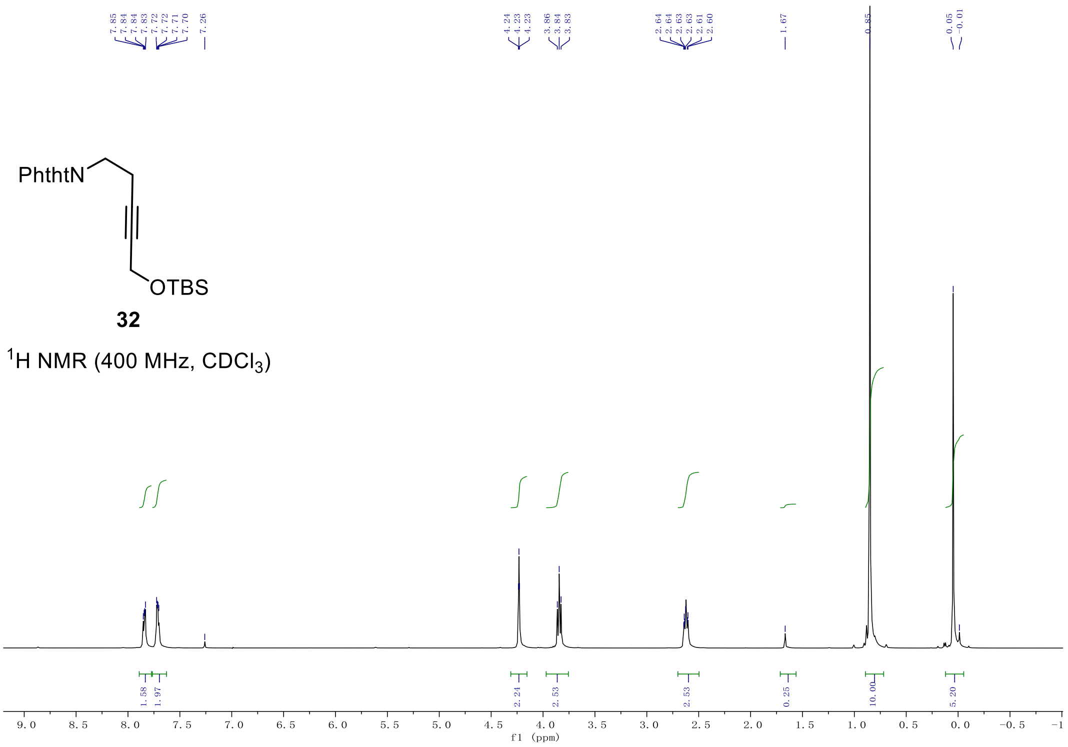


30

^{13}C NMR (100 MHz, CDCl$_3$)

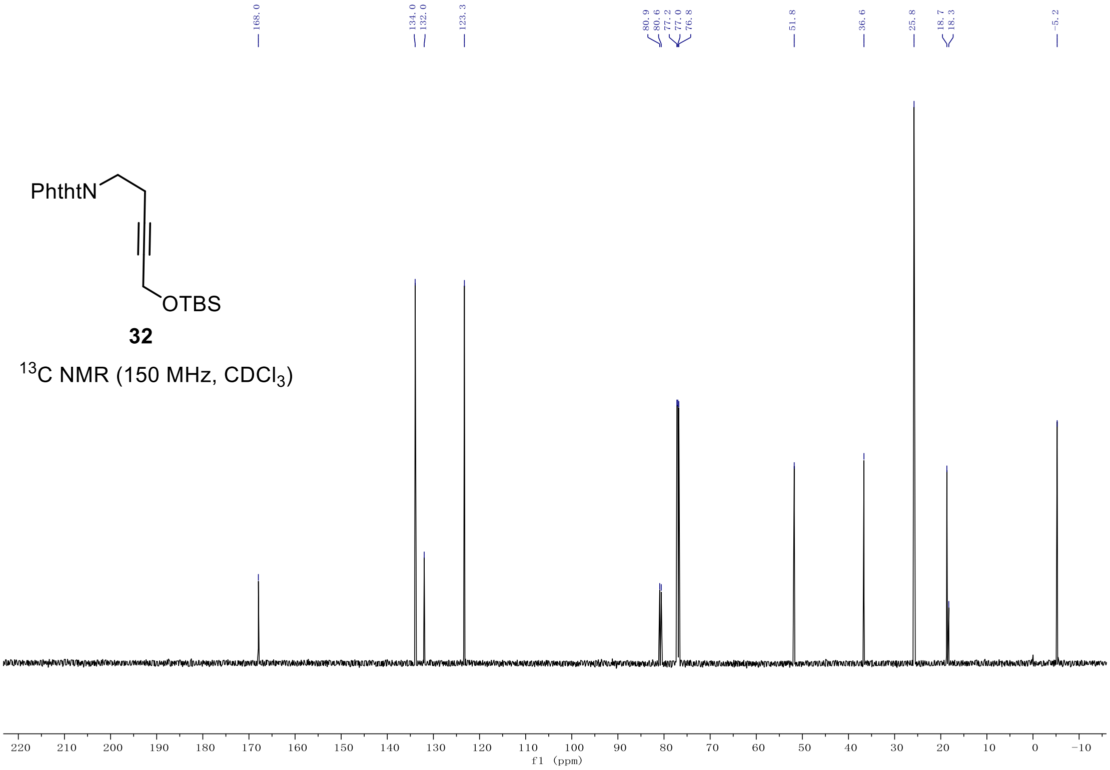

7.86
7.86
7.85
7.84
7.84
7.83
7.82
7.82
7.74
7.73
7.73
7.72
7.71
7.70
7.69
7.69
7.26
4.58
4.58
4.57
3.87
3.85
3.84
2.65
2.64
2.64
2.63
2.63
2.62
2.61
2.61
2.60
2.04
1.71
-0.02
PhthtN
OAc
31
^{1}H NMR (400 MHz, CDCl$_3$)
2.00
2.09
2.15
2.16
2.17
3.11
0.44
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)


170.1
167.9
134.0
132.0
123.3
83.2
77.3
77.0
76.7
76.0
52.4
36.4
20.7
18.7
PhthtN
OAc
31
^{13}C NMR (100 MHz, CDCl$_3$)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



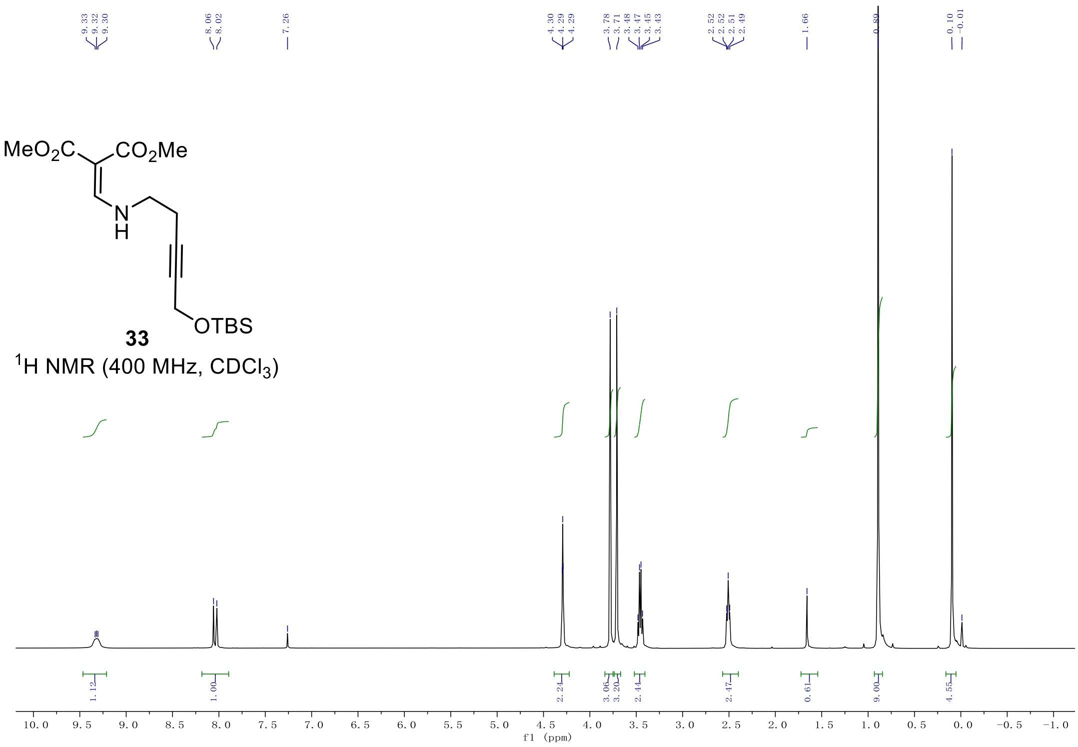
32

^{1}H NMR (400 MHz, CDCl$_3$)



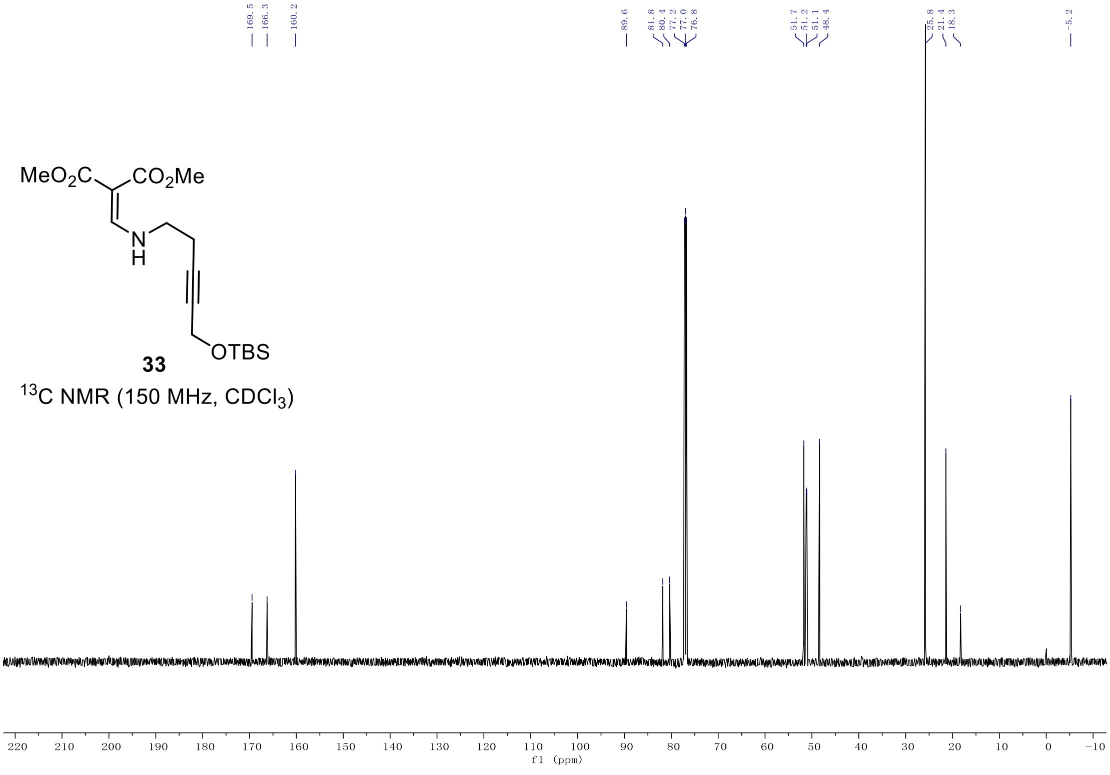
32

^{13}C NMR (150 MHz, CDCl$_3$)



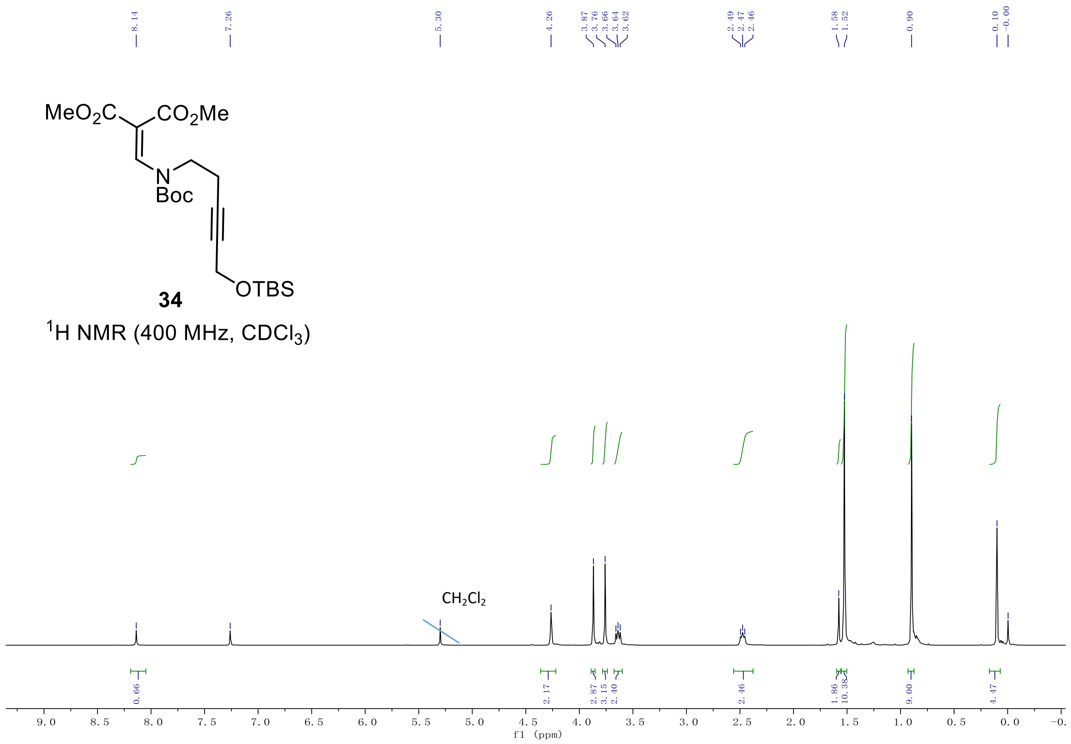
33

^{1}H NMR (400 MHz, CDCl$_3$)



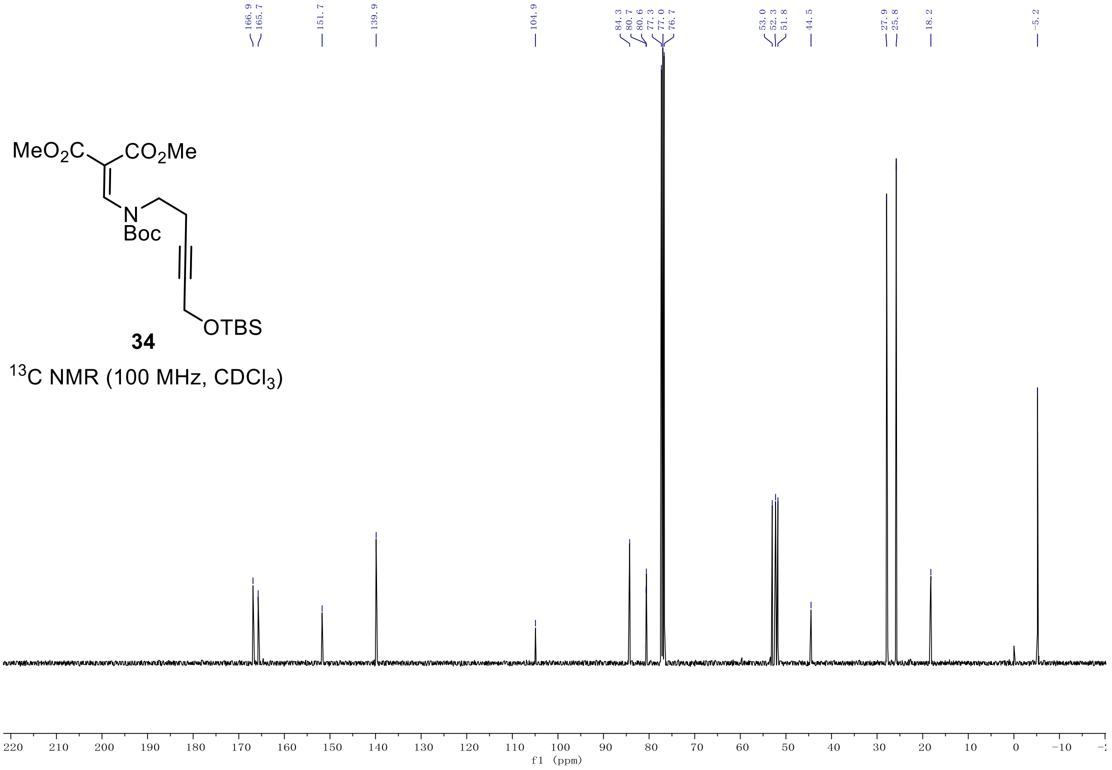
33

^{13}C NMR (150 MHz, CDCl$_3$)



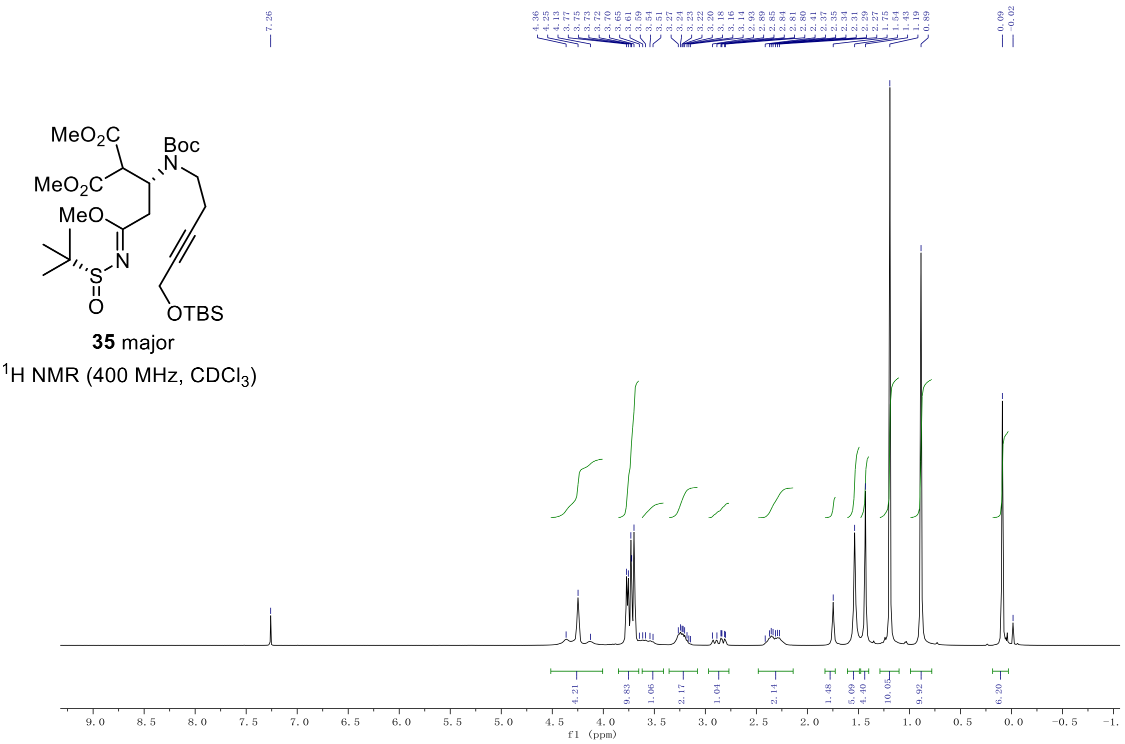
34

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



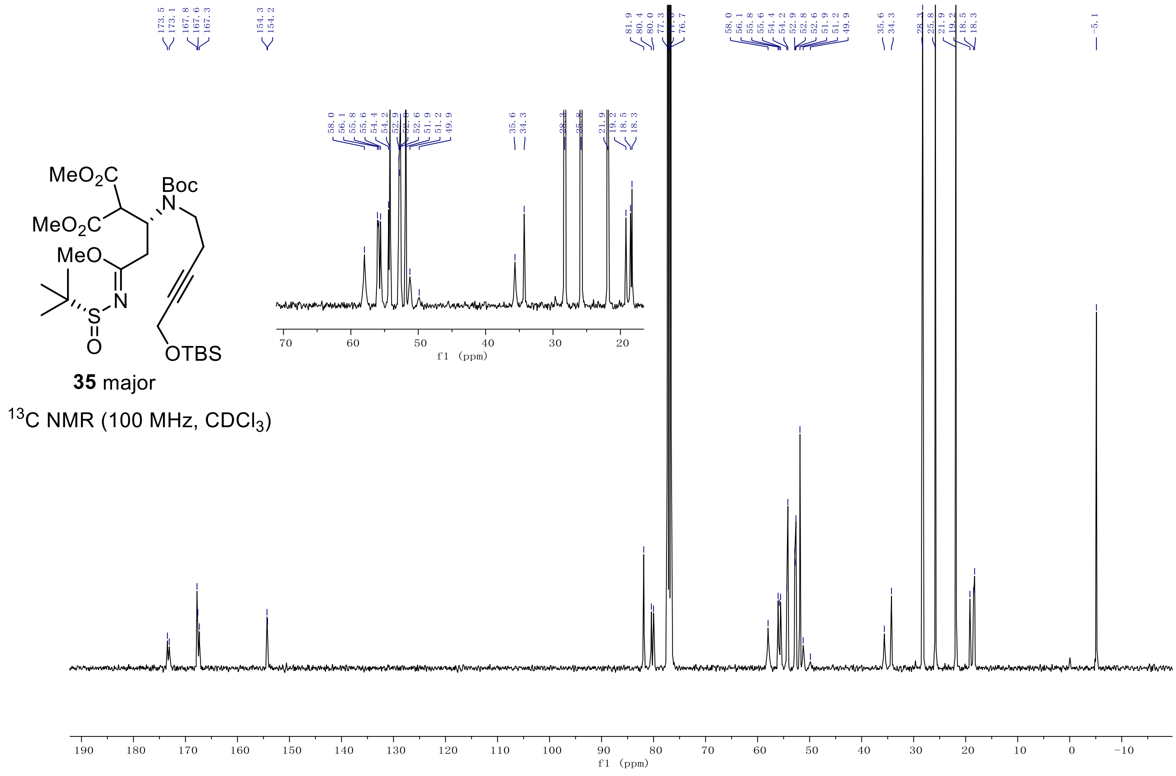
34

^{13}C NMR (100 MHz, $CDCl_3$)



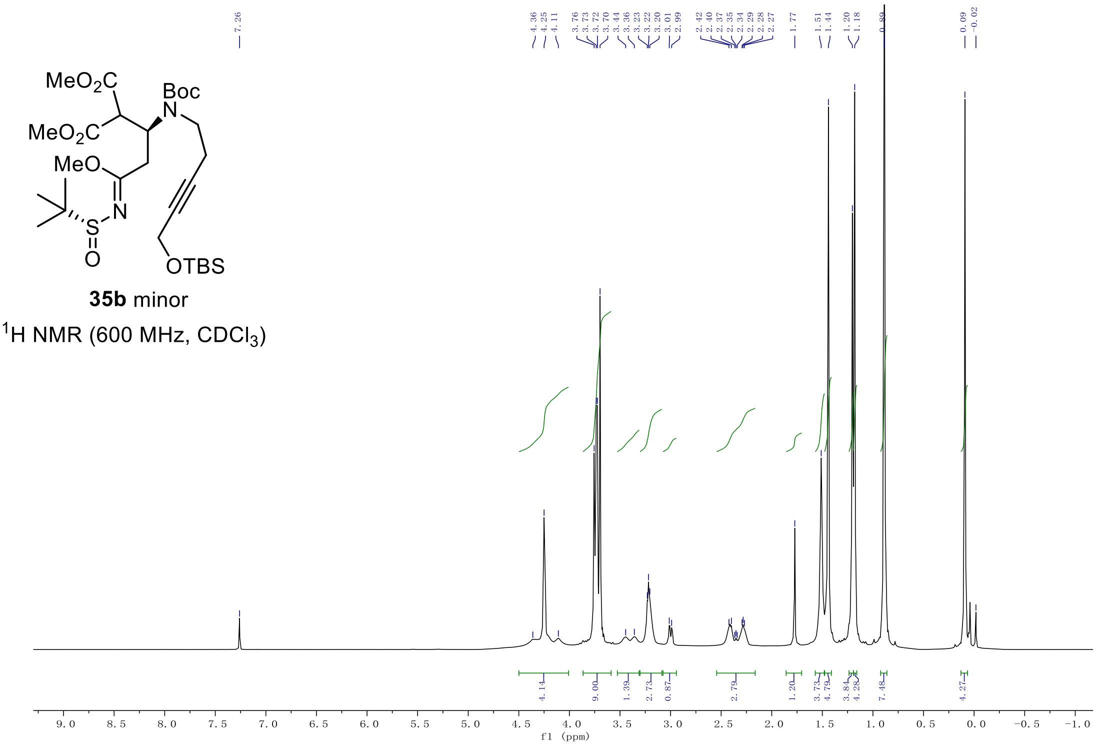
35 major

^{1}H NMR (400 MHz, CDCl$_3$)



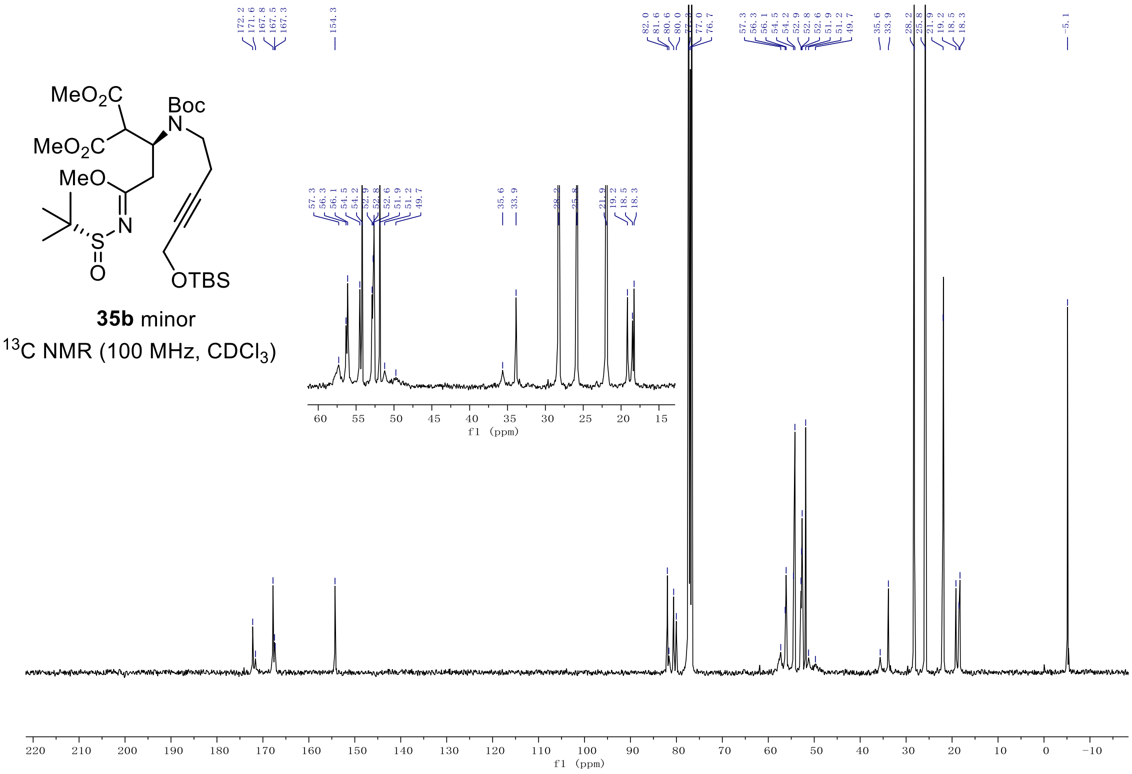
35 major

^{13}C NMR (100 MHz, CDCl$_3$)



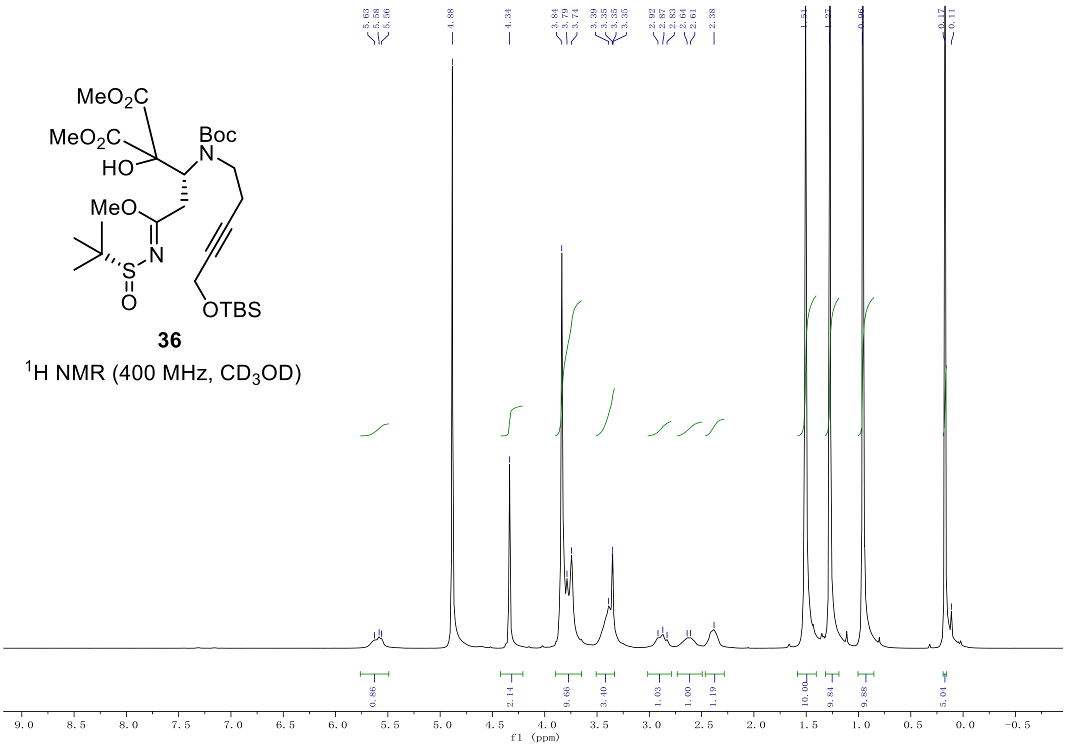
35b minor

^{1}H NMR (600 MHz, CDCl$_3$)



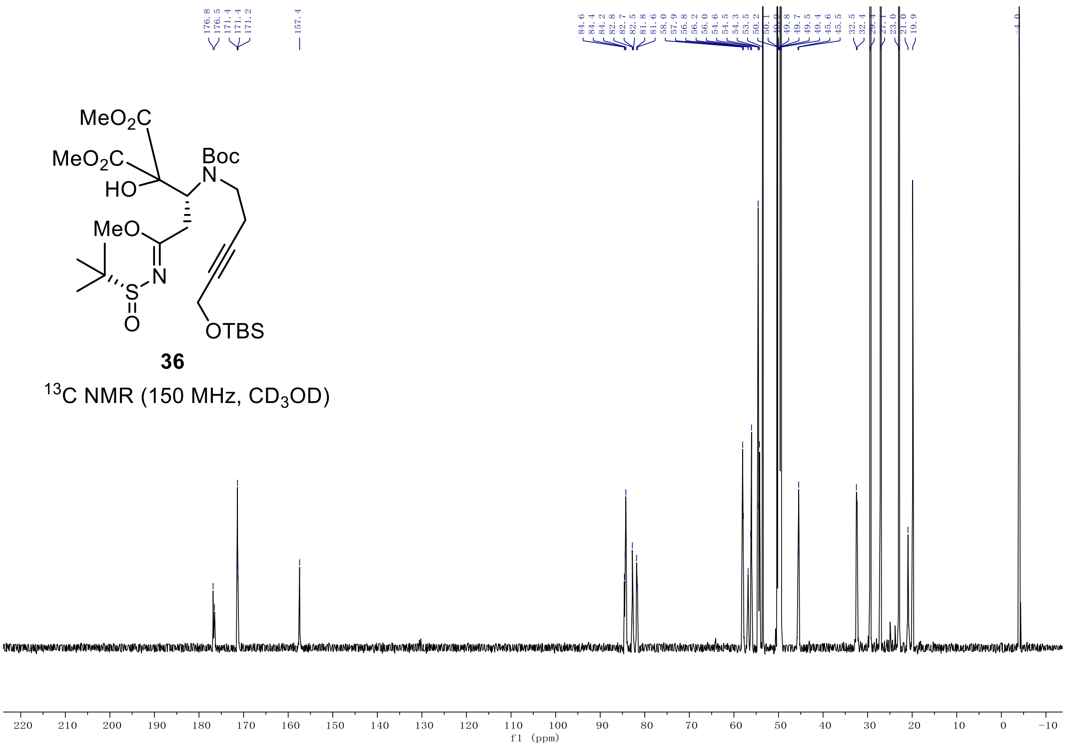
35b minor

^{13}C NMR (100 MHz, CDCl$_3$)



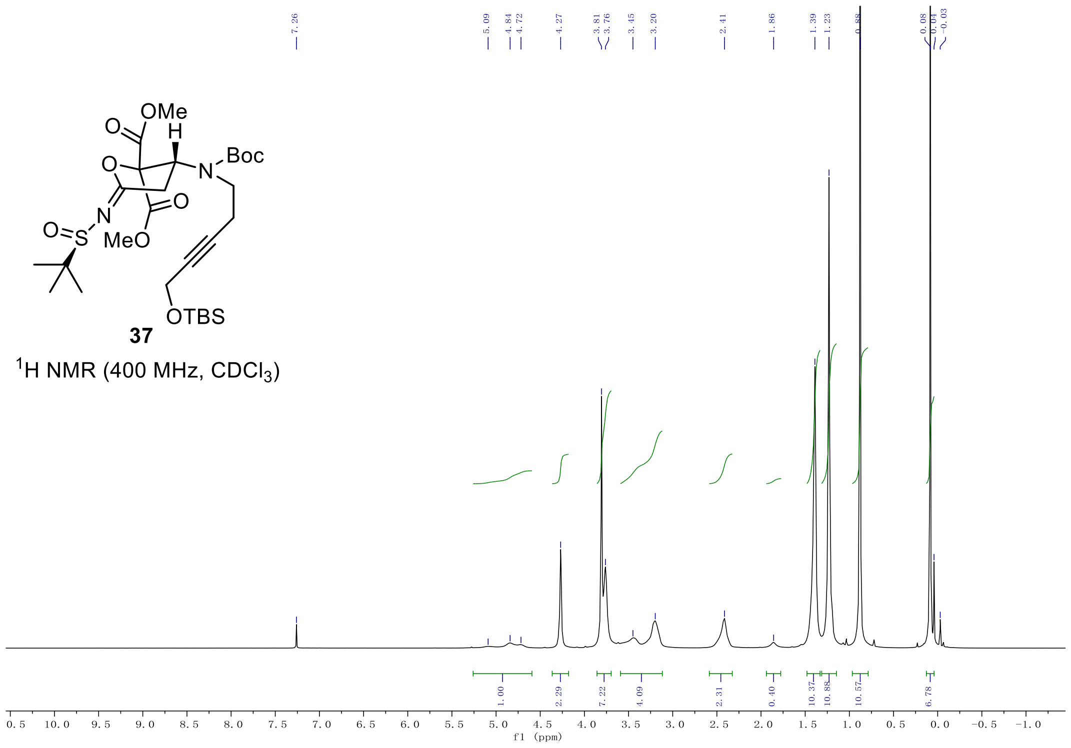
36

^{1}H NMR (400 MHz, CD$_3$OD)



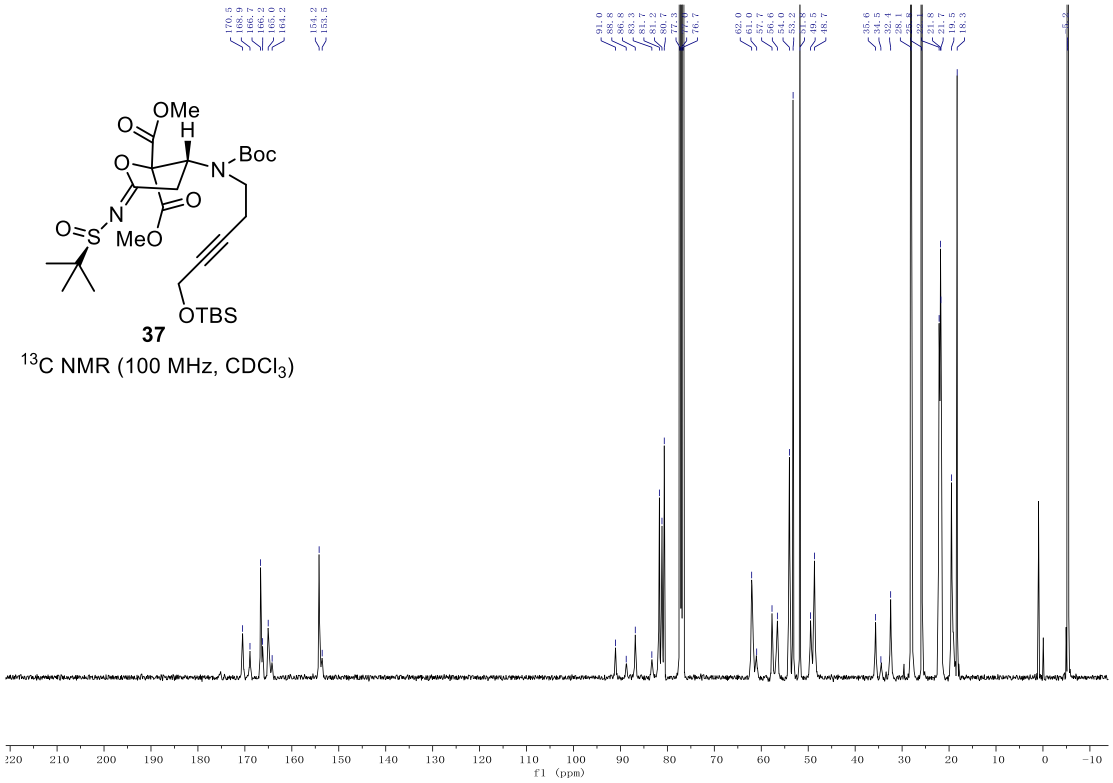
36

^{13}C NMR (150 MHz, CD$_3$OD)



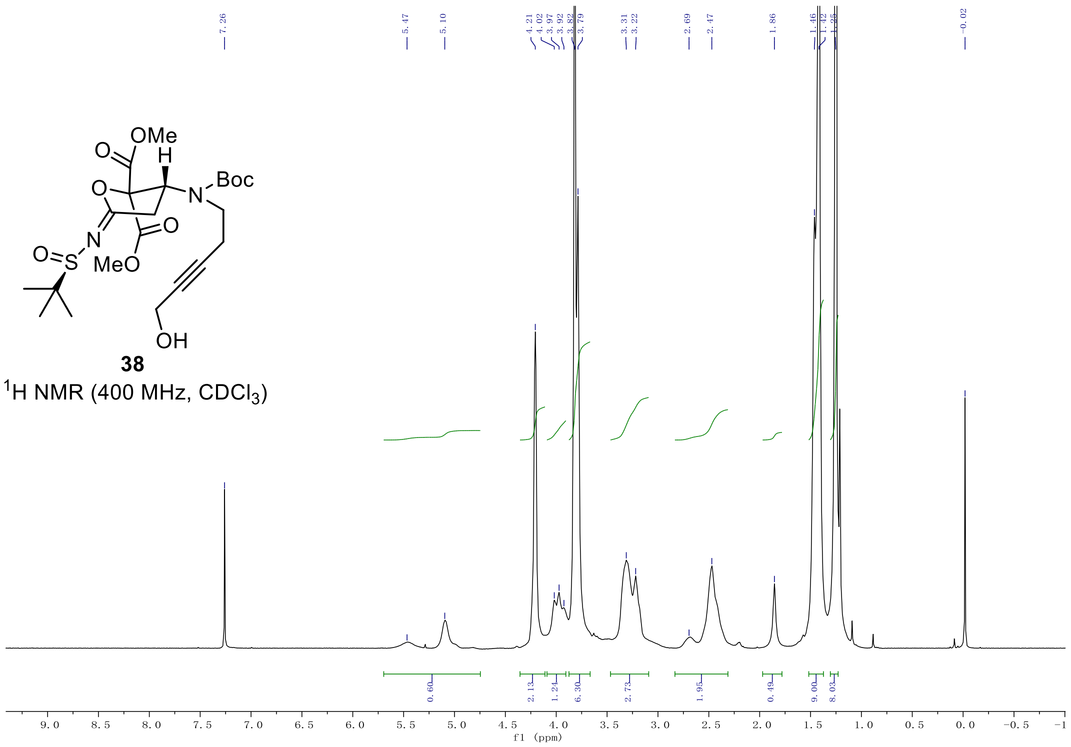
37

^{1}H NMR (400 MHz, CDCl$_3$)



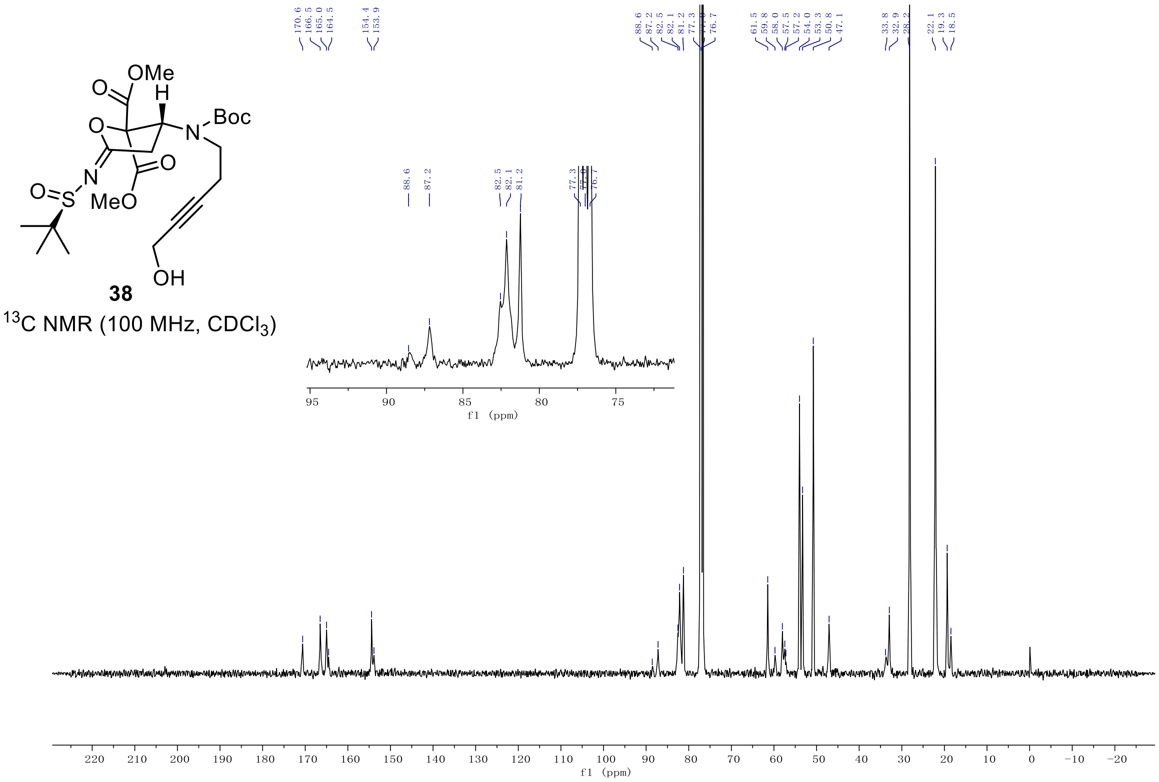
37

^{13}C NMR (100 MHz, CDCl$_3$)



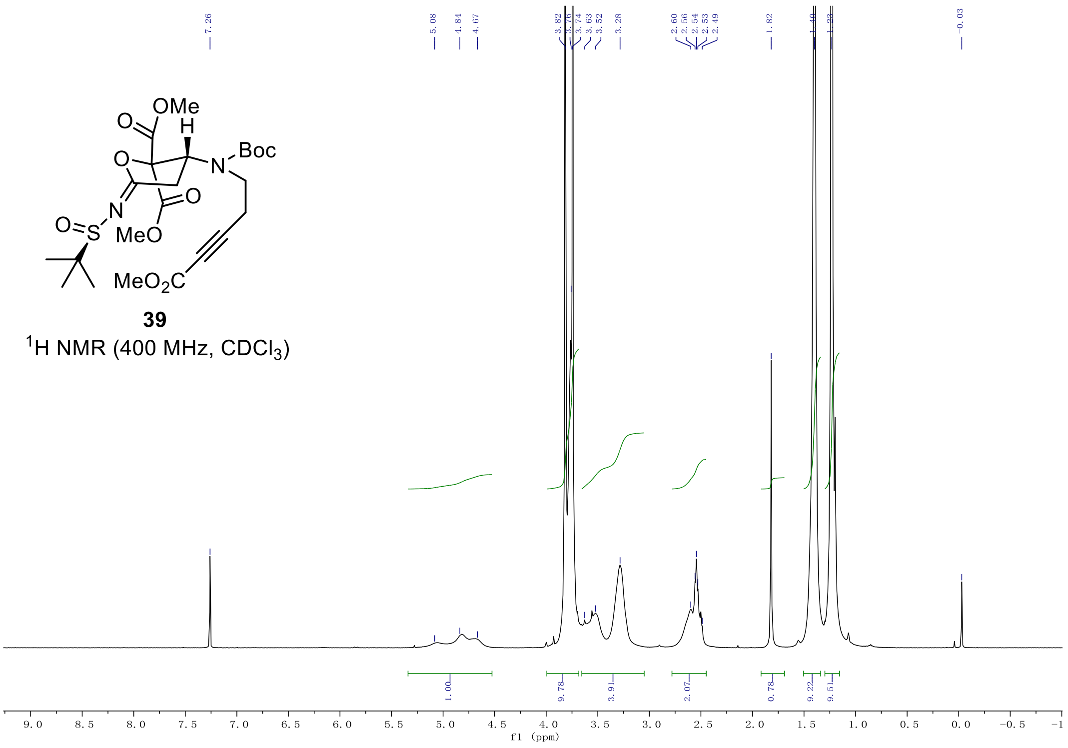
38

^{1}H NMR (400 MHz, CDCl$_3$)



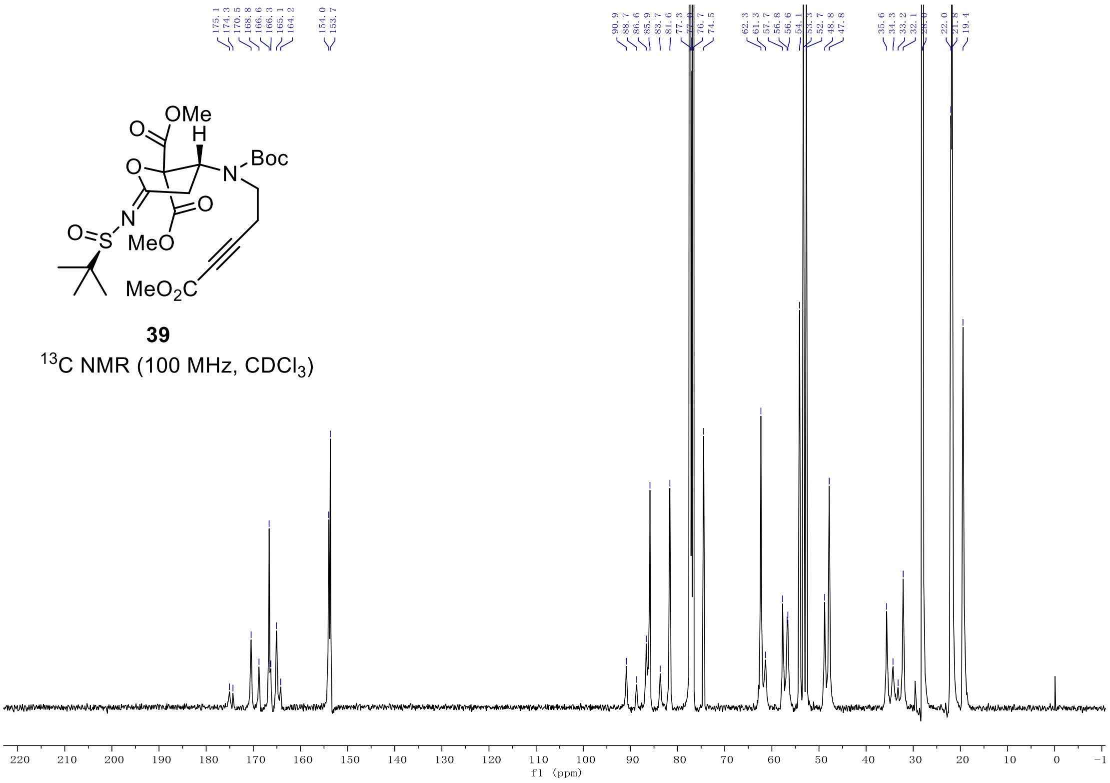
38

^{13}C NMR (100 MHz, CDCl$_3$)



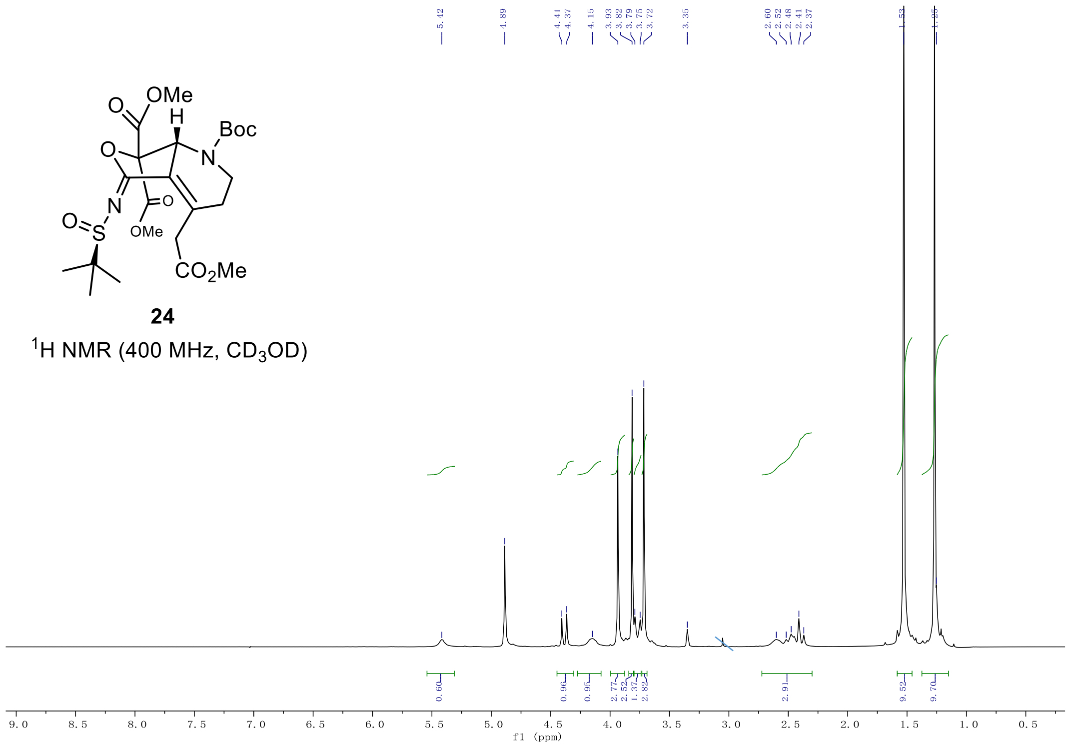
39

^{1}H NMR (400 MHz, CDCl$_3$)



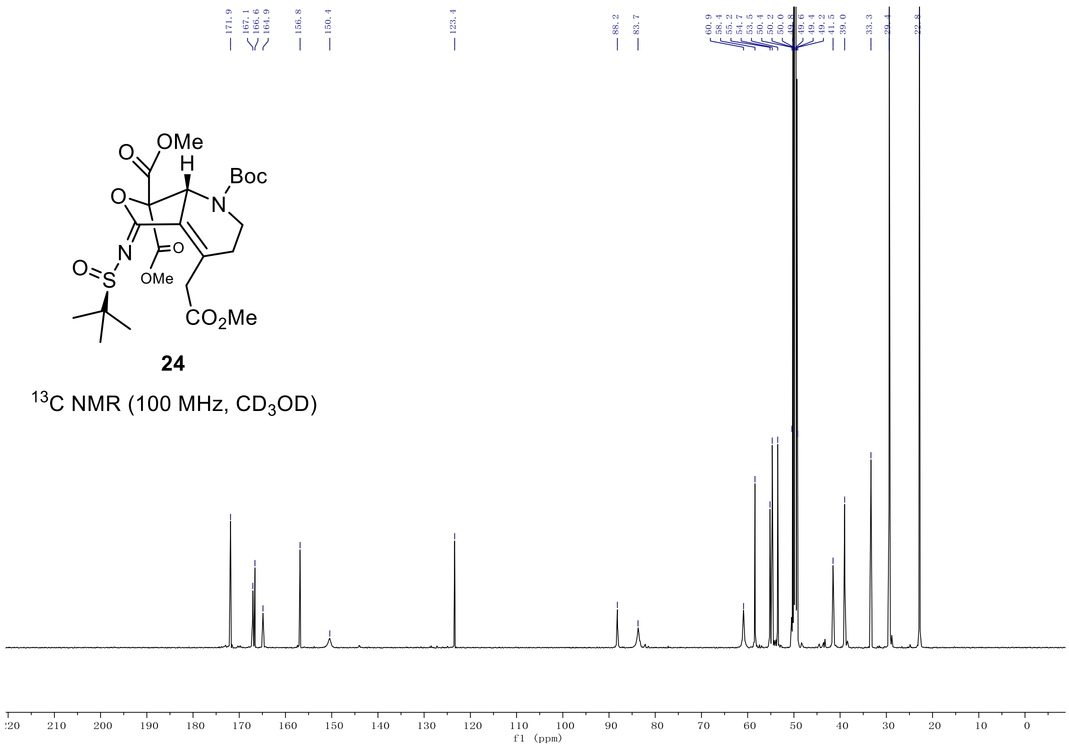
39

^{13}C NMR (100 MHz, CDCl$_3$)



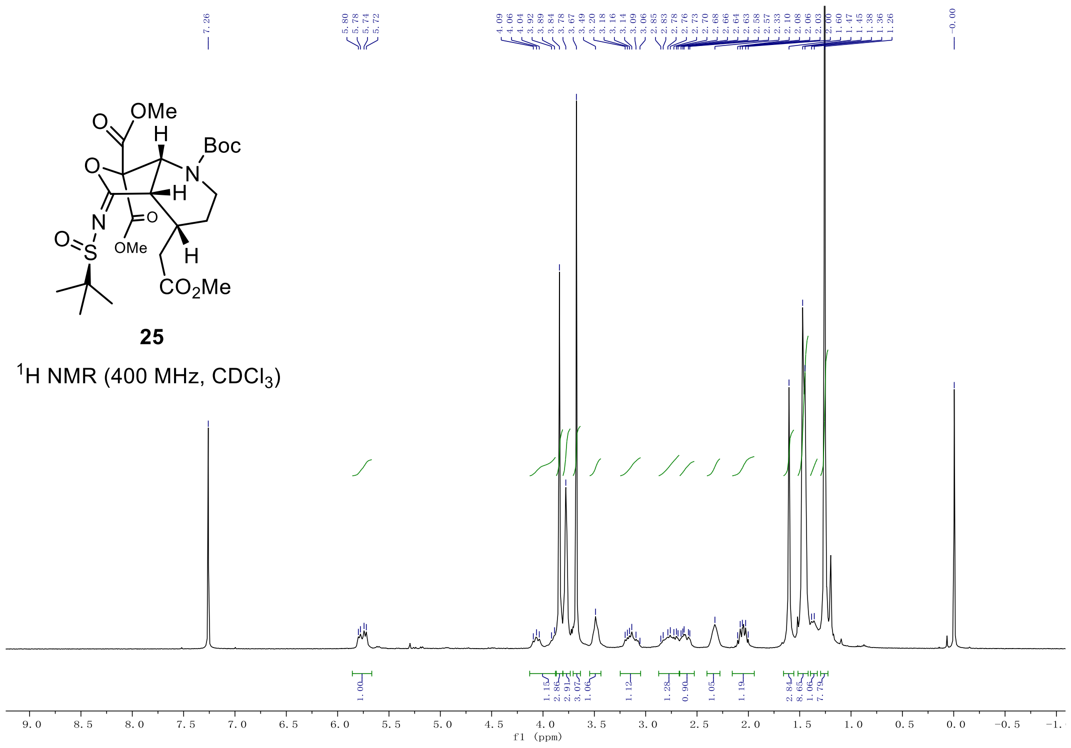
24

^{1}H NMR (400 MHz, CD_3OD)



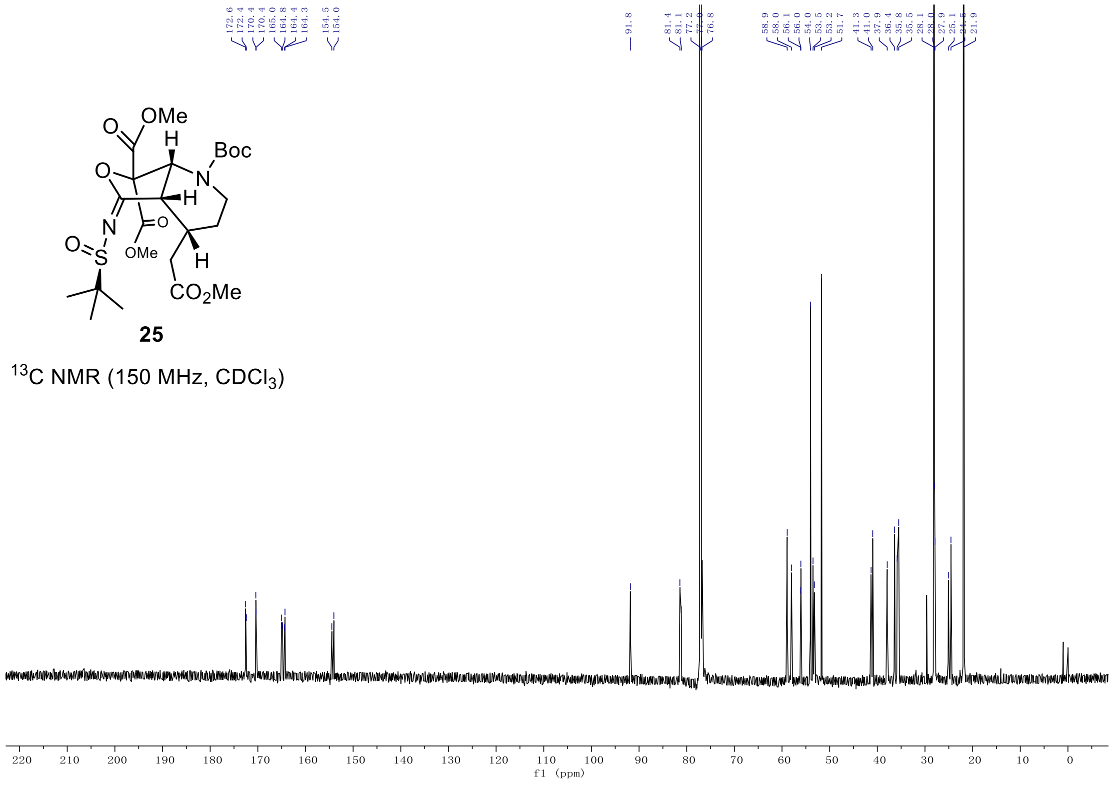
24

^{13}C NMR (100 MHz, CD_3OD)



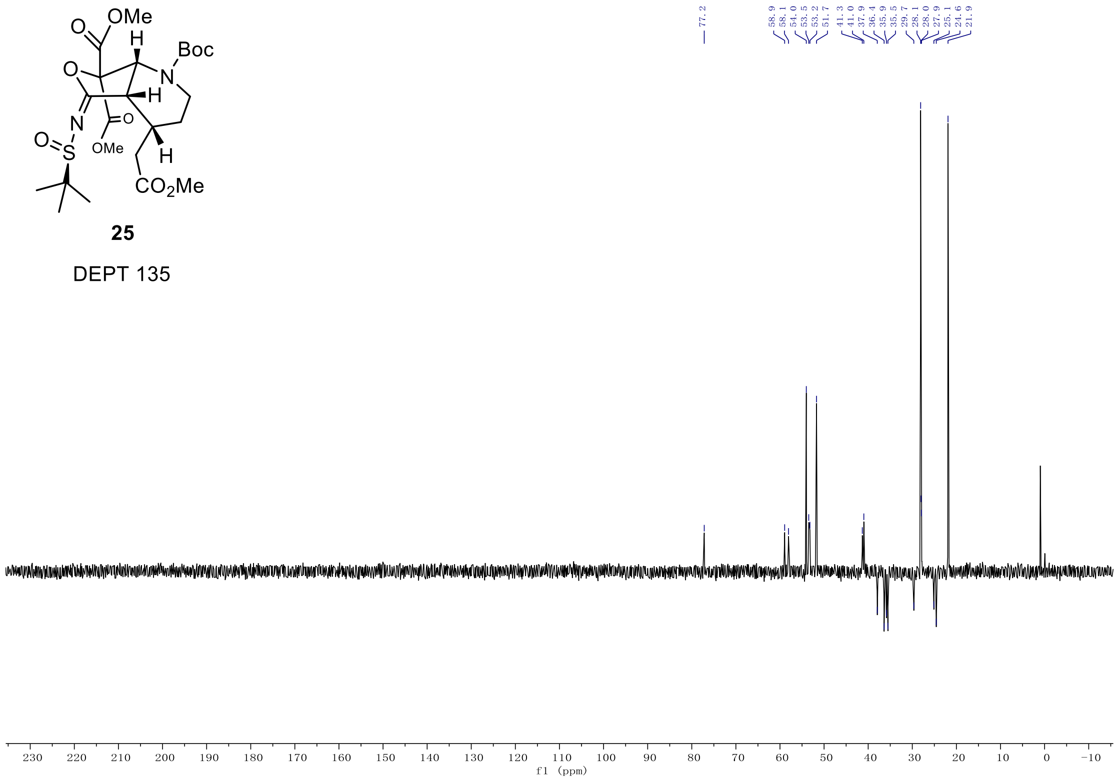
25

^{1}H NMR (400 MHz, CDCl$_3$)



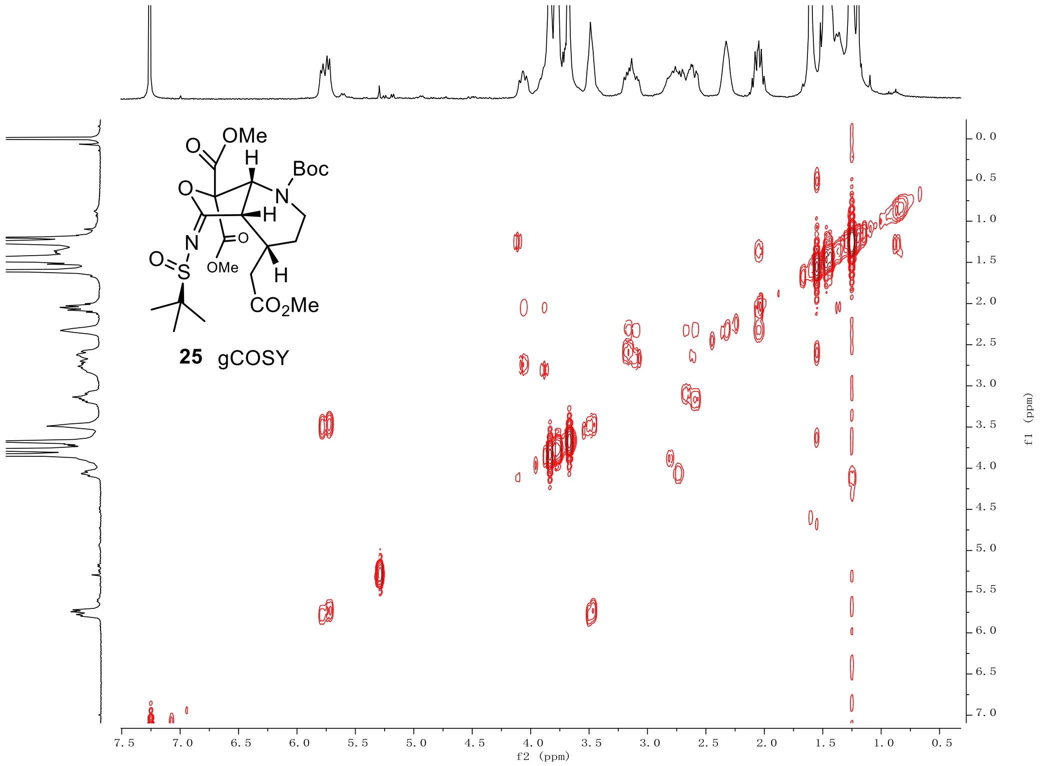
25

^{13}C NMR (150 MHz, CDCl$_3$)

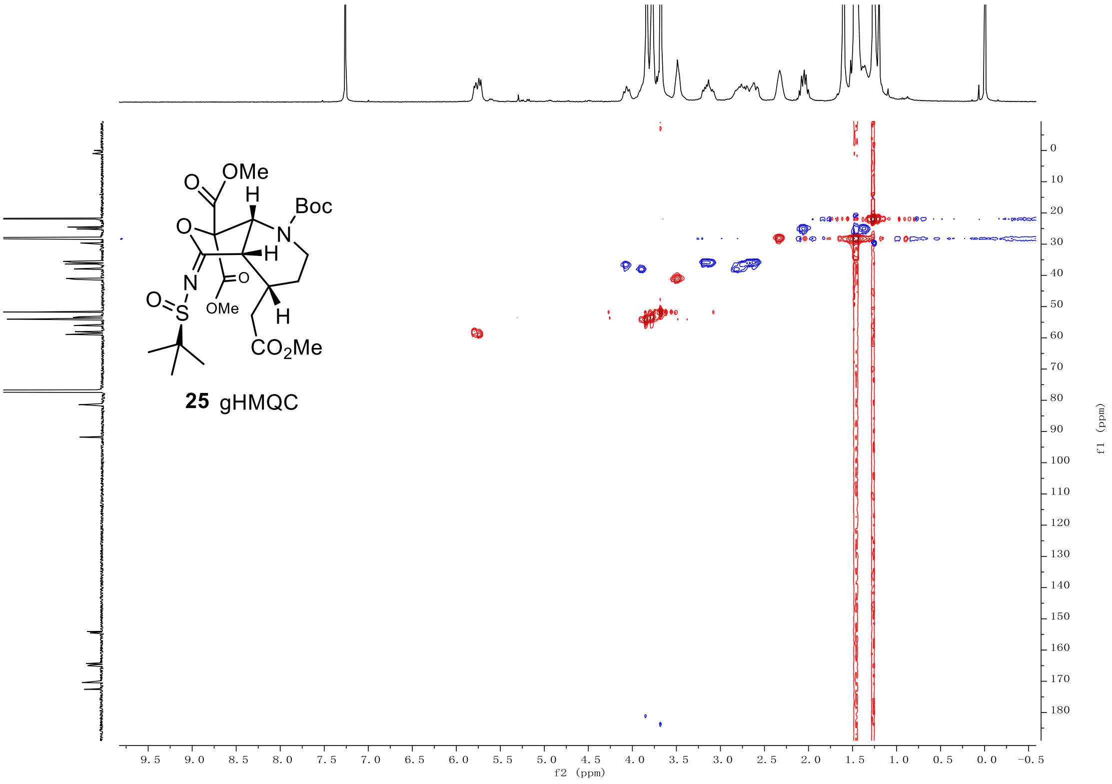


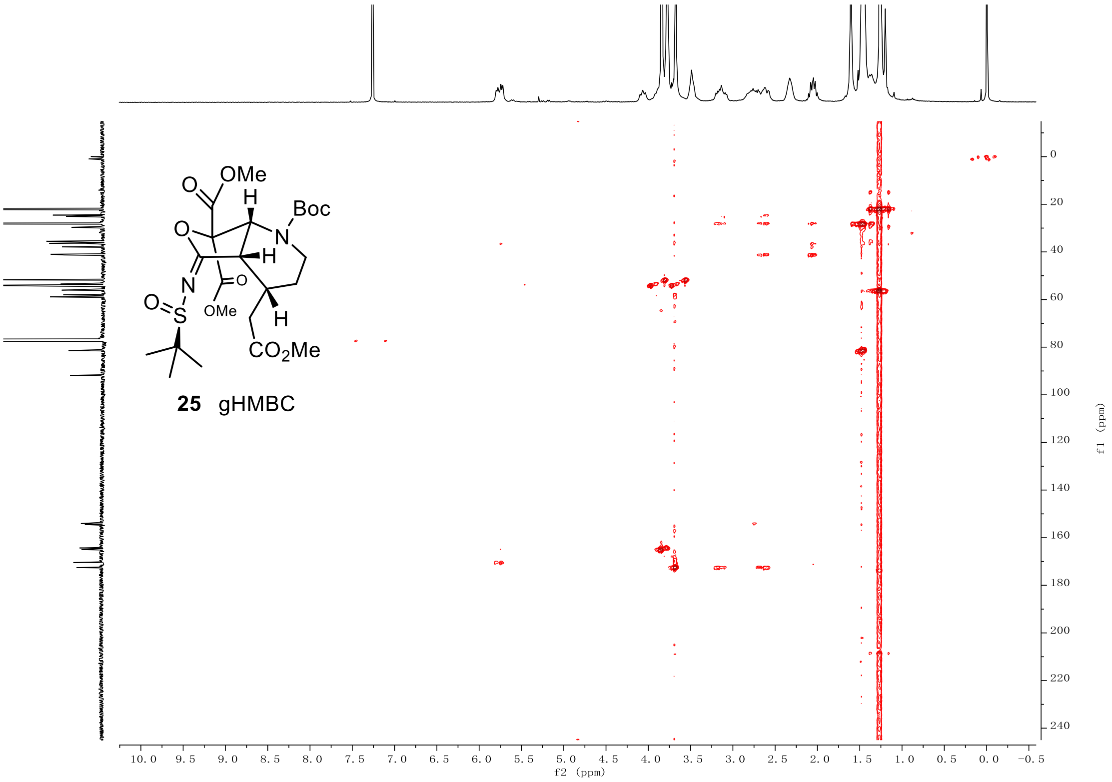
25

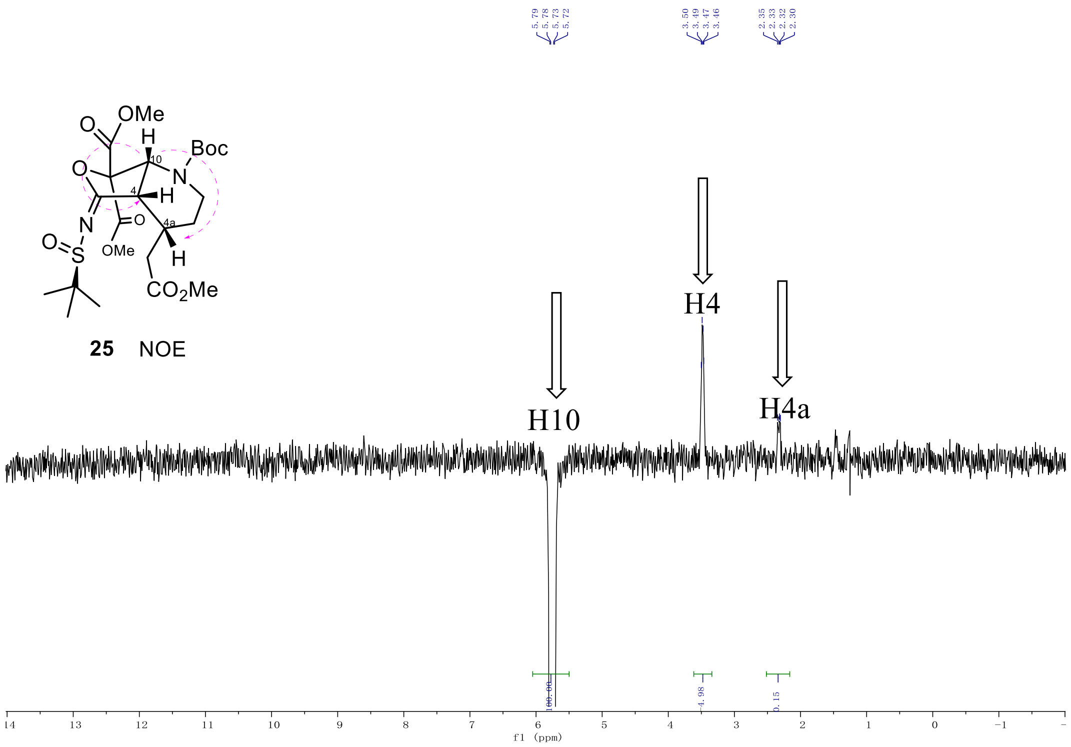
DEPT 135

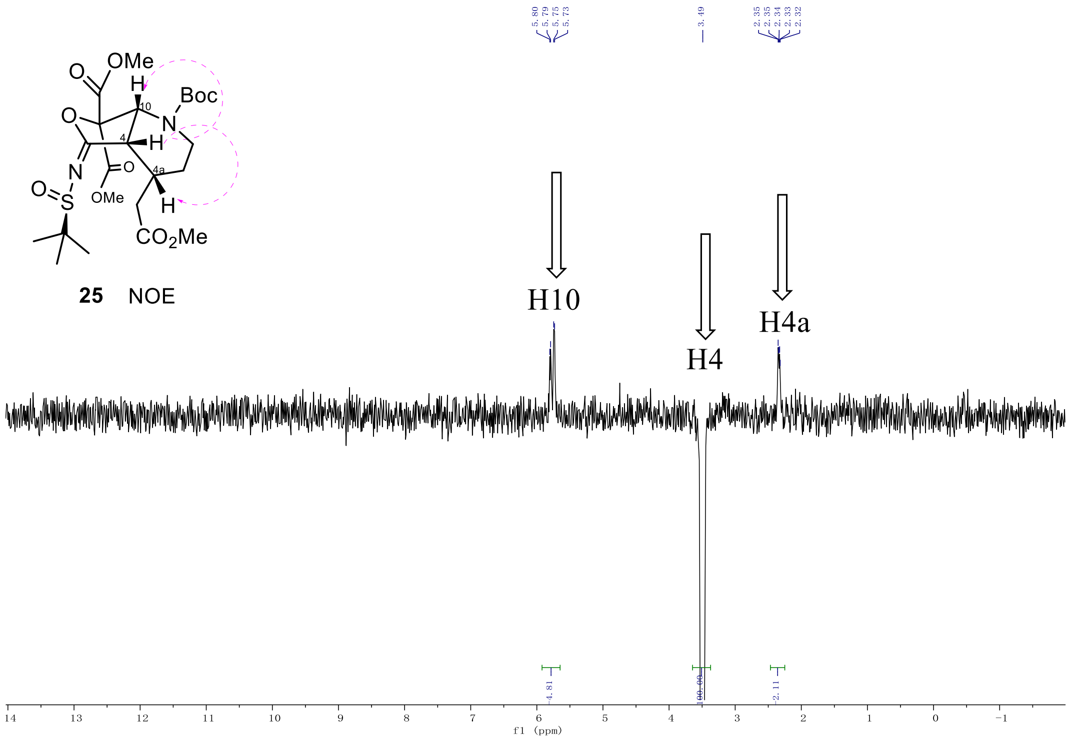


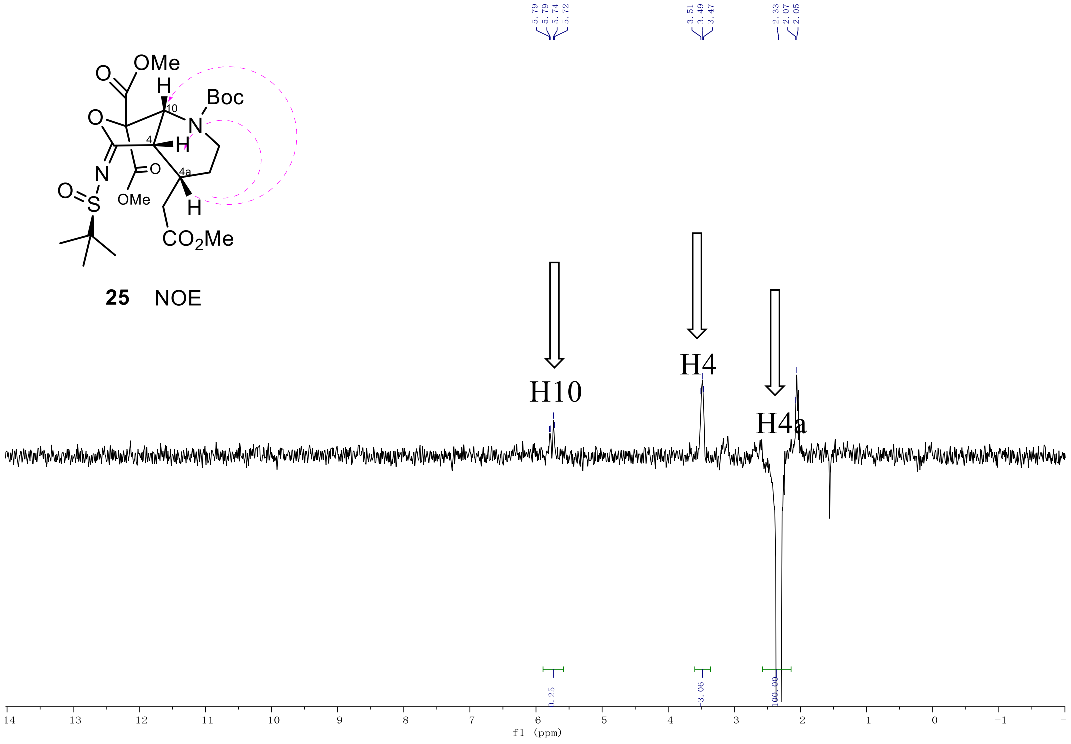
25 gCOSY


OMe
O
H
Boc
O
N
H
O
N
OMe
O
S
H
CO2Me
25 gHMQC
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f2 (ppm)

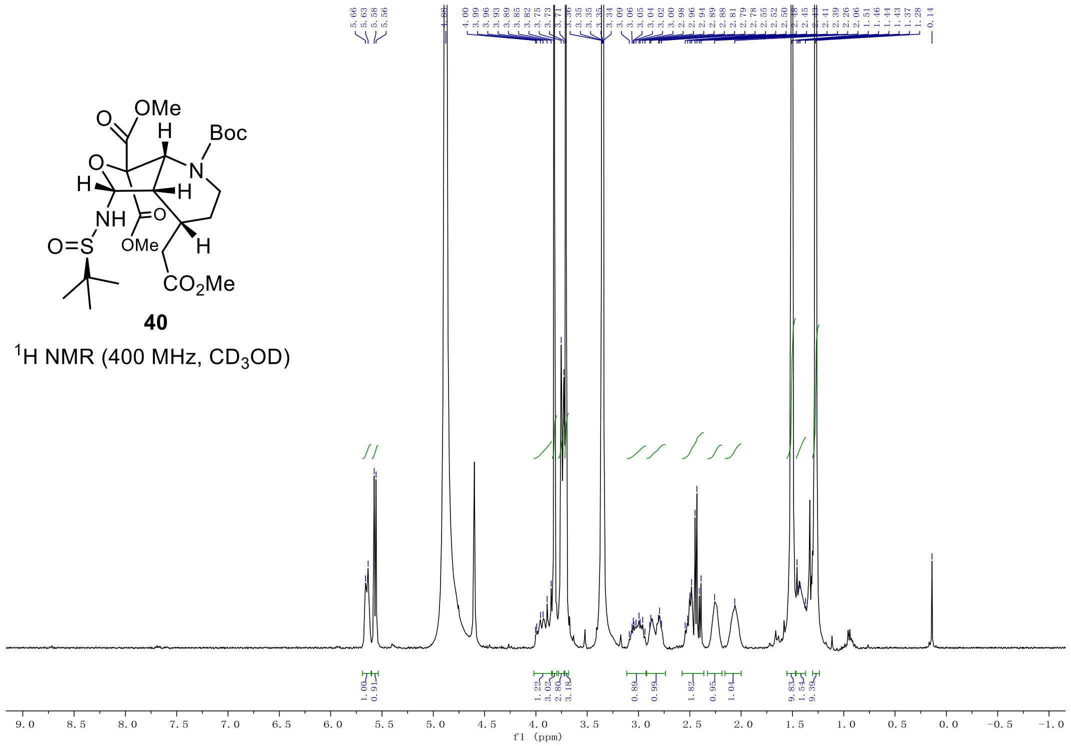

OMe
O
H
Boc
O
N
H
O
N
OMe
O
S
H
CO2Me
25 gHMBC
0
20
40
60
80
100
120
140
160
180
200
220
240
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f2 (ppm)


5.79
5.78
5.73
5.72
3.50
3.49
3.47
3.46
2.35
2.33
2.32
2.30
OMe
O
H
10
Boc
O
N
4
H
4a
O
N
O
S
OMe
H
CO2Me
25 NOE
H4
H10
H4a
100.00
-4.98
0.15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


5.80
5.79
5.75
5.73
3.49
2.35
2.35
2.34
2.33
2.32
OMe
O
H
10
Boc
O
N
4
H
4a
O
N
O
S
OMe
H
CO2Me
25 NOE
H10
H4a
H4
-4.81
100.00
-2.11
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

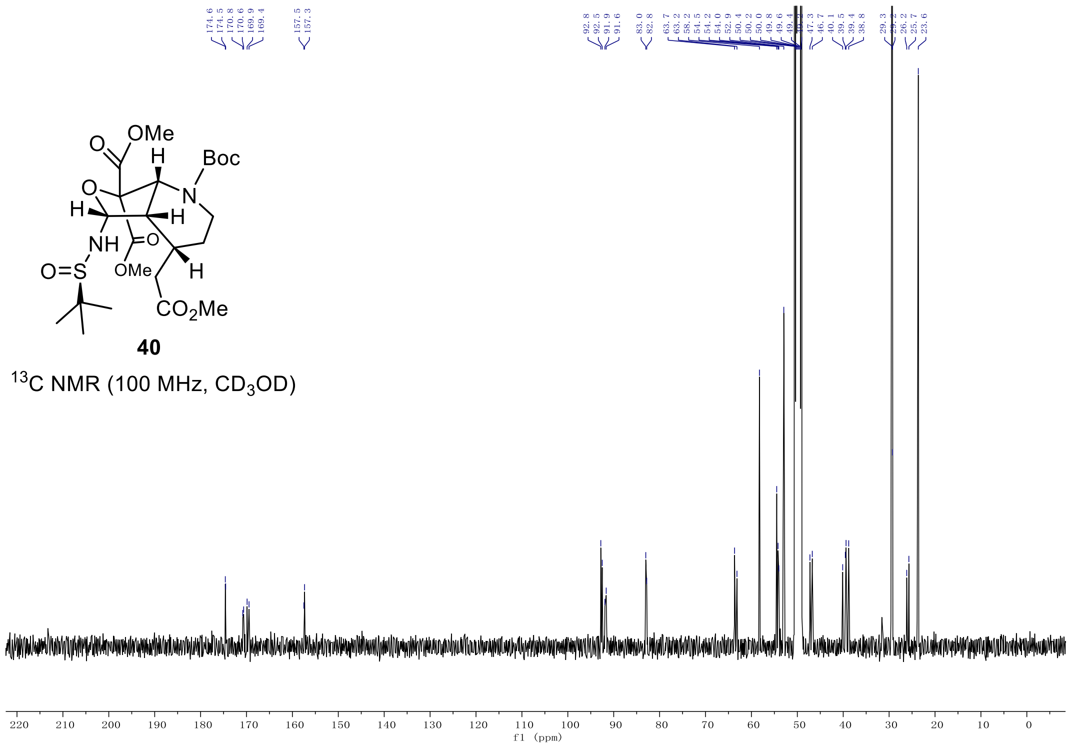


25 NOE



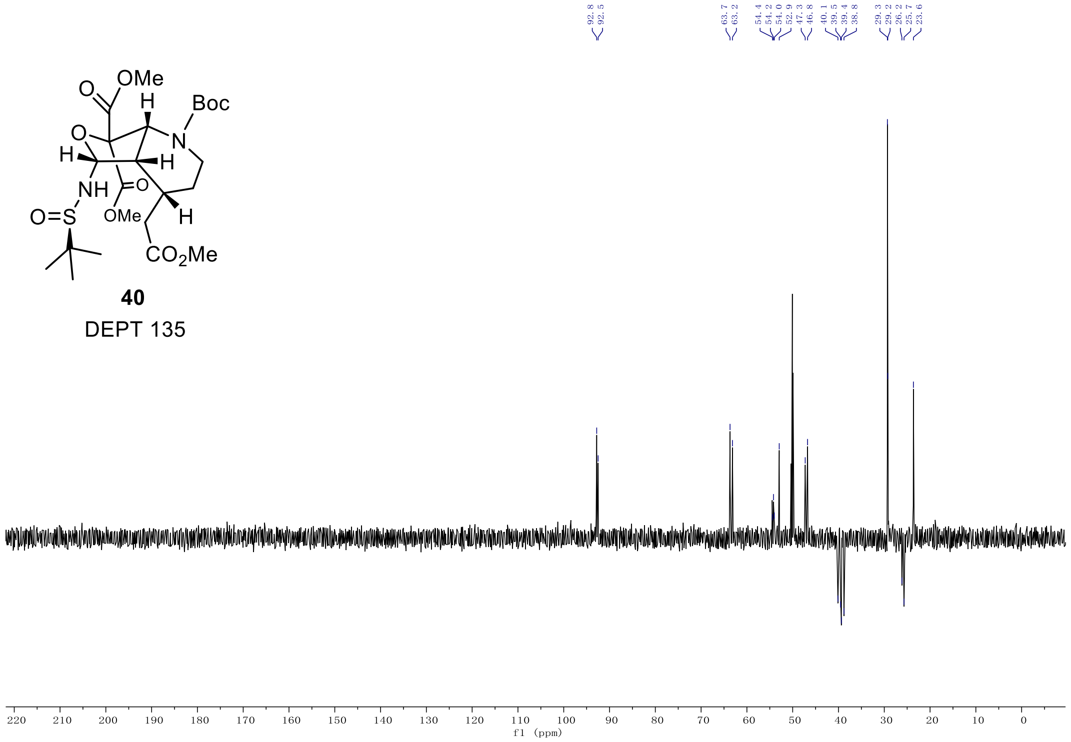
40

^{1}H NMR (400 MHz, CD$_3$OD)



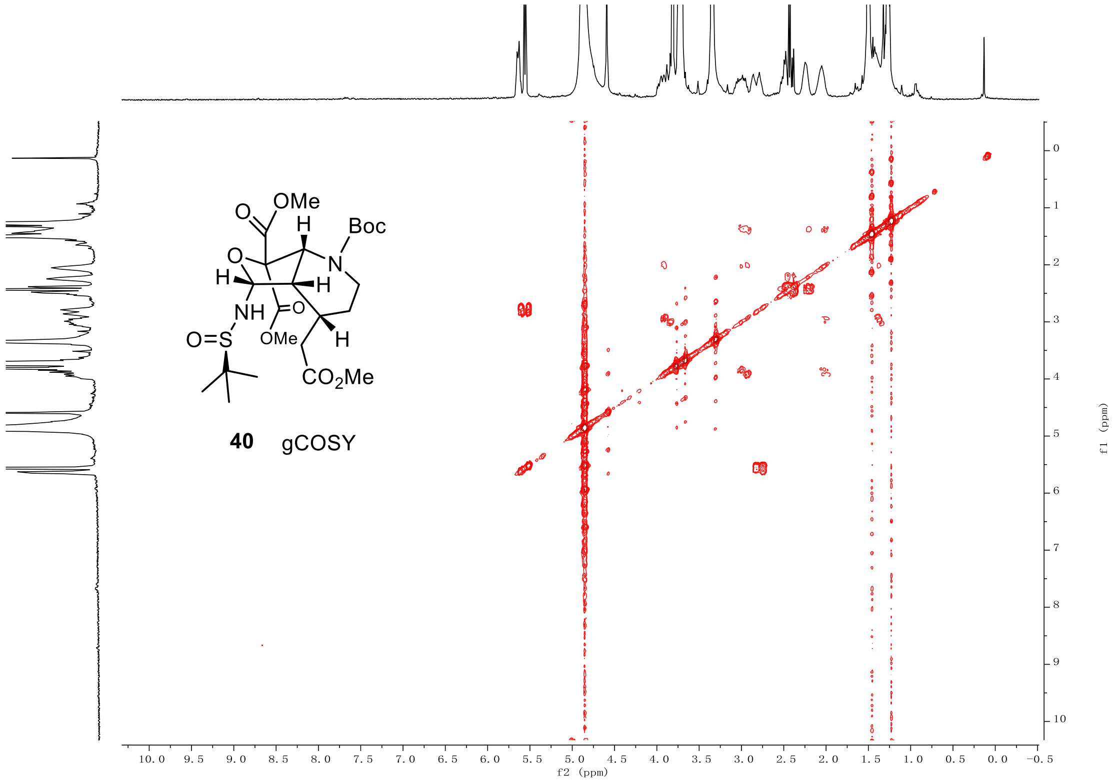
40

^{13}C NMR (100 MHz, CD$_3$OD)

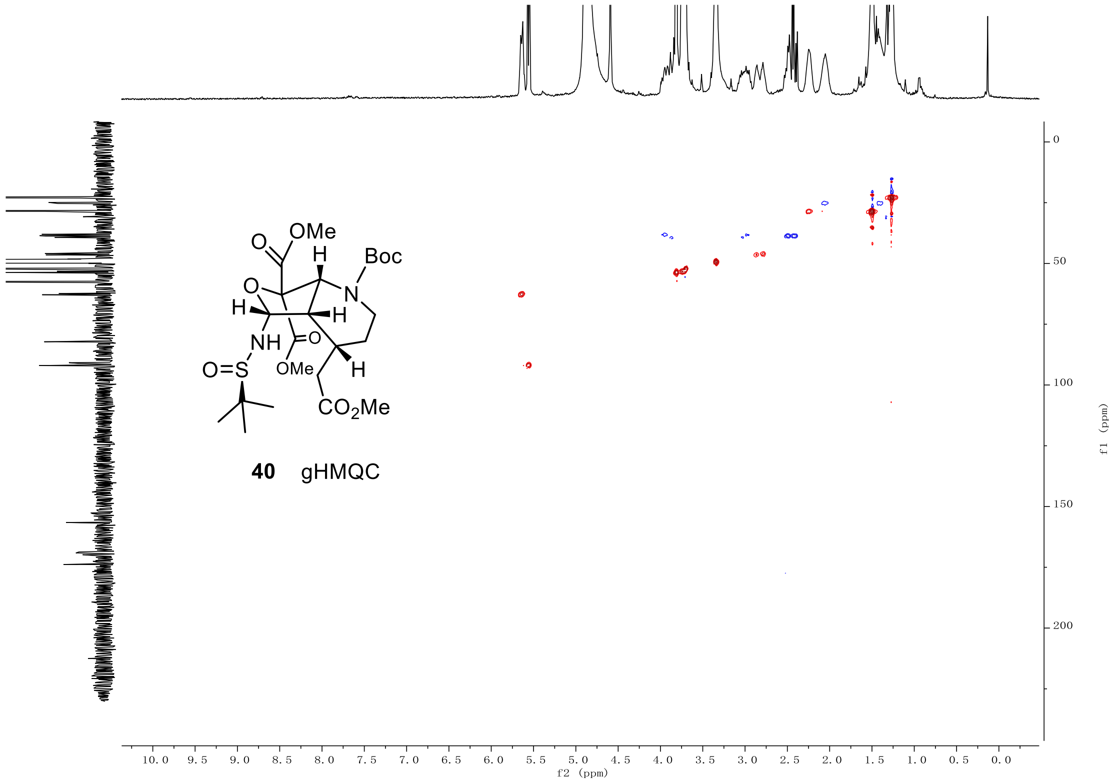


40

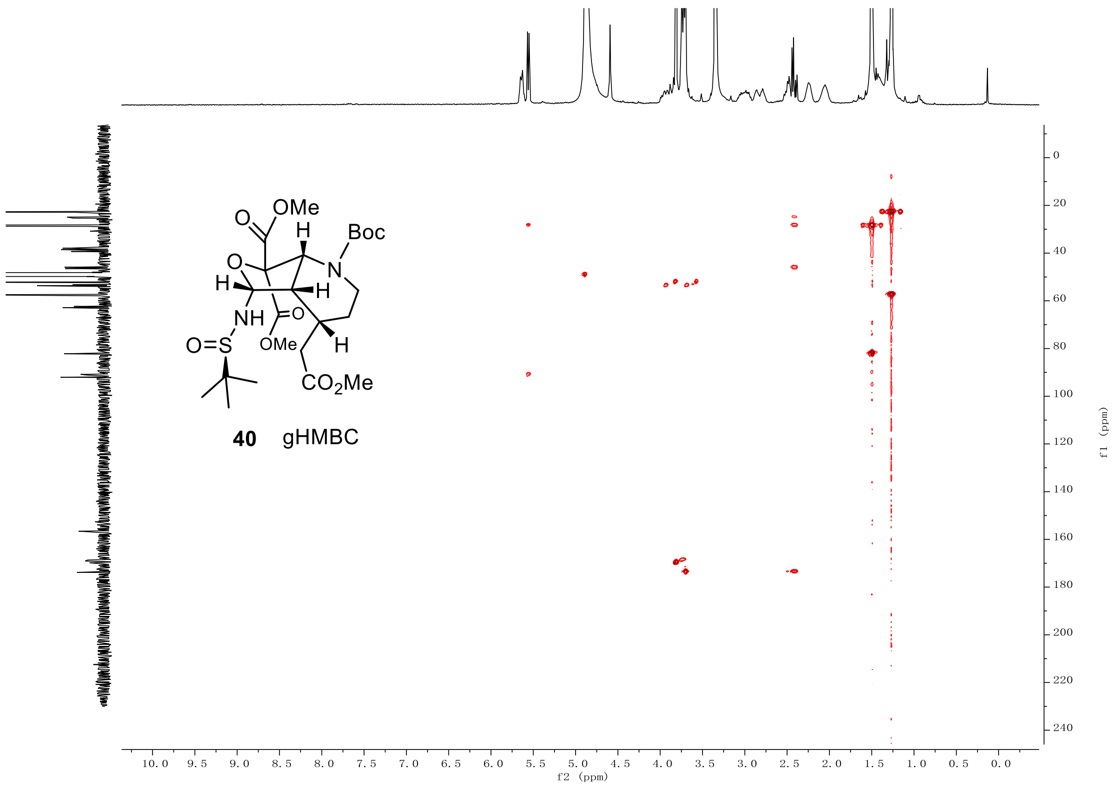
DEPT 135



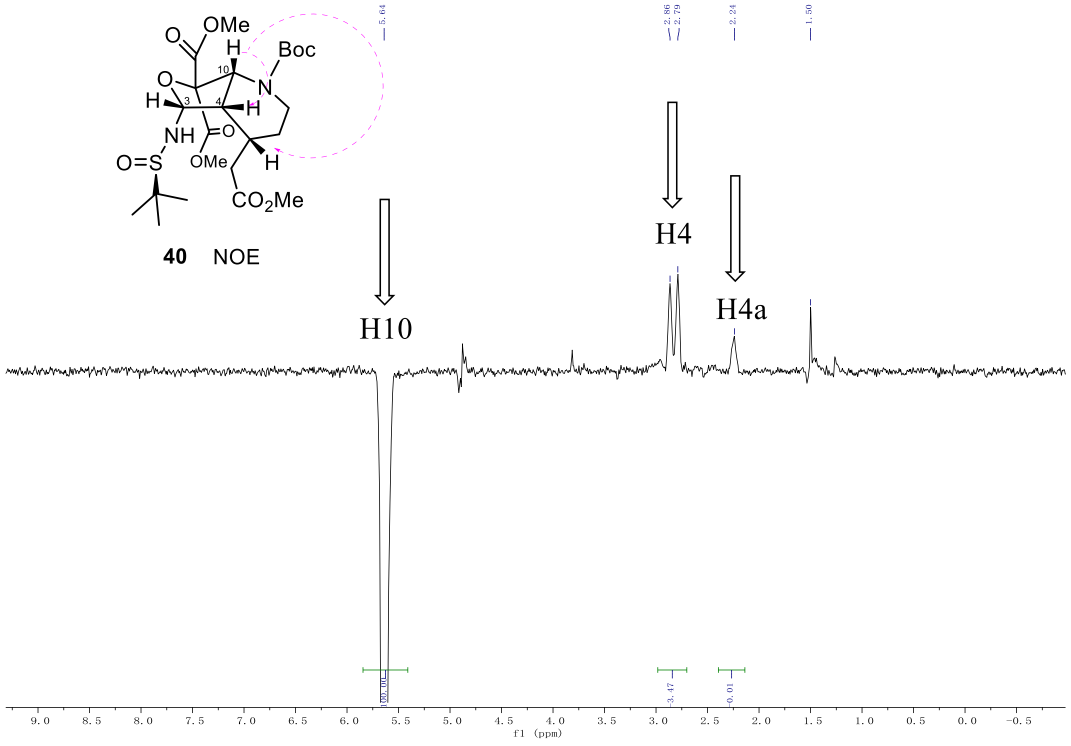
40 gCOSY



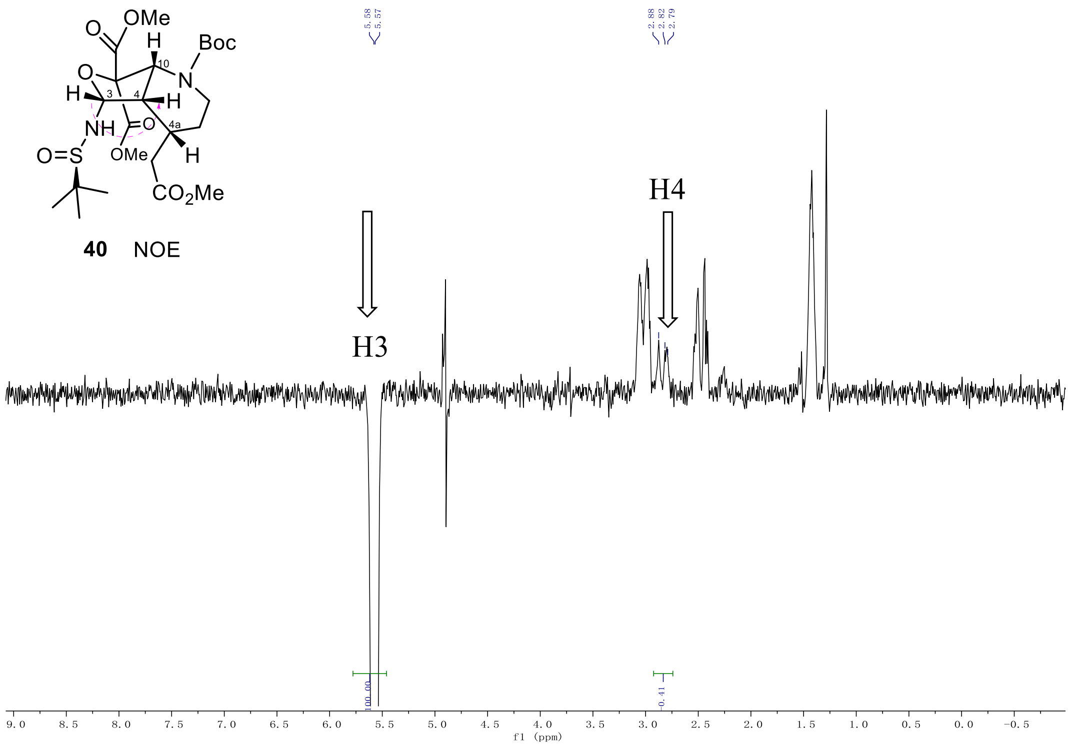
40 gHMQC



40 gHMBC

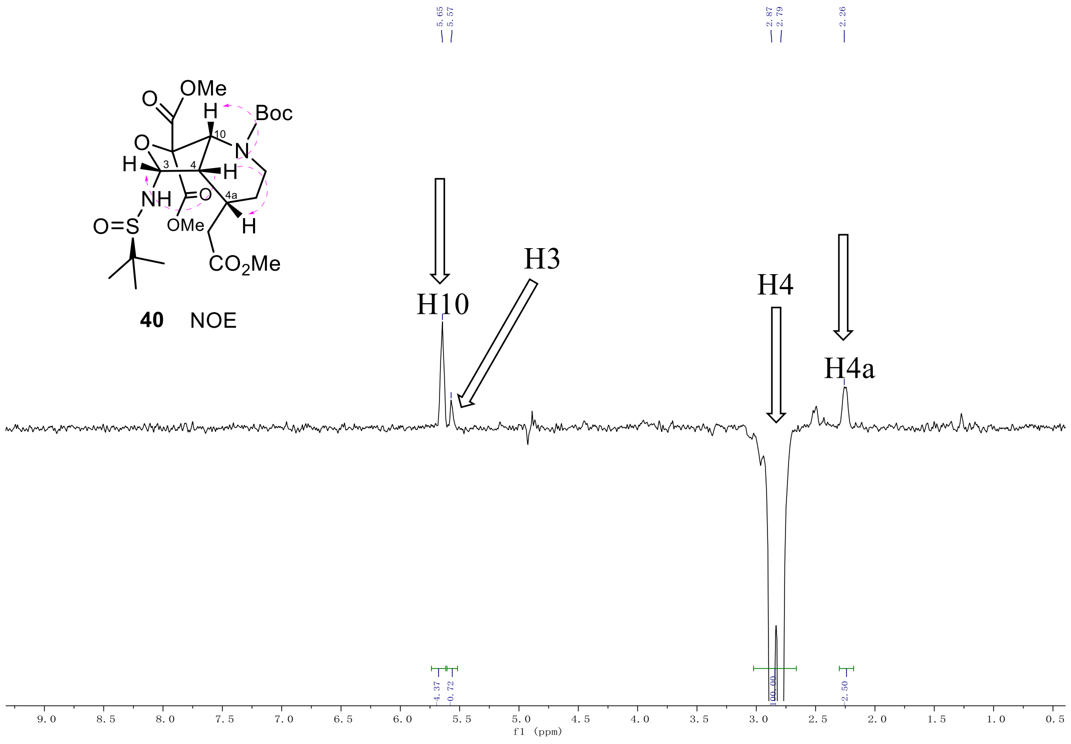


40 NOE



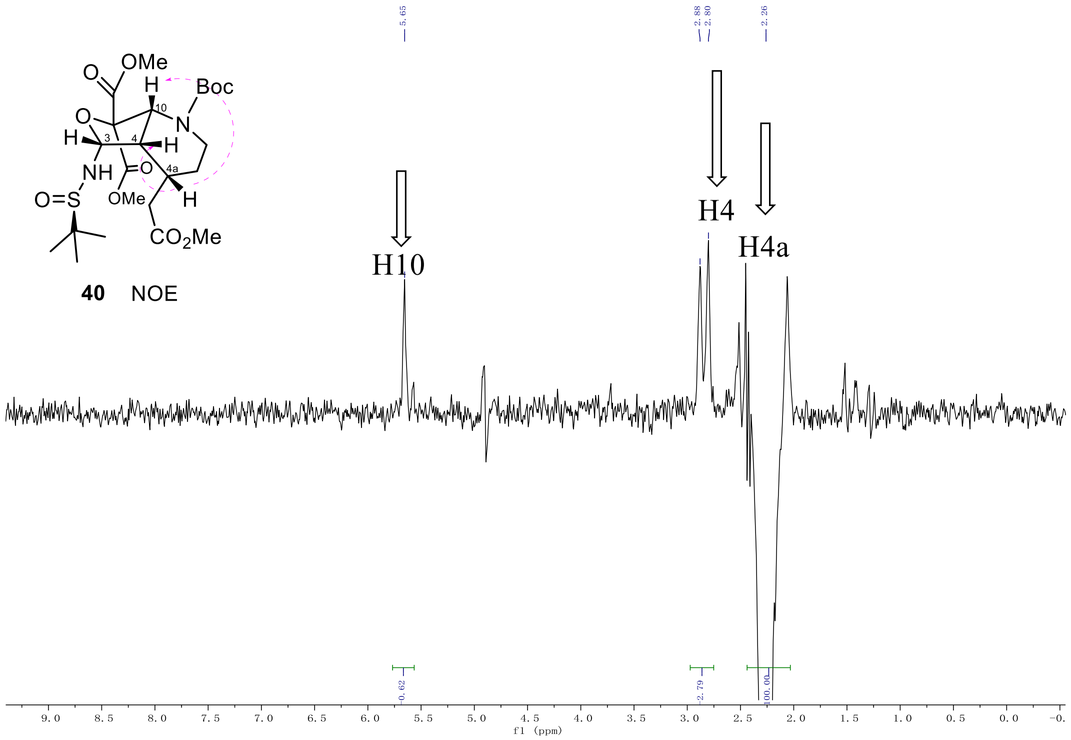
40 NOE

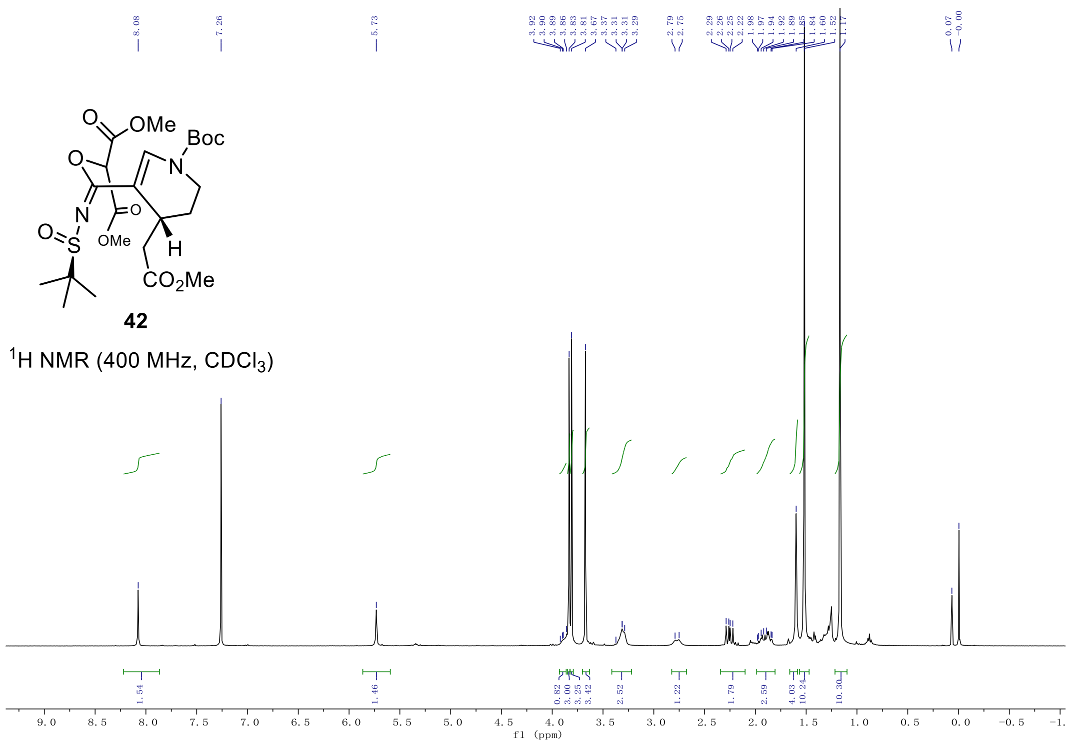
OMe
O
H
10
Boc
N
O
3
4
H
H
NH
O
4a
O=S
OMe
H
CO2Me
5.58
5.57
2.88
2.82
2.79
H4
H3
100.00
0.41
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)



40 NOE

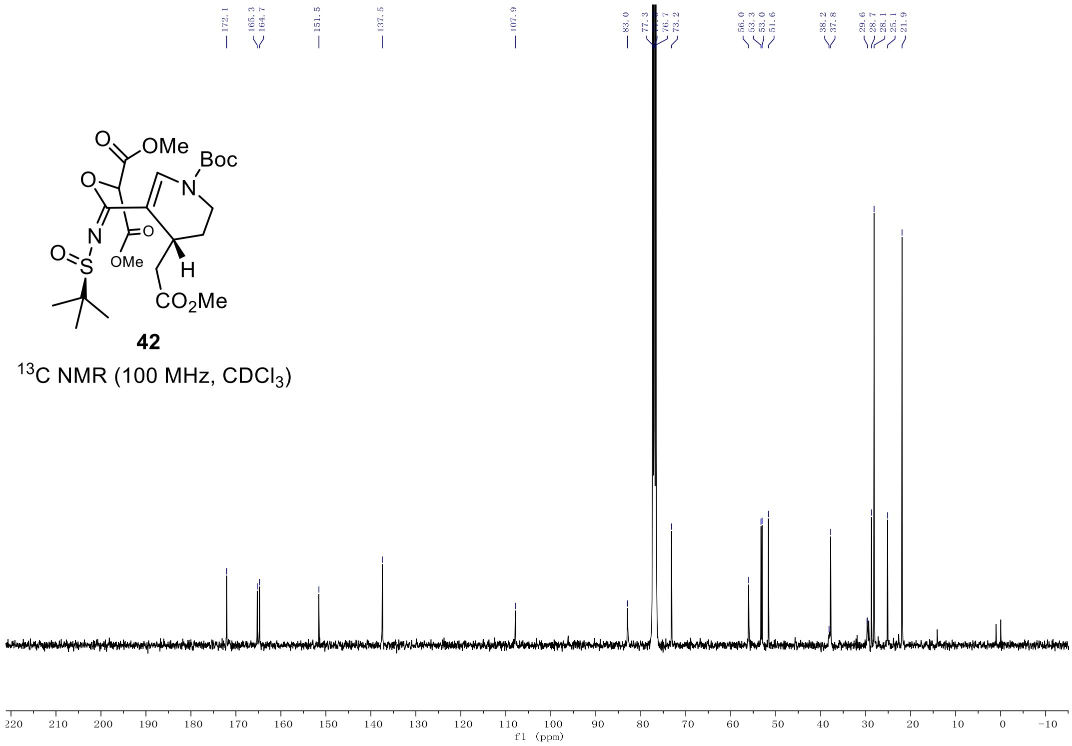
OMe
O
H
10
Boc
N
O
3
4
H
H
NH
O
4a
O=S
OMe
H
CO2Me
5.65
5.57
2.87
2.79
2.26
H10
H3
H4
H4a
4.37
6.72
100.00
2.50
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


5.65
2.88
2.80
2.26
OMe
O
Boc
H
10
N
O
H
3
4
H
NH
O
4a
O=S
OMe
H
CO2Me
40 NOE
H10
H4
H4a
0.62
2.79
100.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.
f1 (ppm)



42

^{1}H NMR (400 MHz, CDCl$_3$)

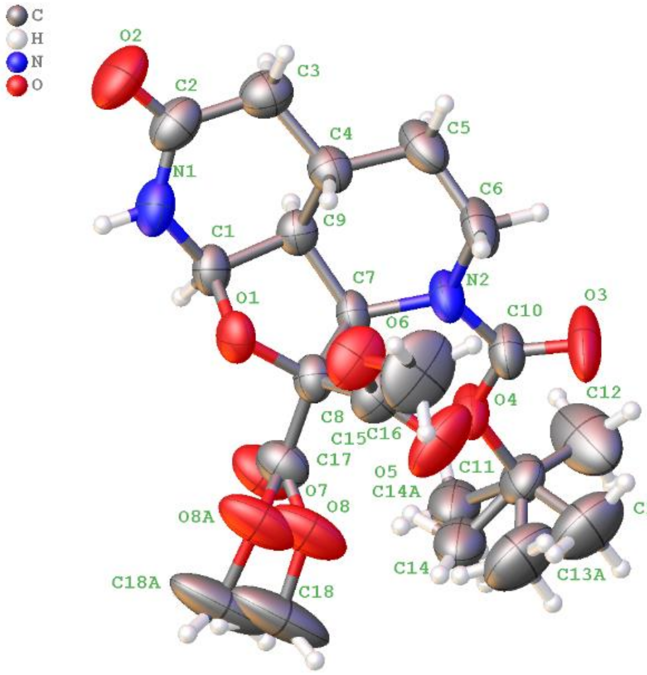


42

^{13}C NMR (100 MHz, CDCl$_3$)

5. Single Crystal X–ray Data

X–ray crystallographic data for 28



Structure deposited at the Cambridge Crystallographic Data Center (CCDC 1974253)

Crystal data and structure refinement for CCDC 1974253

CCDC	1974253
Empirical formula	$C_{18}H_{26}N_2O_8$
Formula weight	398.41
Temperature/K	293.15
Crystal system	monoclinic
Space group	$P2_1$
a/Å	9.4436(6)
b/Å	9.3899(6)
c/Å	11.6167(8)
α/°	90
β/°	91.155(6)
γ/°	90
Volume/Å^3	1029.89(12)
Z	2
ρ_{calc}g/cm^3	1.285
μ/mm^{-1}	0.101
F(000)	424.0
Crystal size/mm^3	0.35 × 0.3 × 0.25
Radiation	MoKα (λ = 0.71073)

2Θ range for data collection/°	6.12 to 52.734
Index ranges	$-11 \leq h \leq 11$, $-10 \leq k \leq 11$, $-14 \leq l \leq 12$
Reflections collected	4893
Independent reflections	3483 [R_{int} = 0.0160, R_{sigma} = 0.0430]
Data/restraints/parameters	3483/1/277
Goodness-of-fit on F^2	1.066
Final R indexes [I>=2σ (I)]	R_1 = 0.0479, wR_2 = 0.0951
Final R indexes [all data]	R_1 = 0.0699, wR_2 = 0.1109
Largest diff. peak/hole / e Å^{-3}	0.13/−0.14
Flack parameter	−0.5(6)