Electronic Supplementary Material (ESI) for ChemComm.

Total Synthesis of (-)-Agelastatin A: An S_H2' Radical Azidation Strategy

Izuru Tsuchimochi,[a,b] Yuta Kitamura,[b] Hiroshi Aoyama,[b] Shuji Akai,[b] Keiyo Nakai[a] and Takehiko Yoshimitsu*[a]

[a]*Division of Pharmaceutical Sciences, Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama University, 1-1-1, Tsushima-naka, Kita-ku, Okayama 700-8530, Japan*

[b]*Graduate School of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita, Osaka 565-0871, Japan*

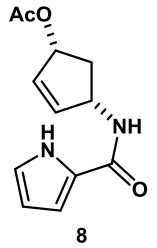
yoshimit@okayama-u.ac.jp

Supplementary Information

Table of Contents

General. All reagents were used as received from commercial suppliers unless otherwise noted. ^{1}H NMR spectra (500, 400 or 300 MHz) and ^{13}C NMR spectra (125 or 100 MHz) were measured in the specified solvents. Chemical shifts are reported in ppm relative to the internal solvent signal [chloroform-*d*: 7.26 ppm (^{1}H NMR), 77.0 ppm (^{13}C NMR); methanol-d_4: 3.31 ppm (^{1}H NMR), 49.0 ppm (^{13}C NMR); acetone-d_6: 2.05 ppm (^{1}H NMR), 29.84 ppm (^{13}C NMR)] or tetramethylsilane [0 ppm] as an internal standard. FT-IR spectra were recorded for samples loaded as neat films on NaCl plates. Mass spectra were obtained according to the specified technique. Analytical thin layer chromatography (TLC) was performed using Kieselgel 60 F_{254} and Silicagel 70 F_{254} TLC Plate *Wako*, and compounds were visualized with UV light and stained with anisaldehyde solution, phosphomolybdic acid solution, $KMnO_4$ solution and iodine.

Experimental Protocols

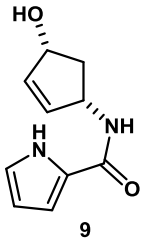


8

(1*R*,4*S*)-4-(1*H*-Pyrrole-2-carboxamido)cyclopent-2-en-1-yl acetate (8):

To a stirred solution of acetate **7** (10.0 g, 41.4 mmol) in MeCN (400 mL) at room temperature were added TMSCl (26.3 mL, 207 mmol) and H_2O (0.90 mL, 49.9 mmol). After 3 h, the solvent was removed under reduced pressure to give the colorless solid, to which MeCN (400 mL) was added. To the resultant suspension were added Et_3N (17.2

mL, 124 mmol), 1*H*-pyrrole-2-carboxylic acid (7.4 g, 66.6 mmol), EDC (12.7 g, 66.2 mmol), and DMAP (506 mg, 4.14 mmol). After being stirred for 14 h, the mixture was concentrated under reduced pressure to afford a solid residue. This crude material was transferred to a separatory funnel where it was partitioned between EtOAc and sat. $NaHCO_3$. The aqueous phase was again extracted with EtOAc. The combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (EtOAc/*n*-Hexane 2:3→ 1:1 v/v) to give amide **8** (8.13 g, 84%) as a colorless amorphous. **Amide 8:** colorless amorphous; $[\alpha]^{21}_{D}$ -73.5 (*c* 1.765, $CHCl_3$); IR (neat) ν 3257, 1714, 1626, 1556, 1519, 1411, 1246 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.58 (brs, 1H), 6.94 (m, 1H), 6.54 (m, 1H), 6.24 (ddd, 1H, *J* = 3.4, 2.9, 2.9 Hz), 6.06 (dd, 1H, *J* = 5.7, 1.7 Hz), 6.03 (ddd, 1H, *J* = 5.2, 2.3, 2.3 Hz), 5.94 (brd, 1H, *J* = 8.6 Hz), 5.60 (m, 1H), 5.15 (m, 1H), 2.91 (ddd, 1H, *J* = 14.9, 7.4, 7.4 Hz), 2.06 (s, 3H), 1.65 (ddd, 1H, *J* = 14.9, 4.0, 4.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 160.4, 136.6, 132.7, 125.5, 121.9, 109.7, 109.0, 77.6, 52.8, 38.5, 21.2; HRMS (MALDI) calcd for $C_{12}H_{14}N_2O_3Na$ $(M+Na)^+$: 257.0897, found: 257.0897.

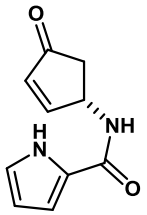


9

***N*-((1*S*,4*R*)-4-Hydroxycyclopent-2-en-1-yl)-1*H*-pyrrole-2-carboxamide (9):**

To a stirred solution of amide **8** (8.13 g, 34.7 mmol) in EtOH-H_2O (267 mL, 3:1 v/v) at room temperature was added $LiOH \cdot H_2O$ (2.2 g, 52.4 mmol). After 15 min, sat. NH_4Cl was added. The whole mixture was transferred to a separatory funnel where it was extracted with EtOAc three times, and the organic phases were combined and dried over $MgSO_4$. The solvent was removed under reduced pressure to afford the residue, which was dissolved in hot EtOAc and was passed through a filter paper. The filtrate was concentrated under reduced pressure to give the residue, which was recrystallized from EtOAc to furnish allylic alcohol **9** (4.67 g, 70%) as thin pale red needles. Further recrystallization of the mother liquor from EtOAc gave additional allylic alcohol **9** (1.18

g, 18%) as a second crop. **Allyl alcohol 9:** thin pale red needles of mp 180-185 ℃ (EtOAc); $[\alpha]_D^{21}$ -141.9 (*c* 1.015, MeOH); IR (KBr) ν 3277, 1598, 1566 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 6.90 (dd, 1H, *J* = 2.4, 1.4 Hz), 6.79 (dd, 1H, *J* = 3.7, 1.4 Hz), 6.15 (dd, 1H, *J* = 3.7, 2.4 Hz), 5.97 (ddd, 1H, *J* = 5.9, 2.0, 2.0 Hz), 5.88 (m, 1H), 4.92 (m, 1H), 4.72 (m, 1H), 2.79 (ddd, 1H, *J* = 13.7, 8.0, 7.4 Hz), 1.52 (ddd, *J* = 13.7, 5.2, 5.1 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 163.0, 137.2, 134.9, 126.6, 123.0, 111.9, 110.2, 75.8, 54.3, 42.0; HRMS (MALDI) calcd for $C_{10}H_{12}N_2O_2Na$ $(M+Na)^+$: 215.0791, found: 215.0791.

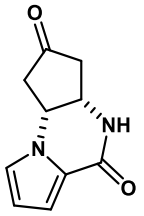


10

(*S*)-*N*-(4-Oxocyclopent-2-en-1-yl)-1*H*-pyrrole-2-carboxamide (10):

To a stirred solution of acetate **9** (3.0 g, 15.6 mmol) in DMF (156 mL) at room temperature was added PDC (14.7 g, 39.0 mmol). After 20 min, *i*-PrOH was added and the mixture was diluted with Et_2O. To the mixture were added Celite and Florisil and the mixture was stirred for 30 min. The mixture was filtered through a pad of Celite/Florisil and the filtrate was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (EtOAc/*n*-Hexane 3:1 v/v) to give enone **10** (2.43 g, 80%) as a colorless solid.

Enone 10: colorless solid of mp 150-152 ºC; $[\alpha]^{20}_D$ -226.2 (*c* 0.5750, $CHCl_3$); IR (neat) ν 3377, 3198, 1709, 1695, 1634, 1520 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.40 (brs, 1H), 7.60 (dd, 1H, *J* = 5.8, 2.4 Hz), 6.96 (ddd, 1H, *J* = 2.7, 2.7, 1.4 Hz), 6.57 (m, 1H), 6.30 (dd, 1H, *J* = 5.8, 2.1 Hz), 6.26 (m, 1H), 5.95 (brd, 1H, *J* = 7.6 Hz), 5.43 (m, 1H), 2.94 (dd, 1H, *J* = 18.8, 6.9 Hz), 2.26 (dd, 1H, *J* = 18.8, 2.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6, 162.0, 160.7, 135.7, 125.0, 122.2, 110.1, 109.5, 49.6, 42.2; HRMS (MALDI) calcd for $C_{10}H_{11}N_2O_2$ $(M+H)^+$: 191.0815, found, 191.0815.

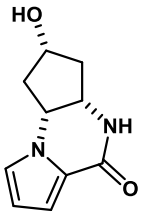


11

(3a*S*,9a*R*)-3a,4-Dihydro-1*H*-cyclopenta[e]pyrrolo[1,2-a]pyrazine-2,5(3*H*,9a*H*)-dione (11):

To a stirred solution of enone **10** (4.31 g, 22.7 mmol) in THF (430 mL) at room temperature was added Cs_2CO_3 (7.38 g, 22.7 mmol). After 7 h, the mixture was filtered through a pad of Celite and the filtrate was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography ($MeOH/CH_2Cl_2$ 1:20 v/v) to give ketone **11** (3.96 g, 92%) as a colorless solid. The spectroscopic and analytical data of this material were in good agreement with those reported.[1]

Ketone 11: colorless solid of mp 185-188 °C; $[\alpha]^{21}_D$ -68.1 (*c* 0.935, MeOH); IR (KBr) ν 3318, 1755, 1663, 1614 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 7.05 (dd, 1H, *J* = 2.8, 1.4 Hz), 6.77 (dd, 1H, *J* = 3.7, 1.4 Hz), 6.28 (dd, 1H, *J* = 3.7, 2.8 Hz), 4.96 (ddd, 1H, *J* = 7.3, 7.3, 5.0 Hz), 4.54 (m, 1H), 2.84 (dd, 1H, *J* = 18.8, 7.8 Hz), 2.72 (dd, 1H, *J* = 18.8, 6.4 Hz), 2.58 (ddd, 1H, *J* = 18.8, 7.3, 1.8 Hz), 2.45 (ddd, 1H, *J* = 18.8, 3.7, 1.8 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 213.1, 162.4, 125.4, 122.8, 115.6, 111.4, 54.9, 53.4, 45.4, 43.7; HRMS (MALDI) calcd for $C_{10}H_{11}N_2O_2$ $(M+H)^+$: 191.0815, found: 191.0814.



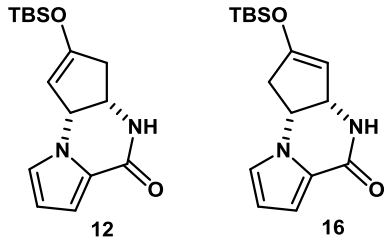
S1

(2*R*,3a*S*,9a*R*)-2-Hydroxy-1,2,3,3a,4,9a-hexahydro-5*H*-cyclopenta[e]pyrrolo [1,2-a]pyrazin-5-one (S1):

To a stirred solution of ketone **11** (10 mg, 0.0526 mmol) in MeOH (1.0 mL) at room temperature was added $NaBH_4$ (3.0 mg, 0.0793 mmol). After 5 min, acetone (8 μL, 0.108 mmol) was added and the mixture was concentrated under reduced pressure. The residue

was purified by flash silica gel column chromatography (MeOH/CH_2Cl_2 1:10 v/v) to give alcohol **S1** (10.1 mg, quant.) as a colorless solid. The optical purity of the alcohol **S1** was determined by the ^{1}H NMR analyses of the corresponding Mosher esters to be >99% ee.

Alcohol S1: colorless solid, ^{1}H NMR (400 MHz, CD_3OD) δ 7.00 (m, 1H), 6.86 (m, 1H), 6.24 (m, 1H), 4.50 (dd, 1H, *J* = 6.9, 13.2 Hz), 4.07 (dd, 1H, *J* = 6.0, 12.3 Hz), 2.58 (ddd, 1H, *J* = 6.9, 7.3, 14.1 Hz), 2.43 (ddd, 1H, *J* = 6.9, 7.3, 14.1 Hz), 2.05 (ddd, 1H, *J* = 5.5, 8.2, 13.7, Hz).



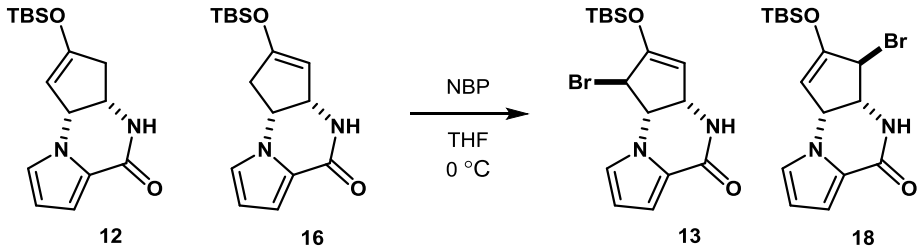
(3a*S*,9a*R*)-2-((*tert*-Butyldimethylsilyl)oxy)-3a,4-dihydro-3*H*-cyclopenta[e]pyrrolo [1,2-a]pyrazin-5(9a*H*)-one (12),

(3a*S*,9a*R*)-2-((*tert*-Butyldimethylsilyl)oxy)-3a,4-dihydro-1*H*-cyclopenta[e]pyrrolo [1,2-a]pyrazin-5(9a*H*)-one (16):

To a stirred solution of ketone **11** (1.91 g, 10.0 mmol) in THF (143 mL) at -78 °C was added NaHMDS (1.9 M in THF; 25.3 mL, 24.1 mmol) dropwise. After 10 min of stirring at the same temperature, a solution of TBSCl (3.63 g, 24.1 mmol) in THF (7 mL) was added and stirring was continued for further 10 min. The mixture was allowed to warm to 0 °C and stirred for 30 min. Sat. NH_4Cl was added to quench the reaction, and the mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (MeOH/CH_2Cl_2 1:30 v/v) to give an inseparable mixture of silyl enol ether **12** and **16** (2.57 g, 84%, **12:16** = 8.3:1) as a colorless solid and unreacted ketone **11** (45 mg, 2%) as a colorless solid. The listed below are the data of regioisomeric silyl enol ethers **12** and **16** that were obtained by careful chromatographic purification.

Silyl enol ether 12: colorless solid of mp 132-152 °C; $[\alpha]^{20}_D$ +103.3 (*c* 0.62, $CHCl_3$); IR

(neat) ν 3223, 1643 cm^{-1}; ^1H NMR (400 MHz, acetone-*d*6) δ 7.01 (brs, 1H), 6.90 (dd, 1H, *J* = 2.5, 1.6 Hz), 6.68 (dd, 1H, *J* = 3.9, 1.6 Hz), 6.17 (dd, 1H, *J* = 3.9, 2.5 Hz), 5.14-5.08 (m, 2H), 4.47-4.39 (m, 1H), 2.72-2.62 (m, 1H), 2.59-2.40 (m, 1H), 0.91 (s, 9H), 0.21 (s, 3H), 0.19 (s, 3H); ^1H NMR (400 MHz, $CDCl_3$) δ 6.93 (dd, 1H, *J* = 3.9, 1.6 Hz), 6.71 (dd, 1H, *J* = 2.5, 1.6 Hz), 6.55-6.35 (brs, 1H), 6.27 (dd, 1H, *J* = 3.9, 2.5 Hz), 5.00 (dd, 1H, *J* = 6.4, 2.3 Hz), 4.94 (m, 1H), 4.35 (ddd, 1H, *J* = 14, 6.8, 3.6 Hz), 2.62 (dd, 1H, *J* = 15.6, 6.9 Hz), 2.49 (dd, 1H, *J* = 15.6, 6.0 Hz), 0.90 (s, 9H), 0.18 (s, 3H), 0.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 158.7, 122.4, 122.3, 112.8, 110.1, 100.5, 57.3, 52.2, 40.9, 25.4, 18.0, -4.7; HRMS (MALDI) calcd for $C_{16}H_{25}N_2O_2Si$ $(M+H)^+$: 305.1680, found: 305.1677. **Silyl enol ether 16:** colorless solid of 152-153 °C; $[\alpha]^{20}_D$ -165.1 (c 0.505, $CHCl_3$) IR (neat) ν 3236, 1651, 1633 cm^{-1}; ^1H NMR (400 MHz, aceton-*d*6) δ 7.00 (dd, 1H, *J* = 2.5, 1.6 Hz), 6.93 (brs, 1H), 6.69 (dd, 1H, *J* = 3.9, 1.6 Hz), 6.18 (dd, 1H, *J* = 3.9, 2.5 Hz), 4.89 (ddd, 1H, *J* = 6.9, 6.4, 5.5 Hz), 4.85 (dd, 1H, *J* = 3.7, 1.4 Hz), 4.76 (m, 1H), 2.89 (m, 1H, overlapped with the signal of H_2O), 2.65 (ddt, 1H, *J* = 15.6, 5.5, 1.4 Hz) 0.91 (s, 9H), 0.19 (s, 3H), 0.17 (s, 3H) ; ^1H NMR (400 MHz, $CDCl_3$) δ 6.94 (dd, 1H, *J* = 3.9, 1.8 Hz), 6.79 (dd, 1H, *J* = 2.5, 1.8 Hz), 6.27 (dd, 1H, *J* = 3.7, 2.7 Hz), 5.61 (brs, 1H), 4.74 (m, 3H), 2.80-2.62, (m, 2H), 0.90 (s, 9H), 0.18 (s, 3H), 0.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 157.3, 122.7, 122.2, 113.3, 110.2, 102.0, 56.2, 53.1, 40.5, 25.4, 18.0, 0.97, -4.78, -4.82; HRMS (MALDI) calcd for $C_{16}H_{25}N_2O_2Si$ $(M+H)^+$: 305.1680, found: 305.1678.



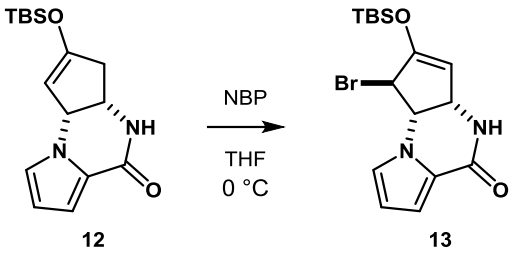
Brominative Olefin Isomerization of Silyl Enol Ether with NBS

(1*R*,3a*S*,9a*S*)-1-Bromo-2-((*tert*-butyldimethylsilyl)oxy)-3a,4-dihydro-1*H*-cyclopenta[e]pyrrolo[1,2-a]pyrazin-5(9a*H*)-one (13),

(3*S*,3a*R*,9a*R*)-3-Bromo-2-((*tert*-butyldimethylsilyl)oxy)-3,3a,4,9a-tetrahydro-5*H*-cyclopenta[e]pyrrolo[1,2-a]pyrazin-5-one (18):

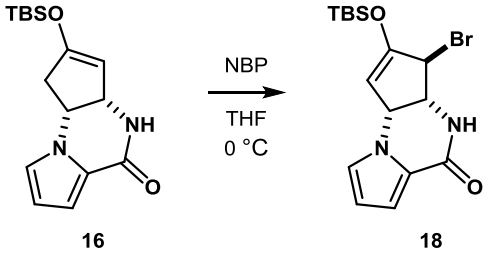
To a stirred solution of silyl enol ether **12** (2.0 g, 6.58 mmol; **12:16** = 8.3:1) in THF (92 mL) at 0 ºC was added *N*-bromophthalimide (NBP) (1.64 mg, 7.26 mmol). After 30 min, sat. $NaHCO_3$ was added and the mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (EtOAc/*n*-Hex 2:3→2:1 v/v) to give less polar bromo enol ether **18** (228 mg, 9%) as a colorless solid and more polar bromo enol ether **13** (1.66 g, 66%) as a colorless solid.

Bromo enol ether 13: colorless solid of mp 145-148 ºC; $[\alpha]_D^{22}$ -4.3 (*c* 0.655, $CHCl_3$); IR (neat) ν 3215, 1666, 1633, 1556 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.05 (dd, 1H, *J* = 2.7, 1.4 Hz), 6.99 (dd, 1H, *J* = 4.1, 1.4 Hz), 4.95-4.91 (m, 2H), 4.85-4.85 (m, 2H), 0.94 (s, 9H), 0.23 (s, 3H), 0.20 (s, 3H); ^1H NMR (400 MHz, acetone-d_6) δ 7.19 (dd, 1H, *J* = 2.7, 1.8 Hz), 6.96 (brs, 1H), 6.74 (dd, 1H, *J* = 4.1, 2.3 Hz), 6.24 (dd, 1H, *J* = 3.7, 2.7 Hz), 5.14 (d, 1H, *J* = 2.3 Hz), 5.09 (d, 1H, *J* = 4.1 Hz), 5.06 (dd, 1H, *J* = 6.4, 4.1 Hz), 4.92-4.87 (m, 1H), 0.94 (s, 9H), 0.24 (s, 3H), 0.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 155.5, 123.3, 121.8, 114.2, 110.8, 104.1, 62.1, 55.8, 54.7, 25.4, 18.1, -4.78, -5.10; HRMS (MALDI) calcd for $C_{16}H_{24}N_2O_2SiBr$ $(M+H)^+$: 383.0785, found: 383.0785. **Allyl bromide 18:** colorless powder of mp 133-135 ºC (Et_2O/*n*-Hexane); $[\alpha]_D^{19}$ -61.7 (*c* 0.675, $CHCl_3$); IR (neat) ν 3213, 1663, 1555 cm^{-1} ;^1H NMR (400 MHz, $CDCl_3$) δ 6.96 (dd, 1H, *J* = 4.0, 1.7 Hz), 6.76 (dd, 1H, *J* = 2.9, 1.7 Hz), 6.58 (brs, 1H), 6.29 (dd, 1H, *J* = 4.0, 2.9 Hz), 5.19-5.17 (m, 1H), 5.00 (d, 1H, *J* = 2.3 Hz), 4.63 (d, 1H, *J* = 5.2 Hz), 4.48-4.52 (m, 1H), 0.94 (s, 9H), 0.24 (s, 3H), 0.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 156.2, 122.7, 122.1, 113.8, 110.7, 102.9, 61.4, 56.4, 56.0, 25.4, 18.1, -4.7, -5.1; HRMS (MALDI) calcd for $C_{16}H_{24}N_2O_2SiBr$ $(M+H)^+$: 383.0785, found: 383.0787.



12 13

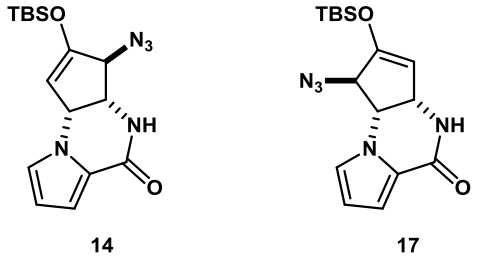
To a stirred solution of silyl enol ether **12** (80 mg, 0.263 mmol) in THF (3 mL) at 0 °C was added *N*-bromophthalimide (NBP) (65.3 mg, 0.289 mmol). After 22 min, sat. $NaHCO_3$ and sat. $Na_2S_2O_3$ were added and the mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (EtOAc/CH_2Cl_2 1:5→1:0 v/v) to give bromo enol ether **13** (72.7 mg, 72%) as a colorless solid.



16 18

To a stirred solution of silyl enol ether **16** (12.7 mg, 0.0417 mmol) in THF (1 mL) at 0 °C was added *N*-bromophthalimide (NBP) (10.4 mg, 0.0460 mmol). After 55 min, sat. $NaHCO_3$ and sat. $Na_2S_2O_3$ were added and the mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (EtOAc/*n*-Hexane 1:5→1:0 v/v) to give bromo enol ether **18** (10.4 mg, 65%) as a colorless solid.

Azidation of Silyl Enol Ether 13 with $BnEt_3N/KMnO_4/TMSN_3$



14 17

(3*S*,3a*R*,9a*R*)-3-Azido-2-((*tert*-butyldimethylsilyl)oxy)-3a,4-dihydro-3*H*-cyclopenta[e]pyrrolo[1,2-a]pyrazin-5(9a*H*)-one (14):

(1*R*,3a*S*,9a*S*)-1-Azido-2-((*tert*-butyldimethylsilyl)oxy)-1,3a,4,9a-tetrahydro-5*H*-cyclopenta[e]pyrrolo[1,2-a]pyrazin-5-one (17):

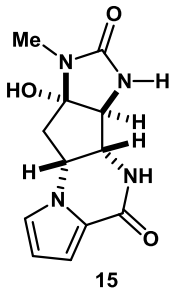
$KMnO_4$ (3.7 mg, 0.0234 mmol) and $BnEt_3NCl$ (5.3 mg, 0.0233 mmol) were added to MeCN (3.0 mL) at room temperature. The mixture was stirred for 30 min at the same temperature and then cooled to 0 °C. After 10 min, $TMSN_3$ (102 μL, 0.753 mmol) was added and stirring was continued for an additional 60 min at the same temperature. To this mixture was added bromo enol ether **13** (30 mg, 0.0783 mmol) as a solid material. The mixture was then allowed to warm to room temperature and stirred for further 40 min. After addition of sat. $NaHCO_3$ and sat. $Na_2S_2O_3$ to the mixture, the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (EtOAc/*n*-Hexane 2:3→1:0 v/v) to give allyl azide **14** (13.4 mg, 50%) as a brown solid, regioisomer **17** (5.8 mg, 21%) as a brown solid and bromide **18** (1.0 mg, 3%) as a colorless solid.

Allyl azide 14: brown solid of mp 157-159 °C; $[\alpha]_D^{20}$ -62.9 (*c* 0.79, $CHCl_3$); IR (neat) ν 3232, 2102, 1649, 1556 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.96 (dd, 1H, *J* = 4.1, 1.4 Hz), 6.69 (dd, 1H, *J* = 2.3, 1.4 Hz), 6.52 (brs, 1H), 6.28 (dd, 1H, *J* = 3.7, 2.7 Hz), 5.13 (d, 1H, *J* = 1.8 Hz), 4.99 (dd, 1H, *J* = 6.4, 2.7 Hz), 4.39 (d, 1H, *J* = 6.4 Hz), 3.93-3.81 (m, 1H), 0.95 (s, 9H), 0.28 (s, 3H), 0.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 157.5, 122.3, 113.7, 110.7, 100.4, 69.6, 58.1, 54.1, 25.3, 18.0, -4.9, -5.0; ^{13}C NMR (100 MHz, acetone-*d*6) δ 158.8, 157.4, 124.0, 123.2, 112.7, 110.6, 103.5, 71.1, 58.8, 55.2, 25.7, 18.6,

-4.89, -4.93; HRMS (MALDI) calcd for $C_{16}H_{23}N_5O_2NaSi$ $(M+Na)^+$: 368.1513, found: 368.1514. **Allyl azide 17:** brown solid of 155-159 ^oC; $[\alpha]_D^{20}$ -13.3 (*c* 0.93, $CHCl_3$); IR (neat) ν 3213, 2110, 1643 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 6.99 (dd, 1H, *J* = 4.0, 1.7 Hz), 6.92 (m, 1H), 6.31 (dd, 1H, *J* = 4.0, 2.9 Hz), 5.55 (brs, 1H), 4.90 (m, 1H), 4.74 (dd, 1H, *J* = 6.9, 2.9 Hz), 4.33 (d, 1H, *J* = 6.9 Hz), 4.30 (dd, 1H, *J* = 6.9, 6.9 Hz), 0.97 (s, 9H), 0.27 (s, 3H), 0.25 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.9, 156.8, 123.5, 121.6, 114.3, 110.9, 102.2, 69.1, 58.6, 53.2, 25.5, 18.1, -4.8; HRMS (MALDI) calcd for $C_{16}H_{24}N_5O_2NaSi$ $(M+Na)^+$: 346.1694, found: 346.1691. The spectroscopic data and analytic data of bromide **18** obtained here were identical with those of authentic material **18**.

Azidation of Silyl Enol Ether 13 with $BnEt_3N/KMnO_4/TMSN_3$ (2.0 g scale)

$KMnO_4$ (247 mg, 1.56 mmol) and $BnEt_3NCl$ (357 mg, 1.57 mmol) were added to MeCN (200 mL) at room temperature. The mixture was stirred for 30 min at the same temperature and then cooled to 0 ^oC. After 10 min, $TMSN_3$ (102 μL, 0.753 mmol) was added and stirring was continued for an additional 60 min at the same temperature. To this mixture was added bromo enol ether **4** (2.0 g, 5.22 mmol) as a solid material. The mixture was then allowed to warm to room temperature and stirred for further 45 min. After addition of sat. $NaHCO_3$ and sat. $Na_2S_2O_3$ to the mixture, the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (EtOAc/*n*-Hexane 2:3→1:0 v/v) to give allyl azide **14** (828 mg, 46%) as a colorless solid, bromide **18** (57.8 mg, 3%) as a brown soild, an inseparable mixture (52 mg) containing allyl azide **14** (27.1 mg, 2%), regioisomer **17** (11.7 mg, 1%), and bromide **13** (13.2 mg, 1%), and additional inseparable mixture (225 mg) containing regioisomer **17** (193 mg, 11%) and bromide **13** (32 mg, 2%). The yields of the products in the above-mentioned inseparable mixture were determined by ^1H NMR analysis.

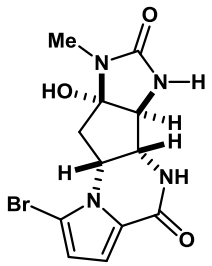


15

Debromoagelastatin A (15) (DeBrAA):

To a stirred solution of azide **14** (200 mg, 0.579 mmol) in MeOH (20 mL) at room temperature was added 10% Pd-C (60 mg, 30% w/w). The mixture was stirred for 100 min under hydrogen atmosphere. The hydrogen gas in the flask was replaced with argon and *N*-methyl-1*H*-imidazole-1-carboxamide (107 mg, 0.869 mmol) was added. After 20 h of stirring, the mixture was filtered through a pad of Celite and a filter cake was washed with MeOH. The filtrate was concentrated under reduced pressure and the residue was dissolved in a mixture of THF (20 mL) and H_2O (0.5 mL). To this was added CsF (88 mg, 0.579 mmol) and the solution was stirred at room temperature. After 1 h, additional H_2O (0.5 mL) was added. After 40 min, H_2O (0.5 mL) was added and the solution was stirred for further 2 h. After removal of the solvent, the residue was purified by flash silica gel column chromatography (MeOH/CH_2Cl_2 1:10→1:5 v/v) to give debromoagelastatin A (**15**) (77.5 mg, 51%) as a colorless solid. The spectroscopic and analytical data were in good agreement with those of the authentic material and those reported.[2]

Debromoagelastatin A (15) (DeBrAA): colorless solid of mp 242-244 ºC; $[\alpha]_D^{18}$ -76.0 (*c* 0.5350, MeOH); IR (KBr) ν 3271, 3234, 16554, 1635 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 7.02 (dd, 1H, *J* = 2.3, 1.7 Hz), 6.88 (dd, 1H, *J* = 4.0, 1.7 Hz), 6.23 (dd, 1H, *J* = 4.0, 2.3 Hz), 4.65 (ddd, 1H, *J* = 10.3, 6.3, 5.7 Hz), 3.99 (dd, 1H, *J* = 5.7, 1.1 Hz), 3.80 (d, 1H, *J* = 1.1 Hz), 2.79 (s, 3H), 2.61 (dd, 1H, *J* = 13.2, 6.3 Hz), 2.28 (dd, 1H, *J* = 13.2, 10.3 Hz); ^{13}C NMR (125 MHz, CD_3OD) δ 162.1, 161.3, 125.7, 122.8, 115.4, 111.1, 95.8, 68.0, 62.8, 55.6, 41.6, 24.3; HRMS (MALDI) calcd for $C_{12}H_{15}N_4O_3$ $(M+H)^+$: 263.1139, found: 263.1144.



1 (AA)

Agelastatin A (1) (AA):

To a stirred solution of debromoagelastatin A (**15**) (46.8 mg, 0.179 mmol) in MeOH-THF (16.5mL, 1:2 v/v) at 0 ^{o}C was added NBS (31.8 mg, 0.179 mmol), and the solution was stirred for 20 min. After removal of the solvent under reduced pressure, the residue was purified by flash silica gel column chromatography (MeOH/CH_2Cl_2 1:10 v/v) to give agelastatin A (**1**) (45.7 mg, 75%) as a colorless solid. The spectroscopic and analytical data were in good agreement with those of the authentic material and those reported.[3] **Agelastatin A (1) (AA):** colorless solid of mp 192-194 ^{o}C (dec); $[\alpha]_D^{20}$ -81.9 (*c* 1.58, MeOH) [lit.[3a] $[\alpha]_D^{20}$ -65.5 (c 0.5, MeOH); lit.[3b] $[\alpha]_D^{20}$ -84.2 (c 1.0, MeOH); lit.[3c] $[\alpha]_D^{20}$ -62.2 (c 0.18, MeOH); lit.[3d] $[\alpha]_D^{14}$ -83.8 (c 0.21, MeOH)]; IR (KBr) ν 3256, 1645, 1553 cm^{-1}; ^{1}H NMR (500 MHz, CD_3OD) δ 6.90 (d, 1H, *J* = 4.6 Hz), 6.32 (d, 1H, *J* = 4.0 Hz), 4.59 (ddd, 1H, *J* = 12.0, 6.3, 5.7 Hz), 4.08 (d, 1H, *J* = 5.2 Hz), 3.87 (s, 1H), 2.80 (s, 3H), 2.64 (dd, 1H, *J* = 13.2, 6.3 Hz), 2.09 (dd, 1H, *J* = 12.6, 12.6 Hz); ^{13}C NMR (125 MHz, CD_3OD) δ 161.4, 161.1, 124.1, 116.0, 113.8, 107.3, 95.7, 67.4, 62.2, 54.4, 40.0, 24.2. HRMS (MALDI) calcd for $C_{12}H_{14}N_4O_3Br$ $(M+H)^+$: 341.02444, found: 341.0245.

Table 1, Entry 1 ***(vide supra)***

Table 1, Entry 2

$KMnO_4$ (2.5 mg, 0.0157 mmol) and $BnEt_3NCl$ (3.6 mg, 0.0157 mmol) were added to MeCN (6.0 mL) at room temperature. The mixture was cooled to 0 ^{o}C and stirred for 10 min. To this was added $TMSN_3$ (205 μL, 1.57 mmol) and stirring was continued for an additional 60 min at the same temperature. To this mixture was added bromo enol ether **13** (60 mg, 0.157 mmol) as a solid material. The mixture was then allowed to warm to room temperature and stirred for further 40 min. After addition of sat. $NaHCO_3$ and sat.

$Na_2S_2O_3$, the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was passed through a short plug of flash silica gel (EtOAc/*n*-Hex 2:3→1:0 v/v) to give a mixture of allyl azide **14** (16.2 mg, 30%), regioisomer **17** (2.1 mg, 4%), bromide **18** (7.2 mg, 12%), and unreacted bromide **13** (17.9 mg, 30%). The chemical yields of each product were determined based on the integrations of their proton signals appeared on the ^{1}H NMR spectra.

Table 1, Entry 3

$KMnO_4$ (2.5 mg, 0.0157 mmol) and $BnEt_3NCl$ (3.6 mg, 0.0157 mmol) were added to MeCN (6.0 mL) at room temperature. The mixture was cooled to 0 ^{o}C and stirred for 10 min. To this was added $TMSN_3$ (205 μL, 1.57 mmol) and stirring was continued for an additional 55 min at the same temperature. After argon in the apparatus was evacuated and the apparatus was re-filled with oxygen, the mixture was stirred for 5 min. To this was added bromo enol ether **13** (60 mg, 0.157 mmol) as a solid material. The mixture was then allowed to warm to room temperature and stirred for further 40 min. After addition of sat. $NaHCO_3$ and sat. $Na_2S_2O_3$, the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was passed through a short plug of flash silica gel (EtOAc/*n*-Hexane 2:3→1:0 v/v) to give a mixture of allyl azide **14** (17 mg, 31%), regioisomer **17** (2.7 mg, 5%), bromide **18** (6.4 mg, 11%) and unreacted bromide **13** (12.8 mg, 21%). The chemical yields of each product were determined based on the integrations of their proton signals appeared on the ^{1}H NMR spectra.

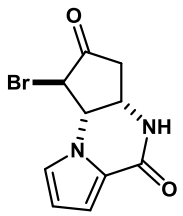
Table 1, entry 4

$KMnO_4$ (7.4 mg, 0.047 mmol) and $BnEt_3NCl$ (10.7 mg, 0.047 mmol) were added to MeCN (3.0 mL) at room temperature. The mixture was cooled to 0 ^{o}C and stirred for 10 min. To this mixture was added $TMSN_3$ (102 μL, 0.783 mmol) and stirring was continued for an additional 60 min at the same temperature. To this mixture was added bromo enol

ether **13** (30 mg, 0.078 mmol) as a solid material. The mixture was then allowed to warm to room temperature and stirred for further 40 min. After addition of sat. $NaHCO_3$ and sat. $Na_2S_2O_3$, the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was passed through a short plug of flash silica gel (EtOAc/*n*-Hexane 2:3 v/v→1:0) to give a mixture of allyl azide **14** (11.7 mg, 43%), regioisomer **17** (2.9 mg, 11%), bromide **18** (1.2 mg, 4%), and unreacted bromide **13** (2.7 mg, 9%). The chemical yields of each product were determined based on the integrations of their proton signals appeared on the ^1H NMR spectra.

Table 1, entry 5, Azidation of Silyl Enol Ether 13 with NaN_3

To a stirred solution of bromo enol ether **13** (10 mg, 0.026 mmol) in DMF (1.0 mL) at room temperature was added NaN_3 (1.9 mg, 0.029 mmol). After 15 min, H_2O was added to the mixture. The whole mixture was transferred to a separatory funnel where it was extracted with EtOAc three times. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (EtOAc/*n*-Hexane 2:1→ 1:0 v/v) to give bromo ketone **S4** (4.1 mg, 60%) as a pale yellow solid.



S4

Bromo ketone (S4): colorless solid of mp 181-183 °C; $[\alpha]_D^{28}$ -69.1 (*c* 0.25, $CHCl_3$); IR (KBr) ν 1772, 1630, 1556 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (brs, 1H), 7.10-7.00 (m, 2H), 6.33 (dd, 1H, *J* = 3.9, 2.7 Hz), 4.77-4.73 (m, 2H), 4.53 (d, 1H, *J* = 8.0), 2.95-2.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.5, 160.6, 124.5, 121.2, 116.0, 111.3, 62.3, 51.0, 50.7, 43.4; HRMS (MALDI) calcd for $C_{10}H_9N_2O_2NaBr$ $(M+Na)^+$: 290.9745, found: 290.9736.

Table 1, entry 6

To a stirred solution of $BnEt_3NCl$ (5.3 mg, 0.024 mmol) in MeCN (3.0 mL) was added $TMSN_3$ (102 μL, 0.78 mmol) at room temperature. After 60 min, bromo enol ether **13** (30 mg, 0.078 mmol) was added and the mixture was stirred for further 75 min. After addition of sat. $NaHCO_3$ and sat. $Na_2S_2O_3$, the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (EtOAc/*n*-Hexane 2:1 v/v) to give unreacted bromo enol ether **13** (27.1 mg, 90%) as a colorless solid.

Table 1, entry 6

To a stirred solution of $TMSN_3$ (102 μL, 0.78 mmol) in MeCN (3.0 mL) at 0 ^oC was added bromo enol ether **13** (30 mg, 0.078 mmol). The mixture was allowed to warm to room temperature and stirred for an additional 70 min. After addition of sat. $NaHCO_3$ and sat. $Na_2S_2O_3$, the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (EtOAc/*n*-Hexane 2:1 v/v) to give unreacted bromo enol ether **13** (26.6 mg, 89%) as a colorless solid.

Table 1, entry 8, Azidation of Silyl Enol Ether 14 with PhIO/$TMSN_3$

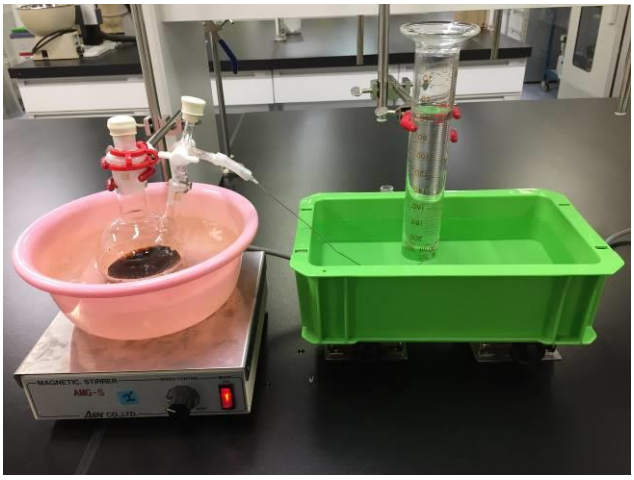
To a stirred solution of bromo enol ether **13** (30 mg, 0.078 mmol) in CH_2Cl_2 (2.3 mL) at -78 ^oC were added $TMSN_3$ (25 μL, 0.19 mmol) and PhIO (20.7 mg, 0.094 mmol). After 40 min, sat. $NaHCO_3$ and sat. $Na_2S_2O_3$ were added and the mixture was allowed to warm to room temperature. The mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (EtOAc/*n*-Hexane 2:3→2:1 v/v) to give a mixture of allyl azide **14** (6.5 mg, 24%), regioisomer **17** (4.6 mg, 17%), bromide **18** (3.9 mg, 14%), and unreacted bromide **13** (1.7 mg, 6%).

Table 1, entry 9

To a stirred solution of bromo enol ether **13** (10 mg, 0.026 mmol) in MeCN (0.5 mL) at room temperature were added $TMSN_3$ (20.5 μL, 0.157 mmol) and $Mn(OAc)_3 \cdot 2H_2O$ (21.0 mg, 0.0783 mmol). After 10.7 h of stirring, $NaHCO_3$ and sat. $Na_2S_2O_3$ were added and the mixture was allowed to warm to room temperature. The mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (EtOAc/*n*-Hexane 2:3→1:0 v/v) to give allyl azide **14** (3.8mg, 42%) as a brown solid and regioisomer **17** (0.7 mg, 8%) as a brown solid.

Evaluation of amounts of N_2 generated by $KMnO_4$/$BnEt_3NCl$/$TMSN_3$ (1:1:33 molar ratio) system:

To a stirred solution of $KMnO_4$ (52.7 mg, 0.333 mmol) and $BnEt_3NCl$ (76.0 mg, 0.333 mmol) in MeCN (17 mL) at 0 °C was added $TMSN_3$ (1.45 mL, 11.1 mmol) dropwise. The nitrogen gas was collected over water, indicating ca. 20~24 mL of moleculer nitrogen (N_2) was produced.



Experimental procedure for preparing a metastable Mn(V) species:

$KMnO_4$ (3.7 mg, 0.024 mmol) and $BnEt_3NCl$ (5.3 mg, 0.024 mmol) were added to MeCN (3.0 mL) at room temperature. The mixture was cooled to 0 °C and stirred for 10 min. At the same temperature, $TMSN_3$ (102 μL, 0.78 mmol) was added to this mixture

and the whole mixture was stirred for an additional 60 min. The mixture was concentrated under reduced pressure to ensure the complete removal of the solvent and unreacted $TMSN_3$. The resultant solid residue was again dissolved in MeCN (3 mL) and the mixture was stirred for 10 min at 0 ^oC. To this mixture was added bromo enol ether **13** (30 mg, 0.078 mmol) as a solid material. The mixture was then allowed to warm to room temperature and stirred for further 12 h. After addition of sat. $NaHCO_3$ and sat. $Na_2S_2O_3$, the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (EtOAc/*n*-Hexane 2:3→1:0 v/v) to give allyl azide **14** (12.4 mg, 46%) as a brown solid, regioisomer **17** (5.5 mg, 20%) as a brown solid, bromide **18** (1.7 mg, 6%) as a colorless soild, and additional inseparable mixture (1.3 mg) containing allyl azide **14** (0.6 mg, 2%), regioisomer **17** (0.5 mg, 2%), and bromide **13** (0.2 mg, 1%). The yields of the products in the inseparable mixture were determined by ^1H NMR analysis.

Azidation of azide 14:

$KMnO_4$ (2.7 mg, 0.017 mmol) and $BnEt_3NCl$ (4.0 mg, 0.018 mmol) were added to MeCN (2.0 mL) at room temperature. The mixture was cooled to 0 ^oC and stirred for 10 min. At the same temperature, $TMSN_3$ (76 μL, 0.60 mmol) was added and the whole mixture was stirred for an additional 60 min. To this mixture was added azide **14** (20 mg, 0.058 mmol) as a solid material. The mixture was then allowed to warm to room temperature and stirred for further 1 h. After addition of sat. $NaHCO_3$ and sat. $Na_2S_2O_3$, the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (EtOAc/*n*-Hexane 2:3→1:0 v/v) to give allyl azide **14** (15.5 mg, 78%) and regioisomer **17** (1.0 mg, 5%), both as a brown solid.

Azidation of bromide 18:

$KMnO_4$ (3.7 mg, 0.024 mmol) and $BnEt_3NCl$ (5.3 mg, 0.024 mmol) were added to

MeCN (3.0 mL) at room temperature. The mixture was cooled to 0 °C and stirred for 10 min. At the same temperature, $TMSN_3$ (102 μL, 0.78 mmol) was added and the whole mixture was stirred for an additional 60 min. To this mixture was added bromo enol ether **17** (30 mg, 0.078 mmol) as a solid material. The mixture was then allowed to warm to room temperature and stirred for further 1 h. After addition of sat. $NaHCO_3$ and sat. $Na_2S_2O_3$, the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (EtOAc/*n*-Hexane 2:3→1:0 v/v) to give allyl azide **14** (7.7 mg, 28%) as a brown solid, regioisomer **17** (5.8 mg, 21%) as a brown solid, bromide **18** (3.5 mg, 12%) as a colorless soild, and additional inseparable mixture (3.4 mg) containing allyl azide **14** (1.5 mg, 6%) and regioisomer **17** (1.9 mg, 7%). The yields of the products in the inseparable mixture were determined by ^1H NMR analysis.

Azidation of azide 17:

$KMnO_4$ (2.1 mg, 0.013 mmol) and $BnEt_3NCl$ (3.0 mg, 0.013 mmol) were added to MeCN (1.5 mL) at room temperature. The mixture was cooled to 0 °C and stirred for 10 min. At the same temperature, $TMSN_3$ (57 μL, 0.43 mmol) was added and the whole mixture was stirred for an additional 60 min. To this mixture was added azide **17** (30 mg, 0.078 mmol) as a solid material. The mixture was then allowed to warm to room temperature and stirred for further 1 h. After addition of sat. $NaHCO_3$ and sat. $Na_2S_2O_3$, the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to afford a solid residue, which was purified by flash silica gel column chromatography (EtOAc/*n*-Hexane 2:3→1:0 v/v) to give allyl azide **14** (1.0 mg, 7%) and regioisomer **17** (11.4 mg, 76%), both as a brown solid.

X-ray analysis of compound 18:

A single crystal of compound **18** was carefully selected under a polarizing microscope and glued to a thin glass fiber and mounted on the goniometer in a liquid nitrogen flow. All measurements were made on a Rigaku R-AXIS RAPID diffractometer using graphite monochromated Cu-Kα radiation. The intensity data sets were reduced by *CrystalClear* software.[4] The structures were solved by direct methods using *SIR2004* program[5] and refined by full-matrix least squares on F^2 using *SHELXL-97* program[6], implemented in program package WinGX.[7] The final models include anisotropic refinement for the non-hydrogen atoms and riding model for H atoms. Figure S1 shows the ORTEP drawing of compound **18**. Further details of the refinements are given Table S1.

Crystallographic data for the structures reported in this paper have been deposited at the Cambridge Crystallographic Data Centre (compound **18**: CCDC-1852628).

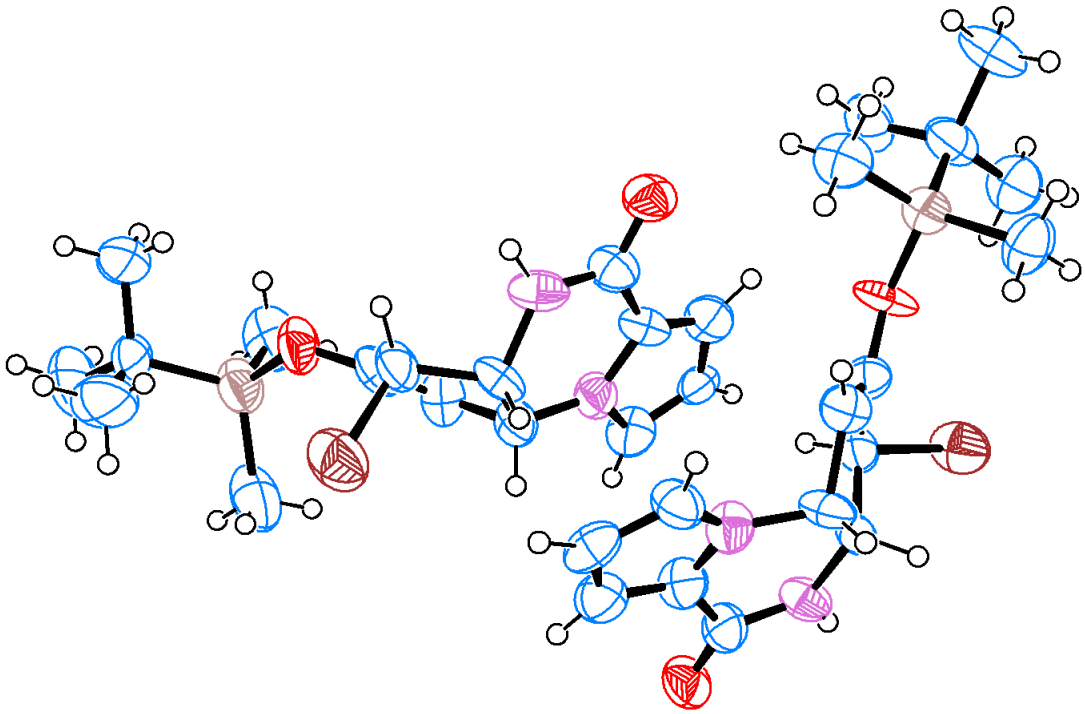


Figure S1. X-ray structure of compound **18** (thermal ellipsoid plot at the 50% probability level)

Table 1. Crystallographic data and structural refinemet for compound **18**

Compound	**18**
Empirical formula	$C_{16}H_{23}BrN_2O_2Si$
Formula weight	383.35
Temperature (K)	163
Crystal system	Monoclinic
Space group	$P2_1$
a (Å)	7.0818 (2)
b (Å)	34.0727 (11)
c (Å)	8.0223 (15)
β (°)	105.239 (2)
V (Å^3)	1867.7 (4)
Z	4
D_{calcd} (g/cm^3)	1.363
R_1 [a]	0.0987
wR_2 [b]	0.3234
Goodness-of-fit [c]	1.091

a $$R1 = \frac{\Sigma\big||Fo| - |Fc|\big|}{\Sigma|Fo|}$$

b $$wR2 = \left\{\frac{\Sigma[w(Fo^2 - Fc^2)^2]}{\Sigma[w(Fo^2)^2]}\right\}^{\frac{1}{2}}$$

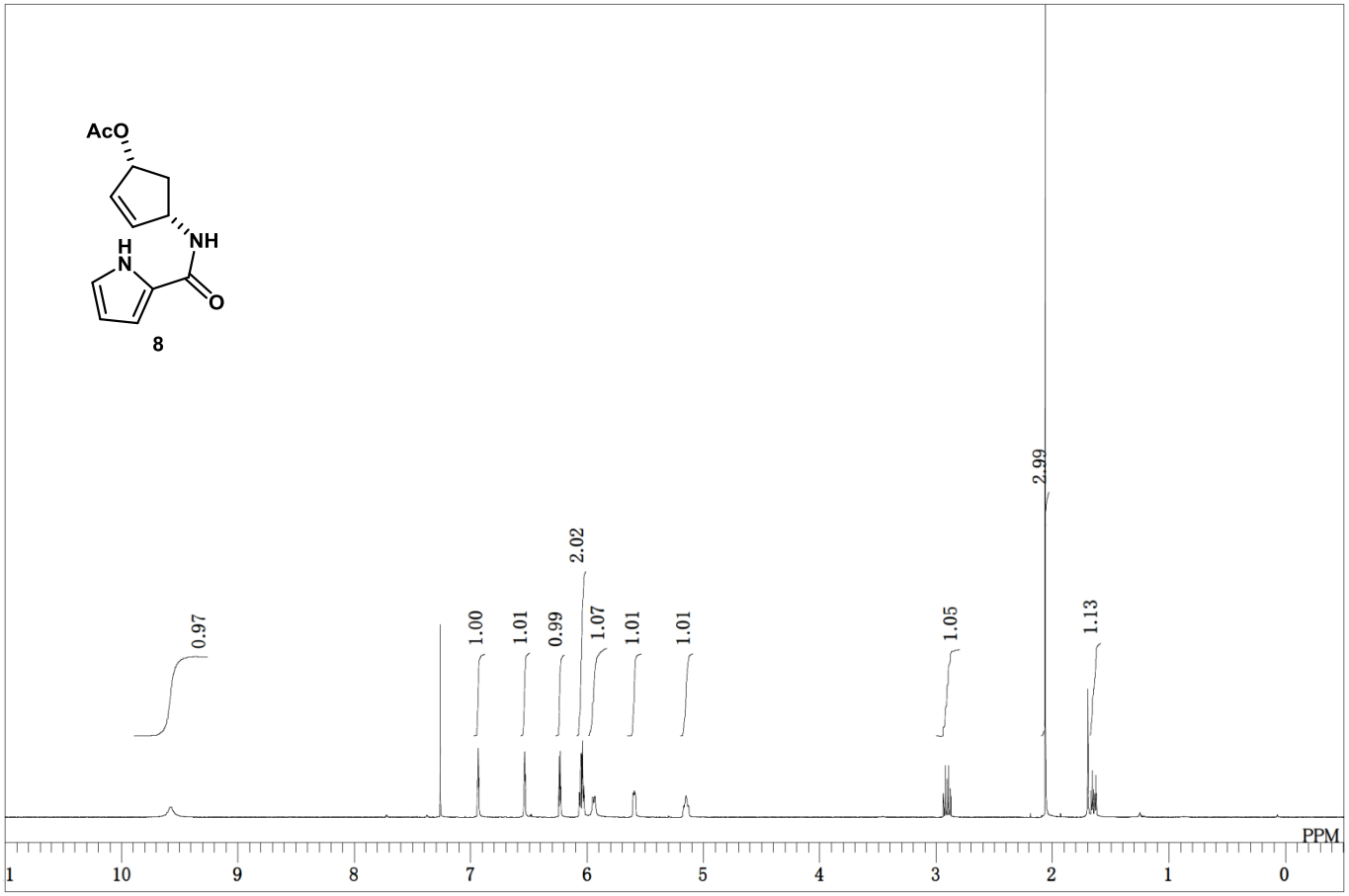
c $$GOF = \left\{\frac{\Sigma[w(Fo^2 - Fc^2)^2]}{n - p}\right\}^{\frac{1}{2}}$$,where n = number of measured data and p = number of parameters.

References

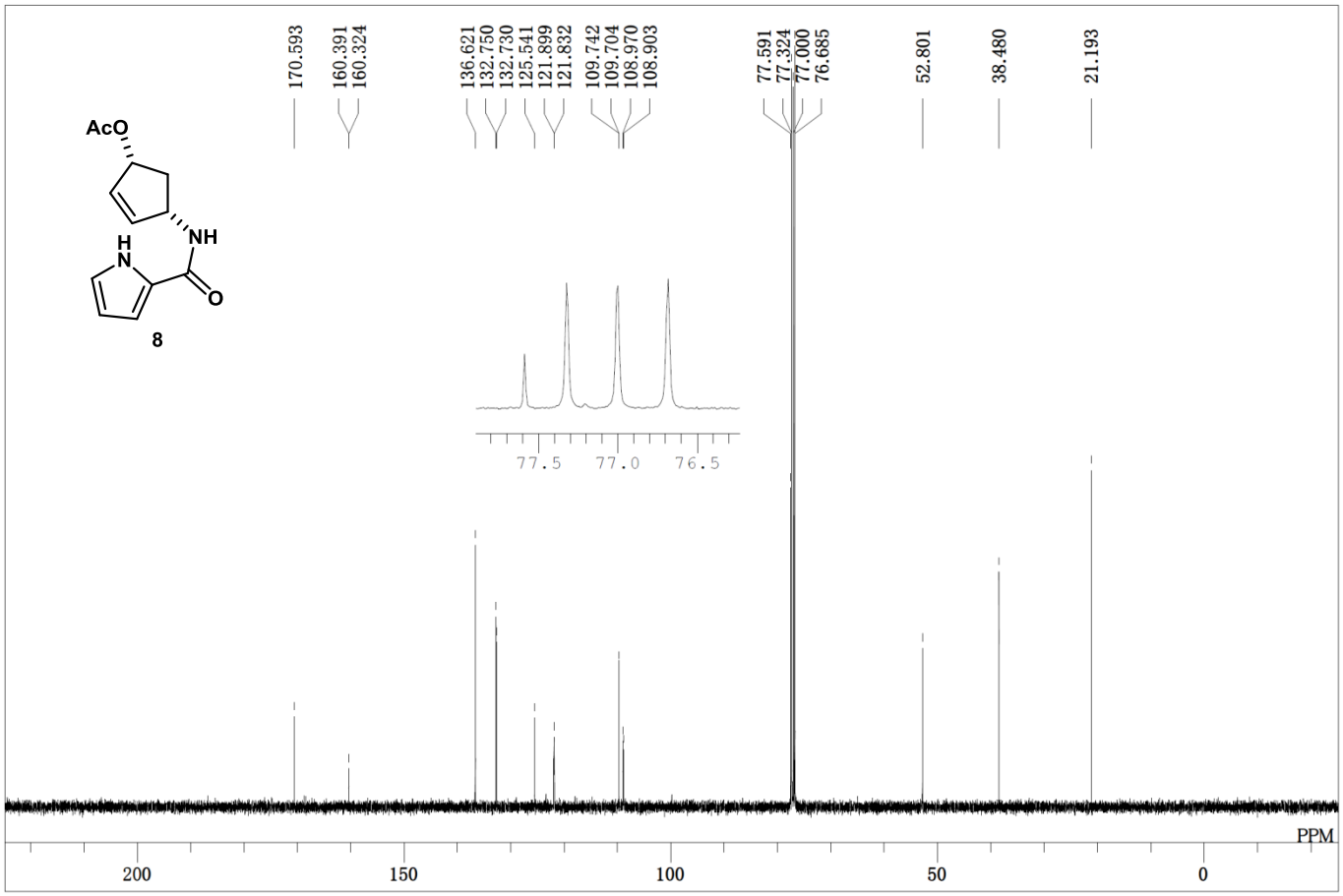
1. D. Shigeoka, T. Kamon and T. Yoshimitsu, *Beilstein J. Org. Chem.*, 2013, **9**, 860.
2. T. Yoshimitsu, T. Ino and T. Tanaka, *Org. Lett*., 2008, **10**, 5457.
3. (a) K. S. Feldman and J. C. Saunders, *J. Am. Chem. Soc*., 2002, **124**, 9060. (b) K. J. Hale, M. M. Domostoj, D. A. Tocher, E. Irving and F. Scheinmann, *Org. Lett*., 2003, **5**, 2927. (c) F. A. Davis and J. Deng, *Org. Lett.*, 2005, **7**, 621. (d) Y. Ichikawa, T. Yamaoka, K. Nakano and H. Kotsuki, *Org. Lett.*, 2007, **9**, 2989.
4. *CrystalClear* Rigaku Corporation, The Woodlands, Texas, USA 1999.
5. M. C. Burla, R. Caliandro, M. Camalli, B. Carrozini, G. L. Cascarano, L. De Caro, C. Giacovazzo, G. Polidor and R. Spagna, *J. Appl. Crystallogr*., 2005, **38**, 381.
6. G. M. Sheldrick, *Acta Cryst*., 2008, **A64**, 112.

7. L. J. Farrugia, *J. Appl. Crystallogr*., 1999, **32**, 837.

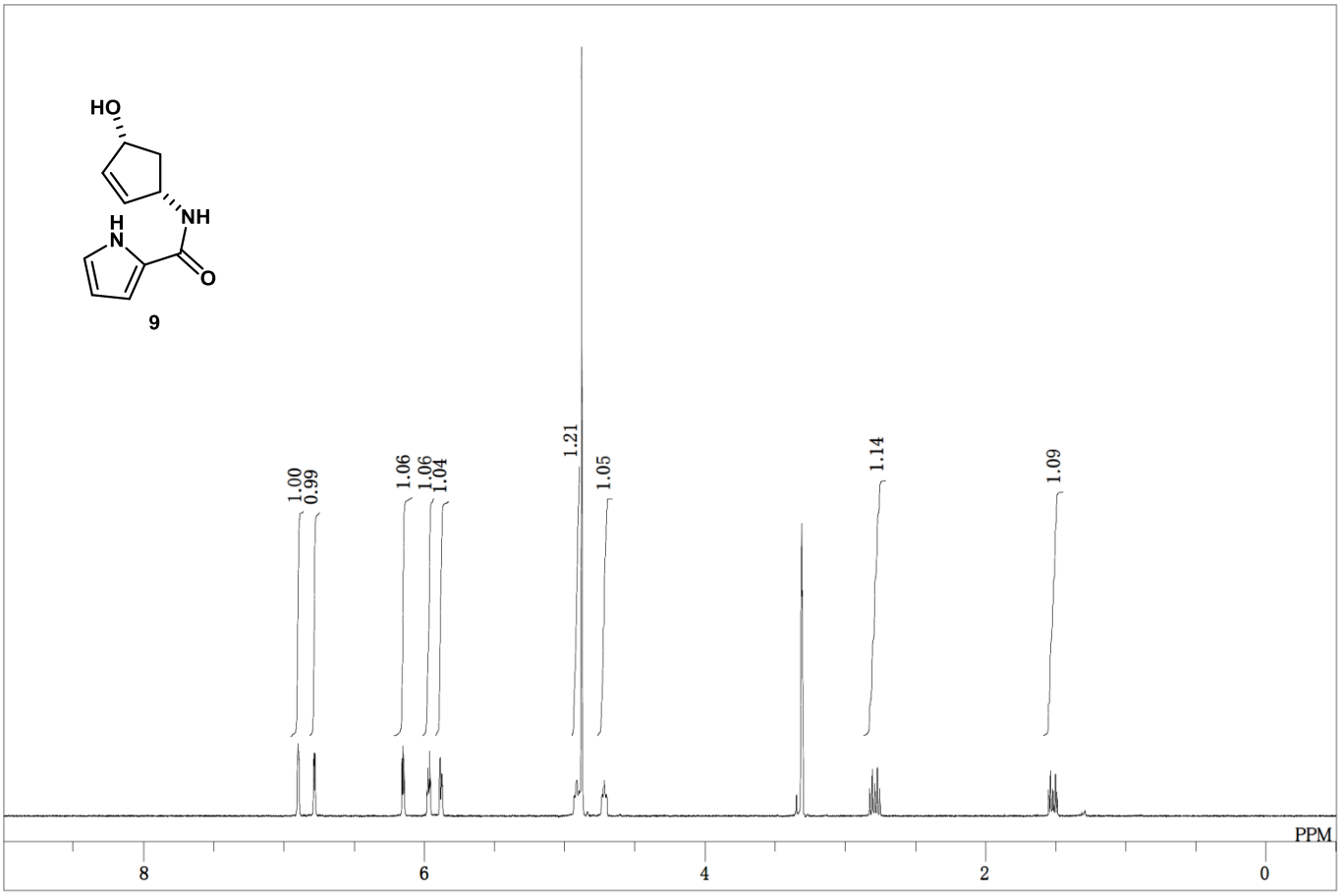
^{1}H NMR (500 MHz, $CDCl_3$)



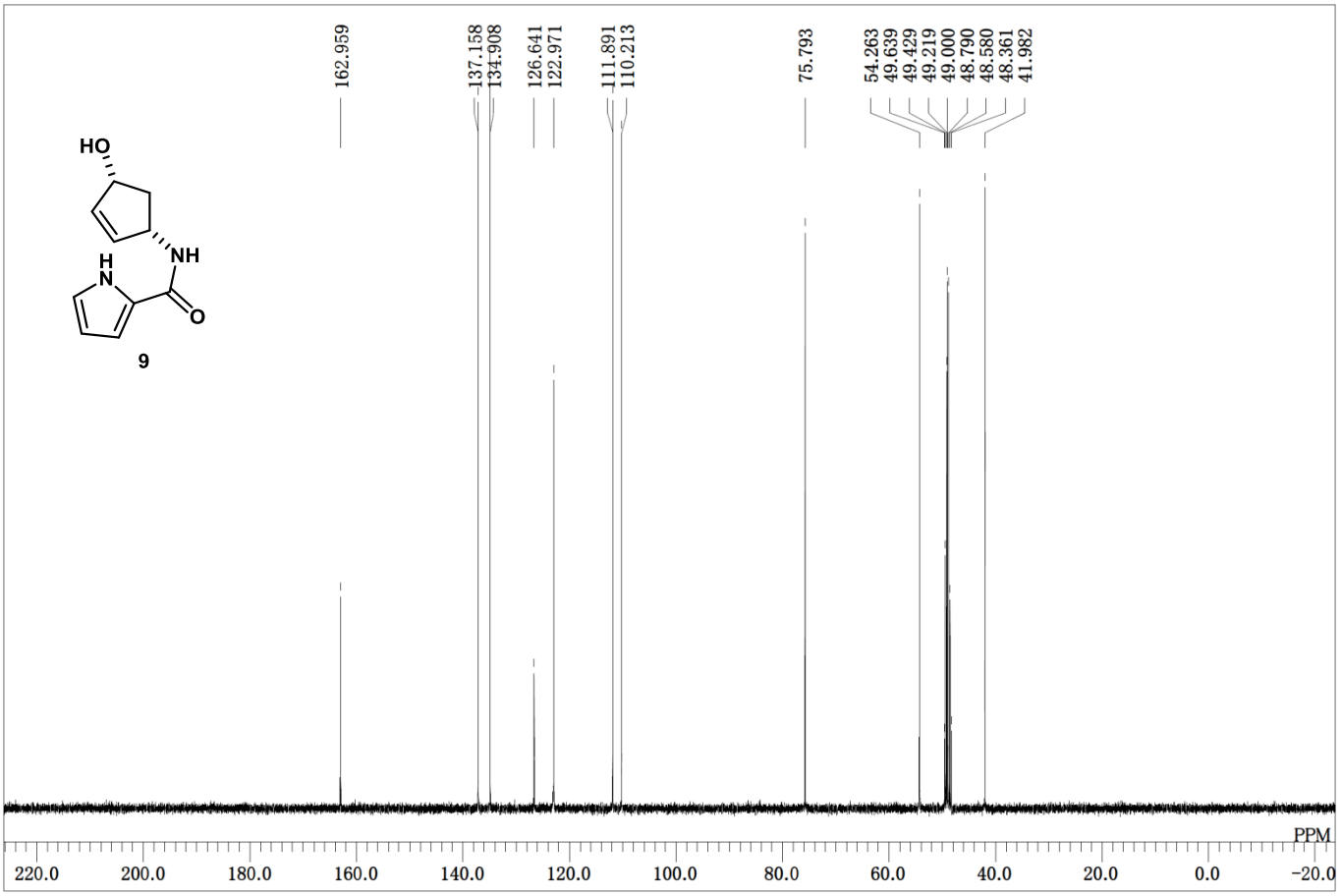
^{13}C NMR (125 MHz, $CDCl_3$)



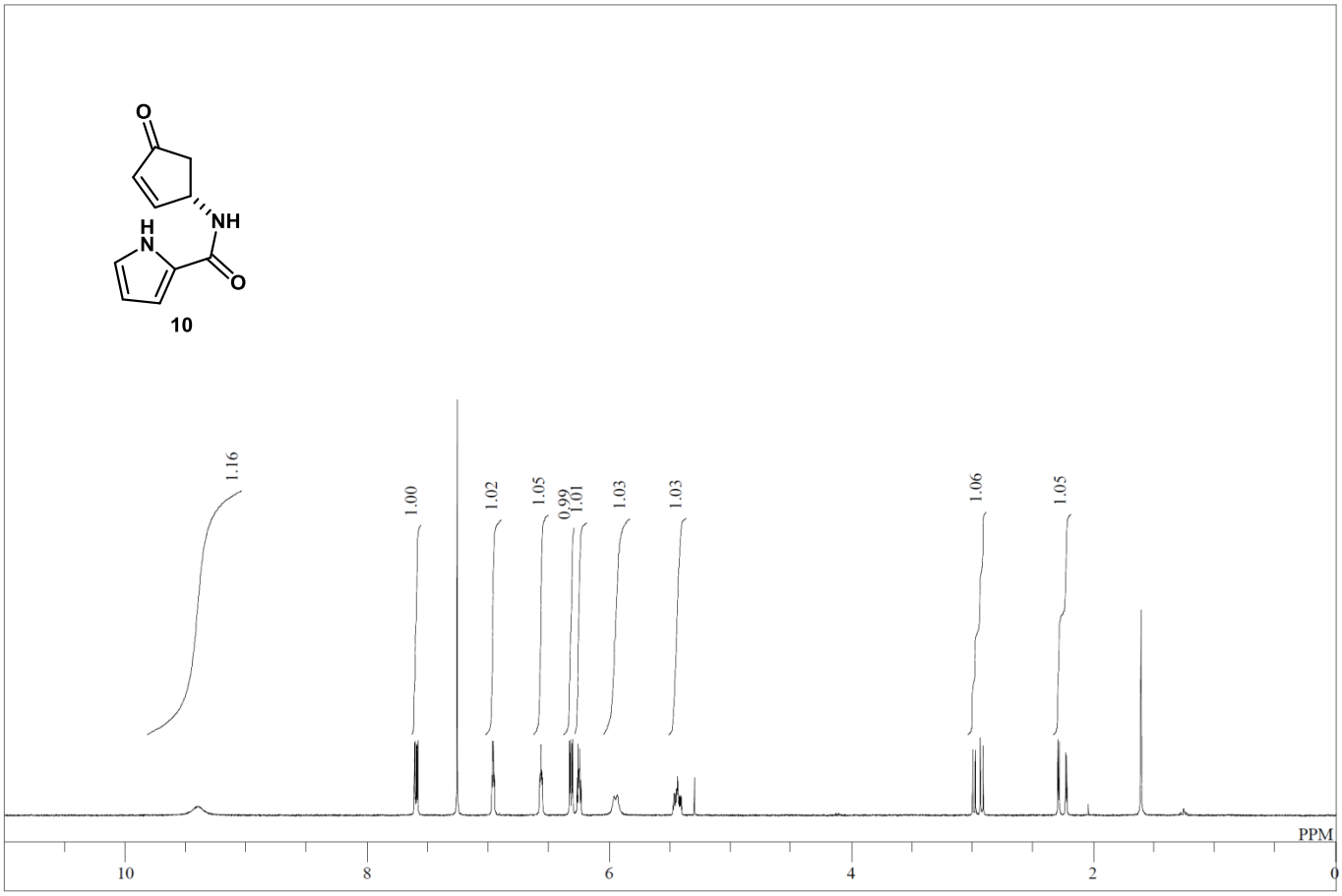
^{1}H NMR (400 MHz, CD_3OD)



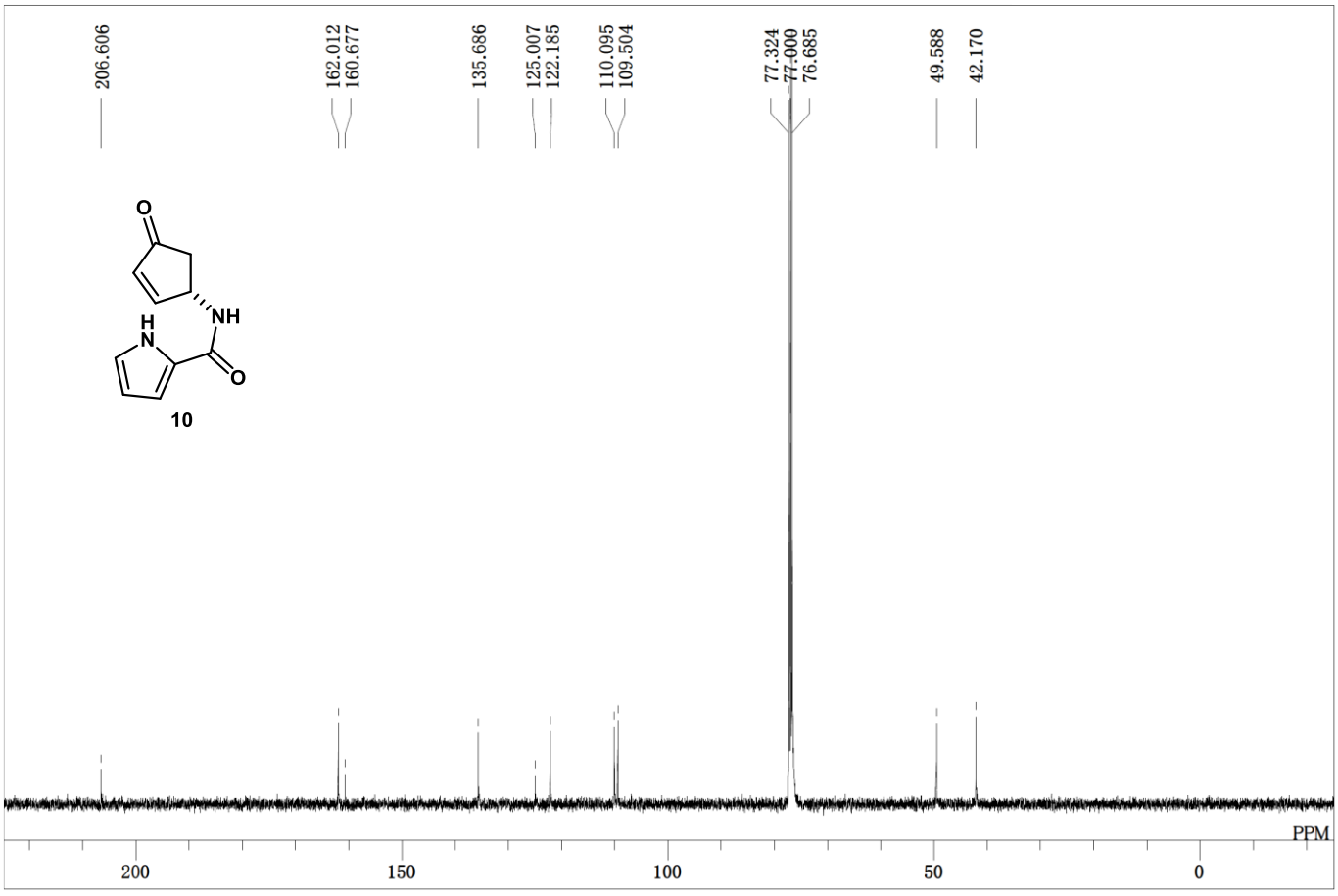
^{13}C NMR (100 MHz, CD_3OD)



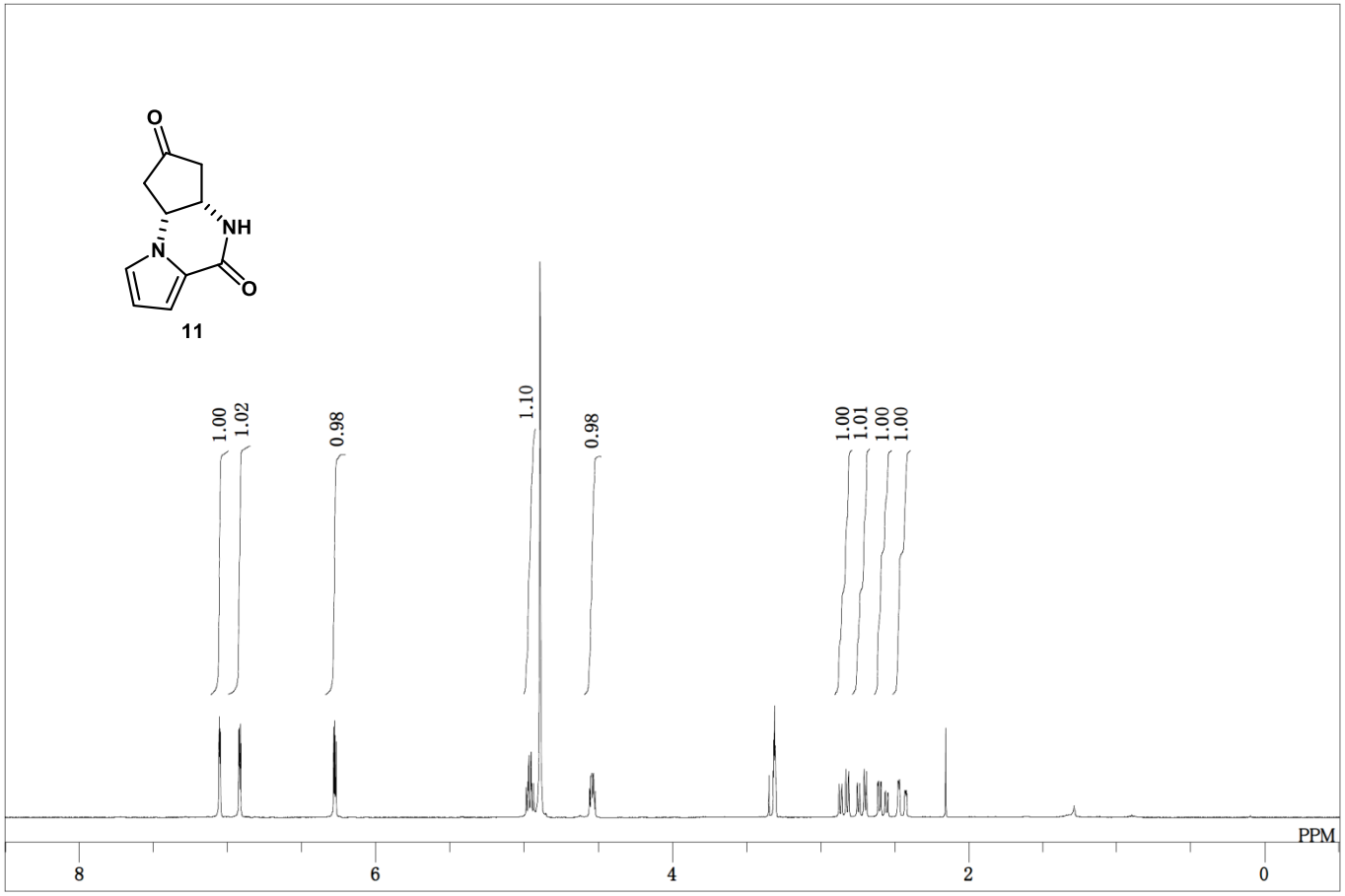
^{1}H NMR (300 MHz, $CDCl_3$)



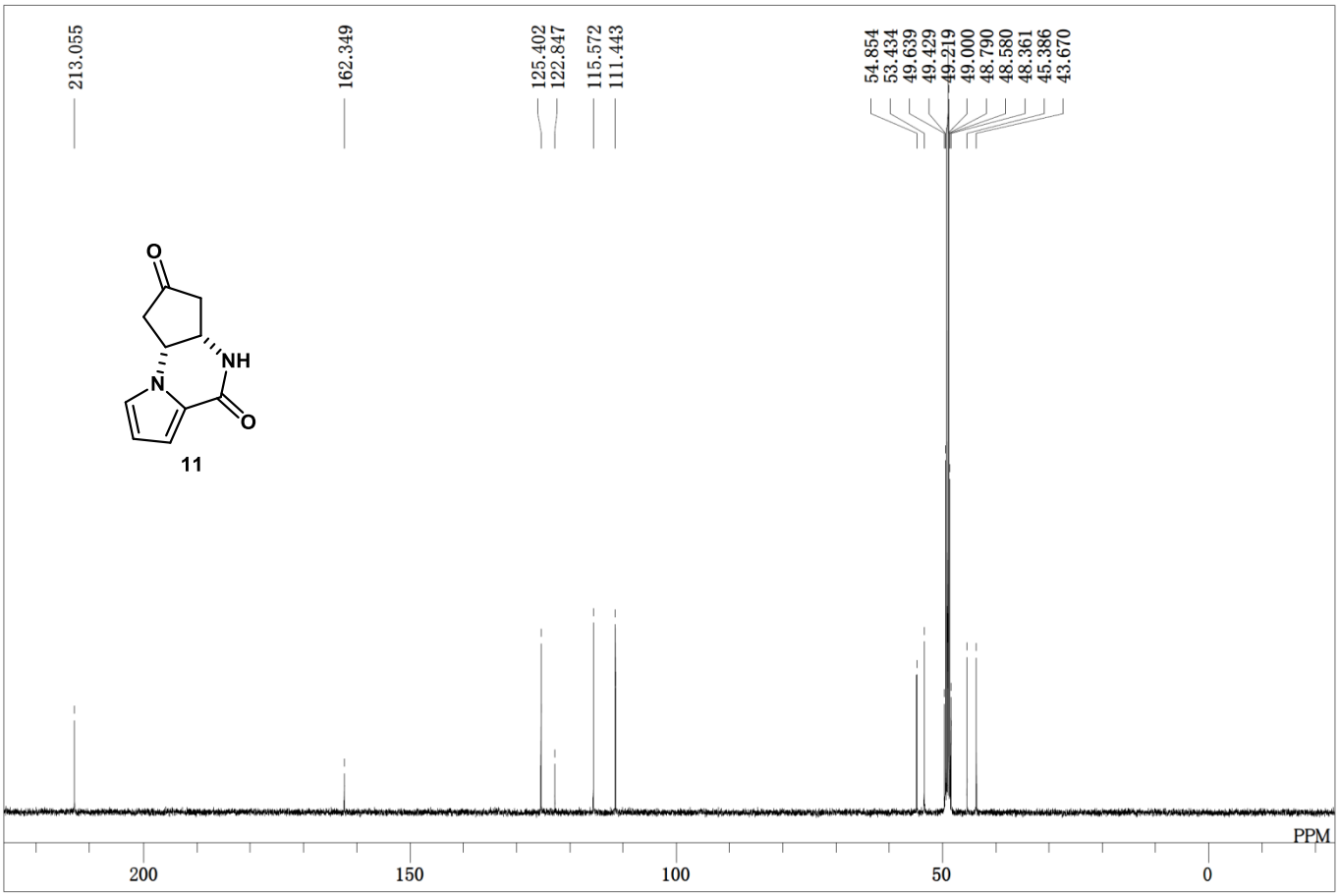
^{13}C NMR (100 MHz, $CDCl_3$)



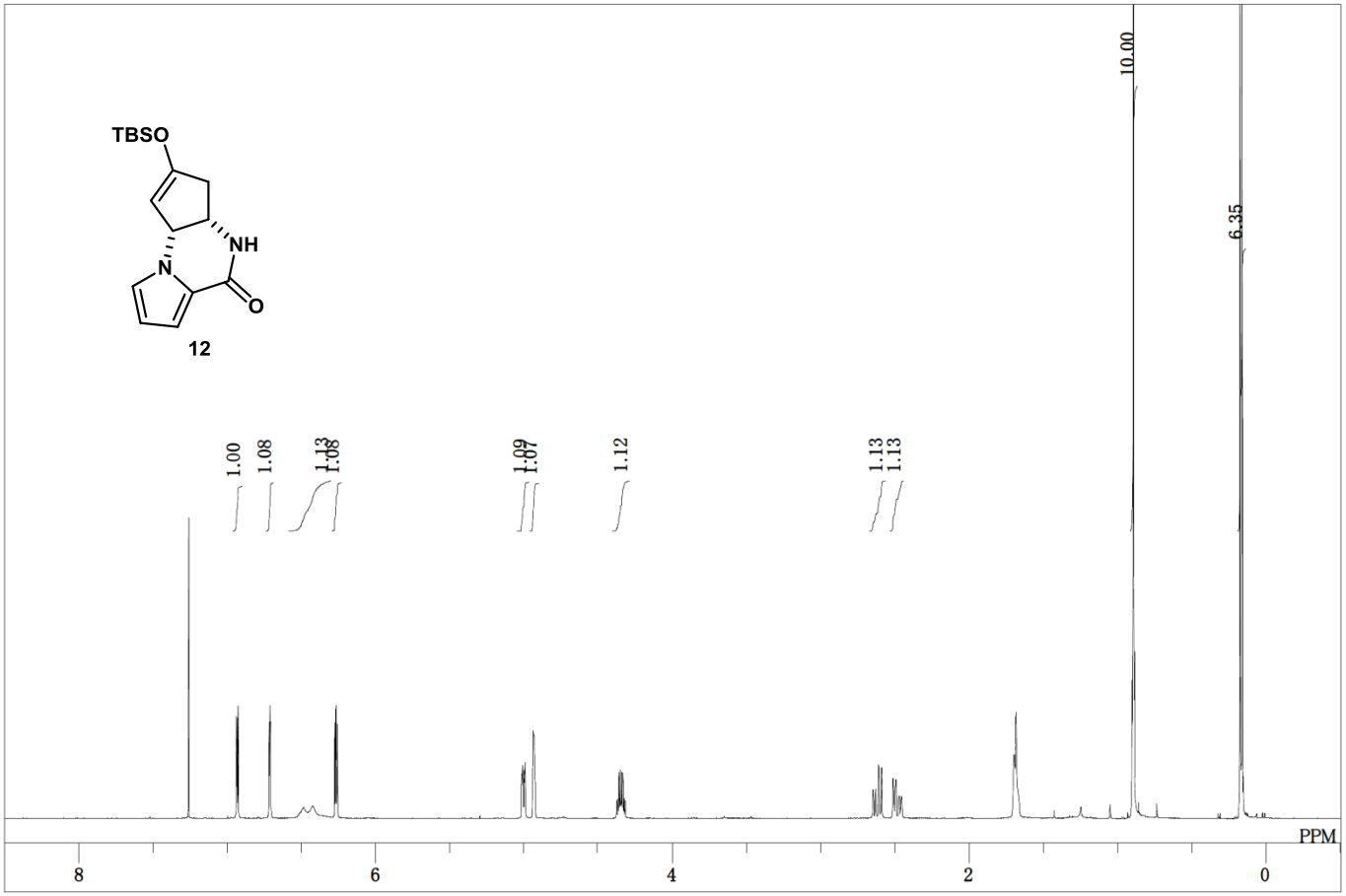
^{1}H NMR (400 MHz, CD_3OD)



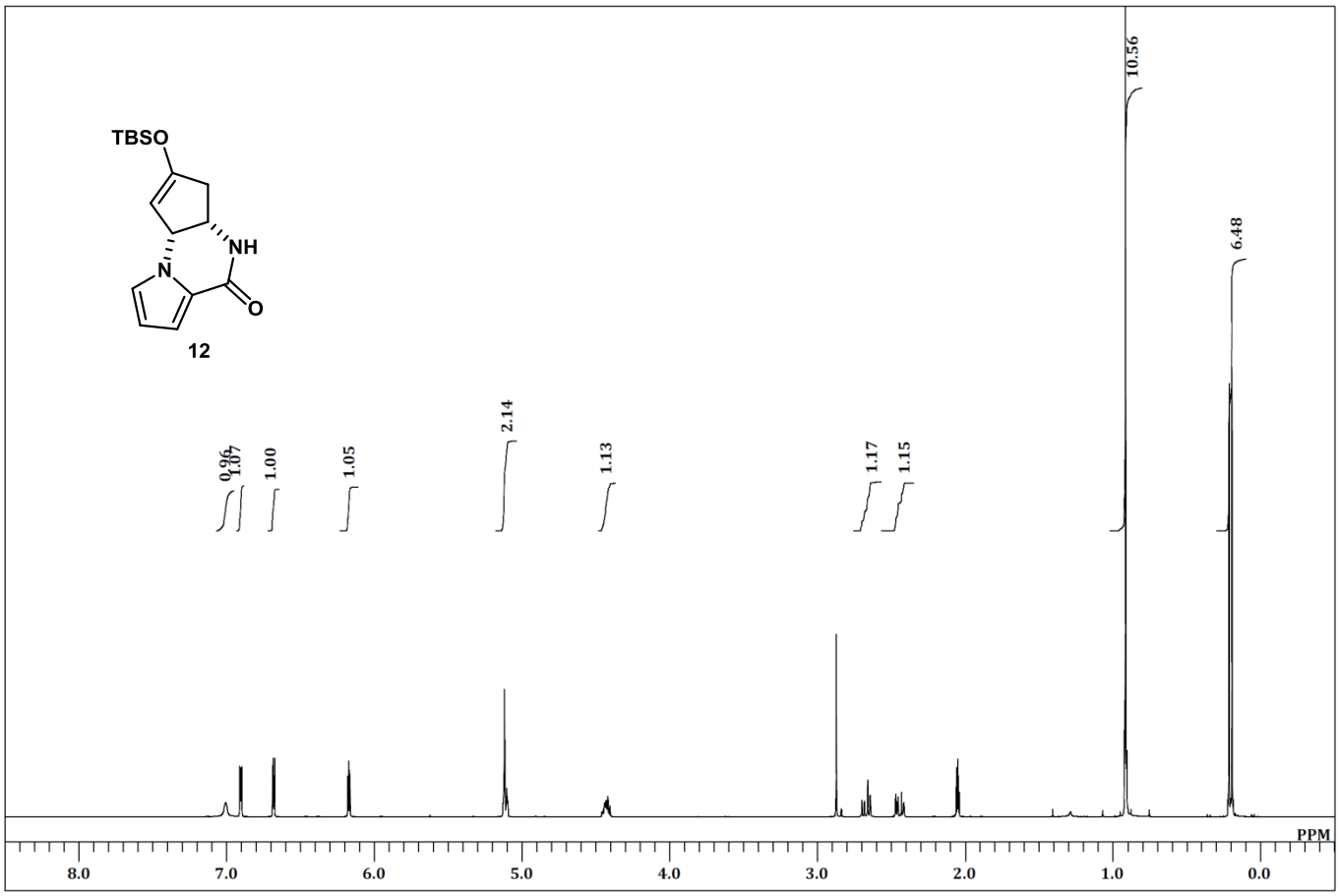
^{13}C NMR (100 MHz, CD_3OD)



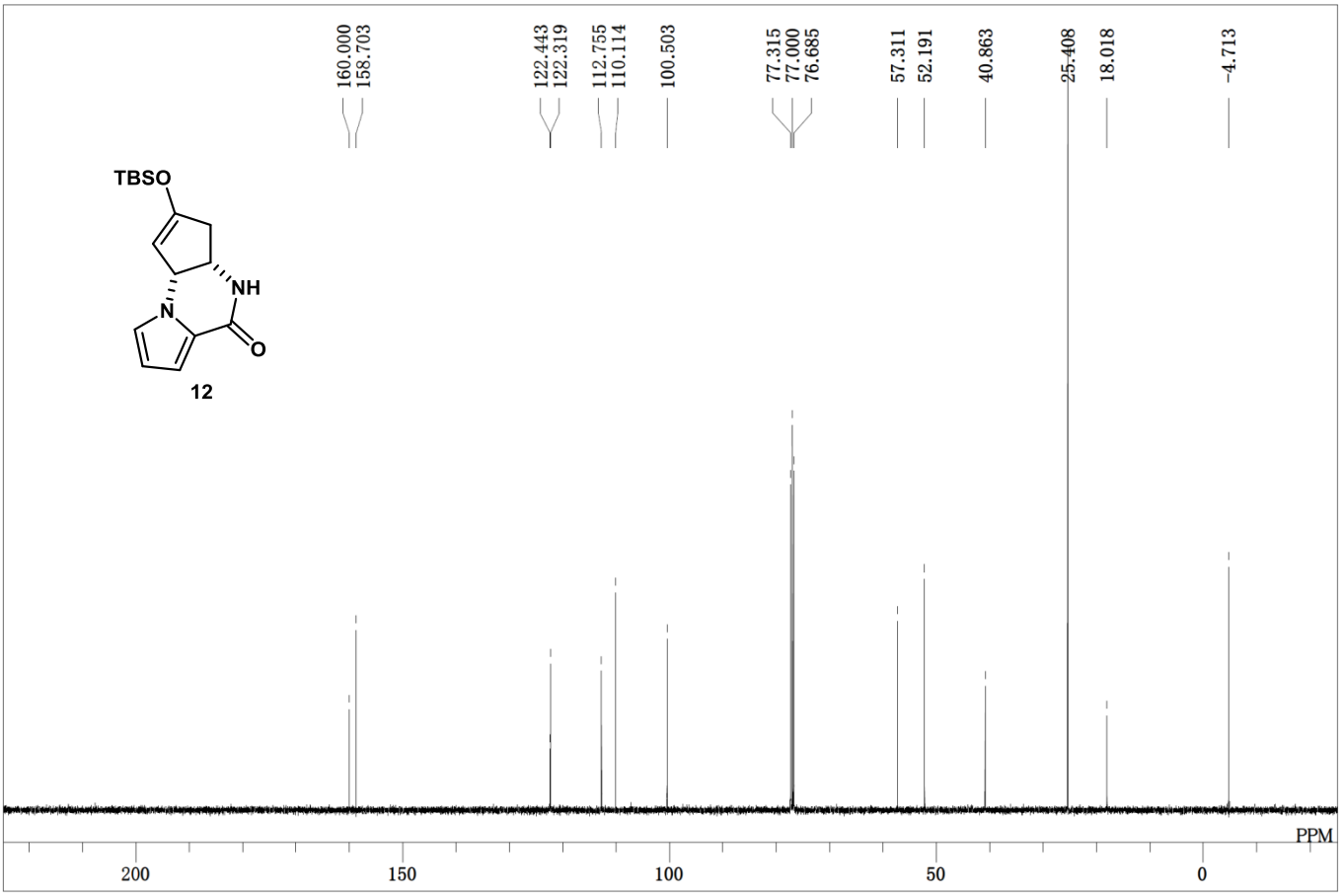
^{1}H NMR (400 MHz, $CDCl_3$)



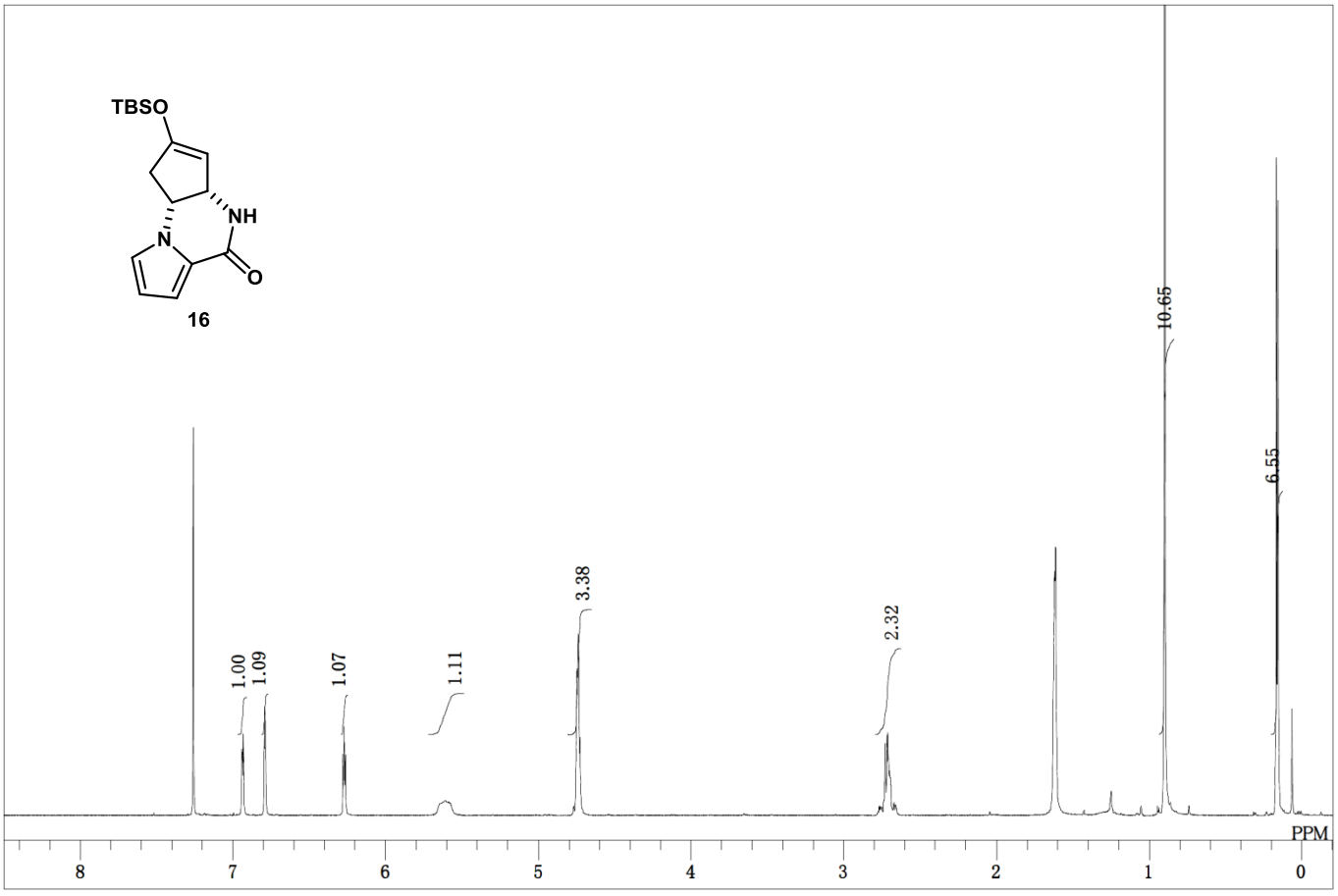
^{1}H NMR (400 MHz, acetone-*d*6)



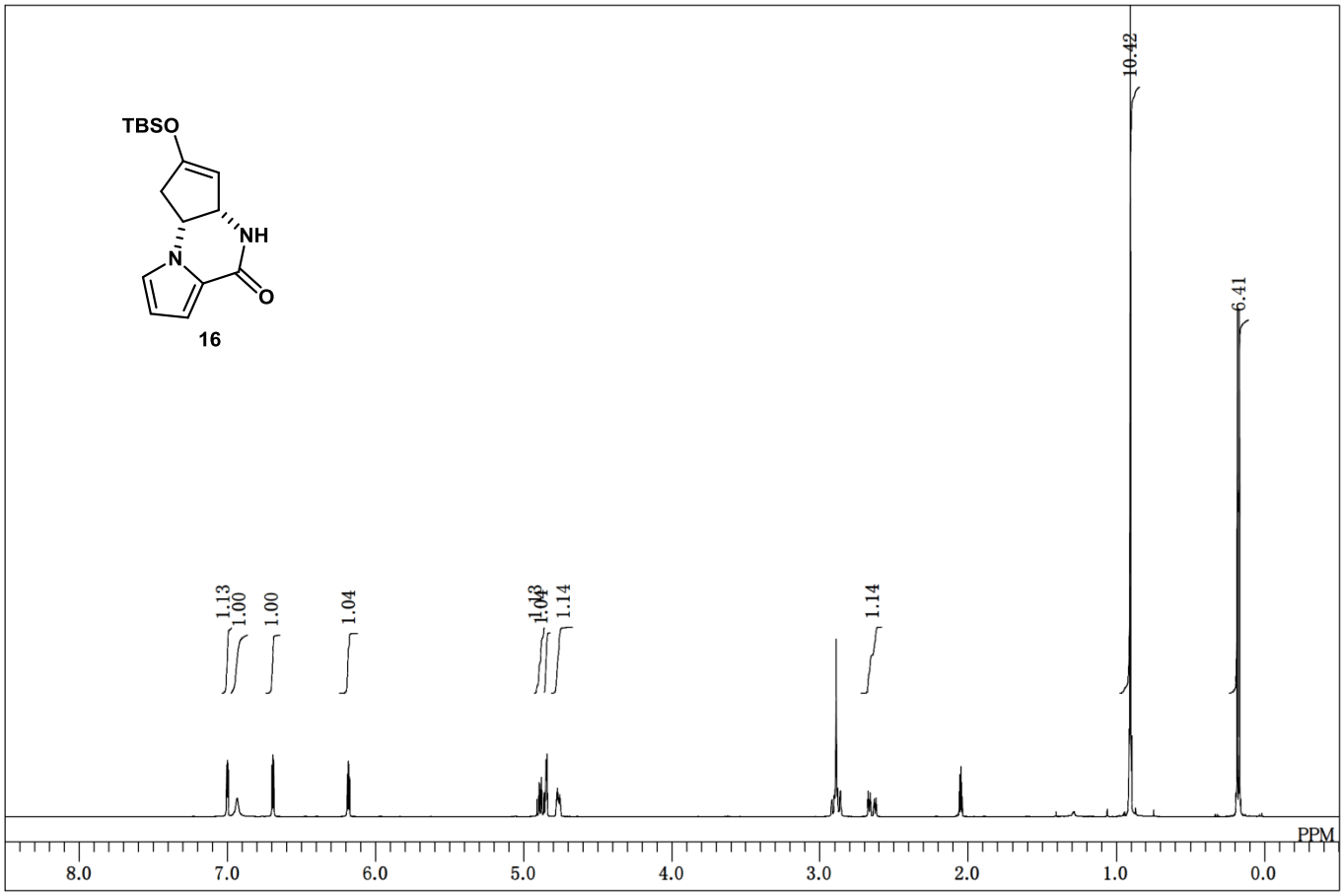
^{13}C NMR (100 MHz, $CDCl_3$)



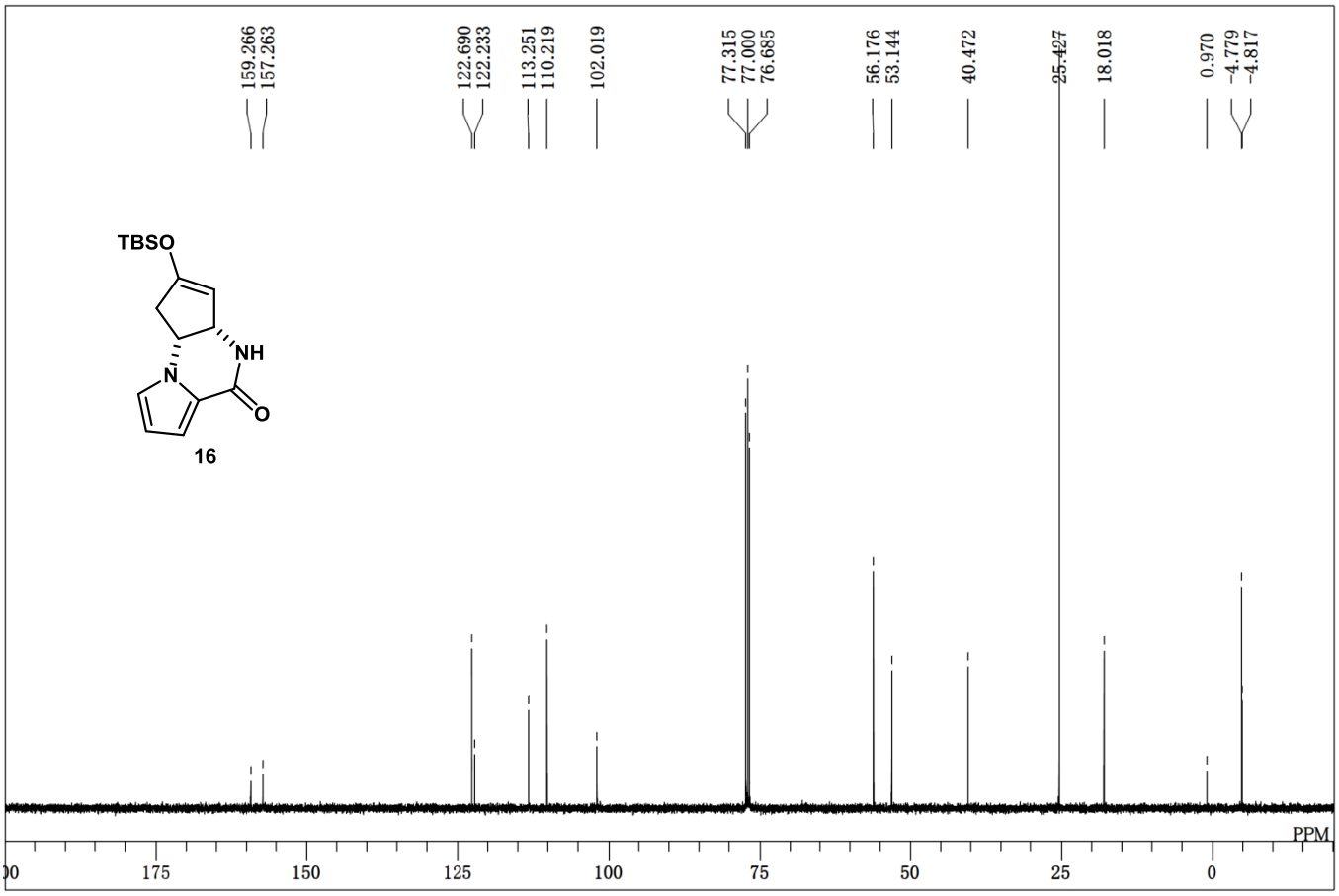
^{1}H NMR (400 MHz, $CDCl_3$)



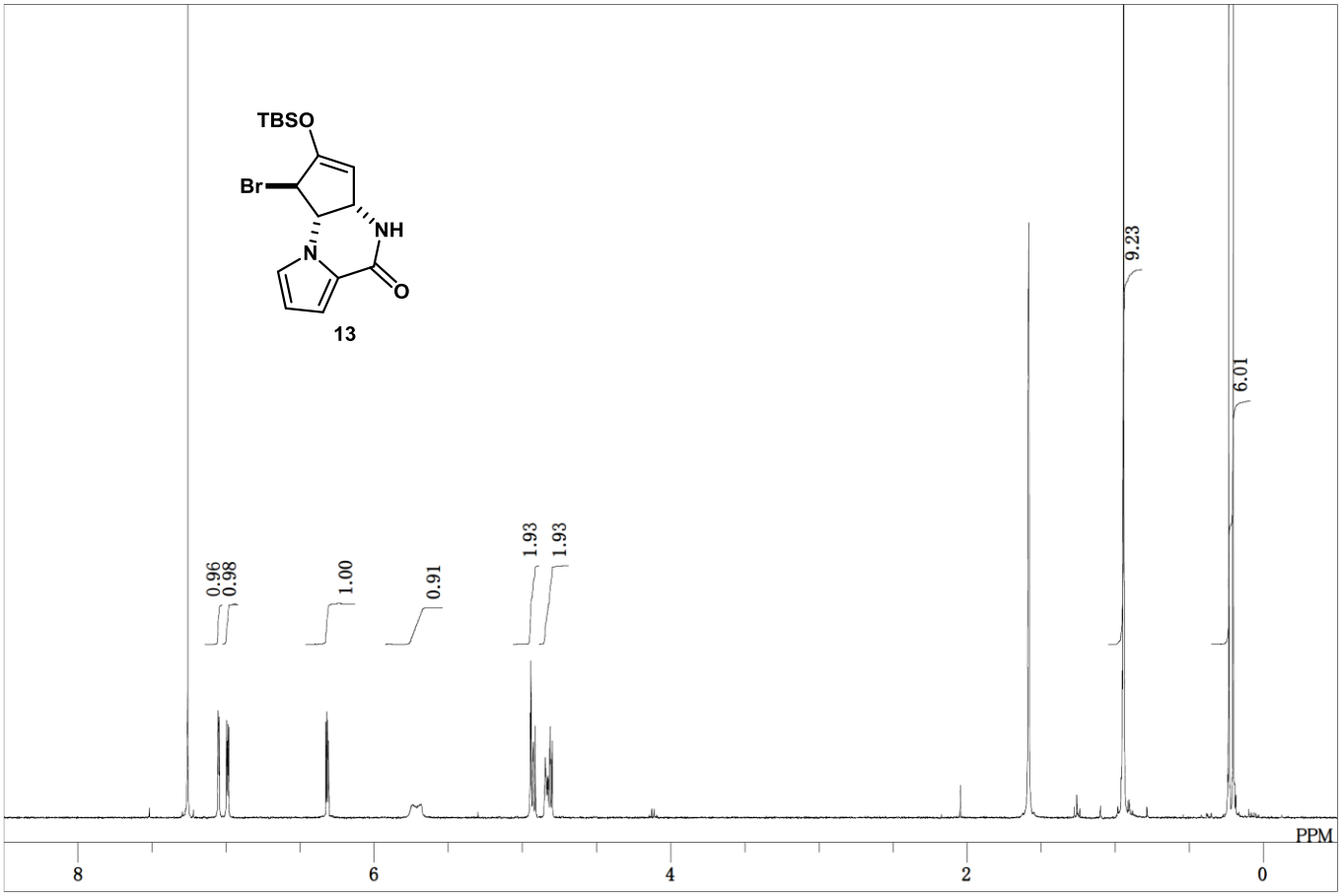
^{1}H NMR (400 MHz, acetone-*d*6)



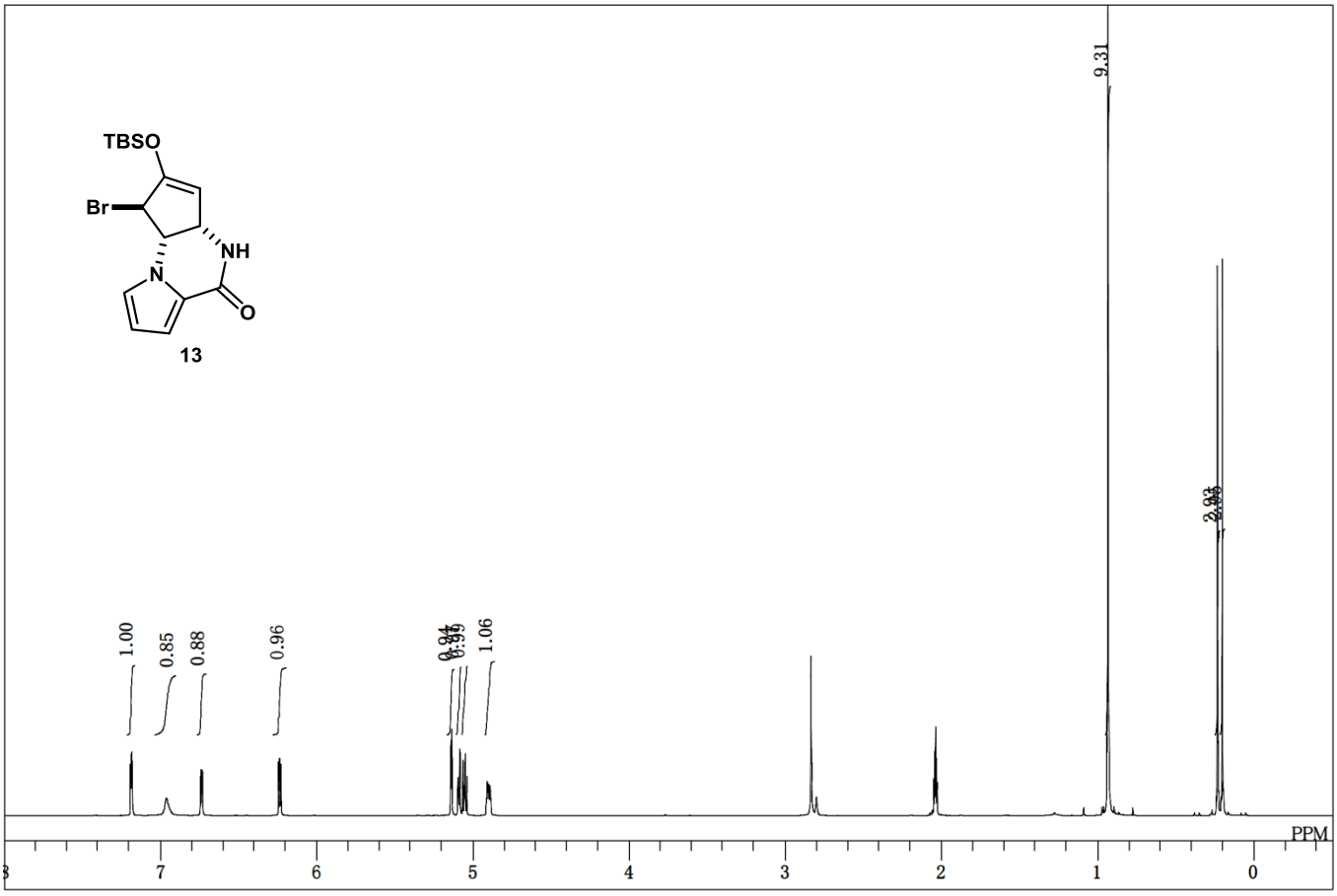
^{13}C NMR (100 MHz, $CDCl_3$)



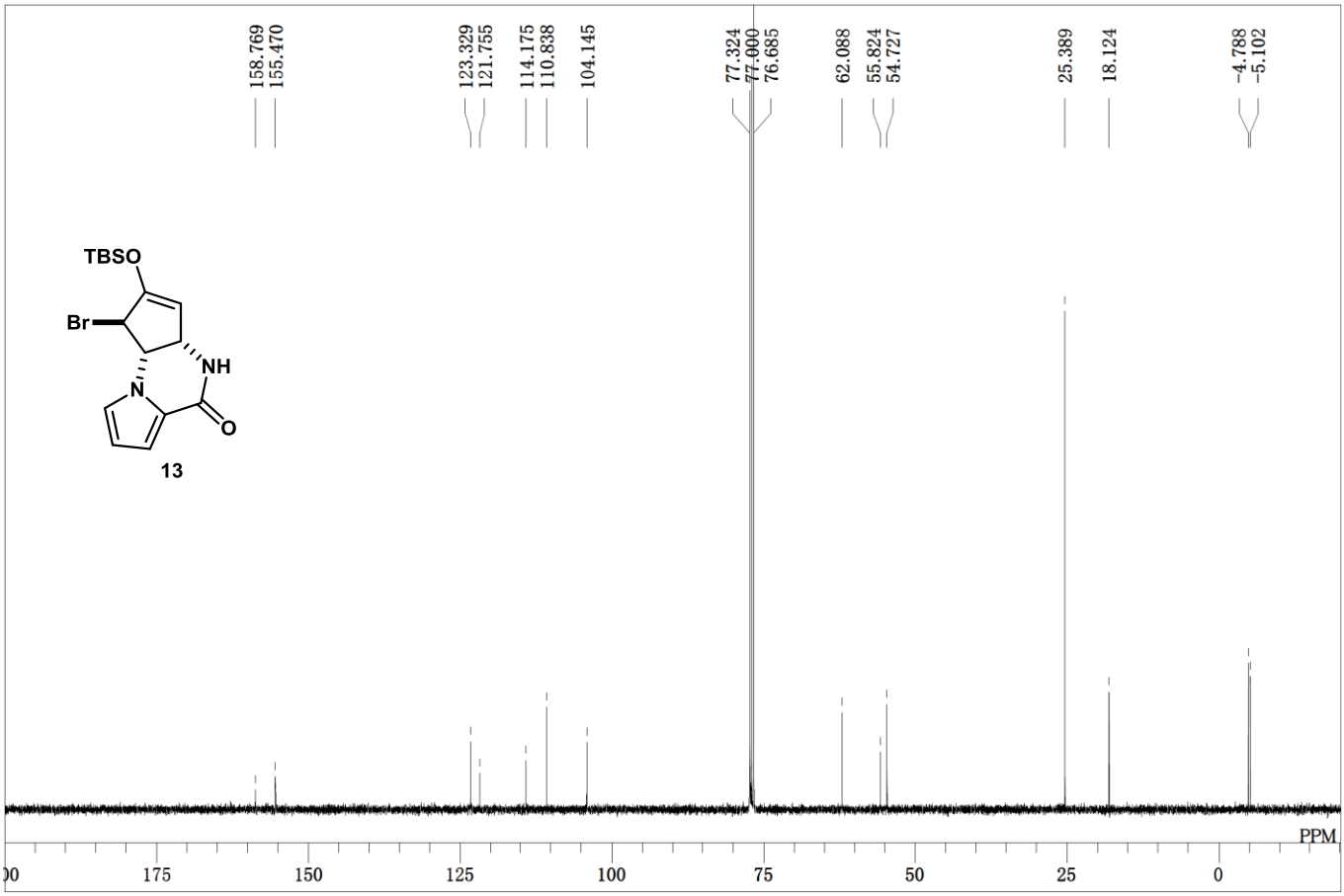
^{1}H NMR (400MHz, $CDCl_3$)



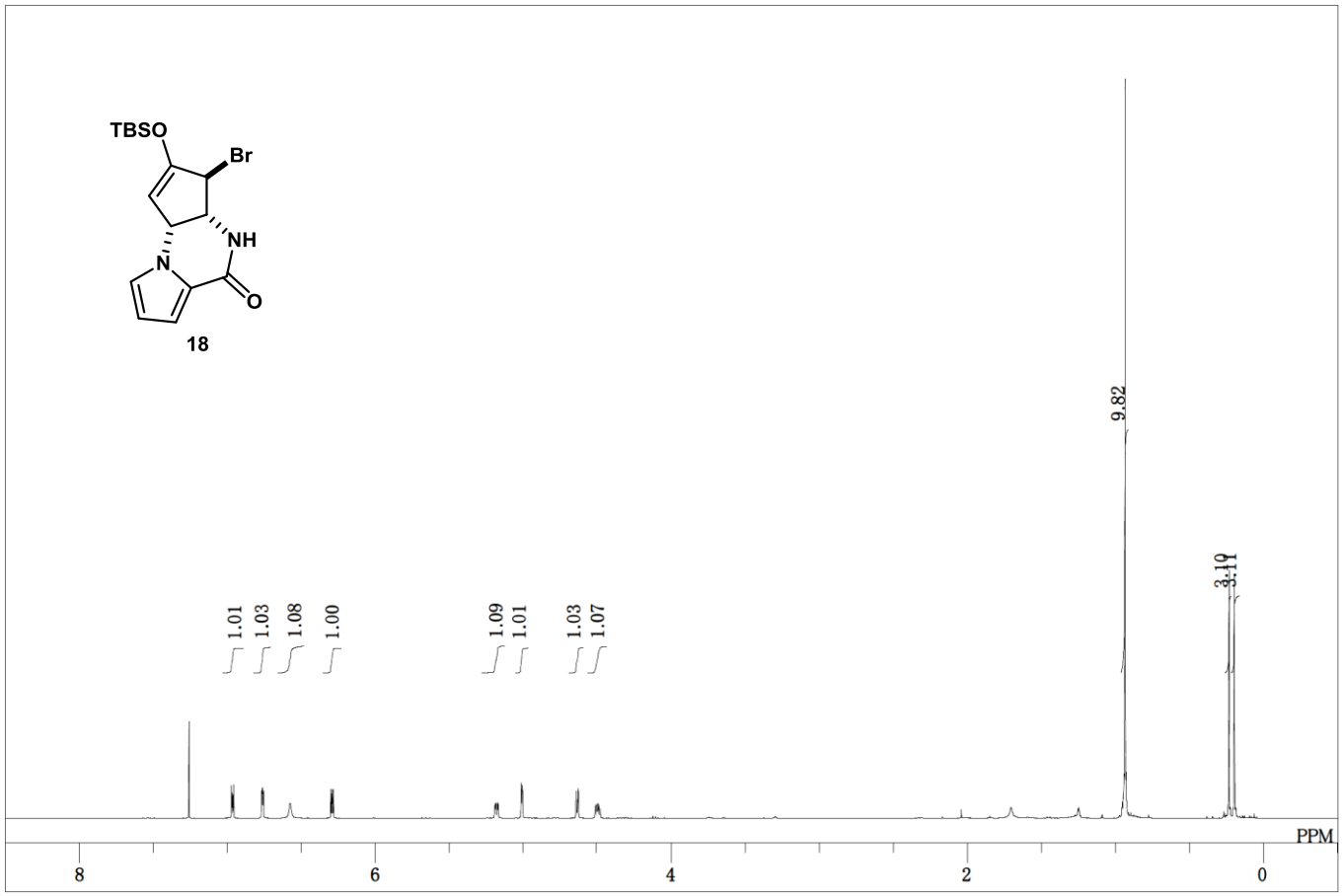
^{1}H NMR (400MHz, acetone-*d*6)



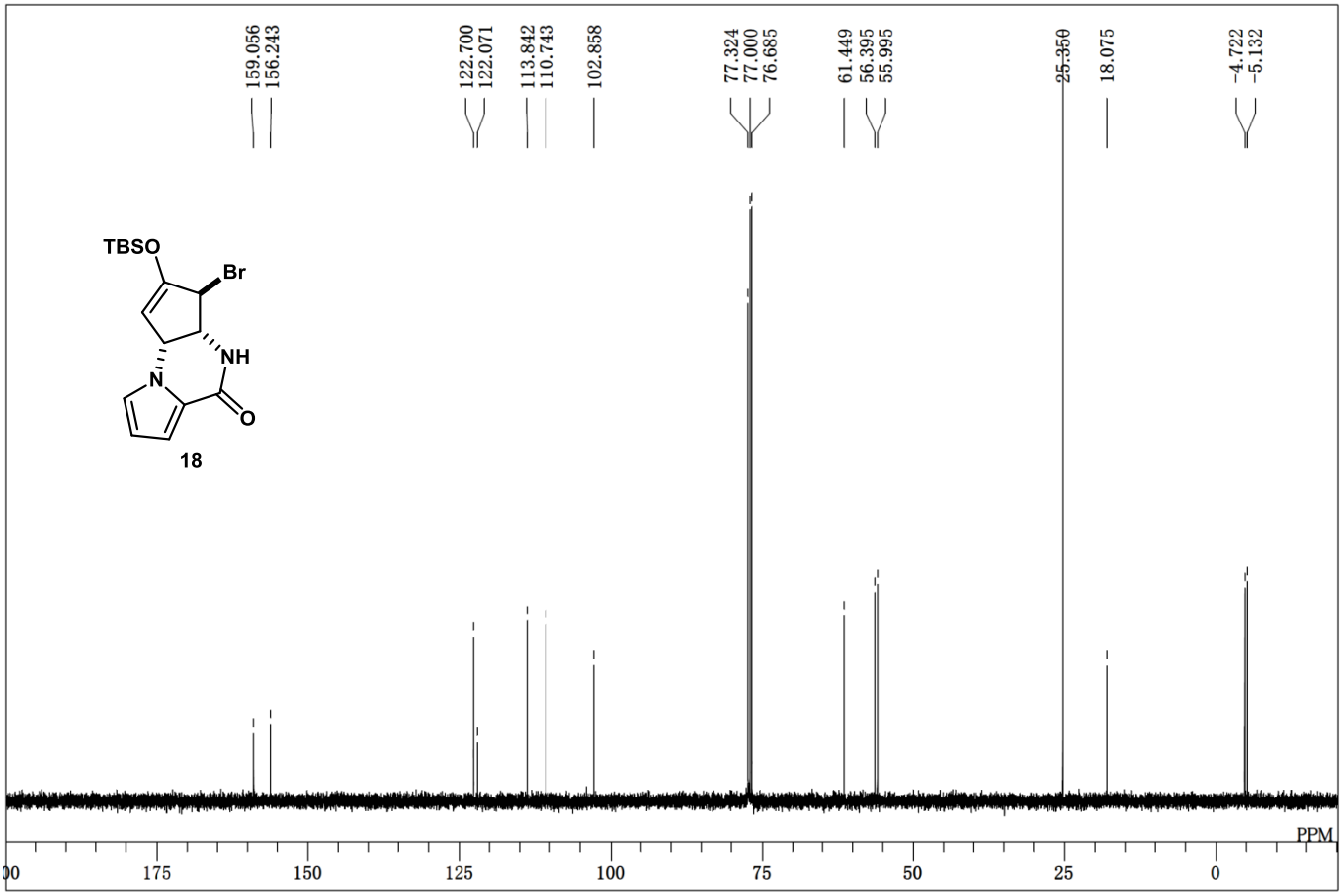
^{13}C NMR (100 MHz, $CDCl_3$)



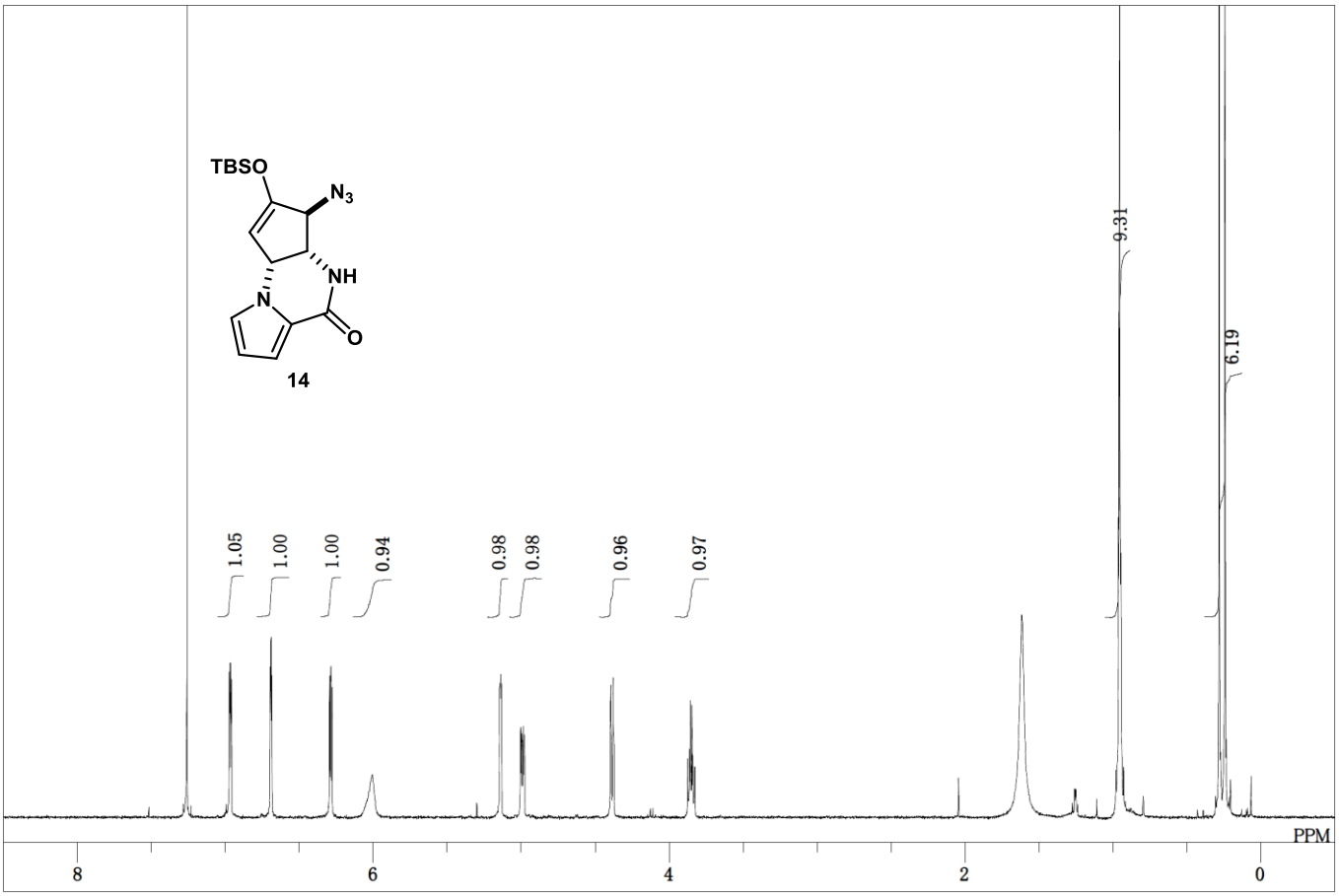
^{1}H NMR (400 MHz, $CDCl_3$)



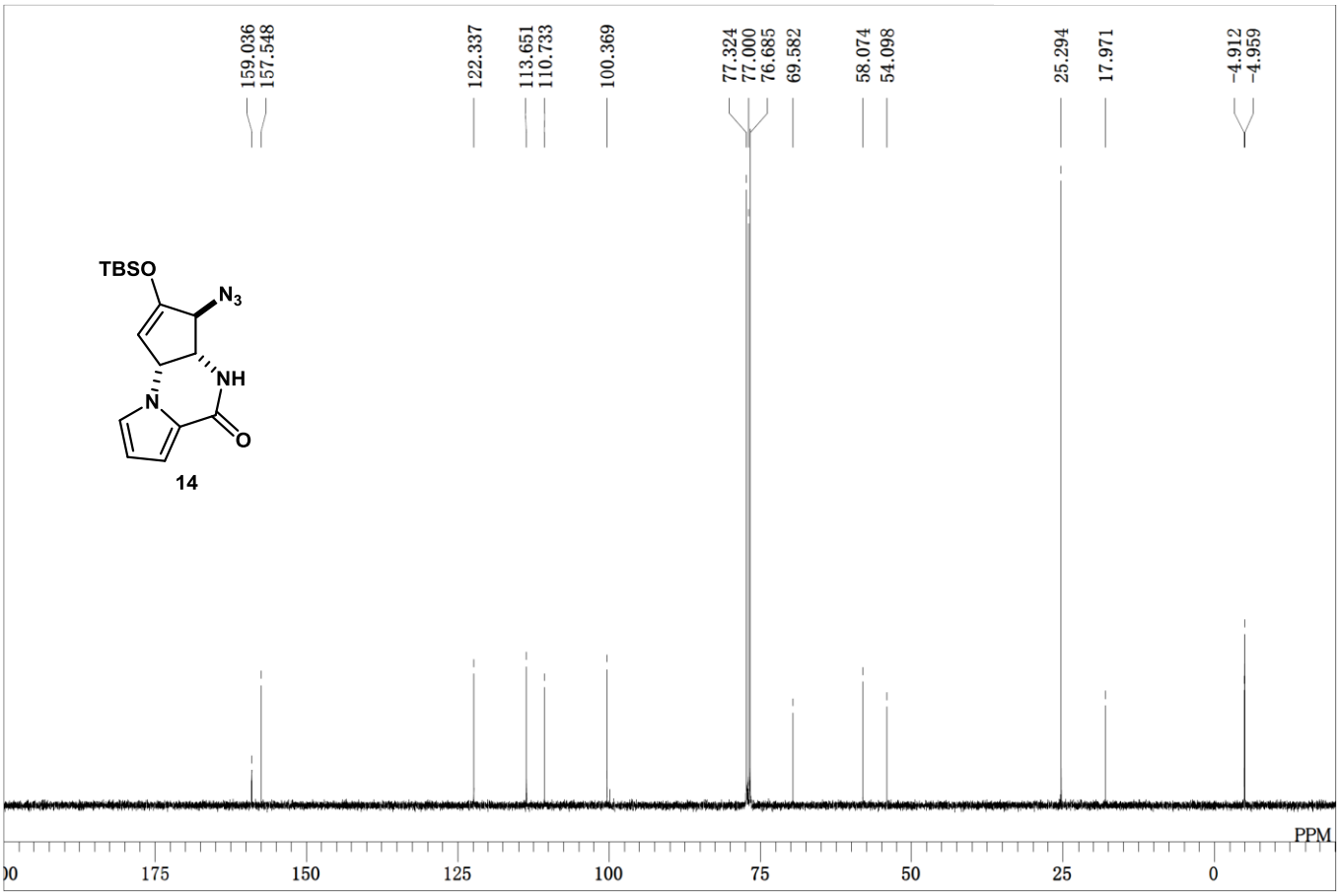
^{13}C NMR (100 MHz, $CDCl_3$)



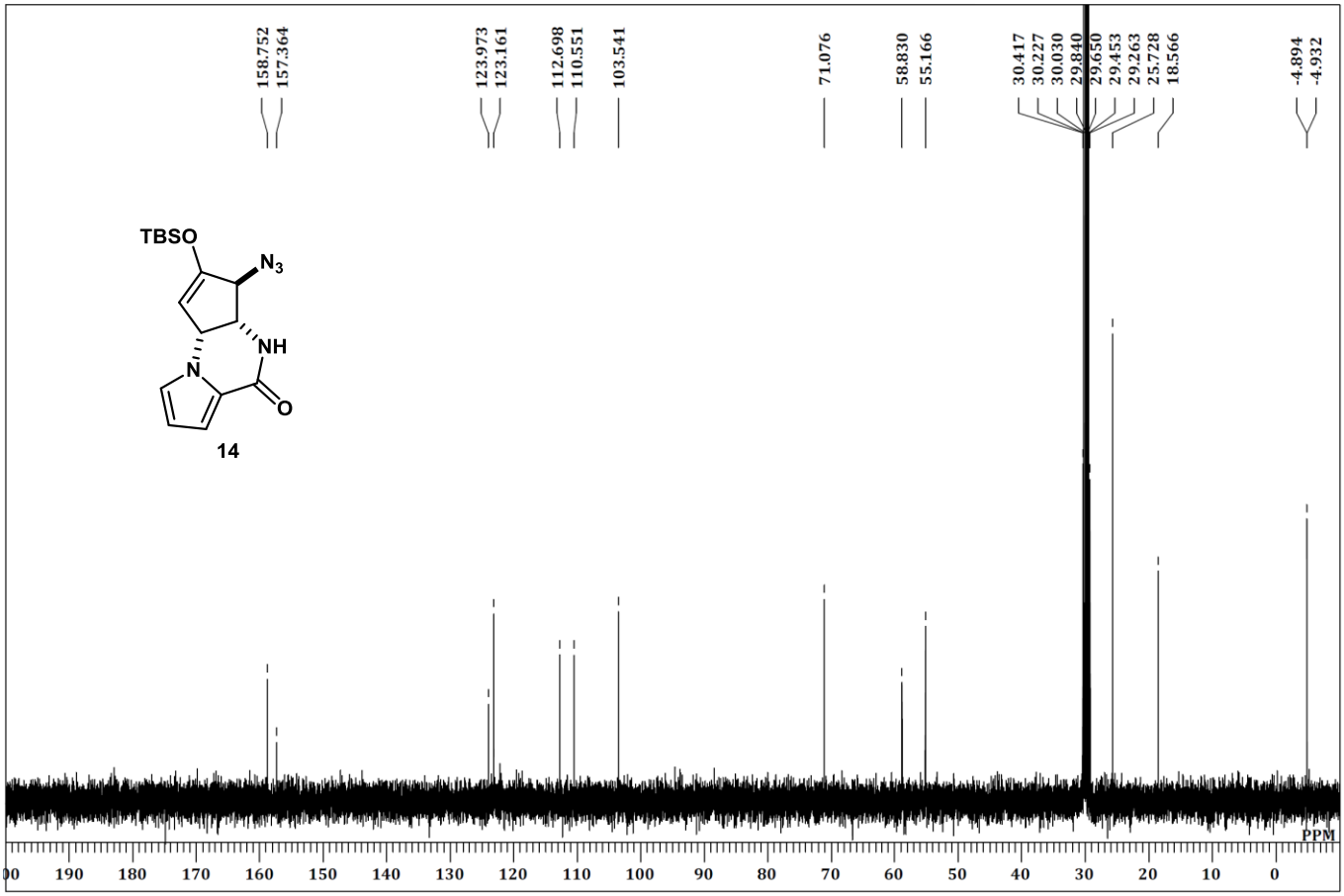
^{1}H NMR (400 MHz, $CDCl_3$)



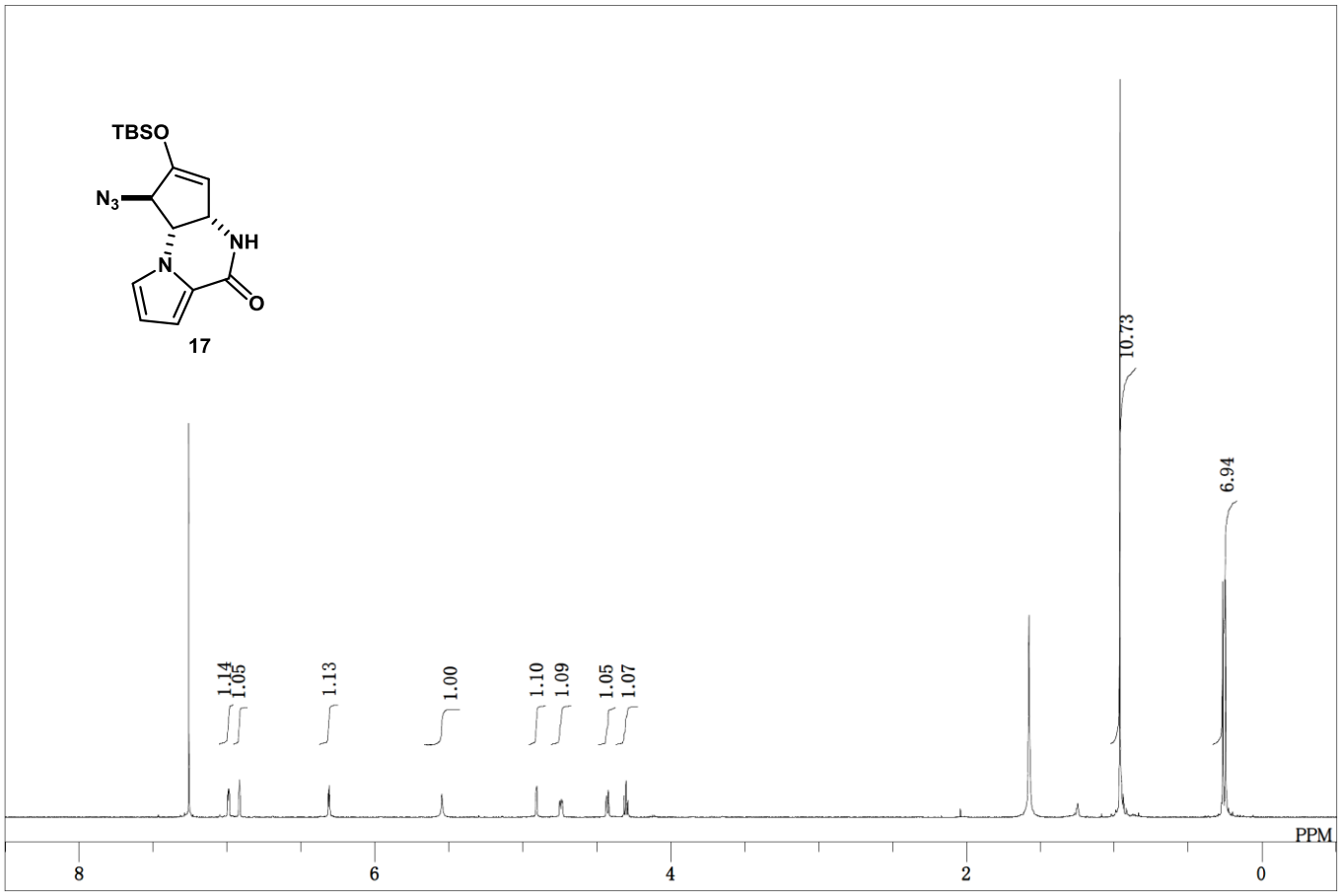
^{1} ^{1}H NMR (400 MHz, $CDCl_3$)



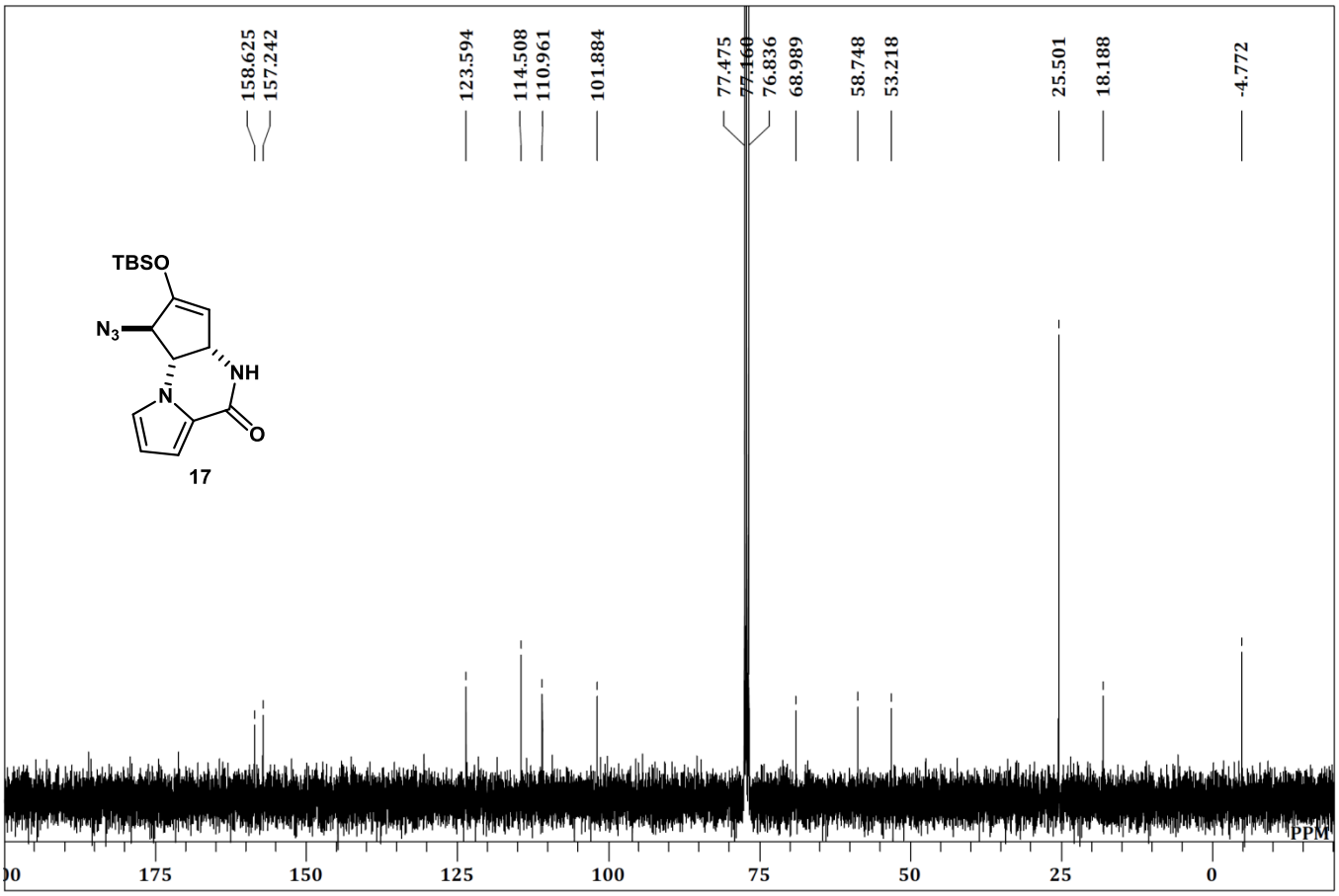
^{13}C NMR (100 MHz, acetone-*d*6)



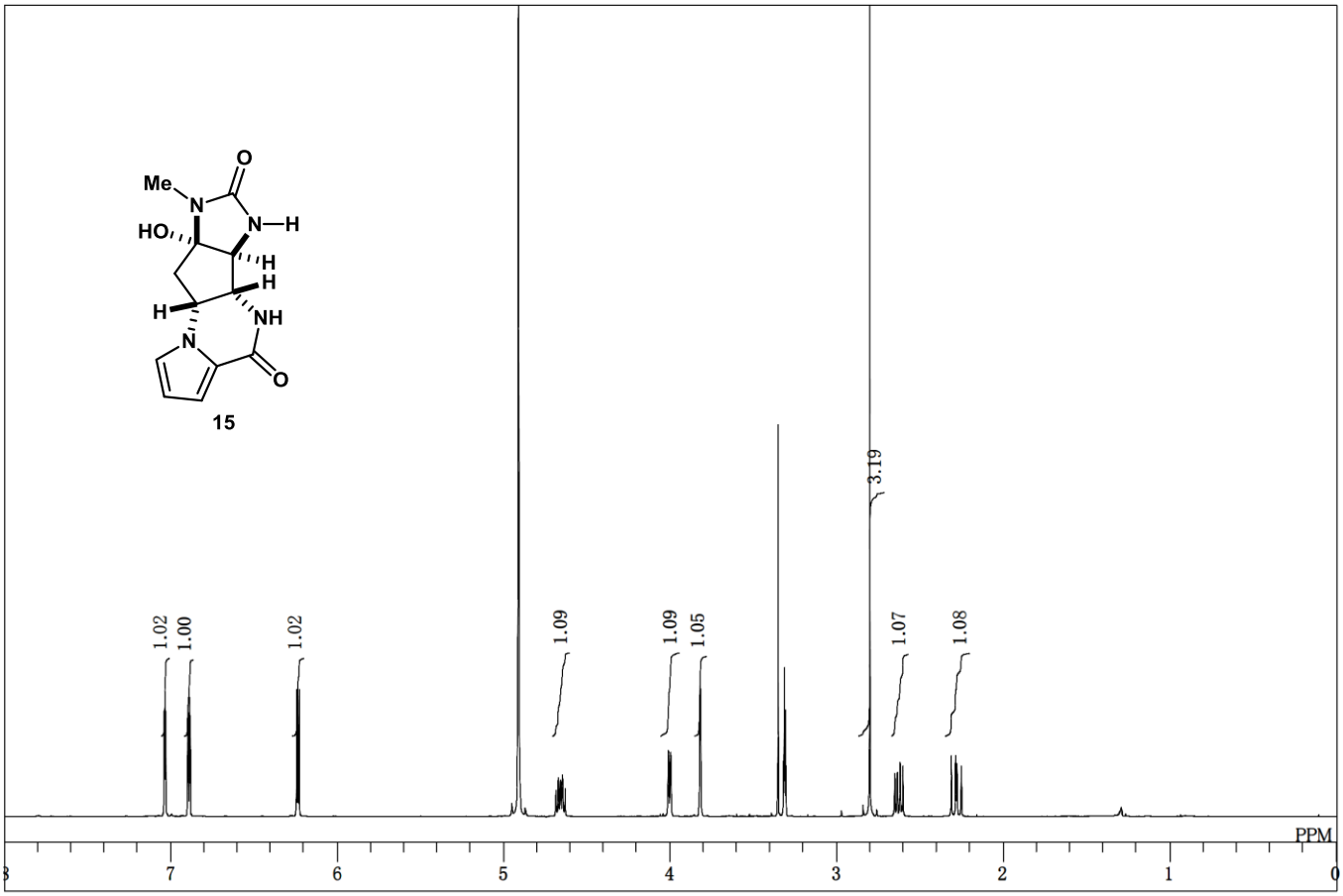
^{13}C NMR (100 MHz, $CDCl_3$)



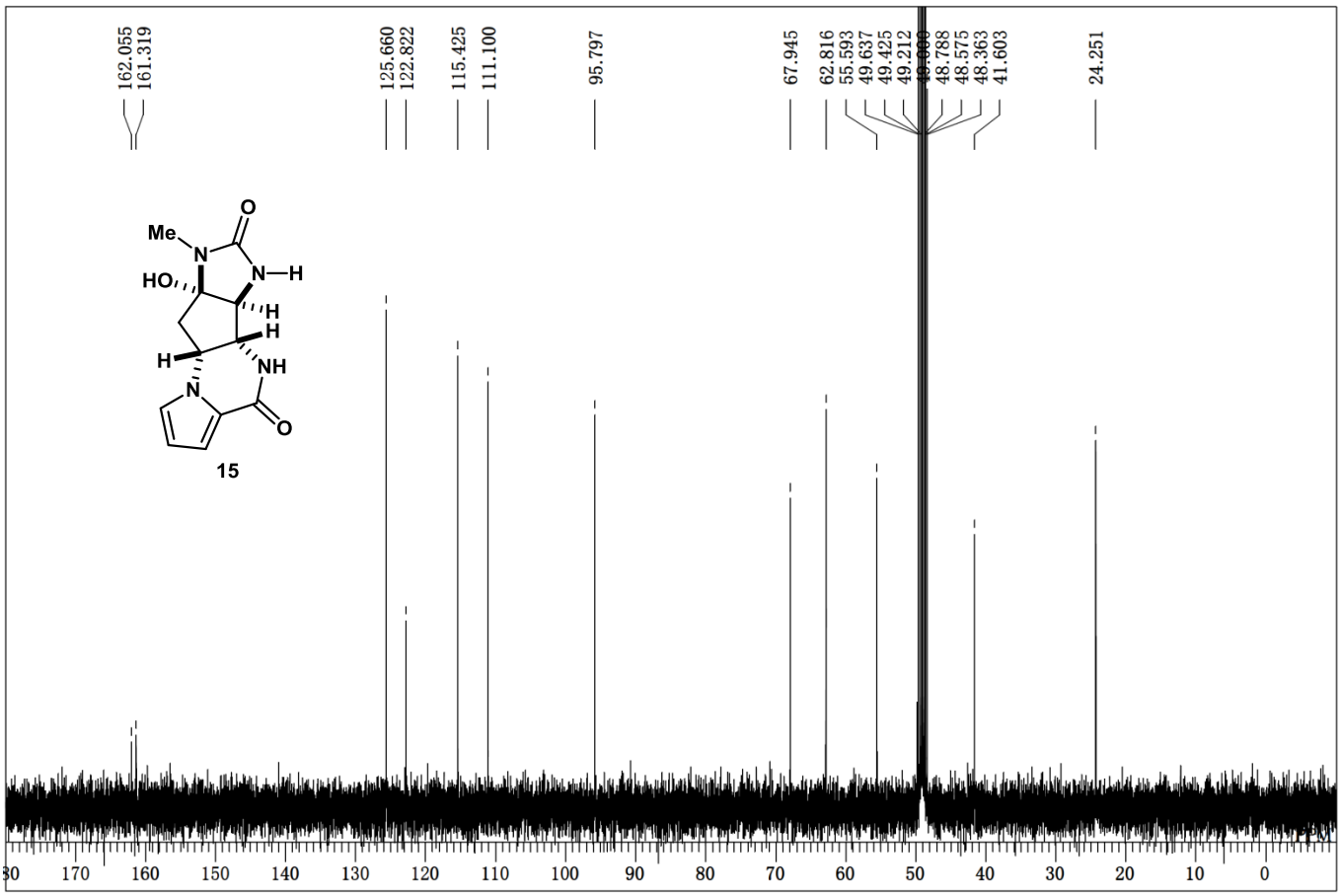
^{13}C NMR (100 MHz, $CDCl_3$)



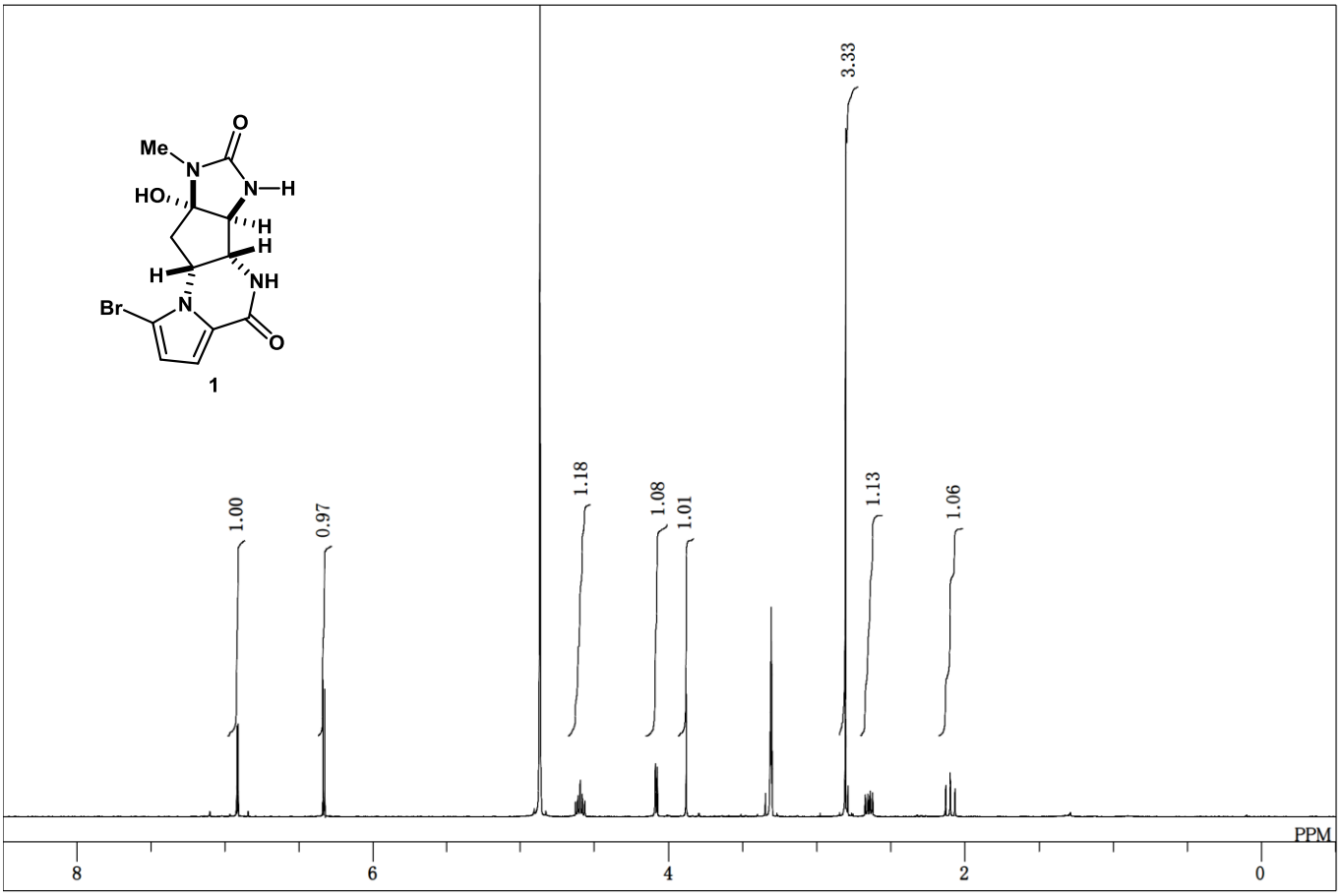
^{1}H NMR (400 MHz, CD_3OD)



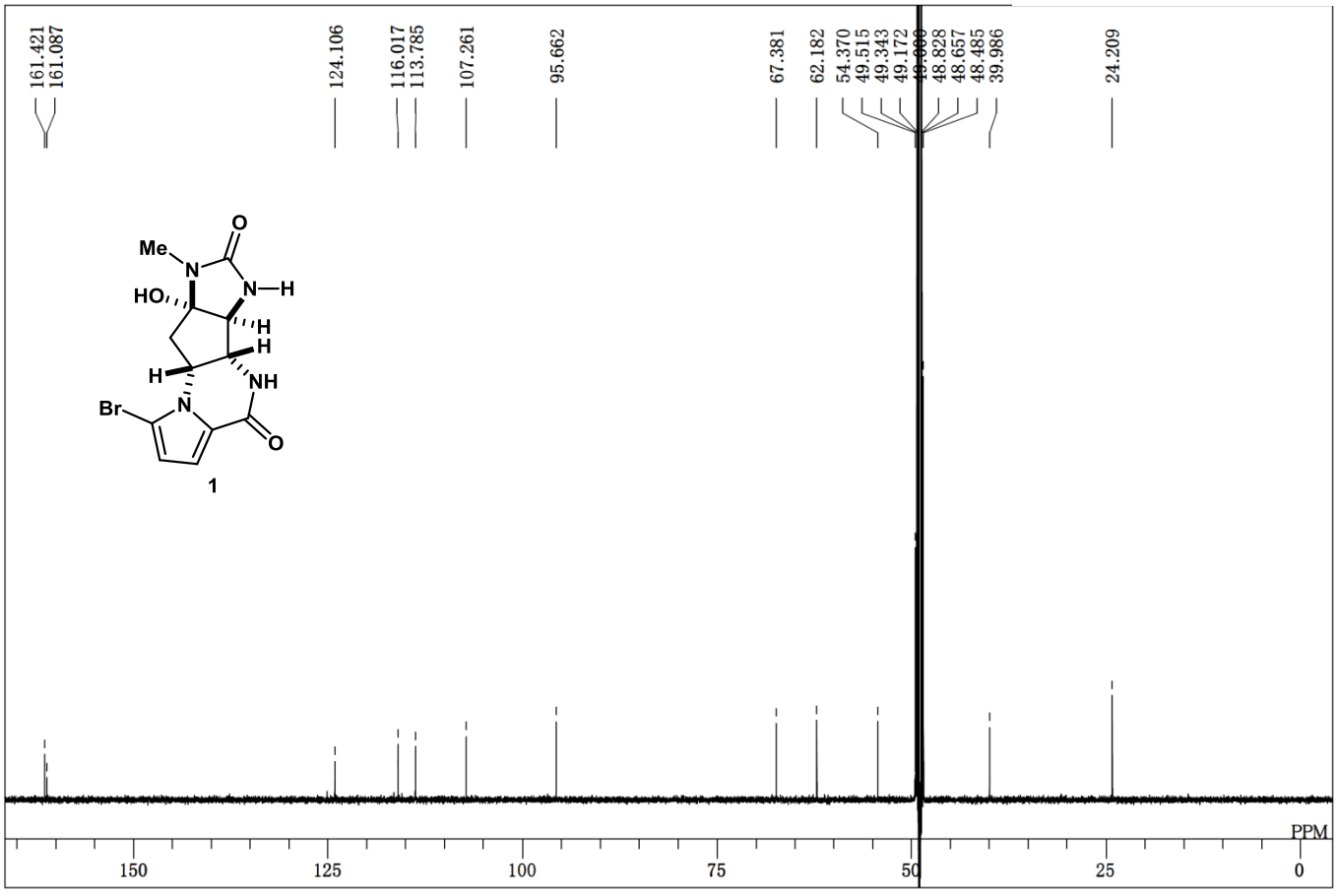
^{13}C NMR (100 MHz, CD_3OD)



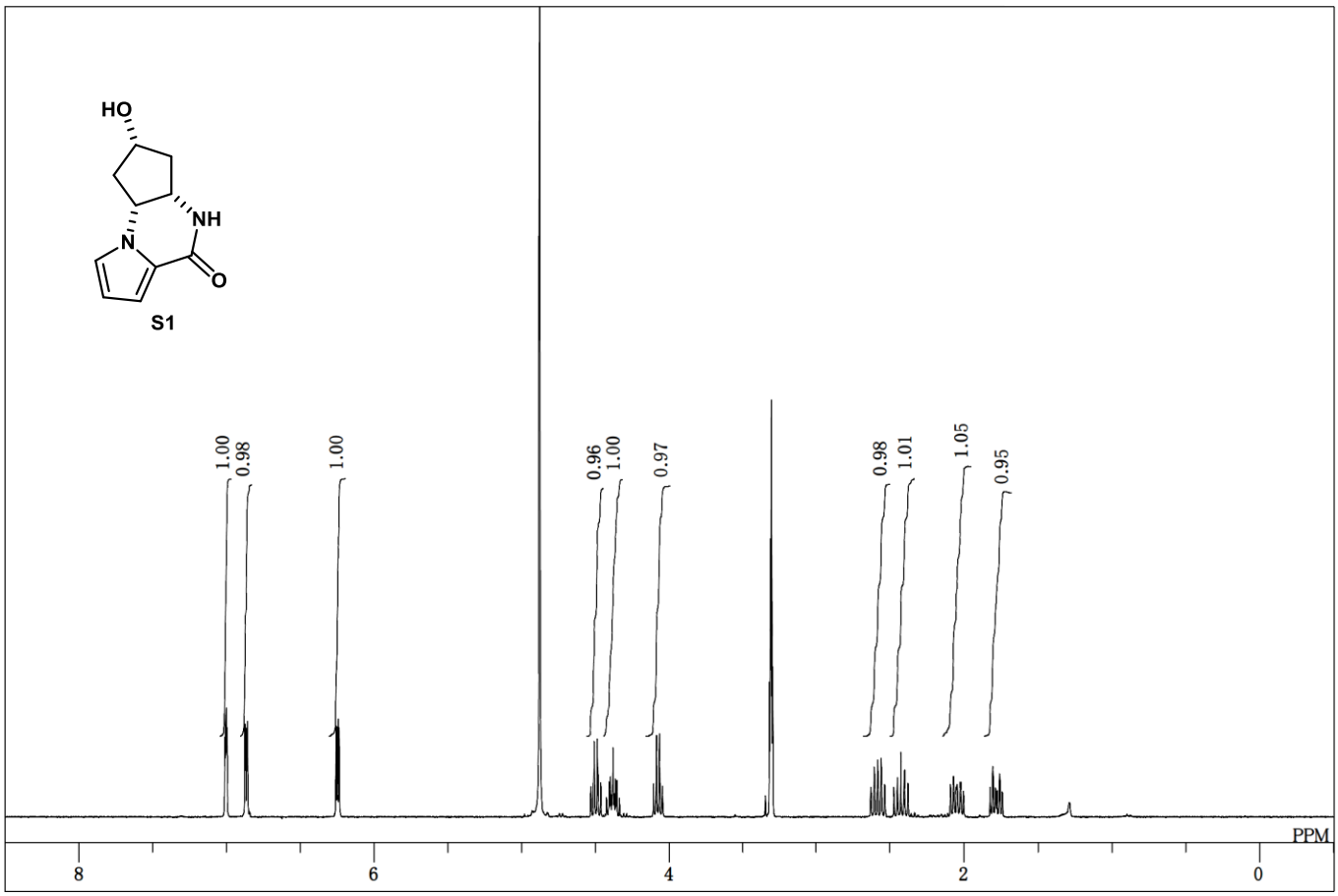
^{1}H NMR (400 MHz, CD_3OD)



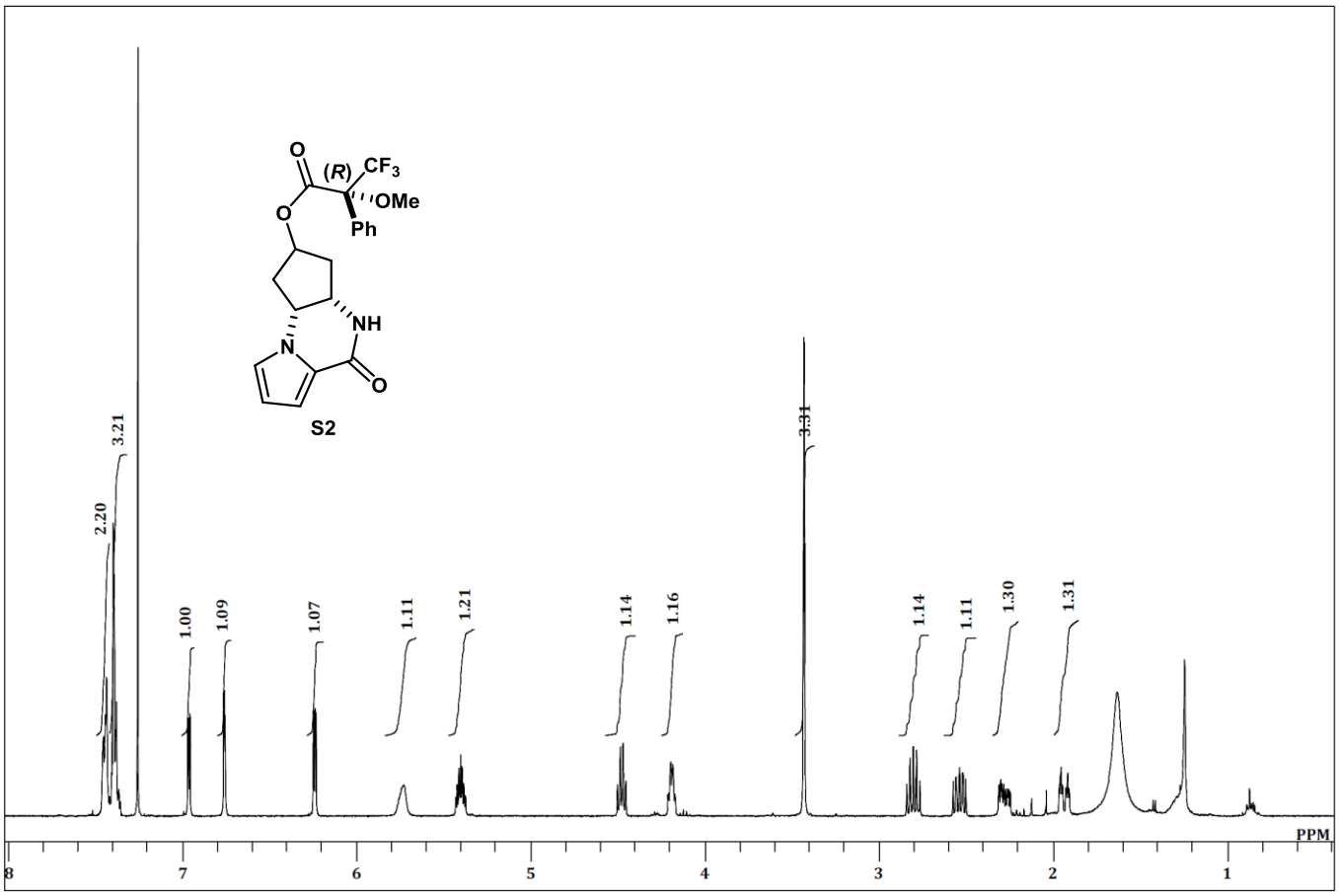
^{13}C NMR (125 MHz, CD_3OD)



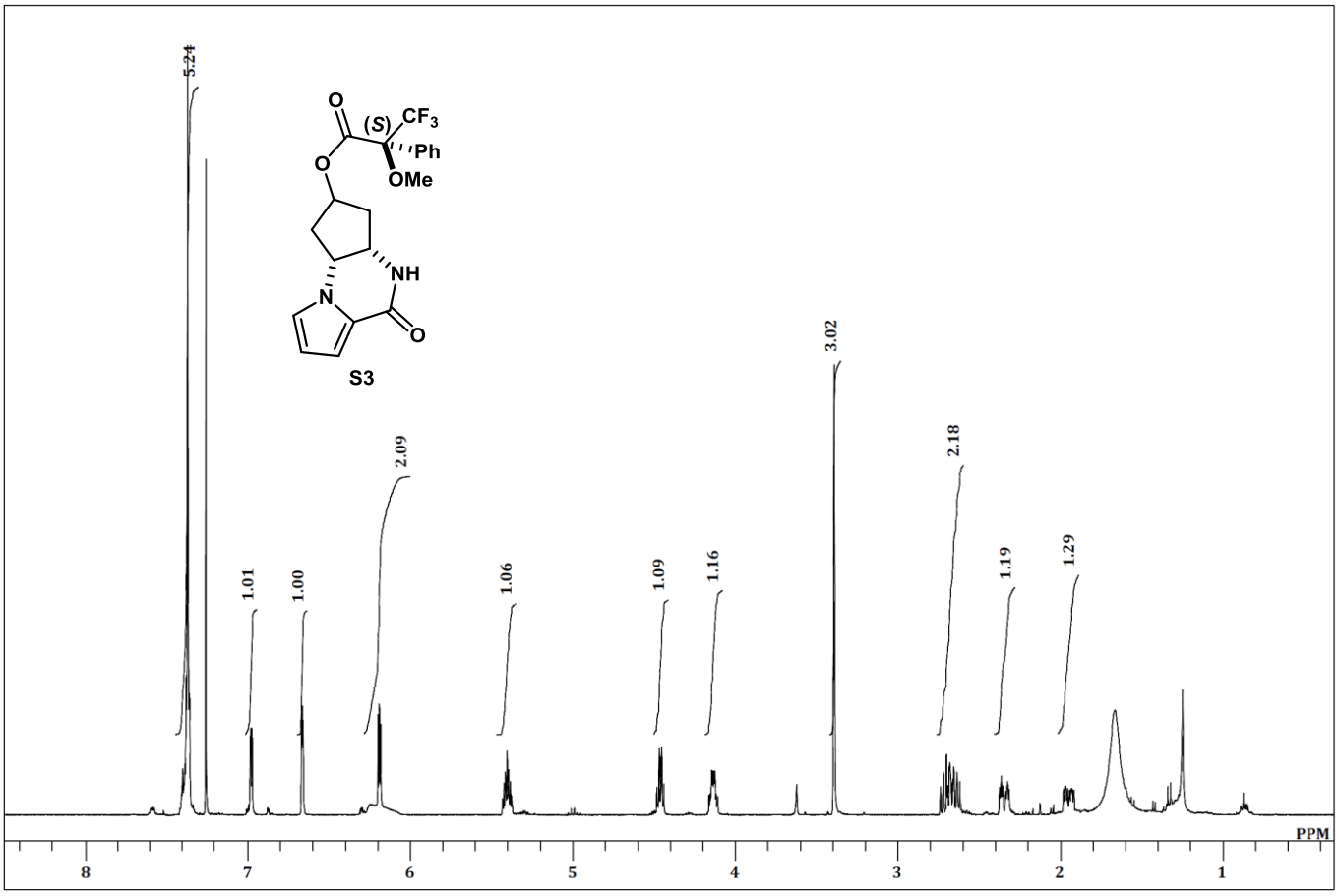
^{1}H NMR (400 MHz, CD_3OD)

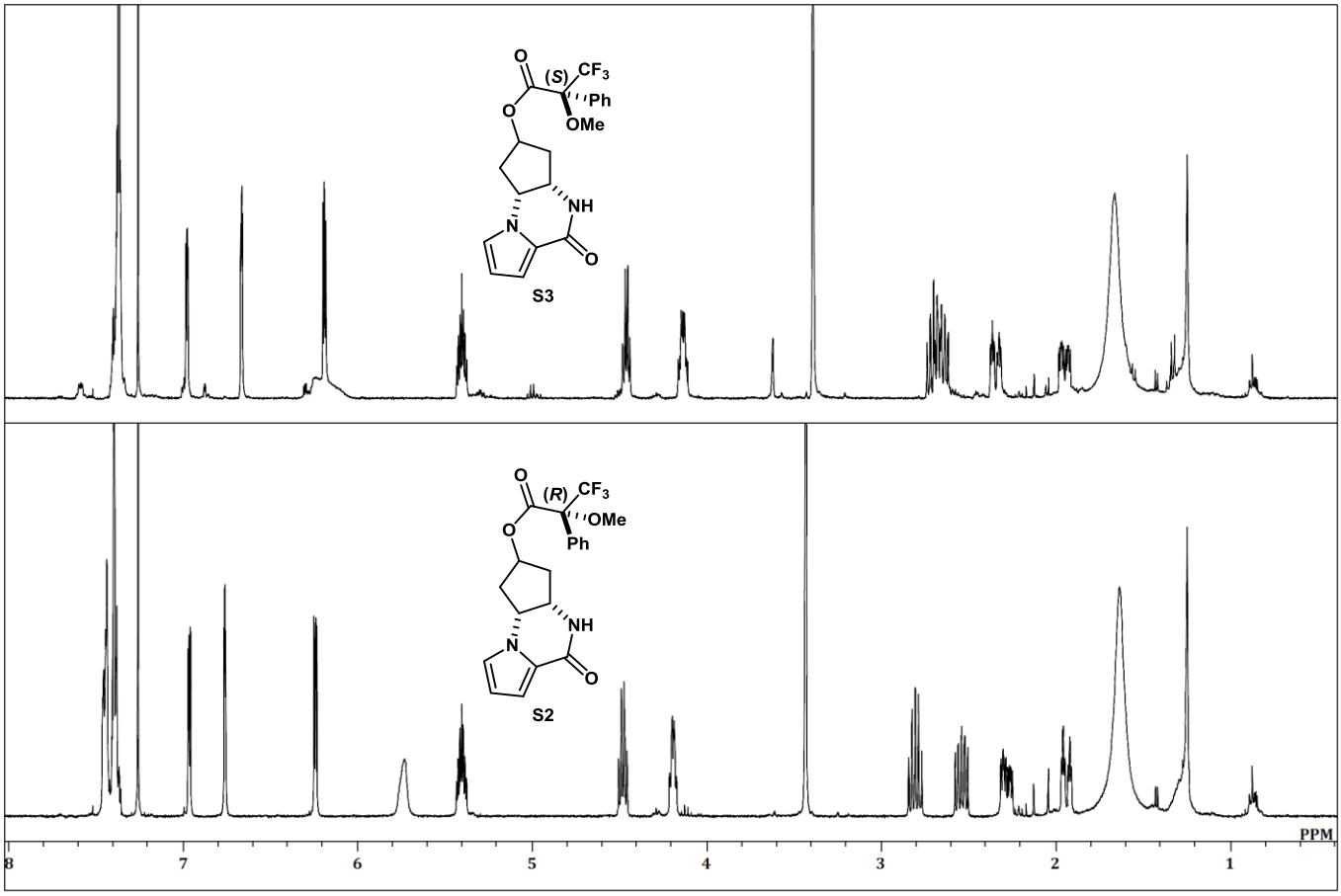


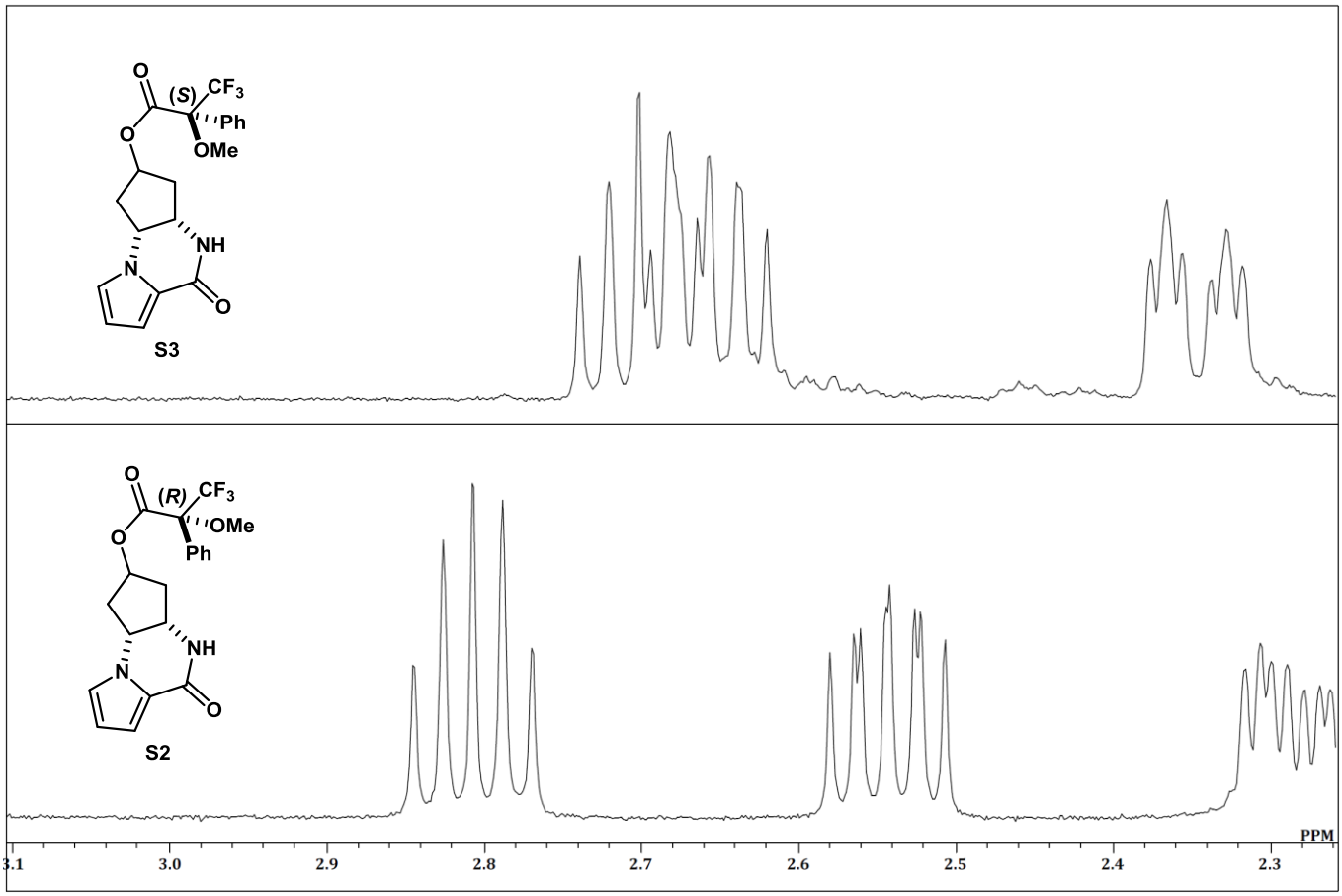
^{1}H NMR (400 MHz, $CDCl_3$)

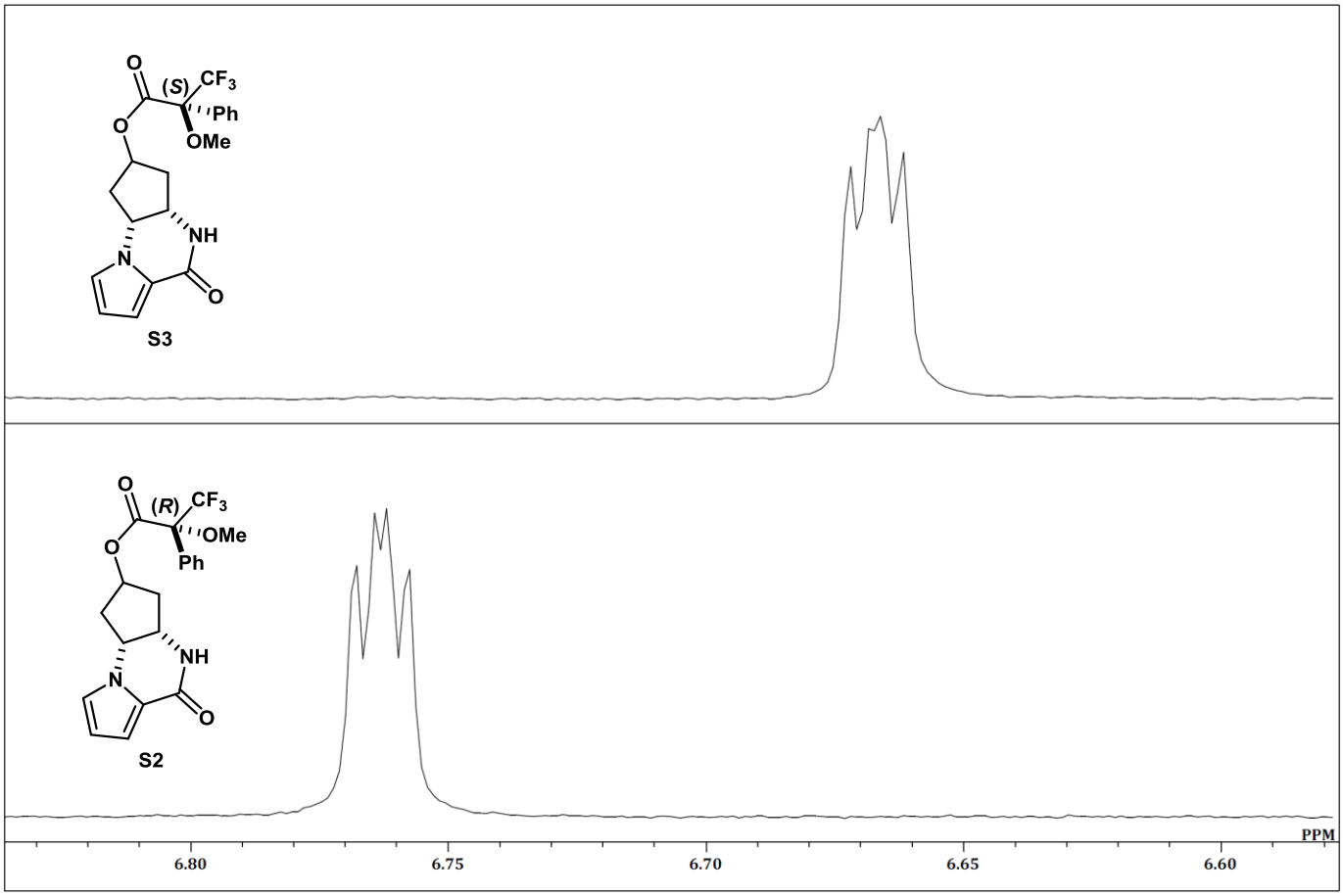


^{1}H NMR (400 MHz, $CDCl_3$)

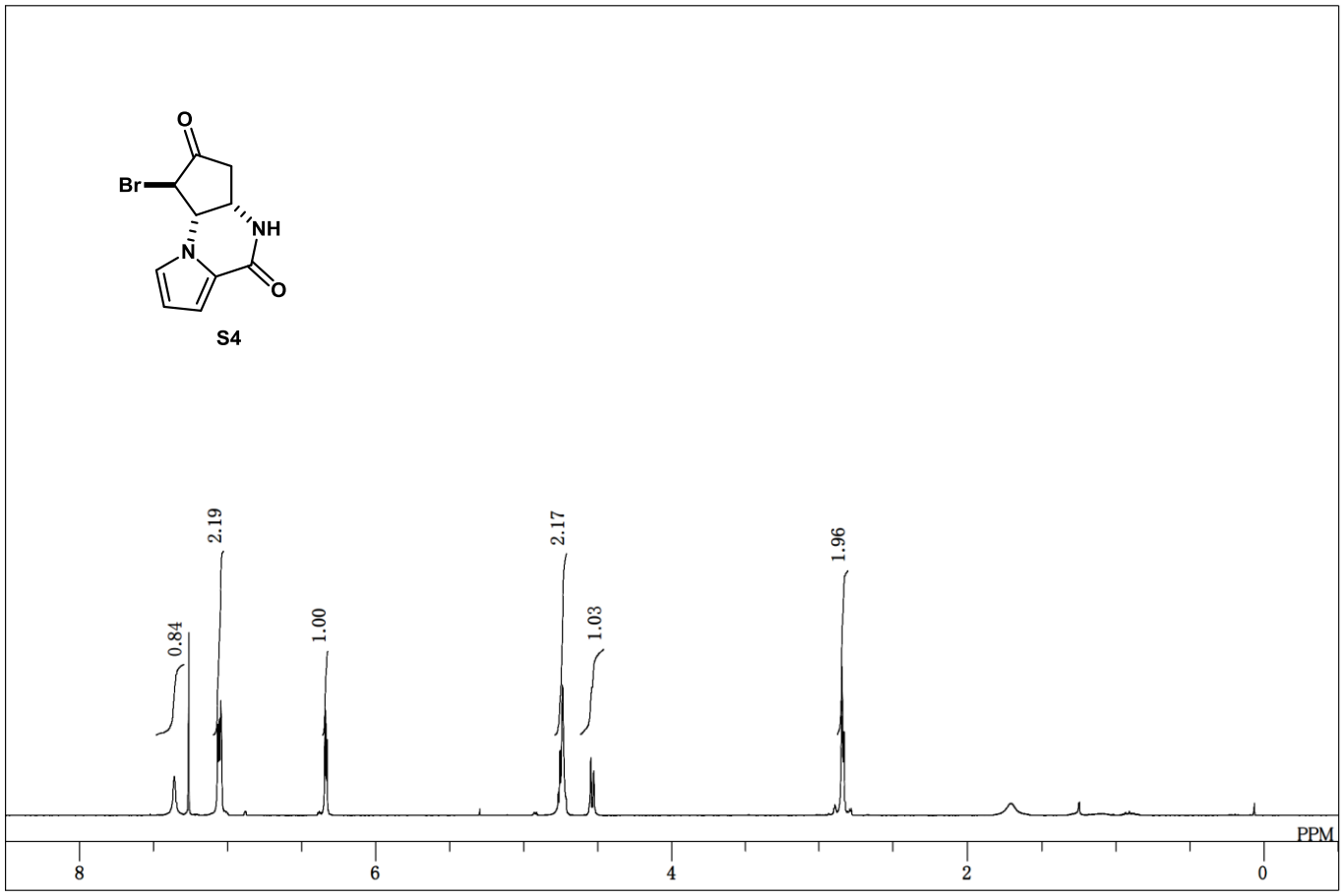





O
(S)
CF3
Ph
OMe
O
NH
N
O
S3
O
(R)
CF3
OMe
Ph
O
NH
N
O
S2
PPM
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3


O
(S)
CF3
Ph
OMe
O
NH
N
O
S3
O
(R)
CF3
OMe
Ph
O
NH
N
O
S2
PPM
6.80
6.75
6.70
6.65
6.60

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



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