Supporting Information

for

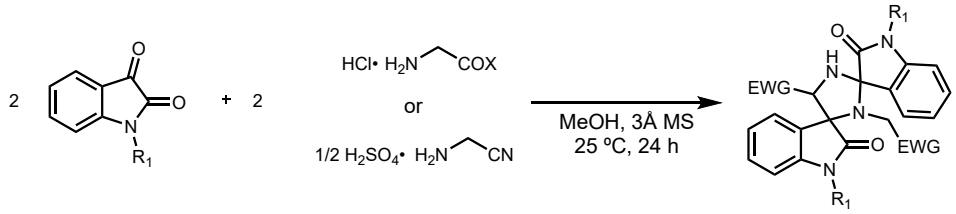
Asymmetric synthesis of spiro[oxindole-3,2'-pyrrolidine]s through the organocatalytic 1,3-dipolar cycloaddition via cycloreversion of precursor isatinimine homodimer

General information

A part of Chemicals and solvents were purchased from commercial suppliers and used as received: isatin and 1-methylisatin (TCI, Japan), amino acid esters (TCI, Japan), unsaturated aldehydes (TCI, Japan/Wako, Japan), THF and EtOH (Wako, Japan), $NaBH_4$ (TCI, Japan), catalysts of diphenylprolinol derivatives (Sigma Aldrich, USA/ TCI, Japan). Products were purified by preparative TLC (PTLC).

NMR spectra were recorded on a JEOL JNM-ECZ600R (600 MHz for ^{1}H, 151 MHz for ^{13}C and 564 MHz for ^{19}F). Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.26 and TMS δ 0.00), carbon (chloroform δ 77.0 and methanol δ 49.3). TFA (δ -76.0 ppm) was used as an external reference for 19F NMR. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), dt (doublet of triplet), dq (doublet of quartet), ddd (doublet of doublet of doublet), m (multiplet). Coupling constants were reported in Hertz (Hz). High-resolution MALDI-TOFMS measurements were performed on a JMS-S3000 Spiral-TOF mass spectrometer. High performance liquid chromatography (HPLC) was performed on Shimadzu 10A instruments using 4.6 mm × 25 cm DAICEL Chiralcel OD-H or Chiralcel IA column.

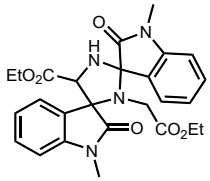
Preparation of DSIs[1]



A 100-mL round bottom flask, equipped with stir bar, was charged with isatin (5 mmol, 1.00 equiv), amino acid ester hydrochloride (6.00 mmol, 1.20 equiv), and 3Å molecular sieves (8 g). Methanol (50 mL) was added to the reaction flask and the resulting mixture was allowed to stir at room temperature for 24 h. The mixture was filtered through celite (rinsed with chloroform) and concentrated. The residues were purified by column chromatography (1:1 hexanes:ethyl acetate) to afford the DSIs as orange or brown solids.

For the synthesis of the substrate **2e**, it's necessary to wash the mixture by a saturated solution of sodium bicarbonate before concentrating.

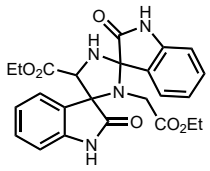
DSI 4a:



^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.78 (d, J = 6.2 Hz, 2H), 7.38-7.32 (m, 2H), 7.16-7.11 (m, 2H), 6.81 (d, J = 8.3 Hz, 2H), 5.00 (s, 1H), 4.16-4.11 (m, 1H), 3.97-3.92 (m, 1H), 3.90-3.81 (broad, 1H), 3.74-3.66 (m, 2H), 3.39 (d, J = 17.2 Hz, 1H), 3.22 (s, 3H), 3.21 (s, 3H), 2.86 (d, J = 17.2 Hz, 1H), 1.04 (t, J = 7.6 Hz, 3H), 0.90 (t, J = 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 177.14, 176.41, 169.53, 167.71, 144.92, 144.63, 130.94, 129.71, 125.83, 125.71, 125.43, 125.30, 123.29, 122.86, 108.25, 107.94, 82.49, 70.95, 68.24, 68.19, 68.14, 61.29, 60.41, 46.71, 26.07, 13.80; HRMS (MALDI-TOF) m/z: calculated for $C_{26}H_{28}N_4O_6[Na]^+$: 515.1901, found 515.1888.

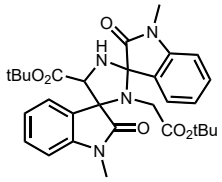
The relative stereochemistry was determined by 2D ^{1}H NMR (COSY, NOESY) which was in accordance with the previously reported DSIs.

DSI 4b:



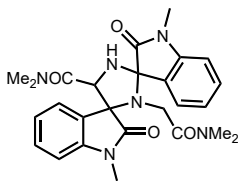
^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.78-7.72 (m, 4H), 7.33-7.26 (m, 2H), 7.16-7.10 (m, 2H), 6.85 (d, J = 7.6 Hz, 2H), 4.97 (s, 1H), 4.18-4.13 (m, 1H), 4.04-3.98 (m, 1H), 3.89-3.80 (broad, 1H), 3.80-3.71 (m, 2H), 3.49 (d, J = 17.2 Hz, 1H), 3.01 (d, J = 17.2 Hz, 1H), 1.08 (t, J = 6.9 Hz, 3H), 0.94 (t, J = 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 179.16, 178.62, 169.73, 167.81, 142.12, 141.93, 130.93, 129.70, 126.11, 126.09, 125.99, 125.72, 123.19, 122.87, 110.37, 110.03, 82.77, 71.52, 68.31, 61.56, 60.58, 46.71, 13.78, 13.70; HRMS (MALDI-TOF) m/z: calculated for $C_{24}H_{24}N_4O_6[Na]^+$: 487.1588, found 487.1569.

DSI 4c:



^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.54 (d, J = 7.6 Hz, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.11 (t, J = 7.6 Hz, 1H), 7.10 (t, J = 7.6 Hz, 1H), 6.81 (d, J = 7.6 Hz, 1H), 6.80 (d, J = 8.3 Hz, 1H), 5.16 (d, J = 12.4 Hz, 1H), 3.46 (d, J = 16.5 Hz, 1H), 3.42 (d, J = 11.7 Hz, 1H), 3.25 (s, 3H), 3.20 (s, 3H), 2.79 (d, J = 16.5 Hz, 1H), 1.01 (s, 9H), 0.95 (s, 9H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 175.35, 173.37, 168.60, 167.04, 145.08, 144.48, 143.92, 131.00, 129.21, 124.86, 124.23, 122.61, 121.48, 108.28, 107.57, 82.84, 81.92, 80.52, 71.32, 68.19, 48.31, 28.13, 27.46, 27.14, 26.43, 26.09; HRMS (MALDI-TOF) m/z: calculated for $C_{30}H_{36}N_4O_6[Na]^+$: 571.2527, found 571.2511.

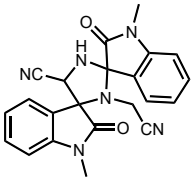
DSI 4d:



^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.94 (d, J = 7.6 Hz, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.09 (t, J = 7.6 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 6.80 (d, J = 8.3 Hz, 1H), 5.28 (d, J = 13.1 Hz, 1H), 4.03 (d, J = 13.1 Hz, 1H), 3.39 (d, J = 14.5 Hz, 1H), 3.29 (s, 3H), 3.24 (s, 3H), 3.04 (d, J = 14.5 Hz, 1H), 2.88 (s, 3H), 2.78 (s, 3H), 2.59 (s, 3H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 151

MHz) δ 177.38, 176.89, 168.06, 166.23, 145.07, 144.93, 130.58, 129.64, 126.19, 125.98, 124.82, 122.63, 122.43, 108.28, 108.24, 81.63, 71.53, 68.04, 48.15, 37.27, 36.52, 35.55, 35.13, 26.30, 26.13; HRMS (MALDI-TOF) m/z: calculated for $C_{26}H_{30}N_6O_4[Na]^+$: 513.2221, found 513.2201.

DSI 4e:



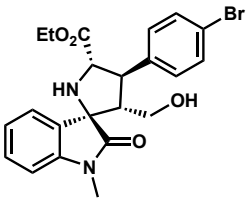
^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.87 (d, J = 7.6 Hz, 1H), 7.69 (d, J = 7.6 Hz, 1H), 7.24 (q, J = 7.6 Hz, 2H), 6.99 (t, J = 8.3 Hz, 1H), 6.91 (t, J = 7.6 Hz, 1H), 5.05 (t, J = 13.1 Hz, 1H), 3.91 (d, J = 12.4 Hz, 1H), 3.39 (d, J = 17.9 Hz, 1H), 3.34 (s, 3H), 3.25 (s, 3H), 3.12 (d, J = 17.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 174.91, 174.86, 144.69, 144.64, 132.19, 131.56, 126.01, 125.64, 124.01, 123.99, 122.63, 121.44, 114.48, 114.30, 109.53, 109.15, 81.70, 70.87, 55.50, 32.62, 26.60, 26.36; HRMS (MALDI-TOF) m/z: calculated for $C_{22}H_{18}N_6O_2[Na]^+$: 421.1383, found 421.1388.

General procedure for [3+2] cycloaddition

DSI (0.08 mmol), an unsaturated aldehyde (0.08 mmol), diphenylprolinol derivatives **C1** (0.016 mmol), and TFA (0.016 mmol) were added to a flask containing 0.4 mL of THF and 0.4 mL of water. The mixture was stirred at 25℃ for 72 hours. Then, $NaBH_4$ (1 mmol) was added and stirred for an additional 10 minutes. The reaction mixture was treated with NH_4Cl saturated solution and extracted three times with chloroform. The combined organic layer was dried over $MgSO_4$, concentrated under reduced pressure, and the residue was isolated by PTLC (3:1 EtOAc/hexane, Rf 0.4-0.6) to afford the purified product.

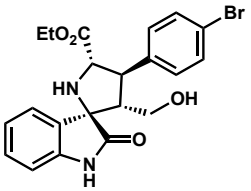
In the synthesis of product **3i**, the reduction step using $NaBH_4$ was omitted, and the crude mixture was isolated by PTLC (1:1 EtOAc/hexane, with 1% Et_3N).

Ethyl (3*R*,3'*S*,4'*R*,5'*S*)-4'-(4-bromophenyl)-3'-(hydroxymethyl)-1-methyl-2-oxospiro[indoline-3,2'-pyrrolidine]-5'-carboxylate (6a)



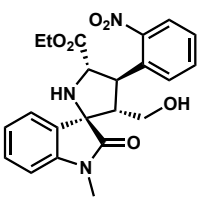
27.9 mg (yield 76%). Colorless solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.49 (d, J = 8.3 Hz, 2H), 7.47 (d, J = 6.9 Hz, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.29 (d, J = 8.3 Hz, 2H), 7.14 (t, J = 7.6 Hz, 1H), 6.86 (d, J = 8.3 Hz, 1H), 4.30 (d, J = 9.6 Hz, 1H), 4.17 (dq, J = 11.0 Hz, 7.6 Hz, 1H), 4.09 (dq, J = 11.0 Hz, 7.6 Hz, 1H), 3.41 (dd, J = 9.6 Hz, 12.4 Hz, 1H), 3.35 (dt, J = 11.7 Hz, 4.1 Hz, 1H), 3.24-3.19 (m, 1H), 3.21 (s, 3H), 3.08 (ddd, J = 4.1 Hz, 9.0 Hz, 12.4 Hz, 1H), 2.87 (s, 1H), 1.14 (t, J = 6.9 Hz, 3H), 0.85 (dd, J = 4.8 Hz, 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 179.25, 173.21, 143.70, 137.65, 131.95, 129.94, 129.64, 129.48, 124.88, 122.81, 121.36, 108.46, 69.95, 67.07, 61.31, 60.80, 58.47, 51.99, 26.56, 14.11; HRMS (MALDI-TOF) m/z: calculated for $C_{22}H_{23}N_2O_4Br[H]^+$: 459.0914, found 459.0926. Enantiomeric excess was determined by HPLC analysis (Chiralpak ODH, hexane/2-propanol = 90:10, 1.0 mL min^{-1}): t_R = 14.6 min (minor), 18.9 min (major).

Ethyl (3*R*,3'*S*,4'*R*,5'*S*)-4'-(4-bromophenyl)-3'-(hydroxymethyl)-2-oxospiro[indoline-3,2'-pyrrolidine]-5'-carboxylate (6b)



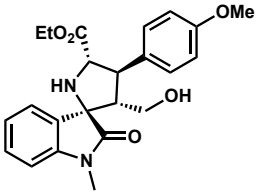
28.3 mg (yield 79%). White solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.72 (s, 1H), 7.46 (d, J = 8.3 Hz, 2H), 7.39 (d, J = 7.6 Hz, 1H), 7.25 (d, J = 9.0 Hz, 2H), 7.23 (t, J = 7.6 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 6.85 (d, J = 8.3 Hz, 1H), 4.22 (d, J = 9.0 Hz, 1H), 4.17 (dq, J = 10.3 Hz, 7.6 Hz, 1H), 4.08 (dq, J = 10.3 Hz, 6.9 Hz, 1H), 3.34 (dt, J = 9.6 Hz, 12.4 Hz, 2H), 3.18 (dt, J = 7.6 Hz, 9.6Hz, 1H), 3.11 (ddd, J = 4.1 Hz, 9.6 Hz, 12.4 Hz, 1H), 2.85 (s, 1H), 1.83 (s, 1H), 1.13 (t, J = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 181.61, 173.27, 140.91, 137.47, 131.94, 130.38, 129.60, 129.38, 125.17, 122.74, 121.37, 110.64, 70.46, 67.12, 61.37, 60.63, 58.38, 51.94, 14.12; HRMS (MALDI-TOF) m/z: calculated for $C_{21}H_{21}N_2O_4Br[H]^+$: 445.0758, found 445.0740. Enantiomeric excess was determined by HPLC analysis (Chiralpak ODH, hexane/2-propanol = 90:10, 1.0 mL min^{-1}): t_R = 20.3 min (minor), 26.4 min (major).

Ethyl (3*R*,3'*S*,4'*R*,5'*S*)-3'-(hydroxymethyl)-1-methyl-4'-(2-nitrophenyl)-2-oxospiro[indoline-3,2'-pyrrolidine]-5'-carboxylate (6c)



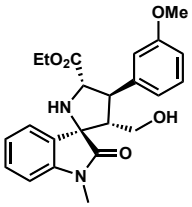
29.1 mg (yield 85%). White solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.96 (d, J = 7.6 Hz, 1H), 7.77 (d, J = 8.3 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.42 (t, J = 8.3 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.14 (t, J = 6.9 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 4.33 (d, J = 6.9 Hz, 1H), 4.14-4.04 (m, 3H), 3.45 (dt, J = 11.0 Hz, 4.8Hz, 1H), 3.32 (dt, J = 9.0 Hz, 12.4 Hz, 1H), 3.26-3.20 (m, 1H), 3.20 (s, 3H), 2.90 (s, 1H), 1.30 (t, J = 5.5 Hz, 1H), 1.07 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 179.28, 172.24, 151.03, 143.63, 133.91, 133.18, 129.54, 129.20, 128.88, 127.92, 124.99, 124.08, 123.03, 108.41, 69.72, 67.73, 61.62, 61.27, 58.79, 45.76, 26.50, 13.74; HRMS (MALDI-TOF) m/z: calculated for $C_{22}H_{22}N_3O_6[Na]^+$: 448.1479, found 448.1472. Enantiomeric excess was determined by HPLC analysis (Chiralpak IA, hexane/2-propanol = 80:20, 1.0 mL min^{-1}): t_R = 16.7 min (major), 29.8 min (minor).

Ethyl (3*R*,3'*S*,4'*R*,5'*S*)-3'-(hydroxymethyl)-4'-(4-methoxyphenyl)-1-methyl-2-oxospiro[indoline-3,2'-pyrrolidine]-5'-carboxylate (6d)



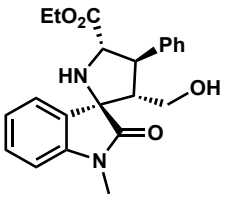
25.4 mg (yield 78%). Colorless solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.49 (d, J = 6.9 Hz, 1H), 7.34 (t, J = 7.6 Hz, 1H), 7.31 (d, J = 8.3 Hz, 2H), 7.13 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 9.0 Hz, 2H), 6.85 (d, J = 7.6 Hz, 1H), 4.28 (d, J = 9.6 Hz, 1H), 4.17 (dq, J = 11.0 Hz, 6.9 Hz, 1H), 4.08 (dq, J = 11.0 Hz, 7.6 Hz, 1H), 3.81 (s, 3H), 3.39 (dd, J = 9.6 Hz, 11.7 Hz, 1H), 3.36 (dt, J = 11.7 Hz, 4.1 Hz, 1H), 3.21 (s, 3H), 3.21-3.16 (m, 1H), 3.11 (ddd, J = 4.1 Hz, 9.0 Hz, 12.4 Hz, 1H), 2.86 (s, 1H), 1.14 (t, J = 7.6 Hz, 3H), 0.83 (dd, J = 4.1 Hz, 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 179.36, 173.62, 158.93, 143.67, 130.25, 130.16, 129.32, 128.86, 124.92, 122.74, 114.20, 108.35, 70.01, 67.31, 61.14, 61.06, 58.57, 55.24, 52.04, 26.54, 14.11; HRMS (MALDI-TOF) m/z: calculated for $C_{23}H_{26}N_2O_5[H]^+$: 411.1914, found 411.1905. Enantiomeric excess was determined by HPLC analysis (Chiralpak ODH, hexane/2-propanol = 80:20, 1.0 mL min^{-1}): t_R = 9.2 min (minor), 15.8 min (major).

Ethyl (3*R*,3'*S*,4'*R*,5'*S*)-3'-(hydroxymethyl)-4'-(3-methoxyphenyl)-1-methyl-2-oxospiro[indoline-3,2'-pyrrolidine]-5'-carboxylate (6e)



26.6 mg (yield 81%). Colorless solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.50 (d, J = 6.2 Hz, 1H), 7.34 (t, J = 7.6 Hz, 1H), 7.26 (t, J = 8.3 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 6.98 (d, J = 7.6 Hz, 1H), 6.95 (s, 1H), 6.86 (d, J = 7.6 Hz, 1H), 6.82 (dd, J = 2.8 Hz, 8.3Hz, 1H), 4.33 (d, J = 9.6 Hz, 1H), 4.18 (dq, J = 10.3 Hz, 6.9 Hz, 1H), 4.09 (dq, J = 11.0 Hz, 7.6 Hz, 1H), 3.82 (s, 3H), 3.42 (dd, J = 9.6 Hz, 11.7 Hz, 1H), 3.40-3.36 (m, 2H), 3.21 (s, 3H), 3.21-3.14 (m, 2H), 2.90 (s, 1H), 1.14 (t, J = 6.9 Hz, 3H), 0.90 (dd, J = 4.1 Hz, 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 179.26, 173.56, 159.93, 143.67, 139.96, 130.16, 129.81, 129.35, 124.92, 122.77, 120.25, 113.37, 112.93, 108.38, 70.12, 67.17, 61.21, 61.03, 58.57, 55.23, 52.67, 26.56, 14.10; HRMS (MALDI-TOF) m/z: calculated for $C_{23}H_{26}N_2O_5[H]^+$: 411.1914, found 411.1903. Enantiomeric excess was determined by HPLC analysis (Chiralpak ODH, hexane/2-propanol = 80:20, 1.0 mL min^{-1}): t_R = 7.5 min (minor), 9.7 min (major).

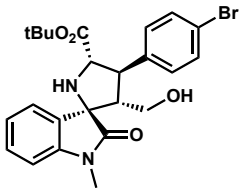
Ethyl (3*R*,3'*S*,4'*R*,5'*S*)-3'-(hydroxymethyl)-1-methyl-2-oxo-4'-phenylspiro[indoline-3,2'-pyrrolidine]-5'-carboxylate (6f)



23.8 mg (yield 78%). White solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.50 (d, J = 7.6 Hz, 1H), 7.40 (d, J = 7.6 Hz, 2H), 7.36 (d, J = 7.6 Hz, 2H), 7.34 (t, J = 7.6 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 4.33 (d, J = 9.6 Hz, 1H), 4.17 (dq, J = 10.3 Hz, 6.9 Hz, 1H), 4.07 (dq, J = 10.3 Hz, 6.9 Hz, 1H), 3.43 (dd, J = 10.3 Hz, 12.4 Hz, 1H), 3.37 (dt, J = 11.0 Hz, 3.4 Hz, 1H), 3.22-3.14 (m, 2H), 3.21 (s, 3H), 2.89 (s, 1H), 1.11 (t, J = 6.9 Hz, 3H), 0.85 (dd, J = 4.1 Hz, 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 179.32, 173.53, 143.69, 138.36, 130.16, 129.36, 128.82, 127.88, 127.55, 124.91, 122.76, 108.38, 70.08, 67.27, 61.17, 60.99, 58.65, 52.74, 26.55, 14.06; HRMS (MALDI-TOF) m/z: calculated for $C_{22}H_{24}N_2O_4[H]^+$: 381.1809, found 381.1817. Enantiomeric excess was determined by HPLC analysis (Chiralpak ODH, hexane/2-propanol = 90:10, 1.0 mL min^{-1}): t_R = 14.1 min (minor), 18.8 min (major).

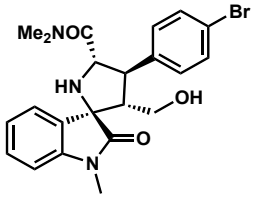
***tert*-Butyl (3*R*,3'*S*,4'*R*,5'*S*)-4'-(4-bromophenyl)-3'-(hydroxymethyl)-1-methyl-2-oxospiro[indoline-3,2'-**

pyrrolidine]-5'-carboxylate (6g)



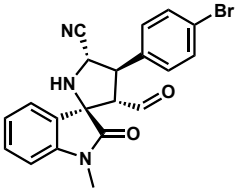
35.7 mg (yield 92%). White solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.48 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 6.9 Hz, 1H), 7.34 (t, J = 6.9 Hz, 1H), 7.29 (d, J = 8.3 Hz, 2H), 7.12 (t, J = 7.6 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 4.19 (d, J = 9.6 Hz, 1H), 3.35 (dd, J = 4.13 Hz, 11.7 Hz, 1H), 3.29 (dd, J = 10.3 Hz, 12.4 Hz, 1H), 3.23-3.18 (m, 1H), 3.20 (s, 3H), 3.08 (ddd, J = 4.1 Hz, 9.0 Hz, 12.4 Hz, 1H), 2.94-2.68 (broad, 1H), 1.32 (s, 9H), 0.98-0.87 (broad, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 179.45, 172.25, 143.75, 137.94, 131.80, 129.99, 129.70, 129.46, 124.79, 122.71, 121.15, 108.42, 81.83, 69.90, 67.69, 60.79, 58.48, 52.63, 27.87, 26.52; HRMS (MALDI-TOF) m/z: calculated for $C_{24}H_{27}N_2O_4Br[Na]^+$: 509.1046, found 509.1022. Enantiomeric excess was determined by HPLC analysis (Chiralpak ODH, hexane/2-propanol = 90:10, 1.0 mL min^{-1}): t_R = 11.1 min (minor), 18.1 min (major).

(3*R*,3'*S*,4'*R*,5'*S*)-4'-(4-bromophenyl)-3'-(hydroxymethyl)-N,N,1-trimethyl-2-oxospiro[indoline-3,2'-pyrrolidine]-5'-carboxamide (6h)



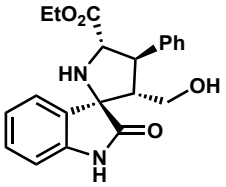
28.5 mg (yield 78%). White solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.67 (d, J = 6.9 Hz, 1H), 7.48 (d, J = 8.3 Hz, 2H), 7.35 (t, J = 7.6 Hz, 1H), 7.33 (d, J = 8.3 Hz, 2H), 4.51 (dd, J = 8.3 Hz, 9.6 Hz, 1H), 3.46 (dd, J = 10.3 Hz, 12.4 Hz, 1H), 3.38 (dt, J = 11.0 Hz, 4.1 Hz, 1H), 3.30-3.19 (m, 2H), 3.21 (s, 3H), 3.01 (d, J = 8.3 Hz, 1H), 2.89 (s, 3H), 2.54 (s, 3H), 1.01 (dd, J = 6.2 Hz, 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 179.93, 171.47, 143.82, 137.47, 132.09, 129.73, 129.58, 129.43, 125.15, 122.89, 121.37, 108.26, 69.99, 64.97, 61.14, 57.70, 53.54, 36.71, 36.04, 26.48; HRMS (MALDI-TOF) m/z: calculated for $C_{22}H_{24}N_3O_3Br[H]^+$: 458.1074, found 458.1069. Enantiomeric excess was determined by HPLC analysis (Chiralpak ODH, hexane/2-propanol = 80:20, 1.0 mL min^{-1}): t_R = 12.8 min (minor), 18.1 min (major).

(3*R*,3'*S*,4'*R*,5'*S*)-4'-(4-bromophenyl)-3'-formyl-1-methyl-2-oxospiro[indoline-3,2'-pyrrolidine]-5'-carbonitrile (6i)



22.5 mg (yield 69%). Colorless needles (recrystallized from $CHCl_3$ and hexane). ^1H NMR ($CDCl_3$, 600 MHz) δ 9.15 (s, 1H), 7.52 (d, J = 8.3 Hz, 2H), 7.41 (d, J = 8.3 Hz, 2H), 7.39 (t, J = 7.6 Hz, 1H), 7.26 (d, J = 6.9 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 6.91 (d, J = 7.6 Hz, 1H), 4.76 (dd, J = 6.2 Hz, 10.3 Hz, 1H), 4.31 (t, J = 9.6 Hz, 1H), 3.54 (d, J = 9.0 Hz, 1H), 3.27 (s, 3H), 2.73 (d, J = 5.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 196.01, 178.45, 143.19, 134.95, 132.39, 130.63, 129.83, 125.81, 125.72, 123.88, 122.49, 118.37, 109.10, 67.61, 63.51, 53.89, 49.00, 26.64; HRMS (MALDI-TOF) m/z: calculated for $C_{20}H_{16}N_3O_2Br[H]^+$: 410.0499, found 410.0513. Enantiomeric excess was determined by HPLC analysis of the alcohol as shown below, obtained by $NaBH_4$ reduction of the aldehyde (Chiralpak ODH, hexane/2-propanol = 90:10, 1.0 mL min^{-1}): t_R = 32.4 min (minor), 38.4 min (major).

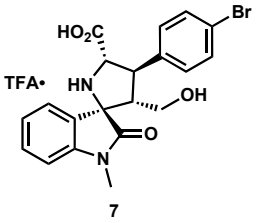
Ethyl (3*R*,3'*S*,4'*R*,5'*S*)-3'-(hydroxymethyl)-1-methyl-2-oxo-4'-phenylspiro[indoline-3,2'-pyrrolidine]-5'-carboxylate (6j)



1.2448 g (yield 68%). Pink solid. ^1H NMR ($CDCl_3$, 600 MHz) δ 8.79 (s, 1H), 7.42 (d, J = 7.6 Hz, 1H), 7.38-7.31 (m, 4H), 7.26 (t, J = 7.2 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.07 (t, J = 7.6 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 4.26 (d, J = 10.3 Hz, 1H), 4.16 (dq, J = 10.3 Hz, 6.9 Hz, 1H), 4.06 (dq, J = 11.0 Hz, 7.6 Hz, 1H), 3.40-3.30 (m, 2H), 3.21-3.11 (m, 2H), 2.99-2.73 (board, 1H), 1.11 (t, J = 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 181.75, 173.58, 140.99, 138.27, 130.58, 129.27, 128.79, 127.85, 127.53, 125.17, 122.63, 110.62, 70.58, 67.32, 61.22, 60.80, 58.51, 52.66, 14.06; HRMS (MALDI-TOF) m/z: calculated for $C_{21}H_{22}N_2O_4[Na]^+$: 389.1472, found 389.1458. Enantiomeric excess was determined by HPLC analysis of the alcohol as shown below, obtained by $NaBH_4$ reduction of the aldehyde (Chiralpak ODH, hexane/2-propanol = 90:10, 1.0 mL min^{-1}): t_R = 17.6 min (minor), 26.7 min (major).

Derivatization of product 6g (7)

Trifluoroacetate salt of (3*R*,3'*S*,4'*R*,5'*S*)-4'-(4-bromophenyl)-3'-(hydroxymethyl)-1-methyl-2-oxospiro[indoline-3,2'-pyrrolidine]-5'-carboxylic acid



7

To the 10 mL flask containing the product **6g** (35.8 mg), dichloromethane (0.2 mL) and TFA (0.2 mL) was added, and the mixture was stirred at room temperature for 4 h. The solvent was removed under reduced pressure, and the residue was purified by PTLC (3:7 MeOH: $CHCl_3$) to afford the product **7** as a white solid (29.5 mg, yield 93%).

^{1}H NMR (CD_3OD, 600 MHz) δ 7.59 (d, J = 7.6 Hz, 1H), 7.47 (d, J = 8.3 Hz, 2H), 7.37 (d, J = 8.3 Hz, 2H), 7.36 (t, J = 7.9 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 6.98 (d, J = 7.6 Hz, 1H), 3.95 (d, J = 9.6 Hz, 1H), 3.27-3.20 (m, 2H), 3.19 (s, 3H), 3.11 (t, J = 10.3 Hz, 1H), 3.05 (dt, J = 3.4 Hz, 11.7 Hz, 1H); ^{13}C NMR (CD_3OD, 151 MHz) δ 181.99, 179.39, 163.36 (q, J = 34.7 Hz), 145.59, 141.31, 132.94, 131.51, 130.67, 126.63, 124.07, 121.83, 118.55 (q, J = 293.5 Hz), 110.02, 71.99, 71.88, 61.72, 60.49, 55.16, 49.30, 27.06; ^{19}F NMR (CD_3OD, 564 MHz) δ -74.64; HRMS (MALDI-TOF) m/z: calculated for $C_{20}H_{19}N_2O_4Br[H]^+$: 431.0601, found 431.0611.

Determination of absolute configuration of 6i.

The absolute configuration of **6i** was determined to be (3*R*,3'*S*,4'*R*,5'*S*) by an X-ray crystallographic analysis. The X-ray diffraction data of the single crystals were collected on a Rigaku XtaLAB P200 diffractometer with Cu Kα X-rays (λ = 1.54184 Å). The structures were solved by direct methods (shelxs-2013)[2] and refined on F^2 by full-matrix least-squares techniques (shelxl-2018)[3] using the Yadokari-XG software package.[4]

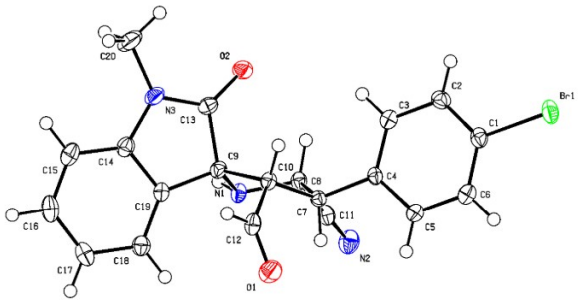


Figure S1. Thermal ellipsoid plot of the crystal structure of **6i**

[Crystal data and structure refinement of 6i]

Bond precision: C-C = 0.0045 A Wavelength=1.54184

Cell: a=7.8995(1) b=10.5371(2) c=21.3743(3)

alpha=90 beta=90 gamma=90

Temperature: 93 K

	Calculated	Reported
Volume	1779.15(5)	1779.15(5)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C20 H16 Br N3 O2	C20 H16 Br N3 O2
Sum formula	C20 H16 Br N3 O2	C20 H16 Br N3 O2
Mr	410.26	410.27
Dx,g cm-3	1.532	1.532
Z	4	4
Mu (mm-1)	3.313	3.313
F000	832.0	832.0

F000’	831.37	
h,k,lmax	9,13,26	9,12,26
Nref	3559[2055]	3451
Tmin,Tmax	0.853,0.967	0.793,1.000
Tmin’	0.516	

Correction method= # Reported T Limits: Tmin=0.793 Tmax=1.000 AbsCorr = MULTI-SCAN

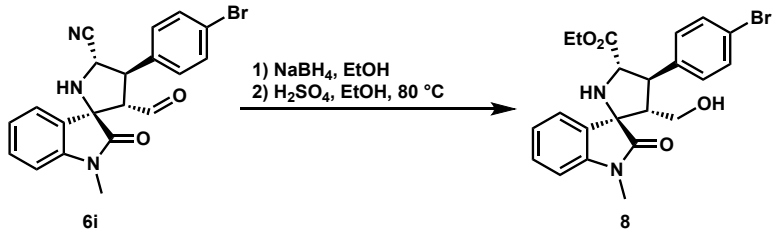
Data completeness= 1.68/0.97 Theta(max)= 73.011

R(reflections)= 0.0248(3322) wR2(reflections)= 0.0673(3451)

S = 1.127 Npar= 239

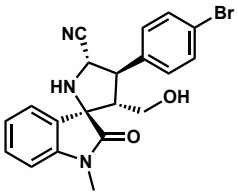
Flack parameter -0.029(10)

Determination of absolute configuration of 6a-6h[5]



6i 8

To a solution of **6i** (11.9 mg, 0.029 mmol) in ethanol (0.5 mL) at room temperature, $NaBH_4$ (0.3 mmol) was added and stirred for 10 minutes. The reaction mixture was treated with NH_4Cl saturated solution and extracted three times with chloroform. The combined organic layer was dried over $MgSO_4$, concentrated under reduced pressure to give the following cyanoalcohol.



^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.53 (d, J = 8.3 Hz, 2H), 7.53 (t, J = 6.9 Hz, 1H), 7.38 (dt, J = 1.4 Hz, 7.6 Hz, 1H), 7.35 (d, J = 9.0 Hz, 2H), 7.18 (t, J = 7.6 Hz, 1H), 6.88 (d, J = 7.6 Hz, 1H), 4.55 (dd, J = 4.8 Hz, 9.6 Hz, 1H), 3.56 (dd, J = 10.3 Hz, 11.7 Hz, 1H), 3.43-3.38 (m, 1H), 3.36-3.29 (m, 1H), 3.21 (s, 3H), 2.96 (ddd, J = 4.1 Hz, 9.0 Hz, 14.1 Hz, 1H), 2.73 (d, J = 5.5 Hz, 1H), 0.91 (t, J = 4.1 Hz, 1H).

Next, to an ethanol (1 mL) solution of this compound (10.2 mg, 0.014 mmol), was added H_2SO_4 (0.28 mL,

0.11 mmol) at room temperature, and the resulting mixture was stirred at 80 °C for 16 h. The reaction was cooled to 0°C, and aqueous NaOH (1 M) was added until *p*H > 8. The organic materials were extracted three times with chloroform. The combined organic layer was dried over $MgSO_4$, concentrated under reduced pressure. The residue was purified by PTLC (3:1 EtOAc/hexane) to afford the product **8**.

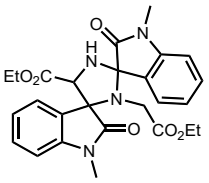
^{1}H NMR ($CDCl_3$, 600 MHz) 7.49 (d, J = 8.3 Hz, 2H), 7.47 (d, J = 6.9 Hz, 1H), 7.35 (t, J = 7.2 Hz, 1H), 7.29 (d, J = 8.3 Hz, 2H), 7.13 (t, J = 7.6 Hz, 1H), 6.87 (d, J = 8.3 Hz, 1H), 4.31 (d, J = 10.3 Hz, 1H), 4.17 (dq, J = 11.0 Hz, 7.6 Hz, 1H), 4.10 (dq, J = 13.7 Hz, 6.9 Hz, 1H), 3.41 (dd, J = 9.6 Hz, 12.4 Hz, 1H), 3.35 (dt, J = 11.0 Hz, 3.4 Hz, 1H), 3.24-3.20 (m, 1H), 3.22 (s, 3H), 3.09 (ddd, J = 4.1 Hz, 9.0 Hz, 12.4 Hz, 1H), 2.91-2.83 (broad, 1H), 1.14 (t, J = 6.9 Hz, 3H), 0.77 (dd, J = 4.8 Hz, 6.9 Hz, 1H). Enantiomeric excess was determined by HPLC analysis (Chiralpak ODH, hexane/2-propanol = 90:10, 1.0 mL min^{-1}): t_R = 17.9 min (minor), 20.3 min (major).

By comparing the NMR and HPLC data of **6a** and **8**, stereochemical structure of **6a** was proved to be (3*R*,3'*S*,4'*R*,5'*S*). Stereochemical structure of other products was determined by analogy.

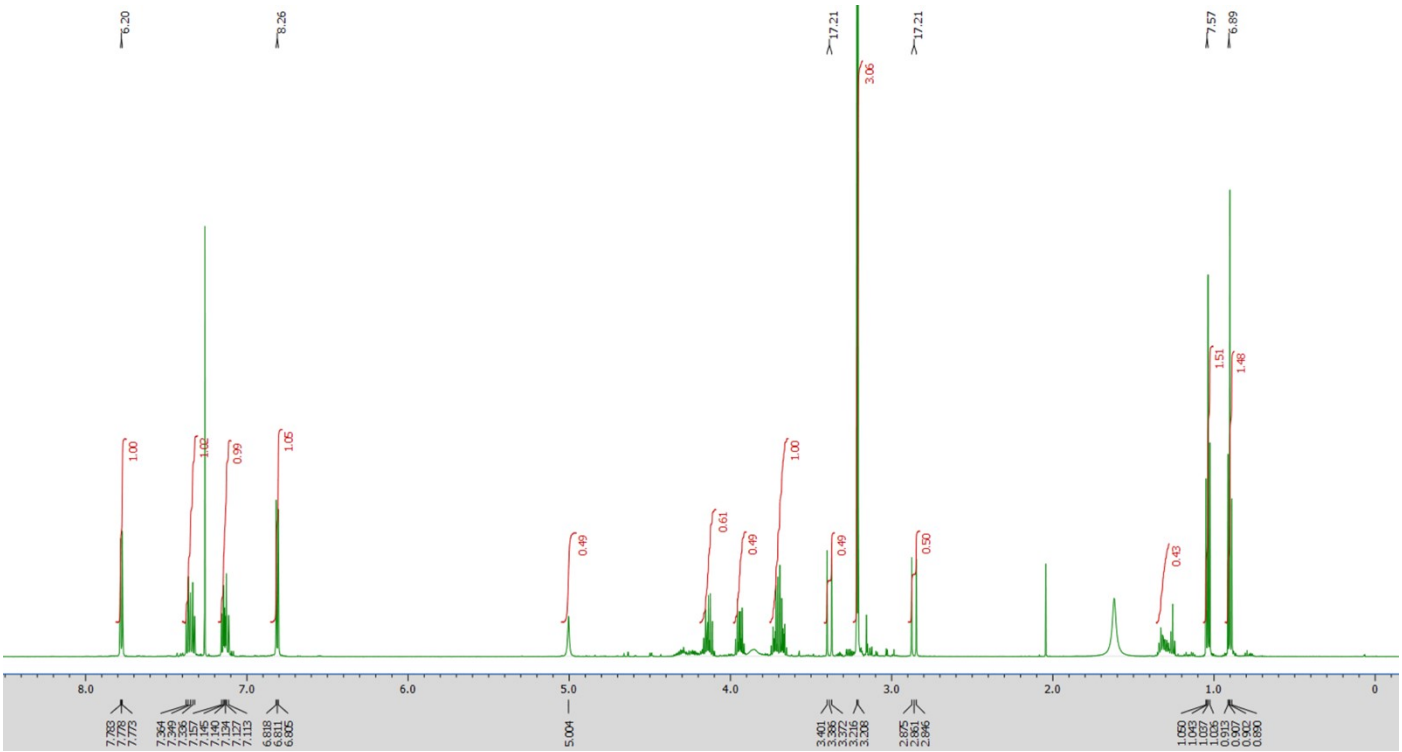
^{1}H and ^{13}C NMR spectra

Substrates

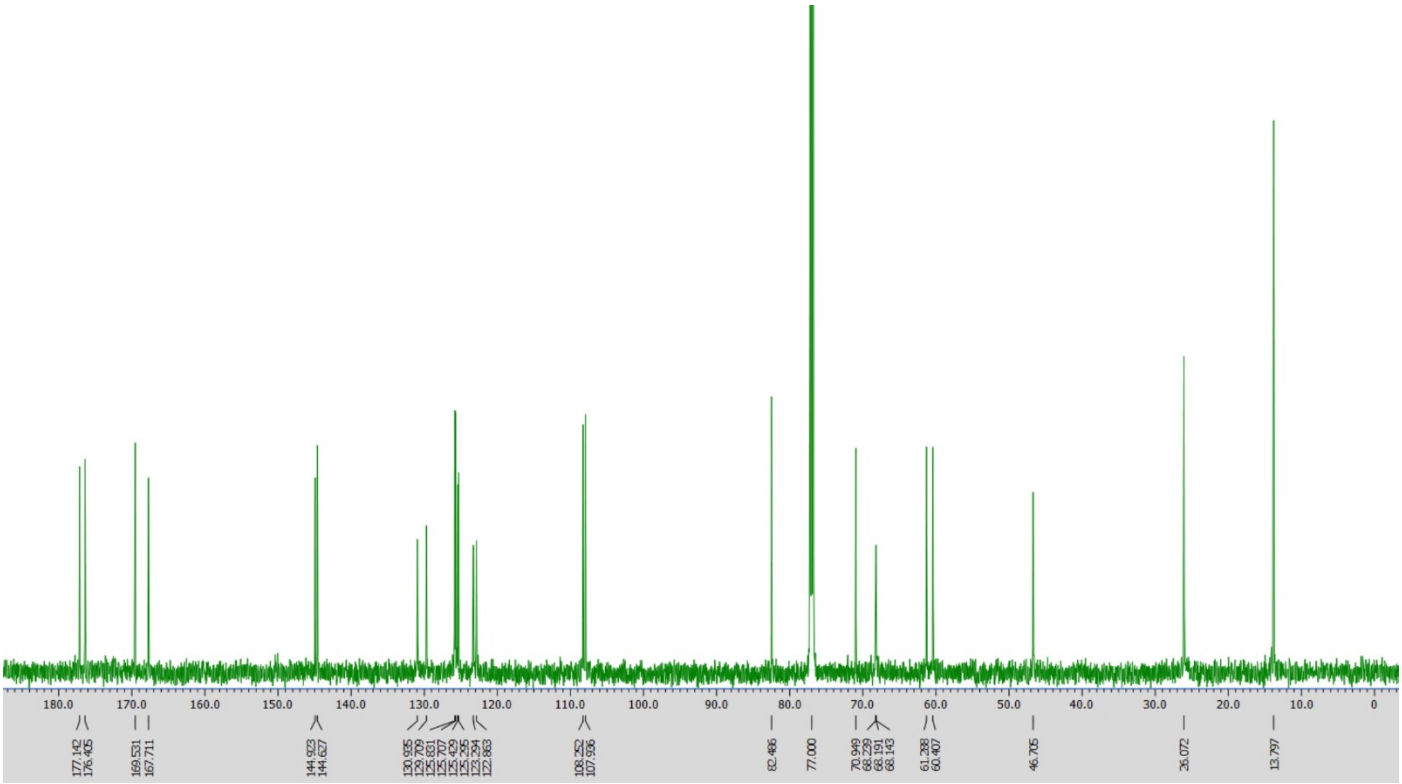
DSI 4a:



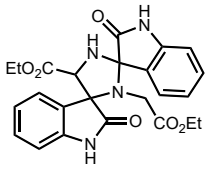
^{1}H-NMR (600 MHz, $CDCl_3$):



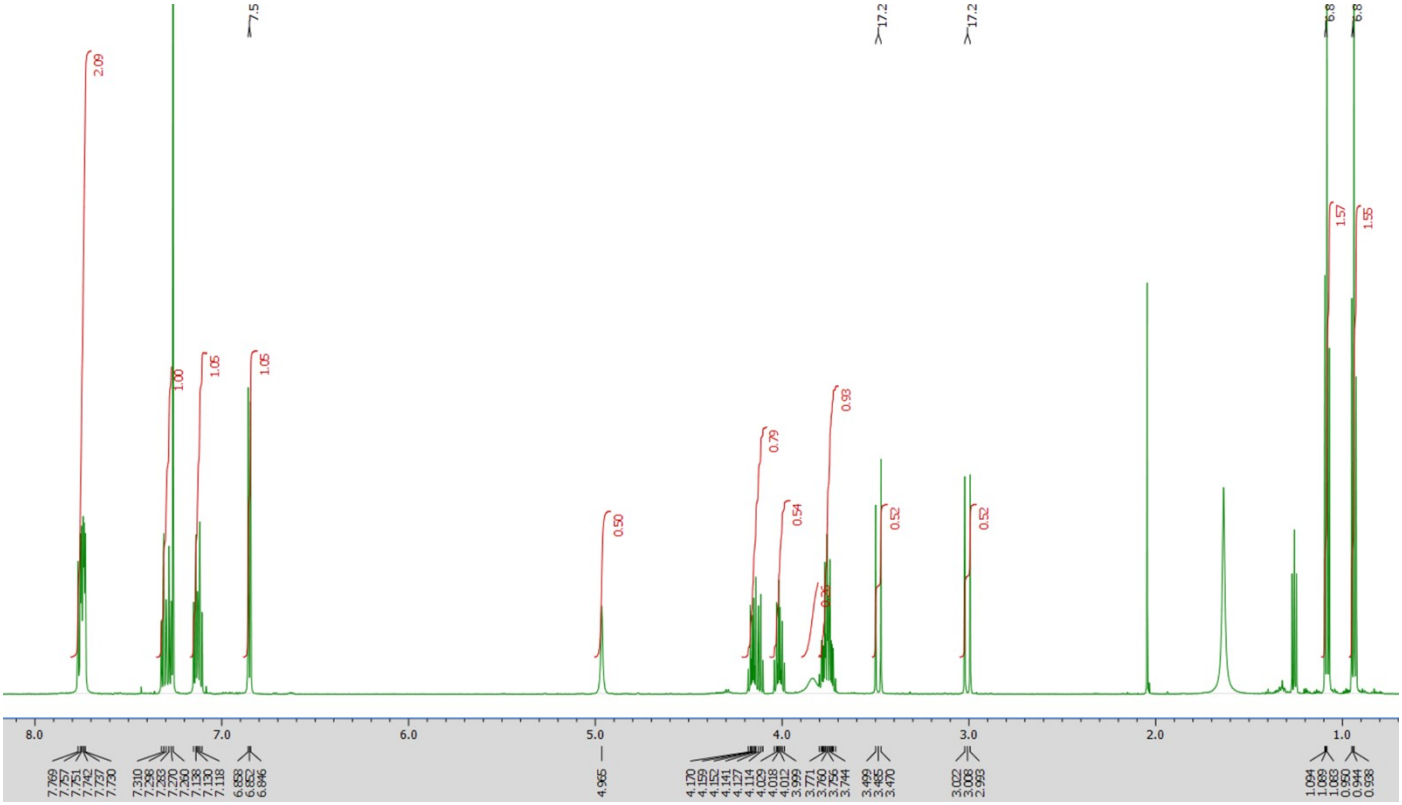
^{13}C-NMR (151 MHz, $CDCl_3$):



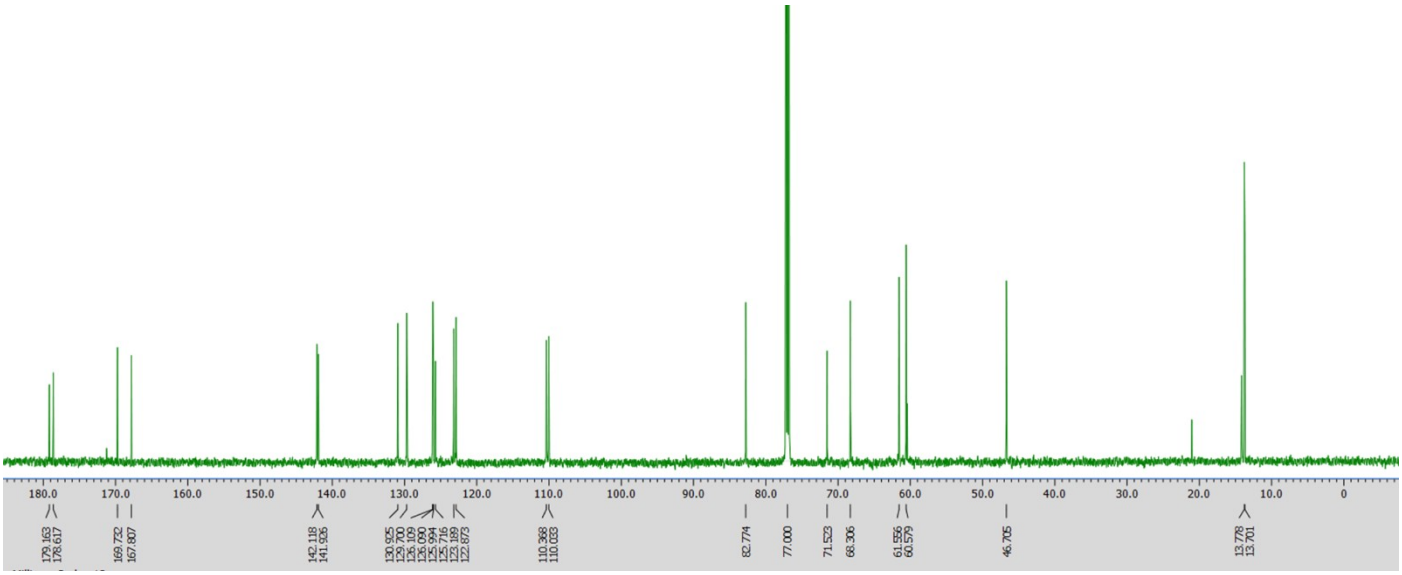
DSI 4b:



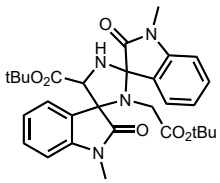
^{1}H-NMR (600 MHz, $CDCl_3$):



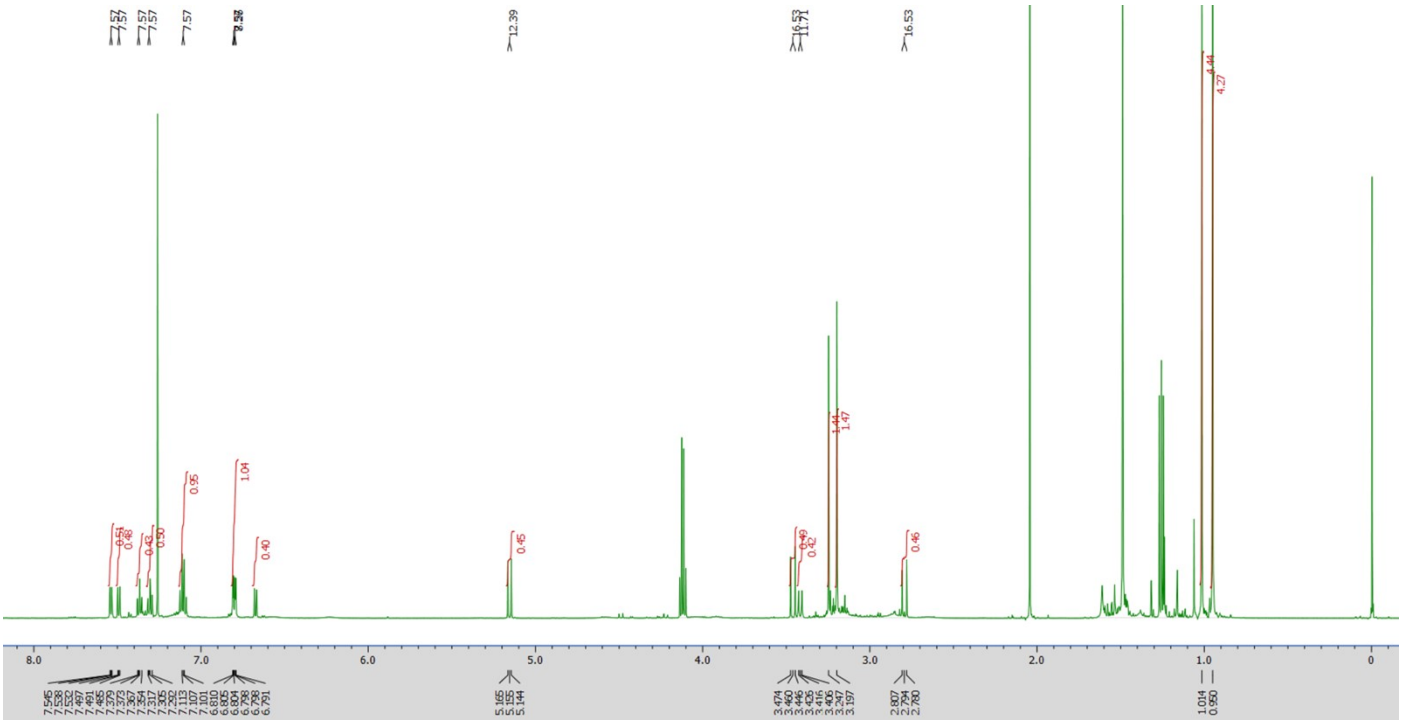
^{13}C-NMR (151 MHz, $CDCl_3$):



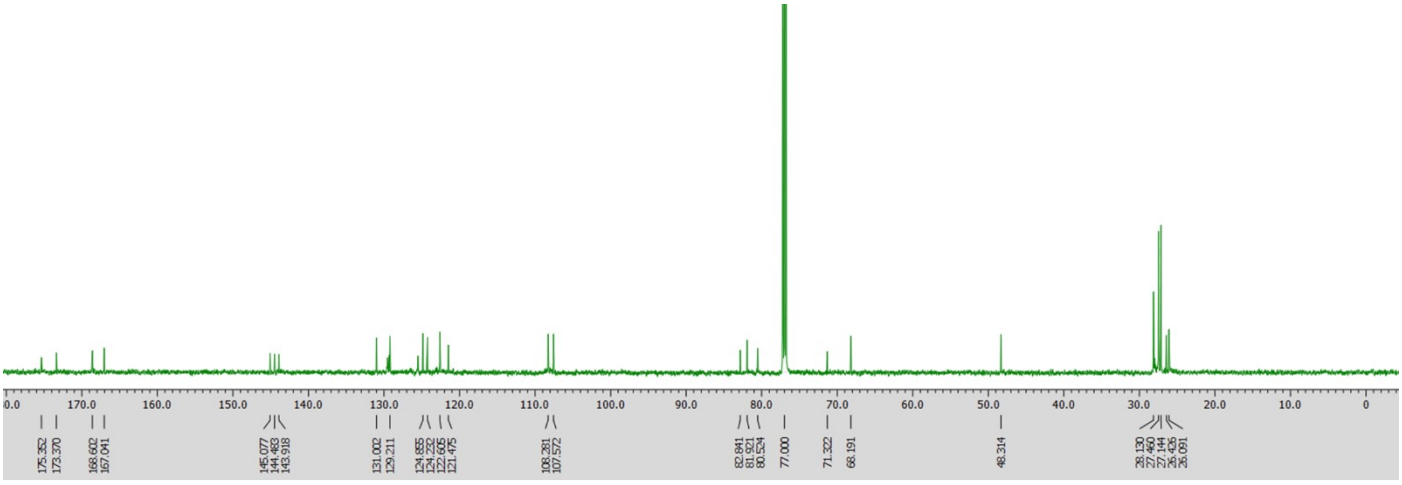
DSI 4c:



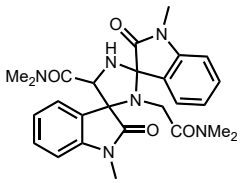
^{1}H-NMR (600 MHz, $CDCl_3$):



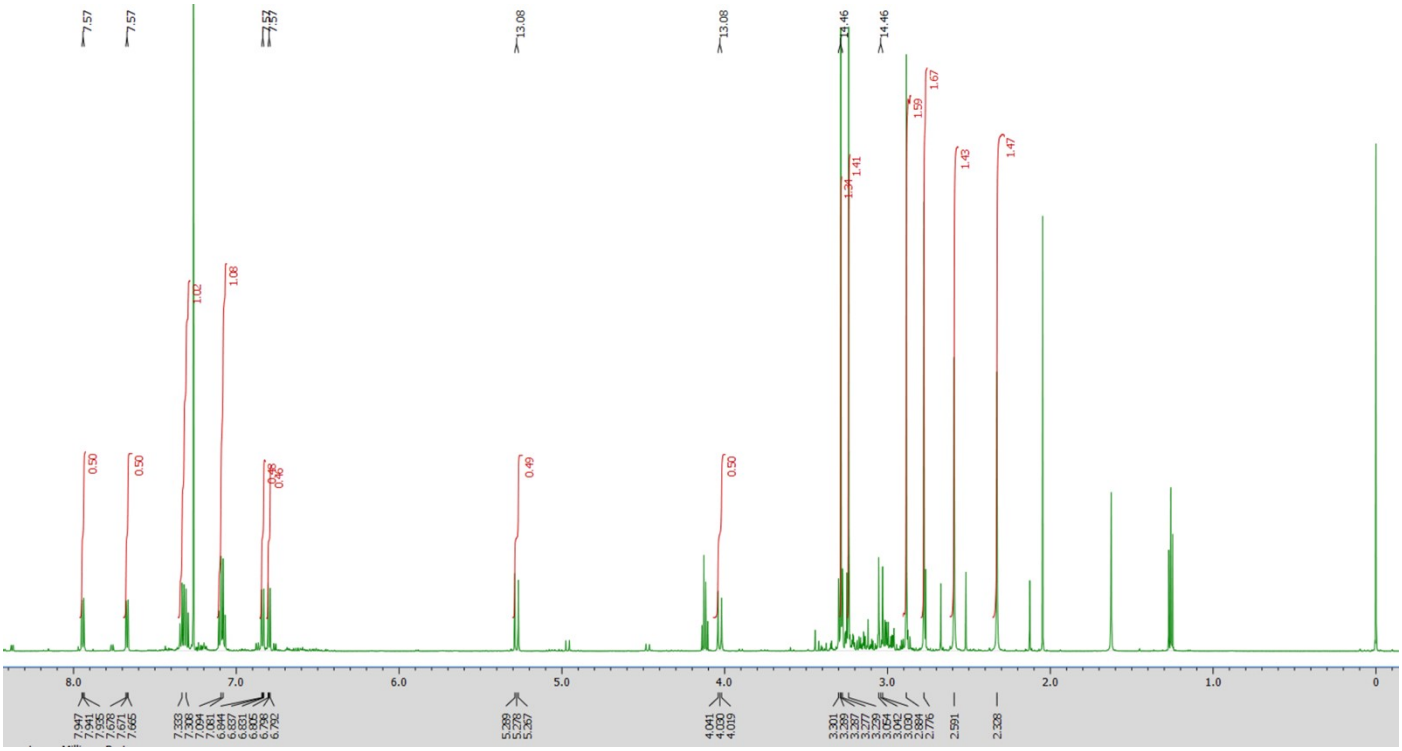
^{13}C-NMR (151 MHz, $CDCl_3$):



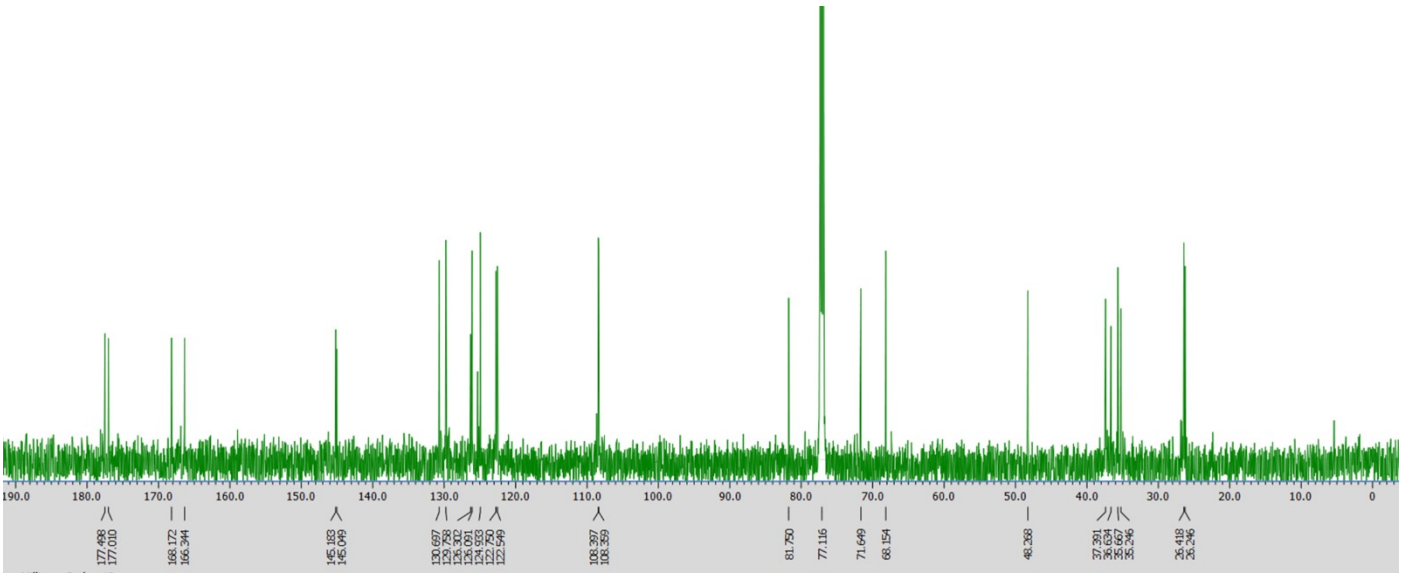
DSI 4d:



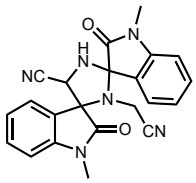
^{1}H-NMR (600 MHz, $CDCl_3$):



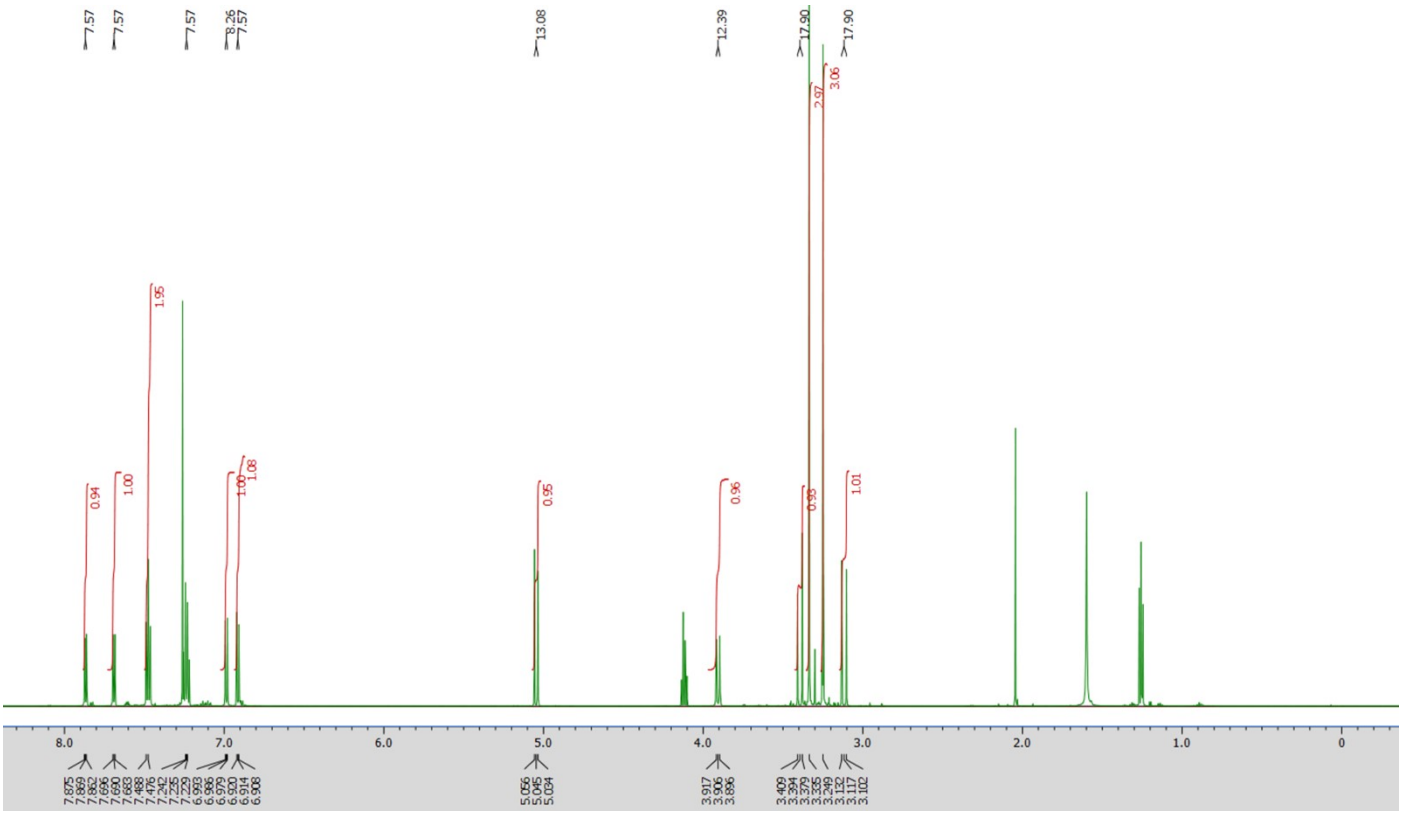
^{13}C-NMR (151 MHz, $CDCl_3$):



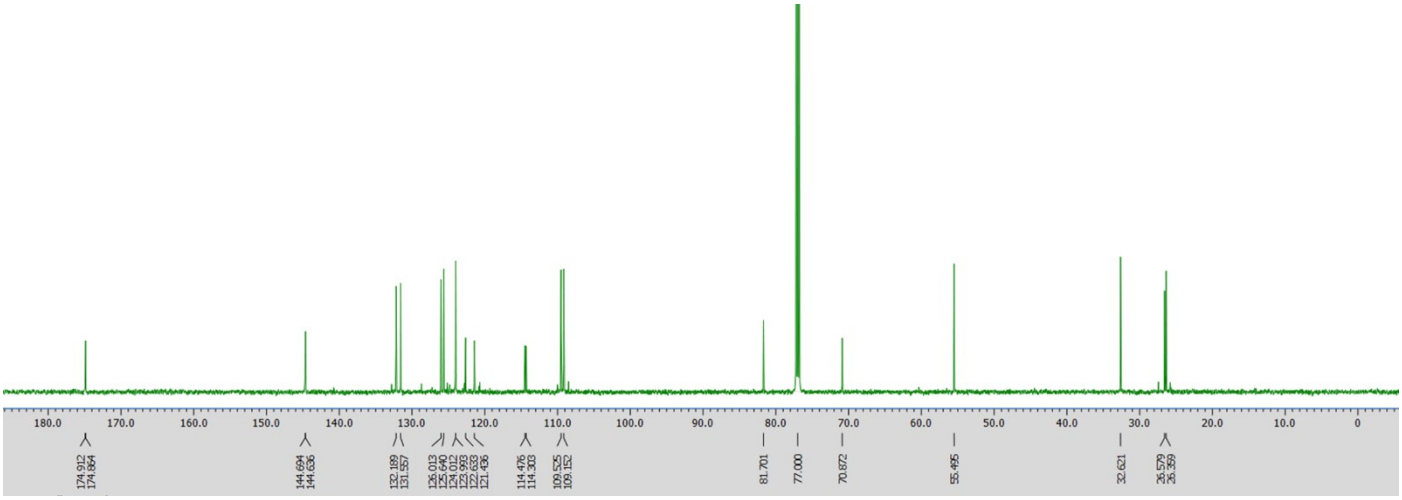
DSI 4e:



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

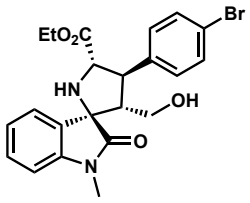


^{13}C-NMR (151 MHz, $CDCl_3$):



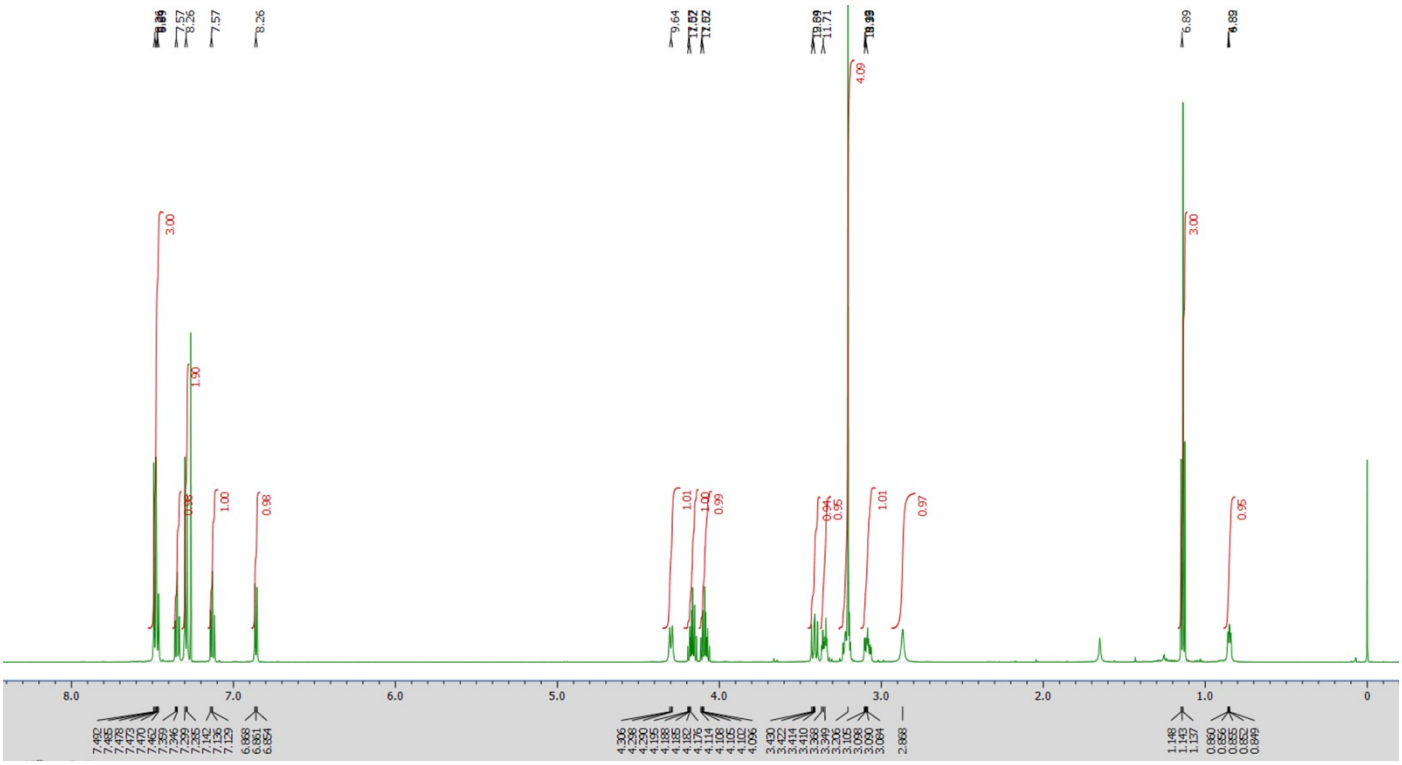
Products

2'-ethyl (2'S,3'R,4'S,5'R)-1-methyl-2-oxo-3'-(4-bromophenyl)-4'-(hydroxymethyl)-spiro[indoline-3,5'-prolinate] (6a)

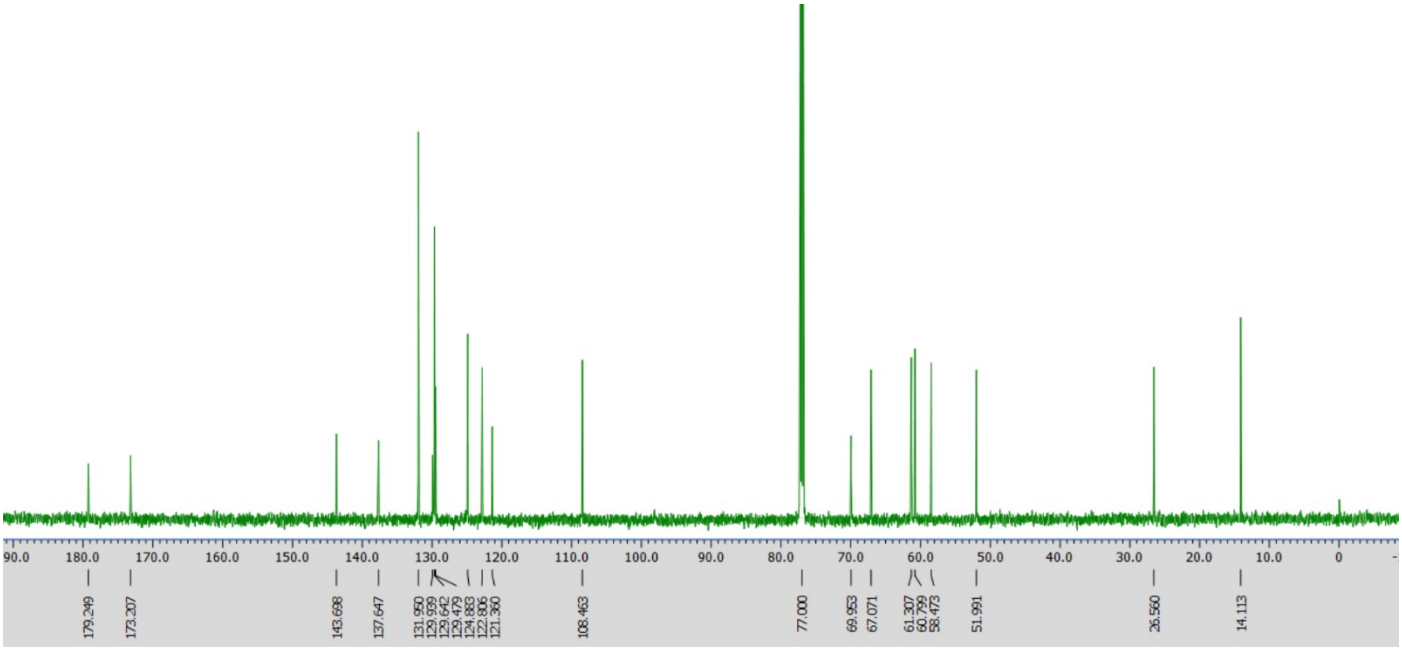


^{1}H-NMR (600 MHz, $CDCl_3$):

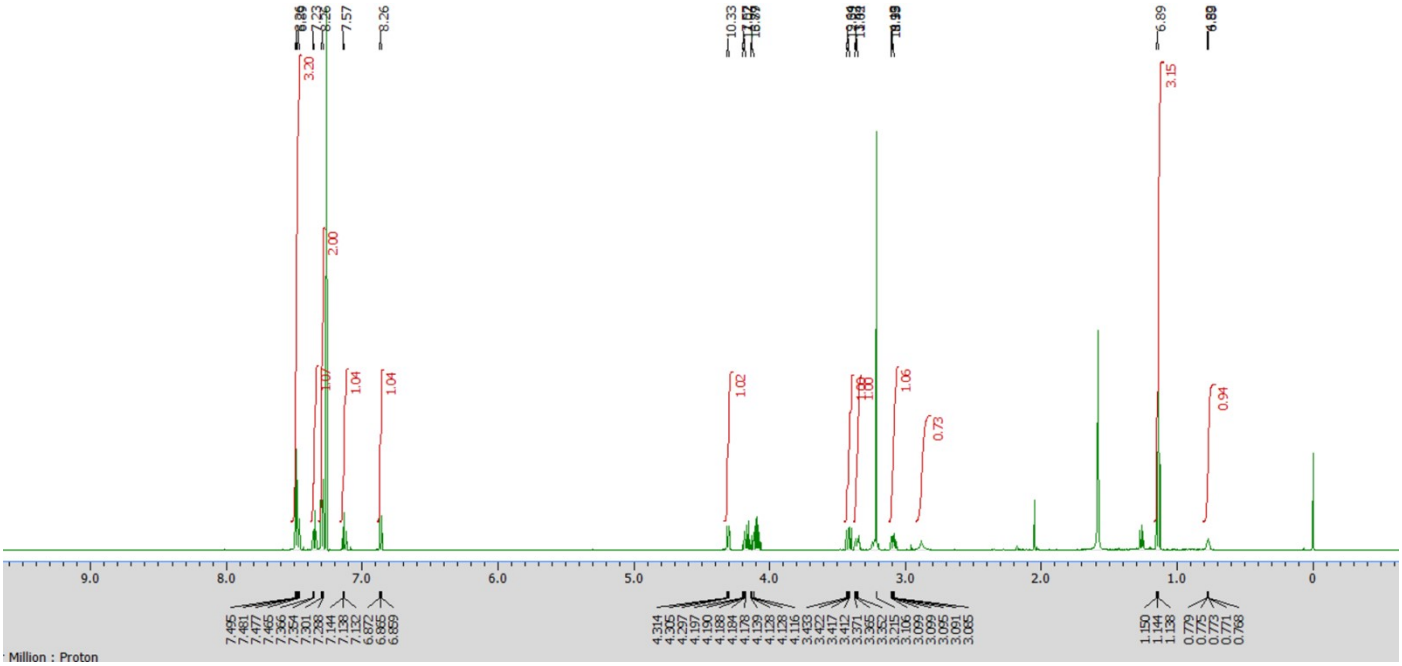
Synthesized by [3+2] cycloaddition



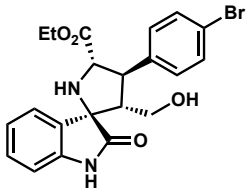
^{13}C-NMR (151 MHz, $CDCl_3$):



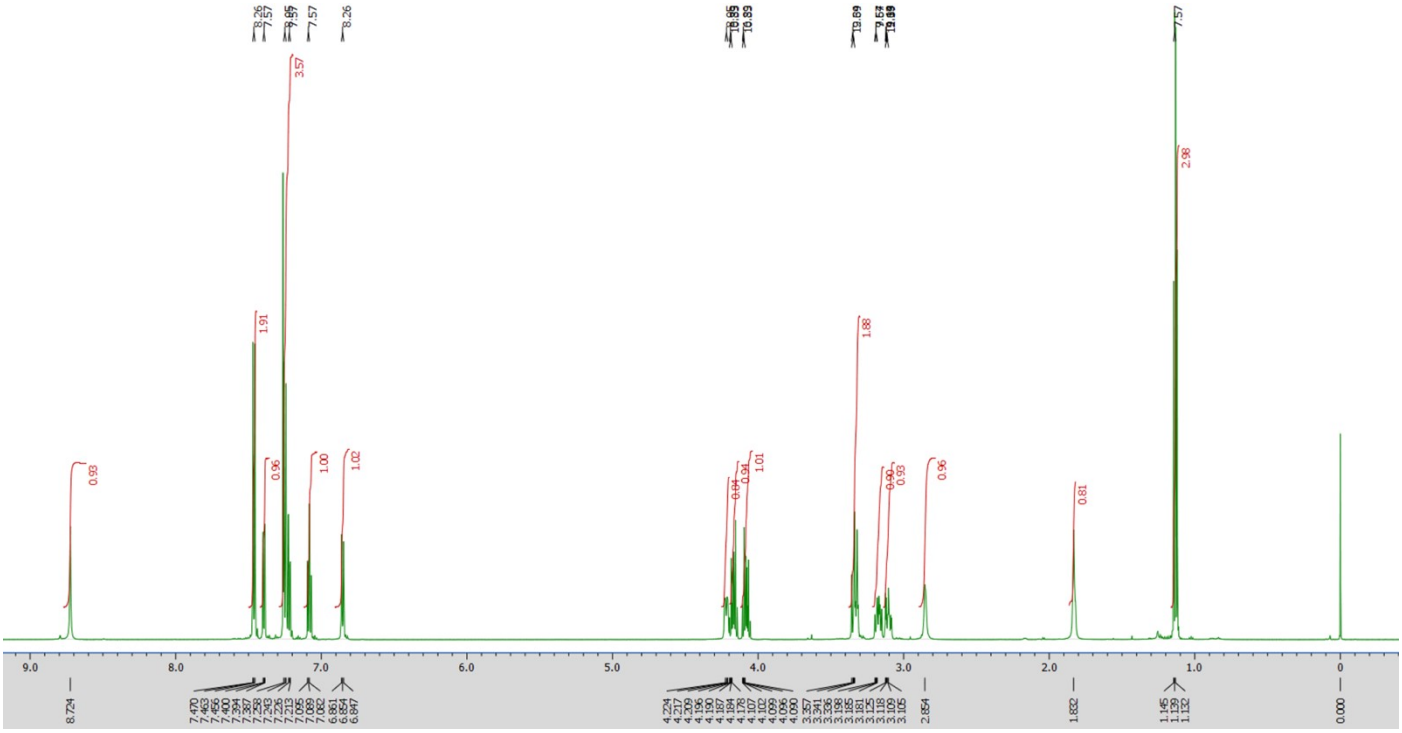
^{1}H-NMR (600 MHz, $CDCl_3$) of **6a** derivatized from CN-product **6i**



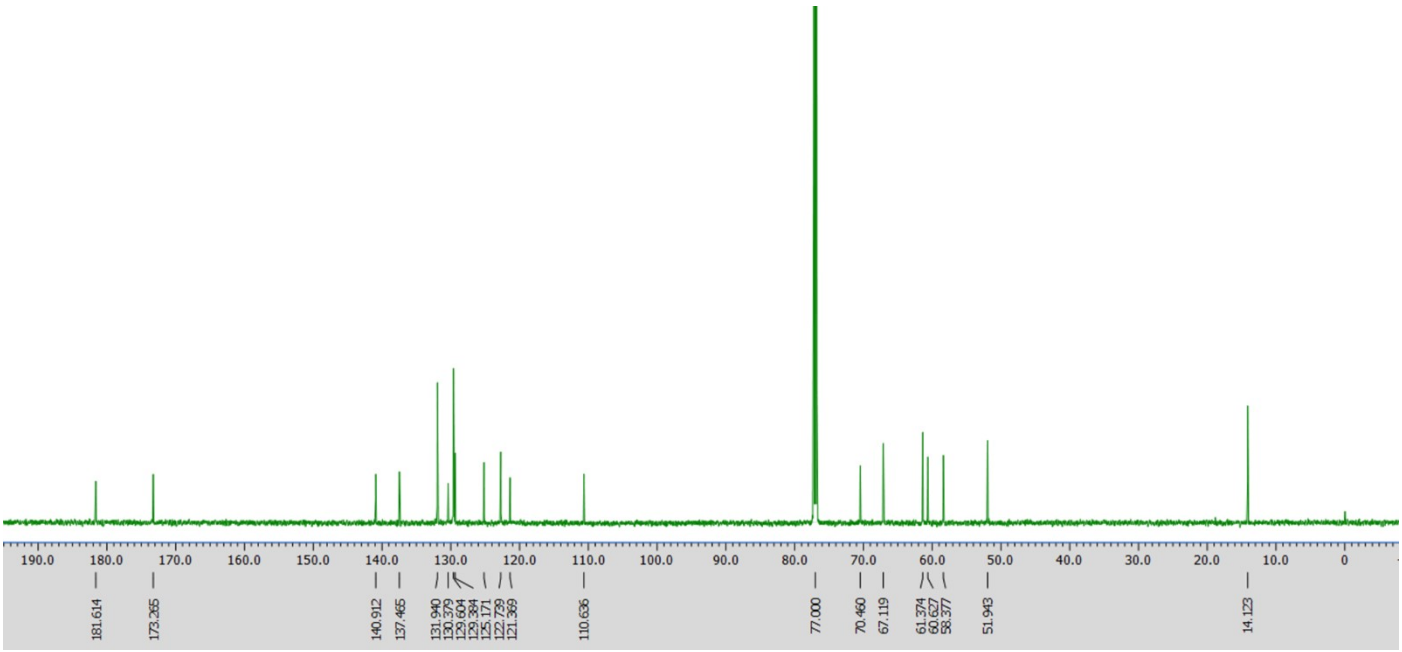
2'-ethyl (2'S,3'R,4'S,5'R)-2-oxo-3'-(4-bromophenyl)-4'-(hydroxymethyl)-spiro[indoline-3,5'-prolinate] (6b)



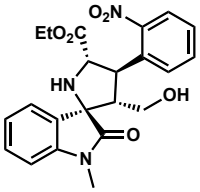
^{1}H-NMR (600 MHz, $CDCl_3$):



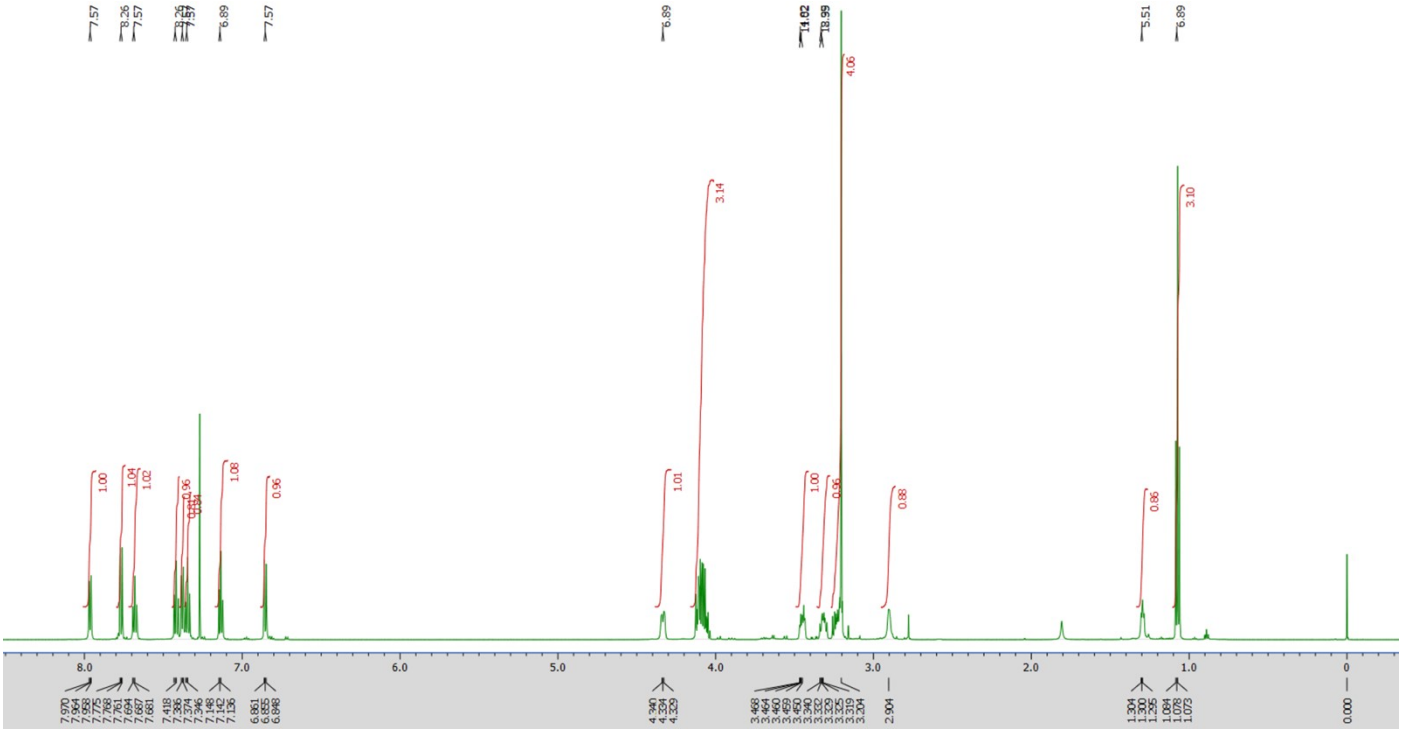
^{13}C-NMR (151 MHz, $CDCl_3$):



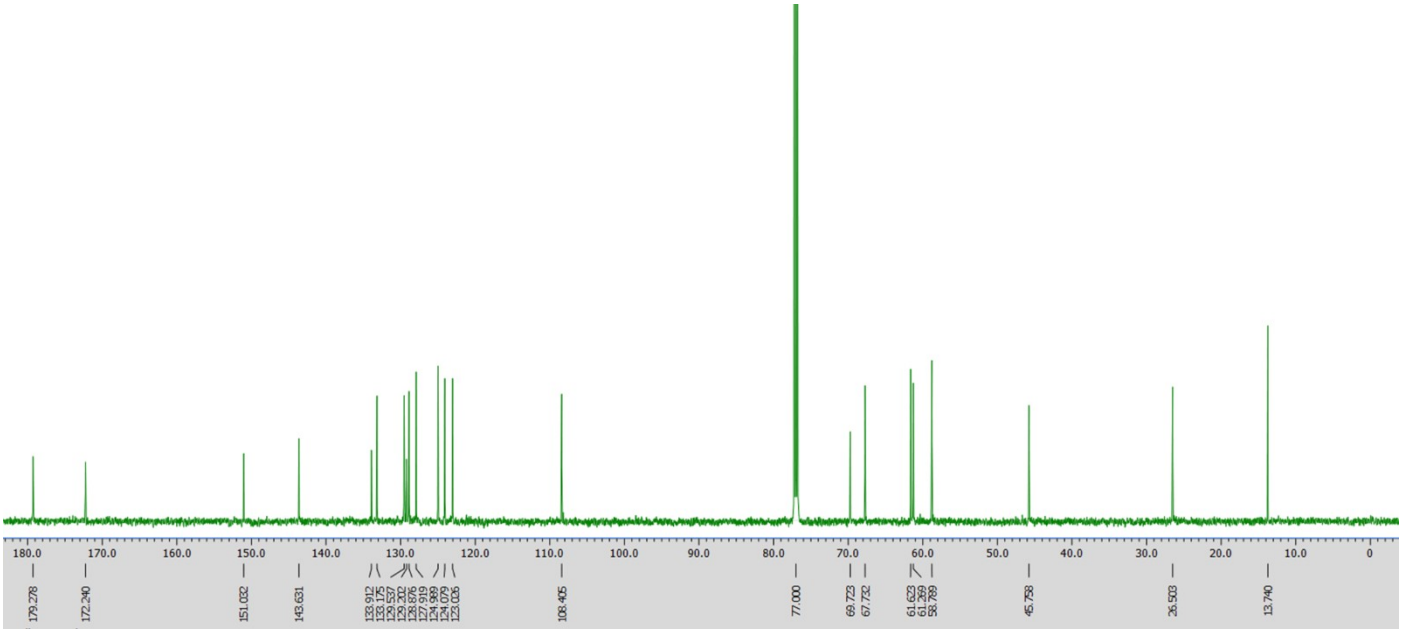
2'-ethyl (2'S,3'R,4'S,5'R)-1-methyl-2-oxo-3'-(2-nitrophenyl)-4'-(hydroxymethyl)-spiro[indoline-3,5'-prolinate] (6c)



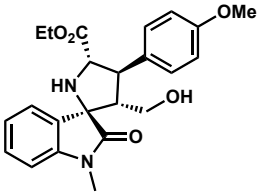
^{1}H-NMR (600 MHz, $CDCl_3$):



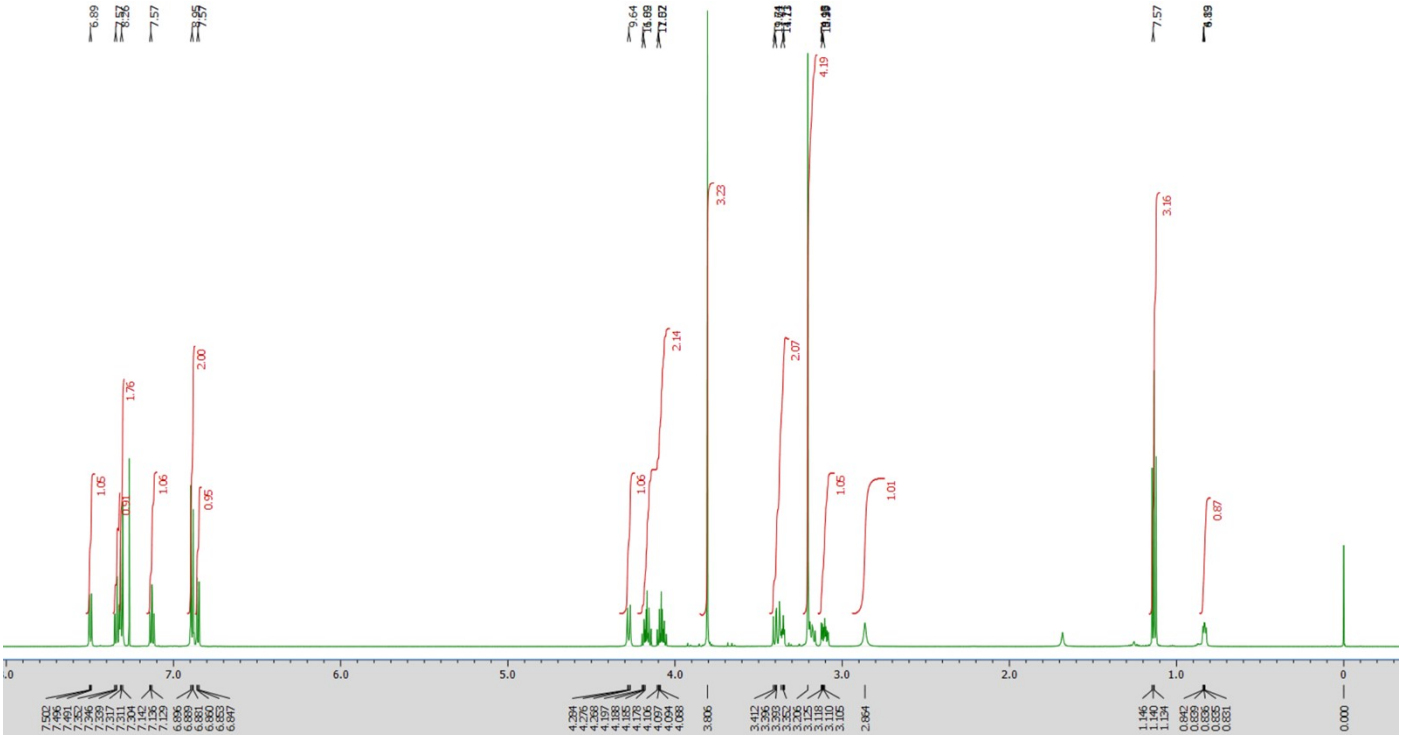
^{13}C-NMR (151 MHz, $CDCl_3$):



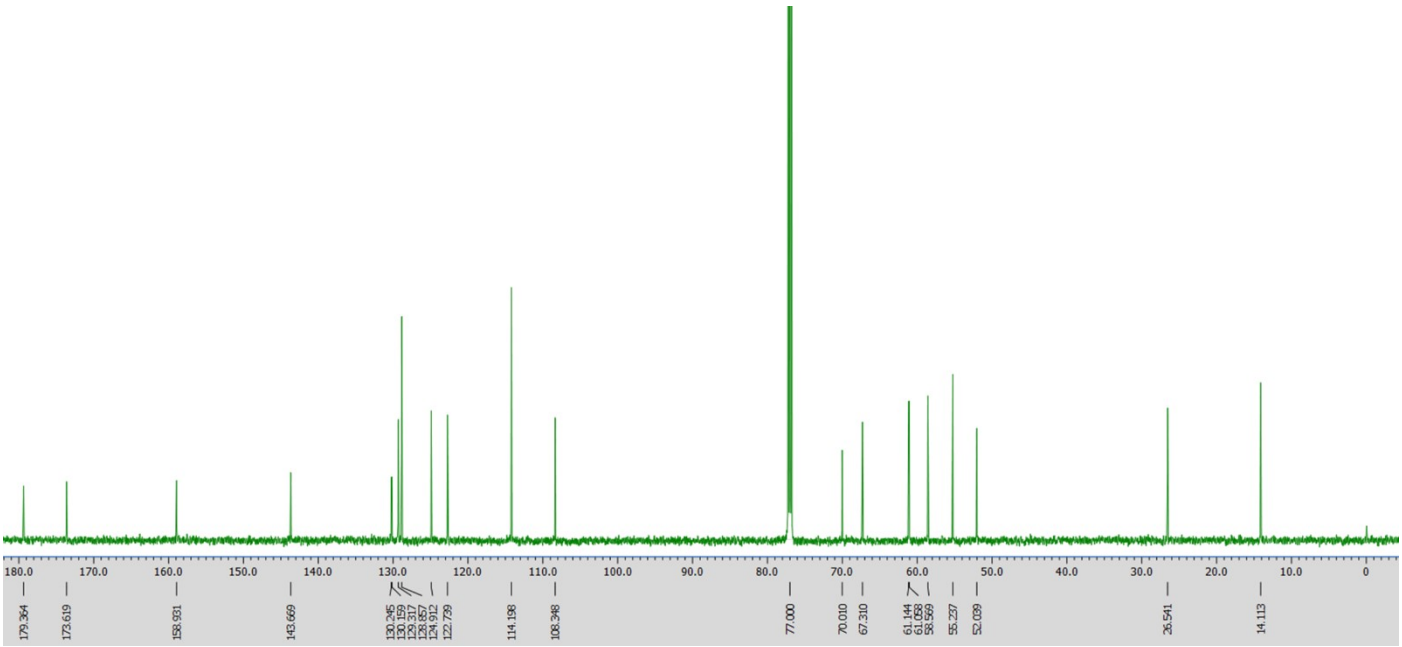
2'-ethyl (2'S,3'R,4'S,5'R)-1-methyl-2-oxo-3'-(4-methoxyphenyl)-4'-(hydroxymethyl)-spiro[indoline-3,5'-prolinate] (6d)



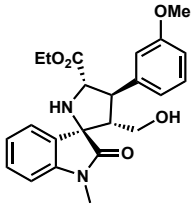
^{1}H-NMR (600 MHz, $CDCl_3$):



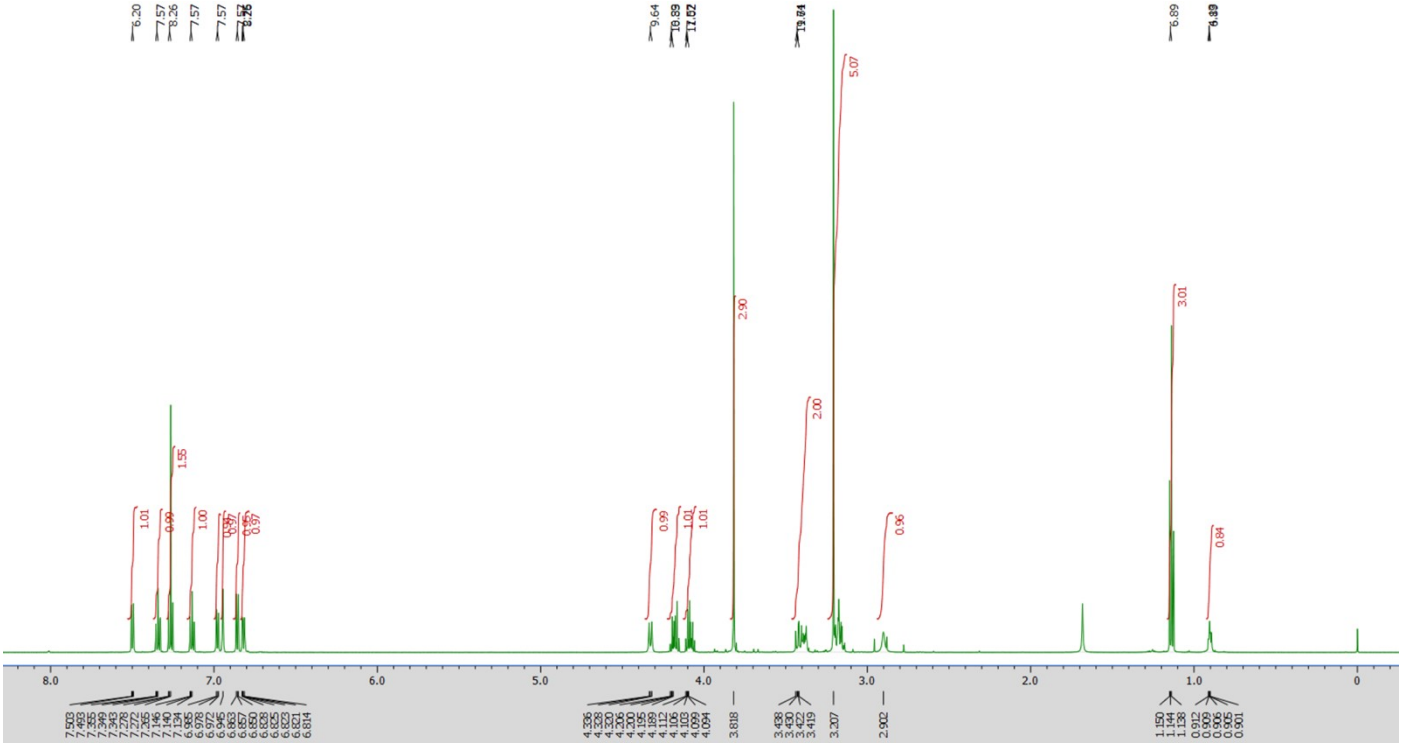
^{13}C-NMR (151 MHz, $CDCl_3$):



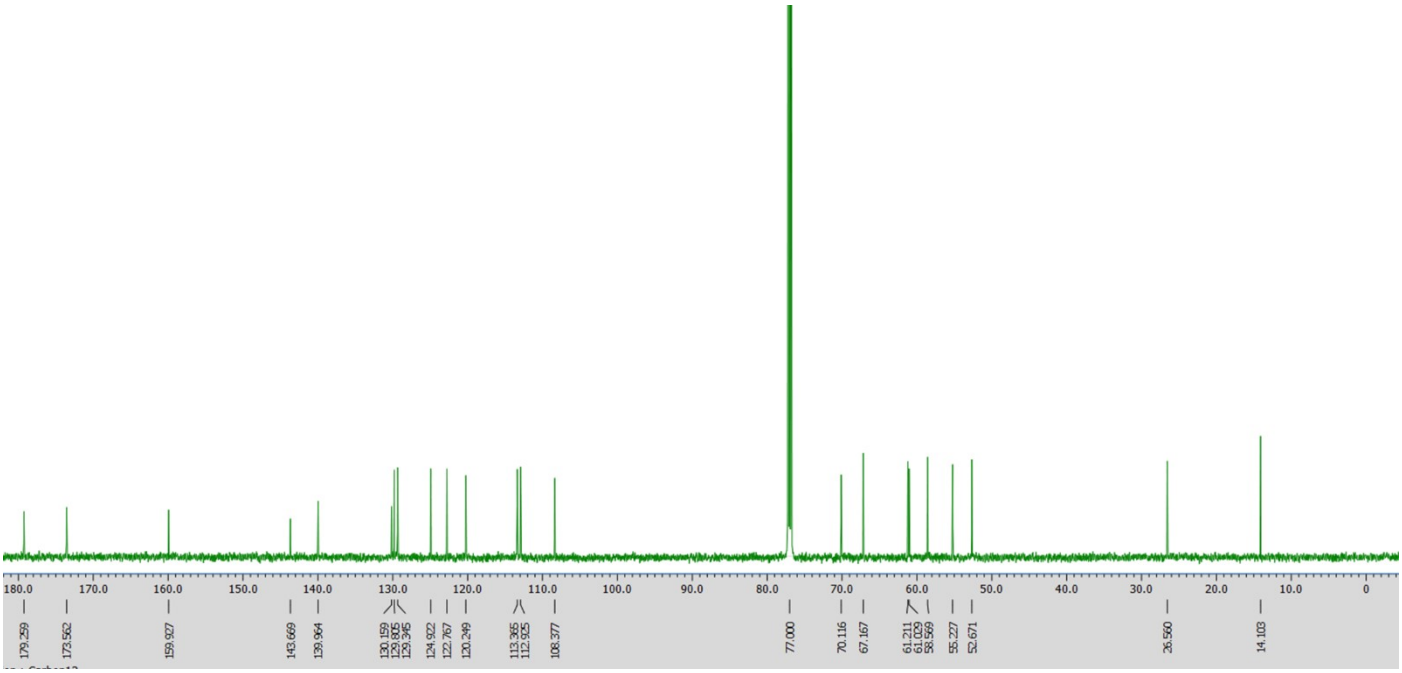
2'-ethyl (2'S,3'R,4'S,5'R)-1-methyl-2-oxo-3'-(3-methoxyphenyl)-4'-(hydroxymethyl)-spiro[indoline-3,5'-prolinate] (6e)



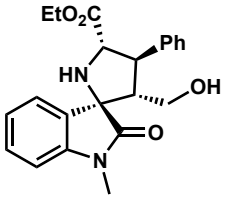
^{1}H-NMR (600 MHz, $CDCl_3$):



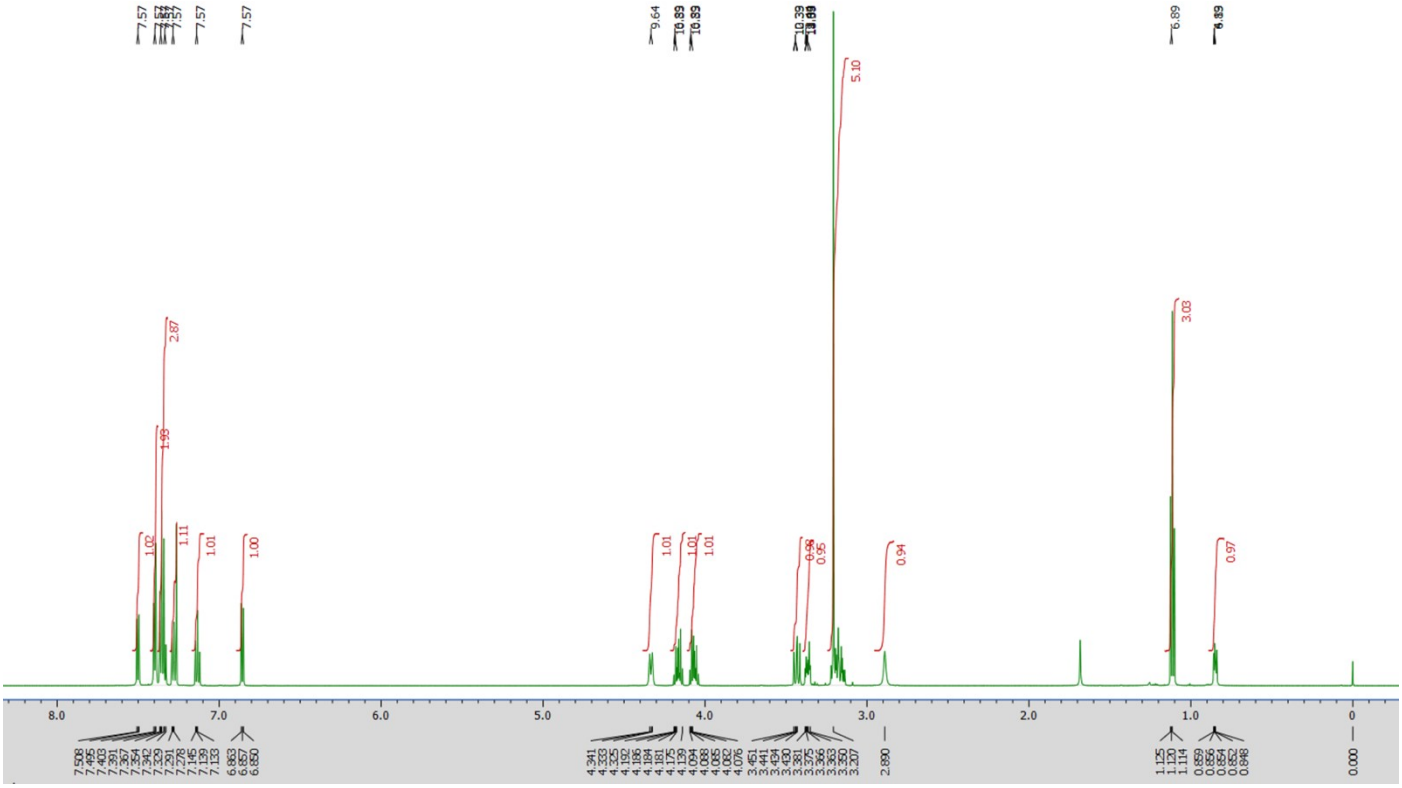
^{13}C-NMR (151 MHz, $CDCl_3$):



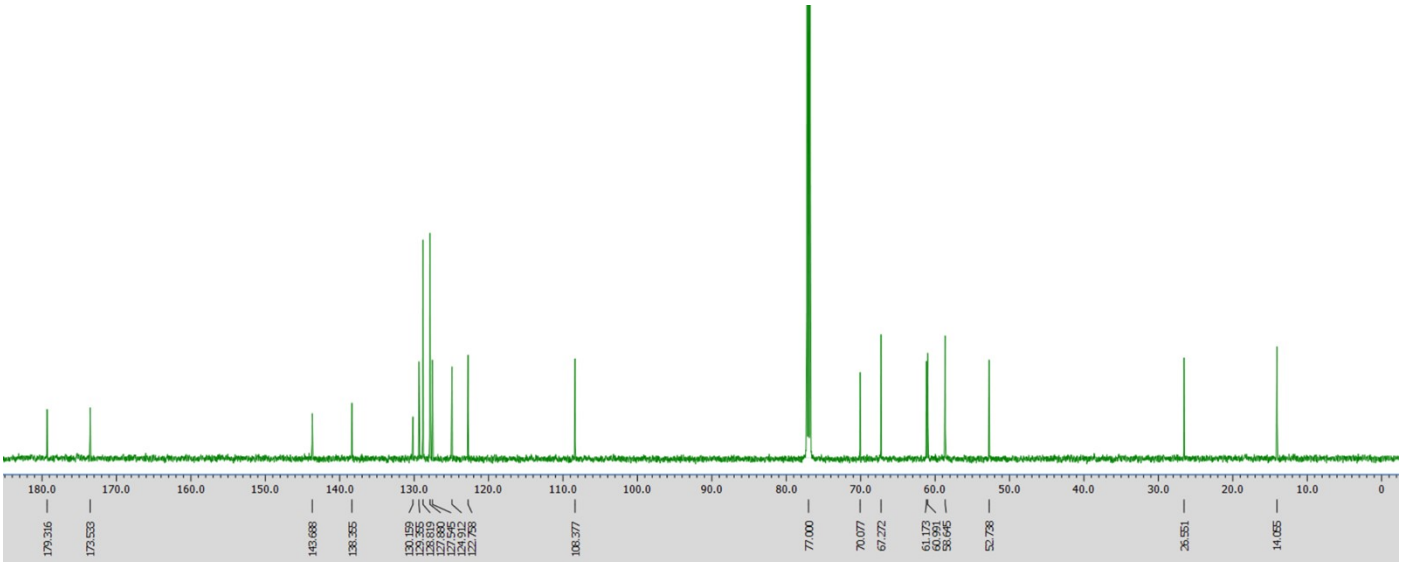
2'-ethyl (2'S,3'R,4'S,5'R)-1-methyl-2-oxo-3'-phenyl-4'-(hydroxymethyl)-spiro[indoline-3,5'- prolinate] (6f)



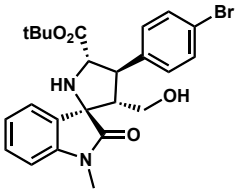
^{1}H-NMR (600 MHz, $CDCl_3$):



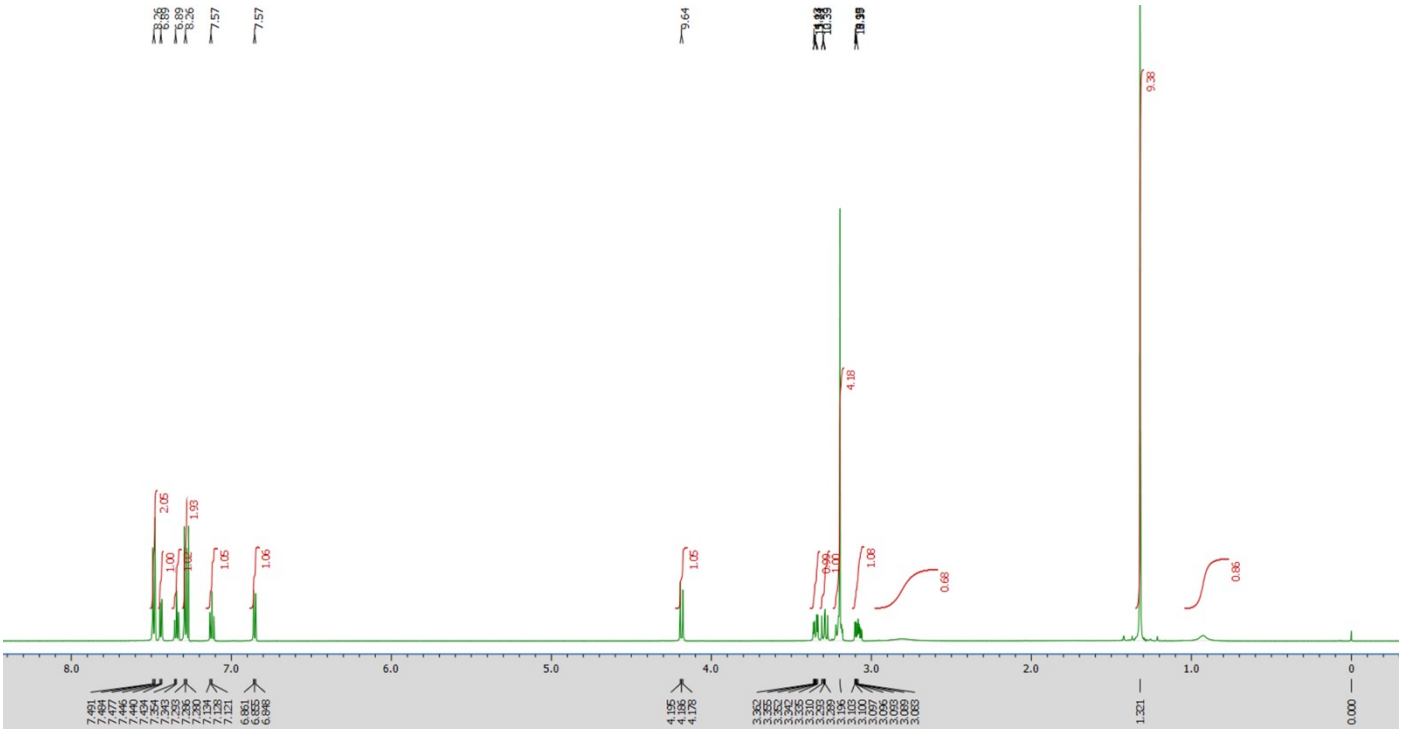
^{13}C-NMR (151 MHz, $CDCl_3$):



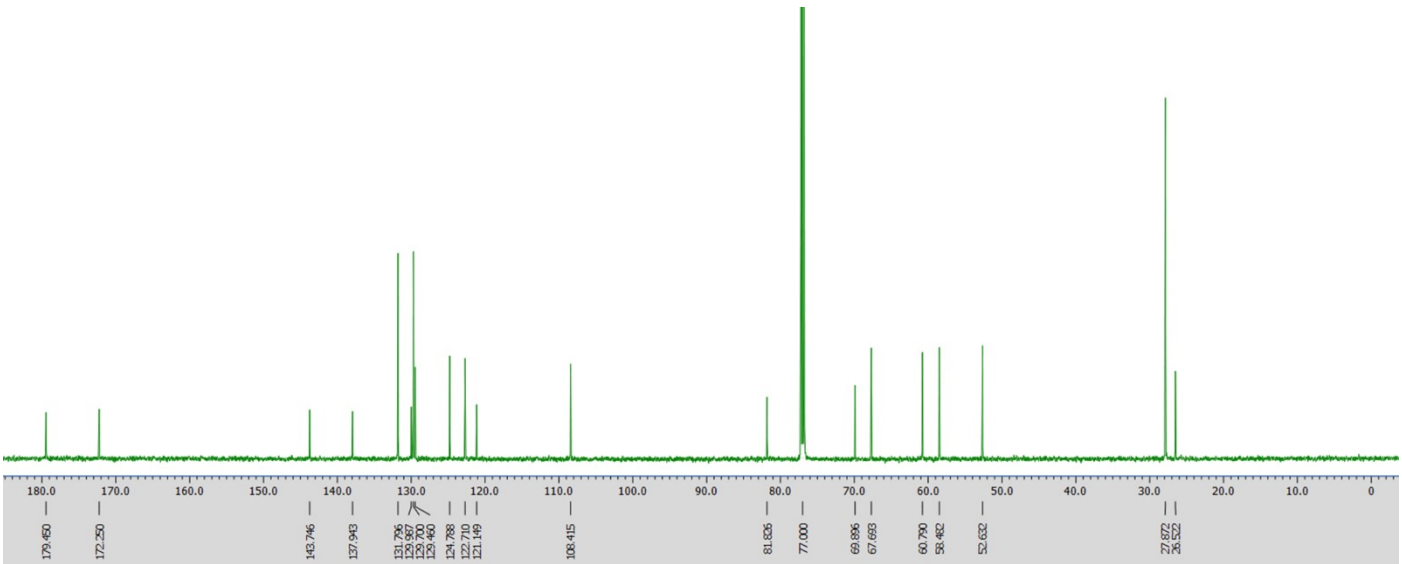
2'-(1,1-dimethylethyl) (2'S,3'R,4'S,5'R)-1-methyl-2-oxo-3'-(4-bromophenyl)-4'-(hydroxymethyl)-spiro[indoline-3,5'-prolinate] (6g)



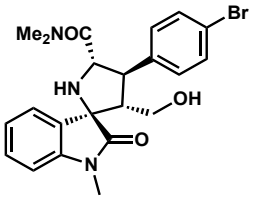
^{1}H-NMR (600 MHz, $CDCl_3$):



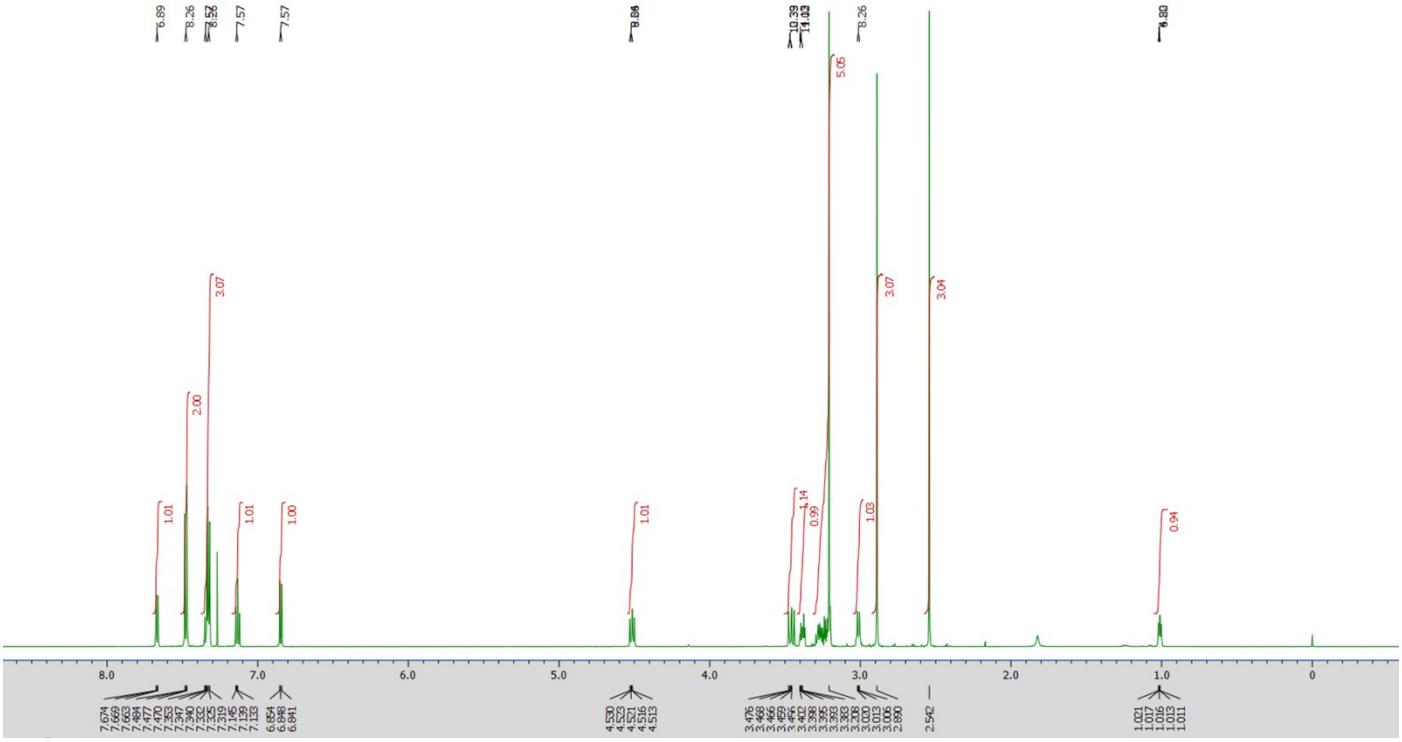
^{13}C-NMR (151 MHz, $CDCl_3$):



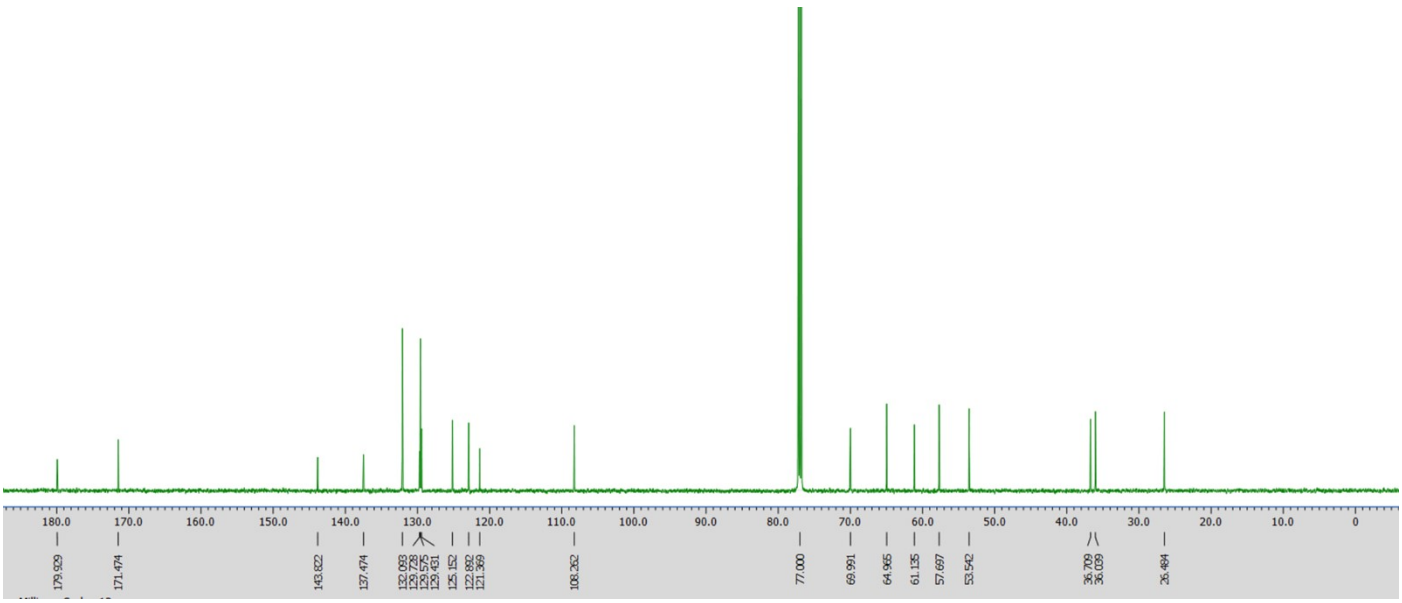
***N,N*-Dimethyl (2'S,3'R,4'S,5'R)-1-methyl-2-oxo-3'-(4-bromophenyl)-4'-(hydroxymethyl)-spiro[indoline-3,5'-prolinamide] (6h)**



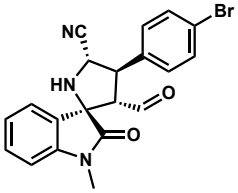
^{1}H-NMR (600 MHz, $CDCl_3$):



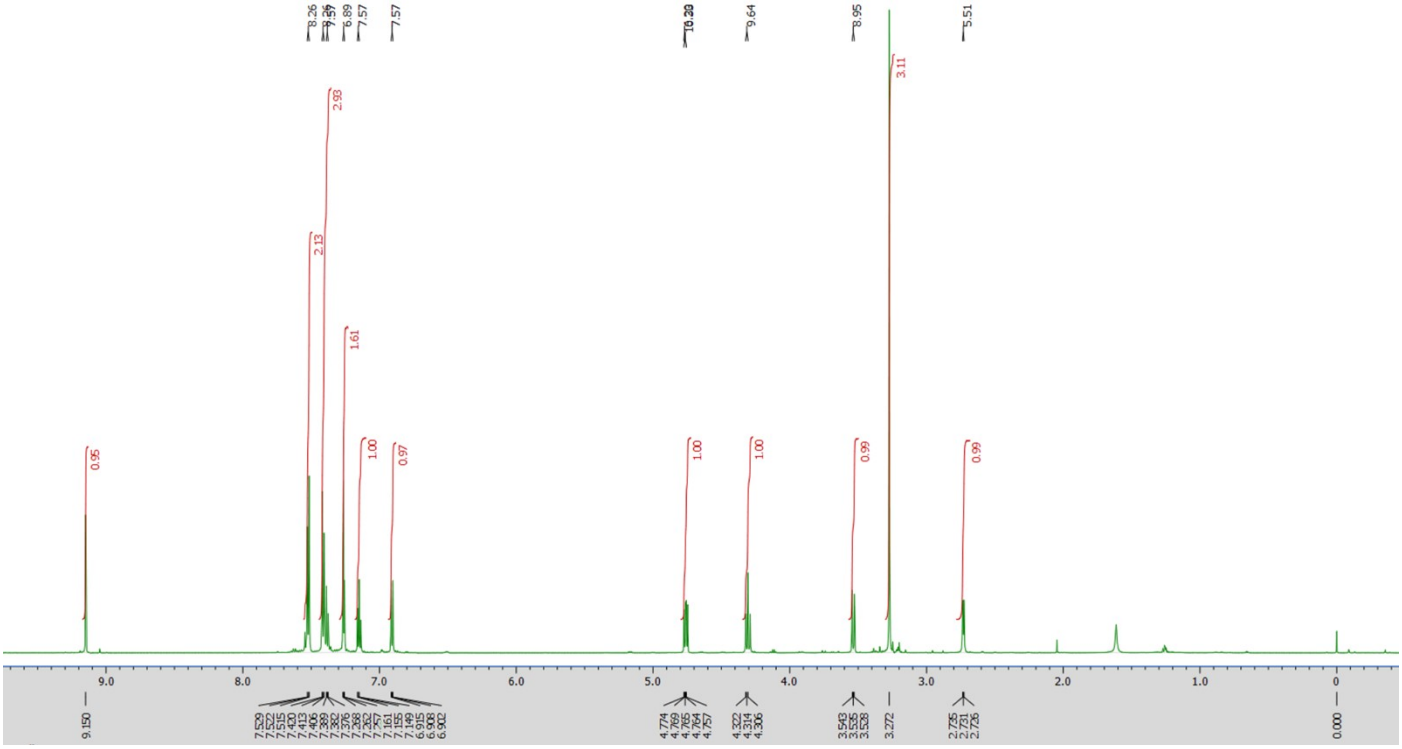
^{13}C-NMR (151 MHz, $CDCl_3$):



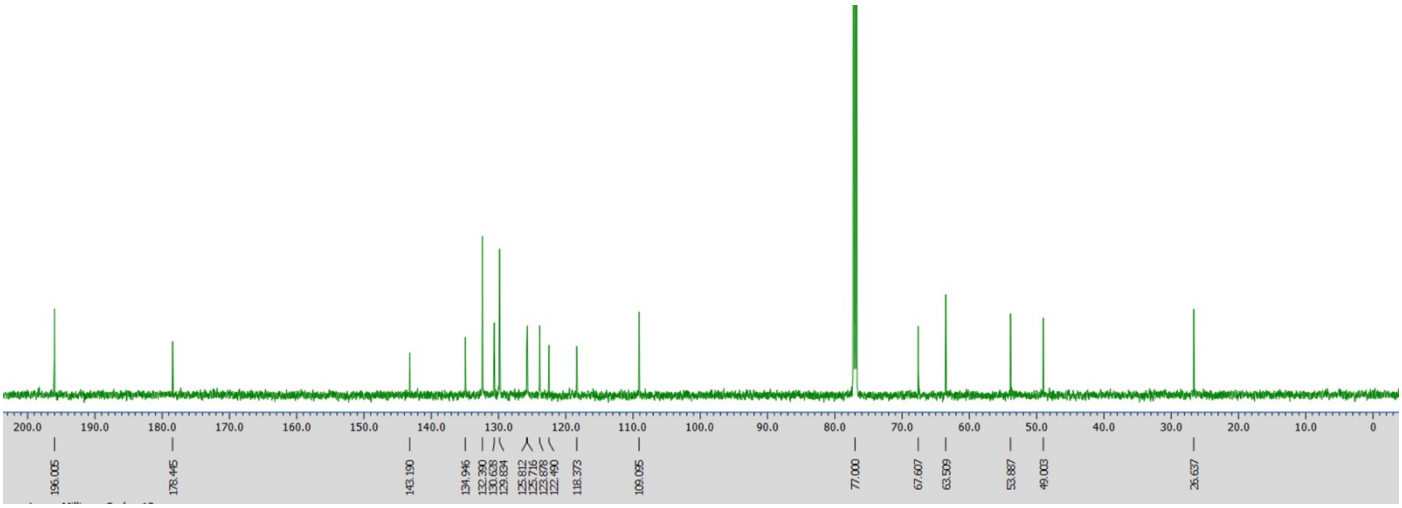
(2'R,3'S,4'R,5'S)-1-methyl-2-oxo-4'-(4-bromophenyl)-5'-carbonitrile-spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde (6i)



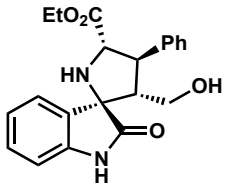
^{1}H-NMR (600 MHz, $CDCl_3$):



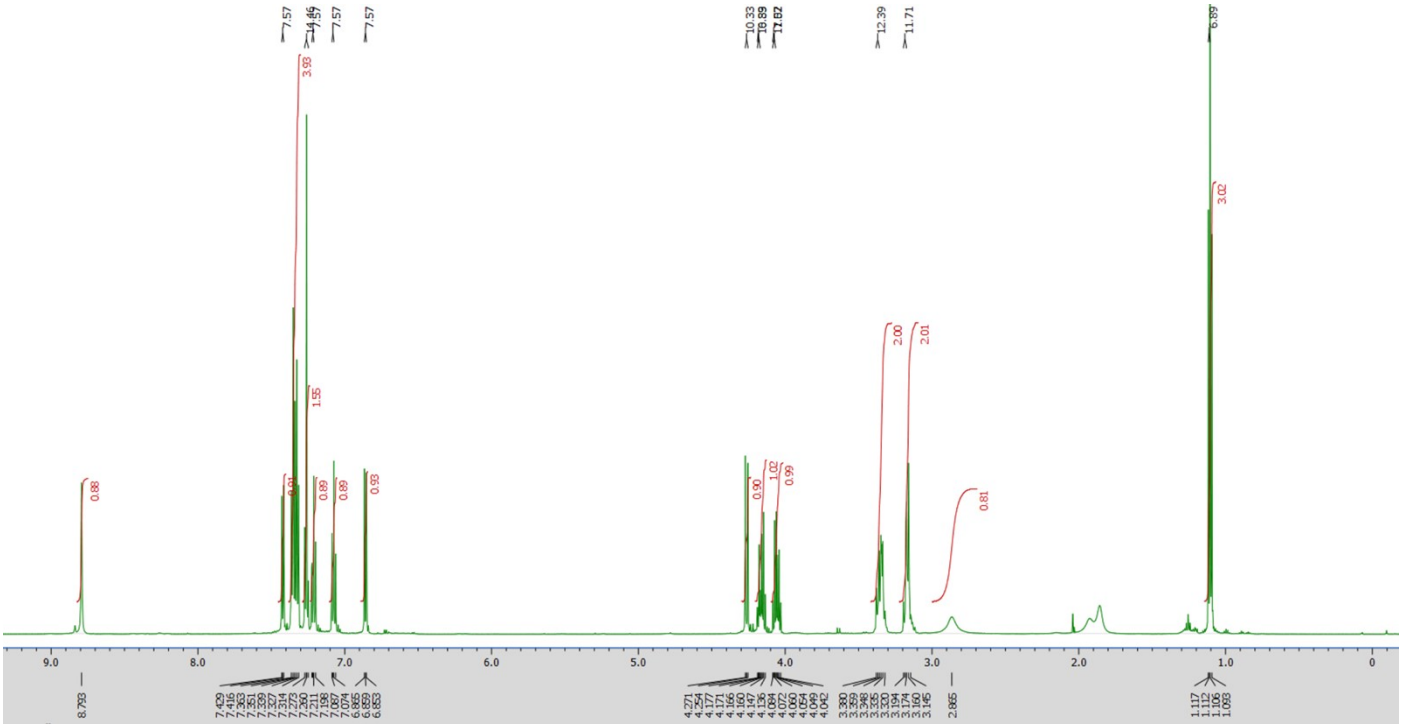
^{13}C-NMR (151 MHz, $CDCl_3$):



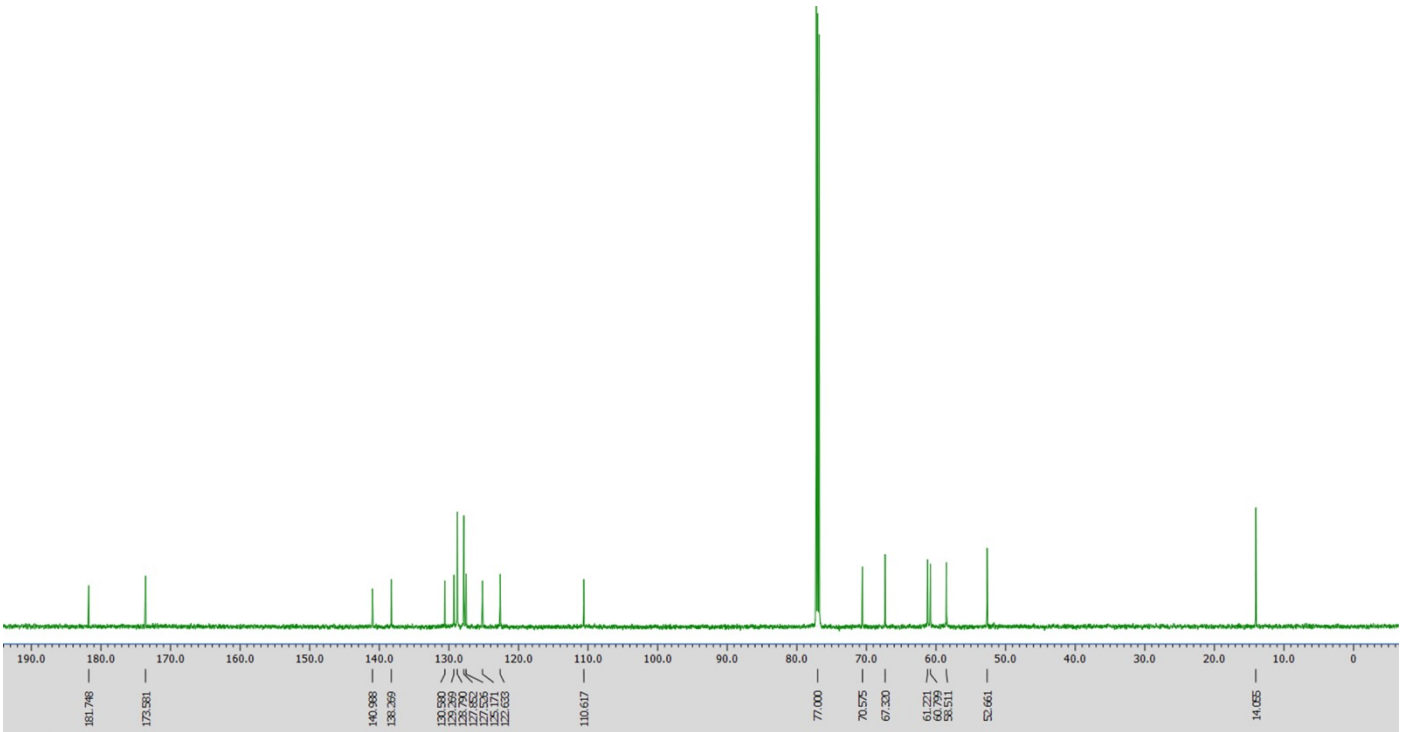
Ethyl (3*R*,3'*S*,4'*R*,5'*S*)-3'-(hydroxymethyl)-1-methyl-2-oxo-4'-phenylspiro[indoline-3,2'-pyrrolidine]-5'-carboxylate (6j)



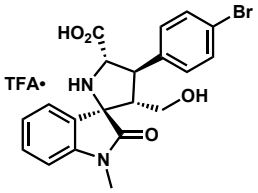
^{1}H-NMR (600 MHz, $CDCl_3$):



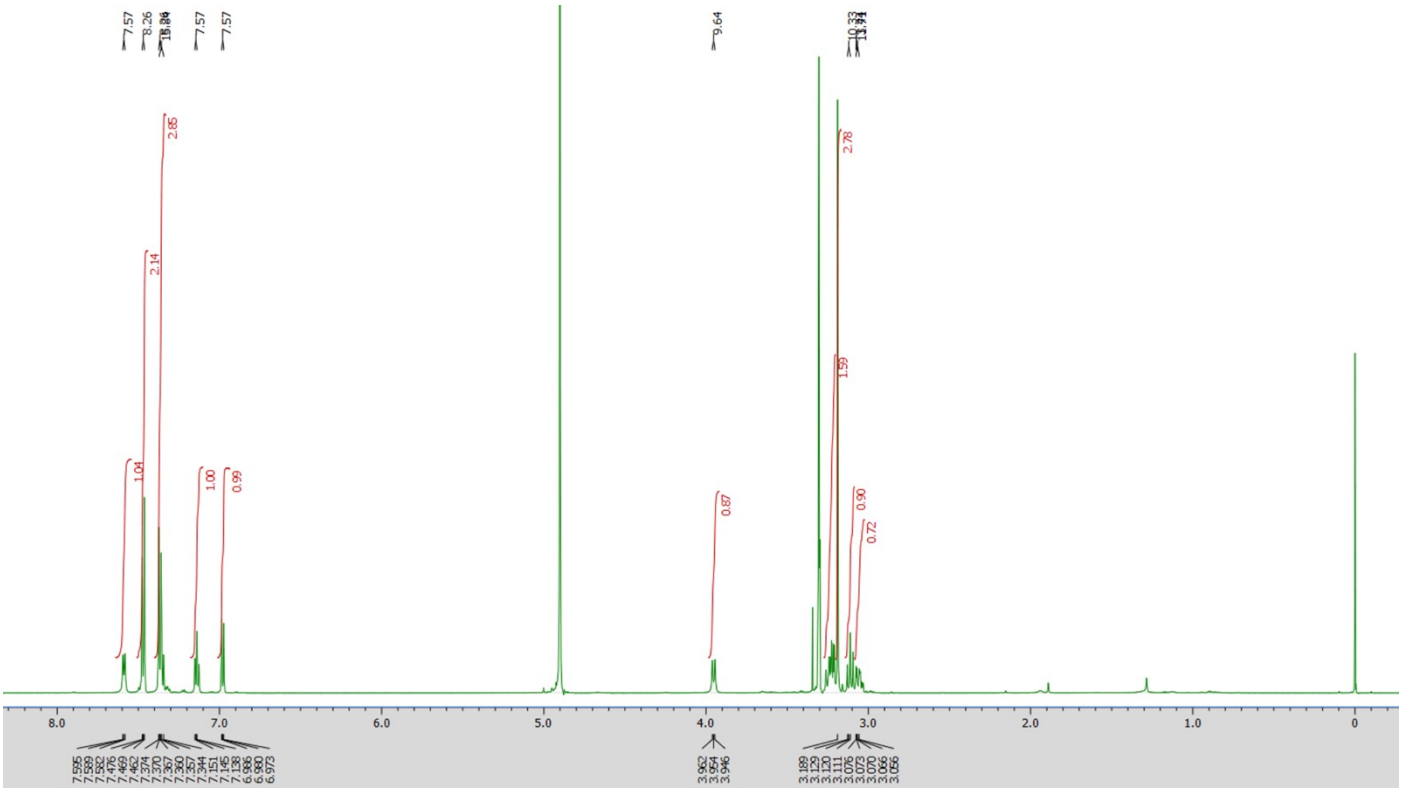
^{13}C-NMR (151 MHz, $CDCl_3$):



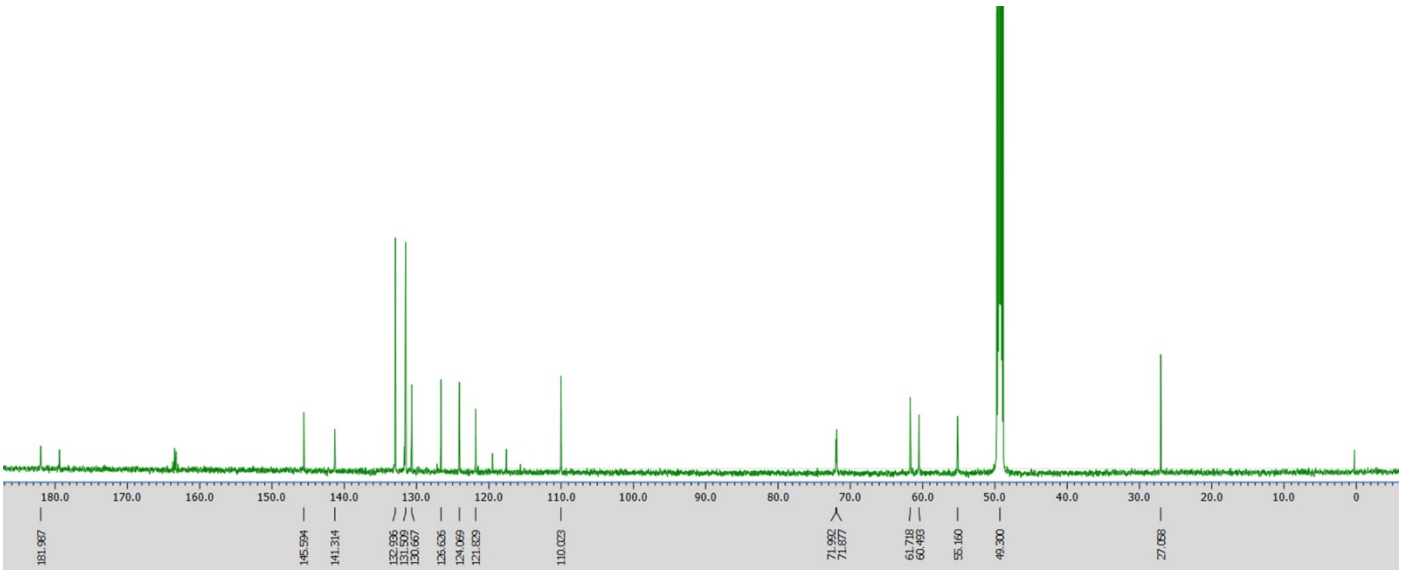
2,2,2-trifluoroacetate salt of (2'S,3'R,4'S,5'R)-1-methyl-2-oxo-3'-(4-bromophenyl)-4'-(hydroxymethyl)-spiro[indoline-3,5'-proline]



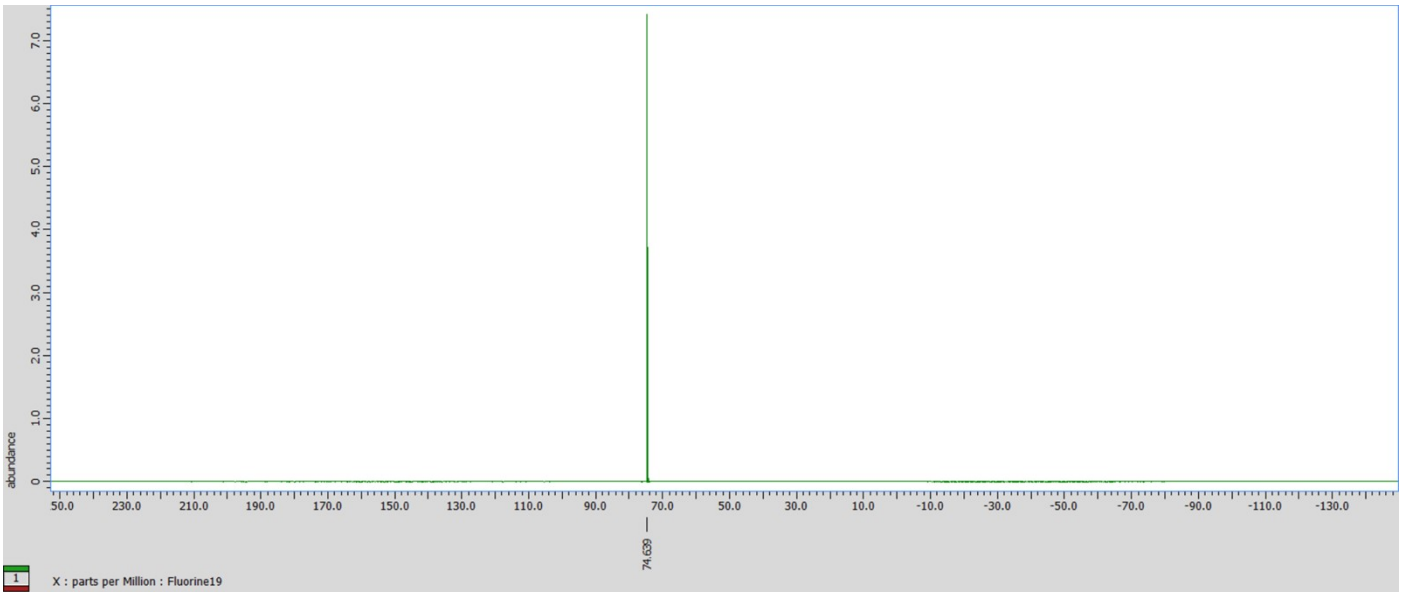
^{1}H-NMR (600 MHz, CD_3OD):



^{13}C-NMR (151 MHz, CD_3OD):

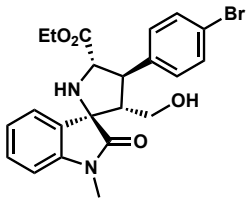


^{19}F NMR (564 MHz, CD_3OD)

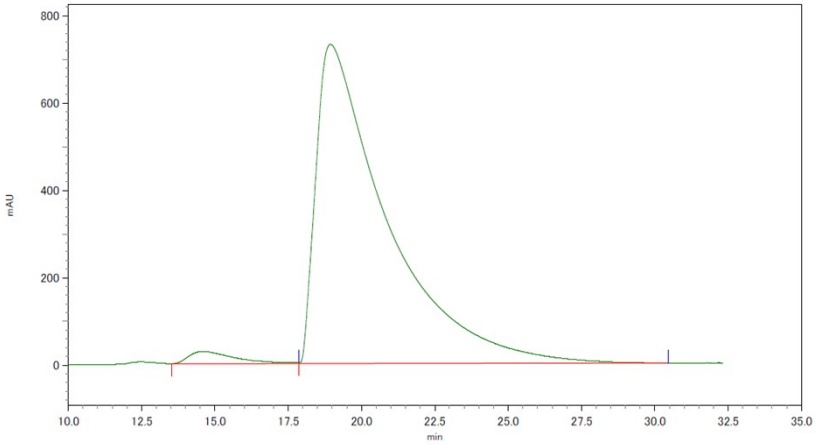


HPLC traces for the products / authentic racemic samples

6a



Chiralpak OD-H, hexane/2-propanol = 90:10, 1.0 mL min^{-1}



1: 254 nm, 8 nm	Retention time (min)	Area	Area%
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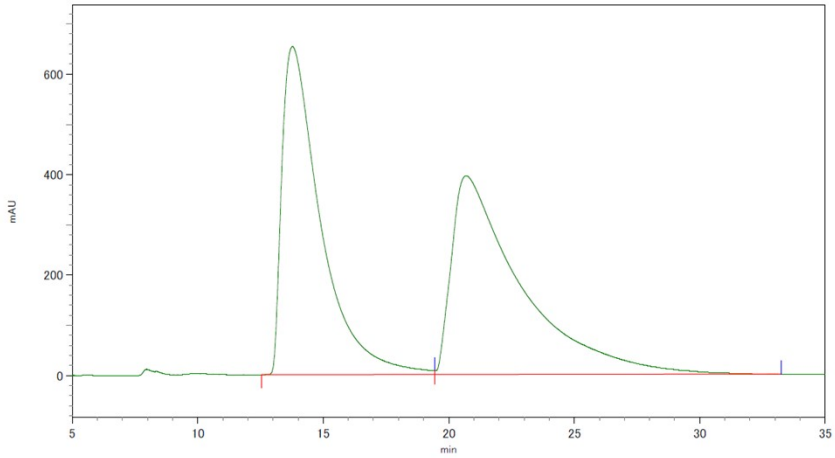
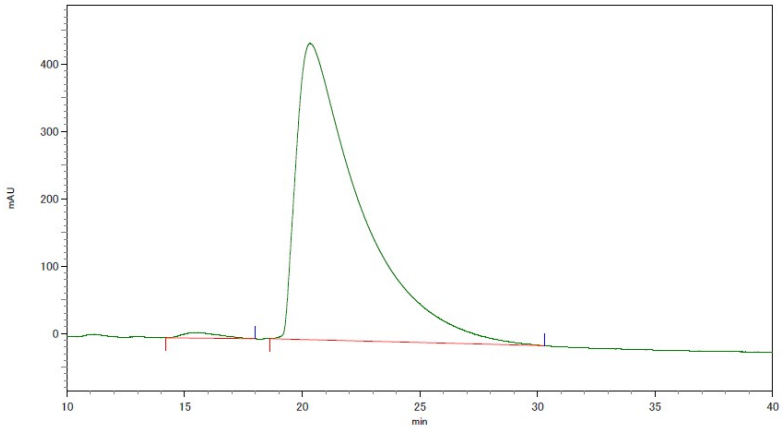
	18.927	122391987	97.58
	Total	125428935	100.00



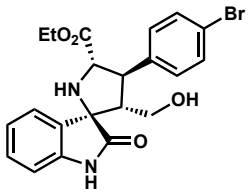
1: 254 nm, 8 nm	Retention time (min)	Area	Area%
	13.765	70151110	48.01
	20.691	75952762	51.99
	Total	146103871	100.00

6a derivatized from CN-product **6i**

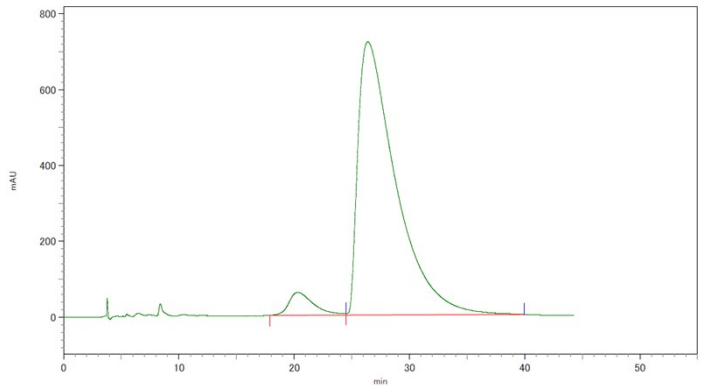


1: 254 nm, 8 nm	Retention time (min)	Area	Area%
	17.903	908610	1.09
	20.320	82214685	98.91
	Total	83123294	100.00

6b



Chiralpak OD-H, hexane/2-propanol = 90:10, 1.0 mL min^{-1}



1: 254 nm, 8 nm	Retention time (min)	Area	Area%
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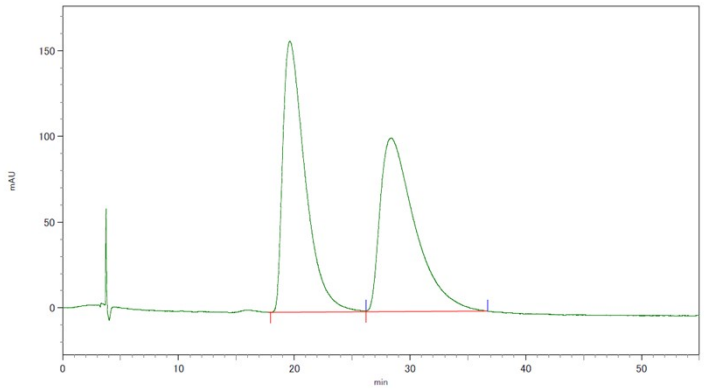
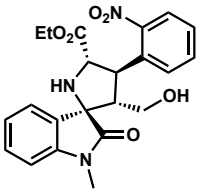
	26.361	164077714	94.77
Total		173139276	100.00

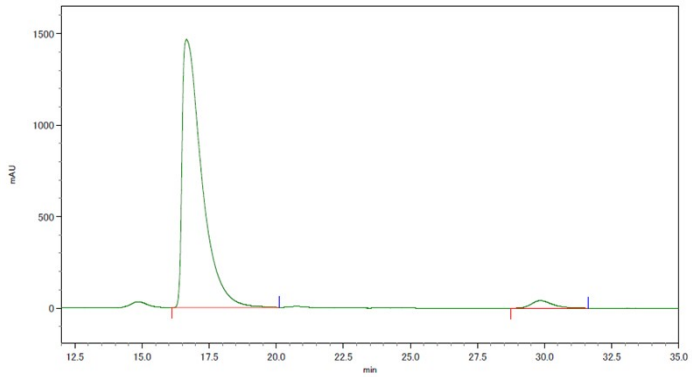


1: 254 nm, 8 nm	Retention time (min)	Area	Area%
	19.620	21274744	50.20
	28.336	21106758	49.80
Total		42381502	100.00

6c



Chiralpak IA, hexane/2-propanol = 80:20, 1.0 mL min^{-1}



1: 270 nm, 8 nm	Retention time (min)	Area	Area%
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	29.834	2236750	2.93
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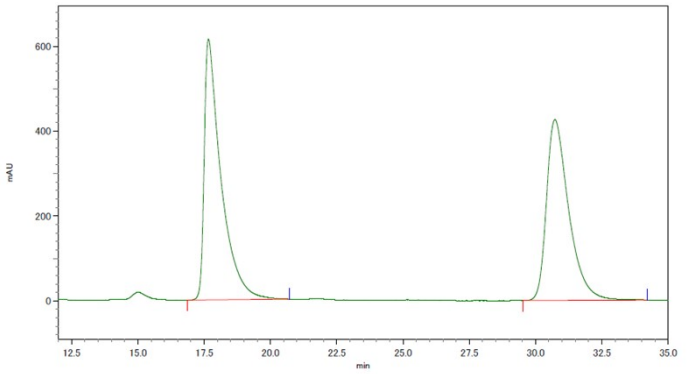
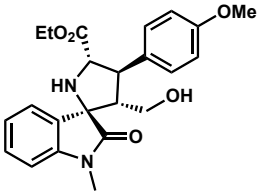
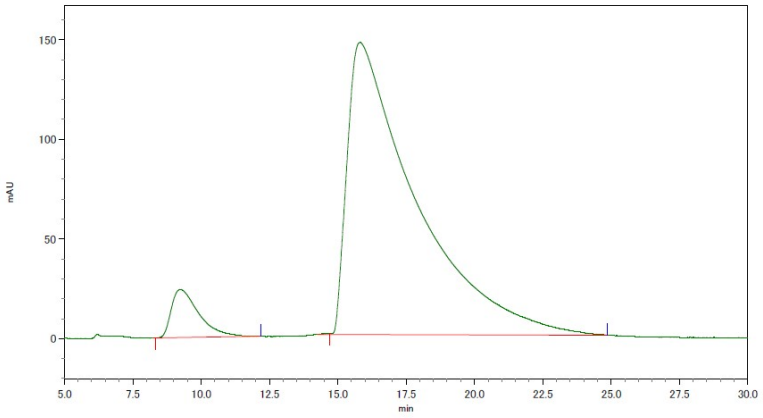


1: 270 nm, 8 nm	Retention time (min)	Area	Area%
	17.659	27010831	52.06
	30.723	24877846	47.94
Total		51888677	100.00

6d



Chiralpak OD-H, hexane/2-propanol = 80:20, 1.0 mL min^{-1}



1: 270 nm, 8 nm	Retention time (min)	Area	Area%
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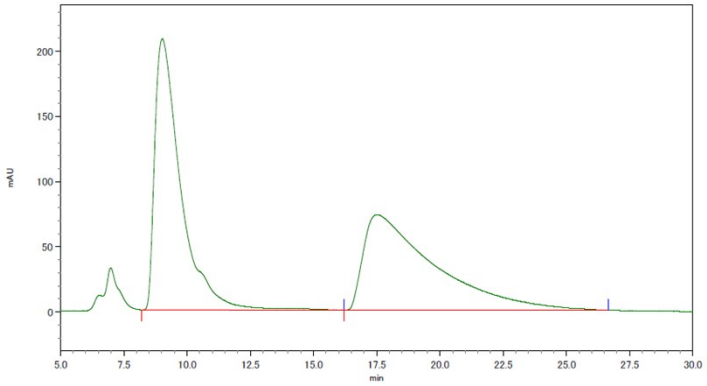
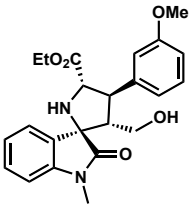
	15.808	25492592	93.78
Total		27183815	100.00

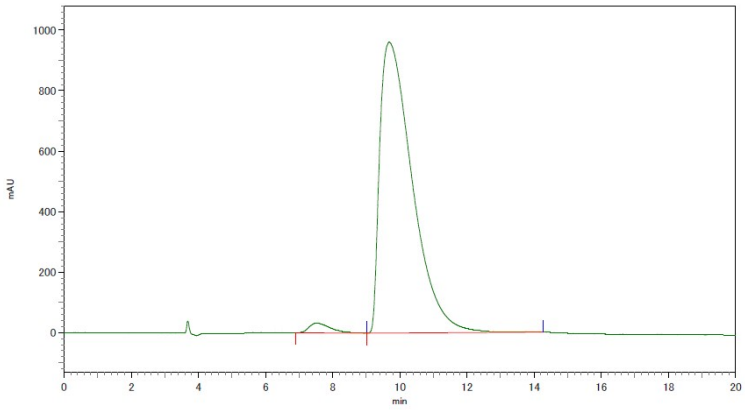


1: 270 nm, 8 nm	Retention time (min)	Area	Area%
	9.012	14817810	51.00
	17.504	14235655	49.00
Total		29053465	100.00

6e



Chiralpak OD-H, hexane/2-propanol = 80:20, 1.0 mL min^{-1}



1: 254 nm, 8 nm	Retention time (min)	Area	Area%
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	9.674	64709491	97.88
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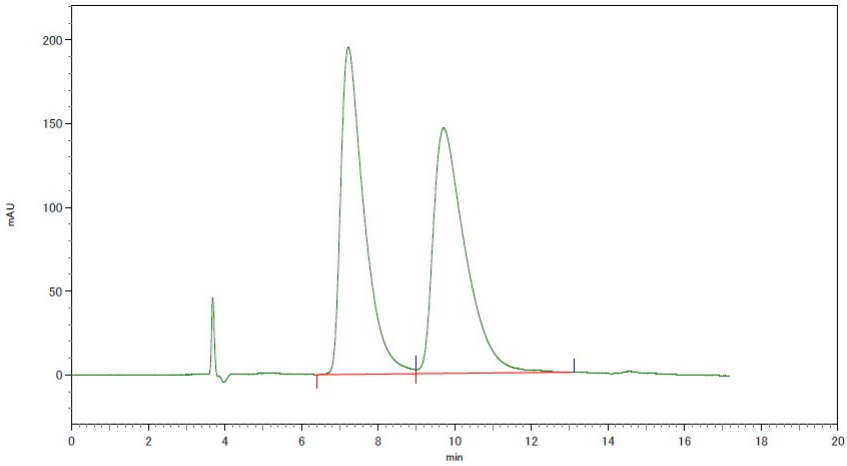
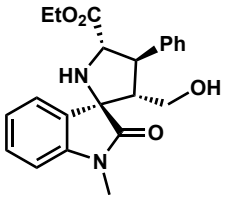
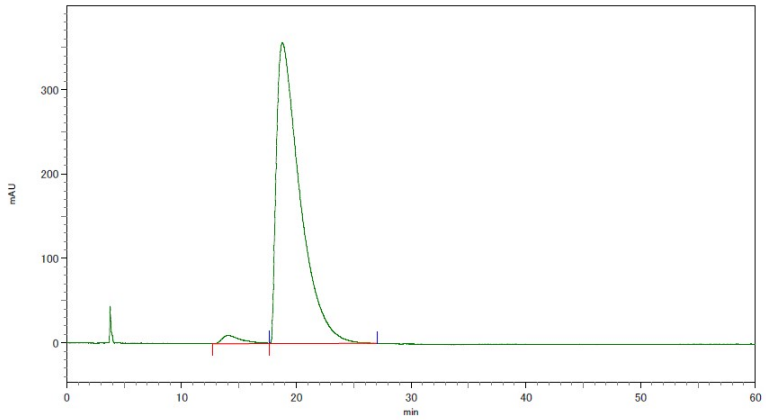


1: 254 nm, 8 nm	Retention time (min)	Area	Area%
	7.217	8270119	49.32
	9.705	8496653	50.68
Total		16766772	100.00

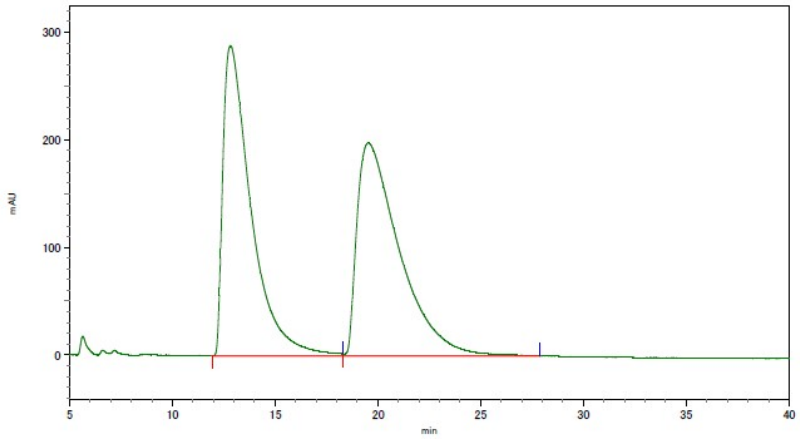
6f



Chiralpak OD-H, hexane/2-propanol = 90:10, 1.0 mL min^{-1}

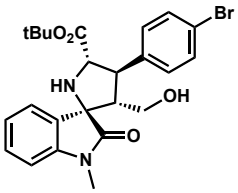


1: 240 nm, 8 nm	Retention time (min)	Area	Area%
	14.077	1193342	2.30
	18.771	50768379	97.70
Total		51961722	100.00

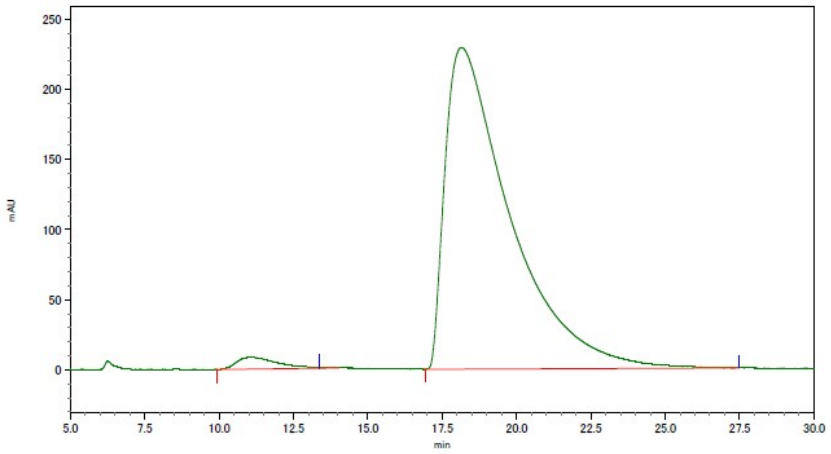


1: 254 nm, 8 nm	Retention time (min)	Area	Area%
	12.828	27364353	49.09
	19.517	28376204	50.91
Total		55740557	100.00

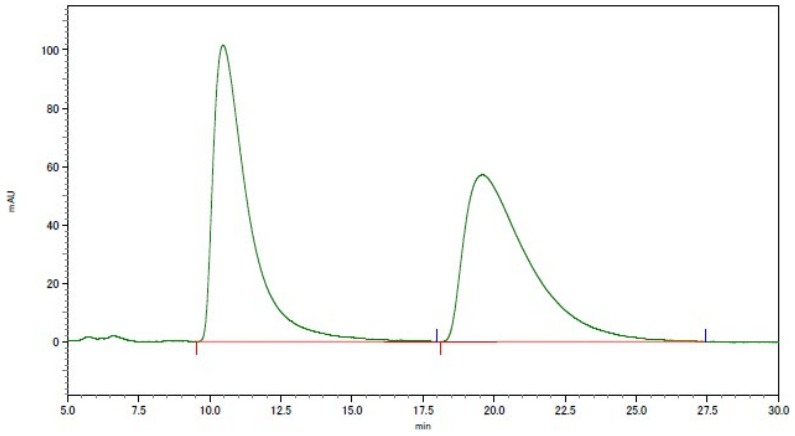
6g



Chiralpak OD-H, hexane/2-propanol = 90:10, 1.0 mL min^{-1}

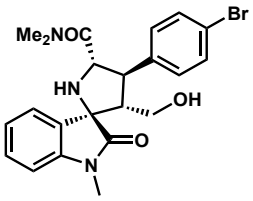


1: 270 nm, 8 nm	Retention time (min)	Area	Area%
	11.069	789403	2.21
	18.140	34857249	97.79
Total		35646653	100.00

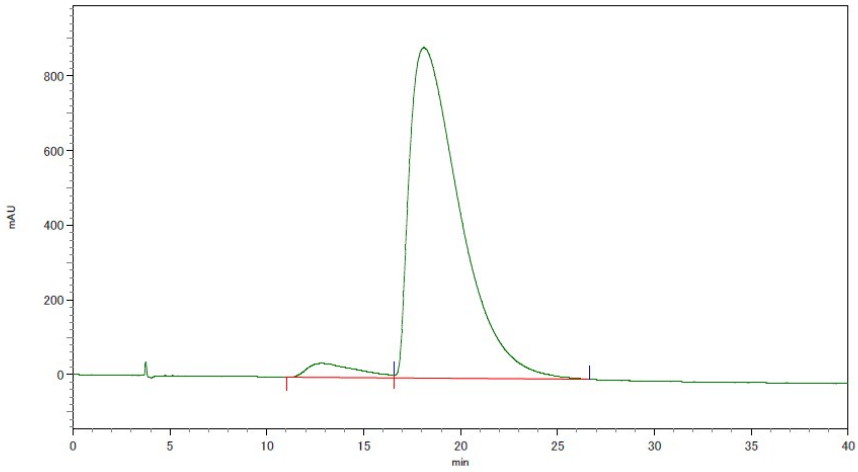


1: 270 nm, 8 nm	Retention time (min)	Area	Area%
	10.459	8744816	49.35
	19.588	8974277	50.65
Total		17719093	100.00

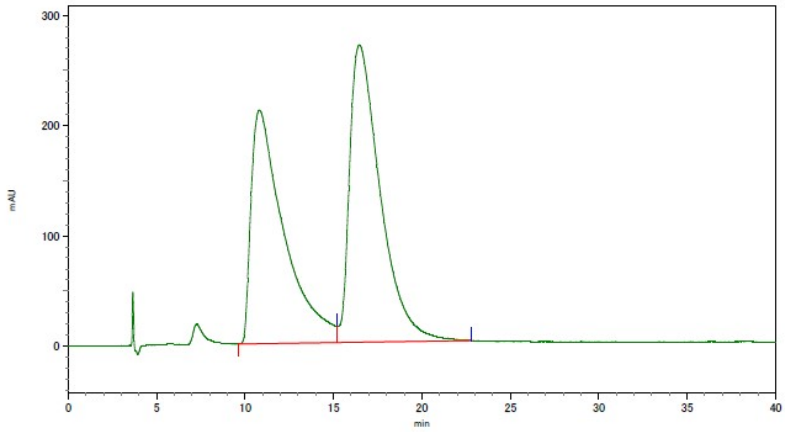
6h



Chiralpak OD-H, hexane/2-propanol = 90:10, 1.0 mL min^{-1}



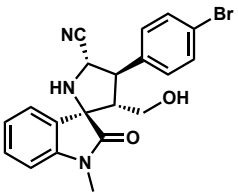
1: 254 nm, 8 nm	Retention time (min)	Area	Area%
	12.836	6801993	4.10
	18.105	159251633	95.90
Total		166053626	100.00



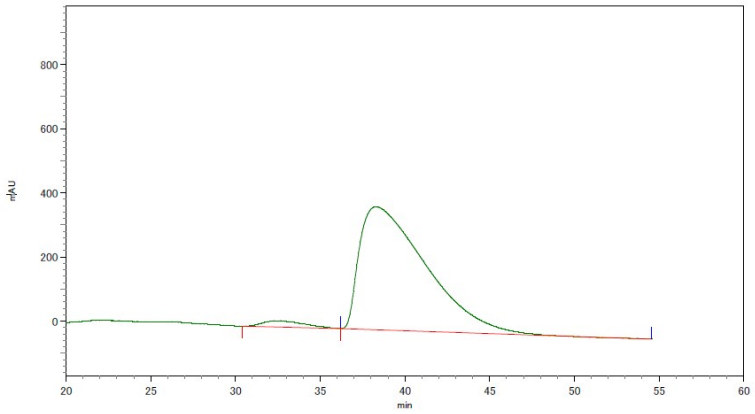
1: 254 nm, 8 nm	Retention time (min)	Area	Area%
	10.810	27418652	45.75
	16.454	32518726	54.25
Total		59937378	100.00

6i

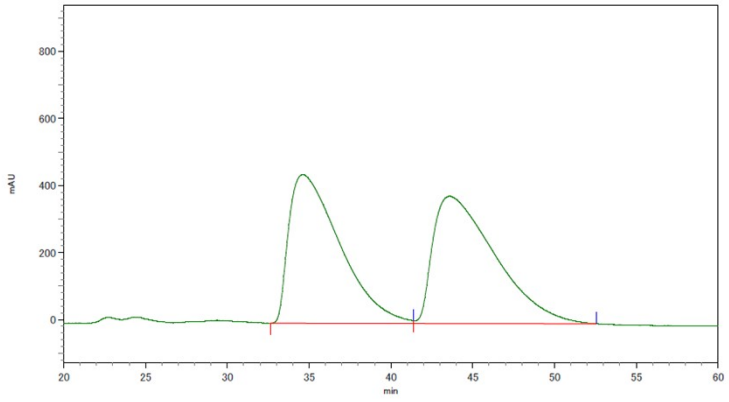
Enantiomeric excess was determined by HPLC analysis of the alcohol as shown below.



Chiralpak OD-H, hexane/2-propanol = 90:10, 1.0 mL min^{-1}

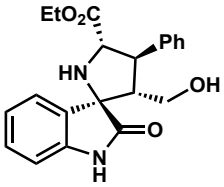


1: 220 nm, 8 nm	Retention time (min)	Area	Area%
	32.395	3340198	3.10
	38.368	104517077	96.90
Total		107857275	100.00

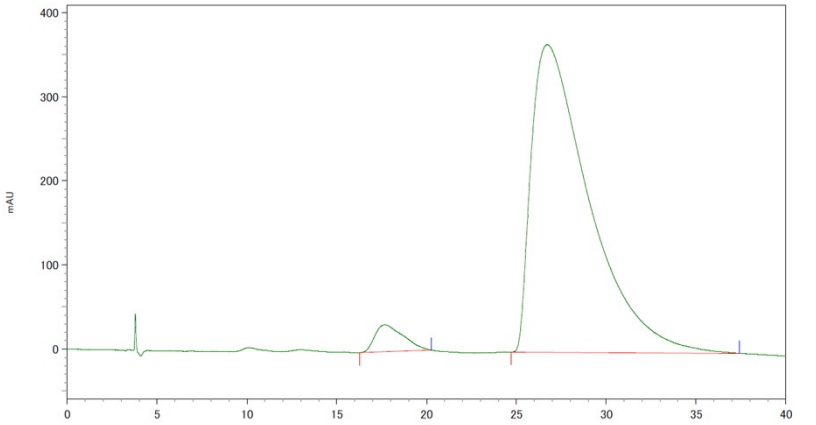


1: 220 nm, 8 nm	Retention time (min)	Area	Area%
	34.607	96189928	48.98
	43.651	100184970	51.02
Total		196374898	100.00

6j

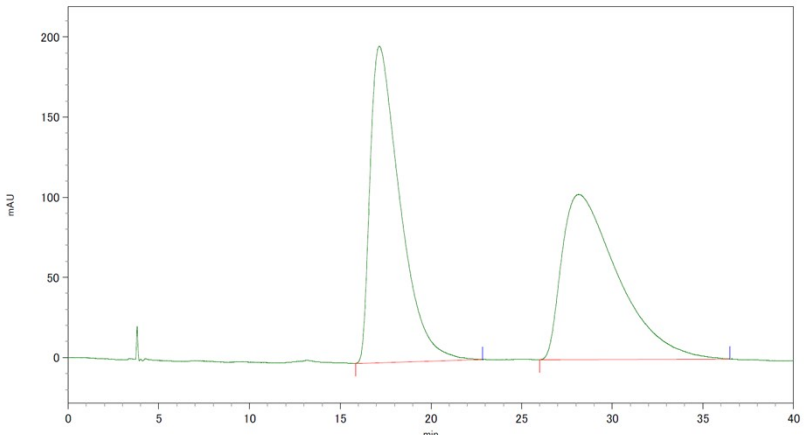


Chiralpak OD-H, hexane/2-propanol = 90:10, 1.0 mL min^{-1}



1: 254 nm, 8 nm

保持時間	Retention time (min)	面積	Area	面積%	Area%
17.658		3494132		4.09	
26.703		82018918		95.91	
Total		85513050		100.00	



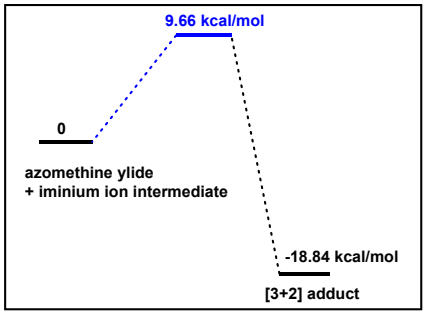
1: 254 nm, 8

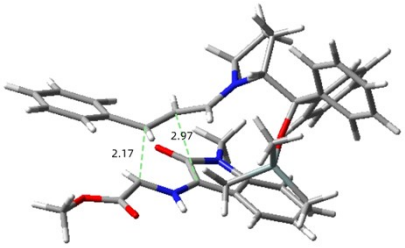
保持時間	Retention time (min)	面積	Area	面積%	Area%
17.153		22598672		50.53	
28.140		22121081		49.47	
Total		44719753		100.00	

Theoretical calculation study

For the solvent effect analysis of the cycloaddition, calculation was performed based on density functional theory (DFT) with M06-2X/6-31G(d,p) method. The solute electron density (SMD) model was applied to simulate the solvent effect. The geometry of the reaction states including initial state (INI), transitional state (TS), and final state (FIN) were optimized. Their Gibbs free energies of [3+2] cycloadditions were computed, as shown in Table S1.

In addition to the transition state structure calculation mentioned in the main text, we also calculated the transition state for minor enantiomer formation in water. In this case, much higher activation energy was observed as shown below.





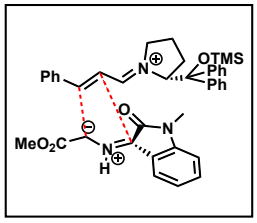


Table S1. The M06-2X/6-31G(d,p) computed energies, enthalpies, Gibbs free energies and imaginary frequencies for the [3+2] cycloadditions

Reaction states (solvent)	Energies	Enthalpies	Gibbs free energies	Number of imaginary frequencies	Imaginary frequencies
INI (THF)	-2342.990779	-2342.989834	-2343.118312	0	-
TS (THF)	-2342.984199	-2342.983255	-2343.108123	1	-317.9144
FIN (THF)	-2343.023416	-2343.022472	-2343.148123	0	-
INI (water)	-2342.980350	-2342.979406	-2343.108346	0	-
TS (water)	-2342.971974	-2342.971030	-2343.094469	1	-362.0139
FIN (water)	-2343.015995	-2343.015051	-2343.141867	0	-
INI (minor enantiomer)	-2342.971185	-2342.970240	-2343.100574	0	-
TS (minor enantiomer)	-2342.960749	-2342.959805	-2343.085188	1	-319.3003
FIN (minor enantiomer)	-2343.008353	-2343.007409	-2343.130619	0	-

M06-2X/6-31G(d,p), THF/water (smd)

THF-INI

C	1.79523900	2.43103200	-0.61471100
C	0.47617700	2.89205300	-0.96353400
C	1.66120200	-0.27625900	1.19304200
N	2.61210100	1.64938000	-1.32566300
C	2.51068000	-0.95445500	0.38023900
C	3.82863700	1.21541600	-1.04650800
C	2.14344600	2.95458800	0.70794400
H	2.24243800	1.28972000	-2.21476300
C	0.39797100	0.10449700	0.63976700
H	1.88742800	-0.09061100	2.23759100
C	4.37951600	0.26232300	-2.00563300
H	2.18346000	-1.15108400	-0.64288300
C	3.80361400	-1.53077400	0.73430300
H	4.33805900	1.55848900	-0.15843600
O	5.64529700	-0.03991500	-1.73210500
O	3.73699400	-0.20299300	-2.93358600
C	6.26034500	-0.98482200	-2.61512800
H	5.66406200	-1.89714300	-2.67747700
H	6.36919400	-0.55166600	-3.61213900
H	7.23778300	-1.19671200	-2.18482300
C	4.37055200	-2.45990000	-0.14973300
C	4.49954000	-1.18158800	1.90266500
C	5.72914600	-1.76316000	2.17779400
C	5.59761400	-3.04802500	0.13403700
C	6.27804500	-2.69975400	1.29852600
H	4.08878100	-0.43919200	2.58058600
H	6.26841100	-1.48425000	3.07721500
H	3.83758100	-2.71654300	-1.06233700

H	6.02428500	-3.77058200	-0.55436200
H	7.23987300	-3.15137700	1.52051500
N	-0.61907900	0.56829000	1.29988100
H	0.22625200	-0.06837300	-0.42054300
N	1.03225200	3.67615800	1.12412900
O	3.18083900	2.80372500	1.34540800
C	0.04044500	3.65981200	0.14357600
C	-0.35940000	2.71895700	-2.06481300
C	-1.62107900	3.31628200	-2.04702700
C	-1.21184600	4.25678800	0.16468200
C	-2.03959100	4.07208300	-0.94727100
H	-0.03720700	2.13972900	-2.92590600
H	-2.28334500	3.19539300	-2.89834900
H	-1.53591200	4.84770800	1.01616800
H	-3.02354600	4.53076000	-0.95624300
C	-0.63458600	0.89875800	2.73491000
C	-1.95926700	0.76505400	0.68856700
C	-1.74163200	1.94376700	2.82603800
C	-2.76052500	1.52014000	1.75982900
H	-1.80847200	1.36611300	-0.21133500
H	0.34480900	1.26660700	3.04483800
H	-0.87903700	-0.01429200	3.29146000
C	-2.56192900	-0.61039400	0.23457600
H	-3.26854400	2.37896100	1.31698600
H	-1.33459400	2.92671900	2.57956000
H	-2.17251600	1.98726800	3.82716100
H	-3.52385400	0.87276900	2.19331700
O	-1.73260000	-0.99861700	-0.84848200
C	-2.42622000	-1.62158200	1.38104300
C	-3.99358700	-0.41244000	-0.27614100
C	-4.32938500	0.74745500	-0.98528600

C	-4.93926700	-1.43917900	-0.19352500
C	-6.18805400	-1.30993700	-0.79906700
C	-5.57821000	0.87995600	-1.58492600
C	-6.51247600	-0.14966000	-1.49596100
H	-4.70488900	-2.35271000	0.34278500
H	-6.90615100	-2.12043800	-0.72254500
H	-3.61244000	1.55635600	-1.09421000
H	-5.81811400	1.78784700	-2.12972500
H	-7.48531300	-0.04713200	-1.96647700
C	-3.33663300	-1.68221600	2.44378100
C	-1.29548200	-2.44430700	1.43356500
C	-1.07115500	-3.29177800	2.51518900
C	-3.11519500	-2.53162400	3.52595400
C	-1.97927700	-3.33604400	3.56941000
H	-0.58029500	-2.42389100	0.61750800
H	-0.18471200	-3.91845200	2.52940100
H	-4.24172300	-1.08333000	2.42433700
H	-3.83941000	-2.56684800	4.33390200
H	-1.80833900	-3.99785800	4.41257600
Si	-1.96768300	-2.10309600	-2.10683200
C	-2.54245400	-3.77909400	-1.50328500
C	-3.14662300	-1.42148500	-3.39021800
C	-0.23441900	-2.23309600	-2.80378400
H	-4.18274200	-1.41308500	-3.03632900
H	-2.87499100	-0.39934500	-3.67477500
H	-3.10447600	-2.04200600	-4.29285800
H	-1.83876400	-4.21998300	-0.79115300
H	-3.52793900	-3.74089900	-1.03145500
H	-2.61562100	-4.45407700	-2.36440100
H	0.15457400	-1.25167500	-3.09810900
H	0.45165300	-2.66850200	-2.06850100

H	-0.21409000	-2.87404100	-3.69150100
C	1.03983200	4.50994600	2.30760700
H	0.81717000	5.54699100	2.04135200
H	2.04032600	4.45326600	2.73803300
H	0.31505000	4.16634900	3.05073100

THF-TS

C	1.78406700	2.36589800	-0.63413600
C	0.51055700	2.91233100	-1.03081100
C	1.69465700	-0.05255900	0.94815300
N	2.60980000	1.61943400	-1.34674700
C	2.61917600	-0.67265400	0.09783700
C	3.66851900	0.92652500	-0.86541300
C	2.12281100	2.91674100	0.71439800
H	2.32337400	1.36465700	-2.29807100
C	0.41529600	0.24597100	0.45618700
H	1.94290300	0.13261800	1.98852500
C	4.41667100	0.19337100	-1.90636500
H	2.22326700	-1.02274200	-0.85649600
C	3.78289600	-1.44619800	0.58210500
H	4.16187900	1.30399700	0.01941500
O	5.63966700	-0.12042700	-1.50547300
O	3.92538900	-0.11496800	-2.97499500
C	6.38720400	-0.96153300	-2.39531900
H	5.80809200	-1.85021200	-2.65308100
H	6.64232300	-0.41250700	-3.30422000
H	7.28832100	-1.23686200	-1.85062200
C	4.20546800	-2.54488400	-0.17423500
C	4.49276900	-1.09461200	1.73617300
C	5.59980100	-1.83958900	2.12682300
C	5.31148300	-3.29120200	0.22039400

C	6.01158600	-2.93862800	1.37178300
H	4.19074300	-0.22500100	2.31437700
H	6.14958100	-1.55865700	3.01954400
H	3.66120500	-2.80973600	-1.07792500
H	5.62634400	-4.14465300	-0.37198100
H	6.87868400	-3.51450000	1.67934000
N	-0.61127600	0.70083100	1.14723900
H	0.19773300	0.02590800	-0.58616800
N	1.02164200	3.66008900	1.08680600
O	3.15809200	2.79392100	1.34827100
C	0.05899400	3.66672600	0.07280900
C	-0.28857600	2.76053600	-2.16189200
C	-1.53579400	3.38057200	-2.17831000
C	-1.18427000	4.28349700	0.06457500
C	-1.97368100	4.12670500	-1.07727400
H	0.05138300	2.17747700	-3.01315300
H	-2.17375500	3.28567700	-3.05047600
H	-1.53027600	4.86481000	0.91357900
H	-2.94963500	4.60110300	-1.11085500
C	-0.58249200	1.03592300	2.57389400
C	-1.97048400	0.81682800	0.58274300
C	-1.74484700	2.01540800	2.72221100
C	-2.76038400	1.60160300	1.64455200
H	-1.88435900	1.36894500	-0.35671000
H	0.38500500	1.47412700	2.83394500
H	-0.73337700	0.12043100	3.16083900
C	-2.56278700	-0.59281100	0.23092800
H	-3.24481000	2.47005100	1.19329400
H	-1.39286100	3.03058000	2.52731900
H	-2.16861300	1.98820200	3.72737800
H	-3.54666300	0.97962800	2.07326100

O	-1.74691800	-1.04550600	-0.83780600
C	-2.39145600	-1.51793800	1.44206600
C	-4.00460100	-0.45345100	-0.27203700
C	-4.37250700	0.65376100	-1.04732000
C	-4.93141300	-1.48891200	-0.11347900
C	-6.19064700	-1.41944200	-0.70678100
C	-5.63130300	0.72701600	-1.63590300
C	-6.54578100	-0.31067800	-1.46977900
H	-4.67191200	-2.36336800	0.47402100
H	-6.89327300	-2.23561000	-0.57029600
H	-3.67359000	1.46820600	-1.21536300
H	-5.89532500	1.59548100	-2.23141400
H	-7.52657700	-0.25426600	-1.93149400
C	-3.29373300	-1.53113400	2.51301700
C	-1.22900400	-2.28984400	1.54886400
C	-0.96585200	-3.03893700	2.69272500
C	-3.03330300	-2.28219400	3.65771000
C	-1.86517700	-3.03349400	3.75586700
H	-0.51602600	-2.29859400	0.73052700
H	-0.05465400	-3.62659600	2.74974000
H	-4.22138900	-0.97048800	2.45412400
H	-3.75077800	-2.28021600	4.47248200
H	-1.66129700	-3.61580200	4.64899700
Si	-1.97810000	-2.24372800	-2.00292000
C	-2.51588500	-3.88317500	-1.27753600
C	-3.18554600	-1.68144500	-3.31791400
C	-0.25358500	-2.39975500	-2.71780400
H	-4.21552100	-1.65189100	-2.94764400
H	-2.92935800	-0.68434900	-3.69183000
H	-3.15240400	-2.37489000	-4.16628900
H	-1.81083100	-4.25260800	-0.52705300

H	-3.50876900	-3.83674100	-0.82219000
H	-2.56082500	-4.62219200	-2.08673800
H	0.11656500	-1.43554800	-3.08452300
H	0.44837700	-2.77320400	-1.96348300
H	-0.23648100	-3.10098600	-3.55888400
C	1.01105900	4.50212500	2.26661600
H	0.76650400	5.53043900	1.98864500
H	2.01187100	4.47208700	2.69842400
H	0.29219500	4.14454100	3.00826400

THF-FIN

C	2.82790600	1.19042400	-0.35786500
C	2.38079000	2.53736100	-0.86459100
C	1.70554100	0.20896300	0.21746000
N	3.60392300	0.42006500	-1.31472300
C	2.09520400	-1.18710600	-0.33241700
C	3.54777700	-0.95990600	-0.86882200
C	3.74500500	1.57707300	0.82926900
H	3.18942400	0.49062200	-2.24489900
C	0.35101100	0.61069000	-0.23418700
H	1.74150700	0.21544300	1.30961300
C	3.82228900	-1.89891000	-2.02121100
H	1.46279400	-1.40962500	-1.20281300
C	1.98076100	-2.32384400	0.65471900
H	4.26399300	-1.12966500	-0.06109800
O	4.27510400	-3.07420300	-1.60079800
O	3.59476900	-1.62130500	-3.17655800
C	4.46759400	-4.06384000	-2.62270500
H	3.52261300	-4.27301100	-3.12842200
H	5.20278100	-3.71676800	-3.35098800
H	4.82922000	-4.95252100	-2.10887300

C	1.24356100	-3.46578700	0.33493400
C	2.64889100	-2.26811100	1.88294600
C	2.57274100	-3.33448700	2.77414400
C	1.16391100	-4.53313700	1.22802700
C	1.82960900	-4.46979600	2.44986800
H	3.24104800	-1.38940400	2.13389200
H	3.09914800	-3.28162700	3.72218500
H	0.73421800	-3.52416200	-0.62443300
H	0.58528600	-5.41349400	0.96577200
H	1.77246600	-5.30079900	3.14589800
N	-0.44208600	1.35528600	0.44252700
H	-0.03009500	0.25340700	-1.18929000
N	3.76242100	2.94009200	0.92582500
O	4.33522100	0.79565800	1.55141800
C	2.96301900	3.52753200	-0.06420700
C	1.54467700	2.88870600	-1.91014200
C	1.29155700	4.24590200	-2.14339500
C	2.72462500	4.87656600	-0.27689600
C	1.87480100	5.21861500	-1.33427600
H	1.09596800	2.12855100	-2.54592500
H	0.64413700	4.54044800	-2.96210300
H	3.18234700	5.63713900	0.34689700
H	1.67170600	6.26712300	-1.52798000
C	-0.11802800	2.05482600	1.70450100
C	-1.84166800	1.65592500	0.02329400
C	-0.96285100	3.31627800	1.57504300
C	-2.26562300	2.80382000	0.95086700
H	-1.78928600	1.96815400	-1.02192000
H	0.95330700	2.24044200	1.77468700
H	-0.44548900	1.41744400	2.53436700
C	-2.69946800	0.34178900	0.08534000

H	-2.79878200	3.57514900	0.39449000
H	-0.46003600	4.01981300	0.90397000
H	-1.11677600	3.79935600	2.54031900
H	-2.93221600	2.43233100	1.73096000
O	-2.19550500	-0.43174500	-0.99128400
C	-2.41960400	-0.36234500	1.41958600
C	-4.17652000	0.66911300	-0.16252600
C	-4.52835100	1.65354100	-1.09324400
C	-5.19390100	-0.10238900	0.40739900
C	-6.52808600	0.11444400	0.06818900
C	-5.86034500	1.87397300	-1.42957600
C	-6.86634800	1.10509400	-0.84867100
H	-4.95087600	-0.88480200	1.11841800
H	-7.30158100	-0.49588900	0.52374600
H	-3.76525800	2.25066100	-1.58313100
H	-6.11030600	2.64485900	-2.15177800
H	-7.90561400	1.27635300	-1.11104300
C	-3.05110400	0.01618300	2.61100900
C	-1.40624700	-1.32461000	1.48463800
C	-1.01762800	-1.88039500	2.70068200
C	-2.66967000	-0.54393900	3.82857700
C	-1.64701700	-1.48739500	3.87954400
H	-0.90789900	-1.64356800	0.57352900
H	-0.22350000	-2.62211000	2.71977700
H	-3.86191000	0.73818000	2.59583400
H	-3.17911000	-0.24058400	4.73789700
H	-1.34806000	-1.91927100	4.82951300
Si	-2.88395200	-1.75176200	-1.80558300
C	-3.38381400	-3.12032400	-0.63182100
C	-4.32623700	-1.23253700	-2.87921700
C	-1.45884700	-2.29840100	-2.88616600

H	-5.22151600	-0.98865800	-2.29932000
H	-4.06958000	-0.36310500	-3.49301100
H	-4.57794900	-2.05628400	-3.55774900
H	-2.53291100	-3.49796100	-0.05570100
H	-4.16218600	-2.81125500	0.07178200
H	-3.78632600	-3.95403000	-1.21955600
H	-1.14225600	-1.49261900	-3.55709200
H	-0.59445000	-2.59986300	-2.28470500
H	-1.74347500	-3.15483300	-3.50630800
C	4.53792500	3.67586200	1.90221000
H	5.27511700	4.30991600	1.40221200
H	5.04997000	2.94968000	2.53331900
H	3.88217000	4.29765400	2.51773300

Water-INI

C	-1.50793500	2.25019600	0.81816600
C	-0.15160000	2.66835500	1.06655800
C	-1.76886900	-0.11174100	-1.40103100
N	-2.24604900	1.39764100	1.53591400
C	-2.59778600	-0.88099400	-0.65316300
C	-3.49600400	1.01175400	1.35661100
C	-1.98354900	2.90856500	-0.39777500
H	-1.76264000	0.92260000	2.31030100
C	-0.43354900	0.05453500	-0.91222000
H	-2.07880300	0.33193800	-2.34155900
C	-3.96917100	-0.05225100	2.22885600
H	-2.18617800	-1.35340700	0.24059200
C	-3.99551200	-1.19071600	-0.93932300
H	-4.10749800	1.47319700	0.59674200
O	-5.26399400	-0.30636300	2.03640800
O	-3.25975500	-0.65242400	3.02567300

C	-5.80426100	-1.39042700	2.80530500
H	-5.24705100	-2.30842100	2.60823600
H	-5.76142000	-1.15173200	3.86963200
H	-6.83703300	-1.49494400	2.47923700
C	-4.58674100	-2.27834800	-0.28182200
C	-4.77181000	-0.40222800	-1.80318000
C	-6.10888100	-0.71259300	-2.01235000
C	-5.92448800	-2.59084800	-0.50008900
C	-6.68613800	-1.80800300	-1.36557000
H	-4.33483200	0.47125000	-2.27840800
H	-6.70908300	-0.09457000	-2.67176400
H	-3.98848700	-2.87171600	0.40526600
H	-6.37383200	-3.43550600	0.01187200
H	-7.73287500	-2.04237300	-1.52984500
N	0.55433500	0.58737800	-1.56160700
H	-0.20216300	-0.32651900	0.07892100
N	-0.92617200	3.67289400	-0.84561700
O	-3.08979200	2.82001200	-0.94520100
C	0.17270800	3.54336500	0.00514700
C	0.79359300	2.39063500	2.05342000
C	2.04869600	2.99313600	1.96133800
C	1.41787900	4.14823500	-0.09131600
C	2.35572600	3.85624500	0.90304300
H	0.55362700	1.73037000	2.88186300
H	2.79705300	2.78963300	2.72054800
H	1.65204800	4.82245800	-0.90893700
H	3.33919200	4.31222600	0.85331700
C	0.43265800	1.18682400	-2.90847000
C	1.95738300	0.66633500	-1.05173700
C	1.70708300	2.00902500	-3.04047500
C	2.73593700	1.18953900	-2.26096700

H	1.94835200	1.41769600	-0.25728700
H	-0.48528400	1.77570300	-2.96882000
H	0.39219100	0.37284000	-3.64019600
C	2.45133500	-0.66659500	-0.39942100
H	3.59587100	1.78010400	-1.94301700
H	1.56997000	2.98647300	-2.57065800
H	1.98425400	2.15592900	-4.08459600
H	3.09079500	0.36120400	-2.87812800
O	1.68383200	-0.76373200	0.79211000
C	2.15512100	-1.85444400	-1.32223500
C	3.93387900	-0.54723700	-0.01066400
C	4.43760200	0.66573600	0.47508900
C	4.76077700	-1.67433900	0.03518900
C	6.05370300	-1.59209000	0.55011000
C	5.73090700	0.75141500	0.98155500
C	6.54446400	-0.37902200	1.02484400
H	4.39944800	-2.62952800	-0.32995900
H	6.67544800	-2.48118300	0.57635200
H	3.82133800	1.55856800	0.47924700
H	6.09846500	1.70394900	1.34984400
H	7.55158500	-0.31416700	1.42372500
C	2.96757900	-2.13401100	-2.42933400
C	1.02357600	-2.64947900	-1.11507700
C	0.70478400	-3.68495800	-1.99232800
C	2.64950700	-3.16699200	-3.30673000
C	1.51353600	-3.94517100	-3.09421000
H	0.38400400	-2.47009100	-0.25716100
H	-0.17908000	-4.28716300	-1.80764500
H	3.87443600	-1.56189700	-2.59694100
H	3.29793700	-3.36701600	-4.15354000
H	1.26711900	-4.75177800	-3.77689600

Si	1.89386300	-1.63474900	2.22626500
C	2.29387400	-3.44144600	1.94324000
C	3.20502800	-0.82797600	3.28936500
C	0.19370400	-1.47056400	2.99204700
H	4.21429900	-1.02463000	2.91225400
H	3.06018100	0.25725500	3.32926200
H	3.14386000	-1.21507200	4.31247800
H	1.48576900	-3.95991600	1.41936500
H	3.21942900	-3.58808800	1.38024400
H	2.42188300	-3.92128600	2.92071600
H	-0.04012200	-0.42625700	3.22380100
H	-0.57088700	-1.84776800	2.30299300
H	0.11811900	-2.04406800	3.92162700
C	-0.97428700	4.50716600	-2.02823500
H	-0.73825000	5.54258500	-1.77052200
H	-1.98596200	4.45745500	-2.43006700
H	-0.26914100	4.15530000	-2.78591300

Water-TS

C	-1.47410600	2.19420900	0.82216600
C	-0.13175400	2.65728100	1.07910800
C	-1.81091400	0.10088600	-1.11223900
N	-2.19389700	1.36221000	1.55355700
C	-2.69644500	-0.59549500	-0.27453500
C	-3.35988000	0.78377900	1.17240200
C	-1.99498100	2.94003900	-0.36573600
H	-1.72871300	0.92635000	2.35831600
C	-0.46053400	0.18344400	-0.74375300
H	-2.15812000	0.51257200	-2.05459300
C	-3.92615300	-0.13229700	2.17876200
H	-2.23268000	-1.22673800	0.48506800

C	-4.01447500	-1.07248100	-0.75528500
H	-4.01461800	1.35255600	0.52710800
O	-5.22274900	-0.33806300	1.98539000
O	-3.25528000	-0.67860100	3.03855600
C	-5.82128700	-1.35404100	2.80713600
H	-5.29851500	-2.30237100	2.66775100
H	-5.78277500	-1.05656000	3.85620500
H	-6.85210200	-1.43259700	2.46841200
C	-4.50449400	-2.29766400	-0.29118000
C	-4.80016900	-0.30178300	-1.62038700
C	-6.04850300	-0.76043800	-2.02571900
C	-5.75541600	-2.75452400	-0.69738400
C	-6.52861300	-1.98769000	-1.56661100
H	-4.44086700	0.66876900	-1.95394300
H	-6.65399200	-0.15520500	-2.69262100
H	-3.90162000	-2.88734700	0.39526800
H	-6.12627200	-3.70694200	-0.33240200
H	-7.50556300	-2.34003200	-1.88129000
N	0.52639900	0.64781800	-1.48285400
H	-0.16888000	-0.21388100	0.22450700
N	-0.94335400	3.70625400	-0.80042900
O	-3.12740000	2.92833500	-0.84085100
C	0.17072800	3.54830500	0.03120800
C	0.82182500	2.35813800	2.05102500
C	2.07211900	2.96491400	1.95676000
C	1.41459700	4.15263800	-0.07508600
C	2.36128100	3.84285300	0.90426700
H	0.58952500	1.67944800	2.86663200
H	2.83076700	2.75507500	2.70328600
H	1.64027300	4.83895600	-0.88449400
H	3.34408100	4.30001100	0.84811800

C	0.33003000	1.23339300	-2.81907100
C	1.95193100	0.68147200	-1.06412500
C	1.61996700	2.01076500	-3.04936600
C	2.67027900	1.16636600	-2.32577800
H	2.03532900	1.43475300	-0.27596200
H	-0.56441100	1.86246400	-2.82591600
H	0.20052800	0.42592100	-3.54961700
C	2.45108800	-0.65906300	-0.43524400
H	3.57003400	1.72987600	-2.07454700
H	1.54326000	2.99678900	-2.58146700
H	1.83545800	2.14181700	-4.11042900
H	2.95568600	0.31829400	-2.95304700
O	1.74622600	-0.73411900	0.79702600
C	2.07220600	-1.84301500	-1.33080800
C	3.95153600	-0.57677600	-0.11323700
C	4.50499100	0.62277200	0.35353000
C	4.75110300	-1.72425100	-0.09807500
C	6.06397300	-1.67638500	0.36853100
C	5.81811100	0.67430400	0.81076700
C	6.60337900	-0.47700000	0.82445900
H	4.34969600	-2.66925900	-0.44757400
H	6.66291400	-2.58148100	0.37253600
H	3.91241700	1.53148000	0.38255000
H	6.22354900	1.61622500	1.16657500
H	7.62560000	-0.43840400	1.18687200
C	2.81787300	-2.17041800	-2.47099700
C	0.91838700	-2.58555500	-1.06086100
C	0.51542600	-3.61882700	-1.90426200
C	2.41598500	-3.20217800	-3.31566400
C	1.26060300	-3.92929300	-3.03780300
H	0.32687300	-2.36363600	-0.17867200

H	-0.38386400	-4.17960700	-1.66965600
H	3.73647100	-1.63562200	-2.69214200
H	3.01371700	-3.44117700	-4.18941600
H	0.94938900	-4.73480600	-3.69507000
Si	1.97459900	-1.63425600	2.20652800
C	2.38604900	-3.43809000	1.91493800
C	3.29706500	-0.82777200	3.25590800
C	0.28018300	-1.50472500	2.99560200
H	4.29762400	-1.00062300	2.84436500
H	3.13640100	0.25429900	3.31975300
H	3.27440100	-1.23409900	4.27301900
H	1.60897400	-3.95124900	1.34111400
H	3.34475700	-3.58462800	1.41074900
H	2.45340800	-3.92571000	2.89511300
H	0.01119300	-0.46423700	3.20565100
H	-0.48139900	-1.92463400	2.32776600
H	0.23656300	-2.05782200	3.93959200
C	-0.99958500	4.57783100	-1.95687100
H	-0.77465800	5.60660200	-1.66561100
H	-2.00931100	4.52851500	-2.36329700
H	-0.28575400	4.25132500	-2.71782500

Water-FIN

C	2.82674800	1.23227500	-0.38228000
C	2.32027200	2.55875500	-0.88782000
C	1.73570700	0.24606500	0.23123900
N	3.59294600	0.46393600	-1.35870300
C	2.11297800	-1.14656500	-0.32936000
C	3.55044500	-0.91342300	-0.89092400
C	3.75641500	1.66417400	0.77371200
H	3.09987400	0.50509300	-2.25323100

C	0.36751700	0.63202200	-0.19793800
H	1.80231100	0.25732600	1.32174800
C	3.80880700	-1.88064000	-2.01689300
H	1.46480400	-1.36134600	-1.18964400
C	2.01437600	-2.29235900	0.64833700
H	4.28277400	-1.06875600	-0.09537700
O	4.14076300	-3.08318200	-1.55830200
O	3.66262700	-1.61367000	-3.19185000
C	4.27764400	-4.11500000	-2.55039400
H	3.33323600	-4.24738100	-3.08119000
H	5.06908800	-3.85441000	-3.25472300
H	4.53682600	-5.01688800	-2.00042300
C	1.30692600	-3.44716100	0.30456300
C	2.66708800	-2.23972800	1.88440000
C	2.60627000	-3.31971600	2.76091200
C	1.24246300	-4.52815200	1.18239900
C	1.89322700	-4.46704800	2.41291500
H	3.23429200	-1.35205300	2.15684500
H	3.11876400	-3.26628600	3.71626700
H	0.80765800	-3.49980300	-0.66022500
H	0.68548200	-5.41687100	0.90279700
H	1.84643700	-5.30808800	3.09721400
N	-0.43165100	1.35221600	0.49550700
H	-0.00670600	0.28464900	-1.15930300
N	3.71299800	3.01873400	0.87823600
O	4.41681600	0.90907800	1.47589500
C	2.85269200	3.57165400	-0.08513400
C	1.45609000	2.87188800	-1.92292600
C	1.12322800	4.21534600	-2.13445100
C	2.53535100	4.90685000	-0.27348100
C	1.65400200	5.21118500	-1.31690500

H	1.04386800	2.09230300	-2.55901800
H	0.44940800	4.48114600	-2.94136600
H	2.95490200	5.68279600	0.35775900
H	1.38490800	6.24763300	-1.49296300
C	-0.11109000	2.04111300	1.76368900
C	-1.83240600	1.64972100	0.07869200
C	-0.96542500	3.29637500	1.64550100
C	-2.26783600	2.77328100	1.02917700
H	-1.77566300	1.98922000	-0.95783400
H	0.95929000	2.23042000	1.83395000
H	-0.43489500	1.39447000	2.58789200
C	-2.67722000	0.32871000	0.10446500
H	-2.81941200	3.54269500	0.48858400
H	-0.47195700	4.00428800	0.97146000
H	-1.11577500	3.77413400	2.61361900
H	-2.91663000	2.37852000	1.81345500
O	-2.16443100	-0.41193100	-0.99115300
C	-2.39698100	-0.40755200	1.42028300
C	-4.15583900	0.64385600	-0.14863600
C	-4.50609900	1.64250700	-1.06506100
C	-5.17064300	-0.15291400	0.39008100
C	-6.50213900	0.05025700	0.03158500
C	-5.83548700	1.84780100	-1.42144100
C	-6.83952500	1.05164000	-0.87421000
H	-4.92868000	-0.94528900	1.09032400
H	-7.27354100	-0.58023000	0.46208500
H	-3.74331400	2.26260800	-1.52560000
H	-6.08457000	2.62909100	-2.13238300
H	-7.87620900	1.21096000	-1.15315300
C	-3.04268300	-0.06685700	2.61504400
C	-1.37103800	-1.35801200	1.46788900

C	-0.98715300	-1.94045800	2.67297100
C	-2.66432800	-0.65301600	3.82128300
C	-1.63155000	-1.58612700	3.85625200
H	-0.85812800	-1.64568100	0.55381600
H	-0.18433500	-2.67296800	2.68155800
H	-3.85881600	0.64892200	2.61085900
H	-3.18302400	-0.37721500	4.73379200
H	-1.33488800	-2.03837400	4.79724400
Si	-2.79910500	-1.75632100	-1.80556900
C	-3.25944400	-3.14081400	-0.63356000
C	-4.25581600	-1.27113500	-2.87798600
C	-1.34564400	-2.24694900	-2.87264300
H	-5.16532700	-1.08374600	-2.29886400
H	-4.02858200	-0.37125200	-3.45844000
H	-4.46675300	-2.08116900	-3.58555000
H	-2.37868300	-3.54568200	-0.12470100
H	-3.97852700	-2.82521000	0.12791500
H	-3.71950000	-3.95226400	-1.20904100
H	-1.07378200	-1.43834500	-3.55896500
H	-0.47128500	-2.47321800	-2.25245900
H	-1.57382000	-3.13513100	-3.47043100
C	4.44166500	3.79418900	1.86256000
H	5.12294100	4.48944900	1.36628700
H	5.01274500	3.10204700	2.48010200
H	3.74501700	4.35559600	2.48984800

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C	-1.89314700	1.86789100	-1.11311500
C	-0.66824500	2.29709200	-1.74229400
C	-1.62772200	-0.68805100	1.59179600
N	-2.70862700	0.87899000	-1.49495300

C	-2.60740300	-1.53502000	1.18778900
C	-3.90916700	0.54725900	-1.06213500
C	-2.19353300	2.77184500	-0.01062200
H	-2.35448400	0.26237900	-2.23796600
C	-0.28652100	-1.13427600	1.36830700
C	-4.48411400	-0.64706300	-1.65681900
C	-4.03300300	-1.44197700	1.47333200
O	-5.75366600	-0.82471300	-1.28812600
O	-3.87446000	-1.39742600	-2.40919500
C	-6.39165800	-1.99547400	-1.81629700
H	-6.45807700	-1.92545300	-2.90388600
H	-5.83376300	-2.89075700	-1.53424600
H	-7.38603200	-2.01363400	-1.37408700
C	-4.62917400	-0.29066100	2.01611700
C	-4.83015200	-2.56056300	1.19061800
C	-6.19609200	-2.53861100	1.45427600
C	-5.99454900	-0.26584400	2.25758600
C	-6.77965600	-1.38964800	1.98155700
H	-4.36825900	-3.44687300	0.76375100
H	-6.80391200	-3.41006800	1.23382100
H	-4.02895800	0.59264500	2.21379300
H	-6.45364100	0.62968100	2.66298800
H	-7.84693300	-1.36360100	2.17680400
N	0.76886400	-0.68418300	1.96794600
H	-0.13450000	-1.98623500	0.70956200
N	-1.19052000	3.71762700	-0.01662000
O	-3.13327200	2.72606000	0.79668600
C	-0.28321700	3.46601900	-1.04652200
C	0.11282200	1.83644200	-2.80168900
C	1.25759600	2.55735700	-3.14958300
C	0.83141300	4.20451500	-1.40993100

C	1.60651500	3.72704200	-2.46957800
H	-0.16650800	0.94087200	-3.35075800
H	1.87517600	2.21059800	-3.97181100
H	1.09732100	5.11438000	-0.88123500
H	2.49226500	4.27809700	-2.76783100
C	0.74766700	0.32788400	3.04859300
C	2.09674000	-1.30298100	1.77763700
C	2.15805500	0.27981900	3.64595200
C	2.77581500	-1.03208800	3.12649800
H	1.91922200	-2.36638500	1.60143400
H	-0.02022300	0.02681500	3.76541300
H	0.48339700	1.30253000	2.63079000
C	2.82437000	-0.74246800	0.50660400
H	2.54050200	-1.85731700	3.80336200
H	2.11522900	0.29317100	4.73537800
H	2.73785300	1.14454100	3.31801400
H	3.86117900	-0.96621900	3.03279100
O	1.87432700	-0.71917000	-0.54277100
C	3.27385200	0.69494600	0.77141400
C	4.01261900	-1.63559900	0.13873400
C	4.39553500	-2.76729900	0.85938800
C	4.72279100	-1.30345700	-1.02159100
C	5.76273700	-2.10645600	-1.47526700
C	5.44696700	-3.56803000	0.41135900
C	6.12537000	-3.24850700	-0.75958900
H	4.44745100	-0.40916000	-1.57572000
H	6.29367900	-1.83947700	-2.38360500
H	3.88385600	-3.05698700	1.77112900
H	5.72728700	-4.44762500	0.98176900
H	6.93722600	-3.87769500	-1.10993400
C	4.54271100	0.96582200	1.29432000

C	2.36606000	1.74621000	0.61714800
C	2.70486200	3.03227000	1.03486400
C	4.88564300	2.25465200	1.69341900
C	3.96045000	3.29008500	1.57992400
H	1.38410100	1.55528000	0.18901000
H	1.98186200	3.83497500	0.93379700
H	5.26596300	0.16376600	1.40498700
H	5.87358200	2.44534600	2.10053700
H	4.21913300	4.29301100	1.90415600
Si	1.49270100	-1.80425800	-1.78886400
C	2.29985600	-1.26307600	-3.38729100
C	1.93998600	-3.57301100	-1.36824200
C	-0.37533200	-1.62018300	-1.92112100
H	3.00926000	-3.77301000	-1.48653600
H	1.65087700	-3.83124700	-0.34328200
H	1.39102500	-4.23863900	-2.04461800
H	1.76628500	-1.70869500	-4.23408000
H	2.25629100	-0.17445100	-3.49872300
H	3.34717600	-1.57120800	-3.44869700
H	-0.90810400	-2.44297800	-1.43192200
H	-0.66259300	-0.68914700	-1.42194400
H	-0.70744800	-1.57668700	-2.96363100
H	-4.41399700	1.14906300	-0.32323800
H	-2.30677700	-2.42653200	0.63606500
H	-1.82236900	0.21641300	2.16070400
C	-1.09181500	4.81181900	0.92542300
H	-1.93085500	4.73504200	1.61639800
H	-0.15562900	4.75236700	1.48694600
H	-1.13897600	5.77194000	0.40526000

Minor enantiomer-TS

C	-1.79946500	1.65526200	-1.17815800
C	-0.59648100	2.16990600	-1.79248200
C	-1.81207300	-0.14436800	1.18996100
N	-2.55675500	0.67143300	-1.61913400
C	-2.86379700	-0.91246900	0.67101800
C	-3.66805100	0.16644900	-1.03670800
C	-2.22701500	2.62890200	-0.12683500
H	-2.19284300	0.11435900	-2.40127300
C	-0.51239100	-0.64836000	1.02734800
C	-4.27639600	-0.93061000	-1.79732000
C	-4.16040900	-1.08167400	1.36362800
O	-5.54607600	-1.12781900	-1.45938400
O	-3.65936600	-1.61110900	-2.60322400
C	-6.16724700	-2.29648000	-2.01714200
H	-6.23808900	-2.20108200	-3.10193200
H	-5.59137300	-3.18702100	-1.75798600
H	-7.15928000	-2.34080900	-1.57227500
C	-4.72777200	-0.08110600	2.16303400
C	-4.83851700	-2.29572700	1.20341600
C	-6.05848700	-2.51404900	1.83625500
C	-5.94658800	-0.30203500	2.79487600
C	-6.61428000	-1.51713100	2.63491600
H	-4.40286100	-3.06719800	0.57252200
H	-6.57263200	-3.46061100	1.70378100
H	-4.22521900	0.87588700	2.27419100
H	-6.38126100	0.47826600	3.41132500
H	-7.56686600	-1.68217100	3.12794500
N	0.54283600	-0.29139700	1.72594700
H	-0.36165600	-1.48930700	0.35600700
N	-1.28362000	3.62188700	-0.14539300
O	-3.22983200	2.59536600	0.58119200

C	-0.32342600	3.38547300	-1.13519500
C	0.22663800	1.72808600	-2.82567200
C	1.32200800	2.51603700	-3.18002700
C	0.74191200	4.18940000	-1.50167500
C	1.56996900	3.72696300	-2.52877100
H	0.01445600	0.79989800	-3.34950800
H	1.97776700	2.19152500	-3.98055100
H	0.92851700	5.13751700	-1.00826800
H	2.42097600	4.32952900	-2.82875600
C	0.47924900	0.70922000	2.80456300
C	1.79362300	-1.07489400	1.72777500
C	1.81439500	0.57400900	3.53793700
C	2.33783100	-0.81659900	3.14188400
H	1.51372500	-2.12109300	1.57576000
H	-0.36962300	0.46178300	3.44992600
H	0.31605000	1.70340700	2.37798600
C	2.74732900	-0.69146900	0.55125500
H	1.93316100	-1.57816500	3.81391500
H	1.67765100	0.65884800	4.61674100
H	2.50467200	1.35802200	3.22085900
H	3.42724500	-0.87289700	3.18085300
O	1.95986900	-0.70048100	-0.63149000
C	3.27978700	0.72460100	0.77658700
C	3.89999200	-1.69366000	0.42974200
C	4.04688000	-2.81528000	1.24518900
C	4.82794400	-1.48357600	-0.59890300
C	5.85490400	-2.39118800	-0.82991600
C	5.08287900	-3.72328600	1.02060500
C	5.98264500	-3.52085000	-0.01995100
H	4.73733100	-0.59890800	-1.22482800
H	6.55897300	-2.21575600	-1.63724200

H	3.35761400	-3.01374300	2.05887100
H	5.17680400	-4.59355100	1.66226200
H	6.78319900	-4.23207800	-0.19622000
C	4.48785200	0.93570100	1.45061100
C	2.49359400	1.82921800	0.43702000
C	2.88995900	3.11318600	0.80882000
C	4.88903600	2.21992700	1.80789600
C	4.08296700	3.31304600	1.49923900
H	1.56001400	1.67974700	-0.10055200
H	2.26273700	3.96244000	0.56015000
H	5.11676800	0.09048700	1.71201400
H	5.82915200	2.36343000	2.33104800
H	4.38520500	4.31503300	1.78675500
Si	1.72925900	-1.84436400	-1.86136300
C	2.65928200	-1.27347700	-3.37998700
C	2.19074900	-3.59887000	-1.39843300
C	-0.12385200	-1.79751800	-2.18193500
H	3.26932600	-3.77748700	-1.37879100
H	1.77352100	-3.88063100	-0.42572400
H	1.74805100	-4.26356900	-2.15034000
H	2.32742700	-1.83936800	-4.25723100
H	2.47072600	-0.21199900	-3.57315900
H	3.73925800	-1.41437000	-3.27660400
H	-0.64183300	-2.62010300	-1.67654600
H	-0.52429600	-0.85916300	-1.79248400
H	-0.35307300	-1.85761900	-3.25075300
H	-4.27057200	0.83148700	-0.43581700
H	-2.56269200	-1.77609600	0.07595200
H	-2.00094300	0.65670100	1.89659200
C	-1.28959400	4.77381600	0.73347600
H	-2.14815400	4.68451000	1.39800500

H	-0.37109900	4.79943200	1.32545600
H	-1.37308900	5.69532700	0.15264500

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C	2.18103300	1.68370600	0.07928100
C	1.21844300	2.22109000	1.10660000
C	1.86882100	0.31247400	-0.60879400
N	3.55613800	1.56893800	0.60740300
C	2.89947100	-0.65138200	0.00651700
C	4.10786000	0.30877000	0.12407400
C	2.14656300	2.78807400	-1.00013000
H	3.49527000	1.49815400	1.62344400
C	0.50604100	-0.25032500	-0.42692500
C	5.11679500	-0.24835200	1.09653800
C	3.12614700	-1.91473400	-0.78315000
O	5.89588700	-1.15917200	0.52400600
O	5.16816300	0.05524700	2.27081800
C	6.82246900	-1.82557400	1.39859100
H	7.52342500	-1.10272300	1.81865400
H	6.28195300	-2.33058200	2.20063700
H	7.34574000	-2.54743400	0.77545300
C	3.50443800	-1.86219200	-2.12961000
C	2.97043500	-3.15801400	-0.16733300
C	3.18654500	-4.33402800	-0.88424700
C	3.72166300	-3.03597000	-2.84460400
C	3.56189600	-4.27475200	-2.22367800
H	2.68014000	-3.20041300	0.87975100
H	3.06159600	-5.29482900	-0.39516600
H	3.63752600	-0.90040900	-2.62010700
H	4.01741400	-2.98451000	-3.88762700
H	3.73182700	-5.18942600	-2.78258600

N	-0.35594200	-0.35620300	-1.36999400
H	0.25130000	-0.68731100	0.53206200
N	1.33832600	3.79133600	-0.56694100
O	2.75551300	2.75312400	-2.06086400
C	0.77926600	3.47966500	0.68417400
C	0.81114000	1.71432400	2.32786700
C	-0.06992900	2.47366300	3.10858200
C	-0.07441800	4.25704200	1.44980500
C	-0.50431500	3.72287900	2.66894600
H	1.18494700	0.75689100	2.67976300
H	-0.40022600	2.09537300	4.06985300
H	-0.39887700	5.23745800	1.11684700
H	-1.17908000	4.30381600	3.28909800
C	-0.13310500	0.18922200	-2.73843300
C	-1.64022100	-1.13145200	-1.27417500
C	-1.48266300	0.04996100	-3.41871300
C	-2.11586500	-1.16749800	-2.73846500
H	-1.36787500	-2.12399600	-0.90255000
H	0.63228600	-0.43321900	-3.21167800
H	0.22464400	1.21709600	-2.66278500
C	-2.63447100	-0.50663800	-0.24751500
H	-1.75454800	-2.08980100	-3.20046100
H	-1.36411000	-0.09786200	-4.49235800
H	-2.08062800	0.94842200	-3.25441100
H	-3.20325400	-1.15377400	-2.81358100
O	-1.97927800	-0.45095300	1.01198900
C	-2.98393200	0.91906100	-0.68656300
C	-3.91058600	-1.34624100	-0.11512900
C	-4.13155800	-2.56881200	-0.74704900
C	-4.88218100	-0.85563600	0.76763600
C	-6.04318500	-1.57386600	1.02097500

C	-5.30155200	-3.28918600	-0.49752500
C	-6.25689300	-2.79838100	0.38525400
H	-4.71720500	0.09790300	1.26333800
H	-6.78147900	-1.17986100	1.71197800
H	-3.39767400	-2.99485000	-1.42384500
H	-5.45659100	-4.24177000	-0.99383000
H	-7.16334600	-3.36271400	0.57939400
C	-4.06472900	1.15054000	-1.54560500
C	-2.17669000	1.99545300	-0.31097900
C	-2.43109700	3.27173500	-0.81177200
C	-4.31523900	2.42480500	-2.04549700
C	-3.49240500	3.48965100	-1.68597400
H	-1.35661300	1.83840900	0.38462400
H	-1.80129700	4.10224600	-0.51007800
H	-4.71529700	0.32991900	-1.83196600
H	-5.15513200	2.58371600	-2.71424900
H	-3.68336400	4.48496400	-2.07428800
Si	-1.84244200	-1.57378800	2.28843200
C	-2.41650200	-0.64552000	3.80067400
C	-2.78017500	-3.18279000	2.10215000
C	-0.04241000	-2.08899000	2.43837500
H	-3.86644400	-3.06666400	2.08343800
H	-2.47229500	-3.74196900	1.21378800
H	-2.51735600	-3.78890600	2.97826900
H	-1.89991200	0.31507000	3.89058400
H	-3.49227400	-0.44832900	3.74726600
H	-2.22112600	-1.22474500	4.70887900
H	0.28349900	-2.65020100	1.55389800
H	0.65843600	-1.26736200	2.60795500
H	0.03694400	-2.76659500	3.29647800
H	4.57531600	0.43133500	-0.85781100

H	2.57825200	-0.90696300	1.02642200
H	2.09836500	0.42946000	-1.67130600
C	1.08385800	5.01765200	-1.29634100
H	1.67508000	4.99120900	-2.21089700
H	0.02343200	5.09570200	-1.54954200
H	1.37828400	5.88203700	-0.69665600

[Reference]

1 C. I. Onyeagusi, X. Shao and S. J. Malcolmson, *Org. Lett.*, 2020, **22**, 1681–1685.

2 G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found.*, 2008, **64**, 112.

3 G. M. Sheldrick, *Acta Crystallogr., Sect. C: Struct. Chem.*, 2015, **71**, 3.

4 C. Kabuto, S. Akine, T. Nemoto and E. Kwon, *Nihon Kessho Gakkaishi*, 2009, **51**, 218.

5 M. Raulin, B. Drouillat, J. Marrot, F. Couty and K. Wright, *Tetrahedron Lett.*, 2022, **94**, 153710.