Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

"Organocatalytic Enantioselective Formal Synthesis of Bromopyrrole Alkaloids via Aza-Michael Addition"

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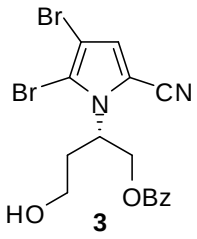
General methods:

All reactions were run under an atmosphere of argon, unless otherwise indicated. Anhydrous solvents were transferred by an oven-dried syringe. Flasks were flame-dried and cooled under a stream of nitrogen. Toluene was distilled from calcium hydride. Chemical reagents were purchased from Aldrich chemical company and used without further purification, unless otherwise noted. Pyrroles **1**[1] and α,β-unsaturated aldehydes **2**[2] were prepared according to the previously reported procedures. Analytical thin-layer chromatography (TLC) was carried out using 0.2-mm commercial silica gel plates (DC-Fertigplatten Krieselgel 60 F_{254}). Preparative column chromatography employing silica gel was performed according to the method of Still.[3] Melting points were determined on a Barnstead melting point apparatus in open capillaries and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer spectrometer. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with a Bruker (400 MHz) spectrometer. Chemical Shifts are reported in delta (δ) units, parts per million (ppm) downfield from trimethylsilane. Coupling constants are reported in Hertz (Hz). Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded with a Bruker 400 (100 MHz) spectrometer. Chemical shifts are reported in delta (δ) units, parts per million (ppm) relative to the center of the triplet at 77.00 ppm for deuteriochloroform. ^{13}C NMR spectra were routinely run with broadbrand decoupling. Mass spectral data were obtained from the Korea Basic Science Institute (Daegu) on a Jeol JMS 700 high resolution mass spectrometer. HPLC analysis was performed on an Agilent 1200 Series with UV detector, using chiral separation column (Chiralpak AD-H).

Representative procedure for the organocatalytic enantioselective conjugate additions:

To a mixture of pyrrole **1** (100 mol %), organocatalyst (20 mol %) and $PhCO_2H$ (40 mol %) in toluene (0.1 M) was added α,β-unsaturated aldehyde **2** (200 mol %) in one portion. The reaction mixture was allowed to stir at –20, –30, or –40 ^oC for 18 hours, at which point the aldehyde was directly reduced with either $NaBH_4$ (110 mol %) in EtOH (0.1 M) or $BH_3 \cdot SMe_2$ (110 mol %) in THF (0.1 M) to alcohol. After 30 min the reaction was quenched by saturated aqueous $NaHCO_3$. The mixture was poured into ethyl acetate, and the layers were separated**.** The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, and dried over $MgSO_4$. The organic layer was filtered and evaporated. The crude residue was purified by silica gel column chromatography.

1. (a) Smith, J. A.; Ng, S.; White, J. *Org. Biomol. Chem.* **2006**, *4*, 2477. (b) Schmuck, C.; Dudaczek, J. *Tetrahedron Lett.* **2005**, *46*, 7101. (c) Loader, C. E.; Anderson, H. J. *Can. J. Chem.* **1981**, *59*, 2673.
2. Avi, M.; Gaisberger, R.; Feichtenhofer, S.; Griengl, H. *Tetrahedron* **2009**, *65*, 5418.
3. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.



3

Colorless Oil

$[\alpha]^{22}_{D}$ +4.0 (c 1, CH_3OH) *in the case of 76% ee (Table 1, entry 1)*

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.6 Hz, 2H), 7.58-7.55 (m, 1H), 7.44-7.40 (m, 2H), 6.99 (s, 1H), 5.33-5.22 (m, 1H), 4.81-4.67 (m, 2H), 3.83-3.77 (m, 1H), 3.50 (dt, *J* = 10.8, 3.6 Hz, 1H), 2.57-2.45 (m, 1H), 2.34-2.23 (m, 1H), 1.73 (s, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 133.3, 129.5, 128.9, 128.4, 124.3, 113.7, 112.7, 102.6, 99.5, 65.2, 57.9, 57.2, 32.6

FTIR (neat) 3487, 3125, 2956, 2221, 1722, 1415, 1314, 1270, 1118, 711 cm^{-1}

HRMS (EI) calcd for $[M]^+$ $C_{16}H_{14}Br_2N_2O_3$ 439.9371, found 439.9373

HPLC Condition to determine enantiomeric excess:

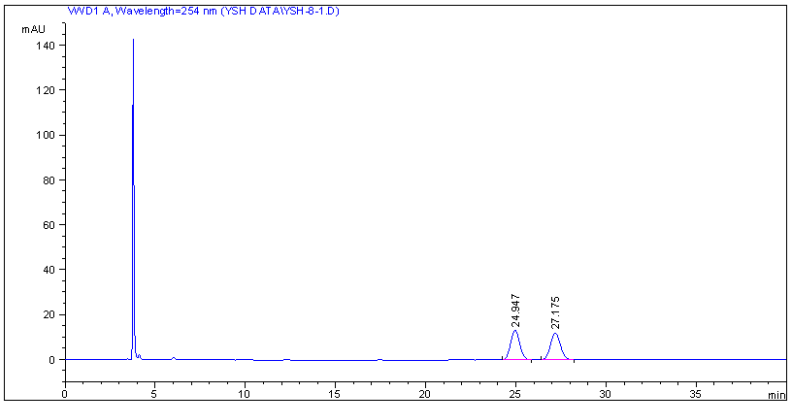
Chiral column: Chiralpak AD-H (250 x 4.6 mm)

Mobile Phase (90/10 = Hexane/IPA)

Flow Rate (0.9 mL/min), Detection Wavelength (254 nm)

Retention Time: 24.9 min (minor isomer), 27.2 min (major isomer)

*Racemate of **3***

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   2  27.175 BB    0.6012  462.62314   12.03768  49.9881

Totals :                   925.46710   25.21658
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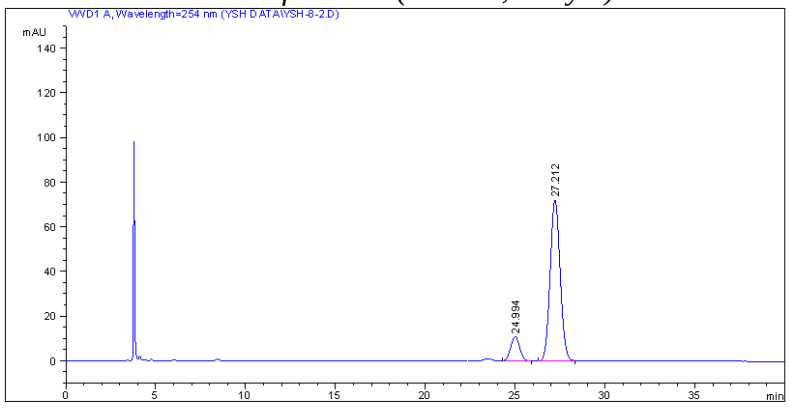
*Enantiomeric excess of **3**: 76% (Table 1, entry 4)*

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Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  24.994 BB    0.5411  384.92709   10.99052  12.1288
   2  27.212 BB    0.6032 2788.73145   72.01487  87.8712

Totals :                  3173.65854   83.00539
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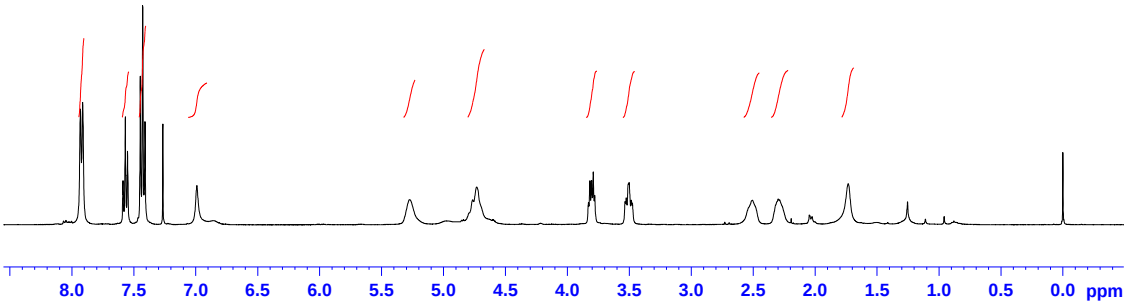
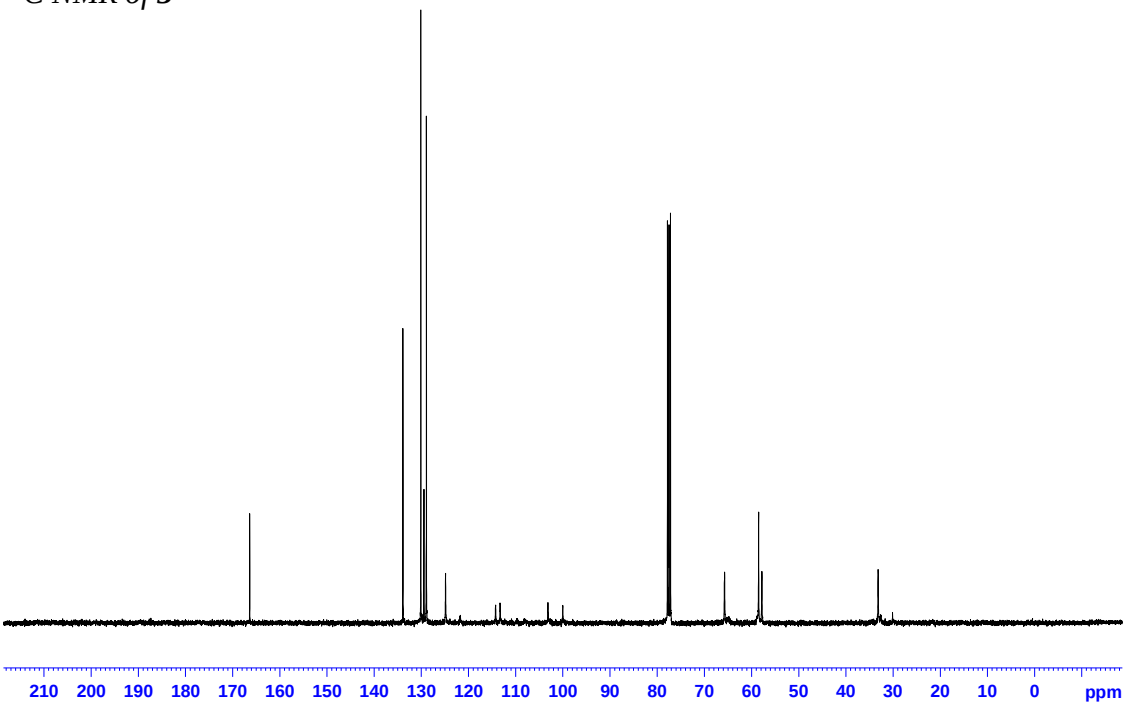
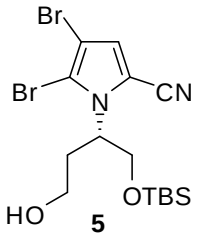
*^{1}H NMR of **3***



*^{13}C NMR of **3***





5

White Solid

M.P. 70~72 °C

$[\alpha]^{22}_{D}$ –12.0 (c 1, CH_3OH) *in the case of 80% ee (Table 1, entry 3)*

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (s, 1H), 4.99-4.88 (m, 1H), 4.09-4.05 (m, 1H), 3.90 (dd, *J* = 10.8, 5.2 Hz, 1H), 3.75-3.71 (m, 1H), 3.53-3.43 (m, 1H), 2.43-2.32 (m, 1H), 2.18-2.08 (m, 1H), 1.48 (s, 1H), 0.79 (s, 9H), 0.01 (s, 3H), −0.05 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 123.7, 114.1, 113.0, 102.3, 98.9, 64.4, 60.5, 58.4, 32.4, 25.4, 17.8, −5.6, −5.8

FTIR (neat) 3438, 2928, 2855, 2221, 1413, 1319, 1249, 1109, 835, 777 cm^{-1}

HRMS (FAB) calcd for $[M+H]^+$ $C_{15}H_{25}O_2N_2Br_2Si$ 451.0052, found 451.0049

HPLC Condition to determine enantiomeric excess:

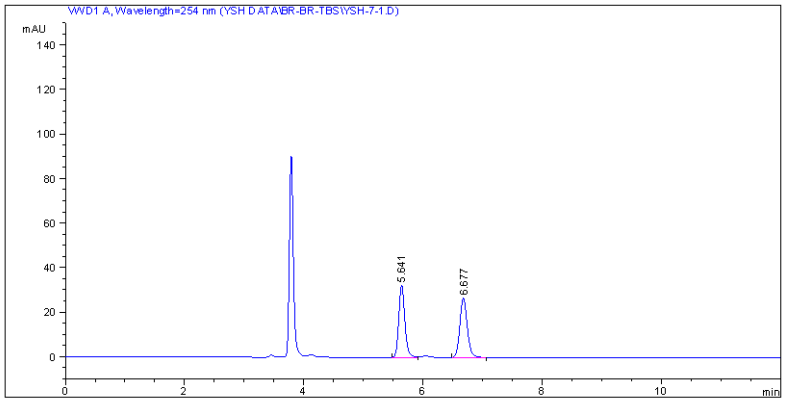
Chiral column: Chiralpak AD-H (250 x 4.6 mm)

Mobile Phase (90/10 = Hexane/IPA)

Flow Rate (0.9 mL/min), Detection Wavelength (254 nm)

Retention Time: 5.6 min (minor isomer), 6.6 min (major isomer)

*Racemate of **5***

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Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
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   2   6.677 BB    0.1333  230.81219   26.59273  50.0186

Totals :                   461.45306   59.00366
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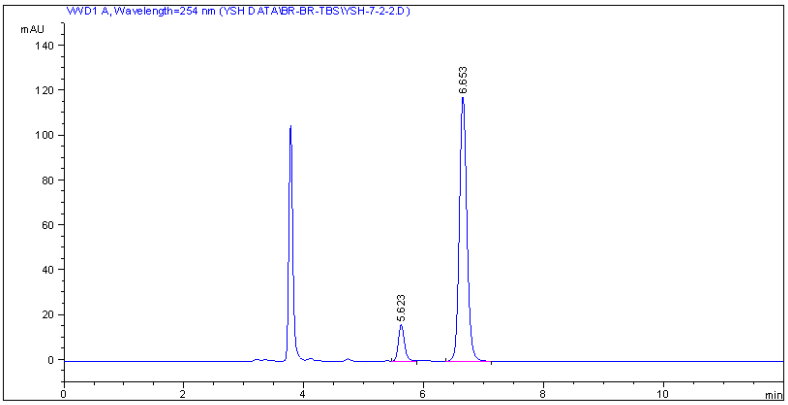
*Enantiomeric excess of **5**: 80% (Table 1, entry 6)*

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Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]       %
----|-------|----|-------|----------|----------|--------|
   1   5.623 VV    0.1101  116.71778   16.23932  10.1279
   2   6.653 BB    0.1345 1035.72546  117.95556  89.8721

Totals :                  1152.44324  134.19488
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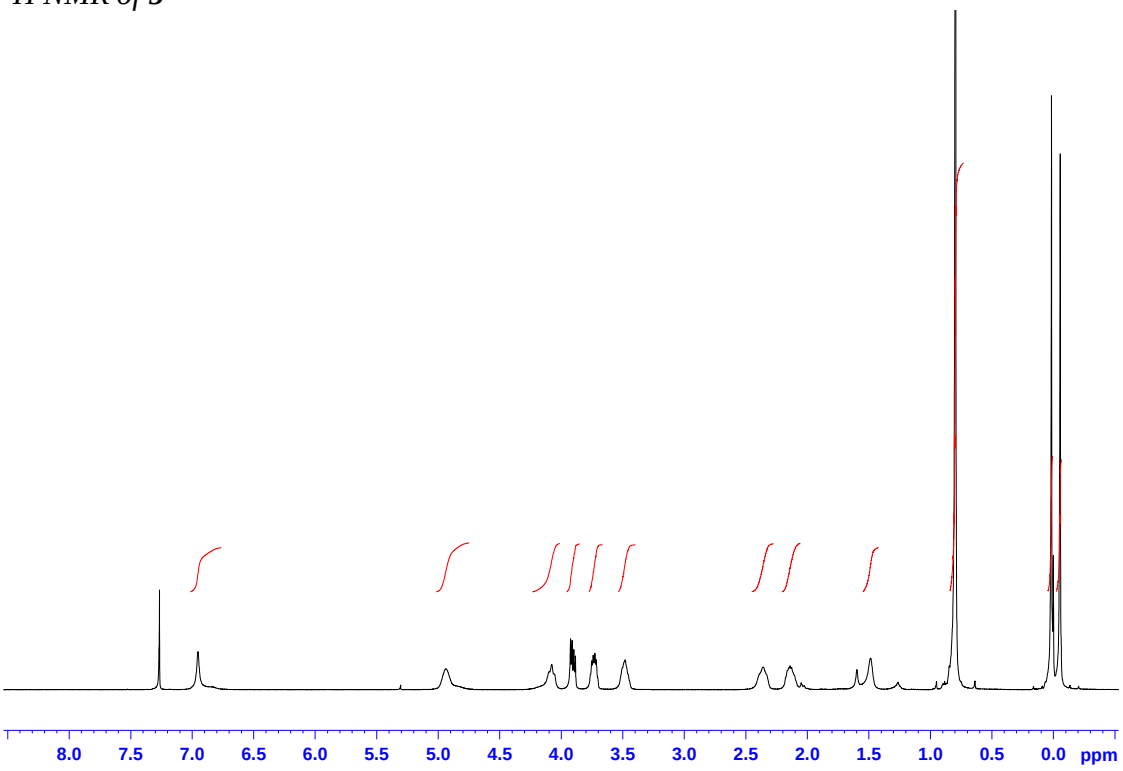
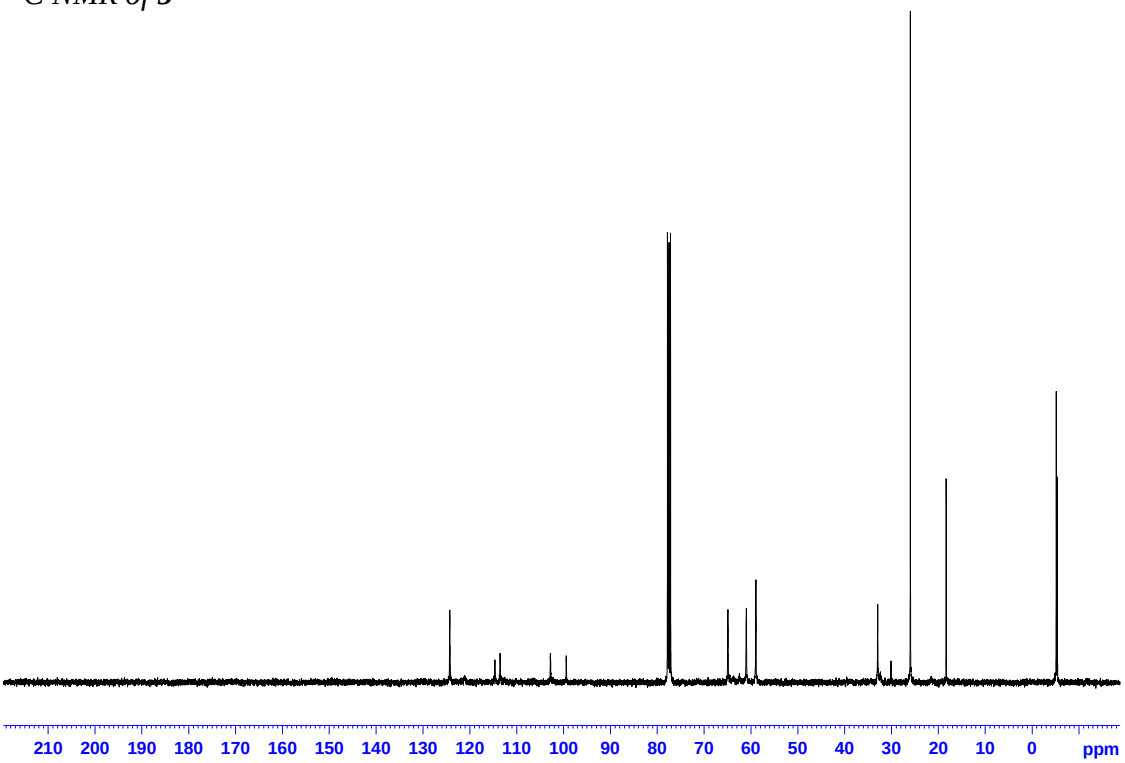
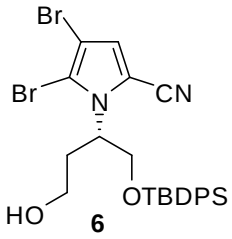
^{1}H *NMR of* ***5***



^{13}C *NMR of* ***5***





6

White Solid

M.P. 99~101 ^{o}C

$[\alpha]^{20}_{D}$ +18.2 (c 1, CH_3OH) *in the case of 93% ee (Table 1, entry 6)*

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.56 (m, 2H), 7.51-7.34 (m, 8H), 6.91 (s, 1H), 5.07-4.96 (m, 1H), 4.11 (t, *J* = 10.0 Hz, 1H), 3.93-3.87 (m, 1H), 3.70-3.63 (m, 1H), 3.47-3.38 (m, 1H), 2.36-2.25 (m, 1H), 2.11-2.00 (m, 1H), 1.42 (s, 1H), 0.96 (s, 9H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.4, 132.6, 132.3, 129.9, 129.8, 127.7, 123.8, 114.2, 112.8, 102.4, 99.0, 65.0, 60.3, 58.2, 32.3, 26.4, 18.9

FTIR (neat) 3391, 2929, 2858, 2223, 2102, 1416, 1311, 1113, 700 cm^{-1}

HRMS (EI) calcd for $[M]^+$ $C_{25}H_{28}Br_2N_2O_2Si$ 574.0287, found 574.0286

HPLC Condition to determine enantiomeric excess:

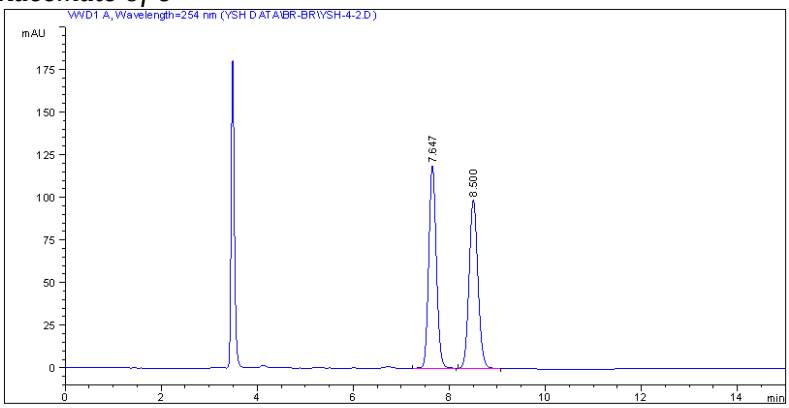
Chiral column: Chiralpak AD-H (250 x 4.6 mm)

Mobile Phase (95/5 = Hexane/IPA)

Flow Rate (1.0 mL/min), Detection Wavelength (254 nm)

Retention Time: 7.8 min (minor isomer), 8.7 min (major isomer)

*Racemate of **6***

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Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
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   1   7.647 VB     0.1686 1302.55652  118.87830  50.6750
   2   8.500 BB     0.1990 1267.85608   98.96604  49.3250

Totals :                  2570.41260  217.84435
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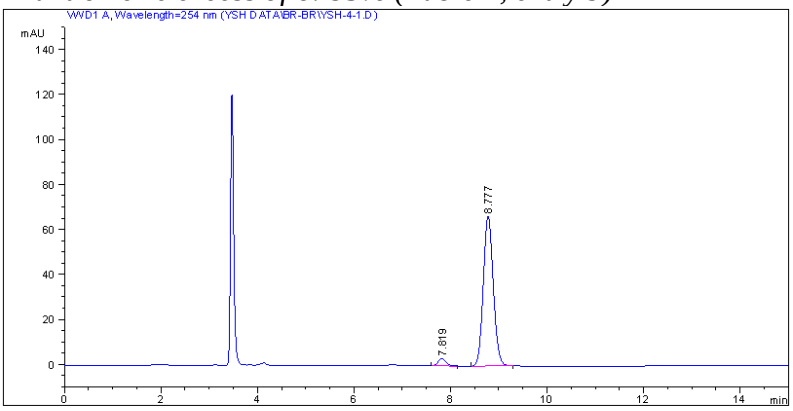
*Enantiomeric excess of **6**: 93% (Table 1, entry 9)*

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Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]       %
----|-------|----|-------|----------|----------|--------|
   1   7.819 BB     0.1813   37.34903    3.16520   3.7491
   2   8.777 BB     0.2235  958.85693   66.52519  96.2509

Totals :                  996.20597   69.69039
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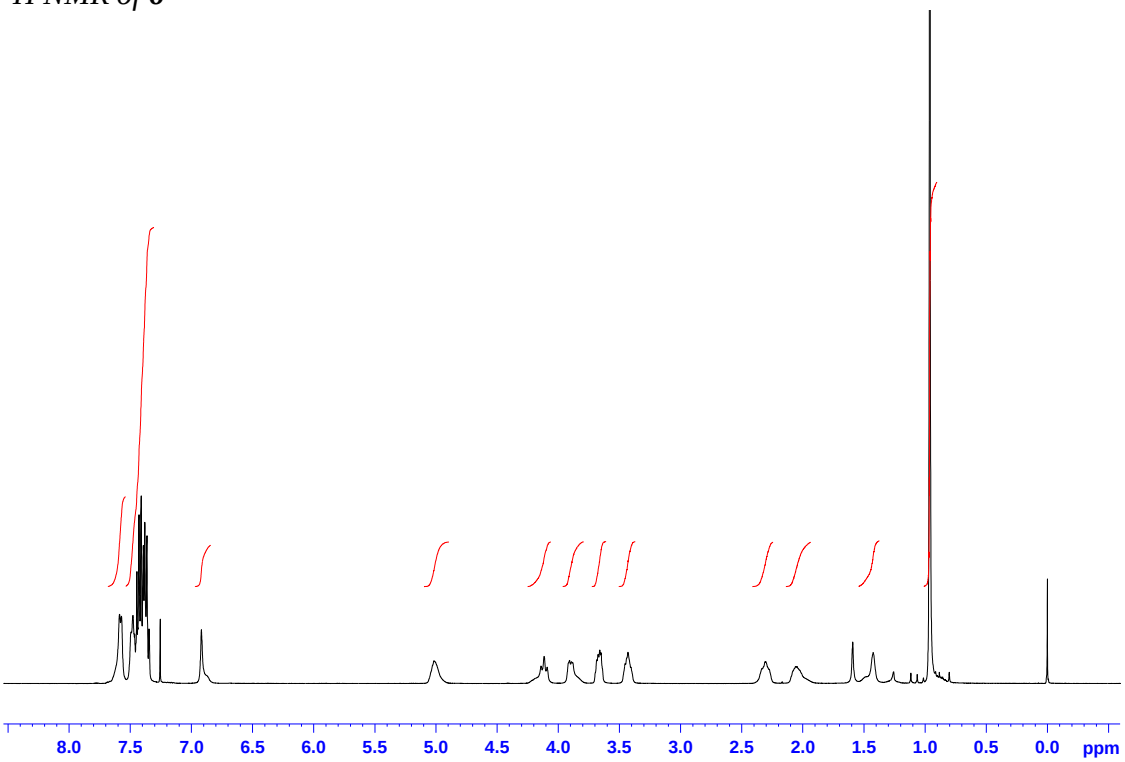
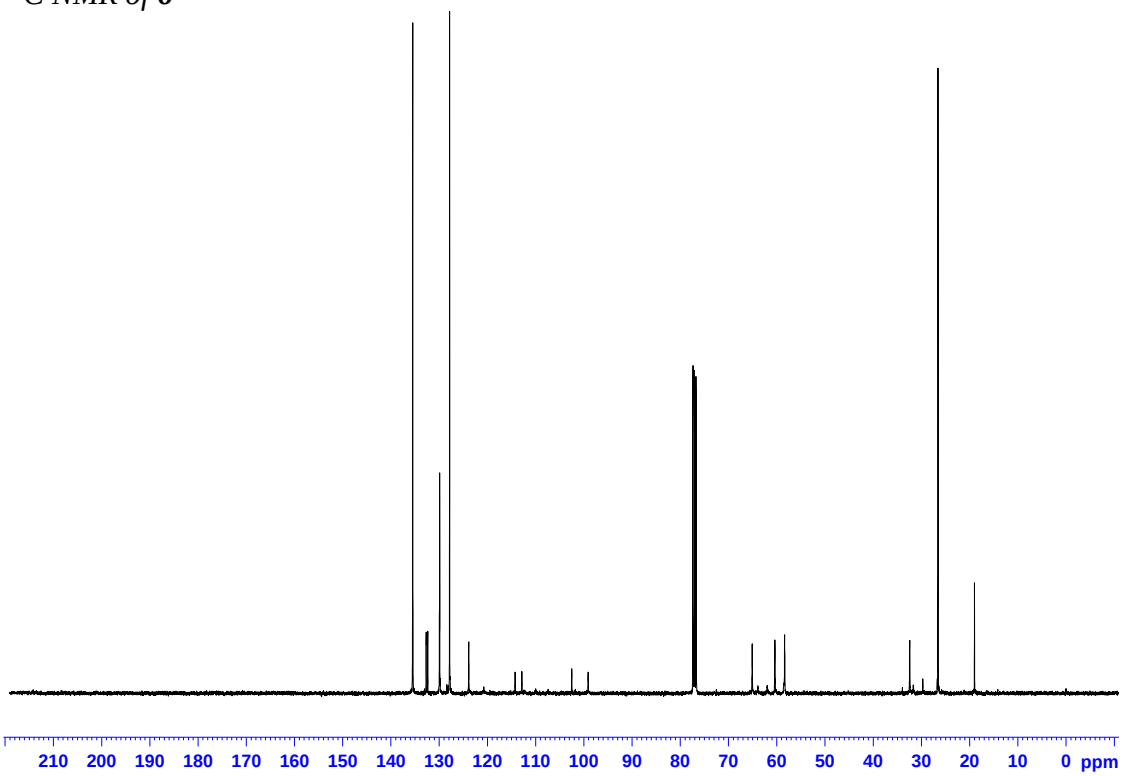
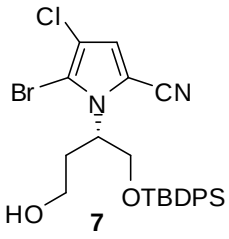
^{1}H NMR of ***6***



^{13}C NMR of ***6***





7

Yellow Oil

$[\alpha]^{21}_{D}$ +26.8 (c 1, CH_3OH)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.55 (m, 2H), 7.51-7.33 (m, 8H), 6.85 (s, 1H), 5.03-4.93 (m, 1H), 4.12 (t, *J* = 9.6 Hz, 1H), 3.93-3.86 (m, 1H), 3.68-3.63 (m, 1H), 3.42 (dt, *J* = 10.0, 3.6 Hz, 1H), 2.36-2.25 (m, 1H), 2.10-1.99 (m, 1H), 1.49 (s, 1H), 0.96 (s, 9H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.4, 132.6, 132.2, 129.9, 129.8, 127.7, 121.1, 113.4, 112.9, 111.7, 101.4, 64.9, 59.8, 58.2, 32.3, 26.4, 18.9

FTIR (neat) 3368, 3114, 2929, 2858, 2224, 1426, 1329, 1113, 825, 701, 508 cm^{-1}

HRMS (EI) calcd for $[M]^+$ $C_{25}H_{28}BrClN_2O_2Si$ 530.0792, found 530.0791

HPLC Condition to determine enantiomeric excess:

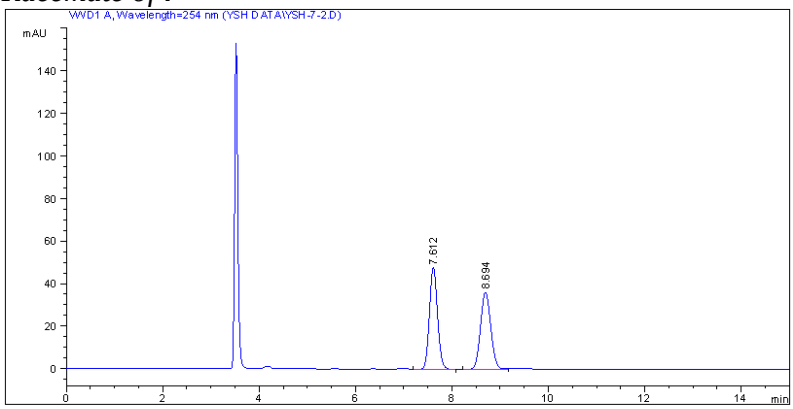
Chiral column: Chiralpak AD-H (250 x 4.6 mm)

Mobile Phase (95/5 = Hexane/IPA)

Flow Rate (1.0 mL/min), Detection Wavelength (254 nm)

Retention Time: 7.4 min (minor isomer), 8.5 min (major isomer)

*Racemate of **7***

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Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   7.612 VB    0.1818  561.38043   47.90997  50.8621
   2   8.694 BB    0.2321  542.34937   36.40378  49.1379

Totals :                  1103.72980   84.31375
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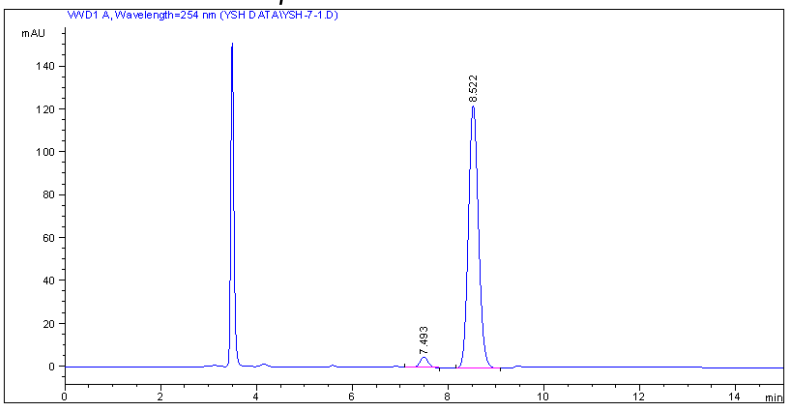
*Enantiomeric excess of **7**: 93%*

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Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   7.493 VB    0.1876   60.13028    4.92578   3.2671
   2   8.522 BB    0.2265 1780.34387  122.39133  96.7329

Totals :                  1840.47415  127.31711
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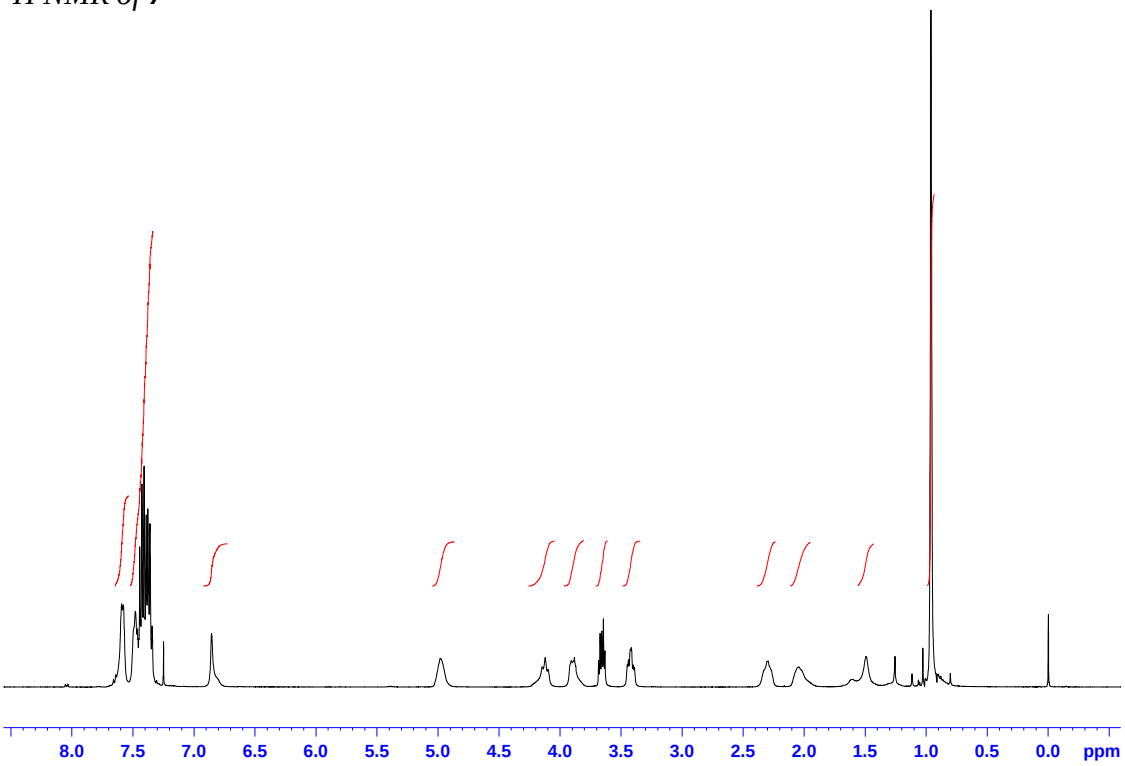
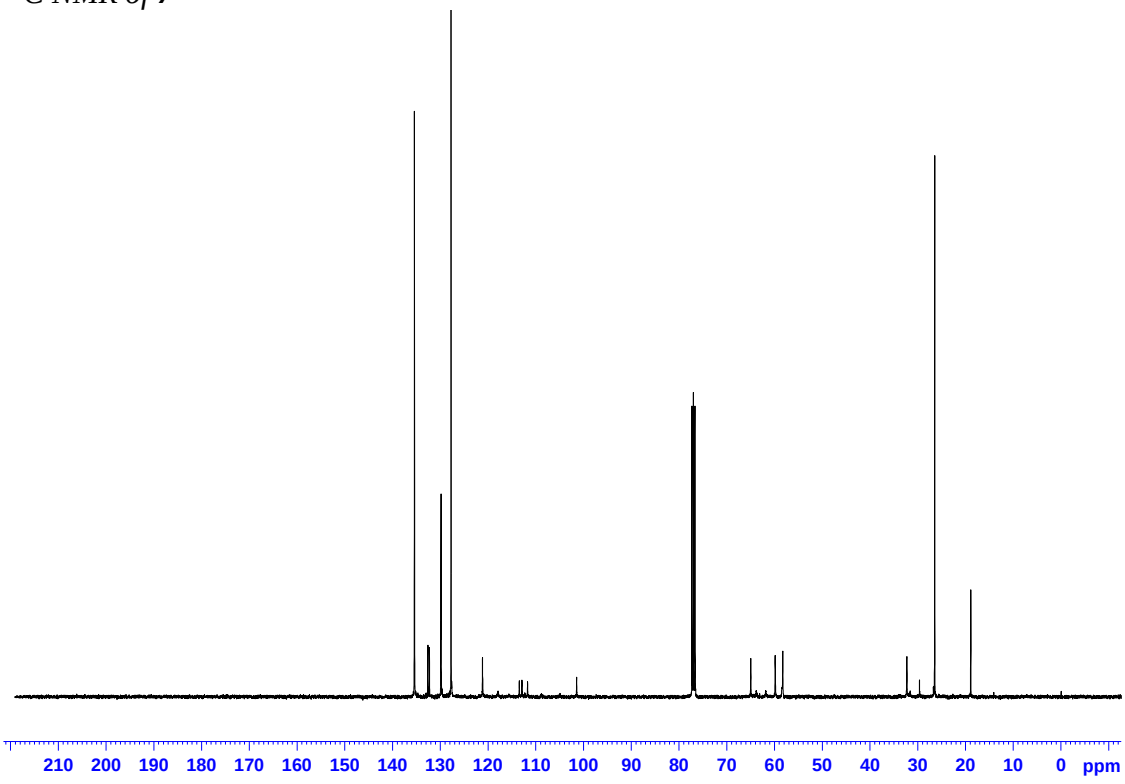
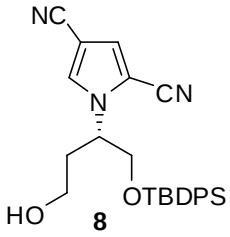
^{1}H NMR of ***7***



^{13}C NMR of ***7***





8

Light Yellow Solid

M.P. 93~95 ^{o}C

$[\alpha]^{22}_{D}$ –9.0 (c 1, CH_3OH)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.37 (m, 10H), 7.32 (d, *J* = 1.2 Hz, 1H), 7.03 (d, *J* = 1.6 Hz, 1H), 4.71-4.65 (m, 1H), 3.91 (dd, *J* = 11.2, 3.6 Hz, 1H), 3.83 (dd, *J* = 11.2, 7.2 Hz, 1H), 3.67-3.62 (m, 1H), 3.44-3.38 (m, 1H), 2.10-1.99 (m, 2H), 1.57 (s, 1H), 1.00 (s, 9H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.4, 135.3, 132.0, 131.9, 130.2, 130.1, 130.0, 127.8, 121.9, 114.2, 111.5, 106.3, 94.5, 65.5, 59.0, 57.8, 33.1, 26.5, 18.9

FTIR (neat) 3447, 3128, 2931, 2858, 2231, 1428, 1114, 702 cm^{-1}

HRMS (EI) calcd for $[M]^+$ $C_{26}H_{29}N_3O_2Si$ 443.2029, found 443.2032

HPLC Condition to determine enantiomeric excess:

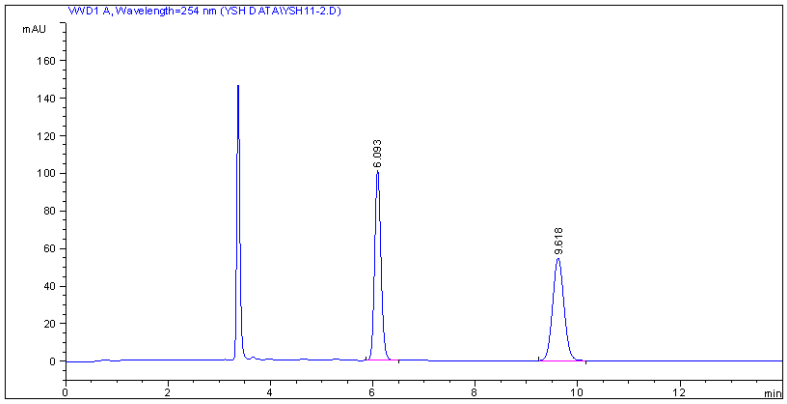
Chiral column: Chiralpak AD-H (250 x 4.6 mm)

Mobile Phase (90/10 = Hexane/IPA)

Flow Rate (1.0 mL/min), Detection Wavelength (254 nm)

Retention Time: 6.0 min (minor isomer), 9.6 min (major isomer)

*Racemate of **8***

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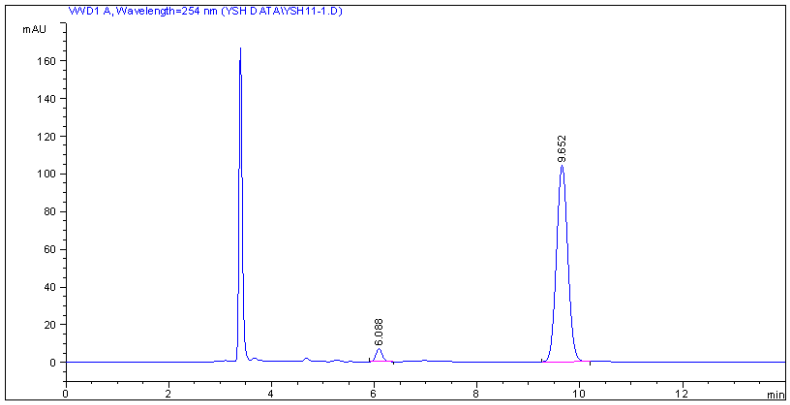
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   6.093 BB    0.1319  865.35352  101.06882  50.8989
   2   9.618 BB    0.2366  834.78906   54.60849  49.1011

Totals :                  1700.14258  155.67732
```

*Enantiomeric excess of **8**: 93%*

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=====================================================================
                        Area Percent Report
=====================================================================

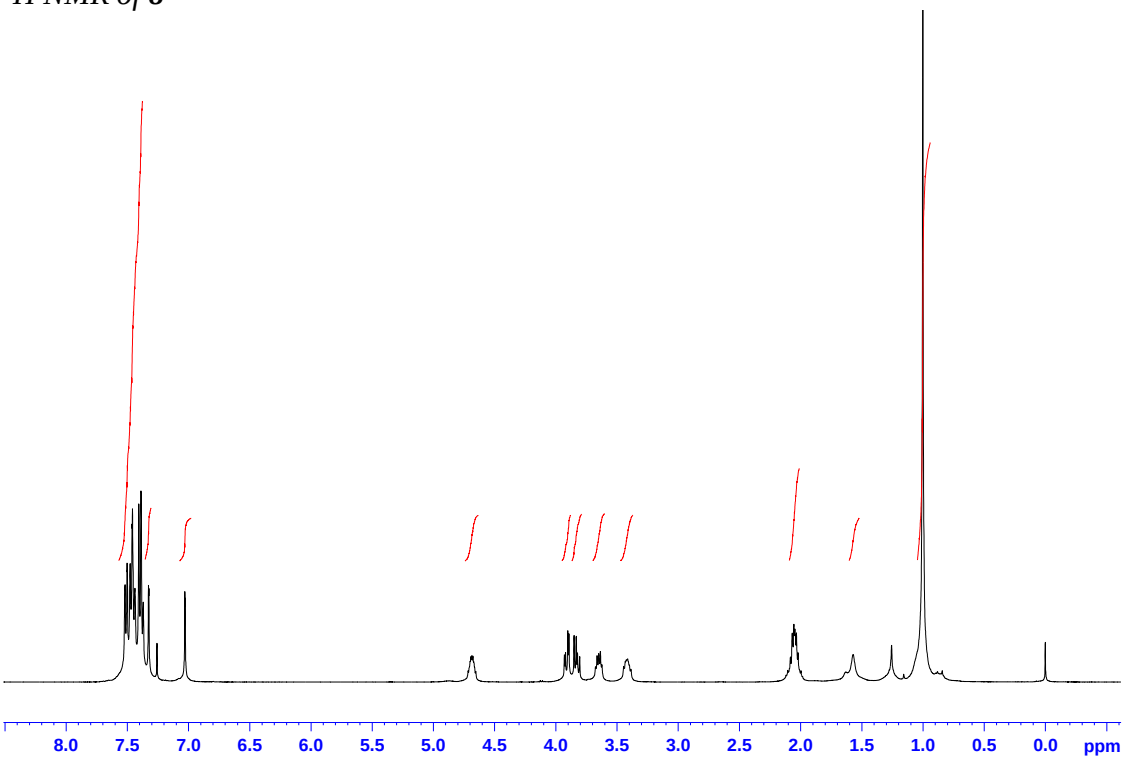
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

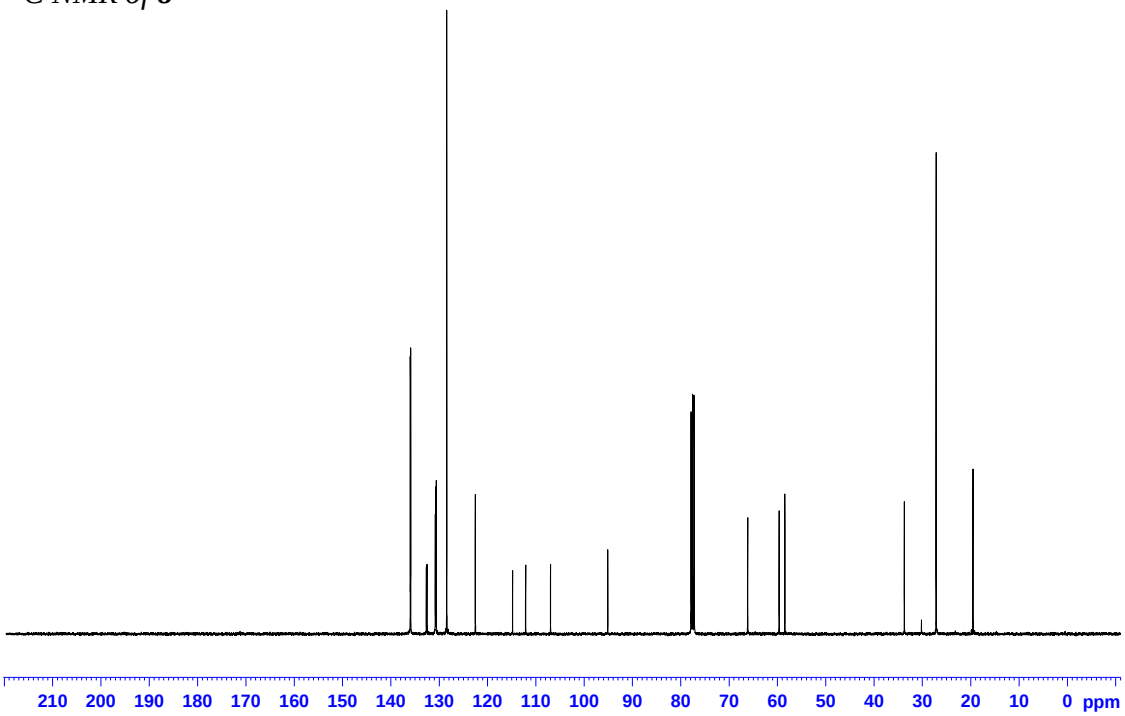
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   6.088 BB    0.1326   59.66602    6.92044   3.6141
   2   9.652 BB    0.2384 1591.25574  103.86515  96.3859

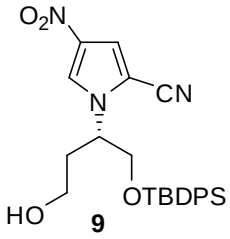
Totals :                  1650.92175  110.78559
```

^{1}H NMR of **8**



^{13}C NMR of **8**





9

Light Yellow Solid

M.P. 88~90 °C

$[\alpha]^{21}_{D}$ +16.1 (c 1, CH_3OH)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 1.6 Hz, 1H), 7.52-7.34 (m, 11H), 4.70-4.66 (m, 1H), 3.94 (dd, *J* = 11.2, 3.2 Hz, 1H), 3.86 (dd, *J* = 11.2, 6.8 Hz, 1H), 3.69-3.64 (m, 1H), 3.48-3.42 (m, 1H), 2.11-2.05 (m, 2H), 1.72 (s, 1H), 1.01 (s, 9H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4, 135.4, 135.3, 132.0, 131.9, 130.1, 130.1, 127.8, 123.9, 114.6, 111.2, 105.7, 65.5, 59.3, 57.9, 33.1, 26.6, 18.9

FTIR (neat) 3419, 3127, 2928, 2857, 2230, 1512, 1389, 1308, 1113, 702 cm^{-1}

HRMS (EI) calcd for $[M]^+$ $C_{25}H_{29}N_3O_4Si$ 463.1927, found 463.1932

HPLC Condition to determine enantiomeric excess:

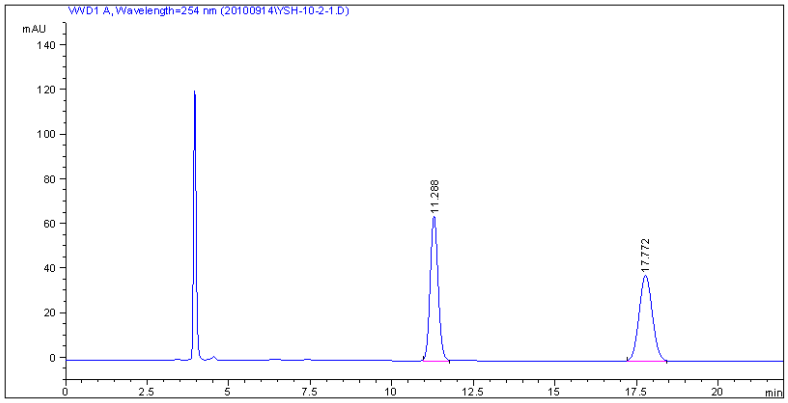
Chiral column: Chiralpak AD-H (250 x 4.6 mm)

Mobile Phase (95/5 = Hexane/IPA)

Flow Rate (0.9 mL/min), Detection Wavelength (254 nm)

Retention Time: 11.2 min (minor isomer), 17.8 min (major isomer)

*Racemate of **9***

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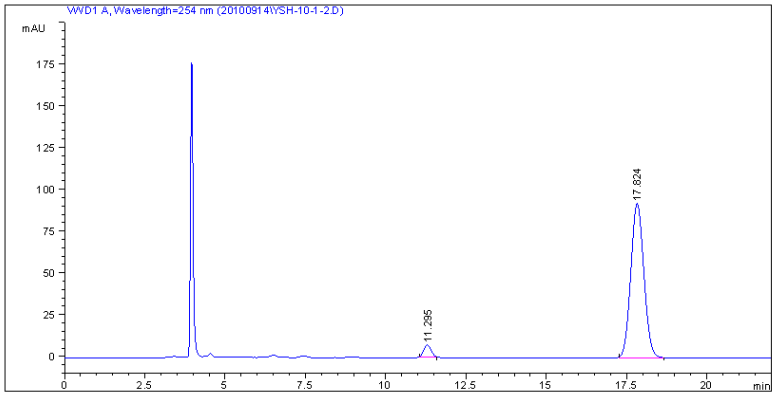
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]       %
----|-------|----|-------|----------|----------|--------|
   1  11.288 MM    0.2811 1095.77185   64.96107  49.7990
   2  17.772 MM    0.4742 1104.61572   38.82713  50.2010
```

*Enantiomeric excess of **9**: 91%*

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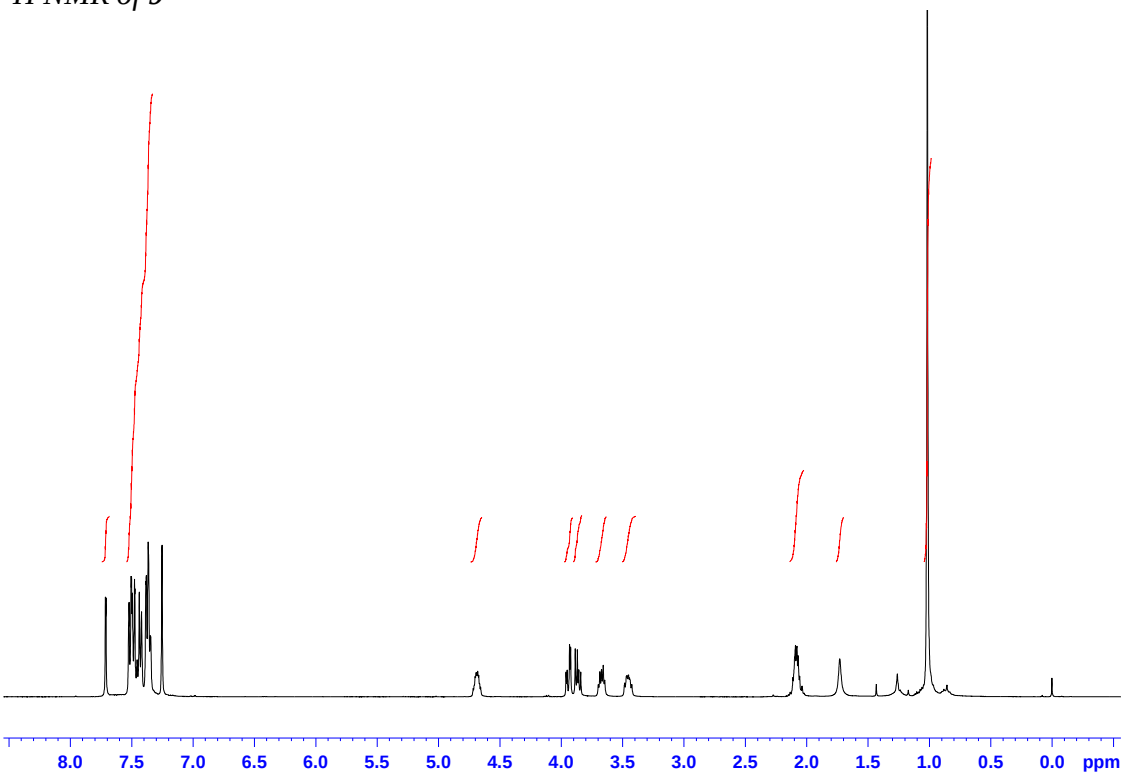
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

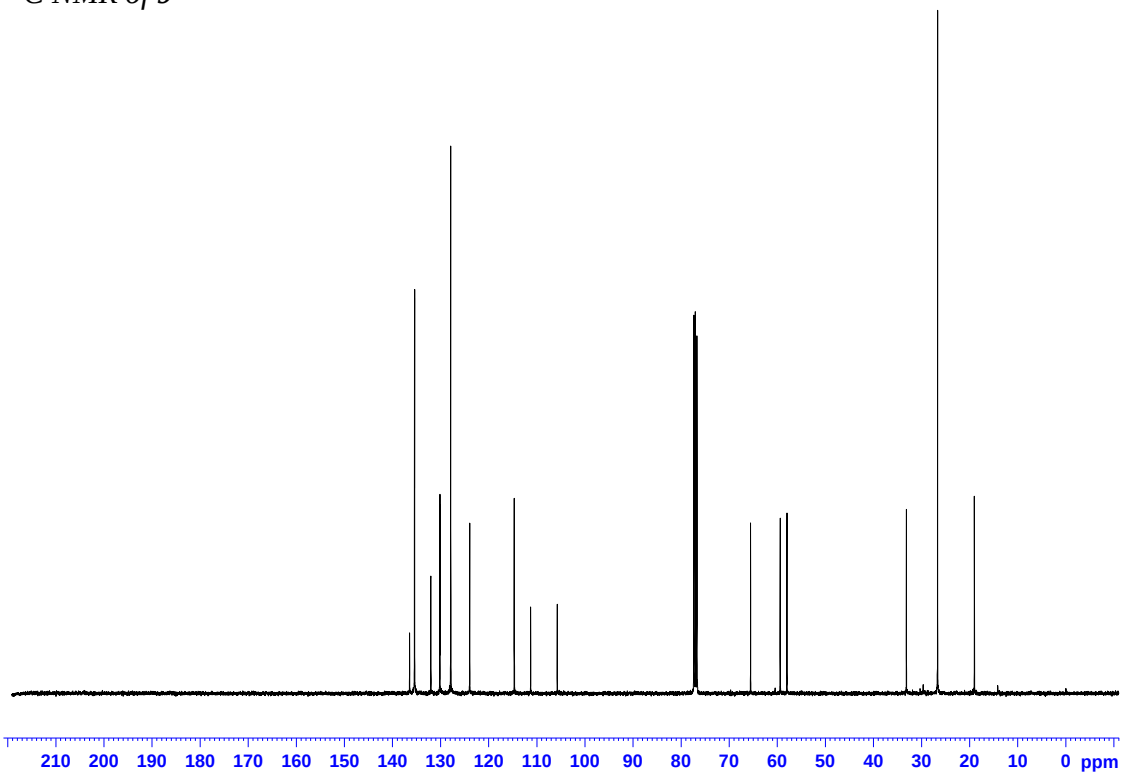

Signal 1: VWD1 A, Wavelength=254 nm

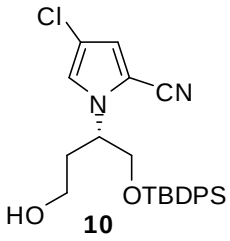
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]       %
----|-------|----|-------|----------|----------|--------|
   1  11.295 MM    0.2763  124.21130    7.49312   4.4963
   2  17.824 MM    0.4753 2638.28662   92.52138  95.5037
```

^{1}H NMR of ***9***



^{13}C NMR of ***9***





10

Colorless Oil

$[\alpha]^{24}_{D}$ –8.2 (c 1, CH_3OH)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.35 (m, 10H), 6.87 (d, *J* = 1.6 Hz, 1H), 6.70 (d, *J* = 1.6 Hz, 1H), 4.61-4.55 (m, 1H), 3.85 (dd, *J* = 10.8, 3.6 Hz, 1H), 3.76 (dd, *J* = 10.8, 6.8 Hz, 1H), 3.65-3.59 (m, 1H), 3.46-3.40 (m, 1H), 2.04-1.98 (m, 2H), 1.58 (s, 1H), 1.00 (s, 9H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 135.4, 132.3, 132.2, 129.9, 129.9, 127.8, 127.8, 121.8, 118.2, 112.9, 112.6, 104.3, 66.1, 58.3, 58.3, 33.5, 26.5, 19.0

FTIR (neat) 3394, 3114, 2930, 2858, 2223, 1427, 1128, 1113, 700 cm^{-1}

HRMS (EI) calcd for $[M]^+$ $C_{25}H_{29}ClN_2O_2Si$ 452.1687, found 452.1684

HPLC Condition to determine enantiomeric excess:

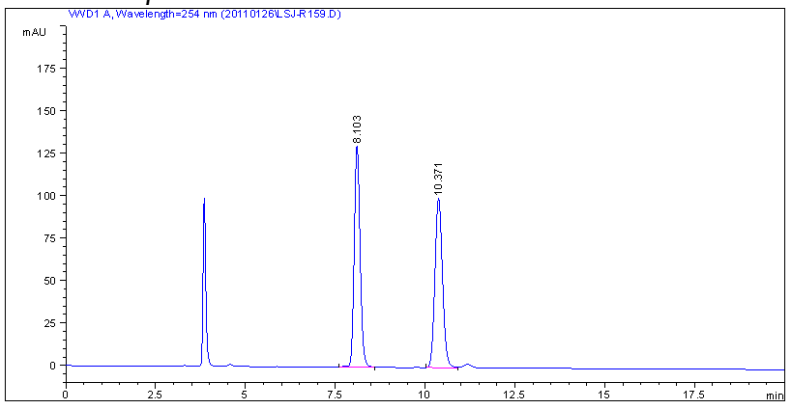
Chiral column: Chiralpak AD-H (250 x 4.6 mm)

Mobile Phase (95/5 = Hexane/IPA)

Flow Rate (0.95 mL/min), Detection Wavelength (254 nm)

Retention Time: 7.8 min (minor isomer), 10.1 min (major isomer)

*Racemate of **10***

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=====================================================================
                      Area Percent Report
=====================================================================

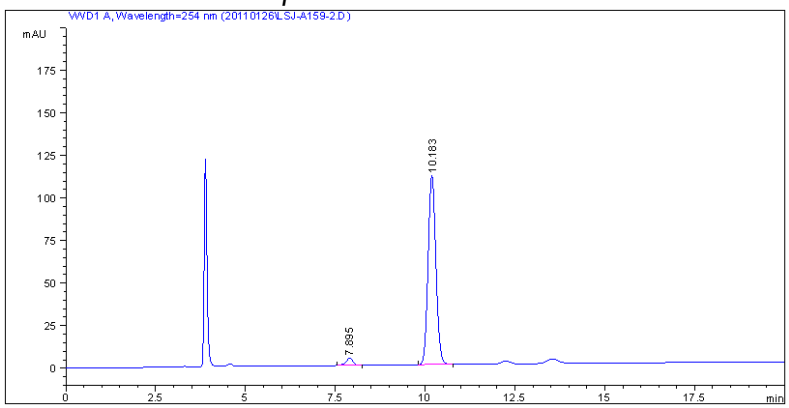
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   8.103 BB    0.1766 1483.76416  130.21782  50.2906
   2  10.371 BV    0.2285 1466.61914   99.63952  49.7094

Totals :                  2950.38330  229.85734
```

*Enantiomeric excess of **10**: 93%*

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=====================================================================
                      Area Percent Report
=====================================================================

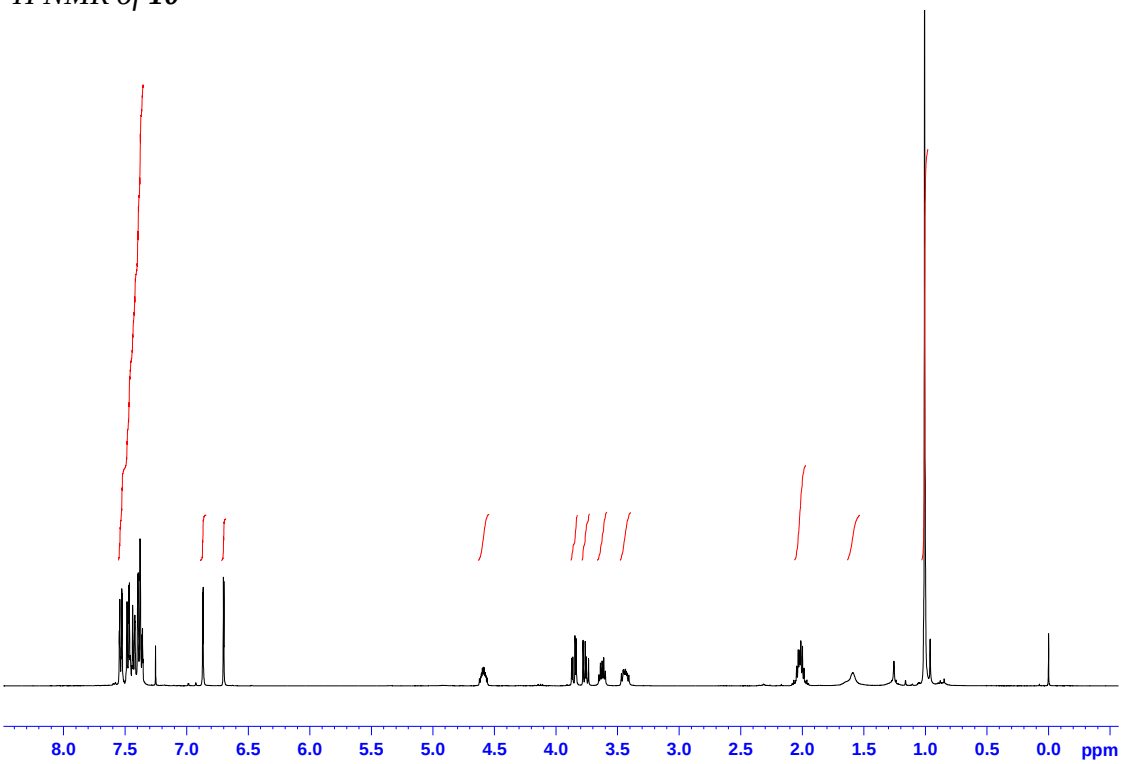
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

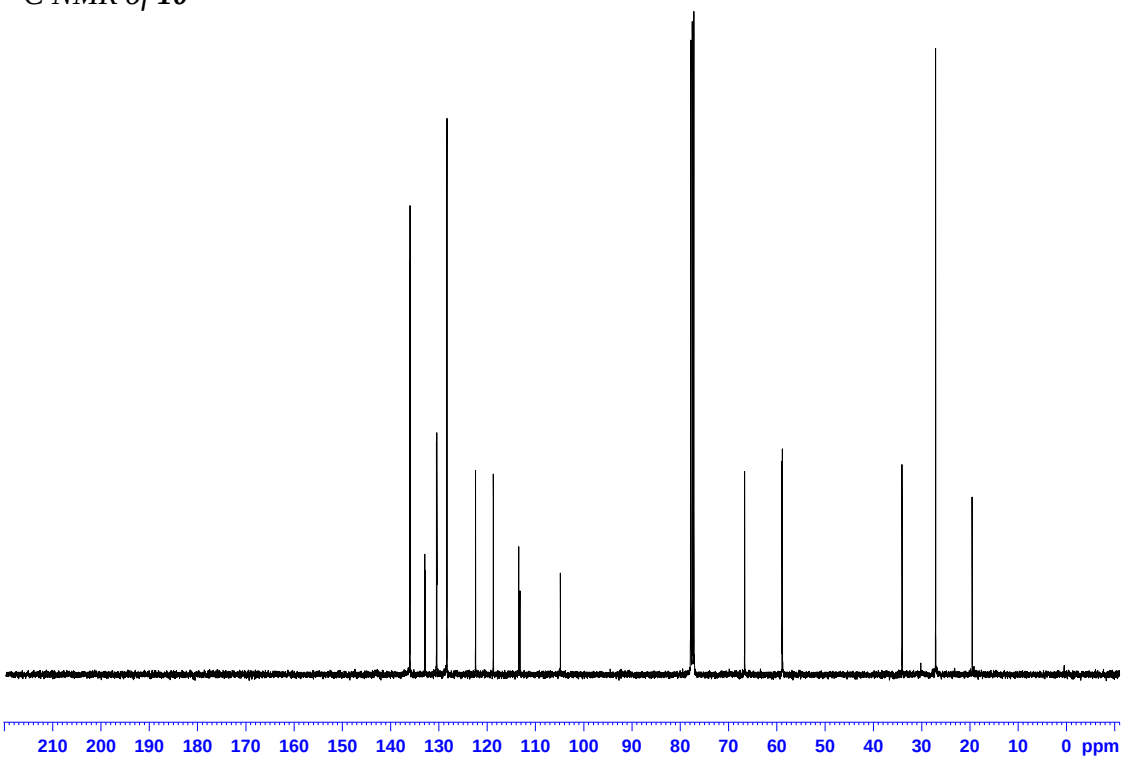
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   7.895 BB    0.1967   57.93516    4.41850   3.3546
   2  10.183 BB    0.2322 1669.08008  111.03948  96.6454

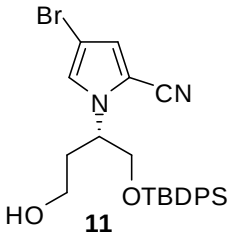
Totals :                  1727.01524  115.45798
```

^{1}H NMR of ***10***



^{13}C NMR of ***10***





11

Yellow Oil

$[\alpha]^{25}_{D}$ –9.3 (c 1, CH_3OH)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.36 (m, 10H), 6.92 (d, *J* = 1.6 Hz, 1H), 6.78 (d, *J* = 1.6 Hz, 1H), 4.64-4.58 (m, 1H), 3.85 (dd, *J* = 10.8, 3.6 Hz, 1H), 3.76 (dd, *J* = 10.8, 6.8 Hz, 1H), 3.67-3.61 (m, 1H), 3.49-3.41 (m, 1H), 2.06-2.00 (m, 2H), 1.47 (s, 1H), 1.00 (s, 9H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.4, 135.4, 132.3, 132.2, 129.9, 129.9, 127.8, 124.3, 120.6, 112.5, 105.2, 96.4, 66.1, 58.3, 58.3, 33.5, 26.5, 19.0

FTIR (neat) 3446, 3071, 2931, 2858, 2221, 1427, 1318, 1113, 758, 702, 504 cm^{-1}

HRMS (EI) calcd for $[M]^+$ $C_{25}H_{29}BrN_2O_2Si$ 496.1182, found 496.1185

HPLC Condition to determine enantiomeric excess:

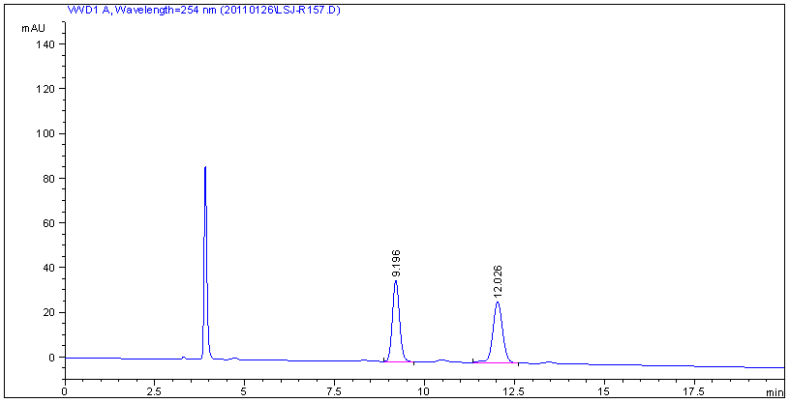
Chiral column: Chiralpak AD-H (250 x 4.6 mm)

Mobile Phase (95/5 = Hexane/IPA)

Flow Rate (0.95 mL/min), Detection Wavelength (254 nm)

Retention Time: 9.0 min (minor isomer), 11.7 min (major isomer)

*Racemate of **11***

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=====================================================================
                      Area Percent Report
=====================================================================

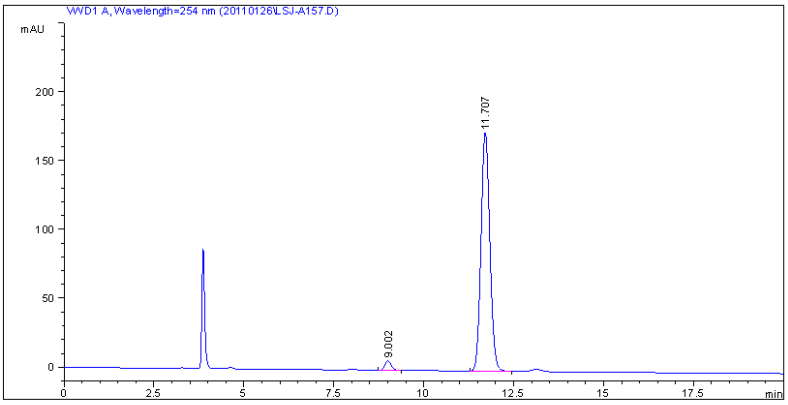
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]       %
----|-------|----|-------|----------|----------|--------|
   1   9.196 BB    0.2118  497.13705   36.39104  49.2742
   2  12.026 BB    0.2892  511.78235   27.40550  50.7258

Totals :                  1008.91940   63.79654
```

*Enantiomeric excess of **11**: 94%*

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                      Area Percent Report
=====================================================================

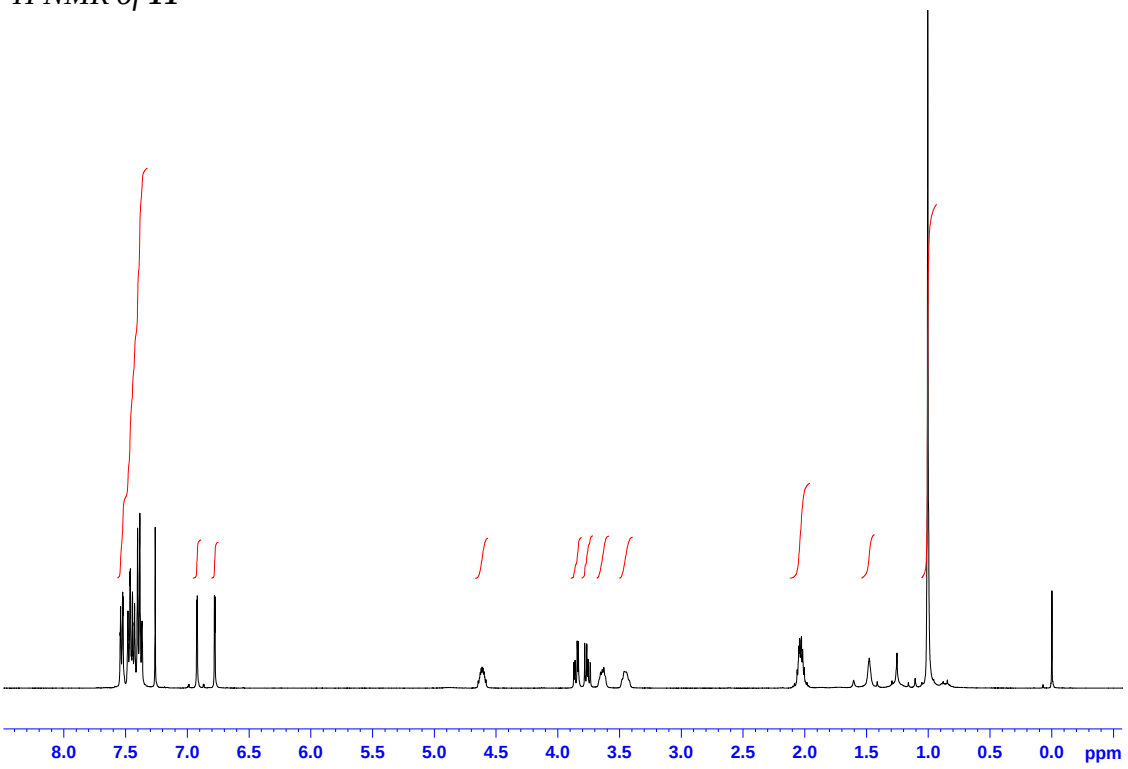
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

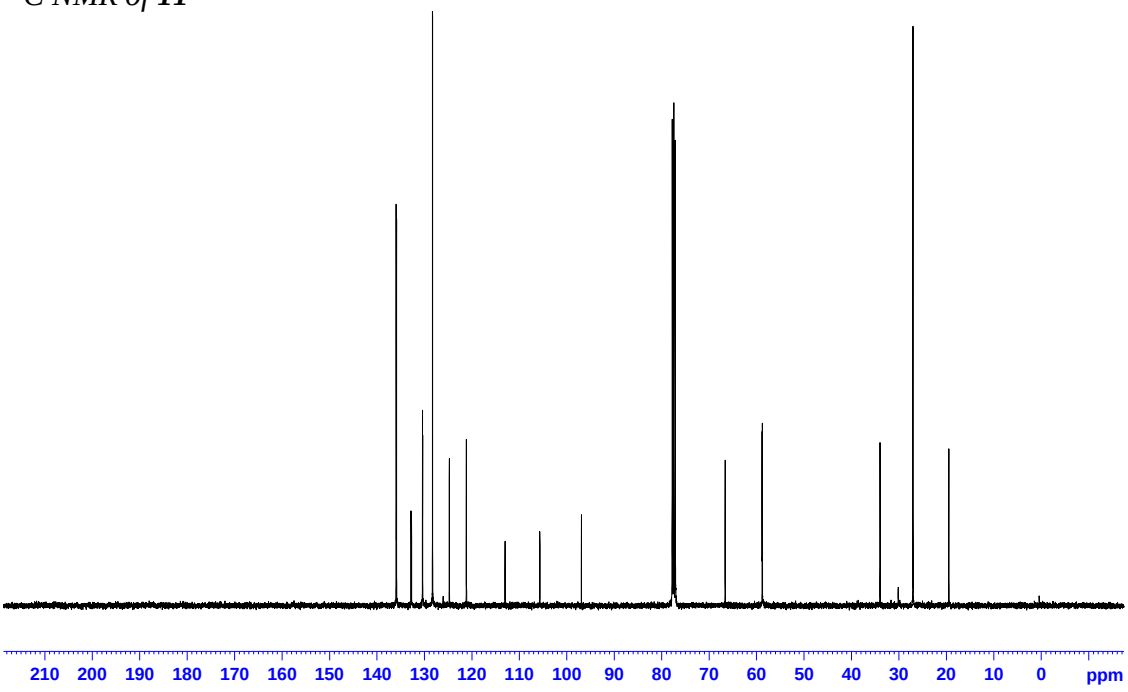
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]       %
----|-------|----|-------|----------|----------|--------|
   1   9.002 BB    0.1979   87.11239    6.84746   2.8538
   2  11.707 BB    0.2651 2965.43652  173.34142  97.1462

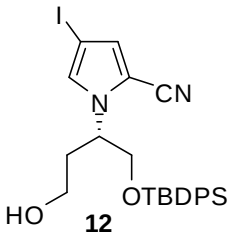
Totals :                  3052.54891  180.18887
```

^{1}H NMR of ***11***



^{13}C NMR of ***11***





12

Light Yellow Oil

$[\alpha]^{21}_{D}$ –19.0 (c 1, CH_3OH)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.35 (m, 10H), 6.98 (d, *J* = 2.0 Hz, 1H), 6.86 (d, *J* = 1.6 Hz, 1H), 4.64-4.58 (m, 1H), 3.84 (dd, *J* = 10.8, 3.6 Hz, 1H), 3.77 (dd, *J* = 10.8, 6.8 Hz, 1H), 3.65-3.60 (m, 1H), 3.47-3.41 (m, 1H), 2.06-2.01 (m, 2H), 1.53 (s, 1H), 1.00 (s, 9H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 135.4, 132.4, 132.3, 129.9, 129.9, 129.2, 127.8, 127.8, 125.6, 112.3, 106.4, 66.2, 59.9, 58.3, 58.2, 33.6, 26.6, 19.0

FTIR (neat) 3447, 3071, 2930, 2857, 2222, 1589, 1460, 1427, 1310, 1114, 758, 702, 504 cm^{-1}

HRMS (EI) calcd for $[M]^+$ $C_{25}H_{28}N_2O_2SiI$ 543.0965, found 543.0968

HPLC Condition to determine enantiomeric excess:

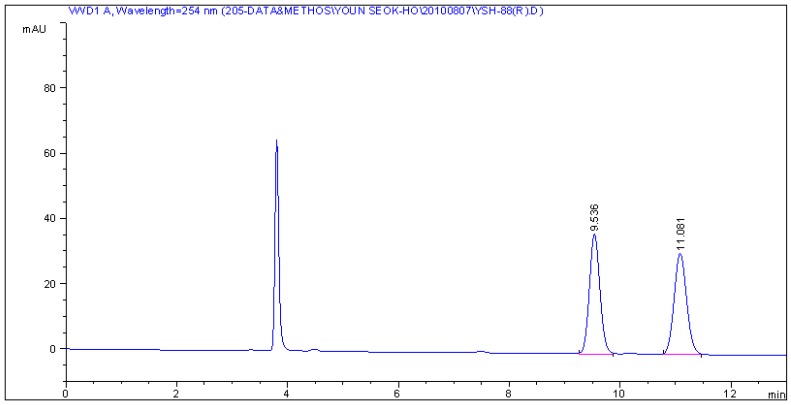
Chiral column: Chiralpak AD-H (250 x 4.6 mm)

Mobile Phase (95/5 = Hexane/IPA)

Flow Rate (1.0 mL/min), Detection Wavelength (254 nm)

Retention Time: 9.4 min (major isomer), 10.9 min (minor isomer)

*Racemate of **12***

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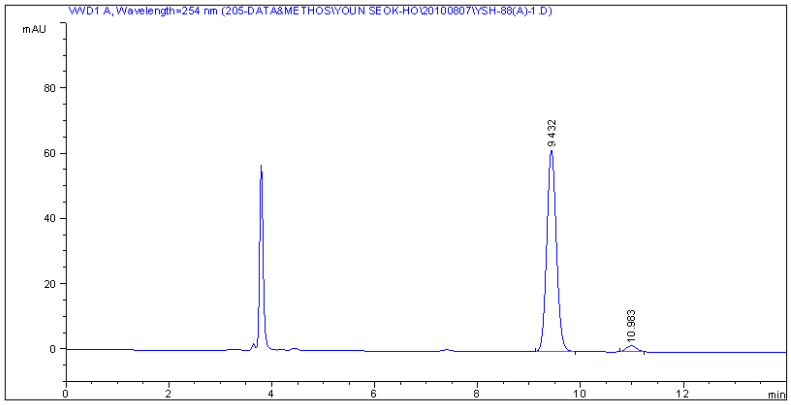
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   9.536 MM    0.2220  491.37085   36.88931  50.3232
   2  11.081 MM    0.2606  485.05893   31.02228  49.6768
```

*Enantiomeric excess of **12**: 93%*

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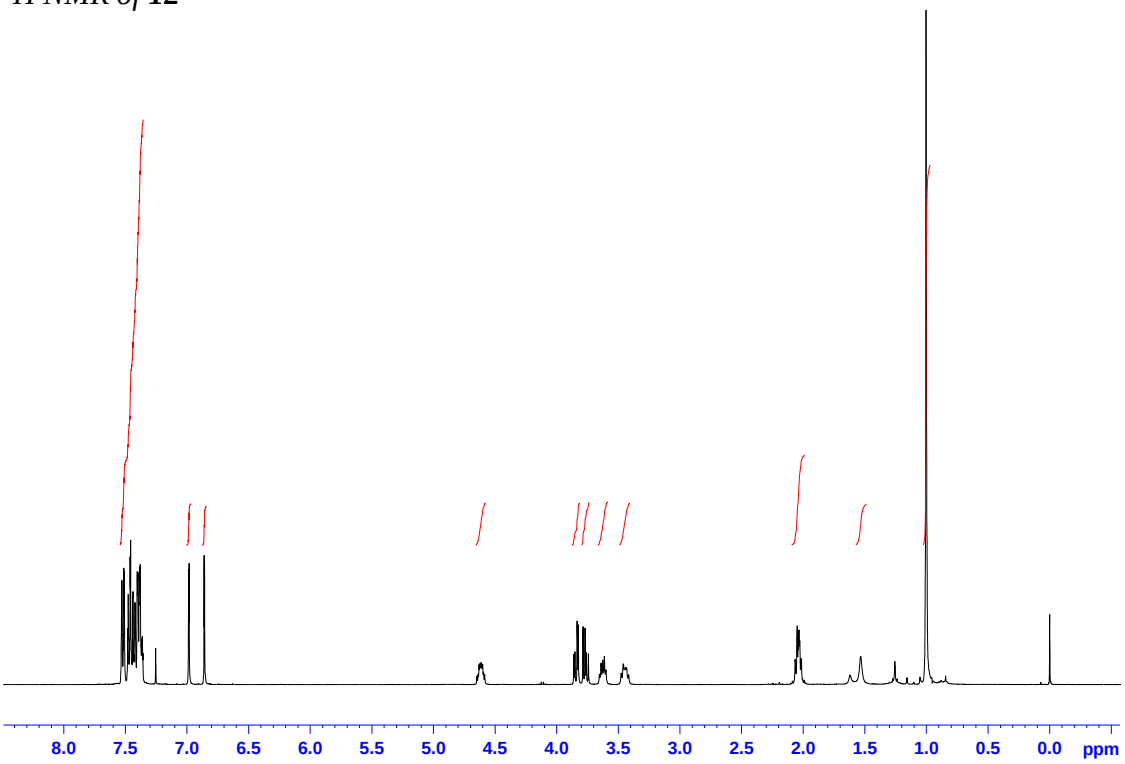
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

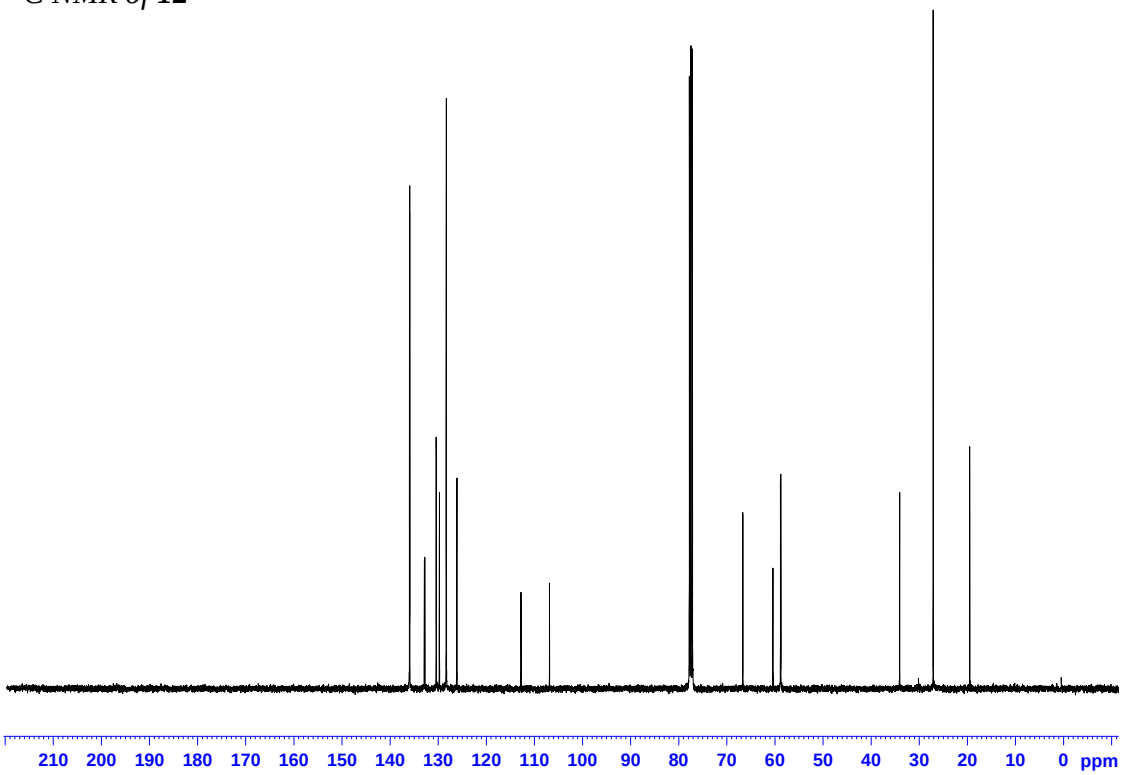

Signal 1: VWD1 A, Wavelength=254 nm

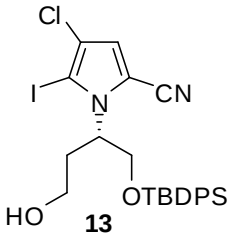
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   9.432 MM    0.2170  806.82196   61.97528  96.5700
   2  10.983 MM    0.2469   28.65729    1.93454   3.4300
```

^{1}H NMR of ***12***



^{13}C NMR of ***12***





13

Colorless Oil

$[\alpha]^{21}_{D}$ –22.5 (c 1, CH_3OH)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.57 (m, 2H), 7.49-7.34 (m, 8H), 6.99 (s, 1H), 4.99-4.92 (m, 1H), 4.14 (dd, *J* = 10.8, 9.6 Hz, 1H), 3.89 (dd, *J* = 11.2, 4.8 Hz, 1H), 3.70-3.63 (m, 1H), 3.44-3.36 (m, 1H), 2.36-2.27 (m, 1H), 2.09-2.00 (m, 1H), 1.42 (s, 1H), 0.96 (s, 9H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.4, 132.6, 132.2, 129.9, 129.8, 127.7, 124.3, 112.6, 106.2, 104.4, 89.4, 65.1, 63.4, 58.2, 32.5, 26.5, 18.9

FTIR (neat) 3448, 3071, 2930, 2857, 2219, 1427, 1306, 1113, 741, 702, 504 cm^{-1}

HRMS (EI) calcd for $[M]^+$ $C_{25}H_{28}ClN_2O_2SiI$ 578.0653, found 578.0648

HPLC Condition to determine enantiomeric excess:

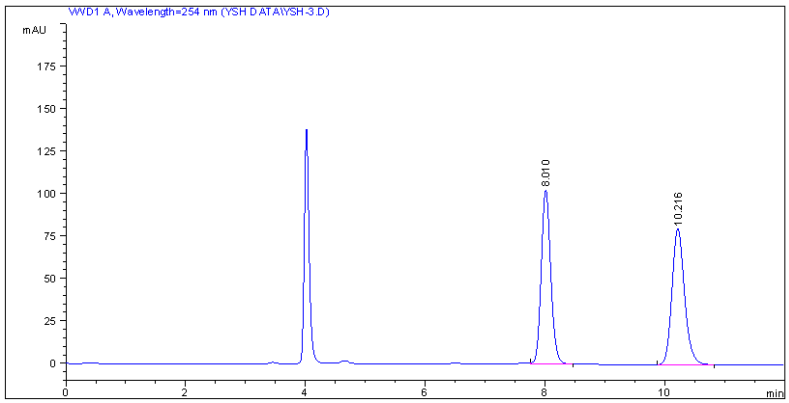
Chiral column: Chiralpak AD-H (250 x 4.6 mm)

Mobile Phase (95/5 = Hexane/IPA)

Flow Rate (0.9 mL/min), Detection Wavelength (254 nm)

Retention Time: 8.0 min (minor isomer), 10.2 min (major isomer)

*Racemate of **13***

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=====================================================================
                      Area Percent Report
=====================================================================

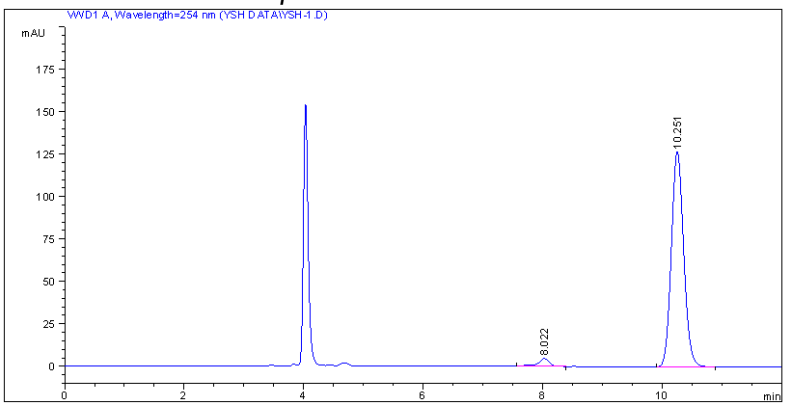
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]       %
----|-------|----|-------|----------|----------|--------|
   1   8.010 VB    0.1696 1133.12988  102.61249  49.2445
   2  10.216 BB    0.2239 1167.89673   80.13323  50.7555

Totals :                  2301.02661  182.74572
```

*Enantiomeric excess of **13**: 93%*

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                      Area Percent Report
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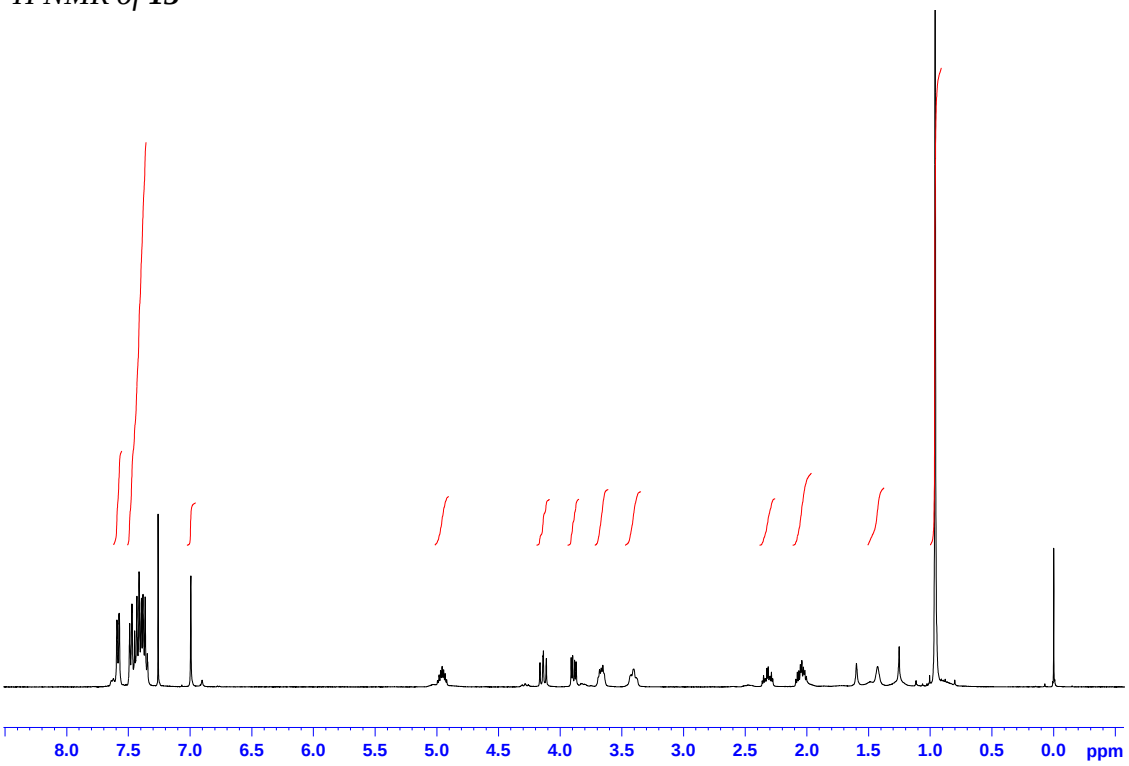
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

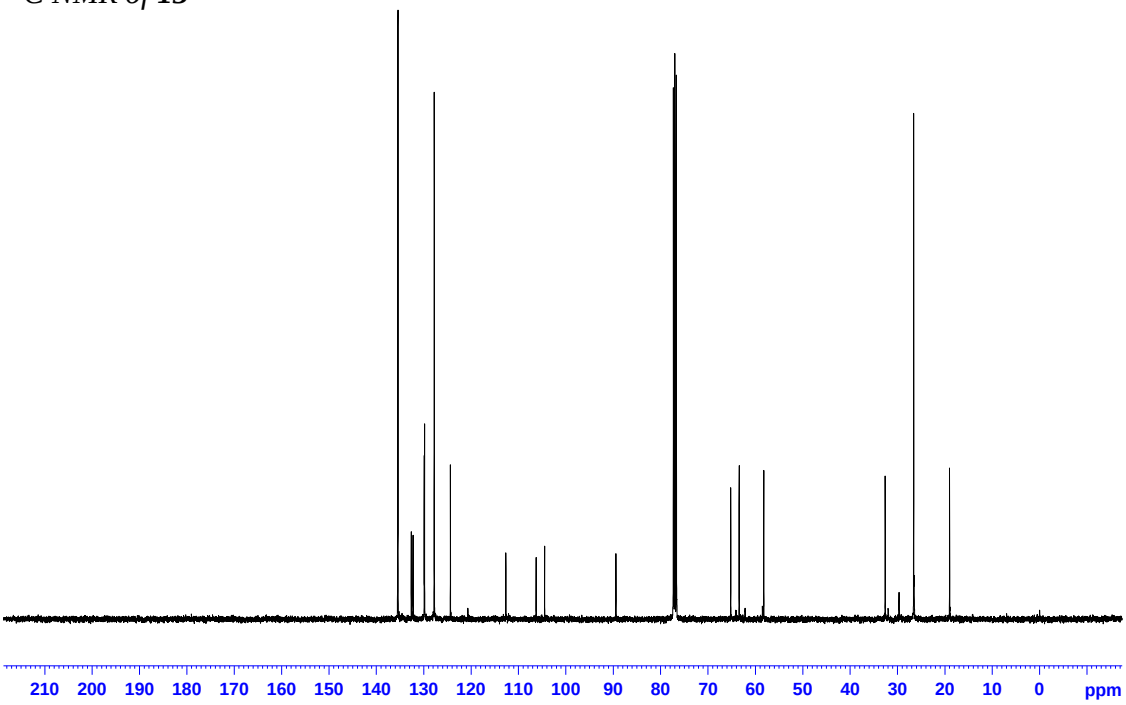
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]       %
----|-------|----|-------|----------|----------|--------|
   1   8.022 BB    0.2031   64.41565    4.63057   3.4199
   2  10.251 BB    0.2213 1819.13977  126.79105  96.5801

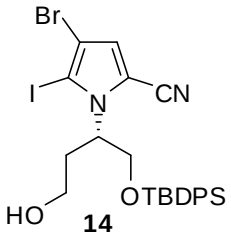
Totals :                  1883.55542  131.42163
```

^{1}H NMR of ***13***



^{13}C NMR of ***13***





14

Yellow Oil

$[\alpha]^{21}_{D}$ –44.8 (c 1, CH_3OH)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.57 (m, 2H), 7.49-7.34 (m, 8H), 6.99 (s, 1H), 4.98-4.92 (m, 1H), 4.14 (dd, *J* = 10.8, 9.6 Hz, 1H), 3.89 (dd, *J* = 11.2, 4.8 Hz, 1H), 3.68-3.63 (m, 1H), 3.40 (dt, *J* = 9.6, 4.0 Hz, 1H), 2.35-2.27 (m, 1H), 2.08-2.00 (m, 1H), 1.47 (s, 1H), 0.96 (s, 9H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 132.6, 132.3, 129.9, 129.8, 127.8, 124.4, 112.6, 106.3, 104.5, 89.3, 65.2, 63.4, 58.3, 32.6, 26.5, 19.0

FTIR (neat) 3456, 3071, 2930, 2219, 1427, 1311, 1114, 758, 702, 504 cm^{-1}

HRMS (EI) calcd for $[M]^+$ $C_{25}H_{28}BrN_2O_2SiI$ 622.0148, found 622.0153

HPLC Condition to determine enantiomeric excess:

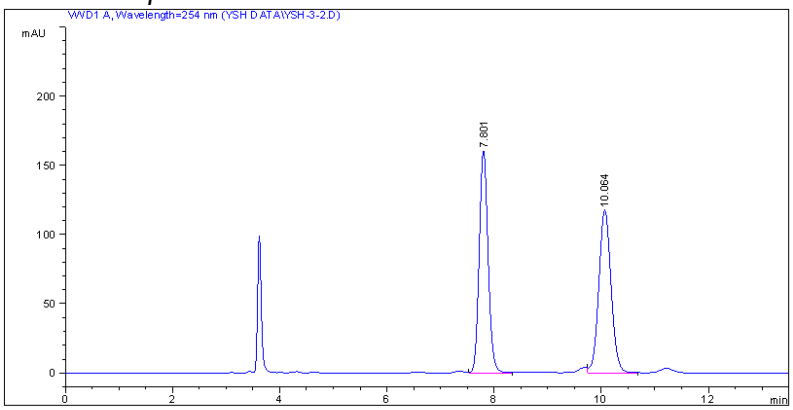
Chiral column: Chiralpak AD-H (250 x 4.6 mm)

Mobile Phase (95/5 = Hexane/IPA)

Flow Rate (1.0 mL/min), Detection Wavelength (254 nm)

Retention Time: 7.8 min (minor isomer), 10.1 min (major isomer)

*Racemate of **14***

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                      Area Percent Report
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Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]       %
----|-------|----|-------|----------|----------|--------|
   1   7.801 VB    0.1779 1848.33374  160.63713  49.7617
   2  10.064 VB    0.2463 1866.03979  117.60342  50.2383

Totals :                  3714.37354  278.24055
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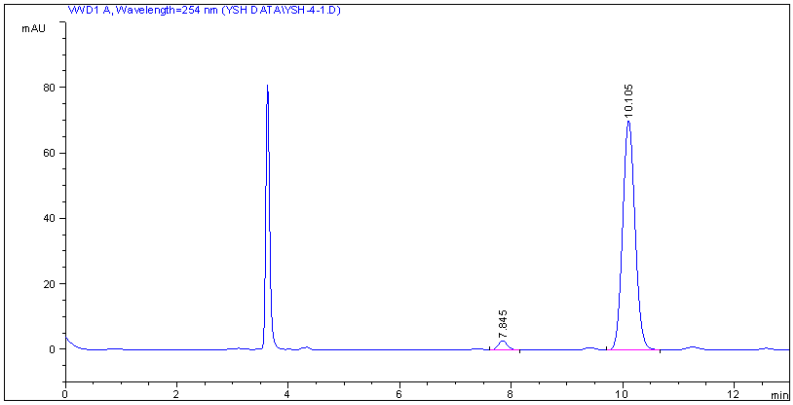
*Enantiomeric excess of **14**: 94%*

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=====================================================================
                      Area Percent Report
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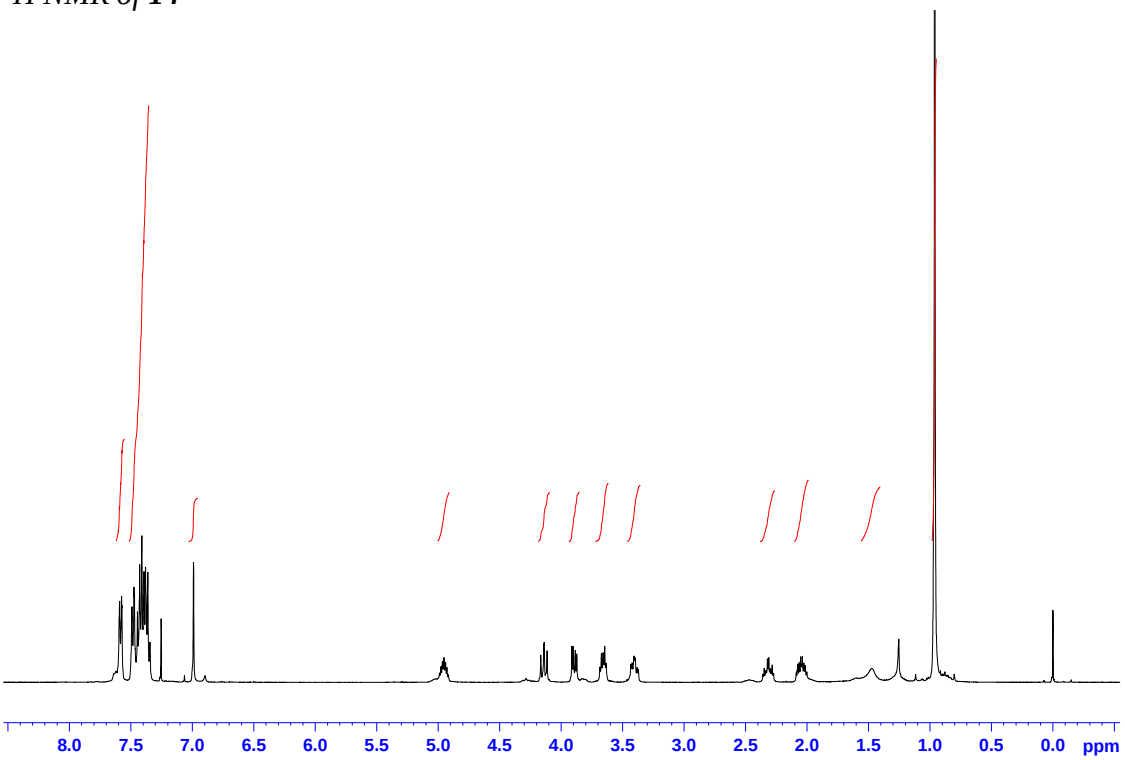
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

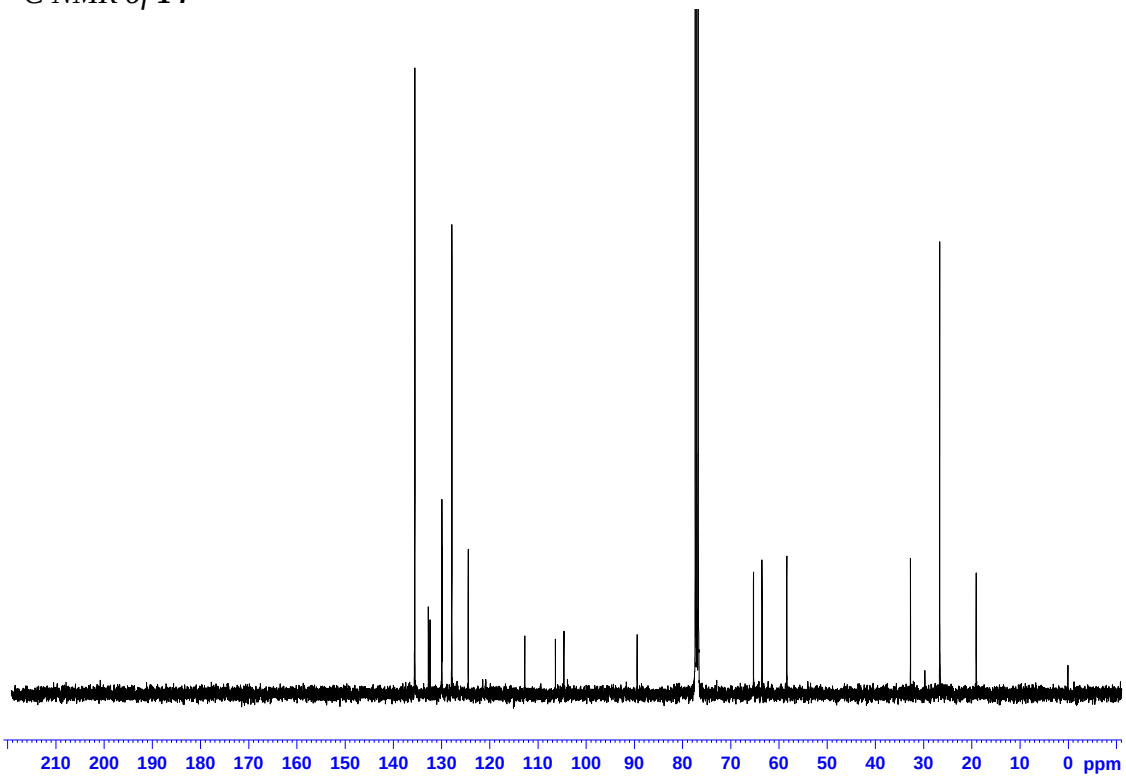
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]       %
----|-------|----|-------|----------|----------|--------|
   1   7.845 VB    0.1788   32.74894    2.82841   2.9481
   2  10.105 VB    0.2393 1078.10925   70.02004  97.0519

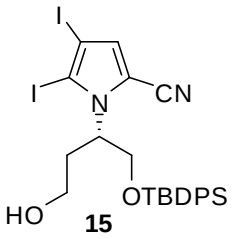
Totals :                  1110.85819   72.84845
```

^{1}H NMR of ***14***



^{13}C NMR of ***14***





15

Light Yellow Oil

$[\alpha]^{21}_{D}$ –36.0 (c 1, CH_3OH)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58-7.56 (m, 2H), 7.48-7.34 (m, 8H), 7.06 (s, 1H), 5.03-4.96 (m, 1H), 4.12 (dd, *J* = 10.8, 9.6 Hz, 1H), 3.88 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.70-3.62 (m, 1H), 3.45-3.37 (m, 1H), 2.35-2.27 (m, 1H), 2.08-1.99 (m, 1H), 1.40 (s, 1H), 0.96 (s, 9H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.4, 132.6, 132.3, 129.9, 129.8, 129.7, 127.8, 127.7, 112.3, 105.5, 95.5, 77.2, 75.5, 65.2, 64.3, 58.2, 32.7, 26.5, 19.0

FTIR (neat) 3452, 3071, 2930, 2218, 1427, 1362, 1298, 1113, 757, 702, 504 cm^{-1}

HRMS (EI) calcd for $[M]^+$ $C_{25}H_{28}N_2O_2SiI_2$ 670.0010, found 670.0005

HPLC Condition to determine enantiomeric excess:

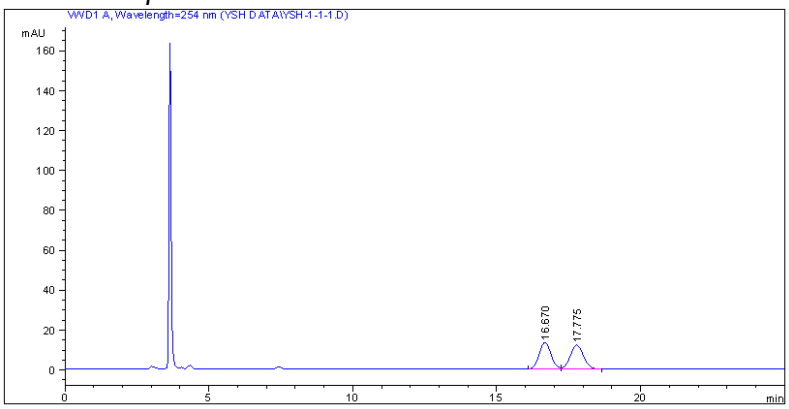
Chiral column: Chiralpak AD-H (250 x 4.6 mm)

Mobile Phase (95/5 = Hexane/IPA)

Flow Rate (0.9 mL/min), Detection Wavelength (254 nm)

Retention Time: 16.6 min (major isomer), 17.7 min (minor isomer)

*Racemate of **15***

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                      Area Percent Report
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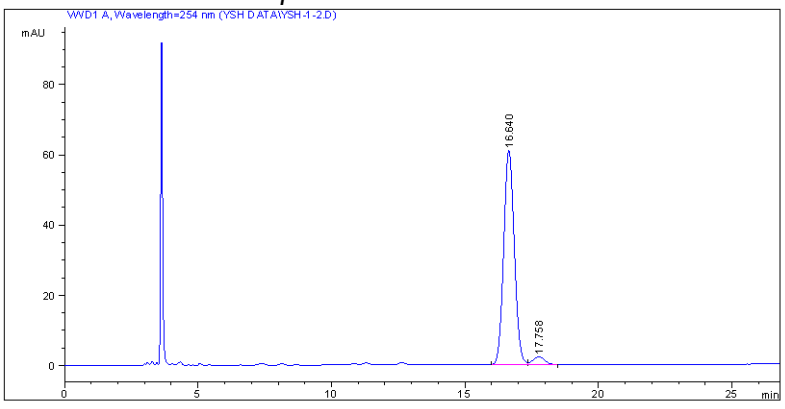
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  16.670 BV    0.4455  382.52658   13.38793  49.9451
   2  17.775 VB    0.5043  383.36755   11.98154  50.0549

Totals :                   765.89413   25.36947
```

*Enantiomeric excess of **15**: 92%*

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=====================================================================
                      Area Percent Report
=====================================================================

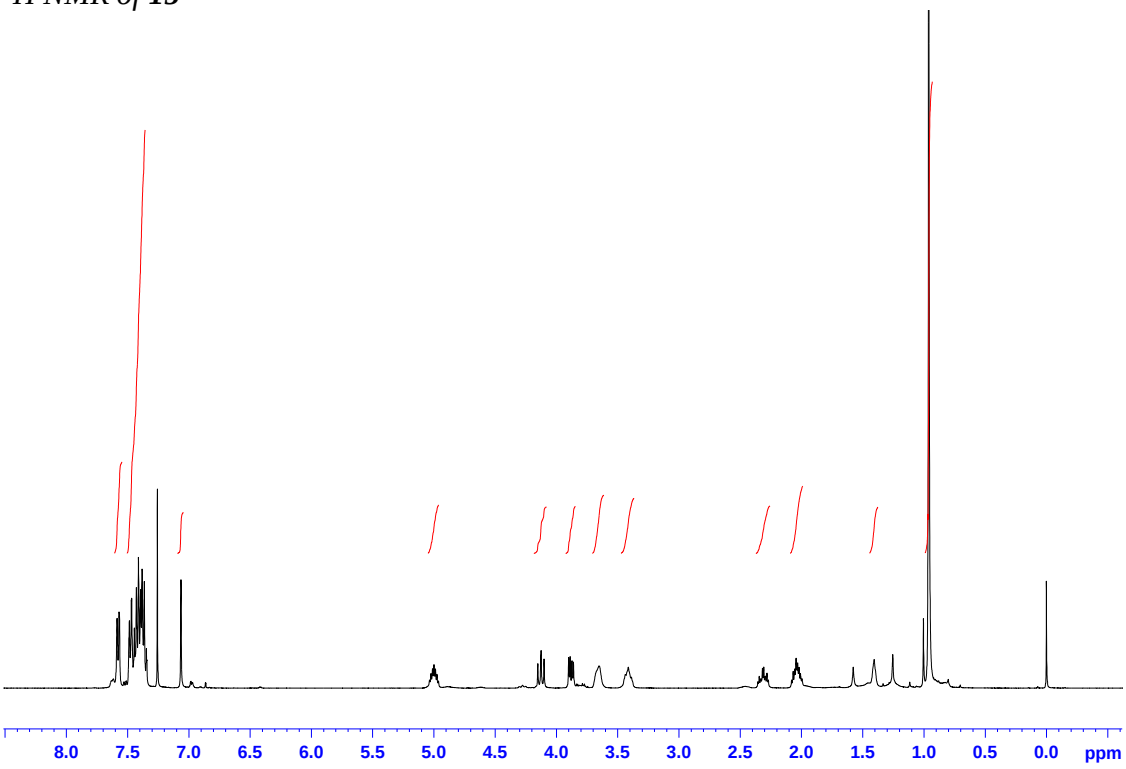
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

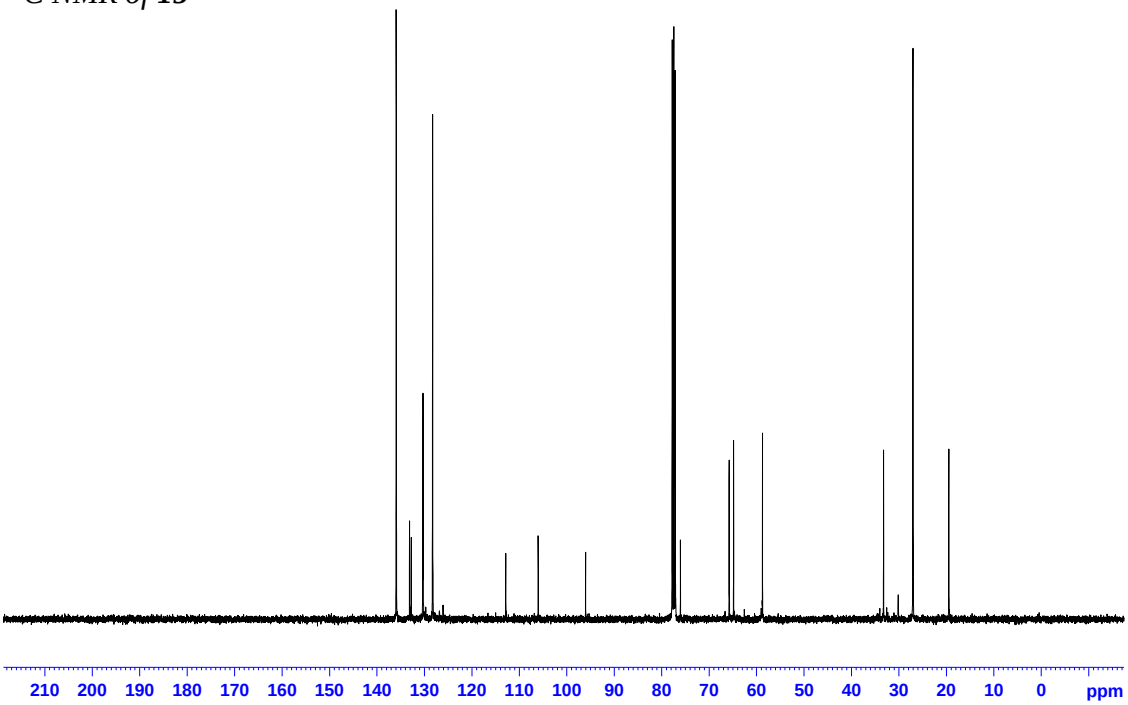
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  16.640 BV    0.4305 1688.97925   61.05460  96.0482
   2  17.758 VB    0.4695   69.49210    2.23233   3.9518

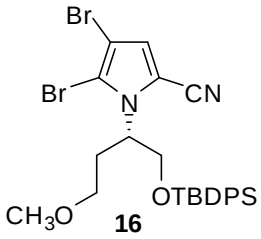
Totals :                  1758.47135   63.28693
```

^{1}H NMR of ***15***



^{13}C NMR of ***15***





16

Iodomethane (6.2 mL, 0.2 M) and silver oxide (431 mg, 1.86 mmol) was added to a solution of the conjugate product **6** (715 mg, 1.24 mmol) in acetonitrile (6.2 mL, 0.2 M) at rt. The mixture was allowed to stir at reflux for 12 h. The solids were removed by filtration and the solvents removed. The residue was purified by flash chromatography (SiO_2: 10% EtOAc in hexanes) to provide the ether **16** in 98% yield (717 mg, 1.22 mmol) as a colorless oil.

Colorless Oil

$[\alpha]^{20}_D$ +30.9 (c 1, CH_3OH)

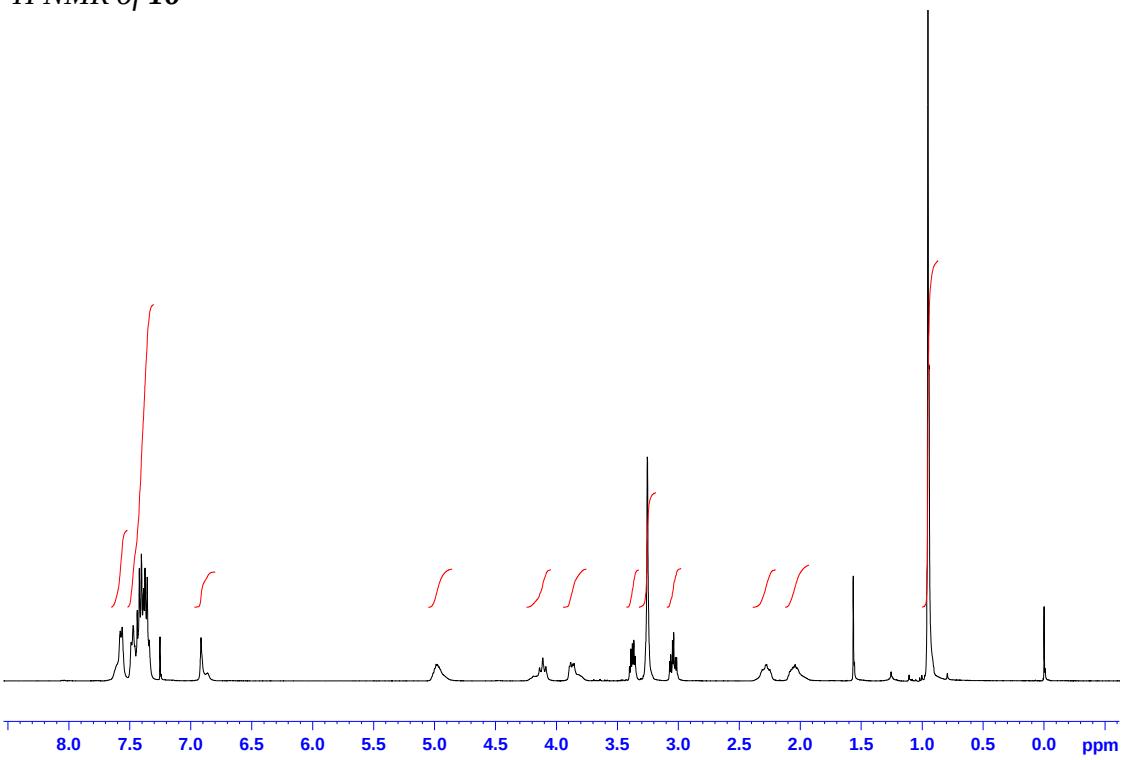
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58-7.56 (m, 2H), 7.49-7.34 (m, 8H), 6.92 (s, 1H), 5.01-4.96 (m, 1H), 4.11 (t, *J* = 10.0 Hz, 1H), 3.87 (dd, *J* = 10.8, 4.4 Hz, 1H), 3.40-3.35 (m, 1H), 3.25 (s, 3H), 3.04 (dt, *J* = 9.6, 4.0 Hz, 1H), 2.31-2.25 (m, 1H), 2.08-2.02 (m, 1H), 0.95 (s, 9H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.4, 132.7, 132.4, 129.8, 129.8, 127.7, 123.7, 114.3, 112.8, 102.4, 98.9, 67.8, 64.9, 60.6, 58.6, 30.1, 26.5, 18.9

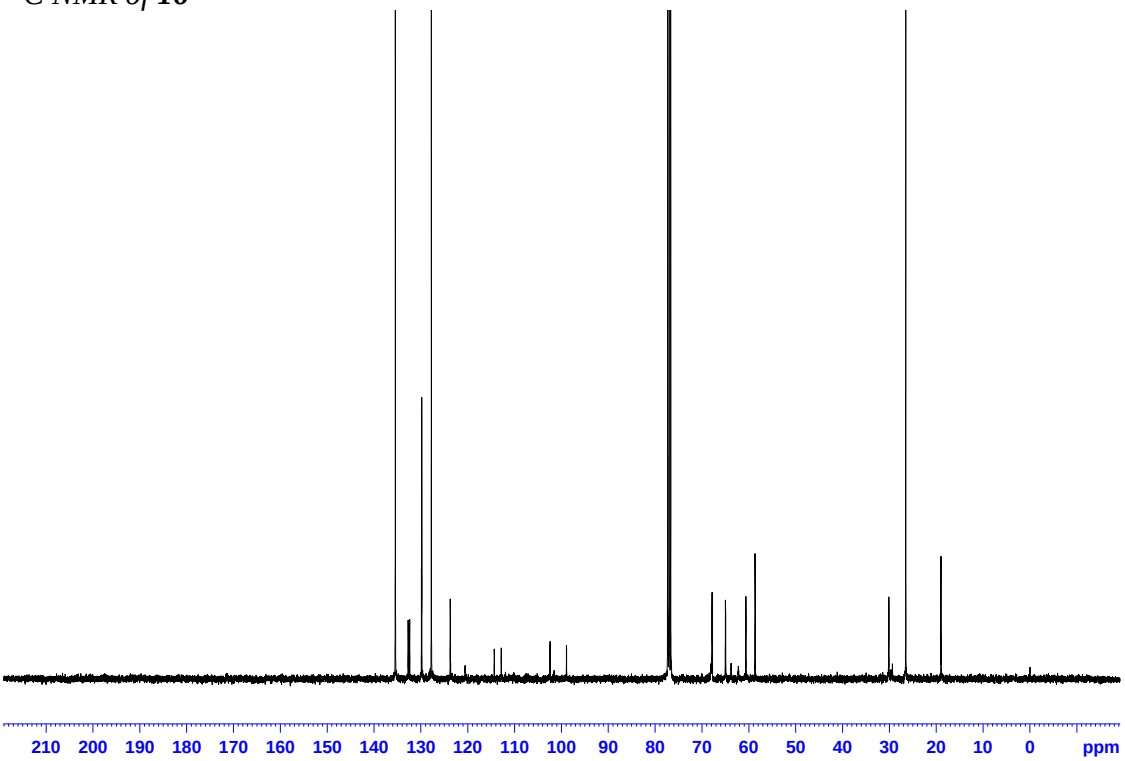
FTIR (neat) 3071, 2930, 2857, 2221, 1415, 1313, 1114, 798, 702, 504 cm^{-1}

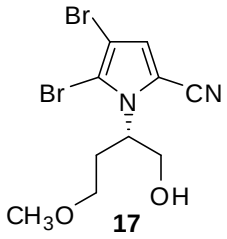
HRMS (EI) calcd for $[M]^+$ $C_{26}H_{30}Br_2N_2O_2Si$ 588.0443, found 588.0442

^{1}H *NMR of* ***16***



^{13}C *NMR of* ***16***





17

1.25 M HCl solution in methanol (6.4 mL, 8.0 mmol) was added to **16** (236 mg, 0.4 mmol). The mixture was stirred at rt for 12 h, at which point 1.25 M HCl solution in methanol (6.4 mL, 8.0 mmol) was added once more and the mixture was stirred at rt for 48 h. The mixture was evaporated to remove methanol and quenched by saturated $NaHCO_3$. The mixture was extracted with ethyl acetate and the organic layer was dried over $MgSO_4$. Filtration, concentration, and purification by flash chromatography (SiO_2: 30% EtOAc in hexanes) provided the alcohol **17** in 90% yield (126 mg, 0.358 mmol) as a white solid.

White Solid

M.P. 63~65 ^{o}C

$[\alpha]^{21}_{D}$ –5.2 (c 1, CH_3OH)

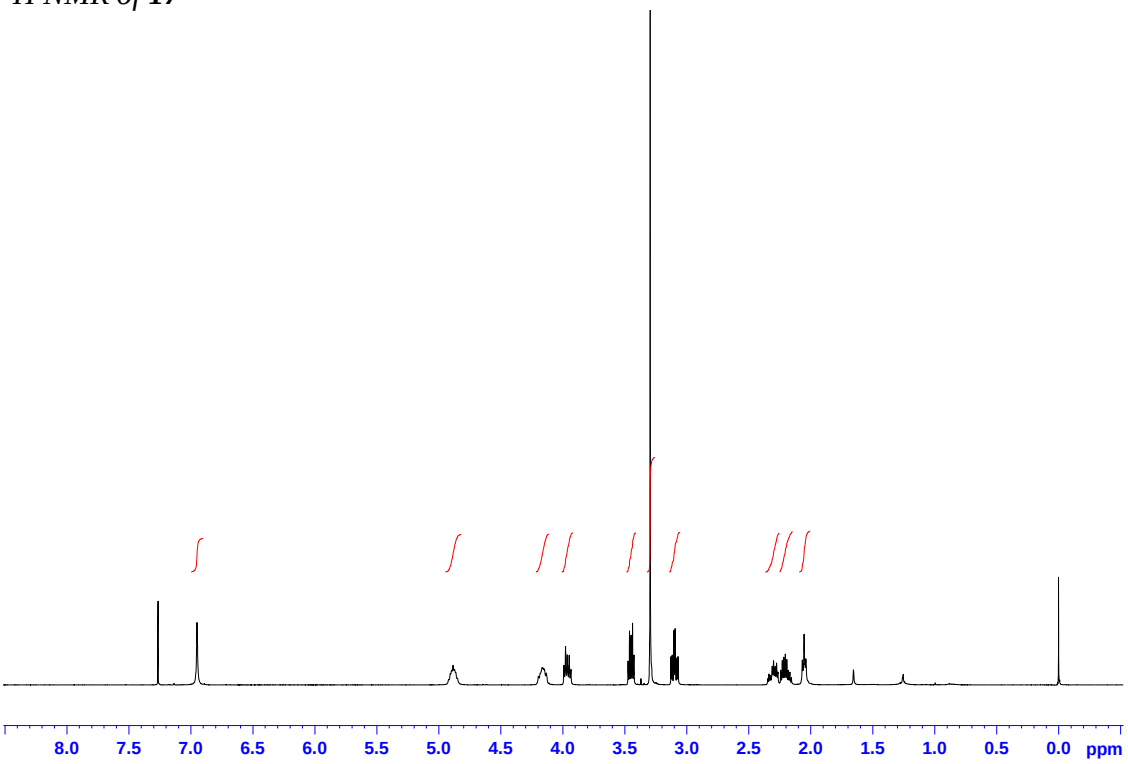
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (s, 1H), 4.90-4.84 (m, 1H), 4.19-4.13 (m, 1H), 3.99-3.93 (m, 1H), 3.47-3.42 (m, 1H), 3.29 (s, 3H), 3.10 (dt, *J* = 9.6, 4.0 Hz, 1H), 2.34-2.26 (m, 1H), 2.24-2.15 (m, 1H), 2.05 (t, *J* = 5.6 Hz, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 123.7, 113.9, 112.7, 102.3, 99.5, 67.9, 63.5, 61.0, 58.6, 30.4

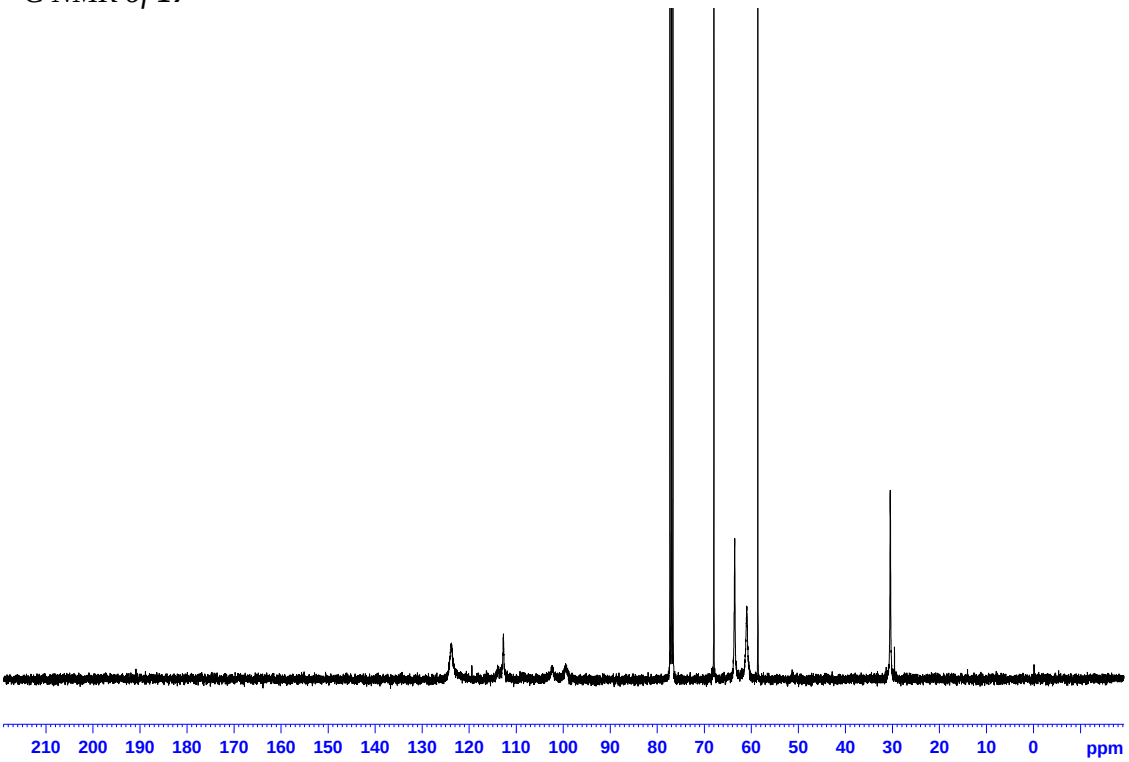
FTIR (neat) 3449, 3124, 2890, 2226, 1411, 1379, 1313, 1121, 1085, 828 cm^{-1}

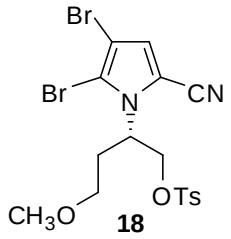
HRMS (EI) calcd for $[M]^+$ $C_{10}H_{12}Br_2N_2O_2$ 349.9265, found 349.9263

^{1}H *NMR of* ***17***



^{13}C *NMR of* ***17***





18

p-Toluenesulfonyl chloride (136 mg, 0.713 mmol) was added to a solution of **17** (114 mg, 0.324 mmol) in pyridine (0.32 mL, 1.0 M). The mixture was allowed to stir at rt for 16 h. The mixture was quenched by water and extracted with ethyl acetate. The organic layer was washed with saturated NH_4Cl and brine, dried over Na_2SO_4. Filtration, concentration, and purification by flash chromatography (SiO_2: 25% EtOAc in hexanes) provided the tosylate **18** in 97% yield (159 mg, 0.314 mmol) as a colorless oil.

Colorless Oil

$[\alpha]^{20}_D$ –12.0 (c 1, CH_3OH)

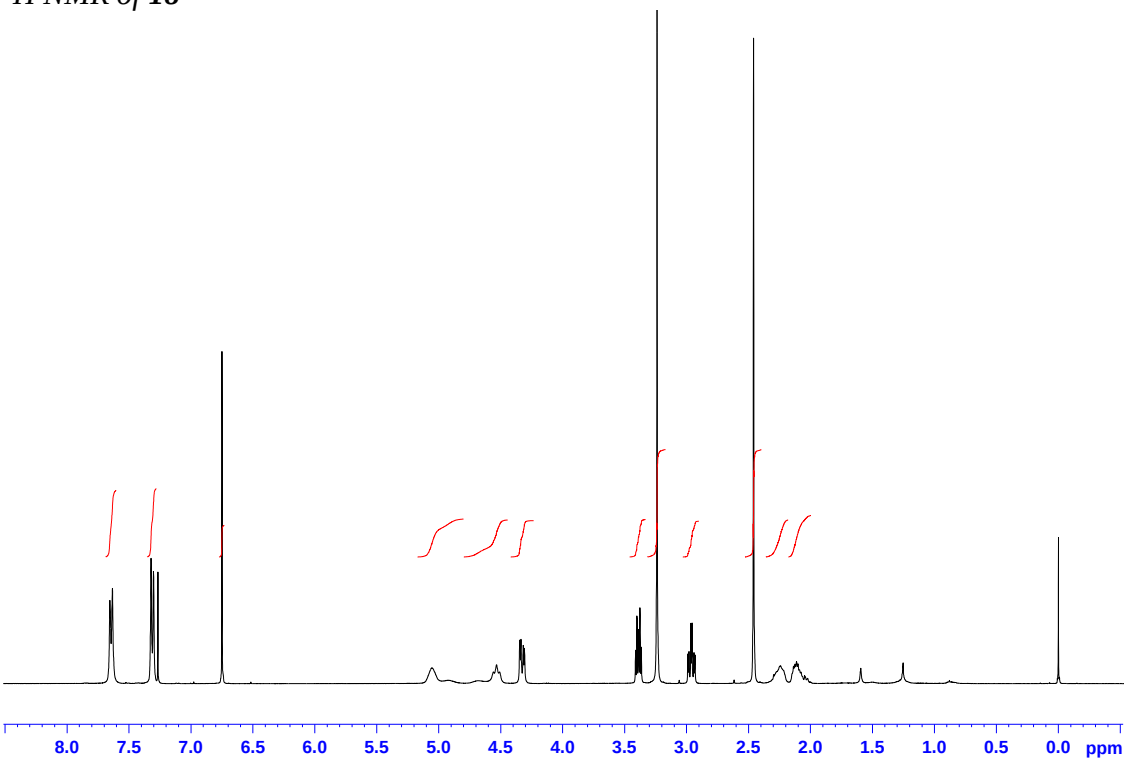
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 6.74 (s, 1H), 5.11-5.01 (m, 1H), 4.53 (t, *J* = 10.2 Hz, 1H), 4.32 (dd, *J* = 10.2, 4.0 Hz, 1H), 3.41-3.36 (m, 1H), 3.23 (s, 3H), 2.96 (dt, *J* = 9.6, 3.6 Hz, 1H), 2.45 (s, 3H), 2.29-2.20 (m, 1H), 2.16-2.07 (m, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 132.0, 129.9, 127.6, 124.0, 113.9, 112.3, 102.1, 99.5, 69.4, 67.2, 58.6, 57.4, 30.3, 21.6

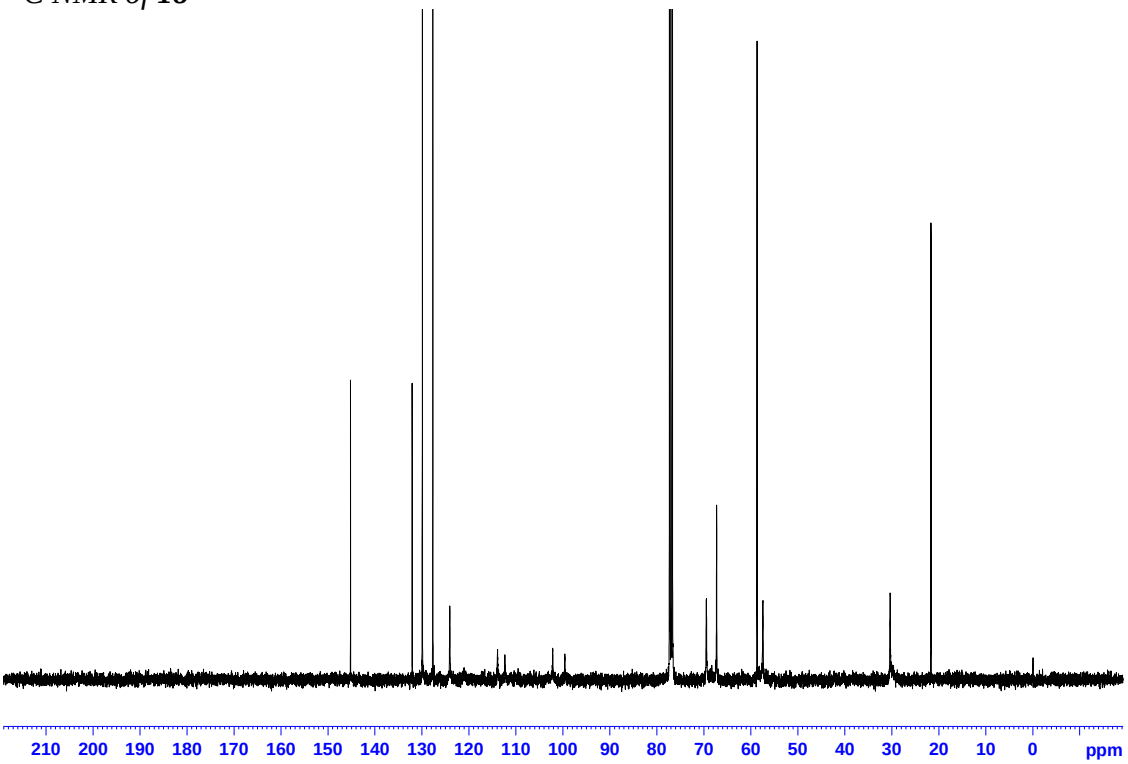
FTIR (neat) 3125, 2927, 2877, 2221, 1598, 1367, 1177, 1122, 981, 813, 666, 554 cm^{-1}

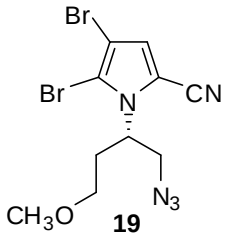
HRMS (EI) calcd for $[M]^+$ $C_{17}H_{18}Br_2N_2O_4S$ 503.9354, found 503.9358

^{1}H NMR of ***18***



^{13}C NMR of ***18***





19

Sodium azide (122 mg, 1.884 mmol) was added to a solution of **18** (159 mg, 0.314 mmol) in dimethyl sulfoxide (3.14 mL, 0.1 M) at rt. The mixture was allowed to stir at 65 ^{o}C for 24 h. The mixture was quenched by water and extracted with ethyl acetate. The organic layers was washed with water and brine, dried over Na_2SO_4. Filtration, concentration, and purification by flash chromatography (SiO_2: 20% EtOAc in hexanes) provided the azide **19** in 82% yield (97 mg, 0.257 mmol) as a white solid.

White Solid

M.P. 45~47 ^{o}C

$[\alpha]^{21}_{D}$ +4.0 (c 1, CH_3OH)

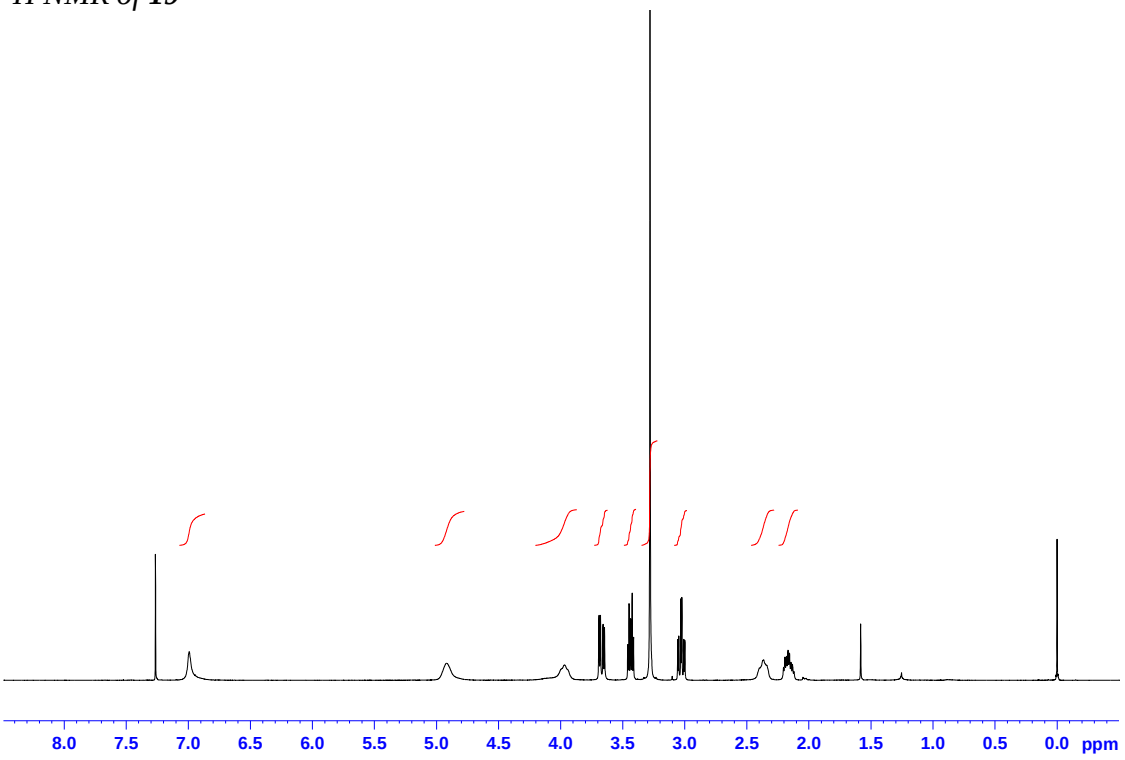
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (s, 1H), 4.97-4.87 (m, 1H), 4.02-3.92 (m, 1H), 3.67 (dd, *J* = 13.2, 5.2 Hz, 1H), 3.46-3.41 (m, 1H), 3.28 (s, 3H), 3.03 (dt, *J* = 10.0, 3.6 Hz, 1H), 2.42-2.32 (m, 1H), 2.20-2.12 (m, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 124.4, 114.0, 112.7, 102.3, 99.7, 67.4, 58.7, 58.2, 53.6, 31.6

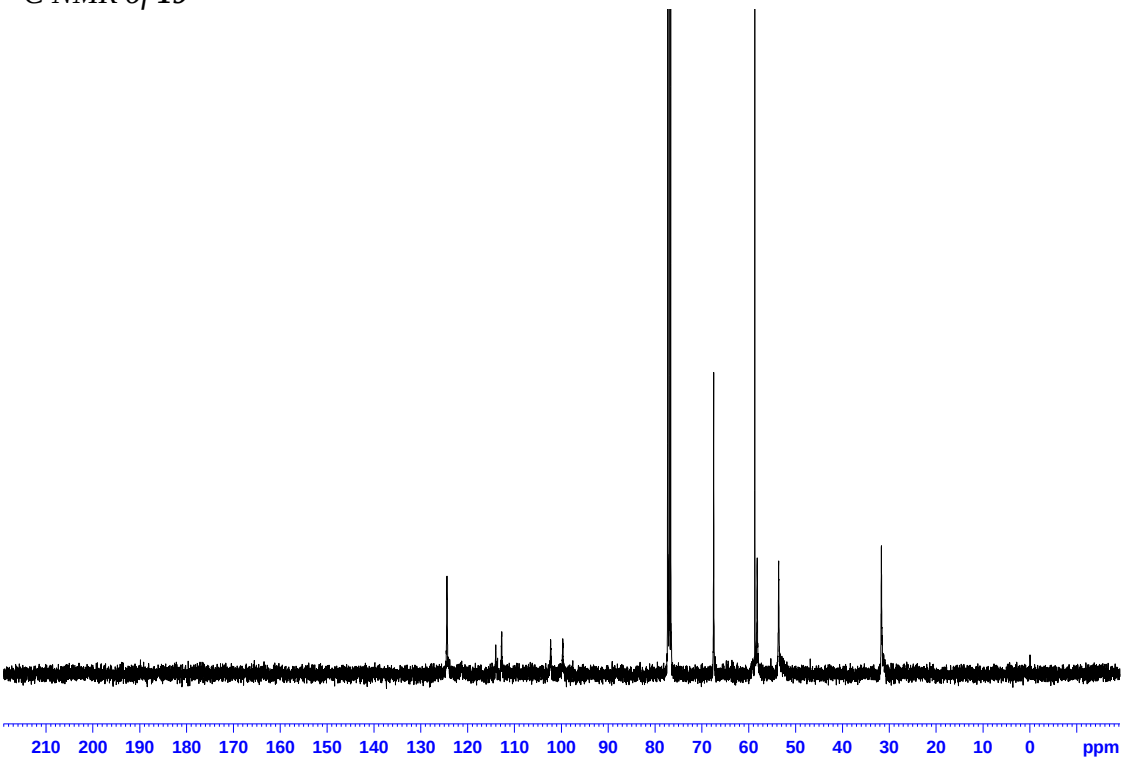
FTIR (neat) 3101, 2936, 2217, 2101, 1413, 1312, 1275, 1121, 1086, 965, 914 cm^{-1}

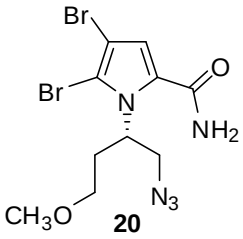
HRMS (EI) calcd for $[M]^+$ $C_{10}H_{11}Br_2N_5O$ 374.9330, found 374.9328

^{1}H NMR of ***19***



^{13}C NMR of ***19***





20

1 N aqueous sodium hydroxide (0.48 mL, 0.48 mmol) and hydrogen peroxide (30 wt. % in H_2O, 0.48 mL, 0.144 mmol) were added to a solution of **19** (91 mg, 0.241 mmol) in methanol−dichloromethane (10 : 1 v/v, 4.82 mL, 0.05 M). The mixture was allowed to stir at rt for 12 h. The mixture was quenched by saturated $Na_2S_2O_2$ and saturated NH_4Cl. The mixture was extracted with dichloromethane and water. The organic layer was dried over $MgSO_4$. Filtration, concentration, and purification by flash chromatography (SiO_2: 40% EtOAc in hexanes) provided the azide−amide **20** in 95% yield (91 mg, 0.229 mmol) as a colorless oil.

Colorless Oil

$[\alpha]^{19}_D$ –36.0 (c 1, CH_3OH)

^{1}H NMR (400 MHz, $CDCl_3$, mixture of two conformers, major : minor = 57 : 43)

δ 6.82 (s, 0.57H) and 6.73 (s, 0.43H), 6.01-5.73 (m, 2.43H) and 4.99-4.89 (m, 0.57H), 4.36 (t, *J* = 11.2 Hz, 0.57H) and 4.10 (t, *J* = 11.2 Hz, 0.43H), 3.62 (dd, *J* = 12.8, 5.2 Hz, 1H), 3.39-3.32 (m, 1H), 3.25 (s, 3H), 3.24-3.17 (m, 0.43H) and 3.06-2.98 (m, 0.57H), 2.50-2.42 (m, 1H), 2.19-2.06 (m, 1H)

^{13}C NMR (100 MHz, $CDCl_3$, mixture of two conformers)

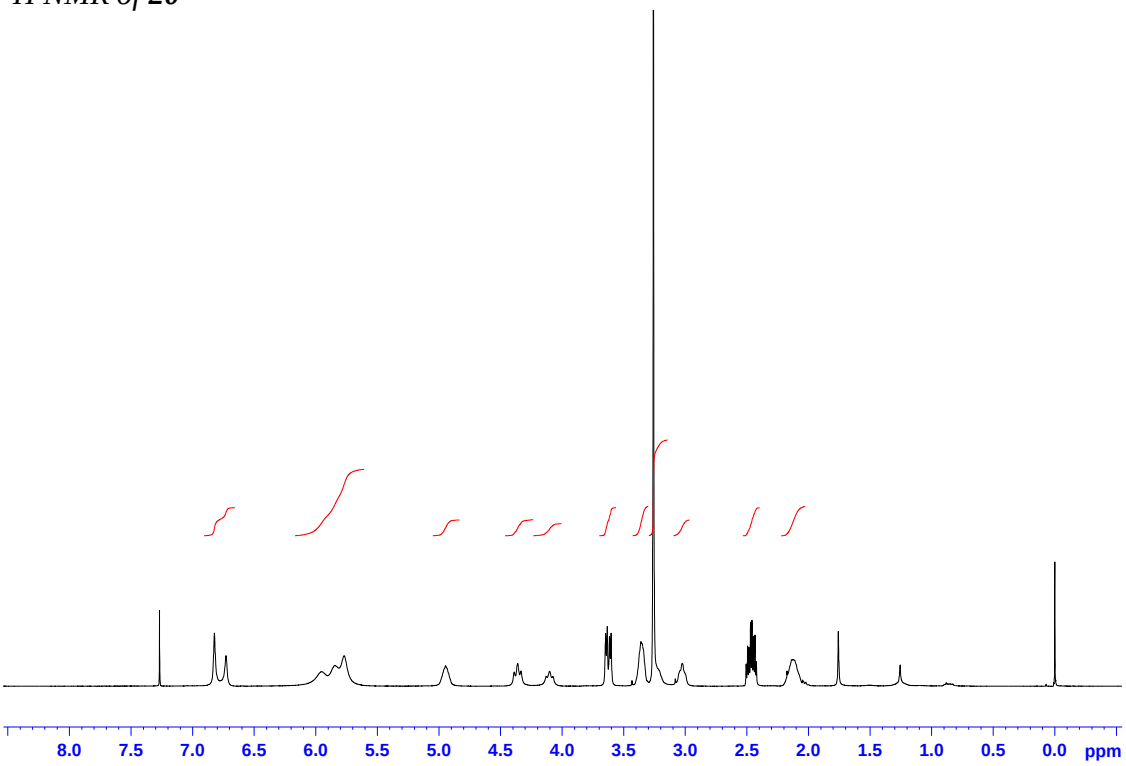
Major: δ 161.9, 126.6, 117.8, 114.7, 98.9, 68.5, 59.0, 58.5, 54.1, 31.9

Minor: δ 161.9, 129.5, 115.8, 107.2, 101.6, 68.8, 58.5, 55.5, 53.1, 31.1

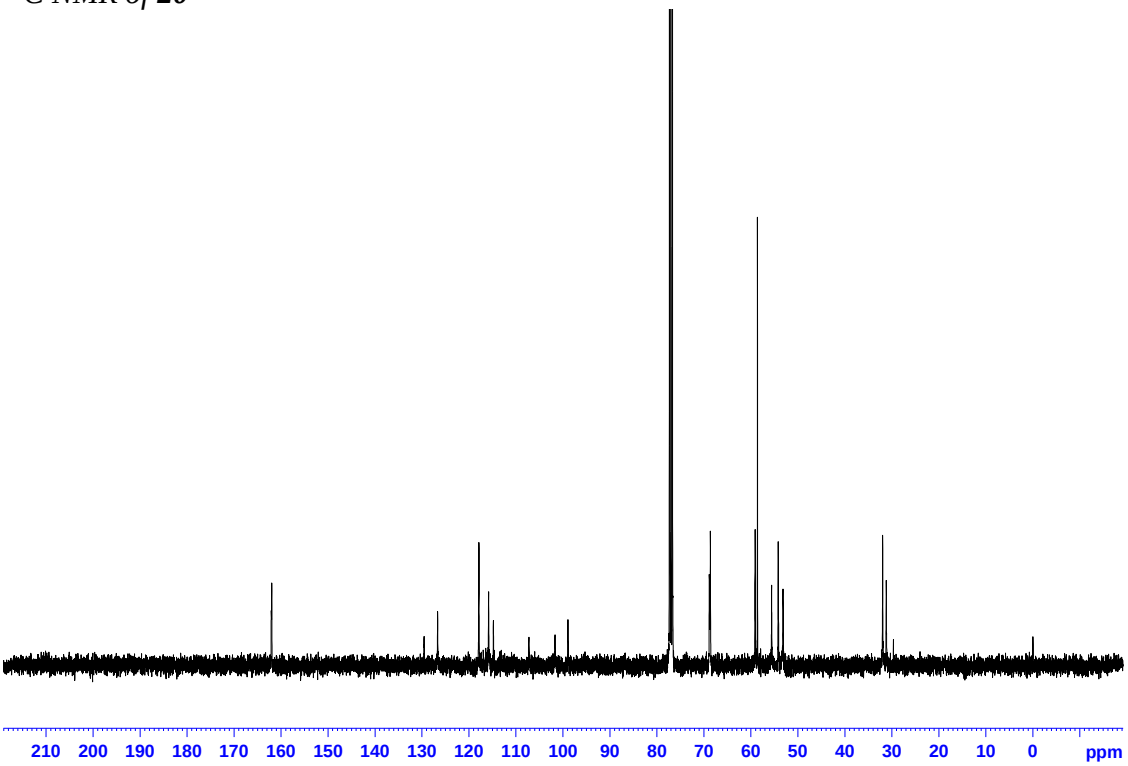
FTIR (neat) 3345, 3188, 2928, 2874, 2102, 1662, 1606, 1420, 1278, 1118, 953, 758 cm^{-1}

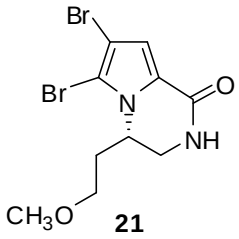
HRMS (EI) calcd for $[M]^+$ $C_{10}H_{13}Br_2N_5O_2$ 392.9436, found 392.9439

^{1}H NMR of ***20***



^{13}C NMR of ***20***





21

Triphenylphosphine (195 mg, 0.75 mmol) was added to a solution of **20** (135 mg, 0.34 mmol) in tetrahydrofuran (3.4 mL, 0.1 M). The mixture was stirred at rt for 1 h, at which point water (0.037 mL, 2.04 mmol) was added and the mixture was refluxed for 20 h. The solvent removed and the residue was purified by flash chromatography (SiO_2: 85% EtOAc in hexanes) to give the pyrrolopiperazinone **21** in 84% yield (100 mg, 0.285 mmol) as a white solid.

White Solid

M.P. 113~115 ^{o}C

$[\alpha]^{21}_{D}$ –27.1 (c 1, CH_3OH)

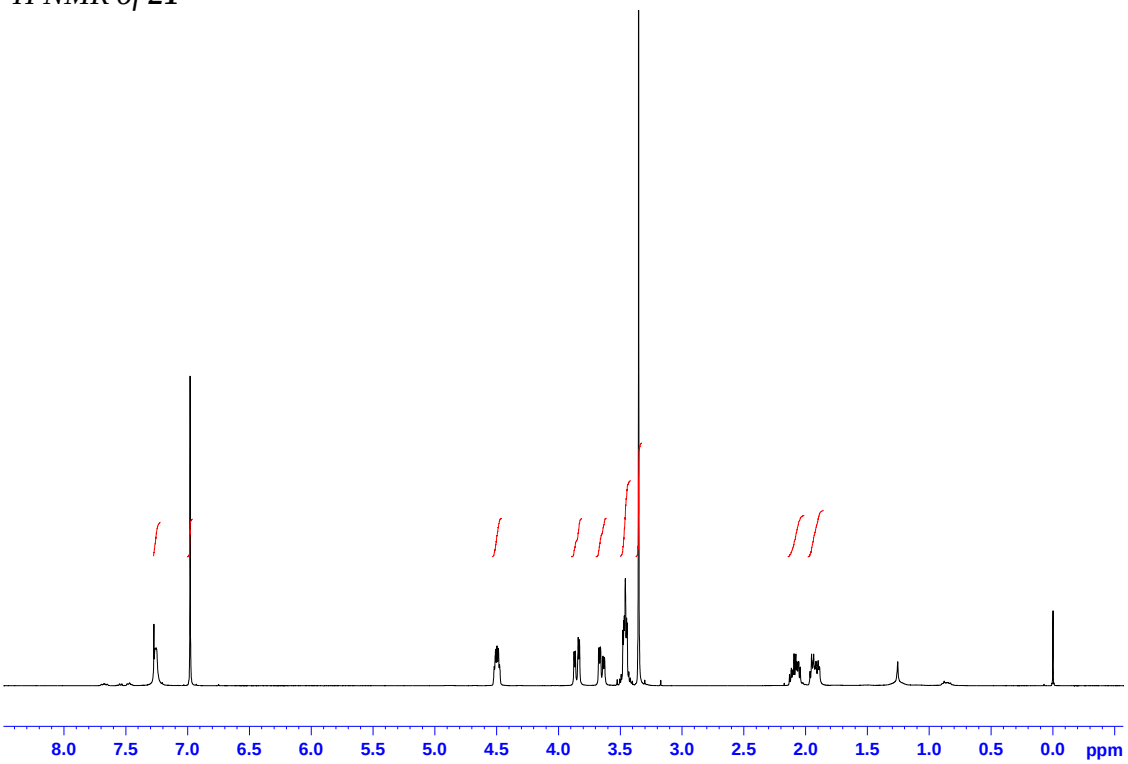
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (br s, 1H), 6.98 (s, 1H), 4.52-4.47 (m, 1H), 3.85 (dd, *J* = 13.2, 4.0 Hz, 1H), 3.65 (dd, *J* = 13.2, 4.8 Hz, 1H), 3.47-3.44 (m, 2H), 3.35 (s, 3H), 2.13-2.04 (m, 1H), 1.96-1.88 (m, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 124.7, 115.6, 106.7, 100.5, 68.7, 58.7, 52.0, 42.9, 31.7

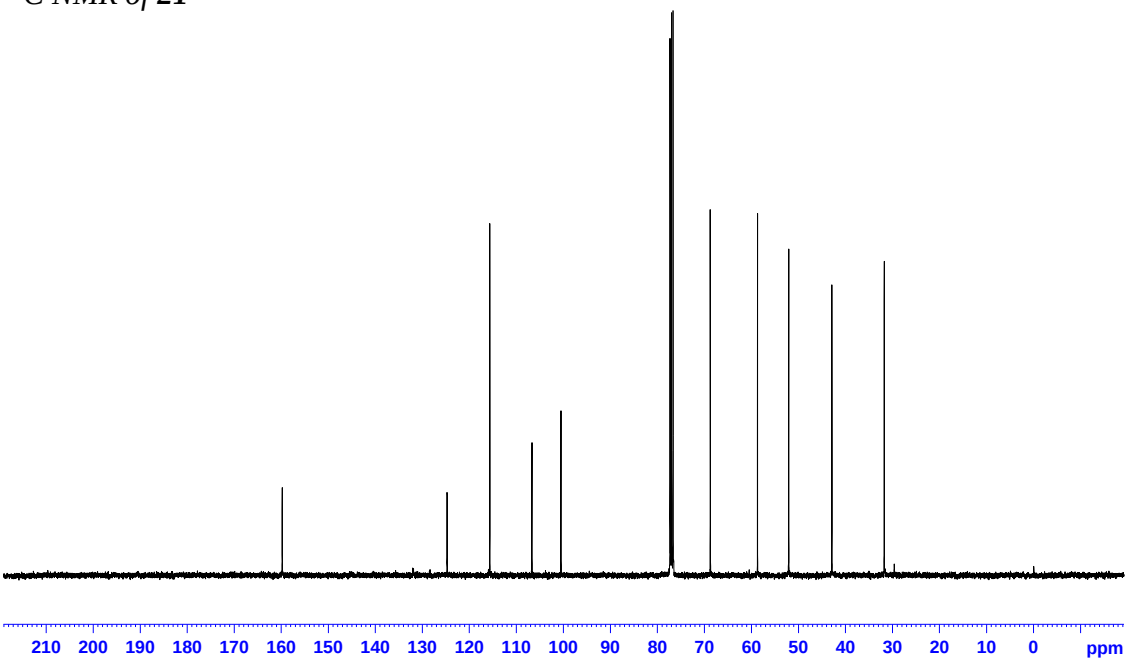
FTIR (neat) 3215, 3083, 2923, 1651, 1547, 1466, 1427, 1332, 1120, 963, 760 cm^{-1}

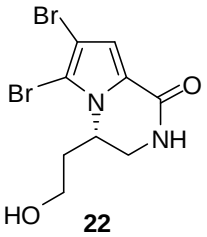
HRMS (EI) calcd for $[M]^+$ $C_{10}H_{12}Br_2N_2O_2$ 349.9265, found 349.9266

^{1}H NMR of ***21***



^{13}C NMR of ***21***





22

Boron tribromide (1 M solution in dichloromethane, 1.2 mL, 1.2 mmol) was slowly added to a solution of **21** (84 mg, 0.24 mmol) in dichloromethane (2.8 mL, 0.085 M) at −20 °C. The mixture was stirred at rt for 6 h and quenched by water. The aqueous layer was extracted twice with ethyl acetate. The combined organic layers were dried over $MgSO_4$. Filtration, concentration, and purification by flash chromatography (SiO_2: 5% MeOH in dichloromethane) provided the key intermediate **22** in 85% yield (69 mg, 0.204 mmol) as a white solid.

White Solid

M.P. 139~141 °C

$[\alpha]^{19}_D$ –28.9 (c 1, CH_3OH)

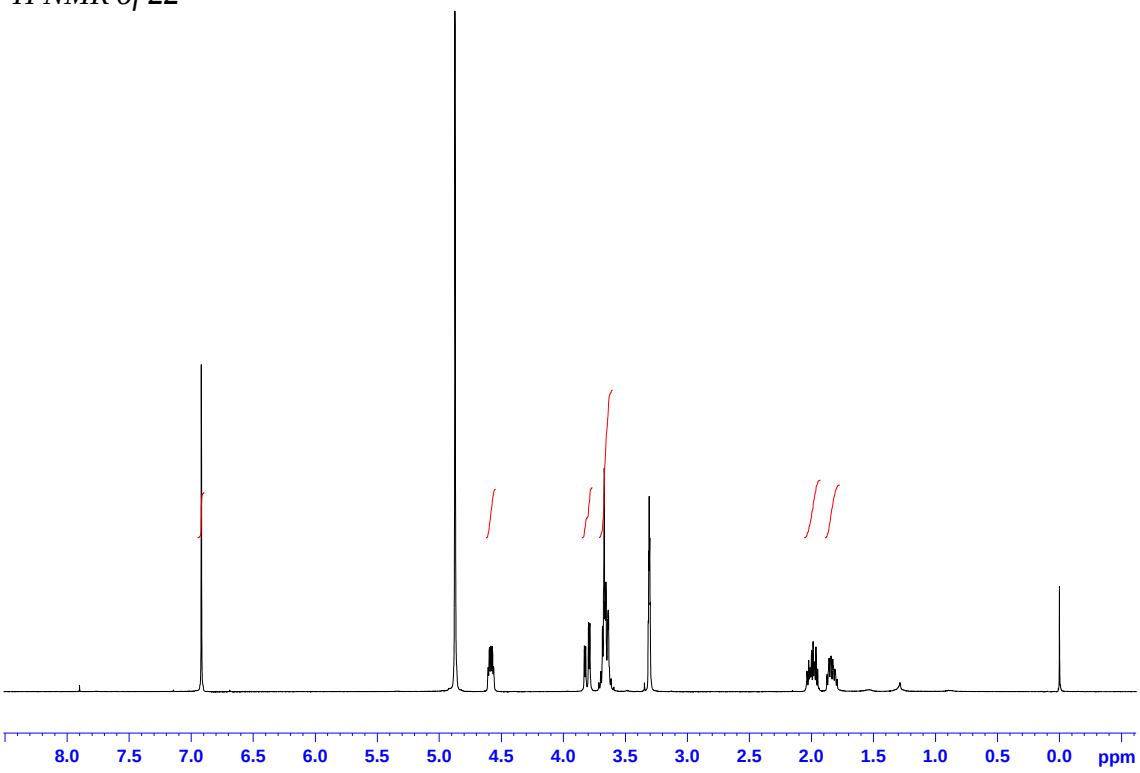
^{1}H NMR (400 MHz, CD_3OD) δ 6.91 (s, 1H), 4.60-4.56 (m, 1H), 3.81 (dd, *J* = 13.6, 4.0 Hz, 1H), 3.68-3.63 (m, 3H), 2.03-1.94 (m, 1H), 1.87-1.79 (m, 1H)

^{13}C NMR (100 MHz, CD_3OD) δ 161.1, 126.1, 116.3, 108.0, 101.2, 59.2, 53.3, 43.3, 35.5

FTIR (neat) 3431, 3243, 2921, 1647, 1617, 1545, 1426, 1335, 1053, 960, 750 cm^{-1}

HRMS (EI) calcd for $[M]^+$ $C_9H_{10}Br_2N_2O_2$ 335.9109, found 335.9109

^{1}H NMR of ***22***



^{13}C NMR of ***22***