Efficient construction of highly functionalized spiro[*γ*-butyrolactone-pyrrolidin-3,3′-oxindole] tricyclic skeletons via an organocatalytic 1,3-dipolar cycloaddition

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Supporting information

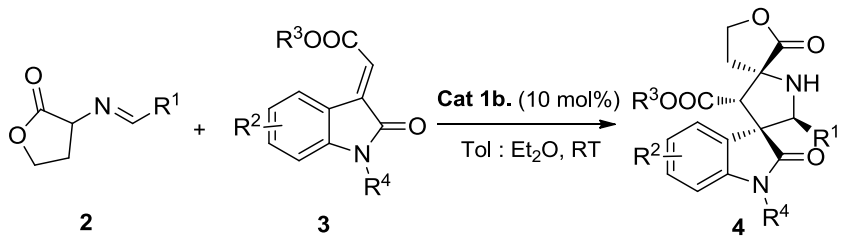
Contents

1.0 General Methods for Procedure of Synthesis

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on Brucker 300 MHz spectrometer in $CDCl_3$ unless otherwise noted and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on Brucker 300 MHz spectrometer in $CDCl_3$ or $(CD_3)_2SO$ using tetramethylsilane (TMS) as internal standard unless otherwise noted. Data are presented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constant in Hertz (Hz). Infrared (IR) spectra were recorded on a FT-IR spectrometer. Optical rotations were recorded on a Perkin-Elmer 341 polarimeter. HR-MS was measured with an APEX II 47e mass spectrometer. The ee values determination was carried out using chiral high-performance liquid chromatography (HPLC) with Daicel Chiracel OD-H column on Waters with a 2996 UV-detector and the dr values determined by 300 Hz ^{1}H NMR.

Materials: Thiourea catalysts were synthesized according to the procedures.[1] cyclic imino esters were synthesized according to the procedures.[2] and methyleneindolinones were synthesized according to the procedures.[3]

2.0 General Procedure



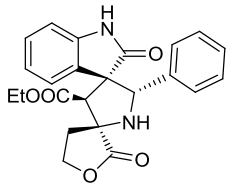
2 **3** **4**

Cyclic imino ester **2** (0.11mmol) and methyleneindolinone **3** (0.10 mmol) were added to a stirred solution of catalyst **1b** (0.01mmol, 10 mol %) in toluene and ether (1.0 mL, 1:1). Then the solution was stirred at room temperature for 24 h. After the reaction was completed (monitored by TLC), the resulting mixture was concentrated under reduced pressure and the residue was purified through column chromatography on silica gel (eluent, EtOAc / PE 1:4), to afford the corresponding product **4**. The enantiomeric purity of the product was determined by using HPLC and the dr values determined by 300 Hz ^{1}H NMR.

The racemates were obtained by using **DABCO** instead of catalyst **1b**.

3.0 Characterization of Products

(4a):

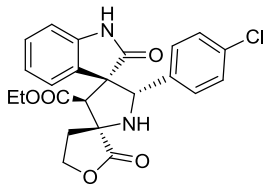


White solid, mp 175 °C, $[\alpha]^{20}_{D}$= -124.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.80(br, 1 H), 7.28-7.31(m, 1 H), 7.09-7.22(m, 5 H), 6.80-6.87(m, 3 H), 4.66-4.74(m, 1 H), 4.54-4.61(m, 2 H), 4.17(s, 1 H), 3.74-3.82(m, 1 H), 3.62-3.70(m, 1 H), 3.32-3.41(m, 1 H), 3.22(br, 1 H), 2.49-2.58(m, 1 H), 0.60-0.65(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 178.8, 177.0, 168.6, 141.3, 134.5, 129.9, 128.9, 128.2, 125.8, 123.3, 122.9, 110.0, 73.9, 66.8, 66.8, 62.1, 61.4, 60.7, 31.4, 13.3. **IR**: 3312.7, 2927.6, 1770.3, 1718.7, 1619.4, 1470.9, 1375.2, 1218.9, 1114.9, 1028.7, 899.8, 748.4, 698.4 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{23}H_{22}N_2O_5$+Na^+: 429.1421; found: 429.1419, 0.3 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 7.53 min, t_{major} = 9.10 min, ee = 95%.

(4b):



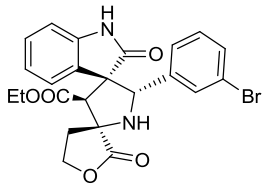
White solid, mp 195 °C, $[\alpha]^{20}_{D}$= -84.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.05(br, 1 H), 7.30-7.33(m, 1 H), 7.09-7.22(m, 4 H), 6.80-6.84(m, 3 H), 4.66-4.73(m, 1 H), 4.53-4.60(m, 2 H), 4.14(s, 1 H), 3.74-3.84(m, 1 H), 3.59-3.70(m, 1 H), 3.31-3.40 (m, 1 H), 2.47-2.56(m, 1 H), 0.60-0.65(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 178.9, 176.9, 168.4, 141.2, 134.0, 133.2, 129.6, 129.1, 128.4, 127.3, 123.3, 123.0, 110.1, 73.1, 66.8, 66.8, 62.0, 61.3, 60.8, 31.4, 13.2. **IR**: 3308.9, 2928.2, 1770.8, 1718.7, 1620.0, 1471.5, 1375.9, 1217.7, 1116.3, 1094.4, 1030.4, 828.2, 7439.2 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{23}H_{21}ClN_2O_5$+Na^+: 463.1031; found: 463.1029, 0.4 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/

Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 8.69 min, t_{major} = 10.16 min, ee = 92%.

(4c):

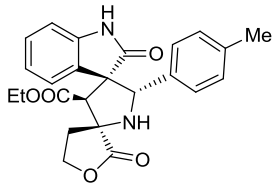


White solid, mp 209 °C, $[\alpha]^{20}_D$= -115.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.30(br, 1 H), 7.29-7.33(m, 2 H), 6.97-7.21(m, 4 H), 6.87-6.90(d, *J* = 7.5 Hz, 1 H), 6.73-6.76(d, *J* = 7.5 Hz, 1 H), 4.66-4.74(m, 1 H), 4.51-4.61(m, 2 H), 4.14(s, 1 H), 3.74-3.85(m, 1 H), 3.60-3.70(m, 1 H), 3.31-3.40 (m, 1 H), 3.13(br, 1 H), 2.46-2.55(m, 1 H), 0.61-0.66(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 178.9, 176.9, 168.4, 141.4, 137.1, 131.2, 129.7, 129.5, 129.2, 129.0, 124.4, 123.2, 123.0, 122.3, 110.3, 72.9, 66.8, 66.8, 61.9, 61.4, 60.8, 31.4, 13.3. **IR**: 3311.0, 2929.0, 1770.9, 1718.3, 1619.8, 1472.0, 1376.1, 1217.4, 1114.1, 1029.2, 882.4, 738.4, 689.4 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{23}H_{21}BrN_2O_5$+Na^+: 507.0526; found: 507.0522, 0.8 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 0.5 mL/min, 230 nm.) Retention time: t_{minor} = 16.97 min, t_{major} = 18.54 min, ee = 90%.

(4d):



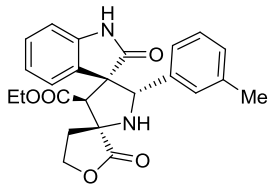
White solid, mp 187 °C, $[\alpha]^{20}_D$= -142.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.39(br, 1 H), 7.25-7.30(m, 1 H), 7.18-7.20(m, 1 H), 7.06-7.11(m, 1 H), 6.91-6.94(d, *J* = 7.8 Hz, 2 H), 6.74-6.80(m, 3 H), 4.62-4.70(m, 1 H), 4.48-4.57(m, 2 H), 4.14(s, 1 H), 3.71-3.80(m, 1 H), 3.57-3.66(m, 1 H), 3.29-3.38(m, 1 H), 3.15-3.20(d, *J* = 14.1 Hz, 1 H), 2.47-2.56(m, 1 H), 2.18(s, 3 H), 0.57-0.61(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 179.4, 177.1, 168.6, 141.5, 137.7, 131.8, 130.0, 128.9, 128.8, 125.7, 123.2, 122.8, 110.1, 73.5, 66.8, 66.7, 62.1, 61.5, 60.7, 31.3, 21.0, 13.2. **IR**: 3366.0, 2926.4, 1770.4, 1716.9,

1619.7, 1471.0, 1375.4, 1219.6, 1118.5, 1029.2, 818.0, 741.4, 701.7 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{24}H_{24}N_2O_5$+Na^+: 443.1577; found: 443.1579, -0.3 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 7.53 min, t_{major} = 9.10 min, ee = 95%.

(4e):

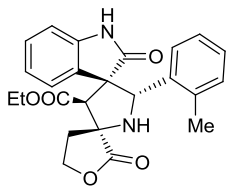


White solid, mp 187 °C, $[\alpha]^{20}_D$= -50.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.33(br, 1 H), 7.25-7.30(m, 1 H), 7.18-7.21(m, 1 H), 7.07-7.12(m, 1 H), 6.96-7.00(m, 2 H), 6.80-6.83(d, *J* = 7.8 Hz, 1 H),6.75(m, 1 H), 6.55-6.56(m, 1 H), 4.64-4.71(m, 1 H), 4.50-4.57(m, 2 H), 4.15(s, 1 H), 3.72-3.83(m, 1 H), 3.57-3.68(m, 1 H), 3.31-3.39 (m, 1 H), 3.20(br, 1 H), 2.47-2.56(m, 1 H), 2.20(s, 3 H), 0.58-0.63(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 179.2, 177.2, 168.6, 141.5, 137.7, 134.5, 130.0, 128.9, 128.0, 126.4, 123.2, 122.9, 122.8, 110.0, 73.7, 66.9, 66.7, 62.1, 61.5, 60.7, 31.3, 21.4, 13.2. **IR**: 3274.1, 2984.4, 1771.1, 1720.7, 1619.0, 1471.6, 1377.3, 1217.8, 1112.4, 1031.0, 897.4, 737.3, 698.7 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{24}H_{24}N_2O_5$+Na^+: 443.1577; found: 443.1581, -0.9 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 6.47 min, t_{major} = 9.36 min, ee = 94%.

(4f):



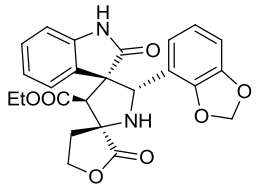
White solid, mp 162 °C, $[\alpha]^{20}_D$= -95.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.43-7.45(d, *J* = 7.8 Hz, 1 H), 7.36(br, 1 H), 7.17-7.23(m, 3 H), 7.04-7.13(m, 2 H),

6.94-6.96(m, 1 H), 6.74-6.76(d, *J* = 7.5 Hz, 1 H), 4.83(s, 1 H), 4.69-4.74(m, 1 H), 4.54-4.61(m, 1 H), 4.33(s, 1 H), 3.79-3.87(m, 1 H), 3.61-3.72(m, 1 H), 3.36-3.45(m, 1 H), 2.57-2.59(m, 1 H), 1.52(s, 3 H), 0.60-0.65(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 177.0, 168.6, 168.2, 141.1, 136.0, 132.4, 130.4, 130.3, 128.8, 128.3, 128.0, 127.1, 125.8, 123.3, 122.8, 109.8, 70.3, 66.9, 66.7, 62.1, 61.2, 60.7, 31.3, 24.9, 19.2, 13.3. **IR**: 3299.8, 2925.5, 1771.2, 1723.4, 1619.6, 1470.5, 1375.9, 1218.8, 1121.8, 1085.3, 1030.4, 738.4, 702.0 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{24}H_{24}N_2O_5$+Na^+: 443.1577; found: 443.1579, -0.3 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 7.88 min, t_{major} = 15.41 min, ee = 97%.

(4g):

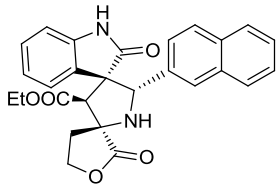


White solid, mp 129 °C, $[\alpha]^{20}_D$= -139.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.23(br, 1 H), 7.25-7.30(m, 1 H), 7.17-7.19(m, 1 H), 7.04-7.12(m, 1 H), 6.84-6.87(d, *J* = 7.8 Hz, 1 H), 6.57-6.59(d, *J* = 8.1 Hz, 1 H), 6.44(m, 1 H), 6.30-6.32(d, *J* = 8.1 Hz, 1 H), 5.86(d, *J* = 1.2 Hz, 1 H), 5.76(d, *J* = 0.9 Hz, 1 H), 4.65-4.73(m, 1 H), 4.53-4.60(m, 1 H), 4.48(s, 1 H), 4.15(s, 1 H), 3.74-3.82(m, 1 H), 3.61-3.71(m, 1 H), 3.30-3.39(m,1 H), 3.05(br, 1 H), 2.47-2.56(m, 1 H), 1.52(s, 3 H), 0.60-0.64(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 179.2, 177.0, 168.6, 147.4, 147.3, 141.4, 129.9, 128.9, 128.2, 123.1, 122.9, 119.5, 110.1, 108.0, 106.5, 101.0, 73.7, 66.8, 66.9, 62.0, 61.3, 60.8, 53.5, 31.4, 13.2. **IR**: 3310.6, 2925.2, 1770.4, 1719.5, 1618.8, 1471.0, 1375.9, 1345.7, 1237.2, 1213.7, 1113.5, 1037.1, 933.6, 738.1 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{24}H_{22}N_2O_7$+Na^+: 473.1319; found: 473.1311, 1.7 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 0.5 mL/min, 230 nm.) Retention time: t_{minor} = 22.58 min, t_{major} = 24.85 min, ee = 92%.

(4h):

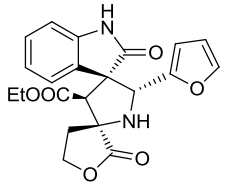


White solid, mp 263 °C, $[\alpha]^{20}_D$= -60.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $(CD_3)_2SO$): δ 10.17(br, 1 H), 7.79-7.82(m, 2 H), 7.68-7.71(m, 2 H), 7.45-7.48(m, 2 H), 7.25-7.34(m, 2 H), 7.07-7.12(m, 1 H), 6.87-6.89(d, *J* = 8.4 Hz, 1 H), 6.77-6.79(d, *J* = 7.5 Hz, 1 H), 4.81-4.94(d, *J* = 8.1 Hz, 1 H), 4.51-4.60(m, 2 H), 4.08(s, 1 H), 4.15(s, 1 H), 3.86-3.89(d, *J* = 8.1 Hz, 2 H), 3.71-3.82(m, 1 H), 3.54-3.65(m, 1 H), 3.17-3.21(m, 1 H), 2.65-2.70(m, 1 H), 0.55-0.56(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, DMSO): δ 177.7, 176.8, 168.3, 142.5, 134.7, 132.5, 132.4, 130.8, 128.6, 127.8, 127.3, 127.0, 126.0, 125.9, 125.1, 124.7, 123.4, 121.9, 109.2, 72.2, 66.0, 65.5, 60.0, 59.8, 58.7, 29.5, 12.9. **IR**: 3317.8, 2925.5, 1770.4, 1720.8, 1619.3, 1470.4, 1374.9, 1218.6, 1123.1, 1029.1, 819.9, 745.2 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{27}H_{25}N_2O_5$+Na^+: 457.1758; found: 457.1751, 1.5 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 5.57 min, t_{major} = 13.13 min, ee = 90%.

(4i):

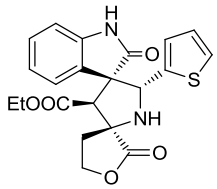


White solid, mp 165 °C, $[\alpha]^{20}_D$= -36.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.30(br, 1 H), 7.25-7.31(m, 2 H), 7.14-7.18 (m, 2 H), 7.05-7.10(m, 1 H), 6.88-6.90(d, *J* = 7.8 Hz, 1 H), 6.21-6.23(q, *J* = 1.8 Hz, 1 H), 6.14-6.15(d, *J* = 3.3 Hz, 1 H), 4.54-4.72(m, 3 H), 4.18(s, 1 H), 3.75-3.86(m, 1 H), 3.61-3.71(m, 1 H), 3.28-3.37 (m, 2 H), 2.46-2.55(m, 1 H), 0.62-0.67(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 179.1, 176.6, 168.3, 148.9, 142.3, 141.4, 129.7,128.9, 123.1, 122.8, 110.5, 110.1, 107.2, 68.5, 67.1, 66.7, 61.3, 61.0, 60.8, 31.2, 13.2. **IR**: 3300.9, 2923.1, 1770.8, 1719.2, 1619.3, 1470.4, 1374.7, 1220.9, 1121.5, 1027.9, 741.4 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{21}H_{20}N_2O_6$+Na^+: 419.1214; found: 419.1212, 0.4 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 8.67 min, t_{major} = 10.15 min, ee = 92%.

(4j):

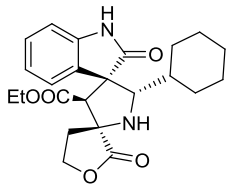


White solid, mp 144 °C, $[\alpha]^{20}_D$= -24.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.16(br, 1 H), 7.30-7.32(m, 1 H), 7.05-7.19(m, 3 H), 6.85-6.88 (d, *J* = 7.8 Hz, 1 H), 6.79-6.82(m, 1 H), 6.70-6.71(d, *J* = 3.3 Hz, 1 H), 4.55-4.73(m, 3 H), 4.20(s, 1 H), 3.75-3.85(m, 1 H), 3.62-3.72(m, 1 H), 3.29-3.38 (m, 2 H), 2.48-2.57(m, 1 H), 0.63-0.67(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 179.1, 176.7, 168.5, 141.6, 136.8, 129.1,129.0, 126.8, 124.7, 124.5, 123.3, 122.9, 110.2, 70.3, 67.0, 66.8, 62.0, 61.3, 60.8, 31.5, 13.3. **IR**: 3310.1, 2924.1, 1770.7, 1717.2, 1619.3, 1469.7, 1375.2, 1217.6, 1116.5, 1028.8, 741.1, 701.9 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{21}H_{20}N_2O_5S$+Na^+: 435.0985; found: 435.0982, 0.8 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 8.23 min, t_{major} = 10.88 min, ee = 91%.

(4k):



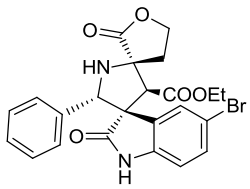
White solid, mp 178 °C, $[\alpha]^{20}_D$= -16.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.82(br, 1 H), 7.22-7.24(m, 1 H), 7.00-7.09(m, 2 H), 6.93-6.96(d, *J* = 7.5 Hz, 1 H), 4.52-4.66(m, 2 H), 3.94(s, 1 H), 3.58-3.72(m, 2 H), 3.18-3.27(m, 2 H), 2.36-2.45(m, 2 H), 1.92-1.99(m, 2 H), 1.64-1.68(m, 1 H), 1.51-1.55(m, 1 H), 1.38-1.42(m, 1 H), 1.16-1.25(m, 2 H), 0.94-1.10(m, 3 H), 0.63-0.68(t, *J* = 7.2 Hz, 3 H),0.44-0.55(m, 1 H); **^{13}C NMR** (75MHz,

$CDCl_3$): δ 186.0, 177.5, 168.5, 141.1, 131.5, 128.6, 123.2, 122.7, 110.1, 76.1, 66.7, 66.3, 64.0, 60.7, 59.9, 38.6, 31.7, 31.4, 30.0, 26.1, 25.5, 13.2. **IR**: 3264.7, 2927.4, 1770.7, 1710.5, 1620.2, 1479.3, 1376.4, 1214.9, 1102.0, 1032.6, 883.9, 738.4 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{23}H_{29}N_2O_5$+Na^+: 413.2071; found: 413.2069, 0.4 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 4.48 min, t_{major} = 5.92 min, ee = 90%.

(4l):

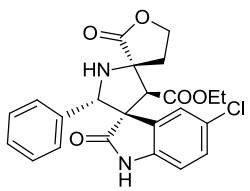


White solid, mp 104 °C, $[\alpha]^{20}_D$= -59.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.33(br, 1 H), 7.39-7.46(m, 2 H), 7.29-7.37(m, 1 H), 7.13-7.19(m, 2 H), 6.84-6.87(m, 2 H), 6.71-6.75(d, *J* = 8.1 Hz, 1 H), 4.65-4.71(m, 1 H), 4.53-4.61(m, 2 H), 4.16(s, 1 H), 3.87-3.93(m, 1 H), 3.67-3.76(m, 1 H), 3.22-3.31(m, 2 H), 2.50-2.55(m, 1 H), 0.68-0.73(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 178.6, 176.9, 168.2, 140.5, 134.1, 132.1, 131.8, 128.7, 128.6, 128.4, 128.3, 126.8, 126.6, 126.3, 125.8, 115.8, 115.2, 111.6, 74.1, 66.9, 66.8, 62.2, 61.5, 61.0, 31.4, 13.4. **IR**: 3292.2, 2925.3, 1771.6, 1724.8, 1622.9, 1474.3, 1375.8, 1302.8, 1218.3, 1122.6, 1029.4, 818.9, 737.4 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{23}H_{21}BrN_2O_5$+Na^+: 507.0526; found: 507.0525, 0.2 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 8.24 min, t_{major} = 9.44 min, ee = 92%.

(4m):



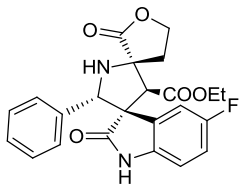
White solid, mp 118 °C, $[\alpha]^{20}_D$= -139.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.15(br, 1 H), 7.29-7.30(m, 1 H), 7.12-7.22(m, 4 H), 6.85-6.87(m, 2 H), 6.76-6.79(d, *J* =

8.1 Hz, 1 H), 4.65-4.73(m, 1 H), 4.54-4.61(m, 2 H), 4.17(s, 1 H), 3.84-3.94(m, 1 H), 3.65-3.76(m, 1 H), 3.22-3.31(m, 2 H), 2.49-2.58(m, 1 H), 0.69-0.73(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 178.7, 176.8, 168.2, 139.9, 134.1, 131.7, 128.9, 128.4, 125.8, 123.6, 111.0, 74.0, 66.9, 66.8, 62.3, 61.5, 61.0, 31.4, 13.4. **IR**: 3294.1, 2926.4, 1771.7, 1723.0, 1619.7, 1478.4, 1375.6, 1220.0, 1123.9, 1029.8, 819.9, 737.9, 698.4 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{23}H_{21}ClN_2O_5+H^+$: 441.1212; found: 441.1214, -0.5 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 7.74 min, t_{major} = 9.35 min, ee = 90%.

(4n):

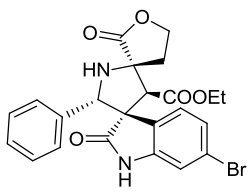


White solid, mp 121 °C, $[\alpha]^{20}_D$= -76.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.95(br, 1 H), 7.14-7.23(m, 3 H), 6.95-7.04(m, 2 H), 6.85-6.87(m, 2 H), 6.75-6.79(m, 1 H), 4.65-4.73(m, 1 H), 4.52-4.61(m, 2 H), 4.19(s, 1 H), 3.82-3.93(m, 1 H), 3.66-3.77(m, 1 H), 3.23-3.31(m, 2 H), 2.48-2.57(m, 1 H), 0.70-0.74(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 178.8, 176.8, 168.3, 137.3, 134.1, 131.4, 128.4, 128.3, 125.8, 115.4, 115.1, 111.5, 111.2, 110.5, 74.2, 66.9, 66.8, 62.5, 61.4, 60.9, 31.4, 13.4. **IR**: 3280.4, 2925.3, 1772.1, 1724.6, 1664.6, 1486.7, 1375.7, 1300.6, 1217.3, 1191.9, 1116.2, 1029.6, 821.0, 735.0 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{23}H_{21}FN_2O_5+H^+$: 441.1507; found: 441.1512, -1.1 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 8.72 min, t_{major} = 12.35 min, ee = 90%.

(4o):

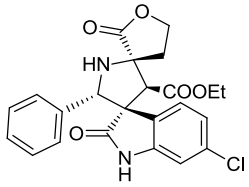


White solid, mp 133 °C, $[\alpha]^{20}_D$= -50.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.44(br, 1 H), 7.23-7.24(m, 1 H), 7.14-7.20(m, 3 H), 6.97(d, *J* = 1.5 Hz, 1 H), 6.84-6.87(m, 2 H), 4.62-4.70(m, 1 H), 4.51-4.59(m, 2 H), 4.13(s, 1 H), 3.78-3.89(m, 1 H), 3.65-3.75(m, 1 H), 3.20-3.31(m, 2 H), 2.46-2.55(m, 1 H), 0.69-0.74(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 179.1, 176.8, 168.3, 142.7, 134.3, 128.9, 128.4, 128.3, 125.7, 125.6, 124.5, 122.4, 113.6, 73.8, 66.9, 66.8, 61.9, 61.4, 61.0, 31.3, 13.4. **IR**: 3320.4, 2926.7, 1771.9, 1725.4, 1656.8, 1610.1, 1456.1, 1331.1, 1223.8, 1124.4, 1069.1,1029.4, 908.2, 737.6, 697.9 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{23}H_{21}BrN_2O_5$-H^+: 458.0707; found: 458.0704, 0.6 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 8.72 min, t_{major} = 12.80 min, ee = 92%.

(4p):

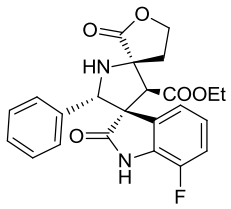


White solid, mp 121 °C, $[\alpha]^{20}_D$= -77.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.32(br, 1 H), 7.08-7.21(m, 5 H), 6.84-6.87(m, 3 H), 4.62-4.71(m, 1 H), 4.54-4.60(m, 1 H), 4.14(s, 1 H), 3.78-3.89(m, 1 H), 3.65-3.76(m, 1 H), 3.23-3.32(m, 1 H), 2.47-2.56(m, 1 H), 0.70-0.75(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 179.1, 176.8, 168.3, 142.5, 134.6, 134.2, 128.4, 128.3, 125.8, 124.2, 122.7, 110.7, 73.8, 66.9, 66.8, 61.8, 61.3, 61.0, 31.3, 13.4. **IR**: 3282.2, 2926.9, 1771.9, 1726.2, 1617.0, 1485.6, 1453.9, 1376.8, 1340.6, 1219.0, 1122.3, 1029.9, 911.4, 735.8 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{23}H_{21}ClN_2O_5$+H^+: 441.1212; found: 441.1211, 0.2 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 8.48 min, t_{major} = 12.42 min, ee = 93%.

(4q):

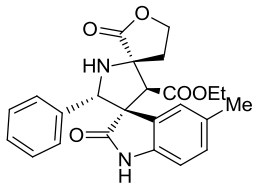


White solid, mp 184 °C, $[\alpha]^{20}_{D}$= -135.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.45(br, 1 H), 7.17-7.24(m, 3 H), 7.01-7.11(m, 3 H), 6.85-6.88(m, 2 H), 4.65-4.72(m, 1 H), 4.52-4.60(m, 2 H), 4.20(s, 1 H), 3.75-3.86(m, 1 H), 3.64-3.73(m, 1 H), 3.22-3.35(m, 2 H), 2.48-2.57(m, 1 H), 0.67-0.72(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 177.6, 176.7, 168.3, 148.4, 145.2, 134.1, 132.8, 132.8, 128.6, 128.4, 128.4, 125.8, 123.6, 123.5, 119.0, 119.0, 116.1, 115.9, 74.3, 66.9, 66.7, 65.9, 62.5, 61.6, 60.8, 31.3, 15.3,13.3. **IR**: 3280.9, 2926.4, 1773.2, 1729.9, 1672.6, 1500.4, 1466.2, 1404.3, 1300.8, 1195.0, 1115.9, 1028.6, 755.7 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{23}H_{21}FN_2O_5$+H^+: 441.1507; found: 441.1497, 2.4 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 8.01 min, t_{major} = 12.75 min, ee = 90%.

(4r):

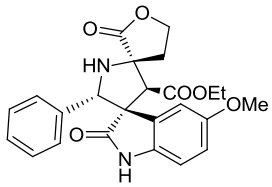


White solid, mp 103 °C, $[\alpha]^{20}_{D}$= -105.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.49(br, 1 H), 7.15-7.19(m, 3 H), 7.06-7.09(d, *J* = 7.5 Hz, 1 H), 6.99(s, 1 H), 6.85-6.87(m, 2 H), 6.69-6.71(d, *J* = 8.1 Hz, 1 H), 4.68-4.75(m, 1 H), 4.55-4.63(m, 2 H), 4.18(s, 1 H), 3.77-3.88(m, 1 H), 3.60-3.71(m, 1 H), 3.33-3.42(m, 1 H), 2.55(m, 1 H), 2.38(s, 3 H), 0.61-0.66(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 178.6, 177.0, 168.7, 138.8, 134.6, 130.0, 129.2, 128.2, 128.1, 125.8, 123.9, 109.6, 73.9, 66.8, 66.7, 62.1, 61.4, 60.7, 31.5, 21.3, 13.3. **IR**: 3277.6, 2925.5, 1771.2, 1719.8, 1665.1, 1493.1, 1456.1, 1376.1, 1301.6, 1206.4, 1121.4, 1029.9, 734.1 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{24}H_{24}N_2O_5$+Na^+: 443.1577; found: 443.1580, -0.6 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 6.83 min, t_{major} = 8.31 min, ee = 93%.

(4s):

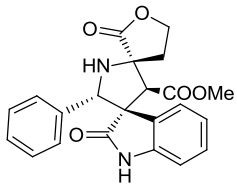


White solid, mp 182 °C, $[\alpha]^{20}_D$= -107.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.21(br, 1 H), 7.13-7.15(m, 3 H), 6.71-6.88(m, 5 H), 4.64-4.71(m, 1 H), 4.51-4.58(m, 2 H), 4.16(s, 1 H), 3.78-3.94(m, 4 H), 3.58-3.72(m, 1 H), 3.27-3.35(m, 1 H), 2.17-3.21(d, *J* = 14.1 Hz, 1 H), 2.46-2.55(m, 1 H), 0.65-0.69(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 179.1, 177.1, 168.5, 155.9, 134.9, 134.6, 131.4, 128.1, 125.8, 112.3, 111.2, 110.4, 74.0, 66.8, 66.8, 62.4, 61.4, 60.8, 55.9, 31.3, 13.3. **IR**: 3281.0, 2926.9, 1771.0, 1713.6, 1604.6, 1490.8, 1376.2, 1300.2, 1206.3, 1121.0, 1030.5, 735.7 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{24}H_{24}N_2O_6$+H^+: 437.1707; found: 437.1710, -0.6 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 9.05 min, t_{major} = 10.98 min, ee = 94%.

(4t):

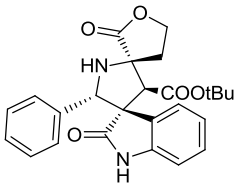


White solid, mp 203 °C, $[\alpha]^{20}_D$= -64.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.09(br, 1 H), 7.26-7.31(m, 1 H), 7.09-7.22(m, 5 H), 6.80-6.85(m, 3 H), 4.63-4.71(m, 1 H), 4.53-4.61(m, 2 H), 4.18(s, 1 H), 3.24-3.39(m, 2 H), 3.21(s, 3 H), 2.49-2.58(m, 1 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 179.0, 177.0, 169.1, 141.2, 134.4, 129.5, 129.0, 128.2, 125.8, 123.2, 122.8, 110.1, 73.8, 66.9, 66.8, 62.2, 61.2, 51.7, 31.5. **IR**: 3286.2, 2954.1, 1770.9, 1716.4, 1619.3, 1470.9, 1353.2, 1219.1, 1116.0, 1028.1, 738.8, 698.0 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{22}H_{20}N_2O_5$+H^+: 393.1445; found: 393.1440, 1.2 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 8.71 min, t_{major} = 12.35 min, ee = 90%.

(4u):

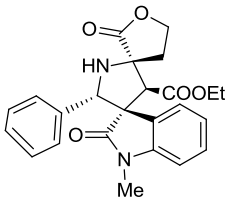


White solid, mp 208 °C, $[\alpha]^{20}_D$= -133.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.81(br, 1 H), 7.25-7.33(m, 1 H), 7.10-7.22(m, 5 H), 6.82-6.88(m, 3 H), 4.69-4.77(m, 1 H), 4.52-4.60(m, 2 H), 4.12(s, 1 H), 3.29-3.37(m, 1 H), 2.46-2.55(m, 1 H), 0.95(s, 9 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 178.9, 177.2, 167.6, 141.5, 134.8, 130.6, 128.8, 128.2, 128.1, 125.8, 123.4, 122.9, 109.9, 82.1, 73.8, 66.8, 66.6, 62.5, 61.9, 31.1, 27.3. **IR**: 3198.6, 2924.8, 1773.9, 1721.9, 1671.4, 1470.9, 1370.5, 1262.9, 1156.6, 1115.5, 1027.1, 752.9, 700.1 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{25}H_{26}N_2O_5+H^+$: 435.1914; found: 435.1911, 0.9 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 5.47 min, t_{major} = 6.54 min, ee = 92%.

(4v):

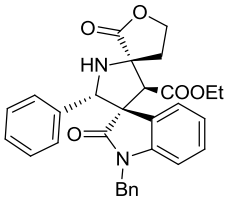


White solid, mp 210 °C, $[\alpha]^{20}_D$= -121.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.32-7.37(m, 1 H), 7.11-7.25(m, 5 H), 6.77-6.79(m, 3 H), 4.65-4.73(m, 1 H), 4.55-4.62(m, 2 H), 4.19(s, 1 H), 3.71-3.82(m, 1 H), 3.59-3.70(m, 1 H), 3.26-3.40(m, 2 H), 2.84(s, 3 H), 2.49-2.58(m, 1 H), 0.61-0.65(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 176.9, 176.8, 168.7, 144.2, 134.6, 129.5, 128.9, 128.1, 125.5, 122.9, 122.8, 108.1, 73.8, 66.8, 66.7, 61.9, 61.1, 60.6, 31.5, 26.1, 13.3. **IR**: 3298.2, 2926.8, 1771.3, 1713.7, 1611.7, 1469.9, 1378.0, 1217.0, 1128.0, 1029.3, 898.3, 752.0, 698.0 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{24}H_{24}N_2O_5$-H^+: 421.1758; found: 421.1755, 0.7 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{minor} = 15.09 min, t_{major} = 17.43 min, ee = 93%.

(4w):

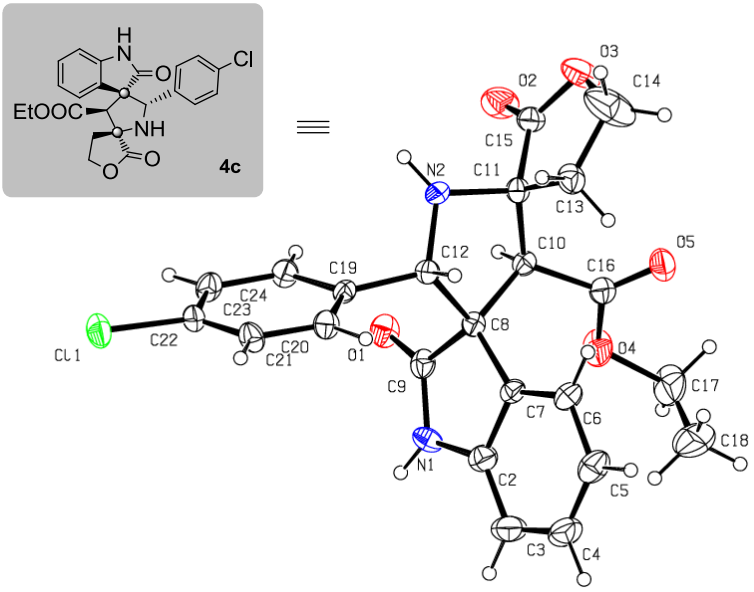


White solid, mp 90 °C, $[\alpha]^{20}_D$= -151.0 (*c*=1.0, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.06-7.21(m, 9 H), 6.90-6.92(m, 2 H), 6.68-6.70(m, 2 H), 6.57-6.59(d, *J* = 7.2 Hz, 1 H), 4.75-4.81(d, *J* = 15.6 Hz, 1 H), 4.68-4.73(m, 2 H), 4.56-4.64(m, 2 H), 4.38-4.43(d, *J* = 15.9 Hz, 1 H), 4.30(s, 1 H), 3.70-3.81(m, 1 H), 3.56-3.67(m, 1 H), 3.35-3.44(m, 2 H), 2.51-2.60(m, 1 H), 0.51-0.55(t, *J* = 7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 177.7, 176.9, 168.7, 143.4, 135.2, 134.3, 129.4, 128.8, 128.5, 128.4, 128.3, 127.3, 127.0, 126.3, 122.9, 122.8, 109.2,74.1, 66.8, 61.8, 61.7, 60.6, 43.9, 31.4, 13.2. **IR**: 3300.5, 2925.3, 1771.2, 1711.4, 1611.1, 1490.7, 1465.5, 1371.4, 1216.5, 1116.3, 1029.8, 738.2, 697.7 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{30}H_{28}N_2O_5$-H^+: 497.2071; found: 497.2071, 0.0 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 230 nm.) Retention time: t_{major} = 27.04 min, ee = >99%.

4.0 The X-ray crystal structure of 4b:



Bond precision:	C-C = 0.0053 A	Wavelength=0.71070
Cell:	a=6.39013(18)	b=16.4094(5) c=20.8853(6)
	alpha=90	beta=90 gamma=90
Temperature:	292 K	
	Calculated	Reported
Volume	2190.00(11)	2190.00(11)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C23 H21 Cl N2 O5	C23 H21 Cl N2 O5
Sum formula	C23 H21 Cl N2 O5	C23 H21 Cl N2 O5
Mr	440.87	440.87
Dx,g cm-3	1.337	1.337
Z	4	4
Mu (mm-1)	0.211	0.211
F000	920.0	920.0
F000’	921.03	
h,k,lmax	8,22,28	8,22,26
Nref	3214[5627]	4150
Tmin,Tmax	0.933,0.943	0.996,1.000
Tmin’	0.933	

Correction method= MULTI-SCAN
Data completeness= 1.29/0.74 Theta(max)= 28.630
R(reflections)= 0.0563(3172) wR2(reflections)= 0.1508(4150)
S = 1.065 Npar= 281

5.0 Plausible reaction mechanism:

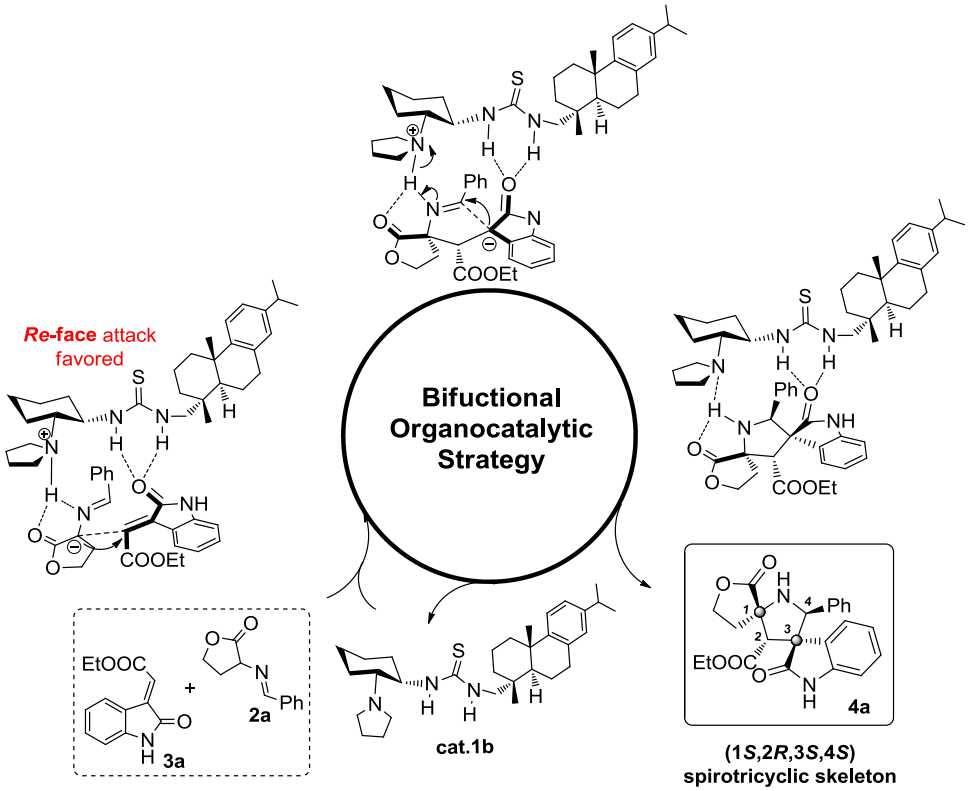


Figure 1. Plausible reaction mechanism.

According to the theoretical works performed by Takemoto and Pápai, [Ref4] we proposed a plausible mechanism featuring a *Re* face process (**Figure 1**). The tertiary amine moiety of the catalyst may interact with the cyclic imino ester via H-bonds, enhancing the electrophilicity of the reacting carbon center, and the thiourea moiety may coordinate to the methyleneindolinone simultaneously. Then *Re*-face selective Michael addition occurs under the synergistic interaction of the catalyst and affords a transient Michael adduct. Subsequent intramolecular Mannich reaction takes place to furnish the cyclization and provide the desired spirocyclic skeleton with a (1*S*,2*R*,3*S*,4*S*) configuration, which is in keeping with the experimental results.

6.0 References

[1] a) X.-X. Jiang and R. Wang, *Org. Lett*. **2009**, *11*, 153; b) X.-X. Jiang and R. Wang, *J. Org. Chem*. **2009**, *74*, 5562.

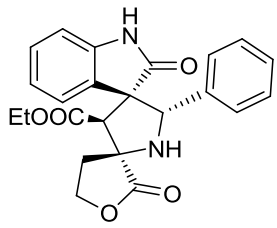
[2] a) S. Thaisrivongs and L. T. Kroll, *J. Med. Chem.* **1988,** *31***,** 1369-1376; b) R. Grigg and M. A. B. Sarker, *Tetrahedron,* **2006**, *62*, 10332-10343.

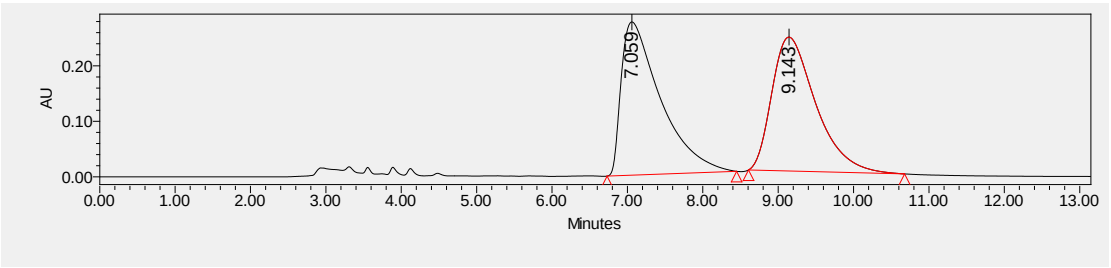
[3] Y.-M. Cao and R. Wang, *Angew. Chem. Int. Ed,* **2011**, *50*, 9124-9127.

[4] a) A. Hamza and I. Pápai, *J. Am. Chem. Soc.*, **2006**, *128*, 13151; b) T. Okino and Y. Takemoto, *J. Am. Chem. Soc.*, **2005**, *127*, 119.

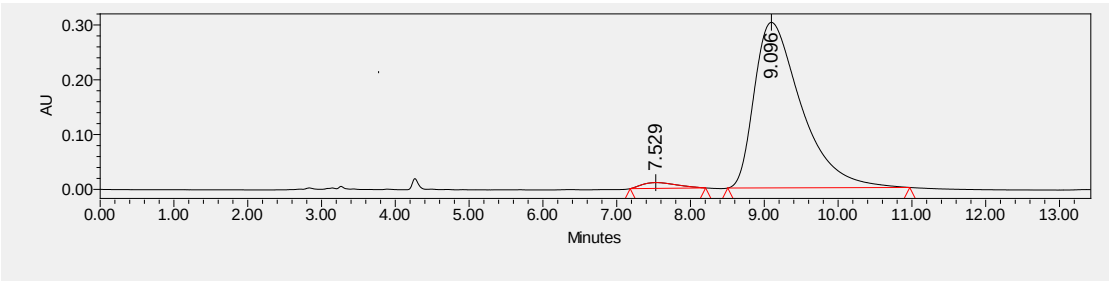
7.0 Copies of HPLC Spectra of Racemic /Chiral Products

(4a):



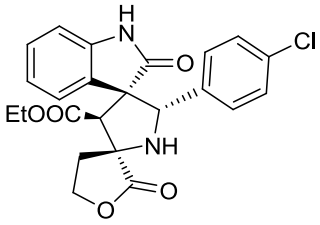


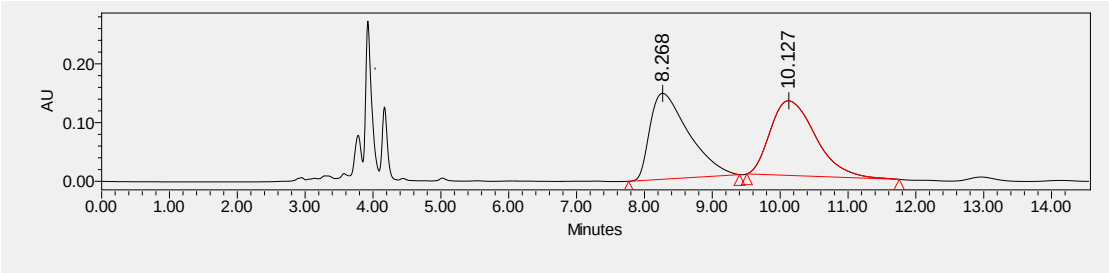
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.059	10028467	50.65	276401	bb	Unknown
2	9.143	9770441	49.35	241438	bb	Unknown



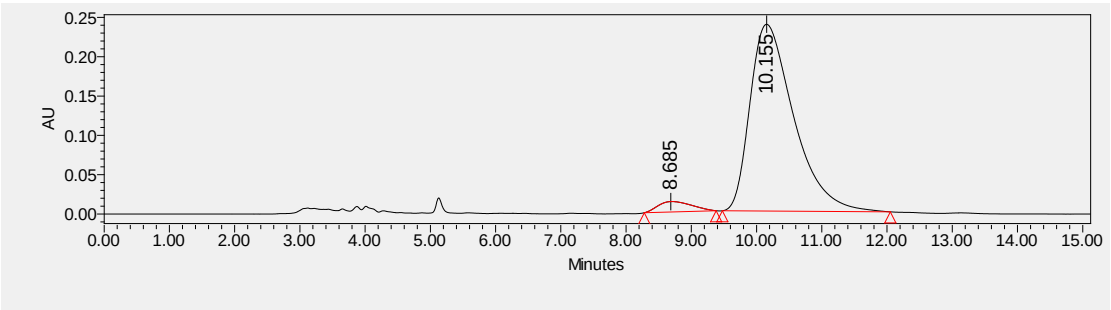
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.529	349109	2.54	10559	bb	Unknown
2	9.096	13377038	97.46	301937	bb	Unknown

(4b):



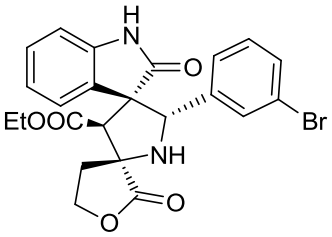


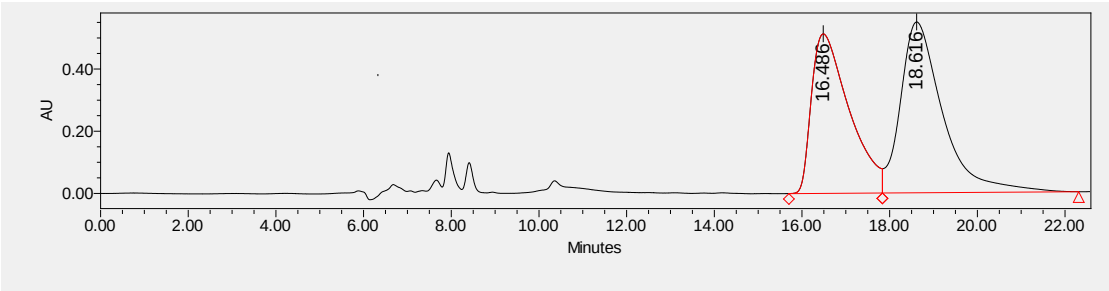
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.268	5781658	49.45	146368	bb	Unknown
2	10.127	5910811	50.55	127098	bb	Unknown



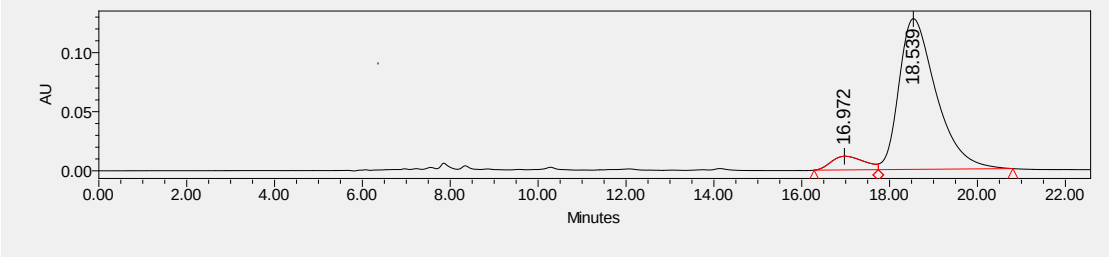
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.685	474126	4.11	13295	bb	Unknown
2	10.155	11070808	95.89	237484	bb	Unknown

(4c):



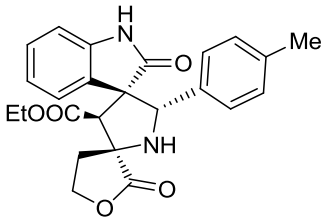


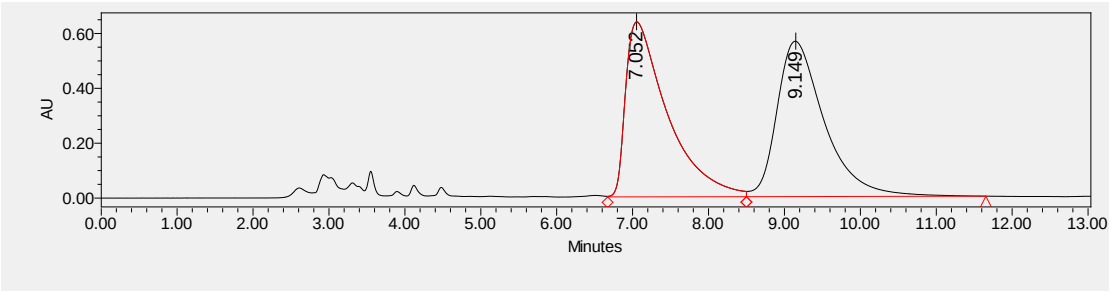
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	16.486	30641236	45.51	513044	VV	Unknown
2	18.616	36692684	54.49	549344	VB	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	16.972	1329188	4.89	32458	bb	Unknown
2	18.539	25832309	95.11	463739	bb	Unknown

(4d):





Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.052	24411893	49.85	638473	VV	Unknown
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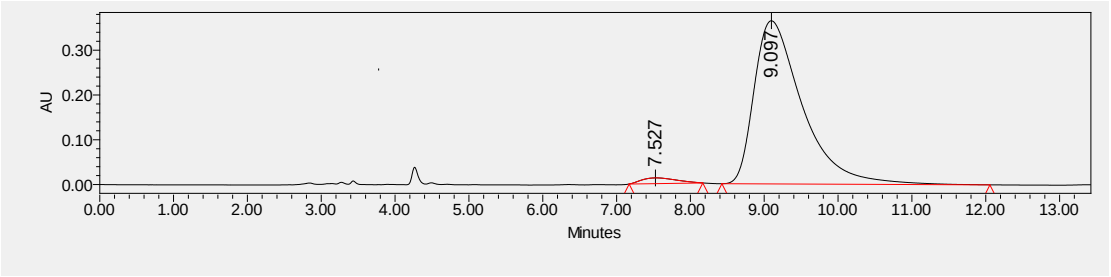

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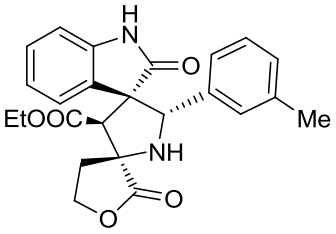
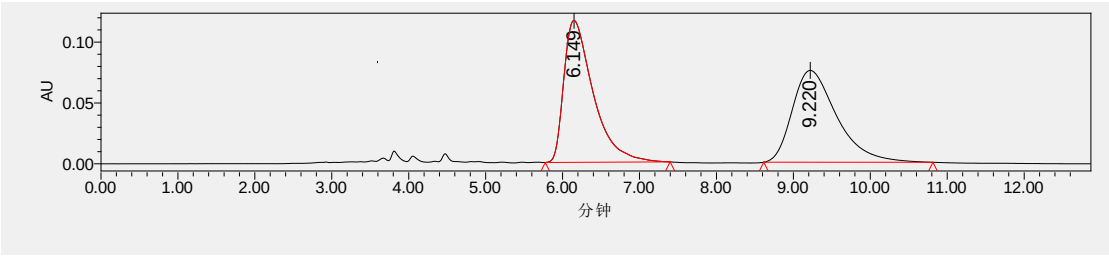
1	7.527	418467	2.47	12792	bb	Unknown
2	9.097	16549664	97.53	364419	bb	Unknown

(4e):





Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	6.149	3091251	50.44	116638	bb	Unknown
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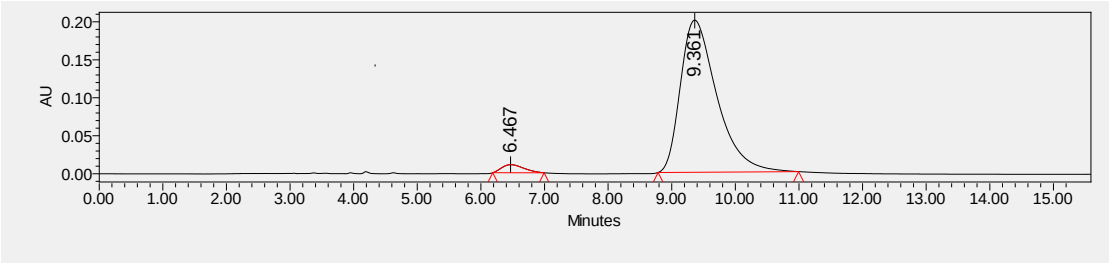

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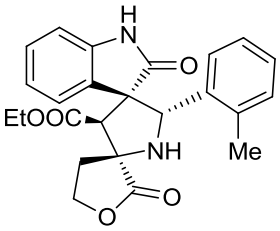
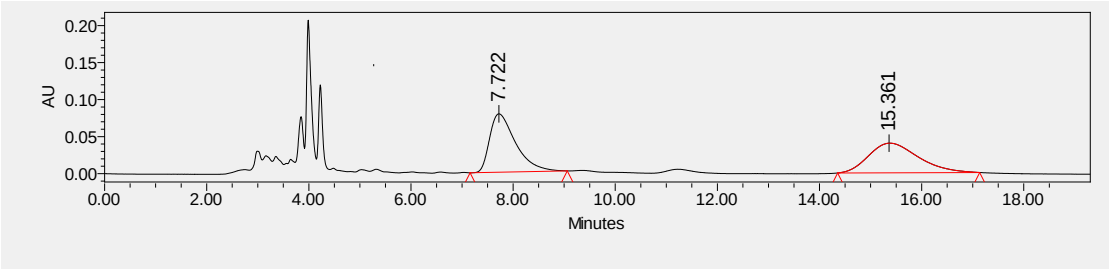
(4f):





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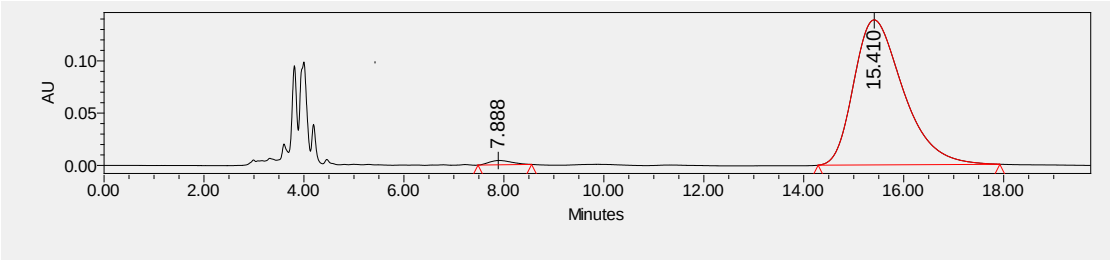
1	7.722	2784211	50.73	78912	bb	Unknown
2	15.361	2704208	49.27	40038	bb	Unknown



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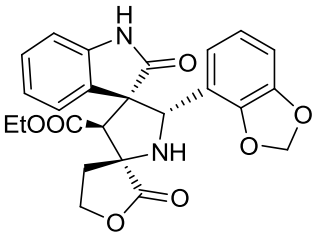
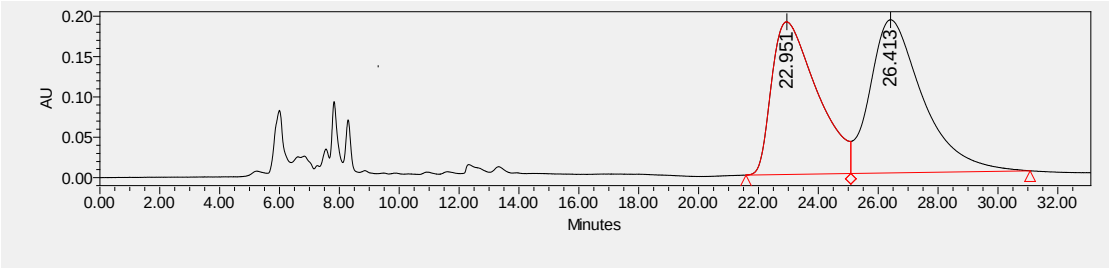
2	15.410	9512212	98.63	138668	bb	Unknown

(4g):





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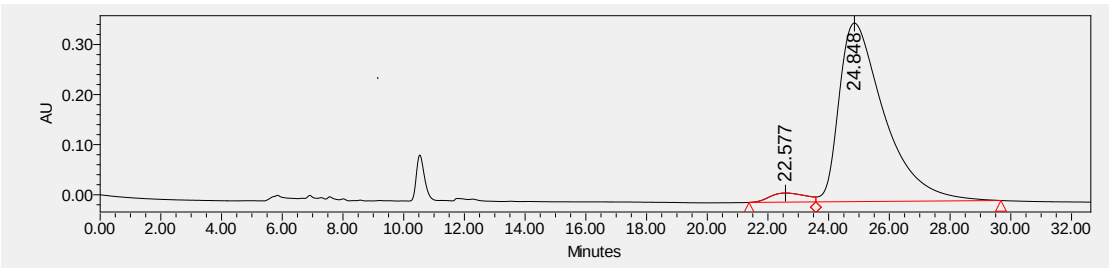
2	26.413	23321143	53.80	189868	VB	Unknown



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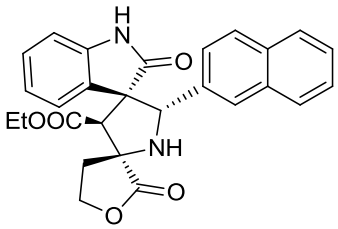
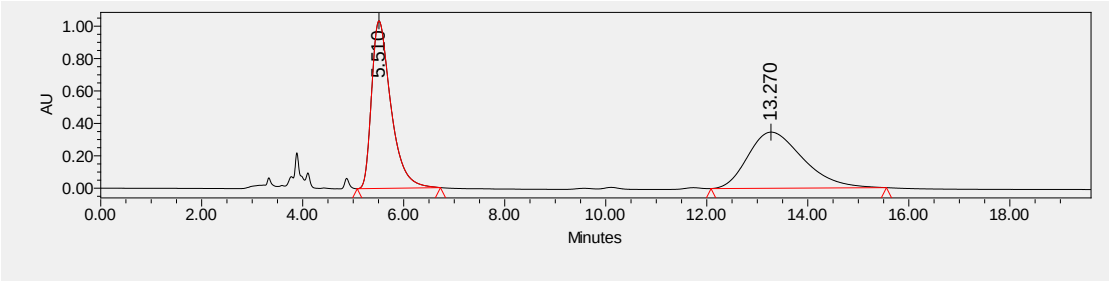
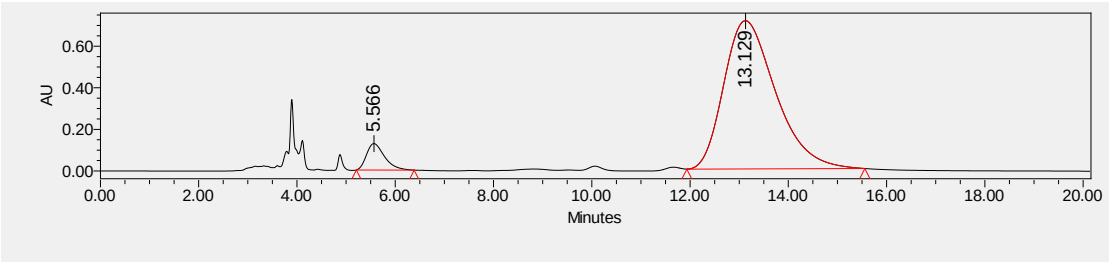
1	22.577	1508668	3.92	18278	BV	Unknown
2	24.848	36965161	96.08	356845	VB	Unknown

(4h):



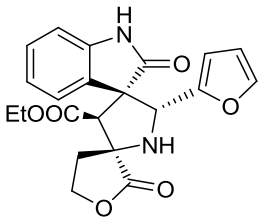


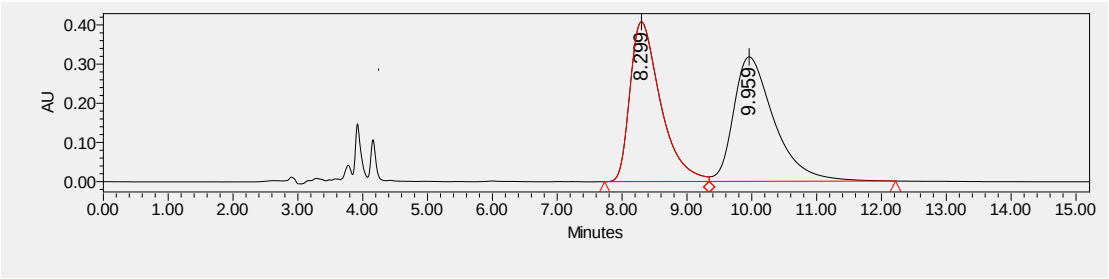
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	5.510	27388430	51.07	1033914	bb	Unknown
2	13.270	26241497	48.93	346533	bb	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	5.566	1955187	5.11	82034	bb	Unknown
2	13.129	36339669	94.89	491978	bb	Unknown

(4i):





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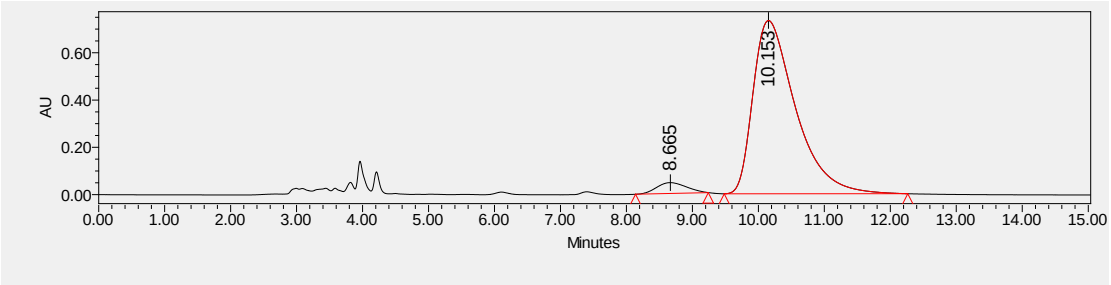

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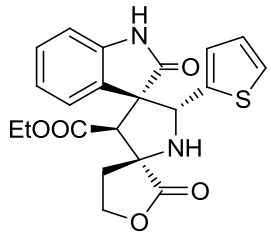
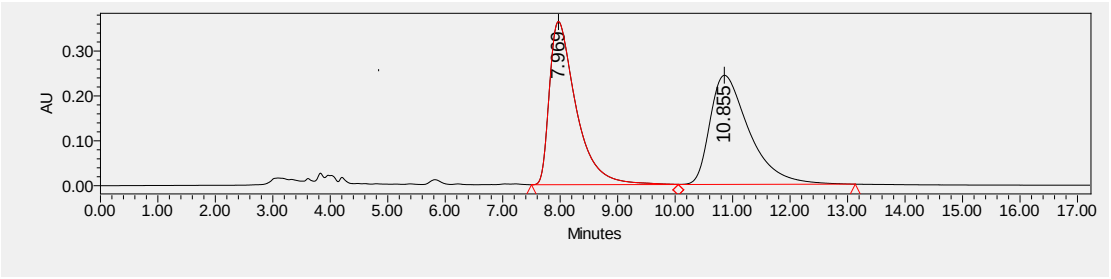
(4j):





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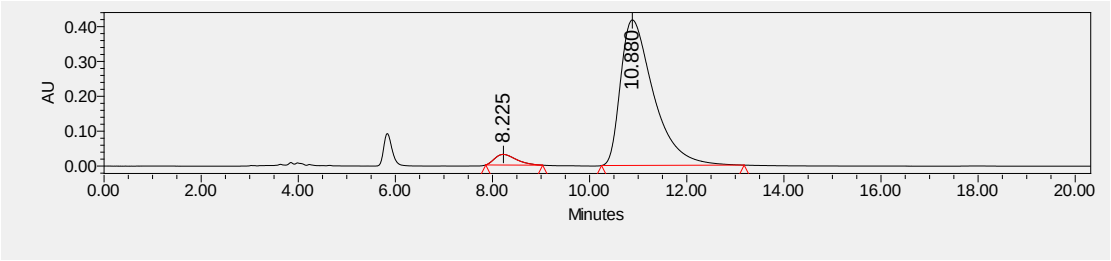

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1	8.225	919835	4.46	30252	bb	Unknown
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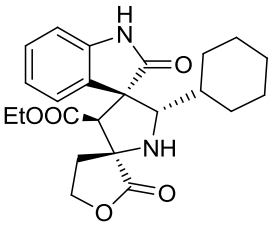
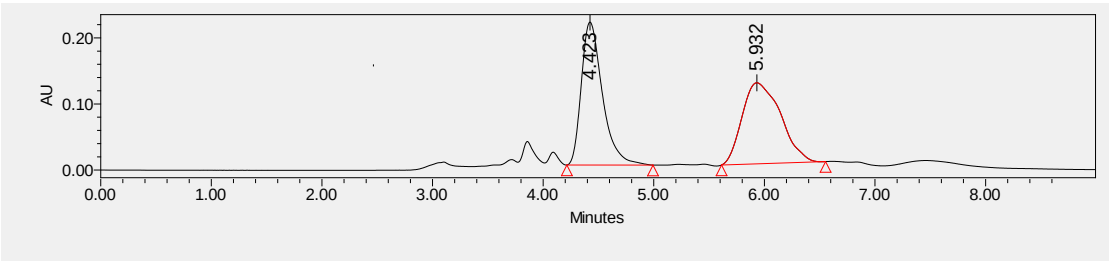
(4k):





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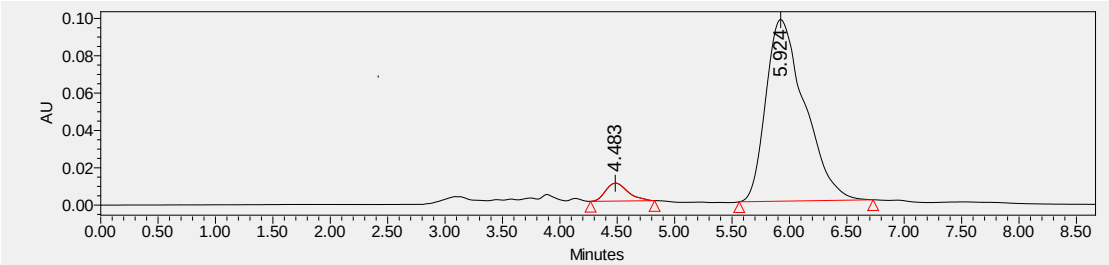

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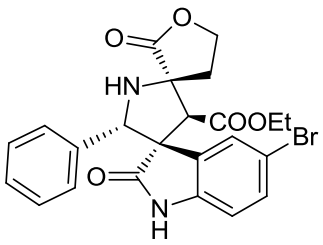
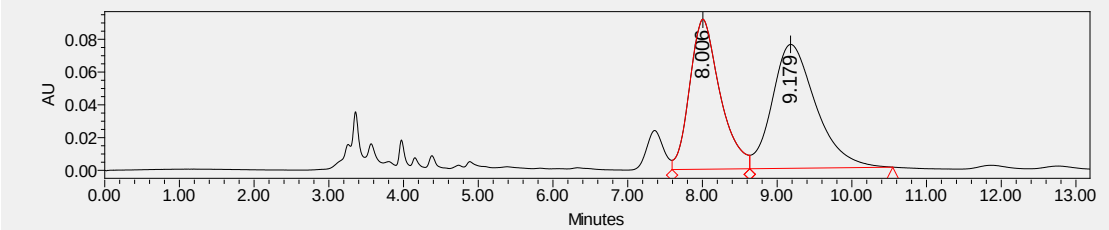
(4l):





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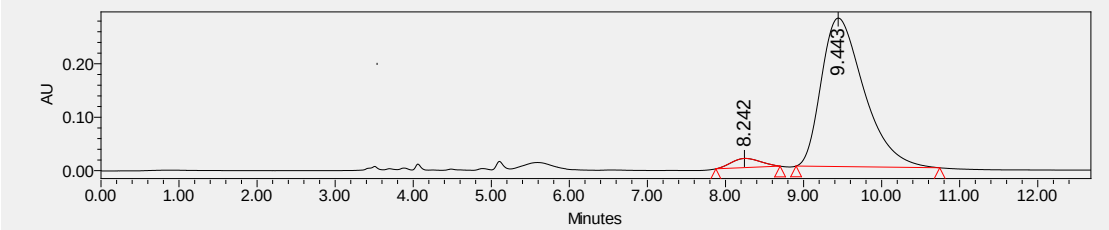
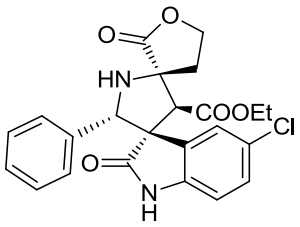
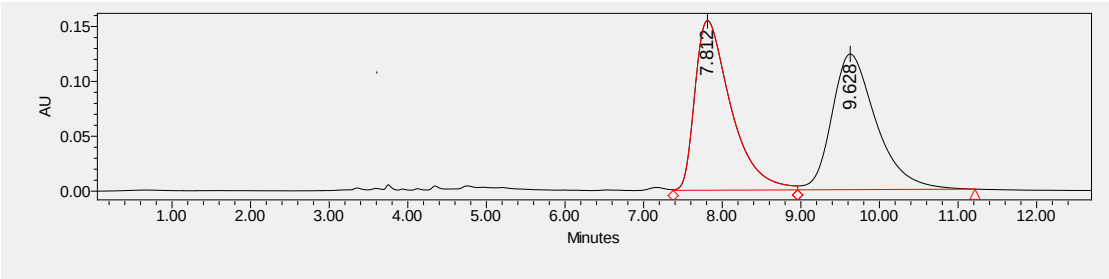
2	9.179	3071669	54.29	75617	Vb	Unknown



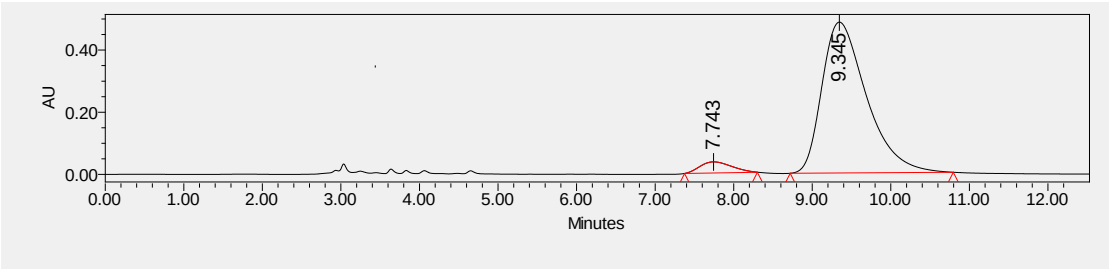
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.242	447168	4.06	17184	bb	Unknown
2	9.443	10562570	95.94	277902	bb	Unknown

(4m):



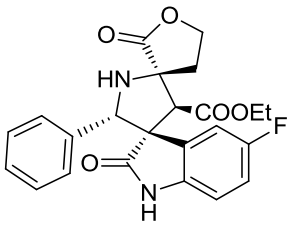


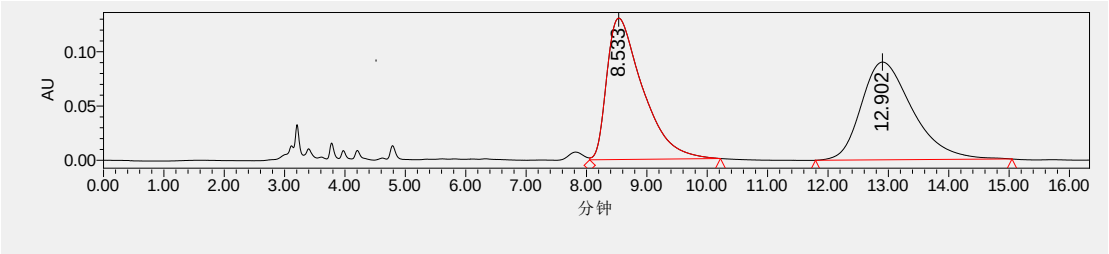
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.812	4911270	50.34	154640	VV	Unknown
2	9.628	4844686	49.66	123586	VB	Unknown



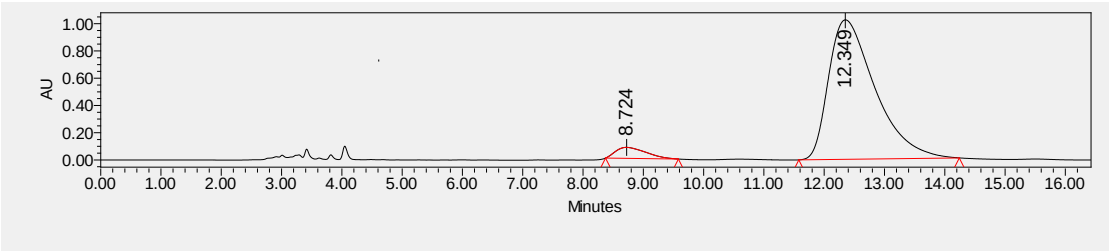
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.743	1002700	4.99	35744	bb	Unknown
2	9.345	19108310	95.01	485629	bb	Unknown

(4n):



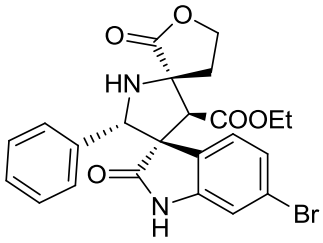


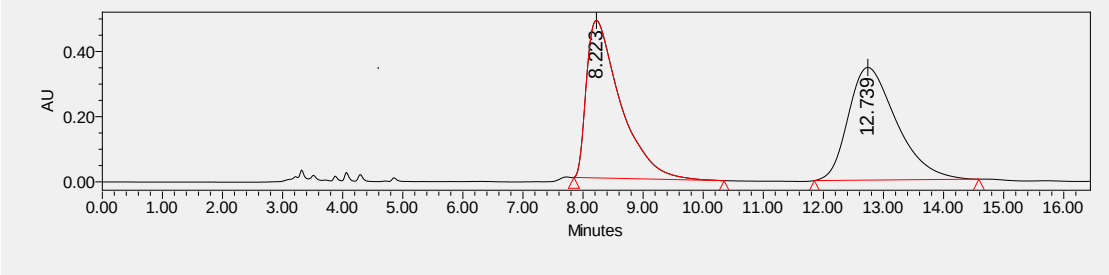
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.533	5386664	50.30	130351	Vb	Unknown
2	12.902	5322738	49.70	90113	Bb	Unknown



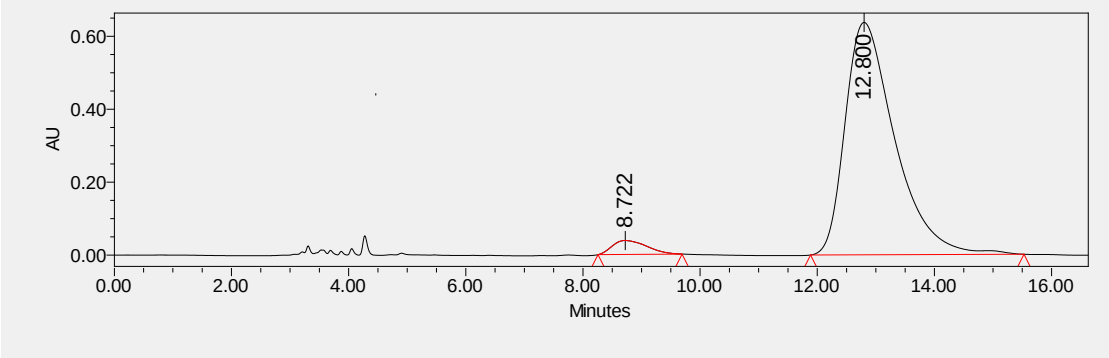
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.724	2821126	4.90	80599	bb	Unknown
2	12.349	54774889	95.10	1023672	bb	Unknown

(4o):



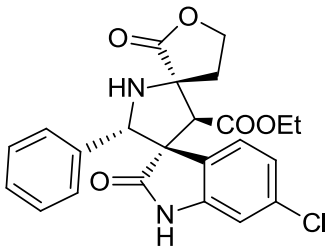


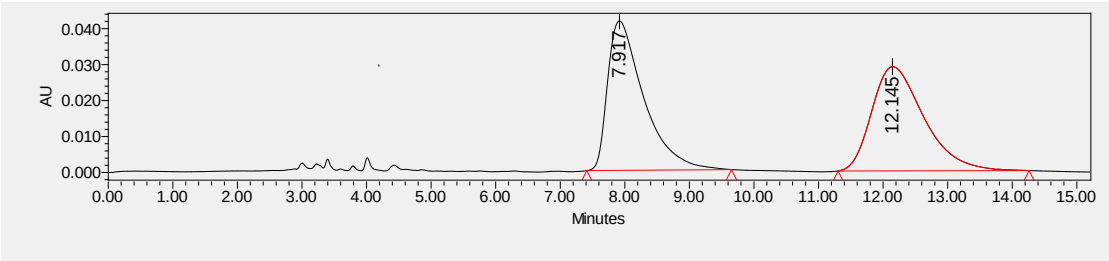
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.223	18991416	49.67	483500	bb	Unknown
2	12.739	19244217	50.33	345632	bb	Unknown



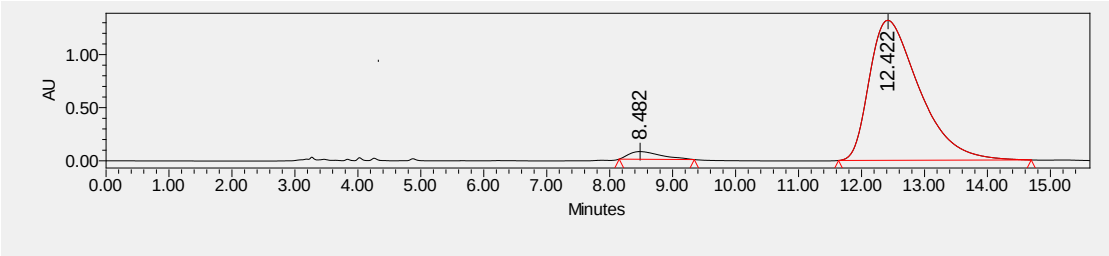
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.722	1561226	3.99	38361	bb	Unknown
2	12.800	37580167	96.01	637384	bb	Unknown

(4p):



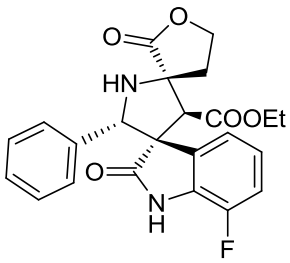


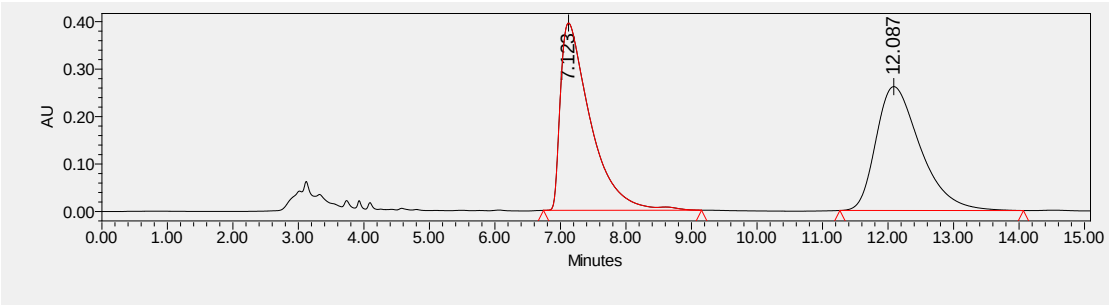
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.917	1618402	49.94	41559	Bb	Unknown
2	12.145	1622182	50.06	28991	Bb	Unknown



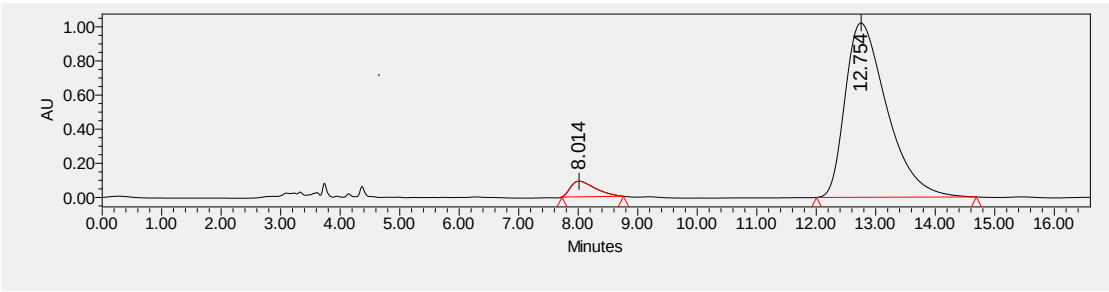
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.482	2572403	3.42	72038	bb	Unknown
2	12.422	72638972	96.58	1317849	bb	Unknown

(4q):



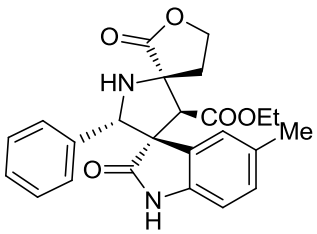


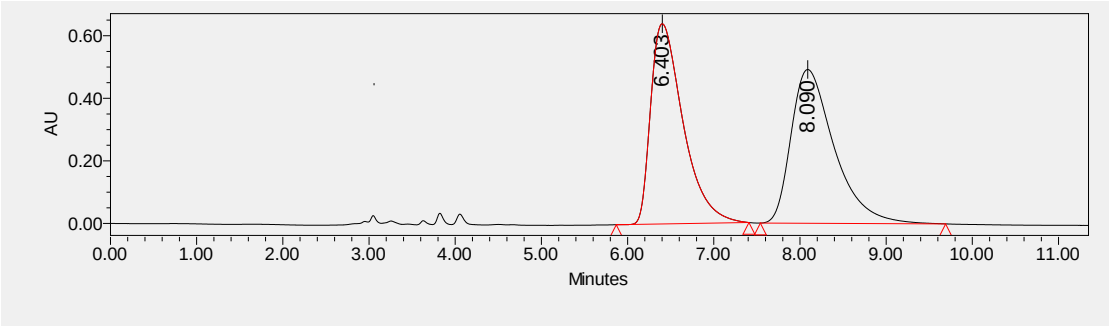
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.123	12553961	50.57	394714	bb	Unknown
2	12.087	12269616	49.43	261102	bb	Unknown



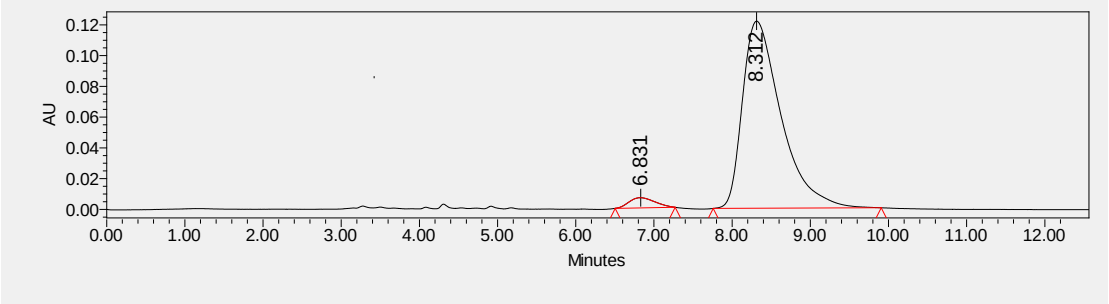
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.014	2639865	5.04	91577	bb	Unknown
2	12.754	49789706	94.96	1022138	bb	Unknown

(4r):



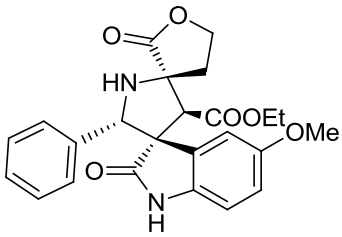


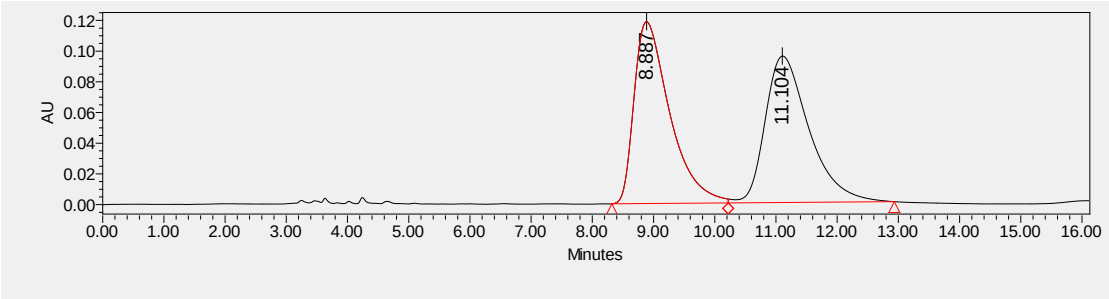
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	6.403	16703875	49.43	639847	bb	Unknown
2	8.090	17088984	50.57	491667	bb	Unknown



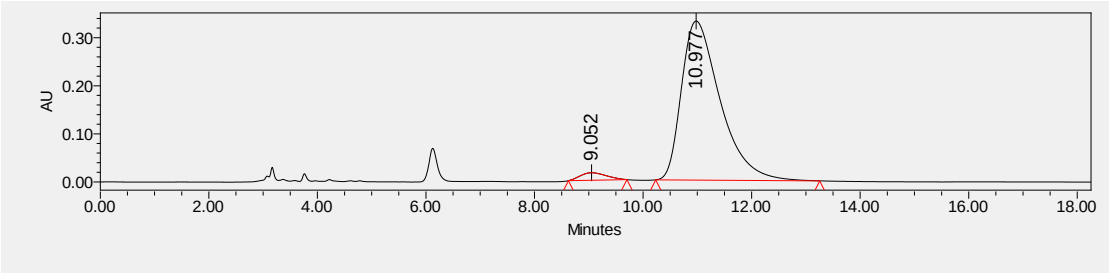
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	6.831	152563	3.53	6656	bb	Unknown
2	8.312	4174023	96.47	121693	bb	Unknown

(4s):



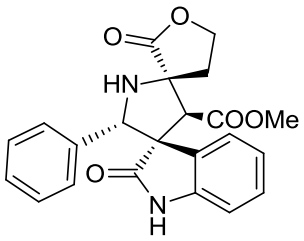


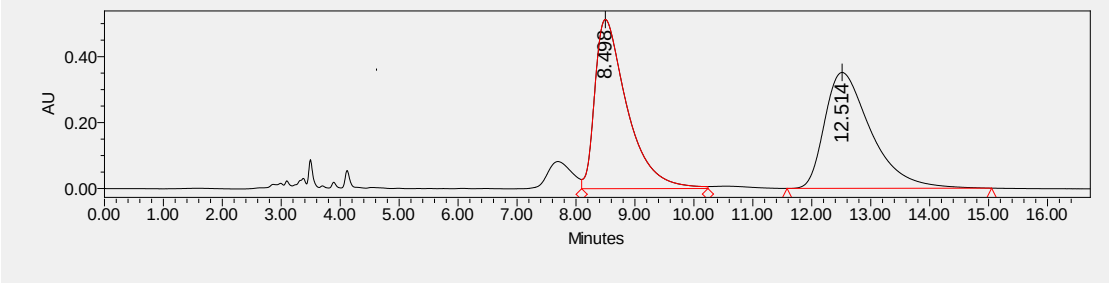
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.887	4793647	50.22	118461	Bv	Unknown
2	11.104	4751546	49.78	95426	vB	Unknown



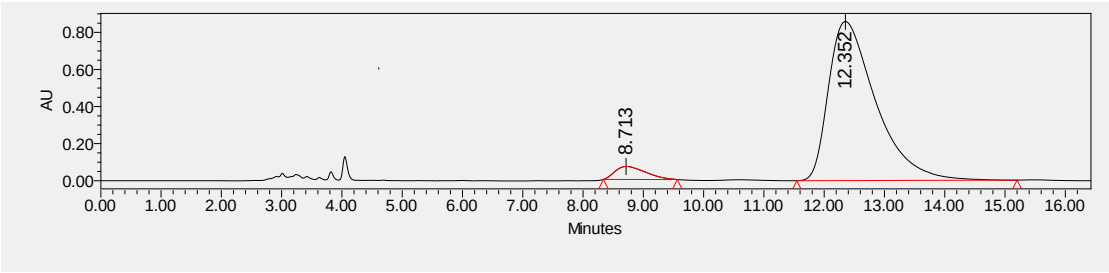
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	9.052	522144	3.09	15647	bb	Unknown
2	10.977	16394122	96.91	330786	bb	Unknown

(4t):



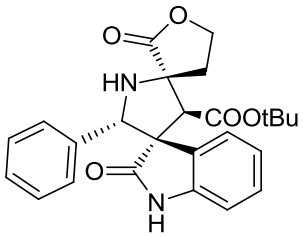


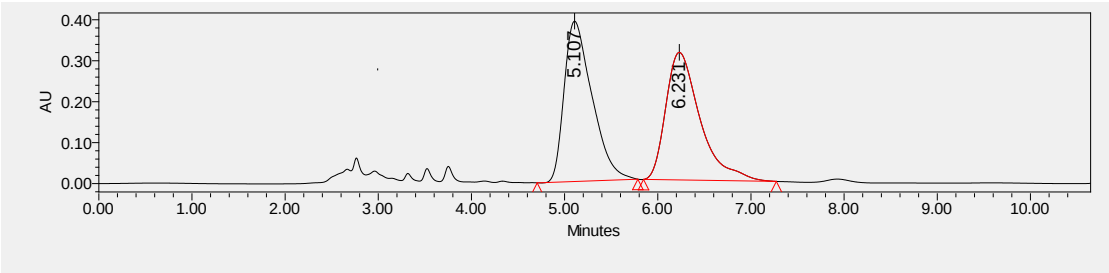
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.498	19512976	50.46	512898	VV	Unknown
2	12.514	19157401	49.54	351490	BB	Unknown



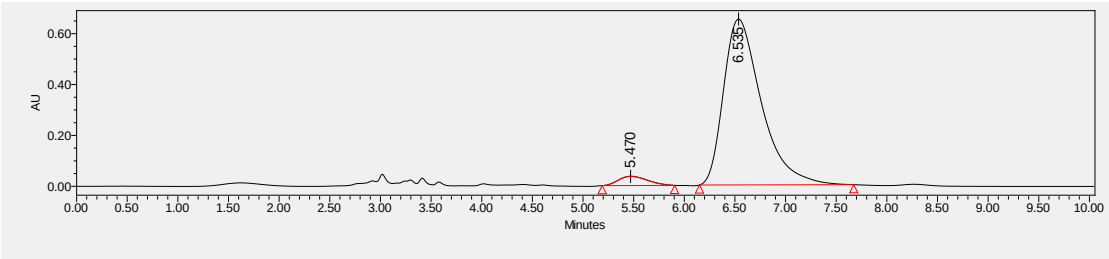
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.713	2475309	5.03	70308	bb	Unknown
2	12.352	46741954	94.97	858279	bb	Unknown

(4u):



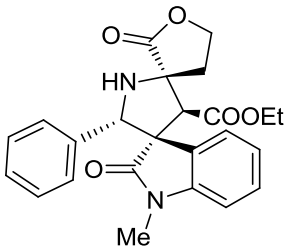


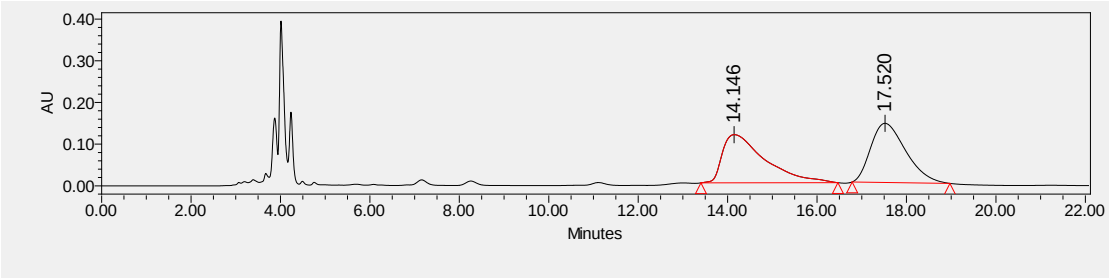
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	5.107	8141261	50.51	391561	bb	Unknown
2	6.231	7977728	49.49	311678	bb	Unknown



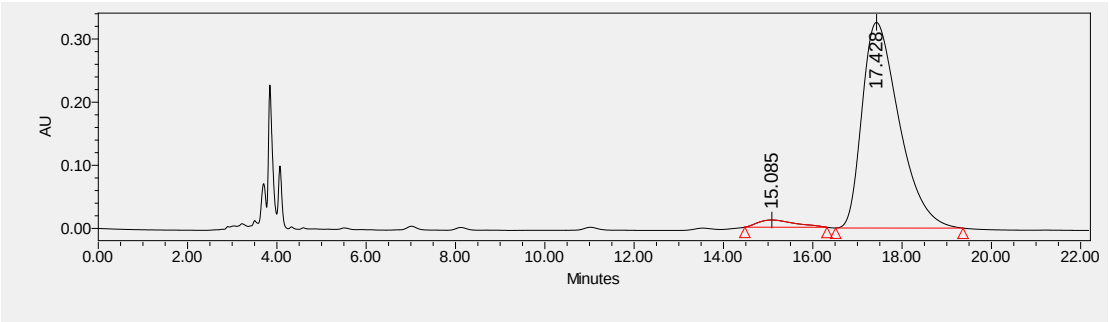
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	5.470	726673	4.11	36366	bb	Unknown
2	6.535	16938554	95.89	651904	bb	Unknown

(4v):



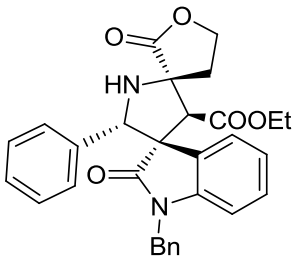


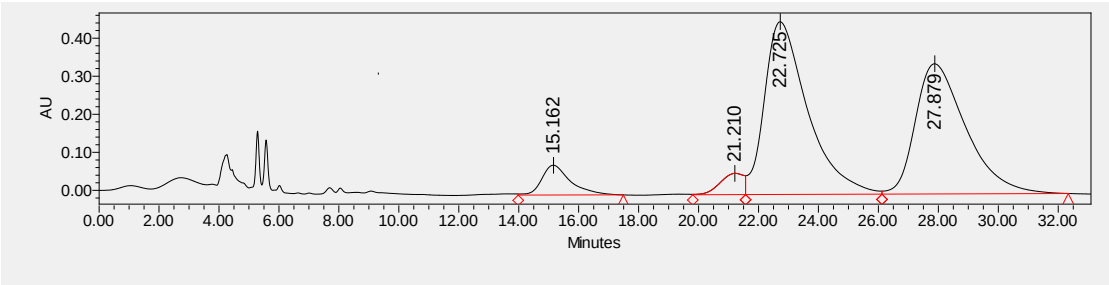
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	14.146	7656016	49.77	115659	bb	Unknown
2	17.520	7728186	50.23	141864	bb	Unknown



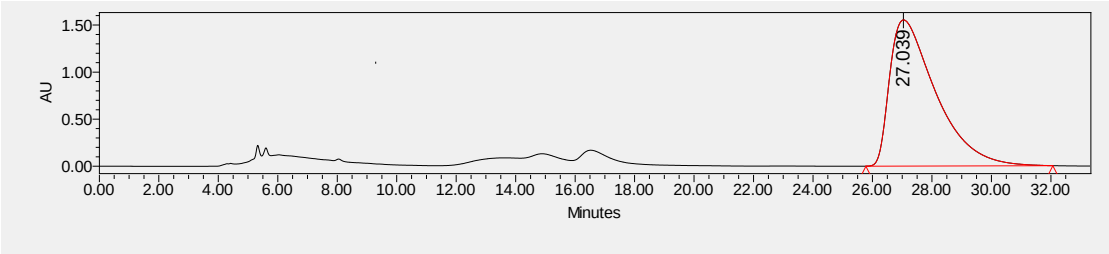
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	15.085	667291	3.44	11456	bb	Unknown
2	17.428	18747899	96.56	325698	bb	Unknown

(4w):





Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	15.162	5222818	5.56	78370	VB	Unknown
2	21.210	3039482	3.24	55996	VV	Unknown
3	22.725	45573762	48.56	453883	VV	Unknown
4	27.879	40016557	42.64	342075	VB	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	27.039	167724648	100.00	1552884	bb	Unknown

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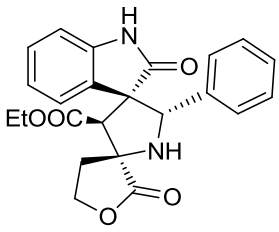
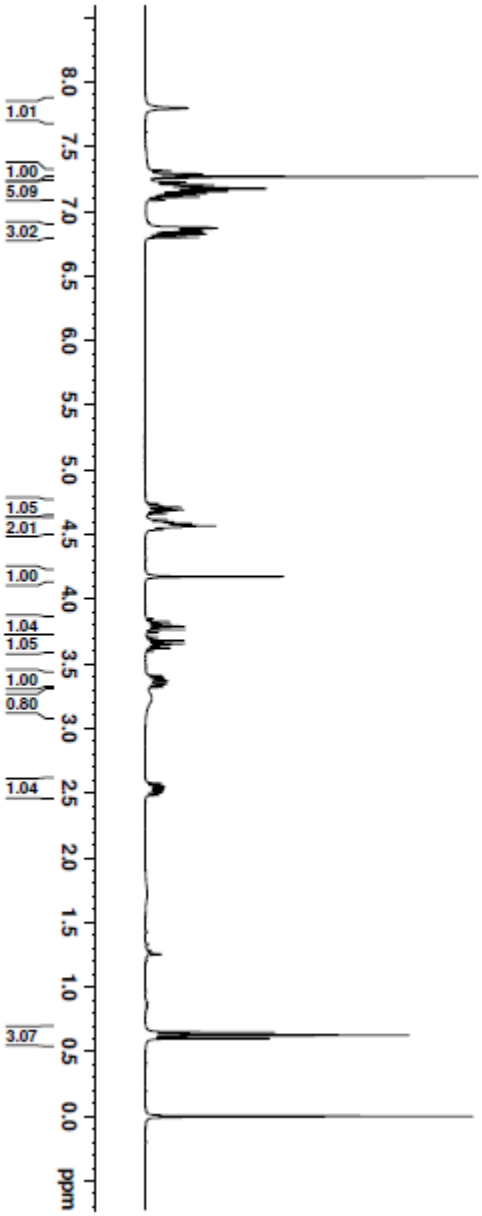
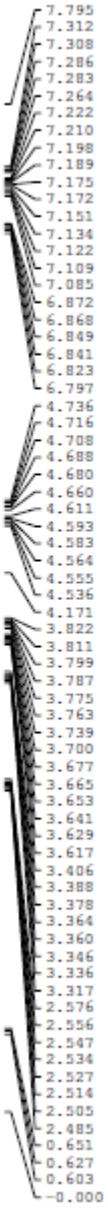
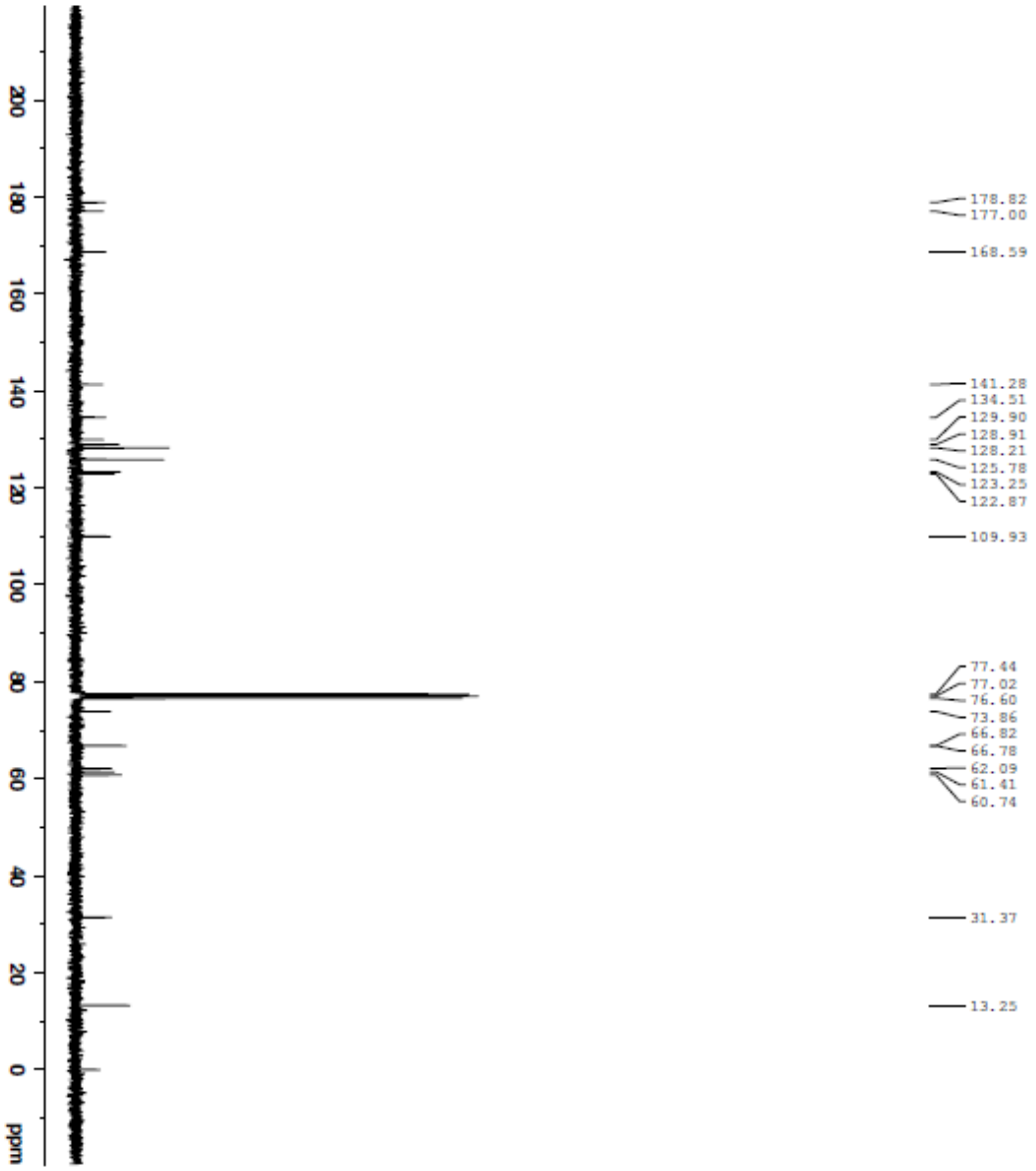
(4a):

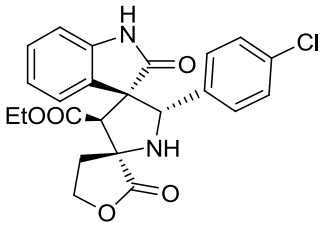








(4b):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Cl
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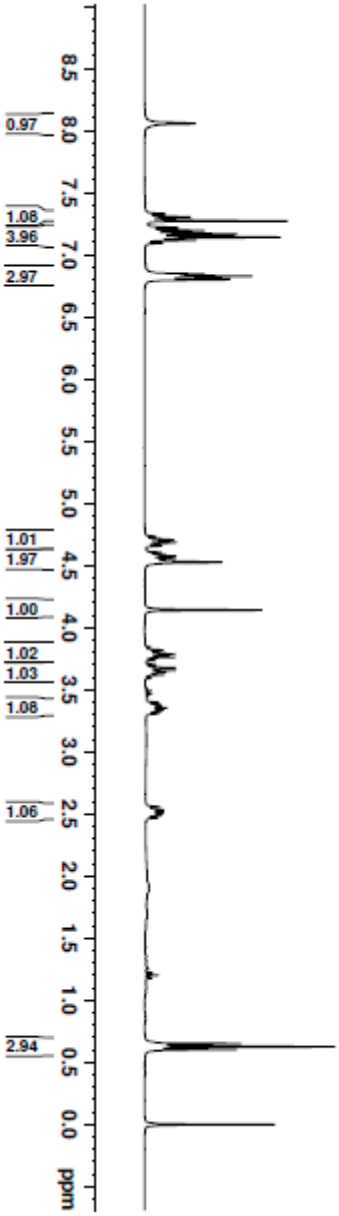
NH
O
O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1.06
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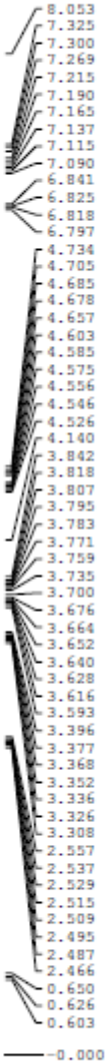
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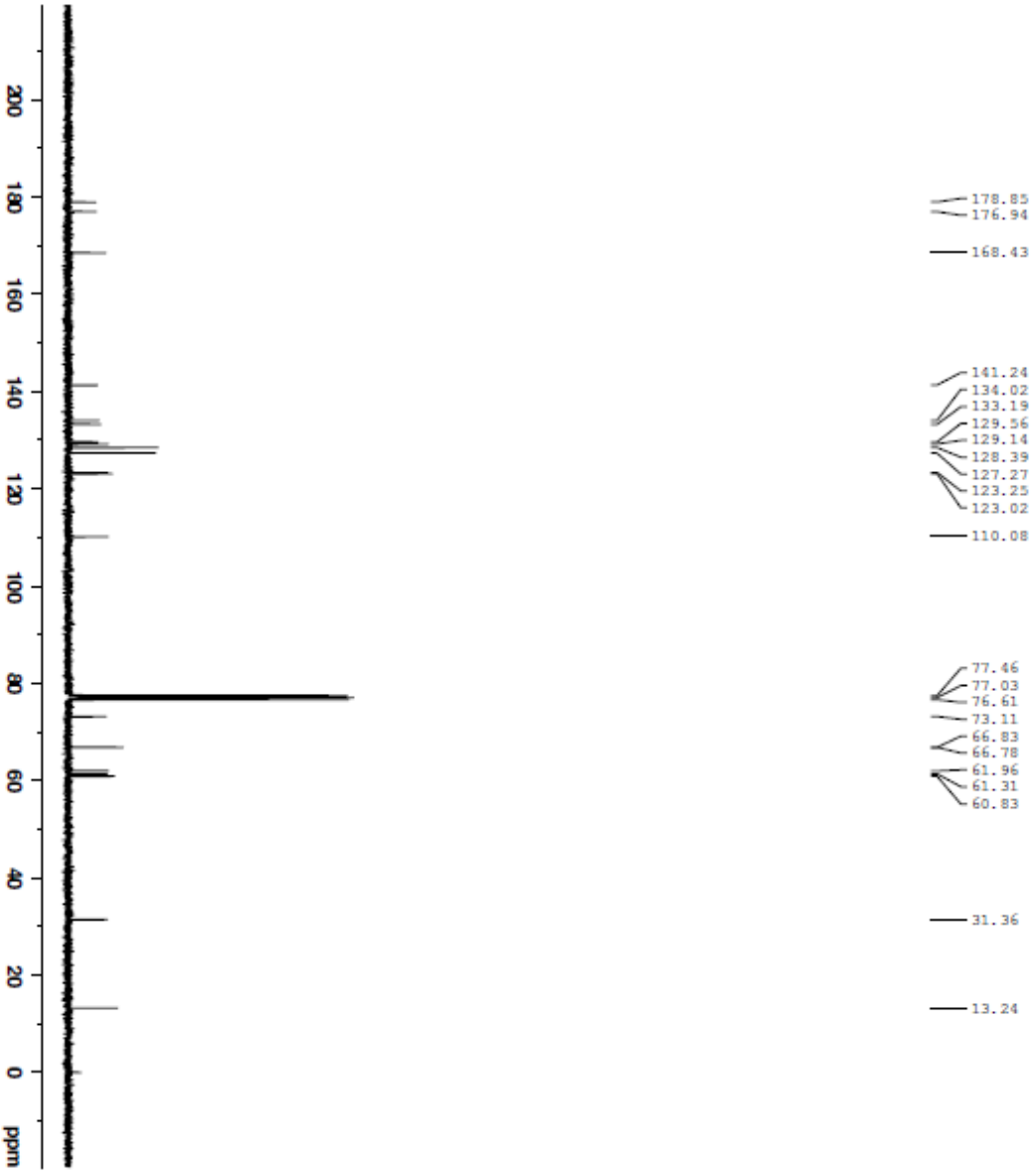
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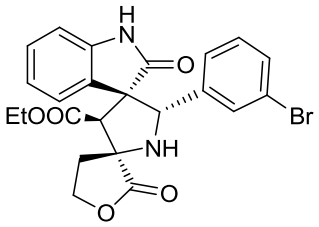
13.24

(4c):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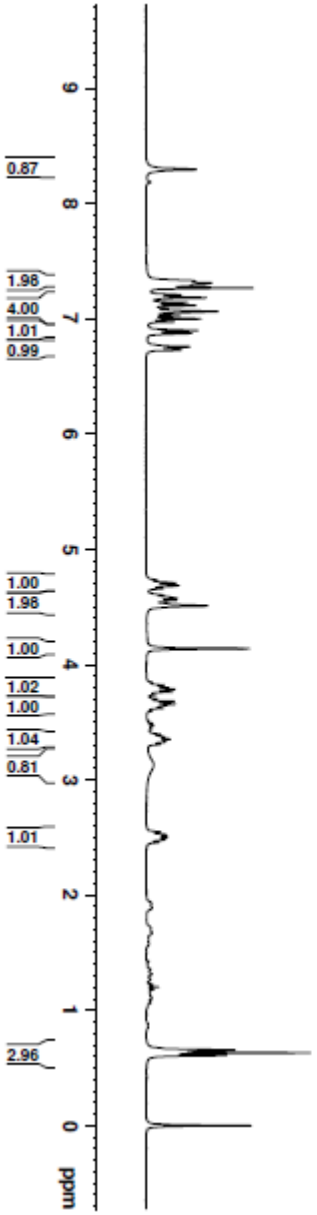
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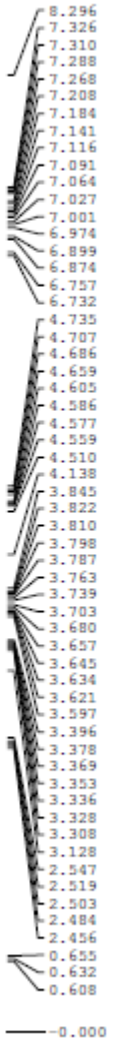
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7.027
7.001
6.974
6.899
6.874
6.757
6.732
4.735
4.707
4.686
4.659
4.605
4.586
4.577
4.559
4.510
4.138
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3.822
3.810
3.798
3.787
3.763
3.739
3.703
3.680
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3.634
3.621
3.597
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3.378
3.369
3.353
3.336
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2.519
2.503
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2.456
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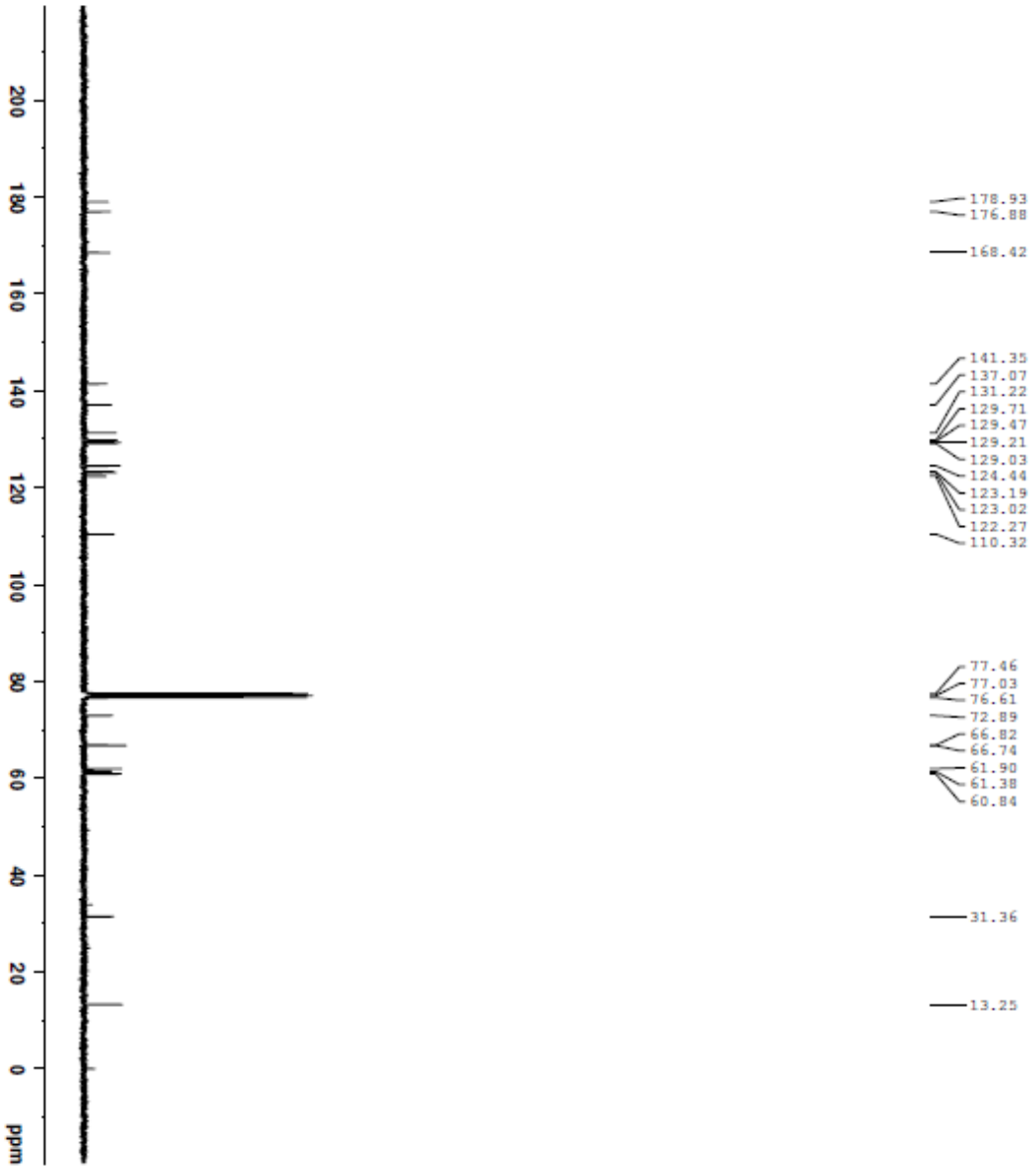
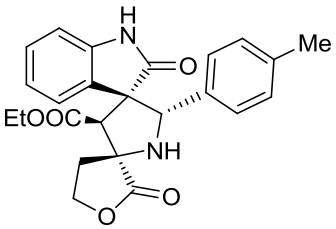
0.632
0.608
-0.000



(4d):


H
N
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EtOOC
NH
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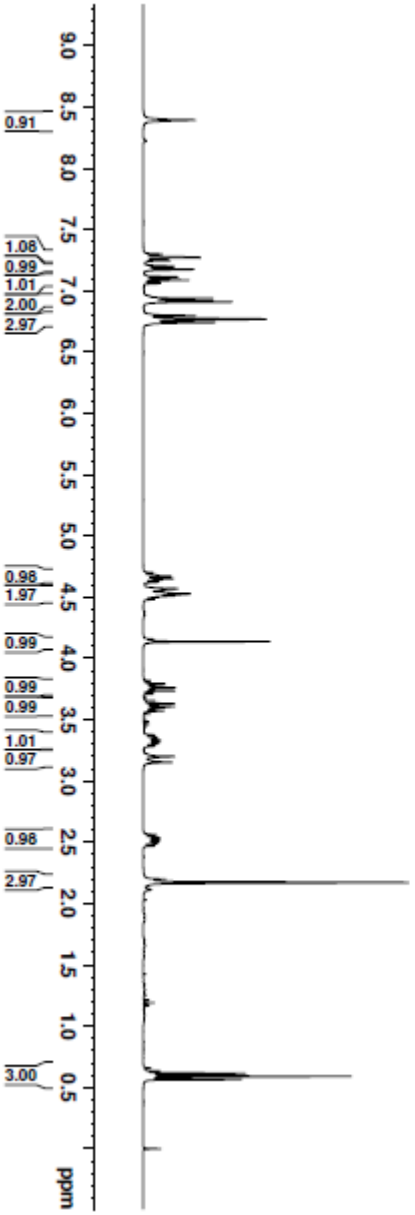
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0.99
0.99
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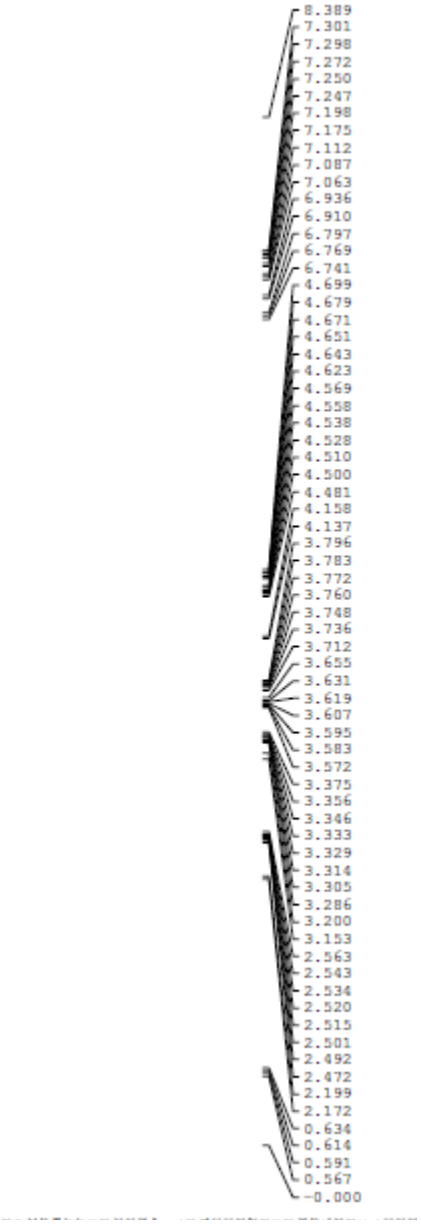
0.97
0.98
2.97
3.00
ppm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7.175
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7.087
7.063
6.936
6.910
6.797
6.769
6.741
4.699
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4.558
4.538
4.528
4.510
4.500
4.481
4.158
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3.796
3.783
3.772
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3.748
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3.712
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3.375
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3.333
3.329
3.314
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3.200
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2.563
2.543
2.534
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2.501
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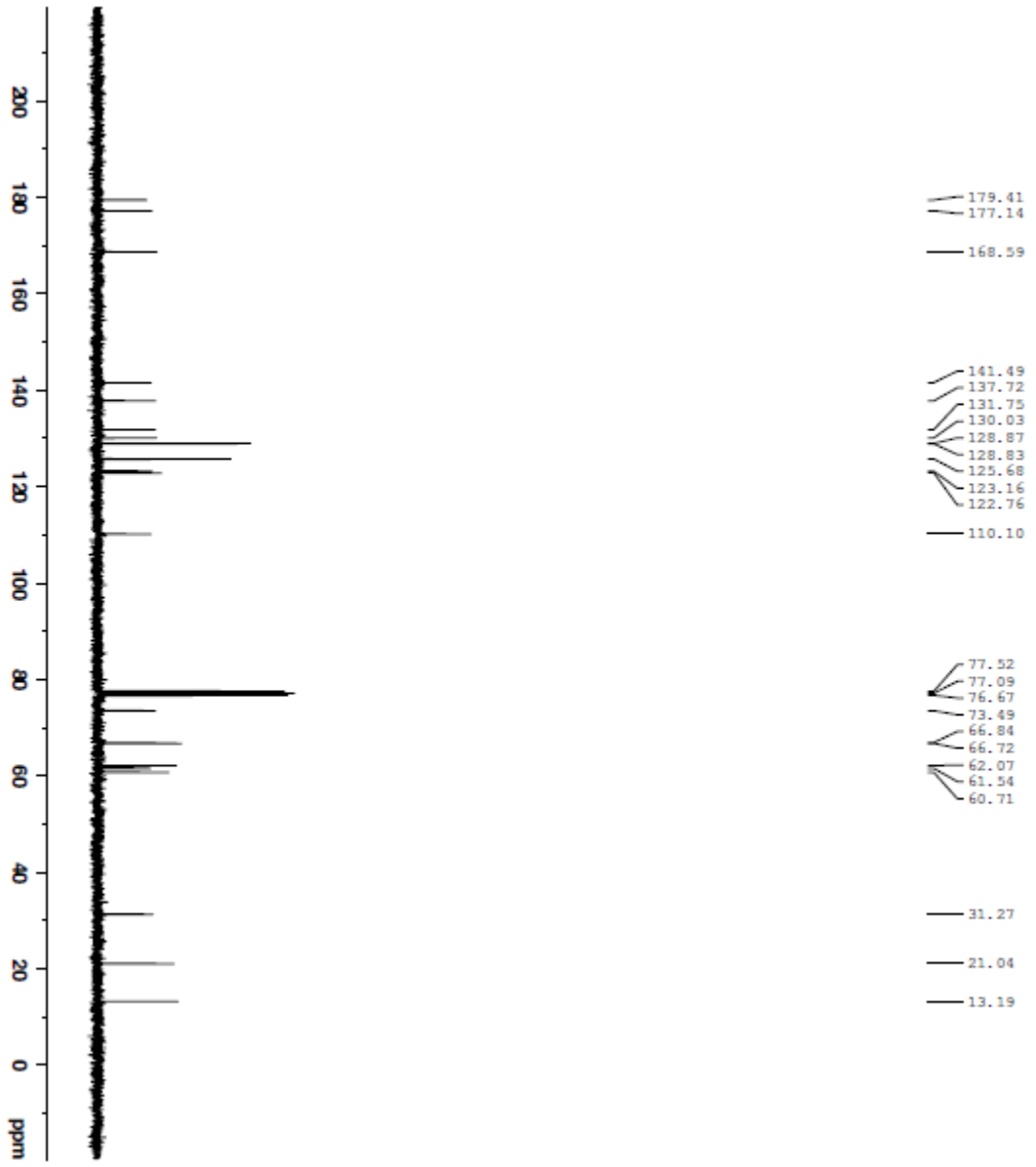
0.591
0.567
-0.000



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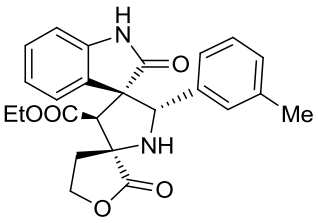
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EtOOC
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NH
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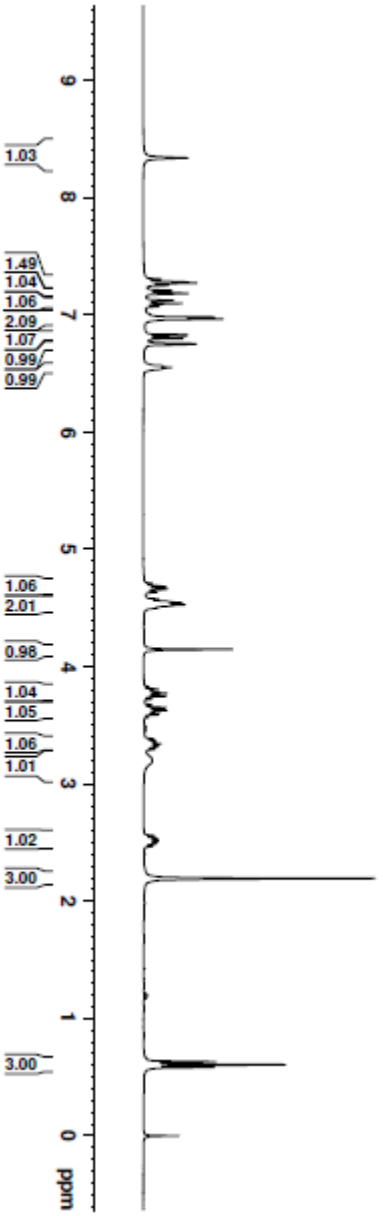
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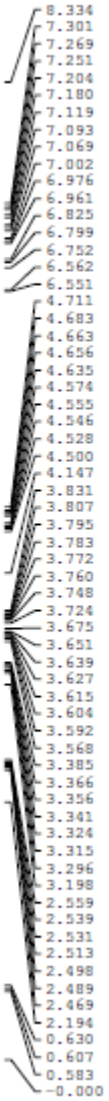
1.07
0.99
0.99
1.06
2.01
0.98
1.04
1.05
1.06
1.01
1.02
3.00
3.00
ppm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7.093
7.069
7.002
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6.961
6.825
6.799
6.752
6.562
6.551
4.711
4.683
4.663
4.656
4.635
4.574
4.555
4.546
4.528
4.500
4.147
3.831
3.807
3.795
3.783
3.772
3.760
3.748
3.724
3.675
3.651
3.639
3.627
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3.604
3.592
3.568
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3.366
3.356
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3.324
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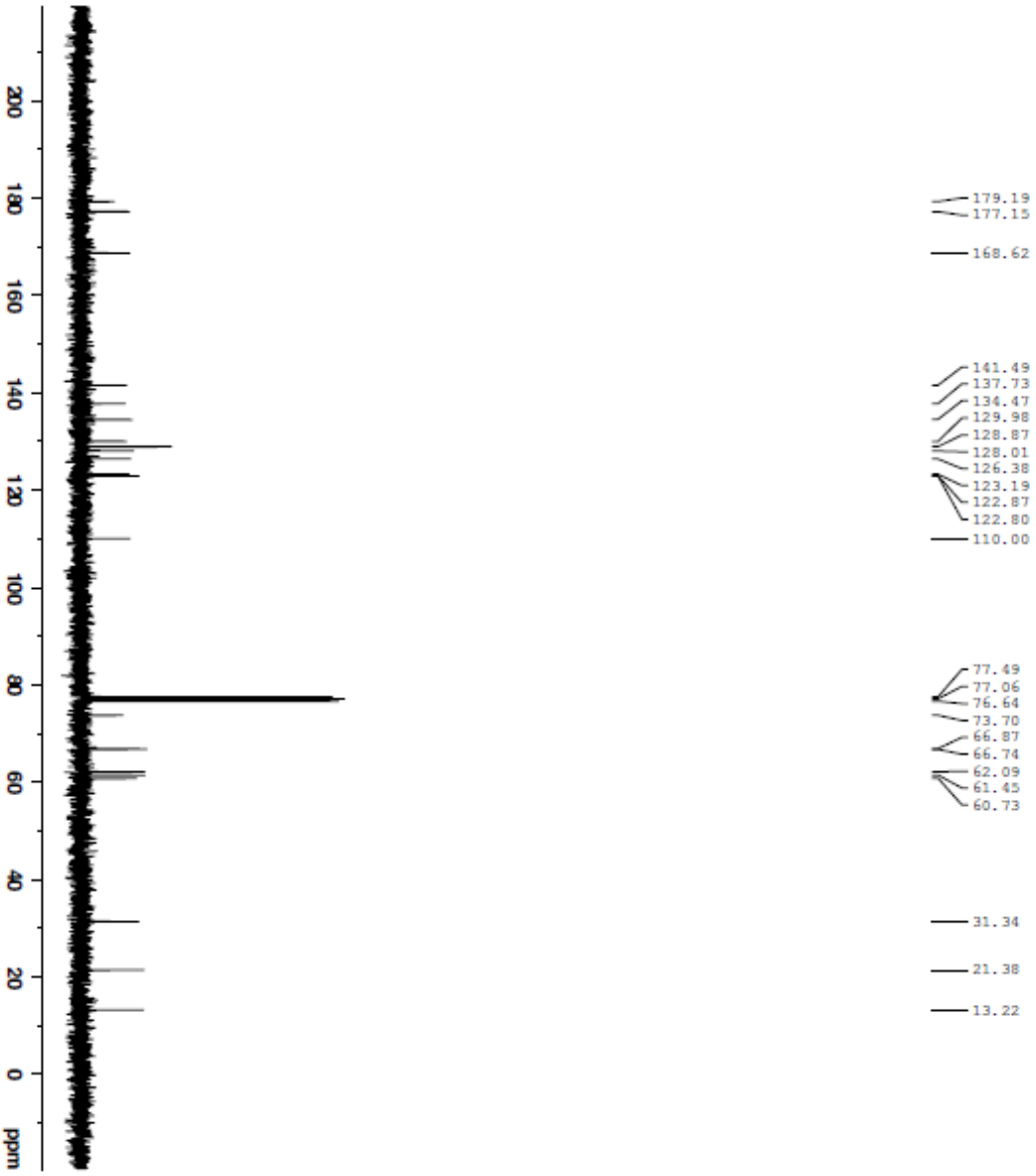

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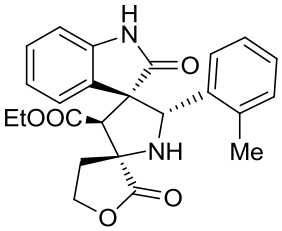
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EtOOC
NH
Me
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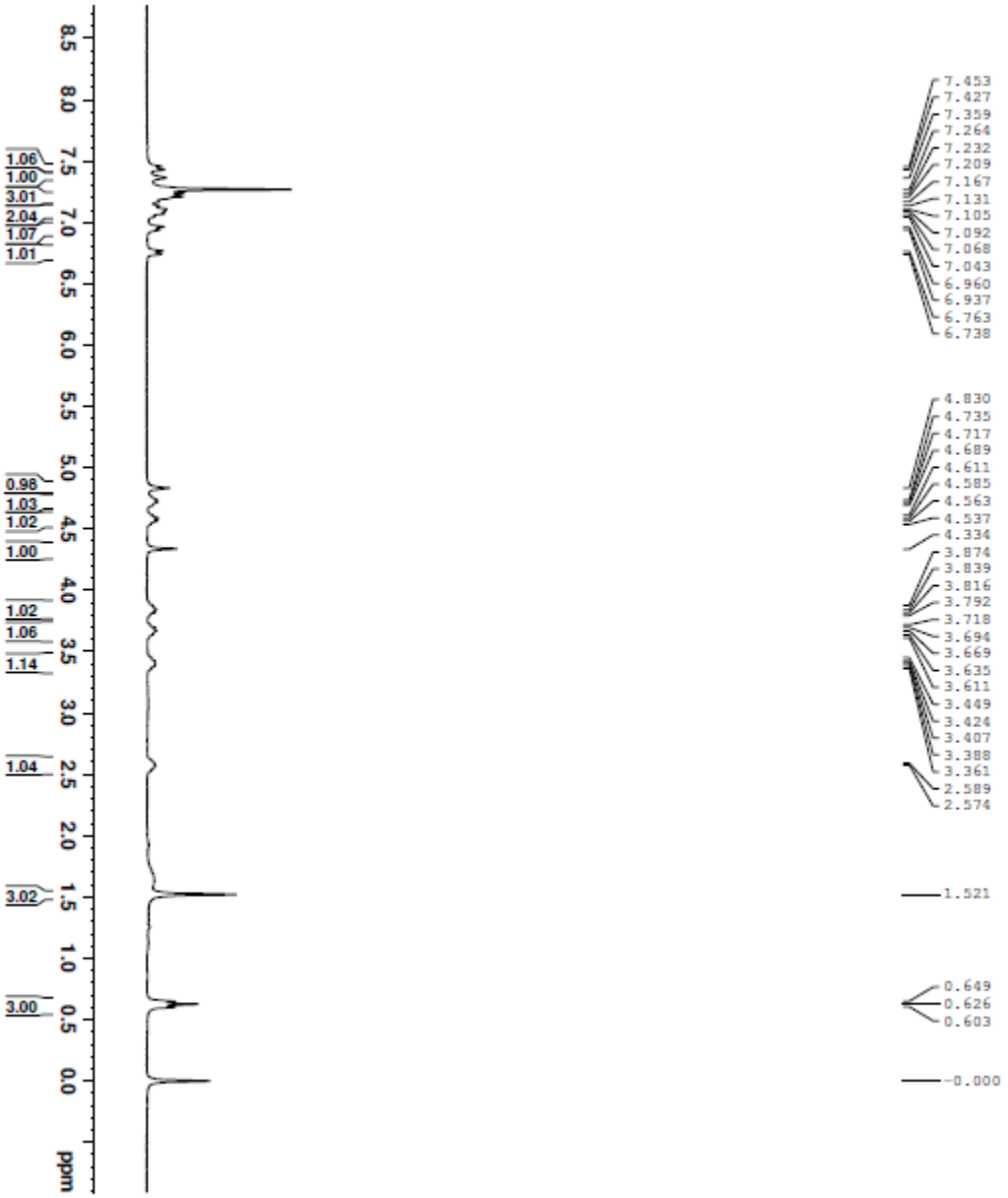
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5.0
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.06
1.00
3.01
2.04
1.07
1.01
0.98
1.03
1.02
1.00
1.02
1.06
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1.04
3.02
3.00
7.453
7.427
7.359
7.264
7.232
7.209
7.167
7.131
7.105
7.092
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7.043
6.960
6.937
6.763
6.738
4.830
4.735
4.717
4.689
4.611
4.585
4.563
4.537
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3.874
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3.816
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3.718
3.694
3.669
3.635
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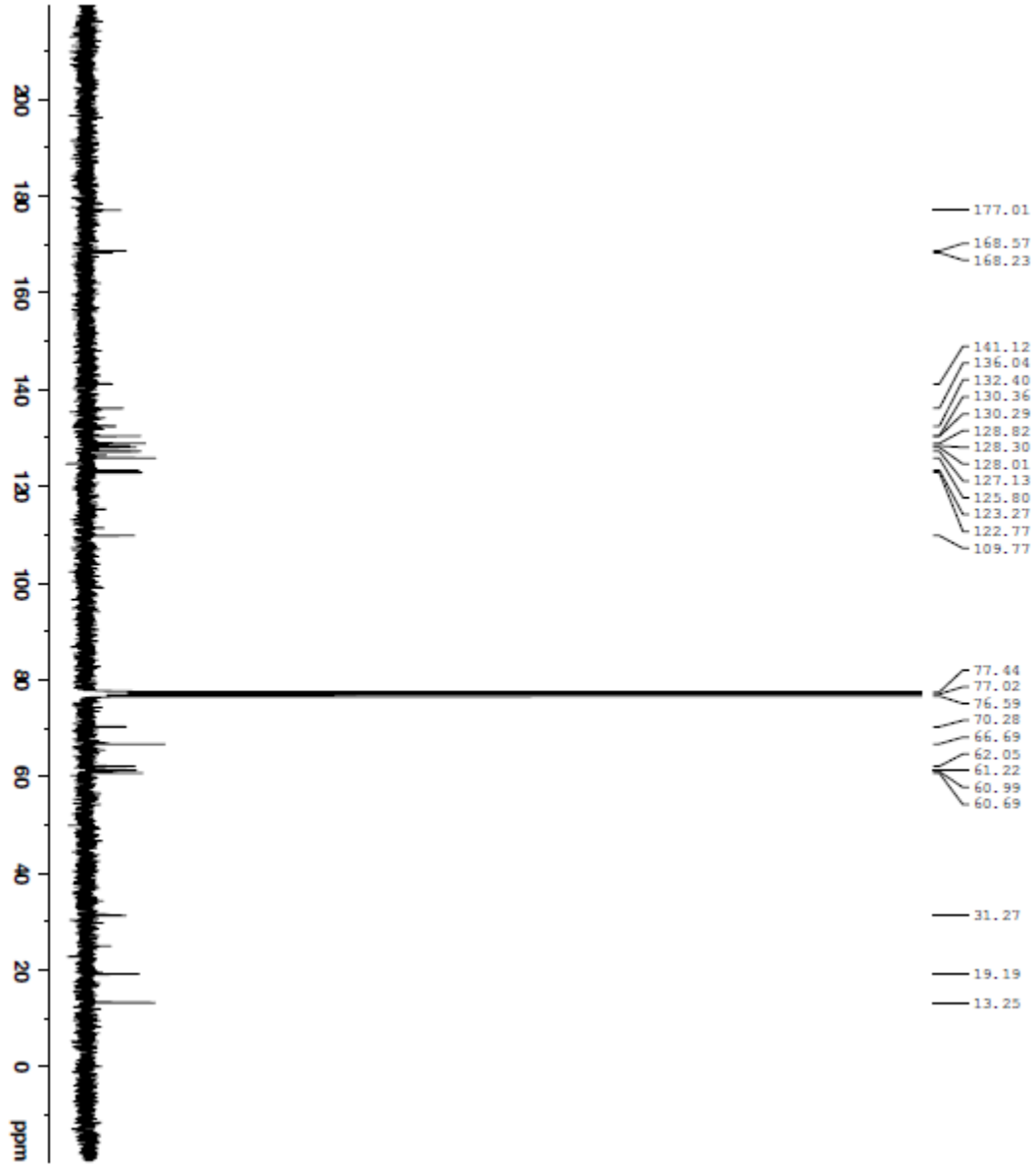
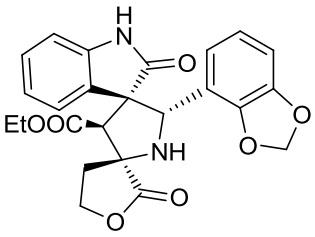


(4g):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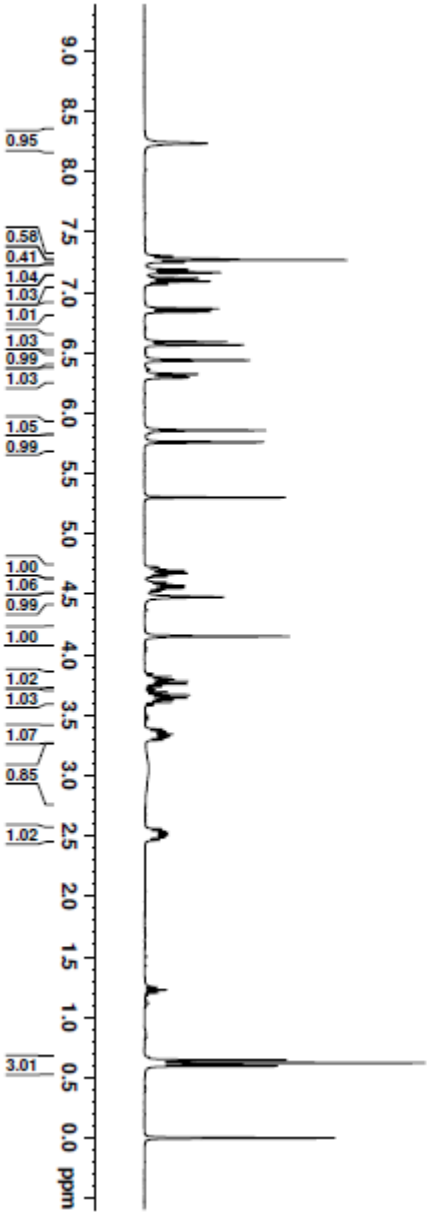
N
O
EtOOC
NH
O
O
O
O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1.03
0.99
1.03
1.05
0.99
1.00
1.06
0.99
1.00
1.02
1.03
1.07
0.85
1.02
3.01
9.0
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8.0
7.5
7.0
6.5
6.0
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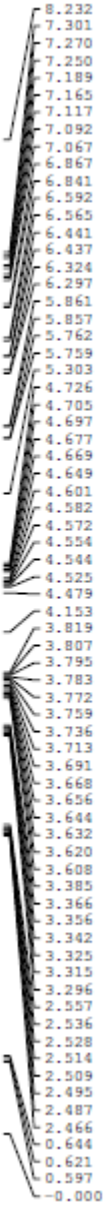
1.5
1.0
0.5
0.0
ppm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6.565
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4.705
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4.677
4.669
4.649
4.601
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4.479
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3.819
3.807
3.795
3.783
3.772
3.759
3.736
3.713
3.691
3.668
3.656
3.644
3.632
3.620
3.608
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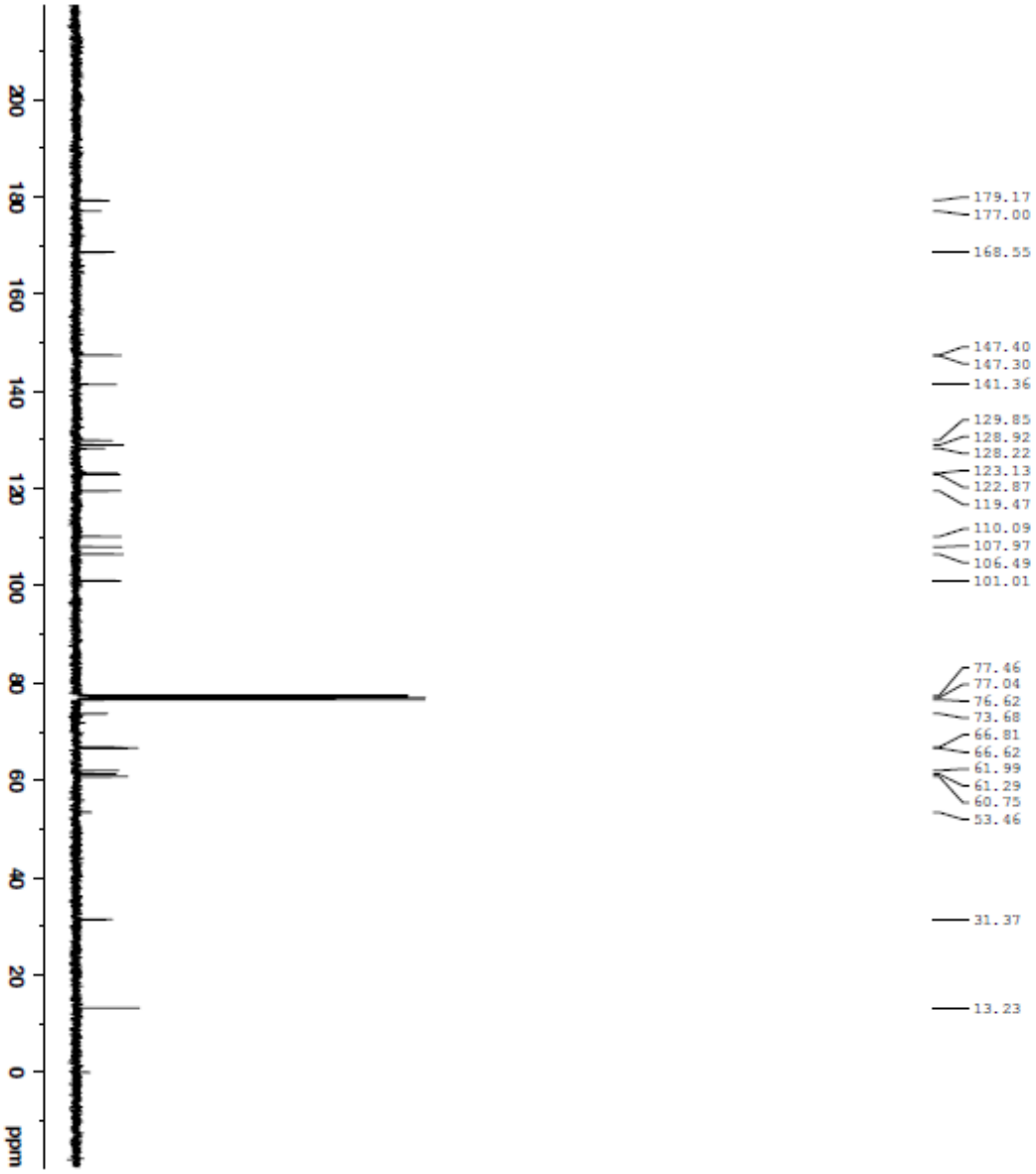
200
180
160
140
120
100
80
60
40
20
0
ppm
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177.00
168.55
147.40
147.30
141.36
129.85
128.92
128.22
123.13
122.87
119.47
110.09
107.97
106.49
101.01
77.46
77.04
76.62
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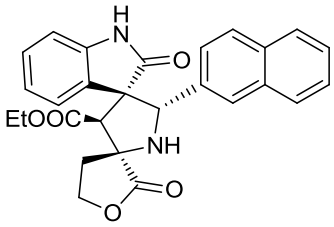
66.81
66.62
61.99
61.29
60.75
53.46
31.37
13.23

(4h):


H
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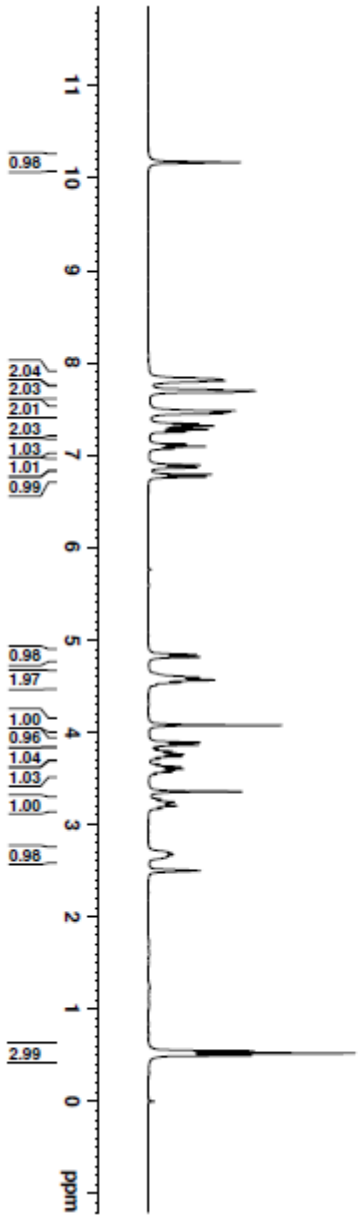
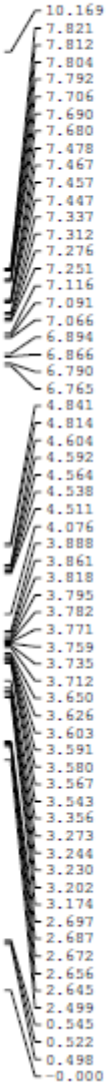
O
EtOOC
NH
O
O


11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.98
2.04
2.03
2.01
2.03
1.03
1.01
0.99
0.98
1.97
1.00
0.96
1.04
1.03
1.00
0.98
2.99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7.447
7.337
7.312
7.276
7.251
7.116
7.091
7.066
6.894
6.866
6.790
6.765
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4.604
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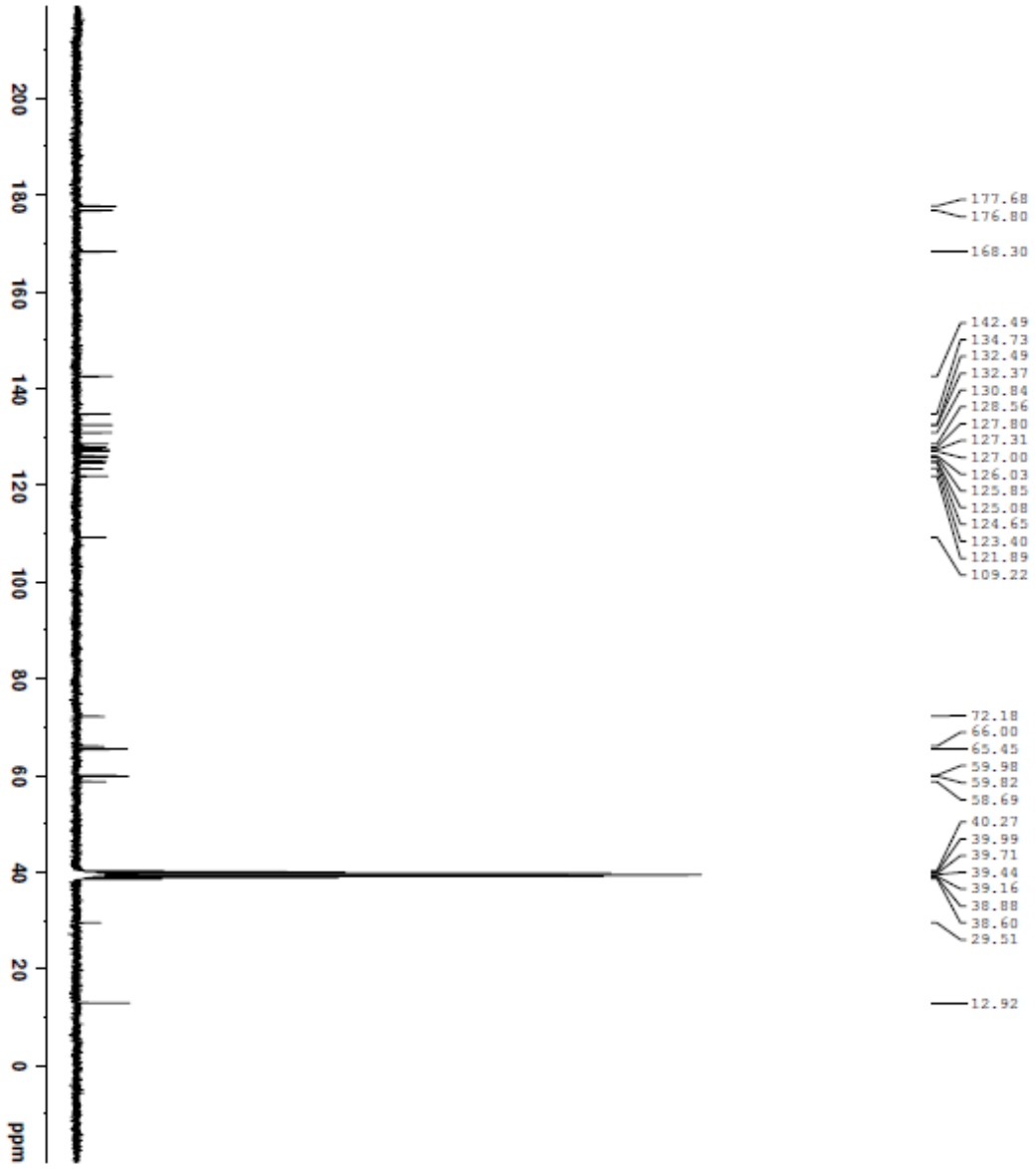
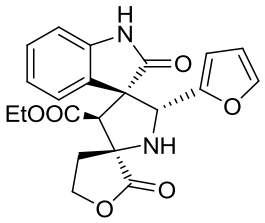
-0.000



(4i):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EtOOC
NH
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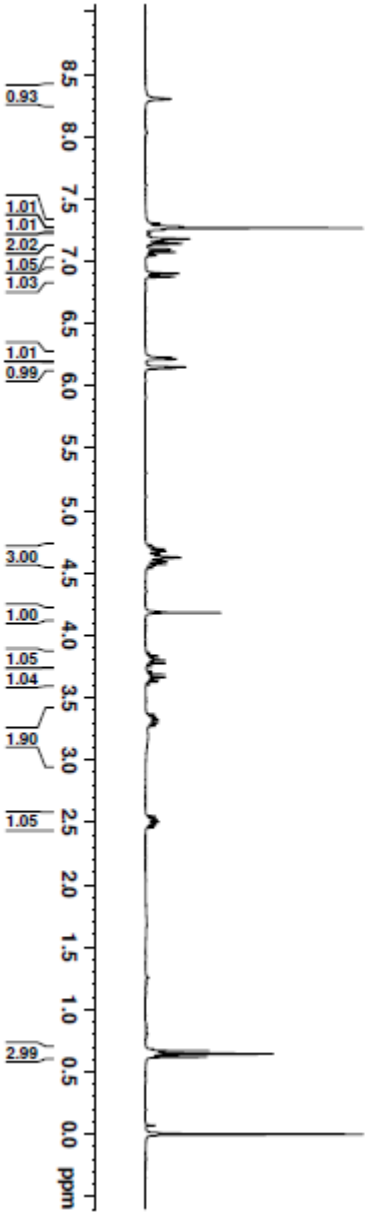
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1.03
1.01
0.99
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1.00
1.05
1.04
1.90
1.05
2.99
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8.0
7.5
7.0
6.5
6.0
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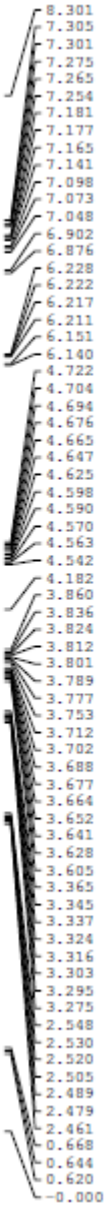
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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7.265
7.254
7.181
7.177
7.165
7.141
7.098
7.073
7.048
6.902
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6.222
6.217
6.211
6.151
6.140
4.722
4.704
4.694
4.676
4.665
4.647
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4.598
4.590
4.570
4.563
4.542
4.182
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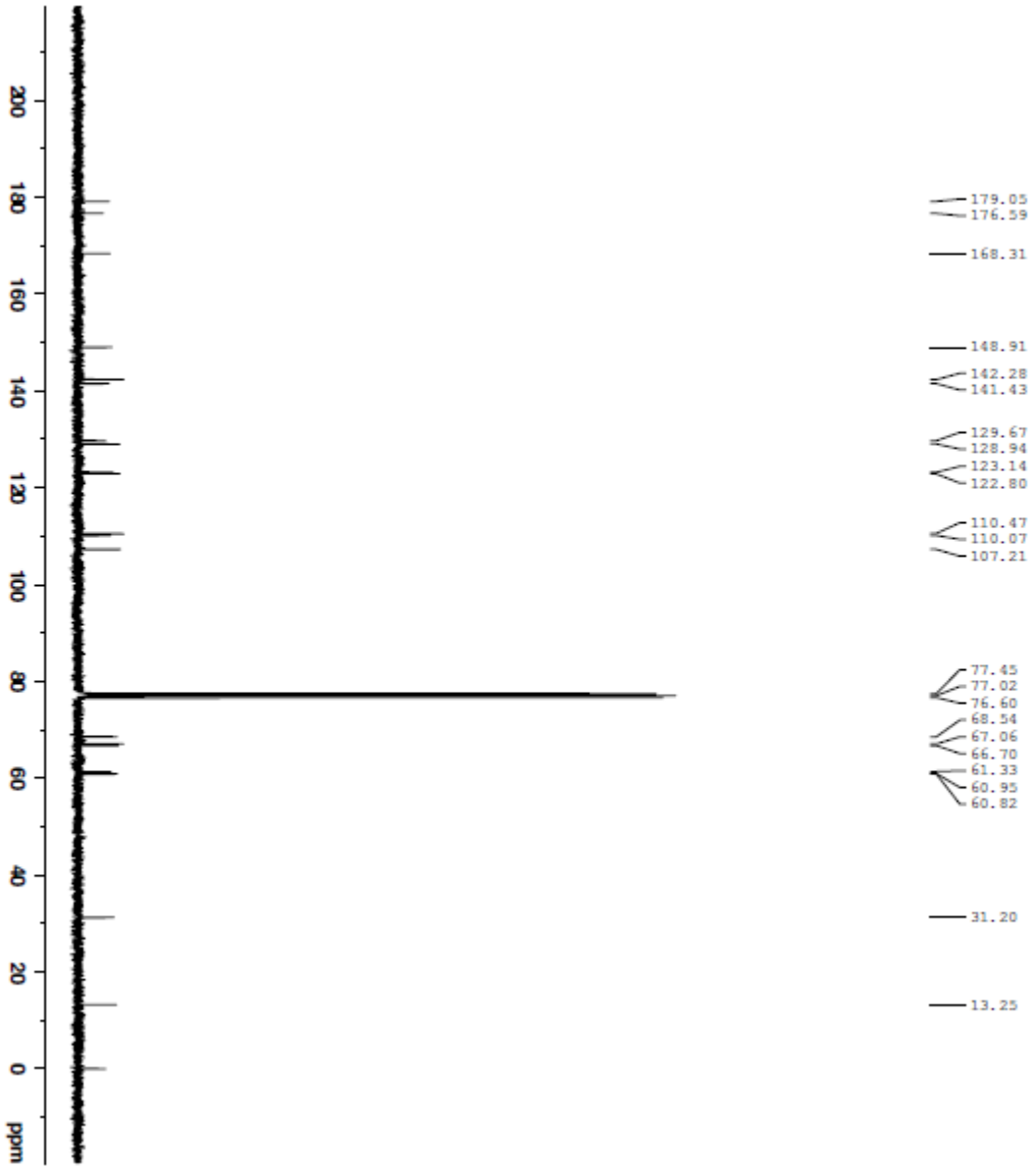
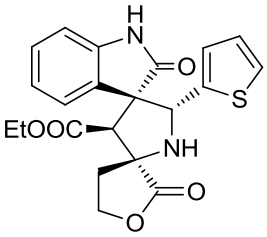


(4j):


H
N
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EtOOC
NH
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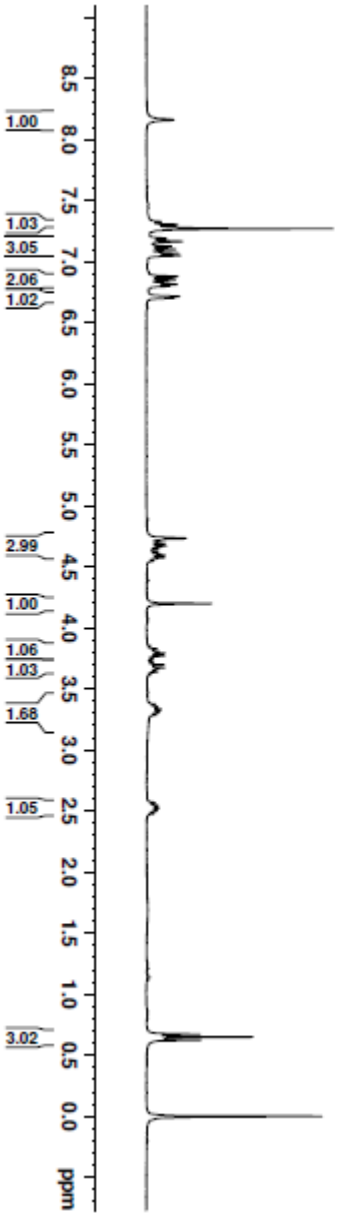
O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1.02
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1.00
1.06
1.03
1.68
1.05
3.02
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7.5
7.0
6.5
6.0
5.5
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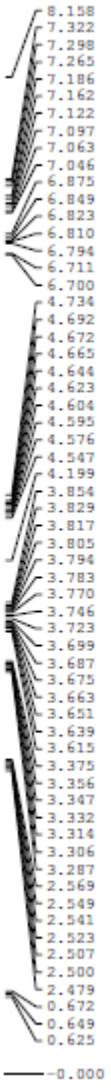
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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7.063
7.046
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6.810
6.794
6.711
6.700
4.734
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4.644
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4.595
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4.199
3.854
3.829
3.817
3.805
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3.723
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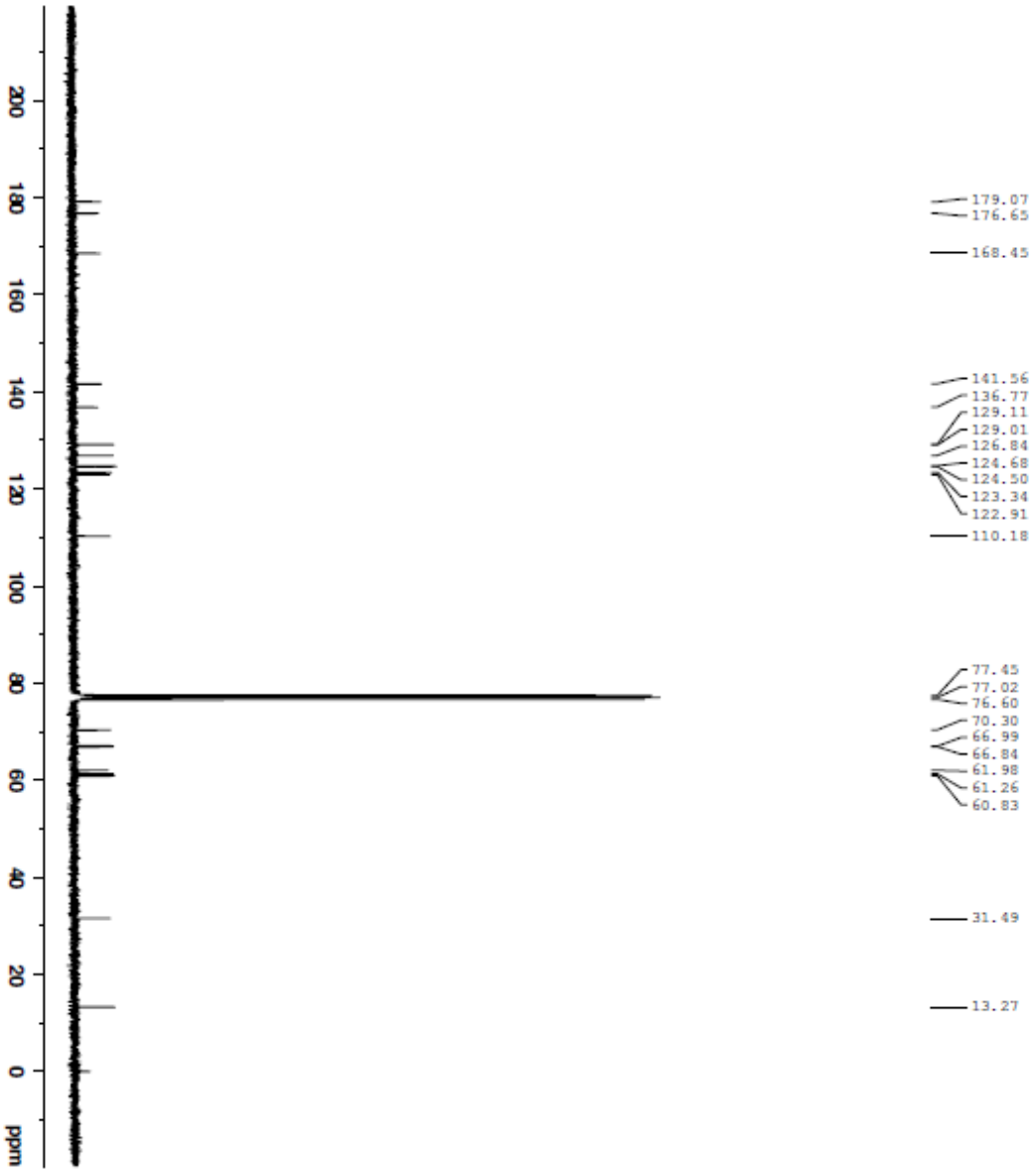
0.649
0.625
-0.000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120
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40
20
0
ppm
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176.65
168.45
141.56
136.77
129.11
129.01
126.84
124.68
124.50
123.34
122.91
110.18
77.45
77.02
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70.30
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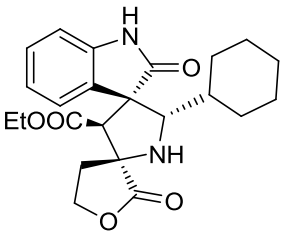
66.84
61.98
61.26
60.83
31.49
13.27

(4k):


H
N
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EtOOC
NH
O
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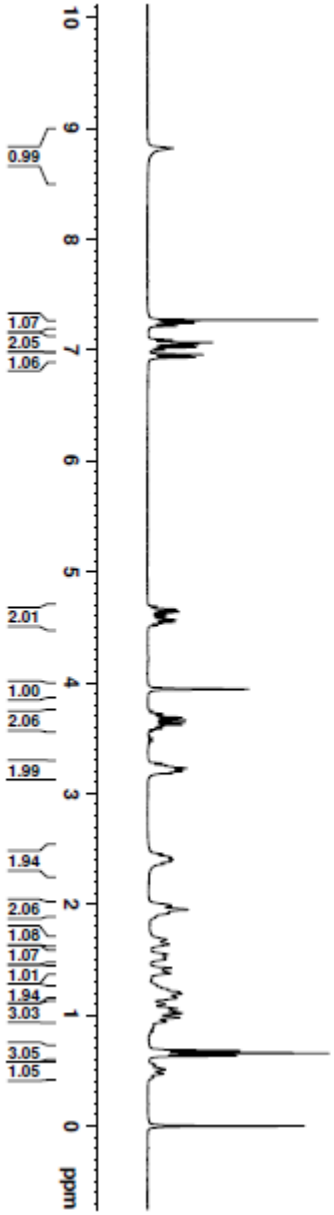
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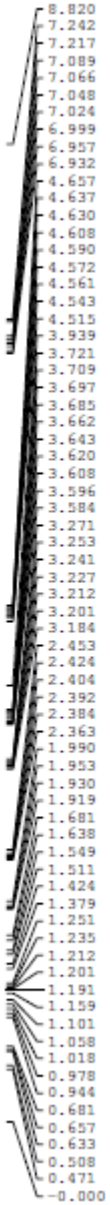
9
8
7
6
5
4
3
2
1
0
ppm
0.99
1.07
2.05
1.06
2.01
1.00
2.06
1.99
1.94
2.06
1.08
1.07
1.01
1.94
3.03
3.05
1.05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6.932
4.657
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4.608
4.590
4.572
4.561
4.543
4.515
3.939
3.721
3.709
3.697
3.685
3.662
3.643
3.620
3.608
3.596
3.584
3.271
3.253
3.241
3.227
3.212
3.201
3.184
2.453
2.424
2.404
2.392
2.384
2.363
1.990
1.953
1.930
1.919
1.681
1.638
1.549
1.511
1.424
1.379
1.251
1.235
1.212
1.201
1.191
1.159
1.101
1.058
1.018
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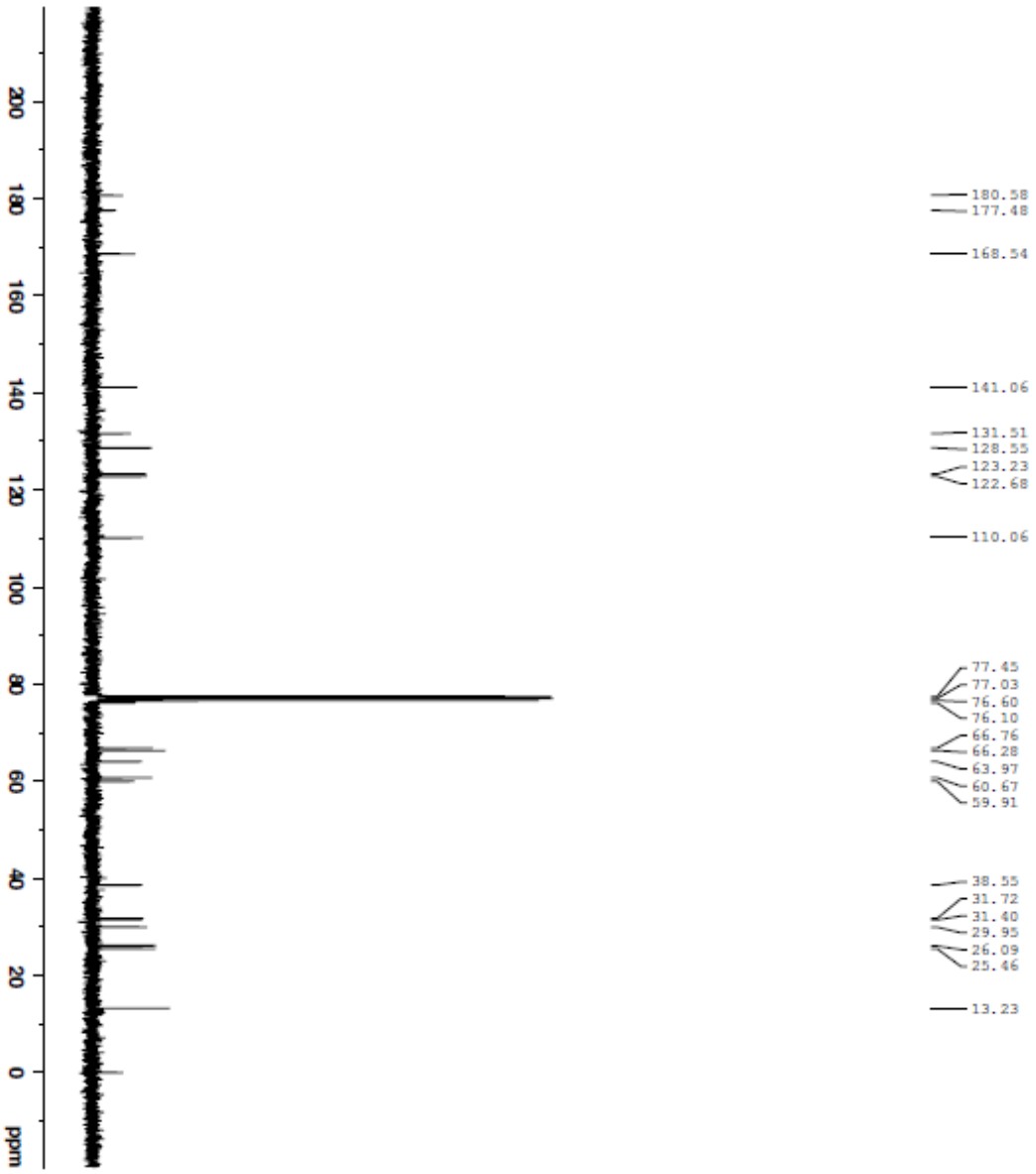
0.944
0.681
0.657
0.633
0.508
0.471
-0.000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180
160
140
120
100
80
60
40
20
0
ppm
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168.54
141.06
131.51
128.55
123.23
122.68
110.06
77.45
77.03
76.60
76.10
66.76
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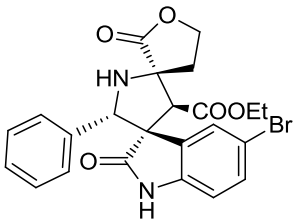
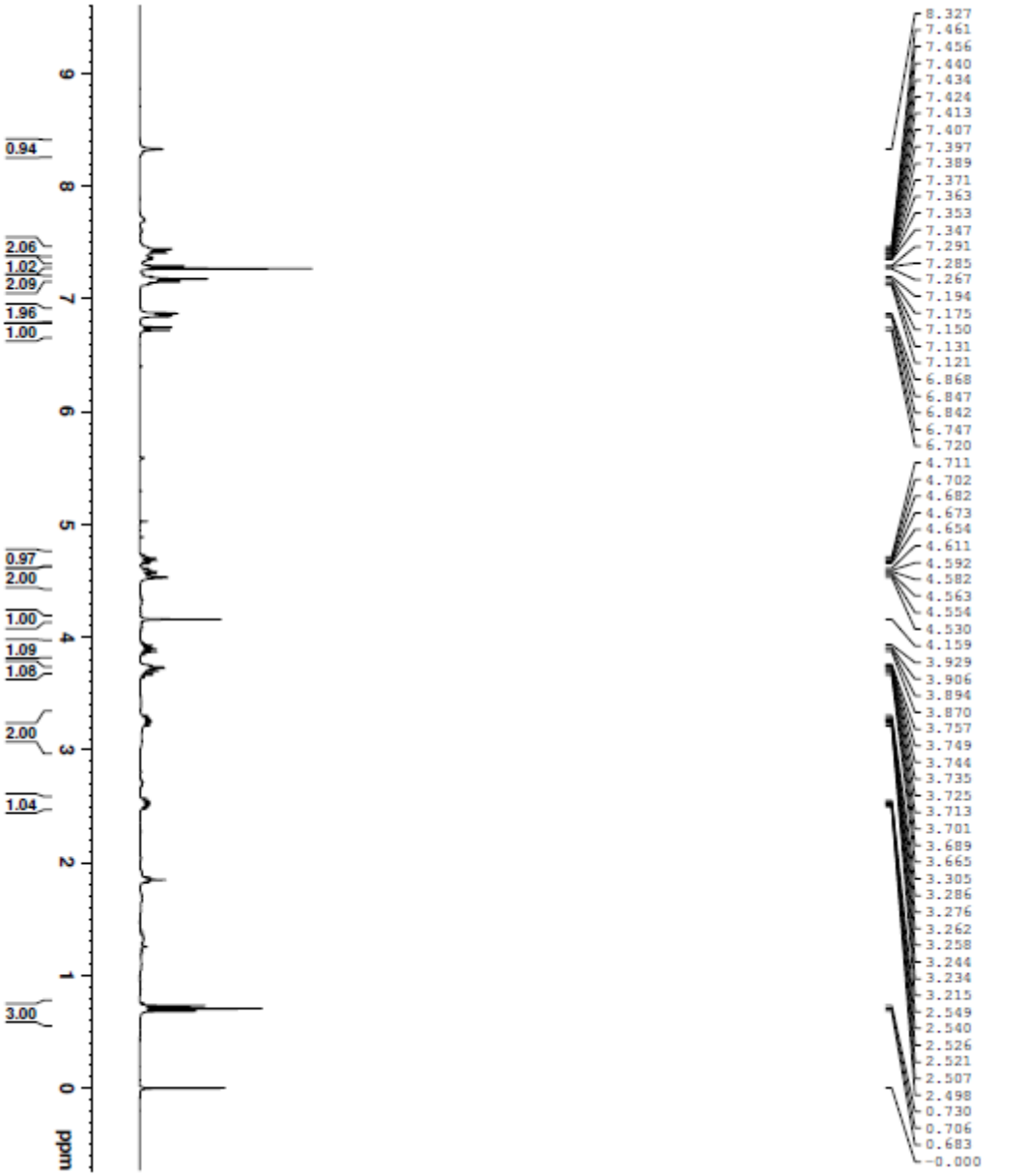
59.91
38.55
31.72
31.40
29.95
26.09
25.46
13.23

(4l):


O
O
HN
COOEt
Br
O
N
H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2.00
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1.09
1.08
2.00
1.04
3.00
ppm
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7.456
7.440
7.434
7.424
7.413
7.407
7.397
7.389
7.371
7.363
7.353
7.347
7.291
7.285
7.267
7.194
7.175
7.150
7.131
7.121
6.868
6.847
6.842
6.747
6.720
4.711
4.702
4.682
4.673
4.654
4.611
4.592
4.582
4.563
4.554
4.530
4.159
3.929
3.906
3.894
3.870
3.757
3.749
3.744
3.735
3.725
3.713
3.701
3.689
3.665
3.305
3.286
3.276
3.262
3.258
3.244
3.234
3.215
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2.540
2.526
2.521
2.507
2.498
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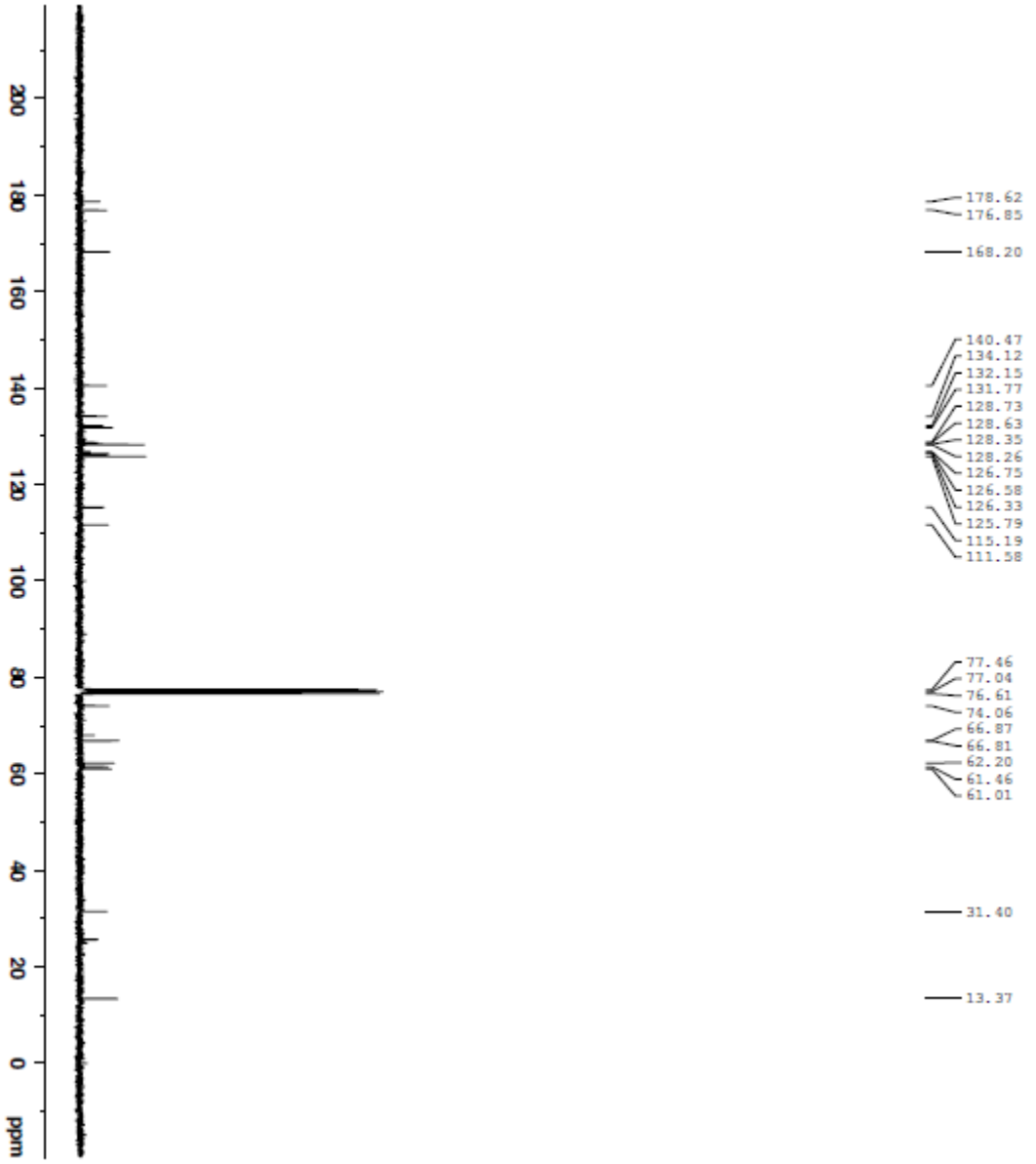
0.706
0.683
-0.000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180
160
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120
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80
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40
20
0
ppm
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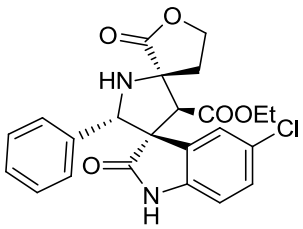
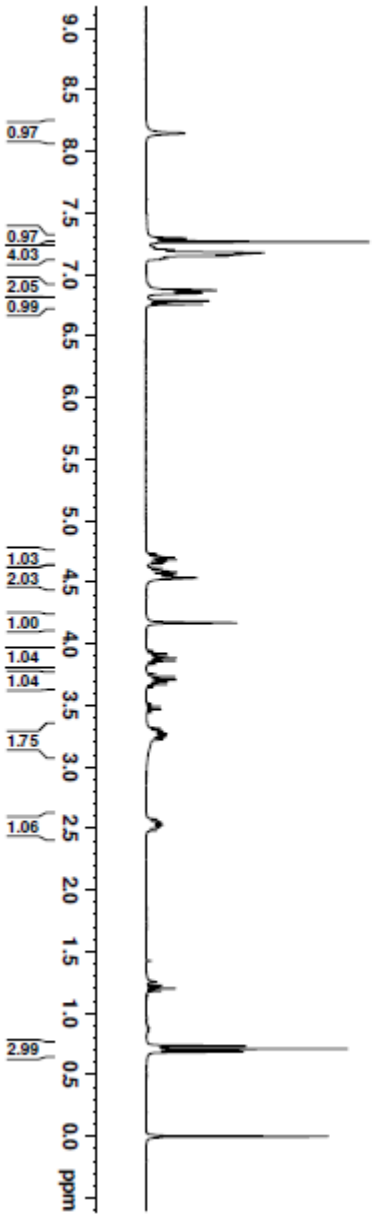
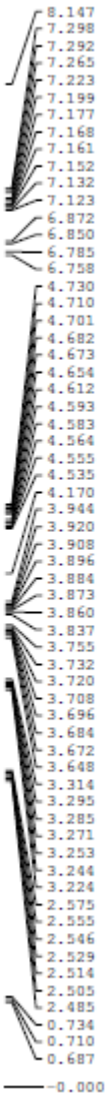
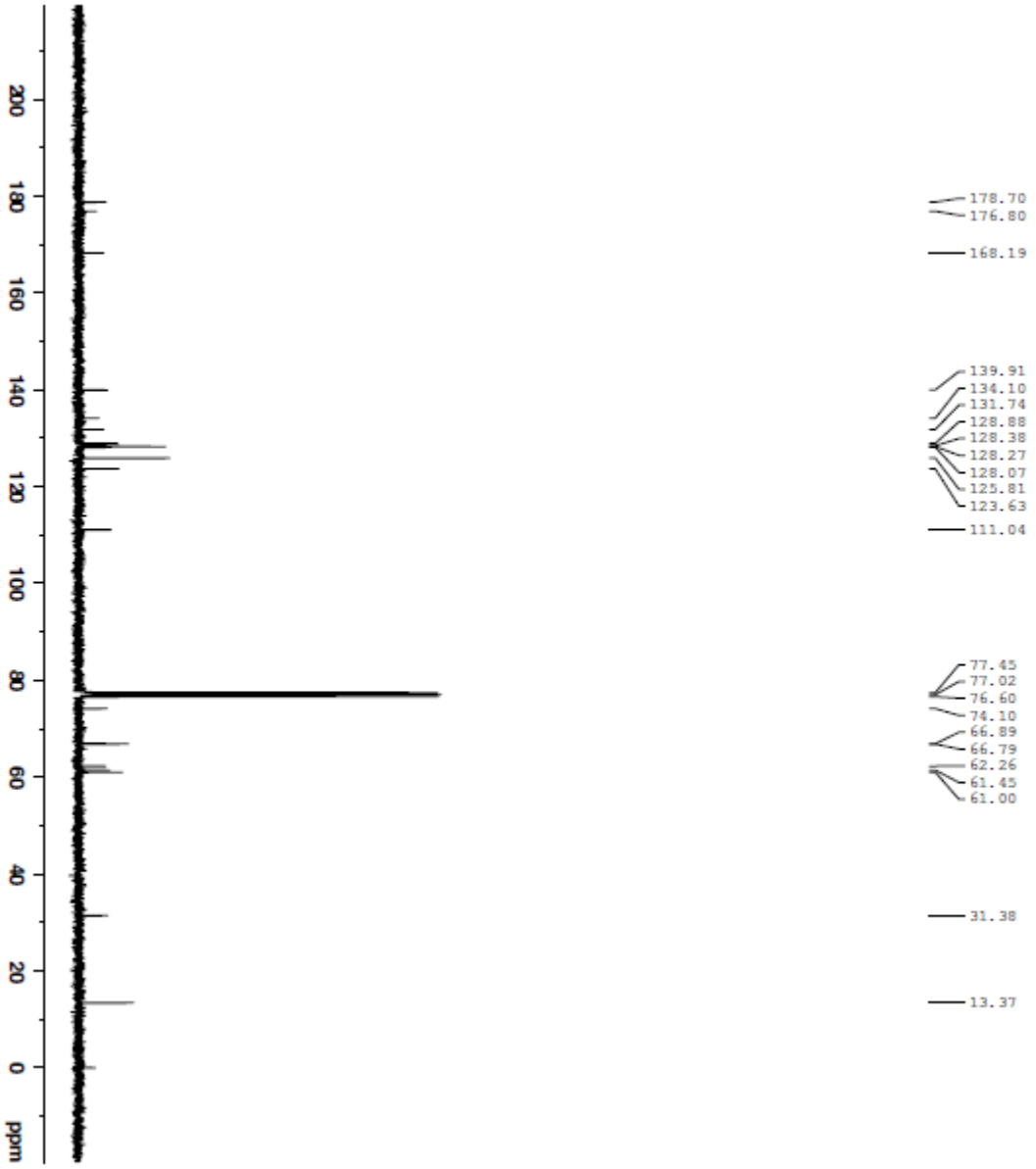
168.20
140.47
134.12
132.15
131.77
128.73
128.63
128.35
128.26
126.75
126.58
126.33
125.79
115.19
111.58
77.46
77.04
76.61
74.06
66.87
66.81
62.20
61.46
61.01
31.40
13.37

(4m):

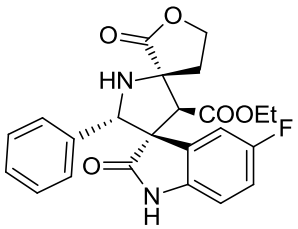


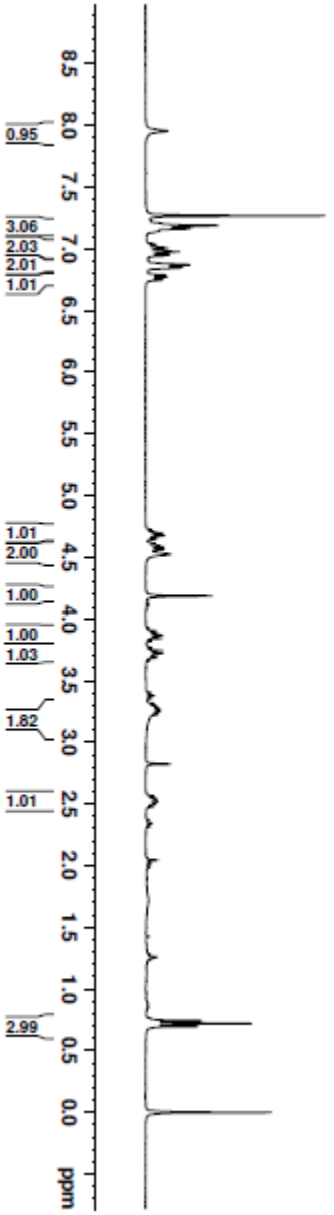






(4n):


O
O
HN
COOEt
F
O
N
H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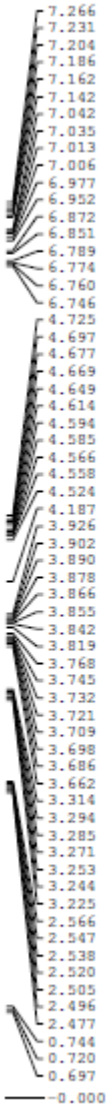
1.01
1.01
2.00
1.00
1.00
1.03
1.82
1.01
2.99
ppm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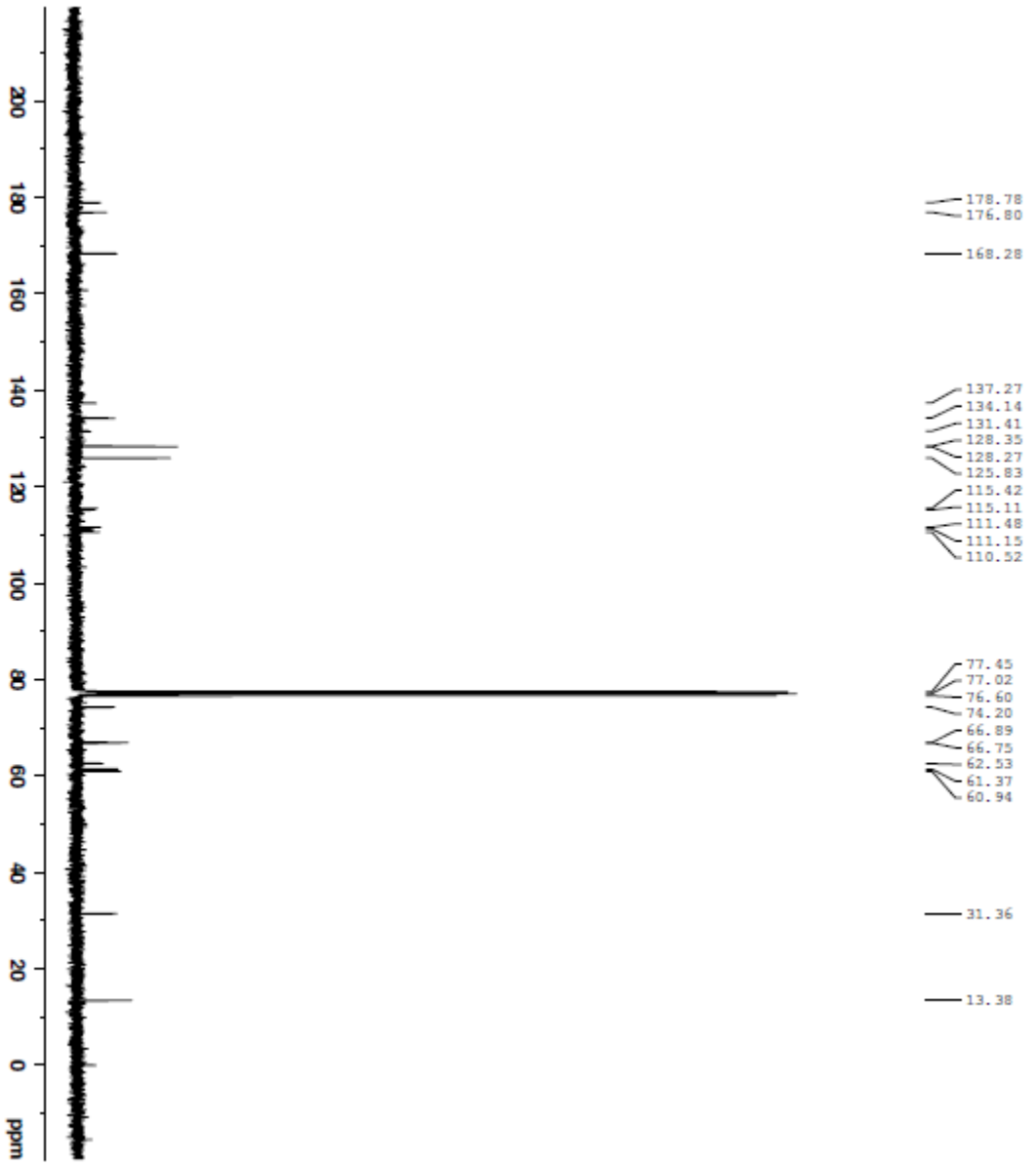
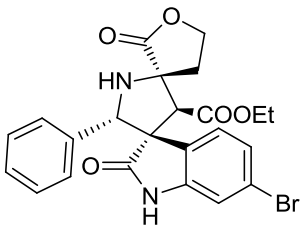
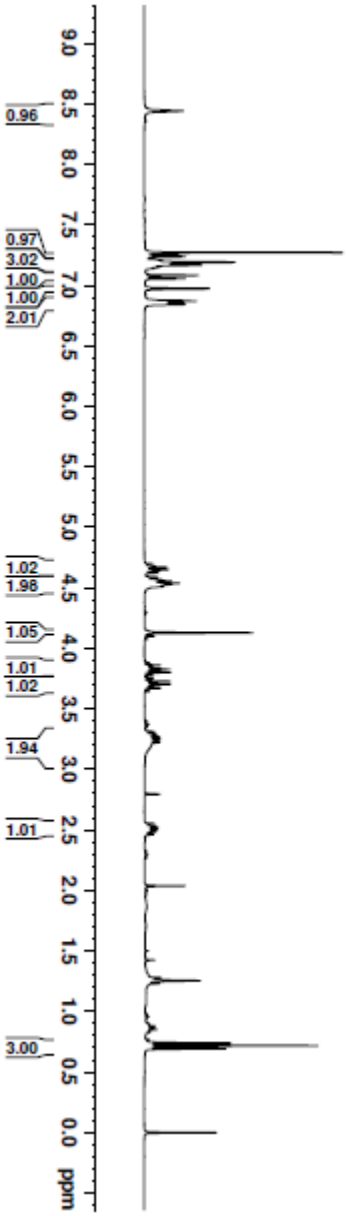
7.231
7.204
7.186
7.162
7.142
7.042
7.035
7.013
7.006
6.977
6.952
6.872
6.851
6.789
6.774
6.760
6.746
4.725
4.697
4.677
4.669
4.649
4.614
4.594
4.585
4.566
4.558
4.524
4.187
3.926
3.902
3.890
3.878
3.866
3.855
3.842
3.819
3.768
3.745
3.732
3.721
3.709
3.698
3.686
3.662
3.314
3.294
3.285
3.271
3.253
3.244
3.225
2.566
2.547
2.538
2.520
2.505
2.496
2.477
0.744
0.720
0.697
0.000



(4o):


O
O
HN
COOEt
O
N
H
Br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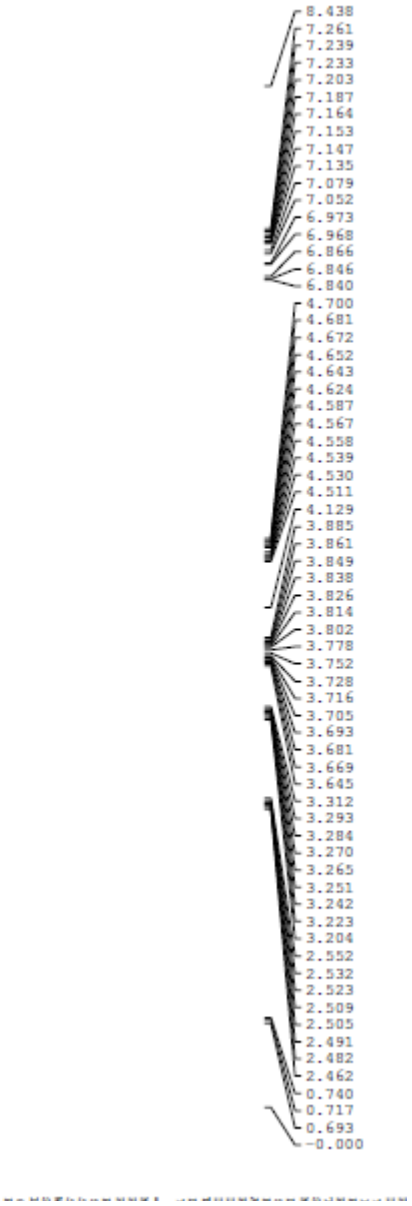
1.00
2.01
1.02
1.98
1.05
1.01
1.02
1.94
1.01
3.00
ppm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7.239
7.233
7.203
7.187
7.164
7.153
7.147
7.135
7.079
7.052
6.973
6.968
6.866
6.846
6.840
4.700
4.681
4.672
4.652
4.643
4.624
4.587
4.567
4.558
4.539
4.530
4.511
4.129
3.885
3.861
3.849
3.838
3.826
3.814
3.802
3.778
3.752
3.728
3.716
3.705
3.693
3.681
3.669
3.645
3.312
3.293
3.284
3.270
3.265
3.251
3.242
3.223
3.204
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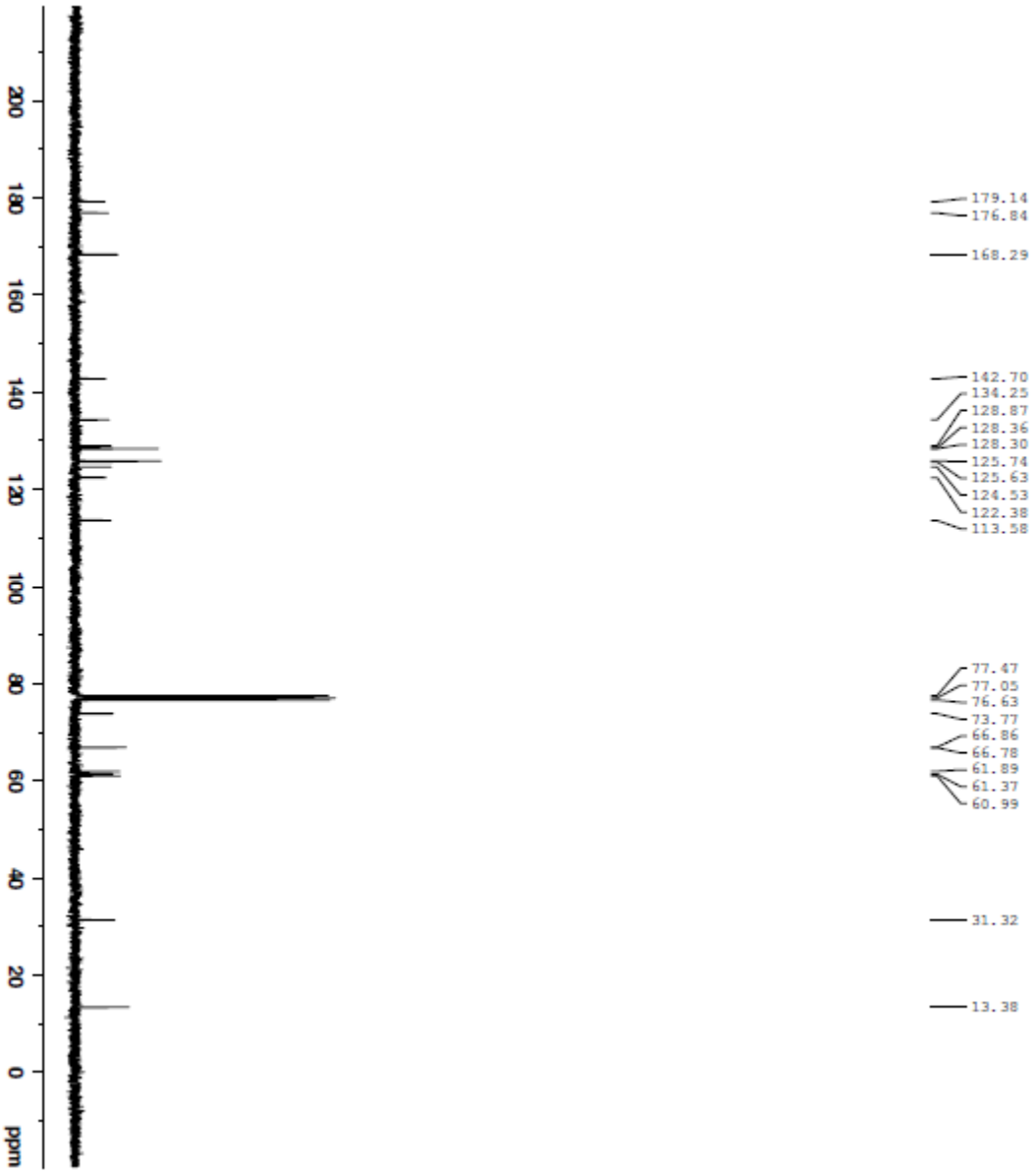
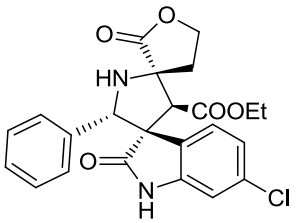
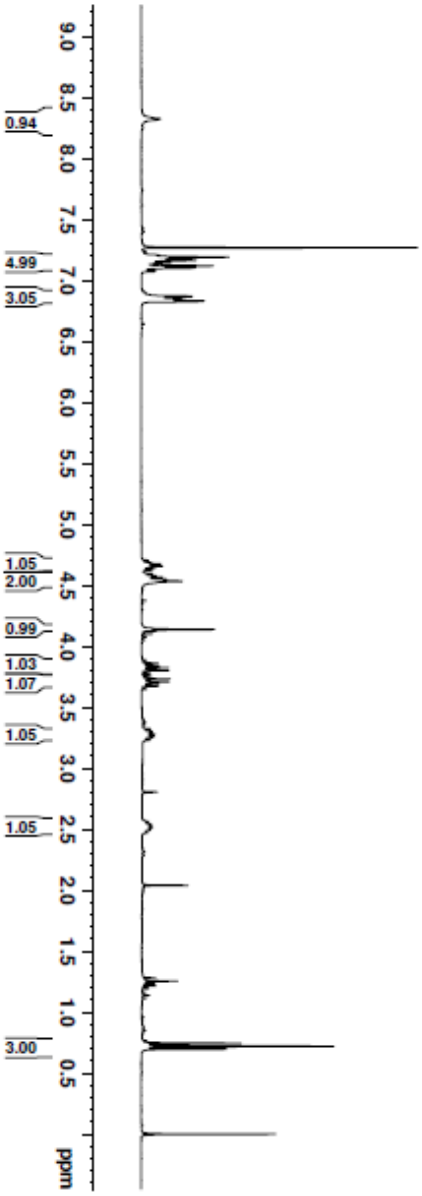
0.693
-0.000



(4p):


O
O
HN
COOEt
O
N
H
Cl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8.0
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7.0
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6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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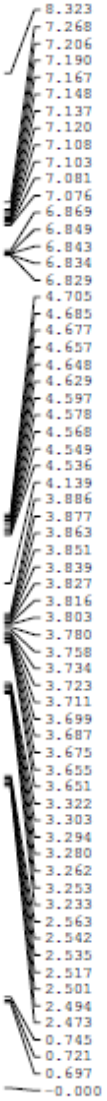
4.99
3.05
1.05
2.00
0.99
1.03
1.07
1.05
1.05
3.00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7.137
7.120
7.108
7.103
7.081
7.076
6.869
6.849
6.843
6.834
6.829
4.705
4.685
4.677
4.657
4.648
4.629
4.597
4.578
4.568
4.549
4.536
4.139
3.886
3.877
3.863
3.851
3.839
3.827
3.816
3.803
3.780
3.758
3.734
3.723
3.711
3.699
3.687
3.675
3.655
3.651
3.322
3.303
3.294
3.280
3.262
3.253
3.233
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2.535
2.517
2.501
2.494
2.473
0.745
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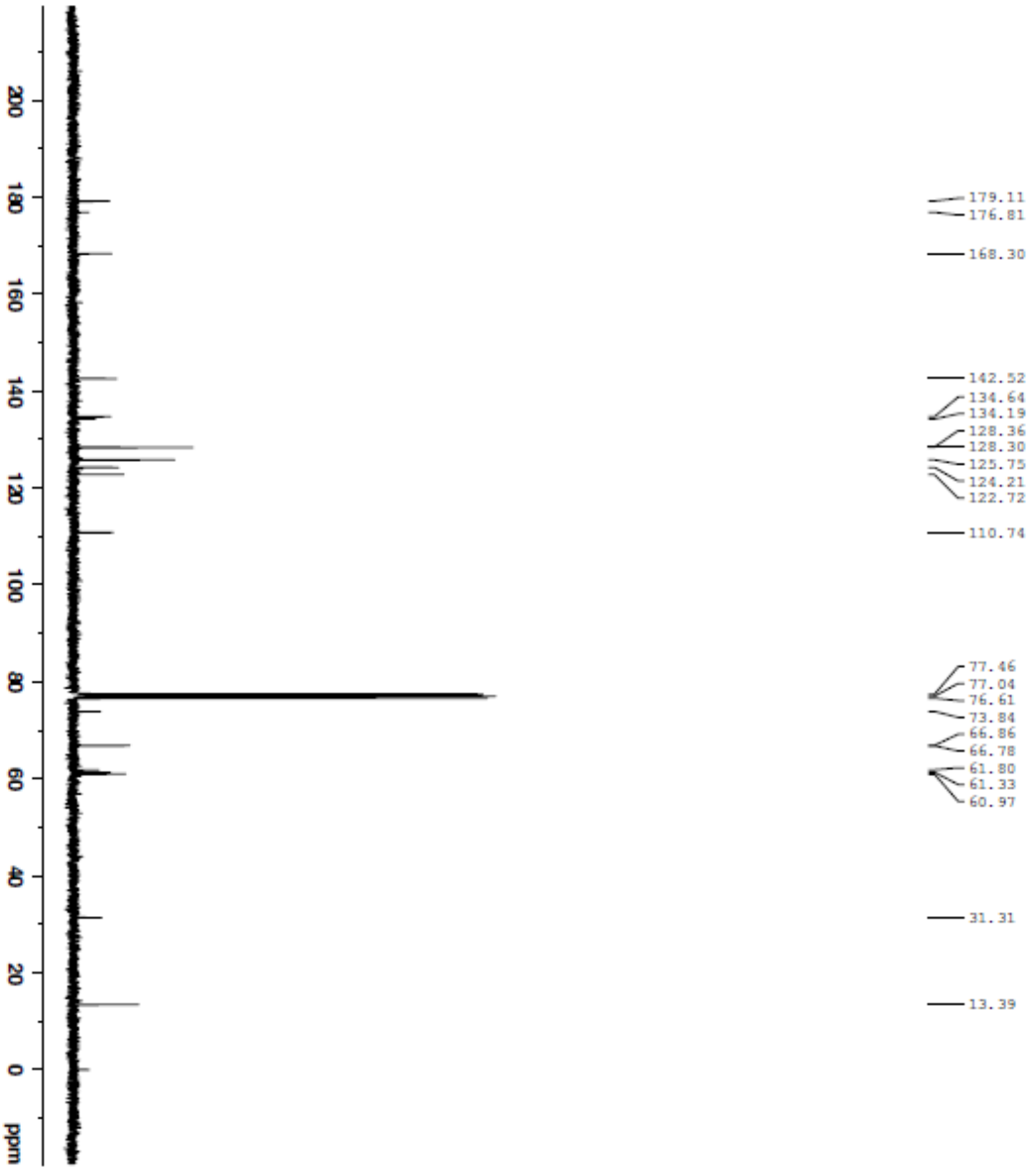
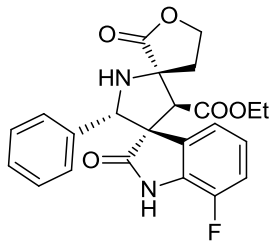
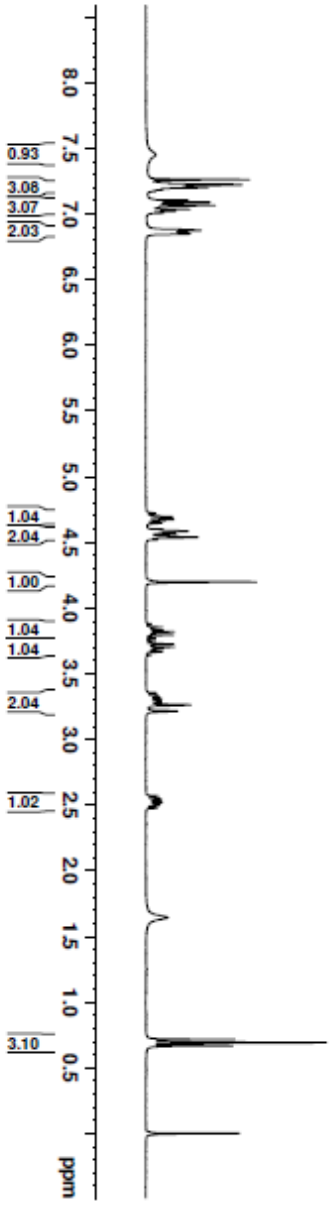
0.697
-0.000



(4q):


O
O
HN
COOEt
O
N
H
F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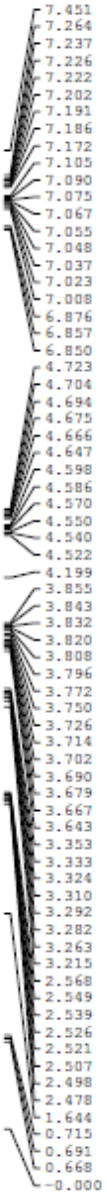
2.04
1.00
1.04
1.04
2.04
1.02
3.10
ppm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7.264
7.237
7.226
7.222
7.202
7.191
7.186
7.172
7.105
7.090
7.075
7.067
7.055
7.048
7.037
7.023
7.008
6.876
6.857
6.850
4.723
4.704
4.694
4.675
4.666
4.647
4.598
4.586
4.570
4.550
4.540
4.522
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3.855
3.843
3.832
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3.808
3.796
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3.750
3.726
3.714
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3.690
3.679
3.667
3.643
3.353
3.333
3.324
3.310
3.292
3.282
3.263
3.215
2.568
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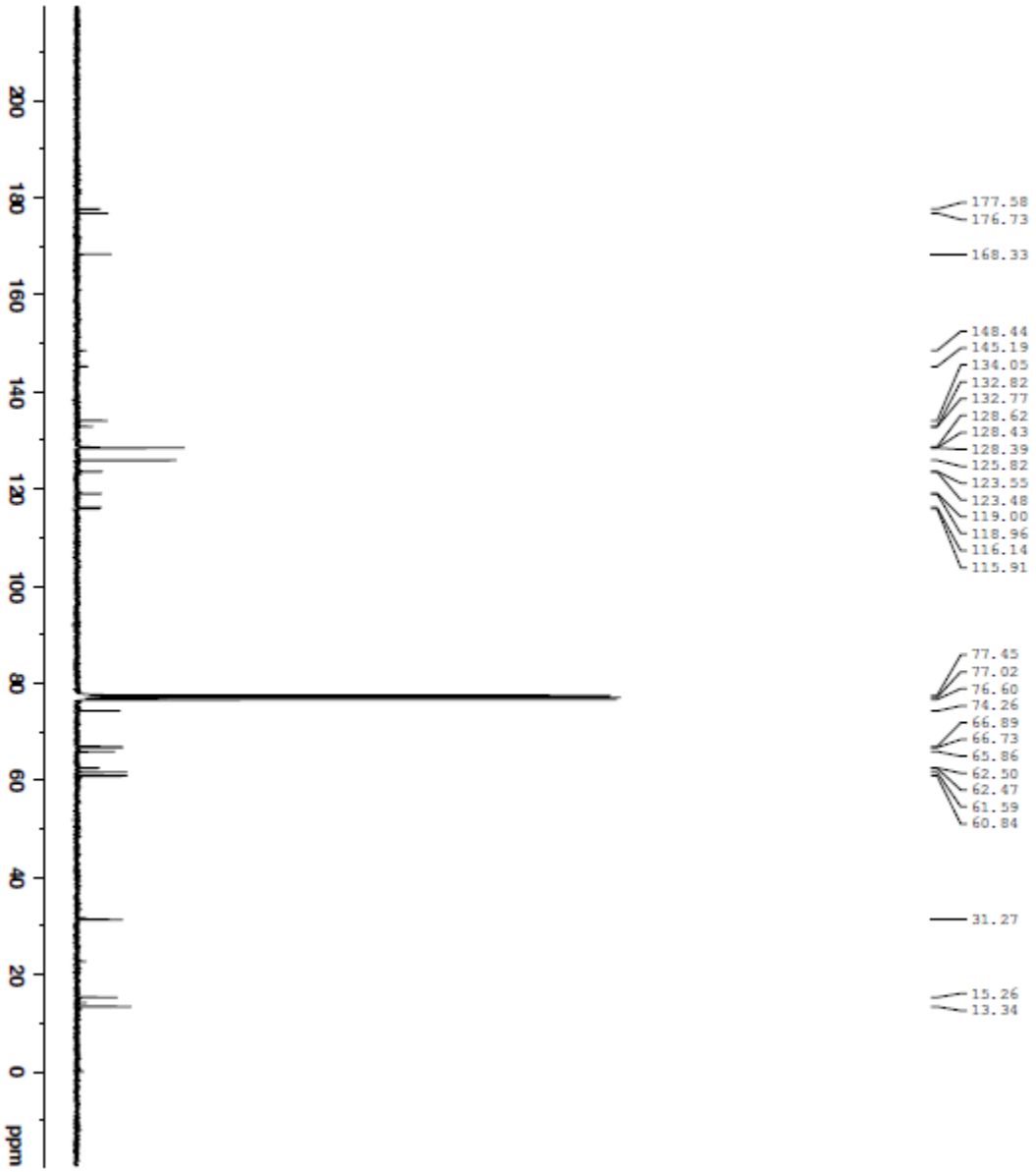
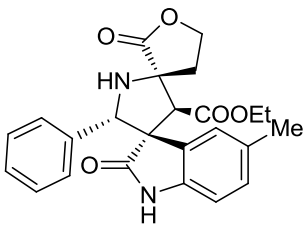
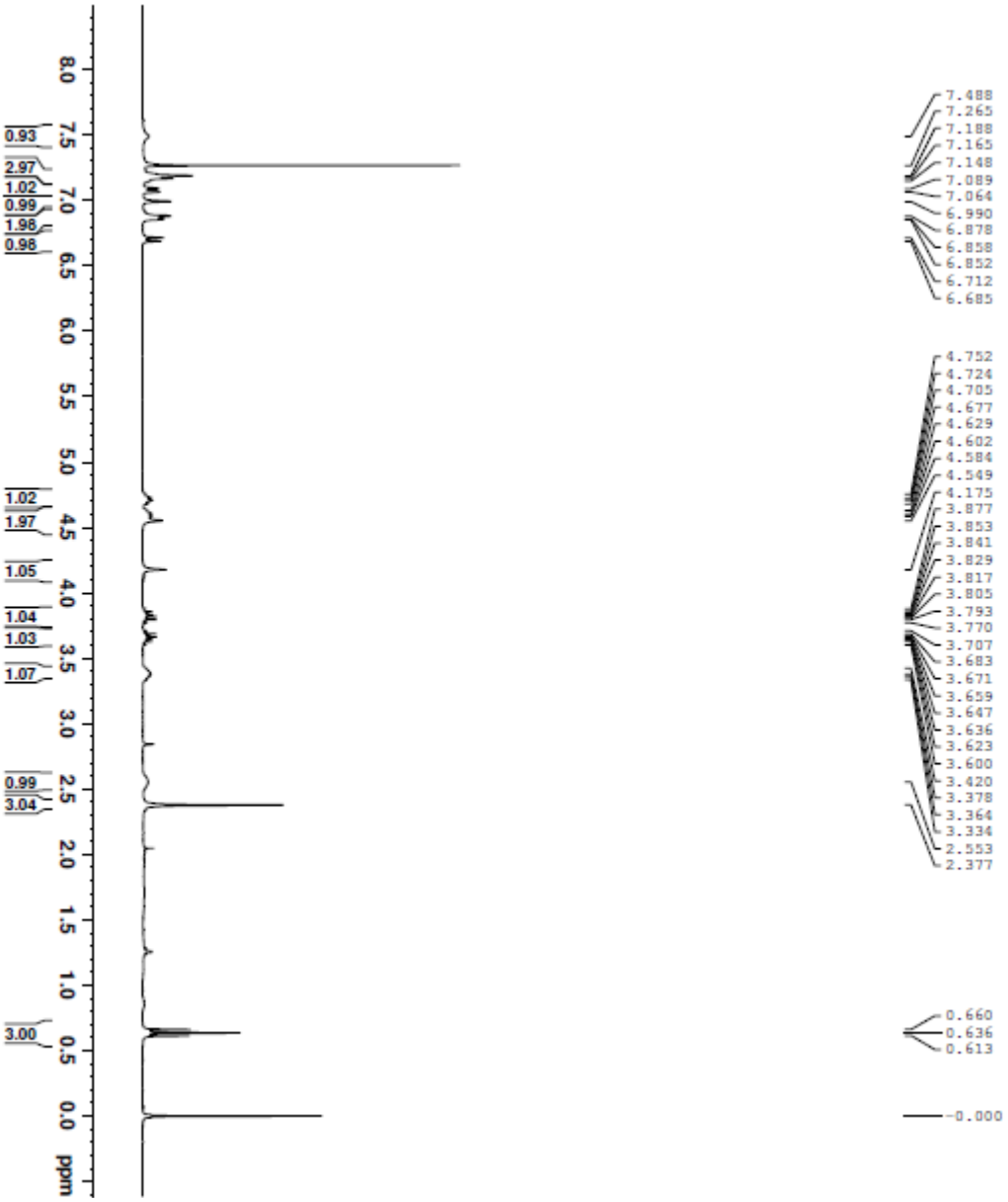
0.668
-0.000



(4r):


O
O
HN
COOEt
Me
O
N
H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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.93
2.97
1.02
0.99
1.98
0.98
1.02
1.97
1.05
1.04
1.03
1.07
0.99
3.04
3.00
7.488
7.265
7.188
7.165
7.148
7.089
7.064
6.990
6.878
6.858
6.852
6.712
6.685
4.752
4.724
4.705
4.677
4.629
4.602
4.584
4.549
4.175
3.877
3.853
3.841
3.829
3.817
3.805
3.793
3.770
3.707
3.683
3.671
3.659
3.647
3.636
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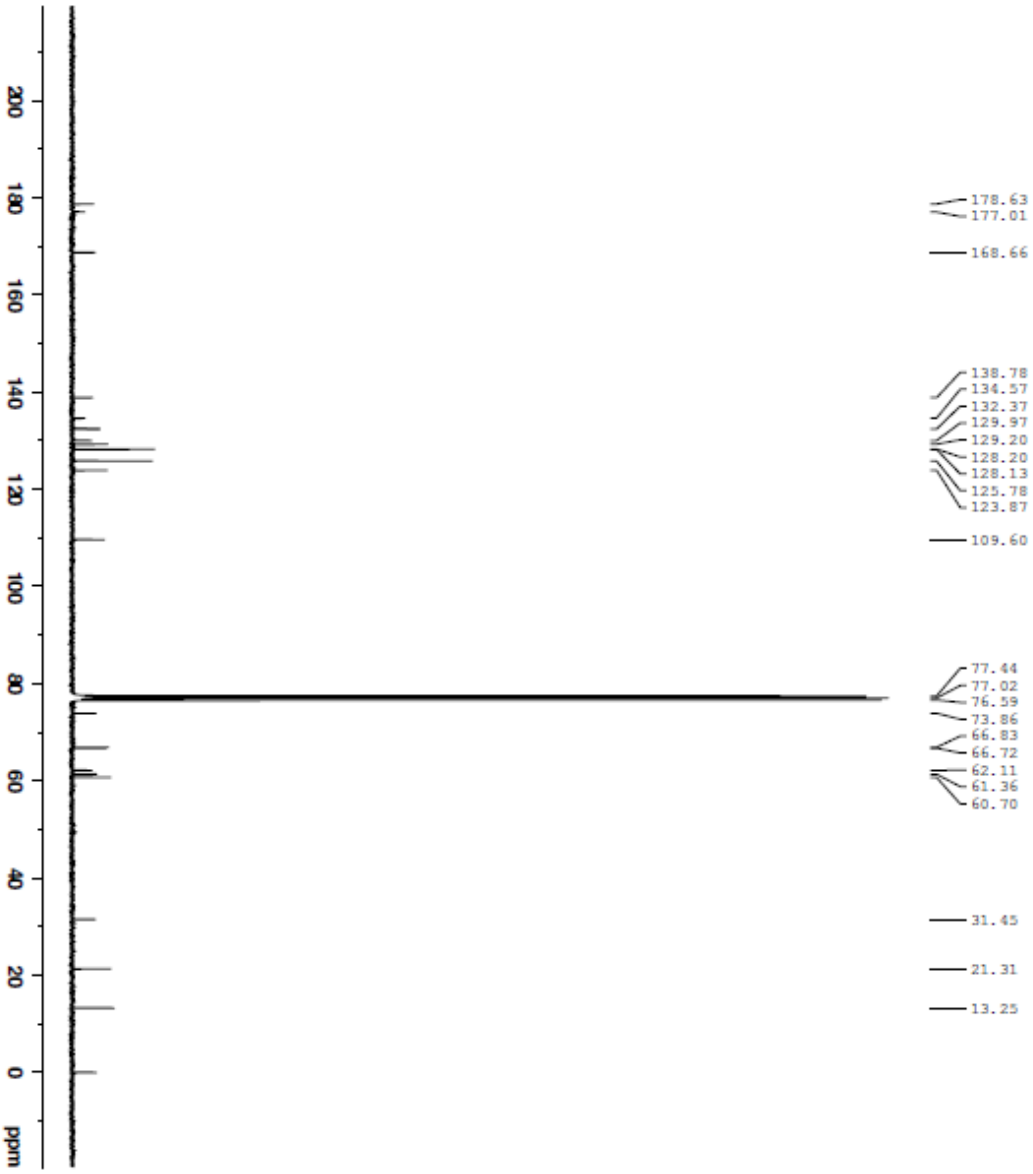
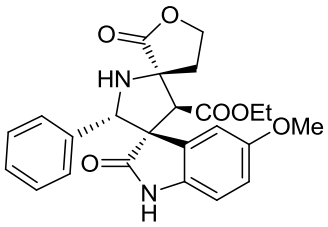
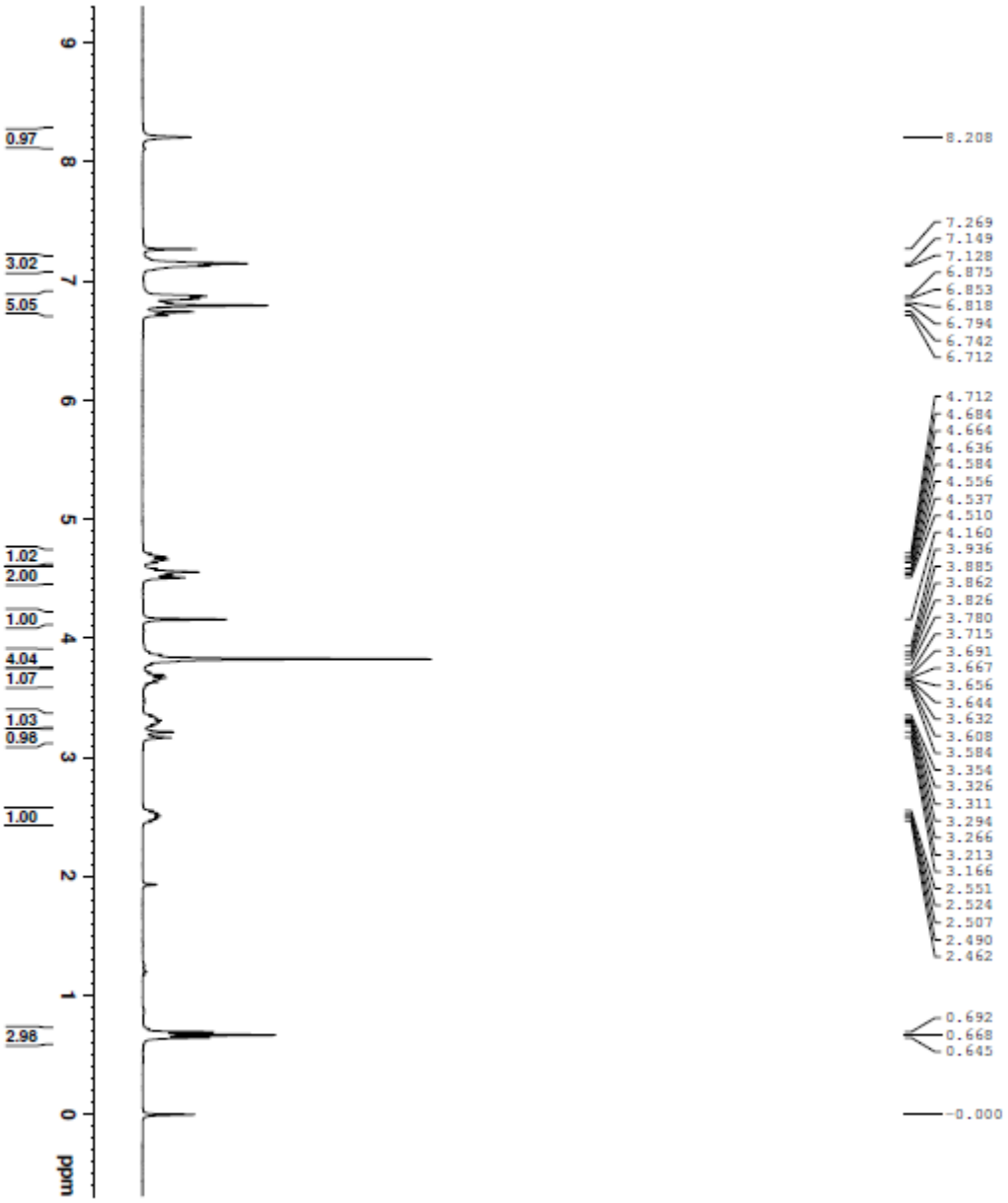
0.613
0.000



(4s):


O
O
HN
COOEt
OMe
O
N
H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3.02
5.05
1.02
2.00
1.00
4.04
1.07
1.03
0.98
1.00
2.98
ppm
8.208
7.269
7.149
7.128
6.875
6.853
6.818
6.794
6.742
6.712
4.712
4.684
4.664
4.636
4.584
4.556
4.537
4.510
4.160
3.936
3.885
3.862
3.826
3.780
3.715
3.691
3.667
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3.608
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3.354
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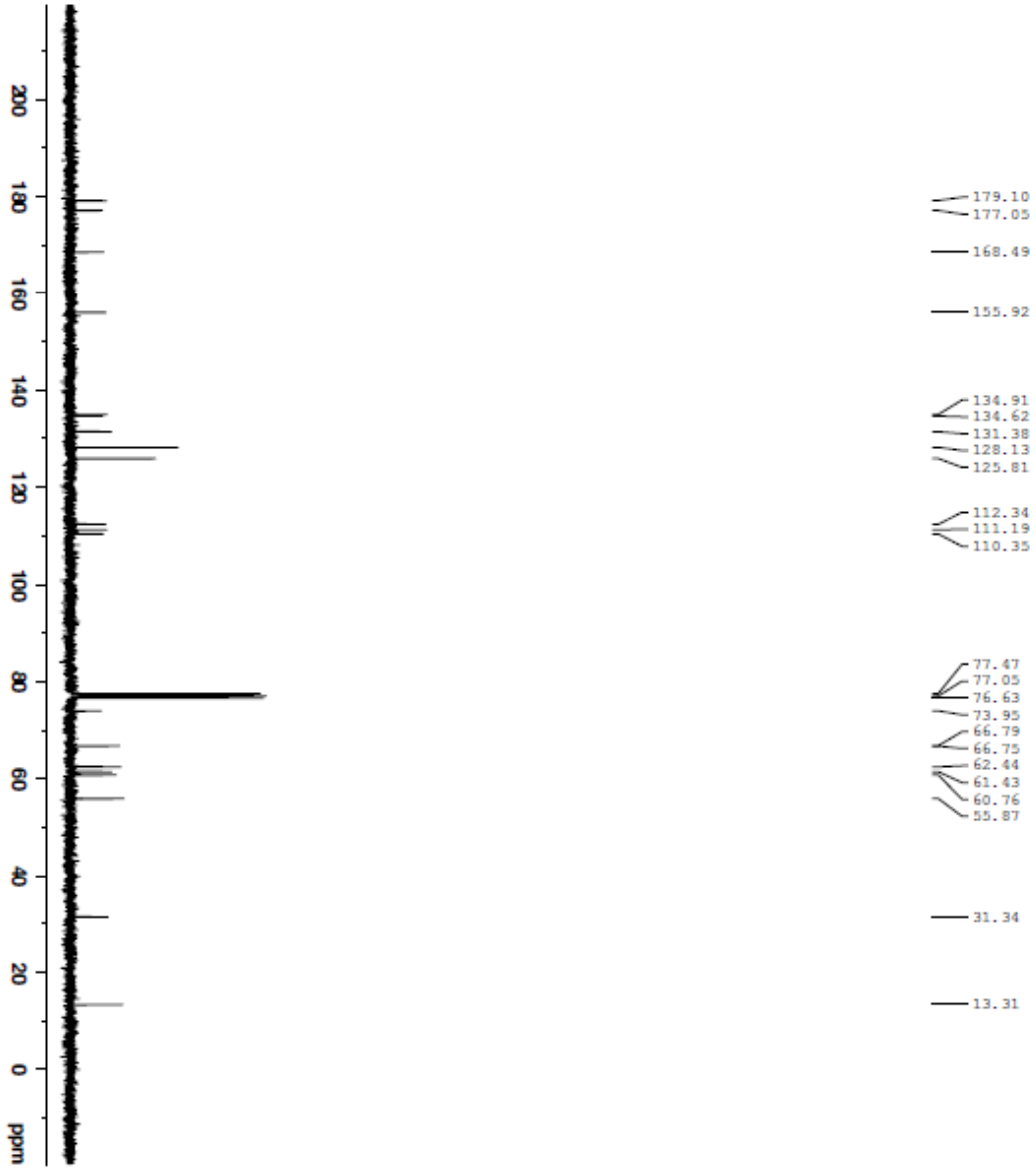
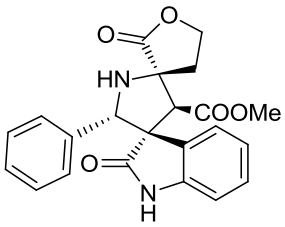
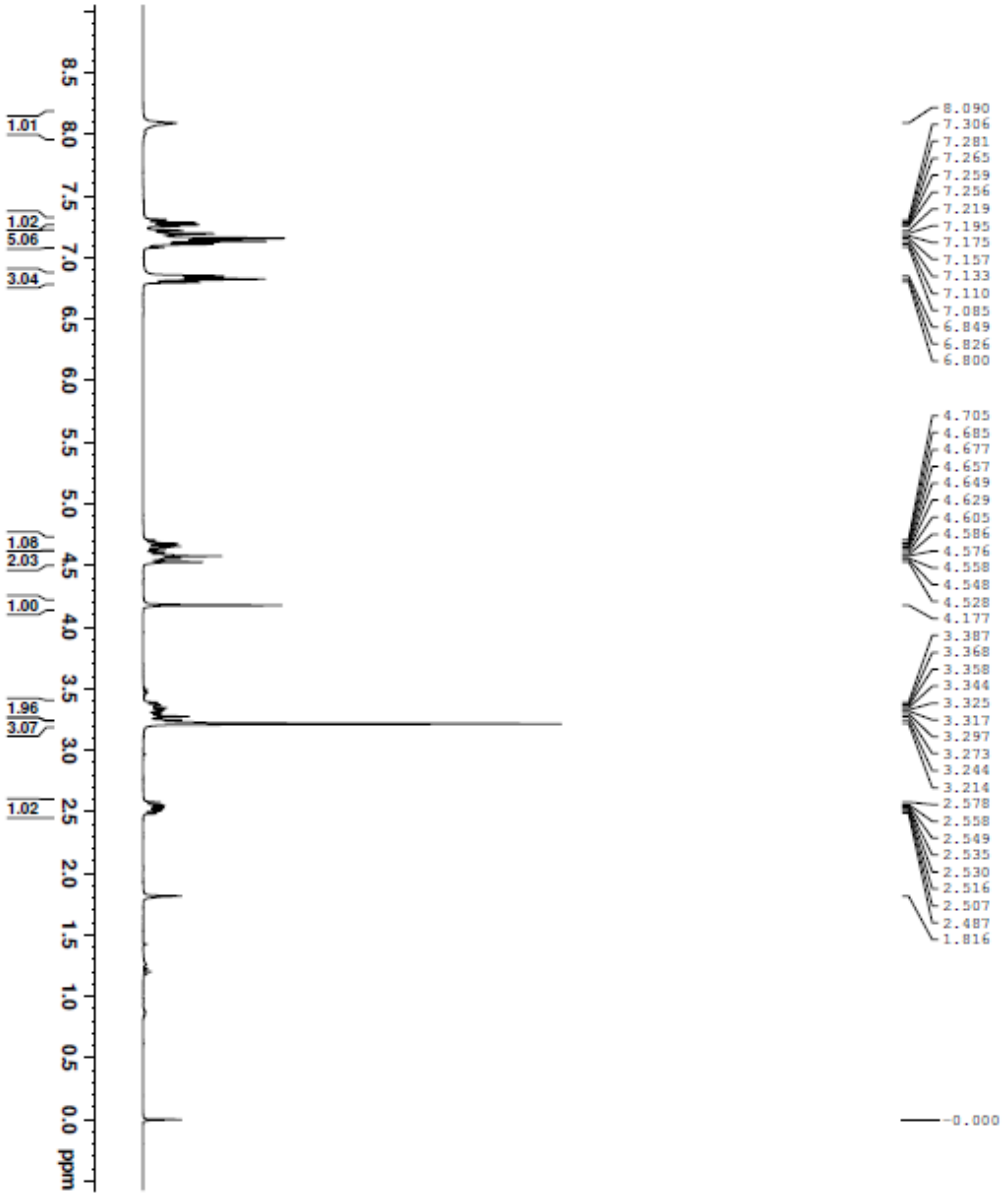
0.000



(4t):


O
O
HN
COOMe
O
N
H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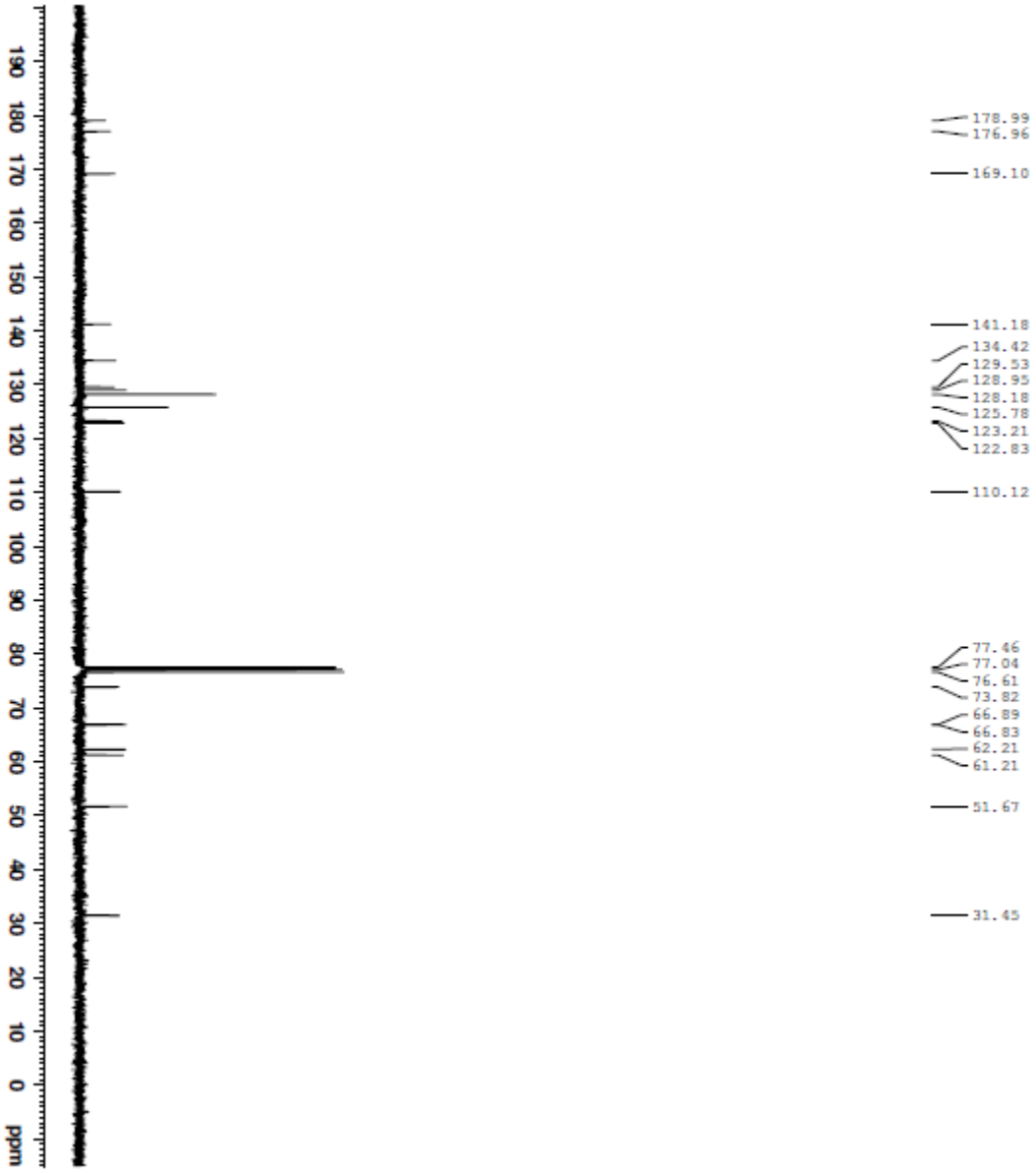
1.02
5.06
3.04
1.08
2.03
1.00
1.96
3.07
1.02
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
8.090
7.306
7.281
7.265
7.259
7.256
7.219
7.195
7.175
7.157
7.133
7.110
7.085
6.849
6.826
6.800
4.705
4.685
4.677
4.657
4.649
4.629
4.605
4.586
4.576
4.558
4.548
4.528
4.177
3.387
3.368
3.358
3.344
3.325
3.317
3.297
3.273
3.244
3.214
2.578
2.558
2.549
2.535
2.530
2.516
2.507
2.487
1.816
0.000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150
140
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120
110
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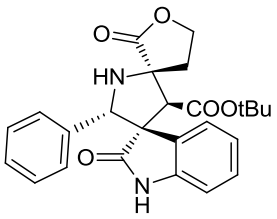
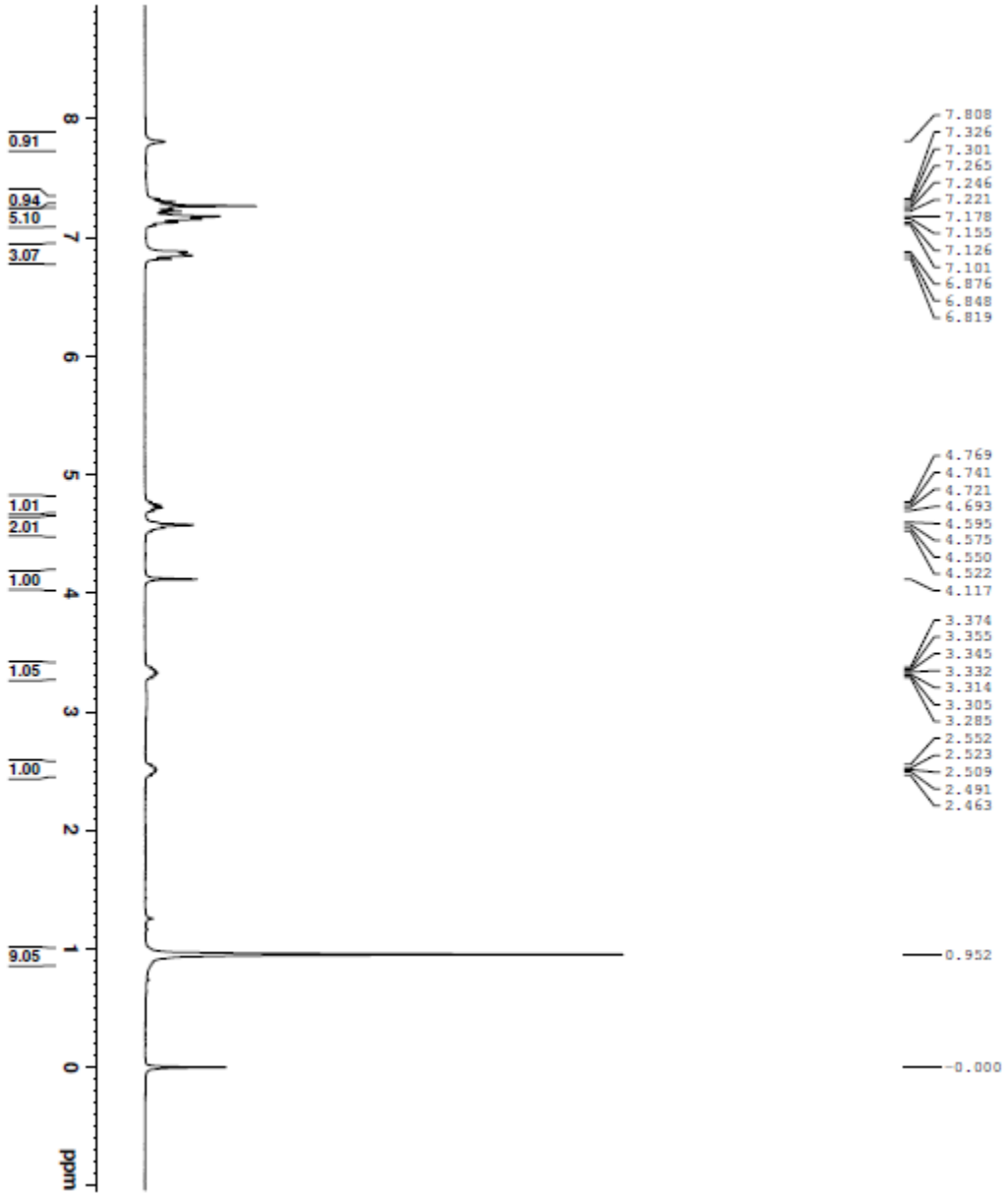
90
80
70
60
50
40
30
20
10
0
ppm
178.99
176.96
169.10
141.18
134.42
129.53
128.95
128.18
125.78
123.21
122.83
110.12
77.46
77.04
76.61
73.82
66.89
66.83
62.21
61.21
51.67
31.45

(4u):


O
O
HN
COOtBu
O
N
H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0.94
5.10
3.07
1.01
2.01
1.00
1.05
1.00
9.05
ppm
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7.326
7.301
7.265
7.246
7.221
7.178
7.155
7.126
7.101
6.876
6.848
6.819
4.769
4.741
4.721
4.693
4.595
4.575
4.550
4.522
4.117
3.374
3.355
3.345
3.332
3.314
3.305
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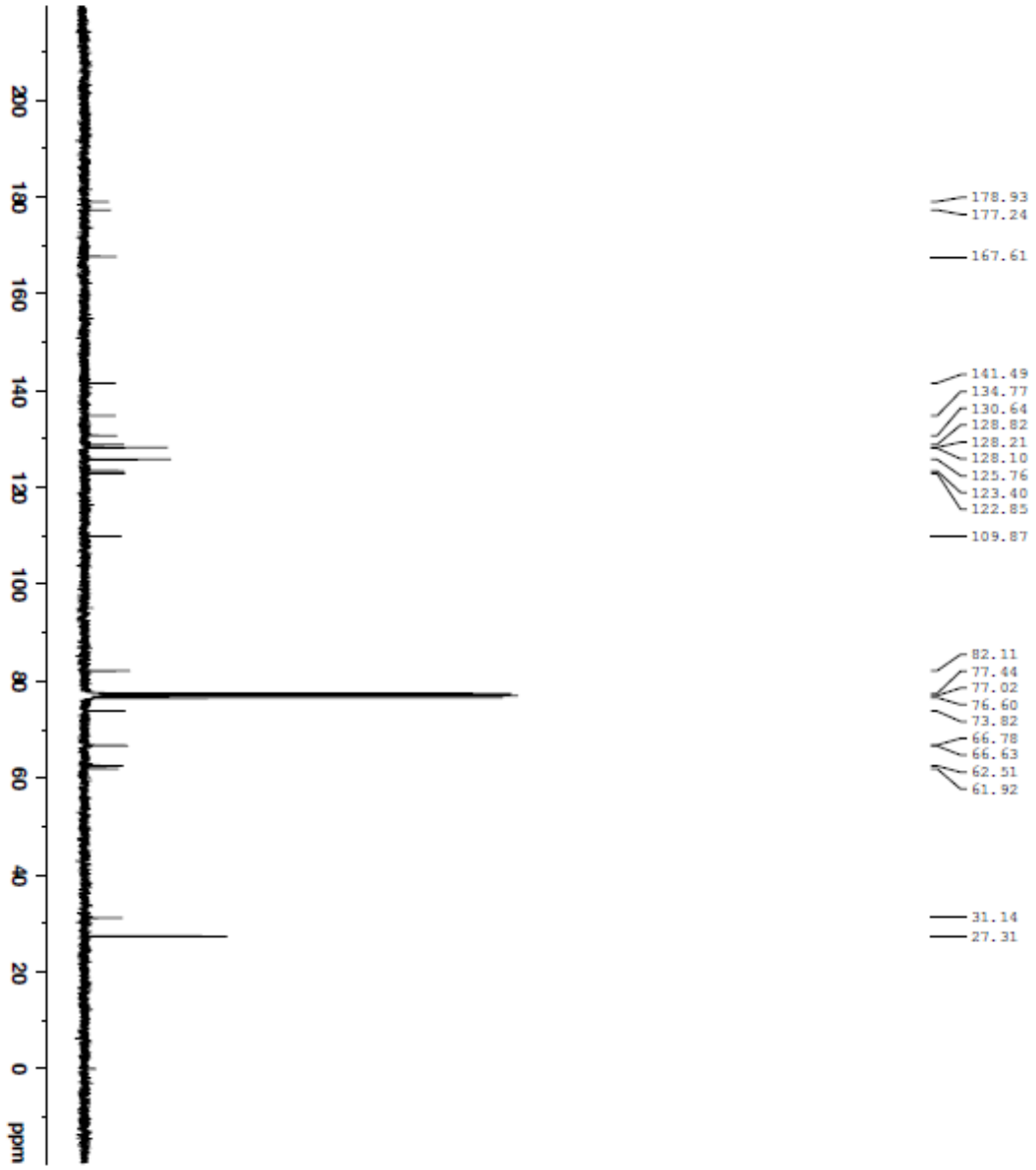
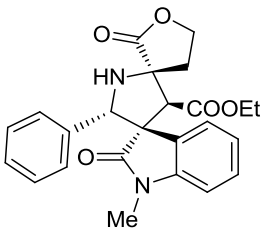
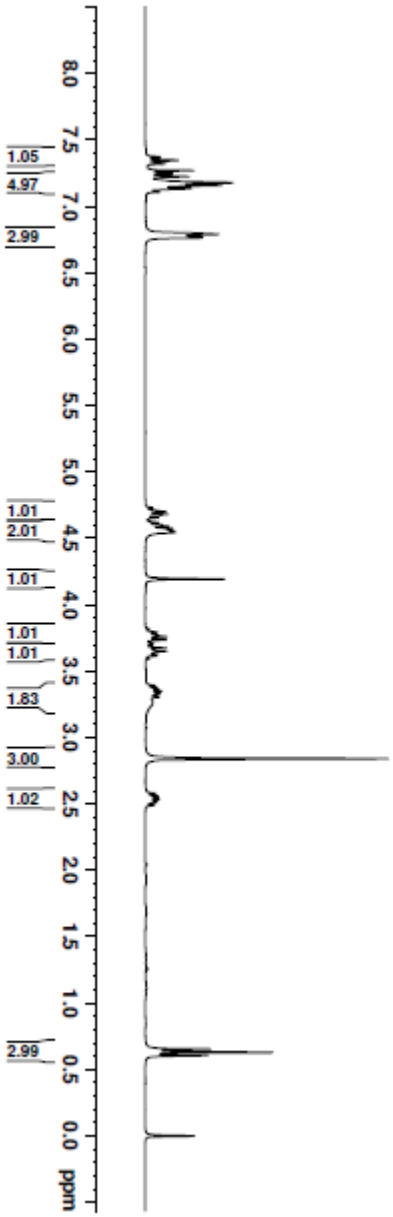
2.463
0.952
-0.000



(4v):


O
O
HN
COOEt
O
N
Me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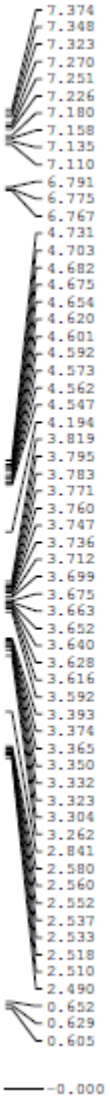
4.97
2.99
1.01
2.01
1.01
1.01
1.01
1.83
3.00
1.02
2.99
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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7.348
7.323
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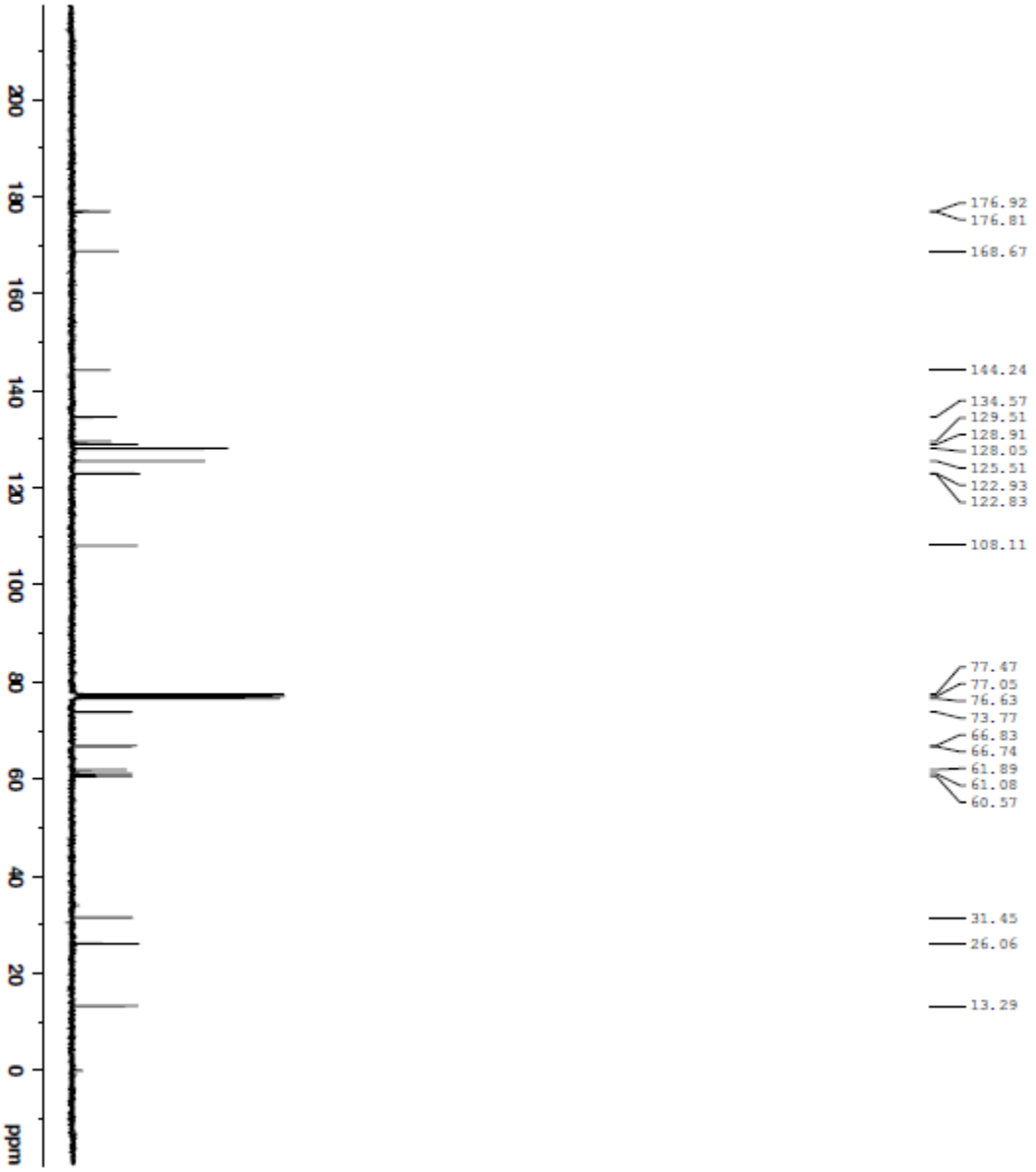
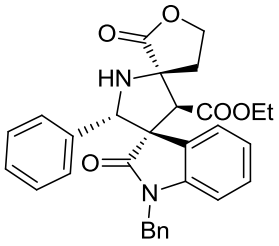
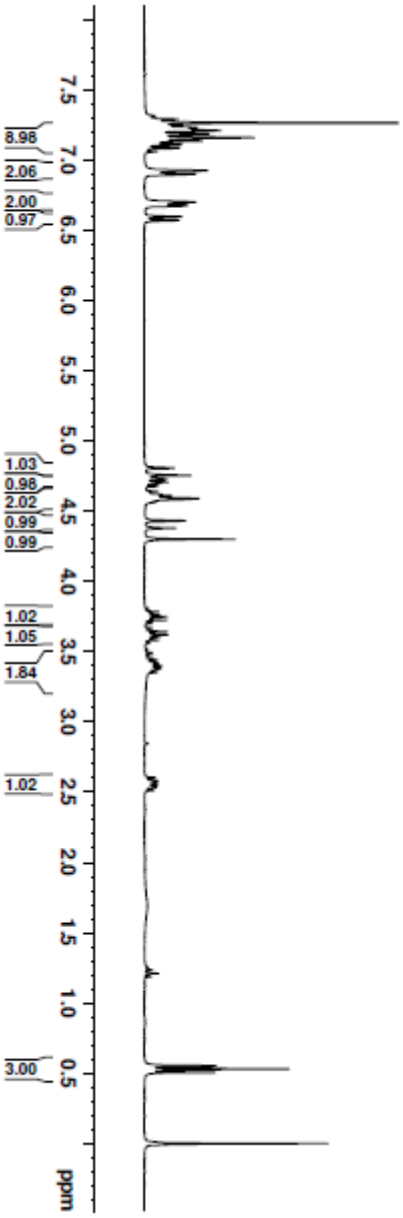
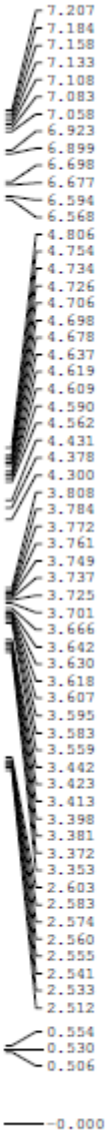
7.251
7.226
7.180
7.158
7.135
7.110
6.791
6.775
6.767
4.731
4.703
4.682
4.675
4.654
4.620
4.601
4.592
4.573
4.562
4.547
4.194
3.819
3.795
3.783
3.771
3.760
3.747
3.736
3.712
3.699
3.675
3.663
3.652
3.640
3.628
3.616
3.592
3.393
3.374
3.365
3.350
3.332
3.323
3.304
3.262
2.841
2.580
2.560
2.552
2.537
2.533
2.518
2.510
2.490
0.652
0.629
0.605
0.000


200
180
160
140
120
100
80
60
40
20
0
ppm
176.92
176.81
168.67
144.24
134.57
129.51
128.91
128.05
125.51
122.93
122.83
108.11
77.47
77.05
76.63
73.77
66.83
66.74
61.89
61.08
60.57
31.45
26.06
13.29

(4w):


O
O
HN
COOEt
O
N
Bn


8.98
2.06
2.00
0.97
1.03
0.98
2.02
0.99
0.99
1.02
1.05
1.84
1.02
3.00
ppm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7.158
7.133
7.108
7.083
7.058
6.923
6.899
6.698
6.677
6.594
6.568
4.806
4.754
4.734
4.726
4.706
4.698
4.678
4.637
4.619
4.609
4.590
4.562
4.431
4.378
4.300
3.808
3.784
3.772
3.761
3.749
3.737
3.725
3.701
3.666
3.642
3.630
3.618
3.607
3.595
3.583
3.559
3.442
3.423
3.413
3.398
3.381
3.372
3.353
2.603
2.583
2.574
2.560
2.555
2.541
2.533
2.512
0.554
0.530
0.506
0.000