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Supporting Information

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Cycle-Specific Organo-Cascade Catalysis: Application to Olefin Hydroamination, Hydro-Oxidation, and Amino-Oxidation. The First Use of Organocascade Catalysis in Complex Natural Product Synthesis

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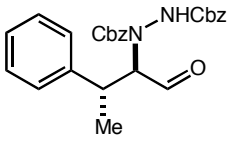
Supporting Information

General Information. Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] All solvents were purified according to the method of Grubbs.[2] Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using an ice-water bath for volatile compounds. Chromatographic purification of products was accomplished by flash chromatography on Silicycle F60 silica gel according to the method of Still[3] (where noted, Iatrobeads 6RS-8060 was used in place of silica gel) or using preparatory TLC on Silicycle SiliaPlates (1000 μm, 20 × 20 cm). Thin-layer chromatography (TLC) was performed on Silicycle 250 μm silica gel plates. Visualization of the developed chromatogram was performed by fluorescence quenching, *p*-anisaldehyde or ceric ammonium molybdate stain. ^{1}H and ^{13}C NMR spectra were recorded on Varian 400 (400 MHz and 100 MHz) or Bruker 500 (500 and 125 MHz) instruments, and are internally referenced to residual protio solvent signals (note: $CDCl_3$ referenced at δ 7.27 and 77.0 ppm respectively). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling constant (Hz) and assignment. Data for ^{13}C NMR are reported in terms of chemical shift and no special nomenclature is used for equivalent carbons. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). High resolution mass spectra were obtained at Princeton University mass spectrometry facilities. Supercritical fluid chromatography (SFC) was performed on a Berger Minigram equipped with a diode array UV detector (λ = 214–258 nm) using a chiral column (25 cm) and guard column (5 cm) as noted for each compound. Gas liquid

chromatography (GLC) was performed on a Hewlett-Packard 6850 Series chromatographs with split-mode capillary injection and FID detection using a chiral column (30 m × 0.25 mm) and guard column as noted for each compound.

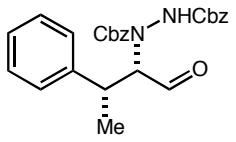


_N_-((1_R_,2_R_)-1-Formyl-2-phenylpropyl)-_N_'-(benzyloxycarbonyl)hydrazinecarboxylic acid benzyl ester:

Procedure A: 3-Phenyl-but-2-enal (36.6 mg, 0.250 mmol), di-*tert*-butyl-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (92.8 mg, 0.300 mmol) and CH_2Cl_2 (500 μL) were charged into a 4 mL vial equipped with septum and a magnetic stir bar and then cooled to –30 °C. After stirring 15 min at –30 °C, the catalysts (2*R*)-2-*tert*-butyl-3-methylimidazolidin-4-one trichloroacetic acid salt (8.0 mg, 0.025 mmol) and L-proline (8.7 mg, 0.075 mmol) were added in one portion with stirring, and the resulting solution was stirred 36 h at –30 °C, at which point a solution of dibenzyl azodicarboxylate (90 wt%, 54.6 mg, 0.165 mmol) in CH_2Cl_2 (1.0 mL) was added, and the reaction mixture was allowed to warm to –15 °C and stirred for an additional 10 h at –15 °C then filtered through an iatrobead pad with EtOAc. Rapid purification (<15 min to avoid partial epimerization at α-amino stereocenter) by flash column chromatography using iatrobeads as the stationary phase (10-50% EtOAc/hexanes) afforded the title compound as a white solid (55.0 mg, 75% yield, 6:1 dr, 99% ee).

Procedure B: 3-Phenyl-but-2-enal (36.6 mg, 0.250 mmol), di-*tert*-butyl-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (92.8 mg, 0.300 mmol) and CH_2Cl_2 (500 μL) were charged into 4 mL vial with magnetic stir bar and cooled to –30 °C. After stirring 15 min at –30 °C, (2*R*)-2-*tert*-butyl-3-methylimidazolidin-4-one trichloroacetic acid salt (8.0 mg, 0.025 mmol) was added in one portion with stirring, and the resulting solution was stirred 36 h at –30 °C, at which point L-proline (8.7 mg, 0.075 mmol) was added followed by a solution of dibenzyl azodicarboxylate (90 wt%, 54.6 mg, 0.165 mmol) in CH_2Cl_2 (1.0 mL) in one portion, and the reaction mixture was allowed to warm to –15 °C. The reaction mixture was stirred for an additional 10 h at –15 °C, then filtered through an iatrobead pad with EtOAc, and concentrated by rotary evaporation.

Rapid purification by flash column chromatography (<15 min to avoid partial epimerization at α-amino stereocenter) using iatrobeads as the stationary phase (10-50% EtOAc/hexanes) afforded the title compound as a white solid (57.0 mg, 77% yield, 8:1 dr, 99% ee). IR (film) 1716, 1402, 1292, 1216, 906 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.15-1.63 (m, 3H, CHC**H**$_3$), 3.25-3.53 (m, 1H, PhMeCH), 4.51-4.78 (m, 1H, NC**H**CHO), 4.91-5.31 (m, 4H, $PhCH_2$), 5.87-6.12 (m, 1H, NH), 7.10-7.48 (m, 15H, PhH), 9.93 (s, 1H, CHO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 37.6, 67.9, 68.4, 72.0, 127.1, 127.2, 127.6, 127.7, 128.3, 128.4, 128.6, 128.7, 128.8, 135.1, 135.3, 142.6, 155.6, 155.8, 197.4 (additional peaks and line broadenings are observed due to rotameric species); HRMS (EI) exact mass calculated for ($C_{26}H_{26}N_2O_5$) requires *m/z* 446.1842, found *m/z* 446.1827. $[\alpha]_D^{23}$ = +56.5 (c = 0.100, $CHCl_3$). The diastereomeric ratio was determined by ^1H NMR analysis of the crude reaction mixture (CHO major 9.93 ppm, minor 9.22 ppm). The enantiomeric ratio was determined by SFC analysis of the corresponding alcohol (following $NaBH_4$ reduction) using a Chiralcel AD-H (25 cm × 0.46 cm) column (5% to 50% MeOH, linear gradient, 100 bar, 35 °C oven, flow = 4.0 mL/min); t_r = 6.48 min (major) and 7.80 min (minor).

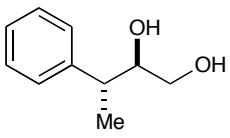


***N*-((1*S*,2*R*)-1-Formyl-2-phenylpropyl)-*N*'-(benzyloxycarbonyl)hydrazinecarboxylic acid benzyl ester:**

Procedure A: 3-Phenyl-but-2-enal (36.6 mg, 0.250 mmol), di-*tert*-butyl-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (92.8 mg, 0.300 mmol) and CH_2Cl_2 (500 μL) were charged into a 4 mL vial equipped with septum and a magnetic stir bar and then cooled to –30 °C. After stirring 15 min at –30 °C, the catalysts (2*R*)-2-*tert*-butyl-3-methylimidazolidin-4-one trichloroacetic acid salt (8.0 mg, 0.025 mmol) and D-proline (8.7 mg, 0.075 mmol) were added in one portion with stirring, and the resulting solution was stirred 36 h at –30 °C, at which point a solution of dibenzyl azodicarboxylate (90 wt%, 54.6 mg, 0.165 mmol) in CH_2Cl_2 (1.0 mL) was added, and the reaction mixture was allowed to warm to –15 °C and stirred for an additional 6 h at –15 °C then filtered through an iatrobead pad with EtOAc. Rapid purification (<15 min to avoid partial epimerization at α-amino stereocenter) by flash column chromatography using

iatrobeads as the stationary phase (10-50% EtOAc/hexanes) afforded the title compound as a white solid (60.3 mg, 82% yield, 8:1 dr, 99% ee).

Procedure B: 3-Phenyl-but-2-enal (36.6 mg, 0.250 mmol), di-*tert*-butyl-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (92.8 mg, 0.300 mmol) and CH_2Cl_2 (500 μL) were charged into a 4 mL vial equipped with septum and a magnetic stir bar and then cooled to –30 °C. After stirring 15 min at –30 °C, (2*R*)-2-*tert*-butyl-3-methylimidazolidin-4-one trichloroacetic acid salt (8.0 mg, 0.025 mmol) was added in one portion with stirring, and the resulting solution was stirred 36 h at –30 °C, at which point D-proline (8.7 mg, 0.075 mmol) was added, followed by a solution of dibenzyl azodicarboxylate (90 wt%, 54.6 mg, 0.165 mmol) in CH_2Cl_2 (1.0 mL) in one portion, and the reaction mixture was allowed to warm to –15 °C and stirred for an additional 6 h at –15 °C then filtered through an iatrobead pad with EtOAc. Rapid purification (<15 min to avoid partial epimerization at α-amino stereocenter) by flash column chromatography using iatrobeads as the stationary phase (10-50% EtOAc/hexanes) afforded the title compound as a white solid (58.8 mg, 80% yield, 10:1 dr, 99% ee). IR (film) 1713, 1293, 1213, 905 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ1.35-1.64 (m, 3H, CHC**H**$_3$), 3.29 (bs, 1H, PhMeCH), 4.75-5.18 (m, 1H, NC**H**CHO), 5.20 (bs, 4H, $PhCH_2$), 6.87 (bs, 1H, NH), 7.18-7.43 (m, 15H, PhH), 9.22 (bs, 1H, CHO); ^{13}C NMR (100 MHz, $CDCl_3$) δ20.3, 38.9, 67.7, 68.6, 72.0, 127.3, 127.6, 128.0, 128.1, 128.3, 128.4, 128.5, 128.8, 129.1, 135.3, 135.4, 141.8, 155.9, 156.6, 199.7 (additional peaks and line broadenings are observed due to rotameric species); HRMS (EI) exact mass calculated for ($C_{26}H_{26}N_2O_5$) requires *m/z* 446.1842, found *m/z* 446.1850. $[\alpha]_D^{23}$ = +15.1 (c = 0.100, $CHCl_3$). The diastereomeric ratio was determined by ^1H NMR analysis of the crude reaction mixture (CHO major 9.22 ppm, minor 9.93 ppm). The enantiomeric ratio was determined by SFC analysis of the corresponding alcohol (following $NaBH_4$ reduction) using a Chiralcel AD-H (25 cm × 0.46 cm) column (5% to 50% MeOH, linear gradient, 100 bar, 35 °C oven, flow = 4.0 mL/min); t_r = 7.17 min (minor) and 7.52 min (major). The relative stereochemistry was proven by chemical derivatization to a known related compound (see below).[4]

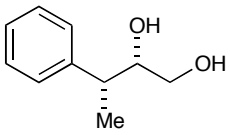


(2*R*,3*R*)-3-Phenylbutane-1,2-diol:

Procedure A: To a 4 mL vial equipped with a magnetic stir bar was added 3-phenyl-but-2-enal (36.6 mg, 0.250 mmol), and di-*tert*-butyl-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (88.4 mg, 0.290 mmol). This mixture was dissolved in chloroform (200 μL) and cooled to –30 °C. After stirring for 10 min, the catalysts (2*R*)-2-*tert*-butyl-3-methyl-imidazolidin-4-one trichloroacetic acid salt (8.0 mg, 25 μmol) and L-proline (8.7 mg, 75 μmol) were added. The reaction was allowed to stir for 24 h then warmed to room temperature after which a solution of nitrosobenzene (22.0 mg, 0.210 mmol) in DMSO (0.750 μL) was added. The reaction mixture was allowed to stir for 30 min (reaction progress followed by TLC and color change from green to orange), then transferred to solution of $NaBH_4$ (28.5 mg, 0.750 mmol) in ethanol (1.0 mL) and allowed to stir for 2 h at room temperature. Excess $NaBH_4$ was quenched with addition of water and extracted with diethyl ether, dried with $MgSO_4$ and concentrated under reduced pressure. The crude reaction mixture was dissolved in ethanol and 10% Pd on charcoal (18.0 mg, 50 wt%) was added. The reaction vessel was purged with hydrogen and stirred under a positive pressure of hydrogen (1 atm) for 12 h. The reaction mixture was filtered through a pad of celite and concentrated under reduced pressure. Purification using silica gel chromatography (50% to 100% Et_2O/pentane) gave the title compound as a colorless oil (25.0 mg, 73% yield, 11:1 dr, 99% ee).

Procedure B: To a 4 mL vial equipped with a magnetic stir bar was added 3-phenyl-but-2-enal (73.1 mg, 0.500 mmol), and di-*tert*-butyl-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (177 mg, 0.580 mmol). This mixture was dissolved in chloroform (400 μL) and cooled to –30 °C. After stirring for 10 min, a (2*R*)-2-*tert*-butyl-3-methyl-imidazolidin-4-one trichloroacetic acid salt (16.0 mg, 50 μmol) was added. The reaction was allowed to stir for 24 h then warmed to room temperature after which L-proline (17.2 mg, 150 μmol) followed by a solution of nitrosobenzene (44.0 mg, 0.420 mmol) in DMSO (1.50 mL) was added. The reaction mixture was allowed to stir for 30 min (reaction progress followed by TLC and color change from green to orange), then transferred to solution of $NaBH_4$ (57.0 mg, 1.50 mmol) in ethanol (2.0 mL) and allowed to stir for 2 h at room temperature. Excess $NaBH_4$ was quenched with addition of water and extracted with diethyl ether, dried with $MgSO_4$ and concentrated under reduced pressure. The crude reaction mixture was dissolved in ethanol and 10% Pd on charcoal (36.0 mg, 50 wt%) was added. The reaction vessel was purged with hydrogen and stirred under a positive pressure

of hydrogen (1 atm) for 12 h. The reaction mixture was filtered through a pad of celite and concentrated under reduced pressure. Purification using silica gel chromatography (10% to 100% EtOAc/hexanes) gave the title compound as a colorless oil (49.3 mg, 71% yield, 16:1 dr, 99% ee). IR (film) 3400, 2965, 2930, 2877, 1717, 1452, 1059 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.28 (d, 3H, J = 7.0 Hz, CH_3), 1.95 (bs, 1H, OH), 2.21 (bs, 1H, OH), 2.88 (app. quintet, 1H, J = 7.0 Hz, ArMeCH), 3.50-3.60 (m, 1H, C**H**OH), 3.70-3.90 (m, 2H, C$\mathbf{H}_2$OH), 7.20-7.50 (m, 5H, ArH); $[\alpha]_D^{23}$ = +14.9 (c = 0.90, $CHCl_3$). The spectroscopic data are consistent with previously reported data.[5] The diastereomeric ratio was determined by ^1H NMR analysis of the crude reaction mixture (CH_3, major 1.28 ppm minor 1.38 ppm). The enantiomeric ratio was determined by SFC analysis using a Chiralcel OJ-H (25 cm × 0.46 cm) column (5% to 10% MeOH, linear gradient, 100 bar, 35 °C oven, flow = 4.0 mL/min); t_r = 3.05 min (minor) and 3.29 min (major).

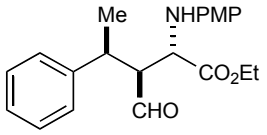


(2*S*,3*R*)-3-Phenylbutane-1,2-diol:

Procedure A: To a 4 mL vial equipped with a magnetic stir bar was added 3-phenyl-but-2-enal (36.6 mg, 0.250 mmol), and di-*tert*-butyl-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (88.4 mg, 0.290 mmol). This mixture was dissolved in chloroform (200 μL) and cooled to –30 °C. After stirring for 10 min, the catalysts (2*R*)-2-*tert*-butyl-3-methyl-imidazolidin-4-one trichloroacetic acid salt (8.0 mg, 25 μmol) and D-proline (8.7 mg, 75 μmol) were added. The reaction was allowed to stir for 24 h then warmed to room temperature after which a solution of nitrosobenzene (22.0 mg, 0.210 mmol) in DMSO (0.750 μL) was added. The reaction mixture was allowed to stir for 30 min (reaction progress followed by TLC and color change from green to orange), then transferred to solution of $NaBH_4$ (28.5 mg, 0.750 mmol) in ethanol (1.0 mL) and allowed to stir for 2 h at room temperature. Excess $NaBH_4$ was quenched with addition of water and extracted with diethyl ether, dried with $MgSO_4$ and concentrated under reduced pressure. The crude reaction mixture was dissolved in ethanol and 10% Pd on charcoal (18.0 mg, 50 wt%) was added. The reaction vessel was purged with hydrogen and stirred under a positive pressure of hydrogen (1 atm) for 12 h. The reaction mixture was filtered through a pad of celite and

concentrated under reduced pressure. Purification using silica gel chromatography (50% to 100% Et_2O/pentane) gave the title compound as a colorless oil (22.0 mg, 65% yield, 3:1 dr, 99% ee).

Procedure B: To a 4 mL vial equipped with a magnetic stir bar was added 3-phenyl-but-2-enal (73.1 mg, 0.500 mmol), and di-*tert*-butyl-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (177 mg, 0.580 mmol). This mixture was dissolved in chloroform (400 μL) and cooled to –30 °C. After stirring for 10 min, (2*R*)-2-*tert*-butyl-3-methyl-imidazolidin-4-one trichloroacetic acid salt (16 mg, 50 μmol) was added. The reaction was allowed to stir for 24 h then warmed to room temperature after which and D-proline (17.2 mg, 150 μmol) followed by a solution of nitrosobenzene (44.0 mg, 0.410 mmol) in DMSO (1.50 mL) was added. The reaction mixture was allowed to stir for 30 min (reaction progress followed by TLC and color change from green to orange), then transferred to solution of $NaBH_4$ (57.0 mg, 1.50 mmol) in ethanol (2.0 mL) and allowed to stir for 2 h at room temperature. Excess $NaBH_4$ was quenched with addition of water and extracted with diethyl ether, dried with $MgSO_4$ and concentrated under reduced pressure. The crude reaction mixture was dissolved in ethanol and 10% Pd on charcoal (36.0 mg, 50 wt%) was added. The reaction vessel was purged with hydrogen and stirred under a positive pressure of hydrogen (1 atm) for 12 h. The reaction mixture was filtered through a pad of celite and concentrated under reduced pressure. Purification using silica gel chromatography (10 to 100% EtOAc/hexanes) gave the title compound as a colorless oil (42.0 mg, 62% yield, 10:1 dr, 99% ee). IR (film) 3369, 2963, 2929, 2877, 1721, 1493, 1452, 1061 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.38 (d, 3H, J = 7.0 Hz, CH_3), 1.95 (bs, 1H, OH), 2.21 (bs, 1H, OH), 2.88 (app. quintet, J = 7.0 Hz, ArMeCH), 3.30-3.40 (m, 1H, C**H**OH), 3.50-3.55 (m, 1H, C**H**OH), 3.70-3.80 (m, 1H, C**H**OH), 7.20-7.50 (m, 5H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.3, 42.8 65.1, 76.1, 126.6 127.5, 128.7, 143.6; HRMS (EI+) exact mass calculated for ($C_{10}H_{14}O_2$) requires m/z 166.0994, found m/z 166.0994. $[\alpha]_D^{23}$ = –2.0 (c = 0.80, $CHCl_3$). The diastereomeric ratio was determined by ^1H NMR analysis of the crude reaction mixture (CH_3, major 1.38 ppm minor 1.28 ppm). The enantiomeric ratio was determined by SFC analysis using a Chiralcel AD-H (25 cm × 0.46 cm) column (5% to 10% MeOH, linear gradient, 100 bar, 35 °C oven, flow = 4.0 mL/min); t_r = 5.61 min (minor) and 5.91 min (major).

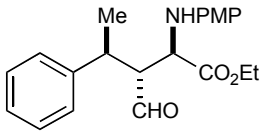


(2*S*,3*S*,4*S*)-Ethyl-2-(4-methoxyphenylamino)-3-formyl-2-4-phenylpentanoate:

Procedure A: To a 4 mL vial equipped with a magnetic stir bar was added 3-phenyl-but-2-enal (21.0 mg, 0.144 mmol) and di-*tert*-butyl-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (53.8 mg, 0.174 mmol). This mixture was dissolved in chloroform (400 μL) and cooled to –30 °C. After stirring for 10 min, the catalysts, (2*R*)-2-*tert*-butyl-3-methyl-imidazolidin-4-one trichloroacetic acid salt (5.1 mg, 16 μmol) and L-proline (5.5 mg, 48 μmol) were added and the reaction was allowed to stir for 24 hr. The reaction mixture was then warmed to room temperature and a premixed solution of (*E*)-ethyl 2-(4-methoxyphenylimino)ethanoate (36 mg, 0.174 mmol) in DMSO (1.5 mL) was added and the resulting mixture was allowed to stir at room temperature for 6 h. A premixed solution (1:1) of saturated NH_4Cl and diethyl ether was added to the reaction with vigorous stirring. The layers were separated and the organic phase was washed with brine. The combined organic phases were dried with $MgSO_4$, concentrated under reduced pressure and purified by chromatography on iatrobeads (10-30% EtOAc/hexane) to give the title compound as a colorless oil (44.0 mg, 86% yield, 14:1 dr, 99% ee).

Procedure B: To a 4 mL vial equipped with a magnetic stir bar was added 3-phenyl-but-2-enal (21.0 mg, 0.144 mmol) and di-*tert*-butyl-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (53.8 mg, 0.174 mmol). This mixture was dissolved in chloroform (200 μL) and cooled to –30 °C. After stirring for 10 min, (2*R*)-2-*tert*-butyl-3-methyl-imidazolidin-4-one trichloroacetic acid salt (5.1 mg, 16 μmol) was added as a solid and the reaction was allowed to stir for 24 hr. The reaction mixture was then warmed to room temperature and a premixed solution of (*E*)-ethyl 2-(4-methoxyphenylimino)ethanoate (36 mg, 0.174 mmol) and L-proline (5.5 mg, 48 μmol) in DMSO (1.5 mL) was added and the resulting mixture was allowed to stir at room temperature for 12 h. A premixed solution (1:1) of saturated NH_4Cl and diethyl ether was added to the reaction with vigorous stirring. The layers were separated and the organic phase was washed with brine. The combined organic phases were dried with $MgSO_4$, concentrated under reduced pressure and purified by chromatography on iatrobeads (10-50% pentane/diethyl ether) to give the title compound as a colorless oil (40.0 mg, 78% yield, 10:1 dr, 99% ee). IR (film) 2989, 2870, 1724,

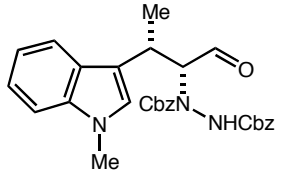
1513, 1239, 1142, cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.25 (dt, 3H, *J* = 4.5, 7.0 Hz, CH_2CH_3), 1.36 (d, 3H, *J* = 7.0 Hz, $CHCH_3$), 2.99 (m, 1H, ArMeCH), 3.45 (m, 1H, CHCHO), 3.72 (s, 3H, $ArOCH_3$), 3.97 (d, 1H, *J* = 4.5 Hz, CHCHN), 4.09-4.14 (m, 2H), 6.38 (d, 2H, *J* = 9.0 Hz, ArH), 6.70 (d, 2H, *J* = 9.5 Hz, ArH), 7.24-7.40 (m, 6H, ArH, NH), 9.83 (d, 1H, *J* = 2.0 Hz, CHO); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 19.9, 37.5, 55.6, 57.5, 59.7, 61.5, 114.7, 115.7, 127.6, 127.7, 128.8, 139.8, 143.3, 153.3, 171.8, 203.4; HRMS (EI+) exact mass calculated for ($C_{21}H_{25}O_4N$) requires *m/z* 355.1784, found *m/z* 355.1787. $[\alpha]_D^{23}$ = −3.60 (*c* = 2.80, $CHCl_3$). The diastereomeric ratio was determined by ^1H NMR analysis of the crude reaction mixture (CHO, major 9.83 ppm minor 9.53 ppm). The enantiomeric ratio was determined by SFC analysis using a Chiralcel OJ-H (25 cm × 0.46 cm) column (5% to 10% MeOH, linear gradient, 100 bar, 35 °C oven, flow = 4.0 mL/min); t_r = 6.51 min (major) and 6.96 min (minor).



((2*R*,3*R*,4*S*)-Ethyl-2-(4-methoxyphenylamino)-3-formyl-4-phenylpentanoate:

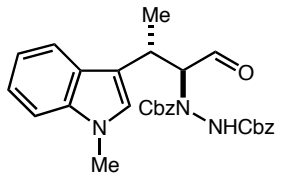
Procedure A: To a 4 mL vial equipped with a magnetic stir bar was added 3-phenyl-but-2-enal (21.0 mg, 0.144 mmol) and di-*tert*-butyl-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (53.8 mg, 0.174 mmol). This mixture was dissolved in chloroform (400 μL) and cooled to –30 °C. After stirring for 10 min, the catalysts, (2*R*)-2-*tert*-butyl-3-methyl-imidazolidin-4-one trichloroacetic acid salt (5.1 mg, 16 μmol) and D-proline (5.5 mg, 48 μmol) were added and the reaction was allowed to stir for 24 hr. The reaction mixture was then warmed to room temperature and a premixed solution of (*E*)-ethyl 2-(4-methoxyphenylimino)ethanoate (36 mg, 0.174 mmol) in DMSO (1.5 mL) was added and the resulting mixture was allowed to stir at room temperature for 6 h. A premixed solution (1:1) of saturated NH_4Cl and diethyl ether was added to the reaction with vigorous stirring. The layers were separated and the organic phase was washed with brine. The combined organic phases were dried with $MgSO_4$, concentrated under reduced pressure and purified by chromatography on iatrobeads (10-30% EtOAc/hexane) to give the title compound as a colorless oil (41.0 mg, 80% yield, 12:1 dr, 99% ee).

Procedure B: To a 4 mL vial equipped with a magnetic stir bar was added 3-phenyl-but-2-enal (21.0 mg, 0.144 mmol), di-*tert*-butyl 1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (53.8 mg, 0.174 mmol). This mixture was dissolved in chloroform (200 μL) and cooled to –30 °C. After stirring for 10 min, (2*R*)-2-*tert*-butyl-3-methyl-imidazolidin-4-one trichloroacetic acid salt (5.1 mg, 16 μmol) was added as a solid and the reaction was allowed to stir for 24 h. The reaction mixture was then warmed to room temperature and a premixed solution of (*E*)-ethyl 2-(4-methoxyphenylimino)ethanoate (36 mg, 0.174 mmol) and D-proline (5.5 mg, 48 μmol) in DMSO (1.5 mL) was added and the resulting mixture was allowed to stir at room temperature for 12 h. A premixed solution (1:1) of saturated NH_4Cl and diethyl ether was added to the reaction with vigorous stirring. The layers were separated and the organic phase was washed with brine. The combined organic phases were dried with $MgSO_4$, concentrated under reduced pressure and purified by chromatography on iatrobeads (10-50% pentane/diethyl ether) to give the title compound as a colorless oil (42.0 mg, 82% yield, 12:1 dr, 99% ee). IR (film) 2989, 2870, 1722, 1513, 1241, 1142, cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.22 (dt, 3H, J = 0.5, 7.0 Hz, $CH_2C\mathbf{H}_3$), 1.48 (d, 3H, J = 7.0 Hz, CH_3), 2.96 (m, 1H, ArCHMe), 3.49 (m, 1H, C**H**CHO), 3.76 (s, 3H, $ArOCH_3$), 4.19-4.14 (q, 2H, J = 7.0 Hz, $C\mathbf{H}_2CH_3$), 4.29 (d, 1H, J = 4.5 Hz, C**H**CNH), 6.63 (d, 2H, J = 8.5 Hz, ArH), 6.78 (d, 2H, J = 9.0 Hz, ArH), 7.32-7.18 (m, 6H, ArH, NH), 9.53 (d, 1H, J = 2.5 Hz, CHO); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 19.9, 37.7, 55.6, 57.1, 58.9, 61.5, 114.8, 115.8, 127.2, 127.8, 128.8, 140.1, 142.4, 153.2, 172.5, 202.9; HRMS (EI+) exact mass calculated for ($C_{21}H_{25}O_4N$) requires m/z 355.1784, found m/z 355.1790. $[\alpha]_D^{23}$ = +30.3 (c = 2.37, $CHCl_3$). The diastereomeric ratio was determined by ^1H NMR analysis of the crude reaction mixture (CHO, major 9.53 ppm minor 9.83 ppm). The enantiomeric ratio was determined by SFC analysis using a Chiralcel OJ-H (25 cm × 0.46 cm) column (5% to 10% MeOH, linear gradient, 100 bar, 35 °C oven, flow = 4.0 mL/min); t_r = 3.41 min (minor) and 3.66 min (major).



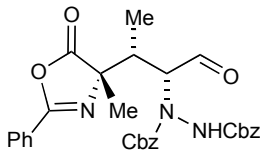
***N*-((1*R*,2*S*)-1-Formyl-2-(1-methyl-1*H*-indol-3-yl))-*N*'-(benzyloxycarbonyl)hydrazine carboxylic acid benzyl ester:** Crotonaldehyde (48 mg, 0.685 mmol), 1-methylindole (30.0 mg,

0.229 mmol) and CH_2Cl_2 (500 μL) were charged into 4 mL vial with magnetic stir bar and cooled to –60 °C. After stirring 15 min at –60 °C, the catalyst (2*S*,5*S*)-2-*tert*-butyl-5-benzyl-3-methylimidazolidin-4-one trifluoroacetic acid salt (8.3 mg, 0.023 mmol) was added in one portion with stirring, and the resulting solution was stirred 12 h at –60 °C, at which point L-proline (5.3 mg, 0.046 mmol) was added, along with a solution of dibenzyl azodicarboxylate (90 wt%, 227 mg, 0.685 mmol) in CH_2Cl_2 (500 μL), and the reaction mixture was allowed to warm to 0 °C. The reaction mixture was stirred further 24 h at 0 °C, and then quickly filtered through an iatrobead pad to stop the reaction. The crude mixture was concentrated by rotary evaporation and then purified quickly (<15 min to avoid partial epimerization at α-amino stereocenter) by flash column chromatography with iatrobeads as the stationary phase (20-30% EtOAc/hexanes) to yield the title compound as a white solid (107 mg, 94% yield, 14:1 dr, 99% ee). IR (film) 1710, 1454, 1283, 1212, 1051 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ1.38-1.78 (m, 3H, CHC**H**$_3$), 3.56-3.64 (m, 1H, ArMeCH), 3.78 (s, 3H, NCH_3), 4.71-4.94 (m, 1H, NC**H**CHO), 4.95-5.28 (m, 4H, $PhCH_2$), 6.20-6.83 (m, 1H, NH), 6.87-7.68 (m, 15H, ArH), 9.28 (bs, 1H, CHO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 29.8, 32.7, 67.7, 68.5, 71.8, 109.5, 114.7, 118.9, 119.3, 121.9, 126.5, 127.6, 128.0, 128.1, 128.4, 128.5, 128.5, 135.2 135.4, 137.1, 155.9, 156.7, 200.9 (additional peaks and line broadenings are observed due to rotameric species); HRMS (EI+) exact mass calculated for ($C_{29}H_{29}N_3O_5$) requires *m/z* 499.2107, found *m/z* 499.2094; $[\alpha]_D^{23}$ = –19.2 (c = 0.100, $CHCl_3$) The diastereomeric ratio was determined by ^1H NMR analysis of the crude reaction mixture (CHO major 9.28 ppm, minor 9.93 ppm). The enantiomeric ratio was determined by SFC analysis of the corresponding alcohol (following $NaBH_4$ reduction) using a Chiralcel AS-H (25 cm × 0.46 cm) column (5% to 25% MeOH, linear gradient, 100 bar, 35 °C oven, flow = 4.0 mL/min); t_r = 8.55 min (minor) and 10.36 min (major).



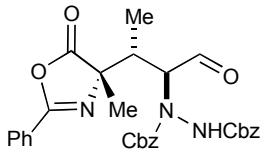
***N*-((1*S*,2*S*)-1-Formyl-2-(1-methyl-1*H*-indol-3-yl))-*N*'-(benzyloxycarbonyl)hydrazine carboxylic acid benzyl ester:** Crotonaldehyde (48 mg, 0.685 mmol), 1-methylindole (30.0 mg,

0.229 mmol) and CH_2Cl_2 (500 μL) were charged into 4 mL vial with magnetic stir bar and cooled to –60 °C. After stirring 15 min at –60 °C, the catalyst (2*S*,5*S*)-2-*tert*-butyl-5-benzyl-3-methylimidazolidin-4-one trifluoroacetic acid salt (8.3 mg, 0.023 mmol) was added in one portion with stirring, and the resulting solution was stirred 12 h at –60 °C, at which point D-proline (5.3 mg, 0.046 mmol) was added, along with a solution of dibenzyl azodicarboxylate (90 wt%, 227 mg, 0.685 mmol) in CH_2Cl_2 (500 μL) and the reaction mixture was allowed to warm to 0 °C. The reaction mixture was stirred further 24 h at 0 °C, and then quickly filtered through an iatrobead pad. The crude mixture was concentrated by rotary evaporation and then purified quickly (<15 min to avoid partial epimerization at α-amino stereocenter) by flash column chromatography with Davisil as the stationary phase (20-30% EtOAc/hexanes) to yield the title compound as a white solid (97.0 mg, 85% yield, 7:1 dr, 99% ee). IR (film) 1712, 1497, 1454, 1213, 1051, 909 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.35-1.58 (m, 3H, CHC**H**$_3$), 3.60-3.86 (m, 4H NCH_3, ArMeCH), 4.75-4.90 (m, 1H, NC**H**CHO), 4.95-5.28 (m, 4H, $PhCH_2$), 6.20-6.60 (m, 1H, N**H**), 6.81-7.65 (m, 16H, ArH), 9.93 (bs, 1H, CHO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2, 28.4, 32.6, 67.7, 68.3, 71.7, 109.5, 115.6, 118.9, 119.2, 121.9, 126.1, 126.5, 127.6 128.0, 128.1, 128.4, 128.5, 135.3, 135.5, 137.1, 155.7, 155.9, 198.0 (additional peaks and line broadenings are observed due to rotameric species); HRMS (EI) exact mass calculated for ($C_{29}H_{29}N_3O_5$) requires *m*/*z* 499.2107, found *m*/*z* 499.2092. $[\alpha]_D^{23}$ = –31.5 (c = 0.100, $CHCl_3$). The diasteriomeric ratio was determined by ^1H NMR analysis of the crude reaction mixture (CHO major 9.93 ppm, minor 9.28 ppm). The enantiomeric ratio was determined by SFC analysis of the corresponding alcohol following $NaBH_4$ reduction using a Chiralcel AS-H (25 cm × 0.46 cm) column (5% to 25% MeOH, linear gradient, 100 bar, 35 °C oven, flow = 4.0 mL/min); t_r = 8.87 min (minor) and 9.23 min (major).



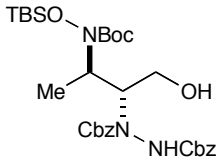
***N*-((1*R*,2*R*)-1-Formyl-2-((*R*)-4,5-dihydro-4-methyl-5-oxo-2-phenyloxazol-4-yl)-*N*'-(benzyloxycarbonyl)hydrazinecarboxylic acid benzyl ester:** Crotonaldehyde (31.0 μL, 0.375 mmol), 4-methyl-2-phenyl-5triisopropylsilanoxy-oxazole (41.5 mg, 0.125 mmol) water (4.5 μL, 0.250 mmol), and MeCN (250 μL) were charged into 4 mL vial with magnetic stir bar and cooled

to –40 °C. After stirring 15 min at –40 °C, the catalyst (2*S*,5*S*)-2-*tert*-butyl-5-benzyl-3-methylimidazolidin-4-one trichloroacetic acid salt (5.3 mg, 0.013 mmol) was added in one portion with stirring, and the resulting solution was stirred 12 h at –40 °C, at which point L-proline (3.0 mg, 0.026 mmol) was added, followed by a solution of dibenzyl azodicarboxylate (90 wt%, 124 mg, 0.375 mmol) in MeCN (700 μL), and the reaction mixture was allowed to warm to –15 °C. The reaction mixture was stirred further 10 h at –15 °C, and then quickly purified by preparatory TLC as the stationary phase (20% EtOAc/hexanes) to yield the title compound as a colorless semi-solid (52.0 mg, 77% yield, 5:1 dr, 99% ee). IR (film) 1721, 1651, 1389, 1283, 1218, 1004 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ0.71-1.26 (m, 3H, CHC**H**$_3$), 1.42-1.81 (m, 3H, CNC**H**$_3$), 2.92-3.15 (m, 1H, ArMeC**H**), 4.37-4.61 (m, 1H, NC**H**CHO), 4.95-5.30 (m, 4H, PhC**H**$_2$), 6.55-6.89 (m, 1H, N**H**), 7.18-8.10 (m, 15H, Ar**H**), 9.82-9.92 (m, 1H, C**H**O); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.9, 21.8, 40.2, 67.9, 68.6, 69.6, 70.8, 127.9, 128.0, 128.2, 128.4, 128.5, 128.7, 128.8, 128.9, 133.2, 133.4, 135.2, 135.5, 151.8, 156.2, 161.3, 179.7, 200.7 (additional peaks and line broadenings are observed due to rotameric species); HRMS (ESI) calculated for ($C_{30}H_{30}N_3O_7$+H) requires *m/z* 544.2084, found *m/z* 544.2079; $[\alpha]_D^{23}$ = +19.9 (c = 2.30, $CHCl_3$). The diasteriomeric ratio was determined by ^1H NMR analysis of the crude reaction mixture (CHO major 9.82-9.92 ppm, minor 9.66-9.81 ppm). The enantiomeric ratio was determined by SFC analysis using a Chiralcel AD-H (25 cm × 0.46 cm) column (5% to 10% MeCN, linear gradient, 100 bar, 35 °C oven, flow = 4.0 mL/min); t_r = 7.52 min (major) and 8.14 min (minor).



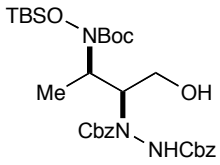
***N*-((1*S*,2*R*)-1-Formyl-2-((*R*)-4,5-dihydro-4-methyl-5-oxo-2-phenyloxazol-4-yl))-*N*'-(benzyloxycarbonyl)hydrazinecarboxylic acid benzyl ester:** Crotonaldehyde (31.0 μL, 0.375 mmol), 4-methyl-2-phenyl-5triisopropylsilanoxy-oxazole (41.5 mg, 0.125 mmol), water (4.5 μL, 0.250 mmol), and MeCN (250 μL) were charged into 4 mL vial with magnetic stir bar and cooled to –40 °C. After stirring 15 min at –40 °C, the catalyst (2*S*,5*S*)-2-*tert*-butyl-5-benzyl-3-methylimidazolidin-4-one trichloroacetic acid salt (5.3 mg, 0.013 mmol) was added in one portion with stirring, and the resulting solution was stirred 12 h at –40 °C, at which point D-

proline (3.0 mg, 0.026 mmol) was added, along with a solution of dibenzyl azodicarboxylate (90 wt%, 124 mg, 0.375 mmol) in MeCN (700 μL), and the reaction mixture was allowed to warm to –15 °C. The reaction mixture was stirred further 14 h at –15 °C, and then quickly purified by preparatory TLC as the stationary phase (20% EtOAc/hexanes) to yield the title compound as a colorless semi-solid (57.0 mg, 84% yield, 13:1 dr, 99% ee). IR (film) 1721, 1648, 1389, 1221, 1029, 679 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ0.82-1.21 (m, 3H, CHC**H**$_3$), 1.43-1.79 (m, 3H, CNCH_3), 2.90-3.10 (m, 1H, ArMeCH), 4.40-4.52 (m, 1H, NC**H**CHO), 4.95-5.30 (m, 4H, PhCH_2), 6.80-6.95 (m, 1H, NH), 7.18-8.09 (m, 15H, ArH), 9.66-9.81 (m, 1H, CHO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.5, 22.6, 40.2, 67.9, 68.6, 69.5, 70.9, 127.9, 128.1, 128.3, 128.5, 128.6, 128.8, 128.9, 129.2, 133.1, 134.6, 135.2, 135.4, 155.7, 156.2, 161.1, 178.8, 200.5 (additional peaks and line broadenings are observed due to rotameric species); HRMS (ESI) calculated for ($C_{30}H_{30}N_3O_7$ +H) requires *m/z* 544.2084, found *m/z* 544.2079. $[\alpha]_D^{23}$ = +2.3 (c = 1.55, $CHCl_3$). The diasteriomeric ratio was determined by ^1H NMR analysis of the crude reaction mixture (CHO major 9.66-9.81 ppm, minor 9.82-9.92 ppm). The enantiomeric ratio was determined by SFC analysis using a Chiralcel AS-H (25 cm × 0.46 cm) column (5% to 25% MeCN, linear gradient, 100 bar, 35 °C oven, flow = 4.0 mL/min); t_r = 6.86 min (major) and 7.97 min (minor).



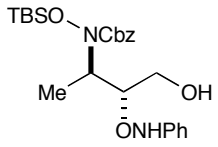
***N*-((2*R*,3*R*)-*tert*-Butyl-(*tert*-butyldimethylsilyloxy)-3-amino-4-hydroxybutan-2-ylcarbamoyl)-*N*'-(benzyloxycarbonyl)hydrazine carboxylic acid benzyl ester:** Crotonaldehyde (50.0 μL, 0.603 mmol), *tert*-butyl-(*tert*-butyldimethylsilyloxy)carbamate (50.0 mg, 0.201 mmol) and $CHCl_3$ (100 μL) were charged into 4 mL vial with magnetic stir bar and cooled to –20 °C. After stirring 15 min at –20 °C, the catalyst (2*S*,5*S*)-2-*tert*-butyl-5-benzyl-3-methylimidazolidin-4-one trifluoroacetic acid salt (7.5 mg, 0.020 mmol) was added in one portion with stirring, and the resulting solution was stirred 48 h at –20 °C, at which point L-proline (4.6 mg, 0.040 mmol) was added, followed by a solution of water (11.0 μL, 0.603 mmol) and dibenzyl azodicarboxylate (90 wt%, 200 mg, 0.603 mmol) in MeCN (1.5 mL). The reaction was allowed to warm to –10 °C, and was stirred an additional 8 h at –10 °C, before being transferred to a solution of $NaBH_4$ (68

mg, 1.8 mmol.) in ethanol (1.0 mL) pre-cooled to –20 °C, the resulting solution was allowed to stir for 30 min at –20 °C and then warm to room temperature. Excess $NaBH_4$ was quenched with addition of half-saturated ammonium chloride at –20 °C and then solution allowed to warm to room temperature and extracted with EtOAc, dried with $MgSO_4$ and concentrated under reduced pressure. The crude mixture was concentrated by rotary evaporation and then purified by flash column chromatography with iatrobeads as the stationary phase (20% EtOAc/hexanes) to yield the title compound as a colorless semi-crystalline solid (103 mg, 84% yield, 7:1 dr, 99% ee). IR (film) 2931, 1721, 1255, 909 cm^{-1}; ^1H NMR (400 MHz, 65 °C, $CDCl_3$) δ0.13-0.22 (m, 6H, SiC**H**$_3$), 0.90-1.00 (m, 9H, SiC(C**H**$_3$)$_3$), 1.17-1.35 (m, 4H, CO**H**, NCHC**H**$_3$), 1.42-1.52 (m, 9H, OC(C**H**$_3$)$_3$), 3.58-3.92 (m, 3H, C**H**$_2$OH, NC**H**), 4.58-4.70 (m, 1H, NC**H**), 5.10-5.30 (m, 4H, PhC**H**$_2$), 6.45-6.95 (m, 1H, N**H**), 7.25-7.43 (m, 10H, Ar**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.4, 15.3, 18.0, 25.9, 28.2, 58.1, 59.7, 64.0, 68.2, 68.9, 82.2, 128.2, 128.2, 128.4, 128.5, 128.6, 128.7, 135.2, 135.4, 155.0, 155.9, 156.8 (additional peaks and line broadenings are observed due to rotameric species); HRMS (ESI) exact mass calculated for ($C_{31}H_{48}N_3O_8Si$+H) requires *m*/*z* 618.3211, found *m*/*z* 618.3209. $[\alpha]_D^{23}$ = –5.6 (c = 0.950, $CHCl_3$). The diasteriomeric ratio was determined by ^1H NMR of the crude reaction mixture before $NaBH_4$ reduction (CHO major 9.60-9.69 ppm, minor 9.75-9.81 ppm). The enantiomeric ratio was determined by SFC analysis of the alcohol using a Chiralcel OJ-H (25 cm × 0.46 cm) column (5-10% MeOH, 100 bar, 35 °C oven, flow = 4.0 mL/min); t_r = 2.31 min (major) and 2.95 min (minor).



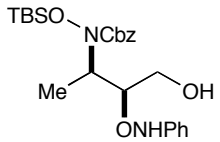
***N*-((2*R*,3*S*)-*tert*-Butyl-(*tert*-butyldimethylsilyloxy)-3-amino-4-hydroxybutan-2-ylcarbamoyl)-*N'*-(benzyloxycarbonyl)hydrazine carboxylic acid benzyl ester:** Crotonaldehyde (50.0 μL, 0.603 mmol), *tert*-butyl-(*tert*-butyldimethylsilyloxy)carbamate (50.0 mg, 0.201 mmol) and $CHCl_3$ (100 μL) were charged into 4 mL vial with magnetic stir bar and cooled to –20 °C. After stirring 15 min at –20 °C, the catalyst (2*S*,5*S*)-2-*tert*-butyl-5-benzyl-3-methylimidazolidin-4-one trifluoroacetic acid salt (7.5 mg, 0.020 mmol) was added in one portion with stirring, and the resulting solution was stirred 48 h at –20 °C, at which point D-proline (4.6 mg, 0.040 mmol) was

added, followed by a solution of water (11.0 μL, 0.603 mmol) and dibenzyl azodicarboxylate (90 wt%, 200 mg, 0.603 mmol) in MeCN (1.5 mL). The reaction mixture was allowed to warm to –10 0 °C. and was stirred an additional 8 h at –10 °C, before being transferred to solution of $NaBH_4$ (68 mg, 1.8 mmol.) in ethanol (1.0 mL) pre-cooled to –20 °C, the resulting solution allowed to stir for 30 min at –20 °C and then warm to room temperature. Excess $NaBH_4$ was quenched with addition of half-saturated ammonium chloride at –20 °C and then solution allowed to warm to room temperature and extracted with EtOAc, dried with $MgSO_4$ and concentrated under reduced pressure. The crude mixture was concentrated by rotary evaporation and then purified by flash column chromatography with iatrobeads as the stationary phase (20% EtOAc/hexanes) to yield the title compound as a colorless semi-crystalline solid (107 mg, 87% yield, 8:1 dr, 99% ee). IR (film) 2931, 1730, 1257, 840 cm^{-1}; ^1H NMR (400 MHz, 65 °C, $CDCl_3$) δ 0.12-0.22 (m, 6H, SiC**H**$_3$), 0.85-0.99 (m, 9H, SiC(C**H**$_3$)$_3$), 1.17-1.32 (m, 4H, CO**H**, NCHC**H**$_3$), 1.39-1.50 (m, 9H, OC(C**H**$_3$)$_3$), 3.40-3.85 (m, 2H, C**H**$_2$OH), 3.91-4.10 (s, 1H, NC**H**), 4.60-4.78 (m, 1H, NC**H**), 5.10-5.30 (m, 4H, PhC**H**$_2$), 7.15-7.22 (m, 1H, N**H**), 7.25-7.43 (m, 10H, Ar**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.3, 18.0, 19.0, 25.9, 28.2, 59.5, 60.3, 60.6, 68.1, 68.3, 82.4, 127.7, 127.8, 127.9, 128.1, 128.5, 128.6, 135.3, 135.9, 155.5, 158.1, 158.4 (additional peaks and line broadenings are observed due to rotameric species); HRMS (ESI) exact mass calculated for ($C_{31}H_{48}N_3O_8Si$ +H) requires *m/z* 618.3211 , found *m/z* 618.3211. $[\alpha]_D^{23}$ = –10.3 (c = 0.730, $CHCl_3$) The diastereomeric ratio was determined by ^1H NMR of the crude reaction mixture before $NaBH_4$ reduction (CHO minor 9.60-9.69 ppm, major 9.75-9.81 ppm). The enantiomeric ratio was determined by SFC analysis using a Chiralcel OJ-H (25 cm × 0.46 cm) column (5% MeCN, 100 bar, 35 °C oven, flow = 4.0 mL/min); t_r = 2.75 min (minor) and 3.21 min (major).



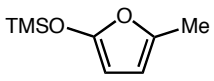
(2*R*,3*R*)-Benzyl-(*tert*-butyldimethylsilyloxy)-3-(*N*-phenyl-aminooxy)-4-hydroxybutan-2-ylcarbamate: Crotonaldehyde (10.0 μL, 0.118 mmol), benzyl-(*tert*-butyldimethylsilyloxy)carbamate (50.0 mg, 0.177 mmol) and $CHCl_3$ (180 μL) were charged into 4 mL vial with magnetic stir bar and cooled to –20 °C. After stirring 15 min at –20 °C, the

catalyst (2*S*,5*S*)-2-*tert*-butyl-5-benzyl-3-methylimidazolidin-4-one trifluoroacetic acid salt (4.3 mg, 0.012 mmol) was added in one portion with stirring, and the resulting solution was stirred 48 h at –20 °C, at which point DMSO (600 μL) and $NaHCO_3$ (5.0 mg, 0.060 mmol) were added and the solution was stirred vigorously and allowed to warm to room temperature over 30 min. L-proline (4.1 mg, 0.036 mmol) and nitrosobenzene (10.1 mg, 0.094 mmol) were added together in one portion, and the reaction mixture was stirred further 30 min at room temperature, and then ethanol (1.0 mL) was added followed by an excess of $NaBH_4$ (18 mg, 0.48 mmol). After stirring 30 min at room temperature, the reaction was quenched with saturated NH_4Cl solution and extracted with EtOAc (3 × 1 mL) then dried over Na_2SO_4. The crude mixture was concentrated by rotary evaporation and then purified by preparatory TLC (30% EtOAc/hexanes) to yield the title compound as a slightly yellow semi-crystalline solid (32.0 mg, 74% yield, 17:1 dr, 99% ee). Note: yield can vary depending on the extent of NO bond cleavage during reductive workup. IR (film) 2929, 1706, 1463, 1253, 1062, 835 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ0.11 (s, 3H, $SiCH_3$), 0.15 (s, 3H, $SiCH_3$), 0.92 (s, 9H, $SiC(CH_3)_3$), 1.38 (d, 3H, *J* = 7.0 Hz, NCHC**H**$_3$), 2.64 (bs, 1H, O**H**), 3.85 (dd, 1H, *J* = 5.3, 13 Hz, CH**H**OH), 3.93 (d, 1H, *J* = 13 Hz, C**H**HOH), 3.99 (m, 1H, C**H**OH), 4.48 (dq, 1H, *J* = *J* = 7.0 Hz , NCH), 5.17 (s, 2H, $PhCH_2$), 6.95 (m, 2H, ArH), 7.23-7.42 (m, 9H, ArH, ArNH); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.6, –4.3, 15.3, 18.2, 25.8, 56.3, 61.1, 68.3, 86.4, 114.5, 122.2, 128.4, 128.5, 128.7, 128.9, 135.4, 148.3, 159.5; HRMS (ESI) exact mass calculated for ($C_{24}H_{36}N_2O_5Si$+H) requires *m*/*z* 461.2472, found *m*/*z* 461.2476. $[\alpha]_D^{23}$ = +0.89 (c = 0.600, $CHCl_3$). The diastereomeric ratio was determined by ^1H NMR of the crude reaction mixture after $NaBH_4$ reductive workup (NCH major dq, 4.48 ppm, minor m, 4.60-4.62 ppm). The enantiomeric ratio was determined by SFC analysis using a Chiralcel AD-H (25 cm × 0.46 cm) column (5% to 10% MeOH, linear gradient, 100 bar, 35 °C oven, flow = 4.0 mL/min); t_r = 5.78 min (minor) and 6.56 min (major).

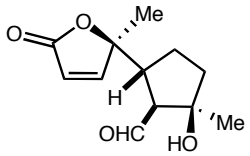


(2*R*,3*S*)-Benzyl-(*tert*-butyldimethylsilyloxy)-3-(*N*-phenyl-aminooxy)-4-hydroxybutan-2-ylcarbamate: Crotonaldehyde (10.0 μL, 0.118 mmol), benzyl-(*tert*-

butyldimethylsilyloxy)carbamate (50.0 mg, 0.177 mmol) and $CHCl_3$ (180 μL) were charged into 4 mL vial with magnetic stir bar and cooled to –20 °C. After stirring 15 min at –20 °C, the catalyst (2*S*,5*S*)-2-*tert*-butyl-5-benzyl-3-methylimidazolidin-4-one trifluoroacetic acid salt (4.3 mg, 0.012 mmol) was added in one portion with stirring, and the resulting solution was stirred 48 h at –20 °C, at which point DMSO (600 μL) and $NaHCO_3$ (5.0 mg, 0.060 mmol) were added and the solution was stirred vigorously and allowed to warm to room temperature over 30 min. D-proline (4.1 mg, 0.036 mmol) and nitrosobenzene (10.1 mg, 0.094 mmol) were added together in one portion, and the reaction mixture was stirred further 30 min at room temperature, and then ethanol (1.0 mL) was added followed by an excess of $NaBH_4$ (18 mg, 0.48 mmol). After stirring 30 min at room temperature, the reaction was quenched with saturated NH_4Cl solution and extracted with EtOAc (3 × 1 mL) then dried over Na_2SO_4. The crude mixture was concentrated by rotary evaporation and then purified by preparatory TLC (30% EtOAc/hexanes) to yield the title compound as a slightly yellow semi-crystalline solid (31.0 mg, 71% yield, 14:1 dr, 99% ee). Note: yield can vary depending on the extent of NO bond cleavage during reductive workup. IR (film) 2952, 1709, 1471, 1301, 1252, 1062, 835 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.13 (s, 3H, $SiCH_3$), 0.16 (s, 3H, $SiCH_3$), 0.94 (s, 9H, $SiC(CH_3)_3$), 1.32 (d, 3H, J = 7.0 Hz, $NCHCH_3$), 2.95 (bs, H, O**H**), 3.79 (m, 1H, C**H**OH), 4.10-4.14 (m, 1H, CH**H**OH), 4.18 (d, 1H, J = 13 Hz, C**H**HOH), 4.60-4.62 (m, 1H, NCH), 5.07-5.15 (m, 2H, $PhCH_2$), 6.96-7.01 (m, 2H, ArH), 7.13-7.31 (m, 8H, ArH), 7.42 (s, 1H, ArNH); ^{13}C NMR (100 MHz, $CDCl_3$) δ–4.4, –4.0, 15.5, 18.4, 25.9, 56.6, 63.5, 68.0, 81.4, 114.8, 122.7, 128.2, 128.3, 128.3, 128.9, 135.6, 147.8, 160.7; HRMS (ESI) exact mass for ($C_{24}H_{36}N_2O_5Si$ +H) requires m/z 461.2472 , found m/z 461.2476. $[\alpha]_D^{23}$ = –19.4 (c = 1.15, $CHCl_3$). The diastereomeric ratio was determined by ^1H NMR of the crude reaction mixture after $NaBH_4$ reductive workup (C**H**N minor dq, 4.48 ppm, major m, 4.60-4.62 ppm). The enantiomeric ratio was determined by SFC analysis using a Chiralcel AD-H (25 cm × 0.46 cm) column (5% to 10% MeOH, linear gradient, 100 bar, 35 °C oven, flow = 4.0 mL/min); t_r = 3.94 min (minor) and 7.10 min (major).

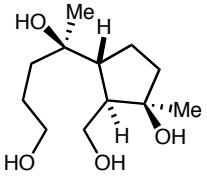


(5-Methylfuran-2-yloxy)trimethylsilane (6): α-Angelica lactone (9.81 g, 100 mmol), dry Et_2O (50.0 mL), and Et_3N (14.4 ml, 103 mmol) were charged into a dry 250 mL round-bottom flask with magnetic stir bar under argon. Contents of flask were cooled to 0 °C. Freshly distilled TMSCl (15.2 mL 102 mmol) was added slowly with stirring, and the resulting solution was allowed to stir overnight gradually warming to ambient temperature. The reaction mixture was filtered, and the solids were washed with dry Et_2O. Filtrate was then concentrated by rotary evaporation and then distilled (44-43 °C, 4 mm Hg) to afford the title compound as a colorless oil (14.8 g, 95% yield). All physical and spectral[6] properties were consistent with reported literature values.



(1*S*,2*R*,5*R*)-5-((*R*)-2,5-Dihydro-2-methyl-5-oxofuran-2-yl)-2-hydroxy-2-methylcyclopentane carbaldehyde (4): 5-Hexen-2-one (250 mg, 2.54 mmol), *E*-crotonaldehyde (267 mg, 3.81 mmol) and CH_2Cl_2 (2.50 mL) were charged into dry 10 mL round-bottom flask equipped with nitrogen inlet, magnetic stirbar and reflux condenser. The solvent was degassed by bubbling a stream of argon into flask for 15 min. Second generation Grubbs catalyst was added (11 mg, 0.013 mmol) and contents of flask heated to 40 °C. After five min stirring at 40 °C, evolution of gas was observed. When evolution of gas had ceased, reflux condenser was removed and contents of flask heated at 35 °C an additional 2 h with nitrogen sweep while flask was vented to open atmosphere (to remove excess crotonaldehyde). Contents of flask were cooled to –50 °C. After five min (2*S*,5*S*)-2-*tert*-butyl-5-benzyl-3-methylimidazolidin-4-one 2-4-dinitrobenzoic acid salt (91.6 mg, 0.200 mmol) was added in one portion as a solution in CH_2Cl_2 (2.00 mL), followed by water (36.0 μL, 2.02 mmol). The resulting solution was stirred another five min at –50 °C at which point (5-methylfuran-2-yloxy)trimethylsilane **6** (158 mg, 1.01 mmol) was added in three equal portions over 12 h. The reaction mixture was further stirred 12 h at –50 °C, and then L-proline (34.5 mg, 0.300 mmol) was added along with EtOAc (4.00 mL). The reaction was allowed to warm to ambient temperature and stirred for 24 h until reaction complete by TLC. The entire reaction mixture was concentrated by rotary evaporation and then purified by flash

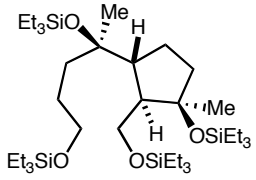
column chromatography (50-90% Et_2O/pentane) to yield the title compound as a colorless oil (145 mg, 64% yield, 5:1 dr, 95% ee). IR (film) 3463, 2968, 1737, 1720, 1379, 1264, 1109, 951 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.28-38 (m, 1H, C**H**HCH_2), 1.40 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 1.68-1.75 (m, 2H, C**H**HCH_2), 1.89 (bs, 1H, O**H**), 1.90-2.05 (m, 1H, C**H**HCH_2), 2.61 (dd, *J* = 2.0, 8.4 Hz, 1H, C**H**CH), 3.10 (ddd, *J* = 10.2, 8.8, 5.2 Hz, 1H, CHC**H**), 6.11 (d, *J* = 6.0 Hz, 1H, CH=C**H**), 7.36 (dd, *J* = 2.0, 6.0 Hz, 1H, C**H**=CH), 9.86 (d, *J* = 2.0 Hz, 1H, CHO); ^{13}C NMR (100 MHz, $CDCl_3$) δ23.4, 24.3, 27.3, 41.2, 44.3, 61.8, 82.5, 90.1, 121.8, 158.9, 172.2, 203.2; HRMS (EI) exact mass calculated for ($C_{12}H_{16}O_4$) requires *m/z* 224.1049, found *m/z* 224.1051. $[\alpha]_D^{23}$ = –12.4 (c = 0.094, $CHCl_3$). The diastereomeric ratio was determined by ^1H NMR analysis of the crude reaction mixture (CHO major = d, 9.86 ppm; CHO minor = d, 9.81 ppm). The enantiomeric ratio was determined by chiral GLC of crude reaction mixture prior to the addition of L-proline (Varian CP-Chirasil Dex-CB 130 °C isotherm 7 min, then 0.7 °C/min to 180 °C) relative to a racemic sample where t_r = 57.9 min (minor) and t_r = 59.1 min (major).



(1*R*,2*R*,3*R*)-2-(Hydroxymethyl)-3-((*R*)-2,5-dihydroxypentan-2-yl)-1-methylcyclopentanol: Butenolide **4** (600 mg, 2.67 mmol) was charged into a dry 25 mL flask along with reagent grade ethanol (10 mL) and 5% Pd/C (600 mg, 100 wt%, Engelhard code 3645). The flask was then gas evacuated and purged with hydrogen gas (~1 atm) and the resulting solution was stirred for 12 h at room temperature. The reaction mixture was directly filtered over Florisil to remove Pd/C and the filtrate was concentrated and purified by passing it through a silica gel plug (100% Et_2O) to remove baseline impurities. Upon concentration, the corresponding butanolide ((1*S*,2*R*,5*R*)-5-((*R*)-tetrahydro-2-methyl-5-oxofuran-2-yl)-2-hydroxy-2-methylcyclopentane carbaldehyde) was obtained as a pure white solid (589 mg, 97% yield). IR (film) 3464, 2970, 1758, 1715, 937 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 1.53-1.61 (m, 1H, C**H**HCH_2), 1.75-1.78 (dd, 2H *J* = 8.4, 6.0 Hz, C**H**HCH_2), 1.86-1.96 (bs, 1H, O**H**), 1.94-2.01 (m, 1H, C**H**HCH_2), 2.06-2.18 (m, 2H, C**H**HCH_2), 2.56-2.74 (m, 3H, C**H**CH, $CO_2C\mathbf{H}_2CH_2$), 3.01-3.07 (m, 1H, CHC**H**), 9.85 (d, *J* = 3.0 Hz, 1H, CHO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.6, 25.4, 27.2,

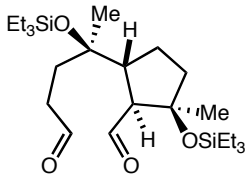
28.8, 31.1, 41.8, 47.5, 62.0, 82.8, 87.8, 176.3, 203.8; HRMS (EI+) exact mass calculated for ($C_{12}H_{18}O_4$–H_2O) requires *m/z* 208.1099, found *m/z* 208.1097. $[\alpha]_D^{23}$ = –79.6 (c = 0.920, EtOH).

The butanolide obtained from the previous step (589 mg, 2.60 mmol) was immediately charged into a dry 50 mL flask along with dry THF (25 mL) and then cooled to 0 °C with stirring. A 2.0 M solution of $LiAlH_4$ in THF (5.2 mL, 10.4 mmol) was added dropwise over 10 min. The resulting solution was allowed to warm gradually to room temperature and then stirred for 12 h. The slurry was then quenched drop-wise carefully with water (320 μL), then 15% NaOH (320 μL), followed again by water (960 μL) to precipitate the aluminum salts from the reaction. After filtration, the organic filtrate was retained, and the solids were dissolved in a concentrated aqueous Rochelle's salt solution and stirred for 30 min, then extracted 3× with CH_2Cl_2, the organic extracts were combined with the organic filtrate and dried with Na_2SO_4, then purified via flash chromatography (10-20% EtOH/CH_2Cl_2) to afford the title compound as a colorless oil (512 mg, 85% yield over 2 steps). IR (film) 3366, 2876, 1375, 1058, 1023 cm^{-1}; δ 3464, 2970, 1758, 1715, 937 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ1.15 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.41-1.70 (m, 7H, CH_2CHH), 1.73-1.79 (m, 2H, CH_2CHH), 1.83-1.89 (m, 1H, CHCH), 2.07-2.14 (td, *J* = 9.3, 6.9 Hz, 1H, CHCH), 3.49-3.62 (m, 3H, CHHOH), 3.79-3.79 (m, 1H, CHHOH); ^{13}C NMR (100 MHz, CD_3OD) δ 25.9, 26.4, 27.7, 28.1, 35.2, 41.9, 52.3, 54.8, 63.8, 64.3, 74.7, 82.3; HRMS (EI+) exact mass calculated for ($C_{12}H_{24}O_4$) requires *m/z* 232.1675, found *m/z* 232.1624. $[\alpha]_D^{23}$ = –5.2 (c = 0.760, EtOH).



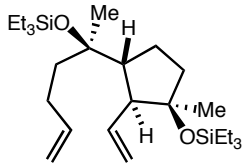
(1*R*,2*R*,3*R*)-2-(Triethyl-silanyloxymethyl)-3-((*R*)-2,5-bis-(triethylsilanyloxypentan-2-yl)-1-methylcyclopentanol-(triethylsilyl) ether: Tetraol from previous step (160 mg, 0.690 mmol) was charged into a dry 25 mL flask along with CH_2Cl_2 (4.0 mL) and lutidine (968 μL, 8.28 mmol). The flask was then cooled to 0 °C and TESOTf was added dropwise over 10 min. The resulting solution was stirred for 45 min at 0 °C. The reaction was quenched with sodium bicarbonate and extracted with CH_2Cl_2 (2 × 3 mL) then washed with water (2 × 3 mL). The

combined organic layers were dried and concentrated and then purified by flash silica gel chromatography (10% Et_2O/pentane) to afford the title compound as a colorless oil (449 mg, 95% yield). IR (film) 2954, 2876, 1458, 1238, 1096, 1006 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ0.50-0.65 (m, 24H, $SiC\mathbf{H}_2CH_3$), 0.91-1.01 (m, 36H, $SiCH_2C\mathbf{H}_3$) 1.18 (s, 3H, CH_3), 1.39 (s, 3H, CH_3) 1.43-1.80 (m, 9H, C**H**HCH_2, CHC**H**) 1.80-1.86 (m, 1H, C**H**CH), 3.52-3.59 (m, 3H, C**H**HOSi), 3.84-3.89 (m, 1H, C**H**HOSi); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.6, 6.6, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 24.8, 26.9, 28.2, 29.1, 38.8, 42.1, 48.8, 52.9, 63.6, 64.0, 78.0, 83.5; HRMS (EI+) exact mass calculated for ($C_{36}H_{80}O_4Si_4$–CH_2CH_3) requires *m/z* 659.4742, found *m/z* 659.4714. $[\alpha]_D^{23}$ = –10.2 (c = 0.844, $CHCl_3$).

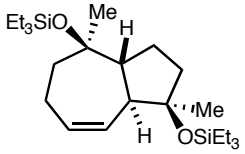


(1*S*,2*R*,5*R*)-5-((*R*)-4-Formyl-2-triethyl-silanyloxybutan-2-yl)-2-triethyl-silanyloxy-2-methylcyclo- pentanecarbaldehyde 8: A 2.0 M solution of oxalyl chloride (2.28 mL, 4.56 mmol) was charged into a dry 15 mL Schlenk flask under argon sweep along with dry CH_2Cl_2 (6.0 mL), then cooled to –78 °C with stirring. Dry DMSO (649 μL, 9.11 mmol) was added as a solution in dry CH_2Cl_2 (4.0 mL). After 15 min, gas evolution had ceased, and a pre-cooled solution of (1*R*,2*R*,3*R*)-2-(triethyl-silanyloxymethyl)-3-((*R*)-2,5-bis-(triethylsilanyloxypentan-2-yl)-1-methylcyclopentanol (triethylsilyl) ether in CH_2Cl_2 (4.0 mL) was added dropwise, then rinsed with dry CH_2Cl_2 (2 × 1.0 mL). The reaction was allowed to stir 20 min at –78 °C then warmed to –40 °C and stirred another 20 min at that temperature. The flask was once again cooled to –78 °C and treated dropwise with triethylamine (2.52 mL, 18.1 mmol). The reaction was stirred 15 min further at –78 °C then allowed to gradually warm to room temperature (with the precipitation of amine-HCl salt). The contents of the reaction flask were poured directly into 25 mL of ice-cold water and then extracted with CH_2Cl_2 (2 × 15 mL). After washing combined organics with brine solution, they were dried with Na_2SO_4, then directly filtered over a pad of silica gel and concentrated. The bisaldehyde **8** formed was unstable, and therefore quickly used in the next step without prolonged storage. IR (film) 2956, 2876, 1721, 1458, 1238, 1121, 1041

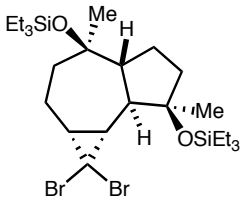
cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.57-0.62 (m, 12H, $SiCH_2CH_3$), 0.92-0.98 (m, 18H, $SiCH_2CH_3$), 1.06 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.62-1.91 (m, 6H, $CHCH_2$), 2.45-2.50 (m, 3H, CHCHO, CHCH), 2.71-2.76 (m, 1H, CHCHCHO), 9.68 (d, J = 3.6 Hz, 1H, CHO), 9.79 (t, J = 0.8 Hz, 1H, CHO); ^{13}C NMR (100 MHz, $CDCl_3$) δ6.7, 7.0, 7.1, 7.2, 24.9, 26.4, 27.8, 33.2, 40.0, 42.2, 47.5, 63.2, 76.3, 86.0, 201.7, 205.2; HRMS (EI+) exact mass calculated for ($C_{24}H_{49}O_4Si_2$–CH_2CH_3) requires m/z 427.2694, found m/z 427.2685. $[\alpha]_D^{23}$ = –19.5° (c = 0.556, $CHCl_3$).



(1*R*,2*S*,3*R*)-3-((*R*)-2-(Triethyl-silanyloxy)-hex-5-en-2-yl)-1-methyl-2-vinylcyclopentanol-(triethylsilyl) ether: To a dry 25 mL flask under argon was added methyltriphenylphosphonium bromide (1.63 g, 4.56 mmol) followed by 6 mL of dry THF. The flask and its contents were then cooled to 0 °C. A 2.5 M solution of *n*-butyl lithium (1.78 mL, 4.45 mmol) was added dropwise (resulting in a bright orange color) and allowed to warm to room temperature and age 30 min. The contents of the flask were again cooled to 0 °C at which point the previous bisaldehyde was added as a solution in THF (6.0 mL). The reaction was allowed to warm to room temperature and further stirred 12 h. When the reaction was deemed complete by TLC, the entire reaction slurry was concentrated and then purified directly via flash chromatography (10% EtOAc/hexanes) to afford the title compound as a colorless oil (371 mg, 72% yield over two steps). IR (film) 2955, 2876, 1458, 1238, 1122, 1009 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.53.-0.62 (m, 12H, $SiCH_2CH_3$), 0.92-0.99 (m, 18H, $SiCH_2CH_3$), 1.15 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 1.42-1.52 (m, 3H, $CHCH_2$), 1.62-1.85 (m, 4H, $CHCH_2$, CHCH), 1.96-2.17 (m, 3H, CH-allyl), 4.90-5.03 (m, 4H, $CH=CH_2$), 5.76-5.85 (m, 2H, $CH=CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$, 77.2) δ6.7, 7.0, 7.2, 7.3, 24.4, 25.7, 26.6, 29.3, 40.9, 42.4, 50.8, 57.63, 78.0, 84.9, 113.9, 115.0, 139.3, 142.4; HRMS (EI+) exact mass calculated for ($C_{26}H_{52}O_2Si_2$) requires m/z 452.3506, found m/z 452.3515. $[\alpha]_D^{23}$ = –29.1 (c = 0.689, $CHCl_3$).

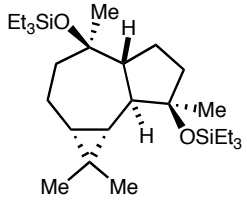


(*Z*,1*R*,3a*R*,4*R*,8a*S*)-1,2,3,3a,4,5,6,8a-Octahydro-1,4-dimethylazulene-1,4-diol-1,4-bis(triethyl-silyl) ether (9): The diene from the previous step (185 mg, 0.409 mmol) and dichloroethane (41 mL) were charged into a dry 100 mL round-bottom flask fitted with a reflux condenser and stirbar. The solvent was degassed by bubbling a stream of argon through the flask for 15 min. Grubbs second generation catalyst (52 mg, 0.0614 mmol) was added in one portion and the contents of the flask placed under argon. The reaction was heated to 70 °C for 1 hour and filtered over a pad of Florisil then concentrated. The crude product was purified by silica flash column chromatography (10% Et_2O/pentane) to yield **8** as a colorless oil (135 mg, 78% yield). IR (film) 2954, 2875, 1457, 1374, 1235, 1101, 1009 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.49-0.57 (m, 12 H, $SiC\mathbf{H}_2CH_3$), 0.88-0.94 (m, 18 H, $SiCH_2C\mathbf{H}_3$), 1.14 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.39-1.45 (m, 1H, $C\mathbf{H}HCH_2$), 1.47-1.54 (m, 1H, $C\mathbf{H}HCH_2$), 1.61-1.82 (m, 5 H, $C\mathbf{H}HCH_2$, $C\mathbf{H}CH$), 1.84-1.92 (m, 1H, CH-allyl), 2.10-2.21 (m, 2H, CH-allyl), 5.68-5.75 (m, 1H, CH=C**H**), 5.80-5.84 (m, 1H, C**H**=CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 6.7, 7.0, 7.1, 7.2, 21.6, 23.7, 23.9, 26.5, 40.2, 42.6, 52.1, 53.5, 78.4, 82.9, 130.1, 132.5; HRMS (EI+) exact mass calculated for ($C_{24}H_{48}O_2Si_2$) requires *m/z* 424.3193, found *m/z* 424.3171. $[\alpha]_D^{23}$ = +10.3 (c = 0.178, $CHCl_3$).



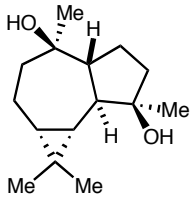
(1a*R*,4*R*,4a*R*,7*R*,7a*R*,7b*S*)-1,1-Dibromo-decahydro-4,7-dimethyl-1*H*-cyclopropa[*e*]azulene-4,7-diol-4,7-bis(triethyl-silyl) ether: A dry 4 mL vial equipped with stirbar, was charged with KO*t*Bu (66.4 mg, 0.590 mmol), **9** (50 mg, 0.118 mmol) and anhydrous hexane (400 μL). The vial was then cooled to 0 °C, and bromoform (149 mg, 0.590 mmol) was added as a solution in hexane (400 μL) over one minute. The heterogeneous white mixture was allowed to age at 0 °C for 2 h. The reaction was quenched into water (3 mL), and then extracted with dichloromethane

(3 × 1 mL). Crude reaction mixture was dried with sodium sulfate and then concentrated. Purification was achieved by silica gel flash column chromatography (10% Et_2O/pentane) to yield title compound as a colorless oil (67.5 mg, 96% yield). IR (film) 2955, 2874, 1457, 1235, 1117, 1002, 700, 671 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.52-0.67 (m, 12 H, $SiC\mathbf{H}_2CH_3$), 0.92-1.05 (m, 19 H, $SiCH_2C\mathbf{H}_3$, CH-cypr), 1.07 (s, 3H, CH_3), 1.20-1.42 (m, 2 H, $C\mathbf{H}HCH_2$, CH-cypr), 1.43 (s, 3H, CH_3), 1.60-1.79 (m, 5H, $C\mathbf{H}HCH_2$), 1.81-1.91 (m, 1H, $C\mathbf{H}HCH_2$), 2.03 (dd, 1H, *J* = 11.4, 9.7 Hz, C**H**CH), 2.09-2.18 (m, 1H, $C\mathbf{H}HCH_2$) 2.22 (td, 1H, *J* = 7.2, 3.6 Hz, C**H**CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 6.60,7.0, 7.1, 7.2, 20.5, 23.9, 24.7, 25.9, 31.9, 32.6, 40.0, 40.1, 42.1, 52.0, 53.8, 78.2, 82.8; HRMS (EI+) exact mass calculated for ($C_{25}H_{48}Br_2O_2Si_2$–Br) requires *m*/*z* 517.2356, found *m*/*z* 517.2368. $[\alpha]_D^{23} = -57.1$ (c = 0.222, $CHCl_3$).



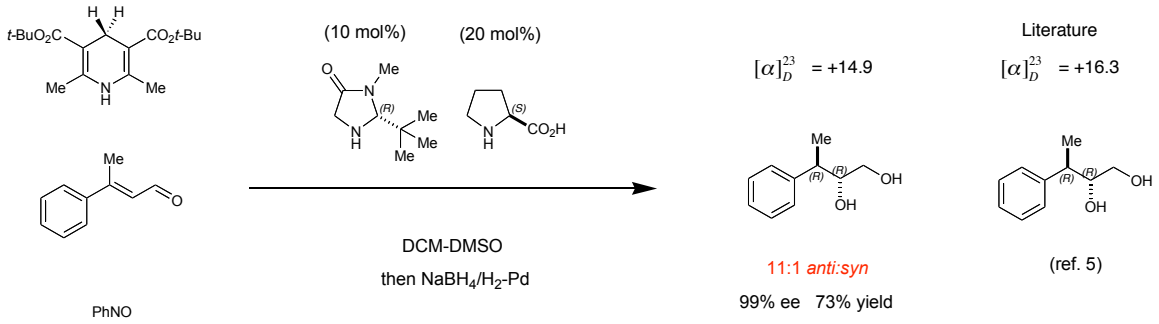
(1a*R*,4*R*,4a*R*,7*R*,7a*S*,7b*R*)-Decahydro-1,1,4,7-tetramethyl-1*H*-cyclopropa[*e*]azulene-4,7-diol-4,7-bis(triethyl-silyl) ether: A dry 15 mL Schlenk tube equipped with stirbar was charged with CuI (320 mg, 1.68 mmol) and anhydrous ether (840 μL). The tube was then cooled to –78 °C, and a 1.6 M solution of MeLi (2.10 ml, 3.35 mmol) was added over 30 min. The heterogeneous white mixture was allowed to warm to –20 °C for 10 min. The homogeneous yellow solution was then re-cooled to –78 °C and dibromide from previous step (100 mg, 0.168 mmol) was then added slowly as a solution in dry ether (250 μL) at –78 °C. The reaction was stirred at 0 °C over the next 48 h. Iodomethane (600 μL, excess) was slowly added at –20 °C and the mixture was allowed to come to room temperature and further stirred 6 h, before being filtered over a pad of Florisil and concentrated. The crude product was purified by silica gel flash column chromatography (10% Et_2O/pentane) to yield the title compound as a colorless oil (78 mg, 99% yield). IR (film) 2953, 2912, 2875, 1457, 1237, 1097, 1004 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ0.48-0.59 (m, 12H, $SiC\mathbf{H}_2CH_3$), 0.71-0.85 (m, 2H, CH-cypr), 0.93-0.98 (m, 22H CH_3, $C\mathbf{H}HCH_2$, $SiCH_2C\mathbf{H}_3$), 1.02 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 1.26-1.36 (m, 2H, $C\mathbf{H}HCH_2$), 1.56-1.86 (m, 6H, C**H**CH, $C\mathbf{H}HCH_2$), 2.18 (td, 1H, *J* = 11.0, 5.0 Hz, C**H**CH); ^{13}C

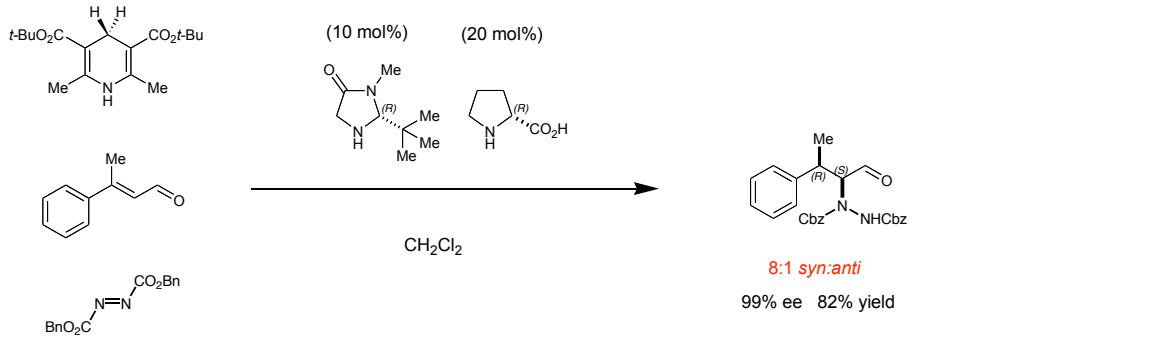
NMR (100 MHz, $CDCl_3$) δ 6.7,7.0, 7.1, 7.2, 16.5, 18.5, 20.7, 20.8, 24.7, 25.4, 25.7, 25.9, 28.8, 40.7, 44.2, 49.2, 54.9, 78.7, 82.8; HRMS (EI) exact mass calculated for ($C_{27}H_{54}O_2Si_2$) requires *m/z* 466.3662, found *m/z* 466.3645. $[\alpha]_D^{23}$ = –39.9 (c = 1.40, $CHCl_3$).

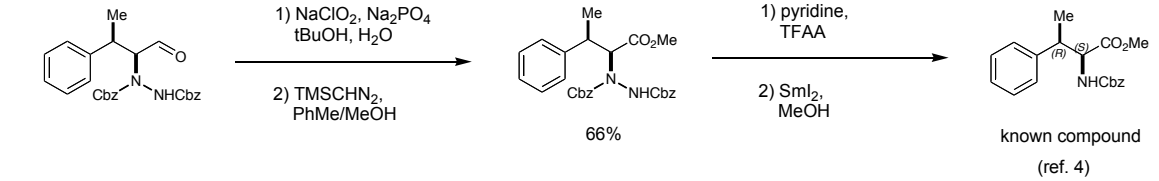


(–)-4α,7α-Aromadendranediol: A 4 mL Teflon vial was equipped with a stir bar and then charged with bisilyl ether from previous step (30 mg, 0643 mmol) and MeCN (750 μL). HF (5 drops, 48% aqueous) was added to the contents of the vial. The solution was allowed to stir 60 min until the silyl group deprotection was deemed complete by TLC. The solution was quenched with saturated sodium bicarbonate solution and extracted with ethyl ether (3 × 1 mL). Extracts were washed with pH 7 phosphate buffer (compound is acid sensitive) then dried over sodium sulfate. The crude product was then purified by preparatory TLC (7:2 $CHCl_3$: acetone, 250 μM plate) to yield the title compound as a white crystalline solid (14.3 mg, 93% yield). IR (film) 3403, 2970, 2950, 1455, 1375, 1172 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.62-0.74 (m, 1H, CH-cypr), 0.82-0.92 (m, 1H, CH-cypr), 0.97 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.26-1.38 (m, 3H, OH, C**H**HCH_2), 1.45-1.59 (ddd 2H, *J* = 10.7, 8.5, 7.6 Hz, C**H**HCH_2), 1.64-1.76 (m, 4H, C**H**HCH_2), 1.82-1.96 (m, 2H, C**H**HCH_2, CHC**H**), 2.13-2.20 (td, 1H, *J* = 10.8, 4.9 Hz, C**H**CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ16.4, 18.9, 19.7, 20.3, 23.7, 24.9, 25.6, 26.1, 28.8, 40.3, 44.2, 47.5, 54.5, 75.5, 80.2; HRMS (EI+) exact mass calculated for ($C_{15}H_{26}O_2$) requires *m/z* 238.1933, found *m/z* 238.1931. $[\alpha]_D^{23}$ = –39.0 (c = 0.100, $CHCl_3$). All spectral data were consistent with the previously reported literature values.[7]

■ Stereochemical Proofs of Selected Cascade Products







■ All spectral data of products are consistent with previously reported data.

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[1] D. D. Perrin, W. L. F. Armarego, *Purification of Laboratory Chemicals* (Pergamon Press, Oxford, 1988) ed 3.
[2] A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen, F. J. Timmers, *Organometallics* **1996**, *15*, 1518.
[3] W. C. Still, M. Kahn, A. J. Mitra, *J. Org. Chem.* **1978,** *43*, 2923 (1978).
[4] L. M. Nogle, C. W. Mann, W. L. Watts, Y. Zhang, *J. Pharm. Biomed. Anal.* **2006**, *40*, 901-909.
[5] M. P. Pasto, A. Moyano, M. A. Pericas, A. Riera, *J. Org. Chem.* **1997**, *62*, 8425.
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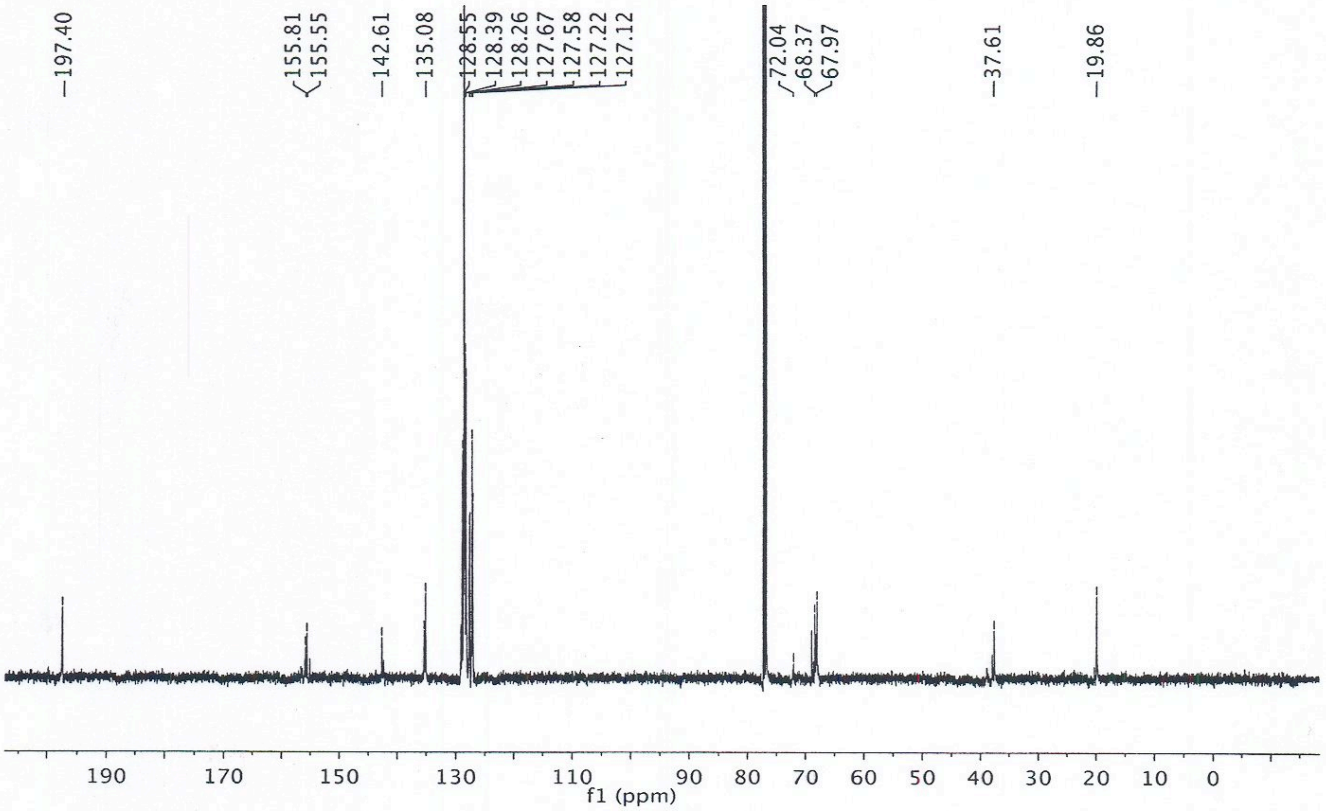
[7] C. M. Beechan, C. Djerassi, H. Eggert, *Tetrahedron.* **1978**, *34*, 2503.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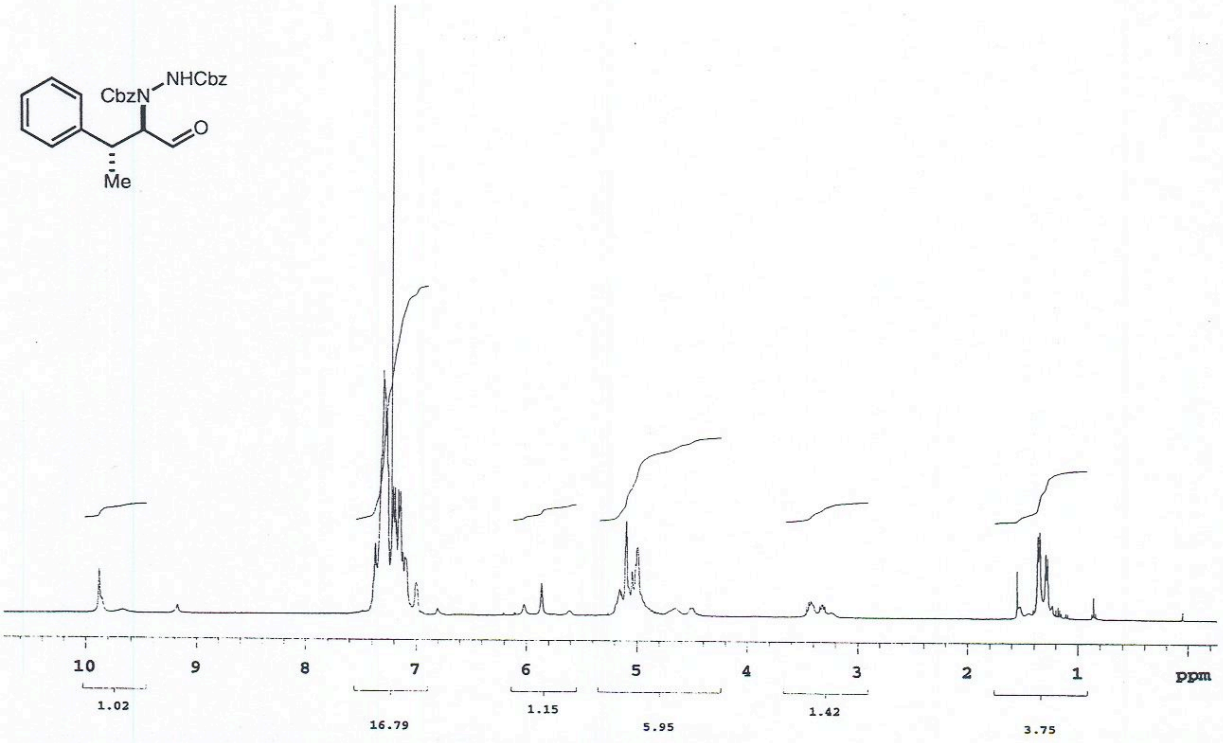
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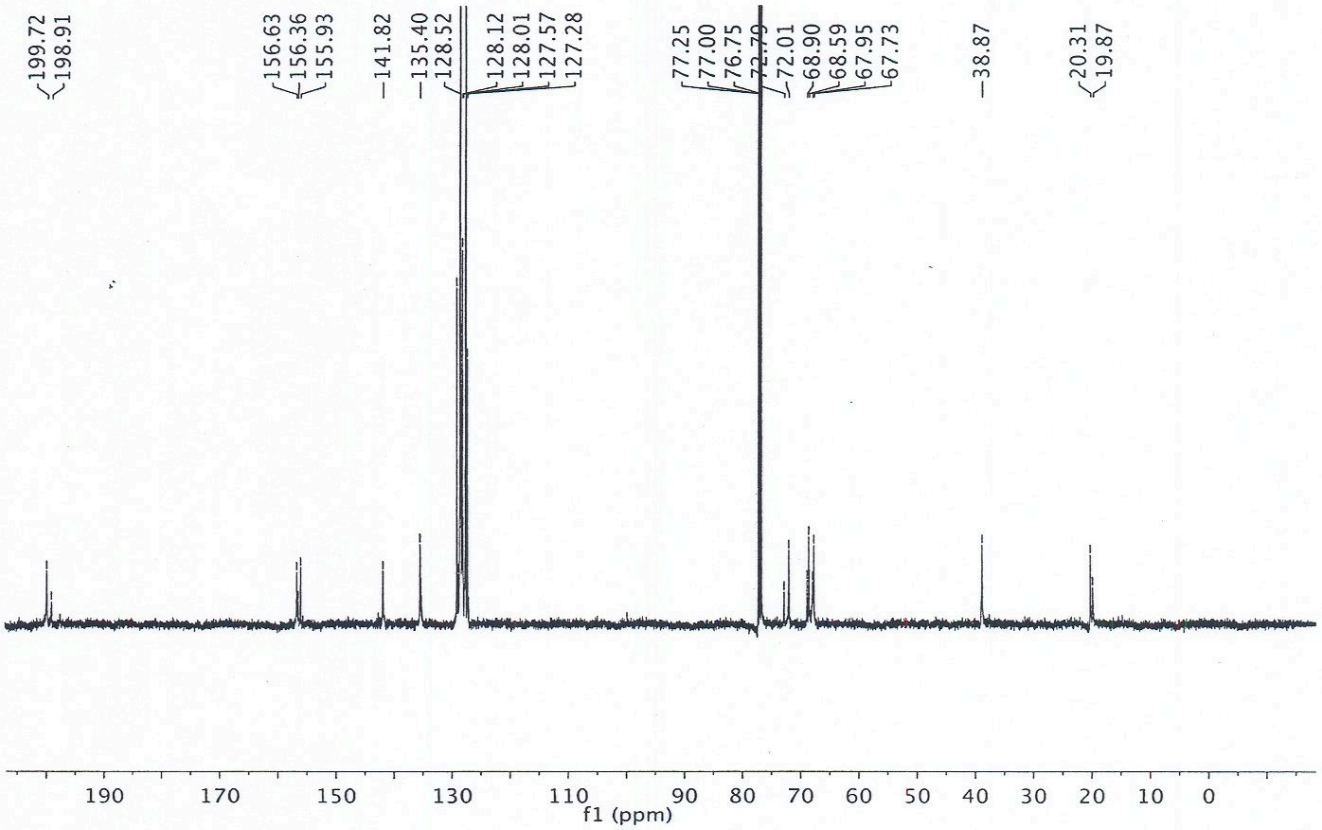
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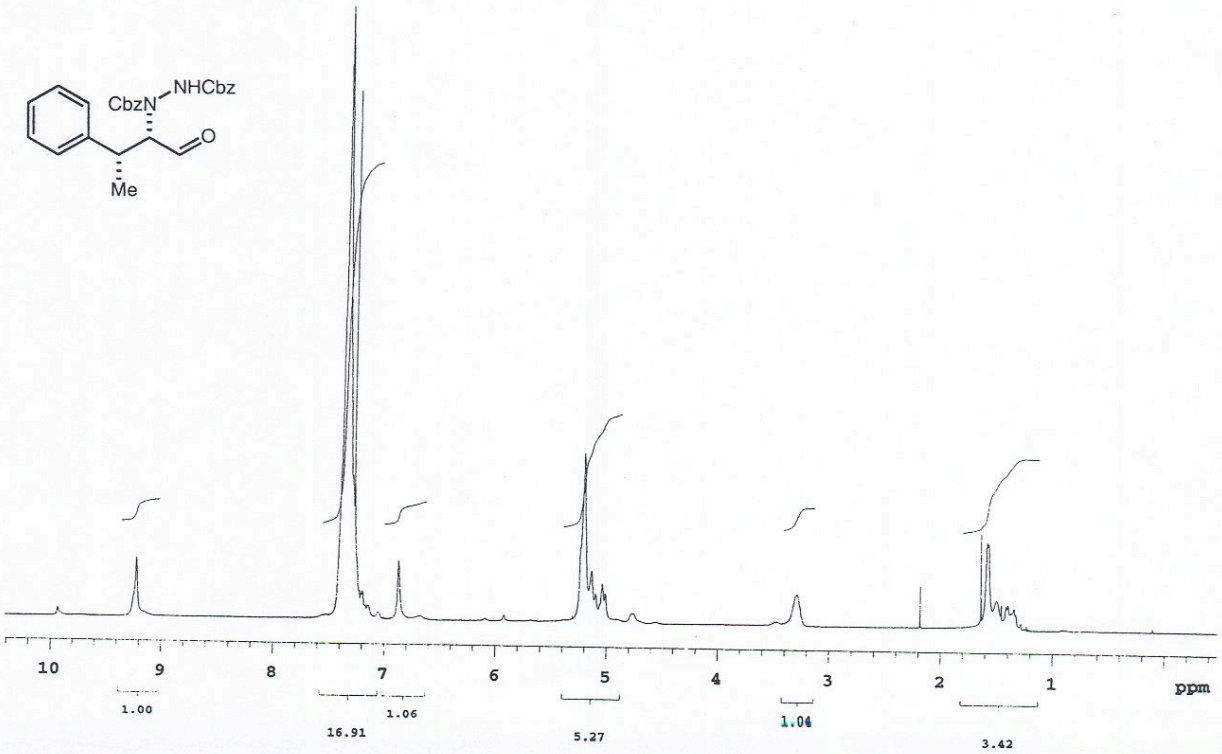
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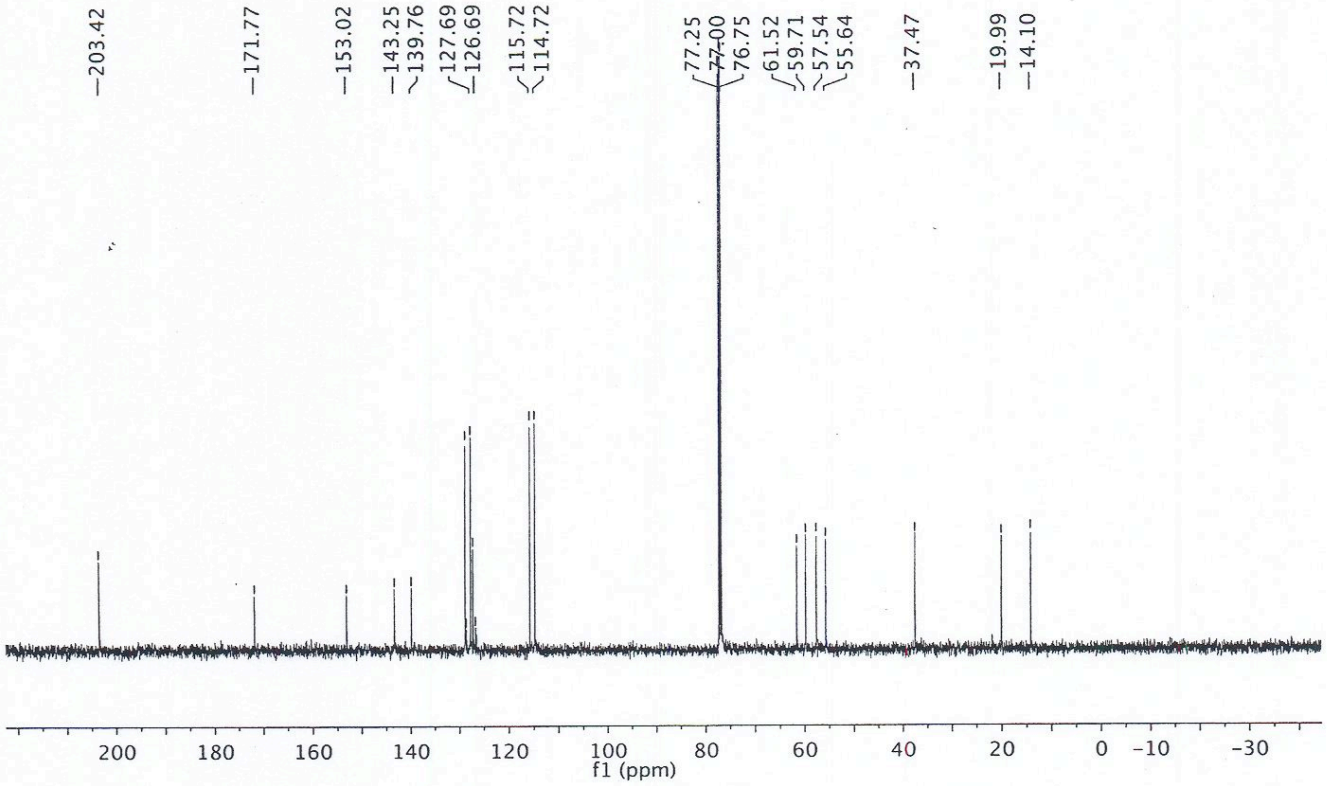
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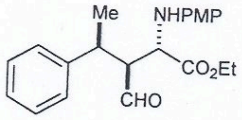
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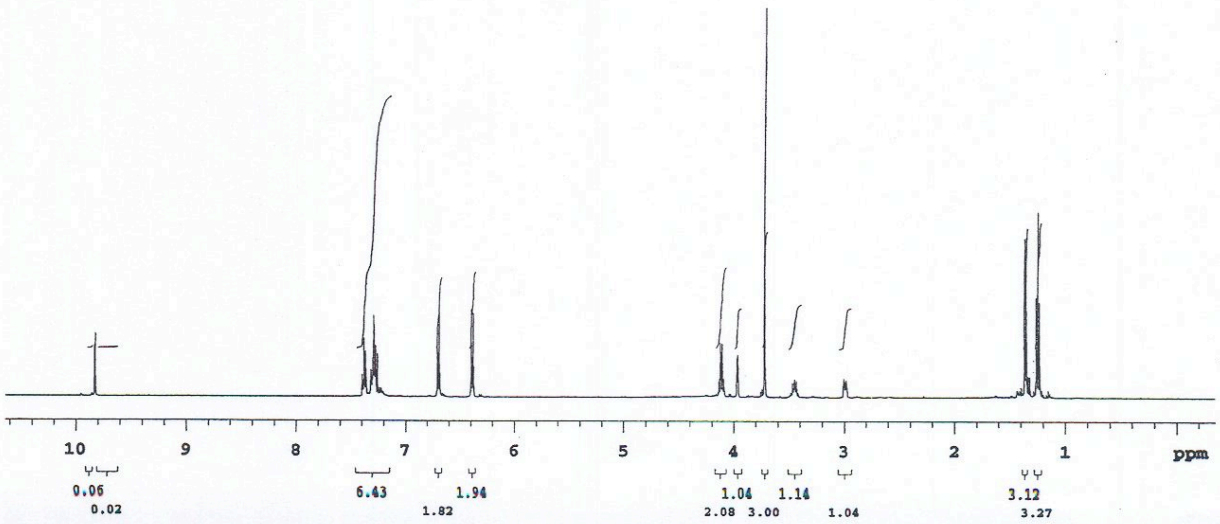
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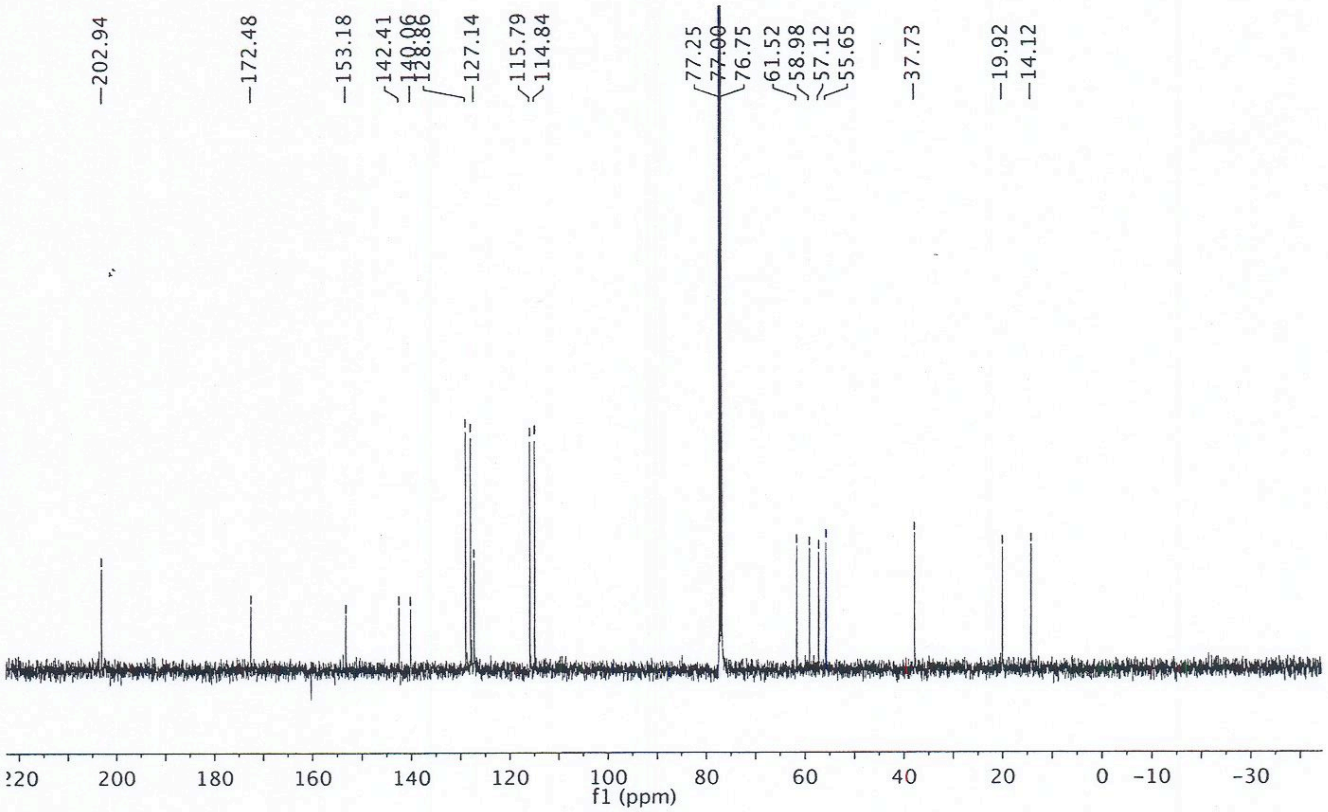
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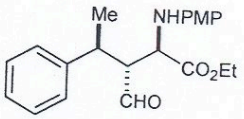
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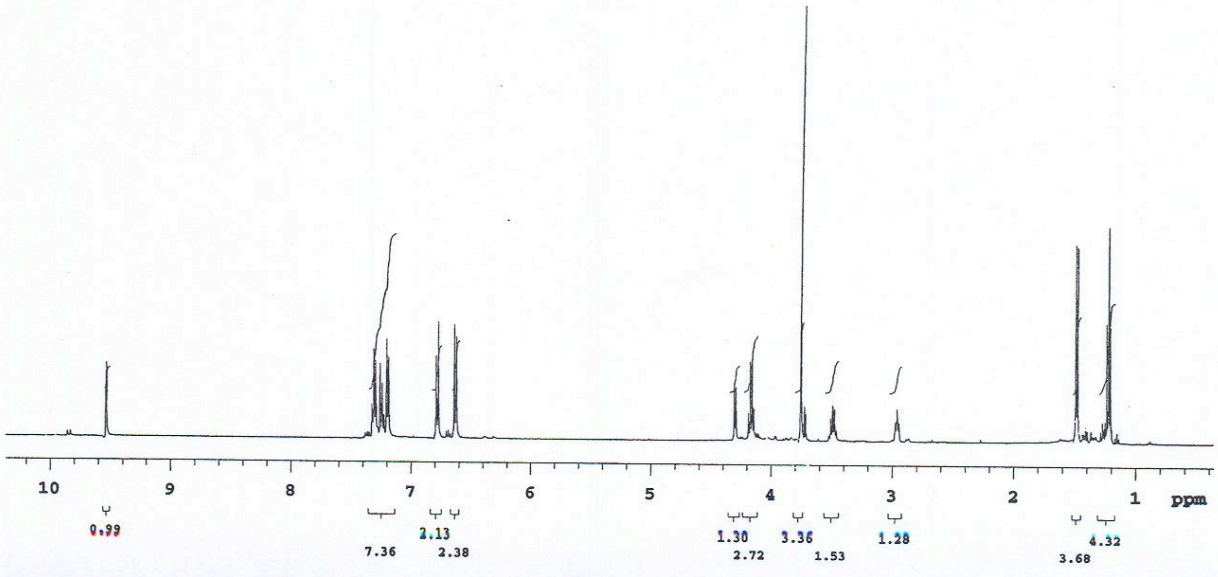
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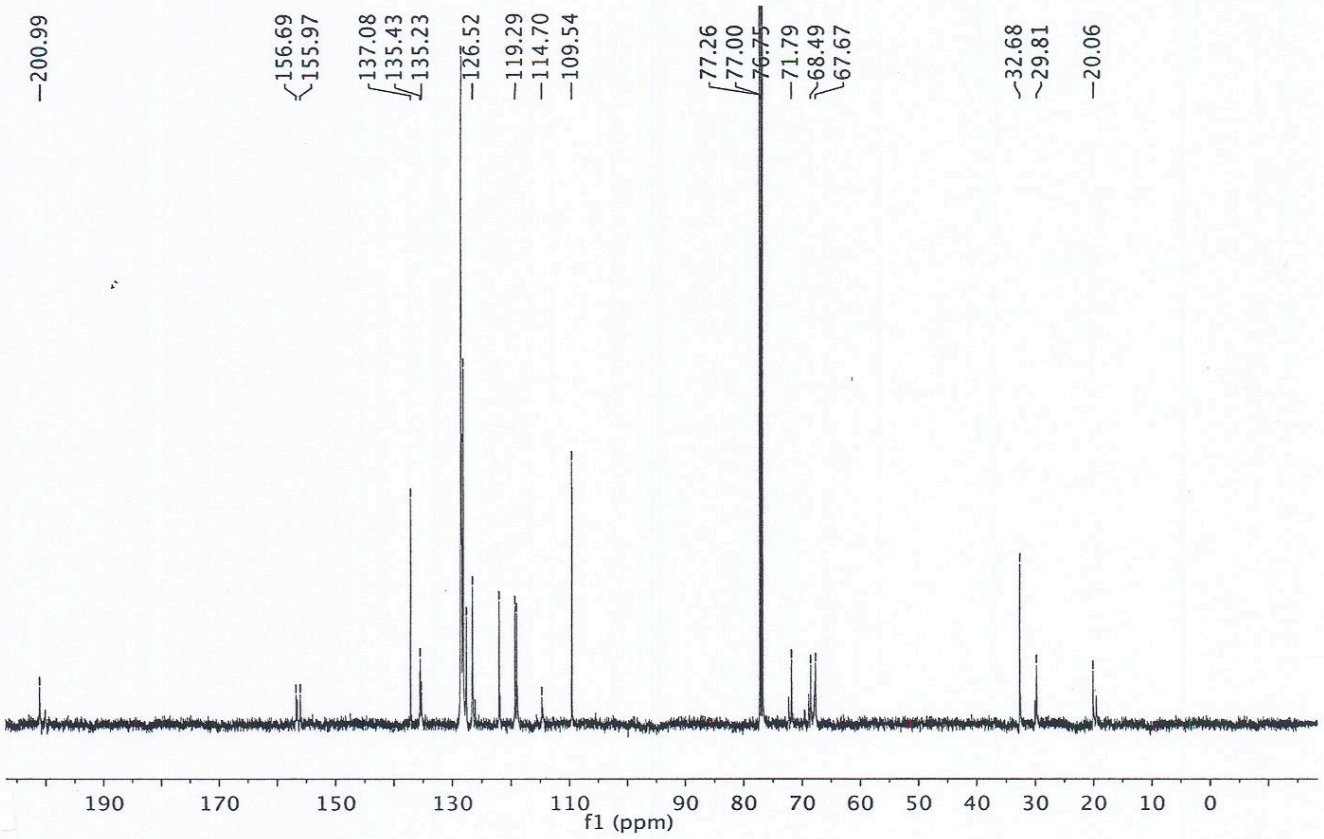
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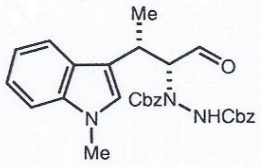
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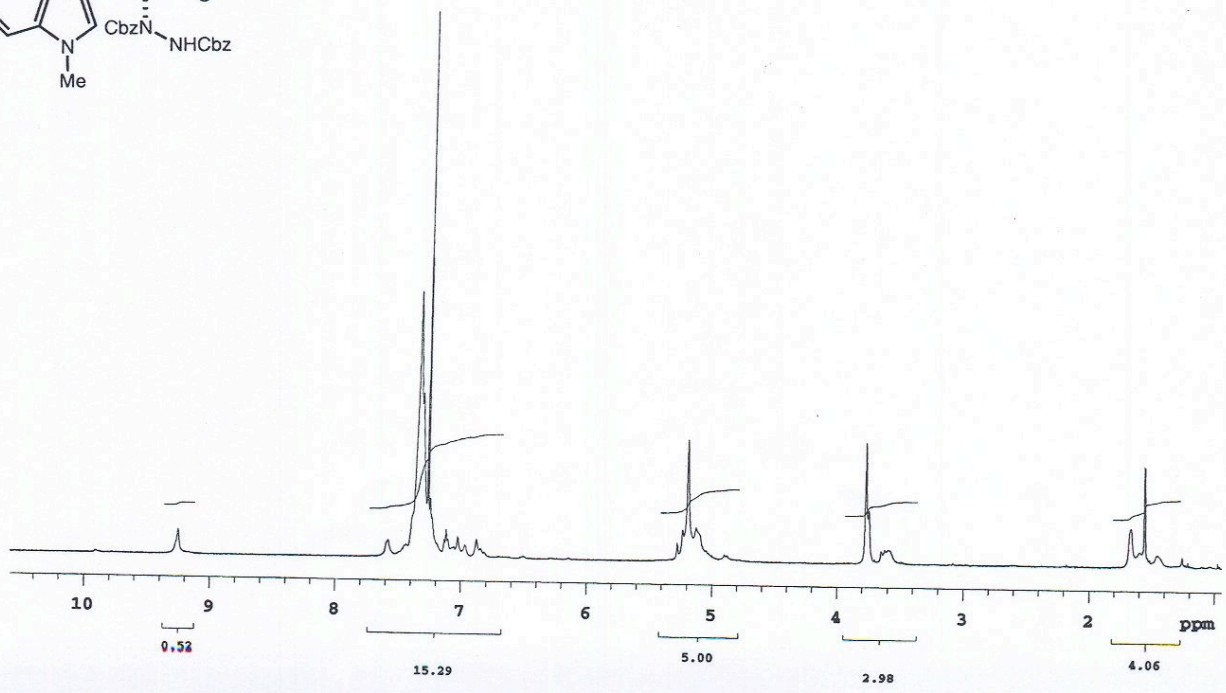
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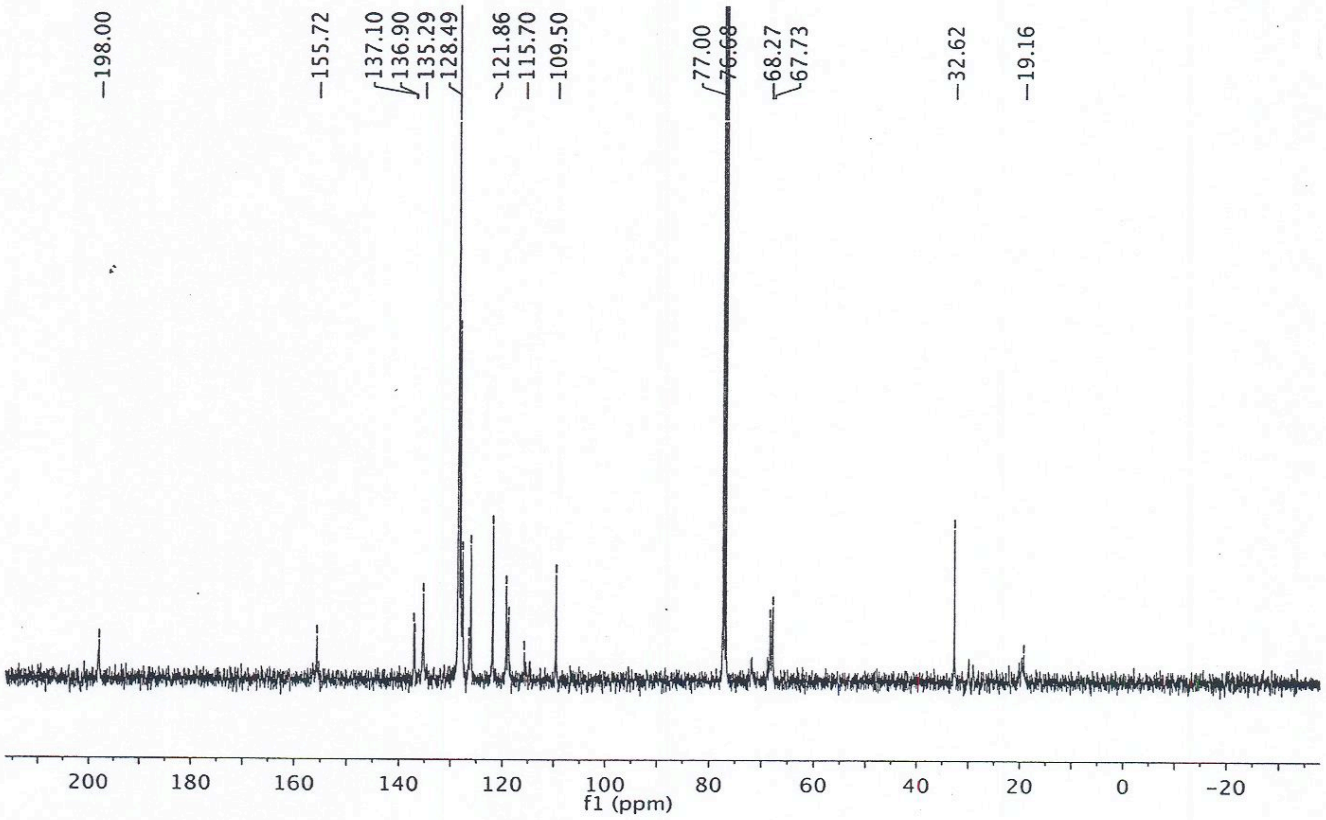
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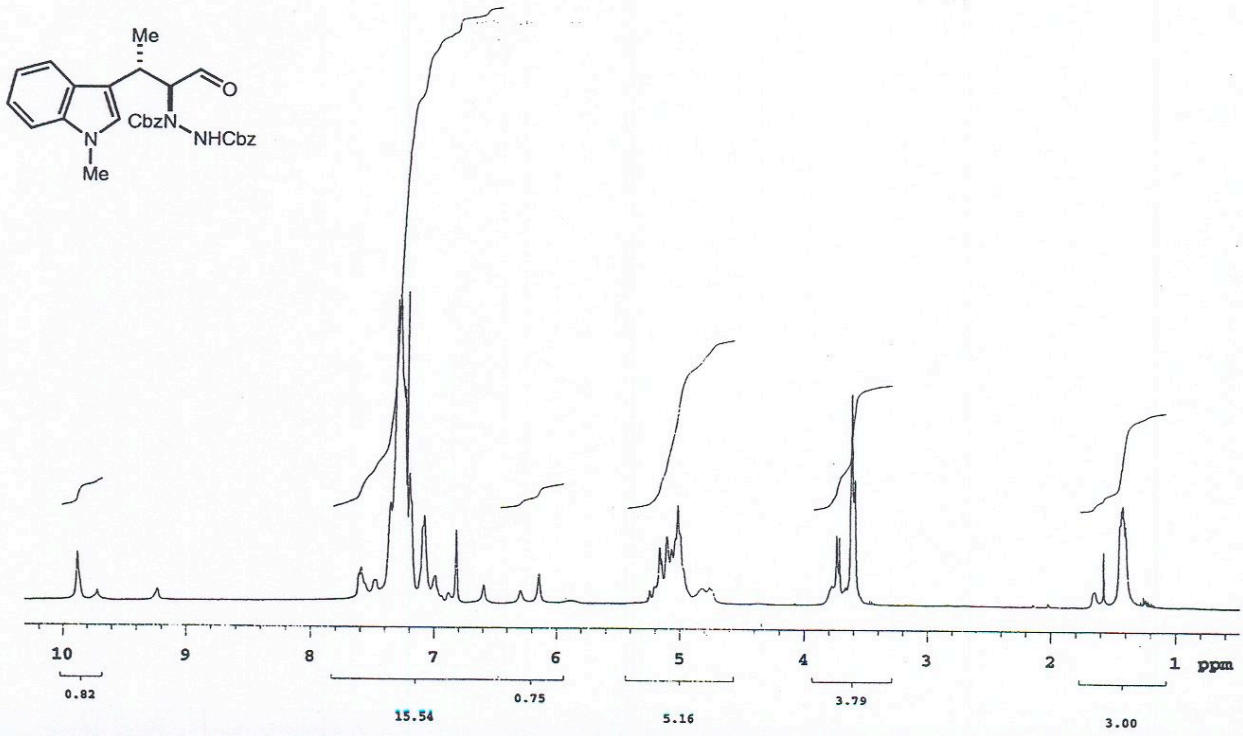
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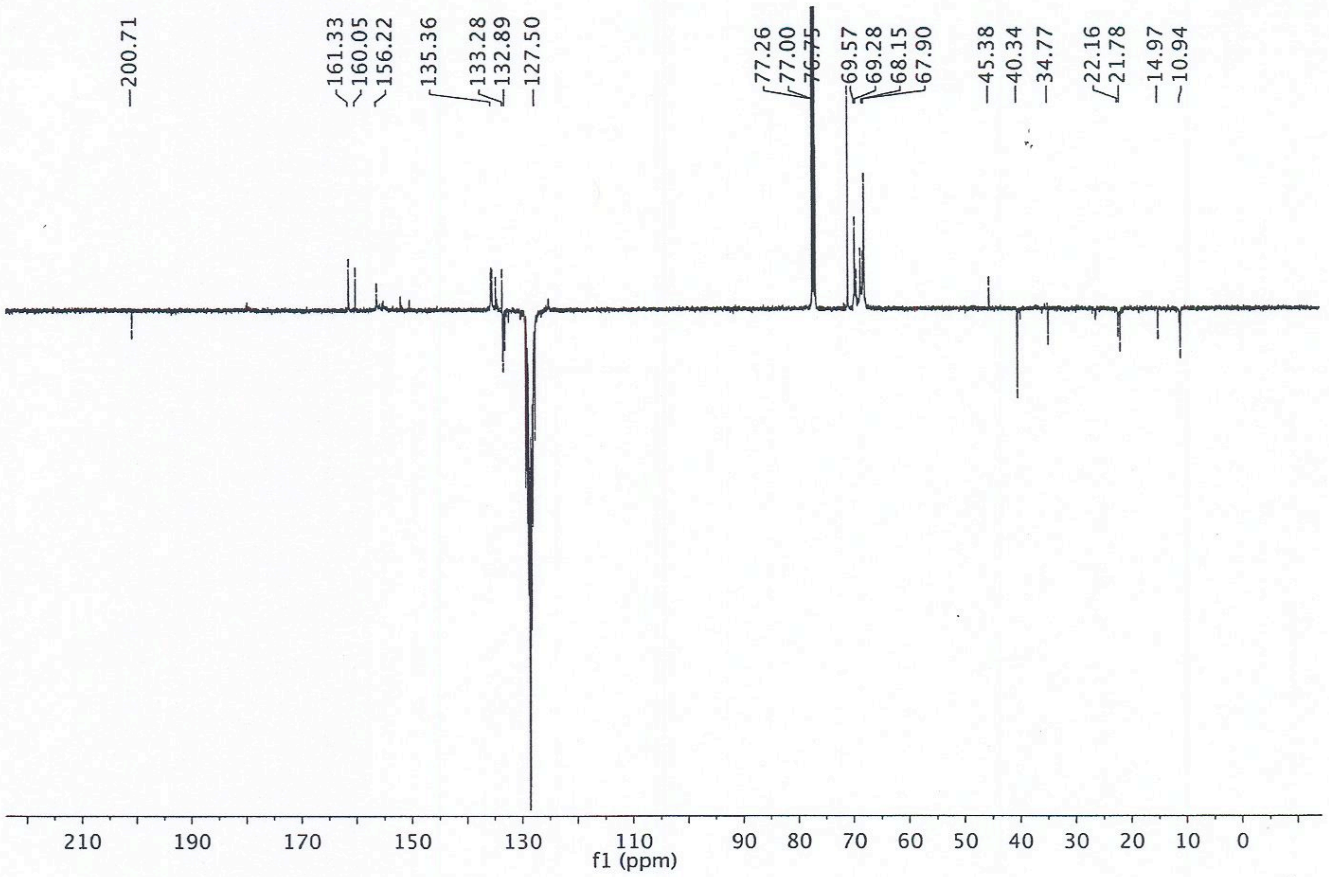
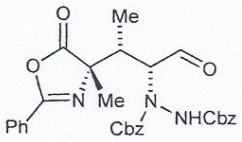
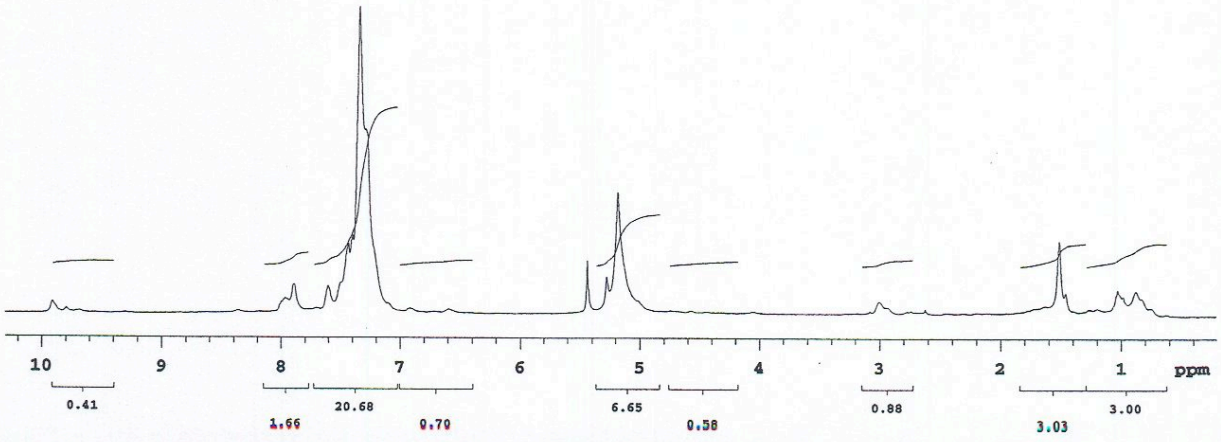
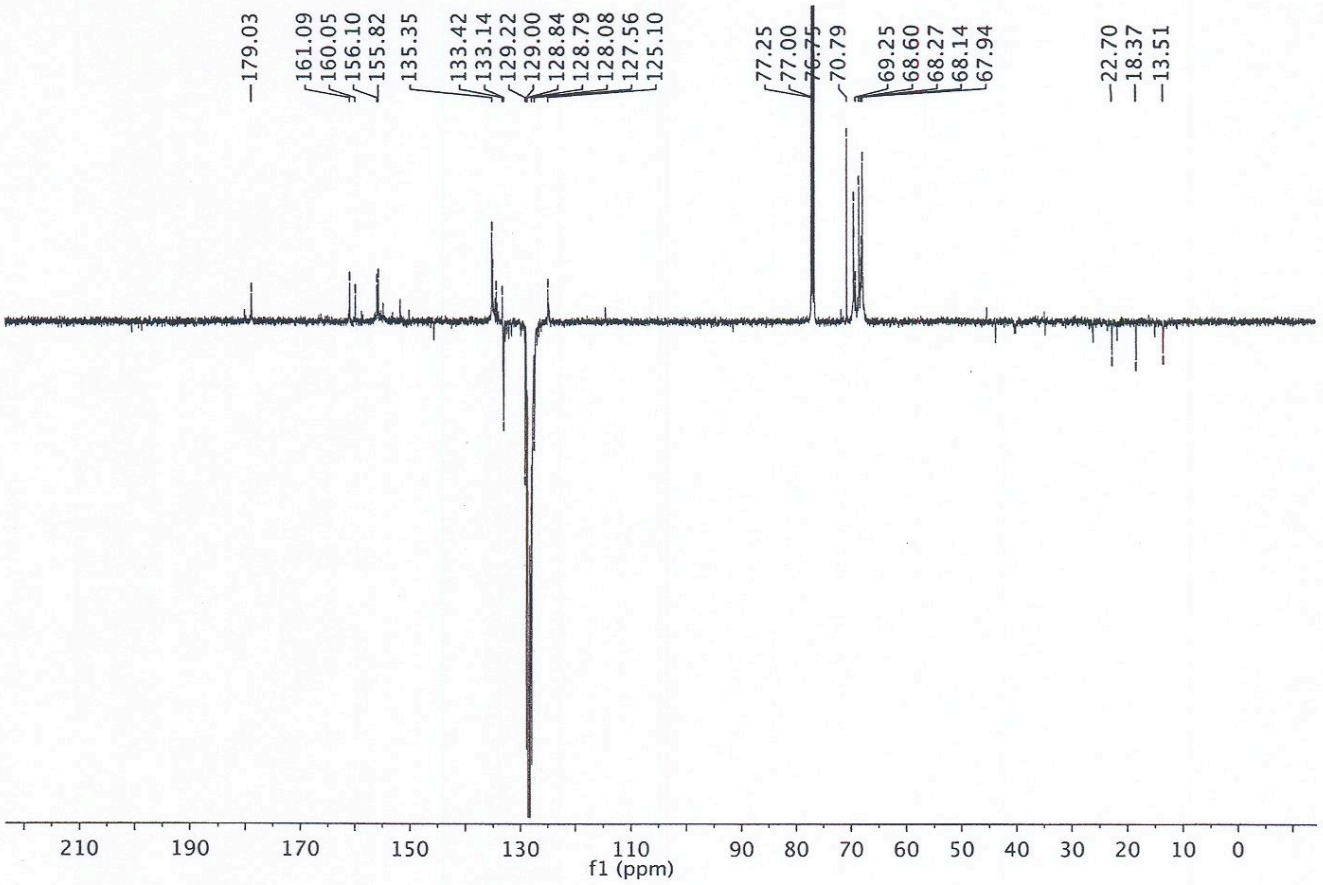
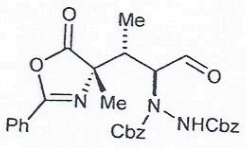
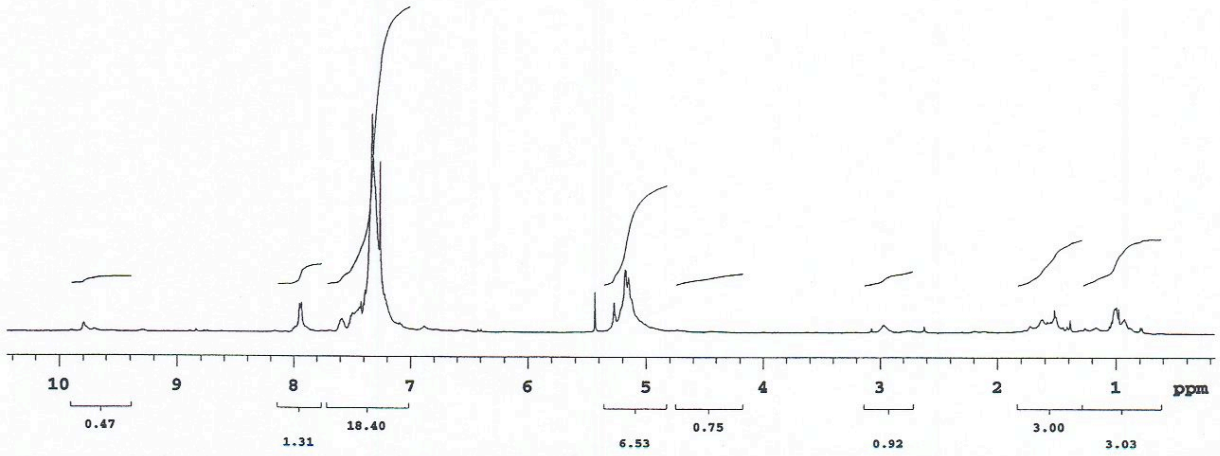

200.71
161.33
160.05
156.22
135.36
133.28
132.89
127.50
77.26
77.00
76.75
69.57
69.28
68.15
67.90
45.38
40.34
34.77
22.16
21.78
14.97
10.94
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

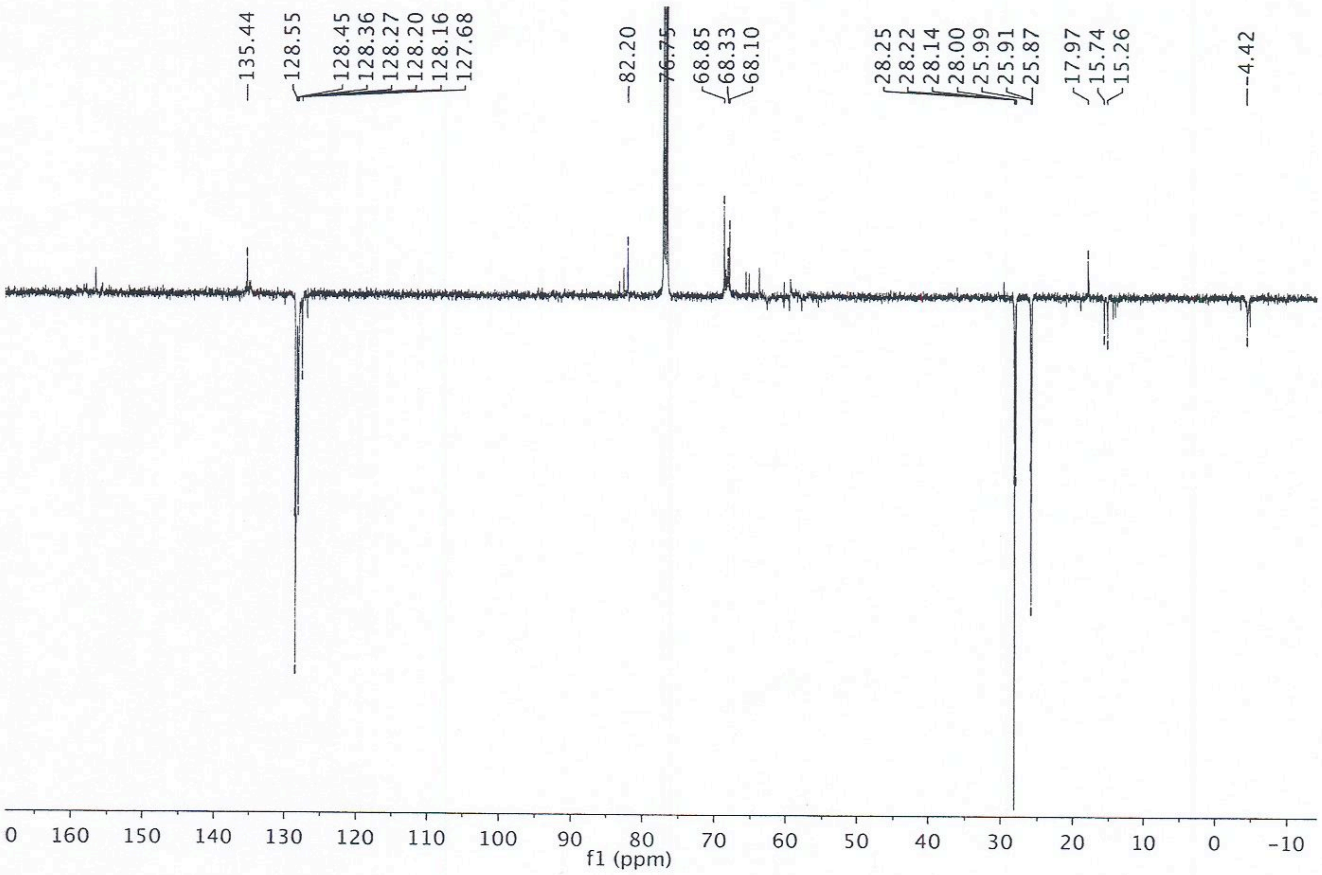

O
Me
O
O
N
Me
N
NHCbz
Ph
Cbz

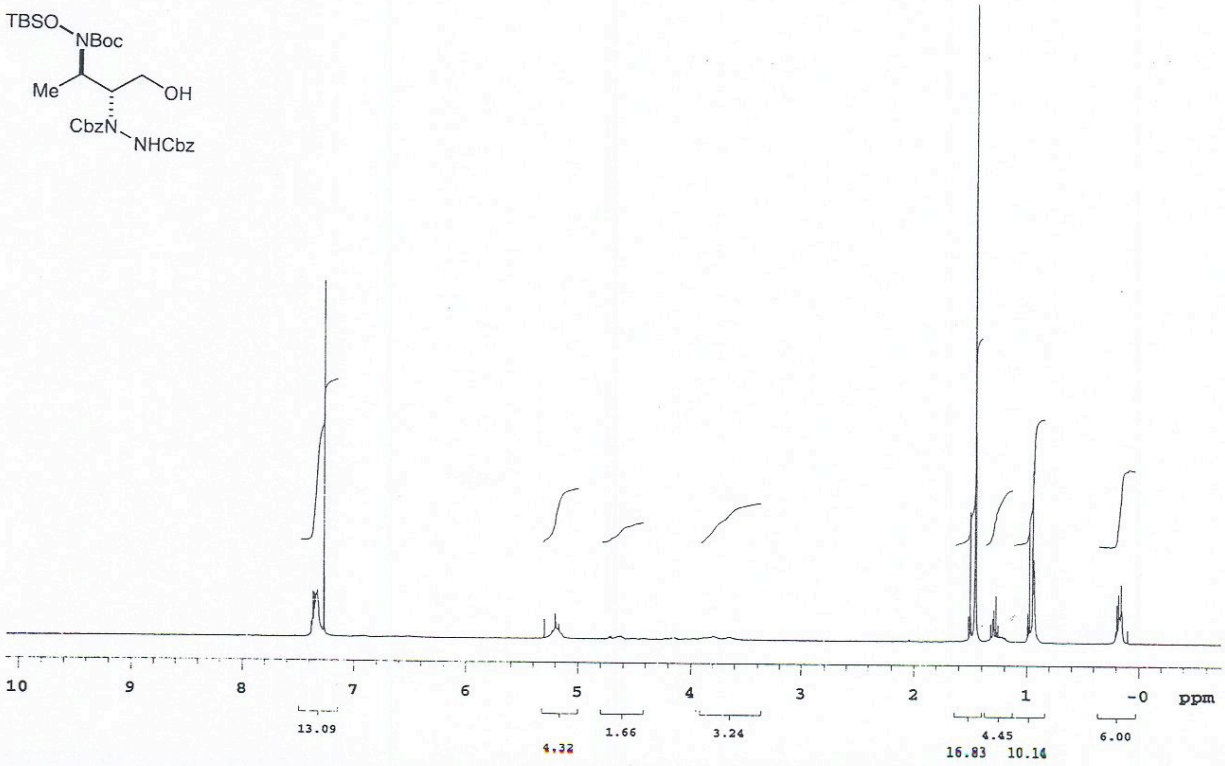

10
9
8
7
6
5
4
3
2
1
ppm
0.41
20.68
6.65
0.88
3.00
1.66
0.79
0.58
3.03

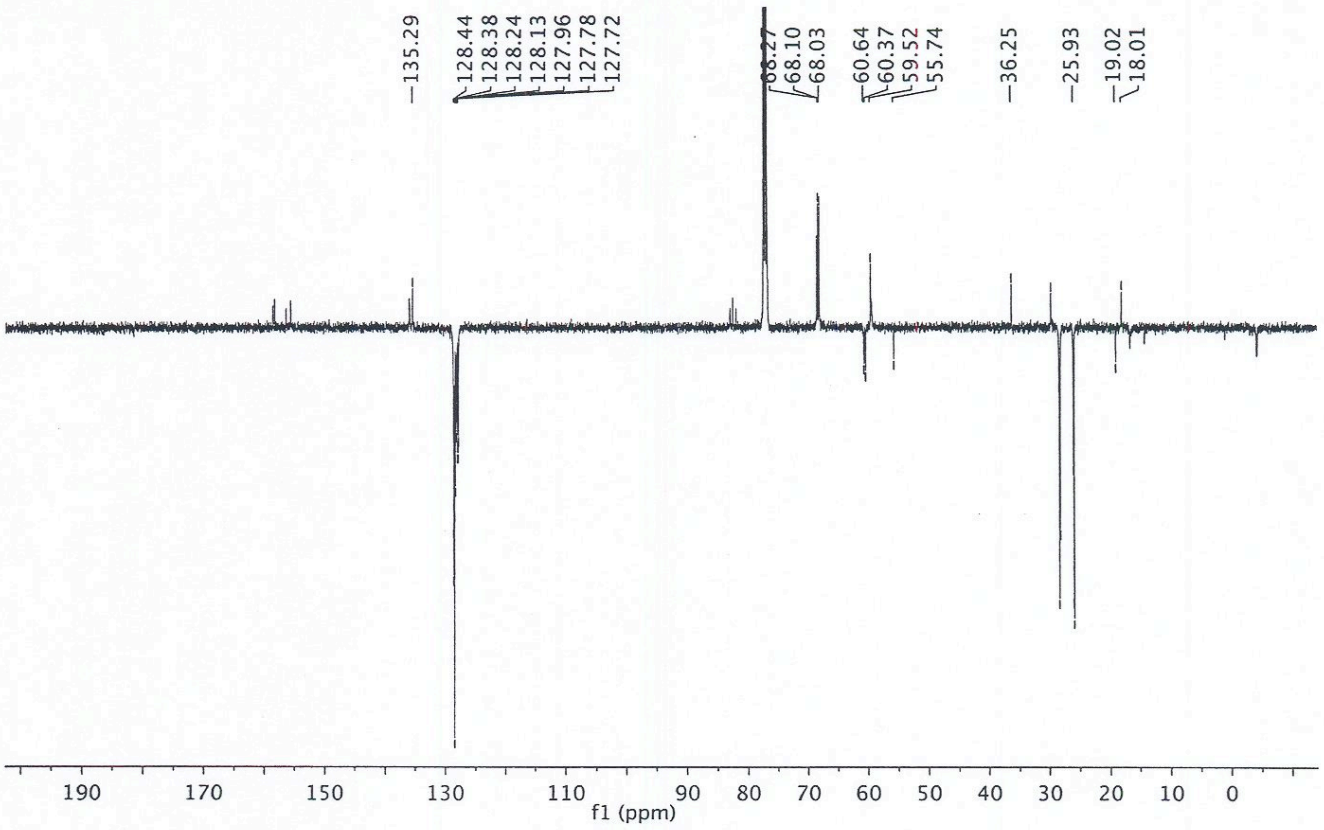

179.03
161.09
160.05
156.10
155.82
135.35
133.42
133.14
129.22
129.00
128.84
128.79
128.08
127.56
125.10
77.25
77.00
76.75
70.79
69.25
68.60
68.27
68.14
67.94
22.70
18.37
13.51
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

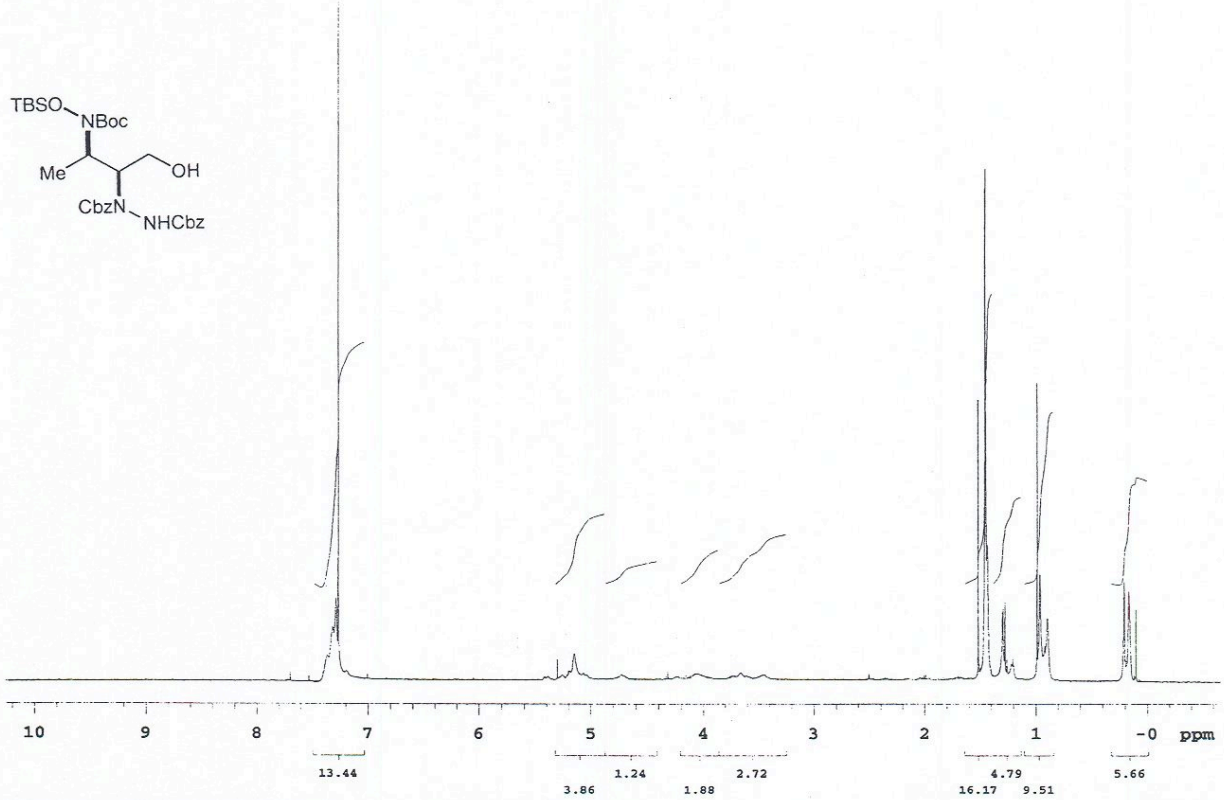

O
Me
O
O
N
Me
N
Ph
Cbz
NHCbz

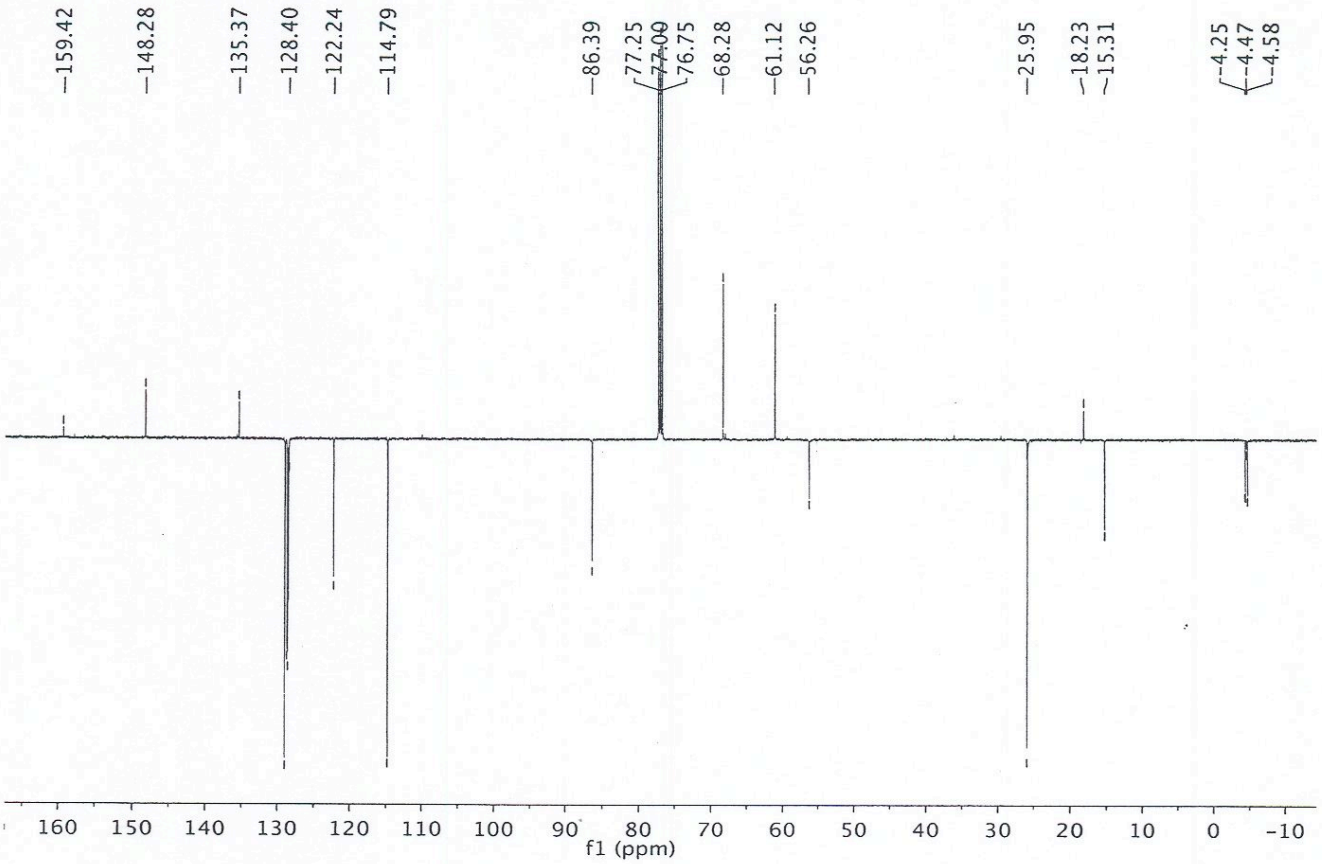

10
9
8
7
6
5
4
3
2
1
ppm
0.47
1.31
18.40
6.53
0.75
0.92
3.00
3.03

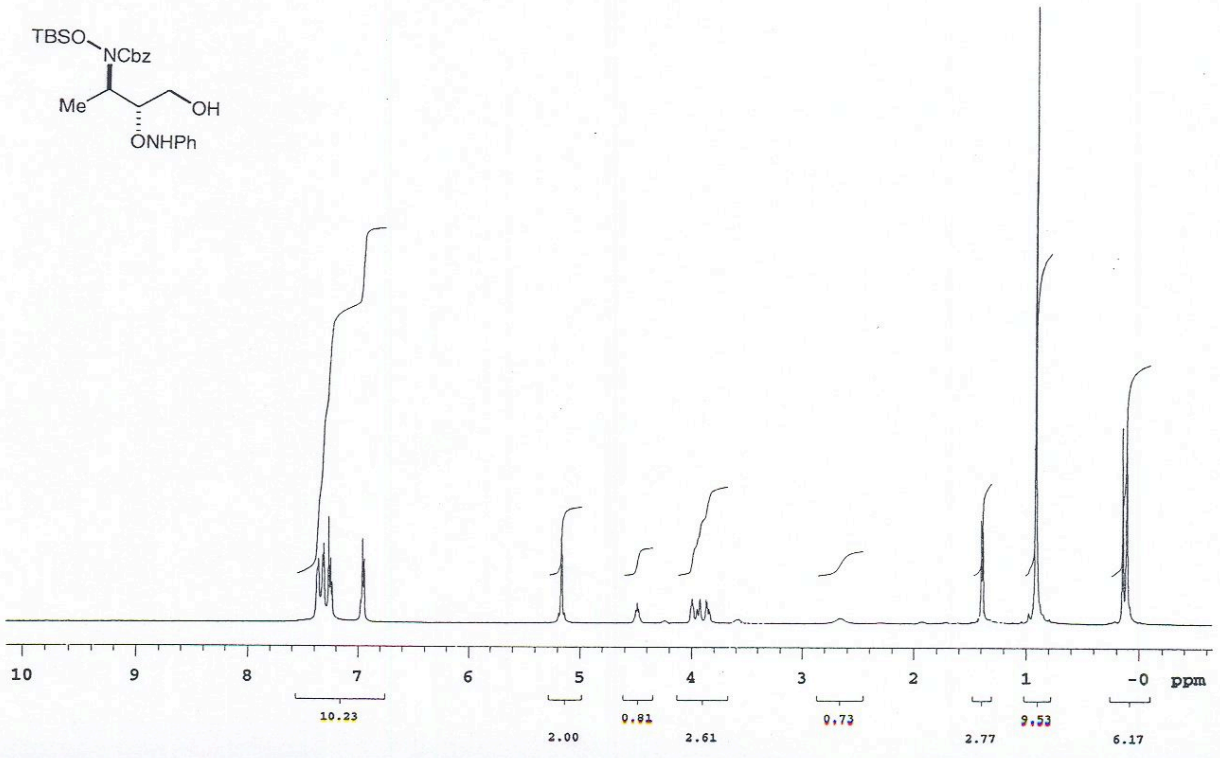

135.44
128.55
128.45
128.36
128.27
128.20
128.16
127.68
82.20
76.75
68.85
68.33
68.10
28.25
28.22
28.14
28.00
25.99
25.91
25.87
17.97
15.74
15.26
-4.42
0 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

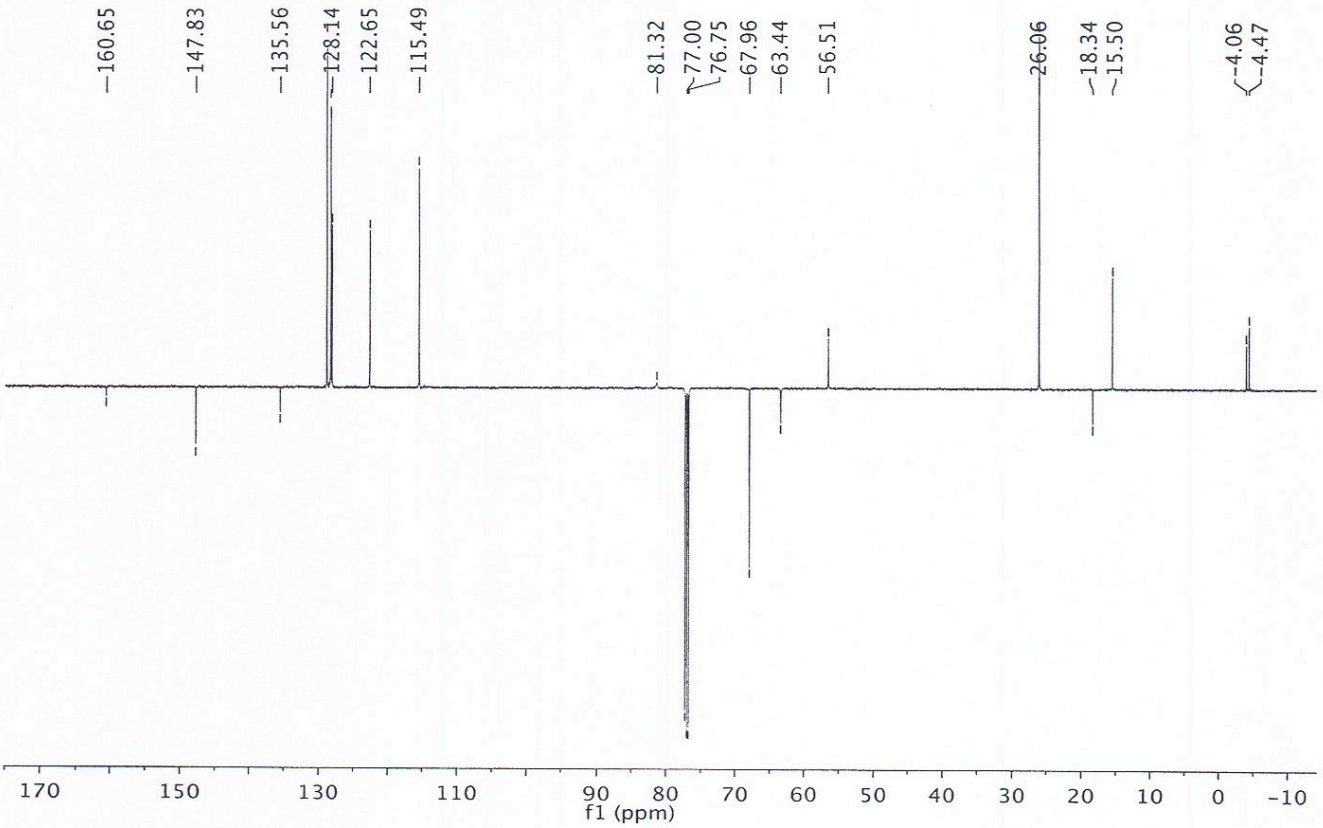

TBSO
NBoc
Me
OH
CbzN
NHCbz
10 9 8 7 6 5 4 3 2 1 -0 ppm
13.09
4.32
1.66
3.24
4.45
16.83
10.14
6.00

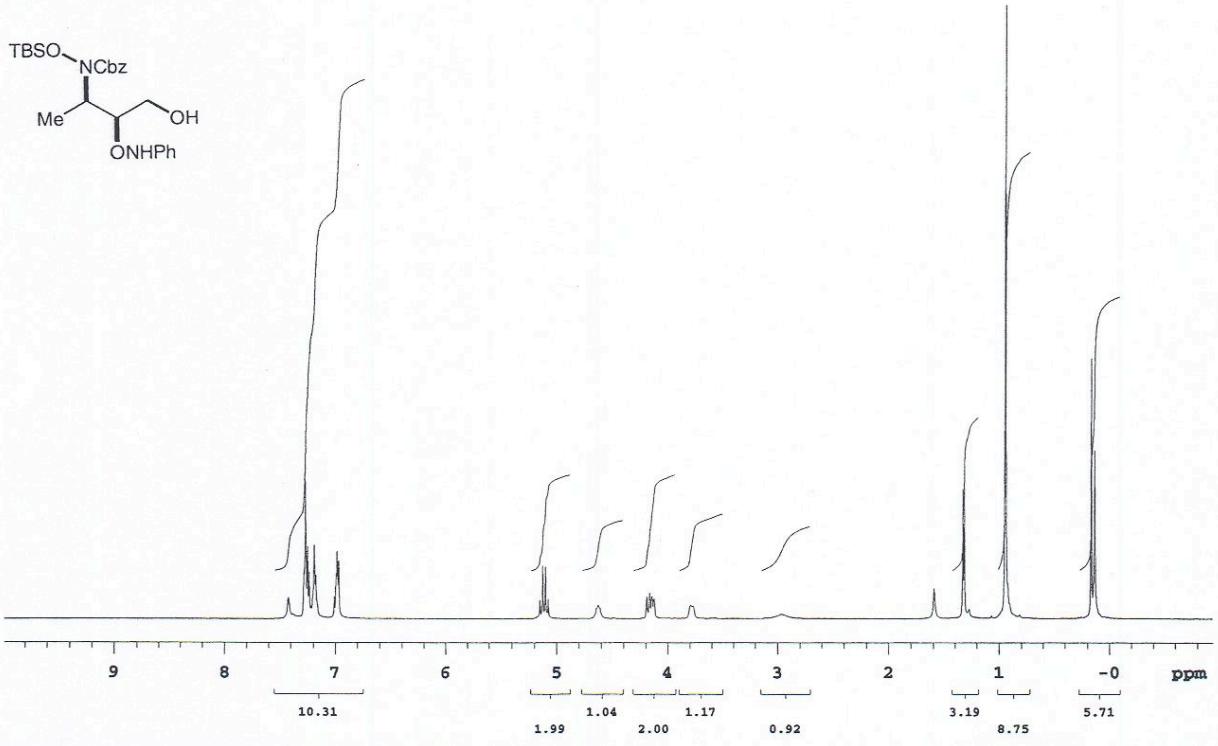

135.29
128.44
128.38
128.24
128.13
127.96
127.78
127.72
68.27
68.10
68.03
60.64
60.37
59.52
55.74
36.25
25.93
19.02
18.01
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

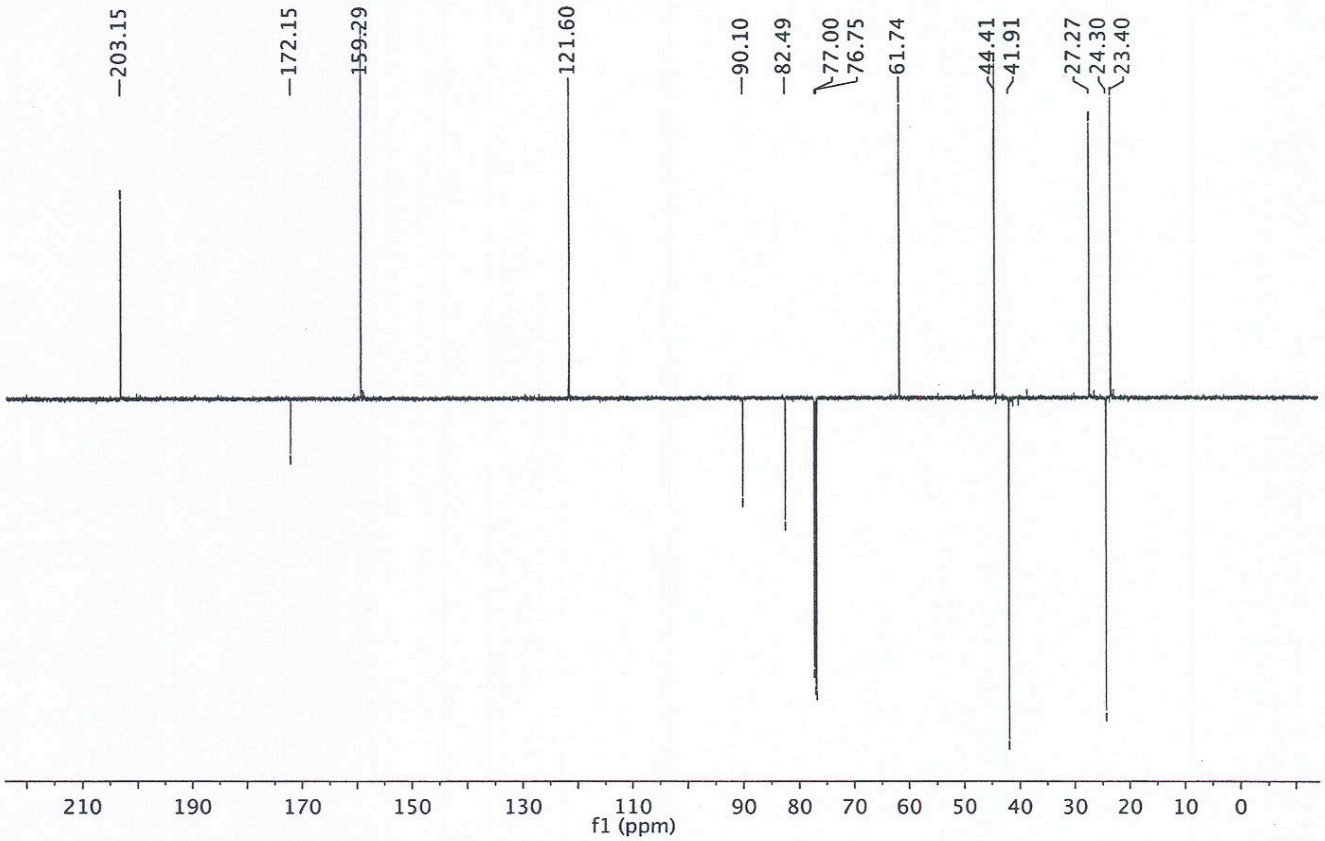

TBSO
NBoc
Me
OH
CbzN
NHCbz
10
9
8
7
6
5
4
3
2
1
-0
ppm
13.44
3.86
1.24
1.88
2.72
16.17
4.79
9.51
5.66

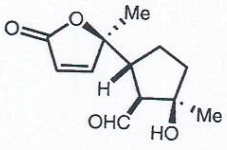

159.42
148.28
135.37
128.40
122.24
114.79
86.39
77.25
77.00
76.75
68.28
61.12
56.26
25.95
18.23
15.31
4.25
4.47
4.58
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


TBSO
NCbz
Me
OH
ONHPh
10 9 8 7 6 5 4 3 2 1 -0 ppm
10.23
2.00
0.81
2.61
0.73
2.77
9.53
6.17


160.65
147.83
135.56
128.14
122.65
115.49
81.32
77.00
76.75
67.96
63.44
56.51
26.06
18.34
15.50
4.06
4.47
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

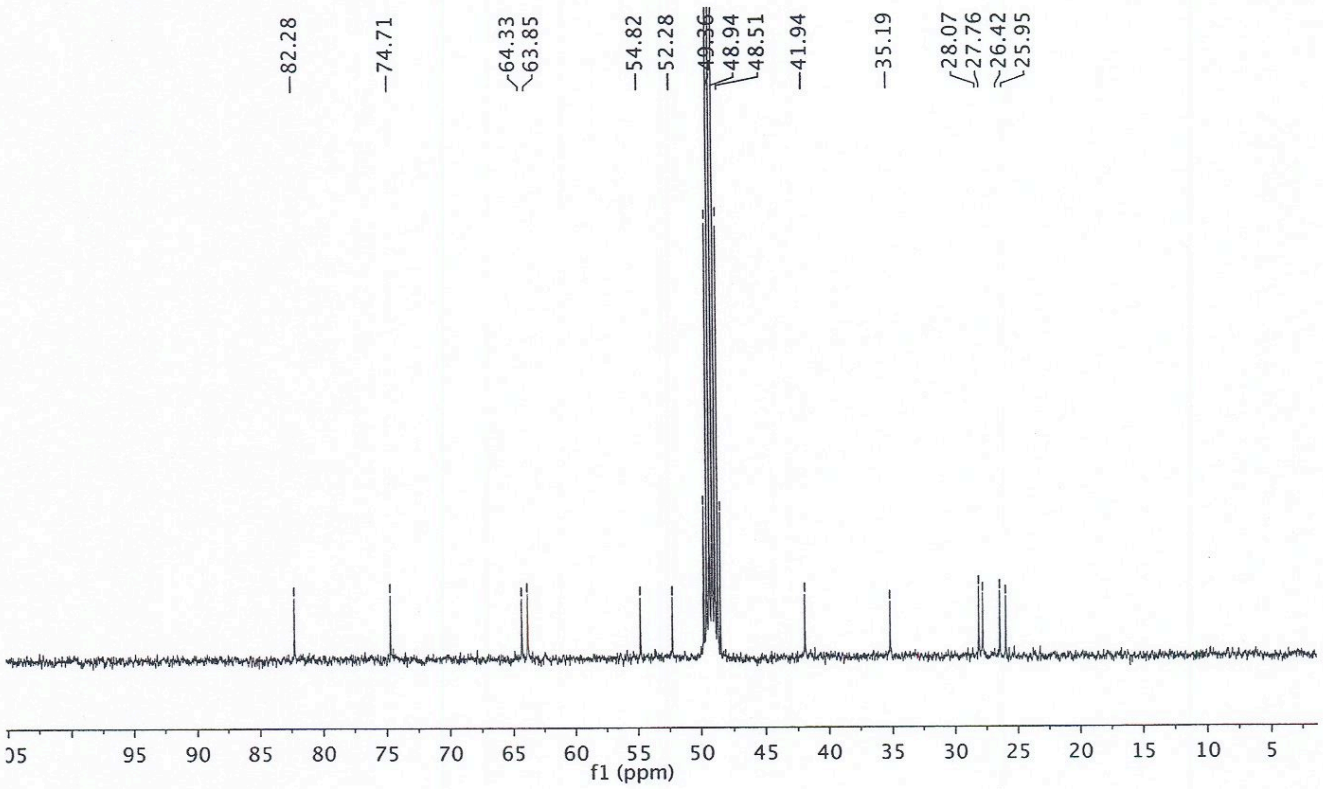

TBSO
NCbz
Me
OH
ONHPh
9
8
7
6
5
4
3
2
1
-0
ppm
10.31
1.99
1.04
2.00
1.17
0.92
3.19
8.75
5.71

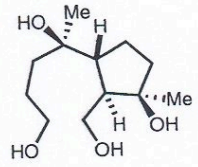

203.15
172.15
159.29
121.60
90.10
82.49
77.00
76.75
61.74
44.41
41.91
27.27
24.30
23.40
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
O
Me
H
OHC
HO
Me

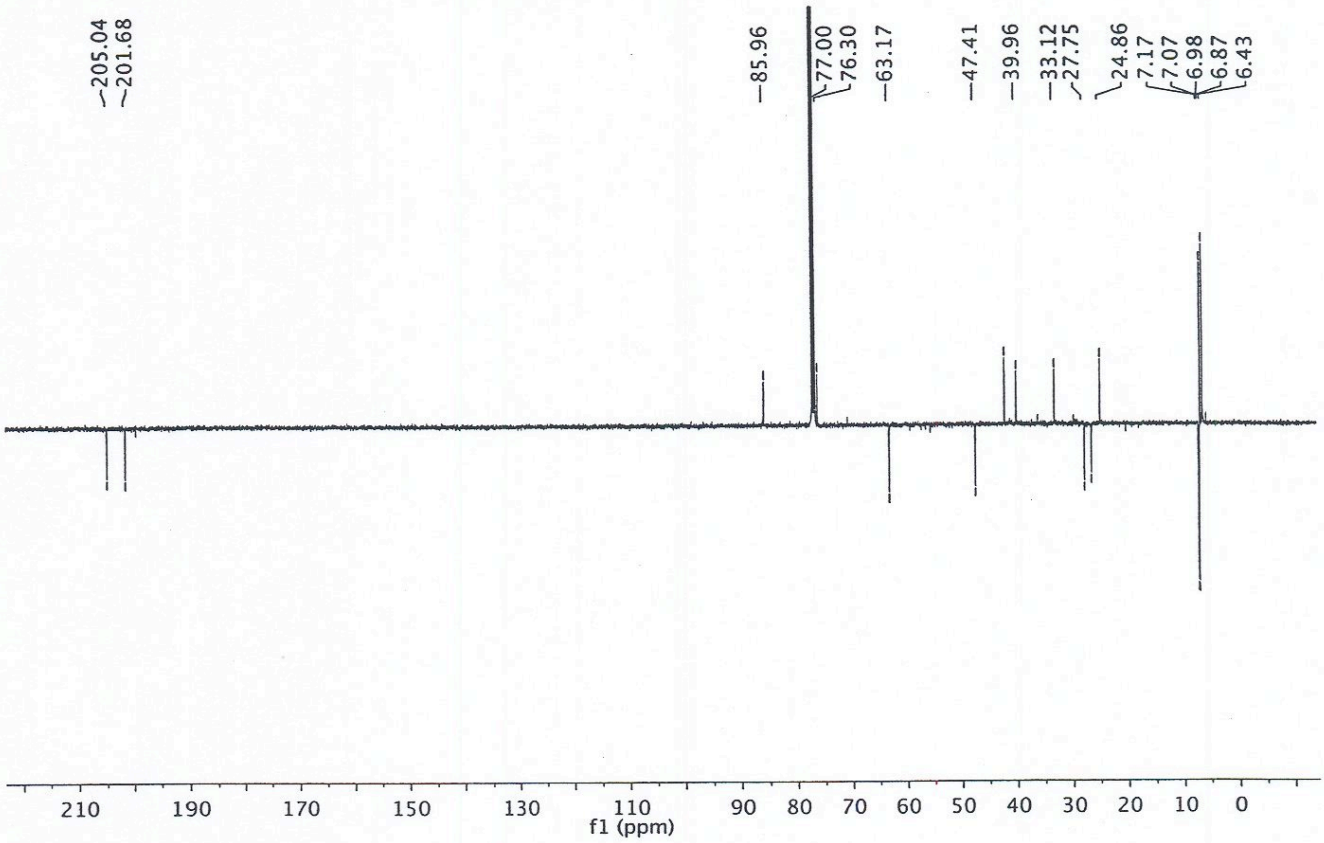
4

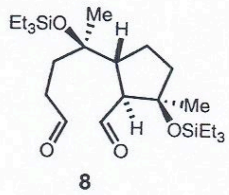
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.15
1.06
1.12
1.09
2.53
4.39
2.14
3.24


82.28
74.71
64.33
63.85
54.82
52.28
49.36
48.94
48.51
41.94
35.19
28.07
27.76
26.42
25.95
95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5
f1 (ppm)


HO
Me
H
Me
H
OH
HO
OH

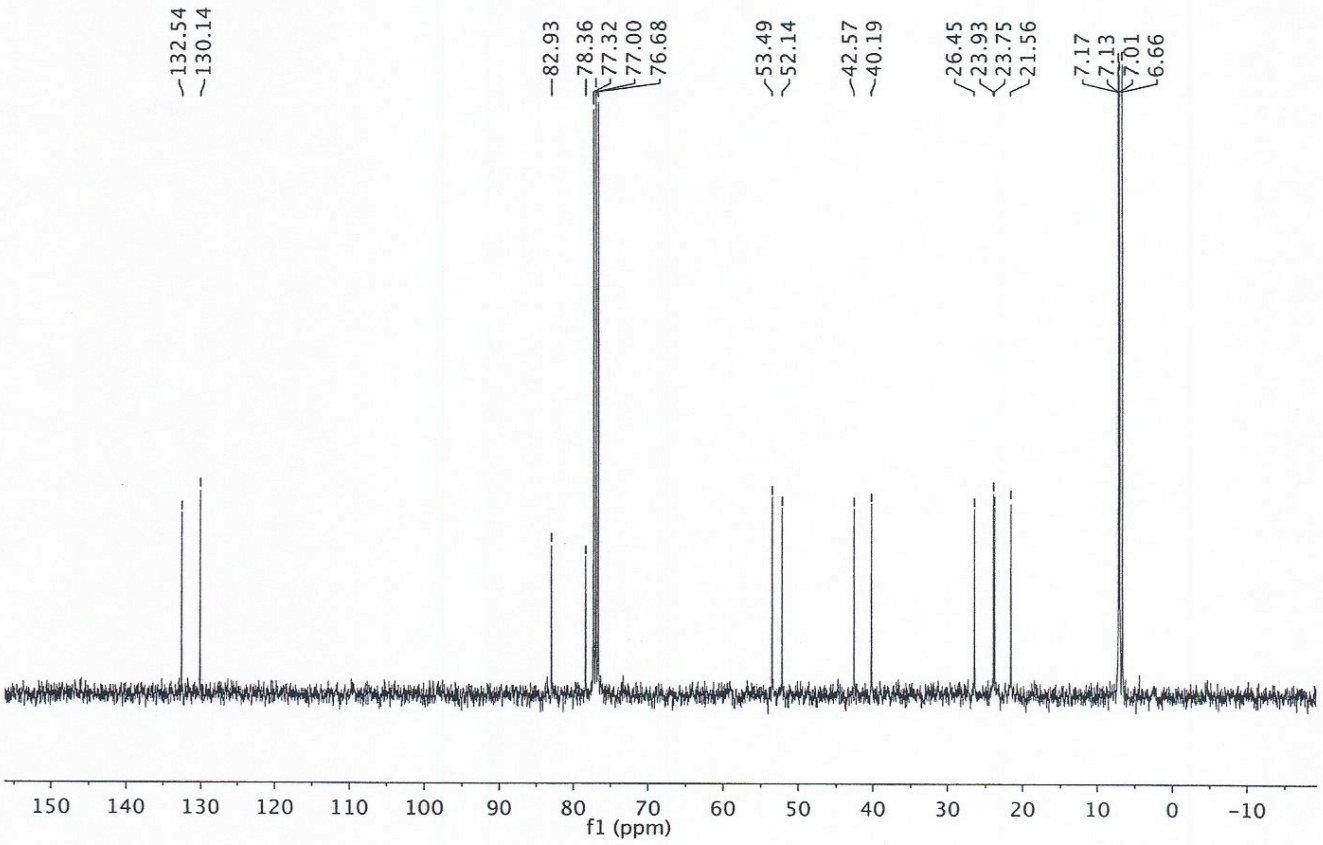
10 9 8 7 6 5 4 3 2 1 ppm
1.00
3.47
0.98
7.97
3.91
2.17
2.89

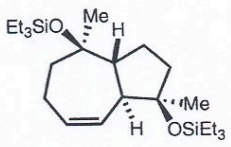

205.04
201.68
85.96
77.00
76.30
63.17
47.41
39.96
33.12
27.75
24.86
7.17
7.07
6.98
6.87
6.43
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Et3SiO
Me
H
Me
H
OSiEt3
O
O

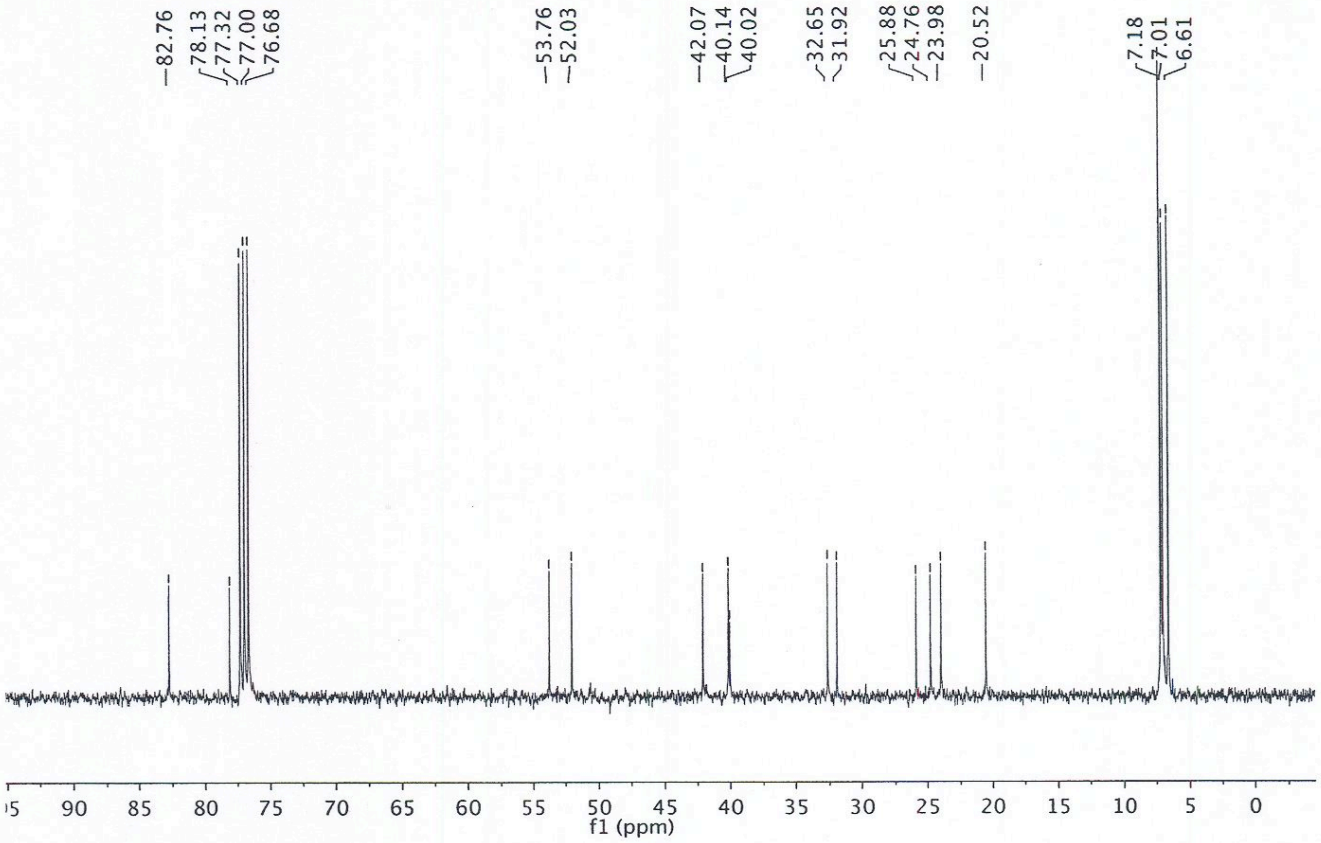
8

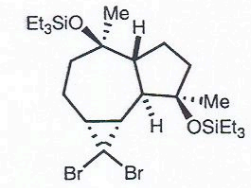
10
9
8
7
6
5
4
3
2
1
ppm
0.76
0.68
0.95
2.62
5.95
2.71
2.78
17.54
10.80


132.54
130.14
82.93
78.36
77.32
77.00
76.68
53.49
52.14
42.57
40.19
26.45
23.93
23.75
21.56
7.17
7.13
7.01
6.66
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

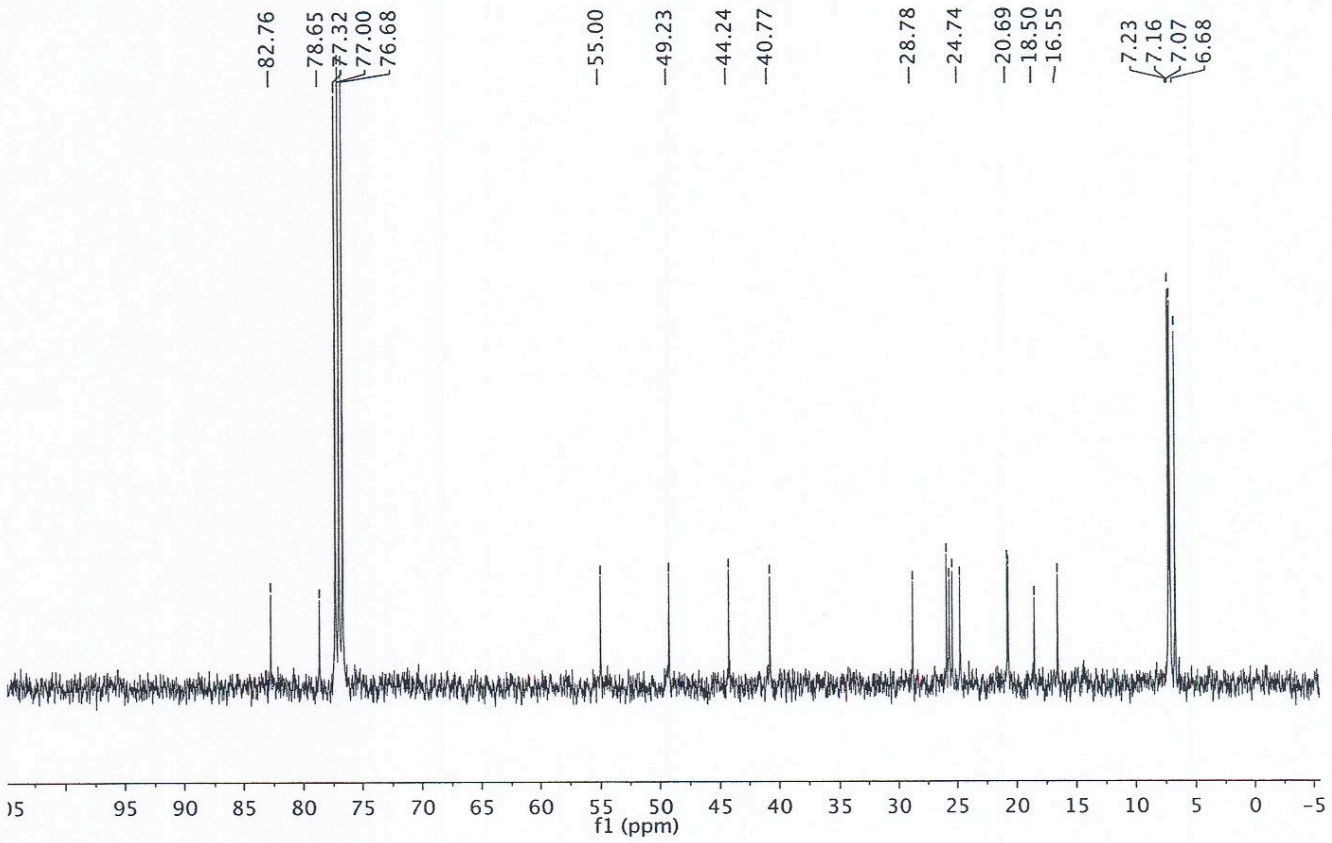

Et3SiO
Me
H
Me
H
OSiEt3

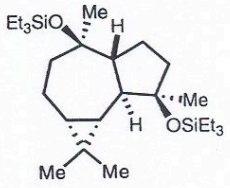
10 9 8 7 6 5 4 3 2 1 ppm
2.00
1.99
8.01
3.12
2.93
18.30
12.20


82.76
78.13
77.32
77.00
76.68
53.76
52.03
42.07
40.14
40.02
32.65
31.92
25.88
24.76
23.98
20.52
7.18
7.01
6.61
f1 (ppm)

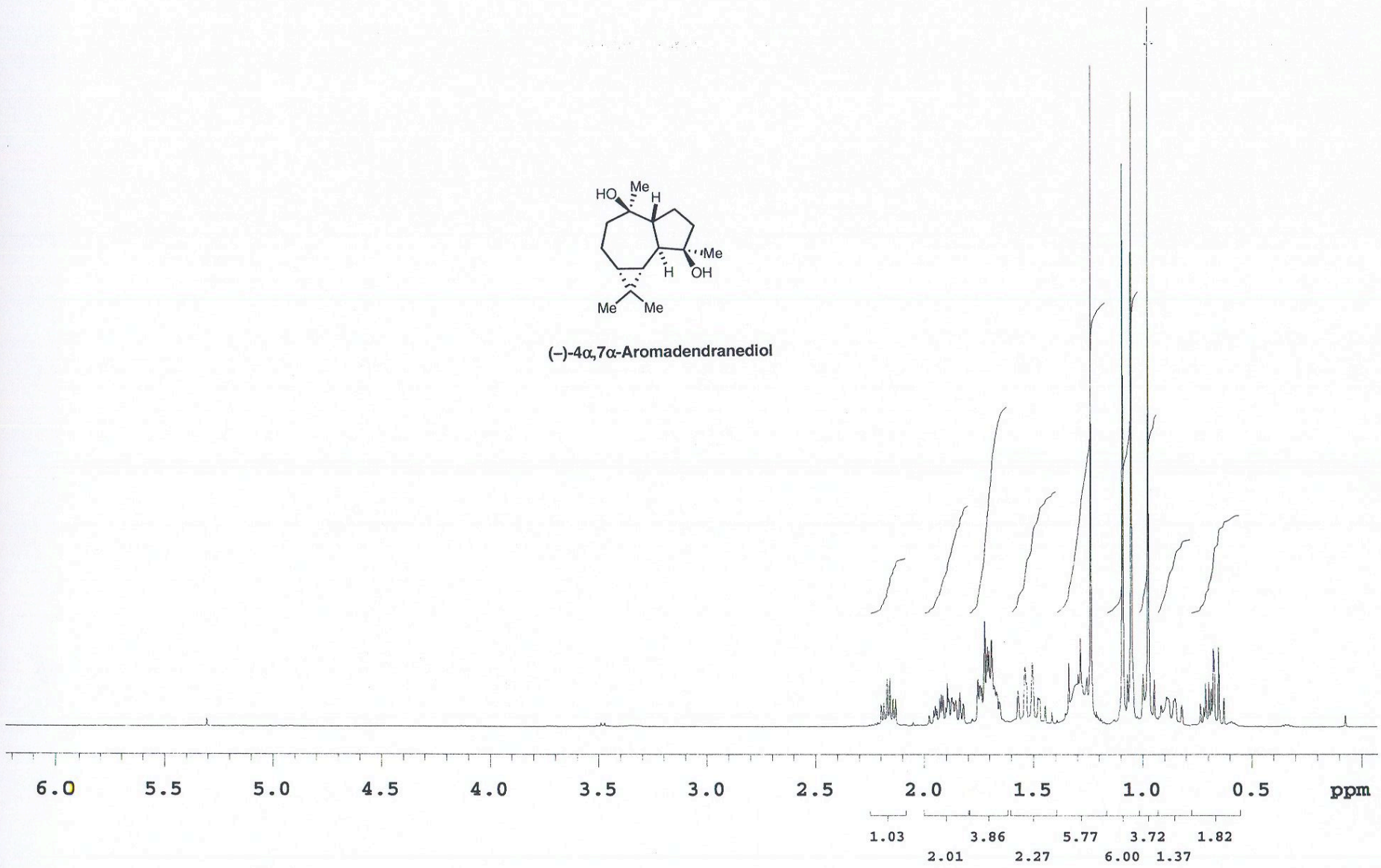

Et3SiO
Me
H
Me
H
OSiEt3
Br
Br

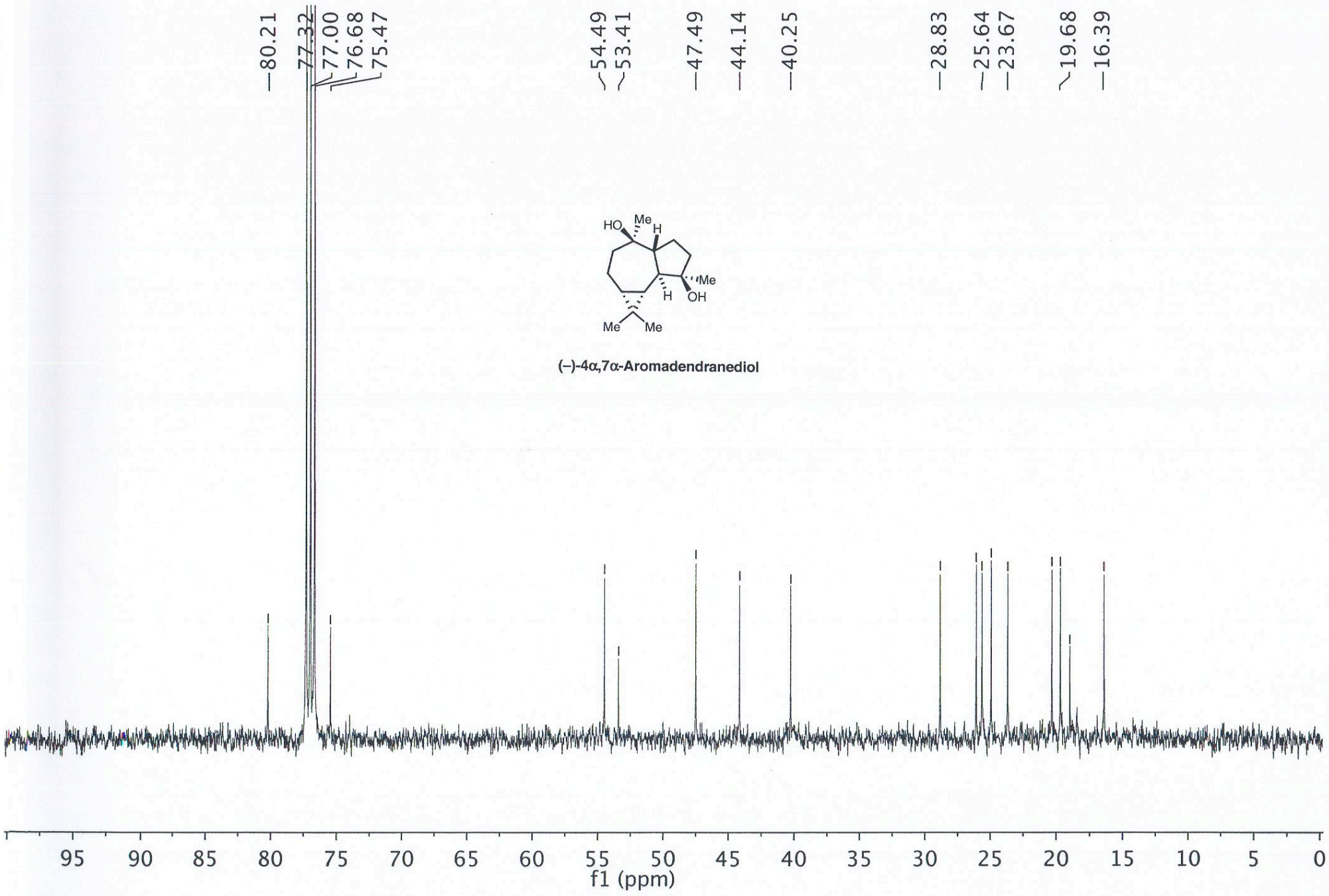
ppm
1.79
1.09
2.73
1.43
18.38
1.00
5.43
1.03
3.07
11.43


82.76
78.65
77.32
77.00
76.68
55.00
49.23
44.24
40.77
28.78
24.74
20.69
18.50
16.55
7.23
7.16
7.07
6.68
95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5
f1 (ppm)


Et3SiO
Me
H
Me
H
OSiEt3
Me
Me

6 5 4 3 2 1 0 ppm
0.87
5.73
1.93
2.29
6.24
17.88
3.04
11.71


HO
Me
H
Me
H
OH
Me
Me
(–)-4α,7α-Aromadendranediol
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
1.03
2.01
3.86
2.27
5.77
6.00
3.72
1.37
1.82



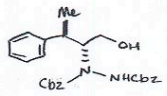
(–)-4α,7α-Aromadendranediol

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 11:19:53 AM
Vial number: 8
Sequence name: bls2
Filename: bls2-86-41

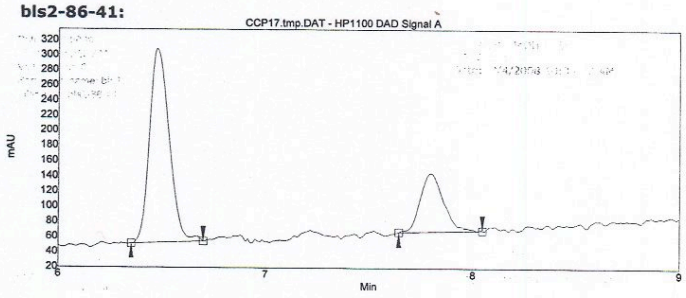
Method Name: ADH_MeOH_5-50
User Name: SFC User
Acquisition Date: 3/4/2008 10:33:52 AM

Run Information:
N.A.



SAMPLE SPIKED WITH BOTH ANTI ENANTIOMERS

bls2-86-41:



The Chromatogram Noise is 0

Results Table:

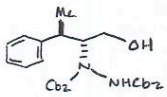
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[uV]	[uV.Min]	[%]
1	UNKNOWN	6.35	6.48	6.70	0.00	73.63	255.9	27.8	73.630
2	UNKNOWN	7.64	7.80	8.05	0.00	26.37	77.1	10.0	26.370
Total						100.00	333.0	37.8	100.000

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 11:25:28 AM
Vial number: 10
Sequence name: BLS6
Filename: bls3-86-D1

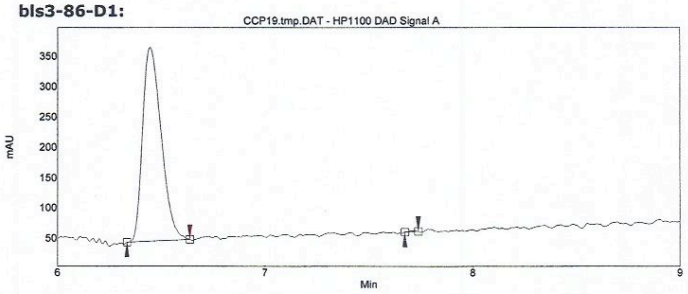
Method Name: ADH_MeOH_5-50
User Name: SFC User
Acquisition Date: 1/21/2008 10:22:35 PM

Run Information:
N.A.



ANTI

bls3-86-D1:



The Chromatogram Noise is 0

Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[uV]	[uV.Min]	[%]
1	UNKNOWN	6.33	6.45	6.64	0.00	99.84	319.4	33.4	99.843
2	UNKNOWN	7.67	7.72	7.74	0.00	0.16	1.9	0.1	0.157
Total						100.00	321.3	33.4	100.000

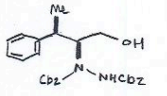
99.6 % ee

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 11:02:21 AM
Vial number: 7
Sequence name: bls-1
Filename: bls3-86-21

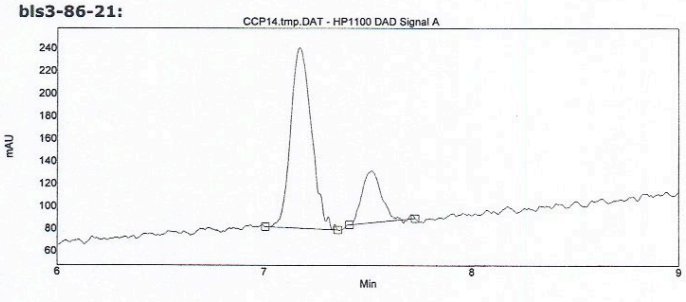
Method Name: ADH_MeOH_5-50
User Name: SFC User
Acquisition Date: 3/4/2008 10:50:36 AM

Run Information:
N.A.



SAMPLE SPIKED WITH BOTH SYN ENANTIOMERS

bls3-86-21:



The Chromatogram Noise is 0

Results Table:

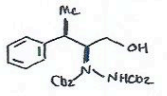
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[uV]	[uV.Min]	[%]
1	UNKNOWN	7.01	7.17	7.35	0.00	78.53	159.9	18.4	78.528
2	UNKNOWN	7.41	7.52	7.73	0.00	21.47	46.1	5.0	21.472
Total						100.00	206.0	23.5	100.000

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 11:50:46 AM
Vial number: 11
Sequence name: bls2
Filename: bls2-86-D21

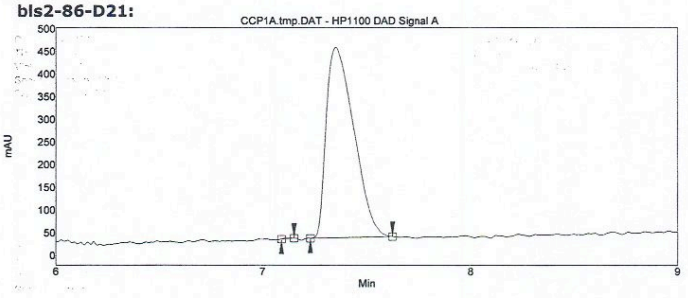
Method Name: ADH_MeOH_5-50
User Name: SFC User
Acquisition Date: 1/21/2008 10:49:30 PM

Run Information:
N.A.



SYN

bls2-86-D21:



The Chromatogram Noise is 0

Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[uV]	[uV.Min]	[%]
2	UNKNOWN	7.09	7.11	7.15	0.00	0.09	1.9	0.1	0.088
1	UNKNOWN	7.23	7.35	7.62	0.00	99.91	419.7	64.0	99.912
Total						100.00	421.6	64.0	100.000

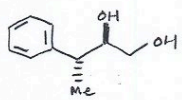
99.8 % ee

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 7:49:29 PM
Vial number: 5
Sequence name: BLS4
Filename: BLS2-H20-RL-racOJH9

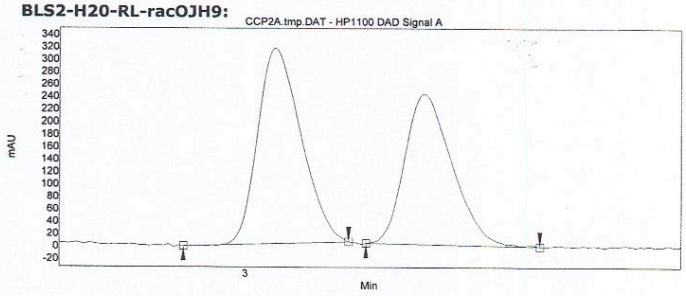
Method Name: OJH_MeOH_5-10
User Name: Administrator
Acquisition Date: 2/5/2009 3:55:12 PM

SAMPLE SPIKED W/ BOTH ANTI ENANTIOMERS



Run Information:
N.A.

BLS2-H20-RL-racOJH9:



The Chromatogram Noise is 0

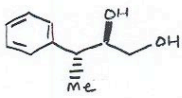
Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[uV]	[uV.Min]	[%]
1	UNKNOWN	2.90	3.05	3.17	0.00	54.62	313.8	25.4	54.621
2	UNKNOWN	3.19	3.29	3.47	0.00	45.38	241.3	21.1	45.379
Total						100.00	555.1	46.6	100.000

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 7:51:18 PM
Vial number: 3
Sequence name: BLS4
Filename: BLS2-H20-RL-OJH11

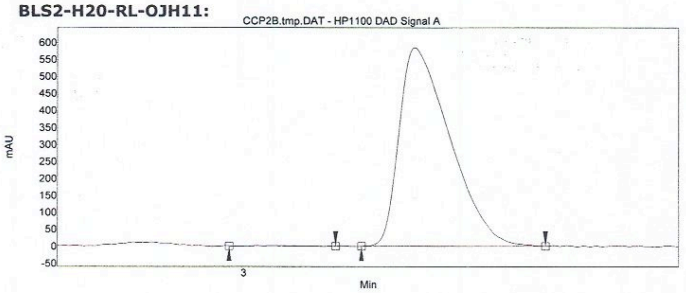
Method Name: OJH_MeOH_5-10
User Name: SFC User
Acquisition Date: 2/5/2009 5:11:57 PM



ANTI

Run Information:
N.A.

BLS2-H20-RL-OJH11:



The Chromatogram Noise is 0

Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[uV]	[uV.Min]	[%]
1	UNKNOWN	2.98	3.02	3.15	0.00	0.15	1.7	0.1	0.145
2	UNKNOWN	3.19	3.28	3.48	0.00	99.85	584.9	55.3	99.855
Total						100.00	586.6	55.4	100.000

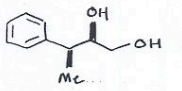
99.7 % ee

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 8:09:00 PM
Vial number: 2
Sequence name: BLS10
Filename: BLS2-H2O-SL10

Method Name: ADH_MeOH_5-10
User Name: SFC User
Acquisition Date: 2/5/2009 12:59:42 PM

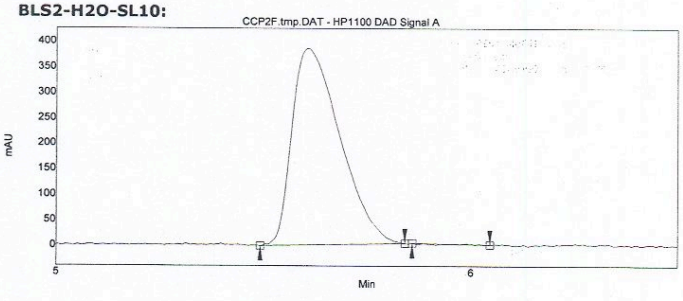
OTHER ENANTIOMER



(2R,3S)-SYN

Run Information:
N.A

BLS2-H2O-SL10:



The Chromatogram Noise is 0

Results Table:

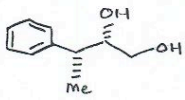
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[uV]	[uV.Min]	[%]
1	UNKNOWN	5.49	5.61	5.84	0.00	99.83	385.2	51.3	99.832
2	UNKNOWN	5.86	5.92	6.05	0.00	0.17	2.7	0.1	0.168
Total						100.00	387.8	51.4	100.000

99.6 % ee

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 8:08:13 PM
Vial number: 1
Sequence name: BLS2
Filename: BLS2-H2O-RD7

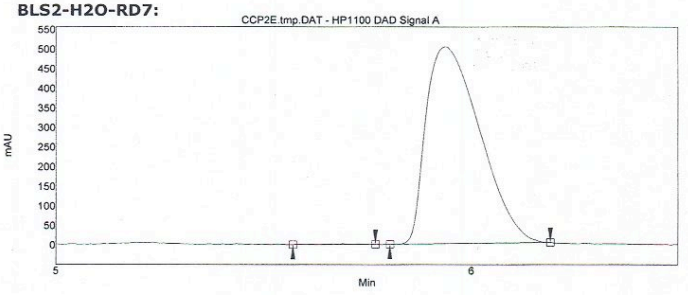
Method Name: ADH_Solv4_5-10
User Name: SFC User
Acquisition Date: 2/5/2009 11:03:36 AM



(2S,3R)-SYN

Run Information:
N.A.

BLS2-H2O-RD7:



The Chromatogram Noise is 0

Results Table:

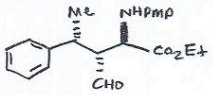
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[uV]	[uV.Min]	[%]
2	UNKNOWN	5.57	5.69	5.77	0.00	0.25	2.1	0.2	0.253
1	UNKNOWN	5.80	5.94	6.19	0.00	99.75	502.9	75.5	99.747
Total						100.00	505.0	75.7	100.000

99.5 % ee

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 8:36:32 PM
Vial number: 4
Sequence name: BLS14
Filename: BLS2-rmSDC5

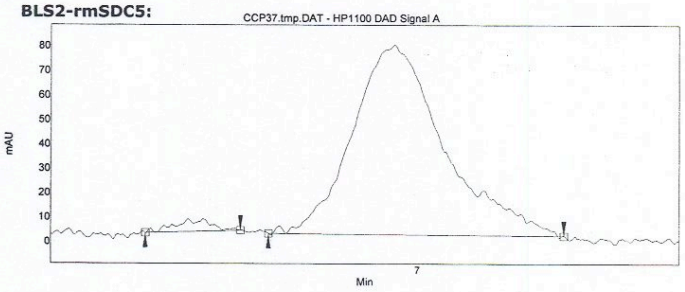
Method Name: OJH_Solv4_5-10
User Name: SFC User
Acquisition Date: 1/30/2009 2:22:14 AM



OTHER ENANTIOMER (2R,3R,4R)

Run Information:
N.A.

BLS2-rmSDC5:



The Chromatogram Noise is 0

Results Table:

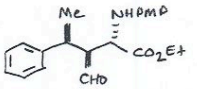
Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	UNKNOWN	6.48	6.56	6.66	0.00	2.44	5.1	0.4	2.439
2	UNKNOWN	6.72	6.96	7.28	0.00	97.56	77.5	15.7	97.561
Total						100.00	82.6	16.1	100.000

97.5 % ee

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 8:37:02 PM
Vial number: 2
Sequence name: BLS10
Filename: BLS2-rmRLC5

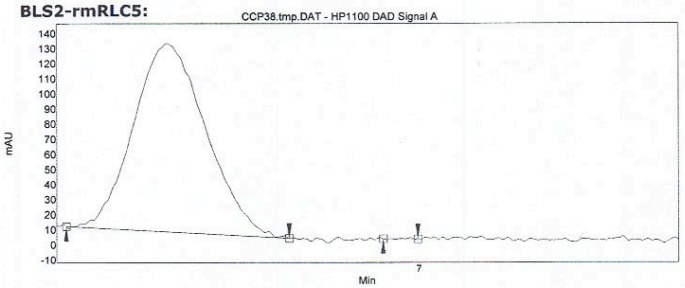
Method Name: OJH_MeOH_5-10
User Name: SFC User
Acquisition Date: 1/30/2009 1:48:49 AM



(2S,3S,4S) *

Run Information:
N.A.

BLS2-rmRLC5:



The Chromatogram Noise is 0

Results Table:

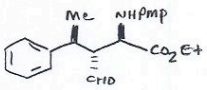
Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	UNKNOWN	6.32	6.51	6.75	0.00	100.00	124.8	20.2	99.996
2	UNKNOWN	6.93	6.98	7.00	0.00	0.00	0.8	0.0	0.004
Total						100.00	125.6	20.2	100.000

99.9 % ee

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 8:14:30 PM
Vial number: 5
Sequence name: BLS16
Filename: BLS2-rmRDrac6

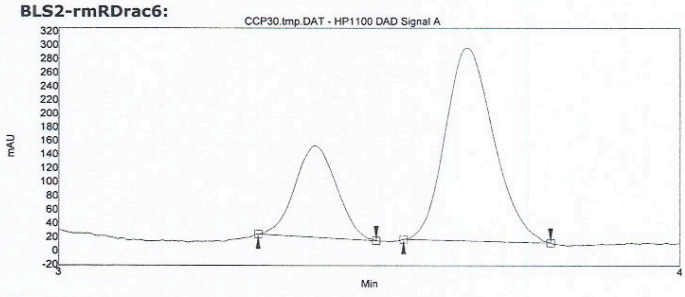
Method Name: OJH_MeOH_5-10
User Name: SFC User
Acquisition Date: 1/30/2009 10:30:06 AM



SAMPLE SPIKED W/ BOTH ENANTIOMERS

Run Information:
N.A.

BLS2-rmRDrac6:



The Chromatogram Noise is 0

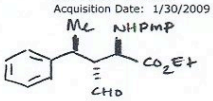
Results Table:

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	UNKNOWN	3.32	3.41	3.51	0.00	28.89	132.4	10.2	28.893
2	UNKNOWN	3.56	3.66	3.79	0.00	71.11	281.0	25.1	71.107
Total						100.00	413.4	35.3	100.000

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 8:16:30 PM
Vial number: 2
Sequence name: BLS10
Filename: BLS2-rmD2C3

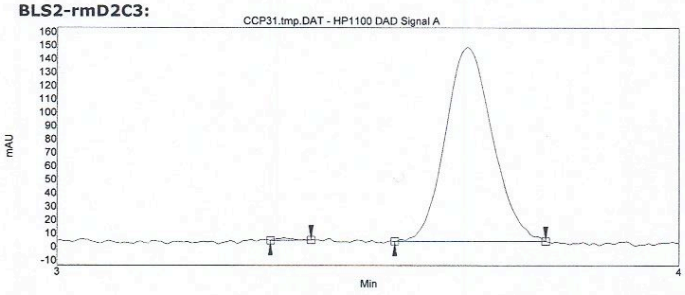
Method Name: OJH_MeOH_5-10
User Name: SFC User
Acquisition Date: 1/30/2009 12:07:51 AM



(2R,3R,4S) *

Run Information:
N.A.

BLS2-rmD2C3:



The Chromatogram Noise is 0

Results Table:

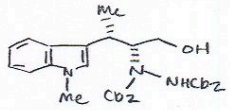
Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
2	UNKNOWN	3.34	3.37	3.41	0.00	0.41	1.8	0.1	0.414
1	UNKNOWN	3.54	3.66	3.78	0.00	99.59	144.1	12.7	99.586
Total						100.00	146.0	12.7	100.000

99.6 % ee

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 4:55:19 PM
Vial number: 2
Sequence name: bls12
Filename: BLS3-260_syn_ASH_5-252

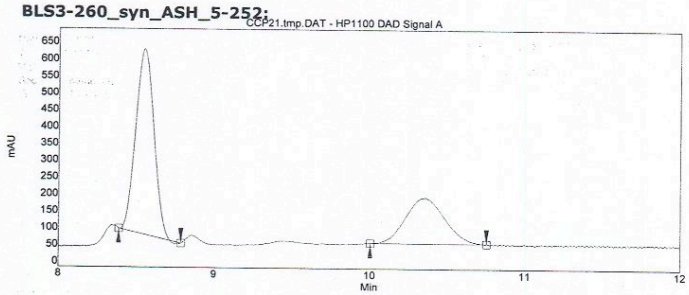
Method Name: ASH_MeOH_5-25
User Name: SFC User
Acquisition Date: 8/16/2008 9:28:23 PM



SYN
SPIKED WITH BOTH ENANTIOMERS

Run Information:
N.A.

BLS3-260_syn_ASH_5-252:



The Chromatogram Noise is 0

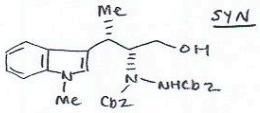
Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.39	8.55	8.79	0.00	65.25	549.0	74.2	65.250
2	UNKNOWN	10.00	10.36	10.75	0.00	34.75	135.7	39.5	34.750
Total						100.00	684.8	113.7	100.000

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 5:43:11 PM
Vial number: 3
Sequence name: jui65
Filename: BLS2-292_ASH_MeOH0

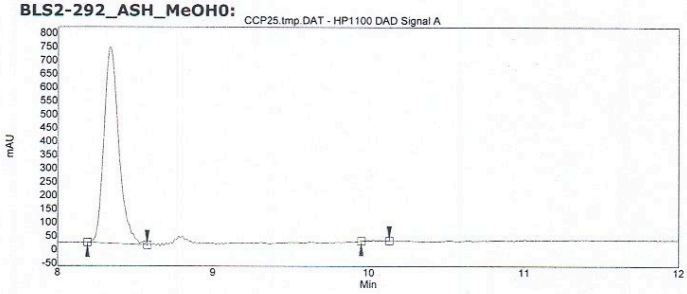
Method Name: ASH_MeOH_5-25
User Name: SFC User
Acquisition Date: 10/8/2008 10:44:25 AM



SYN

Run Information:
N.A.

BLS2-292_ASH_MeOH0:



The Chromatogram Noise is 0

Results Table:

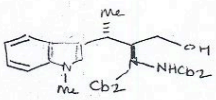
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.19	8.34	8.58	0.00	99.64	725.4	80.2	99.636
2	UNKNOWN	9.95	10.05	10.13	0.00	0.36	3.2	0.3	0.364
Total						100.00	728.5	80.5	100.000

99.2% ee

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 4:29:08 PM
Vial number: 1
Sequence name: bls-1
Filename: BLS3-260_anti_ASH1

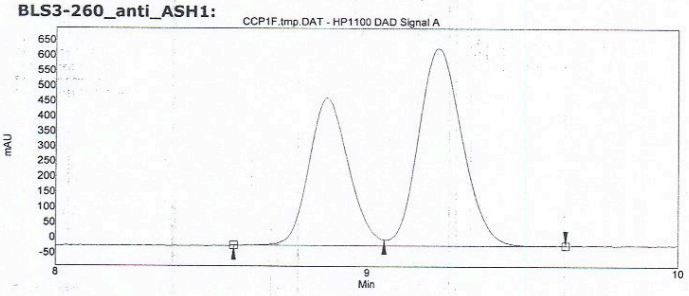
Method Name: ASH_MeOH_5-15
User Name: SFC User
Acquisition Date: 8/16/2008 8:40:04 PM



ANTI
SPIKED WITH BOTH ENANTIOMERS

Run Information:
N.A.

BLS3-260_anti_ASH1:



The Chromatogram Noise is 0

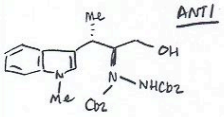
Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.57	8.87	9.06	0.00	40.13	485.7	70.7	40.130
2	UNKNOWN	9.06	9.23	9.64	0.00	59.87	648.9	105.4	59.870
Total						100.00	1134.6	176.1	100.000

BergerSFC Chromatogram Report

Date: 3/1/2009
Time: 10:25:22 PM
Vial number: 1
Sequence name: bls12
Filename: BLS3-260_SS-D_ASH3_2

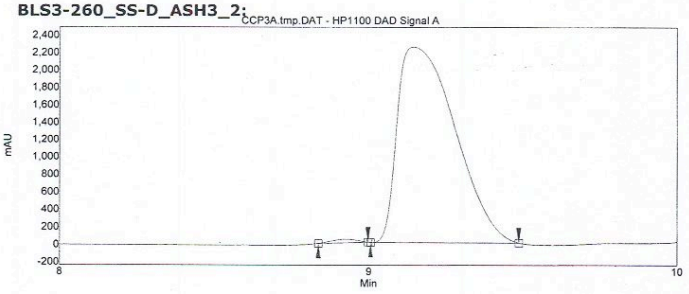
Method Name: ASH_MeOH_5-15
User Name: SFC User
Acquisition Date: 8/16/2008 11:16:32 PM



ANTI

Run Information:
N.A.

BLS3-260_SS-D_ASH3_2:



The Chromatogram Noise is 0

Results Table:

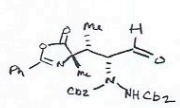
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	8.84	8.92	9.00	0.00	0.75	39.5	3.7	0.753
1	UNKNOWN	9.01	9.14	9.49	0.00	99.25	2241.7	488.3	99.247
Total						100.00	2281.2	492.0	100.000

98.5% ee

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 10:29:00 AM
Vial number: 3
Sequence name: jui48
Filename: BLS2-2BLS2-288-syn_rac_ADH_MeCN5

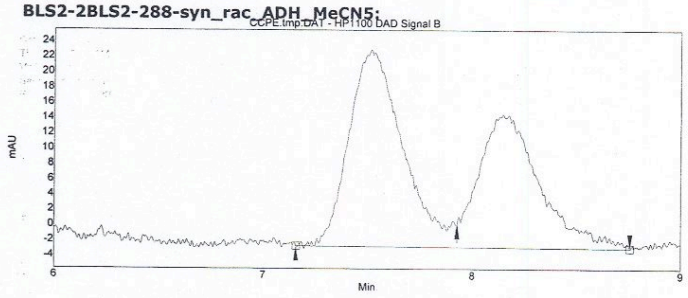
Method Name: ADH_MeCN_5-10
User Name: SFC User
Acquisition Date: 10/8/2008 11:45:59 AM



SYN
SPIKED WITH BOTH ENANTIOMERS

Run Information:
N.A.

BLS2-2BLS2-288-syn_rac_ADH_MeCN5:



The Chromatogram Noise is 0

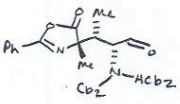
Results Table:

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	UNKNOWN	7.16	7.52	7.93	0.00	56.72	25.7	7.7	56.718
2	UNKNOWN	7.93	8.14	8.76	0.00	43.28	17.4	5.9	43.282
Total						100.00	43.1	13.6	100.000

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 10:34:34 AM
Vial number: 1
Sequence name: jui48
Filename: BLS2-BLS2-288-SS-L_ADH_MeCN6

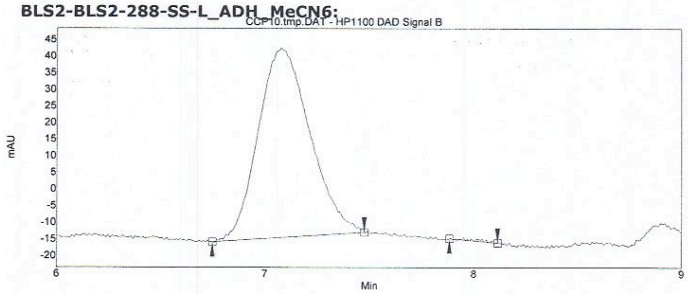
Method Name: ADH_MeCN_5-10
User Name: SFC User
Acquisition Date: 10/8/2008 1:40:53 PM



SYN

Run Information:
N.A.

BLS2-BLS2-288-SS-L_ADH_MeCN6:



The Chromatogram Noise is 0

Results Table:

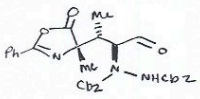
Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	UNKNOWN	6.75	7.08	7.47	0.00	99.78	56.9	16.2	99.783
2	UNKNOWN	7.88	8.04	8.11	0.00	0.22	0.7	0.0	0.217
Total						100.00	57.7	16.2	100.000

99.6% ee

BergerSFC Chromatogram Report

Date: 3/5/2009
Time: 1:21:03 AM
Vial number: 2
Sequence name: jui58
Filename: BLS2-289_anti_ASH_MeCN2

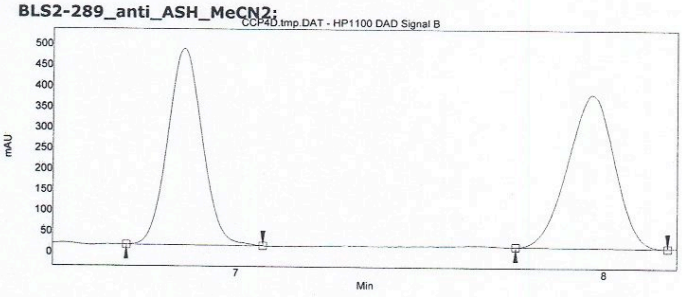
Method Name: ASH_MeCN_5-25
User Name: SFC User
Acquisition Date: 10/7/2008 6:18:36 PM



SAMPLE SPIKED WITH BOTH ANTI ENANTIOMERS

Run Information:
N.A.

BLS2-289_anti_ASH_MeCN2:



The Chromatogram Noise is 0

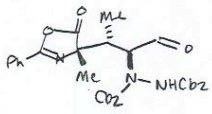
Results Table:

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	UNKNOWN	6.70	6.86	7.07	0.00	48.95	471.9	51.8	48.952
2	UNKNOWN	7.76	7.97	8.17	0.00	51.05	367.5	54.0	51.048
Total						100.00	839.3	105.8	100.000

BergerSFC Chromatogram Report

Date: 3/5/2009
Time: 1:25:31 AM
Vial number: 2
Sequence name: jui58
Filename: BLS2-289_SS-D_ASH_MeCN5

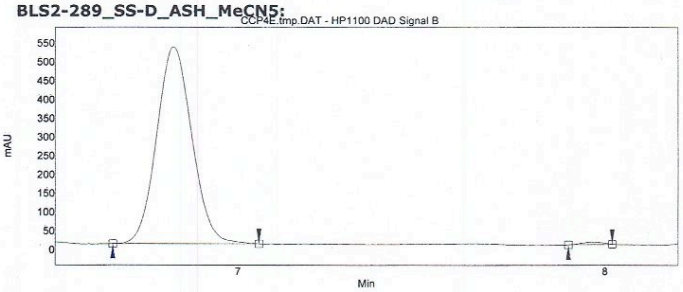
Method Name: ASH_MeCN_5-25
User Name: SFC User
Acquisition Date: 10/8/2008 12:24:54 PM



ANTI

Run Information:
N.A.

BLS2-289_SS-D_ASH_MeCN5:



The Chromatogram Noise is 0

Results Table:

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	UNKNOWN	6.66	6.82	7.06	0.00	99.28	523.9	58.2	99.284
2	UNKNOWN	7.90	7.96	8.02	0.00	0.72	6.4	0.4	0.716
Total						100.00	530.3	58.6	100.000

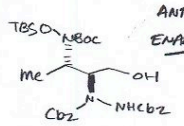
98.6 % ee

BergerSFC Chromatogram Report

Date: 3/2/2009
Time: 11:11:39 AM
Vial number: 4
Sequence name: esther34
Filename: BLS3-208-RR-D_OJH7

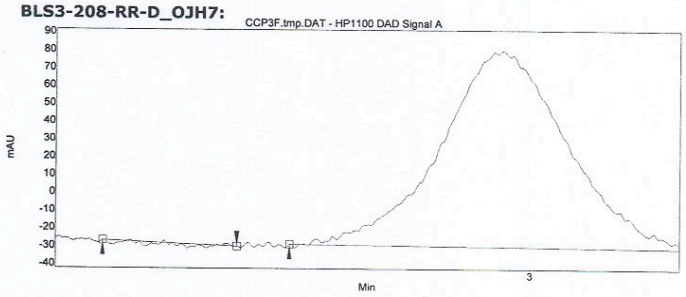
Method Name: OJH_MeOH_5-10
User Name: SFC User
Acquisition Date: 10/18/2008 1:56:15 PM

ANT I
ENANTIOMER



Run Information:
N.A.

BLS3-208-RR-D_OJH7:



The Chromatogram Noise is 0

Results Table:

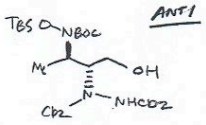
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[uV]	[uV.Min]	[%]
2	UNKNOWN	2.15	2.23	2.41	0.00	0.60	2.5	0.2	0.600
1	UNKNOWN	2.52	2.95	3.37	0.00	99.40	110.2	32.3	99.400
Total						100.00	112.7	32.5	100.000

BergerSFC Chromatogram Report

Date: 3/2/2009
Time: 11:03:32 AM
Vial number: 3
Sequence name: esther32
Filename: BLS3-208-SS-L_OJH7

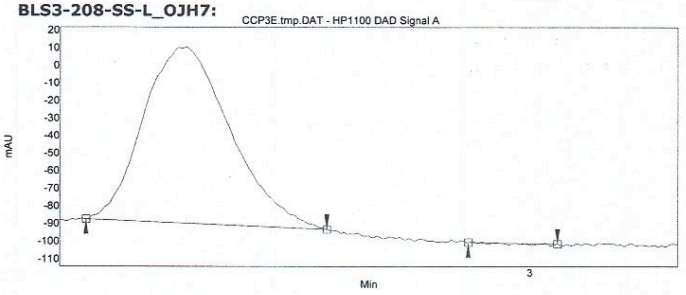
Method Name: OJH_MeOH_5-10
User Name: SFC User
Acquisition Date: 10/18/2008 1:39:27 PM

ANT I



Run Information:
N.A.

BLS3-208-SS-L_OJH7:



The Chromatogram Noise is 0

Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[uV]	[uV.Min]	[%]
1	UNKNOWN	2.10	2.31	2.59	0.00	99.79	100.2	20.4	99.788
2	UNKNOWN	2.87	3.04	3.06	0.00	0.21	1.0	0.0	0.212
Total						100.00	101.2	20.5	100.000

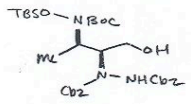
99.6% ee

BergerSFC Chromatogram Report

Date: 3/2/2009
Time: 11:29:20 AM
Vial number: 1
Sequence name: BLSassaydevelopment21
Filename: BLS3-208-syn_OJH_5_MeCN3

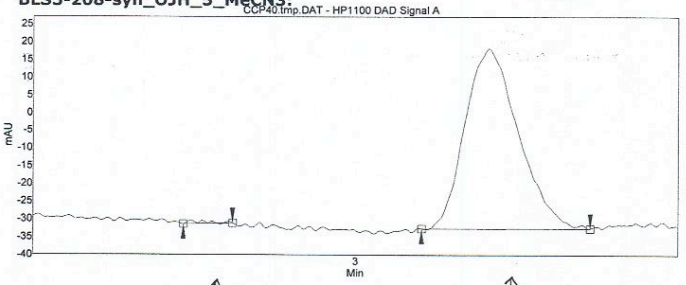
Method Name: OJH_MeCN_5
User Name: SFC User
Acquisition Date: 11/12/2008 7:46:09 PM

SYN



Run Information:
N.A.

BLS3-208-syn_OJH_5_MeCN3:



The Chromatogram Noise is 0

MINOR ENANTIOMER

MAJOR ENANTIOMER

Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[uV]	[uV.Min]	[%]
2	UNKNOWN	2.73	2.75	2.81	0.00	0.53	1.0	0.0	0.534
1	UNKNOWN	3.10	3.21	3.36	0.00	99.47	50.7	4.9	99.466
Total						100.00	51.8	4.9	100.000

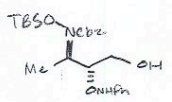
98.9% ee

BergerSFC Chromatogram Report

Date: 3/5/2009
Time: 1:52:57 AM
Vial number: 3
Sequence name: bls2
Filename: BLS3-245-Anti_rac12

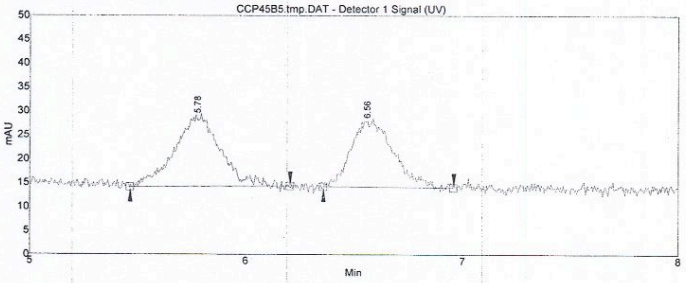
Method Name: ADH_MeOH_5-10
User Name: SFC User
Acquisition Date: 7/14/2008 10:42:21 PM

Run Information:
N.A.



SAMPLE SPIKED WITH BOTH ANTI ENANTIOMERS

BLS3-245-Anti_rac12:



The Chromatogram Noise is 0

Results Table:

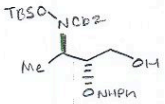
Index	Name	Time [Min]	Width USP [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	UNKNOWN	0.14	0.15	8.36	8.6	0.6	8.359
2	UNKNOWN	0.28	0.05	3.10	8.6	0.2	3.100
3	UNKNOWN	5.78	0.37	47.23	14.4	3.6	47.233
4	UNKNOWN	6.56	0.32	41.31	13.5	3.1	41.308
Total				100.00	45.1	7.6	100.000

BergerSFC Chromatogram Report

Date: 3/5/2009
Time: 1:54:53 AM
Vial number: 8
Sequence name: bls-1
Filename: BLS3-245-L12

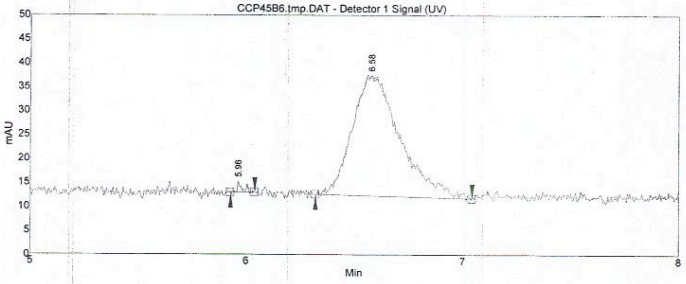
Method Name: ADH_MeOH_5-10
User Name: SFC User
Acquisition Date: 7/14/2008 10:07:21 PM

Run Information:
N.A.



ANTI

BLS3-245-L12:



The Chromatogram Noise is 0

Results Table:

Index	Name	Time [Min]	Width USP [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
2	UNKNOWN	5.96	0.03	0.63	2.2	0.0	0.630
1	UNKNOWN	6.58	0.37	99.37	25.2	6.4	99.370
Total				100.00	27.3	6.4	100.000

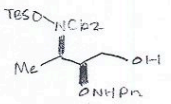
98.8% ee

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 5:51:41 PM
Vial number: 4
Sequence name: bls4
Filename: BLS3-245-Syn_rac13

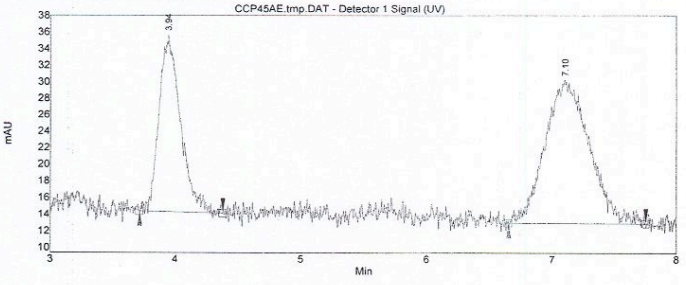
Method Name: ADH_MeOH_5-10
User Name: SFC User
Acquisition Date: 7/14/2008 11:05:36 PM

Run Information:
N.A.



SYN SPIKED WITH BOTH ENANTIOMERS

BLS3-245-Syn_rac13:



The Chromatogram Noise is 0

Results Table:

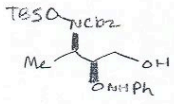
Index	Name	Time [Min]	Width USP [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	UNKNOWN	0.24	0.05	2.91	7.6	0.3	2.911
2	UNKNOWN	3.94	0.34	36.48	21.3	4.2	36.482
3	UNKNOWN	7.10	0.68	60.61	17.3	7.0	60.607
Total				100.00	46.2	11.6	100.000

BergerSFC Chromatogram Report

Date: 2/28/2009
Time: 5:55:41 PM
Vial number: 7
Sequence name: bls2
Filename: BLS3-245-D12

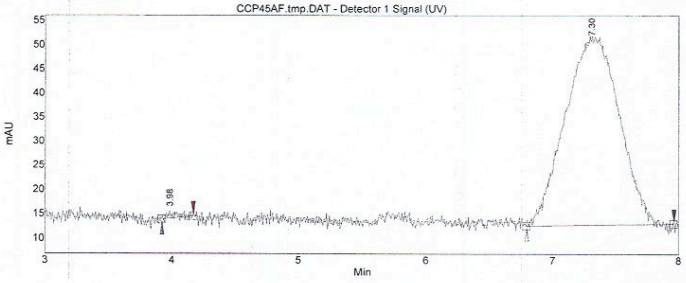
Method Name: ADH_MeOH_5-10
User Name: SFC User
Acquisition Date: 7/14/2008 9:51:09 PM

Run Information:
N.A.



SYN

BLS3-245-D12:



The Chromatogram Noise is 0

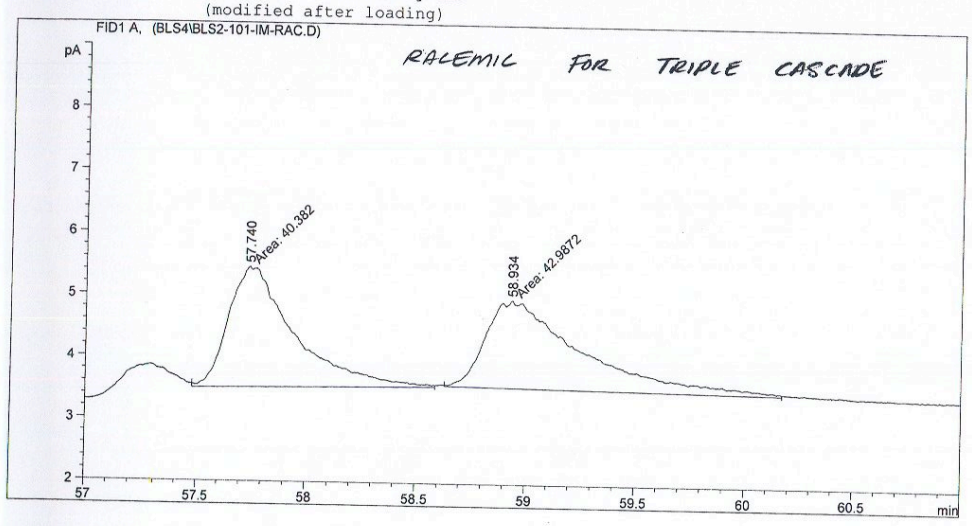
Results Table:

Index	Name	Time [Min]	Width USP [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
2	UNKNOWN	3.98	0.20	0.38	1.6	0.1	0.384
1	UNKNOWN	7.30	0.87	99.62	38.3	19.2	99.616
Total				100.00	39.8	19.3	100.000

99.2% ee

Data File C:\CHEM32\2\DATA\BLS4\BLS2-101-IM-RAC.D
Sample Name: bls2-101-rac

Acq. Operator : bls
Acq. Instrument : Col Mustard
Injection Date : 03-Mar-09, 09:09:18
Seq. Line : 4
Location : Vial 20
Inj : 1
Inj Volume : 1 µl
Different Inj Volume from Sequence ! Actual Inj Volume : 5 µl
Acq. Method : C:\CHEM32\2\METHODS\130-BLS.M
Last changed : 3/3/2009 9:08:12 AM by bls
(modified after loading)
Analysis Method : C:\CHEM32\2\METHODS\130-BLS2C.M
Last changed : 3/5/2009 3:16:08 AM by bls
(modified after loading)



Area Percent Report

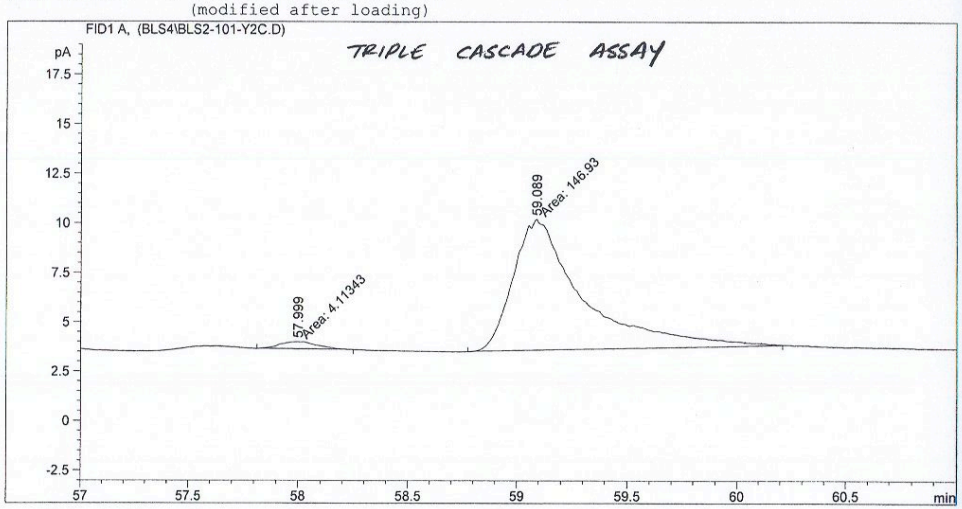
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	57.740	MM	0.3466	40.38200	1.94206	48.43753
2	58.934	MM	0.5055	42.98724	1.41719	51.56247
Totals :				83.36923	3.35925	

Data File C:\CHEM32\2\DATA\BLS4\BLS2-101-Y2C.D
Sample Name: bls2-101-Y

Acq. Operator : bls
Acq. Instrument : Col Mustard
Injection Date : 04-Mar-09, 15:04:20
Seq. Line : 6
Location : Vial 19
Inj : 1
Inj Volume : 1 µl
Different Inj Volume from Sequence ! Actual Inj Volume : 5 µl
Acq. Method : C:\CHEM32\2\METHODS\130-BLS2C.M
Last changed : 3/4/2009 1:02:29 PM by bls
Analysis Method : C:\CHEM32\2\METHODS\130-BLS2C.M
Last changed : 3/5/2009 3:11:38 AM by bls
(modified after loading)



Area Percent Report

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

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	57.999	MM	0.1882	4.11343	3.64213e-1	2.72334
2	59.089	MM	0.3695	146.93028	6.62668	97.27666
Totals :				151.04371	6.99089	

94.6 % ee

*** End of Report ***