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Supporting Information

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Divergent Reactions on a Racemic Mixture: Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

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Experimental Section:

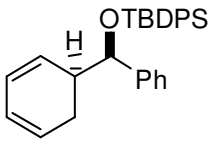
General: All reactions involving air- or moisture-sensitive reagents or intermediates were carried out in heat-gun-dried glassware under an argon atmosphere. THF was freshly distilled from potassium under argon. Diethylether (Et_2O) was freshly distilled from K/Na under argon. Dichloromethane (CH_2Cl_2) was freshly distilled from phosphorus(V)oxide (P_2O_5). Triethylamine (Et_3N) was distilled from CaH_2 and stored under argon. All other solvents and reagents were purified according to standard procedures or were used as received from Aldrich, Acros or Fluka. 2-Nitrosopyridine was synthesized according to the known procedure[1]. ^1H, ^{13}C, GCOSY, GHSQC and 1D-NOE NMR spectroscopy: Bruker Unity plus 600, AMX 400, dpx 300 spectrometer; chemical shifts, δ, were measured in ppm relative to $CHCl_3$ (7.26 ppm), which was used as an

external standard. Polarimetry: optical rotations were measured on Perkin Elmer 241 & 341 polarimeter. TLC: Merck silica gel 60 F 254 plates; detection with UV light or by dipping into a solution of $KMnO_4$ (1.5 g in 400 mL H_2O, 5 g $NaHCO_3$) or a solution of $Ce(SO_4)_2\backslash H_2O$ (10 g), phosphormolybdic acid hydrate (25 g), and conc. H_2SO_4 (60 mL) in H_2O (940 mL), followed by heating. Flash column chromatography (FC): Merck or Fluka silica gel 60 (40-63 µm) at approximately 0.4 bar. HPLC: KNAUER instrument, High Precision KNAUER HPLC Pump, Eurochrom V3.05 software. Column, eluent and retention times for HPLC analysis used for the determination of enantiomer ratios are given below with the details of the relevant experiment. IR: IR spectra were recorded on a *Bruker IFS-28* spectrophotometer. MS: Mass spectra were recorded on a *Finnigan MAT 4200S*, a *Bruker Daltonics Micro Tof*, a *Waters-Micromass Quatro LCZ* (ESI); and peaks are given in *m/z* (% of basis peak).

Syntheses of 1,3-cyclohexadiene derivatives from 1,4-cyclohexadiene

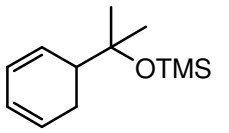
General procedure 1 (GP1): Preparation of cyclohexadienyllithium[2]

The solution of 1,4-cyclohexadiene (1.00 eq.) and tetramethylethylendiamine (TMEDA) (1.08 eq.) in THF (~ 0.2 M) was cooled to -78 °C. Then sec-BuLi (1.08 eq.) was added to the mixture, stirred for 60-90 min at that temperature and the yellowish solution was then used for transmetalation reactions.



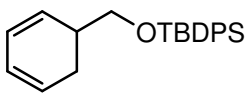
***tert*-Butyl-((*R*)-(*S*)-cyclohexa-2,4-dienyl-phenyl-methoxy)-diphenyl-silane (1a)**: *tert*-Butyldiphenylsilyl chloride (0.34 mL, 1.3 mmol) and imidazole (0.11 g, 1.61 mmol) were added to a solution of (*R*)-(*S*)-cyclohexa-2,4-dienyl-phenyl-methanol[1] (0.20 g, 1.6 mmol) in DMF (0.5 mL) and the solution was stirred at rt for 24 h. The reaction mixture was then diluted with methyl *tert*-butyl ether (MTBE), washed with brine, dried over $MgSO_4$, concentrated in vacuum and the residue was purified by flash column chromatography (pentane:MTBE, 50:1) to afford **1a** as a colorless oil (445 mg, 98 %). TLC: R_f = 0.4 (pentane:MTBE, 50:1). FTIR (neat): ν = 3037, 2931, 2857, 1492. 1471, 1427, 1390, 1110, 1062, 821, 738, 700 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.70-7.67 (m, 2H), 7.46-7.30 (m, 7H), 7.23-7.14 (m, 7H), 5.81-5.72 (m, 2H), 5.51-5.45 (m, 1H), 5.34-5.29 (m, 1H), 4.59 (d, J = 7.8 Hz, 1H),

2.73-2.62 (m, 1H), 2.32-2.14 (m ,1H), 1.03 ppm (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 143.1, 136.1, 134.2, 133.7, 129.5, 129.3, 127.7, 127.5, 127.4, 127.2, 127.1, 125.6, 124.7, 123.7, 77.04, 41.7, 27.1, 25.2, 19.5 ppm. HRMS (ESI) Exact mass calculated for $C_{29}H_{32}O_1Si\,Na$ ($[M + Na]^+$): 447.2115. Found: 447.2105.



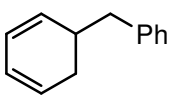
(1-Cyclohexa-2,4-dienyl-1-methyl-ethoxy)-trimethyl-silane (**1b**): Titanium(IV) iso-propoxide (0.66 mL, 2.2 mmol) was added to a solution of cyclohexadienyllithium (2.0 mmol, prepared according to GP 1) at -78 °C and the resulting brown mixture was stirred for 10 min. Acetone (0.12 mL, 1.6 mmol) was then added slowly at -78 °C and stirred for 6 h at that temperature. To the reaction mixture, water and MTBE were then added (white precipitate formed), warmed to rt, phases were separated and the aqueous phase was extracted with MTBE. The organic phase was washed (brine), dried ($MgSO_4$), concentrated in vacuum and the residue was purified by flash column chromatography (pentane:MTBE, 5:1) to afford 2-cyclohexa-2,4-dienyl-propan-2-ol as a colorless oil (0.20 g, 91%). TLC: R_f = 0.2 (pentane/MTBE, 5:1). FTIR (neat): ν = 3383, 3036, 2974, 2938, 2360, 1673, 1379, 1142, 1030, 953, 764, 700 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 6.13- 6.07 (m, 1H), 6.03-5.97 (m, 1H), 5.95-5.89 (m, 2H), 2.55-2.24 (m, 3H), 1.58 (br. s, 1H), 1.35 (s, 3H), 1.34 ppm (s, 3H). ^{13}C-NMR (101 MHz): δ = 126.7, 126.3, 125.3, 123.7, 73.2, 44.5, 27.3, 26.9, 24.1 ppm. MS (EI): 138.2 ($[M]^+$), 120.2, 105.2, 91.2, 80.2.

Trimethylsilyl chloride (0.17 mL, 1.3 mmol) and imidazole (111 mg, 1.63 mmol) were added to a solution of 2-cyclohexa-2,4-dienyl-propan-2-ol (150 mg, 1.08 mmol) in DMF (0.2 mL). The solution was stirred at rt for 8 h. The reaction mixture was then diluted with MTBE, washed with brine, dried over $MgSO_4$, concentrated in vacuum and the residue was purified by flash column chromatography (pentane:MTBE, 40:1) to afford **1b** as a colorless oil (220 mg, 97 %). TLC: R_f = 0.7 (pentane:MTBE, 20:1). FTIR (neat): ν = 2974, 2939, 1681, 1382, 1158, 1031, 756 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 5.93-5.89 (m, 1H), 5.87-5.83 (m, 1H), 5.80-5.75 (m, 2H), 2.42-2.35 (m, 1H), 2.26-2.06 (m, 2H), 1.21 (s, 3H), 1.20 (s, 3H), 0.12 ppm (s, 9H). ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 128.1, 126.3, 124.3, 123.7, 76.1, 45.6, 27.4, 24.2, 2.6 ppm. HRMS (ESI) Exact mass calculated for $C_{12}H_{22}OSiNa$ ($[M + Na]^+$): 233.1332. Found: 233.1325.

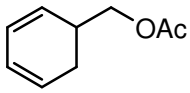


***tert*-Butyl-(cyclohexa-2,4-dienylmethoxy)-diphenyl-silane (1c)** Anhydrous $ZnCl_2$ (327 mg, 2.40 mmol) was added to a solution of cyclohexadienyllithium (4.80 mmol, prepared according to GP 1) at -78 °C and the reaction mixture was stirred for 3 h. Paraformaldehyde (64 mg, 2.0 mmol) was then added at -78 °C and the reaction mixture was stirred for 5 h at that temperature. The mixture was slowly warmed to room temperature and was stirred for 4 h at that temperature. Water and MTBE were then added to the reaction mixture (white precipitate formed), phases were separated and the aqueous phase was extracted with MTBE. The combined organic organic layers were washed (brine), dried ($MgSO_4$), concentrated in vacuum and the residue was purified by flash column chromatography (pentane:MTBE, 2:1) to afford cyclohexa-2,4-dienyl-methanol as a colorless oil (220 mg, 95%, inseparable mixture (9:1) of two isomers). TLC: R_f = 0.3 (pentane:MTBE, 1:1). FTIR (neat): ν = 3362, 3032, 2900, 2875, 1674, 1454, 1207, 1026, 736, 701, 681 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 5.99-5.95 (m, 1H), 5.88-5.85 (m, 1H), 5.79-5.74 (m, 1H), 5.70-5.67 (m, 1H), 3.60-3.58 (m, 2H), 2.54-2.44 (m, 1H), 2.36-2.27 (m, 1H), 2.21-2.13 ppm (m, 1H). ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 126.8, 125.6, 125.4, 123.8, 65.3, 35.7, 25.2 ppm. MS (EI): 110.1 ($[M]^+$), 108.1, 79.1, 51.0.

tert-Butyldiphenylsilyl chloride (0.67 mL, 2.6 mmol) and imidazole (219 mg, 3.21 mmol) were added to a solution of cyclohexa-2,4-dienyl-methanol (237 mg, 2.15 mmol) in DMF (0.5 mL) and the solution was stirred at rt for 24 h. The reaction mixture was then diluted with MTBE, washed with brine, dried over $MgSO_4$, concentrated in vacuum and the residue was purified by flash column chromatography (pentane:MTBE, 100:1) to afford **1c** as a colorless oil (0.73 g, 97 %). TLC: R_f = 0.6 (pentane:MTBE, 50:1). FTIR (neat): ν = 3071, 2901, 2931, 2880, 2858, 1472, 1427, 1390, 1361, 1112, 1007, 823, 740, 702, 613 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.69-7.67 (m, 4H), 7.45-7.37 (m, 6H), 5.94-5.90 (m, 1H), 5.87-5.84 (m, 1H), 5.77-5.69 (m, 2H), 3.63-3.60 (m, 2H), 2.68-2.53 (m, 1H), 2.32-2.15 (m, 2H), 1.07 ppm (s, 9H). ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 135.7, 135.6, 129.5, 127.7, 127.6, 125.6, 124.8, 123.9, 65.8, 36.0, 26.9, 25.2, 19.3 ppm. HRMS (ESI) Exact mass calculated for $C_{23}H_{28}OSiNa$ ($[M + Na]^+$): 371.1802. Found: 371.1801.



Cyclohexa-2,4-dienylmethyl-benzene (1d): Thiocarbonyldiimidazole (TCDI, 0.29 mg, 1.6 mmol) was added to a solution of cyclohexa-2,4-dienyl-phenyl-methanol (0.15 g, 0.81 mmol) in THF (4 mL). The mixture was refluxed at 67 ^{o}C for 6 h. Then the reaction mixture was allowed to cool to rt, concentrated under reduced pressure and passed through a short pad of silica gel (MTBE:pentane, 1:1) to afford the corresponding thiocarbonate derivative. The crude thiocarbonate was then dissolved in PhMe (5 mL). AIBN (32 mg, 0.19 mmol) and Bu_3SnH (0.53 mL, 2.0 mmol) were added to the solution. The reaction mixture was refluxed at 120 ^{o}C for 8 h, was then allowed to cool to rt, was concentrated under vacuum and the residue was purified by silica gel chromatography (pentane:MTBE, 200:1) to afford **1d** as a colorless oil (90 mg, 65 %, over two steps). TLC: R_f = 0.6 (pentane/MTBE, 100:1). FTIR (neat): ν = 3027, 2920, 1601, 1494, 1453, 1029, 737, 699, 720 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.31-7.24 (m, 2H), 7.22- 7.15 (m, 3H), 5.93-5.89 (m, 2H), 5.79-5.67 (m, 2H), 2.75-2.5 (m, 3H), 2.26-2.15 (m, 1H), 2.06-1.94 ppm (m, 1H). ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 140.4, 130.8, 129.1, 128.2, 125.8, 125.5, 124.1, 123.9, 40.1, 34.7, 28.1 ppm. MS (EI): 170.2 ($[M]^+$), 91.2, 79.2.



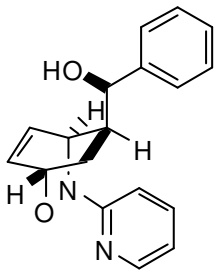
Acetic acid cyclohexa-2,4-dienylmethyl ester (1e): Acetic anhydride (1.03 mL, 10.9 mmol) was added to a solution of cyclohexa-2,4-dienyl-methanol (0.60 g, 5.5 mmol) in pyridine (3.0 mL) and was stirred at rt for 24 h. The reaction mixture was then extracted with CH_2Cl_2 (3x 25 mL), washed with 10% aqueous hydrochloric acid solution and then brine, dried over $MgSO_4$, concentrated in vacuum and the residue was purified by flash column chromatography (pentane:MTBE, 10:1) to afford **1e** as a colorless oil (0.76 g, 92 %). TLC: R_f = 0.3 (pentane:MTBE, 10:1). FTIR (neat) ν = 2970, 2950, 2360, 1740, 1366, 1234, 1036, 686 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 5.99-5.95 (m, 1H), 5.91-5.87 (m, 1H), 5.78-5.74 (m, 1H), 5.67-5.63 (m, 1H), 4.03 (br.s, 1H), 4.01 (br. s, 1H), 2.69-2.58 (m, 1H), 2.33-2.25 (m, 1H), 2.16-2.10 (m, 1H), 2.06 ppm (s; 3H). ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 171.1, 126.1, 125.6, 125.3, 124.0, 65.9, 32.5, 25.2, 20.9 ppm. HRMS (ESI) Exact mass calculated for $C_9H_{12}O_2Na$ ($[M + Na]^+$): 175.0730. Found: 175.0732.

Regiodivergent nitroso Diels-Alder reactions

Representative experimental procedure for the regiodivergent nitroso Diels-Alder reaction using Walphos ligand 8 (GP2)

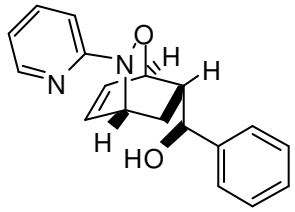
Walphos ligand **8** (5.2 mg, 5.6 µmol, 10 mol%) and $[Cu^{I}(CH_3CN)_4]PF_6$ (2.1 mg, 5.6 µmol, 10 mol%) were added to a flame dried Schlenk tube under argon atmosphere. The catalyst was dried at room temperature for 15 min under vacuum. The Schlenk tube was recharged with argon and anhydrous CH_2Cl_2 (1 mL) was added to the mixture and the resulting solution was stirred under argon for 1 h at rt. The solution was then cooled to -78 °C, a solution of 2-nitrosopyridine (6.7 mg, 62 µmol) in CH_2Cl_2 (0.4 mL) was added dropwise over 10 min and the resulting dark blue solution was stirred for 15 min. A solution of the diene (1.0 eq.) in CH_2Cl_2 (0.5 mL) was added slowly over 1 h at -78 °C. After completion of the addition stirring was continued at -78 °C for 6 h. The mixture was slowly warmed to -20 °C and was stirred for 12 h at that temperature. The solvent was removed under reduced pressure and the crude product was subjected to silica gel chromatography to afford the isomeric adducts.

(1*S*,4*S*,8*S*)-8-[(*R*)-(*tert*-Butyl-diphenyl-silanyloxy)-phenyl-methyl]-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (*ent-anti*-2a) and (1*R*,4*R*,7*R*)-7-[(*S*)-(*tert*-Butyl-diphenyl-silanyloxy)-phenyl-methyl]-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (*anti*-3a): According to GP2 with **8** (14.9 mg, 16.0 µmol, 10 mol%), $[Cu^{I}(CH_3CN)_4]PF_6$ (5.9 mg, 16 µmol, 10 mol%), CH_2Cl_2 (1.5 mL), 2-nitrosopyridine (19.0 mg, 176 µmol), diene **1a** (68.0 mg, 160 µmol) and SiO_2-chromatography (pentane:MTBE, 10:1) to give 84 mg (99%) of *ent-anti*-**2a** and *anti*-**3a** as an inseparable mixture of isomers. The isomer ratio was determined by ^{1}H NMR spectroscopy (*ent-anti*-**2a**:*anti*-**3a** = 0.9:1). For analytical purposes the silyl groups were removed (TBAF). The corresponding regioisomeric alcohols *ent-anti*-**2a**-OH and *anti*-**3a**-OH were separated by SiO_2-chromatography (pentane:MTBE, 1:1).



ent-anti-**2a**-OH: TLC: R_f = 0.3 (pentane:MTBE, 1:1). $[\alpha]^{D}_{25}$ = +74.0° (c = 0.53, $CHCl_3$). FTIR (neat): ν = 3355, 3060, 2930, 1587, 1462,

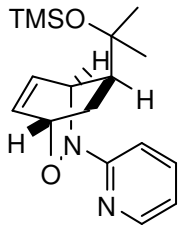
1432, 1371, 1238, 1091, 1002, 953, 910, 832, 785, 764, 732, 702 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$) δ = 8.09 (ddd, *J* = 4.8, 1.8, 1.2 Hz, 1H), 7.48 (ddd, *J* = 8.4, 7.2, 1.8 Hz, 1H), 7.42-7.32 (m, 5H), 6.89-6.87 (m, 1H), 6.73 (ddd, *J* = 7.2, 4.8, 1.2 Hz, 1H), 6.54-6.51 (m, 1H), 6.22-6.20 (m, 1H), 4.93-4.91 (m, 1H), 4.78-4.76 (m, 1H), 4.37 (d, *J* = 8.4 Hz, 1H), 2.82-2.78 (m, 1H), 2.44-2.40 (m ,1H), 2.01 (br.s, 1H), 1.54 ppm (ddd, *J* = 10.8, 3.6, 1.2 Hz, 1H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ = 163.5, 147.1, 142.6, 137.4, 131.6, 130.3, 128.8, 128.1, 126.3, 116.8, 111.7, 77.3, 69.9, 54.6, 40.8, 29.1 ppm. HRMS (ESI) Exact mass calculated for $C_{18}H_{19}N_2O_2$ ($[M + H]^+$): 295.1441. Found: 295.1439. Enantiomeric excess (98% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (95:5); flow: 1.0 mL/min; major enantiomer t_r = 49.2 min, minor enantiomer t_r = 19.8 min.



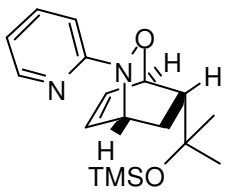
anti-**3a**-OH: TLC: R_f = 0.2 (pentane:MTBE, 1:1). $[\alpha]^D_{25}$ = +146.0° (c = 0.57, $CHCl_3$). FTIR (neat): ν = 3332, 3050, 2920, 1591, 1463, 1432, 1285, 1258, 1088, 1021, 914, 883, 858, 764, 731, 702 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.19-8.18 (m, 1H), 7.49-7.47 (m, 1H), 7.40-7.32 (m, 5H), 6.83-6.81 (m, 1H), 6.78-6.76 (m, 1H), 6.45-6.42 (m, 1H), 6.35-6.33 (m, 1H), 5.40-5.39 (m, 1H), 4.109-4.108 (m, 1H), 4.08 (d, *J* = 9.6 Hz, 1H), 2.81-2.80 (m, 1H), 2.56-2.51 (m, 1H), 1.96 (br.s, 1H), 1.77-1.73 ppm (m, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 163.8, 147.2, 143.1, 138.3, 133.9, 129.3, 129.1, 128.8, 126.6, 117.1, 111.7, 78.0, 71.7, 53.1, 44.7, 26.6 ppm. HRMS (ESI) Exact mass calculated for $C_{18}H_{19}N_2O_2$ ($[M + H]^+$): 295.1441. Found: 295.1429. Enantiomeric excess (92% ee) was determined by chiral HPLC, Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (95:5); flow: 1.0 mL/min; major enantiomer t_r = 31.8 min, minor enantiomer t_r = 15.8 min.

(1*S*,4*S*,8*S*)-8-(1-Methyl-1-trimethylsilanyloxy-ethyl)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (*ent-anti*-**2b**) **and (1*R*,4*R*,7*R*)-7-(1-Methyl-1-trimethylsilanyloxy-ethyl)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene** (*anti*-**3b**): According to GP2 with **8** (8.8 mg, 9.4 µmol), $[Cu^I(CH_3CN)_4]PF_6$ (3.5 mg, 9.4 µmol), CH_2Cl_2 (1.2 mL), 2-nitrosopyridine (11.2 mg, 103 µmol), diene **1b** (19.8 mg, 94.3 µmol)

and SiO_2-chromatography (pentane:MTBE, 5:1) to give 29.7 mg (99%) of *ent-anti*-**2b** and *anti*-**3b** as mixture of isomers. The isomer ratio was determined by chiral HPLC (*ent-anti*-**2b**:*anti*-**3b** = 0.9:1). For analytical purposes a sample was repurified by flash chromatography (pentane:MTBE, 10:1).



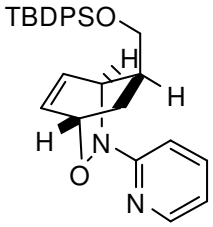
ent-anti-**2b**: TLC: R_f = 0.4 (pentane:MTBE, 10:1). $[\alpha]^{D}_{25}$ = +54.5° (c = 0.51, $CHCl_3$). FTIR (neat): ν = 2969, 2928, 1588, 1462, 1432, 1372, 1290, 1222, 1145, 1046, 1007, 953, 883, 829, 786, 767, 706 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.20-8.19 (m, 1H), 751-7.48 (m, 1H), 6.89-6.88 (m, 1H), 6.76-6.74 (m, 1H), 6.29-6.26 (m, 1H), 6.19-6.16 (m, 1H), 5.41-5.40 (m, 1H), 4.75-4.73 (m, 1H), 2.33-2.27 (m, 2H), 1.27 (s, 3H), 1.26-1.23 (m, 1H), 1.14 (s, 3H), 0.07 ppm (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 163.7, 146.8, 137.7, 132.2, 128.3, 116.4, 111.9, 70.9, 53.96, 44.9, 29.7, 29.3, 28.8, 28.0, 2.5 ppm. HRMS (ESI) Exact mass calculated for $C_{17}H_{27}N_2O_2Si$ ($[M + H]^+$): 319.1836. Found: 319.1827. Enantiomeric excess (95% ee) of the corresponding free alcohol (obtained after removal of the TMS group by treatment with TBAF in THF) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (96:4); flow: 1.0 mL/min; major enantiomer t_r = 19.7min, minor enantiomer t_r = 26.0 min.



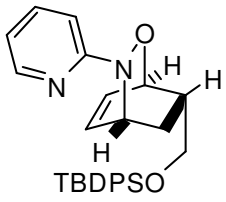
anti-**3b**: TLC: R_f = 0.2 (pentane:MTBE, 10:1). $[\alpha]^{D}_{25}$ = +90.4° (c = 0.41, $CHCl_3$). FTIR (neat): ν = 3056, 2970, 1588, 1568, 1463, 1432, 1366, 1249, 1148, 1087, 1038, 953, 868, 839, 779, 739, 688 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.20-8.19 (m, 1H), 7.53-7.50 (m, 1H), 6.95-6.94 (m, 1H), 6.76 (ddd, *J* = 7.2, 4.8, 0.6Hz, 1H), 6.42-6.40 (m, 1H), 6.25-6.22 (m, 1H), 5.33-5.31 (m, 1H), 4.84-4.82 (m, 1H), 2.43-2.40 (m, 1H), 2.32-2.27 (m, 1H), 1.34-1.31 (m, 1H), 1.20 (s, 3H), 1.05 (s, 3H), 0.09 ppm (s, 9H). ^{13}C-NMR (151 MHz, $CDCl_3$) δ = 163.6, 146.7, 137.7, 130.8, 129.9, 116.4, 111.4, 71.2, 53.3, 48.0, 29.0, 27.4, 25.8, 2.5 ppm. HRMS (ESI) Exact mass calculated for $C_{17}H_{27}N_2O_2Si$ ($[M + H]^+$): 319.1836. Found: 319.1836. Enantiomeric excess (89% ee) of the corresponding free alcohol (obtained after removal of the TMS group by treatment with TBAF in THF) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol

(96:4); flow: 1.0 mL/min; major enantiomer t_r = 27.7 min, minor enantiomer t_r = 57.6 min.

(1*S*,4*S*,8*S*)-8-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (*ent-anti*-**2c**) and **(1*R*,4*R*,7*S*)-7-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene** (*anti*-**3c**): According to GP2 with **8** (7.5 mg, 8.1 µmol), $[Cu^{I}(CH_3CN)_4]PF_6$ (3.0 mg, 8.1 µmol), CH_2Cl_2 (1 mL), 2-nitrosopyridine (9.5 mg, 88 µmol), diene **1c** (28 mg, 80 µmol) and SiO_2-chromatography (pentane:MTBE, 5:1) to give 36 mg (99%) of as mixture of isomers. The isomer ratio was determined by chiral HPLC (*ent-anti*-**2c**: *anti*-**3c**:*syn*-isomers = 3.2:3.5:1.0). For analytical purposes a sample was repurified by flash chromatography (pentane:MTBE, 10:1).



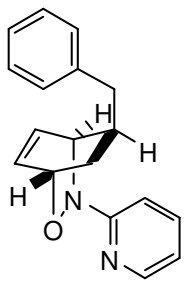
ent-anti-**2c**: TLC: R_f = 0.3 (pentane:MTBE, 10:1). $[\alpha]^{D}_{25}$ = +59.0° (c = 0.53, $CHCl_3$). FTIR (neat): ν = 3070, 2929, 2857, 1587, 1462, 1431, 1387, 1236, 1183, 1112, 1081, 1011, 965, 910, 869, 824, 779, 738, 702 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.25-8.24 (m, 1H), 7.68-7.67 (m, 4H), 7.54-7.51 (m, 1H), 7.45-7.37 (m, 6H), 6.92-6.91 (m, 1H), 6.80-6.78 (m, 1H), 6.41-6.39 (m, 1H), 6.09-6.06 (m, 1H), 5.49- 5.48 (m, 1H), 4.69-4.68 (m, 1H), 3.46 (dd, *J* = 10.2, 6.0 Hz, 1H), 3.37-3.34 (m, 1H), 2.73-2.67 (m, 1H), 2.34-2.29 (m, 1H), 1.09 (s, 9H), 0.89-0.86 ppm (m, 1H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ = 163.8, 147.2, 137.4, 135.6, 135.5, 133.6, 133.5, 130.9, 130.5, 129.63, 129.61, 127.6, 116.6, 111.5, 69.7, 66.3, 54.2, 35.4, 29.7, 28.3, 19.2 ppm. HRMS (ESI) Exact mass calculated for $C_{28}H_{33}N_2O_2Si$ ($[M + H]^+$): 457.2306. Found: 457.2293. Enantiomeric excess (99% ee) was determined by chiral HPLC. Column: Chiralcel OD-RH; solvent: acetonitrile:water (3:1); flow: 0.7 mL/min; major enantiomer t_r = 15.4 min, minor enantiomer t_r = 18.8 min.



anti-**3c**: TLC: R_f = 0.2 (pentane:MTBE, 10:1). $[\alpha]^{D}_{25}$ = +75.6° (c = 0.66, $CHCl_3$). FTIR (neat): ν = 3070, 2929, 2857, 1587, 1568, 1463, 1431, 1382, 1246, 1186, 1112, 1004, 960, 909, 883, 823, 781, 737,

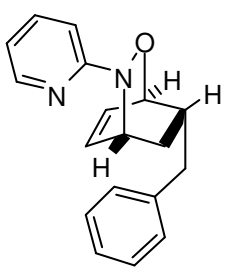
702 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.20-8.19 (m, 1H), 7.66-7.64 (m, 4H), 7.55-7.52 (m, 1H), 7.45-7.37 (m, 6H), 6.97-6.95 (m, 1H), 6.79-6.77 (m, 1H), 6.29-6.26 (m, 1H), 6.23-6.21 (m, 1H), 5.25-5.23 (m, 1H), 4.99-4.97 (m, 1H), 3.56 (dd, *J* = 10.2, 6.0 Hz, 1H), 3.17-3.14 (m, 1H), 2.78-2.72 (m, 1H), 2.29-2.25 (m, 1H), 1.07 (s, 9H), 0.89-0.85 ppm (m, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 163.2, 146.4, 138.0, 135.5, 133.5, 133.4, 132.3, 129.7, 129.1, 127.7, 116.5, 111.6, 71.8, 66.2, 52.3, 38.0, 29.7, 26.9, 26.8, 24.3, 19.2 ppm. HRMS (ESI) Exact mass calculated for $C_{28}H_{33}N_2O_2Si$ ($[M + H]^+$): 457.2306. Found: 457.2302. Enantiomeric excess (88% ee) was determined by chiral HPLC, Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (99.5:0.5); flow: 1.0 mL/min; major enantiomer t_r = 15.9 min, minor enantiomer t_r = 7.4 min.

(1*S*,4*R*,8*S*)-8-Benzyl-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (*ent-anti*-**2d**) and **(1*S*,4*R*,7*R*)-7-Benzyl-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene** (*anti*-**3d**): According to GP2 with **8** (10.8 mg, 11.6 µmol), $[Cu^I(CH_3CN)_4]PF_6$ (4.3 mg, 12 µmol), CH_2Cl_2 (1.2 mL), 2-nitrosopyridine (13.9 mg, 129 µmol), diene **1d** (20 mg, 0.12 mmol) and SiO_2-chromatography (pentane:MTBE, 5:1) to give 32 mg (99%) of *ent-anti*-2d and *anti*-**3d** as mixture isomers. The isomer ratio was determined by chiral HPLC (*ent-anti*-**2d**: *anti*-**3d**:*syn*-isomers = 2.3:2.5:1.0). For analytical purposes a sample was repurified by flash chromatography (pentane:MTBE, 9:1).



ent-anti-**2d**: TLC: R_f = 0.2 (pentane:MTBE, 10:1). FTIR (neat): ν = 3058, 2924, 2853, 1587, 1496, 1461, 1432, 1244, 1146, 1012, 955, 865, 836, 780, 739, 701 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.26-8.15 (m, 1H), 7.61-7.56 (m, 1H), 7.34-7.18 (m, 5H), 6.95-6.91 (m, 1H), 6.87-6.81 (m, 1H), 6.59-6.54 (m, 1H), 6.35-6.32 (m, 1H), 5.33-5.25 (m, 1H), 4.83-4.74 (m, 1H), 2.77-2.66 (m, 1H), 2.45-2.32 (m, 2H), 1.14-1.05 (m, 1H), 0.90-0.81 ppm (m, 1H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ = 139.2, 131.6, 130.2, 129.2, 128.9, 128.5, 126.3, 116.4, 111.8, 70.3, 56.3, 41.3, 34.3, 31.6 ppm. HRMS (ESI) Exact mass calculated for $C_{18}H_{19}N_2O$ ($[M + H]^+$): 279.1492. Found: 279.1487. Enantiomeric excess (98% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent:

cyclohexane:2-propanol (99.5:0.5); flow: 1.0 mL/min; major enantiomer t_r = 28.0 min, minor enantiomer t_r = 40.0 min.

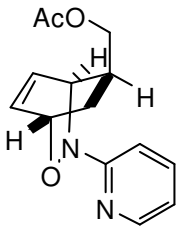


anti-**3d**: TLC: R_f = 0.1 (pentane:MTBE, 10:1). $[\alpha]^{D}_{25}$ = +110.0° (c = 0.46, $CHCl_3$). FTIR (neat): ν = 3058, 2925, 1587, 1567, 1494, 1462, 1431, 1373, 1287, 1258, 1147, 1085, 1061, 1001, 956, 880, 780, 743, 701 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.13-8.12 (m, 1H), 7.43 (ddd, *J* = 10.2, 9.0, 2.4 Hz, 1H), 7.24-7.09 (m, 5H), 6.83-6.81 (m, 1H), 6.70 (ddd, *J* = 9.0, 6.0, 1.2 Hz, 1H), 6.38-6.33 (m, 2H), 5.26-5.23 (m, 1H), 4.43-4.41 (m, 1H), 2.70-2.63 (m, 1H), 2.42-2.28 (m, 3H), 1.19-1.15 ppm (m, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 163.3, 146.5, 139.4, 137.9, 132.7, 129.0, 128.7, 128.5, 126.3, 116.5, 111.6, 72.8, 52.7, 40.9, 37.2, 28.4 ppm. HRMS (ESI) Exact mass calculated for $C_{18}H_{19}N_2O$ ($[M + H]^+$): 279.1492. Found: 279.1485. Enantiomeric excess (84% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (99.5:0.5); flow: 1.0 mL/min; major enantiomer t_r = 29.3 min, minor enantiomer t_r = 20.1 min.

Acetic acid (1*S*,4*S*,5*S*)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-7-en-5-ylmethyl ester (*ent-anti*-**2e**) **and Acetic acid (1*R*,4*R*,6*S*)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-7-en-6-ylmethyl ester** (*anti*-**3e**): According GP2 with **8** (6.0 mg, 6.4 µmol), $[Cu^{I}(CH_3CN)_4]PF_6$ (2.4 mg, 6.4 µmol), CH_2Cl_2 (1 mL), 2-nitrosopyridine (7.8 mg, 72. µmol), diene **1e** (10 mg, 65 µmol) and SiO_2-chromatography (pentane:MTBE, 1:1) to give 17 mg (99%) of *ent-anti*-**2e**, *anti*-**3e** and both *syn*-isomers as an inseparable mixture of isomers. The isomer ratio was determined by chiral HPLC (*ent-anti*-**2e**: *anti*-**3e**:*syn*-isomers = 2.0:2.2:1.0).

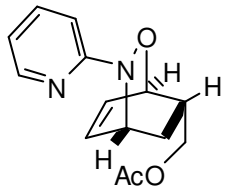
The isomers could not be separated. Therefore, ^{1}H-NMR and ^{13}-NMR data are not provided.

HRMS (ESI) Exact mass calculated for $C_{14}H_{17}N_2O_3$ ($[M + H]^+$): 261.1234. Found: 261.1226



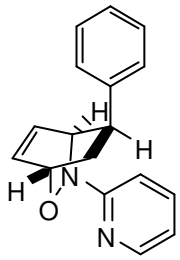
ent-anti-**2e**: Enantiomeric excess (98% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol

(99:1); flow: 1.0 mL/min; major enantiomer t_r = 42.8 min, minor enantiomer t_r = 31.1 min.

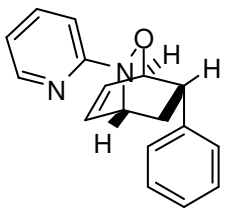


anti-**3e**: Enantiomeric excess (82% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (99:1); flow: 1.0 mL/min; major enantiomer t_r = 37.6 min, minor enantiomer t_r = 20.7 min.

(1*S*,4*S*,8*R*)-8-Phenyl-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (*ent-anti*-**2f**) and **(1*R*,4*R*,7*S*)-7-Phenyl-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene** (*anti*-**3f**): According to GP2 with **8** (10.7 mg, 11.5 µmol), $[Cu^{I}(CH_3CN)_4]PF_6$ (4.3 mg, 12 µmol), CH_2Cl_2 (1.2 mL), 2-nitrosopyridine (13.7 mg, 127 µmol), diene **1d** (18 mg, 0.12 mmol) and SiO_2-chromatography (pentane:MTBE, 5:1) to give 30 mg (99%) of *ent-anti*-**2f** and *anti*-**3f** as mixture isomers. The isomer ratio was determined by chiral HPLC (*ent-anti*-**2f**: *anti*-**3f** = 1.0:1.2). For analytical purposes a sample was repurified by flash chromatography (pentane:MTBE, 10:1).

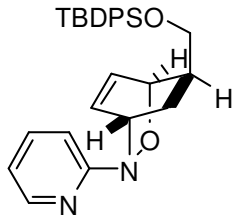


ent-anti-**2f**: TLC: R_f = 0.2 (pentane:MTBE, 5:1). FTIR (neat): ν = 3057, 2932, 1587, 1493, 1461, 1432, 1371, 1280, 1236, 1069, 986, 892, 830, 771, 740, 700 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.19-8.09 (m, 1H), 7.52-7.47 (m, 1H), 7.25-7.12 (m, 5H), 6.92-6.89 (m, 1H), 6.76-6.72 (m, 1H), 6.59-6.54 (m, 1H), 6.19-6.17 (m, 1H), 5.35-5.33 (m, 1H), 4.86-4.83 (m, 1H), 3.66-3.60 (m, 1H), 2.74-2.65 (m, 1H), 1.65-1.59 ppm (m, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 162.9, 146.5, 142.9, 138.1, 131.6, 130.8, 128.4, 128.1, 126.7, 116.7, 111.7, 70.5, 57.8, 38.5, 33.7 ppm. HRMS (ESI) Exact mass calculated for $C_{17}H_{17}N_2O$ ($[M + H]^+$): 265.1335. Found: 265.1339. Enantiomeric excess (98% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (99.5:0.5); flow: 1.0 mL/min; major enantiomer t_r = 25.4 min, minor enantiomer t_r = 71.2 min.

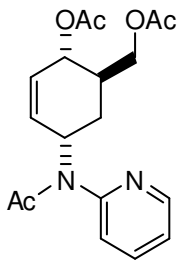


anti- **3f**: TLC: R_f = 0.1 (pentane:MTBE, 5:1). $[\alpha]^{D}_{25}$ = +263.4° (c = 0.55, $CHCl_3$). FTIR (neat): ν = 3054, 2932, 1589, 1493, 1463, 1432, 1373, 1247, 1216, 1069, 1018, 965, 892, 873, 754, 704, 667 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.17-8.15 (m, 1H), 7.52-7.46 (m, 1H), 7.24-7.10 (m, 5H), 6.93-6.91 (m, 1H), 6.76-6.72 (m, 1H), 6.49-6.44 (m, 1H), 6.33-6.28 (m, 1H), 5.45-5.44 (m, 1H), 4.69-4.68 (m, 1H), 3.68-3.63 (m, 1H), 2.75-2.66 (m, 1H), 1.85-1.78 ppm (m, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 163.2, 146.6, 141.8, 137.9, 132.9, 129.7, 128.4, 128.2, 126.7, 116.7, 111.6, 74.2, 52.9, 41.7, 30.3 ppm. HRMS (ESI) Exact mass calculated for $C_{17}H_{17}N_2O$ ($[M + H]^+$): 265.1335. Found: 265.1338. Enantiomeric excess (94% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (99.5:0.5); flow: 1.0 mL/min; major enantiomer t_r = 19.4 min, minor enantiomer t_r = 17.3 min.

Synthesis of peracetylated 2-*epi*-valdamine 11

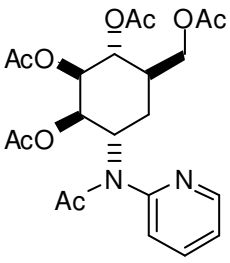


(1*S*,4*S*,7*R*)-7-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (*ent*-*anti*-3c): According to GP2 with *ent*-**8** (360 g, 387 µmol), $[Cu^{I}(CH_3CN)_4]PF_6$ (144 mg, 387 µmol), CH_2Cl_2 (25 mL), 2-nitrosopyridine in 6 mL CH_2Cl_2 (0.46 g, 4.2 mmol), diene **1c** (1.35 g, 3.87 mmol) in CH_2Cl_2 (20 mL) and SiO_2-chromatography (pentane:MTBE, 10:1) to give 775 mg (44%) of *ent*-*anti*-**3c**. Enantiomeric excess (89% ee) was determined by chiral HPLC, Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (99.5:0.5); flow: 1.0 mL/min; major enantiomer t_r = 7.8 min, minor enantiomer t_r = 17.3 min. $[\alpha]^{D}_{25}$ = -74.3° (c = 1.03, $CHCl_3$).



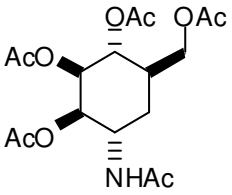
Acetic acid (1*S*,4*S*,6*R*)-6-acetoxymethyl-4-(acetyl-pyridin-2-yl-amino)-cyclohex-2-enyl ester (9): The N-O bond of the *ent*-*anti*-**3c** was cleaved according to the previously reported procedure[3]. $Mo(CO)_6$ (0.14 mg, 0.53 mmol) and $NaBH_4$ (24 mg, 0.65 mmol) was added to the suspension of *ent*-*anti*-**3c** (242 mg, 530 µmol) in MeOH:H_2O (10:1, 4.0 mL). Then the reaction mixture was heated to 65 °C and stirred for 10 h at that

temperature. The precipitate was removed by filtration through a short pad of celite and the filtrate was concentrated in vacuo. The residue was dissolved in CH_2Cl_2, washed (brine), dried ($MgSO_4$) and concentrated under reduced pressure. To remove the silyl group, the resulting residue was dissolved in THF (3 mL), treated with TBAF (2.4 mL, 2.4 mmol) and stirred for 24 h at room temperature. Then the volatiles were removed under reduced pressure and the residue was passed through a short pad of silica gel (MeOH:MTBE, 1:10) to remove the excess TBAF. CH_3MgCl (3 M in THF, 0.71 mL, 2.1 mmol) was added dropwise to the solution of the resulting mass in THF (3.0 mL) at rt and was stirred for 10 min at that temperature. Acetyl chloride (0.23 mL, 3.2 mmol) was then added and stirred at rt for 10 h. The reaction mixture was then diluted with CH_2Cl_2, washed (brine), dried ($MgSO_4$), concentrated under vacuum and subjected to flash column chromatography (MTBE:MeOH, 20:1) to give **9** as a colorless oil (142 mg, 77 %, over three steps). TLC: R_f = 0.2 (MTBE:MeOH, 20:1). $[\alpha]^{D}_{25}$ = -5.6^{o} (c = 1.16, $CHCl_3$). FTIR (neat): ν = 2937, 1737, 1662, 1584, 1469, 1437, 1372, 1315, 1240, 1025, 785, 752. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.58-8.56 (m, 1H), 7.78 (dt, J = 2.0, 7.7 Hz, 1H), 7.33 (ddd, J = 1.0, 4.9, 7.5 Hz, 1H), 7.14 (td, J = 0.9, 7.9 Hz, 1H), 5.87-5.82 (m, 1H), 5.72-5.67 (m, 1H), 5.40-5.35 (m, 1H), 5.01-4.98 (m, 1H), 3.94 (d, J = 5.8 Hz, 2H), 2.11-2.00 (m, 1H), 2.03 (s, 3H), 1.94 (s, 3H), 1.92-1.84 (m, 1H), 1.81 (s, 3H), 1.75-1.64 ppm (m, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 170.9, 170.4, 169.9, 153.5, 149.6, 138.3, 130.5, 128.7, 124.4, 123.5, 67.9, 64.1, 48.1, 34.7, 26.9, 23.2, 21.0, 20.8 ppm. HRMS (ESI) Exact mass calculated for $C_{18}H_{22}N_2O_5Na$ ($[M + Na]^+$): 369.1421. Found: 369.1418.



Acetic acid (1*R*,2*S*,3*R*,4*S*,6*R*)-2,3-diacetoxy-6-acetoxymethyl-4-(acetyl-pyridin-2-yl-amino)-cyclohexyl ester (**10**): K_2OsO_4, $2H_2O$ (25 mg, 65 μmol) and NMO (0.18 mg, 1.5 mmol) were added to a solution of **9** (311 mg, 898 μmol) in acetone:water (9:1, 4 mL). The reaction mixture was then stirred for 24 h at rt. Then the resulting mixture was concentrated under reduced pressure and the residue was passed through a short pad of silica gel (CH_2Cl_2:MeOH, 20:1). The dihydroxylated compound was then dissolved in pyridine (2.5 mL). Acetic anhydride (0.5 mL, 5.29 mmol) was added and the solution was stirred for 24 h at rt. Then the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (MTBE:MeOH, 12:1) to

obtain **10** as a colorless foam (335 mg, 80%, over two steps). TLC: R_f = 0.3 (MTBE:MeOH, 10:1). $[\alpha]^D_{25}$ = +7.5° (c = 0.85, $CHCl_3$). FTIR ($CDCl_3$): ν = 2940, 1745, 1667, 1585, 1469, 1438, 1371, 1231, 1045, 920, 731 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 860-8.58 (m, 1H), 7.85- 7.79 (m, 1H), 7.37-7.32 (m ,1H), 7.17-7.15 (m, 1H), 5.23-4.98 (m, 4H), 4.32-4.26 (m, 1H), 4.21-4.15 (m, 1H), 2.14-1.97 (m, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H), 1.81 ppm (s, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 170.6, 170.3, 169.7, 169.4, 169.2, 149.8, 138.6, 124.0, 123.6, 122.8, 70.0, 69.5, 69.4, 63.6, 50.0, 37.1, 26.8, 23.4, 20.9, 20.84, 20.79, 20.7 ppm. HRMS (ESI) Exact mass calculated for $C_{22}H_{28}N_2O_9Na$ ($[M + Na]^+$): 487.1687. Found: 487.1684.



Acetic acid (1*R*,2*S*,3*R*,4*S*,6*R*)-2,3-diacetoxy-6-acetoxymethyl-4-acetylamino-cyclohexyl ester (11): Rh/C (90 mg, 44 μmol) was added to a solution of **10** (100 mg, 215 μmol) in glacial acetic acid (5 mL) and stirred in an autoclave under hydrogen pressure (74 bar) at 65 °C for 28 h. Then the reaction mixture was filtered through a short pad of celite. The celite pad was washed with CH_2Cl_2:MeOH (1:1), the combined organic layer were concentrated under reduced pressure and the residue was subjected to column chromatography (cyclohexane:isopropanol, 2:1) to yield **11** as a colorless oil (53 mg, 64 %). TLC: R_f = 0.3 (cyclohexane:isopropanol, 2:1). $[\alpha]^D_{25}$ = +16.5° (c = 1.26, $CHCl_3$), (lit[4]. $[\alpha]^D_{24}$ = +18.0° (c = 1.1, $CHCl_3$)). FTIR ($CDCl_3$): ν = 2958, 1746, 1653, 1546, 1370, 1228, 1044 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 5.97 (br.s, 1H), 5.26-5.23 (m, 1H), 5.18-5.09 (m, 2H), 4.31-4.24 (m, 1H), 4.15-4.03 (m, 2H), 2.22-1.90 (m, 2H), 2.09 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H), 1.87-1.78 ppm (m, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 170.7, 169.97, 169.89, 169.79, 169.6, 70.5, 70.1, 69.5, 63.8, 46.4, 36.3, 27.8, 23.3, 20.8, 20.7, 20.6 ppm. HRMS (ESI) Exact mass calculated for $C_{17}H_{25}NO_9Na$ ($[M + Na]^+$): 410.1422. Found: 410.1421.

References:

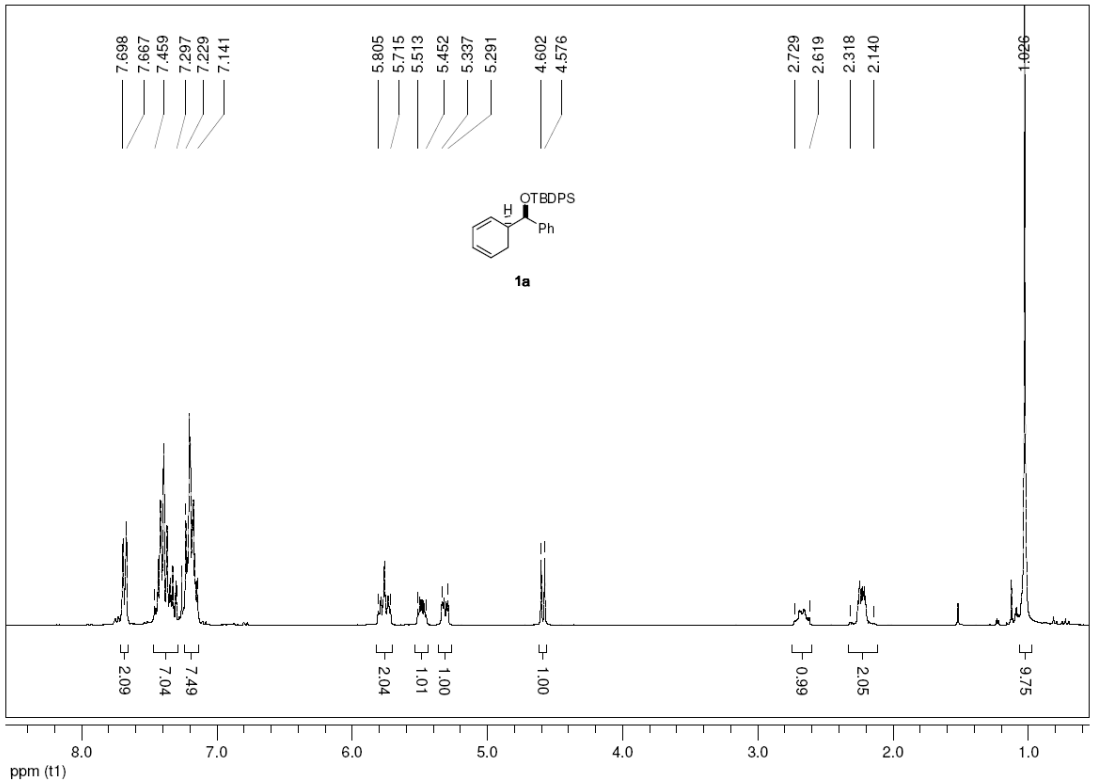
1. Taylor, E. C.; Tseng, C.-P.; Rampal, J. B. *J. Org. Chem*. **1982**, *47*, 552.

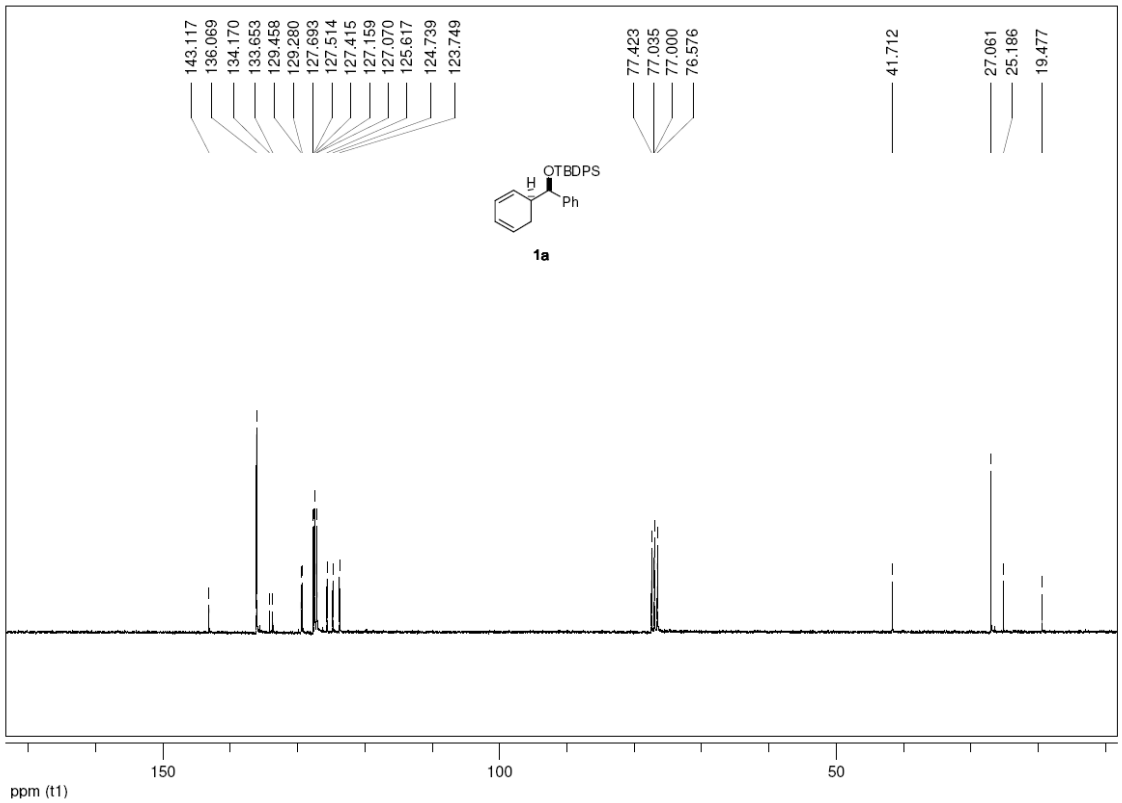
2. (a) Schleth, F.; Vogler, T.; Harms, K.; Studer, A. *Chem. Eur. J.* **2004**, *10*, 4171-4185. (b) Studer, A.; Schleth, F. *Synlett* **2005**, 3033-3041.

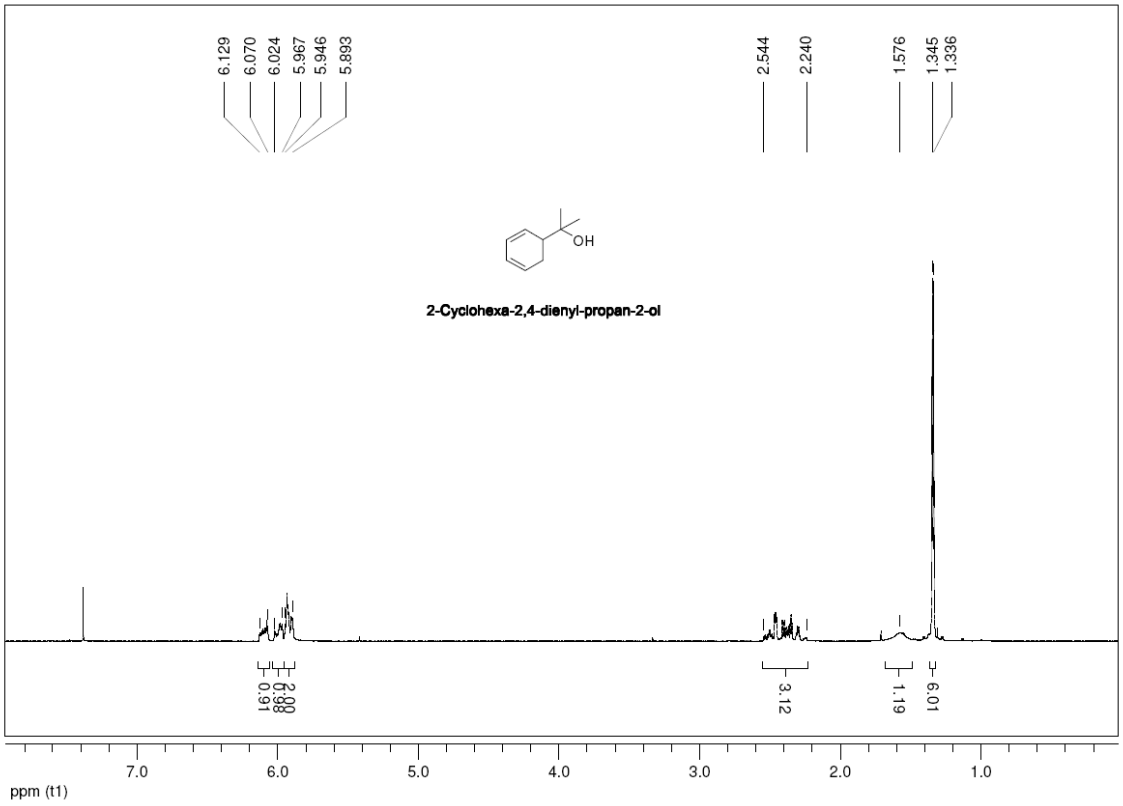
3. (a) Cicchi, S.; Goti, A.; Brandi, A.; Gurana, A.; De Sarlo, F. *Tetrahedron* **1990**, *31*, 3351. (b) Yamamoto, Y.; Yamamoto, H. *J. Am. Chem. Soc.* **2004**, *126*, 4128.

4.Shing, T. K. M.; Tai, V. W.-F. *J. Org. Chem*. **1995**, *60*, 5332.

^{1}H and ^{13}C-NMR Spectra



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0.91
0.98
0.99
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3.0
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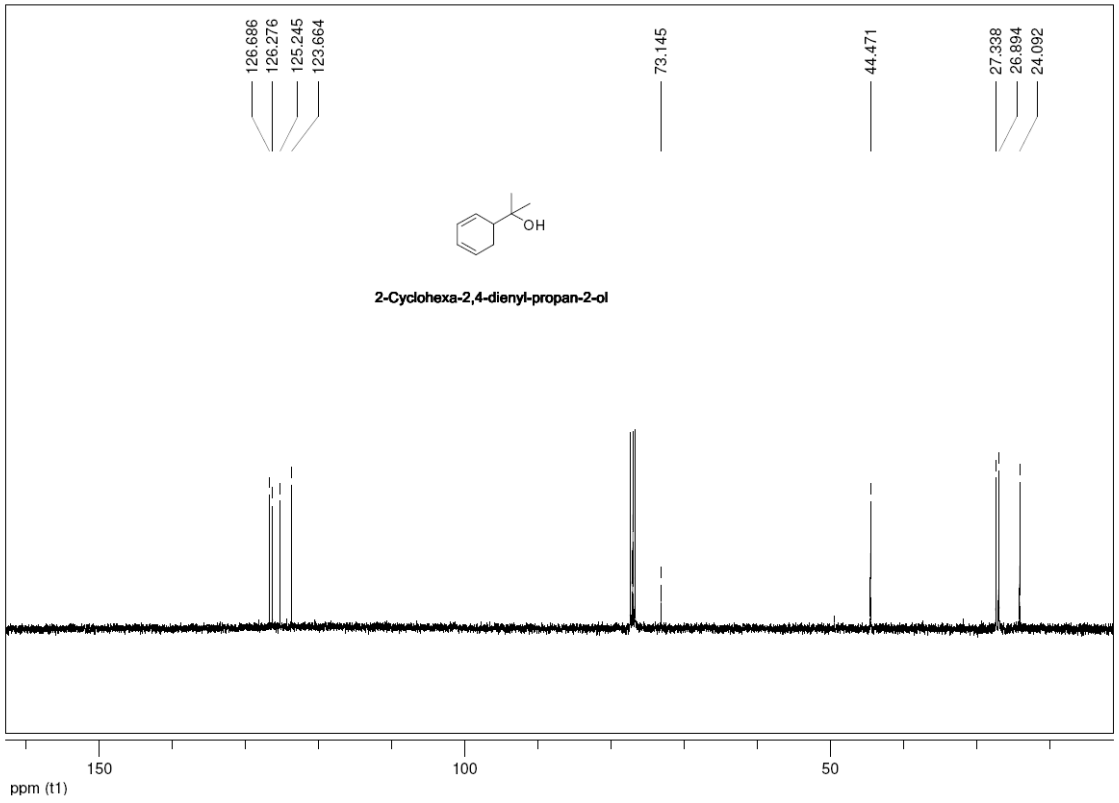
1.0
ppm (t1)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50
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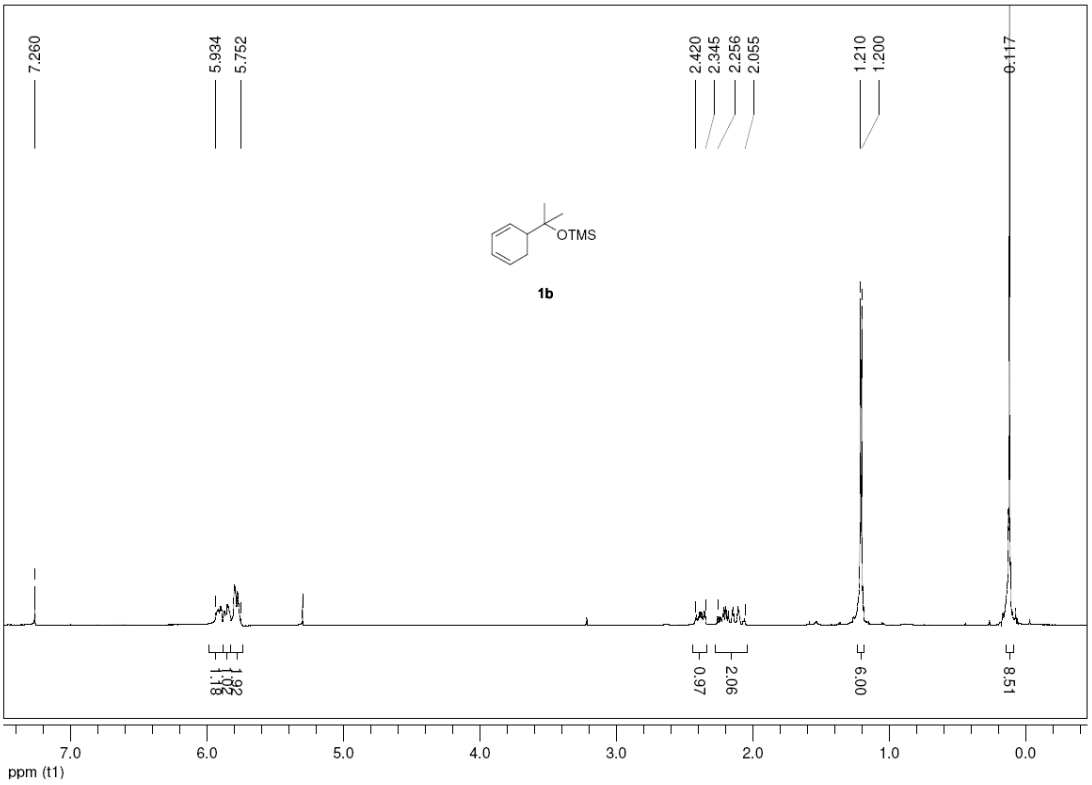
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7.0
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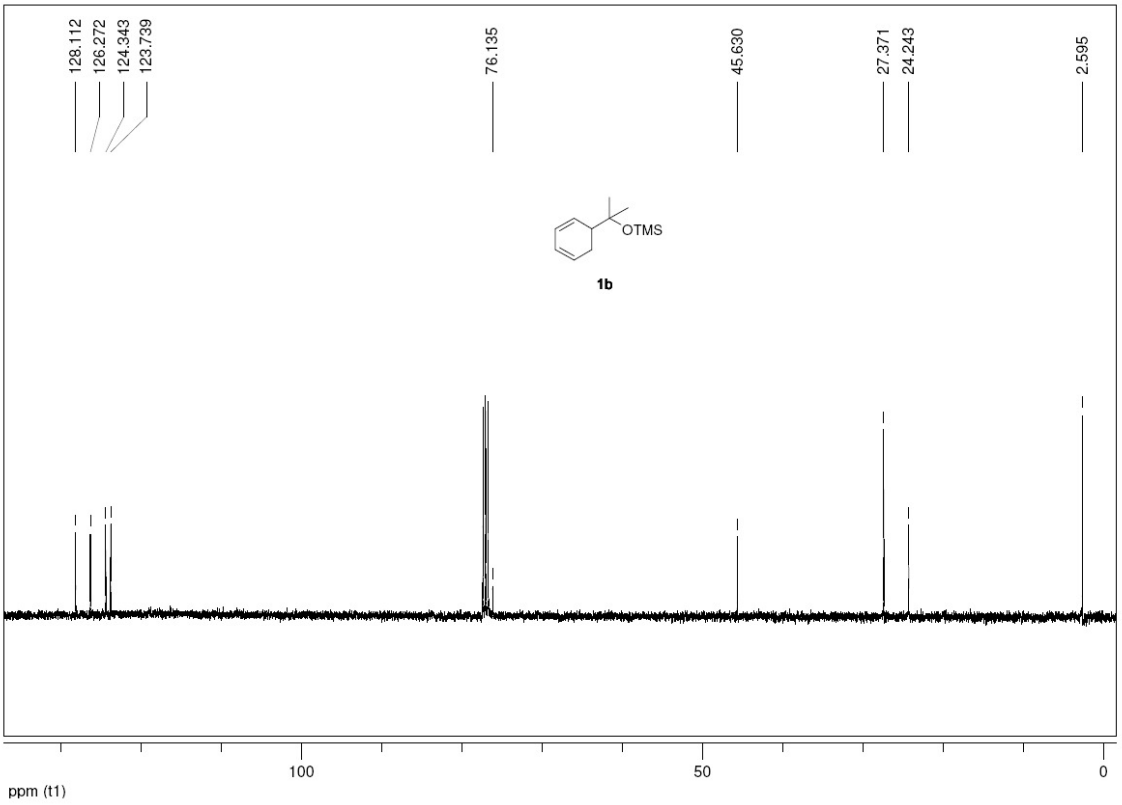
0.0
ppm (t1)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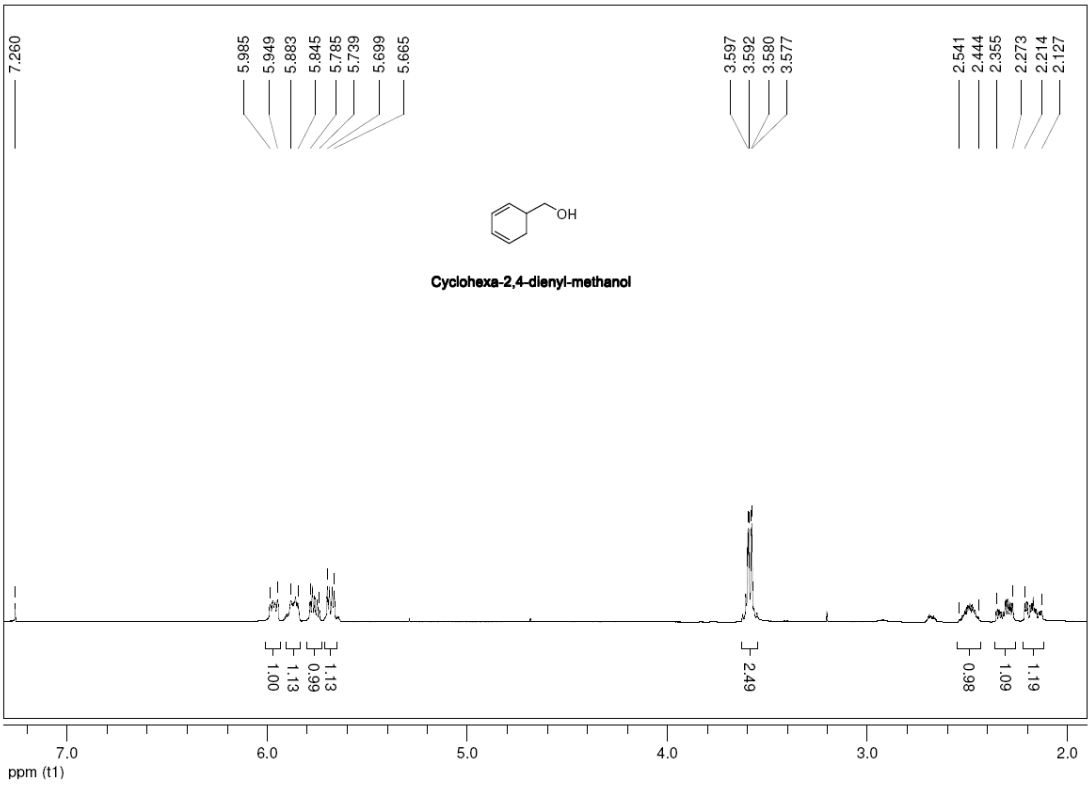
50
0
ppm (t1)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3.580
3.577
2.541
2.444
2.355
2.273
2.214
2.127
OH
Cyclohexa-2,4-dienyl-methanol
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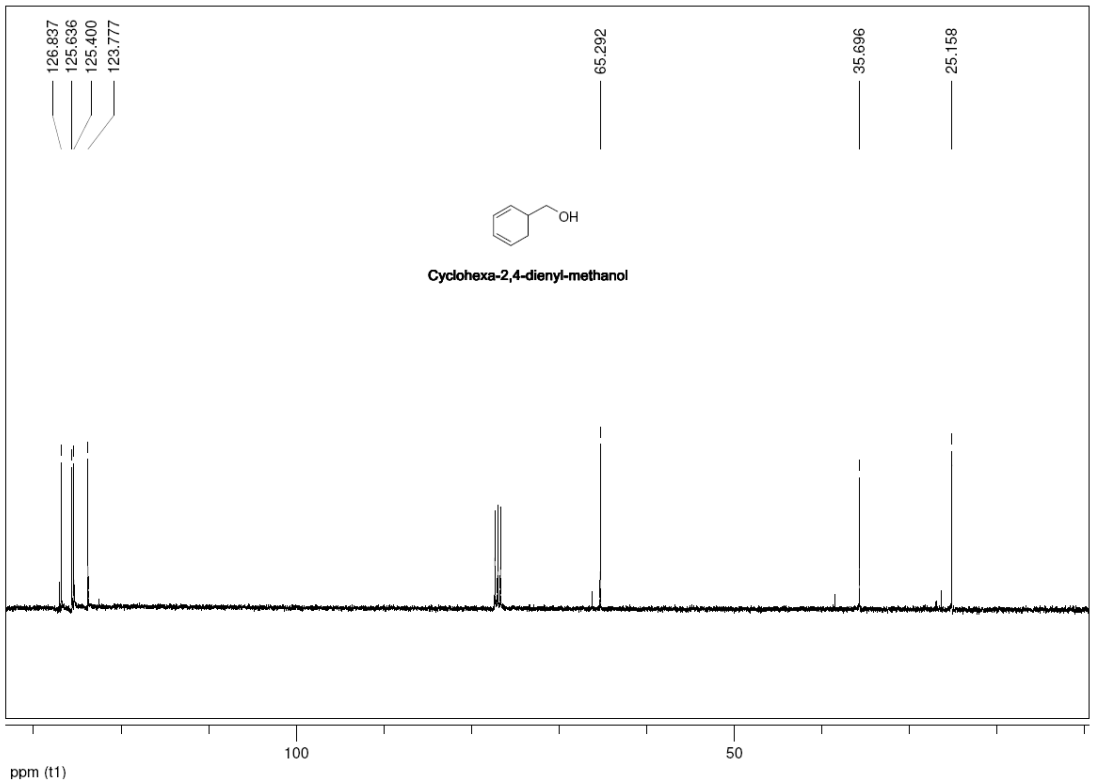
2.0
ppm (t1)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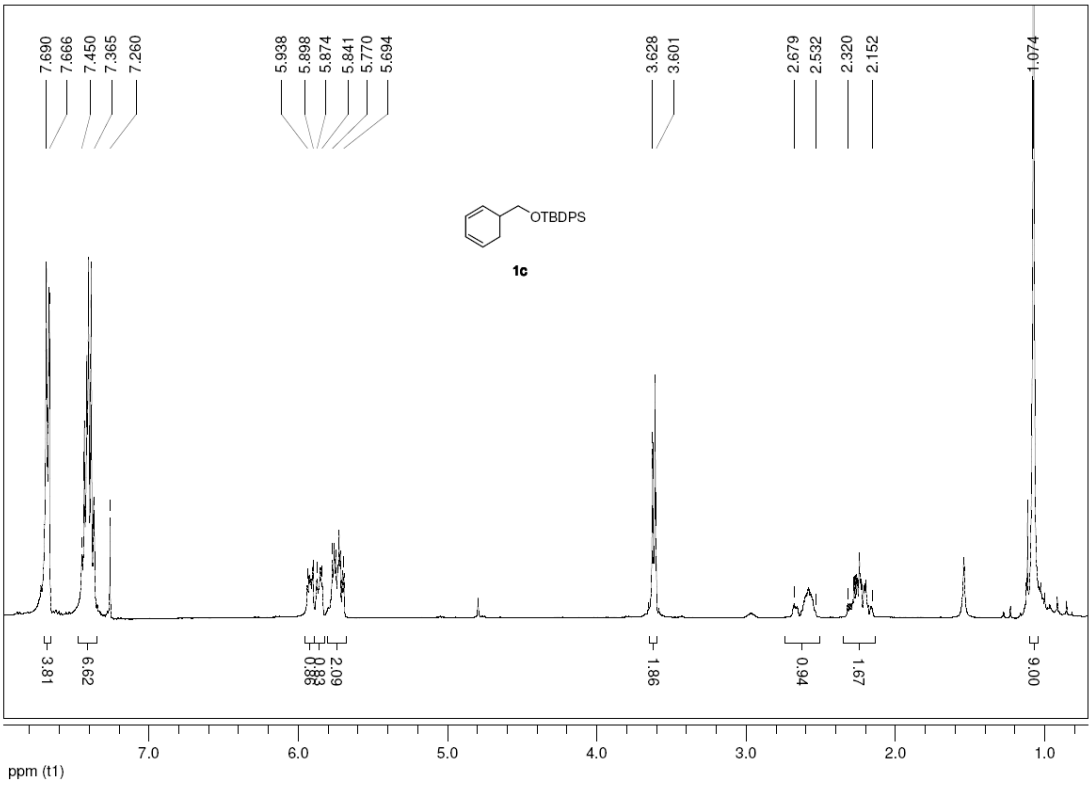
50
ppm (t1)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2.679
2.532
2.320
2.152
1.074
OTBDPS
1c
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2.09
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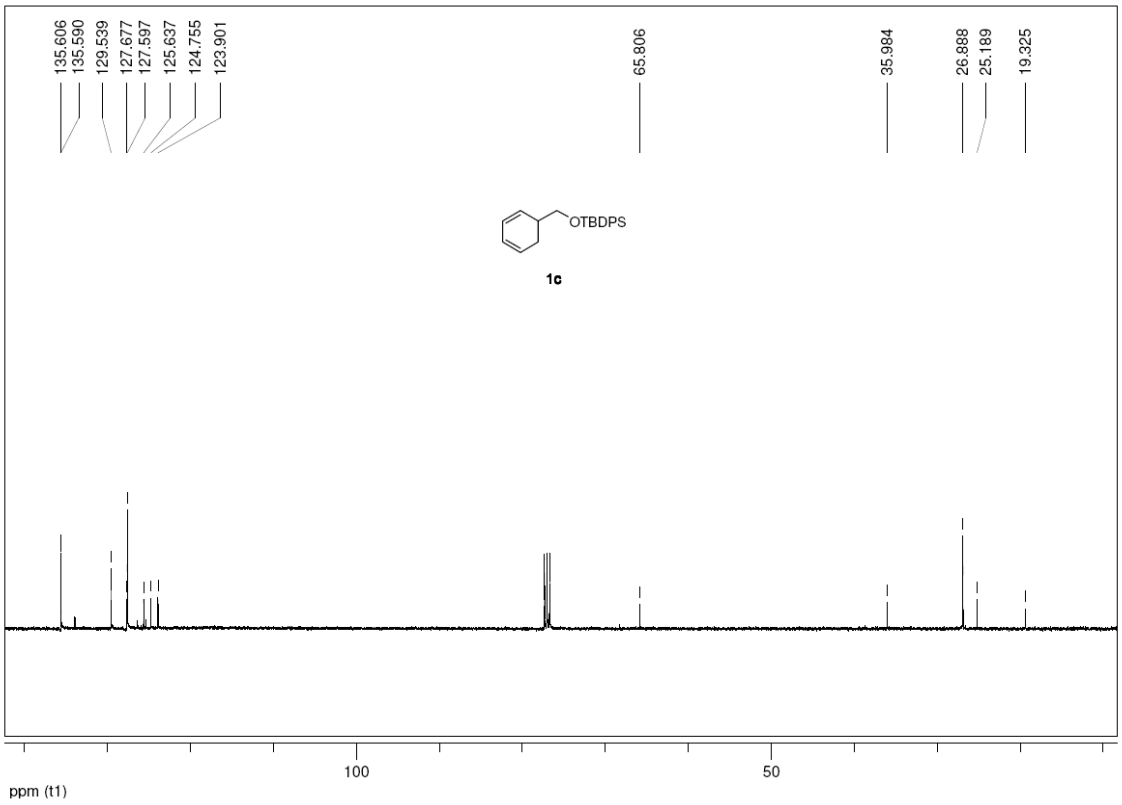
ppm (t1)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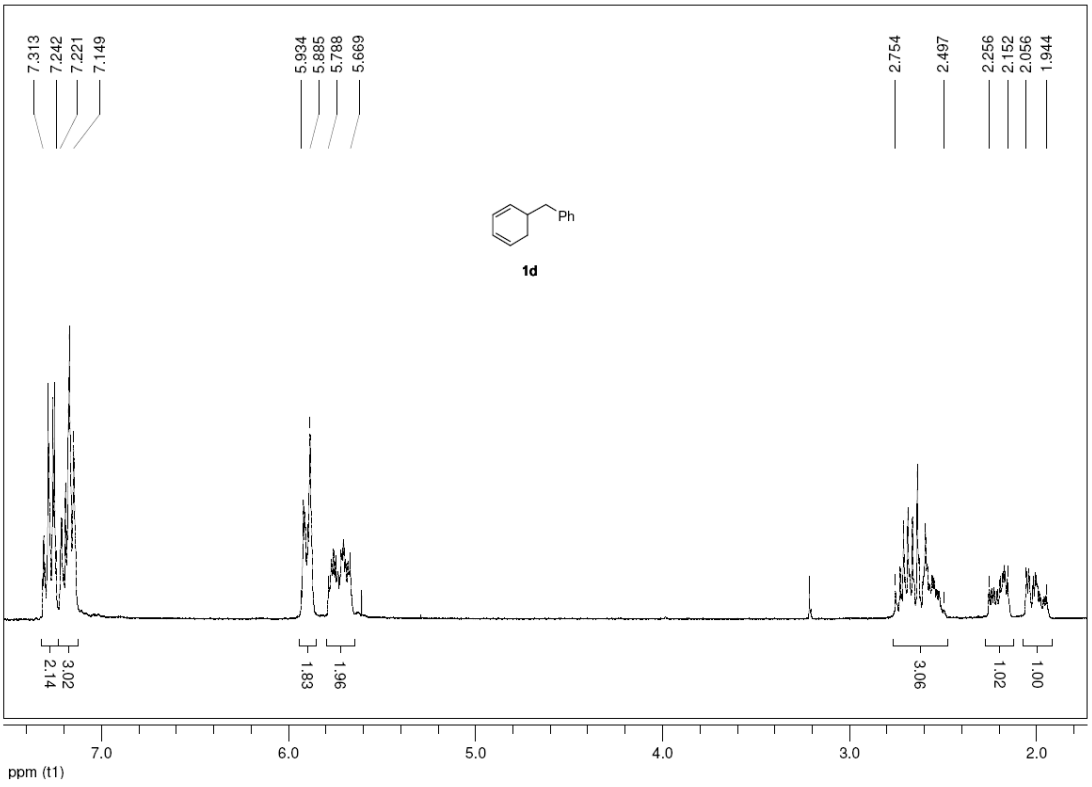
ppm (t1)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1.944
Ph
1d
2.14
3.02
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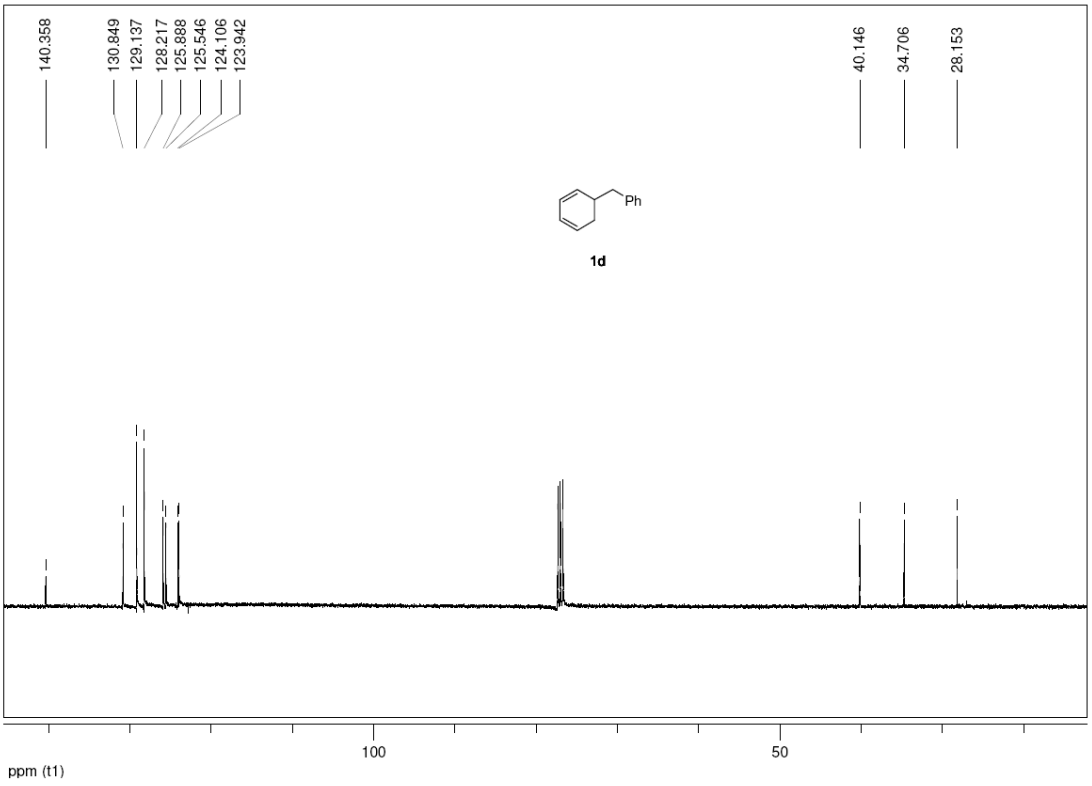
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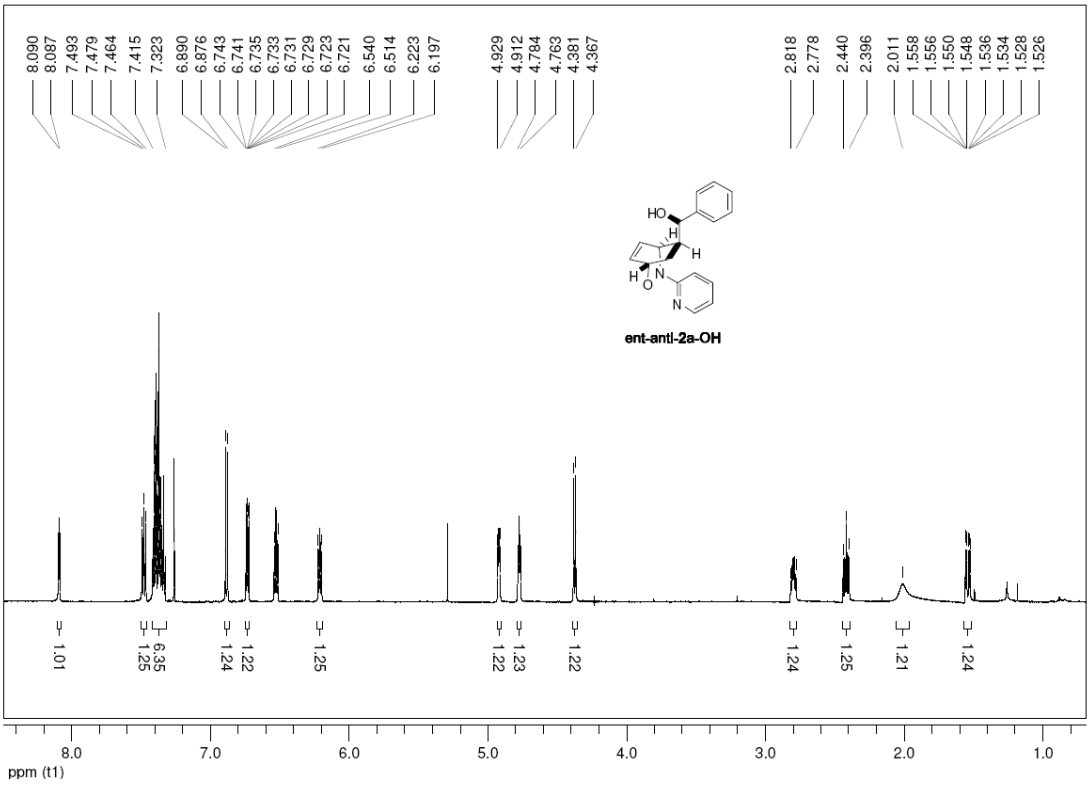
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6.731
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6.197
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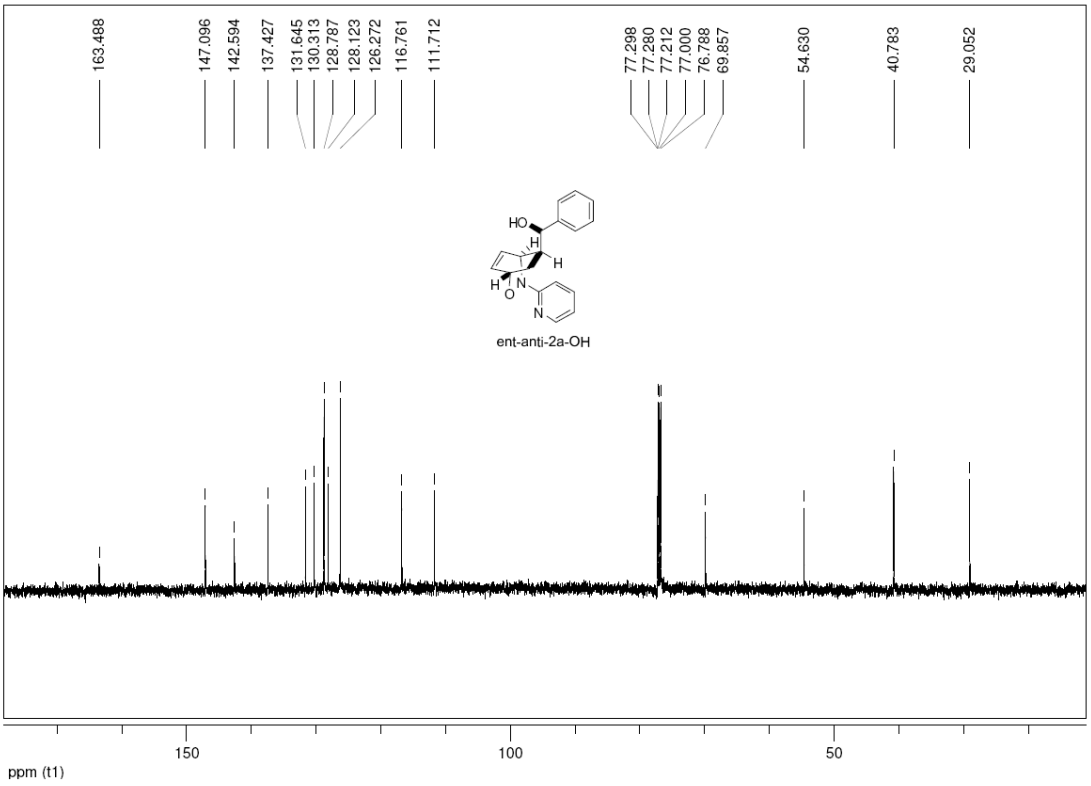
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77.212
77.000
76.788
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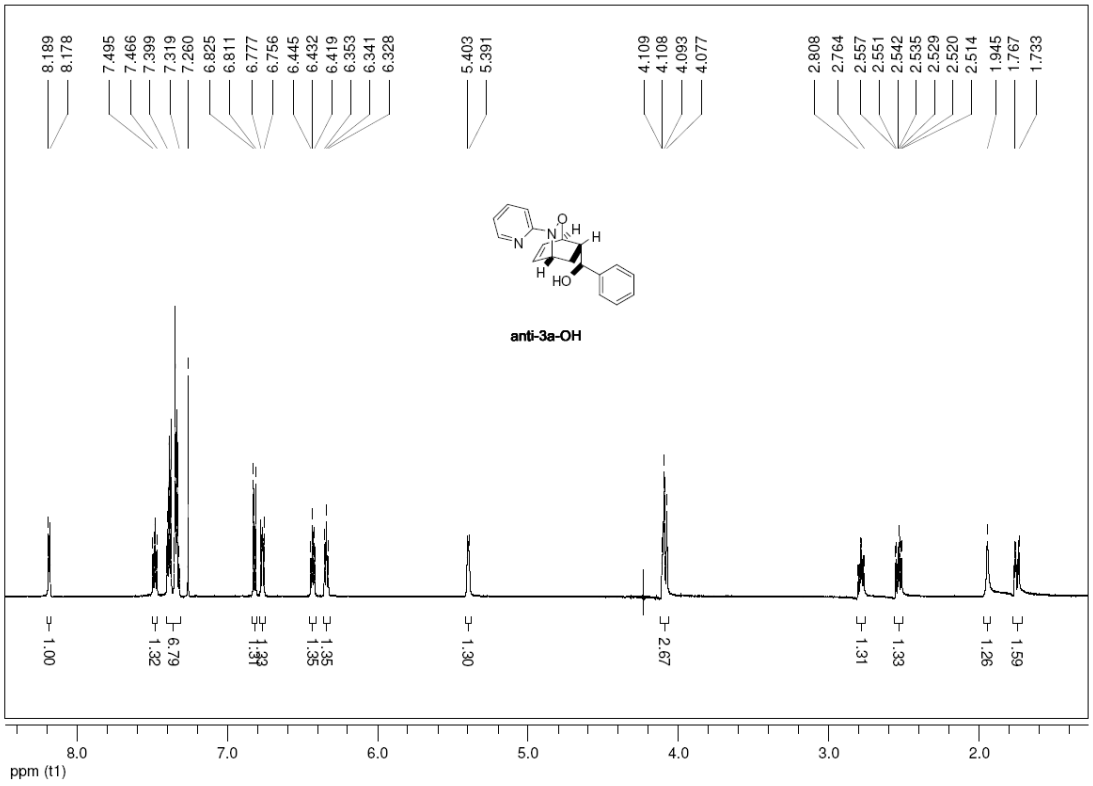
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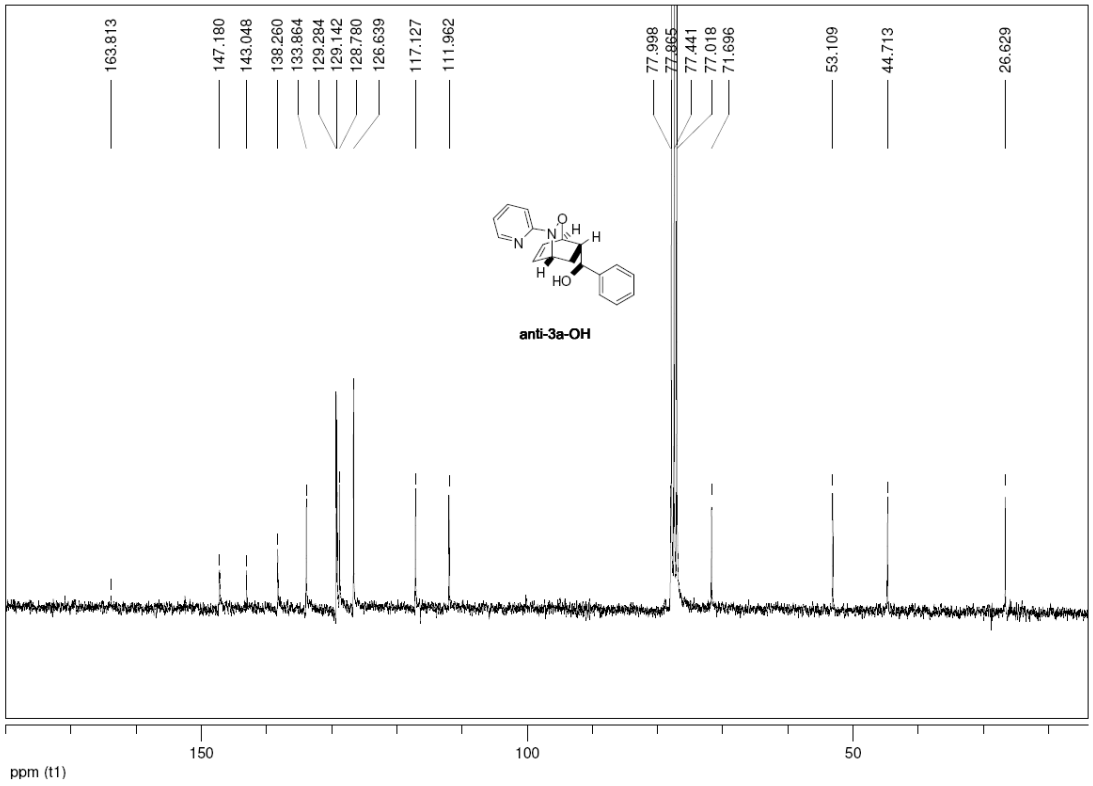
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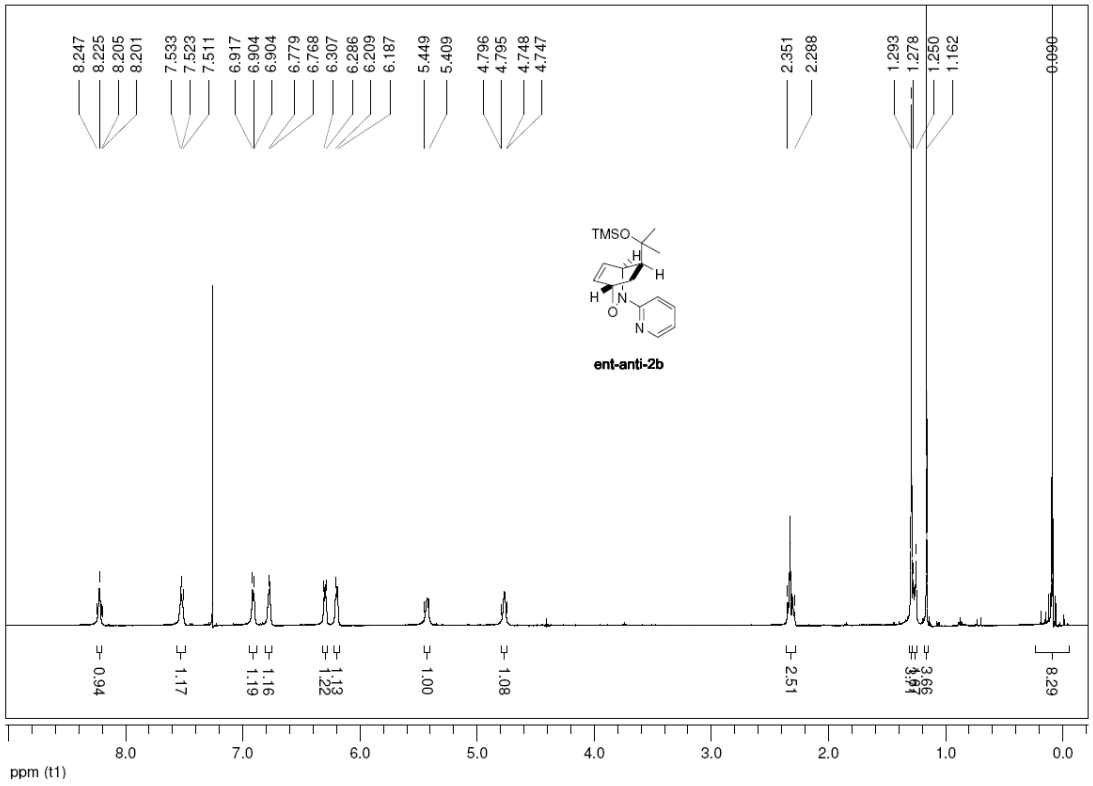
ppm (t1)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H
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O
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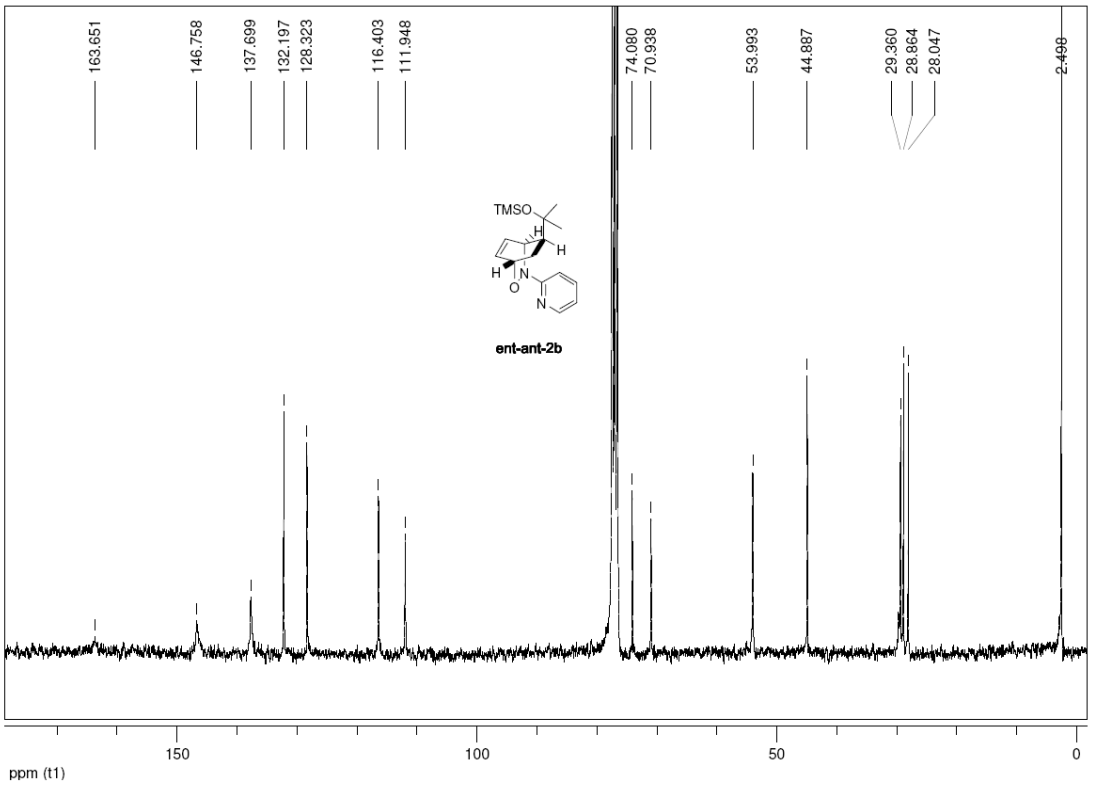
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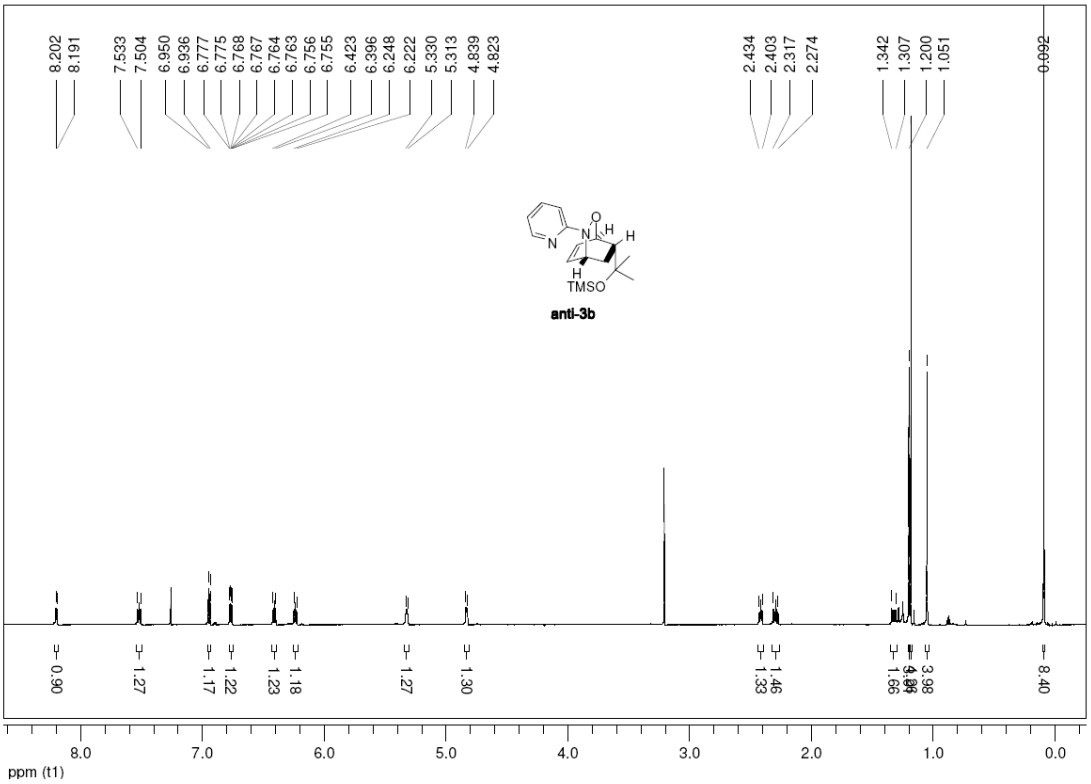
ppm (t1)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1.46
3.98
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7.0
6.0
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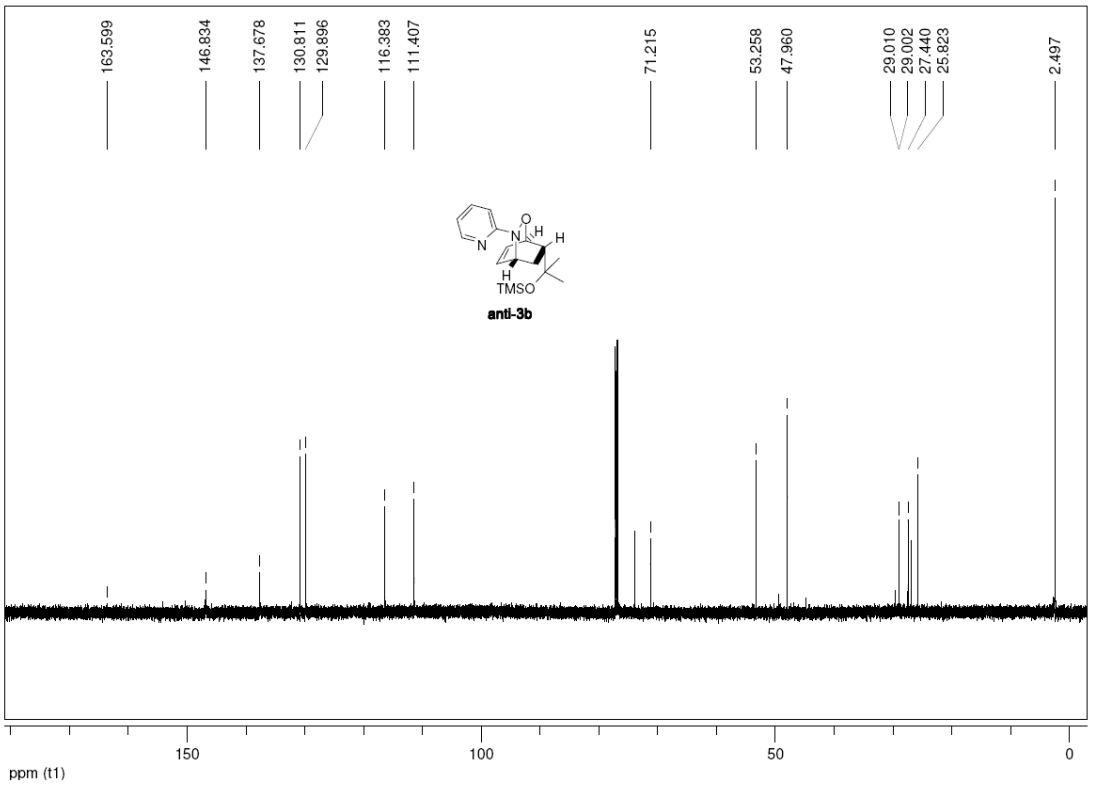
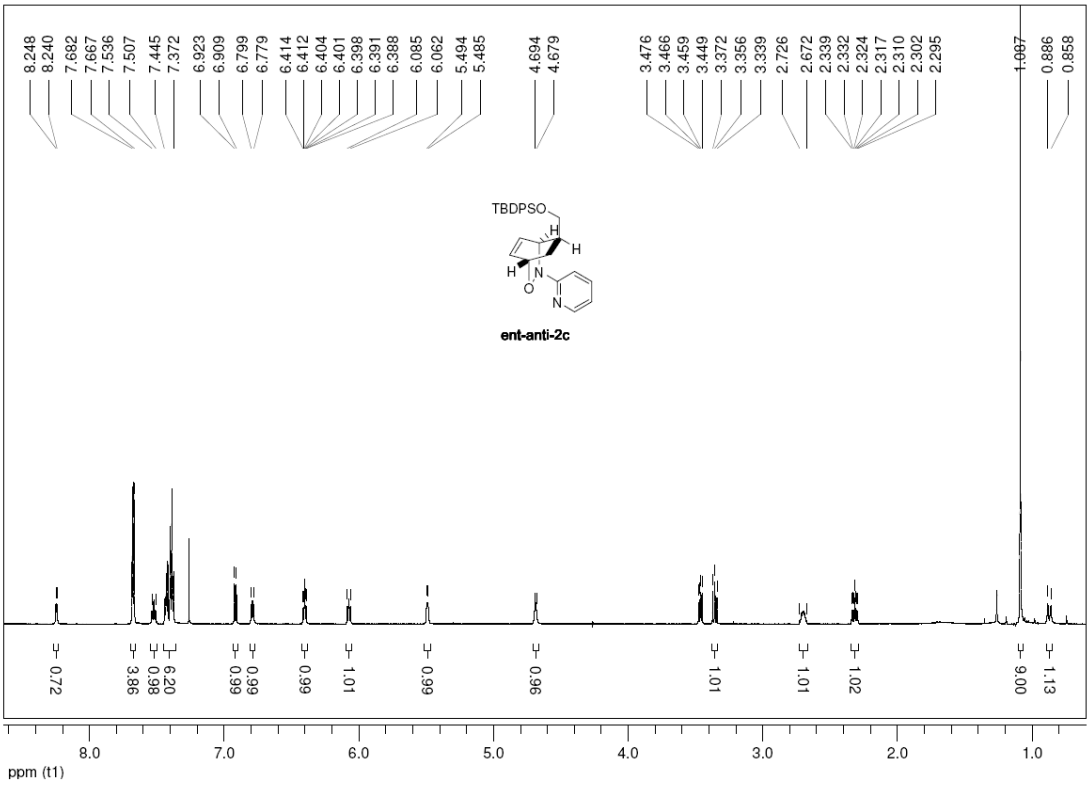
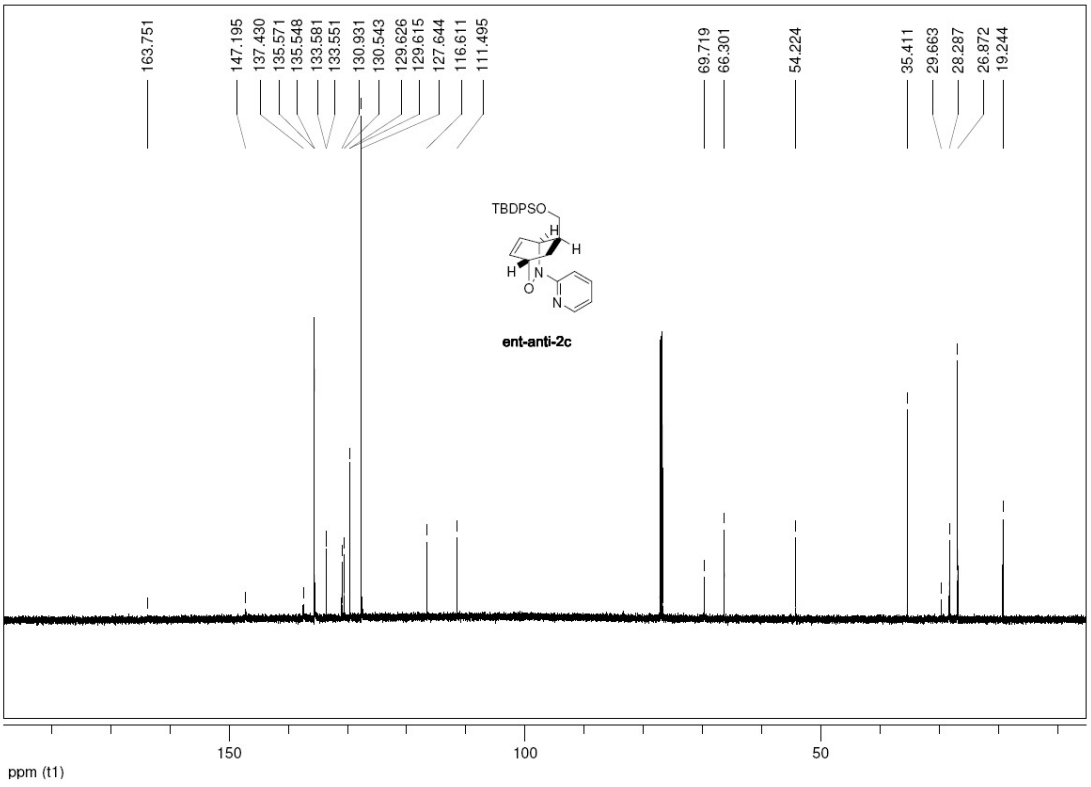
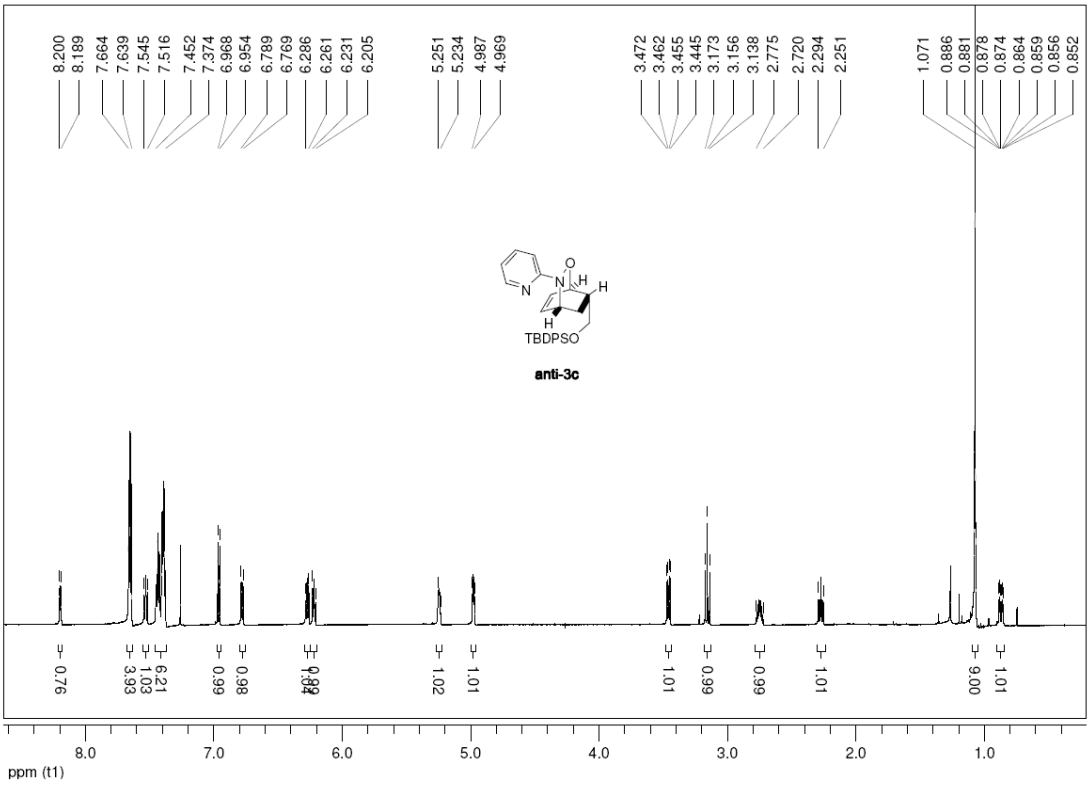
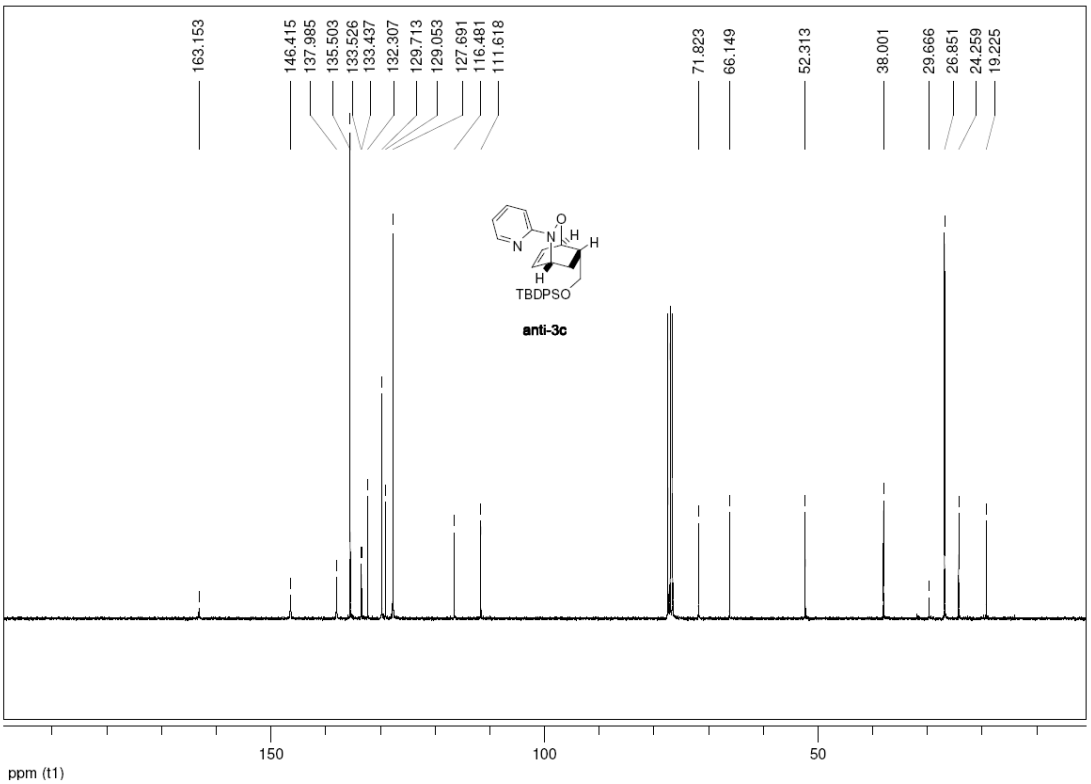
1.0
0.0
ppm (t1)

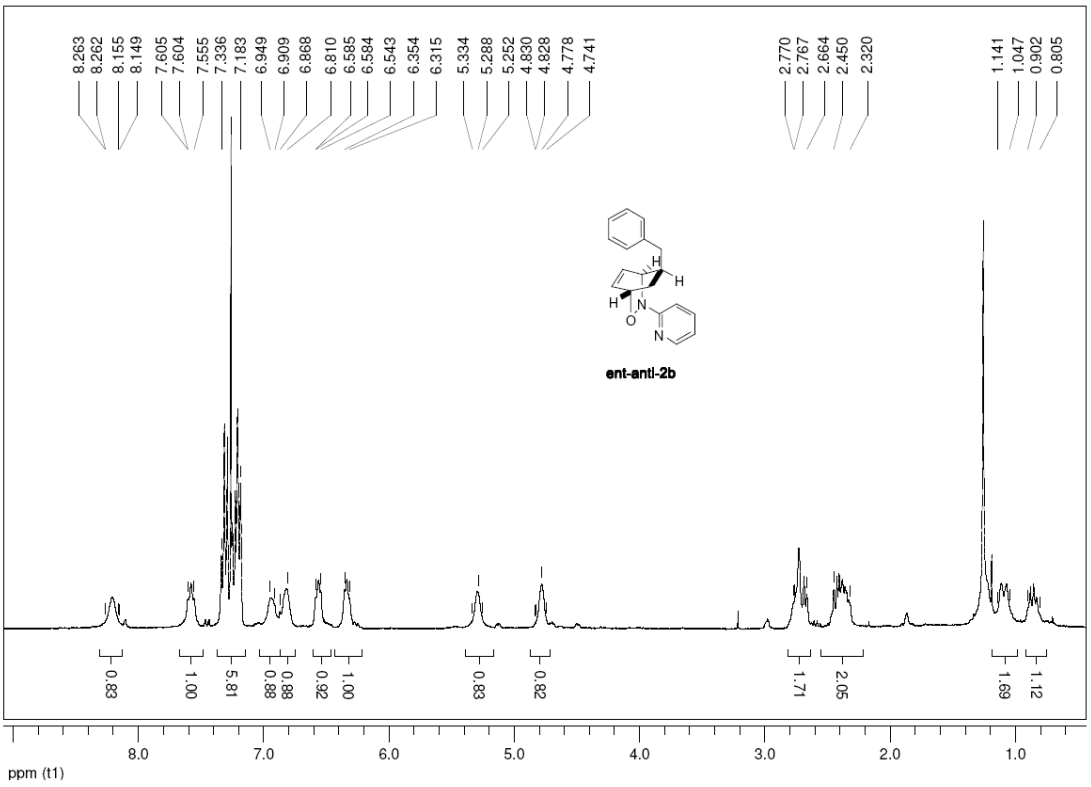

163.599
146.834
137.678
130.811
129.896
116.383
111.407
71.215
53.258
47.960
29.010
29.002
27.440
25.823
2.497
TMSO
anti-3b
150
100
50
0
ppm (t1)

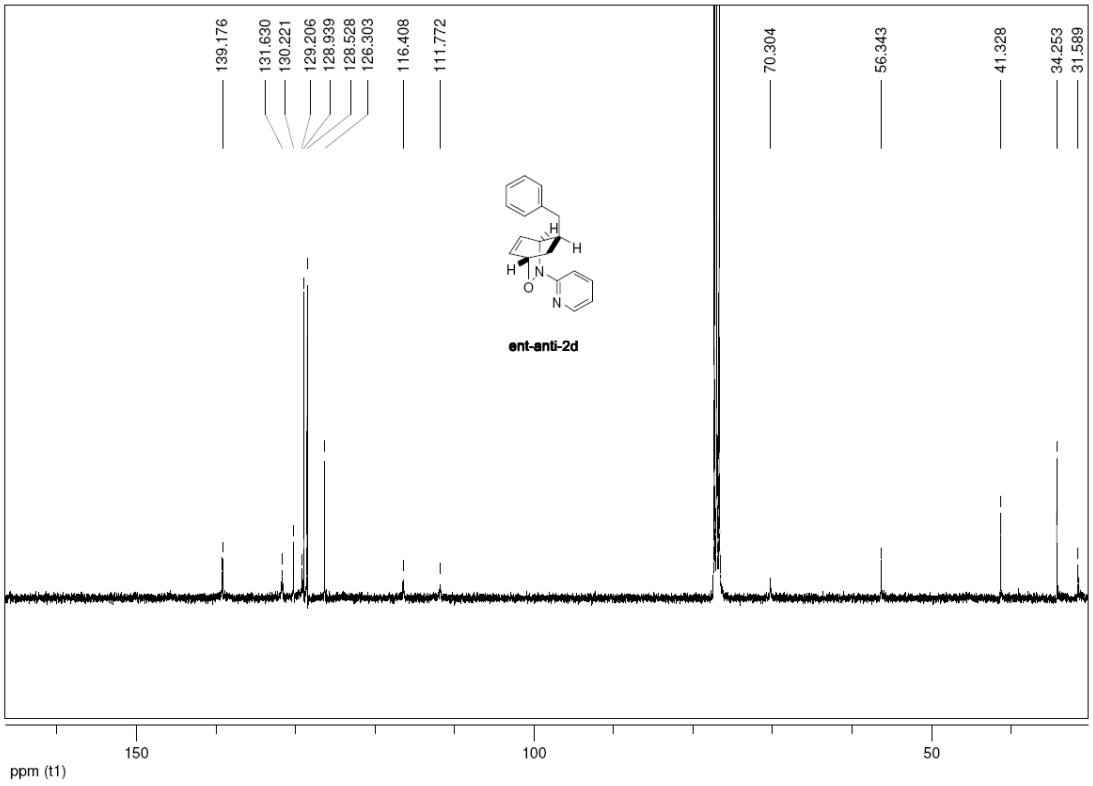

8.248
8.240
7.682
7.667
7.536
7.507
7.445
7.372
6.923
6.909
6.799
6.779
6.414
6.412
6.404
6.401
6.398
6.391
6.388
6.085
6.062
5.494
5.485
4.694
4.679
3.476
3.466
3.459
3.449
3.372
3.356
3.339
2.726
2.672
2.339
2.332
2.324
2.317
2.310
2.302
2.295
1.097
0.886
0.858
TBDPSO
ent-anti-2c
0.72
3.86
0.98
6.20
0.99
0.99
0.99
1.01
0.99
0.96
1.01
1.01
1.02
9.00
1.13
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

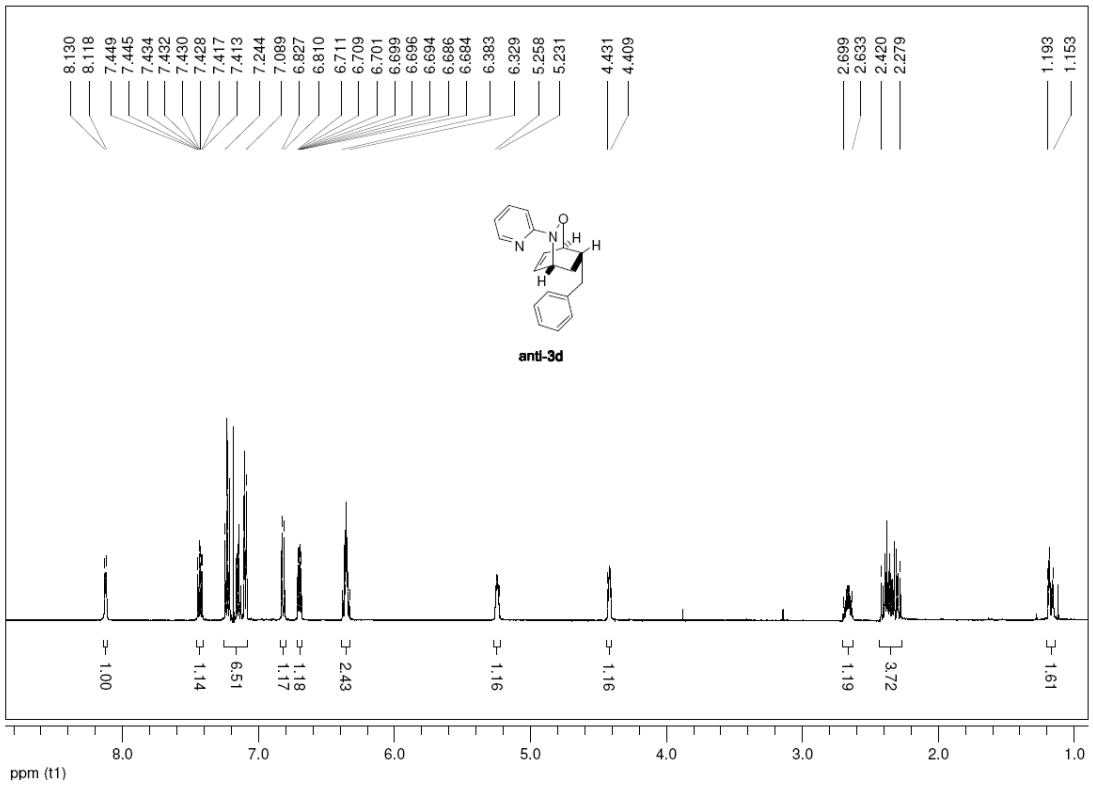

163.751
147.195
137.430
135.571
135.548
133.581
133.551
130.931
130.543
129.626
129.615
127.644
116.611
111.495
69.719
66.301
54.224
35.411
29.663
28.287
26.872
19.244
TBDPSO
ent-anti-2c
150
100
50
ppm (t1)

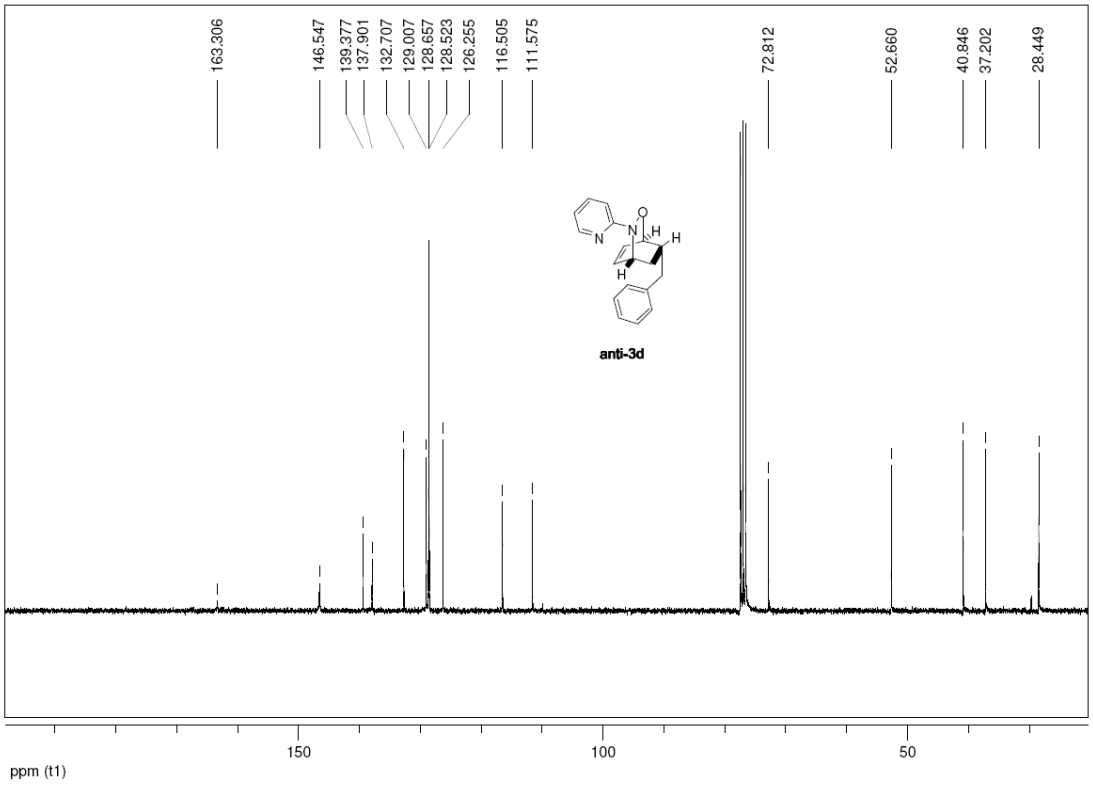

8.200
8.189
7.664
7.639
7.545
7.516
7.452
7.374
6.968
6.954
6.789
6.769
6.286
6.261
6.231
6.205
5.251
5.234
4.987
4.969
3.472
3.462
3.455
3.445
3.173
3.156
3.138
2.775
2.720
2.294
2.251
1.071
0.886
0.881
0.878
0.874
0.864
0.859
0.856
0.852
TBDPSO
anti-3c
0.76
3.33
1.03
6.21
0.99
0.98
1.02
1.01
1.01
0.99
0.99
1.01
9.00
1.01
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

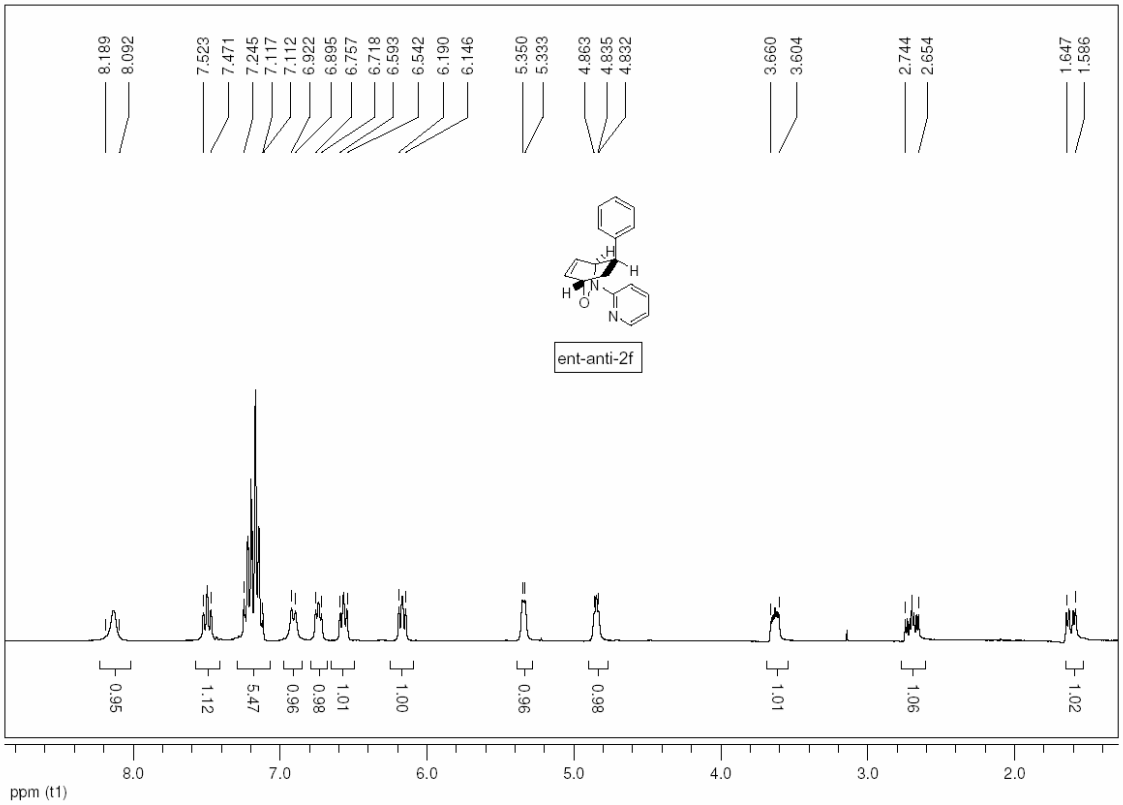

163.153
146.415
137.985
135.503
133.526
133.437
132.307
129.713
129.053
127.691
116.481
111.618
71.823
66.149
52.313
38.001
29.666
26.851
24.259
19.225
TBDPSO
anti-3c
150
100
50
ppm (t1)

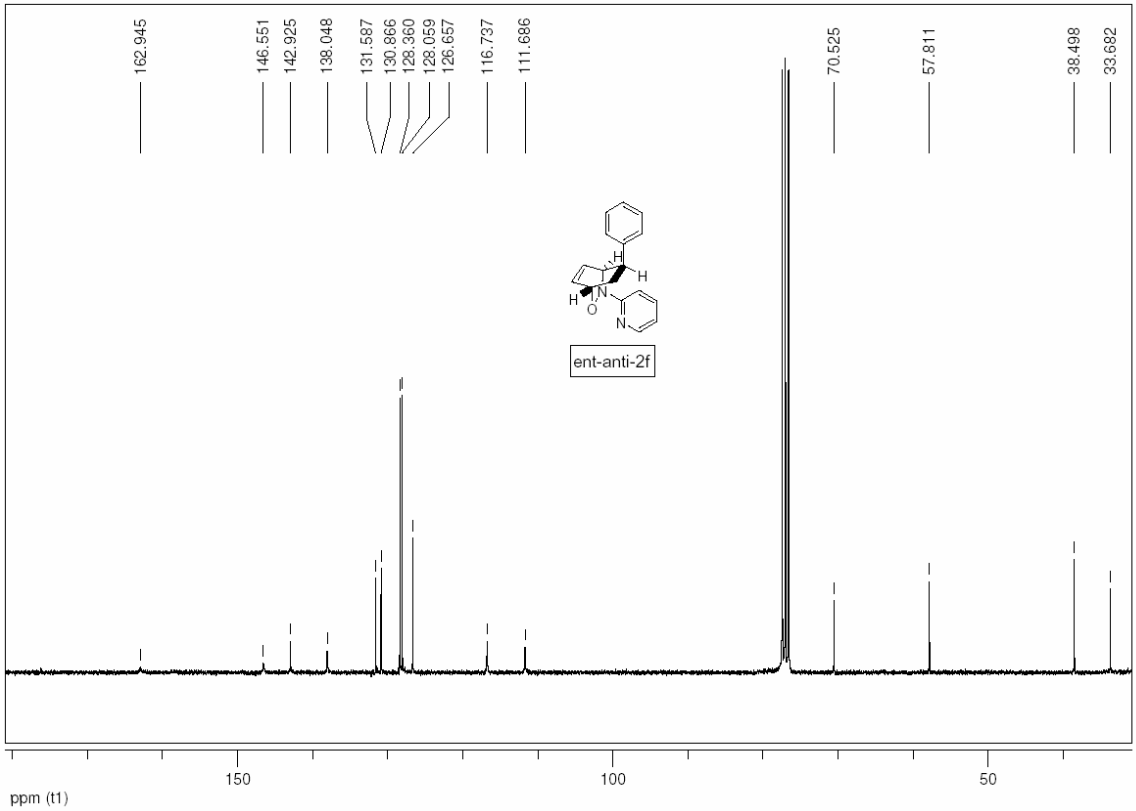

8.263
8.262
8.155
8.149
7.605
7.604
7.555
7.336
7.183
6.949
6.909
6.868
6.810
6.585
6.584
6.543
6.354
6.315
5.334
5.288
5.252
4.830
4.828
4.778
4.741
2.770
2.767
2.664
2.450
2.320
1.141
1.047
0.902
0.805
ent-anti-2b
0.83
1.00
5.18
0.88
0.88
0.92
1.00
0.83
0.82
1.71
2.05
1.69
1.12
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

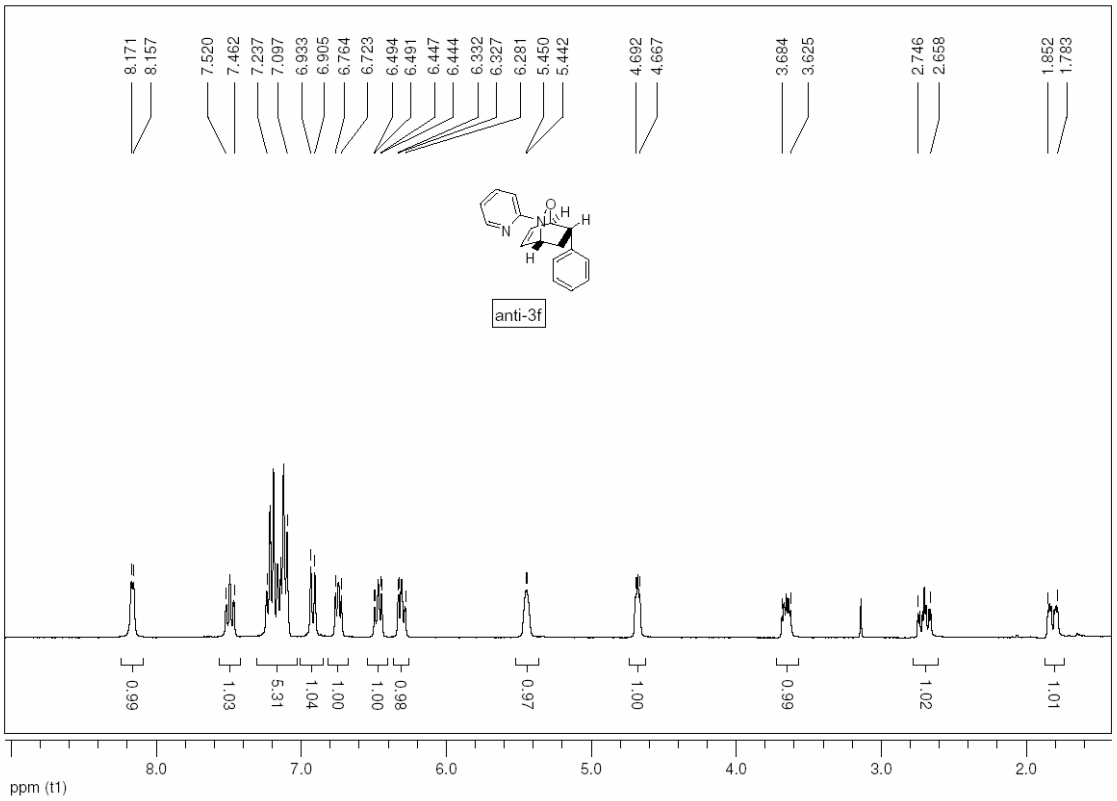

139.176
131.630
130.221
129.206
128.939
128.528
126.303
116.408
111.772
70.304
56.343
41.328
34.253
31.589
ent-anti-2d
150
100
50
ppm (t1)

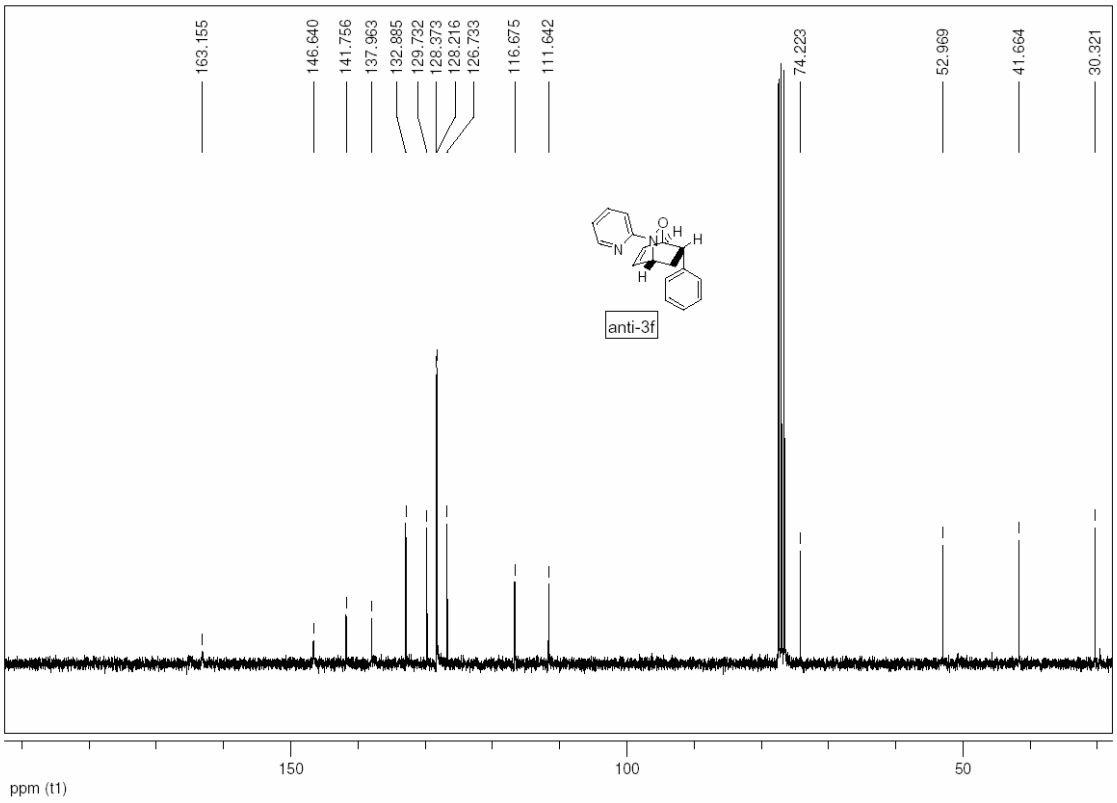

8.130
8.118
7.449
7.445
7.434
7.432
7.430
7.428
7.417
7.413
7.244
7.089
6.827
6.810
6.711
6.709
6.701
6.699
6.696
6.694
6.686
6.684
6.383
6.329
5.258
5.231
4.431
4.409
2.699
2.633
2.420
2.279
1.193
1.153
anti-3d
1.00
1.14
6.51
1.17
1.18
2.43
1.16
1.16
1.19
3.72
1.61
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

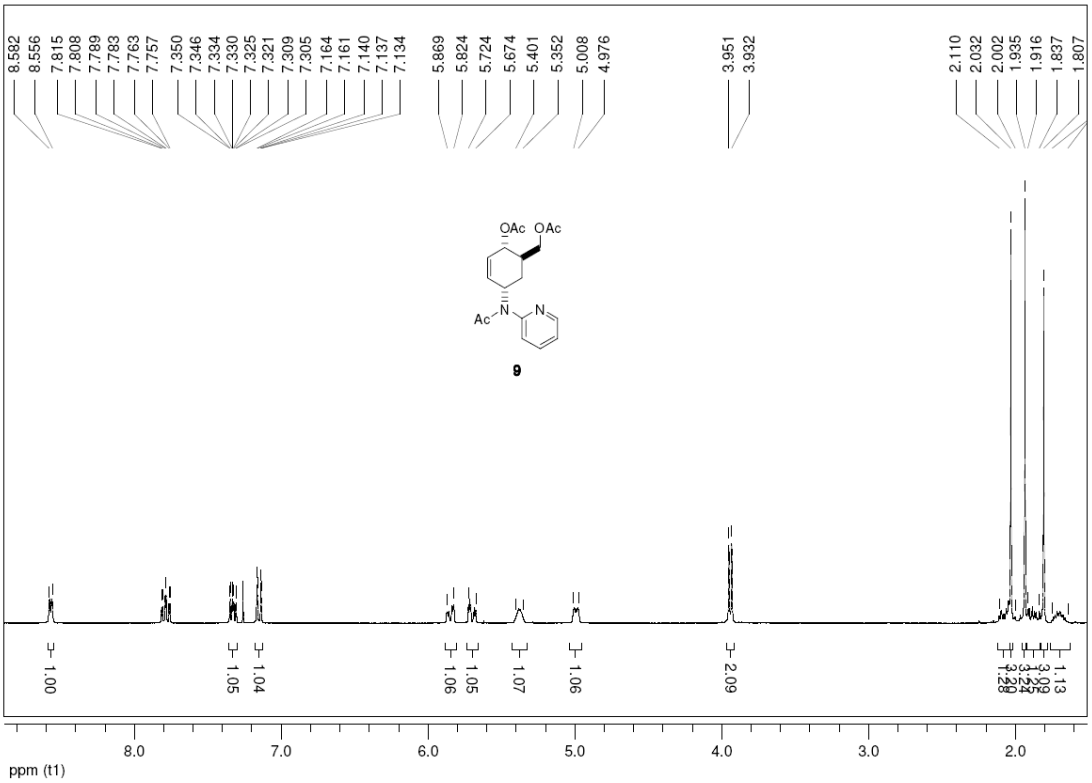

163.306
146.547
139.377
137.901
132.707
129.007
128.657
128.523
126.255
116.505
111.575
72.812
52.660
40.846
37.202
28.449
anti-3d
150
100
50
ppm (t1)

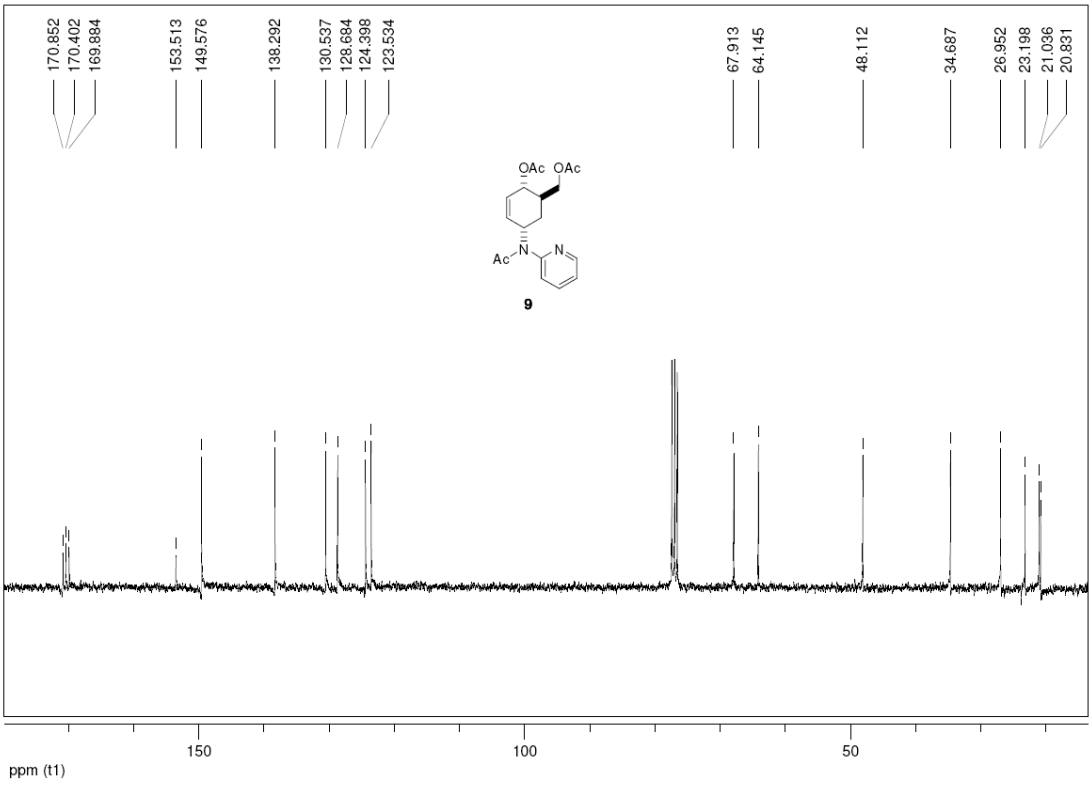

8.189
8.092
7.523
7.471
7.245
7.117
7.112
6.922
6.895
6.757
6.718
6.593
6.542
6.190
6.146
5.350
5.333
4.863
4.835
4.832
3.660
3.604
2.744
2.654
1.647
1.586
ent-anti-2f
0.95
1.12
5.47
0.96
0.98
1.01
1.00
0.96
0.98
1.01
1.06
1.02
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)

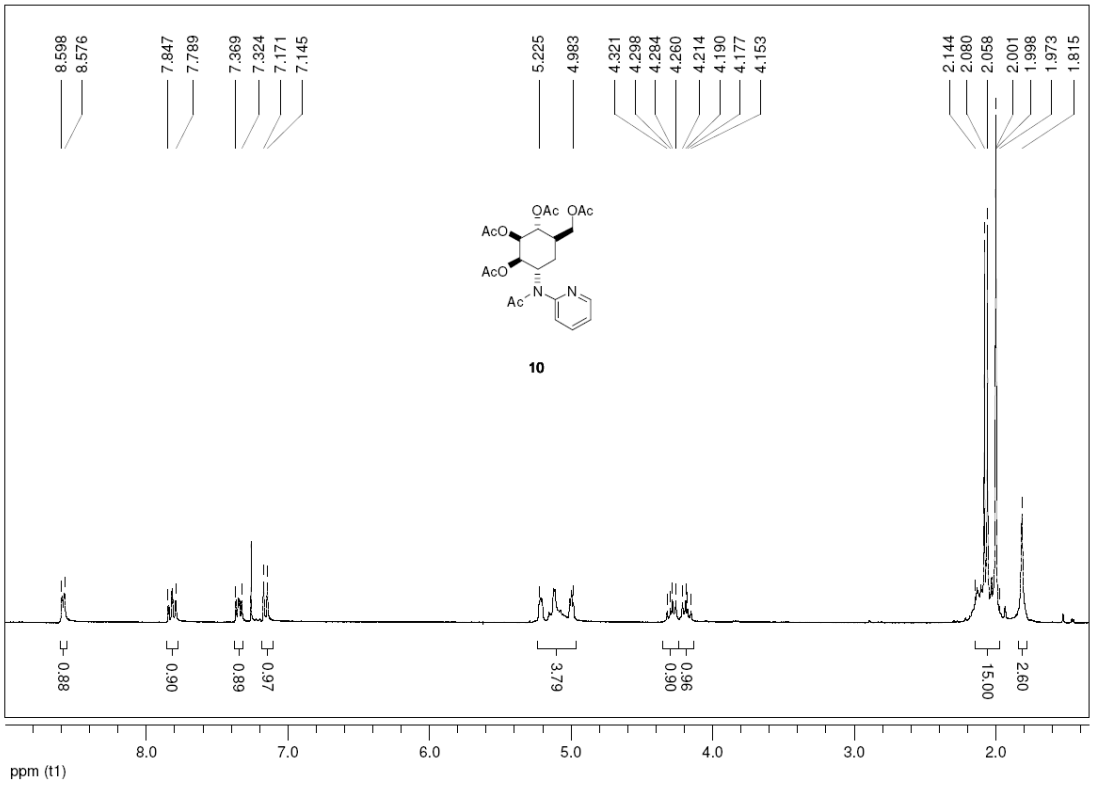

162.945
146.551
142.925
138.048
131.587
130.866
128.360
128.059
126.657
116.737
111.686
70.525
57.811
38.498
33.682
ent-anti-2f
150
100
50
ppm (t1)

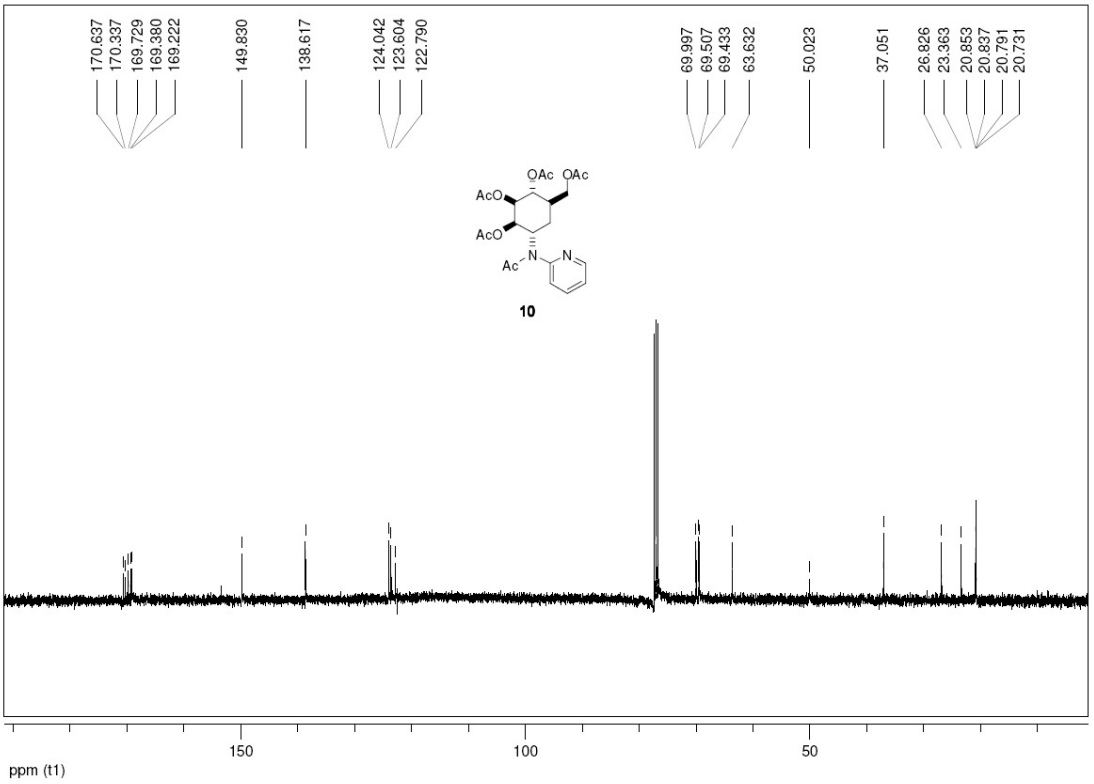

8.171
8.157
7.520
7.462
7.237
7.097
6.933
6.905
6.764
6.723
6.494
6.491
6.447
6.444
6.332
6.327
6.281
5.450
5.442
4.692
4.667
3.684
3.625
2.746
2.658
1.852
1.783
anti-3f
0.99
1.09
5.31
1.04
1.00
1.00
0.98
0.97
1.00
0.99
1.02
1.01
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)

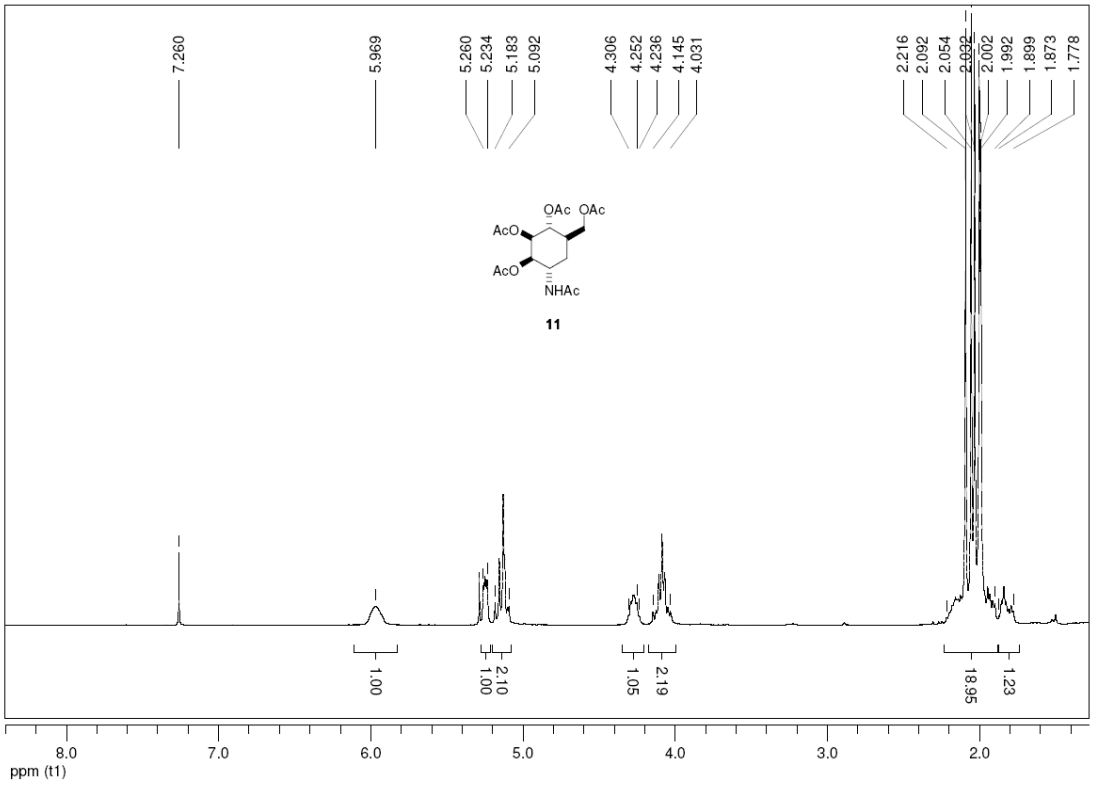

163.155
146.640
141.756
137.963
132.885
129.732
128.373
128.216
126.733
116.675
111.642
74.223
52.969
41.664
30.321
anti-3f
150
100
50
ppm (t1)

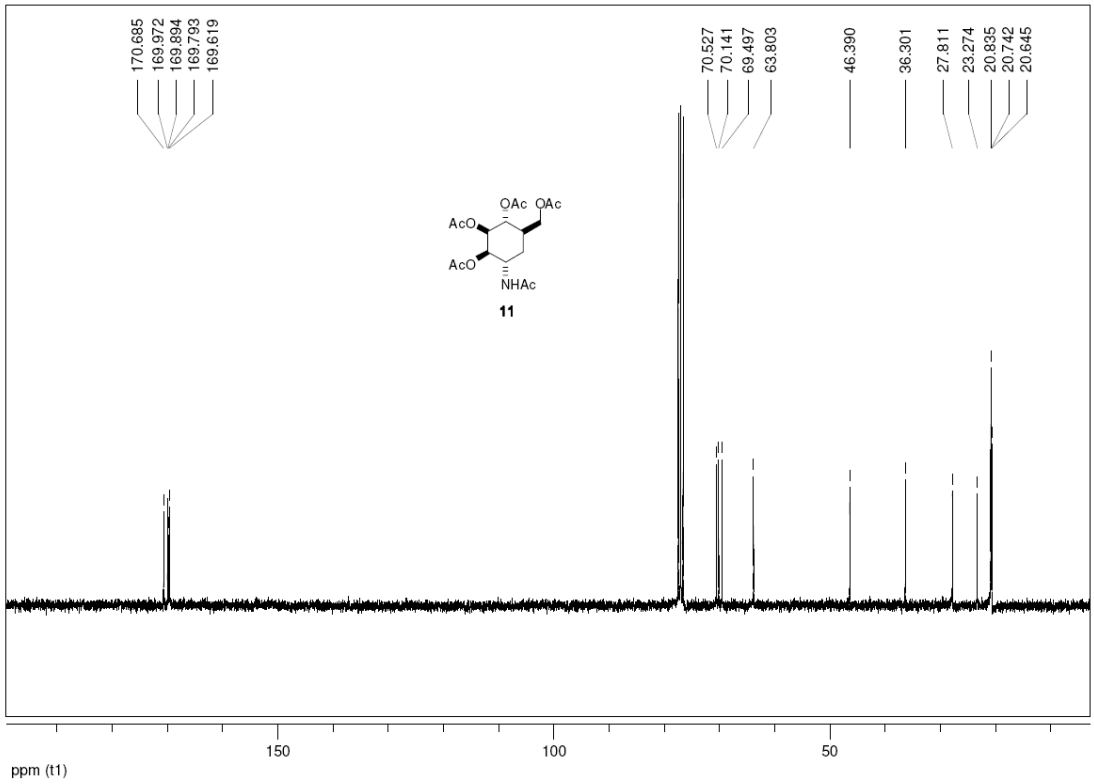

8.582
8.556
7.815
7.808
7.789
7.783
7.763
7.757
7.350
7.346
7.334
7.330
7.325
7.321
7.309
7.305
7.164
7.161
7.140
7.137
7.134
5.869
5.824
5.724
5.674
5.401
5.352
5.008
4.976
3.951
3.932
2.110
2.032
2.002
1.935
1.916
1.837
1.807
OAc OAc
Ac
N
N
9
1.00
1.05
1.04
1.06
1.05
1.07
1.06
2.09
1.13
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)


170.852
170.402
169.884
153.513
149.576
138.292
130.537
128.684
124.398
123.534
67.913
64.145
48.112
34.687
26.952
23.198
21.036
20.831
OAc OAc
Ac
N
N
9
150
100
50
ppm (t1)

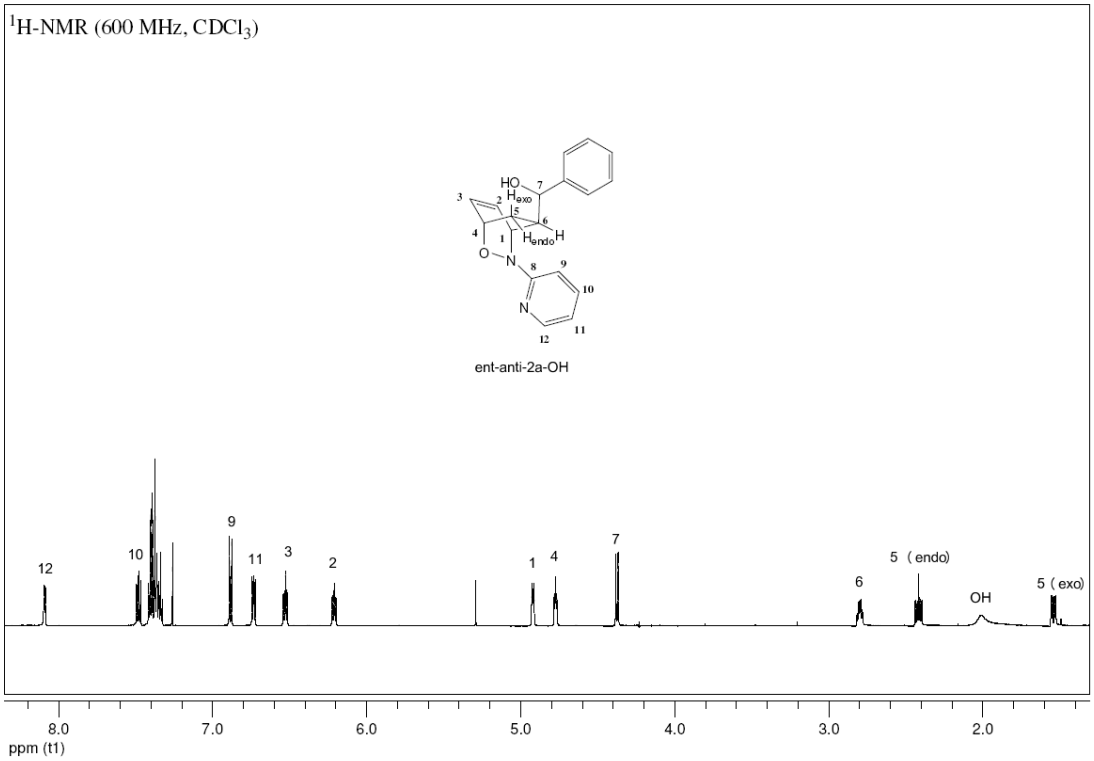

8.598
8.576
7.847
7.789
7.369
7.324
7.171
7.145
5.225
4.983
4.321
4.298
4.284
4.260
4.214
4.190
4.177
4.153
2.144
2.080
2.058
2.001
1.998
1.973
1.815
OAc OAc
AcO
AcO
Ac
N
N
10
0.88
0.90
0.89
0.97
3.79
0.90
0.96
15.00
2.90
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)

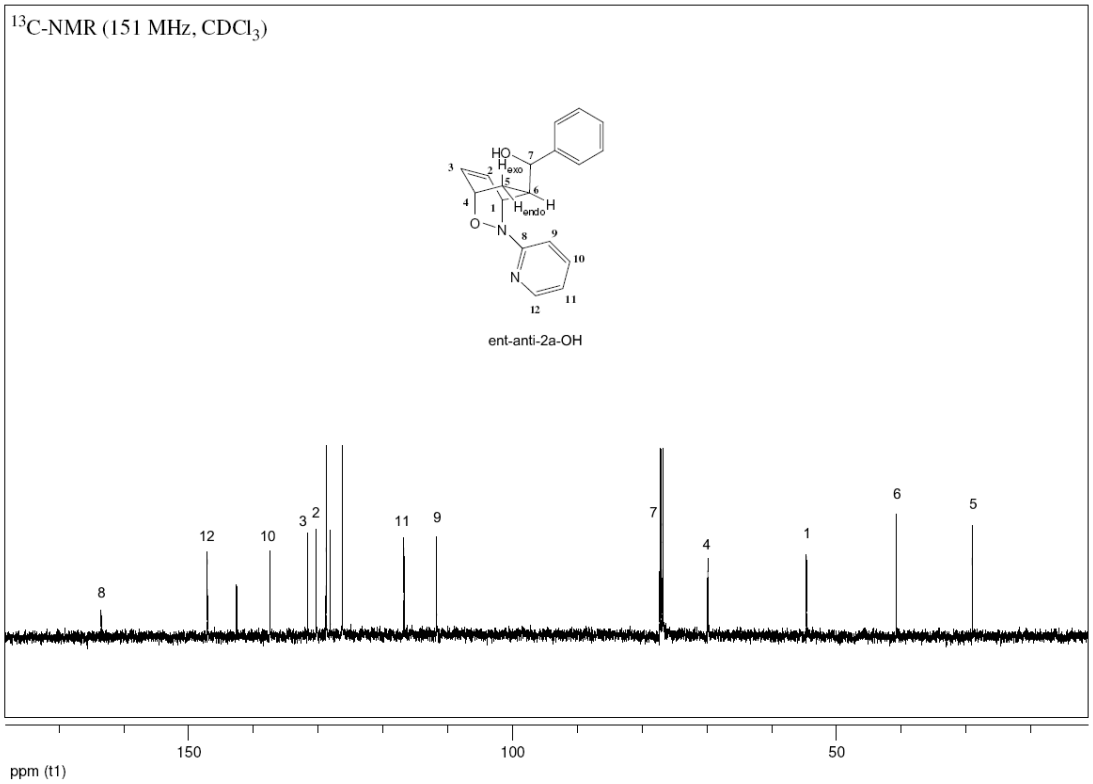

170.637
170.337
169.729
169.380
169.222
149.830
138.617
124.042
123.604
122.790
69.997
69.507
69.433
63.632
50.023
37.051
26.826
23.363
20.853
20.837
20.791
20.731
OAc OAc
AcO
AcO
Ac
N
N
10
150
100
50
ppm (t1)


7.260
5.969
5.260
5.234
5.183
5.092
4.306
4.252
4.236
4.145
4.031
2.216
2.092
2.054
2.032
2.002
1.992
1.899
1.873
1.778
OAc OAc
AcO
AcO
NHAc
11
1.00
1.00
2.10
1.05
2.19
18.95
1.23
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)

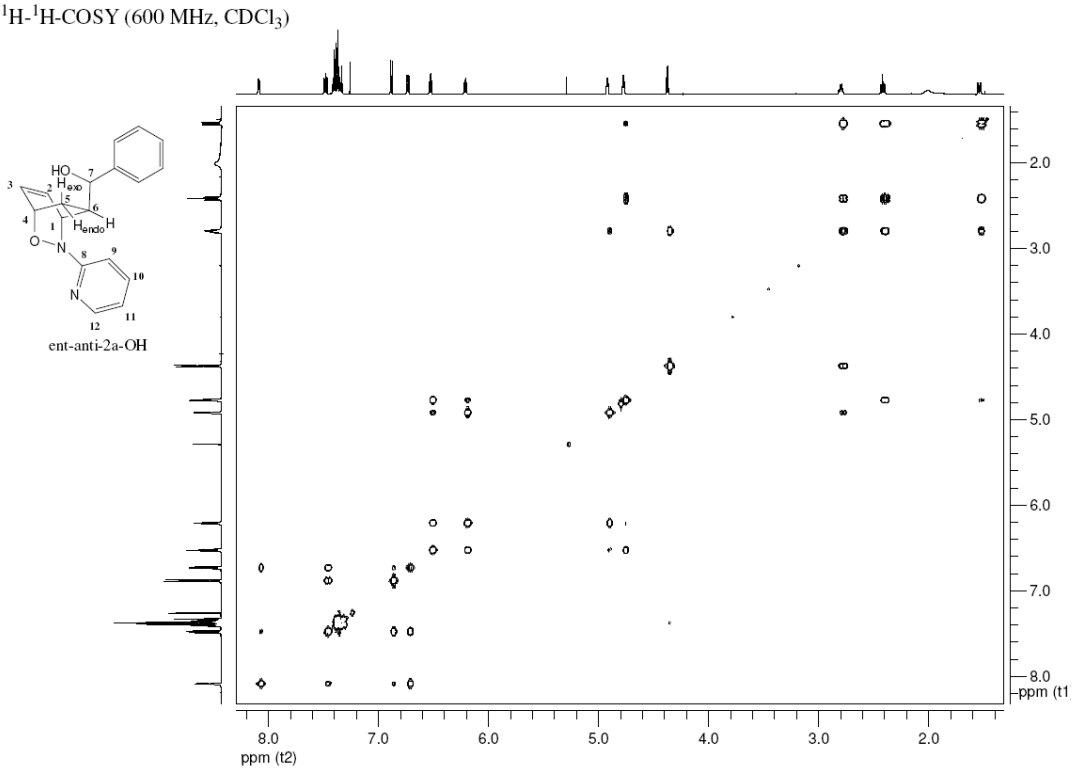

170.685
169.972
169.894
169.793
169.619
70.527
70.141
69.497
63.803
46.390
36.301
27.811
23.274
20.835
20.742
20.645
OAc OAc
AcO
AcO
NHAc
11
150
100
50
ppm (t1)

Determination of Relative Configurations

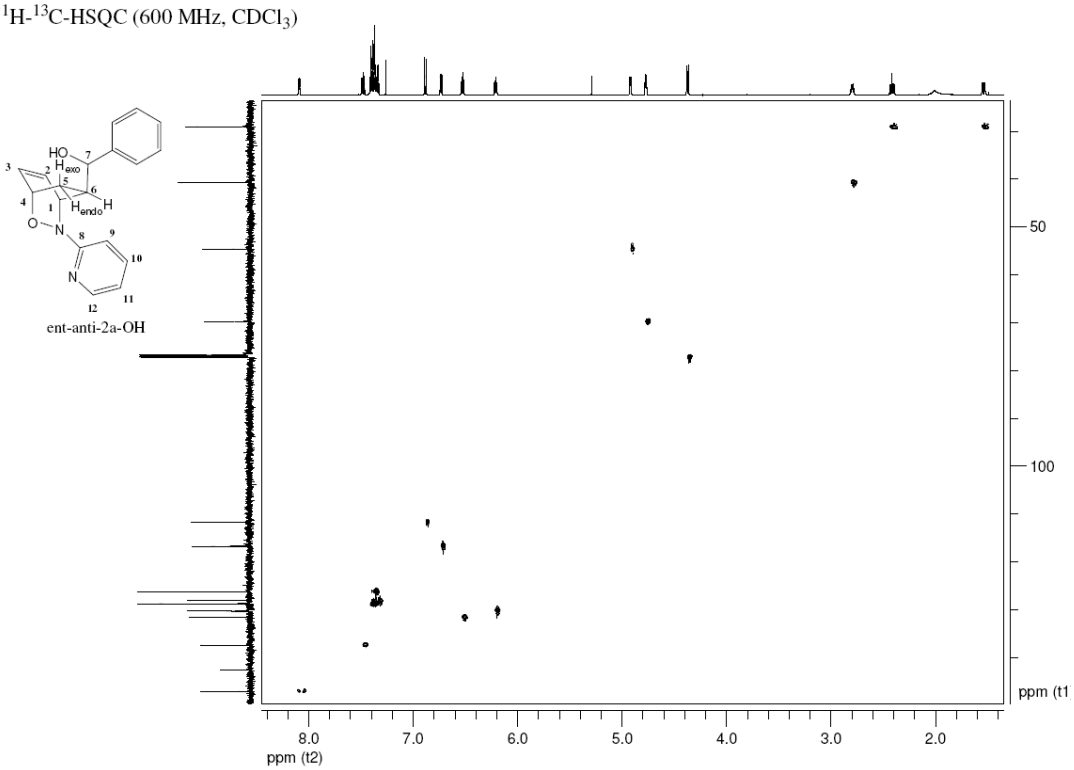


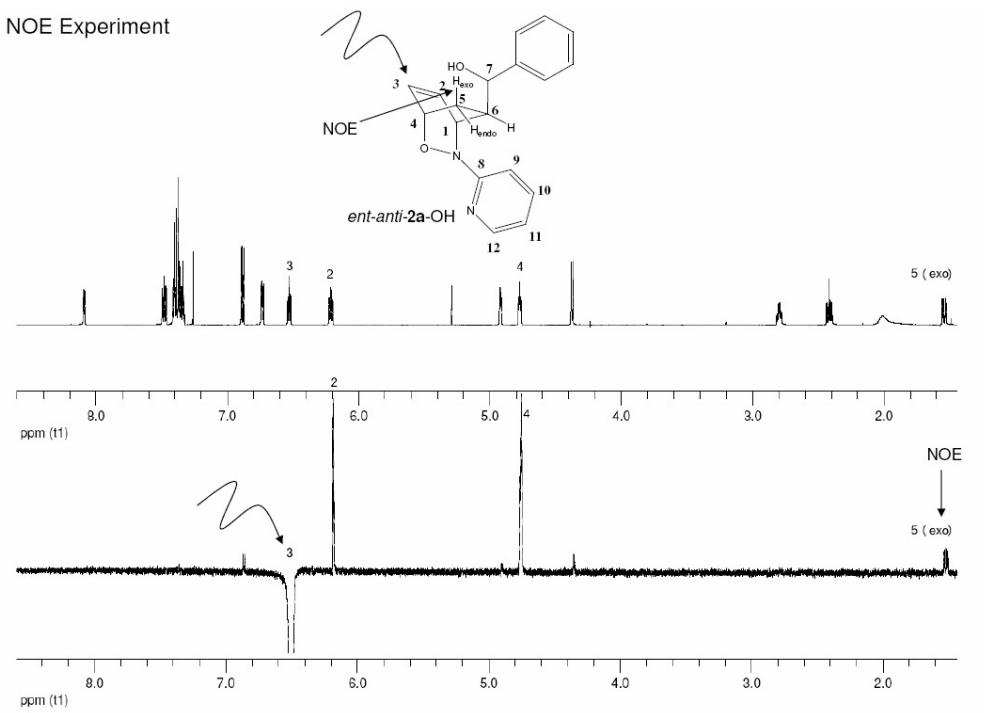


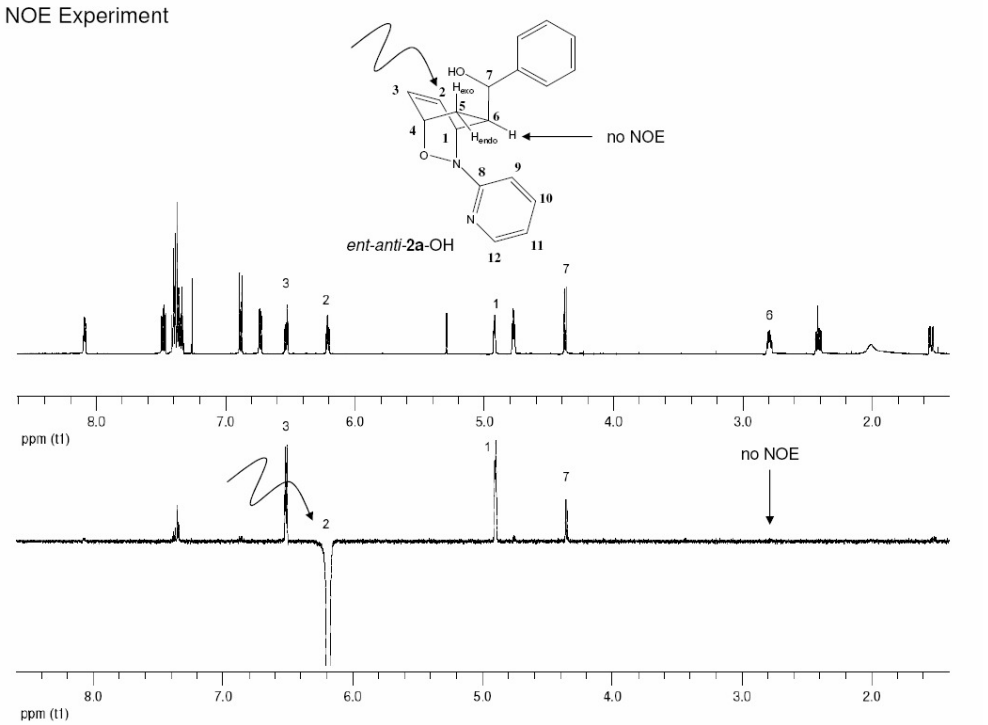
^{1}H-^{1}H-COSY (600 MHz, $CDCl_3$)

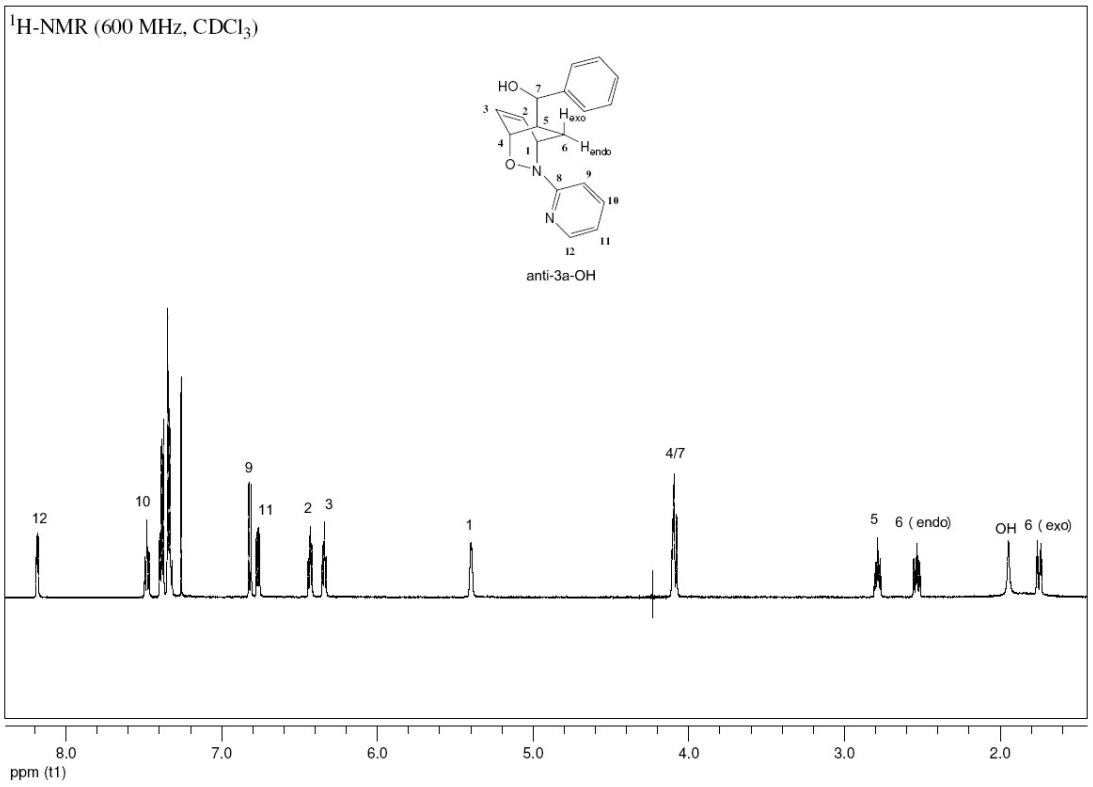


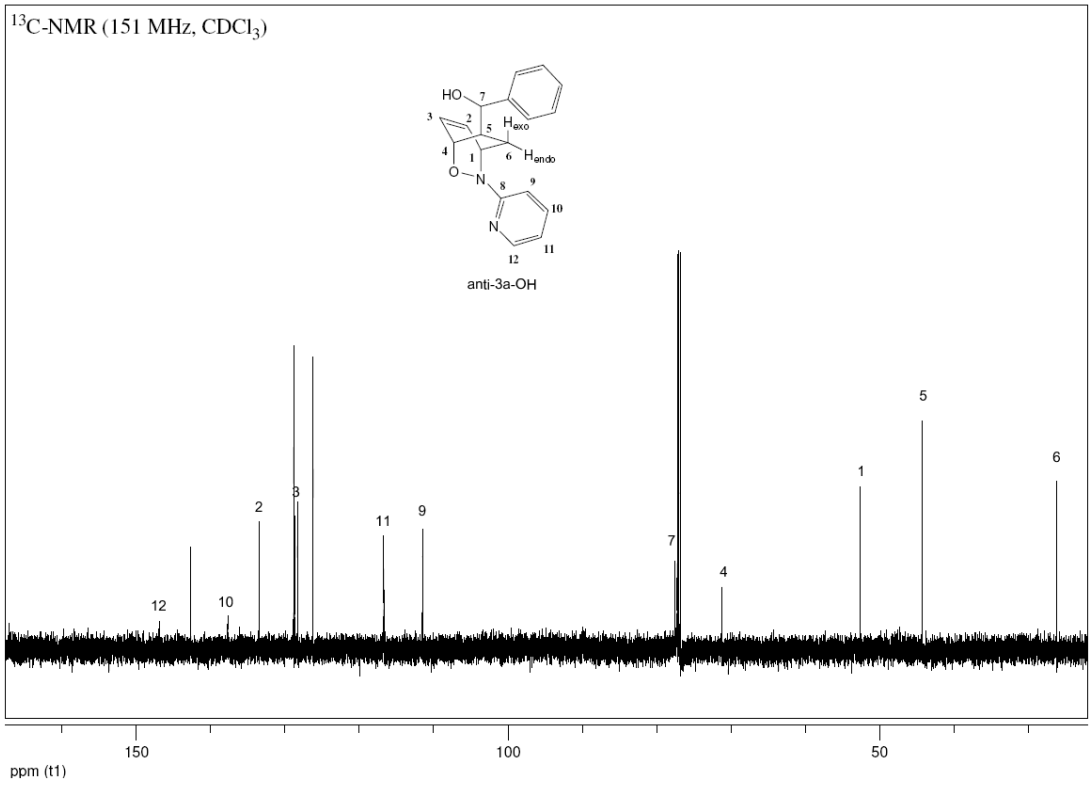
^{1}H-^{13}C-HSQC (600 MHz, $CDCl_3$)



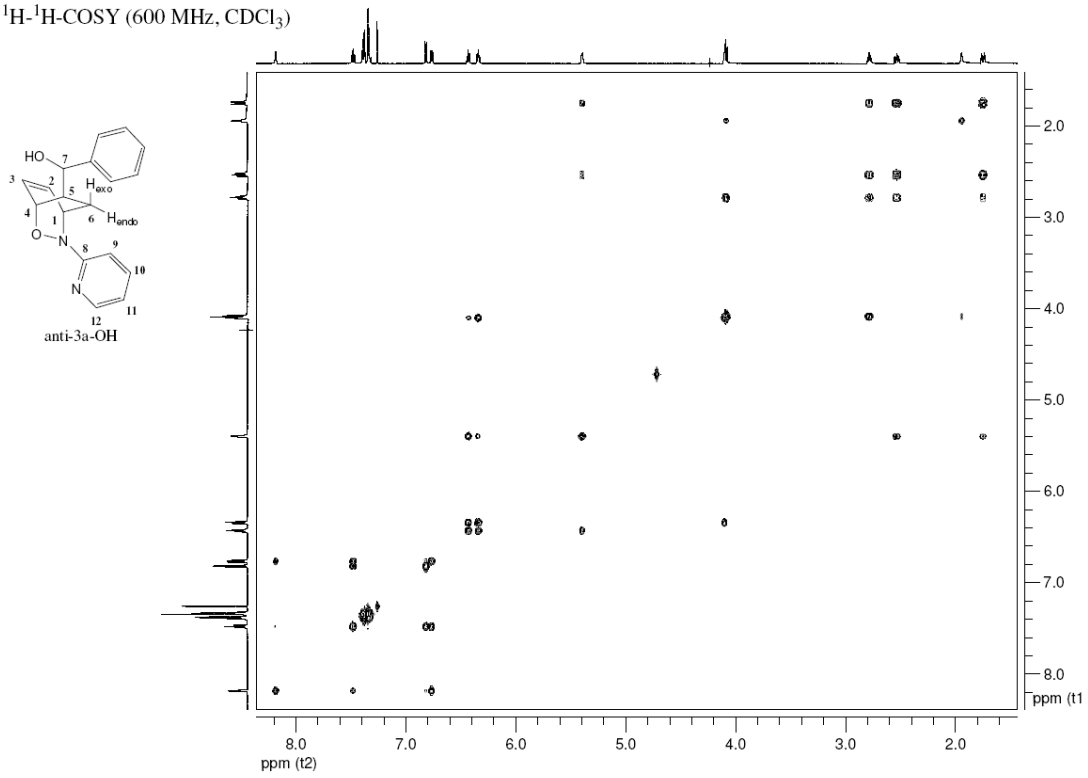

NOE Experiment
NOE
ent-anti-2a-OH
5 (exo)
NOE
5 (exo)
ppm (t1)


NOE Experiment
no NOE
ent-anti-2a-OH
no NOE
ppm (t1)

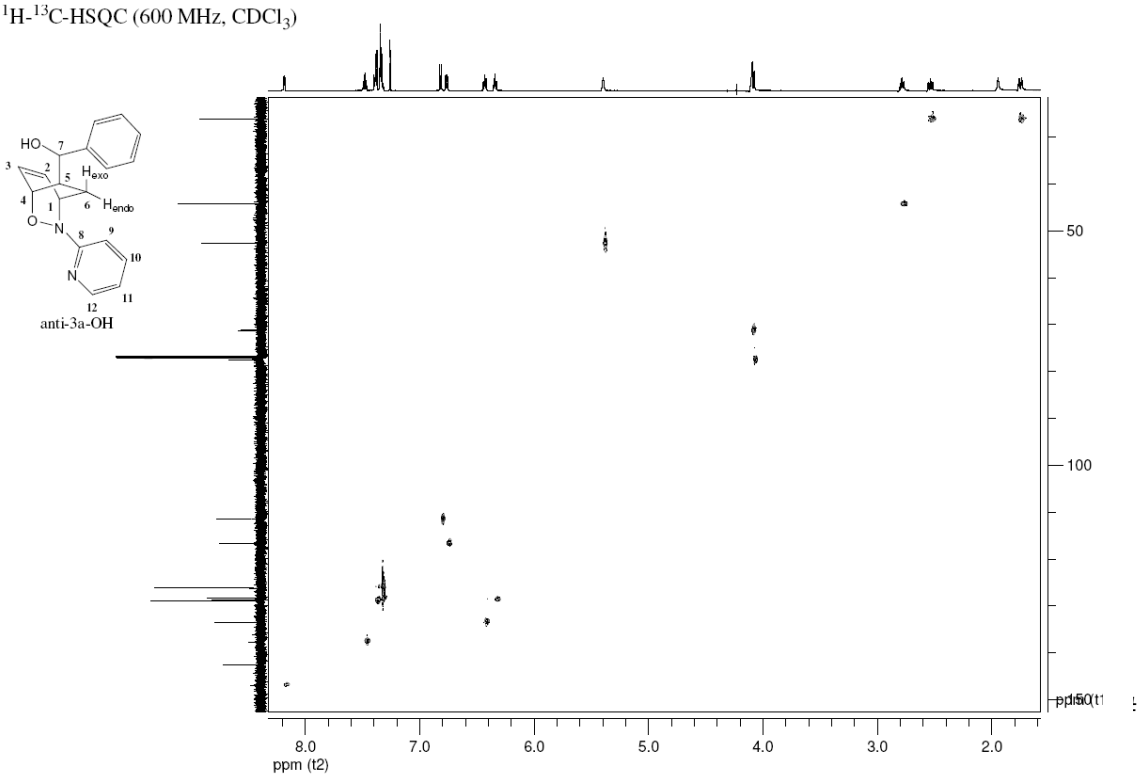

^{1}H-NMR (600 MHz, $CDCl_3$)
anti-3a-OH
12
10
9
11
2
3
1
4/7
5
6 (endo)
OH
6 (exo)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)

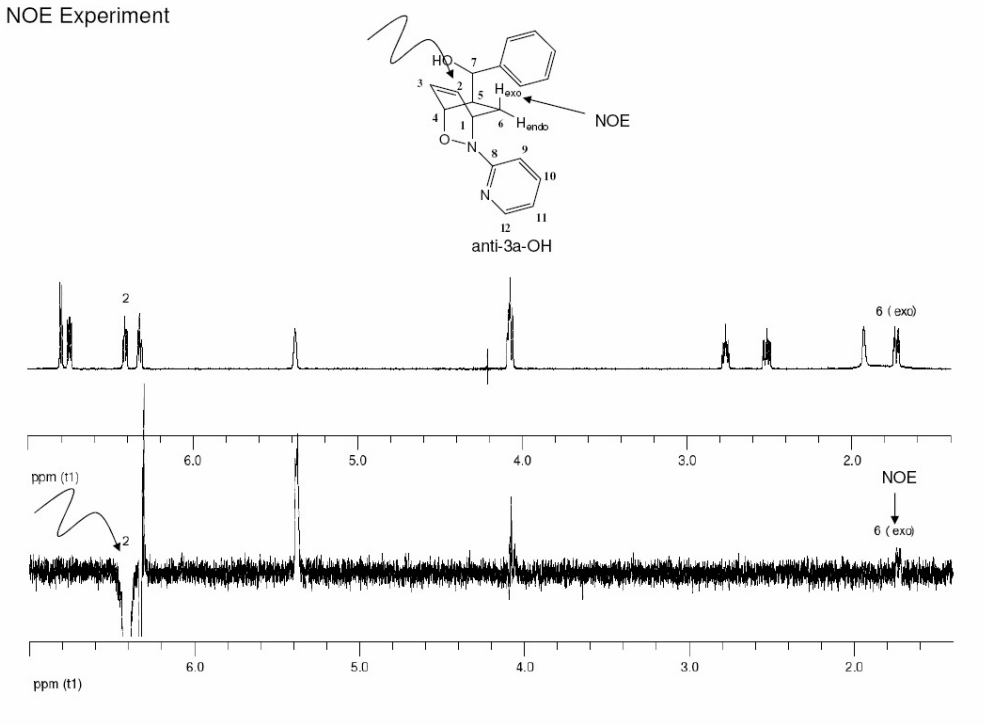

^{13}C-NMR (151 MHz, $CDCl_3$)
anti-3a-OH
12
10
2
3
11
9
7
4
1
5
6
150
100
50
ppm (t1)

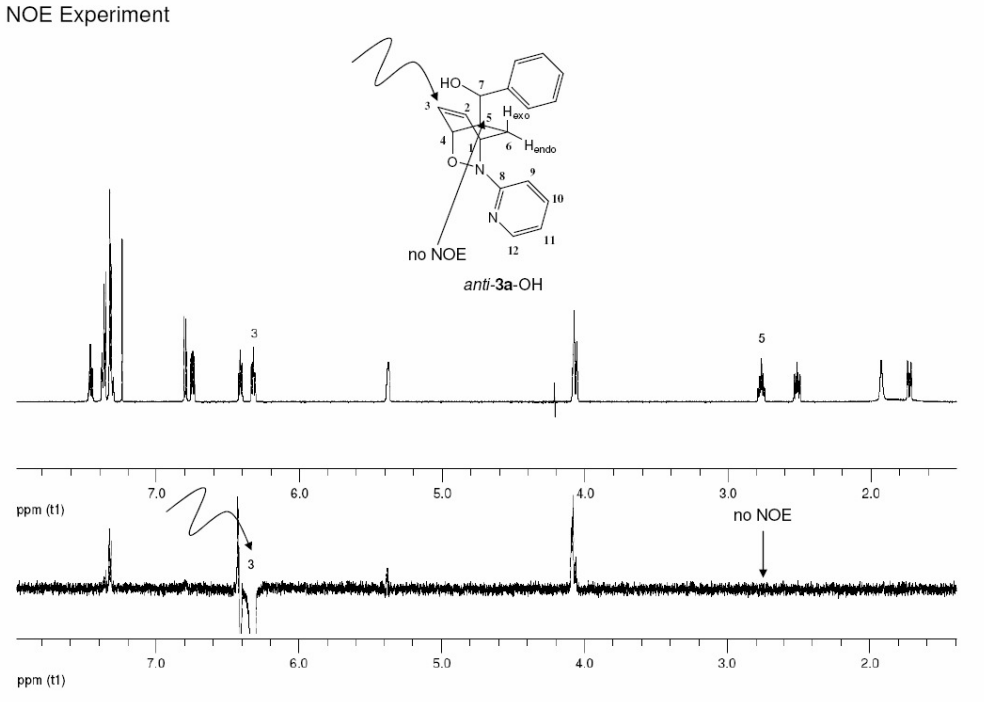
^{1}H-^{1}H-COSY (600 MHz, $CDCl_3$)



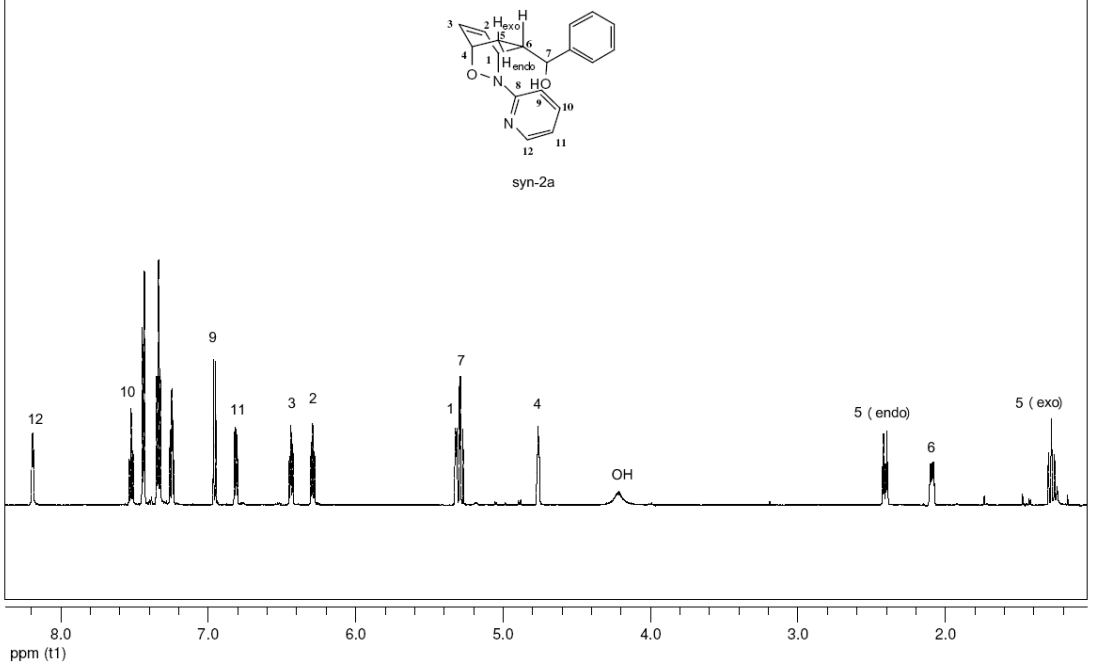
^{1}H-^{13}C-HSQC (600 MHz, $CDCl_3$)



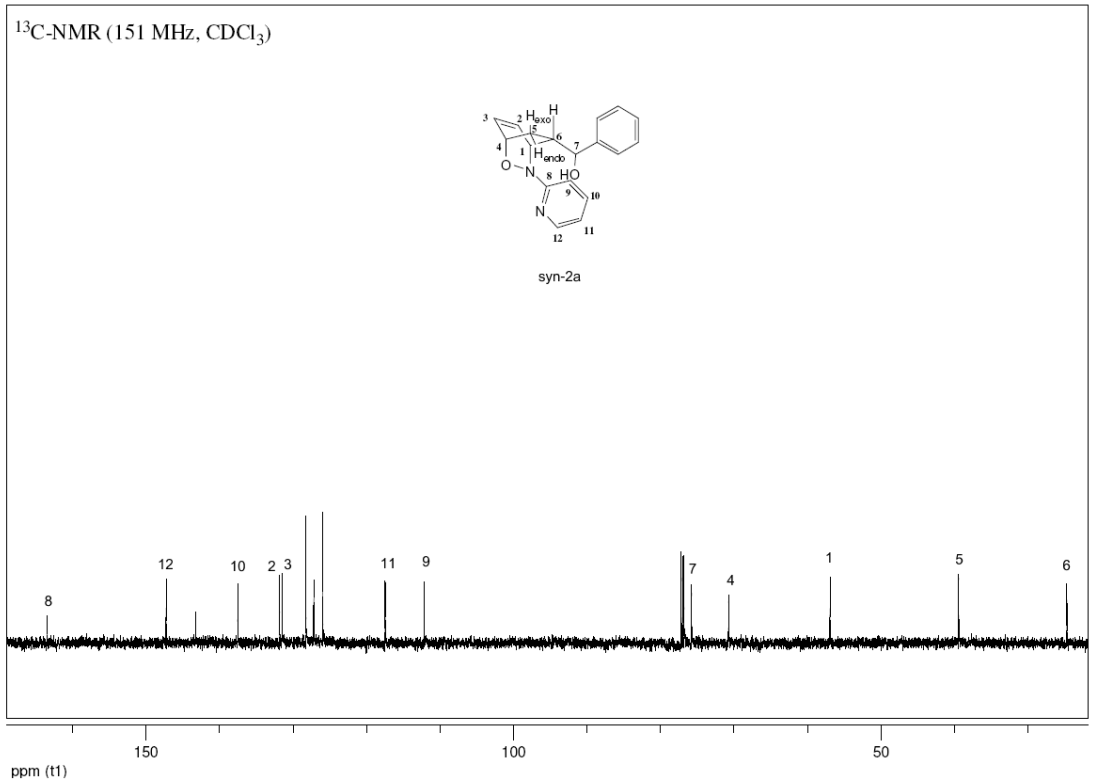

NOE Experiment
HO
7
3
2
5
H_{exo}
4
1
6
H_{endo}
NOE
O
N
8
9
10
N
11
12
anti-3a-OH
2
6 (exo)
6.0
5.0
4.0
3.0
2.0
ppm (t1)
NOE
2
6 (exo)
6.0
5.0
4.0
3.0
2.0
ppm (t1)


NOE Experiment
HO
7
3
2
5
H_{exo}
4
1
6
H_{endo}
O
N
8
9
10
N
11
12
no NOE
anti-3a-OH
3
5
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)
3
no NOE
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)

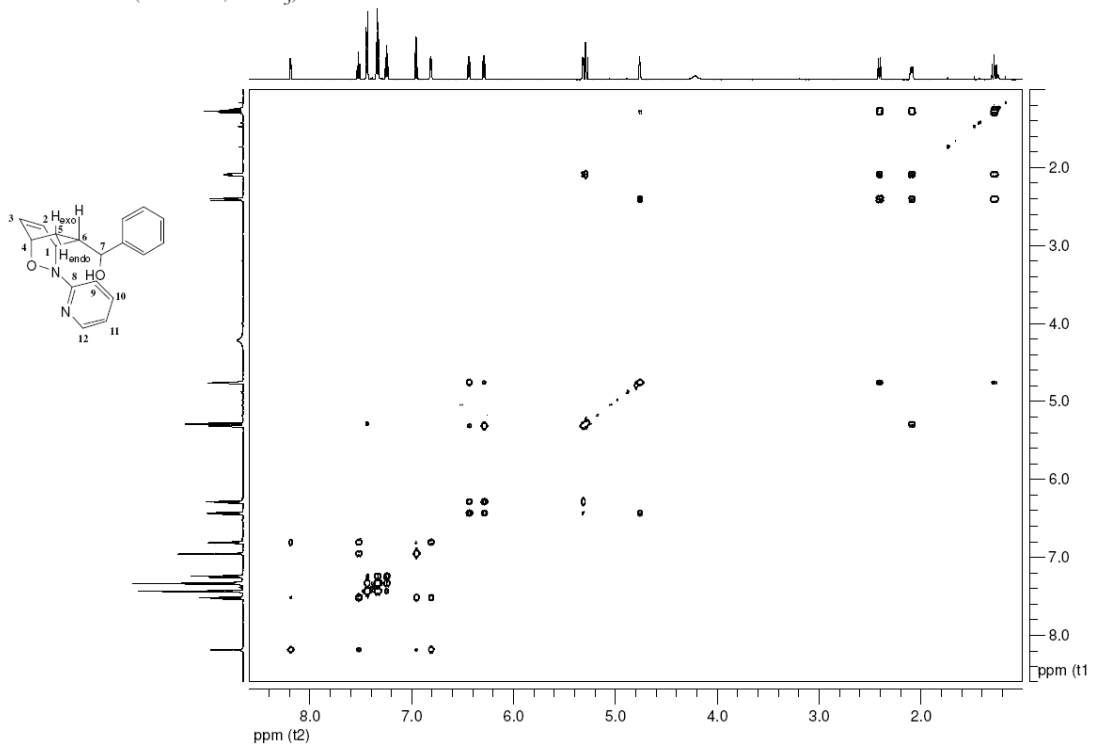
^{1}H-NMR (600 MHz, $CDCl_3$)



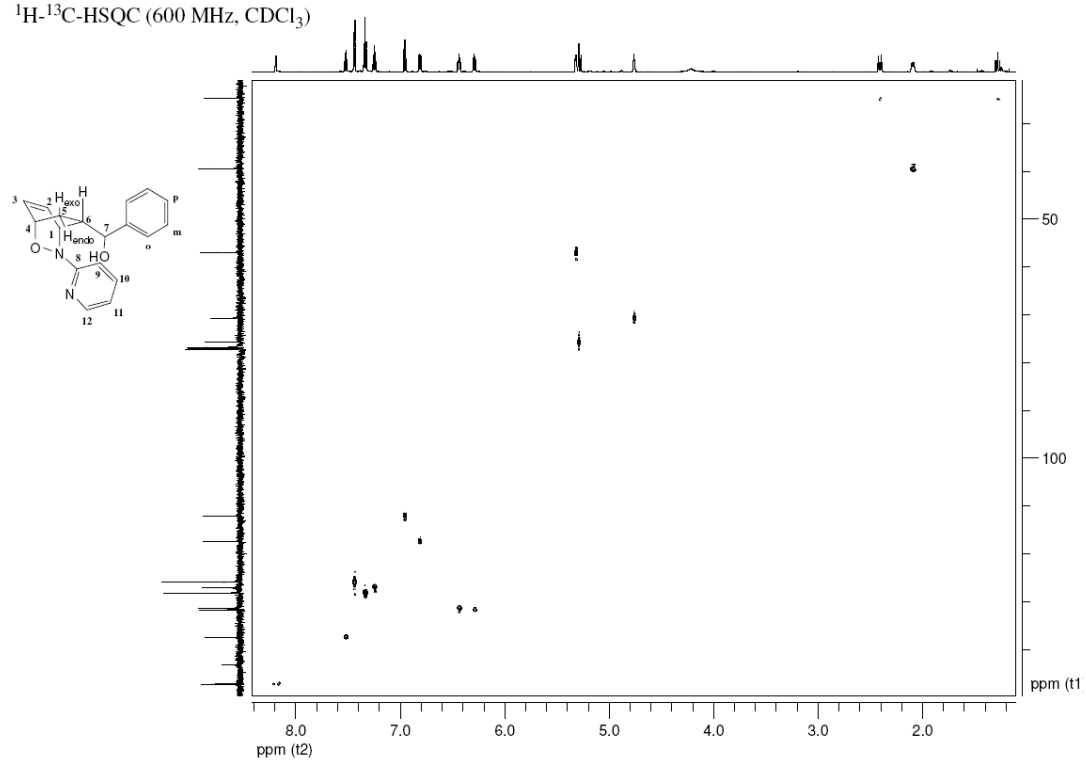
^{13}C-NMR (151 MHz, $CDCl_3$)



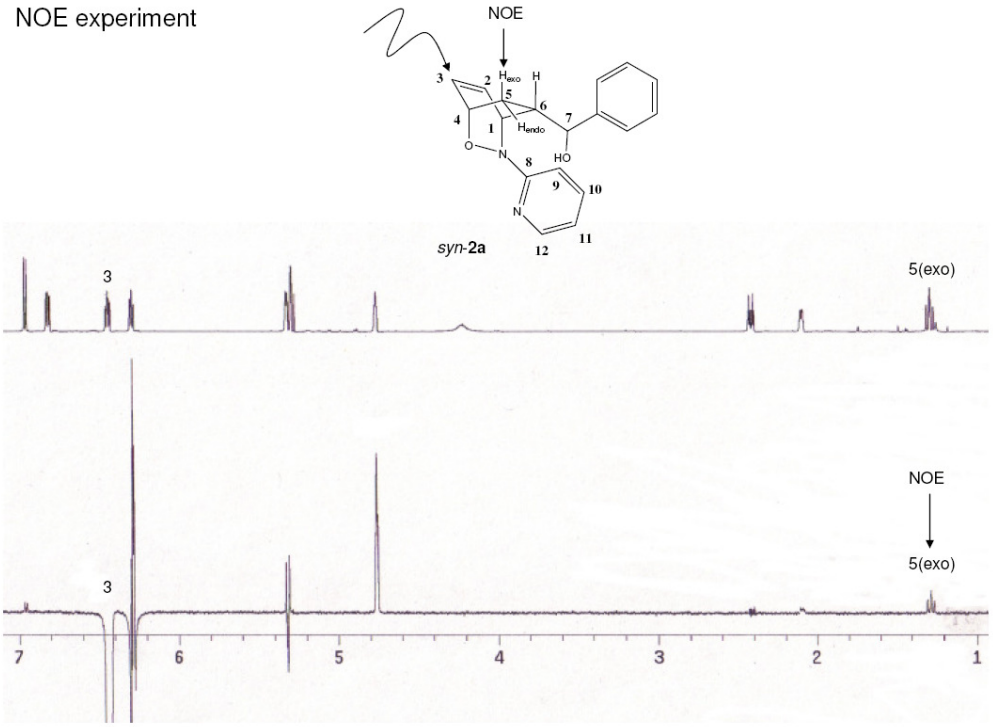
^{1}H-^{1}H-COSY (600 MHz, $CDCl_3$)



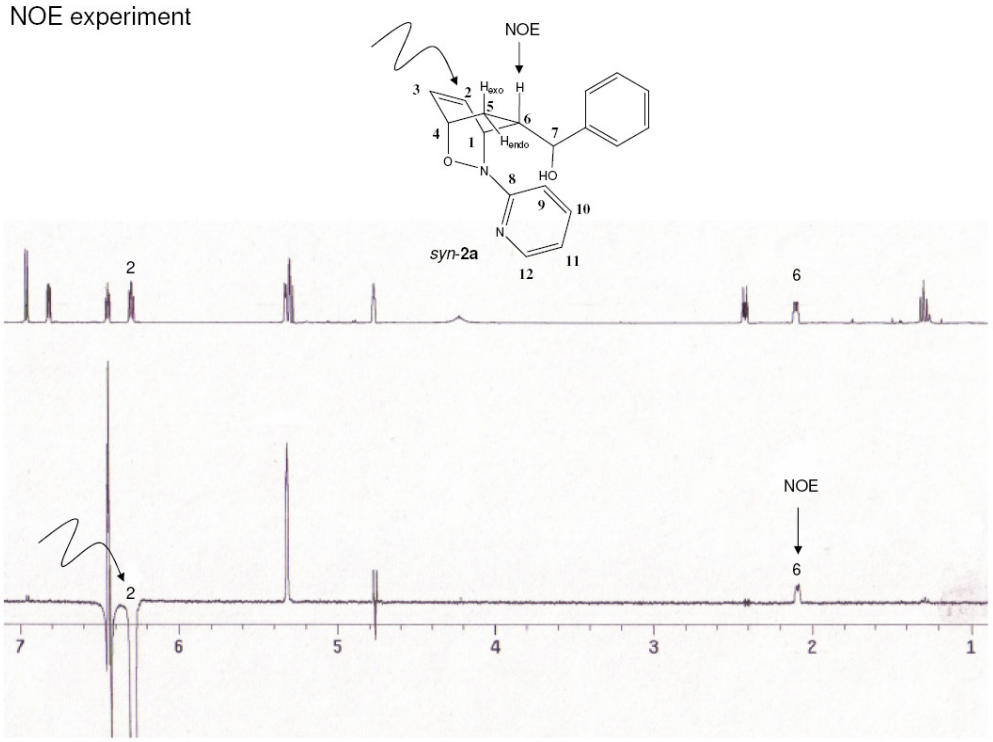
^{1}H-^{13}C-HSQC (600 MHz, $CDCl_3$)

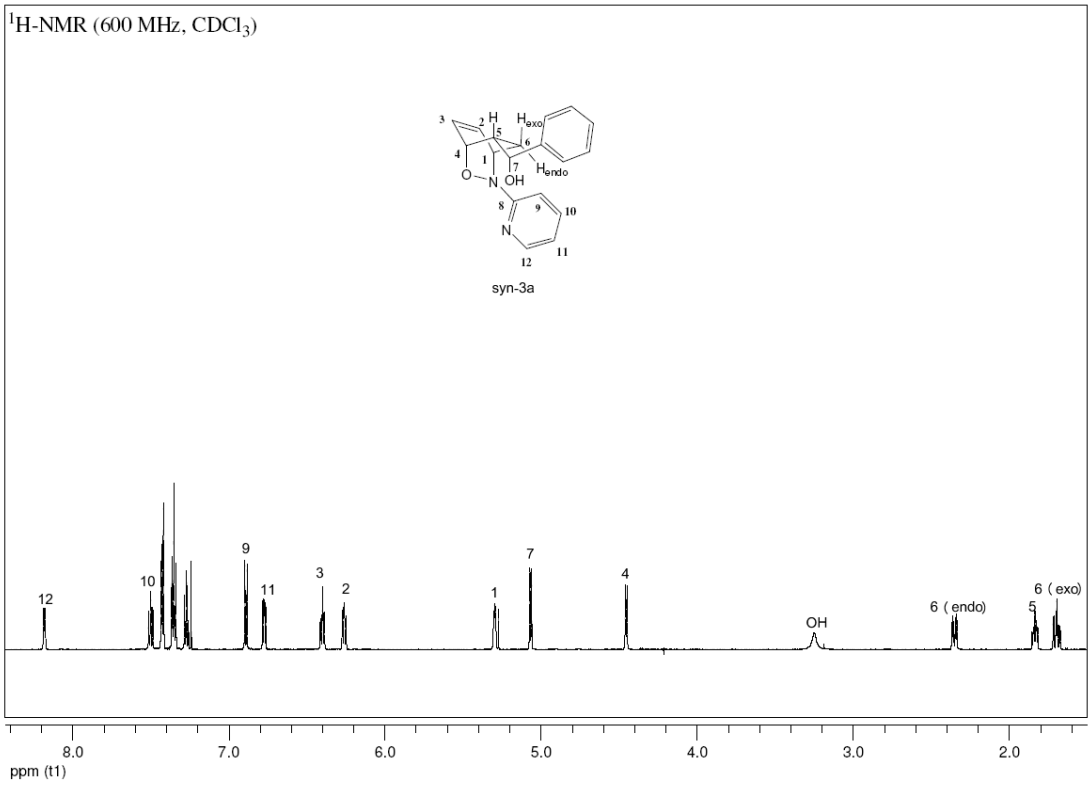


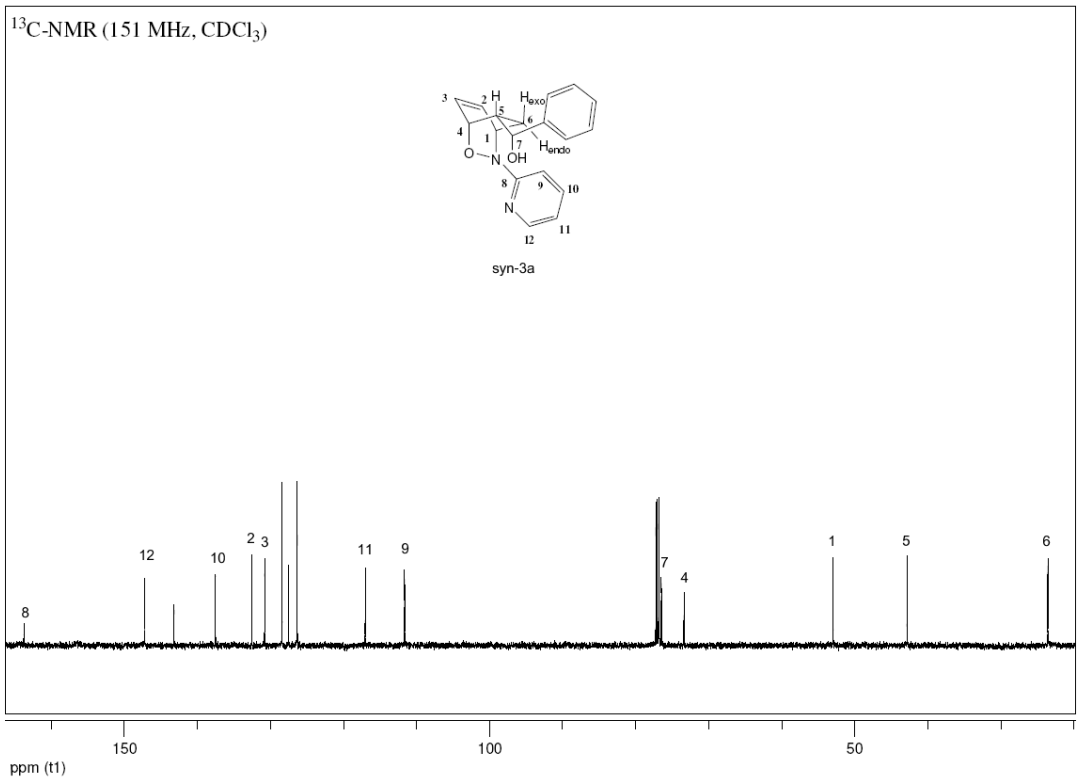
NOE experiment



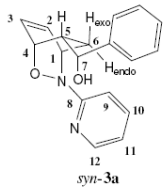
NOE experiment



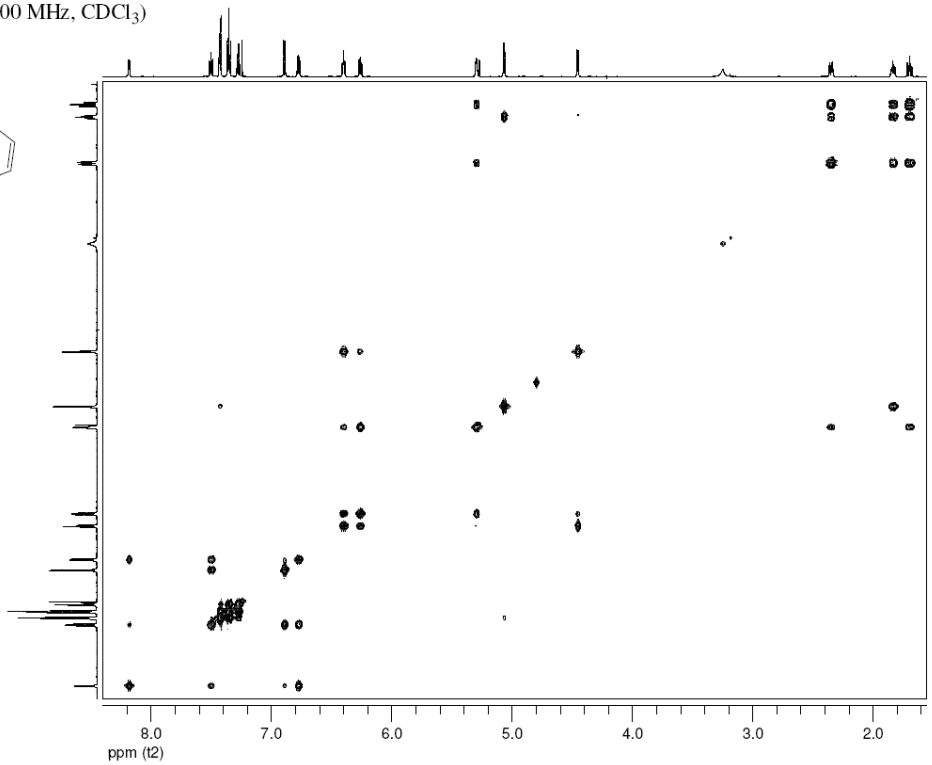

^{1}H-NMR (600 MHz, $CDCl_3$)
syn-3a
12
10
9
11
3
2
1
7
4
OH
6 (endo)
5
6 (exo)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)


^{13}C-NMR (151 MHz, $CDCl_3$)
syn-3a
8
12
10
2
3
11
9
7
4
1
5
6
150
100
50
ppm (t1)

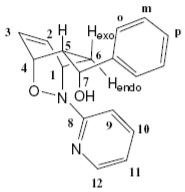
^{1}H-^{1}H-COSY (600 MHz, $CDCl_3$)



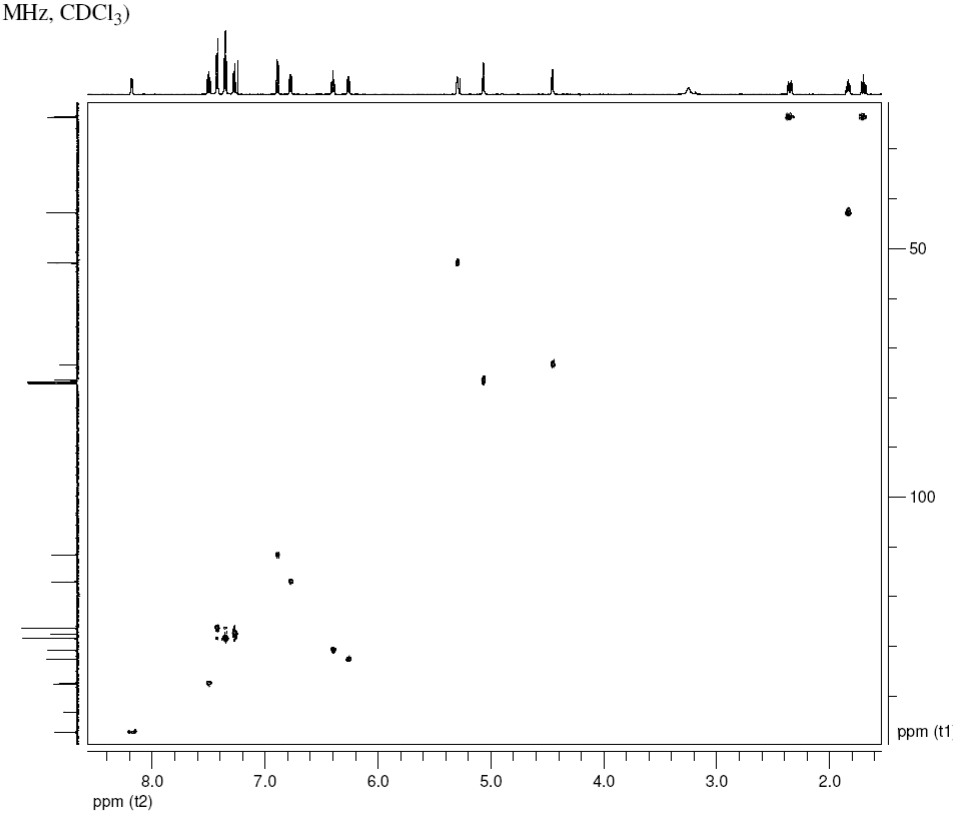
syn-**3a**

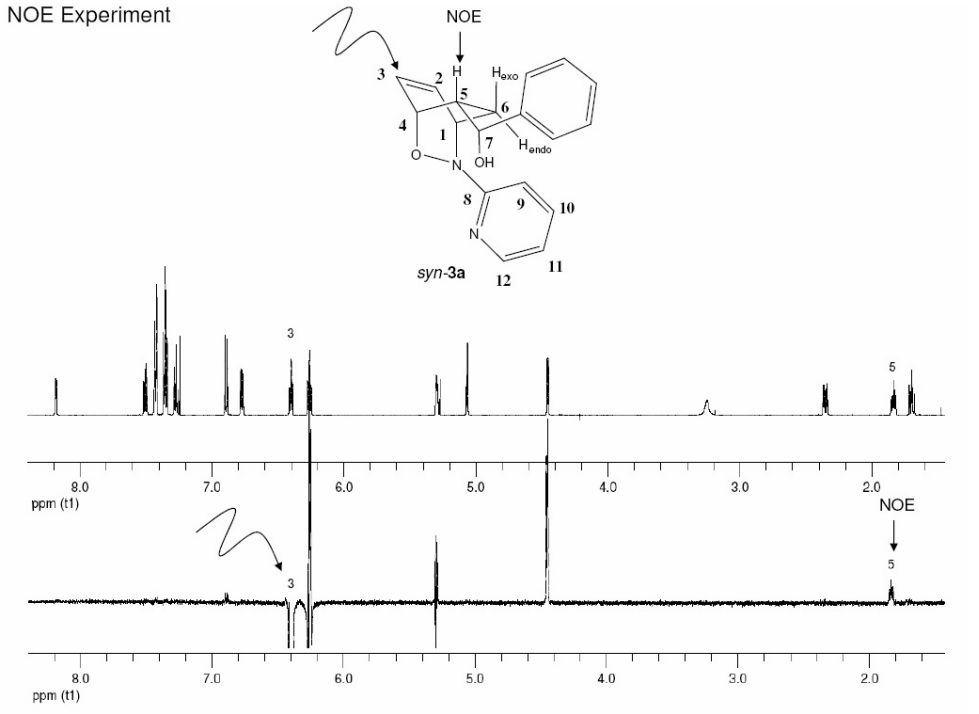


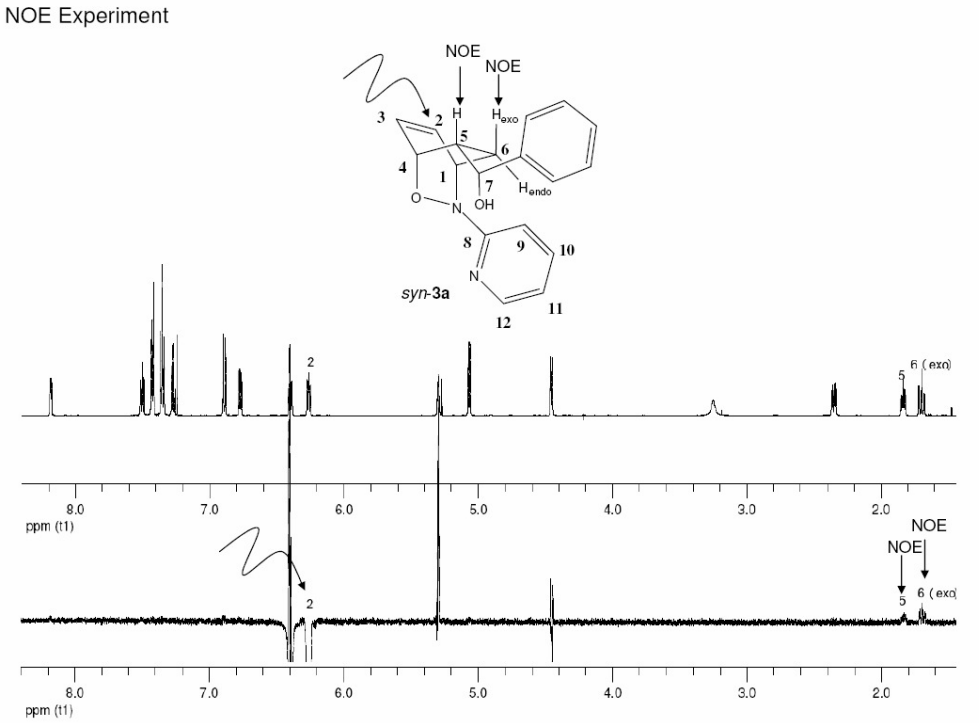
^{1}H-^{13}C-HSQC (600 MHz, $CDCl_3$)



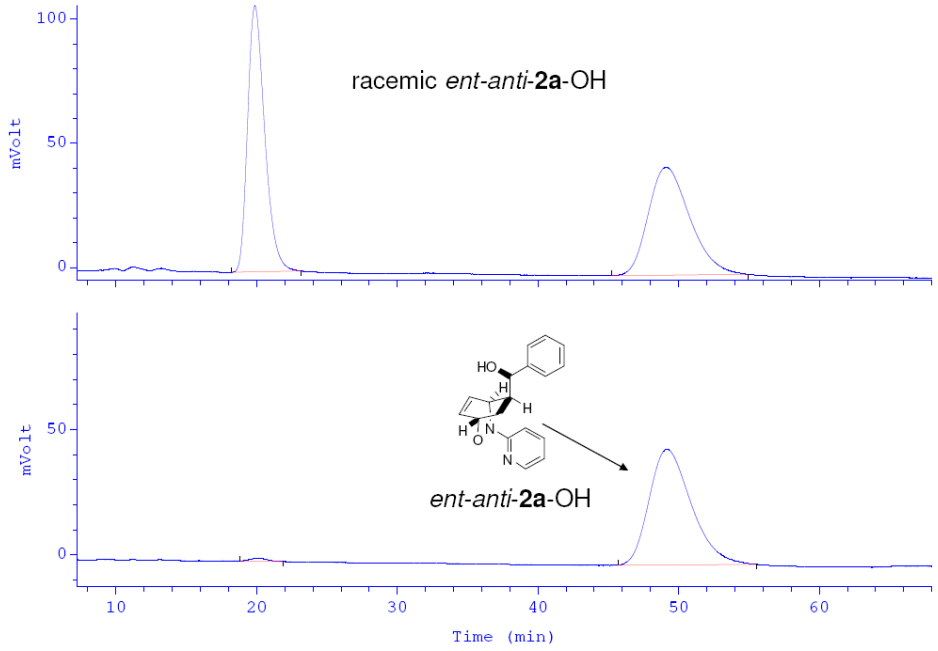
syn-**3a**

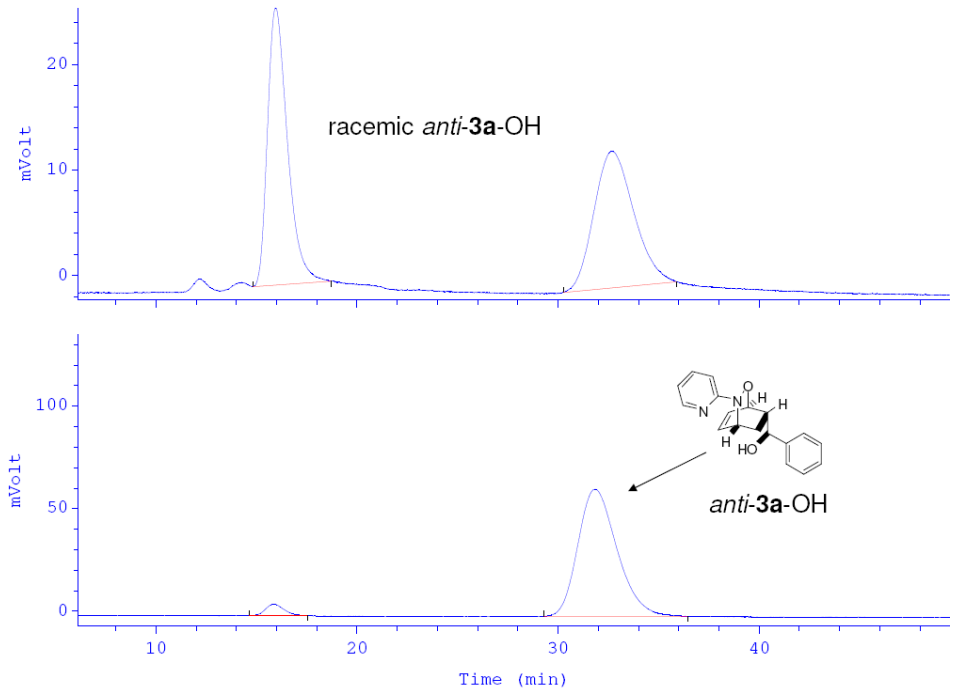


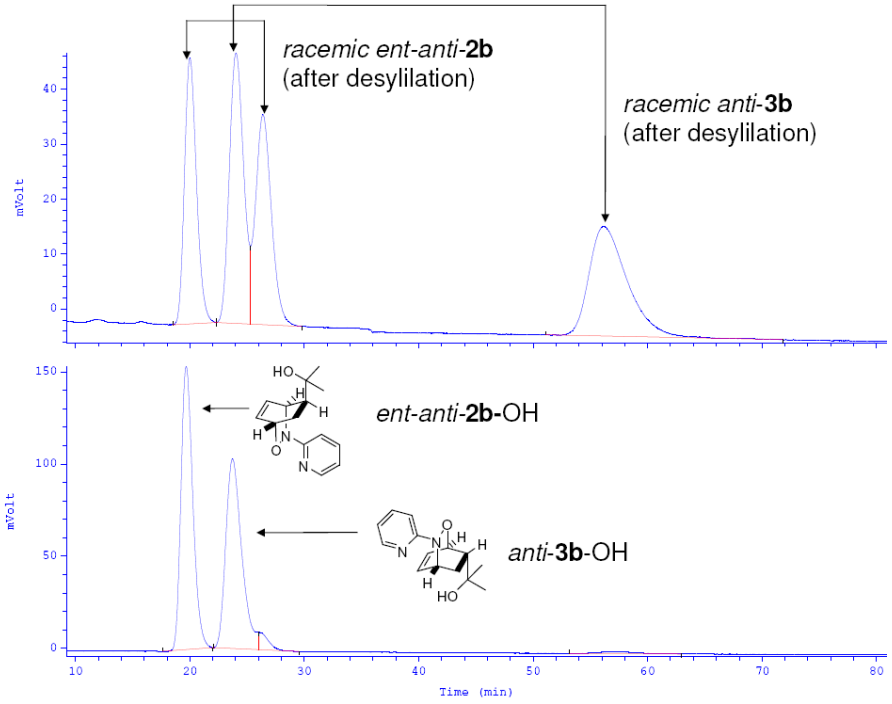

NOE Experiment
NOE
syn-3a
ppm (t1)
NOE

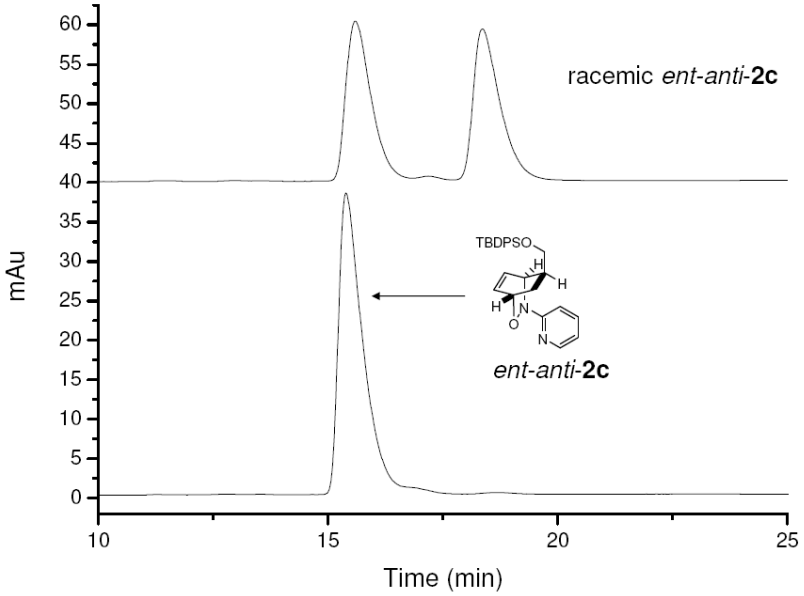

NOE Experiment
NOE
NOE
syn-3a
ppm (t1)
NOE
NOE

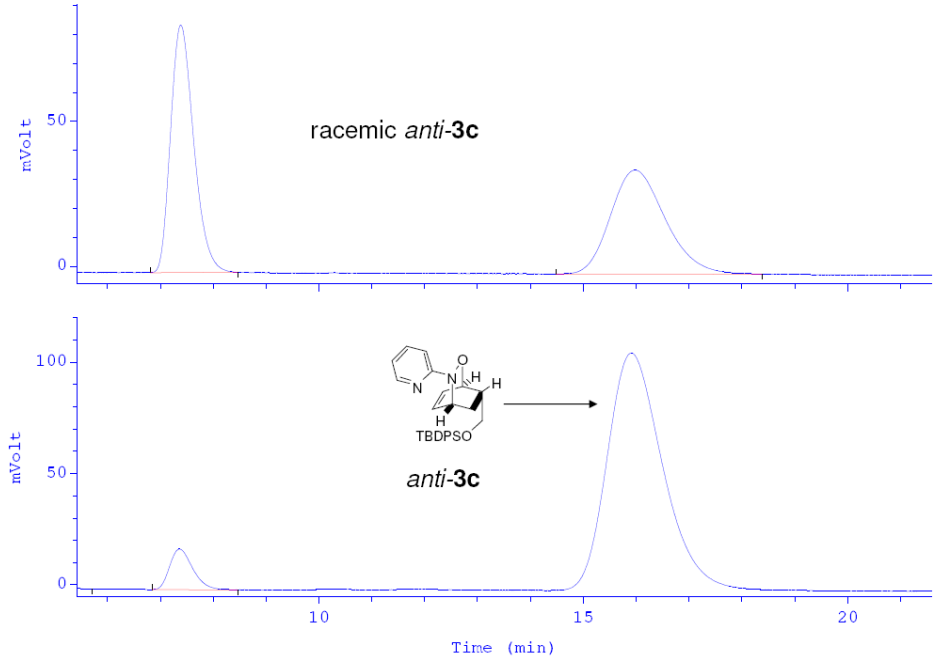
HPLC Traces

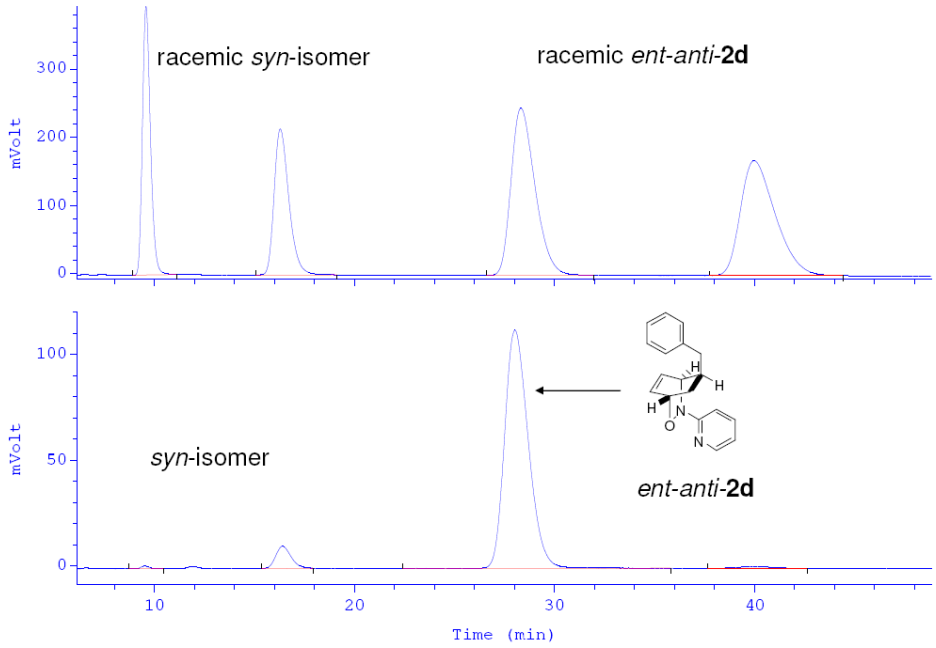

racemic *ent-anti*-**2a**-OH
mVolt
100
50
0
HO
H
H
H
N
O
N
ent-anti-**2a**-OH
10
20
30
40
50
60
Time (min)

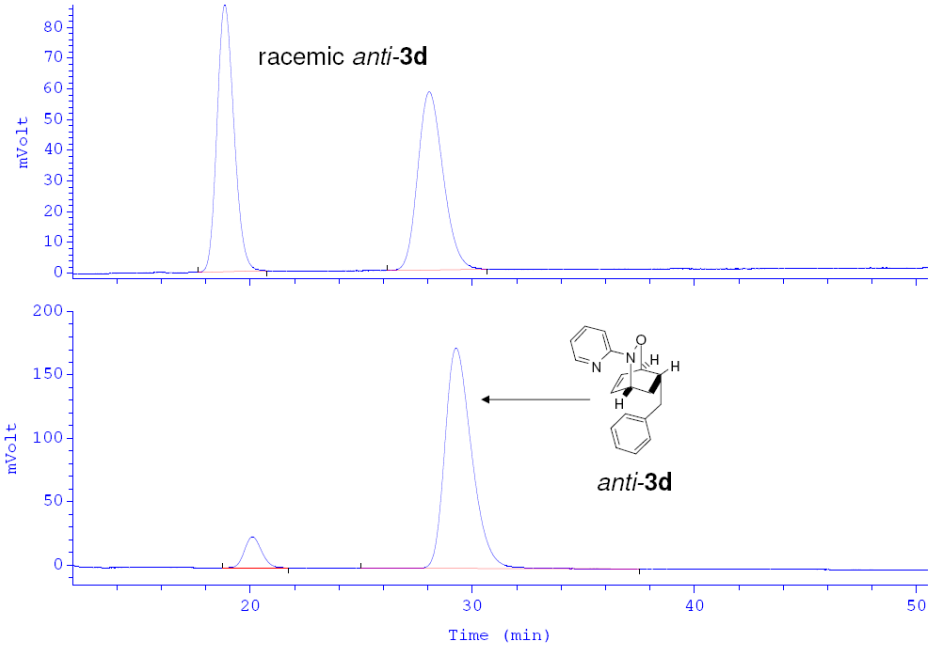

racemic *anti*-**3a**-OH
mVolt
20
10
0
N
N
O
H
H
H
HO
anti-**3a**-OH
100
50
0
10
20
30
40
Time (min)

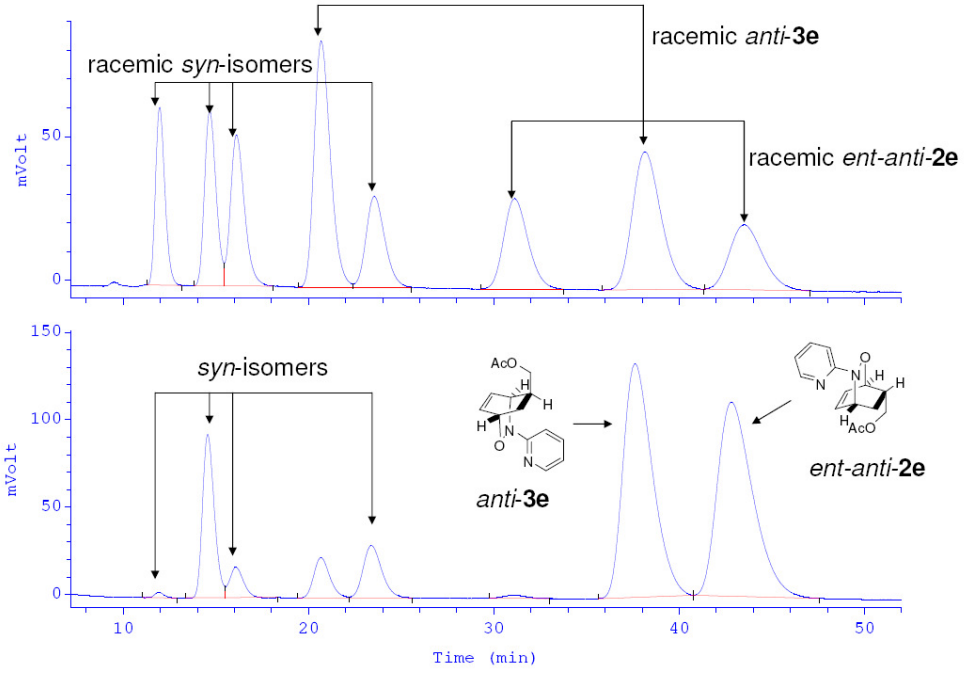

racemic ent-anti-2b
(after desylilation)
racemic anti-3b
(after desylilation)
mVolt
ent-anti-2b-OH
anti-3b-OH
Time (min)

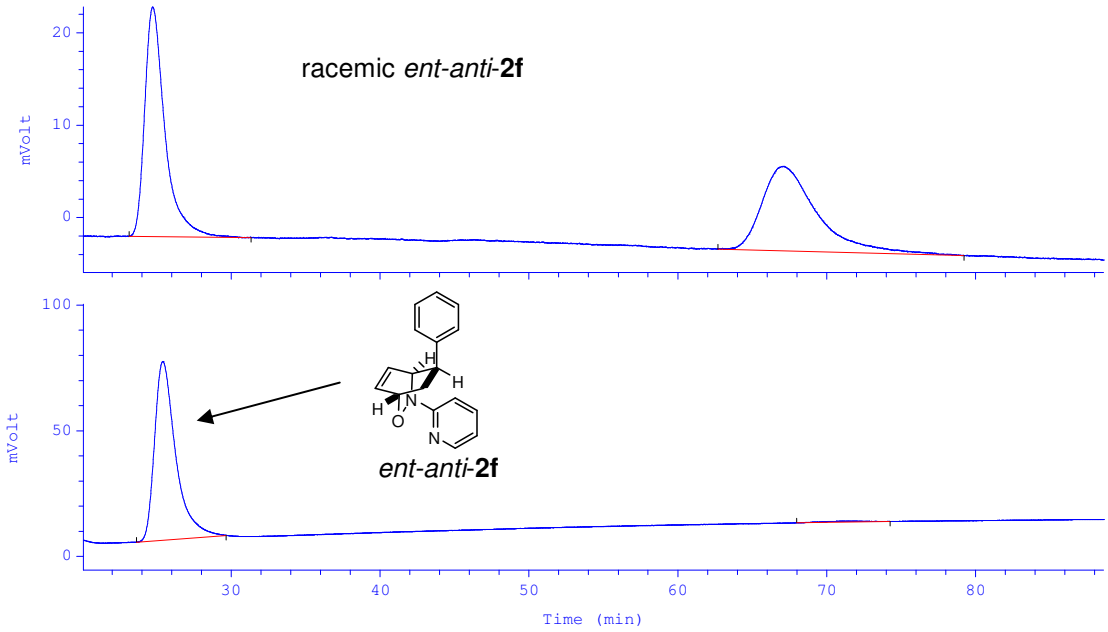

racemic ent-anti-2c
TBDPSO
ent-anti-2c
mAu
Time (min)

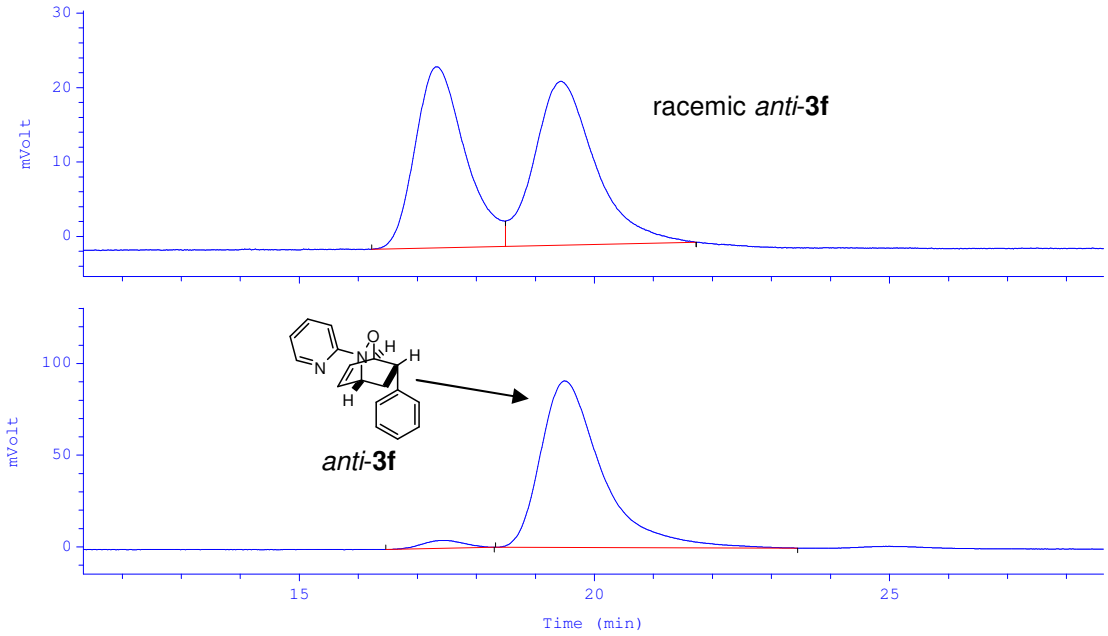

racemic *anti*-**3c**
mVolt
50
0
100
50
0
TBDPSO
anti-**3c**
10
15
20
Time (min)


racemic *syn*-isomer
racemic *ent-anti*-**2d**
mVolt
300
200
100
0
syn-isomer
ent-anti-**2d**
50
10
20
30
40
Time (min)


racemic *anti*-**3d**
mVolt
anti-**3d**
Time (min)


racemic *anti*-**3e**
racemic *syn*-isomers
racemic *ent-anti*-**2e**
mVolt
syn-isomers
anti-**3e**
ent-anti-**2e**
Time (min)


racemic *ent-anti*-**2f**
mVolt
20
10
0
100
50
0
30
40
50
60
70
80
Time (min)
ent-anti-**2f**


racemic *anti*-**3f**
mVolt
30
20
10
0
100
50
0
15
20
25
Time (min)
anti-**3f**