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Supporting Information

Total Synthesis of (+)-*trans*-Dihydronarciclasine via a Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

Chandan Kumar Jana,[†,‡] and Armido Studer*[,‡]

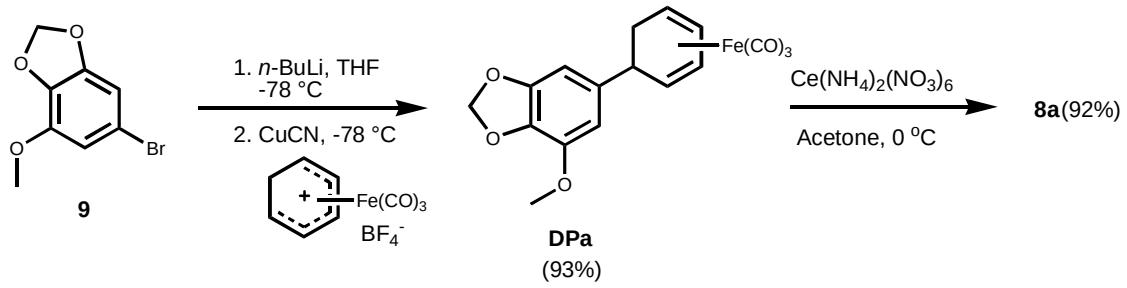
Fachbereich Chemie, Organisch-Chemisches Institut, Westfälische Wilhelms-Universität, Corrensstrasse 40, 48149 Münster, and NRW Graduate School of Chemistry, Westfälische Wilhelms-Universität, Corrensstrasse 36, 48149 Münster.

[‡]Organisch-Chemisches Institut, [†]NRW Graduate School of Chemistry.

Experimental Section:

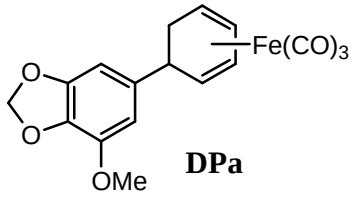
General: All reactions involving air- or moisture-sensitive reagents or intermediates were carried out in heat-gun-dried glassware under an argon atmosphere. THF was freshly distilled from potassium under argon. Diethylether (Et_2O) was freshly distilled from K/Na under argon. Dichloromethane (CH_2Cl_2) 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 a known procedure[1]. ^1H, ^{13}C, GCOSY, GHSQC and 1D-NOE NMR spectroscopy: *Varian Unity plus 600* (at 298 K), *Varian 500 Inova* (at 298 K), *Bruker AMX 400* (at 300 K), *Bruker dpx 300* (at 300 K). Chemical shifts, d (in ppm), are reported relative to TMS (d(^1H) 0.0 ppm, d(^{13}C) 0.0 ppm) which was used as the inner reference. Otherwise the solvents residual proton resonance and carbon resonance ($CHCl_3$, d(^1H) 7.26 ppm, d(^{13}C) 77.0 ppm; C_6D_6, d(^1H) 7.16 ppm, d(^{13}C) 128.0 ppm; CD_3OD, (^1H) 3.31 ppm, d(^{13}C) 49.0 ppm) were used for calibration. 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 $Ce(SO_4)_2$ x 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: Either *KNAUER* instrument, High Precision *KNAUER* HPLC Pump, *Eurochrom V3.05* software or *Hewlett Packard* Binary Pump, analyzed by *Hewlett Packard Series 1100 ChemStation* for LC. 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: spectra were recorded on a *Bruker IFS-28* spectrophotometer. MS: Mass spectra were recorded on a *Finnigan MAT 4200S*, a *Bruker Daltonics MicroTof*, a *Waters Micromass Quatro LCZ* (ESI); and peaks are given in *m/z* (% of basis peak).

Syntheses of different dienes:



Scheme 1: synthesis of diene **8a**.

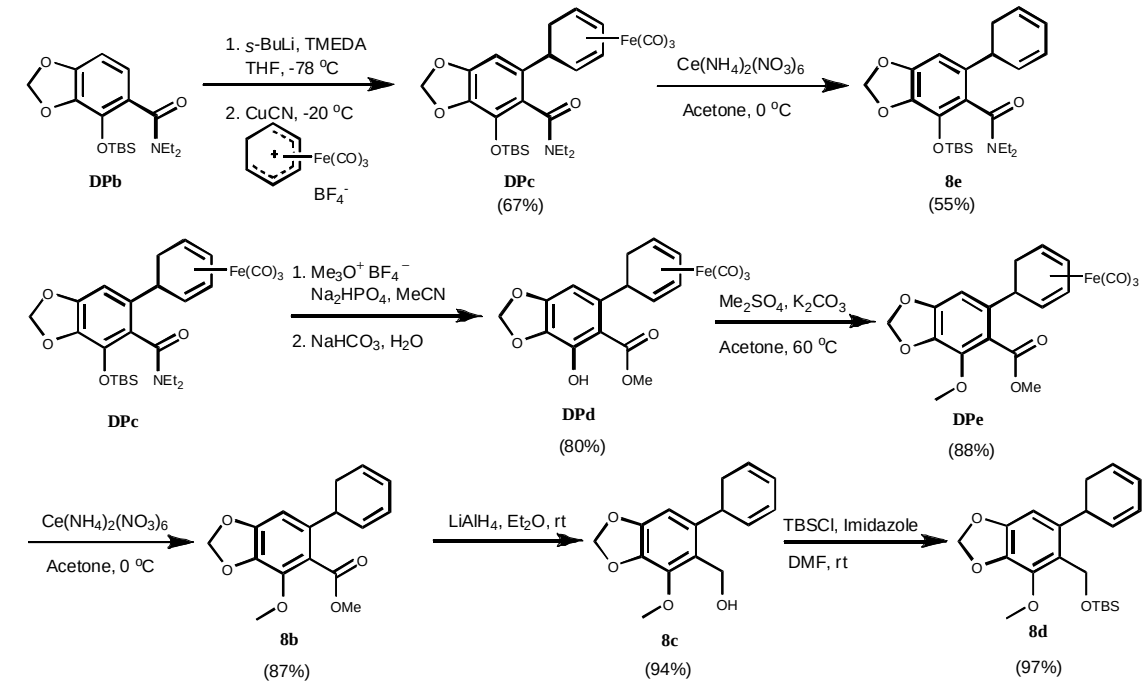
Tricarbonyl[6-[?^{4}-2,4-cyclohexadien-1-yl]-4-methoxy-1,3-benzodioxole]iron (**DPa**):



DPa

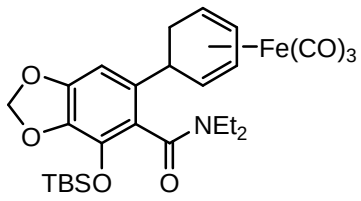
n-BuLi (23 mL, 37 mmol) was added to a solution of **9**[2] (8.0 g, 35 mmol) in THF (140 mL) at -78 °C. After stirring for 2.5 h at that temperature CuCN (1.56 g, 17.5 mmol) was added and stirring was continued for another 3 h. Tricarbonyl(?^{5}-cyclohexa-1,3-diene)iron tetrafluoroborate[4] (3.55 g, 11.6 mmol) was then added. The solution was slowly warmed to room temperature and stirred over night. The reaction was quenched by adding saturated aqueous NH_4Cl solution and the mixture was extracted with Et_2O (3 x 75 mL). The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography (pentane:MTBE, 50:1) to afford **DPa** as a yellowish oil (4.0 g, 11 mmol, 93%). TLC: R_f = 0.1 (pentane:MTBE, 50:1). FTIR (neat): $\tilde{n}$ = 2897, 2042, 1960, 1632, 1508, 1450, 1429, 1315, 1195, 1129, 1090, 1046, 934, 790 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6) d = 6.35 (d, J = 1.0 Hz, 1H), 6.25 (br s, 1H), 5.45 (s, 2H), 4.92 – 4.89 (m, 1H), 4.80 – 4.76 (m, 1H), 3.63 (s, 3H), 3.17 (td, J = 11.1, 3.6 Hz, 1H), 2.87 – 2.83 (m, 1H), 2.75 – 2.70 (m, 1H), 2.16 (ddd, J = 15.1, 11.2, 3.6 Hz, 1H), 1.46 – 1.41 (m, 1H). ^{13}C NMR (75 MHz, C_6D_6) d = 212.5, 149.8, 143.9, 141.7, 134.3, 108.3, 101.1, 100.9, 86.1, 84.5, 67.3, 60.7, 56.7, 44.9, 33.6. HRMS (ESI) exact mass calculated for $C_{17}H_{14}FeO_6Na$ ([M + Na]$^+$): 393.0032, found: 393.0038

6-Cyclohexa-2,4-dienyl-4-methoxy-1,3-benzodioxole (**8a**): Ceric(IV) ammonium nitrate (16.4 g, 29.8 mmol) was added portionwise over 2.5 h to a solution of **DPa** (3.68 g, 9.95 mmol) in acetone (47 mL) at 0 ºC. Then the reaction mixture was stirred for 1 h. Diethylether (200 mL) was added and the solution was washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography (pentane:MTBE, 50:1) to afford **8a** as a colorless oil (2.1 g, 9.1 mmol, 92%). TLC: R_f = 0.3 (pentane:MTBE, 20:1). FTIR (neat): $\tilde{n}$ = 3035, 2937, 1632, 1509, 1450, 1431, 1315, 1191, 1133, 1091, 1046, 827 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) d = 6.43 (d, *J* = 1.3 Hz, 1H), 6.38 (d, *J* = 1.3 Hz, 1H), 5.98 – 5.86 (m, 2H), 5.85 (br.s, 2H), 5.74 – 5.68 (m, 2H), 3.82 (s, 3H), 3.47 – 3.38 (m, 1H), 2.48 –2.37 (m, 1H), 2.30 – 2.17 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) d = 148.8, 143.5, 140.3, 133.7, 129.9, 125.5, 124.5, 123.9, 107.0, 101.8, 101.3, 56.7, 39.9, 31.9. HRMS (ESI) exact mass calculated for $C_{14}H_{14}O_3Na$ ($[M + Na]^+$): 253.0835, found: 253.0833.



Scheme 2. Syntheses of dienes **8b-e**.

Tricarbonyl[6-[?^{4}-2,4-cyclohexadien-1-yl]-4-(*tert*-Butyl-dimethyl-silanyloxy)-1,3-benzodioxole-5-carboxylic acid diethylamide]iron (DPc): *s*-BuLi (15.0 mL, 19.5 mmol) was added to a solution of TMEDA (3.0 mL, 20 mmol) in THF (64 mL) at -78 °C and the reaction mixture was stirred for 15 min. The resulting yellow mixture was then cooled to -90 °C, a solution of amide **DPb**[3] (6.42 g, 18.3 mmol) in THF (38 mL) was added and stirring was continued for 2 h. Then CuCN (819 mg, 9.14 mmol) was added. The mixture was allowed to warm to -20 °C over 4 h, tricarbonyl (?^{5}-cyclohexa-1,3-diene)iron tetrafluoroborate[4] (1.86 g, 6.09 mmol) was added and the reaction mixture was then warmed to 0 ^{o}C. The reaction was quenched by adding saturated aqueous NH_4Cl solution and the mixture was extracted with MTBE (3 x 75 mL). The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography (pentane:MTBE, 5:1) to afford two diastereoisomers arising from atropisomerism (major : minor = 1.5:1) as a yellowish oil (combined 2.3g, 4.1 mmol, 67 %). Major isomer: TLC: R_f = 0.3 (pentane:MTBE, 5:1). FTIR (neat): $\tilde{n}$ = 2963, 2850, 2045, 1967, 1623, 1473, 1261, 1093, 800, 705 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6) d = 6.41 (s, 1H), 5.15 (d, *J* = 0.9 Hz, 1H), 5.14 (d, *J* = 0.9 Hz, 1H), 4.63 – 4.60 (m, 2H), 3.91 –3.79 (m, 1H), 3.30 – 3.24 (m, 1H), 2.89 – 2.77 (m, 2H), 2.76 – 2.64 (m, 2H), 2.44 – 2.39 (m, 1H), 2.24 –2.13 (m, 1H), 1.24 – 1.16 (m, 1H), 1.12 (t, *J* = 7.1 Hz, 3H), 0.96 (s, 9H), 0.73 (t, *J* = 7.1 Hz, 3H), 0.20 (s, 3H), 0.15 (s, 3H). ^{13}C NMR (75 MHz, C_6D_6) d = 212.4, 166.9, 149.1, 137.9, 135.5, 135.3, 125.7, 100.9, 100.7, 85.9, 85.2, 65.3, 61.2, 43.1, 42.2, 39.4, 33.5, 25.9, 18.6, 14.2, 13.3, -4.0, -4.4. HRMS (ESI) exact mass calculated for $C_{27}H_{35}FeNO_7Si$ Na ([M + Na]$^+$): 592.1425, found: 592.1397

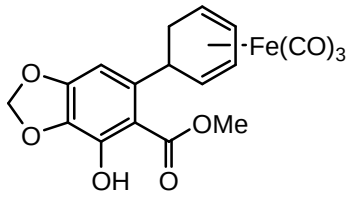


DPc

Minor isomer: TLC: R_f = 0.5 (pentane:MTBE, 5:1). FTIR (neat): $\tilde{n}$ = 2979, 2937, 2043, 1966, 1627, 1474, 1284, 1223, 1090, 1055, 1034, 940, 847, 736 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6) d = 6.23 (s, 1H), 5.16 (d, *J* = 1.1 Hz, 1H), 5.13 (d, *J* = 1.1 Hz, 1H), 4.67 – 4.62 (m, 1H), 4.47 – 4.43 (m, 1H), 3.93 – 3.81 (m, 1H), 3.30 (td, *J* = 11.0, 3.6 Hz, 1H), 3.17 – 3.14 (m, 1H), 2.77 – 2.65 (m, 3H), 2.54 – 2.51 (m, 1H), 1.93 (ddd, *J* = 15.0, 11.0,

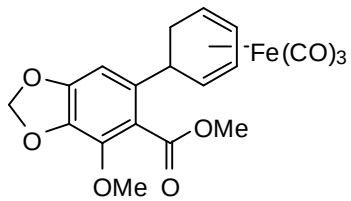
3.8 Hz, 1H), 1.26 – 1.21 (m, 1H), 1.09 (t, J = 7.1 Hz, 3H), 0.97 (s, 9H), 0.66 (t, J = 7.1 Hz, 3H), 0.23 (s, 3H), 0.20 (s, 3H). ^{13}C NMR (75 MHz, C_6D_6) d = 212.3, 167.0, 149.1, 138.2, 135.5, 135.0, 125.8, 100.9, 100.6, 85.7, 84.6, 67.9, 59.9, 43.1, 40.7, 39.4, 33.2, 25.9, 18.6, 14.2, 13.2, -3.9, -4.4. HRMS (ESI) exact mass calculated for $C_{27}H_{35}FeNO_7Si$ Na ([M + Na]$^+$): 592.1425, found: 592.1419.

Tricarbonyl[6-[?^{4}-2,4-cyclohexadien-1-yl]-4-hydroxy-1,3-benzodioxole-5-carboxylic acid methyl ester]iron (DPd): Disodium hydrogen phosphate (Na_2HPO_4, 0.61 g, 4.3 mmol) and trimethyloxonium tetrafluoroborate [$(CH_3)_3OBF_4$, 1.2 g, 8.4 mmol] were added successively to a solution of **DPc** (1.6 g, 2.8 mmol) in 15 mL of CH_3CN at rt and the reaction mixture was stirred for 24 h at rt. Then a saturated aqueous solution of $NaHCO_3$ (50 mL) was slowly added. A portion of solid $NaHCO_3$ (0.6 g) was then added and the reaction mixture was stirred for another 24 h at rt. The resulting mixture was then extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography (pentane:MTBE, 10:1) to afford **DPd** as a yellowish oil (925 mg, 2.23 mmol, 80%). TLC: R_f = 0.2 (pentane:MTBE, 5:1). FTIR (neat): $\tilde{n}$ = 2948, 2042, 1962, 1672, 1438, 1297, 1085, 1034 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6) d = 11.51 (s, 1H), 6.40 (br. s, 1H), 5.31 (dd, J = 9.9, 1.2 Hz, 2H), 4.78 – 4.75 (m, 1H), 4.66 (ddd, J = 5.8, 4.2, 1.5 Hz, 1H), 4.04 –3.98 (m, 1H), 3.33 (s, 3H), 2.63 – 2.57 (m, 2H), 2.05 (ddd, J = 15.1, 11.1, 4.1, Hz, 1H), 1.10 – 1.02 (m, 1H). ^{13}C NMR (75 MHz, C_6D_6) d = 212.4, 171.3, 152.7, 147.1, 145.4, 133.7, 108.6, 102.2, 100.3, 85.7, 85.4, 66.7, 60.2, 51.7, 41.7, 32.7. HRMS (ESI) exact mass calculated for $C_{18}H_{14}FeO_8$ Na ([M + Na]$^+$): 436.9931, found: 436.9929.



DPd

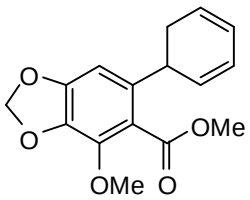
Tricarbonyl[6-[?^{4}-2,4-cyclohexadien-1-yl]-4-methoxy-1,3-benzodioxole-5-carboxylic acid methyl ester]iron (DPe): Dimethyl sulfate (0.25 mL, 2.7 mmol) and K_2CO_3 (461 mg, 3.34 mmol) were added to a solution of **DPd** (922 mg, 2.22 mmol) in acetone (23.0 mL) and the resulting mixture was heated to reflux at



DPe

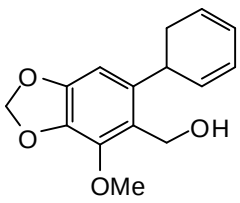
60 ºC for 3 h. Then the reaction mixture was cooled to room temperature, filtered through a pad of celite and concentrated in vacuo. The residue was purified by flash column chromatography (pentane:MTBE, 10:1) to afford **DPe** as a yellowish oil (0.94 g, 2.2 mmol, 98%). TLC: R_f = 0.3 (pentane:MTBE, 5:1). FTIR (neat): $\tilde{n}$ = 2950, 2043, 1964, 1730, 1620, 1477, 1256, 1128, 1092, 1056, 1032, 981, 938 cm^{-1}. ^1H NMR (300 MHz, C_6D_6) d = 6.31 (br. s, 1H), 5.16 – 5.13 (m, 2H), 4.72 – 4.68 (m, 1H), 4.61 – 4.58 (m, 1H), 3.69 (s, 3H), 3.57 (s, 3H), 3.42 (td, *J* = 11.1, 3.6 Hz, 1H), 2.84 – 2.81 (m, 1H), 2.54 – 2.51 (m, 1H), 2.11 (ddd, *J* = 15.2, 11.1, 3.9 Hz, 1H), 1.31 – 1.20 (m, 1H). ^{13}C NMR (75 MHz, C_6D_6) d = 210.9, 166.4, 149.3, 139.4, 137.9, 133.5, 120.2, 99.8, 99.4, 84.5, 83.6, 64.8, 58.9, 58.4, 50.5, 40.5, 31.8. HRMS (ESI) exact mass calculated for $C_{19}H_{16}FeO_8$ Na ($[M + Na]^+$): 451.0087, found: 451.0131.

6-Cyclohexa-2,4-dienyl-4-methoxy-1,3-benzodioxole-5-carboxylic acid methyl ester (8b): Ceric(IV) ammonium nitrate (1.30 g, 2.37 mmol) was added portionwise over 2 h to a solution of **DPe** (339 mg, 0.79 mmol) in acetone (8 mL) at 0 ºC. Then the reaction mixture was stirred for 1 h. Diethylether (50 mL) was added and the mixture was washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography (pentane:MTBE, 10:1) to afford **8b** as a white foam (0.2 g, 0.7 mmol, 87%). TLC: R_f = 0.5 (pentane:MTBE, 5:1). FTIR (neat): $\tilde{n}$ = 2950, 1725, 1619, 1478, 1283, 1244, 1095, 1034, 981, 691 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) d = 6.61 (br.s, 1H), 5.98 –5.92 (m, 1H), 5.86 –5.83 (m, 3H), 5.71 – 5.66 (m, 1H), 5.63 – 5.59 (m, 1H), 3.91 (s, 3H), 3.80 (s, 3H), 3.51 – 3.41 (m, 1H), 2.51 – 2.40 (m, 1H), 2.28 – 2.16 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) d = 168.2, 150.2, 140.2, 137.9, 134.7, 129.2, 125.4, 124.8, 123.6, 120.1, 102.7, 101.3, 60.1, 52.3, 36.9, 31.3. HRMS (ESI) exact mass calculated for $C_{16}H_{16}O_5$ Na ($[M + Na]^+$): 311.0890, found: 311.0896.



8b

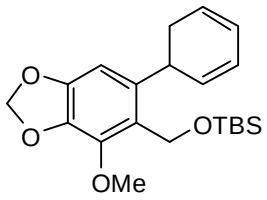
(6-Cyclohexa-2,4-dienyl-4-methoxy-1,3-benzodioxol-5-yl)-methanol (8c): A solution of **8b** (250 mg, 0.87 mmol) in diethylether (2 mL) was added to a suspension of lithium aluminum hydride (65.8 mg, 1.73 mmol) in diethylether (2 mL) and the mixture was stirred for 24 h at rt. The



8c

reaction was quenched by dropwise addition of water (0.2 mL). Then a portion of anhydrous Na_2SO_4 was added to trap excess water. The mixture was stirred for 10 min, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (pentane:MTBE, 1:1) to afford **8c** as a colorless oil (212 mg, 0.815 mmol, 94%). TLC: R_f = 0.3 (pentane:MTBE, 1:1). FTIR (neat): ? = 3403, 3035, 2946, 2895, 1619, 1476, 1377, 1279, 1227, 1052, 1007, 930, 736, 703 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$)[1] d = 6.61– 6.60 (m, 1H), 5.97 – 5.94 (m, 1H), 5.89 – 5.82 (m, 3H), 5.73 – 5.62 (m, 2H), 4.60 – 4.59 (m, 2H), 3.98 – 3.96 (m, 3H), 3.91 – 3.83 (m, 1H), 2.50 – 2.37 (m, 1H), 2.27 – 2.14 (m, 1H), 1.99 (br.s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) d = 148.9, 142.1, 139.1, 134.5, 130.1, 125.4, 124.6, 123.7, 123.3, 102.9, 100.9, 59.9, 56.6, 35.8, 31.8. HRMS (ESI) exact mass calculated for $C_{15}H_{16}O_4Na$ ($[M + Na]^+$): 283.0941, found: 283.0935.

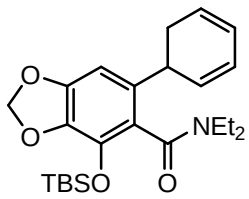
***tert*-Butyl-(6-cyclohexa-2,4-dienyl-4-methoxy-1,3-benzodioxol-5-ylmethoxy)-dimethyl-silane (8d)**: *tert*-Butyldimethylsilyl chloride (71 mg, 0.47 mmol) and imidazole (40 mg, 0.59 mmol) were added to a solution of **8c** (102 mg, 0.392 mmol) in DMF (0.7 mL) and the resulting solution was stirred at 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, 30:1) to afford **8d** as a colorless oil (142 mg, 0.379 mmol, 97%). TLC: R_f = 0.2 (pentane:MTBE, 30:1). FTIR (neat): $\tilde{n}$ = 3036, 2953, 2929, 2885, 2856, 1620, 1476, 1254, 1214, 1037, 1003, 837, 735 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) d = 6.63 – 6.62 (m, 1H), 5.94 – 5.80 (m, 4H), 5.69 – 5.61 (m, 2H), 4.65 – 4.53 (m, 2H), 3.97 – 3.87 (m, 4H), 2.51 – 2.39 (m, 1H), 2.25 – 2.13 (m, 1H), 0.82 – 0.81 (m, 9H), -0.00 (br. s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) d = 148.6, 141.8, 140.5, 135.1, 130.9, 125.5, 124.2, 123.7, 110.0, 103.3, 100.9, 60.2, 55.8, 35.6, 31.8, 26.0, 18.4, -5.4, -5.3. HRMS (ESI) exact mass calculated for $C_{21}H_{30}O_4SiNa$ ($[M + Na]^+$): 397.1806, found: 397.1795



8d

[1] Signals are broadend due to hindered rotation.

4-(*tert*-Butyl-dimethyl-silanyloxy)-6-cyclohexa-2,4-dienyl-1,3-benzodioxole-5-carboxylic acid diethylamide (8e): Ceric(IV) ammonium nitrate (575 mg, 1.05 mmol) was added portionwise over 2 h to a solution of **DPc** (major isomer) (199 mg, 0.35 mmol) in acetone (5 mL) at 0 °C. Then the reaction mixture was stirred for 1 h. Diethylether (30 mL) was added and the mixture was washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography (pentane:MTBE, 10:1) to afford **8e** as a colorless oil (83 mg, 0.19 mmol, 55%). TLC: R_f = 0.3 (pentane:MTBE, 5:1). FTIR (neat): $\tilde{n}$ = 2931, 2858, 1681, 1615, 1473, 1294, 1254, 1224, 1086, 1037, 841 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) d = 6.44 (br. s, 1H), 5.85 – 5.80 (m, 1H), 5.73 – 5.67 (m, 3H), 5.59 – 5.53 (m, 1H), 5.43 (dd, *J* = 9.5, 3.1 Hz, 1H), 3.58 – 3.46 (m, 1H), 3.28 – 3.19 (m, 1H), 3.16 – 3.04 (m, 1H), 3.03 –2.85 (m, 2H), 2.47 – 2.36 (m, 1H), 2.12 – 2.00 (m, 1H), 1.03 (t, *J* = 7.2 Hz, 3H), 0.81 (t, *J* = 7.1 Hz, 3H), 0.75 (s, 9H), 0.04 (s, 3H), -0.00 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) d = 167.5, 148.6, 136.9, 134.8, 134.7, 129.2, 126.4, 125.1, 124.0, 123.1, 102.1, 100.8, 43.1, 39.4, 36.9, 31.7, 25.7, 18.3, 14.0, 13.1, -4.1, -4.4. HRMS (ESI) exact mass calculated for $C_{24}H_{35}NO_4Si\,Na$ ($[M + Na]^+$): 452.2228, found: 452.2223.



8e

Enantioselective regiodivergent nitroso Diels-Alder reaction:

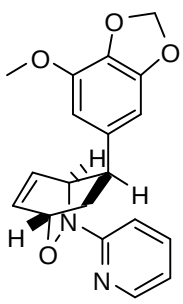
General procedure for the regiodivergent nitroso Diels-Alder reaction with (*R,pR*)-*Walphos* **(GP1)**

(*R,pR*)-*Walphos* ligand (10 mol%) and $[Cu^I(CH_3CN)_4]PF_6$ (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 (~6 mM) with respect to ligand) 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 (1.0 eq.) in CH_2Cl_2 (~15 mM) 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 (~12 mM) was added slowly over 1 h at -78 °C. After completion of 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*R*)-8-(7-Methoxy-1,3-benzodioxol-5-yl)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (7a) and (1*R*,4*R*,7*S*)-7-(7-Methoxy-1,3-benzodioxol-5-yl)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (10a): According to GP1: (*R*,*pR*)-*Walphos* (276 mg, 0.29 mmol), $[Cu^{I}(CH_3CN)_4]PF_6$ (110 mg, 0.29 mmol), CH_2Cl_2 (32 mL), 2-nitrosopyridine (320 mg, 2.96 mmol) in CH_2Cl_2 (6 mL), diene **8a** (681 mg, 2.96 mmol) in CH_2Cl_2 (22 mL) and SiO_2 chromatography (pentane:MTBE, 1:1) gave 1.0 g (2.9 mmol, 99%) of **7a** and **10a** as mixture of isomers. The isomer ratio was determined by chiral HPLC (**7a**: **10a** = 1.0:1.1). The diastereoisomers were separated by flash chromatography (pentane:MTBE, 4:1) to get **7a** (0.47 g, 1.4 mmol, 48 %) and **10a** (0.51 g, 1.5 mmol, 52%).

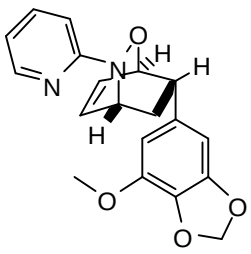
7a: TLC: R_f = 0.1 (pentane:MTBE, 4:1). $[a]_D^{25}$ = - 47.7 (c = 0.78, $CHCl_3$). FTIR (neat):



7a

$\tilde{n}$ = 2937, 1633, 1587, 1510, 1461, 1432, 1138, 1091, 1046, 881, 732 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) d = 8.13 – 8.12 (m, 1H), 7.51 – 7.46 (m, 1H), 6.88 (d, *J* = 8.3 Hz, 1H), 6.73 (dd, *J* = 6.5, 5.2 Hz, 1H), 6.60 – 6.53 (m, 1H), 6.39 (br.s, 1H), 6.29 (d, *J* = 1.3 Hz, 1H), 6.18 – 6.14 (m, 1H), 5.85 (s, 2H), 5.29 – 5.27 (m, 1H), 4.82 – 4.79 (m, 1H), 3.83 (s, 3H), 3.59 – 3.45 (m, 1H), 2.66 (ddd, *J* = 13.3, 9.4, 4.3 Hz, 1H), 1.52 (dd, *J* = 13.3, 5.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) d = 163.0, 148.9, 146.6, 143.3, 138.1, 137.8, 133.9, 131.6, 130.9, 116.8, 111.7, 108.2, 101.9, 101.3, 70.5, 58.1, 56.8, 38.7, 34.1. HRMS (ESI) exact mass calculated for $C_{19}H_{18}N_2O_4H$ ($[M + H]^+$): 339.1339, found: 339.1352. Enantiomeric excess (>99% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (91:9); flow: 1.0 mL/min; major enantiomer t_r = 13.1 min, minor enantiomer t_r = 41.6 min.

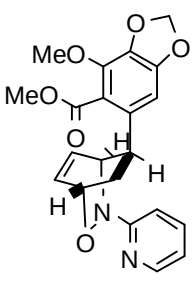
10a: TLC: R_f = 0.1 (pentane:MTBE, 4:1). $[a]_D^{25}$ = +172.9 (c = 1.0, $CHCl_3$). FTIR (neat): $\tilde{n}$ = 2938, 1632, 1589, 1509, 1462, 1431, 1138, 1091, 879, 782 cm^{-1}.[1] ^{1}H NMR (300 MHz, $CDCl_3$) d = 8.16 (br. s, 1H), 7.51 – 7.45 (m, 1H), 6.90 (d, *J* = 8.2 Hz, 1H), 6.74 (dd, *J* = 6.8, 5.1 Hz, 1H), 6.53 – 6.40 (m, 1H), 6.36 – 6.31 (m, 1H), 6.29 (d, *J* = 1.5 Hz, 1H), 6.28 (d, *J* = 1.5 Hz, 1H), 5.85 (s, 2H), 5.43 – 5.40 (m, 1H), 4.67 – 4.57 (m, 1H), 3.82 (s, 3H), 3.57–3.50 (m, 1H), 2.67 (ddd, *J* = 13.2, 9.4, 3.5 Hz, 1H), 1.70 (ddd, *J* = 13.5, 5.0, 2.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) d = 163.1, 148.9, 146.6, 143.3, 138.1, 136.6, 134.0, 132.9, 129.9, 116.7, 111.7, 108.4, 102.1, 101.4, 74.3, 56.8, 52.9, 41.7, 30.9. HRMS (ESI) exact mass calculated for $C_{19}H_{18}N_2O_4H$ ($[M + H]^+$): 339.1339, found: 339.1346. Enantiomeric excess (92% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (91:9); flow: 1.0 mL/min; major enantiomer t_r = 12.9 min, minor enantiomer t_r = 10.1 min.



10a

4-Methoxy-6-((1*S*,4*S*,5*R*)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-7-en-5-yl)-1,3-benzodioxole-5-carboxylic acid methyl ester (7b) and 4-Methoxy-6-((1*R*,4*R*,6*S*)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-7-en-6-yl)-1,3-benzodioxole-5-carboxylic acid methyl ester (10b): According to GP1: (*R*,*pR*)-*Walphos* (12.9 mg, 13.8 µmol), $[Cu^I(CH_3CN)_4]PF_6$ (5.2 mg, 13.8 µmol), CH_2Cl_2 (1.2 mL), 2-nitrosopyridine (15.0 mg, 138 µmol), diene **8b** (40.0 mg, 138 µmol) and SiO_2-chromatography (pentane:MTBE, 1:1) to give 54 mg (0.14 mmol, 99%) of **7b** and **10b** as a mixture of isomers. The isomer ratio was determined by chiral HPLC (*syn* isomer:**7b**:**10b** = 1.0:5.8:4.2). For analytical purposes a sample was repurified by flash chromatography (pentane:MTBE, 3:1).

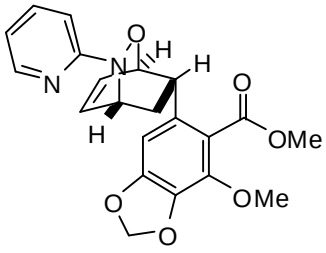
7b: TLC: R_f = 0.4 (pentane:MTBE, 1:1). $[a]_D^{25}$ = -48.9 (c = 0.87, $CHCl_3$). FTIR (neat): $\tilde{n}$ = 2950, 1728, 1618, 1587, 1480, 1432, 1375, 1335, 1261, 1034, 785 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) d = 8.11 (ddd, *J* = 4.8, 1.8, 0.6 Hz, 1H), 7.43 (ddd, *J* = 8.4, 7.3, 2.1 Hz, 1H), 6.83 (td, *J* = 8.4, 0.9 Hz, 1H), 6.69 (ddd, *J* = 7.3, 4.8, 0.9 Hz, 1H), 6.53 (ddd, *J* = 7.9, 5.9, 1.8 Hz, 1H), 6.24 (s, 1H), 6.23 – 6.18 (m, 1H), 5.85 (s, 2H), 5.37 – 5.34 (m, 1H),



7b

4.77 – 4.74 (m, 1H), 3.91 (s, 3H), 3.85 (s, 3H), 3.46 (ddd, *J* = 9.3, 5.4, 2.7 Hz, 1H), 2.62 (ddd, *J* = 13.4, 9.3, 4.5 Hz, 1H), 1.43 (ddd, *J* = 13.4, 5.4, 0.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) d = 167.9, 163.5, 150.1, 147.4, 140.2, 137.4, 135.5, 134.8, 131.5, 131.3, 121.6, 116.8, 111.4, 102.0, 101.4, 70.2, 60.2, 56.7, 52.5, 35.6, 34.5. HRMS (ESI) exact mass calculated for $C_{21}H_{20}N_2O_6$ H ($[M + H]^+$): 397.1394, found: 397.1400. Enantiomeric excess (86% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (96:4); flow: 1.0 mL/min; major enantiomer t_r = 44.9 min, minor enantiomer t_r = 15.8 min.

10b: TLC: R_f = 0.4 (pentane:MTBE, 1:1). $[a]_D^{25}$ = +167.4 (c = 0.47, $CHCl_3$). FTIR (neat): $\tilde{n}$ = 2948, 1730, 1587, 1479, 1432, 1371, 1334, 1257, 1034, 741 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) d = 8.23 – 8.22 (m, 1H), 7.59 – 7.55 (m, 1H), 6.98 (d, *J* = 8.3 Hz, 1H), 6.84 – 6.81 (m, 1H), 6.56 – 6.53 (m, 1H), 6.39 – 6.36 (m, 1H), 6.29 (s, 1H), 5.94 – 5.93 (m, 2H), 5.55 – 5.51 (m, 1H), 4.81 – 4.78 (m, 1H), 4.00 (s, 3H), 3.96 (s, 3H), 3.59 – 3.55 (m, 1H), 2.74 – 2.69 (m, 1H), 1.78 (ddd, *J* = 13.5, 4.6, 2.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) d = 168.1, 162.8, 150.1, 146.4, 139.9, 138.2, 134.8, 133.6, 132.9, 129.9, 121.8, 116.7, 111.8, 102.3, 101.4, 73.6, 60.1, 52.8, 52.6, 38.4, 30.7. HRMS (ESI) Exact mass calculated for $C_{21}H_{20}N_2O_6$ H ($[M + H]^+$): 397.1394, found: 397.1404. Enantiomeric excess (97% ee) was determined by chiral HPLC. Column: Chiralpak IA; solvent: cyclohexane:2-propanol (99.5:0.5); flow: 1.0 mL/min; major enantiomer t_r = 53.6 min, minor enantiomer t_r = 43.5 min.



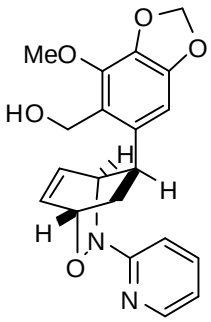
10b

[4-Methoxy-6-((1*S*,4*S*,5*R*)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-7-en-5-yl)-1,3-benzodioxol-5-yl]-methanol (7c) and [4-Methoxy-6-((1*R*,4*R*,6*S*)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-7-en-6-yl)-1,3-benzodioxol-5-yl]-methanol (10c): According to GP1: (*R*,*pR*)-*Walphos* (12.9 mg, 13.8 µmol), $[Cu^I(CH_3CN)_4]PF_6$ (5.2 mg, 13.8 µmol), CH_2Cl_2 (1.2 mL), 2-nitrosopyridine (15.0 mg, 138 µmol), diene **8c** (36.0 mg, 138 µmol) and SiO_2-chromatography (pentane:MTBE, 1:1) to give 50 mg (0.14 mmol,

99%) of **7c** and **10c** as a mixture of isomers. The isomer ratio was determined by chiral HPLC (**7c**:**10c** = 1.2:1.0).

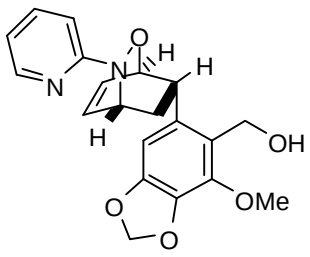
The isomers could not be separated. Therefore, ^{1}H-NMR and ^{13}C-NMR data are not provided. HRMS (ESI) exact mass calculated for $C_{20}H_{21}N_2O_5$ ([M + H]$^+$): 369.1445, found: 369.1430

7c: Enantiomeric excess (92% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (96:4); flow: 1.0 mL/min; major enantiomer t_r = 32.0 min, minor enantiomer t_r = 106.6 min.



7c

10c: Enantiomeric excess (95% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (96:4); flow: 1.0 mL/min; major enantiomer t_r = 73.2 min, minor enantiomer t_r = 83.8 min.

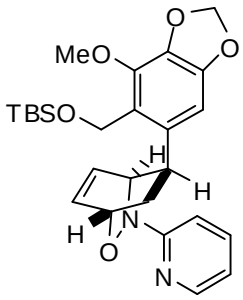


10c

(1*S*,4*S*,8*R*)-8-[6-(*tert*-Butyl-dimethyl-silanyloxymethyl)-7-methoxy-1,3-benzodioxol-5-yl]-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (7d) and (1*R*,4*R*,7*S*)-7-[6-(*tert*-Butyl-dimethyl-silanyloxymethyl)-7-methoxy-1,3-benzodioxol-5-yl]-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (10d): According to GP1: (*R*,*pR*)-*Walphos* (12.9 mg, 13.8 µmol), [Cu^{I}(CH$_3$CN)$_4$]PF$_6$ (5.2 mg, 13.8 µmol), CH$_2$Cl$_2$ (1.2 mL), 2-

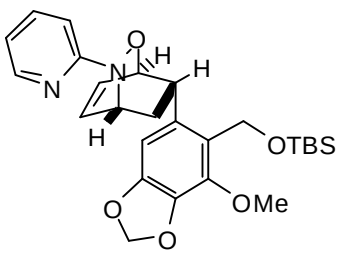
nitrosopyridine (15.0 mg, 138 µmol), diene **8d** (52.0 mg, 138 µmol) and SiO_2-chromatography (pentane:MTBE, 2:1) to give 66 mg (0.14 mmol, 99%) of **7d** and **10d** as a mixture of isomers. The isomer ratio was determined by chiral HPLC (*syn* isomer:**7d**:**10d** = 1.0:3.8:2.4). For analytical purposes a sample was repurified by flash chromatography (pentane:MTBE, 10:1).

7d: TLC: R_f = 0.3 (pentane:MTBE, 5:1). $[a]_D^{25}$ = -27.7 (c = 1.36, $CHCl_3$). FTIR (neat): $\tilde{n}$ = 2953, 2855, 1618, 1588, 1479, 1462, 1432, 1254, 1065, 836, 757 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) d = 8.10 – 8.09 (m, 1H), 7.49 – 7.41 (m, 1H), 6.89 – 6.85 (m, 1H), 6.75 – 6.68 (m, 1H), 6.57 – 6.52 (m, 1H), 6.27 – 6.22 (m, 2H), 5.82 – 5.81 (m, 2H), 5.26 – 5.22 (m, 1H), 4.84 – 4.80 (m, 1H), 4.76 – 4.75 (m, 2H), 4.01 – 3.95 (m, 1H), 3.91 – 3.89 (m, 3H), 2.72 – 2.62 (m, 1H), 1.51 – 1.43 (m, 1H), 0.82 – 0.81 (m, 9H), 0.05 – 042 (m, 3H), 0.01– 0.00 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) d = 163.3, 148.5, 146.7, 141.7, 137.8, 137.7, 135.2, 131.8, 131.3, 125.0, 116.5, 111.6, 102.7, 100.9, 70.8, 60.1, 57.2, 55.9, 35.1, 33.4, 26.1, 18.4, -5.3, -5.2. HRMS (ESI) exact mass calculated for $C_{26}H_{34}N_2O_5Si$ H ($[M + H]^+$): 483.2310, found: 483.2311. Enantiomeric excess (70% 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 = 28.9 min, minor enantiomer t_r = 7.0 min.



7d

10d: TLC: R_f = 0.2 (pentane:MTBE, 5:1). $[a]_D^{25}$ = +157.9 (c = 0.97, $CHCl_3$). FTIR (neat): $\tilde{n}$ = 2953, 2855, 1618, 1588, 1479, 1463, 1432, 1253, 1097, 1038, 838, 777, 757 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) d = 8.07– 8.06 (m, 1H), 7.43 – 7.36 (m, 1H), 6.85 – 6.81 (m, 1H), 6.67 – 6.61 (m, 1H), 6.43 – 6.37 (m, 1H), 6.27 – 6.22 (m, 1H), 6.19 – 6.18 (m, 1H), 5.74 – 5.72 (m, 2H), 5.37 – 5.32 (m, 1H), 4.75 (dd, *J* = 11.1, 4.2 Hz, 1H), 4.67 – 4.62 (m, 1H), 4.57 (dd, *J* = 11.1, 4.2 Hz, 1H), 3.94 – 3.84 (m, 1H), 3.84 (s, 3H), 2.61 – 2.51 (m, 1H), 1.65 – 1.57 (m, 1H), 0.80 – 0.79 (m, 9H), 0.04 – -0.07 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) d = 163.4, 148.5, 146.8, 141.6, 137.8,

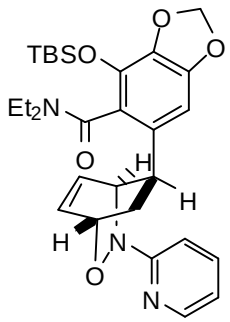


10d

136.5, 135.2, 132.6, 130.5, 125.2, 116.5, 111.6, 102.9, 100.9, 73.9, 60.1, 55.9, 52.9, 36.7, 31.2, 26.1, 18.4, -5.2, -5.2. HRMS (ESI) exact mass calculated for $C_{26}H_{34}N_2O_5Si$ H ([M + H]$^+$): 483.2310, found: 483.2319. 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 = 10.4 min, minor enantiomer t_r = 7.1 min.

4-(*tert*-Butyl-dimethyl-silanyloxy)-6-((1*S*,4*S*,5*R*)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-7-en-5-yl)-1,3-benzodioxole-5-carboxylic acid diethylamide (7e) and 4-(*tert*-Butyl-dimethyl-silanyloxy)-6-((1*R*,4*R*,6*S*)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-7-en-6-yl)-1,3-benzodioxole-5-carboxylic acid diethylamide (10e): According to GP1: (*R*,*pR*)-*Walphos* (7.8 mg, 8.4 µmol), [Cu^I(CH$_3$CN)$_4$]PF$_6$ (3.1 mg, 8.4 µmol), CH_2Cl_2 (1.5 mL), 2-nitrosopyridine (9.1 mg, 84 µmol), diene **8e** (33 mg, 77 µmol) and SiO_2-chromatography (pentane:MTBE, 1:2) to give 41 mg (76 µmol, 99%) of **7e** and **10e** as a mixture of isomers. The isomer ratio was determined (*syn* isomer:**7e:10e** = 1.0:4.2:2.6). For analytical purposes a sample was repurified by flash chromatography (pentane:MTBE, 2:1).

7e: TLC: R_f = 0.1 (pentane:MTBE, 1:1). FTIR (neat): $\tilde{n}$ = 2930, 2857, 1623, 1588, 1473, 1432, 1092, 1035, 841, 731 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$)[2] d = 8.18 – 8.16 (m, 1H), 7.56 – 7.53 (m, 1H), 6.94 – 6.91 (m, 1H), 6.80 – 6.77 (m, 1H), 6.65 – 6.62 (m, 1H), 6.40 – 6.37 (m, 1H), 6.32 (s, 1H), 5.92 (d, *J* = 1.4 Hz, 1H), 5.88 (d, *J* = 1.4 Hz, 1H), 5.34 – 5.29 (m, 1H), 4.85 – 4.82 (m, 1H), 3.92 – 3.85 (m, 1H), 3.56 – 3.52 (m, 1H), 3.36 – 3.30 (m, 2H), 3.26 – 3.20 (m, 1H), 2.82 – 2.76 (m, 1H), 1.49 – 1.45 (m, 1H), 1.23 (t, *J* = 7.2 Hz, 3H), 1.20 (t, *J* = 7.2 Hz, 3H), 0.97 (s, 9H), 0.25 (s, 3H), 0.20 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) d = 167.4, 163.7, 148.6, 137.8, 134.9, 134.8, 132.2, 131.8, 130.9, 130.6, 125.8, 125.4, 116.4, 111.6, 101.2, 100.8, 70.7, 56.1, 43.2, 38.7, 35.8, 34.9, 29.7, 25.6, 18.3, 13.8, 12.8, -4.2, -4.6. HRMS (ESI) exact mass calculated for $C_{29}H_{39}N_3O_5Si$ Na ([M + Na]$^+$): 560.2551, found: 560.2553. Enantiomeric excess (73% ee) was determined by chiral HPLC.

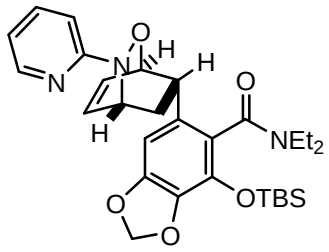


7e

[2] This NMR sample shows a minor set of signals due to hindered rotation (~ 12:1 ratio)

Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (99.5:0.5); flow: 1.0 mL/min; major enantiomer t_r = 36.7 min, minor enantiomer t_r = 9.7 min.

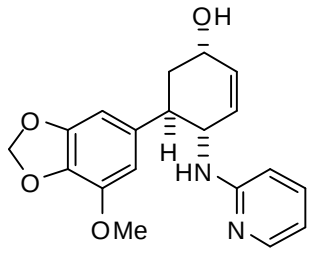
10e: TLC: R_f = 0.1 (pentane:MTBE, 1:1). FTIR (neat): $\tilde{n}$ = 2931, 2858, 1626, 1589, 1472, 1432, 1293, 1125, 1036, 813, 784 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$)[3] d = 8.20 – 8.19 (m, 1H), 7.55 – 7.50 (m, 1H), 6.93 – 6.92 (m, 1H), 6.80 – 6.77 (m, 1H), 6.57– 6.55 (m, 1H), 6.51 – 6.48 (m, 1H), 6.30 (s, 1H), 5.89 (d, *J* = 1.4 Hz, 1H), 5.85 (d, *J* = 1.4 Hz, 1H), 5.41 – 5.38 (m, 1H), 4.55 – 4.52 (m, 1H), 3.93 – 3.87 (m, 1H), 3.59 – 3.56 (m, 1H), 3.24 – 3.17 (m, 3H), 2.77 – 2.72 (m, 1H), 1.63 (ddd, *J* = 13.8, 5.4, 2.4 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H), 0.93 (s, 9H), 0.20 (s, 3H), 0.15 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) d = 167.3, 163.4, 148.5, 146.6, 138.0, 135.1, 134.8, 133.3, 129.8, 125.7, 116.6, 111.5, 101.6, 100.9, 72.9, 53.1, 43.1, 38.8, 37.8, 32.2, 25.6, 18.3, 13.9, 12.9, -4.2, -4.6. HRMS (ESI) exact mass calculated for $C_{29}H_{39}N_3O_5Si$ Na ([M + Na]$^+$): 560.2551, found: 560.2540. Enantiomeric excess (95% 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 = 25.1 min, minor enantiomer t_r = 13.5 min.



10e

Synthesis of (+)-*trans*-Dihydronarciclasine:

(1*S*,4*S*,5*R*)-5-(7-Methoxy-1,3-benzodioxol-5-yl)-4-(pyridin-2-ylamino)-cyclohex-2-enol (**6,** R^1 = H): The N-O bond of **7a** was cleaved according to a previously reported procedure[5]. $Mo(CO)_6$ (411 mg, 1.55 mmol) and $NaBH_4$ (67 mg, 1.8 mmol) was added to a suspension of **7a** (439 mg, 1.29 mmol) in MeOH:H_2O (10:1, 10 mL). Then the reaction mixture was heated to 65 ^oC and stirred for 12 h at that temperature. The precipitate was removed by filtration through a short pad of celite and the

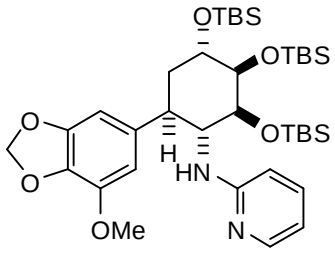


6

[3] This NMR sample shows a minor set of signals due to hindered rotation (~ 5:1 ratio)

filtrate was concentrated in vacuo. The residue was dissolved in CH_2Cl_2, washed (brine), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash column chromatography (pentane:acetone, 1:1) to afford **6** (R^1 = H) as a colorless oil (398 mg, 1.17 mmol, 90%). TLC: R_f = 0.4 (pentane:acetone, 1:1). $[\alpha]_D^{25}$ = +64.5 (c = 1.7, $CHCl_3$). FTIR (neat): $\tilde{\nu}$ = 3385, 2922, 1633, 1511, 1451, 1434, 1361, 1137, 1089, 1045 cm^{-1}.^{1}H NMR (300 MHz, $CDCl_3$) d = 7.93 – 7.90 (m, 1H), 7.26 (ddd, *J* = 8.7, 7.2, 1.8 Hz, 1H), 6.47 – 6.43 (m, 1H), 6.38 (d, *J* = 1.3 Hz, 1H), 6.36 (d, *J* = 1.3 Hz, 1H), 6.20 (d, *J* = 8.5 Hz, 1H), 5.88 (br. s, 2H), 5.82 (s, 2H), 4.77 (d, *J* = 8.0 Hz, 1H), 4.37 – 4.31 (m, 1H), 4.25 – 4.21 (m, 1H), 3.73 (s, 3H), 3.05 – 2.97 (m, 2H), 2.02 – 1.98 (m, 2H) . ^{13}C NMR (75 MHz, $CDCl_3$) d = 157.6, 148.9, 146.9, 143.5, 137.8, 137.7, 133.9, 133.1, 129.5, 112.8, 108.2, 107.6, 101.3, 101.3, 63.8, 56.6, 53.6, 41.5, 38.9. HRMS (ESI) exact mass calculated for $C_{19}H_{20}N_2O_4H$ ($[M + H]^+$): 341.1496, found: 341.1501.

Pyridin-2-yl-[(1*R*,2*S*,3*R*,4*S*,6*R*)-2,3,4-tris-(*tert*-butyl-dimethyl-silanyloxy)-6-(7-methoxy-1,3-benzodioxol-5-yl)-cyclohexyl]-amine (11):

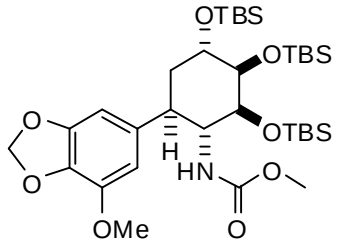


11

K_2OsO_4, $2H_2O$ (31 mg, 85 µmol) and NMO (170 mg, 1.45 mmol) were added to a solution of **6** (R^1 = H) (290 mg, 0.85 mmol) in acetone:water (2:1, 8 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, 10:1). The triol was then dissolved in DMF (5 mL). *tert*-Butyldimethylsilyl chloride (546 mg, 3.62 mmol) and imidazole (369 mg, 5.43 mmol) were added and the solution was stirred for 12 h at 75 ^{o}C. 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:acetone, 20:1) to afford **11** as a colorless oil (470 mg, 656 µoml, 77 %, over two steps). TLC: R_f = 0.4 (pentane:acetone, 10:1). $[\alpha]_D^{25}$ = - 6.4 (c = 0.75, $CHCl_3$). FTIR (neat): $\tilde{\nu}$ = 2953, 2929, 2894, 2857, 1634, 1604, 1511, 1461, 1255, 1193, 1118, 1091, 835, 774 cm^{-1}.^{1}H NMR (300 MHz, $CDCl_3$) d = 7.83 – 7.81 (m, 1H), 7.24 – 7.19 (m, 1H), 6.39 (d, *J* = 8.5 Hz, 1H), 6.33 (dd, *J* = 6.8, 5.4 Hz, 1H), 6.29 (d, *J* = 1.1 Hz, 1H), 6.24 (d, *J* = 1.1 Hz, 1H), 5.80 (s, 2H), 4.29 (d, *J* = 8.3 Hz, 1H), 4.10 – 3.96

(m, 2H), 3.85 – 3.80 (m, 2H), 3.65 (s, 3H), 2.88 – 2.78 (m, 1H), 2.13 – 2.04 (m, 1H), 1.65 – 1.61 (m, 1H), 0.98 (s, 9H), 0.92 (s, 9H), 0.68 (s, 9H), 0.17 (s, 3H), 0.08 (s, 3H), 0.06 (s, 6H), -0.01 (s, 3H), -0.16 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) d = 159.7, 148.7, 147.4, 143.4, 137.8, 136.9, 133.6, 111.9, 106.9, 105.9, 101.5, 101.1, 76.0, 74.5, 71.2, 56.2, 55.2, 44.5, 37.3, 26.0, 25.9, 25.8, 18.2, 18.1, 18.0, -4.2, -4.4, -4.41, -4.7, -4.9, -5.0. HRMS (ESI) Exact mass calculated for $C_{37}H_{64}N_2O_6Si_3$ H ($[M + H]^+$): 717.4145, found: 717.4122

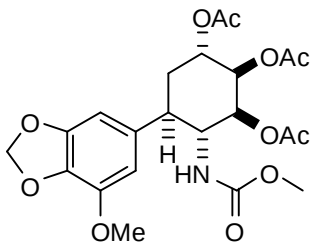
[(1*R*,2*S*,3*R*,4*S*,6*R*)-2,3,4-Tris-(*tert*-butyl-dimethyl-silanyloxy)-6-(7-methoxy-1,3-benzodioxol-5-yl)-cyclohexyl]-carbamic acid methyl ester (12): CH_3MgCl (3M in THF, 0.12 mL, 0.35 mmol) was added dropwise to a solution of **11** (209 mg, 0.29 mmol) in THF (5.0 mL) at rt and the mixture was stirred for 10 min at that temperature. Methyl chloroformate (0.11 mL, 1.45 mmol) was then added and stirring was continued at rt for 12 h. Then the reaction mixture was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were washed (brine), dried ($MgSO_4$) and concentrated in vacuo. The residue was passed through a short pad of silica (pentane:acetone, 10:1). The resulting solution was concentrated in vacuo and the residue was dissolved in CH_2Cl_2 (11 mL). Methyl-trifluoromethanesulfonate (36.0 µL 0.32 mmol) was added dropwise at 0 ^{o}C and the resulting solution was stirred for 12 h at that temperature. Then the solvent was removed in vacuum. The residue was then dissolved in MeOH (6 mL). A aqueous NaOH solution (2M, 2.2 mL) was added and stirring was continued at 50 ^{o}C for 12 h. The solvents were removed and the resulting residue was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography (pentane:acetone, 10:1) to afford **12** as a colorless oil (179 mg, 257 µmol, 88% over three steps). TLC: R_f = 0.3 (pentane:acetone, 10:1). $[a]_D^{25}$ = +5.1 (c = 0.90, $CHCl_3$). FTIR (neat): $\tilde{n}$ = 2953, 2929, 2892, 2857, 1732, 1708, 1635, 1512, 1463, 1254, 1140, 1092, 835, 774 cm^{-1}.^{1}H NMR (300 MHz, $CDCl_3$) d = 6.47 (br. s, 1H), 6.34 (d, *J* = 1.2 Hz, 1H), 5.93 (d, *J* = 1.4 Hz, 1H), 5.91 (d, *J* = 1.4 Hz, 1H), 4.22 – 4.11 (m, 1H), 3.95 – 3.88 (m, 1H), 3.87 (s, 3H), 3.80 (br. s, 2H), 3.48 (br. s, 3H), 2.93 –



12

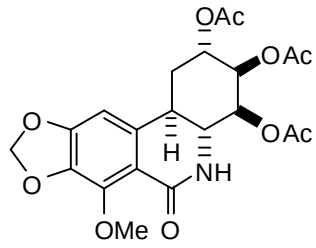
2.77 (m, 1H), 2.09 –2.00 (m, 1H), 1.63 – 1.57 (m, 1H), 0.95 (s, 9H), 0.93 (s, 9H), 0.88 (s, 9H), 0.16 (s, 3H), 0.07 (s, 6H), 0.064 (s, 3H), 0.062 (s, 3H), 0.05 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) d = 156.3, 148.6, 143.6, 137.8, 133.5, 106.3, 101.9, 101.2, 75.6, 72.5, 71.1, 56.4, 54.0, 51.7, 43.6, 37.4, 25.9, 25.8, 25.8, 18.1, 18.0, 18.0, -3.9, -4.4, -4.5, -4.8, -4.9, -5.0. HRMS (ESI) exact mass calculated for $C_{34}H_{63}NO_8Si_3$ Na ([M + Na]$^+$): 720.3754, found: 720.3828

Acetic acid (1*R*,2*S*,3*R*,4*R*,6*S*)-2,6-diacetoxy-4-(7-methoxy-1,3-benzodioxol-5-yl)-3-methoxycarbonylamino-cyclohexyl ester (5): Tetrabutyl ammonium fluoride (5.2 mL, 5.2 mmol) was added to a solution of **12** (240 mg, 0.34 mmol) in THF (7 mL) at 0 ^{o}C and the mixture was stirred at rt for 24 h. Then the solvent was removed in vacuo and the residue was dissolved in pyridine (5 mL). Acetic anhydride (0.33 mL, 3.44 mmol) and DMAP (13 mg, 0.1 mmol) were added to the mixture and stirring was continued for 24 h at rt. Then the solvent was removed and the residue was dissolved in EtOAc (100 mL). The solution was washed with H_2O. The organic layer was dried ($MgSO_4$) and concentrated in vacuum. The residue was purified by flash column chromatography (pentane:acetone, 2:1) to afford **5** as a colorless oil (157 mg, 328 µmol, 95%). TLC: R_f = 0.2. $[a]_D^{25}$ = +63.7 (c = 0.95, $CHCl_3$). FTIR (neat): ? = 3361, 2953, 1748, 1635, 1513, 1370, 1230, 1050, 930, 733 cm^{-1}.^{1}H NMR (300 MHz, $CDCl_3$) d = 6.36 – 6.33 (m, 2H), 5.87 (s, 2H), 5.27 – 5.25 (m, 1H), 5.14 (dd, *J* = 10.5, 2.7 Hz, 1H), 5.98 – 4.95 (m, 1H), 4.43 – 4.40 (m, 1H), 4.17 – 4.01 (m, 1H), 3.83 (s, 3H), 3.43 (s, 3H),2.90 – 2.78 (m, 1H), 2.13 (s, 3H), 2.08 (s, 3H), 1.99 – 1.94 (m, 2H), 1.94 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) d = 170.6, 169.4, 169.3, 156.5, 149.1, 143.5, 134.9, 134.3, 107.5, 101.6, 101.4, 71.2, 69.1, 68.9, 56.8, 53.4, 52.1, 43.4, 33.7, 21.1, 20.9, 20.7. HRMS (ESI) Exact mass calculated for $C_{22}H_{25}NO_{11}Na$ ([M + Na]$^+$): 502.1320, found: 502.1328



5

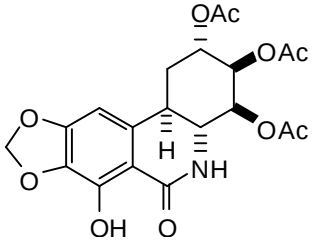
Acetic acid (2*S*,3*R*,4*S*,4a*R*,11b*R*)-2,4-diacetoxy-7-methoxy-6-oxo-1,2,3,4,4a,5,6,11b-octahydro-[1,3]dioxolo[4,5-*j*]phenanthridin-3-yl ester (13):



13

A solution of **5** (150 mg, 0.31 mmol) and DMAP (171 mg, 1.40 mmol) in 25 mL of CH_2Cl_2 was treated with trifluoromethane sulfonic anhydride (0.42 mL, 2.49 mmol) at 0 °C and the solution was stirred for 24 h at 0 - 5 ^oC. Then the solvent was removed and the residue was dissolved in THF (10 mL). A solution of 3 M HCl (1.5 mL) was then added and the resulting solution was stirred for 4 h at rt. Then the reaction was quenched by adding saturated $NaHCO_3$ solution. The mixture was extracted with EtOAc. The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography (pentane:acetone, 1:1) to afford **13** as a colorless oil (90 mg, 0.20 mmol, 64%) and other regioisomer (18%). TLC: R_f = 0.3 (pentane:acetone, 1:1). $[a]_D^{25}$ = +131.3 (c = 0.31, $CHCl_3$). FTIR (neat): $\tilde{n}$ = 3197, 2920, 1750, 1667, 1612, 1480, 1371, 1334, 1222, 1095, 1060, 1032, 844, 731 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) d = 6.61 (br. s, 1H), 6.47 (br. s, 1H), 6.02 (d, *J* = 1.2 Hz, 1H), 5.99 (d, *J* = 1.2 Hz, 1H), 5.43 – 5.40 (m, 1H), 5.19 – 5.14 (m, 2H), 4.05 (s, 3H), 3.71 – 3.63 (m, 1H), 3.12 – 3.02 (m, 1H), 2.43 – 2.37 (m, 1H), 2.13 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H) 1.92 – 1.82 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) d = 170.4, 169.4, 169.1, 164.3, 152.4, 145.2, 137.6, 137.2, 114.9, 101.8, 99.1, 71.4, 68.6, 67.4, 60.8, 52.2, 35.8, 27.0, 21.1, 20.8, 20.7. HRMS (ESI) Exact mass calculated for $C_{21}H_{23}NO_{10}Na$ ($[M + Na]^+$): 472.1214, found: 472.1222

Acetic acid (2*S*,3*R*,4*S*,4a*R*,11b*R*)-2,4-diacetoxy-7-hydroxy-6-oxo-1,2,3,4,4a,5,6,11b-octahydro-[1,3]dioxolo[4,5-*j*]phenanthridin-3-yl ester (13-OH):

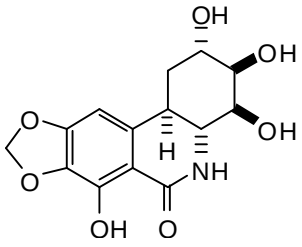


13-OH

Boron tribromide (46 µL, 0.5 mmol) was added to a solution of **13** (84 mg, 0.19 mmol) in CH_2Cl_2 (8 mL) at -78 °C. The reaction mixture was allowed to warm to 0 °C and stirring was continued for 40 min. The reaction was then quenched by adding 25 % aqueous NH_4OH solution (12 mL) and the resulting mixture was stirred for 20 min at 0 °C. Then the reaction mixture was

extracted with EtOAc (3 x 20). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography (pentane:EtOAc, 1:1) to afford **13-OH** (42 mg, 96 µmol, 52%). The physical data are in agreement with those reported in the literature.[6] TLC: R_f = 0.3 (pentane:EtOAc, 1:1). $[\alpha]_D^{25}$ = +80.7 (c = 0.29, $CHCl_3$), (lit[6]. $[\alpha]_D^{20}$ = +81.9 (c = 0.72, $CHCl_3$)). FTIR (neat): $\tilde{\nu}$ = 3336, 2924, 2854, 1745, 1717, 1673, 1625, 1467, 1373, 1225, 1082, 1032, 842 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) d = 12.24 (s, 1H), 6.32 (s, 1H), 6.15 (s, 1H), 6.04 (d, *J* = 1.2 Hz, 1H), 6.03 (d, *J* = 1.2 Hz, 1H), 5.44 – 5.42 (m, 1H), 5.22 – 5.16 (m, 2H), 3.77 (dd, *J* = 12.6, 11.1 Hz, 1H), 3.17 – 3.08 (m, 1H), 2.46 – 2.40 (m, 1H), 2.13 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 1.95 – 1.86 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) d = 170.2, 170.1, 169.3, 169.1, 153.0, 146.5, 135.9, 133.3, 106.9, 102.4, 96.7, 71.6, 68.5, 67.3, 52.8, 34.6, 26.7, 21.0, 20.8, 20.7. HRMS (ESI) exact mass calculated for $C_{20}H_{21}NO_{10}Na$ ($[M + Na]^+$): 458.1058, found: 458.1025.

(+)-*trans*-Dihydronarciclasine (1): 2.5 mL of a sodium methoxide solution (stock: 150 mg in 5 mL methanol) were added to a solution of **13-OH** (30 mg, 69 µmol) in THF (5 mL) and the resulting mixture was stirred for 1 h at rt. The reaction was quenched by adding aqueous NH_4Cl solution and the resulting mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated. The residue was purified by flash column chromatography (EtOAc :MeOH, 10:1) to afford **1** as a white solid (21 mg, 68 µmol, 99%). Spectral data matched literature values. The physical data are in agreement with those reported in the literature.[7] TLC: R_f = 0.3 (EtOAc:MeOH, 10:1). $[\alpha]_D^{25}$ = +4.1 (c = 0.22, THF), (lit[8]. $[\alpha]_D^{20}$ = +4.7 (c = 0.27, THF)). FTIR (neat): $\tilde{\nu}$ = 3355, 2921, 1668, 1623, 1466, 1339, 1076, 1032 cm^{-1}. ^1H NMR (300 MHz, CD_3OD) d = 6.34 (d, *J* = 0.9 Hz, 1H), 5.90 – 5.89 (m, 2H), 3.98 (dd, *J* = 6.0, 3.0 Hz, 1H), 3.81 (t, *J* = 3.0 Hz, 1H), 3.76 (dd, *J* = 9.9, 3.3 Hz, 1H), 3.36 (dd, *J* = 12.9, 9.9 Hz, 1H), 2.95 – 2.85 (m, 1H), 2.15 – 2.09 (m, 1H), 1.79 – 1.67 (m, 1H). ^{13}C NMR (75 MHz, CD_3OD) d = 171.9, 154.3,



1

147.3, 139.7, 133.9, 108.3, 103.4, 97.7, 73.4, 71.6, 70.6, 56.4, 35.3, 29.7. HRMS (ESI) exact mass calculated for $C_{14}H_{15}NO_7Na$ ($[M + Na]^+$): 332.0741, found: 332.0742.

References:

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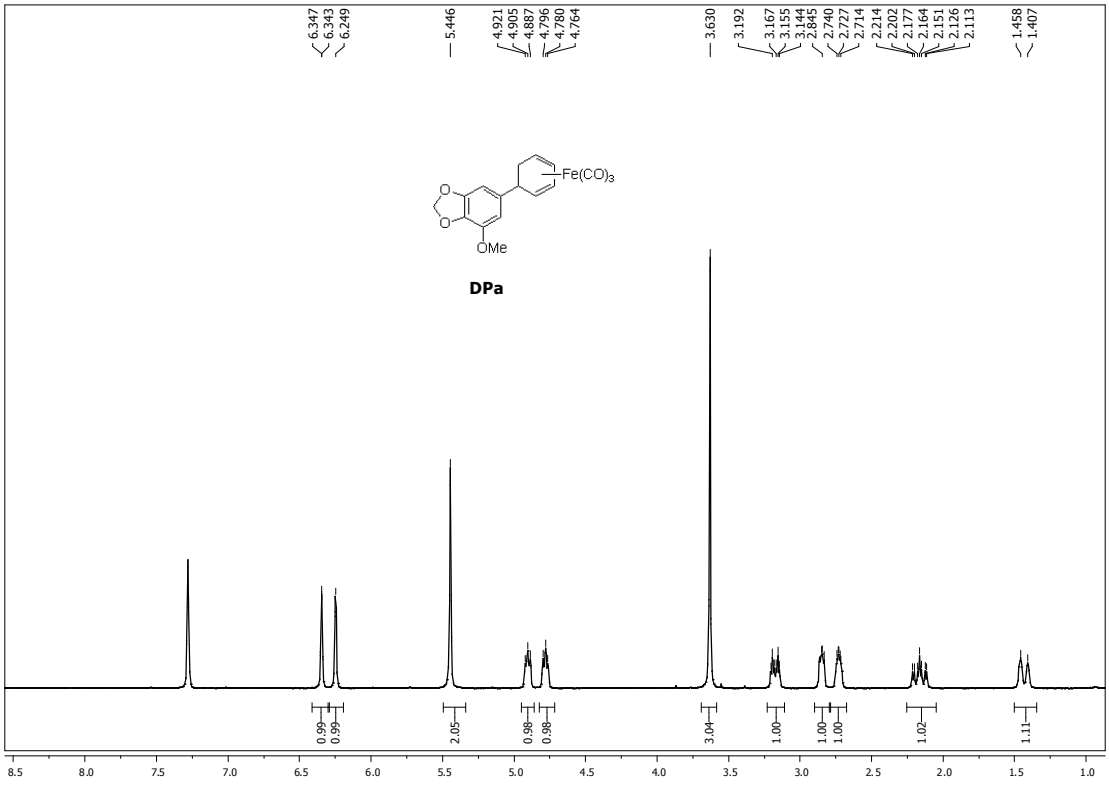
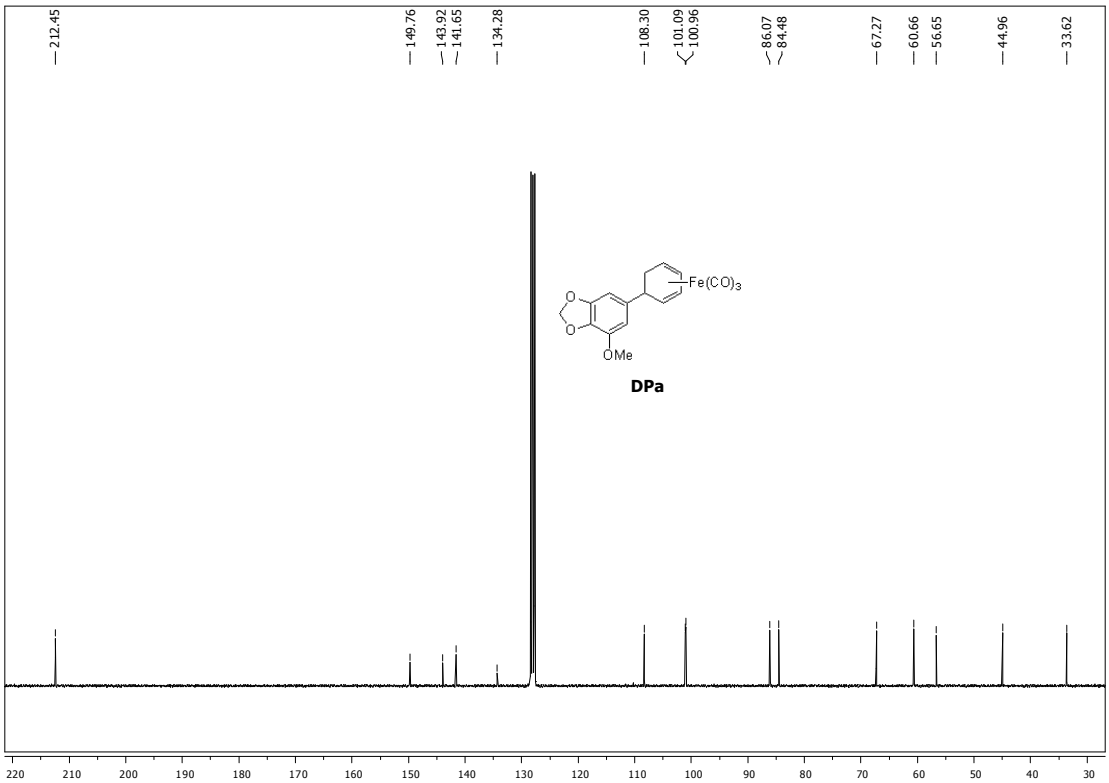
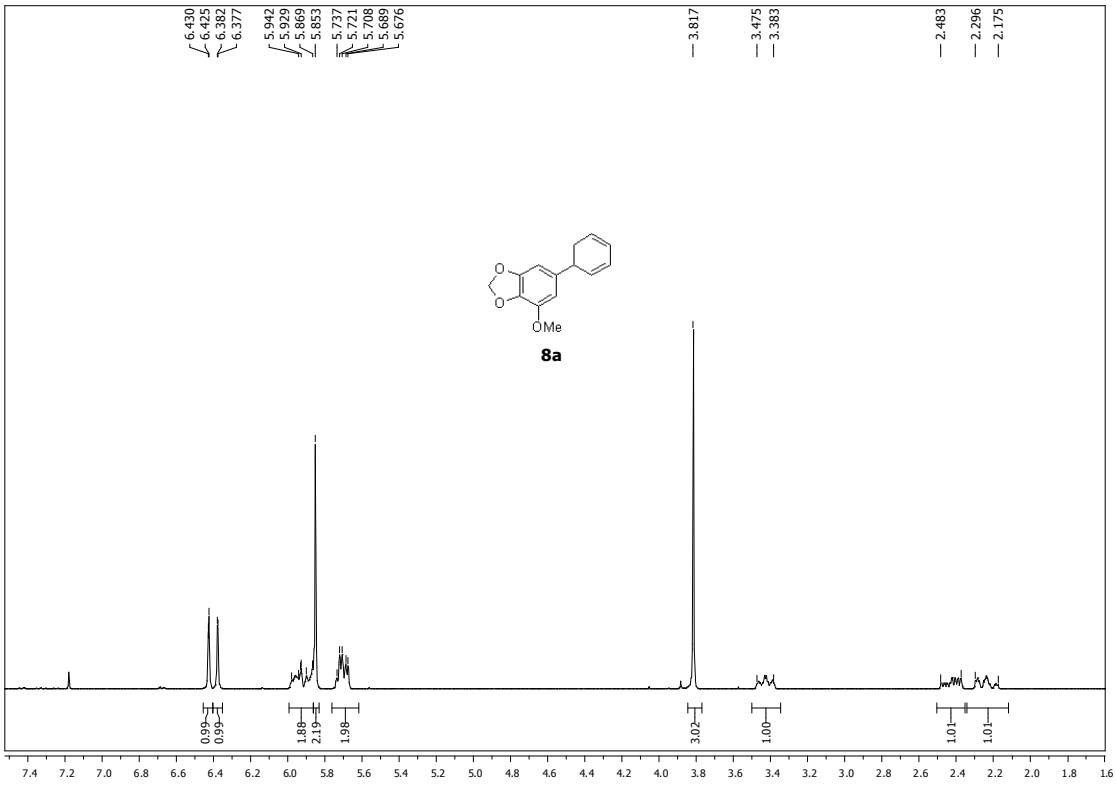
^{1}H and ^{13}C – NMR Spectra



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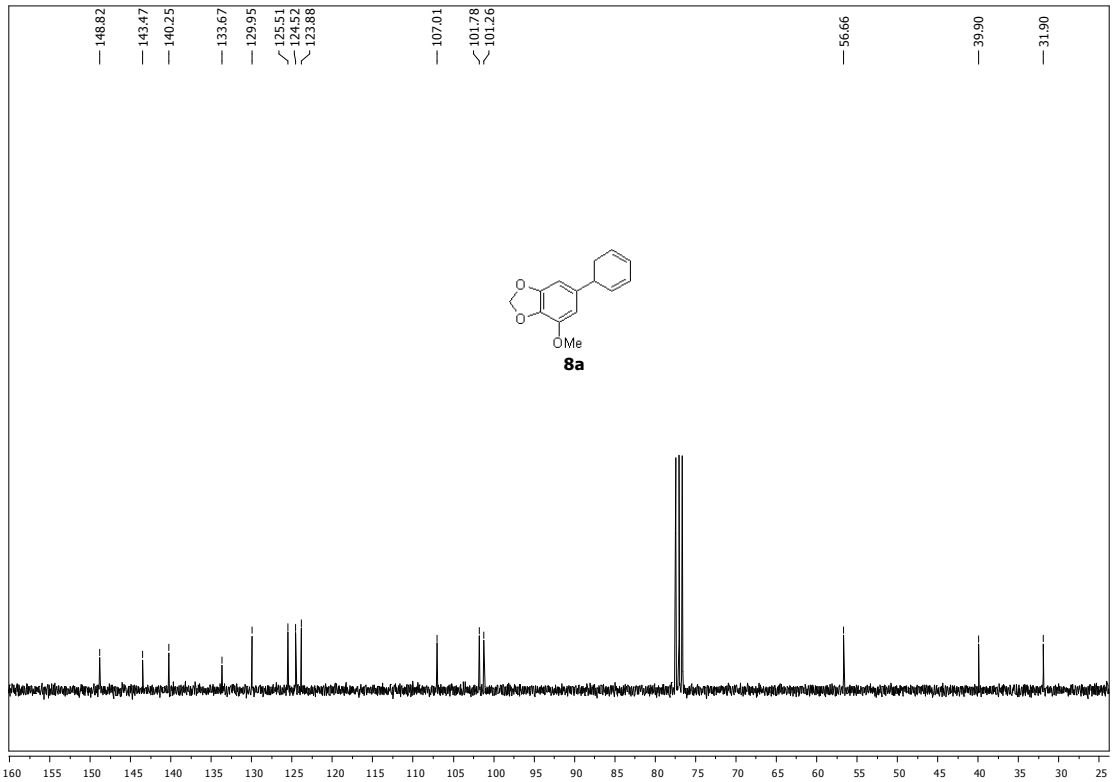
1.01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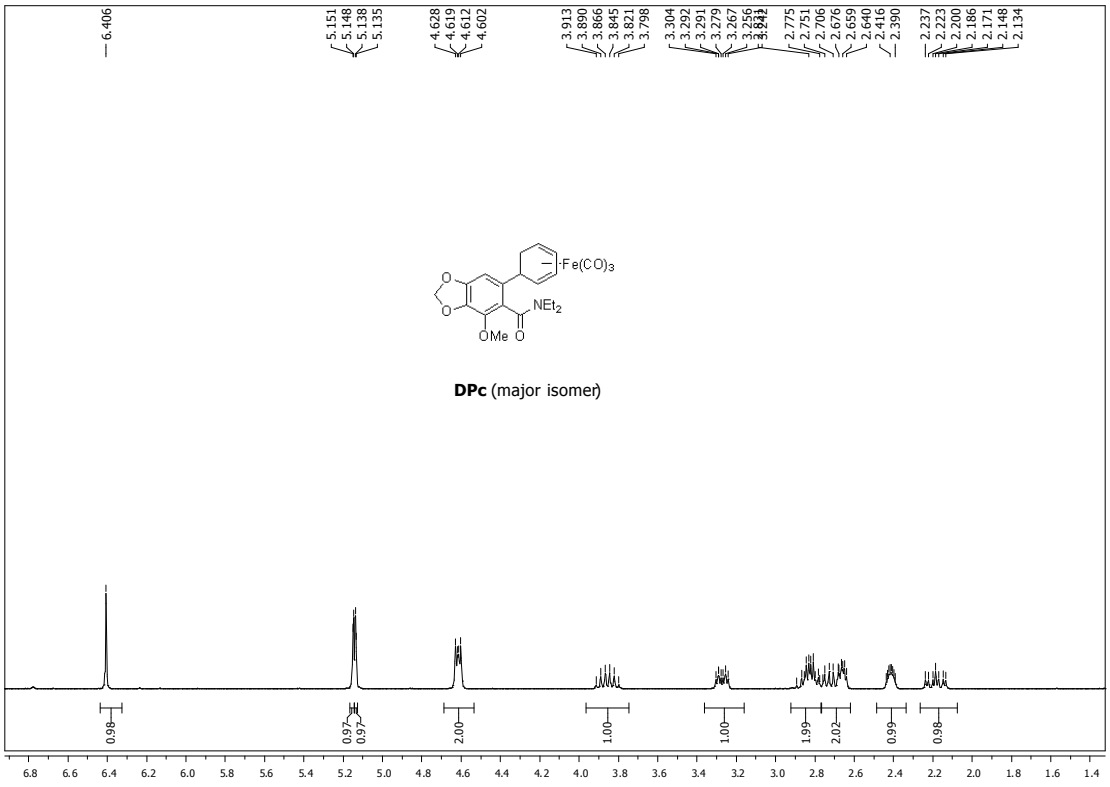

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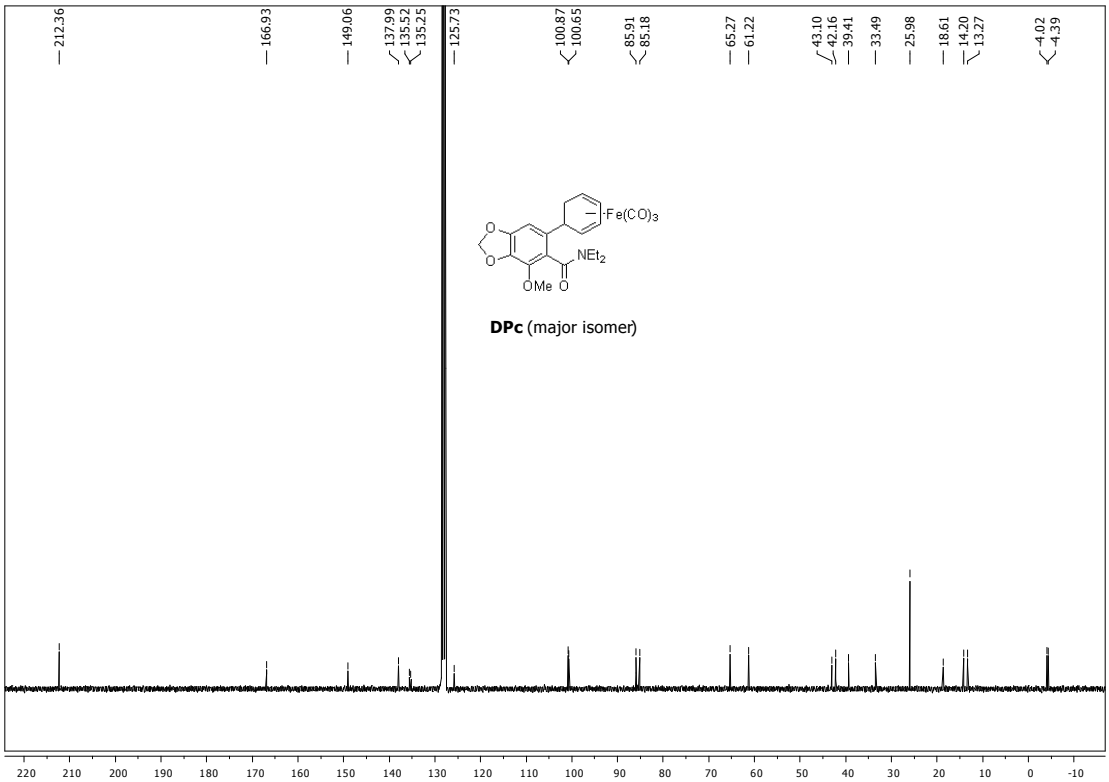

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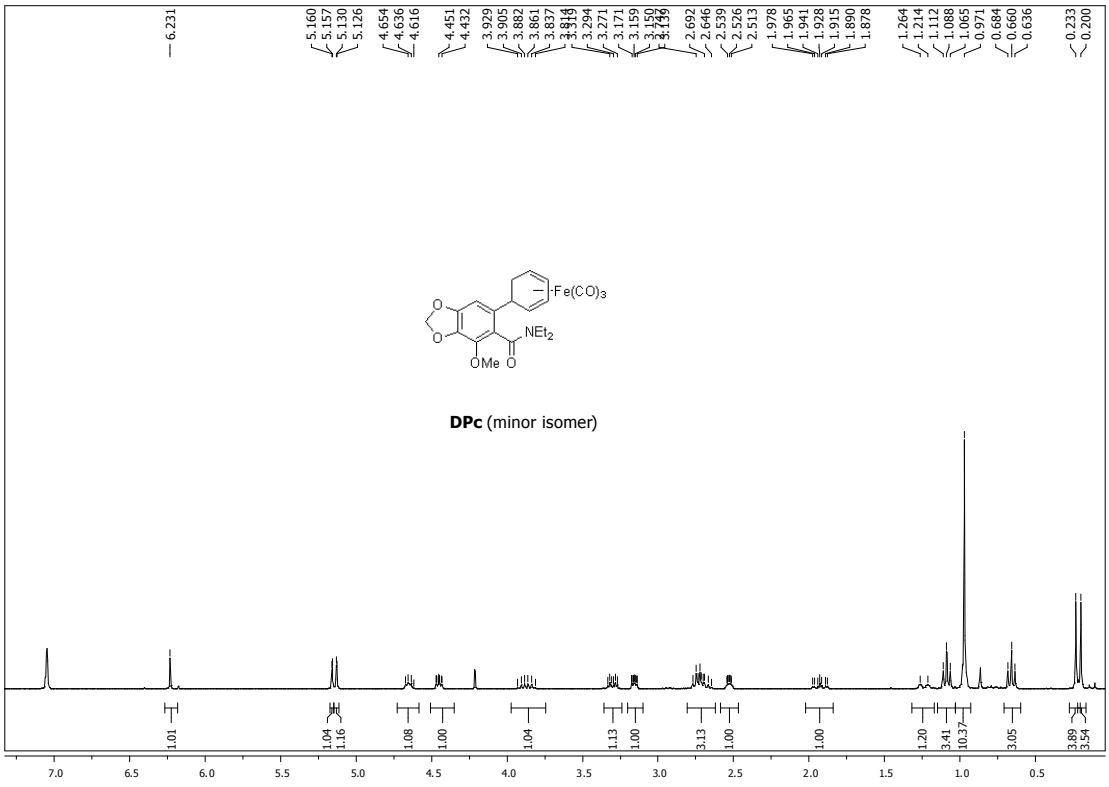

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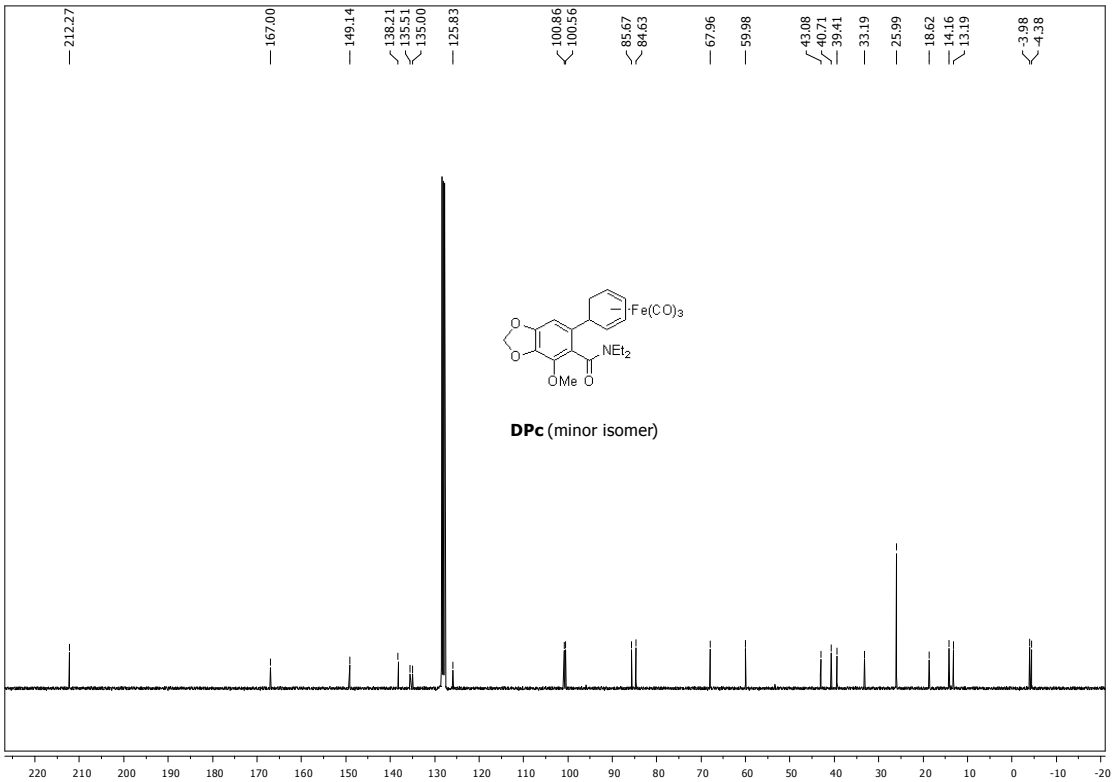

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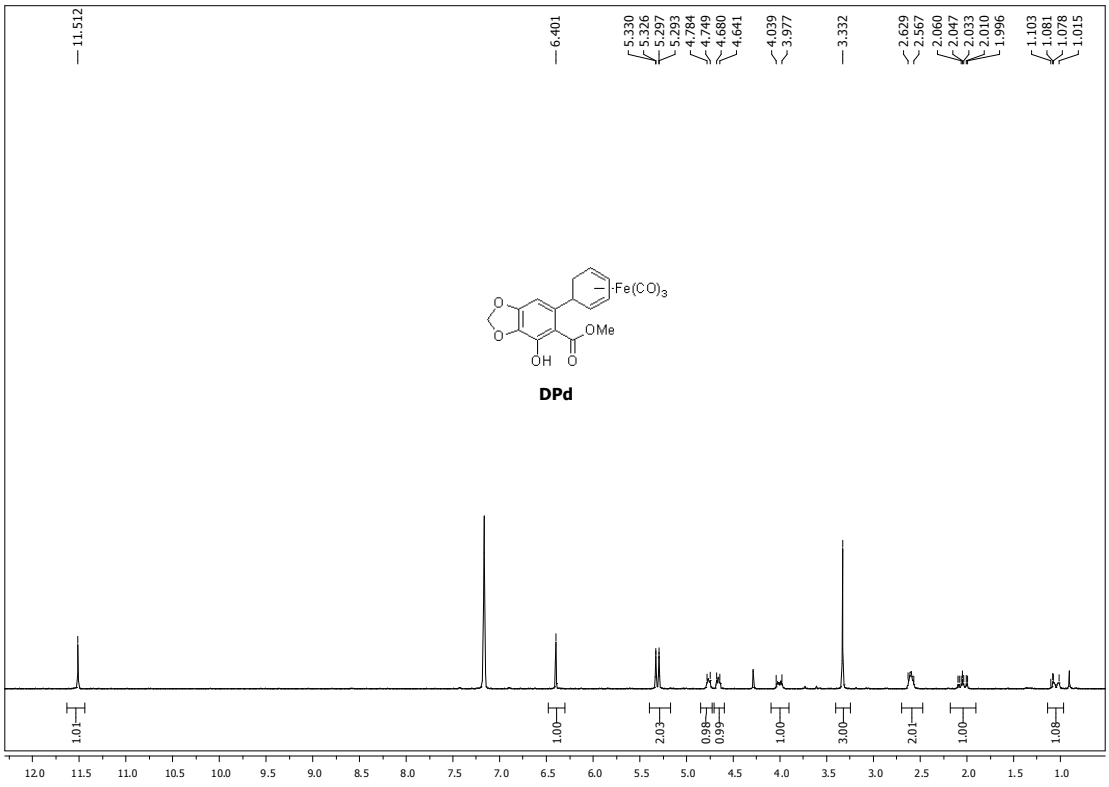
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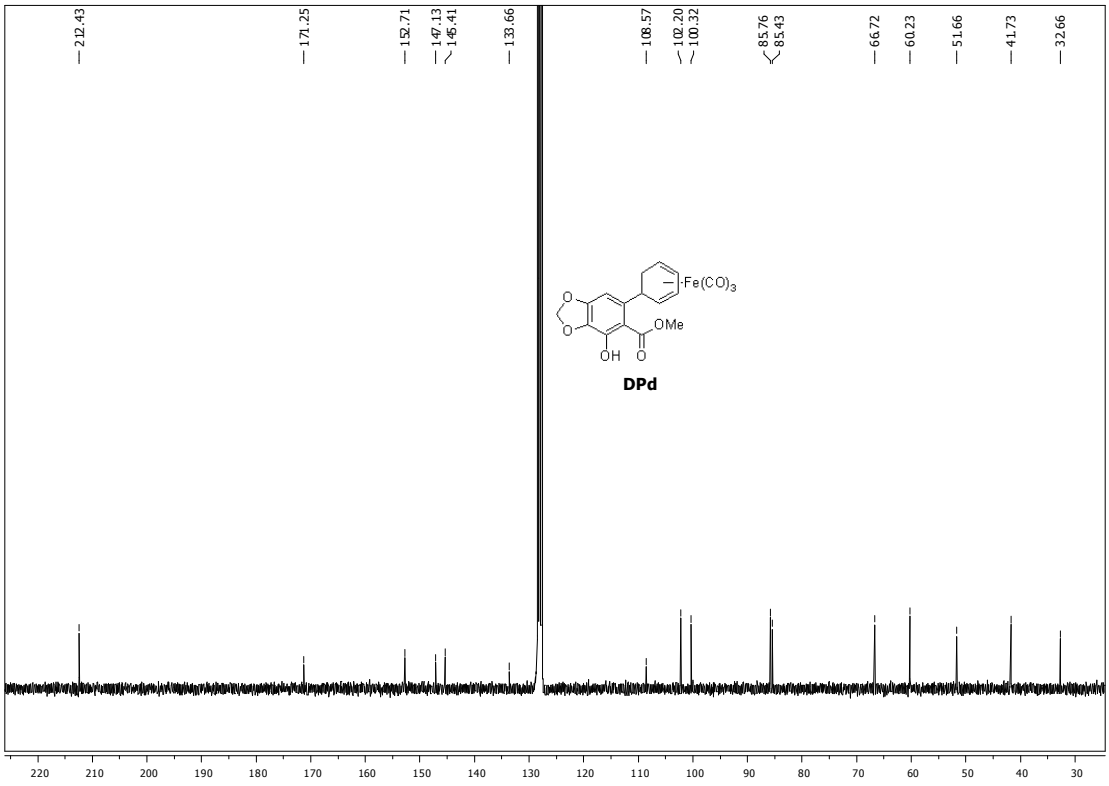
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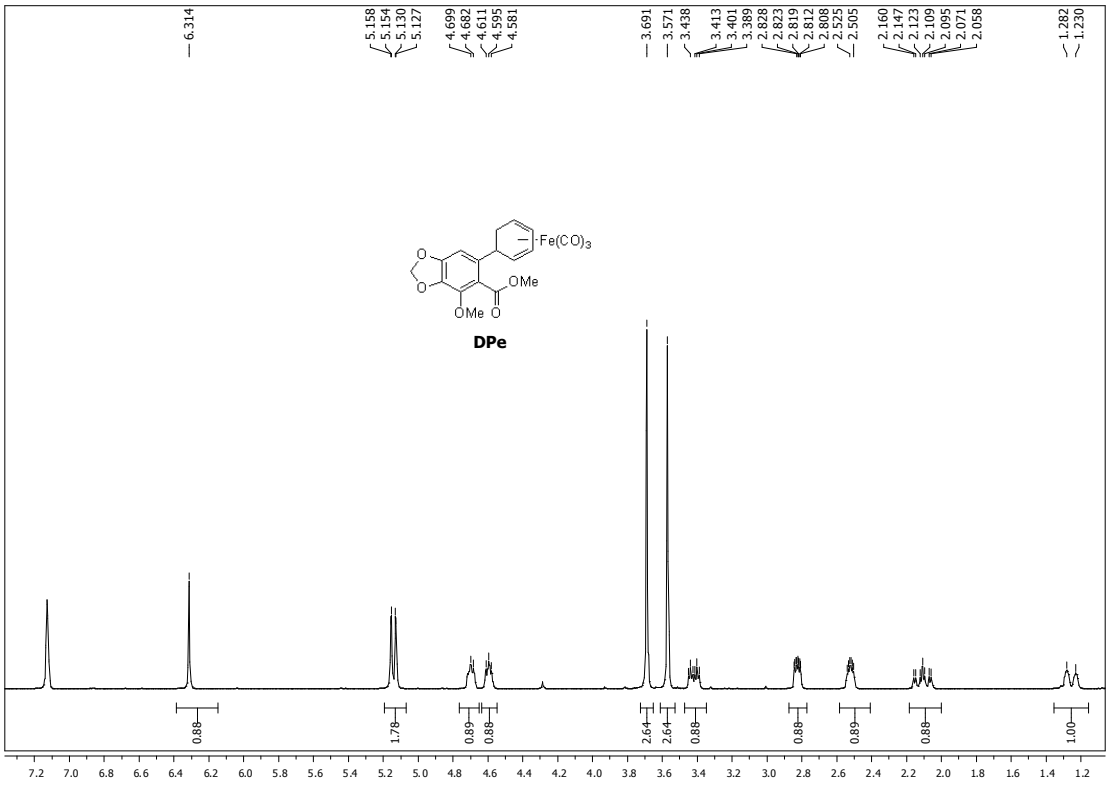
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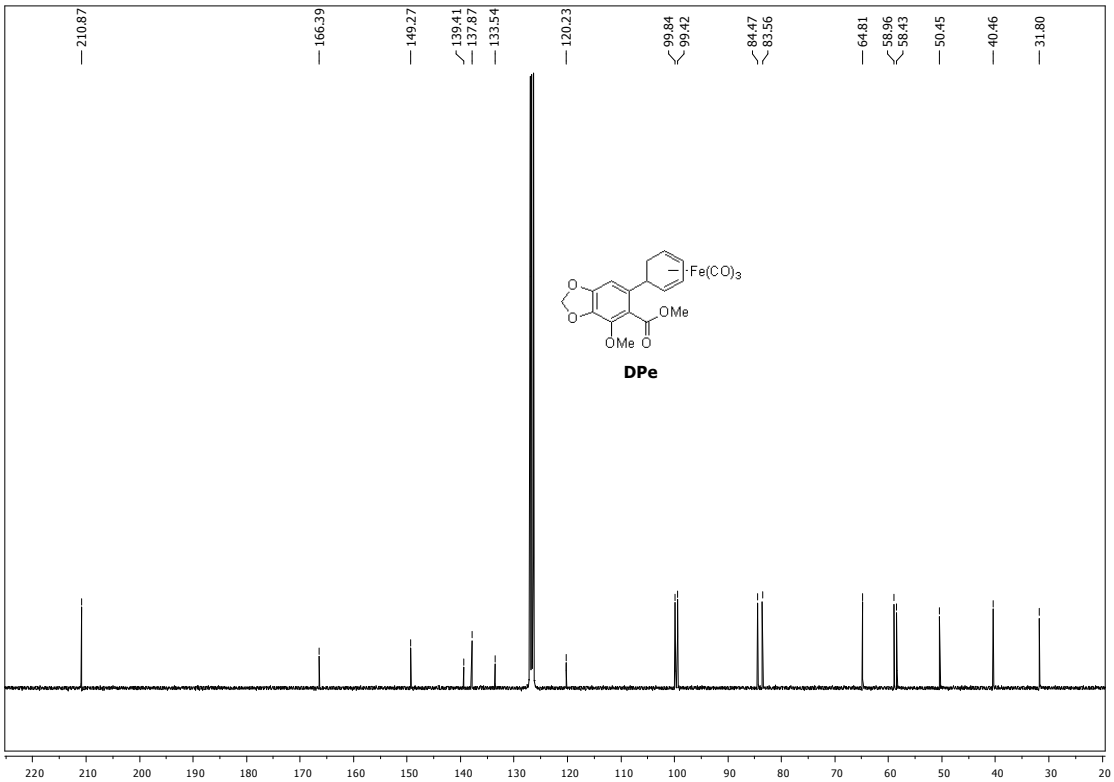
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Fe(CO)3
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OMe O
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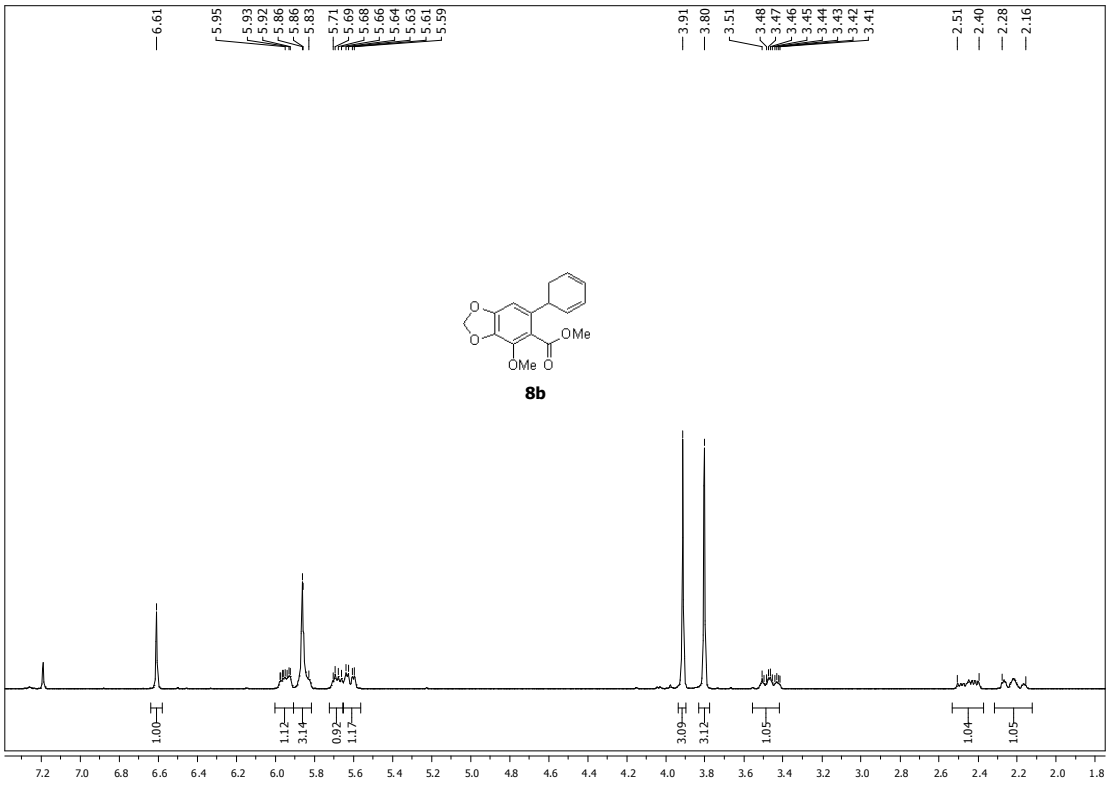
DPe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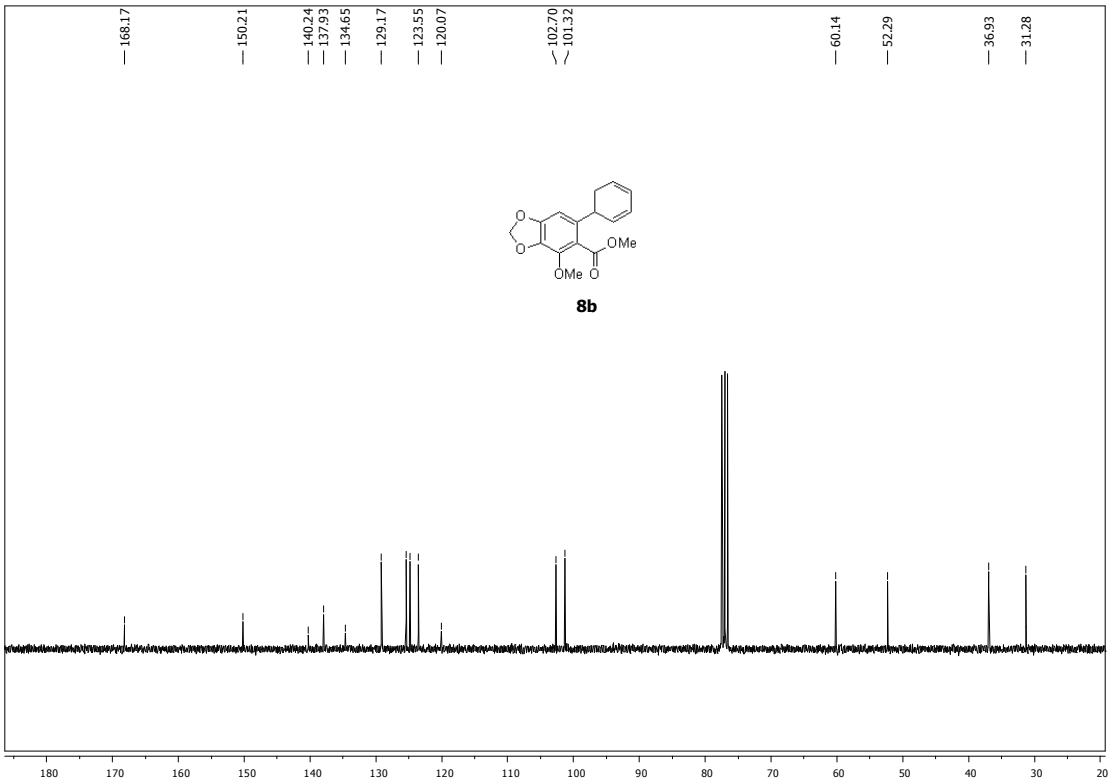
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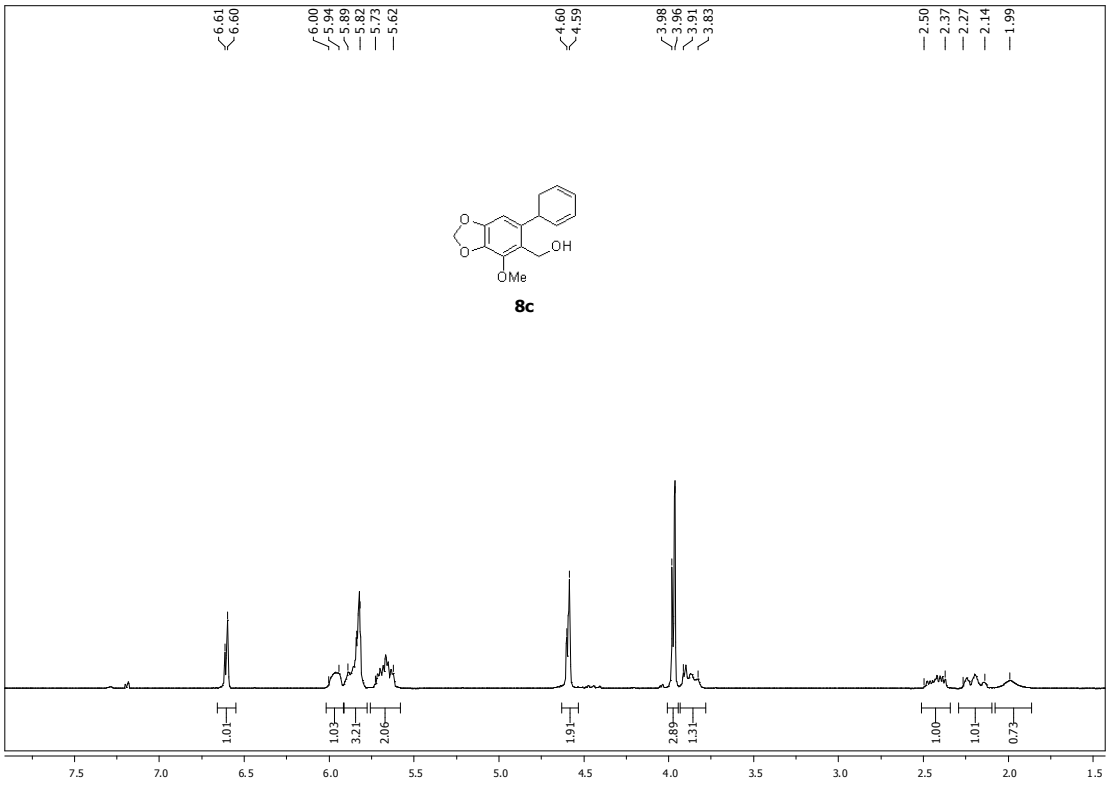
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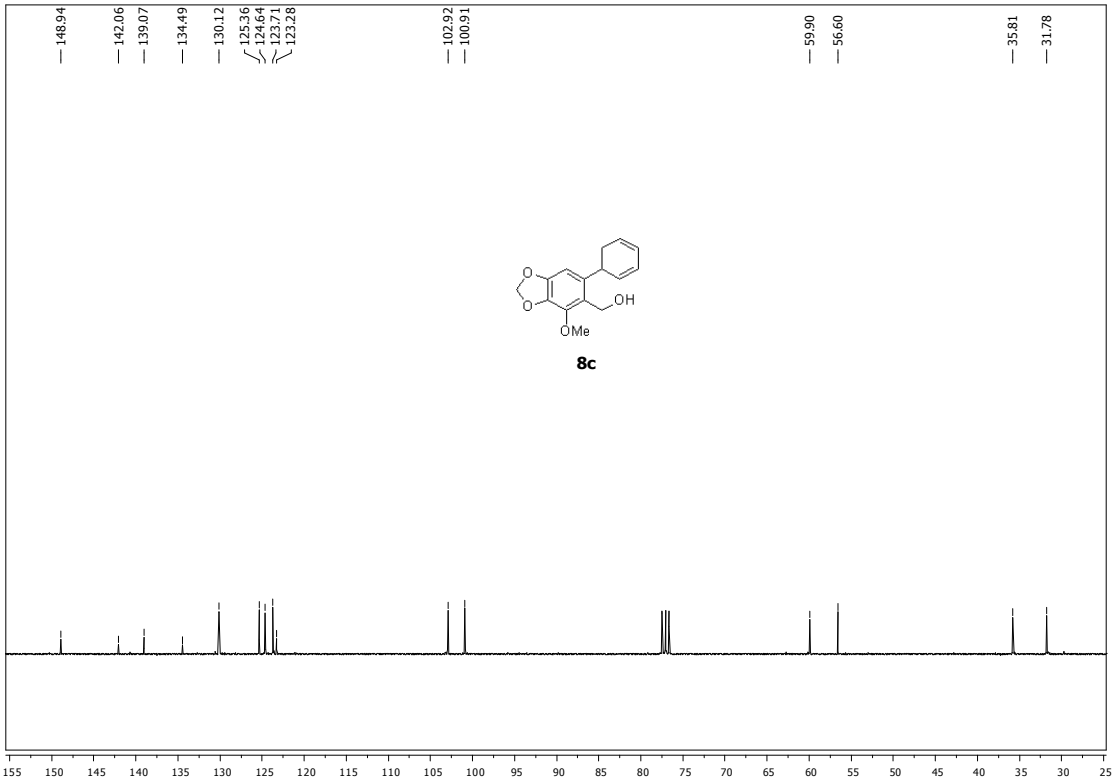
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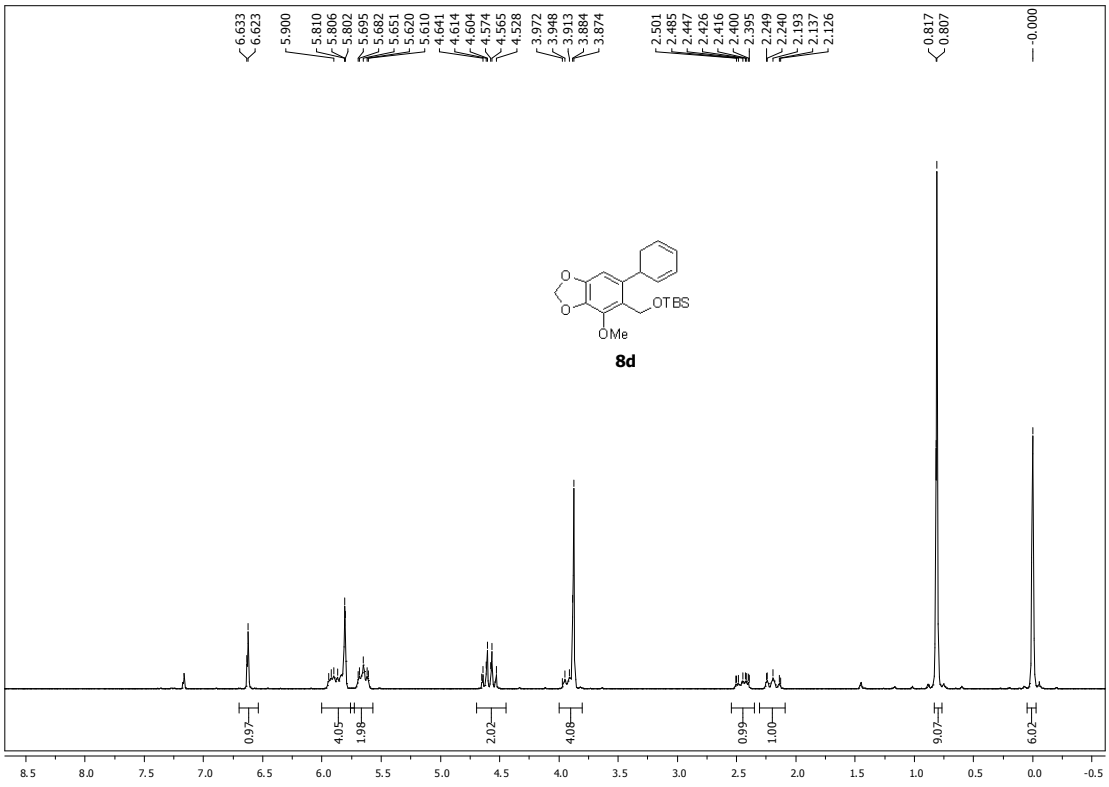
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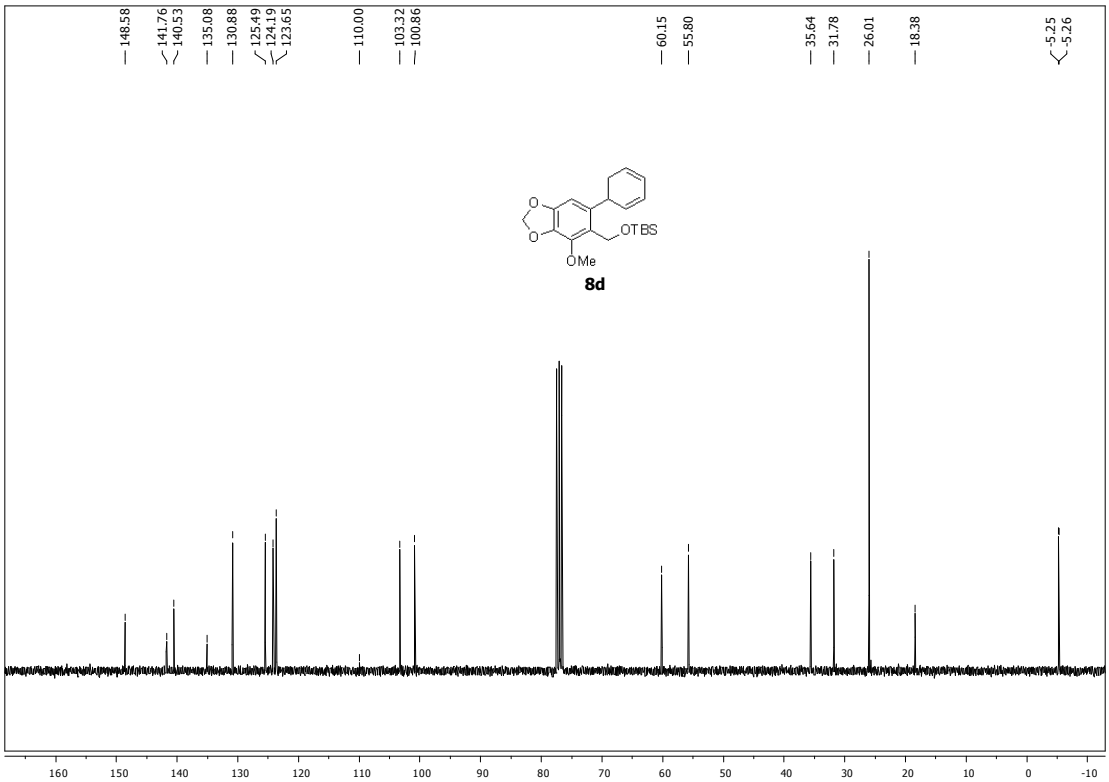
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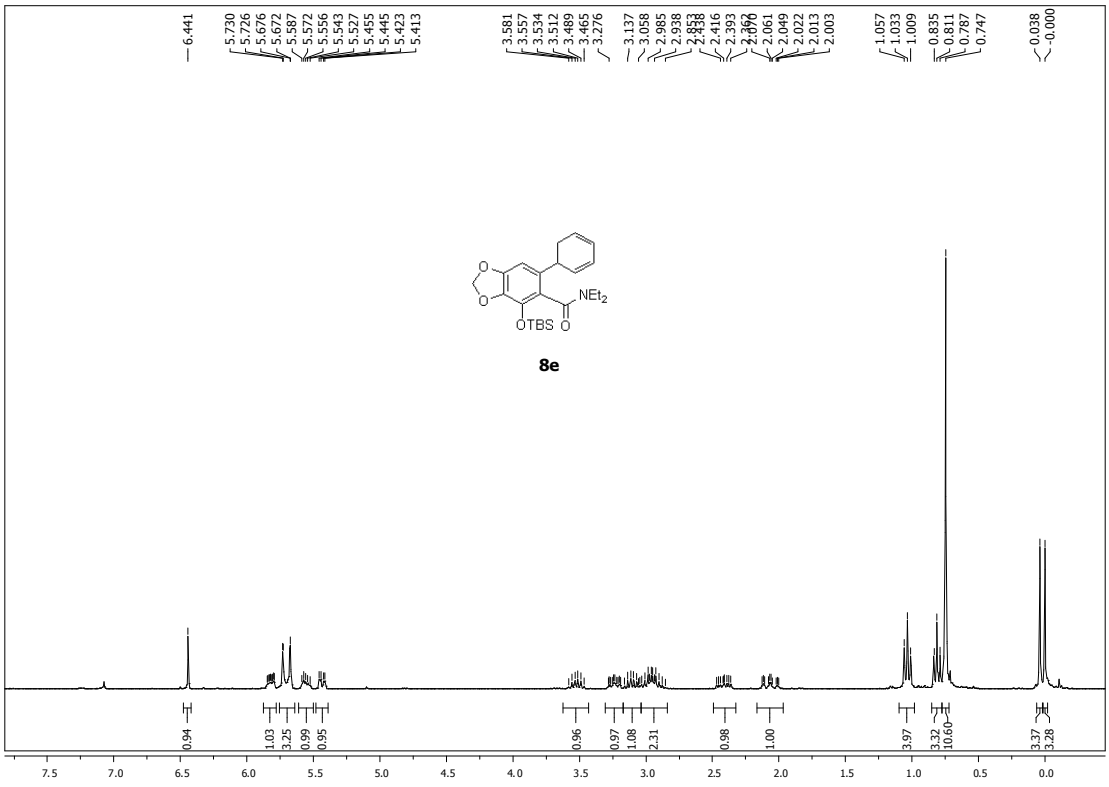
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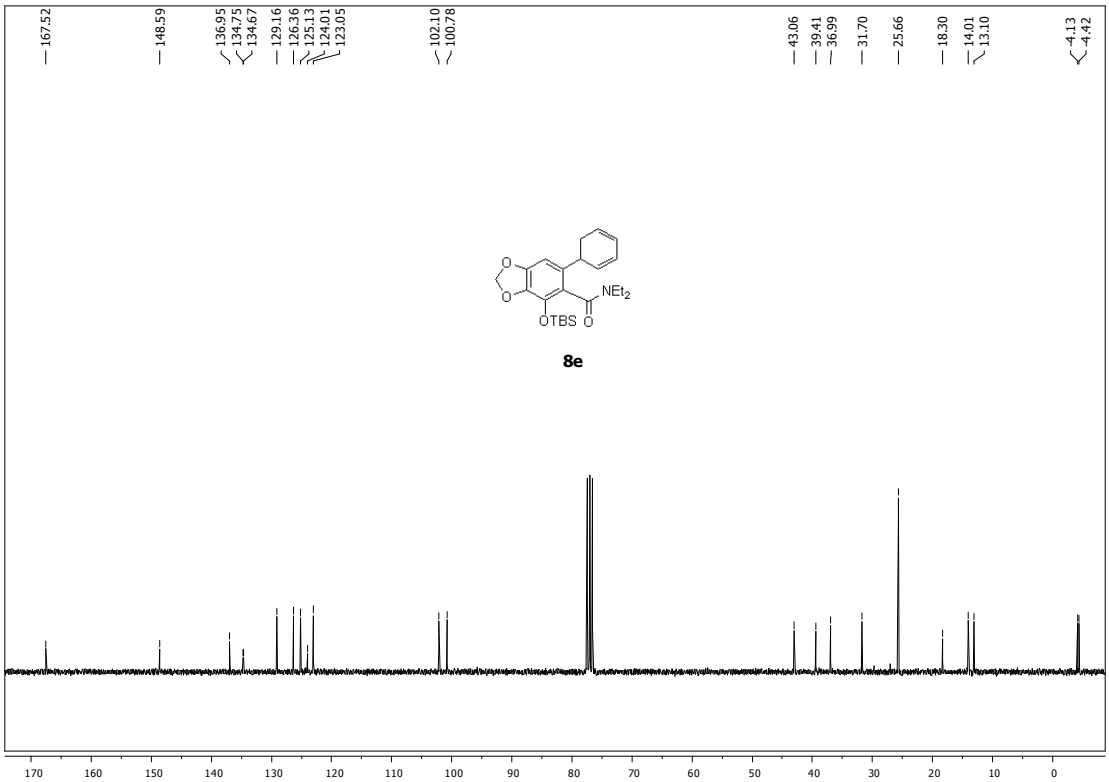
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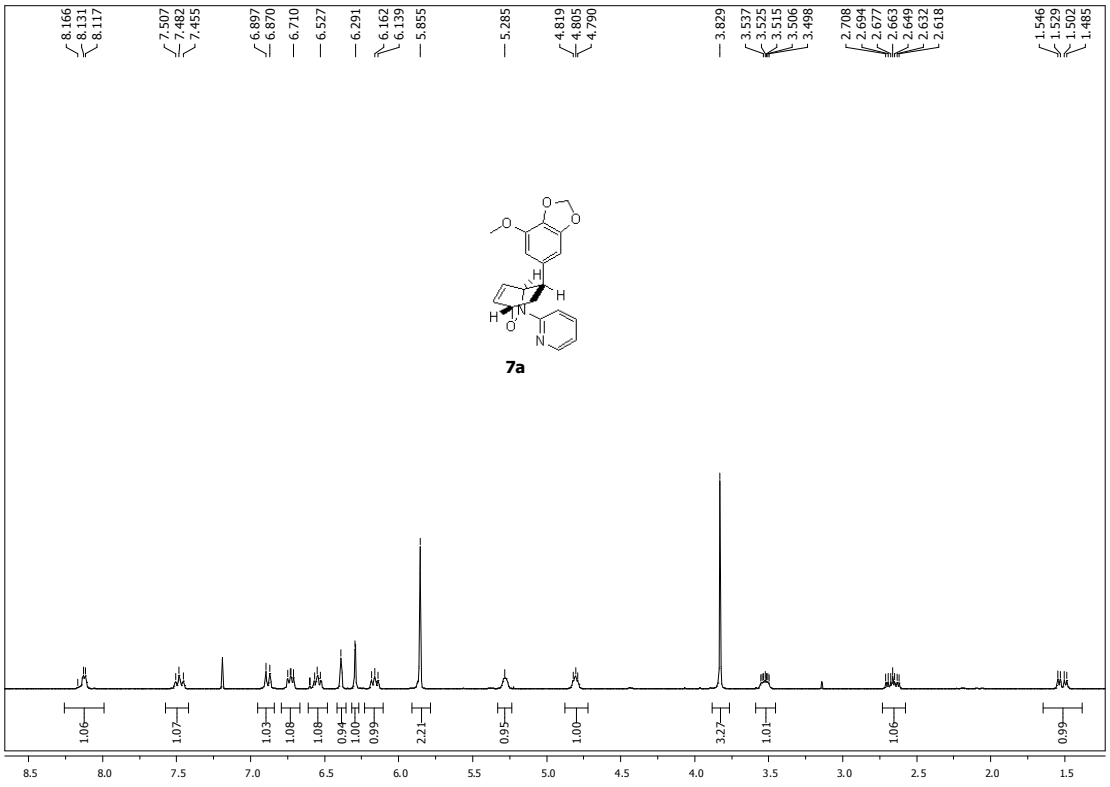
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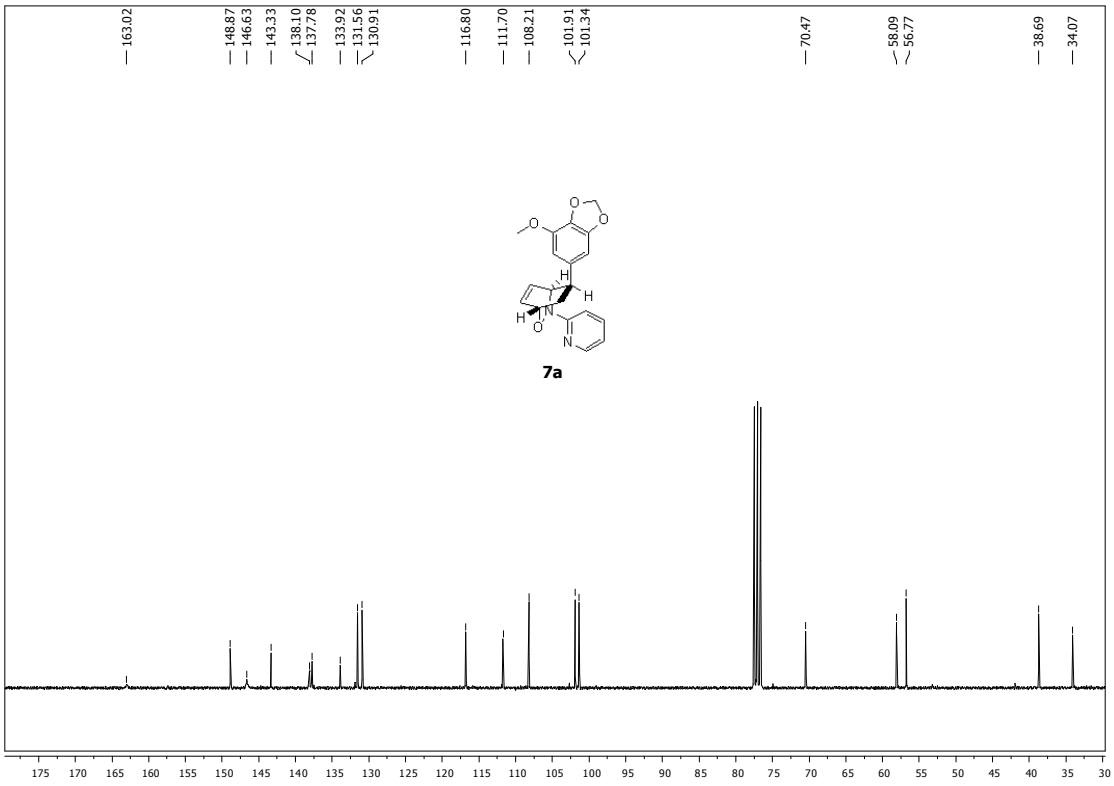
7a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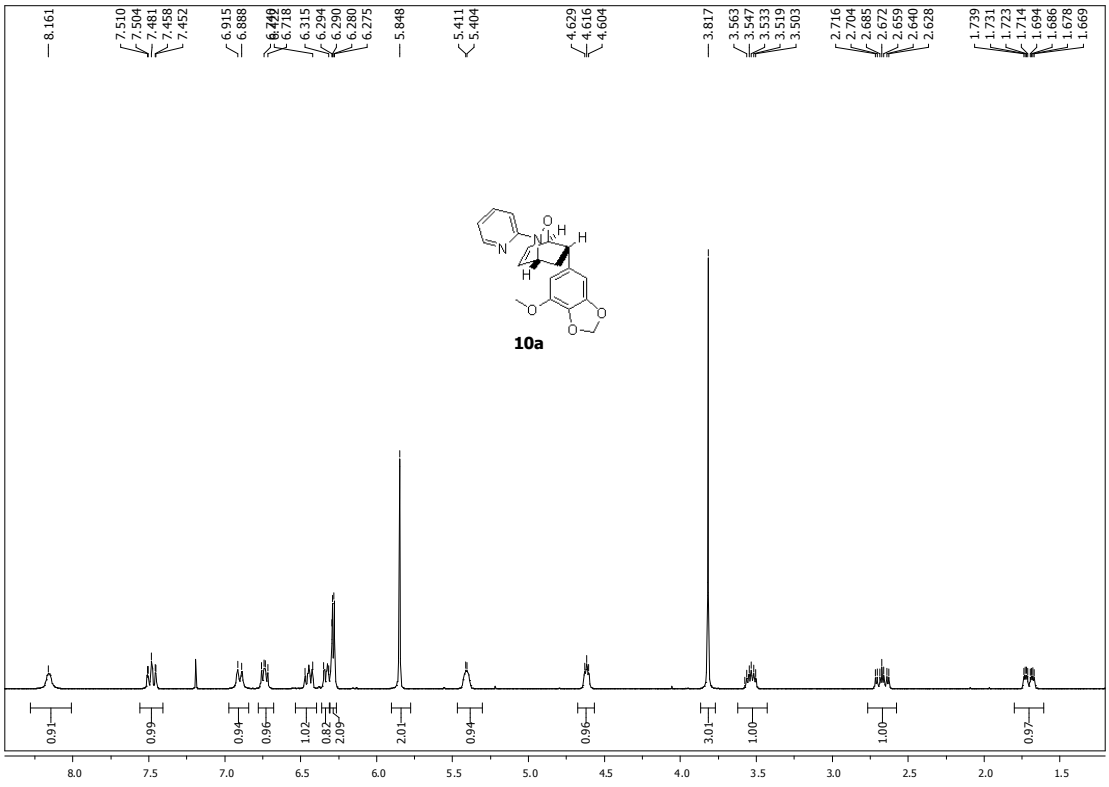
7a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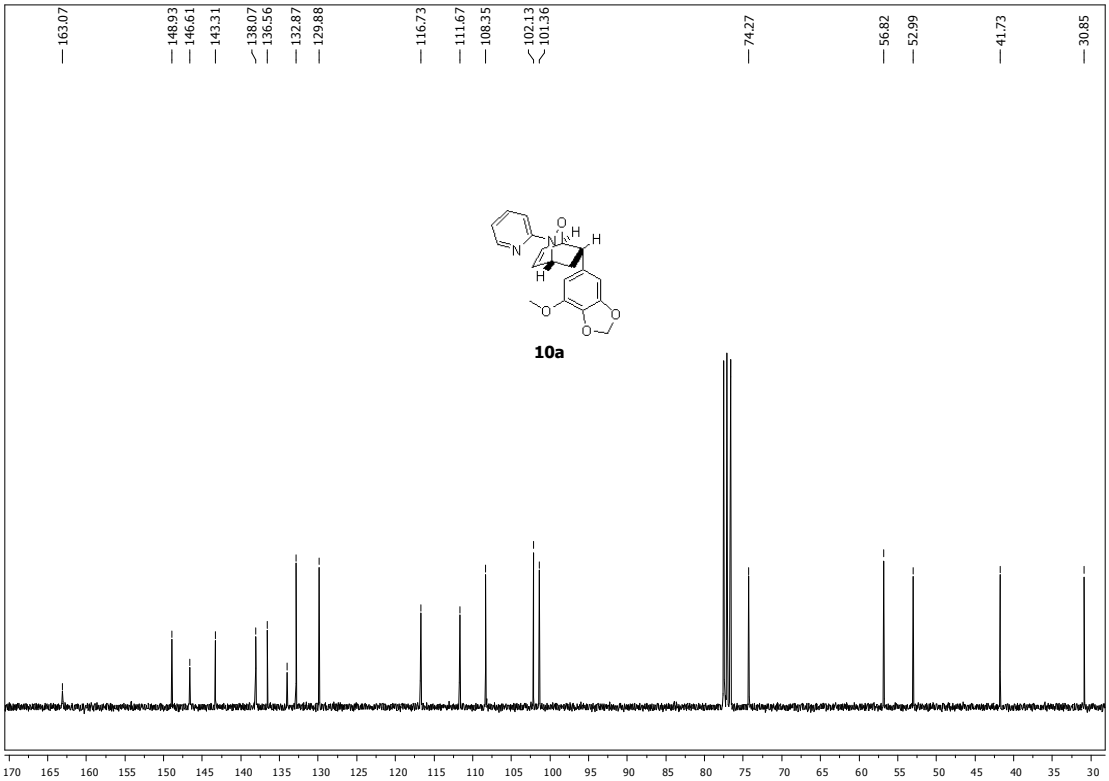
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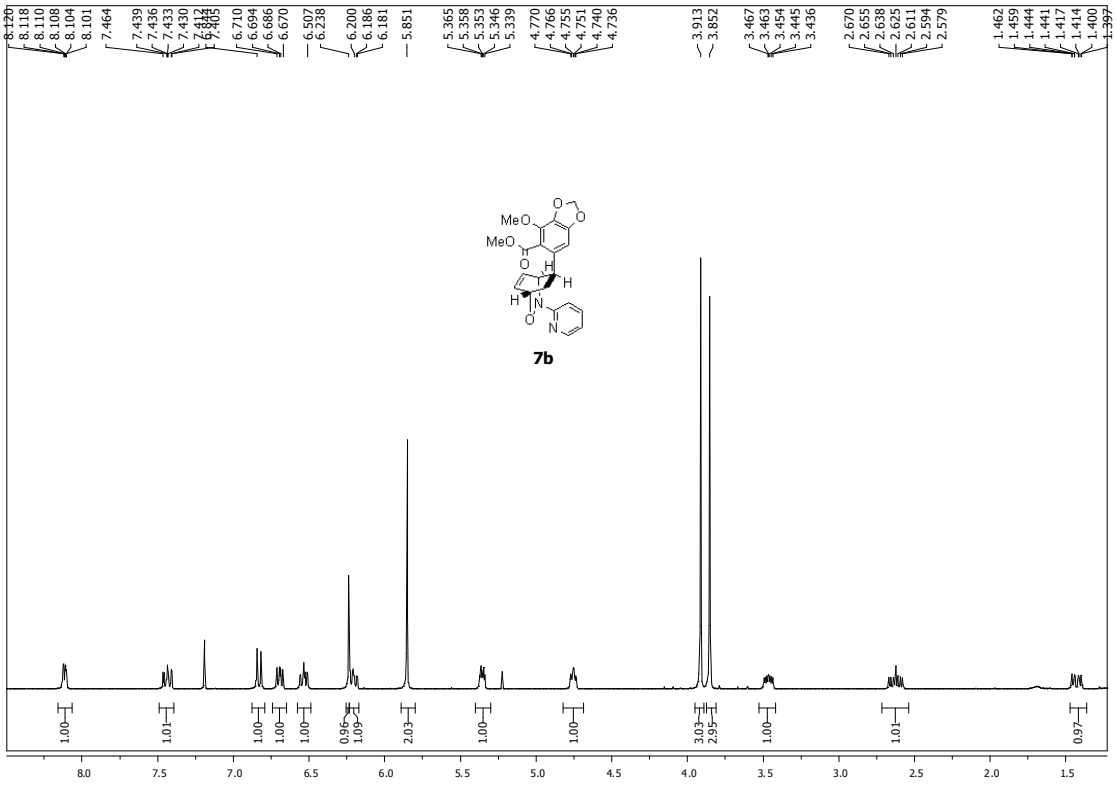
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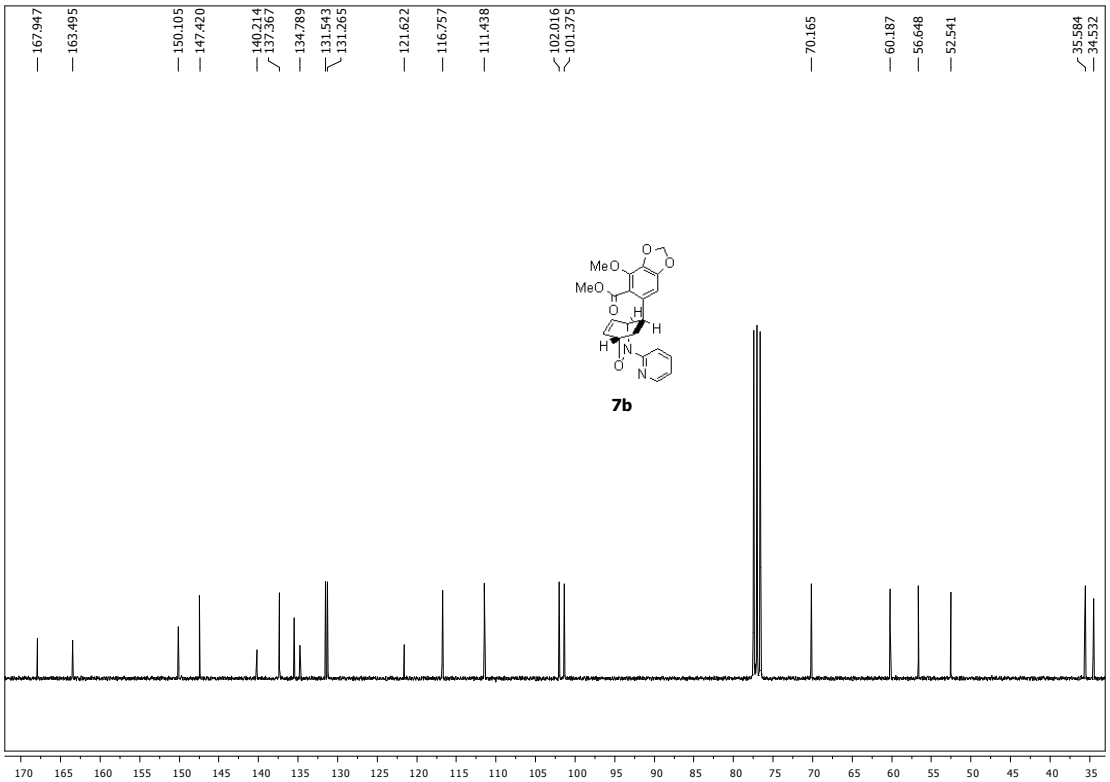
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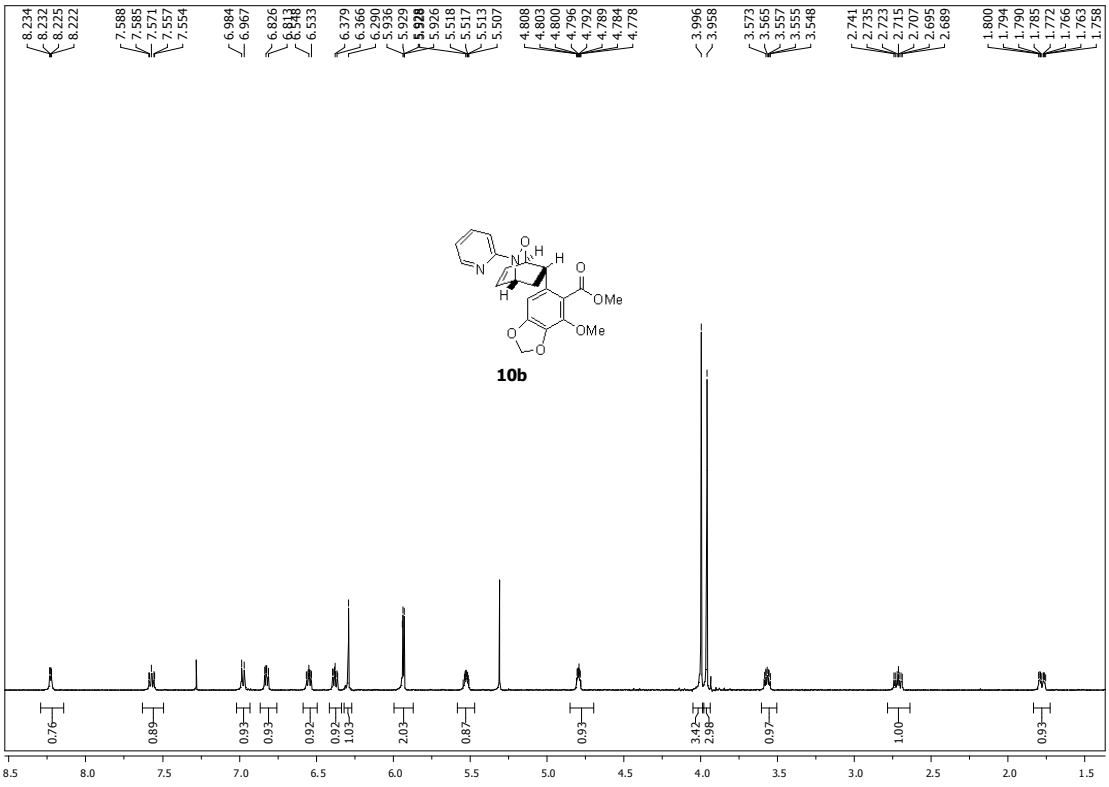
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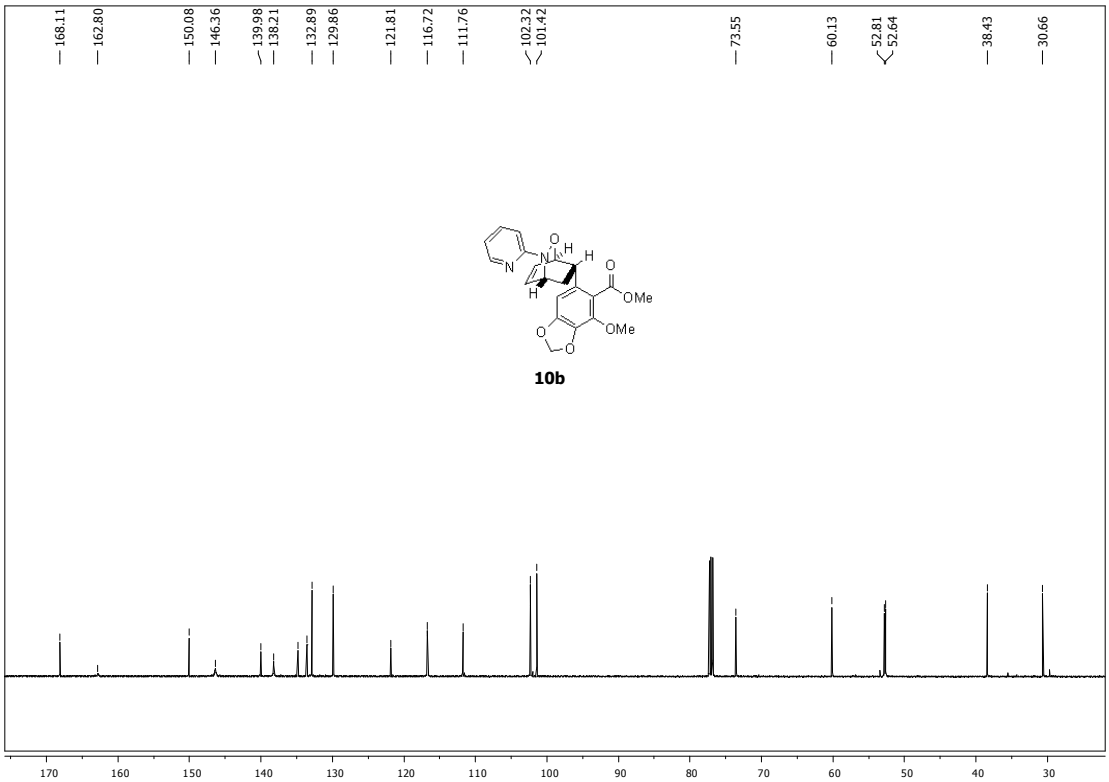
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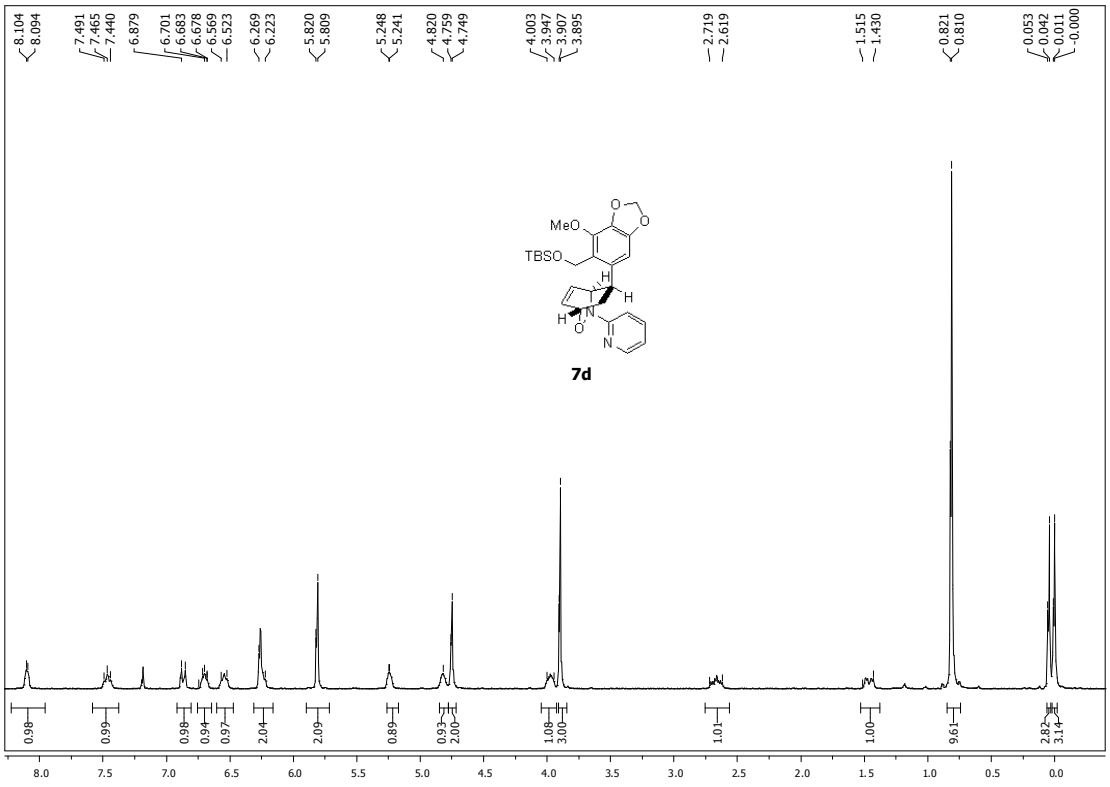
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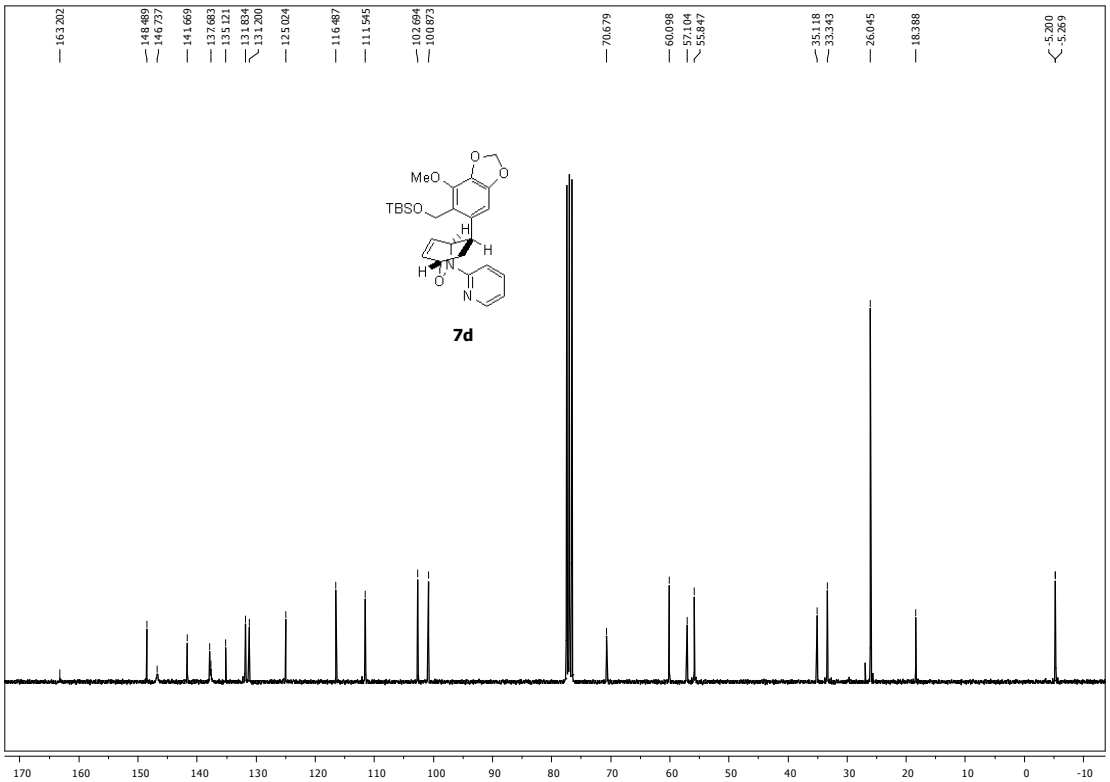
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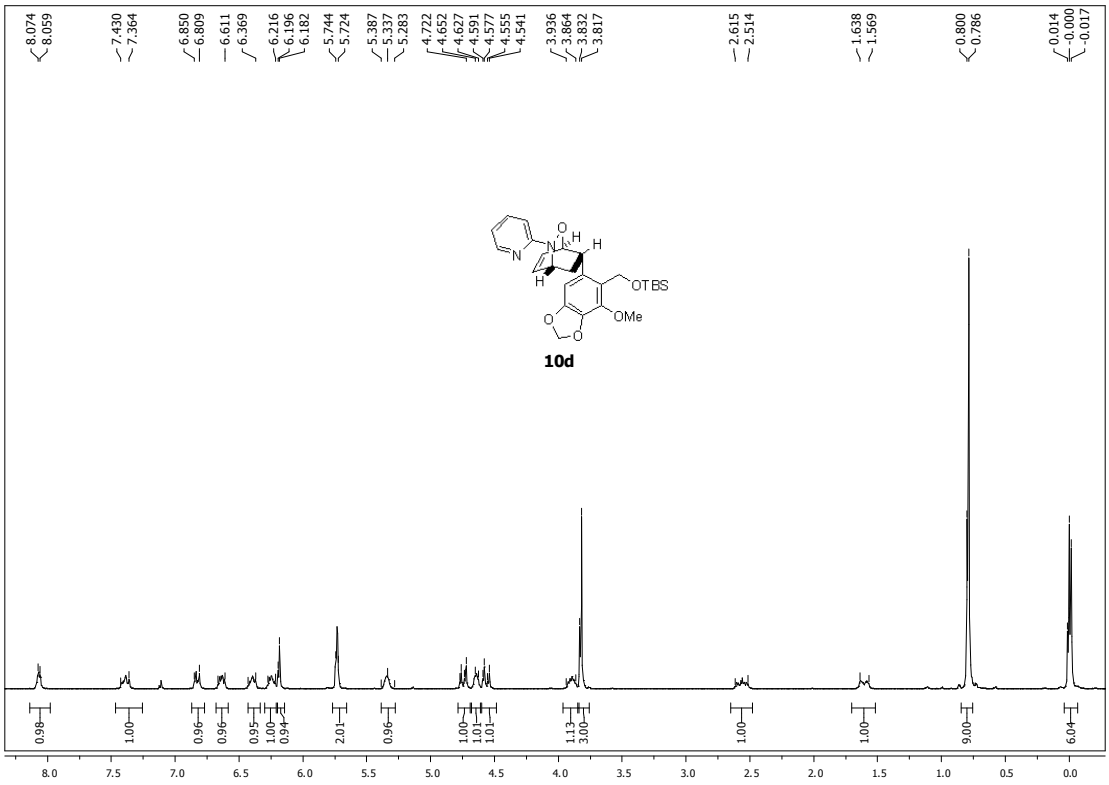
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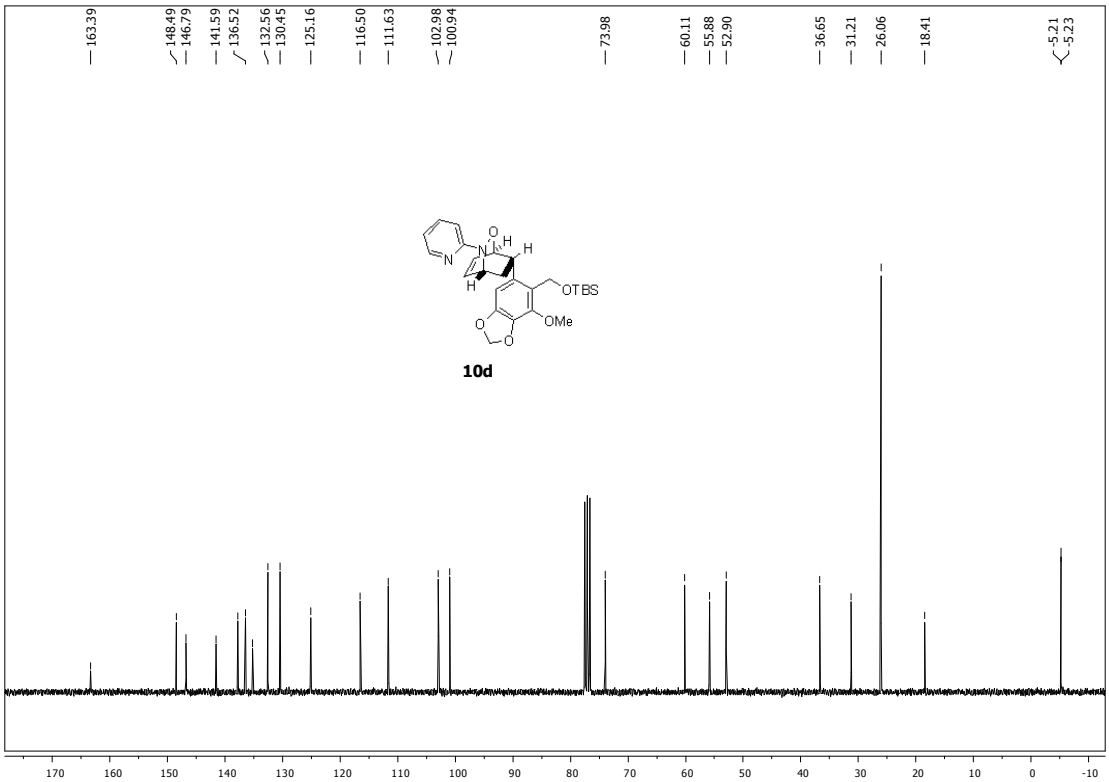
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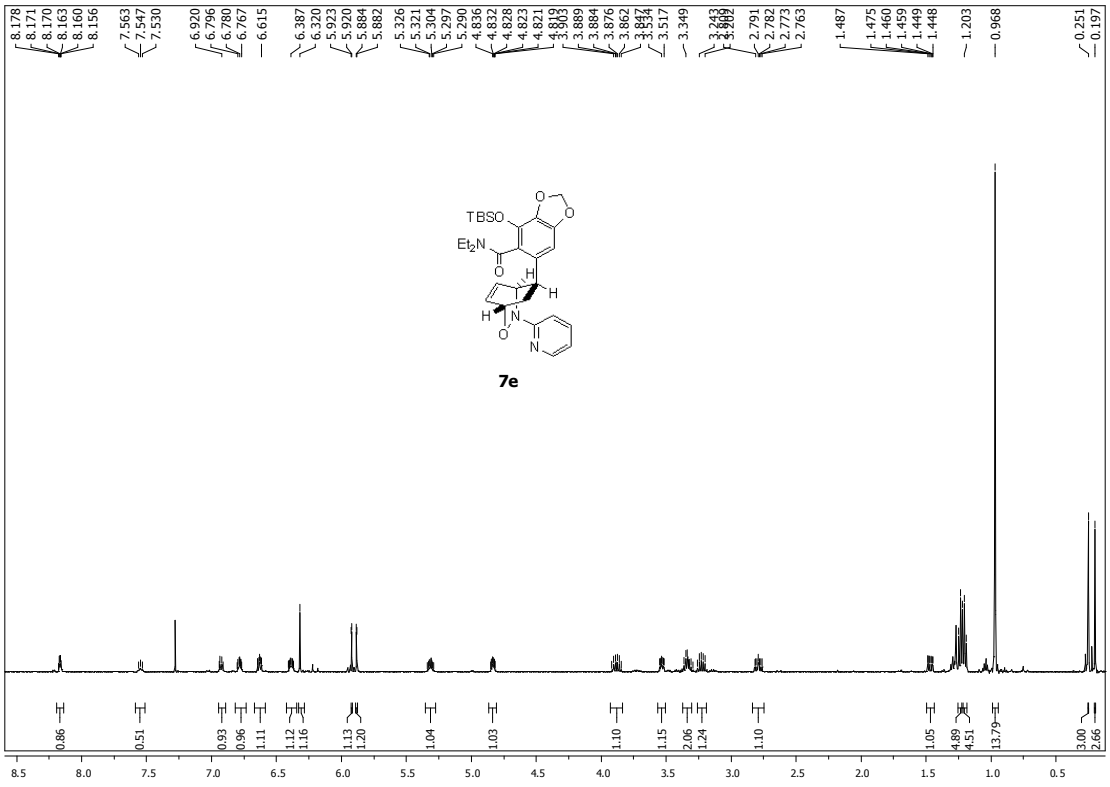
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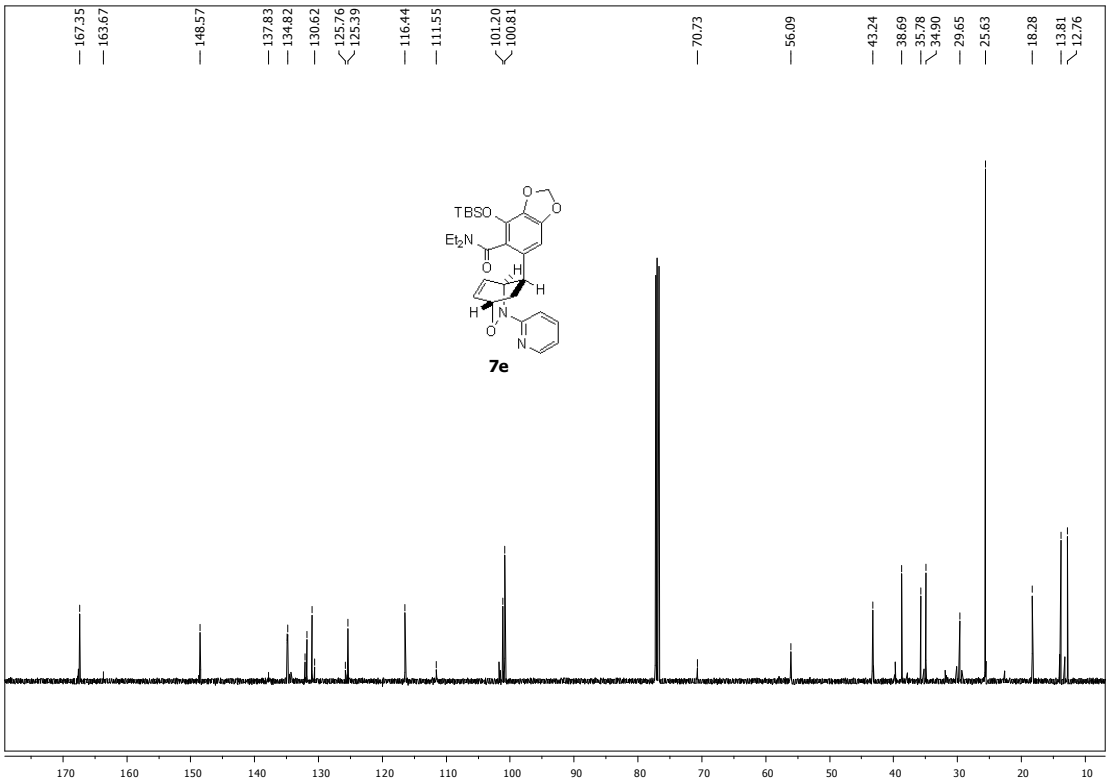
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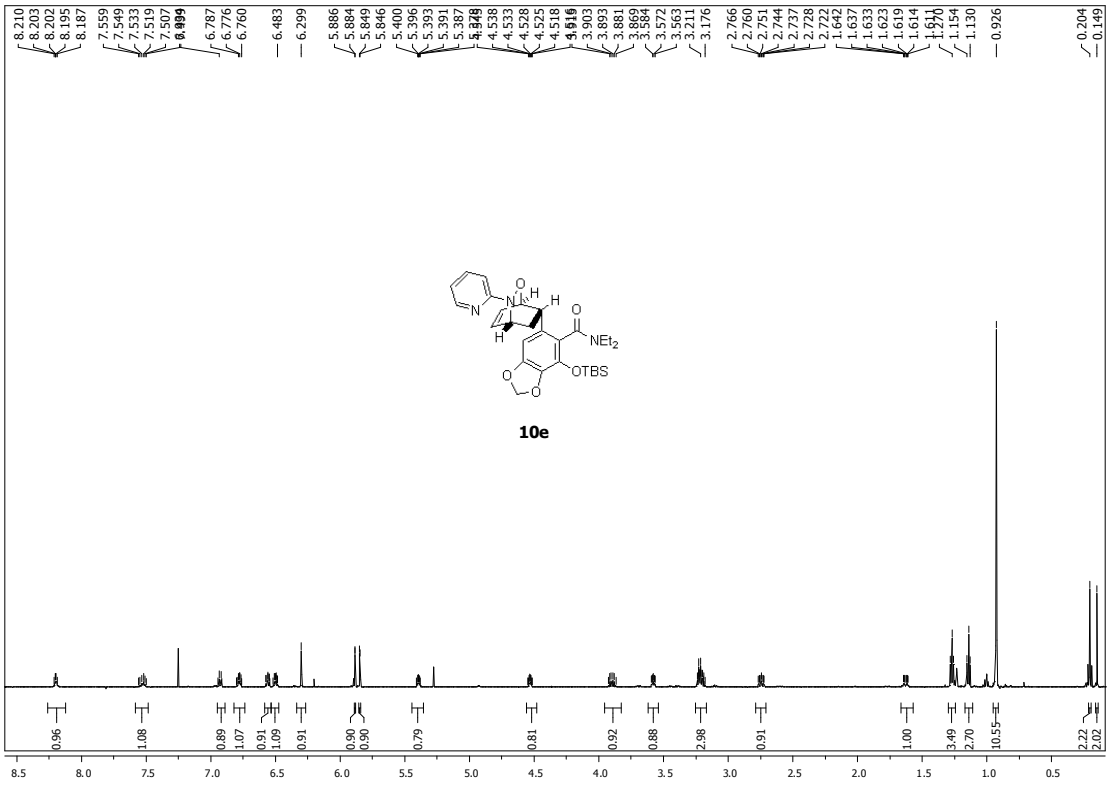
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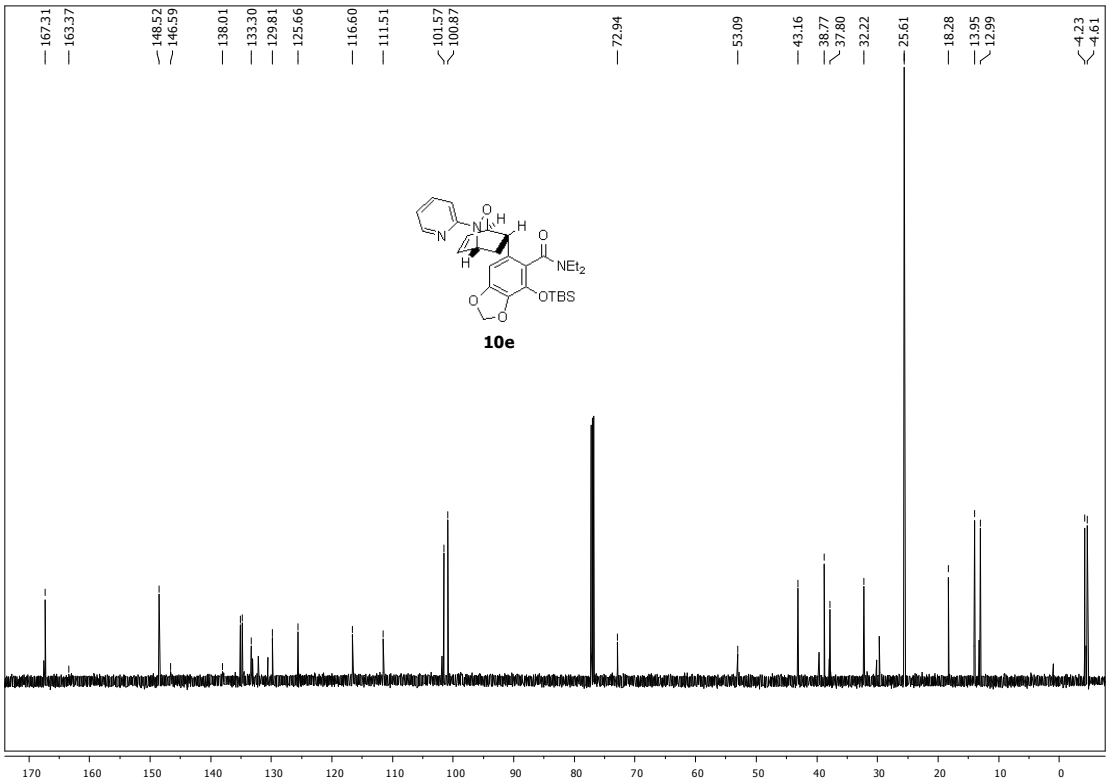
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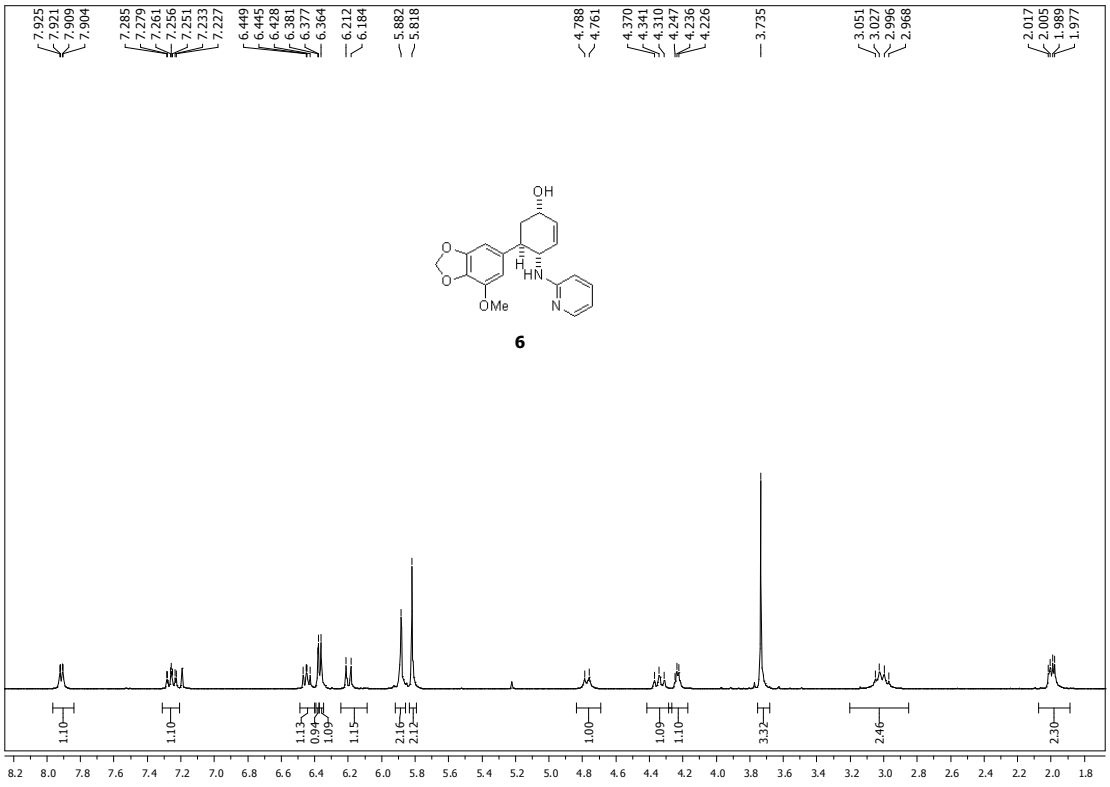
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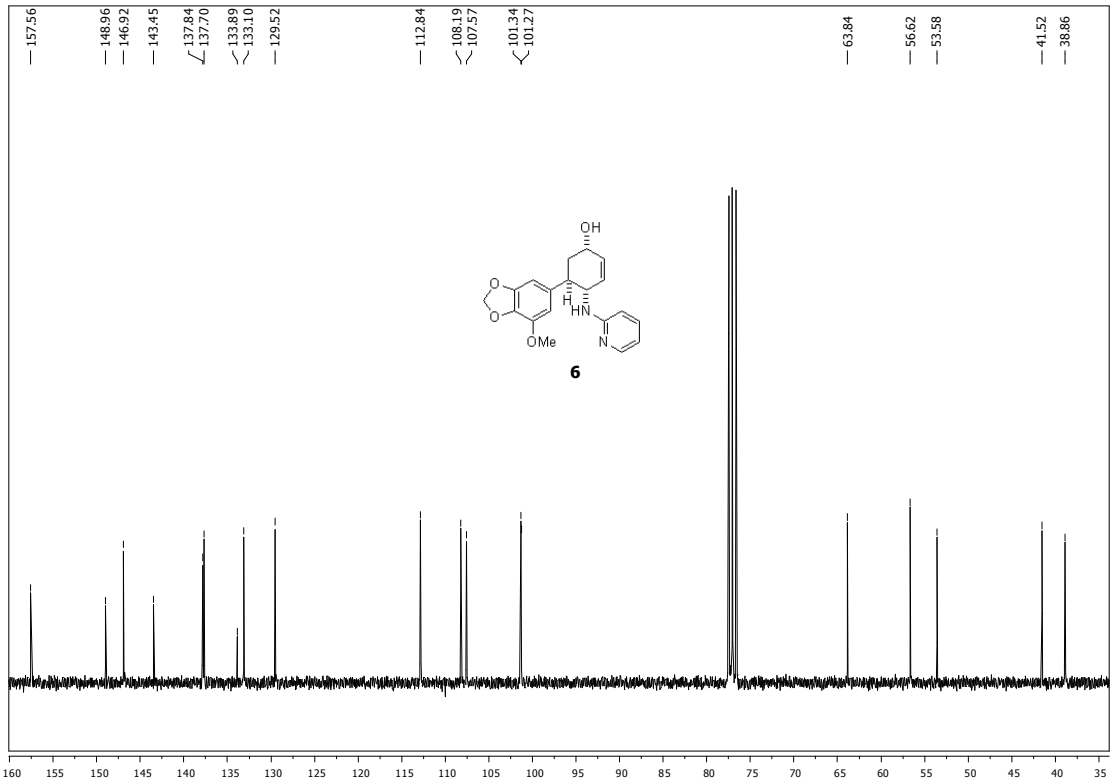
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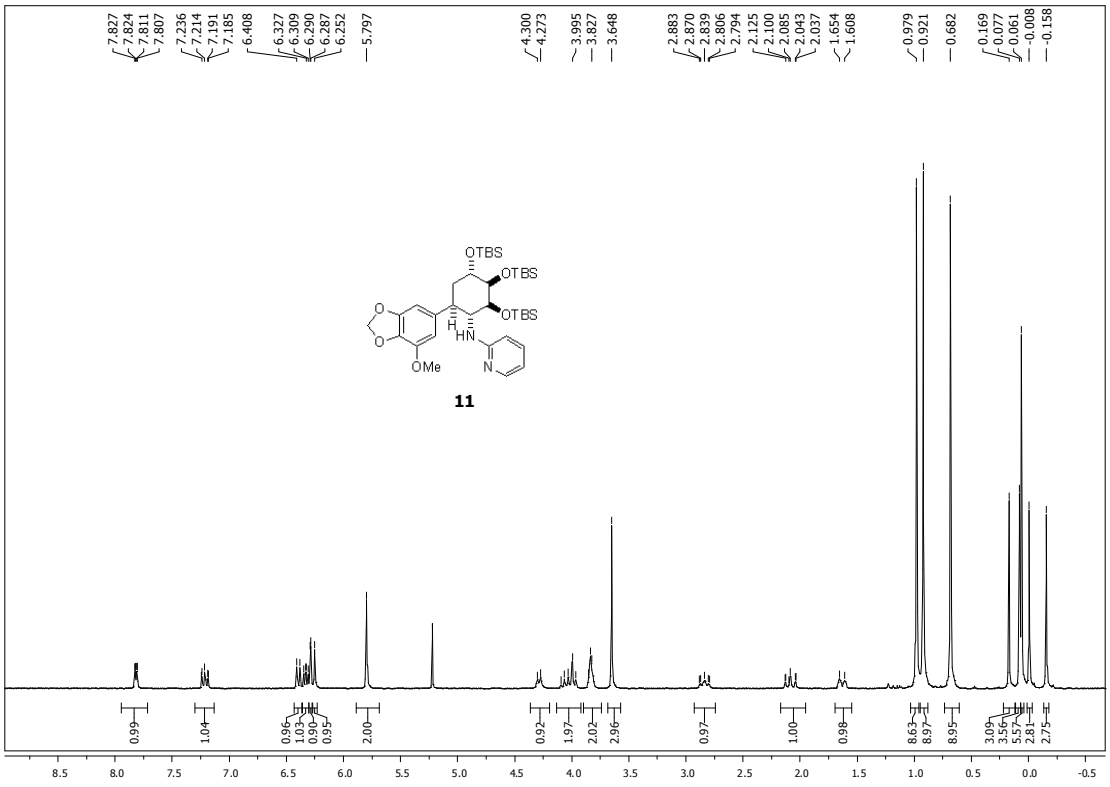
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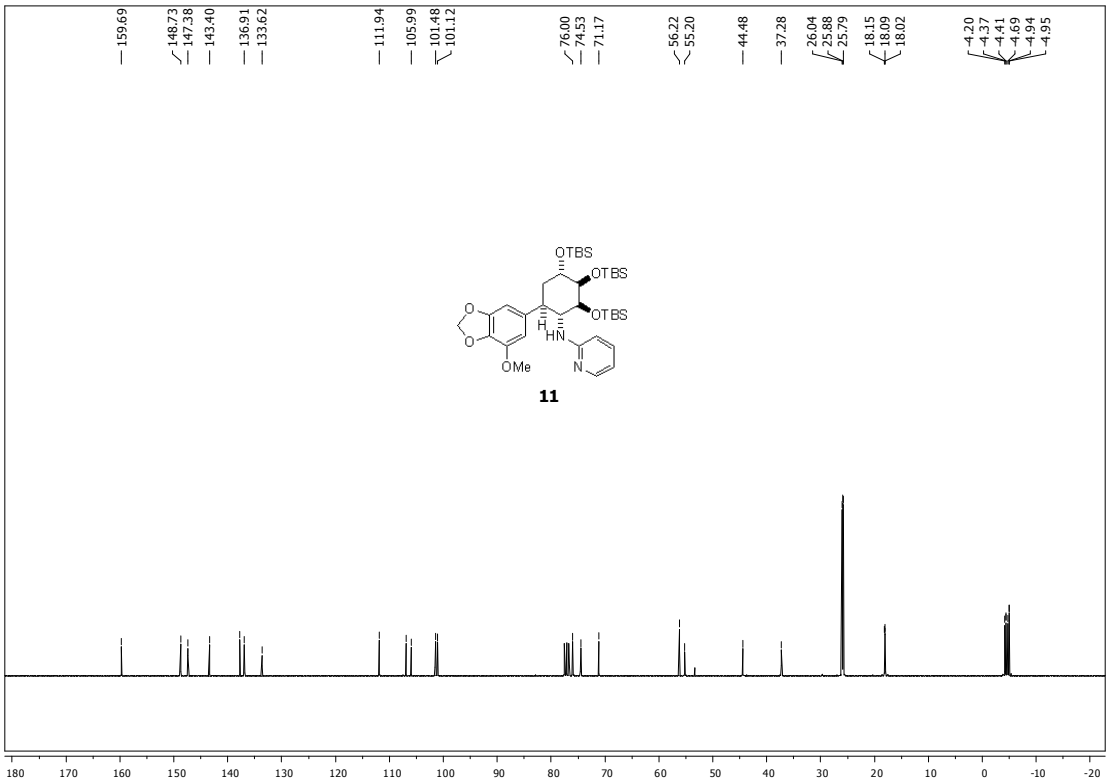
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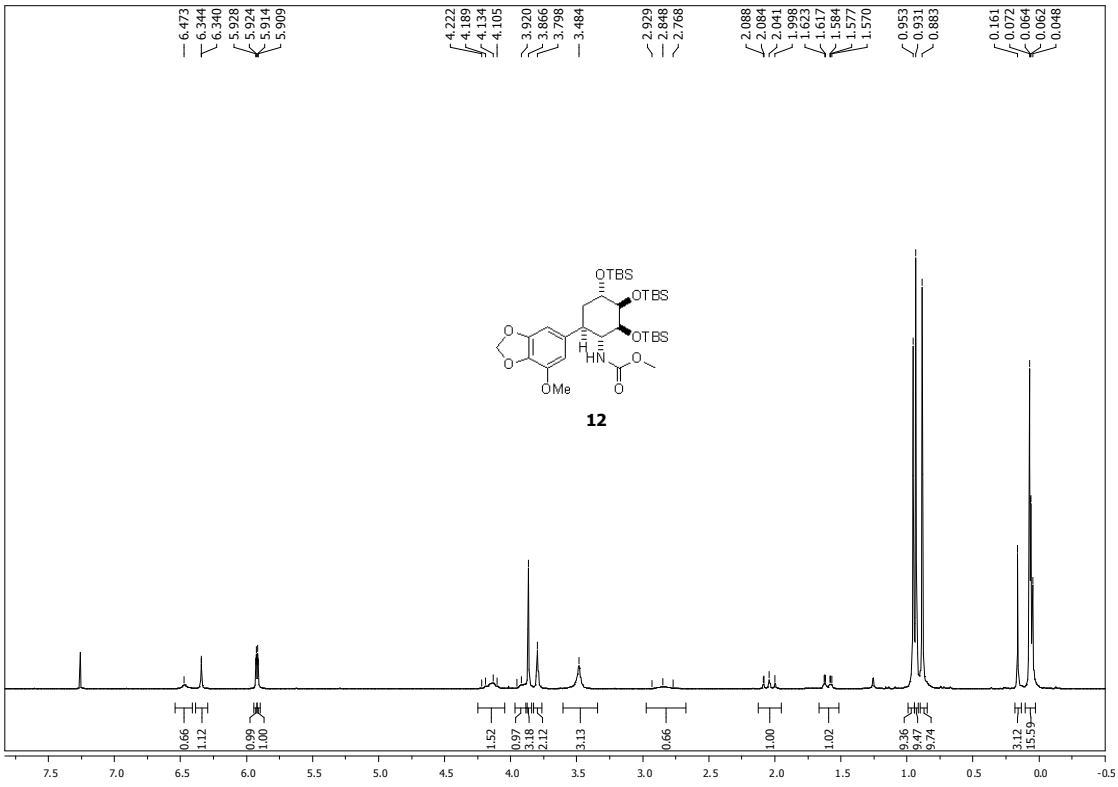
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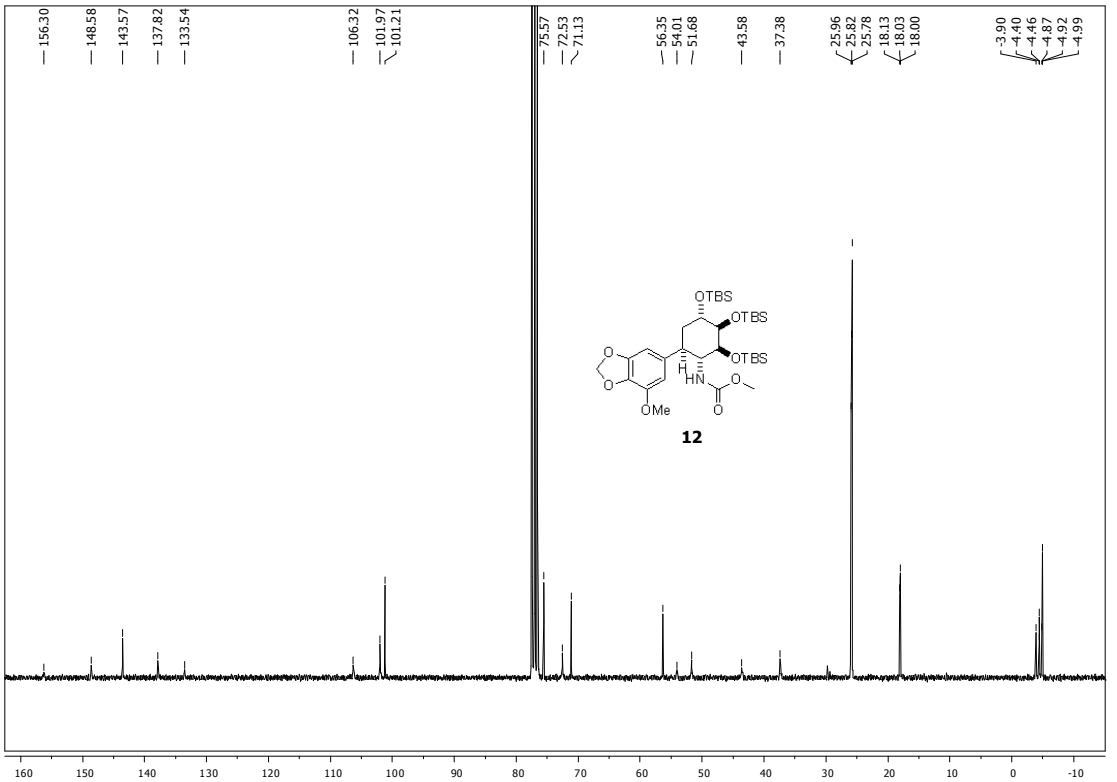
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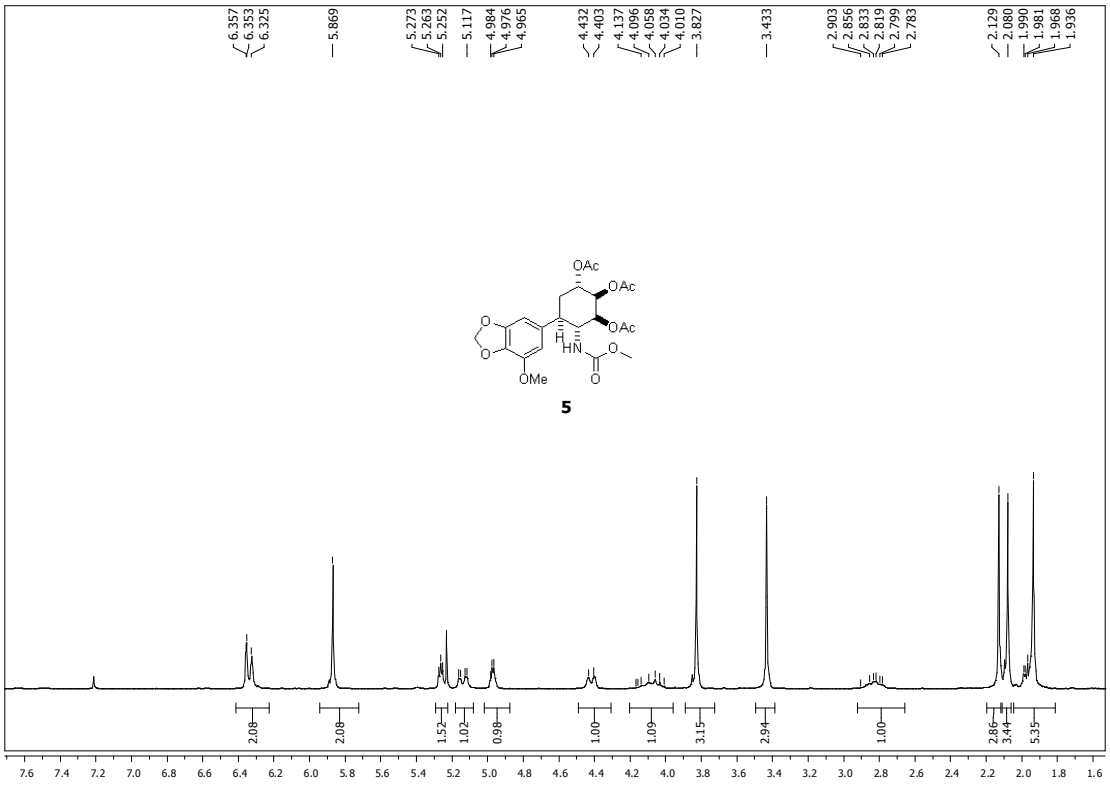
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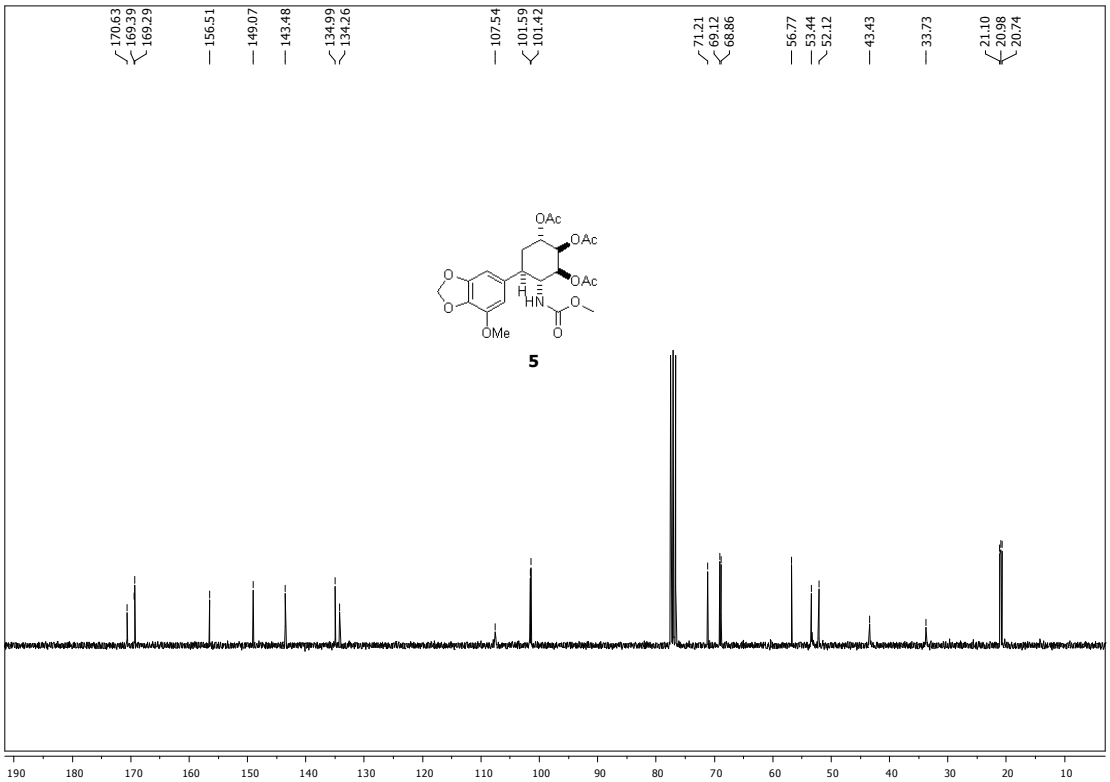
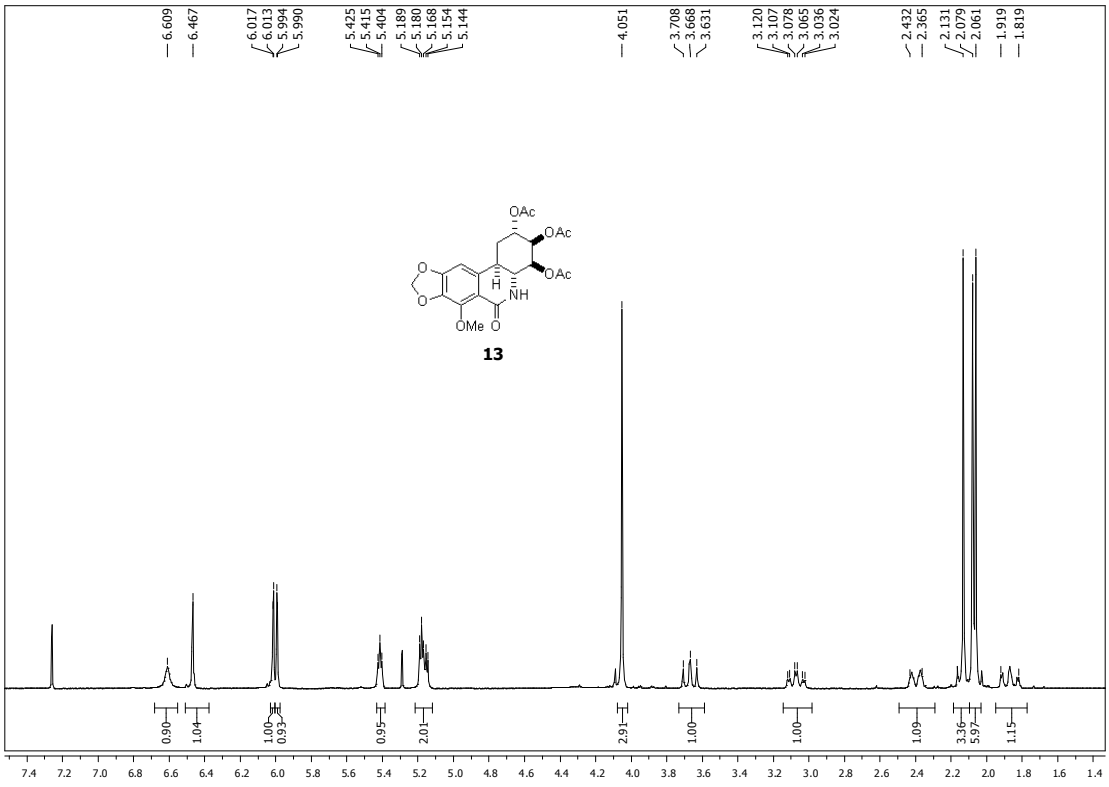
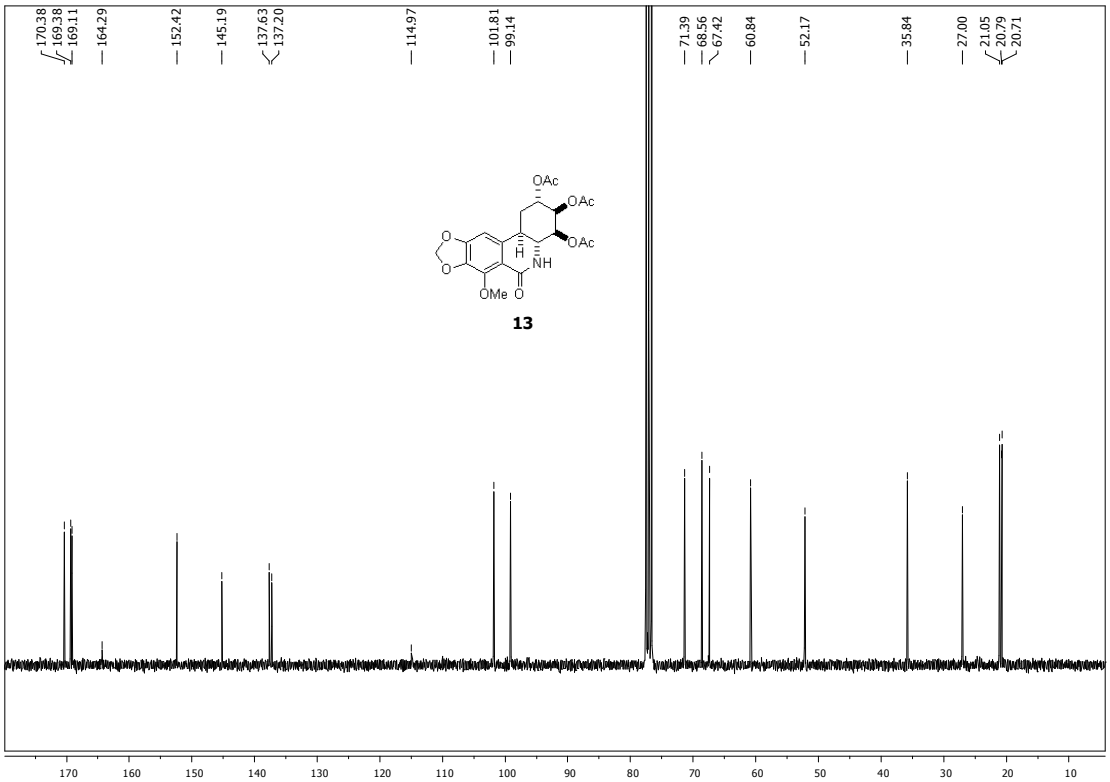
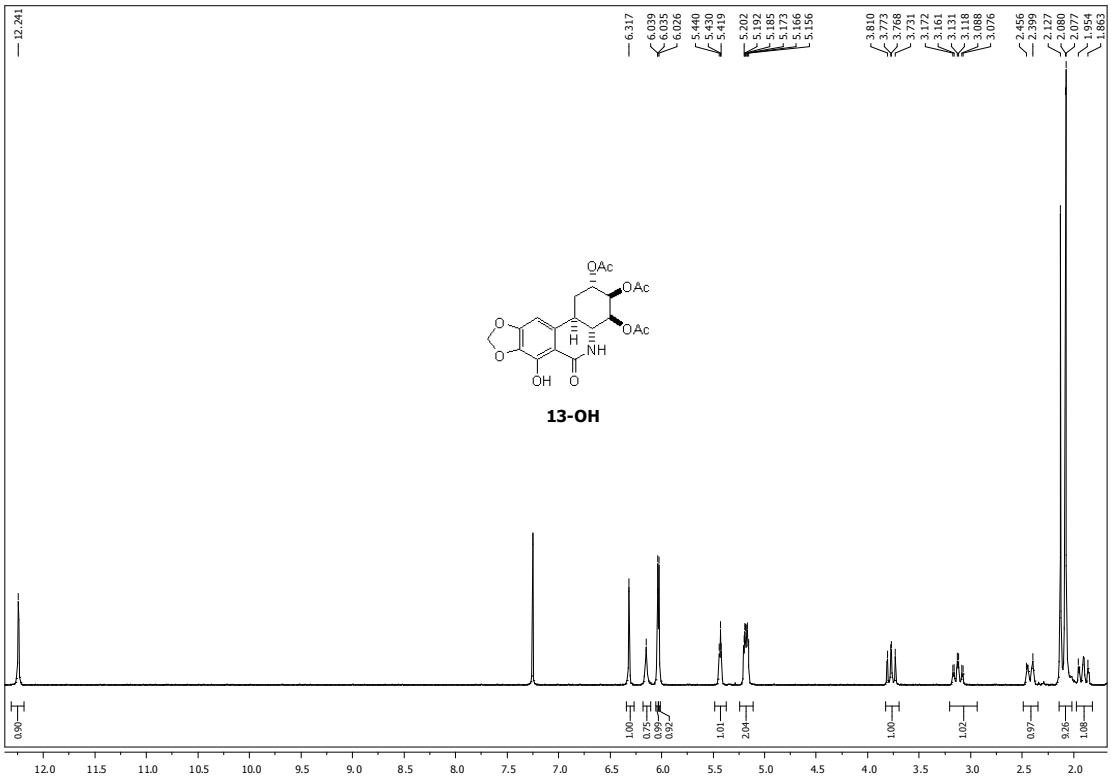
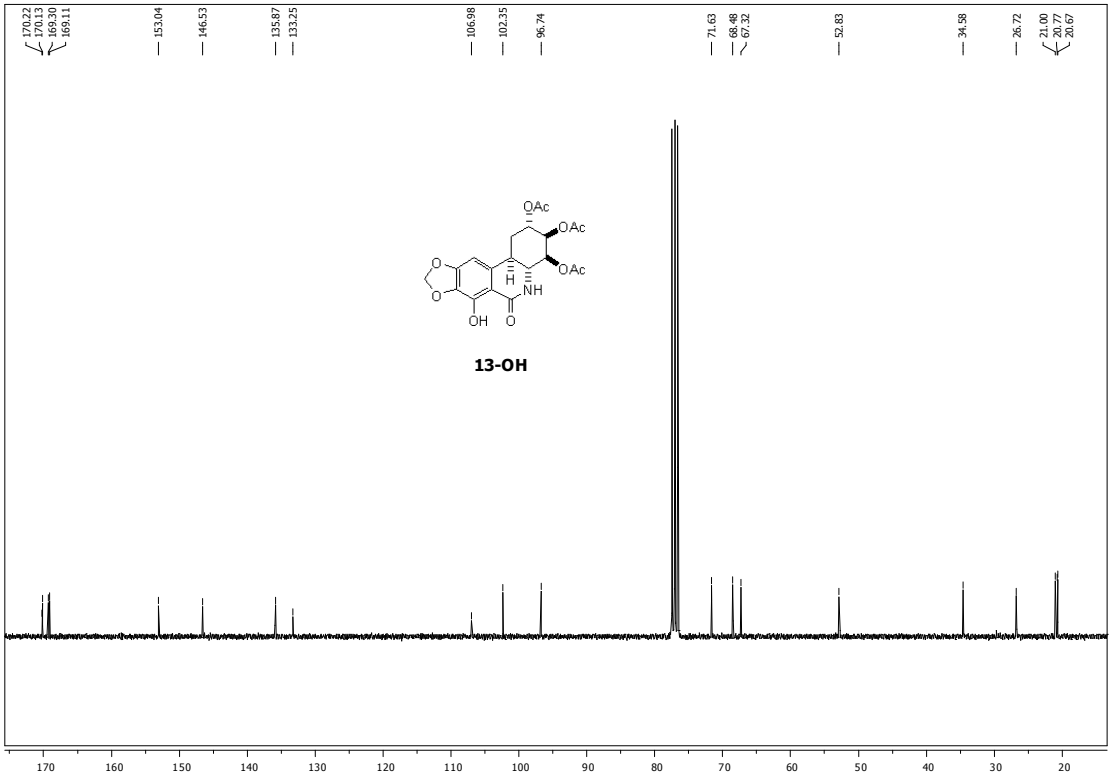
5.263
5.252
5.117
4.984
4.976
4.965
4.432
4.403
4.137
4.096
4.058
4.034
4.010
3.827
3.433
2.903
2.856
2.833
2.819
2.799
2.783
2.129
2.080
1.990
1.981
1.968
1.936
OAc
OAc
OAc
HN
OMe
5
2.08
2.08
1.52
1.02
0.98
1.00
1.09
3.15
2.94
1.00
2.86
3.44
5.35

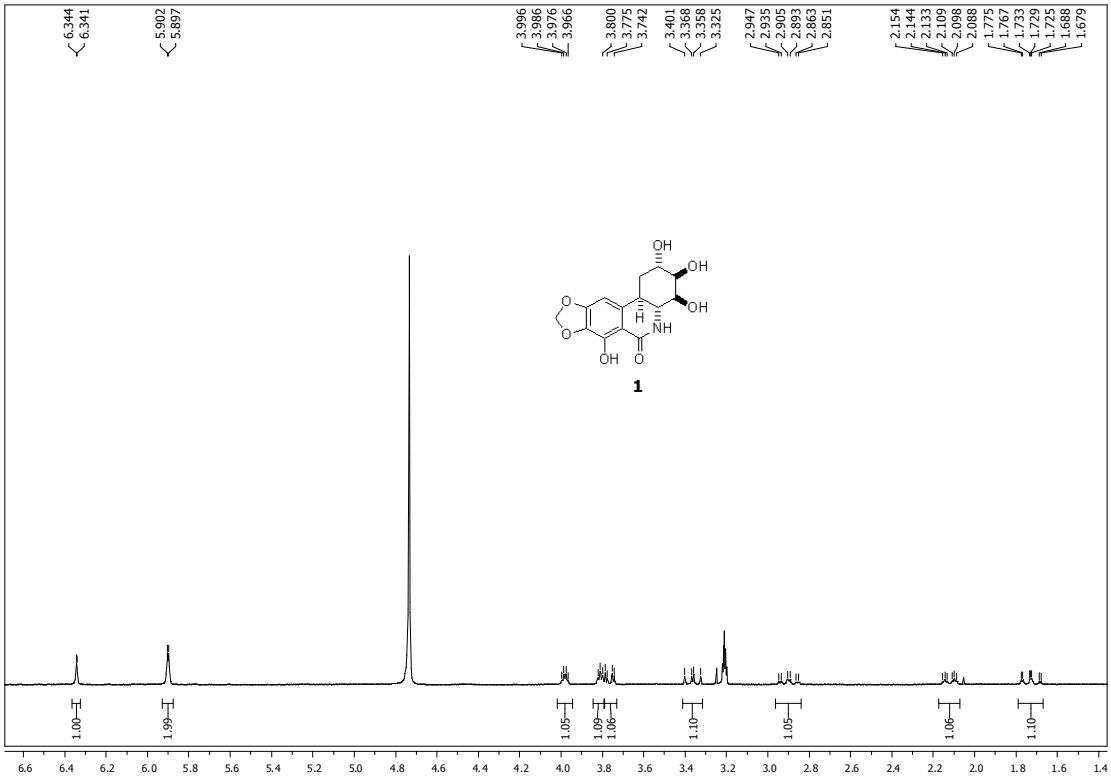

170.63
169.39
169.29
156.51
149.07
143.48
134.99
134.26
107.54
101.59
101.42
71.21
69.12
68.86
56.77
53.44
52.12
43.43
33.73
21.10
20.98
20.74
OAc
OAc
OAc
HN
OMe
5

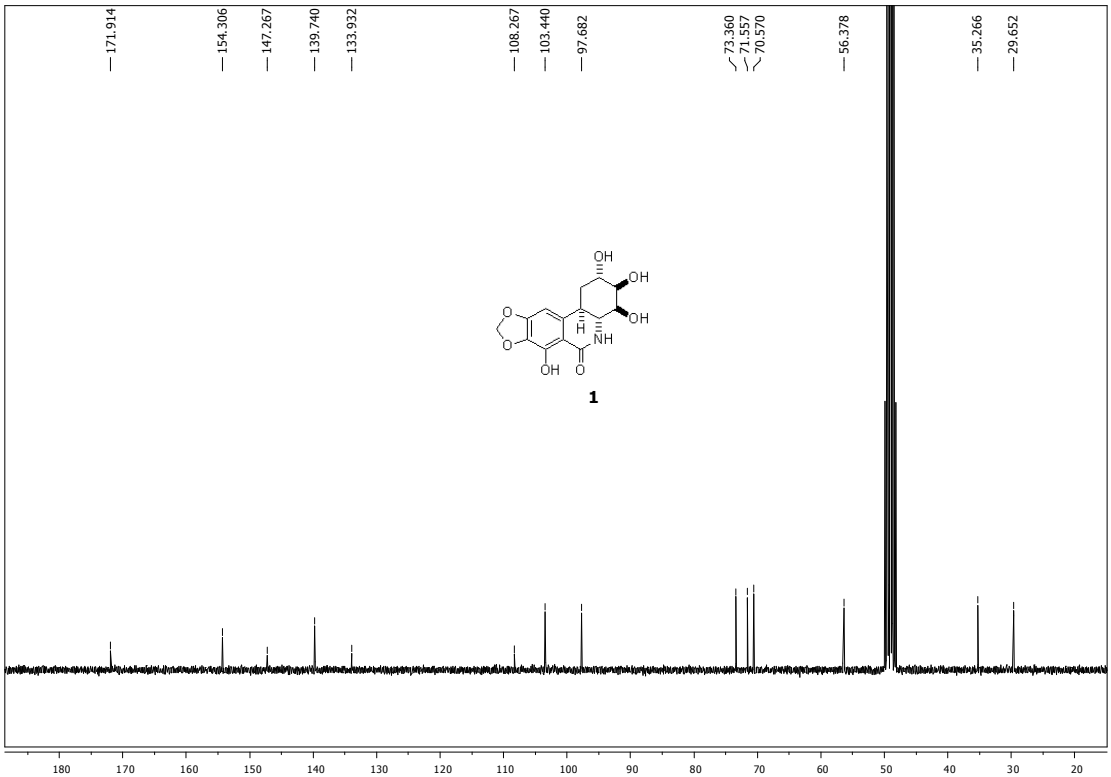

6.609
6.467
6.017
6.013
5.994
5.990
5.425
5.415
5.404
5.189
5.180
5.168
5.154
5.144
4.051
3.708
3.668
3.631
3.120
3.107
3.078
3.065
3.036
3.024
2.432
2.365
2.131
2.079
2.061
1.919
1.819
0.90
1.04
1.00
0.93
0.95
2.01
2.91
1.00
1.00
1.09
3.36
5.97
1.15
OAc
OAc
OAc
H
NH
OMe
O
13


170.38
169.38
169.11
164.29
152.42
145.19
137.63
137.20
114.97
101.81
99.14
71.39
68.56
67.42
60.84
52.17
35.84
27.00
21.05
20.79
20.71
OAc
OAc
OAc
H
NH
OMe
O
13

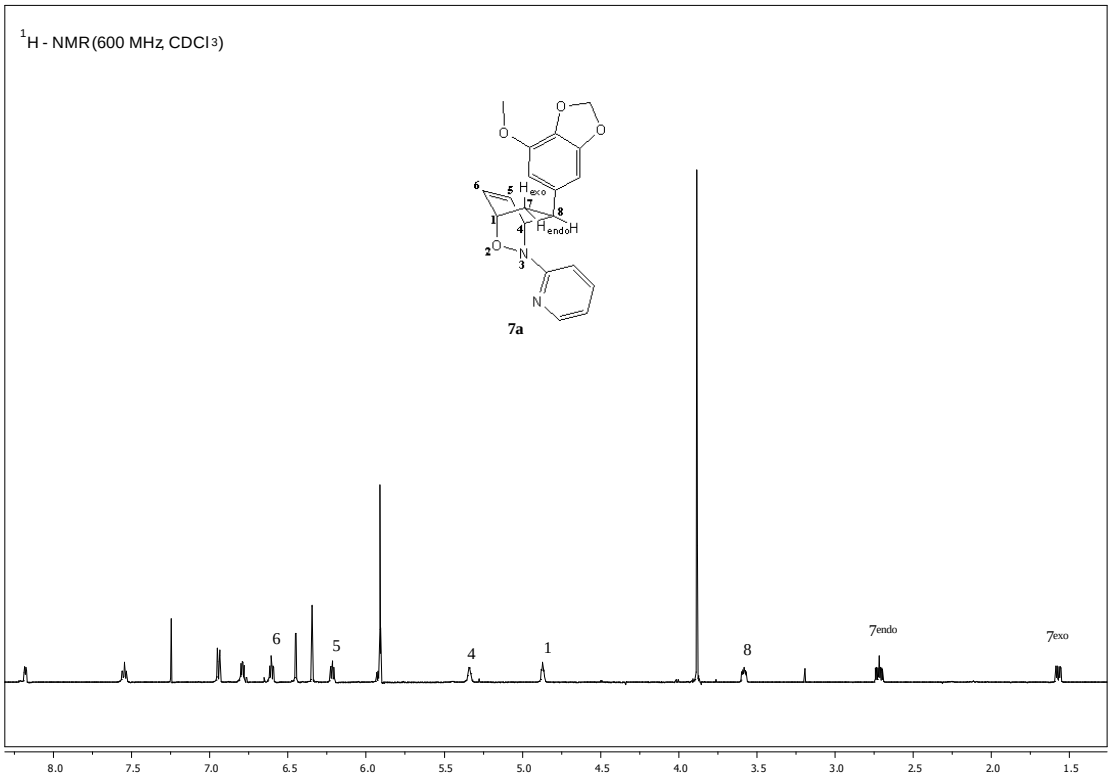

12.241
6.317
6.039
6.035
6.026
5.440
5.430
5.419
5.202
5.192
5.185
5.173
5.166
5.156
3.810
3.773
3.768
3.731
3.172
3.161
3.131
3.118
3.088
3.076
2.456
2.399
2.127
2.090
2.077
1.954
1.863
OAc
OAc
OAc
H
NH
O
O
OH
O
13-OH
0.90
1.00
0.75
0.99
0.92
1.01
2.04
1.00
1.02
0.97
9.26
1.08
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0

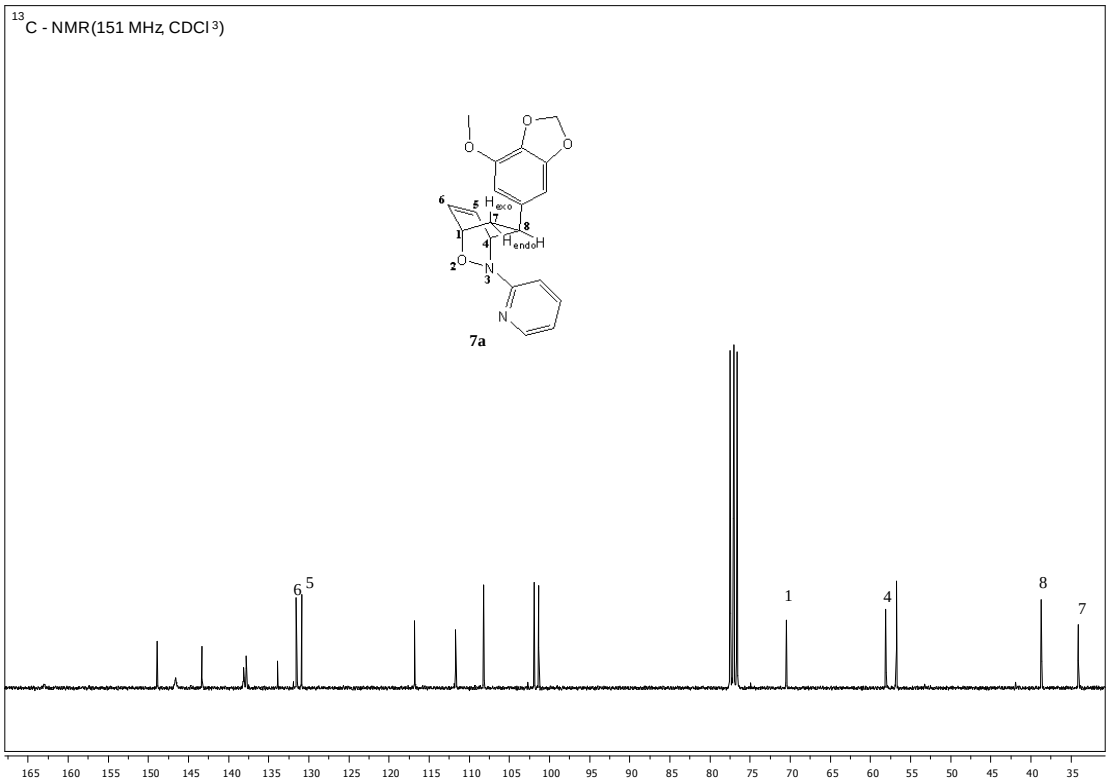

170.22
170.13
169.30
169.11
153.04
146.53
135.87
133.25
106.98
102.35
96.74
71.63
68.48
67.32
52.83
34.58
26.72
21.00
20.77
20.67
OAc
OAc
OAc
H
NH
O
O
OH
O
13-OH
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20


6.344
6.341
5.902
5.897
3.996
3.986
3.976
3.966
3.800
3.775
3.742
3.401
3.368
3.358
3.325
2.947
2.935
2.905
2.893
2.863
2.851
2.154
2.144
2.133
2.109
2.098
2.088
1.775
1.767
1.733
1.729
1.725
1.688
1.679
1.00
1.99
1.05
1.09
1.06
1.10
1.05
1.06
1.10
OH
OH
OH
O
O
H
NH
OH
O
1

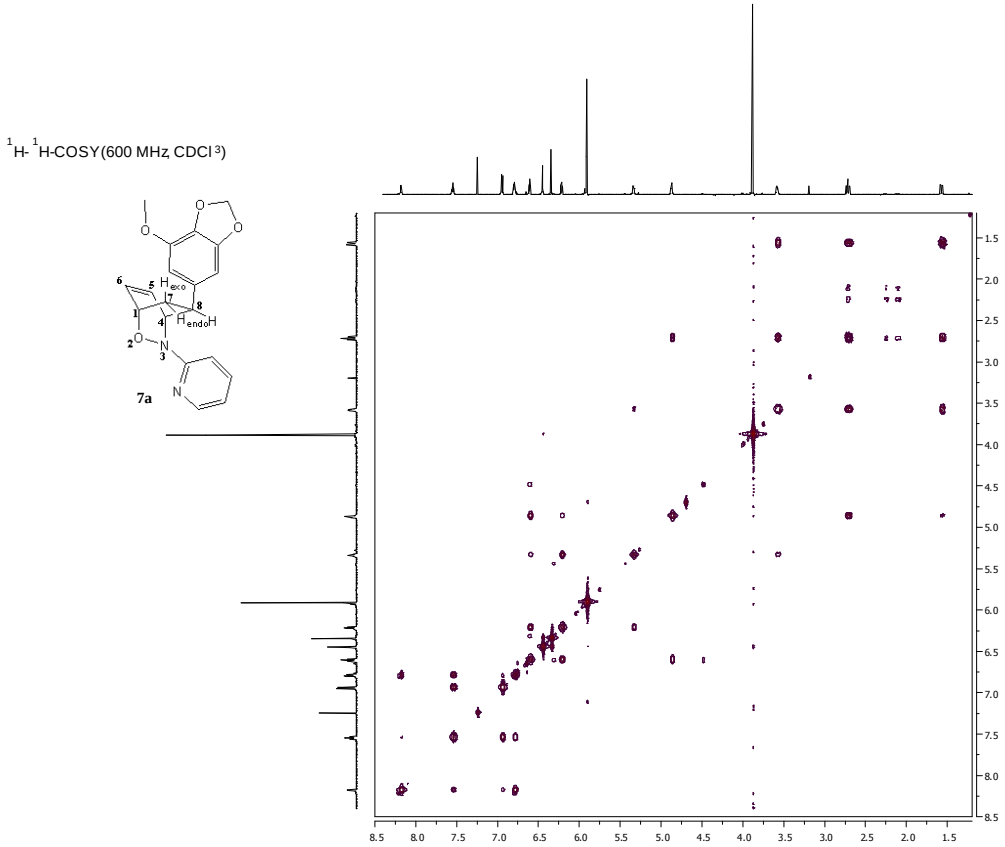

171.914
154.306
147.267
139.740
133.932
108.267
103.440
97.682
73.360
71.557
70.570
56.378
35.266
29.652
OH
OH
OH
O
O
H
NH
OH
O
1

Determination of Relative Configurations

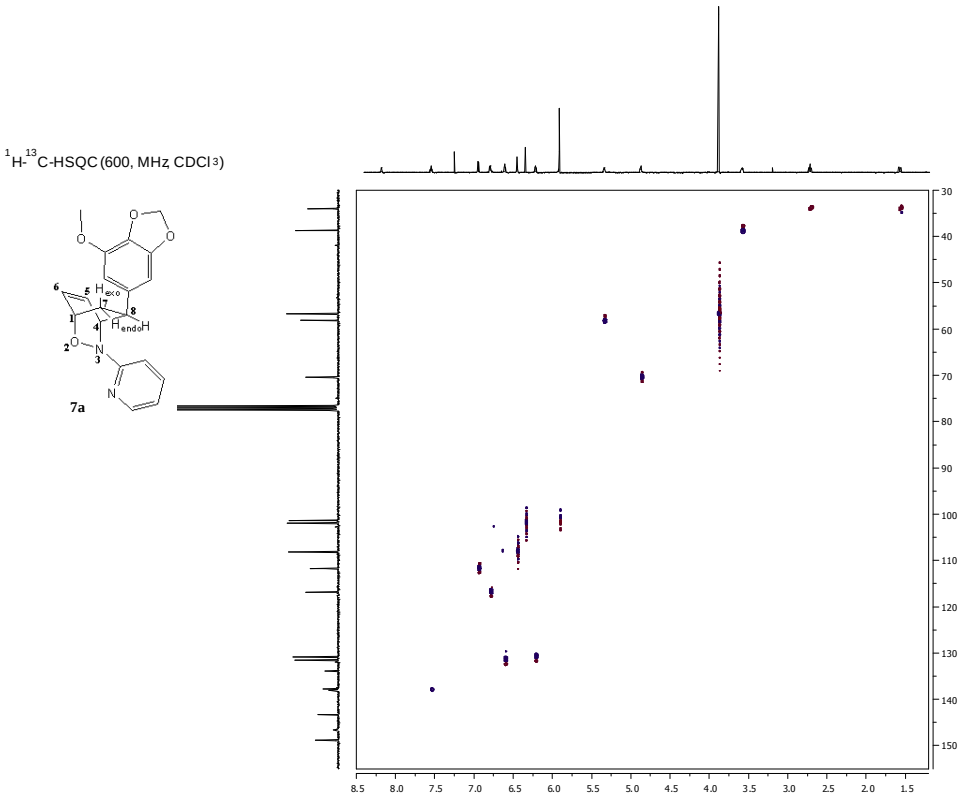


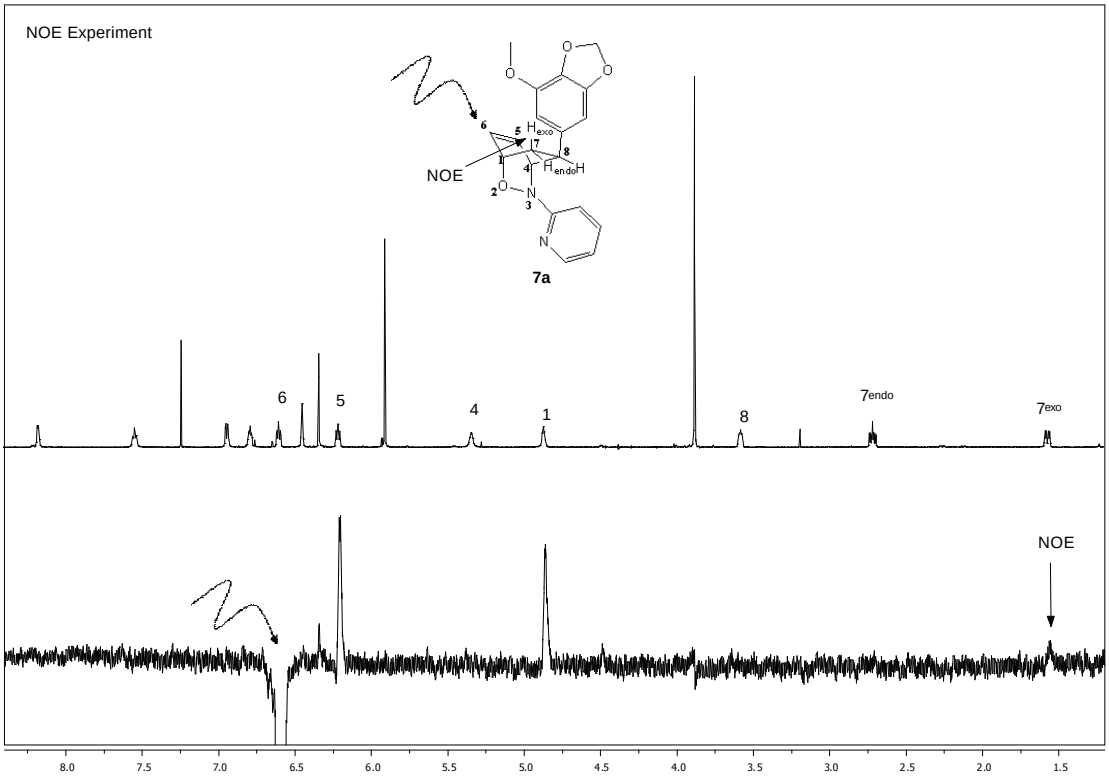


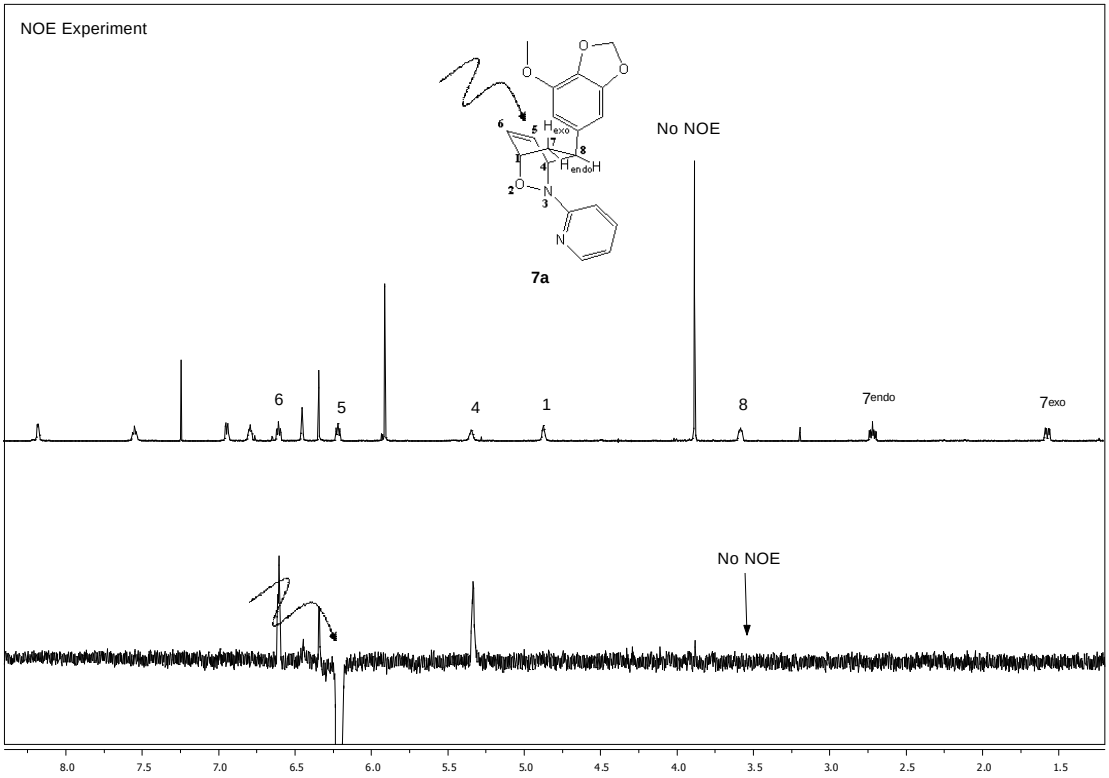
^{1}H-^{1}H-COSY (600 MHz, $CDCl_3$)

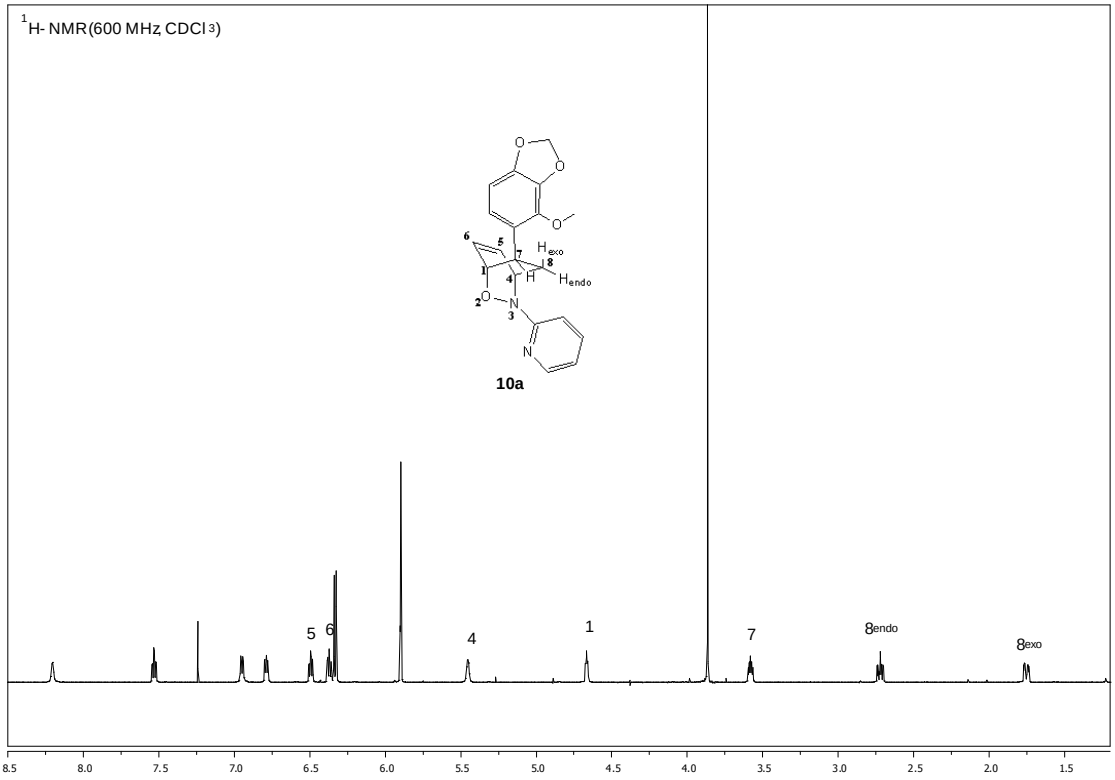


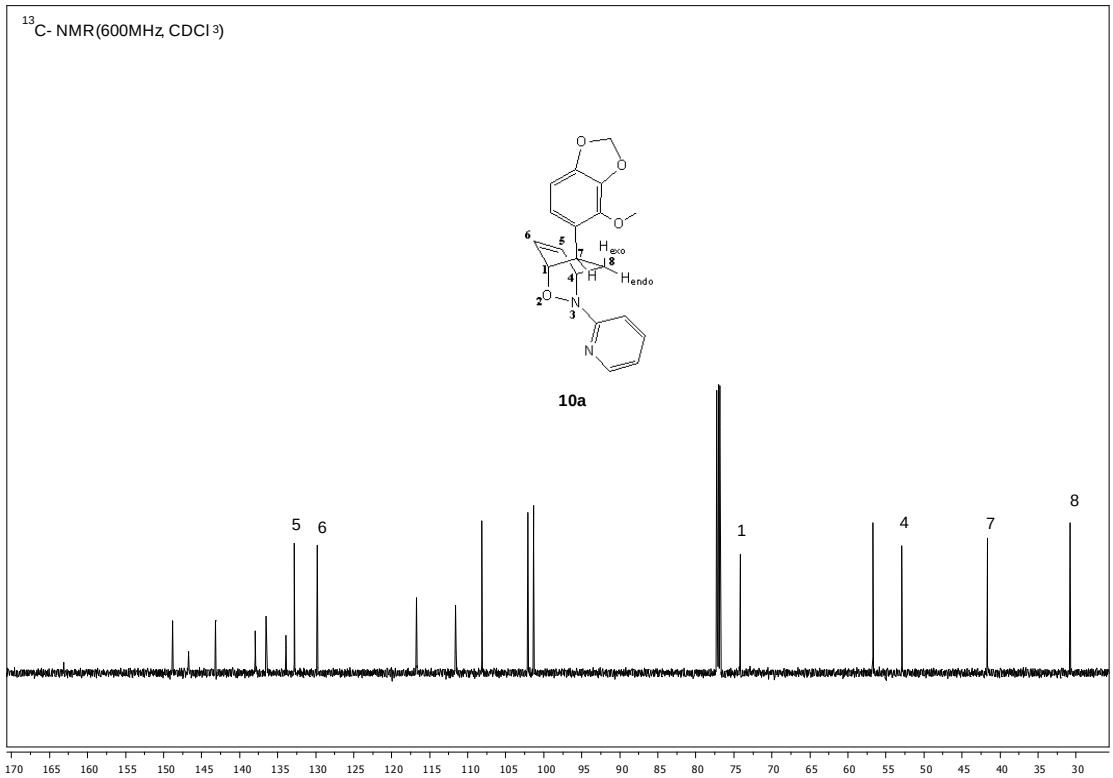
^{1}H-^{13}C-HSQC (600, MHz, $CDCl_3$)



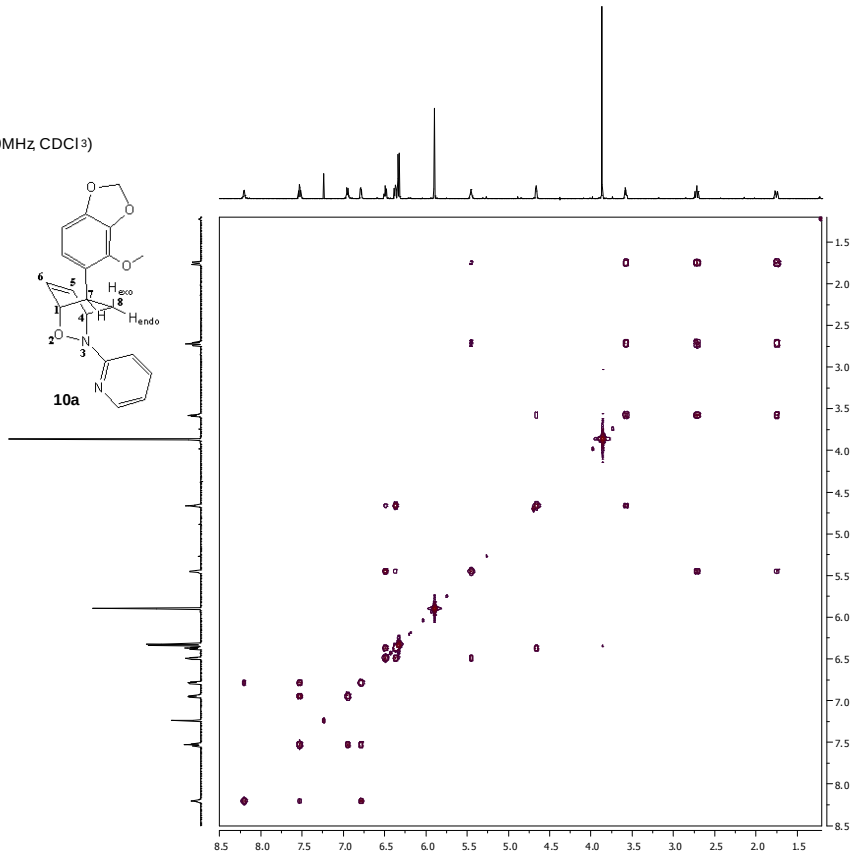

NOE Experiment
NOE
7a
6
5
4
1
8
7endo
7exo
NOE
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5


NOE Experiment
No NOE
7a
6
5
4
1
8
7endo
7exo
No NOE
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

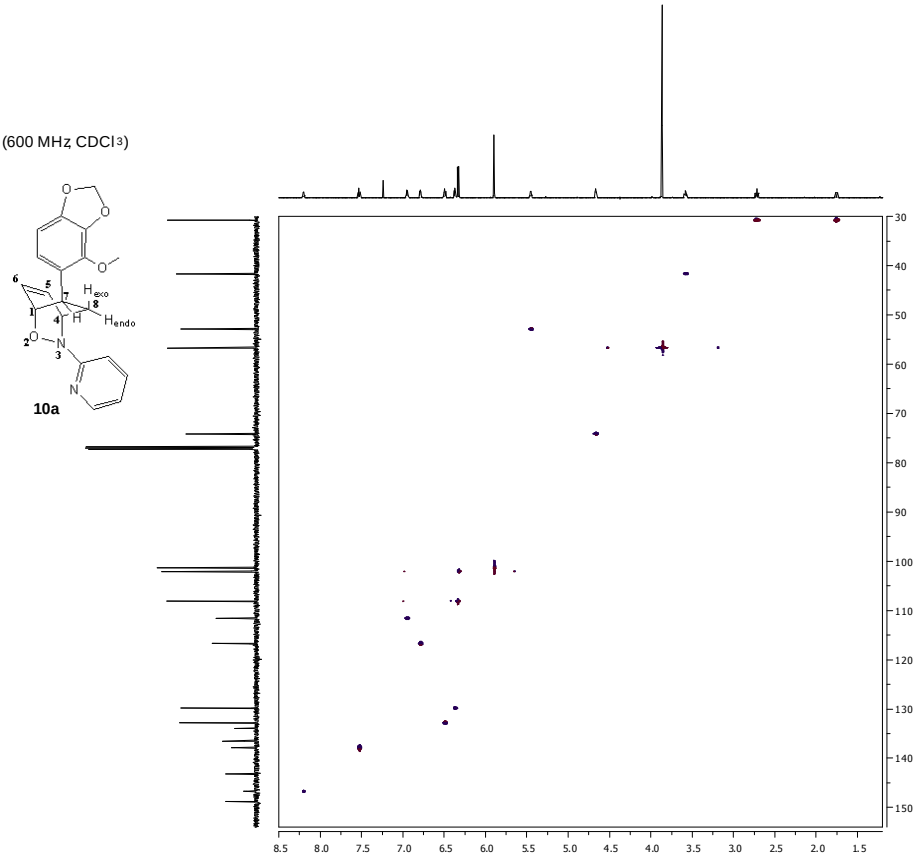

1H- NMR(600 MHz, CDCl3)
10a
5
6
4
1
7
8endo
8exo
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

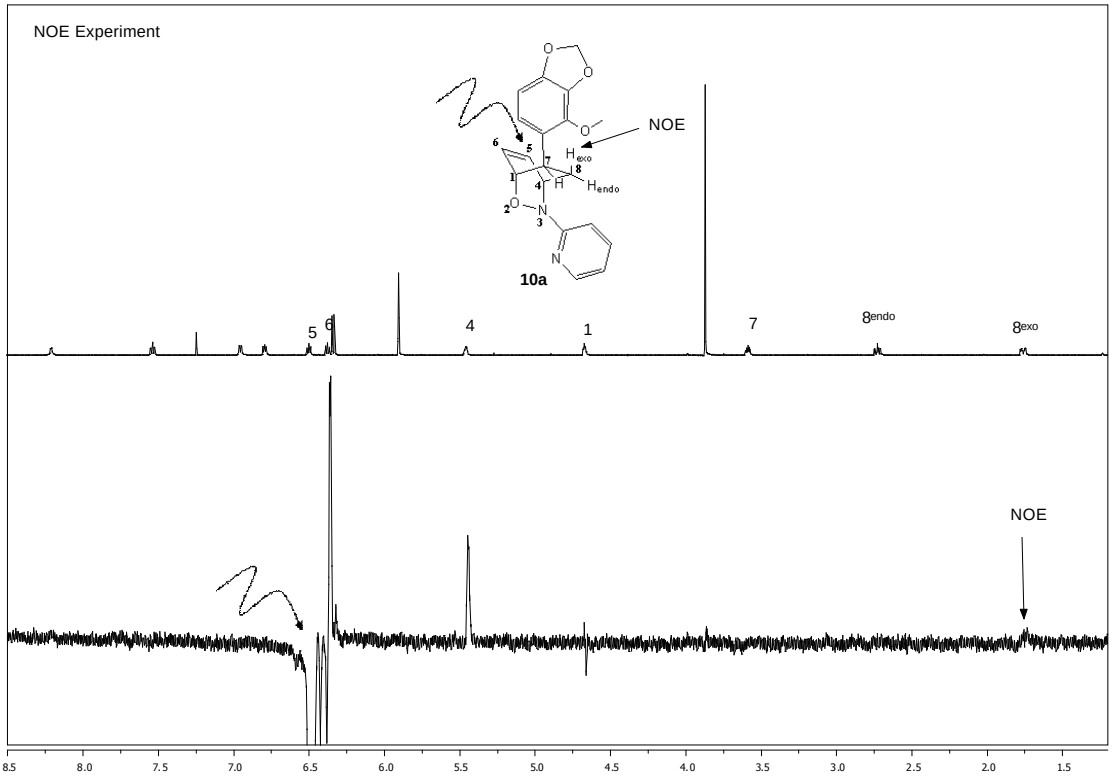

13C- NMR(600MHz, CDCl3)
10a
5
6
1
4
7
8
170
165
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30

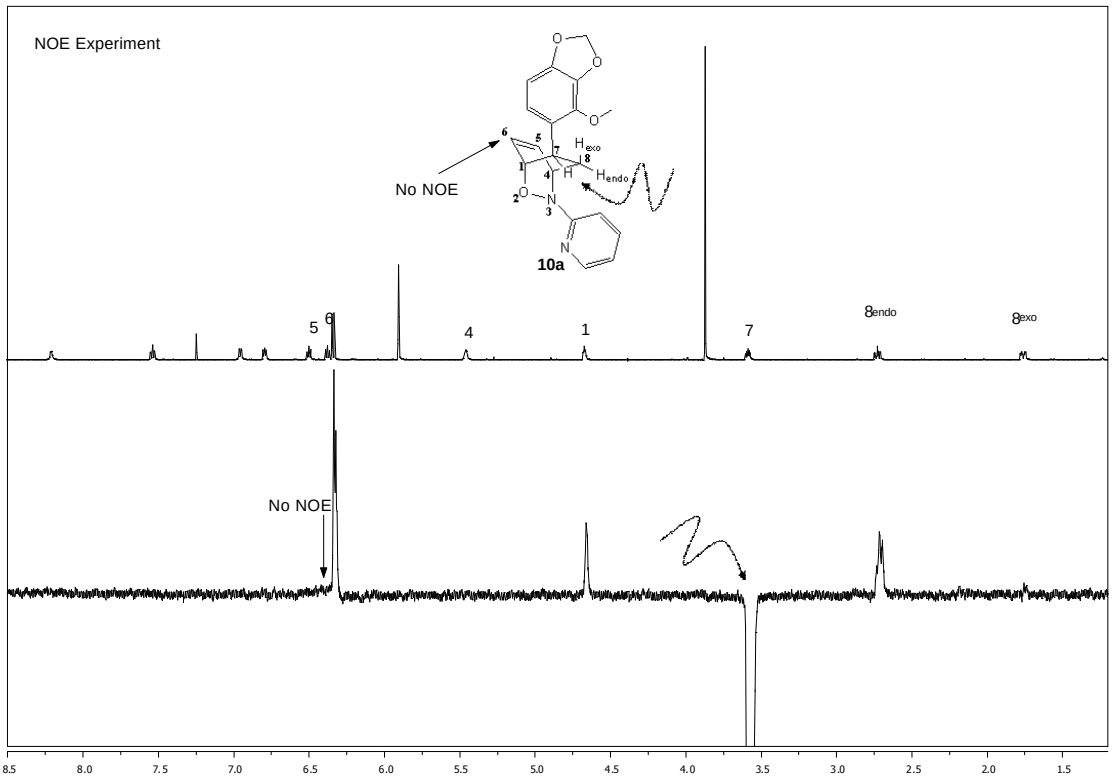
^{1}H-^{1}H-COSY (600MHz, $CDCl_3$)



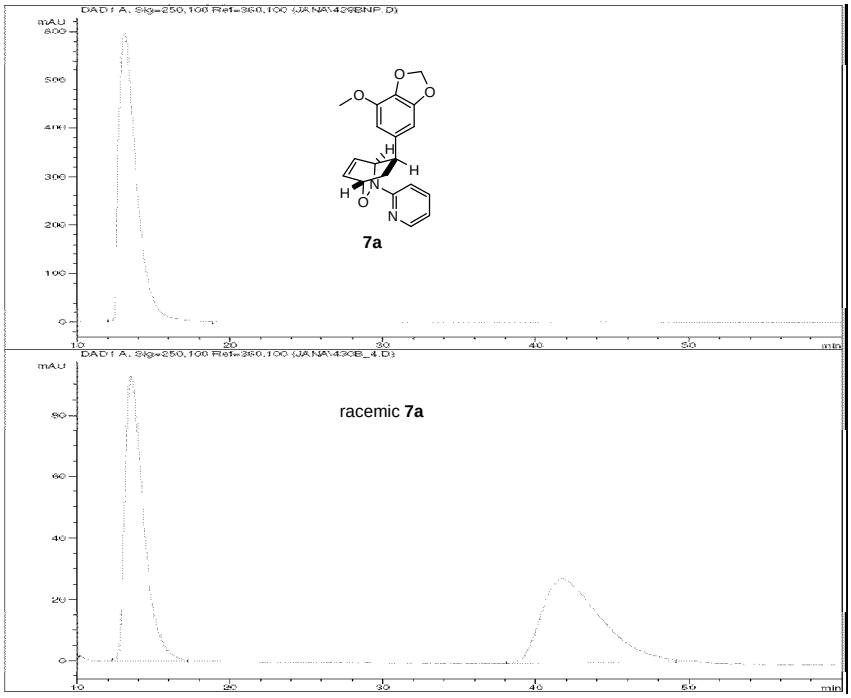
^{1}H-^{13}C-HSQC (600 MHz, $CDCl_3$)

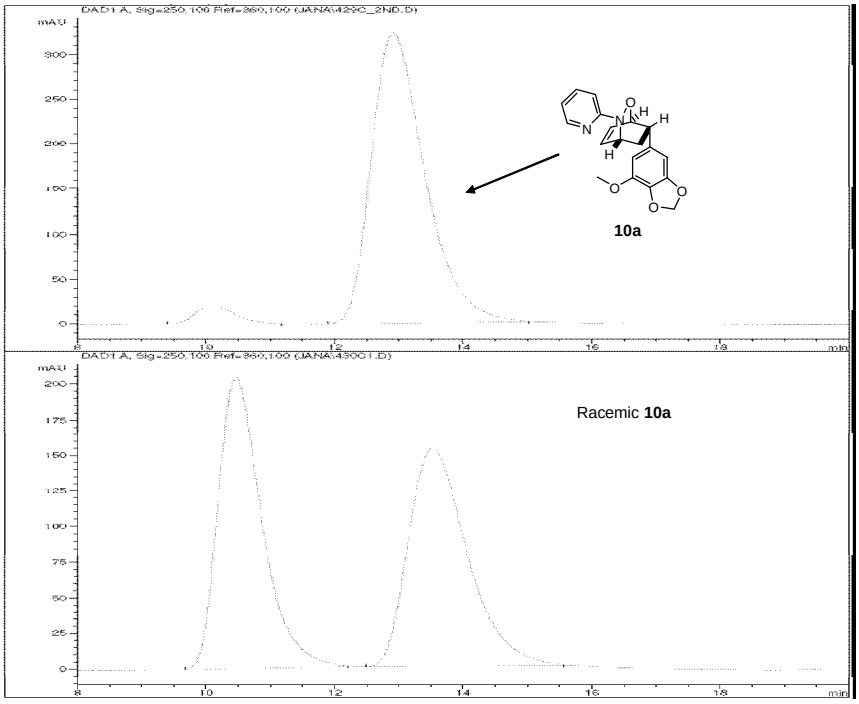


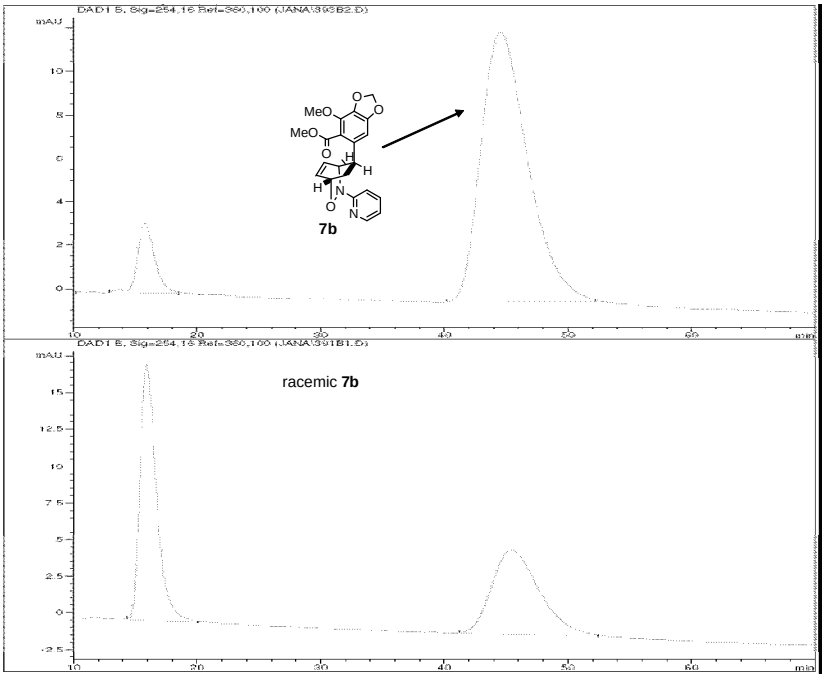

NOE Experiment
NOE
10a
5
6
4
1
7
8endo
8exo
NOE
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

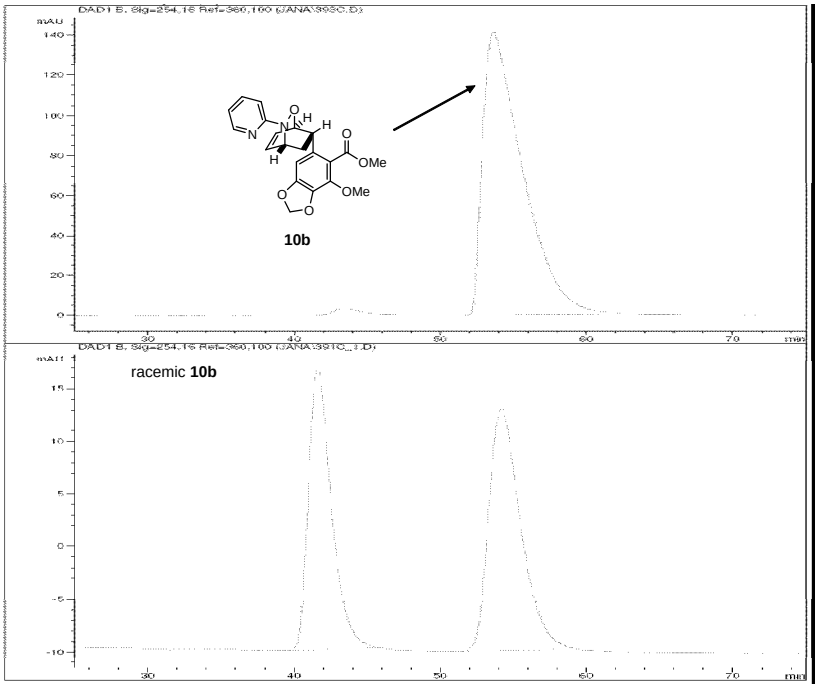

NOE Experiment
No NOE
10a
5
6
4
1
7
8endo
8exo
No NOE
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

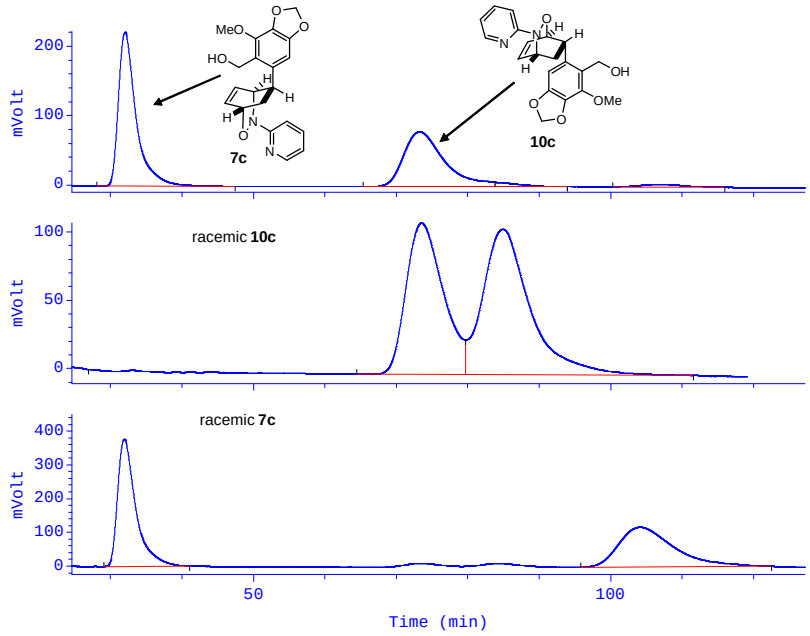
HPLC Traces

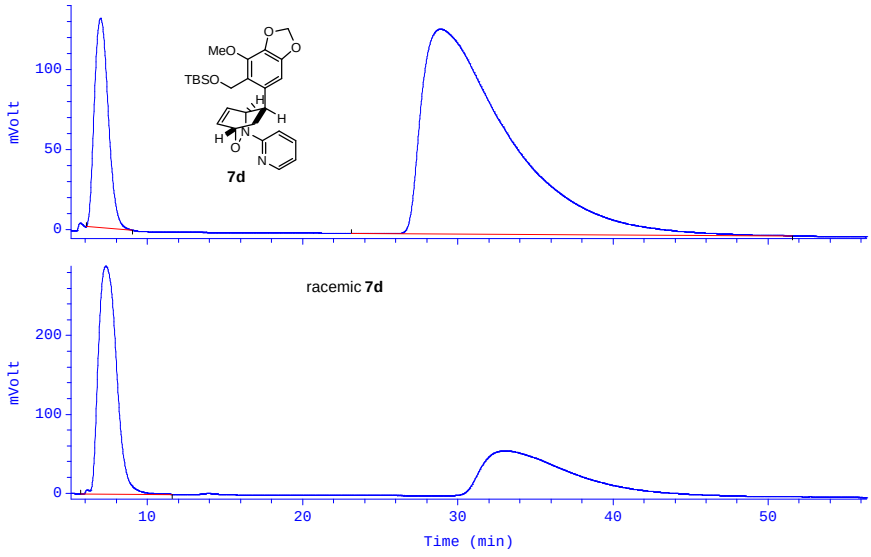


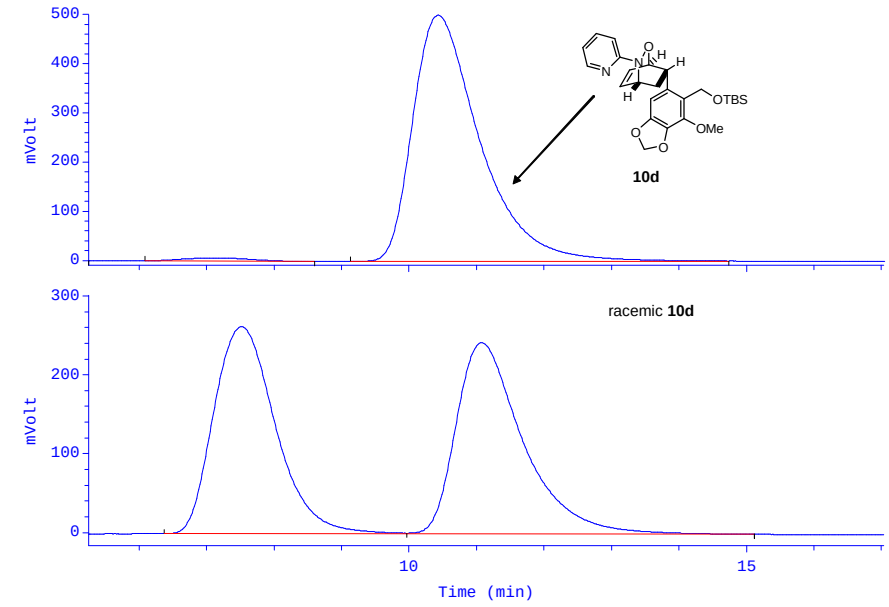


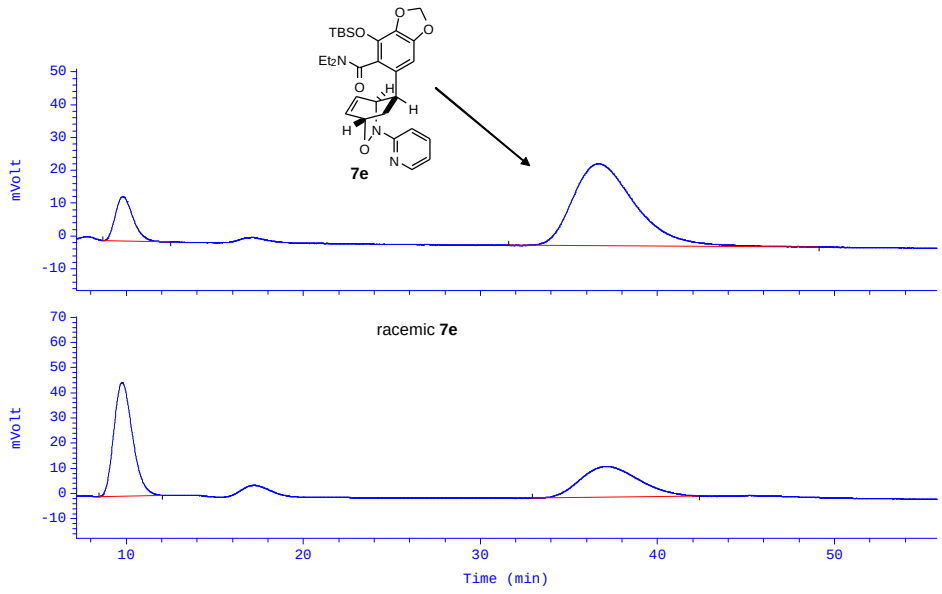

MeO
MeO
O
O
O
H
H
H
N
O
N
7b
racemic 7b

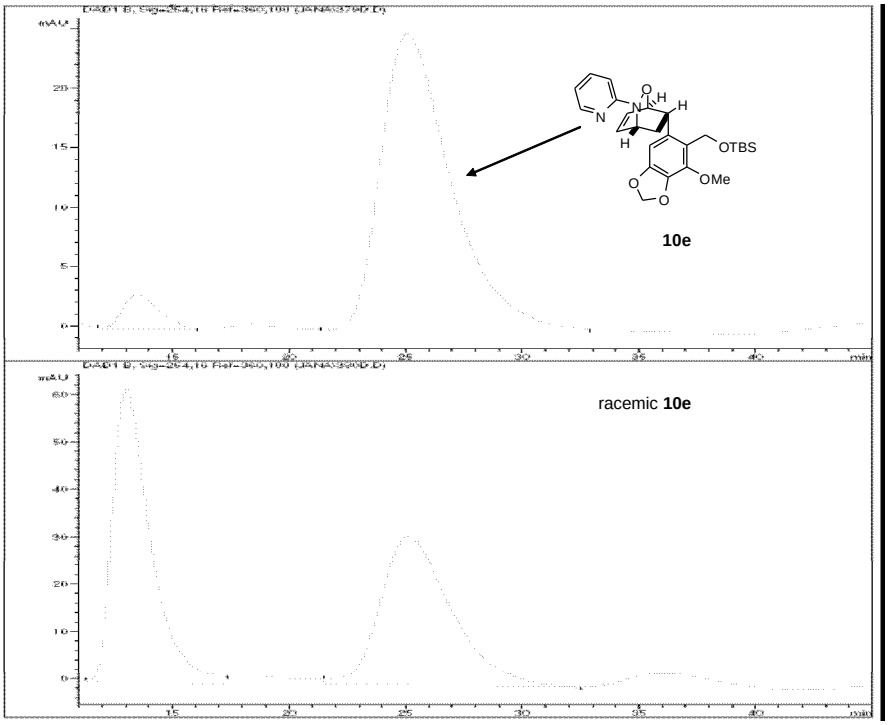

O
H
N
N
H
H
O
OMe
OMe
O
O
10b
racemic 10b


MeO
HO
7c
10c
OH
OMe
mVolt
racemic 10c
racemic 7c
50
100
Time (min)


MeO
TBSO
7d
mVolt
racemic 7d
10
20
30
40
50
Time (min)


500
400
300
200
100
0
mVolt
OTBS
OMe
10d
300
200
100
0
mVolt
racemic 10d
10
15
Time (min)


TBSO
Et2N
7e
50
40
30
20
10
0
-10
mVolt
racemic 7e
70
60
50
40
30
20
10
0
-10
mVolt
10
20
30
40
50
Time (min)


mAU
25
20
15
10
5
0
15
20
25
30
35
40
min
O
H
N
N
H
H
OTBS
OMe
O
O
10e
racemic **10e**
mAU
60
50
40
30
20
10
0
15
20
25
30
35
40
min