Synthesis and Antibacterial Properties of (–)-*nor*-Platencin

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Supporting Material

General procedures: Reactions were conducted in flame or oven-dried glassware under a nitrogen atmosphere and were stirred magnetically. "Concentrated" refers to removal of solvents by means of a rotary-evaporator attached to a diaphragm pump (15-60 Torr) followed by removal of residual solvents at < 1 Torr with a vacuum pump. Flash chromatography was performed on silica gel 60 (230-400 mesh). Analytical thin layer chromatography (TLC) was performed using silica gel 60 F-254 pre-coated glass plates (0.25 mm). TLC Plates were analyzed by short wave UV illumination, by spraying with 1% aqueous $KMnO_4$ solution, or by dipping in vanillin stain (27 g of vanillin in 380 mL of EtOH, 50 mL of water and 20 mL of concentrated sulfuric acid) and heating on a hot plate. THF and ether were dried and purified by distillation from sodium/benzophenone. Pyridine, Et_3N, benzene, toluene, MeOH, and CH_2Cl_2 were distilled from CaH_2. ^1H and ^{13}C NMR spectra were obtained on a 400 MHz spectrometer in $CDCl_3$ with tetramethylsilane as internal standard unless the use of a 500 or 800 MHz spectrometer is specifically indicated. Chemical shifts are reported in δ (ppm downfield from tetramethylsilane). Spectra in $CDCl_3$ are referenced to the residual solvent peaks at δ 7.27 (^1H) and 77.00 (^{13}C). COSY spectra were recorded for all compounds and used to assign ^1H NMR spectra. Coupling constants are reported in Hz with multiplicities denoted as s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), m (multiplet) and br (broad). IR spectra were acquired on an FT-IR spectrometer and are reported in wave numbers (cm^{-1}). High resolution mass spectra were obtained using the following ionization techniques: chemical ionization (CI), electron impact (EI), electrospray ionization (ESI) analyzed by quadrupole time of flight (QTof) . Optical rotation values were measured on a polarimeter using a cell with a path length of 1 dm.

(1*S*,2*R*,4*R*)- and (1*R*,2*R*,4S)-1-(Phenylmethoxymethyl)bicyclo[2.2.2]oct-5-ene-2-carboxaldehyde (6c and 10). (5*S*)-(−)-2,2,3-Trimethyl-5-phenylmethyl-4-imidazolidinone monohydrochloride ((5*S*)-**9**) (286 mg, 1.09 mmol) was dissolved in 20 mL of 95:5 CH_3CN/H_2O and 1.20 mL of acrolein (**8a**) was added. The solution was stirred at 23 ºC for 1 h and treated with a solution of **7b**[8,10] (2.30 g, 11.5 mmol) in 50 mL of 95:5 CH_3CN/H_2O. The reaction flask was wrapped with aluminum foil to prevent polymerization of acrolein and the reaction mixture

was stirred under N_2 at 23 ºC. Additional acrolein (1.2 mL) was added every 24 h. After 5 d, the reaction was concentrated and the residue was dissolved in CH_2Cl_2, which was washed twice with water, dried over $MgSO_4$, and concentrated to give 5 g of an approximately 9:1 mixture of **6c** and **10** as determined by analysis of the ^{1}H NMR spectrum. Flash chromatography on silica gel (100:0 to 95:5 hexanes/EtOAc) gave 124 mg (4.2%) of **10**, followed by 124 mg (4.2%) of **6c** contaminated with **10**, 968 mg (32%) of pure **6c**, and finally 174 mg (5.8%) of **6c** contaminated by regioisomers and other impurities.

Data for **6c**: $[\alpha]^{25.0}_D$ –14.2 (*c* 1.00, $CHCl_3$); ^{1}H NMR 9.26 (d, 1, *J* = 5.0), 7.39-7.27 (m, 5), 6.42 (dd, 1, *J* = 7.2, 8.0), 6.18 (d, 1, *J* = 8.0), 4.55 (d, 1, *J* = 12.0), 4.48 (d, 1, *J* = 12.0), 3.63 (d, 1, *J* = 9.2), 3.45 (d, 1, *J* = 9.2), 2.71-2.65 (m, 1), 2.53 (ddd, 1, *J* = 9.8, 5.0, 4.9), 1.83-1.72 (m, 1), 1.64-1.54 (m, 1), 1.49 (ddd, 1, *J* = 12, 12, 4), 1.48-1.44 (m, 1), 1.40-1.30 (m, 1), 1.15 (ddd, 1, *J* = 12, 12, 4); ^{13}C NMR 203.5, 138.2, 135.4, 132.4, 128.3 (2 C), 127.6 (2 C), 127.5, 74.9, 73.6, 53.8, 41.1, 29.6, 28.8, 28.0, 25.2; IR 3034, 2726, 1718, 1097; HRMS (ESI) calcd. for $C_{17}H_{21}O_2$ (MH^+) 257.1542, found 257.1545.

Chiral HPLC analysis (Supercritical Fluid Chromatography (SFC) System, Chiralpak AS-H Column, 10% MeOH in liquid CO_2, isocratic for 5 min) indicated that the enantiomeric excess was 87% based on retention times of 1.76 min (major) and 1.59 min (minor). Racemic samples used to establish separation conditions were prepared using both a 1:1 mixture of enantiomeric catalysts and a mixture of products prepared using the two enantiomeric catalysts.

Data for *ent*-**6c** prepared using (5*R*)-**9**: $[\alpha]^{18.1}_D$ +12.5 (*c* 1.00, $CHCl_3$), ee 84%.

Data for **10**: $[\alpha]^{18.7}_D$ -11.4 (*c* 1.00 $CHCl_3$); ^{1}H NMR 9.76 (d, 1, *J* = 3.7), 7.38-7.25 (m, 5), 6.34 (dd, 1, *J* = 8.0, 8.0), 6.15 (d, 1, *J* = 8.0), 4.57 (d, 1, *J* = 12.4), 4.53 (d, 1, *J* = 12.4), 3.58 (d, 1, *J* = 9.4), 3.54 (d, 1, *J* = 9.4), 2.64-2.58 (m, 1), 2.44 (ddd, 1, *J* = 11.0, 5.5, 3.7), 1.82 (ddd, 1, *J* = 13.4, 4.9, 2.4), 1.73 (ddd, 1, *J* = 13.4, 10.4, 4.3), 1.61 (dddd, 1, *J* = 12.2, 12.2, 4.9, 2.4), 1.47 (dddd, 1, *J* = 12, 12, 4, 4), 1.36 (ddddd, 1, *J* = 12, 12, 4, 4, 4), 1.07 (dddd, 1, *J* = 12.8, 12.8, 4.9, 2.4); ^{13}C NMR 204.4, 138.2, 135.8, 134.9, 128.3 (2 C), 127.6 (3 C), 74.2, 73.4, 51.0, 41.4, 29.6,

27.4, 25.5, 24.4; IR 3033, 2727, 1716, 1095. HRMS (ESI) calcd. for $C_{17}H_{21}O_2$ (MH^+) 257.1542, found 257.1534.

Equilibration of 6c and 10. A solution of a 7:1 mixture of **6c** and **10** (10 mg) in EtOH (1.00 mL) was treated with aqueous NaOH (1 M, 0.1 mL) at 23 °C. The mixture was stirred at 23 °C overnight. Water (5 mL) was added and the solution was extracted with CH_2Cl_2. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated. Analysis of the ^{1}H NMR spectrum indicated that a 3:1 mixture of **6c** and **10** was present. An identical mixture of products was obtained by equilibration of a 1:6 mixture of **6c** and **10**. Note that epimerization of (–)-**6c** will give (+)-**10**, the enantiomer of the minor exo Diels-Alder adduct (–)-**10** and epimerization of (–)-**10** will give (+)-**6c**, the enantiomer of the major endo Diels-Alder adduct (–)-**6c**.

Background Diels–Alder Reaction of 7b and Acrolein (8a) Without 9. Diene **7b** (55 mg, 0.27 mmol) was dissolved in 1 mL of 95:5 CH_3CN/H_2O and acrolein (0.1 mL, 1.5 mmol) was added at 23 °C. The resulting mixture was stirred under N_2 atmosphere at 23 °C. Aliquots of the reaction were monitored by comparing the alkene peaks for **6c** at δ 6.34 and 6.15 and those for **7b** at δ 5.96-5.89 and 5.83-5.7. The ratio of **7b:6c** was 20:1 after 3 d, 10:1 after 5 d, 2.7:1 after 10 d and 1.3:1 after 20 d.

(*E*) and (*Z*)-(1*S*,2*S*,4*R*)-2-(2-Methoxyethenyl)-1-(phenylmethoxymethyl)-bicyclo[2.2.2]oct-5-ene (11*E*) and (11*Z*).[12] Methoxymethyldiphenylphosphine oxide (710 mg, 2.89 mmol) in dry THF (25 mL) was treated with LDA [from diisopropylamine (0.4 mL) and *n*-BuLi (1.6 M, 1.81 mL)] in THF (25.0) at 0 °C for 10 min. The mixture was cooled to –78 °C and aldehyde **6c** (670 mg, 2.62 mmol) in dry THF (25 mL) was added dropwise. The solution was allowed to warm to 23 °C over 1 h and saturated aqueous NH_4Cl solution (100 mL) and ether (50 mL) were added. The aqueous layer was extracted with ether (3 × 25 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated to give a clear yellow oil that was redissolved in dry THF. The resulting solution was added dropwise to a suspension of NaH (250 mg, 60% suspension in mineral oil) in dry THF (50 mL) at 23 °C. The reaction mixture was

stirred for 24 hours at 23 °C, filtered through Celite, and concentrated to give an approximately 1:1 mixture of crude **11*E*** and **11*Z*** isomers as a yellow-orange oil. Flash chromatography (95:5 hexanes/EtOAc) gave 499 mg (67%) of a 3:2 mixture of **11*E*** and **11*Z***: ^{1}H NMR 7.40-7.15 (m, 5), 6.37-6.24 (m, 1), 6.20 (d, 0.6 × 1, *J* = 12.8), 5.99 (d, 0.4 × 1, *J* = 8.5), 5.90 (d, 0.6 × 1, *J* = 8.5), 5.74 (d, 0.4 × 1, *J* = 6.1), 4.55-4.48 (m, 2), 4.28 (dd, 0.6 × 1, *J* = 12.8, 9.8), 3.97 (dd, 0.4 × 1, *J* = 10.4, 6.1), 3.60-3.37 (m, 2), 3.50 (s, 0.4 × 3), 3.41 (s, 0.6 × 3), 2.78 (ddd, 0.4 × 1, *J* = 10.4, 10.4, 4.9), 2.51-2.42 (m, 1), 2.22 (ddd, 0.6 × 1, *J* = 9.8, 9.8, 4.2), 1.94 (ddd, 0.4 × 1, *J* = 12.5, 10.4, 2.4), 1.88 (ddd, 0.6 × 1, *J* = 12.5, 9.8, 2.4), 1.61-1.17 (m, 4), 1.03-0.90 (m, 1); ^{13}C NMR 146.1, 144.8, 139.2, 138.9, 134.8, 134.7, 133.0, 132.7, 128.2 (2 C), 128.1 (2 C), 127.34 (2 C), 127.29 (2 C), 127.25, 127.15, 112.0, 107.7, 75.2, 75.1, 73.32, 73.26, 59.3, 55.8, 41.14, 41.12, 38.9, 36.5, 36.0, 34.8, 30.4, 30.3, 29.3, 29.1, 26.02, 25.93; IR 3032, 1651, 1453, 1103. HRMS (ESI) calcd. for $C_{19}H_{25}O_2$ (MH^+) 285.1855, found 285.1851.

2-((1*R*,2*S*,4*R*)-1-(Phenylmethoxymethyl)bicyclo[2.2.2]oct-5-ene-1-yl)acetaldehyde (12).[13] A mixture of enol ethers **11*E*** and **11*Z*** (499 mg) in 14 mL of CH_2Cl_2 and 3.5 mL of THF was treated with aqueous HCl (1.8 mL 5 M) and the resulting mixture was vigorously stirred for 5 h at 23 °C. Saturated aqueous sodium bicarbonate saturated solution (50 mL) was added slowly to neutralize the acid, the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography (90:10 hexanes/EtOAc) to give 427 mg (90%) of aldehyde **12**: $[\alpha]^{19.1}_D$ –8.5 (*c* 1.00, $CHCl_3$); ^{1}H NMR 9.62 (t, 1, *J* = 2), 7.37-7.25 (m, 5), 6.32 (dd, 1, *J* = 6.1, 8.6), 5.85 (d, 1, *J* = 8.6), 4.49 (d, 1, *J* = 12), 4.45 (d, 1, *J* = 12), 3.49 (d, 1, *J* = 9), 3.43 (d, 1, *J* = 9), 2.53-2.33 (m, 3), 1.99-1.88 (m, 2), 1.70 (ddd, 1, *J* = 12, 9.8, 3.7), 1.54 (dddd, 1, *J* = 12, 10, 4.3, 2.4), 1.32 (dddd, 1, *J* = 12, 8.6, 6.7, 3.0), 1.16 (ddd, 1, *J* = 12.2, 12.2, 4.3), 0.85 (ddddd, 1, *J* = 12, 12, 4, 4, 4); ^{13}C NMR 203.0, 138.4, 135.2, 131.8, 128.3 (2 C), 127.5 (3 C), 74.1, 73.1, 49.4, 40.6, 35.0, 33.4, 30.4, 30.3, 25.5; IR 3033, 1722, 1453, 1098; HRMS (ESI) calcd. for $C_{18}H_{23}O_2$ (MH^+) 293.1517, found 293.1512.

1-((1*R*,2*S*,4*R*)-1-(Phenylmethoxymethyl)bicyclo[2.2.2]oct-5-en-1-yl)propan-2-ol (**13**). A solution of aldehyde **12** (1.765 g, 6.5 mmol) in 20 mL of THF was added dropwise to a solution of MeMgBr (8.00 mL, 1.4 M in toluene/THF) at 0 °C. The resulting solution was allowed to warm to 23 °C and the reaction was quenched with saturated aqueous NH_4Cl solution, and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$ and concentrated to provide 1.861 g (99.5%) of a mixture of diastereomers **13** that was used for next step.

Flash chromatography of 200 mg (90:10 to 65:35 hexanes/EtOAc) provided 57 mg of the less polar diastereomer, 45 mg of a mixture of diastreomers, and 47 mg of the more polar diastereomer.

Data for the less polar diastereomer of **13**: $[\alpha]^{19.1}_D$ –29.3 (*c* 1.00, $CHCl_3$); ^{1}H NMR 7.38-7.25 (m, 5), 6.27 (dd, 1, *J* = 7.5, 8.5), 5.82 (d, 1, *J* = 8.5), 4.58 (d, 1, *J* = 12.2), 4.52 (d, 1, *J* = 12.2), 3.77-3.66 (m, 1), 3.56 (d, 1, *J* = 9), 3.51 (d, 1, *J* = 9), 2.52-2.46 (m, 1), 2.00-1.91 (m, 1), 1.83 (ddd, 1, *J* = 12.2, 9.7, 3.1), 1.69-1.62 (m, 1), 1.56-1.48 (m, 1), 1.48-1.37 (m, 2), 1.36-1.22 (m, 2), 1.10 (d, 3, *J* = 6.1), 0.94-0.86 (m, 1), 0.81 (ddd, 1, *J* = 13.4, 11.6, 1.8); ^{13}C NMR 138.7, 134.6, 132.5, 128.3 (2 C), 127.6 (2 C), 127.5, 74.3, 73.3, 65.2, 43.3, 40.7, 35.1, 34.2, 30.5 (2 C), 25.8, 24.7; IR 3400, 1452, 1097; HRMS (ESI) calcd. for $C_{19}H_{27}O_2$ (MH^+) 287.2011, found 287.2020.

Data for the more polar diastereomer of **13**: $[\alpha]^{19.1}_D$ –16.8 (*c* 1.00 $CHCl_3$); ^{1}H NMR 7.37-7.24 (m, 5), 6.28 (dd, 1, *J* = 8.5, 8.5), 5.79 (d, 1, *J* = 8.5), 4.56-4.53 (m, 2), 3.81-3.71 (m, 1), 3.61 (d, 1, *J* = 9.2), 3.49 (d, 1, *J* = 9.2), 2.51-2.42 (m, 1), 1.82-1.57 (m, 4), 1.55-1.40 (m, 1), 1.35-1.24 (m, 1), 1.24-0.99 (m, 3), 1.13 (d, 3, *J* = 6.1), 0.97-0.87 (m, 1); ^{13}C NMR 138.5, 134.7, 132.2, 128.3 (2 C), 127.5 (2 C), 127.4, 74.5, 73.3, 66.2, 43.9, 40.9, 35.3, 34.6, 30.7, 30.5, 25.6, 23.0.

1-((2S)-1-(Hydroxymethyl)bicyclo[2.2.2]oct-2-yl)propan-2-ol (**16**). A mixture of the diastereomers of **13** (1.641 g, 5.73 mmol) was dissolved in 10 mL of EtOAc and 250 mg $Pd(OH)_2$/C (Pd content 20%, dry weight basis) was added. The resulting suspension was shaken under hydrogen atmosphere (45 psi) overnight. The catalyst was filtered off and the filtrate was

concentrated to give 272 mg of crude **16**. Flash chromatography (95:5 to 90:10 CH_2Cl_2/MeOH) provided 836 mg (73.6%) of a mixture of the diastereomers **16** followed by 31.4 mg (3%) of the more polar diastereomer of **16**.

Data for the mixture of diastereomers of **16**: ^{1}H NMR 3.96 (qt, 0.5 × 1, *J* = 6, 6), 3.90-3.81 (m, 0.5 × 1), 3.73-2.68 (br, 2, OH), 3.49 (d, 0.5 × 1, *J* = 11.6), 3.43 (d, 0.5 × 1, *J* = 11.6), 3.11 (d, 0.5 × 1, *J* = 11.6), 3.01 (d, 0.5 × 1, *J* = 11.6), 1.96-1.43 (m, 9), 1.43-0.95 (m, 5), 1.21 (d, 0.5 × 3, *J* = 6.1), 1.19 (d, 0.5 × 3, *J* = 6.1);^{13}C NMR 68.6, 68.0, 66.5, 65.4, 41.5, 41.3, 35.0, 34.5, 34.3, 33.8, 31.3, 30.8, 29.9, 29.8, 25.7, 25.6, 25.4, 25.25, 25.23, 25.18, 25.1, 23.3, 23.1, 22.7; IR 3367, 1456, 1034; HRMS (ESI) calcd. for $C_{12}H_{23}O_2$ (MH^+) 199.1698, found 199.1700.

Data for the more polar diastereomer of **16**: $[\alpha]^{19.1}_D$ –62.8 (*c* 1.00 $CHCl_3$); ^{1}H NMR 3.96 (qt, 1, *J* = 6, 6), 3.45 (d, 1, *J* = 11), 3.13 (d, 1, 11), 2.12 (br, 2, $w_{1/2}$ = 6, OH), 1.93-1.77 (m, 1), 1.77-1.58 (m, 3), 1.57-1.43 (m, 4), 1.42-1.25 (m, 4), 1.24-1.01 (m, 2), 1.20 (d, 3, *J* = 6.1); ^{13}C NMR 69.0, 66.7, 41.7, 35.1, 34.6, 31.5, 29.9, 25.6, 25.3, 25.2, 23.1, 22.9.

(8a*S*)- 1,2,3,4,8,8a-Hexahydro-7*H*-2,4a-ethanonaphthalen-7-one (4a).[16] DMSO (1.00 mL, 14.1 mmol) was added slowly to a solution of $(COCl)_2$ (0.6 mL, 7 mmol) in 25 mL of CH_2Cl_2 at –78 °C and the resulting mixture was stirred for 15 min at –78 °C and treated with a solution of diol **16** (89 mg, 0.45 mmol) in 25 mL of CH_2Cl_2 precooled to –78 °C via cannula. The reaction mixture was stirred for 30 min at –78 °C and 4 h at -40 °C. The reaction mixture was cooled to –78 °C, treated with *i*-Pr_2EtN (2.2 mL, 12.6 mmol), and stirred for 30 min at –78 °C and 10 minutes at 0 °C. The reaction was quenched with ice cold saturated aqueous NH_4Cl solution, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated to give 130 mg of crude of (2*S*)-2-(2-oxopropyl)bicyclo[2.2.2]octane-1-carboxaldehyde (**5a**) containing some *i*-Pr_2EtN and other impurities. Crude **5a** was immediately used for the next step without further purification: ^{1}H NMR 9.34 (s, 1), 2.55-2.41 (m, 1), 2.39-2.29 (m, 1), 2.13 (s, 3), 2.05-1.94 (m, 1), 1.76-1.66 (m, 2), 1.65-1.43 (m, 6), 1.37-1.07 (m, 3).

Crude keto aldehyde **5a** was dissolved in 25 mL of EtOH and 150 mg of NaOH was added. The resulting solution was stirred overnight at 23 °C. The reaction was neutralized with 1 M HCl and extracted with ether. The combined organic layers were dried over $MgSO_4$, and concentrated. Flash column chromatography (90:10 hexanes/EtOAc) provided 54 mg (70% from **16**) of pure **4a**: $[\alpha]^{19.5}_D$ –80.2 (*c* 1.00 $CHCl_3$); ^{1}H NMR 6.49 (d, 1, *J* = 10), 5.81 (d, 1, *J* = 10), 2.40 (dd, 1, *J* = 16.5, 4.9), 2.29 (dd, 1, *J* = 16.5, 13.4), 2.22-2.09 (m, 1), 1.98-1.89 (m, 1), 1.76-1.54 (m, 7), 1.50-1.37 (m, 2), 1.12-1.04 (m, 1); ^{13}C NMR 200.6, 158.1, 127.2, 41.8, 35.3, 33.8, 33.0, 31.8, 25.8, 24.8, 24.7, 24.4; IR 1679; HRMS (ESI) calcd. for $C_{12}H_{17}O$ (MH^+) 177.1279, found 177.1271. The data are identical to those previously reported.[17]

(8*S*,8a*S*)- 1,2,3,4,8,8a-Hexahydro-8-methyl-7*H*-2,4a-ethanonaphthalen-7-one (4b).[6b] 1.0 M LiHMDS in toluene (0.8 mL, 0.8 mmol) was added slowly to a solution of enone **4a** (95 mg, 0.54 mmol) in THF (5.0 mL) and HMPA (0.5 mL) at –78 °C. The solution was stirred for 30 min and treated with MeI (0.5 mL, 8.11 mmol) dropwise. The reaction mixture was allowed to warm to 23 °C over 1 h, quenched with saturated aqueous $NaHCO_3$ solution, and extracted three times with EtOAc. The combined organic layers were washed twice with H_2O, brine, dried over $MgSO_4$, and concentrated. Flash chromatography (90:10 hexanes/EtOAc) afforded 75 mg (72.8%) of methyl enone **4b** as single diastereomer followed by 25 mg (13.1%) of a mixture of diastereomers, which was also used for the next step.

Data for the major diastereomer of **4b**: $[\alpha]^{18.7}_D$ –125.5 (*c* 1.00 $CHCl_3$); ^{1}H NMR 6.43 (d, 1, *J* = 9.8), 5.82 (d, 1 *J* = 9.8), 2.24 (dq, 1, *J* = 13, 6.7), 1.97-1.88 (m, 1), 1.82-1.64 (m, 3), 1.64-1.49 (m, 5), 1.47-1.35 (m, 2), 1.17 (dd, 1, *J* = 12.8, 8.5), 1.10 (br d, 3, *J* = 6.7); ^{13}C NMR 202.5, 156.8, 126.6, 43.6, 41.8, 33.5, 33.1, 32.1, 25.8, 25.3, 24.5, 24.5, 11.2; IR 1678; HRMS (ESI) calcd. for $C_{13}H_{19}O$ (MH^+) 191.1436, found 191.1436.

Methyl (8*S*,8a*R*)-1,3,4,7,8,8a-Hexahydro-8-methyl-7-oxo-2*H*-2,4a-ethanonaphthalene-8-propanoate (17).[6h,7b] A solution of *t*-BuOK in *t*-BuOH (2.8 mL, 1 M, 2.8 mmol) was added to a solution of **4b** (71 mg, 0.37 mmol) in ether (2.0 mL) and *t*-BuOH (2.0 mL) at 0 °C. The solution was stirred at 0 °C for 5 min and methyl acrylate (1.00 mL, 11.1 mmol)

was added. The reaction was stirred for 30 min and quenched by the addition of saturated aqueous NH_4Cl solution. The layers were separated and the aqueous layer was extracted three times with ether. The combined organic layers were dried over $MgSO_4$ and concentrated. Flash chromatography (90:10 hexanes/EtOAc) yielded 111 mg of a 5:1 mixture of ester **17** and the diastereomer at the quaternary center. Purification by HPLC (19 × 50 mm Xterra MS C18 10 μm column, 54:45:1 to 39:60:1 $H_2O/CH_3CN/HCOOH$) yielded 39.6 mg (38.7%) of **17** containing less than 5% of the minor diastereomer: $[\alpha]^{19.3}_D$ –69.0 (*c* 0.83, $CHCl_3$); ^{1}H NMR 6.41 (d, 1, *J* = 9.8), 5.79 (d, 1, *J* = 9.8), 3.66 (s, 3), 2.30-2.20 (m, 2), 2.16-2.15 (m, 1), 2.07-1.98 (m, 1), 1.96-1.85 (m, 1), 1.85-1.78 (m, 1), 1.74-1.39 (m, 9), 1.39-1.28 (m, 1), 1.13 (s, 3); ^{13}C NMR 204.6, 174.2, 155.8, 125.6, 51.6, 47.2, 38.5, 35.5, 33.5, 29.6, 29.3, 26.9, 26.6, 25.3, 24.8, 24.7, 21.2; IR 1738, 1673; HRMS (ESI) calcd. for $C_{17}H_{25}O_3$ (MH^+) 277.1804, found 277.1805.

(8*S*,8a*R*)-1,3,4,7,8,8a-Hexahydro-8-methyl-7-oxo-2*H*-2,4a-ethanonaphthalene-8-propanoic Acid (18). [6h,7b] Aqueous NaOH (0.5 mL, 1 M) was added to a solution of ester **17** (12.4 mg, 0.045 mmol) in 0.5 mL of THF at 23 °C and the solution was stirred overnight. The reaction was quenched with water and brine, neutralized with 1 M HCl to pH 3-4, and extracted with ether. The combined organic layers were dried over $MgSO_4$, and concentrated to provide 10.2 mg of crude **18**. Flash chromatography (65:35 hexanes/EtOAc) gave 8.4 mg (71%) of pure **18**: $[\alpha]^{19.2}_D$ –80.8 (*c* 0.50 $CHCl_3$); ^{1}H NMR 6.42 (d, 1, *J* = 9.8), 5.81 (d, 1, *J* = 9.8), 2.36-2.224 (m, 2), 2.17-2.07 (m, 1), 2.07-1.96 (m, 1), 1.96-1.80 (m, 2), 1.70-1.22 (m, 10), 1.15 (s, 3); ^{13}C NMR 204.8, 179.3, 156.0. 125.6, 47.2, 38.6, 35.5, 33.5, 29.3, 29.2, 26.8, 26.6, 25.3, 24.8, 24.7, 21.2; IR 3436, 1708, 1669, 1266, 737; HRMS (ESI) calcd. for $C_{16}H_{23}O_3$ (MH^+) 263.1647, found 263.1642.

2-(Trimethylsilyl)ethyl 3-[[3-[(8*S*,8a*R*)-1,3,4,7,8,8a-Hexahydro-8-methyl-7-oxo-2*H*-2,4a-ethanonaphthalen-8-yl]-1-oxopropyl]amino]-2,4-dihydroxybenzoate (20). [5d,6a] HATU (22.4 mg, 0.060 mmol) and Et_3N (15 μL, 0.11 mmol) were added to a solution of acid **18** (5.2 mg, 0.020 mmol) in DMF (2.00 mL) and the resulting solution was stirred for 10 min and treated with aniline **19**[18] (15.6 mg, 0.060 mmol). The resulting mixture was stirred for 38 h at 23 °C and

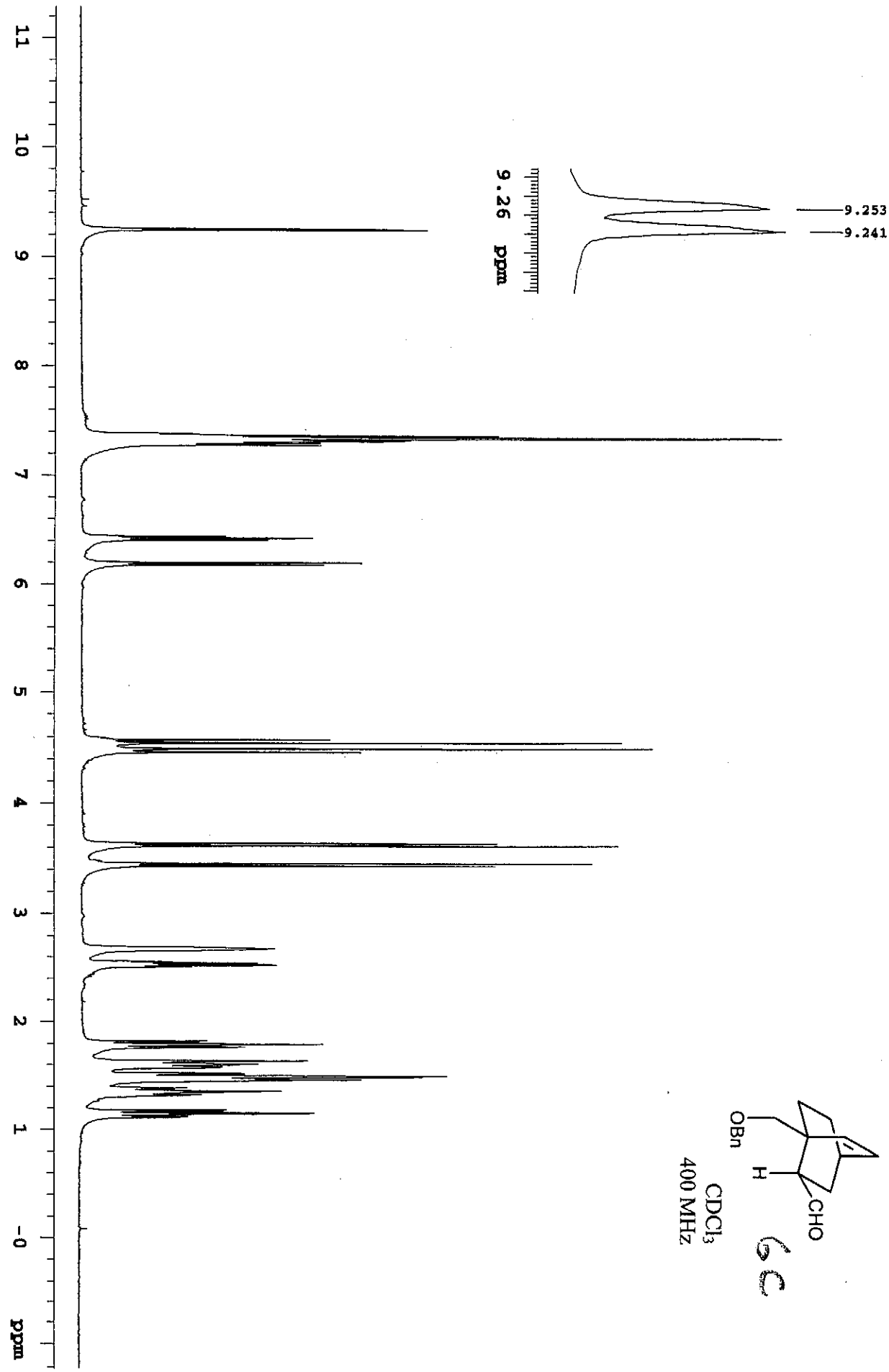
concentrated. Flash chromatography (65:35 hexanes/EtOAc) provided 6.0 mg (58%) of **20**: $[\alpha]^{19.4}_{D}$ –38.0 (*c* 0.29 $CHCl_3$); ^{1}H NMR 11.83 (s, 1, OH), 11.11 (s, 1, OH), 8.24 (s, 1, NH), 7.57 (d, 1, *J* = 9), 6.51 (d, 1, *J* = 9), 6.47 (d, 1, *J* = 10.3), 5.85 (d, 1, *J* = 10.3), 4.42 (dd, 2, *J* = 8.6, 8.5), 2.44 (t, 2, *J* = 8.6), 2.21-2.11 (m, 1), 2.10-2.00 (m, 1), 1.99-1.75 (m, 3), 1.75-1.41 (m, 6), 1.41-1.07 (m, 3), 1.20 (s, 3), 1.14 (dd, 2, *J* = 8.6, 8.5), 0.09 (s, 9); ^{13}C NMR 205.3, 174.3, 170.6, 156.3, 154.6, 153.9, 127.3, 125.6, 114.4, 111.1, 104.4, 63.7, 47.7, 38.7, 35.5, 33.6, 32.5, 30.9, 26.8, 26.6, 25.3, 24.8, 24.7, 21.1, 17.3, -1.5 (3 C); IR 3400, 1659, 1651, 1386, 1258; HRMS (ESI) calcd. for $C_{28}H_{40}NO_6Si$ (MH^+) 514.2625, found 514.2635.

3-[[3-[(8*S*,8a*R*)-1,3,4,7,8,8a-Hexahydro-8-methyl-7-oxo-2*H*-2,4a-ethanonaphthalen-8-yl]-1-oxopropyl]amino]-2,4-dihydroxybenzoic Acid (*nor*-platencin, 3). TASF (25 mg, 0.090 mmol) was added to a solution of **20** (15.4 mg, 0.030 mmol) in DMF (2.0 mL). The resulting mixture was stirred for 1 h at 40 °C and concentrated. Flash chromatography (60:40:1 acetone/hexanes/AcOH) provided 7.0 mg (56%) of **3**: $[\alpha]^{19.4}_{D}$ –63.6 (*c* 0.25 $CHCl_3$); ^{1}H NMR 11.78 (br, 1, $w_{1/2}$ = 22), 11.25 (br, 1, $w_{1/2}$ = 40), 8.33 (s, 1, NH), 7.62 (d, 1, *J* = 9.2), 6.55 (d, 1, *J* = 10), 6.51 (d, 1, *J* = 9.2), 5.89 (d, 1, *J* = 10), 2.60-2.37 (m, 1), 2.23-2.00 (m, 1), 2.00-2.1.79 (m, 1), 1.79-1.43 (m, 9), 1.43-1.03 (m, 3), 1.22 (s, 3), 0.94-0.79 (m, 1); ^{13}C NMR 206.9, 174.3, 172.9, 158.0, 155.3, 154.5, 128.3, 125.3, 114.3, 111.2, 103.5, 47.7, 38.5, 35.4, 33.8, 32.3, 31.0, 26.8, 26.5, 25.3, 24.7, 24.6, 21.4; IR 3386, 3058, 1659, 1651, 1537, 1264, 1243; HRMS (ESI) calcd. for $C_{23}H_{28}NO_6$ (MH^+) 414.1917, found 414.1920.

Minimum Inhibitory Concentration (MIC) of *nor*-Platencin (3) Against Various Bacteria

Org. Type	Org. Specifics	Org. Name	MIC
S. aureus	MSSA	1199	4
S. aureus	MRSA w/o serum	494	4
S. aureus	MRSA w/ serum	494	>32
S. aureus	MRSA macrolide-R and Linezolid-R	NRS 127	4
S. aureus	VISA	Mu50	8
S. aureus	VRSA	VRSA-MI	16
S. aureus	hVISA	Mu3	4
S. aureus	MRSA Daptomycin-R	SA684	4
E. faecalis	macrolide-R	ATCC 29212	16
E. faecium	vancomycin-R	VRE 7303	0.25
E. coli		ATCC 25922	>32

MIC determined according to: *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard –Eighth Edition*. Document M07-A8; Clinical and Laboratory Standards Institute: Wayne, Pennsylvania, 2008. R = resistant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9.26 ppm
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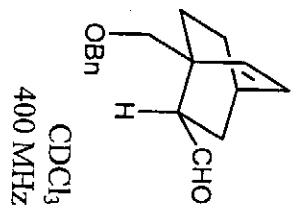
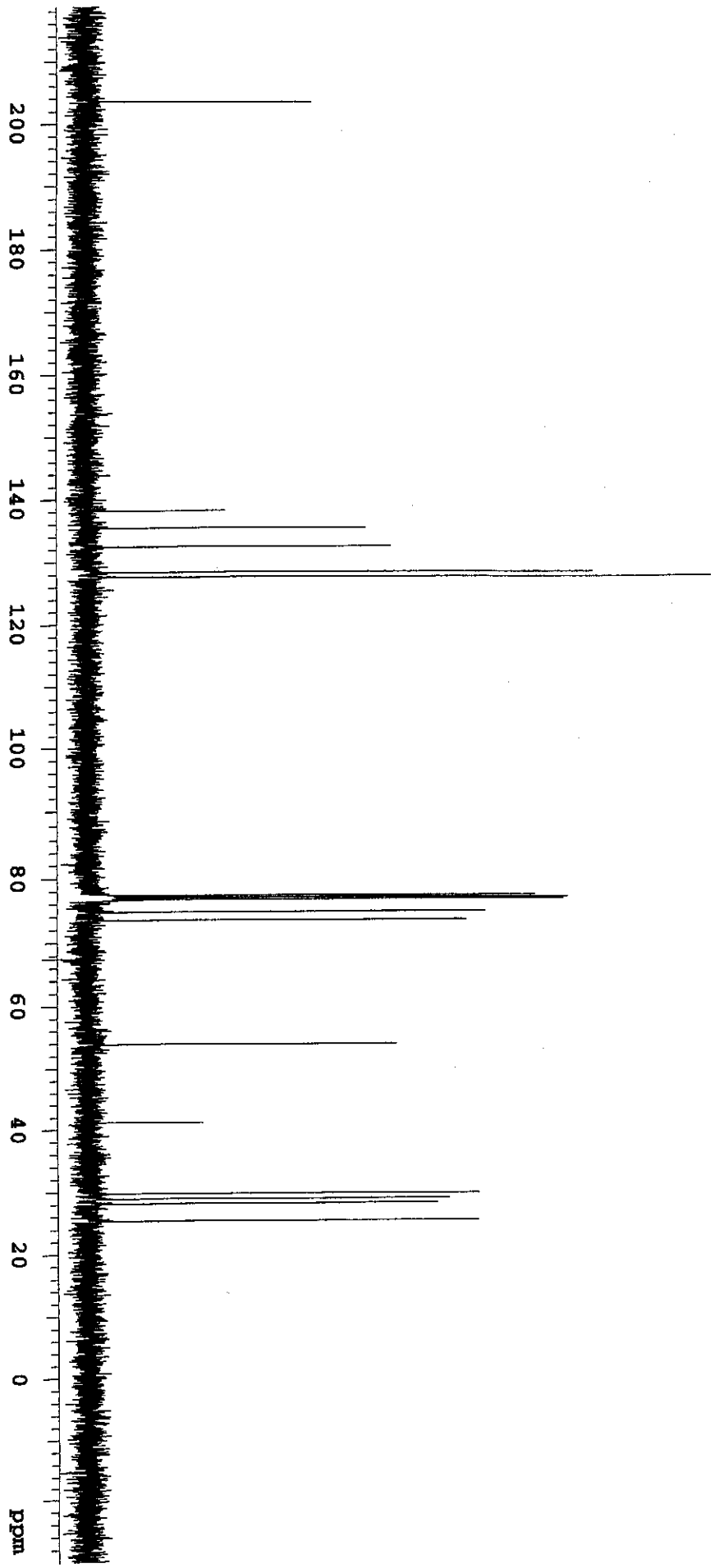
10
9
8
7
6
5
4
3
2
1
-0
ppm
OBn
H
CHO
6c
CDCl3
400 MHz

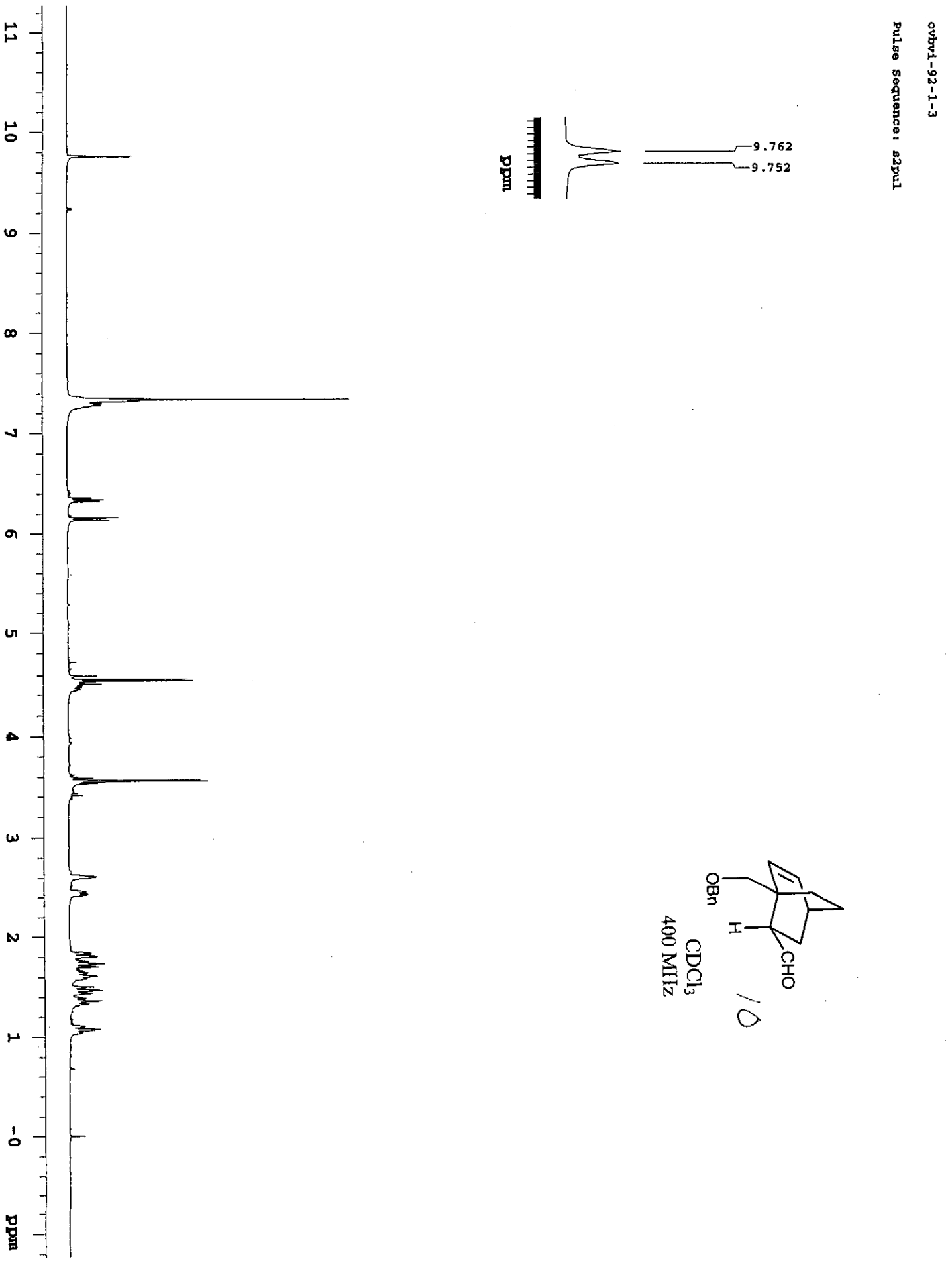
INDEX	FREQUENCY	PPM	HEIGHT
1	20459.871	203.528	36.7
2	13888.473	138.158	23.0
3	13613.806	135.425	45.4
4	13312.436	132.427	49.4
5	12900.436	128.329	82.1
6	12826.429	127.593	101.2
7	12821.088	127.540	58.6
8	7771.801	77.311	72.9
9	7740.519	77.000	78.2
10	7708.475	76.681	77.5
11	7510.104	74.708	64.8
12	7379.638	73.410	61.6
13	5410.431	53.821	50.4
14	4129.417	41.078	19.3
15	2981.158	29.656	63.8
16	2893.417	28.783	58.9
17	2814.832	28.001	57.0
18	2534.061	25.208	63.7



6c

$CDCl_3$
400 MHz

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ppm
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H
CHO
CDCl3
400 MHz
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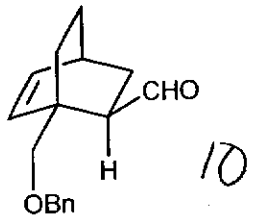
10
9
8
7
6
5
4
3
2
1
-0
ppm

INDEX	FREQUENCY	PPM	HEIGHT
1	20543.034	204.355	13.5
2	13891.525	138.188	10.7
3	13649.666	135.782	21.7
4	13564.214	134.932	24.3
5	12900.436	128.329	38.3
6	12823.377	127.563	79.7
7	7772.564	77.319	13.3
8	7740.519	77.000	13.5
9	7709.238	76.689	13.8
10	7457.460	74.184	23.6
11	7379.638	73.410	27.8
12	5127.372	51.005	23.2
13	4159.172	41.374	15.4
14	2975.054	29.595	28.5
15	2752.269	27.379	23.9
16	2563.054	25.496	26.8
17	2449.373	24.366	24.4



10

$CDCl_3$
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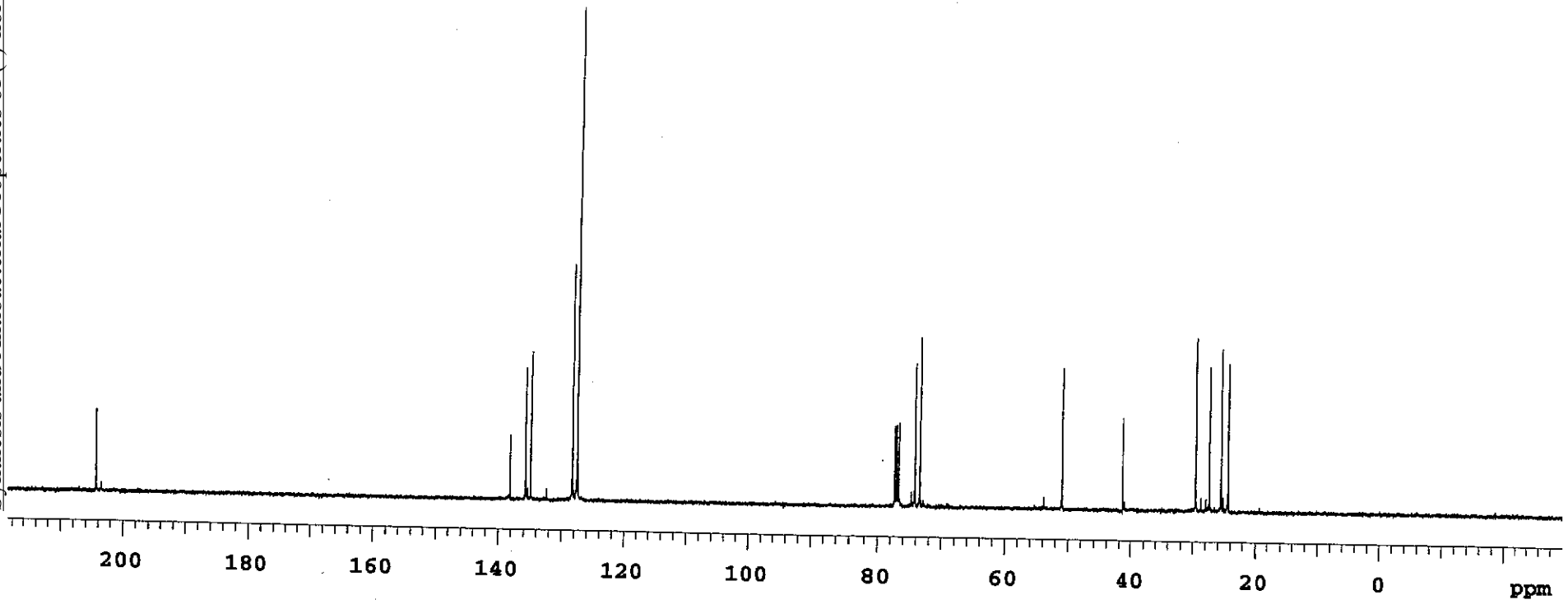

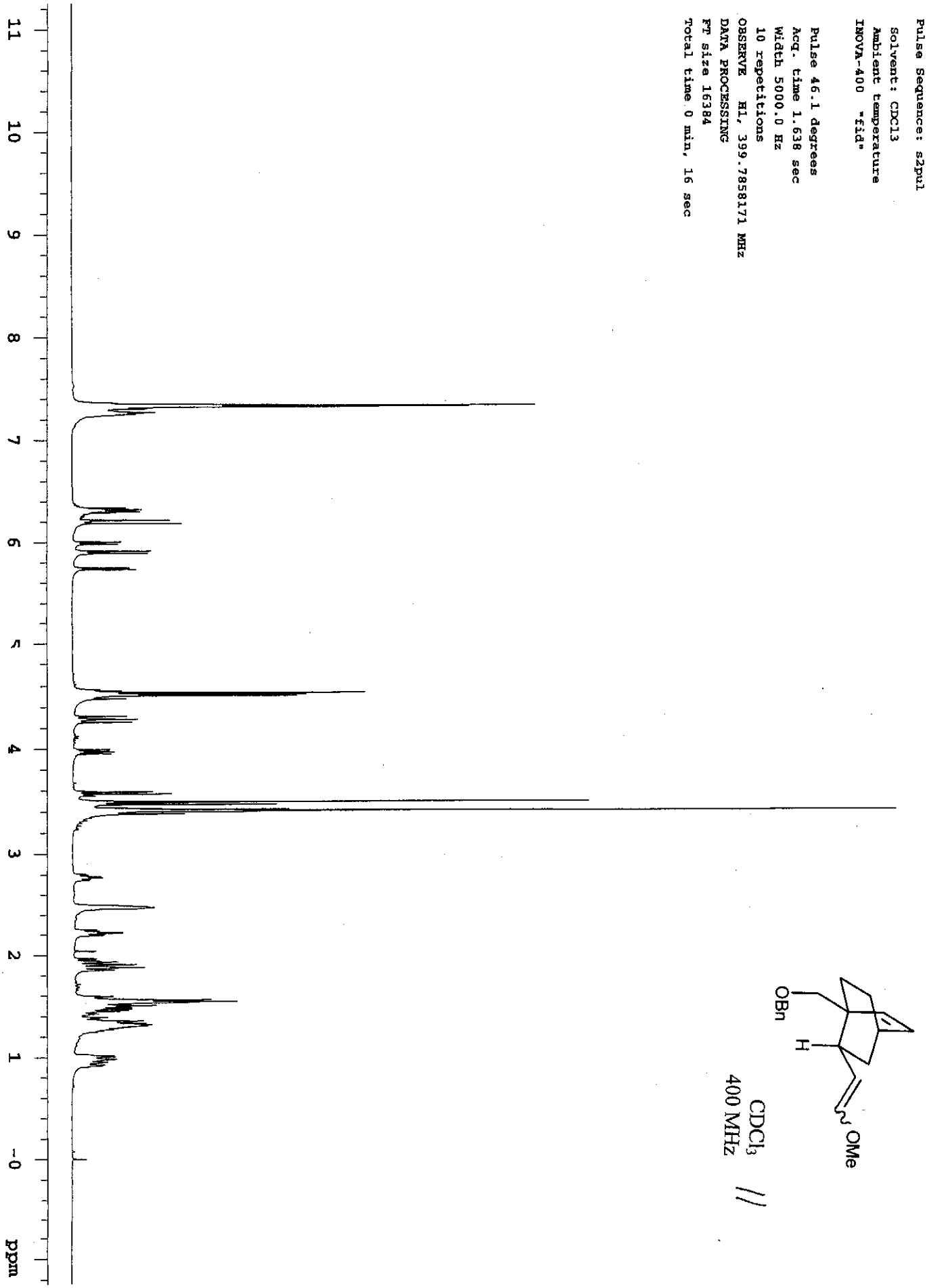
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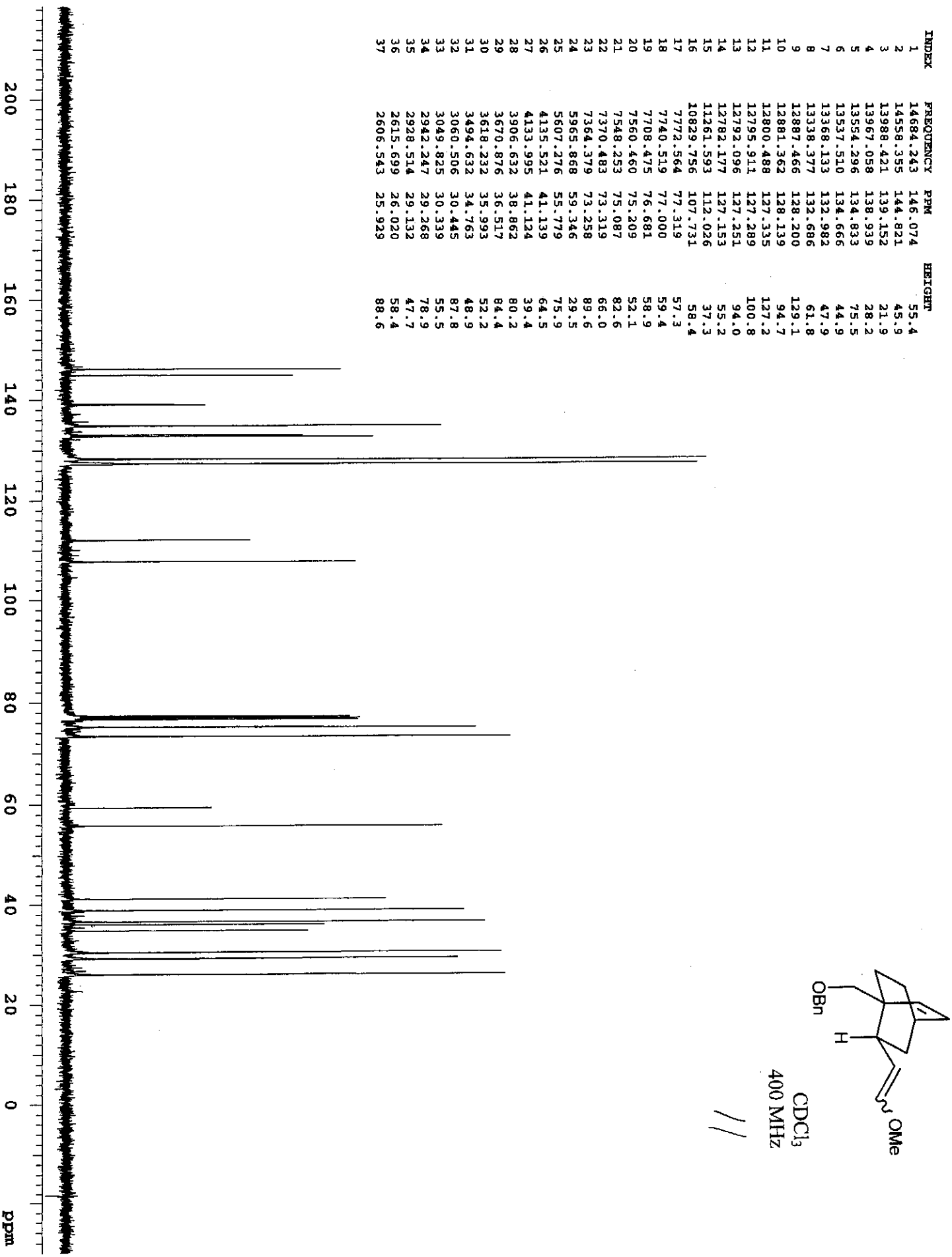
Solvent: CDCl3
Ambient temperature
INOVA-400 "fid"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
10 repetitions
OBSERVE H1, 399.7858171 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 16 sec
OBn
H
OMe
CDCl3
400 MHz
11
10
9
8
7
6
5
4
3
2
1
-0
ppm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4 13967.058 138.939 28.2
5 13554.296 134.833 75.5
6 13537.510 134.666 44.9
7 13368.133 132.982 47.9
8 13338.377 132.686 61.8
9 12887.466 128.200 129.1
10 12881.362 128.139 94.7
11 12800.488 127.335 127.2
12 12795.911 127.289 100.8
13 12792.096 127.251 94.0
14 12782.177 127.153 55.2
15 11261.593 112.026 37.3
16 10829.756 107.731 58.4
17 7772.564 77.319 57.3
18 7740.519 77.000 59.4
19 7708.475 76.681 58.9
20 7560.460 75.209 52.1
21 7548.253 75.087 82.6
22 7370.483 73.319 66.0
23 7364.379 73.258 89.6
24 5965.868 59.346 29.5
25 5607.276 55.779 75.9
26 4135.521 41.139 64.5
27 4133.995 41.124 39.4
28 3906.632 38.862 80.2
29 3670.876 36.517 84.4
30 3618.232 35.993 52.2
31 3494.632 34.763 48.9
32 3060.506 30.445 87.8
33 3049.825 30.339 55.5
34 2942.247 29.268 78.9
35 2928.514 29.132 47.7
36 2615.699 26.020 58.4
37 2606.543 25.929 88.6
OBn
H
OMe
CDCl3
400 MHz
200
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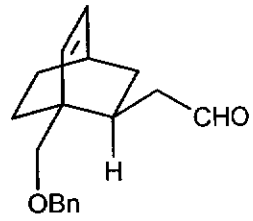
160
140
120
100
80
60
40
20
0
ppm

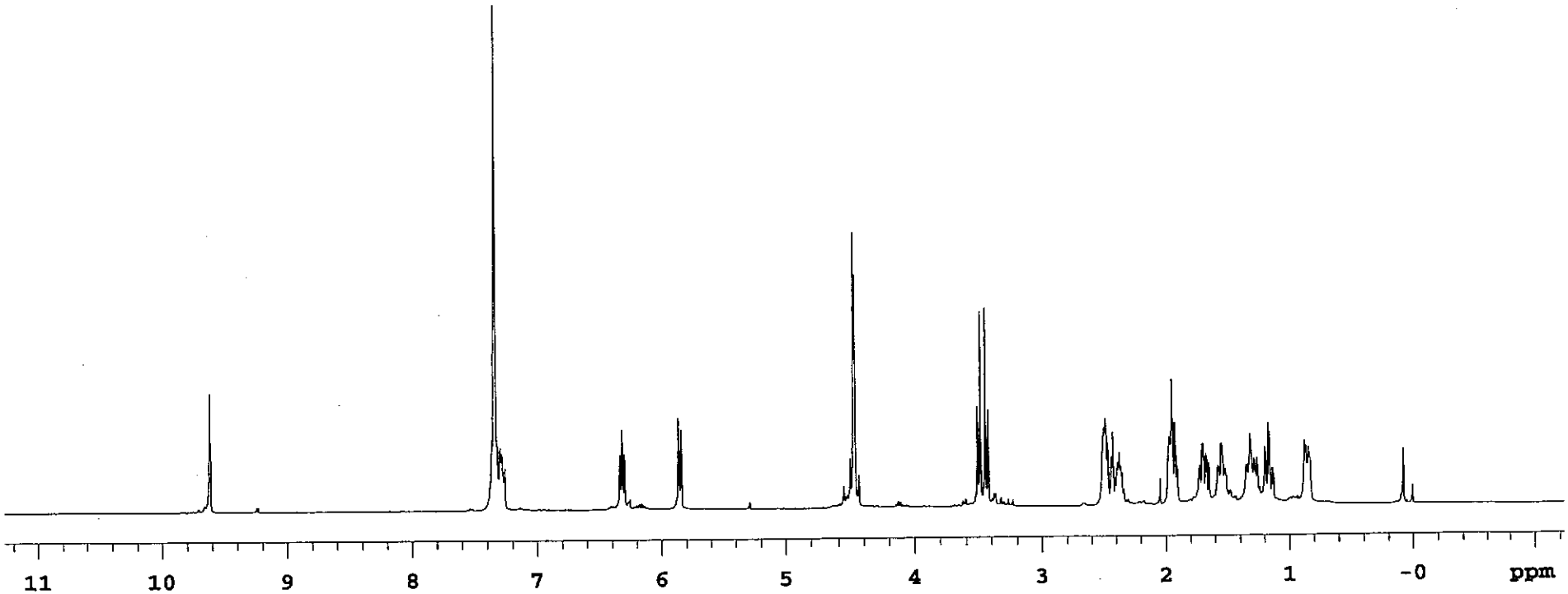
ovbvi-97-10-20

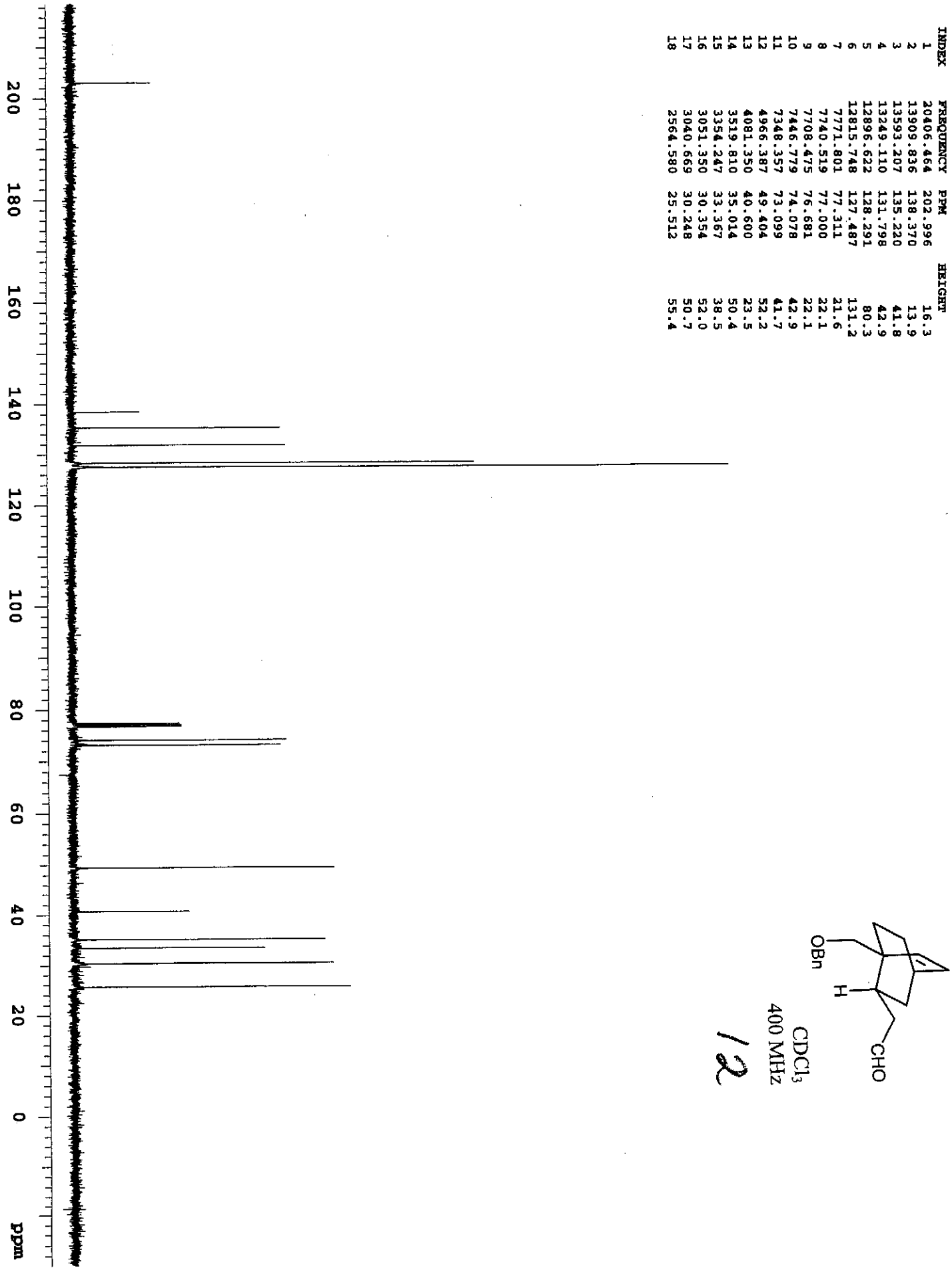
Pulse Sequence: s2pul



$CDCl_3$
400 MHz

12





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3	13593.207	135.220	41.8
4	13249.110	131.798	42.9
5	12896.622	128.291	80.3
6	12815.748	127.487	131.2
7	7771.801	77.311	21.6
8	7740.519	77.000	22.1
9	7708.475	76.681	22.1
10	7446.779	74.078	42.9
11	7348.357	73.099	41.7
12	4966.387	49.404	52.2
13	4081.350	40.600	23.5
14	3519.810	35.014	50.4
15	3354.247	33.367	38.5
16	3051.350	30.354	52.0
17	3040.669	30.248	50.7
18	2564.580	25.512	55.4

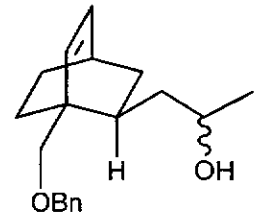
$CDCl_3$
400 MHz

12

ovbvi-98-2-9

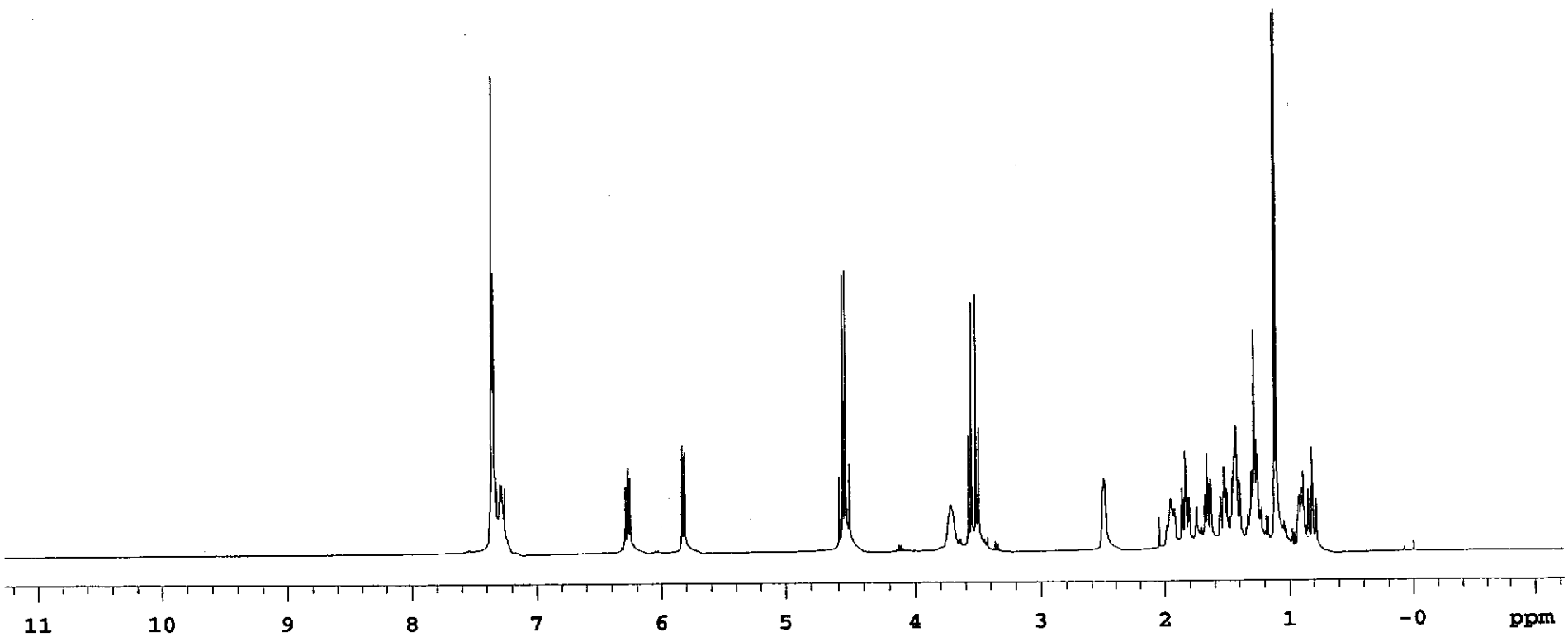
Pulse Sequence: s2pul

less polar diastereoisomer



$CDCl_3$
400 MHz

13



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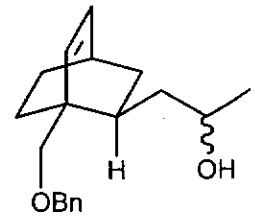
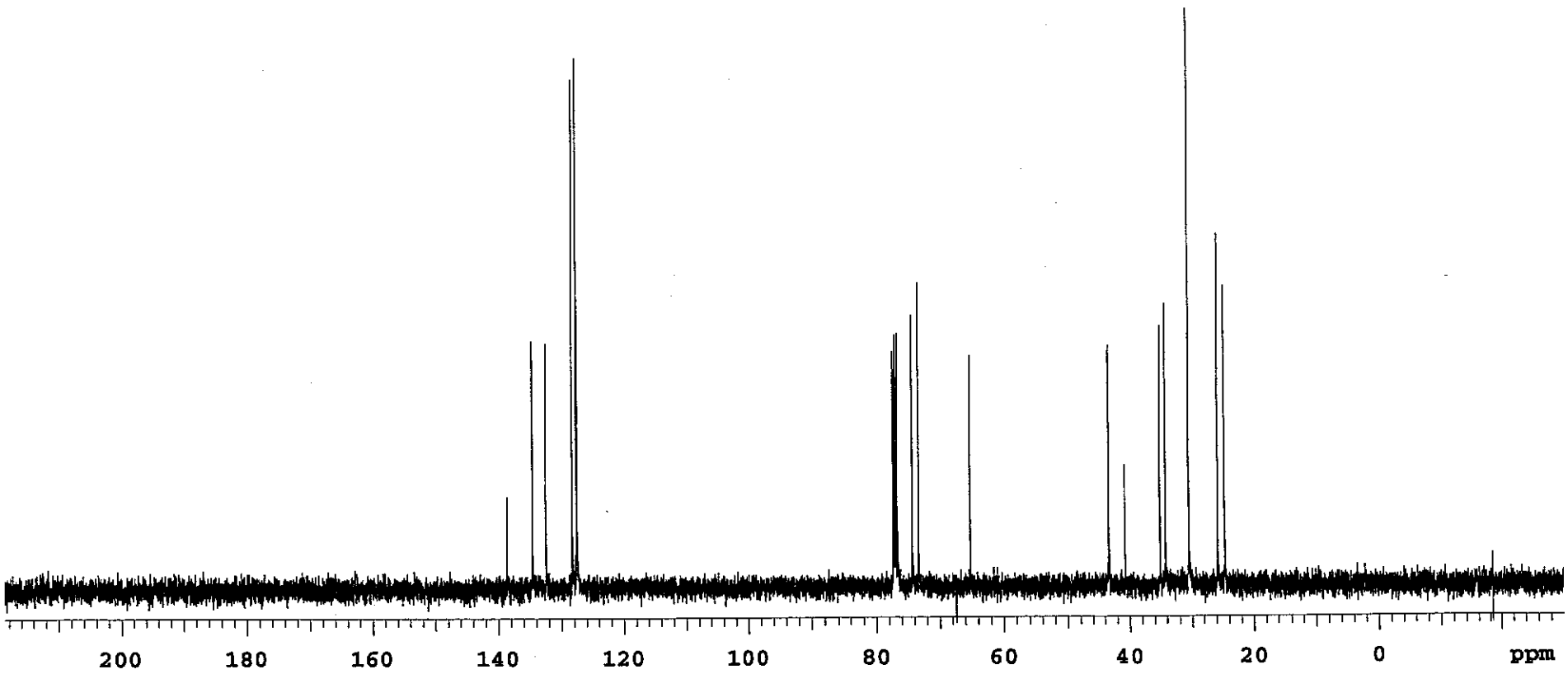
3	13316.251	132.465	39.7
4	12896.621	128.291	82.2
5	12826.429	127.593	85.7
6	12811.933	127.449	47.3
7	7772.564	77.319	38.3
8	7740.519	77.000	41.0
9	7708.475	76.681	41.3
10	7472.719	74.336	44.0
11	7372.771	73.342	49.2
12	6557.164	65.228	37.7
13	4357.543	43.347	39.3
14	4093.557	40.721	20.0
15	3531.254	35.128	42.3
16	3438.172	34.202	45.9
17	3065.084	30.490	93.5
18	2591.284	25.777	57.1
19	2478.365	24.654	48.6

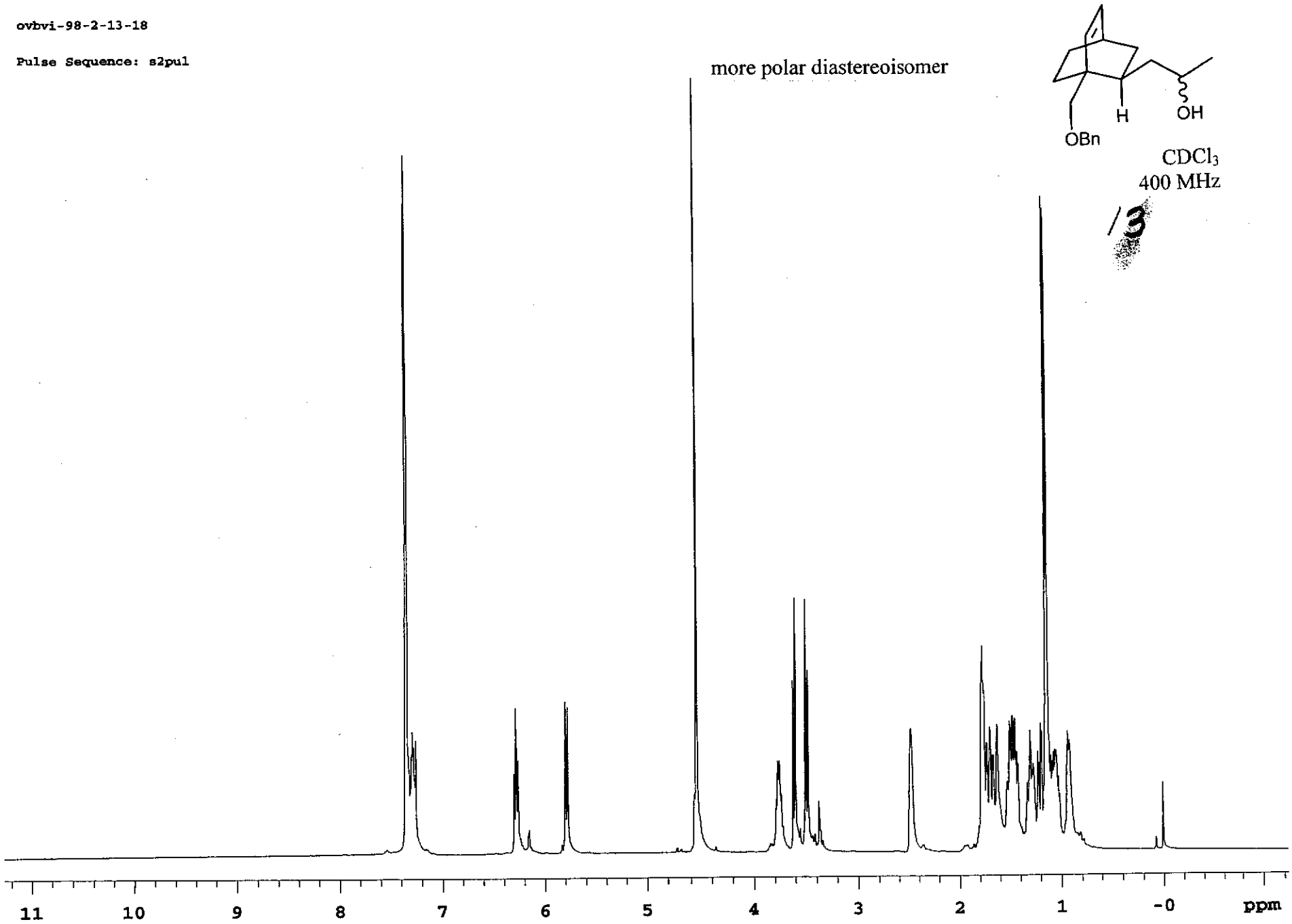
less polar diastereoisomer



$CDCl_3$
400 MHz

13




ovbvi-98-2-13-18
Pulse Sequence: s2pul
more polar diastereoisomer
OBn
H
OH
CDCl3
400 MHz
13
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

INDEX	FREQUENCY	PPM	HEIGHT
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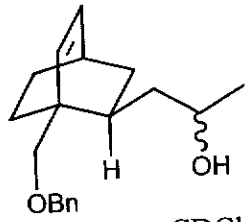
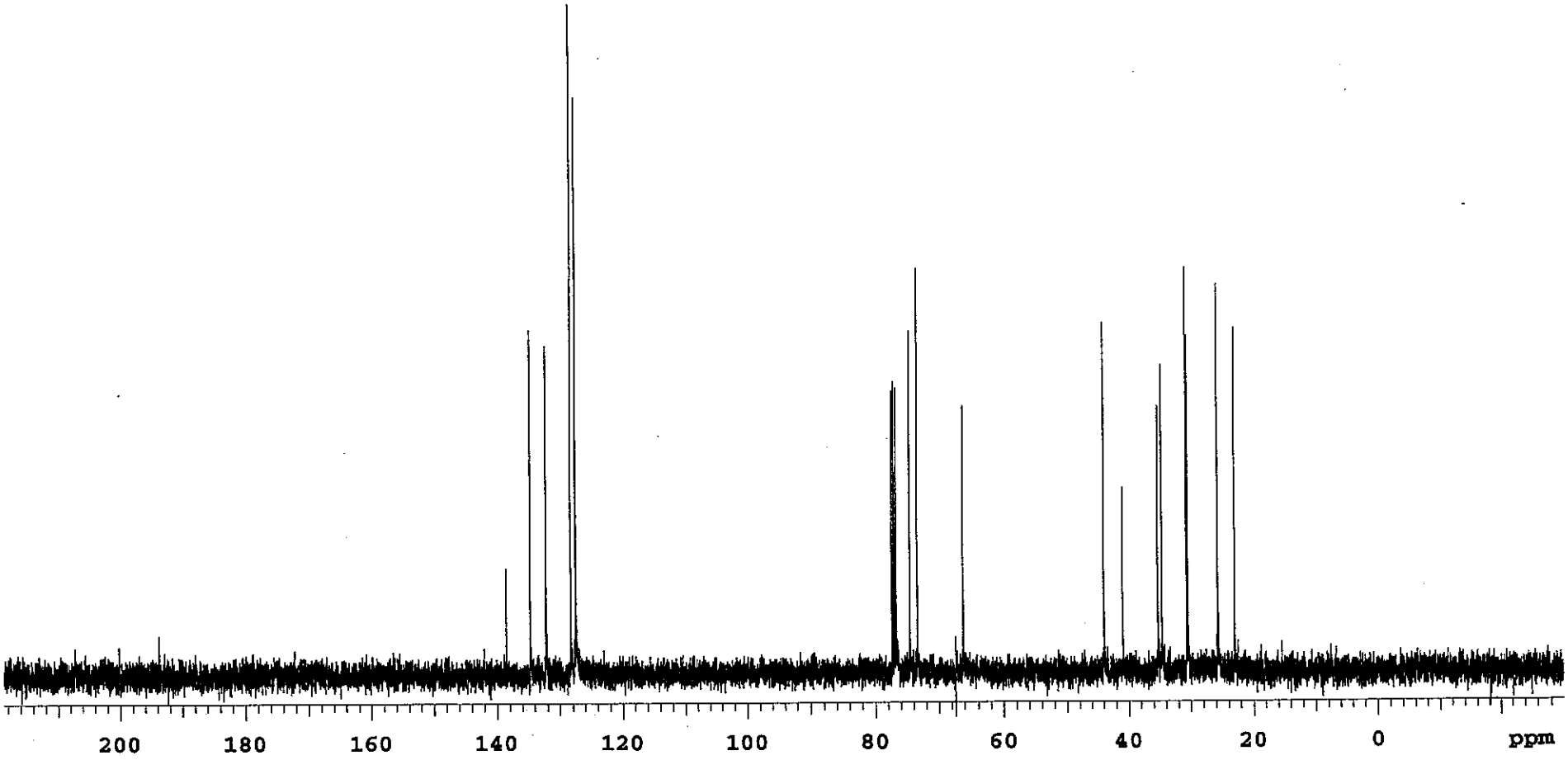
5	12819.562	127.525	93.1
6	12812.696	127.456	67.3
7	7772.564	77.319	45.5
8	7740.519	77.000	47.1
9	7708.475	76.681	46.2
10	7491.031	74.518	55.2
11	7374.297	73.357	65.3
12	6657.875	66.230	43.1
13	4415.528	43.924	56.4
14	4110.343	40.888	30.0
15	3547.276	35.287	43.1
16	3479.373	34.612	49.7
17	3086.447	30.703	65.3
18	3065.847	30.498	54.3
19	2576.788	25.633	62.7
20	2308.225	22.961	55.6

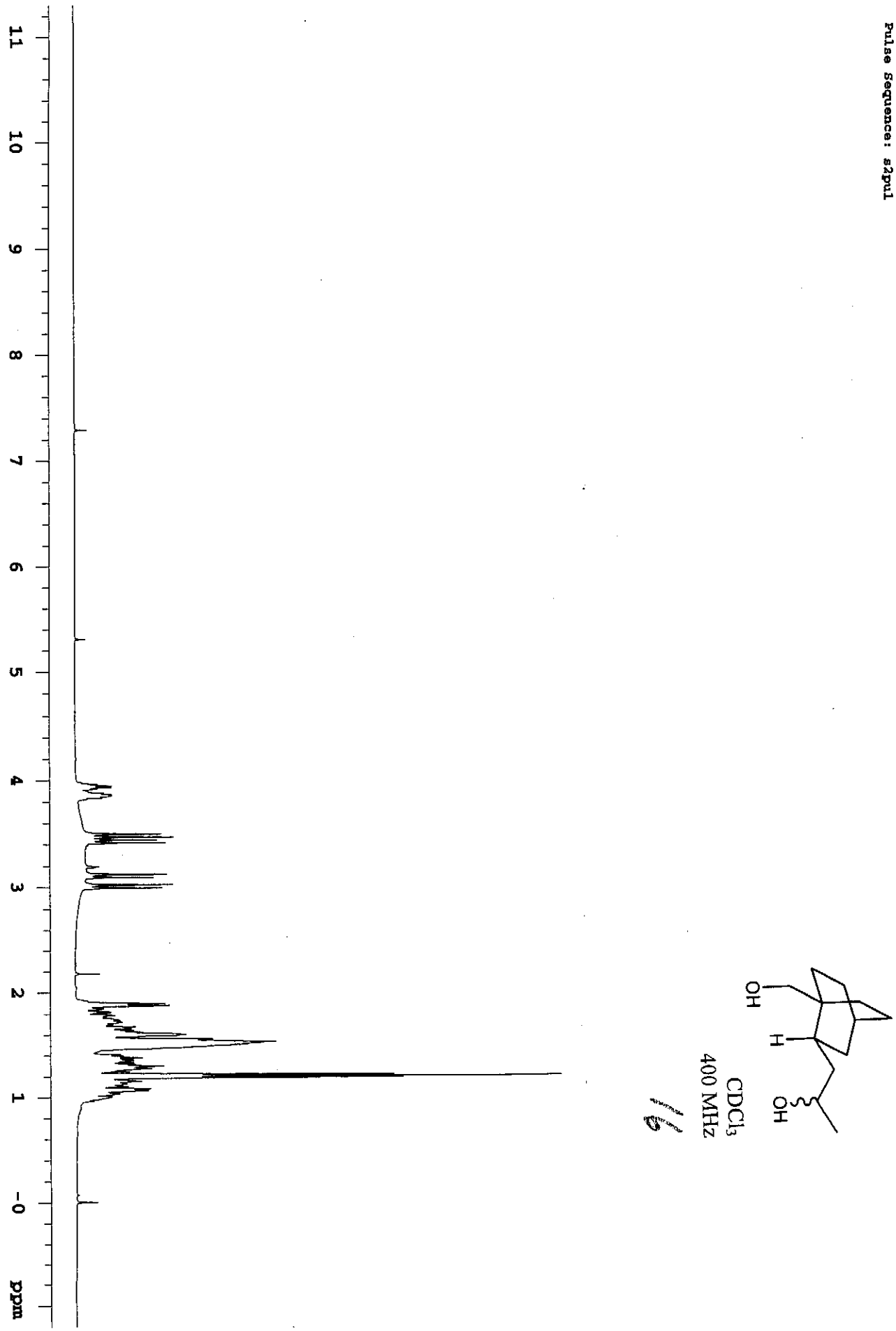
more polar diastereoisomer



$CDCl_3$
400 MHz

13

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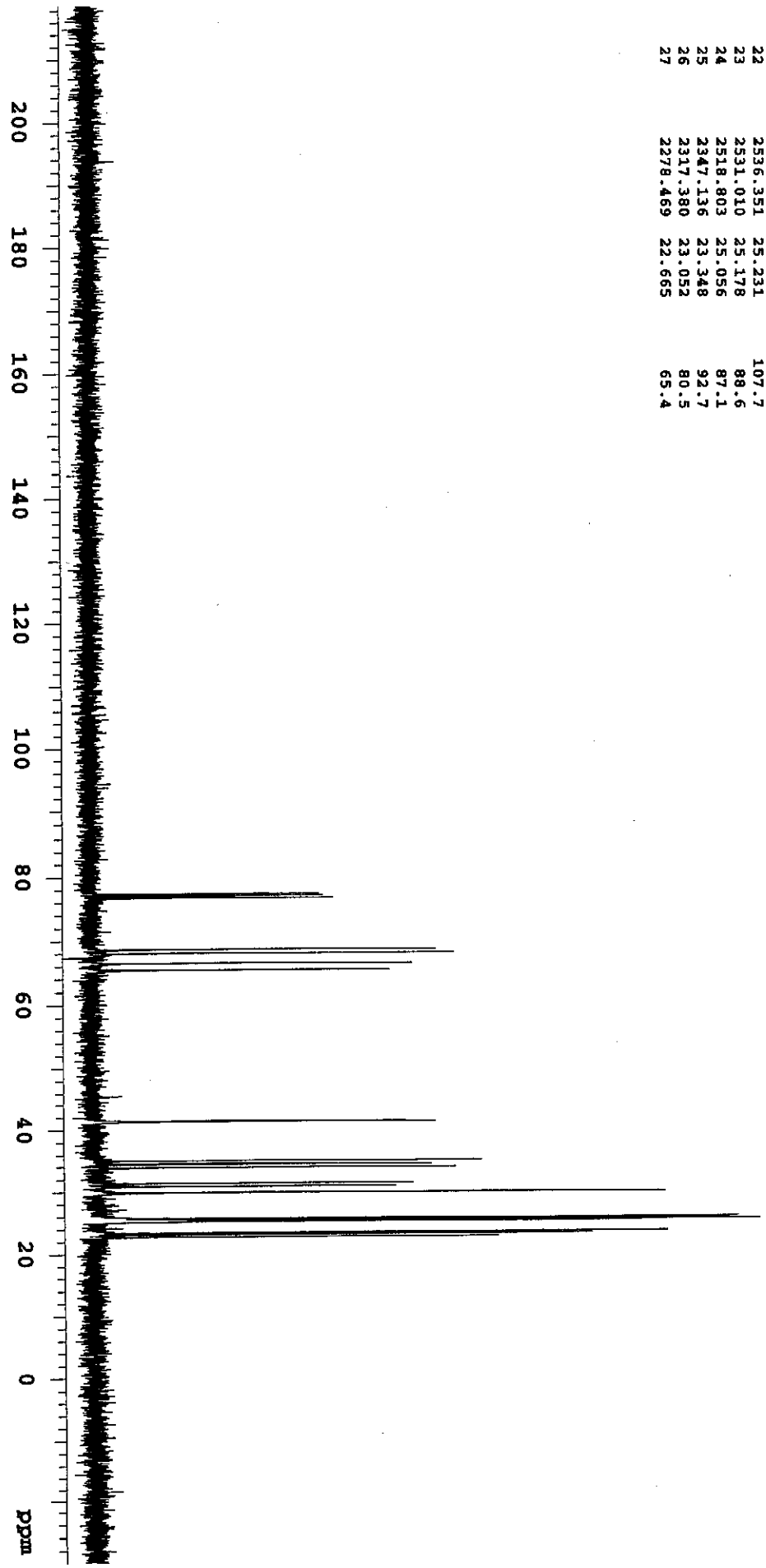
400 MHz
11
11
10
9
8
7
6
5
4
3
2
1
-0
ppm



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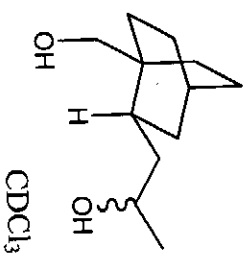
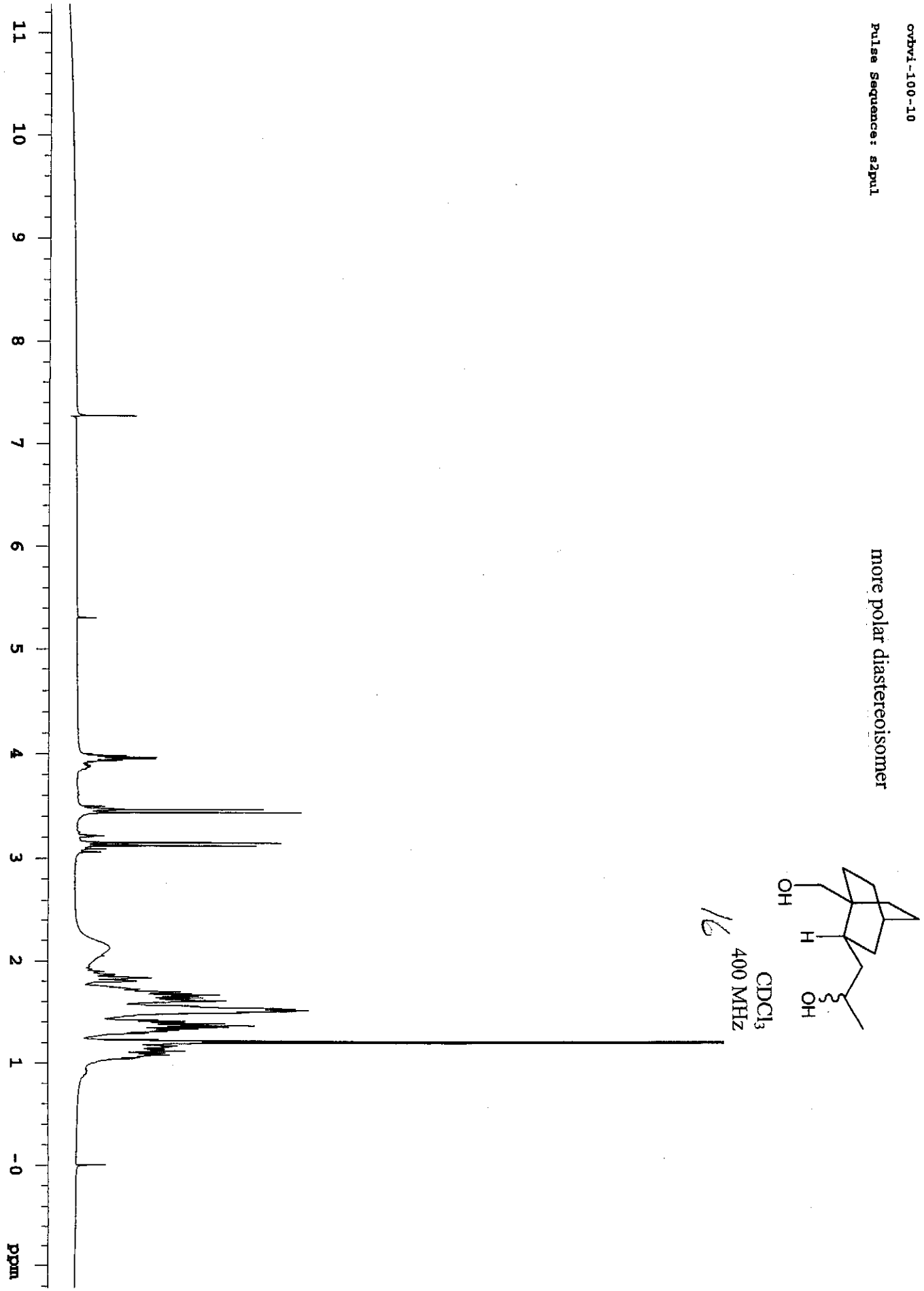
3	7708.475	76.681	39.2
4	6900.498	68.644	55.5
5	6839.461	68.037	58.5
6	6680.001	66.450	51.7
7	6570.898	65.365	48.0
8	4167.565	41.457	50.4
9	4152.306	41.306	55.4
10	3514.469	34.961	62.8
11	3469.454	34.513	39.5
12	3450.380	34.323	54.6
13	3400.025	33.822	58.5
14	3147.484	31.310	51.7
15	3096.365	30.802	48.9
16	3002.521	29.868	85.4
17	2994.891	29.792	92.4
18	2579.077	25.656	104.3
19	2577.551	25.641	94.8
20	2550.847	25.375	102.8
21	2538.640	25.254	105.1
22	2536.351	25.231	107.7
23	2531.010	25.178	88.6
24	2518.803	25.056	87.1
25	2347.136	23.348	92.7
26	2317.380	23.052	80.5
27	2278.469	22.665	65.4

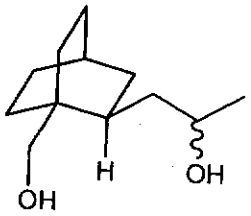


$CDCl_3$
400 MHz
//

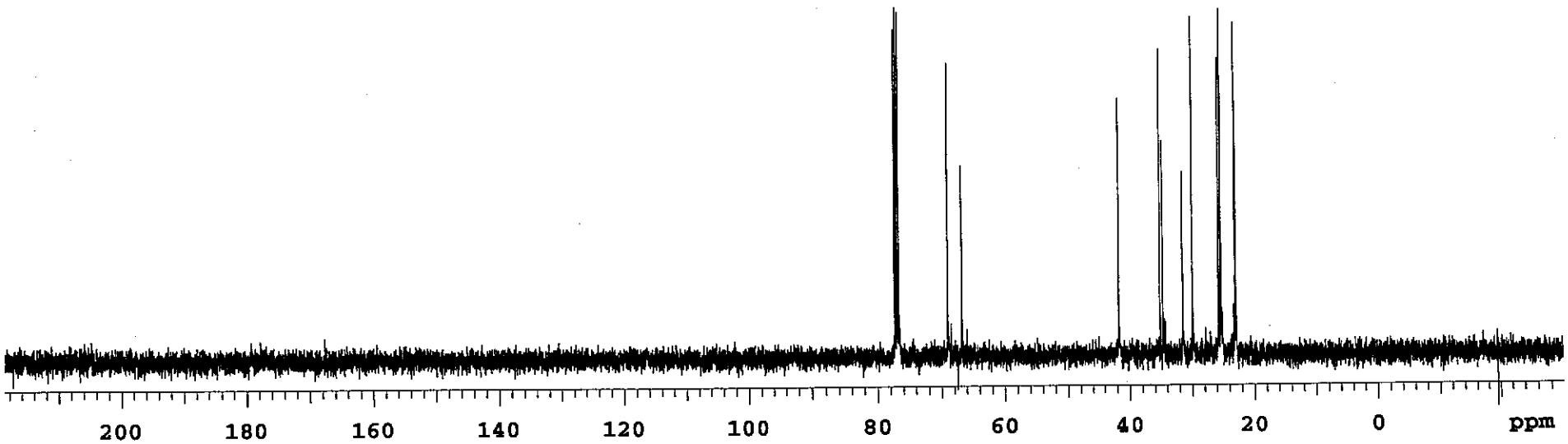

ovbvi-100-10
Pulse Sequence: s2pul
more polar diastereoisomer
OH
H
OH
CDCl3
400 MHz
16
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

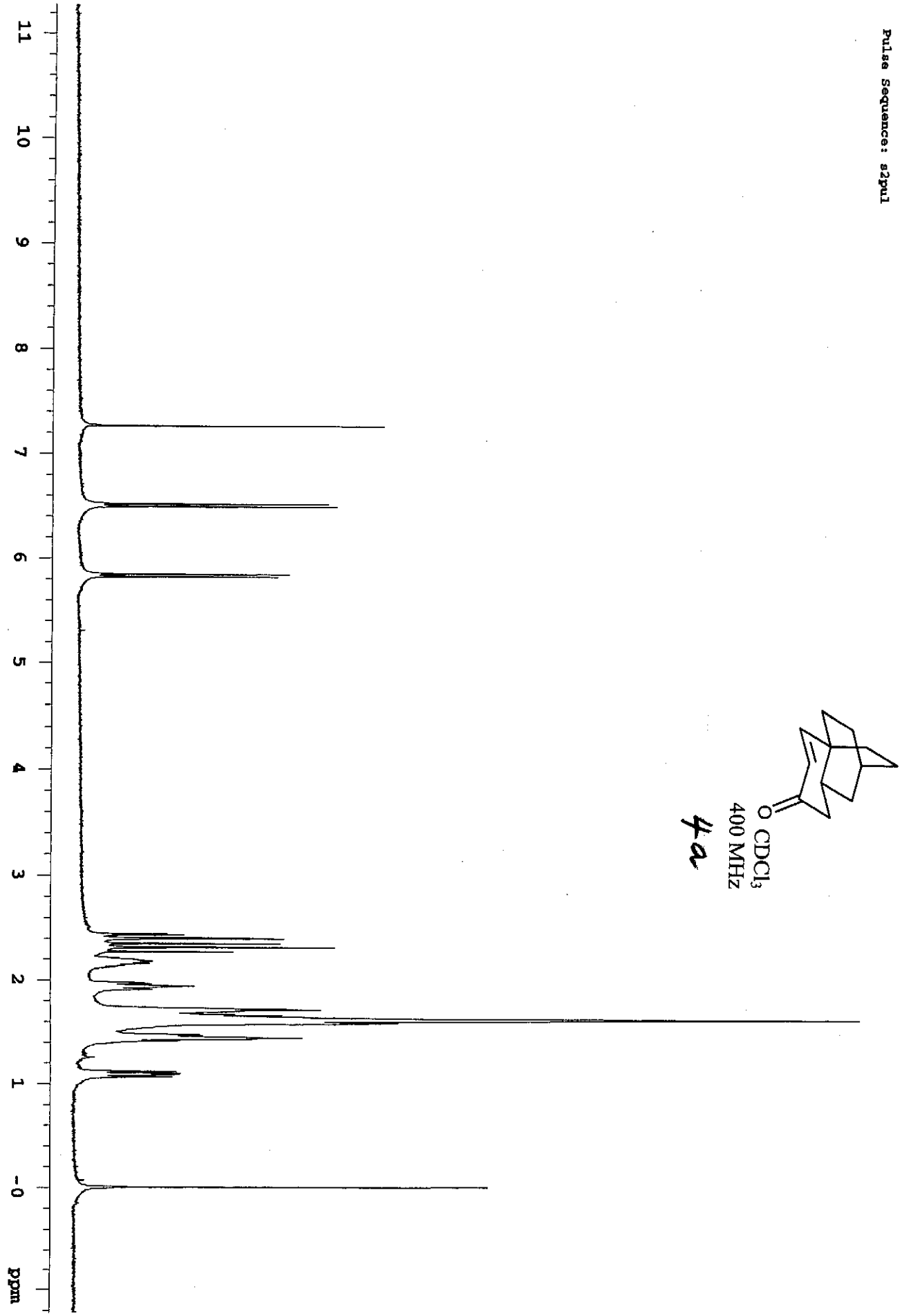
INDEX	FREQUENCY	PPM	HEIGHT
1	7772.564	77.319	53.1
2	7740.519	77.000	56.6
3	7708.475	76.681	55.9
4	6933.305	68.970	47.6
5	6706.705	66.716	31.3
6	4192.742	41.708	41.8
7	3528.202	35.097	49.6
8	3479.372	34.612	35.0
9	3163.506	31.469	30.1
10	3007.098	29.914	54.8
11	2579.076	25.656	48.1
12	2542.454	25.291	56.0
13	2534.824	25.216	45.1
14	2320.432	23.083	53.9
15	2302.121	22.901	41.1

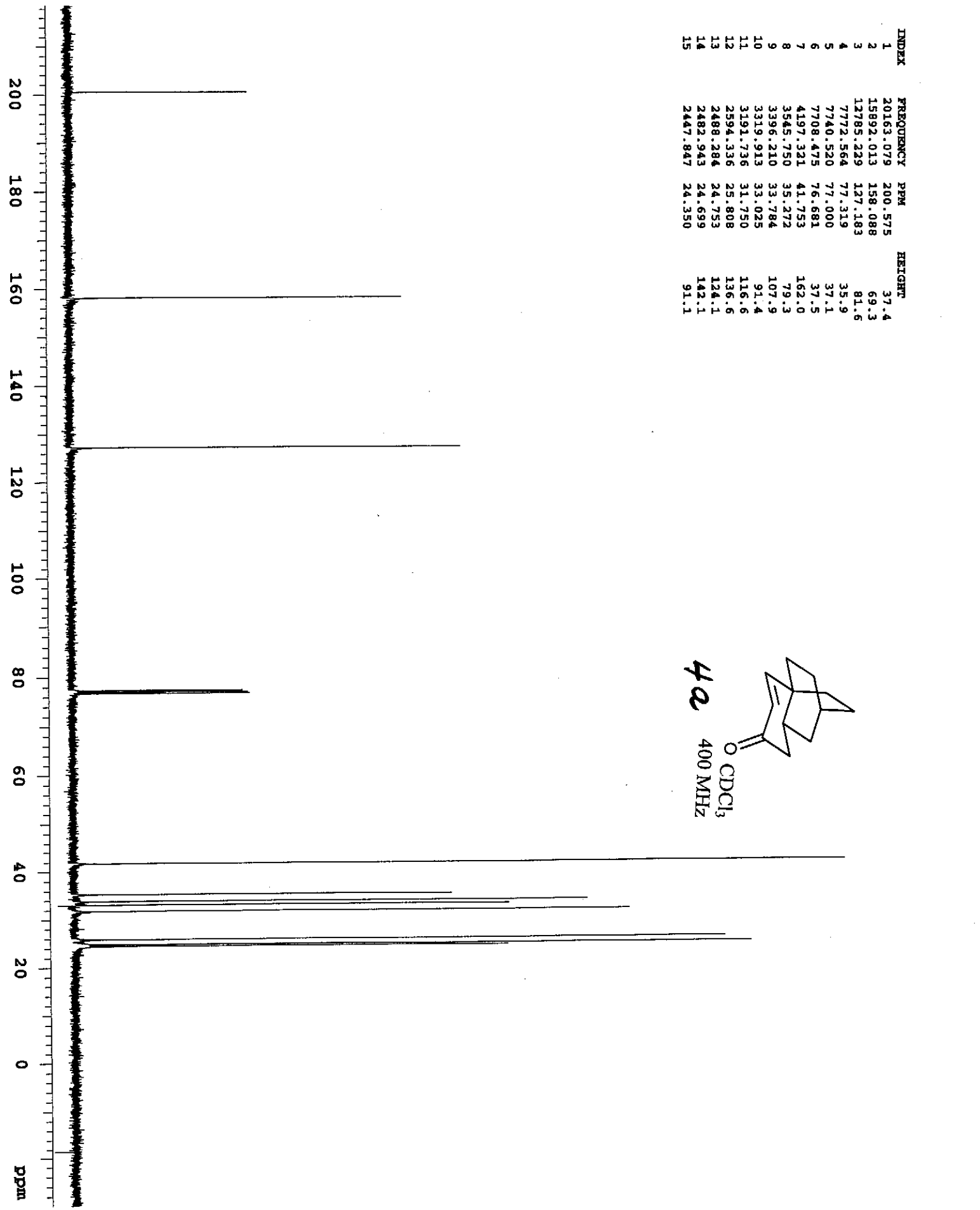
more polar diastereoisomer

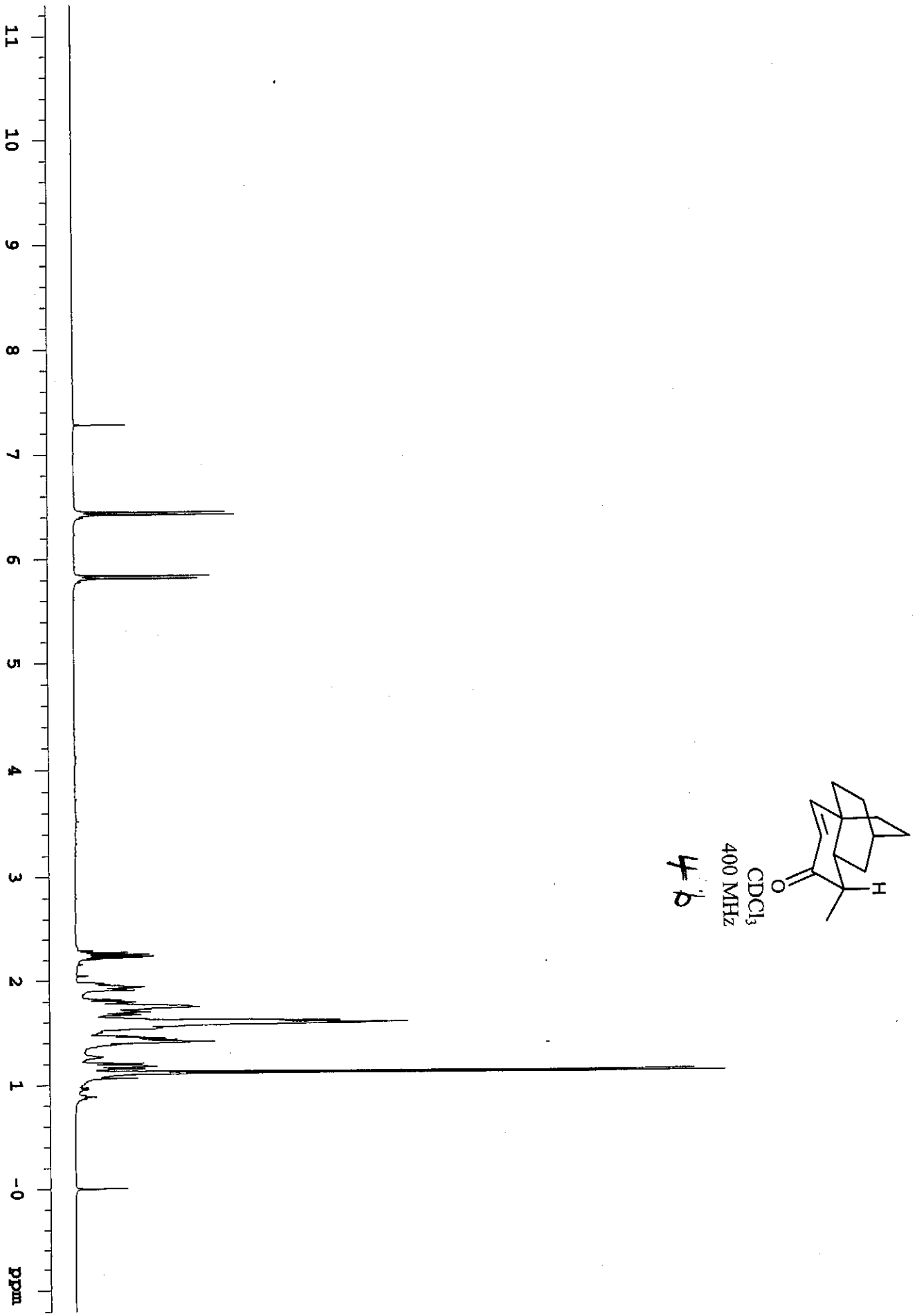


$CDCl_3$
400 MHz
16

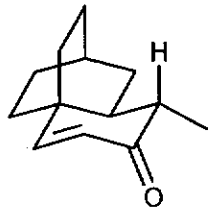



ovbvi-56-14-1
Pulse Sequence: s2pul
O
CDCl3
400 MHz
4a
11
10
9
8
7
6
5
4
3
2
1
-0
ppm


INDEX FREQUENCY PPM HEIGHT
1 20163.079 200.575 37.4
2 15892.013 158.088 69.3
3 12785.229 127.183 81.6
4 7772.564 77.319 35.9
5 7740.520 77.000 37.1
6 7708.475 76.681 37.5
7 4197.321 41.753 162.0
8 3545.750 35.272 79.3
9 3396.210 33.784 107.9
10 3319.913 33.025 91.4
11 3191.736 31.750 116.6
12 2594.336 25.808 136.6
13 2480.284 24.753 124.1
14 2482.943 24.699 142.1
15 2447.847 24.350 91.1
O
4a
CDCl3
400 MHz
200
180
160
140
120
100
80
60
40
20
0
ppm

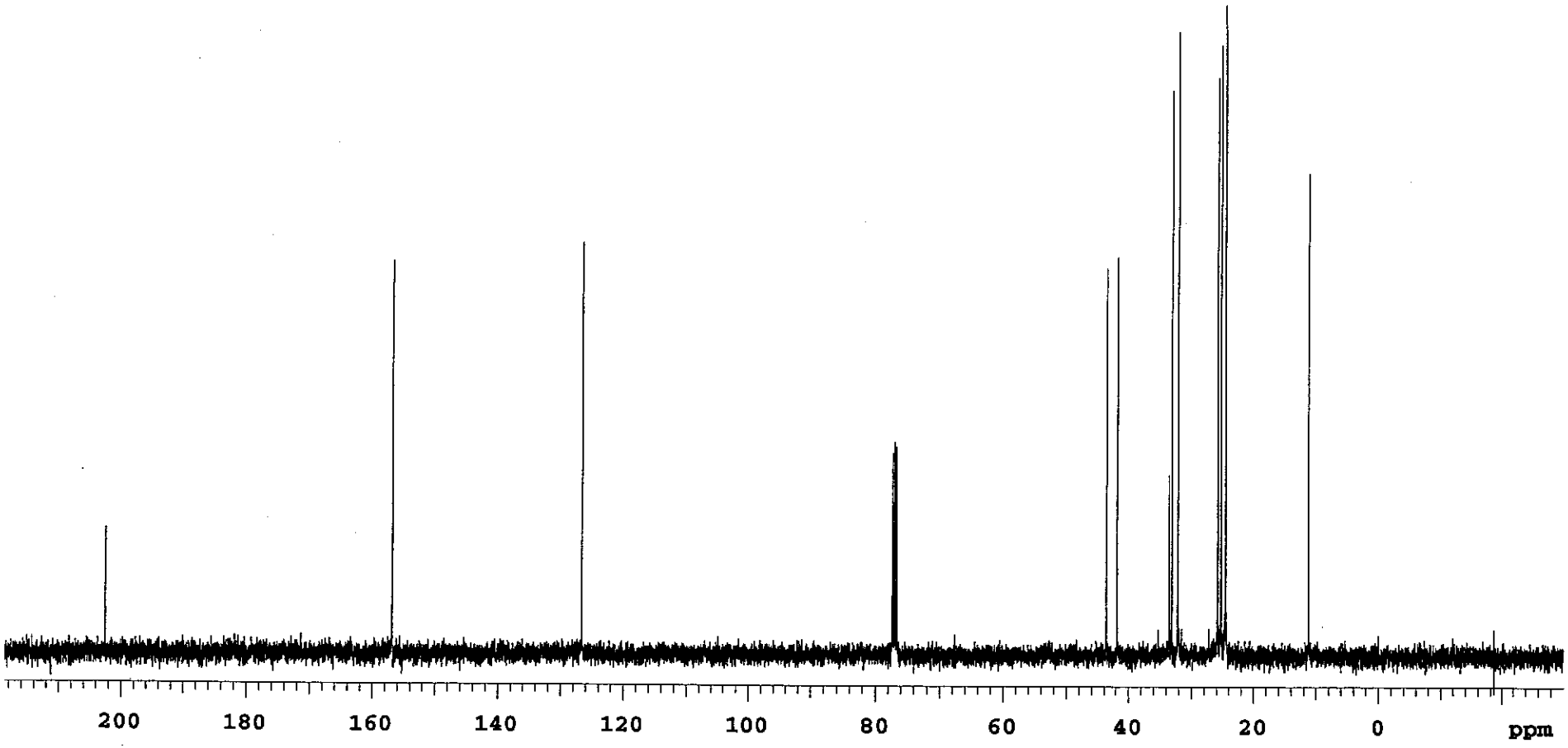

ovbri-60-8
Pulse Sequence: s2pul
CDCl3
400 MHz
4b
O
H
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

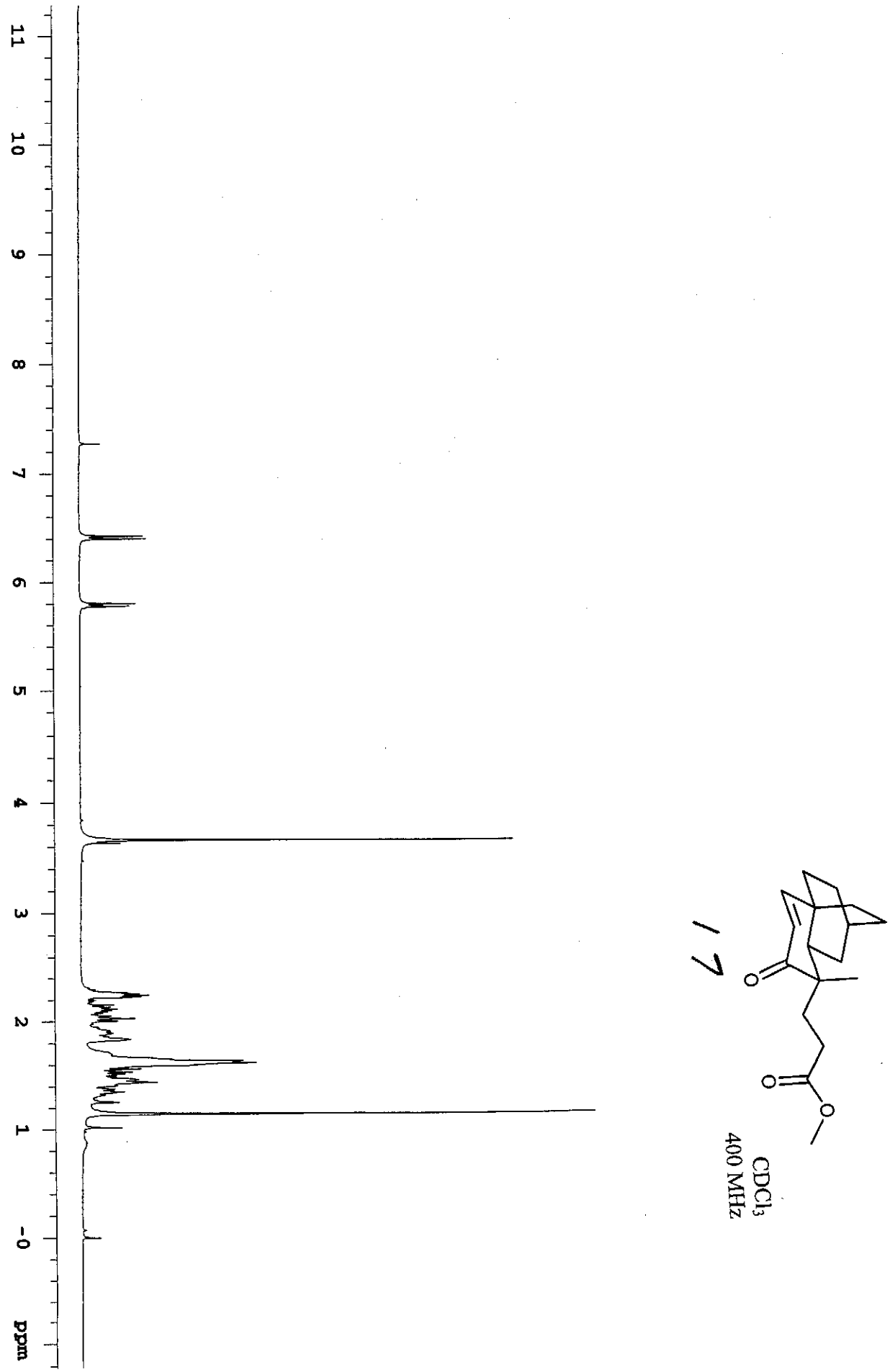
INDEX	FREQUENCY	PPM	HEIGHT
1	20356.871	202.503	20.2
2	15764.599	156.821	63.2
3	12724.955	126.583	66.3
4	7772.564	77.319	33.0
5	7740.519	77.000	34.7
6	7708.475	76.681	34.0
7	4385.009	43.621	62.6
8	4201.898	41.799	64.4
9	3363.402	33.458	29.5
10	3321.439	33.041	91.4
11	3223.780	32.069	100.8
12	2591.284	25.777	93.4
13	2537.877	25.246	98.6
14	2463.106	24.502	105.1
15	2460.054	24.472	101.9
16	1123.344	11.175	77.9



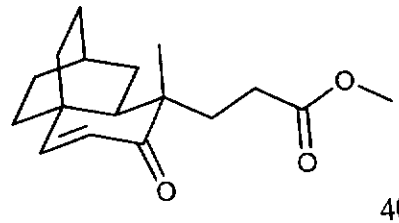
$CDCl_3$
400 MHz

46



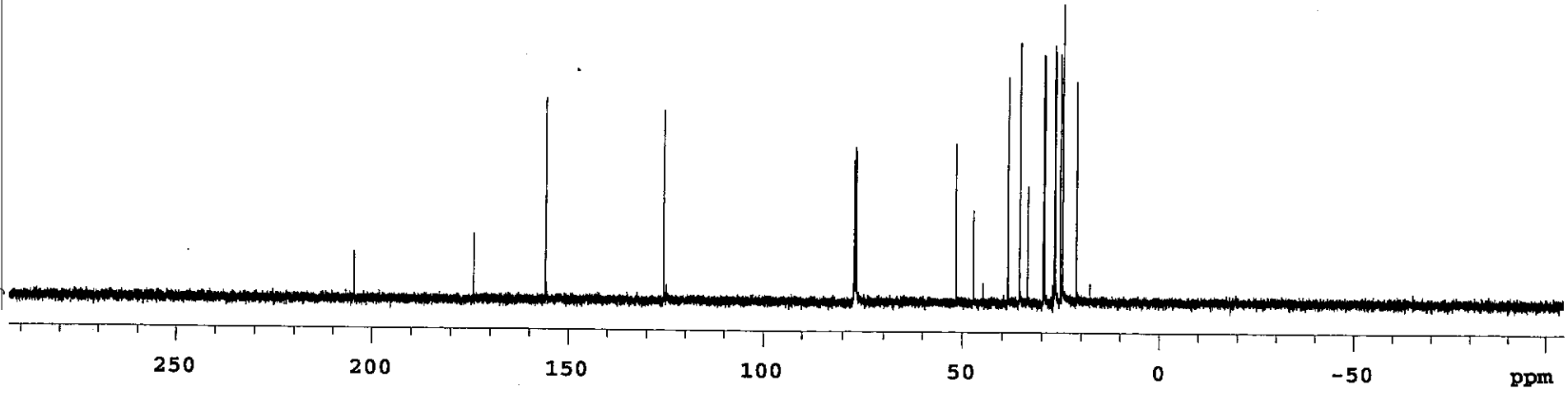

ovbvi-129-comb3
Pulse Sequence: s2pul
11
10
9
8
7
6
5
4
3
2
1
-0
ppm
17
O
O
O
CDCl3
400 MHz

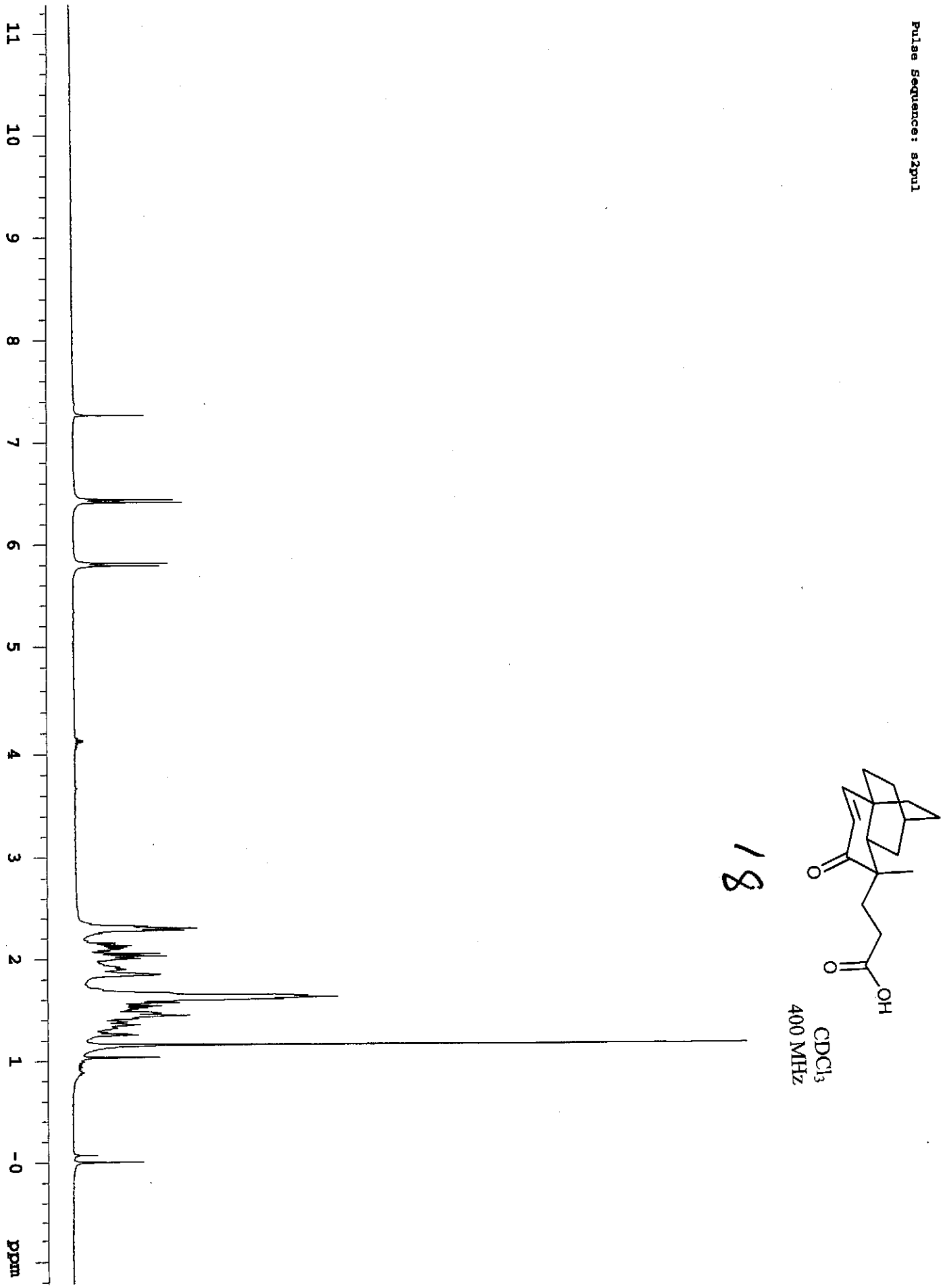
INDEX	FREQUENCY	PPM	HEIGHT
1	20566.643	204.590	7.7
2	17509.955	174.183	10.7
3	15659.341	155.774	32.7
4	12627.679	125.616	30.9
5	7772.258	77.316	23.1
6	7740.519	77.000	25.2
7	7708.781	76.684	24.7
8	5184.328	51.572	25.8
9	4739.985	47.152	15.0
10	3873.883	38.536	36.6
11	3568.703	35.500	42.2
12	3364.842	33.472	18.9
13	2980.315	29.647	40.2
14	2946.745	29.313	40.0
15	2700.159	26.860	41.7
16	2675.134	26.611	40.7
17	2547.569	25.342	40.3
18	2490.805	24.778	38.1
19	2485.312	24.723	48.3
20	2134.965	21.238	35.9



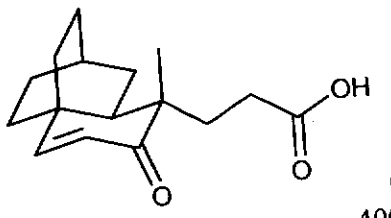
17

$CDCl_3$
400 MHz



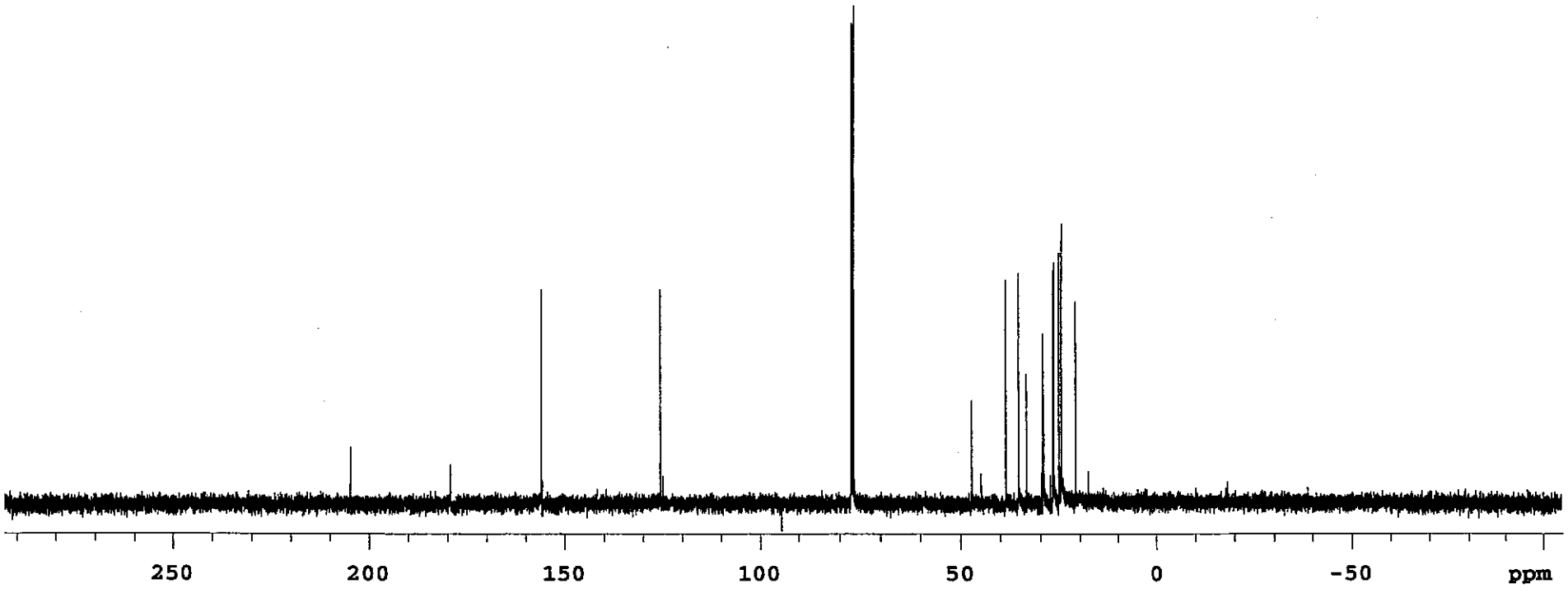

ovbv1-136-3
Pulse Sequence: s2pul
18
CDCl3
400 MHz
O
O
OH
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

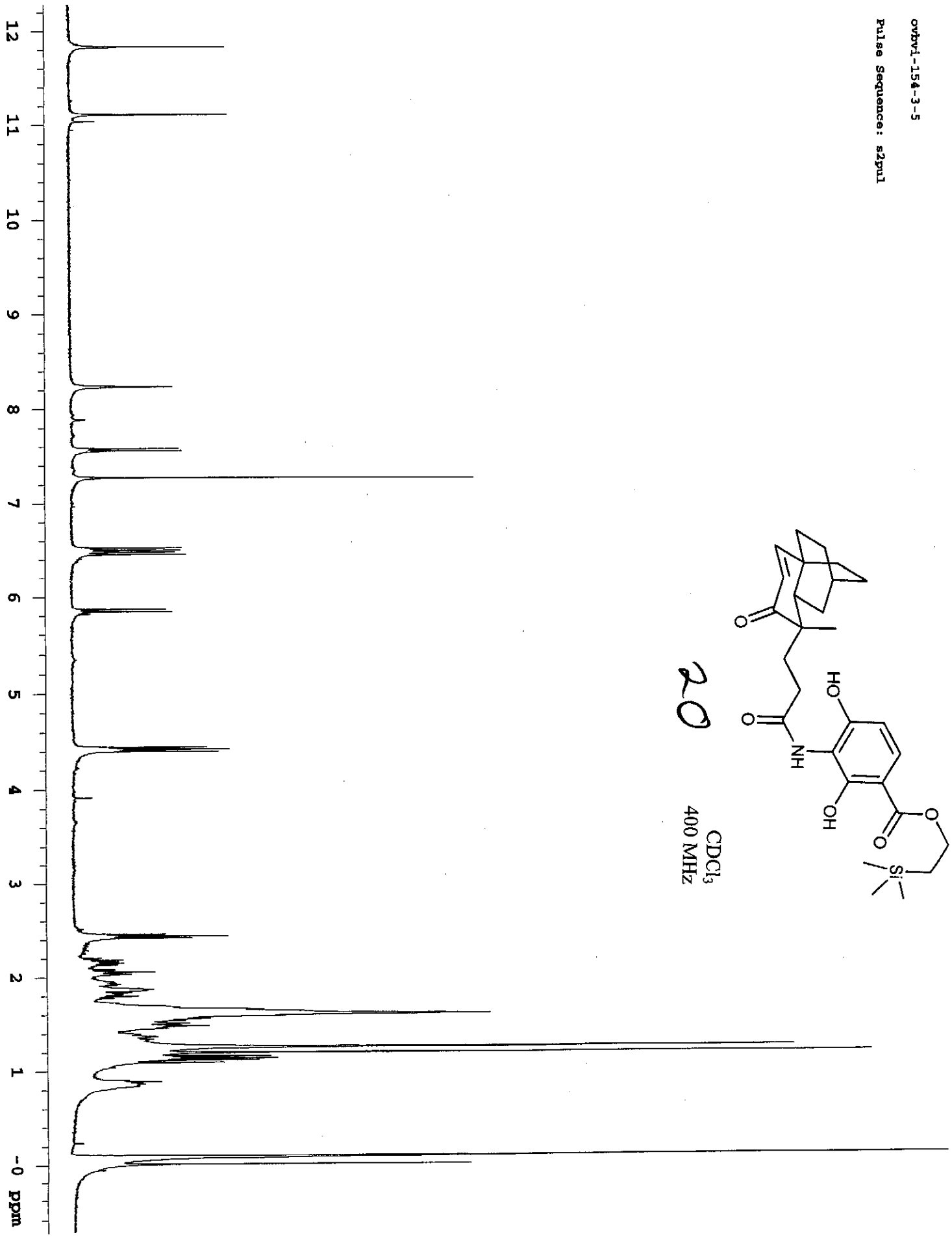
INDEX	FREQUENCY	PPM	HEIGHT
1	20587.395	204.796	9.2
2	18020.827	179.265	6.4
3	15679.483	155.974	34.7
4	12624.627	125.585	34.9
5	7772.868	77.322	77.7
6	7740.519	77.000	77.4
7	7708.780	76.684	80.5
8	4740.596	47.158	16.8
9	3884.870	38.645	36.4
10	3567.482	35.488	37.6
11	3370.335	33.527	21.1
12	2949.186	29.337	27.7
13	2940.031	29.246	21.5
14	2699.549	26.854	37.9
15	2676.965	26.630	39.3
16	2547.569	25.342	40.8
17	2515.220	25.021	5.9
18	2491.416	24.784	42.7
19	2484.091	24.711	45.4
20	2129.472	21.183	33.0



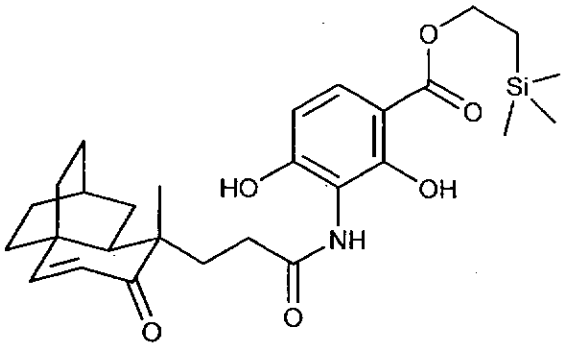
$CDCl_3$
400 MHz

18



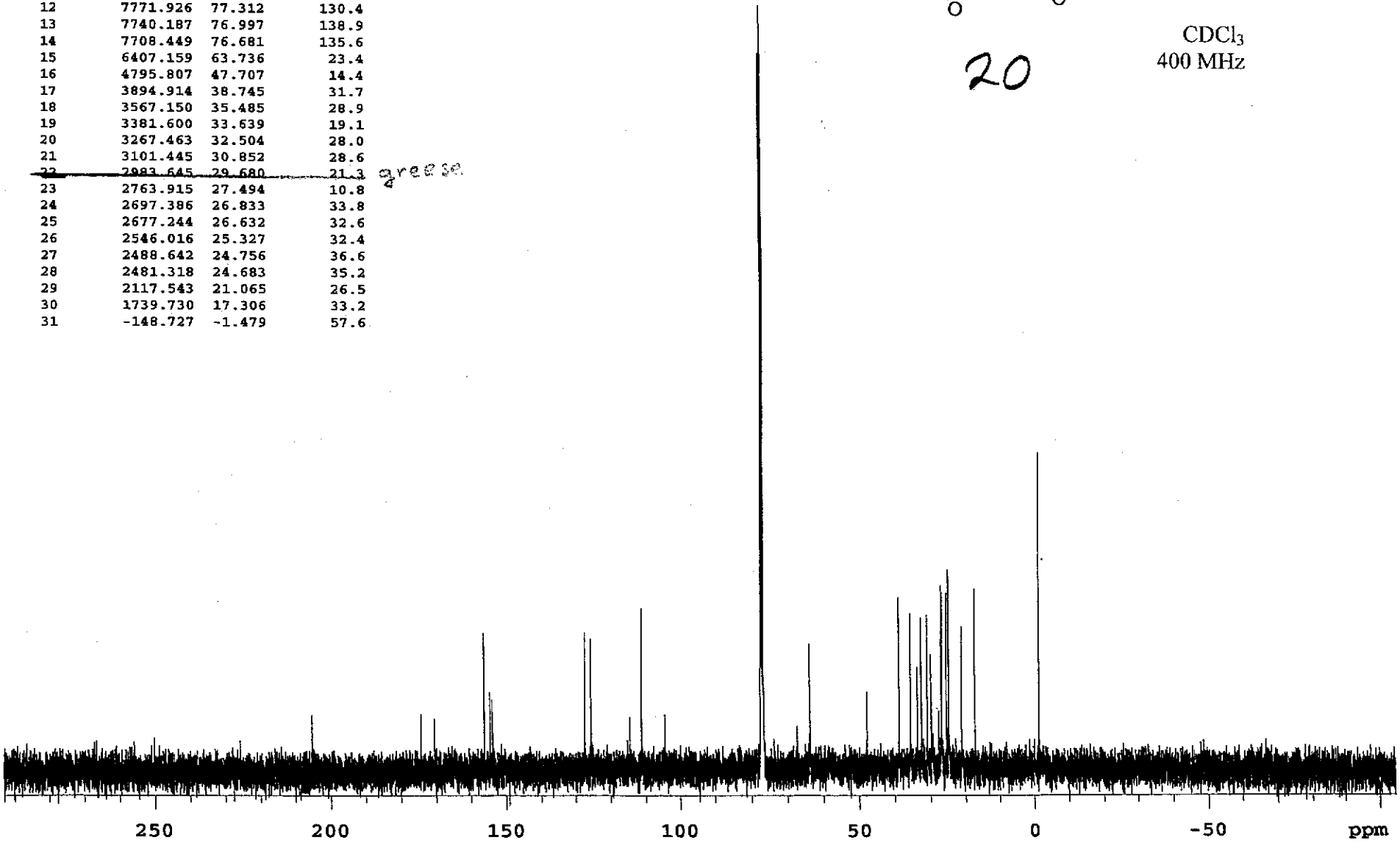

ovbvi-154-3-5
Pulse Sequence: s2pul
20
CDCl3
400 MHz
HO
NH
OH
O
Si
12
11
10
9
8
7
6
5
4
3
2
1
-0 ppm

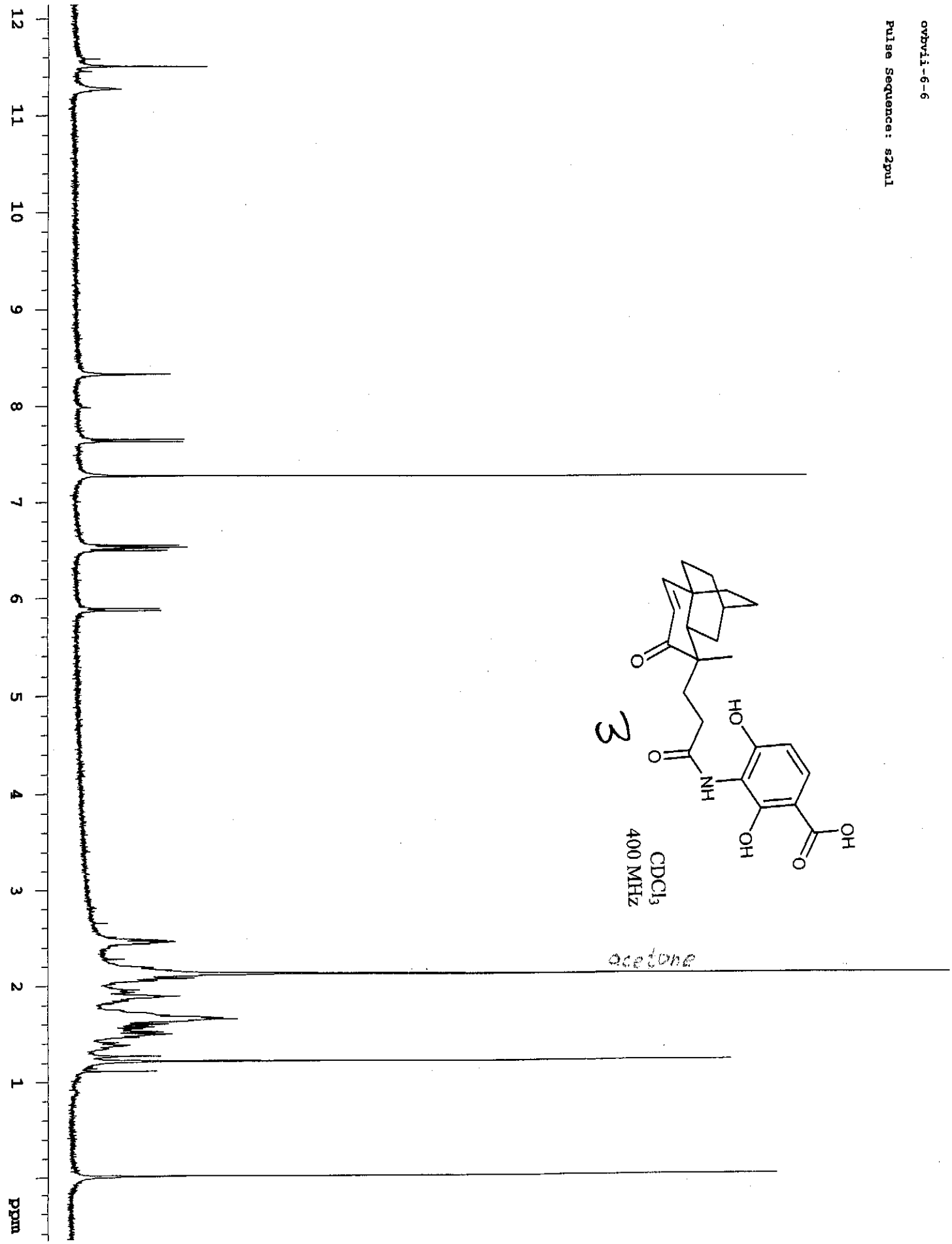
INDEX	FREQUENCY	PPM	HEIGHT
1	20634.061	205.260	10.1
2	17518.779	174.271	10.3
3	17137.303	170.476	9.5
4	15710.890	156.286	25.3
5	15542.430	154.611	14.3
6	15473.460	153.925	13.1
7	12798.858	127.319	25.4
8	12621.854	125.558	24.2
9	11496.959	114.368	9.7
10	11165.533	111.071	29.8
11	10497.187	104.422	10.2
12	7771.926	77.312	130.4
13	7740.187	76.997	138.9
14	7708.449	76.681	135.6
15	6407.159	63.736	23.4
16	4795.807	47.707	14.4
17	3894.914	38.745	31.7
18	3567.150	35.485	28.9
19	3381.600	33.639	19.1
20	3267.463	32.504	28.0
21	3101.445	30.852	28.6
22	2983.645	29.680	21.3 agree so
23	2763.915	27.494	10.8
24	2697.386	26.833	33.8
25	2677.244	26.632	32.6
26	2546.016	25.327	32.4
27	2488.642	24.756	36.6
28	2481.318	24.683	35.2
29	2117.543	21.065	26.5
30	1739.730	17.306	33.2
31	-148.727	-1.479	57.6



20

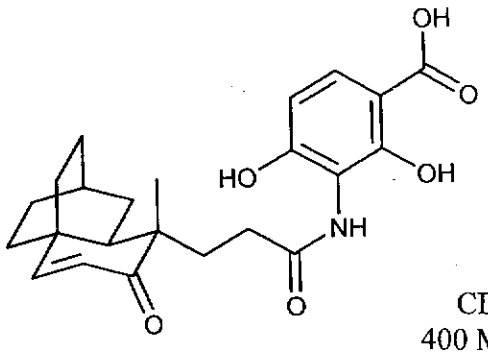
$CDCl_3$
400 MHz




owbvi-6-6
Pulse Sequence: s2pul
CDCl3
400 MHz
acetone
3
HO
OH
OH
NH
O
O
O
12
11
10
9
8
7
6
5
4
3
2
1
ppm

INDEX	FREQUENCY	PPM	HEIGHT
1	17519.389	174.277	17.6
2	17379.006	172.880	10.4
3	15887.895	158.047	23.5
4	15615.674	155.339	17.5
5	15526.561	154.453	13.5
6	12894.075	128.266	26.5
7	12598.050	125.321	28.0
8	11492.076	114.319	10.9
9	11177.129	111.186	24.4
10	7772.536	77.318	195.0
11	7760.940	77.203	59.9
12	7740.798	77.003	200.0
13	7708.449	76.681	198.3
14	4795.806	47.707	14.5
15	3887.589	38.672	11.3
16	3866.227	38.460	29.6
17	3558.605	35.400	33.4
18	3399.301	33.815	24.0
19	3247.321	32.303	24.7
20	3119.145	31.028	31.7
21	2983.645	29.680	23.6
22	2697.386	26.833	39.5
23	2667.478	26.535	35.2
24	2539.913	25.266	39.9
25	2486.201	24.732	48.2
26	2477.045	24.641	43.0
27	2146.840	21.356	34.0

greese



3

$CDCl_3$
400 MHz