General Method……S2

Experimental Procedure……S2

Selected NMR Spectra……..S10

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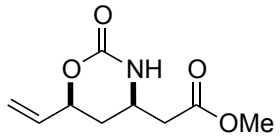
General. Tetrahydrofuran and diethyl ether were dried by filtration through two columns of activated, neutral alumina according to the procedure described by Grubbs.[1] Methanol (MeOH), acetonitrile (MeCN), and dimethylformamide (DMF) were dried by filtration through two columns of activated molecular sieves, and toluene was dried by filtration through one column of activated, neutral alumina followed by one column of Q5 reactant. These solvents were determined to have less than 50 ppm H_2O by Karl Fischer coulometric moisture analysis. Benzene, methylene chloride (CH_2Cl_2), diisopropylamine (*i*-Pr_2NH), triethylamine (Et_3N), diisopropylethylamine (*i*-Pr_2NEt), and pyridine were distilled from calcium hydride immediately prior to use. Zn granules were activated by stirring with 1M HCl for 10 min, filtering, rinsing with D.I. H_2O, MeOH, then Et_2O, and drying under vacuum before use. 2-Deoxy-D-ribose was purchased from Carbosynth. All reagents were reagent grade and used without purification unless otherwise noted, and air or moisture sensitive reagents were weighed in a glove box. All reactions involving air or moisture sensitive reagents or intermediates were performed under an inert atmosphere of nitrogen or argon in glassware that was flame or oven dried. Solutions were degassed using three freeze-pump-thaw cycles under vacuum. Reaction temperatures refer to the temperature of the cooling/heating bath. Volatile solvents were removed under reduced pressure using a Büchi rotary evaporator at 25–30 °C (bath temperature). Thin layer chromatography was run on pre-coated plates of silica gel with a 0.25 mm thickness containing 60F-254 indicator (EMD Millipore). Chromatography was performed using forced flow (flash chromatography) and the indicated solvent system on 230-400 mesh silica gel (Silicycle flash F60) according to the method of Still,[2] unless otherwise noted.

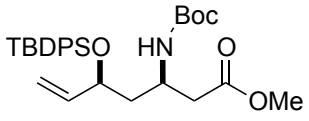
Infrared (IR) spectra were obtained either neat on sodium chloride or as solutions in the solvent indicated and reported as wavenumbers (cm^{-1}). Proton nuclear magnetic resonance (^1H NMR) and carbon nuclear magnetic resonance (^{13}C NMR) spectra were obtained at the indicated field as solutions in $CDCl_3$ unless otherwise indicated. Chemical shifts are referenced to the deuterated solvent (*e.g.,* for $CDCl_3$, δ = 7.26 ppm and 77.0 ppm for ^1H and ^{13}C NMR, respectively) and are reported in parts per million (ppm, δ) relative to tetramethylsilane (TMS, δ = 0.00 ppm). Coupling constants (*J*) are reported in Hz and the splitting abbreviations used are: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; comp, overlapping multiplets of magnetically nonequivalent protons; br, broad; app, apparent.



16

Methyl 2-[(4*R*,6*S*)-6-ethenyl-2-oxo-1,3-oxazinan-4-yl]acetate (16). Compound **14** (20.25 g, 101.5 mmol) was dissolved in dry CH_2Cl_2 (895 mL) and cooled to -10 °C (bath temperature) in an

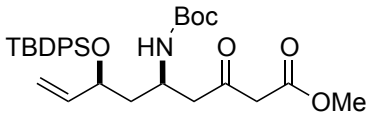
ice/brine bath. NaH (4.31 g, 180.1 mmol, 60% *w/w* dispersion in mineral oil) was added in one portion, and the mixture was stirred under an atmosphere of N_2 (g) at –10 °C for 1.5 h. The reaction was quenched by the slow addition of saturated aqueous NH_4Cl (650 mL), and the aqueous layer was extracted with CH_2Cl_2 (4 x 300 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude residue was purified by recrystallization from methyl *tert*-butylether to give 17.09 g (85%) of **16** as a crystalline mixture (*dr* = 8:1) of diastereomers: $[\alpha]_D^{25}$ –19 (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz, major diastereomer) δ 6.48 (br s, 1 H), 5.92-5.83 (m, 1 H), 5.41 (d, *J* = 17.2 Hz, 1 H), 5.27 (d, *J* = 10.8 Hz, 1 H), 4.75 (q, *J* = 5.6 Hz, 1 H), 3.98-3.91 (m, 1 H), 3.72 (s, 3 H), 2.57 (dd, *J* = 4.4, 3.2 Hz, 2 H), 1.60-1.51 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.8, 153.8, 134.7, 117.4, 76.6, 51.9, 47.0, 39.9, 33.1; IR (neat) 3428, 2951, 1722, 1660, 1436 cm^{-1}; HRMS (CI) *m/z* 200.0924 [$C_9H_{14}NO_4$ (M+H) requires 200.0923].



18

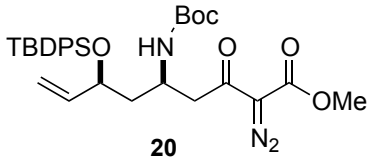
Methyl (3*R*, 5*S*)-3-{[(*tert*-butoxy)carbonyl]amino}-5-[(*tert*-butyldiphenylsilyl)oxy]hept-6-enoate (18). A solution of **17** (22.22 g, 74.2 mmol) and Cs_2CO_3 (2.86 g, 14.8 mmol) in MeOH (370 mL) was stirred at room temperature for 24-48 h until starting material was consumed by TLC (SiO_2, Hex:EtOAc, 1:1). The reaction was then concentrated under reduced pressure to provide 20.28 g of amino alcohol as colorless oil that was taken on without further purification.

A solution of amino alcohol prepared above (20.28 g, 74.2 mmol) in DMF (50 mL) was added to a solution of TBDPSCl (30.59 g, 111.3 mmol), imidazole (6.57 g, 96.46 mmol), and DMAP (0.091 g, 0.742 mmol) in DMF (320 mL), and the reaction was stirred at room temperature overnight. The reaction was quenched with 1 M HCl (300 mL), and the layers were separated. The aqueous layer was extracted with Et_2O (3 x 150 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude residue was purified by flash chromatography eluting with hexanes:EtOAc (5:1) to give 30.38 g (80%) of **18** as a colorless oil: $[\alpha]_D^{25}$ +7.0 (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz, rotamers) δ 7.70-7.63 (comp, 4 H), 7.47-7.33 (comp, 6 H), 5.85 (ddd, *J* = 17.2, 10.2, 6.4 Hz, 1 H), 5.10-5.03 (comp, 2 H), 4.41 (app d, *J* = 8.8 Hz, 1 H), 4.17 (app q, *J* = 6.0 Hz, 1 H), 3.91-3.81 (m, 1 H), 3.60 (s, 3 H), 2.40 (app d, *J* = 4.8 Hz, 2 H), 1.62 (app t, *J* = 6.4 Hz, 2 H), 1.36 (s, 9 H), 1.07 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz, rotamers) δ 171.8, 154.8, 139.4, 135.90, 135.87, 134.1, 133.7, 129.8, 129.6, 127.6, 127.4, 115.5, 79.0, 72.2, 51.5, 44.2, 42.3, 39.6, 28.3, 27.0, 19.2; IR (neat) 3423, 2959, 2932, 2858, 1737, 1716, 1502, 1170, 1111 cm^{-1}; HRMS (ESI) 512.2830 [$C_{29}H_{42}NO_5Si$ (M+H) requires 512.2754].



19

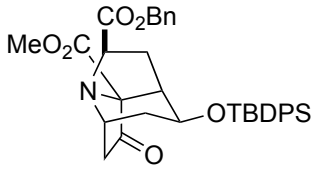
Methyl (5*R*,7*S*)-5-{[(*tert*-butoxy)carbonyl]amino}-7-[(*tert*-butyldiphenylsilyl)oxy]-3-oxonon-8-enoate (19). A solution of freshly distilled methyl acetate (4.75 g, 64.10 mmol) in THF (128 mL) was added dropwise via syringe pump to a solution of NaHMDS (83.33 mmol, 1.8 M in hexane) in THF (167 mL) at –78 ºC. After 30 min, a solution of **18** (3.28 g, 6.41 mmol) in THF (13 mL) was added dropwise to the reaction via syringe pump. During the syringe pump additions the metal needle used to transfer the substrate solutions was passed through a –78 ºC bath to precool the solutions before introduction into the reaction flask. After 1 h at –78 ºC, the reaction was warmed to –10 ºC (ice/brine bath) and stirred for 6 h. The reaction was then quenched by addition of saturated aqueous NH_4Cl (300 mL) and warmed to room temperature. The reaction mixture was extracted with EtOAc (5 x 100 mL), and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude residue was purified by flash chromatography eluting with hexanes:EtOAc (using a gradient from 9:1 to 5:1) to give 3.55 g (75%) of **19** as colorless oil along with 0.56 g (17%) of recovered starting material: ^{1}H NMR ($CDCl_3$, 400 MHz, rotamers) δ 7.69-7.62 (comp, 4 H), 7.47-7.33 (comp, 6 H), 5.83 (ddd, *J* = 17.1, 10.4, 6.4 Hz, 1 H), 5.10-5.03 (comp, 2 H), 4.37 (app d, *J* = 8.0 Hz, 1 H), 4.15 (app q, *J* = 4.0 Hz, 1 H), 3.92-3.83 (m, 1 H), 3.70 (s, 3 H), 3.37 (s, 2 H), 2.61 (app d, *J* = 2.8 Hz, 2 H), 1.68-1.61 (m, 2 H), 1.35 (s, 9 H), 1.07 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz, rotamers) δ 172.6, 167.6, 154.9, 139.4, 135.9, 135.8, 134.0, 133.6, 129.8, 129.6, 127.6, 127.4, 115.5, 79.0, 72.3, 52.2, 49.0, 47.9, 43.9, 42.1, 28.2, 26.9, 19.1; IR (neat) 3417, 2957, 2932, 2858, 1746, 1715, 1714, 1502, 1246, 1169, 1111 cm^{-1}; HRMS (ESI) 576.2750 [$C_{31}H_{43}NO_6SiNa$ (M+Na) requires 576.2757].



20

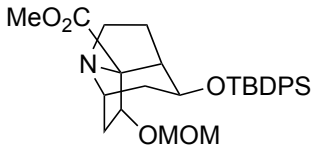
Methyl (5*R*,7*S*)-5-{[(*tert*-butoxy)carbonyl]amino}-7-[(*tert*-butyldiphenylsilyl)oxy]-2-diazo-3-oxonon-8-enoate (20). A solution of **19** (3.55 g, 1.97 mmol), *p*-ABSA (0.708 g, 2.95 mmol), and NEt_3 (0.598 g, 5.91 mmol) in MeCN (6.6 mL) was stirred at room temperature for 16 h. The reaction was concentrated, and the crude residue was triturated with Et_2O (25 mL). The precipitate was removed by filtration, and the solid was rinsed with Et_2O/CH_2Cl_2 (25 mL, 2:1). The combined filtrate and washings were concentrated under reduced pressure. The crude residue was purified by column chromatography eluting with Hex:EtOAc (2:1) to give 1.14 g (92%) of **20** as a yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz,

rotamers) δ 7.71-7.63 (comp, 4 H), 7.46-7.33 (comp, 6 H), 5.83 (ddd, *J* = 17.0, 10.2, 6.4 Hz, 1 H), 5.10-5.03 (comp, 2 H), 4.31 (app d, *J* = 9.6 Hz, 1 H), 4.21-4.13 (m, 1 H), 3.99-3.92 (m, 1 H), 3.81 (s, 3 H), 2.96-2.83 (comp, 2 H), 1.71-1.56 (comp, 2 H), 1.34 (s, 9 H), 1.06 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz, rotamers) δ 190.6, 161.6, 154.9, 139.4, 135.9, 134.1, 133.7, 129.7, 129.6, 128.2, 127.5, 127.4, 115.4, 78.8, 76.2, 72.2, 52.1, 45.6, 44.5, 42.7, 28.2, 26.9, 19.1; IR (neat) 3417, 2959, 2932, 2856, 2136, 1716, 1655, 1500, 1313, 1171, 1112 cm^{-1}; HRMS (ESI) 580.2838 [$C_{31}H_{42}N_3O_6Si$ (M+H) requires 580.2843].



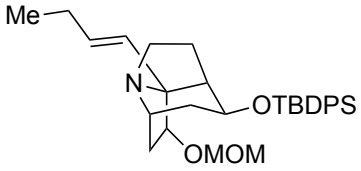
22

6-Benzyl-8-methyl-(6R)-3-[(*tert*-butyldiphenylsilyl)oxy]-9-oxo-7-azatricyclo [5.3.0.0^{4,8}]decane-6,8-dicarboxylate (22). Trifluroroacetic acid (1.58 mL, 20.7 mmol) was added to a precooled solution of **20** (1.20 g, 2.07 mmol) in CH_2Cl_2 (10 mL) at 0 ºC. The reaction was warmed to room temperature and stirred for 2 h. The reaction was concentrated to dryness and pumped down under high vacuum for 2 h to ensure the removal of all excess TFA. The crude residue was dissolved in CH_2Cl_2 (6 mL), 4 Å molecular sieves (1.2 g) were added, and the mixture was cooled to –20 ºC. NEt_3 (0.32 mL, 2.28 mmol) was then added dropwise, and the reaction was warmed to room temperature. A 1 M solution of benzyl glyoxylate (3.11 mL, 3.11 mmol) in CH_2Cl_2 was added, and the reaction was stirred for 16 h at room temperature. The reaction was filtered through Celite, and the filter pad was rinsed with CH_2Cl_2 (12 mL) to give **21** as colorless oil containing an equimolar amount of TFA·NEt_3. The crude residue was dissolved in xylenes (40 mL), $Rh_2(OAc)_4$ (0.027 g, 0.062 mmol) was added, and the mixture was heated under reflux for 24 h. The mixture was concentrated under reduced pressure, and the crude residue was purified by column chromatography eluting with Hex:EtOAc (3:1 to 1:1, with 1% *v*/*v* NEt_3) to give 0.93 g (75%) of **22** as a light yellow oil: $[\alpha]_D^{25}$ –63 (c = 0.3, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.59-7.55 (comp, 4 H), 7.45-7.35 (comp, 11 H), 5.28 (d, *J* = 3.2 Hz, 2 H), 4.15 (app q, *J* = 6.0 Hz, 1 H), 4.08-4.04 (m, 1 H), 3.94-3.89 (m, 1 H), 3.72 (s, 3 H), 2.96 (app q, *J* = 3.2 Hz, 1 H), 2.68 (dd, *J* = 13.6, 5.6 Hz, 1 H), 2.61 (dd, *J* = 16.0, 6.4 Hz, 1 H), 2.15-2.07 (m, 1 H), 1.80 (d, *J* = 17.6 Hz, 1 H), 1.35-1.19 (comp, 2 H), 1.04 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 207.0, 172.5, 169.7, 167.4, 135.5, 135.5, 135.3, 134.7, 133.5, 133.0, 130.0, 129.9, 128.6, 128.5, 127.8, 127.6, 82.4, 67.0, 66.2, 62.3, 54.2, 53.1, 49.7, 44.0, 33.6, 27.0, 26.8, 19.0; IR (neat) 2953, 2857, 1738, 1741, 1428, 1228, 1112 cm^{-1}; HRMS (ESI) *m/z* 598.2614 [$C_{35}H_{40}NO_6Si$ (M+H) requires 598.2625].



31

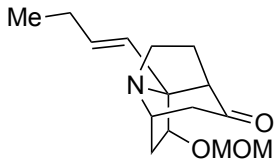
Methyl-3-[(*tert*-butyldiphenylsilyl)oxy]-9-methyloxymethyloxy-7-azatricyclo[5.3.0.0^{4,8}]-decane-8-carboxylate (31). A suspension of **30** (0.340 g, 0.528 mmol) and 10 % *w*/*w* Pd/C (84 mg) in EtOH (11 mL) was stirred under an atmosphere of H_2 (gas) at room temperature for 16 h. The mixture was filtered through a short pad of Celite, which was rinsed with EtOH (30 mL), and the combined filtrate and washings were concentrated to dryness to give 0.292 g (100%) of the corresponding acid as an amorphous solid. The acid thus obtained (0.292 g, 0.528 mmol), 1-hydroxypyridine-2(*1H*)-thione (0.101 g, 0.881 mmol), DCC (0.163 g, 0.881 mmol), and DMAP (0.064 g, 0.528 mmol) were dissolved in $CHCl_3$ (5.3 mL). *t*BuSH (0.59 mL, 5.28 mmol) was added to the solution, and the solution was immediately irradiated with a tungsten filament light bulb (250 W) at room temperature for 1 h. The reaction was concentrated, and the residue was purified by column chromatography eluting with hexanes/EtOAc (2:1) to EtOAc with 1% v/v Et_3N to give 0.170 g (63%) of **31** as yellow oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.71-7.66 (comp, 4 H), 7.42-7.34 (comp, 6 H), 4.72-4.64 (m, 1 H), 4.36-4.29 (comp, 2 H), 3.72 (s, 3 H), 3.22-3.18 (m, 1 H), 3.10 (s, 3 H), 2.93 (dd, *J* = 10.5, 4.2 Hz, 1 H), 2.84 (dd, *J* = 8.4, 5.4 Hz, 1 H), 2.77 (dd, *J* = 5.7, 3.9 Hz, 1 H), 2.48-2.38 (m, 1 H), 2.31-2.22 (m, 1 H), 1.66-1.58 (comp, 2 H), 1.52-1.48 (m, 1 H), 1.41-1.35 (comp, 3 H), 1.13 (dd, *J* = 16.2, 2.4 Hz, 1 H), 1.07 (s, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.7, 135.9, 135.8, 134.8, 134.3, 129.5, 127.4, 127.4, 96.0, 79.3, 78.8, 77.2, 66.4, 60.3, 55.3, 52.4, 47.4, 46.6, 37.7, 34.7, 27.0, 24.7, 19.2; IR (neat) 2951, 2889, 2857, 1737, 1428, 1262, 1229, 1107, 1044 cm^{-1}; HRMS (ESI) *m*/*z* 510.2673 [$C_{29}H_{40}NO_5Si$ (M+H) requires 510.2670].



33

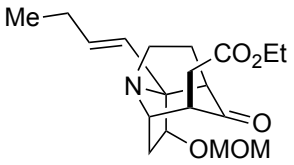
***E*-8-(but-1'-en-1'-yl)-3-[(*tert*-butyldiphenylsilyl)oxy]-9-methyloxymethyloxy-7-azatricyclo[5.3.0.0^{4,8}]decane (33).** To a stirred solution of **32** (0.212 g, 0.44 mmol) and 1-phenyl-5-propylsulfonyl-1*H*-tetrazole (0.335 g, 1.33 mmol) in DME (15 mL) at –55 °C was added KHMDS (3.52 mL, 0.5 M in toluene, 11.76 mmol) dropwise. The resulting solution was stirred for 1 h at –55 °C and warmed to room temperature. After stirring for 1 h at room temperature, the reaction mixture was quenched with sat. NaCl solution (5 mL). The separated aqueous layers were extracted with EtOAc (3 × 10 mL), and the combined organic layers were dried (Na_2SO_4), filtered, and then concentrated. The crude residue was purified by column chromatography eluting with hexanes/EtOAc (3:1 to 1:1) to EtOAc with 1% v/v Et_3N to give 0.240 g (89%) of **33** as colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ

7.72-7.66 (comp, 4 H), 7.41-7.33 (comp, 6 H), 5.54 (dt, *J* = 15.6, 6.3 Hz, 1 H), 5.26 (d, *J* = 15.9 Hz, 1 H), 4.66-4.60 (m, 1 H), 4.35 (d, *J* = 6.6 Hz, 1 H), 4.32 (d, *J* = 6.6 Hz, 1 H), 3.95 (dd, *J* = 10.5, 3.0 Hz, 1 H), 3.14-3.07 (m, 1 H), 3.09 (s, 3 H), 2.88-2.68 (m, 2 H), 2.36-2.29 (m, 1 H), 2.22 (dd, *J* = 6.0, 3.6 Hz, 1 H), 2.12 (ddd, *J* = 12.9, 8.4, 4.5 Hz, 1 H), 2.00 (dt, *J* = 7.5, 1.5 Hz, 2 H), 1.61-1.51 (m, 1 H), 1.42-1.36 (m, 1 H), 1.07 (s, 9 H), 0.95 (t, *J* = 7.2 Hz, 3 H),; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.9, 135.8, 132.4, 130.9, 129.3, 127.4, 96.0, 82.1, 75.7, 66.9, 60.3, 55.1, 47.4, 47.0, 37.3, 35.2, 27.0, 25.5, 24.8, 19.2, 13.7; IR (neat) 2958, 2932, 2886, 2857, 1472, 1428, 1106, 1043, 703 cm^{-1}; HRMS (ESI) *m/z* 506.3092 [$C_{31}H_{44}NO_3Si$ (M+H) requires 506.3085].



34

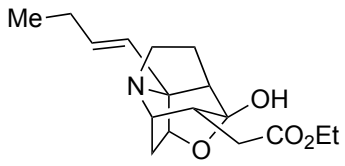
***E*-8-(but-1'-en-1'-yl)-9-methyloxymethyloxy-7-azatricyclo[5.3.0.0^{4,8}]decan-3-one (34).** To a stirred solution of C8 alcohol (0.013 g, 0.049 mmol) in CH_2Cl_2 (1 mL) and DMSO (0.5 mL) at room temperature was added Et_3N (0.068 mL, 0.486 mmol) followed by SO_3·Py (0.039 g, 0.243 mmol). The resulting solution was stirred for 4 h at room temperature and then sat. $NaHCO_3$ solution (2 mL) was added. The separated aqueous layers were extracted with EtOAc (3 × 5 mL), and the combined organic layers were dried (Na_2SO_4), filtered, and then concentrated. The crude residue was purified by column chromatography eluting with hexanes/EtOAc (1:1) to EtOAc with 1% v/v Et_3N to give 0.0099 g (77%) of **34** as colorless oil: $[\alpha]_D^{24}$ –156 (c = 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.74 (dt, *J* = 15.9, 6.9 Hz, 1 H), 5.41 (dt, *J* = 15.9, 1.5 Hz, 1 H), 4.59 (s, 2 H), 4.21 (d, J = 8.7 Hz, 1 H), 3.53 (t, J = 6.3 Hz, 1 H), 3.33 (s, 3 H), 3.16-3.00 (m, 2 H), 2.85 (d, J = 6.6 Hz, 1 H), 2.58-2.50 (m, 1 H), 2.45-2.36 (m, 1 H), 2.19-2.11 (m, 1 H), 2.07 (dt, *J* = 7.8, 1.5 Hz, 2 H), 1.69-1.60 (comp, 2 H), 0.99 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 209.3, 132.2, 129.9, 95.8, 82.0, 79.7, 60.4, 56.9, 55.6, 46.6, 41.2, 38.6, 30.9, 25.5, 13.6; IR (neat) 2958, 2893, 1722, 1106, 1091, 1040 cm^{-1}; HRMS (ESI) *m/z* 266.1754 [$C_{15}H_{24}NO_3$ (M+H) requires 266.1751].



35

***E*-8-(But-1'-en-1'-yl)-3-ethoxycarbonylmethyl-9-methyloxymethyloxy-7-azatricyclo[5.3.0.0^{4,8}]decan-3-one (35).** Freshly prepared LDA (0.42 mL, 0.2 M in THF, 0.084 mmol) was added to a stirred solution of **34** (0.016 g, 0.060 mmol) in THF (1.2 mL) at –10 ºC, and the resulting solution was stirred for 1 h at –10 ºC, whereupon ethyl iodoacetate (0.011 mL, 0.090 mmol) was added

at –10 ºC. The resulting solution was stirred for 30 min. DABCO (20 mg) was added, and the solution was warmed to room temperature. Brine (5 mL) and EtOAc (5 mL) were added, and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 10 mL), and the combined organic layers were dried (Na_2SO_4), filtered, and then concentrated under reduced pressure The crude residue was purified by column chromatography eluting with hexanes/EtOAc (1:1) to EtOAc with 1% v/v Et_3N to give 0.013 g (62%) of **35** as colorless oil along with 0.0025 g (16%) of starting material: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.72 (dt, *J* = 15.6, 6.3 Hz, 1 H), 5.41 (d, *J* = 15.6 Hz, 1 H), 4.57 (s, 2 H), 4.22-4.14 (comp, 3 H), 3.40 (d, J = 5.7 Hz, 1 H), 3.33 (s, 3 H), 3.18-3.07 (m, 2 H), 2.88-2.75 (comp. 3 H), 2.54 (dd, J = 15.6, 10.8 Hz, 1 H), 2.41-2.32 (m, 1 H), 2.19-2.02 (comp, 3 H), 1.74 (d, *J* = 12.9 Hz, 1 H), 1.70-1.62 (m, 1 H), 1.27 (t, *J* = 7.2 Hz, 3 H), 0.99 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.7, 132.3, 129.3, 95.6, 82.2, 78.9, 63.0, 60.9, 56.6, 55.7, 48.3, 45.7, 41.8, 38.9, 30.2, 25.5, 14.2, 13.6; IR (neat) 2960, 1732, 1715, 1151, 1106, 1039 cm^{-1}; HRMS (ESI) *m/z* 352.2123 [$C_{19}H_{30}NO_5$ (M+H) requires 352.2119].



36

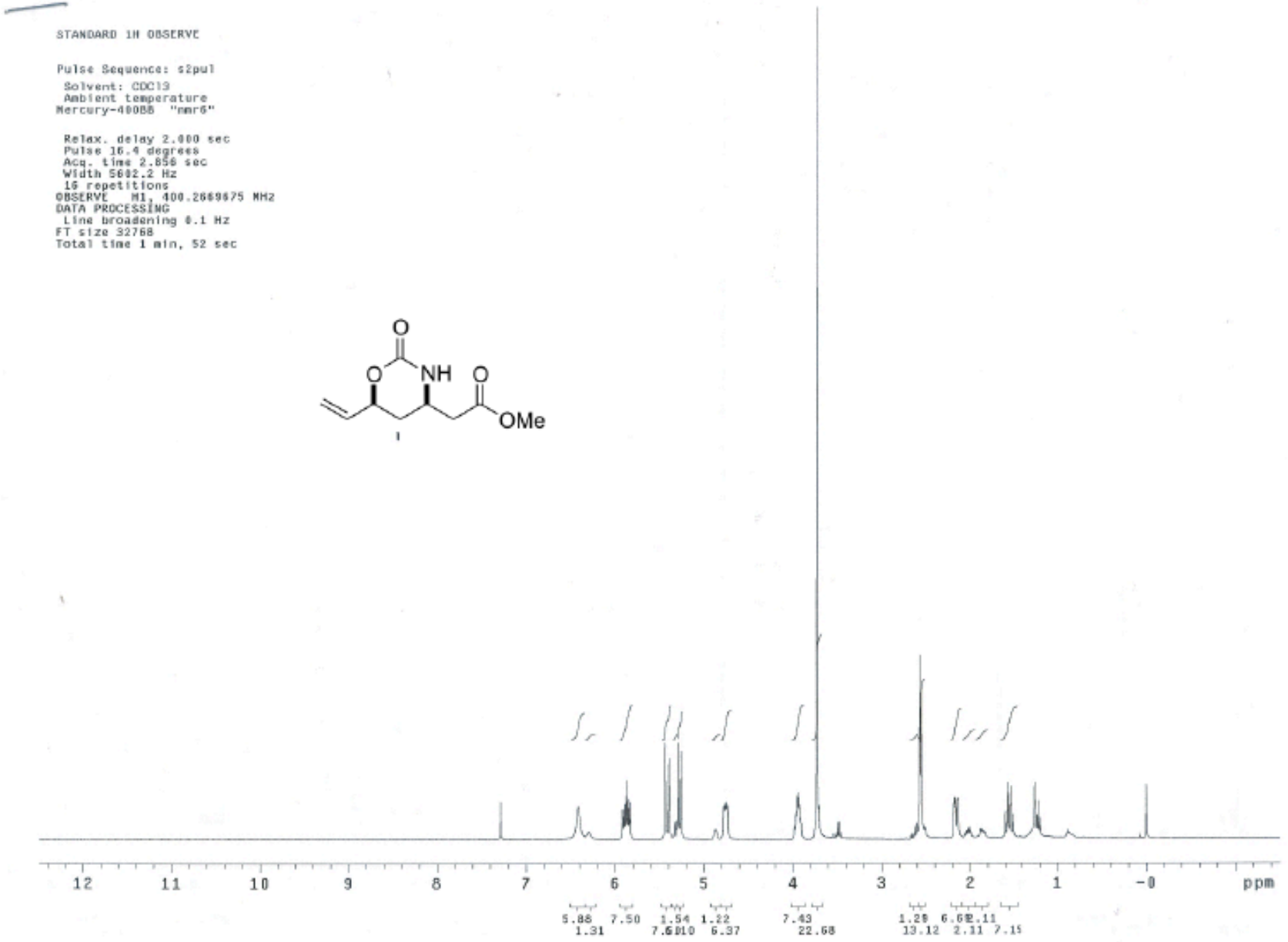
***E*-2-(But-1'-en-1'-yl)-10-ethoxycarbonylmethyl-11-oxa-3-azatetracyclo[5.3.1.0^{2,6}.0^{3,9}]undecan-7-ol (36).** DBU (0.024 mL, 0.16 mmol) was added to a stirred solution of **35** (0.014 g, 0.040 mmol) in toluene (0.4 mL) in a 5 mL vial at room temperature. The vial was sealed and heated with stirring at 130 ºC (bath temperature) for 4 h. The reaction was cooled to room temperature and filtered through a pad of silica gel (EtOAc to EtOAc-MeOH 10:1) to afford the epimerized product as yellow oil (0.014 g, ~100%), which was dissolved in CH_2Cl_2 (0.4 mL) and cooled to 0 ºC. TFA (0.31 mL, 4.0 mmol) was then added with stirring, and the resulting solution was warmed to room temperature and stirred for 1 h. 5 M NaOH (1 mL), CH_2Cl_2 (5 mL), and $NaHCO_3$(5 mL) were then added sequentially, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by column chromatography eluting with EtOAc with 1% v/v Et_3N to give 0.010 g (81%) of **36** as light yellow oil: $[\alpha]_D^{25}$ +17 (c = 0.5, $CHCl_3$); IR (neat) 3349, 2962, 1733, 1325, 1273, 1227, 1179, 1038, 972 cm^{-1}; HRMS (ESI) *m/z* 308.1859 [$C_{17}H_{26}NO_4$ (M+H) requires 308.1856]; The ^{1}H and ^{13}C NMR data were consistent with those reported by Overman (see Table 1 and 2).[3]

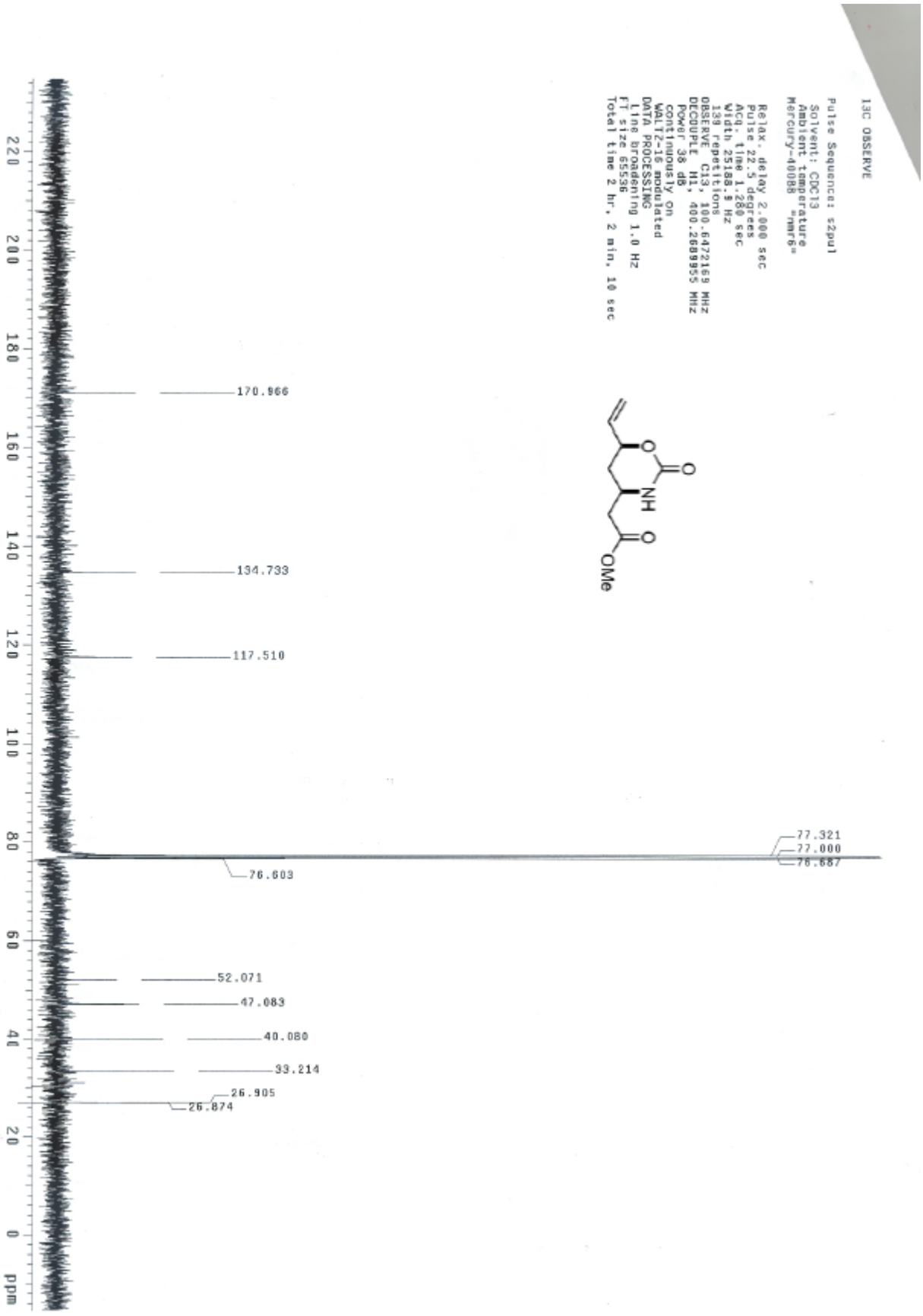
Table 1 Comparison of ^{1}H NMR data of **36** with reported literature values

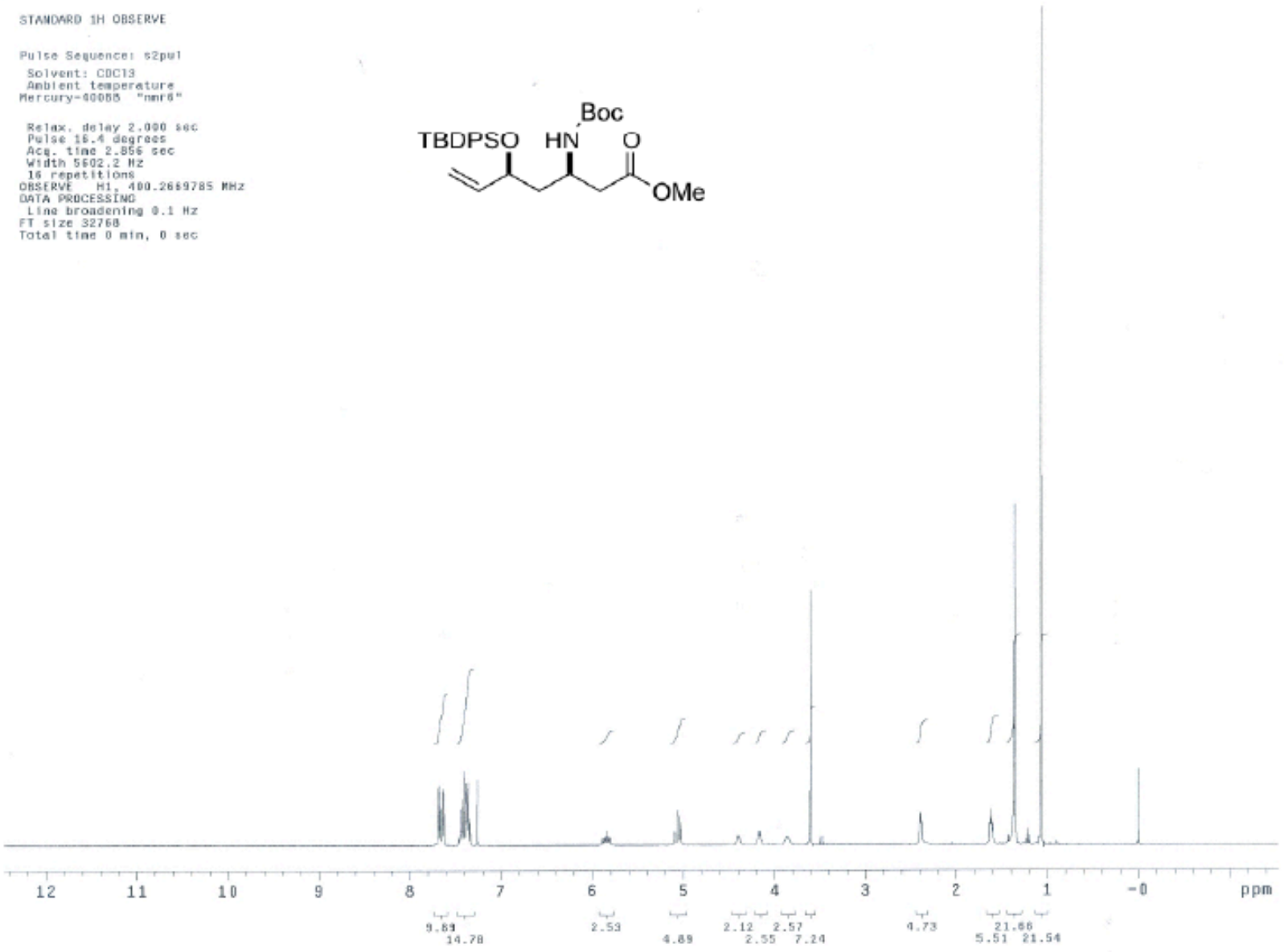
^{1}H (Hz) Overman[3]	^{1}H (Hz)
5.70 dt (15.5, 6.3)	5.72, dt (15.5, 6.0)
5.47 dt (15.5, 1.4)	5.48 d (15.5)
4.23 br t (2.0)	4.25 br s
4.16 qd (7.2, 1.3)	4.19 qd (7.0, 2.0)
3.21-3.16 br s	3.19 br s
3.08-2.95 m	3.06-2.96 m
2.91 dd (17.0, 9.3)	2.92 dd (17.0, 9.5)
2.44 t (3.4)	2.45 t (3.5)
2.23-2.17 m	2.23-2.19 m
2.09-2.00 m	2.09-2.03 m
1.89-1.78 m	1.89-1.81 comp
1.63 dt (12.2, 3.2)	1.64 dt (12.0, 3.0)
1.26 t (7.2)	1.28 t (7.0)
0.97 t (7.4)	0.99 t (7.5)

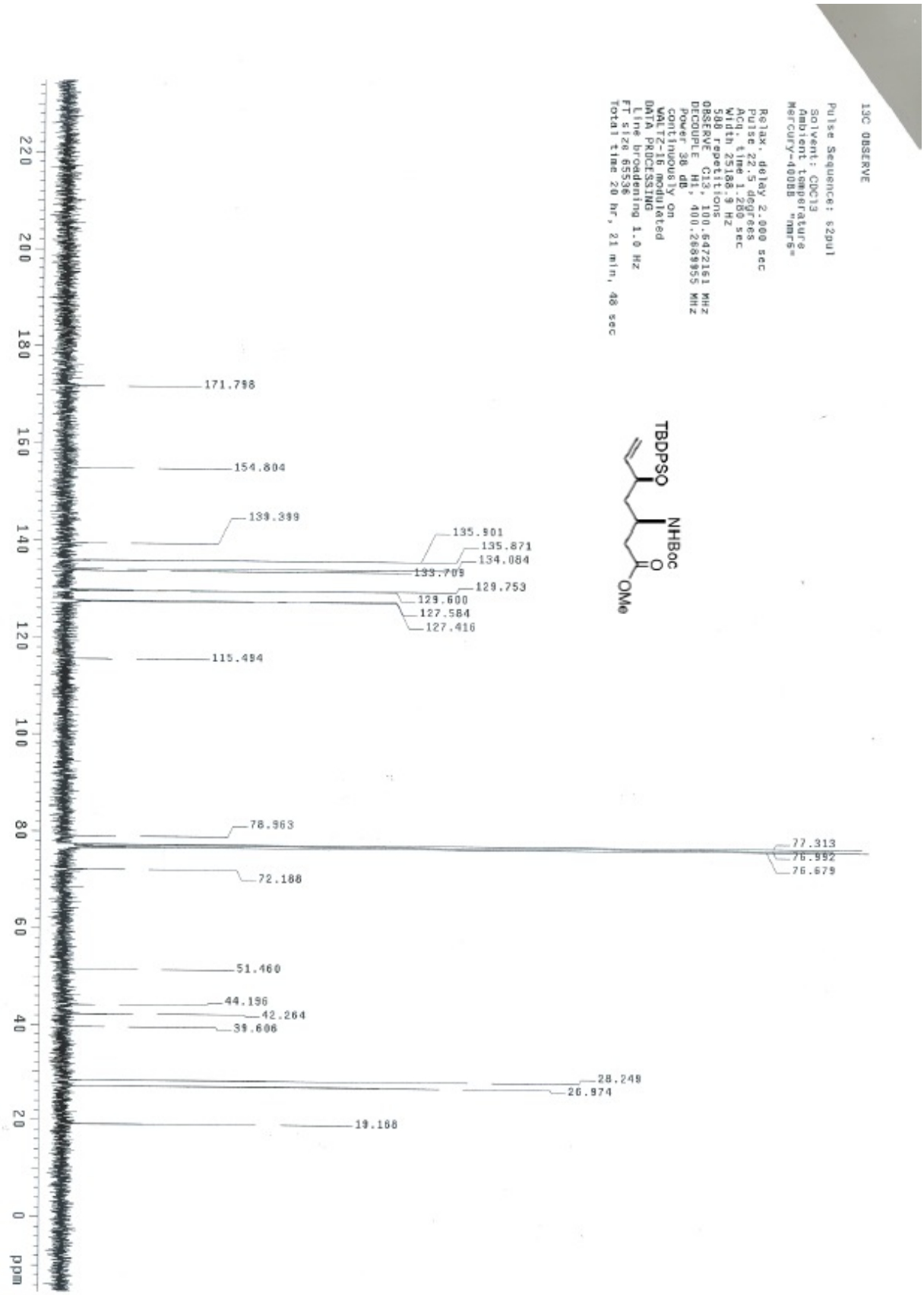
Table 2 Comparison of ^{13}C NMR data of **36** with reported literature values

^{13}C Overman[3]	^{13}C
175.5	175.6
132.6	132.6
126.9	127.2
104.8	104.8
82.1	82.3
81.6	81.6
65.2	65.3
61.5	61.5
55.9	56.0
47.7	47.8
36.8	36.9
33.1	33.2
32.4	32.5
26.6	26.8
25.3	25.4
14.1	14.1
13.5	13.6


STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "nmr6"
Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.858 sec
Width 5602.2 Hz
16 repetitions
OBSERVE H1, 400.2669675 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 1 min, 52 sec
O
O
NH
O
OMe
12
11
10
9
8
7
6
5
4
3
2
1
-0
ppm
5.88
1.31
7.50
1.54
7.61
1.10
1.22
6.37
7.43
22.68
1.28
13.12
6.68
2.11
2.11
7.15


13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "mmr6"
Relax. delay 2.000 sec
Pulse 22.5 degrees
Acq. time 1.280 sec
Width 25188.8 Hz
139 repetitions
OBSERVE C13, 100.6472169 MHz
DECOUPLE H1, 400.2689955 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 2 hr, 2 min, 10 sec
NH
O
OMe
170.966
134.733
117.510
77.321
77.000
76.687
76.603
52.071
47.083
40.080
33.214
26.905
26.874
220
200
180
160
140
120
100
80
60
40
20
0
ppm


STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "nmr6"
Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
16 repetitions
OBSERVE H1, 400.2669785 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 0 min, 0 sec
Boc
TBDPSO
HN
O
OMe
12
11
10
9
8
7
6
5
4
3
2
1
-0
ppm
9.83
14.78
2.53
4.89
2.12
2.57
2.55
7.24
4.73
21.66
5.51
21.54

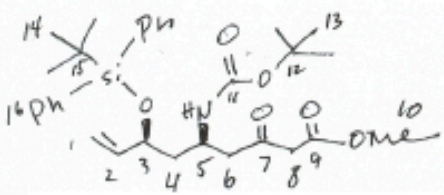

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "mars"
Relax. delay 2.000 sec
Pulse 22.5 degrees
Acq. time 1.280 sec
Width 25188.9 Hz
588 repetitions
OBSERVE C13, 100.6472161 MHz
DECOUPLE H1, 400.2689955 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 20 hr, 21 min, 48 sec
TBDPSO
NHBoc
O
OMe
171.798
154.804
139.399
135.901
135.871
134.084
133.709
129.753
129.600
127.584
127.416
115.494
78.963
77.313
76.992
76.679
72.188
51.460
44.196
42.264
39.606
28.249
26.974
19.188
220
200
180
160
140
120
100
80
60
40
20
0
ppm

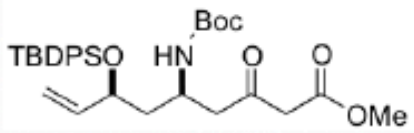
STANDARD 1H OBSERVE

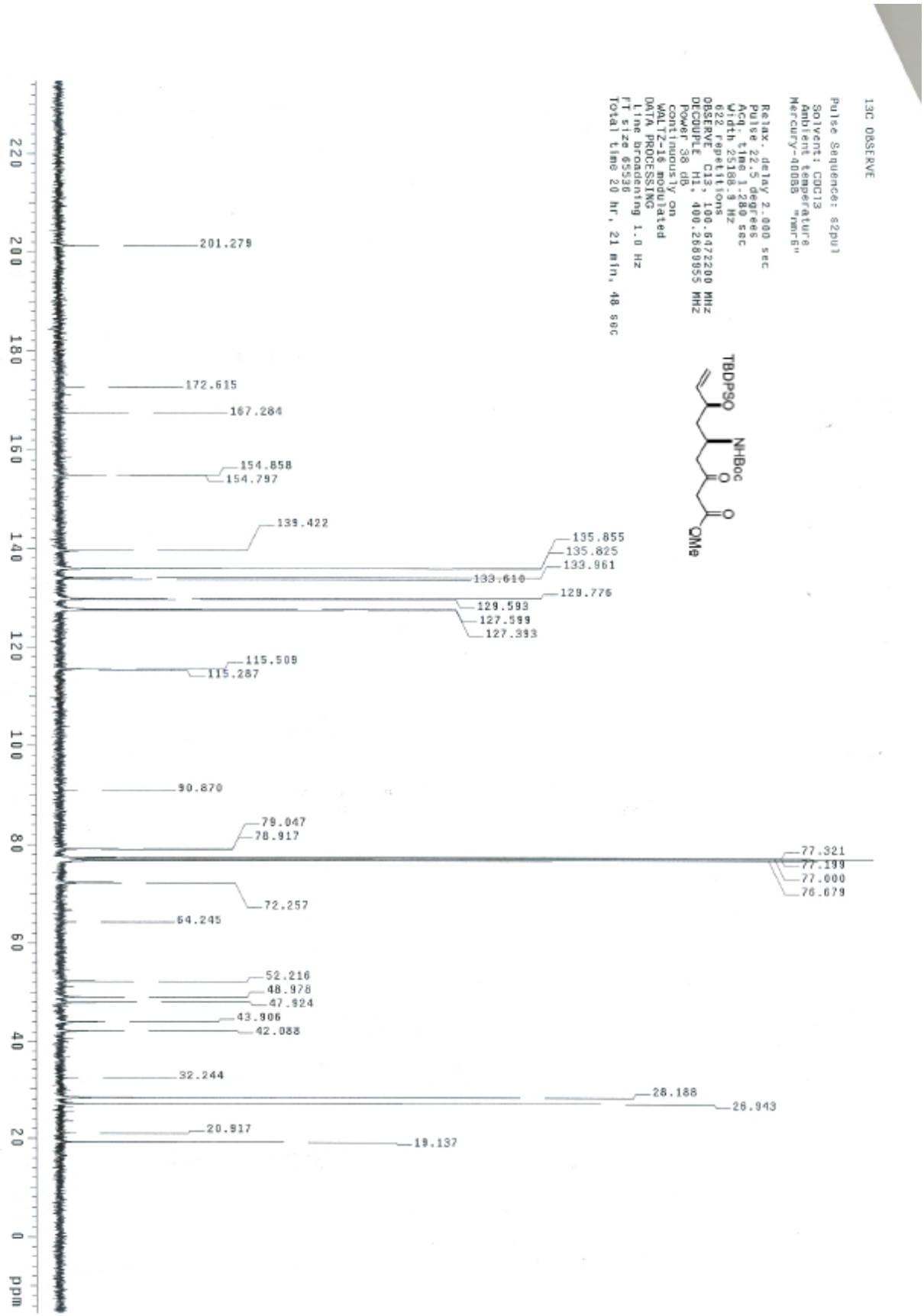
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "nmr6"

Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
11 repetitions
OBSERVE H1, 400.2669769 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 1 min, 52 sec

^{13}C attached





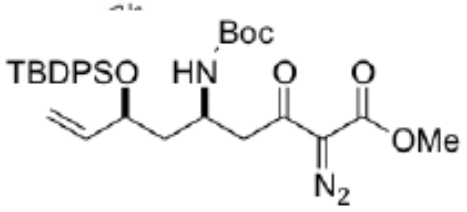

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "mmr6"
Relax. delay 2.000 sec
Pulse 22.5 degrees
Acq. time 1.280 sec
Width 25188.9 Hz
622 repetitions
OBSERVE C13, 100.6472200 MHz
DECOUPLE H1, 400.2688955 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 20 hr, 21 min, 48 sec
TBDPSO
NHBoc
O
O
OMe
201.279
172.615
167.284
154.858
154.797
139.422
135.855
135.825
133.961
133.610
129.776
129.593
127.599
127.393
115.509
115.287
90.870
79.047
78.917
77.321
77.199
77.000
76.679
72.257
64.245
52.216
48.978
47.924
43.906
42.088
32.244
28.188
26.943
20.917
19.137
220
200
180
160
140
120
100
80
60
40
20
0
ppm

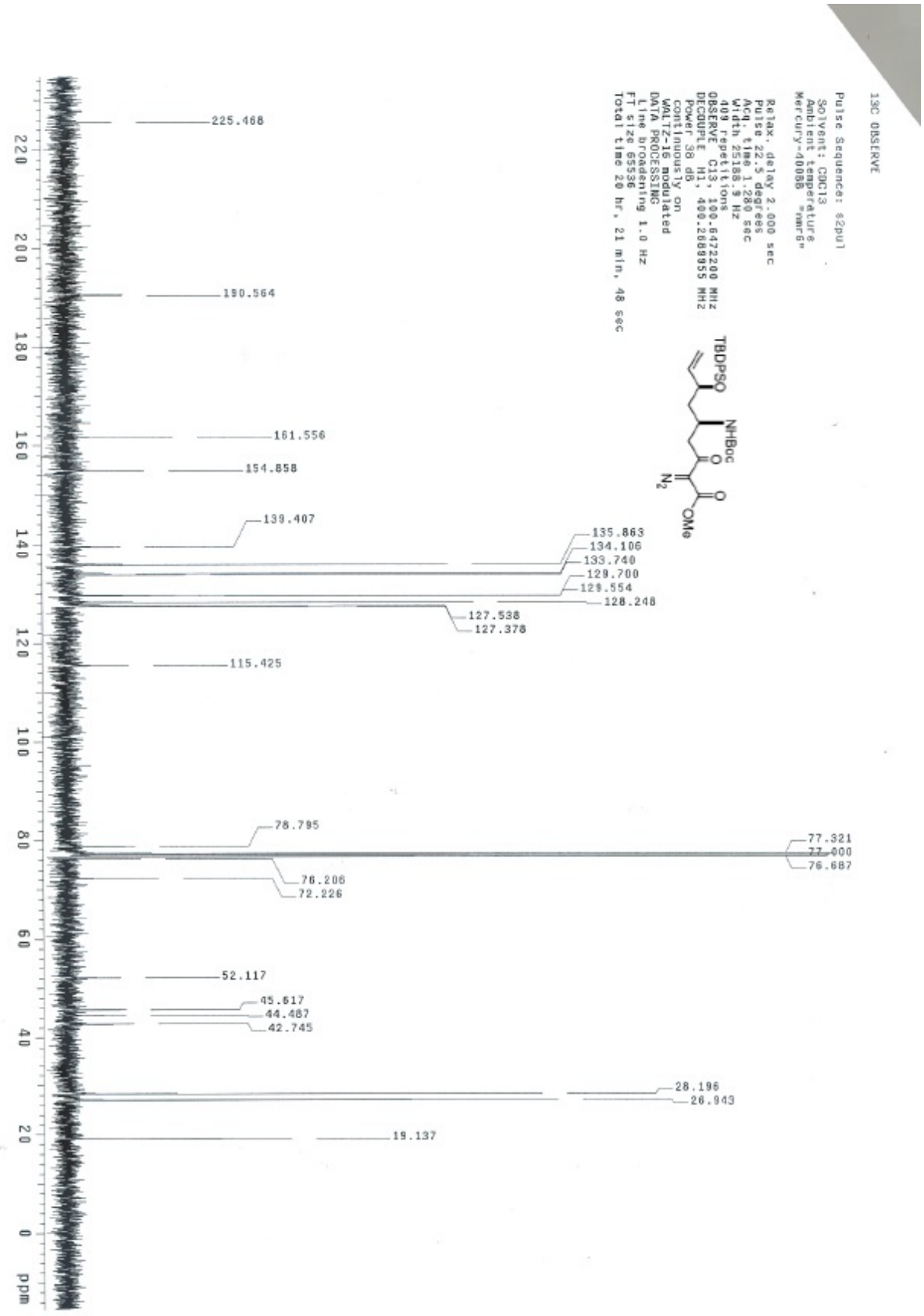
STANDARD 1H OBSERVE

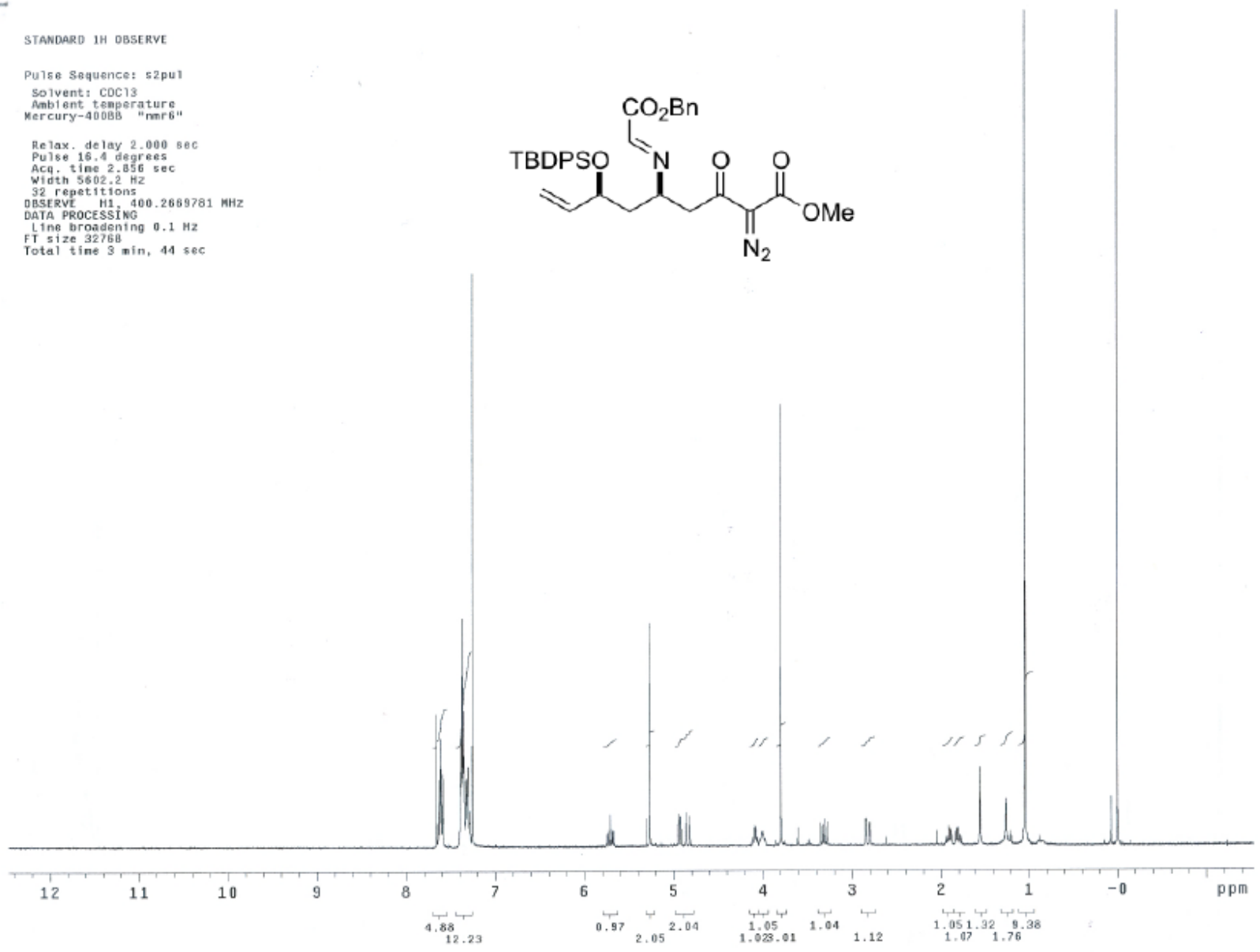
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "rmr6"

Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
16 repetitions
OBSERVE H1, 400.2669839 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 0 min, 0 sec

Attached ^{13}C-NMR



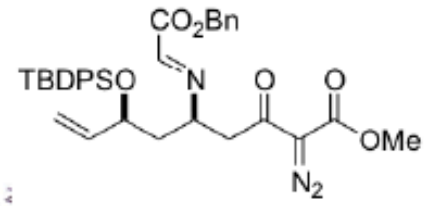

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 22.5 degrees
Acq. time 1.280 sec
Width 25188.9 Hz
409 repetitions
OBSERVE C13, 100.6472200 MHz
DECOUPLE H1, 400.2688955 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 20 hr, 21 min, 48 sec
TBDPSO
NHBoc
O
O
N2
O
OMe
225.468
190.564
161.556
154.858
139.407
135.863
134.106
133.740
129.700
129.554
128.248
127.538
127.378
115.425
78.795
77.321
77.000
76.687
76.206
72.226
52.117
45.617
44.487
42.745
28.196
26.943
19.137
220
200
180
160
140
120
100
80
60
40
20
0
ppm


STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "nmr6"
Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
32 repetitions
OBSERVE H1, 400.2669781 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 44 sec
CO2Bn
TBDPSO
N
O
O
OMe
N2
12
11
10
9
8
7
6
5
4
3
2
1
-0
ppm
4.88
12.23
0.97
2.05
2.04
1.05
1.023.01
1.04
1.12
1.05
1.07
1.32
1.76
9.38

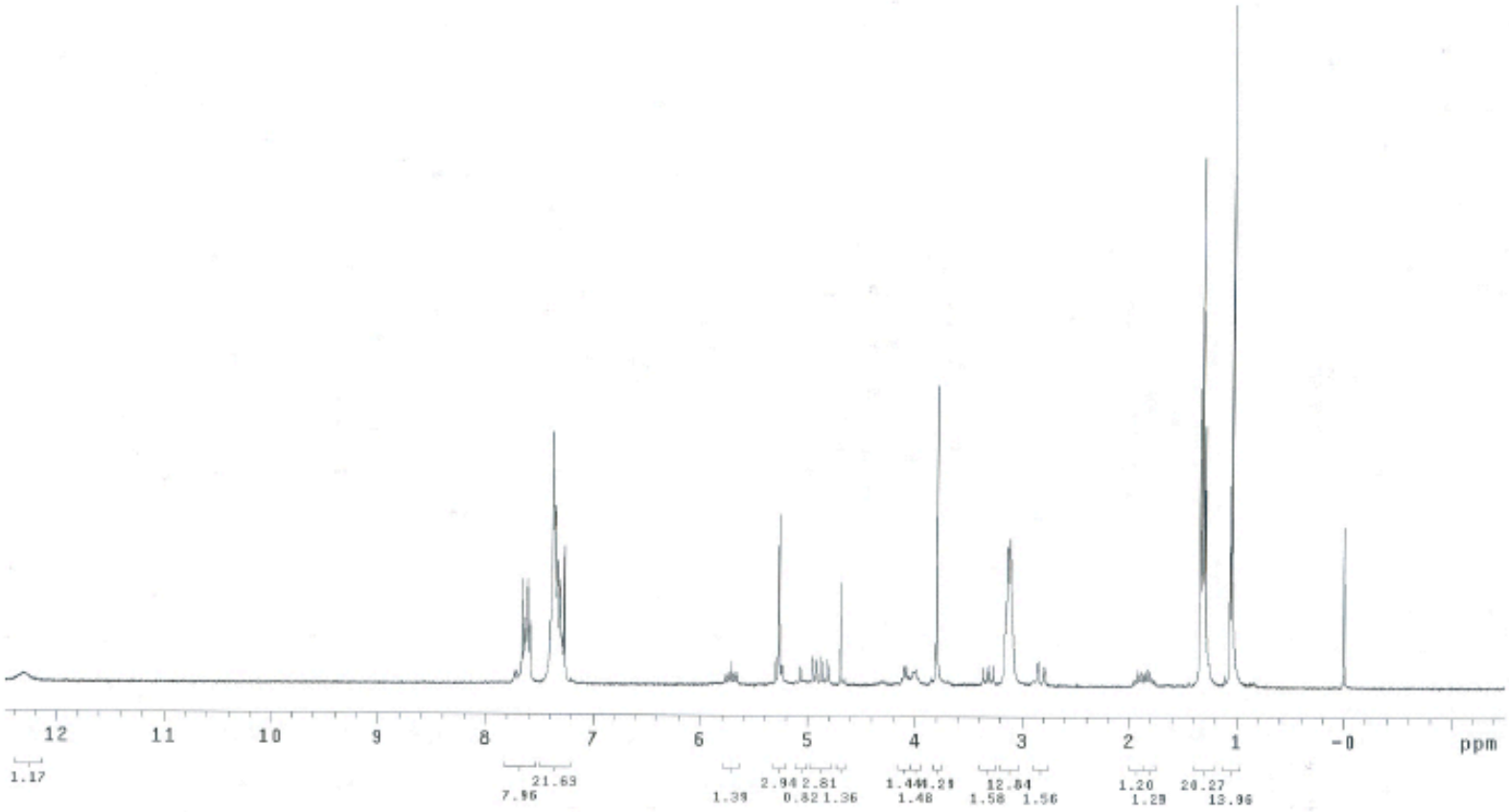
CF-I-046

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
UNITYplus-300 "nmr2"

Relax. delay 1.000 sec
Pulse 15.0 degrees
Acq. time 3.813 sec
Width 4196.4 Hz
16 repetitions
OBSERVE H1, 300.1390295 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 1 min, 17 sec



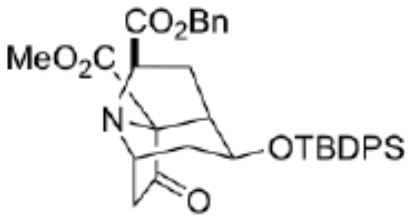
with TFA•NEt_3



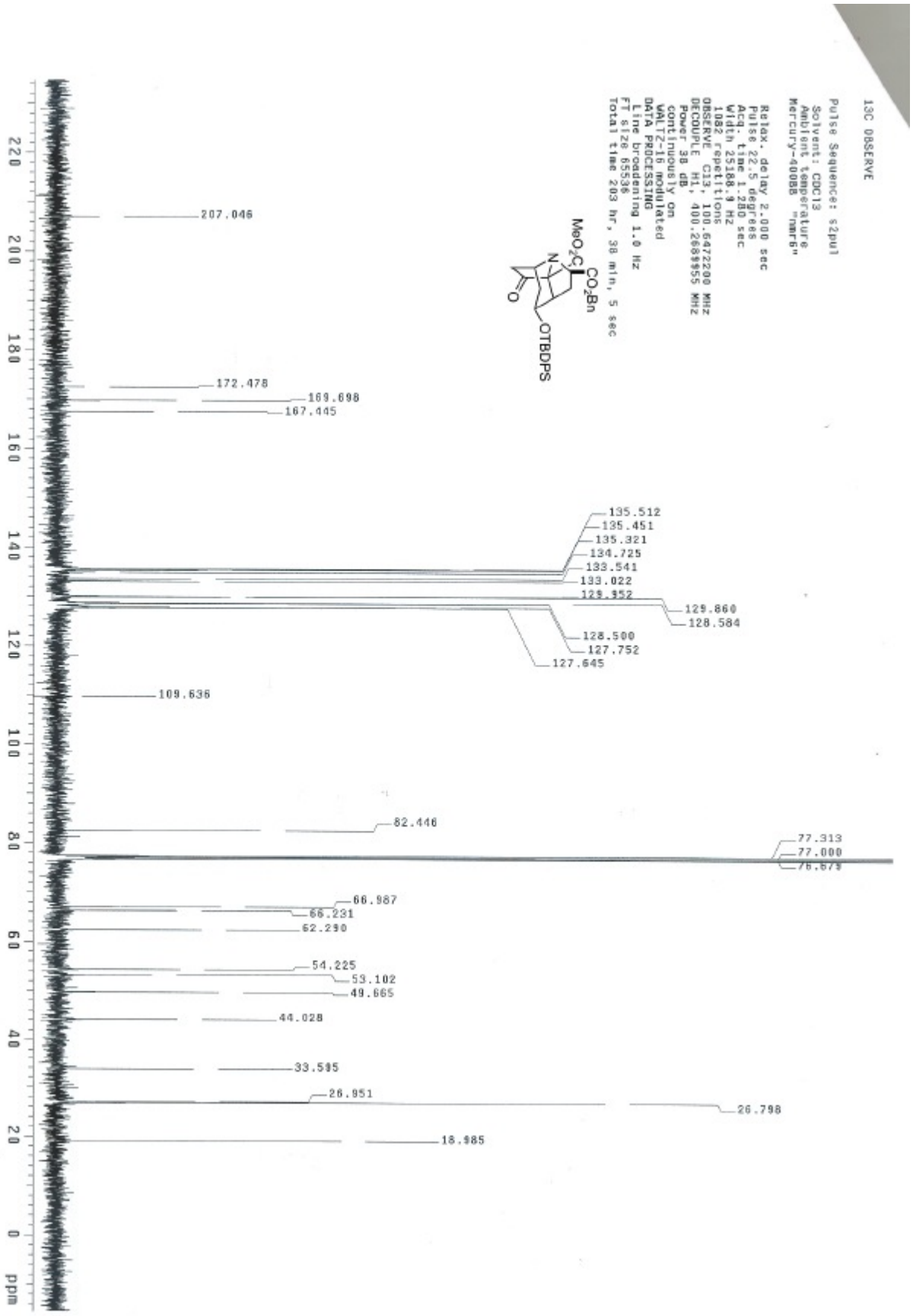
STANDARD 1H OBSERVE

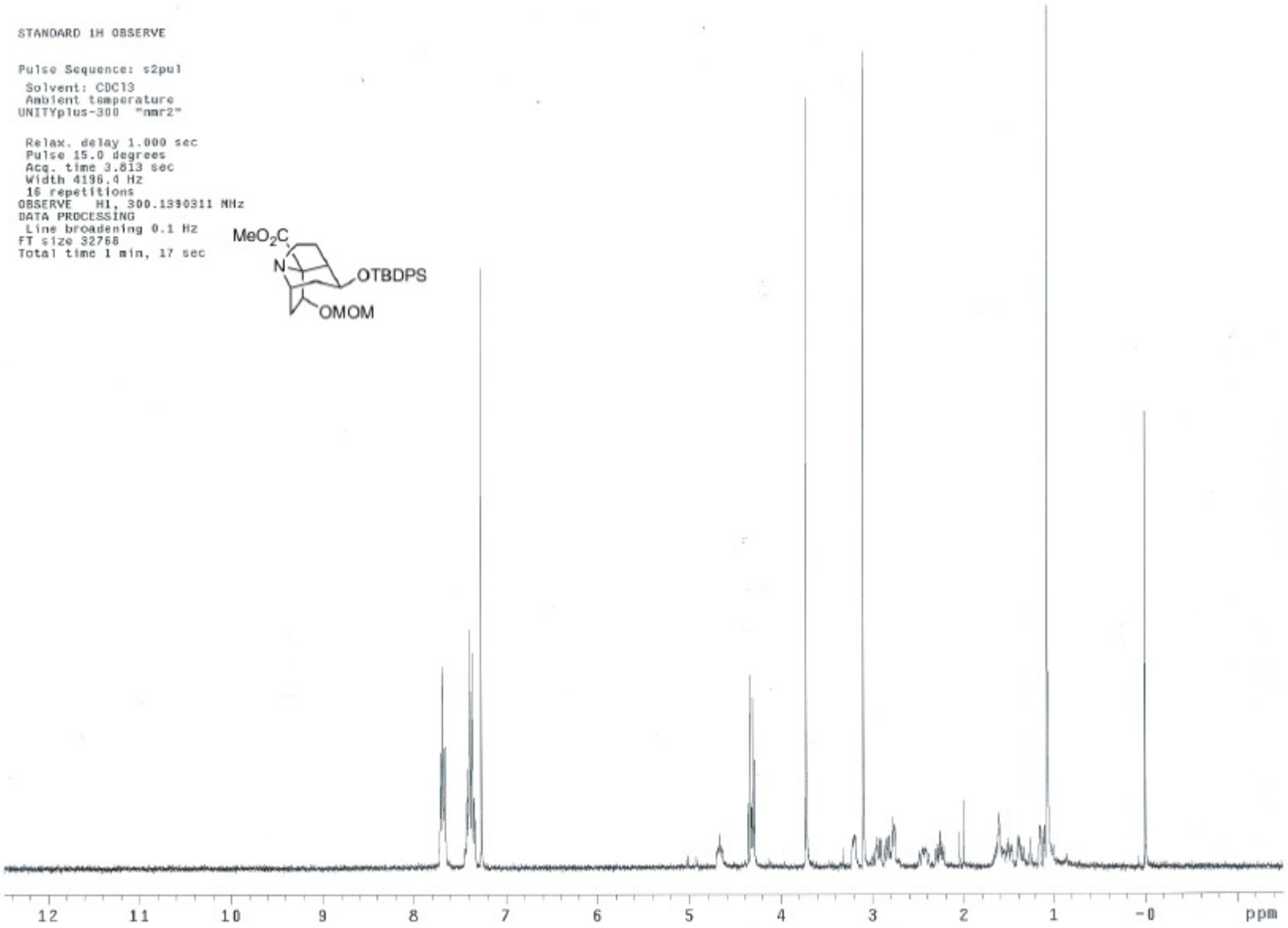
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "nmr6"

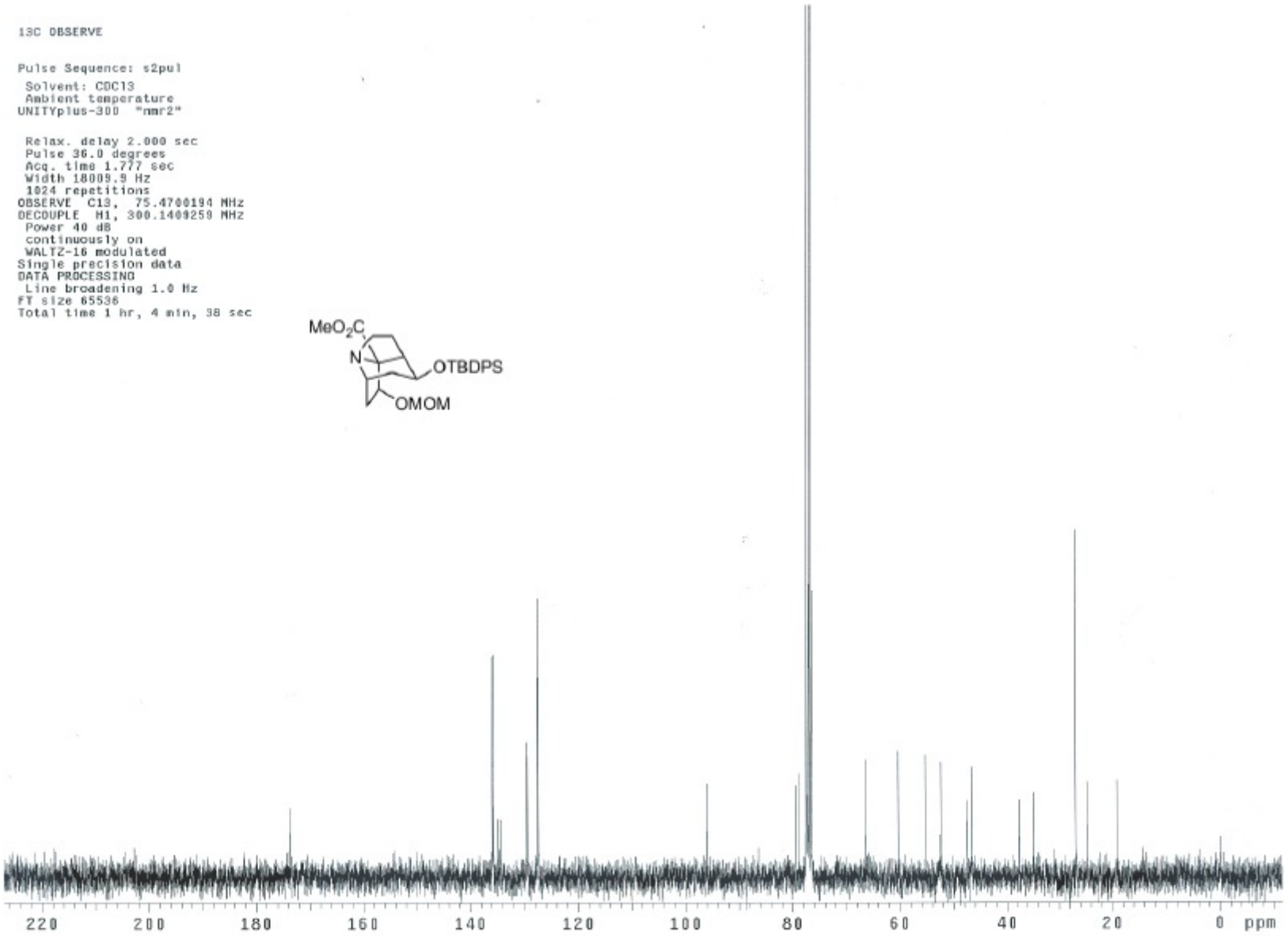
Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
32 repetitions
OBSERVE H1, 400.2669795 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 0 min, 0 sec

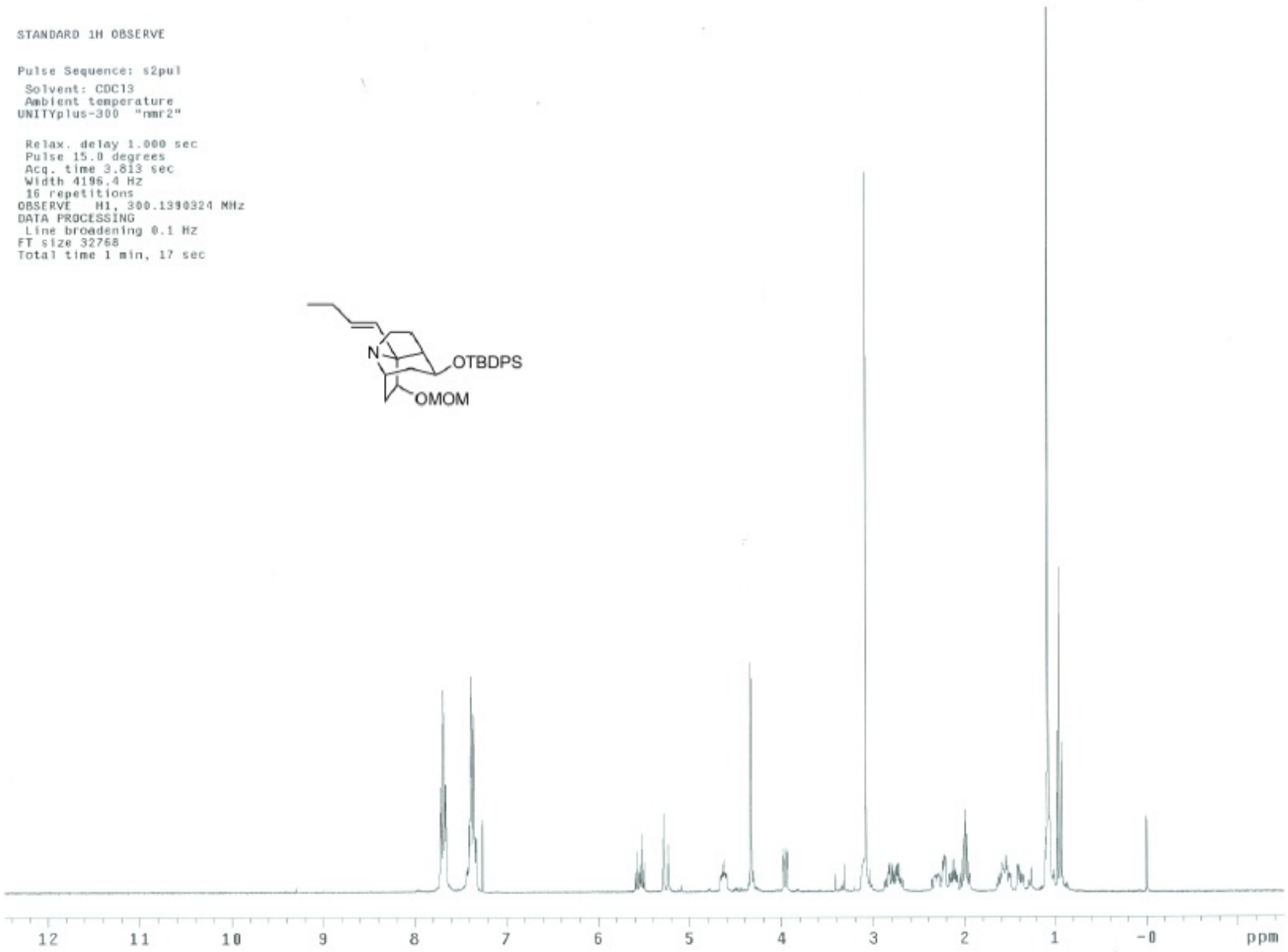


13C-attached


13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "nmrb"
Relax. delay 2.000 sec
Pulse 22.5 degrees
Acq. time 1.280 sec
Width 25188.9 Hz
1082 repetitions
OBSERVE C13, 100.6472200 MHz
DECOUPLE H1, 400.2689955 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 203 hr, 38 min, 5 sec
MeO2C
CO2Bn
N
O
OTBDPS
207.046
172.478
169.698
167.445
135.512
135.451
135.321
134.725
133.541
133.022
129.952
129.860
128.584
128.500
127.752
127.645
109.636
82.446
77.313
77.000
76.679
66.987
66.231
62.290
54.225
53.102
49.665
44.028
33.595
26.951
26.798
18.985
220
200
180
160
140
120
100
80
60
40
20
0
ppm


STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
UNITYplus-300 "nmr2"
Relax. delay 1.000 sec
Pulse 15.0 degrees
Acq. time 3.813 sec
Width 4196.4 Hz
16 repetitions
OBSERVE H1, 300.1390311 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 1 min, 17 sec
MeO2C
N
OTBDPS
OMOM
12
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

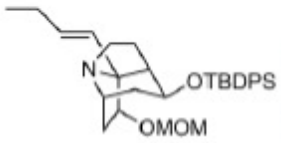

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
UNITYplus-300 "nmr2"
Relax. delay 2.000 sec
Pulse 36.0 degrees
Acq. time 1.777 sec
Width 18009.9 Hz
1024 repetitions
OBSERVE C13, 75.4700194 MHz
DECOUPLE H1, 300.1409259 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
Single precision data
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 4 min, 38 sec
MeO2C
N
OTBDPS
OMOM
220
200
180
160
140
120
100
80
60
40
20
0
ppm

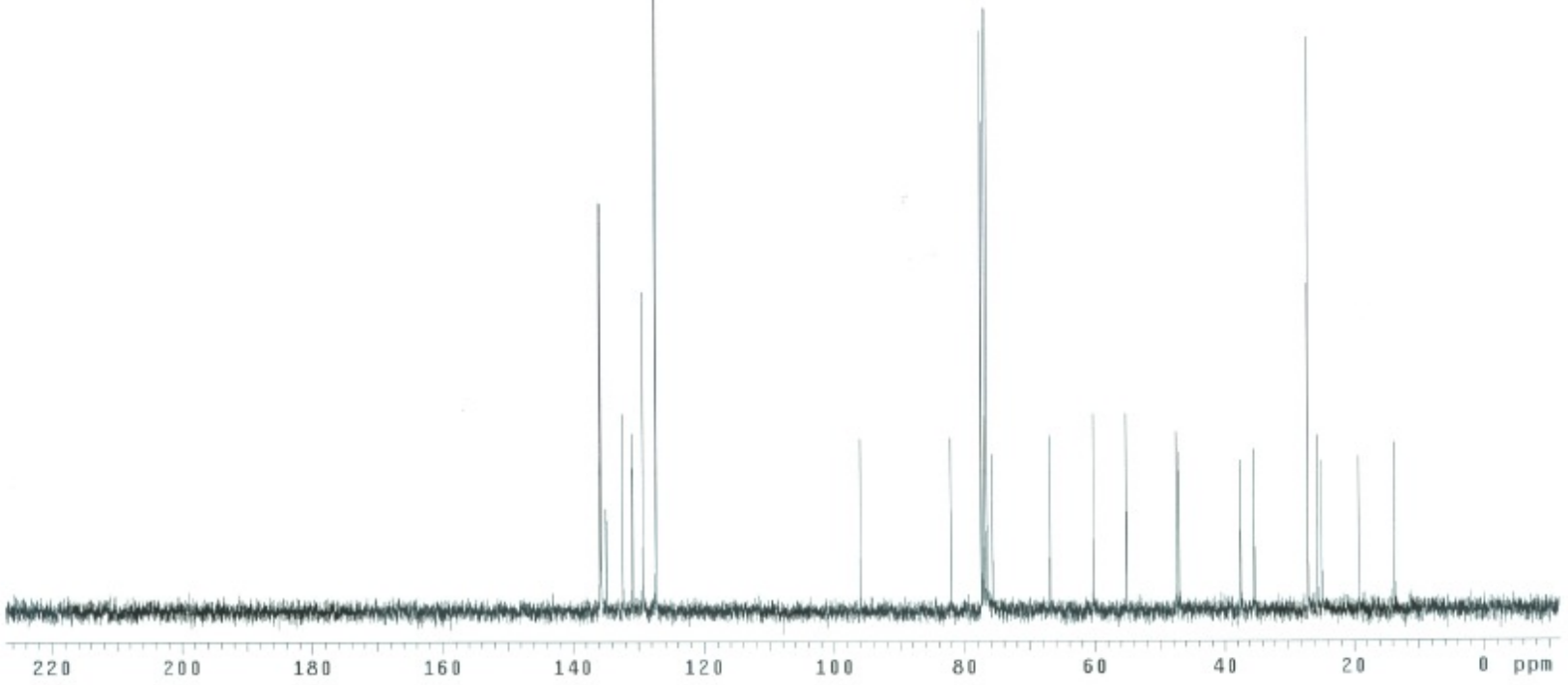

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
UNITYplus-300 "nmr2"
Relax. delay 1.000 sec
Pulse 15.0 degrees
Acq. time 3.813 sec
Width 4196.4 Hz
16 repetitions
OBSERVE H1, 300.1390324 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 1 min, 17 sec
N
OTBDPS
OMOM
12
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

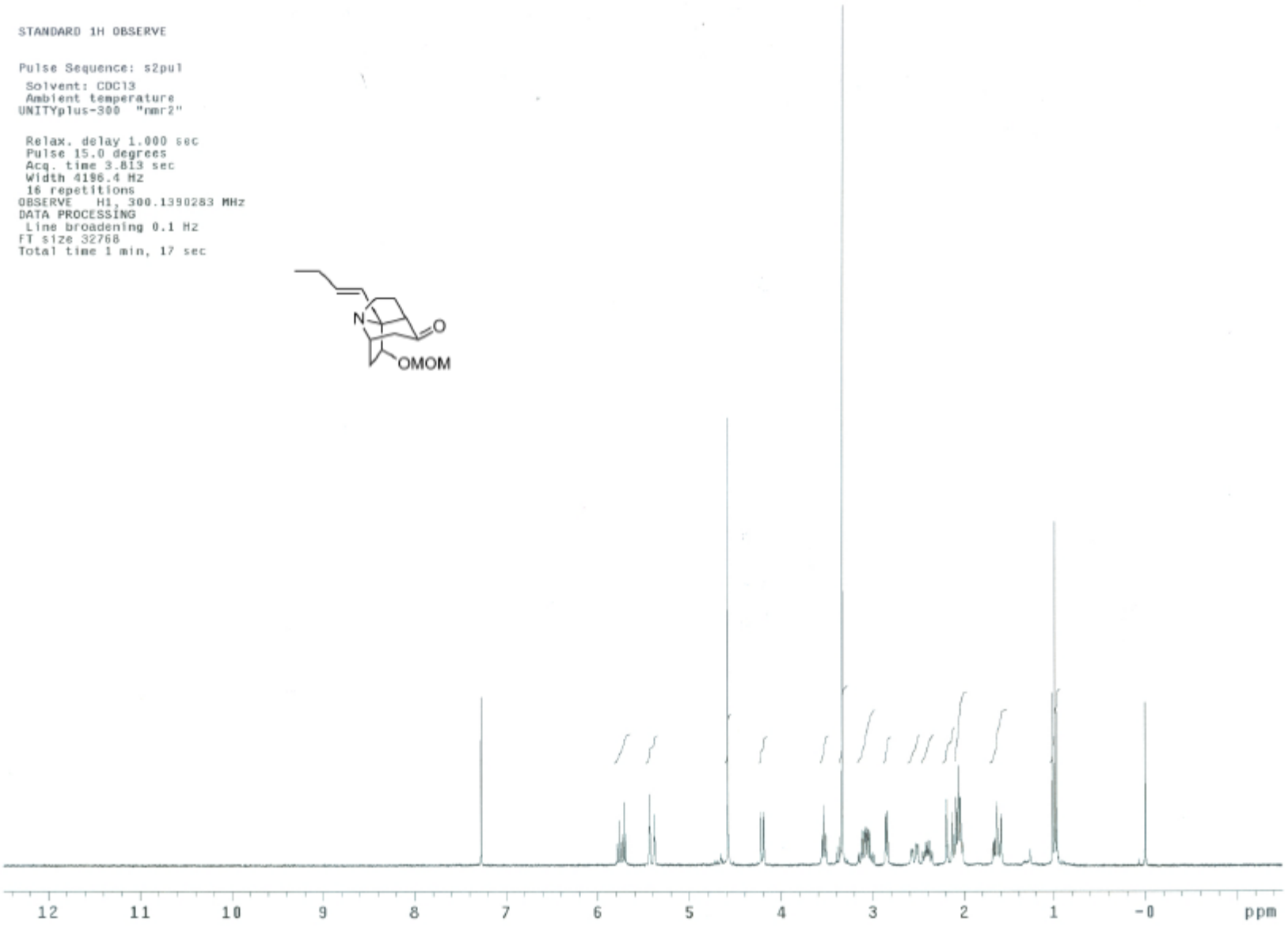
13C OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
UNITYplus-300 "nmr2"

 Relax. delay 2.000 sec
 Pulse 36.0 degrees
 Acq. time 1.777 sec
 Width 18009.9 Hz
 520 repetitions
OBSERVE C13, 75.4700205 MHz
DECOUPLE H1, 300.1409259 MHz
 Power 40 dB
 continuously on
 WALTZ-16 modulated
Single precision data
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 4 min, 38 sec



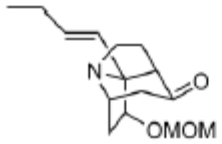


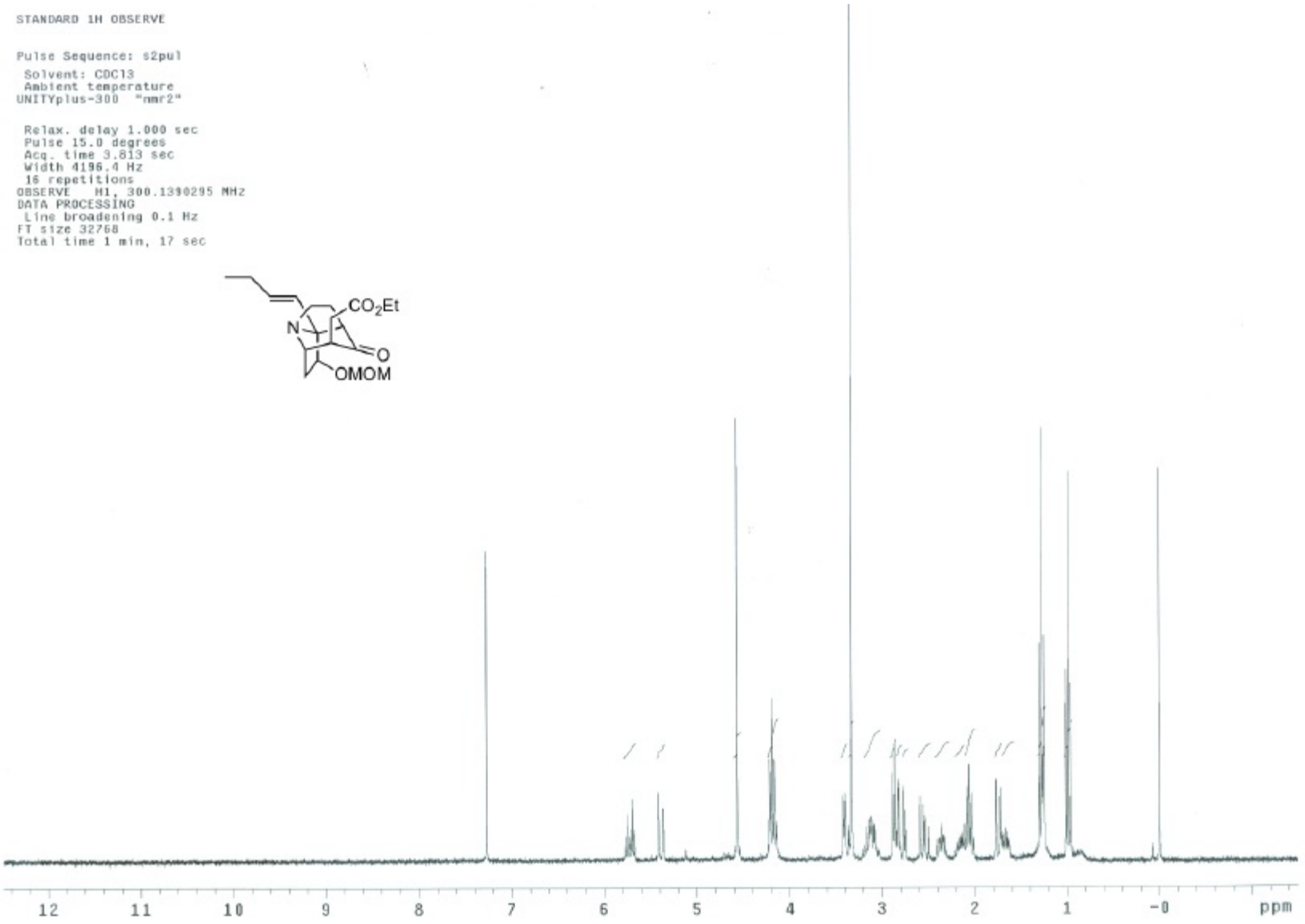

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
UNITYplus-300 "nmr2"
Relax. delay 1.000 sec
Pulse 15.0 degrees
Acq. time 3.813 sec
Width 4196.4 Hz
16 repetitions
OBSERVE H1, 300.1390283 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 1 min, 17 sec
N
O
OMOM
12
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

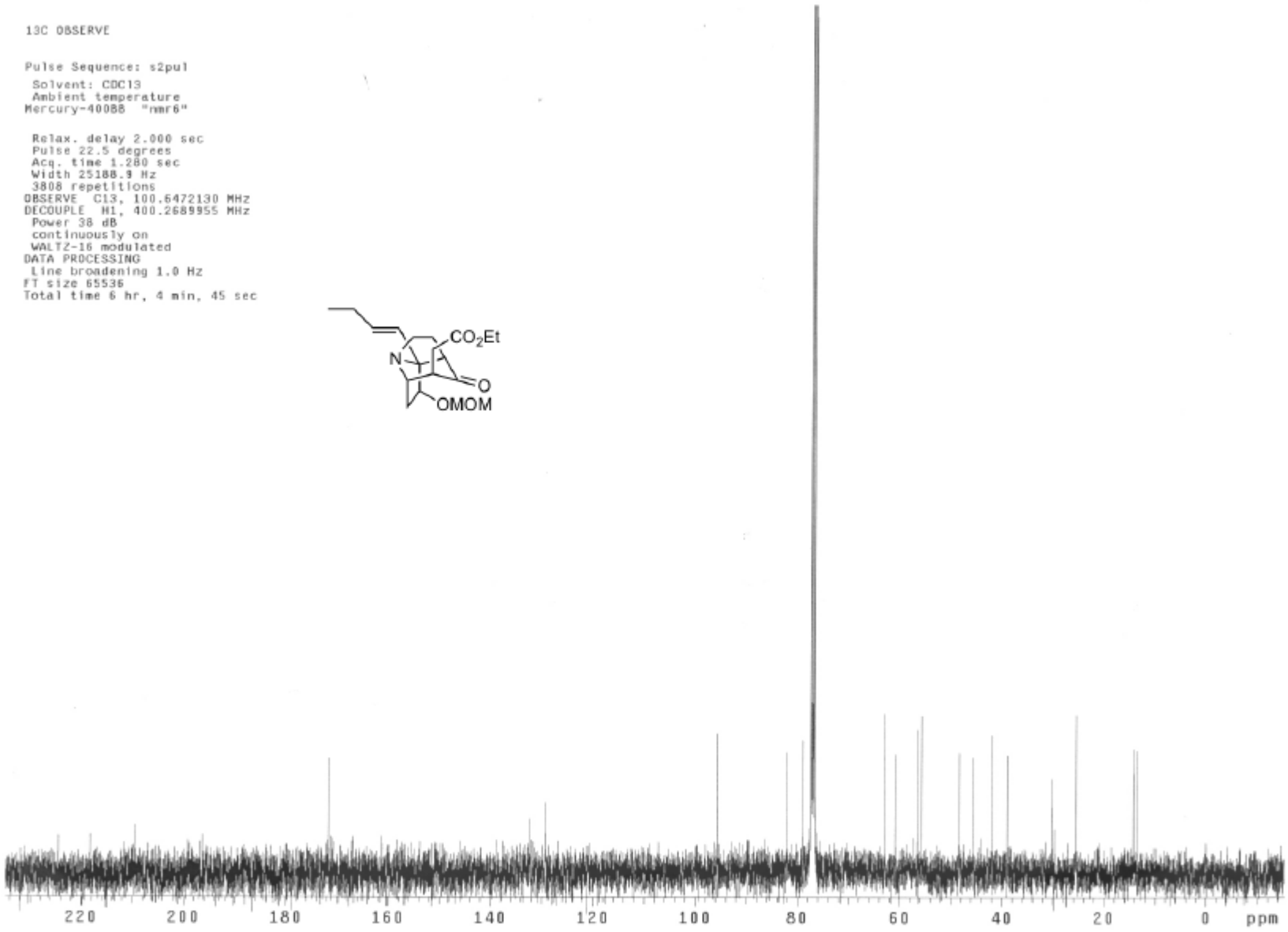
13C OBSERVE

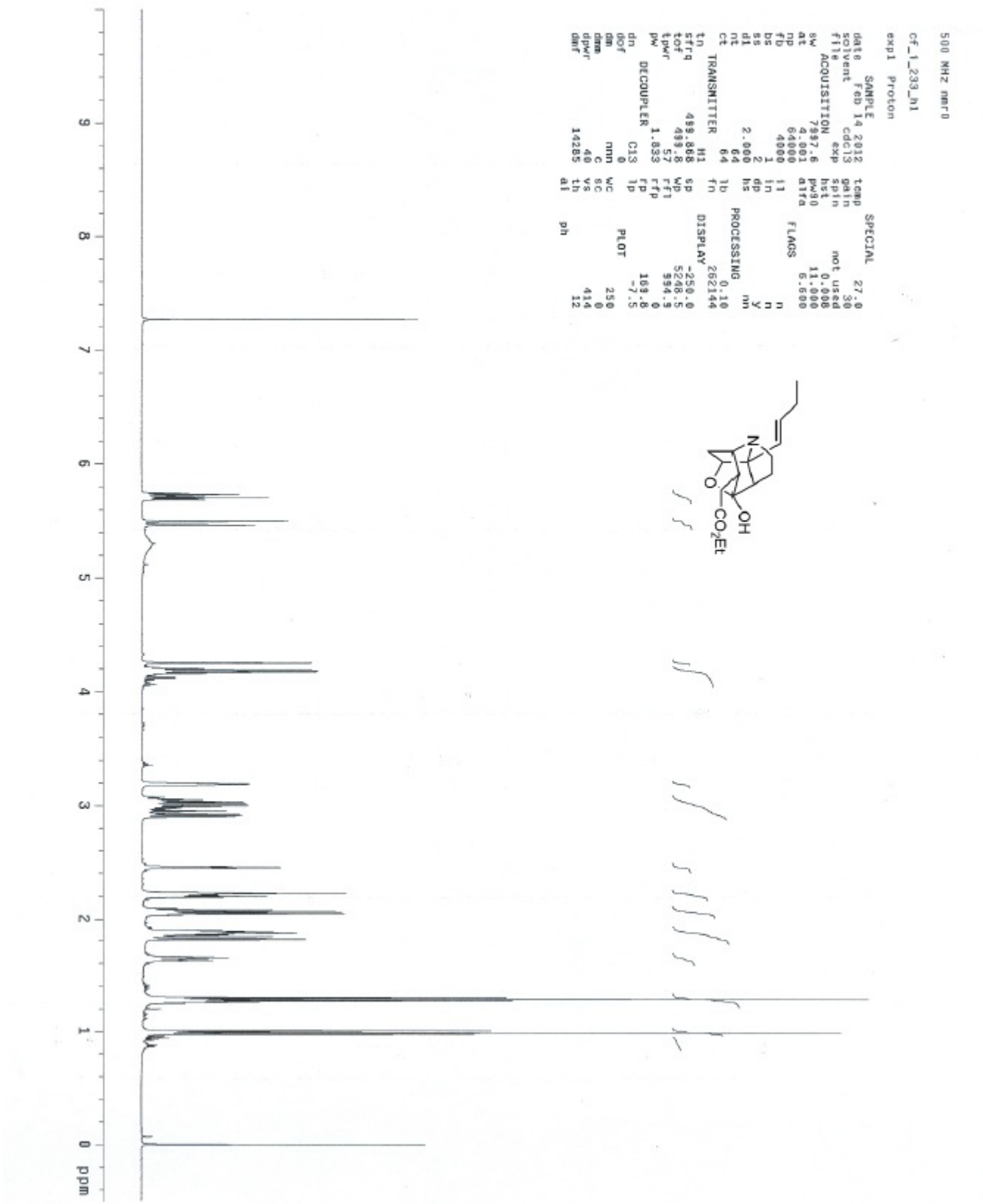
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
UNITYplus-300 "nmr2"

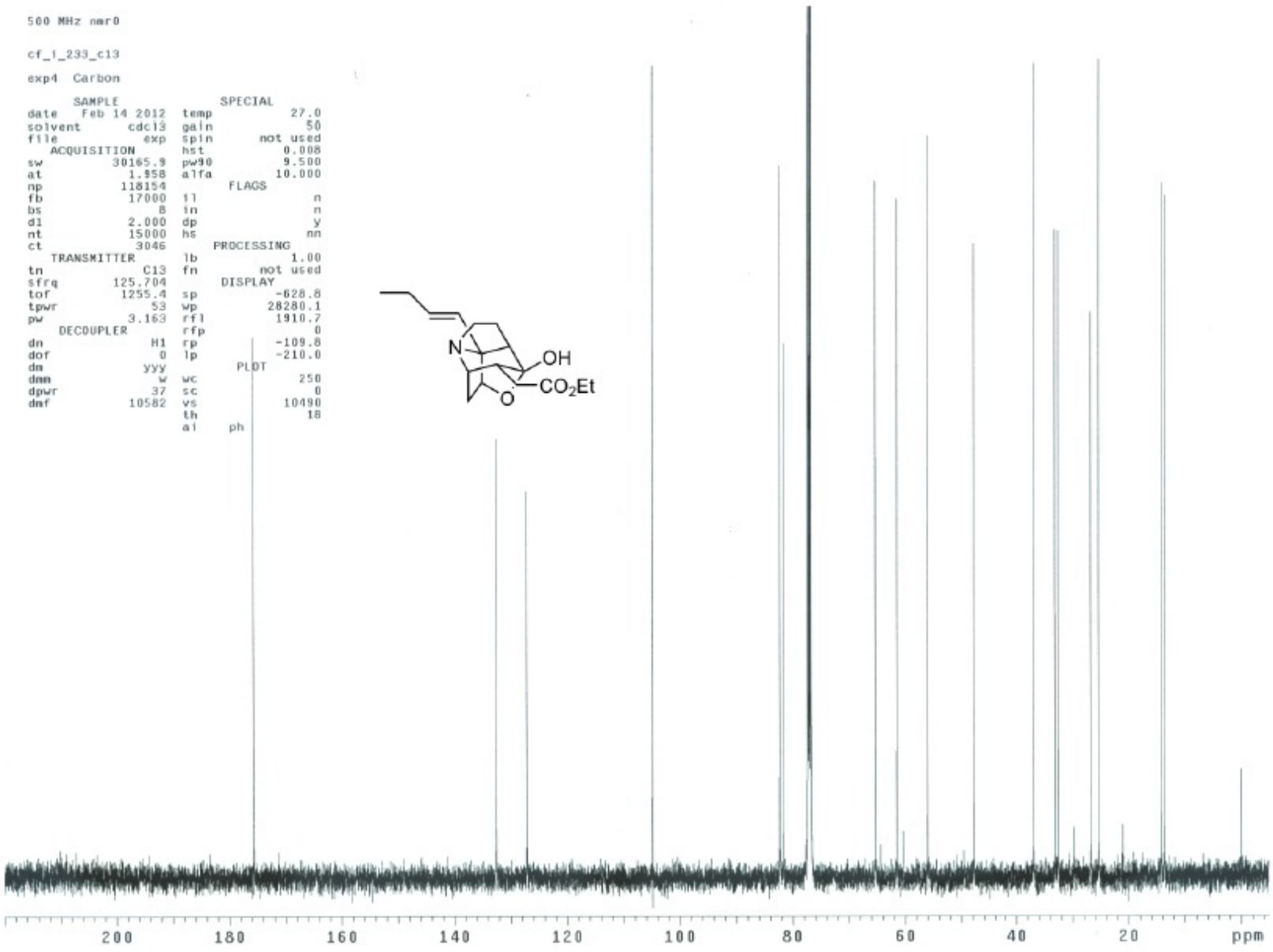
Relax. delay 2.000 sec
Pulse 36.0 degrees
Acq. time 1.777 sec
Width 18009.9 Hz
835 repetitions
OBSERVE C13, 75.4700178 MHz
DECOUPLE H1, 300.1409259 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
Single precision data
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 4 min, 38




STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
UNITYplus-300 "nmr2"
Relax. delay 1.000 sec
Pulse 15.0 degrees
Acq. time 3.813 sec
Width 4196.4 Hz
16 repetitions
OBSERVE H1, 300.1390295 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 1 min, 17 sec
CO2Et
N
O
OMOM
12
11
10
9
8
7
6
5
4
3
2
1
-0
ppm


13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "nmr6"
Relax. delay 2.000 sec
Pulse 22.5 degrees
Acq. time 1.280 sec
Width 25188.9 Hz
3808 repetitions
OBSERVE C13, 100.6472130 MHz
DECOUPLE H1, 400.2689955 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 6 hr, 4 min, 45 sec
CO2Et
N
O
OMOM
220
200
180
160
140
120
100
80
60
40
20
0
ppm


500 MHz nmr0
cf_1_233_h1
expl Proton
SAMPLE
date Feb 14 2012
solvent cdcl3
file
ACQUISITION
sw 7997.6
at 4.001
np 64000
fb 40000
bs
ss 2
d1 2.000
nt 64
ct 64
TRANSMITTER
tn H1
sfrq 499.868
tof 499.8
tpwr 57
pw 1.833
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 40
dmf 14285
SPECIAL
temp 27.0
gain 30
spin not used
hst 0.000
pw90 11.000
atfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.10
fn 262144
DISPLAY
sp -250.0
wp 5248.5
rfl 994.9
rfp 0
rp 169.8
lp -7.5
PLOT
wc 250
sc 0
vs 414
th 12
ai
ph
N
O
OH
CO2Et
9
8
7
6
5
4
3
2
1
0 ppm


500 MHz nmr0
cf_l_233_c13
exp4 Carbon
SAMPLE
date Feb 14 2012
solvent cdcl3
file exp
ACQUISITION
sw 30165.9
at 1.958
np 118154
fb 17000
bs 8
d1 2.000
nt 15000
ct 3046
TRANSMITTER
tn C13
sfrq 125.704
tof 1255.4
tpwr 53
pw 3.163
DECOUPLER
dn H1
dof 0
dm yyy
dmm w
dpwr 37
dmf 10582
SPECIAL
temp 27.0
gain 50
spin not used
hst 0.008
pw90 9.500
alfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 1.00
fn not used
DISPLAY
sp -628.8
wp 28280.1
rfl 1910.7
rfp 0
rp -109.8
lp -210.0
PLOT
wc 250
sc 0
vs 10490
th 18
ai ph
N
OH
O
CO2Et
200
180
160
140
120
100
80
60
40
20
ppm

Reference:

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2. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923-2925.

3. Brüggemann, M.; McDonald, A. I.; Overman, L. E.; Rosen, M. D.; Schwink, L.; Scott, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 15284-15285.