Supporting Information

Enantioselective Total Synthesis Of (+)-Sieboldine A

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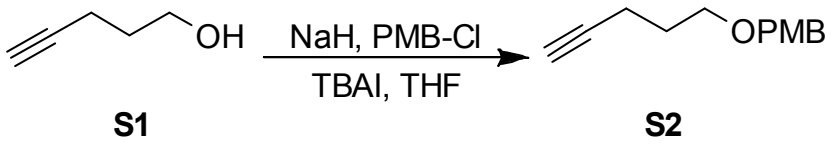
General notes:

All commercially obtained reagents and solvents were used as received unless additional purification is stated in the procedure. All glassware was oven-dried at 150 °C and cooled in desiccator immediately before use. Experiments were conducted under inert atmospheres of Nitrogen or Argon using standard syringe–septa techniques. Reactions performed at room temperature were at approximately 24 °C. Thin layer chromatography (TLC) was performed on Merck analytical glass plates pre-coated with silica gel 60 F254 (0.25 mm thick). Visualization was effected by exposure to UV light (254 nm) and staining with *p*-anisaldehyde or phosphomolybdic acid stains followed by a brief heating on a hot plate. Concentration under reduced pressure was performed by rotary evaporation (~30 mmHg) at 20-40 °C. Flash column chromatography was performed as described by W. C. Still *et al.* (*J. Org. Chem.***1978**, *43*, 2923.) using forced flow of the indicated solvent system on Kanto® Chemical silica gel 60N (spherical, neutral, 40–50 μm,). Melting points were determined on YANAGIMOTO micro melting point apparatus and were uncorrected. Infrared spectra were recorded on a ThermoFisher Nicolet iS5 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). NMR spectra were recorded on JNM-ECS400 or JNM-ECA600 spectrometers. Chemical shift (δ) values are reported in parts per million relative to internal standard tetramethylsilane (δ 0.00 ppm) and residual $CDCl_3$ (δ 7.27 ppm) for proton spectra and to residual $CDCl_3$ (δ 77.23 ppm) for carbon spectra. Coupling constants are reported in Hertz. The following abbreviations were used for spin multiplicity: s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublet; ddd, doublet of doublet of doublet; td, triplet of doublet; m, multiplet; br m, broad multiplet. High-resolution mass spectra were measured with JMS-T100TD (DART) mass spectrometer. Optical rotations were measured with a JASCO P-2200 polarimeter with a sodium lamp and reported as followed: $[\alpha]^{T}_{D}$ (concentration g/100 mL, solvent). Single-crystal X-ray diffraction was measured with R-AXIS RAPID II.

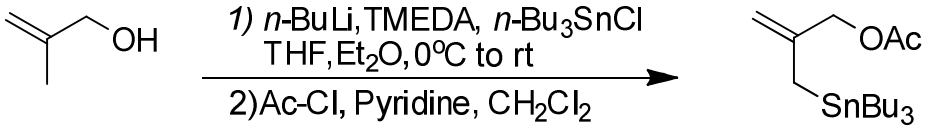
1-Methoxy-4-((pent-4-ynyloxy)methyl)benzene S2



S1 **S2**

1-Methoxy-4-((pent-4-ynyloxy)methyl)benzene **S2** was prepared from 4-pentyn-1-ol **S1** according to the method described by Chandrasekhar *et al*.[1]

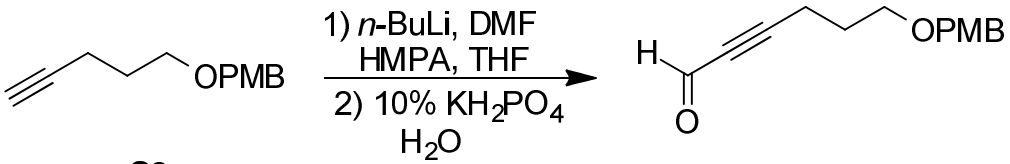
2-((Tributylstannyl)methyl)allyl acetate S4



S3 **S4**

2-((Tributylstannyl)methyl)allyl acetate **S4** was prepared from methallyl alcohol **S3** according to the procedure described by Trost and Bonk.[2]

6-((4-Methoxybenzyl)oxy)hex-2-ynal 9



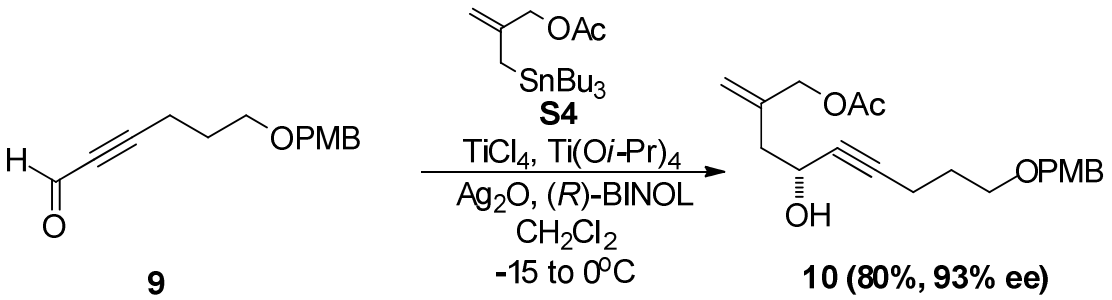
S2 **9 (81%)**

To a solution of alkyne **S3** (10 g, 49 mmol) and hexamethylphosphoramide HMPA (21.5 mL, 122.5 mmol) in THF (100 mL) at -45 °C was added *n*-BuLi (1.43 M in hexane, 51.5 mL, 73.5 mmol). After stirring for 30 min at the same temperature, DMF (15 mL, 196 mmol) was added at once and the reaction mixture was warmed up to room temperature over 1 h. The reaction was quenched with 10% aq KH_2PO_4 (270 mL) and the mixture was partitioned between EtOAc and brine. The layers were separated and the aqueous layer was extracted three times with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography using

(1) Chandrasekhar, S; Rao, C. L.; Seenaiah, M.; Naresh, P.; Jagadeesh, B.; Manjeera, D.; Sarkar, A.; Bhadra, M. P. *J. Org. Chem*. **2009**, *74*, 401.
(2) Trost, B. M.; Bonk, P. J. *J. Am. Chem. Soc*. **1985**, *107*, 1778.

(hexanes/EtOAc, 6:1) as an eluent to afford aldehyde **9** as pale yellow oil (9.2 g, 81% yield): ^{1}H NMR (600 MHz, $CDCl_3$); δ 9.11 (s, 1H), 7.24 (dd, *J* = 8.2, 4.1, 2H), 6.86 (dd, *J* = 8.6, 4.3, 2H), 4.42 (s, 2H), 3.76 (s, 3H), 3.51 (t, *J* = 6.0, 2H), 2.51 (td, *J* = 7.0, 3.5, 2H), 1.85-1.84 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 176.9, 159.0, 130.0, 129.0, 113.5, 98.3, 81.5, 72.4, 67.5, 54.9, 27.5, 15.8; IR (thin film, cm^{-1}) 2200, 1664, 1243, 1030; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{14}H_{17}O_3$ 233.1177, found 233.1190.

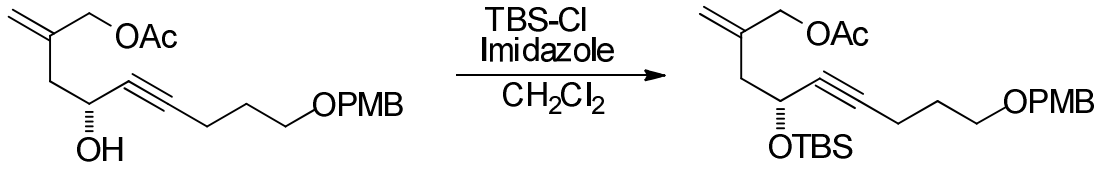
(*R*)-4-Hydroxy-9-((4-methoxybenzyl)oxy)-2-methylenenon-5-yn-1-yl acetate 10



To a stirred solution of $TiCl_4$ (22 μL, 0.2 mmol) in CH_2Cl_2 (3 mL) at 0 °C under argon was added Ti(O*i*-Pr)$_4$ (180 μL, 0.6 mmol). The reaction mixture was allowed to warm to room temperature and stirred for 1 h. Silver(I) oxide Ag_2O (93 mg, 0.4 mmol) was added and the reaction mixture was stirred for 5 h at the same temperature under exclusion of direct light. The reaction mixture was diluted with CH_2Cl_2 (8 mL), and (*R*)-BINOL (229 mg, 0.8 mmol) was added. After stirring for 2 h, the reaction mixture was cooled to -15 °C and a solution of aldehyde **9** (232 mg, 1 mmol) in CH_2Cl_2 (2.5 mL) and a solution of allylstannane **S4** (806 mg, 2 mmol) in CH_2Cl_2 (2.5 mL) were added sequentially via cannula. The reaction was allowed to warm to 0 °C and stirred at the same temperature for 10 h. The reaction mixture was quenched with saturated aq $NaHCO_3$ and the heterogeneous suspension was filtered through Celite.® The Celite® was washed thoroughly with Et_2O. The layers were separated and the aqueous layer was extracted three times with Et_2O. The combined organic extracts were washed with water and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography using (hexanes/EtOAc, 2:1) as an eluent to afford alcohol **10** as colorless oil (277 mg, 80% yield, 93% ee): $[\alpha]^{30}_D$ = +13.2 (*c* 1.1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$); δ 7.25 (d, *J* = 8.6, 2H), 6.87 (d, *J* = 8.6, 2H), 5.17 (d, *J* = 1.4, 1H),

5.09 (s, 1H), 4.58 (s, 2H), 4.48-4.46 (m, 1H), 4.43 (s, 2H), 3.79 (s, 3H), 3.50 (t, *J* = 6.2, 2H), 2.58 (d, *J* = 5.2, 1H), 2.44 (d, *J* = 10.8, 2H), 2.31 (td, *J* = 7.1, 1.8, 2H), 2.08 (s, 3H), 1.80-1.75 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 170.6, 159.0, 139.5, 130.3, 129.1, 115.9, 113.6, 85.0, 80.8, 72.4, 68.2, 66.7, 61.0, 55.1, 41.9, 28.5, 20.8, 15.4; IR (thin film, cm^{-1}) 3414, 1696, 1511, 1172; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{20}H_{27}O_5$ 347.1858, found 347.1857; HPLC: Daicel CHIRALPAK® OD-H column; λ = 254 nm; eluent: hexane/isopropanol = 90/10; flow rate: 1.0 mL/min; major enantiomer t_R = 18.0 min, minor enantiomer t_R = 20.2 min; ee = 93%.

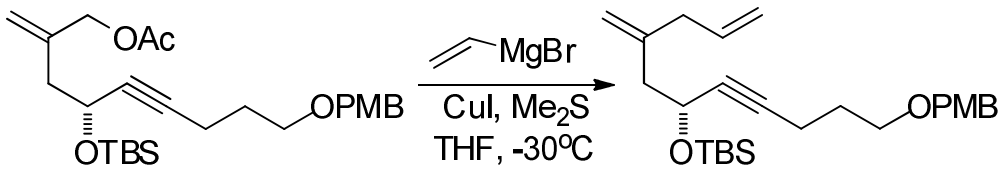
(*R*)-4-((*tert*-Butyldimethylsilyl)oxy)-9-((4-methoxybenzyl)oxy)-2-methylenenon-5-yn-1-yl acetate 11



10 **11 (99%)**

To a solution of alcohol **10** (3.1 g, 8.95 mmol) in CH_2Cl_2 (30 mL) were added imidazole (1.8 g, 26.85 mmol) and TBS-Cl (2.7 g, 17.9 mmol) at room temperature. After stirring for 4 h at the same temperature, the reaction mixture was quenched with water. The layers were separated and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was chromatographed using (hexanes/EtOAc, from 10:1) as an eluent to afford **11** as colorless oil (4.06 g, 99% yield): $[\alpha]^{30}_D$ = +22.9 (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.16 (d, *J* = 8.7, 2H), 6.78 (d, *J* = 8.7, 2H), 5.04 (d, *J* = 1.4, 1H), 4.95 (s, 1H), 4.48 (s, 2H), 4.39-4.36 (m, 1H), 4.33 (s, 2H), 3.70 (s, 3H), 3.42 (t, *J* = 6.4, 2H), 2.31 (d, *J* = 6.4, 2H), 2.20 (td, *J* = 7.3, 1.8, 2H), 1.99 (s, 3H), 1.69-1.68 (m, 2H), 0.80 (s, 9H), 0.02 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$); δ170.5, 159.1, 139.9, 130.5, 129.1, 115.5, 113.7, 84.5, 81.3, 72.6, 68.5, 67.0, 62.4, 55.1, 42.7, 28.7, 25.7, 20.9, 18.1, 15.5, -4.5, -5.1; IR (thin film, cm^{-1}) 1733, 1514, 1249, 1078; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{26}H_{41}O_5Si$ 461.2723, found 461.2730.

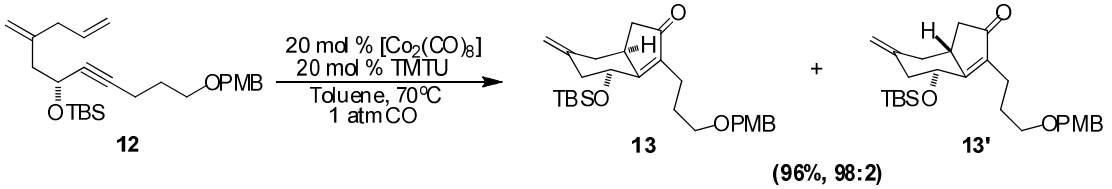
(*R*)-*tert*-Butyl((11-((4-methoxybenzyl)oxy)-4-methyleneundec-1-en-7-yn-6-yl)oxy)dimethylsilane 12



11 **12 (85%)**

To a stirred solution of **11** (2.3 g, 5 mmol) in THF (18 mL) and dimethylsulfide Me_2S (1.8 mL) at room temperature under argon, was added CuI (190 mg, 1.0 mmol). The reaction mixture was cooled to -30 °C, and vinylmagnesium bromide (10 mL, 10 mmol, 1.0 M in THF) was added slowly over 20 min. After stirring for 30 min at the same temperature, the reaction was quenched with saturated aq $NaHCO_3$ and diluted with Et_2O. The layers were separated and the aqueous layer was extracted three times with Et_2O. The combined organic extracts were washed with water and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography using (hexanes/EtOAc, 20:1) as an eluent to afford dienyne **12** as colorless oil (1.82 g, 85%). $[\alpha]^{30}_D$ = +22.8 (*c* 0.9, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$); δ 7.14 (d, *J* = 8.6, 2H), 6.76 (d, *J* = 8.6, 2H), 5.72-5.67 (m, 1H), 4.96-4.95 (m, 2H), 4.77-4.76 (m, 2H), 4.36-4.35 (m, 1H), 4.32 (s, 2H), 3.66 (s, 3H), 3.41 (t, *J* = 6.4, 2H), 2.71 (d, *J* = 6.9, 2H), 2.27-2.26 (m, 2H), 2.20 (td, *J* = 7.0, 1.7, 2H), 1.69-1.65 (m, 2H), 0.81 (s, 9H), 0.03 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 159.0, 143.7, 136.0, 130.4, 129.0, 116.1, 113.5, 113.3, 84.0, 81.8, 72.5, 68.4, 62.3, 54.9, 45.1, 40.9, 28.7, 25.7, 18.1, 15.4, -4.6, -5.1; IR (thin film, cm^{-1}) 2952, 1513, 1248, 1079; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{26}H_{41}O_3Si$ 429.2825, found 429.2827.

(4*R*,7a*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(3-((4-methoxybenzyl)-oxy)propyl)-6-methylene-5,6,7,7a-tetrahydro-1*H*-inden-2(4*H*)-one 13 and (4*R*,7a*R*)-4-((*tert*-butyldimethylsilyl)oxy)-3-(3-((4-methoxybenz-yl)oxy)propyl)-6-methylene-5,6,7,7a-tetrahydro-1*H*-inden-2(4*H*)-one 13'

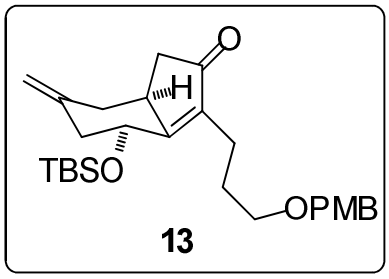


12 **13** **13'** **(96%, 98:2)**

To a stirred solution of dienyne **12** (4.8 g, 11.2 mmol) in toluene (70 mL) were added

$Co_2(CO)_8$ (766 mg, 20 mol %) and tetramethulthiourea TMTU (296 mg, 20 mol %) at room temperature. The reaction was stirred for 4 h at 70 °C under 1 atm CO. The black suspension was concentrated under reduced pressure. The residue was chromatographed with (hexanes/EtOAc, 9:1) eluting first **13** as colorless oil (4.8 g, 94%) followed by **13'** as colorless oil (0.1 g, 2%).

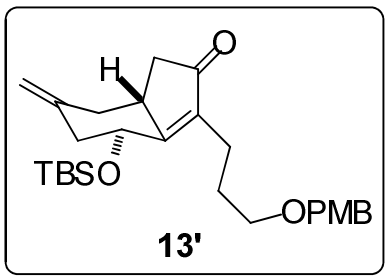
(4*R*,7a*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(3-((4-methoxybenzyl)-oxy)propyl)-6-methylene-5,6,7,7a-tetrahydro-1*H*-inden-2(4*H*)-one 13



13

$[\alpha]^{30}_D$ = -62.1 (*c* 1.0 , $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$); δ 7.18 (d, *J* = 7.6, 2H), 6.79 (d, *J* = 7.6, 2H), 4.82 (s, 2H), 4.71 (s, 1H), 4.34 (s, 2H), 3.72 (s, 3H), 3.36-3.33 (m, 2H), 2.98-2.96 (m, 1H), 2.65 (dd, *J* = 6.5, 3.4, 1H), 2.47 (dd, *J* = 19.2, 6.5, 1H), 2.41 (d, *J* = 13.7, 1H), 2.23-2.22 (m, 2H), 2.09 (d, *J* = 13.7, 1H), 1.88 (d, *J* = 19.2, 1H) 1.71-1.70 (m, 1H), 1.62-1.60 (m, 2H), 0.78 (s, 9H), 0.00 (s, 3H), -0.11 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 209.1, 173.9, 159.0, 141.8, 136.1, 130.5, 129.0, 113.6, 112.5, 72.3, 69.1, 65.0, 55.1, 43.4, 43.3, 41.1, 36.6, 28.4, 25.5, 19.5, 17.9, -4.8, -4.9; IR (thin film, cm^{-1}) 2928, 1702, 1247, 1071; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{27}H_{41}O_4Si$ 457.2774, found 457.2770.

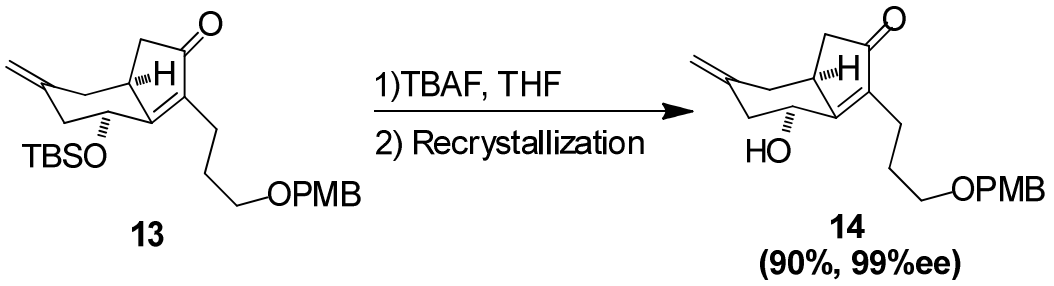
(4*R*,7a*R*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(3-((4-methoxy-benzyl)oxy)-propyl)-6-methylene-5,6,7,7a-tetrahydro-1*H*-inden-2(4*H*)-one 13'



13'

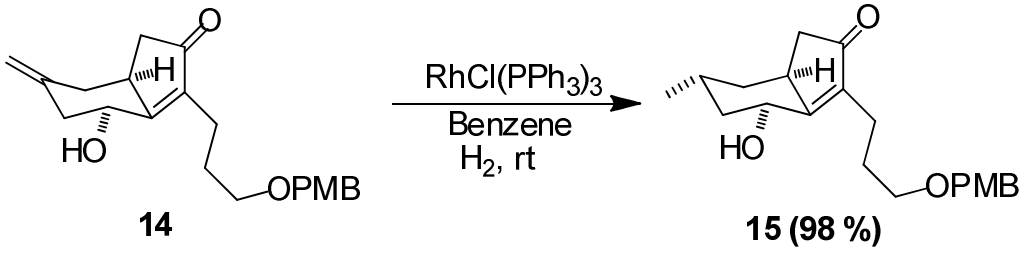
$[\alpha]^{25}_D$ = +21.0 (*c* 3.1 , $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$); δ 7.25-7.23 (m, 2H), 6.85 (d, *J* = 8.6, 2H), 4.83 (s, 2H), 4.47 (dd, *J* = 11.7, 5.5, 1H), 4.41 (d, *J* = 11.6, 1H), 4.39 (d, *J* = 11.6, 1H), 3.79 (s, 3H), 3.42 (t, *J* = 7.0, 2H), 2.64-2.60 (m, 2H), 2.54-2.52 (m, 3H), 2.48-2.45 (m, 1H), 2.24 (t, *J* = 11.9, 1H), 1.96 (d, *J* = 17.2, 1H), 1.77-1.71 (m, 2H), 1.64-1.62 (m, 1H), 0.92 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 208.4, 173.0, 159.0, 143.2, 138.0, 130.8, 129.3, 113.6, 111.6, 74.3, 72.3, 70.0, 55.2, 45.8, 42.8, 40.5, 39.1, 29.7, 25.9, 19.4, 18.2, -4.6, -5.0; IR (thin film, cm^{-1}) 2952, 1702, 1243, 1093; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{27}H_{41}O_4Si$ 457.2774, found 457.2779.

(4*R*,7a*S*)-4-Hydroxy-3-(3-((4-methoxybenzyl)oxy)propyl)-6-methylene-5,6,7,7a-tetrahydro-1*H*-inden-2(4*H*)-one 14



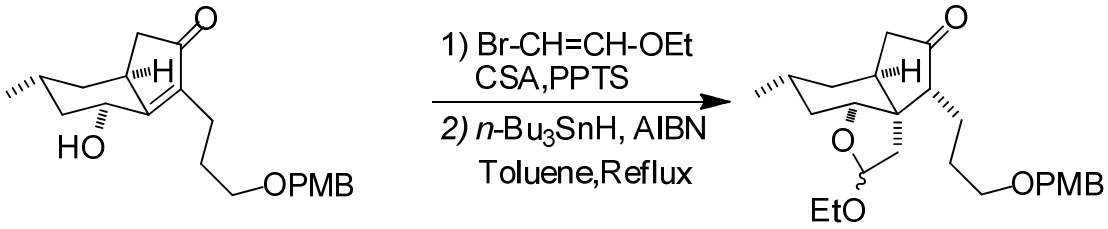
To a solution of indenone **13** (1.63 g, 3.6 mmol) in THF (36 mL) at room temperature was added tetrabutylammonium fluoride TBAF (5.4 mL, 5.4 mmol, 1.0 M in THF). After stirring for 3 h at the same temperature, the reaction was quenched with saturated aq NH_4Cl and diluted by addition of EtOAc. The layers were separated and the aqueous layer was extracted three times with EtOAc. The combined organic extracts were washed with water and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was chromatographed with (hexanes/EtOAc, 2:1) as an eluent. The crude eluted fractions were evaporated and the remaining solid residue was recrystallized from (EtOAc/hexanes) to give **14** as colorless needles (1.1 g, 90%, 99% ee): $[\alpha]^{30}_D$ = -117.7 (*c* 1.0 , $CHCl_3$); mp = 68-69 °C; ^{1}H NMR (600 MHz, $CDCl_3$); δ 7.23 (d, *J* = 8.6, 2H), 6.86 (d, *J* = 8.6, 2H), 4.98 (brs, 1H), 4.91-4.90 (m, 2H), 4.40 (d, *J* = 11.3, 1H), 4.38 (d, *J* = 11.3, 1H), 3.79 (s, 3H), 3.41 (t, *J* = 6.2, 2H), 3.04-3.00 (m, 1H), 2.79 (d, *J* = 4.8, 1H), 2.73 (dd, *J* = 12.7, 4.5, 1H), 2.60-2.53 (m, 2H), 2.32-2.30 (m, 3H), 1.97 (dd, *J* = 18.7, 1.9, 1H) 1.77-1.72 (m, 3H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 208.7, 172.8, 159.0, 141.6, 137.6, 130.1, 129.2, 113.7, 113.5, 72.0, 68.7, 64.2, 55.1, 42.5, 42.0, 41.0, 36.7, 27.7, 19.2; IR (thin film, cm^{-1}) 3411, 1697, 1512, 1247, 1036; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{21}H_{27}O_4$ 343.1909, found 343.1906; HPLC: Daicel CHIRALPAK® OD-H column; λ = 254 nm; eluent: hexane/isopropanol = 94/6; flow rate: 1.0 mL/min; major enantiomer t_R = 32.9 min; ee = 99%.

(4*R*,6*R*,7a*S*)-4-Hydroxy-3-(3-((4-methoxybenzyl)oxy)propyl)-6-methyl-5,6,7,7a-tetrahydro-1*H*-inden-2(4*H*)-one 15



To a stirred solution of **14** (5.5 g, 16 mmol) in benzene (60 mL) at room temperature was added $RhCl(PPh_3)_3$ (740 mg, 5 mol %). The reaction was stirred for 6 h at room temperature under 1 atm H_2. The brown mixture was concentrated under reduced pressure and the residue was chromatographed with (hexanes/EtOAc, 1:1) as an eluent to give **15** as colorless oil (5.4 g, 98%): $[\alpha]^{25}_D$ = -80.4 (*c* 2.2 , $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$); δ 7.22 (d, *J* = 8.6, 2H), 6.87 (d, *J* = 8.6, 2H), 4.83 (brs, 1H), 4.40 (d, *J* = 11.7, 1H), 4.36 (d, *J* = 11.7, 1H), 3.80 (s, 3H), 3.41 (t, *J* = 5.3, 2H), 3.17-3.14 (m, 1H), 3.07 (s, 1H), 2.57 (dd, *J* = 18.9, 6.5, 1H), 2.31 (dd, *J* = 6.8, 6.5, 2H), 2.01-2.00 (m, 1H), 1.95-1.90 (m, 3H), 1.78-1.71 (m, 3H), 1.28-1.27 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 209.6, 175.1, 159.2, 137.4, 129.9, 129.3, 113.7, 71.8, 68.4, 64.2, 55.2, 41.5, 40.2, 37.9, 31.0, 27.0, 26.9, 20.5, 19.1; IR (thin film, cm^{-1}) 3426, 1701, 1512, 1174; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{21}H_{29}O_4$ 345.2065, found 345.2064.

(3a*S*,4R,6a*S*,8*R*,9a*R*)-2-Ethoxy-4-(3-((4-methoxybenzyl)oxy)propyl)-8-methyloctahydroindeno[4,3a-b]furan-5(4*H*)-one 16



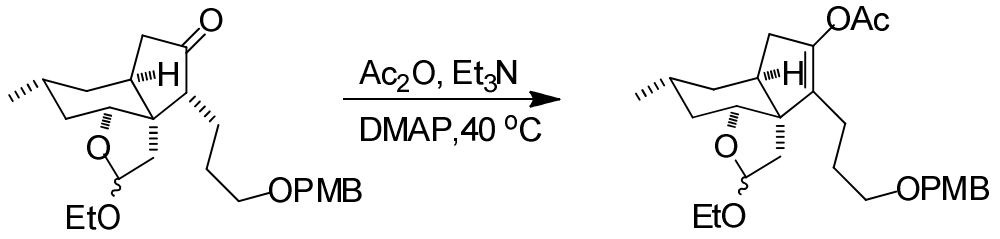
15 **16 (91 %)**

Pyridinium *p*-toluenesulfonate PPTS (263 mg, 1.05 mmol) and camphorsulfonic acid CSA (244 mg, 1.05 mmol) were added to a solution of alcohol **15** (1.8 g, 5.23 mmol) and (*Z*/*E*)-2-bromovinyl ethyl ether [3] (3.15 g, 20.9 mmol) at room temperature. After stirring for 2 h, the reaction was diluted by Et_2O and quenched with saturated aq $NaHCO_3$ at 0 °C. The layers were separated and the aqueous layer was extracted three times with Et_2O. The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was passed through a short pad of silica gel using (hexanes/EtOAc, from 10:1 to 3:1) as an eluent. The crude eluted fractions were evaporated and dissolved in toluene. Tributyltin hydride *n*-Bu_3SnH (7.0 mL, 26.15 mmol) and Azobisisobutyronitrile AIBN were added (0.43 g, 2.62 mmol) at room

(3) (*Z*/*E*)-2-Bromovinyl ethyl ether was freshly prepared as described by Stalick, W. M.; Khorrami, A.; Hatton, K. S. *J. Org. Chem.* **1986**, *51*, 3577.

temperature. The reaction was heated under reflux for 4 h. The solvent was evaporated under reduced pressure and the residue was chromatographed with (hexanes/EtOAc, from 6:1 to 2:1) to afford cyclic acetal **16** as colorless oil (1.97 g, 91%, two diastereomers, 3:1): $[\alpha]^{25}_{D}$ = +3.4 (*c* 1.9 , $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, major isomer); δ 7.25-7.24 (m, 2H), 6.87 (d, *J* = 8.6, 2H), 5.12 (dd, *J* = 5.7, 2.6, 1H), 4.41 (s, 2H), 3.95 (t, *J* = 5.3, 1H), 3.80 (s, 3H), 3.75-3.71 (m, 1H), 3.46-3.41 (m, 3H), 2.44 (dd, *J* = 19.2, 8.9, 1H), 2.36-2.35 (m, 1H), 2.26 (dd, *J* = 9.3, 4.8, 1H), 2.00-1.96 (m, 2H), 1.89-1.87 (m, 2H), 1.77-1.73 (m, 2H), 1.68-1.64 (m, 1H), 1.53-1.45 (br m, 3H), 1.39-1.34 (m, 1H), 1.28-1.25 (m, 1H), 1.17 (t, *J* = 7.0, 3H), 1.07 (d, *J* = 6.9, 3H); ^{13}C NMR (151 MHz, $CDCl_3$, major isomer); δ 219.4, 159.1, 130.6, 129.2, 113.7, 102.0, 78.7, 72.4, 69.9, 62.9, 55.2, 52.3, 50.0, 42.1, 38.0, 33.8, 33.6, 33.4, 27.8, 24.9, 23.2, 20.7, 15.3; IR (thin film, cm^{-1}) 2924, 1736, 1513, 1247, 1098; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{25}H_{37}O_5$ 417.2641, found 417.2639.

(3a*S*,6a*S*,8*R*,9a*R*)-2-Ethoxy-4-(3-((4-methoxybenzyl)oxy)propyl)-8-methyl-2,3,6,6a,7,8,9,9a-octahydroindeno[4,3a-b]furan-5-yl acetate 17



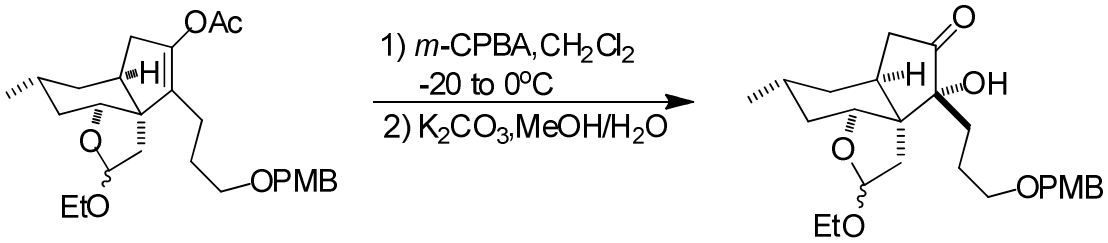
16 **17 (92%)**

Dimethylaminopyridine DMAP (410.5 mg, 3.36 mmol) and Et_3N (11.6 mL, 84 mmol) were added to a solution of **16** (3.5 g, 8.4 mmol) and acetic anhydride [4] (23.8 mL, 252 mmol) at room temperature. The reaction mixture was stirred at 40 °C for 48 h. The color changed from pale yellow to dark brown during the course of the reaction. The reaction was diluted by EtOAc at 0 °C and quenched with saturated aq $NaHCO_3$. The heterogeneous mixture was filtered through Celite® and the Celite® was washed thoroughly with EtOAc. The layers were separated and the aqueous layer was extracted three times with EtOAc. The combined organic layers were washed with saturated aq copper(II) sulfate and brine, dried over anhydrous Na_2SO_4,

(4) Acetic anhydride was distilled from K_2CO_3 prior to use.

filtered and concentrated under reduced pressure. The residue was purified by column chromatography using (hexanes/EtOAc, from 9:1 to 6:1) as an eluent to afford vinyl acetate derivative **17** as pale yellow oil (3.54 g, 92%, two diastereomers, 3:1): $[\alpha]^{24}_{D}$ = -13.1 (*c* 1.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, major isomer); δ 7.26 (d, *J* = 8.6, 2H), 6.87 (d, *J* = 8.6, 2H), 5.11 (dd, *J* = 6.0, 3.3, 1H), 4.41 (s, 2H), 4.05 (t, *J* = 4.6, 1H), 3.80 (s, 3H), 3.75-3.73 (m, 1H), 3.45-3.40 (m, 3H), 2.57 (dd, *J* = 15.1, 7.9, 1H), 2.18-2.13 (br m, 5H), 2.08 (s, 3H), 1.92 (dd, *J* = 13.9, 3.3, 1H), 1.77-1.68 (m, 4H), 1.60-1.56 (m, 1H), 1.48-1.46 (m, 1H), 1.39-1.34 (m, 1H), 1.17 (t, *J* = 7.0, 3H), 1.03 (d, *J* = 6.9, 3H); ^{13}C NMR (151 MHz, $CDCl_3$, major isomer); δ 168.7, 159.0, 146.1, 130.7, 129.1, 128.4, 113.7, 102.2, 78.0, 72.3, 69.8, 63.1, 55.2, 54.1, 44.0, 39.0, 35.3, 33.7, 32.7, 28.5, 23.9, 21.7, 20.8, 20.5, 15.3; IR (thin film, cm^{-1}) 3292, 1754, 1512, 1246, 1100; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{27}H_{39}O_6$ 459.2747, found 459.2749.

(3a*R*,4*R*,6a*S*,8*R*,9a*R*)-2-Ethoxy-4-hydroxy-4-(3-((4-methoxybenzyl)-oxy)propyl)-8-methyloctahydroindeno[4,3a-b]furan-5(4*H*)-one 18



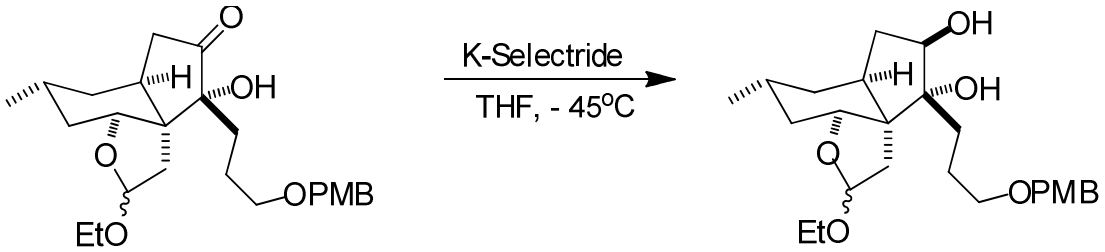
17 **18 (96%)**

To a solution of **17** (2.0 g, 4.36 mmol) in CH_2Cl_2 (40 mL) at -20 °C was added a solution of *m*-CPBA[5] (2.26 g, 13.0 mmol) in CH_2Cl_2 (25 mL). The reaction mixture was gradually warmed to 0 °C and stirred for 2 h at the same temperature. The reaction was quenched with saturated aq $NaHCO_3$ and $Na_2S_2O_3$. The layers were separated and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was dissolved in MeOH/H_2O (15 mL: 1.5 mL). Potassium carbonate K_2CO_3 (241 mg, 1.74 mmol) was added and the reaction mixture was stirred for 4 h at room temperature. The reaction mixture was partitioned between EtOAc and brine. The

(5) *m*-CPBA was purified and recrystallized from CH_2Cl_2 as described by Traylor, T. G.; Miksztal, A. R. *J. Am. Chem. Soc.* **1987**, *109*, 2770.

layers were separated and the aqueous layer was extracted three times with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography using (hexanes/EtOAc, 4:1) as an eluent to give α-hydroxy ketone **18** as colorless oil (1.8 g, 96% yield, two diastereomers, 3:1): $[\alpha]^{24}_D$ = +42.5 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, major isomer); δ 7.23 (d, *J* = 8.7, 2H), 6.87 (d, *J* = 8.7, 2H), 5.05 (dd, *J* = 6.4, 4.6, 1H), 4.94 (s, 1H), 4.49 (d, *J* = 11.4, 1H), 4.42 (d, *J* = 11.4, 1H), 3.80 (s, 3H), 3.77-3.74 (m, 1H), 3.55-3.53 (m, 2H), 3.45-3.42 (m, 2H), 2.83-2.80 (m, 1H), 2.71 (dd, *J* = 14.7, 6.4, 1H), 2.63 (dd, *J* = 19.5, 10.3, 1H), 2.15-2.10 (m, 1H), 2.04-1.92 (m, 1H), 1.87-1.84 (m, 4H), 1.51-1.44 (m, 4H), 1.35-1.31 (m, 1H), 1.21 (t, *J* = 7.1, 3H), 0.92 (d, *J* = 5.5, 3H); ^{13}C NMR (151 MHz, $CDCl_3$, major isomer); δ 215.8, 159.3, 129.6, 129.5, 113.8, 104.5, 80.4, 77.4, 72.7, 70.8, 63.5, 56.0, 55.2, 39.5, 39.2, 34.8, 33.6, 32.9, 28.3, 24.0, 22.9, 21.9, 15.4; IR (thin film, cm^{-1}) 3357, 1741, 1246, 1090; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{25}H_{37}O_6$ 433.25901, found 433.25905.

(3a*R*,4*R*,5*R*,6a*S*,8*R*,9a*R*)-2-Ethoxy-4-(3-((4-methoxybenzyl)oxy)-propyl)-8-methyldecahydroindeno[4,3a-b]furan-4,5-diol 19

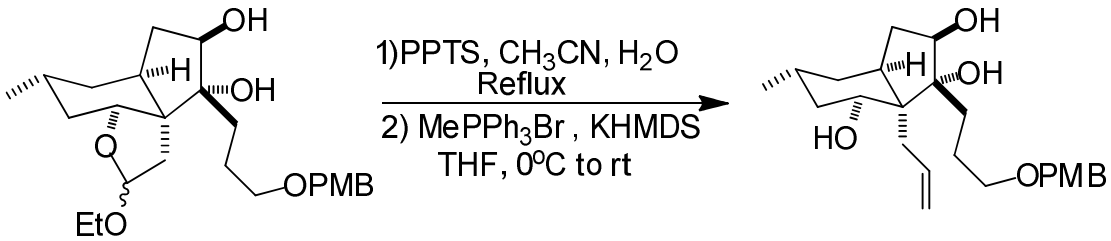


18 **19 (86%)**

K-Selectride (5.5 mL, 5.5 mmol, 1.0M solution in THF) was added dropwise to a solution of **18** (1.8 g, 4.16 mmol) in THF (40 mL) at -45 °C under argon. After stirring for 6h at the same temperature, the reaction was quenched with 3 M aq NaOH and 30% aq H_2O_2. The mixture was diluted with EtOAc and the layers were separated. The aqueous layer was extracted three times with EtOAc. The combined organic extracts were washed with saturated aq $Na_2S_2O_3$ and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography using (hexanes/EtOAc, from 2:1 to 1:1) as an eluent to give *trans*-diol **19** as colorless oil (1.54 g, 86% yield, two diastereomers, 3:1): $[\alpha]^{24}_D$ = -9.3 (*c* 0.8, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$); δ

7.24-7.23 (m, 2H), 6.88-6.87 (m, 2H), 5.12-5.04 (m, 1H), 4.49-4.45 (m, 3H) 4.00-3.98 (m, 1H), 3.80 (d, *J* = 10.0, 3H), 3.77-3.73 (m, 1H), 3.49-3.43 (m, 3H), 2.63-2.62 (m, 1H), 2.54-2.48 (m, 2H), 2.41-2.38 (m, 1H), 2.15-2.08 (m, 2H), 1.83-1.76 (m, 4H), 1.61-1.59 (m, 1H), 1.46-1.44 (m, 1H), 1.34-1.29 (m, 4H), 1.21-1.18 (m, 3H), 0.91-0.89 (m, 3H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 159.2, 129.6, 129.5, 129.4, 113.8, 103.9, 102.4, 86.0, 85.6, 77.9, 77.4, 77.2, 72.9, 72.8, 70.6, 70.3, 63.4, 63.3, 57.3, 55.2, 54.8, 40.0, 39.6, 38.4, 37.8, 37.4, 36.8, 36.2, 34.1, 34.0, 28.8, 27.5, 24.3, 23.9, 23.8, 22.1, 22.0, 15.4; IR (thin film, cm^{-1}) 3430, 1512, 1301, 1091; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{25}H_{39}O_6$ 435.2746, found 435.2742.

(1*R*,2*R*,3a*S*,5*R*,7*R*,7a*R*)-7a-Allyl-1-(3-((4-methoxybenzyl)oxy)-propyl)-5-methyloctahydro-1*H*-indene-1,2,7-triol 20

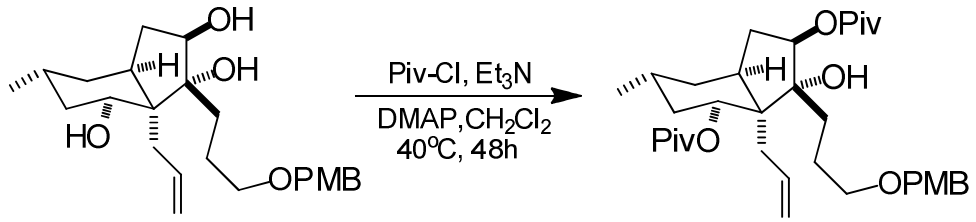


19 **20 (55%)**

PPTS (123 mg, 0.49 mmol) was added to a solution of **19** (1.06 g, 2.44 mmol) in CH_3CN/H_2O (10 mL: 2 mL) at room temperature. The reaction mixture was heated under reflux for 4 h. The reaction was quenched with saturated aq $NaHCO_3$ and the mixture was partitioned between EtOAc and brine. The layers were separated and the aqueous layer was extracted three times with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was passed through a short pad of silica gel using (hexanes/EtOAc, 1:2) as an eluent. The crude eluted fractions were evaporated, dissolved in THF (10 mL) and cooled at 0°C. In a previously prepared second flask, methyltriphenylphosphonium bromide PPh_3MeBr (6.1 g, 17.08 mmol) was dried at 80 °C under vacuum for 3 hours. After the salt has cooled THF (24 mL) was added and the slurry was cooled to 0 °C under argon. Potassium bis(trimehtylsilyl)amide KHMDS (16.8 mL, 16.8 mmol, 1.0 M in THF) was added dropwise at the same temperature resulting in a bright yellow color. After stirring for 30 min at the same temperature, the bright yellow ylide slurry was cannulated to the first reaction flask at 0°C under argon. The reaction mixture was stirred at the same temperature for 2h then warmed gradually to room temperature and stirred overnight. The reaction was

quenched with saturated aq NH_4Cl and the mixture was diluted with EtOAc. The layers were separated and the aqueous layer was extracted three times with EtOAc. The combined organic extracts were washed with water and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography with (hexanes/EtOAc, 2:1) as eluent to afford triol **20** as colorless oil (0.54 g, 55% yield): $[\alpha]^{24}_D$ = -13.4 (*c* 0.8, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$); δ 7.26-7.24 (m, 2H), 6.87 (d, *J* = 9.3, 2H), 6.22-6.15 (m, 1H), 5.14 (dd, *J* = 17.2, 1.7, 1H), 5.03 (dd, *J* = 10.0, 1.7, 1H), 4.49 (d, *J* = 11.7, 1H), 4.46 (d, *J* = 11.7, 1H), 4.31-4.27 (m, 1H), 3.94-3.93 (m, 1H), 3.80 (s, 3H), 3.57-3.54 (m, 1H), 3.46 (td, *J* = 8.5, 3.9, 1H), 3.33 (d, *J* = 2.7, 1H) 2.53-2.49 (m, 2H), 2.35-2.31 (m, 1H), 2.29-2.25 (m, 1H), 2.17 (s, 1H), 2.15-2.10 (m, 1H), 1.93-1.88 (m, 1H), 1.84-1.80 (m, 2H), 1.75-1.74 (m, 1H), 1.67-1.64 (m, 1H), 1.49-1.44 (m, 2H), 1.19-1.16 (m, 2H), 1.12-1.09 (m, 1H), 0.92 (d, *J* = 6.5, 3H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 159.3, 139.1, 129.8, 129.5, 116.5, 113.8, 89.3, 77.8, 72.8, 70.1, 69.2, 55.2, 53.0, 41.3, 39.7, 36.0, 32.5, 32.1, 29.4, 25.6, 24.0, 22.1; IR (thin film, cm^{-1}) 3424, 1513, 1247, 1035; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{24}H_{37}O_5$ 405.2641, found 405.2640.

(2*R*,3*R*,3a*R*,4*R*,6*R*,7a*S*)-3a-Allyl-3-hydroxy-3-(3-((4-methoxybenzyl)-oxy)propyl)-6-methyloctahydro-1*H*-indene-2,4-diyl bis(2,2-dimethyl-propanoate) 21

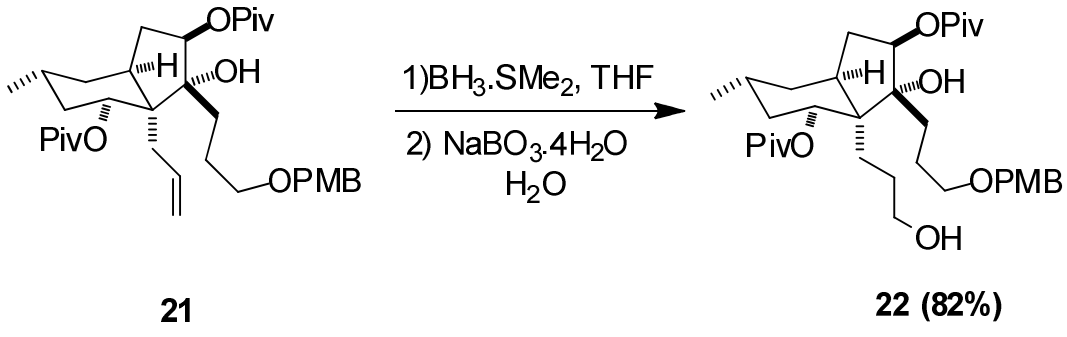


20 **21 (71%)**

DMAP (35.5 mg, 0.29 mmol) and Et_3N (8 mL, 58 mmol) were added to a solution of triol **20** (235 mg, 0.58 mmol) in CH_2Cl_2 (4 mL) at room temperature. The reaction was cooled to 0 °C and pivaloyl chloride (7.1 mL, 58 mmol) was added dropwise. After the addition, the reaction was stirred at 0 °C for 1 h and then warmed to 40 °C and stirred for 48 h. The reaction mixture was diluted with CH_2Cl_2 at 0 °C and quenched with saturated aq $NaHCO_3$. The layers were separated and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were

washed with saturated aq copper(II) sulfate and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography using (hexanes/EtOAc, from 18:1 to 6:1) as an eluent to afford **21** as colorless oil (234.5 mg, 71% yield)): $[\alpha]^{25}_D$ = -17.8 (*c* 3.3, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$); δ 7.22 (d, *J* = 8.6, 2H), 6.86 (d, *J* = 8.6, 2H), 6.19-6.15 (m, 1H), 5.22 (dd, *J* = 11.5, 4.6, 1H), 5.12 (dd, *J* = 17.0, 1.5, 1H), 5.03 (dd, *J* = 10.1, 1.5, 1H), 4.80 (dd, *J* = 8.2, 3.1, 1H), 4.42 (d, *J* = 11.3, 1H), 4.39 (d, *J* = 11.3, 1H), 3.80 (s, 3H), 3.48-3.44 (m, 1H), 3.39 (br s, 1H), 3.34-3.30 (m, 1H), 2.65-2.63 (m, 1H), 2.55 (dd, *J* = 15.1, 7.2, 1H), 2.50-2.45 (m, 2H), 1.77-1.75 (m, 1H), 1.70-1.66 (m, 3H), 1.62-1.61 (m, 1H), 1.46-1.43 (m, 2H), 1.35-1.31 (m, 2H), 1.21 (s, 9H), 1.17 (s, 9H), 1.11-1.06 (m, 1H), 0.90 (d, *J* = 6.5, 3H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 177.4, 177.2, 159.2, 138.3, 130.0, 129.3, 116.4, 113.7, 88.1, 79.0, 72.7, 72.4, 70.5, 55.2, 51.8, 40.1, 38.8, 36.5, 35.5, 33.2, 32.6, 30.3, 27.1, 27.0, 26.8, 25.2, 24.0, 21.9; IR (thin film, cm^{-1}) 3443, 2924, 1721, 1158; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{34}H_{53}O_7$ 573.3791, found 573.3794.

(2*R*,3*R*,3a*R*,4*R*,6*R*,7a*S*)-3-Hydroxy-3a-(3-hydroxypropyl)-3-(3-((4-methoxybenzyl)oxy)propyl)-6-methyloctahydro-1*H*-indene-2,4-diyl bis(2,2-dimethylpropanoate) 22

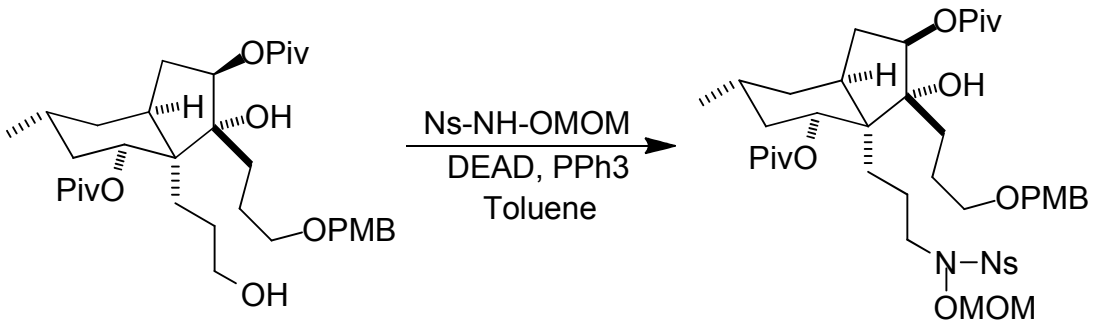


21 **22 (82%)**

Borane dimethyl sulfide complex $BH_3.SMe_2$ (0.5 mL, 4.95 mmol) was added to a solution of allyl derivative **21** (566 mg, 0.99 mmol) in THF (10 mL) at 0 °C under argon. After stirring for 2 h at the same temperature, water H_2O (2 mL) and $NaBO_3.4H_2O$ (762 mg, 4.95 mmol) were added. The reaction was warmed to room temperature and stirred for 4 h. The reaction mixture was partitioned between EtOAc and brine and the layers were separated. The aqueous layer was extracted three times with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was chromatographed

using (hexanes/EtOAc, from 2:1 to 1:1) as an eluent to afford primary alcohol **22** as colorless oil (480 mg, 82% yield): $[\alpha]^{25}_{D}$ = -19.8 (*c* 3.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$); δ 7.23 (d, *J* = 8.2, 2H), 6.87 (d, *J* = 8.2, 2H), 5.21 (dd, *J* = 11.5, 4.6, 1H), 4.81 (dd, *J* = 8.9, 3.4, 1H), 4.43 (d, *J* = 11.5, 1H), 4.39 (d, *J* = 11.5, 1H), 3.81 (s, 3H), 3.64-3.63 (m, 2H), 3.50-3.47 (m, 2H), 3.33-3.31 (m, 1H), 2.65-2.62 (m, 1H), 2.51-2.45 (m, 1H), 1.95-1.93 (m, 1H), 1.77-1.69 (m, 4H), 1.66-1.61 (m, 5H), 1.50-1.48 (m, 2H), 1.32-1.26 (m, 3H), 1.21 (s, 9H), 1.16 (s, 9H), 0.89 (d, *J* = 6.5, 3H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 177.4, 177.3, 159.3, 129.8, 129.4, 113.8, 87.9, 79.5, 72.8, 72.7, 70.5, 64.3, 55.3, 50.9, 40.4, 38.8, 38.5, 36.6, 35.6, 33.5, 30.2, 29.2, 27.1, 26.8, 25.2, 24.6, 24.1, 21.9; IR (thin film, cm^{-1}) 3426, 1721, 1284, 1156; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{34}H_{55}O_8$ 591.3897, found 591.3890.

(2*R*,3*R*,3a*R*,4*R*,6*R*,7aS)-3-Hydroxy-3-(3-((4-methoxybenzyl)-oxy)propyl)-3a-(3-(N-(methoxymethoxy)-2-nitrophenylsulfonamido)-propyl)-6-methyloctahydro-1*H*-indene-2,4-diyl bis(2,2-dimethyl-propanoate) 23



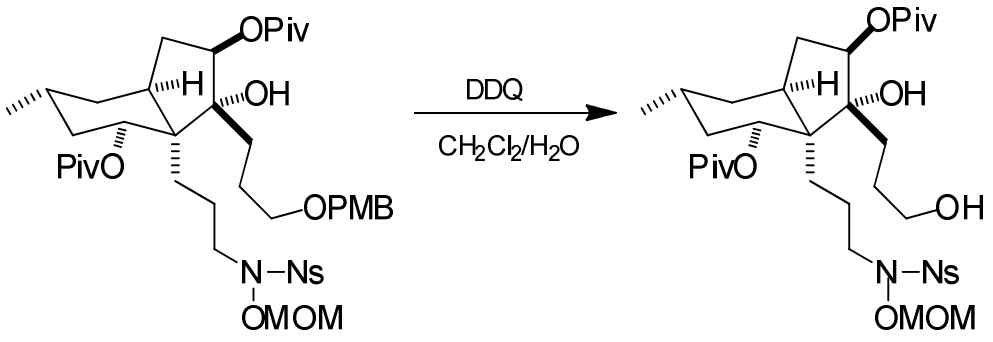
22 **23 (88%)**

N-(Methoxymethoxy)-2-nitrobenzenesulfonamide[6] **S5** Ns-NH-OMOM (47 mg, 0.18 mmol) and triphenylphosphine (168 mg, 0.64 mmol) were added to a solution of primary alcohol **22** (94 mg, 0.16 mmol) in toluene (3 mL) at -20 °C. Diethyl azodicarboxylate DEAD (348 μL, 0.8 mmol, 40% in toluene) was added dropwise to the reaction mixture at the same temperature. The yellow suspension was warmed gradually to room temperature and stirred for 1 h. The orange suspension was concentrated under reduced pressure and the residue was chromatographed with (hexanes/Et_2O, from 1:1 to 1:2) to afford **23** as pale yellow oil (114 mg, 88%): $[\alpha]^{25}_{D}$

(6) N-(Methoxymethoxy)-2-nitrobenzenesulfonamide **S5** was prepared as described by Canham, S. M.; France, D. J.; Overman, L. E. *J. Am. Chem. Soc.* **2010**, *132*, 7876.

= -39.2 (*c* 1.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$); δ 8.04 (dd, *J* = 7.9, 1.0, 1H), 7.79-7.72 (m, 2H), 7.59 (dd, *J* = 7.7, 1.2, 1H), 7.20 (d, *J* = 8.6, 2H), 6.86 (d, *J* = 8.6, 2H), 5.19 (dd, *J* = 11.5, 4.6, 1H), 5.02 (d, *J* = 8.3, 1H), 4.99 (d, *J* = 8.3, 1H), 4.79 (dd, *J* = 8.6, 3.1, 1H), 4.40 (d, *J* = 11.0, 1H), 4.38 (d, *J* = 11.0, 1H), 3.80 (s, 3H), 3.49-3.44 (m, 1H), 3.43 (s, 3H), 3.33-3.32 (m, 1H), 3.24-3.23 (m, 2H), 2.62-2.58 (m, 1H), 2.49-2.45 (m, 1H), 2.07-2.04 (m, 1H), 1.78-1.75 (m, 3H), 1.63-1.62 (m, 3H), 1.49-1.43 (m, 2H), 1.29-1.26 (m, 4H), 1.21 (s, 9H), 1.15 (s, 9H), 1.10-1.06 (m, 2H), 0.89 (d, *J* = 6.5, 3H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 177.4, 177.3, 159.2, 149.8, 134.8, 132.3, 130.9, 130.0, 129.2, 126.6, 123.8, 113.7, 102.7, 87.9, 79.3, 72.7, 72.6, 70.5, 57.6, 55.3, 54.5, 51.0, 39.8, 38.8, 36.5, 35.5, 33.3, 30.2, 29.7, 27.1, 26.8, 25.5, 25.2, 24.2, 23.2, 21.8; IR (thin film, cm^{-1}) 3372, 2923, 1722, 1178; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{42}H_{63}N_2O_{13}S$ 835.4051, found 835.4050.

(2*R*,3*R*,3a*R*,4*R*,6*R*,7a*S*)-3-Hydroxy-3-(3-hydroxypropyl)-3a-(3-(N-(methoxymethoxy)-2-nitrophenylsulfonamido)propyl)-6-methyloctahydro-1*H*-indene-2,4-diyl bis(2,2-dimethylpropanoate) 24

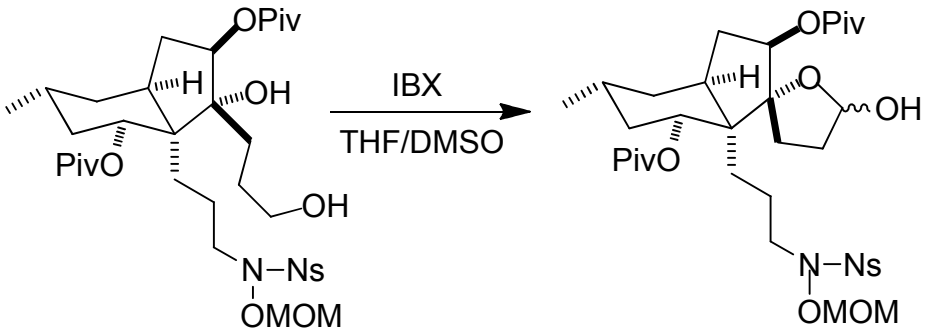


23 **24 (85 %)**

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone DDQ (102 mg, 0.45 mmol) was added to a solution of **23** (250 mg, 0.3 mmol) in CH_2Cl_2/H_2O (4 mL: 1 mL) at room temperature. After stirring for 4 h at the same temperature, the reaction was quenched with saturated aq $NaHCO_3$. The layers were separated and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with H_2O and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography using (hexane/EtOAc, from 1:1 to 1:2) as an eluent to afford diol **24** as pale yellow oil (182 mg, 85% yield): $[\alpha]^{25}_D$ = -12.2 (*c* 0.22, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$); δ 8.05 (dd, *J* = 7.9, 2.1,

1H), 7.82-7.79 (m, 1H), 7.77-7.76 (m, 1H), 7.60 (d, *J* = 7.9, 1H), 5.21 (dd, *J* = 11.5, 4.6, 1H), 5.06 (d, *J* = 7.9, 1H), 5.01 (d, *J* = 7.9, 1H), 4.82 (dd, *J* = 8.1, 2.9, 1H), 3.70-3.68 (m, 1H), 3.55-3.53 (m, 1H), 3.47 (s, 3H), 3.28-3.21 (m, 3H), 2.62-2.59 (m, 1H), 2.50-2.44 (m, 1H), 2.07-2.05 (m, 1H), 1.84-1.75 (m, 5H), 1.64-1.63 (m, 2H), 1.50-1.44 (m, 2H), 1.34-1.25 (m, 3H), 1.22 (s, 9H), 1.18 (s, 9H), 1.11-1.09 (m, 2H), 0.90 (d, *J* = 6.5, 3H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 177.5, 177.3, 149.8, 134.9, 132.3, 131.0, 126.6, 123.8, 102.7, 87.9, 79.2, 72.6, 63.3, 57.7, 54.5, 51.0, 39.9, 38.9, 38.6, 36.5, 35.5, 33.3, 29.8, 27.1, 26.8, 25.4, 25.2, 23.1, 21.8, 14.2; IR (thin film, cm^{-1}) 3476, 1721, 1711, 1156; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{34}H_{55}N_2O_{12}S$ 715.3476, found 715.3472.

(1'*R*,2'*R*,3a'*S*,5'*R*,7'*R*,7a'*R*)-5-Hydroxy-7a'-(3-(N-(methoxymethoxy)-2-nitrophenylsulfonamido)propyl)-5'-methyldecahydro-3*H*-spiro[furan-2,1'-indene]-2',7'-diyl bis(2,2-dimethylpropanoate) 25



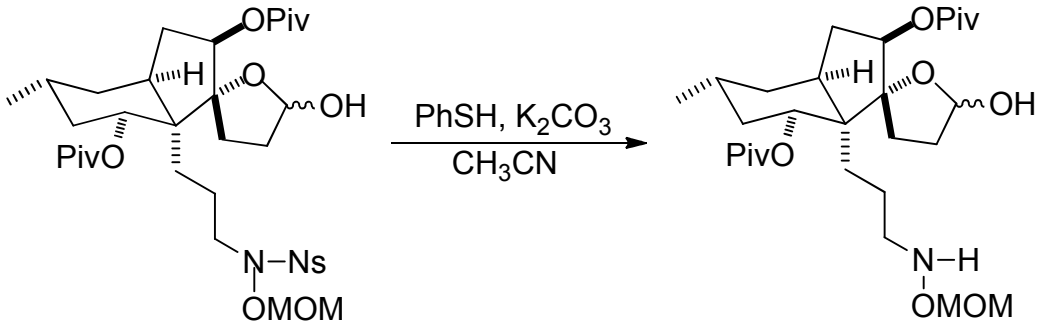
24 **25 (83 %)**

2-Iodoxybenzoic acid IBX[7] (29 mg, 0.105 mmol) was added to a solution of diol **24** (49 mg, 0.07 mmol) in THF/DMSO (1.0 mL: 1.0 mL) at room temperature. After stirring for 6 h at the same temperature, the reaction was quenched with saturated aq $NaHCO_3$ and partitioned between EtOAc and brine. The layers were separated and the aqueous layer was extracted three times with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography using (hexanes/EtOAc, 1:1) as an eluent to afford spirolactol **25** as colorless oil (41.5 mg, 83% yield, two diastereomers, 3:1): $[\alpha]^{24}_D$ = -8.8 (*c* 0.24, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$); δ 8.08-8.05 (m, 1H), 7.79-7.74 (m, 2H), 7.61-7.60 (m, 1H), 5.46-5.41

(7) IBX was freshly prepared as described by Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537.

(m, 1H), 5.13-5.10 (m, 1H), 5.02-4.97 (m, 2H), 4.80-4.78 (m, 1H), 3.47 (d, *J* = 11.0, 3H), 3.28-3.23 (m, 2H), 2.55-2.48 (m, 1H), 2.42-2.38 (m, 1H), 2.21-2.17 (m, 1H), 2.11-2.03 (m, 1H), 1.81-1.77 (m, 4H), 1.70-1.65 (m, 4H), 1.54-1.50 (m, 2H), 1.44-1.32 (m, 2H), 1.22 (d, *J* = 5.5, 9H), 1.17 (d, *J* = 1.8, 9H), 1.08-1.05 (m, 1H), 0.91-0.89 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$); δ 177.7, 177.3, 158.4, 145.4, 134.8, 132.3, 132.0, 131.1, 123.9, 123.8, 102.3, 100.0, 99.3, 97.0, 78.1, 72.3, 72.1, 57.8, 55.0, 48.8, 39.3, 38.8, 38.6, 36.1, 34.6, 33.2, 32.9, 31.8, 27.2, 27.1, 26.9, 25.0, 24.3, 23.9, 23.4, 21.9; IR (thin film, cm^{-1}) 3492, 1719, 1283, 1158; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{34}H_{53}N_2O_{12}S$ 713.3319, found 713.3313.

(1'*R*,2'*R*,3a'*S*,5'*R*,7'*R*,7a'*R*)-5-Hydroxy-7a'-(3-((methoxymethoxy)-amino)propyl)-5'-methyldecahydro-3*H*-spiro[furan-2,1'-indene]-2',7'-diyl bis(2,2-dimethylpropanoate) 26

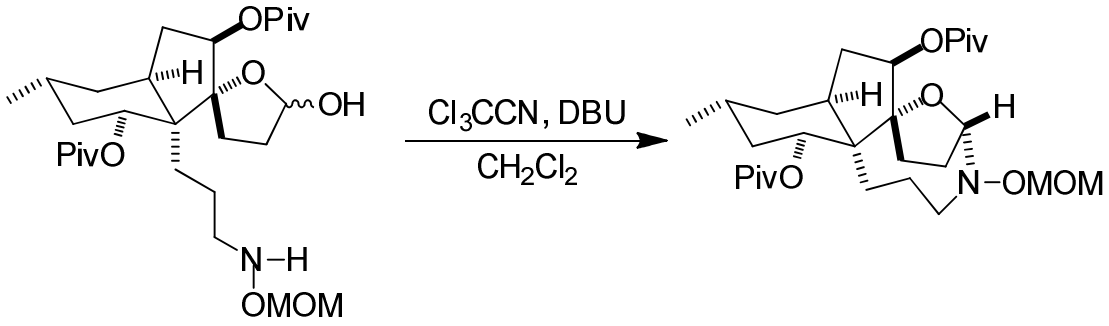


25 **26 (90 %)**

K_2CO_3 (29.0 mg, 0.21 mmol) and thiophenol PhSH (140 μL, 0.14 mmol, 1.0M in CH_3CN) were added to a solution of **25** (50 mg, 0.07 mmol) in CH_3CN (4 mL) at room temperature. After stirring for 6 h at the same temperature, the mixture was partitioned between EtOAc and brine. The layers were separated and the aqueous layer was extracted three times with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography using (hexanes/EtOAc, from 1:1 to 1:2) as an eluent to afford aminolactol **26** as colorless oil (33.2 mg, 90% yield, two diastereomers, 3:1): $[\alpha]^{24}_D$ = -6.5 (*c* 0.4, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$); δ 5.44-5.43 (m, 1H), 5.11-5.09 (m, 1H), 4.82-4.80 (m, 1H), 4.76 (d, *J* = 2.4, 2H), 3.42 (s, 3H), 3.18-3.16 (m, 1H), 2.92-2.87 (m, 1H), 2.56-2.54 (m, 1H), 2.43-2.38 (m, 1H), 2.13-2.09 (m, 1H), 2.06-2.04 (m, 1H), 1.84-1.75 (m, 5H), 1.70-1.63 (m, 2H), 1.54-1.52 (m, 2H), 1.43-1.38 (m, 1H), 1.27-1.25 (m, 1H), 1.23 (d,

J = 7.2, 9H), 1.17 (d, *J* = 9.3, 9H), 1.12-1.08 (m, 2H), 0.90-0.89 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 177.6, 177.3, 100.2, 99.2, 98.9, 97.0, 78.3, 72.4, 55.9, 53.1, 48.7, 40.0, 39.3, 38.9, 38.6, 36.4, 34.7, 33.3, 33.2, 27.2, 27.1, 26.9, 25.0, 24.5, 23.9, 23.0, 21.9; IR (thin film, cm^{-1}) 3733, 1723, 1151; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{28}H_{50}NO_8$ 528.3536, found 528.3544.

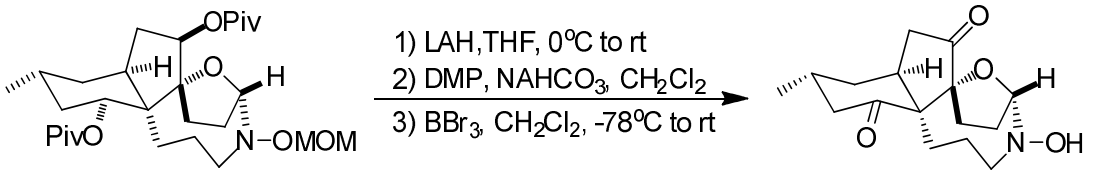
(5*S*,7a*R*,8*R*,9a*S*,11*R*,13*R*,13a*R*)-4-(Methoxymethoxy)-11-methyltetradecahydro-5,7a-epoxyindeno[1,7a-e]azonine-8,13-diyl bis(2,2-dimethylpropanoate) 27



26 **27 (63%)**

1,8-Diazabicyclo[5.4.0]undec-7-ene DBU (550 µL, 1.32 mmol, 2.4 M in CH_2Cl_2) was added dropwise to a solution of aminolactol **26** (32.0 mg, 0.06 mmol) in CH_2Cl_2 (4.0 mL) at 0 °C under argon. Trichloroacetonitrile (660 µL, 3.3 mmol, 5.0 M in CH_2Cl_2) was added dropwise to the reaction mixture at the same temperature. After stirring at 0 °C for 2 h, the reaction mixture was gradually warmed to room temperature and stirred for 36 h. The color changed from pale yellow to dark brown during the course of the reaction. The dark brown solution was concentrated under reduced pressure and the residue was purified by flash chromatography using (hexanes/acetone, 40:3) as an eluent to afford tetracyclic derivative **27** as a colorless film: (19.4 mg, 63% yield). $[\alpha]^{24}_D$ = +85.5 (*c* 0.33, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$); δ 5.19 (dd, *J* = 11.5, 4.6, 1H), 5.09 (t, *J* = 5.7, 1H), 4.90 (dd, *J* = 8.9, 3.6, 1H), 4.75 (s, 2H), 3.42 (s, 3H), 3.34-3.31 (m, 1H), 3.14-3.12 (m, 1H), 2.73-2.68 (m, 1H), 2.47-2.41 (m, 1H), 2.37-2.33 (m, 1H), 2.21-2.16 (m, 1H), 2.01-1.96 (m, 4H), 1.77-1.70 (m, 3H), 1.55-1.52 (m, 1H), 1.48-1.43 (m, 2H), 1.21 (s, 9H), 1.20 (s, 9H), 1.16-1.15 (m, 2H), 0.89 (d, *J* = 6.2, 3H); ^{13}C NMR (151 MHz, $CDCl_3$); δ 177.8, 177.0, 98.8, 96.5, 95.6, 80.5, 72.1, 56.1, 54.2, 49.5, 38.9, 38.6, 38.4, 35.2, 34.2, 31.3, 29.0, 27.1, 26.9, 26.5, 25.2, 25.0, 21.9, 19.3; IR (thin film, cm^{-1}) 2956, 1723, 1153; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{28}H_{48}NO_7$ 510.3431, found 510.3432.

(+)-Sieboldine A (1)



27 **(+)-Sieboldine A (1) (53%)**

Lithium aluminium hydride LAH (57 mg, 1.5 mmol) was added to a solution of **27** (11 mg, 0.021 mmol) in THF (3 mL) at 0 °C under argon. After stirring for 2 h at the same temperature, the reaction mixture was gradually warmed to room temperature and stirred for 18 h. The reaction was diluted with EtOAc at 0 °C and a saturated aq solution of Rochelle's salt was added. The mixture was allowed to warm to room temperature and stirred for 2h. The layers were separated and the aqueous layer was extracted three times with EtOAc. The combined organic layers were washed with H_2O and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure.

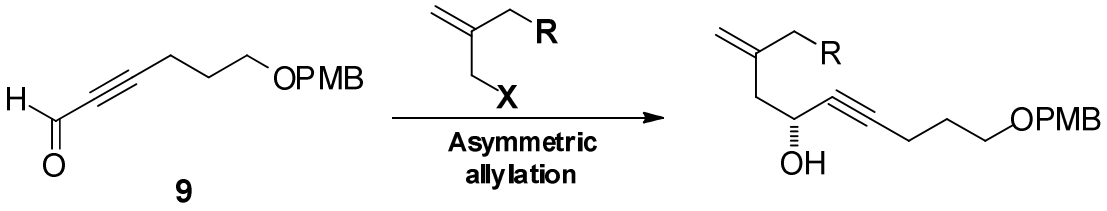
The residue was dissolved in CH_2Cl_2 (3 mL). $NaHCO_3$ (13 mg, 0.15 mmol) and Dess martin periodinane DMP (0.5 mL, 0.15 mmol, 0.3 M in CH_2Cl_2) were added to the reaction mixture at room temperature under argon. After stirring for 2 h, the reaction was quenched with saturated aq $NaHCO_3$. The layers were separated and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with H_2O and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure.

The residue was dissolved in CH_2Cl_2 (3 mL) and cooled to -78 °C under argon. Boron tribromide BBr_3 (105 µL, 0.105 mmol, 1.0 M in CH_2Cl_2) was added dropwise to the reaction mixture at the same temperature. The reaction mixture was gradually warmed to 0 °C and stirred for 2 h and was then warmed to room temperature and stirred for 18h. The reaction was quenched with saturated aq $NaHCO_3$. The layers were separated and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with H_2O and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography using (hexanes/acetone, 1:1) as an eluent to afford (+)-sieboldine A (**1**) as a colorless powder (3.3 mg, 53% yield): $[\alpha]^{25}_D$ = +140.0 (*c* 0.33, CH_3OH); ^1H NMR (600 MHz, CD_3OD); δ; 4.89-4.87 (m, 1H), 3.27-3.22 (m, 1H),

3.20-3.18 (m, 1H), 2.90 (ddd, *J* = 14.8, 7.4, 3.7, 1H), 2.57-2.55 (m, 1H), 2.51 (dd, *J* = 12.9, 12.5, 1H), 2.47-2.45 (m, 1H), 2.43 (dd, *J* = 21.3, 10.7, 1H), 2.40-2.38 (m, 1H), 2.11-2.10 (m, 1H), 2.08-2.07 (m, 1H), 2.05-2.04 (m, 1H), 2.03-2.01 (m, 1H), 1.98-1.96 (m, 1H), 1.92 (dd, *J* = 19.6, 10.7, 1H), 1.79-1.77 (m, 2H), 1.76-1.75 (m, 1H), 1.62-1.60 (m, 1H), 1.05 (d, *J* = 6.2, 3H); ^{13}C NMR (151 MHz, CD_3OD); δ 216.5, 212.7, 98.5, 92.8, 62.3, 54.5, 47.6, 38.7, 37.2, 32.5, 31.8, 31.4, 28.3, 26.1, 22.5, 19.4; IR (thin film, cm^{-1}) 3400, 1754, 1698; DART HRMS *m/z* $[M+H]^+$ calcd for $C_{16}H_{24}NO_4$ 294.1705, found 294.1701.

Optimization of asymmetric allylation of aldehyde 9 (Table S1):

Table S1. Asymmetric allylation of aldehyde **9**

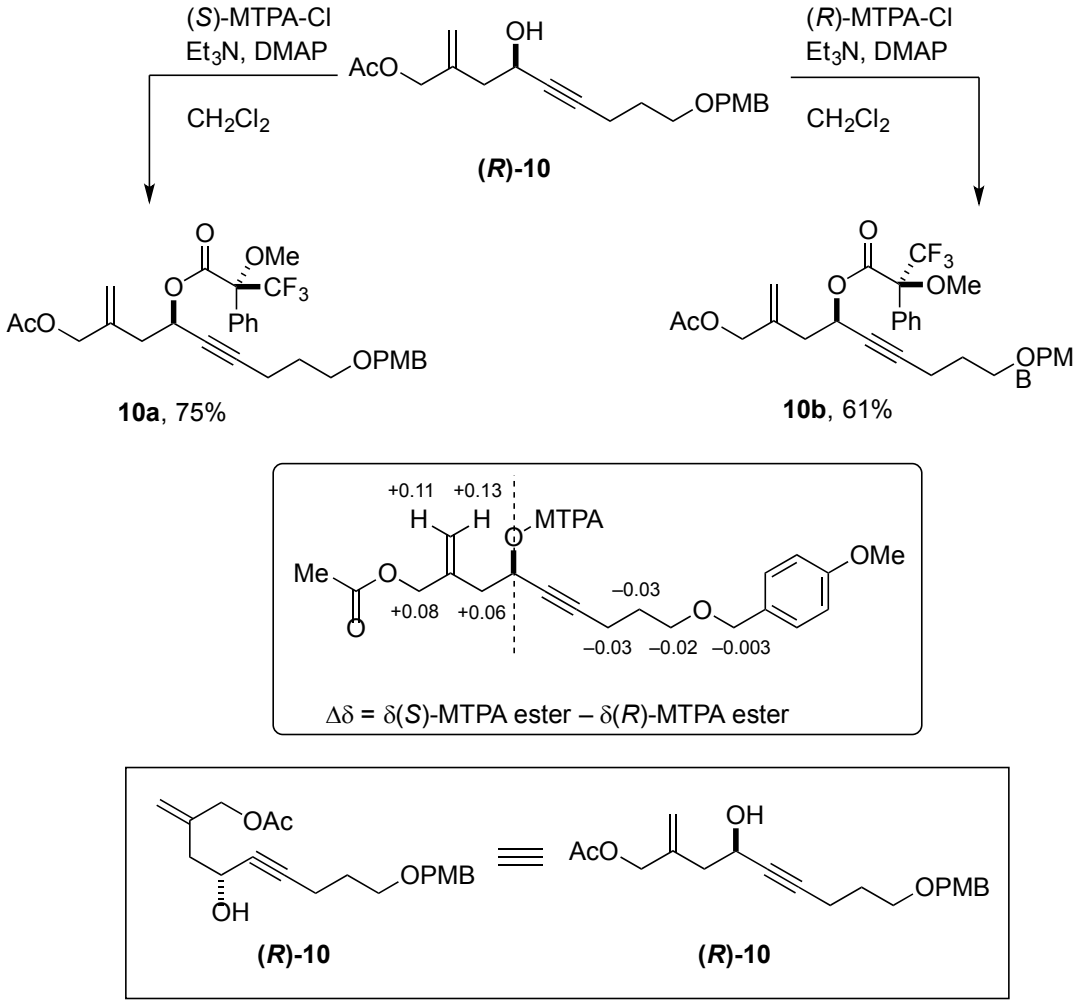


Entry	R	X	Reagent	Solvent	Temp (^{o}C)	Yield (%)	ee[a] (%)
1	-CH=CH_2	I	In^0, (+)-Ipc_2BCl	THF	-78 to rt	7	75
2	-CH=CH_2	I	In^0, (+)-Ipc_2BCl	THF	-98 to rt	35	77
3	-OTBDPS	I	In^0, (+)-Ipc_2BCl	THF	-78 to rt	15	75
4	-OTBDPS	$SnBu_3$	$TiCl_4$,Ti(O*i*-Pr)$_4$ (*R*)-BINOL	CH_2Cl_2	-15 to rt	80	89
5	-OAc	$SnBu_3$	$TiCl_4$,Ti(O*i*-Pr)$_4$ (*R*)-BINOL	CH_2Cl_2	-15 to rt	80	93

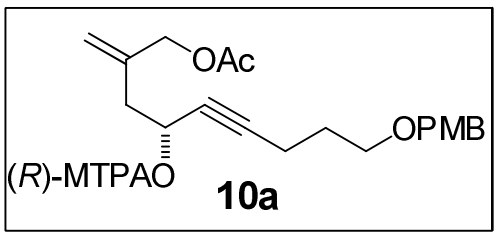
a) ee was determined by HPLC analysis (Daicel CHIRALPAK® OD-H)

Determination of the absolute configuration of (*R*)-10 (Scheme S1):

Scheme S1.



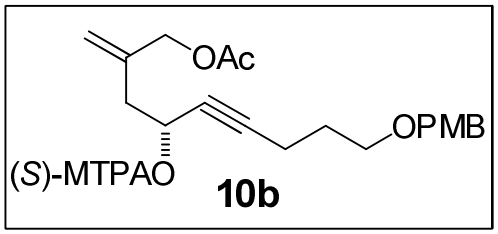
(*R*)-MTPA ester of (*R*)-10 (10a)



To a solution of **(*R*)-10** (14 mg, 0.040 mmol) in CH_2Cl_2 (0.40 mL) were added Et_3N (50 μL, 0.36 mmol), DMAP (1.0 mg, 8.0 x10^{-3} mmol) and (*S*)-MTPA-Cl (15 mg, 6.0 x10^{-2} mmol) at room temperature. After stirring for 1.5 h at the same temperature, the reaction was quenched with saturated aq NH_4Cl. The layers were separated and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column

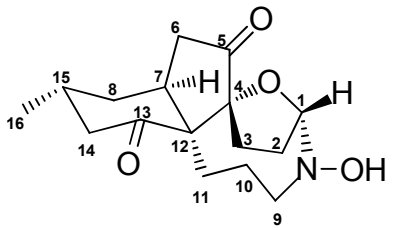
chromatography using (hexanes/EtOAc, 6:1) as an eluent to afford **10a** (17 mg, 75%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.55-7.53 (m, 2H), 7.39-7.36 (m, 3H), 7.26-7.23 (m, 2H), 6.88-6.86 (m, 2H), 5.71-5.68 (m, 1H), 5.09 (s, 1H), 4.95 (s, 1H), 4.46-4.45 (m, 2H), 4.41 (s, 2H), 3.80 (s, 3H), 3.58 (s, 3H), 3.49 (t, *J* = 6.2, 2H), 2.58-2.49 (m, 2H), 2.33 (td, *J* = 7.1, 1.8, 2H), 2.07 (s, 3H), 1.81-1.74 (m, 2H).

(*S*)-MTPA ester of (*R*)-10 (10b)



In the same manner as that described for preparation of **10a**, **(*R*)-10** (14 mg, 0.040 mmol) with (*R*)-MTPA-Cl (15 mg, 6.0 x 10^{-2} mmol) afforded **10b** (14 mg, 61 %) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.53-7.51 (m, 2H), 7.40-7.35 (m, 3H), 7.26-7.23 (m, 2H), 6.89-6.85 (m, 2H), 5.70-5.65 (m, 1H), 5.20 (s, 1H), 5.09 (s, 1H), 4.53 (s, 2H), 4.41 (s, 2H), 3.80 (s, 3H), 3.53 (s, 3H), 3.48 (t, *J* = 6.2, 2H), 2.65-2.53 (m, 2H), 2.30 (td, *J* = 7.1, 1.8, 2H), 2.07 (s, 3H), 1.78-1.72 (m, 2H).

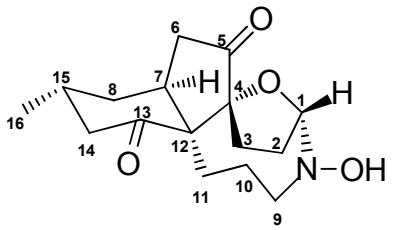
(+)-Sieboldine A ^{13}C spectra comparison:



(+)-Sieboldine A

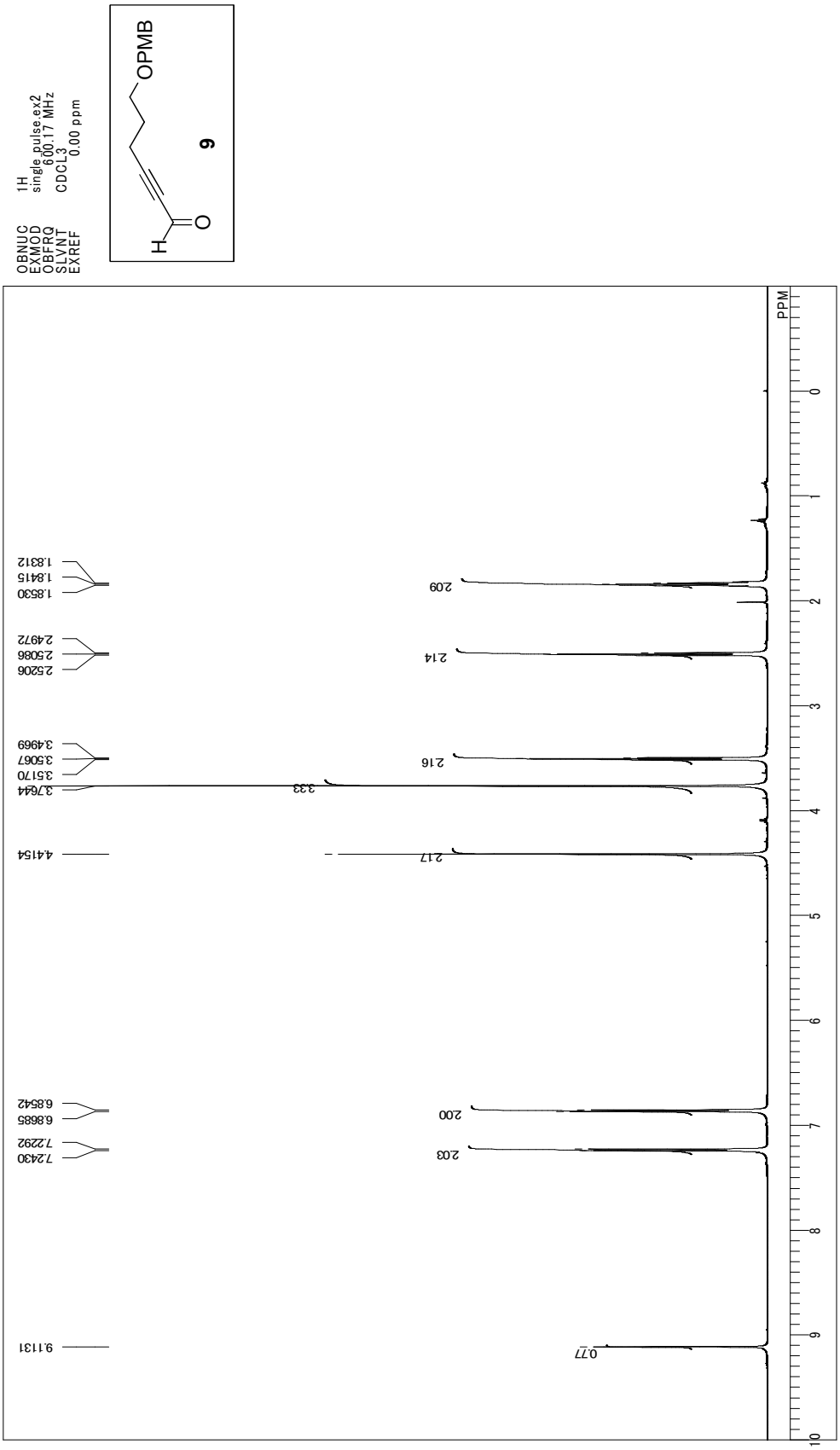
Position	^{13}C NMR (δ) Natural isolate (CD_3OD)	^{13}C NMR (δ) Synthetic sample (151 MHz, CD_3OD)
1	98.5	98.5
2	31.4	31.4
3	26.1	26.1
4	92.8	92.8
5	212.6	212.7
6	37.2	37.2
7	38.7	38.7
8	31.8	31.8
9	54.5	54.5
10	19.4	19.4
11	28.3	28.3
12	62.3	62.3
13	216.5	216.5
14	47.4	47.6
15	32.5	32.5
16	22.5	22.5

(+)-Sieboldine A ^{1}H spectra comparison:



(+)-Sieboldine A

Position	^{1}H NMR (δ) Natural isolate (CD_3OD)	^{1}H NMR (δ) Synthetic sample (600 MHz, CD_3OD)
1	4.89 (m, 1H)	4.89-4.87 (m, 1H)
2a	1.98 (m, 1H)	1.98-1.96 (m, 1H)
2b	2.12 (m, 1H)	2.11-2.10 (m, 1H)
3a	2.08 (m, 1H)	2.08-2.07 (m, 1H)
3b	2.40 (m, 1H)	2.40-2.38 (m, 1H)
6a	1.93 (dd, *J* = 19.6, 10.9, 1H)	1.92 (dd, *J* = 19.6, 10.7, 1H)
6b	2.45 (dd, *J* = 19.6, 9.2, 1H)	2.43 (dd, *J* = 21.3, 10.7, 1H)
7	3.25 (m, 1H)	3.27-3.22 (m, 1H)
8a	1.76 (m, 1H)	1.76-1.75 (m, 1H)
8b	1.77 (m, 1H)	1.79-1.77 (m, 1H)
9a	2.91 (ddd, *J* = 14.8, 8.0, 3.7, 1H)	2.90 (ddd, *J* = 14.8, 7.4, 3.7, 1H)
9b	3.19 (m, 1H)	3.20-3.18 (m, 1H)
10a	1.63 (m, 1H)	1.62-1.60 (m, 1H)
10b	2.57 (m, 1H)	2.57-2.55 (m, 1H)
11a	1.77 (m, 1H)	1.79-1.77 (m, 1H)
11b	2.46 (m, 1H)	2.47-2.45 (m, 1H)
14a	2.03 (m, 1H)	2.03-2.01 (m, 1H)
14b	2.54 (dd, *J* = 12.7, 12.7, 1H)	2.51 (dd, *J* = 12.9, 12.5, 1H)
15	2.06 (m, 1H)	2.05-2.04 (m, 1H)
16	1.06 (d, *J* = 6.2, 3H)	1.05 (d, *J* = 6.2, 3H)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7
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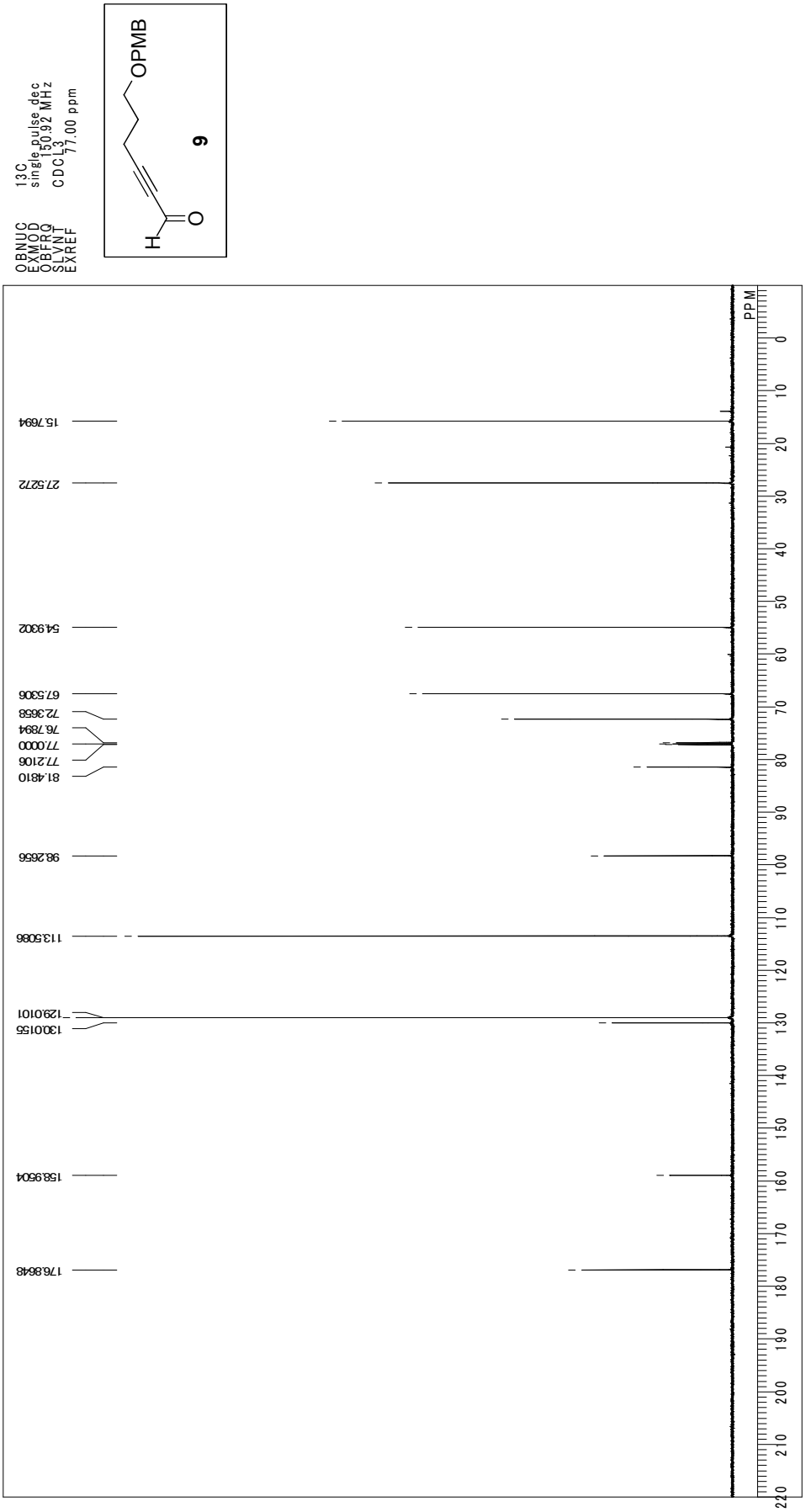
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PPM
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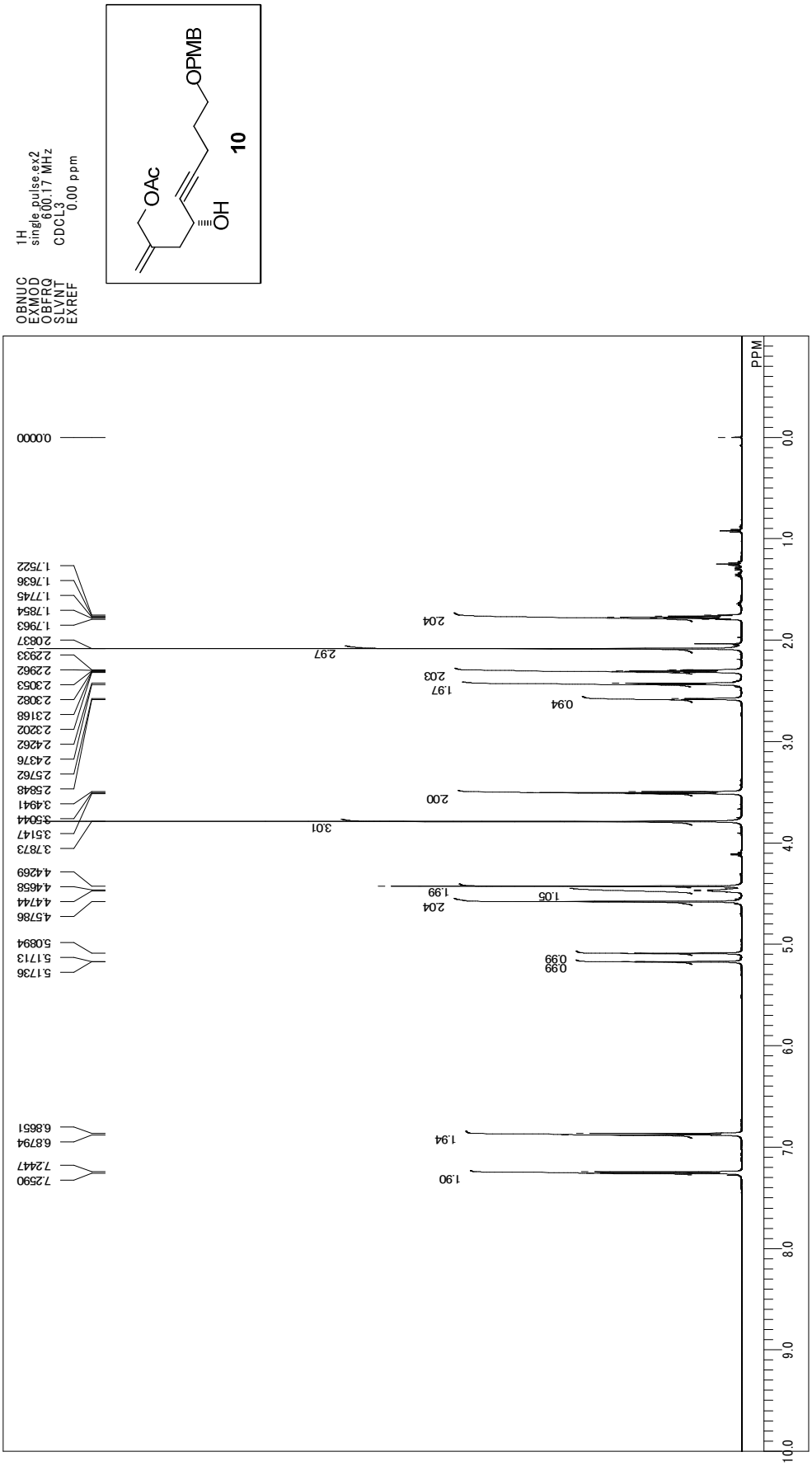
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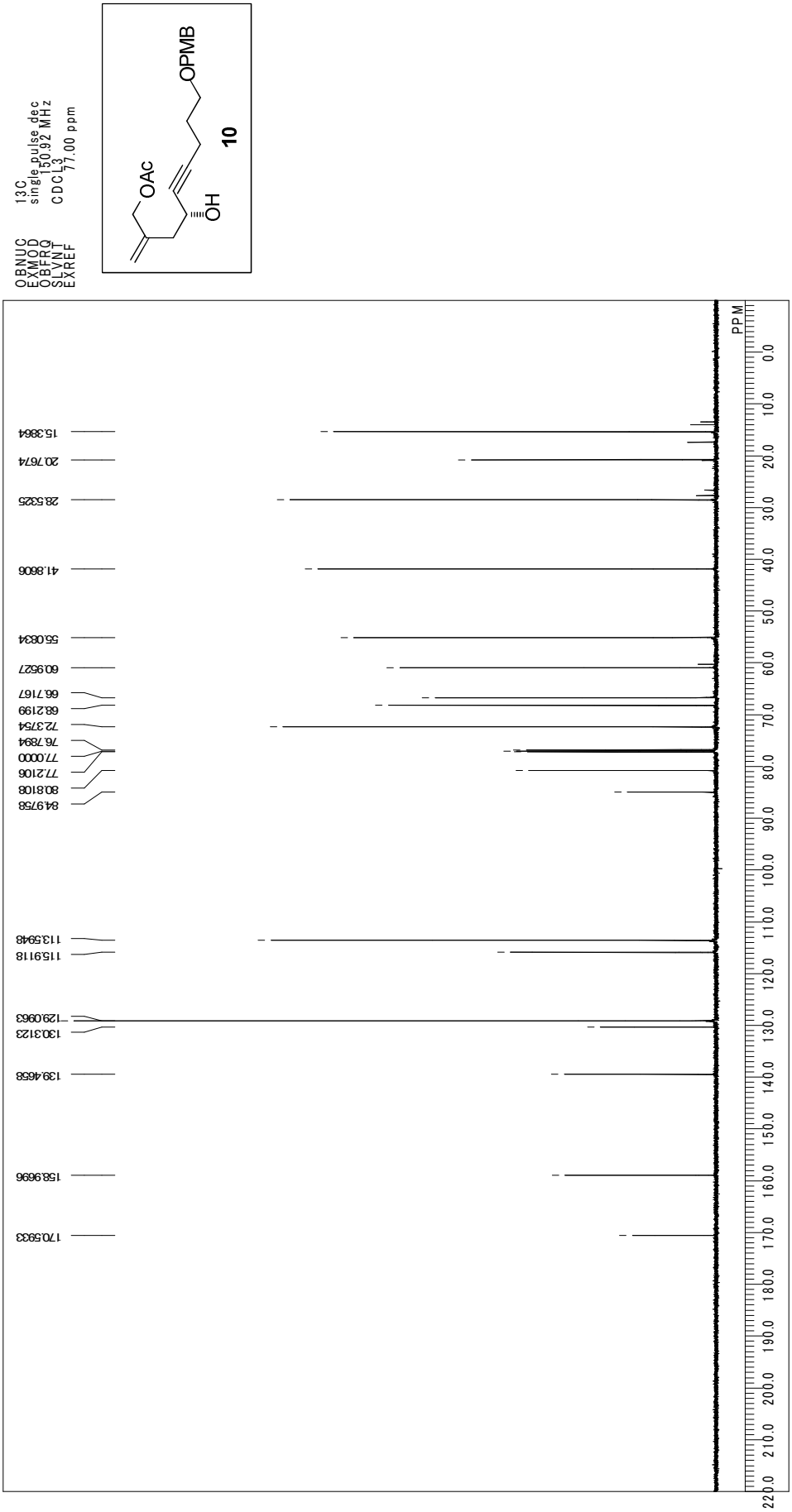
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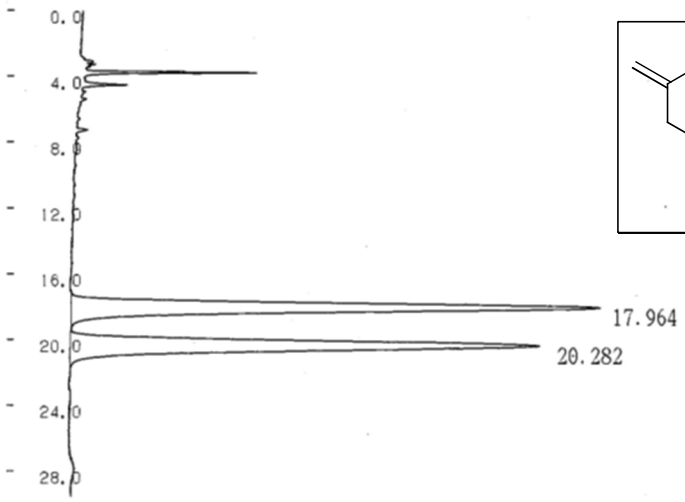

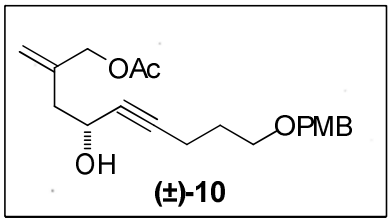

(±)-10

** 定量計算結果 **

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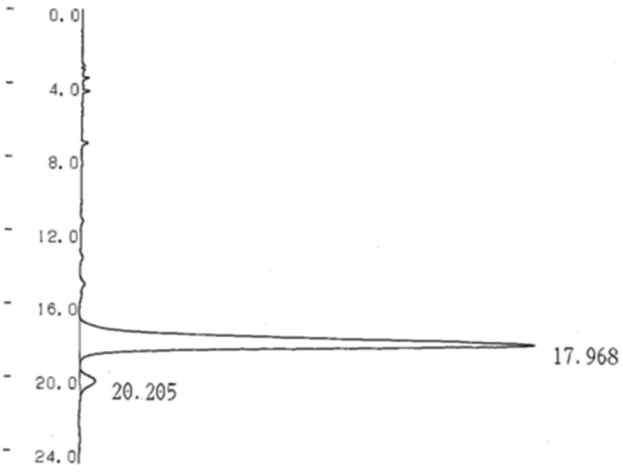

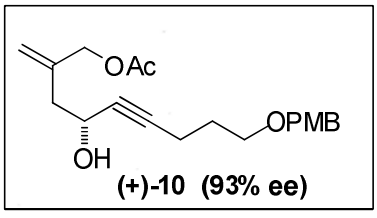

(+)-10 (93% ee)

** 定量計算結果 **

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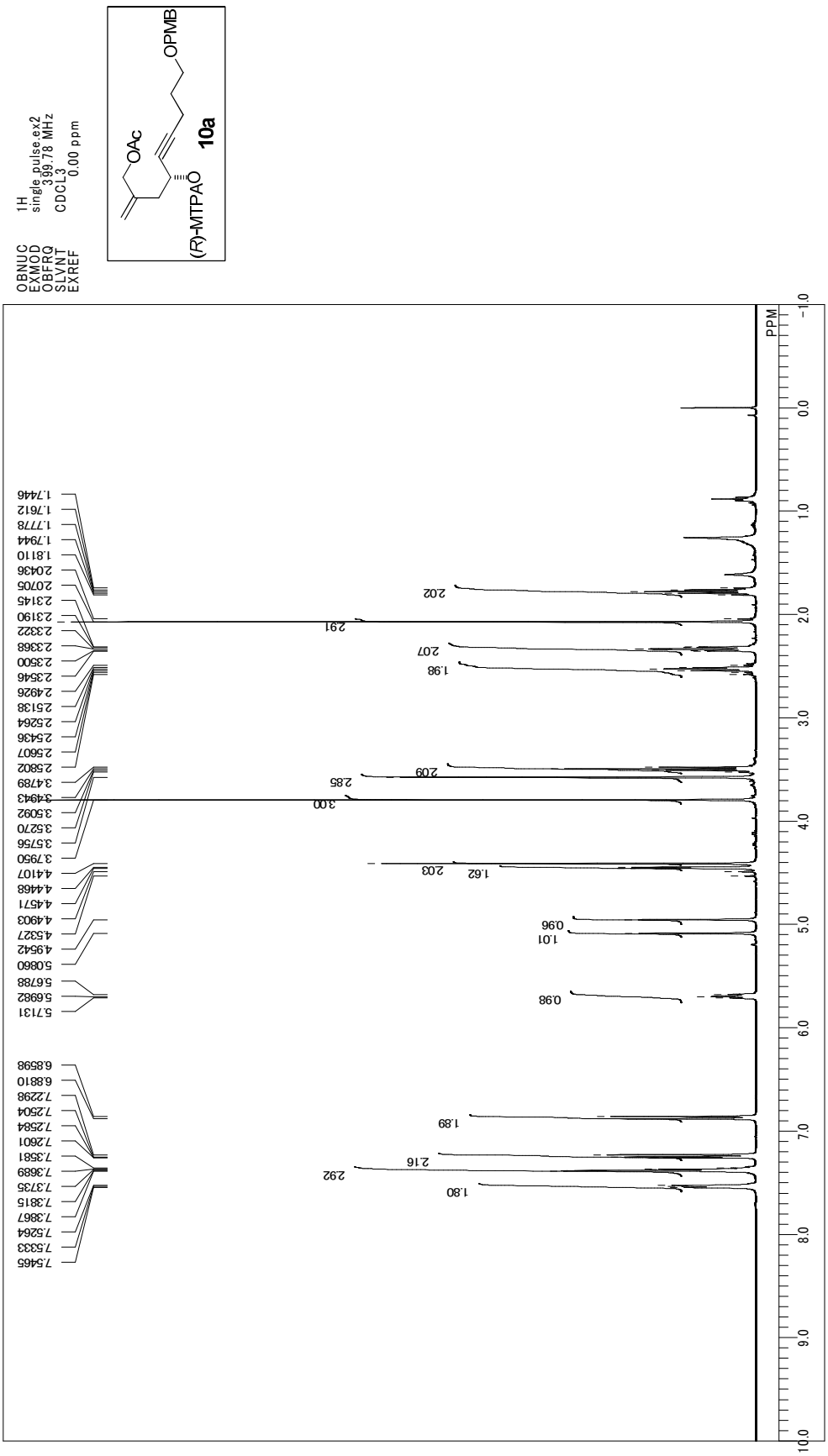
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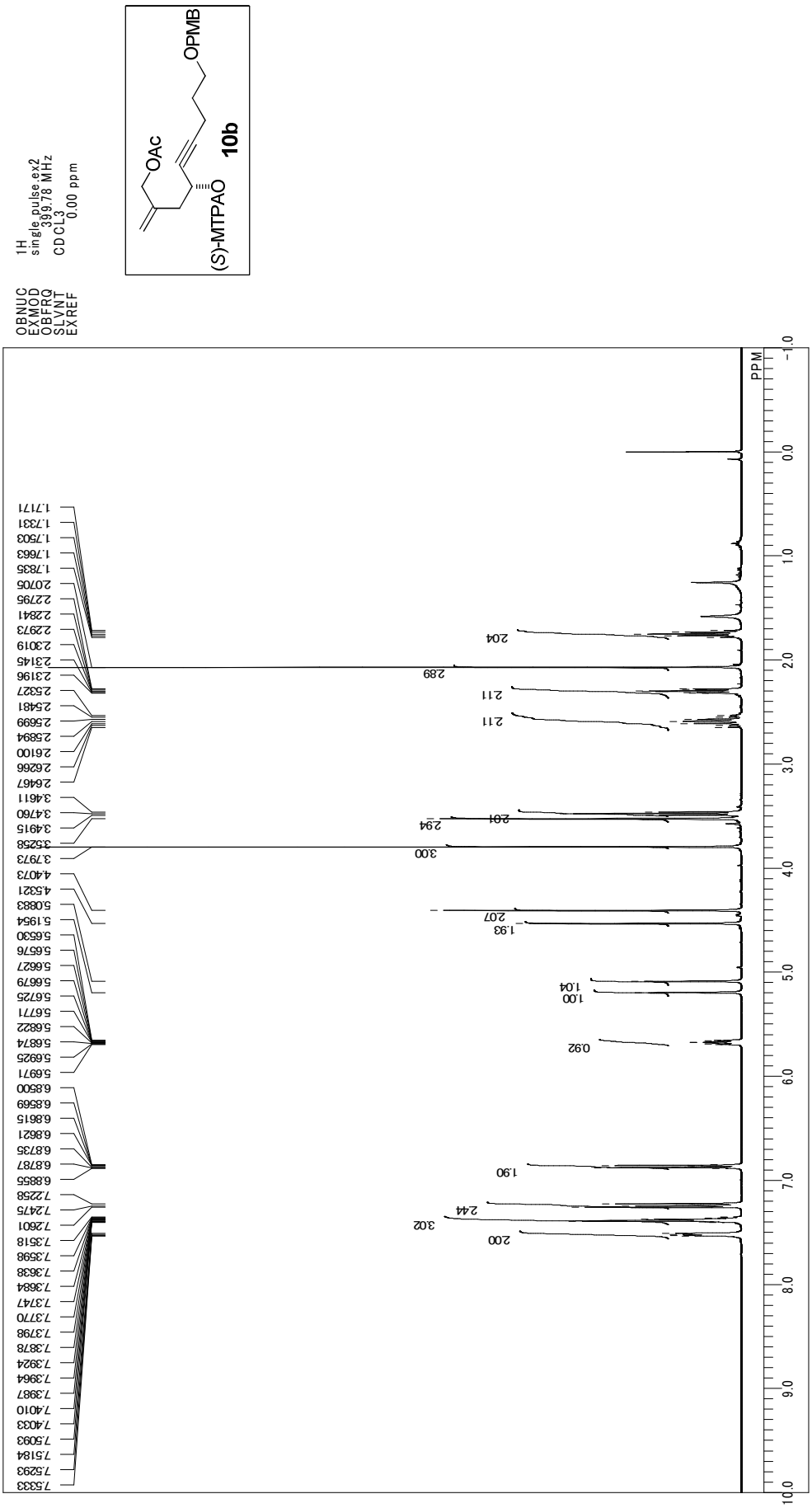
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EXREF
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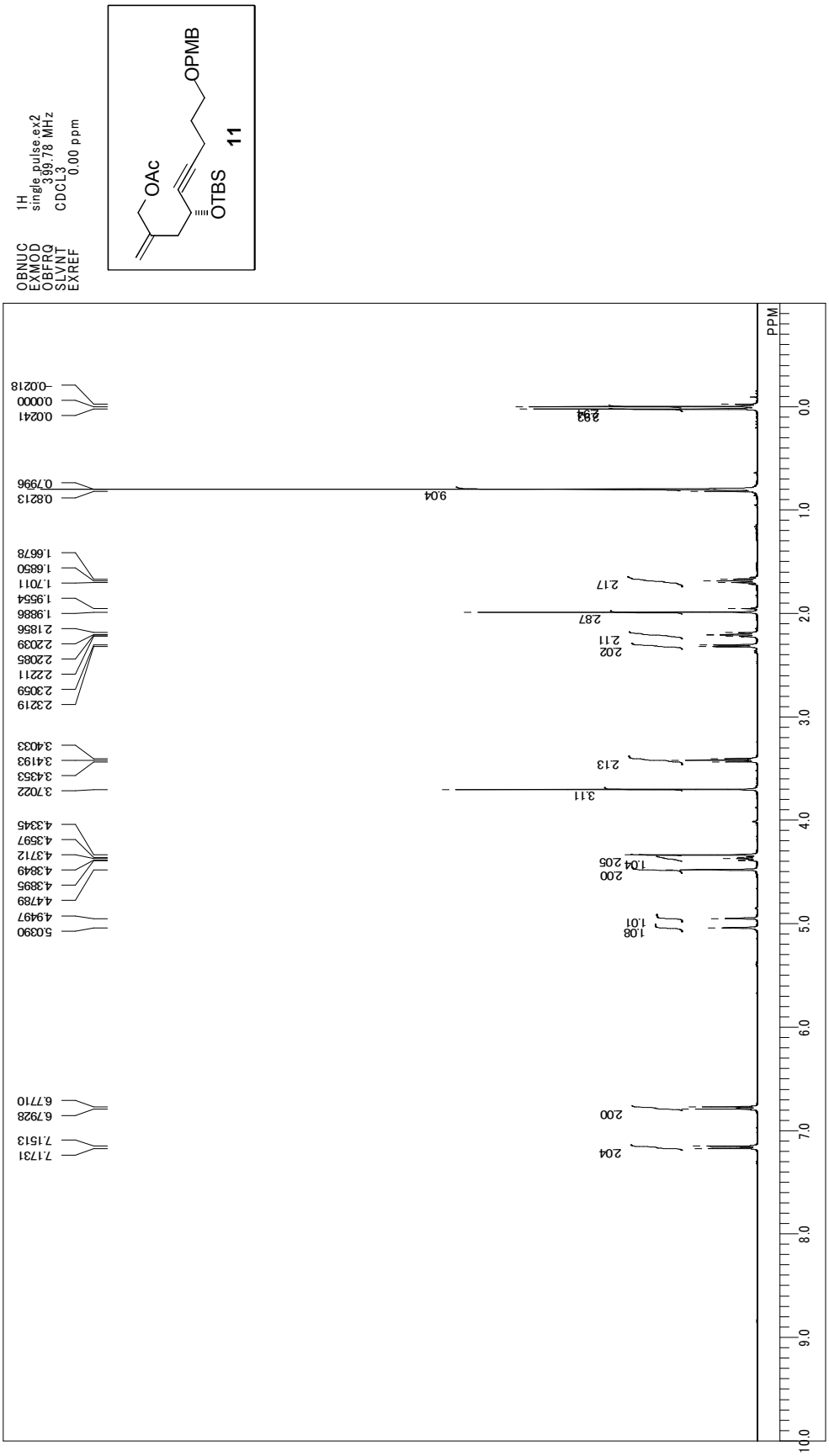
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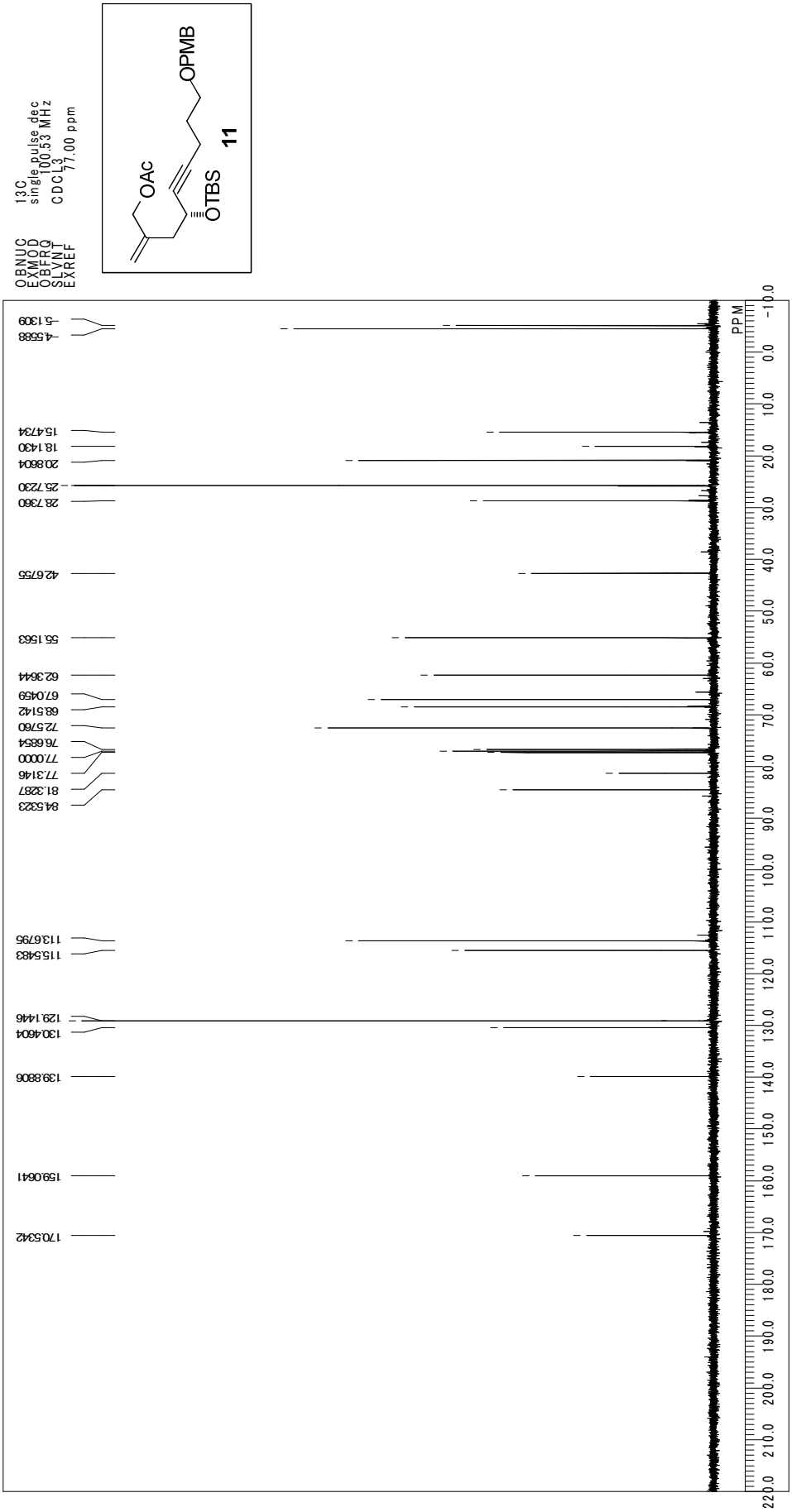
PPM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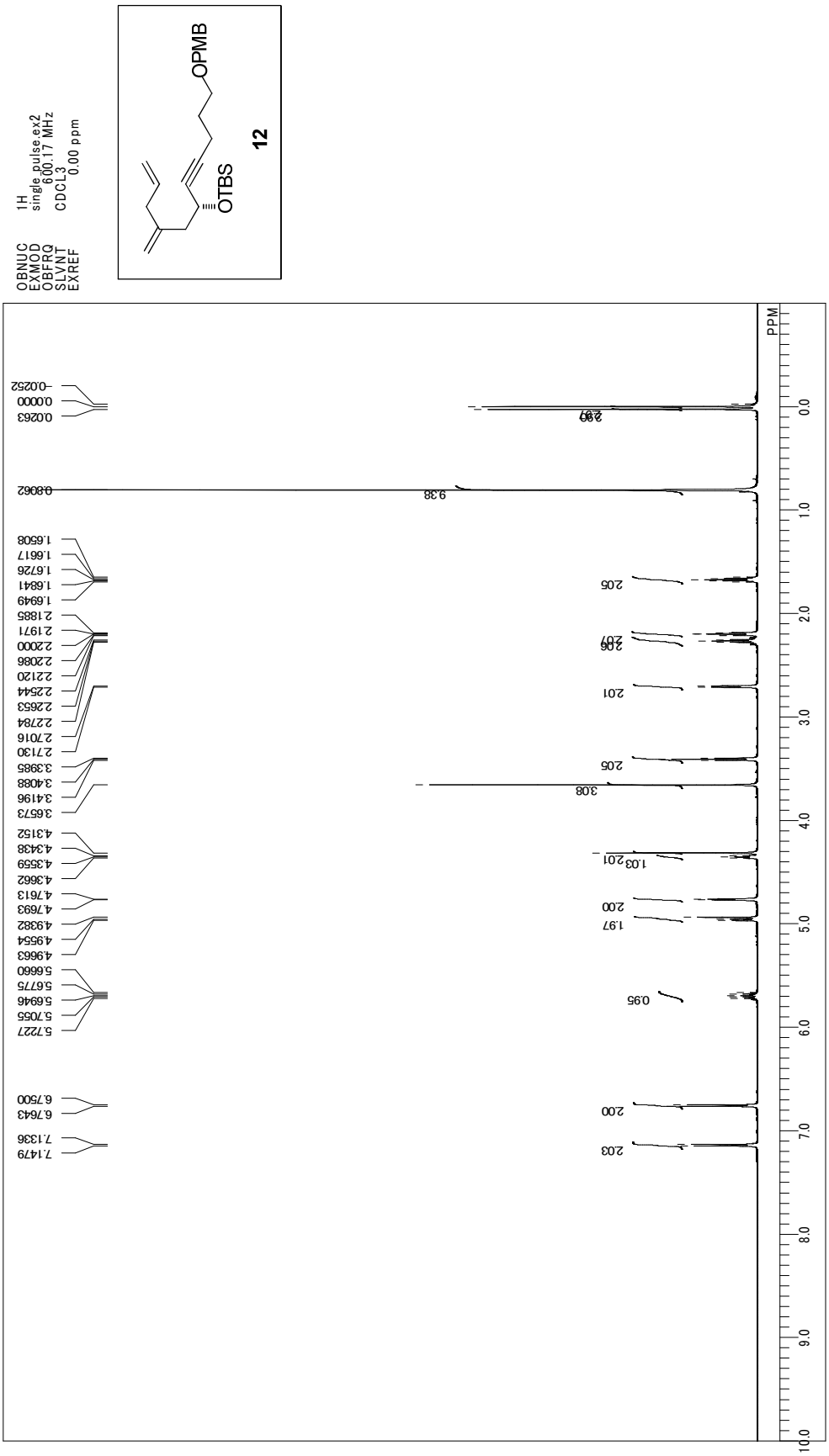
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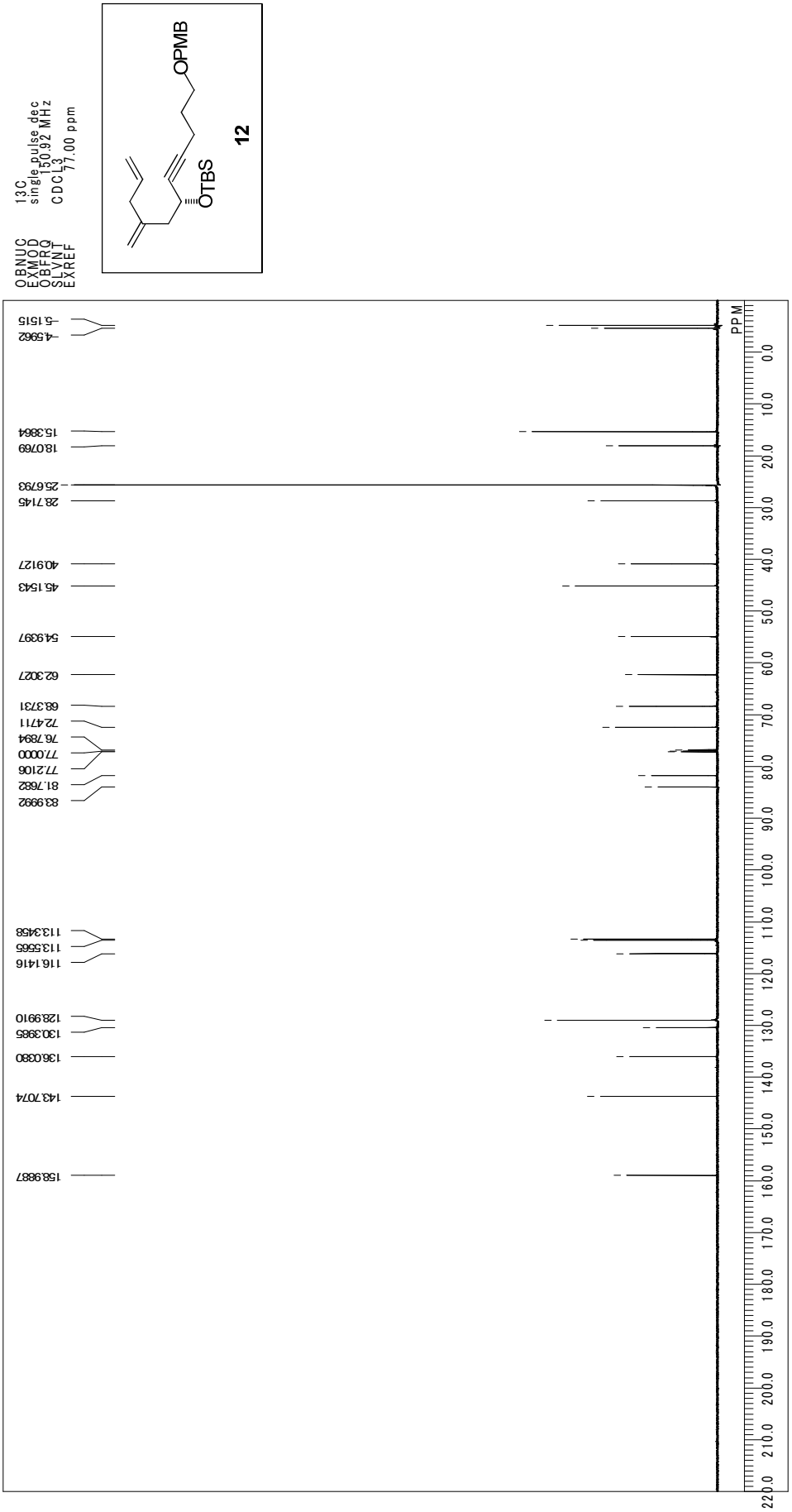
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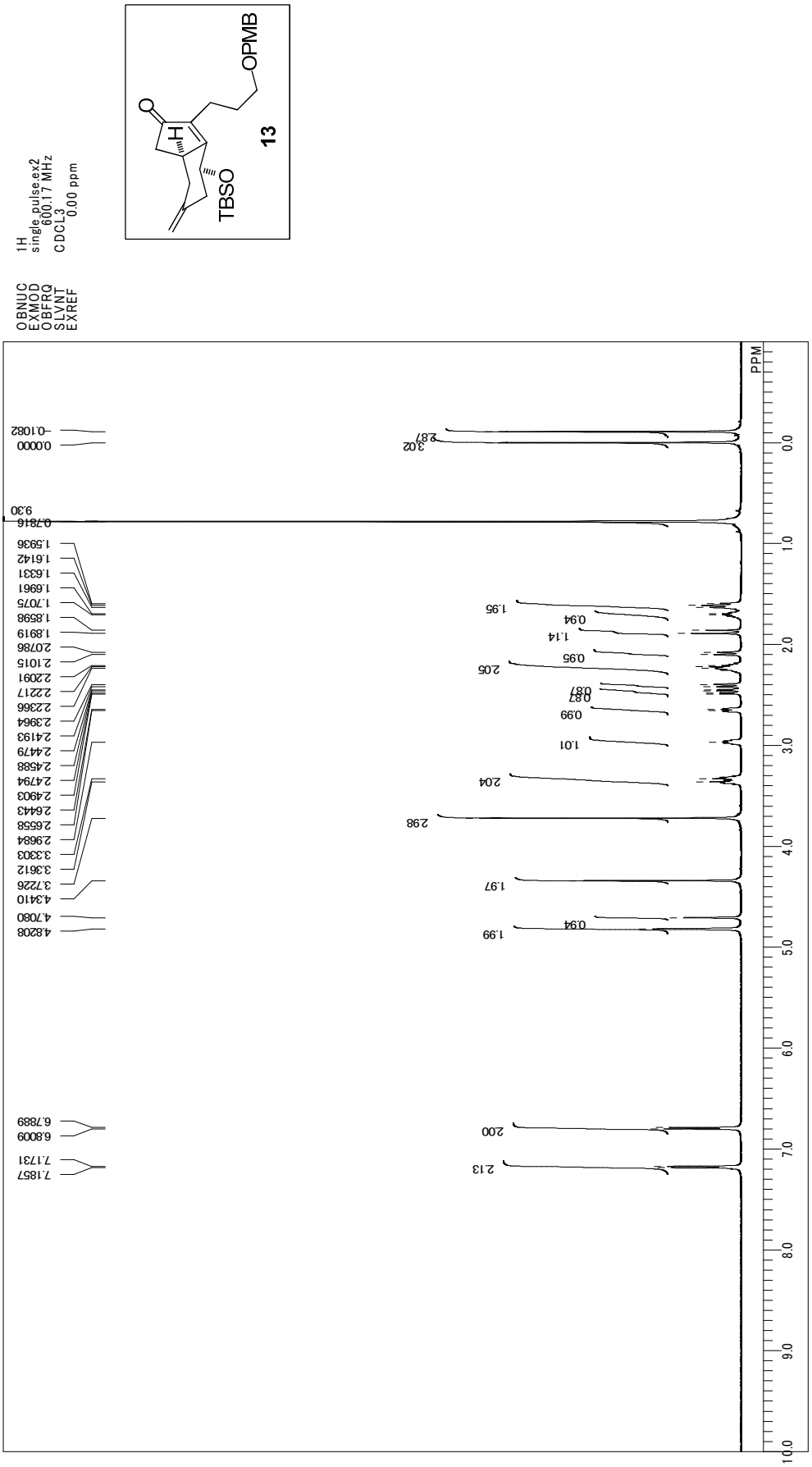
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TBSO
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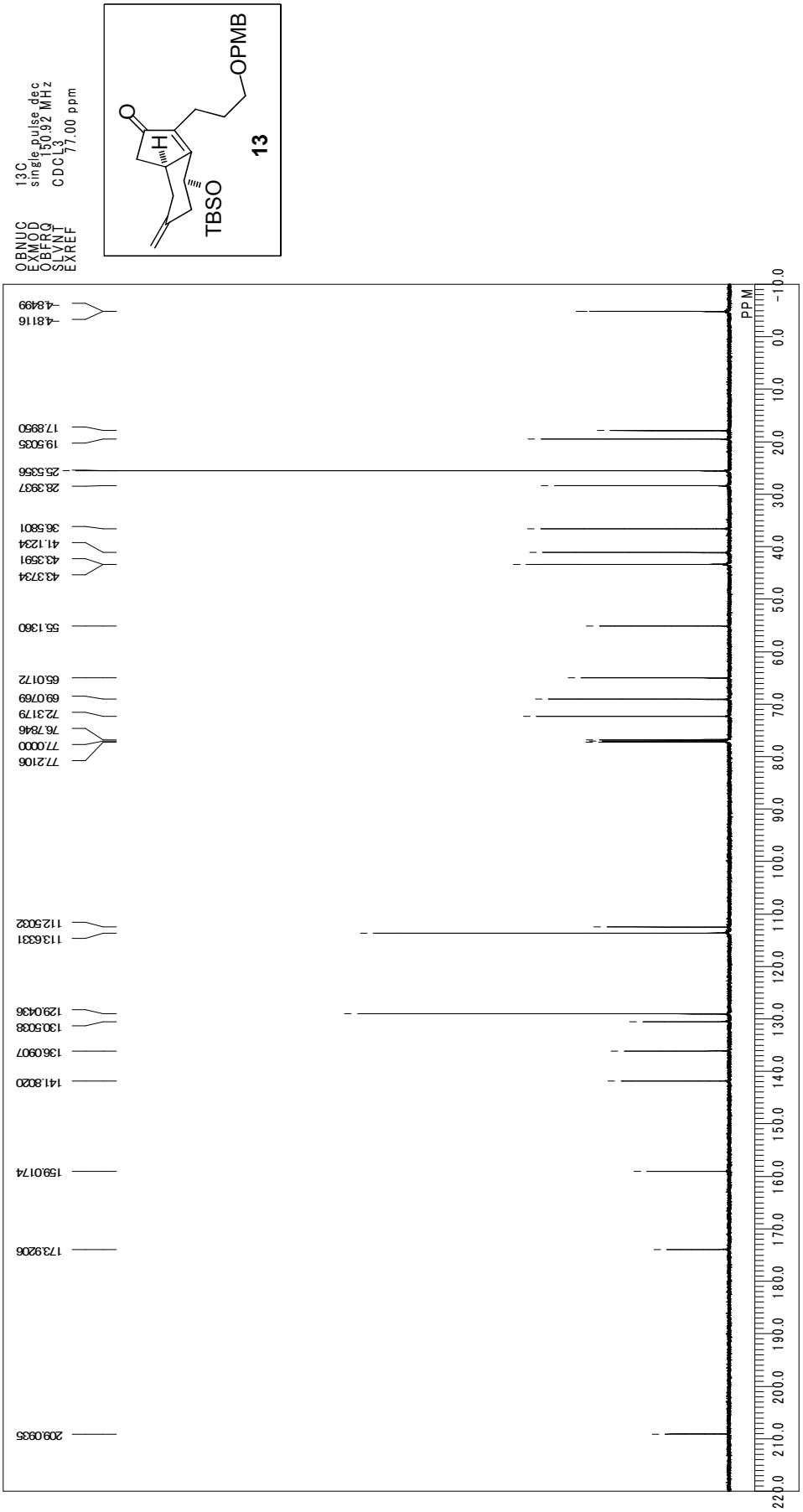
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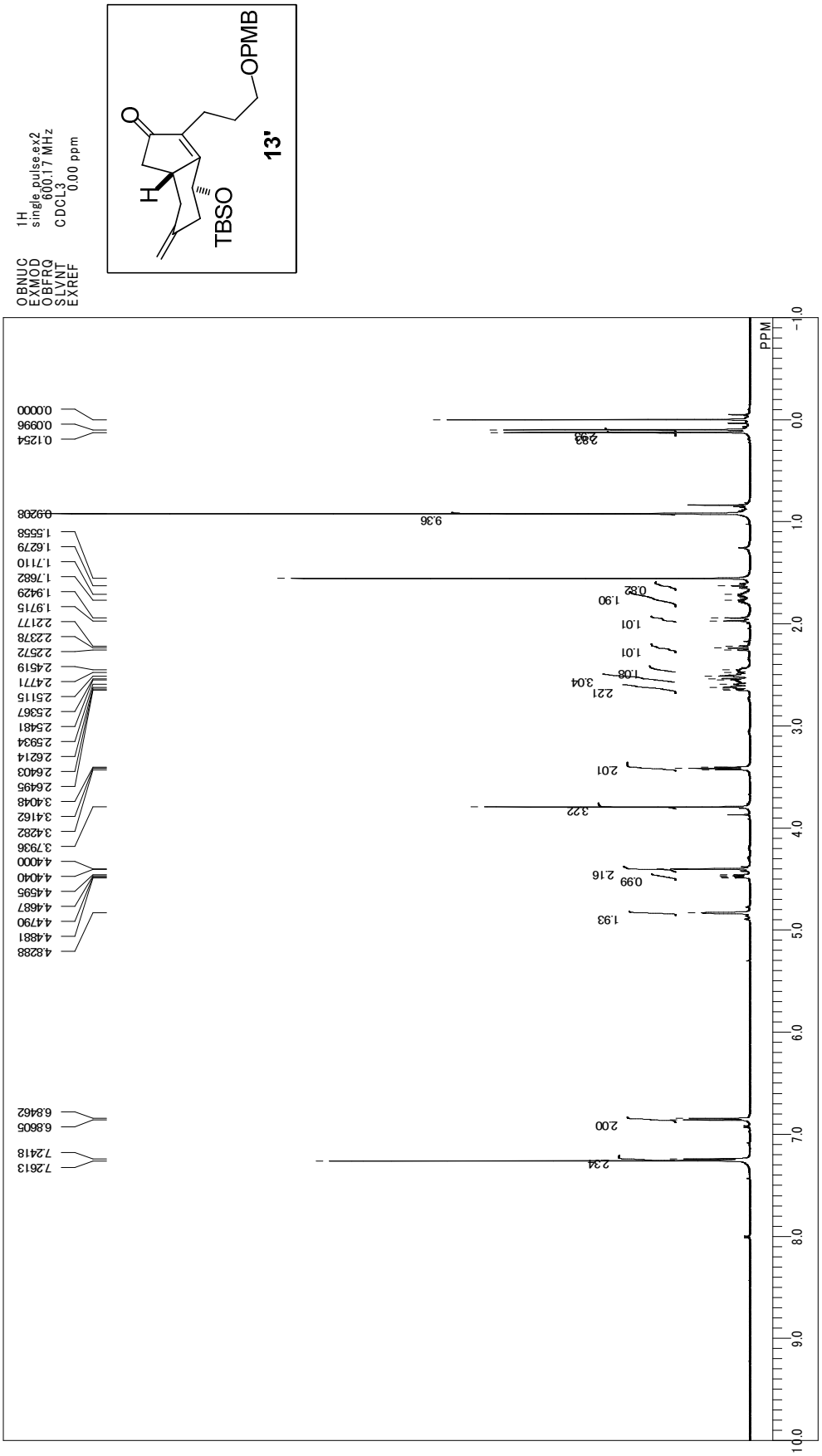
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EXREF
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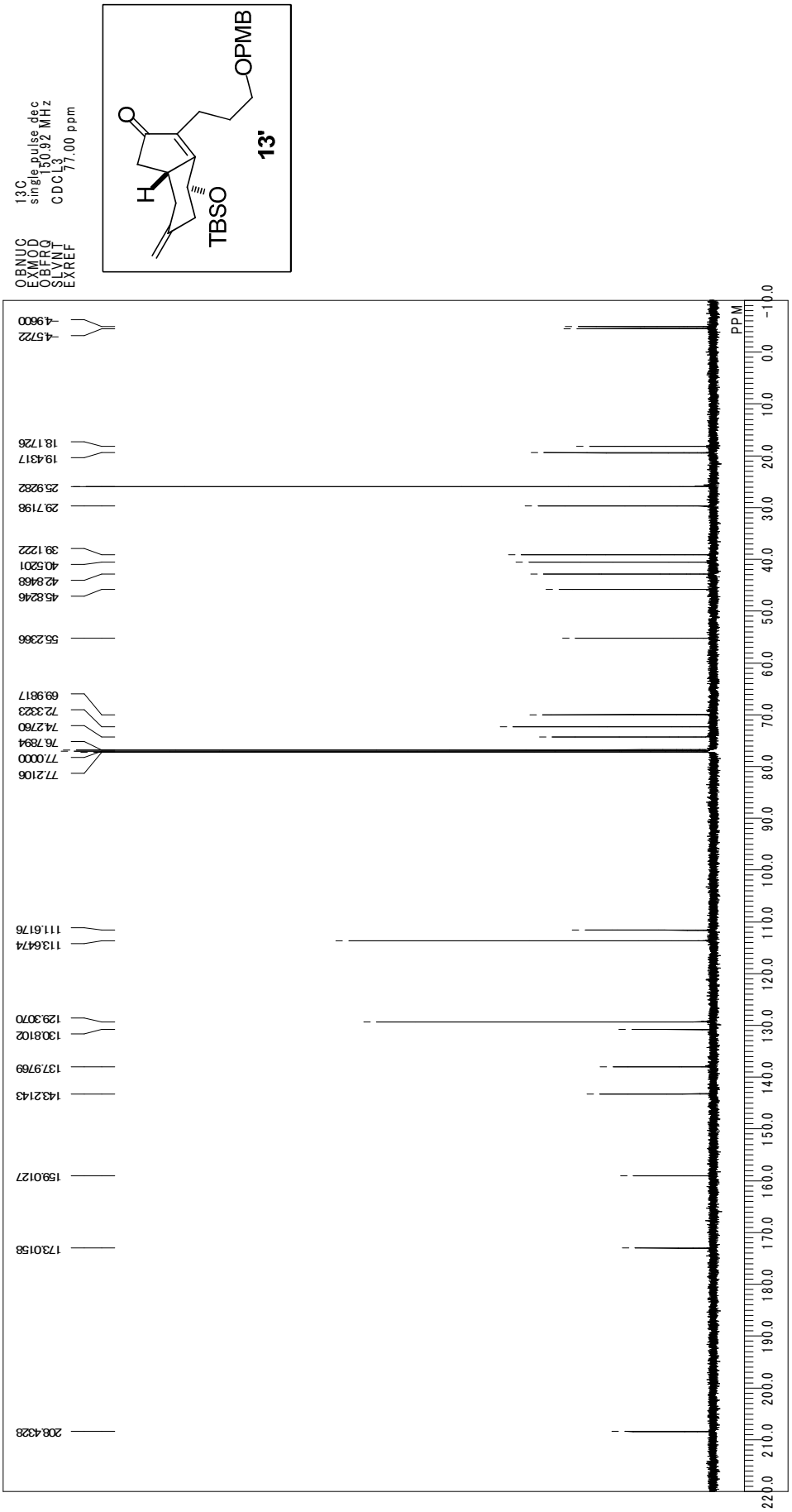
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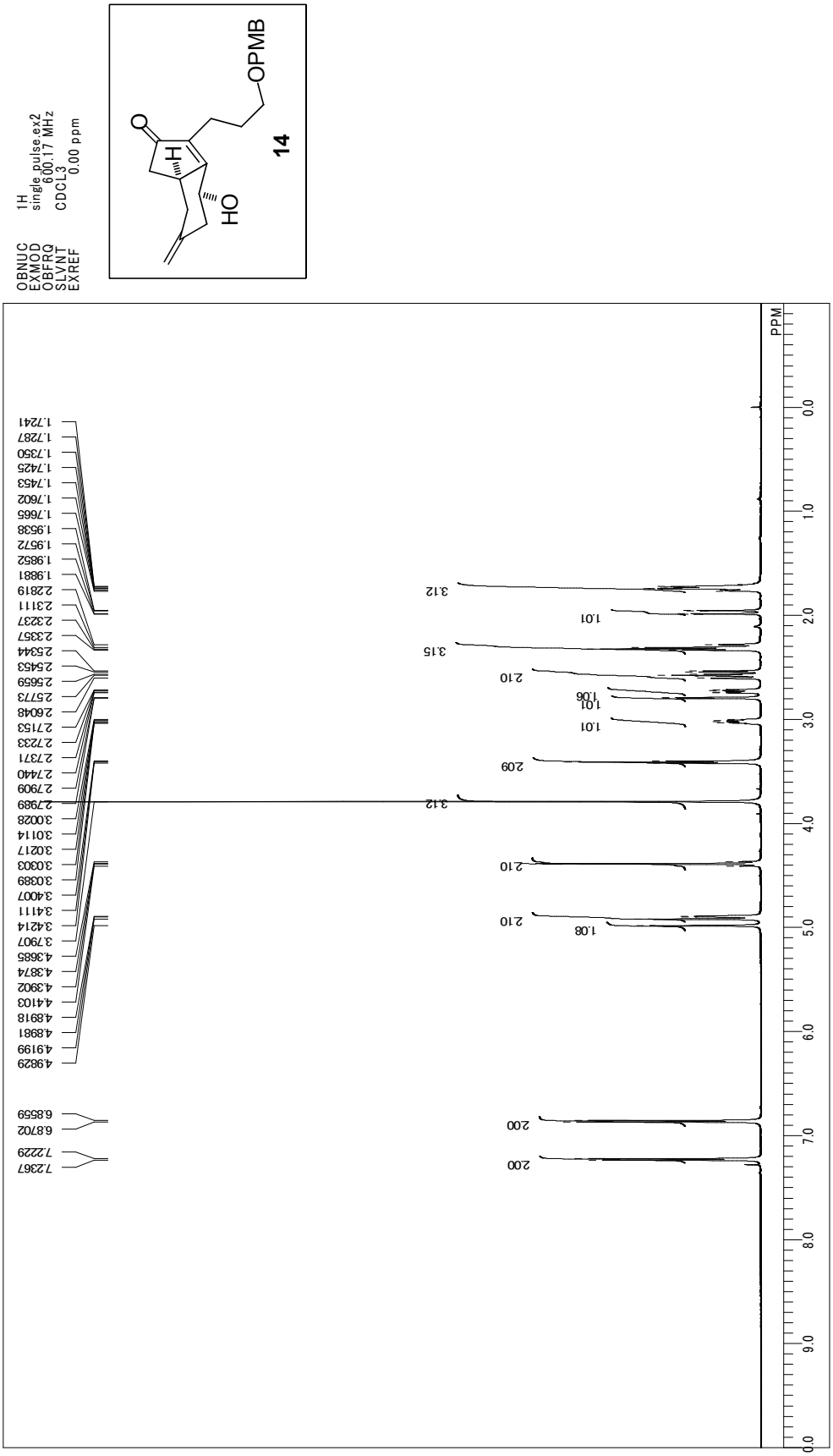
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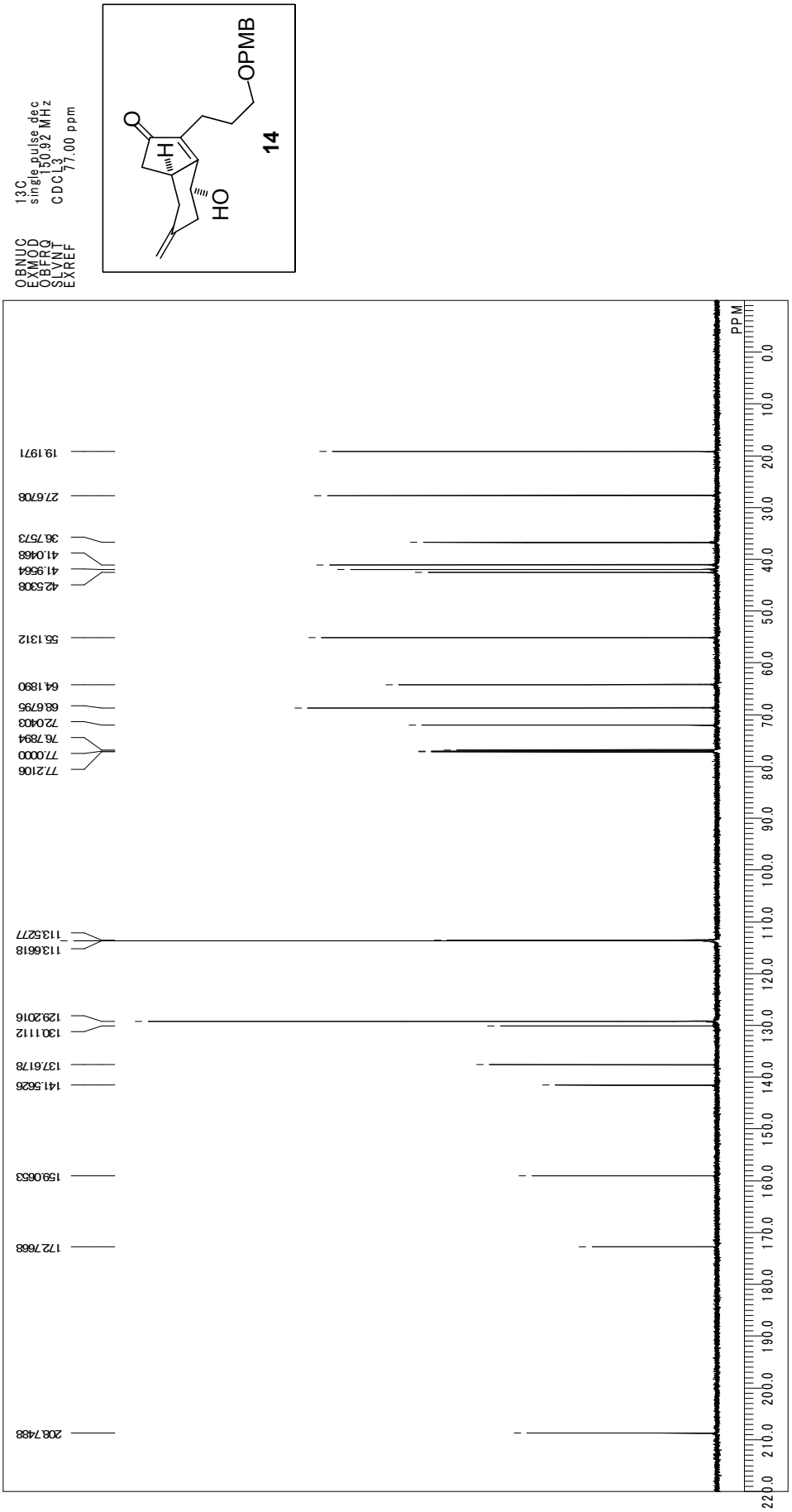
PPM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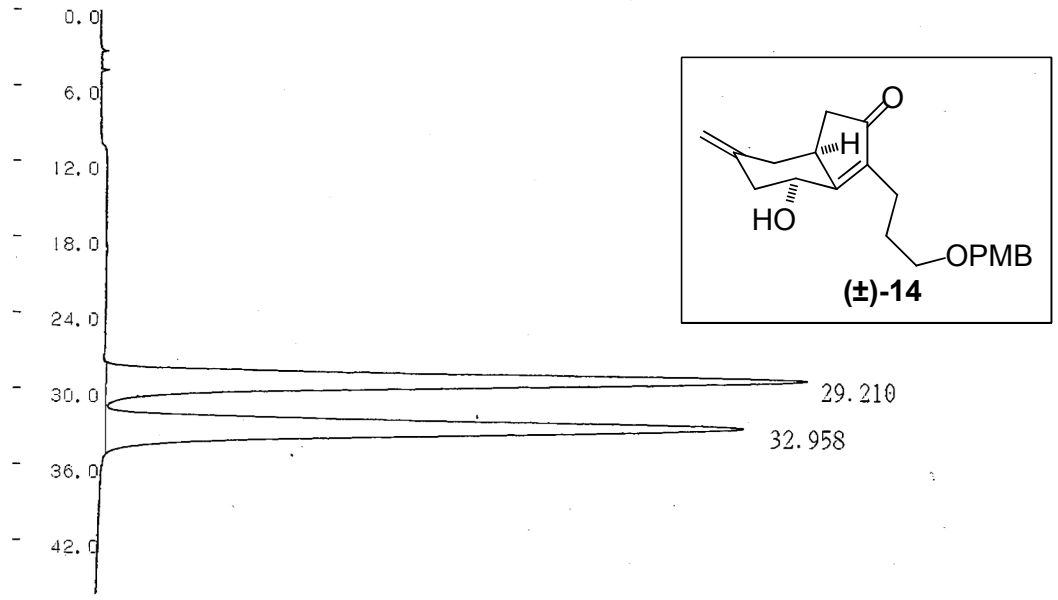
208.7488

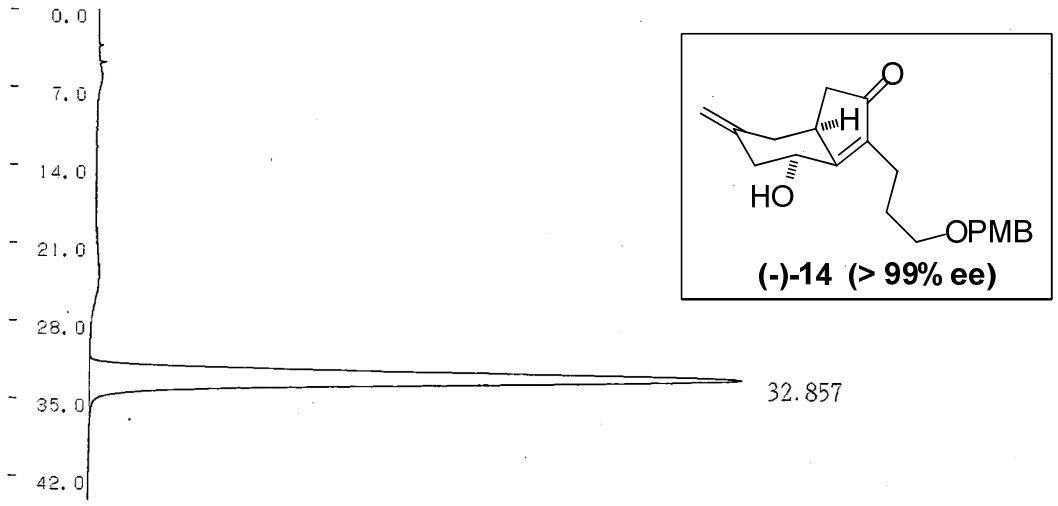
CHROMATOPAC C-R7A CH=1 REPORT No.=5 ｸﾛﾏﾄ=1:@CHRM1.C00 13/07/04 12:00:52



** 定量計算結果 **

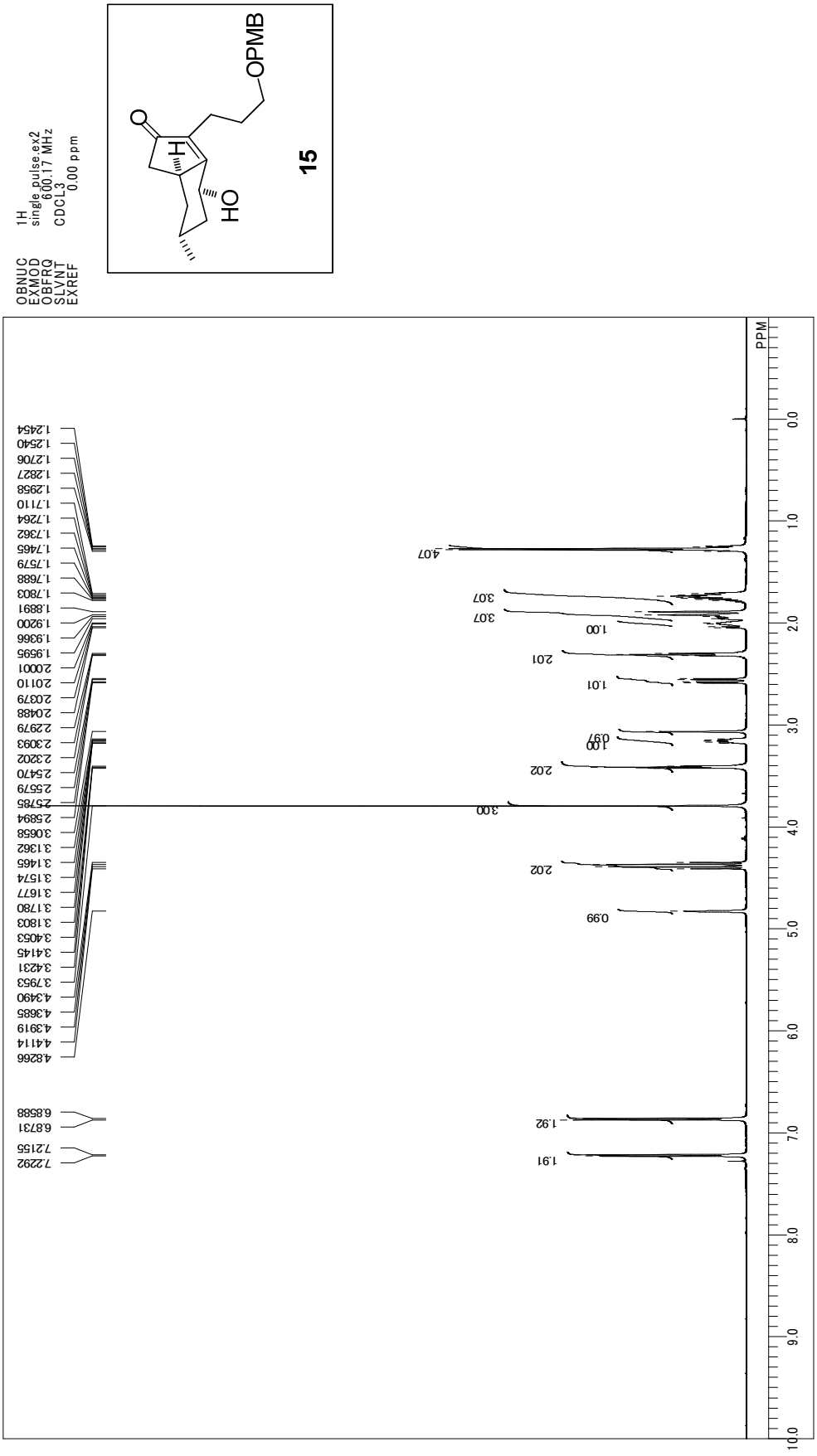
CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	29.21	456676	6245			49.9458	
	2	32.958	457667	5681			50.0542	
		TOTAL	914343	11926			100	

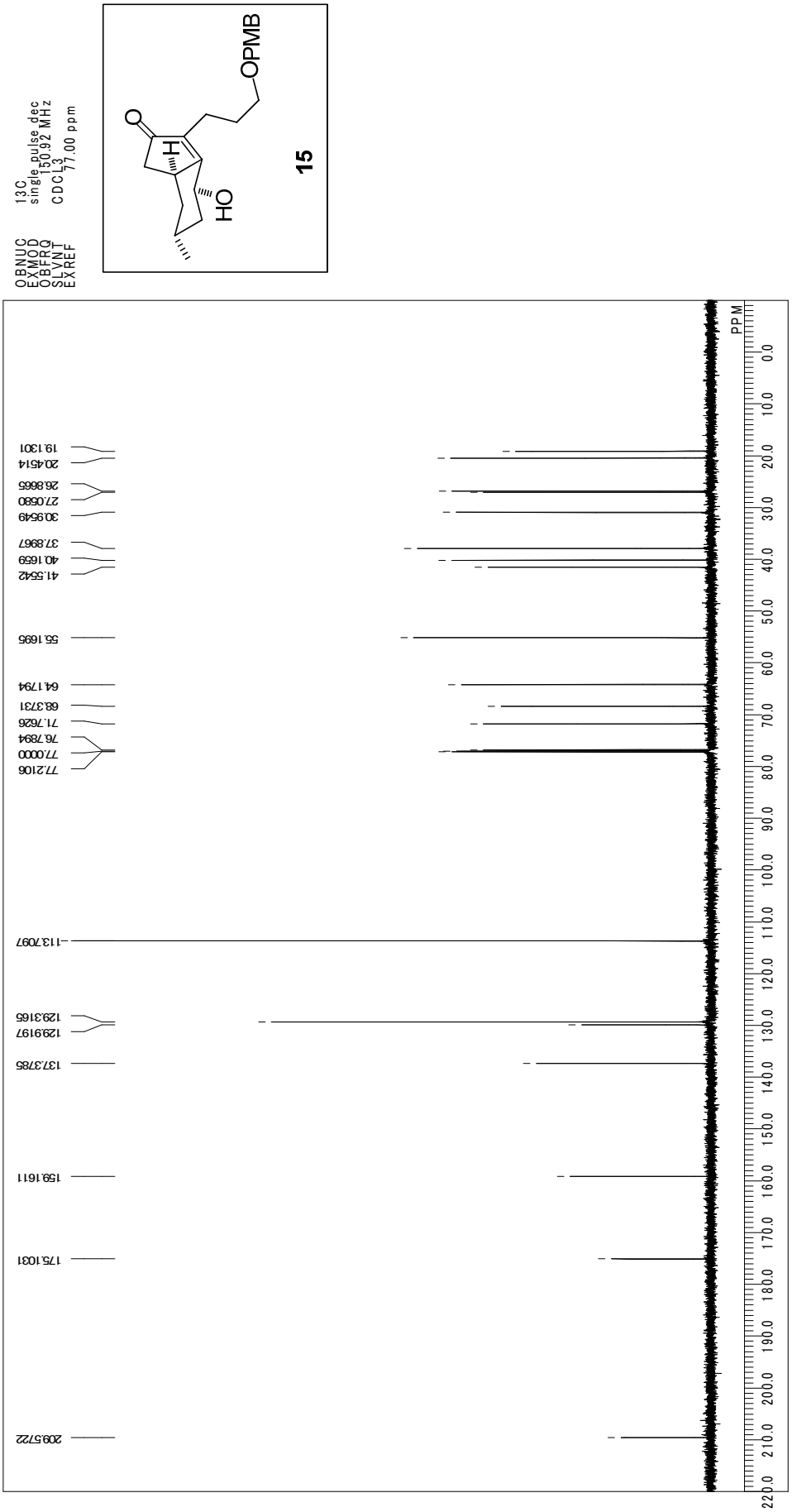
CHROMATOPAC C-R7A CH=1 REPORT No.=2 ｸﾛﾏﾄ=1:@CHRM1.C00 13/07/04 08:57:06

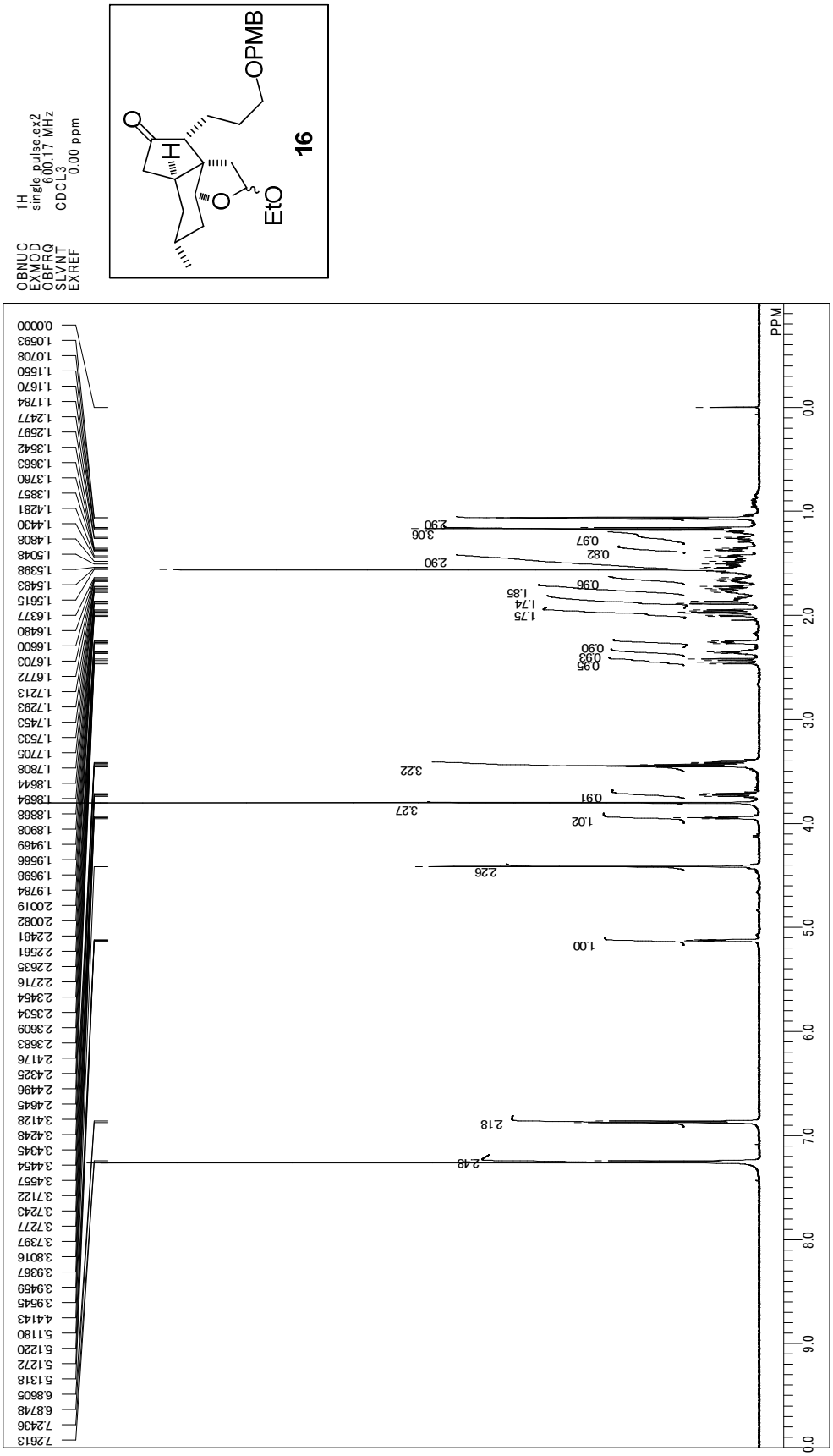


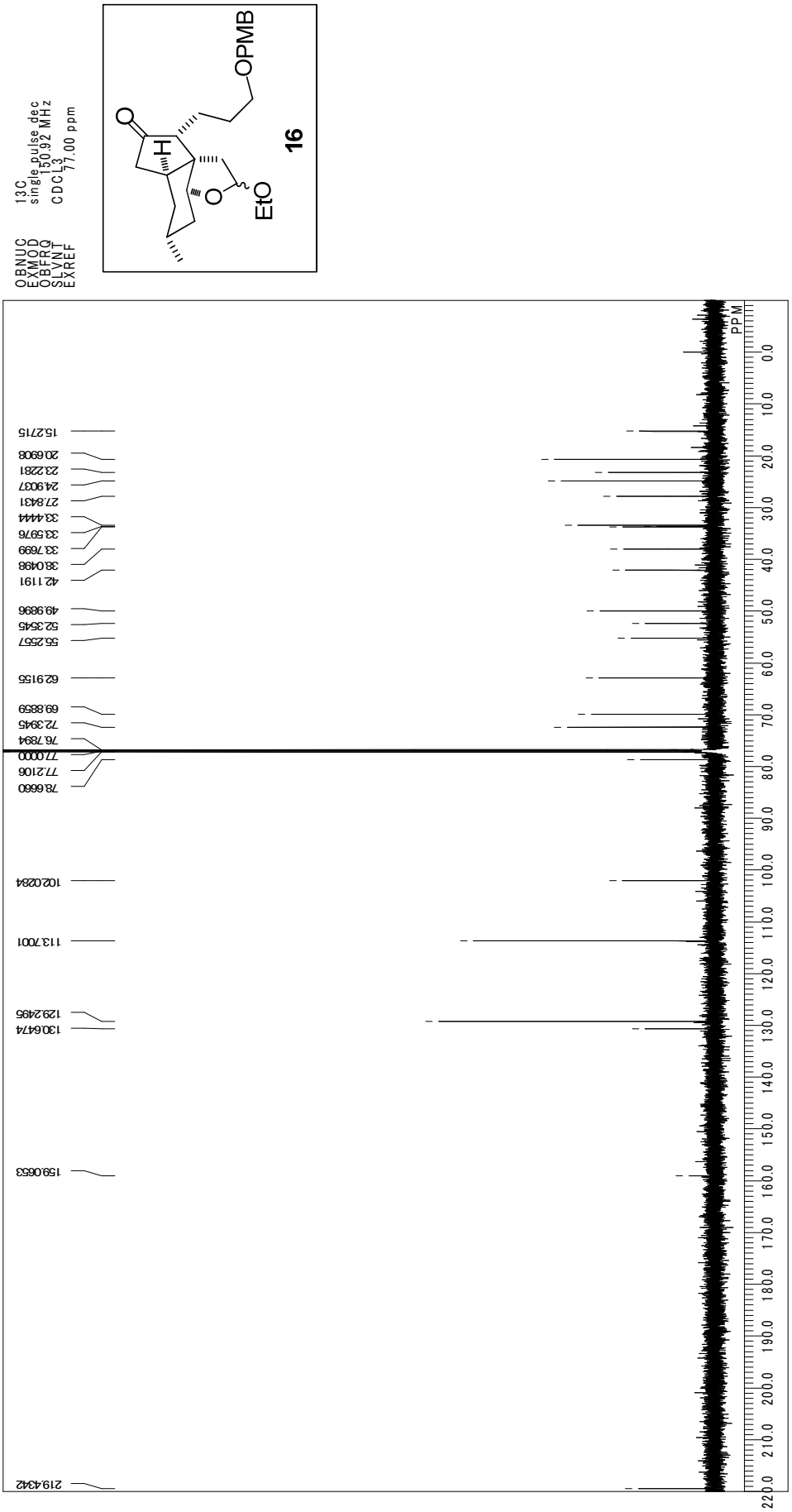
** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	32.857	951164	11653			100	
		TOTAL	951164	11653			100	


OPMB
HO
H
15
1H
single pulse.ex2
600.17 MHz
CDCL3
0.00 ppm
OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
PPM


OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
13C
single pulse dec
150.92 MHz
CDCl3
77.00 ppm
OPMB
HO
15
PPM
209.5722
175.1031
159.1611
137.3786
129.9197
129.3165
113.7097
77.2106
77.0000
76.7894
71.7626
68.3731
64.1794
55.1695
41.5542
40.1659
37.8967
30.9549
27.0580
26.8665
20.4514
19.1301


OPMB
EtO
16
1H
single pulse.ex2
600.17 MHz
CDCL3
0.00 ppm
OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
PPM


OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
13C
single pulse dec
150.92 MHz
CDCl3
77.00 ppm
OPMB
H
O
O
EtO
16
PPM
15.2715
20.6908
23.2281
24.9037
27.8431
33.4444
33.5976
33.7699
38.0498
42.1191
49.9896
52.3545
55.2557
62.9155
69.8859
72.3945
76.7894
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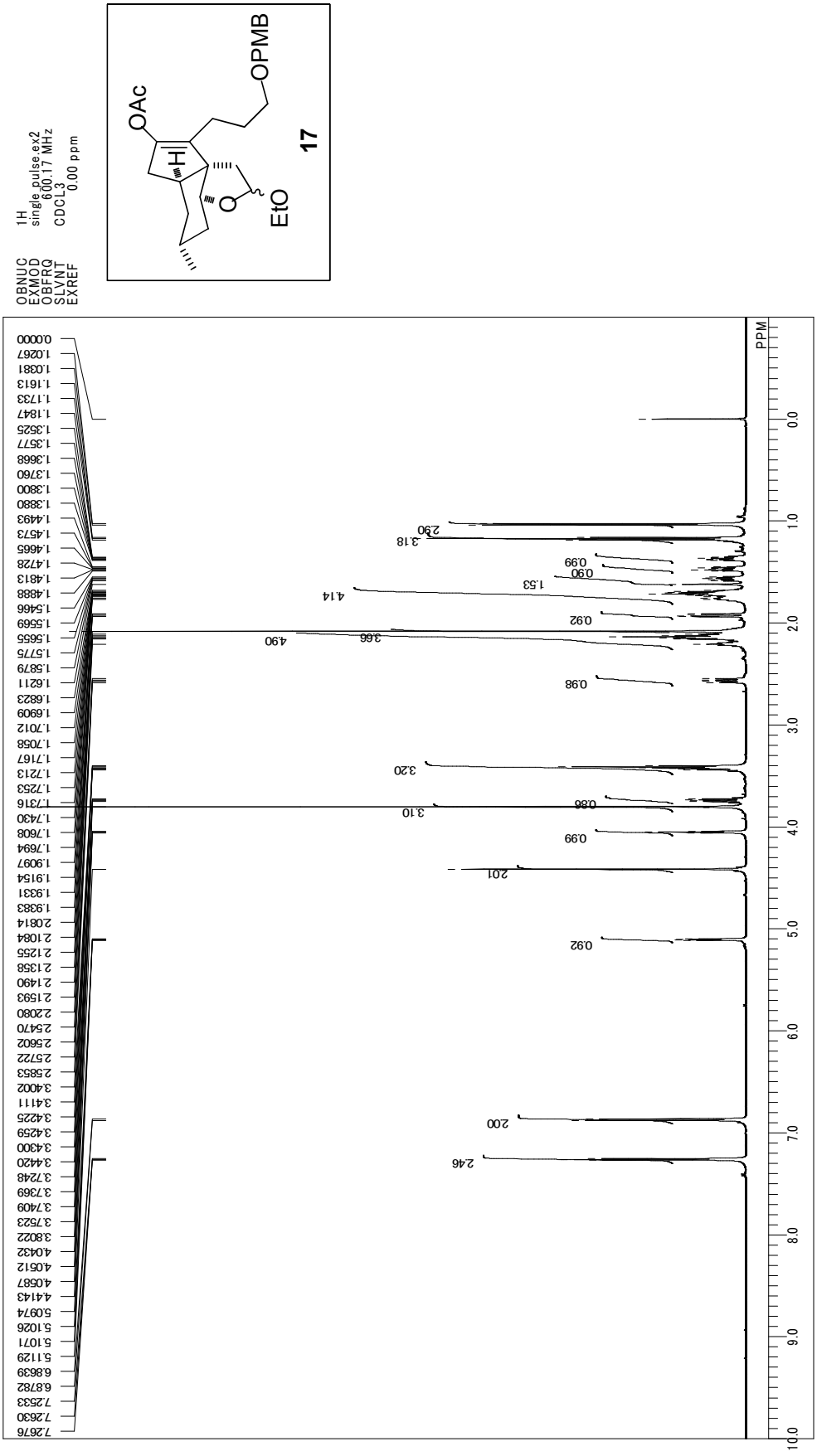
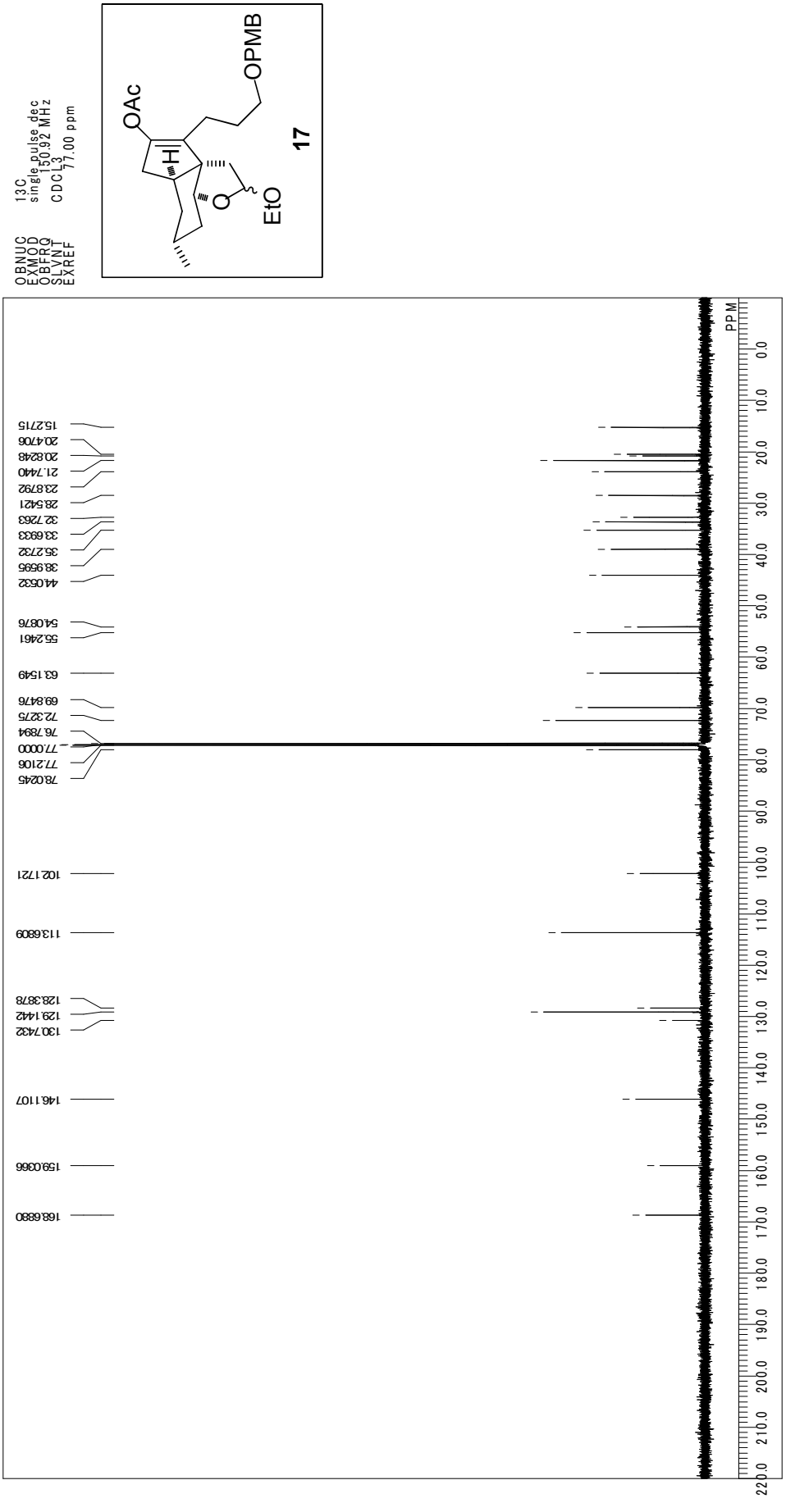
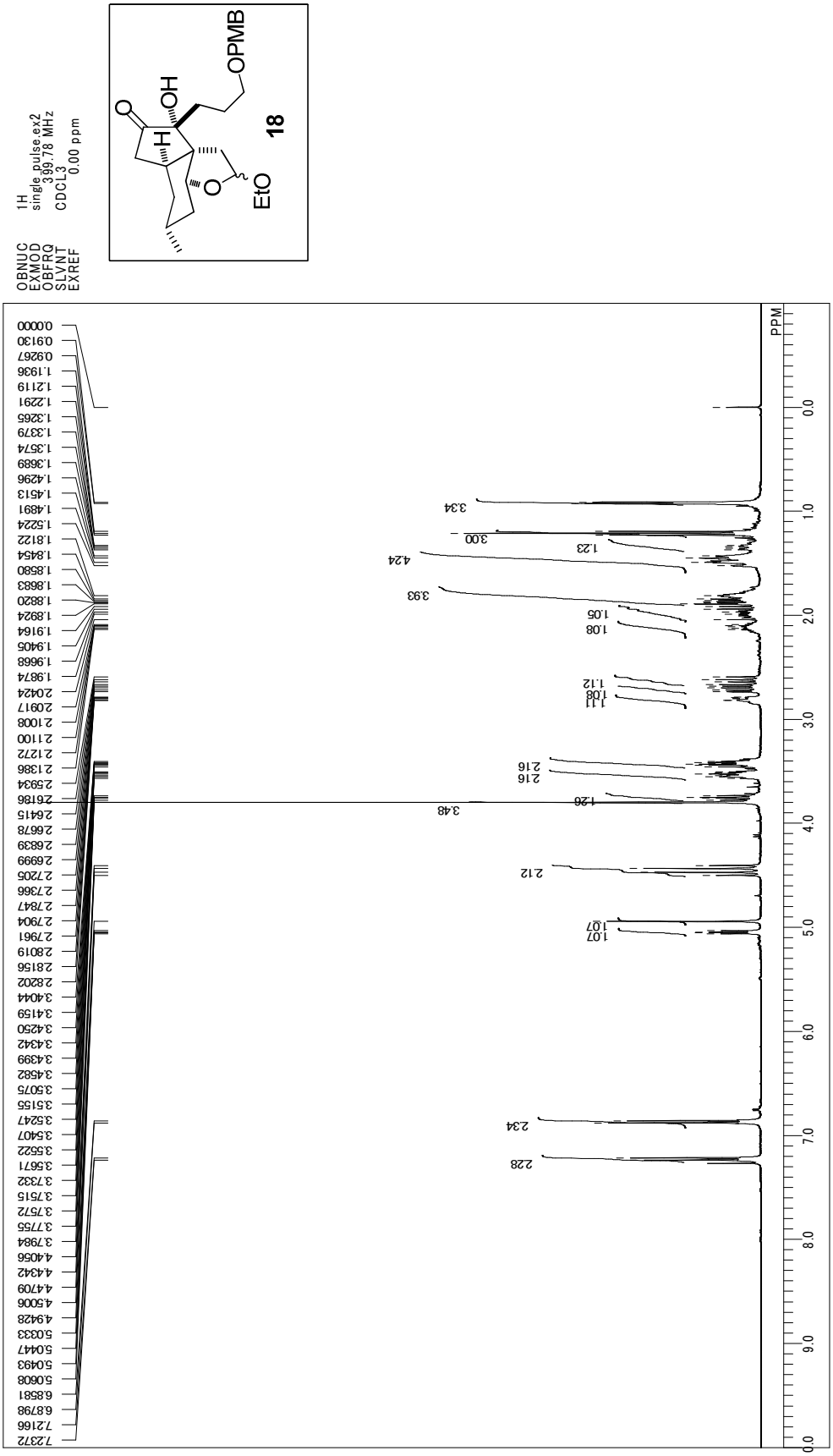
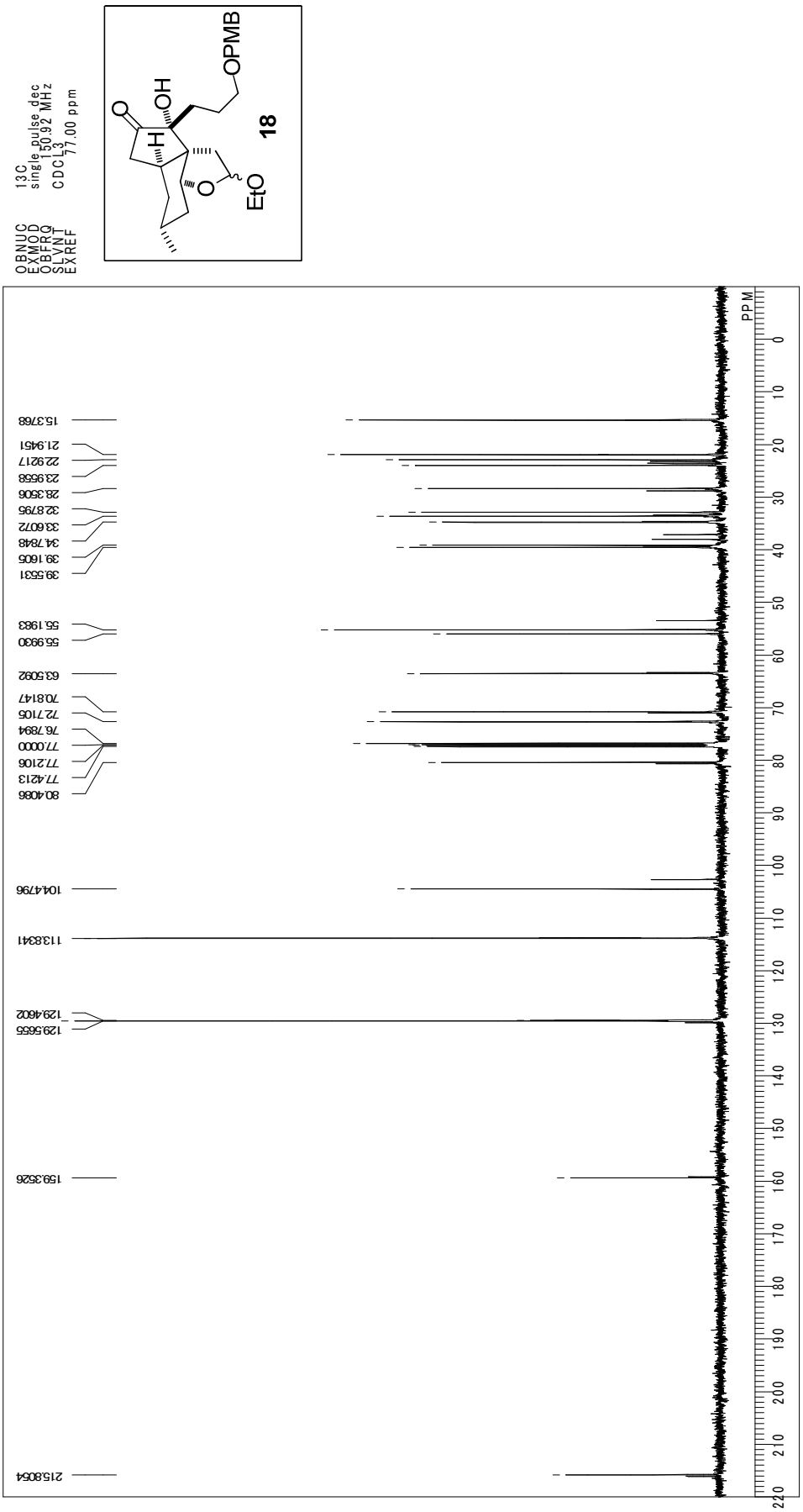
78.6660
102.0284
113.7001
129.2495
130.6474
159.0653
219.4342


OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
1H
single pulse.ex2
600.17 MHz
CDCL3
0.00 ppm
OAc
OPMB
EtO
17
PPM
2.90
3.18
0.99
0.90
1.53
4.14
0.92
3.66
4.90
0.98
3.20
0.86
3.10
0.99
2.01
0.92
2.00
2.46


OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
13C
single pulse dec
150.92 MHz
CDCl3
77.00 ppm
OAc
OPMB
EtO
17
PPM
15.2715
20.4706
20.8248
21.7440
23.8792
28.5421
32.7263
33.6933
35.2732
38.9596
44.0532
54.0876
55.2461
63.1549
69.8476
72.3275
76.7894
77.0000
77.2106
78.0245
102.1721
113.6809
128.3878
129.1442
130.7432
146.1107
159.0366
168.6880


OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
1H
single_pulse.ex2
399.78 MHz
CDCL3
0.00 ppm
OPMB
OH
H
O
O
EtO
18
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
3.34
3.00
1.23
4.24
3.93
1.05
1.08
1.11
1.08
1.12
2.16
2.16
3.48
1.26
2.12
1.07
1.07
2.34
2.28


OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
13C
single pulse dec
150.92 MHz
CDCl3
77.00 ppm
OPMB
OH
H
O
EtO
18
PPM
153768
21.9451
22.9217
23.9558
28.3506
32.8796
33.6072
34.7848
39.1605
39.5531
55.1983
55.9930
63.5092
70.8147
72.7105
76.7894
77.0000
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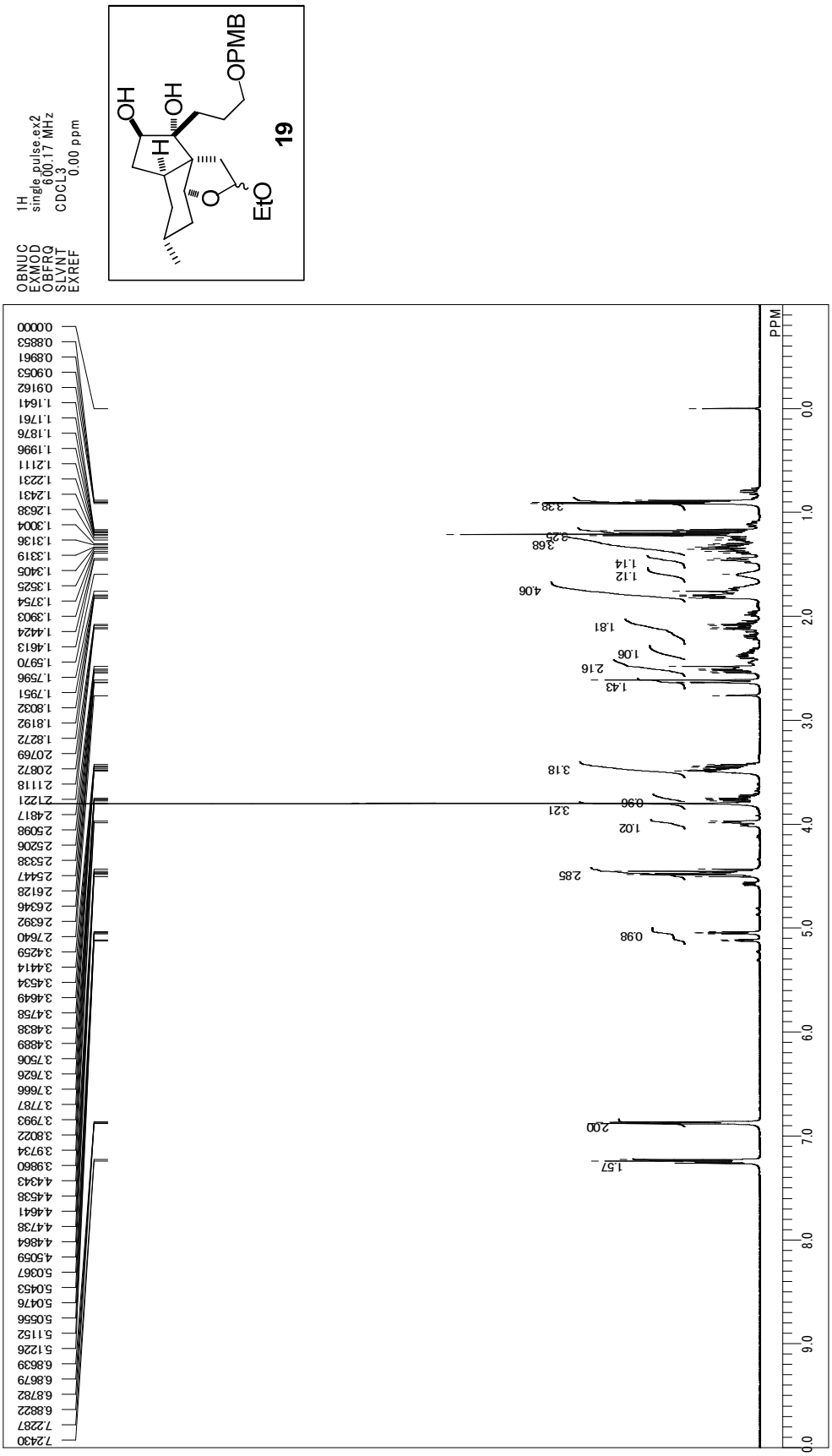
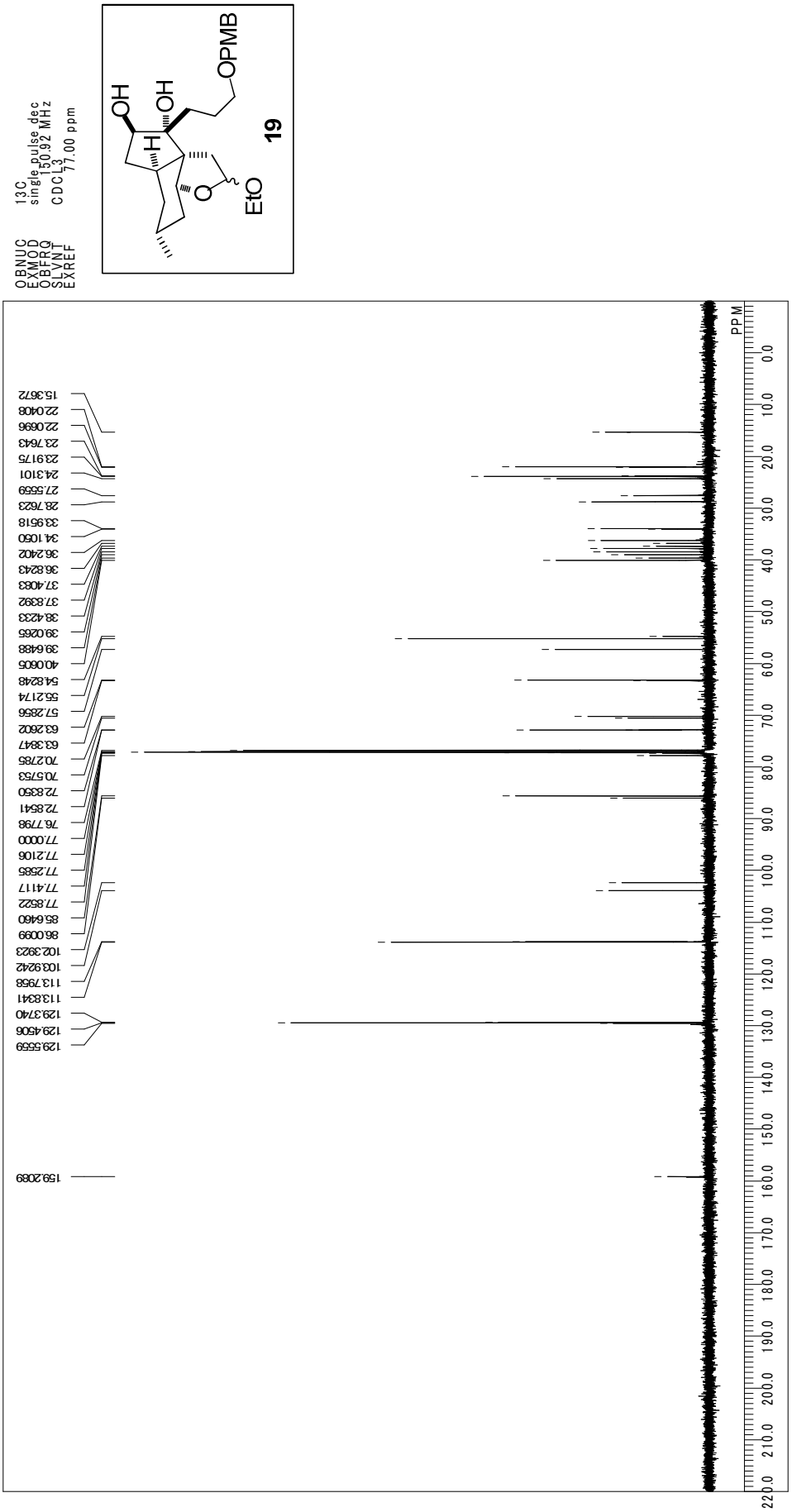
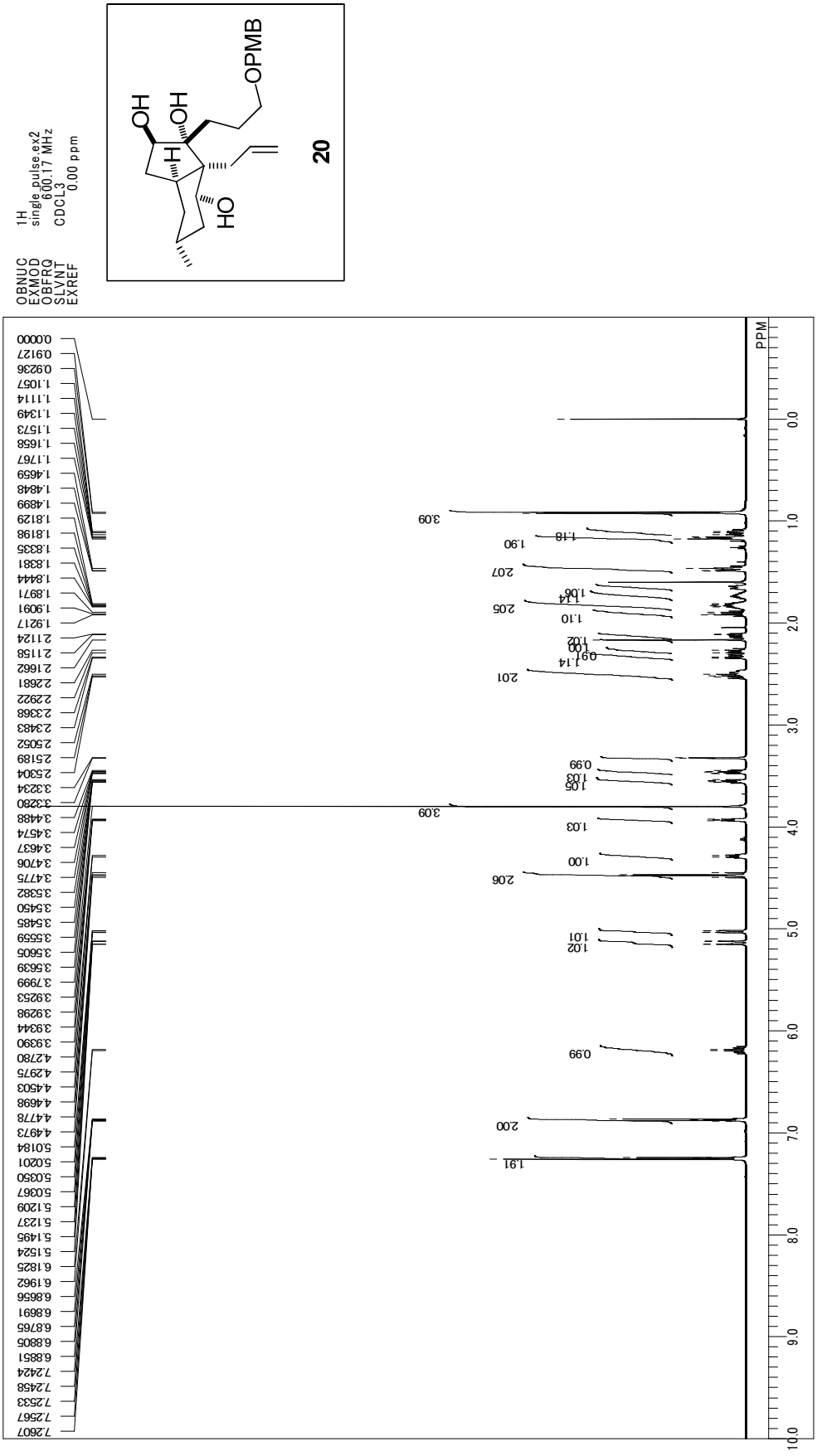
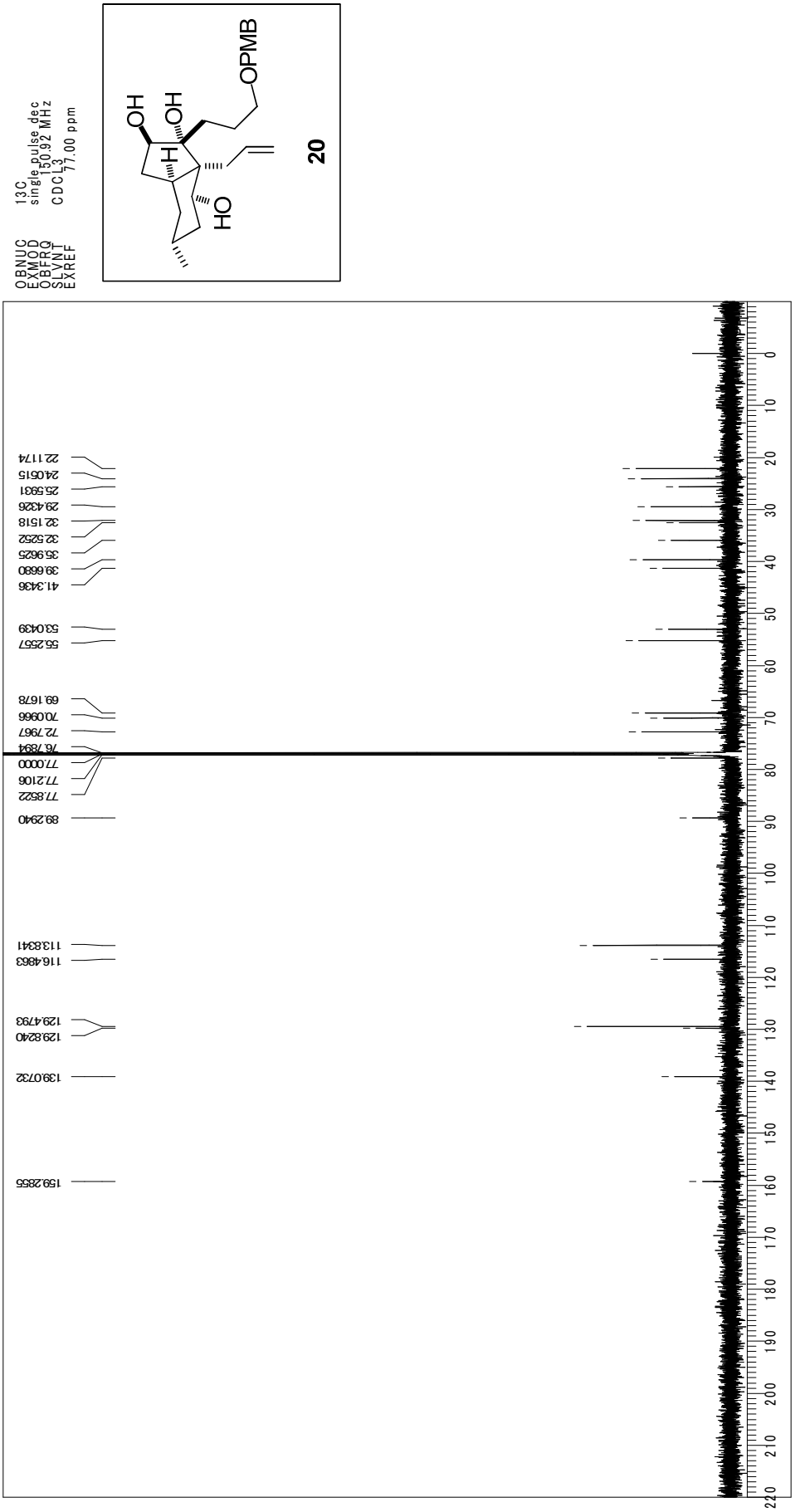
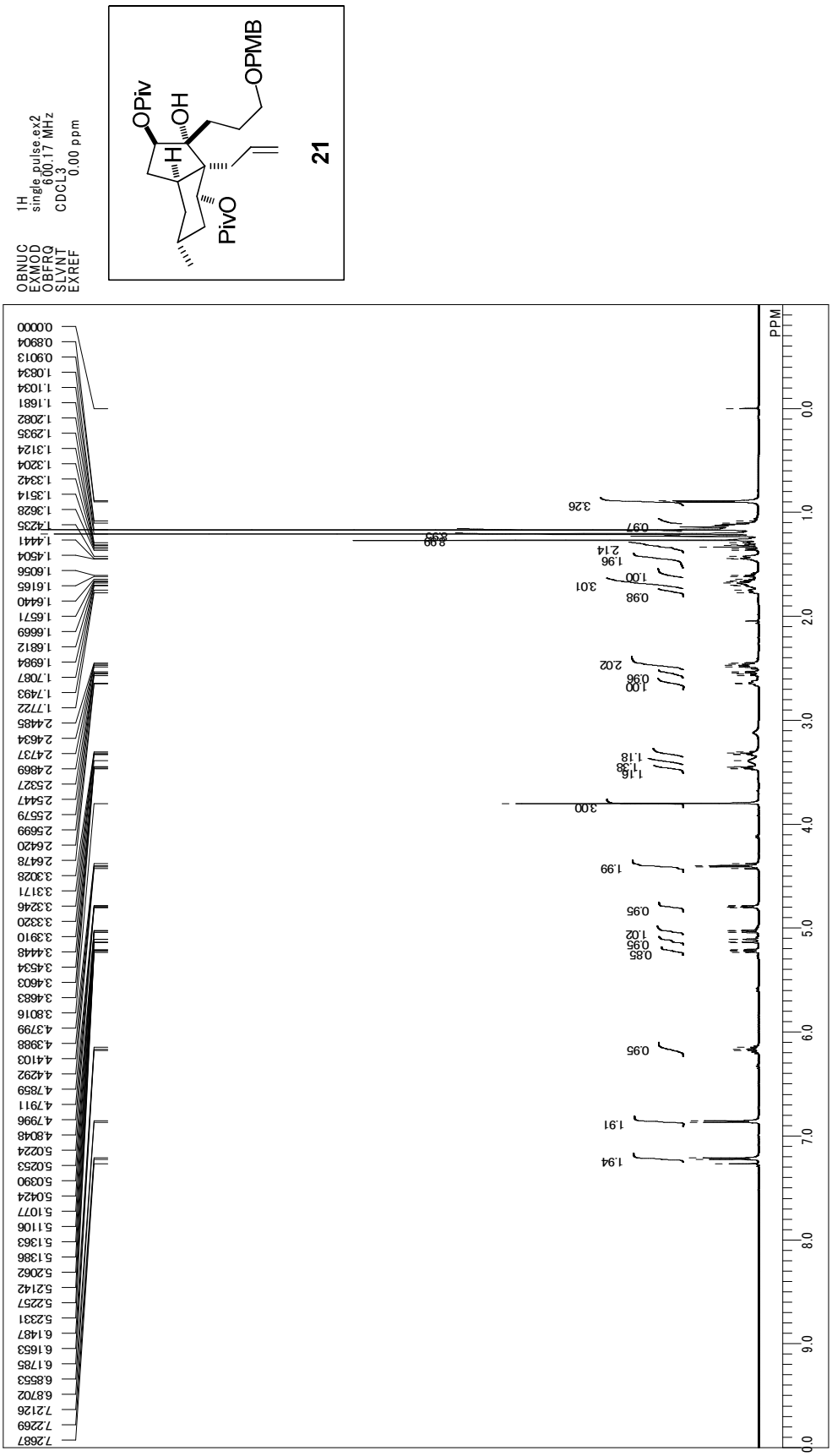
77.4213
80.4086
104.4796
113.8341
129.4602
129.5655
159.3526
215.8054

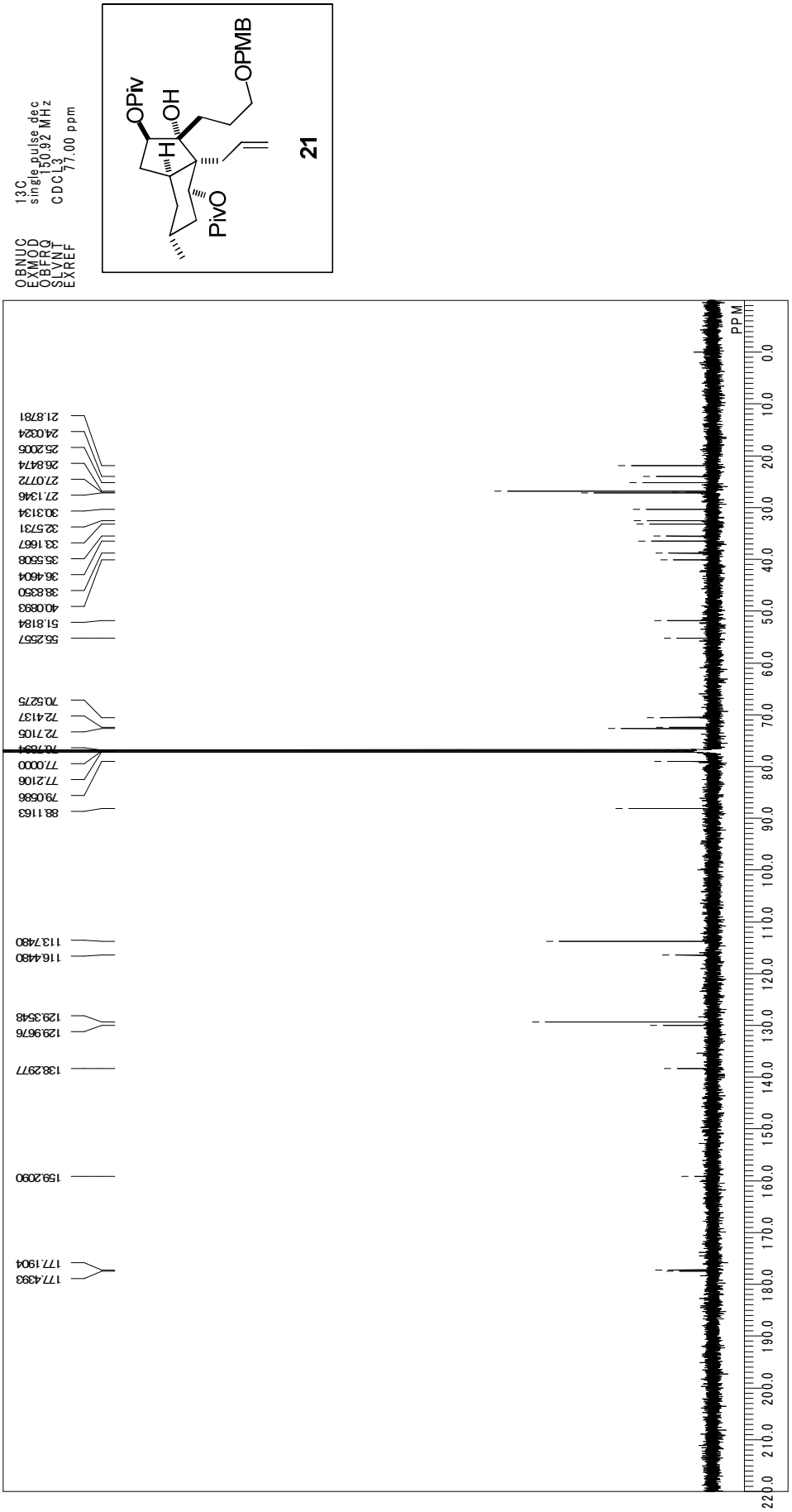

OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
1H
single pulse.ex2
600.17 MHz
CDCL3
0.00 ppm
OH
OH
H
OPMB
EtO
19
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
1.57
2.00
0.98
2.85
1.02
0.96
3.21
3.18
2.16
1.06
1.43
1.81
4.06
1.12
1.14
3.68
3.25
3.38


OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
13C
single pulse dec
150.92 MHz
CDCl3
77.00 ppm
OH
OH
H
O
OPMB
EtO
19
PPM
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0
210.0
220.0
15.3672
22.0408
22.0696
23.7643
23.9175
24.3101
27.5559
28.7623
33.9518
34.1060
36.2402
36.8243
37.4083
37.8392
38.4233
39.0265
39.6488
40.0605
54.8248
55.2174
57.2856
63.2602
63.3847
70.2785
70.5753
72.8350
72.8541
76.7798
77.0000
77.2106
77.2585
77.4117
77.8522
85.6460
86.0099
102.3823
103.9242
113.7958
113.8341
129.3740
129.4506
129.5559
159.2089


OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
1H
single_pulse.ex2
600.17 MHz
CDCL3
0.00 ppm
OH
OH
H
HO
OPMB
20
PPM


OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
13C
single pulse dec
150.92 MHz
CDCl3
77.00 ppm
OH
OH
H
HO
OPMB
20
22.1174
24.0515
25.5931
29.4326
32.1518
32.5252
35.9625
39.6680
41.3436
53.0439
55.2557
69.1678
70.0966
72.7967
76.7894
77.0000
77.2106
77.8522
89.2940
113.8341
116.4863
129.4793
129.8240
139.0732
159.2855


OPiv
OH
H
OPMB
PivO
21
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 600.17 MHz
SLVNT CDCL3
EXREF 0.00 ppm
PPM


OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
13C
single pulse dec
150.92 MHz
CDCl3
77.00 ppm
OPiv
OH
H
PivO
OPMB
21
PPM
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0
210.0
220.0
21.8781
24.0324
25.2005
26.8474
27.0772
27.1346
30.3134
32.5731
33.1667
35.5508
36.4604
38.8350
40.0893
51.8184
55.2557
70.5275
72.4137
72.7105
76.7694
77.0000
77.2106
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113.7480
116.4480
129.3548
129.9676
138.2977
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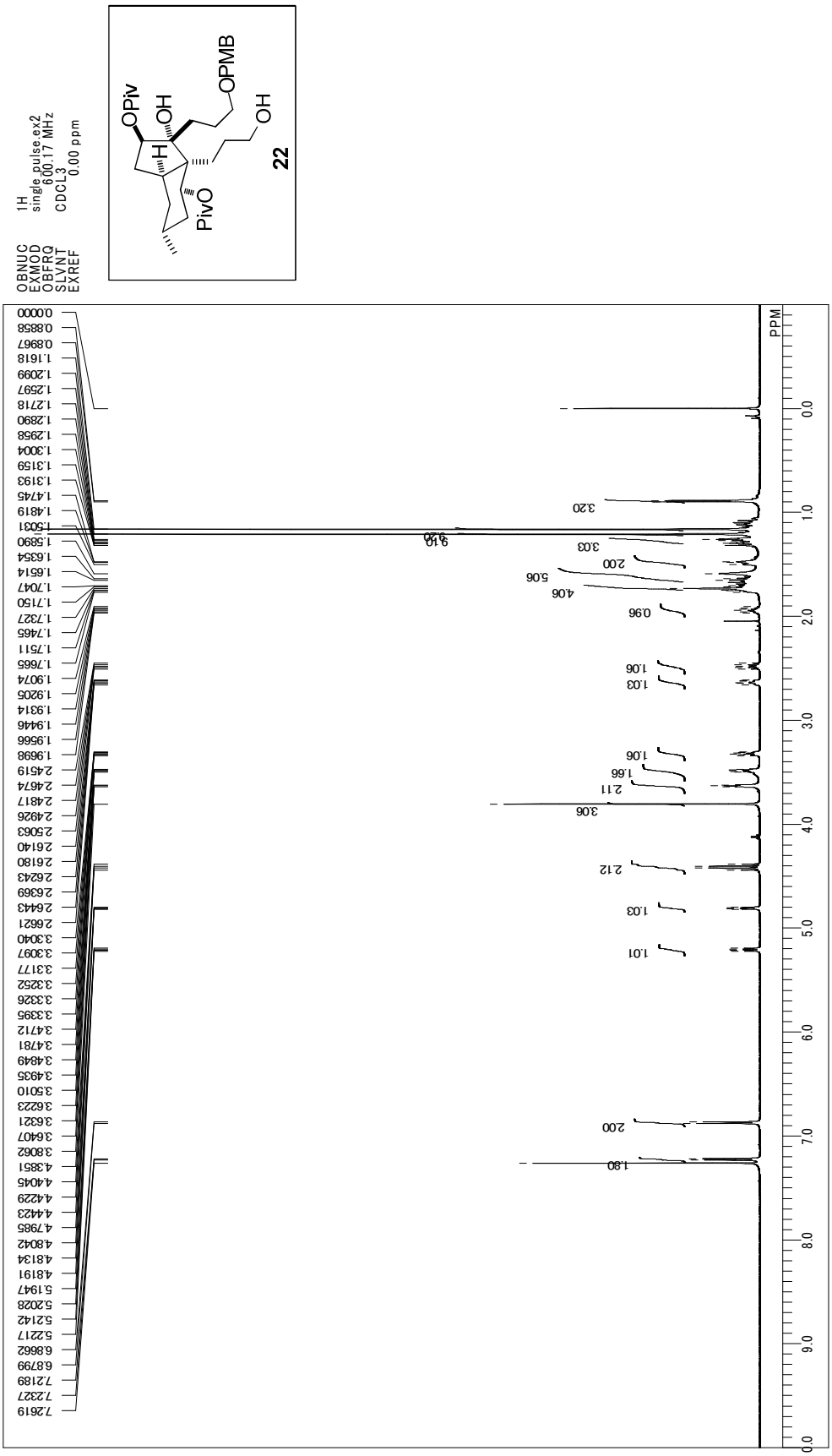
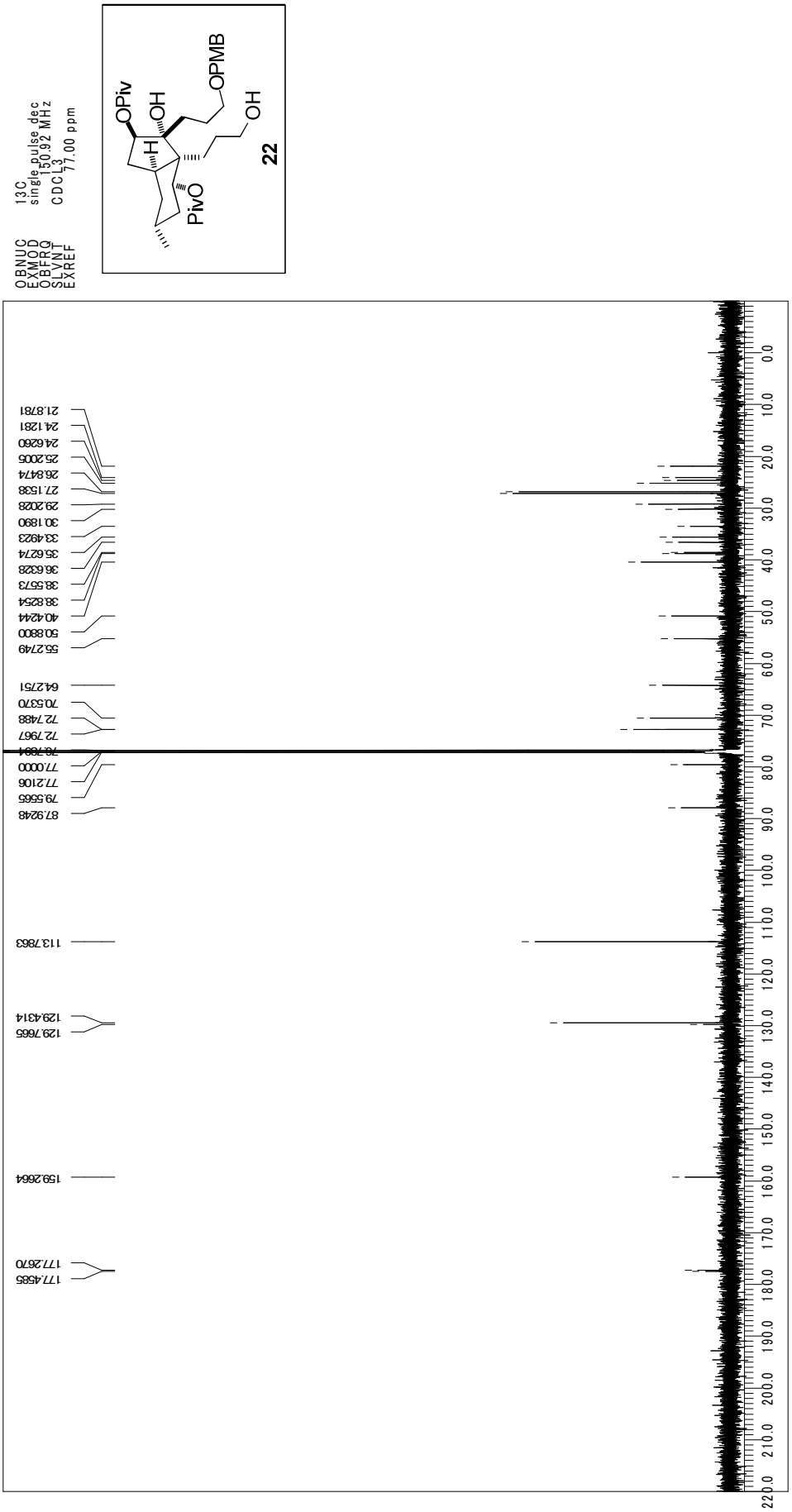
177.1904
177.4393


OPiv
OH
H
OPMB
OH
PivO
22
OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
1H
single pulse.ex2
600.17 MHz
CDCL3
0.00 ppm
PPM
9.20
9.10
5.06
4.06
3.20
3.03
3.06
2.12
2.11
2.00
1.80
1.66
1.06
1.03
1.01
0.96


OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
13C
single pulse dec
150.92 MHz
CDCl3
77.00 ppm
OPiv
OH
H
PivO
OPMB
OH
22
21.8781
24.1281
24.6260
25.2005
26.8474
27.1538
29.2028
30.1890
33.4923
35.6274
36.6328
38.5573
38.8254
40.4244
50.8800
55.2749
64.2751
70.5370
72.7488
72.7967
78.7891
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79.5565
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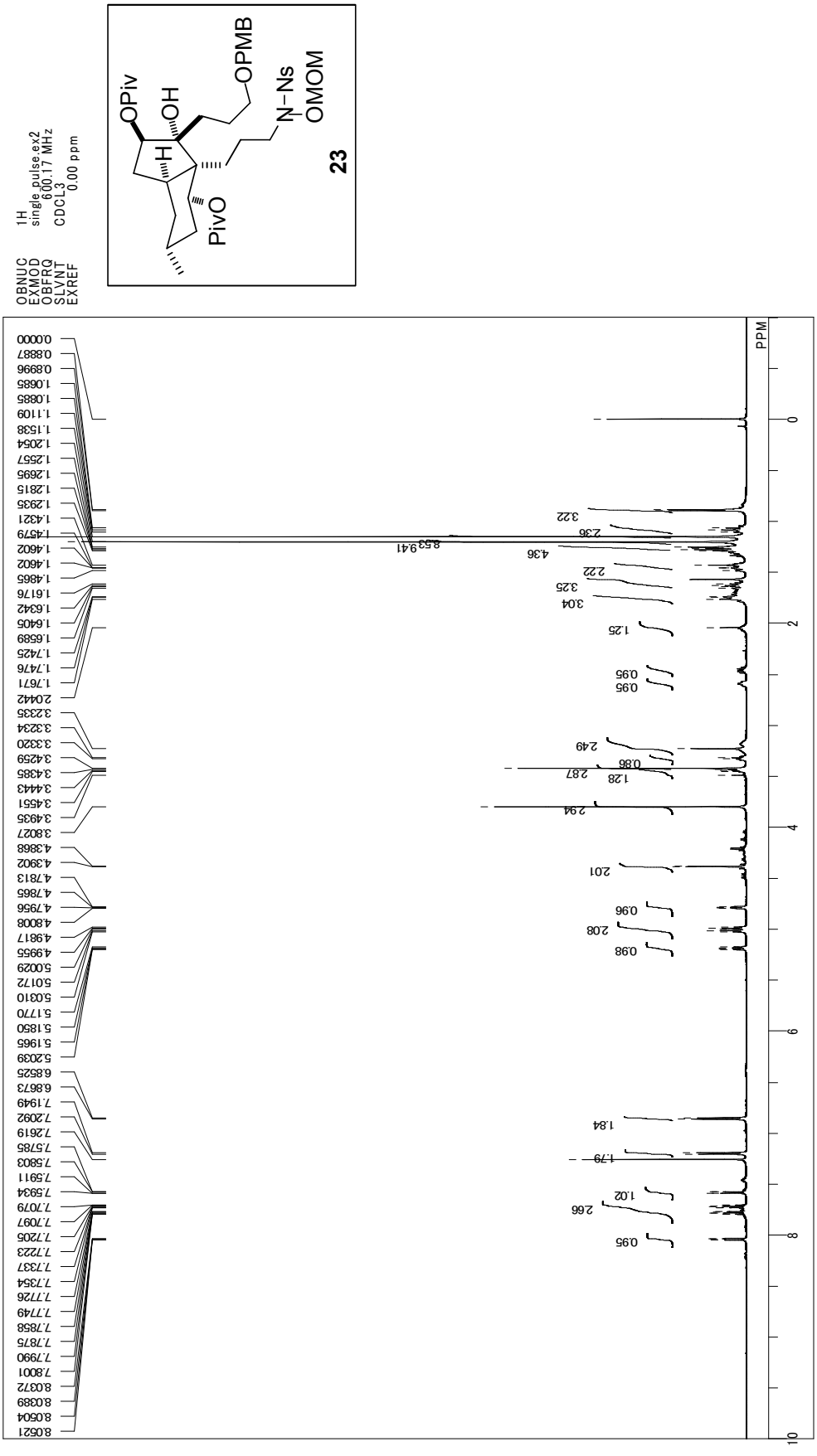
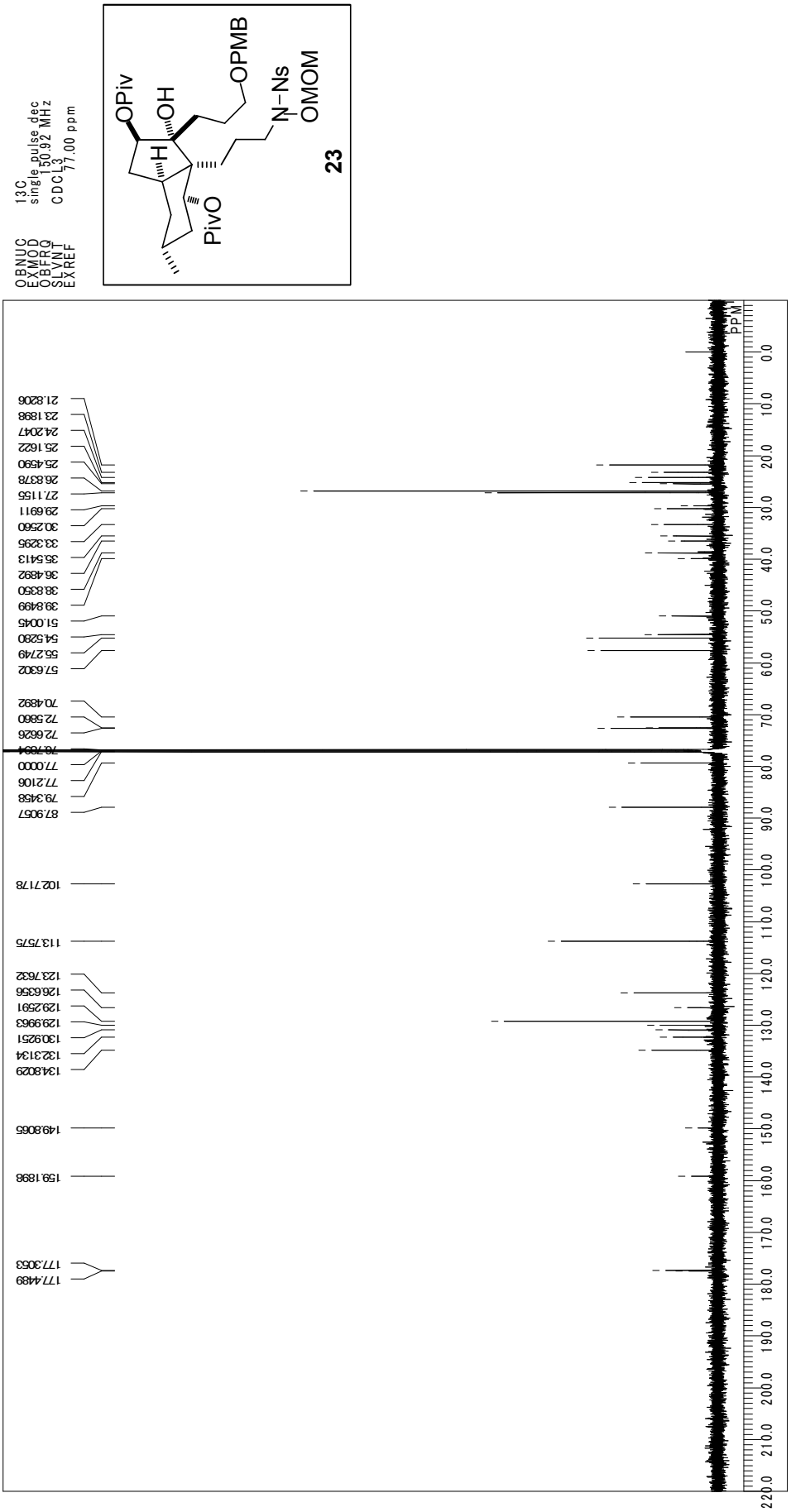
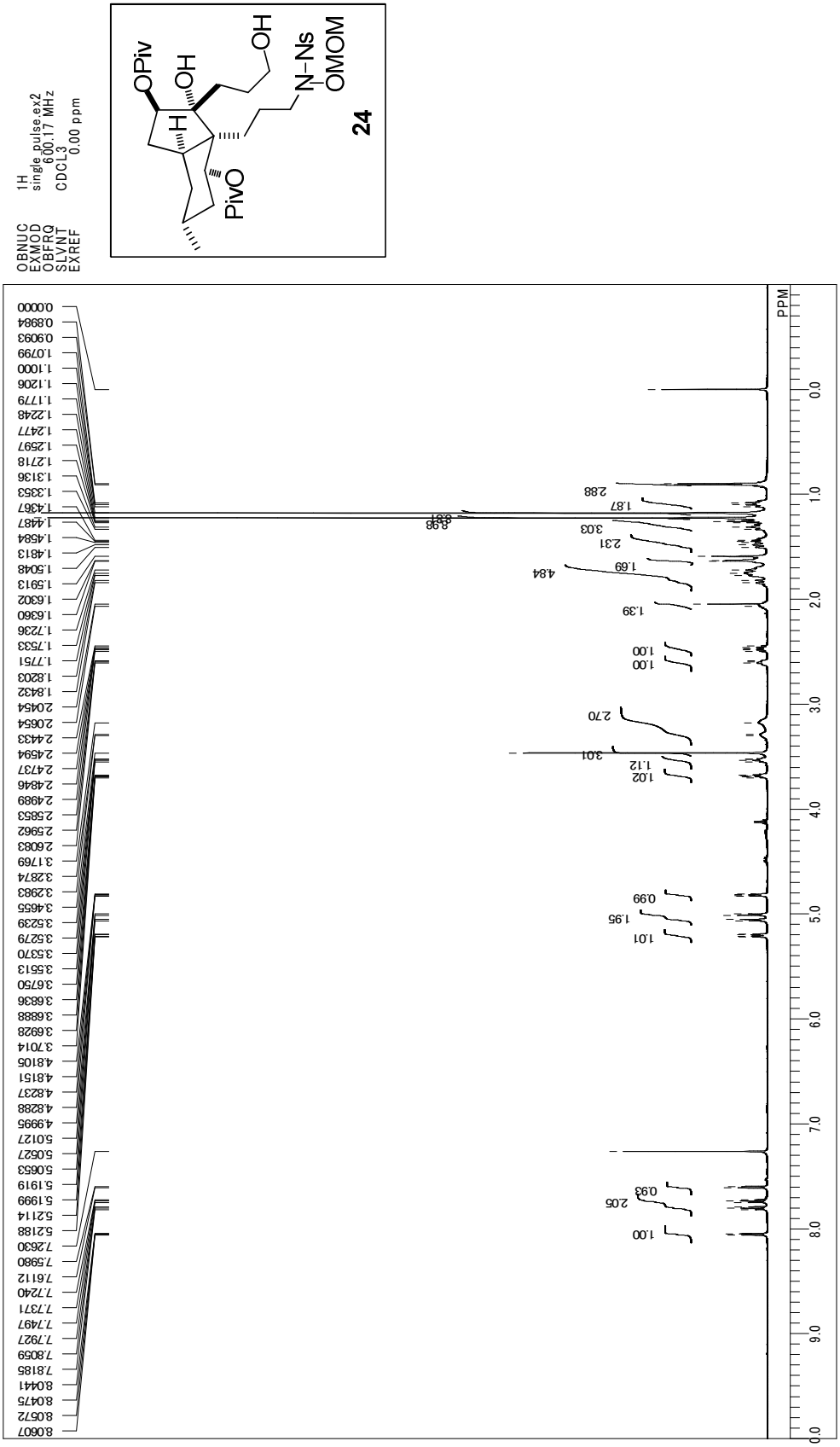
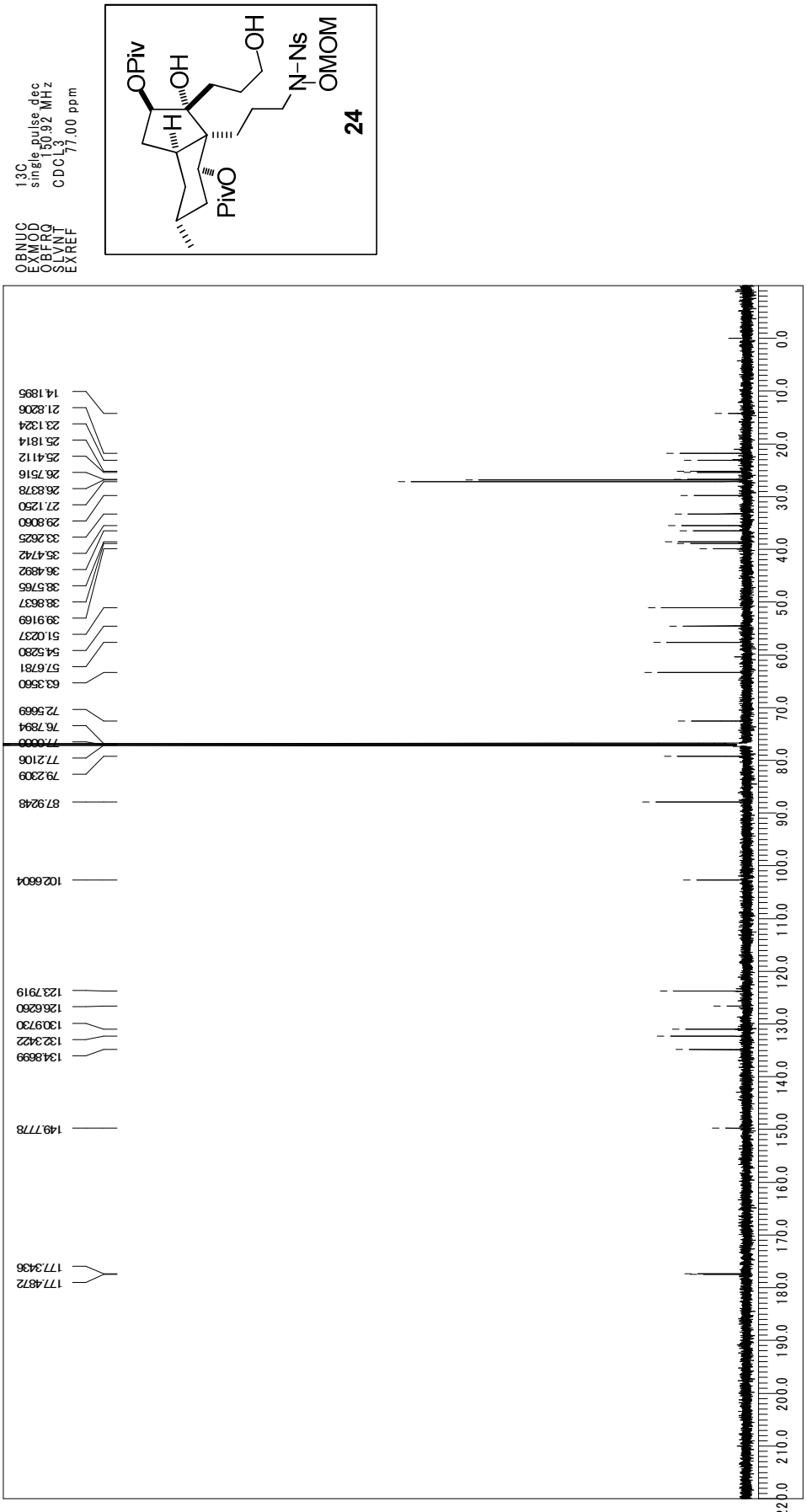
129.7665
129.4314
159.2664
177.4585
177.2670


OPiv
OH
H
PivO
OPMB
N–Ns
OMOM
23
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 600.17 MHz
SLVNT CDCL3
EXREF 0.00 ppm
PPM


OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
13C
single pulse dec
150.92 MHz
CDCl3
77.00 ppm
OPiv
OH
H
PivO
OPMB
N–Ns
OMOM
23
PPM
21.8206
23.1898
24.2047
25.1622
25.4590
26.8378
27.1155
29.6911
30.2560
33.3296
35.5413
36.4892
38.8350
39.8499
51.0045
54.5280
55.2749
57.6302
70.4892
72.5860
72.6626
78.7894
77.0000
77.2106
79.3458
87.9057
102.7178
113.7575
123.7632
126.6356
129.2591
129.9963
130.9251
132.3134
134.8029
149.8065
159.1898
177.4489
177.3063


OPiv
OH
H
PivO
OH
N–Ns
OMOM
24
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 600.17 MHz
SLVNT CDCL3
EXREF 0.00 ppm
PPM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EXMOD single pulse dec
OBFRQ 150.92 MHz
SLVNT CDCL3
EXREF 77.00 ppm
OPiv
OH
H
PivO
OH
N–Ns
OMOM
24
14.1895
21.8206
23.1324
25.1814
25.4112
26.7516
26.8378
27.1250
29.8060
33.2625
35.4742
36.4892
38.5765
38.8637
39.9169
51.0237
54.5280
57.6781
63.3560
72.5669
76.7894
77.0000
77.2106
79.2309
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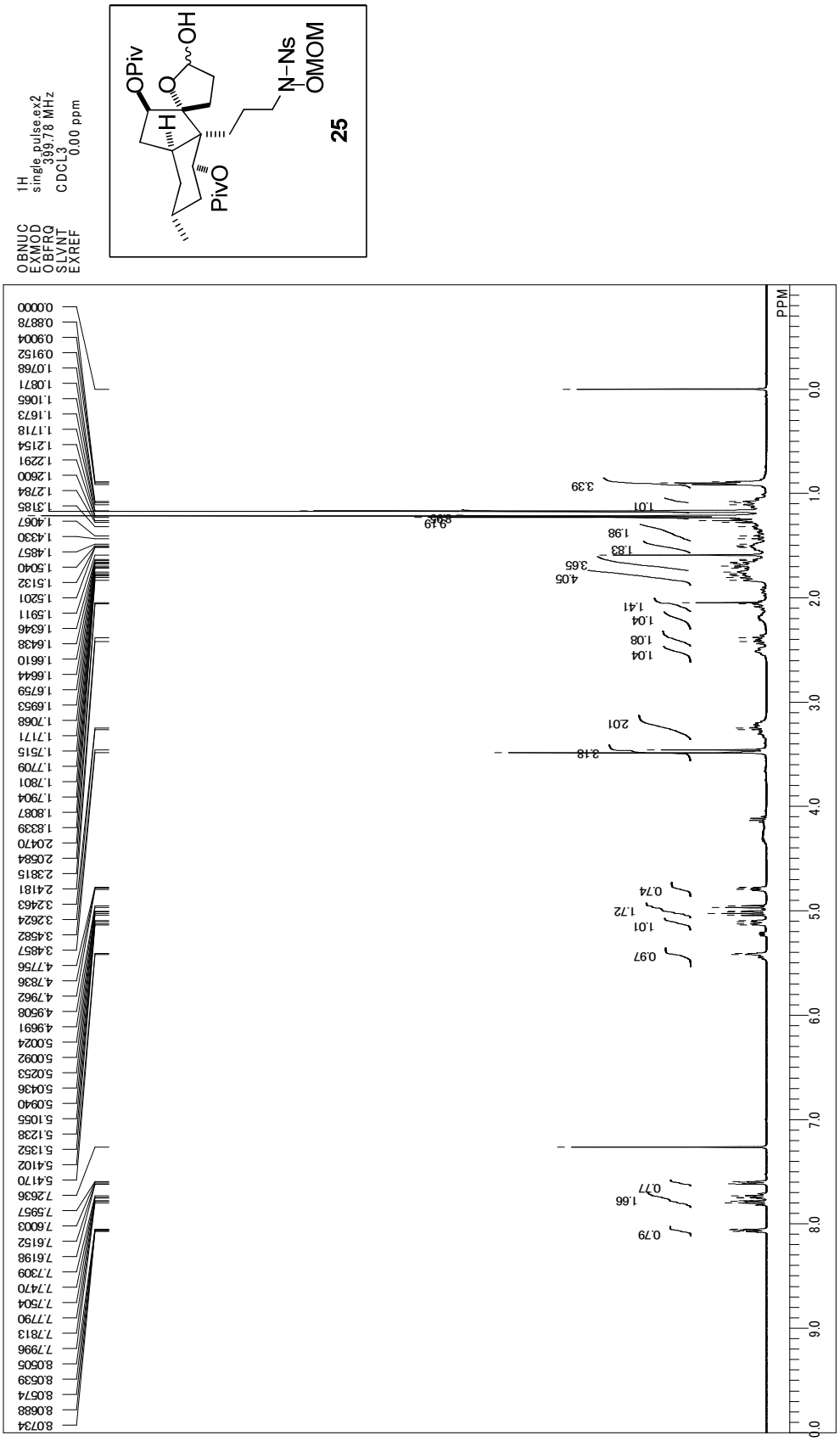
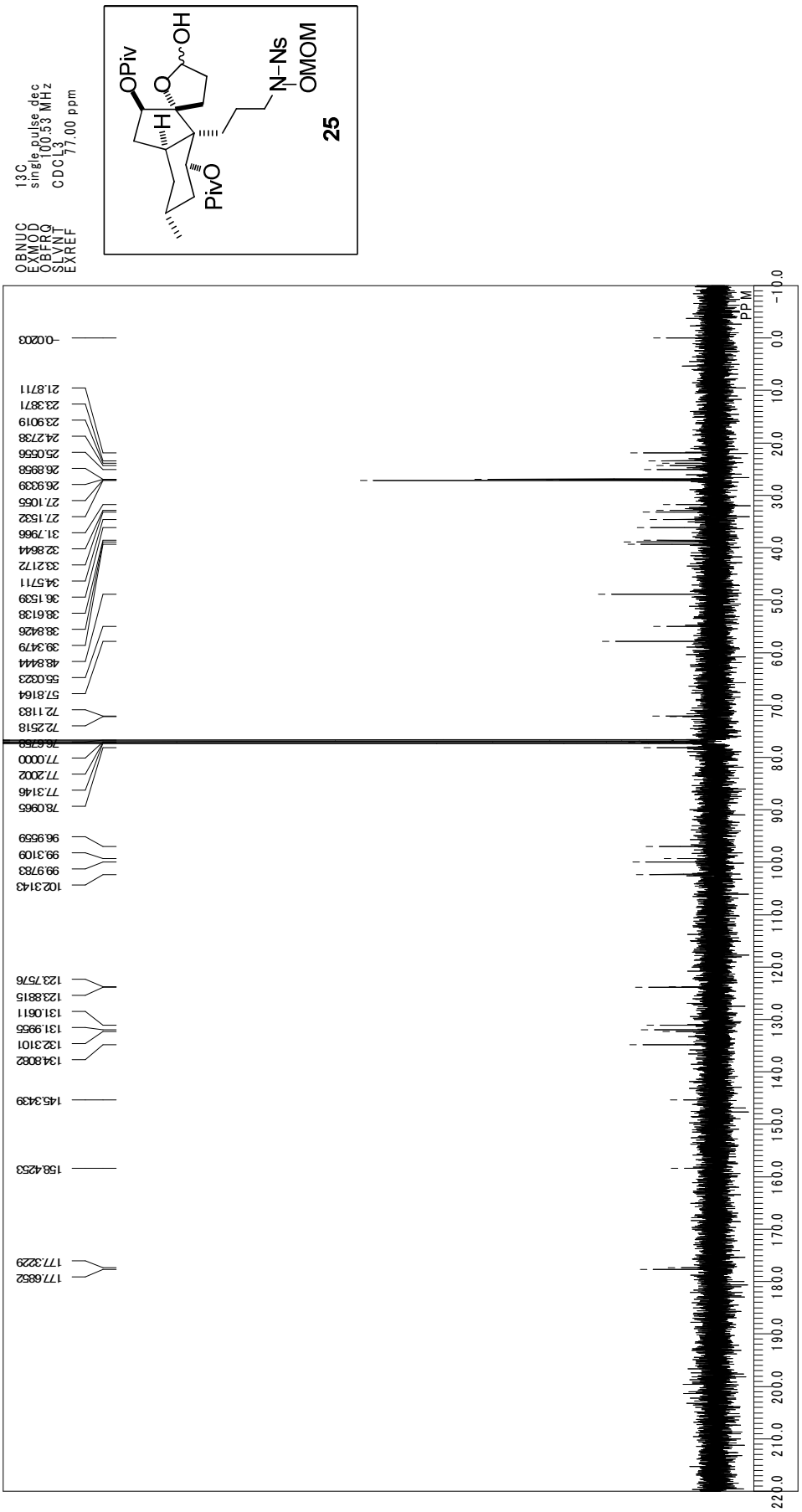
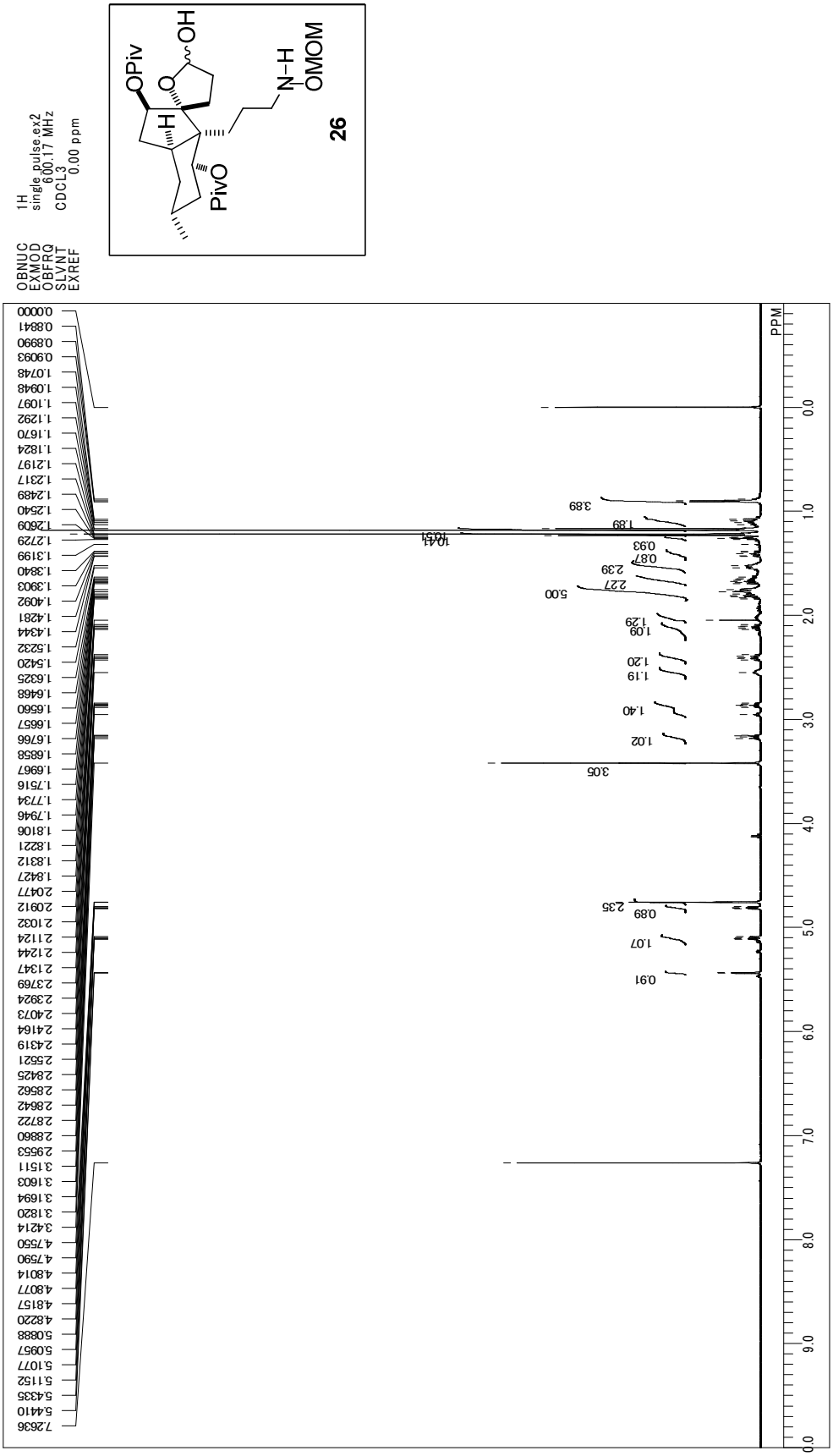
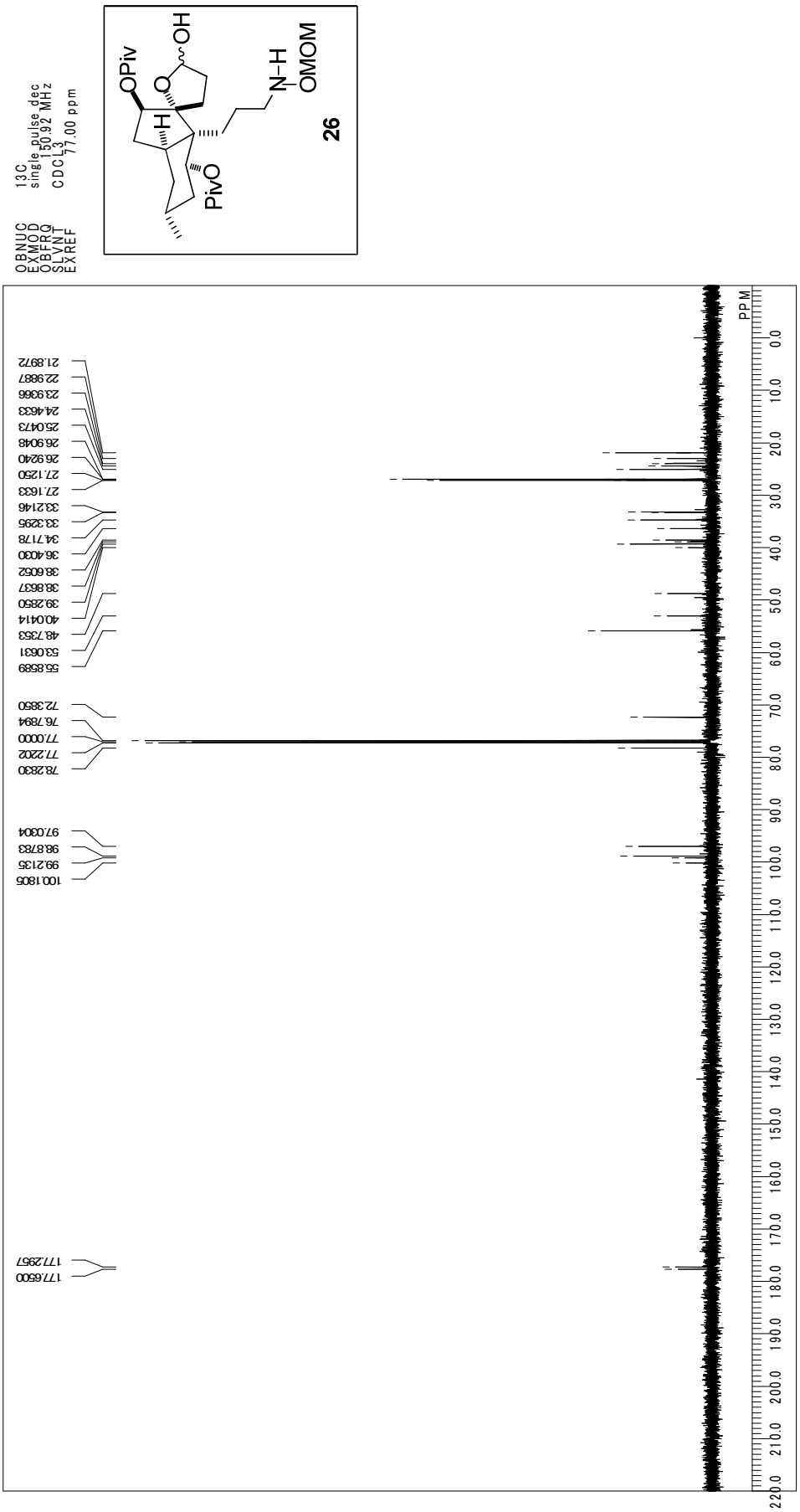
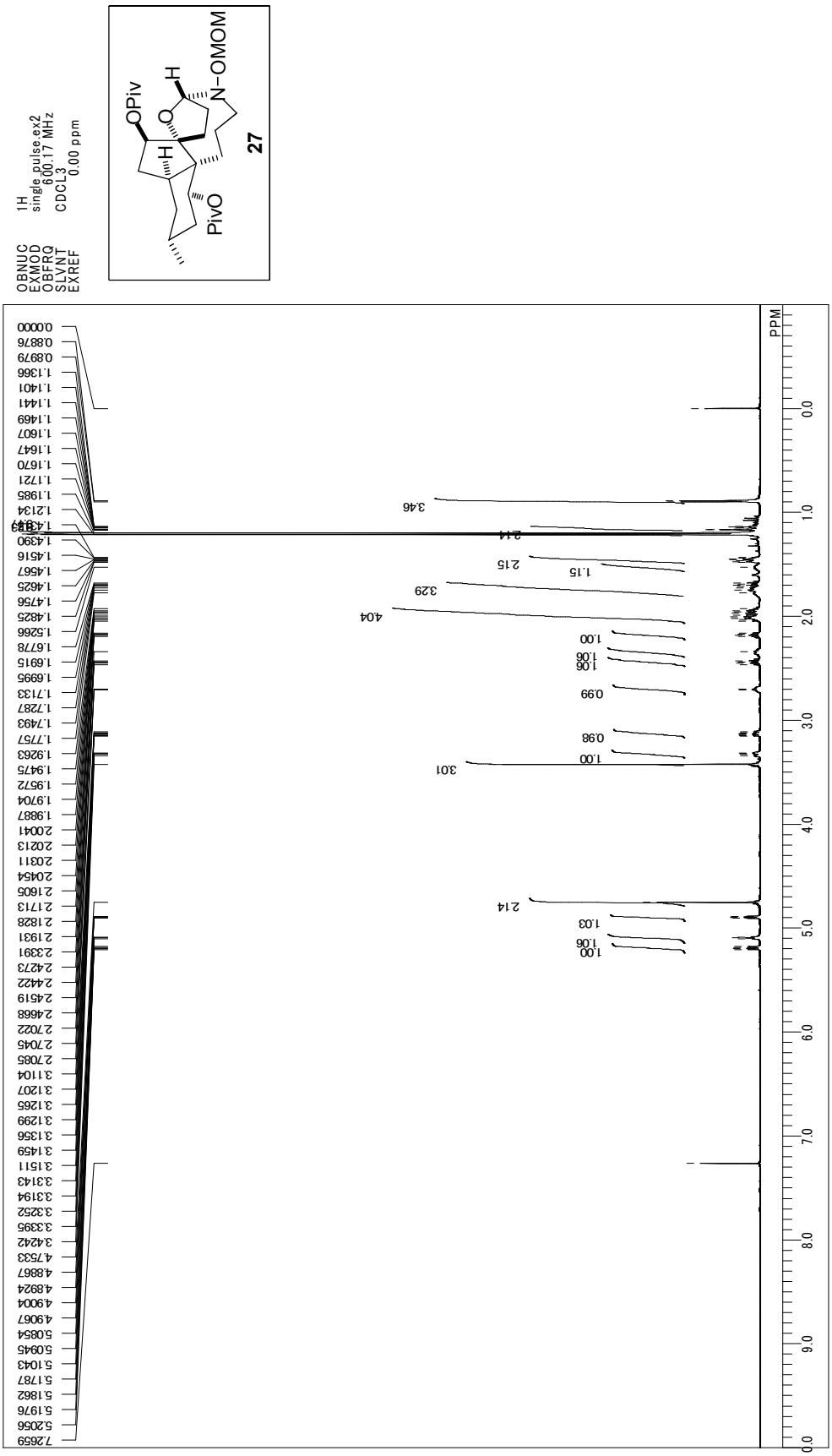
123.7919
126.6260
130.9730
132.3422
134.8699
149.7778
177.3436
177.4872

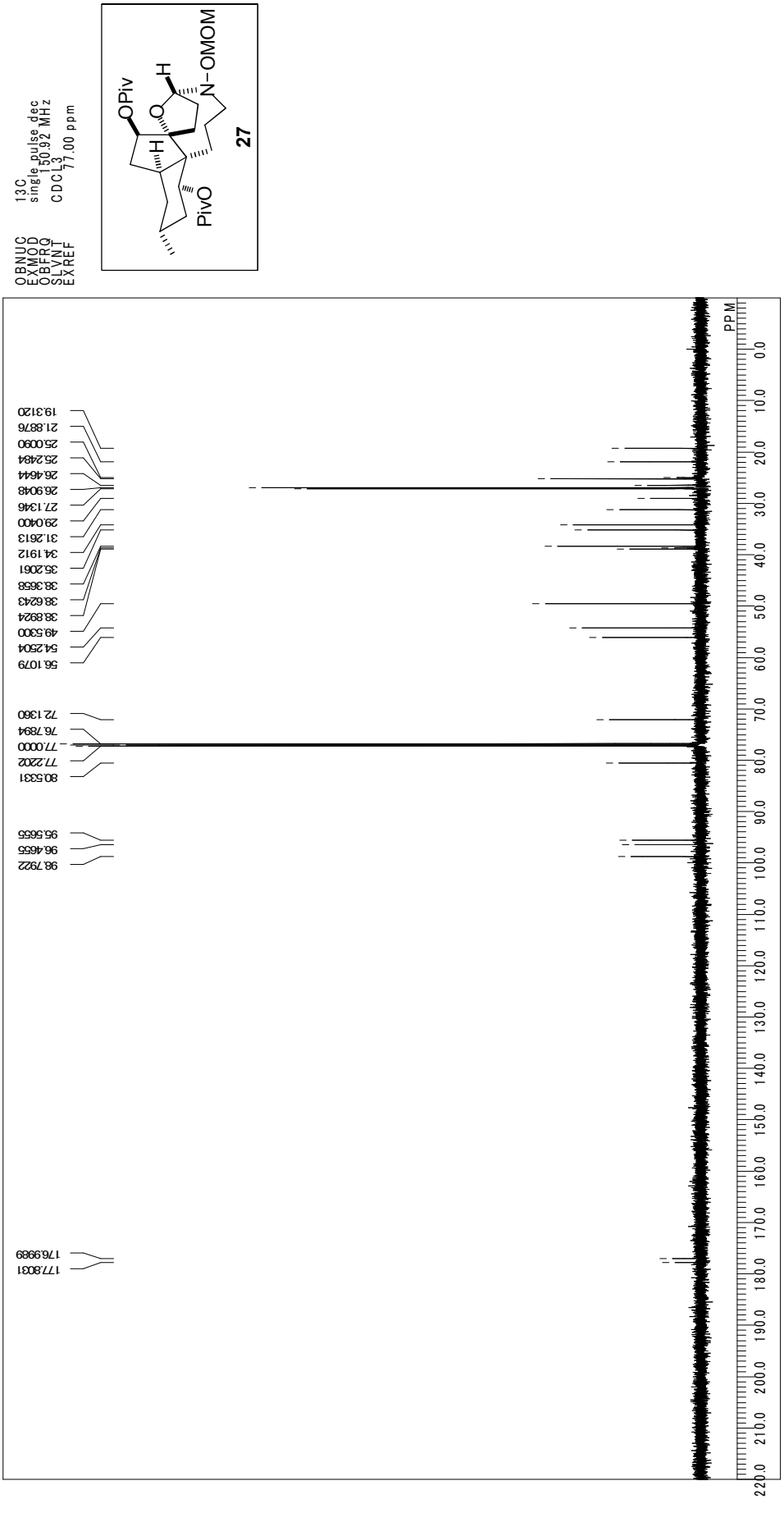

OPiv
OH
O
H
PivO
N–Ns
OMOM
25
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 399.78 MHz
SLVNT CDCL3
EXREF 0.00 ppm
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
3.39
1.01
9.19
1.98
1.83
3.65
4.05
1.41
1.04
1.08
1.04
2.01
3.18
0.74
1.72
1.01
0.97
0.79
1.66
0.77

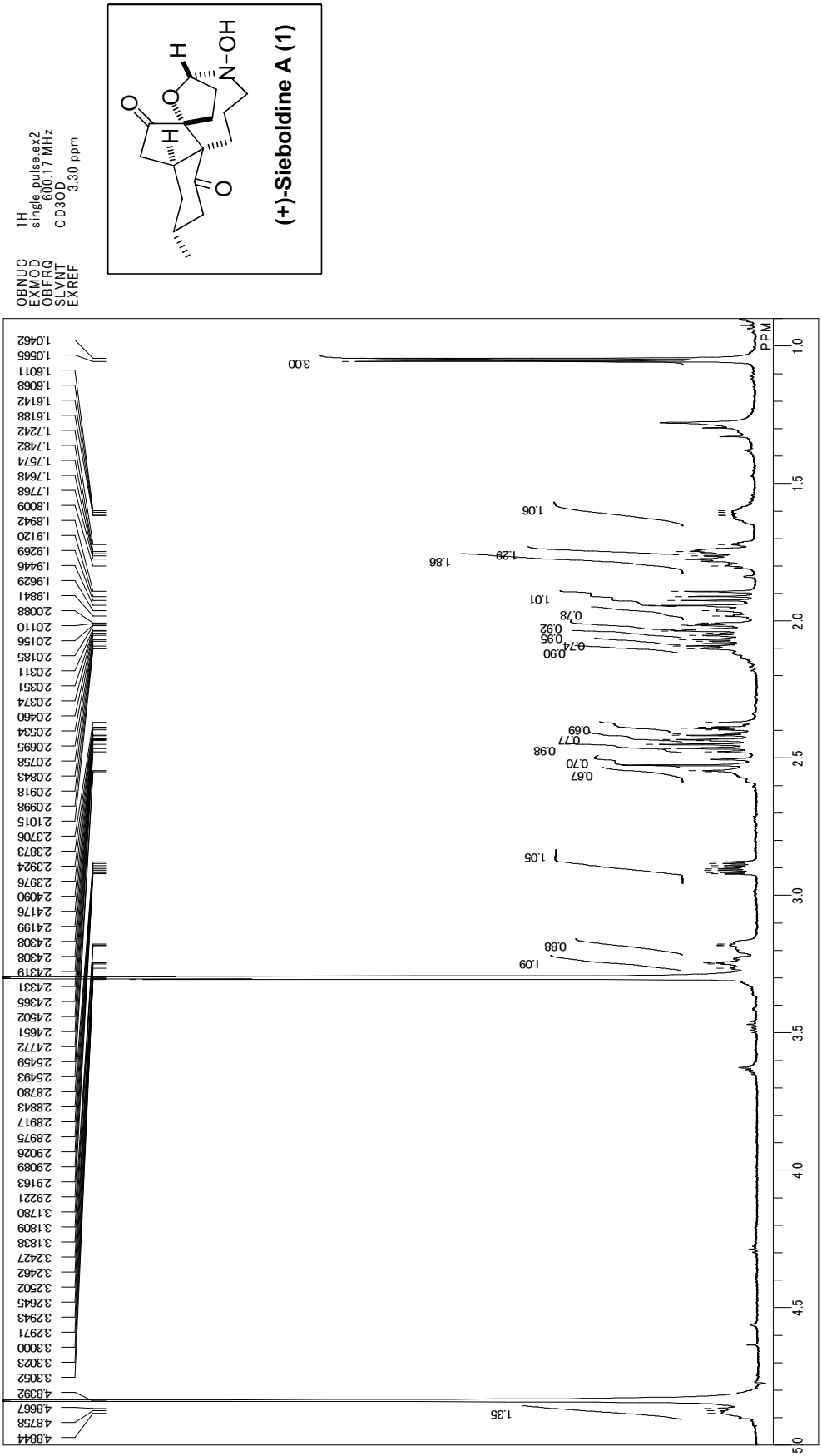

OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
13C
single pulse dec
100.53 MHz
CDCl3
77.00 ppm
OPiv
OH
O
H
PivO
N–Ns
OMOM
25
PPM
-00203
21.8711
23.3871
23.9019
24.2738
25.0556
26.8958
26.9339
27.1065
27.1532
31.7966
32.8644
33.2172
34.5711
36.1539
38.6138
38.8426
39.3479
48.8444
55.0323
57.8164
72.1183
72.2518
76.6758
77.0000
77.2002
77.3146
78.0965
96.9559
99.3109
99.9783
102.3143
123.7576
123.8815
131.0611
131.9955
132.3101
134.8082
145.3439
158.4253
177.3229
177.6852

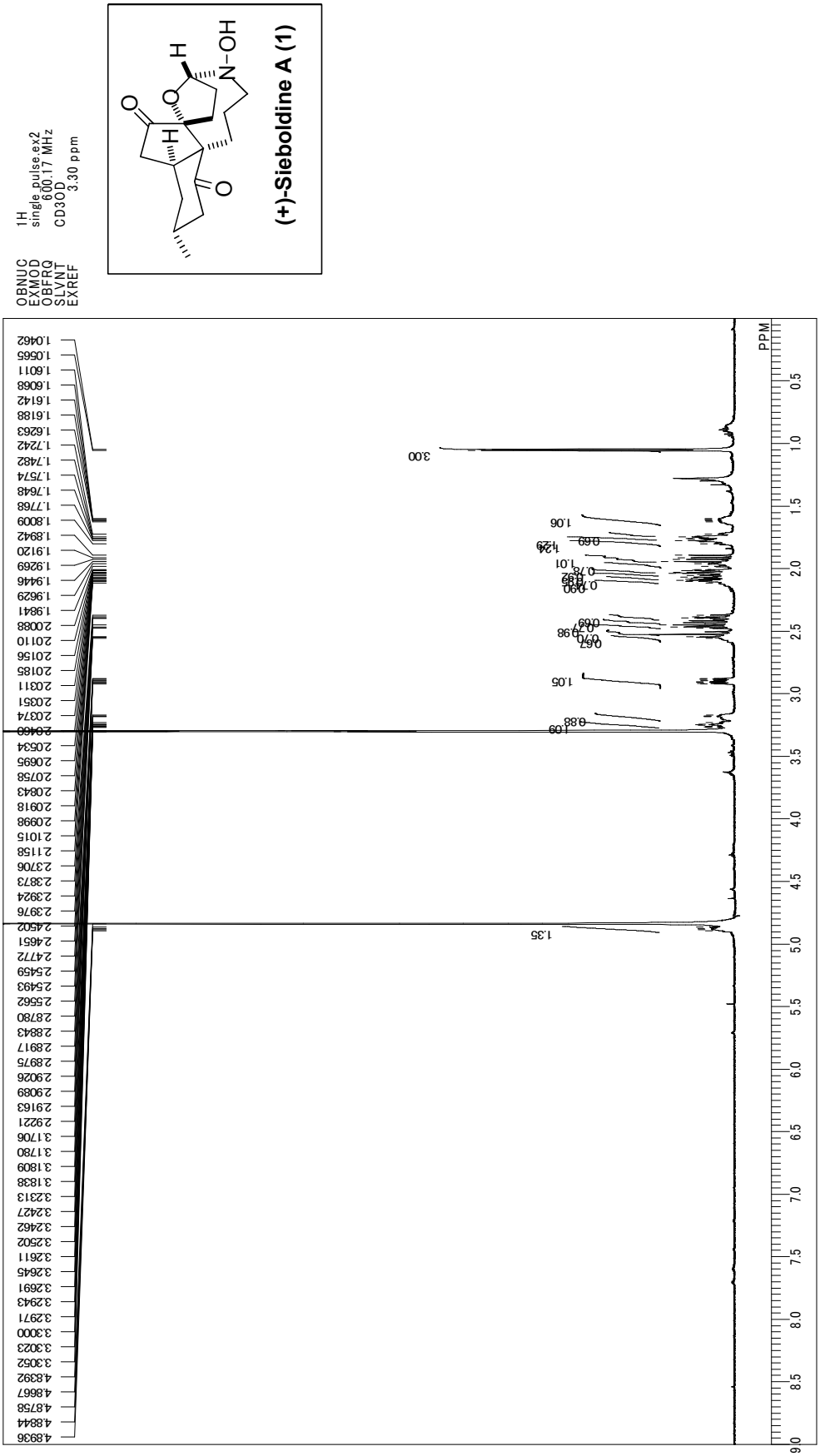

OPiv
OH
O
H
PivO
N–H
OMOM
26
OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
1H
single_pulse.ex2
600.17 MHz
CDCL3
0.00 ppm
PPM

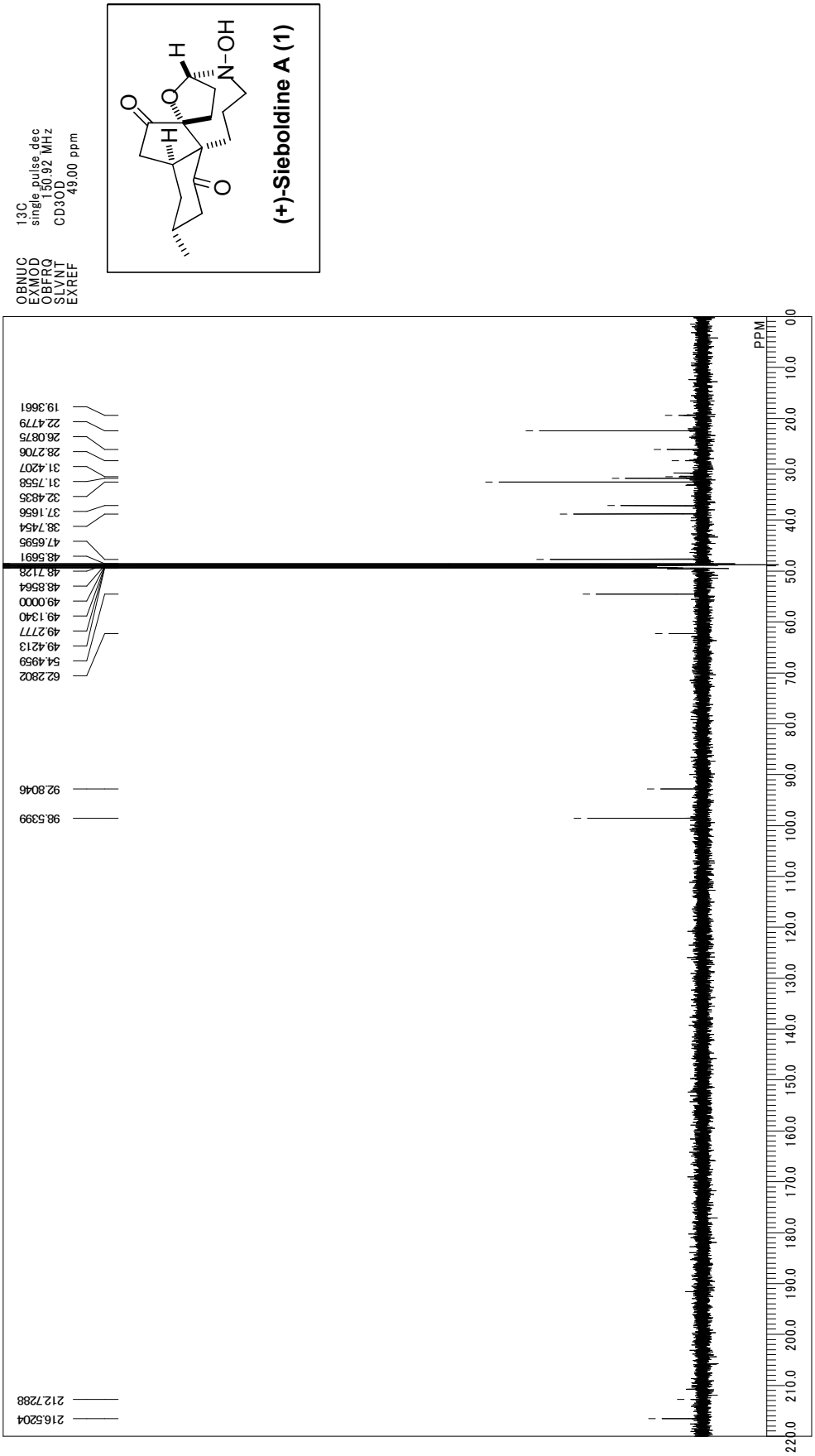

OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
13C
single pulse dec
150.92 MHz
CDCl3
77.00 ppm
OPiv
OH
PivO
N-H
OMOM
26
PPM
21.8972
22.9887
23.9366
24.4633
25.0473
26.9048
26.9240
27.1250
27.1633
33.2146
33.3295
34.7178
36.4030
38.6052
38.8637
39.2850
40.0414
48.7353
53.0631
55.8589
72.3850
76.7894
77.0000
77.2202
78.2830
97.0304
98.8783
99.2135
100.1805
177.6500
177.2957


OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
1H
single pulse.ex2
600.17 MHz
CDCL3
0.00 ppm
OPiv
H
O
H
N–OMOM
PivO
27
PPM
3.46
2.14
2.15
1.15
3.29
4.04
1.00
1.06
1.06
0.99
0.98
1.00
3.01
2.14
1.03
1.00
1.06


OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
13C
single pulse dec
150.92 MHz
CDCl3
77.00 ppm
OPiv
H
O
N–OMOM
H
PivO
27
19.3120
21.8876
25.0090
25.2484
26.4644
26.9048
27.1346
29.0400
31.2613
34.1912
35.2061
38.3658
38.6243
38.8924
49.5300
54.2504
56.1079
72.1360
76.7894
77.0000
77.2202
80.5331
95.5655
96.4655
98.7922
176.9989
177.8031
PPM


(+)-Sieboldine A (1)
1H
single_pulse.ex2
600.17 MHz
CD3OD
3.30 ppm
OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
PPM


(+)-Sieboldine A (1)
1H
single pulse.ex2
600.17 MHz
CD3OD
3.30 ppm
OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
PPM


(+)-Sieboldine A (1)
HO–N
O
H
O
H
O
OBNUC
EXMOD
OBFRQ
SLVNT
EXREF
13C
single pulse.dec
150.92 MHz
CD3OD
49.00 ppm
PPM
19.3661
22.4779
26.0875
28.2706
31.4207
31.7558
32.4835
37.1656
38.7454
47.6595
48.5691
48.7128
48.8564
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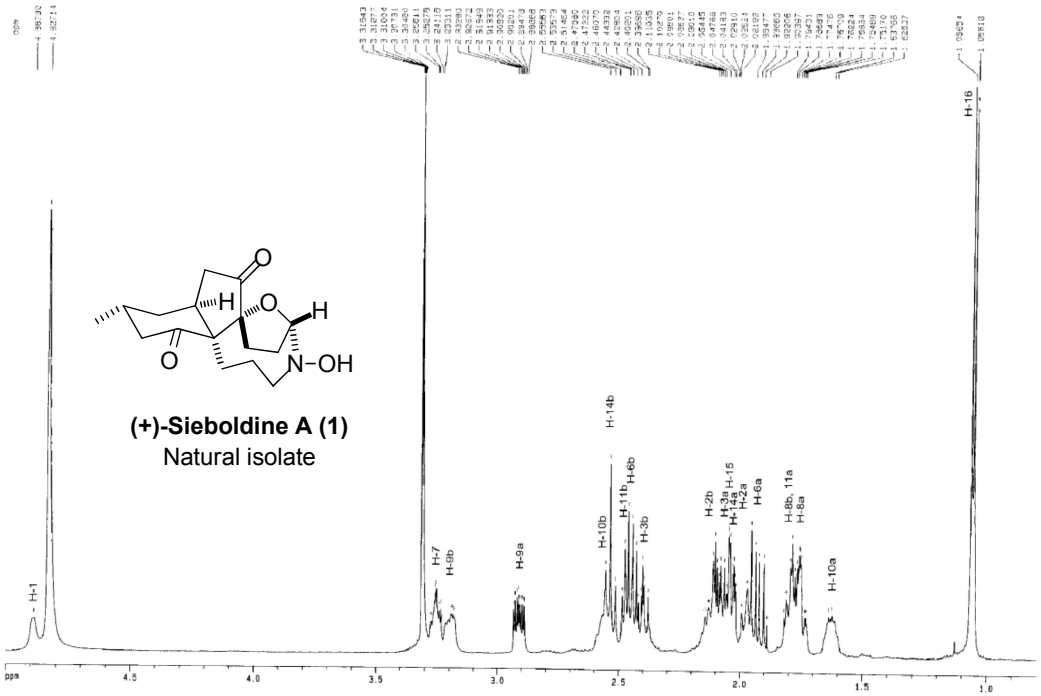
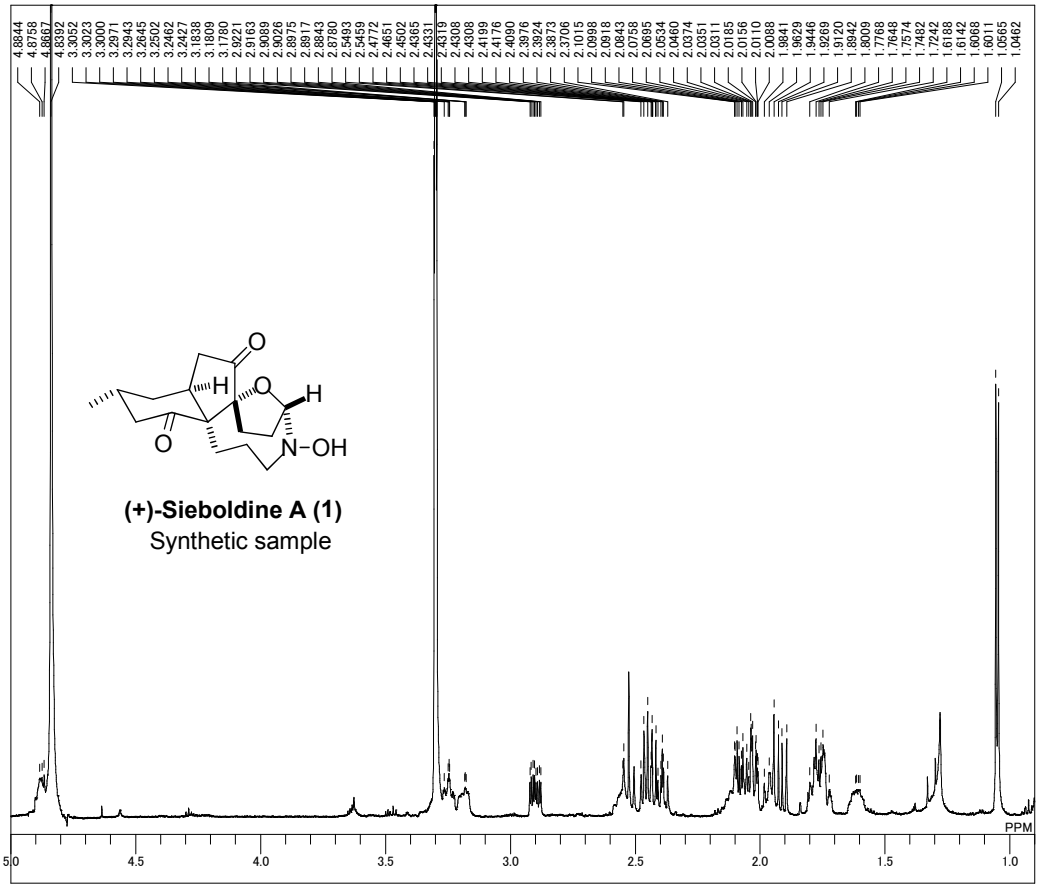
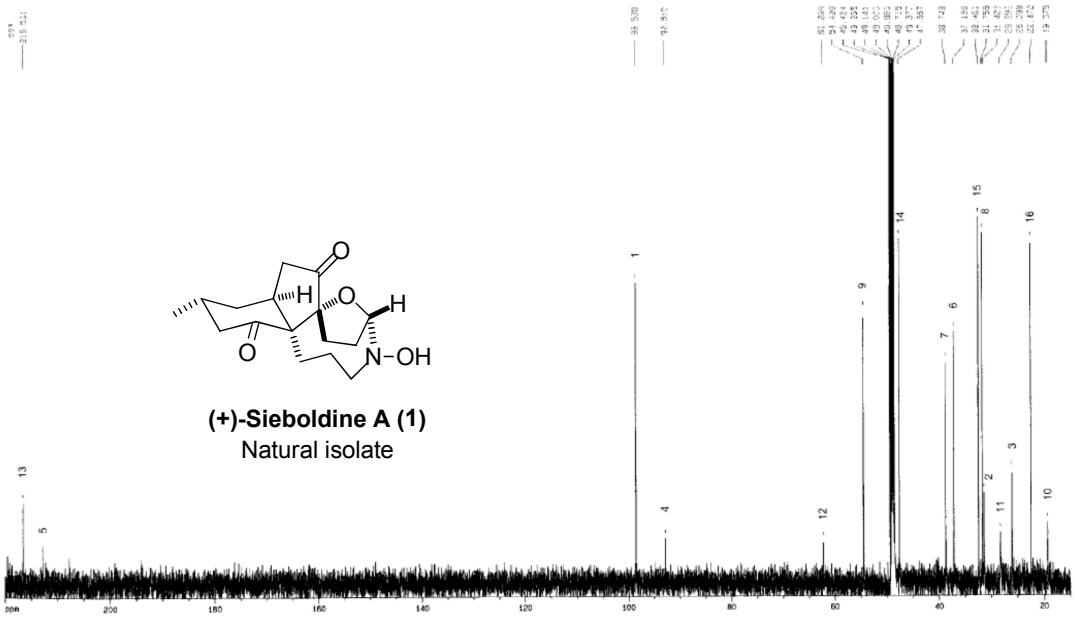
62.2802
92.8046
98.5399
212.7288
216.5204



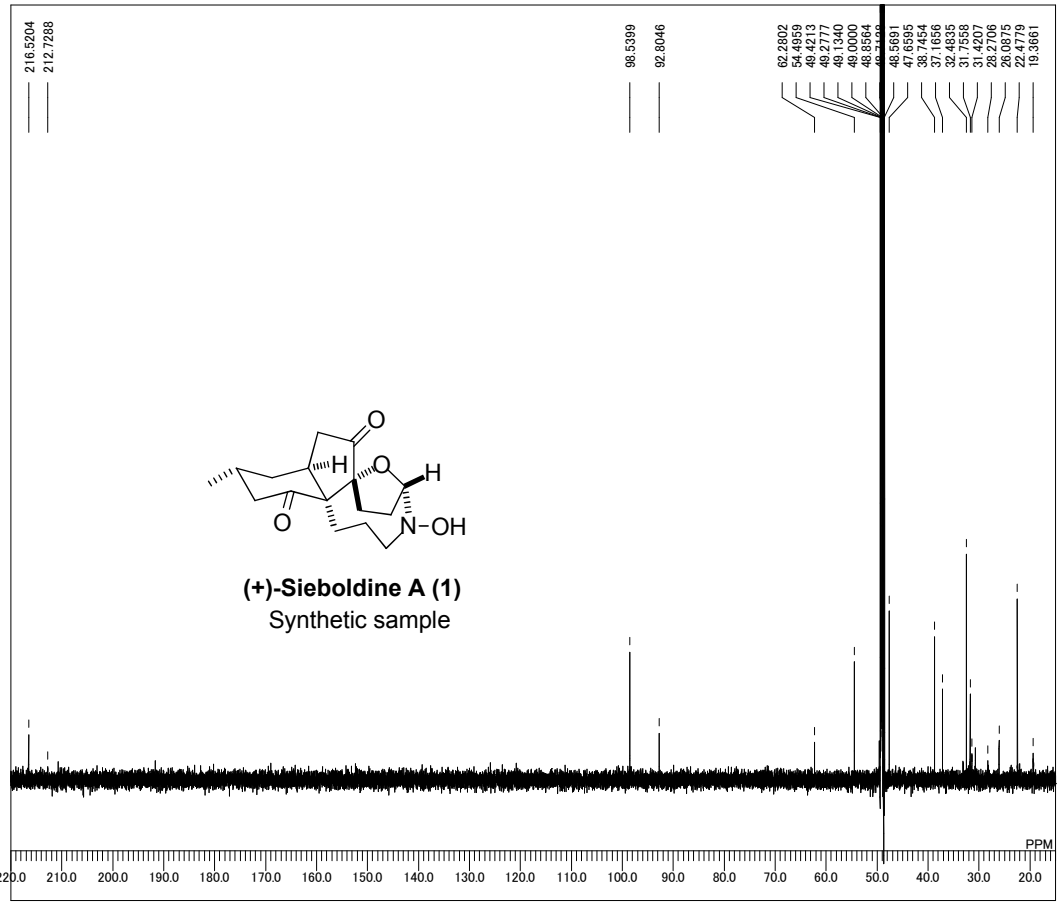
(+)-Sieboldine A (1)
Natural isolate



(+)-Sieboldine A (1)
Synthetic sample



(+)-Sieboldine A (1)
Natural isolate



(+)-Sieboldine A (1)
Synthetic sample