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Supplementary Information

Synthesis of NH006—a photostable fungicide effective against *Botrytis cinerea*—according to the asymmetric total synthesis of MK8383

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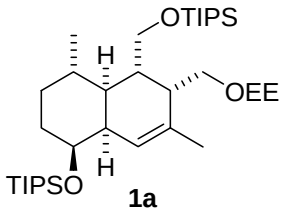
General Information. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL AL-400 spectrometer or JEOL Lambda 500 or Bruker AVANCE 600 spectrometer. ^{1}H and ^{13}C chemical shifts are reported in ppm downfield from tetramethylsilane (TMS, δ scale) with the solvent resonances as internal standards. The following abbreviations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; band, several overlapping signals; br, broad. IR spectra were recorded on a JASCO FT/IR-8300 or a HORIBA FT-730. Optical rotations were measured using a 2 ml cell with a 1 dm path length on a JASCO DIP-1000. Melting points (mp) are uncorrected, recorded on a Yanaco micro melting point apparatus MP-500P. Mass spectra and elemental analyses were provided at the Materials Characterization Central Laboratory, Waseda University. All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. All reactions were monitored by thin-layer chromatography carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and phosphomolybdic acid and heat as developing agents. KANTO CHEMICAL silica gel (spherical, neutral, particle size 0.040-0.050 mm or 0.063-0.210) was used for flash chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on self-made 0.3 mm E. Merck silica gel plates (60F-254).

Materials. THF and Et_2O were distilled from sodium/benzophenone ketyl. Toluene was distilled from sodium. MeOH was distilled with a small amount of magnesium and I_2. Benzene, MeCN were distilled from CaH_2, and all other reagents were purchased from Aldrich, TCI, or Kanto Chemical Co. Ltd.

Total synthesis of compound 12

(1*S*,4*S*,4a*S*,5*S*,6*S*,8a*S*)-6-(1-Ethoxy-ethoxymethyl)-4,7-dimethyl-1-triisopropylsilanyloxy-5-triisopropylsilanyloxymethyl-1,2,3,4,4a,5,6,8a-octahydro-naphthalene (1a)

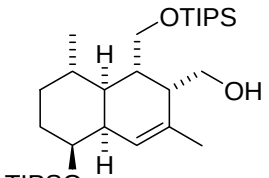


1a

To a stirred solution of alcohol **1** (0.0464 g, 0.149 mmol) in CH_2Cl_2 at –78 ºC was added DBU (0.111 mL, 0.742 mmol) and TIPSOTf (0.0950 mL, 0.341 mmol) successively, and stirring was continued for 10 min at the same temperature. The reaction was quenched with saturated aqueous NH_4Cl solution (6 mL), and the aqueous layer was extracted with CH_2Cl_2 (6 mL×3). The combined organic layer was dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 50/1) to afford TIPS ether **1a** (0.0892 g, 96%) as a colorless oil:

R_f = 0.38 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.68 (1H, s), 4.68 (1/2H, q, *J*=5.4 Hz), 4.64 (1/2H, q, *J*=5.4 Hz), 3.88-3.78 (3/2H, m), 3.70 (1H, ddd, *J*=11.2, 4.6, 4.6 Hz), 3.66-3.60 (1H, m), 3.60-3.43 (3H, m), 3.23 (1/2H, dd, *J*=9.3, 9.3 Hz), 2.66-2.59 (1H, m), 2.44-2.35 (1H, m), 2.32-2.22 (1H, m), 1.73-1.56 (6H, m), 1.43-1.25 (5H, m), 1.20 (3H, t, *J*=7.1 Hz), 1.12-0.92 (43H, m), 0.84 (3H, d, *J*=6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.4, 132.4, 123.5, 123.5, 100.1, 99.7, 73.7, 65.8, 65.1, 60.8, 60.7, 60.7, 60.5, 40.5, 40.4, 38.1, 37.9, 37.8, 37.6, 37.5, 33.8, 32.0, 28.3, 22.0, 22.0, 19.8, 19.8, 19.1, 18.2, 18.1, 15.4, 15.4, 12.5, 12.0; IR ($CHCl_3$) ν_{max} 2943, 2866, 1464, 1381, 1257, 1099, 1066, 1012, 995, 883, 814 cm^{-1}; FAB HRMS $[M\text{-}OEt]^+$ calcd for $C_{34}H_{67}O_3Si_2$: 579.4629, found: 579.4629.

(-)-(1*S*,2*S*,4a*S*,5*S*,8*S*,8a*S*)-(3,8-Dimethyl-5-triisopropylsilanyloxy-1-triisopropylsilanyloxymethyl-1,2,4a,5,6,7,8,8a-octahydro-naphthalen-2-yl)-methanol (2)

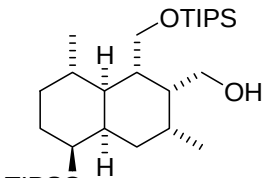


2

To a stirred solution of TIPS ether **1a** (0.0071 g, 0.0114 mmol) in ethanol (0.7 mL) was added acetic acid (0.14 mL) at room temperature, and the solution was stirred at 60 ºC for 2 days. After cooling the reaction mixture, saturated aqueous $NaHCO_3$ solution was added to the reaction mixture till no evolution of CO_2 gas was observed, and the aqueous layer was extracted with Et_2O (5 mL×3). The combined organic layer was washed with brine (5 mL) and dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 30/1) to afford alcohol **2** (0.0047 g, 75%) as a colorless oil:

R_f = 0.73 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65 (1H, s), 3.98-3.84 (2H, m), 3.71 (1H, dd, *J*=10.0, 10.0 Hz), 3.66 (1H, ddd, *J*=11.5, 4.6, 4.6 Hz), 3.48 (1H, dd, *J*=10.0, 1.5 Hz), 2.42-2.33 (1H, m), 2.31-2.19 (2H, m), 1.70 (3H, s), 1.65-1.55 (2H, m), 1.43-1.31 (1H, m), 1.30-1.00 (45H, m), 1.00-0.90 (1H, m), 0.87 (3H, d, *J*=6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.7, 122.4, 73.4, 67.2, 62.2, 46.2, 40.8, 39.2, 38.5, 33.3, 31.6, 28.6, 21.7, 18.9, 18.1, 17.9, 12.3, 11.8; IR ($CHCl_3$) ν_{max} 3502, 2943, 2866, 1464, 1383, 1248, 1215, 1111, 1068, 1014, 997, 883, 814, 798, 758 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{32}H_{65}O_3Si_2$: 553.4472, found: 553.4453; $[\alpha]_D^{28}$ –27.3 (*c* 0.53, $CHCl_3$).

(+)-(1*S*,2*R*,3*R*,4a*R*,5*S*,8*S*,8a*S*)-(3,8-Dimethyl-5-triisopropylsilanyloxy-1-triisopropylsilanyloxymethyl-decahydro-naphthalen-2-yl)-methanol (3)



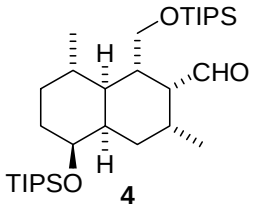
3

To a stirred suspension of Rh-Al_2O_3 (0.307 g, 5 wt. %) in a degassed mixed solvent (methanol/acetic acid = 5/1, 1.5 mL) was added a solution of alcohol **2** (0.0954 g, 0.173 mmol) in a degassed mixed

solvent (methanol/acetic acid = 5/1, 2.5 mL), and the mixture was stirred under hydrogen atmosphere at room temperature for 4 h. After completion of the reaction, the reaction mixture was filtered through a pad of Celite. The residue on Celite was washed with a small amount of Et_2O, and the filtrate and washings were partitioned between Et_2O (7 mL) and saturated aqueous $NaHCO_3$ solution (7 ml). The aqueous layer was extracted with Et_2O (7 mL×3). The combined organic layer was washed with brine (5 mL) and dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 20/1) to afford alcohol **3** (0.0426 g, 81%) as a colorless oil and **2** (0.0133 g, 14%).

R_f = 0.67 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (1H, dd, *J*=9.5, 5.9 Hz), 3.80-3.70 (2H, m), 3.65-3.55 (2H, m), 2.18-1.89 (5H, m), 1.76-1.50 (6H, m), 1.36-1.28 (1H, m), 1.16-0.94 (43H, m), 0.88 (3H, d, *J*=7.3 Hz), 0.84 (3H, d, *J*=6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 73.8, 65.1, 64.3, 45.0, 40.0, 39.8, 34.3, 34.2, 30.2, 28.7, 26.8, 26.5, 19.7, 18.1, 18.0, 16.1, 12.4, 11.9; IR ($CHCl_3$) ν_{max} 3378, 2943, 2866, 1464, 1383, 1248, 1215, 1093, 1066, 1012, 883, 816, 760 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{32}H_{67}O_3Si_2$: 555.4629, found: 555.4613; $[\alpha]_D^{26}$ +7.3 (*c* 0.70, $CHCl_3$).

(-)-(1*S*,2*R*,3*R*,4a*R*,5*S*,8*S*,8a*S*)-3,8-Dimethyl-5-triisopropylsilanyloxy-1-triisopropylsilanyloxymethyl-decahydro-naphthalene-2-carbaldehyde (4)



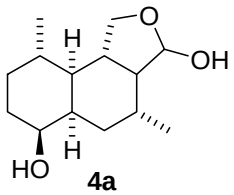
4

To a stirred solution of alcohol **3** (0.1393 g, 0.251 mmol) in CH_2Cl_2 (3 mL) was added Dess-Martin periodinane (0.748 g, 1.76 mmol), and the mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with Et_2O (3 mL), and to the solution was added saturated aqueous $NaHCO_3$ solution (3 mL) and saturated aqueous $Na_2S_2O_3$ solution (6 mL), and the aqueous layer was extracted with Et_2O (7 mL × 3). The combined organic layer was washed with brine (5 mL), dried over Na_2SO_4,

and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 60/1) to afford aldehyde **4** (0.131 g, 95%) as a colorless oil:

R_f = 0.60 (hexane/ethyl acetate = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (1H,s), 3.78 (1H, ddd, *J*=10.5, 4.9, 4.9 Hz), 3.74-3.66 (2H, m), 2.65-2.57 (1H, m), 2.55-2.46 (1H, m), 2.44-2.38 (1H, m), 2.21-2.11 (1H, m), 1.78-1.49 (6H, m), 1.42-1.34 (1H, m), 1.14-1.01 (43H, m), 0.98 (3H, d, *J*=7.1 Hz), 0.89 (3H, d, *J*=6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.5, 73.6, 64.5, 51.2, 43.2, 39.5, 34.1, 30.1, 27.1, 27.0, 26.0, 19.6, 18.1, 18.0, 18.0, 16.6, 12.3, 12.0; IR ($CHCl_3$) ν_{max} 2943, 2893, 1724, 1464, 1383, 1246, 1095, 1068, 1012, 995, 881, 825, 793 cm^{-1}; FAB HRMS $[M-H]^+$ calcd for $C_{32}H_{63}O_3Si_2$: 551.4316, found: 551.4324; $[\alpha]_D^{26}$ –10.3 (*c* 0.58, $CHCl_3$).

(4R,5aR,6S,9S,9aS,9bS)-dodecahydro-4,9-dimethylnaphtho[2,1-c]furan-3,6-diol (4a)

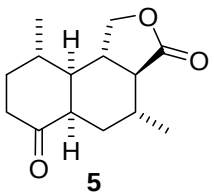


4a

To a stirred solution of **4** (0.0458 g, 0.0828 mmol) in THF (1 mL) was added a solution of TBAF in THF (0.415 mL, 1.0 M), and the reaction mixture was stirred at room temperature for 0.5 h, and then, refluxed for 1 h. The reaction was quenched with saturated aqueous NH_4Cl solution (2 mL), and extracted with EtOAc (2 mL × 3). The combined organic layer was washed with brine (3 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 1/1) to afford hydroxylactol **4a** as a colorless oil, which was immediately used for the next reaction:

R_f = 0.26 (hexane/ethyl acetate = 1/1).

(3aS,4R,5aR,9S,9aS,9bS)-decahydro-4,9-dimethylnaphtho[2,1-c]furan-3,6-dione (5)

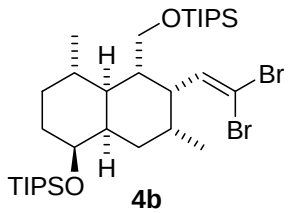


5

To a stirred solution of hydroxylactol **4a** in CH_2Cl_2 (1.5 mL) was added Dess-Martin periodinane (0.1280 g, 0.302 mmol), and the mixture was stirred over night. The reaction mixture was diluted with Et_2O (1.5 mL), and to the solution was added saturated aqueous $NaHCO_3$ solution (1.5 mL) and saturated aqueous $Na_2S_2O_3$ solution (3 mL), and the aqueous layer was extracted with Et_2O (4 mL × 3). The combined organic layer was washed with brine (4 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 60/1) to afford ketolactone **5**, which was further purified by recrystallization (CH_2Cl_2/hexane) to afford pure **5** (0.0078 g, 40% (2 steps)) as a white crystal. A single crystal was obtained by recrystallization (Et_2O/hexane):

R_f = 0.54 (hexane/ethyl acetate = 1/1); mp 159-161 ºC

(+)-(1*S*,2*R*,3*R*,4a*R*,5*S*,8*S*,8a*S*)-2-(2,2-Dibromo-vinyl)-3,8-dimethyl-5-triisopropylsilanyloxy-1-triisopropylsilanyloxymethyl-decahydro-naphthalene (4b)

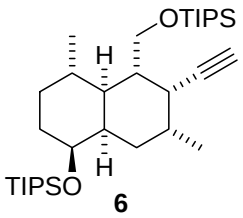


4b

To a stirred solution of CBr_4 (0.0303 g, 0.0914 mmol) in CH_2Cl_2 (0.5 mL) was added PPh_3 (0.0601 g, 0.229 mmol), and the mixture was stirred at room temperature for 10 min. To the reaction mixture was added a solution of aldehyde **4** (0.0293 g, 0.0529 mmol) in CH_2Cl_2 (0.5 mL), and the resultant solution was stirred at room temperature. After 1 h, to the reaction mixture was added a solution prepared by mixing CBr_4 (0.0306 g, 0.0923 mmol) and PPh_3 (0.0576 g, 0.220 mmol) in CH_2Cl_2 (0.5 mL), and the reaction mixture was stirred for 1 h. The reaction was quenched with saturated aqueous $NaHCO_3$ solution (4 mL), and the aqueous layer was extracted with CH_2Cl_2 (4 mL × 3). The combined organic layer was dried over Na_2SO_4 and evaporated. The residue was diluted with hexane, and the precipitate was removed filtration. The filtrate was evaporated and the residue was purified by flash chromatography (hexane) to afford dibromide **4b** (0.0314 g, 84%) as a colorless oil:

R_f = 0.68 (hexane/ethyl acetate = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.59 (1H, d, *J*=9.8 Hz), 3.78 (1H, ddd, *J*=10.2, 4.9, 4.9 Hz), 3.70 (1H, dd, *J*=9.5, 9.5 Hz), 3.65 (1H, dd, *J*=9.5, 4.1 Hz), 2.77-2.71 (1H, m), 2.16-2.05 (2H, m), 2.04-1.95 (1H, m), 1.79-1.53 (6H, m), 1.46-1.39 (1H, m), 1.14-0.99 (43H, m), 0.91 (3H, d, *J*=7.6 Hz), 0.89 (3H, d, *J*=7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.2, 88.2, 73.7, 63.3, 43.3, 43.1, 42.3, 32.7, 30.4, 30.2, 27.2, 19.8, 18.1, 18.1, 18.1, 18.0, 16.6, 12.4, 12.0; IR ($CHCl_3$) ν_{max} 2943, 2891, 1601, 1464, 1383, 1244, 1095, 1068, 1012, 995, 883, 831 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{33}H_{65}Br_2O_2Si_2$: 707.2890, found: 707.2870; $[\alpha]_D^{30}$ +20.9 (*c* 0.59, $CHCl_3$).

(-)-(1*S*,2*R*,3*R*,4a*R*,5*S*,8*S*,8a*S*)-2-Ethynyl-3,8-dimethyl-5-triisopropylsilanyloxy-1-triisopropylsilanyloxymethyl-decahydro-naphthalene (6)

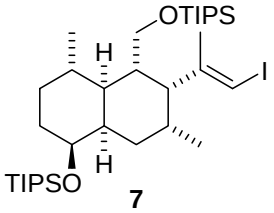


6

To a stirred solution of dibromide **4b** (0.0747 g, 0.105 mmol) in THF (1 mL) was added *n*-BuLi in hexane (0.141 mL, 1.57 M) dropwise at –78 ºC, and the reaction mixture was stirred at the same temperature for 15 min. The reaction was quenched with saturated aqueous NH_4Cl solution (2 mL), and the aqueous layer was extracted with Et_2O (3 mL×3). The combined organic layer was washed with brine (3 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 60/1) to afford alkyne **6** (0.0560 g, 97%) as a colorless oil:

R_f = 0.38 (hexane/ethyl acetate = 30/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.99-3.88 (1H, m), 3.85-3.75 (1H, m), 3.70 (1H, dd, *J*=9.3, 9.0 Hz), 2.88-2.81 (1H, m), 2.23-1.99 (4H, m), 1.78-1.68 (1H, m), 1.67-1.48 (5H, m), 1.43-1.35 (1H, m), 1.13-1.01 (43H, m), 0.97 (3H, d, *J*=7.1 Hz), 0.87 (3H, d, *J*=6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 86.0, 73.8, 70.8, 63.5, 42.6, 42.0, 32.8, 30.9, 30.0, 27.9, 19.6, 18.2, 18.1, 18.1, 17.6, 12.5, 12.3, 12.0, 11.7; IR ($CHCl_3$) ν_{max} 3311, 2943, 2866, 1464, 1381, 1246, 1093, 1068, 1012, 995, 883, 816, 798 cm^{-1}; FAB HRMS $[M-H]^+$ calcd for $C_{33}H_{63}O_2Si_2$: 547.4367, found: 547.4358; $[\alpha]_D^{26}$ –3.0 (*c* 0.66, $CHCl_3$).

(+)-(1*S*,2*R*,3*R*,4a*R*,5*S*,8*S*,8a*S*)-2-[(*E*)-2-Iodo-1-methyl-vinyl]-3,8-dimethyl-5-triisopropylsilanyloxy-1-triisopropylsilanyloxymethyl-decahydro-naphthalene (7)

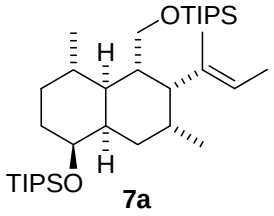


7

To a stirred solution of Cp_2ZrCl_2 (0.302 g, 1.03 mmol) in CH_2Cl_2 (1 mL) was added Me_3Al in hexane (2.91 mL, 1.05 M) at 0 ºC, and the reaction mixture was warmed to room temperature. After 30 min, the reaction mixture was cooled to –30 ºC, and to the reaction mixture was added H_2O (0.0184 mL, 1.02 mmol) dropwise and warmed to –10 ºC. After 10 min, the reaction mixture was cooled to –30 ºC again, and to the reaction mixture was added a solution of alkyne **6** in CH_2Cl_2 (1.8 mL). The reaction mixture was stirred at the same temperature for 2.5 h. After checking the disappearance of the starting material by TLC, a solution of I_2 (0.388 g, 1.53 mmol) in THF (1 mL) was added to the reaction mixture, and stirring was continued at the same temperature for 1 h. The reaction was quenched with saturated aqueous NH_4Cl solution (5 mL), and the aqueous layer was extracted with Et_2O (10 mL×3). The combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane) to afford iodoalkene **7** (0.0585 g, 83%) as a colorless oil:

R_f = 0.48 (hexane/ethyl acetate = 30/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.08 (1H, s), 3.77 (1H, ddd, *J*=10.7, 5.1, 5.1 Hz), 3.66-3.56 (2H, m), 2.41-2.28 (3H, m), 2.19-2.10 (1H, m), 1.90 (3H, s), 1.74-1.48 (6H, m), 1.46-1.39 (1H, m), 1.16-0.98 (43H, m), 0.85 (3H, d, *J*=6.3 Hz), 0.75 (3H, d, *J*=7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.4, 73.8, 63.2, 46.2, 44.8, 41.7, 34.3, 33.3, 30.4, 29.6, 27.2, 26.8, 24.6, 19.7, 18.1, 18.1, 18.1, 18.0, 15.7, 12.3, 11.9; IR ($CHCl_3$) ν_{max} 2941, 2866, 1601, 1462, 1383, 1257, 1092, 1066, 1012, 995, 918, 883, 822, 787 cm^{-1}; FAB HRMS $[M-H]^+$ calcd for $C_{34}H_{66}IO_2Si_2$: 689.3646, found: 689.3652; $[\alpha]_D^{27}$ +4.9 (*c* 0.71, $CHCl_3$).

(+)-(1*S*,2*R*,3*R*,4a*R*,5*S*,8*S*,8a*S*)-3,8-Dimethyl-2-[(*E*)-1-methyl-propenyl]-5-triisopropylsilanyloxy-1-triisopropylsilanyloxymethyl-decahydro-naphthalene (7a)

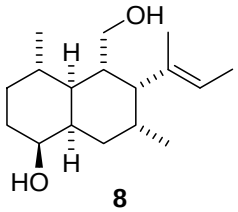


7a

To a mixture of $PdCl_2(PPh_3)_2$ (0.0030g, 0.00427 mmol) and iodoalkene **7** (0.0585 g, 0.0847 mmol) in THF (1 mL) was added a solution of Me_2Zn in THF (0.127 mL, 1.0 M) dropwise at room temperature, and the reaction mixture was stirred at the same temperature for 30 min. The reaction was quenched with saturated aqueous NH_4Cl solution (2 mL), and the aqueous layer was extracted with Et_2O (3 mL×3). The combined organic layer was washed with brine (3 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane) to afford alkene **7a** (0.0472 g, 96%) as a colorless oil:

R_f = 0.42 (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.36 (1H, q, *J*=6.1 Hz), 3.77 (1H, ddd, *J*=10.7, 5.1, 5.1 Hz), 3.67 (1H, dd, *J*=9.0, 1.0 Hz), 3.57 (1H, dd, *J*=9.0, 9.0 Hz), 2.34-2.21 (3H, m), 2.21-2.10 (1H, m), 1.74-1.54 (12H, m), 1.47-1.40 (1H, m), 1.10-0.99 (43H, m), 0.85 (3H, d, *J*=6.1 Hz), 0.74 (3H, d, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.5, 117.9, 74.0, 63.0, 44.5, 44.0, 41.2, 34.4, 33.5, 30.5, 29.1, 27.2, 27.0, 19.8, 18.2, 18.1, 18.1, 18.0, 15.7, 15.1, 13.6, 12.4, 12.0; IR ($CHCl_3$) ν_{max} 2941, 2866, 1658, 1464, 1383, 1257, 1092, 1066, 1012, 995, 908, 883, 818, 766, 737 cm^{-1}; FAB HRMS $[M-H]^+$ calcd for $C_{35}H_{69}O_2Si_2$: 577.4836, found: 577.4846; $[\alpha]_D^{28}$ +8.9 (*c* 0.57, $CHCl_3$).

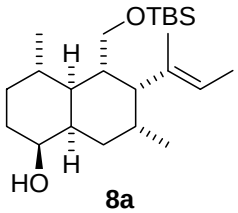
(+)-(1*S*,4*S*,4a*S*,5*S*,6*R*,7*R*,8a*R*)-5-Hydroxymethyl-4,7-dimethyl-6-[(*E*)-1-methyl-propenyl]-decahydro-naphthalen-1-ol (8)



8

To a stirred solution of **7a** (0.0447 g, 0.0772 mmol) in THF (1.5 mL) was added a solution of TBAF in THF (0.772 mL, 1.0 M), and the reaction mixture was refluxed for 1 h. The reaction was quenched with saturated aqueous NH_4Cl solution (3 mL), and extracted with Et_2O (4 mL × 3). The combined organic layer was washed with brine (3 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 1/2) to afford diol **8** (0.0206 g, 100%) as a colorless oil: R_f = 0.23 (hexane/ethyl acetate = 1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.36 (1H, q, *J*=6.1 Hz), 3.77 (1H, ddd, *J*=11.7, 4.9, 4.9 Hz), 3.71 (1H, dd, *J*=10.5, 1.7 Hz), 3.57 (1H, dd, *J*=10.5, 8.5 Hz), 2.39-2.18 (4H, m), 1.80-1.45 (14H, m), 1.44-1.35 (1H, m), 1.16-1.02 (1H, m), 0.89 (3H, d, *J*=6.3 Hz), 0.80 (3H, d, *J*=7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.2, 118.3, 73.3, 62.9, 44.5, 43.9, 40.9, 33.9, 32.7, 29.8, 28.8, 27.1, 26.7, 19.6, 15.8, 15.4, 13.7; IR ($CHCl_3$) ν_{max} 3400, 2929, 2870, 1631, 1454, 1381, 1215, 1034, 1001, 758 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{17}H_{31}O_2$: 267.2324, found: 267.2324; $[\alpha]_D^{27}$ +2.8 (*c* 0.63, $CHCl_3$).

(+)-(1*S*,4*S*,4a*S*,5*S*,6*R*,7*R*,8a*R*)-5-(*tert*-Butyl-dimethyl-silanyloxymethyl)-4,7-dimethyl-6-[(*E*)-1-methyl-propenyl]-decahydro-naphthalen-1-ol (8a)



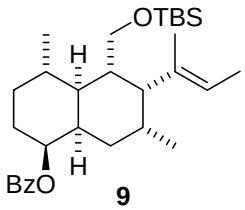
8a

To a stirred solution of diol **8** (0.0223 g, 0.0837 mmol) in CH_2Cl_2 (1 mL) was added imidazole (0.0325 g, 0.477 mmol) and TBSCl (0.0271 g, 0.180 mmol) successively at room temperature, and the reaction mixture was stirred at the same temperature for 2.5 h. The reaction was quenched with saturated

aqueous NH_4Cl solution (2 mL), and extracted with CH_2Cl_2 (3 mL × 3). The combined organic layer was dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 10/1) to afford TBS ether **8a** as a white solid:

R_f = 0.82 (hexane/ethyl acetate = 1/1); mp 84-88 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.32 (1H, q, *J*=6.6 Hz), 3.73 (1H, ddd, *J*=11.7, 4.9, 4.9 Hz), 3.55 (1H, dd, *J*=9.5, 1.7 Hz), 3.45 (1H, dd, *J*=9.5, 8.8 Hz), 2.34-2.12 (4H, m), 1.77-1.35 (14H, m), 1.11-0.98 (1H, m), 0.90-0.84 (9H, m), 0.83 (3H, d, *J*=6.3 Hz), 0.77 (3H, d, *J*=7.3 Hz), 0.06-0.00 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 118.0, 73.5, 62.5, 44.2, 40.8, 34.1, 32.6, 29.9, 28.8, 27.1, 26.8, 25.9, 19.7, 18.2, 16.0, 15.3, 13.7, -5.2, -5.3; IR ($CHCl_3$) ν_{max} 3367, 2929, 2858, 1462, 1381, 1362, 1255, 1215, 1080, 1005, 835, 762 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{23}H_{45}O_2Si$: 381.3189, found: 381.3187; $[\alpha]_D^{26}$ +11.6 (*c* 0.51, $CHCl_3$).

(+)-Benzoic acid (1*S*,4*S*,4a*S*,5*S*,6*R*,7*R*,8a*R*)-5-(*tert*-butyl-dimethyl-silanyloxymethyl)-4,7-dimethyl-6-[(*E*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl ester (9)



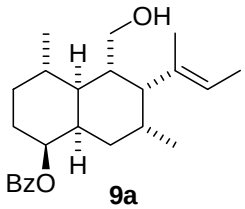
9

To a stirred solution of TBS ether **8a** (0.0228 g, 0.0599 mmol) in CH_2Cl_2 (1 mL) was added DMAP (0.0373 g, 0.305 mmol) and Bz_2O (0.0417 g, 0.184 mmol) successively, and the reaction mixture was stirred at room temperature for 3 h. The reaction was quenched with saturated aqueous NH_4Cl solution (2 mL), and extracted with CH_2Cl_2 (3 mL × 3). The combined organic layer was dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 50/1) to afford benzoate **9** as a colorless oil:

R_f = 0.35 (hexane/ethyl acetate = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-7.98 (2H, m), 7.56-7.48 (1H, m), 7.45-7.37 (2H, m), 5.31 (1H, q, *J*=6.1 Hz), 5.08 (1H, ddd, *J*=11.2, 4.9, 4.9 Hz), 3.53 (1H, dd, *J*=9.8, 1.7 Hz), 3.45 (1H, dd, *J*=9.5, 8.5 Hz), 2.45-2.35 (1H, m), 2.33-2.21 (3H, m), 1.88-1.68 (5H, m), 1.64-1.50 (8H, m), 1.26-1.10 (1H, m), 0.91-0.83 (12H, m), 0.73 (3H, d, *J*=6.8 Hz), 0.07-0.00 (6H, m);

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 136.2, 132.7, 131.0, 129.5, 128.3, 118.2, 76.4, 62.4, 44.0, 43.9, 40.9, 33.8, 30.3, 28.8, 28.2, 27.3, 26.4, 25.9, 19.7, 18.2, 16.0, 15.3, 13.7, -5.2, -5.3; IR ($CHCl_3$) ν_{max} 2929, 2856, 1716, 1603, 1585, 1450, 1381, 1362, 1315, 1275, 1217, 1176, 1115, 1070, 1026, 982, 837, 760 cm^{-1}; FAB HRMS $[M-H]^+$ calcd for $C_{30}H_{47}O_3Si$: 483.3294, found: 483.3284; $[\alpha]_D^{28}$ +44.7 (*c* 0.63, $CHCl_3$).

(+)-Benzoic acid (1*S*,4*S*,4a*S*,5*S*,6*R*,7*R*,8a*R*)-5-hydroxymethyl-4,7-dimethyl-6-[(*E*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl ester (9a)

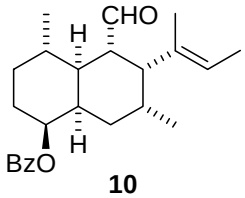


9a

To a stirred solution of benzoate **9** (0.0352 g, 0.0726 mmol) in THF (2 mL) was added a solution of TBAF in THF (0.436 mL, 1.0M) at room temperature, and the reaction mixture was stirred at the same temperature for 2 days. The reaction was quenched with saturated aqueous NH_4Cl solution (4 mL), and extracted with Et_2O (6 mL × 3). The combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 8/1) to afford diol **9a** (0.0264, 98%) as a colorless oil:

R_f = 0.30 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09-8.00 (2H, m), 7.59-7.51 (1H, m), 7.48-7.40 (2H, m), 5.37 (1H, q, *J*=6.6 Hz), 5.13 (1H, ddd, *J*=11.5, 4.9, 4.9 Hz), 3.69 (1H, dd, *J*=10.0, 2.0 Hz), 3.59 (1H, dd, *J*=10.0, 8.8 Hz), 2.53-2.43 (1H, m), 2.38-2.26 (3H, m), 1.91-1.50 (14H, m), 1.28-1.16 (1H, m), 0.94 (3H, d, *J*=6.3 Hz), 0.77 (3H, d, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 136.1, 132.7, 130.9, 129.5, 128.3, 118.5, 76.2, 62.8, 44.2, 43.9, 40.8, 35.6, 30.3, 28.8, 28.0, 27.3, 26.4, 19.6, 15.9, 15.4, 13.7; IR ($CHCl_3$) ν_{max} 3452, 2929, 1712, 1603, 1585, 1450, 1381, 1315, 1282, 1217, 1176, 1117, 1070, 1026, 980, 758 cm^{-1}; FAB HRMS $[M-H]^+$ calcd for $C_{24}H_{35}O_3$: 371.2586, found: 371.2583; $[\alpha]_D^{25}$ +30.2 (*c* 0.67, $CHCl_3$).

(+)-Benzoic acid (1*S*,4*S*,4a*R*,5*S*,6*R*,7*R*,8a*R*)-5-formyl-4,7-dimethyl-6-[(*E*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl ester (10)

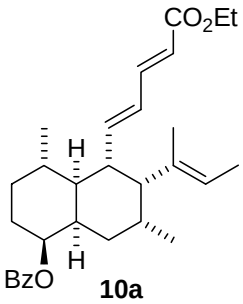


10

To a stirred solution of alcohol **9a** (0.0220 g, 0.0594 mmol) in CH_2Cl_2 (1.5 mL) was added Dess-Martin periodinane (0.0768 g, 0.181 mmol), and the mixture was stirred at room temperature. After disappearance of the starting material, the reaction mixture was diluted with Et_2O (1.5 mL), and to the solution was added saturated aqueous $NaHCO_3$ solution (1.5 mL) and saturated aqueous $Na_2S_2O_3$ solution (3 mL), and the aqueous layer was extracted with Et_2O (5 mL × 3). The combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 20/1) to afford **10** (0.0198 g, 90%) as a colorless oil:

R_f = 0.60 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (1H,s), 8.04-7.98 (2H, m), 7.57-7.51 (1H, m), 7.47-7.40 (2H, m), 5.34 (1H, q, *J*=6.6 Hz), 5.15 (1H, ddd, *J*=11.7, 4.9, 4.9 Hz), 2.91-2.84 (1H, m), 2.61-2.54 (1H, m), 2.54-2.44 (1H, m), 2.35-2.26 (1H, m), 2.12-2.04 (1H, m), 1.98-1.74 (4H, m), 1.72 (3H, s), 1.71-1.62 (5H, m), 1.34-1.20 (1H, m),0.89 (3H, d, *J*=6.7 Hz), 0.85 (3H, d, *J*=7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.4, 165.6, 134.8, 132.7, 130.9, 129.5, 128.3, 119.7, 75.2, 48.9, 43.3, 42.0, 33.3, 31.2, 29.3, 27.6, 27.0, 26.3, 19.3, 15.7, 15.0, 13.7; IR ($CHCl_3$) ν_{max} 2933, 2873, 2727, 1712, 1603, 1583, 1450, 1381, 1313, 1277, 1176, 1115, 1070, 1026, 980, 756 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{24}H_{32}O_3Na$: 391.2249, found: 391.2252; $[\alpha]_D^{25}$ +105.9 (*c* 0.60, $CHCl_3$).

(+)-Benzoic acid (1*S*,4*S*,4a*S*,5*S*,6*R*,7*R*,8a*R*)-5-[(1*E*,3*E*)-4-ethoxycarbonyl-buta-1,3-dienyl]-4,7-dimethyl-6-[(*E*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl ester (10a)

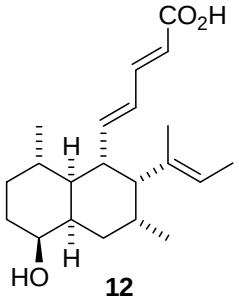


10a

To a stirred solution of phosphonate **11** (0.0430 g, 0.172 mmol) in THF (0.3 mL) was added a solution of LiHMDS in THF (0.126 mL, 1.07 M) dropwise at –78 ºC, and the reaction mixture was stirred at the same temperature. After 30 min, to the reaction mixture was added a solution of aldehyde **10** (0.0198 g, 0.0537 mmol) in THF (1 mL) at –78 ºC. The reaction mixture was stirred at the same temperature for 2 h, and then, warmed to 0 ºC and stirred for 2 h. The reaction was quenched with saturated aqueous NH_4Cl solution (1.5 mL), and the aqueous layer was extracted with Et_2O (3 mL × 3). The combined organic layer was washed with brine (3 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 20/1) to afford a mixture of ester **10a** containing aldehyde **10**. This mixture was subjected to the reaction described above under the same conditions to afford ester **10a** (0.0228 g, 91%) as a colorless oil:

R_f = 0.60 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-7.99 (2H, m), 7.59-7.51 (1H, m), 7.48-7.41 (2H, m), 7.27 (1H, dd, *J*=15.4, 10.7 Hz), 6.61-6.42 (1H, m), 6.19 (1H, dd, *J*=15.6, 10.7 Hz), 5.80 (1H, d, *J*=15.4 Hz), 5.31 (1H, q, *J*=6.1 Hz), 5.14-5.05 (1H, m), 4.20 (2H, q, *J*=7.1 Hz), 3.00-2.93 (1H, m), 2.49-2.27 (3H, m), 2.01-1.69 (5H, m), 1.68-1.59 (7H, m), 1.56-1.48 (1H, m), 1.29 (3H, t, *J*=7.1 Hz), 1.25-1.16 (1H, m), 0.95 (3H, d, *J*=6.3 Hz), 0.91 (3H, d, *J*=7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 165.8, 149.6, 145.5, 136.1, 132.7, 130.9, 129.5, 128.3, 127.1, 119.0, 75.8, 65.5, 60.1, 49.6, 44.5, 39.9, 33.7, 30.6, 29.5, 27.4, 26.2, 19.5, 19.2, 16.4, 16.0, 14.3, 13.7; IR ($CHCl_3$) ν_{max} 2931, 2873, 1716, 1633, 1450, 1381, 1367, 1267, 1176, 1132, 1115, 1070, 1026, 1003, 978, 756 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{30}H_{41}O_4$: 465.3005, found: 465.3006; $[\alpha]_D^{23}$ +134.2 (*c* 0.70, $CHCl_3$).

(+)-(2*E*,4*E*)-5-{(1*S*,2R,3*R*,4a*R*,5*S*,8*S*,8a*S*)-5-Hydroxy-3,8-dimethyl-2-[(*E*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl}-penta-2,4-dienoic acid (12)



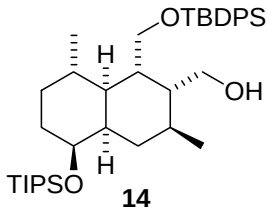
12

To a stirred solution of ester **10a** (0.0265 g, 0.0570 mmol) in a mixed solvent (EtOH/H_2O = 10/1, 1.1 mL) was added LiOH·H_2O (0.0266 g, 0.634 mmol), and the reaction mixture was stirred at room temperature for 1 day. The reaction was quenched with saturated aqueous NH_4Cl solution (3 mL), and the aqueous layer was extracted with EtOAc (5 mL × 3). The combined organic layer was washed with brine (3 mL), dried over Na_2SO_4, and evaporated. The residue was purified by recrystallization (CH_2Cl_2/hexane) to afford hydroxycarboxylic acid **12** (0.0170 g, 89%) as a white solid:

R_f = 0.27 (hexane/ethyl acetate = 1/1); mp 169-173 ºC; ^{1}H NMR (600 MHz, CD_3OD) δ 7.14 (1H, dd, *J*=15.4, 10.8 Hz), 6.55-6.42 (1H, m), 6.15 (1H, dd, *J*=15.1, 10.8 Hz), 5.69 (1H, d, *J*=15.4 Hz), 5.26 (1H, q, *J*=6.7 Hz), 3.58 (1H, ddd, *J*=11.0, 4.9, 4.9 Hz), 2.92-2.84 (1H, m), 2.35-2.23 (2H, m), 2.17-2.08 (1H, m), 1.78-1.63 (3H, m), 1.61-1.44 (10H, m), 1.36-1.25 (1H, m), 1.05-0.95 (1H, m), 0.88 (3H, d, *J*=7.2 Hz), 0.81 (3H, d, *J*=6.4 Hz); ^{13}C NMR (150 MHz, CD_3OD) δ 170.8, 151.6, 147.5, 137.8, 128.4, 120.5, 120.0, 73.8, 51.2, 46.1, 41.5, 35.2, 34.1, 31.0, 30.1, 28.5, 27.5, 19.9, 16.8, 16.2, 13.8; IR (KBr) ν_{max} 3386, 2927, 2870, 1691, 1630, 1458, 1415, 1383, 1304, 1259, 1146, 1051, 1001 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{21}H_{32}O_3Na$: 355.2249, found: 355.2252; $[\alpha]_D^{24}$ +66.9 (*c* 0.43, CH_3OH).

Total synthesis of compound 16

(-)-[(1*S*,2*R*,3*S*,4a*R*,5*S*,8*S*,8a*S*)-1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3,8-dimethyl-5-triisopropylsilanyloxy-decahydro-naphthalen-2-yl]-methanol (14)

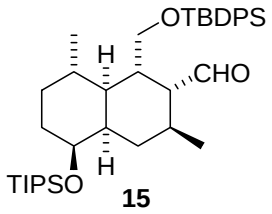


14

To a stirred solution of $[Ir(cod)pyr(PCy_3)]PF_6$ (Crabtree's catalyst) (0.0084 g, 0.0104 mmol) in degassed $(CH_2Cl)_2$ (0.4 mL) was added a solution of alcohol **13** (0.0330 g, 0.0520 mmol) in $(CH_2Cl)_2$ (2.5 mL) at room temperature, and the mixture was stirred under hydrogen atmosphere at 60 ºC for 2 h. After completion of the reaction, to the reaction mixture was added saturated aqueous NH_4Cl solution (4 mL), and extracted with EtOAc (5 mL × 3). The combined organic layer was washed with brine (3 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 20/1) to afford alcohol **14** (0.0279 g, 84%) as a colorless oil:

R_f = 0.35 (benzene/ethyl acetate = 100/1, development×2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75-7.66 (4H, m), 7.49-7.33 (6H, m), 4.09 (1H, dd, *J*=10.2, 9.0 Hz), 3.84-3.76 (1H, m), 3.74-3.66 (1H, m), 3.58-3.49 (2H, m), 3.41 (1H, dd, *J*=10.5, 2.7 Hz), 2.25-2.18 (1H, m), 1.76-1.42 (8H, m), 1.17-0.86 (36H, m), 0.77 (3H, d, *J*=6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.6, 135.5, 134.8, 133.0, 132.9, 129.9, 129.9, 129.5, 127.9 127.8, 127.7, 73.6, 67.1, 63.6, 37.7, 42.7, 40.1, 39.7, 34.0, 30.0, 29.5, 28.7, 26.9, 26.7, 26.6, 20.3, 19.3, 19.0, 18.1, 18.1, 17.7, 12.3; IR ($CHCl_3$) ν_{max} 3460, 2948, 2868, 1464, 1428, 1390, 1245, 1114, 1068, 1056, 1012, 998, 882, 822, 760 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{39}H_{65}O_3Si2$: 637.4472, found: 637.4481; $[\alpha]_D^{20}$ –3.0 (*c* 0.52, $CHCl_3$).

(-)-(1*S*,2*R*,3*S*,4a*R*,5*S*,8*S*,8a*S*)-1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3,8-dimethyl-5-triisopropylsilanyloxy-decahydro-naphthalene-2-carbaldehyde (15)

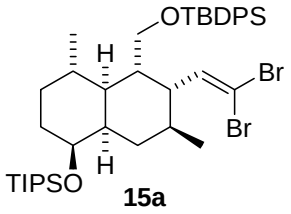


15

Compound **15** (0.0611 g, 95%), a colorless oil, was prepared from **14** (0.0613 g, 0.0962 mmol) according to the procedure for aldehyde **4** and purified by flash chromatography (hexane/ethyl acetate = 50/1):

R_f = 0.67 (hexane/ethyl acetate = 4/1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.70 (1H, d, *J*=2.7 Hz), 7.68-7.59 (4H, m), 7.46-7.34 (6H, m), 3.86 (1H, dd, *J*=10.2, 8.3 Hz), 3.68-3.60 (1H, m), 3.54 (1H, dd, *J*=10.2, 6.3 Hz), 2.51-2.41 (1H, m), 2.09 (1H, ddd, *J*=11.7, 3.4, 3.4 Hz), 1.99-1.84 (2H, m), 1.78 (1H, ddd, *J*=17.3, 3.7, 3.7 Hz), 1.74-1.49 (4H, m), 1.15-0.98 (33H, m), 0.96 (3H, d, *J*=6.1 Hz), 0.84 (3H, d, *J*=6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.7, 135.6, 133.4, 129.7, 129.7, 127.7, 73.5, 64.1, 54.7, 43.9, 40.8, 38.7, 34.0, 30.0, 28.5, 27.0, 26.9, 26.7, 21.0, 19.3, 19.1, 18.1, 12.4; IR (neat) ν_{max} 2944, 2868, 1724, 1464, 1428, 1390, 1245, 1114, 998, 882, 824 cm^{-1}; FAB HRMS $[M-H]^+$ calcd for $C_{39}H_{61}O_3Si_2$: 633.4159, found: 633.4141; $[\alpha]_D^{20}$ –8.7 (*c* 0.54, $CHCl_3$).

(+)-(1*S*,2*R*,3*S*,4a*R*,5*S*,8*S*,8a*S*)-1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-(2,2-dibromo-vinyl)-3,8-dimethyl-5-triisopropylsilanyloxy-decahydro-naphthalene (15a)

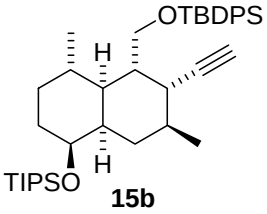


15a

Compound **15a** (0.0581 g, 83%), a colorless oil, was prepared from **15** (0.0564 g, 0.0880 mmol) according to the procedure for dibromide **4b** and purified by flash chromatography (hexane/ethyl acetate = 100/1):

R_f = 0.64 (hexane/ethyl acetate = 10/1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71-7.62 (4H, m), 7.47-7.36 (6H, m), 6.18 (1H, d, *J*=9.0 Hz), 3.78-3.66 (3H, m), 2.29-2.20 (2H, m), 2.10-2.01 (1H, m), 1.80-1.66 (3H, m), 1.64-1.50 (3H, m), 1.49-1.37 (1H, m), 1.13-0.98 (32H, m), 0.91 (3H, d, *J*=6.1 Hz), 0.81 (3H, d, *J*=6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0, 135.5, 135.4, 133.9, 133.5, 129.6, 129.6, 127.8, 127.7, 87.5, 73.8, 62.6, 46.7, 43.2, 41.7, 38.3, 34.3, 31.7, 30.2, 28.9, 27.2, 26.8, 21.1, 19.7, 19.2, 18.1, 12.4; IR ($CHCl_3$) ν_{max} 2929, 2866, 1589, 1462, 1427, 1381, 1242, 1217, 1111, 1068, 1012, 997, 883, 812, 760 cm^{-1}; FAB HRMS $[M-H]^+$ calcd for $C_{40}H_{61}Br_2O_2Si_2$: 787.2577, found: 787.2546; $[\alpha]_D^{27}$ +31.6(*c* 0.56, $CHCl_3$).

(-)-(1*S*,2*R*,3*S*,4a*R*,5*S*,8*S*,8a*S*)-1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-ethynyl-3,8-dimethyl-5-triisopropylsilanyloxy-decahydro-naphthalene (15b)

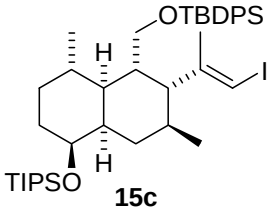


15b

Compound **15b** (0.0439 g, 96%), a colorless oil, was prepared from **15a** (0.0572 g, 0.0723 mmol) according to the procedure for alkyne **6** and purified by flash chromatography (hexane/ethyl acetate = 100/1):

R_f = 0.41 (hexane/ethyl acetate = 20/1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72-7.62 (4H, m), 7.44-7.32 (6H, m), 4.13 (1H, dd, *J*=10.2, 3.7 Hz), 3.85-3.71 (2H, m), 2.32-2.17 (2H, m), 2.14-2.06 (1H, m), 1.90 (1H, d, *J*=2.4 Hz), 1.78-1.67 (3H, m), 1.67-1.58 (3H, m), 1.38-1.24 (1H, m), 1.10-0.97 (35H, m), 0.90 (3H, d, *J*=6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.6, 135.5, 134.2, 134.0, 129.5, 127.6, 127.5, 86.1, 73.8, 70.6, 61.8, 41.6, 41.6, 38.0, 34.8, 34.3, 32.5, 30.2, 28.6, 27.2, 26.8, 21.5, 19.6, 19.3, 18.2, 12.4; IR ($CHCl_3$) ν_{max} 3309, 2941, 2866, 1462, 1427, 1383, 1248, 1217, 1113, 1068, 1011, 997, 883, 818, 760, 741 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{40}H_{63}O_2Si_2$: 631.4367, found: 631.4376; $[\alpha]_D^{26}$ –4.2 (*c* 0.52, $CHCl_3$).

(+)-(1*S*,2*R*,3*S*,4a*R*,5*S*,8*S*,8a*S*)-1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-[(*E*)-2-iodo-1-methyl-vinyl]-3,8-dimethyl-5-triisopropylsilanyloxy-decahydro-naphthalene (15c)

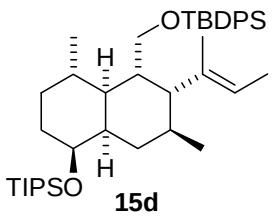


15c

Compound **15c** (0.0393 g, 99%), a colorless oil, was prepared from **15b** (0.0323 g, 0.0512 mmol) according to the procedure for iodoalkene **7** and purified by flash chromatography (hexane/ethyl acetate = 100/1):

R_f = 0.62 (hexane/ethyl acetate = 20/1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.58 (4H, m), 7.46-7.34 (6H, m), 5.66 (1H, s), 3.77 (1H, ddd, *J*=10.5, 5.1, 5.1 Hz), 3.64 (1H, dd, *J*=10.0, 9.8 Hz), 3.54 (1H, dd, *J*=10.0, 3.9 Hz), 2.14-2.00 (3H, m), 1.82-1.62 (5H, m), 1.61 (3H, s), 1.58-1.48 (2H, m), 1.10-1.00 (32H, m), 0.87 (3H, d, *J*=5.4 Hz), 0.79 (3H, d, *J*=6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 135.5, 135.4, 134.1, 133.8, 129.6, 129.5, 127.7, 127.6, 76.6, 73.9, 61.7, 51.5, 42.5, 41.2, 37.9, 34.3, 30.3, 29.7, 29.3, 27.1, 26.9, 25.1, 21.4, 19.5, 19.3, 18.2, 12.4; IR ($CHCl_3$) ν_{max} 2941, 2866, 1589, 1462, 1427, 1379, 1257, 1242, 1217, 1113, 1068, 1012, 997, 883, 820, 760 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{41}H_{66}IO_2Si_2$: 773.3646, found: 773.3630; $[\alpha]_D^{26}$ +18.2 (*c* 0.58, $CHCl_3$).

(+)-(1*S*,2*R*,3*S*,4a*R*,5*S*,8*S*,8a*S*)-1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3,8-dimethyl-2-[(*E*)-1-methyl-propenyl]-5-triisopropylsilanyloxy-decahydro-naphthalene (15d)

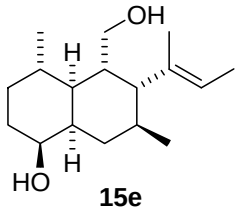


15d

Compound **15d** (0.0307 g, 91%), a colorless oil, was prepared from **15c** (0.0393 g, 0.0508 mmol) according to the procedure for alkene **7a** and purified by flash chromatography (hexane/ethyl acetate = 100/1):

R_f = 0.44 (hexane/ethyl acetate = 30/1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.58 (4H, m), 7.44-7.30 (6H, m), 4.93 (1H, q, *J*=6.6 Hz), 3.78 (1H, ddd, *J*=10.2, 5.1, 5.1 Hz), 3.66 (1H, dd, *J*=10.0, 10.0 Hz), 3.58 (1H, dd, *J*=10.0, 4.4 Hz), 2.16-2.08 (1H, m), 2.06-1.97 (1H, m), 1.81-1.68 (5H, m), 1.66-1.45 (4H, m), 1.40 (3H, d, *J*=6.6 Hz), 1.38 (3H, s), 1.10-0.96 (31H, m), 0.89 (3H, d, *J*=4.9 Hz), 0.77 (3H, d, *J*=6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.6, 135.5, 135.4, 134.5, 134.1, 129.4, 127.5, 127.5, 119.6, 74.2, 61.8, 50.0, 42.4, 41.3, 38.0, 34.5, 30.3, 29.4, 29.1, 27.1, 26.8, 21.5, 19.5, 19.3, 18.2, 16.6, 13.1, 12.5; IR ($CHCl_3$) ν_{max} 2941, 2866, 1589, 1462, 1427, 1381, 1255, 1217, 1111, 1068, 1012, 997, 883, 822, 760 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{42}H_{69}O_2Si_2$: 661.4836, found: 661.4843; $[\alpha]_D^{26}$ +8.0 (*c* 0.60, $CHCl_3$).

(+)-(1*S*,4*S*,4a*S*,5*S*,6*R*,7*S*,8a*R*)-5-Hydroxymethyl-4,7-dimethyl-6-[(*E*)-1-methyl-propenyl]-decahydro-naphthalen-1-ol (15e)



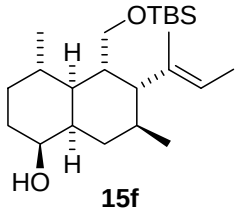
15e

Compound **15e** (0.0154 g, 99%), a white solid, was prepared from **15d** (0.0387 g, 0.0585 mmol) according to the procedure for diol **8** and purified by flash chromatography (hexane/ethyl acetate = 1/2):

R_f = 0.14 (hexane/ethyl acetate = 1/1); mp 174-177 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 5.11-4.98 (1H, m), 3.63-3.39 (3H, m), 2.12-1.98 (1H, m), 1.97-1.86 (1H, m), 1.85-1.39 (15H, m), 1.14-0.90 (3H, m), 0.85-0.72 (6H, m); ^{13}C NMR (100 MHz, CD_3OD) δ 137.1, 121.1, 74.0, 60.9, 51.3, 43.5, 42.2, 38.2, 35.4, 30.4, 30.1, 28.4, 21.9, 19.7, 17.1, 13.4; IR (KBr) ν_{max} 3365, 2925, 2866, 1633, 1456, 1408, 1375, 1286,

1223, 1099, 1063, 1034, 957 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{17}H_{31}O_2$: 267.2324, found: 267.2324; $[\alpha]_D^{27}$ +61.0 (*c* 0.54, CH_3OH).

(+)-(1*S*,4*S*,4a*S*,5*S*,6*R*,7*S*,8a*R*)-5-(*tert*-Butyl-dimethyl-silanyloxymethyl)-4,7-dimethyl-6-[(*E*)-1-methyl-propenyl]-decahydro-naphthalen-1-ol (15f)

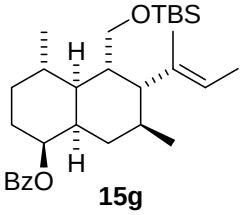


15f

Compound **15f** (0.0214 g, 85%), a colorless oil, was prepared from **15e** (0.0176 g, 0.0660 mmol) according to the procedure for TBS ether **8a** and purified by flash chromatography (hexane/ethyl acetate = 10/1):

R_f = 0.79 (hexane/ethyl acetate = 1/1); ^1H NMR (400 MHz, $CDCl_3$) δ 5.10 (1H, q, *J*=6.6 Hz), 3.70 (1H, ddd, *J*=11.7, 4.9, 4.9 Hz), 3.61-3.53 (2H, m), 2.16 -2.08 (1H, m), 1.96-1.89 (1H, m), 1.85-1.78 (1H, m), 1.78-1.47 (14H, m), 1.18-0.98 (2H, m), 0.91-0.86 (9H, m), 0.85 (3H, d, *J*=6.1 Hz), 0.83 (3H, d, *J*=5.9 Hz), 0.04-0.00 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 120.0, 73.4, 60.9, 50.0, 42.1, 41.3, 37.0, 34.2, 29.7, 29.1, 29.0, 27.0, 26.0, 21.4, 19.3, 18.2, 16.7, 13.3, -5.3, -5.4; IR ($CHCl_3$) ν_{max} 3311, 2929, 2858, 1462, 1377, 1362, 1255, 1215, 1088, 1045, 1007, 835, 773, 760 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{23}H_{45}O_2Si$: 381.3189, found: 381.3191; $[\alpha]_D^{27}$ +58.1 (*c* 0.51, $CHCl_3$).

(+)-Benzoic acid (1*S*,4*S*,4a*S*,5*S*,6*R*,7*S*,8a*R*)-5-(*tert*-butyl-dimethyl-silanyloxymethyl)-4,7-dimethyl-6-[(*E*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl ester (15g)

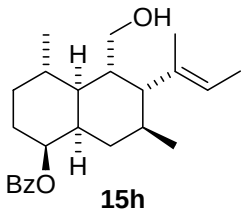


15g

Compound **15g** (0.0211 g, 100%), a colorless oil, was prepared from **15f** (0.0166 g, 0.0436 mmol) according to the procedure for benzoate **9** and purified by flash chromatography (hexane/ethyl acetate = 8/1):

R_f = 0.77 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 -8.02 (2H, m), 7.57 -7.51 (1H, m), 7.46-7.40 (2H, m), 5.14-5.00 (2H, m), 3.59 -3.50 (2H, m), 2.39 -2.30 (1H, m), 1.98-1.90 (1H, m), 1.89-1.73 (8H, m), 1.60 (3H, d, *J*=7.1 Hz), 1.58 (3H, s), 1.38-1.28 (1H, m), 1.24-1.14 (1H, m), 0.91-0.85 (12H, m), 0.84 (3H, d, *J*=6.1 Hz), 0.08- -0.00 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 136.1, 132.9, 131.4, 129.8, 128.6, 120.4, 76.7, 61.3, 50.2, 42.5, 41.7, 34.9, 34.2, 30.5, 30.0, 29.2, 27.5, 26.6, 26.3, 21.8, 19.7, 18.5, 17.0, 13.6, -5.0, -5.0; IR ($CHCl_3$) ν_{max} 2927, 2856, 1716, 1603, 1585, 1452, 1379, 1362, 1315, 1277, 1176, 1115, 1090, 1026, 1007, 984, 939, 835, 760 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{30}H_{49}O_3Si$: 485.3451, found: 485.3434; $[\alpha]_D^{26}$ +59.3 (*c* 0.68, $CHCl_3$).

(+)-Benzoic acid (1*S*,4*S*,4a*S*,5*S*,6*R*,7*S*,8a*R*)-5-hydroxymethyl-4,7-dimethyl-6-[(*E*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl ester (15h)



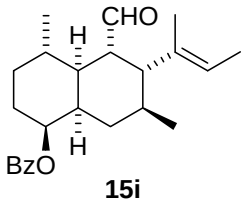
15h

Compound **15h** (0.0161 g, 100%), a colorless oil, was prepared from **15g** (0.0216g, 0.0435 mmol) according to the procedure for alcohol **9a** and purified by flash chromatography (hexane/ethyl acetate = 4/1):

R_f = 0.24 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11-8.00 (2H, m), 7.61-7.52 (1H, m), 7.51-7.40 (2H, m), 5.21 (1H, q, *J*=6.3 Hz), 5.06 (1H, ddd, *J*=11.0, 5.1, 5.1 Hz),, 3.81 (1H, dd, *J*=11.0, 6.1 Hz), 3.48 (1H, dd, *J*=11.0, 7.1 Hz), 2.29-2.18 (1H, m), 2.13-2.04 (1H, m), 1.91-1.57 (14H, m), 1.56-1.47 (1H, m), 1.42-1.28 (1H, m), 1.24-1.13 (1H, m), 0.93 (3H, d, *J*=6.1 Hz), 0.88 (3H, d, *J*=5.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 137.0, 132.7, 130.8, 129.5, 128.3, 119.4, 76.1, 63.2, 49.3,

44.7, 41.3, 35.1, 33.6, 29.9, 28.5, 27.1, 26.2, 21.1, 19.2, 17.4, 13.4; IR ($CHCl_3$) ν_{max} 3444, 2927, 2871, 1714, 1623, 1585, 1450, 1379, 1317, 1279, 1217, 1176, 1119, 1070, 1026, 982, 935, 758 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{24}H_{35}O_3$: 371.2586, found: 371.2588; $[\alpha]_D^{31}$ +55.9 (*c* 0.79, $CHCl_3$).

(+)-Benzoic acid (1*S*,4*S*,4aR,5*S*,6*R*,7*S*,8a*R*)-5-formyl-4,7-dimethyl-6-[(*E*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl ester (15i)

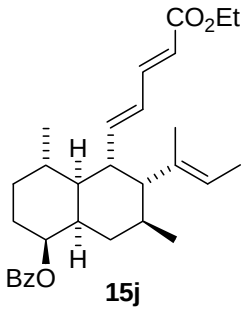


15i

Compound **15i** (0.0151 g, 91%), a colorless oil, was prepared from **15h** (0.0167 g, 0.0451 mmol) according to the procedure for aldehyde **10** and purified by flash chromatography (hexane/ethyl acetate = 20/1):

R_f = 0.56 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (1H, d, *J*=2.0 Hz), 8.10-7.99 (2H, m), 7.59-7.52 (1H, m), 7.49-7.40 (2H, m), 5.34 (1H, q, *J*=6.1 Hz), 5.06 (1H, ddd, *J*=11.7, 4.9, 4.9 Hz), 2.61-2.54 (1H, m), 2.37-2.26 (1H, m), 2.06-1.69 (8H, m), 1.68-1.58 (6H, m), 1.47-1.34 (1H, m), 1.32-1.16 (1H, m), 0.95 (3H, d, *J*=5.9 Hz), 0.91 (3H, d, *J*=5.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.9, 165.7, 134.2, 132.7, 130.8, 129.5, 128.3, 121.7, 75.3, 51.4, 49.1, 43.6, 36.7, 33.3, 30.6, 29.9, 27.0, 26.1, 20.7, 19.1, 16.6, 13.4; IR ($CHCl_3$) ν_{max} 2929, 2871, 2742, 1716, 1603, 1583, 1450, 1381, 1315, 1277, 1176, 1115, 1070, 1026, 984, 758 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{24}H_{33}O_3$: 369.2430, found: 369.2433; $[\alpha]_D^{27}$ +118.7 (*c* 0.67, $CHCl_3$).

(+)-Benzoic acid (1*S*,4*S*,4a*S*,5*S*,6*R*,7*S*,8a*R*)-5-[(1*E*,3*E*)-4-ethoxycarbonyl-buta-1,3-dienyl]-4,7-dimethyl-6-[(*E*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl ester (15j)

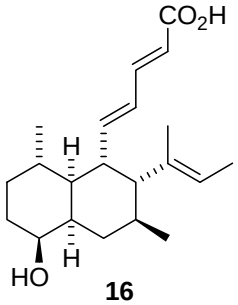


15j

Compound **15j** (0.0186 g, 98%), a colorless oil, was prepared from **15i** (0.0151 g, 0.0410 mmol) according to the procedure for ester **10a** and purified by flash chromatography (hexane/ethyl acetate = 20/1). Aldehyde **15i** did not remain in the reaction with phosophonate **11**, thus, all the starting material was consumed in one reaction in contrast with the reaction of aldehyde **10**:

R_f = 0.56 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14-8.01 (2H, m), 7.63-7.52 (1H, m), 7.51-7.40 (2H, m), 7.24 (1H, dd, *J*=15.4, 11.0 Hz), 6.44 (1H, dd, *J*=15.1, 9.3 Hz), 6.07 (1H, dd, *J*=15.1, 11.0 Hz), 5.77 (1H, d, *J*=15.4 Hz), 5.15 (1H, q, *J*=6.6 Hz), 5.00 (1H, ddd, *J*=11.0, 5.1, 5.1 Hz), 4.26-4.13 (2H, m), 2.67-2.56 (1H, m), 2.48-2.32 (1H, m), 1.96-1.72 (6H, m), 1.69-1.60 (1H, m), 1.55 (3H, d, *J*=6.6 Hz), 1.45 (3H, s), 1.40-1.11 (6H, m), 0.95 (3H, d, *J*=6.3 Hz), 0.85 (3H, d, *J*=5.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 165.8, 146.4, 145.1, 136.3, 132.8, 130.8, 129.5, 128.6, 128.3, 120.6, 119.4, 75.9, 60.1, 51.4, 49.5, 45.0, 35.4, 33.5, 30.1, 28.7, 27.6, 26.2, 20.8, 19.2, 15.5, 14.3, 13.2; IR ($CHCl_3$) ν_{max} 2927, 2871, 1712, 1637, 1450, 1369, 1277, 1176, 1157, 1134, 1115, 1070, 1026, 1001,984, 758 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{30}H_{41}O_4$: 465.3005, found: 465.2997; $[\alpha]_D^{26}$ +246.6 (*c* 0.50, $CHCl_3$).

(+)-(2*E*,4*E*)-5-{(1*S*,2R,3*S*,4a*R*,5*S*,8*S*,8a*S*)--5-Hydroxy-3,8-dimethyl-2-[(*E*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl}-penta-2,4-dienoic acid (16)



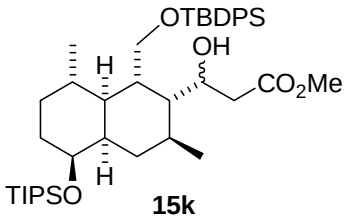
16

Compound **16** (0.0125 g, 94%), a colorless oil, was prepared from **15j** (0.0186 g, 0.0400 mmol) according to the procedure for hydroxycarboxylic acid **12** and purified by flash chromatography (hexane/ethyl acetate = 1/1);

R_f = 0.14 (hexane/ethyl acetate = 1/1); ^{1}H NMR (600 MHz, CD_3OD) δ 7.23 (1H, dd, *J*=15.1, 11.0 Hz), 6.54 (1H, dd, *J*=14.8, 9.5 Hz), 6.09 (1H, dd, *J*=14.8, 11.0 Hz), 5.76 (1H, d, *J*=15.1 Hz), 5.18 (1H, q, *J*=6.7 Hz), 3.58 (1H, ddd, *J*=10.2, 5.1, 5.1 Hz), 2.68-2.58 (1H, m), 2.19-2.12 (1H, m), 1.96-1.69 (6H, m), 1.67-1.53 (5H, m), 1.49 (3H, s), 1.30-1.04 (2H, m), 0.91 (3H, d, *J*=6.4 Hz), 0.84 (3H, d, *J*=6.1 Hz); ^{13}C NMR (150 MHz, CD_3OD) δ 170.9, 148.5, 147.0, 137.8, 129.8, 121.5, 120.5, 73.8, 53.1, 51.5, 46.5, 39.3, 35.1, 30.4, 30.2, 30.0, 28.8, 21.3, 19.7, 15.9, 13.3; IR ($CHCl_3$) ν_{max} 3384, 2927, 2870, 1687, 1633, 1456, 1417, 1377, 1304, 1265, 1238, 1157, 1045, 1001, 758 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{21}H_{33}O_3$: 333.2430, found: 333.2435; $[\alpha]_D^{25}$ +157.4 (*c* 0.70, $CHCl_3$).

Total synthesis of NH006

3-[(1*S*,2*R*,3*S*,4a*R*,5*S*,8*S*,8a*S*)-1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3,8-dimethyl-5-triisopropylsilanyloxy-decahydro-naphthalen-2-yl]-3-hydroxy-propionic acid methyl ester (15k)

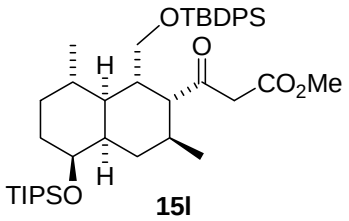


15k

To a stirred solution of *i*-Pr_2NH (0.0365 mL, 0.260 mmol) in THF (0.5 mL) was added *n*-BuLi in hexane (0.1439 mL, 1.63 M) at 0 ºC. After 10 min, the reaction mixture was cooled to –78 ºC, and to which was added MeOAc (0.0207 mL, 0.261 mmol). After 10 min, to the reaction mixture was added a solution of aldehyde **15** (0.0331 g, 0.0521 mmol) in THF (1.2 mL) at –78 ºC, and the resulting mixture was stirred at the same temperature for 1 h. The reaction was quenched with saturated aqueous NH_4Cl solution (2 mL), and the aqueous layer was extracted with Et_2O (4 mL × 3). The combined organic layer was washed with brine (3 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 10/1) to afford hydroxyester **15k**, which was immediately used for the next reaction:

R_f = 0.40 (hexane/ethyl acetate = 1/1).

(-)-3-[(1*S*,2*R*,3*S*,4a*R*,5*S*,8*S*,8a*S*)-1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3,8-dimethyl-5-triisopropylsilanyloxy-decahydro-naphthalen-2-yl]-3-oxo-propionic acid methyl ester (15l)



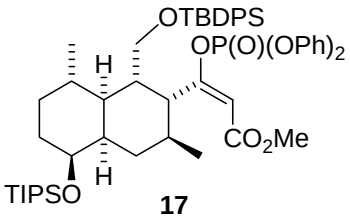
15l

To a stirred solution of hydroxyester **15k** obtained as above in CH_2Cl_2 (2 mL) was added Dess-Martin periodinane (0.0436 g, 0.103 mmol), and the mixture was stirred at room temperature for 1 h. The

reaction mixture was diluted with Et_2O (2 mL), and to the solution was added saturated aqueous $NaHCO_3$ solution (2 mL) and saturated aqueous $Na_2S_2O_3$ solution (4 mL), and the aqueous layer was extracted with Et_2O (6 mL × 3). The combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 30/1) to afford ketoester **15l** (0.0310 g, 84% (2 steps)) as a colorless oil:

R_f = 0.27 (hexane/ethyl acetate = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.57 (4H, m), 7.46-7.31 (6H, m), 3.73-3.67 (1H, m), 3.66 (3H, s), 3.60 (1H, dd, *J*=10.5, 8.3 Hz), 3.48 (1H, dd, *J*=10.5, 5.6 Hz), 3.36 (1H, d, *J*=14.9 Hz), 3.17 (1H, d, *J*=14.9 Hz), 2.51 (1H, dd, *J*=11.5, 4.1 Hz), 2.35-2.24 (1H, m), 1.96-1.49 (8H, m), 1.12-0.95 (32H, m), 0.92 (3H, d, *J*=5.9 Hz), 0.83 (3H, d, *J*=6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.3, 167.7, 135.5, 135.4, 133.5, 133.5, 129.7, 129.6, 127.7, 73.5, 62.5, 54.3, 52.1, 48.4, 43.2, 39.5, 37.8, 34.0, 30.0, 27.9, 27.6, 26.9, 26.8, 21.0, 19.4, 19.2, 18.1, 18.1, 12.3; IR (neat) ν_{max} 2944, 2868, 1750, 1714, 1654, 1622, 1464, 1428, 1376, 1324, 1290, 1242, 1112, 1086, 1014, 998, 882, 822, 760, 742 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{42}H_{67}O_5Si_2$: 707.4534, found: 707.4527; $[\alpha]_D^{18}$ – 29.2 (*c* 0.50, $CHCl_3$).

(+)-(*E*)-3-[(1*S*,2*R*,3*S*,4a*R*,5*S*,8*S*,8a*S*)-1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3,8-dimethyl-5-triisopropylsilanyloxy-decahydro-naphthalen-2-yl]-3-(diphenoxy-phosphoryloxy)-acrylic acid methyl ester (17)



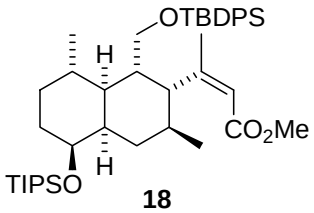
17

To a stirred solution of ketoester **15l** (0.0310 g, 0.0438 mmol) in HMPA (1.5 mL) was added Et_3N (0.0611 mL, 0.438 mmol) at 0 ºC, and stirring was continued at the same temperature. After 2 h, to the reaction mixture was added $ClP(O)(OPh)_2$ (0.0907 mL, 0.260 mmol) and DMAP (0.0005 g, 0.00409 mmol) successively at 0 ºC, and the reaction mixture was stirred at room temperature for 1 h. The

reaction was quenched with saturated aqueous NH_4Cl solution (3 mL), and the aqueous layer was extracted with Et_2O (6 mL × 3). The combined organic layer was washed with brine (3 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 10/1) to afford enol phosphonate **17** (0.0403 g, 98%):

R_f = 0.51 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.54 (4H, m), 7.44-7.26 (6H, m), 7.23-7.16 (2H, m), 7.16-7.05 (4H, m), 7.01-6.94 (2H, m), 6.91-6.84 (2H, m), 5.90 (1H, s), 3.77-3.55 (6H, m), 2.26-2.17 (1H, m), 1.97-1.88 (1H, m), 1.86-1.69 (3H, m), 1.64-1.51 (3H, m), 1.15-0.97 (34H, m), 0.94 (3H, d, *J*=5.4 Hz), 0.65 (3H, d, *J*=5.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 168.8, 165.9, 150.0, 150.0, 135.6, 135.5, 134.1, 133.8, 129.8, 129.7, 129.6, 129.5, 127.7, 127.6, 125.8, 125.7, 120.1, 120.1, 120.0, 120.0, 105.4, 105.4, 73.9, 61.4, 51.4, 43.3, 43.2, 42.4, 41.5, 37.7, 34.5, 30.2, 28.5, 28.1, 27.0, 26.8, 21.0, 19.7, 19.3, 18.2, 12.4; IR ($CHCl_3$) ν_{max} 2940, 2868, 1724, 1640, 1592, 1490, 1462, 1428, 1380, 1300, 1236, 1214, 1188, 1162, 1132, 1112, 1084, 1044, 1026, 1010, 970, 944, 882, 860, 822, 756 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for$C_{54}H_{75}O_8PSi_2Na$: 961.4636, found: 961.4654; $[\alpha]_D^{19}$ +51.4 (*c* 0.50, $CHCl_3$).

(+)-(*Z*)-3-[(1*S*,2*R*,3*S*,4a*R*,5*S*,8*S*,8a*S*)-1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3,8-dimethyl-5-triisopropylsilanyloxy-decahydro-naphthalen-2-yl]-but-2-enoic acid methyl ester (18)



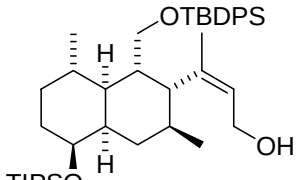
18

To a stirred solution of MeMgCl in THF (2.37 mL, 3.0 M) was added a solution of the enol phosphonate **17** (0.111 g, 0.118 mmol) and $Fe(acac)_3$ (0.208 g, 0.591 mmol) in NMP (4 mL) dropwise at 0 ºC, and the reaction mixture was stirred at 0 ºC for 1h. The reaction was quenched with saturated aqueous NH_4Cl (7 mL) and the aqueous layer was extracted with Et_2O (10 mL×3). The combined organic layer was washed with brine (3 mL), dried over $MgSO_4$, filtered, and evaporated. The residue

was purified by silica gel chromatography (hexane/ethyl acetate=50/1) to give the ester **18** (0.0763 g, 91%) as a colorless oil:

R_f = 0.58 (hexane/ethyl acetate = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.57 (4H, m), 7.45-7.30 (6H, m), 5.60 (1H, s), 3.78-3.59 (6H, m), 2.21-2.14 (1H, m), 2.06-1.97 (1H, m), 1.89-1.71 (2H, m), 1.65 (3H, s), 1.63-1.53 (4H, m), 1.19-1.10 (34H, m), 0.96 (3H, d, *J*=6.1 Hz), 0.76 (3H, d, *J*=6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 163.8, 135.5, 135.5, 134.4, 134.0, 133.8, 129.5, 127.6, 127.5, 118.2, 74.0, 63.2, 50.7, 44.1, 43.5, 43.3, 38.5, 34.5, 30.2, 29.2, 29.0, 27.0, 26.7, 22.6, 21.8, 20.0, 19.2, 18.2, 12.4; IR ($CHCl_3$) ν_{max} 2944, 2868, 1718, 1632, 1592, 1464, 1430, 1380, 1220, 1192, 1150, 1114, 1092, 1014, 998, 952, 918, 882, 866, 822, 758 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{43}H_{68}O_4Si_2Na$: 727.4554, found: 727.4544; $[\alpha]_D^{19}$ +89.8 (*c* 0.47, $CHCl_3$).

(+)-(*Z*)-3-[(1*S*,2*R*,3*S*,4a*R*,5*S*,8*S*,8a*S*)-1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3,8-dimethyl-5-triisopropylsilanyloxy-decahydro-naphthalen-2-yl]-but-2-en-1-ol (18a)

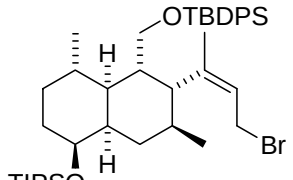


18a

To a stirred solution of the ester **18** (0.0763 g, 0.108 mmol) in CH_2Cl_2 (3 mL) was added DIBAL in hexane (0.414 mL, 0.98 M) at −78 ºC and the reaction mixture was stirred at the same temperature for 30 min. To the reaction mixture was added MeOH at −78 ºC until no gas evolution was observed, and the mixture was warmed up to room temperature. To the mixture was added saturated aqueous Rochelle salt (9 mL), and the resultant mixture was stirred at room temperature for 30 min. The aqueous layer was extracted with CH_2Cl_2 (10 mL×3). The combined organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate=10/1) to give the alcohol **18a** (0.0720 g, 98%) as a colorless oil:

R_f = 0.17 (hexane/ethyl acetate = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.56 (4H, m), 7.46-7.30 (6H, m), 5.36-5.28 (1H, m), 4.22-4.12 (1H, m), 4.04-3.95 (1H, m), 3.80-3.68 (2H, m), 3.64 (1H, dd, *J*=9.5, 5.1 Hz), 2.39-2.30 (1H, m), 2.11-2.02 (1H, m), 1.92-1.66 (4H, m), 1.66-1.50 (4H, m), 1.47 (3H, s), 1.16-0.96 (32H, m), 0.87 (3H, d, *J*=5.1 Hz), 0.76 (3H, d, *J*=6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 135.5, 135.4, 134.1, 133.9, 129.5, 129.5, 127.6, 127.5, 127.0, 73.9, 62.2, 58.5, 44.8, 42.5, 37.9, 34.5, 30.2, 29.0, 28.9, 27.1, 26.8, 22.0, 21.4, 19.9, 19.2, 18.2, 12.4 ; IR ($CHCl_3$) ν_{max} 3372, 2940, 2868, 1717, 1639, 1550, 1464, 1428, 1384, 1256, 1218, 1112, 1092, 1008, 882, 820, 760 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{42}H_{68}O_3Si_2Na$: 699.4605, found: 699.4576; $[\alpha]_D^{21}$ +41.6 (*c* 0.52, $CHCl_3$).

(1*S*,2*R*,3*S*,4a*R*,5*S*,8*S*,8a*S*)-2-[(*Z*)-3-Bromo-1-methyl-propenyl]-1-(*tert*-butyl-diphenyl-silanyloxymethyl)-3,8-dimethyl-5-triisopropylsilanyloxy-decahydro-naphthalene (18b)

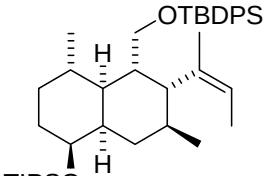


18b

To a solution of alcohol **18a** (0.0720 g, 0.106 mmol) in Et_2O (3 mL) was added pyridine (0.0258 mL, 0.319 mmol) and PBr_3 (0.111 mL, 1.063 mmol) successively at 0 ºC, and the reaction mixture was stirred at the same temperature for 30 min. After completion of the reaction, the reaction mixture was directly purified by flash chromatography (Et_2O) to afford allylic bromide **18b**, which was immediately used for the next reaction:

R_f = 0.64 (hexane/ethyl acetate = 10/1).

(+)-(1*S*,2*R*,3*S*,4a*R*,5*S*,8*S*,8a*S*)-1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3,8-dimethyl-2-[(*Z*)-1-methyl-propenyl]-5-triisopropylsilanyloxy-decahydro-naphthalene (19)

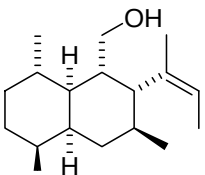


19

To a solution of allylic bromide **18b** obtained as above in Et_2O (3 mL) was added $LiAlH_4$ (0.0274 g, 0.578 mmol) portionwise at 0 ºC, and the reaction mixture was stirred at room temperature for 30 min. To the reaction mixture was added saturated aqueous Na_2SO_4 at 0 ºC until no gas evolution was observed, and white precipitates were filtered through Celite. The residue on Celite was washed with Et_2O, and the filtrate and washings were combined and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate=100/1) to give the alcohol **19** (0.0513 g, 73% (2 steps)) as a colorless oil:

R_f = 0.22 (hexane/ethyl acetate = 30/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.59 (4H, m), 7.44-7.30 (6H, m), 5.19-5.11 (1H, m), 3.82-3.70 (2H, m), 3.66 (1H, dd, *J*=9.8, 5.1 Hz), 2.40-2.33 (1H, m), 2.14-1.99 (2H, m), 1.84-1.70 (5H, m), 1.66-1.57 (2H, m), 1.55 (3H, d, *J*=6.1 Hz), 1.39 (3H, s), 1.14-0.98 (32H, m), 0.89 (3H, d, *J*=5.6 Hz), 0.75 (3H, d, *J*=6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 135.5, 135.5, 134.4, 134.1, 129.5, 127.6, 127.5, 121.7, 100.6, 74.2, 62.4, 43.2, 42.3, 41.8, 38.0, 34.7, 30.3, 30.3, 29.3, 29.1, 27.2, 26.8, 22.1, 21.5, 20.0, 19.3, 18.2, 12.8, 12.5; IR (neat) ν_{max} 2936, 2892, 2868, 1561, 1464, 1428, 1382, 1205, 1112, 1092, 1028, 1014, 998, 882, 820, 738 cm^{-1}; FAB HRMS $[M-H]^+$ calcd for $C_{42}H_{67}O_2Si_2$: 659.4680, found: 659.4687; $[\alpha]_D^{17}$ +48.7 (*c* 0.50, $CHCl_3$).

(+)-(1*S*,4*S*,4a*S*,5*S*,6*R*,7*S*,8a*R*)-5-Hydroxymethyl-4,7-dimethyl-6-[(*Z*)-1-methyl-propenyl]-decahydro-naphthalen-1-ol (19a)

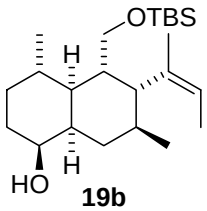


19a

Compound **19a** (0.0190 g, 92%), a white solid, was prepared from **19** (0.0513 g, 0.0776 mmol) according to the procedure for diol **8** and purified by flash chromatography (hexane/ethyl acetate = 1/1):

R_f = 0.21 (hexane/ethyl acetate = 1/1); mp 167-169 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 5.26 (1H, q, *J*=6.8 Hz), 3.62-3.46 (3H, m), 2.43-2.32 (1H, m), 2.06-1.96 (1H, m), 1.96-1.85 (1H, m), 1.79-1.39 (15H, m), 1.12-0.92 (2H, m), 0.83 (3H, d, *J*=6.1 Hz), 0.73 (3H, d, *J*=5.9 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 139.0, 123.1, 74.0, 61.4, 44.4, 43.3, 43.0, 38.1, 35.6, 35.5, 30.2, 30.0, 28.4, 22.5, 22.0, 20.3, 13.2; IR (KBr) ν_{max} 3368, 2944, 2896, 1654, 1457, 1411, 1375, 1333, 1225, 1102, 1065, 1034, 1003, 942, 818 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{17}H_{31}O_2$: 267.2324, found: 267.2333; $[\alpha]_D^{19}$ +81.5 (*c* 0.27, CH_3OH).

(+)-(1*S*,4*S*,4a*S*,5*S*,6*R*,7*S*,8a*R*)-5-(*tert*-Butyl-dimethyl-silanyloxymethyl)-4,7-dimethyl-6-[(*Z*)-1-methyl-propenyl]-decahydro-naphthalen-1-ol (19b)

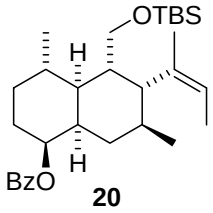


19b

Compound **19b** (0.0262 g, 97%), a colorless oil, was prepared from **19a** (0.0190 g, 0.0713 mmol) according to the procedure for TBS ether **8a** and purified by flash chromatography (hexane/ethyl acetate = 10/1):

R_f = 0.80 (hexane/ethyl acetate = 1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.31 (1H, q, *J*=6.8 Hz), 3.72-3.56 (3H, m), 2.46-2.35 (1H, m), 2.16-2.06 (1H, m), 1.97-1.88 (1H, m), 1.83-1.70 (2H, m), 1.70-1.48 (12H, m), 1.18-0.98 (2H, m), 0.89-0.83 (12H, m), 0.79 (3H, d, *J*=6.1 Hz), 0.03-0.00 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 122.0, 73.4, 61.5, 42.8, 42.1, 41.8, 37.1, 34.3, 29.6, 29.0, 28.9, 27.1, 25.9, 22.0, 21.6, 19.9, 18.2, 12.8, -5.3, -5.4; IR ($CHCl_3$) ν_{max} 3364, 2932, 1464, 1380, 1362, 1256, 1216, 1092, 1060, 1010, 917, 836, 762 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{23}H_{44}O_2SiNa$: 403.3008, found: 403.2998; $[\alpha]_D^{22}$ +86.8 (*c* 0.23, $CHCl_3$).

(+)-Benzoic acid (1*S*,4*S*,4a*S*,5*S*,6*R*,7*S*,8a*R*)-5-(*tert*-butyl-dimethyl-silanyloxymethyl)-4,7-dimethyl-6-[(*Z*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl ester (20)

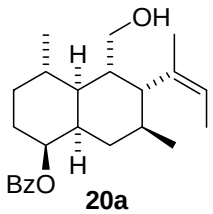


20

Compound **20** (0.0311 g, 90%), a colorless oil, was prepared from TBS ether **19b** (0.0262 g, 0.0688 mmol) according to the procedure for benzoate **9** and purified by flash chromatography (hexane/ethyl acetate = 50/1):

R_f = 0.70 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09-8.02 (2H, m), 7.58-7.52 (1H, m), 7.48-7.41 (2H, m), 5.33 (1H, q, *J*=6.3 Hz), 5.06 (1H, ddd, *J*=11.5, 4.6, 4.6 Hz), 3.69-3.58 (2H, m), 2.50-2.30 (2H, m), 1.99-1.55 (15H, m), 1.39-1.27 (1H, m), 0.92 (3H, d, *J*=6.1 Hz), 0.90-0.86 (9H, m), 0.82 (3H, d, *J*=5.9 Hz), 0.06-0.01 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 137.6, 132.6, 131.0, 129.5, 128.3, 122.0, 76.3, 61.6, 42.8, 42.3, 41.7, 34.7, 34.0, 30.0, 28.9, 27.2, 26.2, 25.9, 22.0, 21.5, 19.9, 18.2, 12.8, -5.3, -5.4; IR (neat) ν_{max} 2932, 2860, 1720, 1561, 1539, 1452, 1380, 1316, 1278, 1176, 1116, 1090, 1046, 1006, 984, 961, 916, 883, 836 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{30}H_{48}O_3SiNa$: 507.3270, found: 507.3264; $[\alpha]_D^{18}$ +60.7 (*c* 0.28, $CHCl_3$).

(+)-Benzoic acid (1*S*,4*S*,4a*S*,5*S*,6*R*,7*S*,8a*R*)-5-hydroxymethyl-4,7-dimethyl-6-[(*Z*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl ester (20a)

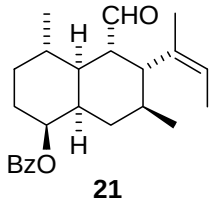


20a

Compound **20a** (0.0232 g, 100%), a colorless oil, was prepared from benzoate **20** (0.0311 g, 0.0626 mmol) according to the procedure for alcohol **9a** and purified by flash chromatography (hexane/ethyl acetate = 8/1):

R_f = 0.30 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08-8.00 (2H, m), 7.59-7.50 (1H, m), 7.49-7.39 (2H, m), 5.36 (1H, q, *J*=6.6 Hz), 5.07 (1H, ddd, *J*=10.7, 5.1, 5.1 Hz), 3.77 (1H, dd, *J*=9.8, 5.4 Hz), 3.65 (1H, dd, *J*=9.8, 9.8 Hz), 2.53-2.41 (1H, m), 2.36-2.26 (1H, m), 2.07-1.53 (16H, m), 1.41-1.28 (1H, m), 0.96 (3H, d, *J*=6.3 Hz), 0.84 (3H, d, *J*=5.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 137.3, 132.7, 130.9, 129.5, 128.3, 122.6, 76.2, 62.1, 43.3, 43.1, 41.3, 34.7, 33.9, 29.8, 28.7, 27.2, 26.1, 21.9, 21.4, 19.8, 12.9; IR ($CHCl_3$) ν_{max} 3484, 2928, 2872, 1708, 1572, 1539, 1452, 1382, 1318, 1294, 1280, 1216, 1178, 1120, 1072, 1026, 982, 754 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{24}H_{34}O_3Na$: 393.2406, found:393.2404; $[\alpha]_D^{21}$ +47.0 (*c* 0.27, $CHCl_3$).

(+)-Benzoic acid (1*S*,4*S*,4a*R*,5*S*,6*R*,7*S*,8a*R*)-5-formyl-4,7-dimethyl-6-[(*Z*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl ester (21)



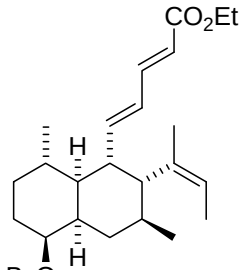
21

Compound **21** (0.0210 g, 88%), a colorless oil, was prepared from alcohol **20a** (0.0240 g, 0.0648 mmol) according to the procedure for aldehyde **10** and purified by flash chromatography (hexane/ethyl acetate = 20/1):

R_f = 0.52 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.0 (1H, d, *J*=2.7 Hz), 8.08-8.02 (2H, m), 7.59-7.52 (1H, m), 7.48-7.41 (2H, m), 5.42 (1H, q, *J*=5.6 Hz), 5.08 (1H, ddd, *J*=11.7, 4.9, 4.9 Hz), 2.68-2.58 (2H, m), 2.48-2.38 (1H, m), 1.98-1.57 (14H, m), 1.47-1.35 (1H, m), 0.94 (3H, d, *J*=6.1 Hz), 0.89 (3H, d, *J*=6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.8, 165.7, 135.7, 132.8, 130.7, 129.5, 128.3, 123.6, 75.3, 53.9, 43.3, 41.6, 41.5, 36.5, 33.4, 30.2, 29.9, 27.1, 26.0, 21.1, 19.5, 13.0; IR ($CHCl_3$)

ν_{max} 2932, 2876, 2740, 1720, 1604, 1586, 1452, 1382, 1318, 1278, 1176, 1116, 1072, 1026, 982, 758 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{24}H_{33}O_3$: 369.2430, found: 369.2424; $[\alpha]_D^{21}$ +121.7 (*c* 0.28, $CHCl_3$).

(+)-Benzoic acid (1*S*,4*S*,4a*S*,5*S*,6*R*,7*S*,8a*R*)-5-[(1*E*,3*E*)-4-ethoxycarbonyl-buta-1,3-dienyl]-4,7-dimethyl-6-[(*Z*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl ester (21a)

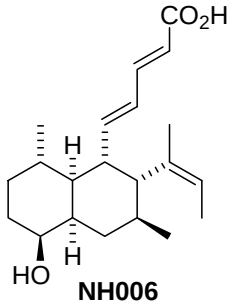


21a

Compound **21a** (0.0260 g, 98%), a colorless oil, was prepared from **21** (0.0210 g, 0.0570 mmol) according to the procedure for ester **10a** and purified by flash chromatography (hexane/ethyl acetate = 20/1). Aldehyde **21** did not remain in the reaction with phosophonate **11**, thus, all the starting material was consumed in one reaction in contrast with the reaction of aldehyde **10**:

R_f = 0.52 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10-8.02 (2H, m), 7.60-7.51 (1H, m), 7.50-7.41 (2H, m), 7.26 (1H, dd, *J*=15.4, 11.2 Hz), 6.54 (1H, dd, *J*=14.9, 9.8 Hz), 6.10 (1H, dd, *J*=14.9, 11.2 Hz), 5.78 (1H, d, *J*=15.4 Hz), 5.27 (1H, q, *J*=6.3 Hz), 5.01 (1H, ddd, *J*=11.0, 5.1, 5.1 Hz), 4.25-4.14 (2H, m), 2.60-2.40 (3H, m), 2.01-1.76 (6H, m), 1.60 (3H, d, *J*=6.3 Hz), 1.50 (3H, s), 1.46-1.32 (1H, m), 1.32-1.22 (5H, m), 0.98 (3H, d, *J*=6.3 Hz), 0.84 (3H, d, *J*=5.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 165.8, 146.4, 144.9, 137.2, 132.8, 130.8, 129.5, 128.5, 128.3, 121.5, 119.8, 75.9, 60.2, 49.9, 45.4, 42.8, 35.3, 33.6, 30.0, 28.6, 27.7, 26.1, 21.0, 20.9, 19.5, 14.3, 12.7; IR ($CHCl_3$) ν_{max} 2932, 2876, 1714, 1638, 1452, 1380, 1278, 1178, 1158, 1134, 1116, 1070, 1028, 1002, 984, 758 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{30}H_{40}O_4Na$: 487.2824, found: 487.2815; $[\alpha]_D^{20}$ +308.1 (*c* 019, $CHCl_3$).

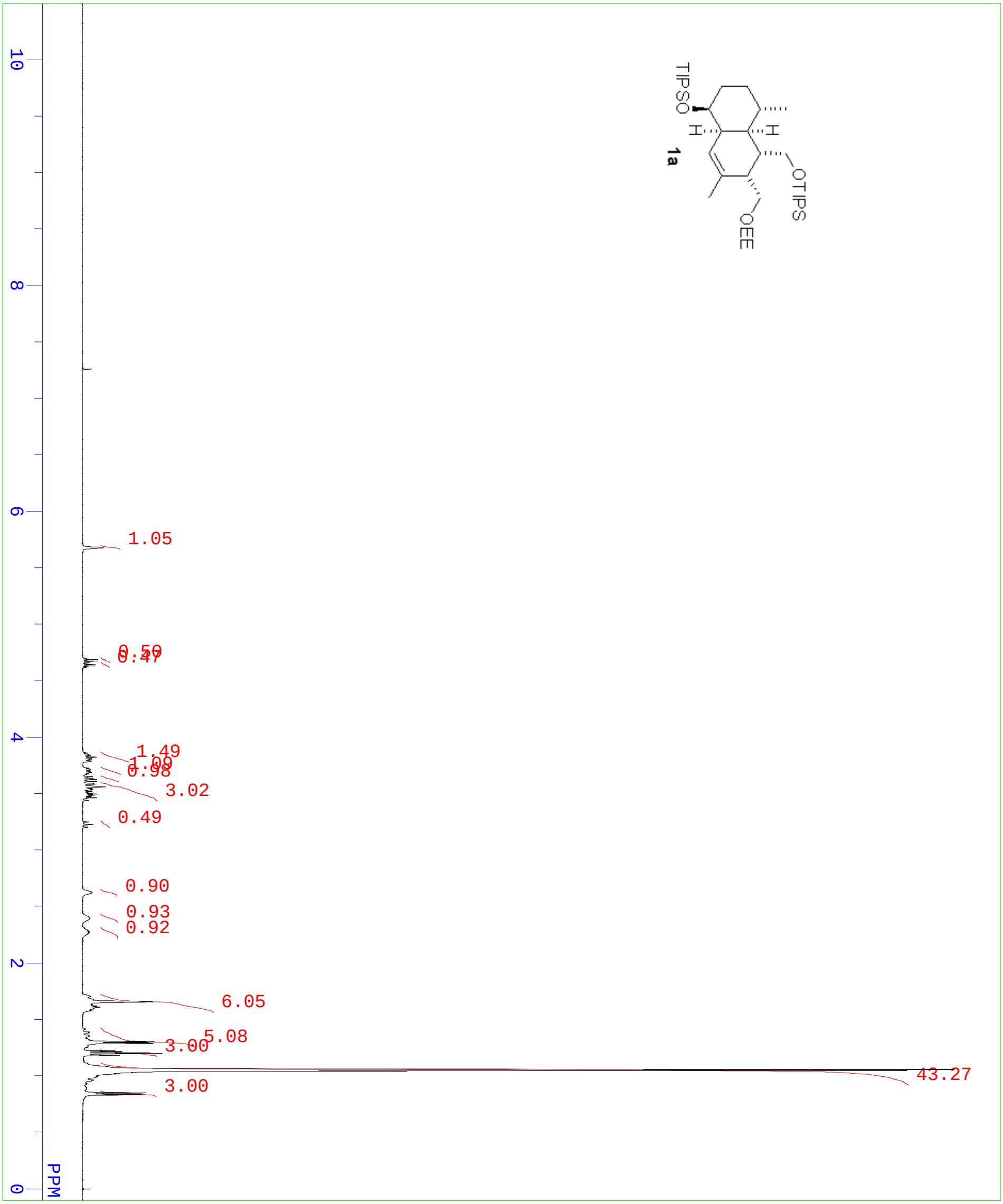
(+)-(2*E*,4*E*)-5-{(1*S*,2R,3*S*,4a*R*,5*S*,8*S*,8a*S*)--5-Hydroxy-3,8-dimethyl-2-[(*Z*)-1-methyl-propenyl]-decahydro-naphthalen-1-yl}-penta-2,4-dienoic acid (NH006)



NH006

NH006 (0.0152 g, 82%), a colorless oil, was prepared from ester **21a** (0.0260 g, 0.0560 mmol) according to the procedure for hydroxycarboxylic acid **12** and purified by flash chromatography (hexane/ethyl acetate = 2/1).

R_f = 0.29 (hexane/ethyl acetate = 1/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (1H, dd, *J*=15.4, 11.0 Hz), 6.62 (1H, dd, *J*=14.8, 10.2 Hz), 6.13 (1H, dd, *J*=14.8, 11.0 Hz), 5.79 (1H, d, *J*=15.4 Hz), 5.27 (1H, qd, *J*=6.7, 1.3 Hz), 3.67 (1H, ddd, *J*=11.8, 4.9, 4.9 Hz), 2.58-2.46 (2H, m), 2.23-2.16 (1H, m), 1.90-1.72 (4H, m), 1.69-1.64 (1H, m), 1.63-1.53 (5H, m), 1.51 (3H, s), 1.24-1.16 (1H, m), 1.16-1.10 (1H, m), 1.08-1.00 (1H, m), 0.93 (3H, d, *J*=6.4 Hz), 0.83 (3H, d, *J*=6.1 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.5, 148.5, 147.3, 137.8, 128.2, 121.5, 118.5, 73.1, 50.3, 45.6, 43.0, 38.1, 33.9, 29.7, 29.5, 29.0, 28.8, 27.7, 21.0, 19.5, 12.7; IR ($CHCl_3$) ν_{max} 3388, 2924, 1690, 1636, 1614, 1456, 1416, 1380, 1306, 1270, 1244, 1160, 1106, 1076, 1050, 1002, 952, 754 cm^{-1}; FAB HRMS $[M+Na]^+$ calcd for $C_{21}H_{32}O_3Na$: 355.2249, found: 355.2233; $[\alpha]_D^{19}$ +267.5 (*c* 033, $CHCl_3$).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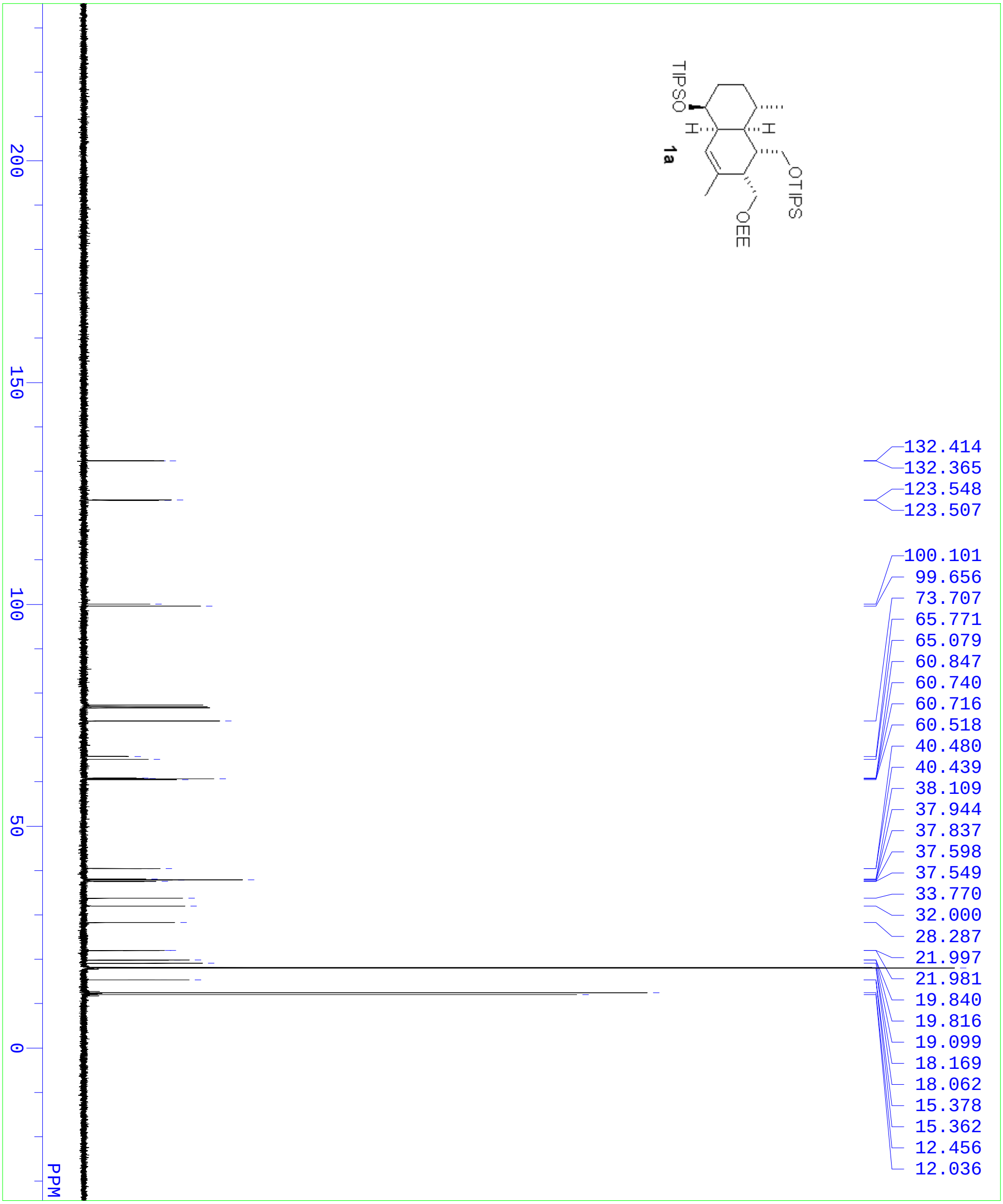
3.00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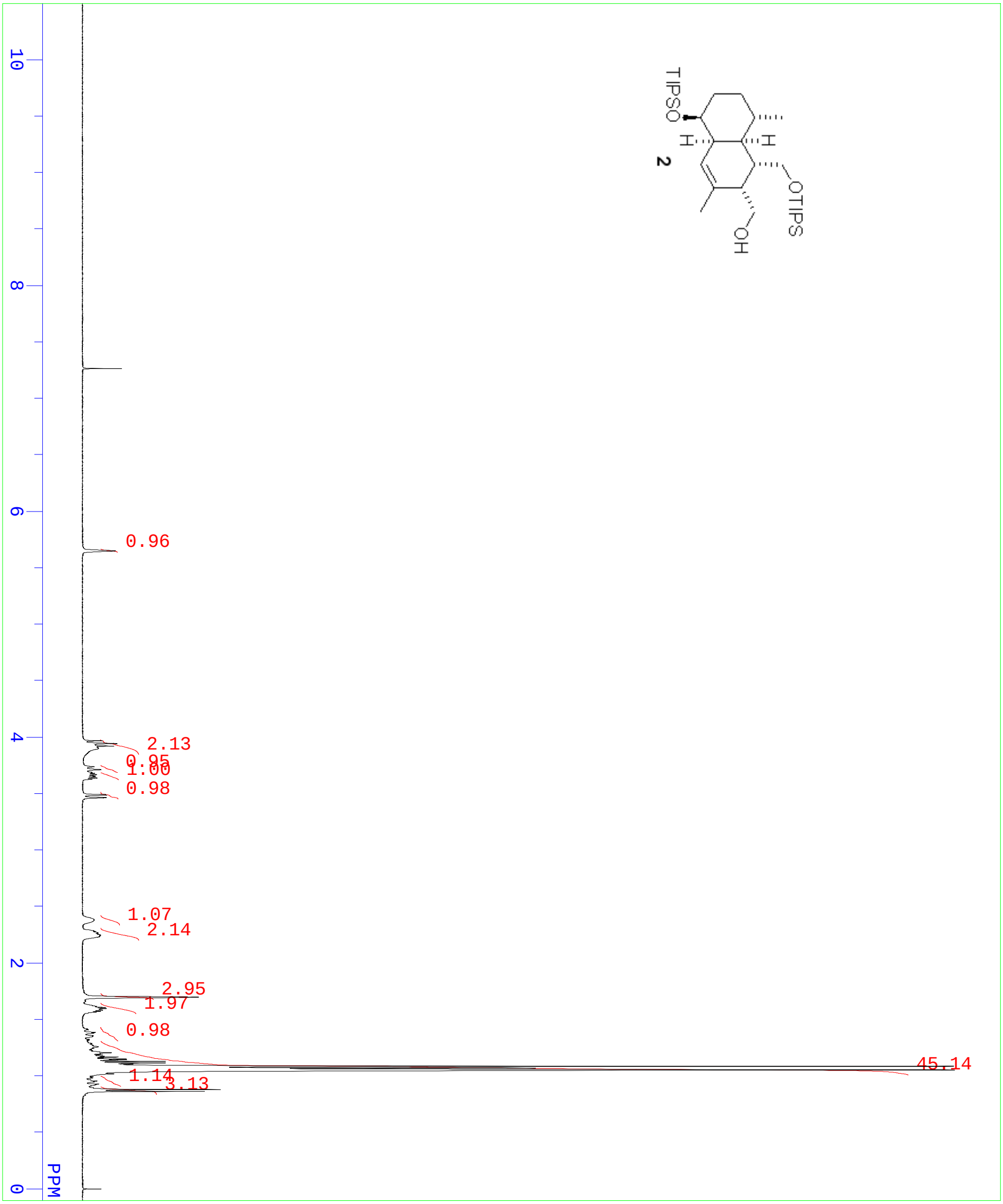
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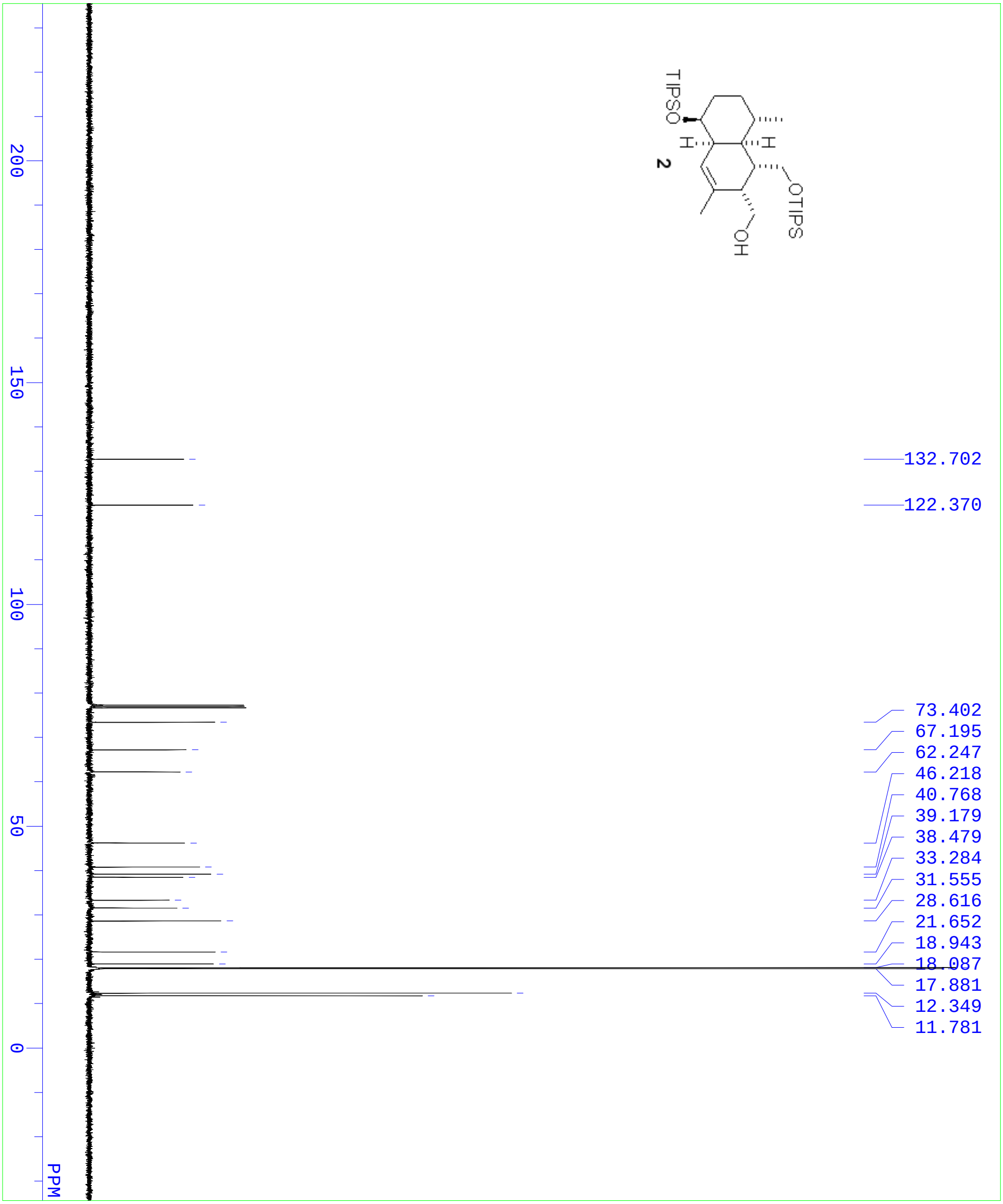
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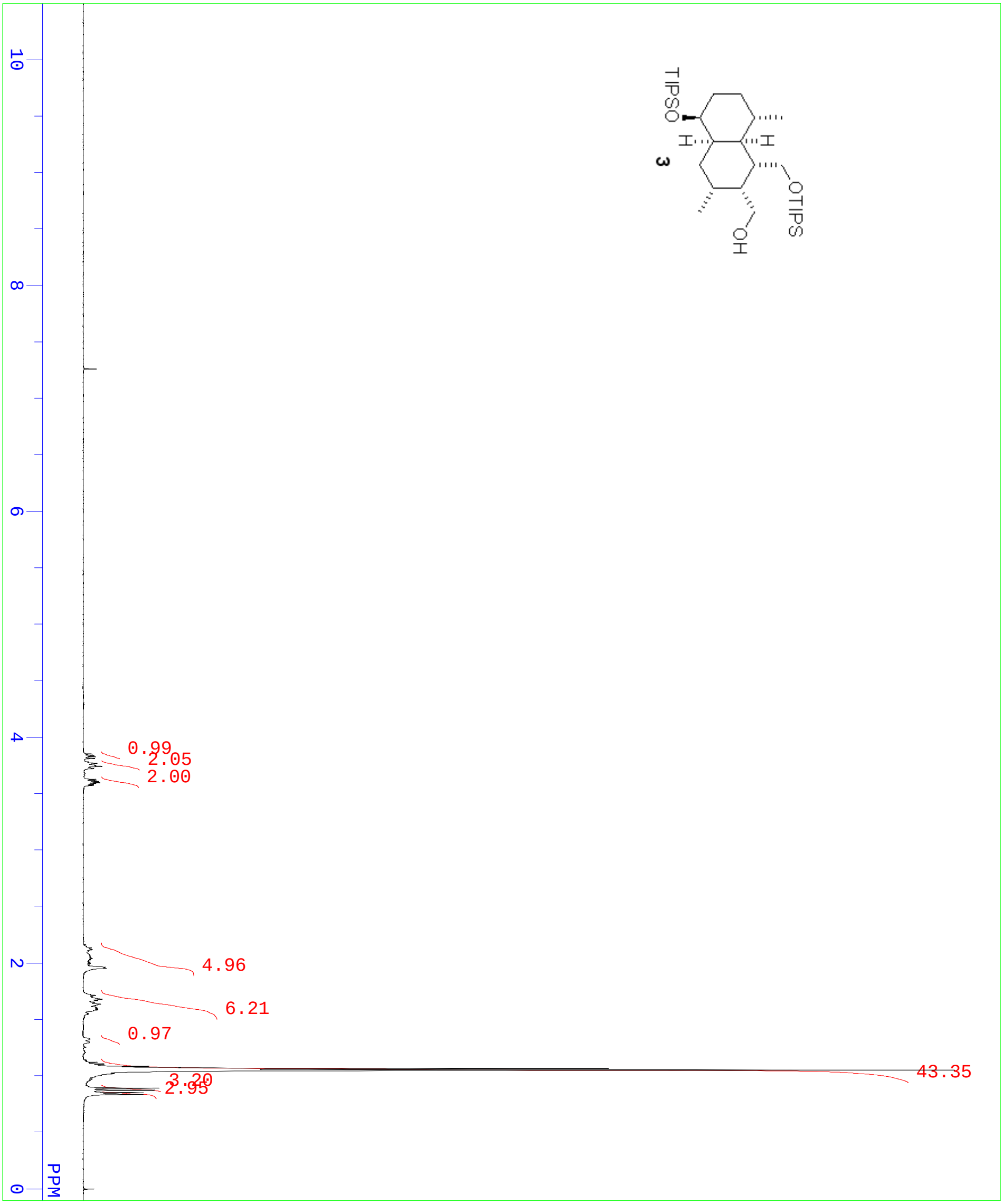
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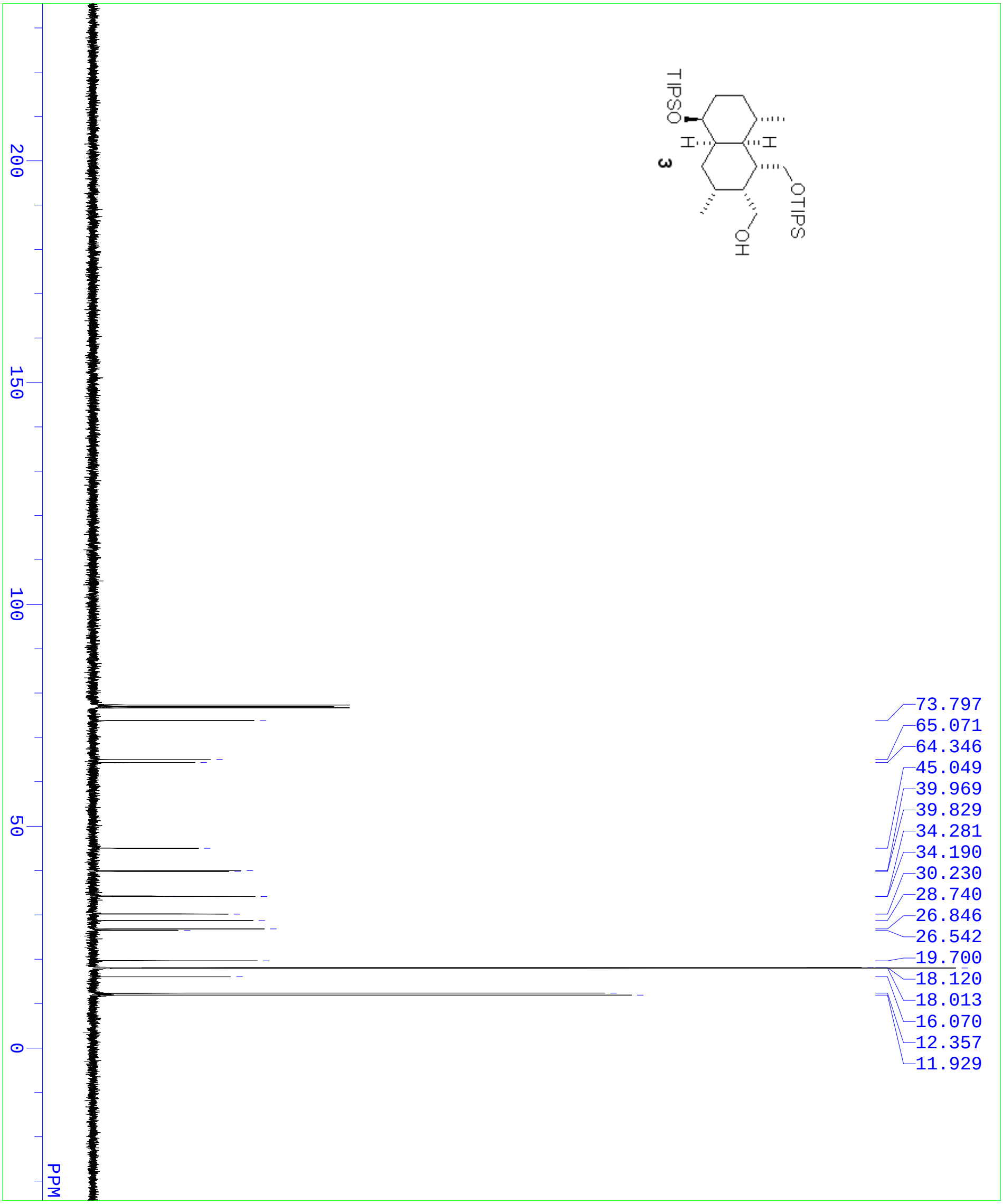
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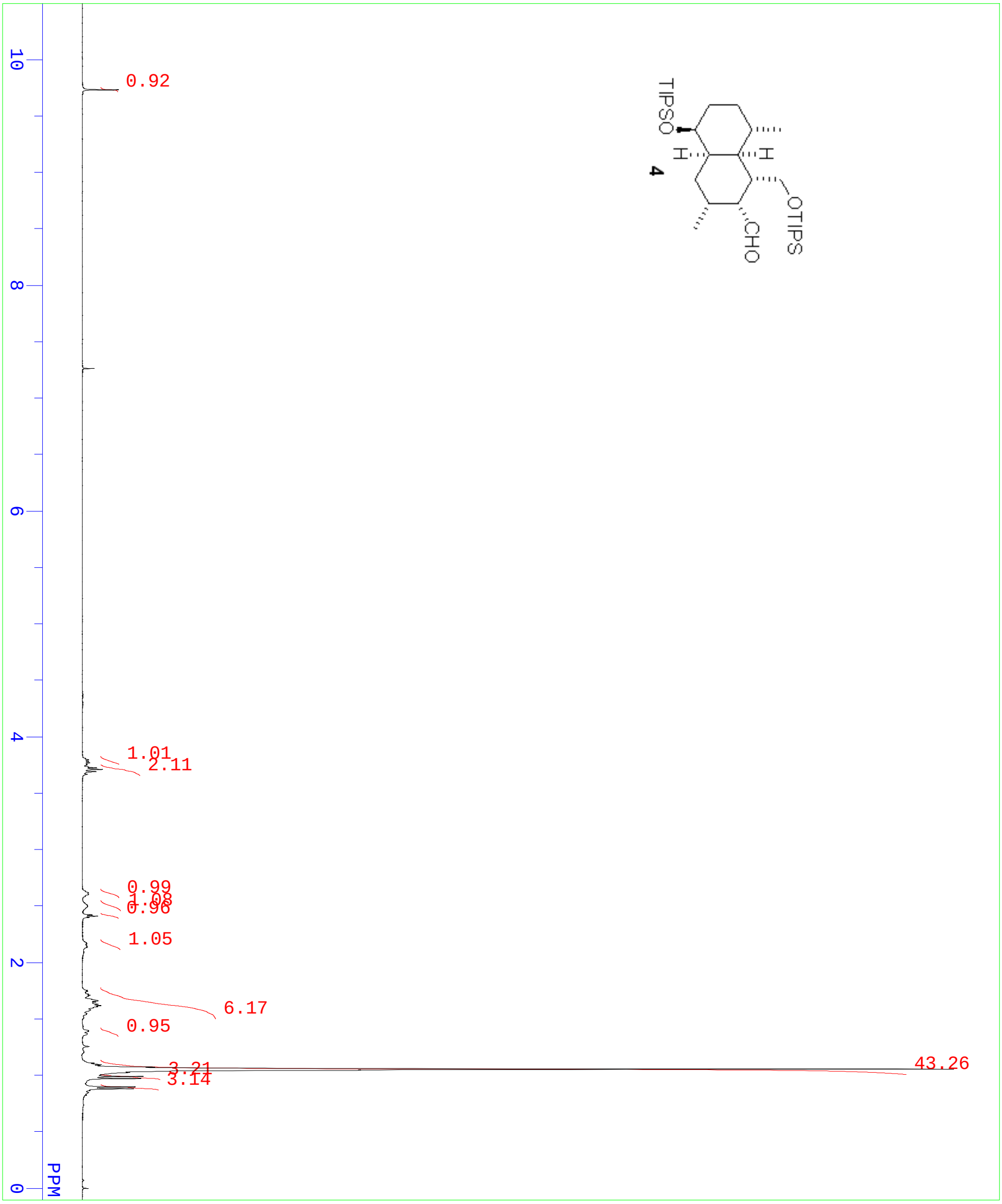
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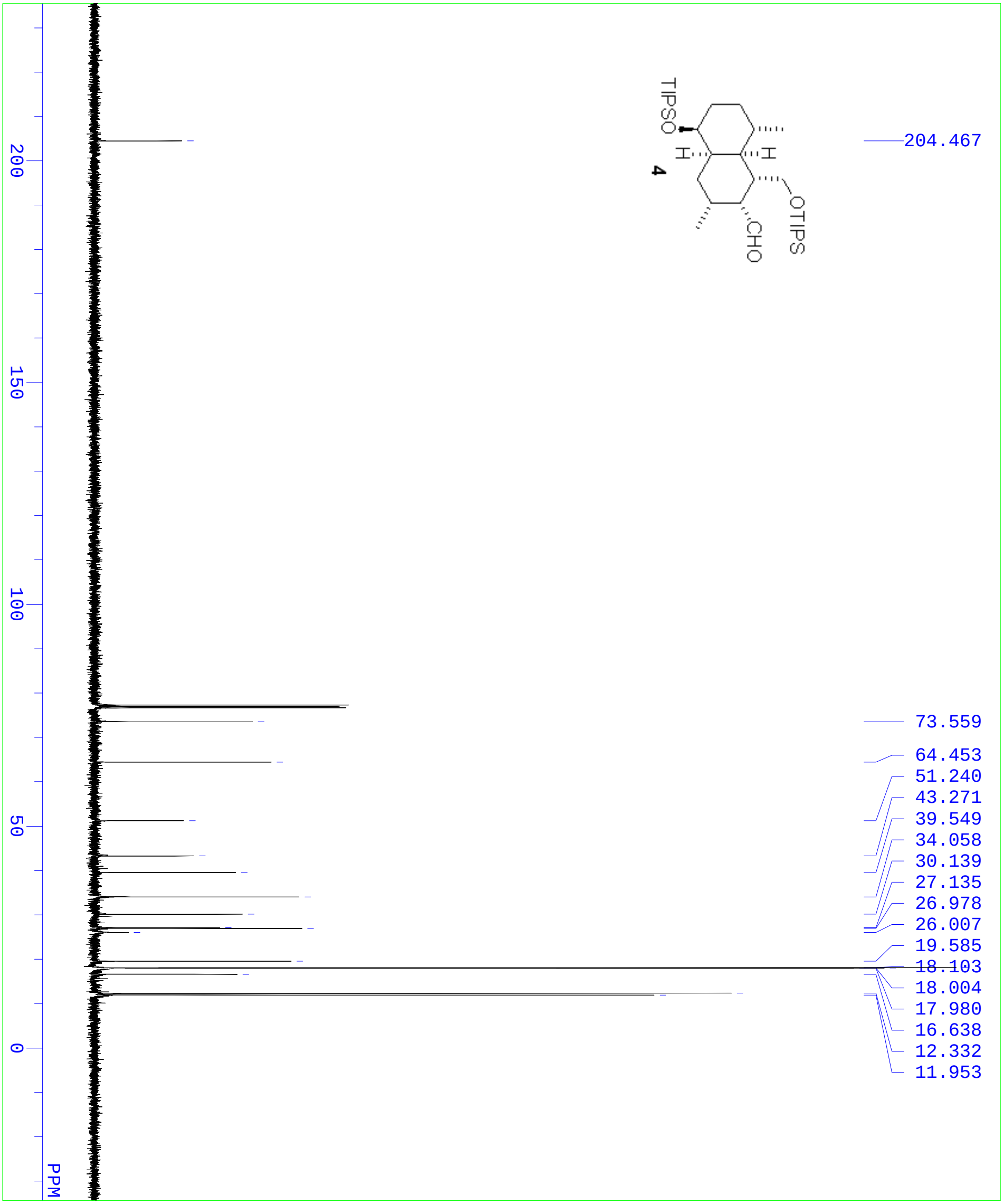
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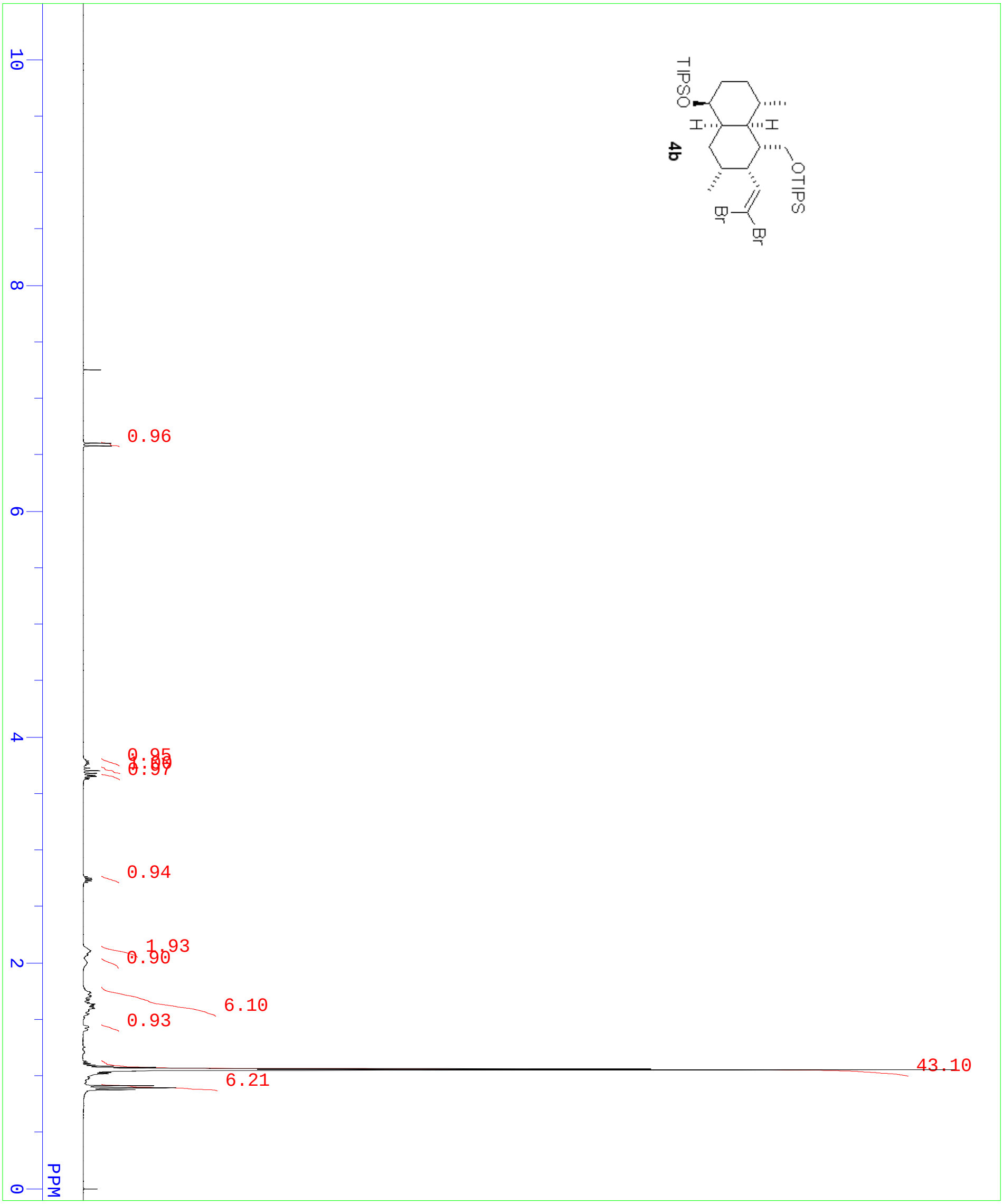
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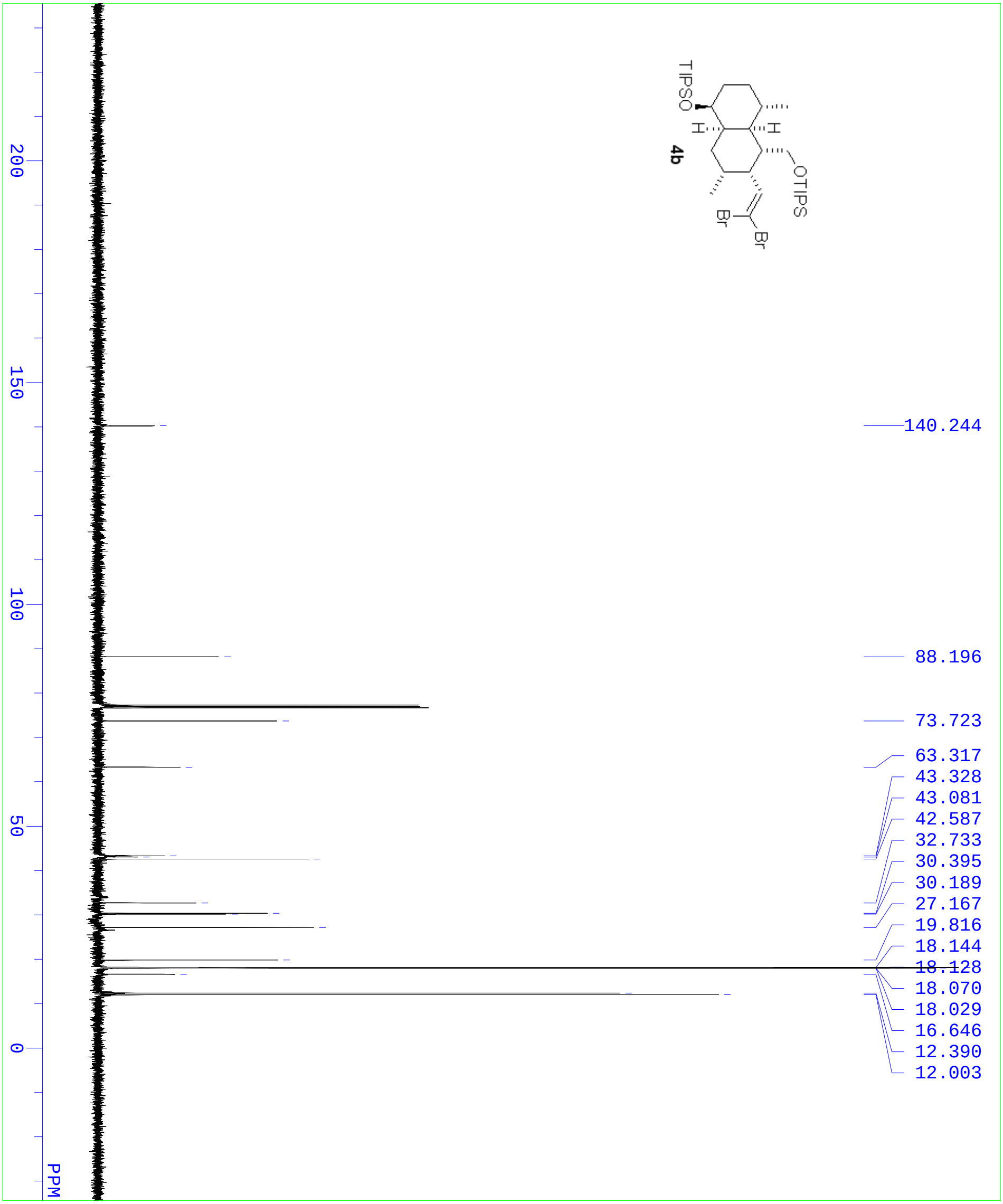
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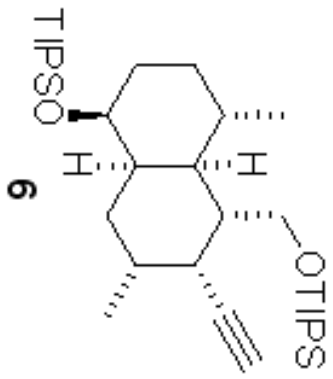
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OTIPS

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10
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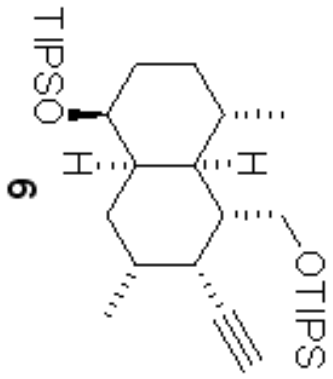
PPM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H
OTIPS

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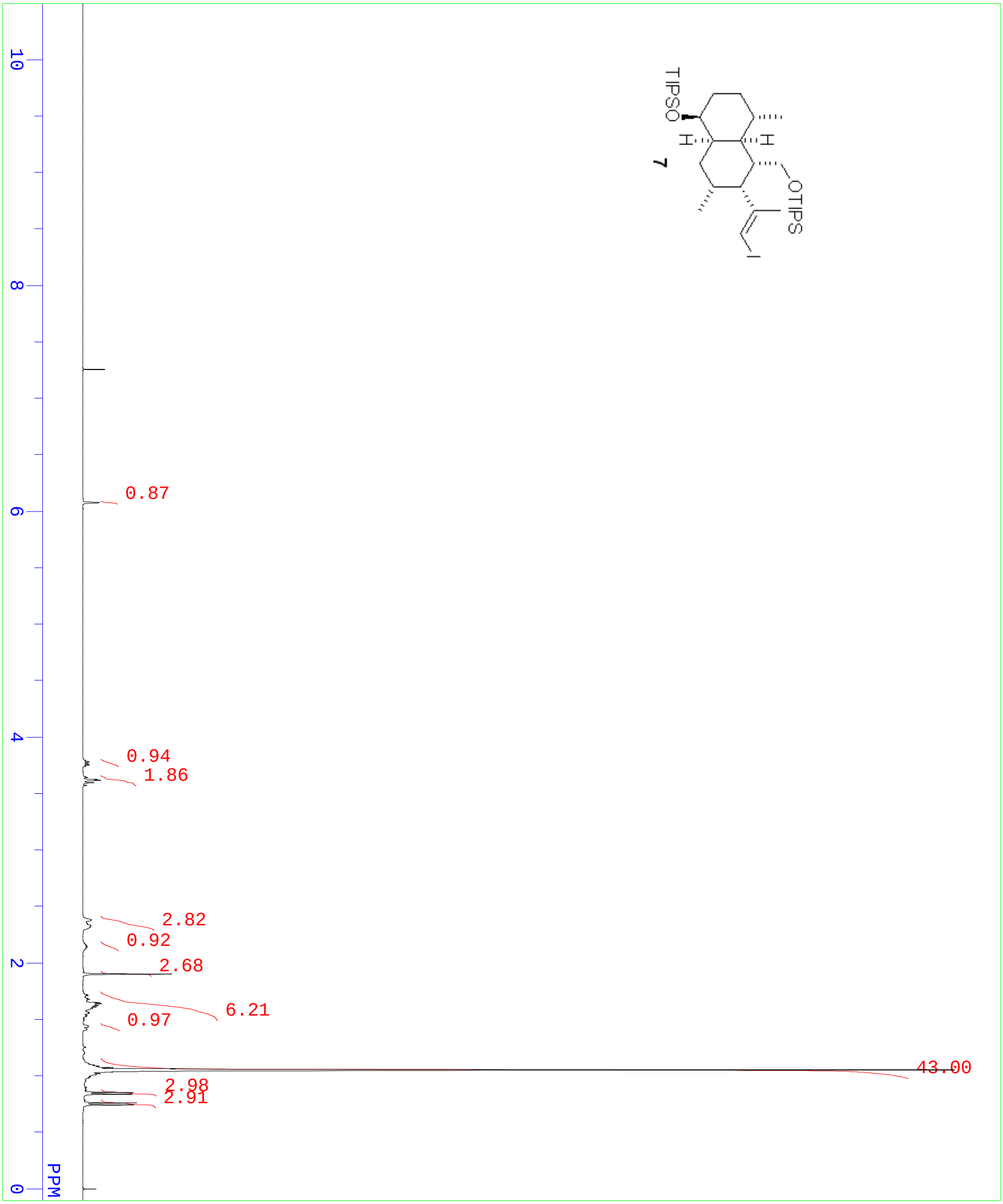
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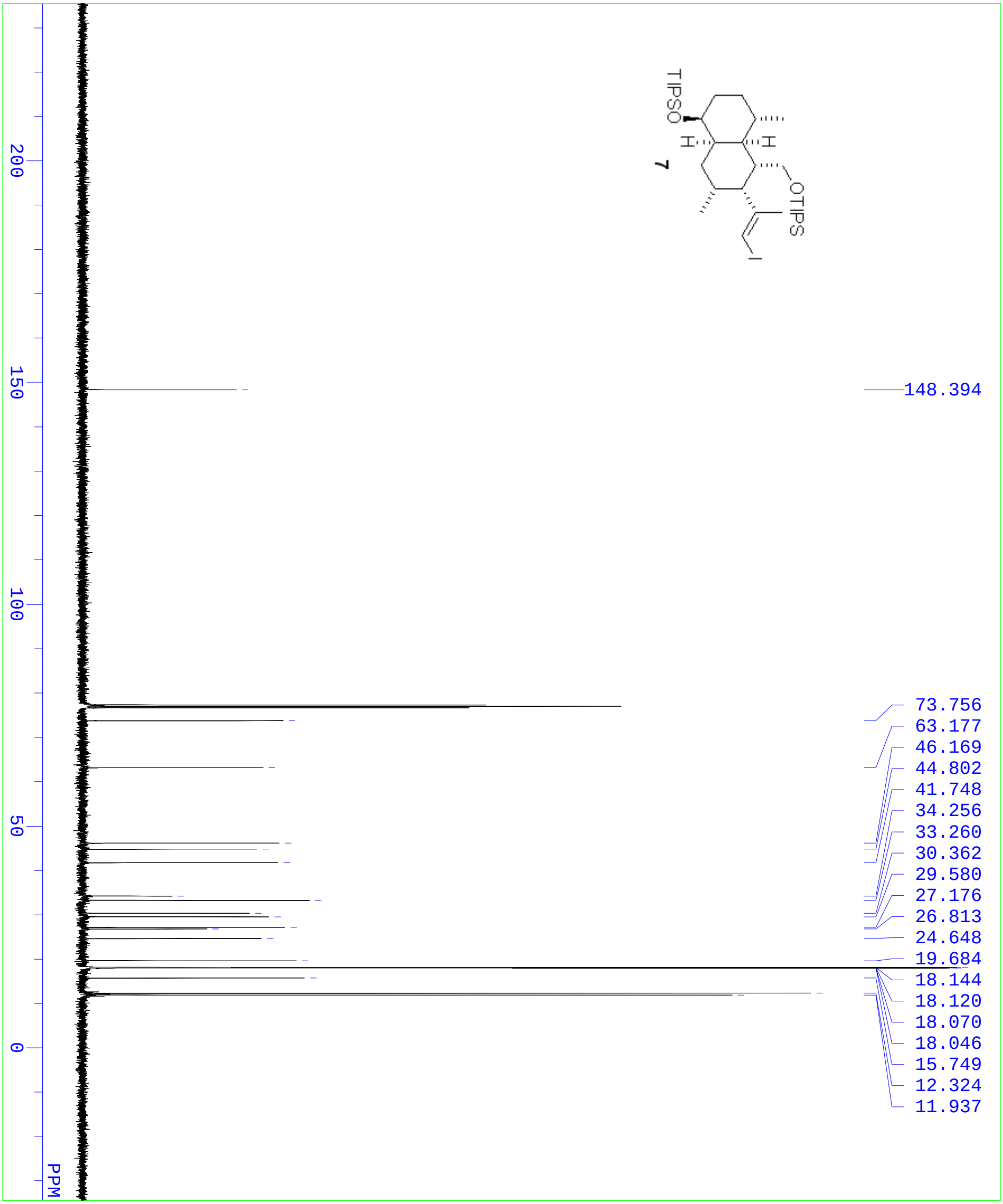
H
OTIPS
7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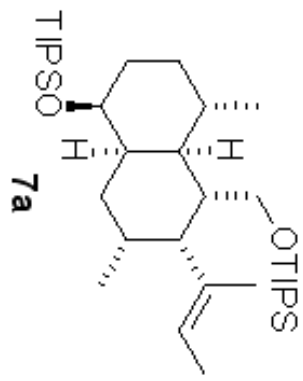
PPM


TIPSO
H
H
OTIPS

7a

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2.83
10
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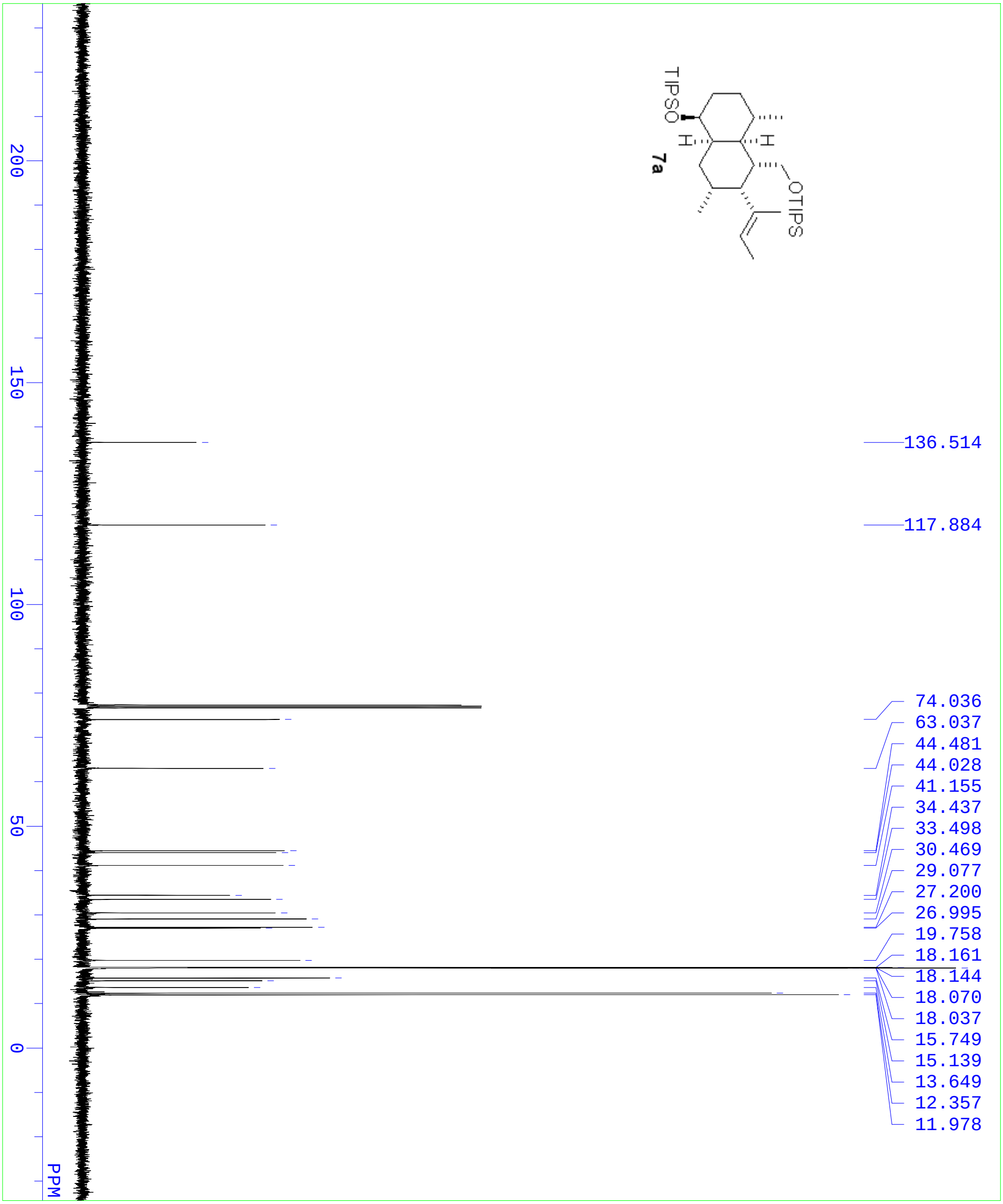
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OTIPS
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41.155
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30.469
29.077
27.200
26.995
19.758
18.161
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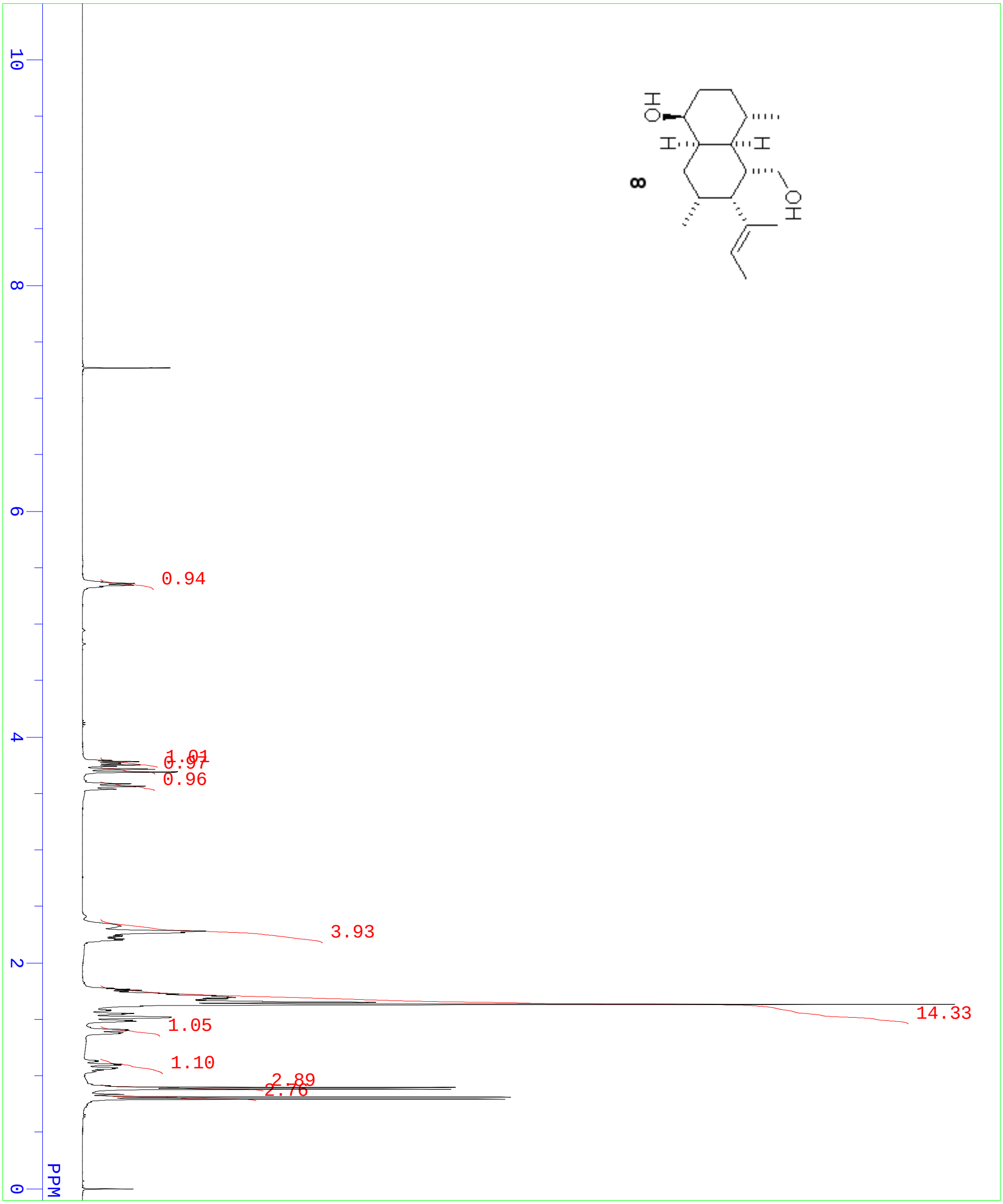
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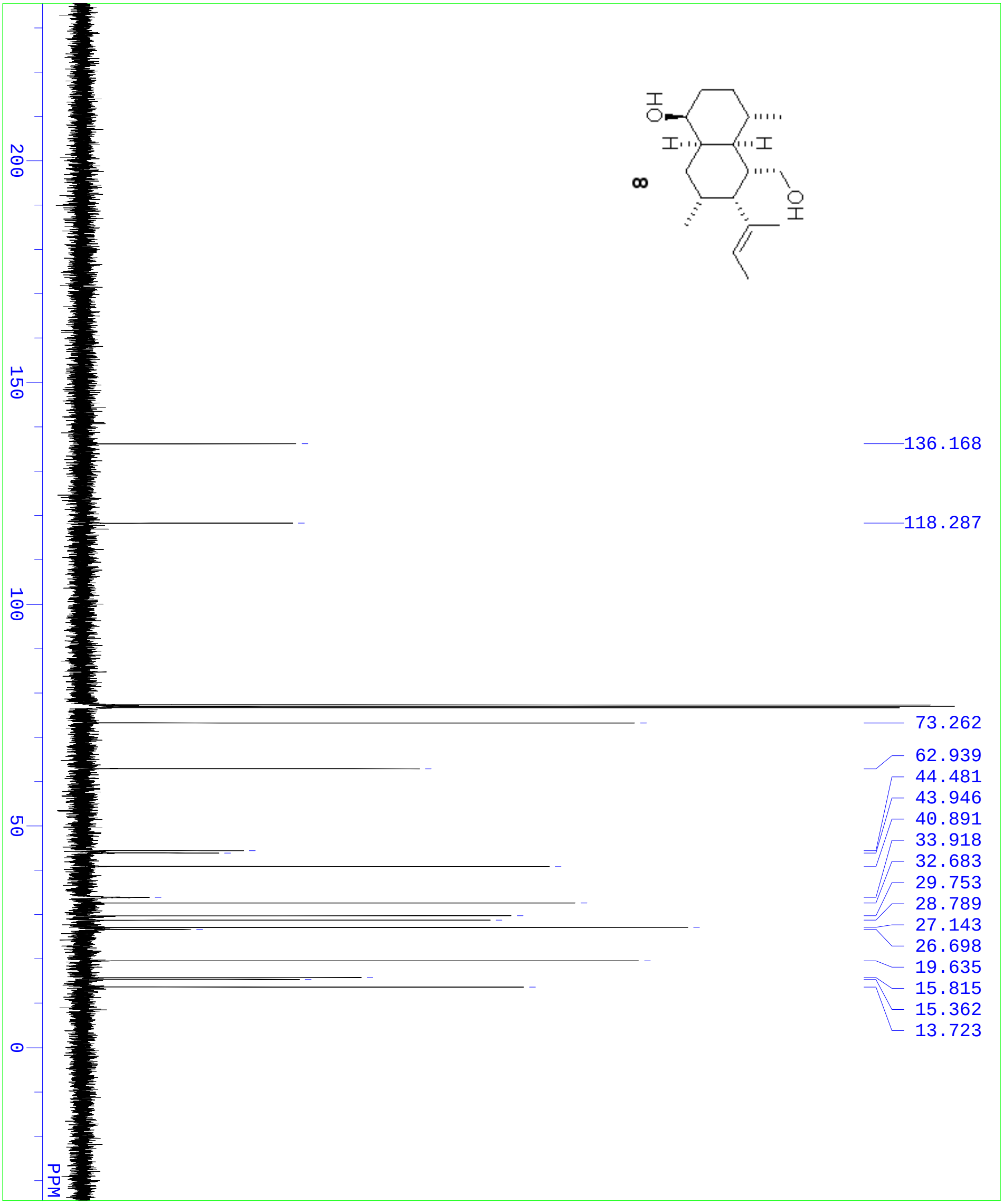
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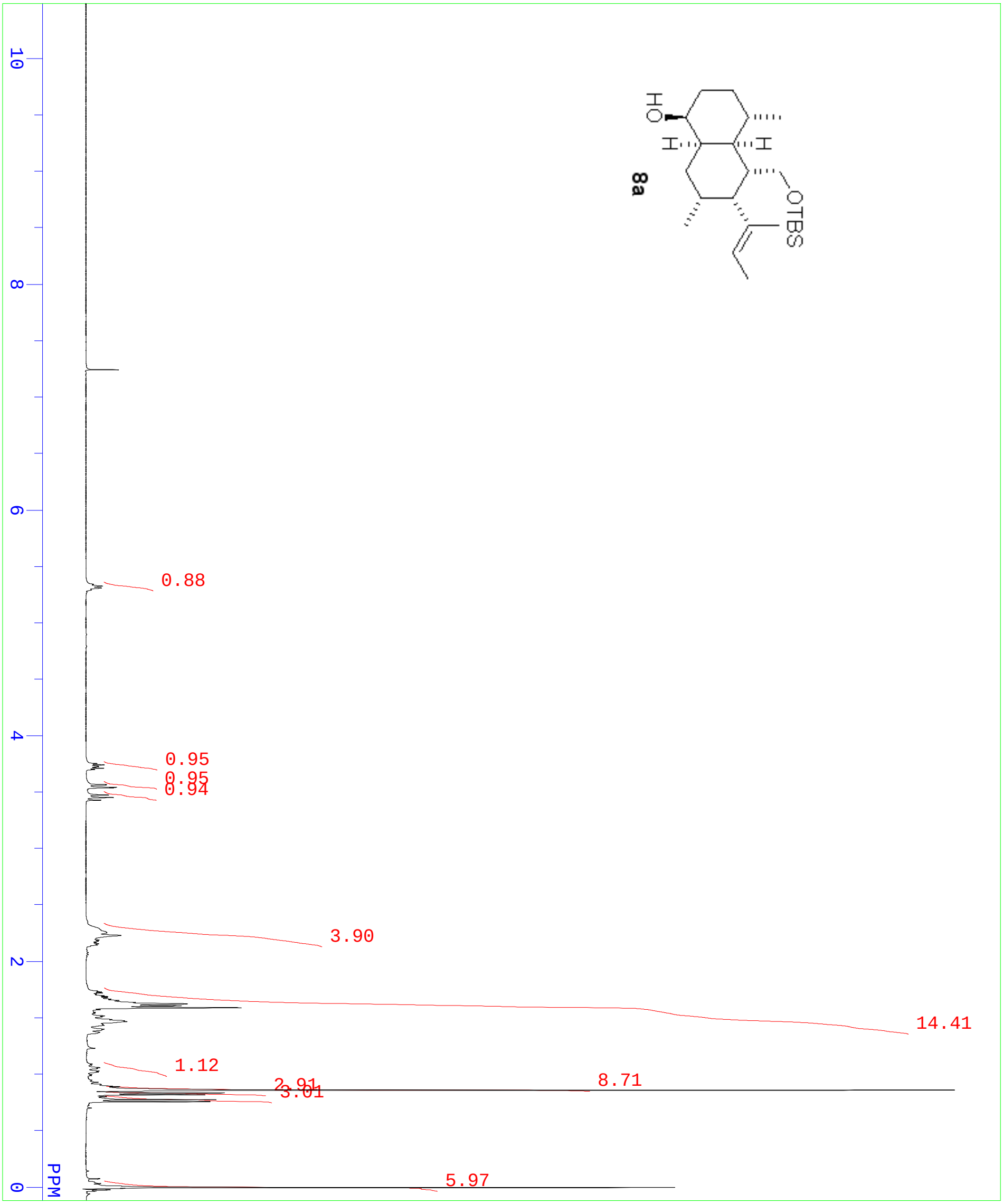
15.362
13.723


HO
H
H
OTBS
8a
10
8
6
4
2
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PPM
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0.95
0.94
3.90
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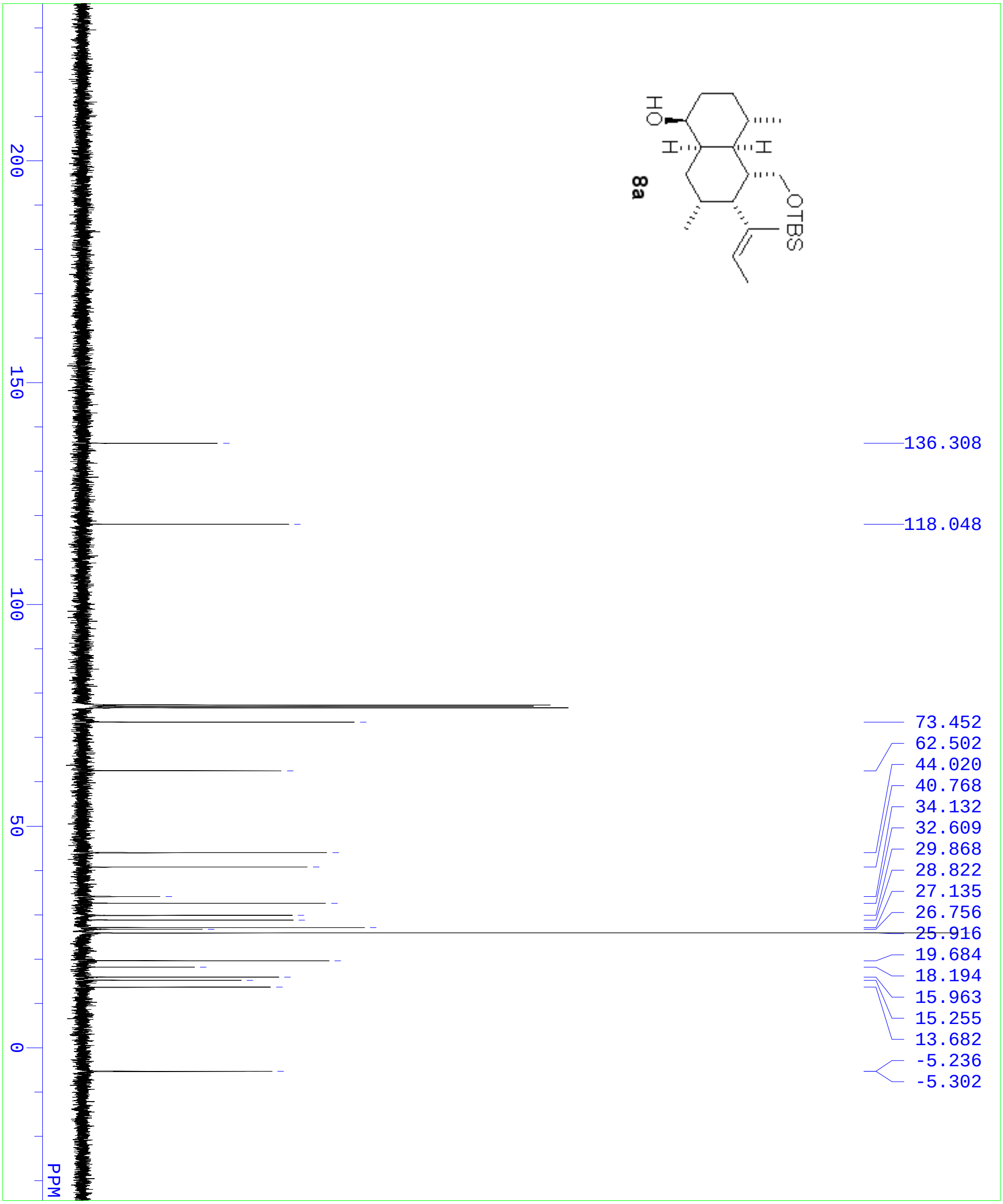
1.12
2.91
3.01
8.71
5.97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H
H
OTBS
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44.020
40.768
34.132
32.609
29.868
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26.756
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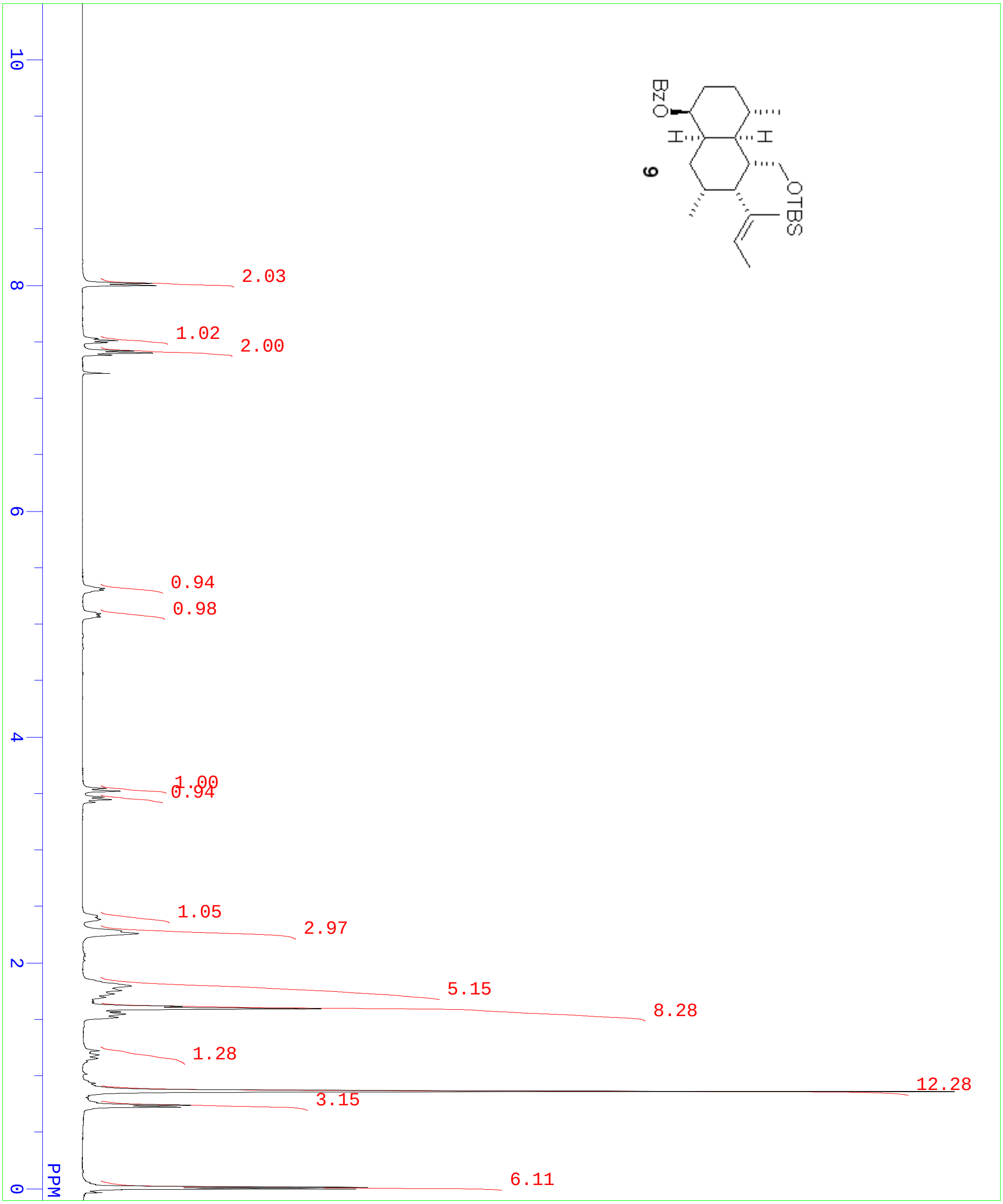
15.963
15.255
13.682
-5.236
-5.302


BzO
H
H
OTBS
9
10
8
6
4
2
0
PPM
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2.00
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0.94
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2.97
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8.28
1.28
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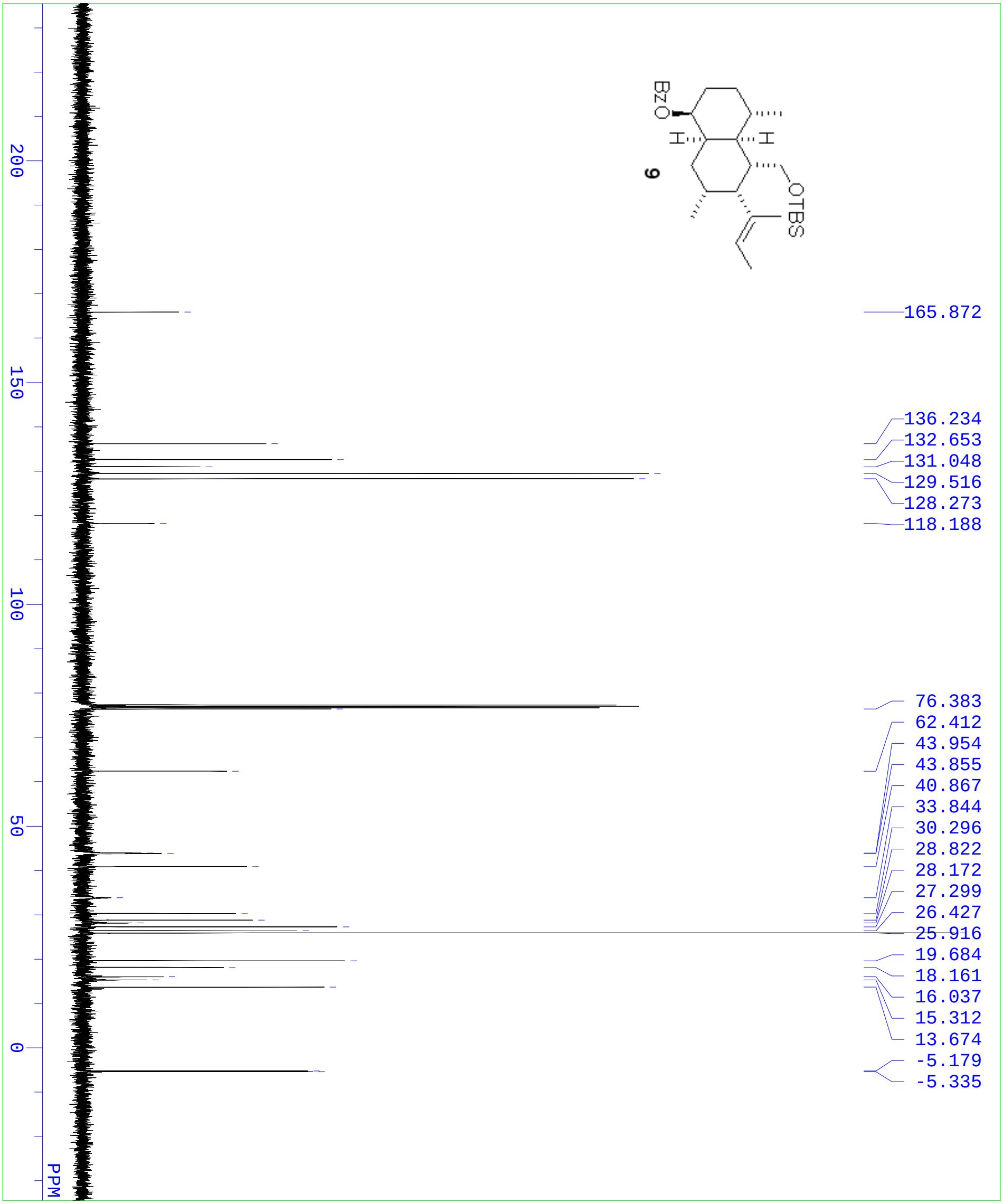
3.15
6.11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129.516
128.273
118.188
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62.412
43.954
43.855
40.867
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30.296
28.822
28.172
27.299
26.427
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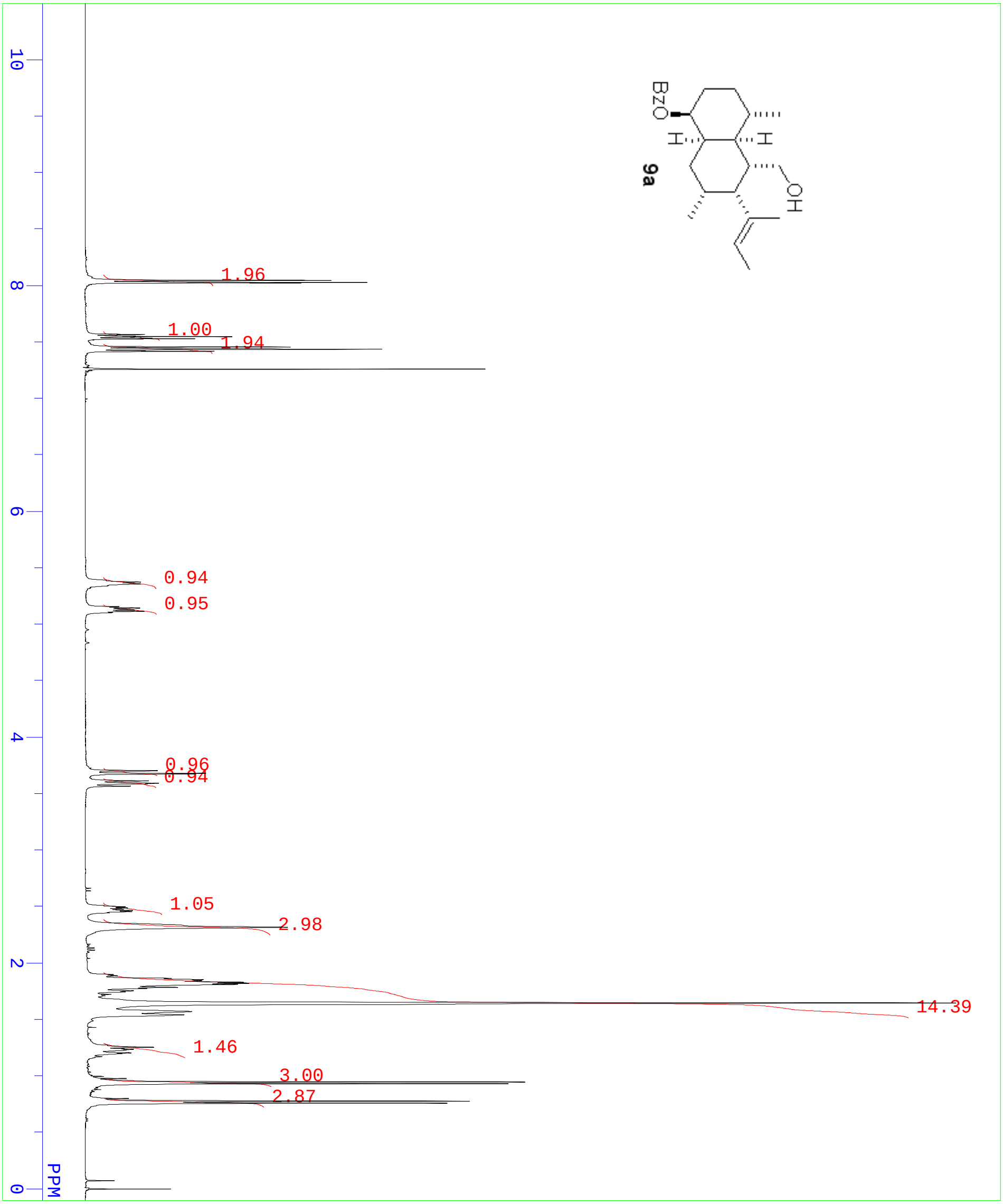
0
PPM


BzO
H
H
OH
9a
10
8
6
4
2
0
PPM
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1.94
0.94
0.95
0.96
0.94
1.05
2.98
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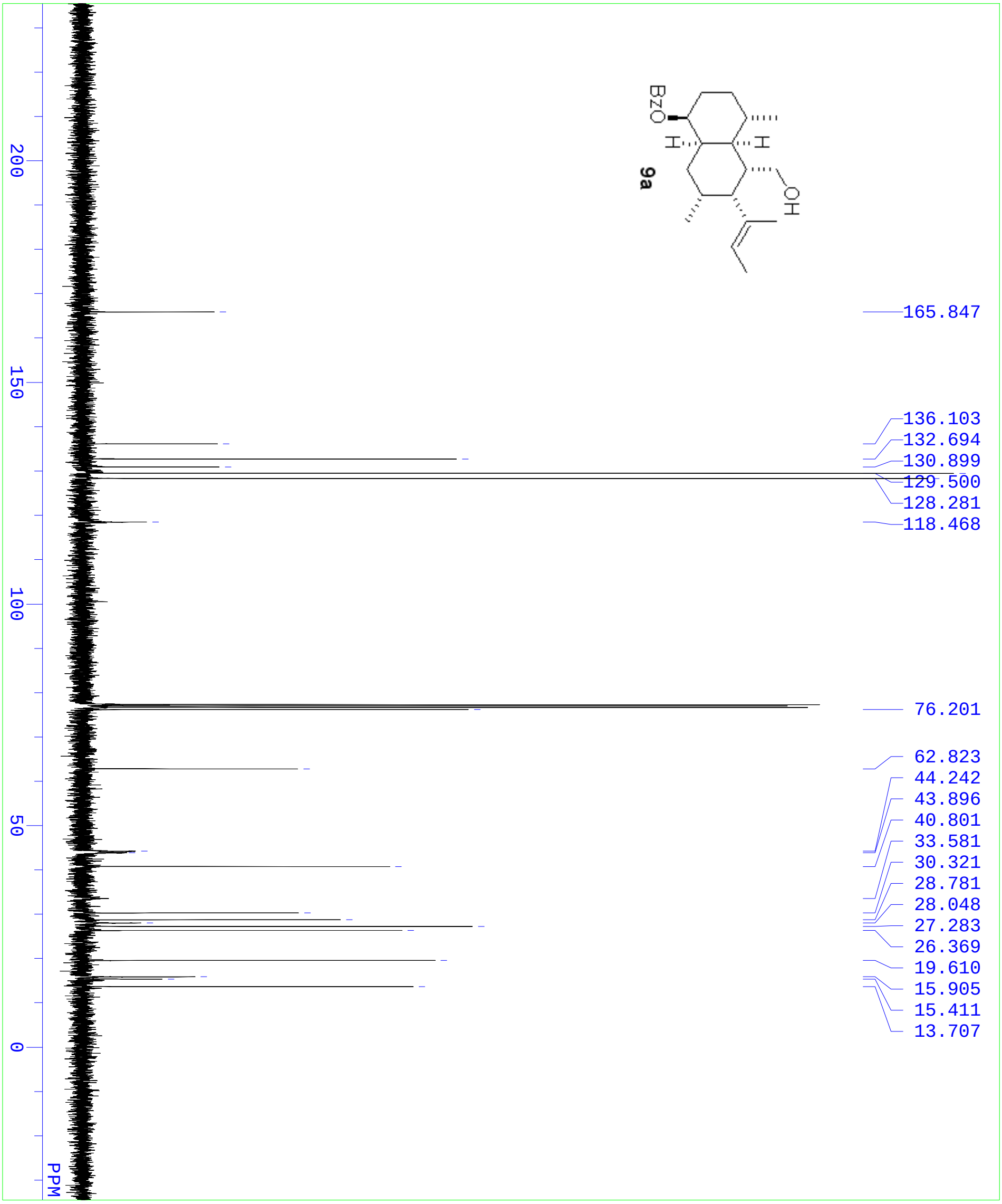
1.46
3.00
2.87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H
OH
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128.281
118.468
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62.823
44.242
43.896
40.801
33.581
30.321
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28.048
27.283
26.369
19.610
15.905
15.411
13.707
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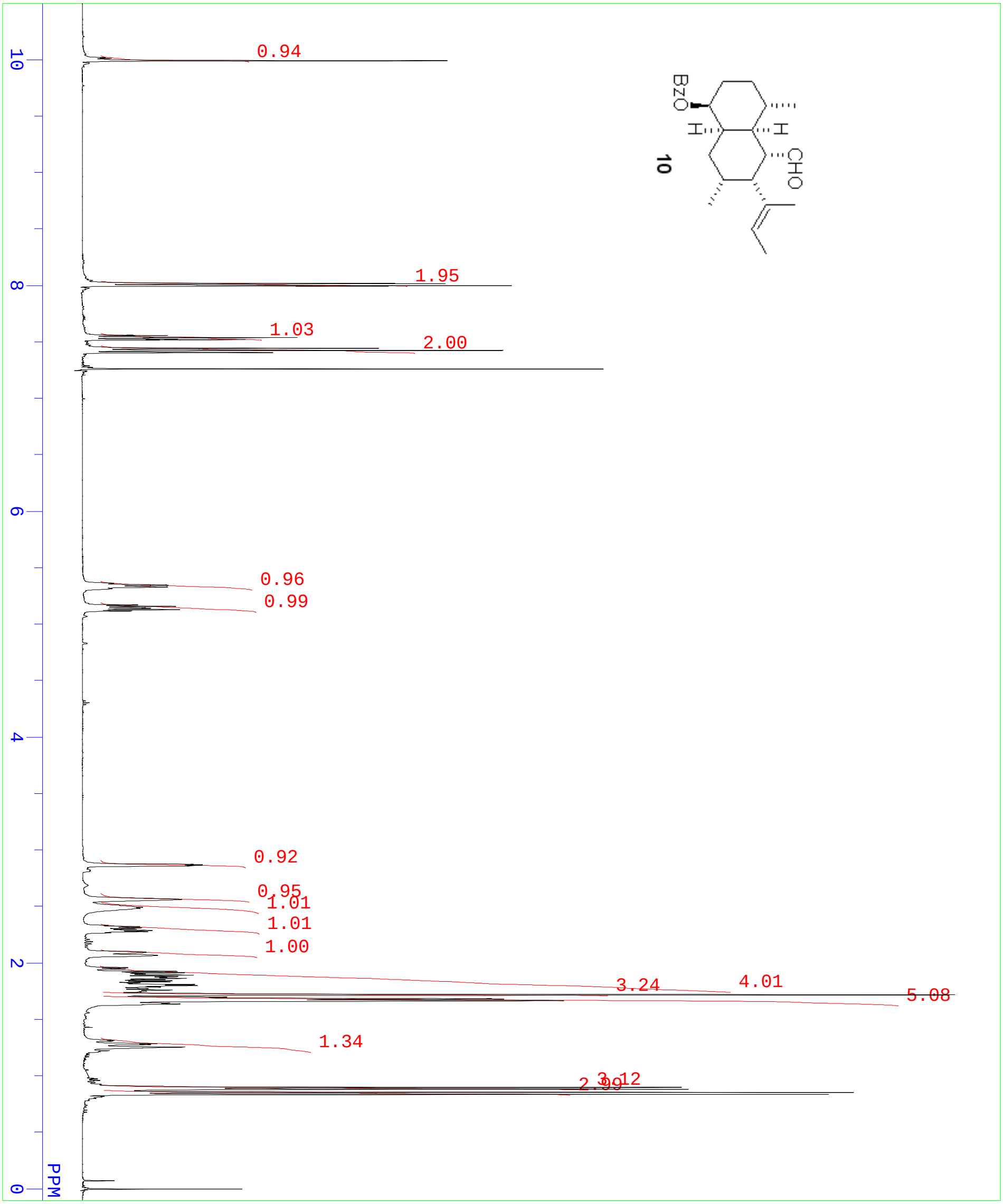
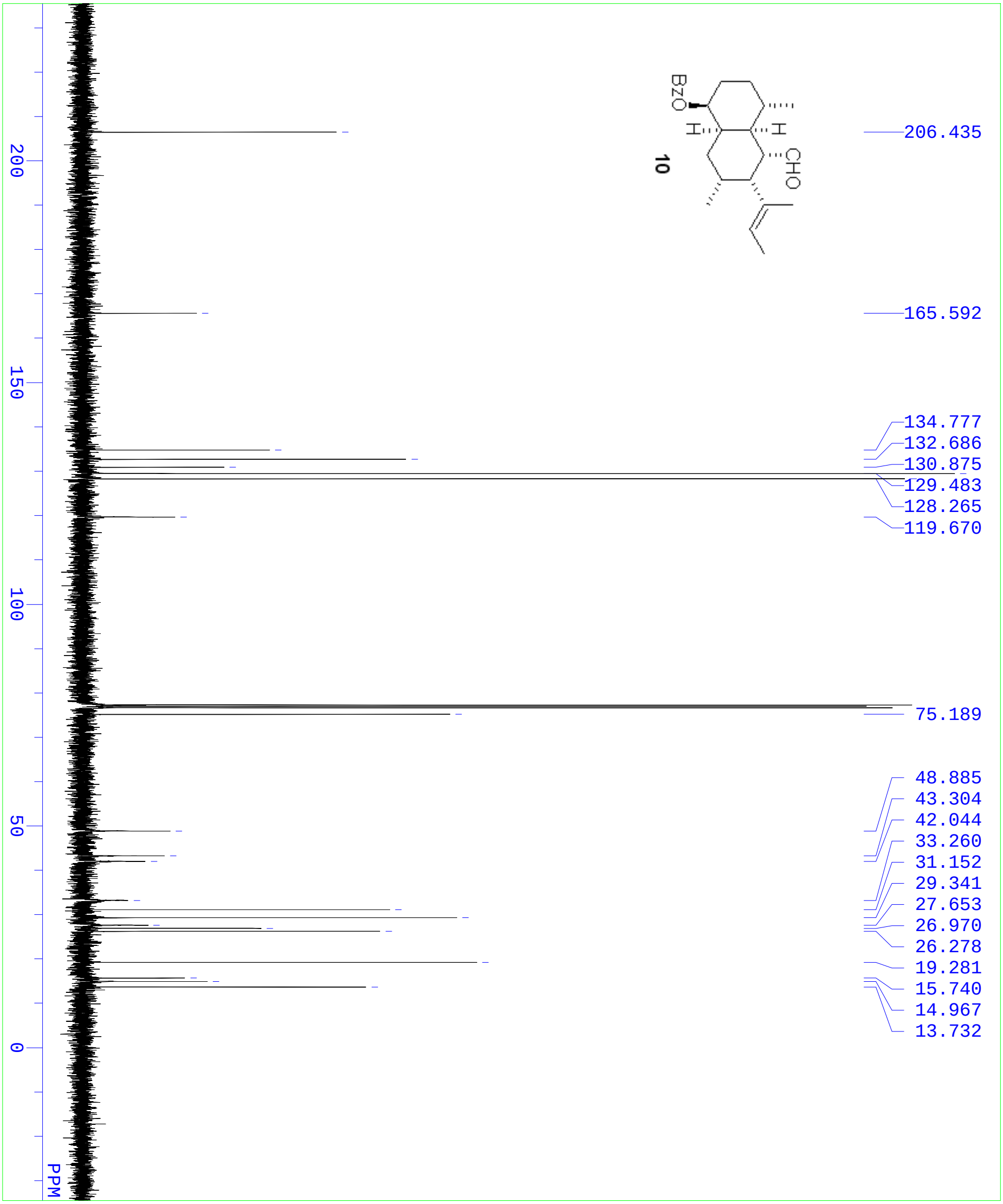
150
100
50
0
PPM


10
8
6
4
2
0
PPM
0.94
1.95
1.03
2.00
0.96
0.99
0.92
0.95
1.01
1.01
1.00
3.24
4.01
5.08
1.34
2.99
3.12
BzO
H
H
CHO
10


BzO
H
H
CHO
10
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132.686
130.875
129.483
128.265
119.670
75.189
48.885
43.304
42.044
33.260
31.152
29.341
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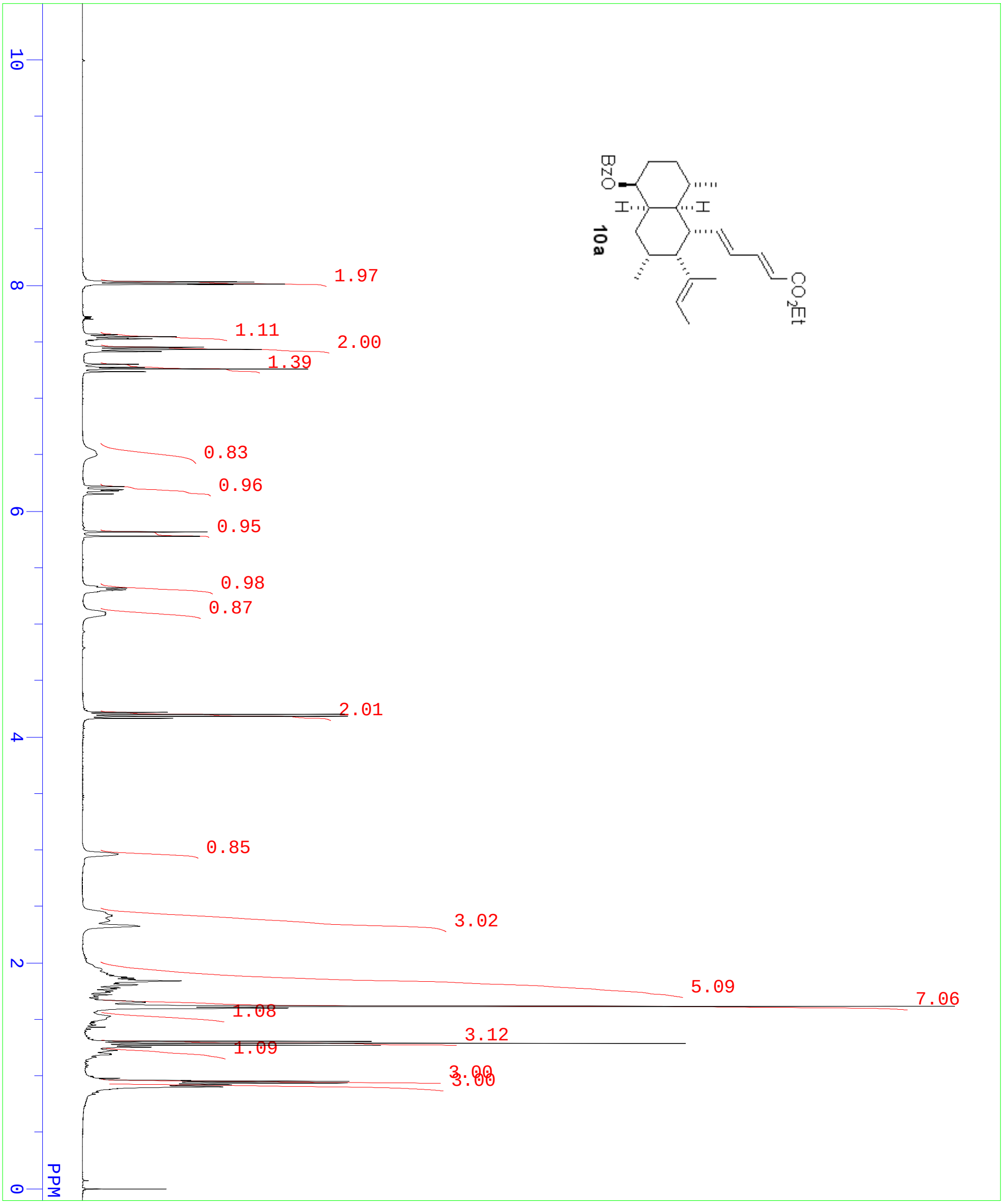
26.970
26.278
19.281
15.740
14.967
13.732
200
150
100
50
0
PPM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8
6
4
2
0
PPM
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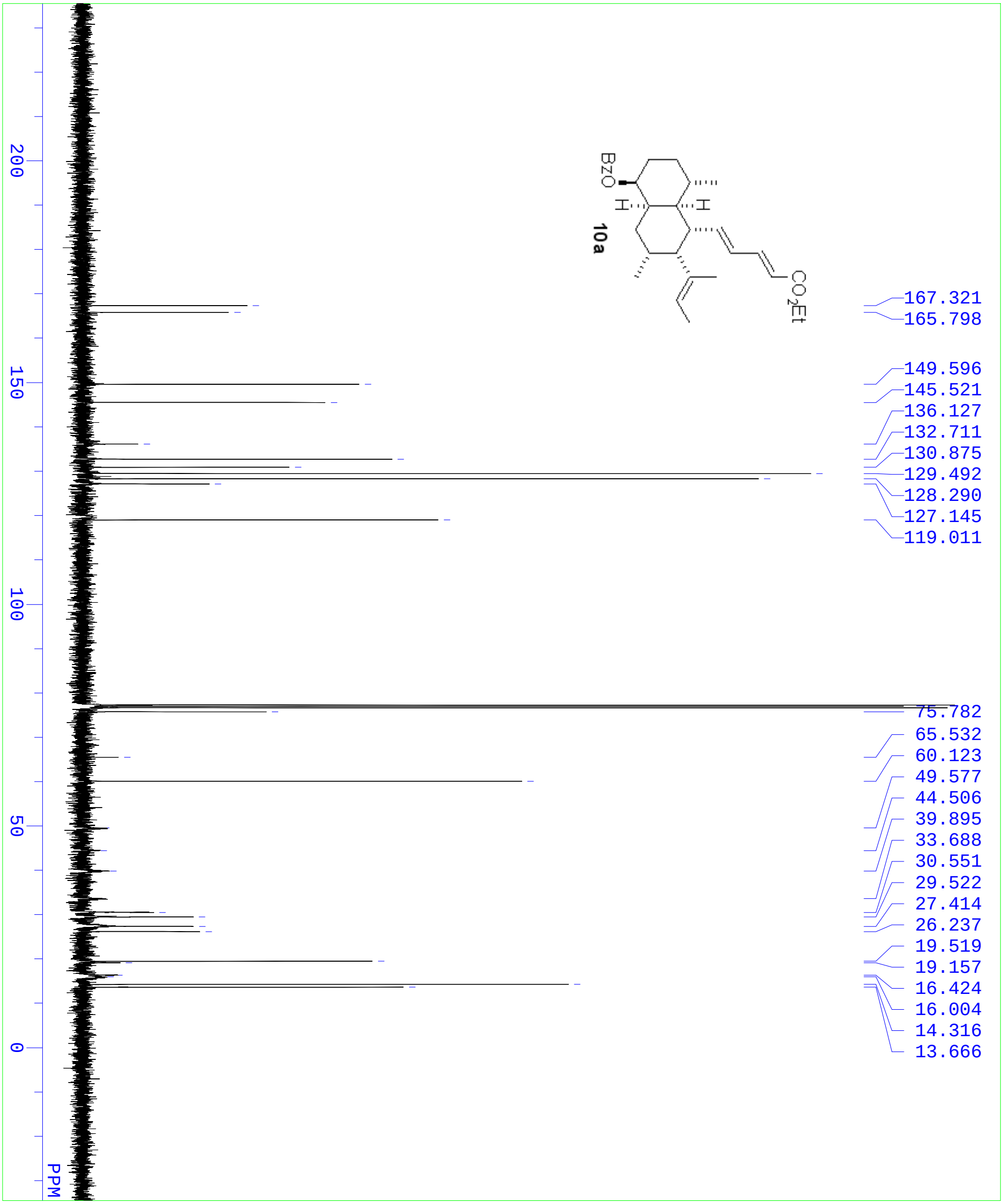
1.11
2.00
1.39
0.83
0.96
0.95
0.98
0.87
2.01
0.85
3.02
5.09
7.06
1.08
3.12
1.09
3.00
3.00
BzO
H
H
CO2Et
10a


BzO
H
H
CO2Et
10a
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165.798
149.596
145.521
136.127
132.711
130.875
129.492
128.290
127.145
119.011
75.782
65.532
60.123
49.577
44.506
39.895
33.688
30.551
29.522
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19.519
19.157
16.424
16.004
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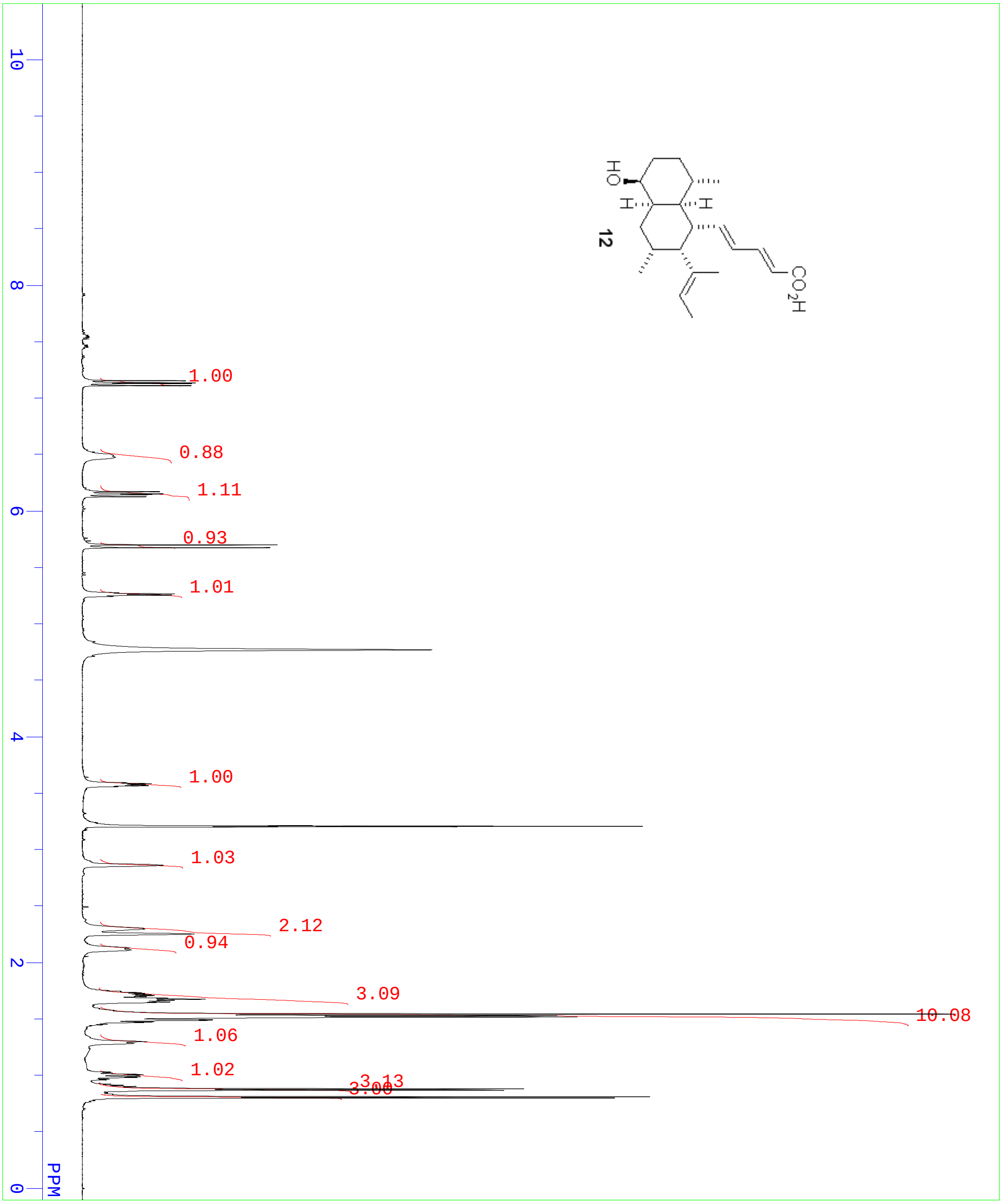
13.666
200
150
100
50
0
PPM


12
HO
H
H
CO2H
10
8
6
4
2
0
PPM
1.00
0.88
1.11
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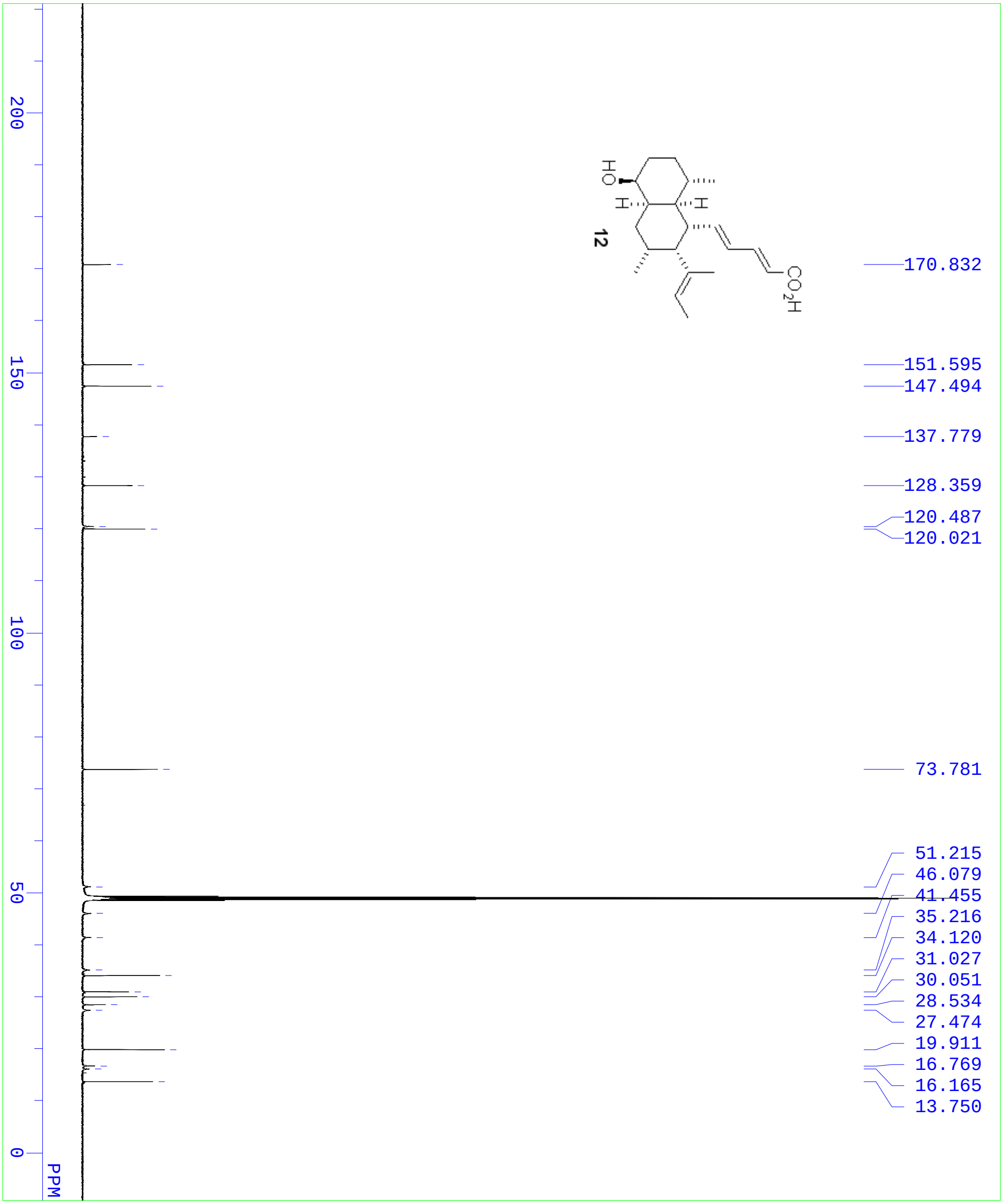
1.01
1.00
1.03
2.12
0.94
3.09
10.08
1.06
1.02
3.00
3.13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150
100
50
0
PPM
HO
H
H
12
CO2H
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151.595
147.494
137.779
128.359
120.487
120.021
73.781
51.215
46.079
41.455
35.216
34.120
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30.051
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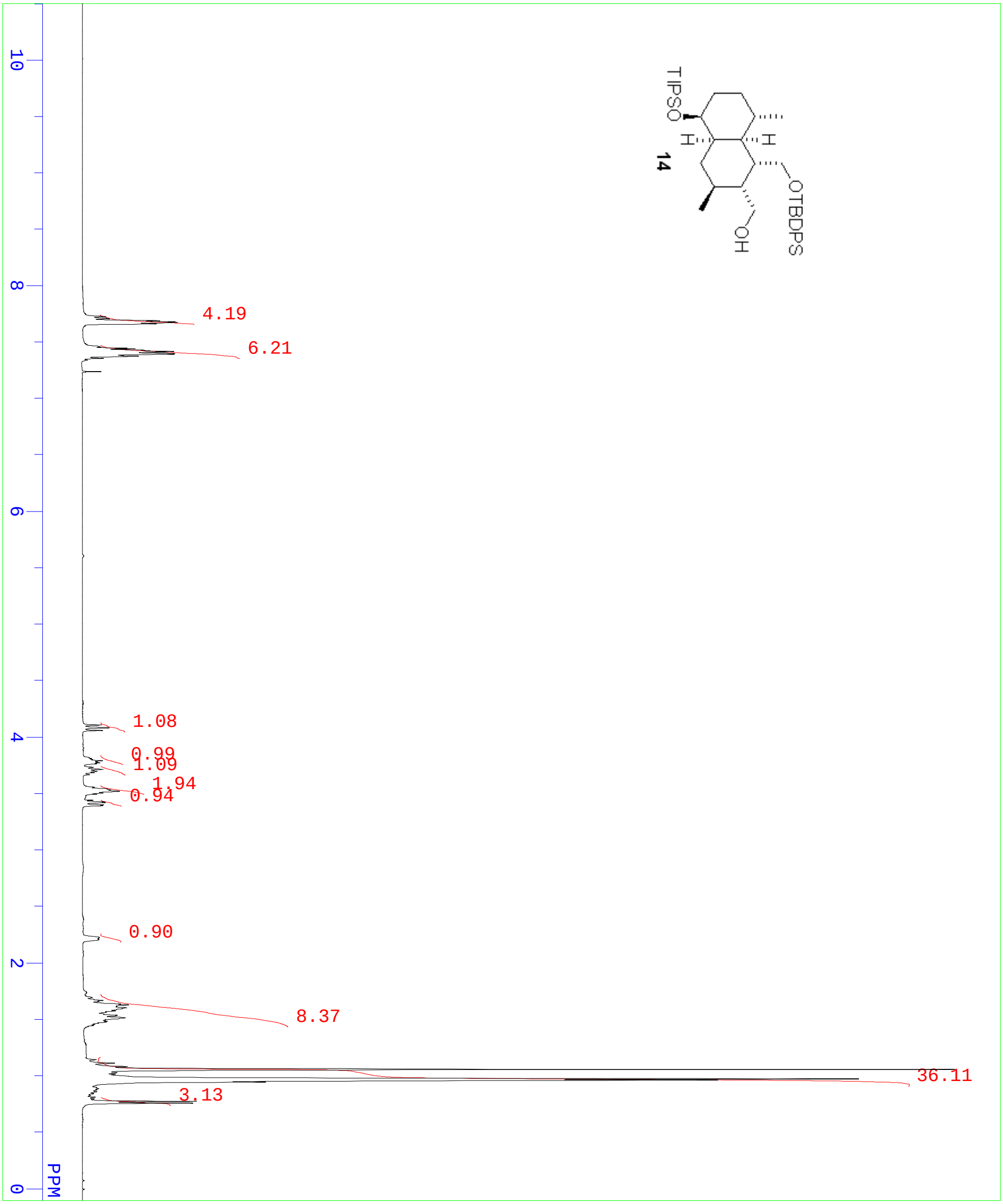
16.165
13.750


TIPSO
H
H
OTBDPS
OH
14
10
8
6
4
2
0
PPM
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6.21
1.08
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1.09
1.94
0.94
0.90
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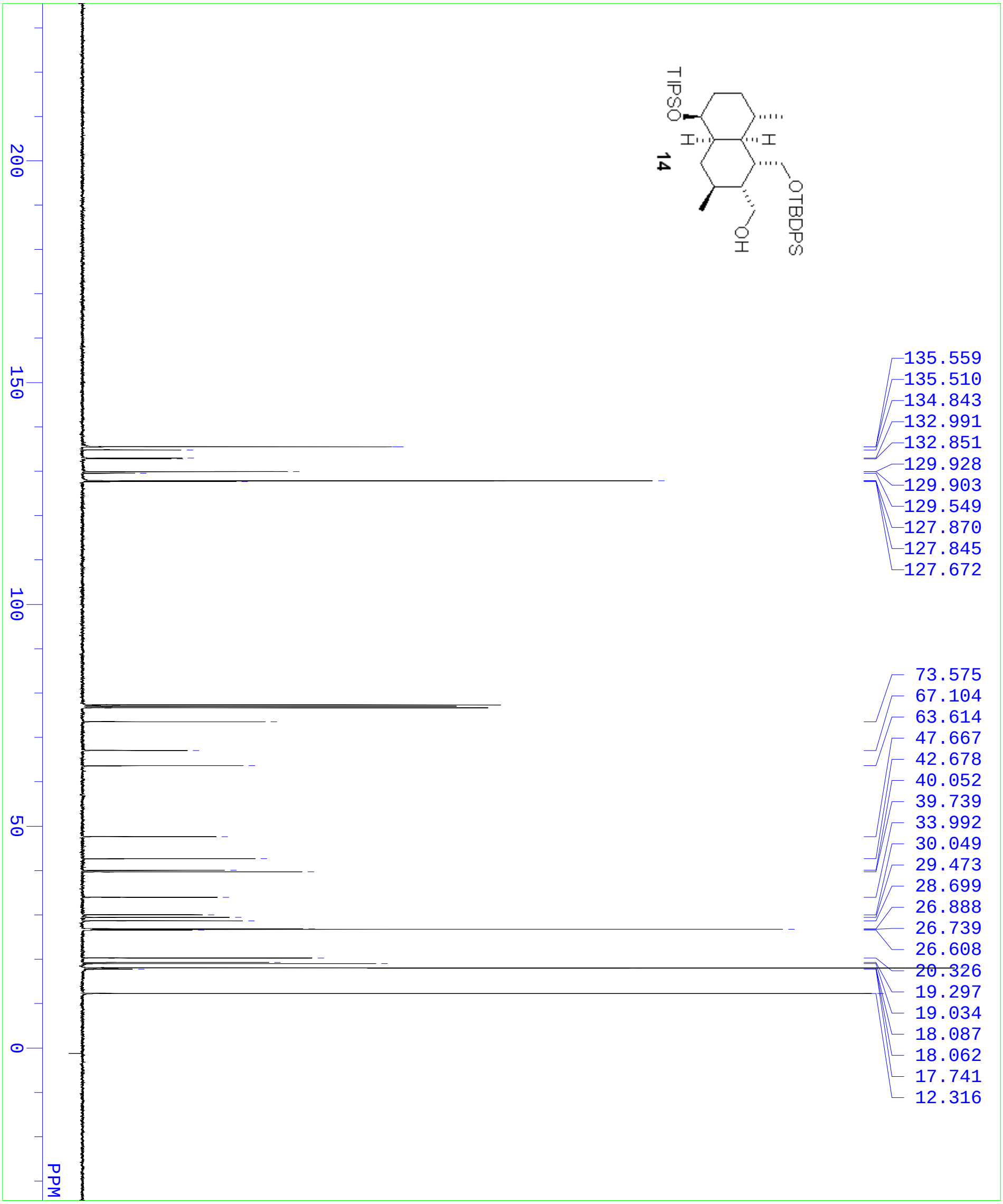
36.11
3.13


TIPSO
H
H
OTBDPS
OH
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132.851
129.928
129.903
129.549
127.870
127.845
127.672
73.575
67.104
63.614
47.667
42.678
40.052
39.739
33.992
30.049
29.473
28.699
26.888
26.739
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19.034
18.087
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17.741
12.316
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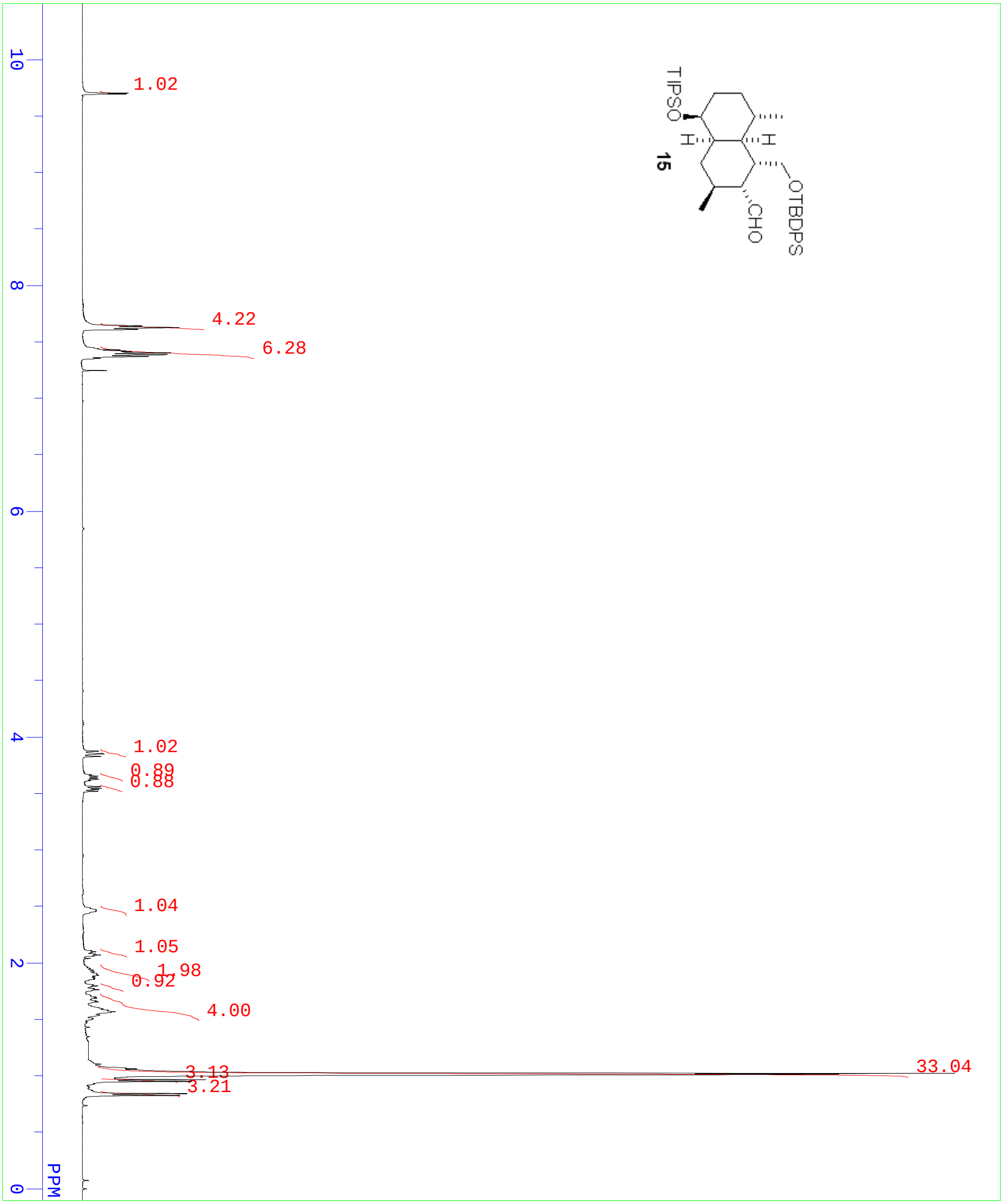
100
50
0
PPM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8
6
4
2
0
PPM
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1.02
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0.88
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1.05
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0.92
4.00
3.13
3.21
33.04
TIPSO
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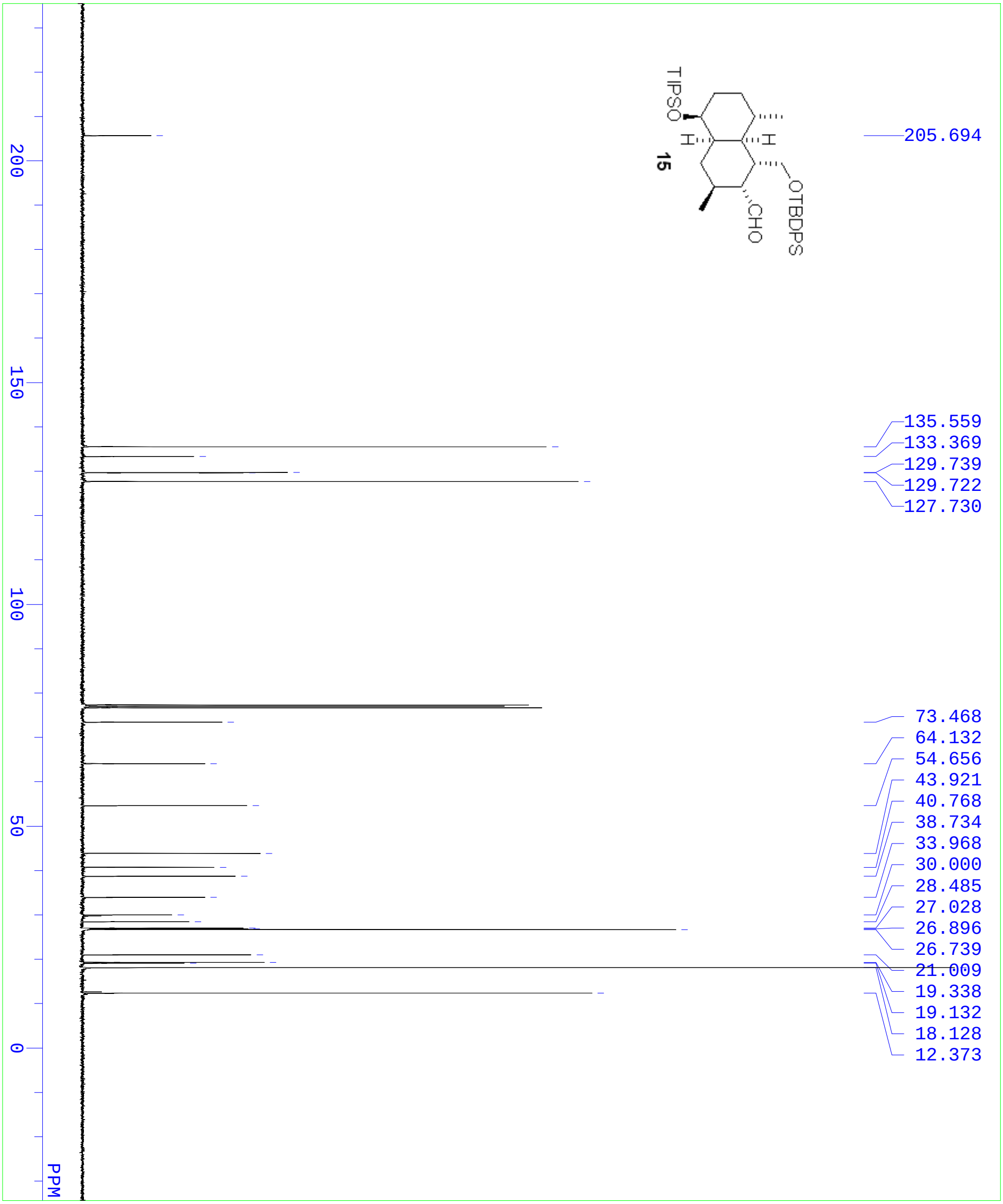
H
OTBDPS
CHO
15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H
OTBDPS
CHO
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54.656
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40.768
38.734
33.968
30.000
28.485
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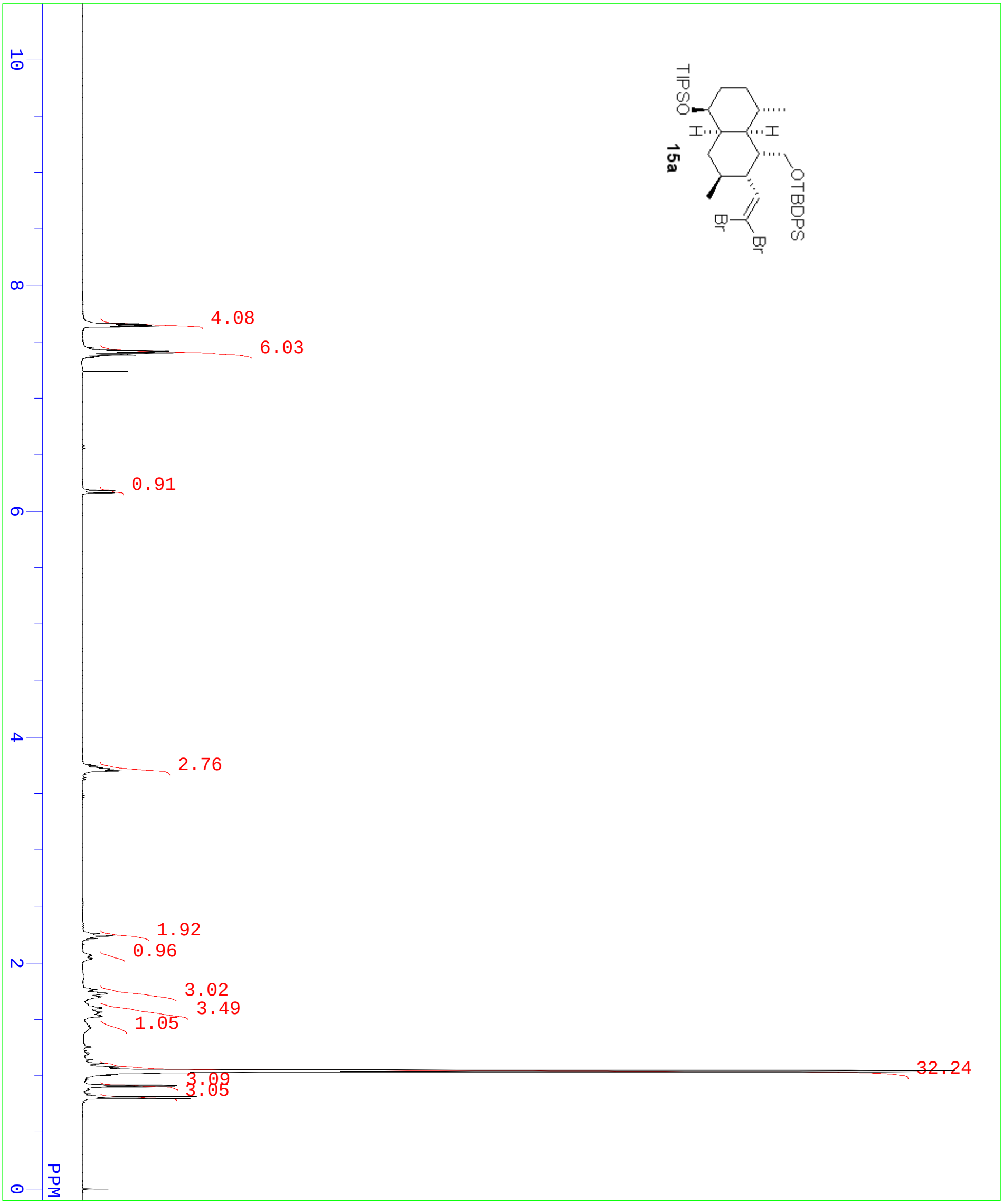
100
50
0
PPM


TIPSO
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H
OTBDPS
Br
Br
15a
10
8
6
4
2
0
PPM
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0.96
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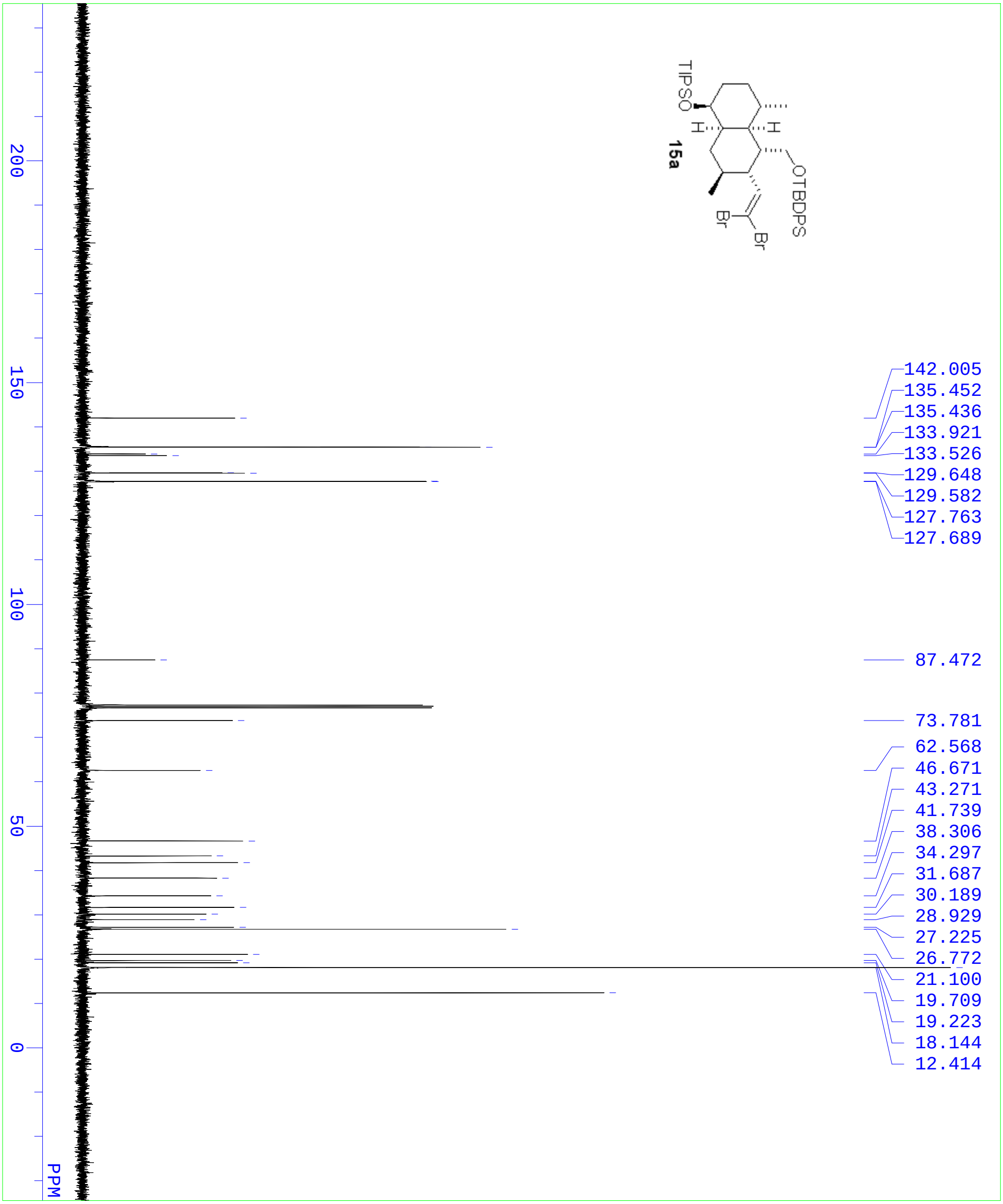
3.09
3.05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H
OTBDPS
Br
Br
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133.526
129.648
129.582
127.763
127.689
87.472
73.781
62.568
46.671
43.271
41.739
38.306
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31.687
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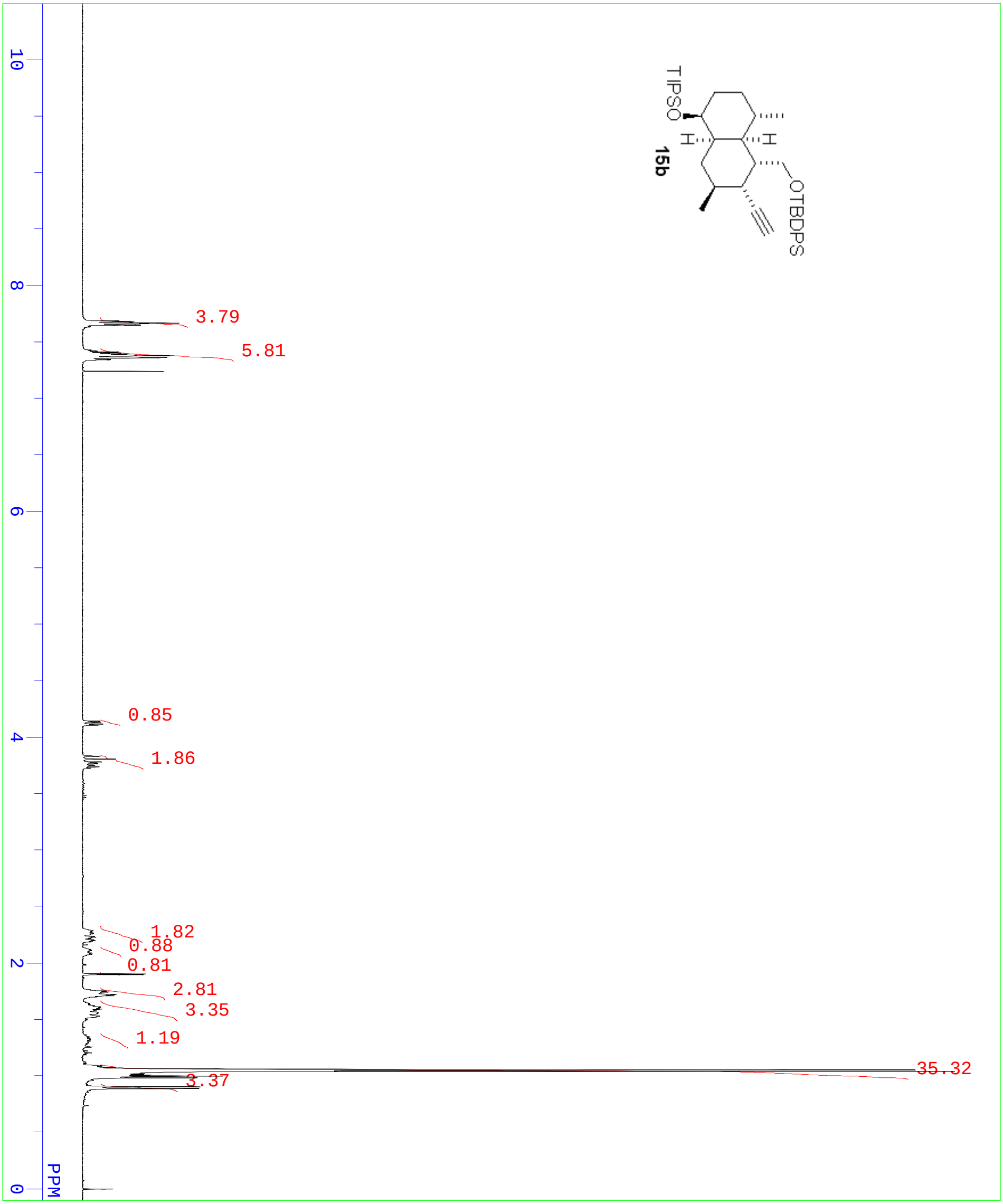
PPM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H
OTBDPS
15b
10
8
6
4
2
0
PPM
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0.88
0.81
2.81
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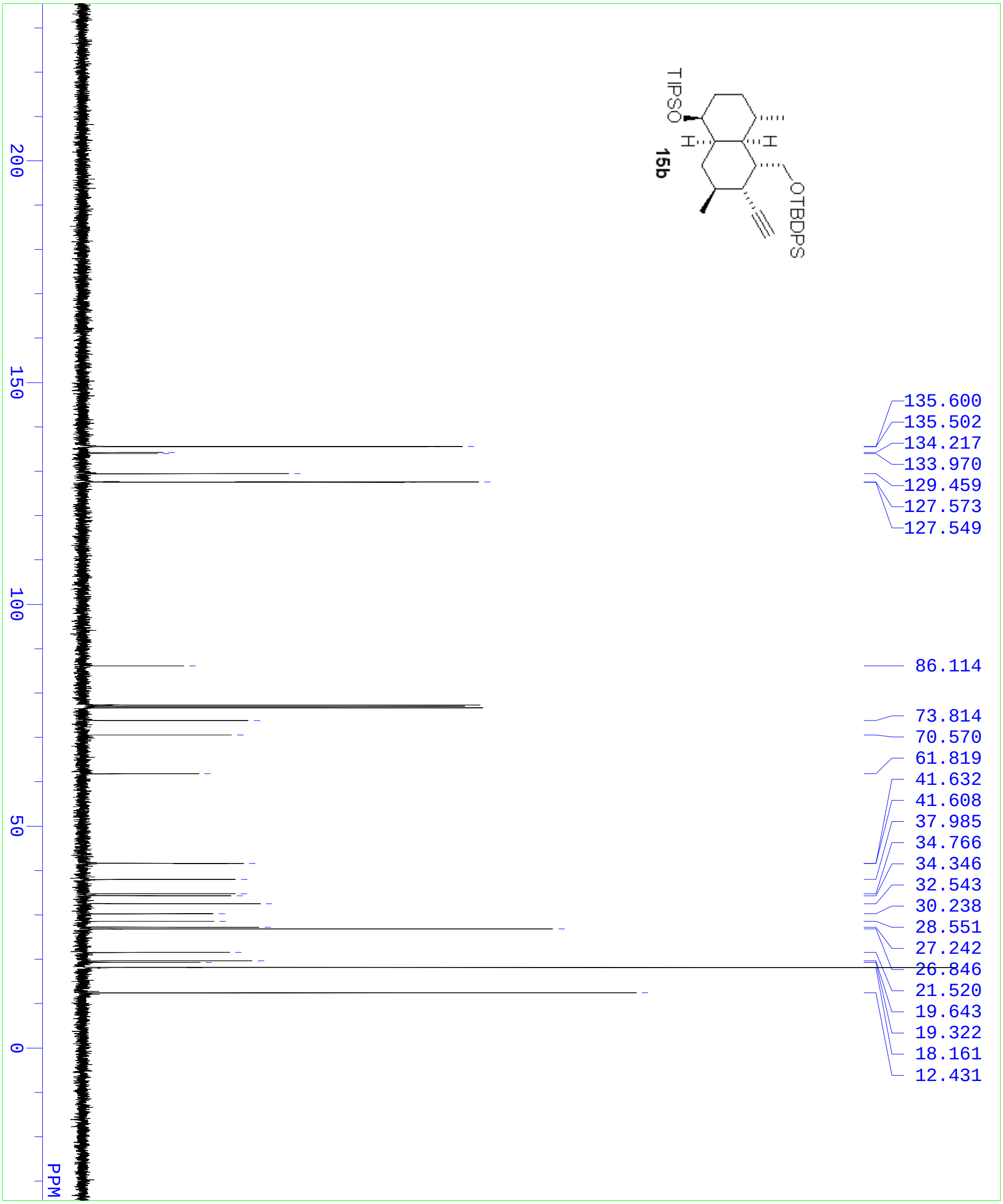
1.19
35.32
3.37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H
OTBDPS
15b
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133.970
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127.573
127.549
86.114
73.814
70.570
61.819
41.632
41.608
37.985
34.766
34.346
32.543
30.238
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21.520
19.643
19.322
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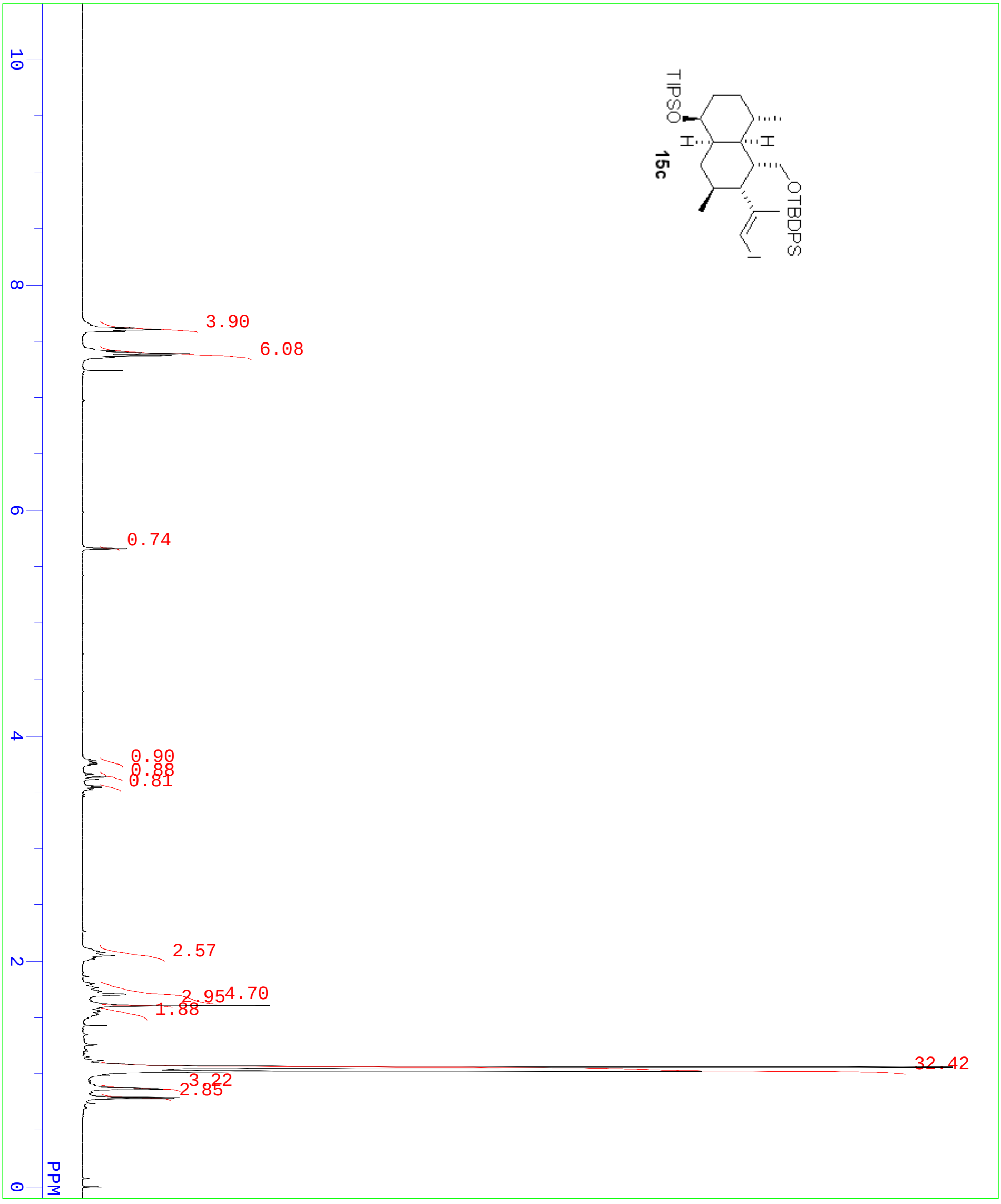
12.431
200
150
100
50
0
PPM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H
OTBDPS
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10
8
6
4
2
0
PPM
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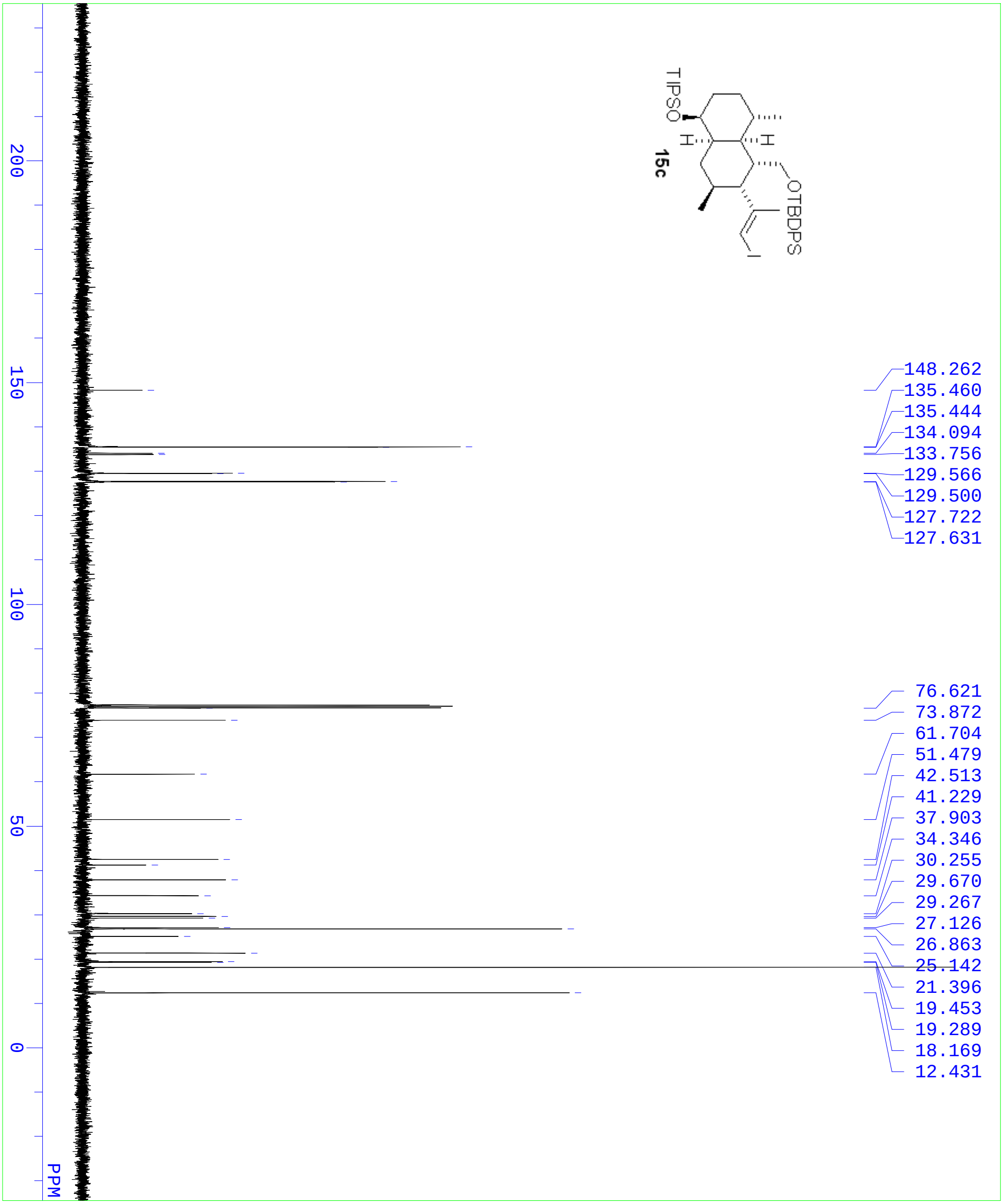
3.22
2.85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H
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129.500
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127.631
76.621
73.872
61.704
51.479
42.513
41.229
37.903
34.346
30.255
29.670
29.267
27.126
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25.142
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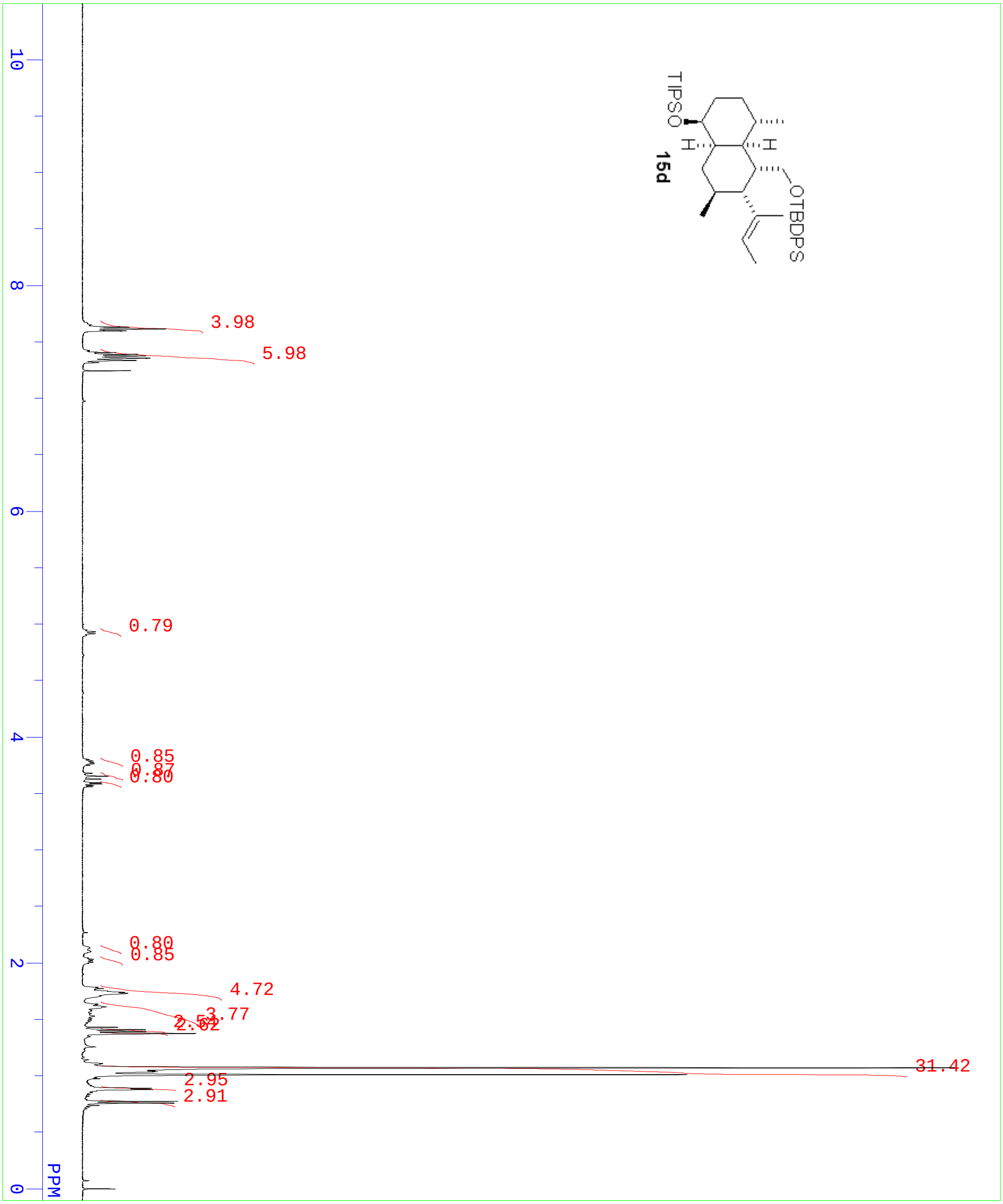
12.431
200
150
100
50
0
PPM


TIPSO
H
H
OTBDPS
15d
10
8
6
4
2
0
PPM
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5.98
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0.80
0.85
4.72
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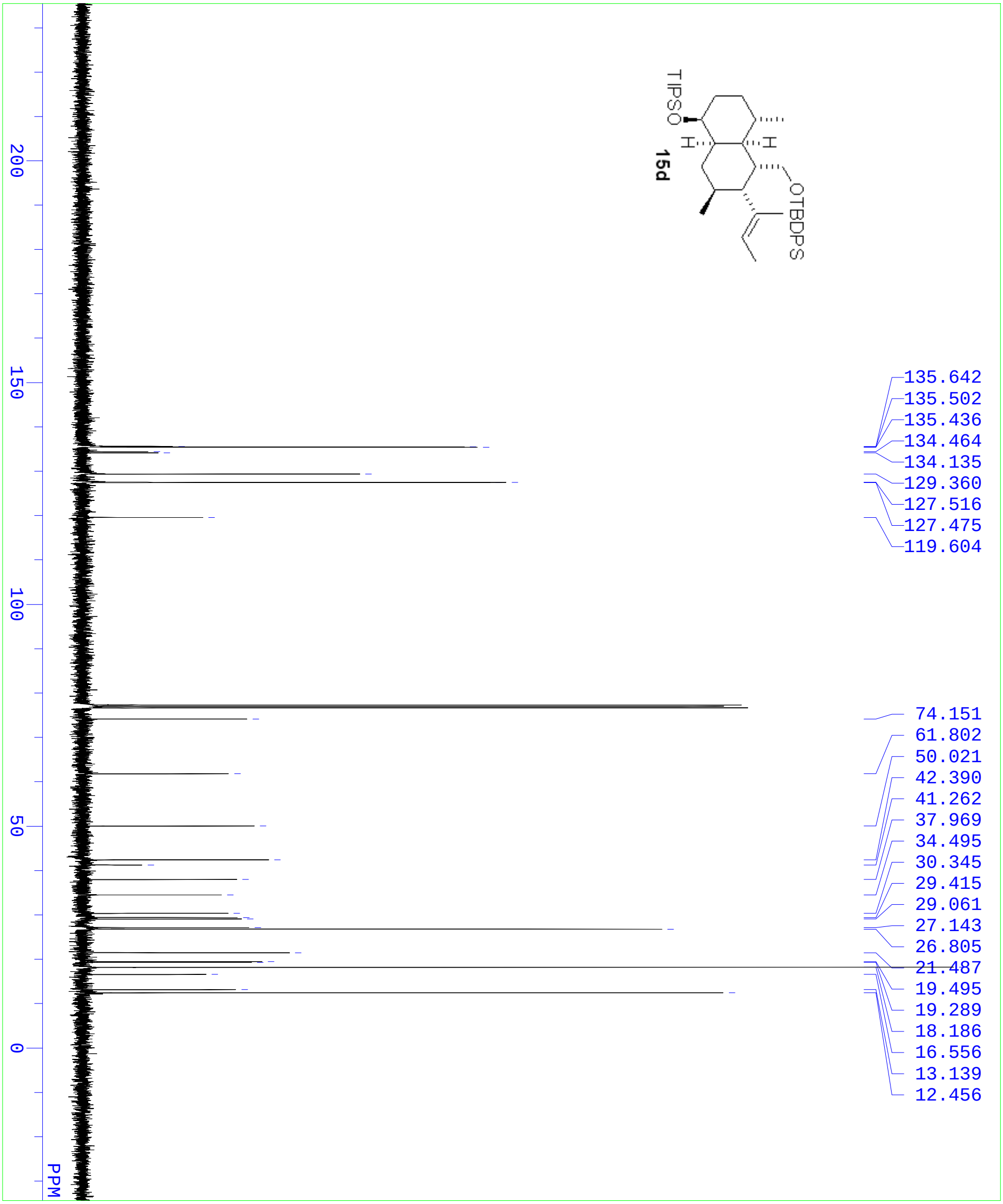
2.54
2.62
31.42
2.95
2.91


TIPSO
H
H
OTBDPS
15d
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135.436
134.464
134.135
129.360
127.516
127.475
119.604
74.151
61.802
50.021
42.390
41.262
37.969
34.495
30.345
29.415
29.061
27.143
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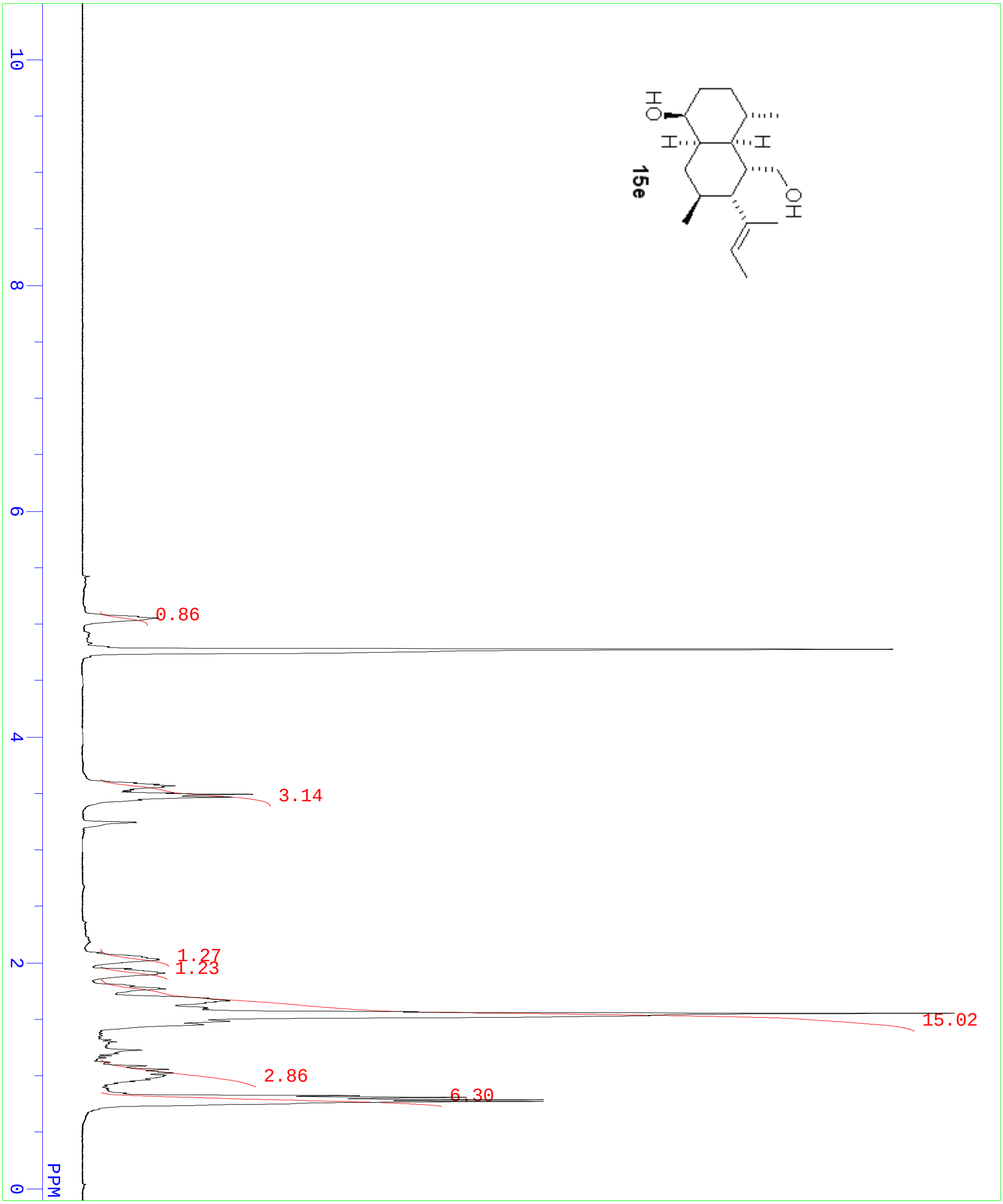
16.556
13.139
12.456
200
150
100
50
0
PPM


15e
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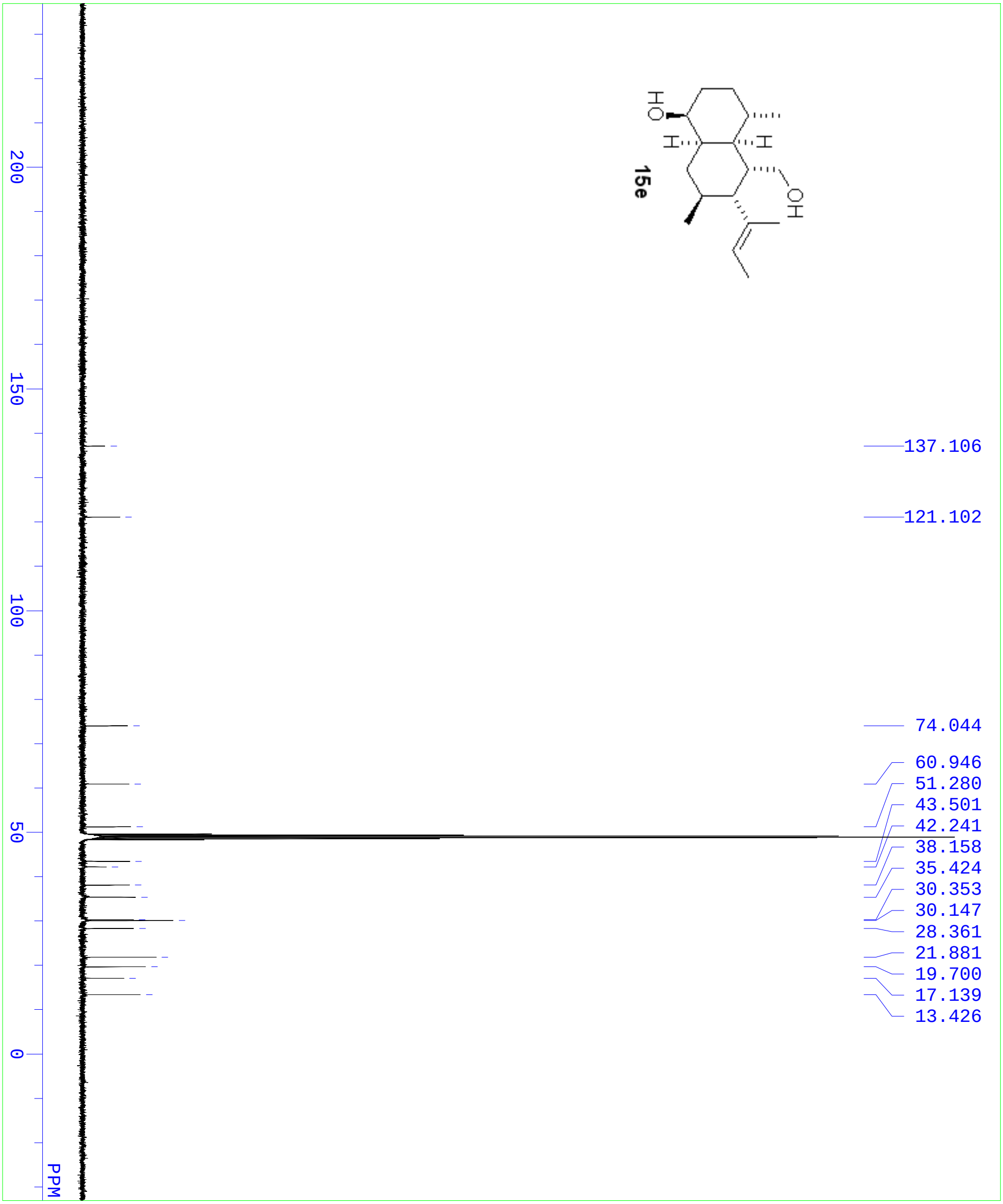
1.27
1.23
15.02
2.86
6.30
10
8
6
4
2
0
PPM


15e
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74.044
60.946
51.280
43.501
42.241
38.158
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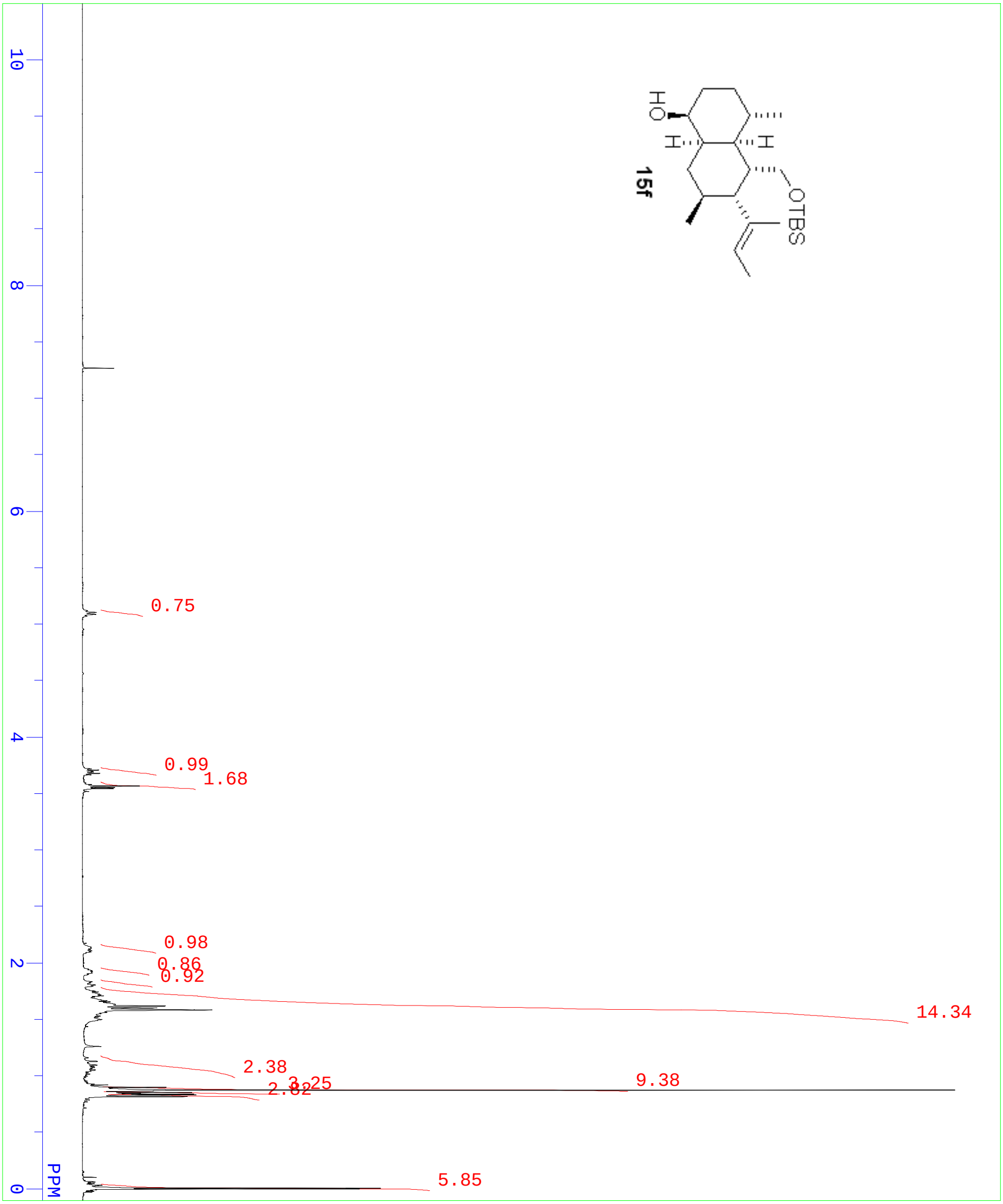
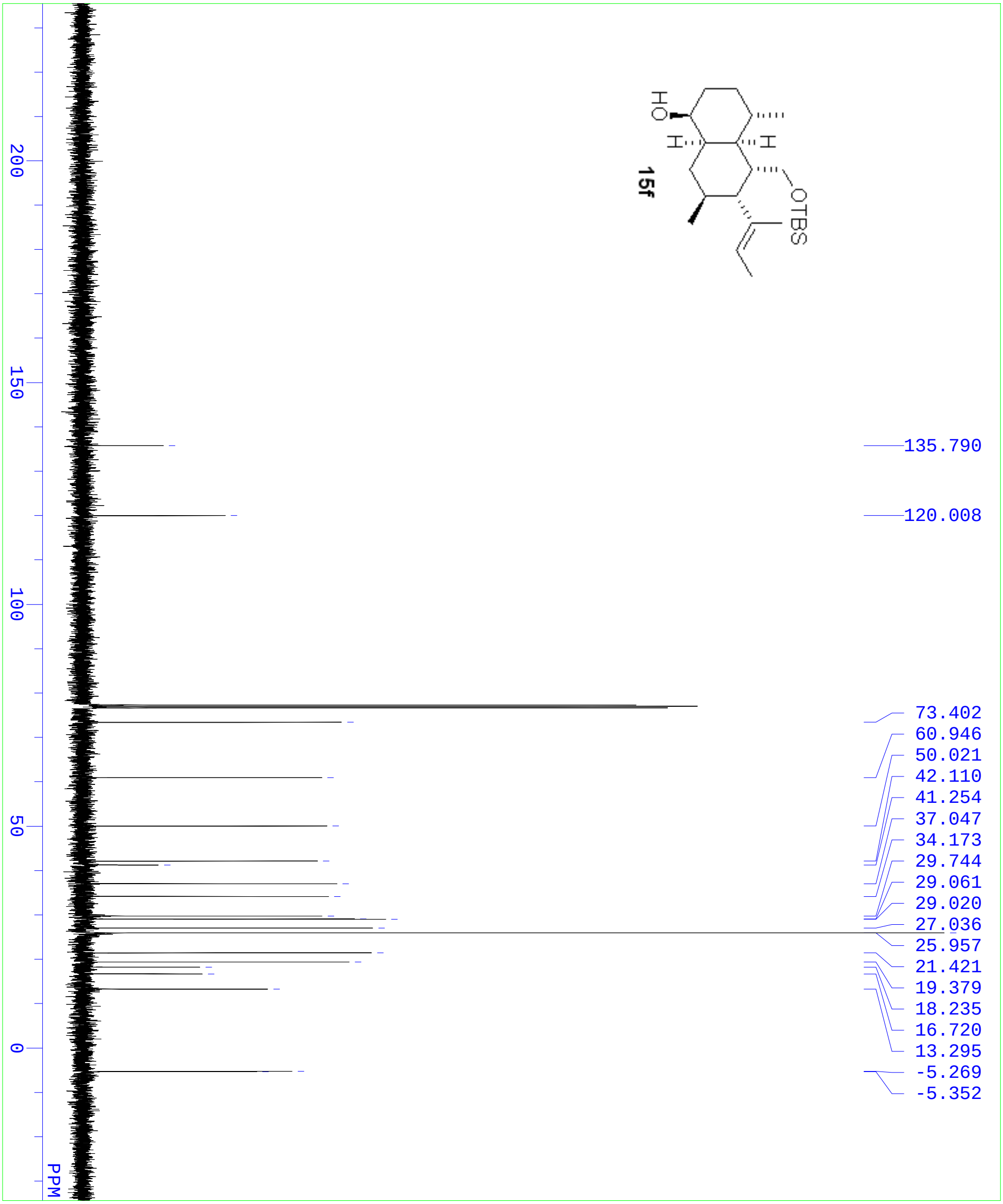
30.147
28.361
21.881
19.700
17.139
13.426
200
150
100
50
0
PPM


HO
H
H
OTBS
15f
10
8
6
4
2
0
PPM
0.75
0.99
1.68
0.98
0.86
0.92
14.34
2.38
2.82
3.25
9.38
5.85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H
H
OTBS
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42.110
41.254
37.047
34.173
29.744
29.061
29.020
27.036
25.957
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-5.352
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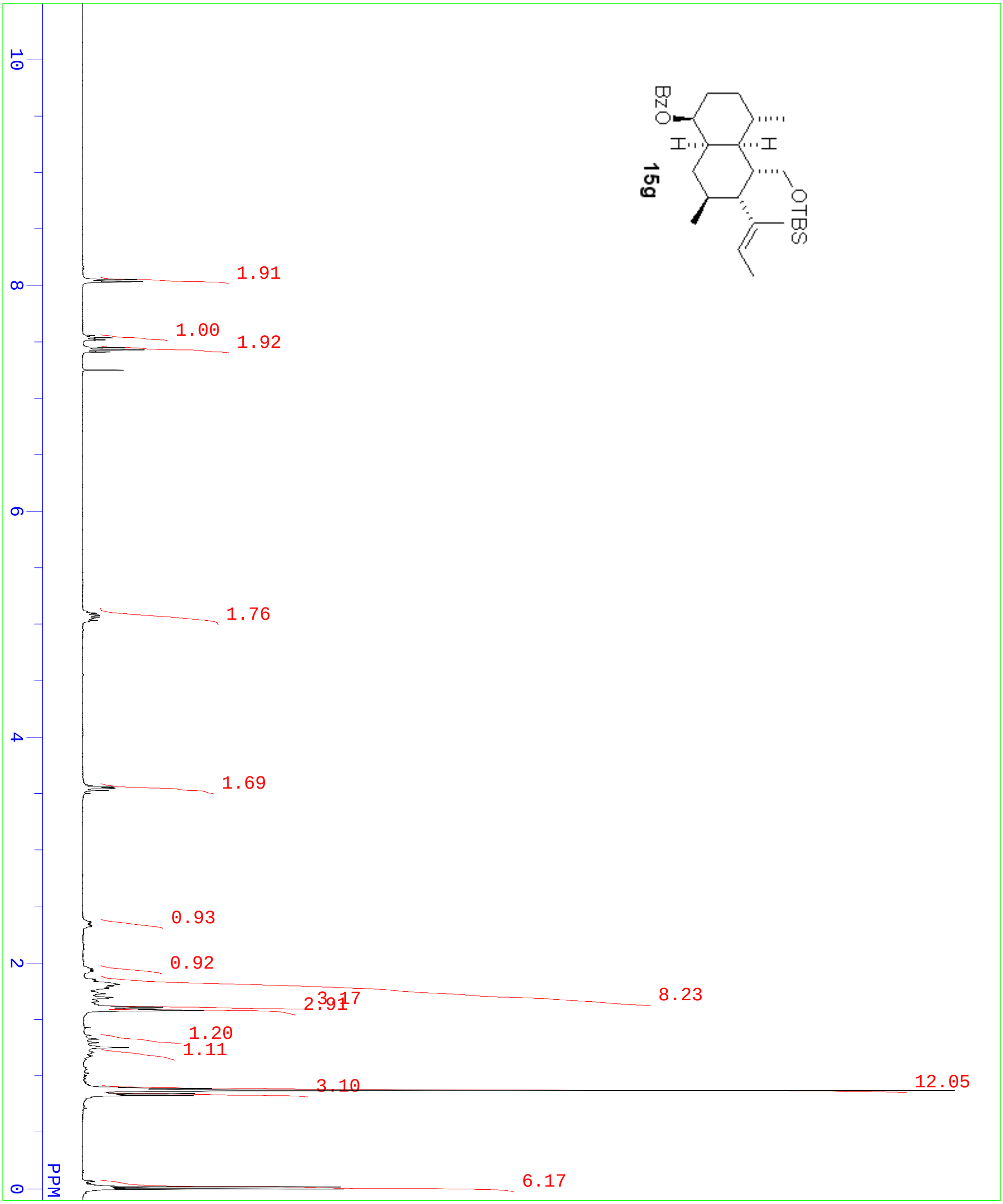
PPM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H
H
OTBS
15g
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1.00
1.92
1.76
1.69
0.93
0.92
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1.20
1.11
3.10
12.05
6.17
10
8
6
4
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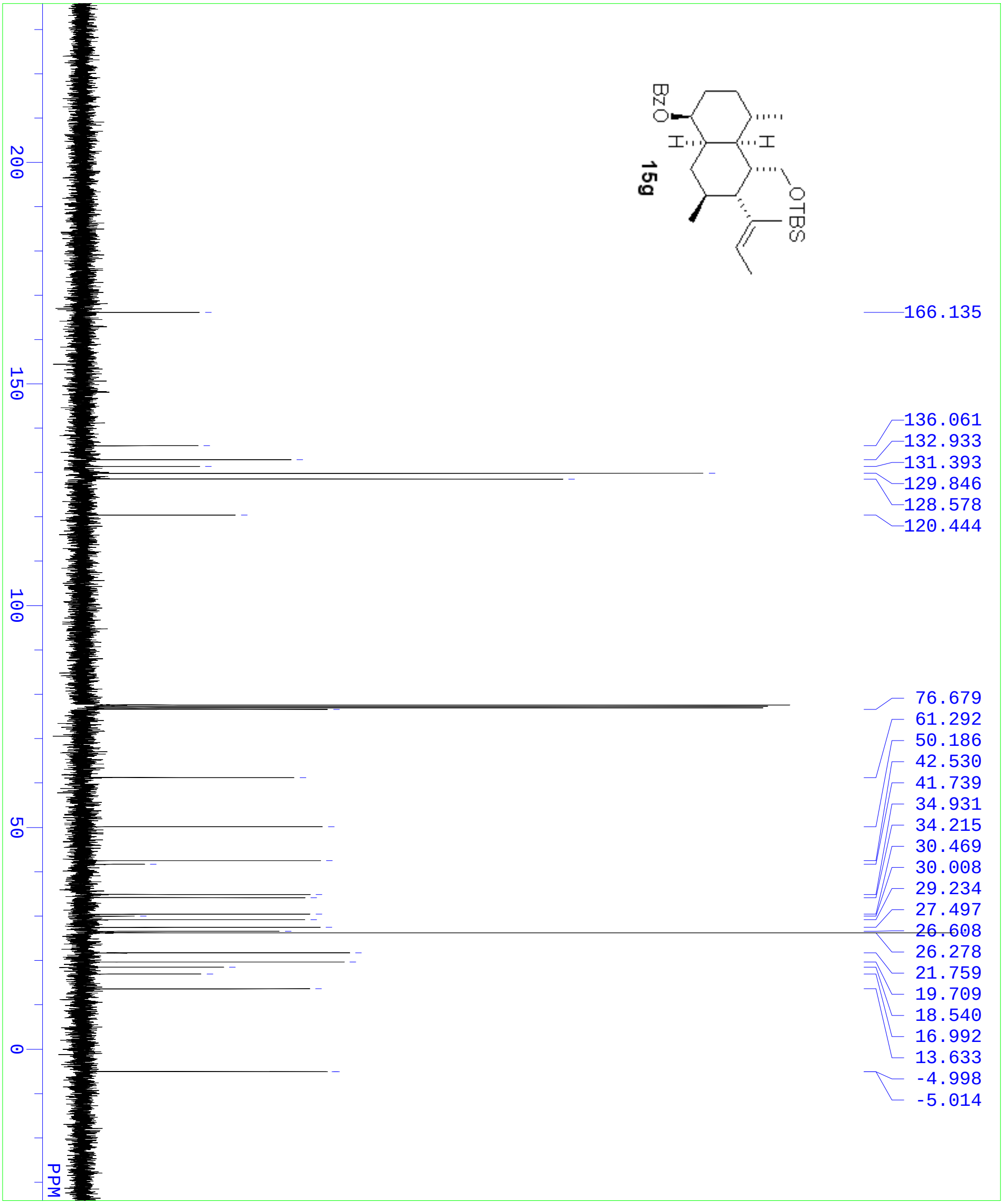
0
PPM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H
H
OTBS
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131.393
129.846
128.578
120.444
76.679
61.292
50.186
42.530
41.739
34.931
34.215
30.469
30.008
29.234
27.497
26.608
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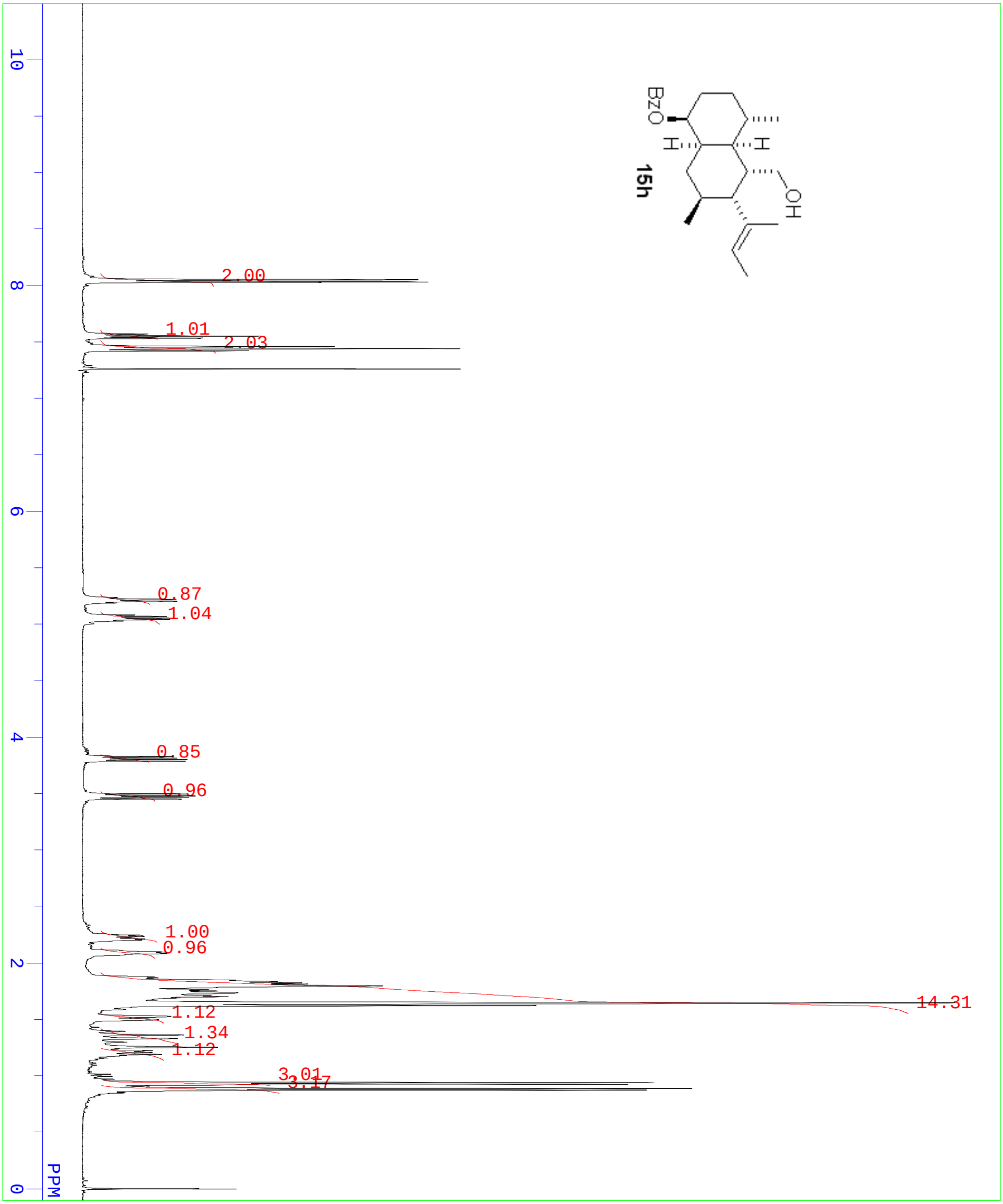
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H
H
OH
15h
10
8
6
4
2
0
PPM
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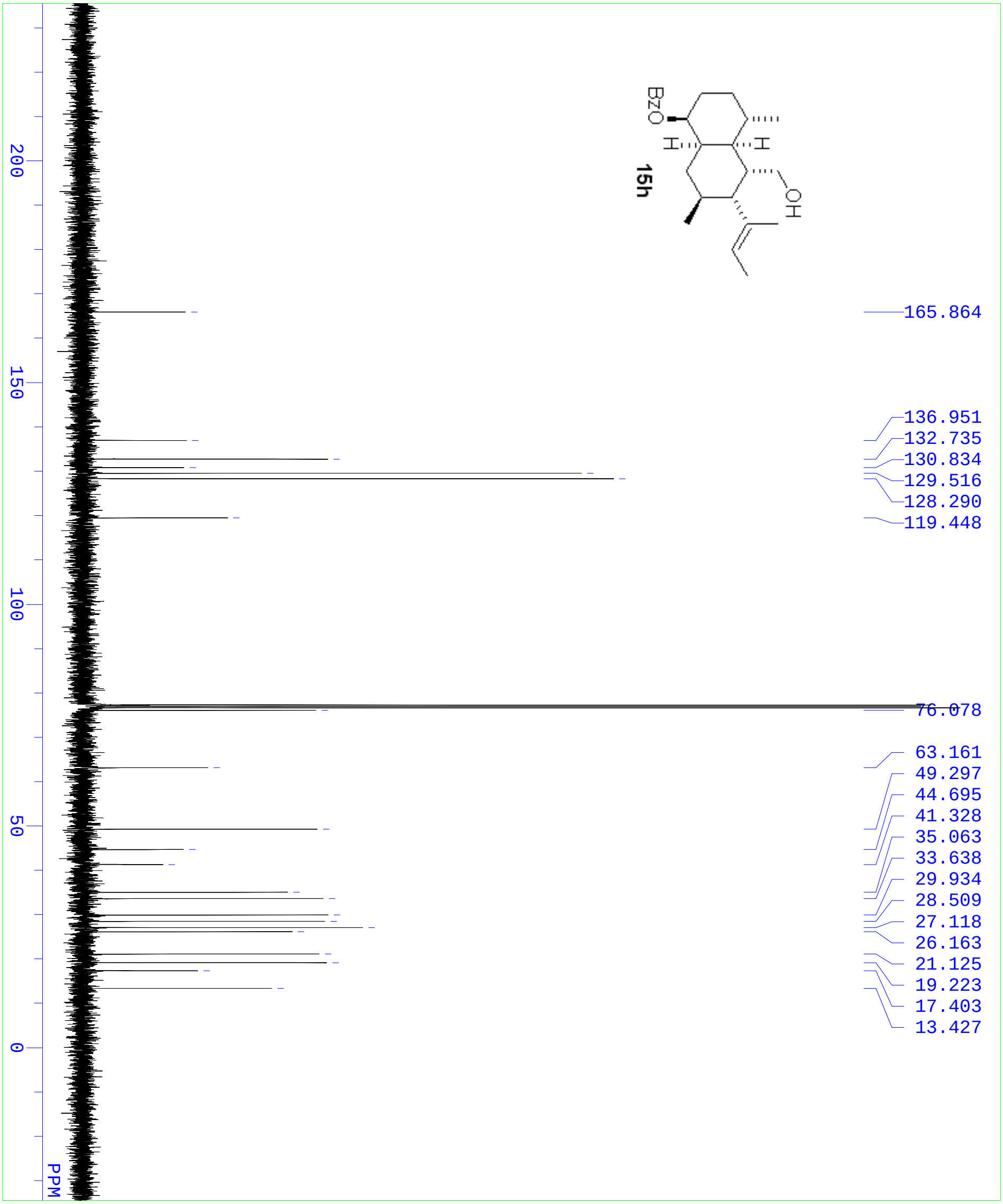
1.01
2.03
0.87
1.04
0.85
0.96
1.00
0.96
14.31
1.12
1.34
1.12
3.01
3.17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H
H
OH
15h
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136.951
132.735
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129.516
128.290
119.448
76.078
63.161
49.297
44.695
41.328
35.063
33.638
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27.118
26.163
21.125
19.223
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13.427
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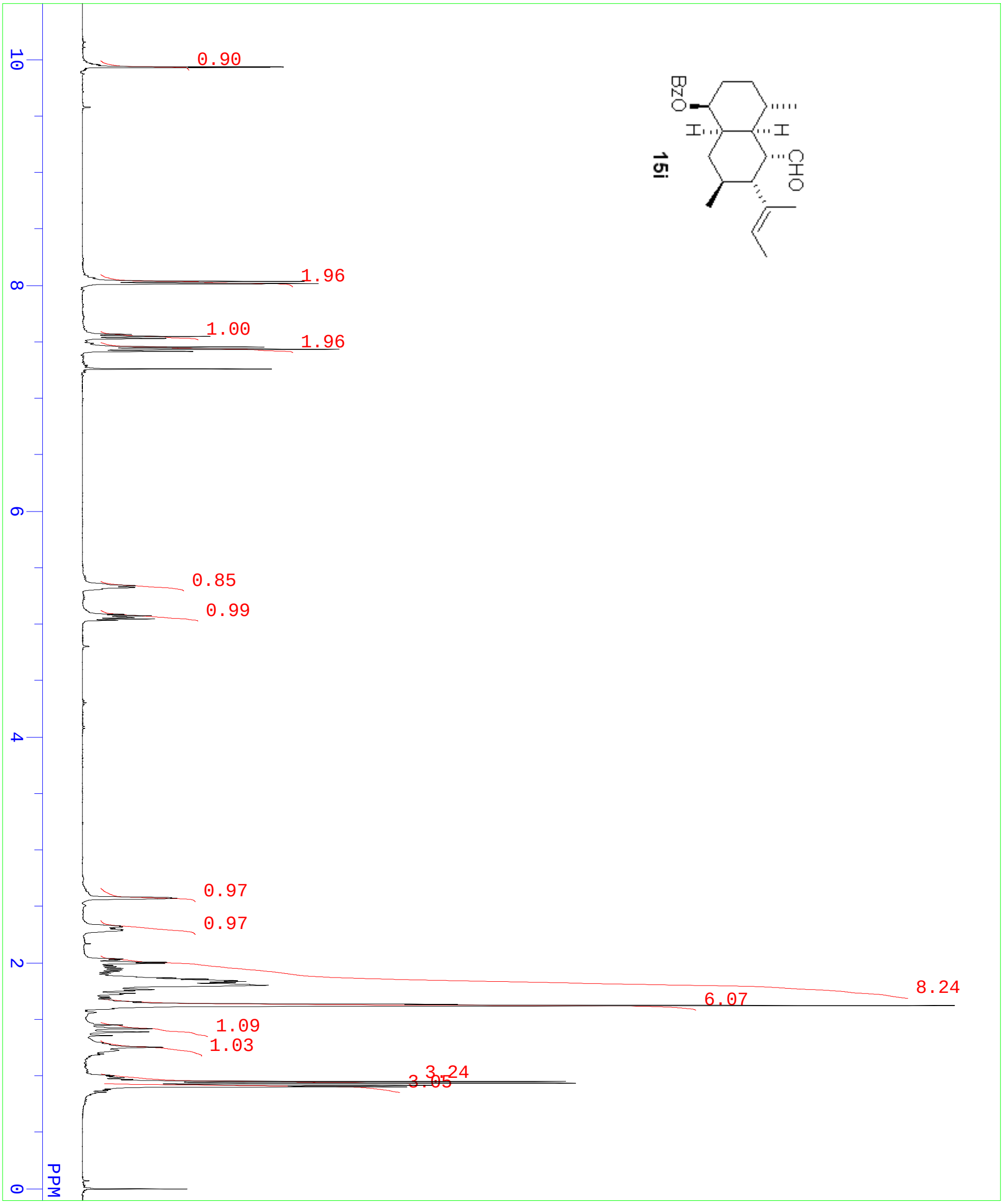
150
100
50
0
PPM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1.00
1.96
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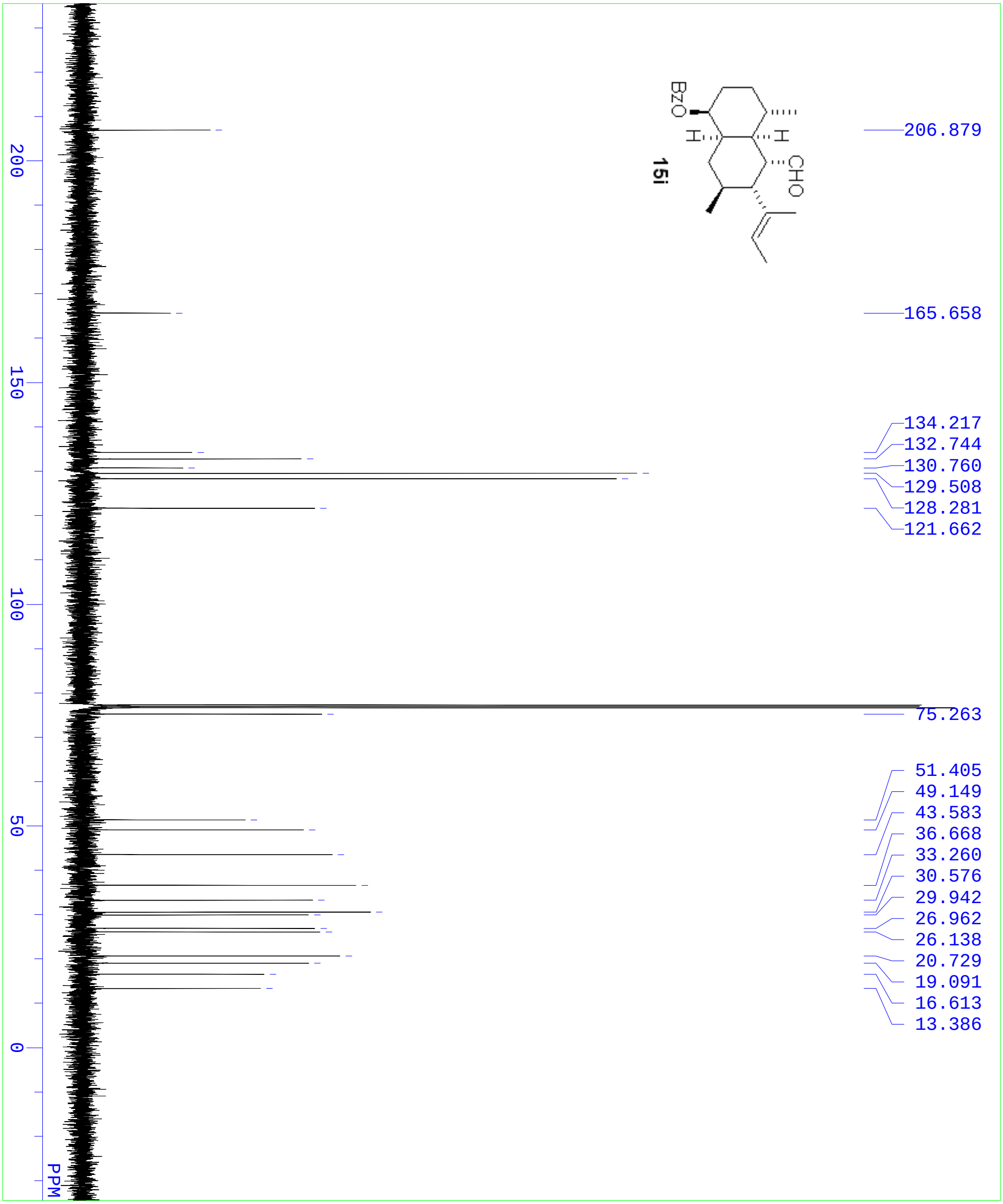
0.99
0.97
0.97
8.24
6.07
1.09
1.03
3.24
3.05
10
8
6
4
2
0
PPM

BzO
H
H
CHO

15i


BzO
H
H
CHO
15i
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130.760
129.508
128.281
121.662
75.263
51.405
49.149
43.583
36.668
33.260
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26.962
26.138
20.729
19.091
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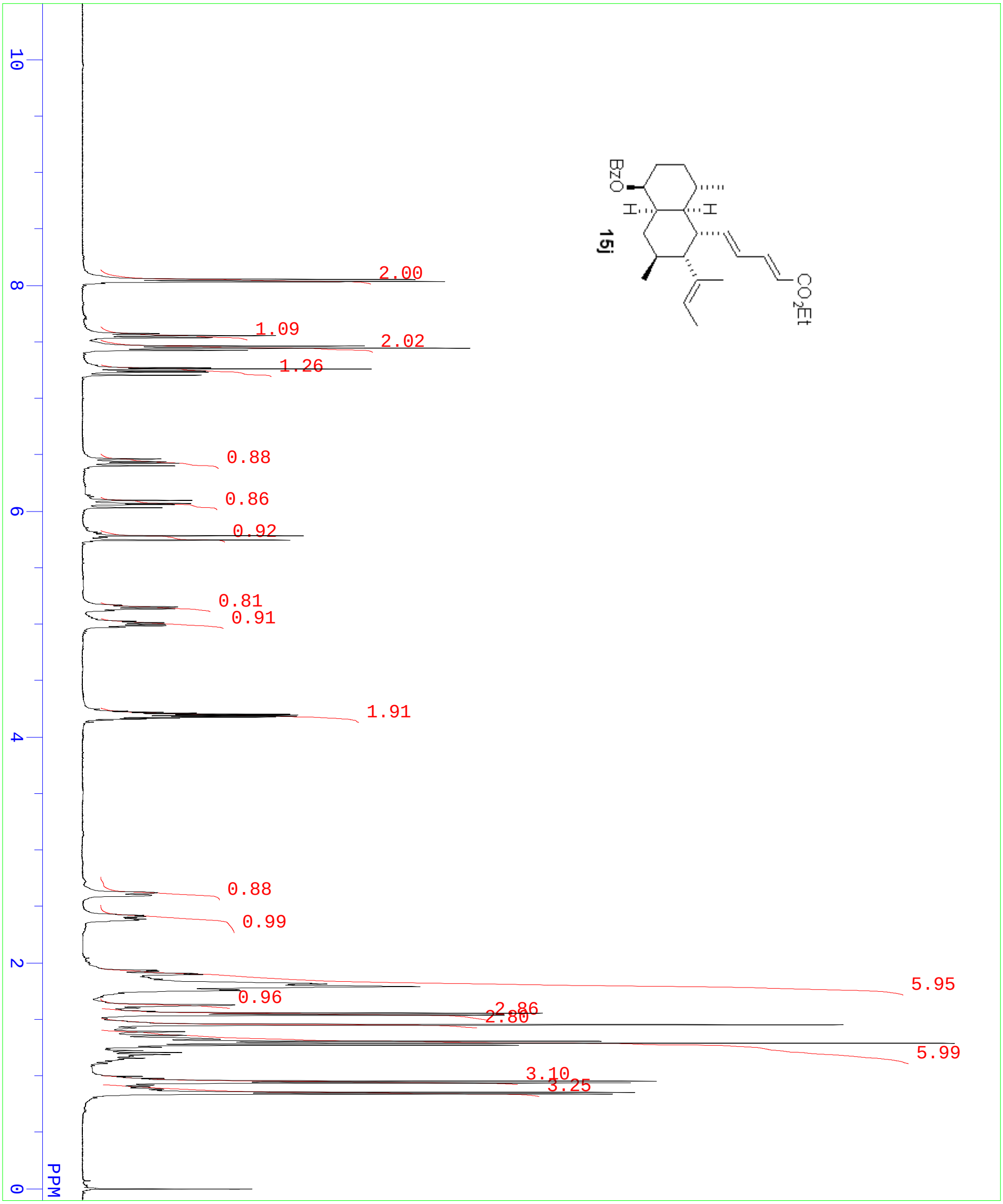
13.386
200
150
100
50
0
PPM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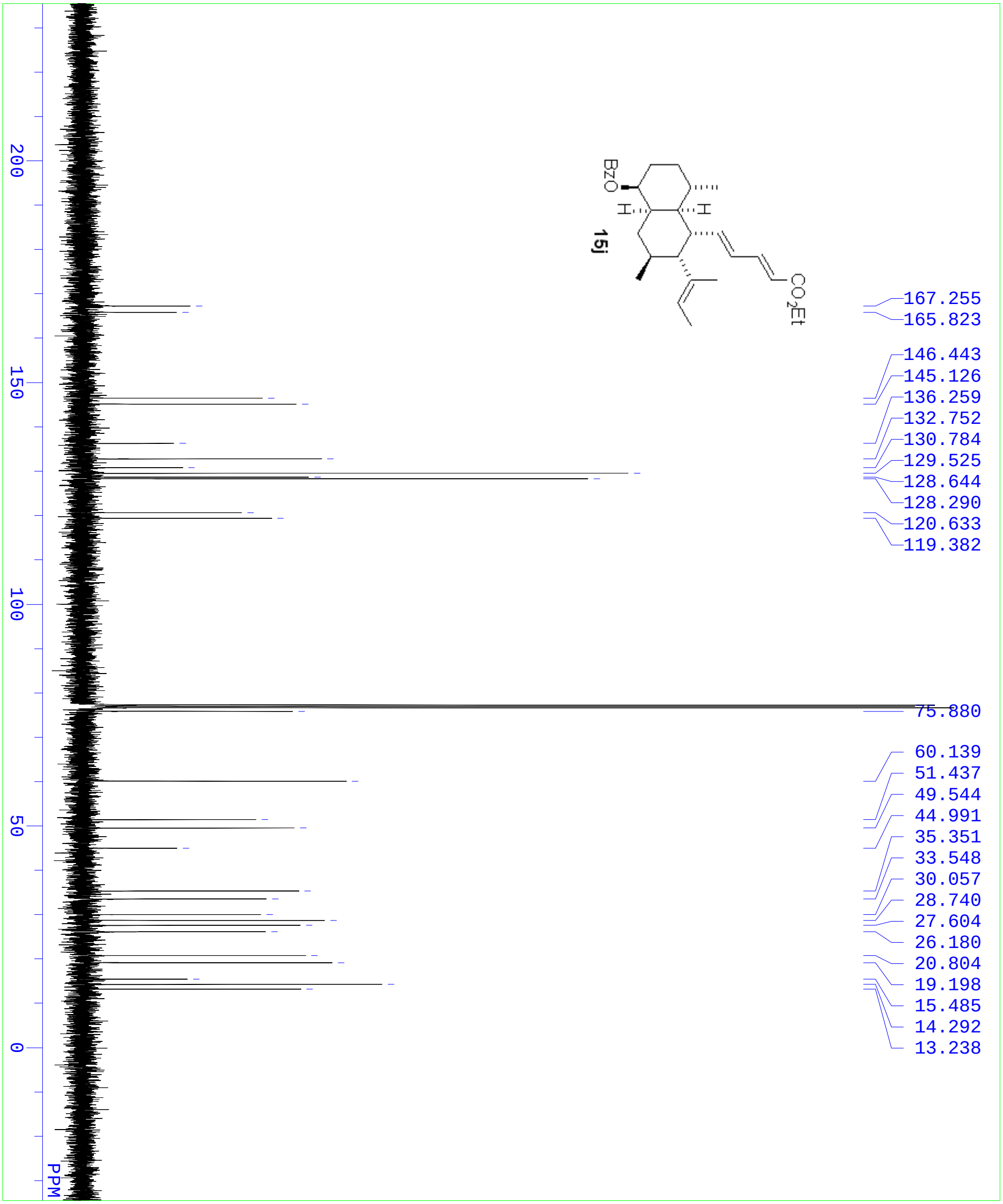
8
6
4
2
0
PPM
2.00
1.09
2.02
1.26
0.88
0.86
0.92
0.81
0.91
1.91
0.88
0.99
0.96
2.86
2.80
5.95
5.99
3.10
3.25
BzO
H
H
15j
CO2Et


200
150
100
50
0
PPM
BzO
H
H
CO2Et
15j
167.255
165.823
146.443
145.126
136.259
132.752
130.784
129.525
128.644
128.290
120.633
119.382
75.880
60.139
51.437
49.544
44.991
35.351
33.548
30.057
28.740
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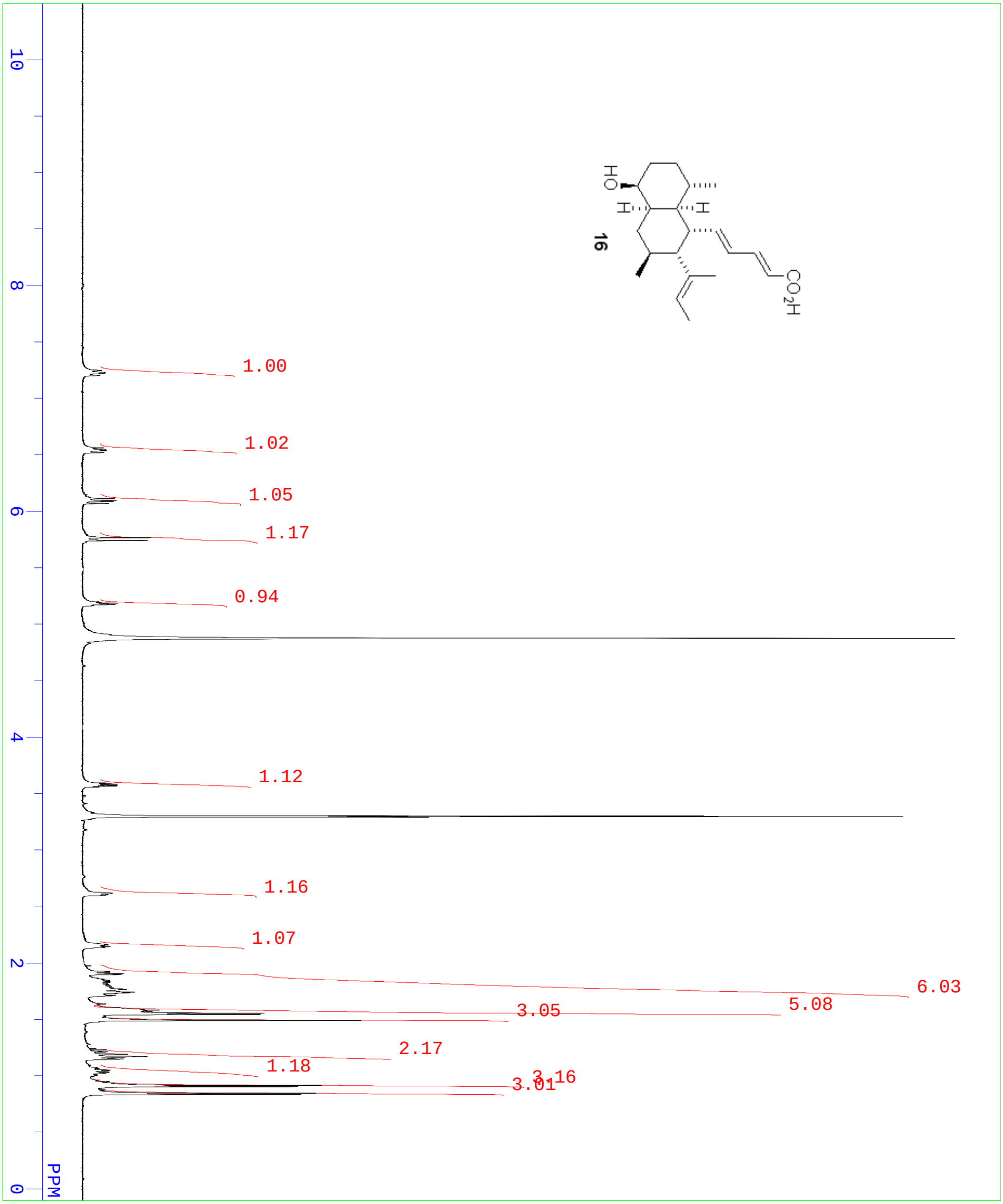
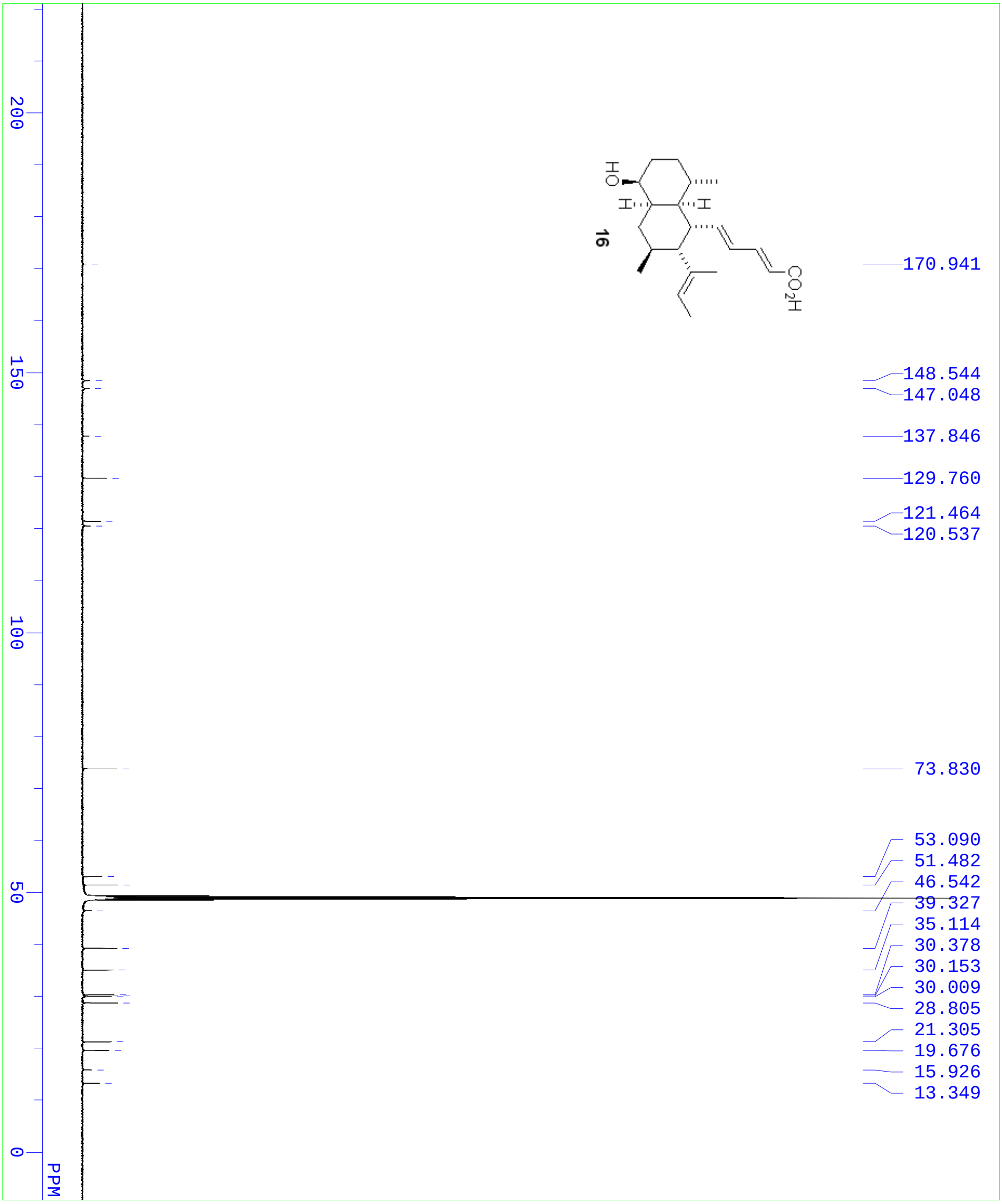
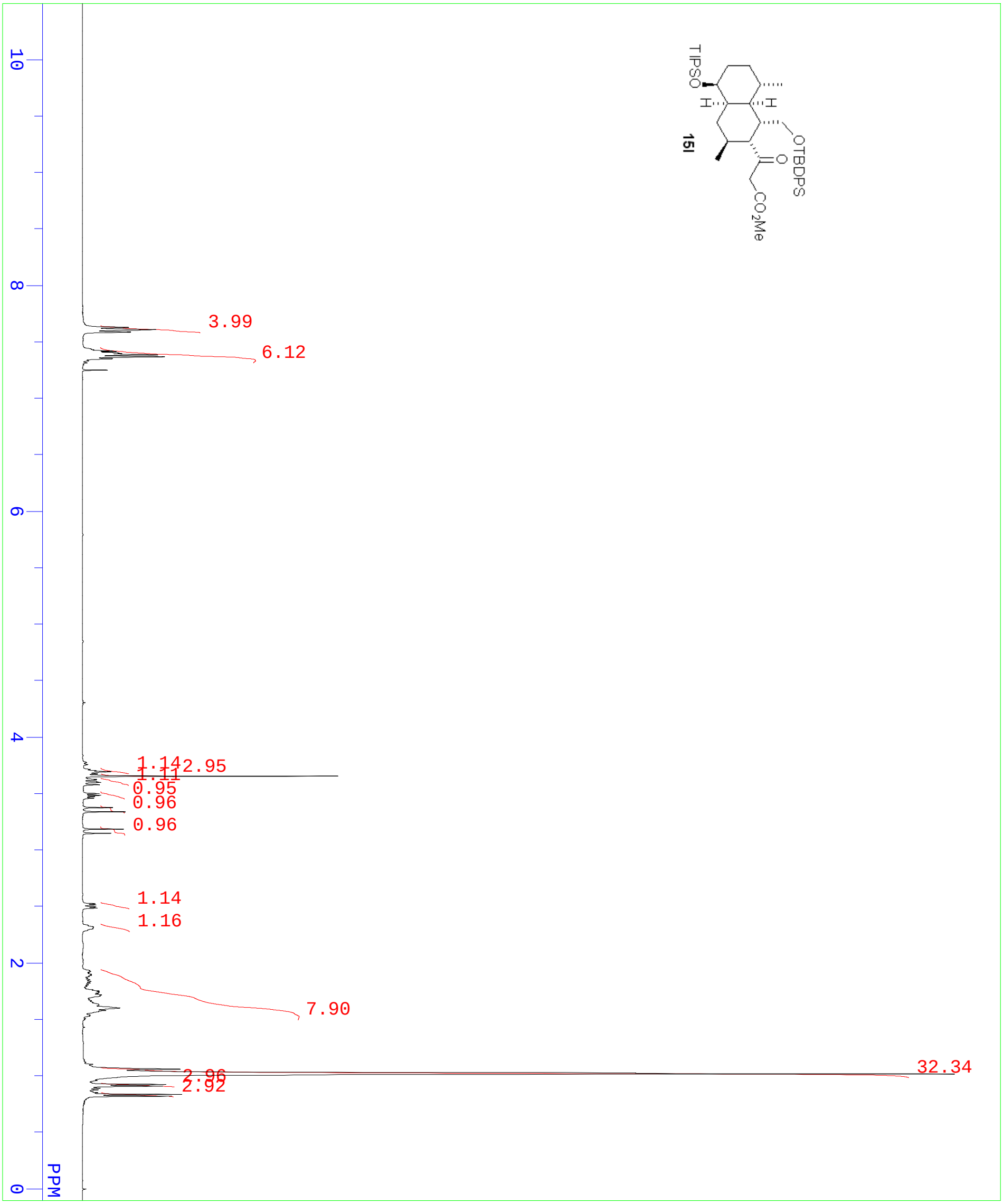
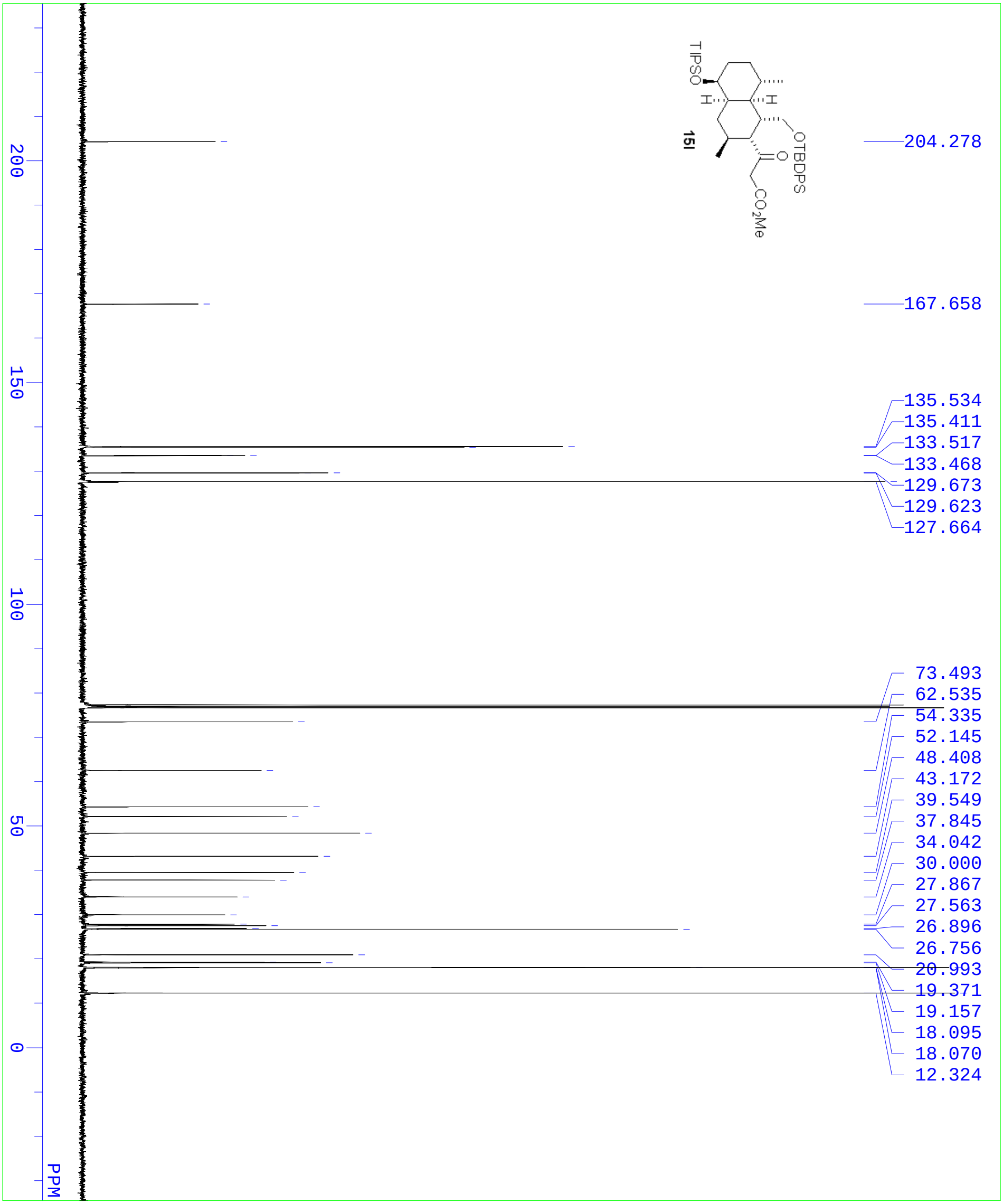
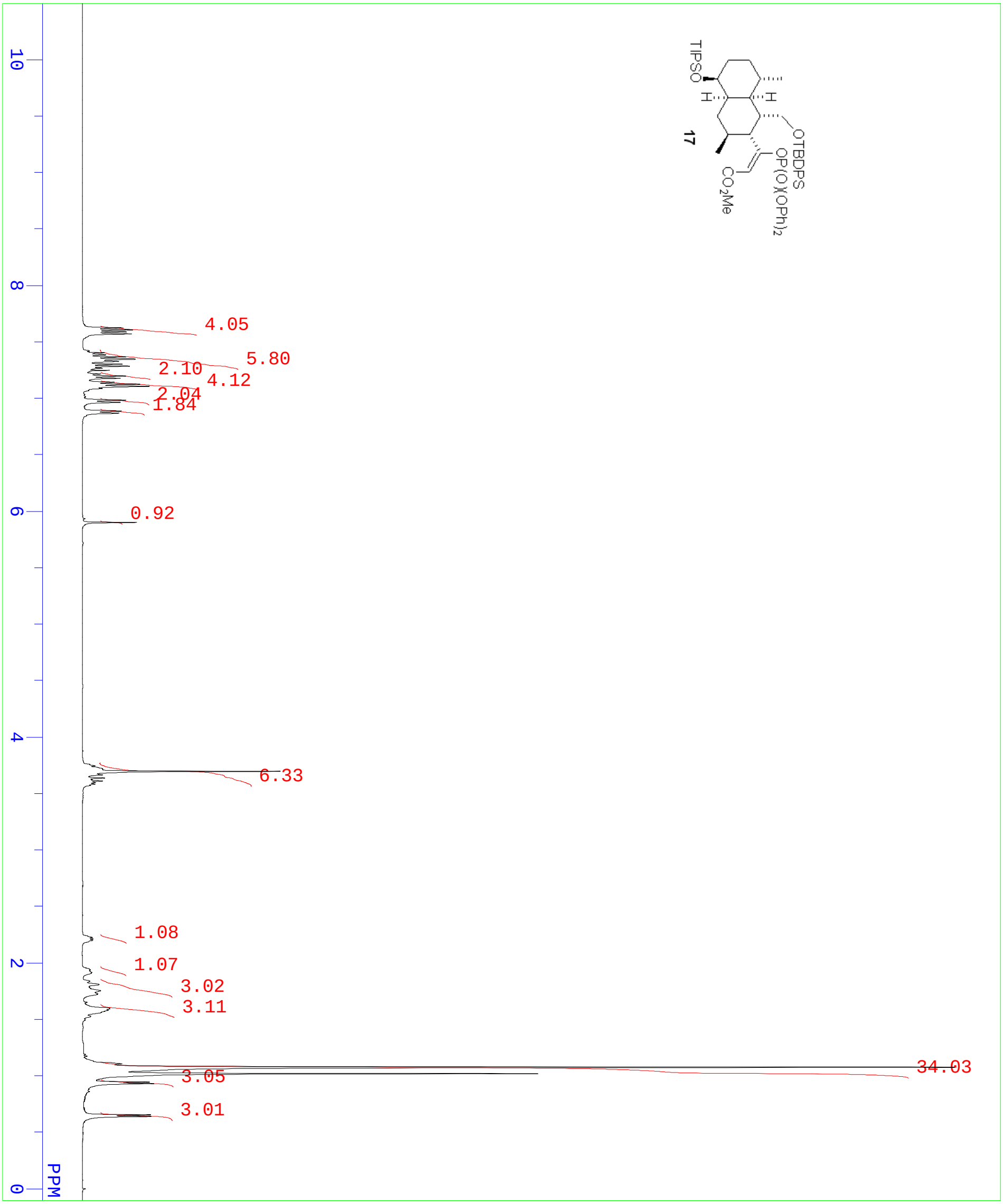
26.180
20.804
19.198
15.485
14.292
13.238

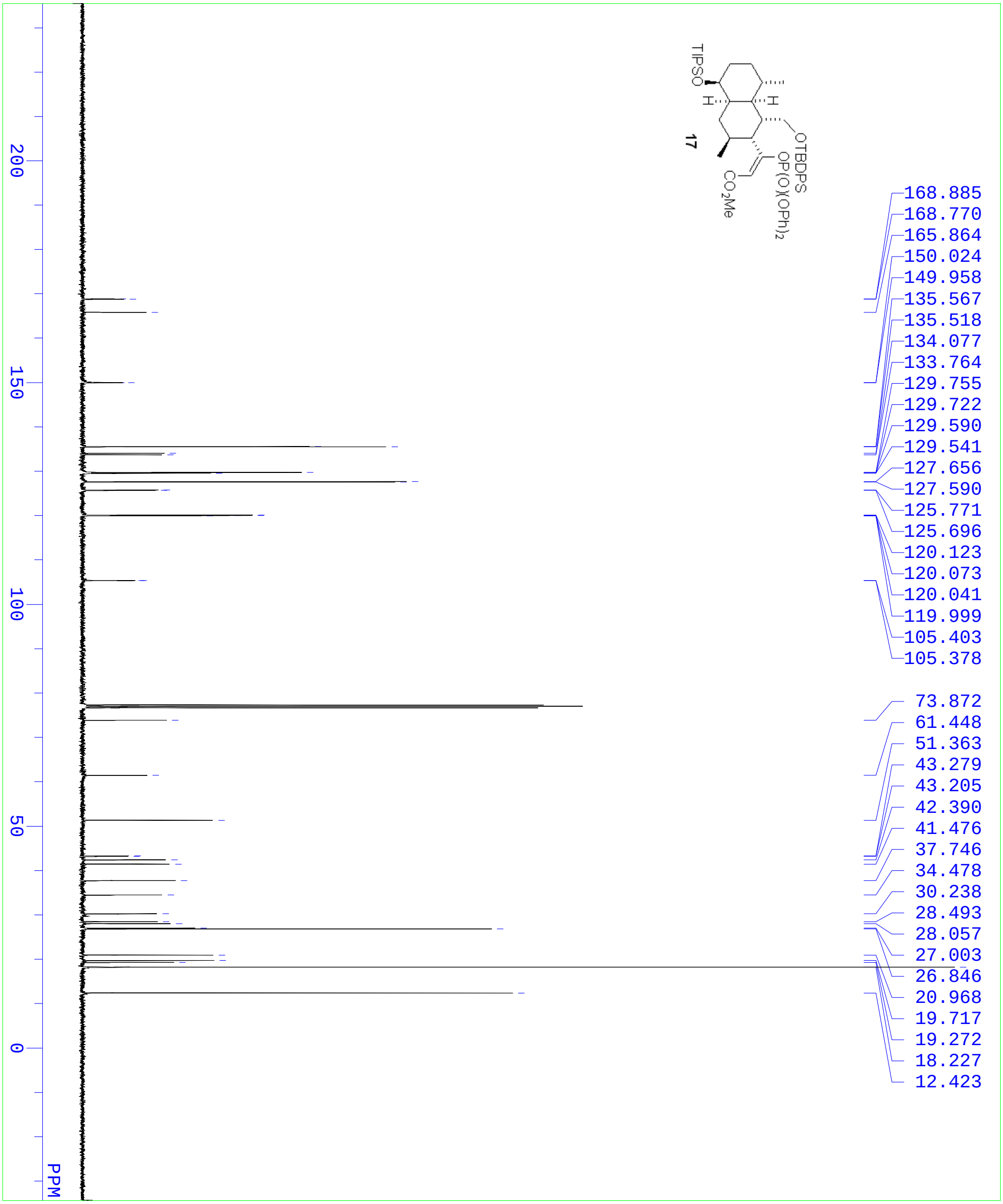

10
8
6
4
2
0
PPM
1.00
1.02
1.05
1.17
0.94
1.12
1.16
1.07
6.03
5.08
3.05
2.17
1.18
3.16
3.01
HO
H
H
16
CO2H

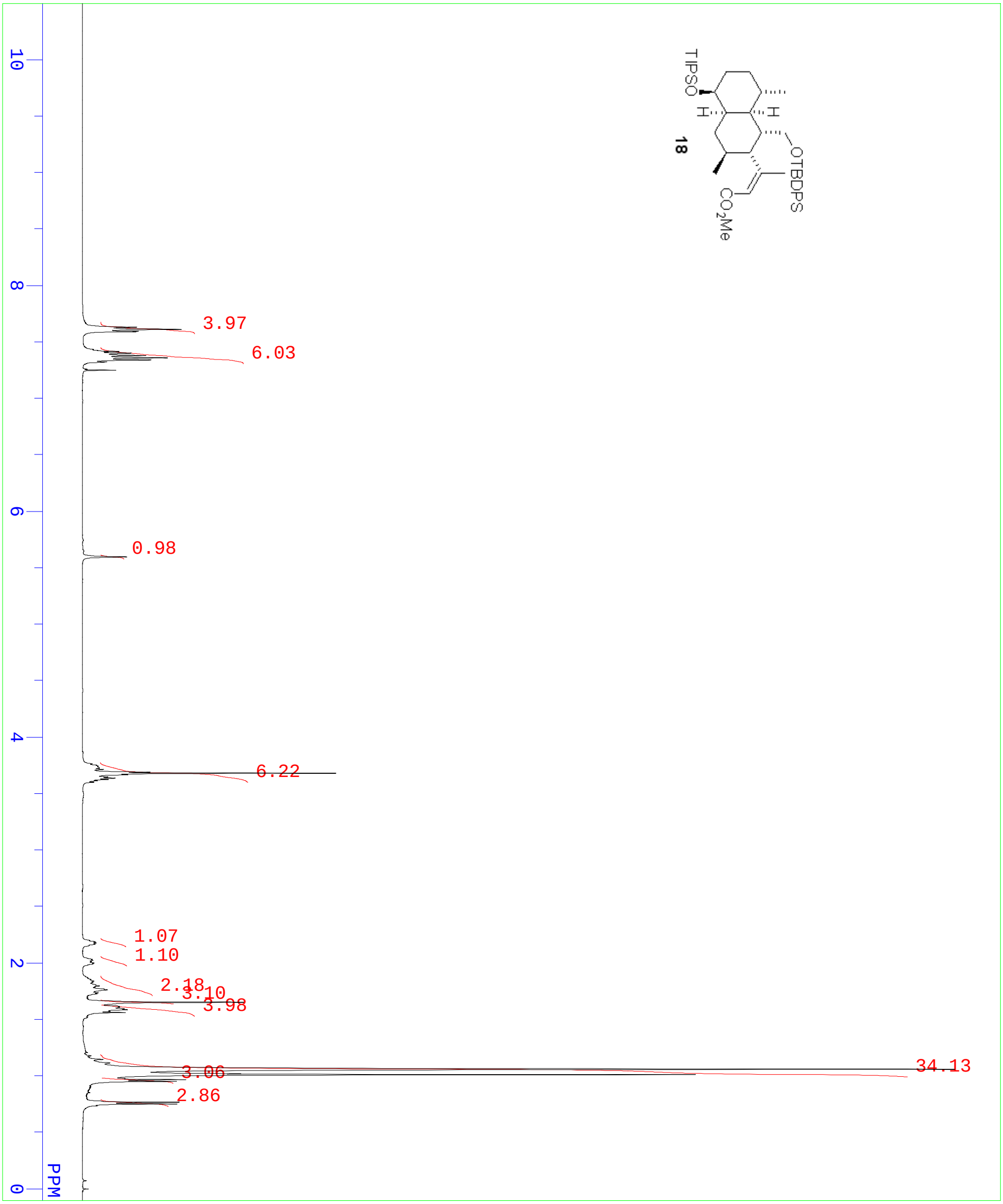

200
150
100
50
0
PPM
HO
H
H
16
CO2H
170.941
148.544
147.048
137.846
129.760
121.464
120.537
73.830
53.090
51.482
46.542
39.327
35.114
30.378
30.153
30.009
28.805
21.305
19.676
15.926
13.349

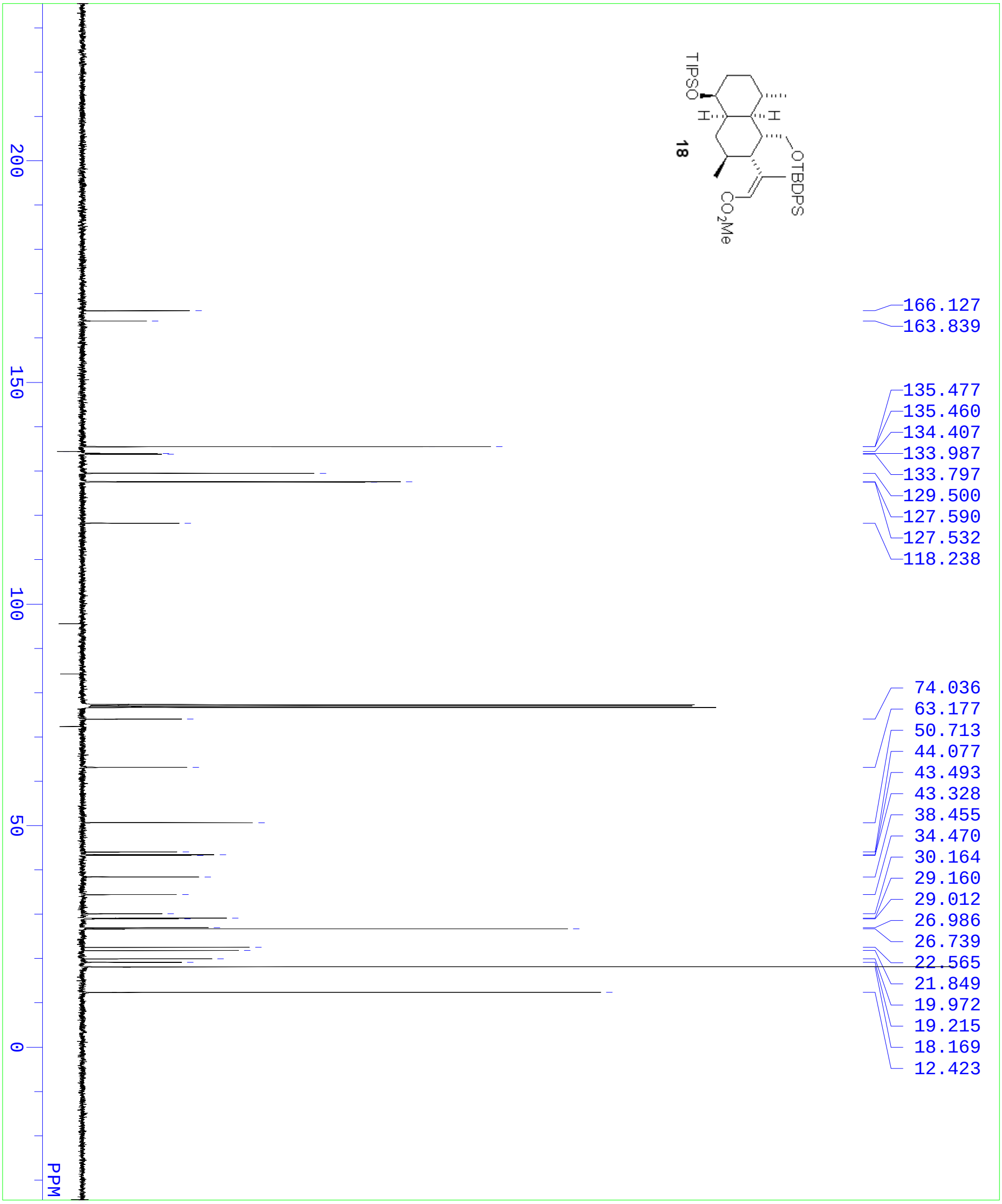

TIPSO
H
H
OTBDPS
O
CO2Me
15l
10
8
6
4
2
0
PPM
3.99
6.12
1.14
2.95
1.11
0.95
0.96
0.96
1.14
1.16
7.90
2.96
2.92
32.34


TIPSO
H
H
OTBDPS
O
CO2Me
151
204.278
167.658
135.534
135.411
133.517
133.468
129.673
129.623
127.664
73.493
62.535
54.335
52.145
48.408
43.172
39.549
37.845
34.042
30.000
27.867
27.563
26.896
26.756
20.993
19.371
19.157
18.095
18.070
12.324
200
150
100
50
0
PPM


TIPSO
H
H
OTBDPS
OP(O)(OPh)2
CO2Me
17
10
8
6
4
2
0
PPM
4.05
5.80
2.10
4.12
2.04
1.84
0.92
6.33
1.08
1.07
3.02
3.11
34.03
3.05
3.01


TIPSO
H
H
OTBDPS
OP(O)(OPh)2
CO2Me
17
168.885
168.770
165.864
150.024
149.958
135.567
135.518
134.077
133.764
129.755
129.722
129.590
129.541
127.656
127.590
125.771
125.696
120.123
120.073
120.041
119.999
105.403
105.378
73.872
61.448
51.363
43.279
43.205
42.390
41.476
37.746
34.478
30.238
28.493
28.057
27.003
26.846
20.968
19.717
19.272
18.227
12.423
200
150
100
50
0
PPM


TIPSO
H
H
OTBDPS
CO2Me
18
10
8
6
4
2
0
PPM
3.97
6.03
0.98
6.22
1.07
1.10
2.18
3.10
3.98
34.13
3.06
2.86


TIPSO
H
H
OTBDPS
CO2Me
18
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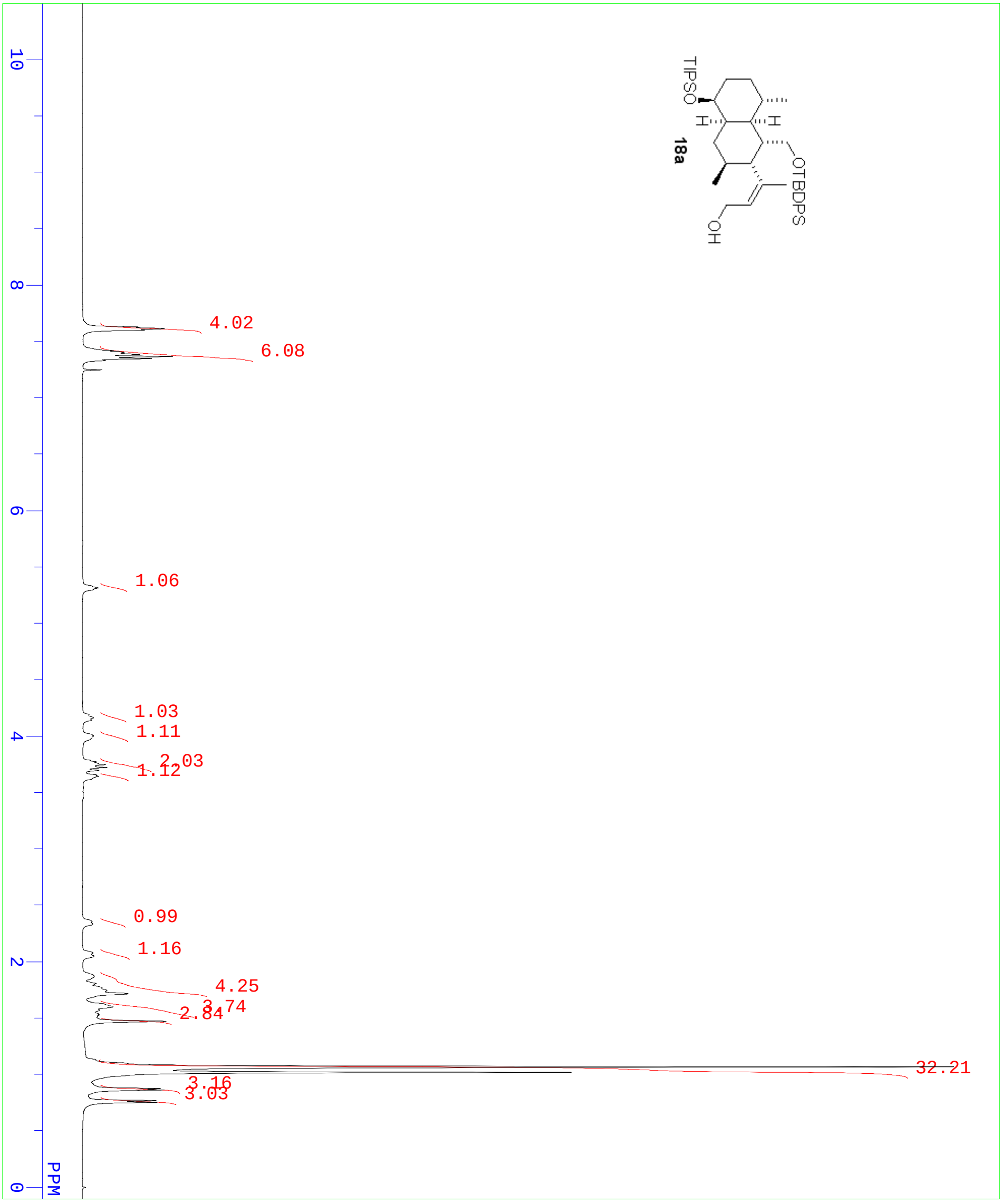
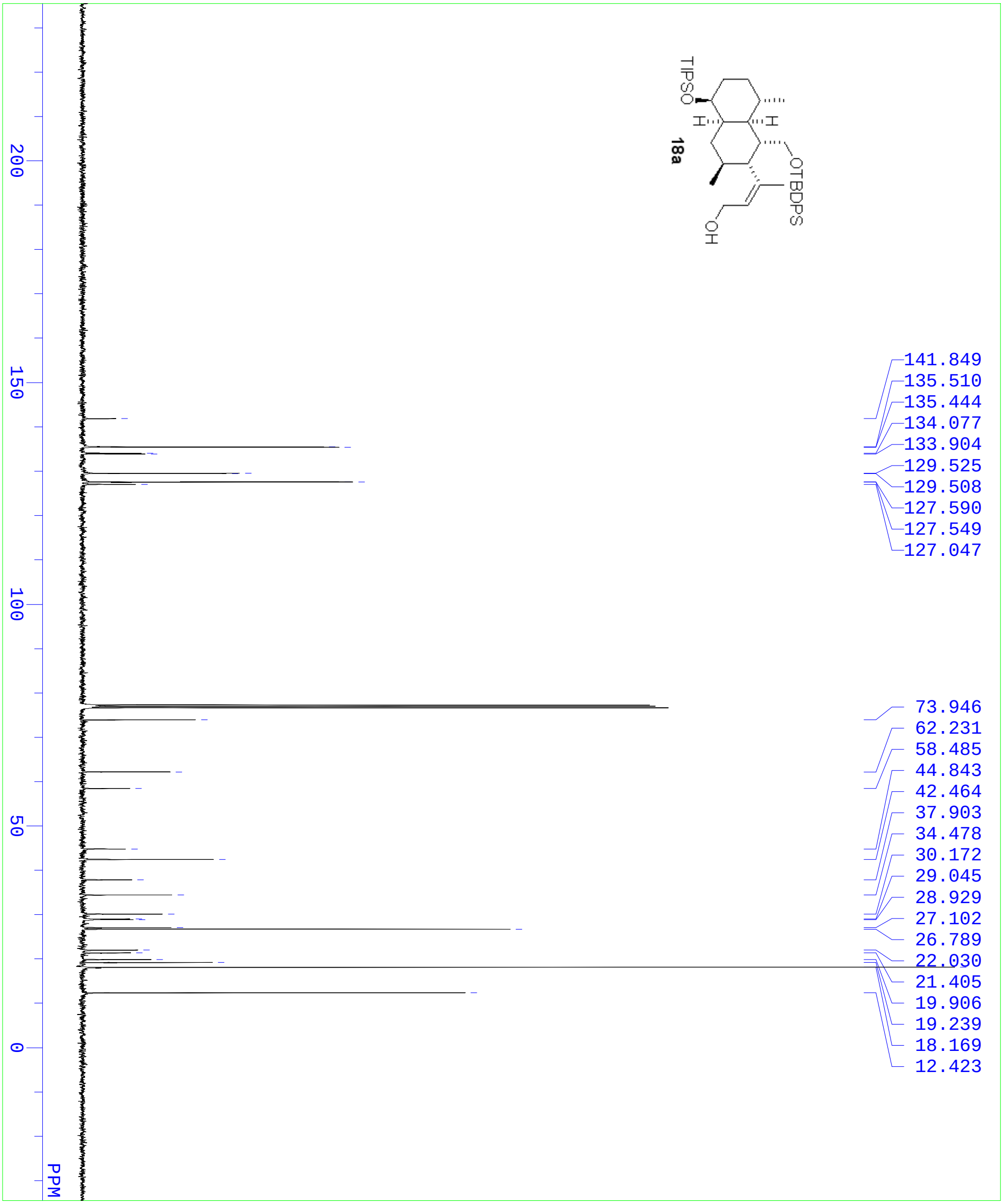
135.460
134.407
133.987
133.797
129.500
127.590
127.532
118.238
74.036
63.177
50.713
44.077
43.493
43.328
38.455
34.470
30.164
29.160
29.012
26.986
26.739
22.565
21.849
19.972
19.215
18.169
12.423
200
150
100
50
0
PPM


TIPSO
H
H
OTBDPS
OH
18a
10
8
6
4
2
0
PPM
4.02
6.08
1.06
1.03
1.11
2.03
1.12
0.99
1.16
4.25
3.74
2.84
32.21
3.16
3.03


TIPSO
H
H
OTBDPS
OH
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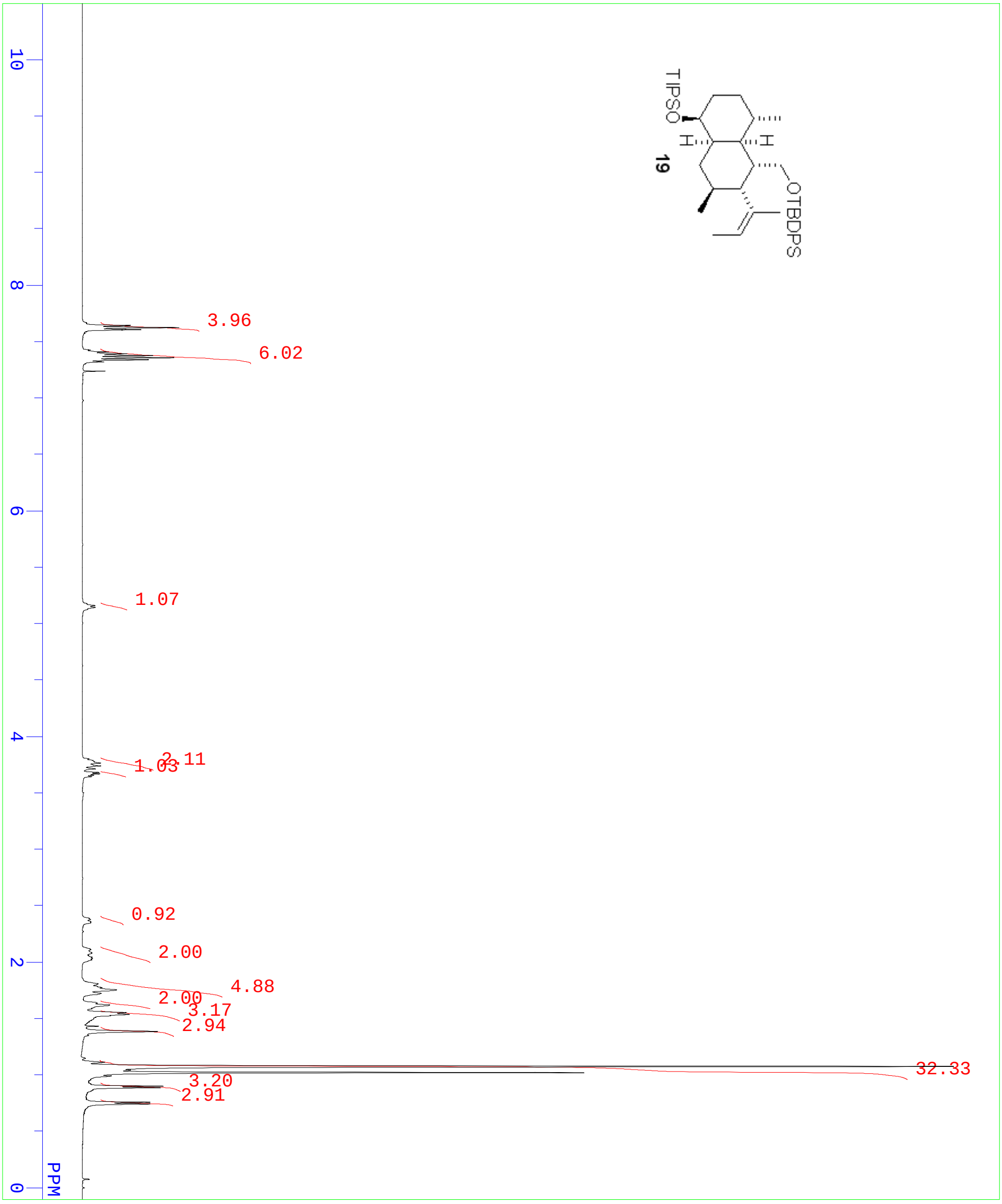
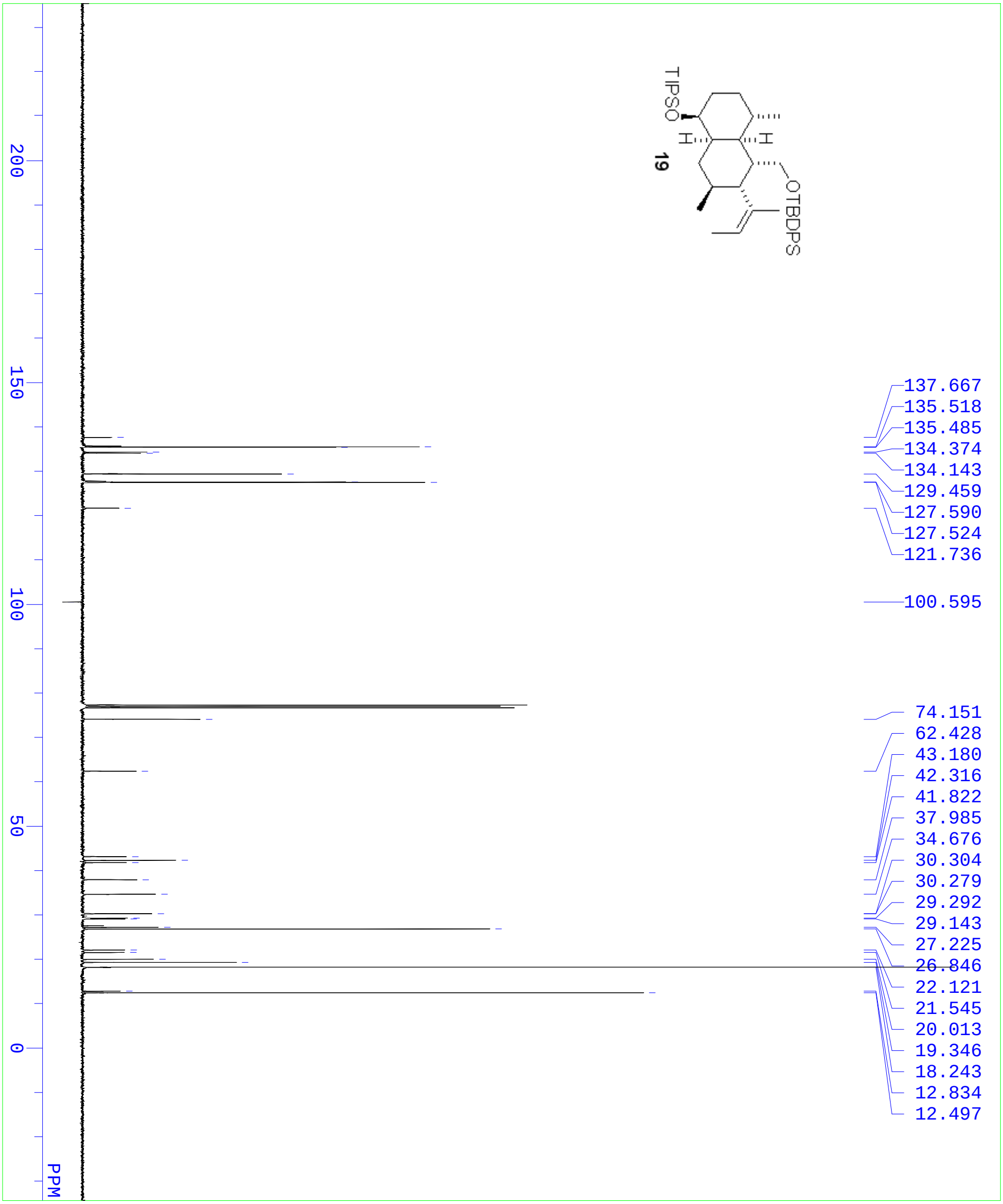
134.077
133.904
129.525
129.508
127.590
127.549
127.047
73.946
62.231
58.485
44.843
42.464
37.903
34.478
30.172
29.045
28.929
27.102
26.789
22.030
21.405
19.906
19.239
18.169
12.423
200
150
100
50
0
PPM


TIPSO
H
H
OTBDPS
19
3.96
6.02
1.07
2.11
1.03
0.92
2.00
4.88
2.00
3.17
2.94
32.33
3.20
2.91
10
8
6
4
2
0
PPM


TIPSO
H
H
OTBDPS
19
200
150
100
50
0
PPM
137.667
135.518
135.485
134.374
134.143
129.459
127.590
127.524
121.736
100.595
74.151
62.428
43.180
42.316
41.822
37.985
34.676
30.304
30.279
29.292
29.143
27.225
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21.545
20.013
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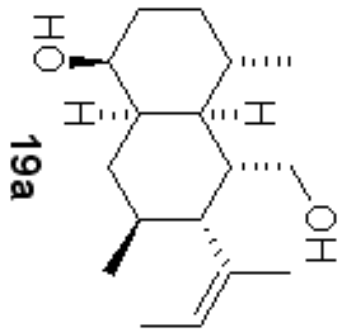
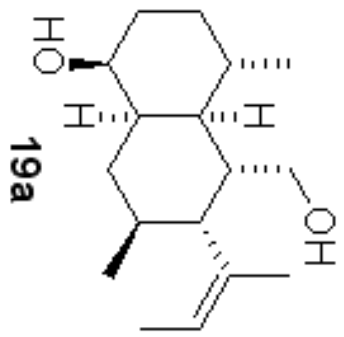
12.497

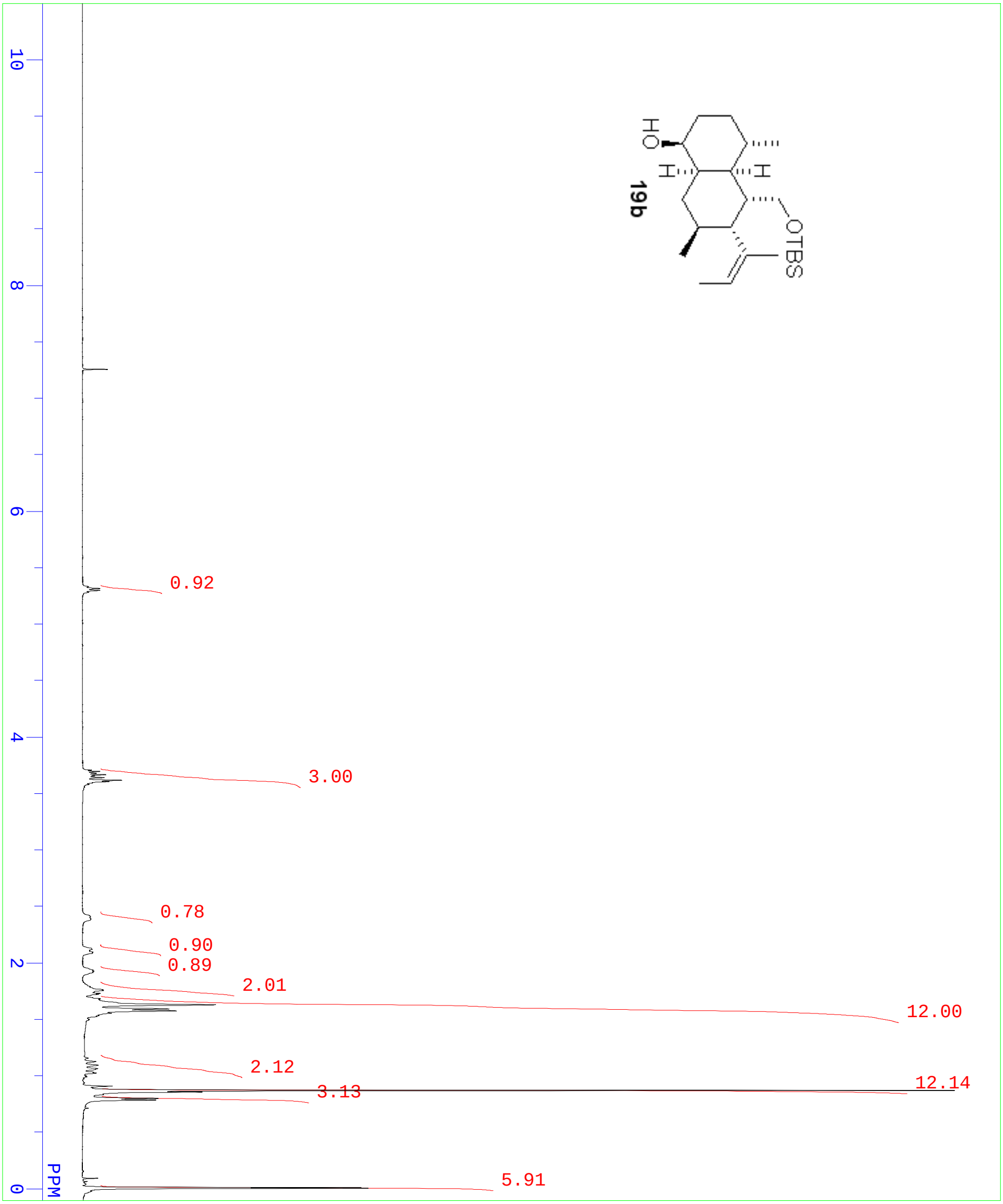


19a


HO
H
H
OH

19a

200
150
100
50
0
PPM
138.967
123.111
74.019
61.390
44.357
43.311
43.048
38.125
35.572
35.540
30.180
30.048
28.394
22.491
22.046
20.293
13.155


HO
H
H
OTBS
19b
10
8
6
4
2
0
PPM
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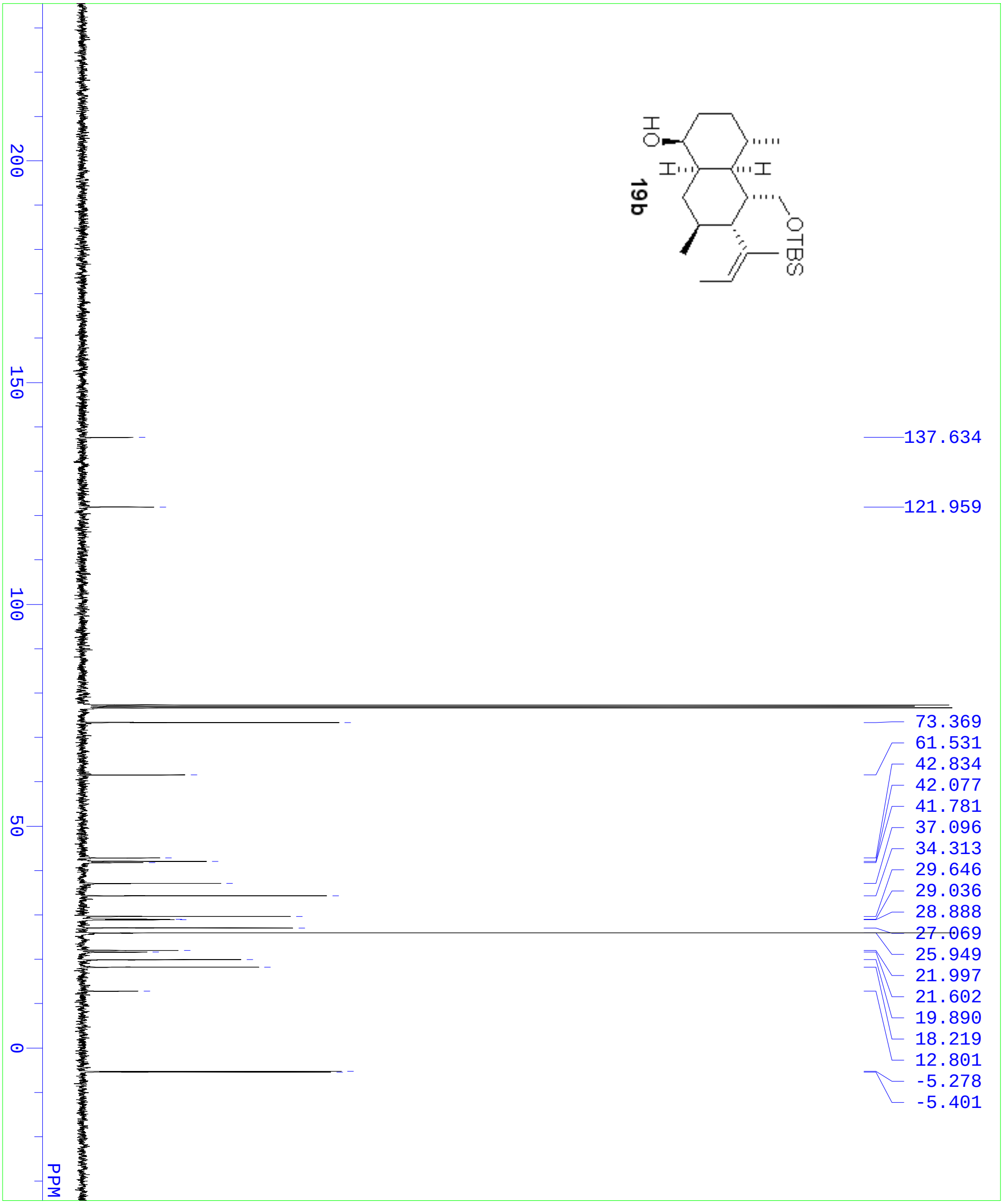
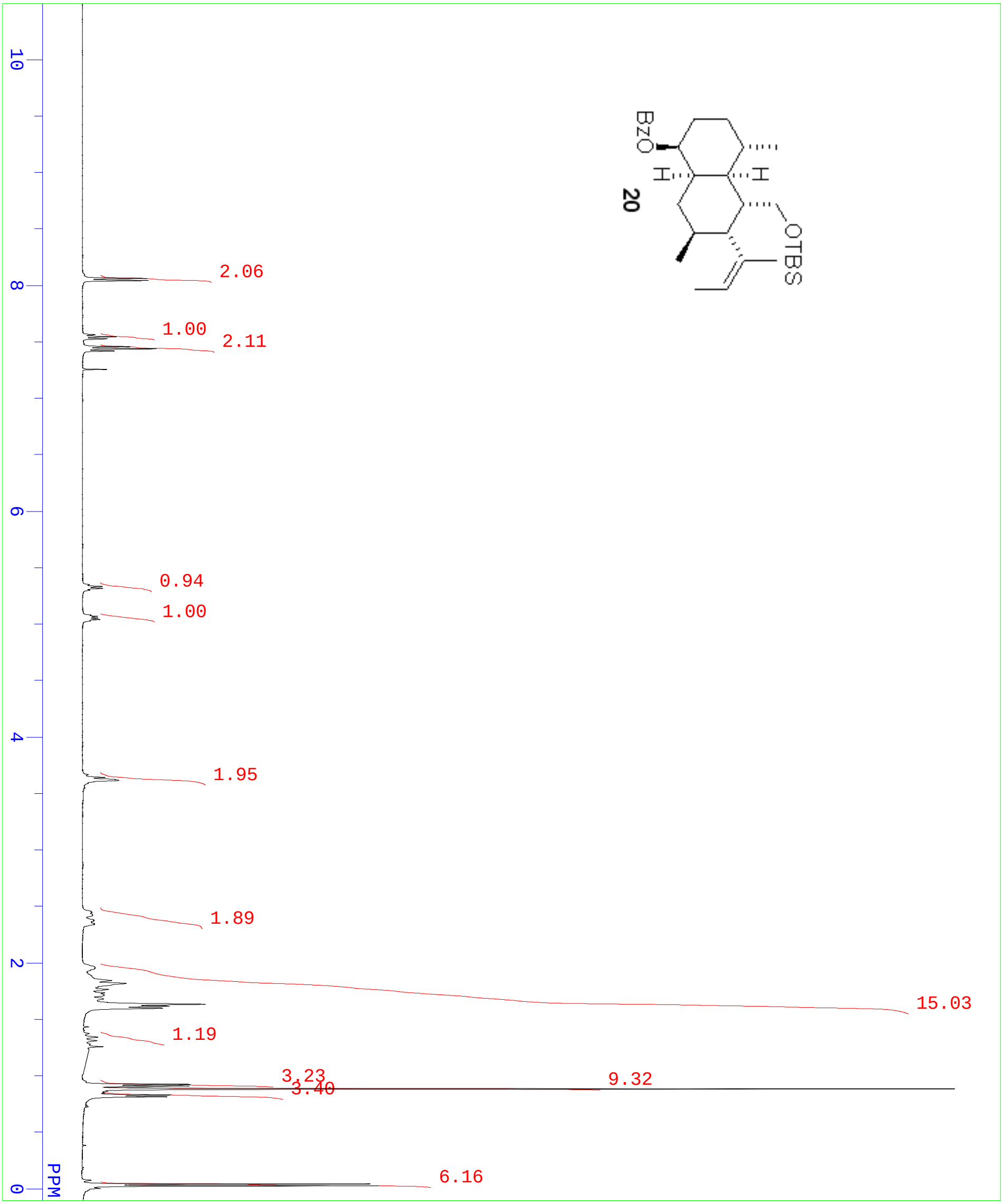
0.78
0.90
0.89
2.01
12.00
2.12
3.13
12.14
5.91


200
150
100
50
0
PPM
HO
H
H
OTBS
19b
137.634
121.959
73.369
61.531
42.834
42.077
41.781
37.096
34.313
29.646
29.036
28.888
27.069
25.949
21.997
21.602
19.890
18.219
12.801
-5.278
-5.401


BzO
H
H
OTBS
20
2.06
1.00
2.11
0.94
1.00
1.95
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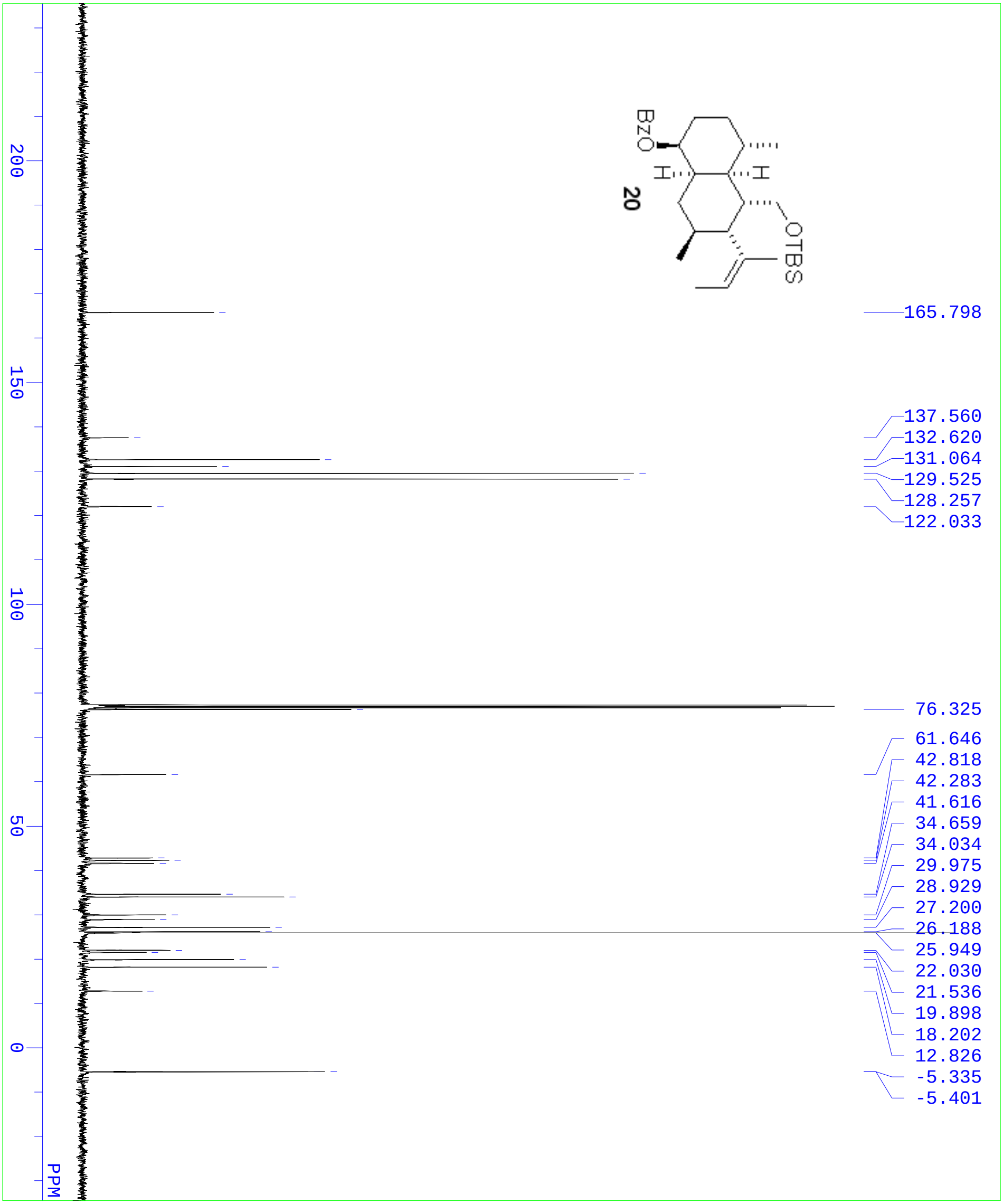
1.19
3.23
3.40
9.32
6.16
10
8
6
4
2
0
PPM


BzO
H
H
OTBS
20
165.798
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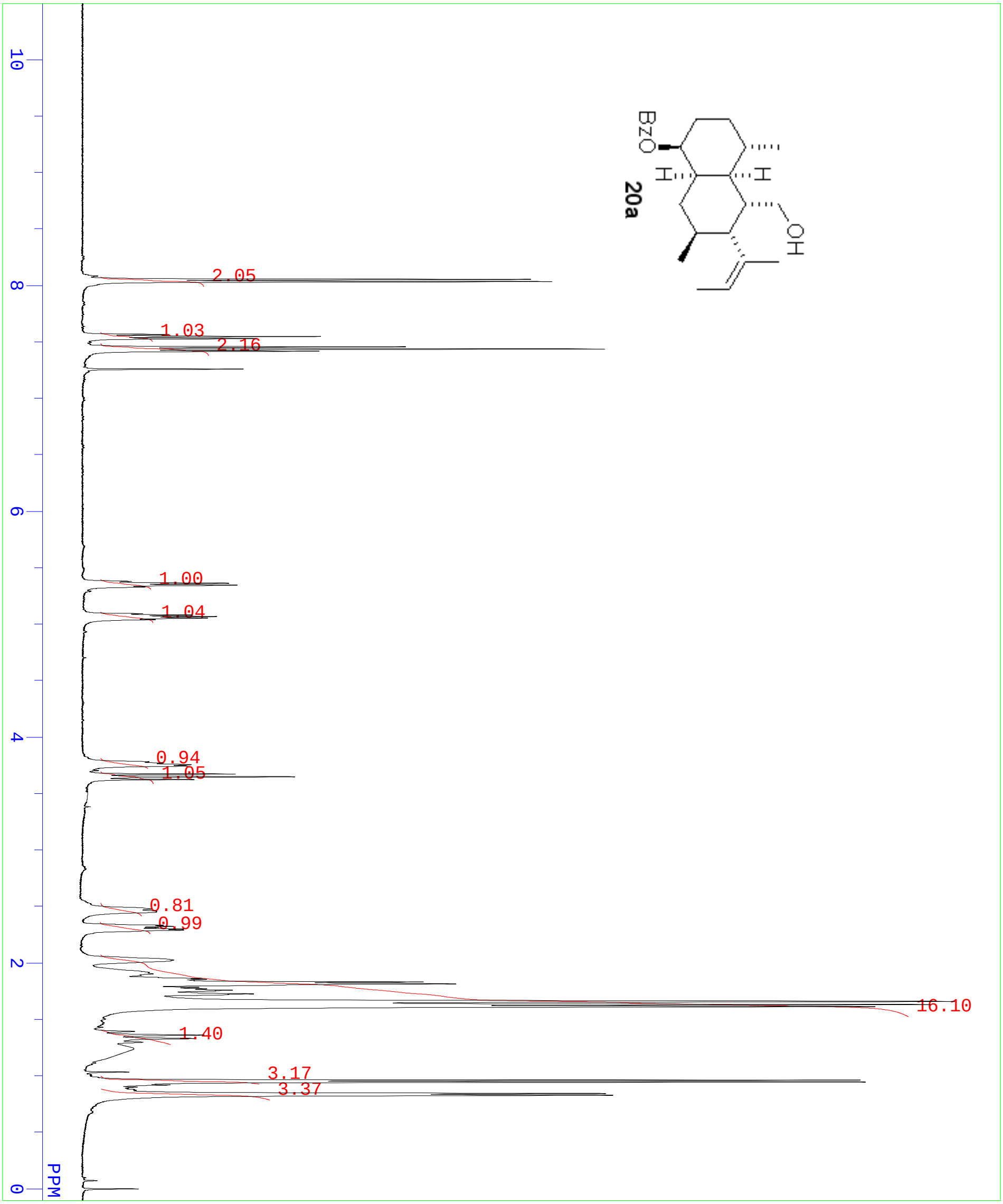
132.620
131.064
129.525
128.257
122.033
76.325
61.646
42.818
42.283
41.616
34.659
34.034
29.975
28.929
27.200
26.188
25.949
22.030
21.536
19.898
18.202
12.826
-5.335
-5.401
200
150
100
50
0
PPM


10
8
6
4
2
0
PPM
2.05
1.03
2.16
1.00
1.04
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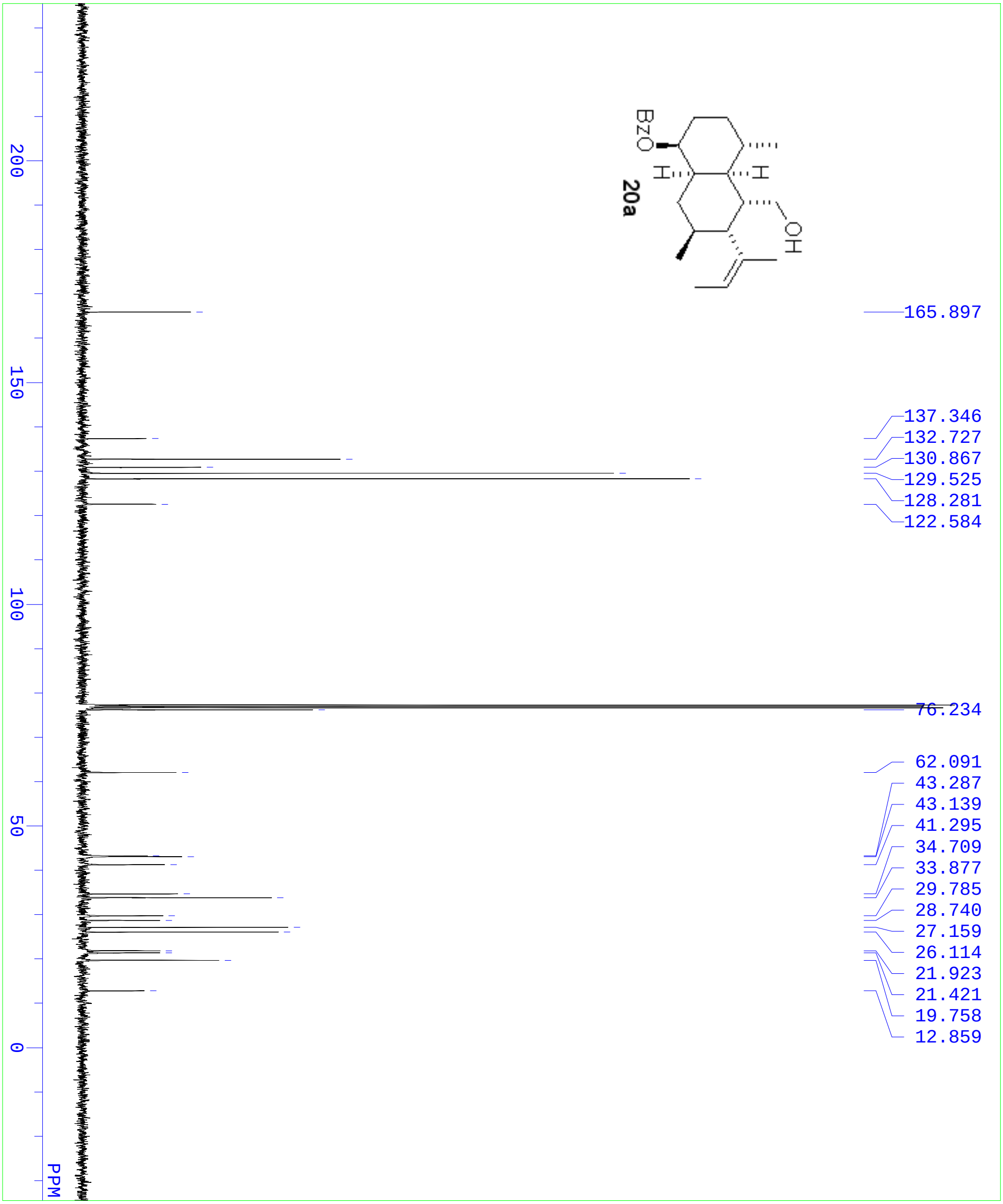
1.05
0.81
0.99
16.10
1.40
3.17
3.37
BzO
H
H
OH
20a


BzO
H
H
OH
20a
165.897
137.346
132.727
130.867
129.525
128.281
122.584
76.234
62.091
43.287
43.139
41.295
34.709
33.877
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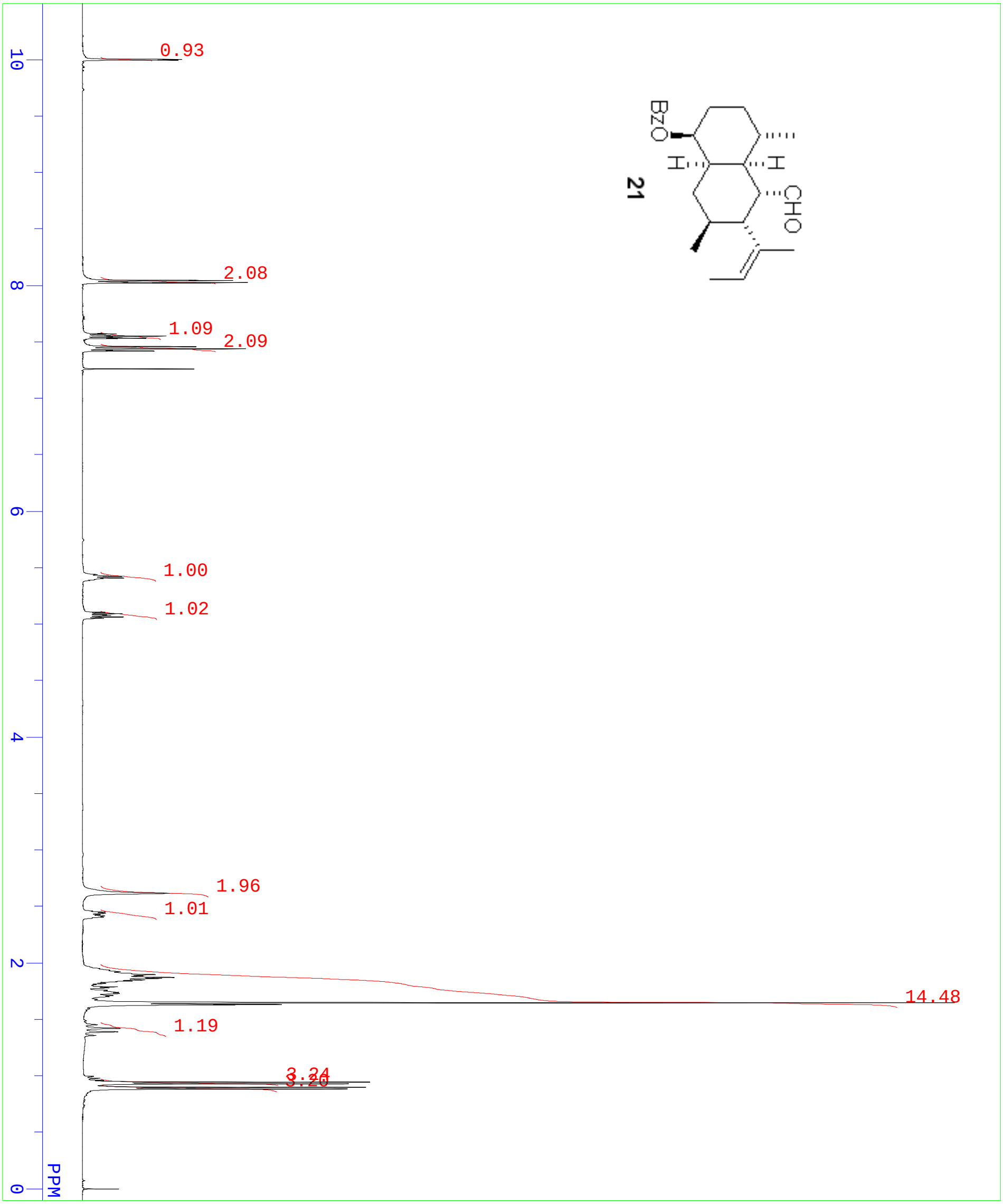
28.740
27.159
26.114
21.923
21.421
19.758
12.859
200
150
100
50
0
PPM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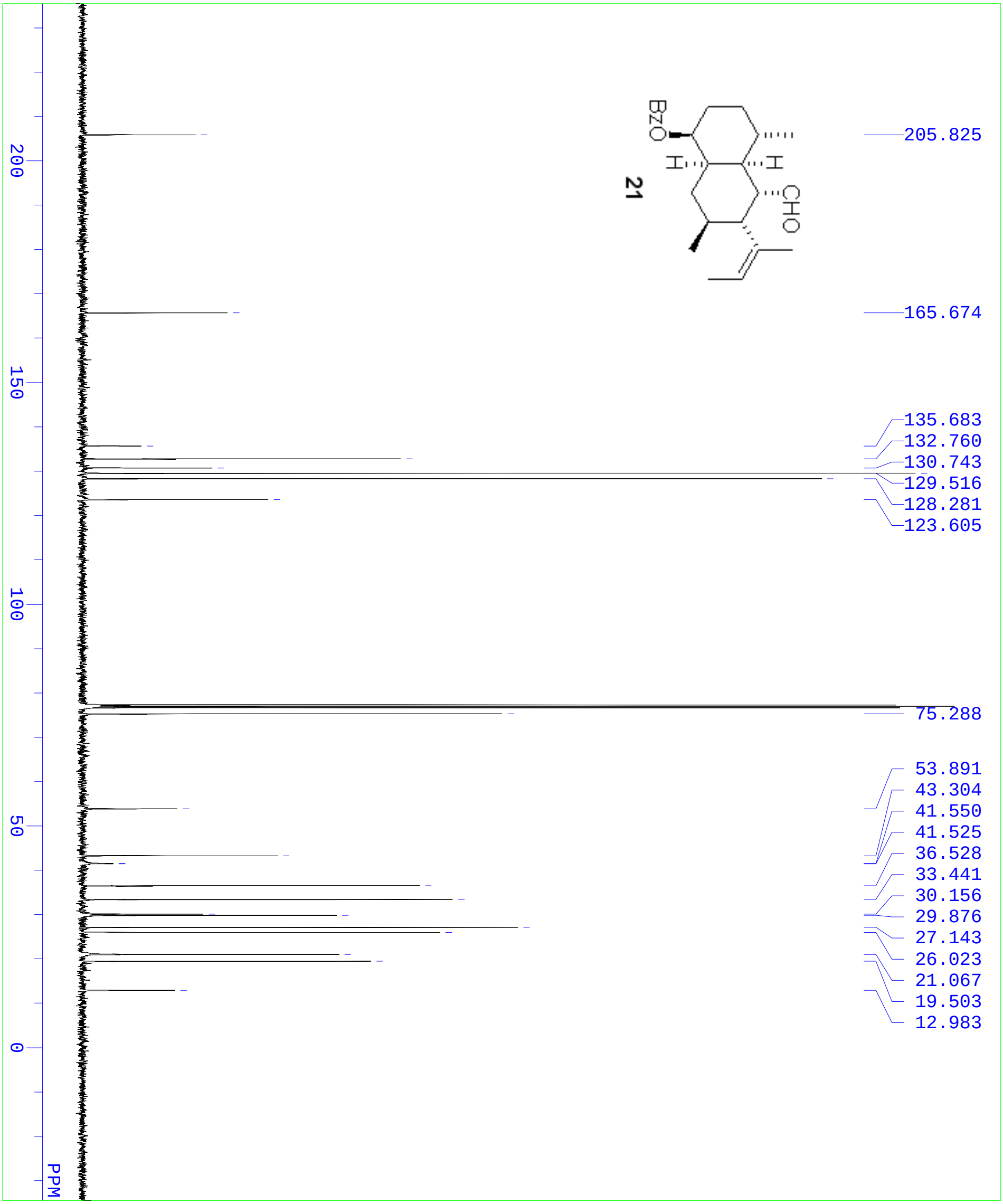
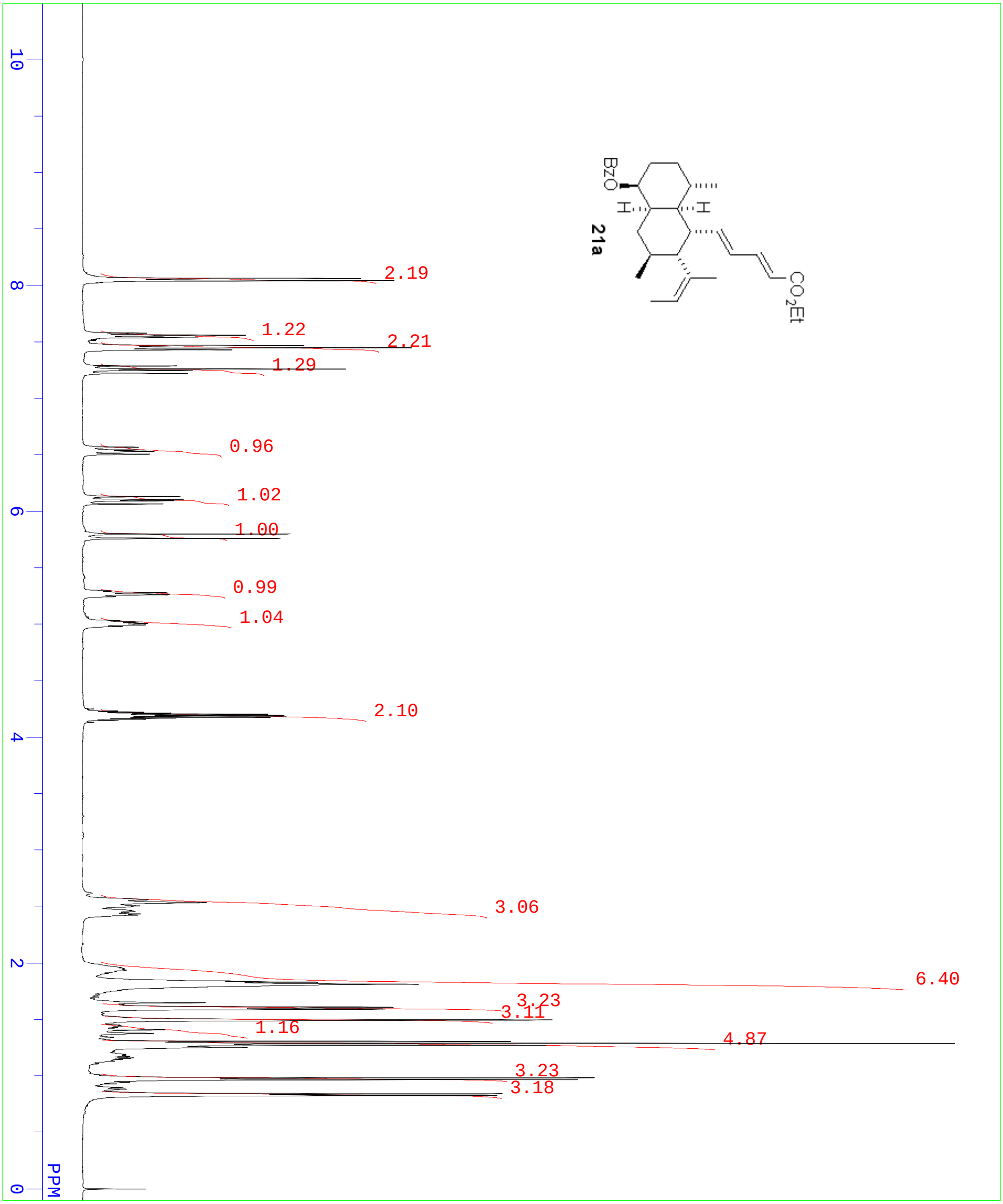
1.00
1.02
1.96
1.01
14.48
1.19
3.24
3.20
10
8
6
4
2
0
PPM

BzO
H
H
CHO

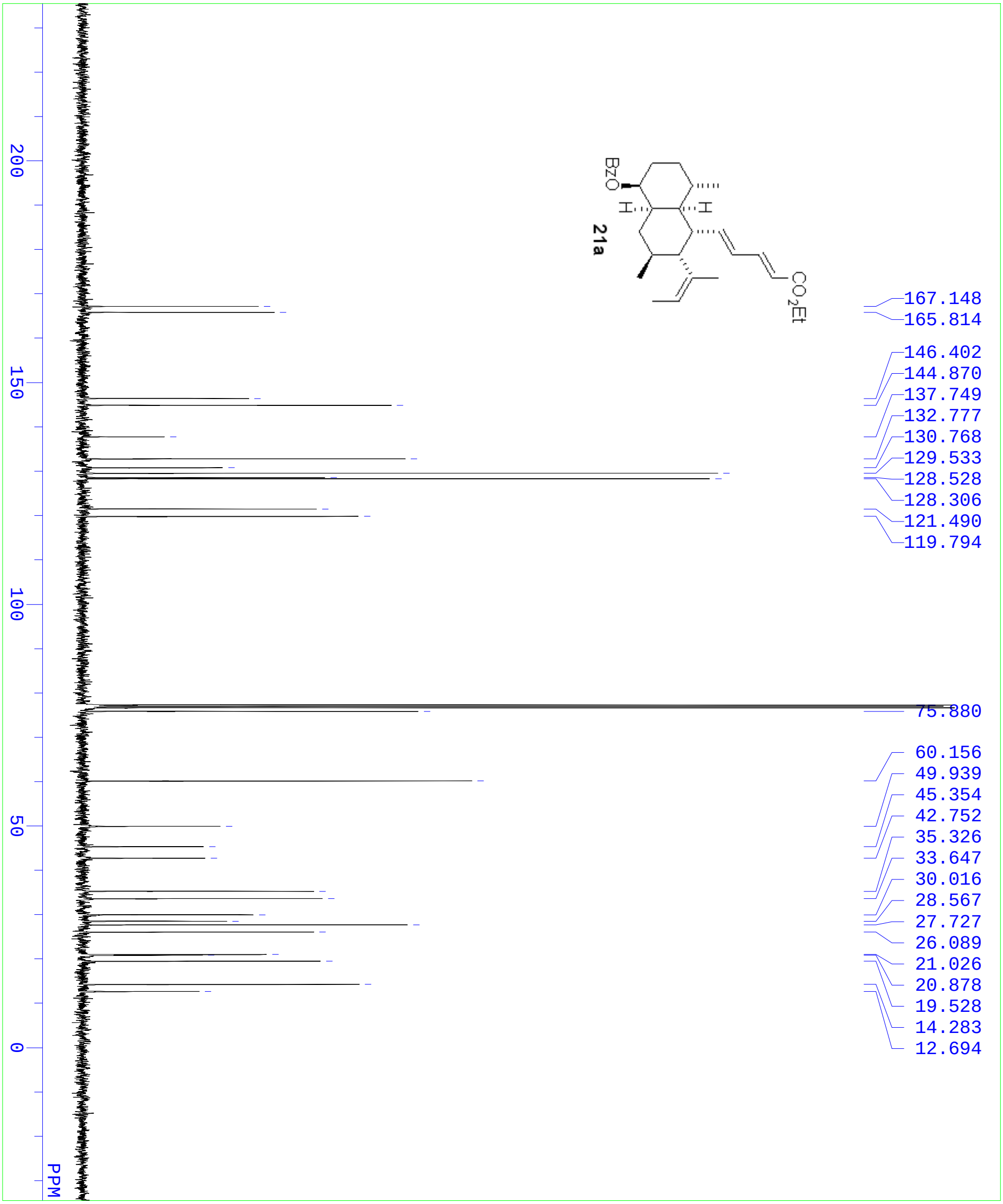
21

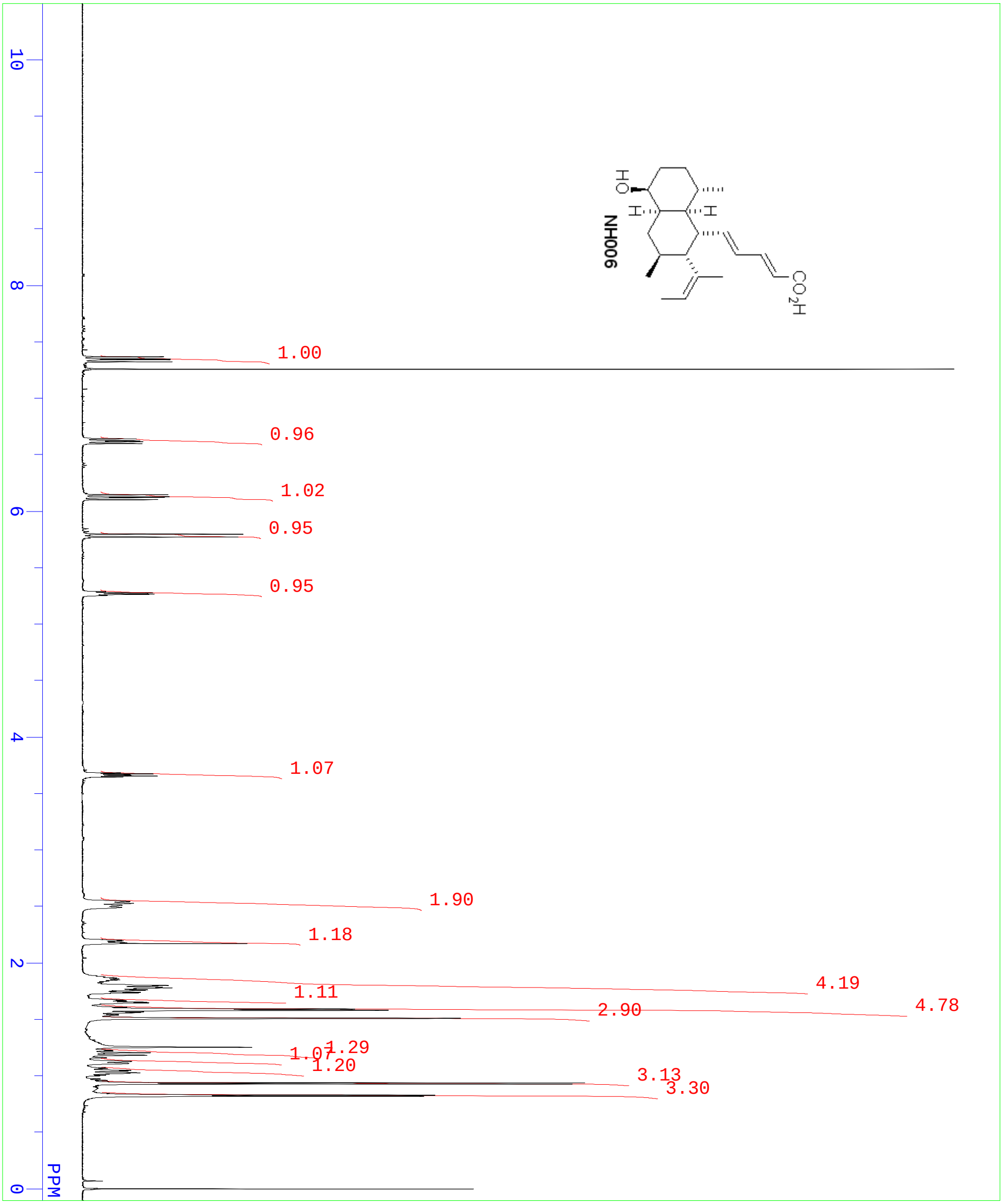

BzO
H
H
CHO
21
205.825
165.674
135.683
132.760
130.743
129.516
128.281
123.605
75.288
53.891
43.304
41.550
41.525
36.528
33.441
30.156
29.876
27.143
26.023
21.067
19.503
12.983
200
150
100
50
0
PPM

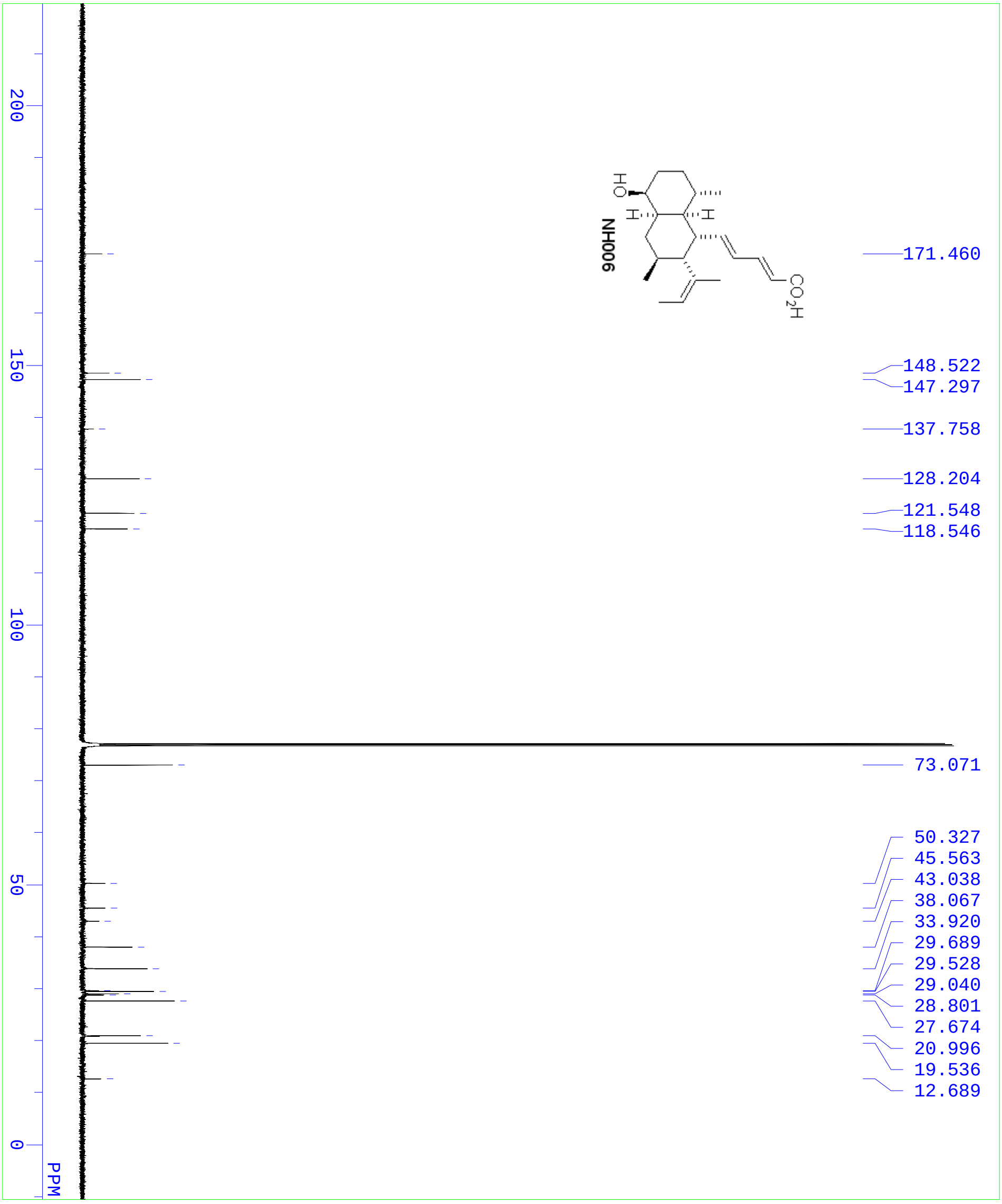

10
8
6
4
2
0
PPM
2.19
1.22
2.21
1.29
0.96
1.02
1.00
0.99
1.04
2.10
3.06
6.40
3.23
3.11
1.16
4.87
3.23
3.18

BzO
H
H
CO2Et

21a


200
150
100
50
0
PPM
BzO
H
H
21a
CO2Et
167.148
165.814
146.402
144.870
137.749
132.777
130.768
129.533
128.528
128.306
121.490
119.794
75.880
60.156
49.939
45.354
42.752
35.326
33.647
30.016
28.567
27.727
26.089
21.026
20.878
19.528
14.283
12.694


900HN
HO
H
H
CO2H
1.00
0.96
1.02
0.95
0.95
1.07
1.90
1.18
4.19
1.11
4.78
2.90
1.29
1.07
1.20
3.13
3.30
10
8
6
4
2
0
PPM


200
150
100
50
0
PPM
900HN
OH
H
H
CO2H
171.460
148.522
147.297
137.758
128.204
121.548
118.546
73.071
50.327
45.563
43.038
38.067
33.920
29.689
29.528
29.040
28.801
27.674
20.996
19.536
12.689