Enantio- and diastereocontrolled synthesis of (+)-juvabione employing organocatalytic desymmetrisation and photoinduced fragmentation

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Supporting Information

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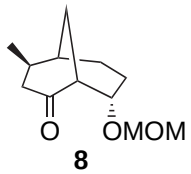
1. General.

Dess-Martin periodinane[1] and 1-methyl-2-azaadamantane-*N*-oxyl (1-Me-AZADO)[2] (**19**) were prepared according to the literature procedures. Other chemicals and solvents were purchased from commercial suppliers or purified by standard techniques. All reactions were stirred magnetically, under an argon atmosphere, unless otherwise noted, and monitored with analytical TLC (Merck Kieselgel 60 F_{254}). Column chromatography was carried out with silica gel 60 particle size 0.063-0.210 mm. Melting points were taken with Yazawa BY-2 and are uncorrected. NMR spectra were measured in JEOL JNM-AL400 (400 MHz). Chemical shifts were reported in the δ scale relative to tetramethylsilane (TMS) (0.00 ppm for ^{1}H ($CDCl_3$)) and residual $CHCl_3$ (7.26 ppm for ^{1}H and 77.00 ppm for ^{13}C), as internal reference. The infrared (IR) spectra were recorded on JASCO FT/IR-410. Mass spectra were measured on JEOL JMS-DX303 (for low resolution MS) and JMS-AX500 or JMS-700 (for high resolution MS) instruments. The specific rotations were measured on JASCO DIP-370. Elemental analyses utilized Yanaco CHN CORDER MT-6.

2. Experimental procedures.

(1) Preparation of substrates for the Norrish Ireactions

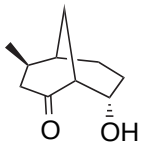


8

(1*R*,4*R*,5*R*,8*S*)-8-Methoxymethoxy-4-methylbicyclo[3.3.1]nonan-2-one [(–)-8]: 1.04 M MeLi in Et_2O (22.0 ml, 23.0 mmol) was added to the suspension of CuI (2.20 g, 11.6 mmol) in THF (35 ml) at –40 °C. The mixture was stirred for 30 min at the same temperature. Then, to this mixture was added dropwisely a solution of (1*R*,5*R*,8*S*)-8-methoxymethoxybicyclo[3.3.1]non-3-en-2-one [(+)-**7**][3] (900 mg, 4.59 mmol, > 99% ee) in THF (17 ml) at –40 °C and stirring was continued for 90 min at the same temperature. After the reaction mixture was quenched with saturated aqueous NH_4Cl, the mixture was extracted with Et_2O and washed with H_2O. The aqueous layer was extracted with Et_2O and the combined organic extract was washed with brine, dried over $MgSO_4$, and

concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane-AcOEt (19:1 v/v)] to afford ketone (–)-**8** (954 mg, 98%) as a colorless oil.

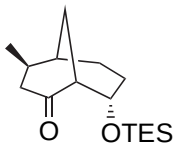
$[\alpha]_D^{28}$ = –45.5° (*c* 1.03, $CHCl_3$); IR (neat): 1704 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.77 (d, 1H, *J* = 6.8 Hz), 4.62 (d, 1H, *J* = 7.1 Hz), 3.82 (m, 1H), 3.38 (s, 3H), 2.80 (br s, 1H), 2.62 (dd, 1H *J* = 17.3, 8.1 Hz), 2.22-2.10 (m, 3H), 2.03 (m, 1H), 1.90-1.60 (m, 5H), 1.05 (d, 3H, *J* = 7.1 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 212.1, 94.1, 75.1, 55.3, 49.4, 47.7, 33.9, 32.8, 31.1, 27.6, 27.5, 23.4; MS *m/z* : 212 (M^+), 45 (100%); HRMS Calcd. $C_{12}H_{20}O_3$: 212.1411. Found: 212.1422; *Anal*. Calcd. for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.60; H, 9.30.



9

(1*R*,4*R*,5*R*,8*S*)-8-Hydroxy-4-methylbicyclo[3.3.1]nonan-2-one [(–)-9]: To a solution of MOM ether (–)-**8** (777 mg, 3.66 mmol) in 1,4-dioxane (43 ml) were added $LiBF_4$ (1.89 g, 20.2 mmol) and H_2O (1.42 ml) at room temperature. The mixture was heated to 50-70 °C and stirred for 7 h. After cooling, the reaction mixture was diluted with Et_2O and the organic solution was washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with AcOEt and the combined organic extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane-AcOEt (4:1 v/v)] to afford alcohol (–)-**9** (513 mg, 83%) as colorless crystals and the recovered starting material (–)-**8** (51 mg, 6.5%).

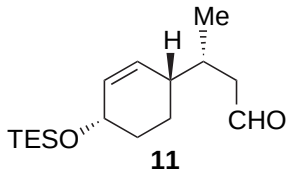
mp 51-53 ˚C; $[\alpha]_D^{28}$ = –96.5° (*c* 0.66, $CHCl_3$); IR ($CHCl_3$ solution): 3272, 1697 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.70 (m, 1H), 3.34 (d, 1H, *J* = 8.6 Hz), 2.56 (br s, 1H), 2.43 (dd, 1H, *J* = 16.1, 6.8 Hz), 2.20-2.11 (m, 2H), 1.95-1.55 (m, 6H), 1.26 (dq, 1H, *J* = 6.9, 12.9 Hz) , 1.05 (dd, 3H, *J* = 7.0, 1.5 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 218.6, 72.2, 49.0, 47.2, 33.2, 31.28, 31.26, 29.5, 27.4, 23.6; MS *m/z* : 168 (M^+), 168 (100%); HRMS Calcd. $C_{10}H_{16}O_2$: 168.1149. Found: 168.1139.



10

(1*R*,4*R*,5*R*,8*S*)-8-Triethylsiloxy-4-methylbicyclo[3.3.1]nonan-2-one [(+)-10]: TESCl (0.613 ml, 3.66 mmol) and imidazole (414 mg, 6.08 mmol) were added to a solution of alcohol (–)-**9** (512 mg, 3.04 mmol) in DMF (10 ml) at room temperature. The reaction mixture was stirred for 12 h at the same temperature. Then, the reaction mixture was diluted with Et_2O and washed with H_2O. The aqueous layer was extracted with Et_2O and the combined organic extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane-AcOEt (97:3~19:1 v/v)] to afford TES ether (+)-**10** (784 mg, 91%) as a colorless oil. $[\alpha]_D^{29}$ = +29.0° (*c* 0.86, $CHCl_3$); IR (neat): 1708 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.86 (m, 1H), 2.63 (dd, 1H, *J* = 17.6, 8.6 Hz), 2.60 (br s, 1H), 2.19-2.13 (m, 2H), 2.07 (m, 1H), 1.94 (m, 1H), 1.85-1.71 (m, 3H), 1.63 (br s, 1.5H), 1.59 (br s, 0.5H), 1.03 (dd, 3H, *J* = 7.1, 1.6 Hz) , 0.94 (dt, 9H, *J* = 1.7, 8.8 Hz), 0.58 (dq, 6H, *J* = 1.4, 8.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 211.6, 71.3, 53.5, 48.0, 34.6, 32.8, 31.2, 30.7, 28.1, 23.3, 6.7, 4.8; MS *m/z* : 253 (M^+–Et), 253 (100%); HRMS Calcd. $C_{14}H_{25}O_2Si$ (M^+–Et): 253.1622. Found: 253.1605.

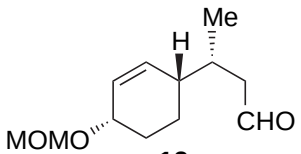
(1) Typical procedures for the Norrsih Ireactions



11

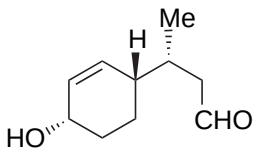
(3*R*)-((1*S*,4*S*)-4-Triethylsiloxycyclohex-2-enyl)butyraldehyde [(–)-11]: A solution of (+)-**10** (720 mg, 2.55 mmol) in MeOH (170 ml) in Pyrex tubes was degassed by bubbling of argon gas through the solution for 25 min. The solution was irradiated using a Rayonet Photochemical Reactor (Lamp 300 nm) for 90 min at room temperature. Then, the solution was concentrated under reduced pressure and the residue was purified by silica gel column chromatography [hexane-AcOEt (97:3~19:1 v/v)] to afford aldehyde (–)-**11** (477

mg, 66%) as a colorless oil with inseparable small amount of impurities.
$[\alpha]_D^{29}$ = –56.1° (*c* 1.00, $CHCl_3$); IR (neat): 1728 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 9.77 (dd, 1H, *J* = 2.7, 1.7 Hz), 5.77 (dm, 1H, *J* = 10.2 Hz), 5.64 (dm, 1H, *J* = 10.2 Hz), 4.13 (m, 1H), 2.52 (m, 1H), 2.26-2.15 (m, 2H), 2.00 (br s, 1H), 1.77-1.45 (m, 4H), 0.94 (m, 12H), 0.61 (q, 6H, *J* = 8.0 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 202.8, 132.0, 131.2, 64.3, 48.3, 40.2, 31.8, 31.2, 20.0, 17.0, 6.8, 5.0; MS *m/z* : 282 (M^+), 133 (100%); HRMS Calcd. $C_{16}H_{30}O_2Si$: 282.2013. Found: 282.2032.



12

(3*R*)-((1*S*,4*S*)-4-Methoxymethoxycyclohex-2-enyl)butyraldehyde [(–)-12]: A solution of (–)-**8** (215 mg, 1.01 mmol) in MeOH (100 ml) in Pyrex tubes was degassed by bubbling of argon gas through the solution for 25 min. The solution was irradiated using a Rayonet Photochemical Reactor (Lamp 300 nm) for 90 min at room temperature. Then, the solution was concentrated under reduced pressure and the residue was purified by silica gel column chromatography [hexane-AcOEt (19:1~9:1 v/v)] to afford aldehyde (–)-**12** (149 mg, 69%) as a colorless oil.
$[\alpha]_D^{29}$ = –66.6° (*c* 0.93, $CHCl_3$); IR (neat): 1725 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 9.77 (t, 1H, *J* = 1.8 Hz), 5.89 (m, 1H), 5.76 (br d, 1H, *J* = 10.8 Hz), 4.71 (dd, 1H, *J* = 6.8, 1.2 Hz), 4.67 (dd, 1H, *J* = 6.8, 1.2 Hz), 4.01 (br s, 1H), 3.37 (d, 3H, *J* = 1.4 Hz), 2.50 (m, 1H), 2.31-2.18 (m, 2H), 2.07 (br s, 1H), 1.93 (m, 1H), 1.64-1.48 (m, 3H), 0.96 (d, 3H, *J* = 7.6 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 202.6, 134.3, 128.1, 95.0, 68.6, 55.1, 48.2, 40.4, 31.6, 28.0, 19.8, 16.7; MS *m/z* : 212 (M^+), 123 (100%); HRMS Calcd. $C_{12}H_{20}O_3$: 212.1411. Found: 212.1391.

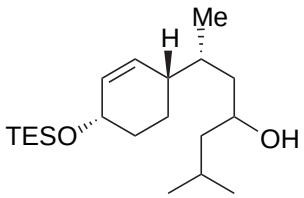


13

(3*R*)-((1*S*,4*S*)-4-hydroxycyclohex-2-enyl)butyraldehyde [(–)-13]: A solution of (–)-**9** (40 mg, 0.238 mmol) in MeOH (12 ml) in Pyrex tubes was degassed by bubbling of argon gas through the solution for 25 min. The solution was irradiated using a Rayonet Photochemical Reactor (Lamp 300 nm) for 2 h at room temperature. Then, the solution was concentrated under reduced pressure and the residue was purified by silica gel column chromatography [hexane-AcOEt (17:3~4:1 v/v)] to afford aldehyde (–)-**13** (24 mg, 60%) as a colorless oil.

$[\alpha]_D^{27}$ = –65.9° (*c* 0.35, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 9.78 (t, 1H, *J* = 2.1 Hz), 5.89 (dm, 1H, *J* = 10.1 Hz), 5.73 (dm, 1H, *J* = 10.2 Hz), 4.15 (m, 1H), 2.51 (ddd, 1H, *J* = 15.9, 4.8, 1.9 Hz), 2.33-2.19 (m, 2H), 2.08 (m, 1H), 1.85 (m, 1H), 1.72-1.61 (m, 2H), 1.54-1.47 (m, 2H), 0.96 (d, 3H, *J* = 6.8 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 202.5, 134.1, 129.8, 63.6, 48.2, 40.3, 31.6, 30.5, 19.2, 16.6.

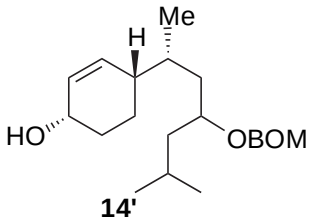
(3) Synthesis of (+)-Juvabione



14

(6*R*)-2-Methyl-6-((1*S*,4*S*)-4-triethylsiloxycyclohex-2-enyl)heptan-4-ol [14]: A stirred powder of $CeCl_3$ (1.30 g, 5.27 mmol) was heated to 140 °C under reduced pressure for 2 h and argon gas was introduced to the flask. To this dry $CeCl_3$[4] was added THF (10 ml) at 0 °C and the mixture was stirred for 12 h at room temperature. Then, 2.0 M *i*-BuMgBr in Et_2O (2.64 ml, 5.28 mmol) was added dropwisely to the suspension at –5 °C and stirring was continued for 2 h at 0 °C. To this mixture was added dropwisely a solution of aldehyde (–)-**11** (450 mg, 1.59 mmol) in THF (10 ml) at 0 °C and stirring was continued for 2 h at the same temperature. After the reaction mixture was quenched with saturated aqueous NH_4Cl, the mixture was extracted with Et_2O and washed with H_2O. The aqueous layer was extracted with Et_2O and the combined organic extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane-AcOEt

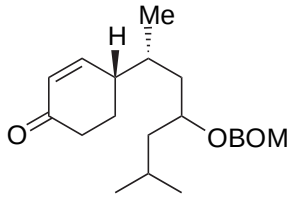
(19:1 v/v)] to afford alcohol **14** (437 mg, 81%) as a colorless oil.
IR (neat): 3350, 1648 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.73 (m, 1H), 5.65 (br t, 1H, *J* = 11.5 Hz), 4.11 (m, 1H), 3.74 (m, 1H), 2.02 (br s, 0.5H), 1.94 (br s, 0.5H), 1.82-1.20 (m, 11H), 0.98-0.87 (m, 18H), 0.60 (q, 6H, *J* = 8.0 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 134.0, 133.6, 130.2, 68.3, 67.7, 64.5, 64.4, 47.8, 47.0, 42.7, 42.5, 41.1, 39.8, 33.6, 33.0, 31.5, 24.6, 24.5, 23.5, 23.3, 22.2, 21.9, 19.5, 18.9, 16.8, 15.9, 6.8, 5.0; MS *m/z* : 340 (M^+), 238 (100%); HRMS Calcd. $C_{20}H_{40}O_2Si$: 340.2795. Found: 340.2807.



14'

(1*S*,4*S*)-4-((1*R*)-3-Benzyloxymethoxy-1,5-dimethylhexyl)cyclohex-2-enol [14']: BOMCl (1.41 ml, 10.2 mmol), *i*-Pr_2EtN (3.34 ml, 19.2 mmol) and TBAI (47 mg, 0.13 mmol) was added to a stirred solution of alcohol **14** (435 mg, 1.28 mmol) at room temperature and the mixture was stirred for 47 h at the same temperature. Then, the reaction mixture was diluted with Et_2O and washed with H_2O. The aqueous layer was extracted with Et_2O and the combined organic extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane-AcOEt (19:1~9:1 v/v)] to afford BOM ether as a colorless oil. To a solution of this BOM ether in THF (7.0 ml) was added 1.0 M TBAF in THF (3.0ml, 3.0 mmol) at room temperature and stirring was continued overnight. Then, the reaction mixture was diluted with Et_2O and washed with H_2O. The aqueous layer was extracted with Et_2O and the combined organic extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane-AcOEt (4:1 v/v)] to afford alcohol **14'** (416 mg, 94%) as a colorless oil.
IR (neat): 3410, 1645 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.35-7.27 (m, 5H), 5.84 (m, 1H), 5.70 (br t, 1H, *J* = 13.4 Hz), 4.81-4.75 (m, 2H), 4.64-4.59 (m, 2H), 4.11

(br s, 1H), 3.75 (m, 1H), 2.07 (br s, 0.5H), 2.00 (br s, 0.5H), 1.87-1.42 (m, 9.5H), 1.33-1.26 (m, 1.5H), 0.93-0.85 (m, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 137.9, 135.8, 135.7, 129.0, 128.9, 128.4, 127.8, 127.7, 127.6, 93.4, 93.1, 74.5, 74.3, 69.64, 69.61, 63.7, 44.7, 44.1, 41.1, 40.3, 39.7, 39.3, 33.2, 32.9, 30.9, 30.8, 24.6, 24.4, 23.4, 23.0, 22.8, 22.4, 18.7, 18.3, 16.2, 16.1; MS *m/z* : 328 (M^+–H_2O), 91 (100%); HRMS Calcd. $C_{22}H_{32}O_2$ (M^+–H_2O): 328.2401. Found: 328.2382.

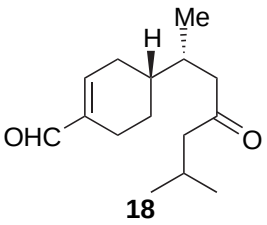


15

(4*S*)-4-((1*R*)-3-Benzyloxymethoxy-1,5-dimethylhexyl)cyclohex-2-enone

[15]: Mn_2O (1.00 g, 11.5 mmol) was added to a solution of alcohol **14'** (400 mg, 1.15 mmol) in CH_2Cl_2 (8.0 ml) and the mixture was stirred for 12 h at room temperature. Then, the reaction mixture was filtered through a Celite pad eluting with Et_2O, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane-AcOEt (9:1 v/v)] to afford enone **15** (389 mg, 98%) as a colorless oil.

IR (neat): 1683 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.35-7.27 (m, 5H), 6.81 (d, 0.5H, *J* = 10.5 Hz), 6.74 (d, 0.5H, *J* = 10.5 Hz), 6.02 (d, 0.5H, *J* = 10.0 Hz), 5.99 (d, 0.5H, *J* = 10.2 Hz), 4.82-4.76 (m, 2H), 4.68-4.59 (m, 2H), 3.75 (br t, 1H, *J* = 6.0 Hz), 2.52-2.28 (m, 3H), 1.99-1.25 (m, 8H), 0.94-0.89 (m, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 199.95, 199.86, 155.0, 154.8, 137.82, 137.80, 129.9, 129.8, 128.5, 128.4, 127.7, 127.65, 127.63, 93.32, 93.28, 74.4, 74.2, 69.7, 69.6, 44.6, 44.1, 41.7, 40.7, 39.7, 39.2, 37.5, 37.4, 33.0, 32.8, 24.7, 24.5, 24.3, 23.7, 23.3, 23.1, 22.7, 22.5, 16.5, 16.2; MS *m/z* : 344 (M^+), 91 (100%); HRMS Calcd. $C_{22}H_{32}O_3$: 344.2350. Found: 344.2336.



18

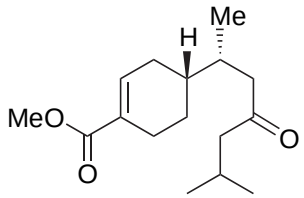
(4*R*)-4-((1*R*)-1,5-Dimethyl-3-oxohexyl)cyclohex-1-enecarbaldehyde [(+)-18]: 1.6 M *n*-BuLi in hexane (1.60 ml, 2.56 mmol) was added to a suspension of Ph_3PCH_2OMeCl (880 mg, 2.57 mmol) in THF (5.0 ml) at –10 °C and the mixture was stirred for 30 min at the same temperature. Then, to this mixture was added dropwisely a solution of enone **15** (295 mg, 0.856 mmol) in THF (5.0 ml) at –30 °C and stirring was continued for 2 h at the same temperature. After the reaction mixture was quenched with saturated aqueous NH_4Cl, the mixture was extracted with Et_2O and washed with H_2O. The aqueous layer was extracted with Et_2O and the combined organic extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane-AcOEt (97:3 v/v)] to afford corresponding methyl dienol ether as a pale yellow oil and this product was immediately used for the next transformation. To a solution of this methyl dienol ether in THF (10 ml) was added 10% aq. HCl (10 ml) and the mixture was stirred for 2 days at room temperature. After neutralization with 3 N aq. NaOH, the reaction mixture was extracted with AcOEt. The aqueous layer was extracted with AcOEt and the combined organic solution was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane-AcOEt (4:1 v/v)] to afford hydroxy-α, β-unsaturated aldehyde **17** as a colorless oil. Dess-Martin periodinane (1.09 g, 2.57 mmol) was added to a solution of this hydroxyaldehyde **17** in CH_2Cl_2 (5.0 ml) at room temperature and the mixture was stirred for 1 h at the same temperature. Then, the reaction mixture was diluted with Et_2O, filtered through a Celite pad, and the organic solution was washed with saturated aqueous $NaHCO_3$ and H_2O. The aqueous layer was extracted with Et_2O and the combined organic solution was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane-AcOEt (9:1 v/v)] to afford keto-aldehyde (+)-**18**

(103 mg, 51%) as a colorless oil.

(Alternative method of oxidation): 1-Me-AZADO[2] (0.77 mg, 4.6 μmol) and BAIB (50 mg, 0.155 mmol) were added to a solution of hydroxyaldehyde **17** (22.0 mg, 0.0923 mmol) in CH_2Cl_2 (1.0 ml) at room temperature and the mixture was stirred for 7.5 h at the same temperature. Then, the reaction mixture was quenched with aqueous Na_2SO_3, extracted with Et_2O, and washed with saturated aqueous $NaHCO_3$ and H_2O. The aqueous layer was extracted with Et_2O and the combined organic solution was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane-AcOEt (19:1~9:1 v/v)] to afford keto-aldehyde (+)-**18** (20.4 mg, 94%) as a colorless oil.

$[\alpha]_D^{27}$ = +95.5° (*c* 0.79, $CHCl_3$); IR (neat): 1710, 1684, 1645 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 9.42 (s, 1H), 6.79 (m, 1H), 2.51-1.98 (m, 8H), 2.28 (d, 2H, *J* = 7.1 Hz), 1.82 (m, 1H), 1.54 (m, 1H), 1.20 (m, 1H), 0.92 (d, 3H, *J* = 6.8 Hz), 0.915 (d, 3H, *J* = 7.1 Hz), 0.90 (d, 3H, *J* = 7.0 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 210.4, 193.9, 150.8, 141.5, 52.5, 47.8, 38.3, 32.5, 30.5, 24.6, 23.8, 22.6, 22.5, 21.8, 16.3; MS *m/z* : 236 (M^+), 136 (100%); HRMS Calcd. $C_{15}H_{24}O_2$: 236.1775. Found: 236.1758.

These spectral data were identical with those reported.[5]



(+)-Juvabione (**4**)

(4*R*)-4-((1*R*)-1,5-Dimethyl-3-oxohexyl)cyclohex-1-enecarboxylic acid methyl ester [(+)-Juvabione] [(+)-4]: To a solution of α, β-unsaturated aldehyde (+)-**18** (25.0 mg, 0.106 mg) in MeOH (4.0 ml) was added NaCN (39 mg, 0.796 mmol), MnO_2 (276 mg, 3.17 mmol), and AcOH (ca. 20 mg) at room temperature and the mixture was stirred for 24 h at the same temperature. Then, the reaction mixture was diluted with Et_2O, filtered through a Celite pad, and the organic solution was washed with 0.2 N aq. NaOH and H_2O. The aqueous layer was extracted with Et_2O and the combined organic solution was

washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane-AcOEt (19:1 v/v)] to afford (+)-Juvabione [(+)-**4**] (22 mg, 78%) as a colorless oil.
$[\alpha]_D^{27}$ = +69.1° (*c* 1.00, benzene). [lit.[6] $[\alpha]_D^{25}$ = +66.9° (*c* 2.57, benzene)]; IR (neat): 1714, 1652 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.95 (m, 1H), 3.72 (s, 3H), 2.48 (m, 1H), 2.44 (dd, 1H, *J* = 16.2, 4.7 Hz), 2.27 (d, 2H, *J* = 7.1 Hz), 2.27-1.89 (m, 6H), 1.80 (m, 1H), 1.44 (m, 1H), 1.21 (m, 1H), 0.92 (d, 3H, *J* = 6.6 Hz), 0.91 (d, 3H, *J* = 6.6 Hz), 0.88 (d, 3H, *J* = 6.8 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 210.6, 167.8, 139.3, 130.2, 52.5, 51.5, 47.8, 37.7, 32.6, 29.7, 24.8, 24.7, 24.5, 22.6, 22.5, 16.5; MS *m/z* : 266 (M^+), 134 (100%); HRMS Calcd. $C_{16}H_{26}O_3$: 266.1881. Found: 266.1888.
These spectral data were identical with those reported.[6]

3. References

(1) (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4156. (b) Ireland, R. E.; Liu, L. *J. Org. Chem.* **1993**, *58*, 2899.

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(3) (a) Itagaki, N.; Sugahara, T.; Iwabuchi, Y. *Org. Lett.* **2005**, *7*, 4181. (b) Itagaki, N.; Kimura, M.; Sugahara, T.; Iwabuchi, Y. *Org. Lett.* **2005**, *7*, 4185.

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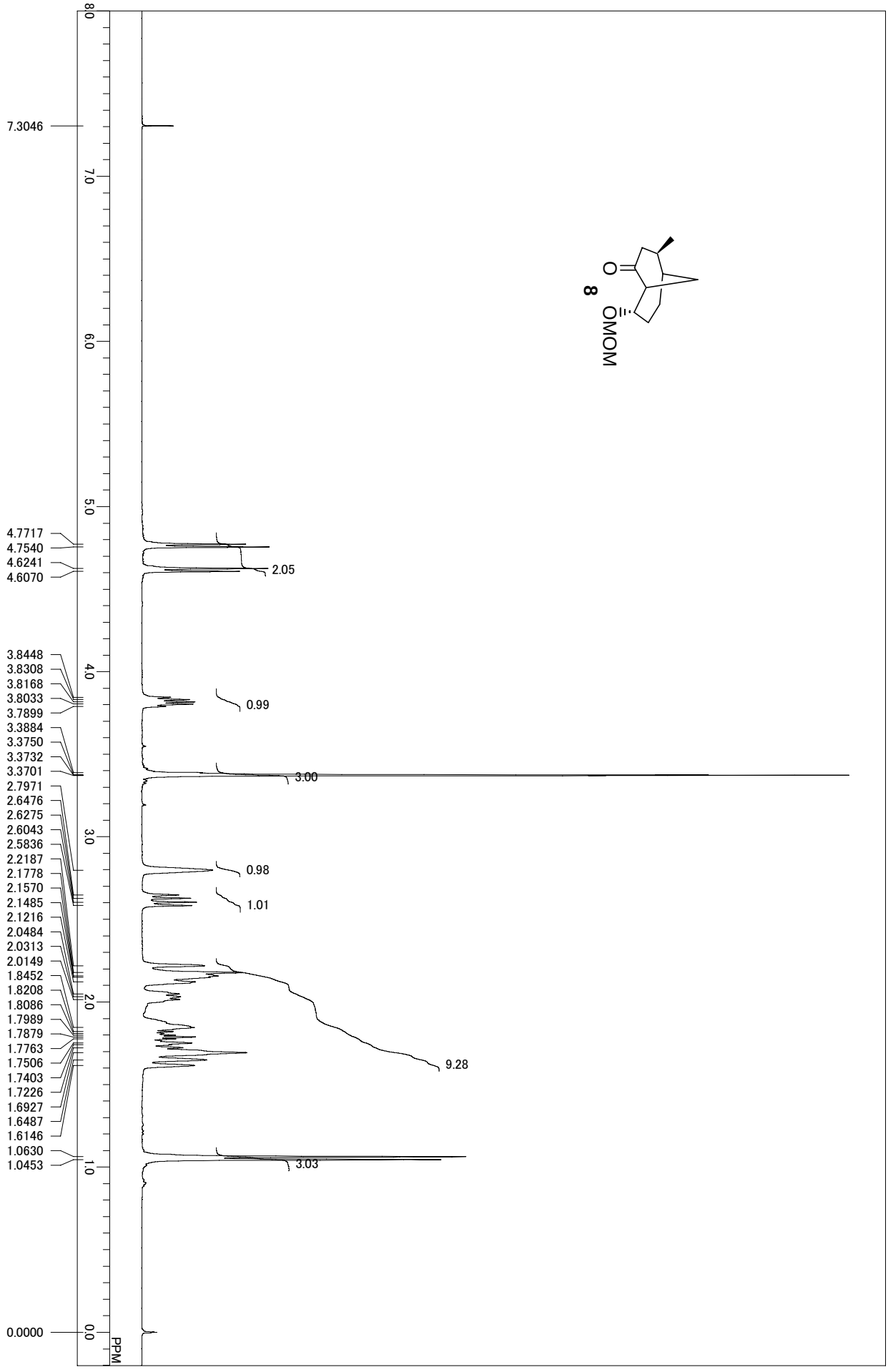
(6) Bergner, E. J.; Helmchen, G. *J. Org. Chem.* **2000**, *65*, 5072.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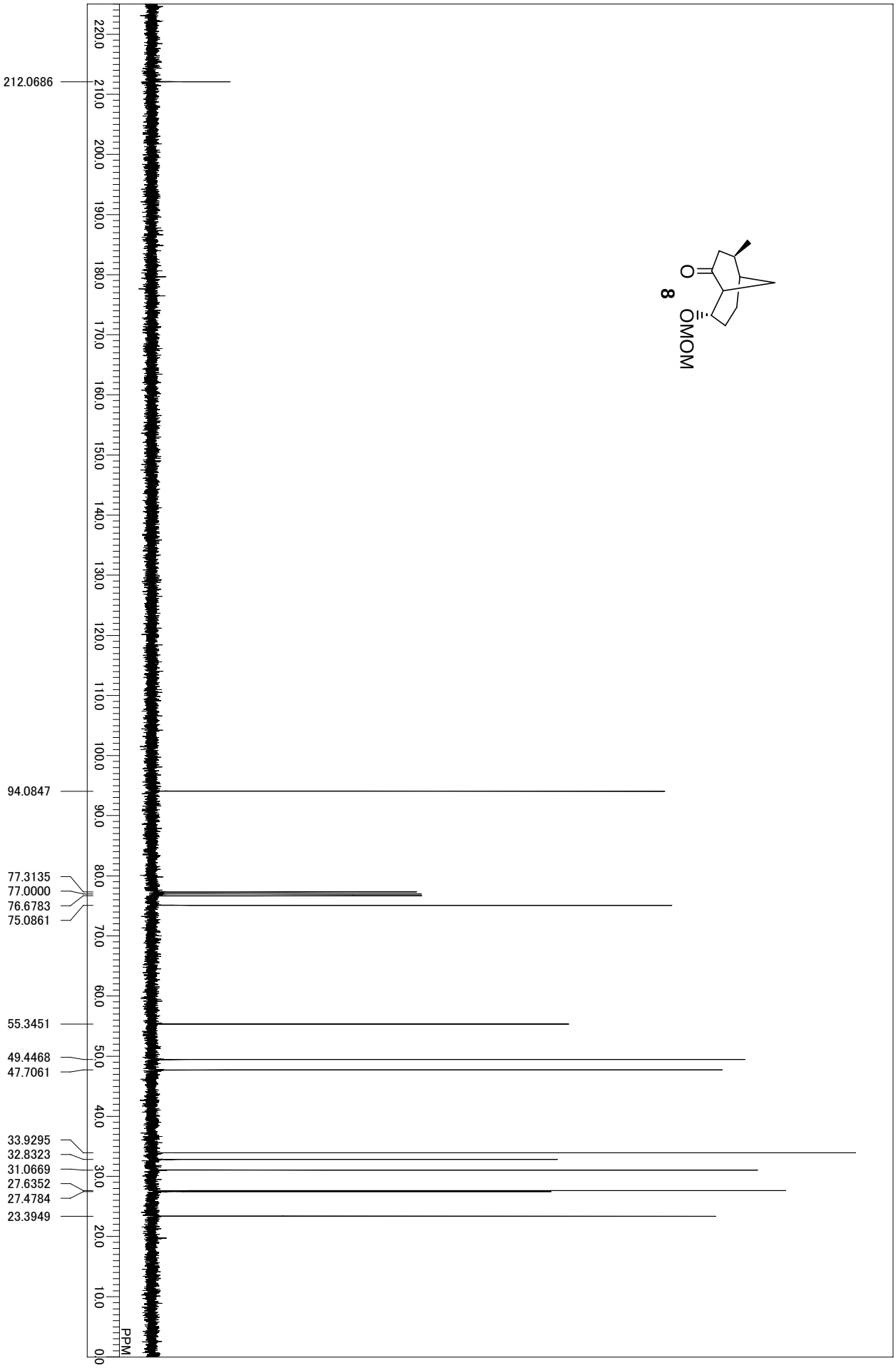
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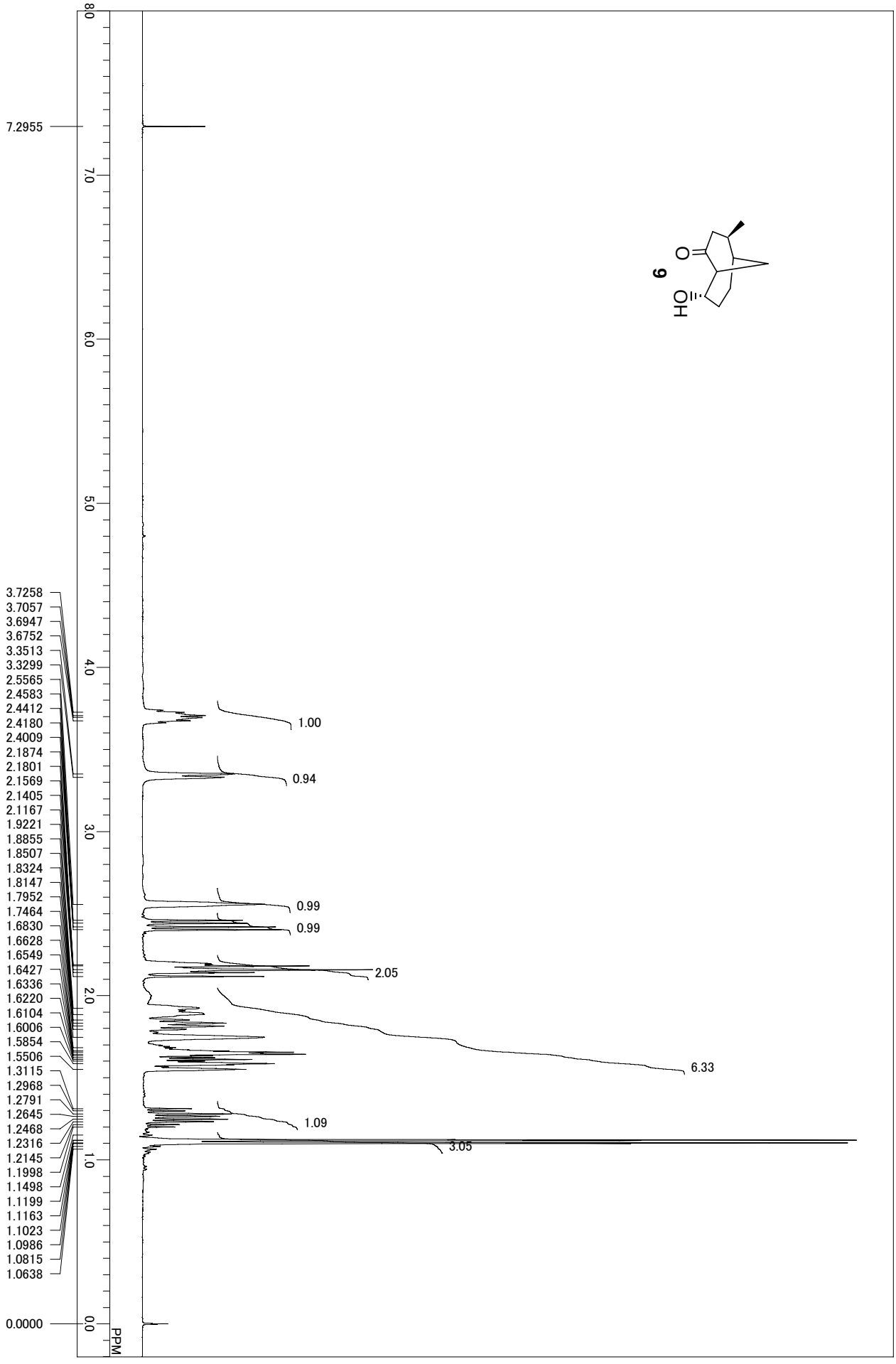
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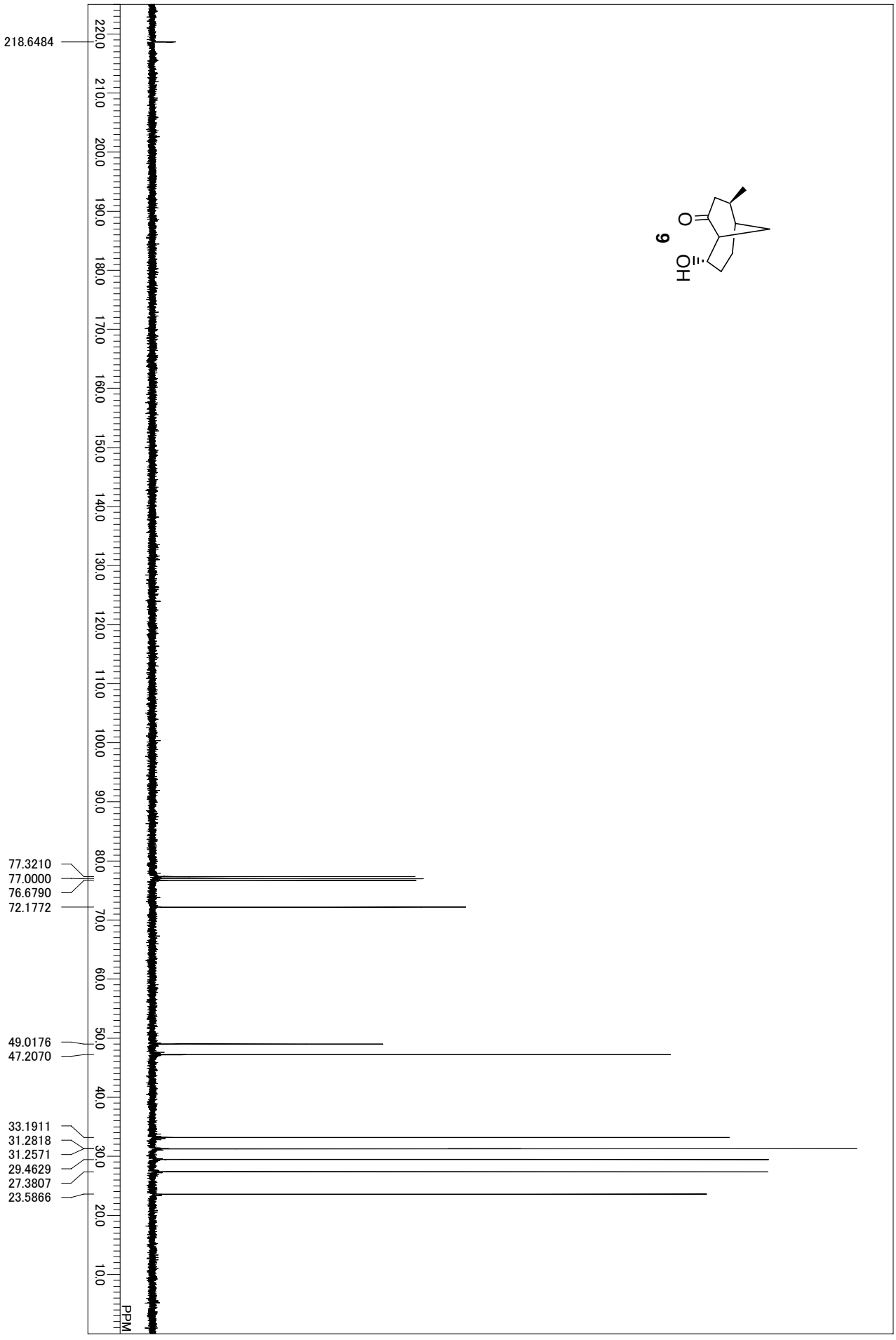
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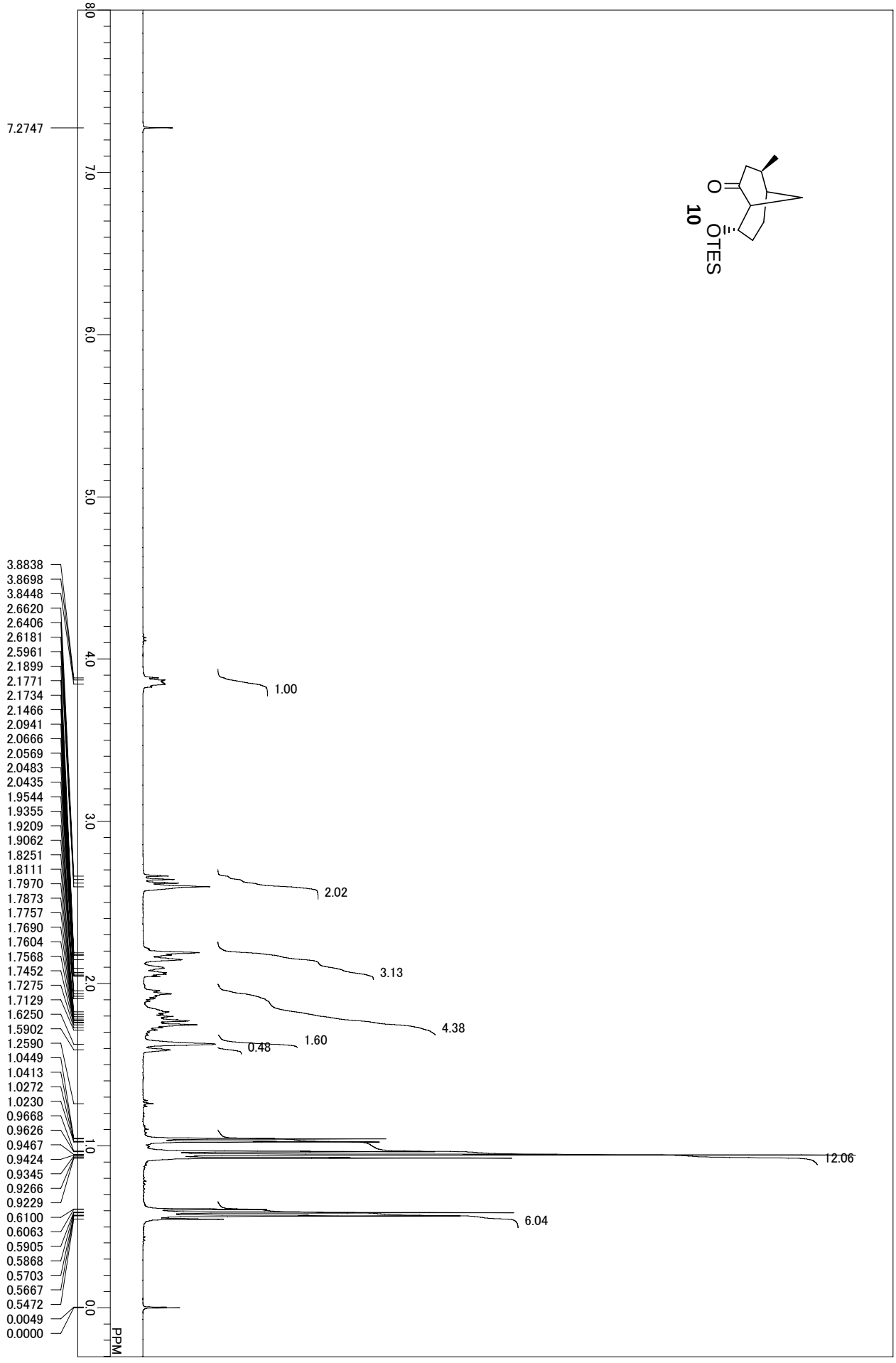
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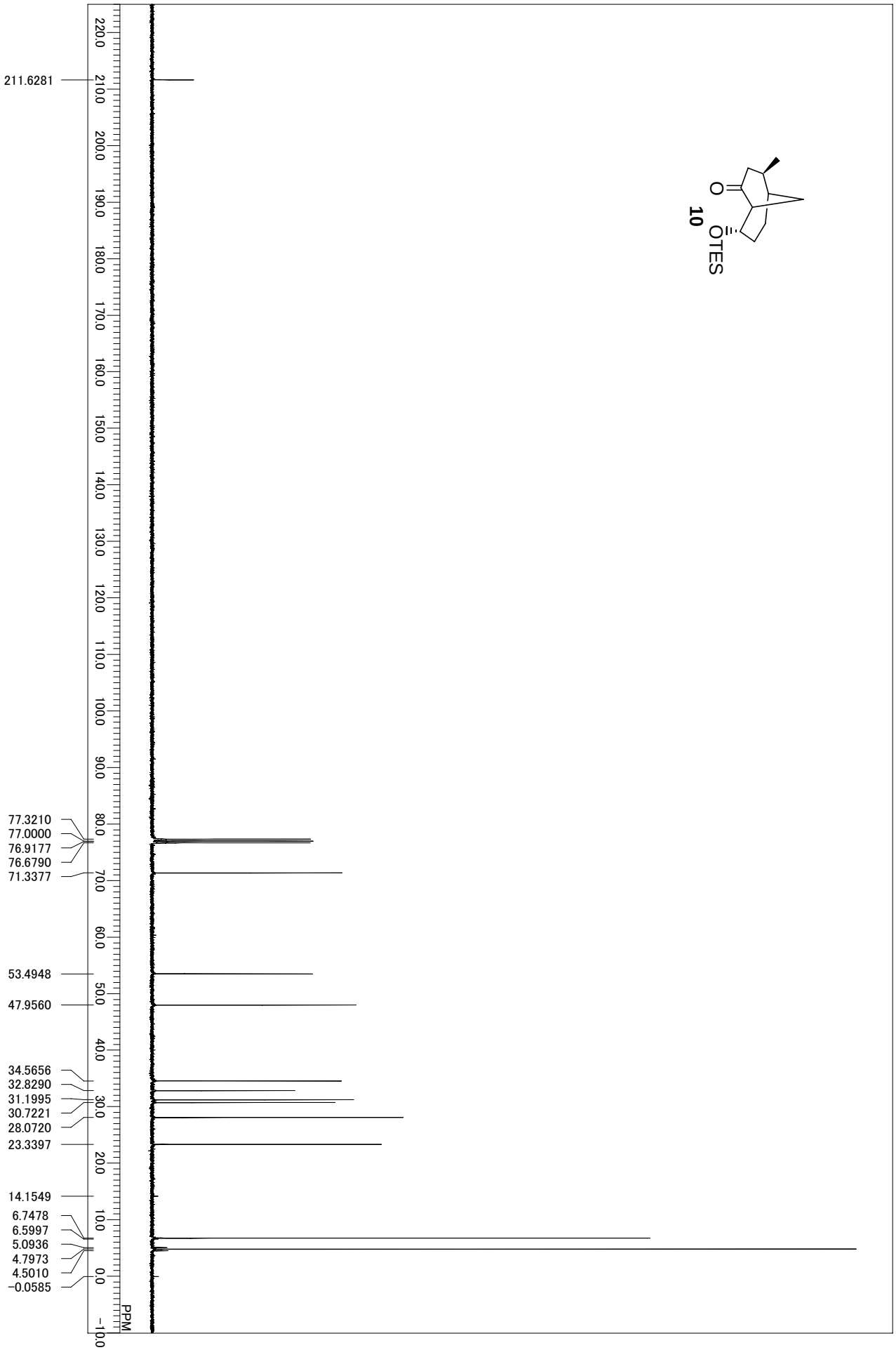
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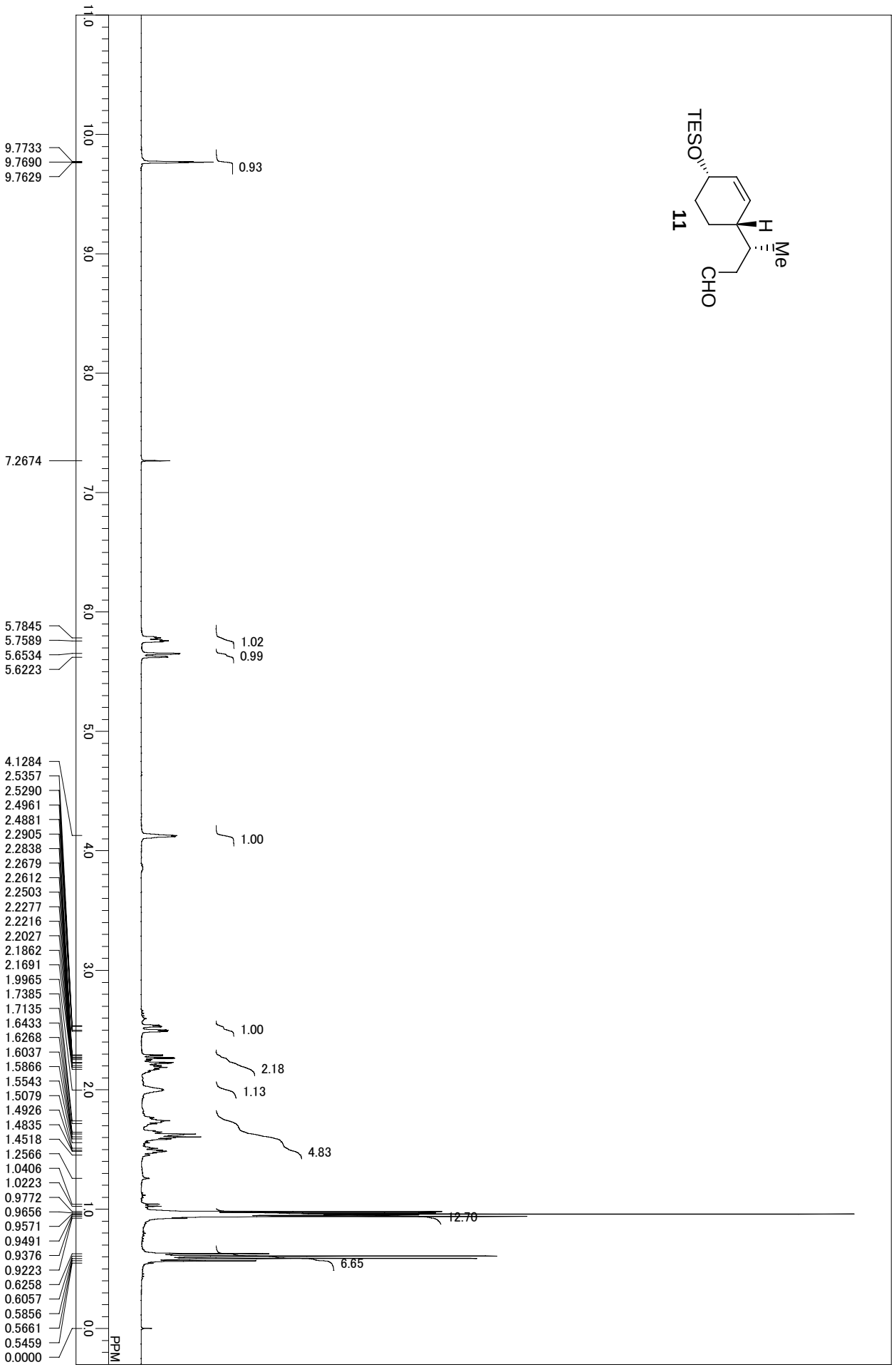
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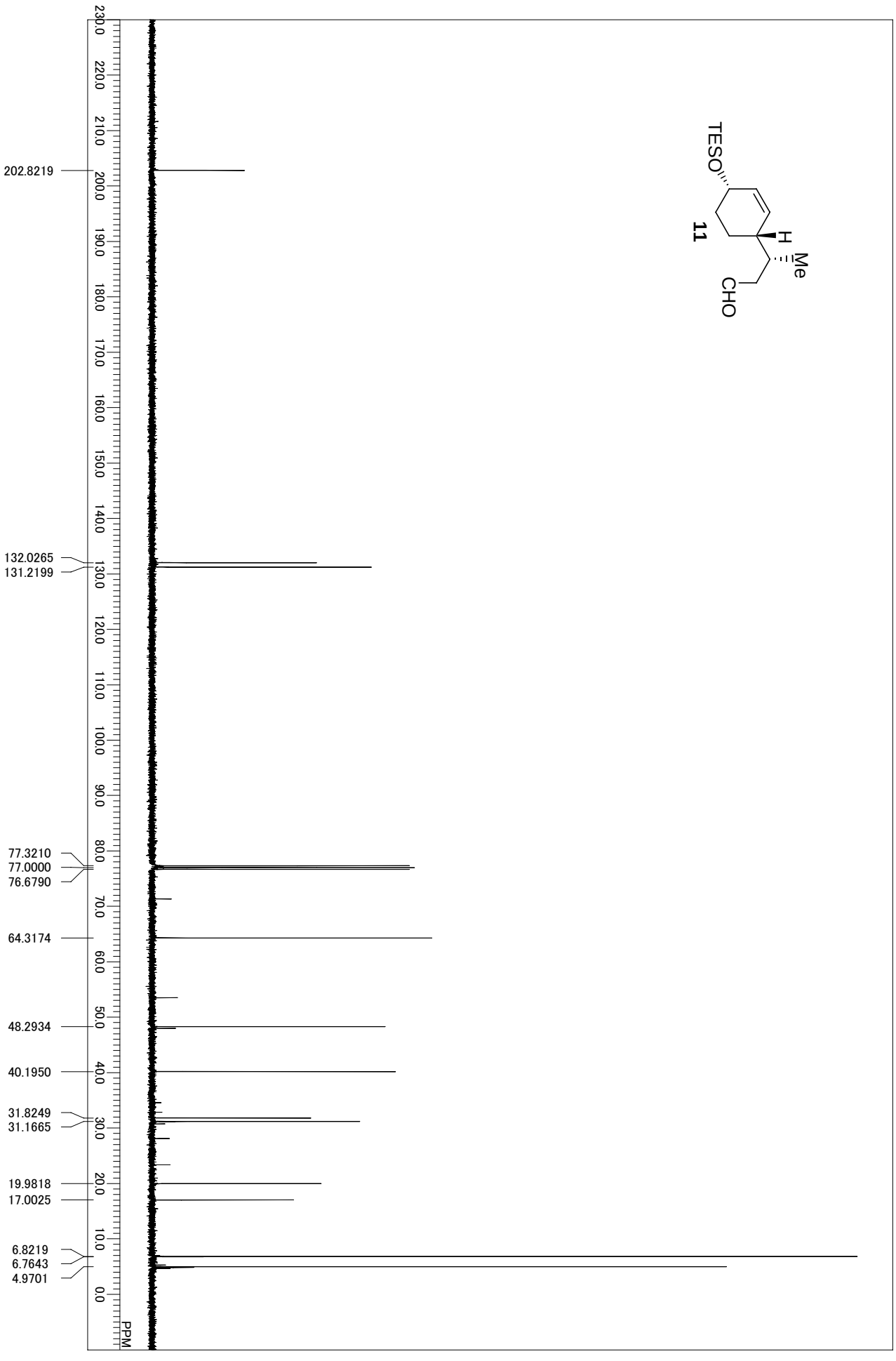
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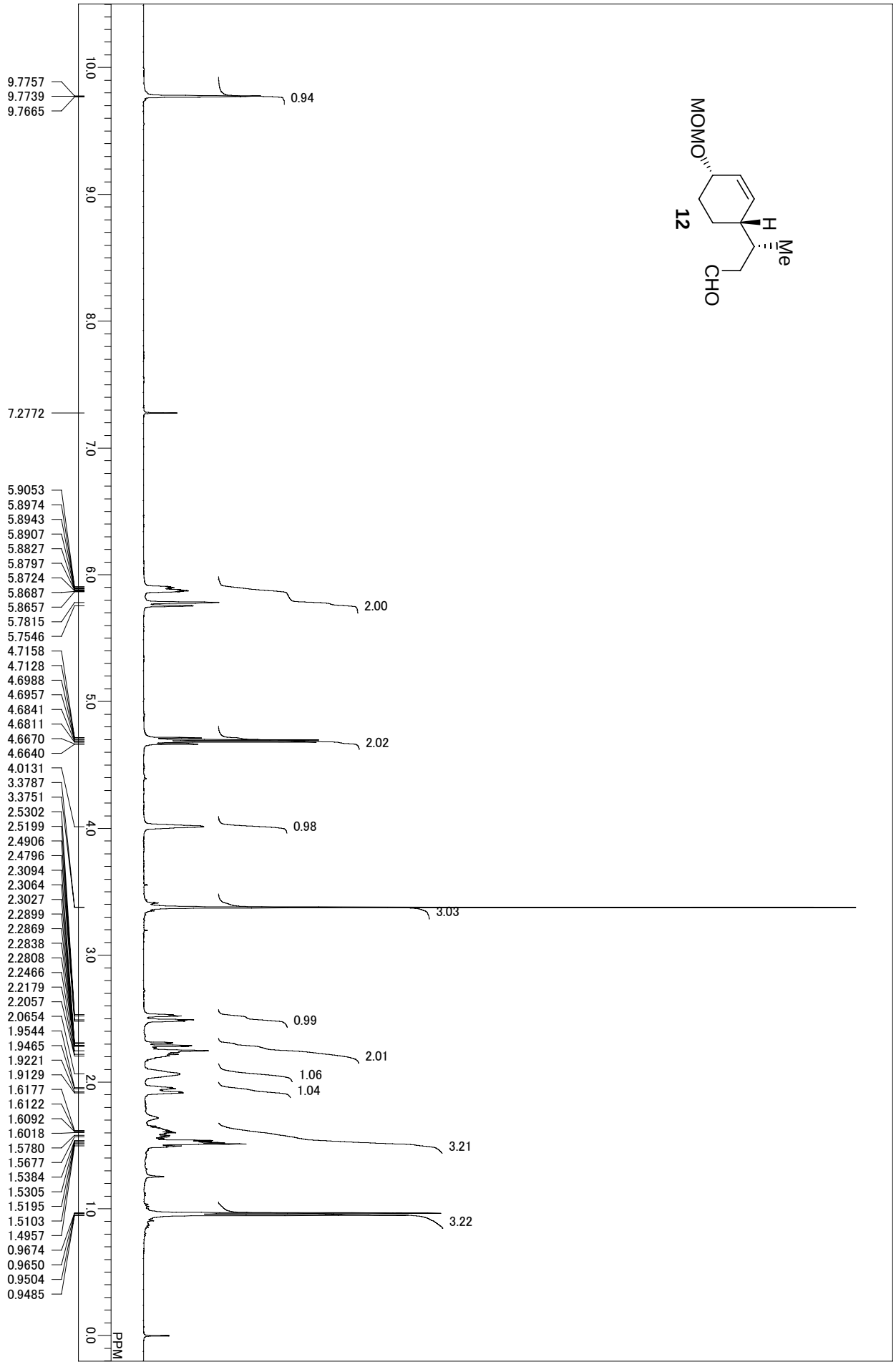
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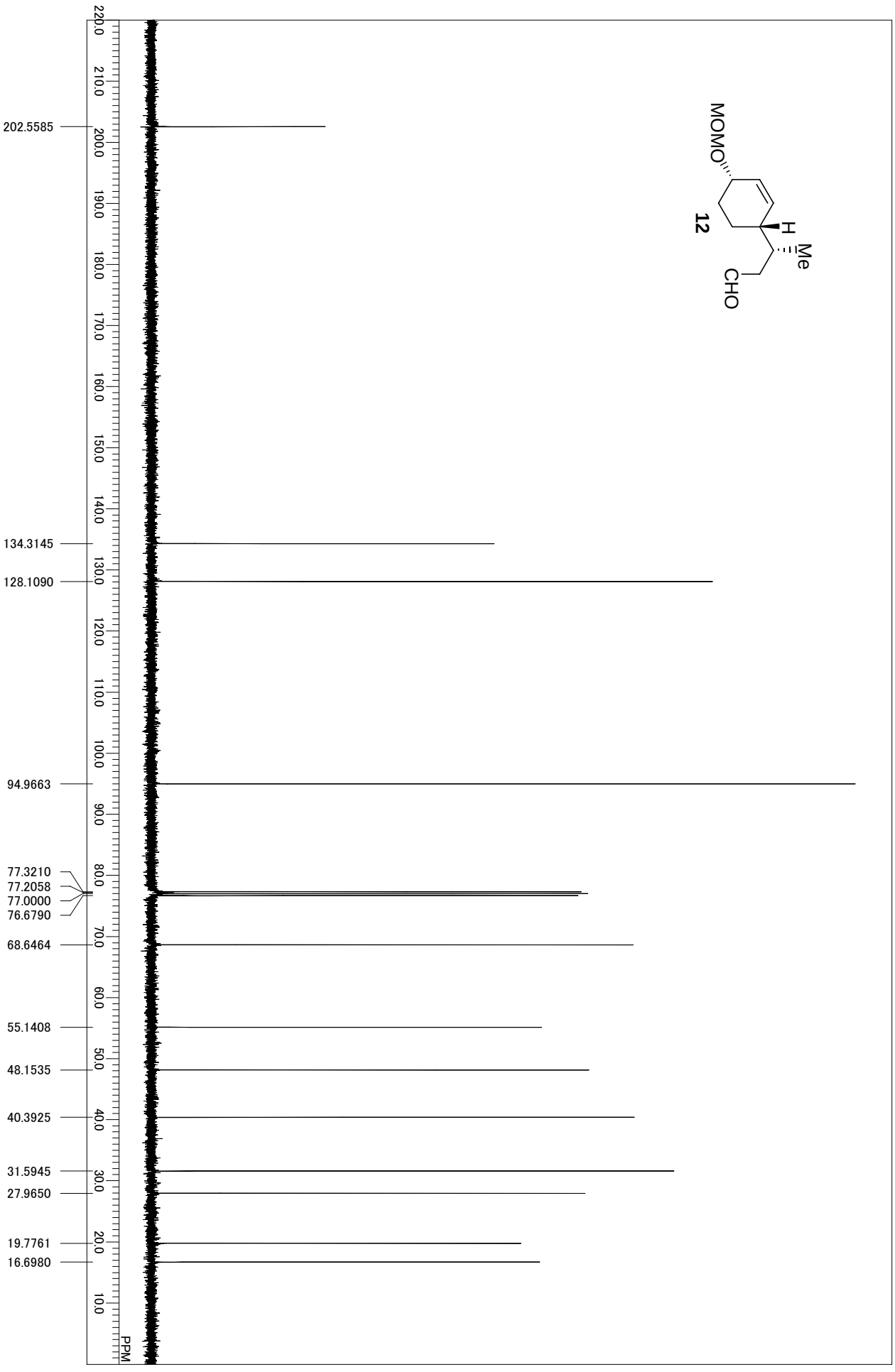
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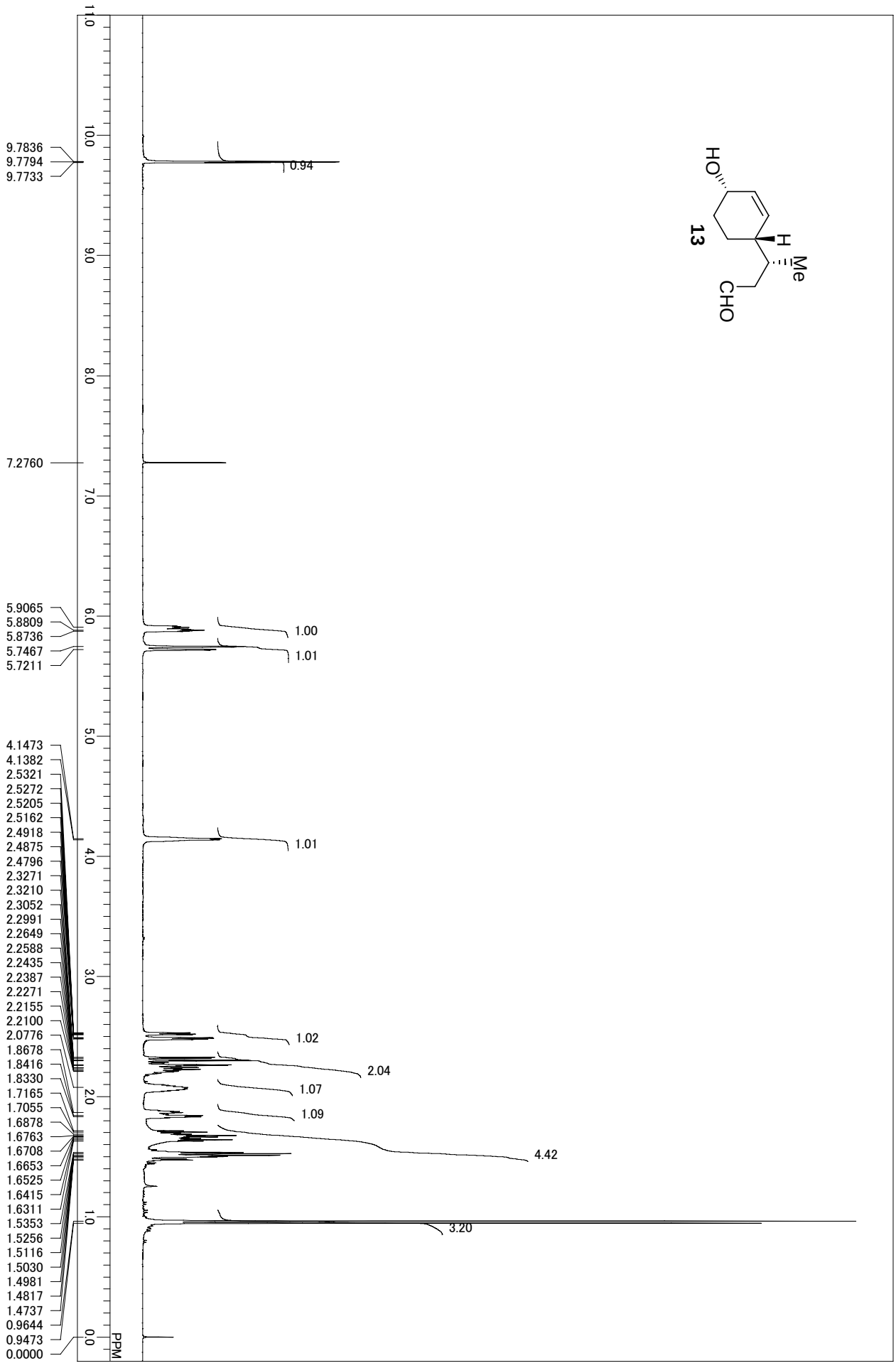
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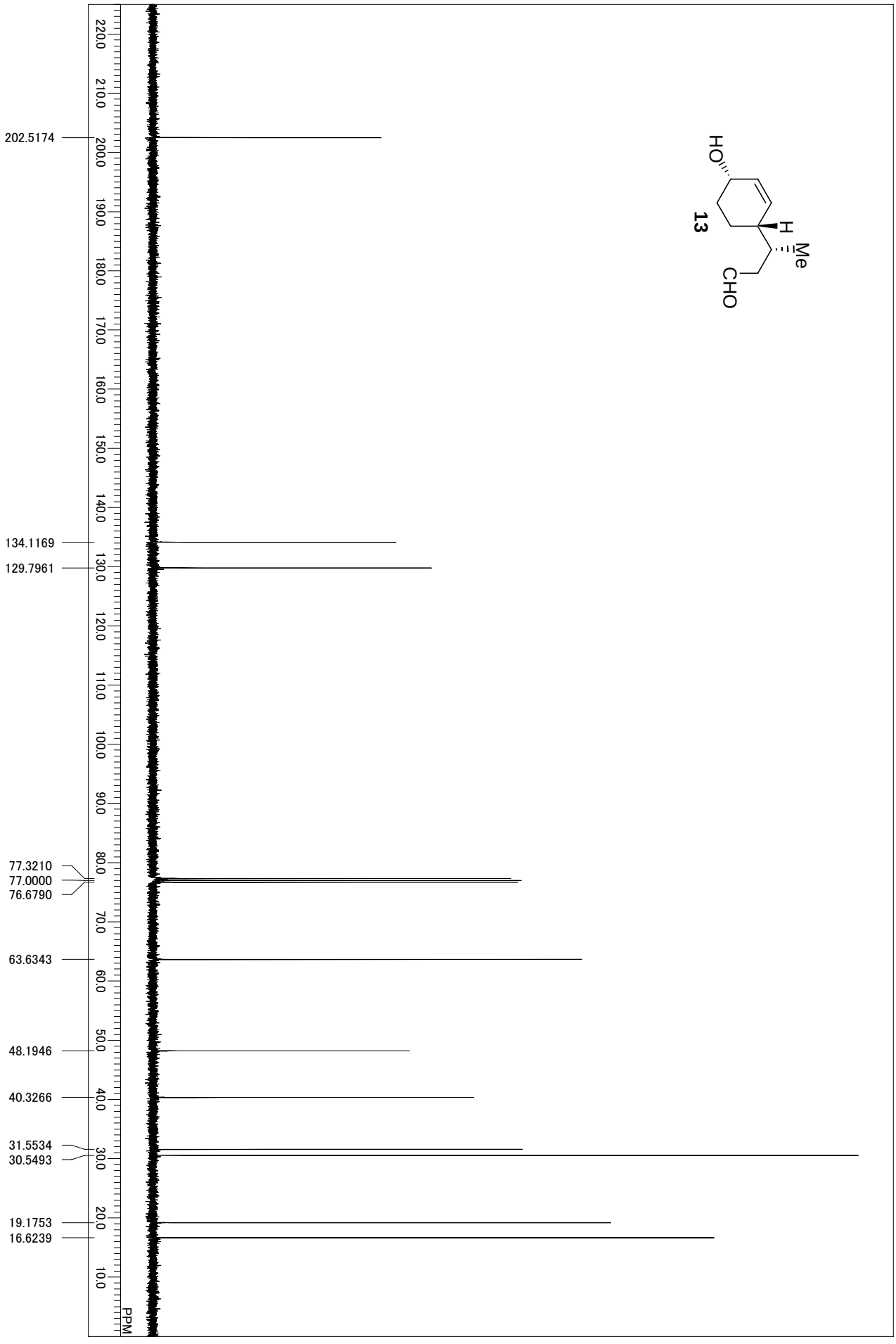
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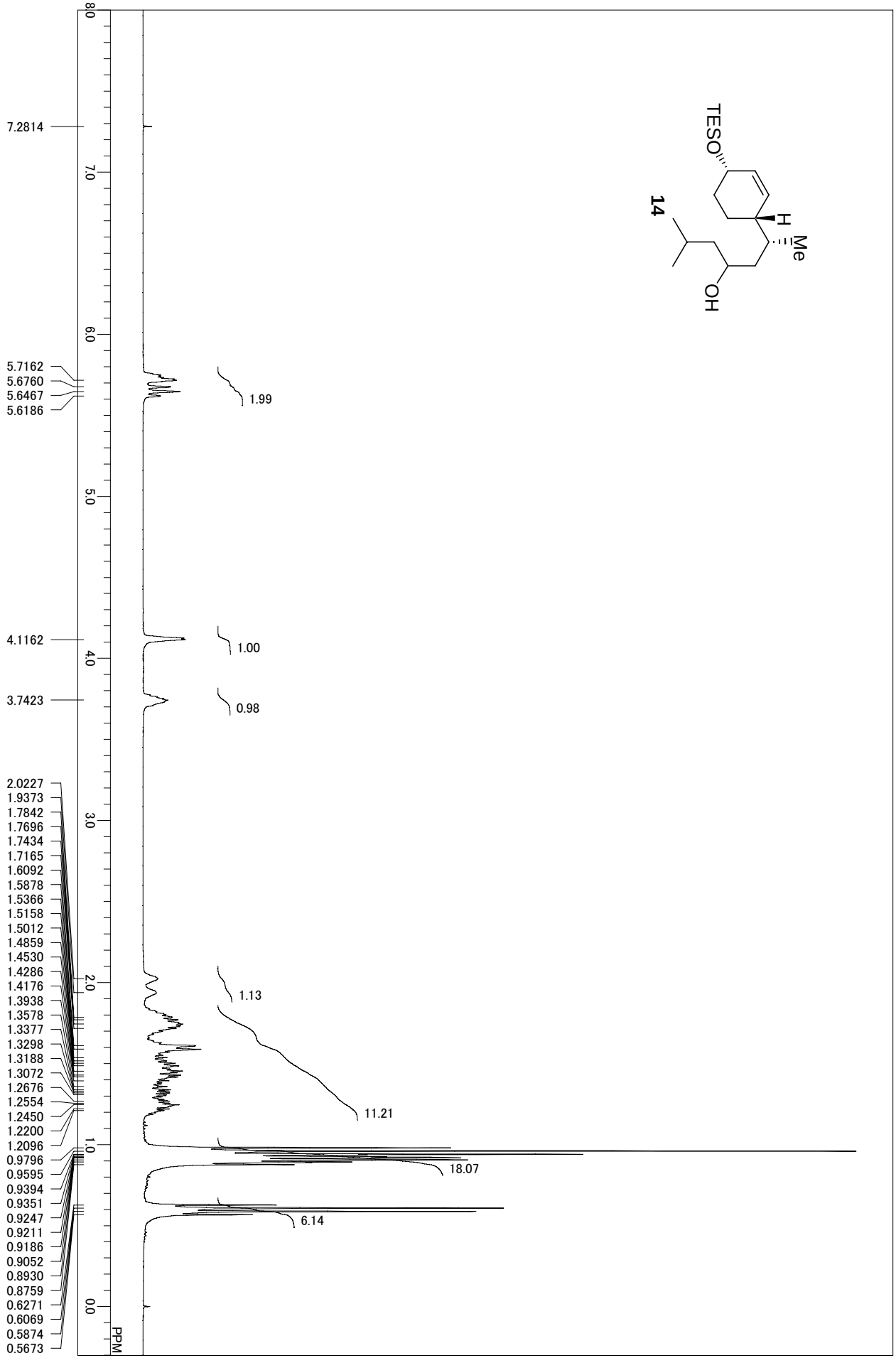
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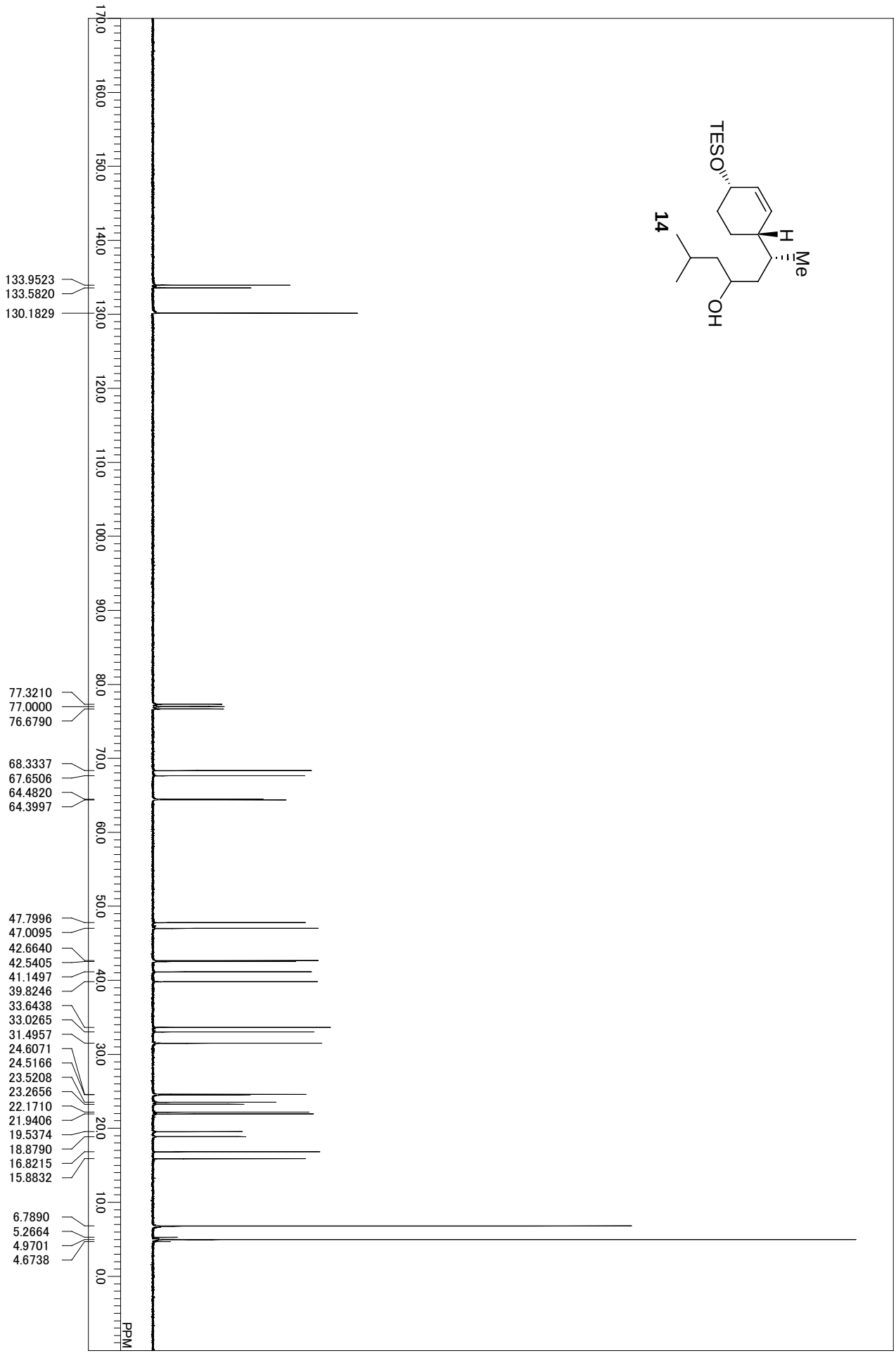
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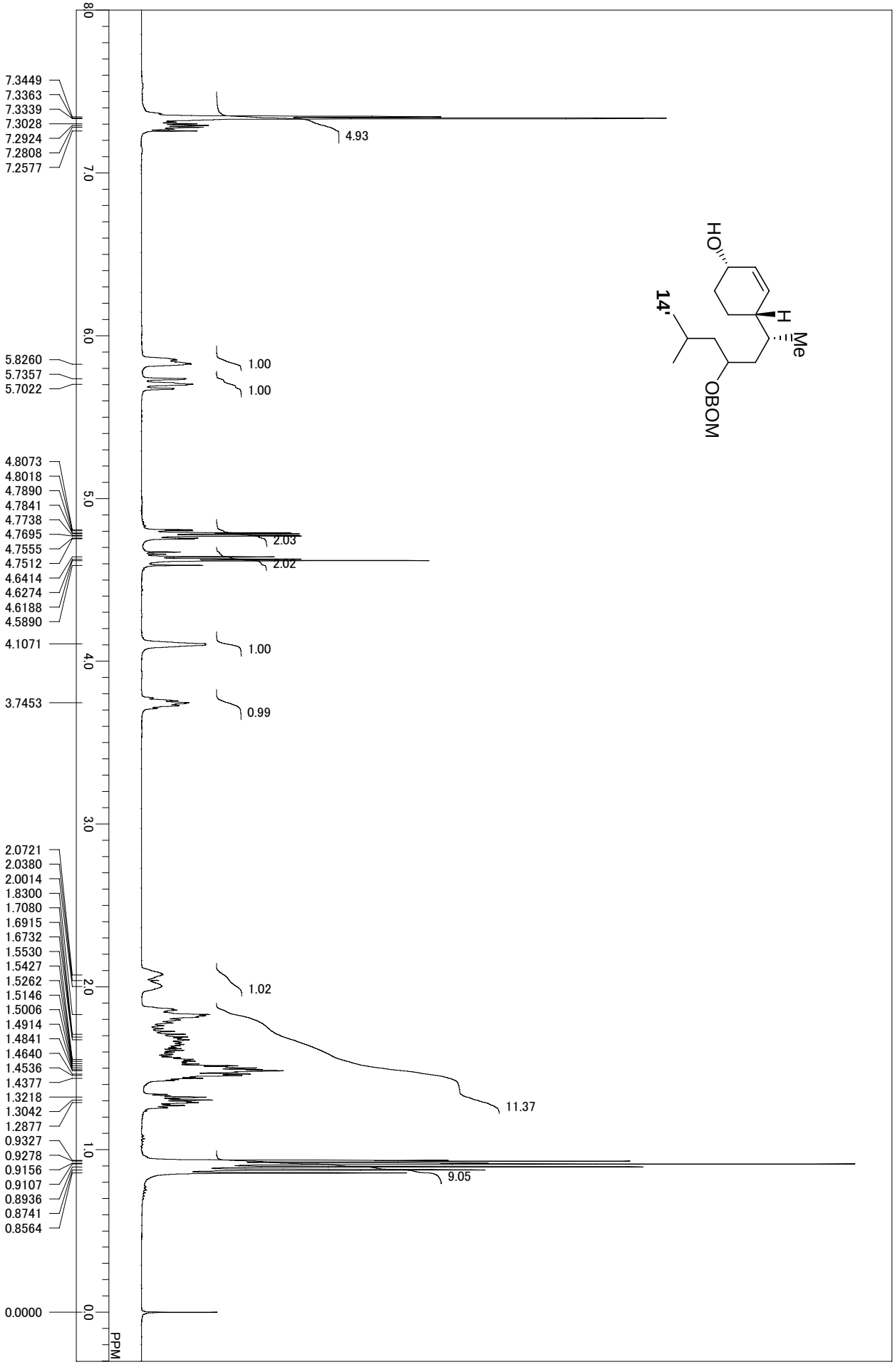
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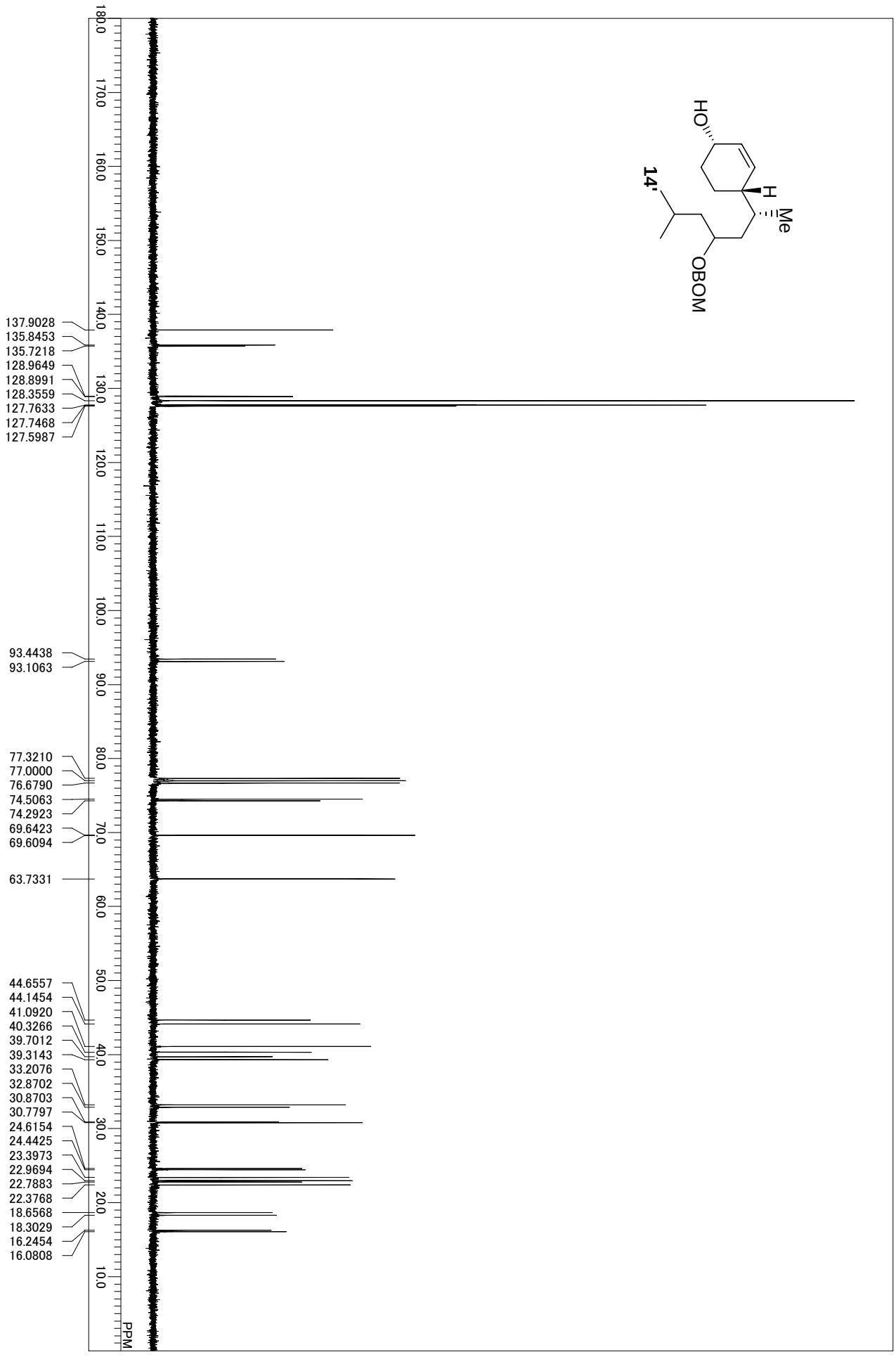
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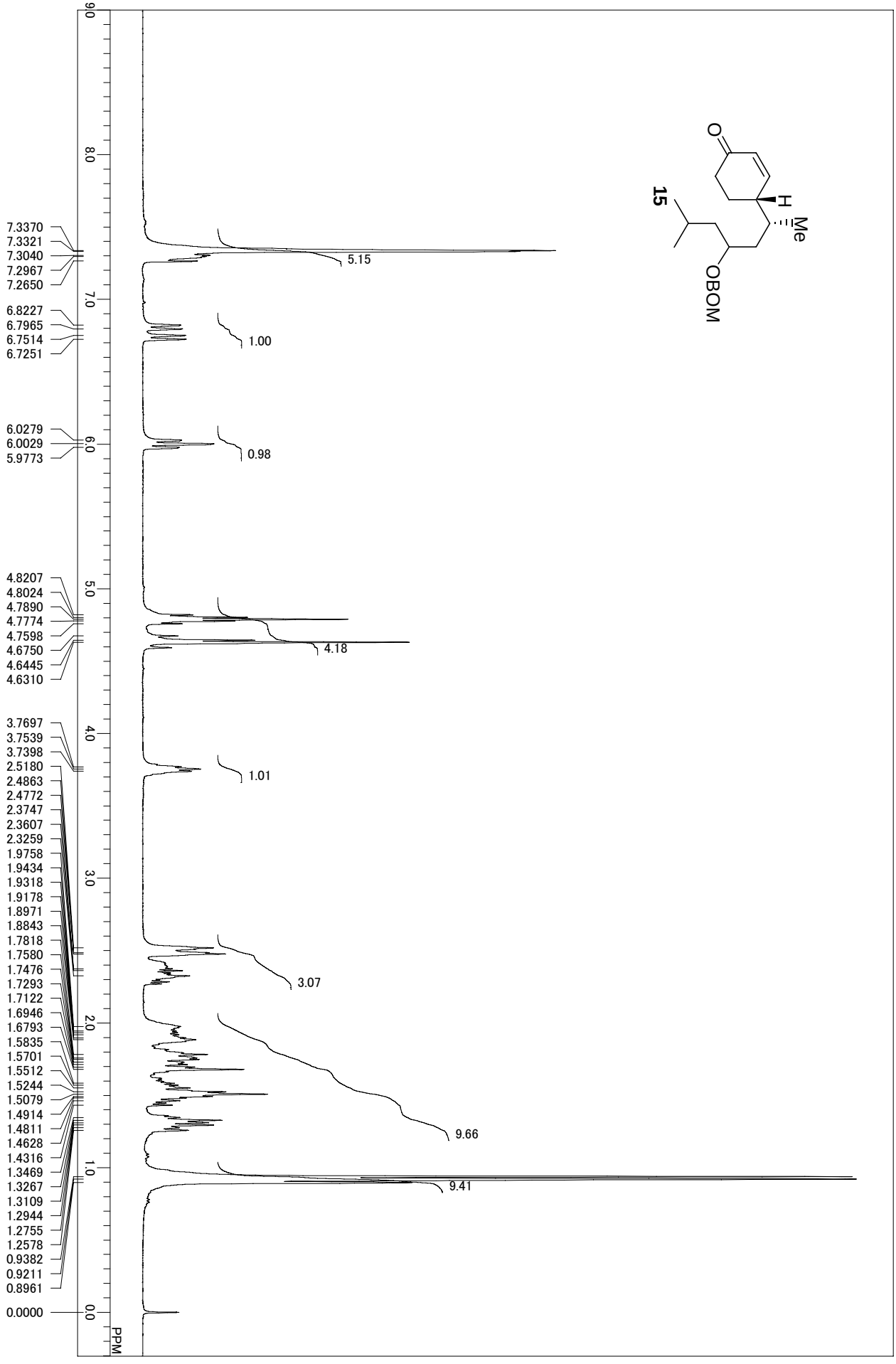
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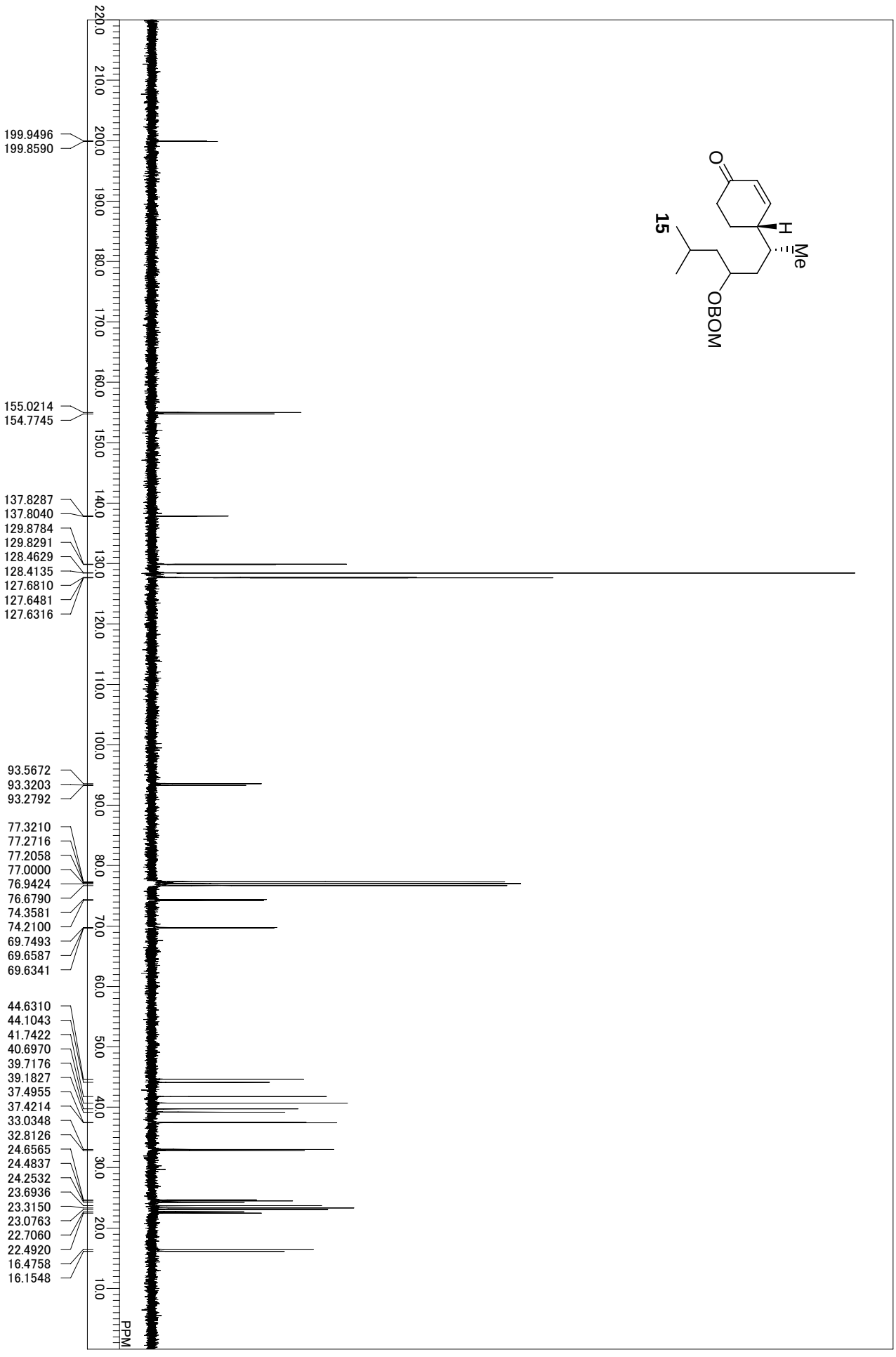
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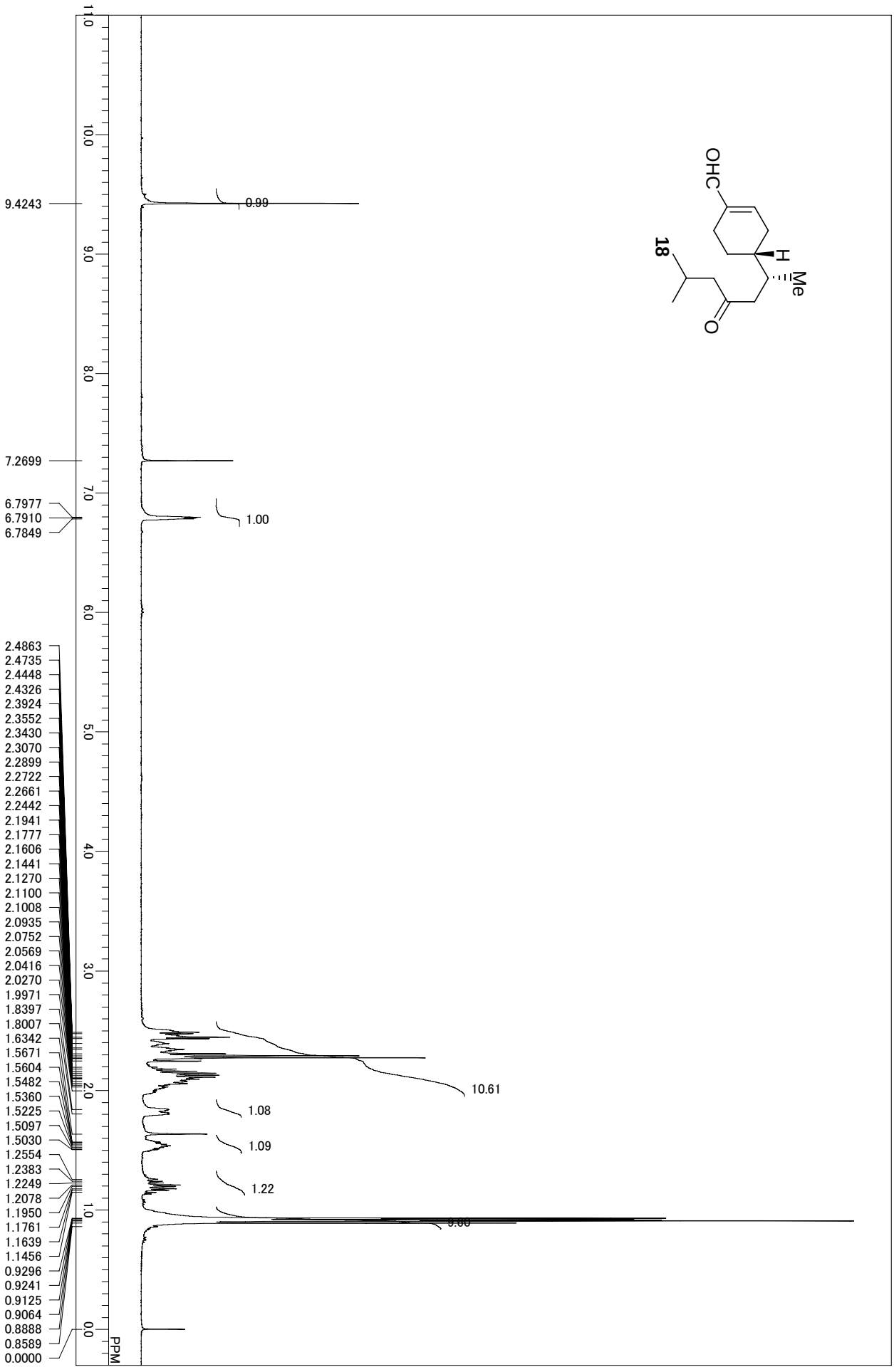
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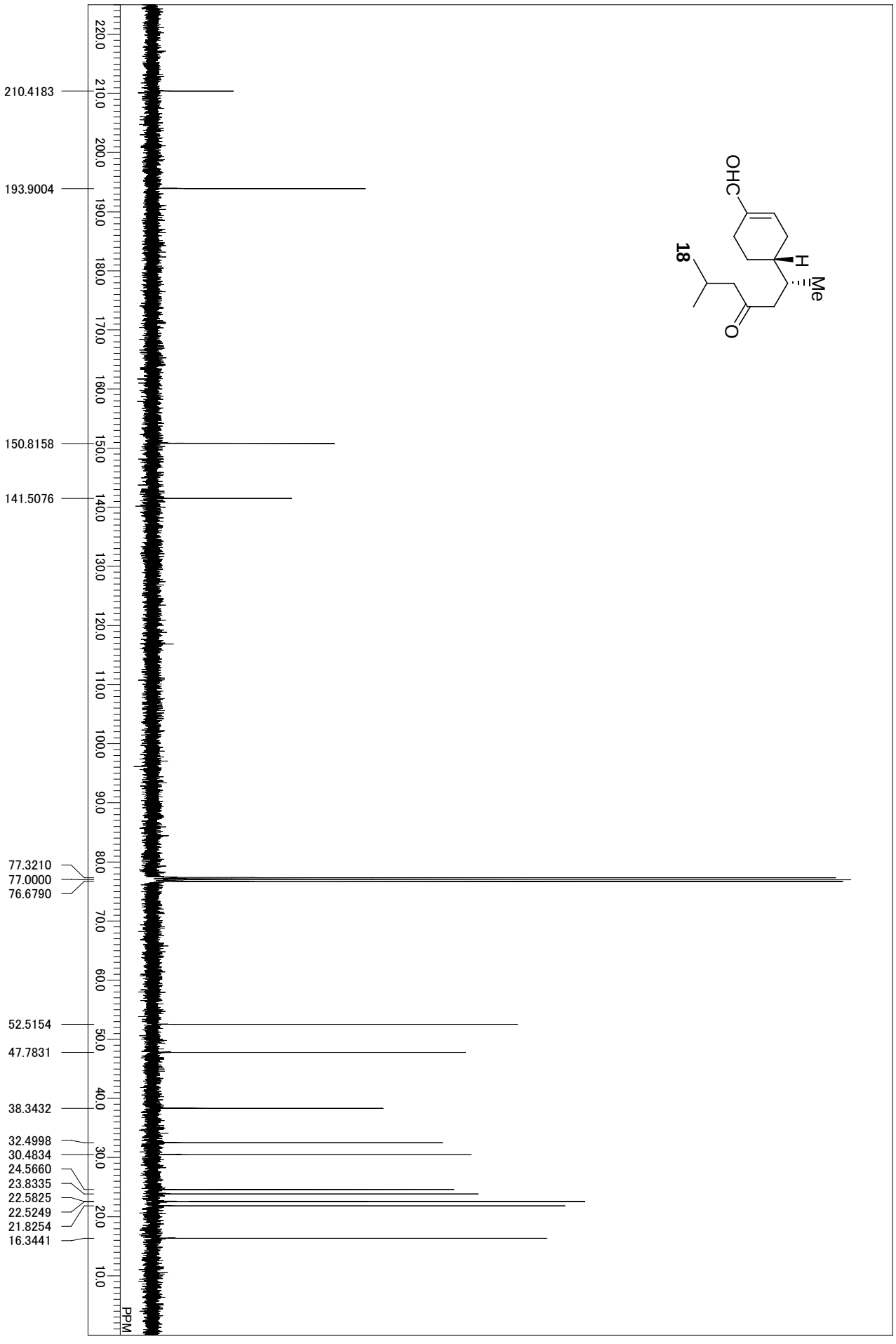
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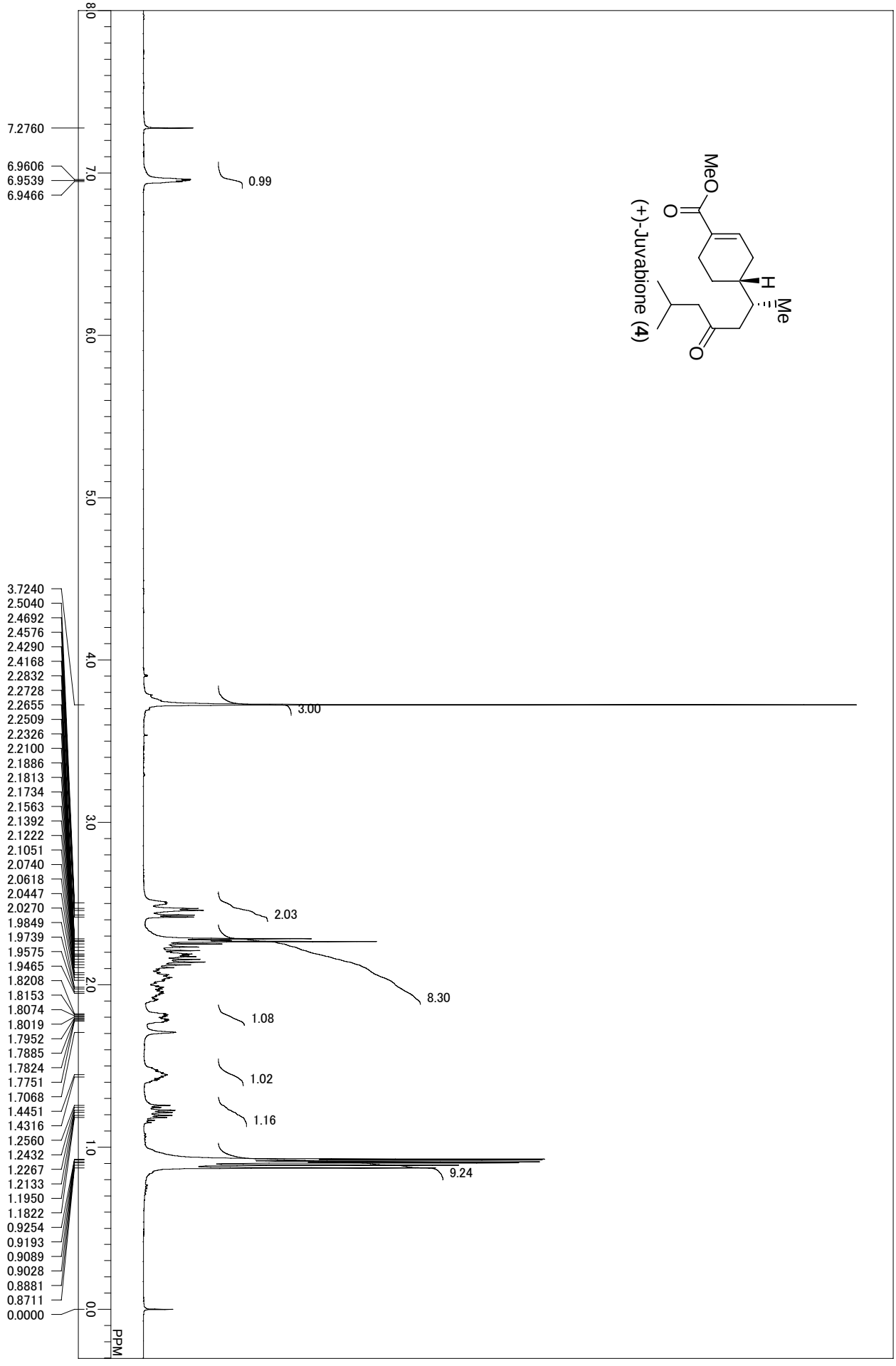
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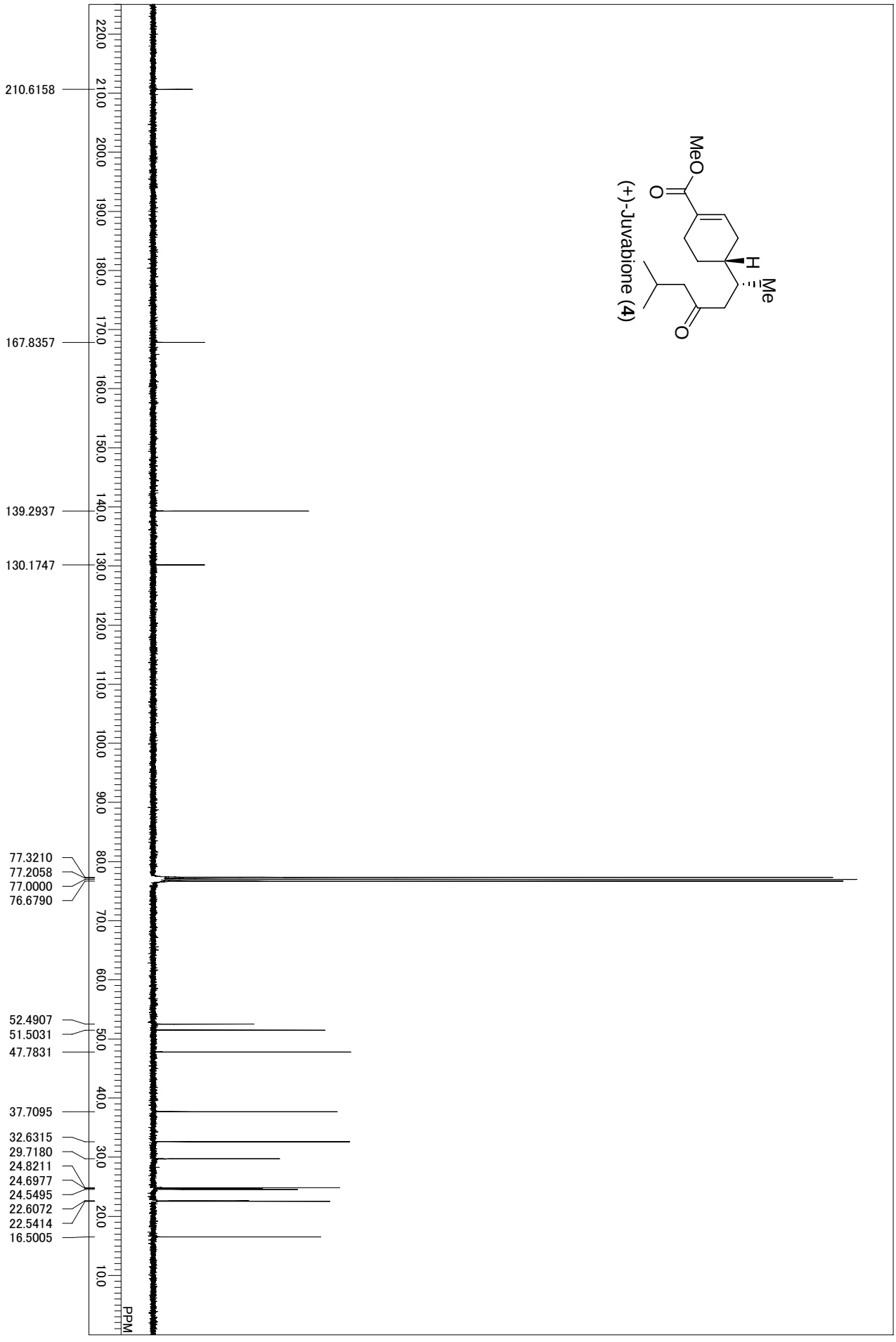
(+)-Juvabione (4)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PPM
MeO
O
H
Me
O
(+)-Juvabione (4)