Electronic Supporting information

A straightforward and efficient synthetic access to biologically active marine sesterterpenoids, sesterstatin 4 and 5

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Melting points were obtained in open capillary tubes using a micro melting point apparatus SGW X-4, which were uncorrected.

Mass spectra were recorded by the HP5989A service; HRMS (EI) spectra were obtained on a Finigann MAT8401 instrument.

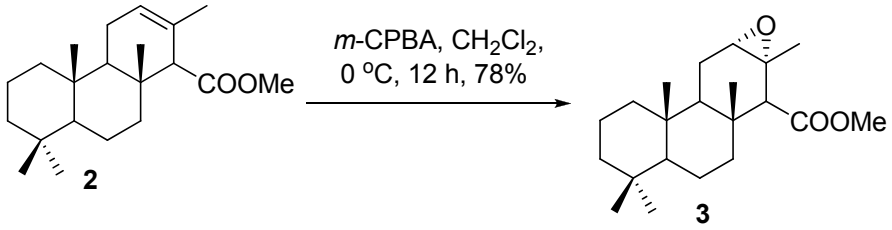
Optical rotations were measured on a AUTOPOLO III polarimeter operating at the sodium D line (589 nm) and are reported as follows: $[a]_D^T$, concentration (g/100 ml), and solvent.

^{1}H nuclear magnetic resonance (NMR) spectra were recorded using an internal deuterium lock for the residual protons in $CDCl_3$ (δ_H = 7.26), CD_2Cl_2 (δ_H = 5.32) and $(CD_3)_2SO$ (δ_H = 2.50) at ambient temperatures on the following instruments: Bruker AVANCE DPX-400 (400 MHz). Data are presented as follows: Chemical shift (in ppm on the scale relative to δ_{TMS} = 0), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet), coupling constant (*J*/Hz) and interpretation. **^{13}C NMR** spectra were recorded by broadband spin decoupling using an internal deuterium lock for $CDCl_3$ (δ = 77.2), CD_2Cl_2 (δ_c = 53.84) and $(CD_3)_2SO$ (δ = 39.5) at ambient temperatures on the following instruments: Bruker AVANCE DPX-400 (100.6 MHz). Chemical shift values are reported in ppm on the scale (δ_{TMS} = 0).

Infrared spectra were recorded on NICOLET 5SXC instrument as thin films, frequencies are given in wavenumbers (cm^{-1}).

All reagents and solvents were used as purchased if not otherwise stated.

Preparation of compound 3

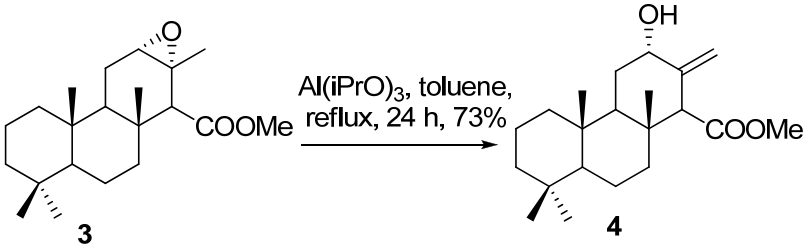


2 **3**

To an ice-cooled solution of **2** (7.00 g, 22.0 mmol) in dry CH_2Cl_2 (150 mL) was added *m*-CPBA (85%, 5.4 g, 26.6 mmol), the mixture was stirred at 0 °C for 12 h. The CH_2Cl_2 solution was filtered, and the filtrate was washed successively with saturated

Na_2SO_3 (80 mL), then washed with 0.1 M NaOH (3×50 mL) and saturated brine, dried over Na_2SO_4 and concentrated *in vacuo* to give a solid residue, which after crystallisation from $CHCl_3$-MeOH furnished pure **3** (5.73 g, 78%), the procedure of Rúveda, E. A. *et. al* was used.[1]

Preparation of compound 4



To a solution of **3** (5.00 g, 14.9 mmol) in toluene (70 mL) was added 0.92 g (4.5 mmol) of Al(^{i}PrO)$_3$, the mixture was stirred at 140 ^{o}C for 24 h, then diluted with water (10 mL) and extracted with EtOAc (3×30 mL). The organic layer was washed with a 10% aqueous solution of NaOH (30 mL) and brine, dried over Na_2SO_4, concentrated *in vacuo* and purified by column chromatography (10%, EtOAc/Petroleum ether) to give **4** (3.65 g, 73%) as a white solid.

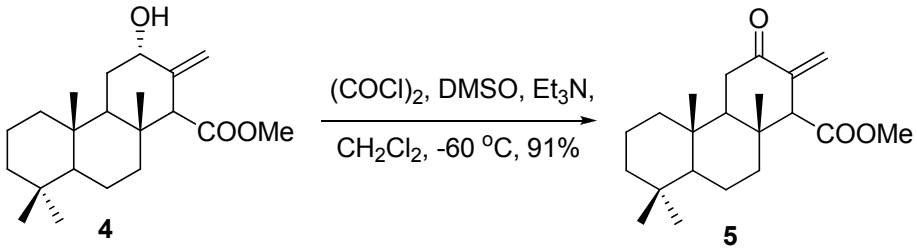
Mp: 153-154 ^{o}C (lit.[2] 156-158 ^{o}C)

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.04 (s, 1H), 4.85 (s, 1H), 4.38 (s, 1H), 3.64 (s, 3H), 3.35 (s, 1H), 1.82 (m, 2H), 1.69-1.59 (m, 3H), 1.55 (m, 2H), 1.46-1.30 (m, 4H), 1.22-1.10 (m, 1H), 1.03 (s, 3H), 0.95-0.89 (m, 2H), 0.86 (s, 3H), 0.84 (s, 3H), 0.81 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 145.1, 111.2, 72.9, 57.4, 56.7, 51.7, 50.9, 41.9, 40.2, 40.0, 39.7, 37.2, 33.3, 33.2, 29.1, 21.4, 18.6, 18.4, 16.0, 14.1.

The data is in agreement with that reported by Basabe *et. al.*[2]

Preparation of compound 5



A solution of dimethyl sulphoxide (3.4 mL, 47.4 mmol) in CH_2Cl_2 (12 mL) was added dropwise to a stirred solution of oxalyl chloride (2.0 mL, 21.7 mmol) in CH_2Cl_2

(72 mL) under dry nitrogen at -60 °C. After 3 min at -60 °C, a solution of **4** (6.60 g, 19.7 mmol) in CH_2Cl_2:DMSO (3:1, 29 mL) was added dropwise. The reaction was stirred for a further 20 min. Triethyl amine (13.7 mL, 103.0 mmol) was added at -60 °C, and stirred for a further 10 min. The cooling bath was removed, water was added at rt, and the product was extracted with CH_2Cl_2 (3×30 mL). The organic layer was washed with saturated brine, dried over Na_2SO_4, concentrated *in vacuo* and purified by flash chromatography (5%, EtOAc/Petroleum ether) to give **5** (5.97 g, 91%) as a white solid.

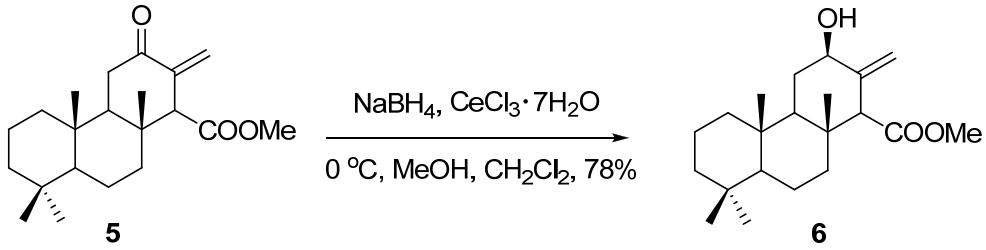
Mp: 144-146 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.11 (s, 1H), 5.17 (s, 1H), 3.72 (s, 3H), 3.21 (s, 1H), 2.55 (dd, *J* = 5.2, 18.5 Hz, 1H), 2.36 (dd, *J* = 13.4, 18.4 Hz, 1H), 1.68-1.59 (m, 3H), 1.59-1.49 (m, 3H), 1.46-1.36 (m, 4H), 1.16 (m, 1H), 1.10 (s, 3H), 0.90 (s, 3H), 0.88 (s, 3H), 0.83 (s, 3H), 0.79 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 200.4, 171.4, 141.0, 122.3, 61.6, 56.3, 55.4, 51.3, 41.7, 39.9, 39.2, 38.1, 37.8, 36.7, 33.3, 33.1, 21.5, 18.4, 18.2, 15.0, 14.7.

IR (film): 3457, 2923, 2848, 1732, 1693, 1616, 1400, 1173, 1127 cm^{-1}.

Preparation of compound 6



5 6

To a solution of **5** (6.00 g, 18.0 mmol) in MeOH (100 mL) and CH_2Cl_2 (5 mL) at 0 °C was added $CeCl_3$•$7H_2O$ (6.70 g, 18.0 mmol), followed by $NaBH_4$ (683.0 mg, 18.1 mmol). Once the reaction was finished as judged by TLC, solvent was removed *in vacuo*. CH_2Cl_2 was added, the organic solution was washed with saturated NaCl, dried over Na_2SO_4, concentrated *in vacuo* and purified by column chromatography (10%, EtOAc/Petroleum ether) to give **6** (4.71 g, 78%) as a white solid.

Mp: 162-163 °C

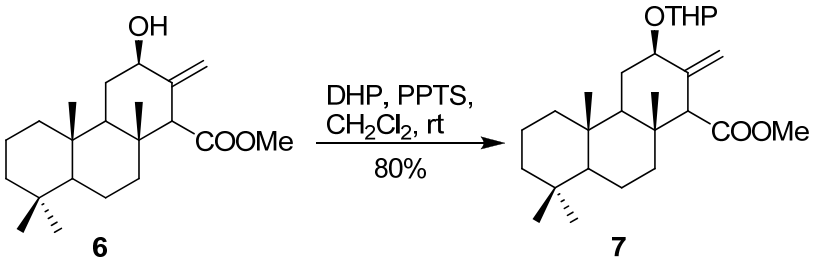
MS(EI) m/z 334.3 M^+, 335.3 $(M+H)^+$

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.17 (s, 1H), 4.91 (s, 1H), 4.05 (br, 1H), 3.66 (s, 3H), 2.71 (s, 1H), 2.05 (m, 1H), 1.78 (s, 1H), 1.72-1.57 (m, 4H), 1.47-1.25 (m, 5H), 1.19-1.07 (m, 2H), 1.05 (s, 3H), 0.87 (m, 1H), 0.85 (s, 3H), 0.84 (s, 3H), 0.81 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 145.2, 105.2, 72.4, 60.9, 57.1, 56.6, 50.9, 41.9, 39.9, 39.8, 39.6, 37.5, 33.3, 33.1, 31.9, 21.4, 18.5, 18.4, 16.1, 14.9.

IR (film): 3494, 2953, 2920, 1721, 1391, 1215, 1175, 1032, 899 cm^{-1}.

Preparation of compound 7



6 **7**

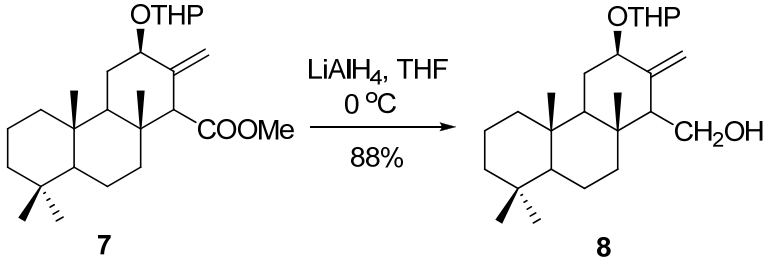
A solution of **6** (3.00 g, 8.97 mmol) and dihydropyran (1.10 g, 13.1 mmol) in dry DCM (30 mL) containing PPTS (2.25 g, 8.95 mmol) was stirred over night at room temperature. The solution was diluted with ether and washed once with brine to remove the catalyst. After evaporation of the solvent, the residue was purified by column chromatography (5%, EtOAc/Petroleum ether) to give **6** (3.00 g, 80%) as a white solid.

MS(EI) m/z 418.3 M^+

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.38 (s, 1H), 5.03 (s, 1.1H), 4.90 (s, 1H), 4.88 (s, 1.1H), 4.86 (m, 1H), 4.64 (dd, *J* = 2.9, 4.8 Hz, 1.1H), 4.06 (m, 2.1H), 3.91 (m, 2.1H), 3.65 (s, 6.3H), 3.50 (m, 2.1H), 2.73 (s, 1H), 2.67 (s,1.1H), 1.07 (s, 3H), 1.06 (s, 3.3H), 0.85 (s, 6.3H), 0.84 (s, 6.3H), 0.80 (s, 6.3H).

IR (film): 2944, 1738, 1389,1126, 1164, 1025, 909 cm^{-1}.

Preparation of compound 8



7 **8**

To a solution of **7** (3.00 g, 7.17 mmol) in dry THF (40 mL) $LiAlH_4$ (272 mg, 7.17 mmol) was added at 0 °C, the mixture was stirred at 0 °C for 6 h. Once the reaction was finished as judged by TLC, water (2 mL) was added to quench any unreacted

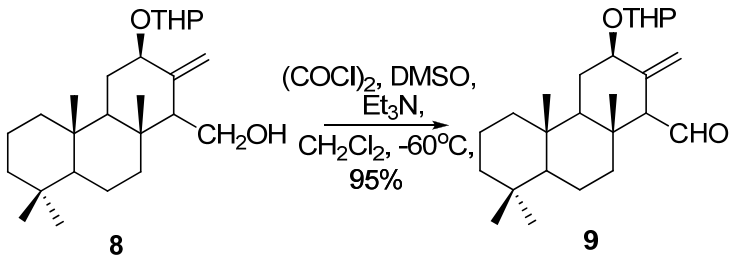
$LiAlH_4$. The mixture was extracted with CH_2Cl_2 (3×10 mL), and the organic phase was washed with saturated NaCl, dried over Na_2SO_4, concentrated *in vacuo* and purified by column chromatography (10%, EtOAc/Petroleum ether) to give **8** (2.46 g, 88%) as a white solid.

MS(EI) m/z 390.3 M^+

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.49 (s, 1H), 5.16 (s, 1.3H), 4.85 (t, *J* = 3.4 Hz, 1 H), 4.80 (s, 1H), 4.76 (s, 1.3H), 4.65 (dd, *J* = 5.1, 2.8 Hz, 1.3H), 3.96 (m, 4.6H), 3.83 (m, 4.6 H), 3.49 (m, 2.3H), 0.86 (s, 6.9H), 0.81 (s, 6.9H), 0.80 (s, 6.9H), 0.73 (s, 3H), 0.71 (s, 3.9H).

IR (film): 3438, 2940, 2869, 2849, 1387, 1120, 1021, 978, 896 cm^{-1}.

Preparation of compound 9



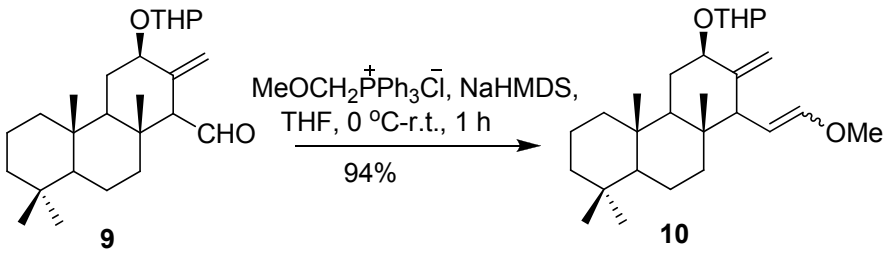
8 **9**

This experimental procedure was the same as that for the synthesis of compound **5**. After short silica gel column filtration and evaporation *in vacuo,* product **9** was obtained in 95% yield as white solid. ^{1}H NMR spectroscopy confirmed adequate purity for next step.

MS(EI) m/z 388.3 M^+

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.90 (d, *J* = 4.4 Hz, 1H), 9.90 (d, *J* = 4.2 Hz, 0.5H), 5.50 (s, 1H), 5.16 (s, 0.5H), 4.88 (t, *J* = 3.3 Hz, 1H), 4.74 (s, 1H), 4.71 (s, 0.5H), 4.63 (dd, *J* = 2.8, 4.9 Hz, 0.5H), 4.06 (m, 1.5H) , 3.96 (m, 0.5H), 3.87 (m, 1H), 3.51 (m, 1.5H), 1.17 (s, 3H), 1.15 (s, 1.5H), 0.88 (s, 4.5H), 0.87 (s, 4.5H), 0.82 (m, 4.5H).

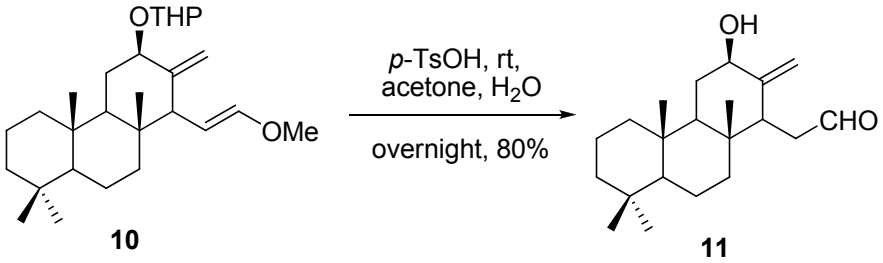
Preparation of compound 10



9 **10**

To a suspension of methoxymethyltriphenylphosphonium chloride ($MeOCH_2PPh_3Cl$) (2.65 g, 7.73 mmol) in THF (20 mL) at 0 ^oC under an argon atmosphere, a solution of NaHMDS in THF (2.0 M, 3.8 mL, 7.6 mmol) was added dropwise. The solution was stirred for a further 20 min, then a solution of aldehyde **9** (1.50 g, 3.86 mmol) in THF (10 mL) was added dropwise. The mixture was stirred for 2 h, then quenched with aqueous NH_4Cl (2 mL) and extracted with Et_2O (3×10 mL)[2]. The organic layer was washed with saturated brine and dried over Na_2SO_4. The residue was obtained after removing the solvent and was purified by flash chromatography (5%, EtOAc/Petroleum ether) affording **10** (1.51 g, 94%), which was directly used for the next step.

Preparation of compound 11



10 **11**

To a solution of **10** (0.60 g, 1.44 mmol) in acetone (50 mL) and water (1 mL), *p*-TsOH (0.55 g, 2.83 mmol) was added at room temperature. After being stirred for 7 h, the reaction mixture was concentrated *in vacuo*, diluted with water and extracted with Et_2O (3×10 mL). The extracts were washed with saturated $NaHCO_3$ solution, dried over Na_2SO_4, concentrated *in vacuo* and purified by column chromatography (10%, EtOAc/Petroleum ether) to give **11** (0.37 g, 80%) as a white solid.

Mp: 148-150 ^oC

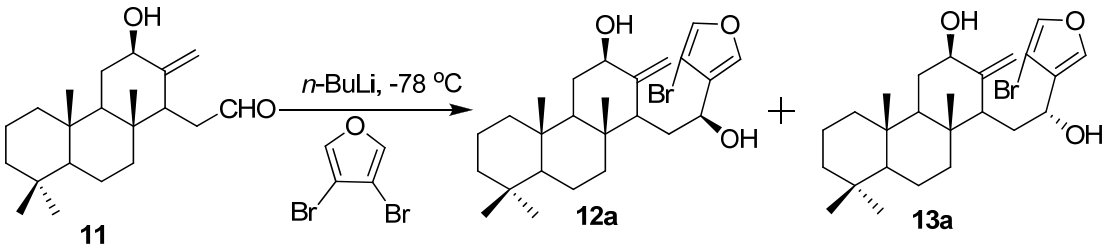
MS (EI) m/z 319.3 $(M+H)^+$

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.65 (d, *J* = 2.4 Hz, 1H), 5.17 (s, 1H), 4.57 (s, 1H), 4.08 (m, 1H), 2.64-2.53 (m, 1H), 2.47 (dd, *J* = 16.8, 3.7 Hz, 1H), 2.29 (d, *J* = 10.2 Hz, 1H), 2.10 (dd, *J* = 5.4, 10.9 Hz, 1H), 1.73-1.59 (m, 5H), 1.50-1.35 (m, 3H), 1.34-1.27 (m, 1H), 1.24 (m, 1H), 1.21-1.10 (m, 2H), 0.88 (s, 1H), 0.86 (s, 3H), 0.83 (s, 3H), 0.81 (s, 3H), 0.70 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 202.8, 150.4, 104.6 73.3, 57.4, 56.5, 49.2, 41.9, 40.7 40.0, 39.5, 38.9, 37.7, 33.3, 33.3, 32.4, 21.4, 18.9, 18.6, 16.2, 15.5.

IR (film): 3447, 2959, 2922, 2853, 1722, 1385, 1059 cm^{-1}.

Preparation of compounds 12a and 13a



To a solution of 2,3-dibromofuran (0.50 g, 2.23 mmol) in THF (4 mL) at -78 °C a solution of *n*-BuLi in hexanes (0.72 mL, 2.5 M, 1.8 mmol) was added dropwise. The mixture was stirred for 10 min, after which a solution of **11** (0.24 g, 0.75 mmol) in THF (5 mL) was added dropwise *via* syringe. After 1 h at -78 °C, the reaction was quenched with a saturated NH_4Cl solution (1 mL), diluted with ethyl acetate, and washed with water (10 mL) and brine (10 mL). The organic layer was dried, filtered and concentrated. The product was purified by column chromatography (15% EtOAc/Petroleum ether) to give **12a** (150 mg, 43%) and **13a** (98 mg, 28%) as white solids.

Data for **12a**

MS (EI) m/z 464.2 M^+

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, *J* = 1.8Hz, 1H), 7.39 (d, *J* = 1.8 Hz, 1H), 5.24 (s, 1H), 4.83 (s, 1H), 4.68 (m, 1H), 4.05 (m, 1H), 2.14-2.05 (m, 2H), 1.94-1.88 (m, 2H), 1.83-1.77 (m, 1H), 1.73-1.66 (m, 1H), 1.66-1.62 (m, 1H), 1.47-1.41 (m, 1H), 1.41-1.34 (m, 2H), 1.34-1.28 (m, 1H), 1.27-1.22 (m, 2H), 1.21-1.10 (m, 3H), 0.91-0.88 (m, 1H), 0.86 (s, 3H), 0.82 (s, 3H), 0.81 (s, 3H), 0.68 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): 150.3, 141.6, 139.9, 129.8, 103.3, 99.6, 73.9, 64.4, 57.7, 56.5, 50.4, 42.0, 40.4, 40.1, 39.2, 37.7, 33.3, 33.3, 33.0, 31.2, 21.4, 19.0, 18.6, 16.2, 15.7.

Data for **13a**

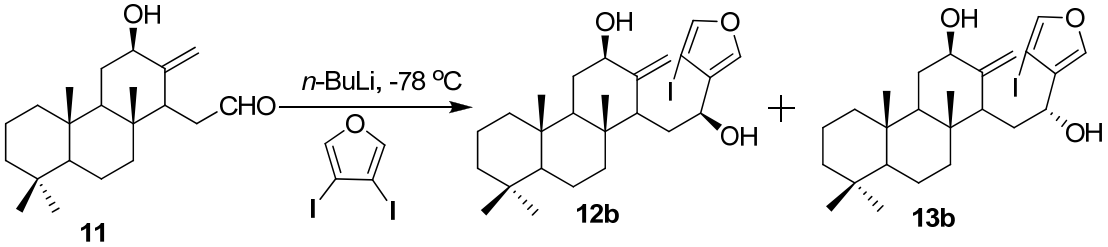
MS (EI) m/z 464.2 M^+

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, *J* = 1.7 Hz, 1H), 7.35 (d, *J* = 1.7 Hz, 1H), 5.25 (s, 1H), 4.91 (s, 1H), 4.70 (dd, d, *J* = 5.4, 8.9 Hz, 1H), 3.90 (dd, *J* = 5.2, 10.9 Hz, 1H), 2.16-1.99 (m, 4H), 1.82 (dt, *J* = 3.2, 12.7 Hz, 1H), 1.59-1.55 (m, 2H), 1.46-1.40 (m, 2H), 1.39-1.33 (m, 2H), 1.29-1.24 (m, 2H), 1.22-1.10 (m, 2H), 1.05-0.94 (m, 2H), 0.85 (s, 3H), 0.79 (s, 6H), 0.69 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 150.9, 141.8, 140.6, 128.0, 103.3, 99.9, 73.8,

66.2, 57.4, 56.4, 51.6, 41.9, 40.3, 40.0, 39.6, 37.7, 33.3, 33.3, 32.9, 31.1, 21.4, 19.0, 18.6, 16.2, 15.6.

Preparation of compounds 12b and 13b



To a solution of 2,3-diiodofuran (1.00 g, 3.13 mmol) in THF (6 mL) at –78 °C a solution of *n*-BuLi in hexanes (1.0 mL, 2.5 M, 2.5 mmol) was added dropwise. The mixture was stirred for 10 min, after which a solution of **11** (0.30 g, 0.94 mmol) in THF (7 mL) was added dropwise *via* syringe. After 1 h at –78 °C, the reaction was quenched with a saturated NH_4Cl solution (1 mL), diluted with ethyl acetate, and washed with water (10 mL) and brine (10 mL). The organic layer was dried, filtered, and concentrated. The product was purified by column chromatography (15% EtOAc/Petroleum ether) to give **12b** (225 mg, 47%) and **13b** (154 mg, 32%) as a white solid.

Data for **12b**

Mp: 105-107 ^oC $[\alpha]_D^{29}$ = -61.5 (*c* 0.2, CH_2Cl_2)

HRMS-EI (m/z) calcd. for $C_{25}H_{37}IO_3$ $[M+H]^+$ 513.1878, found: 513.1892.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 1.4 Hz, 1H), 7.38 (d, *J* = 1.4 Hz, 1H), 5.24 (s, 1H), 4.84 (s, 1H), 4.61 (m, 1H), 4.05 (m, 1H), 2.14-2.04 (m, 2H), 1.96-1.86 (m, 2H), 1.86-1.75 (m, 2H), 1.71 (m, 1H), 1.66 (m, 1H), 1.59 (s, 1H), 1.45-1.26 (m, 3H), 1.28-1.20 (m, 2H), 1.19-1.13 (m, 2H), 0.89 (s, 1H), 0.86 (s, 3H), 0.82 (s, 3H), 0.81 (s, 3H), 0.68 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 150.4, 146.2, 139.9, 131.6, 103.4, 73.9, 65.8, 65.4, 57.7, 56.5, 50.4, 42.0, 40.4, 40.1, 39.2, 37.7, 33.3, 33.3, 33.0, 31.1, 21.4, 19.0, 18.6, 16.2, 15.7.

IR (film): 3409, 2934, 2869, 1650, 1387, 1049 cm^{-1}.

Data for **13b**

Mp: 100-102 ^oC $[\alpha]_D^{29}$ = -4.2 (*c*, 0.205, CH_2Cl_2)

MS (EI) m/z 512.2$(M)^+$, 513.2 $(M+H)^+$

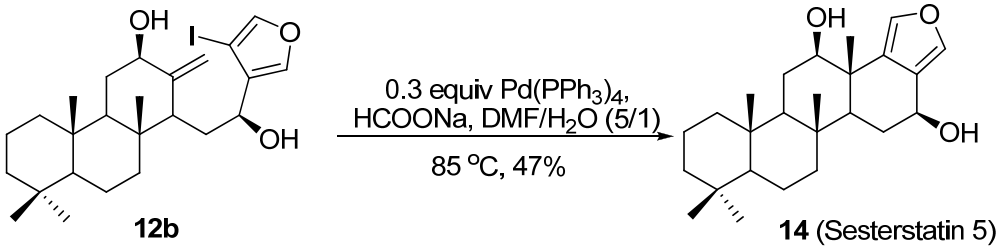
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, *J* = 1.5 Hz, 1H), 7.33 (d, *J* = 1.5 Hz,

1H), 5.25 (s, 1H), 4.92 (s, 1H), 4.65 (m, 1H), 3.91 (m, 1H), 2.13-2.05 (m, 2H), 2.03-1.98 (m, 1H), 1.87-1.79 (m, 2H), 1.72-1.61 (m, 2H), 1.45-1.32 (m, 4H), 1.28-1.10 (m, 3H), 1.04-0.94 (m, 2H), 0.87 (s, 1H), 0.85 (s, 3H), 0.79 (s, 6H), 0.69 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 150.9, 146.4, 140.5, 129.9, 103.4, 73.8, 67.2, 66.0, 57.4, 56.4, 51.6, 41.9, 40.4, 40.0, 39.7, 37.7, 33.3, 33.3, 32.9, 31.2, 21.4, 19.0, 18.6, 16.2, 15.6.

IR (film): 3422, 2931, 2850, 1650, 1401, 1046 cm^{-1}.

Preparation of compound 14 (Sesterstatin 5)



A mixture of compound **12b** (23.0 mg, 0.045 mmol), HCOONa (4.6 mg, 0.067 mmol), $Pd(PPh_3)_4$ (15.0 mg, 0.013 mmol) in DMF:H_2O (5:1, 2 mL) was loaded into a Schlenk tube and flushed with nitrogen. The reaction was heated with continuous stirring at 85 ^oC for 30 h.[4] Once the reaction was complete as judged by TLC, the reaction solvent was removed under reduced pressure. The residue was purified by column chromatography (30% EtOAc/Petroleum ether) to give sesterstatin 5 (8.1 mg, 47%) as a white solid.

Mp 242-244 ^oC (lit.[3] 245 ^oC). $[\alpha]_D^{23}$ +28.1 (*c* 0.09, $CHCl_3$) lit.[3] $[\alpha]_D^{25}$ +27 (*c* 0.09, $CHCl_3$)

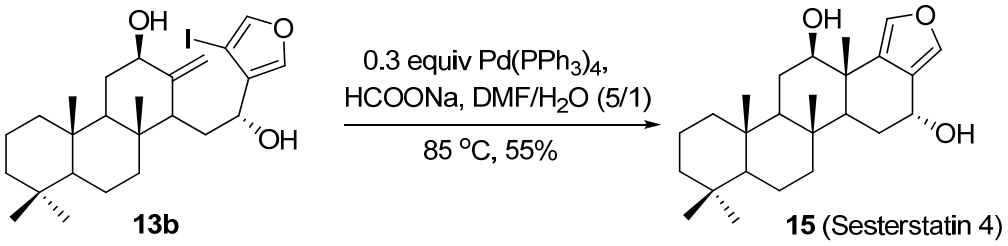
HRMS-EI (m/z) calcd. for $C_{25}H_{39}O_3$ $[M+H]^+$ 387.2899, found: 387.2903.

^{1}H NMR (400 MHz, DMSO): δ 7.49 (s, 1H), 7.39 (s, 1H), 5.12 (d, *J* = 6.2 Hz, 1H), 4.87 (d, *J* = 5.1 Hz, 1H), 4.52 (m, 1H), 3.38 (m, 1H), 1.91 (dd, *J* = 6.4, 12.2 Hz, 1 H), 1.84 (d, *J* = 12.1 Hz, 1H), 1.72-1.61 (m, 3H), 1.57-1.51 (m, 2H), 1.51-1.35 (m, 5H), 1.18 (s, 3H), 1.17-1.11 (m, 1H), 1.04 (d, *J* = 11.7 Hz, 1H), 0.98-0.92 (m, 2H), 0.89 (s, 3H), 0.89 (s, 3H), 0.87 (s, 3H), 0.85 (s, 4H).

^{13}C NMR (100 MHz, DMSO): δ 138.04, 136.92, 135.18, 126.83, 78.44, 65.43, 58.50, 56.46, 54.36, 42.08, 41.53, 40.55, 39.80, 37.39, 37.27, 33.55, 33.42, 29.14, 27.67, 21.63, 20,37, 18.63, 18.25, 17.98, 16.45.

FT-IR (film): 3450, 2932, 1401, 1386, 1041 cm^{-1}.

Preparation of compound 15 (Sesterstatin 4)



A mixture of compound **13b** (23.0 mg, 0.045 mmol), HCOONa (4.6 mg, 0.067 mmol), $Pd(PPh_3)_4$ (15.0 mg, 0.013 mmol) in DMF:H_2O (5:1, 2 mL) was loaded into a Schlenk tube and flushed with nitrogen. The reaction was heated with continuous stirring at 85 ^oC for 30 h. Once the reaction was complete as judged by TLC, the reaction solvent was removed under reduced pressure. The residue was purified by column chromatography (30% EtOAc/Petroleum ether) to give sesterstatin 4 (9.5 mg, 55%) as a white solid.

M.p. 253-255 ^oC (lit.[3] 252-254 ^oC). $[\alpha]_D^{23}$ -15.9 (*c* 0.138, $CHCl_3$) lit.[3] $[\alpha]_D^{25}$ -10 (*c* 0.09, $CHCl_3$)

HRMS-EI (m/z) calcd. for $C_{25}H_{39}O_3$ $[M+H]^+$ 387.2899, found: 387.2911.

^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.43 (s, 1H), 7.28 (s, 1H), 4.82 (s, 1H), 3.55 (m, 1H),1.83-1.66 (m, 4H), 1.66-1.56 (m, 3H), 1.44-1.34 (m, 4H), 1.32-1.26 (m, 2H), 1.18 (s, 2H), 1.04 (s, 3H), 0.95-0.87 (m, 2H), 0.82 (s, 3H), 0.79 (s, 3H), 0.76 (s, 3H), 0.74 (s, 3H).

^{13}C NMR (101 MHz, CD_2Cl_2): δ 138.24, 136.71, 132.84, 123.38, 78.81, 60.42, 58.04, 55.78, 48.44, 41.28, 40.73, 39.59, 39.07, 36.67, 36.11, 32.43, 32.23, 27.18, 26.94, 20.27, 17.88, 17.49, 17.38, 16.76, 15.27.

FT-IR (film): 3488, 2964, 1400, 1388, 1262, 1092, 1039, 800 cm^{-1}.

Reference

1. P. M. Imamura, E. A. Rúveda, *J. Org. Chem.,* 1980, **45**, 510.
2. P. Basabe, S. Delgado, I. S. Marcos, D. Diez, A. Diego, M. Román, F. Sanzb, J. G. Urones, *Tetrahedron,* 2007**, 63**, 8939.
3. G. R. Pettit, R. Tan, N. Melody, Z. A. Cichacz, D. L. Herald, M. S. Hoard, R. K. Pettit and J.-C. Chapuis, *Bioorg. Med. Chem. Lett.*, 1998, **8**, 2093-2098.
4. K. C. Majumdar, S. Chakravorty, T. Ghosh, B. Sridhar, *Synlett.,* 2009, 3127.

Crystal data and structure refinement for sesterstatin 4

Empirical formula	$C_{25}H_{38}O_3$
Formula weight	386.55
Temperature	293 (2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, *P*2(1)2(1)2(1)
Unit cell dimensions	*a* = 7.6282 (8) Å alpha = 90 deg.
	b = 9.5689 (10) Å beta = 90 deg.
	c = 29.068 (3) Å gamma = 90 deg.
Volume	2121.8 (4) Å ^3
Z, Calculated density	4, 1.210 Mg /m^3
Absorption coefficient	0.077 mm^-1
F (000)	848
Crystal size	0.402 × 0.329 × 0.257 mm
Theta range for data collection	2.24 to 26.00 deg.
Limiting indices	-9<=h<=9, -11<=k<=11, -30<=l<=35
Reflections collected / unique	11634 / 2406 [R (int) = 0.0497]
Completeness to theta = 26.00	99.8%
Absorption correction	Empirical
Max. and min. transmission	1.00000 and 0.76154
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2406 / 1 /260
Goodness-of-fit on F^2	1.126
Final R indices [I>2sigma (I)]	R1=0.0532, wR2 = 0.1203
R indices (all data)	R1 = 0.0612 wR2 = 0.1240
Absolute structure parameter	10 (10)
Largest diff. peak and hole	0.246 and -0.192 e. Å ^3

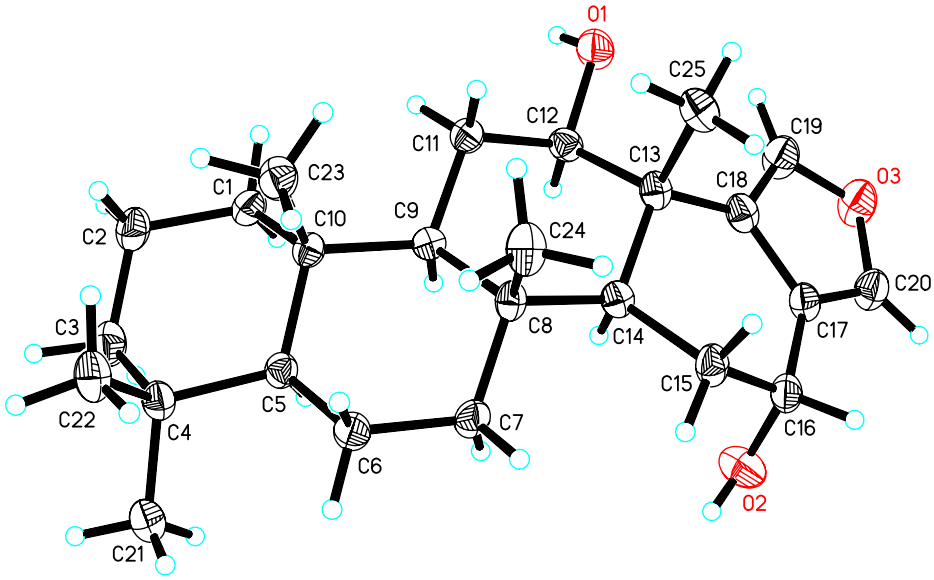
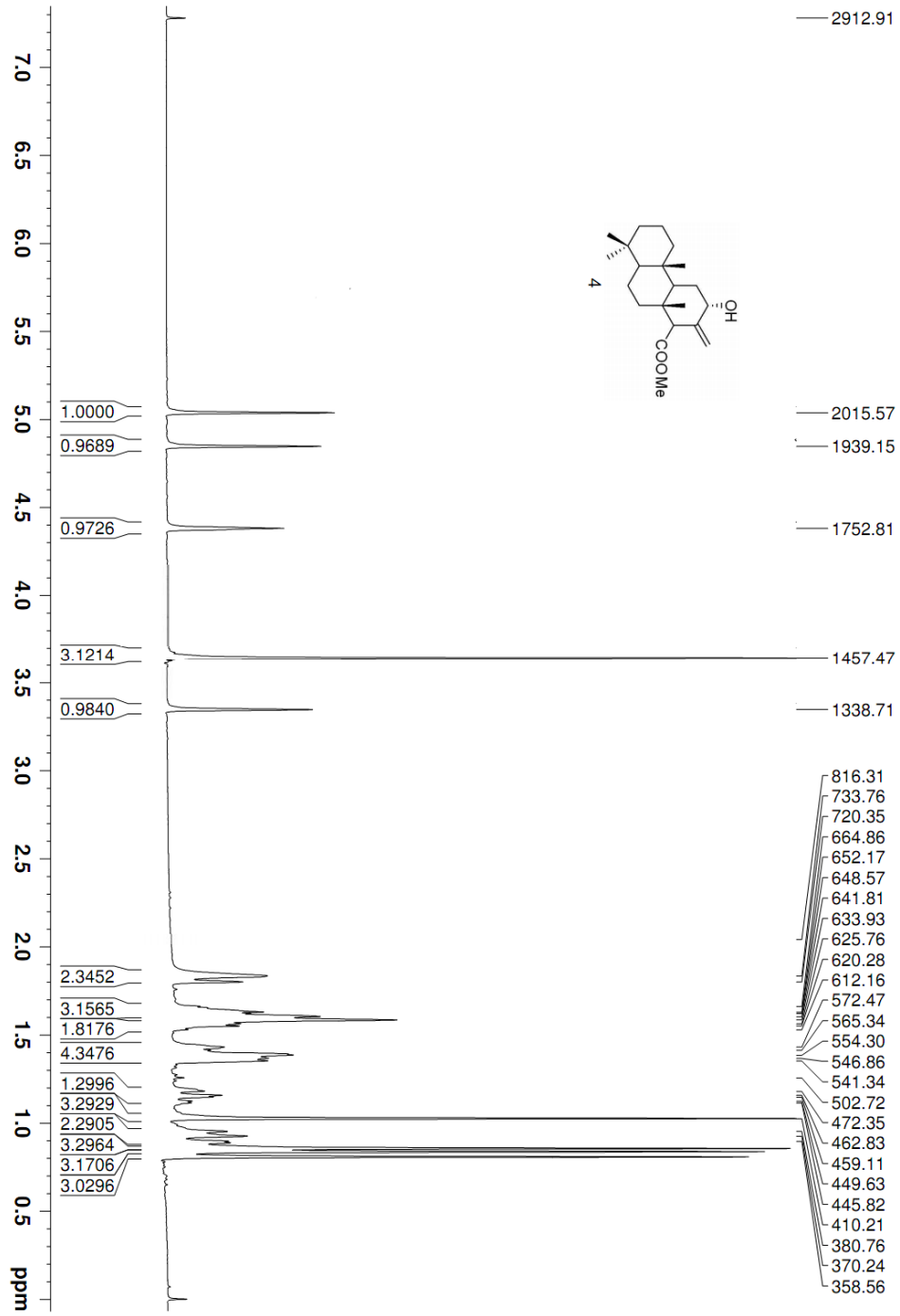


Figure 3. ORTEP drawing of sesterstatin 4.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0.5
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2.2905
3.2964
3.1706
3.0296
2912.91
2015.57
1939.15
1752.81
1457.47
1338.71
816.31
733.76
720.35
664.86
652.17
648.57
641.81
633.93
625.76
620.28
612.16
572.47
565.34
554.30
546.86
541.34
502.72
472.35
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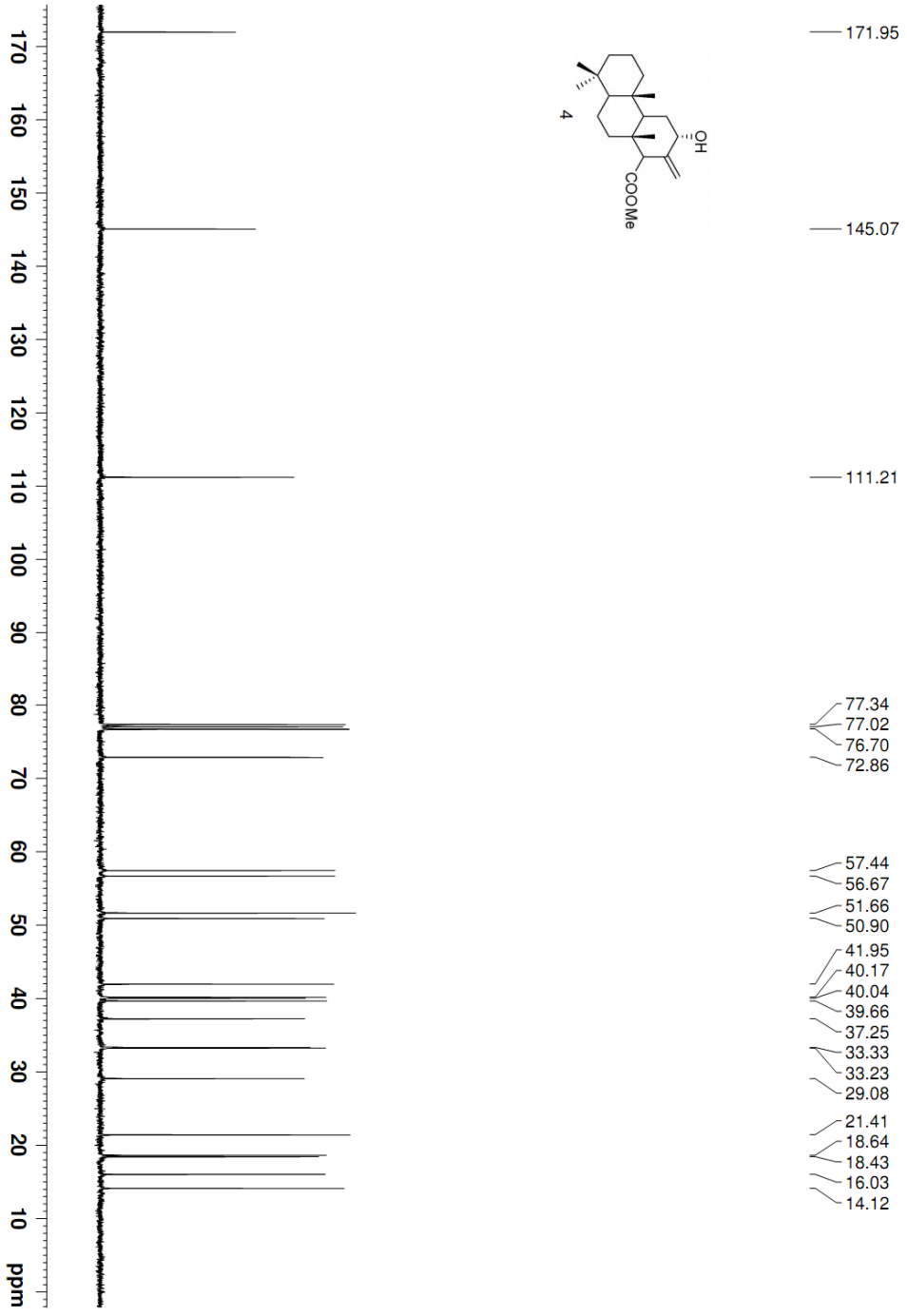
459.11
449.63
445.82
410.21
380.76
370.24
358.56
4
OH
COOMe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145.07
111.21
77.34
77.02
76.70
72.86
57.44
56.67
51.66
50.90
41.95
40.17
40.04
39.66
37.25
33.33
33.23
29.08
21.41
18.64
18.43
16.03
14.12
4
HO
COOMe
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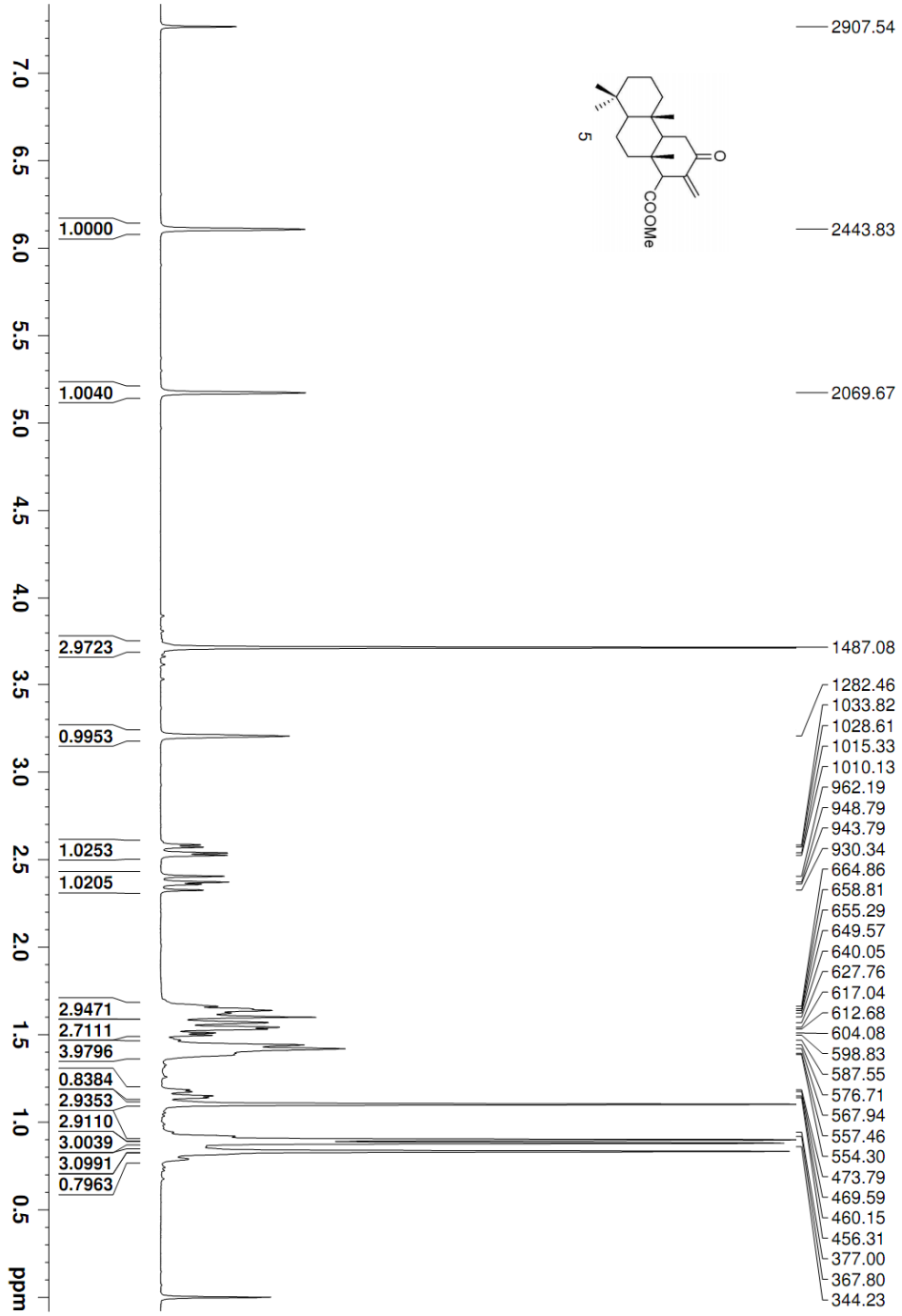
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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3.5
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1.0
0.5
ppm
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1.0253
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2.7111
3.9796
0.8384
2.9353
2.9110
3.0039
3.0991
0.7963
5
O
COOMe
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1033.82
1028.61
1015.33
1010.13
962.19
948.79
943.79
930.34
664.86
658.81
655.29
649.57
640.05
627.76
617.04
612.68
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598.83
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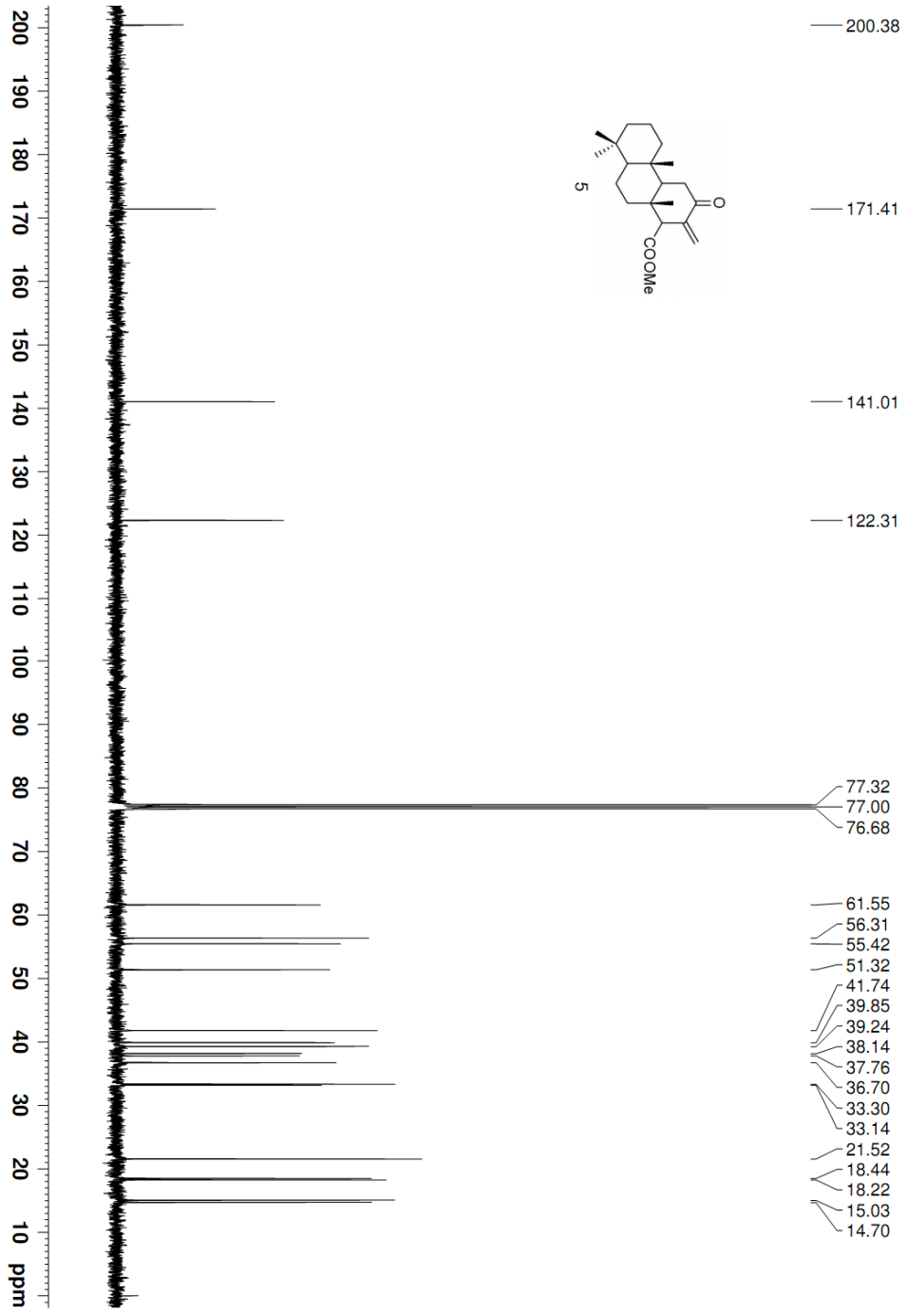
344.23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77.00
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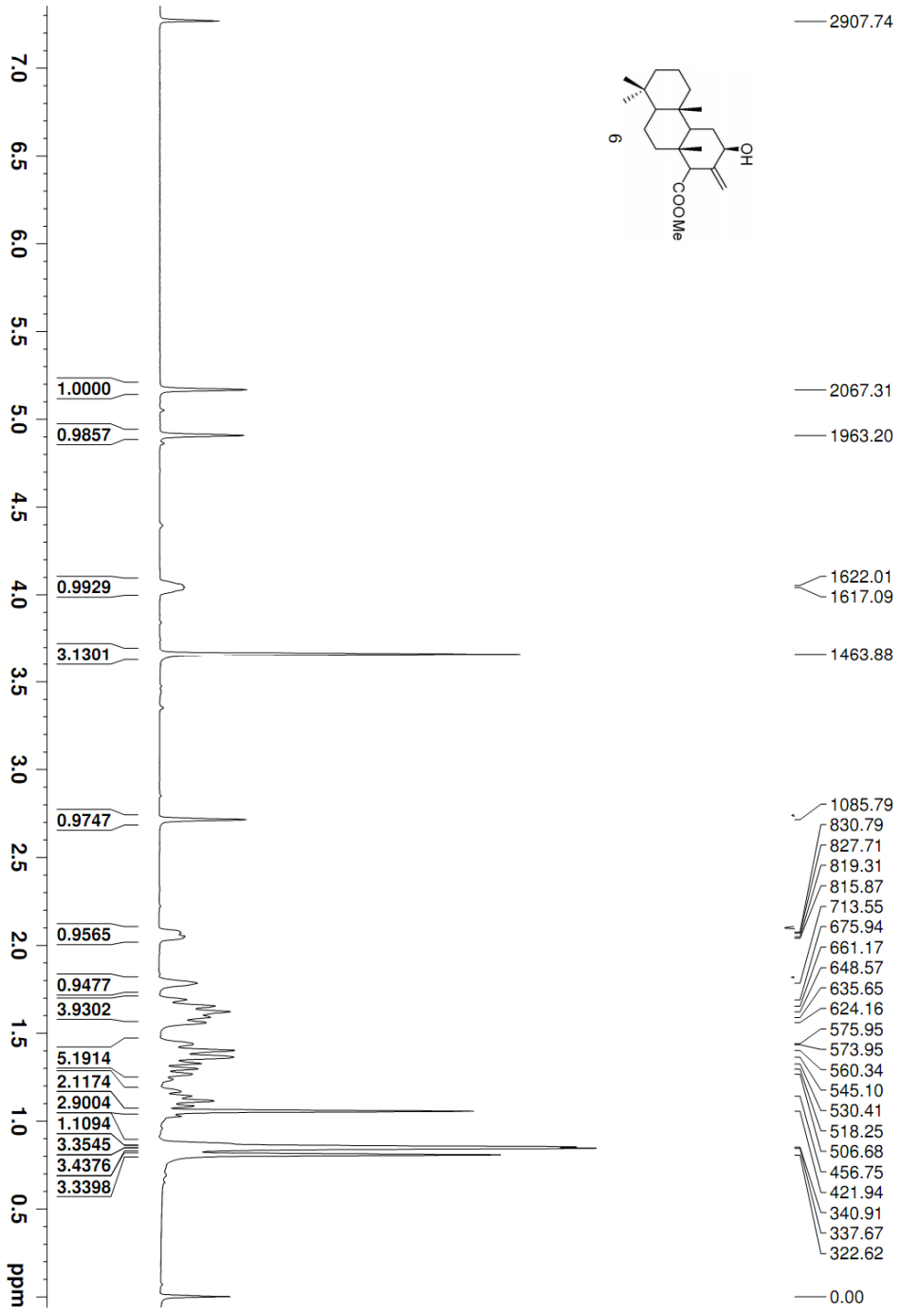
39.85
39.24
38.14
37.76
36.70
33.30
33.14
21.52
18.44
18.22
15.03
14.70
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
5
O
COOMe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4.0
3.5
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2.5
2.0
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1.0
0.5
ppm
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0.9929
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0.9477
3.9302
5.1914
2.1174
2.9004
1.1094
3.3545
3.4376
3.3398
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1085.79
830.79
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819.31
815.87
713.55
675.94
661.17
648.57
635.65
624.16
575.95
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530.41
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506.68
456.75
421.94
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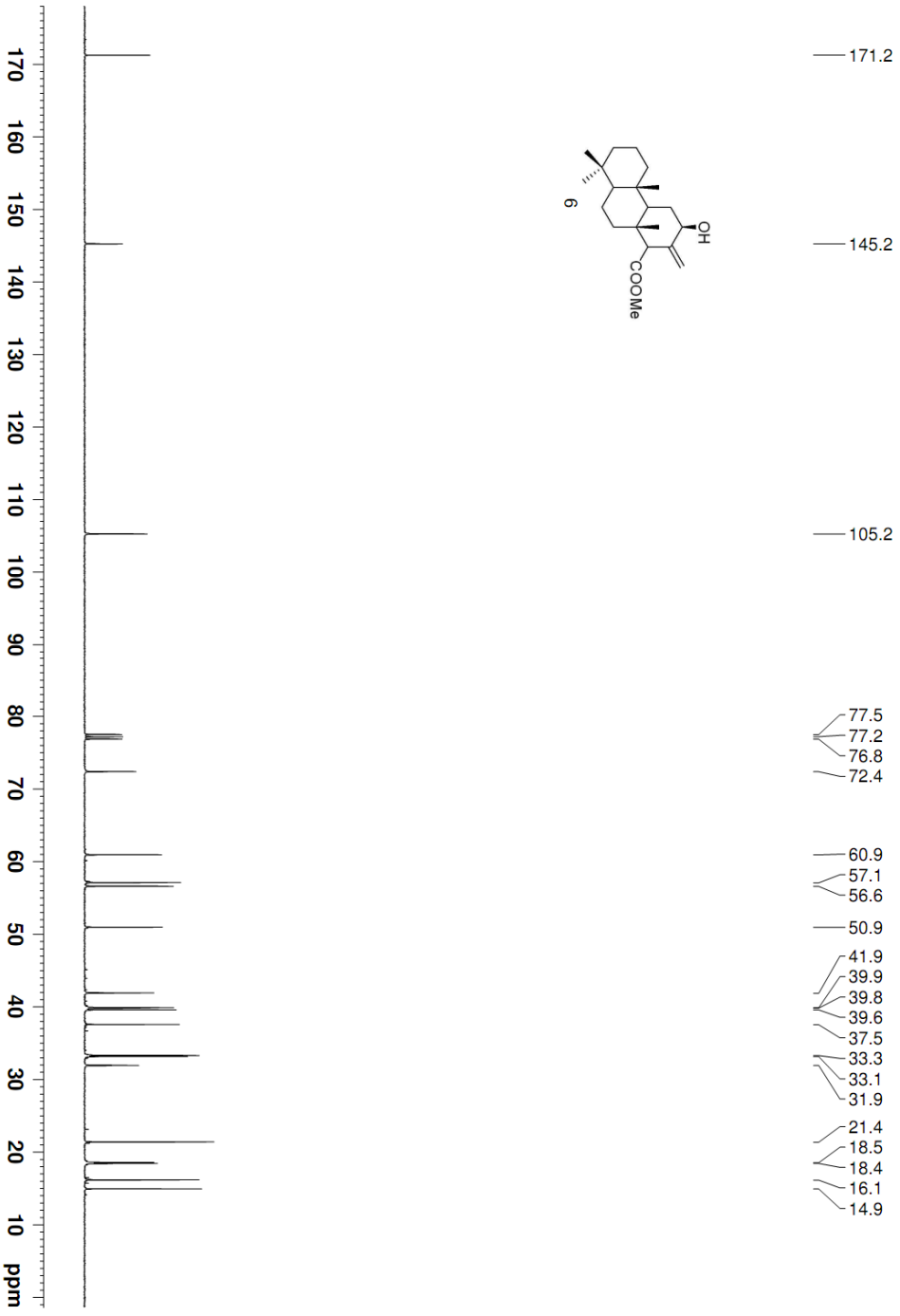
322.62
0.00


9
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COOMe
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77.2
76.8
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41.9
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37.5
33.3
33.1
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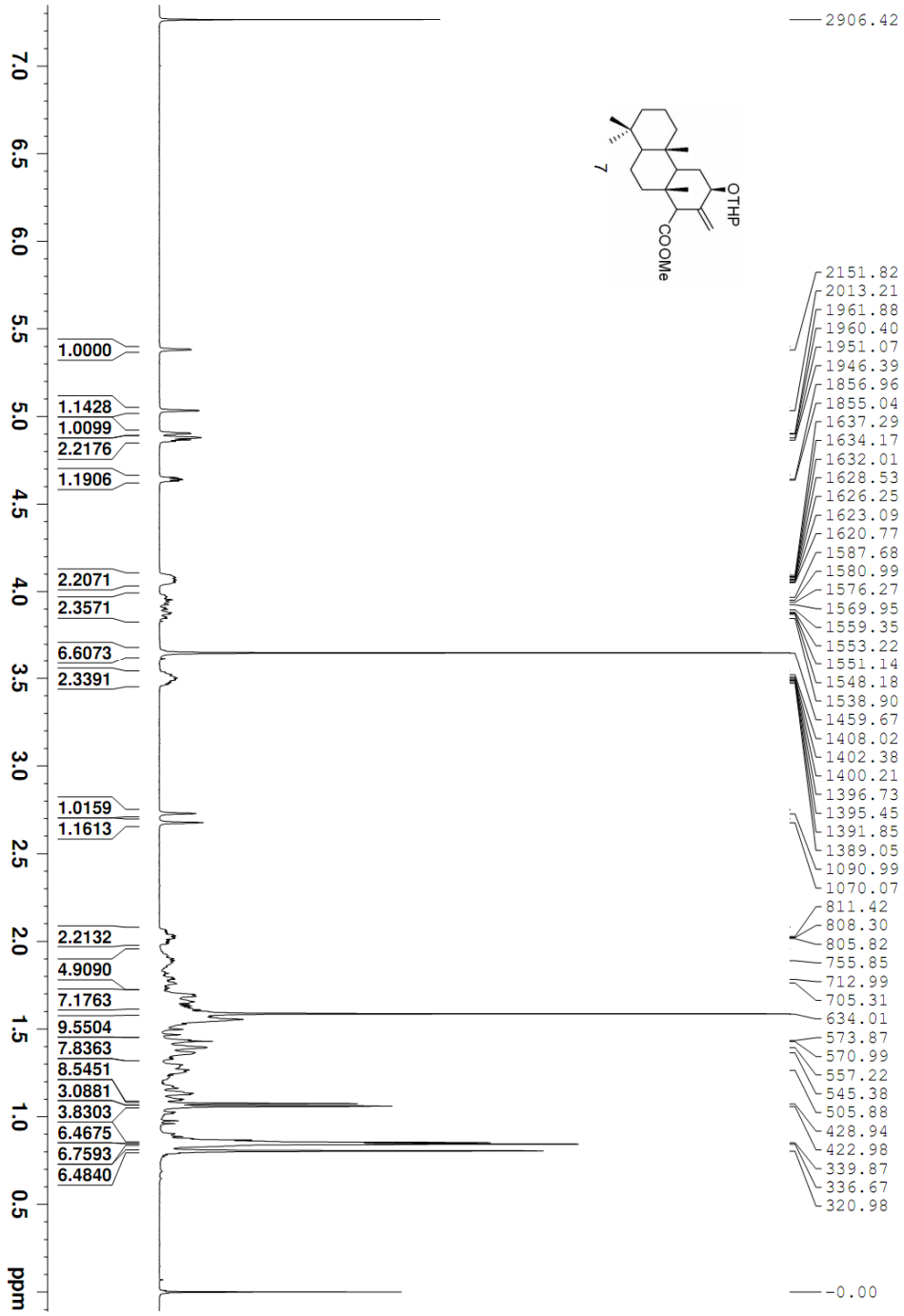
16.1
14.9
ppm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705.31
634.01
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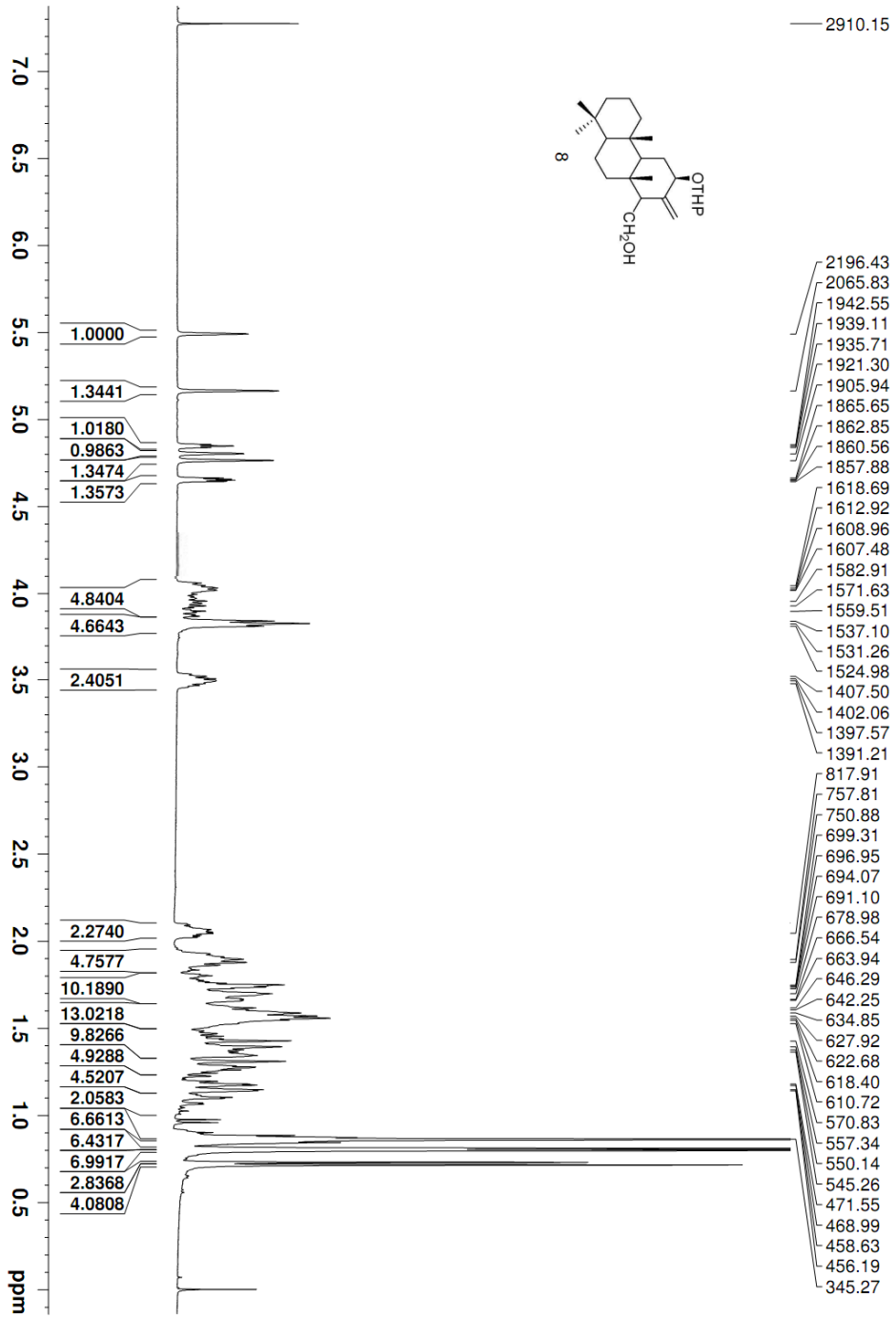
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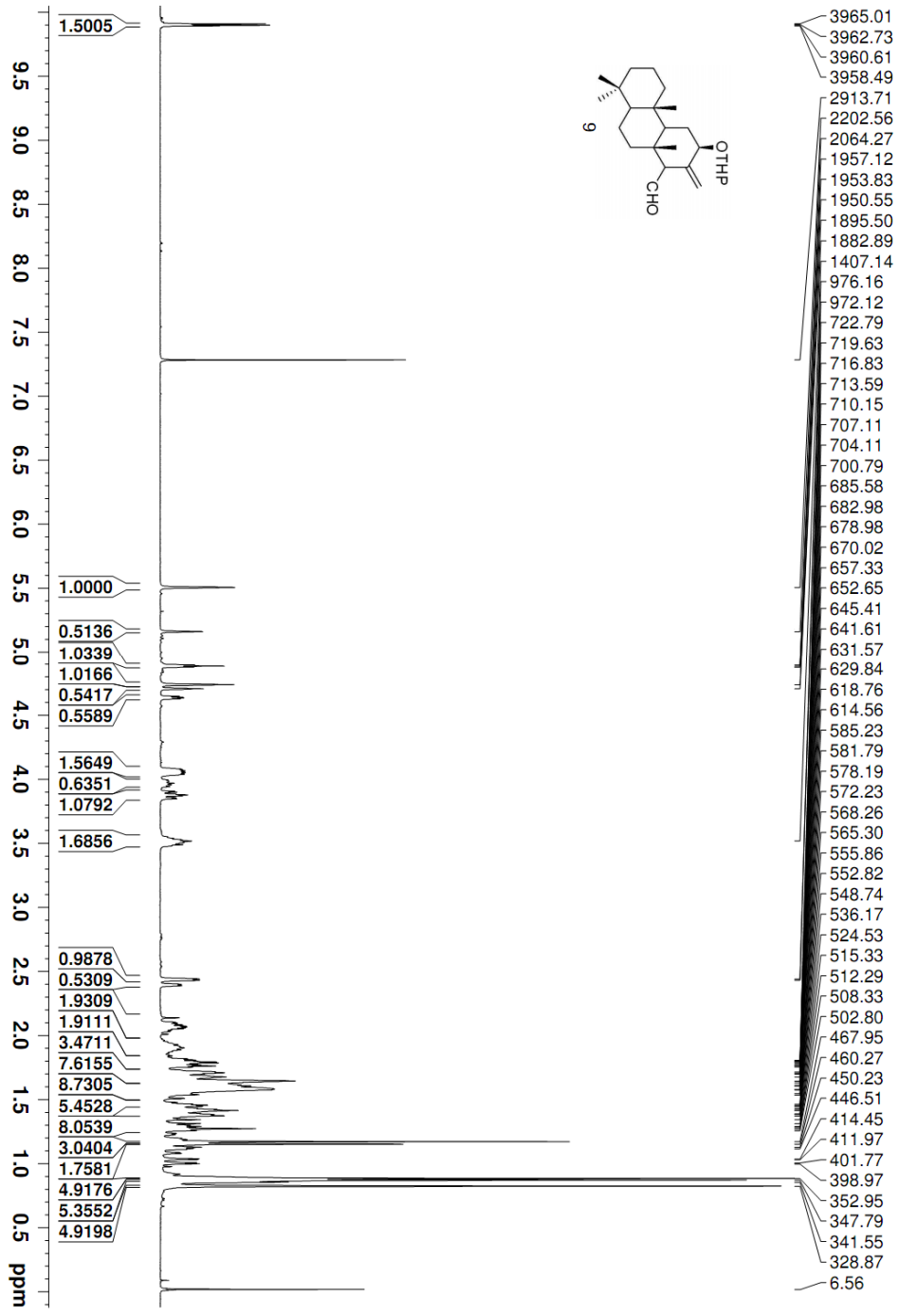
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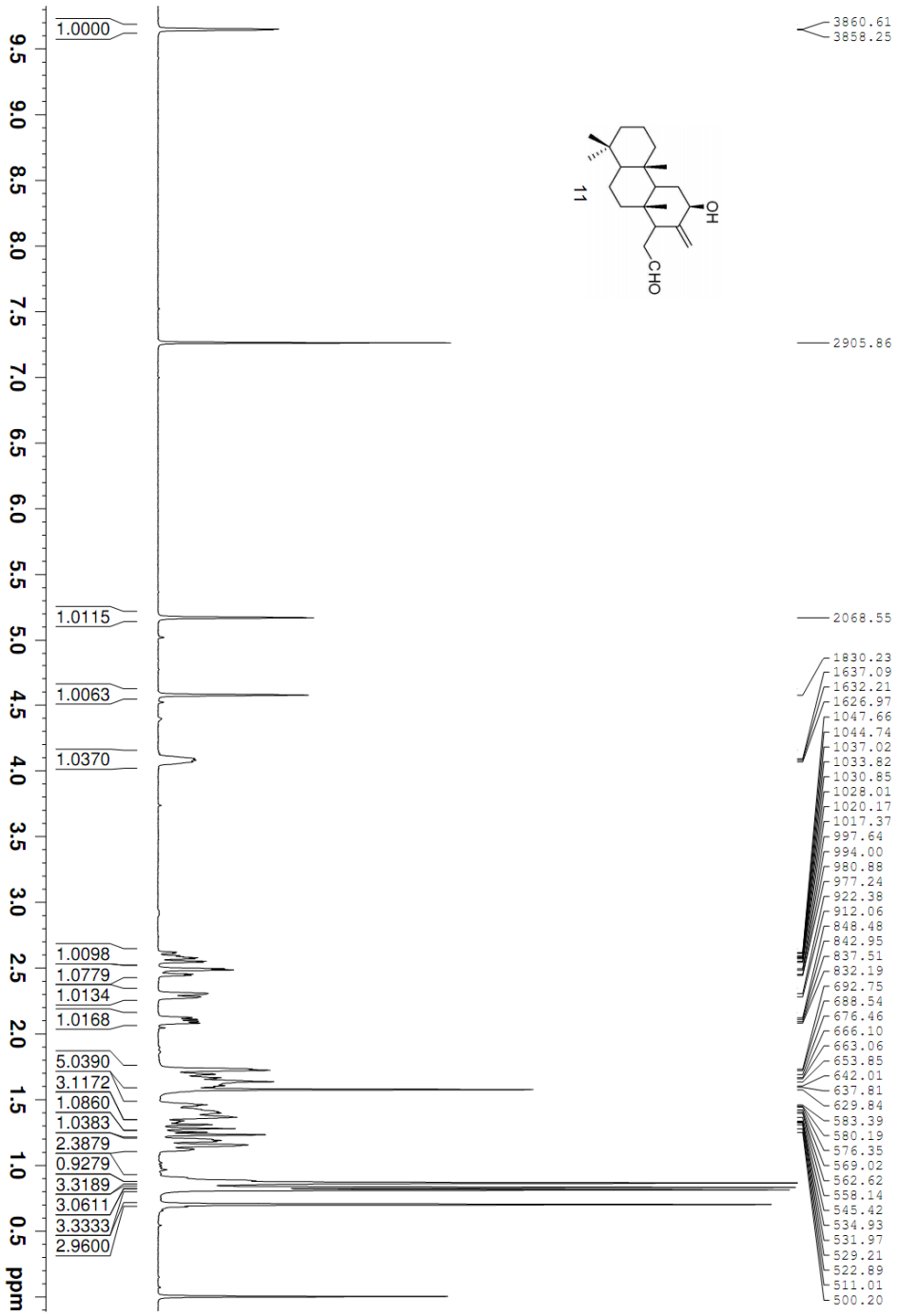
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1028.01
1020.17
1017.37
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994.00
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977.24
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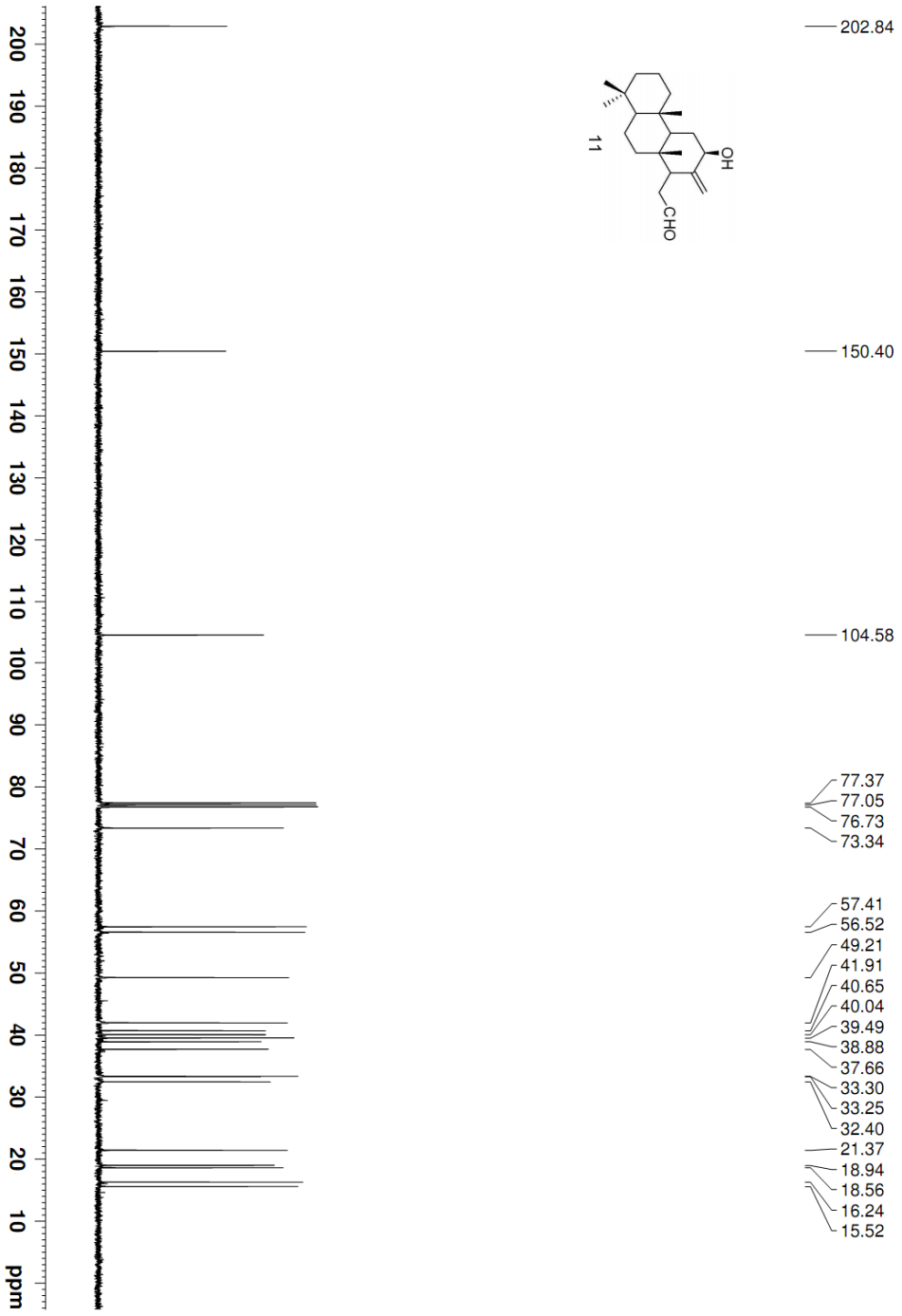
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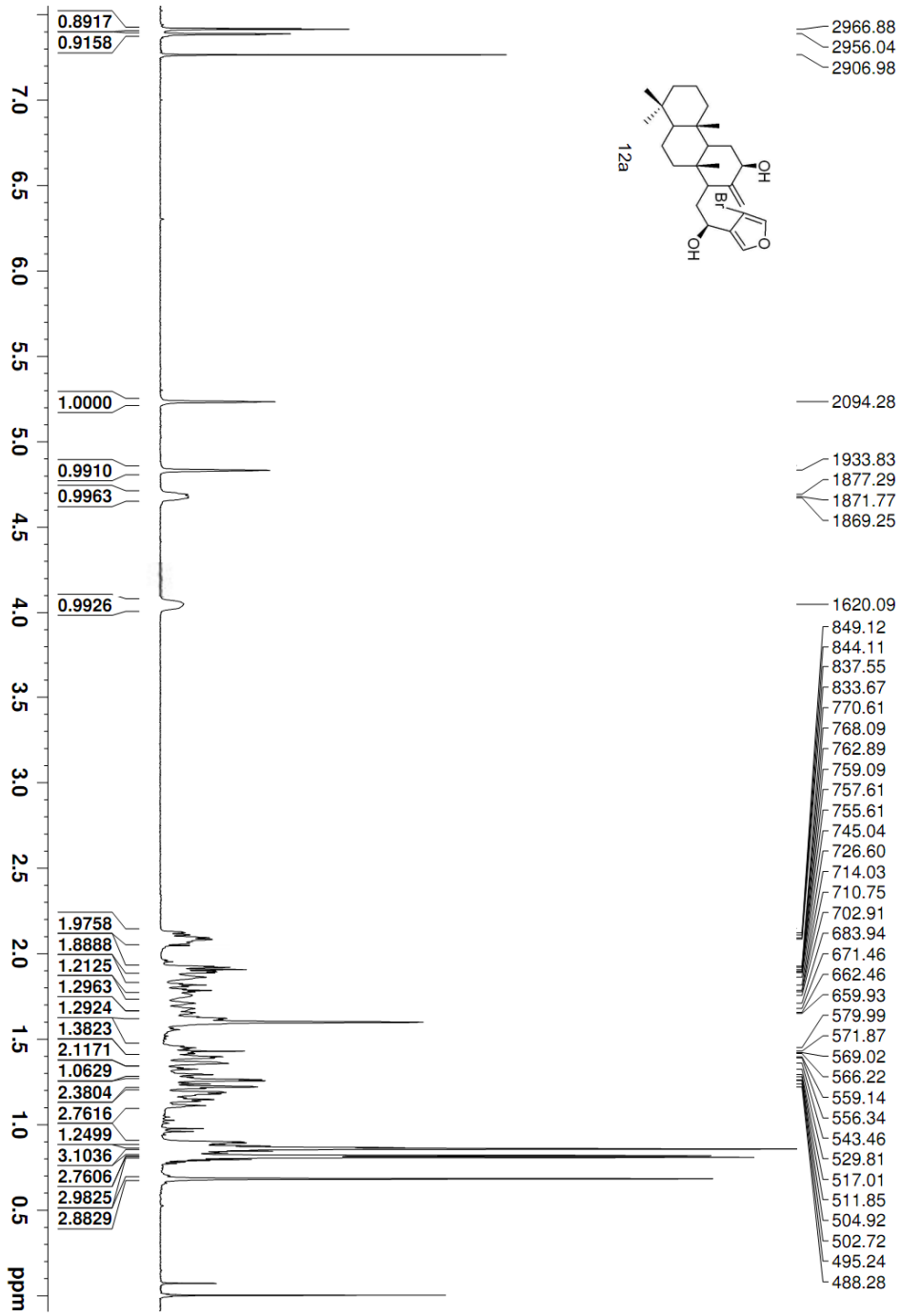
15.52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2.3804
2.7616
1.2499
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6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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12a
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Br
OH
O
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1869.25
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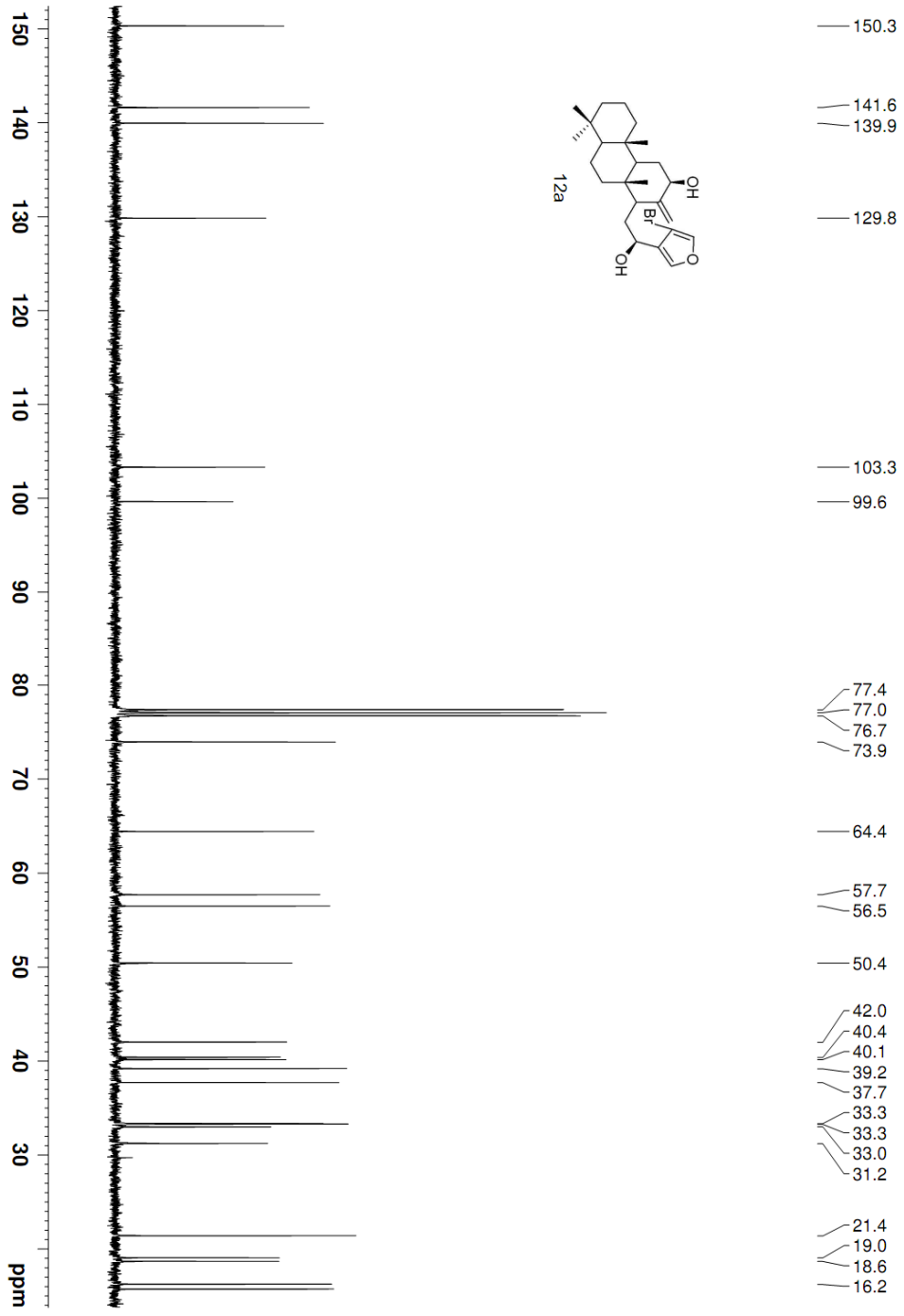
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42.0
40.4
40.1
39.2
37.7
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31.2
21.4
19.0
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16.2
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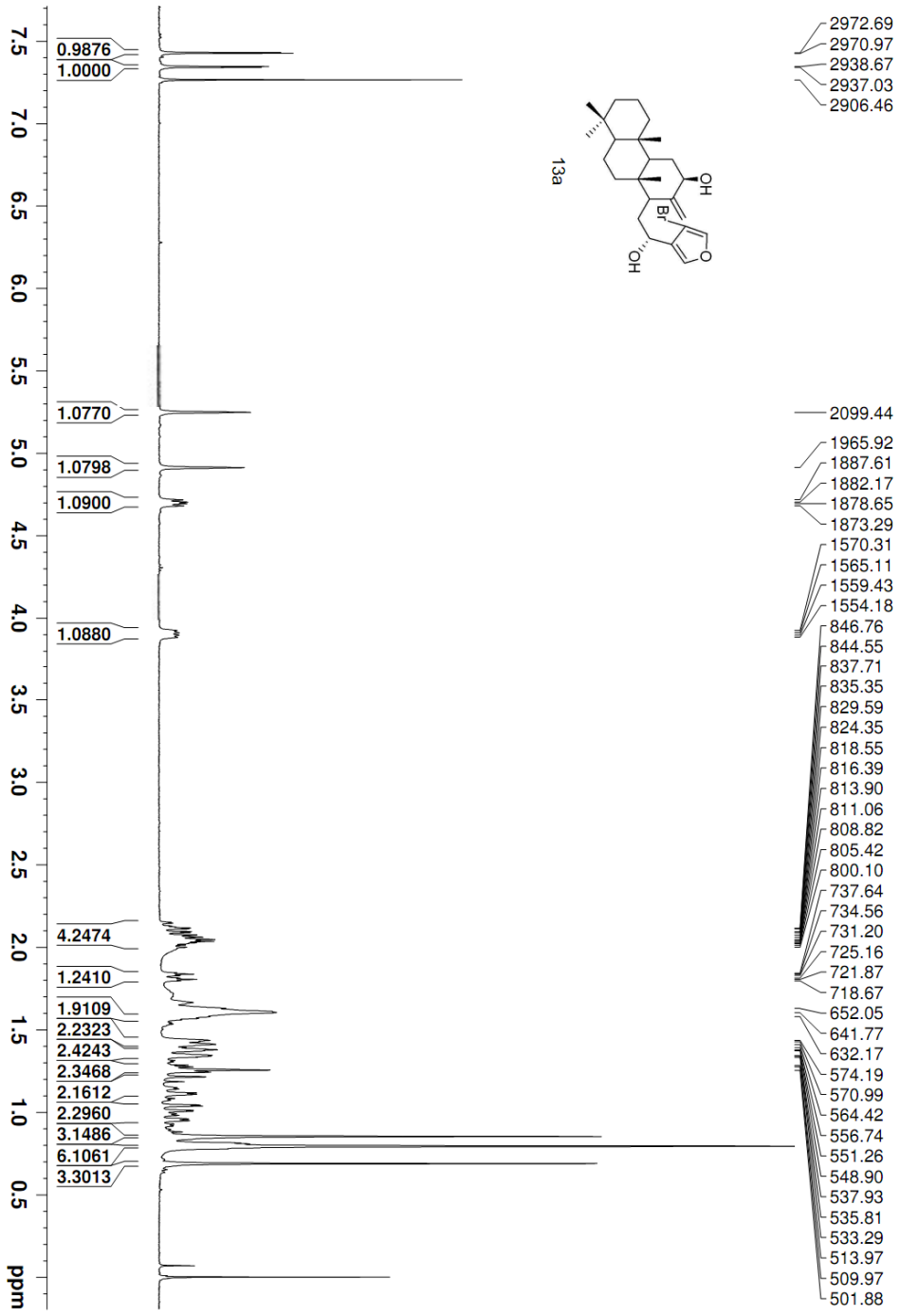
OH
Br
OH
O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Br
O
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1.9109
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2.4243
2.3468
2.1612
2.2960
3.1486
6.1061
3.3013
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2970.97
2938.67
2937.03
2906.46
2099.44
1965.92
1887.61
1882.17
1878.65
1873.29
1570.31
1565.11
1559.43
1554.18
846.76
844.55
837.71
835.35
829.59
824.35
818.55
816.39
813.90
811.06
808.82
805.42
800.10
737.64
734.56
731.20
725.16
721.87
718.67
652.05
641.77
632.17
574.19
570.99
564.42
556.74
551.26
548.90
537.93
535.81
533.29
513.97
509.97
501.88
7.5
7.0
6.5
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4.0
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2.0
1.5
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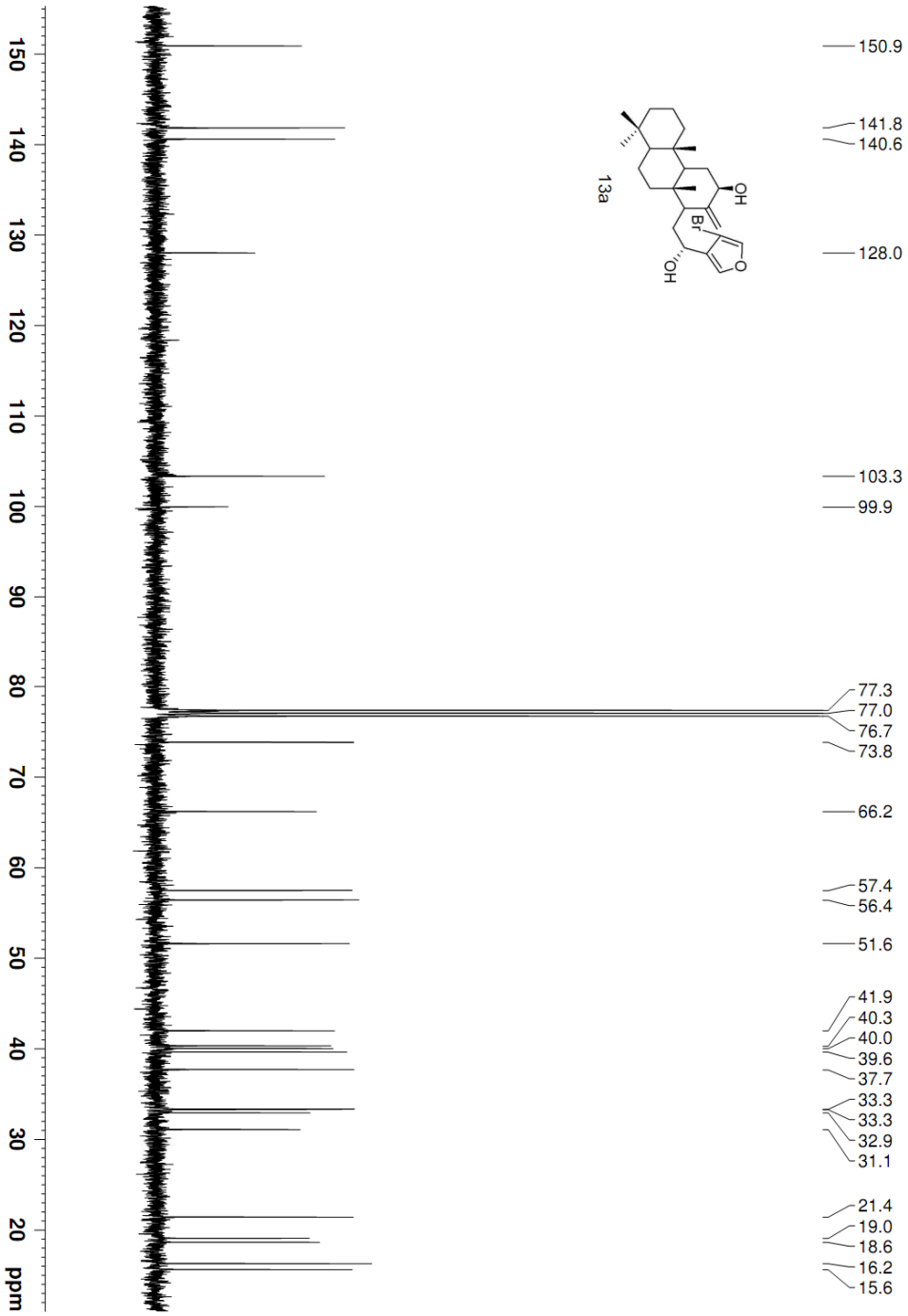
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41.9
40.3
40.0
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37.7
33.3
33.3
32.9
31.1
21.4
19.0
18.6
16.2
15.6
13a
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Br
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O
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140
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120
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100
90
80
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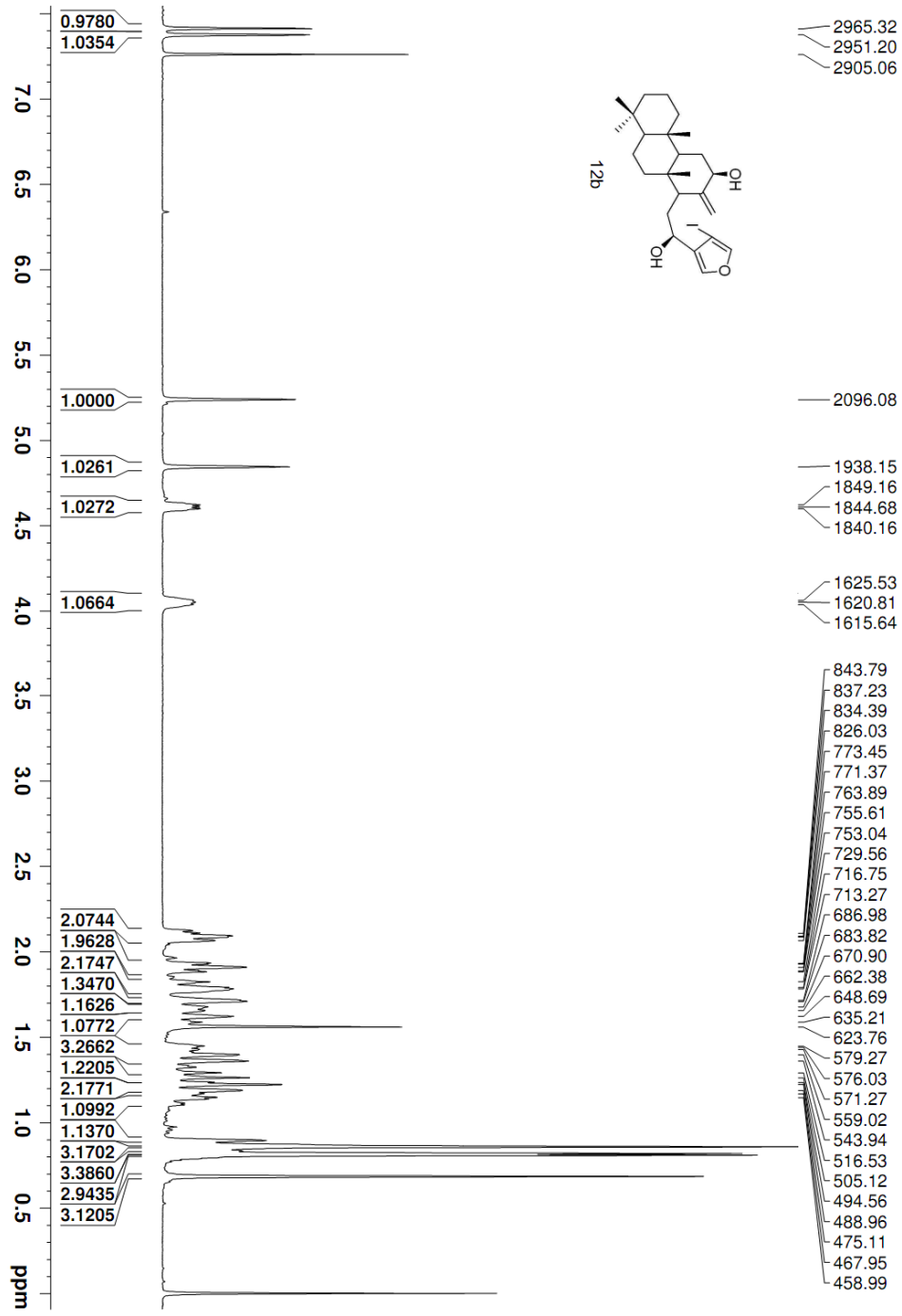
60
50
40
30
20
ppm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1.1370
3.1702
3.3860
2.9435
3.1205
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
12b
OH
OH
O
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2951.20
2905.06
2096.08
1938.15
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1844.68
1840.16
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1620.81
1615.64
843.79
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834.39
826.03
773.45
771.37
763.89
755.61
753.04
729.56
716.75
713.27
686.98
683.82
670.90
662.38
648.69
635.21
623.76
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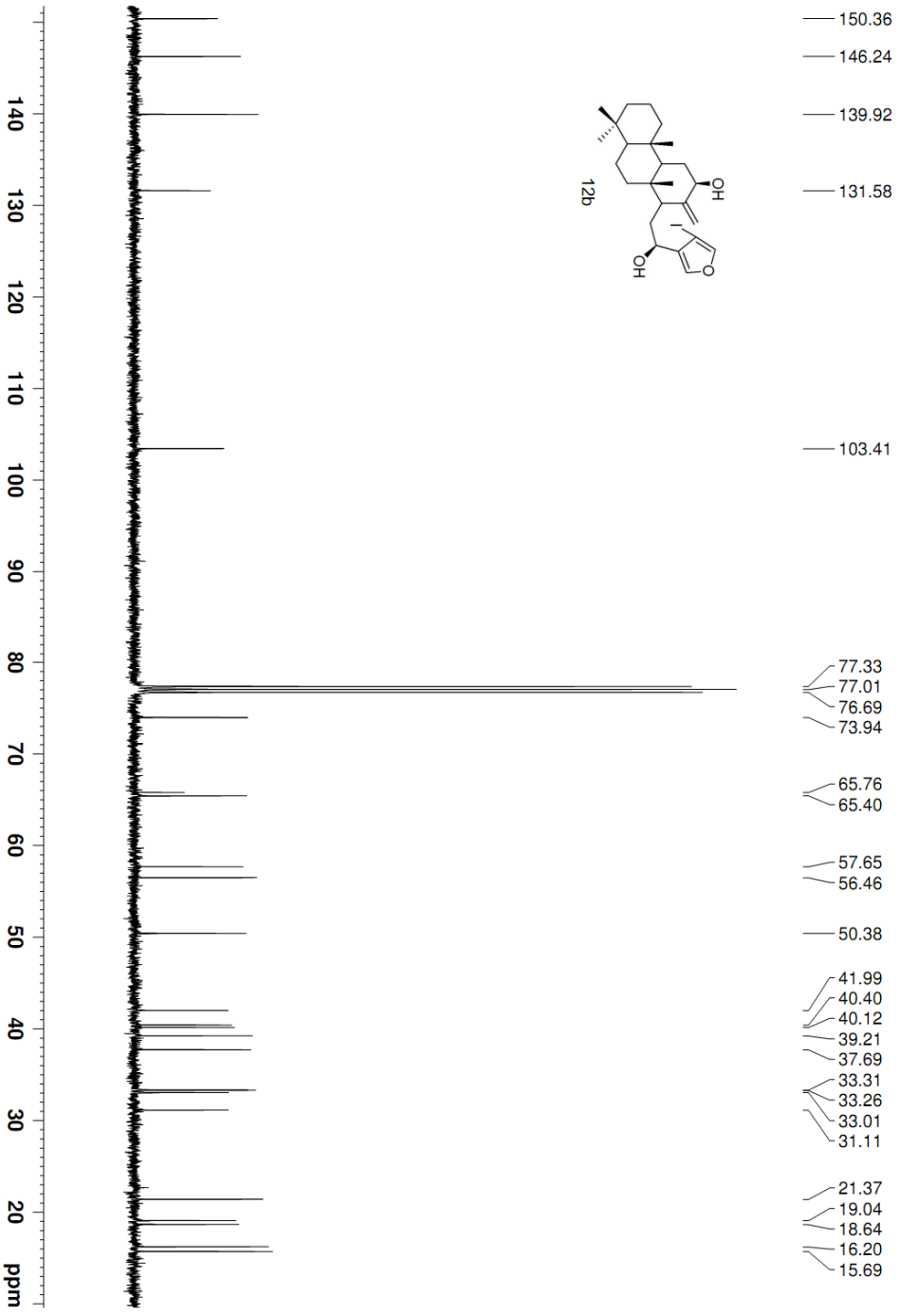
458.99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50.38
41.99
40.40
40.12
39.21
37.69
33.31
33.26
33.01
31.11
21.37
19.04
18.64
16.20
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OH
O
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130
120
110
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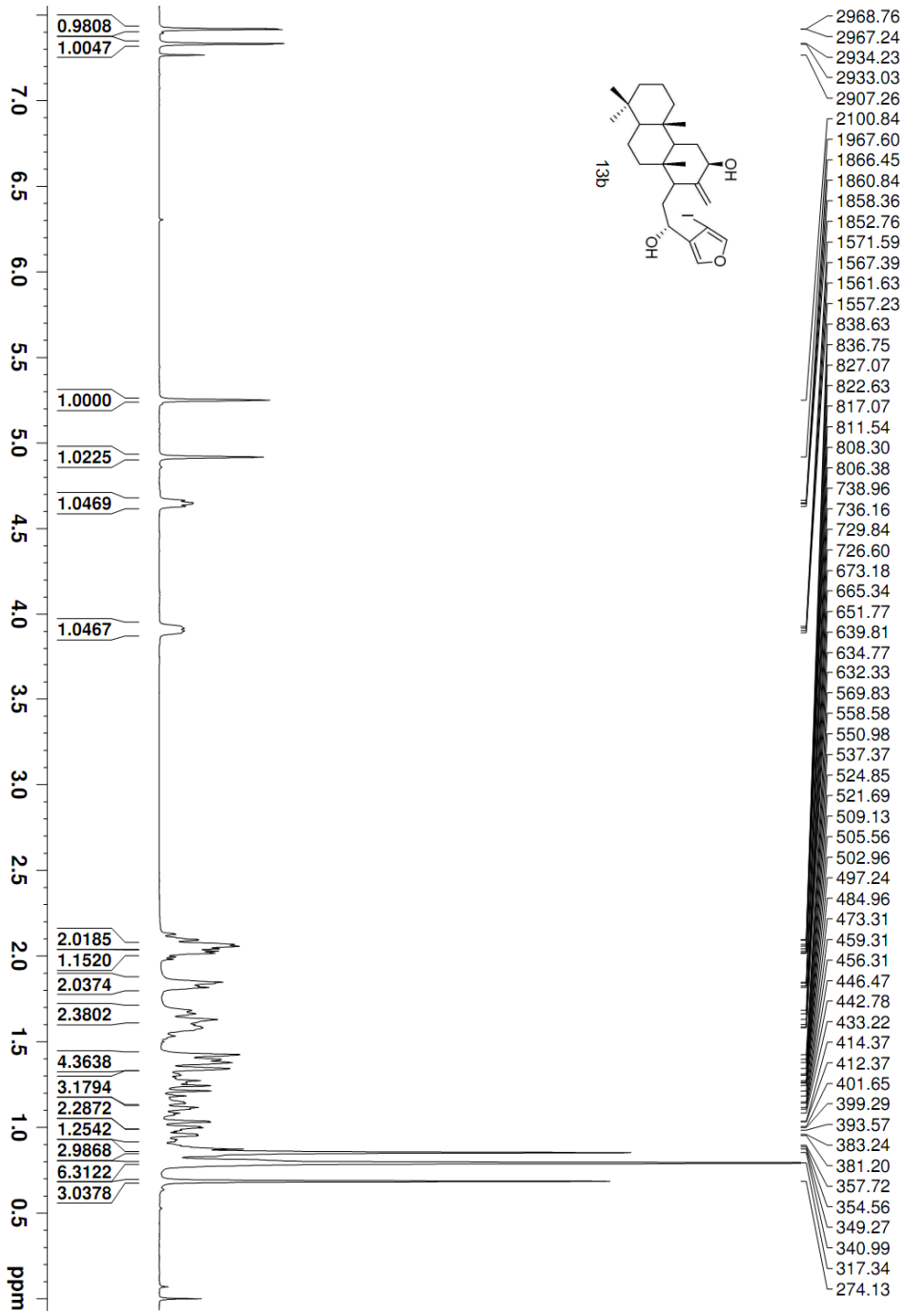
40
30
20
ppm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2.2872
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6.3122
3.0378
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6.5
6.0
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5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
13b
OH
OH
O
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2934.23
2933.03
2907.26
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1967.60
1866.45
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1858.36
1852.76
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1567.39
1561.63
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838.63
836.75
827.07
822.63
817.07
811.54
808.30
806.38
738.96
736.16
729.84
726.60
673.18
665.34
651.77
639.81
634.77
632.33
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558.58
550.98
537.37
524.85
521.69
509.13
505.56
502.96
497.24
484.96
473.31
459.31
456.31
446.47
442.78
433.22
414.37
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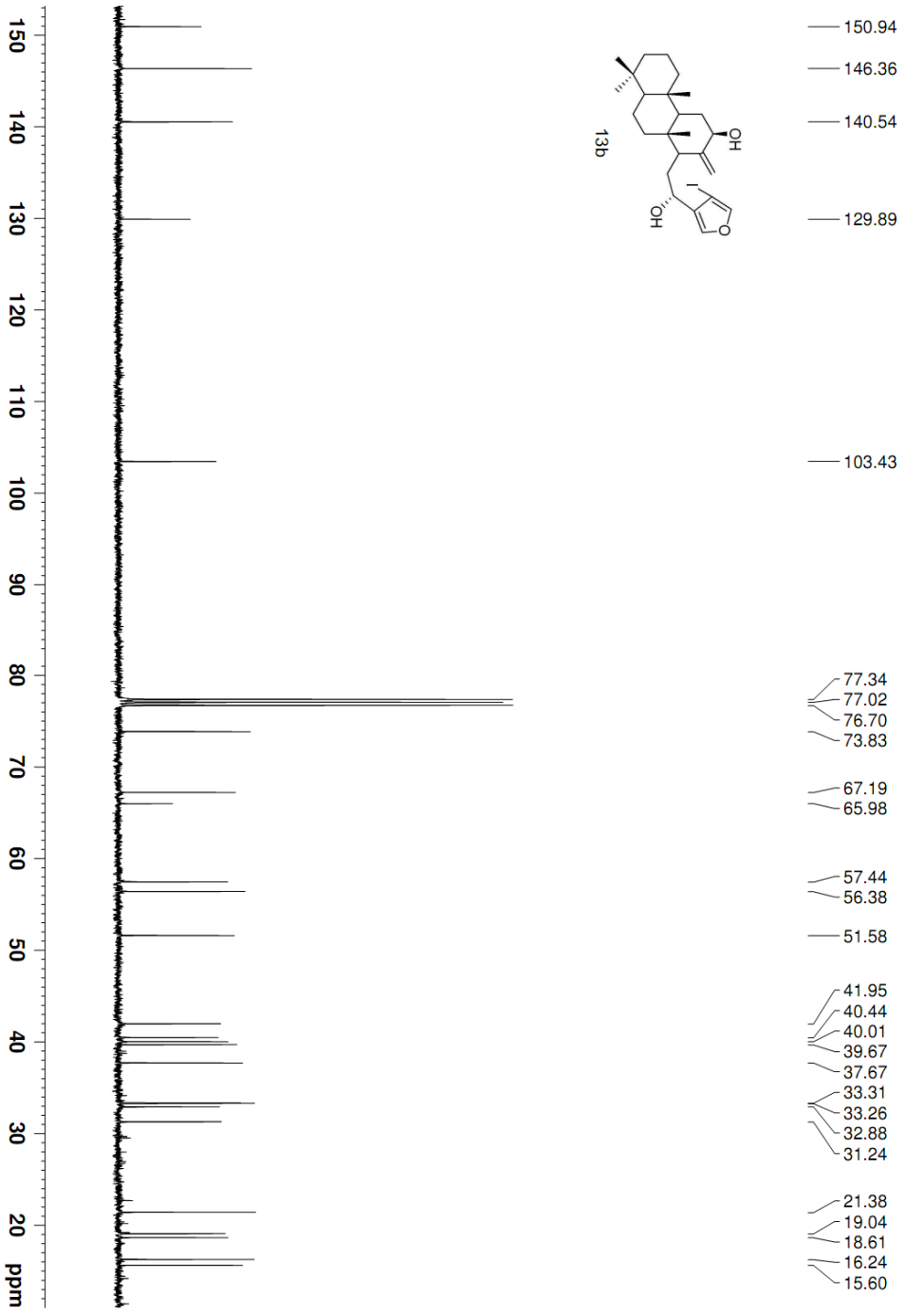
340.99
317.34
274.13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51.58
41.95
40.44
40.01
39.67
37.67
33.31
33.26
32.88
31.24
21.38
19.04
18.61
16.24
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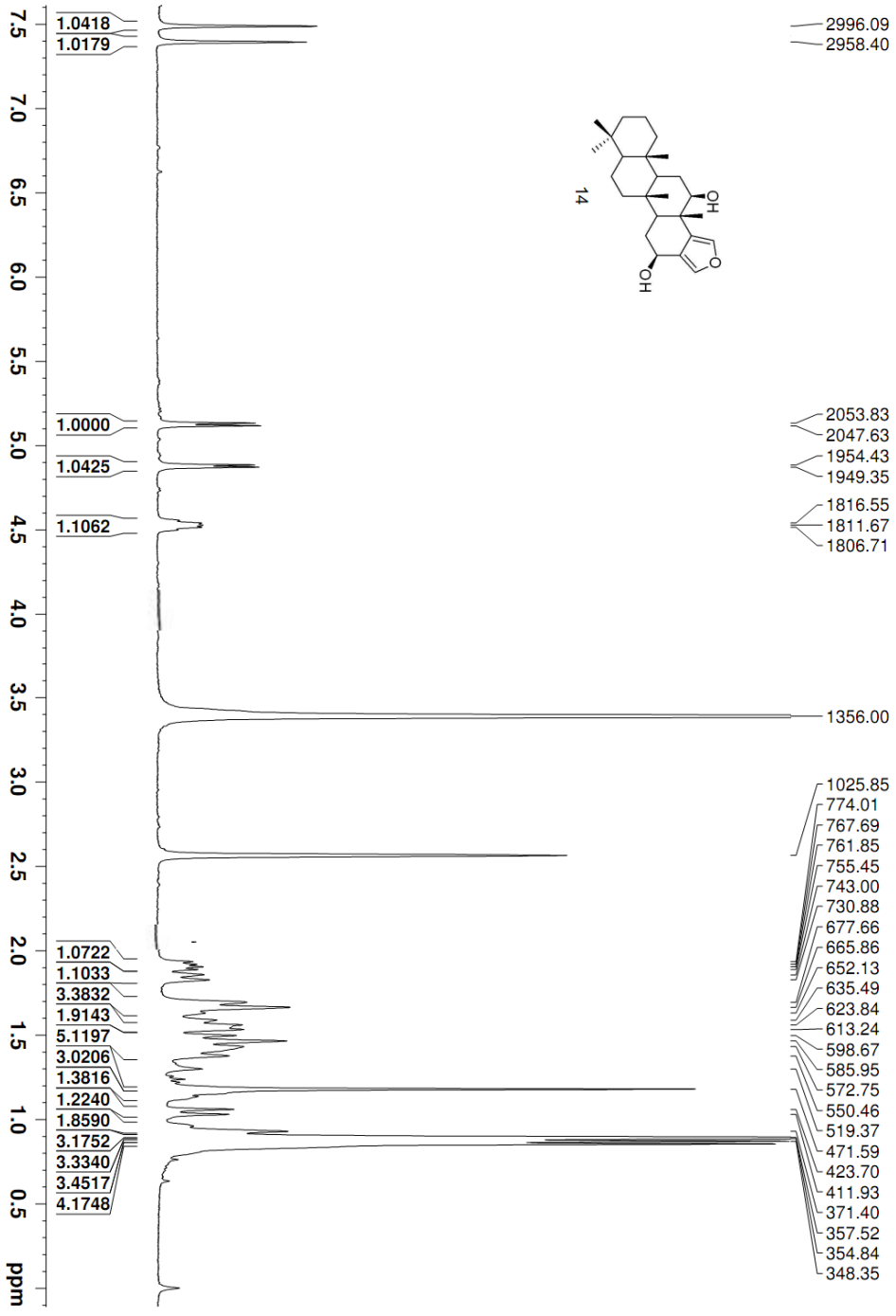
13b
OH
HO
O
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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4.0
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3.0
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2.0
1.5
1.0
0.5
ppm
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1.0722
1.1033
3.3832
1.9143
5.1197
3.0206
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1.2240
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3.4517
4.1748
2996.09
2958.40
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2047.63
1954.43
1949.35
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1806.71
1356.00
1025.85
774.01
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761.85
755.45
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677.66
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652.13
635.49
623.84
613.24
598.67
585.95
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371.40
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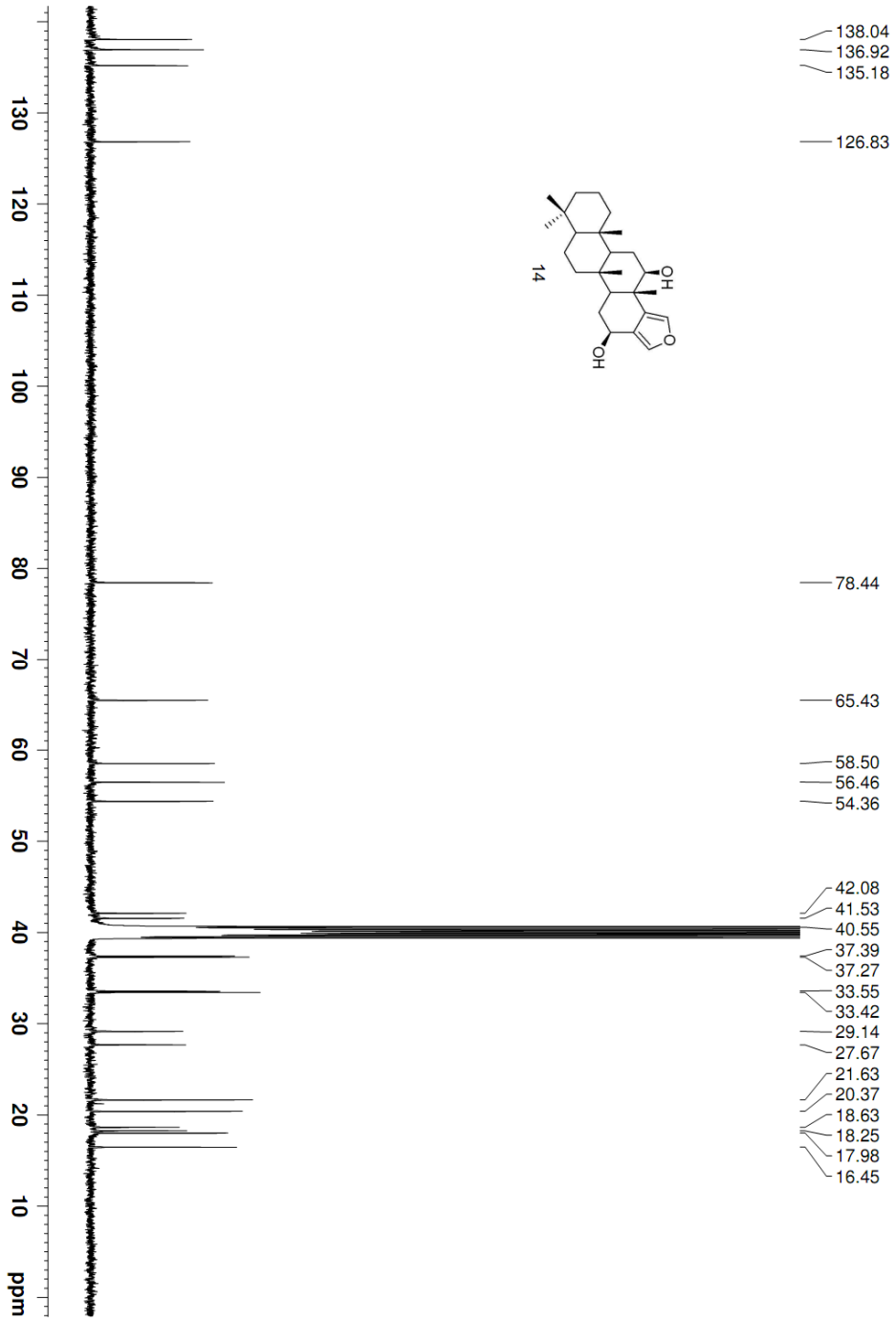
354.84
348.35
14
HO
HO
O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37.39
37.27
33.55
33.42
29.14
27.67
21.63
20.37
18.63
18.25
17.98
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14
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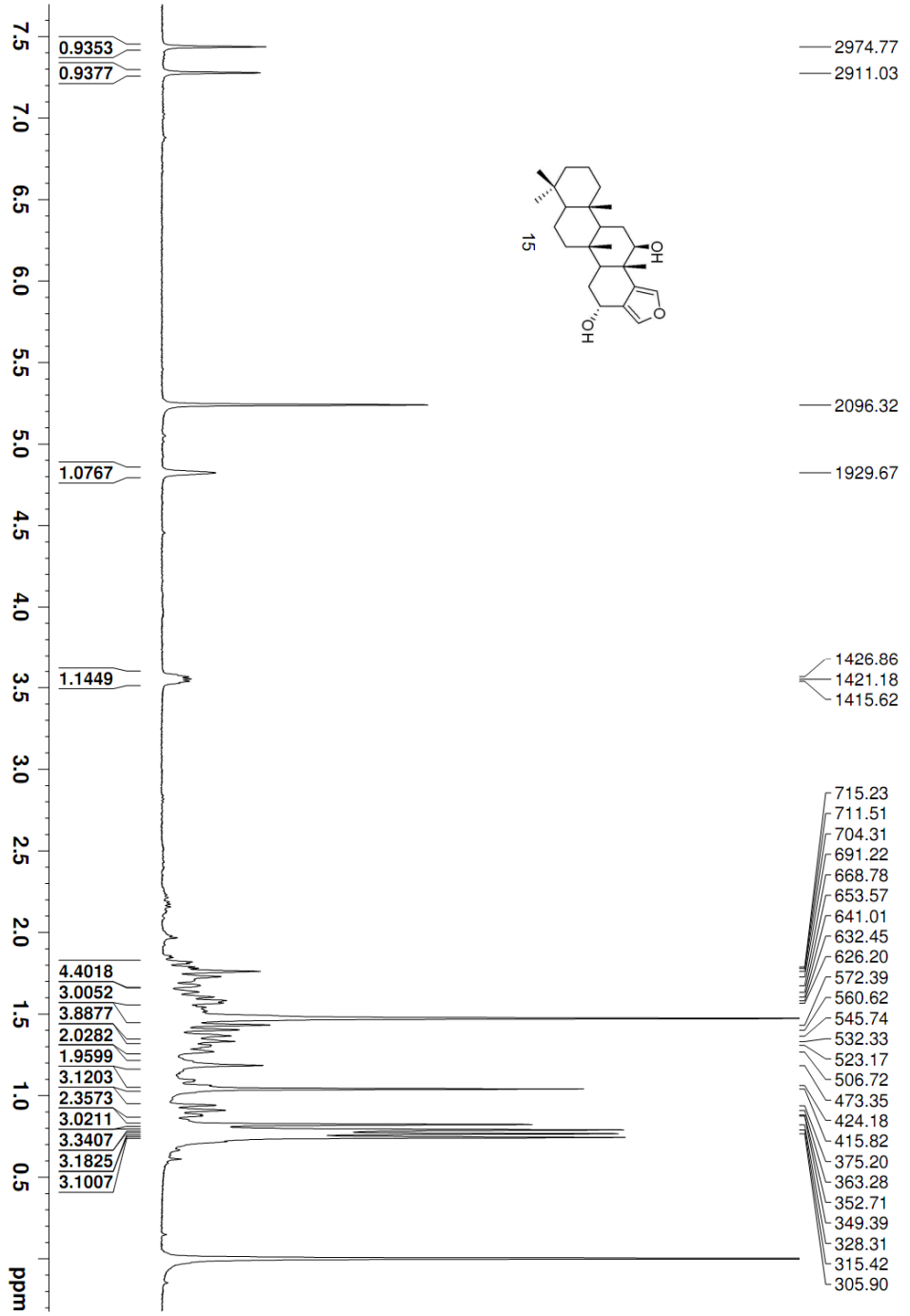
OH
O
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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3.3407
3.1825
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2974.77
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2096.32
1929.67
1426.86
1421.18
1415.62
715.23
711.51
704.31
691.22
668.78
653.57
641.01
632.45
626.20
572.39
560.62
545.74
532.33
523.17
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328.31
315.42
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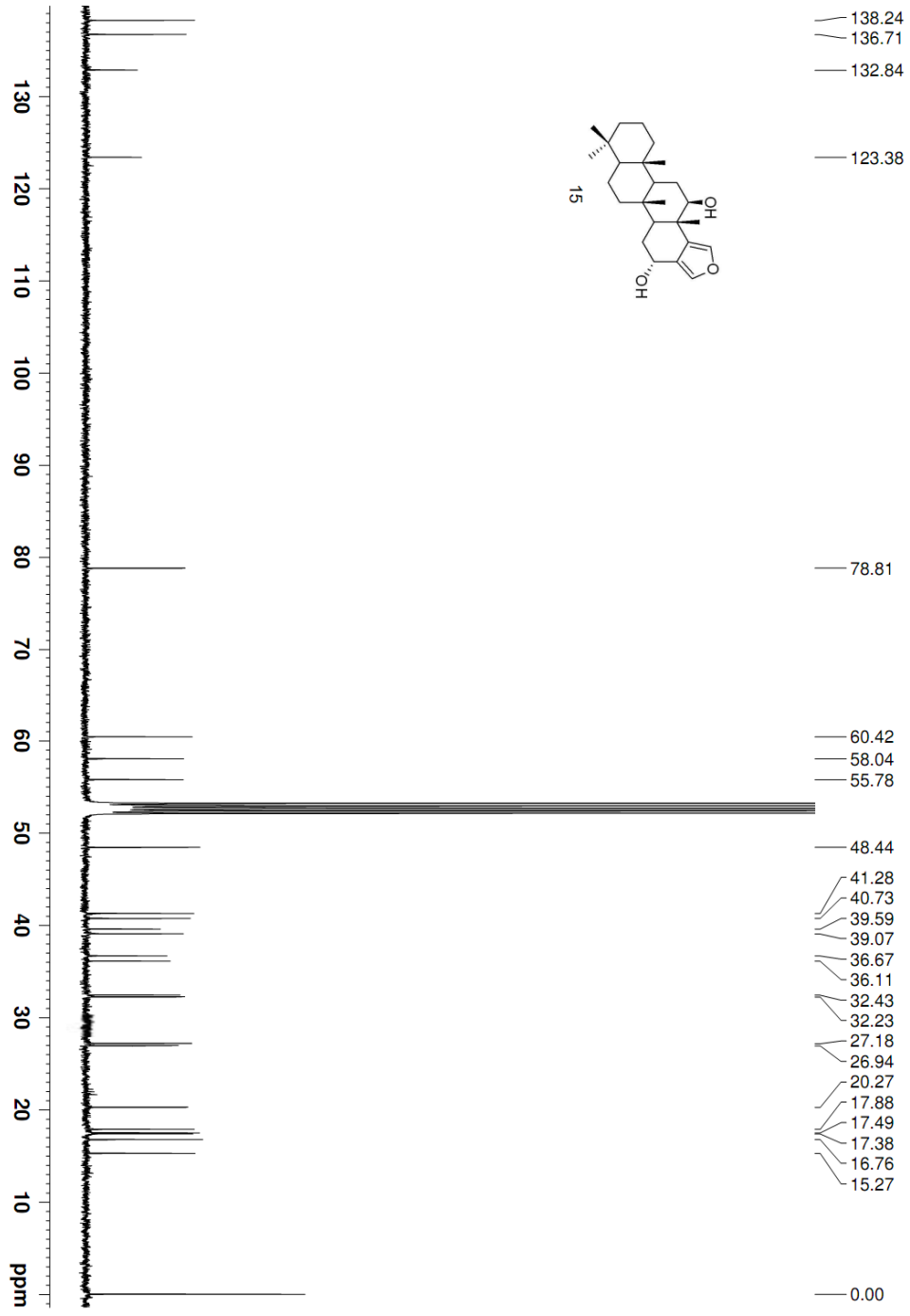
15
HO
HO
O
ppm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39.59
39.07
36.67
36.11
32.43
32.23
27.18
26.94
20.27
17.88
17.49
17.38
16.76
15.27
0.00
ppm
OH
OH
O
15