Electronic Supplementary Information (ESI)

Synthesis and Antioxidant Capacity of Novel Stable 5-Tellurofuranose Derivatives

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General Experimental Methods; Details of procedures used to determine rate constants; Experimental procedures for new compounds; ^{1}H and ^{13}C NMR spectra of compounds **1** to **7**.

General Experimental Methods.

^{1}H and ^{13}C NMR spectra were recorded at 500 or 400 MHz, and 125 MHz, respectively. ^{125}Te NMR spectra were recorded at 158 MHz. High-resolution ESI mass spectra were acquired on an Orbitrap Exactive Plus mass spectrometer (Thermo Fisher Scientific San Jose, CA). Parent ions are denoted as "$(M+H)^{+}$" or "$(M+Ag)^{+}$" when silver nitrate was used for sample ionization. Optical specific rotations $[\alpha]_D$ were measured using a Jasco DIP-1000 digital polarimeter at 20 °C, in a cell with a 1 dm path length; concentrations (c) are expressed in g/100 cm^3.

Analytical thin layer chromatography was performed using pre-coated 0.25 mm thick Merk 60 F_{254} silica gel plates. TLC plated were visualized thermally following immersion in an ethanolic solution of phosphomolybdic acid or sulfuric acid. Flash chromatography was carried out on silica gel [Merck Kieselgel 60 (230-400 mesh)] with nitrogen pressure.

Methods for determination of rate constants.

Scavenging of HOCl and HOBr by the Te-compounds was investigated using a competition kinetics approach in which oxidation of Fmoc-methionine (FmocMet) to Fmoc-methionine sulfoxide (FmocMetSO) was used as a reference reaction.[1] This method is based on the quantification of the loss of FmocMet (and decreased formation of FmocMetSO), using UPLC, in the presence of increasing concentrations of a competing target. FmocMet and FmocMetSO were quantified by fluorescence (λ_{ex} 340 nm, λ_{em} 440 nm), with the second order rate constant for this reaction, k_2 taken as 1.5 x 10^8 M^{-1} s^{-1}. [1] Fresh Fmoc-Met (5 μM) and Te-derivatives (0–50 μM in 10 mM phosphate buffer, pH 7.4) were mixed and treated with 2 μM HOCl/HOBr for 20 min at 21 °C, after which 6 μL of each sample was injected on to the UPLC column (Shimpack column XR-ODS, Shimadzu, 100 x 4.6 mm, 2.2. μm) at 40 °C, with the Fmoc-Met and Fmoc-Met-SO eluted using a gradient system as described previously[2] (buffer A: 5% of 1M sodium acetate, 2.5% THF, 20% MeOH and 72.5% water; buffer B: 5% of 1M sodium acetate, 2.5% THF, 80% MeOH and 12.5% water) and quantified by fluorescence. The rate constants for reaction of HOCl/HOBr with the Te compounds were calculated from the gradient of the resulting scavenger plots arising from the equation:

$$\frac{Y_{max}}{Y_{scav}} \cdot [FmocMet] = \frac{k_{scav}}{k_{FmocMet}} \cdot [scav] + [FmocMet]$$

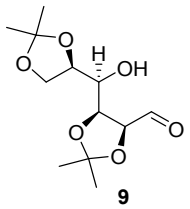
where Y_{max} and Y_{scav} correspond to the yield of FmocMetSO in the absence and presence of Te-compound, [FmocMet] and [scav] are the concentrations of FmocMet and added Te compound respectively, and $k_{FmocMet}$ is the rate constant for reaction of FmocMet with HOCl or HOBr.

Rate constants for reaction of ONOOH with the Te-compounds were determined by stopped-flow spectroscopy (Applied Photophysics), by monitoring the decay of ONOOH at 302 nm in the absence and presence of added Te compound as described previously.[3] Rate constants for the reactions of the Te sugars (0.2–3 mM) with ONOOH (200 μM) were determined by fitting exponential decay curves to the experimental data (8–10 measurements), with the resulting pseudo-first-order rate constants (k_{obs}) subsequently plotted against the Te-sugar concentration, to give the second order rate constant k_2.

References

1 C. Storkey, M. J. Davies and D. I. Pattison, *Free Radic Biol Med*, 2014, **73**, 60.
2 D. I. Pattison and M. J. Davies, *Biochemistry*, 2004, **43**, 4799
3 C. Storkey, D. I. Pattison, M. T. Ignasiak, C. H. Schiesser and M. J. Davies, *Free Radic Biol Med*, 2015, **89**, 1049.

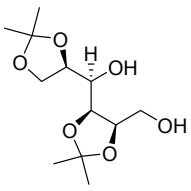
Standard procedure A: 2,3,4,6-Di-isopropylidene-1,5-di-*O*-hydroxy-D-mannitol (9)



9

To a suspension of D-mannose (10 g, 55.5 mmol) and *p*-toluenesulfonic acid monohydrate (1.06 g, 5.55 mmol) in anhydrous acetone (200 mL) at 0 ^{o}C was added 2,2-dimethoxypropane (50 mL, 406 mmol) dropwise over 30 minutes. The suspension was allowed to warm to room temperature and stirred for 18h. The resulting pale yellow solution was quenched by the addition of $NaHCO_3$ (2 g). Filtration and removal of the solvent in vacuo gave a yellow oil which was partitioned between EtOAc (150 mL) and H_2O (150 mL). The organic layer was separated and the aqueous phase was extracted with EtOAc (3 x 80 mL). The combined organic extracts washed with brine (2 x 80 mL), dried over $MgSO_4$ and evaporated in vacuo to give a pale yellow solid which was recrystallized from EtOAc and petroleum ether (Pet) to give compound **9** as a white powder (8.25 g, 85%). R_f 0.21 (EtOAc:Pet 2:8); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.35 (d, *J*= 2.6 Hz, 1H), 4.78 (dd, *J*= 5.9, 3.7 Hz, 1H), 4.58 (d, *J*= 5.9 Hz, 1H), 4.38 (ddd, *J*= 6.9, 6.2, 4.9 Hz, 1H), 4.15 (dd, *J*= 7.1, 3.6 Hz, 1H), 4.07-4.02 (m, 2H), 3.62-3.60 (m, 1H), 1.44 (s, 3H), 1.43 (s, 3H), 1.35 (s, 3H), 1.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 112.7, 109.2, 101.3, 85.6, 80.2, 79.7, 73.4, 66.6, 26.9, 25.9, 25.2, 24.5; HRMS (ESI$^+$) 261.13328 (261.13326 $[M + H]^+$ calc. for $C_{12}H_{21}O_6$).

Standard procedure B: 2,3;5,6-Di-isopropylidene-1,4-di-*O*-hydroxy-D-mannitol (10)

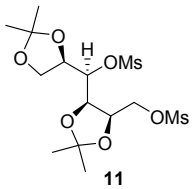


10

To a solution of compound **9** (8.25 g, 31.6 mmol) in CH_3OH (180 mL) at 0 ºC was added $NaBH_4$ (1.70 g, 45 mmol) portion wise. After stirring at room temperature for 16h, the solvent was removed in vacuo and the resulting residue was taken up in EtOAc (180 mL) and washed with H_2O (2 x 80 mL). The organic layer was collected, dried over $MgSO_4$, evaporated under reduced pressure and purified by flash column chromatography (30%, 40%, 50% EtOAc/Pet) to afford the compound (**10**) as a white solid (7.65 g, 90%). R_f 0.38 (EtOAc:Pet 40%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.39 (dd, *J*= 7.3, 1.6 Hz, 1H), 4.31 (dt, *J*=

7.3, 4.5 Hz, 1H), 4.12 (dd, *J*= 8.0, 5.8 Hz, 1H), 4.08-4.00 (m, 2H), 3.92-3.79 (m, 2H), 3.58 (ddd, *J*= 7.8, 6.3, 1.5 Hz, 1H), 3.10 (d, *J*= 6.3 Hz, 1H), 2.64 (t, *J*= 6.1 Hz, 1H), 1.52 (s, 3H), 1.41 (s, 3H), 1.40 (s, 3H), 1.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 109.6, 108.5, 77.4, 76.2, 75.8, 70.4, 67.8, 61.2, 26.94, 26.92, 25.4, 24.9; HRMS (ESI^+) 263.14882 (263.14891 $[M + H]^+$ calc. for $C_{12}H_{23}O_6$).

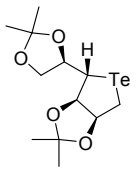
Standard procedure C: 2,3;5,6-Di-isopropylidene-1,4-bis(methanesulfonyl)-D-mannitol (11)



11

To diol **10** (7.65 g, 29.1 mmol) in CH_2Cl_2 (180 mL) at 0 ºC was added NEt_3 (12.2 mL) followed by methanosulfonyl chloride (6.8 mL, 88.1 mmol). After stirring at 0 ºC for 20 min, the ice bath was removed and the reaction mixture was stirred for 1h at room temperature. The reaction mixture was quenched with H_2O (80 mL), extracted with CH_2Cl_2 (2 x 80 mL), dried and evaporated under reduced pressure to give a yellow residue. This crude material was purified by flash column chromatography (40% EtOAc/Pet) to afford the compound **11** as a clear yellow syrup (11.2 g, 82%). R_f 0.68 (EtOAc:Pet 40%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.76 (t, *J*= 7.4 Hz, 1H), 4.48-4.35 (m, 4H), 4.23-4.10 (m, 2H), 4.02 (dd, *J*= 8.1, 6.6 Hz, 1H), 3.14 (s, 3H), 3.09 (s, 3H), 1.53 (s, 3H), 1.45 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 110.8, 109.9, 78.8, 76.9, 75.1, 75.0, 68.0, 67.4, 39.4, 37.8, 27.4, 26.2, 25.9, 25.3. HRMS (ESI^+) 419.10387 (419.10401 $[M + H]^+$ calc. for $C_{14}H_{27}O_{10}S_2$).

Standard procedure D: 2,3;5,6-Di-isopropylidene-1,4-anhydro-4-telluro-D-talitol (12)

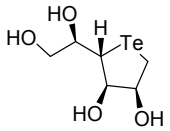


12

To a stirred suspension of tellurim powder (0.0974 g, 0.75 mmol) in PEG-400 (5 mL) under a steady flow of N_2 at room temperature was added $NaBH_4$ (0.076 g, 2 mmol) and the mixture was stirred at 55 ºC until the black coloured suspension had turned clear (approx. 50 min). The dimesylate (**11**) (0.2405 g, 0.5 mmol) was then added and stirred at 55 ºC for an additional 1 h. The reaction mixture was diluted with EtOAc (30 mL) and washed with H_2O

(20 mL). The aqueous phase was further extracted with EtOAc (20 mL) and the combined organic phases were washed with brine (2 x 30 mL), dried over $MgSO_4$ and evaporated under reduced pressure to give an orange residue. This crude material was purified by flash column chromatography (20% EtOAc/Pet) to afford the compound (**12**) as a yellow solid (0.1163 g, 65%). R_f 0.55 (EtOAc:Pet 20%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.98-4.94 (m, 1H), 4.55 (t, *J*= 5.5 Hz, 1H), 4.18 (t, *J*= 5.5 Hz, 1H), 4.15-4.10 (m, 2H), 3.69-3.65(m, 1H), 3.38 (dd, *J*= 11.4, 6.2 Hz, 1H), 3.30 (dd, *J*= 11.4, 4.4 Hz, 1H), 1.52 (s, 3H), 1.45 (s, 3H), 1.33 (s, 3H), 1.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 111.1, 109.4, 90.4, 87.1, 79.2, 70.5, 36.6, 27.7, 26.7, 25.6, 25.1, 6.3; HRMS (ESI$^+$) calculated for $C_{12}H_{20}O_4TeAg$ 464.94693 $[M + Ag]^+$, found 464.94649.

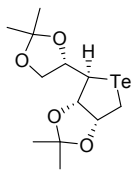
Standard procedure E: 1,4-Anhydro-4-telluro-D-talitol (1)



1

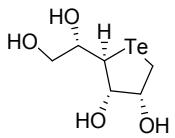
To the bis-acetonide **12** (0.3580 g, 1 mmol) in CH_2Cl_2 (4 mL) at 0 ºC was added H_2O (0.2 mL) followed by trifluoric acid (0.2 mL). The solution was stirred at room temperature for 1h. The reaction mixture was quenched by the addition of $NaHCO_3$ until the pH turned between 6–7. This crude material was filtered, dried over $MgSO_4$ and the solvent was removed. The resulting residue was purified by flash column chromatography (EtOAc/MeOH 4:1) to afford the compound (**1**) as a yellow solid (0.1474 g, 53%). R_f 0.50 (EtOAc:MeOH 4:1); $[\alpha]_D^{20}$ – 42.09 (*c* 1, MeOH); ^{1}H NMR (CD_3OD, 400 MHz) δ 4.51 (q, *J*= 3.5 Hz, 1H), 4.06 (dd, *J*= 8.5, 5.4 Hz, 1H), 3.98 (dd, *J*= 8.5, 2.8 Hz, 1H), 3.63-3.58 (m, 1H), 3.52 (dd, *J*= 11.2, 4.9 Hz, 1H), 3.45 (dd, *J*= 11.2, 5.2 Hz, 1H), 3.23 (dd, *J*= 10.7, 4.4 Hz, 1H), 2.80 (dd, *J*= 10.7, 3.4 Hz, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ 111.1, 109.4, 90.4, 87.1, 79.2, 70.5, 36.6, 27.7, 26.7, 25.6, 25.1, 6.3; ^{125}Te NMR (CD_3OD, 158 MHz) δ 201.8; HRMS (ESI$^+$) m/z 276.9885 (276.9858 calcd. for $C_6H_{13}O_4Te$).

Synthesis of 2,3;5,6-Di-isopropylidene-1,4-anhydro-4-telluro-L-talitol



The title compound was prepared following standard procedures A, B, C and D starting with L-mannose. Yellow solid (0.1163 g, 65%). R_f 0.55 (EtOAc:Pet 20%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.93-4.90 (m, 1H), 4.51 (t, *J*= 5.5 Hz, 1H), 4.13 (t, *J*= 5.4 Hz, 1H), 4.11-4.06 (m, 2H), 3.63 (td, *J*= 8.9, 4.9 Hz, 1H), 3.33 (dd, *J*= 11.3, 6.2 Hz, 1H), 3.25 (dd, *J*= 11.3, 4.3 Hz, 1H), 1.47 (s, 3H), 1.41 (s, 3H), 1.28 (s, 3H), 1.25 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 111.0, 109.4, 90.3, 87.0, 79.1, 70.4, 36.5, 27.7, 26.6, 25.5, 25.1, 6.3; HRMS (ESI$^+$) calculated for $C_{12}H_{20}O_4TeAg$ 464.94693 [M + Ag]$^+$, found 464.94632.

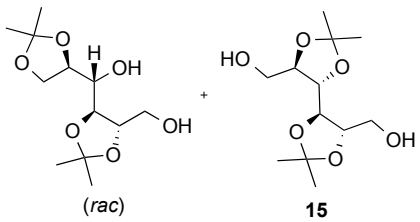
Synthesis of 1,4-anhydro-4-telluro-L-talitol (2)



2

The compound **2** was prepared from 2,3;5,6-Di-isopropylidene-1,4-anhydro-4-telluro-L-talitol using standard procedure E. Yellow solid; R_f 0.50 (EtOAc:MeOH 4:1); Yield: 0.1529 g (57%) $[\alpha]_D^{20}$ + 35.66 (*c* 1, MeOH); ^{1}H NMR (CD_3OD, 400 MHz) δ 4.51 (q, *J*= 3.5 Hz, 1H), 4.06 (dd, *J*= 8.5, 5.4 Hz, 1H), 3.98 (dd, *J*= 8.5, 2.8 Hz, 1H), 3.63-3.58 (m, 1H), 3.52 (dd, *J*= 11.2, 4.9 Hz, 1H), 3.45 (dd, *J*= 11.2, 5.2 Hz, 1H), 3.23 (dd, *J*= 10.7, 4.4 Hz, 1H), 2.80 (dd, *J*= 10.7, 3.4 Hz, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ 111.1, 109.4, 90.4, 87.1, 79.2, 70.5, 36.6, 27.7, 26.7, 25.6, 25.1, 6.3; HRMS (ESI$^+$) calculated for $C_6H_{12}O_4TeAg$ 384.88433 [M + Ag]$^+$, found 384.88354.

2,3;5,6-Di-isopropylidene-1,4-di-*O*-hydroxy-D-galactitol (14) and 2,3;4,5-di-isopropylidene-1,6-di-hydroxy-D,L-galactiol (15)

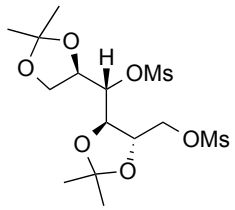


14 **15**

Dulcitol (**13**) (10 g, 55 mmol), anhydrous $CuSO_4$ (16.9 g, 105.6 mmol) and conc. H_2SO_4 (0.2 mL) in anhydrous acetone (180 mL) were stirred vigorously for 8 days at room temperature, after which time the reaction was filtered. The filtered was neutralized with K_2CO_3 (10 g) and

stirred for 1h, filtered again and cooled to help deposit the first crop of crop of crystals which were collected to give compound **14** as a white solid (2.92 g, 20%). The mother liquor was then reduced to half its volume and cooled again to give the symmetrical diol **15** as a white solid (2.62 g, 18%). Compound **14**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.25 (td, *J*= 6.5, 4.8 Hz, 1H), 4.08 (ddd, *J*= 9.5, 8.1, 5.6 Hz, 2H), 3.92 (dd, *J*= 8.6, 6.4 Hz, 1H), 3.83-3.78 (m, 2H), 3.73 (dd, *J*= 8.6, 7.8 Hz, 1H), 3.53-3.48 (m, 1H), 2.64 (d, *J*= 5.6 Hz, 1H), 2.53 (dd, *J*= 7.7, 4.9 Hz, 1H), 1.45 (s, 3H), 1.40 (s, 3H), 1.38 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 109.52, 109.50, 81.2, 78.6, 76.6, 73.4, 66.4, 63.2, 27.2, 27.0, 26.7, 25.3; HRMS (ESI$^+$) 263.14887 (263.14891 [M + H]$^+$ calc. for $C_{12}H_{23}O_6$). Compound (**15**): ^{1}H NMR($CDCl_3$, 500 MHz) δ 4.07 (ddd, *J*= 9.5, 4.4, 2.1 Hz, 2H), 3.88-3.71 (m, 6H), 2.26 (dd, *J*= 8.8, 4.2 Hz, 2H), 1.42 (s, 6H), 1.39 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 110.1, 81.4, 79.0, 62.6, 27.1, 27.0; HRMS (ESI$^+$) 263.14888 (263.14891 [M + H]$^+$ calc. for $C_{12}H_{23}O_6$).

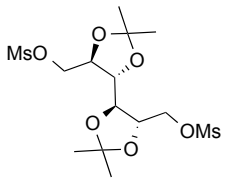
2,3;5,6-Di-isopropylidene-1,4-bis(methanesulfonyl)-D-galactitol (16)



16

Compound **16** was prepared using standard procedure C. Diol **14** (1.46 g, 5.5 mmol), Et_3N (2.3 mL, 16.5 mmol), MsCl (1.3 mL, 16.5 mmol) and CH_2Cl_2 (70 mL) followed by column chromatography (EtOAc/Pet 40%) afforded compound (**16**) as a clear yellow syrup (2.07 g, 90%). R_f 0.37 (EtOAc:Pet 10%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.70 (dd, *J*= 7.4, 5.5 Hz, 1H), 4.54 (dd, *J*= 11.1, 2.1 Hz, 1H), 4.44-4.37 (m, 2H), 4.29 (dd, *J*= 12.1, 6.1 Hz, 1H), 4.12 (dd, *J*= 9.2, 6.6 Hz, 1H), 4.03 (dt, *J*= 9.1, 6.8 Hz, 2H), 3.18 (s, 3H), 3.06 (s, 3H), 1.45 (s, 3H), 1.43 (s, 6H), 1.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 110.9, 110.1, 82.0, 77.2, 76.2, 75.7, 74.7, 69.1, 66.1, 39.3, 37.7, 27.0, 26.9, 26.3, 25.5; HRMS (ESI$^+$) 419.10400 (419.10401 [M + H]$^+$ calc. for $C_{14}H_{27}O_{10}S_2$).

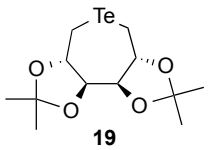
2,3;5,6-Di-isopropylidene-1,6-bis(methanesulfonyl)-galactitol (18)



17

Compound **17** was prepared using standard procedure C. Diol **15** (1.31 g, 4.93 mmol), Et_3N (2.1 mL, 14.8 mmol), MsCl (1.2 mL, 14.8 mmol) and CH_2Cl_2 (65 mL) followed by column chromatography (40, 50, 60% gradient, EtOAc/Pet) afforded compound **18** as a clear yellow solid (1.83 g, 89%). R_f 0.37 (EtOAc:Pet 40%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.51 (dd, J= 11.3, 2.4 Hz, 2H), 4.32 (dd, J= 11.3, 5.3 Hz, 1H), 4.21 (ddd, J= 7.6, 5.2, 2.3 Hz, 1H), 3.83-3.71 (m, 2H), 3.70 (s, 6H), 1.42 (s, 6H), 1.39 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 111.2, 78.8, 77.5, 68.7, 37.9, 27.1, 27.0; HRMS (ESI$^+$) 419.10405 (419.10401 $[M + H]^+$ calc. for $C_{14}H_{27}O_{10}S_2$).

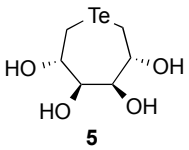
2,3;4,5-Di-O-isopropylidene-1,6-anhydro-6-tellurogalactitol (19)



19

Compound **19** was prepared using standard procedure D. Tellurium powder (0.0974 g, 0.75 mmol), $NaBH_4$ (0.076 g, 2 mmol), dimesylate (**16**) (0.2090 g, 0.5 mmol) in PEG-400 (5 mL) followed by column chromatography (EtOAc/Pet 20%) afforded compound (**19**) as an orange solid (0.2147 g, 60%). R_f 0.60 (EtOAc:Pet 25%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.27-4.22 (m, 2H), 4.09-4.04 (m, 2H), 3.22 (dd, J= 11.5, 3.8 Hz, 2H), 2.97 (dd, J= 11.5, 9.8 Hz, 2H), 1.45 (s, 6H), 1.43 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 109.7, 78.4, 76.8, 26.8, 26.7, -1.1; HRMS (ESI$^+$) calculated for $C_{12}H_{20}O_4TeAg$ 464.94693 $[M + Ag]^+$, found 464.94456.

1,4-Anhydro-6-tellurogalactitol (5)

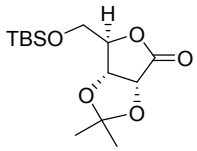


5

Compound **5** was prepared using standard procedure E. Compound (**19**) (0.3580 g, 1.0 mmol), H_2O (0.2 mL), TFA (0.2 mL) in DCM (5 mL) followed by column chromatography (5% CH_3OH in EtOAc) afforded compound (**5**) as an orange solid (0.2359 g, 53%). R_f 0.45

(EtOAc:CH_3OH 4:1); ^1H NMR ($CDCl_3$, 500 MHz) δ 4.17-4.14 (m, 2H), 4.07-4.02 (m, 2H), 3.50 (dd, *J*= 11.7, 6.3 Hz, 2H), 3.42 (dd, *J*= 11.7, 6.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 76.3, 71.2, 27.9; HRMS (ESI^+) calculated for $C_6H_{12}O_4TeAg$ 384.88433 $[M + Ag]^+$, found 384.88213.

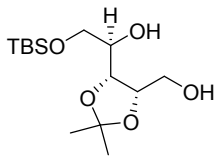
5-O-(tert-Butyldimethylsilyl)2,3-di-O-isopropylidene-D-ribono-1,4-lactone (21)



21

To a suspension of t-butyldimethylsilyl chloride (1.6 g, 10.6 mmol) and 2,3-isopropylidene-D-ribono-1,4-lactone (**20**) (1.0 g, 5.31 mmol) in dimethylformamide (DMF) (10 mL) at room temperature was added imidazole (0.72 g, 10.6 mmol) was stirred for 14 h. Then H_2O (10 mL) was added to the reaction mixture and the product was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts was dried over $MgSO_4$ and evaporated in vacuo to give a colourless oil. Further drying under reduced pressure using a high vacuum system gave the compound **21** as a white powder (1.58 g, 99%) that was further reacted without additional purification. R_f 0.86 (30% EtOAc in Pet); ^1H NMR ($CDCl_3$, 400 MHz) δ 4.72 (q, *J*= 5.6 Hz, 2H), 4.60 (t, *J*= 1.7 Hz, 1H), 3.89 (dd, *J*= 11.3, 2.1 Hz, 1H), 3.80 (dd, *J*= 11.3, 1.4 Hz, 1H), 1.47 (s, 3H), 1.39 (s, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.3, 113.1, 82.4, 78.6, 75.9, 63.1, 26.9, 25.9, 25.7, 18.4, - 5.5, - 5.6; HRMS (ESI^+) 303.16193 (303.16223 $[M + H]^+$calc. for $C_{14}H_{27}O_5Si$).

5-O-(tert-Butyldimethylsilyl)2,3-di-O-isopropylidene-D-ribitol (22)

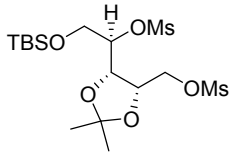


22

Compound **22** was prepared using standard procedure B. Compound **21** (1.58 g, 5.24 mmol) and $NaBH_4$ (0.05 g, 1.32 mmol) in THF (6 mL) and CH_3OH (12 mL) followed by column chromatography (EtOAc/Pet 20%) afforded compound (**22**) as a white solid (1.31 g, 82%). R_f 0.25 (EtOAc:Pet 20%); ^1H NMR ($CDCl_3$, 400 MHz) δ 4.37 (dt, *J*= 7.7, 5.5 Hz, 1H), 4.06 (dd, *J*= 9.6, 6.0 Hz, 1H), 3.92-3.84 (m, 2H), 3.83-3.74 (m, 2H), 3.66 (dd, *J*= 9.9, 6.0 Hz, 1H), 3.15 (dd, *J*= 8.9, 4.9 Hz, 1H), 3.03 (d, *J*= 4.5 Hz, 1H), 1.40 (s, 3H), 1.34 (s, 3H), 0.91 (s, 9H), 0.10 (s, 6H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 243.4, 108.7, 77.7, 76.7, 69.6, 64.5, 61.0, 28.0, 26.0, 25.4, 18.5, -5.2, -5.3; HRMS (ESI$^+$) 307.19385 (307.19353 $[M + H]^+$ calc. for $C_{14}H_{31}O_5Si$).

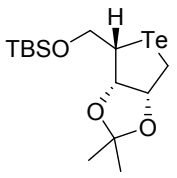
5-O-(tert-Butyldimethylsilyl)-1,4-bis(methanesulfonyl)-2,3-di-O-isopropylidene-D-ribitol



A

Compound **A** was prepared using standard procedure C. Diol **22** (1.33 g, 4.4 mmol), Et_3N (1.82 mL, 13.1 mmol), MsCl (1.0 mL, 12.9 mmol) and CH_2Cl_2 (27 mL) followed by column chromatography (40% EtOAc/Pet) afforded compound (**23**) as a clear yellow oil (1.83 g, 90%). R_f 0.66 (EtOAc:Pet 40%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.81 (ddd, *J*= 7.1, 4.2, 2.8 Hz, 1H), 4.52 (dd, *J*= 10.7, 3.4 Hz, 1H), 4.48-4.44 (m, 1H), 4.36 (dt, *J*= 10.6, 6.3 Hz, 2H), 4.07 (dd, *J*= 12.1, 2.8 Hz, 1H), 3.89 (dd, *J*= 12.1, 4.2 Hz, 1H), 3.13 (s, 3H), 3.07 (s, 3H), 1.49 (s, 3H), 1.37 (s, 3H), 0.91 (s, 3H), 0.1 (s, 3H), 0.09 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 109.6, 79.8, 75.2, 74.2, 68.7, 62.8, 39.4, 37.7, 27.7, 25.9, 25.5, 18.5, 5.35, -5.4; HRMS (ESI$^+$) 463.14870 (463.14863 $[M + H]^+$ calc. for $C_{16}H_{36}O_9S_2Si$).

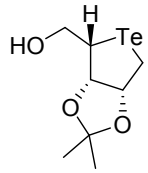
1,4-Anhydro-5-O-(tert-butyldimethylsilyl)-2,3-di-O-isopropylidene-4-telluro-L-lyxitol (B)



B

Compound **B** was prepared using standard procedure D. Tellurium powder (0.3896 g, 3 mmol), $NaBH_4$ (0.304 g, 8 mmol), dimesylate (**A**) (0.9260 g, 2 mmol) in PEG-400 (20 mL) followed by column chromatography (EtOAc/Pet 15%) afforded compound (**24**) as a yellow solid (0.7636 g, 95%). R_f 0.50 (EtOAc:Pet 20%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.85 (dt, *J*= 5.3, 2.5 Hz, 1H), 4.62 (t, *J*= 4.6 Hz, 1H), 4.36 (ddd, *J*= 7.2, 4.4, 2.8 Hz, 1H), 4.13-4.09 (m, 1H), 3.83 (dd, *J*= 10.0, 8.6 Hz, 1H), 3.45 (dd, *J*= 12.0, 5.3 Hz, 1H), 3.13 (dd, *J*= 12.0, 2.5 Hz, 1H), 1.53 (s, 3H), 1.30 (s, 3H), 0.88 (s, 9H), 0.06 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 109.8, 87.4, 84.8, 63.9, 36.1, 26.5, 25.9, 24.7, 18.2, 9.8, -5.30, -5.33; HRMS (ESI$^+$) calculated for $C_{14}H_{28}O_3SiTeAg$ 508.99154 $[M + Ag]^+$, found 508.99103.

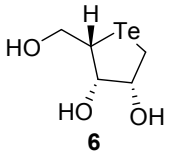
1,4-Anhydro-2,3-di-O-isopropylidene-4-telluro-L-lyxitol (C)



C

To a suspension of compound **B** (0.7636 g, 1.89 mmol) in THF (15 mL) at -20 ºC was added tetrabutylammonium fluoride (TBAF) (1.0 M in THF, 2.1 mL, 2.1 mmol) dropwise. The reaction mixture was warmed to room temperature over 1 h at which time H_2O (15 mL) was added and the product extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts was dried over $MgSO_4$ and evaporated in vacuo and the resulting residue was purified by column chromatography (40% EtOAc/Pet) afforded compound (**25**) as a yellow solid (0.3810 g, 70%). R_f 0.40 (40% EtOAc in Pet); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.89 (td, *J*= 5.7, 3.8 Hz, 1H), 4.79 (t, *J*= 5.6 Hz, 1H), 4.24 (dt, *J*= 7.8, 4.8 Hz, 1H), 4.01 (dt, J= 11.6, 7.3 Hz, 1H), 3.89-3.84 (m, 1H), 3.39 (dd, *J*= 11.8, 5.4 Hz, 1H), 3.28 (dd, *J*= 11.8, 3.7 Hz, 1H), 2.67 (t, *J*= 6.3 Hz, 1H), 1.56 (s, 3H), 1.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 106.2, 82.9, 82.7, 59.5, 29.2, 21.7, 21.6, 4.7; HRMS (ESI$^+$) calculated for $C_8H_{14}O_3TeAg$ 394.90506 $[M + Ag]^+$, found 394.90470.

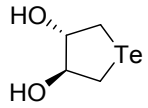
1,4-Anhydro-4-telluro-L-lyxitol (6)



6

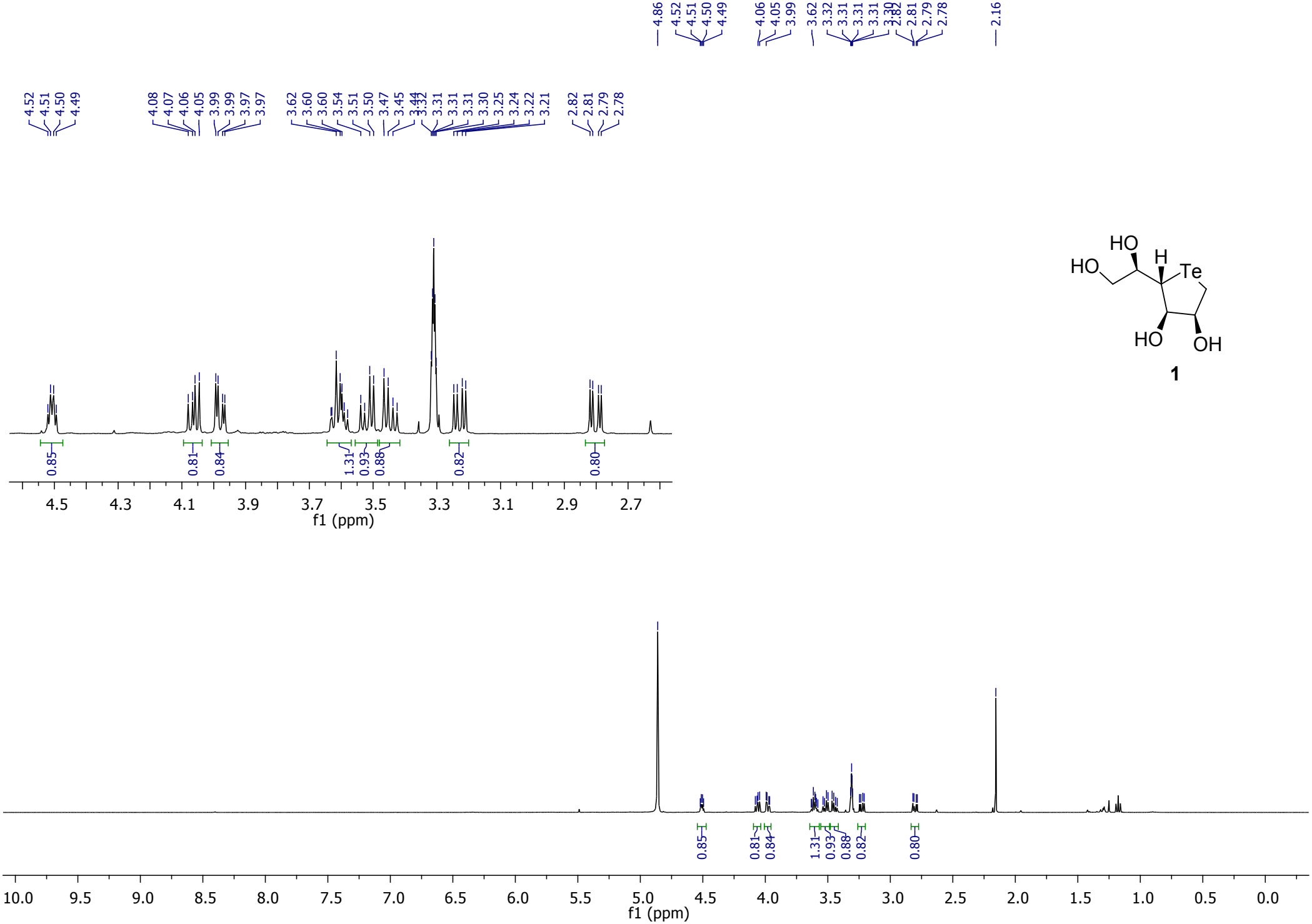
Compound **6** was prepared using standard procedure E. Compound **C** (0.3810 g, 1 mmol), H_2O (0.2 mL), TFA (0.2 mL) in DCM (5 mL) followed by column chromatography (10% CH_3OH in EtOAc) to afford compound **5** as a yellow solid (0.0661 g, 65%). R_f 0.30 (EtOAc:CH_3OH 9:1); $[\alpha]_D^{20}$ –33.84 (*c* 1, MeOH); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.27 (dd, *J*= 3.8, 2.7 Hz, 1H), 4.16 (td, *J*= 7.5, 3.9 Hz, 1H), 4.09-4.04 (m, 1H), 4.02-3.99 (m, 1H), 3.63 (dd, J= 10.9, 7.7Hz, 1H), 3.20 (dd, *J*= 10.4, 9.0 Hz, 1H), 3.07 (dd, *J*= 9.0, 6.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 81.0, 75.6, 74.7, 68.3, 63.2, 27.5, 2.8; HRMS (ESI$^+$) calculated for $C_5H_{10}O_3TeAg$ 354.87376 $[M + Ag]^+$, found 354.87282.

D/L-*trans*-3,4-dihydroxy-1-tellurolane (7)



7

To a suspension of tellurium powder (1.299 g, 10 mmol) in H_2O (10 mL) at 0 ºC was added $NaBH_4$ (0.836 g, 22 mmol) in H_2O (10 mL). The reaction mixture was warmed to room temperature and stirred for 1 hour then was added $NaBH_4$ (0.304 g, 8 mmol) portionwise. When the black coloured suspension had turned clear (approx. 5 min) the 1,3-butadiene bisepoxide (**26**) (0.7 mL, 8.45 mmol) was then added stirred at room temperature for an additional 1 h. The reaction mixture was diluted with EtOAc (30 mL) and washed with satured NaCl (2 × 30 mL), dried over $MgSO_4$ and evaporated under reduced pressure to give product **7** as a yellow solid, in almost quantitative yield (1.8405 g, 98%) without additional purification. R_f 0.50 (EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.02-3.97 (m, 2H), 3.29 (dd, *J*= 10.1, 4.9 Hz, 2H), 3.12 (dd, *J*= 10.1, 6.8 Hz, 2H), 2.06 (d, *J*= 4.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 80.1, 4.85; ^{125}Te NMR (CD_3OD, 158 MHz) δ 112.1; HRMS (ESI$^+$) m/z 324.86245 (324.86224 [M + Ag]$^+$ calc. for $C_4H_8O_2Te$).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3.30
2.82
2.81
2.79
2.78
2.16
4.52
4.51
4.50
4.49
4.08
4.07
4.06
4.05
3.99
3.99
3.97
3.97
3.62
3.60
3.60
3.54
3.51
3.50
3.47
3.45
3.44
3.32
3.31
3.31
3.31
3.30
3.25
3.24
3.22
3.21
2.82
2.81
2.79
2.78
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0.81
0.84
1.31
0.93
0.88
0.82
0.80
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4.3
4.1
3.9
3.7
3.5
3.3
3.1
2.9
2.7
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HO
Te
HO
OH
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1.31
0.93
0.88
0.82
0.80
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9.0
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6.0
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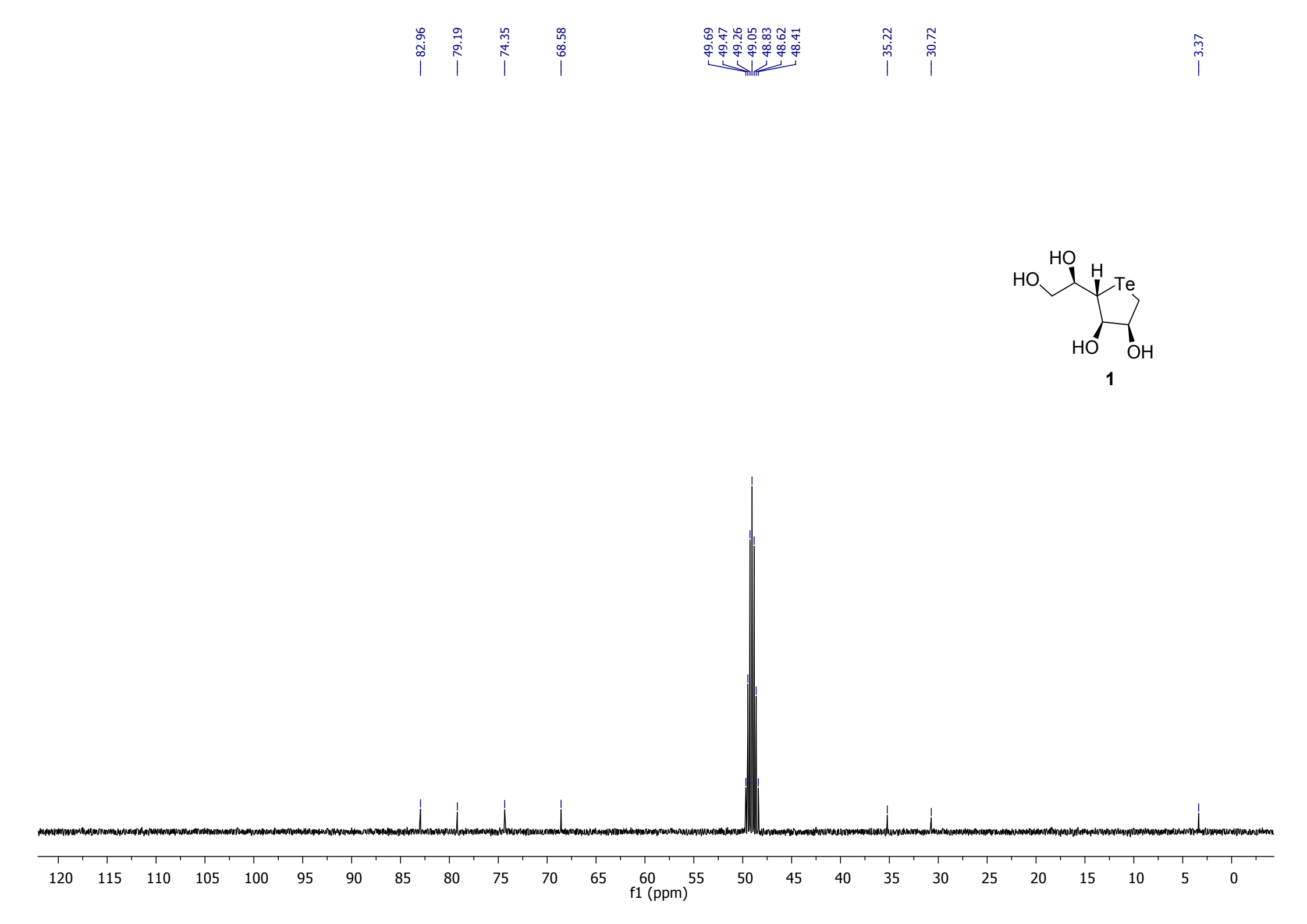
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49.05
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3.37
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H
HO
Te
HO
OH
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110
105
100
95
90
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25
20
15
10
5
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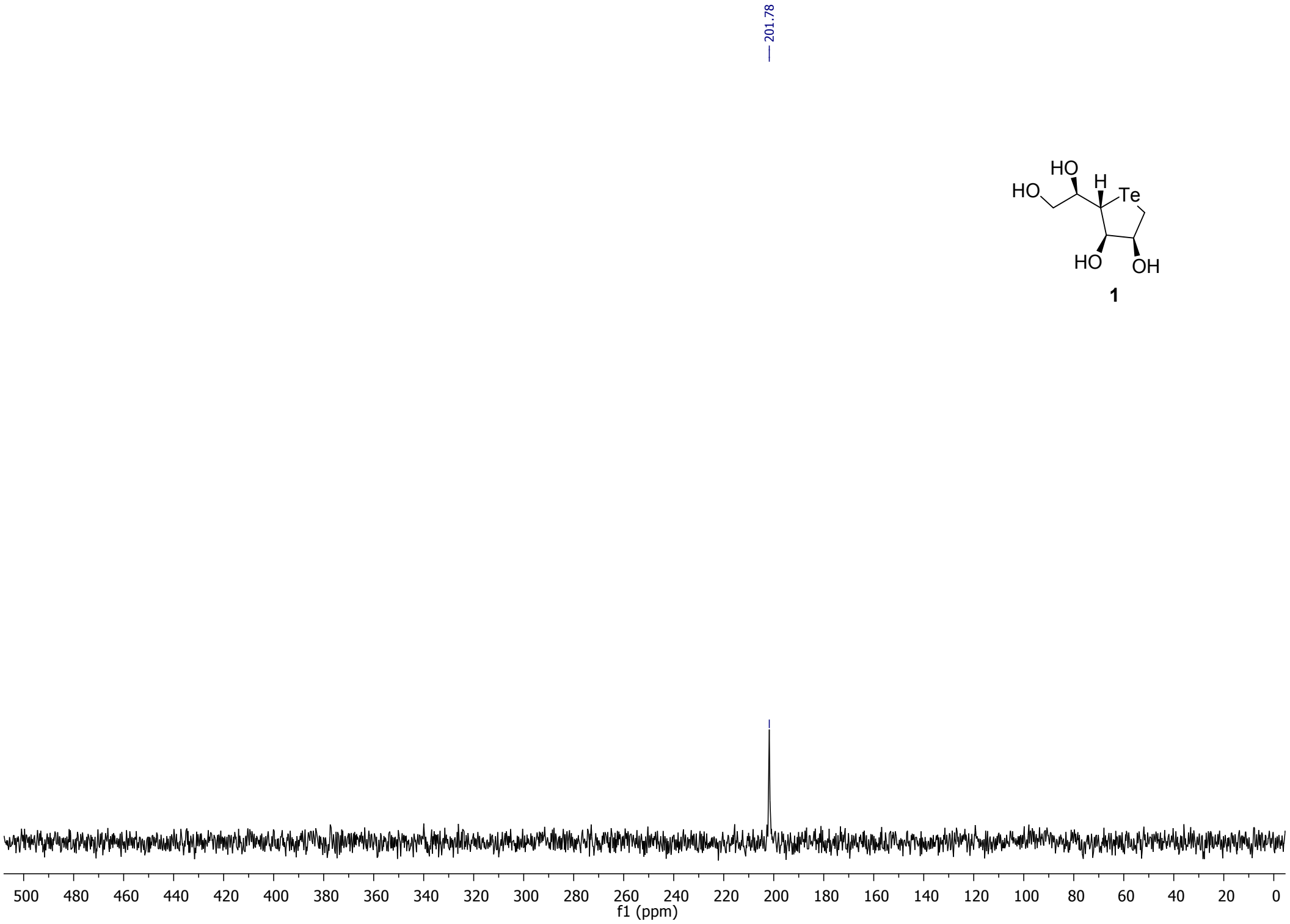
f1 (ppm)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20
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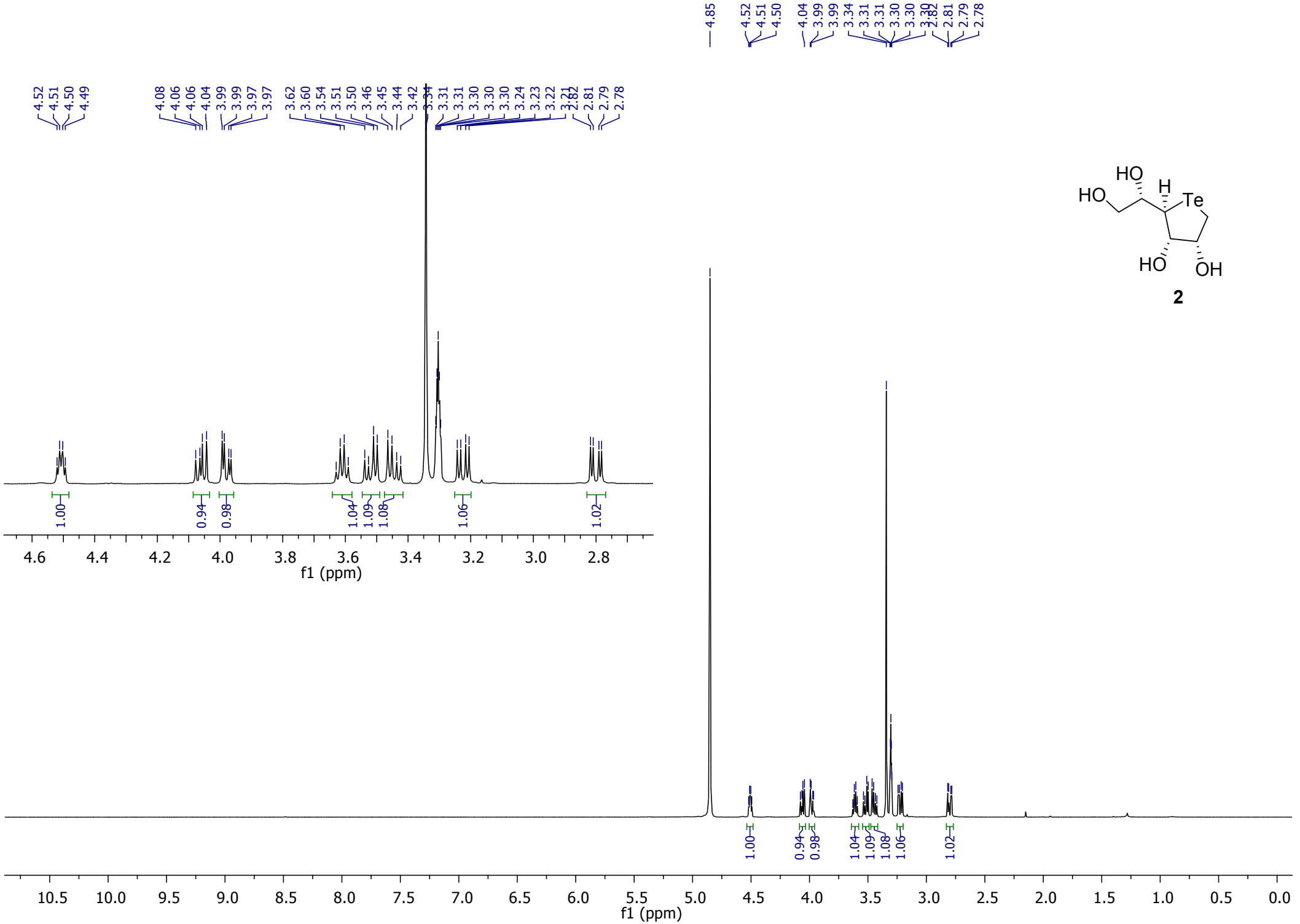
f1 (ppm)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3.99
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3.31
3.30
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3.30
3.30
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3.23
3.22
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2.79
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1.08
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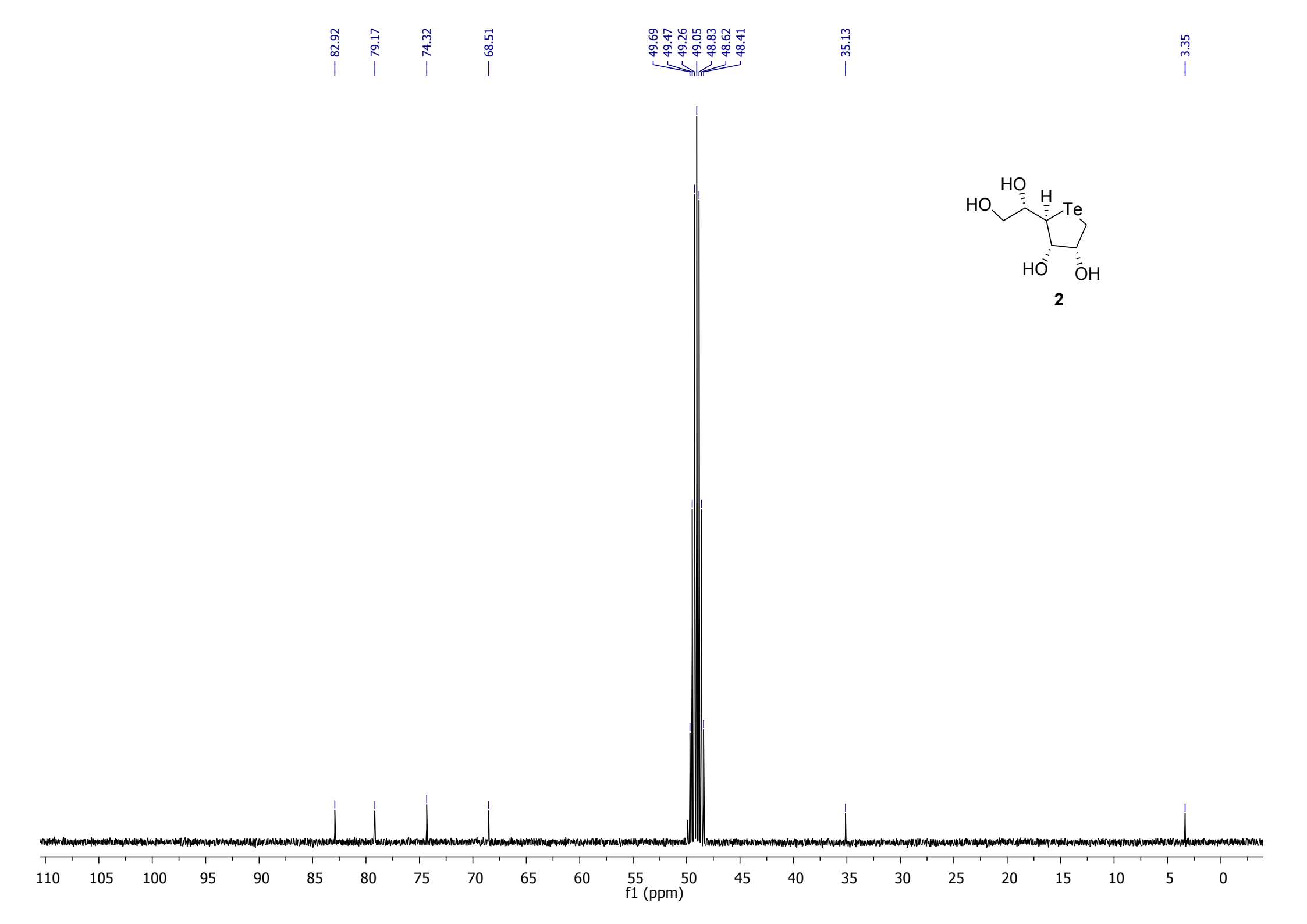
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90
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25
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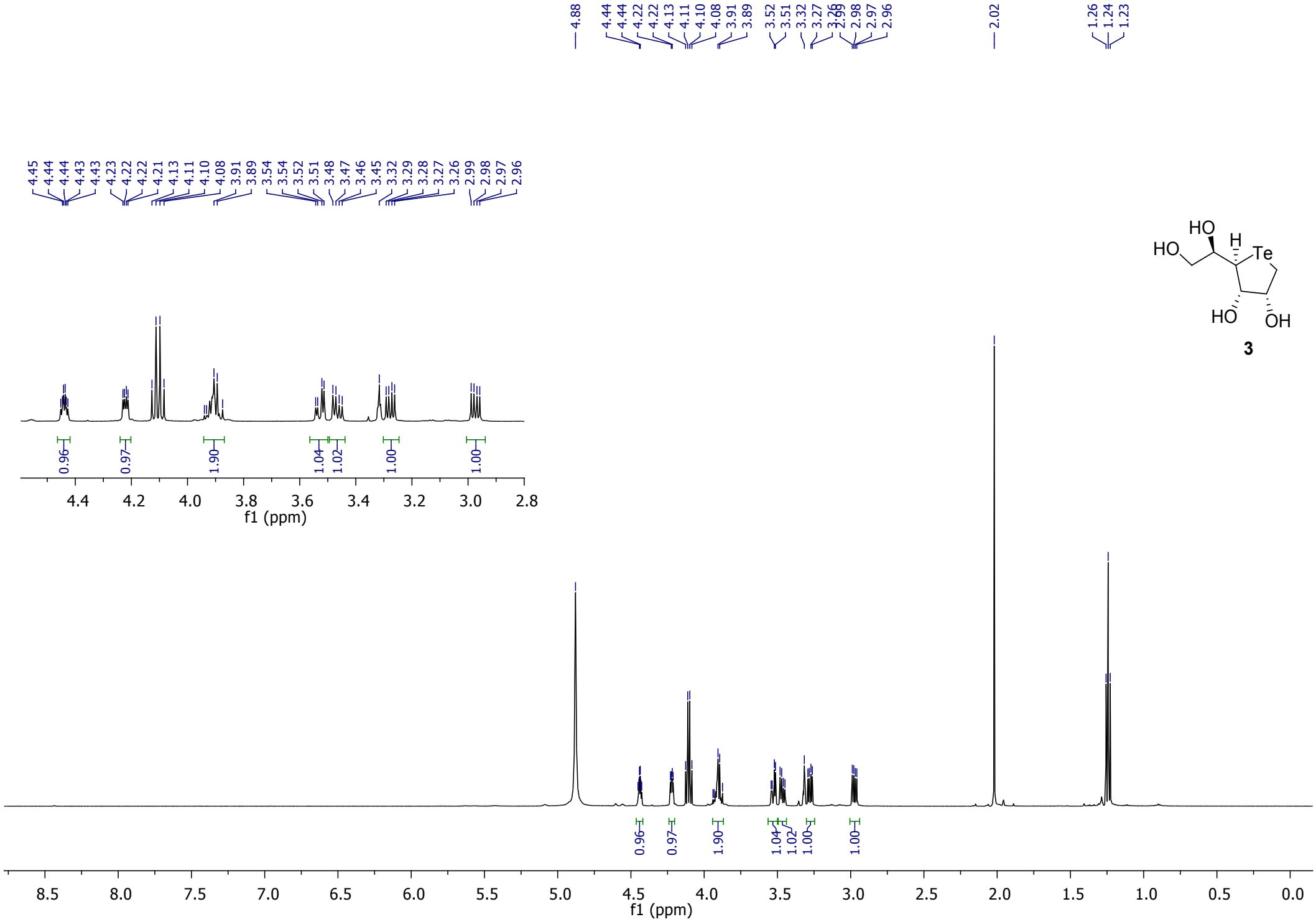
f1 (ppm)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3.26
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2.98
2.97
2.96
0.96
0.97
1.90
1.04
1.02
1.00
1.00
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4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
f1 (ppm)
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HO
H
Te
HO
OH
3
0.96
0.97
1.90
1.04
1.02
1.00
1.00
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8.0
7.5
7.0
6.5
6.0
5.5
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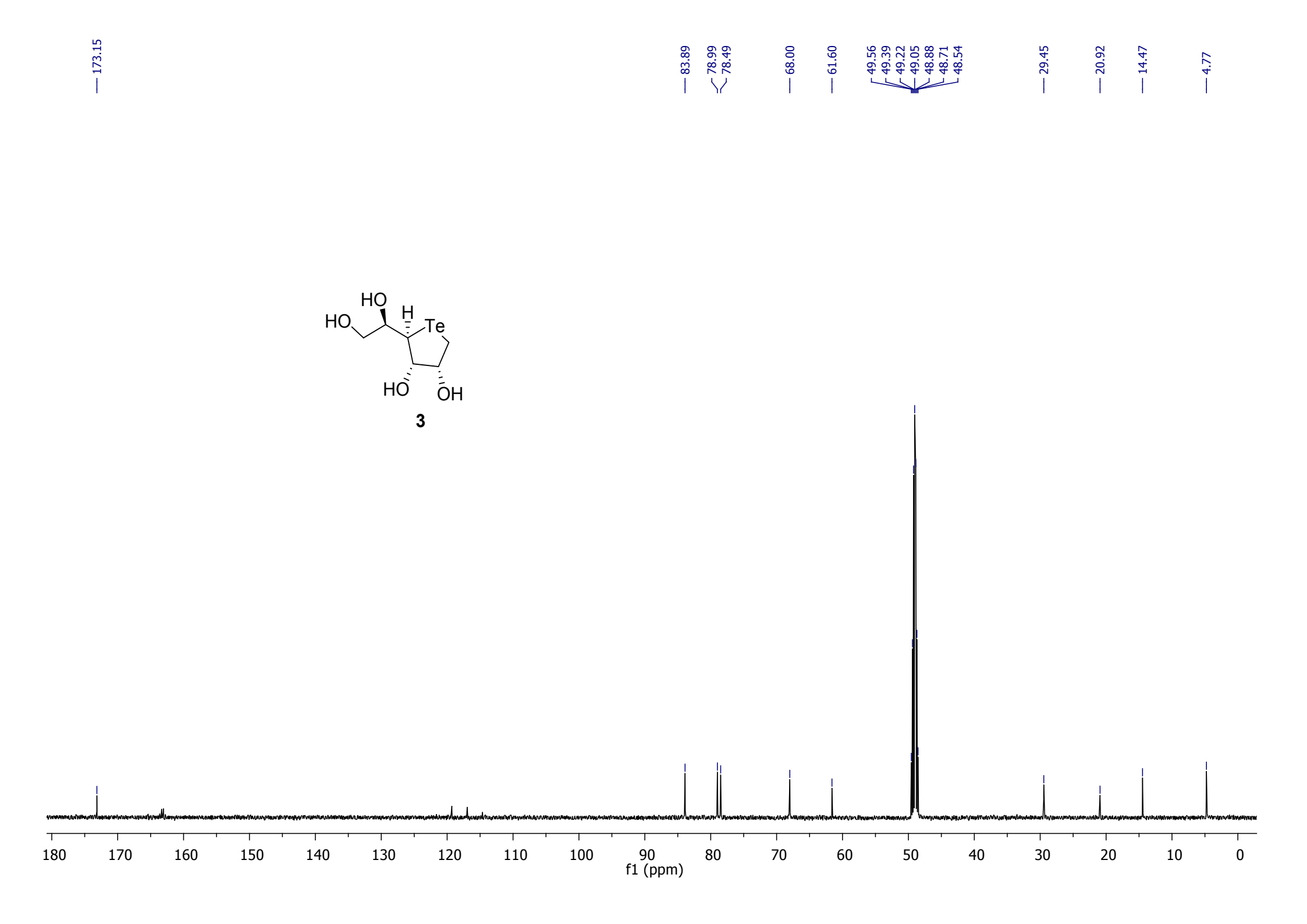
f1 (ppm)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78.49
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OH
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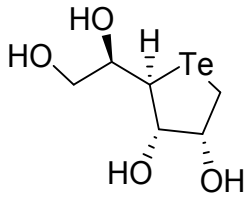
f1 (ppm)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HO
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HO
OH

3

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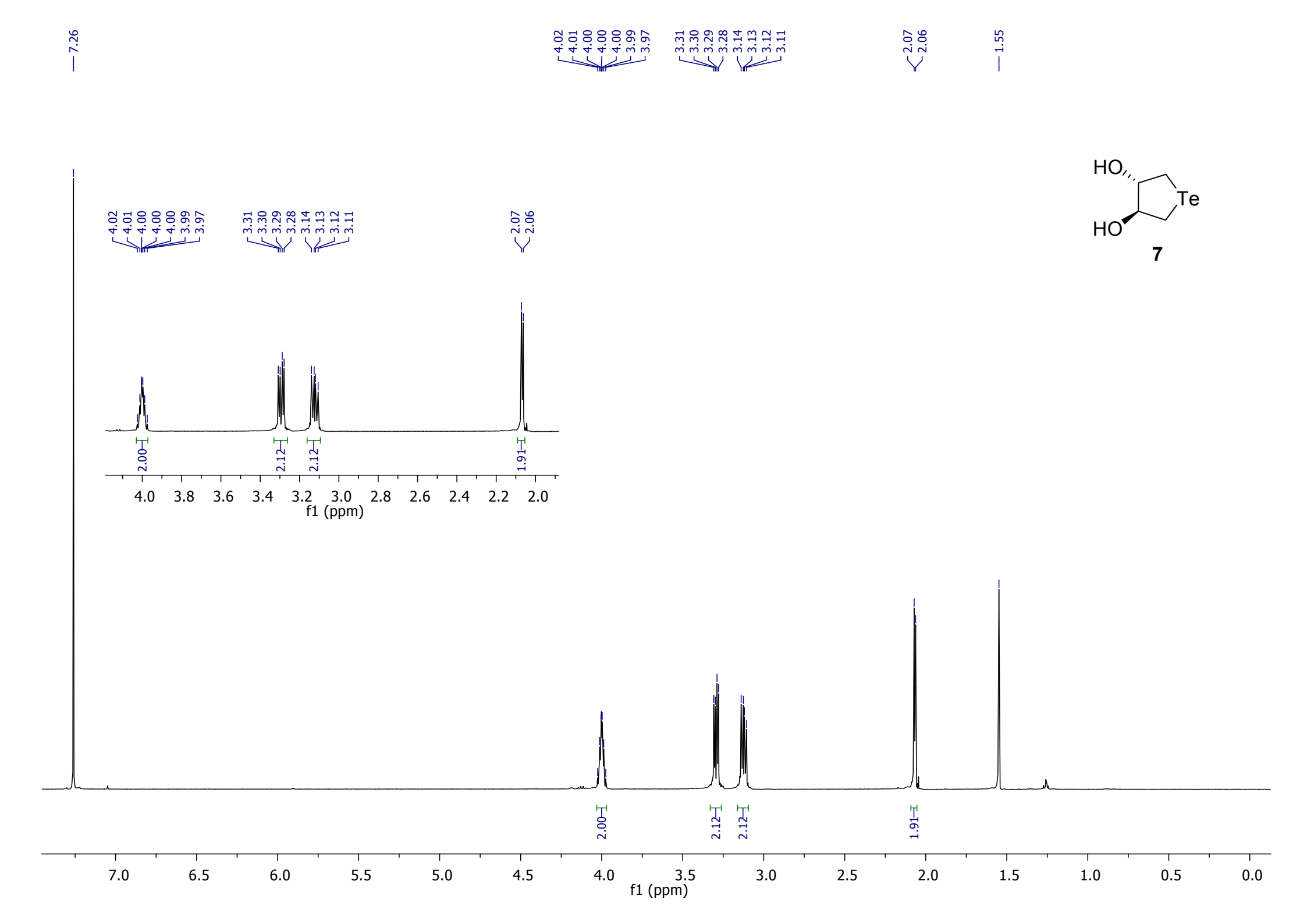
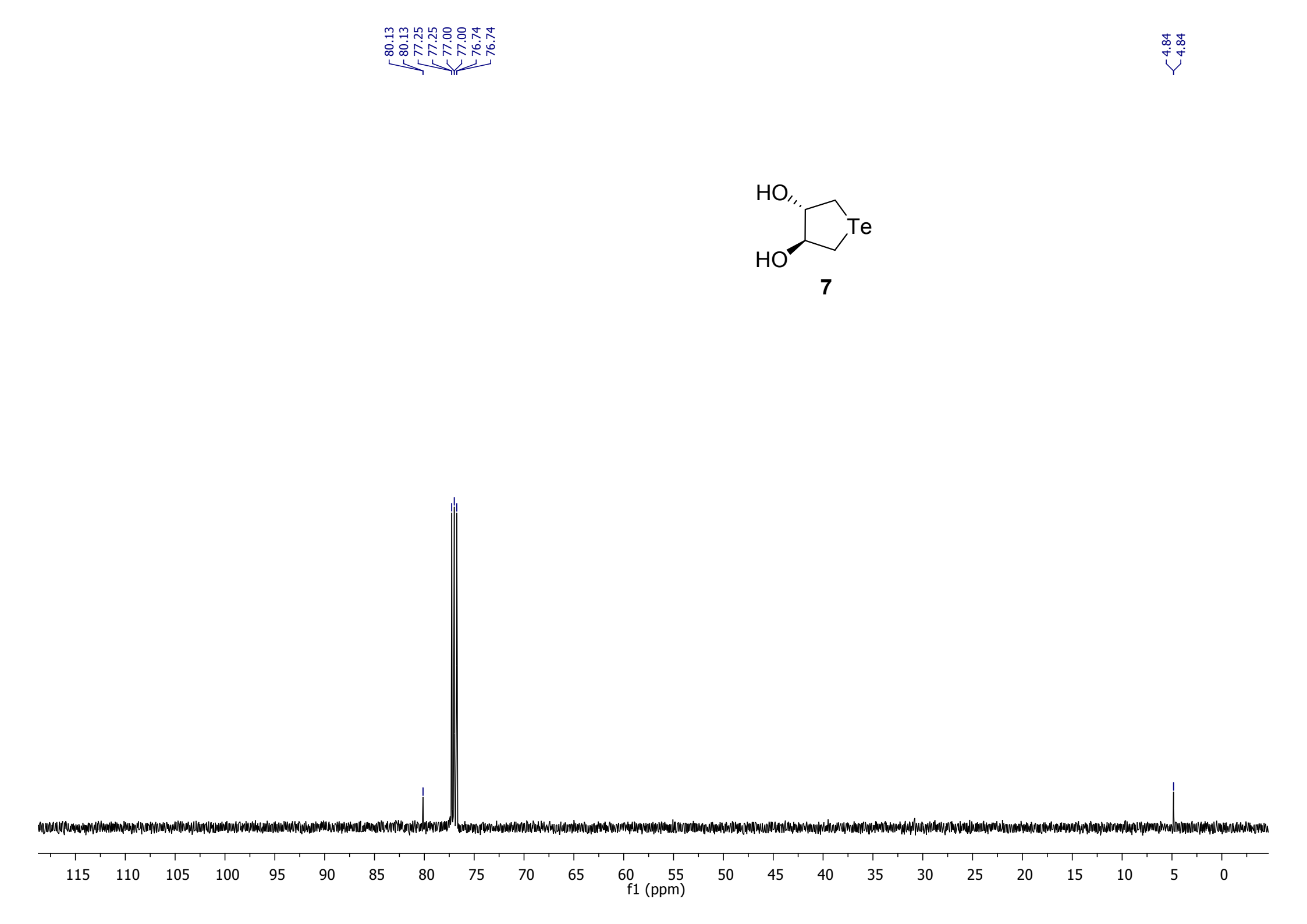
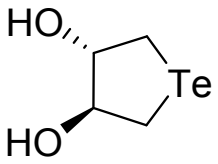
100
80
60
40
f1 (ppm)

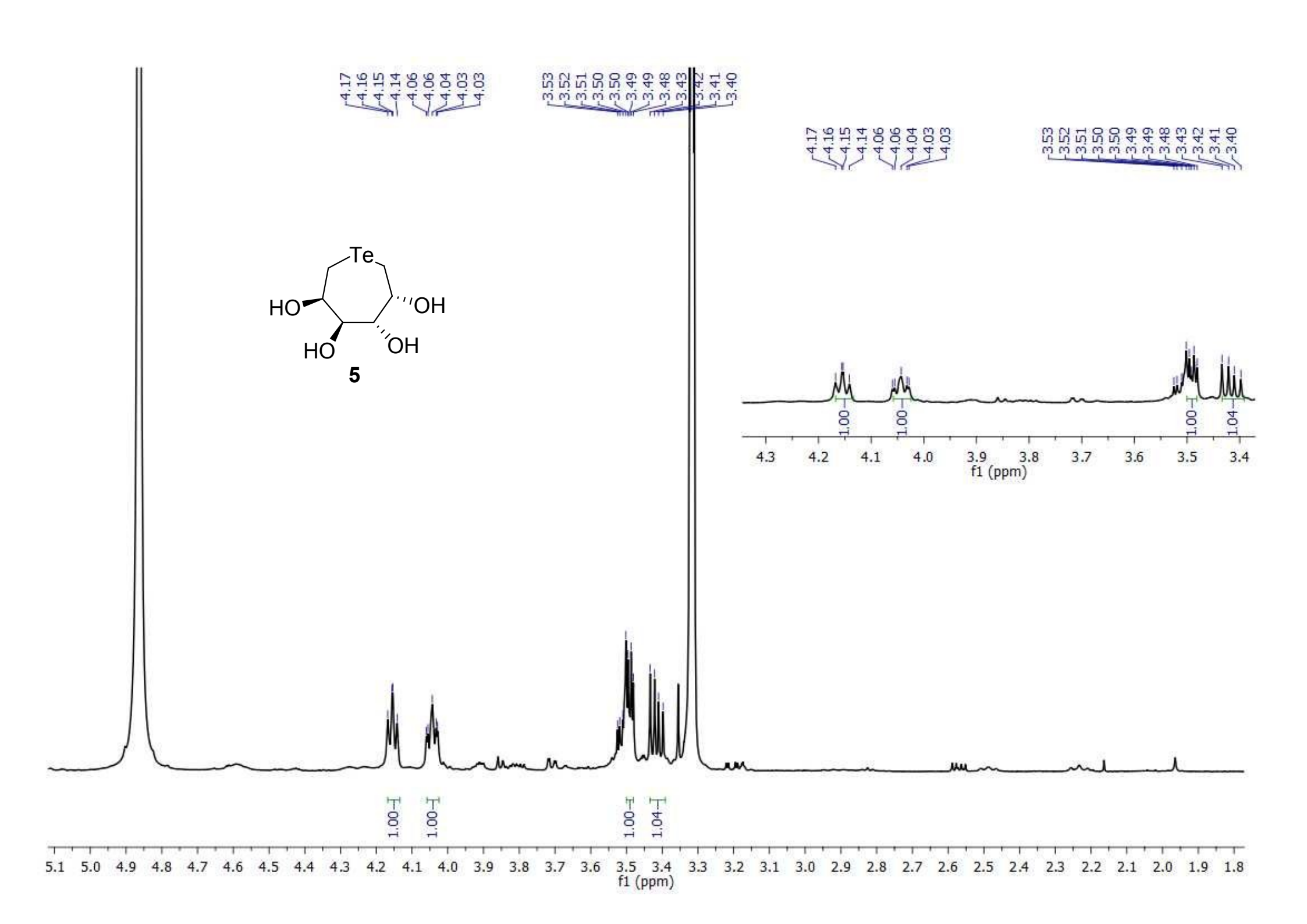

7.26
4.02
4.01
4.00
4.00
4.00
3.99
3.97
3.31
3.30
3.29
3.28
3.14
3.13
3.12
3.11
2.07
2.06
1.55
HO
Te
HO
7
2.00
2.12
2.12
1.91
f1 (ppm)

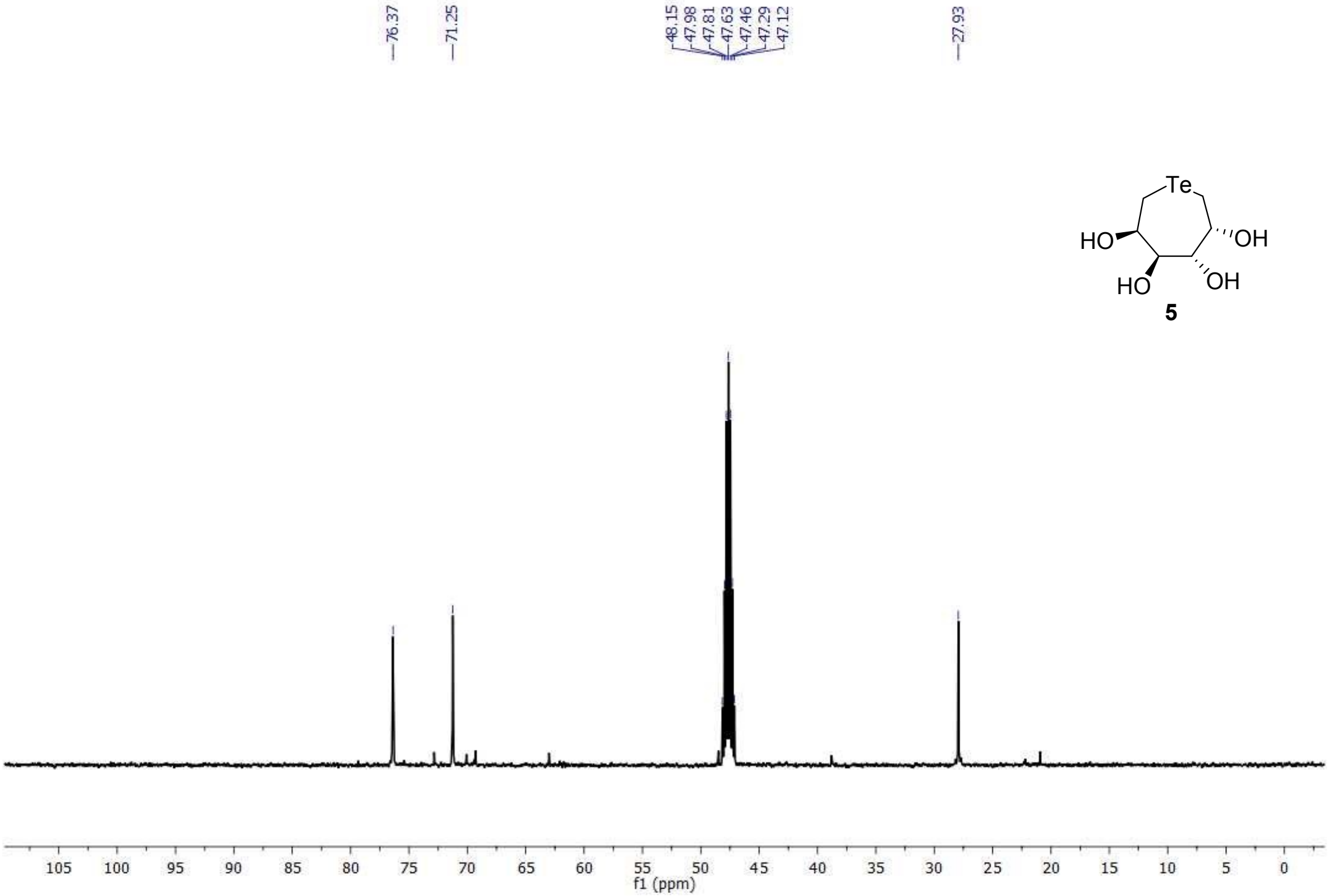

80.13
80.13
77.25
77.25
77.00
77.00
76.74
76.74
4.84
4.84
HO
Te
HO
7
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
f1 (ppm)

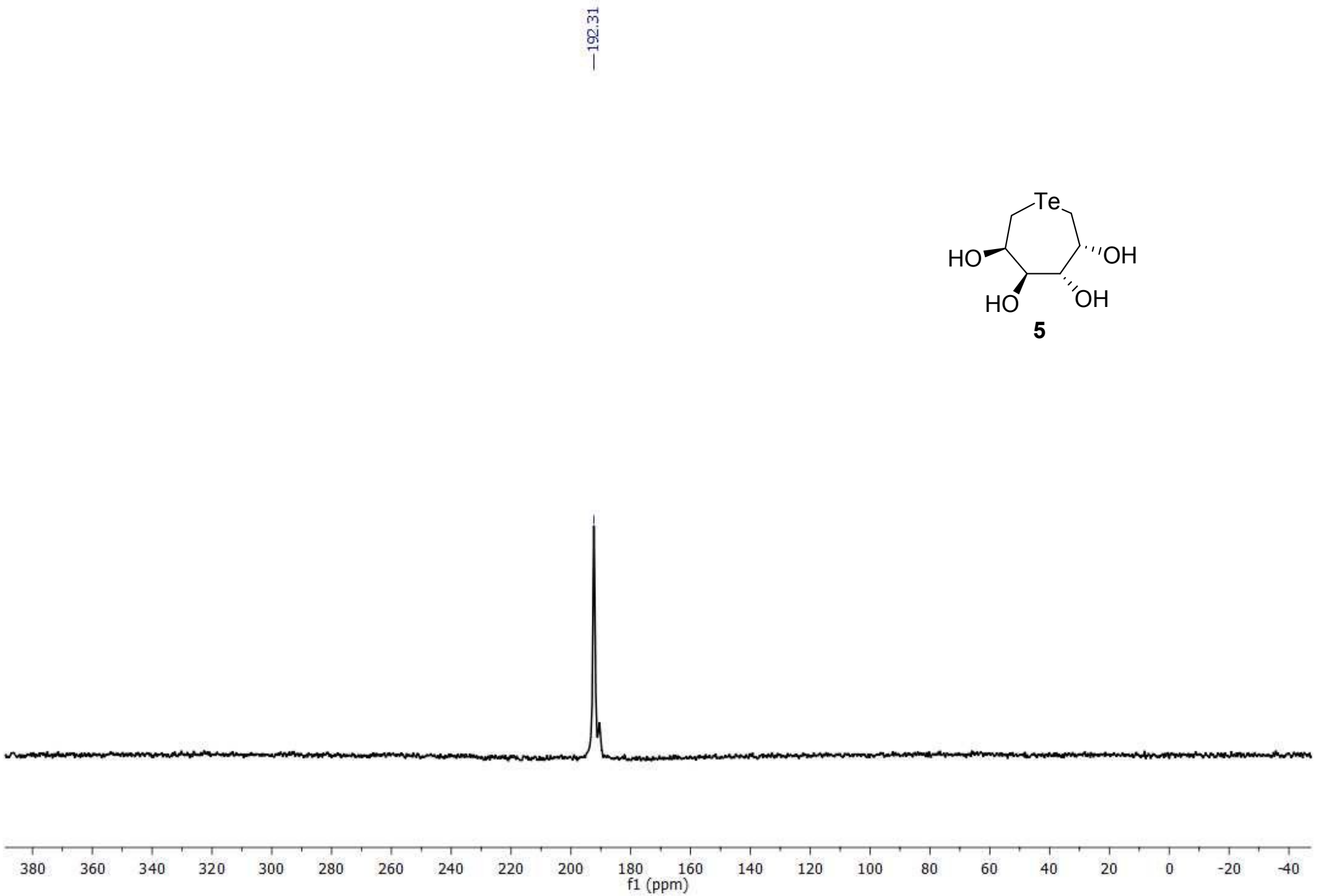

HO
Te
HO

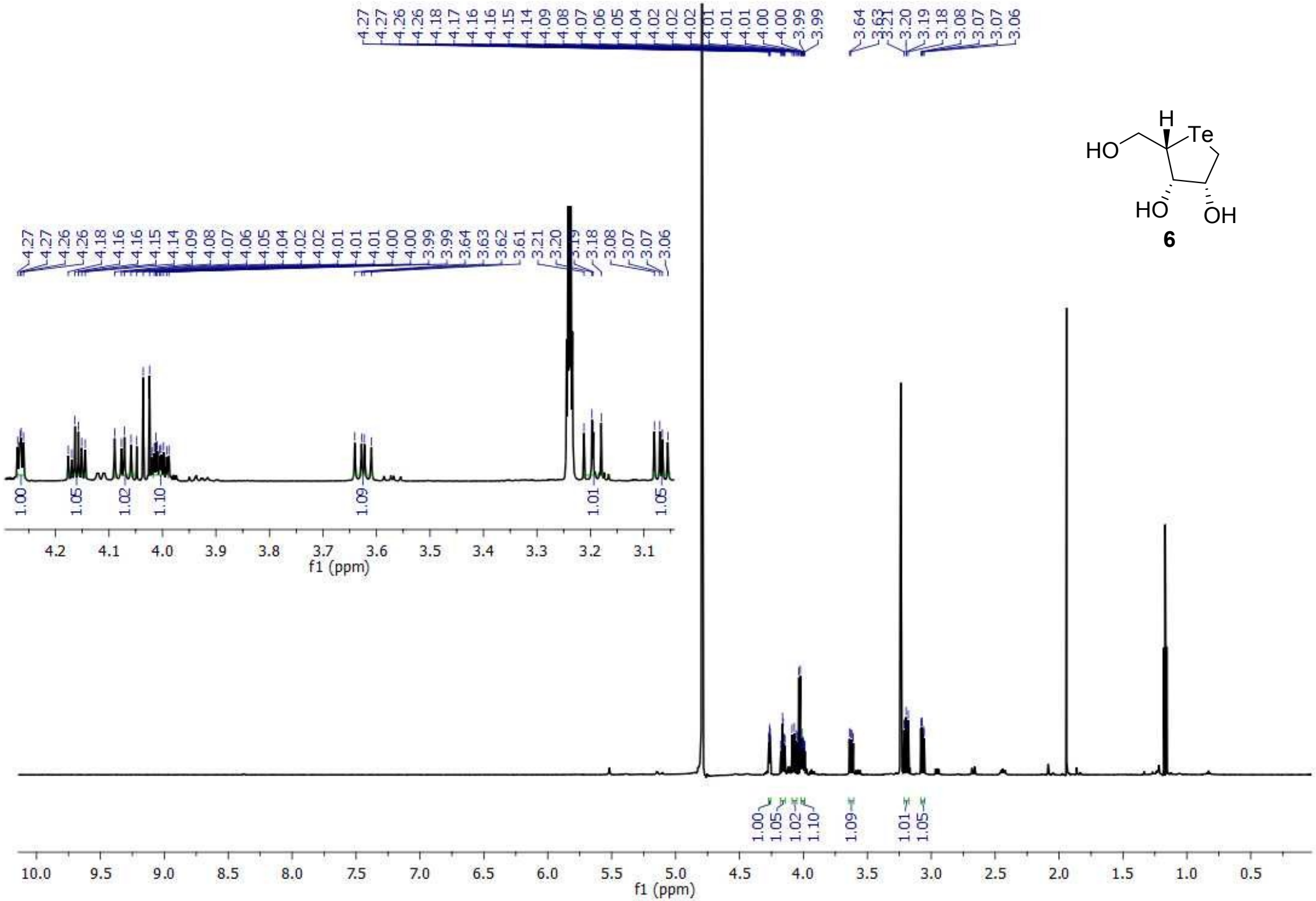
7

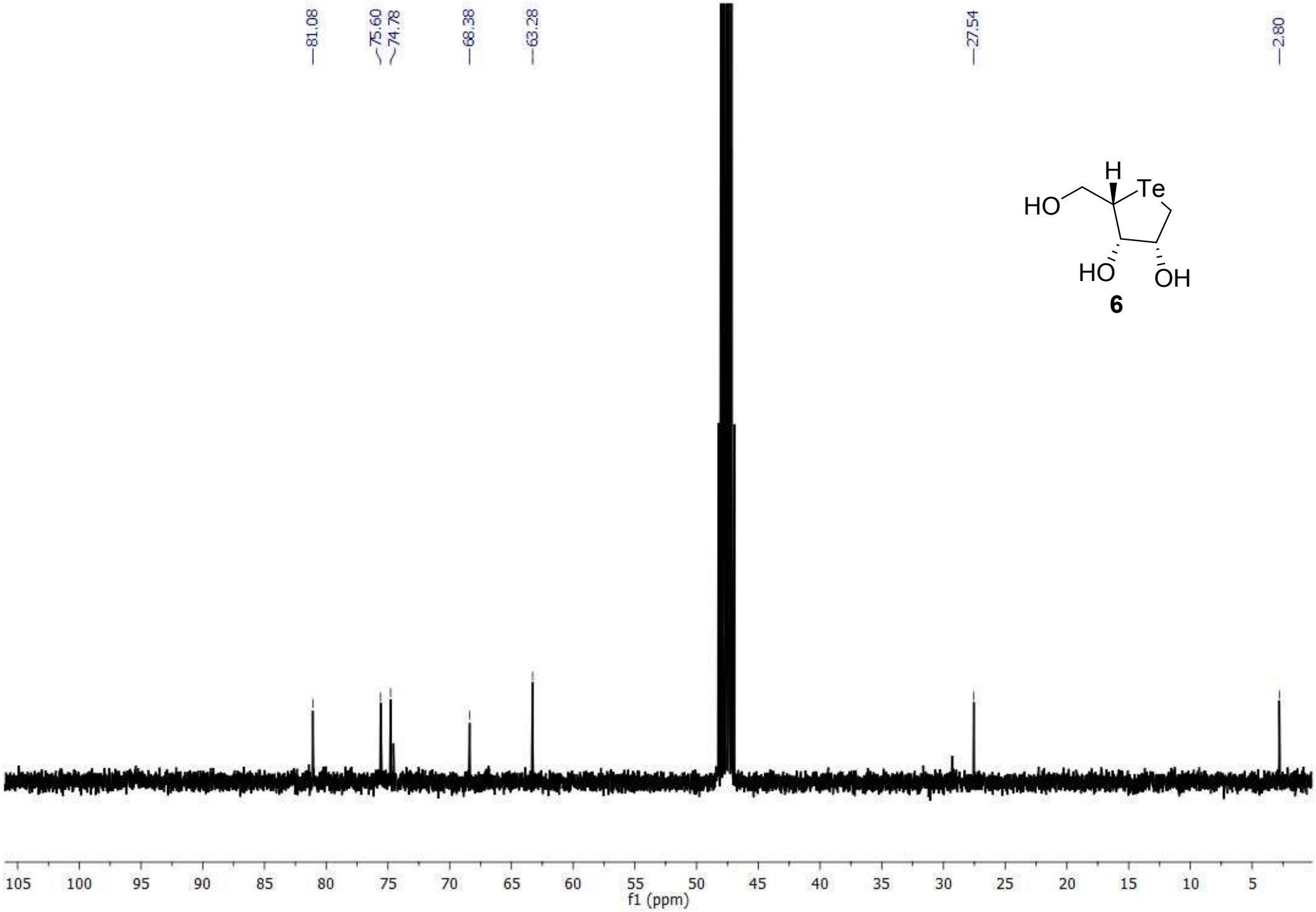
112.08
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
-40
f1 (ppm)

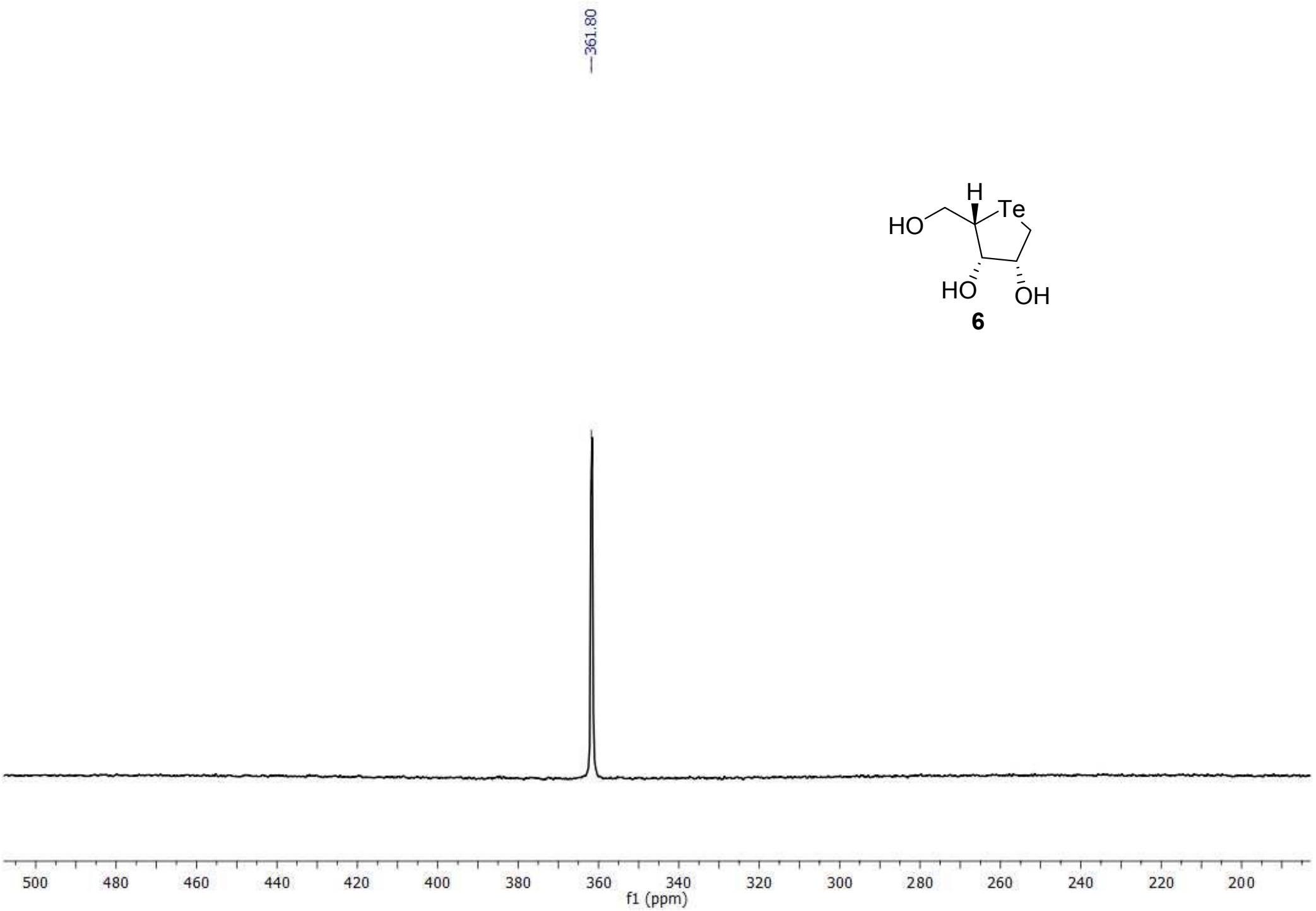

4.17
4.16
4.15
4.14
4.06
4.06
4.04
4.03
4.03
3.53
3.52
3.51
3.50
3.50
3.49
3.49
3.48
3.43
3.42
3.41
3.40
Te
HO
OH
HO
OH
5
1.00
1.00
1.00
1.04
f1 (ppm)


76.37
71.25
48.15
47.98
47.81
47.63
47.46
47.29
47.12
27.93
Te
HO
OH
HO
OH
5
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
f1 (ppm)


192.31
Te
HO
OH
HO
OH
5
380
360
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
-40
f1 (ppm)


4.27 4.27 4.26 4.26 4.18 4.17 4.16 4.16 4.15 4.14 4.09 4.08 4.07 4.06 4.05 4.04 4.02 4.02 4.02 4.01 4.01 4.01 4.00 4.00 3.99 3.99
3.64 3.63 3.21 3.20 3.19 3.18 3.08 3.07 3.07 3.06
1.00 1.05 1.02 1.10 1.09 1.01 1.05
10.0 9.5 9.0 8.5 8.0 7.5 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
f1 (ppm)
4.27 4.27 4.26 4.26 4.18 4.16 4.16 4.15 4.14 4.09 4.08 4.07 4.06 4.05 4.04 4.02 4.02 4.01 4.01 4.01 4.00 4.00 3.99 3.99 3.64 3.63 3.62 3.61 3.21 3.20 3.19 3.18 3.08 3.07 3.07 3.06
1.00 1.05 1.02 1.10 1.09 1.01 1.05
4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1
f1 (ppm)
H
Te
HO
HO
OH
6


81.08
75.60
74.78
68.38
63.28
27.54
2.80
H
Te
HO
HO
OH
6
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
f1 (ppm)


361.80
H
Te
HO
HO
OH
6
500
480
460
440
420
400
380
360
340
320
300
280
260
240
220
200
f1 (ppm)