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Synthesis and Antioxidant Capacity of 5-Selenopyranose Derivatives

Corin Storkey,*[a,b,c] Michael J. Davies,[c] Jonathan M. White,[b] and Carl H. Schiesser*[a,b]

[a] *ARC Centre of Excellence for Free Radical Chemistry and Biotechnology*
[b] *School of Chemistry and Bio21 Molecular Science and Biotechnology Institute, The University of Melbourne, Victoria, 3010, Australia. Fax: +61 3 9347 8189; Tel: +61 3 8344 2432; E-mail: carlhs@unimelb.edu.au*
[c] *Heart Research Institute, Newtown, 2042, NSW, Australia. Fax: +61 2 9565 5584; Tel: +61 2 8208 8900; E-mail: daviesm@hri.org.au, storkeyc@hri.org.au.*

Experimental procedures for new compounds; ^{1}H and ^{13}C NMR spectra of compounds **8** – **11**; crystal structures for compounds **8** – **10**. (19 pages).

2,3,4,6-Di-isopropylidene-1,5-di-*O*-hydroxy-D-mannitol (13). To a suspension of D-mannose **(12)** (10 g, 55.5 mmol) and *p*-toluenesulfonic acid monohydrate (1.06 g, 5.55 mmol) over 4 Å molecular sieves in dry DMF (80 mL) at 0 °C was added 2-methoxypropene (10.6 mL, 8.0 g, 222 mmol) dropwise over 30 minutes. The suspension was maintained at 5 - 10 °C for 8 hours and allowed to warm to room temperature. The resulting pale yellow solution was quenched by the addition of $NaCO_3$ (2 g). Filtration and removal of the solvent in vacuo gave a yellow oil. The residue was partitioned between EtOAc (200 mL) and water (200 mL) and the organic layer was separated. The aqueous phase was extracted with EtOAc (3 x 100 mL) and the combined organic extracts washed with brine (2 x 80 mL) and dried over $MgSO_4$. Evaporation afforded the crude di-isopropylidene as the major of three products, two of which were inseperable by column chromatography Rf 0.18 (Hex:EtOAc 3:1). The crude mixture was then dissolved in anhydrous MeOH (100 mL) under nitrogen at 0 °C before the portionwise addition of $NaBH_4$ (2.9 g, 77 mmol). Vigorous effervescence occurred and the solution was stirred at 0 °C for 30 minutes and then at room temperature for 4 hours. Two new products were observed by TLC, the major of which being the desired diol 29 (R_f 0.36) the minor product (R_f 0.52 Hex:EtOAc 1:2) was now able to be seperated. The solvent was removed in vacuo and the residue was partitioned between EtOAc (150 mL) and water (150 mL) and the organic layer was separated. The aqueous phase was extracted with EtOAc (5 x 50 mL) and the combined organic extracts washed with brine (2 x 50 mL) and dried over $MgSO_4$. Evaporation and chromatography (25% - 67% EtOAc in Pet.) afforded the diol **(13)** as a colourless oil (9.36 g, 36 mmol, 67% over 2 steps). R_f 0.36 (Hex:EtOAc 1:2); $[\alpha]_D^{22}$ = -12.8 ° (c 1.0 in DCM); ^{1}H NMR (500 MHz, CDCl3) δ 4.47 (dd, *J* = 2.3, 6.7 Hz, 1H), 4.31 (dt, *J* = 4.8, 6.7 Hz, 1H), 3.97 - 3.89 (m, 2H), 3.81 (m, 2H), 3.70 (dd, *J* = 2.3, 8.8 Hz, 1H), 3.64 (td, *J* = 2.6, 10.3 Hz, 1H), 1.53 (s, 3H), 1.49 (s, 3H), 1.41 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (125 MHz, CDCl3) δ 109.10, 99.43, 77.88, 74.90, 72.58, 64.94, 63.98, 61.66, 28.29, 26.90, 25.80, 19.65; IR(neat)/cm^{-1}: 3433, 2986, 1217, 1066; MS (ESI$^+$) *m/z* (rel intensity) 263.09 [100, (M+Na)$^+$]; HRMS (ESI$^+$) *m/z* 263.1489 (263.1489 calcd for $C_{12}H_{22}O_6Na$).

2,3,4,6-Di-*O*-isopropylidene-1,5-di-*O*-methanesulfonyl-D-mannitol (14). To a stirred solution of the diol **(13)** (5 g, 19 mmol), DMAP (250 mg, 2 mmol) and anhydrous pyridine (10 mL) in dry DCM (150 mL) under nitrogen at 0 °C was added dropwise methanesulfonyl chloride (4.5 mL, 59 mmol). The solution was stirred at 0 °C for 30 minutes and then warmed to room temperature and stirred for 6 hours. The reaction was quenched by the addition of saturated $NaHCO_3$ (50 mL) before being extracted with DCM (3 x 50 mL). The combined organic extracts were then washed with brine (2 x 100 mL) and dried over $MgSO_4$. Evaporation and chromatography (Hex:EtOAc 1:1) afforded the dimesylate **(14)** as a white amorphous solid (6.76 g, 16 mmol, 85%). R_f 0.15 (Hex:EtOAc 3:1); $[\alpha]_D^{22}$ = +19.9 ° (*c* 1.0 in DCM); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.82 (ddd, *J* = 5.1, 7.3, 8.8 Hz, 1H), 4.55 (ddd, *J* = 4.1, 6.3, 7.5 Hz, 1H), 4.50 (dd, *J* = 7.5, 10.3 Hz, 1H) 4.40 (dd, *J* = 1.1, 6.3 Hz, 1H), 4.38 (dd, *J* = 4.1, 10.3 Hz, 1H), 4.13 (dd, *J* = 5.1, 12.0 Hz, 1H), 3.88 (dd, *J* = 7.3, 12.1 Hz, 1H), 3.81 (dd, *J* = 1.1, 8.8 Hz, 1H), 3.08 (s, 3H), 3.07 (s, 3H), 1.52 (s, 3H), 1.50 (s, 3H), 1.41 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 110.46, 100.01, 74.87, 73.86, 72.25, 69.55, 68.19, 62.62, 38.12, 38.04, 27.36, 26.80, 25.84, 20.32; IR

(neat)/cm^{-1}: 2970, 1738, 1365, 1217; MS (ESI$^+$) *m/z* (rel intensity) 441.18 [100, (M+Na)$^+$]; HRMS (ESI$^+$) *m/z* 441.0860 (441.0859 calcd for $C_{14}H_{26}O_{10}S_2Na$).

2,3,4,6-Di-*O*-isopropylidene-1,5-anhydro-5-thio-L-gulitol (15).To a solution of the dimesylate **(14)** (1 g, 2.4 mmol) in DMF (15 mL) under nitrogen was added $Na_2S.9H_2O$ (0.68 g, 3.0 mmol). The solution was stirred at 100 °C for 15 hours and was then allowed to cool to room temperature. The reaction mixture was then concentrated *in vacuo*, poured into water (50 mL), and extracted with DCM (3 x 50 mL). The combined organic fractions were washed with water (2 x 40 mL) and brine (10 mL), dried over $MgSO_4$ and concentrated to afford a viscous clear yellow oil. Flash chromatography (Hex:EtOAc 3:1) afforded the thio-gulitol **(15)** as a white amorphous solid (0.53 g, 2.0 mmol, 85%). R_f 0.52 (Hex:EtOAc 3:1); $[\alpha]_D^{22}$ = -84.0^o (*c* 0.1 in DCM); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.47 (t, *J* = 2.9 Hz, 1H), 4.39 (td, *J* = 4.1, 6.7 Hz, 1H), 4.19 (dd, *J* = 3.0, 12.5 Hz, 1H), 4.12 (*J* = 2.9, 6.4 Hz, 1H), 3.77 (dd, *J* = 2.1, 12.5 Hz 1H), 3.05 (dd, *J* = 4.1, 13.5 Hz, 1H), 2.97 (ddd, *J* = 2.0, 2.7, 6.9 Hz, 1H), 2.65 (dd, *J* = 7.0, 13.6 Hz, 1H), 1.52 (s, 3H), 1.47 (s, 3H), 1.44 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 108.52, 99.52, 74.95, 70.61, 67.18, 64.23, 35.11, 29.33, 29.22, 27.41, 25.49, 19.22; IR (neat)/cm^{-1}: 2989, 2925, 1738, 1380, 1218, 1055; MS (ESI$^+$) *m/z* (rel intensity) 627.27 [100, (M+367)$^+$]; HRMS (ESI$^+$) *m/z* 283.0976 (283.0975 calcd for $C_{12}H_{20}O_4SNa$); Anal. Calcd. for $C_{12}H_{20}O_4S + Me_2CO$: C 56.58; H 8.23. Found: C 56.17; H 7.91.

2,3,4,6-Di-*O*-isopropylidene-1,5-anhydro-5-seleno-L-gulitol (16). To a stirred suspension of the selenium powder (0.85 g, 10.8 mmol) in degassed EtOH (40 mL) under argon at 0 °C was added a saturated solution of $NaBH_4$ (~1 g) in degassed EtOH (10 mL). The suspension was stirred at 0 °C for 10 minutes and at room temperature for 1 hour during which time the black selenium colour disappeared. The clear solution was then cooled to 0 °C for the addition of the dimesylate **(14)** (3 g, 7.2 mmol) in THF (5 mL). The reaction mixture was heated and stirred at 70 °C for 12 hours. The solvent was removed *in vacuo* before the residue was partitioned between DCM (50 mL) and water (50 mL) and the organic layer was separated. The aqueous phase was extracted with EtOAc (3 x 30 mL) and the combined organic extracts were washed with brine (2 x 30 mL) and dried over $MgSO_4$. Evaporation and chromatography (25% EtOAc in Pet.) afforded the seleno-gulitol **(16)** as a white amorphous solid (1.34 g, 4.4 mmol, 61%). R_f 0.49 (Hex:EtOAc 3:1); $[\alpha]_D^{22}$ = -33.1^o (*c* 0.5 in DCM); ^{1}H NMR (500 MHz, $CDCl_3$) 4.43 (ddd, *J* = 2.4, 5.4, 5.8 Hz, 1H), 4.37 (t, *J* = 3.2 Hz, 1H), 4.22 (dd, *J* = 2.7, 12.6 Hz, 1H) 4.13 (*J* = 3.5, 5.9 Hz, 1H), 3.78 (dd, *J* = 2.0, 12.7 Hz, 1H), 3.21 (dd, *J* = 3.3, 12.6 Hz, 1H), 3.18 (dd, *J* = 2.0, 2.7, 6.9 Hz, 1H), 2.68 (dd, *J* = 5.9, 12.6 Hz, $J_{H,Se}$ = 12.4 Hz, 1H), 1.53 (s, 3H), 1.47 (s, 3H), 1.45 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 108.48, 99.48, 75.44, 70.29, 67.67, 65.01, 29.49, 28.22, 27.00, 25.16, 20.99, 19.37; ^{77}Se NMR (95 MHz, $CDCl_3$) δ 63; IR (neat)/cm^{-1}: 2970, 1739, 1366, 1217; MS (ESI$^+$) *m/z* (rel intensity) 360.55 [100, (M+53)$^+$]; HRMS (ESI$^+$) *m/z* 331.0420 (331.0419 calcd for $C_{12}H_{20}O_4SeNa$). Anal. Calcd. for $C_{12}H_{20}O_4Se$: C 46.92; H 6.56; O 20.84; Se 25.68. Found: C 47.02; H 6.49; O 20.90.

1,5-Anhydro-5-thio-L-gulitol (8). To a stirred solution of the protected thio-sugar **(15)** (0.5 g, 1.9 mmol) in DCM (10 mL) under nitrogen at 0 °C was added TFA (1 mL). The solution was stirred at 0 °C for 10 minutes and at room temperature for 3 hours. The solvent was removed *in vacuo* and the residue was purified by column chromatography (30% MeOH in DCM) to afford the deprotected thio-sugar **(8)** as a white amorphous solid (0.23 g, 1.29 mmol, 68%). R_f 0.49 (MeOH:EtOAc 1:5); $[\alpha]_D^{22}$ = -17.6 (*c* 0.1 in MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 4.09 (ddd, *J* = 2.5, 4.0, 11.4 Hz, 1H), 4.06 (td, *J* = 2.0, 7.0 Hz, 1H) 3.82 (m, 1H), 3.72 (dd, *J* = 7.0, 11.1 Hz, 1H), 3.61 (dd, *J* = 6.7, 11.0 Hz, 1H), 3.36 (dd, *J* = 1.6, 5.3 Hz, 1H), 2.95 (t, *J* = 11.8 Hz, 1H), 2.35 (dd, *J* = 3.9, 12.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 77.75, 73.16, 68.75, 62.69, 44.19, 28.61; IR (neat)/cm^{-1}: 3308, 2921, 1393, 1024; MS (ESI$^+$) *m/z* (rel intensity) 203.17 [100, (M+Na)$^+$]; HRMS (ESI$^+$) *m/z* 203.0349 (203.0349 calcd for $C_6H_{12}O_4SNa$).

1,5-Anhydro-5-seleno-L-gulitol (9). To a stirred solution of the protected seleno-sugar **(16)** (0.5 g, 1.6 mmol) in DCM (10 mL) under nitrogen at 0 °C was added TFA (1 mL). The solution was stirred at 0 °C for 10 minutes and at room temperature for 3 hours. The solvent was removed *in vacuo* and the residue was purified by column chromatography (30% MeOH in DCM) to afford the deprotected seleno-sugar **83** as a white amorphous solid (0.21 g, 0.91 mmol, 57%). R_f 0.50 (MeOH:EtOAc 1:5); $[\alpha]_D^{22}$ = -17.7^o (*c* 0.1 in MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 4.15 (ddd, *J* = 2.5, 4.0, 11.4 Hz, 1H), 4.12 (dd, *J* = 2.5, 5.4 Hz, 1H,), 3.80 (dd, *J* = 1.6, 5.3 Hz, 1H), 3.76 (dd, *J* = 7.2, 11.0 Hz, 1H), 3.65 (dd, *J* = 6.8, 11.0 Hz, 1H), 3.59 (td, *J* = 2.0, 7.0 Hz, 1H), 3.04 (t, *J* = 11.3 Hz, 1H), 2.28 (dd, *J* = 3.9, 11.5 Hz, $J_{H,Se}$ = 12.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 73.69, 72.32, 68.83, 63.42, 39.04, 19.21; IR (neat)/cm^{-1}: 3321, 2126, 1638; MS (ESI$^+$) *m/z* (rel intensity) 360.45 [100, (M+133.33)$^+$]; HRMS (ESI$^+$) *m/z* 250.9793 (250.9799 calcd for $C_6H_{12}O_4SeNa$); Anal. Calcd. for $C_6H_{12}O_4Se$: C 31.74; H 5.33; O 28.19; Se 34.74. Found: C 32.01; H 5.15.

2,3,4,6-Di-isopropylidene-1-*tert*-butyl-dimethylsilyl-5-*O*-hydroxy-D-mannitol (17). To a solution of the diol **(13)** (5 g, 19.1 mmol) in dry DCM (100 mL) under nitrogen at 0 °C was added imidazole (3.2 g, 47.7 mmol) followed by TBDMSCl (3.16 g, 21.0 mmol). The solution was stirred at 0 °C for 10 minutes and was then allowed to warm to room temperature and stirred for 2 hours, during which time a solid white precipitate formed. The reaction mixture was then diluted with DCM (100 mL) and poured into water (100 mL). The organic fraction was washed with saturated $NaHCO_3$ (2 x 40 mL), dried over $MgSO_4$ and concentrated to afford a viscous clear yellow oil. Flash chromatography (Hex:EtOAc 4:1) afforded the silyl ether **(17)** as a colourless oil (6.82 g, 18.1 mmol, 95%). R_f 0.48 (Hex:EtOAc 3:1); $[\alpha]_D^{22}$= -58.7^o (*c* 1.0 in DCM); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.37 (dd, *J* = 3.1, 6.2 Hz, 1H), 4.32 (dd, *J* = 5.8, 13.1, Hz, 1H), 3.92 - 3.78 (m, 5H), 3.64 - 3.57 (m, 1H), 2.77 (bs, 1H), 1.48 (s, 6H), 1.41 (s, 3H), 1.37 (s, 3H), 0.91 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 109.02, 98.81, 77.51, 76.06, 72.42, 65.12, 64.43, 62.17, 28.61, 27.17, 26.05, 19.60, 18.51, -5.16, -5.22; IR (neat)/cm^{-1}: 3530, 2985, 2930, 1379, 1251, 1075; MS (ESI$^+$) *m/z* (rel intensity) 449.18 [100, (M+72)$^+$];

HRMS (ESI^+) *m/z* 377.2353 (377.2354 calcd for $C_{18}H_{36}O_6Si$); Anal. Calcd. for $C_{18}H_{36}O_6Si$: C 57.41; H 9.64; O 25.49; Si 7.46. Found: C 57.27; H 9.48.

2,3,4,6-Di-isopropylidene-1-*tert*-butyl-dimethylsilyl-D-man-5-anone (18). To a solution of DMSO (3.72 mL, 54.1 mmol) in dry DCM (100 mL) under nitrogen at -78 °C was added oxalyl chloride (3.43 mL, 39.4 mmol) dropwise, maintaining the temperature at -78 °C. Afer stirring for 30 minutes the alcohol **(17) (**5.0 g, 13.3 mmol) in DCM (25 mL) was added dropwise. After stirring for 1 hour Et_3N (14.68 mL, 105 mmol) was added dropwise and the solution was stirred for an additional hour at -78°C and was then slowly warmed to room temperature. The reaction mixture was then diluted with DCM (100 mL) and poured into water (100 mL). The organic fraction was washed with saturated $NaHCO_3$ (2 x 50 mL) and brine (50 mL), dried over MgSO4 and concentrated to afford a viscous clear yellow oil. Flash chromatography (Hex:EtOAc 5:1) afforded the ketone **(18)** as a colourless oil (4.43 g, 11.84 mmol, 89%). R_f 0.47 (Hex:EtOAc 5:1); $[\alpha]_D^{22}$= -47.6° (*c* 1.0 in DCM); ^1H NMR (500 MHz, $CDCl_3$) δ 4.65 (dd, *J* = 6.6, 3.8 Hz, 1H), 4.59 (dd, *J* = 3.8, 1.4 Hz, 1H), 4.38 - 4.32 (m, 1H), 4.29 (dd, *J* = 16.7, 1.5 Hz, 2H), 3.98 (d, *J* = 16.7 Hz, 1H), 3.86 (dd, *J* = 6.3, 4.0 Hz, 2H), 1.50 (s, 3H), 1.48 (s, 3H), 1.47 (s, 3H), 1.35 (s, 3H), 0.88 (s, 9H), 0.07 (s, 3H); ^{13}C NMR (125 MHz; $CDCl_3$) δ 207.81, 109.36, 101.08, 76.65, 75.37, 74.01, 66.96, 61.95, 26.75, 25.96, 25.68, 23.95, 18.32, -5.25, -5.29; IR (neat)/cm^{-1}: 2932, 2859, 1750, 1381, 1254, 1090; MS (ESI^+) *m/z* (rel intensity) 483.12 [100, $(M+Ag)^+$]; HRMS (ESI^+) *m/z* 483.1168 (483.1167 calcd for $C_{18}H_{34}O_6SiAg$).

2,3,4,6-Di-isopropylidene-1-*tert*-butyl-dimethylsilyl-5-*O*-hydroxy-L-gulitol (19). To a solution of the ketone **(18)** (5.0 g, 13 mmol) in dry MeOH (150 mL) at - 78°C was added $CeCl_3.7H_2O$ (5.35 g, 14.3 mmol). The solution was stirred for 5 minutes before the portionwise addition of $NaBH_4$ (0.76 mg, 20 mmol). The solution was then allowed to warm to room temperature before being filtered through celite and the solvent removed *in vacuo*. The remaining residue was dissolved in EtOAc (100 mL) and water (75 mL). The organic layer was then separated and the aqueous layer was extracted with EtOAc (50 mL). The combined organic fractions were washed with saturated $NaHCO_3$ (75 mL), then brine (75 mL) and dried over $MgSO_4$. Evaporation of the solvent afforded a viscous clear oil. Flash chromatography (Hex:EtOAc 4:1) afforded the alcohol **(19)** as a colourless oil (4.6 g, 12.2 mmol, 94%). R_f 0.38 (Hex:EtOAc 3:1); $[\alpha]_D^{22}$= -10.7° (*c* 1.0 in DCM); ^1H NMR (500 MHz, $CDCl_3$) δ 4.40 (t, *J* = 5.7 Hz, 1H), 4.22 (ddd, *J* = 8.4, 5.7, 4.3 Hz, 1H), 4.10 (dd, *J* = 5.8, 1.3 Hz, 1H), 4.00 (dd, *J* = 12.2, 1.5 Hz, 1H), 3.82 - 3.76 (m, 1H), 3.76 - 3.72 (m, 1H), 3.70 (dd, *J* = 10.5, 4.3 Hz, 1H), 1.49 (s, 6H), 1.47 (s, 3H), 1.37 (s, 3H), 0.89 (s, 9H), 0.07 (d, *J* = 0.7 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 109.11, 99.02, 78.22, 76.88, 69.41, 65.59, 65.17, 61.97, 29.51, 27.37, 26.05, 25.84, 25.70, 18.54, -5.16, -5.22; IR (neat)/cm^{-1}: 3525, 2990, 2931, 1380, 1252, 1074; MS (ESI^+) *m/z* (rel intensity) 399.17 [100, $(M+Na)^+$]; HRMS (ESI^+) *m/z* 399.2173 (399.2173 calcd for $C_{18}H_{36}O_6SiNa$). Anal. Calcd. for $C_{18}H_{36}O_6Si$: C 57.41; H 9.64; O 25.49; Si 7.46. Found: C 57.35; H 9.49.

2,3,4,6-Di-isopropylidene-1,5-di-*O*-hydroxy-L-gulitol (20). To a stirred solution of **(19)** (3 g, 7.97 mmol) in dry THF (50 mL) under nitrogen at room temperature was added TBAF (7.4 mL of a 1.0 M solution in THF, 7.4 mmol) dropwise. After 3 hours the solvent was concentrated *in vacuo*, before the residue was diluted with EtOAc (100 mL) and washed with water (2 x 50 mL) followed by brine (50 mL). Drying over $MgSO_4$ and concentration *in vacuo* afforded compound **(20)** as a colourless oil (1.90 g, 7.25 mmol, 91 %). R_f 0.18 (EtOAc); $[\alpha]_D^{22}$ = -3.6° (*c* 1.0 in DCM); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.40 (dd, *J* = 6.3, 4.5 Hz, 1H), 4.33 - 4.27 (m, 1H), 4.03 (ddd, *J* = 5.8, 3.0, 0.9 Hz, 2H), 3.84 (dd, *J* = 12.4, 2.1 Hz, 1H), 3.79 - 3.73 (m, 2H), 3.61 (ddd, *J* = 6.7, 3.6, 1.6 Hz, 1H), 1.55 (s, 3H), 1.50 (s, 6H), 1.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 109.44, 99.28, 78.02, 77.77, 69.31, 65.58, 65.53, 61.37, 29.38, 27.14, 25.66, 18.46; IR (neat)/cm^{-1}: 3449, 2989, 2926, 1381, 1221, 1041; MS (ESI$^+$) *m/z* (rel intensity) 285.18 [100, (M+Na)$^+$]; HRMS (ESI$^+$) *m/z* 285.1309 (285.1309 calcd for $C_{12}H_{22}O_6Na$); Anal. Calcd. for $C_{12}H_{22}O_6$: C 54.95; H 8.45. Found: C 54.97; H 8.43.

2,3,4,6-Di-isopropylidene-1,5-di-*O*-methanesulfonyl-L-gulitol (21). To a stirred solution of the diol **(20)** (5 g, 19 mmol), DMAP (250 mg, 2 mmol) and anhydrous pyridine (10 mL) in dry DCM (150 mL) under nitrogen at 0 °C was added dropwise methanesulfonyl chloride (4.5 mL, 59 mmol). The solution was stirred at 0 °C for 30 minutes and then warmed to room temperature for 6 hours. The reaction was quenched by the addition of saturated $NaHCO_3$ (50 mL) before being extracted with DCM (3 x 50 mL). The combined organic extracts were then washed with brine (2 x 100 mL) and dried over $MgSO_4$. Evaporation and chromatography (Hex:EtOAc 1:1) afforded the dimesylate **(21)** as a white amorphous solid (6.76 g, 18.1 mmol, 95%). R_f 0.36 (Hex:EtOAc 1:1); $[\alpha]_D^{22}$ = +15.2° (*c* 1.0 in DCM); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.75 (q, *J* = 2.1 Hz, 1H), 4.56 - 4.50 (m, 1H), 4.43 (dd, *J* = 7.3, 5.3 Hz, 1H), 4.37 (dd, *J* = 10.7, 6.7 Hz, 1H), 4.28 (dd, *J* = 7.3, 1.7 Hz, 1H), 4.22 (dd, *J* = 10.7, 4.8 Hz, 1H), 4.18 (dd, *J* = 13.6, 2.0 Hz, 1H), 4.09 (dd, *J* = 13.6, 2.3 Hz, 1H), 3.18 (s, 3H), 3.10 (s, 3H), 1.55 (s, 3H), 1.53 (s, 3H), 1.51 (s, 3H), 1.42 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 109.60, 99.69, 76.28, 74.67, 73.49, 71.24, 69.36, 68.12, 67.94, 67.17, 62.68, 62.42, 39.12, 37.93, 37.73, 28.75, 27.86, 26.58, 25.62, 25.49, 20.13, 18.85; IR (neat)/cm^{-1}: 2992, 2940, 1351, 1173; MS (ESI$^+$) *m/z* (rel intensity) 436.27 [100, (M+18)$^+$]; HRMS (ESI$^+$) *m/z* 441.0860 (441.0860 calcd for $C_{14}H_{26}O_{10}S_2Na$); Anal. Calcd. for $C_{14}H_{26}O_{10}S_2$: C 40.18; H 6.26. Found: C 40.09; H 6.28.

2,3,4,6-Di-O-isopropylidene-1,5-anhydro-5-thio-D-mannitol (22). To a solution of the dimesylate **(21)** (1 g, 2.4 mmol) in DMF (15 mL) under nitrogen was added $Na_2S.9H_2O$ (0.68 g, 3.0 mmol). The solution was stirred at 100 °C for 15 hours and was then allowed to cool to room temperature. The reaction mixture was then concentrated *in vacuo*, poured into water (50 mL), and extracted with DCM (3 x 50 mL). The combined organic fractions were washed with water (2 x 40 mL), brine (10 mL), dried over $MgSO_4$ and concentrated to afford a viscous clear yellow oil. Flash chromatography (Hex:EtOAc 3:1) afforded the thio-gulitol **(22)** as a white amorphous solid (0.54 g, 2.1 mmol, 86%). R_f 0.52 (Hex:EtOAc 3:1); $[\alpha]_D^{22}$ = -25.7° (*c* 1.0 in DCM); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.45 (ddd, *J* = 7.8, 6.1, 4.3 Hz, 1H), 4.07 - 3.99 (m, 2H), 3.89 - 3.76 (m, 2H), 2.91 - 2.78 (m, 3H), 1.55 (s, 3H), 1.54

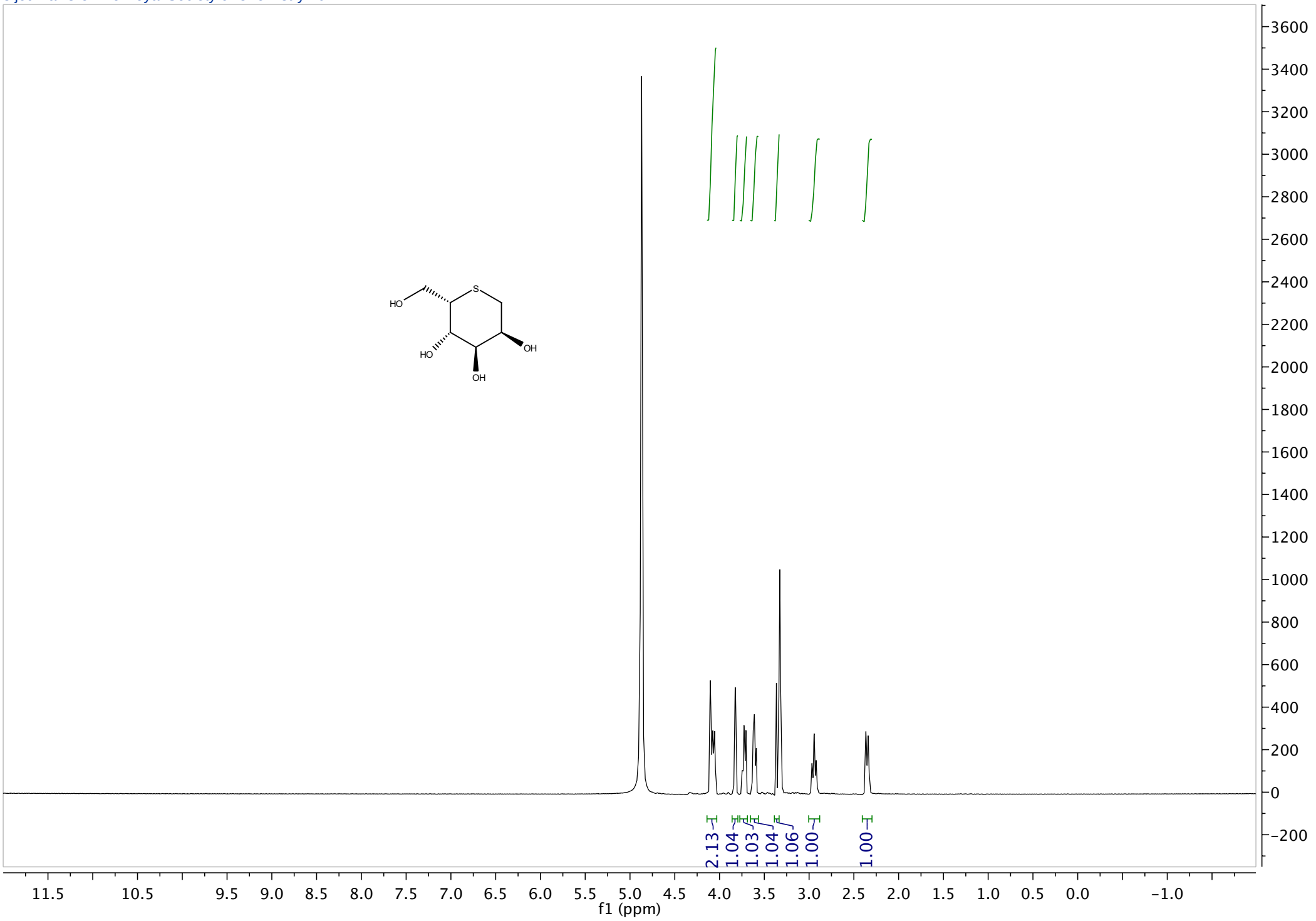
(s, 3H), 1.46 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 109.32, 99.46, 77.40, 74.32, 73.77, 63.34, 35.59, 29.49, 27.73, 27.09, 25.44, 18.98; IR (neat)/cm^{-1}: 2990, 2937, 1373, 1198, 1064; MS (ESI$^+$) *m/z* (rel intensity) 203.17 [100, (M-57)$^+$]; HRMS (ESI$^+$) *m/z* 283.0975 (283.0975 calcd for $C_{12}H_{20}O_4SNa$). Anal. Calcd. for $C_{12}H_{20}O_4S$: C 55.36; H 7.74. Found: C 55.28; H 7.94.

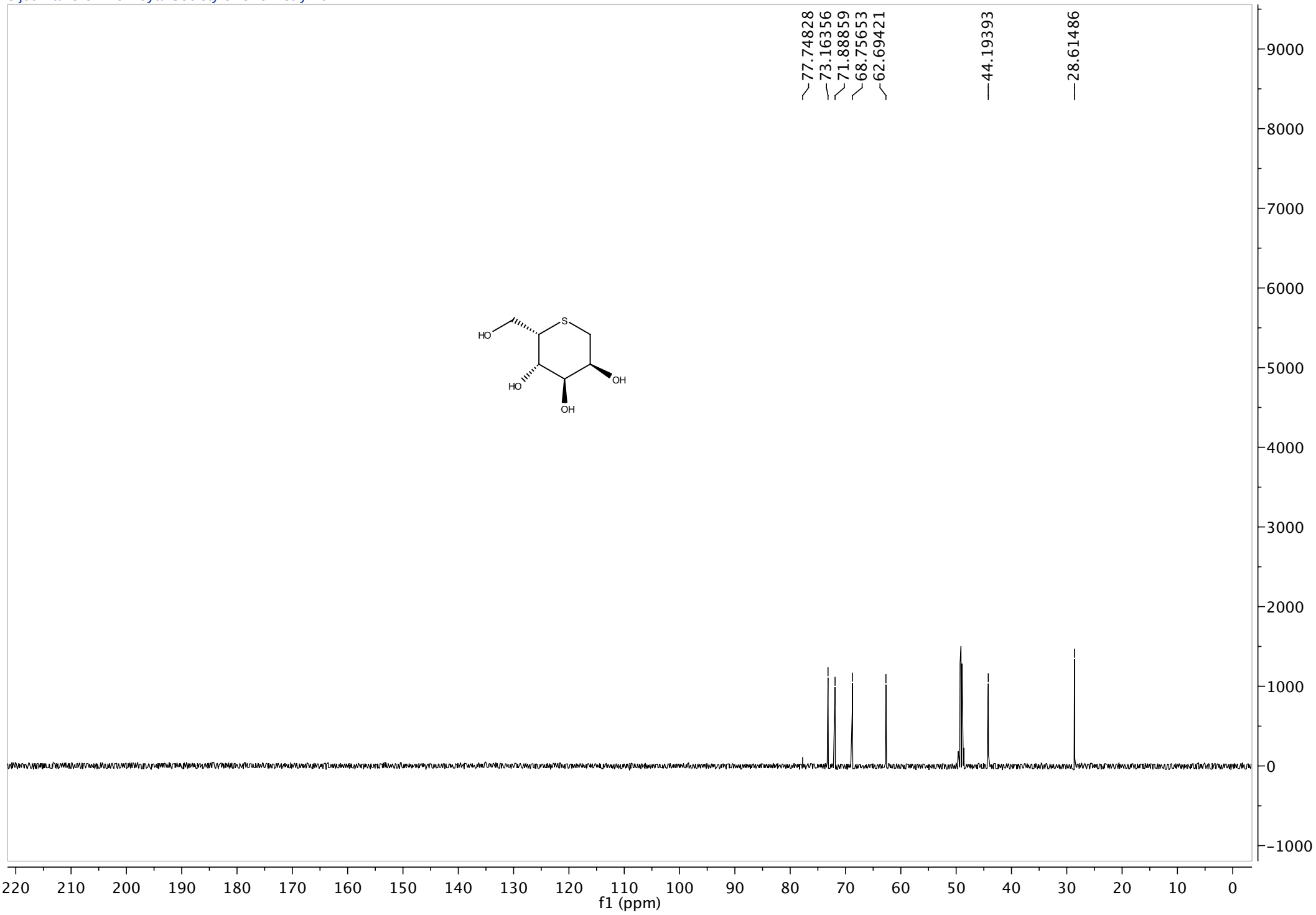
2,3,4,6-Di-O-isopropylidene-1,5-anhydro-5-seleno-D-mannitol (23). To a stirred suspension of the selenium powder (1 g, 12.7 mmol) in degassed EtOH (40 mL) under argon at 0 °C was added a saturated solution of $NaBH_4$ (~1 g) in degassed EtOH (10 mL). The suspension was stirred at 0 °C for 10 minutes and at room temperature for 1 hour during which time the black selenium colour disappeared. The clear solution was then cooled to 0 °C for the addition of the dimesylate **(21)** (3 g, 7.2 mmol) in THF (5 mL). The reaction mixture was heated and stirred at 70 °C for 12 hours. The solvent was removed *in vacuo* before the residue was partitioned between EtOAc (50 mL) and water (50 mL) and the organic layer was separated. The aqueous phase was extracted with EtOAc (3 x 30 mL) and the combined organic extracts were washed with brine (2 x 30 mL) and dried over $MgSO_4$. Evaporation and chromatography (Hex:EtOAc 3:1) afforded the seleno-gulitol **(23)** as a white crystalline solid (1.36 g, 4.5 mmol, 63%). R_f 0.51 (Hex:EtOAc 3:1); $[\alpha]_D^{22}$ = +21.3^o (*c* 1.0 in DCM); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.53 - 4.44 (m, 1H), 4.11 - 3.97 (m, 3H), 3.85 (dd, *J* = 11.6, 5.1 Hz, 1H), 3.13 (td, *J* = 11.2, 5.2 Hz, 1H), 2.83 (t, *J* = 11.3 Hz, 1H), 2.63 (dd, *J* = 11.5, 4.5 Hz, $J_{H,Se}$ = 12.4 Hz, 1H), 1.57 (s, 3H), 1.51 (s, 3H), 1.46 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 109.07, 99.45, 77.49, 75.72, 73.49, 64.55, 29.61, 27.67, 27.58, 25.03, 19.14, 18.01; ^{77}Se NMR (95 MHz; $CDCl_3$) δ 103.02; IR (neat)/cm^{-1}: 2990, 2938, 1373, 1198, 1057; MS (ESI$^+$) *m/z* (rel intensity) 251.18 [100, (M-56)$^+$]; HRMS (ESI$^+$) *m/z* 414.9574 (414.9572 calcd for $C_{12}H_{20}O_4Ag$); Anal. Calcd. for $C_{12}H_{20}O_4Se$: C 45.92; H 6.56. Found: C 47.01; H 6.52.

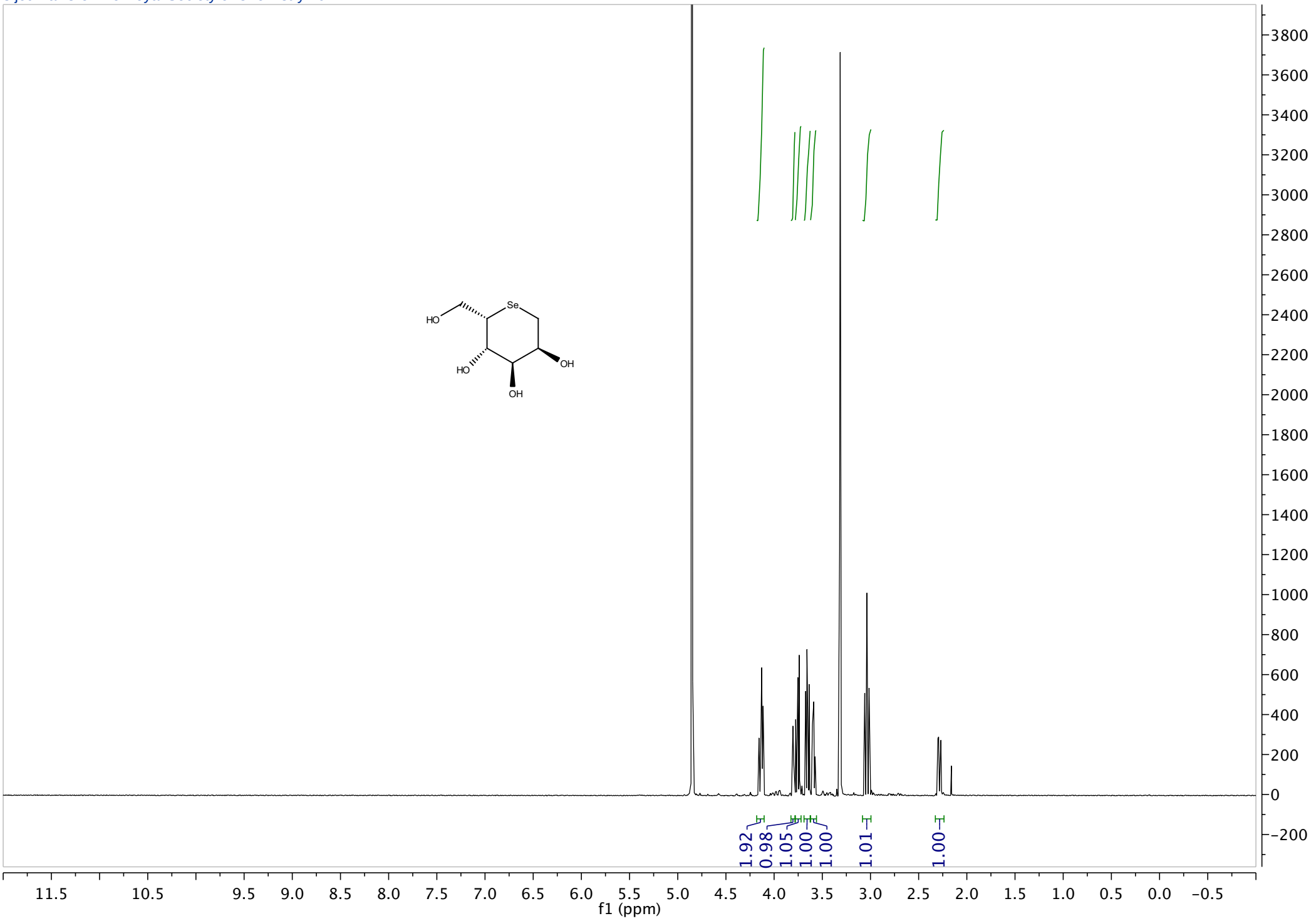
1,5-Anhydro-5-thio-D-mannitol (10). To a stirred solution of the protected thio-sugar **(22)** (0.5 g, 1.9 mmol) in dry DCM (10 mL) under nitrogen at 0 °C was added TFA (1 mL). The solution was stirred at 0 °C for 10 minutes and at room temperature for 3 hours. The solvent was removed *in vacuo* and the residue was purified by column chromatography (30% MeOH in DCM) to afford the deprotected thio-sugar **(10)** as a colourless crystalline solid (0.24 g, 1.35 mmol, 71%). R_f 0.25 (EtOAc:MeOH 5:1); M.p: 127-128 ^{o}C (MeOH); $[\alpha]_D^{22}$= -41.4^o *c* 0.1 in MeOH; ^{1}H NMR (500 MHz, CD_3OD) δ 4.17 - 4.11 (m, 1H), 3.96 (dd, *J* = 11.4, 4.3 Hz, 1H), 3.82 (t, *J* = 8.7 Hz, 1H), 3.74 (dd, *J* = 11.4, 6.9 Hz, 1H), 3.37 (dd, *J* = 8.5, 2.9 Hz, 1H), 2.85 (dd, *J* = 14.0, 2.1 Hz, 1H), 2.81 (ddd, *J* = 8.9, 6.9, 4.3 Hz, 1H), 2.70 (dd, *J* = 14.0, 5.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 79.28, 74.73, 72.73, 65.90, 52.70, 35.50; IR (neat)/cm^{-1}: 3309, 2884, 1413, 1048; MS (ESI$^+$) *m/z* (rel intensity) 203.17 [100, (M+Na)$^+$]; HRMS (ESI$^+$) *m/z* 203.0349 (203.0349 calcd for $C_6H_{12}O_4SNa$); Anal. Calcd. for $C_6H_{12}O_4S$: C 39.99; H 6.71. Found: C 39.75; H 6.64.

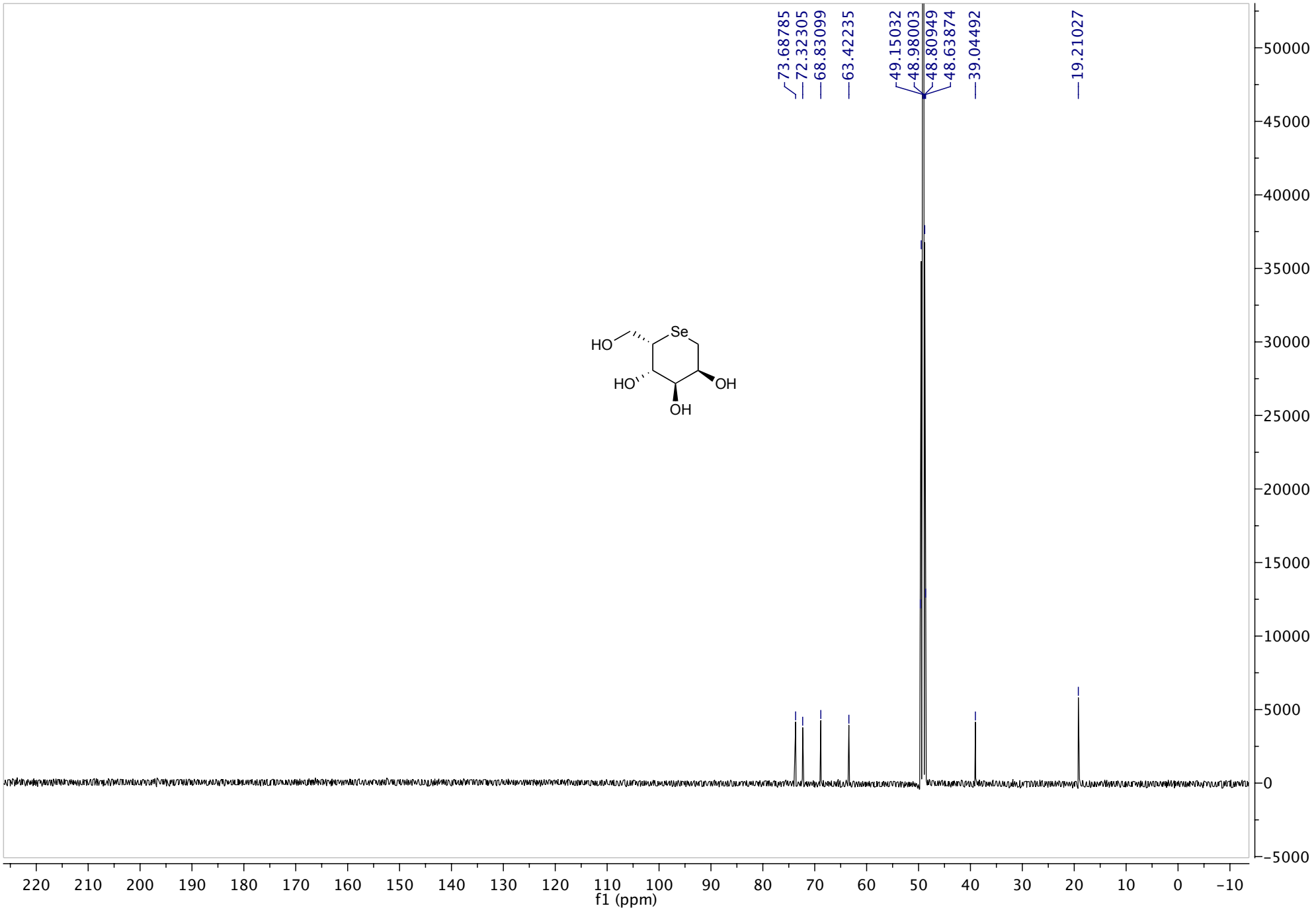
1,5-Anhydro-5-seleno-D-mannitol (11). To a stirred solution of the protected seleno-sugar **(23)** (0.5 g, 1.6 mmol) in dry DCM (10 mL) under nitrogen at 0 °C was added TFA (1 mL). The solution was

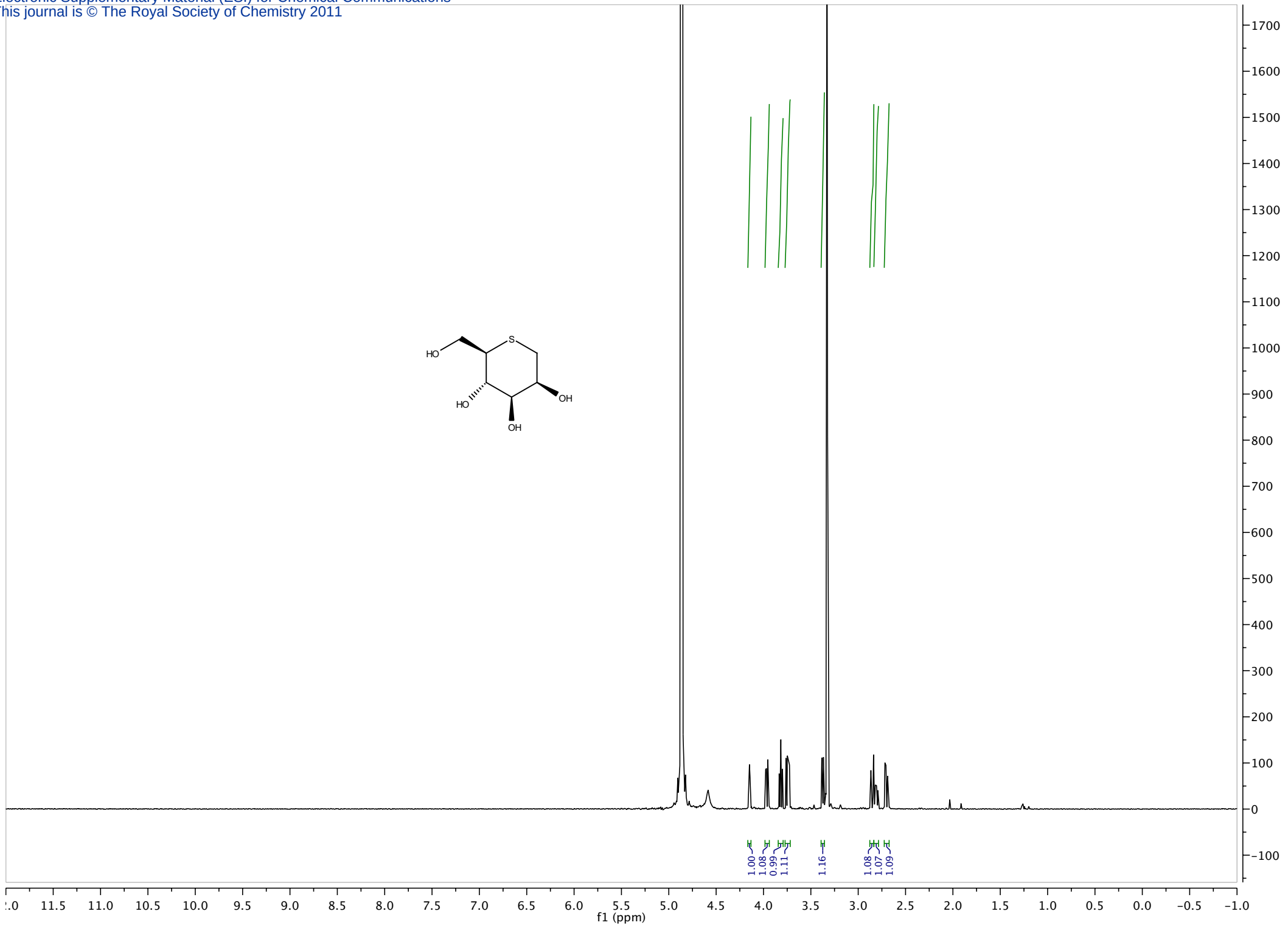
stirred at 0 °C for 10 minutes and at room temperature for 3 hours. The solvent was removed *in vacuo* and the residue was purified by column chromatography (30% MeOH in DCM) to afford the deprotected seleno-sugar **(11)** as a white amorphous solid (0.22 g, 0.92 mmol, 61%). R_f 0.29 (EtOAc:MeOH 5:1); $[\alpha]_D^{22}$ = -41.4° *c* 0.1 in MeOH; ^{1}H NMR (500 MHz, CD_3OD) δ 4.30 (td, *J* = 5.5, 3.2 Hz, 1H), 4.24 (dd, *J* = 5.3, 3.2 Hz, 1H), 3.70 (ddd, *J* = 9.2, 6.1, 3.3 Hz, 1H), 3.63 (dd, *J* = 11.4, 3.3 Hz, 1H), 3.48 (ddd, *J* = 11.4, 6.1, 0.6 Hz, 1H), 3.42 (dd, *J* = 8.6, 5.4 Hz, 1H), 2.98 (dd, *J* = 9.9, 5.1 Hz, 1H), 2.79 (dd, *J* = 9.9, 6.0 Hz, $J_{H,Se}$ = 12.4 Hz, 1H); ^{13}C NMR (126 MHz, CD_3OD) δ 78.50, 76.04, 75.10, 65.27, 44.53, 23.84; IR (neat)/cm^{-1}: 3346, 2885, 1415, 1051; MS (ESI$^+$) *m/z* (rel intensity) 243.17 [100, (M+16)$^+$]; HRMS (ESI$^+$) *m/z* 250.9793 (250.9793 calcd for $C_6H_{12}O_4SeNa$); Anal. Calcd. for $C_6H_{12}O_4Se$: C 31.74; H 5.33. Found: C 31.63; H 5.33.

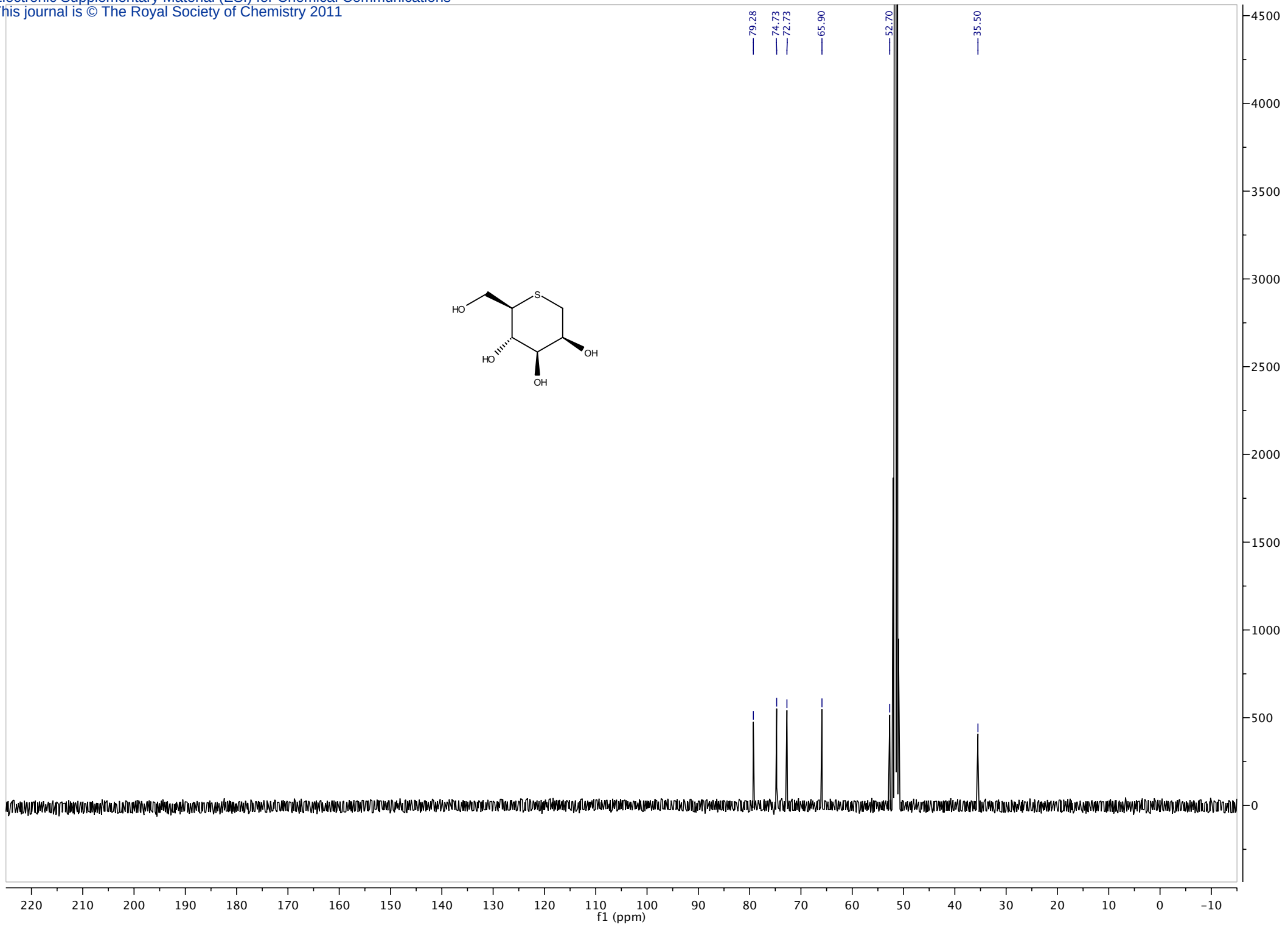


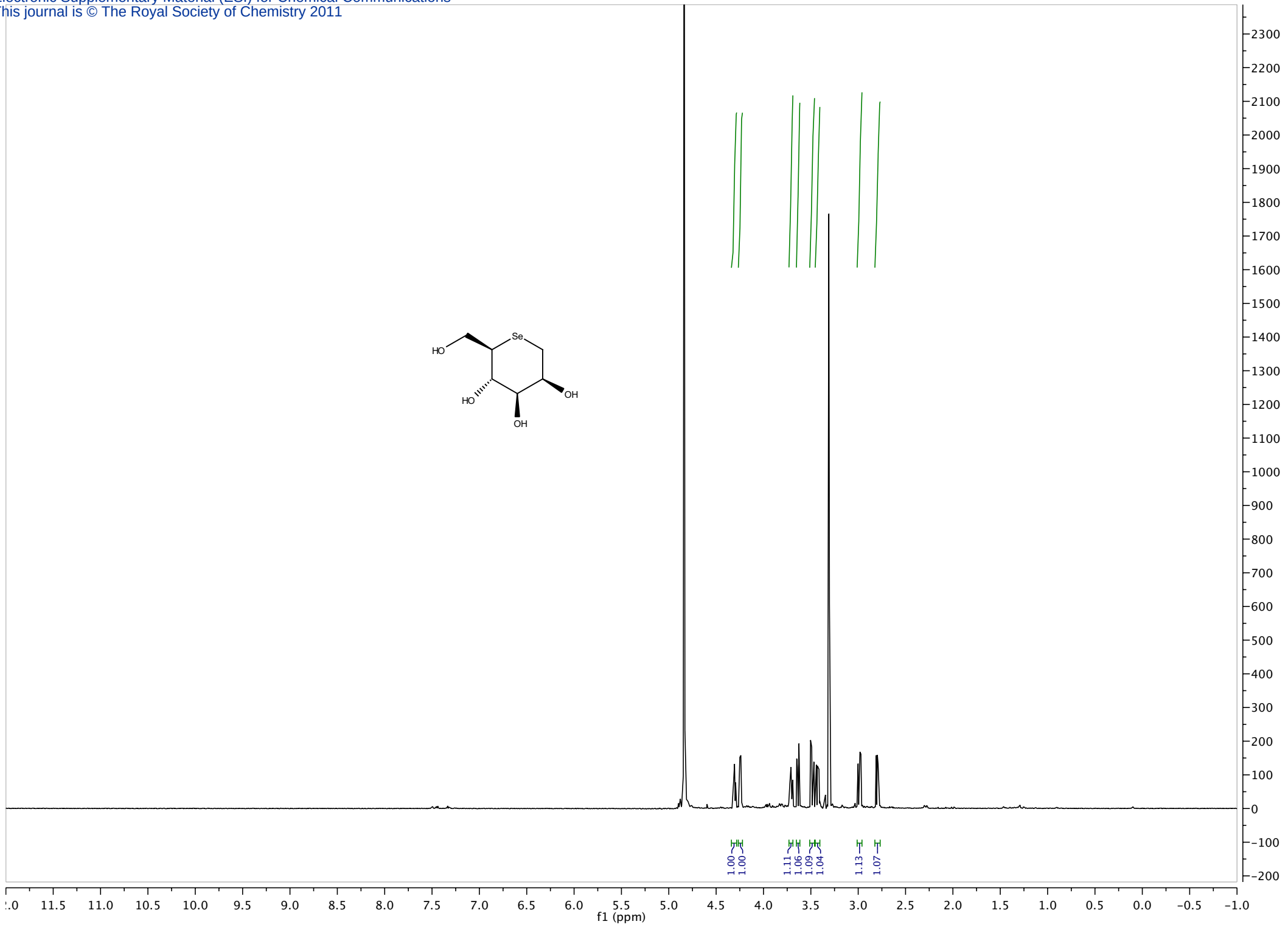


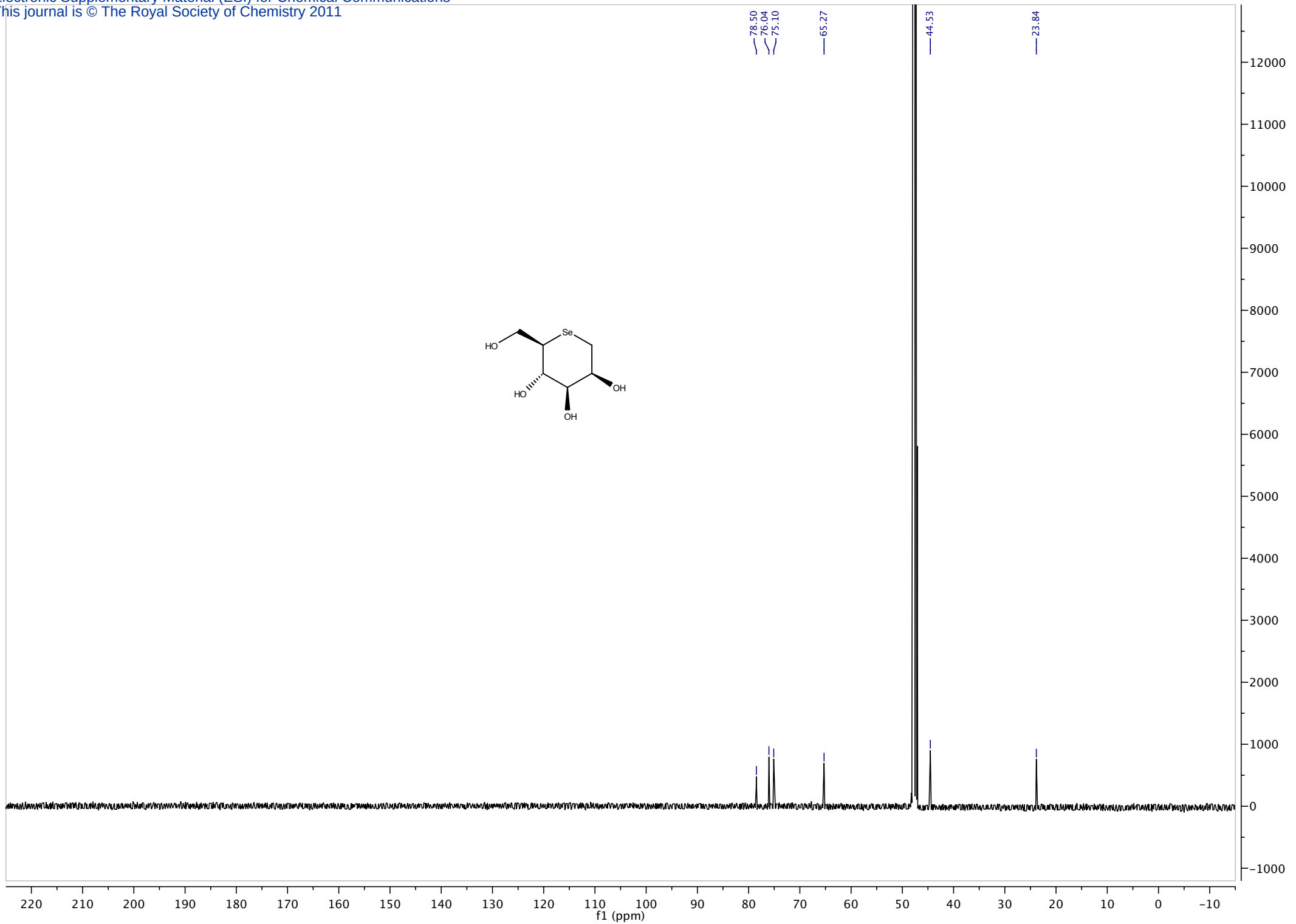




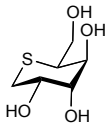


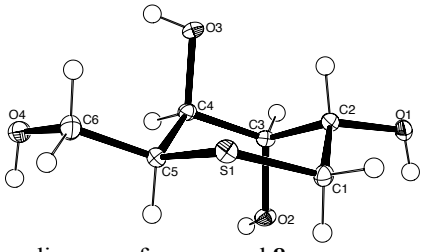






1,5-Anhydro-5-thio-L-gulitol (**8**)



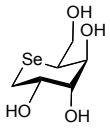


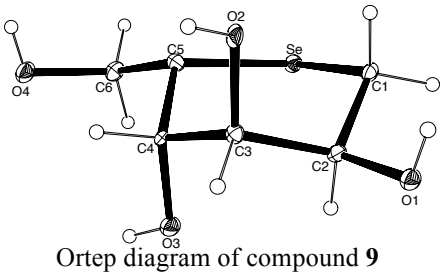
Ortep diagram of compound **8**

Table 1. Crystal data and structure refinement for **8**.

Empirical formula	C6 H12 O4 S	
Formula weight	180.22	
Temperature	130.0 K	
Wavelength	0.7107 ≈	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 5.53550(10) ≈	α= 90∞.
	b = 11.5250(2) ≈	β= 90∞.
	c = 11.6990(2) ≈	γ = 90∞.
Volume	746.36(2) ≈^{3}	
Z	4	
Density (calculated)	1.604 Mg/m^3	
Absorption coefficient	0.396 mm^{-1}	
F(000)	384	
Crystal size	0.6387 x 0.4061 x 0.3169 mm^3	
Theta range for data collection	3.48 to 29.08∞.	
Index ranges	-7<=h<=7, -15<=k<=15, -15<=l<=15	
Reflections collected	9451	
Independent reflections	1877 [R(int) = 0.0214]	
Completeness to theta = 29.08∞	98.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.65385	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1877 / 0 / 117	
Goodness-of-fit on F^2	1.081	
Final R indices [I>2sigma(I)]	R1 = 0.0192, wR2 = 0.0488	
R indices (all data)	R1 = 0.0198, wR2 = 0.0491	
Absolute structure parameter	0.03(5)	
Extinction coefficient	0.007(3)	
Largest diff. peak and hole	0.310 and -0.164 e.≈$^{-3}$	

1,5-Anhydro-5-seleno-L-gulitol (**9**).



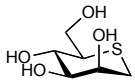


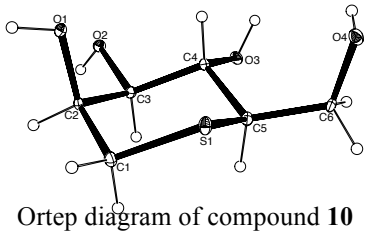
Ortep diagram of compound **9**

Table 1. Crystal data and structure refinement for **9**.

Empirical formula	C6 H12 O4 Se	
Formula weight	227.12	
Temperature	130(2) K	
Wavelength	1.54184 ≈	
Crystal system	Orthorhombic	
Space group	P212121	
Unit cell dimensions	a = 5.5827(2) ≈	α= 90∞.
	b = 11.6100(3) ≈	β= 90∞.
	c = 11.8442(3) ≈	γ = 90∞.
Volume	767.68(4) ≈^{3}	
Z	4	
Density (calculated)	1.965 Mg/m^3	
Absorption coefficient	6.390 mm^{-1}	
F(000)	456	
Crystal size	0.4004 x 0.0560 x 0.0500 mm^3	
Theta range for data collection	5.34 to 72.85∞.	
Index ranges	-6<=h<=4, -13<=k<=14, -10<=l<=14	
Reflections collected	2269	
Independent reflections	1284 [R(int) = 0.0317]	
Completeness to theta = 72.85∞	98.6 %	
Absorption correction	Gaussian	
Max. and min. transmission	0.748 and 0.336	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1284 / 0 / 104	
Goodness-of-fit on F^2	1.050	
Final R indices [I>2sigma(I)]	R1 = 0.0331, wR2 = 0.0744	
R indices (all data)	R1 = 0.0350, wR2 = 0.0751	
Absolute structure parameter	0.03(5)	
Largest diff. peak and hole	0.617 and -0.415 e.≈$^{-3}$	

1,5-Anhydro-5-thio-D-mannitol (**10**)





Ortep diagram of compound **10**

Table 1. Crystal data and structure refinement for **10**.

Empirical formula	C6 H12 O4 S	
Formula weight	180.22	
Temperature	130(2) K	
Wavelength	1.5418 ≈	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 4.7741(3) ≈	α= 90∞.
	b = 8.1111(4) ≈	β= 94.245(5)∞.
	c = 9.6763(5) ≈	γ = 90∞.
Volume	373.67(4) ≈^{3}	
Z	2	
Density (calculated)	1.602 Mg/m^3	
Absorption coefficient	3.604 mm^{-1}	
F(000)	192	
Crystal size	0.3249 x 0.1500 x 0.0900 mm^3	
Theta range for data collection	4.58 to 73.24∞.	
Index ranges	-5<=h<=5, -4<=k<=9, -11<=l<=11	
Reflections collected	1413	
Independent reflections	920 [R(int) = 0.0182]	
Completeness to theta = 73.24∞	97.5 %	
Absorption correction	Gaussian	
Max. and min. transmission	0.736 and 0.524	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	920 / 1 / 117	
Goodness-of-fit on F^2	1.098	
Final R indices [I>2sigma(I)]	R1 = 0.0282, wR2 = 0.0750	
R indices (all data)	R1 = 0.0294, wR2 = 0.0752	
Absolute structure parameter	0.03(2)	
Extinction coefficient	0.024(4)	
Largest diff. peak and hole	0.326 and -0.240 e.≈$^{-3}$	