

Supplementary Information for

**Novel functionalized organotellurides with enhanced thiol peroxidase catalytic activity**

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## **1. Synthesis of $\beta$ -hydroxy tellurides (1), $\beta$ -amino tellurides (4) and dithiatellurepanes (7).<sup>1</sup>**

$\text{Li}_2\text{Te}$  was generated according to literature<sup>2</sup> from 1 mL of a 1 M THF solution of  $\text{LiEt}_3\text{BH}$  (1.0 mmol, 2.0 eq.) and elemental tellurium powder (63 mg, 0.5 mmol, 1.0 eq.), stirred at ambient temperature under inert atmosphere ( $\text{N}_2$ ) for 6 h. The chalky-white suspension of  $\text{Li}_2\text{Te}$  in THF was *in situ* treated with the electrophile (epoxide, aziridine or thiirane - 1.0 mmol, 2.0 eq.) and the reaction was stirred for 12 h at ambient temperature. Afterwards, the mixture was diluted with  $\text{Et}_2\text{O}$  (10 mL), filtered through a short pad of celite, washed with sat. aq.  $\text{NH}_4\text{Cl}$  and then with  $\text{H}_2\text{O}$  (2 x 5 mL). The organic phase was dried over  $\text{Na}_2\text{SO}_4$ , filtered and evaporated under reduced pressure. The crude residue was then purified by flash chromatography to yield  $\beta$ -functionalised tellurides.<sup>3</sup>

## **2. Synthesis of $\beta$ -hydroxyethyltellurides (2).**

$\text{Li}_2\text{Te}_2$  was generated from 0.5 mL of a 1 M THF solution of  $\text{LiEt}_3\text{BH}$  (0.5 mmol, 2.0 eq.) and 63 mg of elemental tellurium powder (0.5 mmol, 1.0 eq.), stirred at ambient temperature under inert atmosphere ( $\text{N}_2$ ) for 6 h. The dark red suspension of  $\text{Li}_2\text{Te}_2$  in THF was *in situ* treated with the suitable epoxide (0.5 mmol, 1.0 eq.) and the reaction was stirred for 12 h at ambient temperature. Afterwards, the mixture was diluted with  $\text{Et}_2\text{O}$  (5 mL), filtered through a short pad of celite, washed with  $\text{NH}_4\text{Cl}$  (sat. aq. solution), and then with  $\text{H}_2\text{O}$  (2 x 3 mL). The organic phase was dried over  $\text{Na}_2\text{SO}_4$ , filtered and evaporated under reduced pressure. The crude residue was then purified by flash chromatography to yield  $\beta$ -hydroxyethyl tellurides **2**.

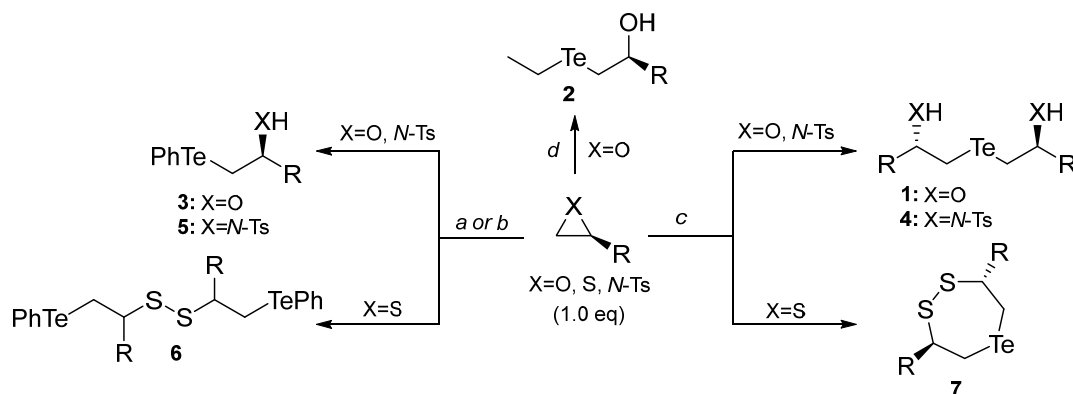
## **3. Synthesis of $\beta$ -phenyltelluro alcohols (3)**

$\text{NaBH}_4$  (28 mg, 0.75 mmol, 3.0 eq.) was portionwise added to a solution of diphenyl ditelluride (0.25 mmol, 1.0 eq.) in  $\text{EtOH}$  (2 mL) at  $0^\circ\text{C}$  under inert atmosphere ( $\text{N}_2$ ). After 30 min, the epoxide (0.45 mmol, 1.8 eq.) was slowly added and the reaction mixture was stirred at room temperature until complete consumption of the starting material was observed by TLC. The reaction was quenched by addition of saturated aq.  $\text{NH}_4\text{Cl}$  (2 mL) and diluted with  $\text{Et}_2\text{O}$  (5 mL). The layers were separated and the organic layer was washed with  $\text{H}_2\text{O}$  (3 mL), dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated under vacuum. The crude material was purified by flash chromatography to yield  $\beta$ -phenyltelluro alcohols **3**.

## **4. Synthesis of $\beta$ -phenyltelluro disulfide (6)**

A solution of 2-((benzyloxy)methyl)thiirane (0.2 mmol) and  $\text{PhTeSiMe}_3$  (0.24 mmol) in dry THF (1 mL) was cooled under inert atmosphere ( $\text{N}_2$ ) at  $0^\circ\text{C}$ , and treated with TBAF (72  $\mu\text{L}$  of 1 M THF

solution, 0.072 mmol). The reaction was stirred for 12 h at ambient temperature and then 2 mL of  $\text{NH}_4\text{Cl}$  (sat. aq. solution) was added. The solution was diluted with diethyl ether (5 mL), washed with water (1 x 5 mL), and dried over  $\text{Na}_2\text{SO}_4$ . The solvent was evaporated under vacuum and the crude product was purified by flash chromatography to give  $\beta$ -phenyltelluro disulfide **6**.

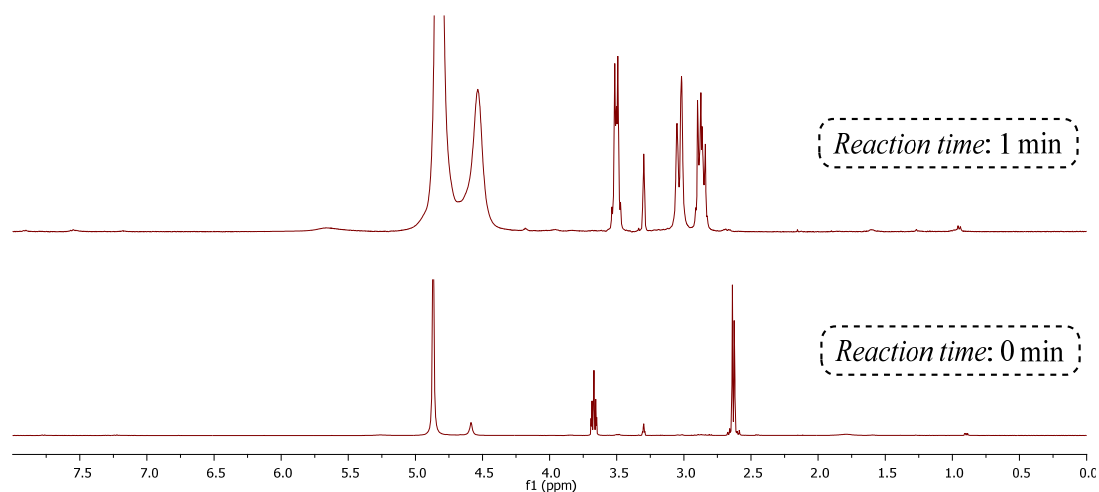
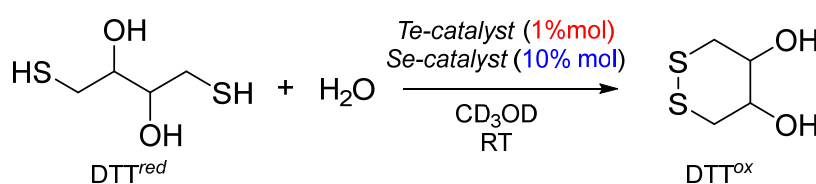


**Scheme S1:** Synthesis of  $\beta$ -functionalized tellurides. Reagent and conditions: a)  $\text{PhTeSiMe}_3$  (1.2 eq.), TBAF (0.36 eq.), THF. b)  $\text{PhTeTePh}$  (0.5 eq.),  $\text{NaBH}_4$  (1.5 eq.), EtOH. c) Elemental Te (0.5 eq.),  $\text{LiEt}_3\text{BH}$  (1.0 eq.), THF. d) Elemental Te (1.0 eq.),  $\text{LiEt}_3\text{BH}$  (1.0 eq.), THF.

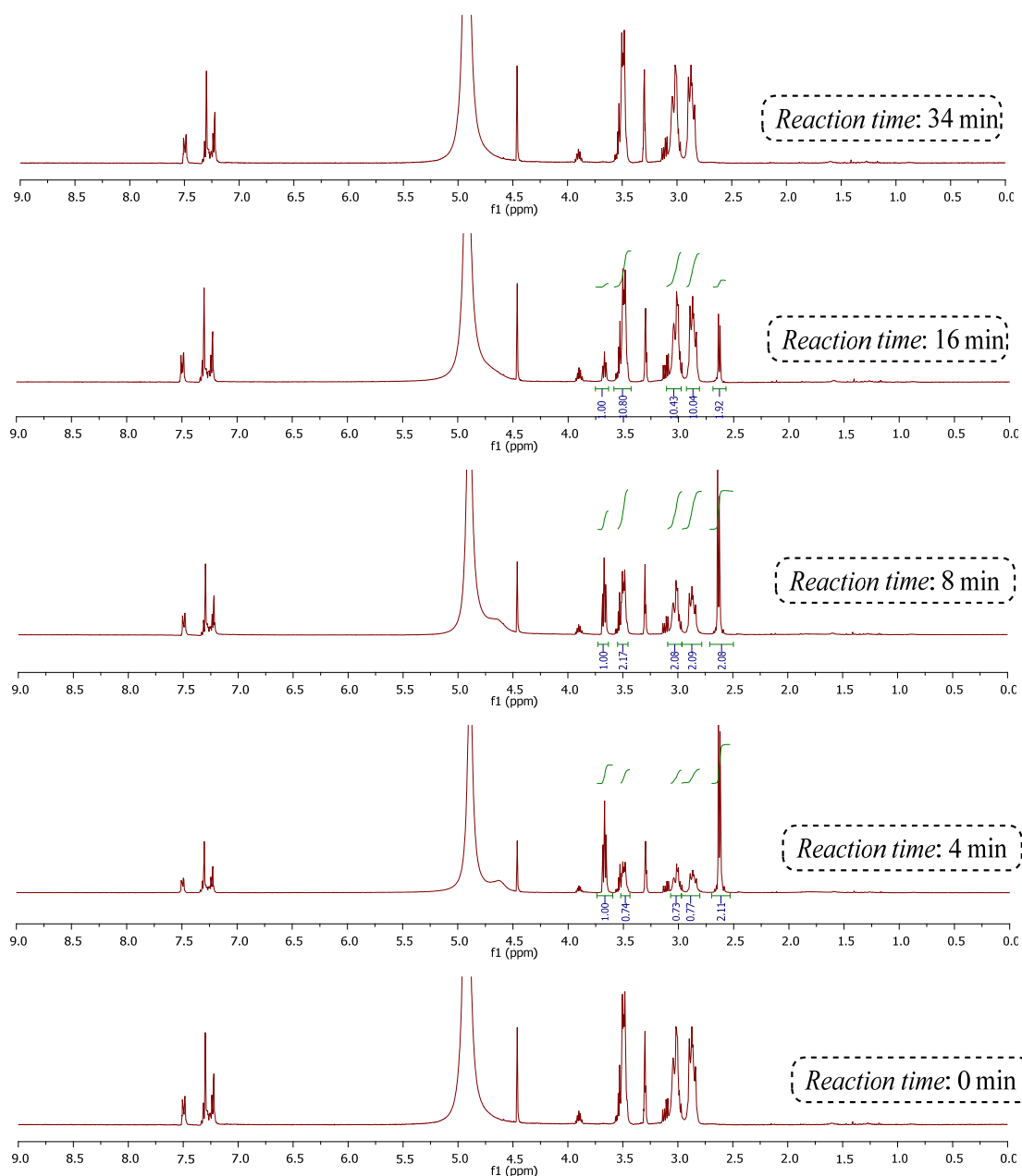
## 5. GPx-like catalytic activity measurements

### NMR Assay (DTT oxidation)

In the NMR assay, DTT<sup>red</sup> (0.15 mmol) and Te-catalyst (0.0015 mmol) were dissolved in CD<sub>3</sub>OD (1.1 mL), and the solution was added to 35% H<sub>2</sub>O<sub>2</sub> (15 μL, 0.15 mmol) to start the reaction. <sup>1</sup>H NMR spectra were measured at a variable reaction time at 25 °C. The relative populations of DTT<sup>red</sup> and DTT<sup>ox</sup> were determined by integration of the <sup>1</sup>H NMR signals (Scheme S2 and Figures S1, S2 related to exemplificative catalytic activity of a telluride and a selenide).<sup>3</sup>



**Figure S1.** Series of <sup>1</sup>H NMR spectra obtained in the oxidation of DTT red (0.15 mmol) with H<sub>2</sub>O<sub>2</sub> (0.15 mmol) in the presence of catalytic amount of amino telluride **9** (0.0015 mmol)



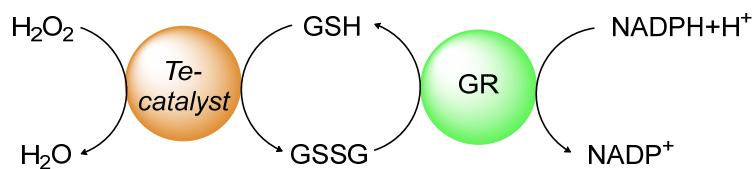
**Figure S2.** Series of <sup>1</sup>H NMR spectra obtained in the oxidation of DTT red (0.15 mmol) with H<sub>2</sub>O<sub>2</sub> (0.15 mmol) in the presence of catalytic amount of β-phenyltelluro hydroxy selenide **13a** (0.015 mmol)

### *PhSH oxidation*

Catalytic GPX model reaction was initiated by the addition of H<sub>2</sub>O<sub>2</sub> (88 μL of a 200 mM solution) to 2 mL of a 1.9 mM solution of PhSH in methanol containing a selenium catalyst (0.05 mM) at 25 °C. The reaction progress was monitored by UV spectroscopy at 305 nm.<sup>4</sup>

### ***GSH and NADPH-Glutathione Reductase (GR) coupled assay***

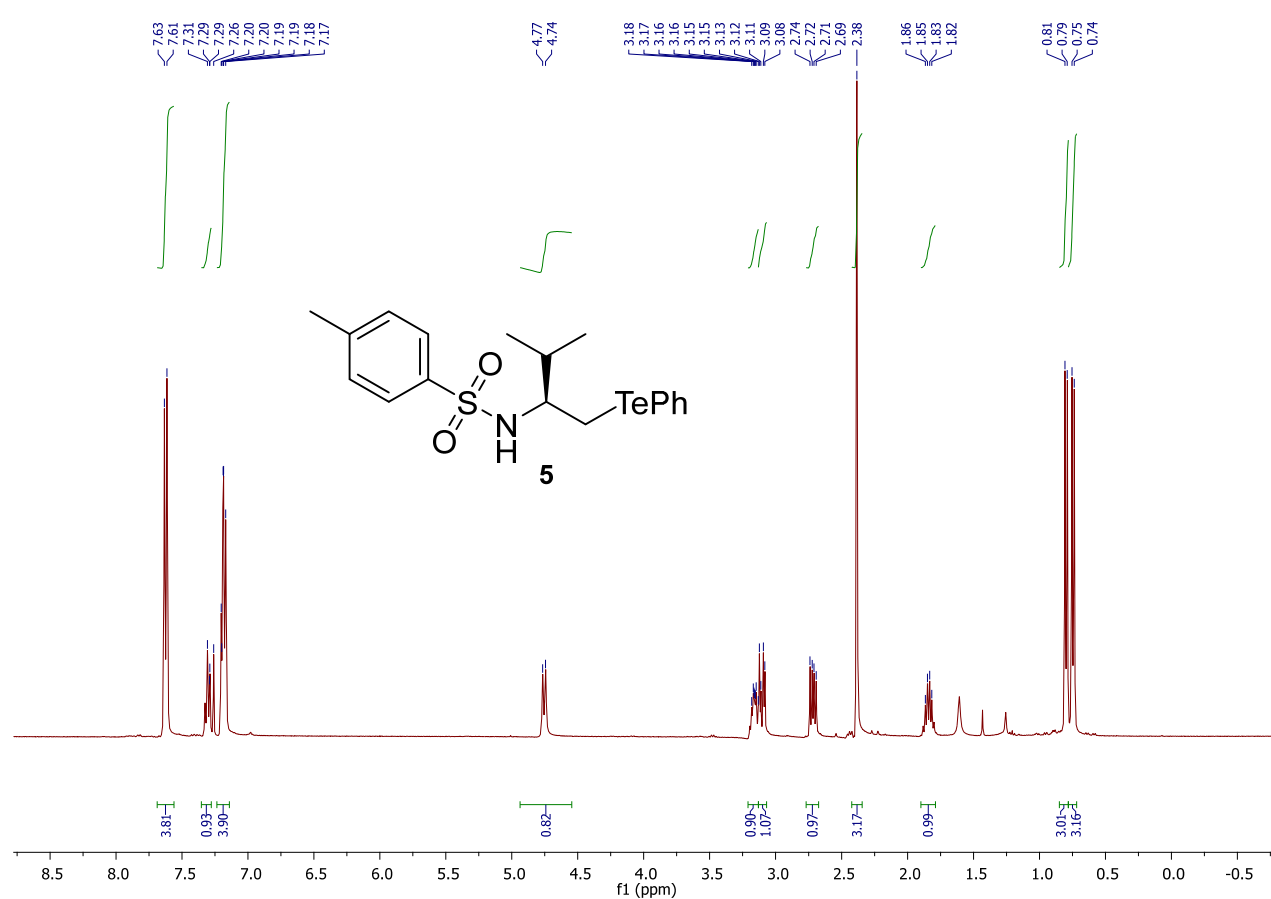
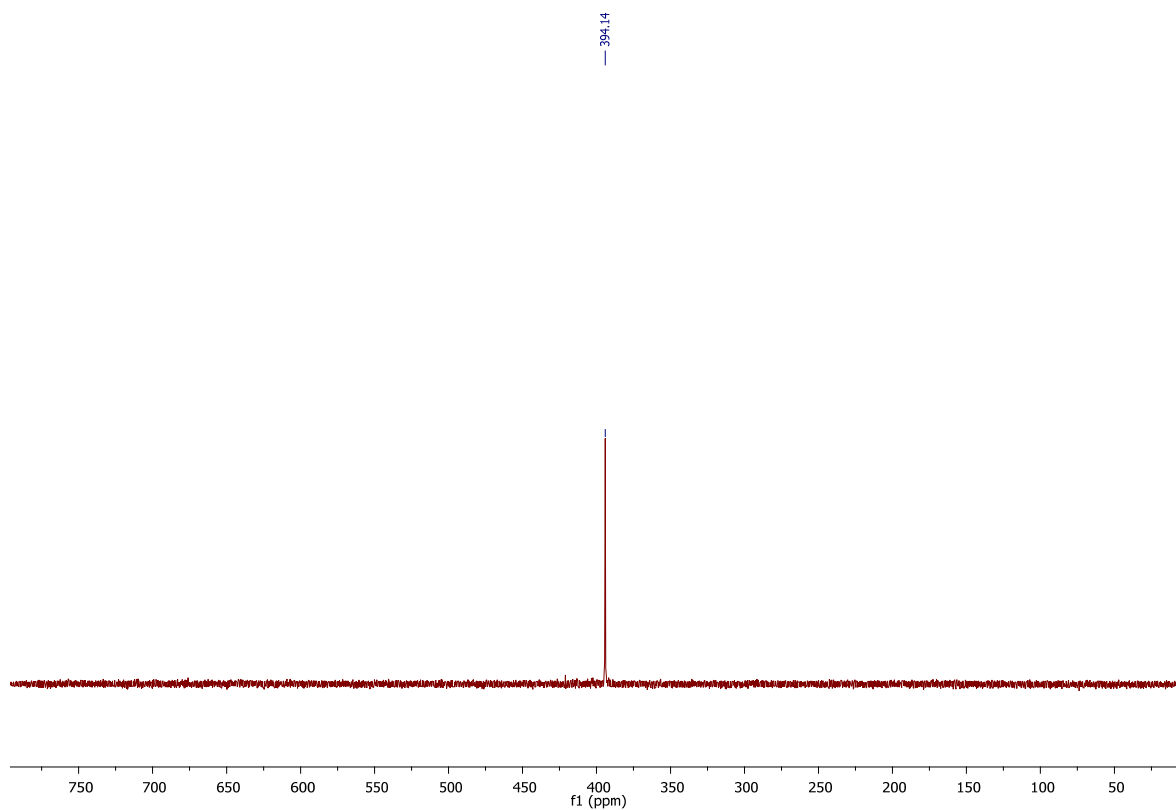
In the NADPH/GR coupled assay, 272  $\mu\text{L}$  of a 0.5 mM solution of telluride in a 100 mM phosphate buffer pH 7.4 was added to 988  $\mu\text{L}$  of phosphate buffer solution. Then, 600  $\mu\text{L}$  of a test solution, prepared by mixing 5823  $\mu\text{L}$  of a 100 mM phosphate/6mM EDTA buffer solution at pH 7.4 containing NADPH (6  $\mu\text{mol}$ ) and GSH (20.4  $\mu\text{mol}$ ) with a GR solution (600 U/mL, 135  $\mu\text{L}$ ), were added to the telluride solution. The reaction was started by addition of 140  $\mu\text{L}$  of a 36 mM aqueous solution of  $\text{H}_2\text{O}_2$ . The progress of the reaction was monitored following the consumption of NADPH by UV spectroscopy (340 nm).<sup>5</sup>



**Figure S3.** Te-catalyst (6 mol % with respect to GSH). Reaction progress followed monitoring absorption change at 340 nm due to consumption of NADPH

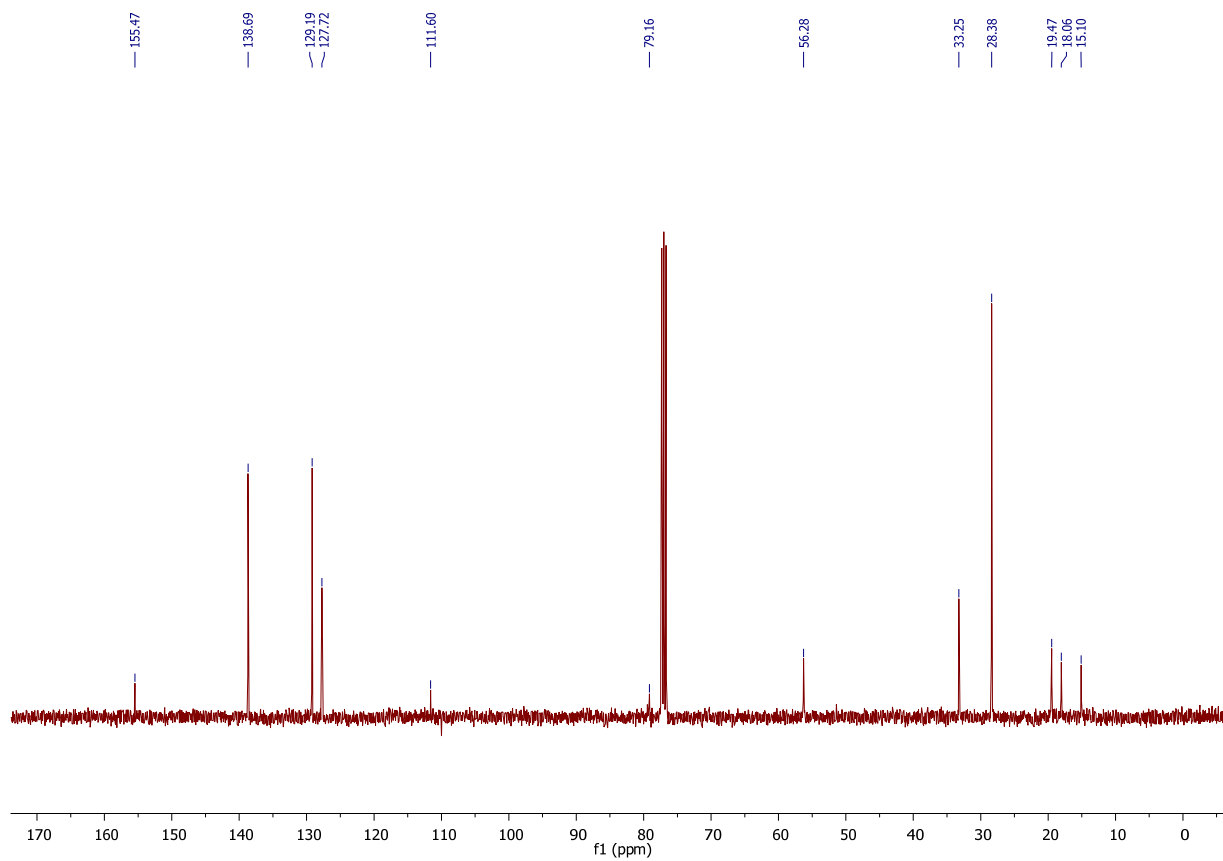


$^{125}\text{Te}$  NMR spectrum of compound **3c**

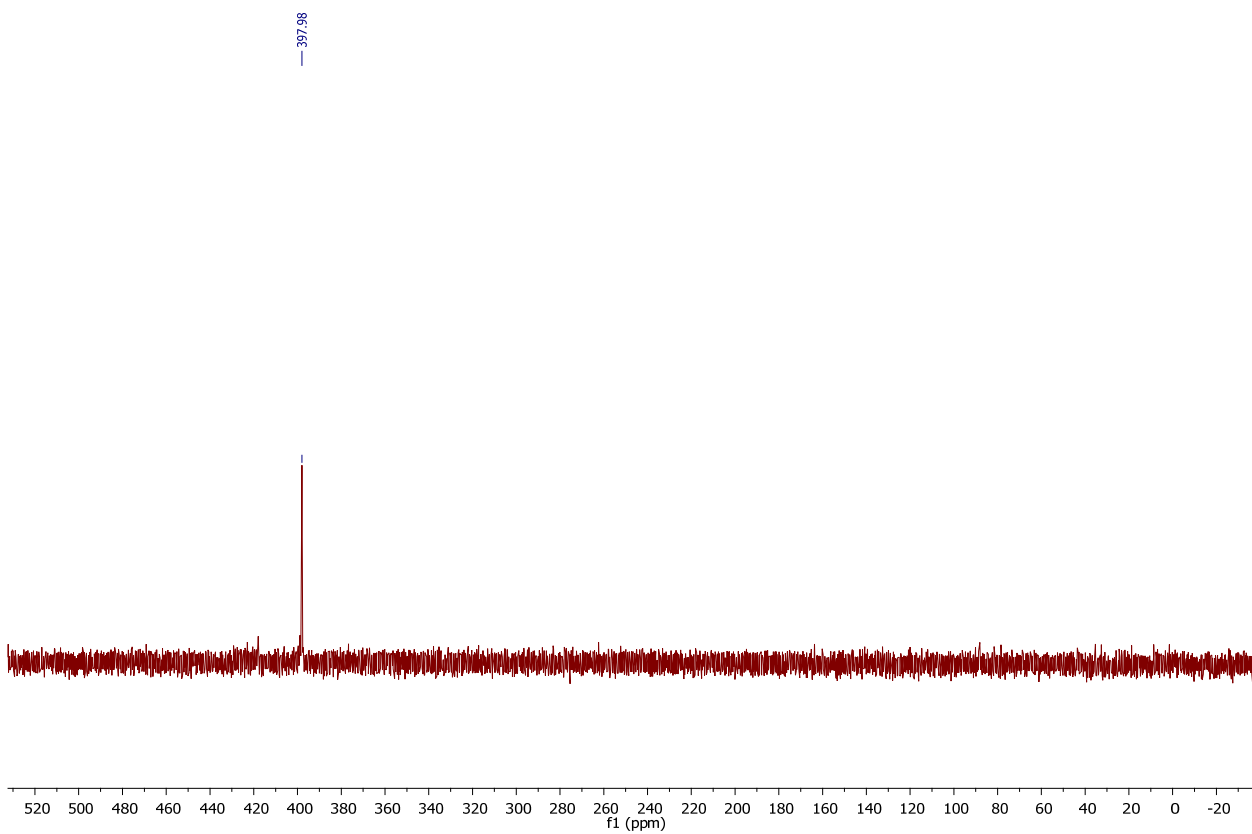


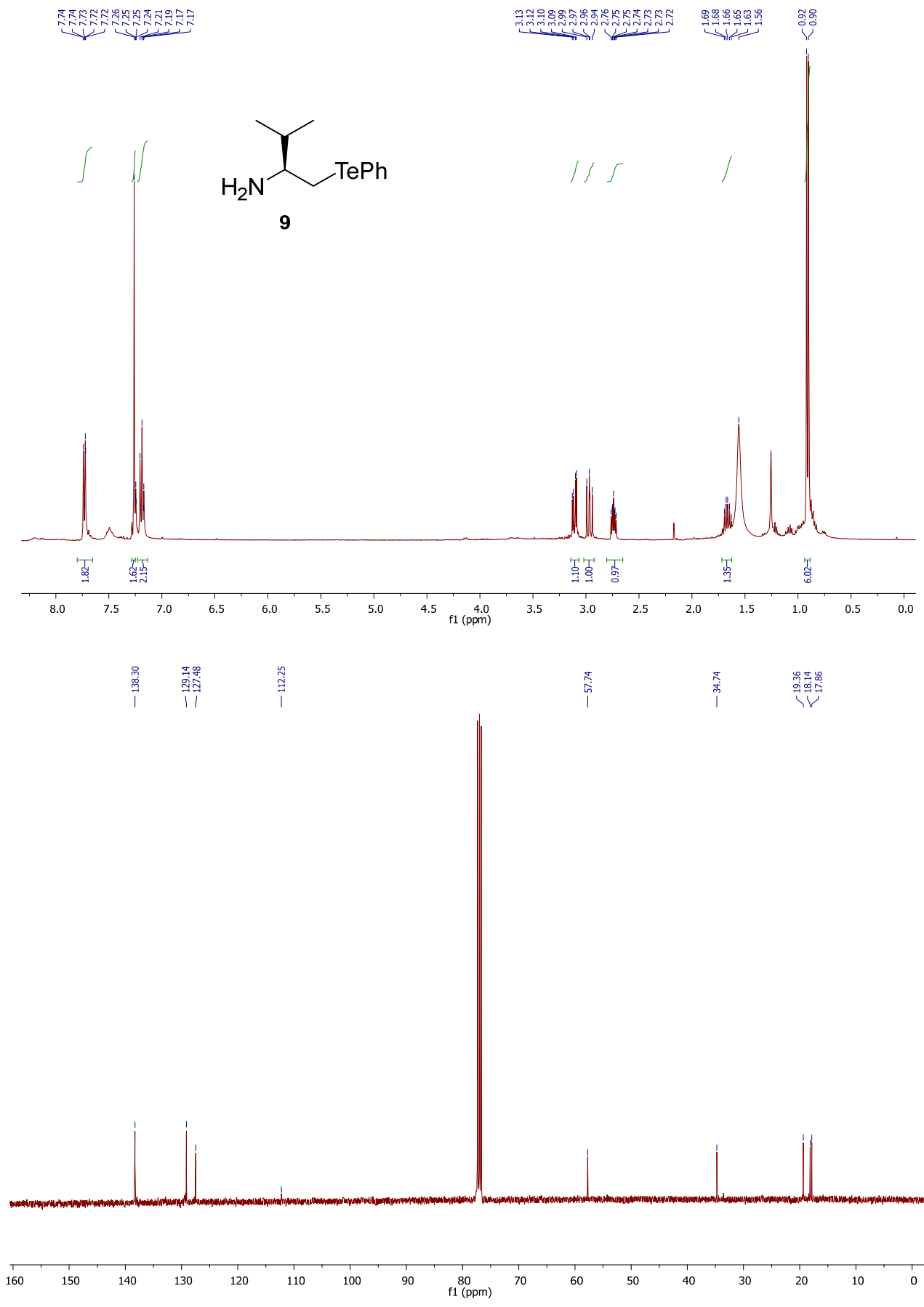




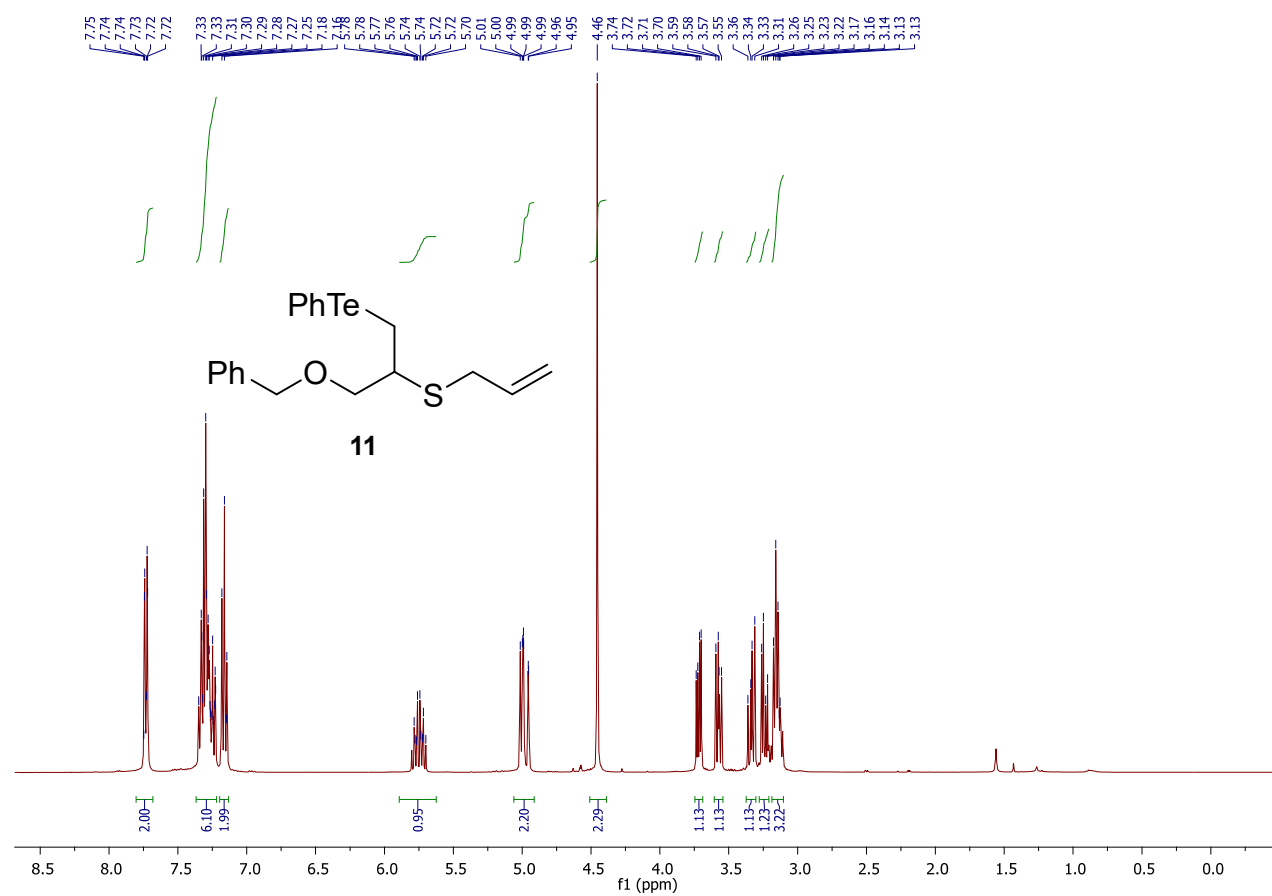
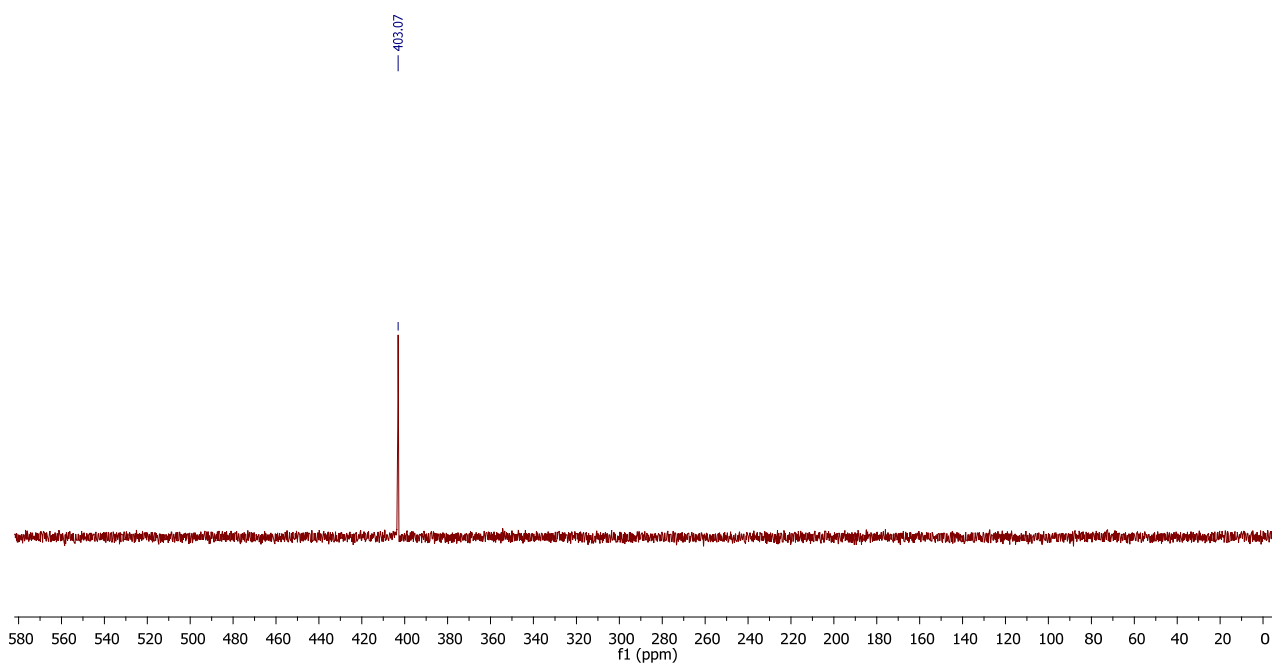


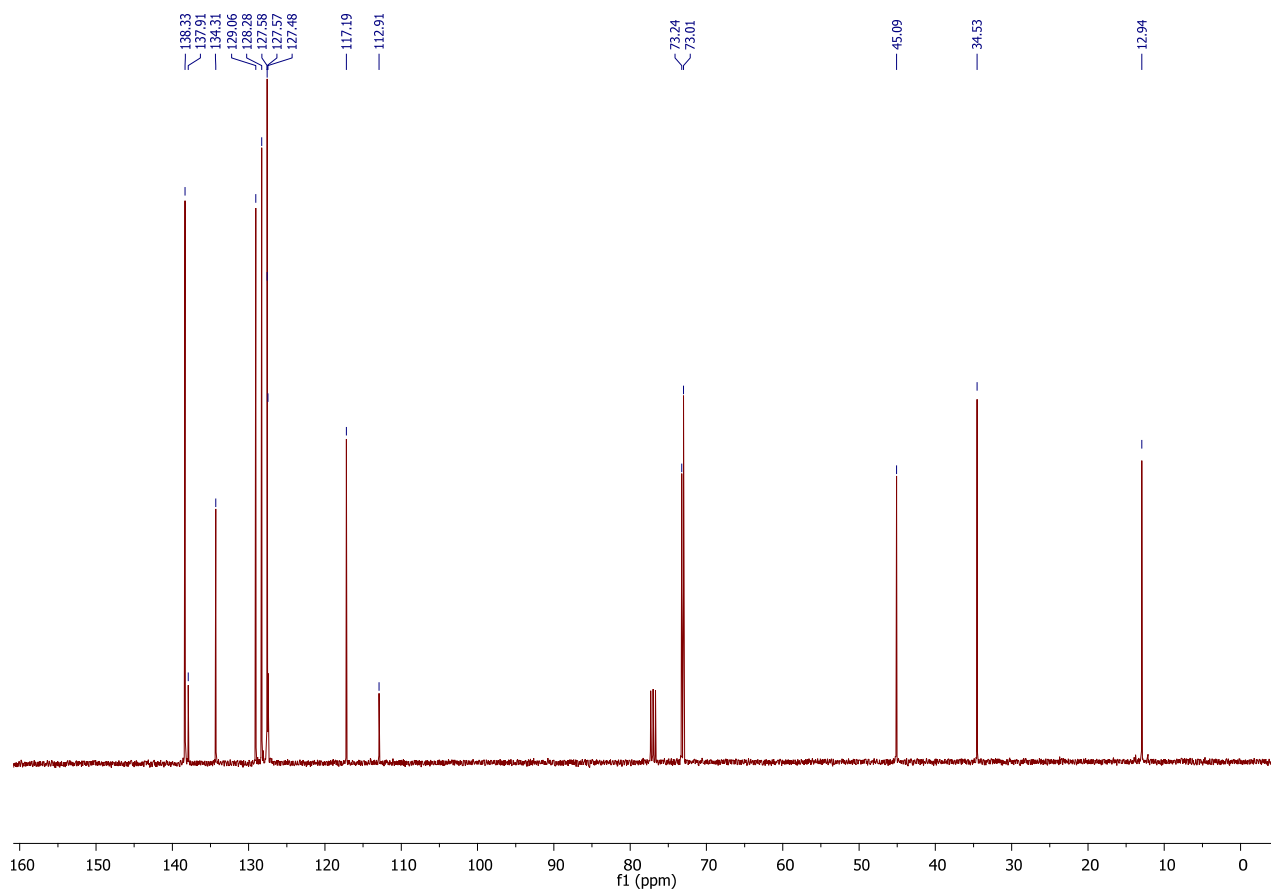
$^{125}\text{Te}$  NMR spectrum of compound **8**



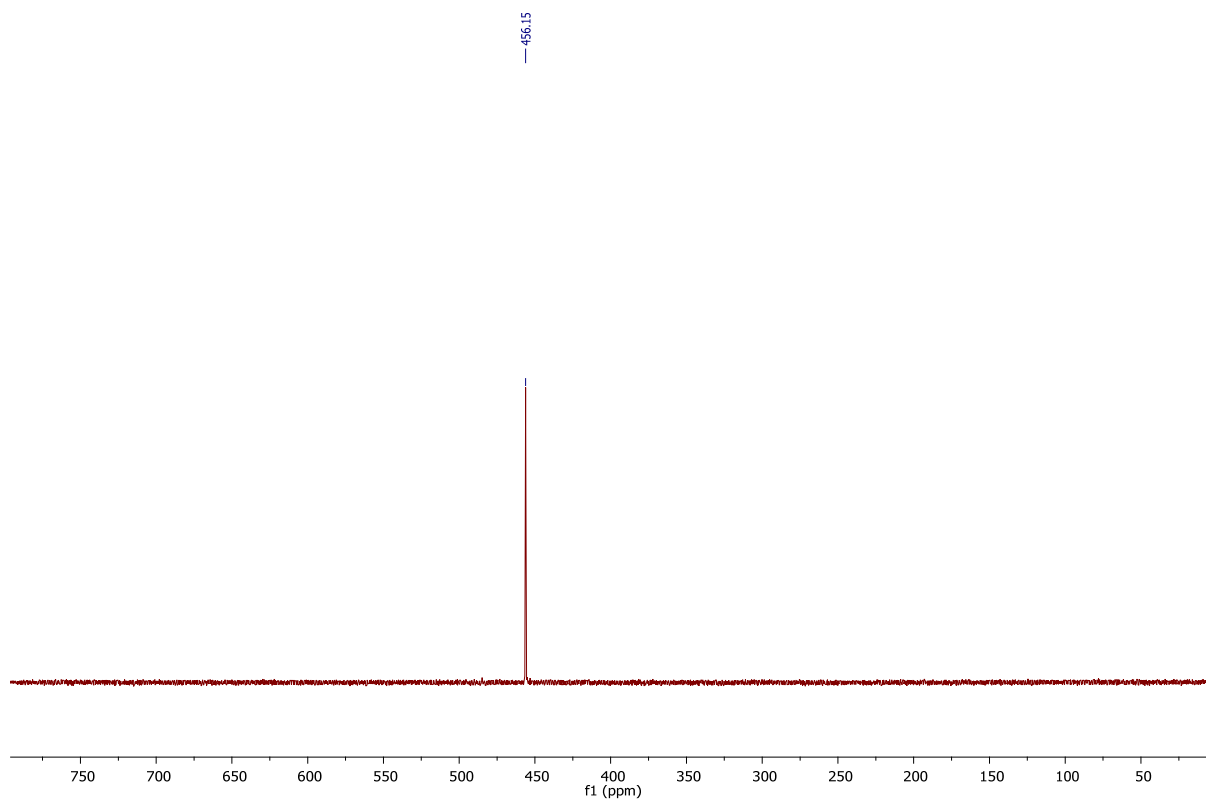


$^{125}\text{Te}$  NMR spectrum of compound **9**





$^{125}\text{Te}$  NMR spectrum of compound **11**



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