Supplementary Information for

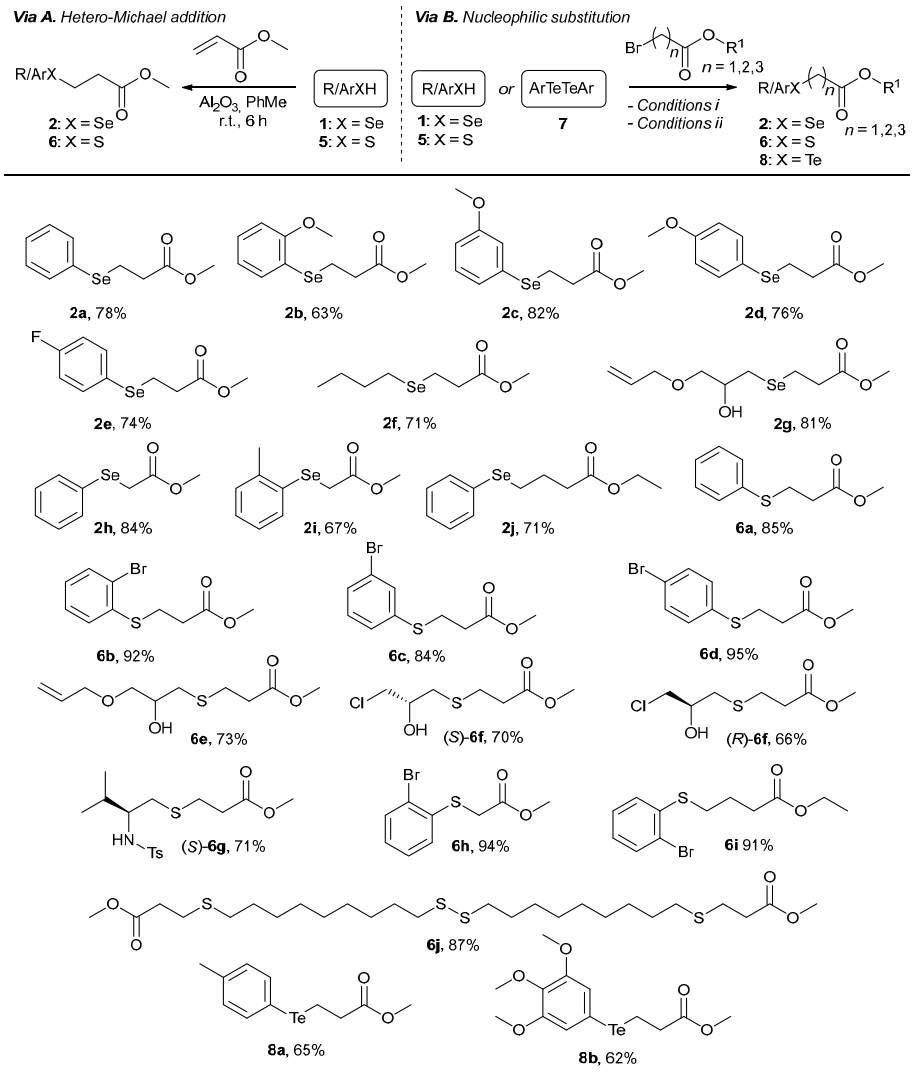
Direct biocatalysed synthesis of first sulfur-, selenium- and tellurium containing L-ascorbyl hybrid derivatives with radical trapping and GPx-like properties

Damiano Tanini,* Beatrice Lupori, Gianni Malevolti, Moira Ambrosi, Pierandrea Lo Nostro, Antonella Capperucci*

Dipartimento di Chimica "Ugo Schiff", Università di Firenze, Via della Lastruccia 3-13, 50019 Sesto Fiorentino, Italy. Email: damiano.tanini@unifi.it; antonella.capperucci@unifi.it.

Table of contents

1. α, β, and γ-chalcogenoesters used in this work



Via B. Reagents and conditions. *Conditions i*: R/ArSH **1** or R/ArSeH **5** (1.0 equiv.), Cs_2CO_3 (1.0 equiv.), TBAI (1.0 equiv.), dry DMF, 0°C, bromoester (1.1 equiv.), then 0°C to r.t. for 4h; *Conditions ii*: ArTeTeAr **7** (1.0 equiv.), $NaBH_4$ (3.0 equiv.), 0°C for 30 min, bromoester (2.2 equiv.), then 0°C to r.t. for 4h.

Scheme S1. Synthesis of selenoesters **2**, thioesters **6**, and telluroesters **8** through hetero-Michael addition (*via **A***) and nucleophilic substitution (*via **B***). Isolated yields are reported.

2. General experimental

All reactions were carried out in an oven-dried glassware under inert atmosphere (N_2). Solvents were dried using a solvent purification system (Pure-Solv™). All commercial materials were purchased from various commercial sources and used as received, without further purification. Flash column chromatography purifications were performed with Silica gel 60 (230-400 mesh). Thin layer chromatography was performed with TLC plates Silica gel 60 F_{254}, which was visualised under UV light, or by staining with an ethanolic acid solution of *p*-anisaldehyde followed by heating. High resolution mass spectra (HRMS) were recorded by Electrospray Ionization (ESI).

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or CD_3OD using Varian Mercury 400, Bruker 400 Ultrashield, and Varian Gemini 200 spectrometers operating at 400 MHz and 200 MHz (for ^{1}H), 100 MHz and 50 MHz (for ^{13}C). ^{19}F NMR spectra were recorded using a Varian Mercury 400 spectrometer operating at 376 MHz. ^{77}Se NMR and ^{125}Te spectra were recorded using a Bruker 400 Ultrashield spectrometer, operating at 76 MHz and 126 MHz, respectively. NMR signals were referenced to nondeuterated residual solvent signals ($CDCl_3$: 7.26 ppm for ^{1}H, 77.0 ppm for ^{13}C; CD_3OD: 3.31 ppm for ^{1}H, 49.0 ppm for ^{13}C). Diphenyl diselenide $(PhSe)_2$ was used as an external reference for ^{77}Se NMR (δ = 461 ppm). Diphenyl ditelluride $(PhTe)_2$ was used as an external reference for ^{125}Te NMR (δ = 420 ppm). Chemical shifts (δ) are given in parts per million (ppm), and coupling constants (J) are given in Hertz (Hz), rounded to the nearest 0.1 Hz. ^{1}H NMR data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, ap d = apparent doublet, m = multiplet, dd = doublet of doublet, bs = broad singlet, bd = broad doublet, ecc.), coupling constant (J) or line separation (ls), and assignment. Where reported, NMR assignments are made according to spin systems, using, where appropriate, 2D NMR experiments (COSY, HSQC, HMBC) to assist the assignment.

β-Hydroxy-[1] and β-amino-thiols,[2] alkyl-[3] and aryl-selenols[4] were synthesised from the corresponding epoxides and aziridines following a reported procedure.

DSC experiments were performed on a Q2000 differential scanning calorimeter (TA Instruments) by using hermetic aluminium pans. Naming of Compounds. Compound names are those generated by ChemBioDraw 15.0 software (PerkinElmer), following IUPAC nomenclature.

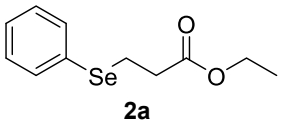
3. General procedures

General procedure for the synthesis of β-selenoesters and β-thioesters through seleno-Michael and thia-Michael addition (GP1). Neutral Al_2O_3 (61 mg, 0.60 mmol, 3.0 eq.) was added to a stirred solution of selenol **1** or thiol **5** (0.20 mmol, 1.0 eq.) and methyl acrylate (0.30 mmol, 1.5 eq) in dry toluene (3 mL) at ambient temperature under inert atmosphere (N_2). The reaction mixture was stirred for 8 h, then diluted with Et_2O (5 mL) and filtered through a short pad of Celite. The Celite was washed with Et_2O (2 x 5 mL) and the solvent was removed *in vacuo*. The crude material was subjected to flash column chromatography to afford pure β-selenoesters **2a-g** or β-thioesters **6a-h**.[5]

General procedure for the synthesis of chalcogen-containing 6-O-ascorbyl esters through bio-catalysed transesterification (GP2). Lipase B da *C. antarctica* (Lipase immobilized, beads, 2 U/mg; 100 U, 100 U/mmol with respect to L-ascorbic acid) and 4 A molecular sieves (300 mg) were added to a solution of L-ascorbic acid (1 mmol, 1.0 eq.) and the suitable α-, β-, or γ-chalcogen containing ester **2**, **6** or **7** (3 mmol, 3.0 eq.) in acetone (2 mL) at room temperature, under inert atmosphere (N_2). The vial was sealed and the reaction mixture was heated to 45ºC and stirred for 48 h. Afterwards, the mixture was cooled to room temperature, diluted with ethyl acetate (10 mL), and filtered through a short pad of Celite. Then, the mixture was washed with brine (3 x 5 mL) and the organic layer was dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. Pure chalcogen-containing 6-*O*-ascorbyl esters **4**, **9** or **10** were obtained by precipitation from the crude material (hexane/EtOAc).

4. Synthesis of chalcogen-containing methyl and ethyl esters

*Synthesis of methyl 3-(phenylselanyl)propanoate (**2a**)*



2a

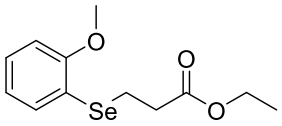
Following the general procedure ***GP1***, benzeneselenol **1a** (47 mg, 0.3 mmol) and methyl acrylate (41 μL, 0.45 mmol) gave, after purification by flash column chromatography (Petroleum ether/Et_2O 10:1), **2a** (57 mg, 78%) as a pale yellowish oil.

^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 2.71 (2H, t, CH_2Se, J = 7.4 Hz); 3.08 (2H, t, $CH_2C(O)$, J = 7.4 Hz); 3.64 (3H, s, OCH_3); 7.23-7.26 (2H, m); 7.48-7.51 (2H, m).

^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 21.80; 35.20; 51.78; 127.36; 129.20; 133.34; 162.59.

MS (ESI, positive): 267.2 $[M+Na]^+$.

*Synthesis of ethyl 3-((2-methoxyphenyl)selanyl)propanoate (**2b**)*



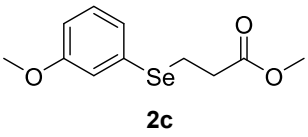
2b

Following the general procedure ***GP1***, 2-methoxybenzeneselenol **1b** (56 mg, 0.30 mmol) and ethyl acrylate (49 μL, 0.45 mmol) gave, after purification by flash column chromatography (petroleum ether/Et_2O 8:1), **2b** (54 mg, 63%) as a pale yellowish oil.

^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 1.25 (3H, t, *J* = 7.1 Hz); 2.69-2.77 (2H, m); 3.06-3.14 (2H, m); 3.88 (3H, s, OCH_3); 4.13 (2H, q, *J* = 7.1 Hz); 6.85 (1H, dd, *J* = 1.2, 8.3 Hz); 6.92 (1H, dd, *J* = 1.3, 7.5 Hz); 7.23-7.27 (1H, m); 7.38 (1H, dd, *J* = 1.6, 7.6 Hz).

MS (ESI, positive): 310.8 $[M+Na]^+$.

*Synthesis of methyl 3-((3-methoxyphenyl)selanyl)propanoate (**2c**)*



2c

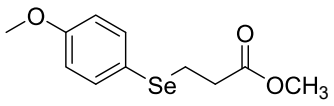
Following the general procedure ***GP1***, 3-methoxybenzeneselenol **1c** (56 mg, 0.30 mmol) and methyl acrylate (41 µL, 0.45 mmol) gave, after purification by flash column chromatography (petroleum ether/Et_2O 8:1), **2c** (71 mg, 82%) as a yellowish oil.

^{1}H NMR (200 MHz, $CDCl_3$) *δ* (ppm): 2.74 (2H, t, CH_2Se, *J* = 7.2 Hz), 3.10 (2H, t, C**H$_2$**CO, *J* = 7.2 Hz), 3.67 (3H, s, ArOC**H$_3$**), 3.80 (3H, s, C(O)OC**H$_3$**), 6.75-6.80 (2H, m), 7.15-7.20 (2H, m).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm): 21.7; 35.1; 51.8; 55.3; 113.1; 118.5; 125.2; 129.9; 130.2; 159.8; 172.6.

MS (ESI, positive): 311.2 $[M+Na]^+$.

*Synthesis of methyl 3-((4-methoxyphenyl)selanyl)propanoate (**2d**)*



2d

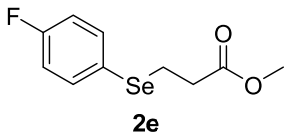
Following the general procedure ***GP1***, 4-methoxybenzeneselenol **1d** (37 mg, 0.20 mmol) and methyl acrylate (27 µL, 0.30 mmol) gave, after purification by flash column chromatography (petroleum ether/Et_2O 8:1), **2d** (43 mg, 76%) as a yellowish oil.

^{1}H NMR (200 MHz, $CDCl_3$) *δ* (ppm): 2.68 (2H, t, CH_2Se, *J* = 7.4 Hz); 3.0 (2H, t, CH_2CO, *J* = 7.4 Hz); 3.66 (3H, s, C(O)OCH_3); 3.79 (3H, s, ArOCH_3); 6.82 (2H, ap d, *J* = 7.9 Hz); 7.49 (2H, ap d, *J* = 7.9 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 23.3; 35.8; 52.3; 55.8; 115.4; 119.5; 136.9; 160.2; 173.2.

MS (ESI, positive): 311.0 $[M+Na]^+$.

*Synthesis of methyl 3-((4-fluorophenyl)selanyl)propanoate (**2e**)*



2e

Following the general procedure ***GP1***, 4-fluorobenzeneselenol **1e** (53 mg, 0.30 mmol) and methyl acrylate (41 µL, 0.45 mmol) gave, after purification by flash column chromatography (petroleum ether/Et_2O 9:1), **2e** (58 mg, 74%) as a yellowish oil.

^{1}H NMR (200 MHz, $CDCl_3$) *δ* (ppm): 2.68 (2H, t, CH_2Se, *J* = 7.4 Hz); 3.04 (2H, t, $CH_2C(O)$, *J* = 7.4 Hz); 3.66 (3H, s, OCH_3); 6.92-7.01(2H, m); 7.47-7.55 (2H, m).

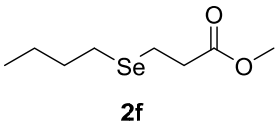
^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 22.5; 35.0; 51.6; 116.2 (d, $^2J_{C\text{-}F}$ = 21.3 Hz); 123.4 (d, $^4J_{C\text{-}F}$ = 3 Hz); 135.9 (d, $^3J_{C\text{-}F}$ = 8.3 Hz); 162.4 (d, $^1J_{C\text{-}F}$ = 246.3 Hz); 172.3.

^{77}Se NMR (76 MHz, $CDCl_3$) δ (ppm): 310.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): -114.1.

MS (ESI, positive): 263.1 $[M+H]^+$.

*Synthesis of methyl 3-(butylselanyl)propanoate (**2f**)*

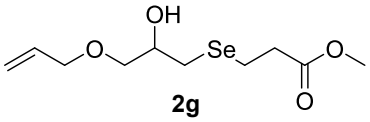


2f

$NaBH_4$ (29 mg, 0.75 mmol) was slowly added to a solution of 1,2-dibutyldiselane (68 mg, 0.25 mmol) in dry ethanol (4 mL) at 0°C under inert atmosphere. The mixture was stirred for 30 minutes and then methyl 3-bromopropionate (92 mg, 0.55 mmol) was added. The reaction was allowed to warm to room temperature and stirred for 4 h. Afterwards, the reaction was diluted with Et_2O (8 mL) and saturated *aq.* NH_4Cl (4 mL) was added. The organic phase was washed with brine (3 x 5 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/Et_2O 20:1) to yield methyl 3-(butylselanyl)propanoate **2f** (81 mg, 71%) as a yellowish oil.

^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 0.91 (3H, t, $CH_2C\mathbf{H_3}$, J = 8 Hz); 1.3-1.5 (2H, m, $CH_3C\mathbf{H_2}$); 1.55-1.75(2H, m, $C\mathbf{H_2}CH_2CH_3$); 2.59 (2H, t, $C\mathbf{H_2}CH_2CH_2CH_3$, J = 8Hz); 2.7-2.85 (4H, m); 3.69 (3H, s, OCH_3).

*Synthesis of methyl 3-((3-(allyloxy)-2-hydroxypropyl)selanyl)propanoate (**2g**)*



2g

Following the general procedure ***GP1***, 1-(allyloxy)-3-hydroselenopropan-2-ol **1f** (39 mg, 0.20 mmol) and methyl acrylate (28 µL, 0.30 mmol) gave, after purification by flash column chromatography (petroleum ether/EtOAc 2:1), **2g** (46 mg, 81%) as a yellowish oil.[5]

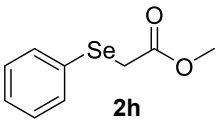
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.66-2.83 (7H, m); 3.46 (1H, dd, J = 3.9, 9.6 Hz, $C\mathbf{H_a}H_b$); 3.51 (1H, dd, J = 4.2, 9.6 Hz, $CH_a\mathbf{H_b}$); 3.69 (3H, s); 3.89-3.97 (1H, m); 3.96-4.05 (2H, m); 5.14-5.30 (2H, m); 5.82-5.95 (1H, m).

^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 18.3; 28.3; 35.4; 51.8; 69.8; 72.3; 73.1; 117.3; 134.3; 172.6.

^{77}Se NMR ($CDCl_3$, 76 MHz) δ (ppm): 134.0.

HRMS (ESI) calc. $C_{10}H_{19}O_4Se$ $[M+H]^+$ 283.0449, found 283.0437.

*Synthesis of methyl 2-(phenylselanyl)acetate (**2h**)*



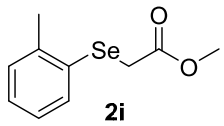
2h

A solution of benzeneselenol **1a** (79 mg, 0.50 mmol) in dry DMF (4 mL) was cooled at 0°C and treated with Cs_2CO_3 (163 mg, 0.50 mmol) and tetrabutylammonium iodide (TBAI, 185 mg, 0.50 mmol). Then, methyl bromoacetate (84 mg, 0.55 mmol) was

slowly added and the mixture was allowed to warm to room temperature and stirred for additional 4 h. Afterwards, the reaction was diluted with Et_2O (10 mL) and saturated *aq.* NH_4Cl (5 mL) was added. The organic phase was washed with brine (3 x 8 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/Et_2O 8:1) to yield methyl 2-(phenylselanyl)acetate **2h** (96 mg, 84%) as a yellowish oil.

^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 3.59 (2H, s, CH_2Se); 3.74 (3H, s, CH_3O); 7.31-7.39 (3H, m); 7.57-7.68 (2H, m).

*Synthesis of methyl 2-(o-tolylselanyl)acetate (**2i**)*



2i

A solution of 2-methylbenzeneselenol **1g** (43 mg, 0.25 mmol) in dry DMF (2 mL) was cooled at 0°C and treated with Cs_2CO_3 (82 mg, 0.25 mmol) and tetrabutylammonium iodide (TBAI, 93 mg, 0.25 mmol). Then, methyl bromoacetate (42 mg, 0.28 mmol) was slowly added and the mixture was allowed to warm to room temperature and stirred for additional 4 h. Afterwards, the reaction was diluted with Et_2O (8 mL) and saturated *aq.* NH_4Cl (3 mL) was added. The organic phase was washed with brine (3 x 5 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/Et_2O 9:1) to yield methyl 2-(*o*-tolylselanyl)acetate **2i** (41 mg, 67%) as a yellowish oil.

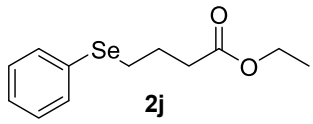
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.46 (3H, s); 3.53 (2H, s, CH_2Se); 3.68 (3H, s); 7.13-7.17 (1H, m); 7.21-7.24 (2H, m); 7.58 (1H, ap d, J = 7.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 22.9; 26.9; 53.0; 127.4; 128.6; 130.6; 130.7; 133.9; 140.6; 171.7.

^{77}Se NMR (76 MHz, $CDCl_3$) δ (ppm): 283.3.

MS (ESI, positive): 245.2 $[M+H]^+$.

*Synthesis of ethyl 4-(phenylselanyl)butanoate (**2j**)*



2j

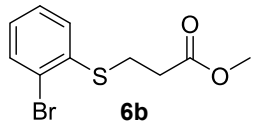
A solution of benzeneselenol **1a** (40 mg, 0.25 mmol) in dry DMF (2 mL) was cooled at 0°C and treated with Cs_2CO_3 (82 mg, 0.25 mmol) and tetrabutylammonium iodide (TBAI, 93 mg, 0.25 mmol). Then, ethyl 4-bromobutyrate (53 mg, 0.28 mmol) was slowly added and the mixture was allowed to warm to room temperature and stirred for additional 4 h. Afterwards, the reaction was diluted with Et_2O (8 mL) and saturated *aq.* NH_4Cl (3 mL) was added. The organic phase was washed with brine (3 x 5 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/Et_2O 9:1) to yield ethyl 4-(phenylselanyl)butanoate **2j** (48 mg, 71%) as a yellowish oil.

^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 1.31 (3H, t, J = 7.1 Hz); 2.0-2.14 (2H, m); 2.51 (2H, t, J = 7.2 Hz); 3.0 (2H, t, J = 7.2 Hz); 4.18 (2H, q, J = 7.1 Hz); 7.28-7.35 (3H, m); 7.52-7.59 (2H, m).

^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm):14.2; 15.4; 27.1; 34.0; 60.4; 126.9; 129.1; 130.0; 132.7.

MS (ESI, positive): 262.5 $[M+H]^+$.

*Synthesis of methyl 3-((2-bromophenyl)thio)propanoate (**6b**)*



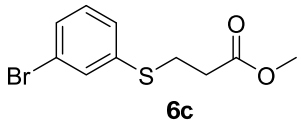
6b

Following the general procedure ***GP1***, 2-bromobenzenethiol **5b** (95 mg, 0.50 mmol) and methyl acrylate (68 µL, 0.75 mmol) gave, after purification by flash column chromatography (Petroleum ether/Et_2O 8:1), methyl 3-((2-bromophenyl)thio)propanoate **6b** (127 mg, 92%) as a yellowish oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.67 (2H, t, J = 7.4 Hz); 3.19 (2H, t, J = 7.4 Hz); 3.68 (3H, s); 7.02 (1H, ddd, J = 3.3 Hz, J = 5.7 Hz, J = 7.9 Hz); 7.25-7.30 (1H, m); 7.51-7.56 (1H, m).

MS (ESI, positive): 297.3 $[M+Na]^+$.

*Synthesis of methyl 3-((3-bromophenyl)thio)propanoate (**6c**)*



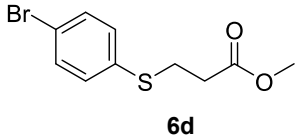
6c

Following the general procedure ***GP1***, 3-bromobenzenethiol **5c** (95 mg, 0.50 mmol) and methyl acrylate (68 µL, 0.75 mmol) gave, after purification by flash column chromatography (Petroleum ether/Et_2O 8:1), methyl 3-((3-bromophenyl)thio)propanoate **6c** (116 mg, 84%) as a yellowish oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.71 (2H, t, J = 7.4 Hz); 3.24 (2H, t, J = 7.4 Hz); 3.75 (3H, s); 7.21 (1H, t, J = 7.8 Hz); 7.31-7.33 (1H, m); 7.37-7.38 (1H, m); 7.55 (1H, t, J = 1.8 Hz).

MS (ESI, positive): 274.6 $[M+H]^+$.

*Synthesis of methyl 3-((4-bromophenyl)thio)propanoate (**6d**)*

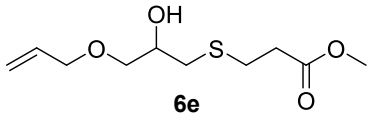


6d

Following the general procedure ***GP1***, 4-bromobenzenethiol **5d** (95 mg, 0.50 mmol) and methyl acrylate (68 µL, 0.75 mmol) gave, after purification by flash column chromatography (Petroleum ether/Et_2O 8:1), methyl 3-((4-bromophenyl)thio)propanoate **6d** (131 mg, 95%) as a yellowish oil. All spectroscopic data matched those previously reported in the literature.[6]

^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm): 2.62 (2H, t, J = 7.4 Hz); 3.15 (2H, t, J = 7.4 Hz); 3.69 (3H, s); 7.23 (2H, ap d, J = 8.4 Hz); 7.42 (2H, ap d, J = 8.4 Hz).

*Synthesis of methyl 3-((3-(allyloxy)-2-hydroxypropyl)thio)propanoate (**6e**)*



6e

Following the general procedure ***GP1***, 1-(allyloxy)-3-mercaptopropan-2-ol **5e** (45 mg, 0.30 mmol) and methyl acrylate (41 µL, 0.45 mmol) gave, after purification by flash column chromatography (Petroleum ether/Et_2O 5:1),

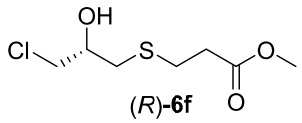
methyl 3-((3-(allyloxy)-2-hydroxypropyl)thio)propanoate **6e** (51 mg, 73%) as a yellowish oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.42 (1H, bs, OH); 2.60-2.65 (3H, m); 2.71-2.85 (3H, m); 3.46 (1H, dd, J = 6.2, 9.6 Hz; C**H**$_a$H$_b$O); 3.52(1H, dd, J = 4.2, 9.6 Hz; CH$_a$**H**$_b$O); .3.69 (3H,s,OC**H**$_3$); 3.87-3.93 (1H, C**H**OH); 4.01-4.03 (2H, m); 5.18-5.29 (2H, m); 5.84-5.94 (1H, m).

^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 27.5; 34.6; 35.9; 51.8; 69.4; 72.3; 72.6; 117.4; 134.4; 172.3.

MS (ESI, positive): 256.7 [M+Na]$^+$.

*Synthesis of methyl (R)-3-((3-chloro-2-hydroxypropyl)thio)propanoate ((R)-**6f**)*



(*R*)-**6f**

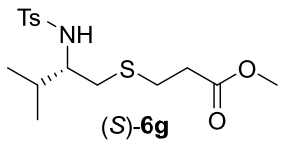
Following the general procedure ***GP1***, methyl 1-chloro-3-mercaptopropan-2-ol (*R*)-**5f** (50 mg, 0.40 mmol) and methyl acrylate (54 µL, 0.60 mmol) gave, after purification by flash column chromatography (Petroleum ether/Et_2O 4:1), (*R*)-3-((3-chloro-2-hydroxypropyl)thio)propanoate (*R*)-**6f** (56 mg, 66%) as a yellowish oil.

^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm): 2.37 (1H, bs, OH); 2.59-2.89 (6H, m); 3.62-3.66 (2H, m, C**H**$_2$Cl); 3.71 (3H, s; C**H**$_3$O); 3.90-4.01 (1H, m, C**H**OH).

^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm): 27.6; 34.6; 36.5; 47.9; 51.9; 70.2; 172.3.

MS (ESI, positive): 235.4 [M+Na]$^+$.

*Synthesis of methyl (S)-3-((3-methyl-2-((4-methylphenyl)sulfonamido)butyl)thio)propanoate ((S)-**6g**)*



(*S*)-**6g**

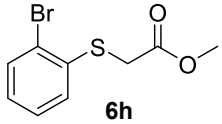
Following the general procedure ***GP1***, (*S*)-*N*-(1-mercapto-3-methylbutan-2-yl)-4-methylbenzenesulfonamide (*S*)-**5g** (82 mg, 0.3 mmol) and methyl acrylate (41 µL, 0.45 mmol) gave, after purification by flash column chromatography (Petroleum ether/EtOAc 3:1), (*S*)-**6g** (77 mg, 71%) as a yellowish glassy solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.81 (6H, d, J = 6.8 Hz); 1.89-1.97 (1H, m); 2.43 (3H, s); 2.47-2.52 (3H, m); 2.59-2.63 (2H, m); 2.67 (1H, dd, J = 5.0, J = 13.5 Hz); 3.14-3.20 (1H, m, C**H**NH); 3.71 (3H, s); 5.01 (1H, d, J = 8.4 Hz, NH); 7.31 (ap d, J = 8.0 Hz); 7.79 (ap d, J = 8.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 17.5; 18.9; 21.4; 27.6; 30.0; 34.4; 34.9; 51.8; 58.4; 127.2; 129.6; 137.8; 143.3; 172.1.

MS (ESI, positive): 360.3 [M+H]$^+$.

*Synthesis of methyl 2-((2-bromophenyl)thio)acetate (**6h**)*



6h

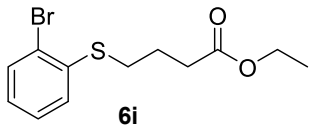
A solution of 2-bromobenzenethiol **5b** (95 mg, 0.50 mmol) in dry DMF (4 mL) was cooled at 0°C and treated with Cs_2CO_3 (163 mg, 0.50 mmol) and tetrabutylammonium

iodide (TBAI, 185 mg, 0.50 mmol). Then, methyl bromoacetate (84 mg, 0.55 mmol) was slowly added and the mixture was allowed to warm to room temperature and stirred overnight. Afterwards, the reaction was diluted with Et_2O (10 mL) and saturated *aq.* NH_4Cl (5 mL) was added. The organic phase was washed with brine (3 x 8 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/Et_2O 5:1) to yield methyl 2-((2-bromophenyl)thio)acetate **6h** (116 mg, 94%).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 3.71 (2H, s, C**H$_2$**S); 3.75 (3H, s); 7.10 (1H, td, J = 1.6, 7.8 Hz); 7.30 (1H, td, J = 1.3, 7.8 Hz); 7.39 (1H, dd, J = 1.6, 7.9 Hz); 7.58 (1H, dd, J = 1.3, 7.9 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 35.3; 52.6; 124.1; 127.7; 128.0; 129.3; 133.1; 136.2; 169.5.

*Synthesis of ethyl 4-((2-bromophenyl)thio)butanoate (**6i**)*



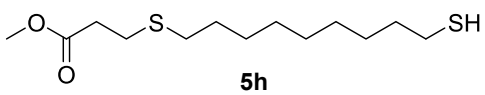
6i

A solution of 2-bromobenzenethiol **5b** (48 mg, 0.25 mmol) in dry DMF (3 mL) was cooled at 0°C and treated with Cs_2CO_3 (82 mg, 0.25 mmol) and tetrabutylammonium iodide (TBAI, 93 mg, 0.25 mmol). Then, ethyl 4-bromobutyrate (53 mg, 0.28 mmol) was slowly added and the mixture was allowed to warm to room temperature and stirred overnight. Afterwards, the reaction was diluted with Et_2O (8 mL) and saturated *aq.* NH_4Cl (4 mL) was added. The organic phase was washed with brine (3 x 5 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/Et_2O 5:1) to yield methyl ethyl 4-((2-bromophenyl)thio)butanoate **6i** (69 mg, 91%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 1.30 (3H, d, J = 7.1 Hz); 1.98-2.13 (2H, m); 2.55 (2H, t, J = 7.2 Hz); 3.04 (2H, t, J = 7.2 Hz); 4.19 (2H, q, J = 7.2 Hz); 7.02-7.12 (1H, m); 7.31-7.35 (2H, m); 7.56-7.62 (1H, m).

MS (ESI, positive): 325.1 $[M+Na]^+$.

*Synthesis of methyl 3-((9-mercaptononyl)thio)propanoate (**5h**)*



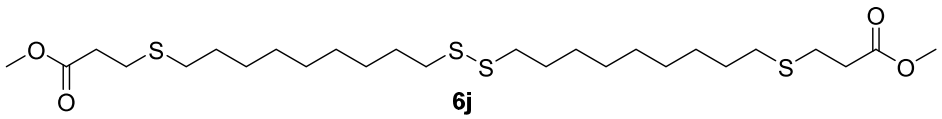
5h

Al_2O_3 (61 mg, 0.6 mmol) was added to a solution of 1,9-nonanedithiol (58 mg, 0.3 mmol) and methyl acrylate (22 µL, 0.24 mmol) in dry toluene (2 mL) and the mixture was stirred at room temperature for 6 h, then diluted with Et_2O (5 mL) and filtered through a short pad of Celite®. The Celite was washed with Et_2O (2 x 5 mL) and the solvent was removed *in vacuo*. The crude material was subjected to flash column chromatography (petroleum ether/Et_2O 10:1) to afford thiol **5h** (43 mg, 64%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 1.22-1.43 (9H, m); 1.50-1.66 (4H, m); 2.46-2.64 (6H. m); 2.74-2.82 (2H, m); 3.70 (3H, s).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 24.5; 26.9; 28.2; 28.7; 28.9; 29.0; 29.2; 29.4; 32.1; 33.9; 34.6; 51.6; 172.3.

*Synthesis of dimethyl 3,3'-((disulfanediylbis(nonane-9,1-diyl))bis(sulfanediyl))dipropionate (**6j**)*



6j

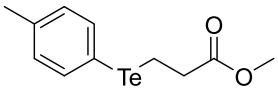
Dimethyl dicyanofumarate (21 mg, 0.11 mmol) was added to a solution of thiol **5h** (30 mg, 0.11 mmol) in dry dichloromethane (3 mL) at 0°C.[7] The mixture was stirred for 12 h at room temperature, the solvent was evaporated under vacuum, and the crude material was purified by flash chromatography (petroleum ether /ethyl acetate 10:1) to yield disulfide **6j** (52 mg, 87%) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.21-1.44 (18H, m); 1.50-1.66 (8H, m); 2.46-2.64 (12H, m); 2.74-2.82 (4H, m); 3.70 (6H, s).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 24.5; 26.9; 28.2; 28.7; 28.9; 29.0; :29.2; 29.4.32.1,33.9,34.6,51.6; 172.3.

MS (ESI, positive): 577.6 $[M+Na]^+$.

*Synthesis of methyl 3-(p-tolyltellanyl)propanoate (**8a**)*



8a

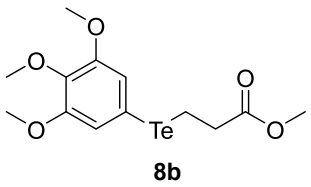
$NaBH_4$ (12 mg, 0.3 mmol) was slowly added to a solution of 1,2-di-*p*-tolylditellane **7a** (44 mg, 0.1 mmol) in dry ethanol (2 mL) at 0°C under inert atmosphere. The mixture was stirred for 30 minutes and then methyl 3-bromopropionate (33 mg, 0.22 mmol) was added. The reaction was allowed to warm to room temperature and stirred for 4 h. Afterwards, the reaction was diluted with Et_2O (6 mL) and saturated *aq.* NH_4Cl (3 mL) was added. The organic phase was washed with brine (3 x 4 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/Et_2O 12:1) to yield methyl 3-(p-tolyltellanyl)propanoate **8a** (40 mg, 65%) as a yellowish oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):2.34 (3H, s); 2.86-2.90 (2H, m); 2.96-3.0 (2H, m); 3.66 (3H, s); 7.04 (2H, ap d, J = 7.8 Hz); 7.65 (2H, ap d, J = 7.8 Hz).

^{13}C NMR (100 MHz $CDCl_3$) δ (ppm): 0.3 (CH_2Te); 21.2 (CH_3); 36.6 (CH_2CO); 51.7 (CH_3O); 107.2 (CTe); 130.2; 138.0; 139.3; 173.6.

^{125}Te NMR (126 MHz $CDCl_3$) δ (ppm): 515.1.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-((2-bromophenyl)thio)propanoate (**8b**)*



8b

$NaBH_4$ (12 mg, 0.3 mmol) was slowly added to a solution of 1,2-bis(3,4,5-trimethoxyphenyl)ditellane **7b** (59 mg, 0.1 mmol) in dry ethanol (2 mL) at 0°C under inert atmosphere. The mixture was stirred for 30 minutes and then methyl 3-bromopropionate (33 mg, 0.22 mmol) was added. The reaction was allowed to warm to room temperature and stirred for 4 h. Afterwards, the reaction was diluted with Et_2O (6 mL) and saturated *aq.* NH_4Cl (3 mL) was added. The organic phase was washed with brine (3 x 4 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/EtOAc 4:1) to yield methyl 3-((3,4,5-trimethoxyphenyl)tellanyl)propanoate **8b** (47 mg, 62%) as a yellowish oil.

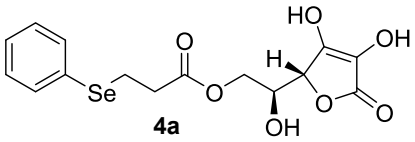
^{1}H NMR (400MHz, $CDCl_3$) δ (ppm): 2.91-2.95 (2H, m); 3.01-3.05 (2H, m); 3.67 (3H, s); 3.84 (3H, s); 3.86 (6H, s); 6.98 (2H, s).

^{13}C NMR (100MHz, $CDCl_3$) δ (ppm): 1.1(CH_2Te); 36.6 (CH_2CO); 51.8; 56.3; 60.9; 104.0 (CTe); 116.9; 138.5; 153.3; 173.6.

MS (ESI, positive): 384.5 $[M+H]^+$.

5. Synthesis of chalcogen-containing 6-*O*-ascorbyl esters

*S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-(phenylselanyl)propanoate (**4a**)*



4a

According to the general procedure ***GP2***, L-ascorbic acid (18 mg, 0.10 mmol) and β-selenoester **2a** (73 mg, 0.30 mmol) gave 6-*O*-L-ascorbyl ester **4a** (30 mg, 77%) as a white glassy solid.

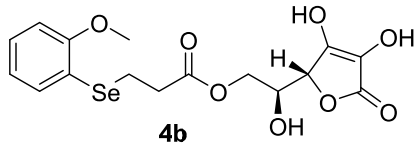
^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 2.79 (2H, t, CH_2Se, J = 7.1 Hz); 3.14 (2H, t, $CH_2C(O)O$ J = 7.1 Hz); 4.08-4.12 (1H, m, C**H**OH); 4.21 (1H, dd, J = 5.7, 11.1 Hz, C$\mathbf{H_a}H_bO$); 4.26 (1H, dd, J = 7.1, 11.1 Hz, $CH_a\mathbf{H_b}O$); 4.74 (1H, d, J = 2.1 Hz, C**H**OH); 7.26-7.32 (3H, m); 7.50-7.56 (2H, m).

^{13}C NMR (100 MHz, CD_3OD) δ (ppm): 21.7; 35.3; 65.3; 67.2; 76.5; 119.2; 127.6; 129.5; 129.8; 133.4; 153.8; 172.5; 172.8.

^{77}Se NMR (76 MHz, CD_3OD) δ (ppm): 310.0.

HRMS (ESI) calc. $C_{15}H_{16}NaO_7Se$ $[M+Na]^+$ 410.9959, found 410.9970.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-((2-methoxyphenyl)selanyl)propanoate (**4b**)*



4b

According to the general procedure ***GP2***, L-ascorbic acid (9 mg, 0.05 mmol) and β-selenoester **2b** (41 mg, 0.15 mmol) gave 6-*O*-L-ascorbyl ester **4b** (14 mg, 67%) as a colourless glassy solid.

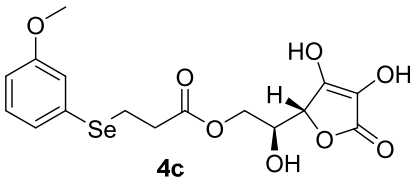
^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 2.77 (2H, t, J = 7.2 Hz); 3.09 (2H, t, J = 7.2 Hz); 3.84 (3H, s, OCH_3); 4.06-4.10 (1H, m, C**H**OH); 4.19 (1H, dd, J = 5.8, 11.1 Hz, C**H$_a$**H$_b$O); 4.24 (1H, dd, J = 7.1, 11.1 Hz, CH$_a$**H$_b$**O); 4.72 (1H, d, J = 2.1 Hz, C**H**CHOH); 6.89 (1H, td, J = 1.2, 7.5 Hz); 6.93 (1H, dd, J = 1.2, 8.2 Hz); 7.21-7.25 (1H, m); 7.37 (1H, dd, J = 2.8, 5.6 Hz).

^{13}C NMR (100 MHz, CD_3OD) δ (ppm): 18.9; 35.2; 55.5; 65.3; 67.2; 76.4; 111.1; 118.9; 119.2; 121.7; 128.5; 132.1; 153.8; 158.8; 172.5; 172.9.

^{77}Se NMR (76 MHz, CD_3OD) δ (ppm): 247.2.

HRMS (ESI) calc. $C_{16}H_{18}NaO_8Se$ $[M+Na]^+$ 441.0065, found 441.0051.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-((3-methoxyphenyl)selanyl)propanoate (**4c**)*



4c

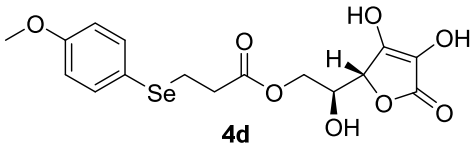
According to the general procedure ***GP2***, L-ascorbic acid (18 mg, 0.1 mmol) and β-selenoester **2c** (82 mg, 0.3 mmol) gave 6-*O*-L-ascorbyl ester **4c** (27 mg, 64%) as a white glassy solid.

^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 2.77 (2H, t, CH_2Se, J = 7.1 Hz); 3.11 (2H, t, $CH_2C(O)O$ J = 7.1 Hz); 3.76 (3H, s); 4.07-4.11 (1H, m, C**H**OH); 4.18 (1H, dd, J = 5.7, 11.1 Hz, C**H$_a$**H$_b$O); 4.24 (1H, dd, J = 7.1, 11.1 Hz, CH$_a$**H$_b$**O); 4.72 (1H, d, J = 2.1 Hz, C**H**OH); 6.78-6.83 (1H, m); 7.03-7.07 (2H, m); 7.18 (2H, ap t, J = 8.2 Hz).

^{13}C NMR (100 MHz, CD_3OD) δ (ppm): 21.8; 35.5; 55.3; 65.6; 67.4; 76.6; 113.4; 118.8; 119.5; 125.5; 130.5; 131.0; 153.6; 160.8; 172.6; 173.0.

HRMS (ESI) calc. $C_{16}H_{18}NaO_8Se$ $[M+Na]^+$ 441.0065, found 441.0047.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-((4-methoxyphenyl)selanyl)propanoate (**4d**)*



4d

According to the general procedure ***GP2***, L-ascorbic acid (9 mg, 0.05 mmol) and β-selenoester **2d** (41 mg, 0.15 mmol) gave 6-*O*-L-ascorbyl ester **4d** (15 mg, 71%) as a white glassy solid.

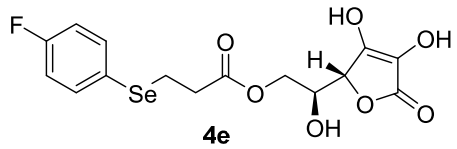
^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 2.73 (2H, t, CH_2Se, J = 7.1 Hz); 3.02 (2H, t, $CH_2C(O)O$ J = 7.1 Hz); 3.79 (3H, s); 4.07-4.13 (1H, m, C**H**OH); 4.20 (1H, dd, J = 5.7, 11.1 Hz, C**H$_a$**H$_b$O); 4.25 (1H, dd, J = 7.1,

11.1 Hz, CH_aH_bO); 4.74 (1H, d, *J* = 2.0 Hz, C**H**OH); 6.87 (2H, ap d, *J* = 8.8 Hz); 7.49 (2H, ap d, *J* = 8.8 Hz).

^{13}C NMR (100 MHz, CD_3OD) δ (ppm): 22.6; 35.3; 55.0; 65.3; 67.2; 76.6; 115.2; 118.9; 119.4; 136.5; 154.8; 160.4; 172.7; 172.8.

HRMS (ESI) calc. $C_{16}H_{18}NaO_8Se$ $[M+Na]^+$ 441.0065, found 441.0054.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-((4-fluorophenyl)selanyl)propanoate (**4e**)*



4e

According to the general procedure ***GP2***, L-ascorbic acid (18 mg, 0.10 mmol) and β-selenoester **2e** (78 mg, 0.30 mmol) gave 6-*O*-L-ascorbyl ester **4e** (28 mg, 69%) as a yellowish glassy solid.

^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 2.75 (2H, t, *J* = 7.1 Hz); 3.09 (2H, t, *J* = 7.1 Hz); 4.06-4.10 (1H, m, C**H**OH); 4.19 (1H, dd, *J* = 5.7, 11.2 Hz, CH_aCH_bO); 4.24 (1H, dd, *J* = 7.1, 11.2 Hz, CH_aCH_bO); 4.72 (1H, d, *J* = 2.1 Hz, C**H**CHOH); 7.04 (2H, ap t, *J* = 8.9 Hz); 7.55-7.58 (2H, m).

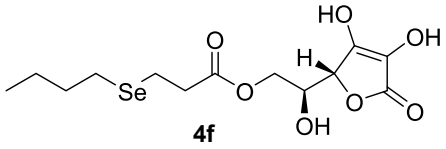
^{13}C NMR (100 MHz, CD_3OD) δ (ppm): 21.8; 34.6; 64.7; 66.6; 75.8; 115.8 (d, $^{2}J_{C\text{-}F}$ = 21.8 Hz); 118.6; 123.8 (d, $^{4}J_{C\text{-}F}$ = 3.3 Hz); 135.7 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz); 152.9; 162.5 (d, $^{1}J_{C\text{-}F}$ = 245.8 Hz); 171.8-171.9.

^{77}Se NMR (76 MHz, CD_3OD) δ (ppm): 307.2.

^{19}F NMR (376 MHz, CD_3OD) δ (ppm): -116.7.

HRMS (ESI) calc. $C_{15}H_{15}FNaO_7Se$ $[M+Na]^+$ 428.9865, found 428.9873.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-(butylselanyl)propanoate (**4f**)*



4f

According to the general procedure ***GP2***, L-ascorbic acid (18 mg, 0.10 mmol) and β-selenoester **2f** (67 mg, 0.30 mmol) gave 6-*O*-L-ascorbyl ester **4f** (26 mg, 72%) as a yellowish oil.

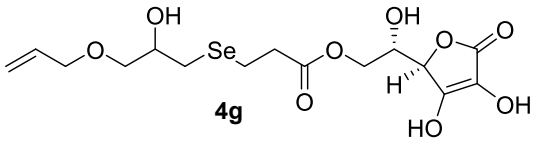
^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 0.92 (3H, t, *J* = 7.4 Hz, CH_3); 1.36-1.46 (2H, m); 1.60-1.67 (2H, m); 2.61 (2H, t, *J* = 7.4 Hz); 2.78 (4H, m); 4.09-4.13 (1H, m, C**H**OH); 4.23 (1H, dd, *J* = 5.9, 11.1 Hz, CH_aCH_bO); 4.27 (1H, dd, *J* = 7.1, 11.1 Hz, CH_aCH_bO); 4.77 (1H, d, *J* = 2.0 Hz, C**H**CHOH).

^{13}C NMR (100 MHz, CD_3OD) δ (ppm): 13.1; 17.3; 23.1; 23.8; 33.0; 35.8; 65.2; 67.2; 76.4; 119.3; 153.5; 172.4; 173.1.

^{77}Se NMR (76 MHz, CD_3OD) δ (ppm): 177.3.

HRMS (ESI) calc. $C_{13}H_{20}NaO_7Se$ $[M+Na]^+$ 391.0272, found 391.0255.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-((3-(allyloxy)-2-hydroxypropyl)selanyl)propanoate (**4g**)*



4g

According to the general procedure ***GP2***, L-ascorbic acid (9 mg, 0.05 mmol) and β-selenoester **2g** (42 mg, 0.15 mmol) gave 6-*O*-L-ascorbyl ester **4g** (12 mg, 58%, white glassy solid) as an equimolar mixture of diastereoisomers.

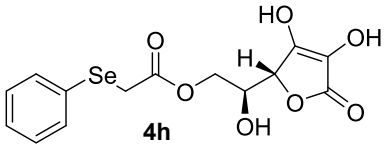
^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 2.70 (1H, dd, J = 6.6, 12.7 Hz); 2.78-2.87 (5H, m); 3.5 (1H, dd, J = 5.6, 9.8 Hz, C**H$_a$**H$_b$O); 3.53 (1H, dd, J = 4.8, 9.8 Hz, CH$_a$**H$_b$**O); 3.88-3.94 (1H, m, C**H**OH); 4.02-4.06 (2H, m, **CH$_2$**CH=CH$_2$); 4.11-4.15 (1H, m, CH**CH**OH); 4.25 (1H, dd, J = 5.8, 11.2 Hz, C**H$_a$**H$_b$OC(O)); 4.30 (1H, dd, J = 7.1, 11.2 Hz; CH$_a$**H$_b$**OC(O)); 4.78 (1H, d, J = 2 Hz, OC**H**CH); 5.17-5.33 (2H, m); 5.89-5.99 (1H, m).

^{13}C NMR (100 MHz, CD_3OD) δ (ppm): 18.3; 27.9; 35.8; 65.3; 67.2; 70.9; 72.5; 73.6; 76.4; 116.5; 119.2; 135.3; 153.6; 172.4; 172.9.

^{77}Se NMR (76 MHz, CD_3OD) δ (ppm): 145.6; 145.7.

HRMS (ESI) calc. $C_{15}H_{23}O_9Se$ $[M+H]^+$ 427.0507, found 427.0501.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 2-(phenylselanyl)acetate (**4h**)*



4h

According to the general procedure ***GP2***, L-ascorbic acid (18 mg, 0.10 mmol) and α-selenoester **2h** (69 mg, 0.30 mmol) gave 6-*O*-L-ascorbyl ester **4h** (28 mg, 73%) as a yellowish oil.

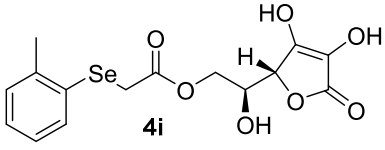
^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 3.62-3.63 (2H, m CH_2Se); 3.99-4.03 (1H, m, C**H**OH); 4,15 (1H, dd, J = 6.7, 11.0 Hz, C**H$_a$**H$_b$O); 4.23 (1H, dd, J = 6.7, 11.0 Hz, CH$_a$**H$_b$**O); 4.52 (1H, d, J = 2.0 Hz, C**H**CHOH); 7.29-7.34 (3H, m); 7.59-7.63 (2H, m).

^{13}C NMR (100 MHz, CD_3OD) δ (ppm): 27.0; 65.4; 66.8; 76.1; 119.2 (HO**C**C = O); 128.2; 129.5; 133.7; 153.6 (HO**C**CH); 171.6; 172.4.

^{77}Se NMR (76 MHz, CD_3OD) δ (ppm): 333.8.

HRMS (ESI) calc. $C_{14}H_{14}NaO_7Se$ $[M+Na]^+$ 396.9802, found 396.9791.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 2-(o-tolylselanyl)acetate (**4i**)*



4i

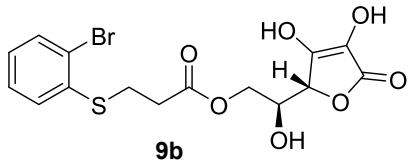
According to the general procedure ***GP2***, L-ascorbic acid (9 mg, 0.05 mmol) and α-selenoester **2i** (36 mg, 0.15 mmol) gave 6-*O*-L-ascorbyl ester **4i** (11 mg, 56%) as a white glassy solid.

^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 3.59 (2H, ap d, J = 1.7 Hz, CH_2Se); 3.95-3.99 (1H, m, C**H**OH); 4.10 (1H, dd, J = 6.6, 11.0 Hz, C**H$_a$**H$_b$O); 4.17 (1H, dd, J = 6.7, 11.0 Hz, CH$_a$**H$_b$**O); 4.42 (1H, d, J = 2.1 Hz, C**H**CHOH); 7.09-7.13 (1H, m); 7.16-7.23 (2H, m); 7.58-7.60 (1H, m).

^{13}C NMR (100 MHz, CD_3OD) δ (ppm): 21.6-26.0 (CH_2Se); 65.4; 66.9; 76.3; 118.6; 127.0; 128.4; 130.3; 134.0; 167.4; 171.4.

HRMS (ESI) calc. $C_{15}H_{16}NaO_7Se$ $[M+Na]^+$ 410.9959, found 410.9971.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-((2-bromophenyl)thio)propanoate **(9b)***



9b

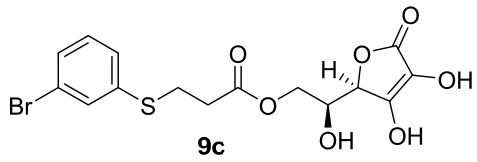
According to the general procedure ***GP2***, L-ascorbic acid (18 mg, 0.10 mmol) and β-thioester **6b** (82 mg, 0.30 mmol) gave 6-*O*-L-ascorbyl ester **9b** (26 mg, 62%) as a white solid.

^{1}H NMR (CD_3OD, 400 MHz) δ (ppm): 2.74 (2H, t, J = 7.2 Hz); 3.25 (2H, t, J = 7.2 Hz); 4.09-4.13 (1H, m, CHC**H**OH); 4.23 (1H, dd, J = 5.7, 11.1 Hz, C**H$_a$**H$_b$O); 4.28 (1H, dd, J = 7.1, 11.1 Hz, CH$_a$**H$_b$**OH); 4.74 (1H, d, J = 1.7 Hz, C**H**CHOH); 7.06-7.11 (1H, m); 7.32-7.36 (1H, m); 7.40 (1H, dd, J = 1.0, 7.8 Hz); 7.57 (1H, d, J = 7.8 Hz).

^{13}C NMR (CD_3OD, 100 MHz) δ (ppm): 27.3; 33.2; 64.8; 66.6; 75.8; 118.5; 123.4; 126.8; 127.8; 128.5; 132.8; 136.9; 153.3; 171.5; 171.9.

HRMS (ESI) calc. $C_{15}H_{15}BrNaO_7S$ $[M+Na]^+$ 440.9620, found 440.9607.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-((3-bromophenyl)thio)propanoate **(9c)***



9c

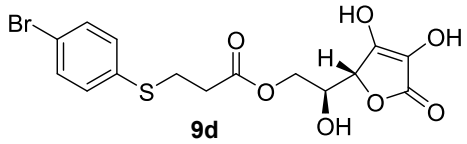
According to the general procedure ***GP2***, L-ascorbic acid (18 mg, 0.10 mmol) and β-thioester **6c** (82 mg, 0.30 mmol) gave 6-*O*-L-ascorbyl ester **9c** (31 mg, 75%) as a white solid.

^{1}H NMR (CD_3OD, 400 MHz) δ (ppm): 2.72 (2H, t, J = 7.1 Hz); 3.25 (2H, t, J = 7.1 Hz); 4.1-4.13 (1H, m, CHC**H**OH); 4.23 (1H, dd, J = 5.7, 11.1 Hz, C**H$_a$**H$_b$O); 4.29 (1H, dd, J = 7.1, 11.1 Hz, CH$_a$**H$_b$**O); 4.75 (1H, d, J = 2.1 Hz, **CH**CHOH); 7.24 (1H, ap t, J = 7.9 Hz); 7.34-7.39 (2H m); 7.54 (1H, ap t, J = 1.8 Hz).

^{13}C NMR (CD_3OD, 100 MHz) δ (ppm): 28.1; 33.5; 64.8; 66.6; 75.8; 118.6; 122.3; 127.7; 129.0; 130.2; 131.4; 138.2; 152.8; 171.5; 171.7.

HRMS (ESI) calc. $C_{15}H_{15}BrNaO_7S$ $[M+Na]^+$ 440.9620, found 440.9603.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-((4-bromophenyl)thio)propanoate (**9d**)*



9d

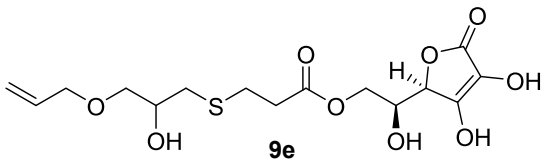
According to the general procedure ***GP2***, L-ascorbic acid (18 mg, 0.10 mmol) and β-thioester **6d** (82 mg, 0.30 mmol) gave 6-*O*-L-ascorbyl ester **9d** (35 mg, 83%) as a white solid.

^{1}H NMR (CD_3OD, 400 MHz) δ (ppm): 2.70 (2H, t, J = 7.1 Hz); 3.22 (2H, t; J = 7.1 Hz); 4.08-4.14 (1H, m, CH**C**H**O**H); 4,23 (1H, dd, J = 5.7, 11.2 Hz, C**H$_a$**H$_b$O); 4.29 (1H, dd, J = 7.1, 11.2 Hz, CH$_a$**H$_b$**O); 475 (1H, d, J = 2.1 Hz, C**H**CHOH); 7.31 (2H, ap d, J = 8.6 Hz); 7.47 (2H, ap d, J = 8.6 Hz).

^{13}C NMR (CD_3OD, 100 MHz) δ (ppm): 28.9; 34.2; 65.4; 67.2; 76.4; 119.3; 120.3; 131.7; 132.4; 135.6; 153.4; 172.2; 172.4.

HRMS (ESI) calc. $C_{15}H_{16}BrO_7S$ $[M+H]^+$ 418.9800, found 418.9783.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-((3-(allyloxy)-2-hydroxypropyl)thio)propanoate (**9e**)*



9e

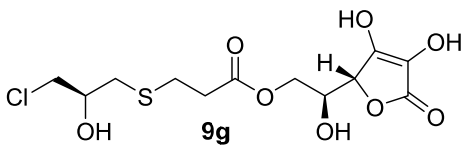
According to the general procedure ***GP2***, L-ascorbic acid (18 mg, 0.10 mmol) and hydroxy-substituted β-thioester **6e** (70 mg, 0.30 mmol) gave 6-*O*-L-ascorbyl ester **9e** (23 mg, 61%) as a colourless glassy solid.

^{1}H NMR (CD_3OD, 400 MHz) δ (ppm): 2.50-2.89 (6H, m); 3.49 (1H, dd; J = 5.8, 10.0 Hz, C**H$_a$**H$_b$O); 3.53 (1H, dd; J = 4.8, 10.0 Hz, CH$_a$**H$_b$**O); 3.84-3.90 (1H, m; C**H**OH); 4.03-4.04 (2H, m; C**H$_2$**CH=CH$_2$); 4.11-4.15 (1H, m; CHC**H**OH); 4.25 (1H, dd; J = 6.1, 12.2 Hz; C**H$_a$**H$_b$OC(O)); 4.30 (1H, dd; J = 7.2, 11.2 Hz; CH$_a$**H$_b$**OC(O)); 4.78 (1H, d, J = 2.0 Hz; C**H**COH); 5.16-5.33 (2H, m); 5.89-5.99 (1H, m).

^{13}C NMR (CD_3OD, 100 MHz) δ (ppm): 27.8; 35.7; 65.3;67.2;70.5; 72.5; 73.2; 76.4;116.5;119.2; 135.3; 153.7; 172.5; 172.6.

HRMS (ESI) calc. $C_{15}H_{22}NaO_9S$ $[M+Na]^+$ 401.0882, found 401.0891.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-(((R)-3-chloro-2-hydroxypropyl)thio)propanoate (**9g**)*



9g

According to the general procedure ***GP2***, L-ascorbic acid (12 mg, 0.07 mmol) and hydroxy-substituted β-thioester (*R*)-**6f** (43 mg, 0.20 mmol) gave 6-*O*-L-ascorbyl ester **9g** (15 mg, 58%) as a colourless glassy solid.

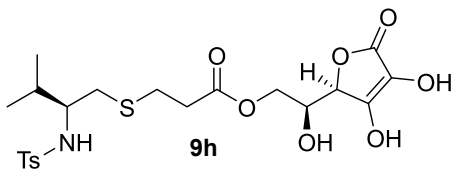
^{1}H NMR (CD_3OD, 400 MHz) δ (ppm): 2.66-2.72 (3H, m); 2.78 (1H, dd, J = 5.7, 13.8 Hz); 2.85-2.88 (2H, m); 3.61 (1H, dd, J = 5.5, 11.2 Hz, C**H$_a$**H$_b$Cl); 3.67 (1 H, dd, J = 4.7, 11.2 Hz, CH$_a$**H$_b$**Cl); 3.88-3.94 (1H, m,

C**H**OH); 4.09-4.13 (1H, m, CHC**H**OH); 4.23 (1 H, dd, *J* = 5.3, 11.6 Hz, C**H**$_a$H$_b$O); 4.28 (1H, dd, *J* = 7.1, 11.6 Hz, CH$_a$**H**$_b$O); 4.74 (1H, d, *J* = 2.1 Hz, **CH**CHOH).

^{13}C NMR (CD_3OD, 100 MHz) δ (ppm): 27.2; 34.3; 35.2; 47.2; 64.7; 66.6; 70.7; 75.9; 118.4; 153.7; 171.9; 172.0.

HRMS (ESI) calc. $C_{12}H_{18}ClO_8S$ $[M+H]^+$ 357.0411, found 357.0398.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-(((S)-3-methyl-2-((4-methylphenyl)sulfonamido)butyl)thio)propanoate (**9h**)*



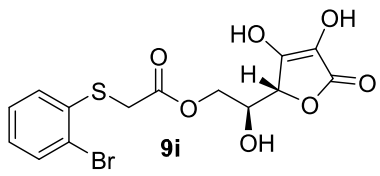
According to the general procedure ***GP2***, L-ascorbic acid (12 mg, 0.07 mmol) and amino-substituted β-thioester (*S*)-**6g** (72 mg, 0.20 mmol) gave 6-*O*-L-ascorbyl ester **9h** (22 mg, 62%) as a white glassy solid.

^{1}H NMR (CD_3OD, 400 MHz) δ (ppm): 0.79 (3H, d, *J* = 6.8 Hz); 0.85 (3H, d, *J* = 6.8 Hz); 1.90-2.02 (1H, m); 2.39 (1H, dd, *J* = 5.4, 3.6 Hz); 2.45 (3H,s); 2.48-2.62 (5H, m); 3.13-3.19 (1H, m, C**H**N); 411-4.15 (1H, m, CH**CH**OH); 4.23(1H, dd, *J* = 5.9, 11.1 Hz, C**H**$_a$H$_b$O); 4.30 (1H, dd, *J* = 7.0, 11.1 Hz, CH$_a$**H**$_b$O); 4.77 (1H, d, *J* = 2.0 Hz, **CH**CHOH); 7.39 (2H, ap d, *J* = 8.2 Hz); 7.78 (2H, ap d, *J* = 8.2 Hz).

^{13}C NMR (CD_3OD, 100 MHz) δ (ppm): 16.4; 18.9; 20.7; 27.5; 30.3; 34.5; 34.7; 59.1; 65.2; 67.2; 76.4; 119.2; 127.4; 129.9; 139.4; 143.8; 153.8; 172.3; 172.5.

HRMS (ESI) calc. $C_{21}H_{30}NO_9S_2$ $[M+H]^+$ 504.1362, found 504.1354.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 2-((2-bromophenyl)thio)acetate (**9i**)*



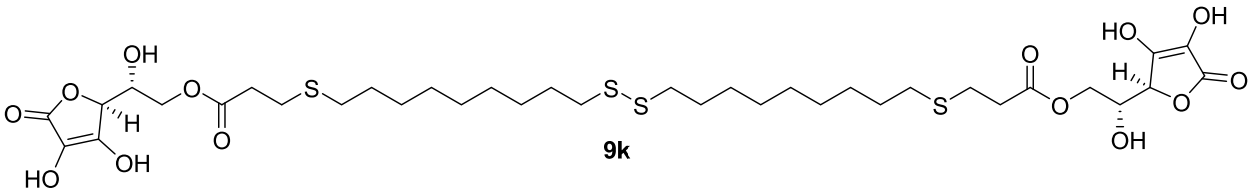
According to the general procedure ***GP2***, L-ascorbic acid (18 mg, 0.10 mmol) and α-thioester **6h** (78 mg, 0.30 mmol) gave 6-*O*-L-ascorbyl ester **9i** (31 mg, 76%) as a white glassy solid.

^{1}H NMR (CD_3OD, 400 MHz) δ (ppm): 3.88 (2H, s, CH_2S); 4.07-4.12 (1H, m, CHC**H**OH); 4.23 (1H, dd, *J* = 6.1, *J* = 11.1 Hz, C**H**$_a$H$_b$O); 4.31 (1H, dd, *J* = 6.8, 11.31 Hz, CH$_a$**H**$_b$O); 4.65 (1H, d, *J* = 2.1. Hz, C**H**OH); 7.09-7.13 (1H, m); 7.37.32-7.36 (1H, m); 7.44(1H, dd, *J* = 2.5, 7.9 Hz) 7.58 (1H, dd, *J* = 1.3, 8.0 Hz).

^{13}C NMR (CD_3OD, 100 MHz) δ (ppm): 35.0; 65.9; 67.0; 76.2; 119.3; 123.6; 127.9; 128.5; 129.5; 133.4; 136.9; 153.4; 169.8; 172.3.

HRMS (ESI) calc. $C_{14}H_{13}BrNaO_7S$ $[M+Na]^+$ 426.9463, found 426.9470.

*bis((R)-2-((S)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl) 3,3'-((disulfanediylbis(nonane-9,1-diyl))bis(sulfanediyl))dipropionate (**9k**)*



9k

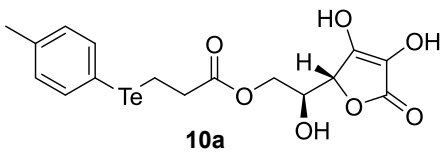
According to a slightly modified general procedure ***GP2***, L-ascorbic acid (88 mg, 0.50 mmol) and disulfide **6j** (56 mg, 0.10 mmol) gave the bis 6-*O*-L-ascorbyl ester **9k** (54 mg, 64%) as a white glassy solid.

^{1}H NMR (CD_3OD, 400 MHz) δ (ppm): 1.31-1.44 (20H, m); 1.57-1.64 (4H, m); 1.67-1.74 (4H, m); 2.52-2.61 (4H, m); 2.67-2.75 (8H, m); 2.76-2.82 (4H, m); 4.10-4.15 (2H, m, CHC**H**OH); 4.25 (2H, dd, J = 5.9, 11.1 Hz); 4.30 (2H, dd, J = 7.1, 11.1 Hz); 4.79 (2H, d, J = 2.0 Hz, C**H**OH).

^{13}C NMR (CD_3OD, 100 MHz) δ (ppm): 26.5; 28.0; 28.4; 28.7; 28.8; 29.1; 29.3; 31.5; 34.4; 38.4; 64.6; 66.6; 75.8; 118.6; 152.8; 171.8; 172.0.

HRMS (ESI) calc. $C_{36}H_{59}O_{14}S_4$ $[M+H]^+$ 843.2788, found 843.2799.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-(p-tolyltellanyl)propanoate (**10a**)*



10a

According to the general procedure ***GP2***, L-ascorbic acid (9 mg, 0.05 mmol) and β-telluroester **8a** (46 mg, 0.15 mmol) gave 6-*O*-L-ascorbyl ester **10a** (17 mg, 74%) as a yellowish glassy solid.

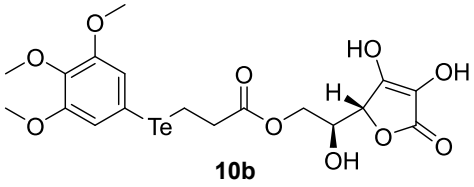
^{1}H NMR (400 MHz) δ (ppm): 2.35 (3H, s); 2.94-2.98 (2H, m); 3.0-3.04 (2H, m); 4.07-4.11 (1H, m, C**H**OH); 4.19 (1H, dd, J = 5.7, 11.1 Hz, C$\mathbf{H_a}H_bO$); 4.24 (1H, dd, J = 7.2, 11.1 Hz, $CH_a\mathbf{H_b}O$); 4.73 (1H, d, J = 2.0 Hz, C**H**CHOH); 7.07 (2H, ap d, J = 7.8 Hz); 7.66 (2H, ap d, J = 7.8 Hz).

^{13}C NMR (100 MHz, CD_3OD) δ (ppm): -0.2 (CH_2Te); 20.4 (CH_3); 36.8 ($CH_2C(O)$); 65.3; 67.2; 76.4; 107.7; 119.3; 130.4;138.4; 139.5; 153.2; 172.3; 173.7.

^{125}Te NMR (126MHz, CD_3OD) δ (ppm): 514.5.

HRMS (ESI) calc. $C_{16}H_{19}O_7Te$ $[M+H]^+$ 453.0193, found 453.0179.

*(S)-2-((R)-3,4-dihydroxy-5-oxo-2,5-dihydrofuran-2-yl)-2-hydroxyethyl 3-((3,4,5-trimethoxyphenyl)tellanyl)propanoate (**10b**)*



10b

According to the general procedure ***GP2***, L-ascorbic acid (9 mg, 0.05 mmol) and β-telluroester **8b** (57 mg, 0.15 mmol) gave 6-*O*-L-ascorbyl ester **10b** (18 mg, 67%) as a yellowish glassy solid.

^{1}H NMR (CD_3OD, 400 MHz) δ (ppm): 2.97-3.0 (2H, m, C**H$_2$**C(O)); 3.05-3.09 (2H, m, C**H$_2$**Te); 3.75 (3H, s); 3.83 (6H, s); 4.06-4.10 (1H, m, C**H**OH); 4.19 (1H, dd, J = 5.8, 11.2 Hz, C**H$_a$**H$_b$O); 4.24 (1H, dd, J = 7.1, 11.2 Hz, CH$_a$**H$_b$**O), 4.74 (1H, d, J = 2 Hz, C**H**CHOH); 7.03 (2H, s Ar-H).

^{13}C NMR (CD_3OD, 100 MHz) δ (ppm): -.01 (CH_2Te);36.2 (CH_2C(O)); 55.4 (2C, **C**H$_3$O); 59.7 (**C**H$_3$O); 64.7 (**C**H$_2$O); 66.6 (**C**HOH); 75.8 (**C**HCHOH); 104.4; 116.4 (**C**H); 118.7; 138.1; 152.5; 153.3; 171.7; 173.1.

^{125}Te NMR (126MHz CD_3OD) δ (ppm): 569.8.

HRMS (ESI) calc. $C_{18}H_{22}NaO_{10}Te$ $[M+Na]^+$ 551.0173, found 551.0192.

6. Differential scanning calorimetry (DSC)

Samples were equilibrated at 25 °C before undergoing a heating - cooling - heating cycle. The solids were first heated to 110 °C, then cooled down to -20 °C and finally heated up again to 110 °C. Both heating ramps were performed at 5 °C/min, while cooling was carried out at two different rates, 5 °C/min and 50 °C/min. The measurements were performed under a nitrogen atmosphere flow (50 mL/min). The crystallization and melting temperatures were taken as the temperature of the corresponding exothermic and endothermic peak, respectively.

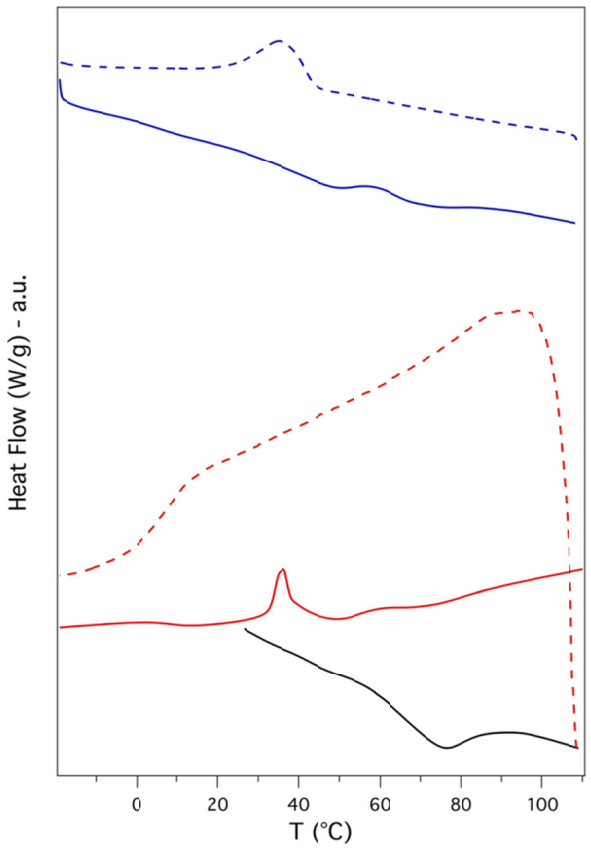
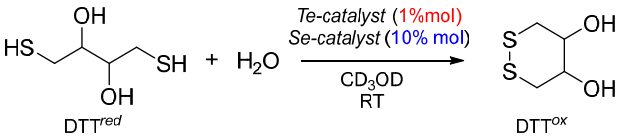


Figure S1. DSC curves for **9c** (black) First heating cycle , (dashed red) cooling cycle at 50 °C/min, (red), second heating cycle, (dashed blu) cooling cycle at 5 °C/min, (blu) second heating cycle. The curves have been displaced vertically for clarity.

7. GPx-like catalytic activity measurements

NMR Assay (DTT oxidation)

In the NMR assay, DTT^{red} (0.15 mmol) and Te-catalyst (0.0015 mmol) were dissolved in CD_3OD (1.1 mL), and the solution was added to 35% H_2O_2 (15 µL, 0.15 mmol) to start the reaction. ^1H NMR spectra were measured at a variable reaction time at 25 °C. The relative populations of DTT^{red} and DTT^{ox} were determined by integration of the ^1H NMR signals (Scheme S2 and Figures S2, related to exemplificative catalytic activity of L-ascorbyl derivative **4a)**.[8]



Scheme S2. Catalysed oxidation of DTT^{red} to DTT^{ox} (DTT oxidation NMR assay)

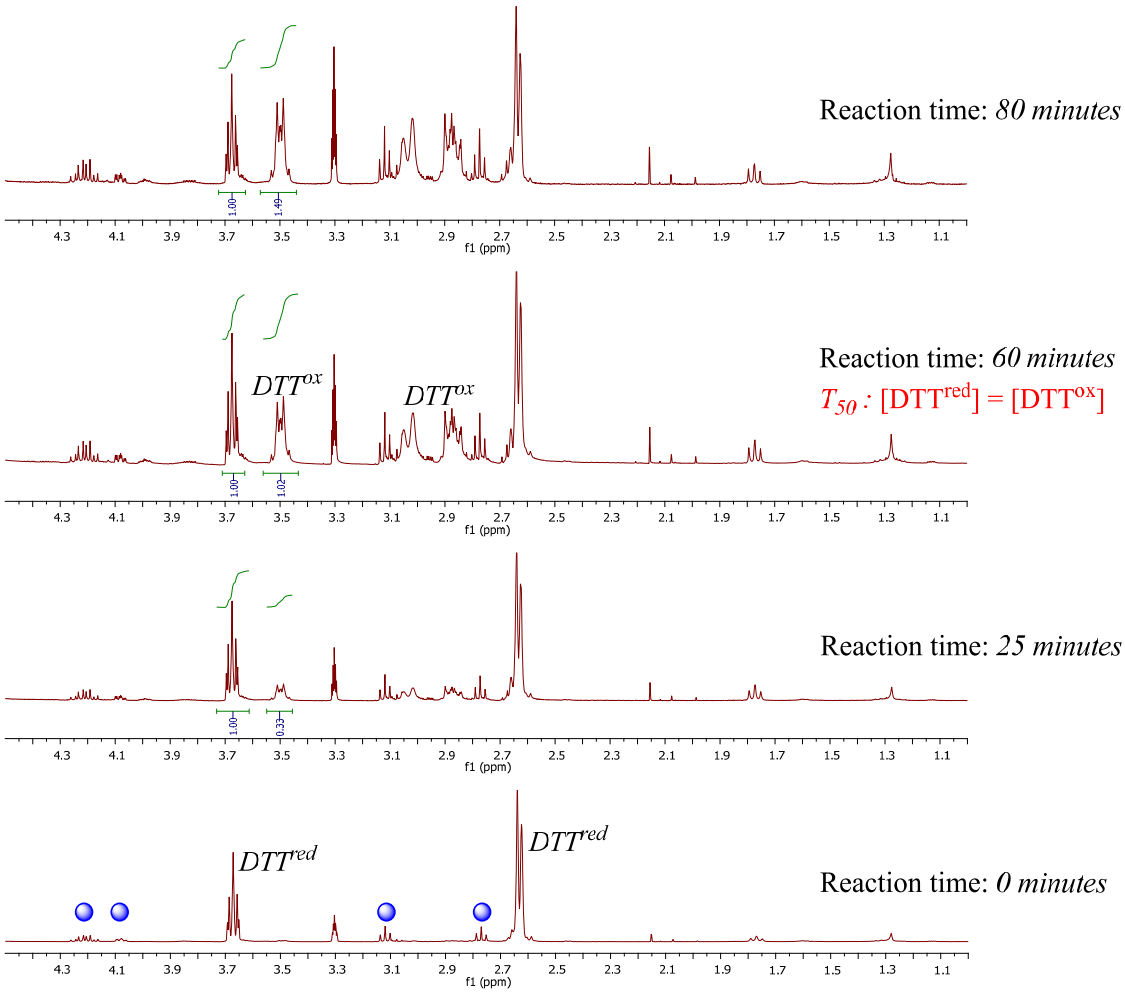


Figure S2. Series of ^1H NMR spectra obtained in the oxidation of DTT^{red} (0.15 mmol) with H_2O_2 (0.15 mmol) in the presence of catalytic amount of L-ascorbyl selenoester **4a** (0.015 mmol). ● = signals of catalyst.

GSH and NADPH-Glutathione Reductase (GR) coupled assay

In the NADPH/GR coupled assay, 272 µL of a 0.5 mM solution of telluride in a 100 mM phosphate buffer pH 7.4 was added to 988 µL of phosphate buffer solution. Then, 600 µL of a test solution, prepared by mixing 5823 µL of a 100 mM phosphate/6mM EDTA buffer solution at pH 7.4 containing NADPH (6 µmol) and GSH (20.4 µmol) with a GR solution (600 U/mL, 135 µL), were added to the telluride solution. The reaction was started by addition of 140 µL of a 36 mM aqueous solution of H_2O_2. The progress of the reaction was monitored following the consumption of NADPH by UV spectroscopy (340 nm).[8,9]

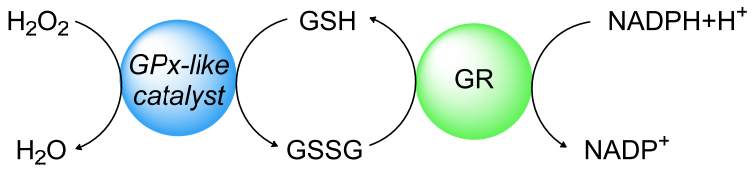


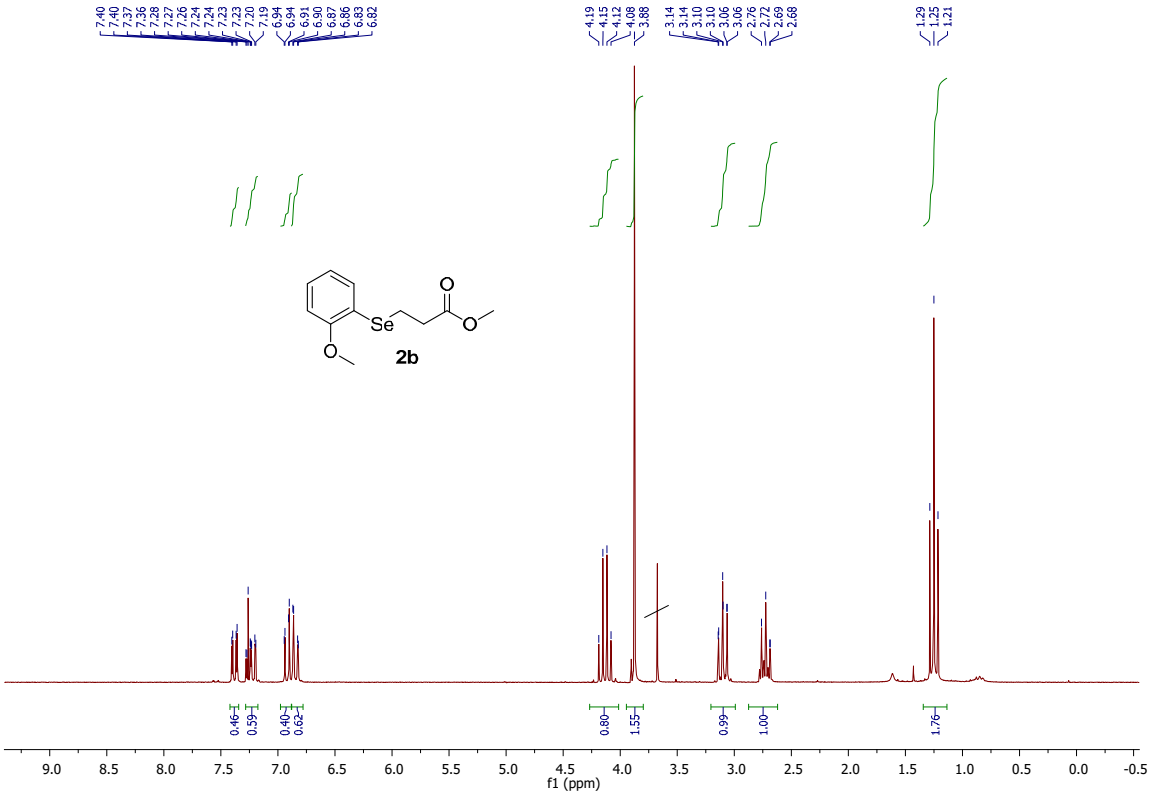
Figure S3. Te-catalyst (6 mol % with respect to GSH). Reaction progress followed monitoring absorption change at 340 nm due to consumption of NADPH

8. 2,2-Diphenyl-1-picrylhydrazyl (DPPH) assay

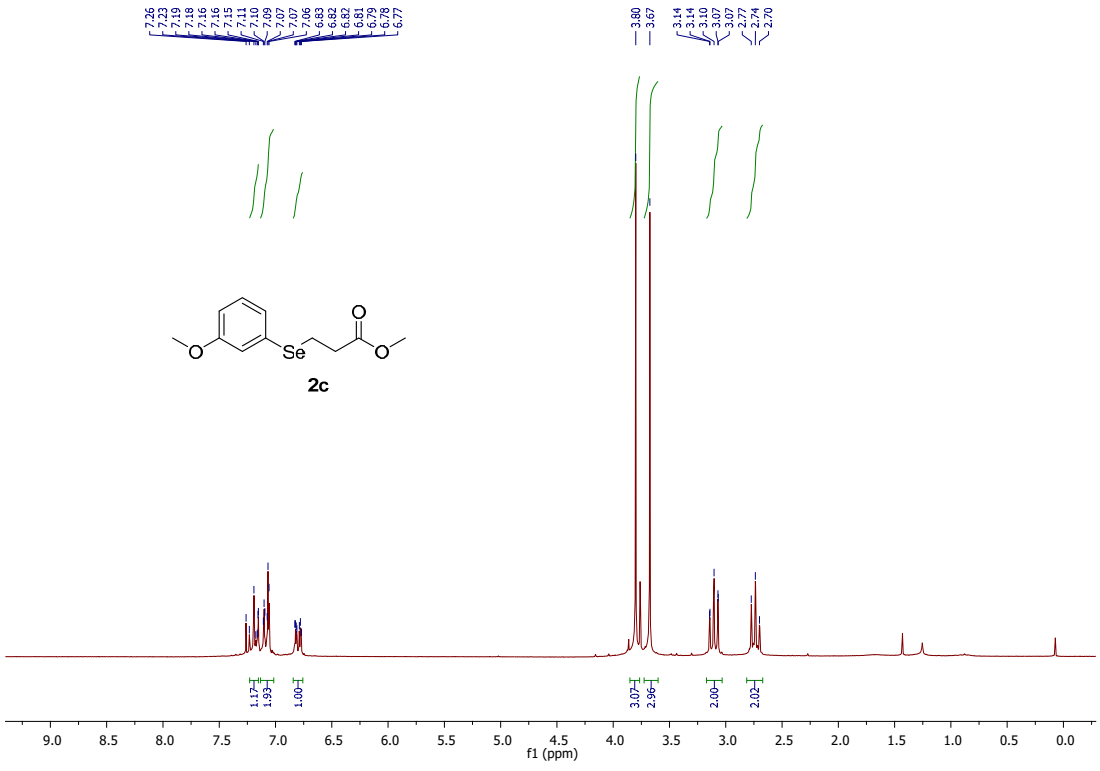
The assay was performed according to a literature reported procedure.[10] To 1.98 mL of 200 µM DPPH in ethanol 20 µL of 10 mM ethanolic solution of compounds **4**, **9** or **10** were added and rapidly mixed. The reaction was followed by spectrophotometric analysis measuring the absorbance at 515 nm. In order to determine the stoichiometry of the reaction (*n*, number of radical trapped), the assay was also performed by using an excess of DPPH. Thus, 20 µL of 5 mM ethanolic solution of compounds **4**, **9** or **10** were added to 1.98 mL of 200 µM DPPH in ethanol and rapidly mixed. The progress of the reaction was moitored by spectrophotometric analysis measuring the absorbance at 515 nm every 20 seconds for 10 minutes.

9. NMR Spectra of New Compounds

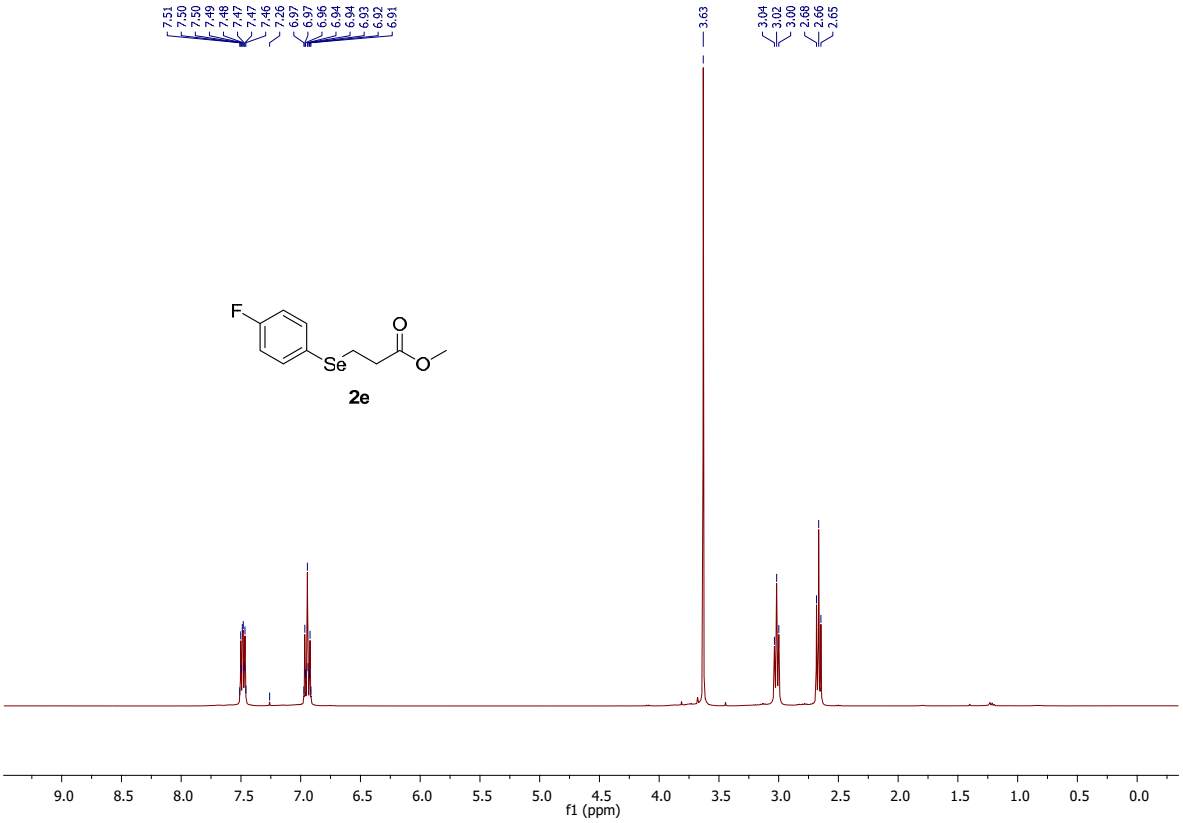
^{1}H NMR spectrum of compound **2b** (200 MHz, $CDCl_3$)



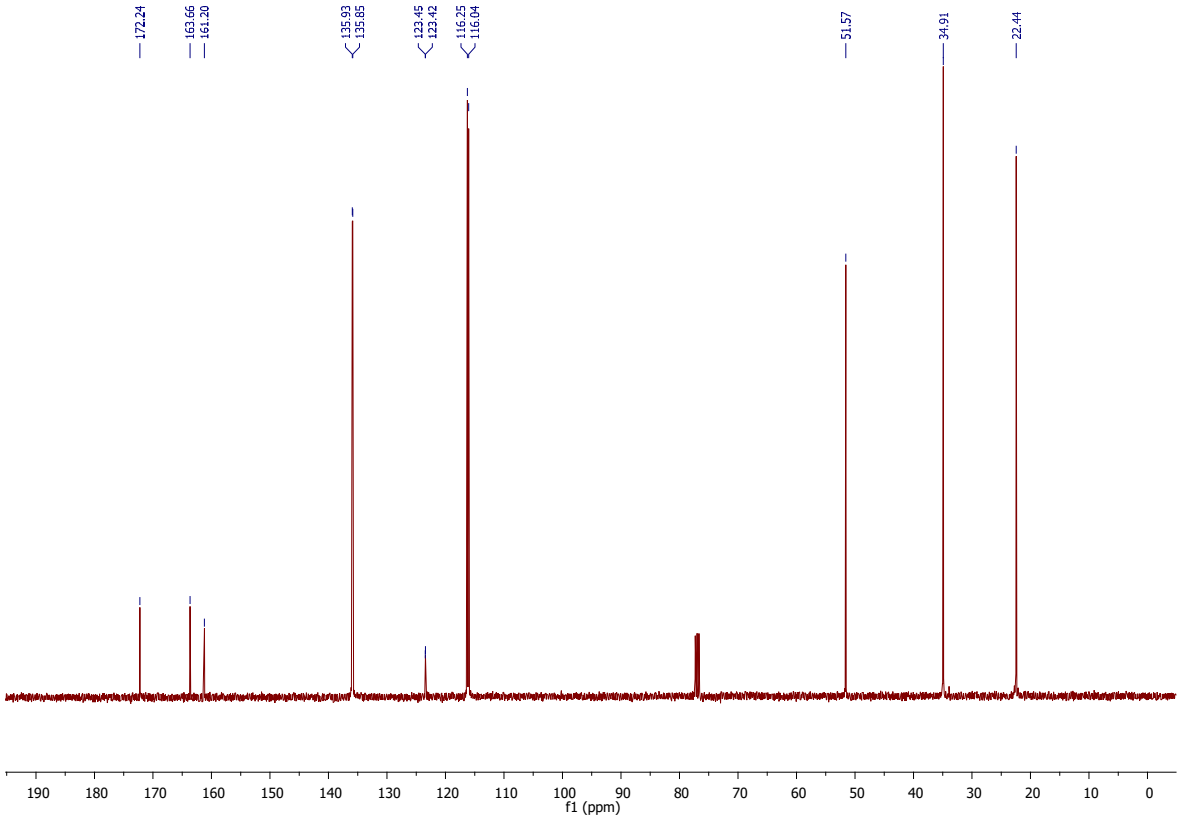
^{1}H NMR spectrum of compound **2c** (200 MHz, $CDCl_3$)



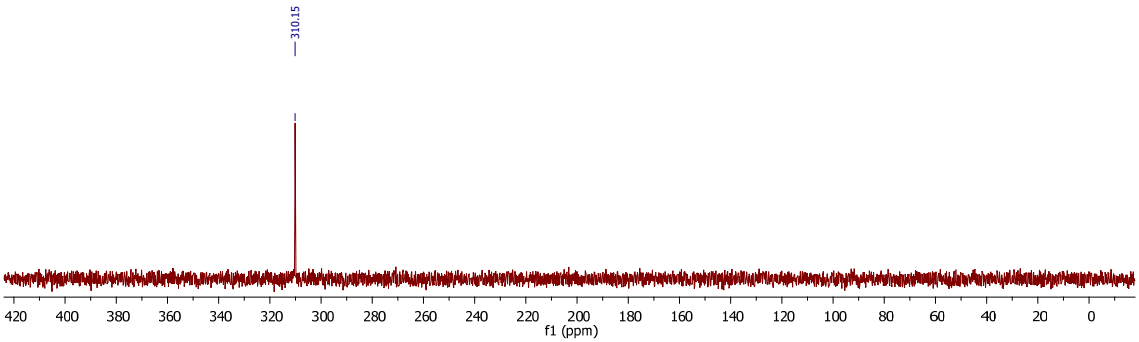
^{1}H NMR spectrum of compound **2e** (400 MHz, $CDCl_3$)



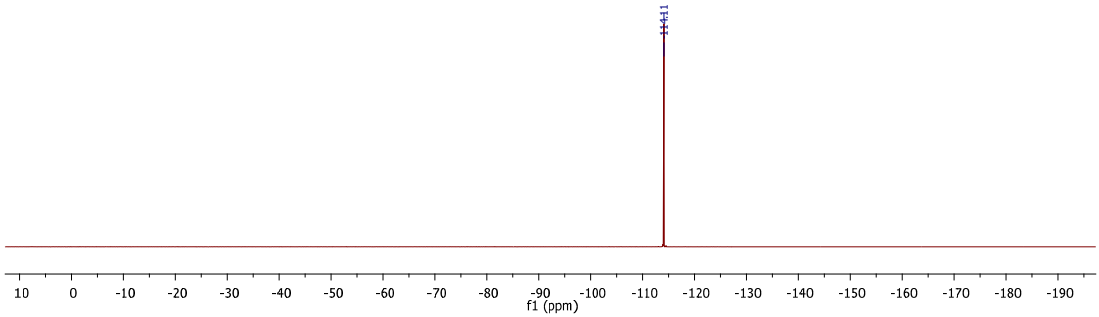
^{13}C NMR spectrum of compound **2e** (100 MHz, $CDCl_3$)



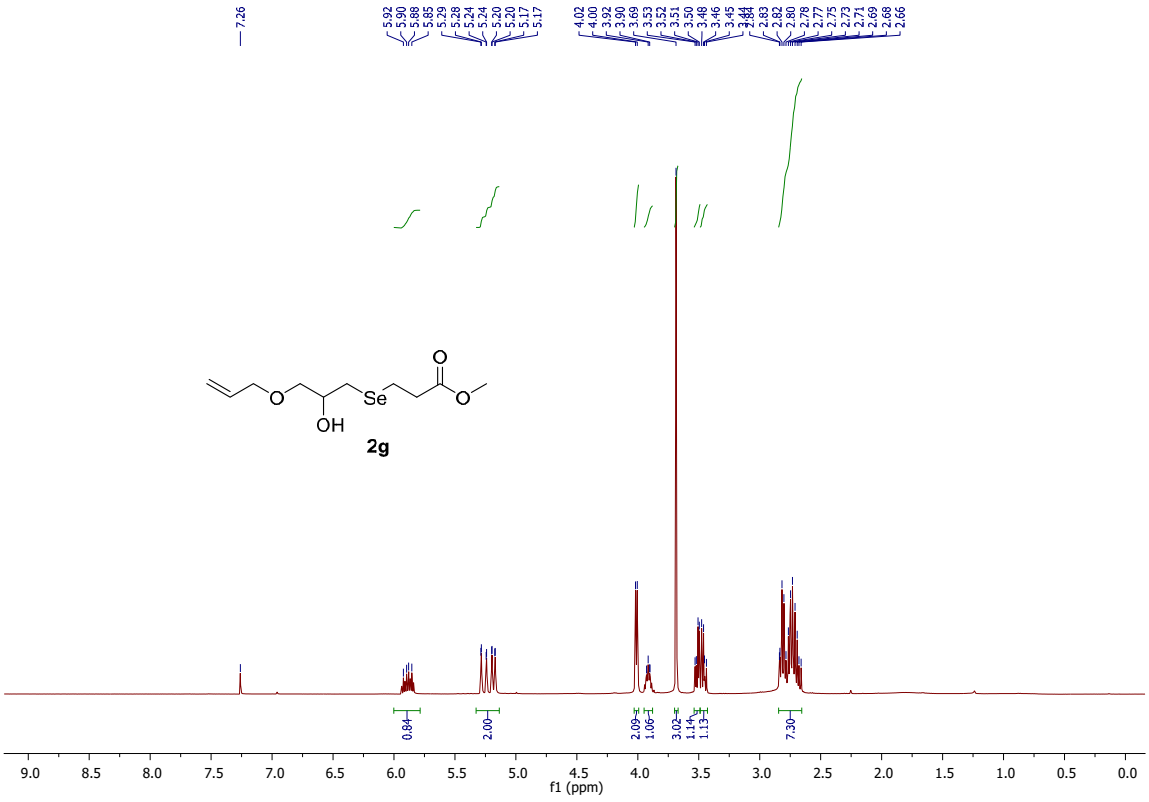
^{77}Se NMR spectrum of compound **2e** (76 MHz, $CDCl_3$)



^{19}F NMR spectrum of compound **2e** (376 MHz, $CDCl_3$)

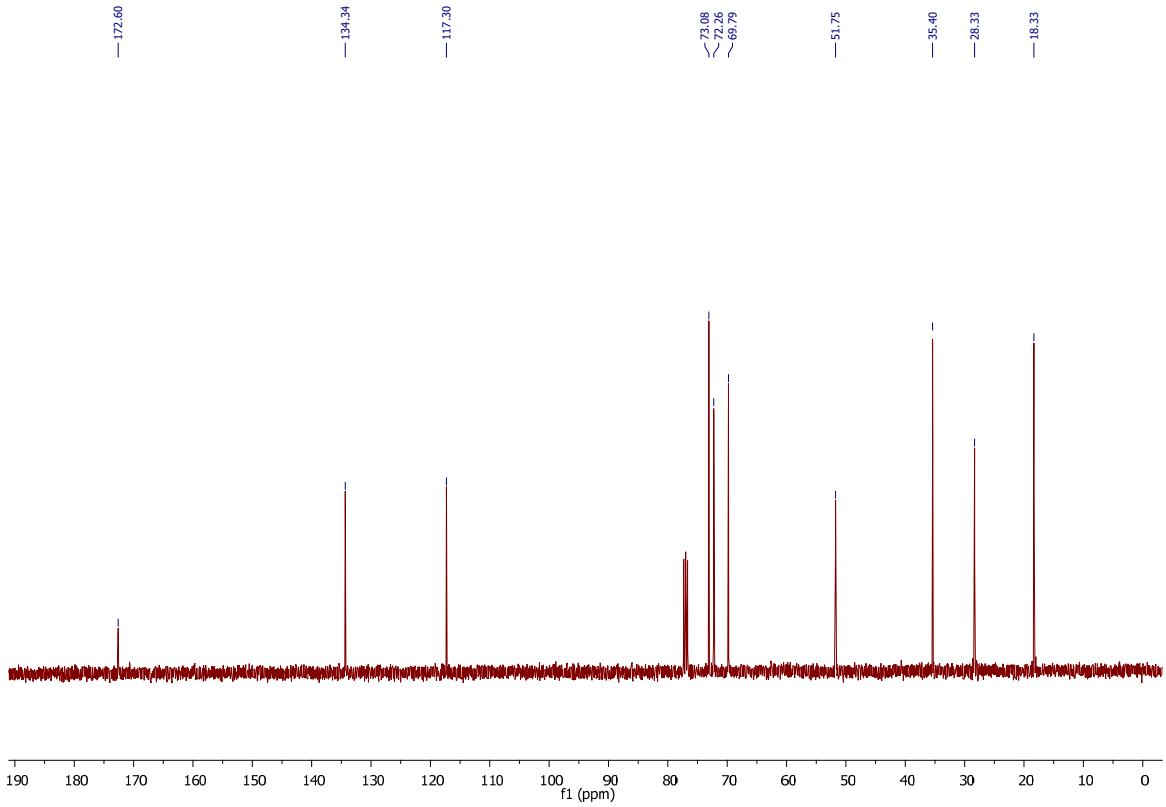


^{1}H NMR spectrum of compound **2g** (400 MHz, $CDCl_3$)

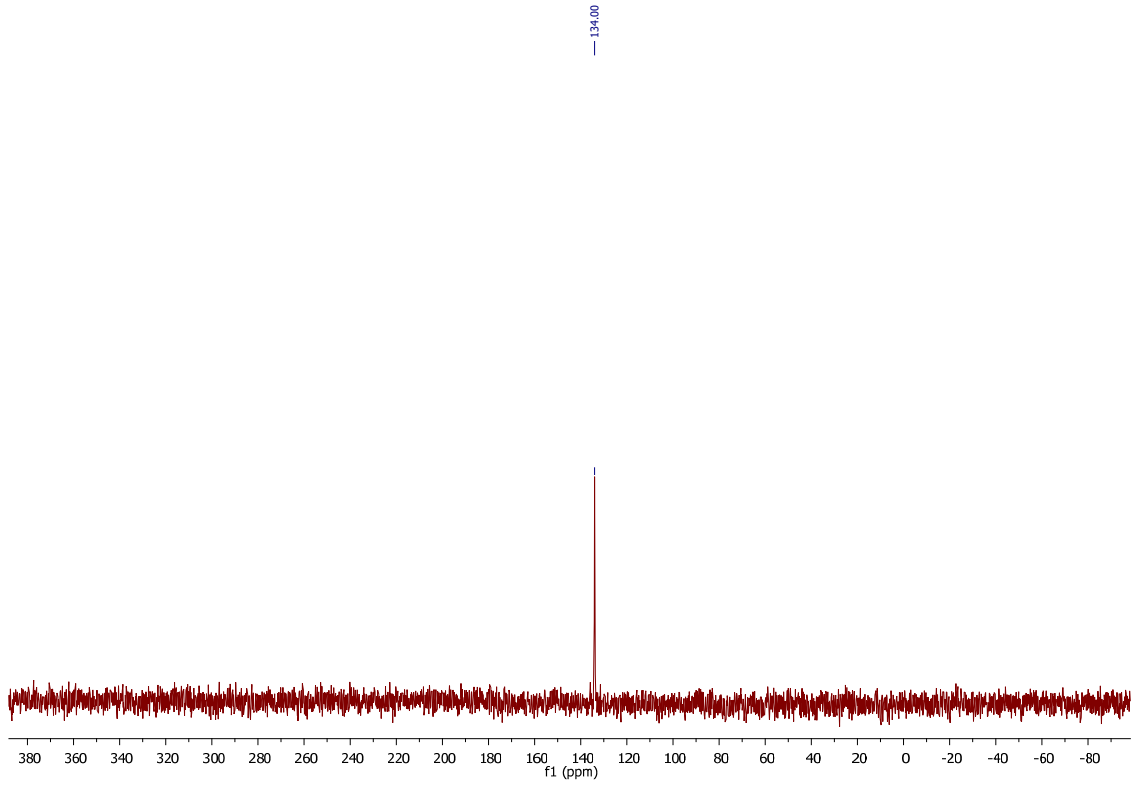


2g

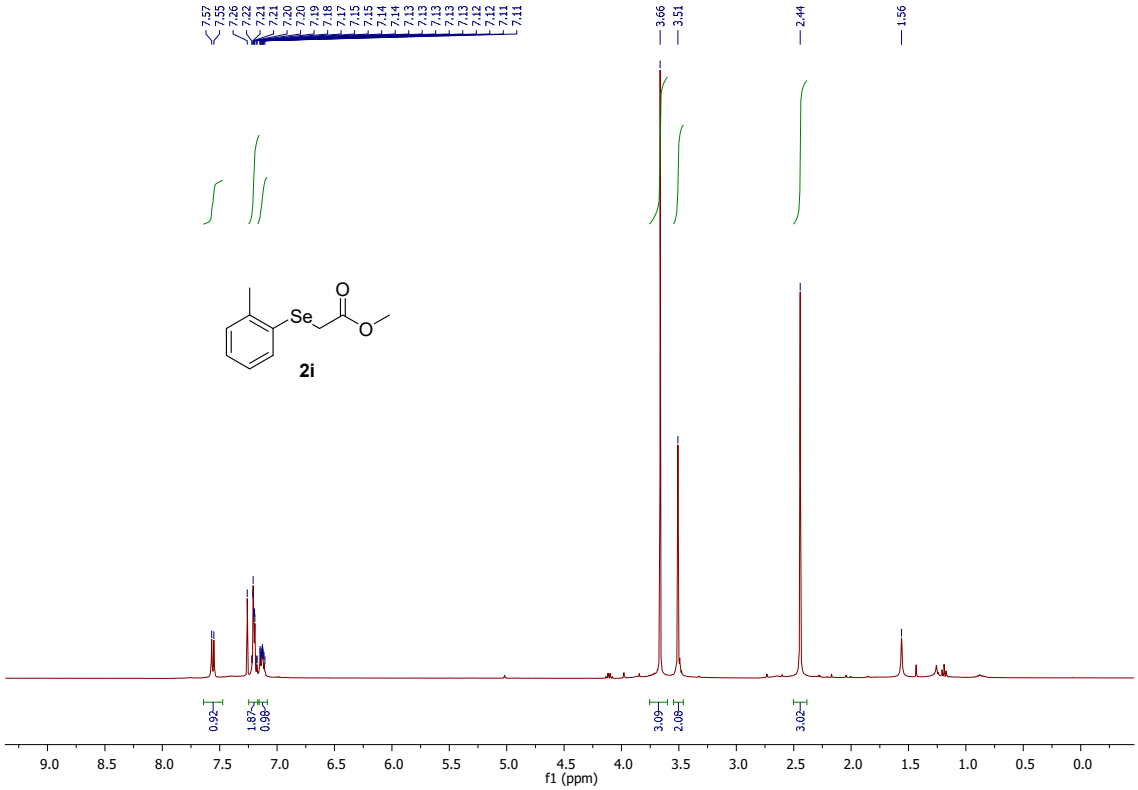
^{13}C NMR spectrum of compound **2g** (100 MHz, $CDCl_3$)



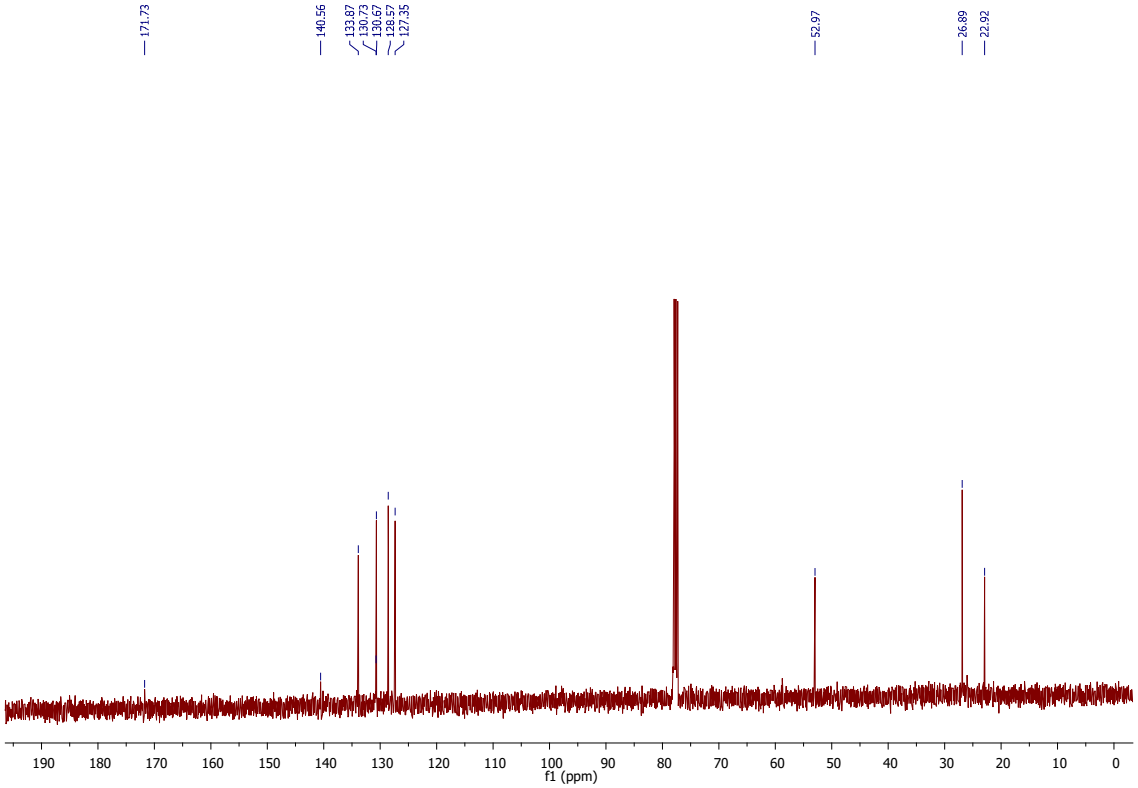
^{77}Se NMR spectrum of compound **2g** (76 MHz, $CDCl_3$)



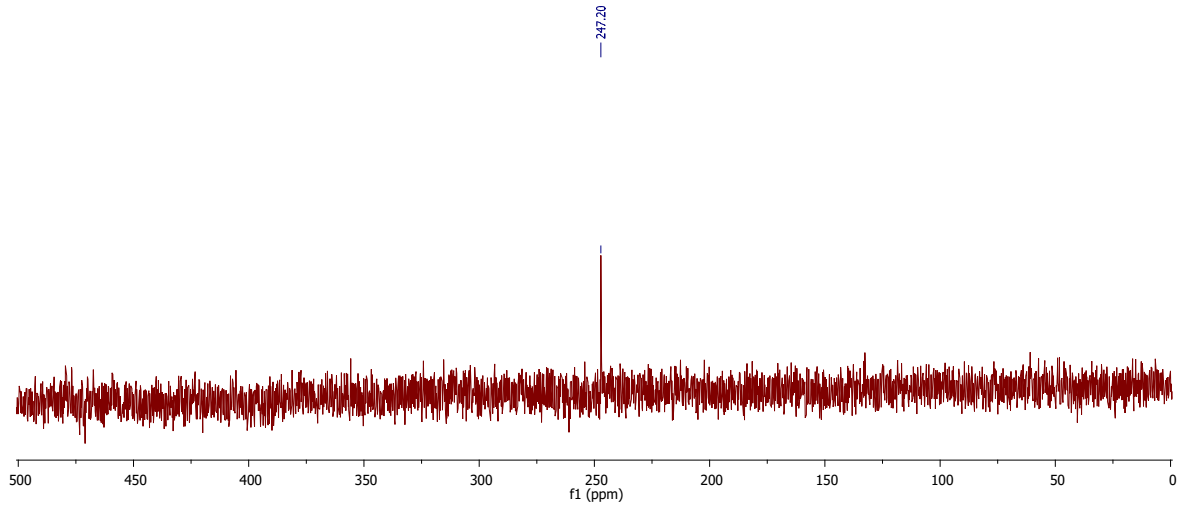
^{1}H NMR spectrum of compound **2i** (400 MHz, $CDCl_3$)



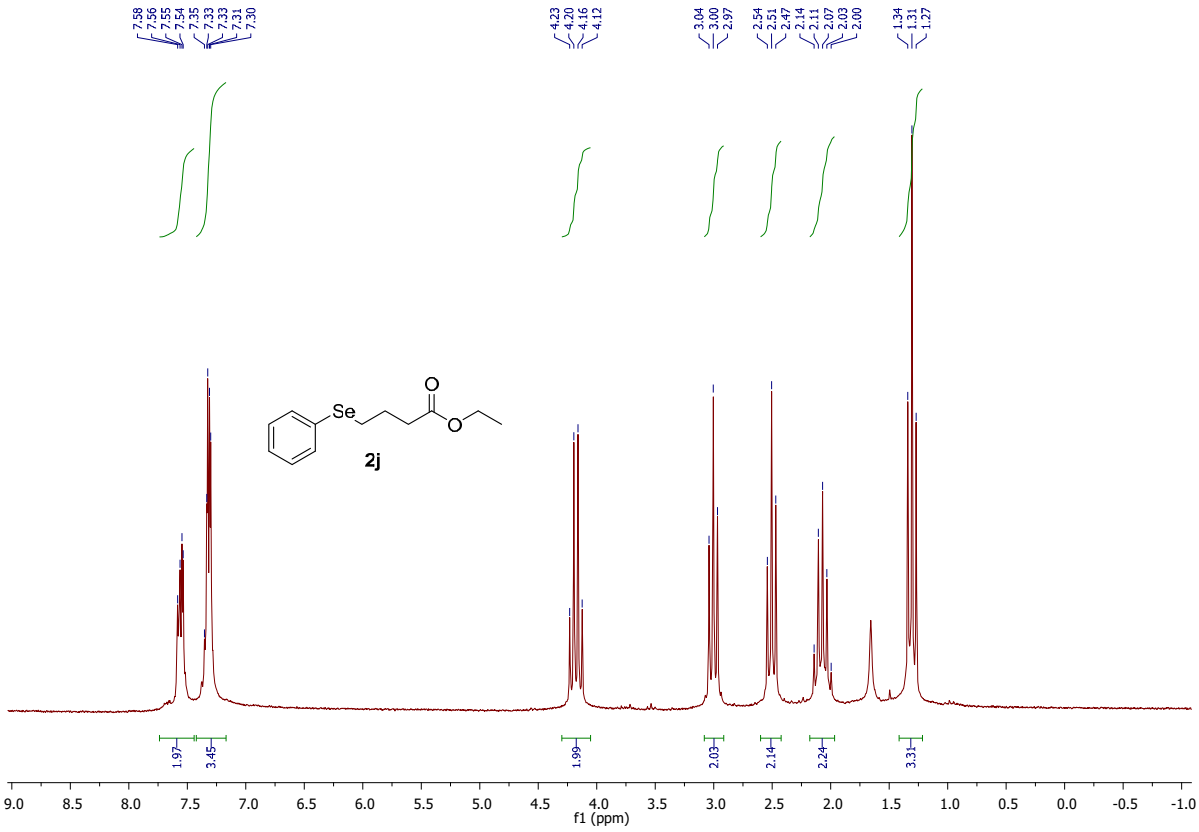
^{13}C NMR spectrum of compound **2i** (100 MHz, $CDCl_3$)



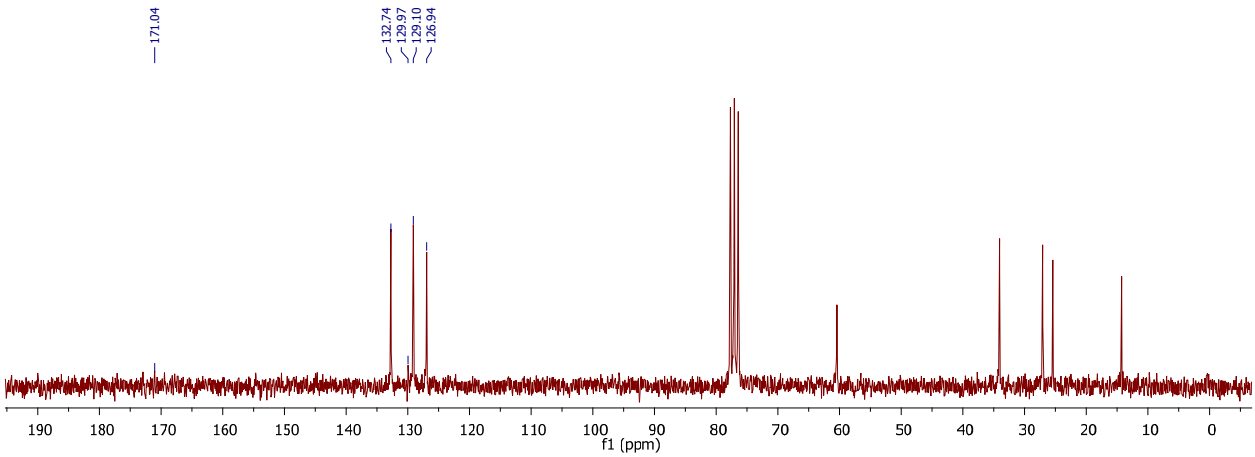
^{77}Se NMR spectrum of compound **2i** (76 MHz, $CDCl_3$)



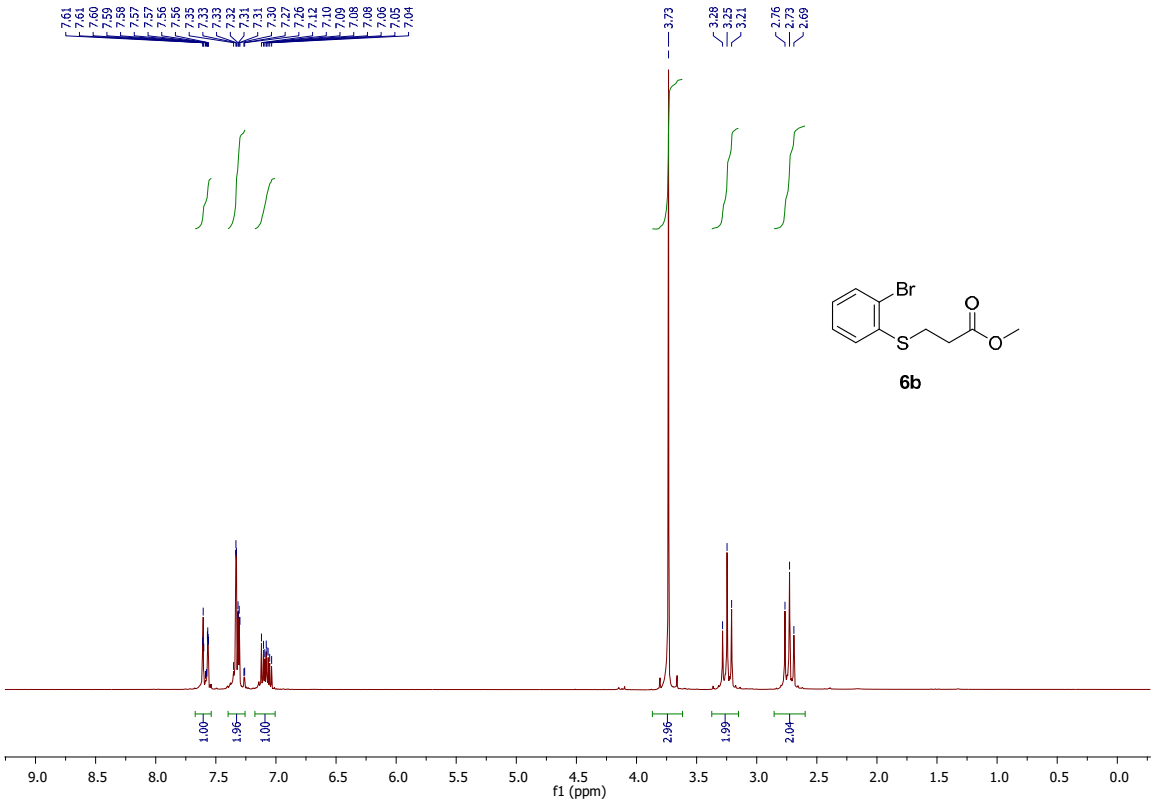
^{1}H NMR spectrum of compound **2j** (200 MHz, $CDCl_3$)



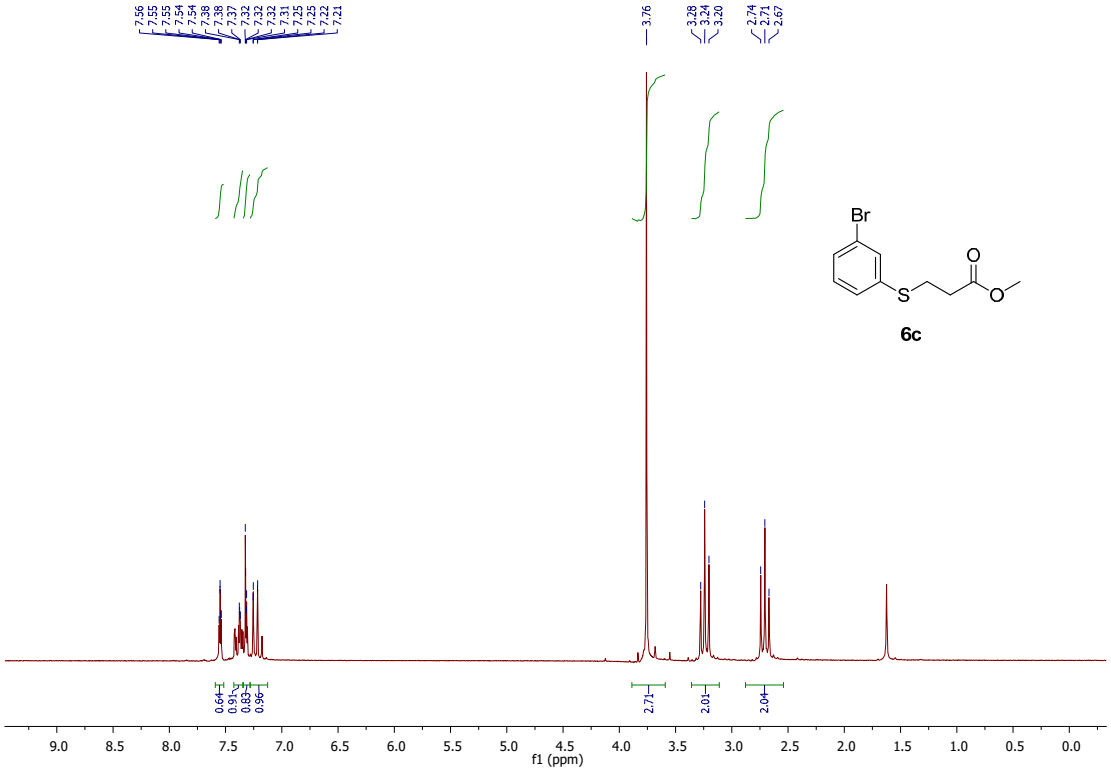
^{13}C NMR spectrum of compound **2j** (50 MHz, $CDCl_3$)



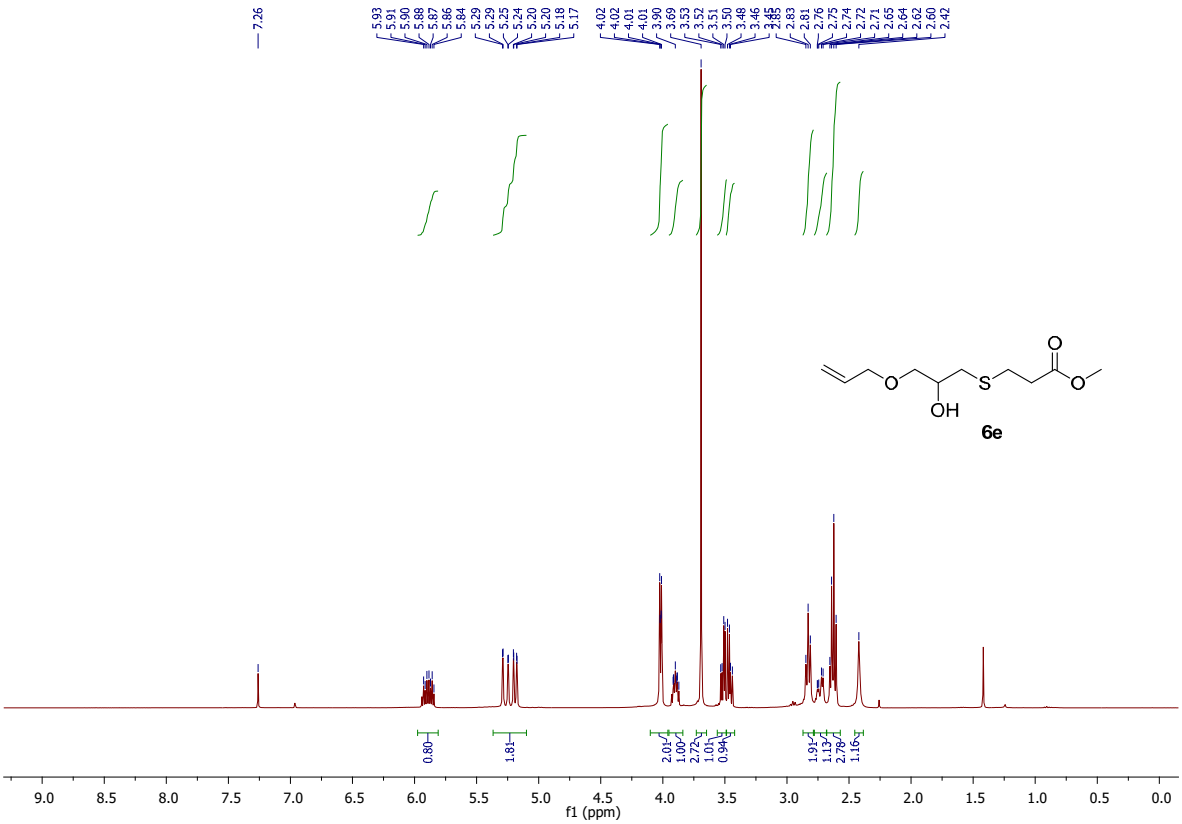
^{1}H NMR spectrum of compound **6b** (400 MHz, $CDCl_3$)



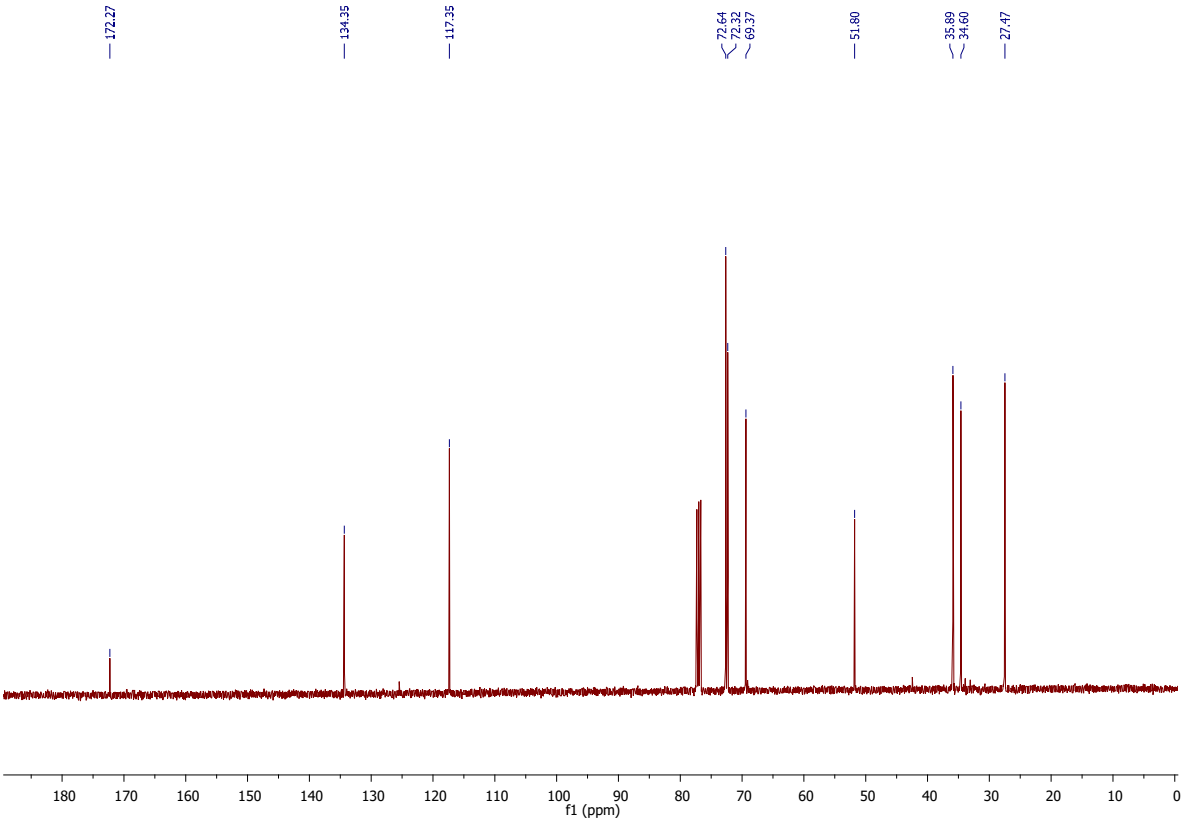
^{1}H NMR spectrum of compound **6c** (400 MHz, $CDCl_3$)



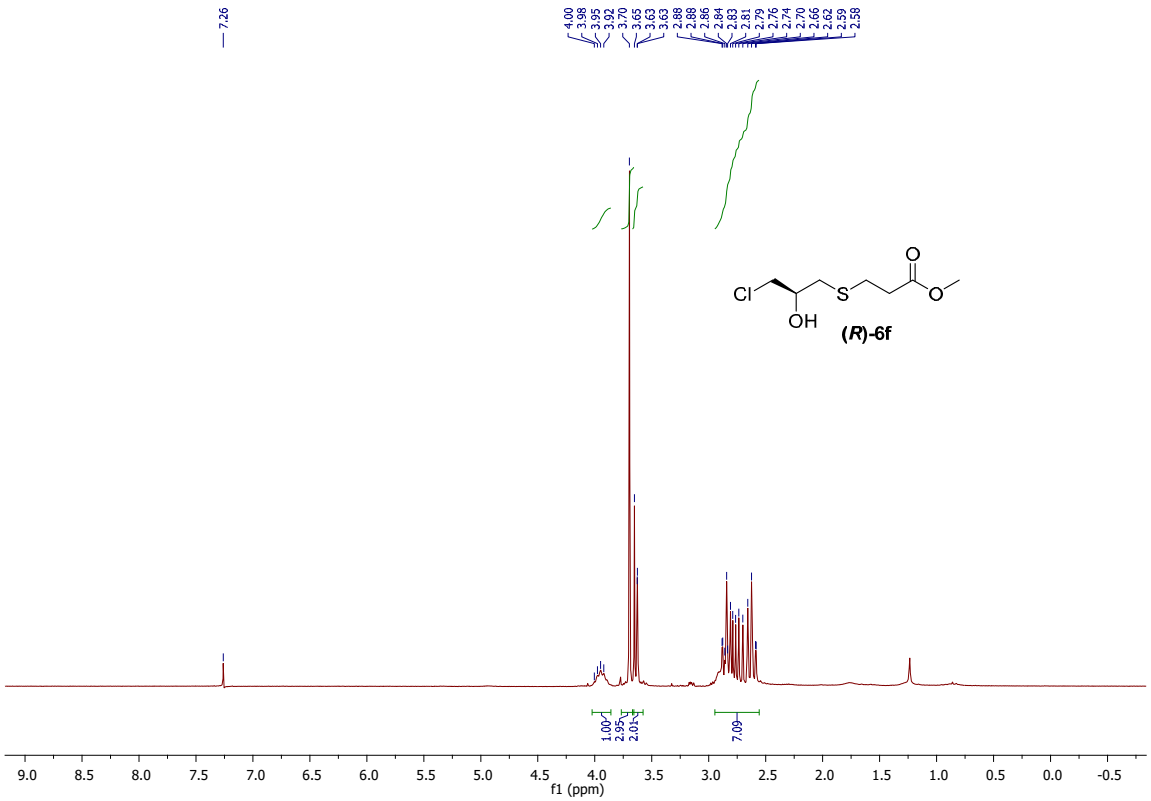
^{1}H NMR spectrum of compound **6e** (400 MHz, $CDCl_3$)



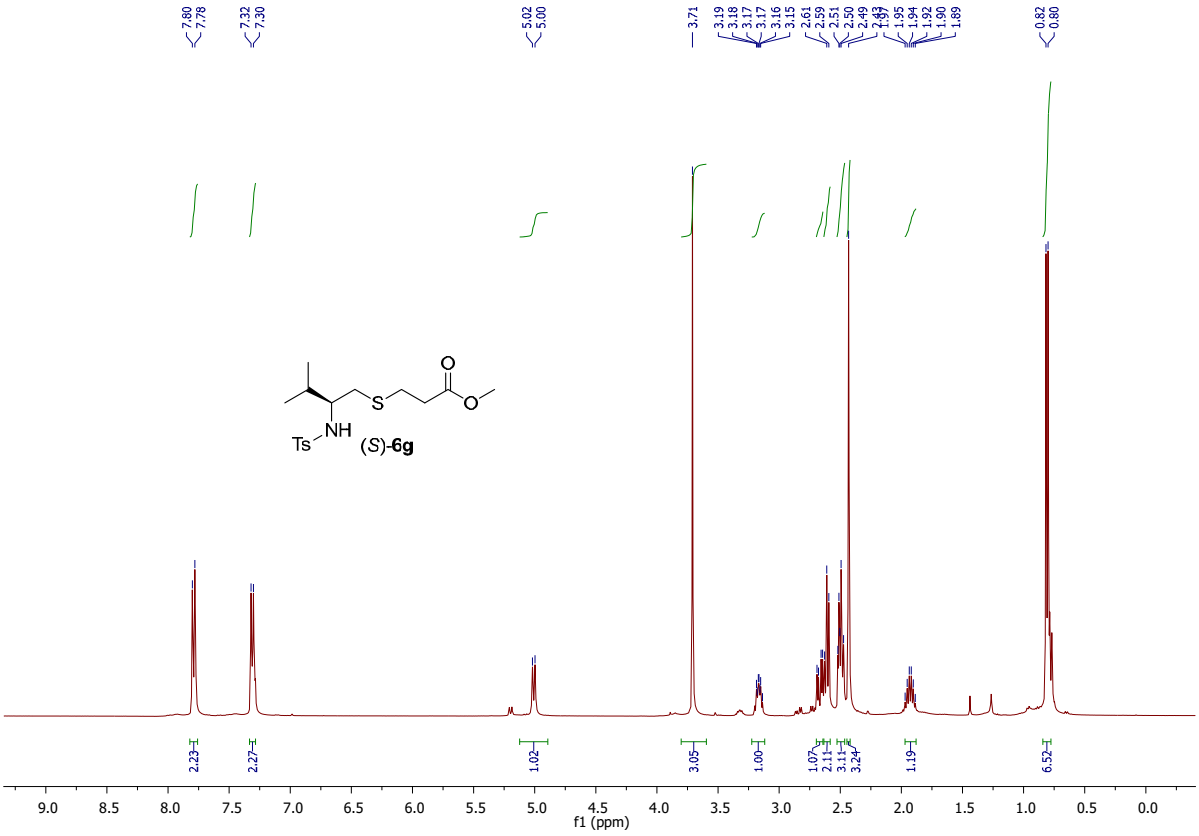
^{13}C NMR spectrum of compound **6e** (100 MHz, $CDCl_3$)



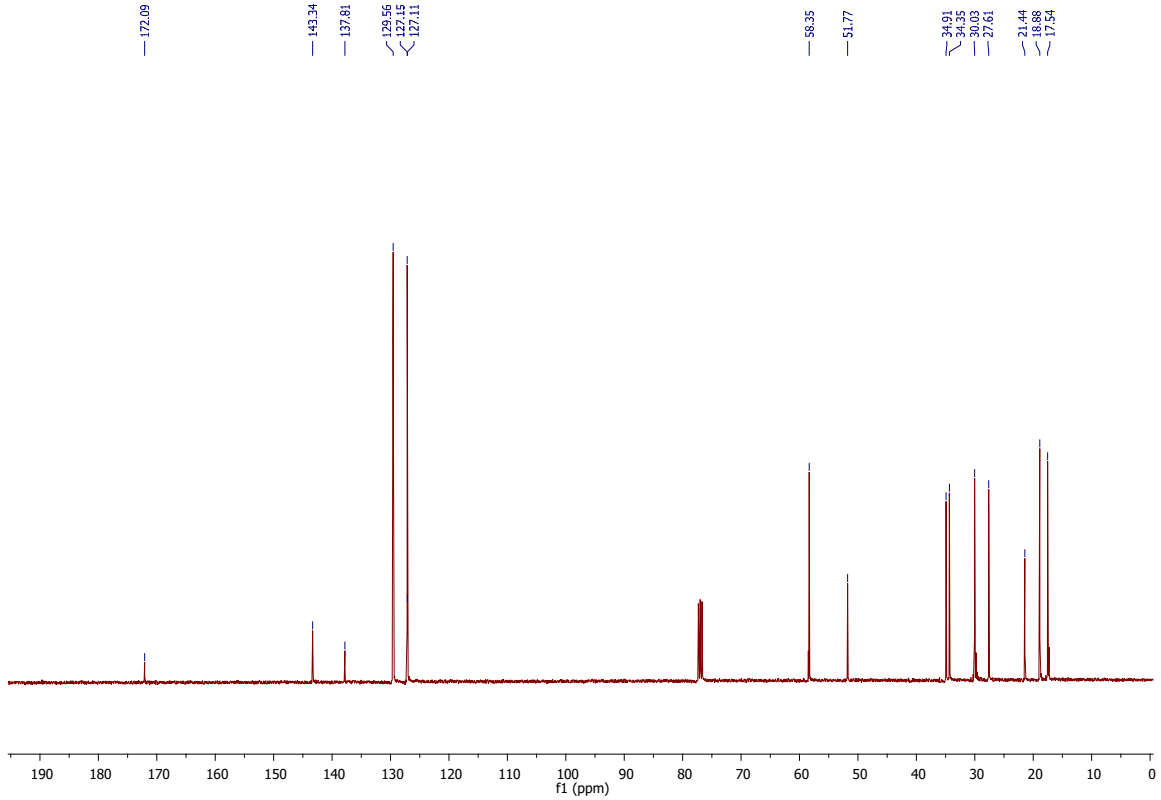
^{1}H NMR spectrum of compound (*R*)-**6f** (200 MHz, $CDCl_3$)



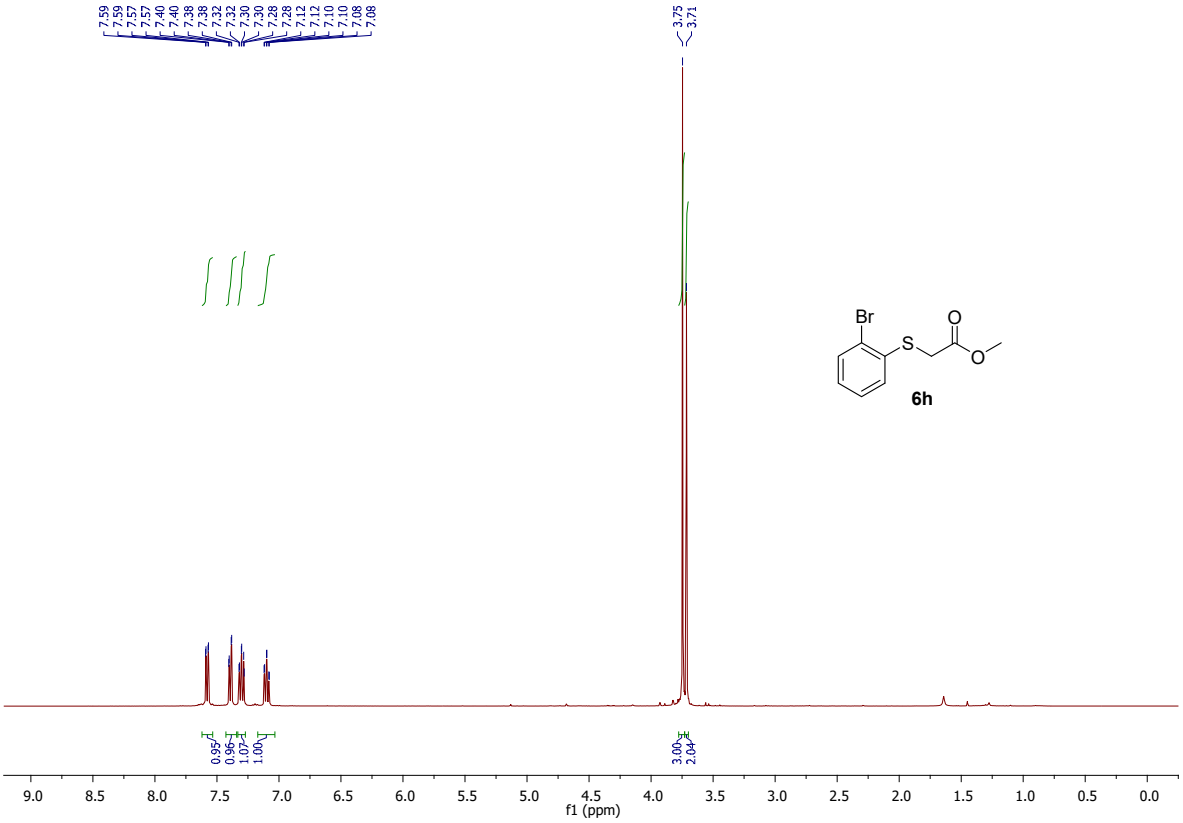
^{1}H NMR spectrum of compound (*S*)-**6g** (400 MHz, $CDCl_3$)



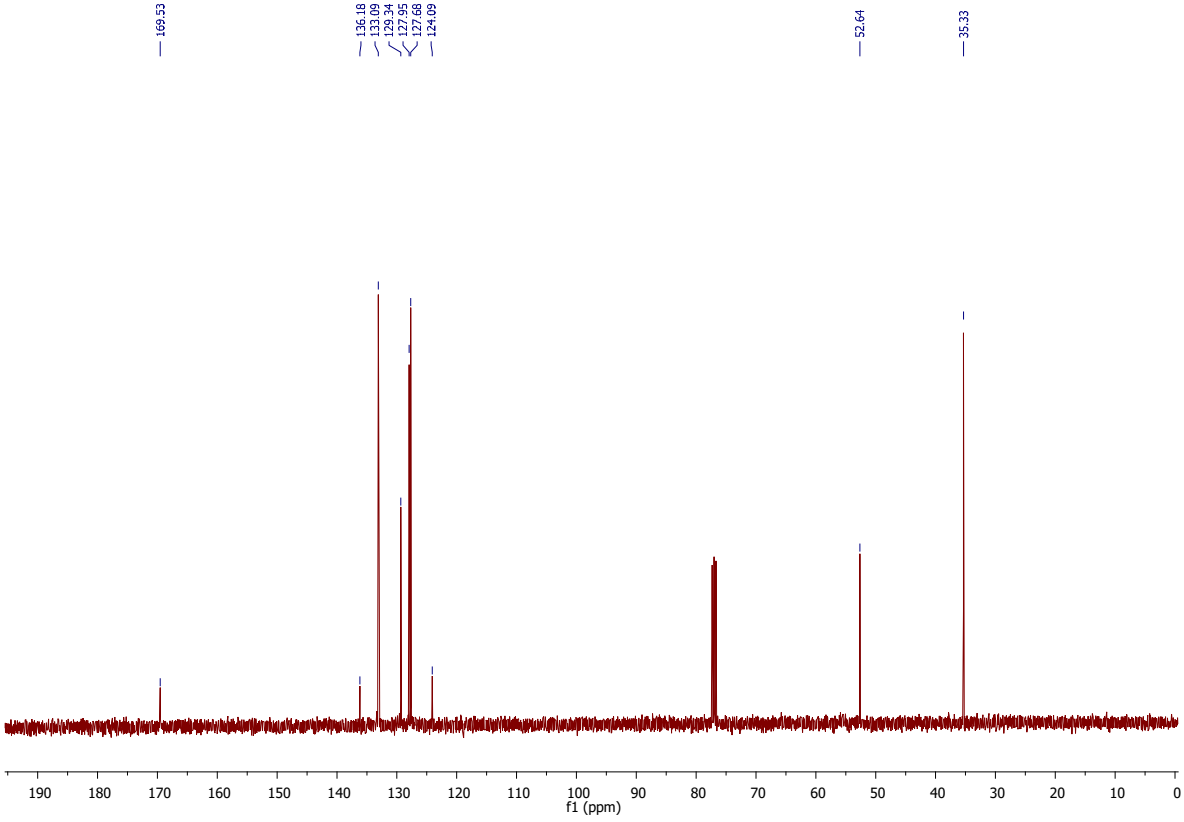
^{13}C NMR spectrum of compound (*S*)-**6g** (100 MHz, $CDCl_3$)



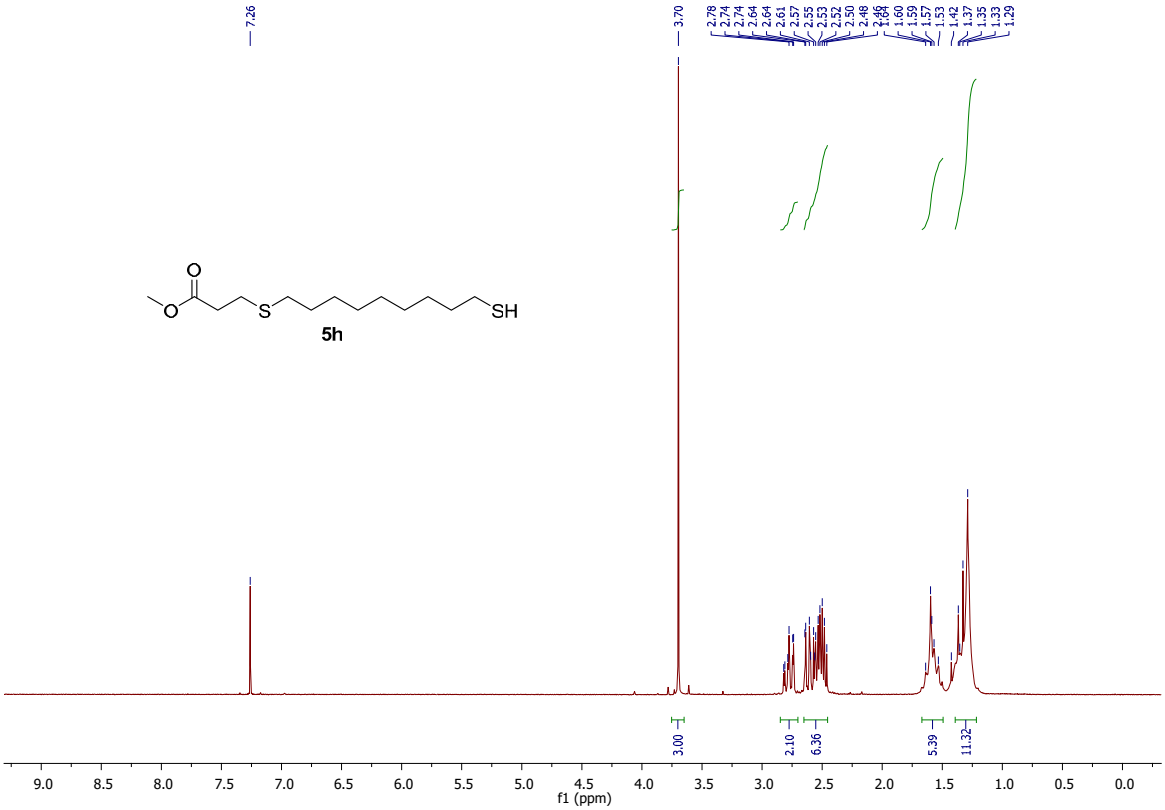
^{1}H NMR spectrum of compound **6h** (400 MHz, $CDCl_3$)



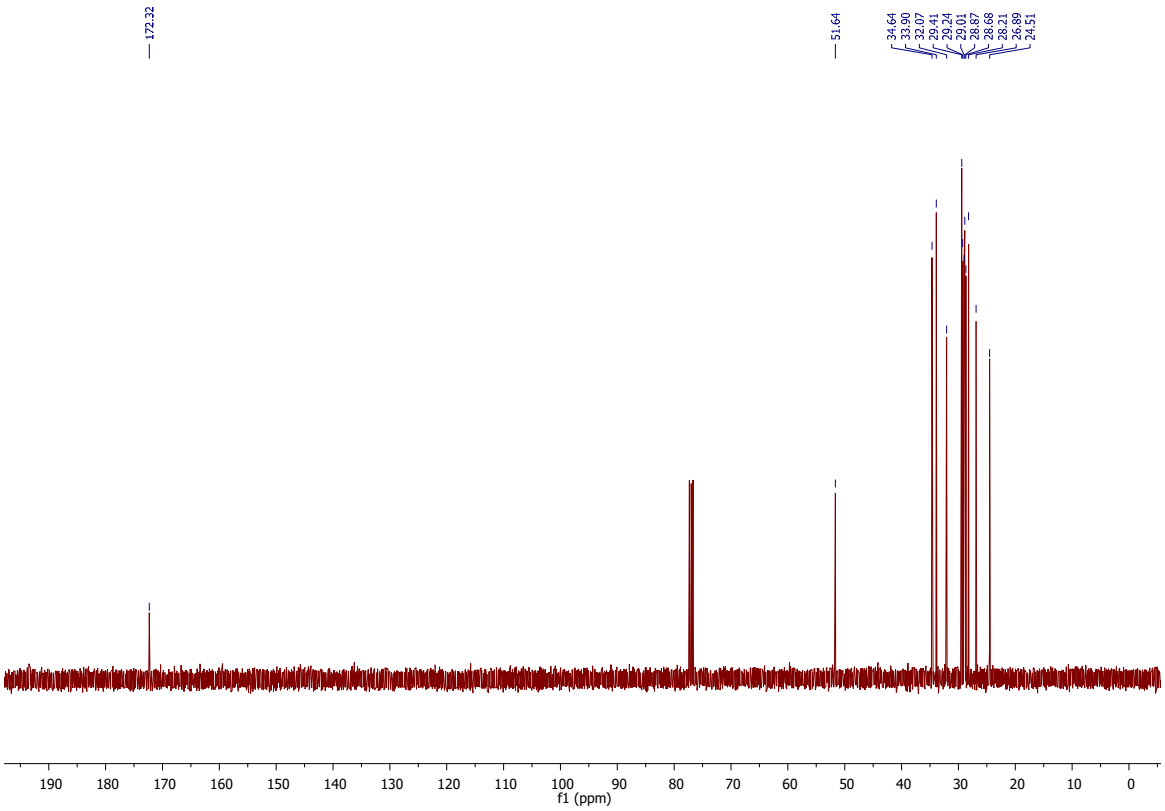
^{13}C NMR spectrum of compound **6h** (100 MHz, $CDCl_3$)



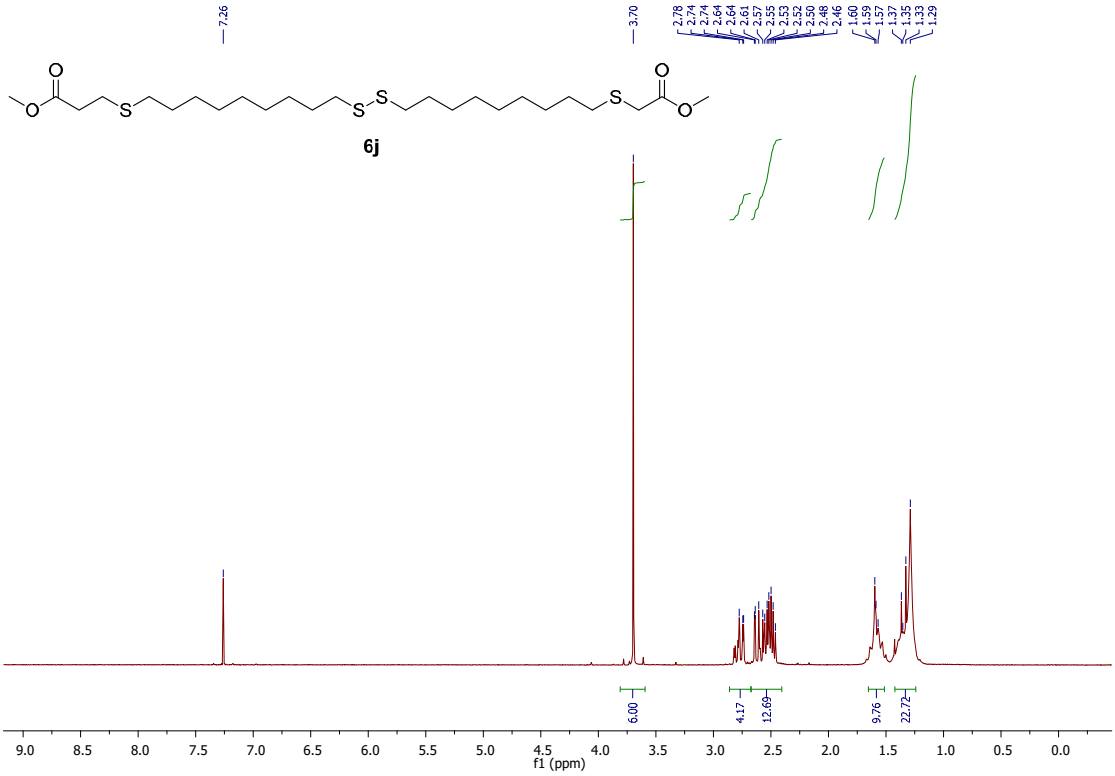
^{1}H NMR spectrum of compound **5h** (200 MHz, $CDCl_3$)



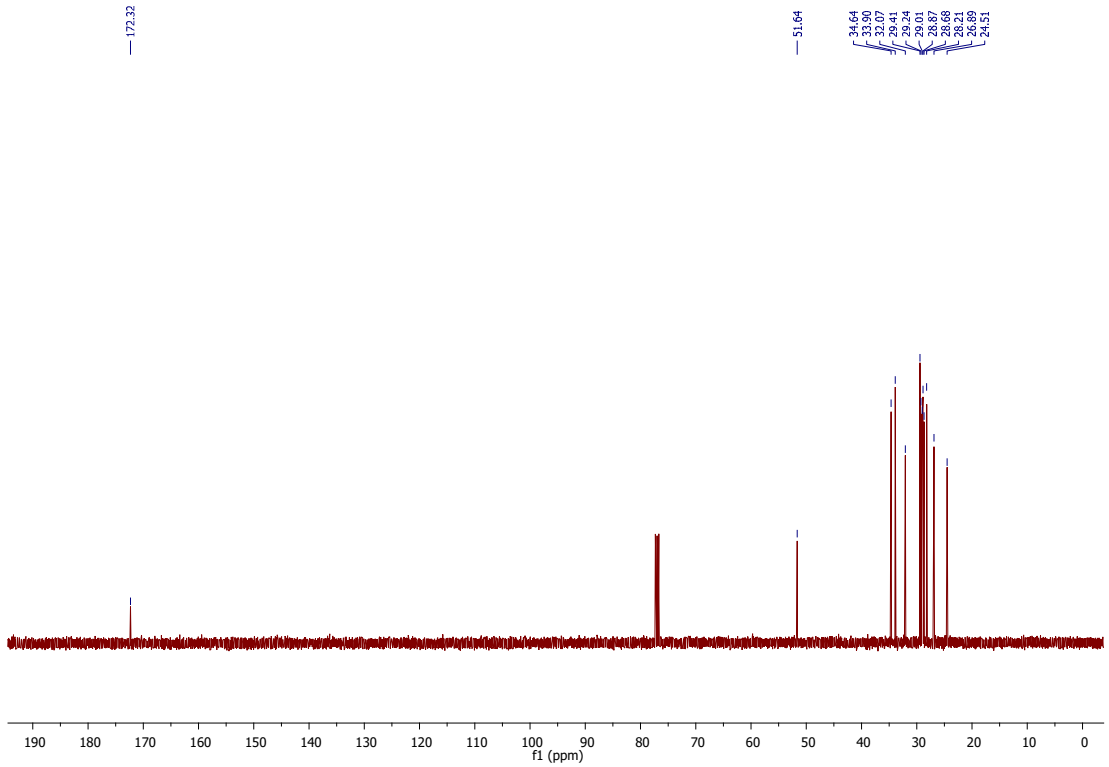
^{13}C NMR spectrum of compound **5h** (100 MHz, $CDCl_3$)



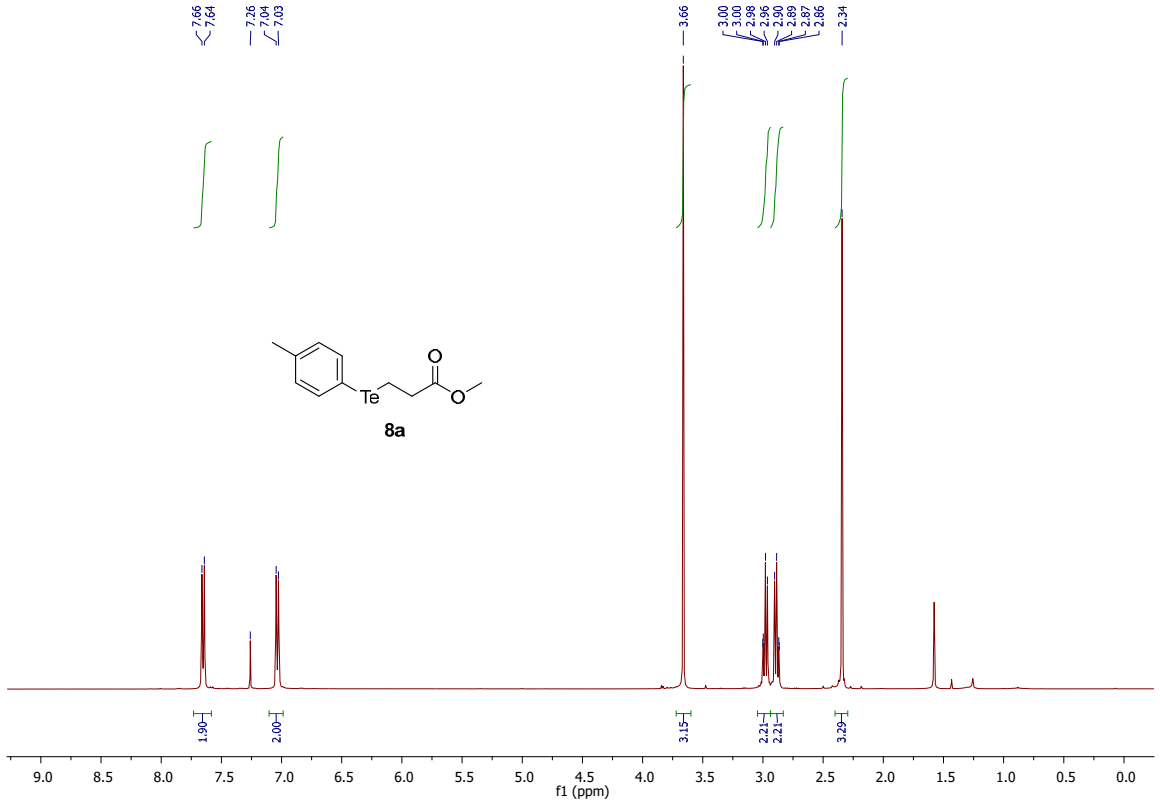
^{1}H NMR spectrum of compound **6j** (400 MHz, $CDCl_3$)



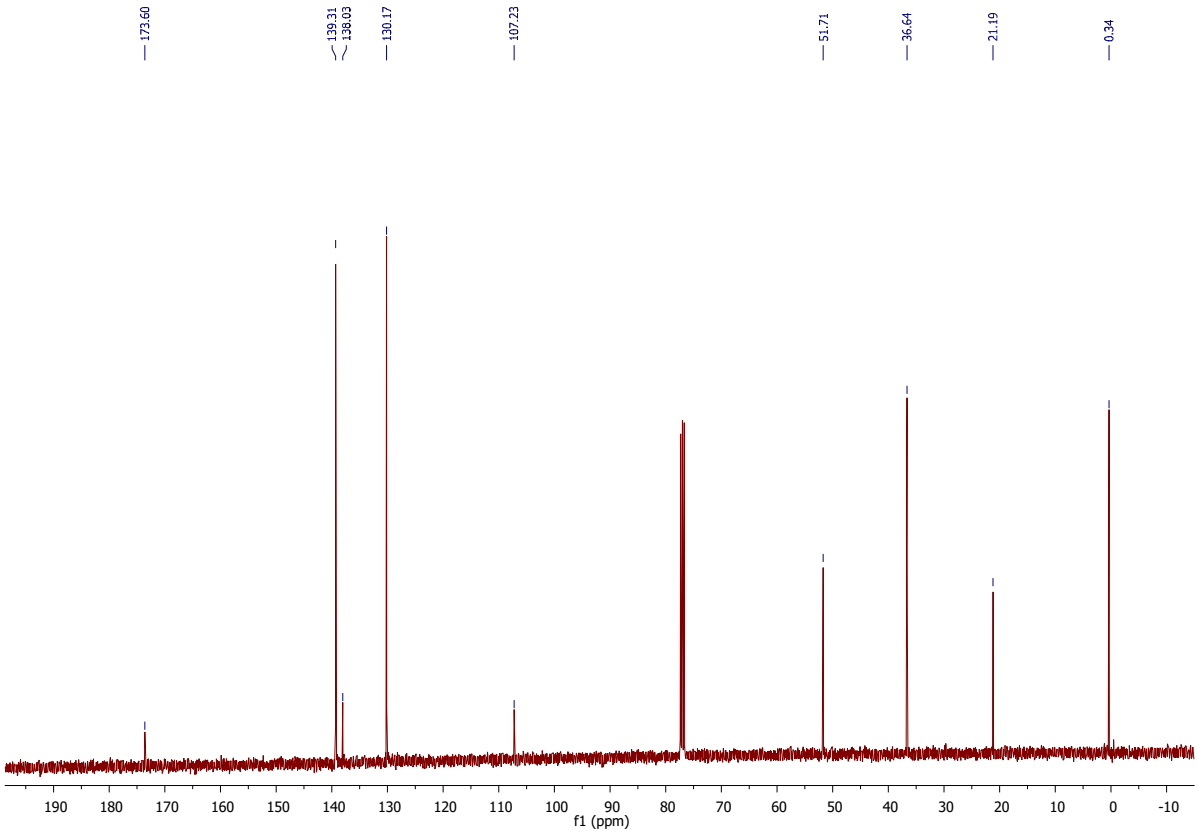
^{13}C NMR spectrum of compound **6j** (100 MHz, $CDCl_3$)



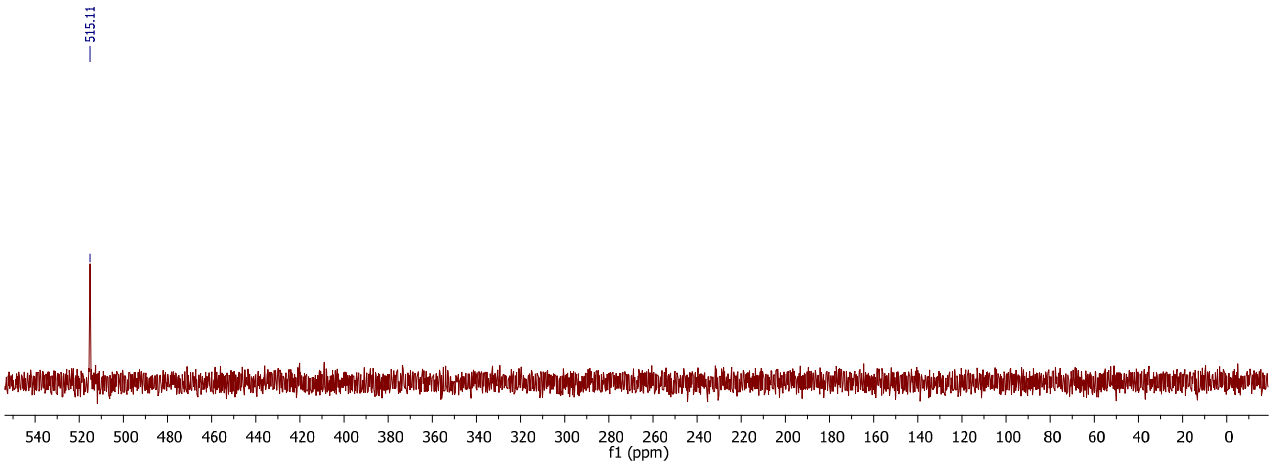
^{1}H NMR spectrum of compound **8a** (400 MHz, $CDCl_3$)



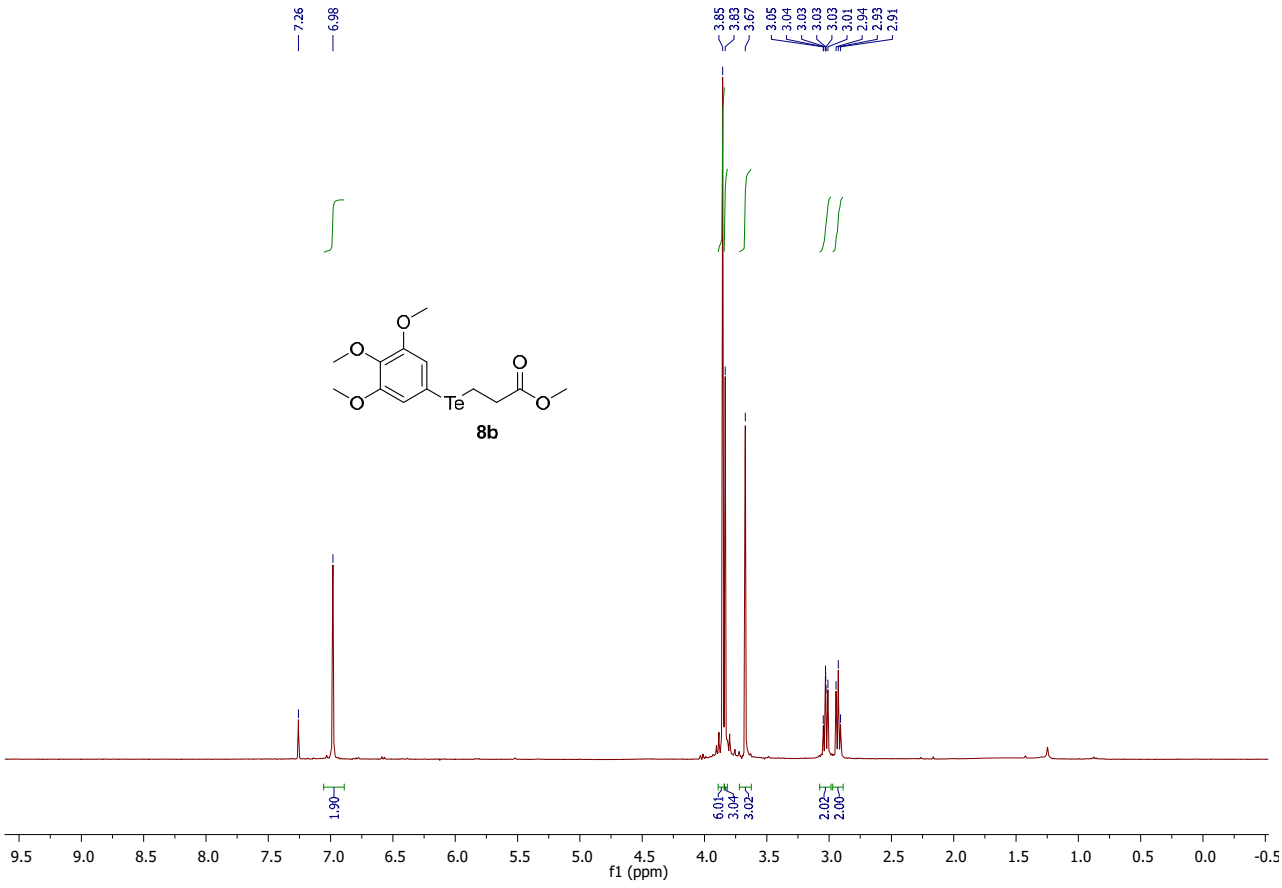
^{13}C NMR spectrum of compound **8a** (100 MHz, $CDCl_3$)



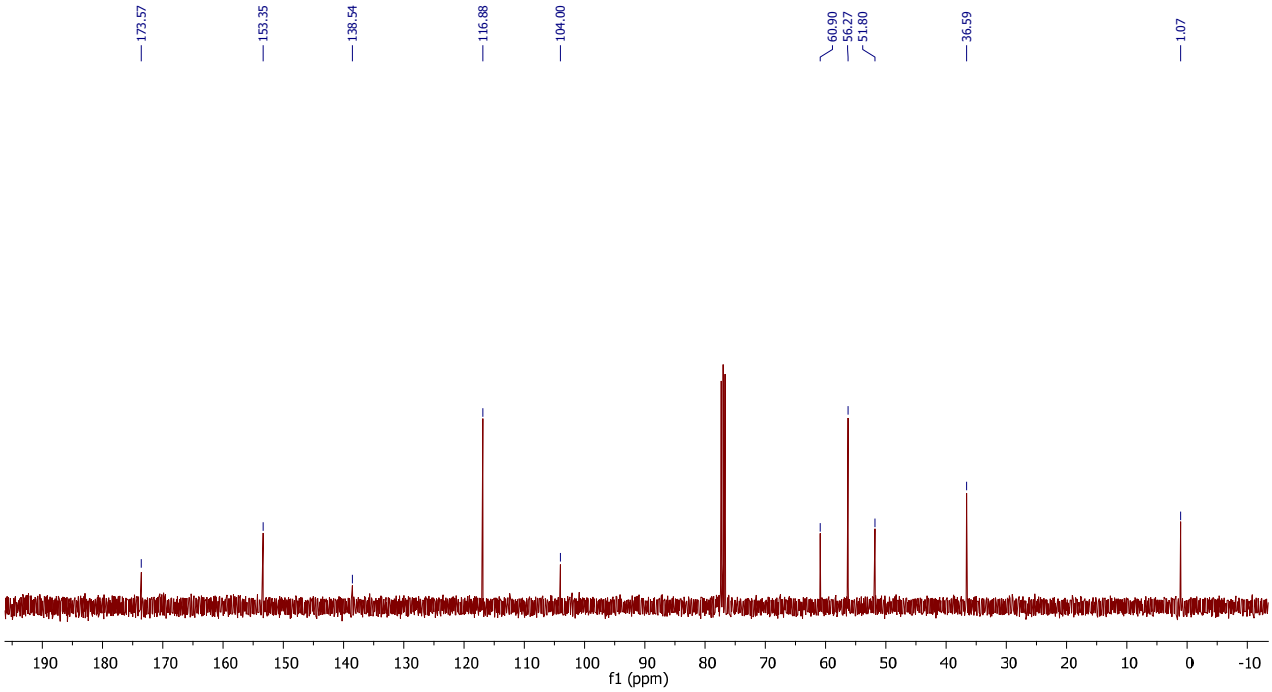
^{125}Te NMR spectrum of compound **8a** (126 MHz, $CDCl_3$)



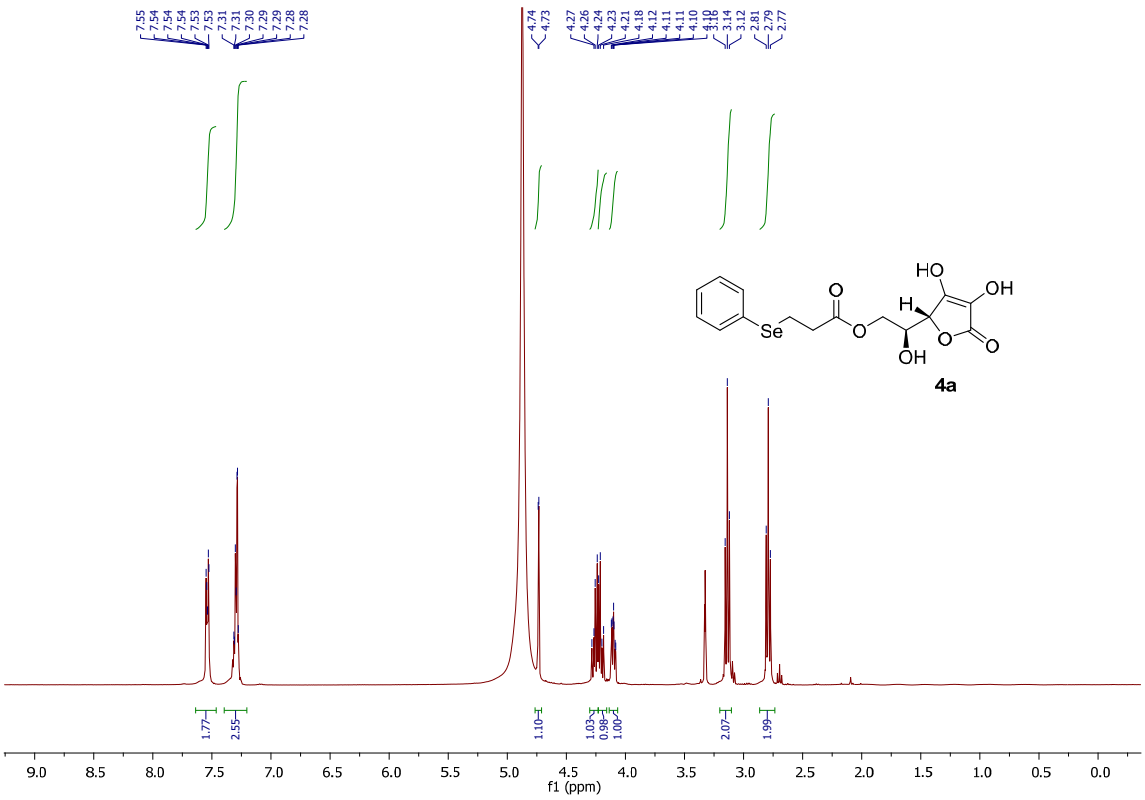
^{1}H NMR spectrum of compound **8b** (400 MHz, $CDCl_3$)



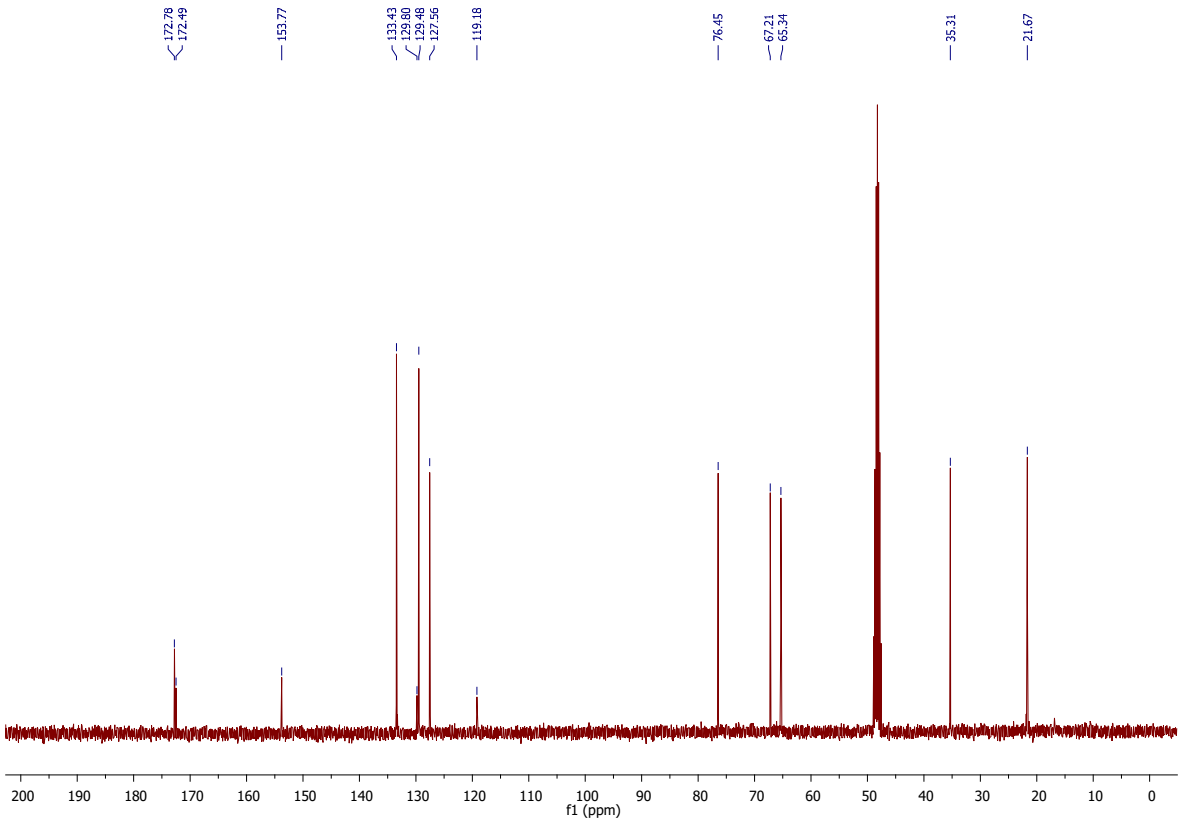
^{13}C NMR spectrum of compound **8b** (100 MHz, $CDCl_3$)



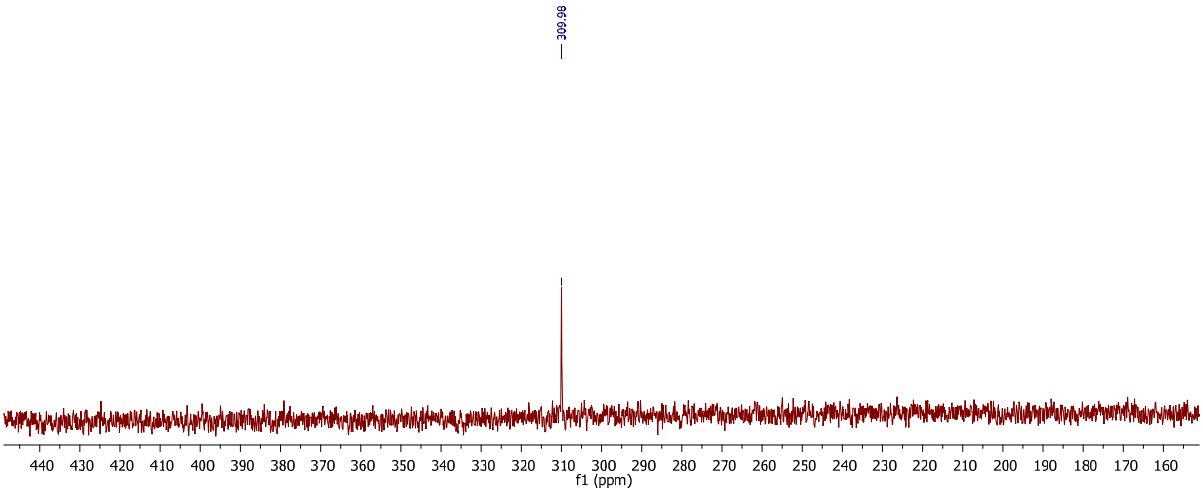
^{1}H NMR spectrum of compound **4a** (400 MHz, CD_3OD)



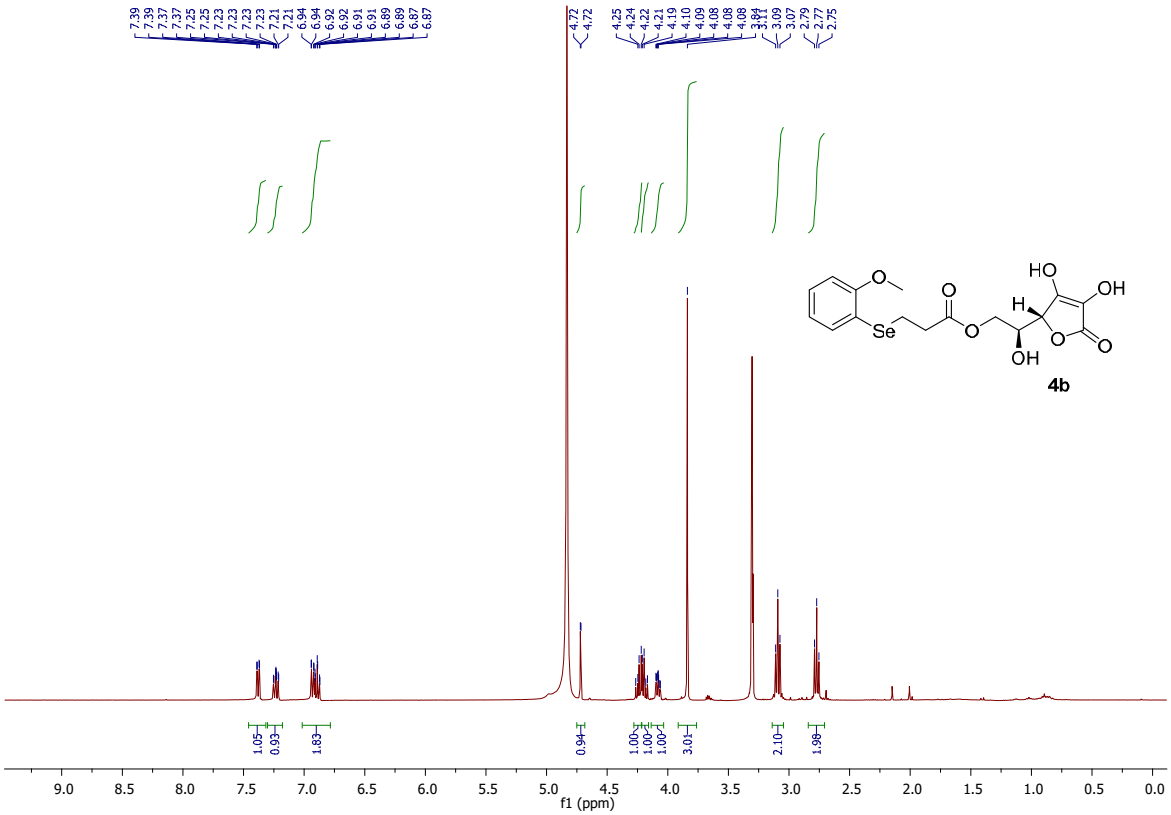
^{13}C NMR spectrum of compound **4a** (100 MHz, CD_3OD)



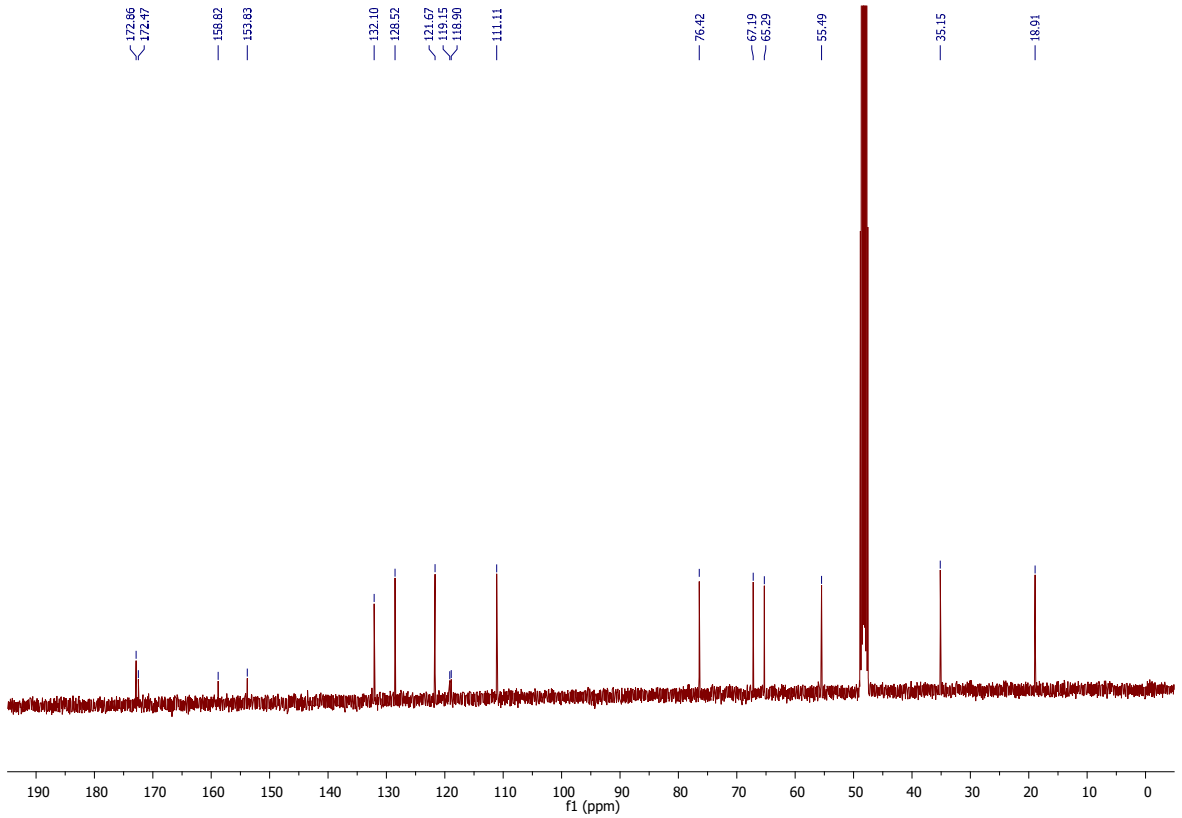
^{77}Se NMR spectrum of compound **4a** (76 MHz, CD_3OD)



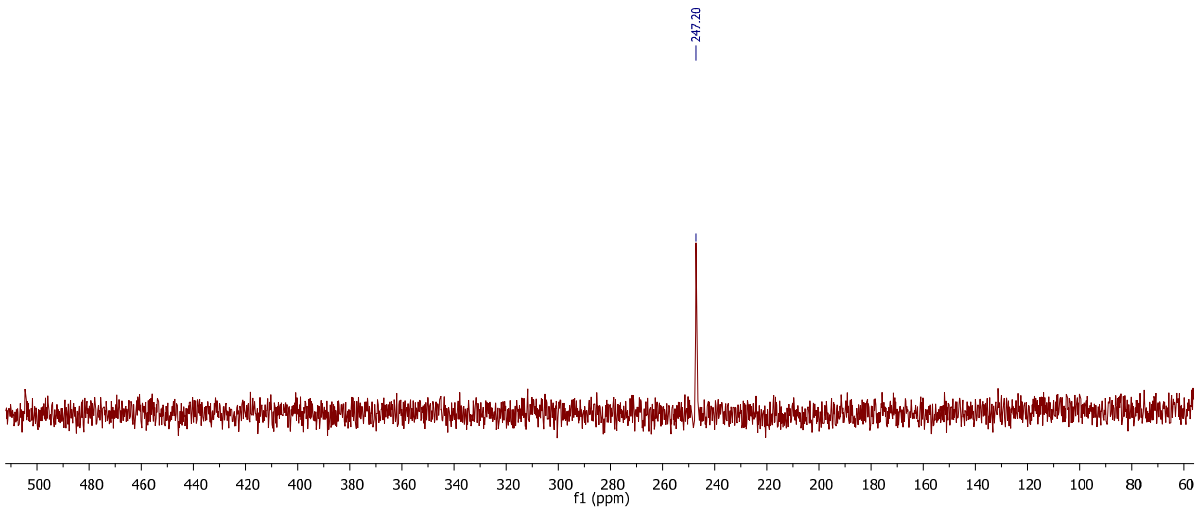
^{1}H NMR spectrum of compound **4b** (400 MHz, CD_3OD)



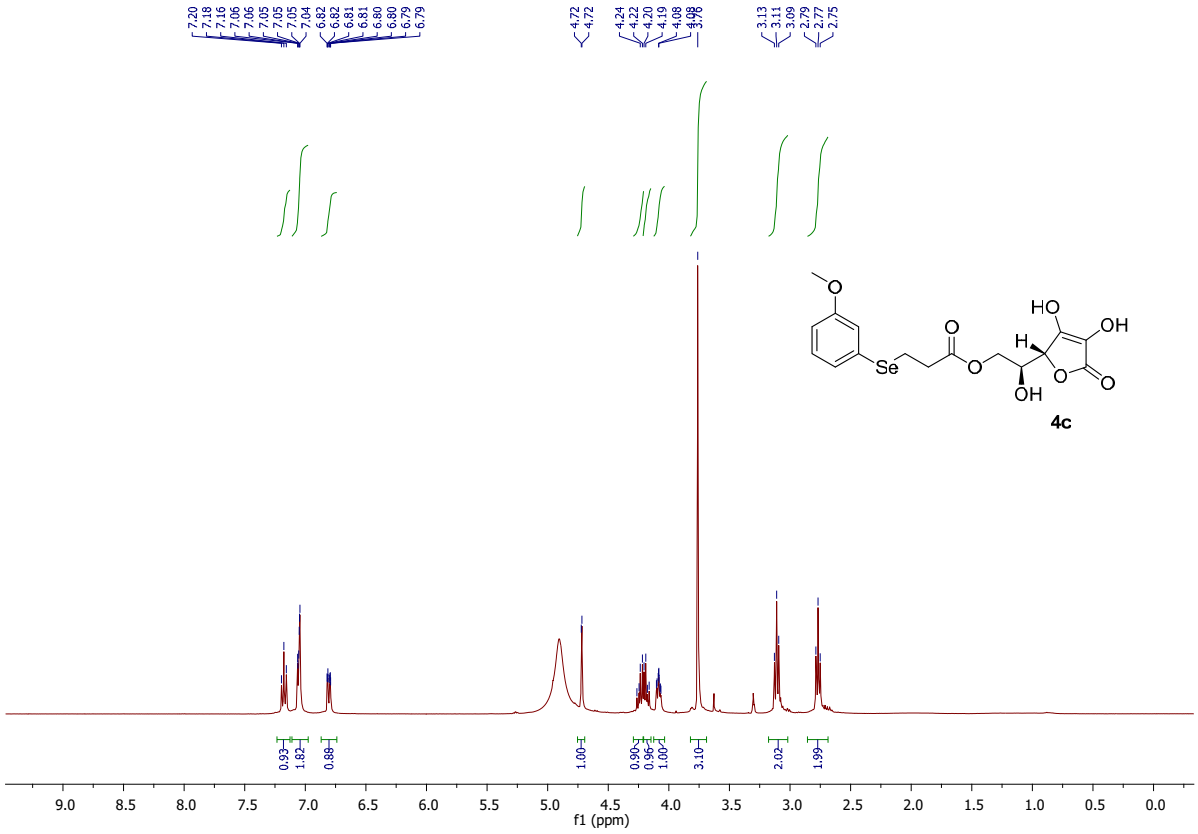
^{13}C NMR spectrum of compound **4b** (100 MHz, CD_3OD)



^{77}Se NMR spectrum of compound **4b** (76 MHz, CD_3OD)

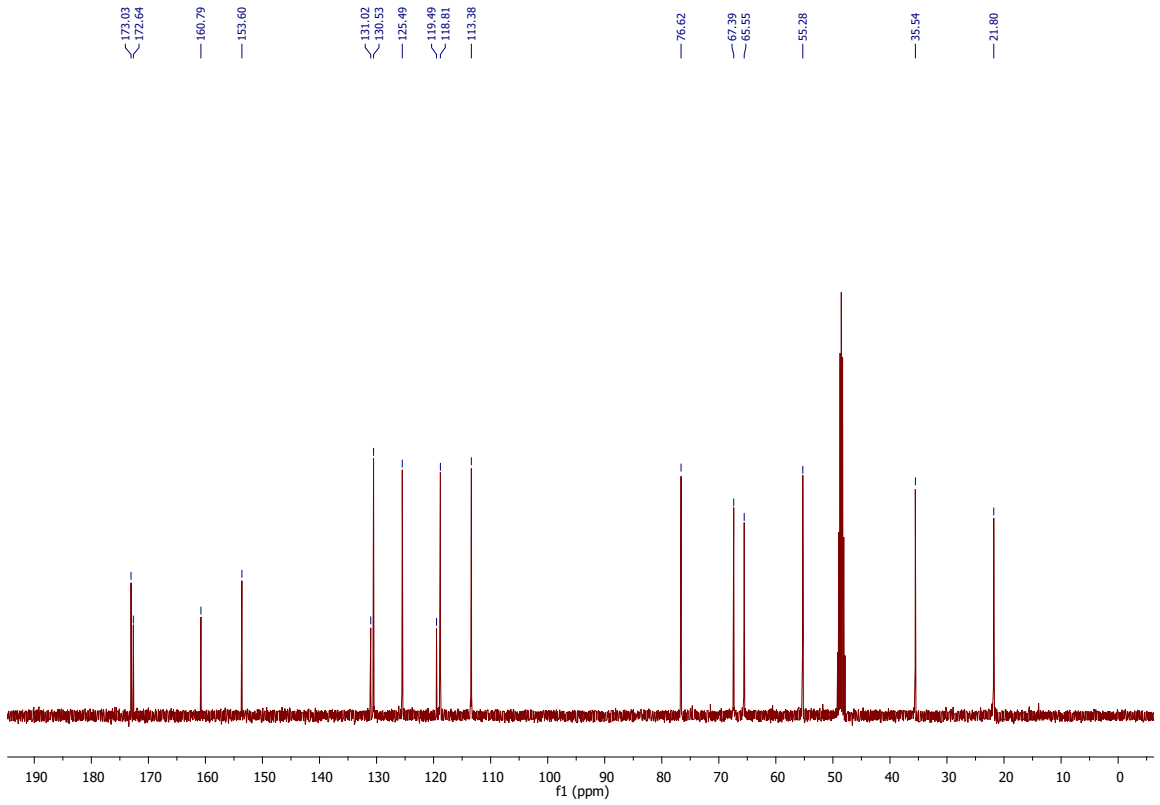


^{1}H NMR spectrum of compound **4c** (400 MHz, CD_3OD)

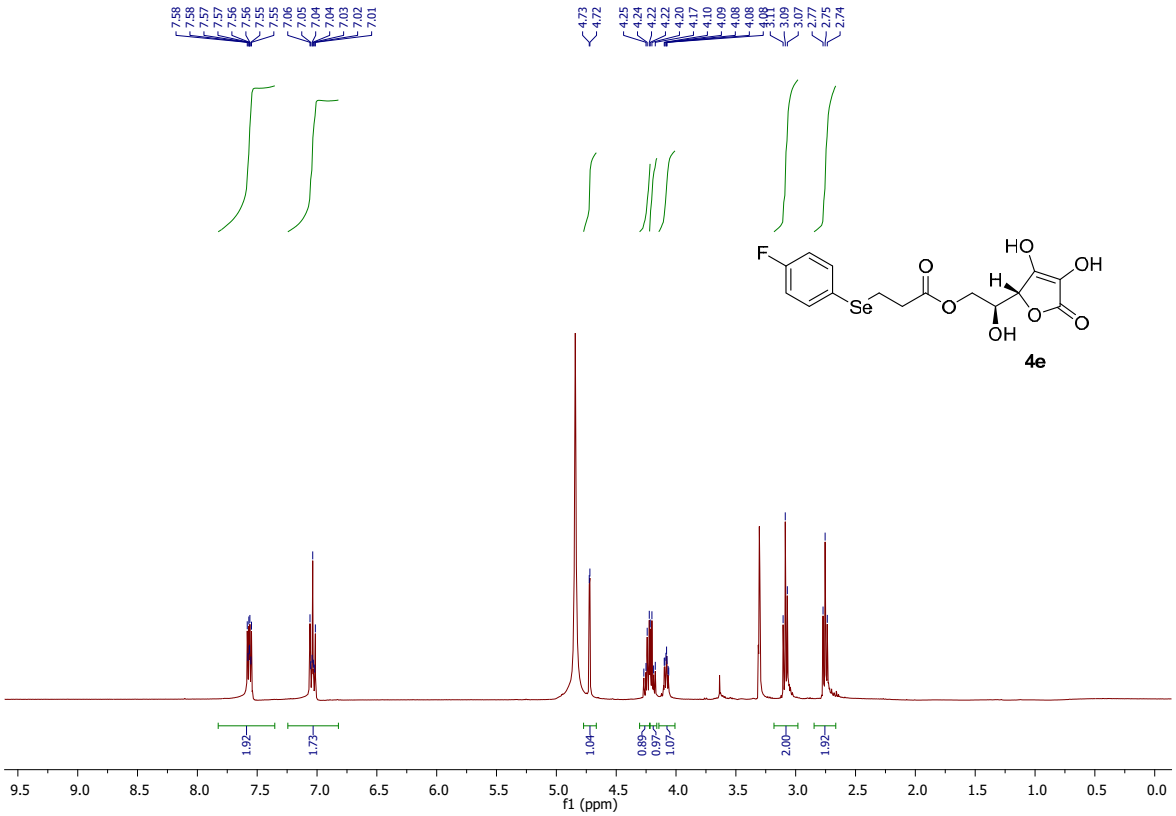


4c

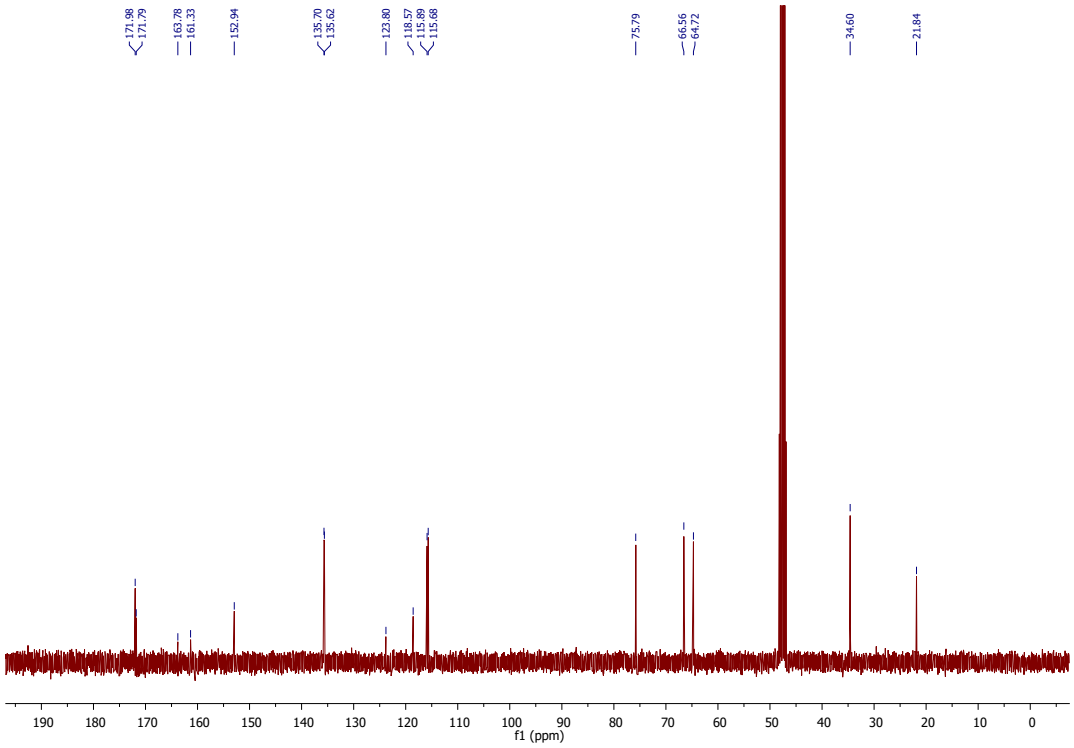
^{13}C NMR spectrum of compound **4c** (100 MHz, CD_3OD)



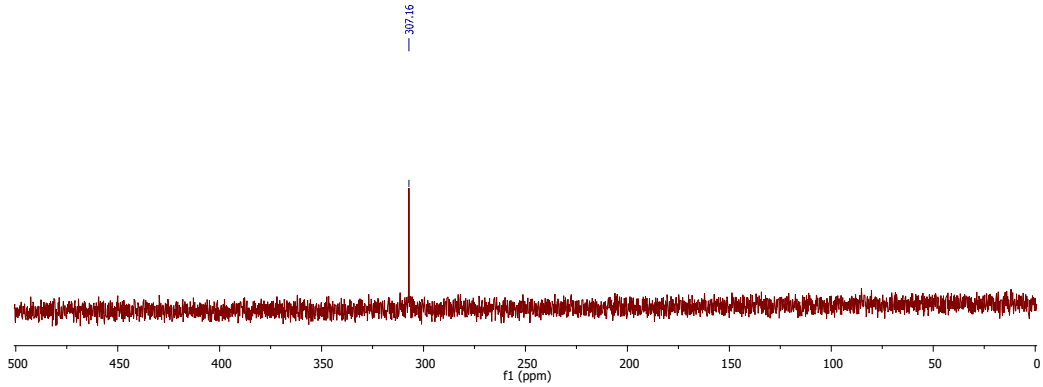
^{1}H NMR spectrum of compound **4e** (400 MHz, CD_3OD)



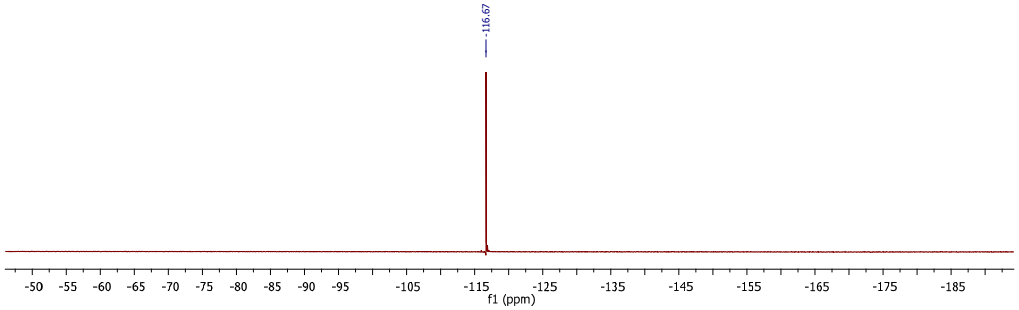
^{13}C NMR spectrum of compound **4e** (100 MHz, CD_3OD)



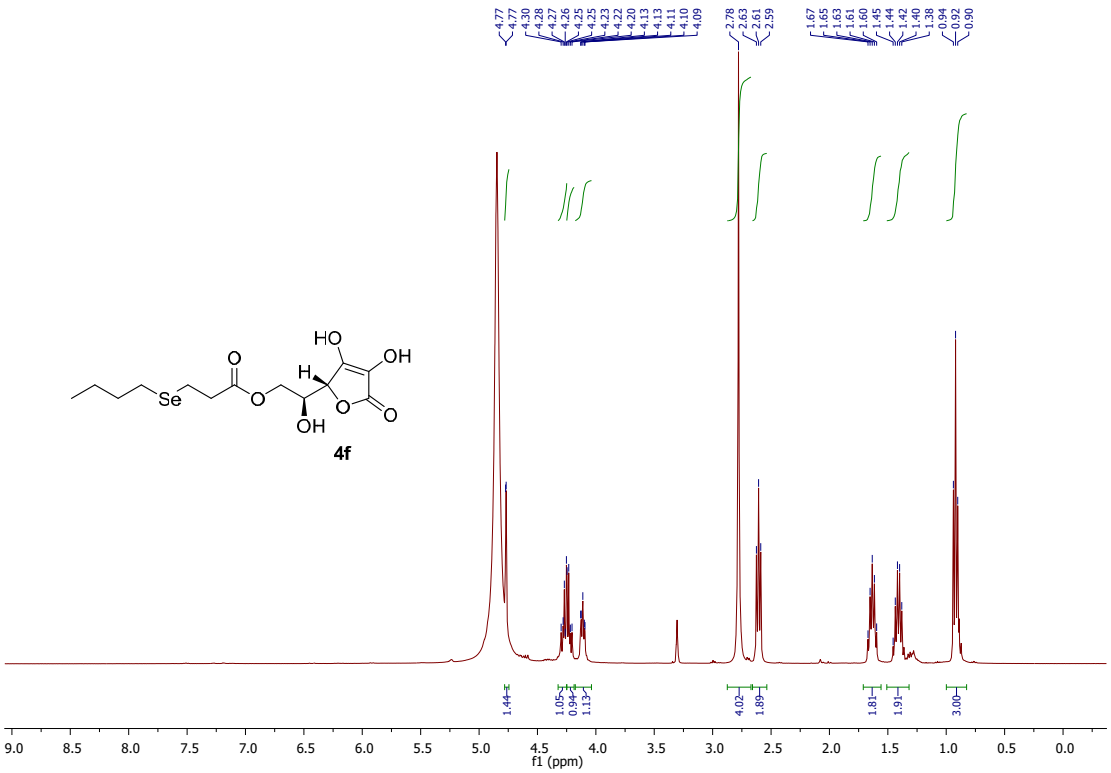
^{77}Se NMR spectrum of compound **4e** (76 MHz, CD_3OD)



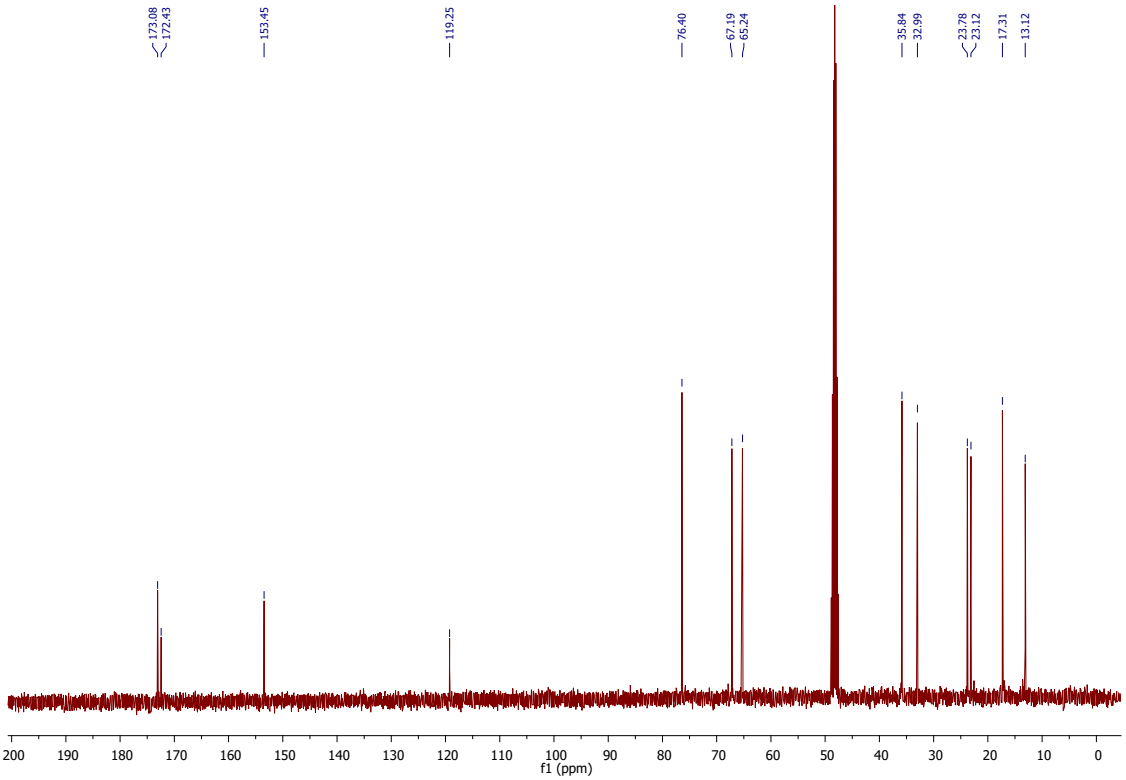
^{19}F NMR spectrum of compound **4e** (376 MHz, CD_3OD)



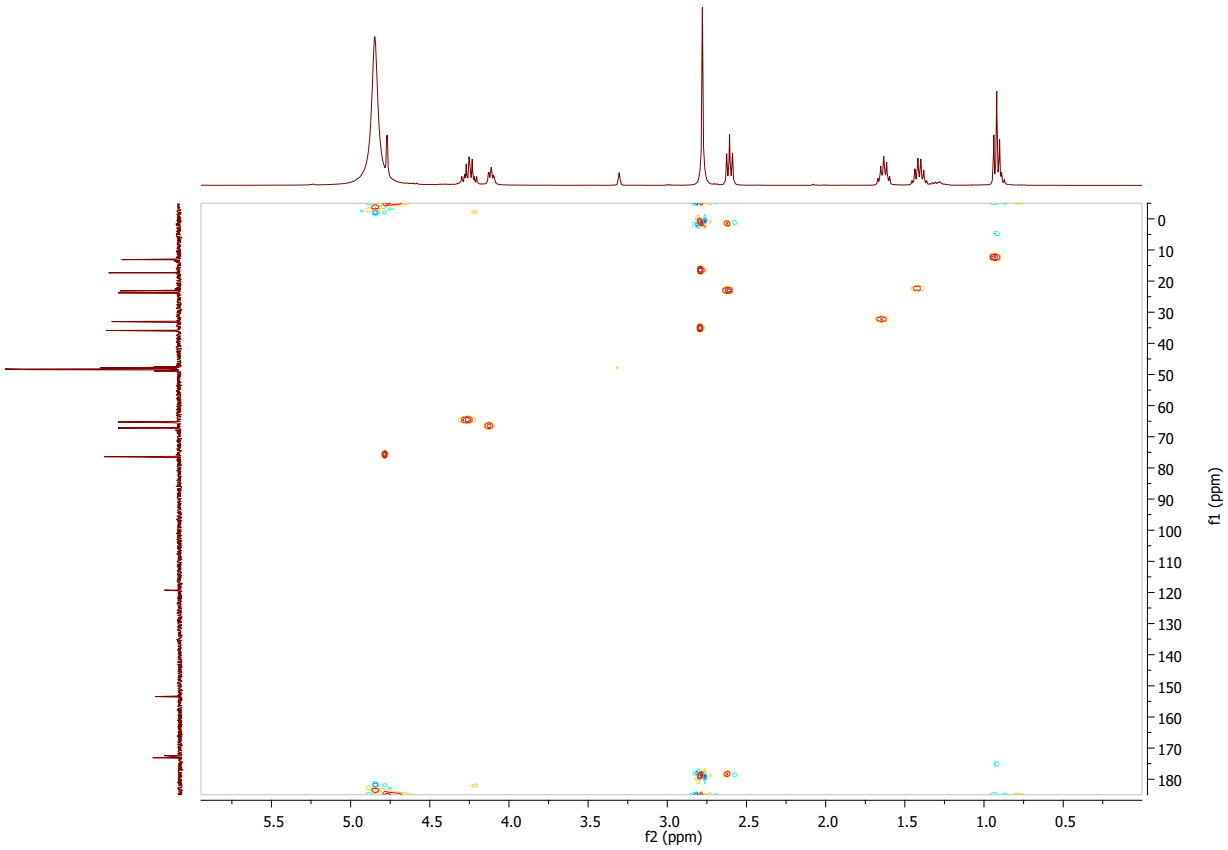
^{1}H NMR spectrum of compound **4f** (400 MHz, CD_3OD)



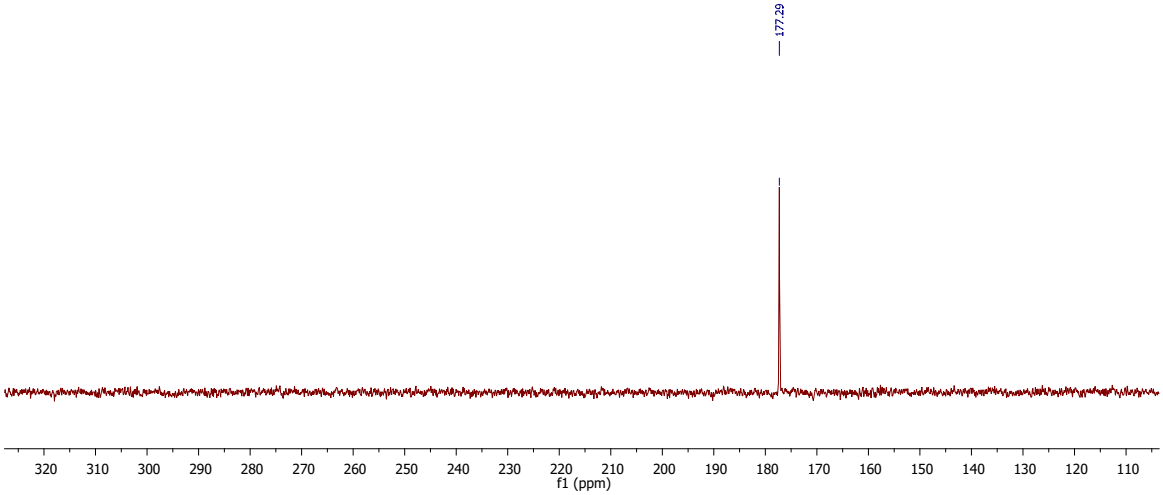
^{13}C NMR spectrum of compound **4f** (100 MHz, CD_3OD)



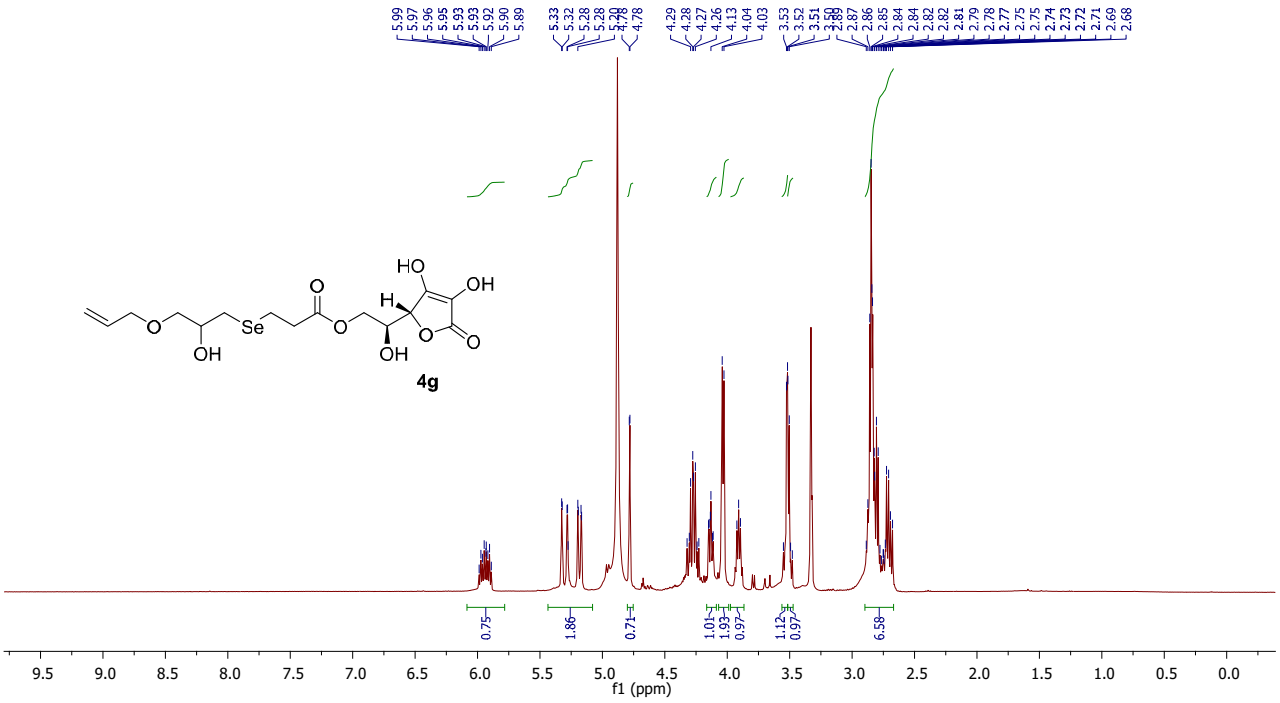
^{1}H-^{13}C HSQC NMR of compound **4f** (400 MHz, CD_3OD)



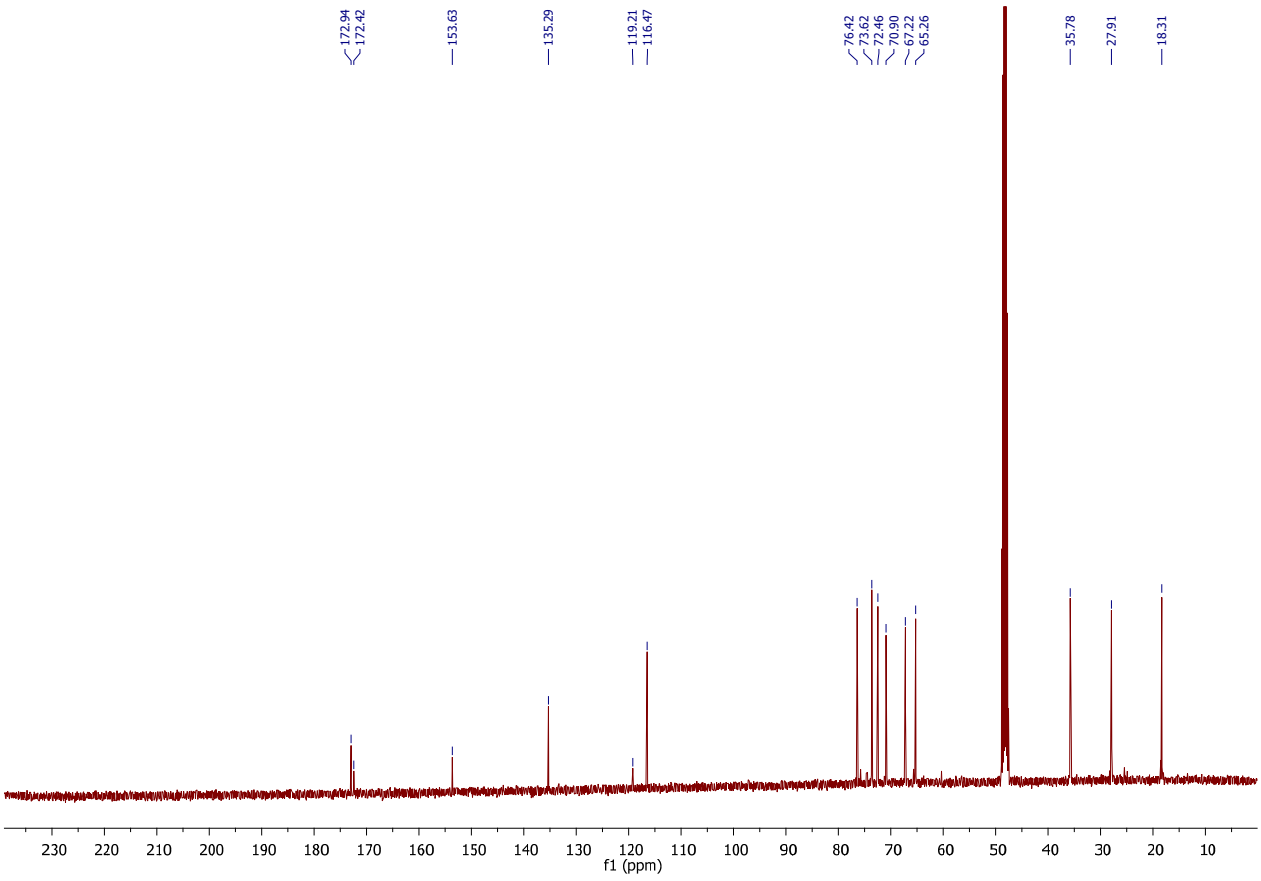
^{77}Se NMR spectrum of compound **4f** (76 MHz, CD_3OD)



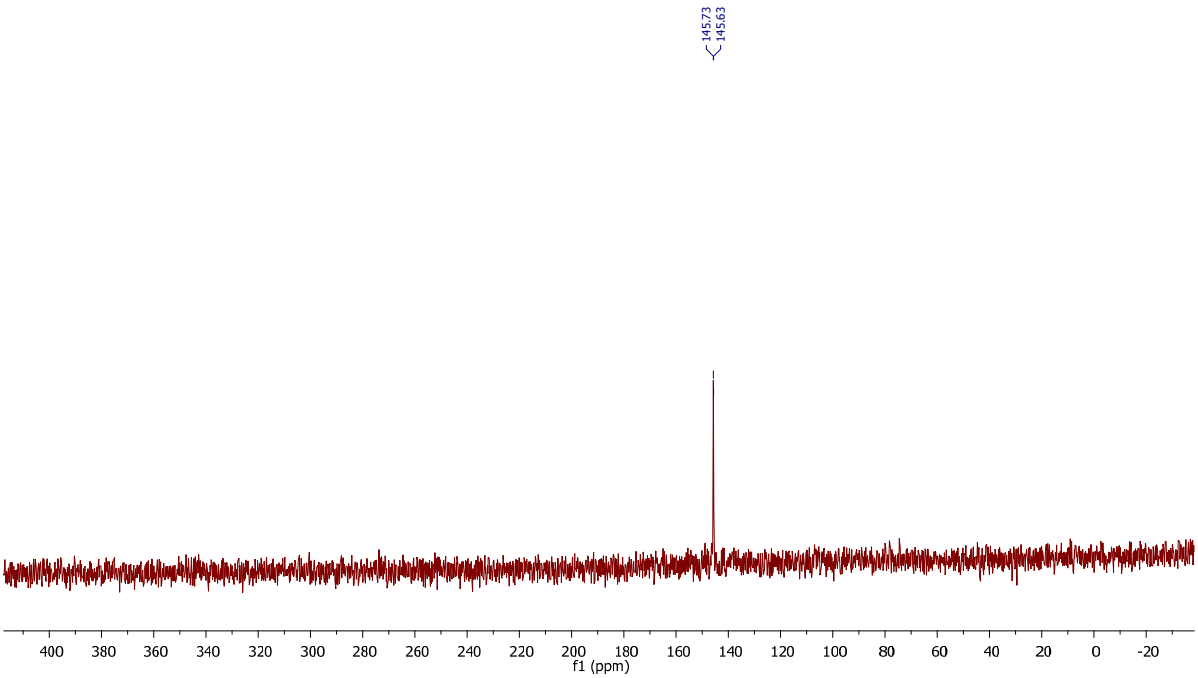
^{1}H NMR spectrum of compound **4g** (400 MHz, CD_3OD)



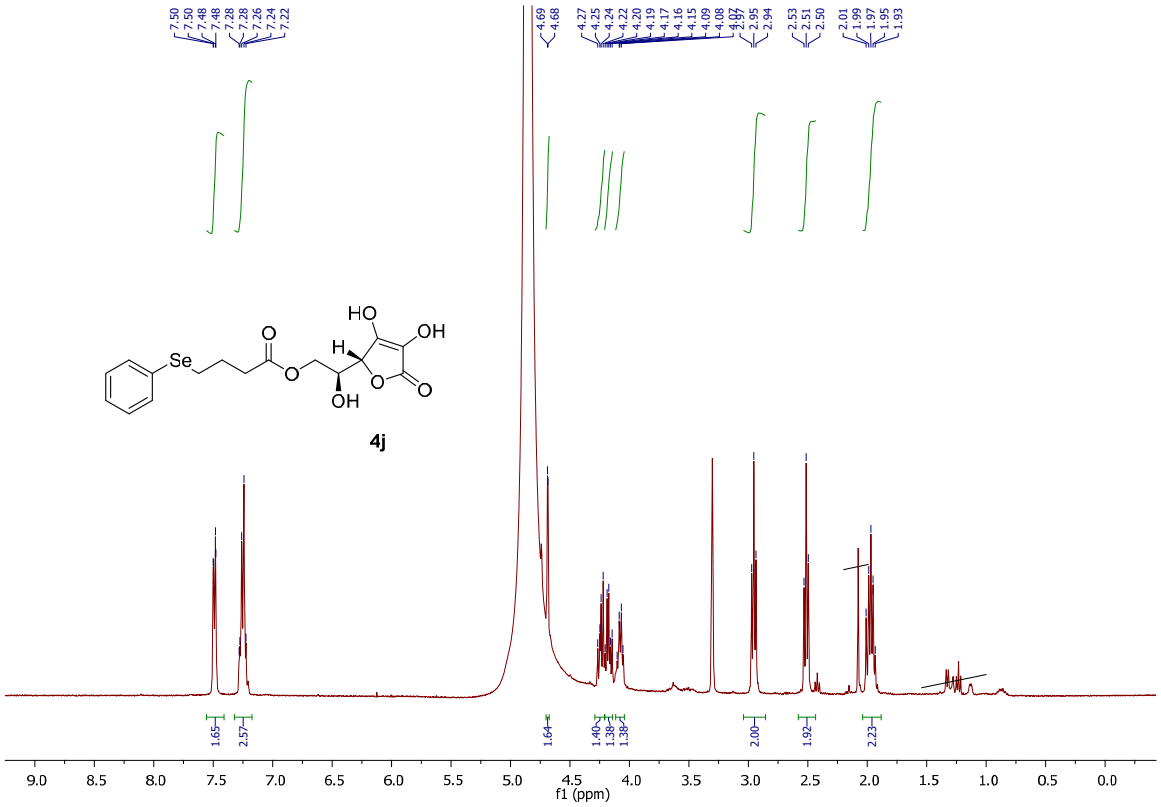
^{13}C NMR spectrum of compound **4g** (100 MHz, CD_3OD)



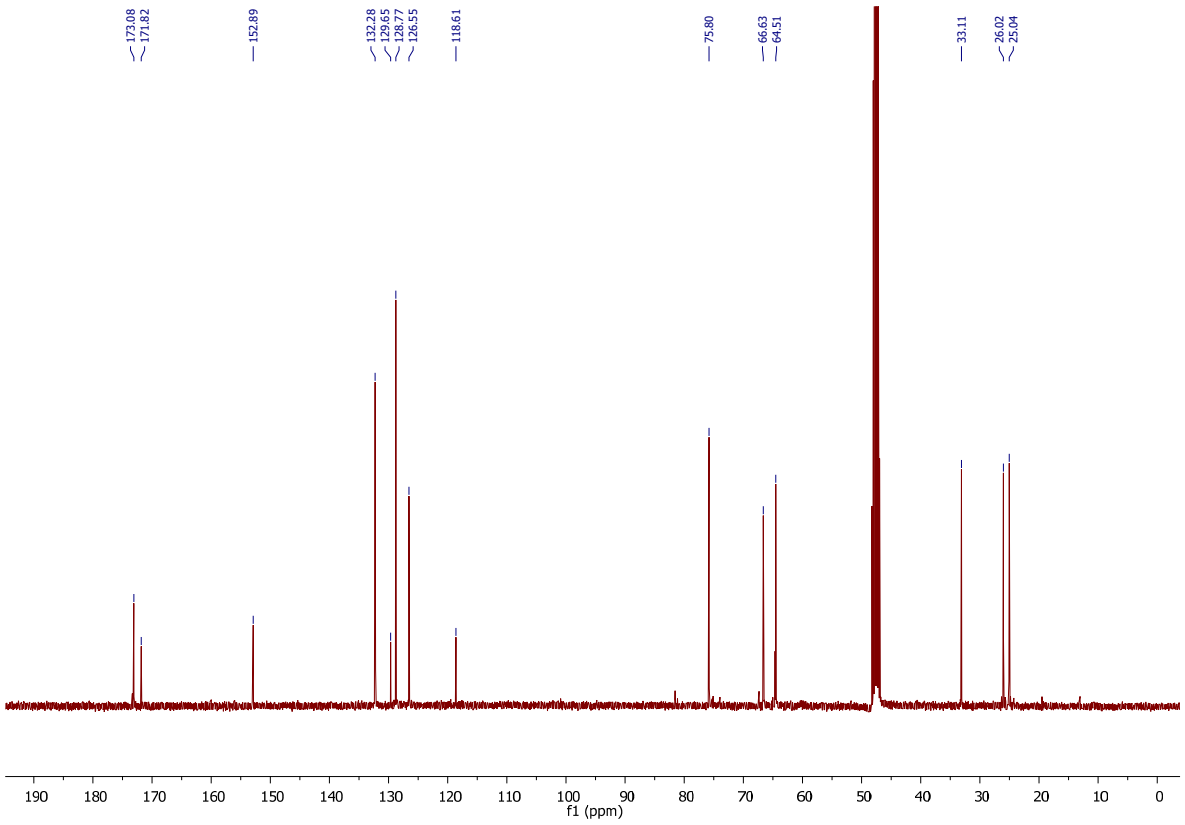
^{77}Se NMR spectrum of compound **4g** (76 MHz, CD_3OD)



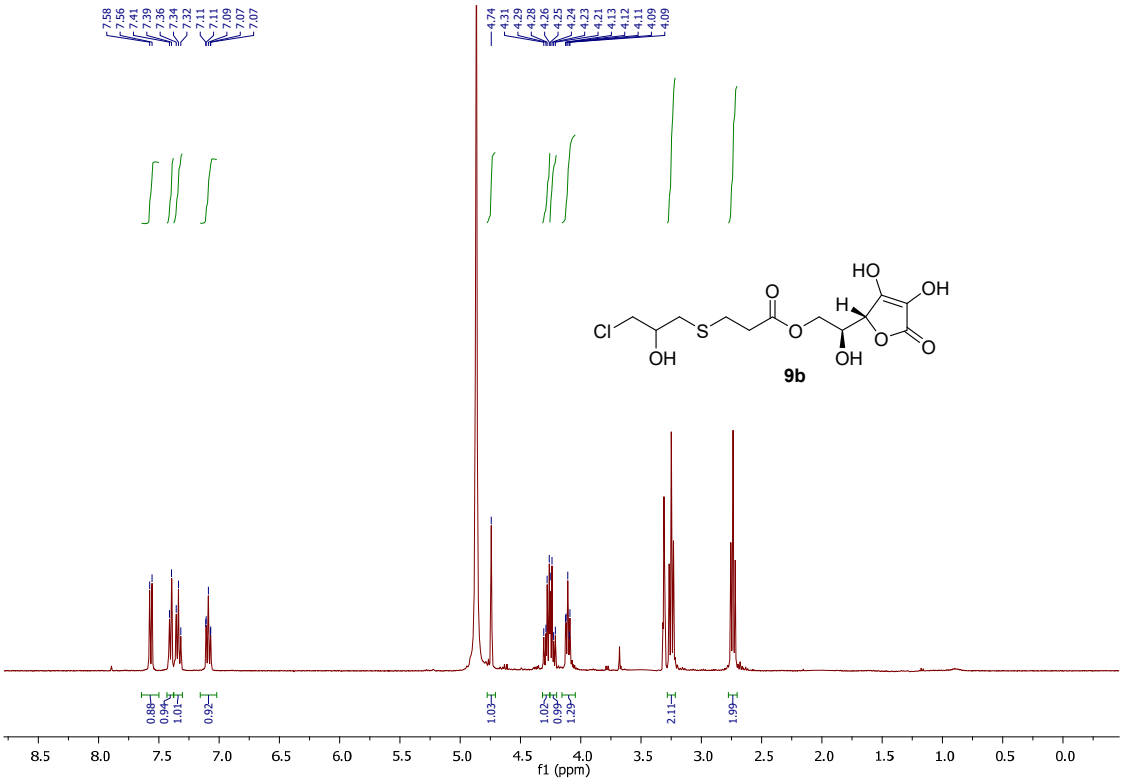
^{1}H NMR spectrum of compound **4j** (400 MHz, CD_3OD)



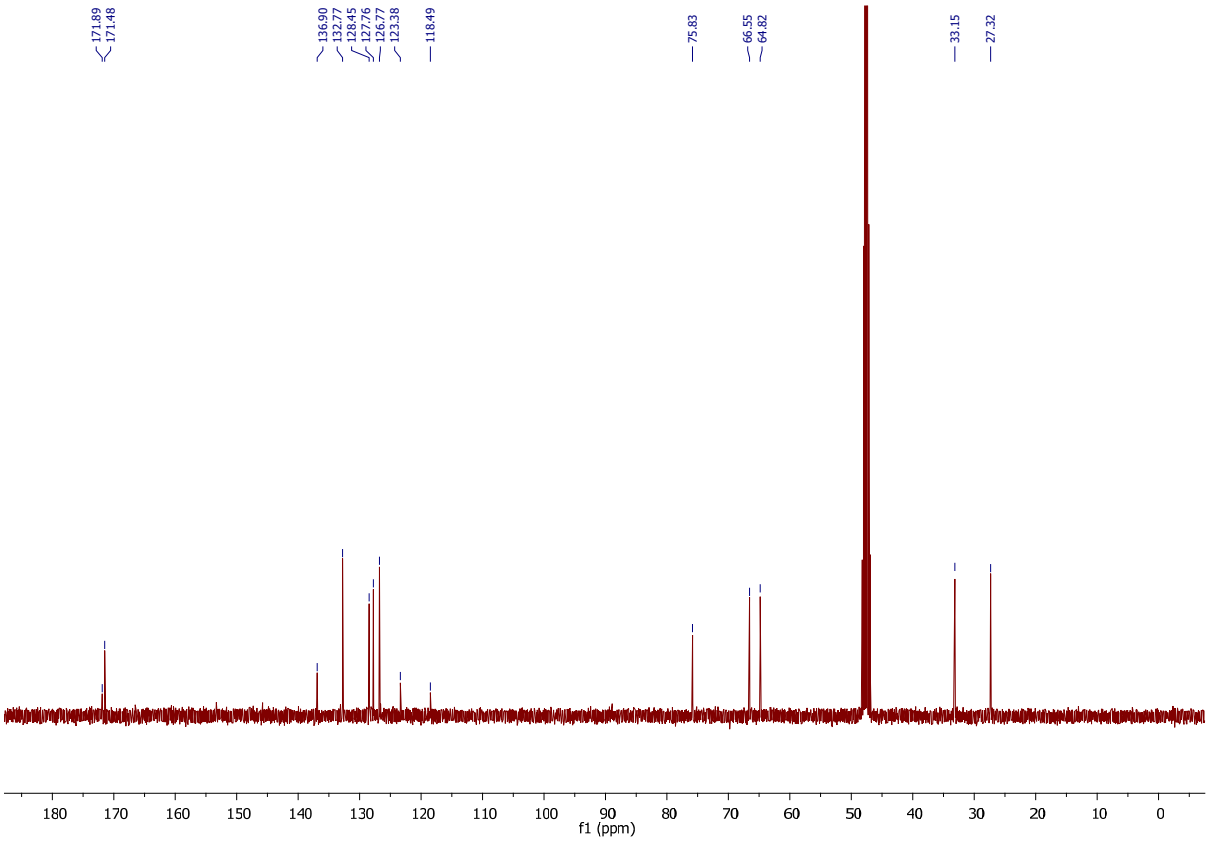
^{13}C NMR spectrum of compound **4j** (100 MHz, CD_3OD)



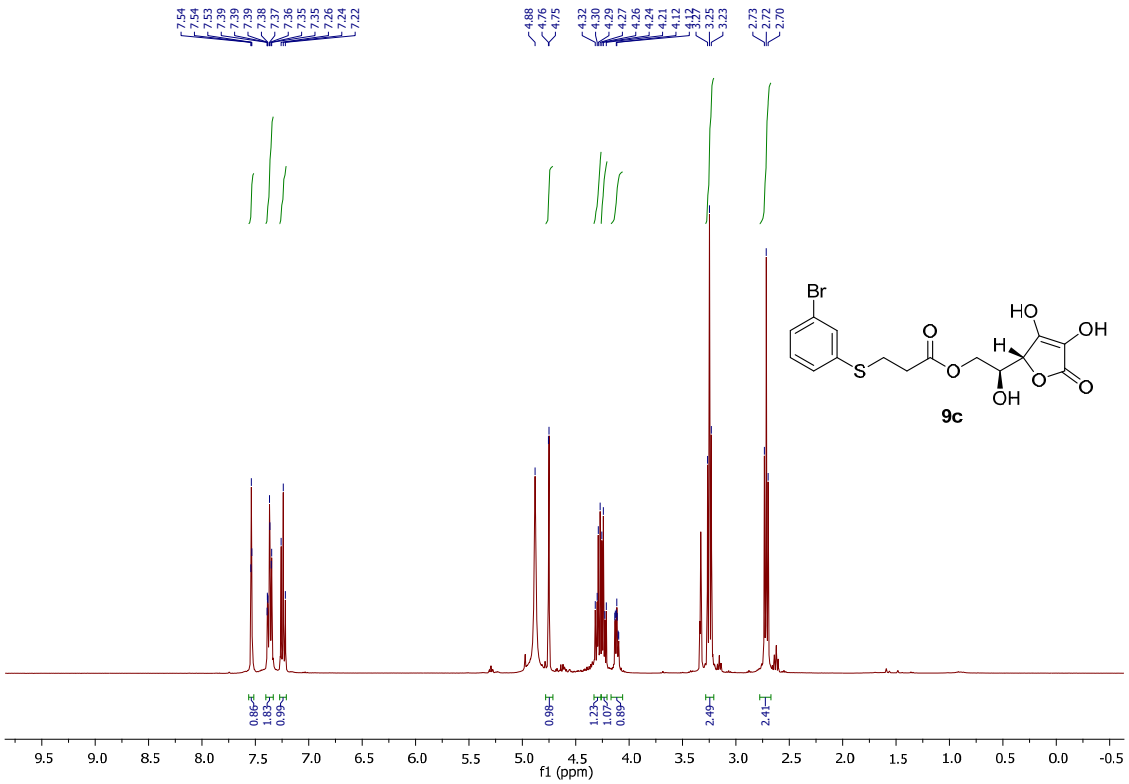
^{1}H NMR spectrum of compound **9b** (400 MHz, CD_3OD)



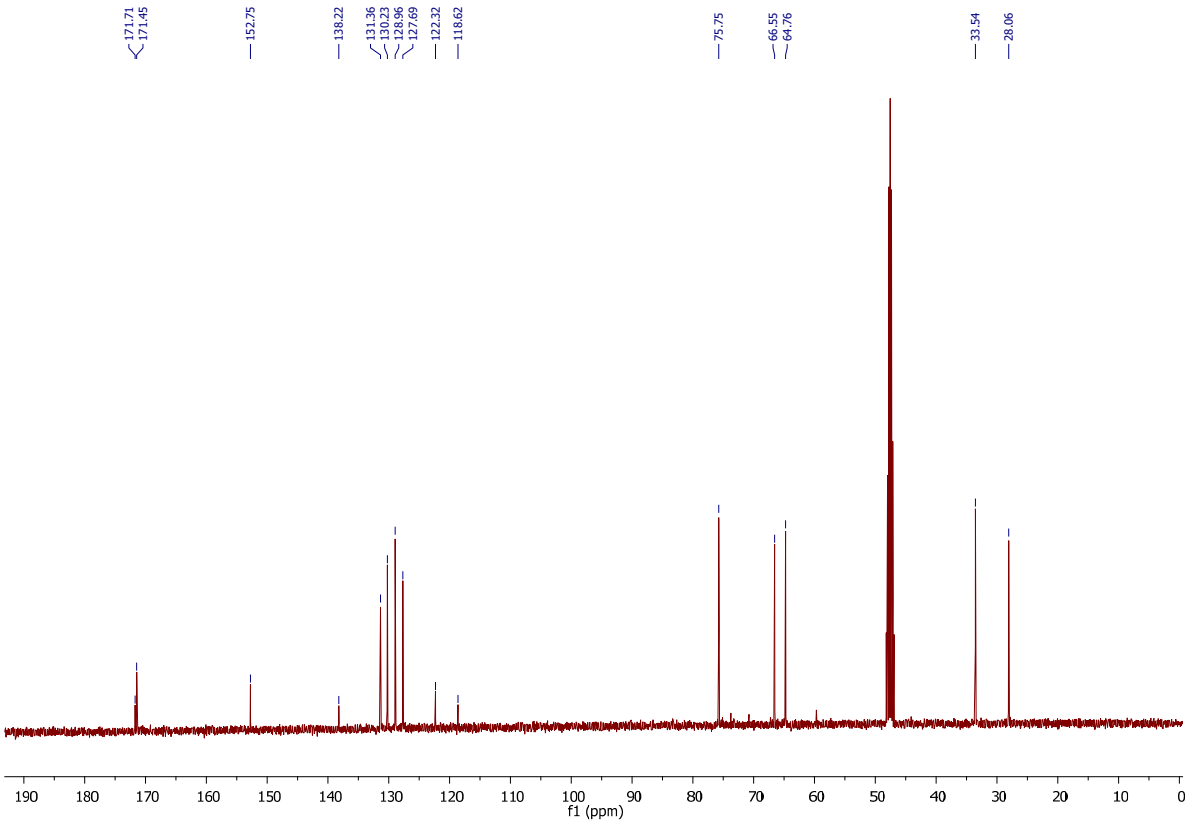
^{13}C NMR spectrum of compound **9b** (100 MHz, CD_3OD)



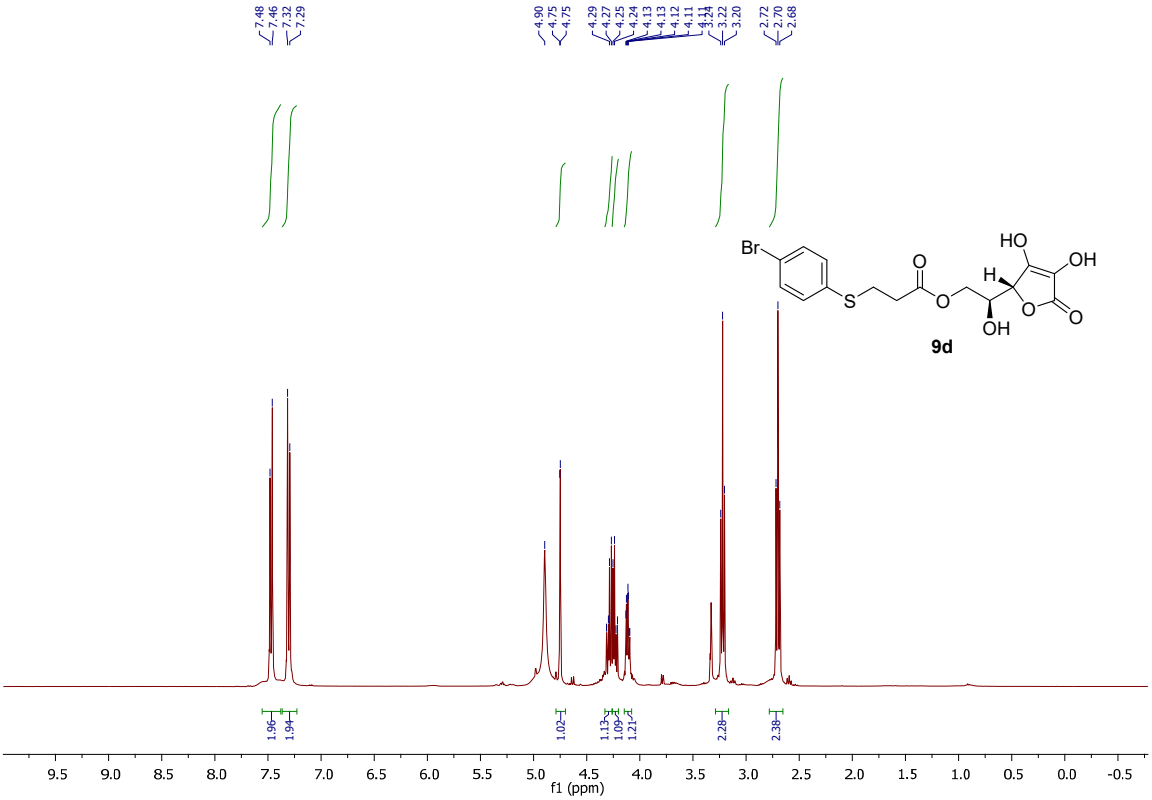
^{1}H NMR spectrum of compound **9c** (400 MHz, CD_3OD)



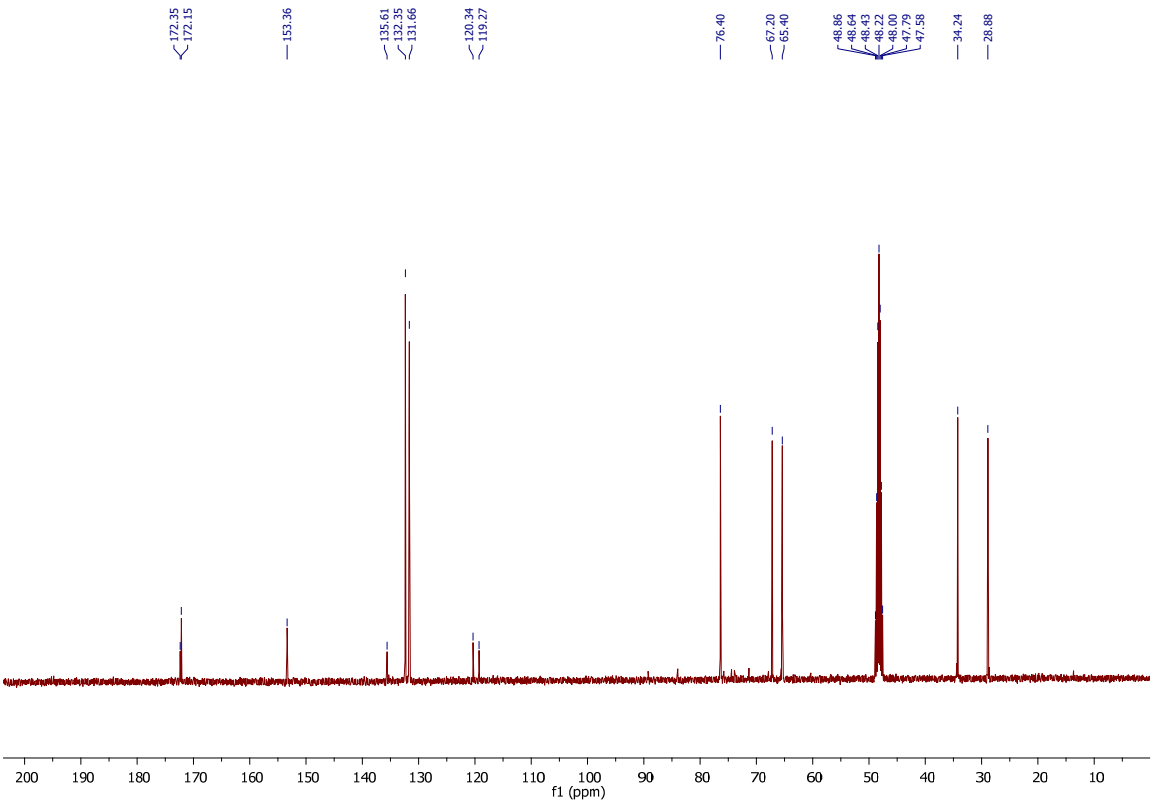
^{13}C NMR spectrum of compound **9c** (100 MHz, CD_3OD)



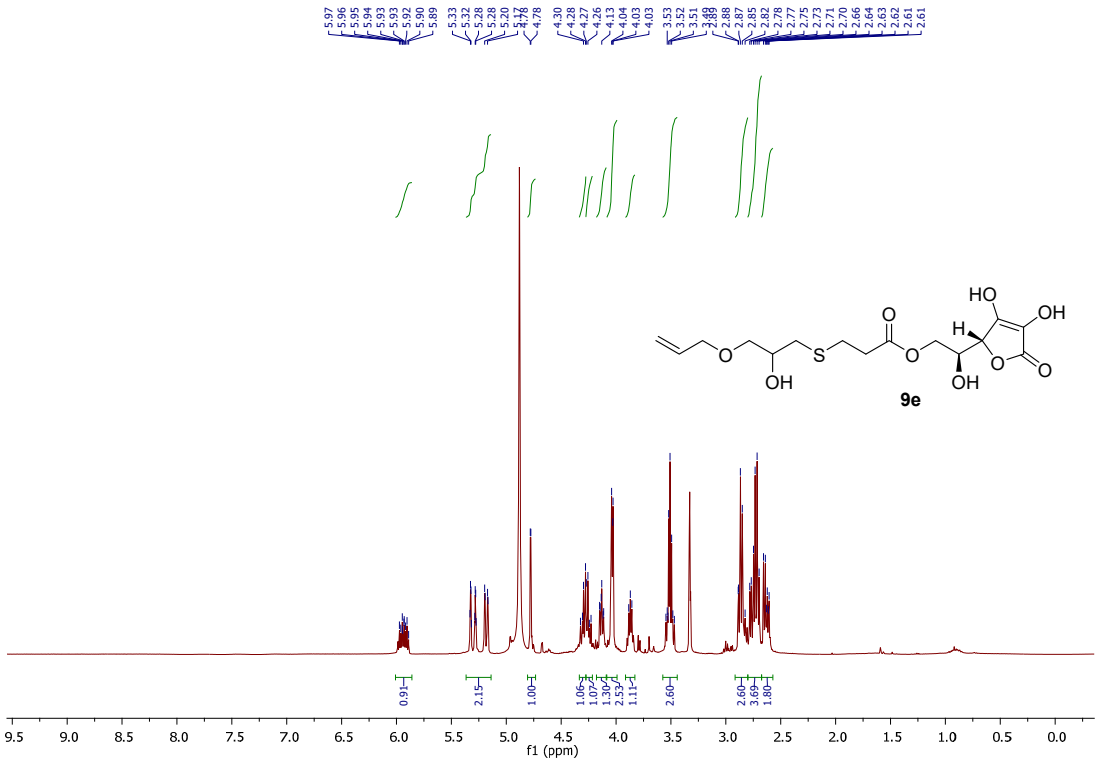
^{1}H NMR spectrum of compound **9d** (400 MHz, CD_3OD)



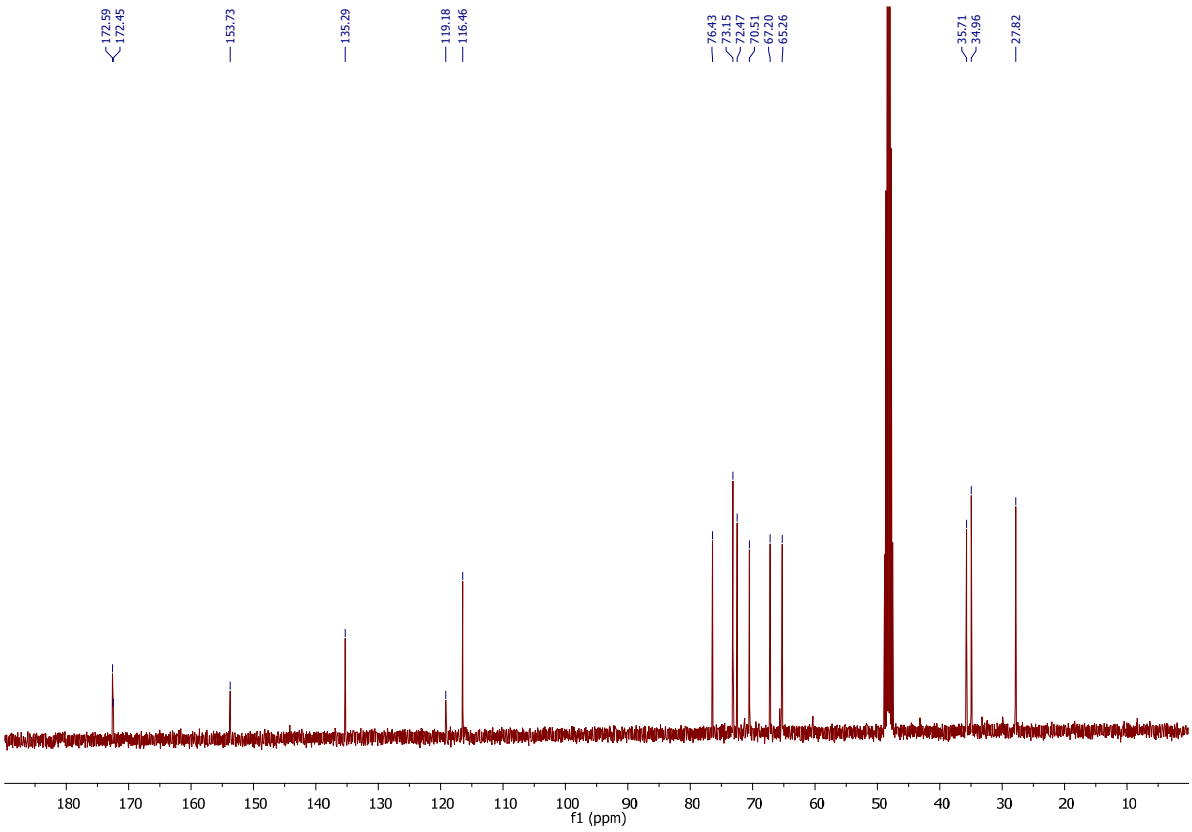
^{13}C NMR spectrum of compound **9d** (100 MHz, CD_3OD)



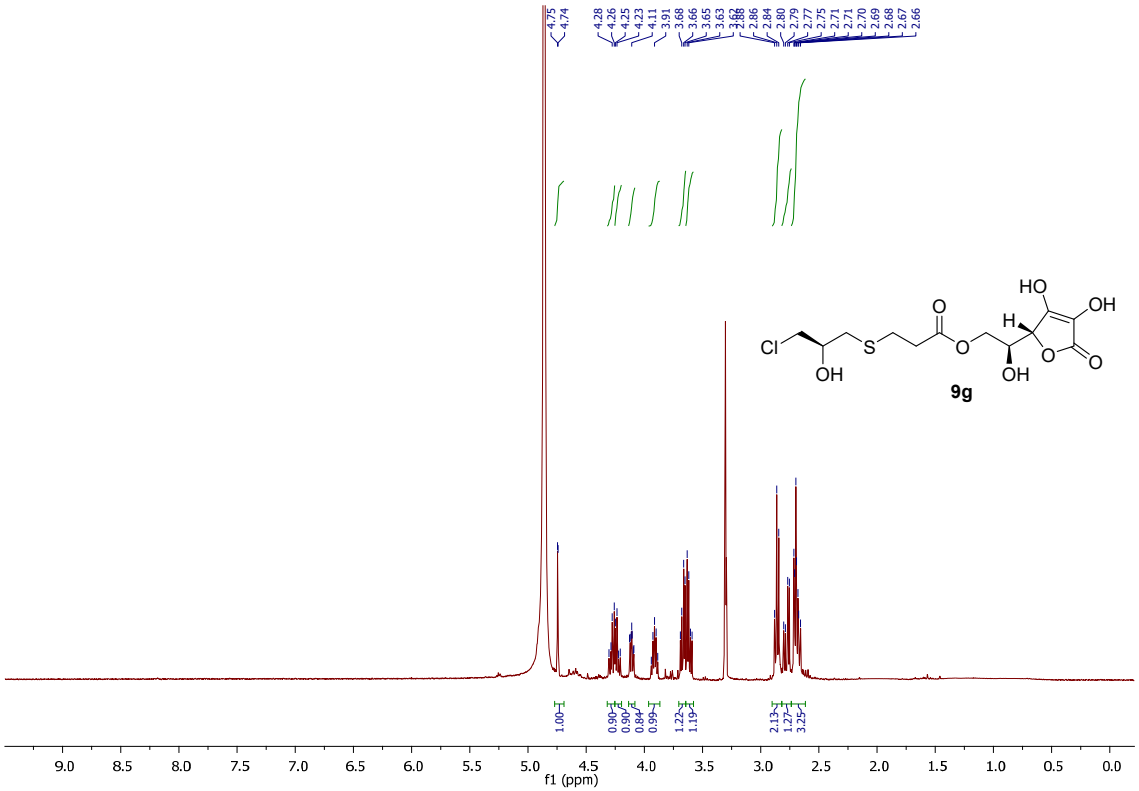
^{1}H NMR spectrum of compound **9e** (400 MHz, CD_3OD)



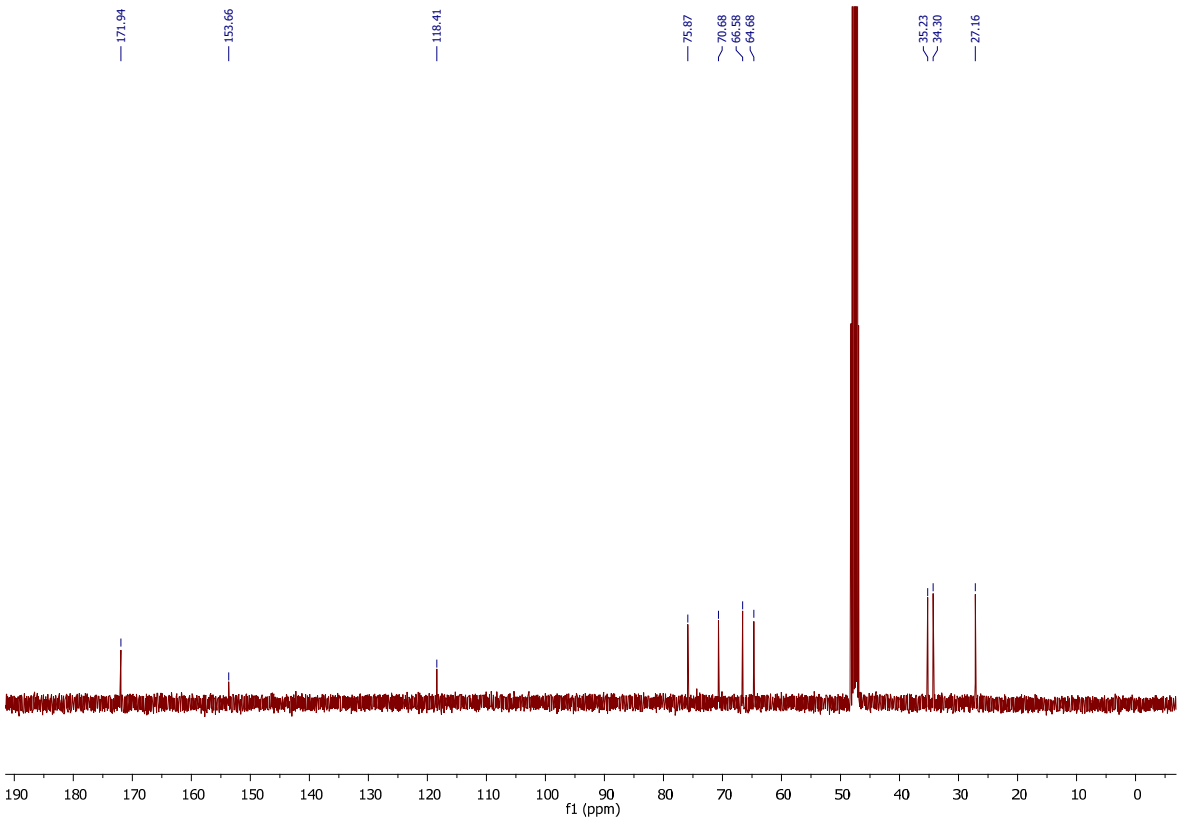
^{13}C NMR spectrum of compound **9e** (100 MHz, CD_3OD)



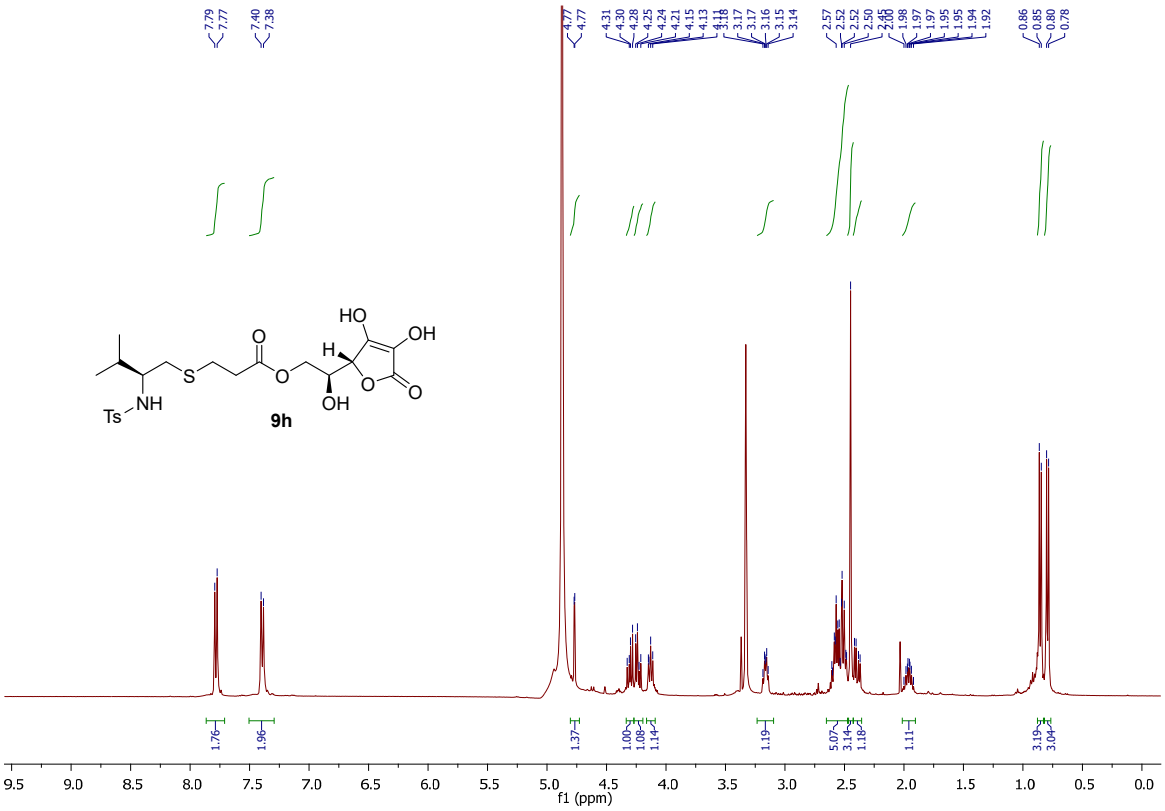
^{1}H NMR spectrum of compound **9g** (400 MHz, CD_3OD)



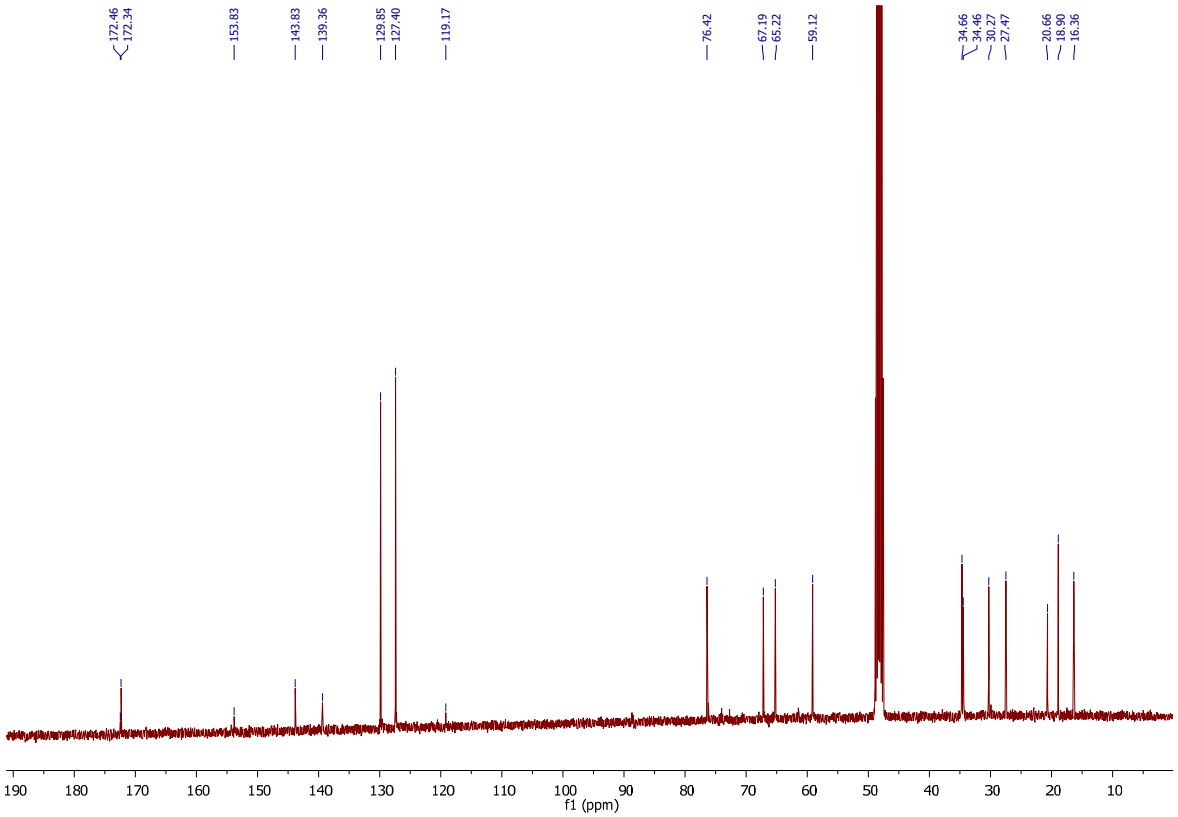
^{13}C NMR spectrum of compound **9g** (100 MHz, CD_3OD)



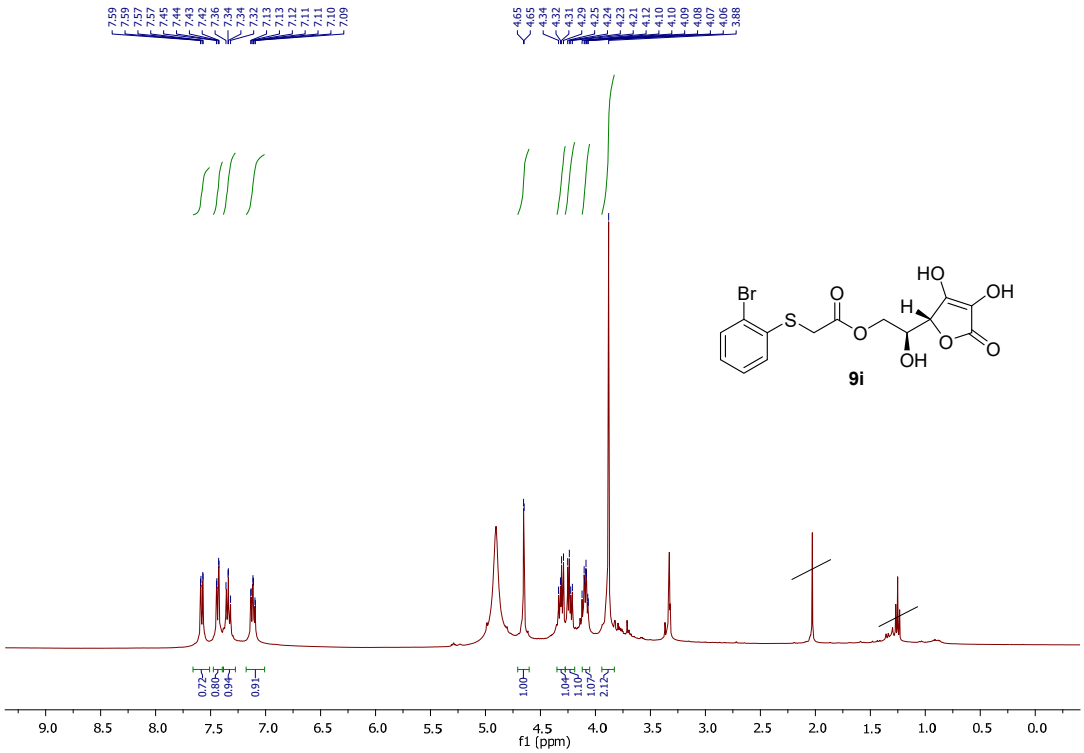
^{1}H NMR spectrum of compound **9h** (400 MHz, CD_3OD)



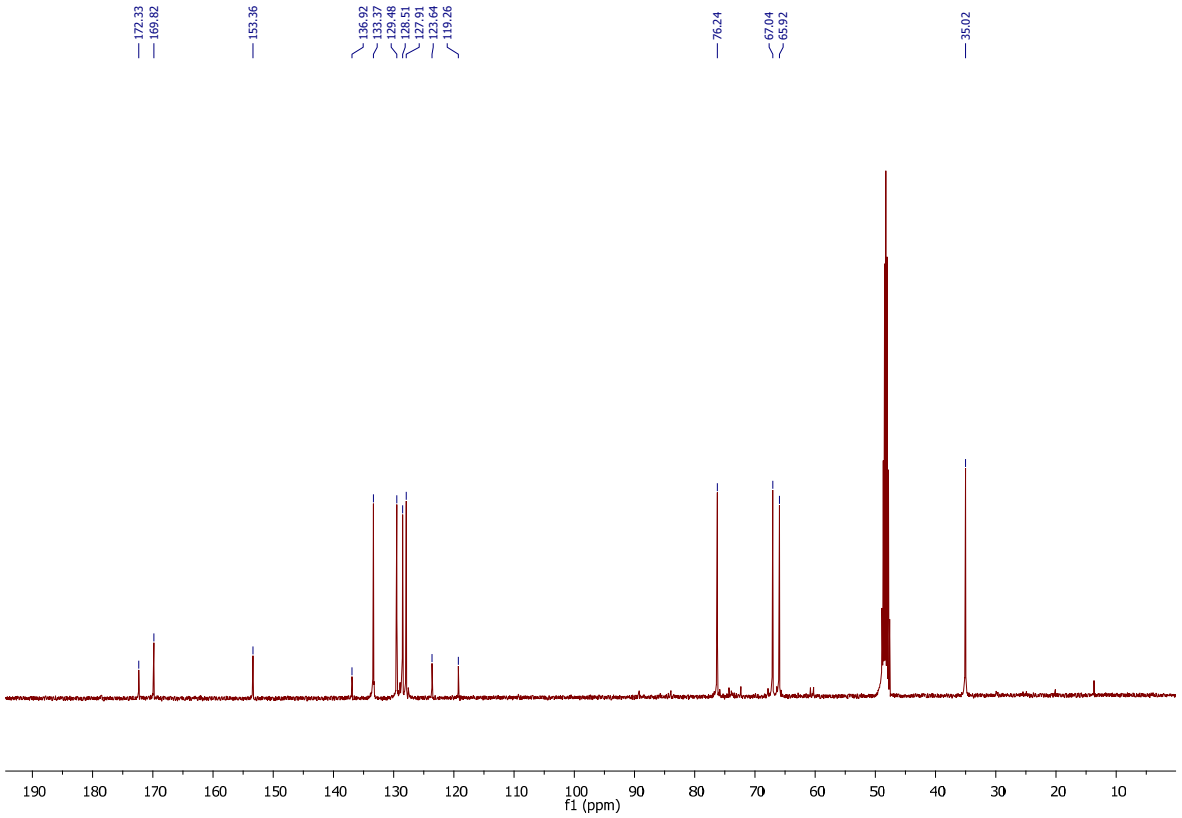
^{13}C NMR spectrum of compound **9h** (100 MHz, CD_3OD)



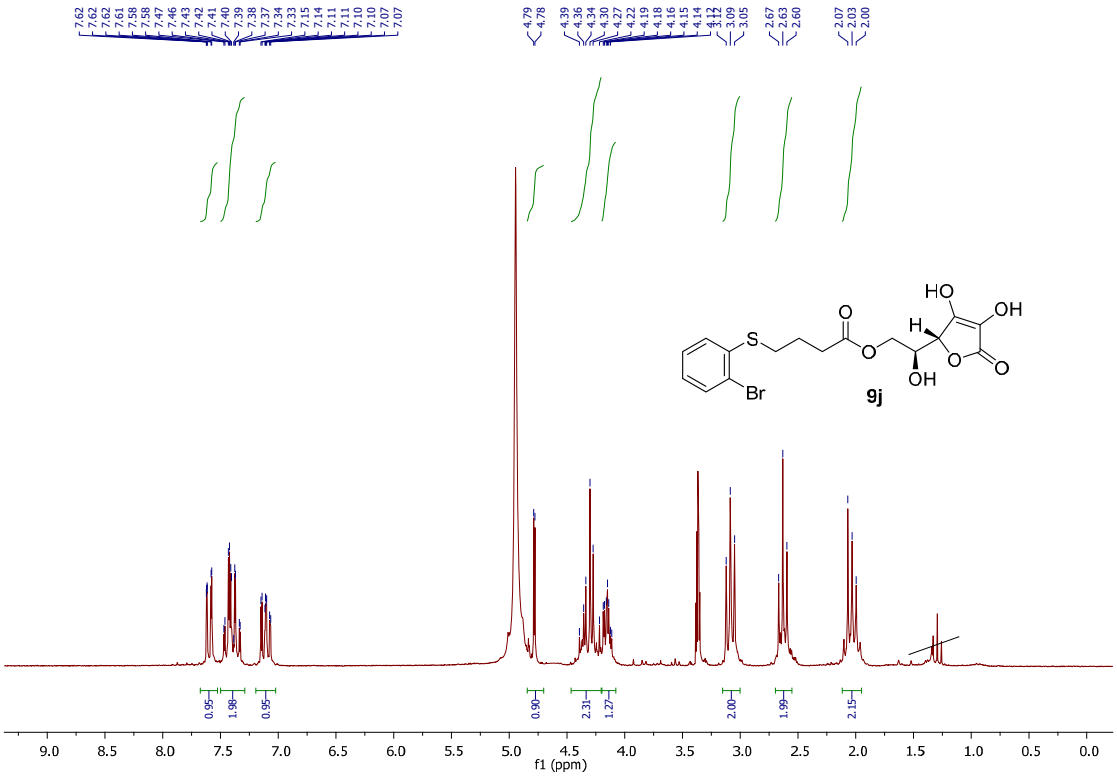
^{1}H NMR spectrum of compound **9i** (400 MHz, CD_3OD)



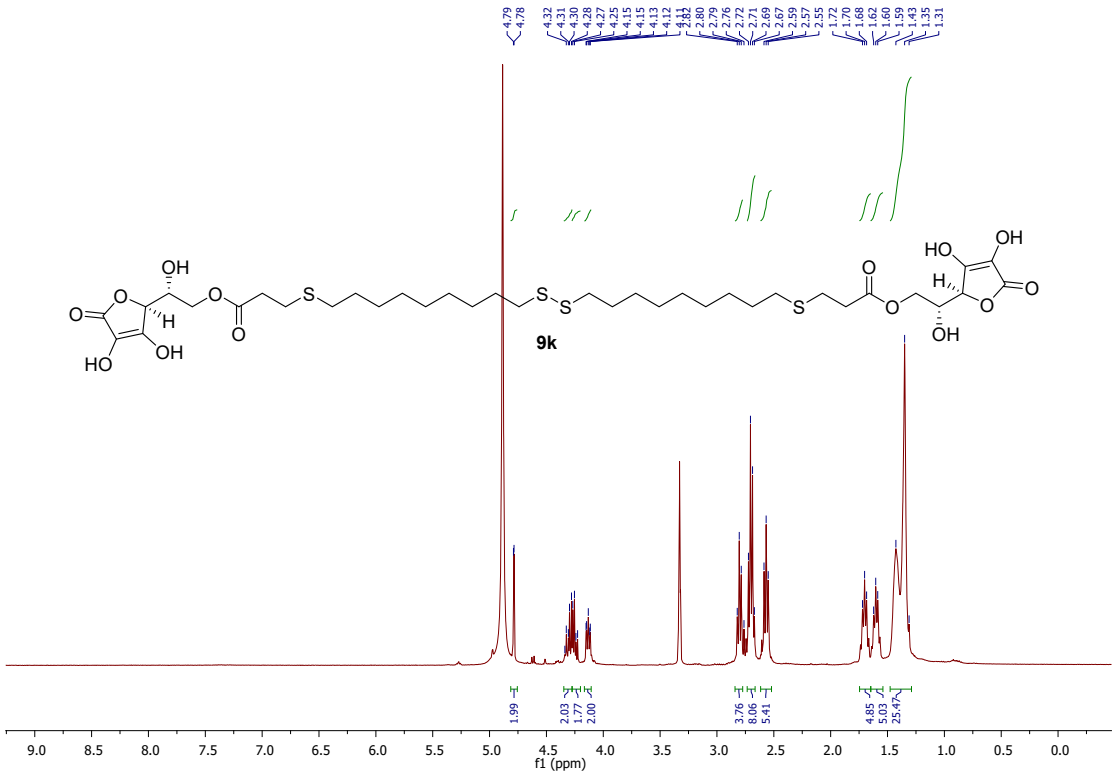
^{13}C NMR spectrum of compound **9i** (100 MHz, CD_3OD)



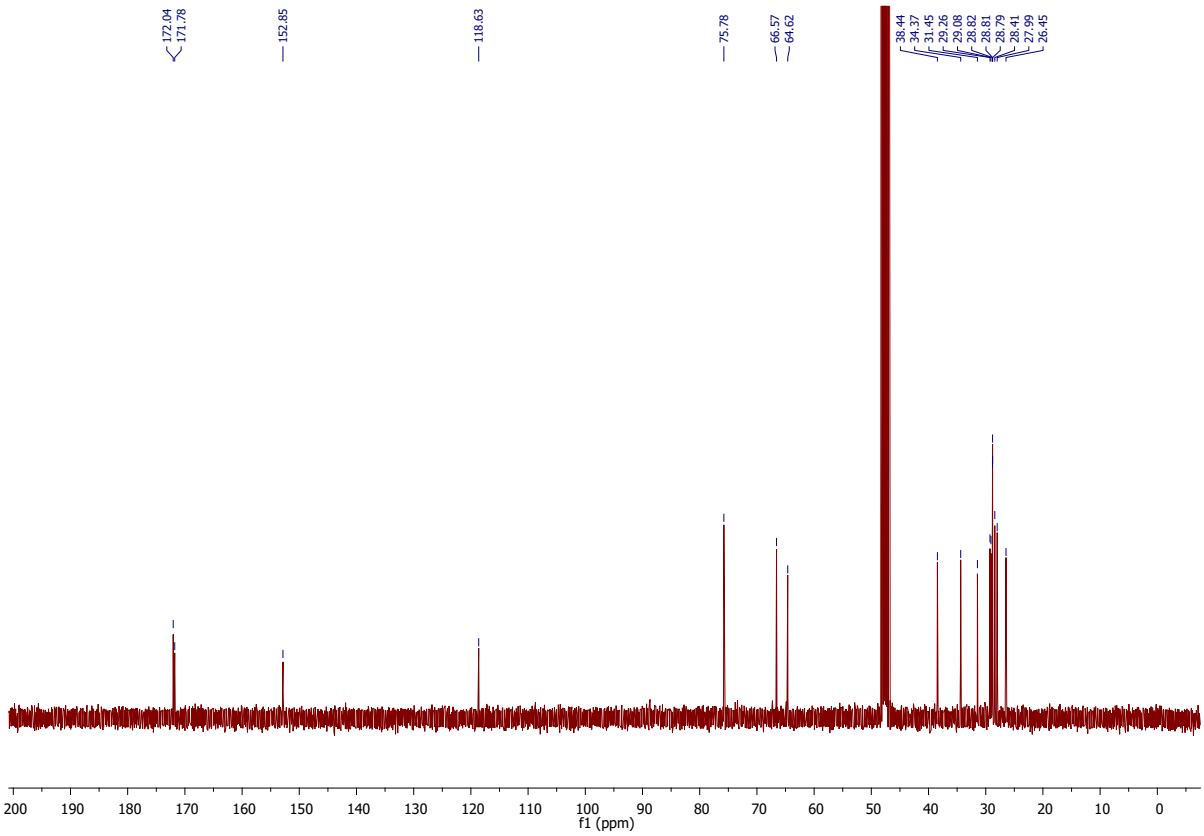
^{1}H NMR spectrum of compound **9j** (400 MHz, CD_3OD)



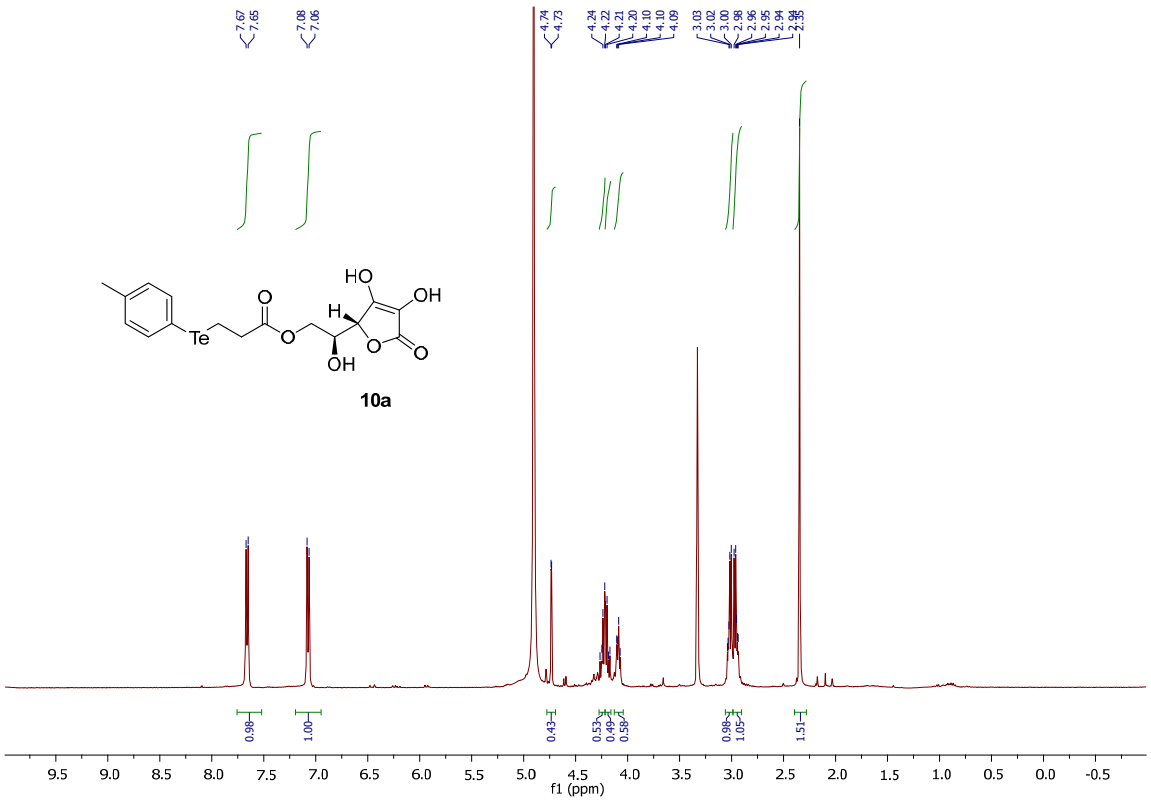
^{1}H NMR spectrum of compound **9k** (400 MHz, CD_3OD)



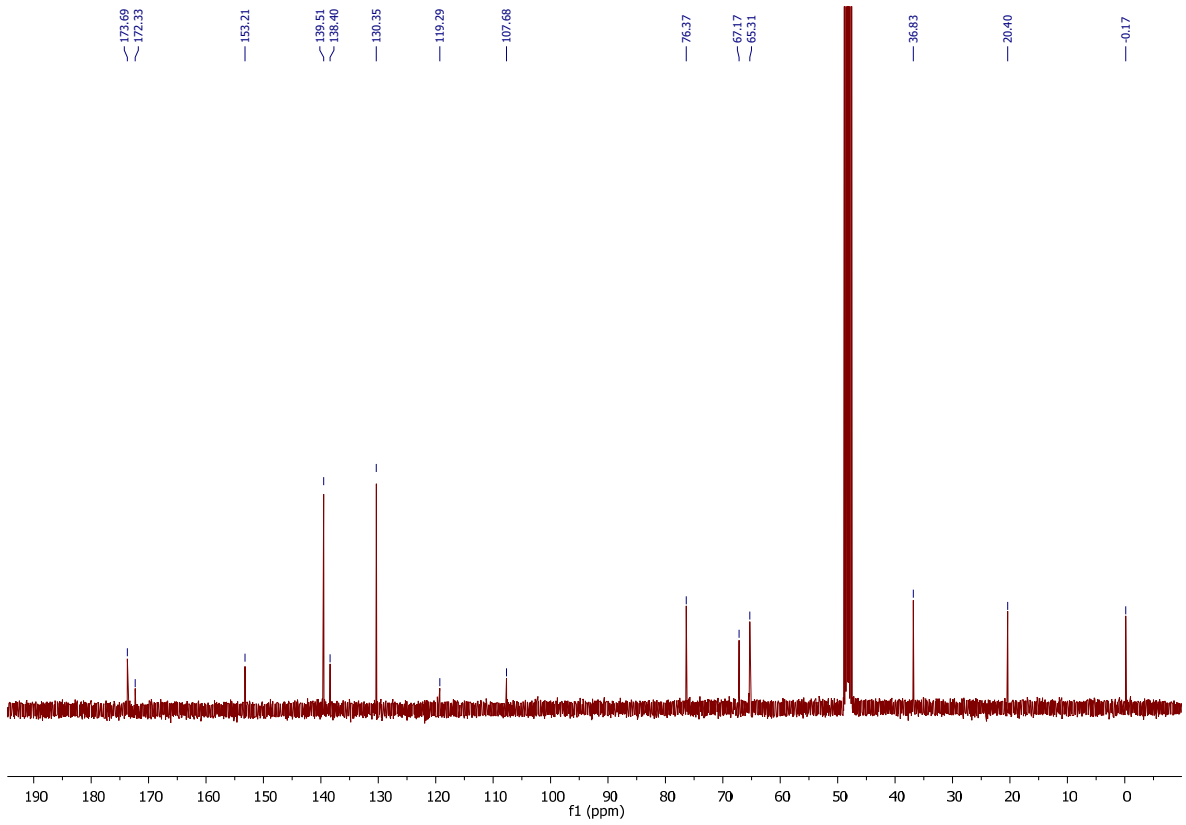
^{13}C NMR spectrum of compound **9k** (100 MHz, CD_3OD)



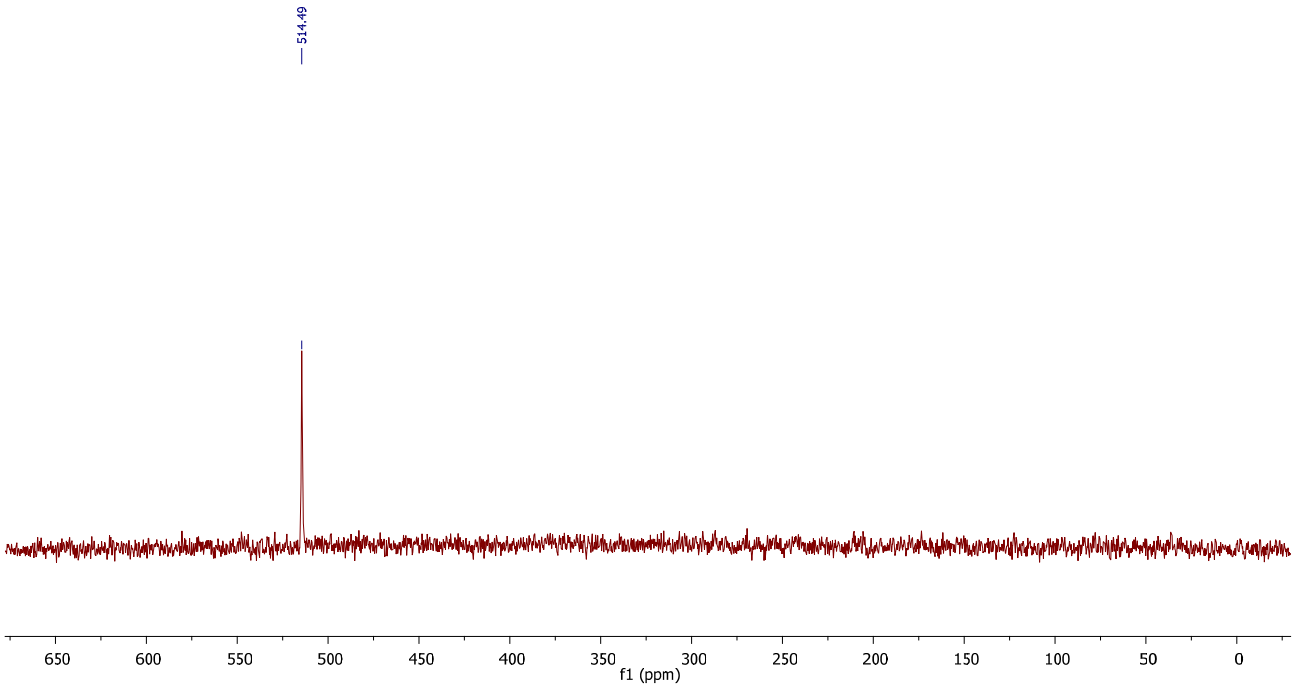
^{1}H NMR spectrum of compound **10a** (400 MHz, CD_3OD)



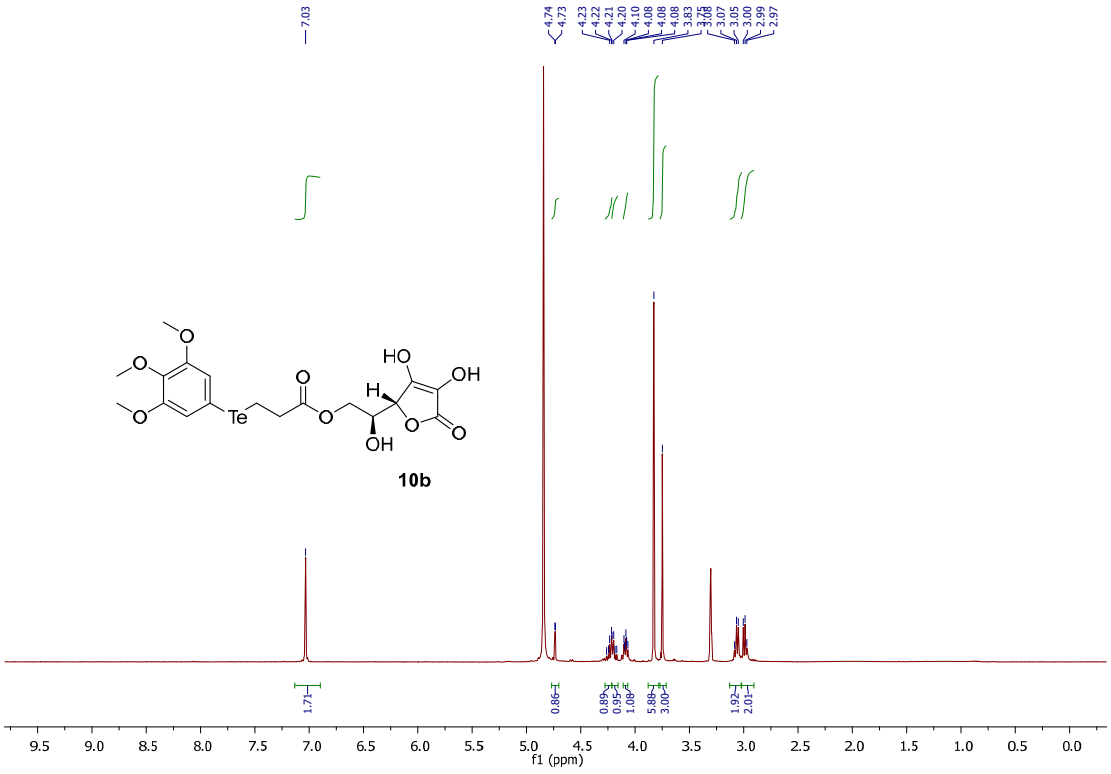
^{13}C NMR spectrum of compound **10a** (100 MHz, CD_3OD)



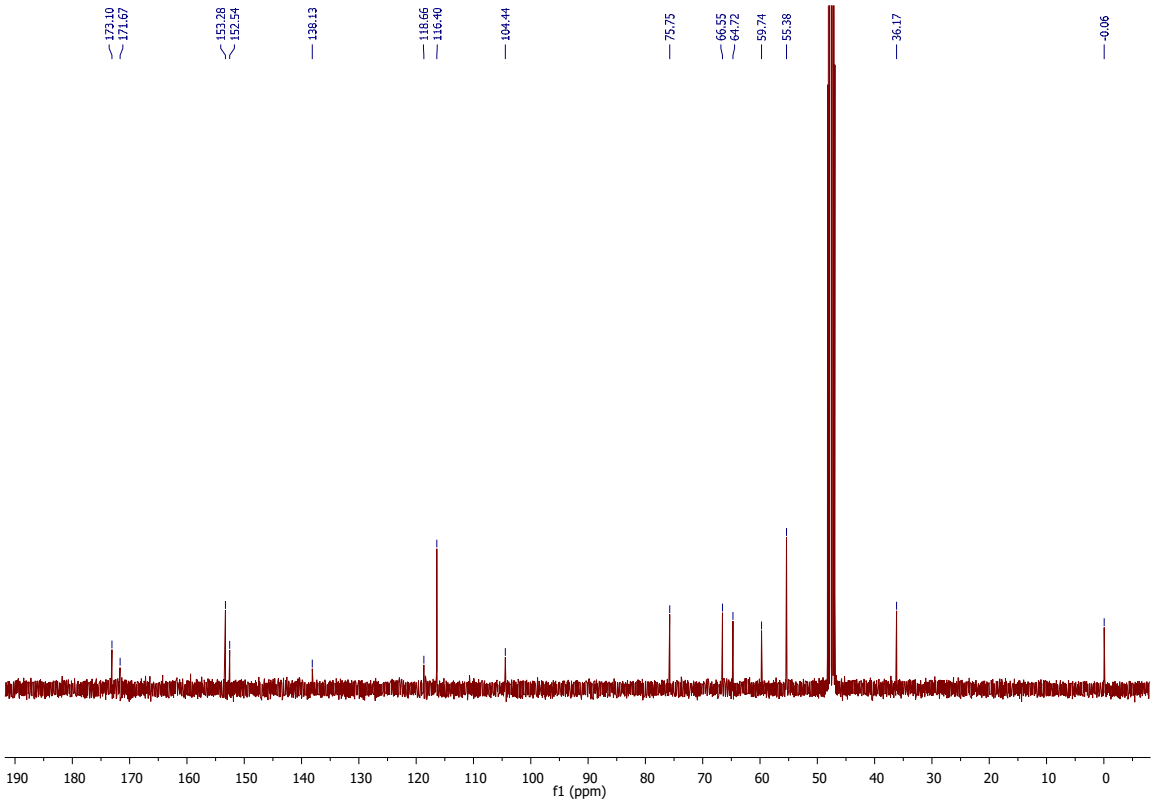
^{125}Te NMR spectrum of compound **10a** (126 MHz, CD_3OD)



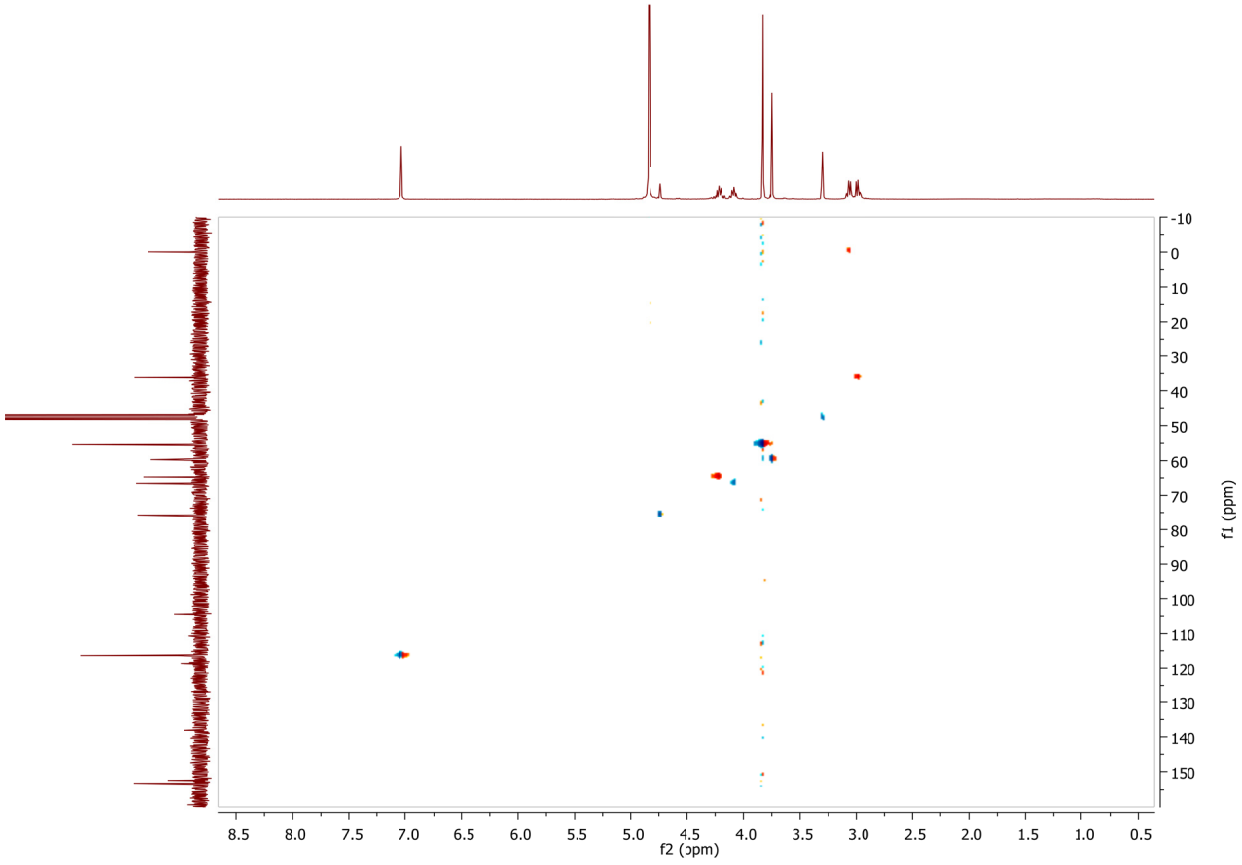
^{1}H NMR spectrum of compound **10b** (400 MHz, CD_3OD)



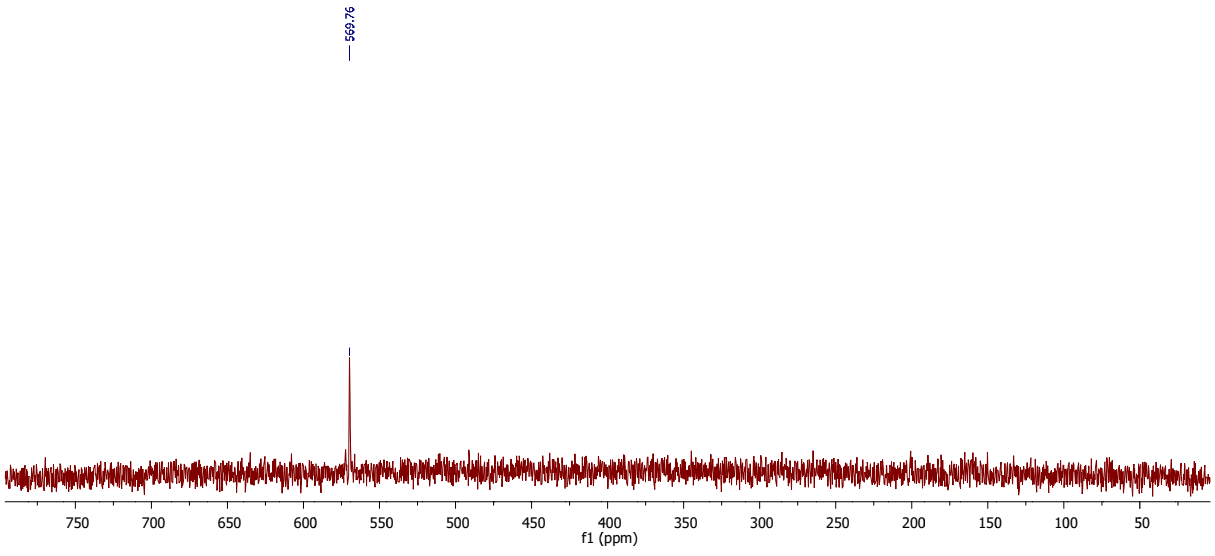
^{13}C NMR spectrum of compound **10b** (100 MHz, CD_3OD)



^{1}H-^{13}C HSQC NMR of compound **10b** (400 MHz, CD_3OD)



^{125}Te NMR spectrum of compound **10b** (126 MHz, CD_3OD)



10. References

1. (a) A. Degl'Innocenti, A. Capperucci, A. Cerreti, S. Pollicino, S. Scapecchi, I. Malesci and G. Castagnoli, *Synlett* 2005, 3063; (b) E. Obijalska, M. Pawelec, G. Mlostoń, A. Capperucci, D. Tanini and H. Heimgartner, *Eur. J. Org. Chem*., 2018, 3716.
2. (a) D. Tanini, G. Barchielli, F. Benelli, A. Degl'Innocenti and A. Capperucci, *Phosphorus Sulfur Silicon Relat. Elem.,* 2015, **190**, 1265; (b) D. Tanini, C. Borgogni, A. Capperucci, *New J. Chem.,* 2019, **43**, 6388.
3. D. Tanini, C. Tiberi, C. Gellini, P. R. Salvi, A. Capperucci, *Adv, Synth. Catal*., 2018, **360**, 3367.
4. A. Angeli, D. Tanini, A. Nocentini, A. Capperucci, M. Ferraroni, P. Gratteri and C.T. Supuran, *Chem. Commun*., 2019, **55**, 648.
5. D. Tanini, S. Scarpelli, E. Ermini, A. Capperucci, *Adv. Synth. Catal*., 2019, DOI 10.1002/adsc.201900168.
6. C. B. W. Phippen, J. K. Beattie and C. S. P. McErlean, *Chem. Commun*., 2010, **46**, 8234.
7. G. Mlostoń, A. Capperucci, D. Tanini, R. Hamera-Fałdyga and H. Heimgartner, *Eur. J. Org. Chem*., 2017, 6831.
8. (a) D. Tanini, A. Grechi, L. Ricci, S. Dei, E. Teodori, A. Capperucci, *New J. Chem*., 2018, **42**, 6077; (b) F. Kumakura, B. Mishra, K. I. Priyadarsini and M. Iwaoka, *Eur. J. Org. Chem*., 2010, 440.
9. P. Pascual, E. Martinez-Lara, J. A. Bàrcena, J. Lòpez-Barca and F. Toribio, *J. Chromatogr., Biomed. Appl.,* 1992, **581**, 49.
10. P. Goupy, C. Dufour, M. Loonis and O. Dangles, *J. Agric. Food Chem.,* 2003, **51**, 615.