

Organotellurium scaffolds for mass cytometry reagent development

Supplementary Information

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1. Abbreviations and Definitions:

CDCl_3 = deuterated chloroform

DART MS = direct analysis in real time mass spectrometry

DCC = *N,N'*-dicyclohexylcarbodiimide

DCU = dicyclourea

DCM = dichloro methane

DME = dimethyl ethane

DMSO = dimethyl sulfoxide

ESI = electrospray ionization

EtOAc = ethyl acetate

FBS = fetal bovine serum

HPLC = high performance liquid chromatography

LC-MS = liquid chromatography mass spectrometry

MC = mass cytometry

NHS = *N*-hydroxysuccinimide

NMR = nuclear magnetic resonance

O.N = over night

PBS: phosphate buffered saline

p-NP = para-nitrophenol

ppm = parts per million

RPMI = Roswell Park Memorial Institute

THF = tetrahydrofuran

TLC = thin layer chromatography

WST-1 = water soluble tetrazolium salt 1

2. Instrumentation:

Heidolph rotary evaporator was used to perform all rotary evaporations. NMR spectrum were collected at room temperature on one of the following spectrometers: Agilent DD2 600 MHz with the OneNMR H/F{x} probe, Agilent DD2 500 MHz with the Xsense Cold probe or Varian 400 MHz with the AutoX probe. High resolution mass spectrometry was obtained by one of the following: JEOL AccuTOF model JMS-T1000LC mass spectrometer equipped with DART ion source or Agilent 6538 Q-TOF mass spectrometer equipped with Agilent 1200 HPLC and an ESI ion source.

3. Experimental Conditions:

All reactions were performed under inert atmosphere using N₂ gas. Dry THF (Acros Organics), methanol (Acros Organics), pyridine (Acros Organics), and all other reagents (Sigma Aldrich) were used as supplied.

3-methyltellanyl-1-ethanol (1): Tellurium metal (granular, -5-+50 mesh, 500 mg, 3.9 mmol) was grounded to a fine powder using a mortar and pestle and suspended in THF (50 mL). Methyl lithium (2.5 mL, 4.0 mmol) was added drop-wise to the suspension until the solution became a homogenous yellow solution at room temperature. The resulting mixture was cooled to -196°C in a liquid nitrogen bath. Upon freezing, 2-chloro-ethanol (0.261 mL, 3.9 mmol) was added in one portion and the reaction was warmed to room temperature. The reaction mixture was stirred at room temperature for 2.5 hours. Once the reaction was complete by TLC, sat. NH₄Cl (100 mL) was added to the mixture. The solution was extracted into diethyl ether (2 x 100 mL). The combined organic layer was washed with brine (1 x 100 mL), dried over MgSO₄, filtered and concentrated. The crude compound was purified by column chromatography on silica gel (10% EtOAc in Pentane) and dried under vacuum to give a viscous yellow oil. Yield: 66%, 488 mgs. ¹H NMR (500 MHz, CDCl₃, δ): 3.78 (s, -CH₂OH, 2H), 2.80 (t, *J* = 6.8 Hz, -CH₂CH₂OH, 2H), 1.88 (s, -TeCH₃, 3H); ¹³C NMR (125 MHz, CDCl₃, δ): 62.59 (-CH₂OH), 8.40 (-CH₂-Te), -22.41 (-Te-CH₃). [M+NH₄]⁺ = 207.99829.

3-methyltellanyl-1-propanol (2): Tellurium metal (granular, -5-+50 mesh, 500 mg, 3.9 mmol) was ground to a fine powder using a mortar and pestle and suspended in THF (50 mL). Methyl lithium (2.5 mL, 4.0 mmol) was added drop-wise to the suspension until the solution turned yellow at room temperature. The resulting mixture was cooled to -196°C in a liquid nitrogen bath. Upon freezing, 1-chloro-3-propanol (0.326 mL, 3.9 mmol) was added in one portion and the reaction was warmed to room temperature. The reaction mixture was stirred at room temperature for 2.5 hours. Once the reaction was complete by TLC, sat. NH₄Cl (100 mL) was added to the mixture. The solution was extracted into diethyl ether (2 x 100 mL). The combined organic layer was washed with brine (1 x 100 mL), dried over MgSO₄, filtered, concentrated and dried under vacuum to give a viscous dark orange oil product. Yield: 74%, 581 mgs.

Characterization equivalent to that of literature. *Angew. Chem. Int. Ed. Engl.*, 2014, **53**, 11473-11477.

methyl 3-methyltellanyl-propionate (3): Tellurium metal (granular, -5-+50 mesh, 500 mg, 3.9 mmol) was ground to a fine powder using a mortar and pestle and suspended in THF (50 mL). Methyl lithium (2.5 mL, 4.0 mmol) was added drop-wise to the suspension until the solution turned yellow at room temperature. Water (0.18 mL) was added to the solution, inducing a color change to a dark brown mixture. The resulting mixture was cooled to -196°C in a liquid nitrogen bath. Upon freezing, methyl acrylate (0.355 mL, 3.9 mmol) was added in one portion and the reaction was warmed to room temperature. The reaction mixture was stirred at room temperature for 0.5 hours. Once the reaction was complete by TLC, sat. NH₄Cl (100 mL) was added to the mixture. The solution was extracted into diethyl ether (2 x 100 mL). The combined organic layer was washed with brine (1 x 100 mL), dried over MgSO₄, filtered, concentrated and dried under vacuum to give a viscous dark yellow oil. Yield: 85%, 775 mgs. ¹H NMR (500 MHz, CDCl₃, δ): 3.68 (s, -COOCH₃, 3H), 2.86 (m, -CH₂COOCH₃, 2H), 2.76 (m, -CH₂CH₂Te-, 2H), 1.92 (s, -Te-CH₃, 3H); ¹³C NMR (125 MHz, CDCl₃, δ): 173.87 (C=O), 52.11 (-COOCH₃), 37.17 (-CH₂COOCH₃), -4.72 (-TeCH₂CH₂-), -21.35 (-Te-CH₃). [M+H]⁺ = 232.98149.

methyl 4-methyltellanyl-butanoate (4): Tellurium metal (granular, -5-+50 mesh, 500 mg, 3.9 mmol) was ground to a fine powder using a mortar and pestle and suspended in THF (50 mL). Methyl lithium (2.5 mL, 4.0 mmol) was added drop-wise to the suspension until the solution turned yellow at room temperature. The resulting mixture was cooled to -196°C in a liquid nitrogen bath. Upon freezing, methyl-4-chlorobutyrate (0.478 mL, 3.9 mmol) was added in one portion and the reaction was warmed to room temperature. The reaction mixture was stirred at room temperature for 2.5 hours. Once the reaction was complete by TLC, sat. NH₄Cl (100 mL) was added to the mixture. The solution was extracted into diethyl ether (2 x 100 mL). The combined organic layer was washed with brine (1 x 100 mL), dried over MgSO₄, filtered, concentrated and dried under vacuum to give a viscous dark yellow oil. Yield: 91%, 877 mgs. ¹H NMR (500 MHz, CDCl₃, δ): 3.64 (s, -COOCH₃, 3H), 2.60 (t, *J* = 7.6 Hz, -TeCH₂- 2H), 2.39 (t, *J* = 7.4 Hz, -CH₂COOCH₃, 2H), 2.01 (m, -CH₂CH₂CH₂-, 2H), 1.86 (s, -TeCH₃, 3H); ¹³C NMR (125 MHz, CDCl₃, δ): 173.09 (C=O), 51.36 (-COOCH₃), 35.71 (-CH₂C=O-), 26.76 (-CH₂CH₂C=O-), 1.92 (-TeCH₂CH₂-), -22.52 (-TeCH₃). [M+H]⁺ = 246.99690.

methyl 4-((trifluoromethyl)tellanyl)butanoate (5): Tellurium metal (granular, -5-+50 mesh, 500 mg, 3.9 mmol) was ground to a fine powder using a mortar and pestle and suspended in 7 mL of DME. The solution was cooled to -60 °C using a 40% ethylene glycol 60% ethanol and dry ice cooling bath. Upon cooling, trimethyl(trifluoromethyl)silane (0.356 mL, 2.61 mmol) and tetramethylammonium fluoride (243 mg, 2.61 mmol) were added to the reaction mixture. The reaction was stirred vigorously for 1 hour at -60°C and for 3 hours at room temperature. Once the reaction was complete, the yellow supernatant was decanted off and the solid residues

remaining were washed with DME. The supernatant and the washes were combined and concentrated. To the concentrated crude mixture, 3 mL of DME and methyl 4-bromobutyrate (0.230 mL, 1.82 mmol) were added. The reaction mixture was stirred over-night at room temperature. Once the reaction was complete, the DME was removed by rotary-vaporization and the remaining crude mixture was taken up in EtOAc. This organic layer was washed with water (3x), brine (1x), dried over MgSO₄, filtered and concentrated. The crude mixture was purified by column chromatography (Toluene on silica gel). Yield: 50%, 270 mgs. ¹H NMR (500 MHz, CDCl₃, δ): 3.68 (s, -COOCH₃, 3H), 3.13 (t, *J* = 7.7 Hz, -TeCH₂-, 2H), 2.47 (t, *J* = 7.7 Hz, -CH₂COOCH₃, -2H), 2.26 (p, *J* = 7.1 Hz, -CH₂CH₂CH₂-, 2H); ¹³C NMR (125 MHz, CDCl₃, δ): 172.82 (C=O), 103.79-95.40 (q, *J* = 351.5 Hz, -Te-CF₃), 51.763 (-COOCH₃), 35.41 (-CH₂CH₂CH₂Te-), 27.08 (-CH₂CH₂CH₂-), 8.20 (-TeCH₂-). [M+NH₄]⁺ = 317.99529

(bromoethynyl)triisopropylsilane: *N*-bromosuccinimide (5.15g, 29 mmol), silver nitrate (4.28g, 25.2 mmol) and TIPS-acetylene (5.6 mL, 25.2 mmol) were added to 200 mL of acetone. The solution mixture was stirred vigorously for 3 hours at room temperature. Once the reaction was complete, 150 mL of water was added to the mixture. The solution was extracted into hexane (3 x 125 mL). The combined organic layer was washed with brine (2x), dried over MgSO₄, filtered, concentrated and dried under vacuum to give a clear oil product. Yield: 6.51 g, 98%. *Org. Lett.* 2011, **13**, 537-539.

hepta-4,6-diynoic acid intermediate: Cadiot-Chodkiewicz coupling was completed according to literature. (J. P. Marino, H. N. Nguyen, *J. Org. Chem.*, **2002**, 67, 6841-6844.) CuCl (15 mg, 0.15 mmol) was added to an aqueous solution of 30% BuNH₂ (25 mL) at room temperature which generated a transparent blue solution. A few hydroxylamine hydrochloride crystals were added to this solution mixture to discharge the color. 4-pentynoic acid (901 mg, 9.2 mmol) was added to the mixture at once, resulting in a yellow suspension. This solution was cooled using an ice-water bath. Upon cooling, 2-bromo-1-triisopropylsilyl acetylene (2 g, 7.6 mmol) was added dropwise. Additional crystals of hydroxylamine hydrochloride were added to maintain the yellow solution when blue-green color changes occurred. The reaction was stirred vigorously for 0.5 hours. Once the reaction was complete by TLC, the solution was extracted with EtOAc (2 x 100 mL). The combined organic layer was washed with 1M HCl (1 x 100 mL), brine (1 x 100 mL), dried with MgSO₄, filtered, concentrated and dried under vacuum to give a dark brown crude crystalline product. This product is directly deprotected. The product 6-(triisopropylsilyl)hepta-4,6-diynoic acid (388 mg, 1.39 mmol) was dissolved in THF (15 mL). This solution mixture was cooled using an ice-water bath. While cooling, tetrabutylammonium fluoride (1.39 mL, 1M in THF) was added dropwise until the solution reached room temperature. The reaction was stirred vigorously for 3 hours. Once the reaction was complete, the solution was extracted with EtOAc (3 x 100 mL). The combined organic layer was washed with 1M citric acid (3 x 100 mL), brine (3 x 100 mL), dried with MgSO₄, filtered, concentrated and dried

under vacuum to give a brown crude oil product. The compound was taken directly to the next step of 2-(tellurophene-2-yl)propanoic acid synthesis.

2-(tellurophen-2-yl)propanoic acid (6): Tellurium metal (granular, -5-+50 mesh, 3.0 g, 23.5 mmol) was ground to a fine powder using a mortar and pestle. The tellurium powder was added to an aqueous solution of 1M NaOH (30 mL). To the reaction mixture, sodium hydroxymethylsulfinate (6.0 g, 38.9 mmol) was added and stirred vigorously. The reaction solution was heated using an oil bath, to 95°C for 0.5 hours and the solution turned a deep purple color. The reaction solution was cooled to 60°C and stirred for an additional 5 mins. In 5 mL of ethanol, hepta-4,6-diynoic acid (388 mg, 3.17 mmol) was added to the reaction mixture. This solution mixture was stirred for 1.5 hours at 60°C. The reaction was then exposed to oxygen by removing the septa and allowing in atmosphere. The reaction was allowed to cool to room temperature and stirred for 15 mins. Upon cooling, the reaction was diluted with a sat. NH₄Cl solution (100 mL). The solution was extracted with EtOAc (2 x 100 mL). The combined organic layer was washed with 1M HCl (2 x 100 mL), brine (2 x 100 mL), dried over MgSO₄, filtered, concentrated, and dried under vacuum to give a dark yellow solid crude product. The crude product was purified by flash chromatography (5%-50% EtOAc/Hexanes on silica gel) to give a light yellow solid (563 mg, 70%). ¹H NMR (500 MHz, CDCl₃, δ): 8.71 (dd, *J* = 6.9, 1.2 Hz, -HCTe-, 1H), 7.59 (m, -HCHCTe-, 1H), 7.38 (m, -TeCCH-, 1H), 3.22 (t, *J* = 7.3, Tephene-CH₂-, 2H), 2.73 (t, *J* = 7.3, -CH₂CH₂COOH, 2H); ¹³C NMR (125 MHz, CDCl₃, δ): 178.94 (C=O), 148.69 (-TeCCH-), 137.42 (-HCHCTe-), 136.15 (-TeCCH-), 125.29 (-HCTe-), 37.95 (Tephene-CH₂-), 32.01 (-CH₂CH₂COOH). [M+H]⁺=254.96665

hexa-3,5-diyn-1-ol intermediate: Cadiot-Chodkiewicz coupling. CuCl (7.5 mg, 0.08 mmol) was added to an aqueous solution of 30% BuNH₂ (25 mL) at room temperature that generated a transparent blue solution. A few hydroxylamine hydrochloride crystals were added to this solution mixture to discharge the color. 3-Butyn-1-ol (1 g, 3.83 mmol) was added to the mixture resulting in a yellow suspension. This solution was cooled using an ice-water bath. Upon cooling, 2-bromo-1-triisopropylsilyl acetylene (832 mg, 3.19 mmol) was added drop-wise. Additional crystals of hydroxylamine hydrochloride were added to prevent the solution from turning a blue-green color. The reaction was stirred vigorously for 0.5 hours. Once the reaction was complete by TLC, the solution was extracted with EtOAc (2 x 100 mL). The combined organic layer was washed with 1M HCl (1 x 100 mL), brine (1 x 100 mL), dried with MgSO₄, filtered, concentrated and dried under vacuum to give a neat dark brown oil. This product is directly deprotected. The product, 6-(triisopropylsilyl)hexa-3,5-diyn-1-ol (873 mg, 1.44 mmol) was dissolved in THF (15 mL). This solution mixture was cooled using an ice-water (1:1) bath. Upon cooling, tetrabutylammonium fluoride (1.44 mL, 1M in THF) was added dropwise and the solution was allowed to warm to room temperature. The reaction was stirred vigorously for 3 hours. Once the reaction was complete by TLC,

the solution was extracted with EtOAc (3 x 100 mL). The combined organic layer was washed with 1 M citric acid (3 x 100 mL), brine (3 x 100 mL), dried with MgSO₄, filtered, concentrated and dried under vacuum to give a brown oil. This crude product was immediately taken to the next step for the synthesis of 2-(tellurophen-2-yl)ethan-ol since the compound possess limited stability as a free diacetylene.

2-(tellurophen-2-yl)ethan-ol (7): Tellurium metal (granular, -5-+50 mesh, 3.0 g, 23.5 mmol) was ground to a fine powder using a mortar and pestle. The tellurium powder was added to an aqueous solution of 1M NaOH (30 mL). To the reaction mixture, sodium hydroxymethylsulfinate (6.0 g, 38.9 mmol) was added and stirred vigorously. The reaction solution was heated using an oil bath, to 95°C for 0.5 hours and the solution turned a deep purple color. The reaction solution was cooled to 60°C and stirred for an additional 5 mins. In ethanol (5 mL), hexa-3,5-diyn-1-ol (600 mg, 6.37 mmol) was added to the reaction mixture. This solution mixture was stirred for 1.5 hours at 60°C. At this point, the reaction was exposed to oxygen by removing the septa and exposing the reaction to atmosphere. The reaction was cooled to room temperature and allowed to stir for 15 mins. Upon cooling, the reaction was diluted with a sat. NH₄Cl solution (100 mL). The solution was extracted with EtOAc (2 x 100 mL). The combined organic layer was washed with 1M HCl (2 x 100 mL), brine (2 x 100 mL), dried with MgSO₄, filtered concentrated, and dried under vacuum to give a dark yellow oil crude product. The crude product was purified by flash chromatography (10%-30% EtOAc/Hexanes on silica gel stationary phase) to give a light yellow oil (949 mg, 66%). ¹H NMR (400 MHz, CDCl₃, δ): 8.71 (dd, *J* = 6.9, 1.2 Hz, -HCTe-, 1H), 7.65 (m, -HCHCTe-, 1H), 7.44 (m, -TeCCH-, 1H), 3.82 (t, *J* = 6.0 Hz, Tephene-CH₂-, 2H), 3.13 (t, *J* = 6.4 Hz, -CH₂CH₂OH, 2H), 2.68 (s, -OH, 1H). ¹³C NMR (100 MHz, CDCl₃): 145.37 (-TeCCH-), 136.34 (-HCHCTe-), 135.48 (-TeCCH-), 124.89 (-HCTe-), 63.64 (-CH₂CH₂OH), 38.85 (-Tephene-CH₂-). [M+H]⁺ = 254.96665

3-(methyltellanyl)propyl benzylecarbamate (8): The *p*-NP-carbamate intermediate was synthesized from **2** using a literature protocol (Telox. *Angew. Chem. Int. Ed. Engl.*, 2014, **53**, 11473-11477). In an oven dried 25 mL round bottom flask, benzylamine (42 μL, 0.38 mmol) and pyridine (92 μL, 114 mmol) were added to methanol (5 mL). Upon mixing, a dilute solution of the *p*-NP-carbamate intermediate (139 mg, 0.38 mmol in 1 mL methanol) was added dropwise via a syringe over 1 minute. The reaction mixture was stirred for 3 hours at room temperature. The methanol solvent was removed by rotary evaporation and the crude compound was purified by flash chromatography (5-20% EtOAc/Pentanes on silica gel stationary phase) to afford a light yellow crystal **8** (98 mg, 77%). ¹H NMR (500 MHz, CDCl₃, δ): 7.34 (m, aryl-, 5H), 4.97 (s, -NH-, 1H), 4.37 (d, *J* = 5.7 Hz, aryl-CH₂NH-, 2H), 4.14 (t, *J* = 6.2 Hz, -OCH₂CH₂CH₂Te-, 2H), 2.64 (t, *J* = 7.4 Hz, -OCH₂CH₂CH₂Te- 2H), 2.06 (m, -OCH₂CH₂CH₂Te-, 2H), 1.90 (s, -TeCH₃, 3H). ¹³C NMR (125 MHz, CDCl₃, δ): 156.77 (C=O), (138.35, 130.80, 130.57, 128.59 & 127.42, aryl), 68.86 (-OCH₂CH₂CH₂Te-), 30.76 (-CH₂CH₂CH₂Te-), -2.25 (-CH₂TeCH₃, -22.24 (-TeCH₃). [M+NH₄]⁺ = 354.0376

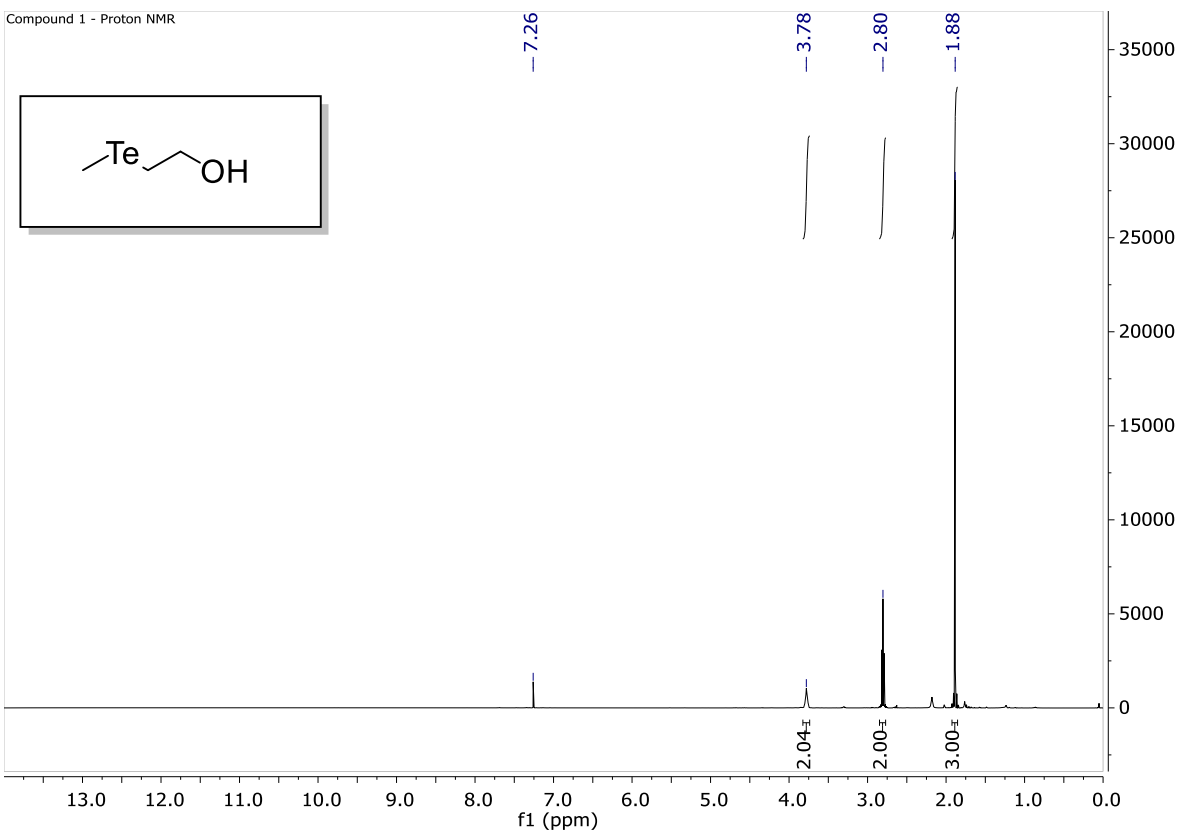
***N*-benzyl-4-(methyltellanyl)butanamide (9):** Compound **4** (400 mg, 1.64 mmol) was dissolved in THF (25 mL) and stirred vigorously. To the mixture, 1 M NaOH (25 mL) was added and a biphasic mixture was generated. This solution was stirred for 1 hour. The reaction was then diluted with H₂O (50 mL) and 1 M citric acid was added until the reaction mixture was acidic by pH paper. The resulting mixture was extracted into diethyl ether (3 x 100 mL) and washed with brine (2 x 100 mL). The solvent was removed from the combined organic layers by rotary evaporation. This compound was re-dissolved in DCM (5 mL) and added to a new round bottom flask where DCC (355 mg, 1.72 mmol) was added and stirred for 5 minutes. Once the mixture became a milky solution, NHS (198.2 mg, 1.72 mmol) was added to the mixture and stirred for an additional 5 minutes. To this resulting solution, a mixture of benzylamine (215 μ L, 1.97 mmol) and TEA (275 μ L, 1.97 mmol) in DCM (5 mL) were added at room temperature. The reaction was stirred overnight. Once the reaction was complete by TLC, the stir bar was removed and the solvent was removed by rotary evaporation. The resulting product was re-dissolved in cold EtOAc (100 mL) where white precipitate formed in the solution. The precipitate, presumed to be DCU, was removed by filtration. This process was repeated 3 times to remove the DCU. The filtrate was washed with 0.5 M citric acid (2 x 100 mL), NaHCO₃ (2 x 100 mL) and brine (1 x 100 mL). The organic layers were combined, dried with MgSO₄, filtered, concentrated and dried under vacuum to give a light yellow solid product (440 mg, 81%). ¹H NMR (500 MHz, CDCl₃, δ): 7.33 (m, aryl-, 5H), 5.92 (s, -NH-1H), 4.40 (d, *J* = 5.8 Hz, aryl-CH₂NH- 2H), 2.62 (t, *J* = 7.4 Hz, -TeCH₂-, 2H), 2.29 (t, *J* = 7.3 Hz, -COCH₂CH₂CH₂Te-, 2H), 2.06 (m, -COCH₂CH₂CH₂Te-, 2H), 1.86 (s, -TeCH₃, 3H). ¹³C NMR (125 MHz, CDCl₃, δ): 172.25 (C=O), (138.63, 129.08, 128.17 & 127.89, aryl), 43.99 (aryl-CH₂-NH-), 38.66 (-CH₂CH₂CH₂Te-), 27.78 (-CH₂CH₂CH₂Te-), 2.90 (-CH₂TeCH₃), -21.95 (-TeCH₃). [M+H]⁺ = 322.04378

***N*-benzyl-4-((trifluoromethyl)tellanyl)butanamide (10):** Compound **5** (400 mg, 1.4 mmol) was dissolved in 25 mL of THF and stirred vigorously. To the mixture, 25 mL of 1 M NaOH was added and a biphasic mixture was generated. This solution was stirred for 1 hour. Upon completion, the reaction was diluted and 1 M citric acid was added until the reaction mixture was acidic. The resulting mixture was extracted into ethyl acetate (3 x 100 mL) and washed with brine (2 x 100 mL). The combined organic layers were combined and the solvent was removed by rotary evaporation. This compound was re-dissolved in DCM (5 mL) and added to a new round bottom flask where DCC (303 mg, 1.47 mmol) was added and stirred for 5 minutes. Once the mixture became a milky solution, NHS (169 mg, 1.47 mmol) was added to the mixture and stirred for an addition 5 minutes. To this resulting solution, a mixture of benzylamine (180 μ L, 1.68 mmol) and TEA (235 μ L, 1.68 mmol) in 5 mL of DCM was added at room temperature. The reaction was stirred overnight. Upon completion, the stir bar was removed and the solvent was removed by rotary evaporation. The resulting product was redissolved in cold EtOAc (100 mL) where white precipitate formed. The precipitate, presumed to be DCU, was removed by filtration. The filtrate was washed with 0.5 M citric acid (2 x 100 mL), NaHCO₃ (2 x 100 mL) and brine (1 x

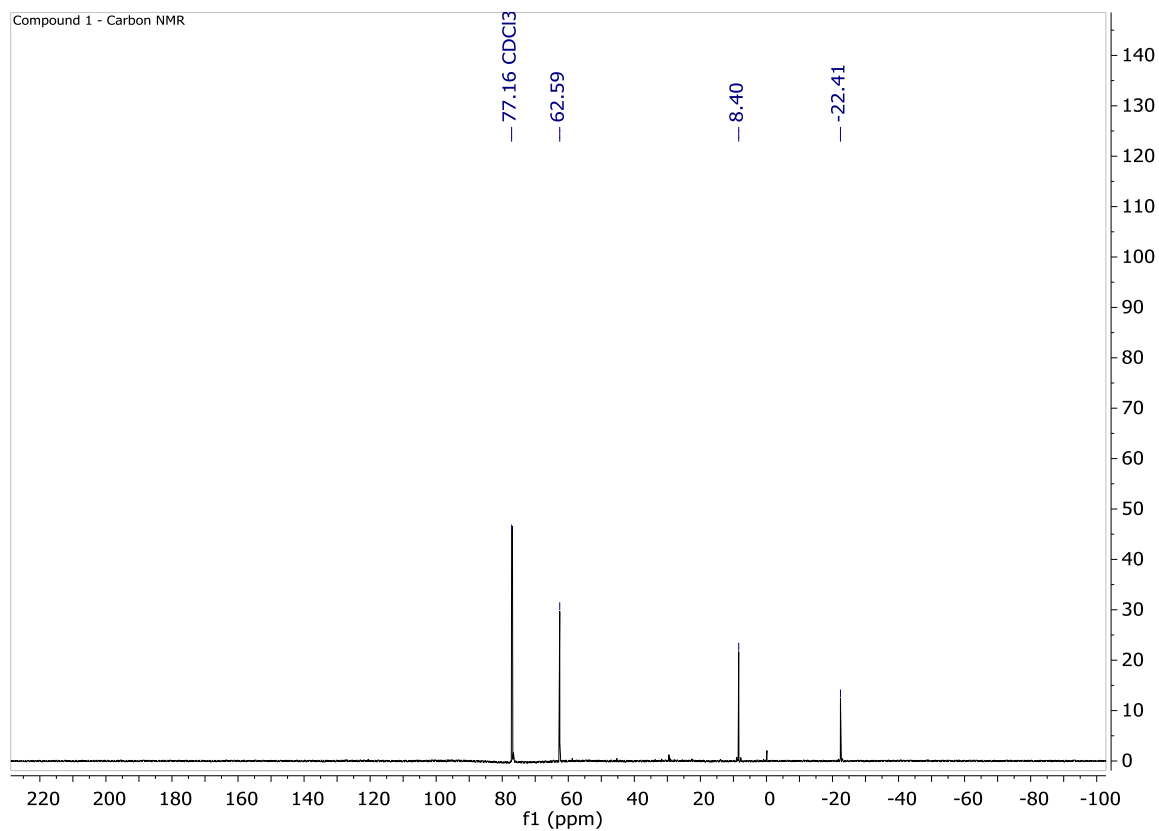
100 mL). The organic layers were combined, dried with MgSO_4 , filtered, concentrated and dried under vacuum to give a yellow solid product (157 mg, 30%). ^1H NMR (500 MHz, CDCl_3 , δ): 7.33 (m, aryl-, 5H), 5.79 (s, -NH-, 1H), 4.41 (d, $J = 5.7$ Hz, aryl- CH_2NH -, 2H), 3.14 (t, $J = 6.9$ Hz, - CH_2Te -, 2H), 2.34 (m, - $\text{CH}_2\text{CH}_2\text{CH}_2\text{Te}$ -, 2H), 2.28 (p, $J = 6.8$, - $\text{CH}_2\text{CH}_2\text{CH}_2\text{Te}$ -, 2H). ^{13}C NMR (125 MHz, CDCl_3 , δ): 171.87 (C=O), (138.40, 129.19, 128.26 & 128.07, aryl), (104.84-96.44, - CF_3), 44.15 (aryl- CH_2NH -), 37.94 (- $\text{CH}_2\text{CH}_2\text{CH}_2\text{Te}$ -), 27.75 (- $\text{CH}_2\text{CH}_2\text{CH}_2\text{Te}$ -), 9.05 (- $\text{CH}_2\text{CH}_2\text{CH}_2\text{Te}$ -). $[\text{M}+\text{H}]^+ = 376.0175$

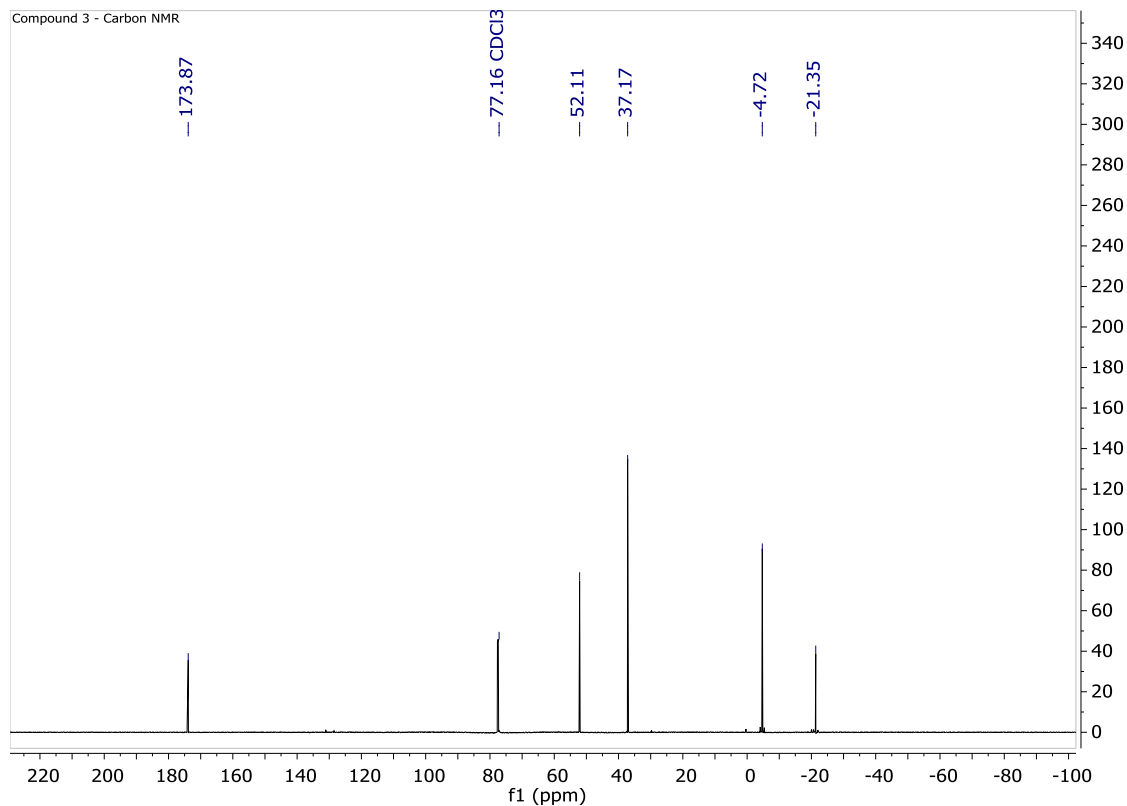
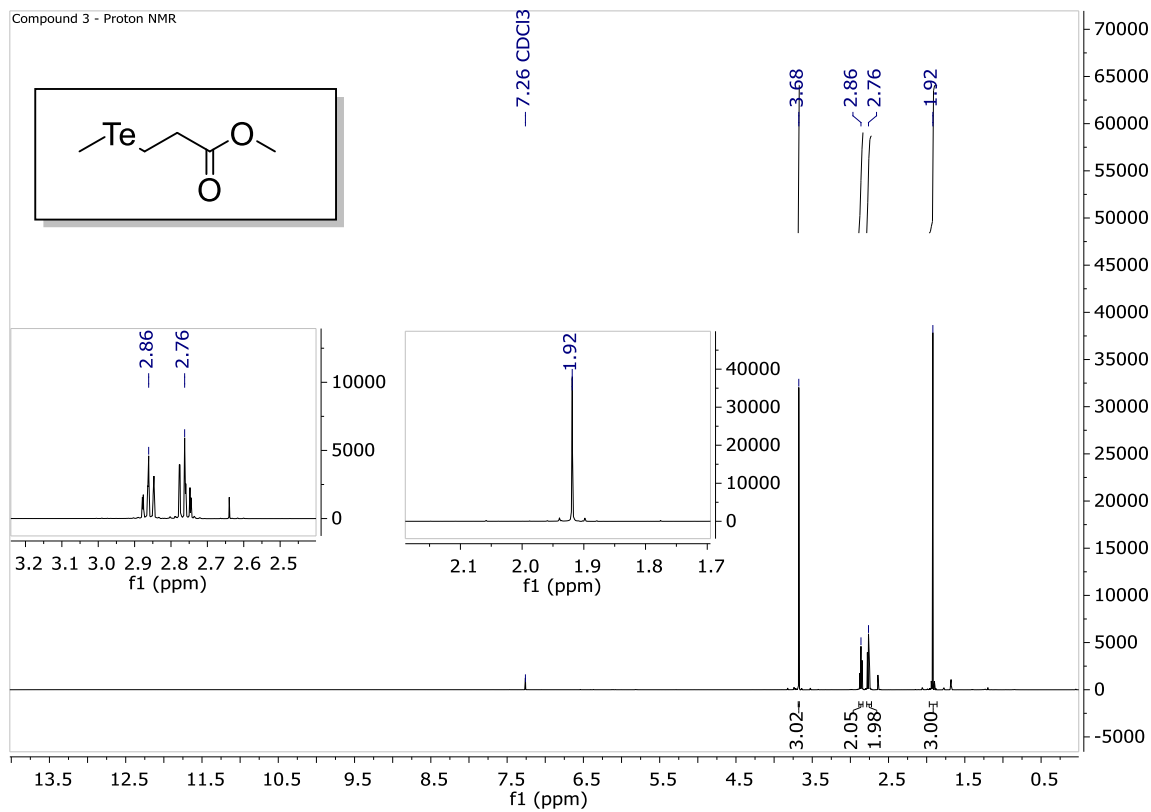
N-benzyl-3-(tellurophen-2-yl)propanamide (11): Compound **6** (100mg, 0.4 mmol) was dissolved in DCM (5 mL) and DCC (86 mg, 0.42 mmol) was added and stirred for 5 minutes. Once the mixture became a milky solution, NHS (48 mg, 0.42 mmol) was added and stirred for an additional 5 minutes. To this resulting solution, a mixture of benzylamine (52 μL , 0.48 mmol) and TEA (67 μL , 0.48 mmol) in 5 mL of DCM was added at room temperature. The reaction was stirred overnight. Upon completion, the stir bar was removed and the solvent was removed by rotary evaporation. The resulting product was redissolved in cold EtOAc (150 mL) where white precipitate crashed out of solution. The precipitate, presumed to be DCU, was removed by filtration and the filtrate was washed with 0.5 M citric acid (2 x 150 mL), NaHCO_3 (2 x 150 mL) and brine (1 x 150 mL). The organic layers were combined, dried with MgSO_4 , filtered, concentrated and dried under vacuum to give a yellow solid. The product was purified by flash chromatography (5%-25% EtOAc/Hexanes) to give a yellow solid (440 mg, 81%). ^1H NMR (500 MHz, CDCl_3 , δ): 8.71 (dd, $J = 6.9$, 1.3 Hz, - HCTe -, 1H), 7.57 (m, - HCHCTe -, 1H), 7.31 (m, - TeCCH - & aryl, 7H), 5.76 (s, -NH-, 1H), 4.41 (d, $J = 5.7$ Hz, aryl- CH_2NH -, 2H), 3.25 (t, $J = 7.6$ Hz, Tephene- CH_2CH_2 -, 2H), 2.53 (t, $J = 7.6$ Hz, Tephene- CH_2CH_2 -, 2H). ^{13}C NMR (125 MHz, CDCl_3 , δ): 171.31 (C=O), 148.96 (- TeCCH -), 137.85 (- HCHCTe -), 136.73 (- TeCCH -), (135.54, 128.84, 128.56, 127.7, 127.39 & 124.87, aryl), 43.58 (aryl- CH_2NH -), 39.88 (Tephene- CH_2CH_2 -), 32.33 (Tephene- CH_2CH_2 -). $[\text{M}+\text{H}]^+ = 344.02941$

Compound 1 - Proton NMR

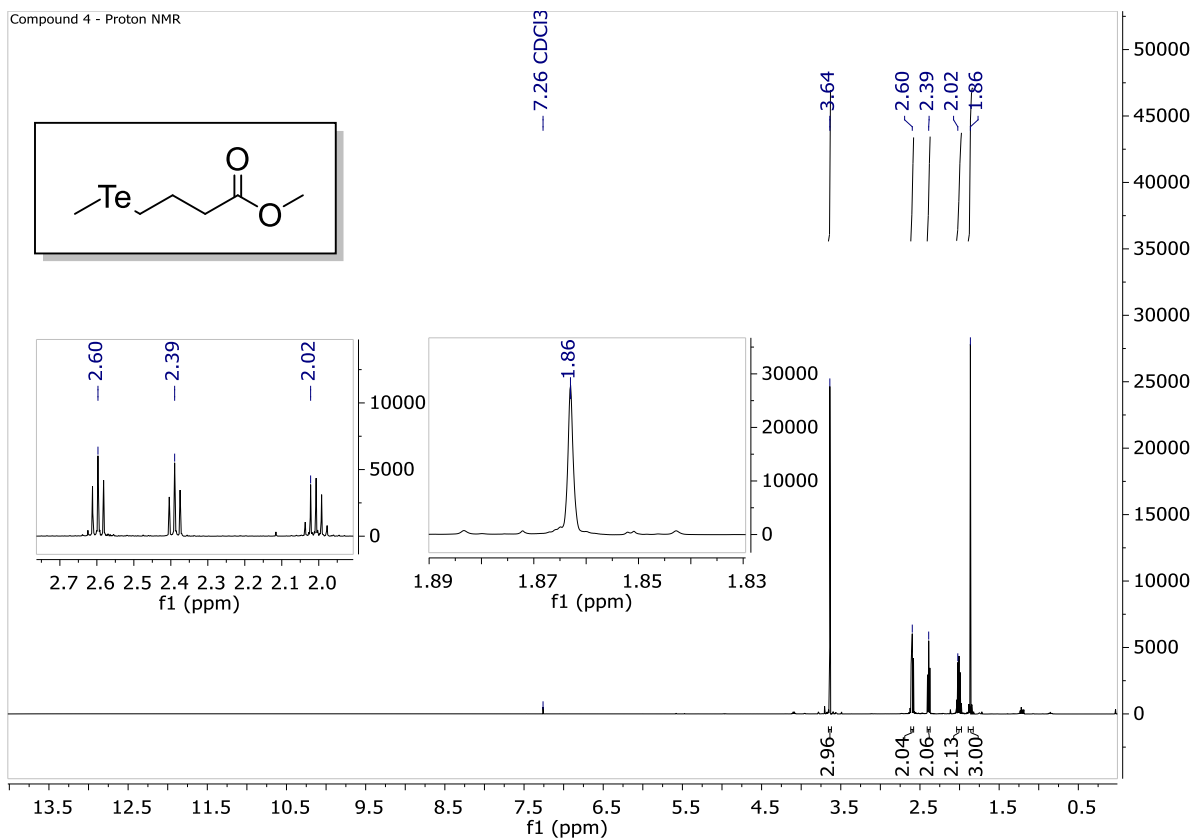


Compound 1 - Carbon NMR

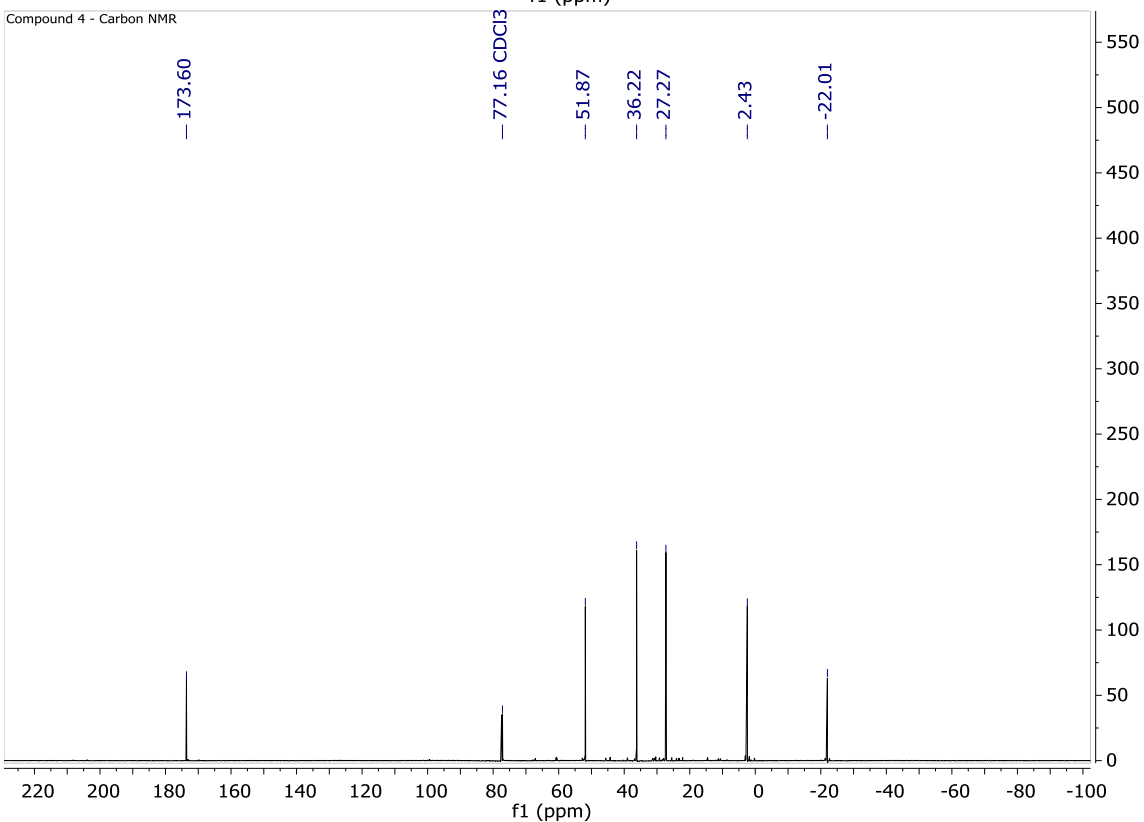




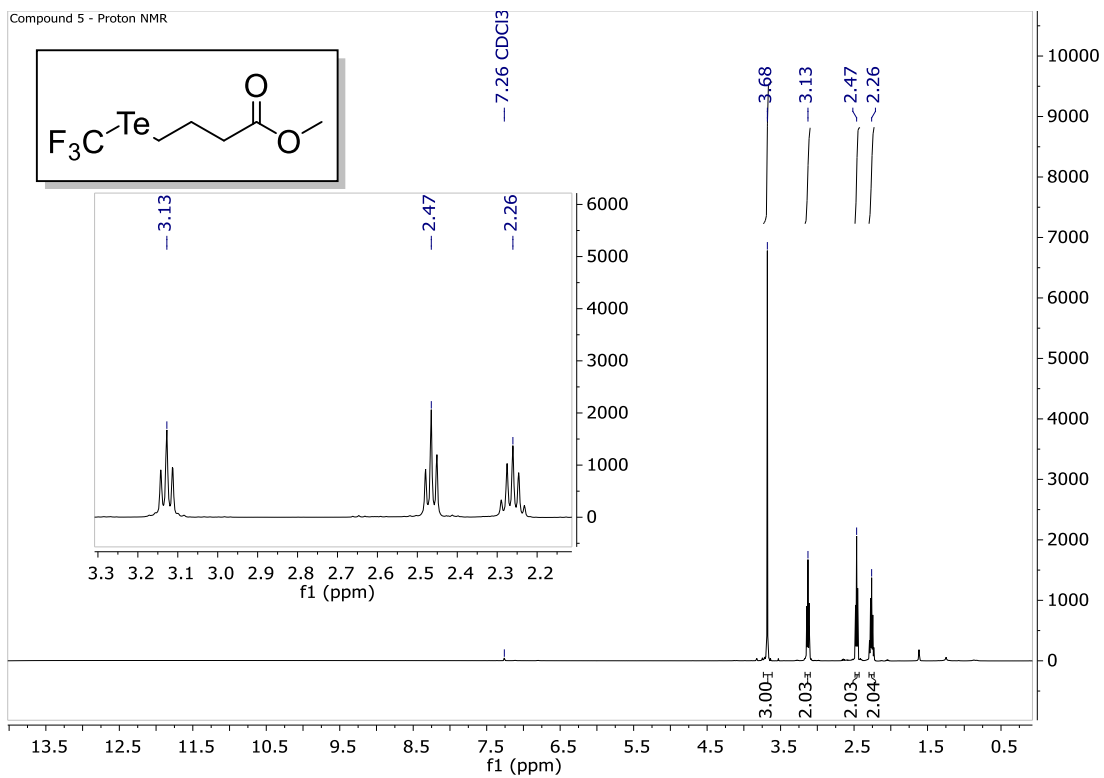
Compound 4 - Proton NMR



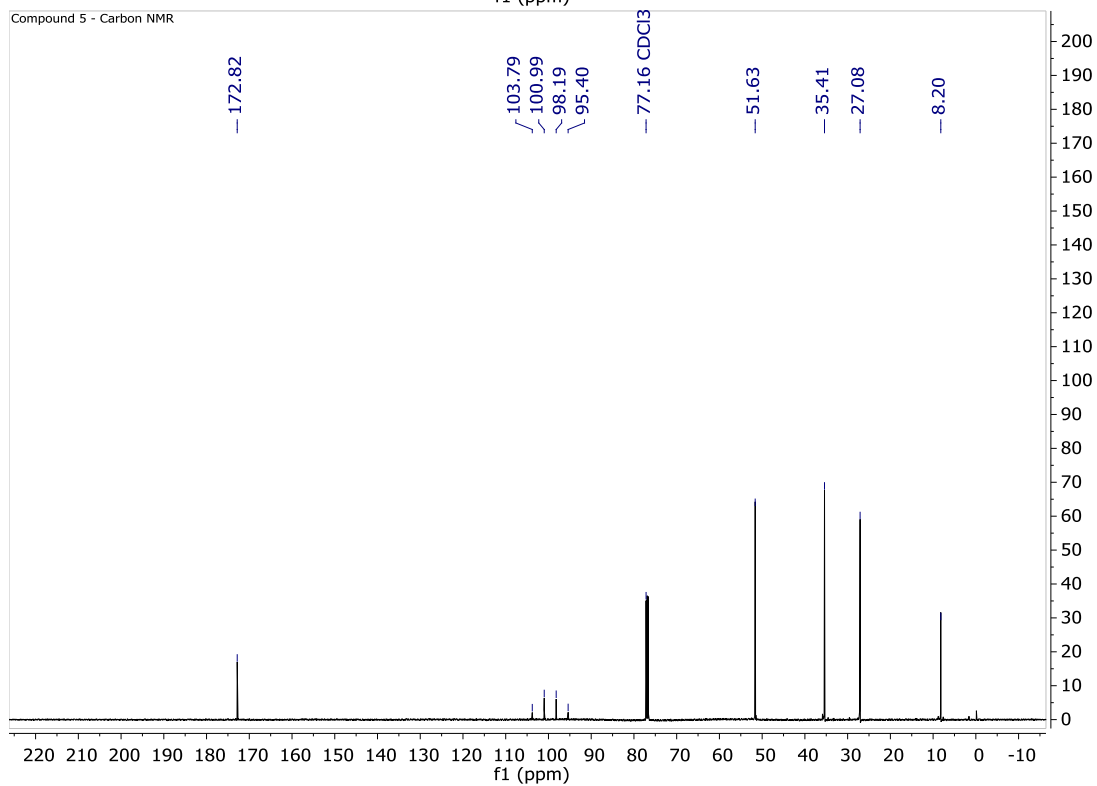
Compound 4 - Carbon NMR



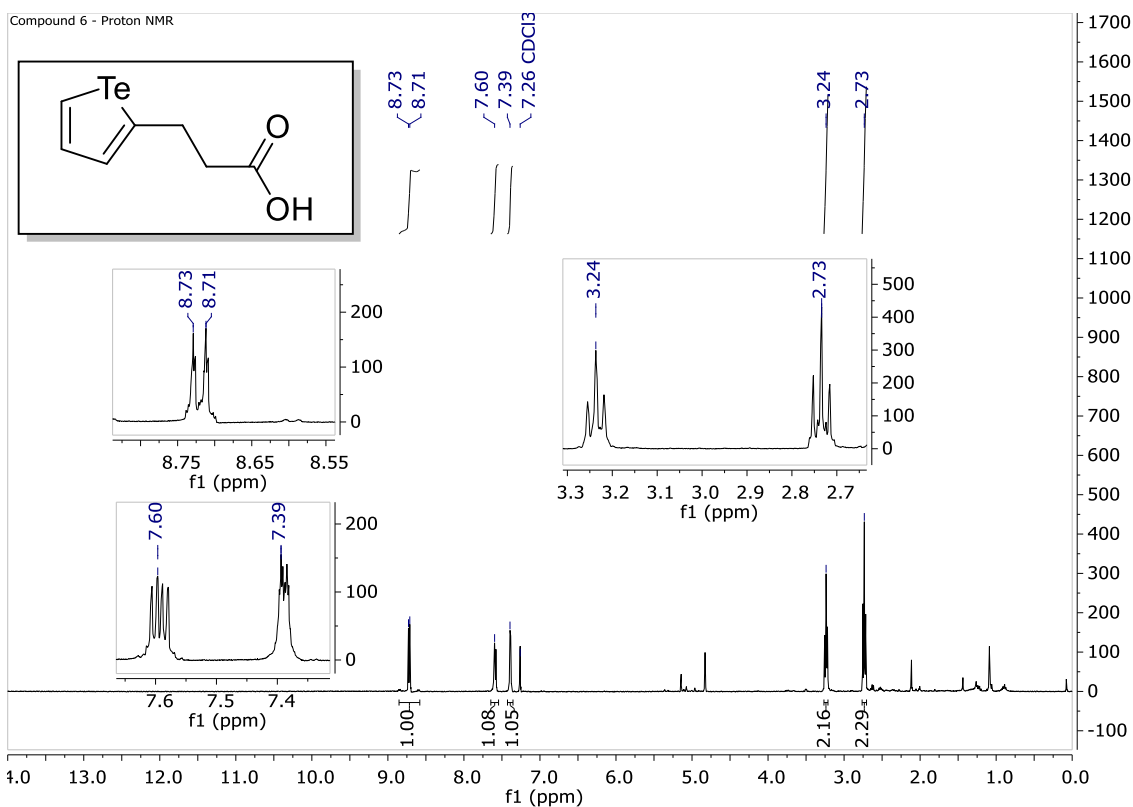
Compound 5 - Proton NMR



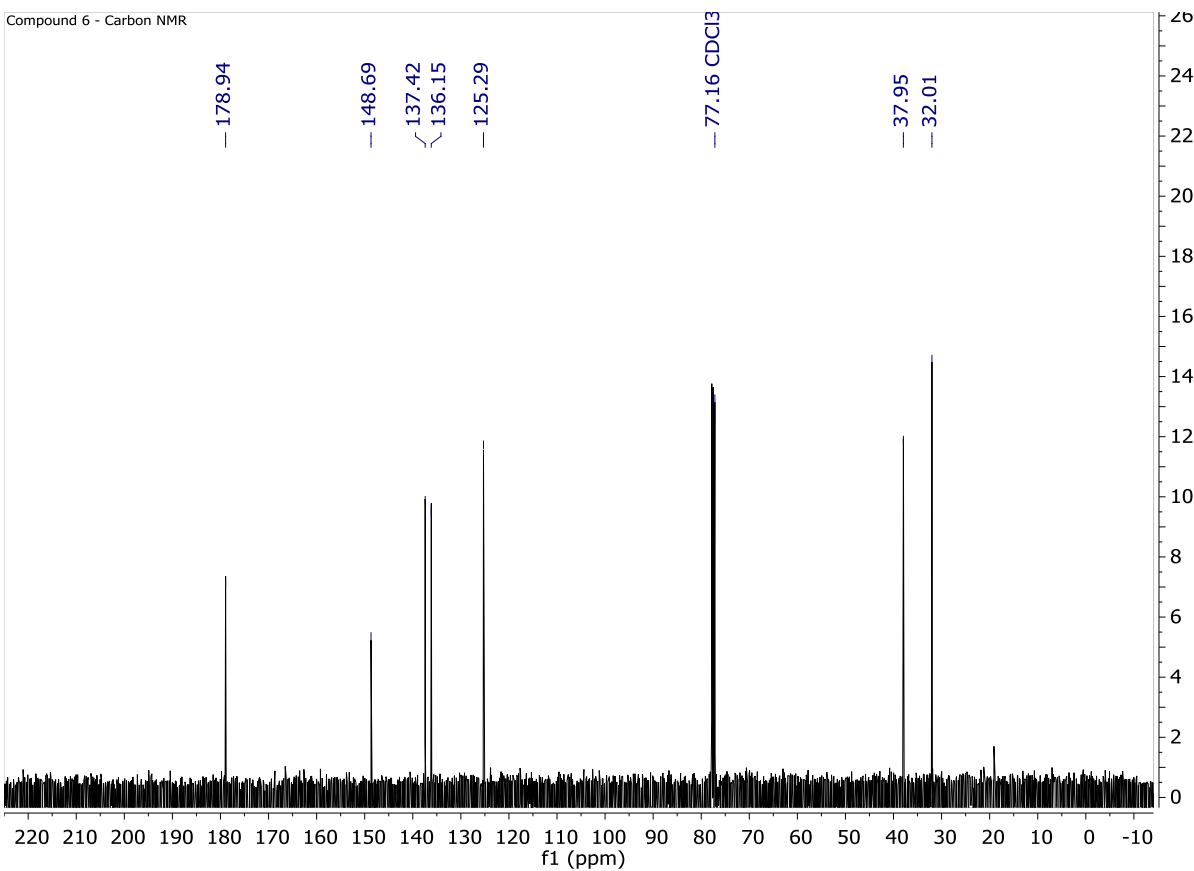
Compound 5 - Carbon NMR



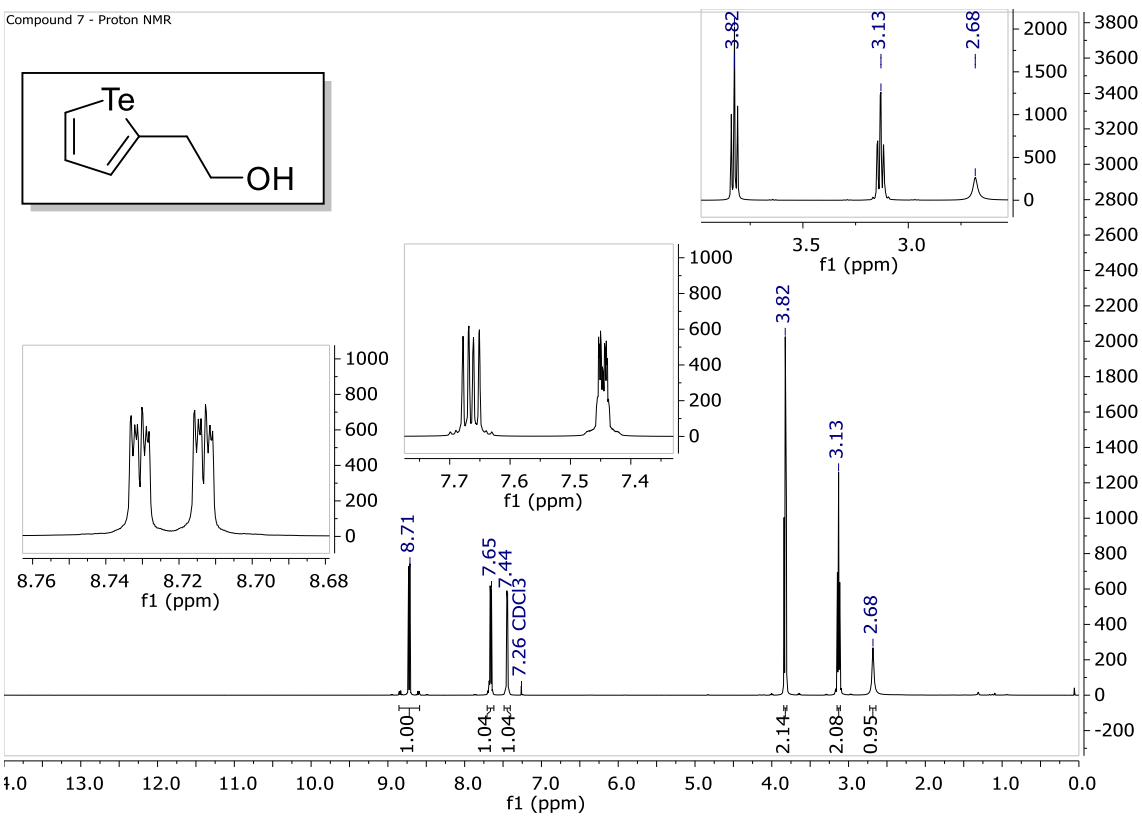
Compound 6 - Proton NMR



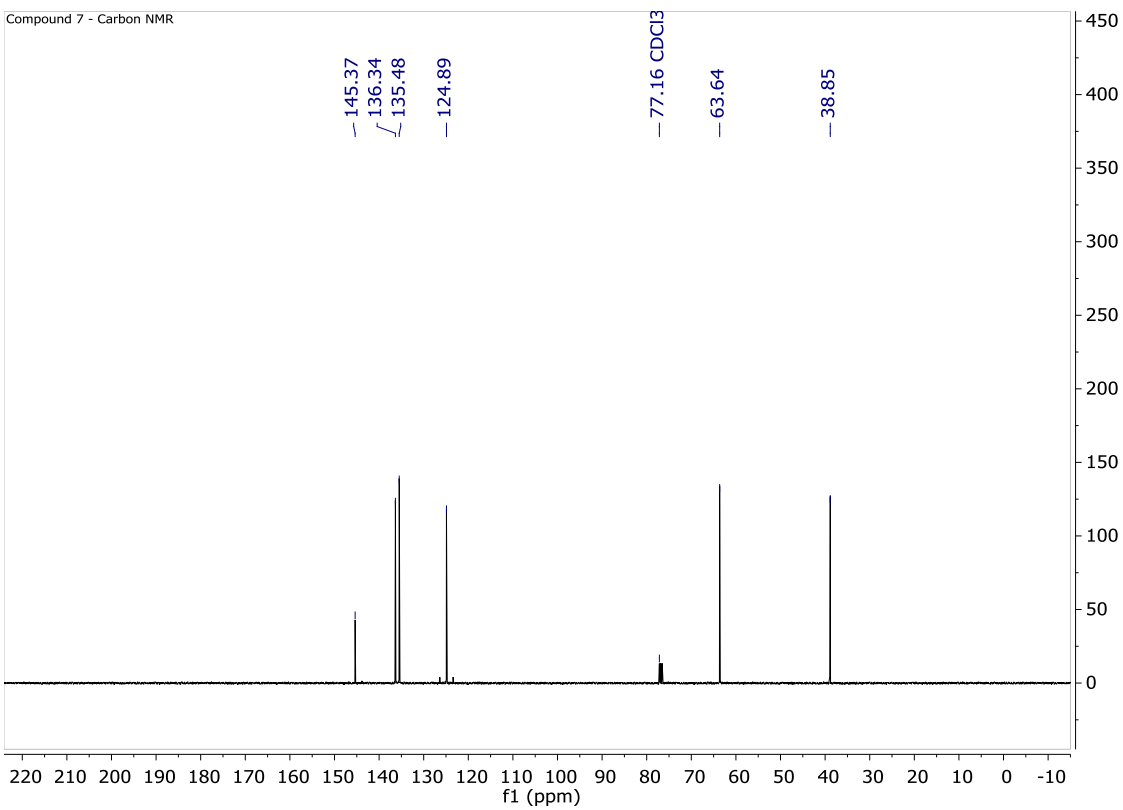
Compound 6 - Carbon NMR



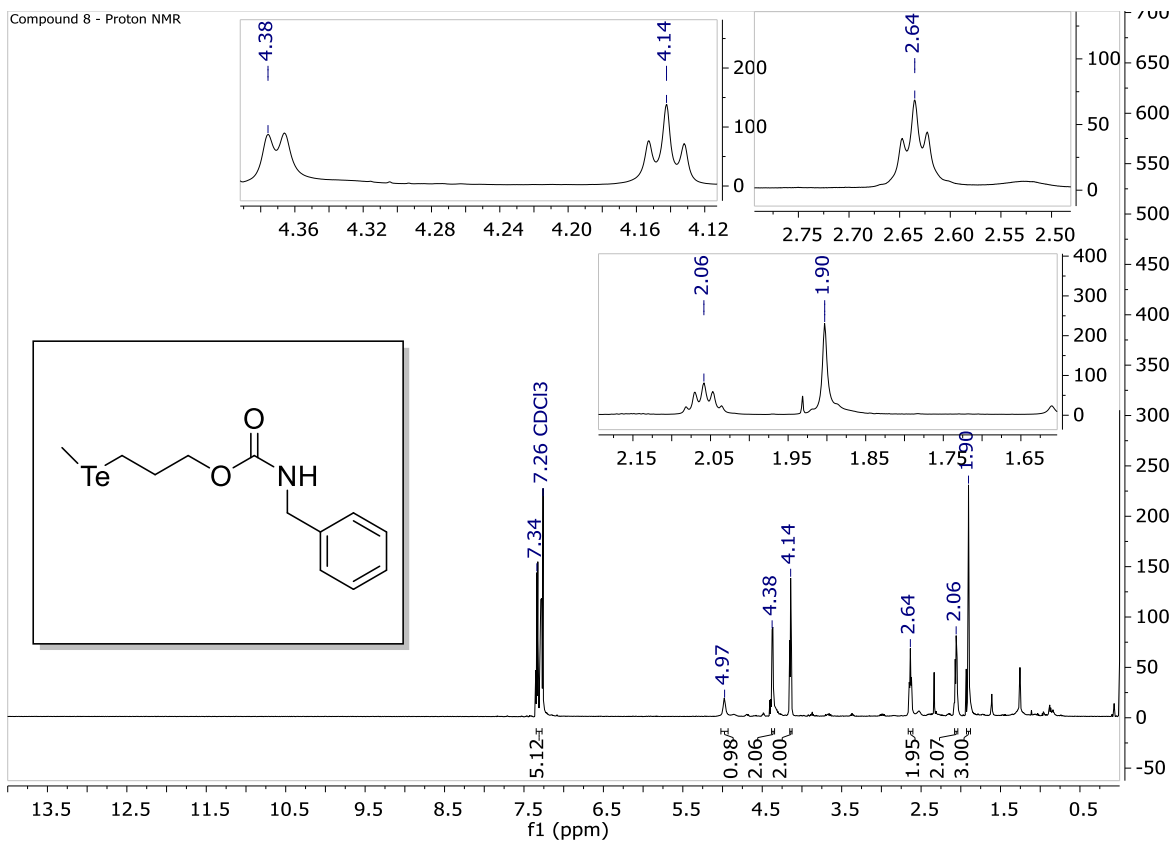
Compound 7 - Proton NMR



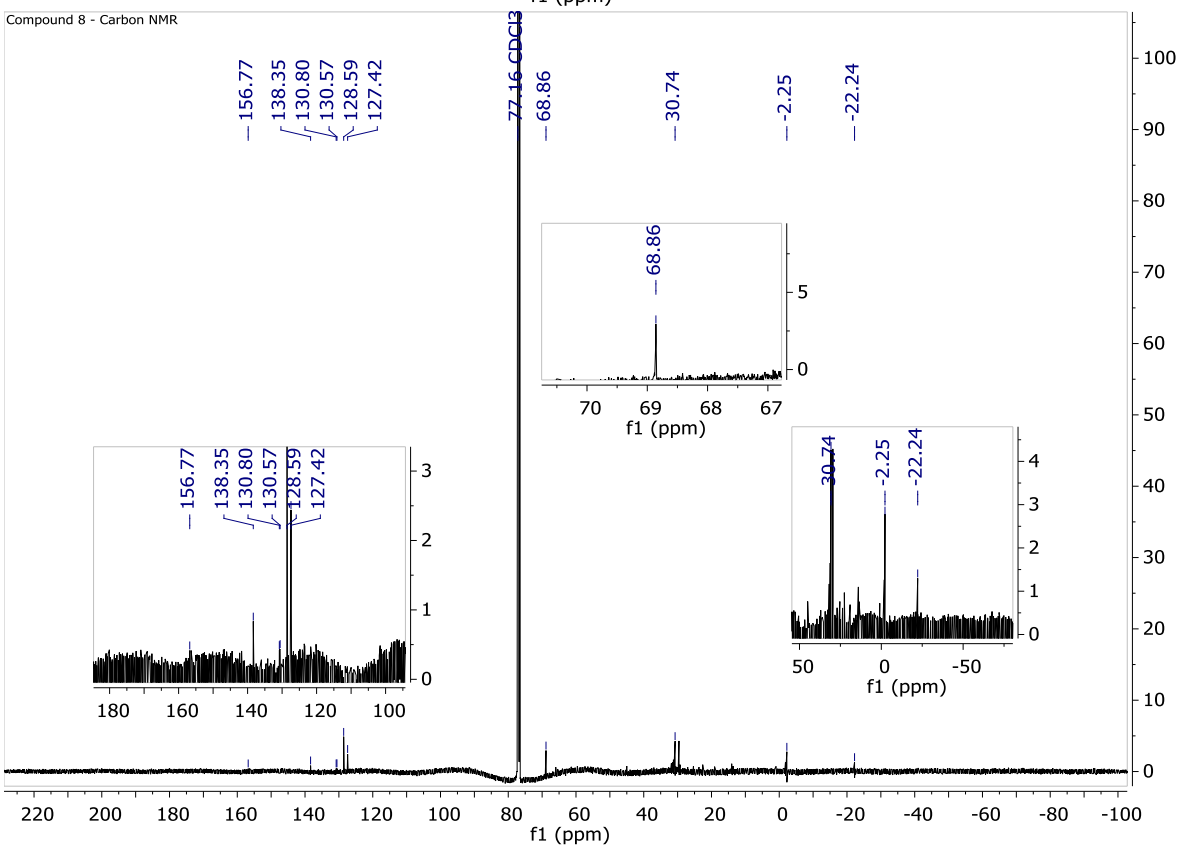
Compound 7 - Carbon NMR



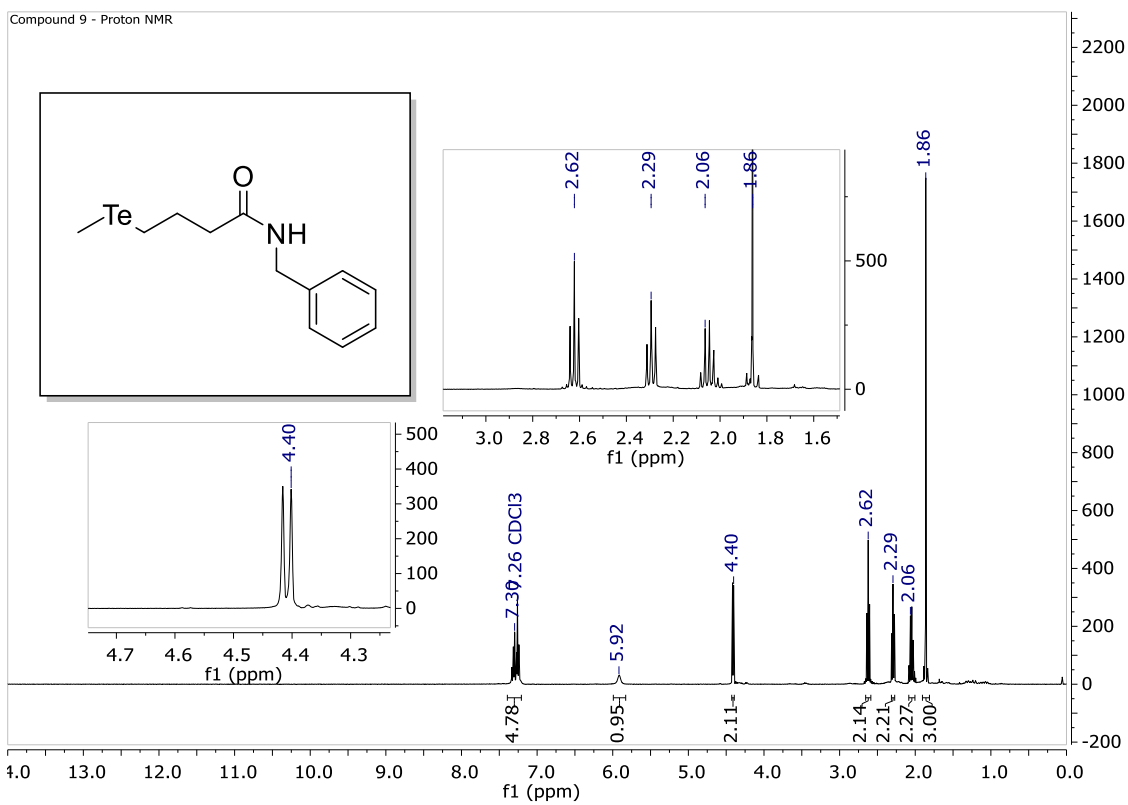
Compound 8 - Proton NMR



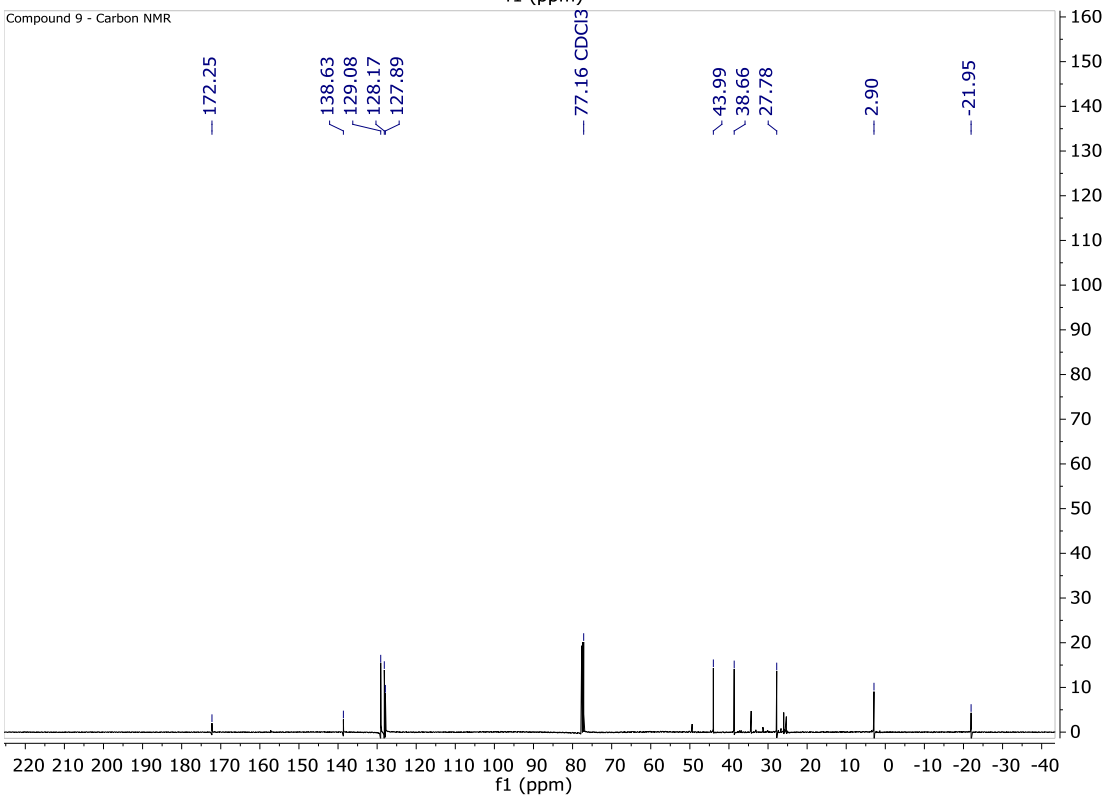
Compound 8 - Carbon NMR



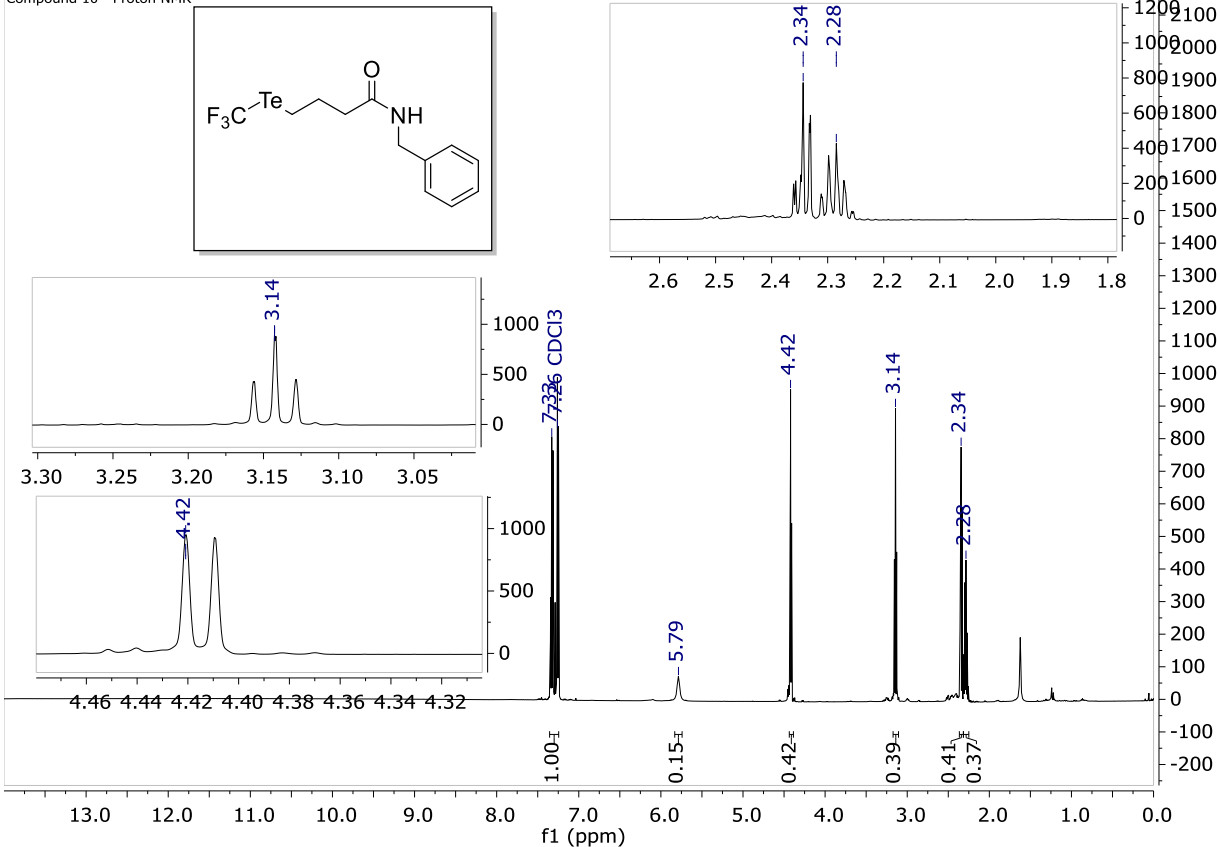
Compound 9 - Proton NMR



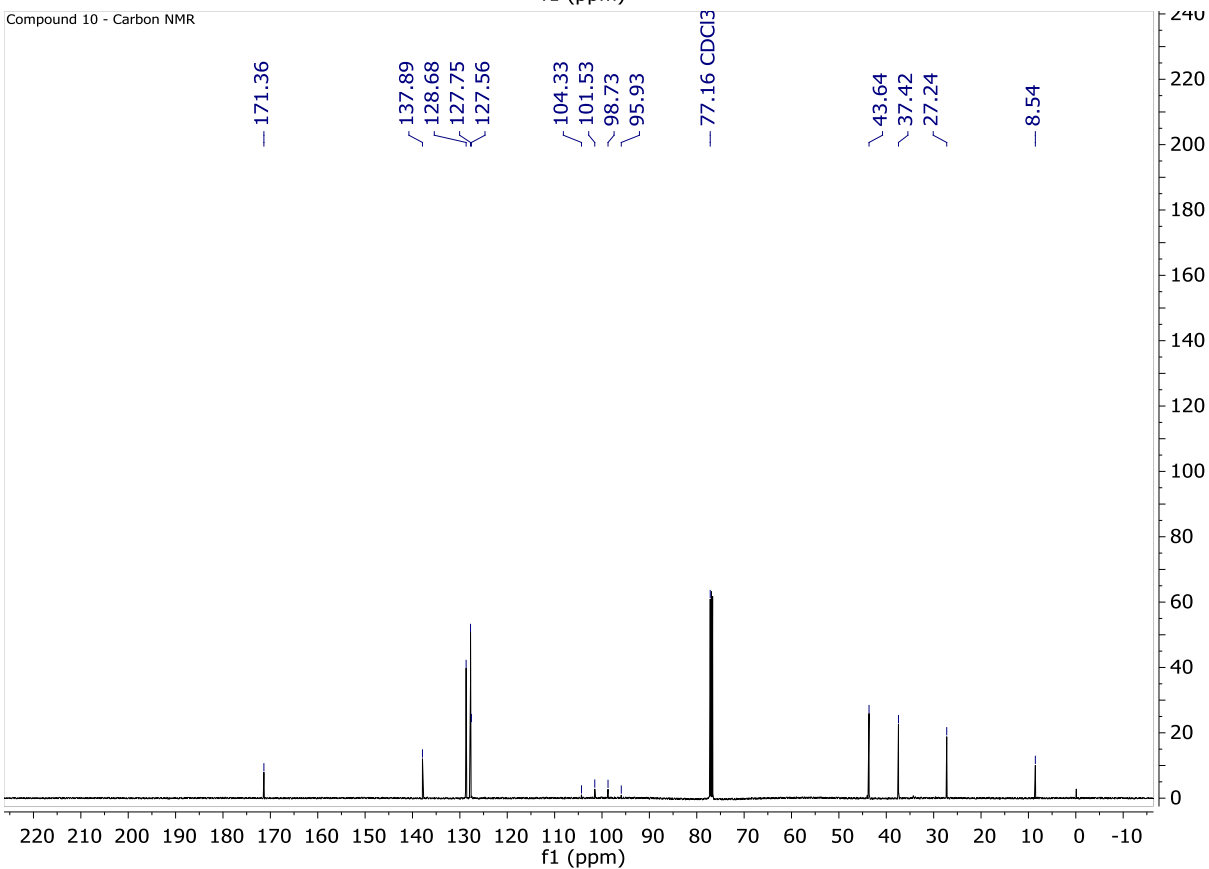
Compound 9 - Carbon NMR



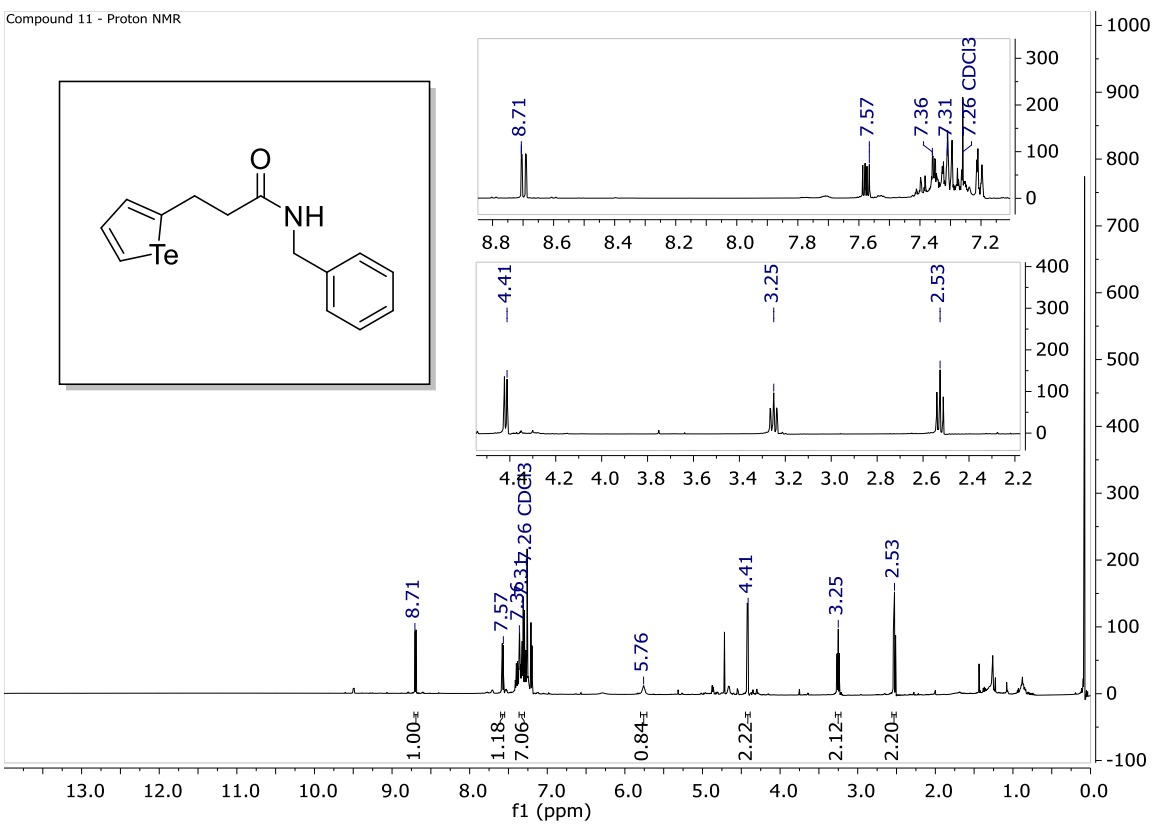
Compound 10 - Proton NMR



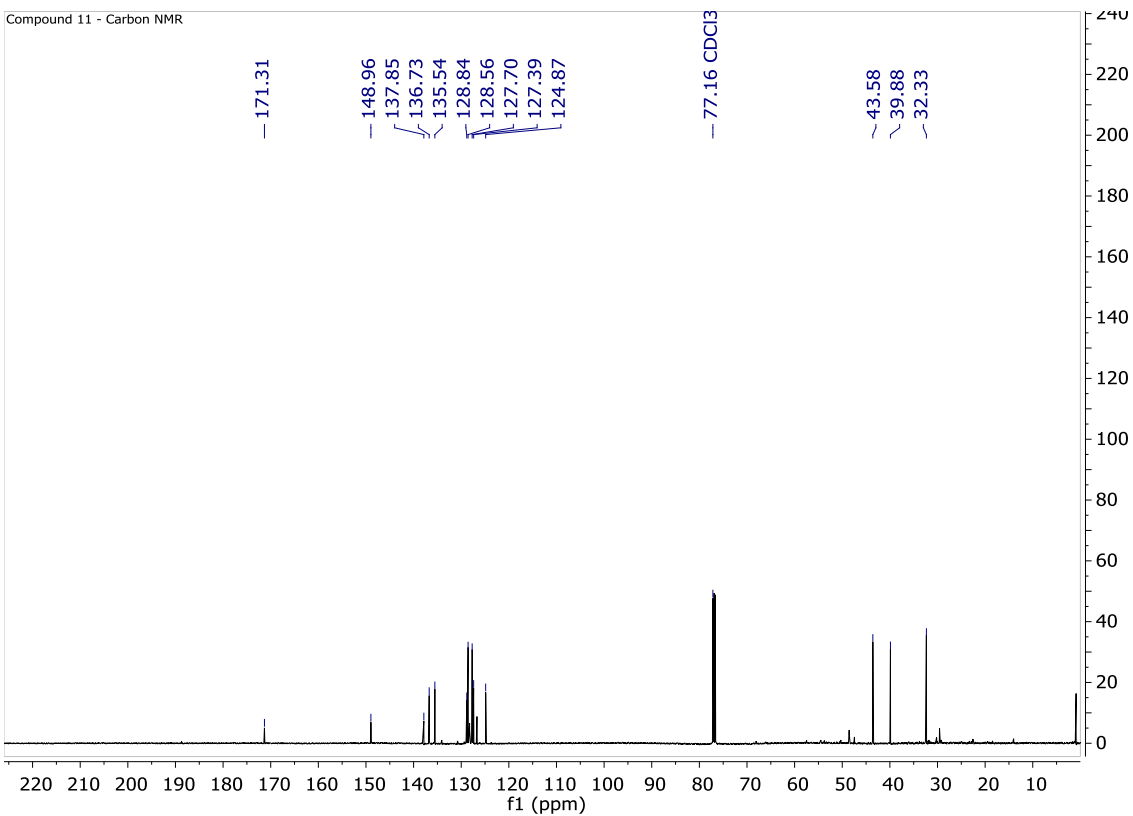
Compound 10 - Carbon NMR



Compound 11 - Proton NMR



Compound 11 - Carbon NMR



4. NMR Stability Experimental Procedures and Methods

^1H NMR Stability Experiment:

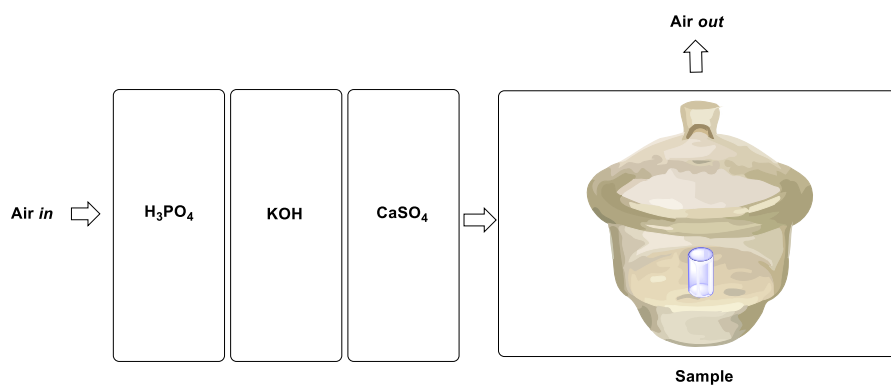
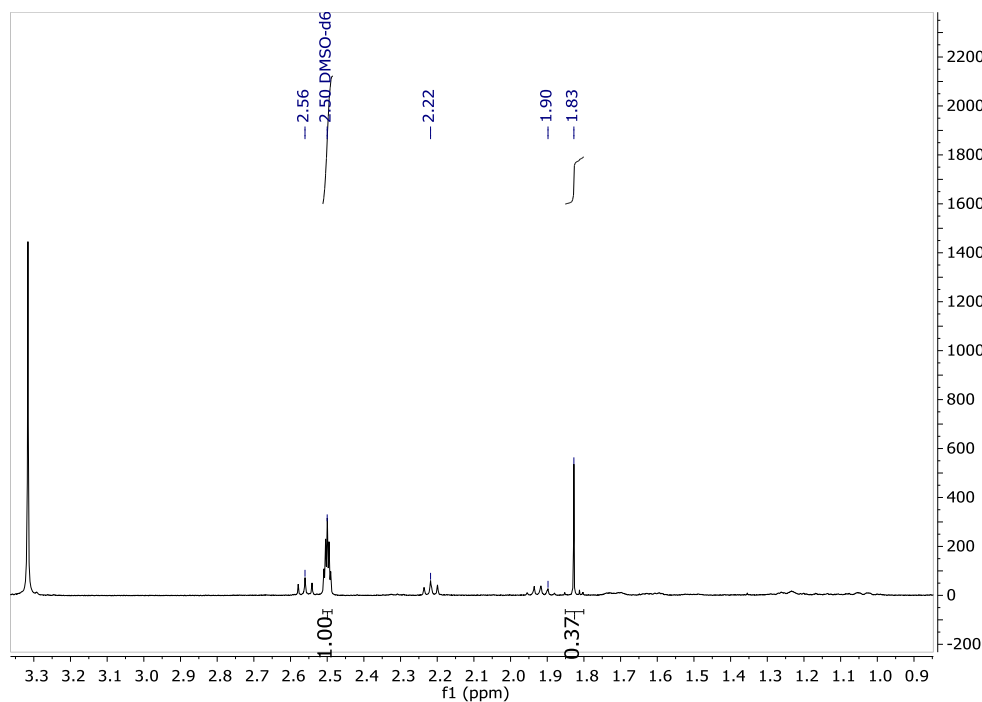


Figure 1. Experimental Set Up: House air was filtered using phosphoric acid, potassium hydroxide and calcium sulfate to remove moisture. Each sample was contained inside a desiccator. The desiccator was maintained moisture by spreading a layer of calcium sulfate on the bottom.



$$i_{\text{standard}} = 1, i_x = 0.37$$

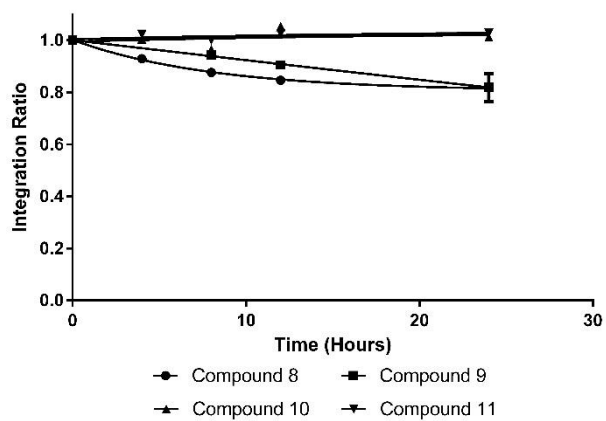
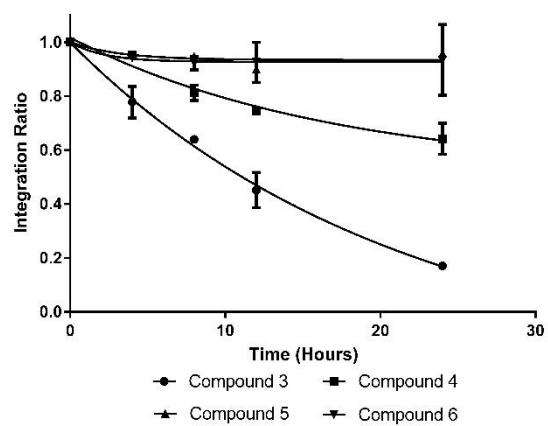
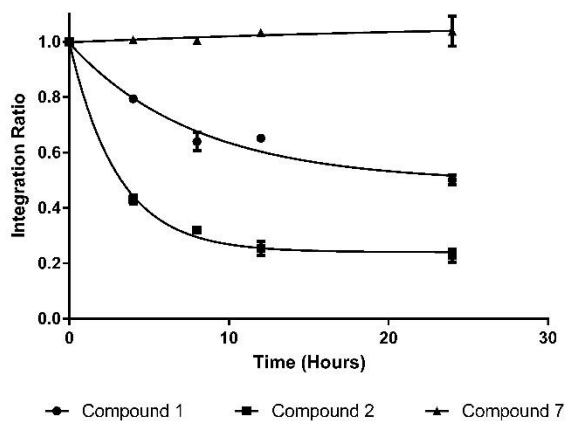
Figure 2. NMR Analysis Example: All values obtained from the NMR calculations were normalized to 1 for plotting.

4. NMR Experimental Procedure:

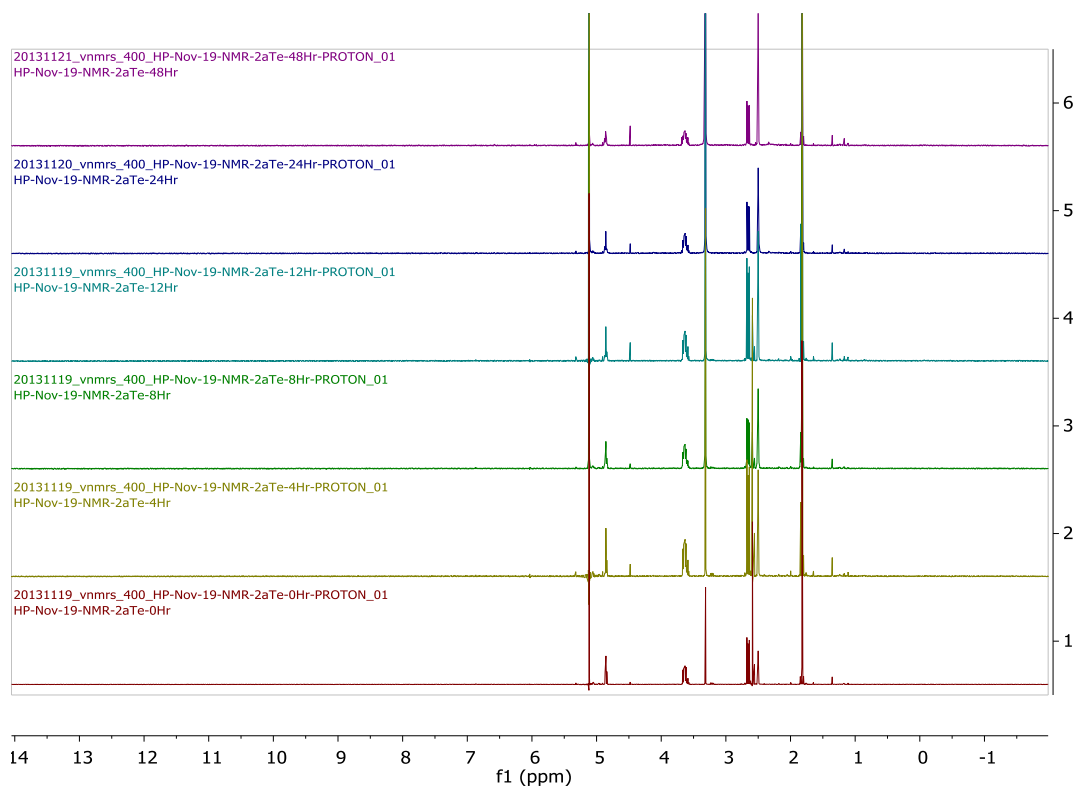
The organotellurium compound of study was dissolved in d6-DMSO in a relative 3:1 concentration ratio with 1,3,5 – trioxane, the secondary internal standard of study. The compounds were kept in 20 mL vials sealed with parafilm. The film layer was punctured 4 times to create 4 small holes for oxygen to enter. The vials were kept in a moisture free environment for 24 hours. House air was filtered using sulfuric acid, potassium hydroxide and calcium sulfate to remove moisture. Each sample was contained inside a clear glass desiccator. The desiccator was maintained moisture free by spreading a layer of calcium sulfate on the bottom. No efforts were made to exclude ambient light. Aliquots were taken from each sample and ^1H NMR was taken at 0, 4, 8, 12 and 24 Hours. An organotellurium proton signal that could be integrated with confidence and the DMSO absorbance at 2.5 ppm were integrated. The ratio between the DMSO and the organotellurium protons were normalized to 1 generate a degradation plot $s(i/i_{\text{std}})$.

Experimental error was calculated taking into consideration the confidence of integration. Each NMR peak was integrated to its minimum value ($X_{\text{ppm}}-Y_{\text{ppm}}$) centered on the peak of interest. The confidence of integration was taken by taking a second integration of ($X_{+0.01\text{ppm}}-Y_{\text{ppm}}$) and a third integration of ($X_{\text{ppm}}-Y_{\text{ppm}-0.01\text{ppm}}$). Taking the error of deviation of these three values takes into consideration potential integration bias, integration changes that may arise from instrumental drift and peak broadening due to the observed precipitates.

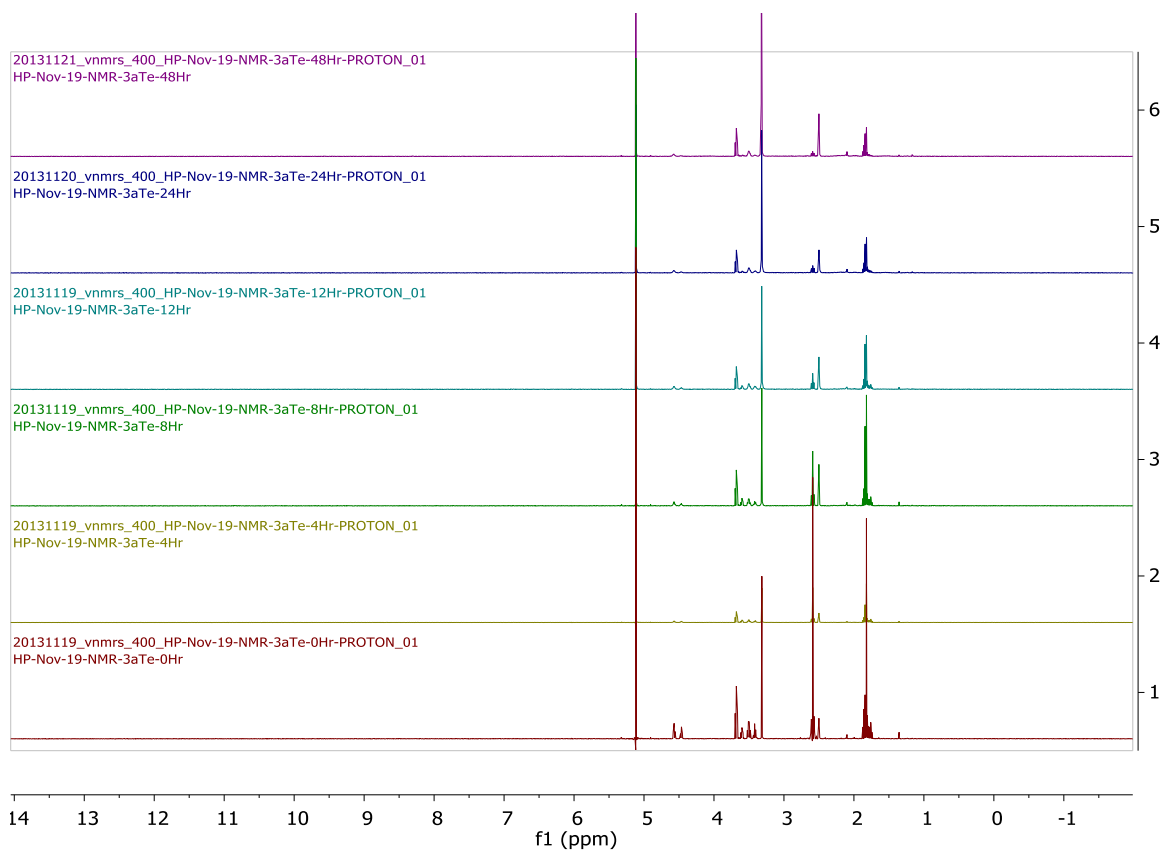
Degradation Plots:



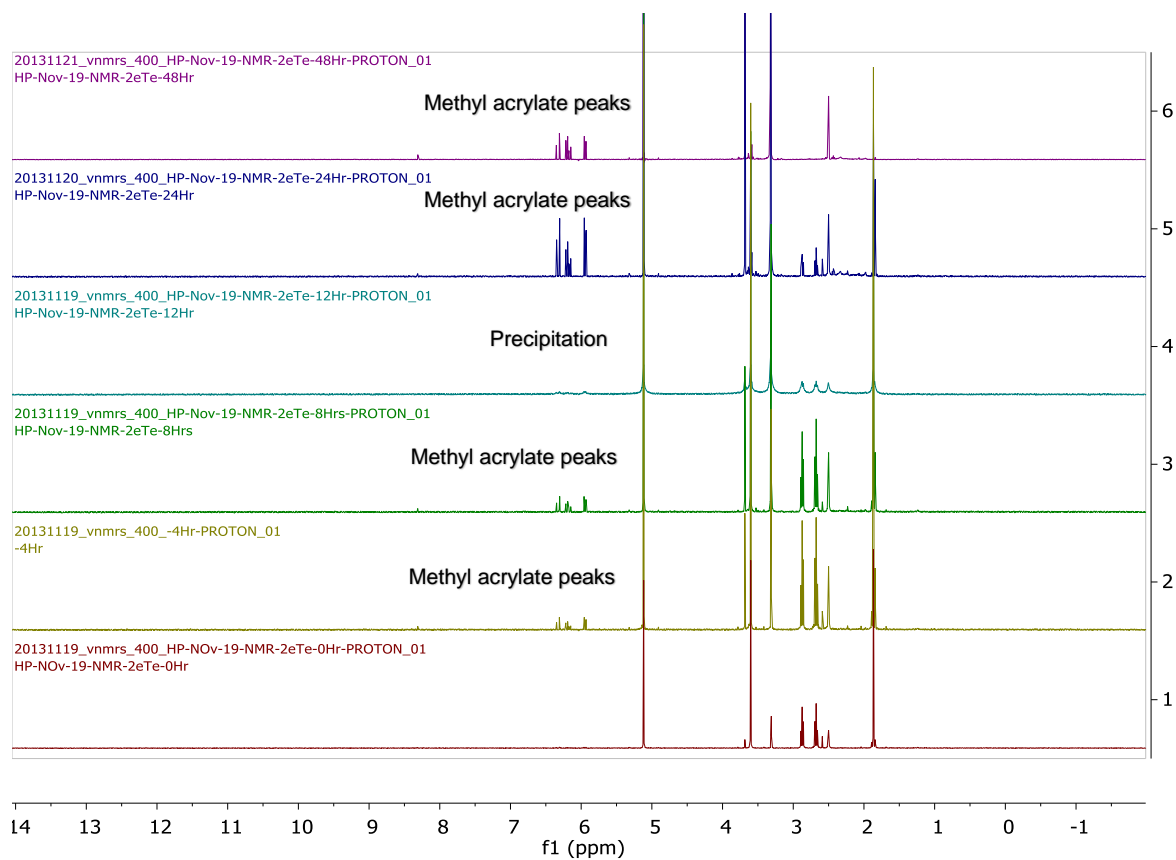
Stacked Preliminary NMR Plots:



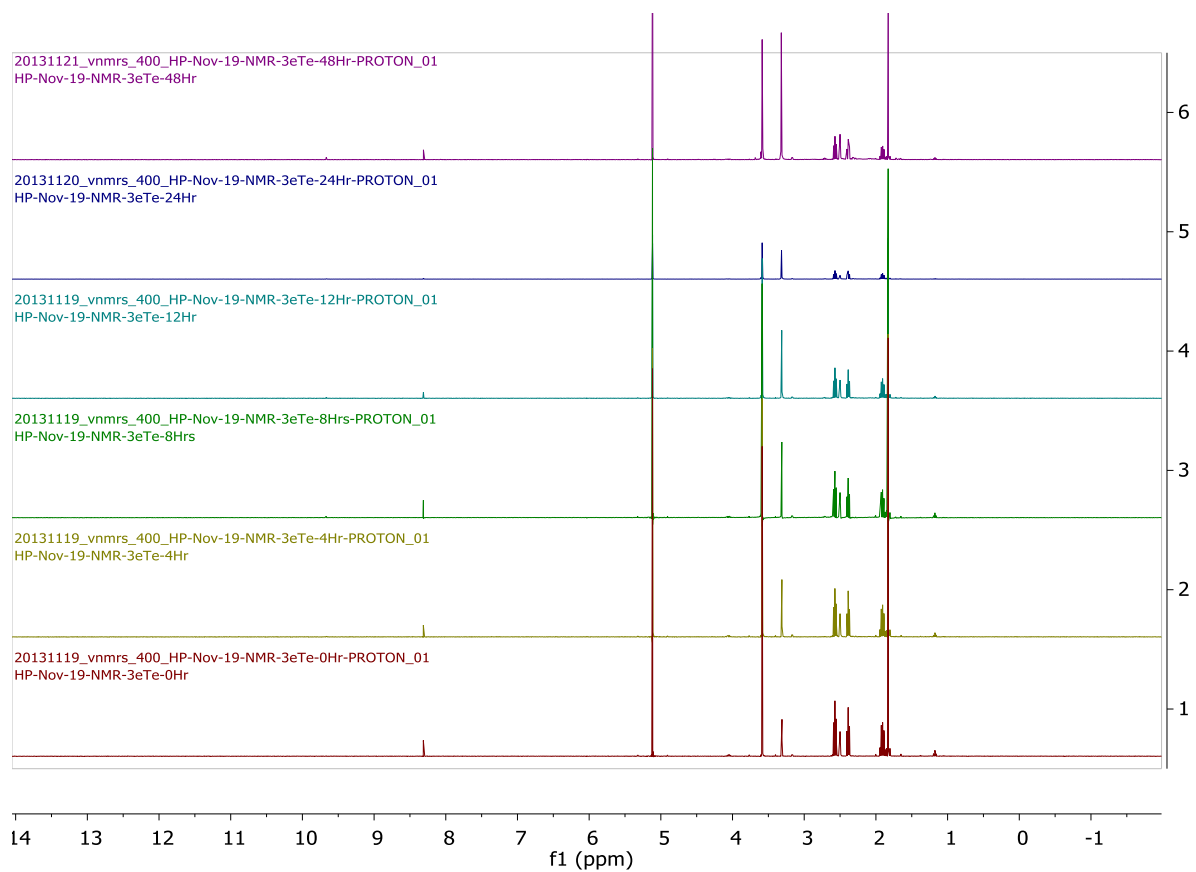
Compound 1.



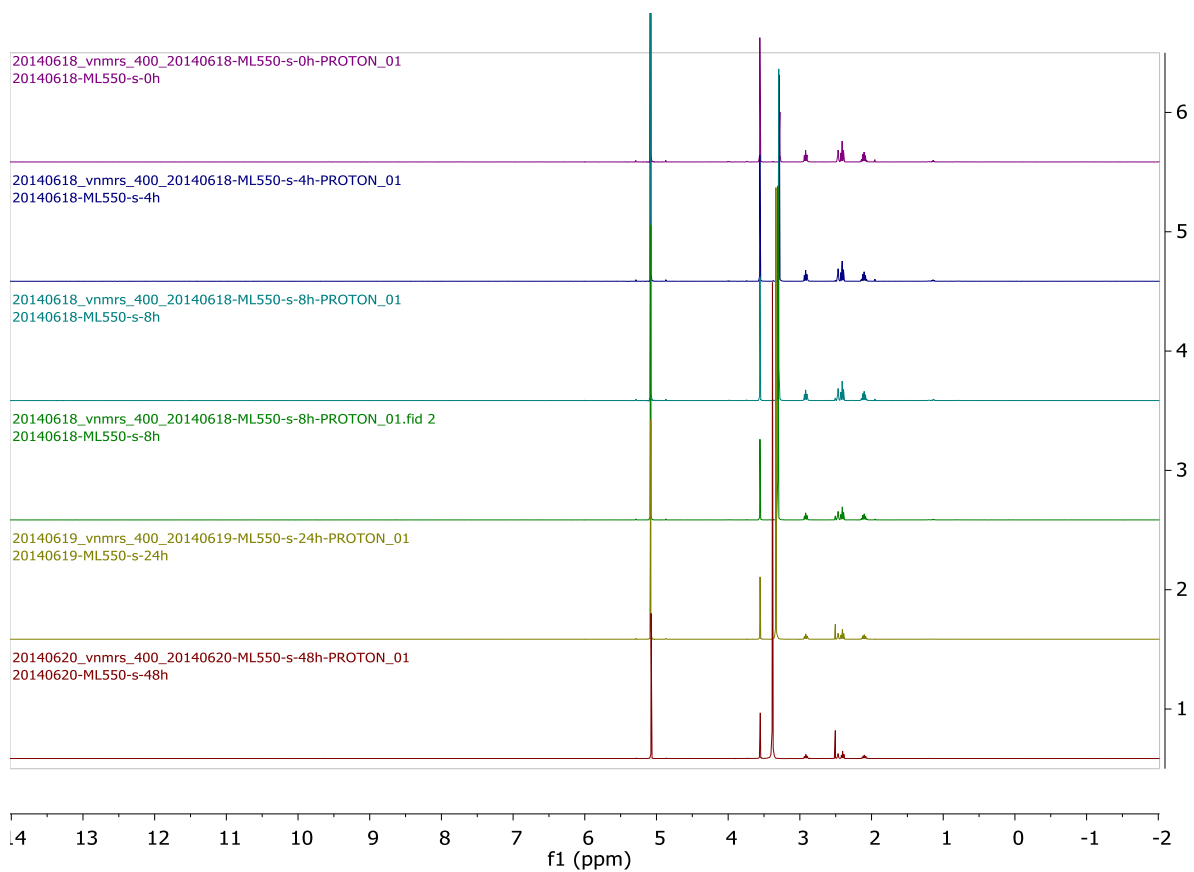
Compound 2.



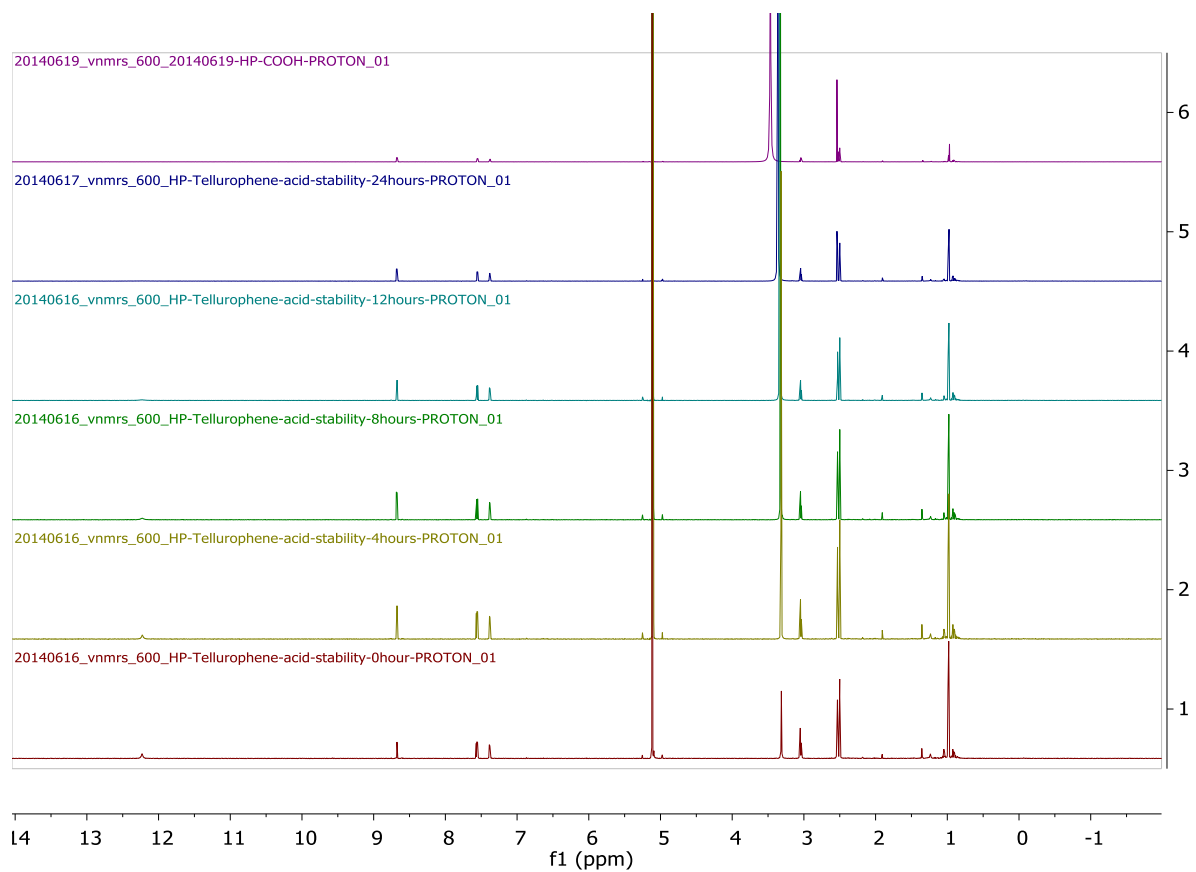
Compound 3.



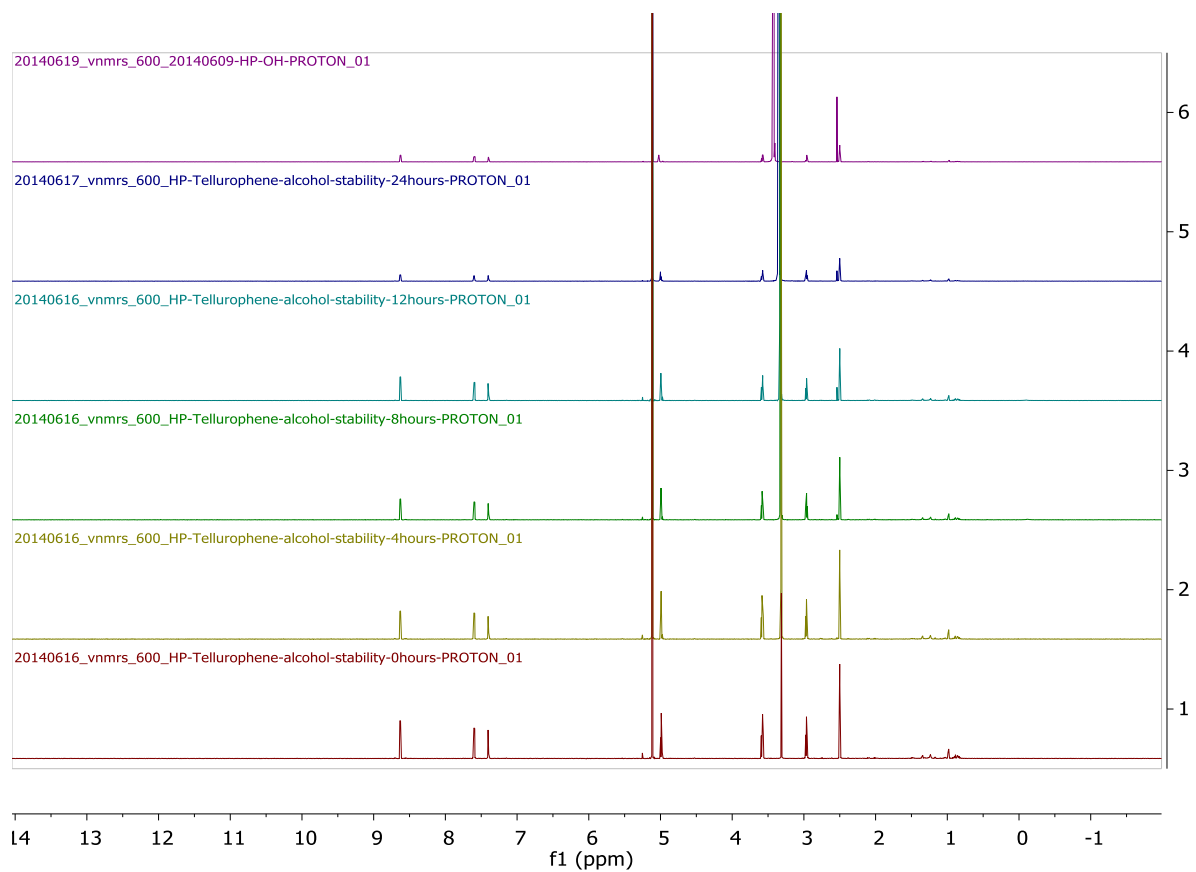
Compound 4.



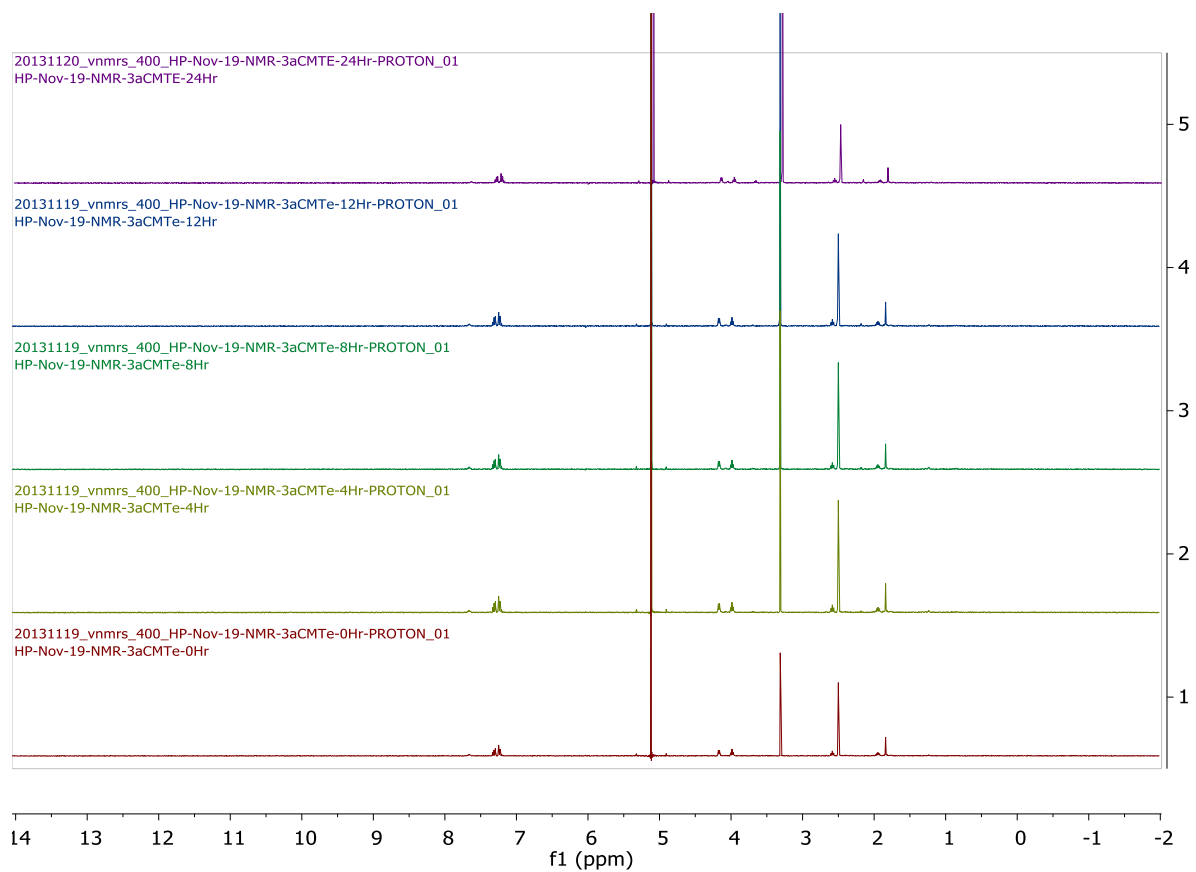
Compound 5



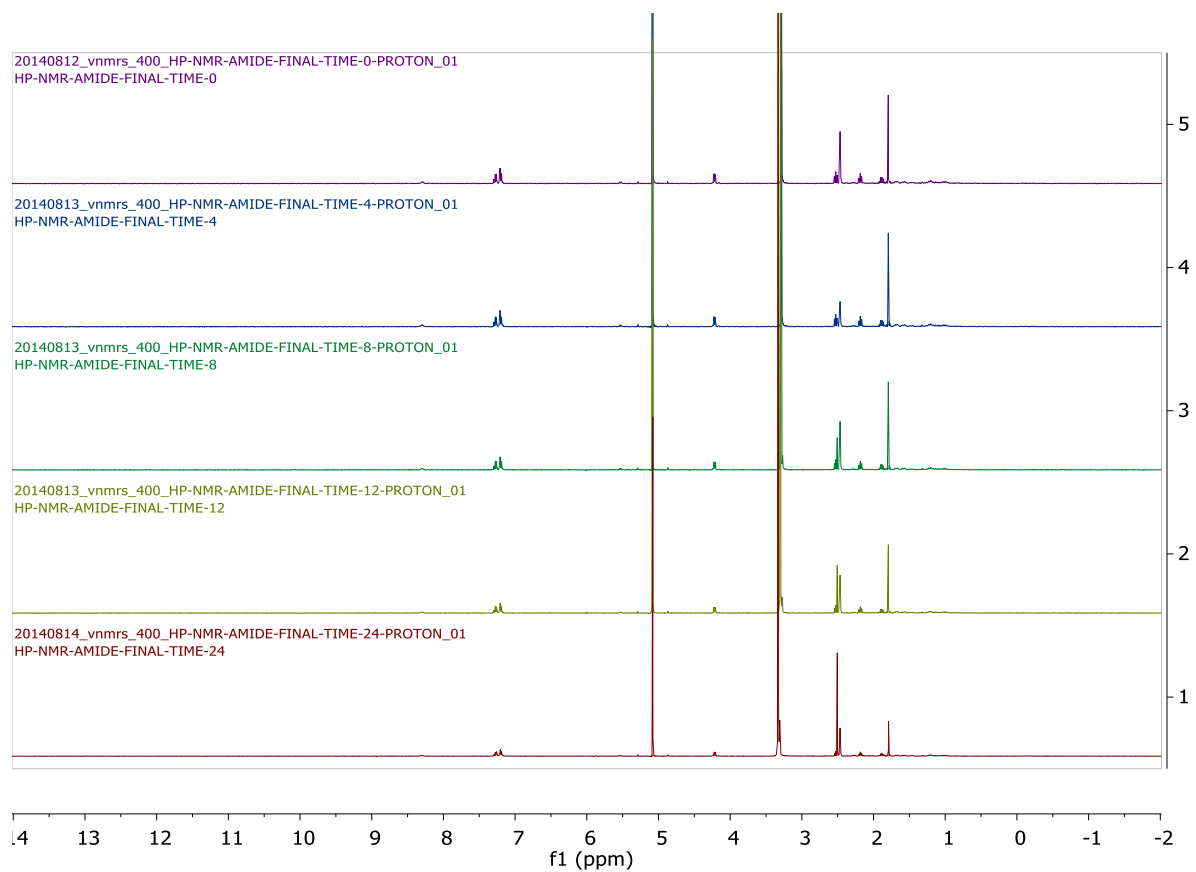
Compound 6



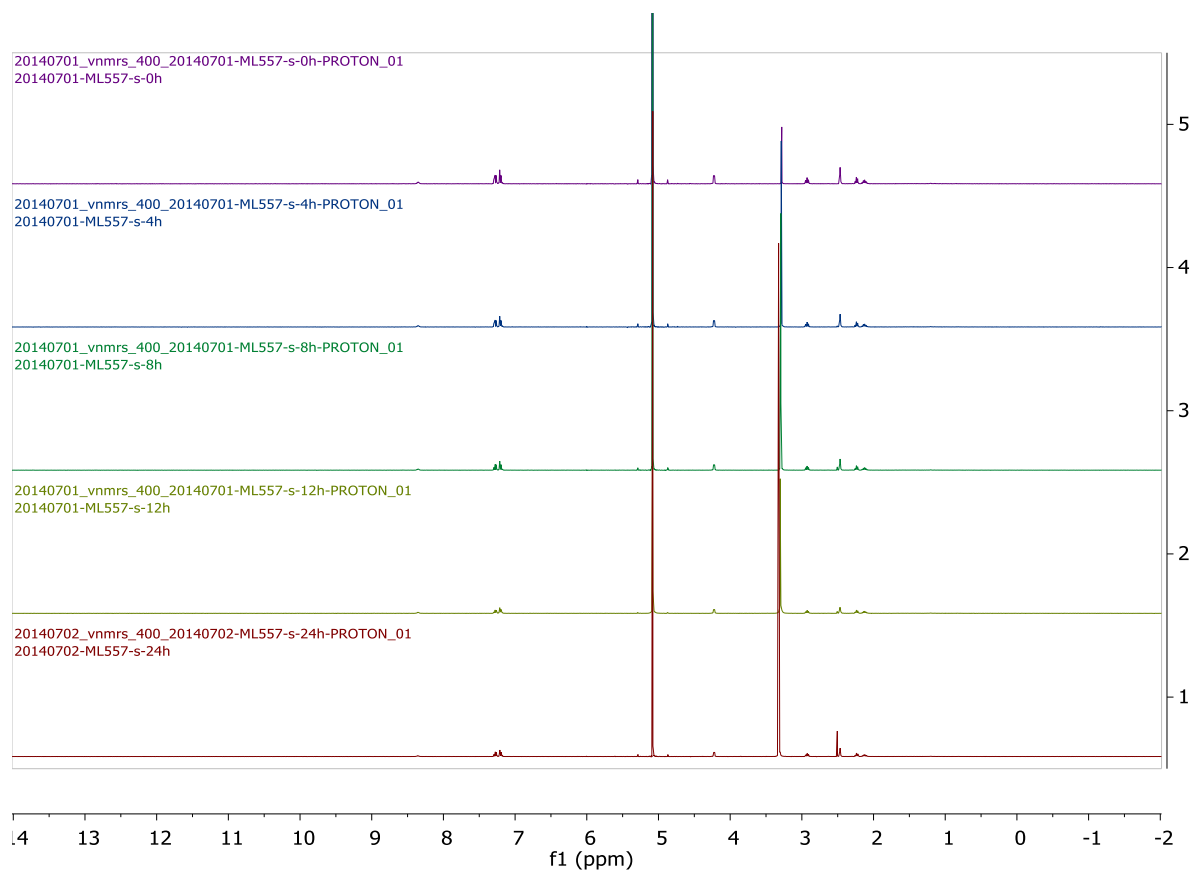
Compound 7



Compound 8

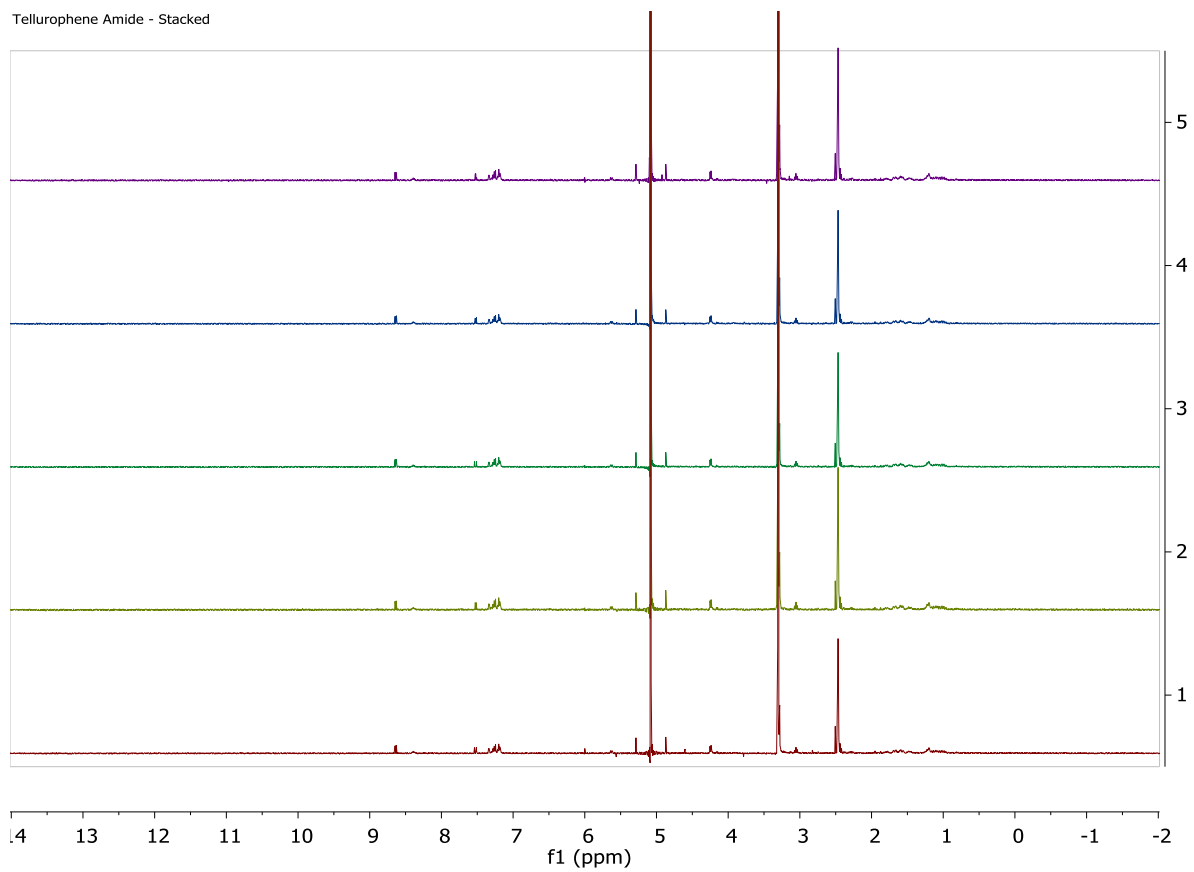


Compound 9



Compound 10

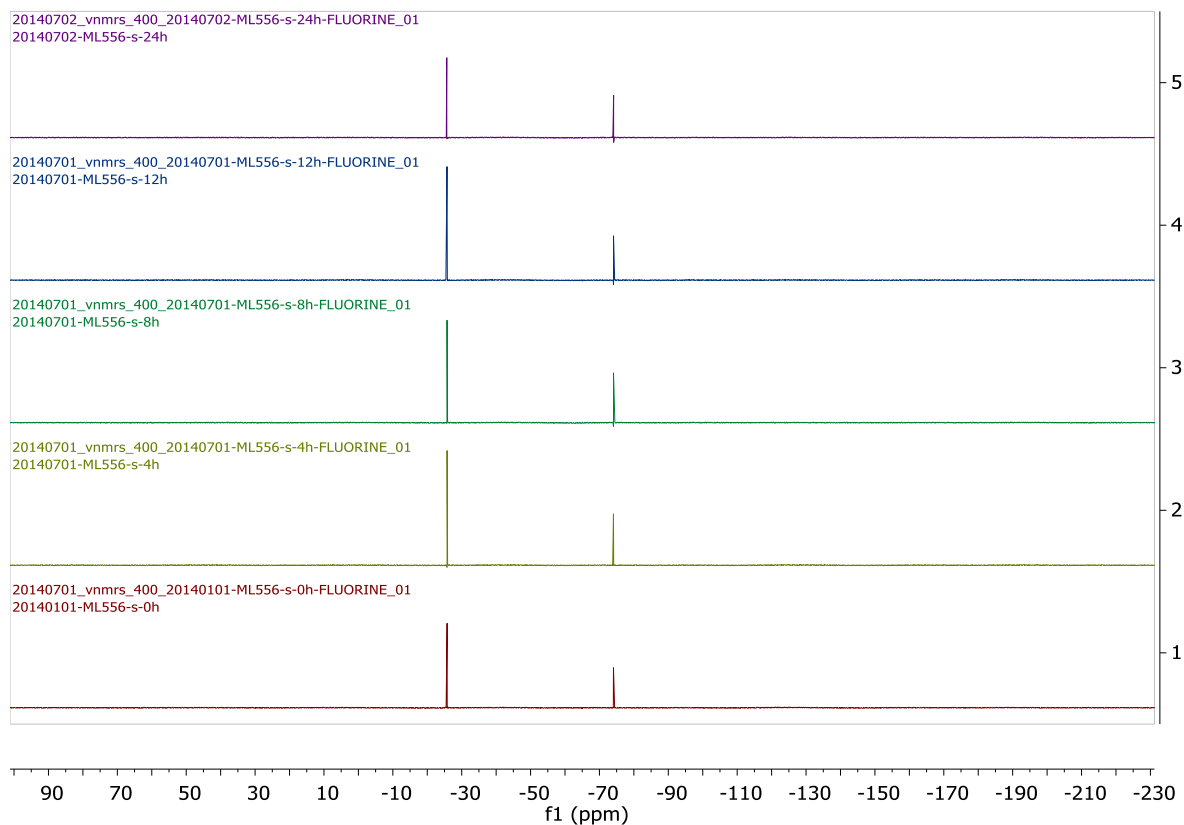
Tellurophene Amide - Stacked



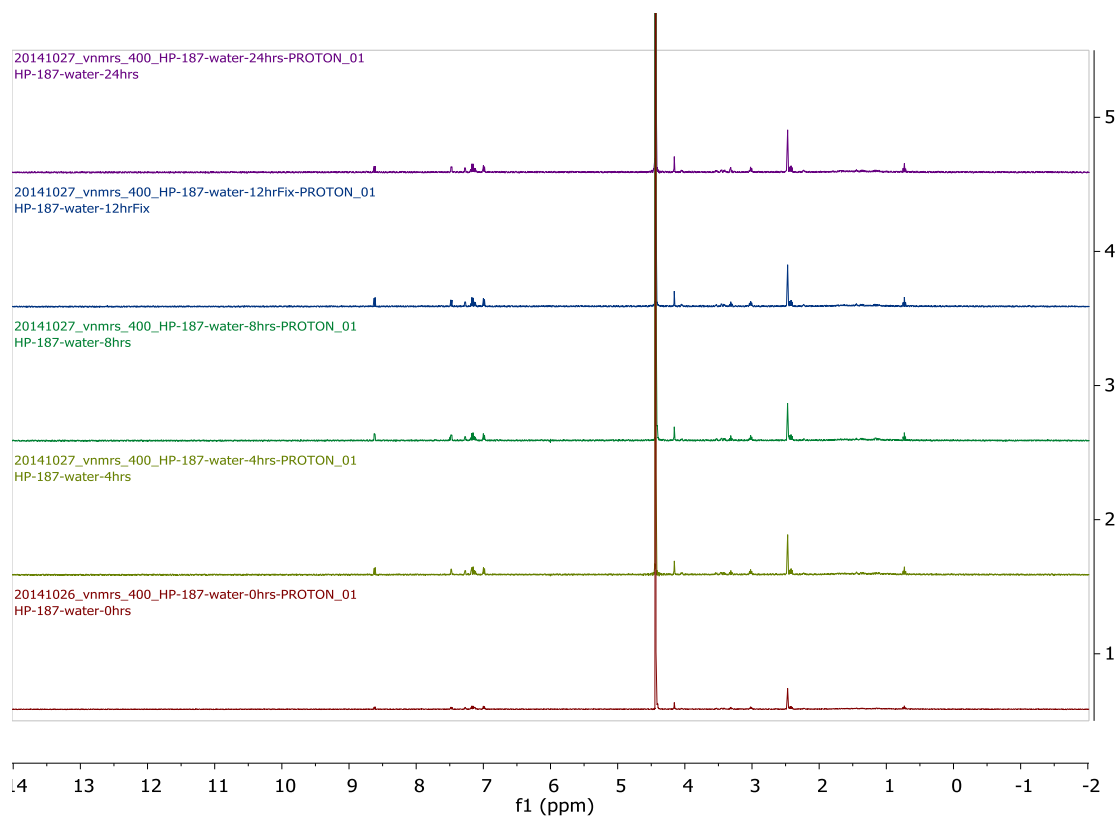
Compound 11

NMR Stability Experiment in PBS Buffer:

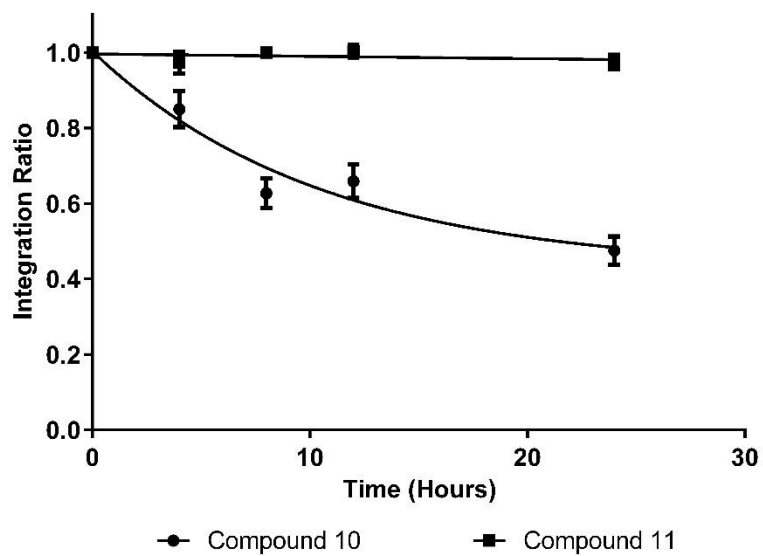
Compounds **10** and **11** were dissolved in a 50/50 v/v ratio of *d*-DMSO/*d*-PBS solution. The compounds were exposed to atmosphere and light at room temperature. Aliquot NMR spectra were taken at 4 hour intervals until the 12 hour time frame and a final 24 hour time point NMR was taken. ^{19}F NMR was taken for compound **10** where fluoroacetic acid was used as the internal standard, and ^1H NMR was taken for compound **11** where DMSO was used as the internal standard. *d*-PBS was made using D_2O .



Compound **10**



Compound 11



5. Biological Methods and Experiments:

WST – 1 Assay Protocol:

Jurkat cells were maintained in RPMI media supplemented with 10% (FBS) at 37°C with 5% CO₂. Each compound was dissolved in DMSO at 100 mM to generate a stock solution, which was used immediately. Compounds were diluted in fresh media to 2-8 mM, depending on the solubility of the compound, and then two-fold serial dilutions were prepared in media. In 12-well plates, 250 μ L of diluted compound was mixed with 250 μ L Jurkat cells at 10⁶ cells/mL and incubated at 37°C for 24 h. Cell viability was measured using the WST-1 reagent (Roche Diagnostics, Laval, Quebec) as per manufacturer's instructions.

LD₅₀ Curves of 8-11:

