

Supporting Information

Copper-Catalyzed Radical Selenodifluoromethylation of Alkenes: Access to CF₂-Containing γ -Lactams

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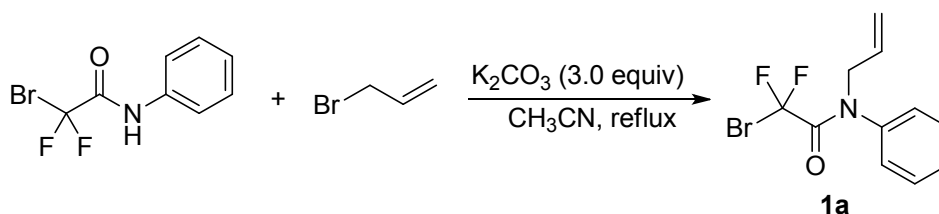
I. General Remarks:

All reagents were purchased from commercial sources and used without further treatment, unless otherwise indicated. All reactions were run under air with no precautions taken to exclude moisture. ^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded at 25 °C on a Varian (400 MHz, 100 MHz and 376 MHz). Melting points were obtained with a micro melting point XT4A Beijing Keyi electrooptic apparatus and are uncorrected. High resolution mass spectra were recorded on Bruker microtof. All reactions were monitored by TLC with Taizhou GF254 silica gel coated plates. Flash column chromatography was carried out using 200-300 mesh silica gel at increased pressure.

Attention: As the boiling point of dichloroethane (DCE) is 83 °C, reaction operation in DCE at 120 °C in a screw-capped test tube may have potential risk. However, in this reaction, we found the selenodifluoromethylation could proceed smoothly.

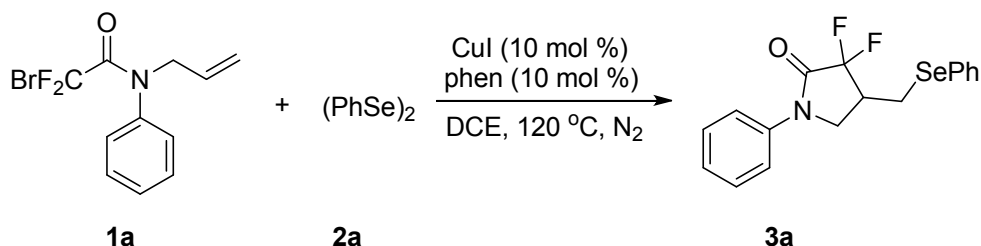
II. Synthesis Procedure

Synthesis procedure for compounds 1 (1a as an example):



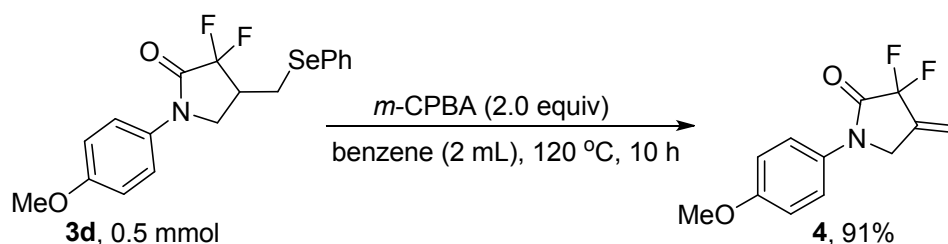
In a round-bottomed flask (50 mL) equipped with a magnetic stirrer, a solution of 2-bromo-2,2-difluoro-N-phenylacetamide (1.25 g, 5.0 mmol) with CH_3CN (25 mL) was prepared. K_2CO_3 (2.07 g, 15 mmol) was added to the solution and the reaction mixture was stirred magnetically at 90 °C and monitored by TLC. After the amide was exhausted, the mixture was purified by silica gel column chromatography to give the corresponding product **1a** (87.9 mg, 75%).

Synthesis procedure for compounds 3 (3a as an example):



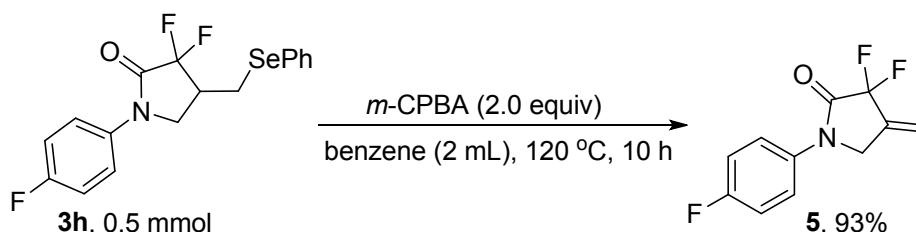
To a solution of the *N*-allyl-2-bromo-2,2-difluoro-*N*-phenylacetamide **1a** (87.1 mg, 0.3 mmol) in DCE (3.0 mL) was added the 1,2-diphenyldiselenane **2a** (103.0 mg, 0.33 mmol), phenanthroline (5.4 mg, 0.03 mmol), CuI (5.7 mg, 0.03 mmol) in screw-cap test tube. The reaction mixture was stirred at 120 °C for 12 h under a N_2 atmosphere. After the reaction finished, the reaction mixture was cooled to room temperature and quenched by water. The mixture was extracted with EtOAc (5.0 mL \times 3), the combined organic phases were dried over anhydrous Na_2SO_4 and the solvent was evaporated under vacuum. The residue was purified by column chromatography to give the corresponding product **3a** (85.7 mg, 78%).

Synthesis procedure for compounds 4:



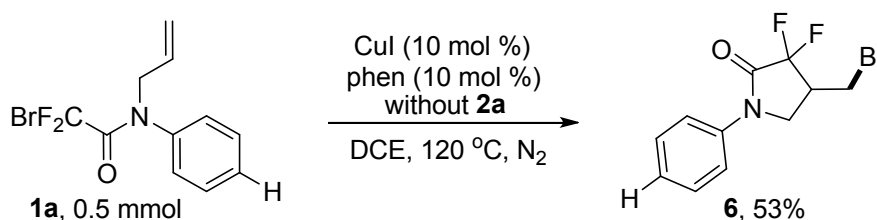
To a solution of **3d** (198.1 mg, 0.5 mmol) in benzene (2.0 mL), *m*-chloroperoxybenzoic acid (*m*-CPBA, 172.6 mg, 1.0 mmol) was added. The reaction mixture was stirred at 120 °C for 10 h under an air atmosphere. After the reaction finished, the reaction mixture was cooled to room temperature and quenched by water. The mixture was extracted with EtOAc (5.0 mL×3), the combined organic phases were dried over anhydrous Na₂SO₄ and the solvent was evaporated under vacuum. The residue was purified by column chromatography to give the corresponding product **4** (108.7 mg, 91%).

Synthesis procedure for compounds 5:



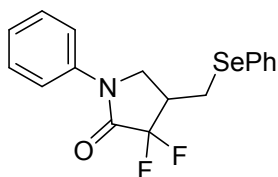
To a solution of **3h** (192.5 mg, 0.5 mmol) in benzene (2.0 mL), *m*-chloroperoxybenzoic acid (*m*-CPBA, 172.6 mg, 1.0 mmol) was added. The reaction mixture was stirred at 120 °C for 10 h under an air atmosphere. After the reaction finished, the reaction mixture was cooled to room temperature and quenched by water. The mixture was extracted with EtOAc (5.0 mL×3), the combined organic phases were dried over anhydrous Na₂SO₄ and the solvent was evaporated under vacuum. The residue was purified by column chromatography to give the corresponding product **5** (105.5 mg, 93%).

Synthesis procedure for compounds 6:



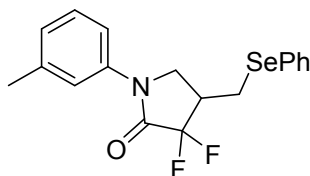
To a solution of **1a** (145.0 mg, 0.5 mmol) in DCE (3.0 mL), 1,10-phenanthroline (9.0 mg, 0.05 mmol), CuI (9.5 mg, 0.05 mmol) in screw-cap test tube. The reaction mixture was stirred at 120 °C for 12 h under a N₂ atmosphere. After the reaction finished, the reaction mixture was cooled to room temperature and quenched by water. The mixture was extracted with EtOAc (5.0 mL×3), the combined organic phases were dried over anhydrous Na₂SO₄ and the solvent was evaporated under vacuum. The residue was purified by column chromatography to give the corresponding product **6** (76.9 mg, 53%).

III. Analytical Data of Compounds 3, 4, 5 and 6



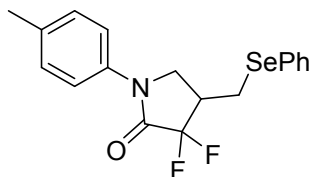
3,3-Difluoro-1-phenyl-4-((phenylselanyl)methyl)pyrrolidin-2-one (3a).

The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white solid (85.7 mg, 78%); mp: 103-106 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.63-7.56 (m, 4H), 7.26 (t, J = 7.9 Hz, 2H), 7.31 (dd, J = 5.8, 2.2 Hz, 4H), 4.01 (d, J = 9.6 Hz, 1H), 3.65 (t, J = 8.8 Hz, 1H), 4.41 (dd, J = 12.8, 4.0 Hz, 1H), 2.96 (t, J = 15.8 Hz, 1H), 2.85-2.81 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.0, 161.7, 161.4, 133.6, 129.6, 129.4, 129.3, 129.2, 129.0, 128.1, 127.9, 126.2, 119.9, 48.9, 48.8, 40.5, 40.3, 40.0, 22.4, 22.3. ^{19}F NMR (376 MHz, CDCl_3) δ -110.0 (d, J = 267.0 Hz, 1F), -116.9 (d, J = 267.0 Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{17}\text{H}_{16}\text{F}_2\text{ONSe}$, $[\text{M}+\text{H}]^+$ 368.0366; Found 368.0361.



3,3-Difluoro-4-((phenylselanyl)methyl)-1-(*m*-tolyl)pyrrolidin-2-one (3b).

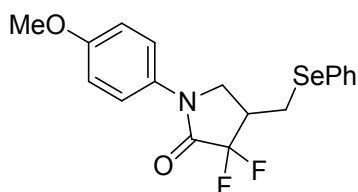
The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white oil (71.9 mg, 63%); ^1H NMR (400 MHz, CDCl_3) δ 7.58 (t, J = 3.6 Hz, 2H), 7.44-7.38 (m, 2H), 7.35-7.27 (m, 4H), 7.07 (d, J = 7.6 Hz, 1H), 3.98 (t, J = 9.0 Hz, 1H), 3.62 (t, J = 8.6 Hz, 1H), 3.52 (dd, J = 12.8, 4.4 Hz, 1H), 2.93 (d, J = 12.4 Hz, 1H), 2.85-2.80 (m, 1H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.3, 162.0, 161.7, 139.2, 137.8, 133.6, 129.6, 129.0, 128.1, 128.0, 127.1, 120.7, 117.1, 49.0, 48.9, 40.5, 40.3, 40.1, 22.4, 22.3, 21.5. ^{19}F NMR (376 MHz, CDCl_3) δ -109.8 (d, J = 267.0 Hz, 1F), -116.9 (d, J = 267.0 Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{18}\text{H}_{18}\text{F}_2\text{ONSe}$, $[\text{M}+\text{H}]^+$ 382.0522; Found 382.0526.



3,3-Difluoro-4-((phenylselanyl)methyl)-1-(*p*-tolyl)pyrrolidin-2-one (3c).

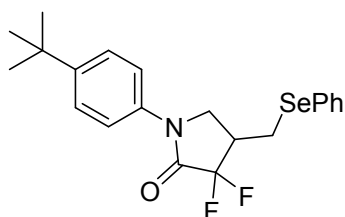
The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white solid (86.7 mg, 76%); mp: 90-92 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.57 (dd, J = 6.6, 3.0 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.34-7.27 (m, 3H), 7.21 (d, J = 8.4 Hz, 2H), 3.98 (t, J = 9.0 Hz, 1H), 3.64-3.59 (m, 1H), 3.40 (dd, J = 12.6, 4.2 Hz, 1H), 2.95 (t, J = 7.6 Hz, 1H), 2.85-2.79 (m, 1H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 161.9, 161.6, 136.1, 135.3, 133.6, 129.7, 129.6, 128.5, 128.1, 128.0, 126.5, 120.0, 49.0, 48.9, 40.5, 40.3, 40.1, 22.4, 22.3, 20.9. ^{19}F NMR (376 MHz, CDCl_3) δ -109.8 (d, J = 267.0 Hz, 1F), -116.8 (d, J = 267.0 Hz, 1F). HRMS (ESI-TOF) Calcd

for $C_{18}H_{18}F_2ONSe$, $[M+H]^+$ 382.0522; Found 382.0527.



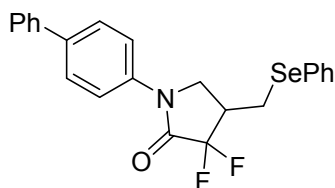
3,3-Difluoro-1-(4-methoxyphenyl)-4-((phenylselanyl)methyl)pyrrolidin-2-one (3d).

The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white oil (97.5 mg, 82%); 1H NMR (400 MHz, $CDCl_3$) δ 7.57 (t, J = 3.0 Hz, 2H), 7.52 (t, J = 10.8 Hz, 2H), 7.34-7.27 (m, 3H), 6.93 (d, J = 9.2 Hz, 2H), 3.95 (t, J = 9.0 Hz, 1H), 3.82 (s, 3H), 3.60 (t, J = 8.8 Hz, 1H), 3.39 (dd, J = 12.8, 4.0 Hz, 1H), 2.94 (t, J = 11.2 Hz, 1H), 2.85-2.81 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 161.7, 161.4, 157.7, 133.5, 130.9, 129.6, 128.1, 128.0, 121.6, 114.3, 77.4, 55.5, 49.2, 49.1, 40.5, 40.3, 40.1, 22.4, 22.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.5 (d, J = 267.0 Hz, 1F), -116.6 (d, J = 267.0 Hz, 1F). HRMS (ESI-TOF) Calcd for $C_{18}H_{18}F_2O_2NSe$, $[M+H]^+$ 398.0472; Found 398.0467.



1-(4-(tert-butyl)phenyl)-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one (3e).

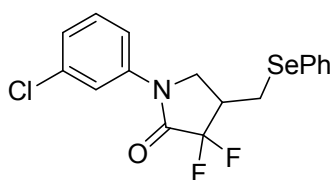
The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white solid (93.8 mg, 74%); mp: 69-72 °C; 1H NMR (400 MHz, $CDCl_3$) δ 7.58-7.52 (m, 4H), 7.43 (d, J = 8.8 Hz, 2H), 7.34 (dd, J = 5.4, 2.2 Hz, 3H), 3.98 (t, J = 9.0 Hz, 1H), 3.63 (t, J = 8.8 Hz, 1H), 3.40 (dd, J = 12.6, 4.2 Hz, 1H), 2.95 (t, J = 11.8 Hz, 1H), 2.84-2.80 (m, 1H), 1.33 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 161.9, 161.6, 149.4, 135.2, 133.6, 129.6, 128.1, 127.9, 126.2, 126.1, 119.9, 119.8, 119.7, 48.9, 48.8, 40.5, 40.3, 40.1, 34.5, 31.3, 22.4, 22.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.9 (d, J = 267.0 Hz, 1F), -116.9 (d, J = 267.0 Hz, 1F). HRMS (ESI-TOF) Calcd for $C_{21}H_{24}F_2ONSe$, $[M+H]^+$ 424.0991; Found 424.0998.



1-([1,1'-Biphenyl]-4-yl)-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one (3f).

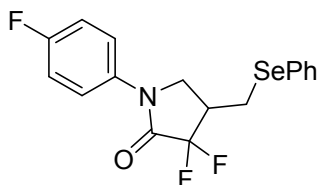
The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white solid (106.2 mg, 80%); mp: 143-146 °C; 1H NMR (400 MHz, $CDCl_3$) δ 7.72-7.58 (m, 8H), 7.47 (t, J = 7.4 Hz, 2H),

7.40-7.27 (m, 4H), 4.04 (t, $J = 8.8$ Hz, 1H), 3.68 (t, $J = 8.8$ Hz, 1H), 3.42 (dd, $J = 12.8, 4.0$ Hz, 1H), 2.97 (t, $J = 11.4$ Hz, 1H), 2.88-2.85 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.1, 161.8, 140.0, 139.1, 137.0, 133.6, 129.6, 128.9, 128.1, 127.8, 127.6, 127.0, 120.1, 48.9, 48.8, 40.5, 40.3, 40.1, 22.4, 22.3. ^{19}F NMR (376 MHz, CDCl_3) δ -109.8 (d, $J = 267.0$ Hz, 1F), -116.8 (d, $J = 267.0$ Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{23}\text{H}_{20}\text{F}_2\text{ONSe}$, $[\text{M}+\text{H}]^+$ 444.0676; Found 444.0679.



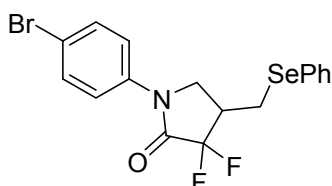
1-(3-chlorophenyl)-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one (3g).

The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 8:1), white solid (84.1 mg, 70%): mp: 103-104 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.57 (dd, $J = 9.2, 3.6$ Hz, 4H), 7.39-7.27 (m, 5H), 3.97 (t, $J = 9.0$ Hz, 1H), 3.61 (t, $J = 8.4$ Hz, 1H), 3.39 (dd, $J = 12.4, 4.0$ Hz, 1H), 2.95 (t, $J = 11.8$ Hz, 1H), 2.86-2.82 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.1, 161.7, 136.4, 133.5, 131.5, 129.6, 129.3, 128.1, 127.9, 121.0, 48.8, 48.7, 40.4, 40.2, 40.0, 22.3, 22.2. ^{19}F NMR (376 MHz, CDCl_3) δ -111.1 (d, $J = 267.0$ Hz, 1F), -119.4 (d, $J = 267.0$ Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{17}\text{H}_{15}\text{F}_2\text{ONSe}$, $[\text{M}+\text{H}]^+$ 396.0029; Found 396.0035.



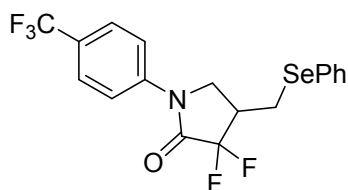
3,3-Difluoro-1-(4-fluorophenyl)-4-((phenylselanyl)methyl)pyrrolidin-2-one (3h).

The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 8:1), white solid (84.2 mg, 73%): mp: 78-79 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.60-7.55 (m, 4H), 7.34-7.27 (m, 3H), 7.11 (t, $J = 8.6$ Hz, 2H), 3.99 (t, $J = 8.4$ Hz, 1H), 3.62 (t, $J = 8.2$ Hz, 1H), 3.40 (dd, $J = 12.6, 4.2$ Hz, 1H), 2.95 (t, $J = 11.6$ Hz, 1H), 2.91-2.82 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.3, 162.0, 161.6, 159.2, 133.9, 133.8, 133.5, 129.6, 128.1, 127.9, 121.8, 121.7, 116.1, 115.9, 49.1, 49.0, 40.4, 40.2, 40.0, 22.3, 22.2. ^{19}F NMR (376 MHz, CDCl_3) δ -109.8 (d, $J = 267.0$ Hz, 1F), -114.9 (s, 1F), -116.7 (t, $J = 270.7$ Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{17}\text{H}_{15}\text{F}_3\text{ONSe}$, $[\text{M}+\text{H}]^+$ 386.0271; Found 386.0278.

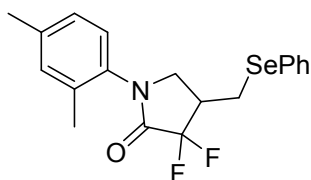


1-(4-Bromophenyl)-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one (3i).

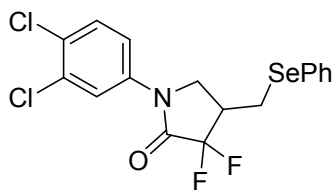
The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white solid (94.8 mg, 71%): mp: 102-104 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.58-7.51 (m, 6H), 7.34-7.27 (m, 3H), 3.96 (t, J = 9.0 Hz, 1H), 3.59 (t, J = 8.4 Hz, 1H), 3.39 (dd, J = 12.8, 4.0 Hz, 1H), 2.94 (t, J = 11.6 Hz, 1H), 2.85-2.79 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.4, 162.1, 161.8, 136.9, 133.5, 132.2, 129.6, 128.2, 127.9, 121.2, 119.3, 48.7, 48.6, 40.3, 40.1, 39.9, 22.2, 22.1. ^{19}F NMR (376 MHz, CDCl_3) δ -109.9 (d, J = 267.0 Hz, 1F), -116.7 (d, J = 267.0 Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{17}\text{H}_{15}\text{F}_2\text{OBrNSe}$, $[\text{M}+\text{H}]^+$ 445.9471; Found 445.9474.

**3,3-Difluoro-4-((phenylselanyl)methyl)-1-(4-(trifluoromethyl)phenyl)pyrrolidin-2-one (3j).**

The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white solid (97.7 mg, 75%): mp: 67-69 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.61-7.55 (m, 4H), 7.34-7.27 (m, 3H), 7.11 (t, J = 8.4 Hz, 2H), 3.97 (t, J = 9.0 Hz, 1H), 3.62 (t, J = 8.6 Hz, 1H), 3.40 (dd, J = 12.6, 3.8 Hz, 1H), 2.95 (t, J = 11.6 Hz, 1H), 2.86-2.82 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.0, 161.6, 159.1, 133.9, 133.5, 129.6, 128.1, 127.9, 121.8, 121.7, 116.1, 115.9, 49.1, 40.4, 40.2, 40.0, 22.3, 22.2. ^{19}F NMR (376 MHz, CDCl_3) δ -109.8 (dd, J = 268.8, 13.2 Hz, 1F), -114.9 (d, J = 11.3 Hz), -116.7 (dd, J = 267.0, 11.3 Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{18}\text{H}_{15}\text{F}_5\text{ONSe}$, $[\text{M}+\text{H}]^+$ 436.0239; Found 436.0244.

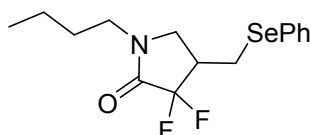
**1-(2,4-Dimethylphenyl)-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one (3k).**

The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white oil (75.7 mg, 64%): ^1H NMR (400 MHz, CDCl_3) δ 7.57 (t, J = 3.6 Hz, 2H), 7.39 (s, 1H), 7.35-7.27 (m, 4H), 7.16 (d, J = 8.4 Hz, 1H), 3.96 (t, J = 9.0 Hz, 1H), 3.60 (t, J = 8.8 Hz, 1H), 3.39 (dd, J = 12.8, 4.4 Hz, 1H), 2.94 (t, J = 11.4 Hz, 1H), 2.84-2.78 (m, 1H), 2.29 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.2, 161.9, 161.6, 137.6, 135.5, 134.9, 133.6, 130.2, 130.1, 129.6, 128.1, 128.0, 121.3, 117.5, 114.5, 49.1, 49.0, 40.5, 40.3, 40.1, 26.9, 22.5, 22.4, 20.0, 19.3. ^{19}F NMR (376 MHz, CDCl_3) δ -109.7 (d, J = 267.0 Hz, 1F), -116.8 (d, J = 267.0 Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{19}\text{H}_{20}\text{F}_2\text{ONSe}$, $[\text{M}+\text{H}]^+$ 396.0678; Found 396.0684.



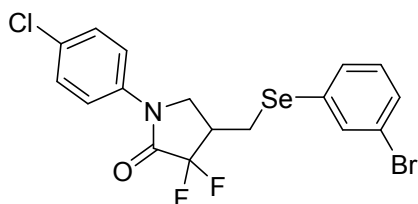
1-(3,4-Dichlorophenyl)-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one (3l).

The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white solid (90.1 mg, 69%): mp: 70-72 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.75 (d, J = 2.8 Hz, 1H), 7.59-7.54 (m, 3H), 7.47 (d, J = 8.8 Hz, 1H), 7.35 (t, J = 2.6 Hz, 3H), 3.96 (t, J = 8.8 Hz, 1H), 3.60 (t, J = 8.6 Hz, 1H), 3.40 (dd, J = 12.8, 4.0 Hz, 1H), 2.94 (t, J = 11.8 Hz, 1H), 2.86-2.82 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.0, 161.7, 161.4, 157.7, 137.8, 137.5, 133.6, 129.6, 129.2, 128.11, 127.9, 126.2, 119.9, 48.9, 48.8, 40.5, 40.3, 40.0, 22.4, 22.3. ^{19}F NMR (376 MHz, CDCl_3) δ -110.1 (d, J = 267.0 Hz, 1F), -116.7 (d, J = 270.7 Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{17}\text{H}_{14}\text{F}_2\text{OCl}_2\text{NSe}$, $[\text{M}+\text{H}]^+$ 435.9588; Found 435.9582.



1-Butyl-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one (3m).

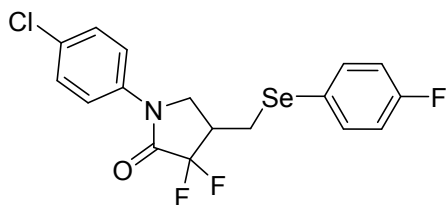
The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 6:1), white oil (47.8 mg, 46%): ^1H NMR (400 MHz, CDCl_3) δ 7.54 (dd, J = 6.2, 3.0 Hz, 2H), 7.33 (t, J = 3.0 Hz, 3H), 3.53 (t, J = 8.0 Hz, 1H), 3.51-3.17 (m, 4H), 2.84 (t, J = 11.8 Hz, 1H), 2.70-2.67 (m, 1H), 1.51 (dd, J = 15.2, 7.6 Hz, 2H), 1.30 (t, J = 7.6 Hz, 2H), 1.27 (d, J = 11.2 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.3, 162.3, 161.6, 137.5, 133.4, 129.5, 129.3, 128.1, 128.0, 47.8, 47.7, 43.2, 40.8, 40.6, 40.4, 28.8, 22.7, 22.6, 19.8, 13.6. ^{19}F NMR (376 MHz, CDCl_3) δ -110.5 (d, J = 267.0 Hz, 1F), -117.0 (d, J = 267.0 Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{15}\text{H}_{20}\text{F}_2\text{ONSe}$, $[\text{M}+\text{H}]^+$ 348.0678; Found 348.0686.



4-(((3-Bromophenyl)selanyl)methyl)-1-(4-chlorophenyl)-3,3-difluoropyrrolidin-2-one (3n).

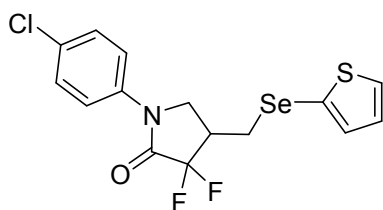
The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white solid (105.0 mg, 73%): mp: 105-107 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.59-7.55 (m, 4H), 7.39-7.32 (m, 4H), 3.97 (t, J = 9.0 Hz, 1H), 3.60 (t, J = 8.8 Hz, 1H), 3.49 (dd, J = 12.6, 4.2 Hz, 1H), 2.95 (t, J = 11.8 Hz, 1H), 2.86-2.81 (m, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 162.4, 162.1, 161.7, 136.4, 133.5, 131.5, 129.6, 129.3, 128.1, 127.9, 121.0, 48.8, 48.7, 40.4, 40.2, 40.0, 22.3, 22.2. ^{19}F NMR (376 MHz, CDCl_3) δ -109.8 (d, J = 267.0 Hz, 1F), -116.7 (d, J = 267.0 Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{17}\text{H}_{14}\text{F}_2\text{OCINBrSe}$, $[\text{M}+\text{H}]^+$ 479.9081; Found 479.9075.



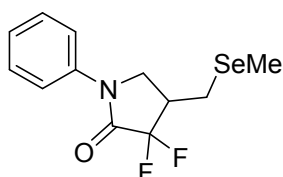
1-(4-Chlorophenyl)-3,3-difluoro-4-(((4-fluorophenyl)selenanyl)methyl)pyrrolidin-2-one (3o).

The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white solid (94.2 mg, 75%): mp: 105-107 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.61-7.55 (m, 4H), 7.40 (t, J = 2.4 Hz, 2H), 7.04 (t, J = 8.8 Hz, 2H), 3.98 (t, J = 9.0 Hz, 1H), 3.62 (t, J = 8.4 Hz, 1H), 3.34 (dd, J = 12.8, 4.4 Hz, 1H), 2.92 (t, J = 11.4 Hz, 1H), 2.83-2.77 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.4, 162.0, 161.7, 136.3, 136.2, 136.1, 131.6, 129.3, 121.0, 117.0, 116.8, 48.8, 48.7, 40.3, 40.1, 39.9, 34.7, 34.5. ^{19}F NMR (376 MHz, CDCl_3) δ -109.7 (d, J = 270.7 Hz, 1F), -112.6 (s, 1F), -116.8 (d, J = 270.7 Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{17}\text{H}_{14}\text{F}_3\text{OCINSe}$, $[\text{M}+\text{H}]^+$ 419.9881; Found 419.9888.



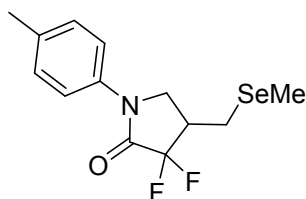
1-(4-Chlorophenyl)-3,3-difluoro-4-((thiophen-2-yl)selenanyl)methyl)pyrrolidin-2-one (3p).

The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white oil (68.3 mg, 56%); ^1H NMR (400 MHz, CDCl_3) δ 7.61 (d, J = 8.8 Hz, 2H), 7.46 (d, J = 5.2 Hz, 1H), 7.38 (d, J = 8.8 Hz, 2H), 7.28 (d, J = 3.6 Hz, 1H), 7.03 (dd, J = 5.2, 3.6 Hz, 1H), 4.04 (t, J = 8.2 Hz, 1H), 3.63 (t, J = 7.8 Hz, 1H), 3.27 (d, J = 8.4 Hz, 1H), 2.86-2.81 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.3, 162.0, 161.7, 136.9, 136.4, 132.0, 131.5, 129.3, 128.6, 121.2, 121.0, 48.7, 48.6, 40.1, 39.9, 39.7, 25.5, 25.4. ^{19}F NMR (376 MHz, CDCl_3) δ -109.4 (d, J = 270.7 Hz, 1F), -116.2 (d, J = 267.0 Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{15}\text{H}_{13}\text{F}_2\text{OSCINSe}$, $[\text{M}+\text{H}]^+$ 407.9541; Found 407.9537.



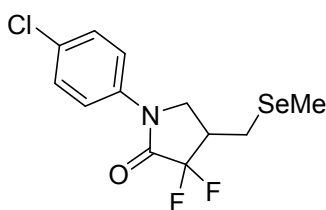
3,3-Difluoro-4-((methylselanyl)methyl)-1-phenylpyrrolidin-2-one (3q).

The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white solid (73.0 mg, 80%); mp: 104-107 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.67 (d, J = 8.0 Hz, 2H), 7.44 (t, J = 8.0 Hz, 2H), 7.27 (t, J = 6.2 Hz, 1H), 4.09 (t, J = 9.0 Hz, 1H), 3.67 (t, J = 8.8 Hz, 1H), 3.03 (dd, J = 8.6, 4.6 Hz, 1H), 2.93-2.89 (m, 1H), 2.67 (dd, J = 12.0, 10.8 Hz, 1H), 2.11 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.2, 161.9, 161.6, 137.8, 129.3, 129.2, 126.3, 120.0, 49.1, 49.0, 40.6, 40.4, 40.2, 19.4, 19.3, 4.9. ^{19}F NMR (376 MHz, CDCl_3) δ -109.7 (d, J = 267.0 Hz, 1F), -117.3 (d, J = 267.0 Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{12}\text{H}_{14}\text{F}_2\text{ONSe}$, $[\text{M}+\text{H}]^+$ 306.0209; Found 306.0217.



3,3-Difluoro-4-((methylselanyl)methyl)-1-(*p*-tolyl)pyrrolidin-2-one (3r).

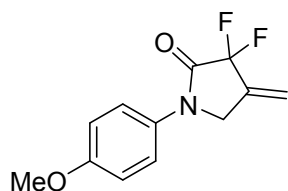
The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white oil (78.3 mg, 82%); ^1H NMR (400 MHz, CDCl_3) δ 7.54 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H), 4.06 (t, J = 9.0 Hz, 1H), 3.64 (t, J = 8.8 Hz, 1H), 3.02 (dd, J = 12.4, 4.8 Hz, 1H), 2.90 (t, J = 2.8 Hz, 1H), 2.69-2.63 (m, 1H), 2.37 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.3, 162.0, 161.7, 136.4, 136.2, 135.4, 129.8, 129.7, 120.1, 120.0, 119.5, 117.0, 116.9, 114.5, 49.2, 49.1, 40.6, 40.4, 40.2, 21.0, 19.5, 19.4, 4.9. ^{19}F NMR (376 MHz, CDCl_3) δ -109.5 (d, J = 267.0 Hz, 1F), -117.2 (d, J = 267.0 Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{13}\text{H}_{16}\text{F}_2\text{ONSe}$, $[\text{M}+\text{H}]^+$ 320.0365; Found 320.0369.



1-(4-Chlorophenyl)-3,3-difluoro-4-((methylselanyl)methyl)pyrrolidin-2-one (3s).

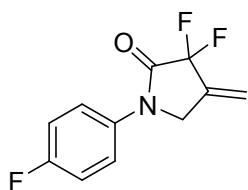
The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white oil (92.5 mg, 91%); ^1H NMR (400 MHz, CDCl_3) δ 7.63 (d, J = 7.2 Hz, 2H), 7.39 (dd, J = 7.2, 2.0 Hz, 2H), 4.06 (t, J = 8.8 Hz, 1H), 3.63 (t, J = 8.4 Hz, 1H), 3.01 (dd, J = 12.6, 4.6 Hz, 1H), 2.93-2.89 (m, 1H), 2.65 (dd, J = 11.8, 10.6 Hz, 1H), 2.10 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.5, 162.2, 161.9, 136.4, 131.5, 129.4, 129.3, 121.2, 121.1, 119.2, 116.8, 116.7, 114.2, 49.0, 48.9, 40.4, 40.2, 40.0, 19.3, 19.2, 4.90. ^{19}F NMR (376 MHz, CDCl_3) δ -109.7 (d, J = 270.7 Hz, 1F), -117.1 (d, J = 270.7 Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{12}\text{H}_{13}\text{F}_2\text{OClNSe}$, $[\text{M}+\text{H}]^+$ 339.9818;

Found 339.9812.



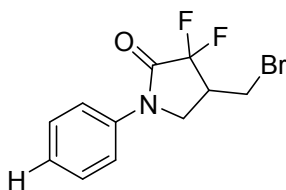
3,3-Difluoro-1-(4-methoxyphenyl)-4-methylenepyrrolidin-2-one (4).

The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1), white solid (108.7 mg, 91%): mp: 120-121 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.60 (d, J = 8.8 Hz, 2H), 6.94 (d, J = 9.2 Hz, 2H), 6.05 (s, 1H), 5.75 (s, 1H), 4.46 (t, J = 2.0 Hz, 2H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 161.9, 161.6, 161.3, 157.8, 133.0, 132.8, 132.6, 130.6, 121.9, 118.1, 114.4, 113.4, 111.0, 108.5, 55.5, 48.7. ^{19}F NMR (376 MHz, CDCl_3) δ -102.7 (s, 2F). HRMS (ESI-TOF) Calcd for $\text{C}_{12}\text{H}_{12}\text{F}_2\text{NO}_2$, $[\text{M}+\text{H}]^+$ 240.0830; Found 240.0836.



3,3-Difluoro-1-(4-fluorophenyl)-4-methylenepyrrolidin-2-one (5).

The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 9:1), white solid (105.5 mg, 93%): mp: 99-100 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.70 (dd, J = 4.8, 2.4 Hz, 2H), 7.17-7.11 (m, 2H), 6.09 (d, J = 2.4 Hz, 1H), 5.79 (d, J = 1.2 Hz, 1H), 4.49 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.0, 161.9, 161.7, 161.6, 159.3, 133.7, 133.6, 132.6, 132.2, 122.1, 122.0, 118.5, 116.3, 116.0, 110.7, 48.7, 48.6, 48.5. ^{19}F NMR (376 MHz, CDCl_3) δ -102.8 (s, 2F), -114.6 (s, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{11}\text{H}_9\text{F}_3\text{NO}$, $[\text{M}+\text{H}]^+$ 228.0630; Found 228.0626.

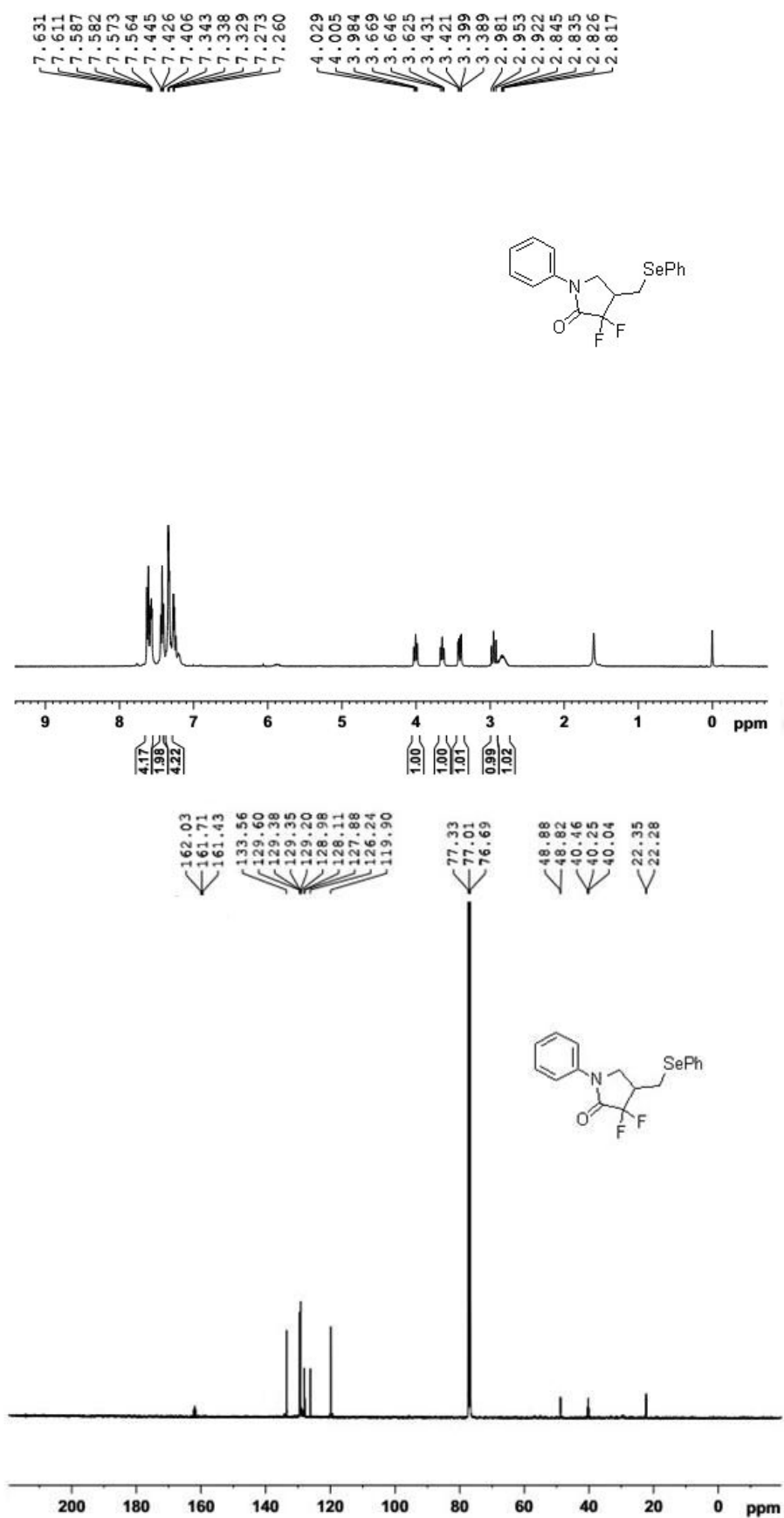


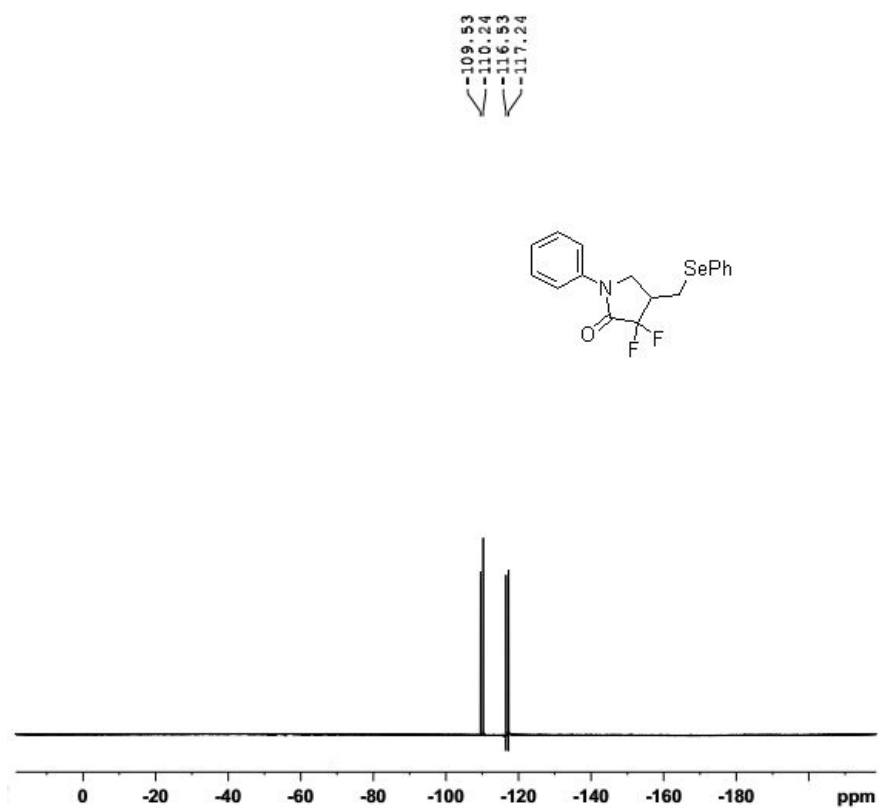
4-(Bromomethyl)-3,3-difluoro-1-phenylpyrrolidin-2-one (6).

The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1), white solid (76.9 mg, 53%): mp: 50-51 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.66 (d, J = 7.6 Hz, 2H), 7.43 (dd, J = 8.0, 6.4 Hz, 2H), 7.30-7.26 (m, 1H), 4.12 (d, J = 8.0 Hz, 1H), 3.96 (dd, J = 11.4, 5.0 Hz, 1H), 3.79-3.70 (m, 2H), 3.13-3.07 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 161.4, 137.6, 129.3, 126.5, 120.1, 47.4, 47.3, 42.1, 41.9, 41.7, 39.3, 39.2. ^{19}F NMR (376 MHz, CDCl_3) δ -107.4 (d, J = 274.5 Hz, 1F), -117.5 (d, J = 27.07 Hz, 1F). HRMS (ESI-TOF) Calcd for $\text{C}_{11}\text{H}_{11}\text{FBrNO}_2$, $[\text{M}+\text{H}]^+$ 286.9951; Found 286.9958.

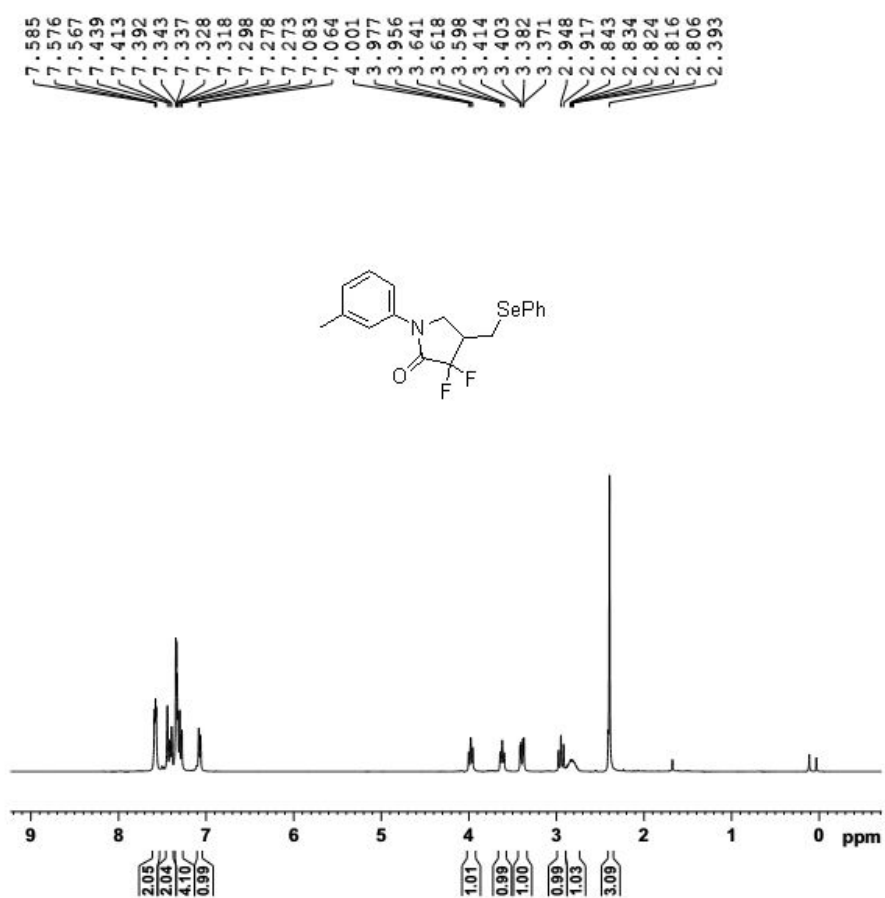
IV. ^1H NMR and ^{13}C NMR Spectra Copies of Synthesized Compounds

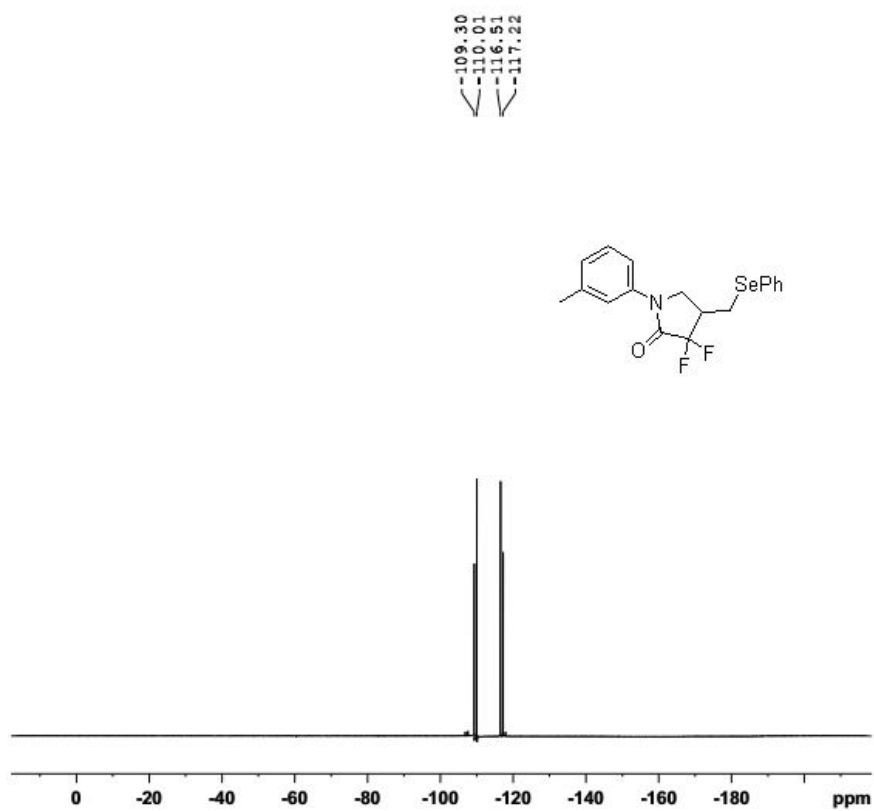
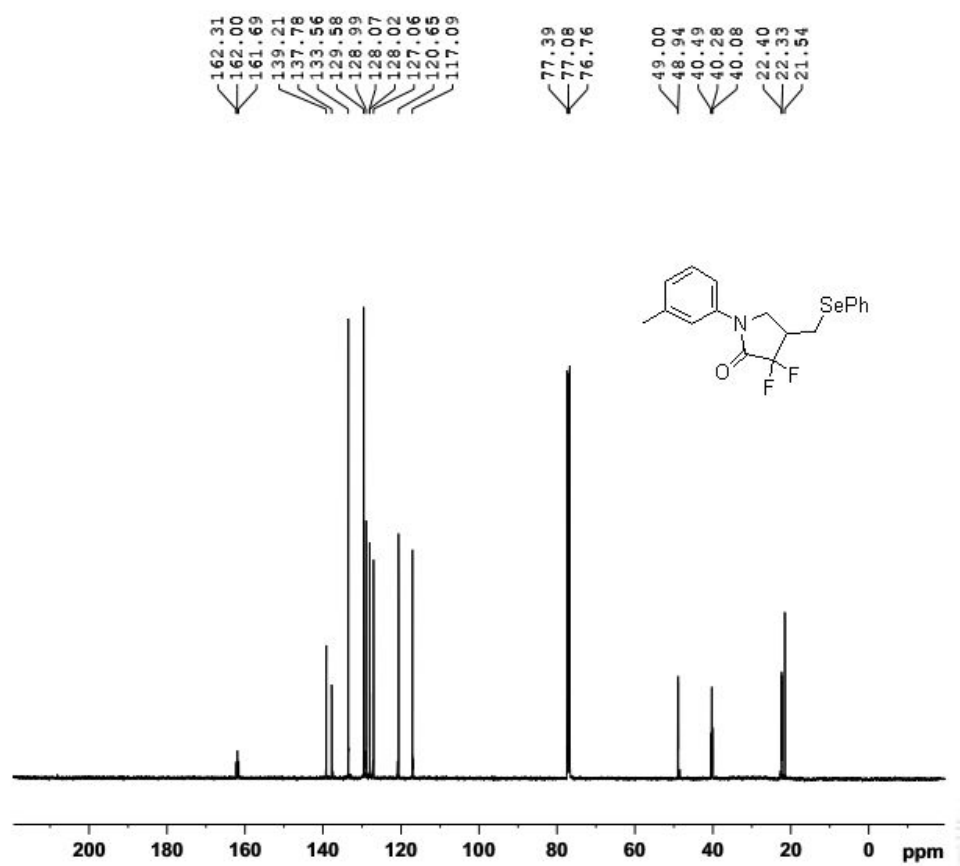
Compound 3a



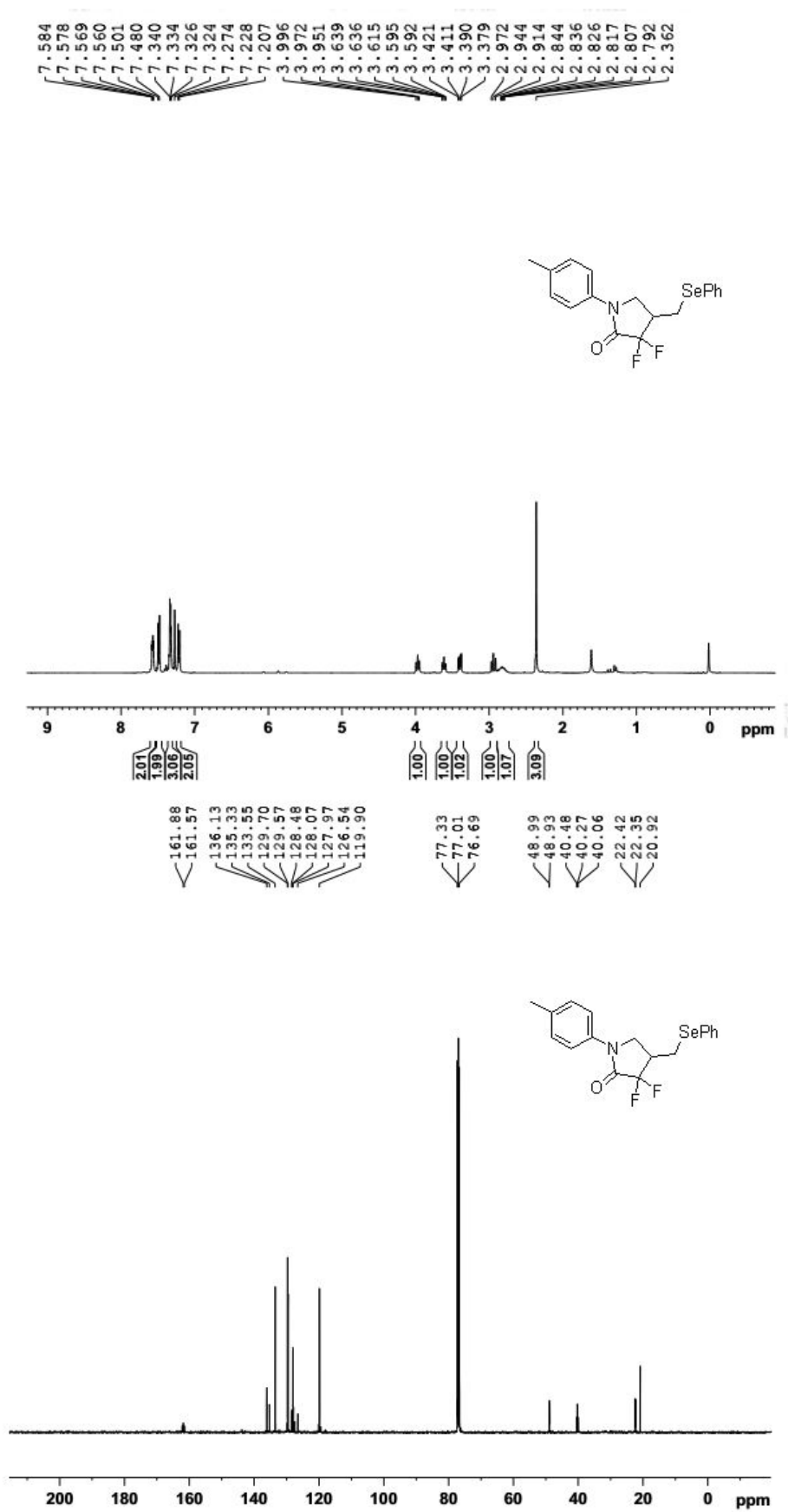


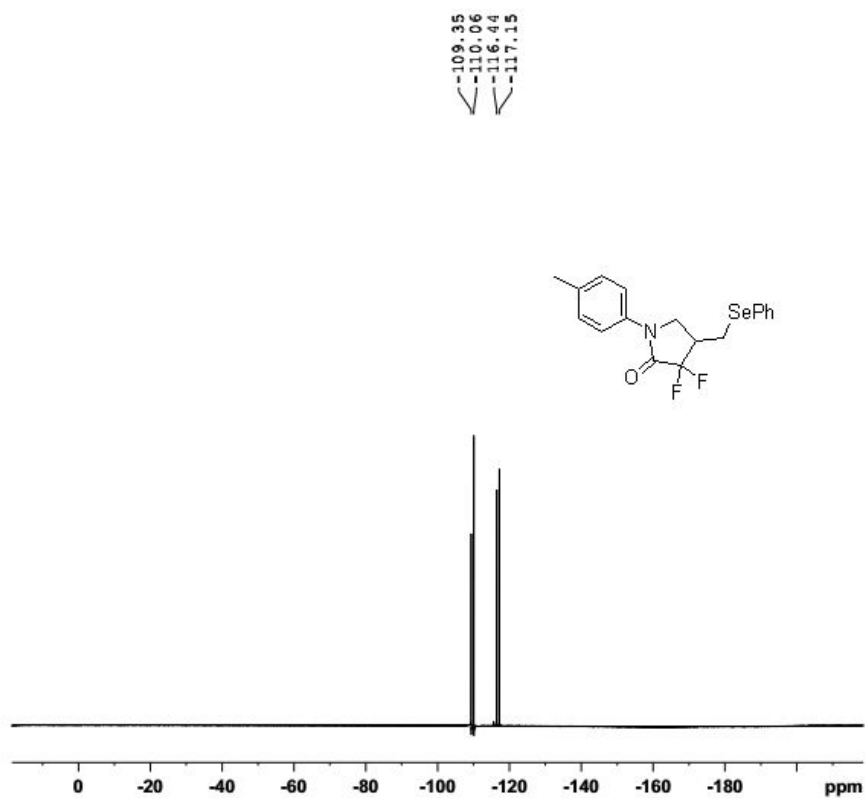
Compound 3b



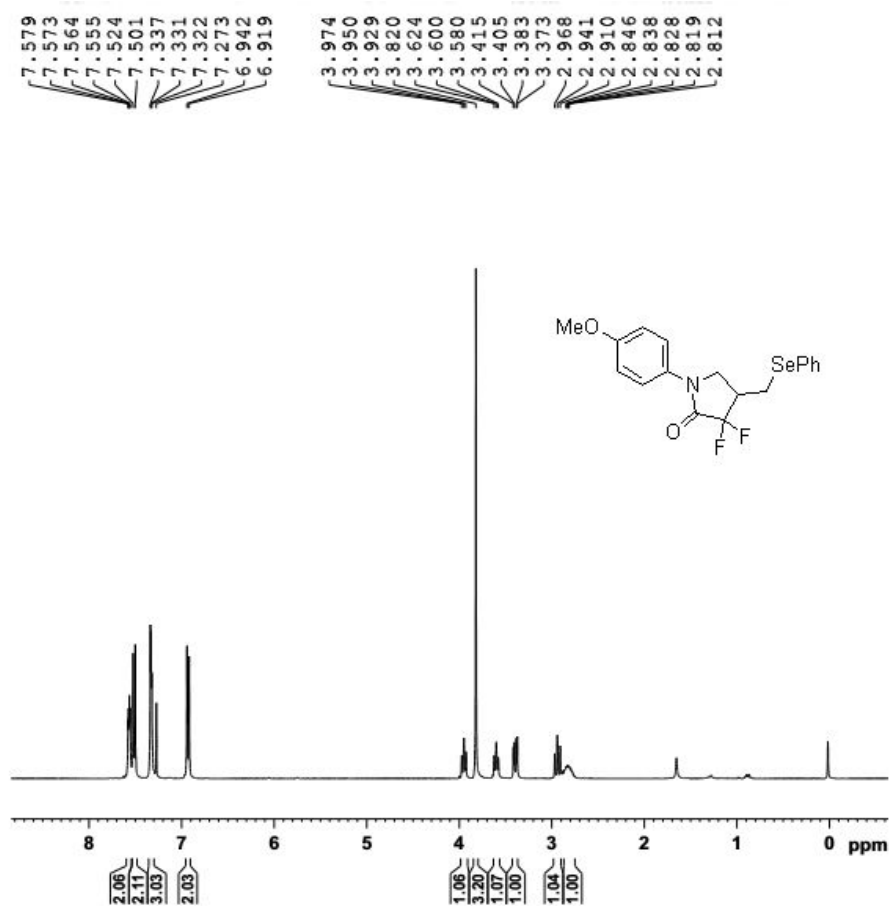


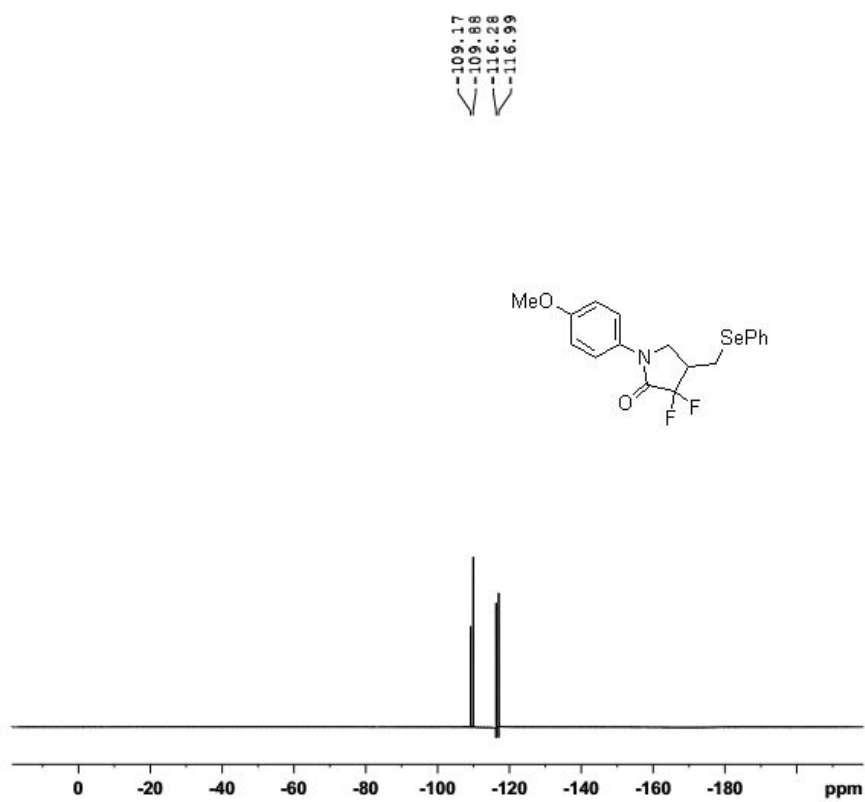
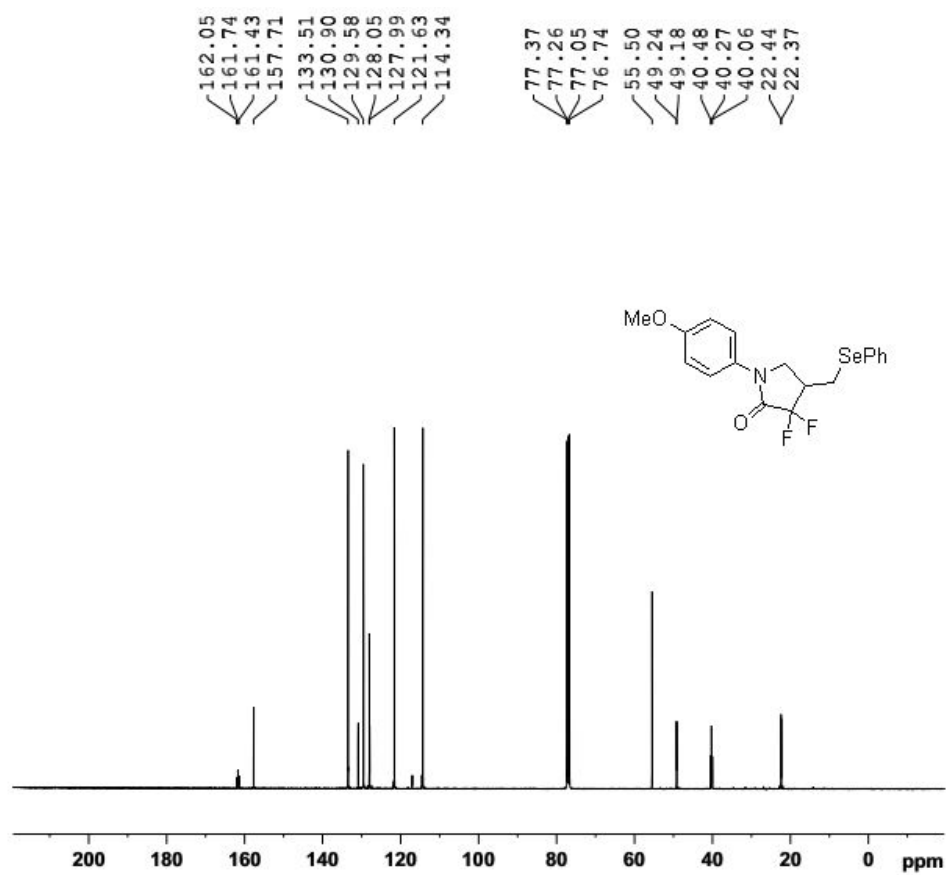
Compound 3c



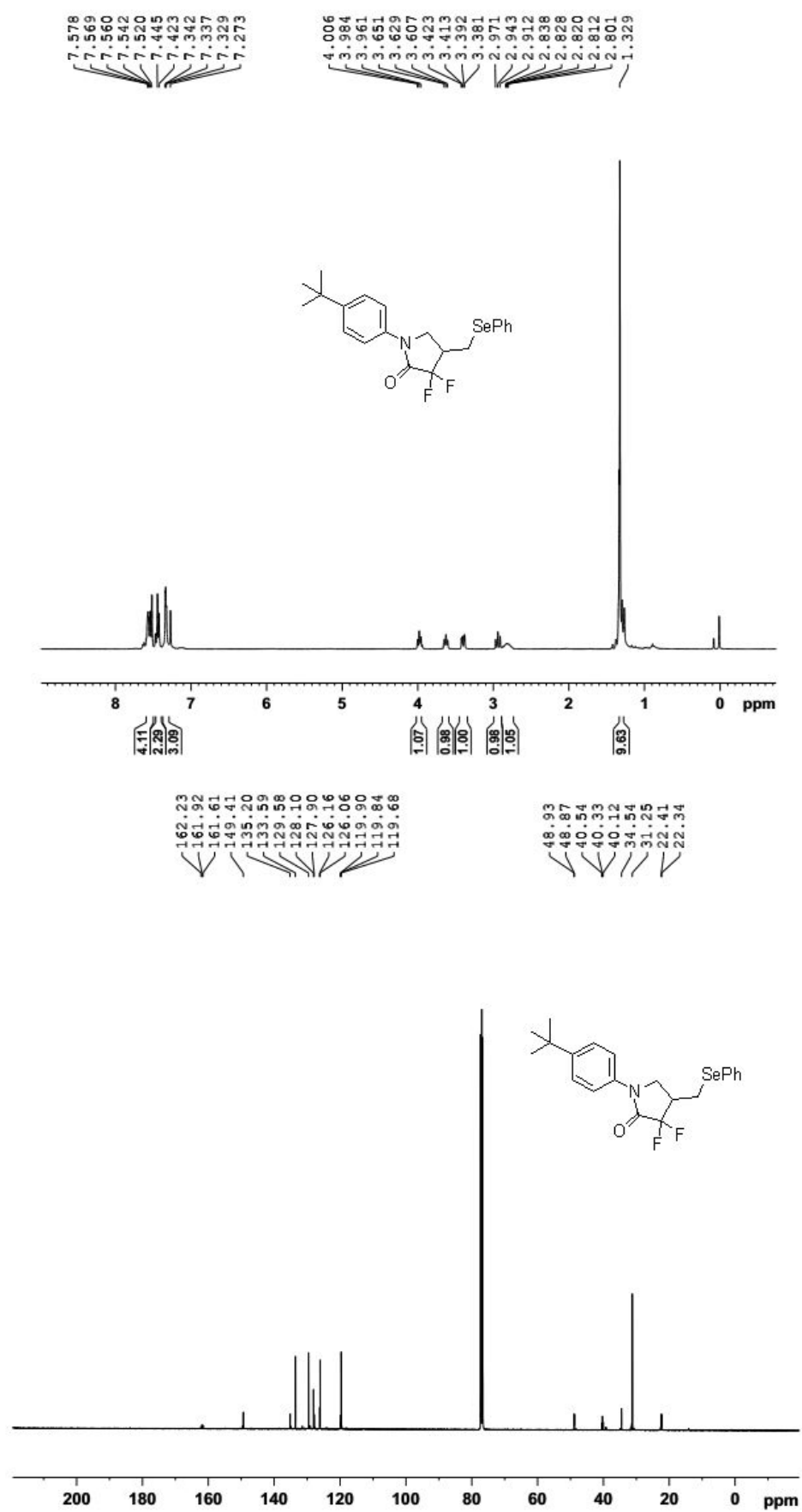


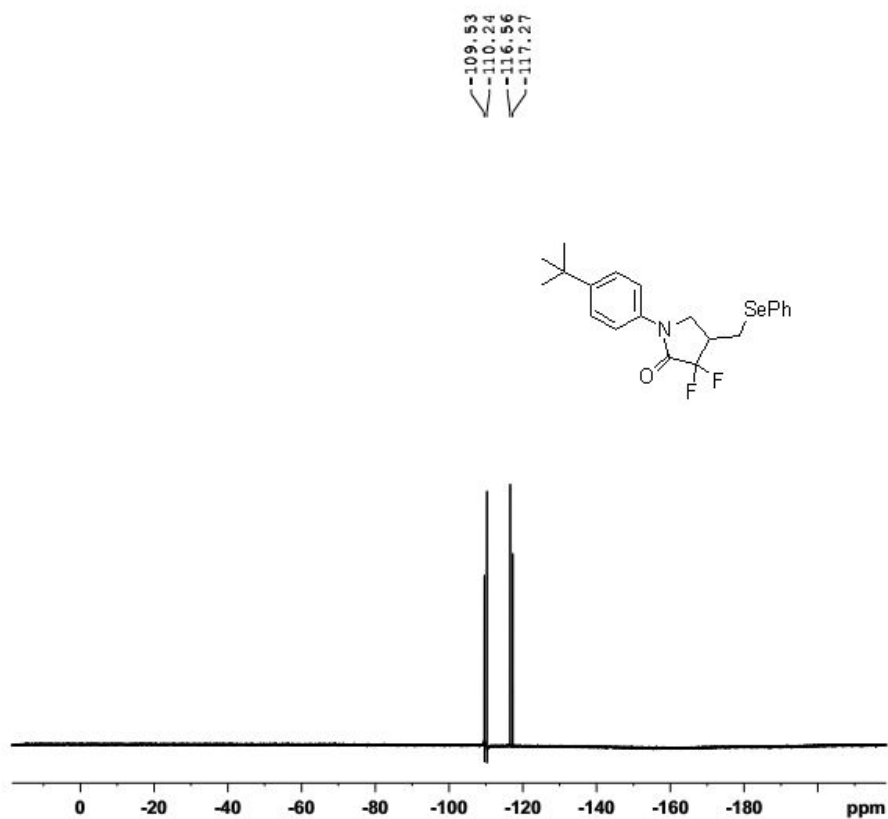
Compound 3d



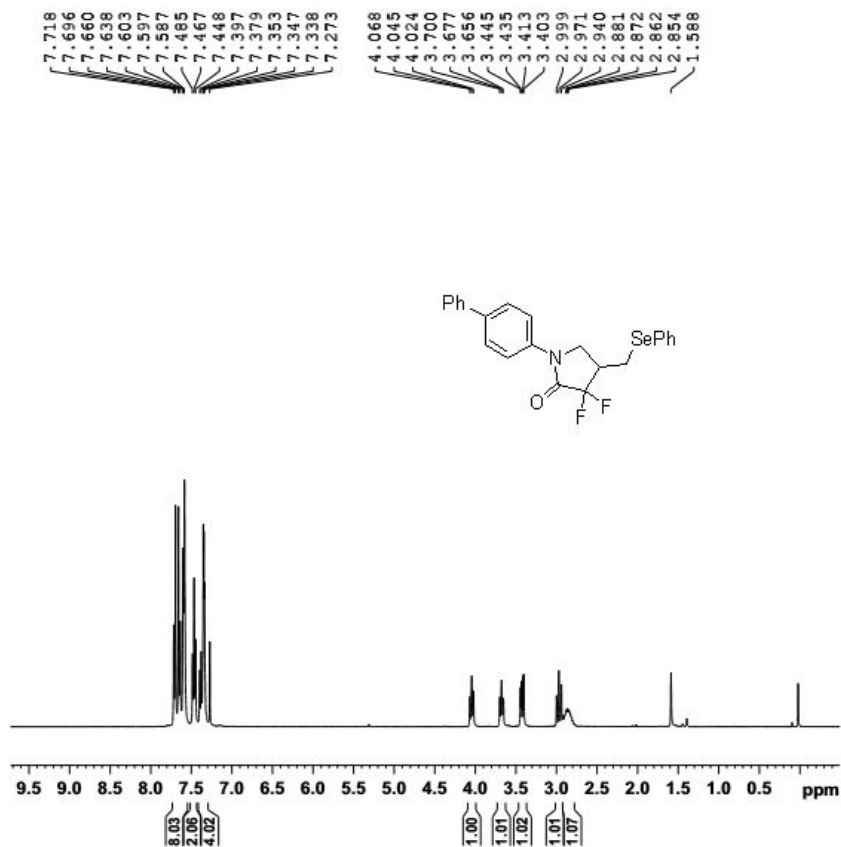


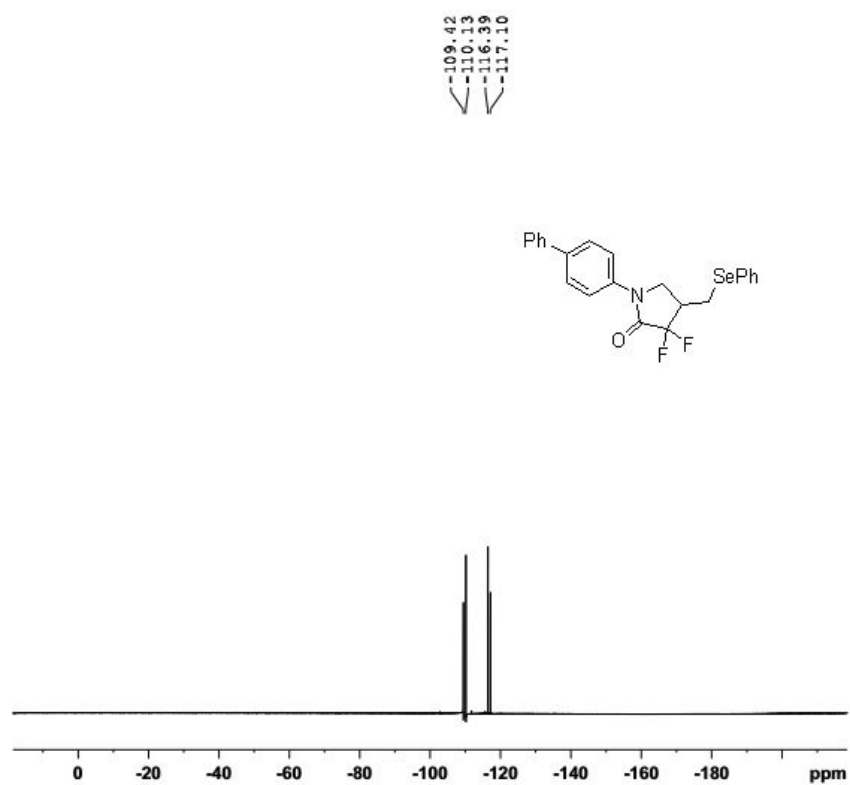
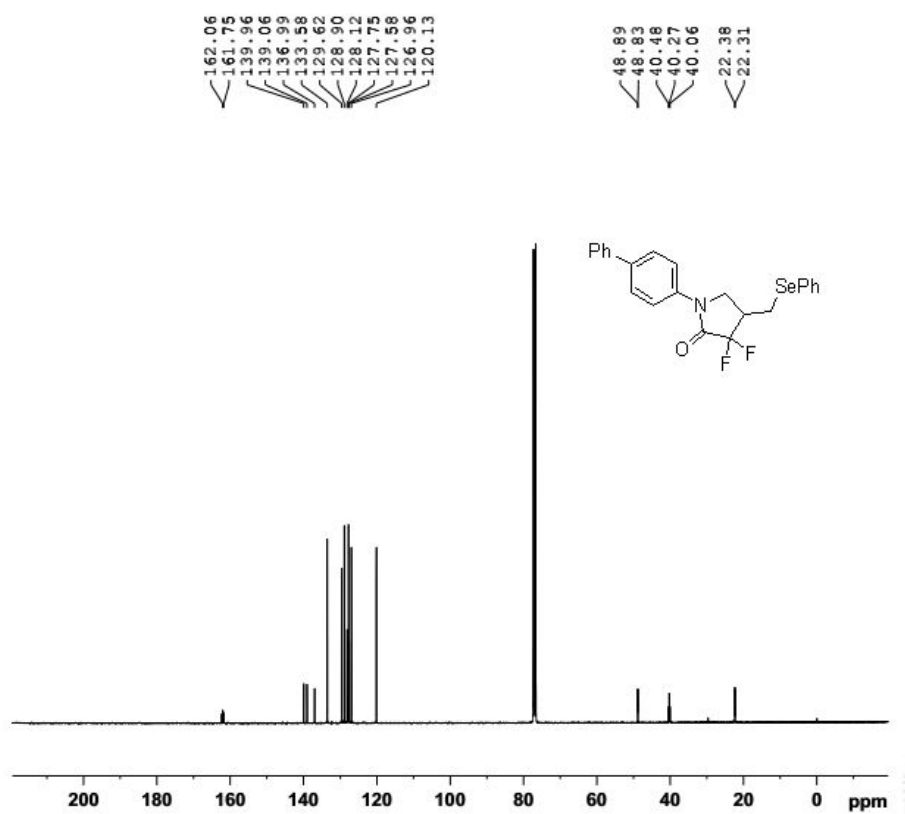
Compound 3e



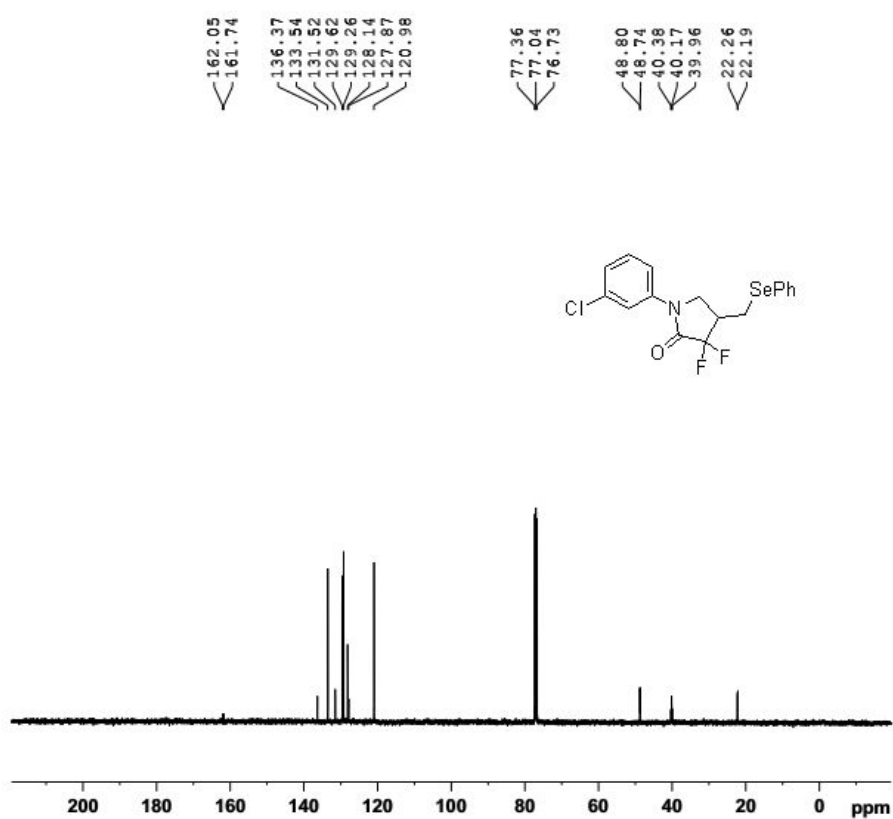
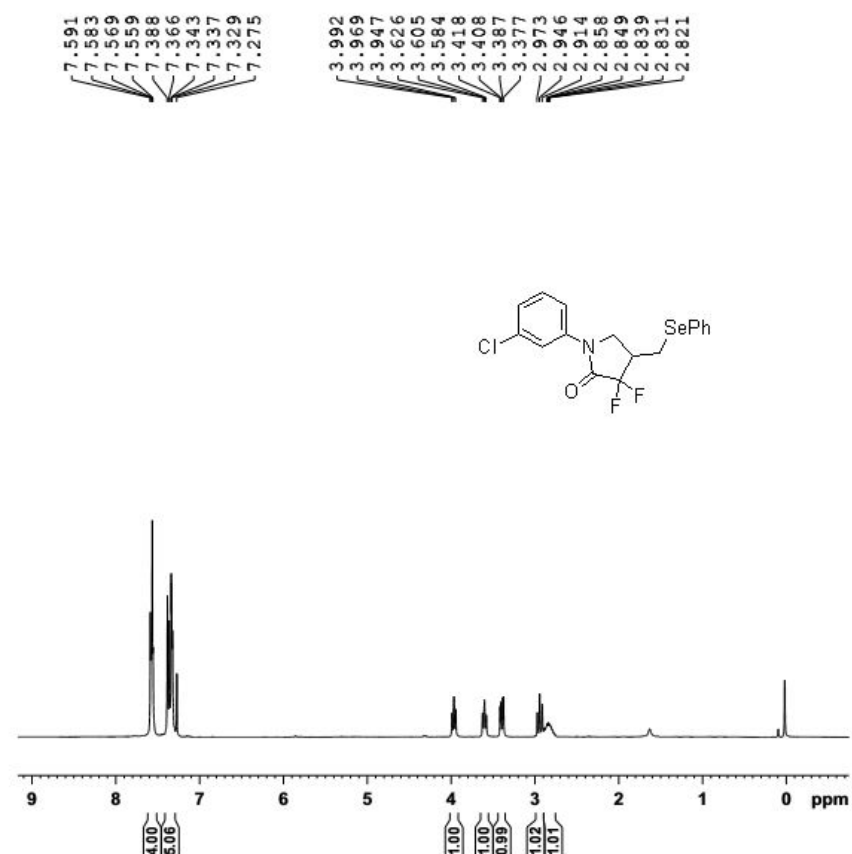


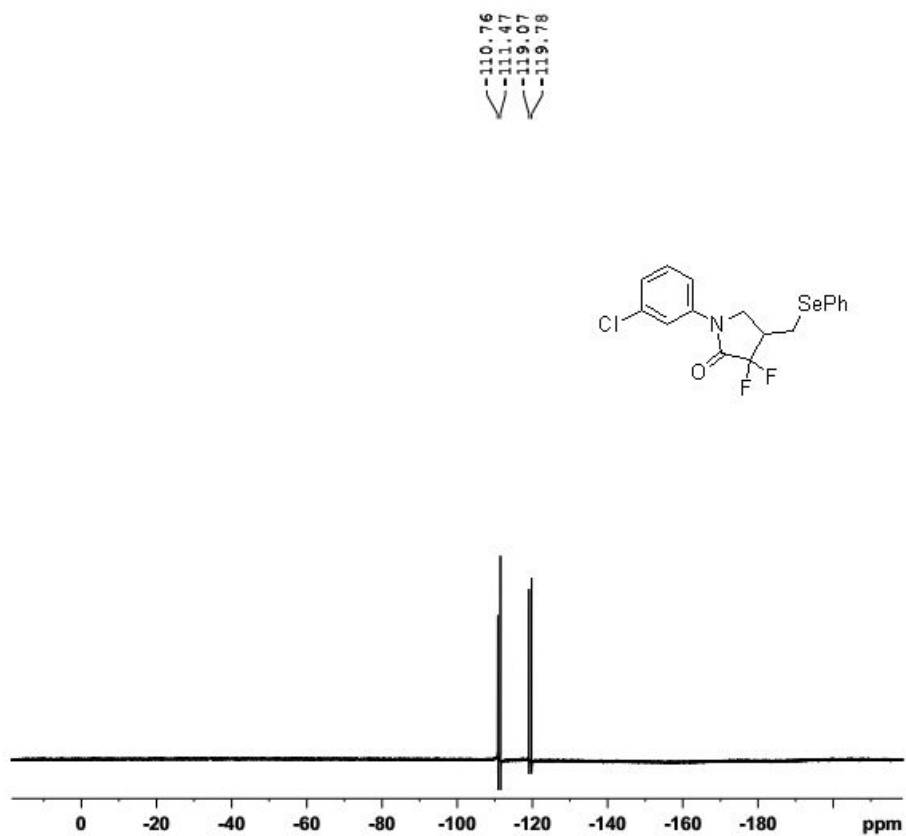
Compound 3f



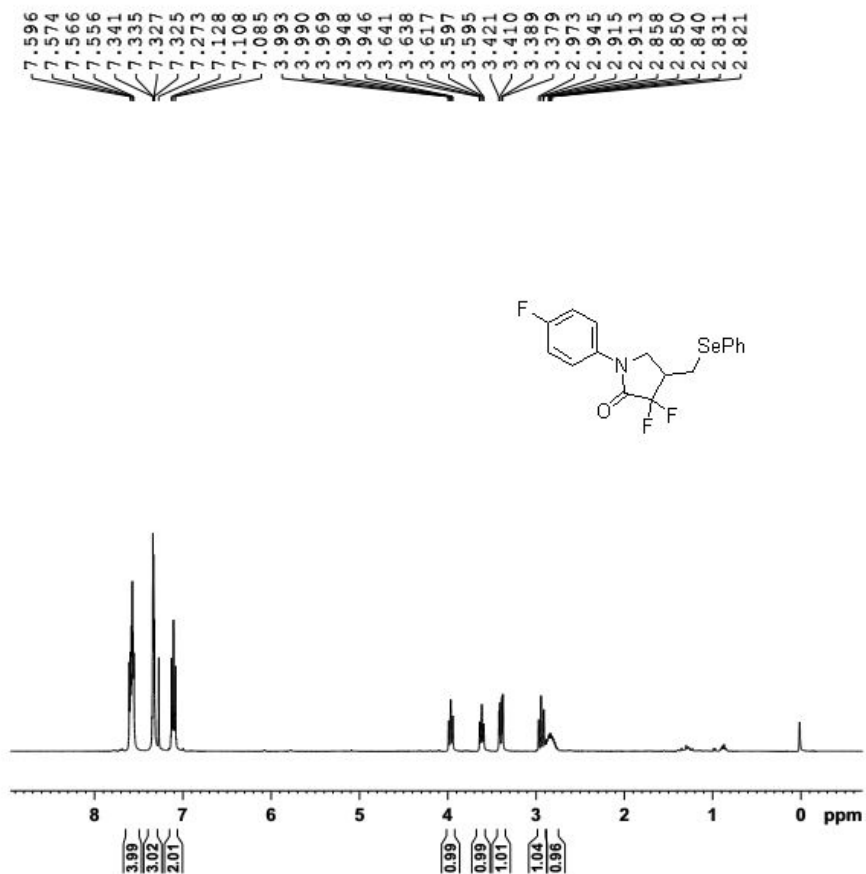


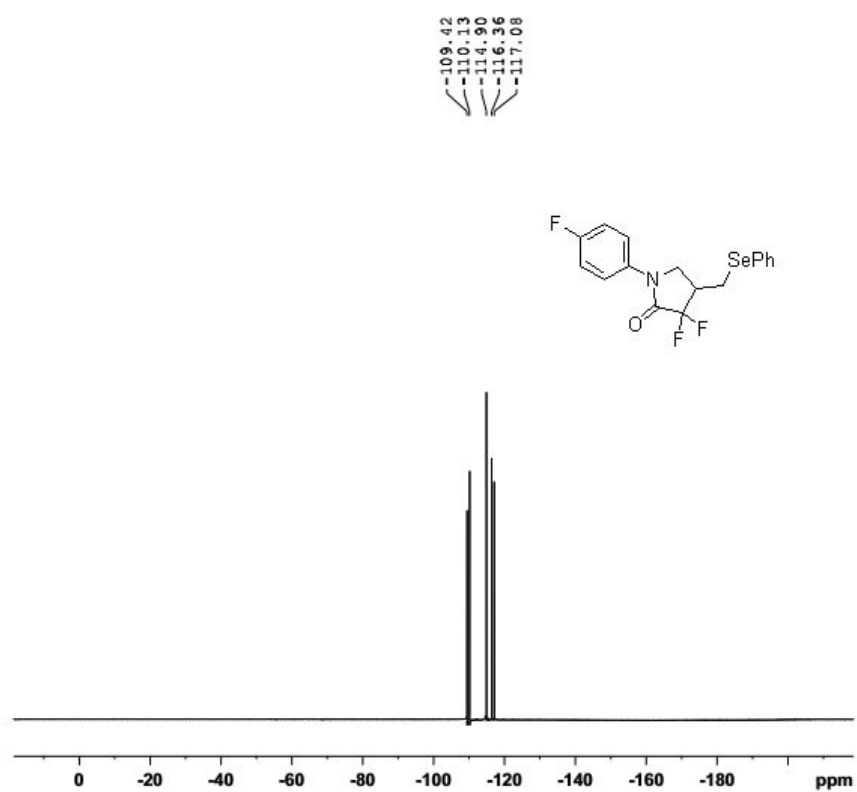
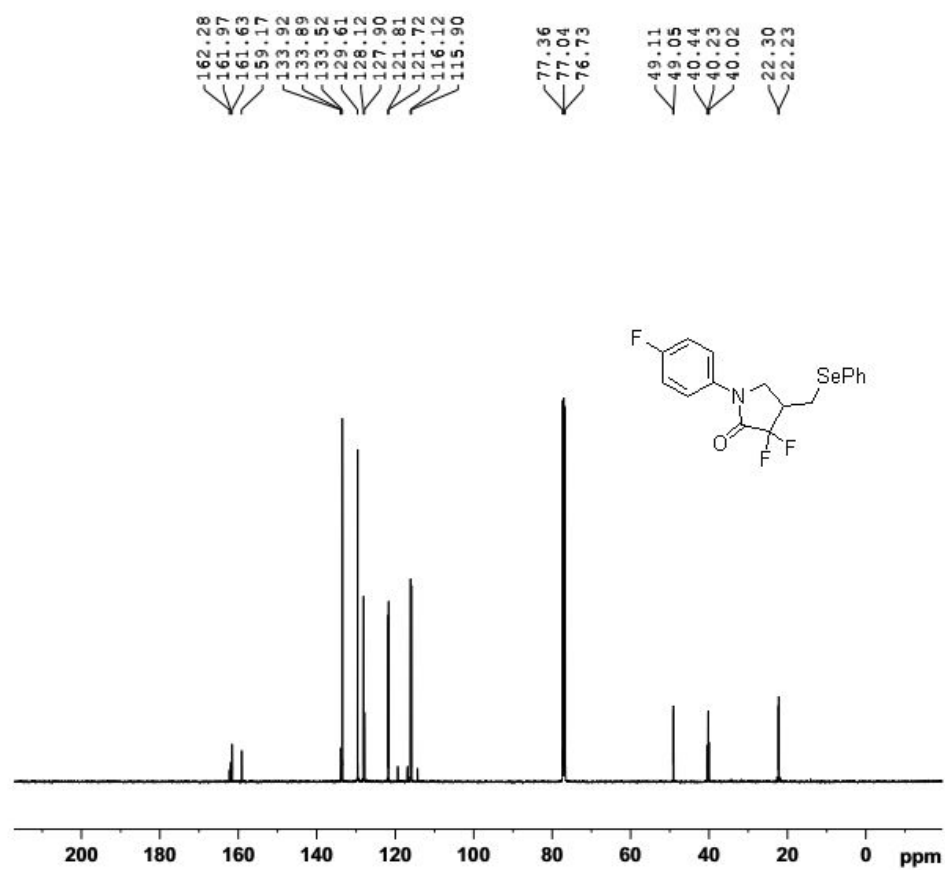
Compound 3g



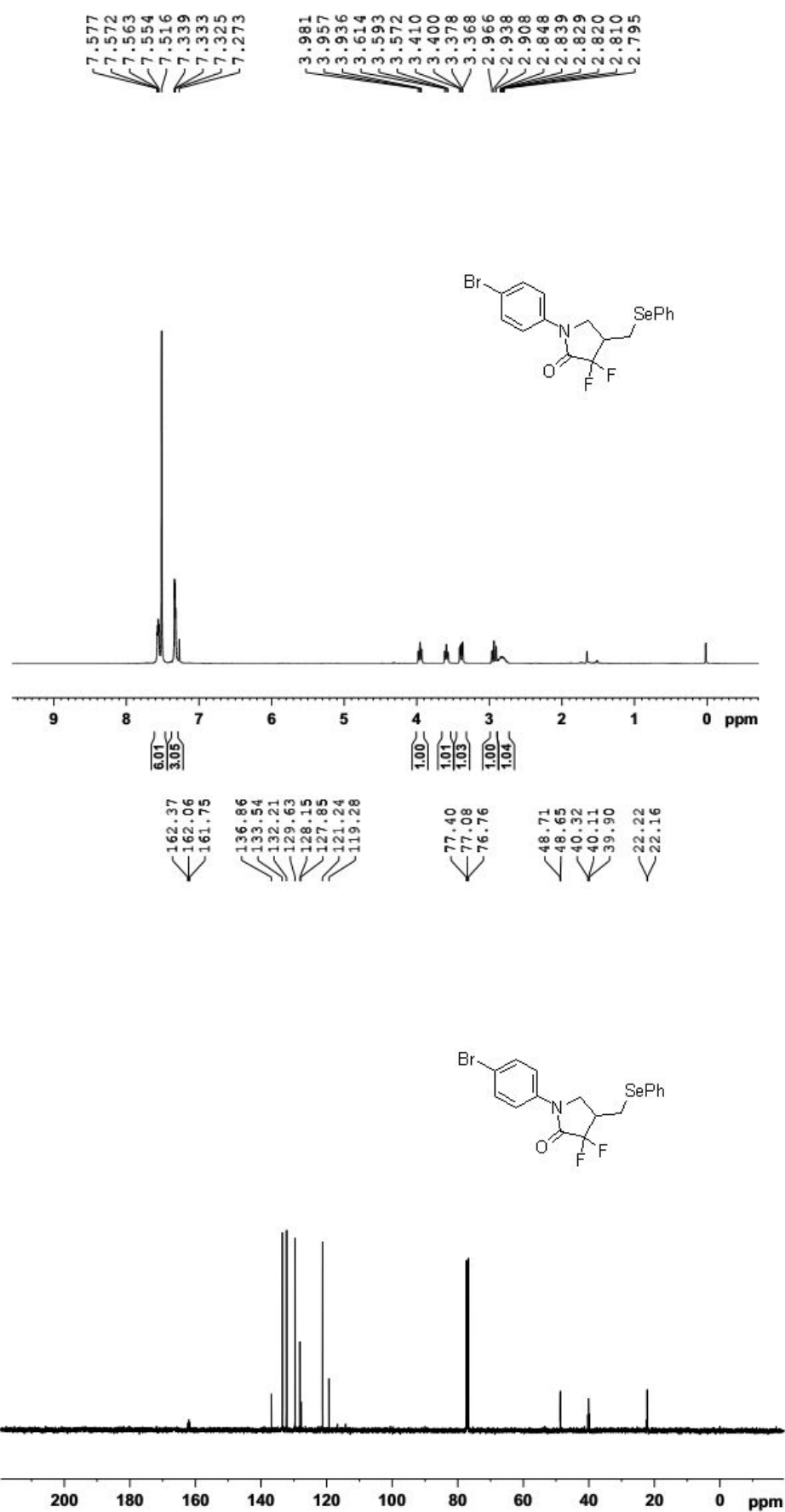


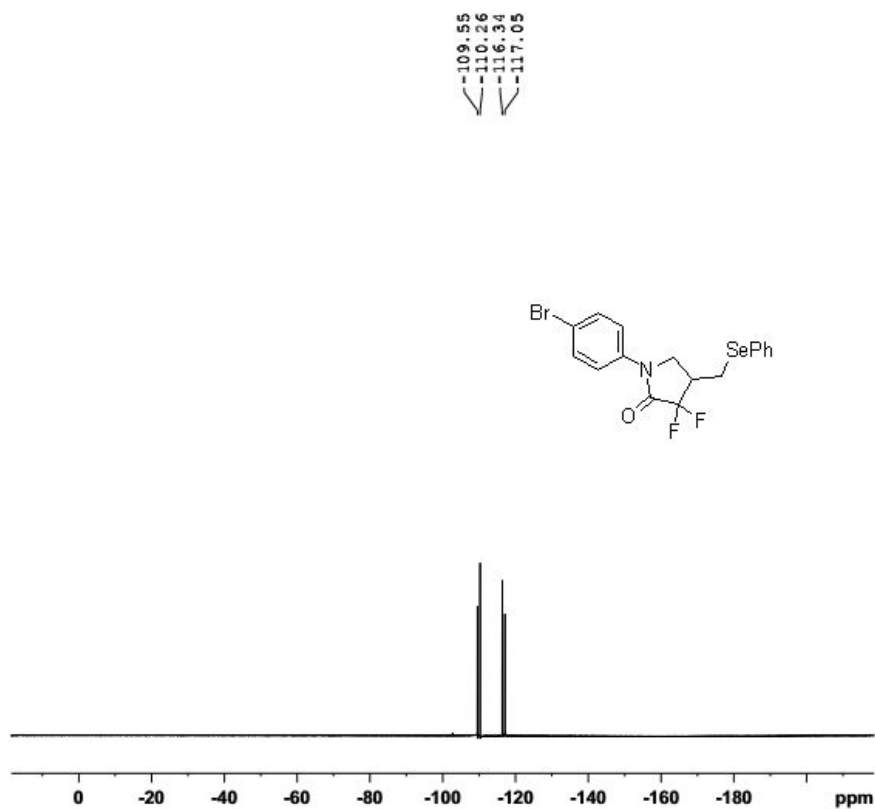
Compound 3h



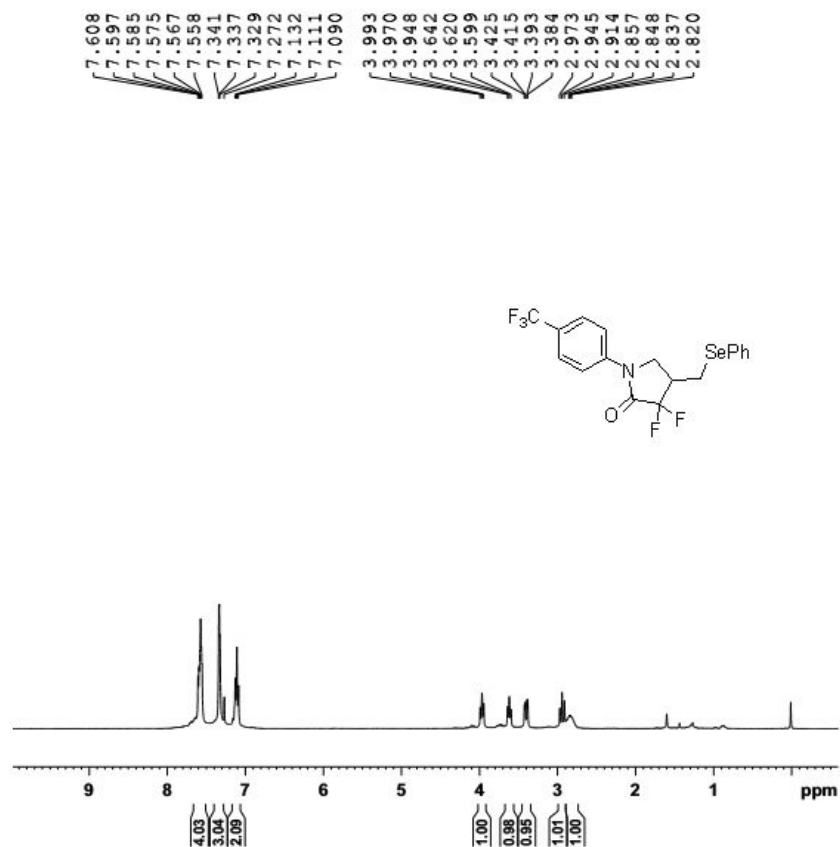


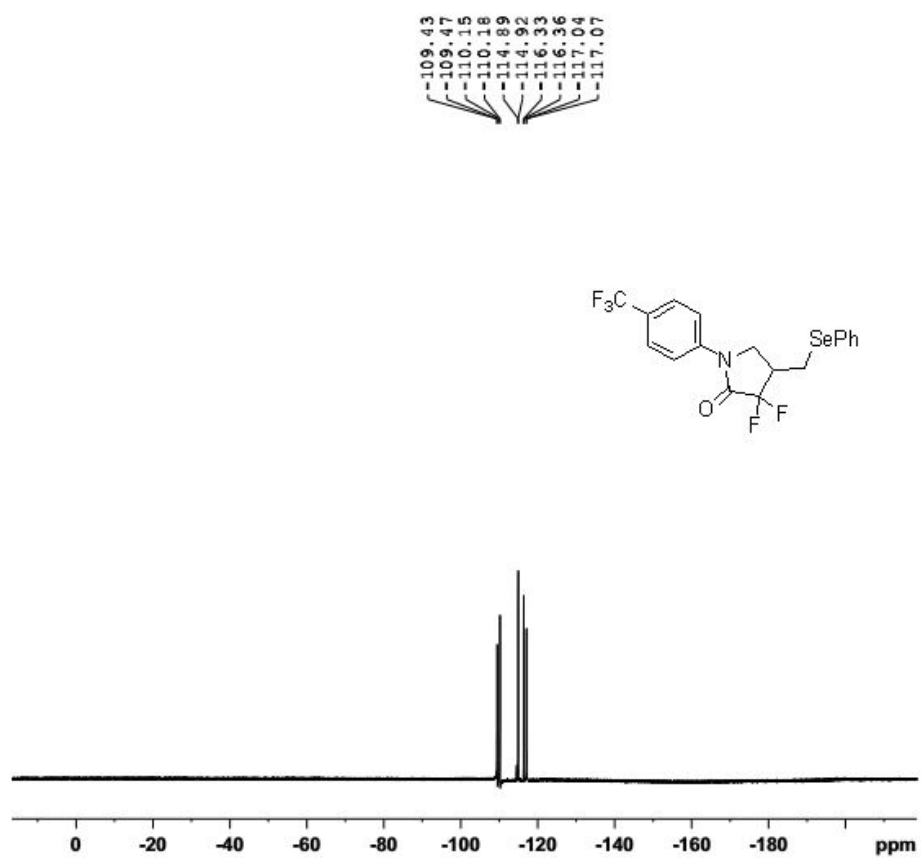
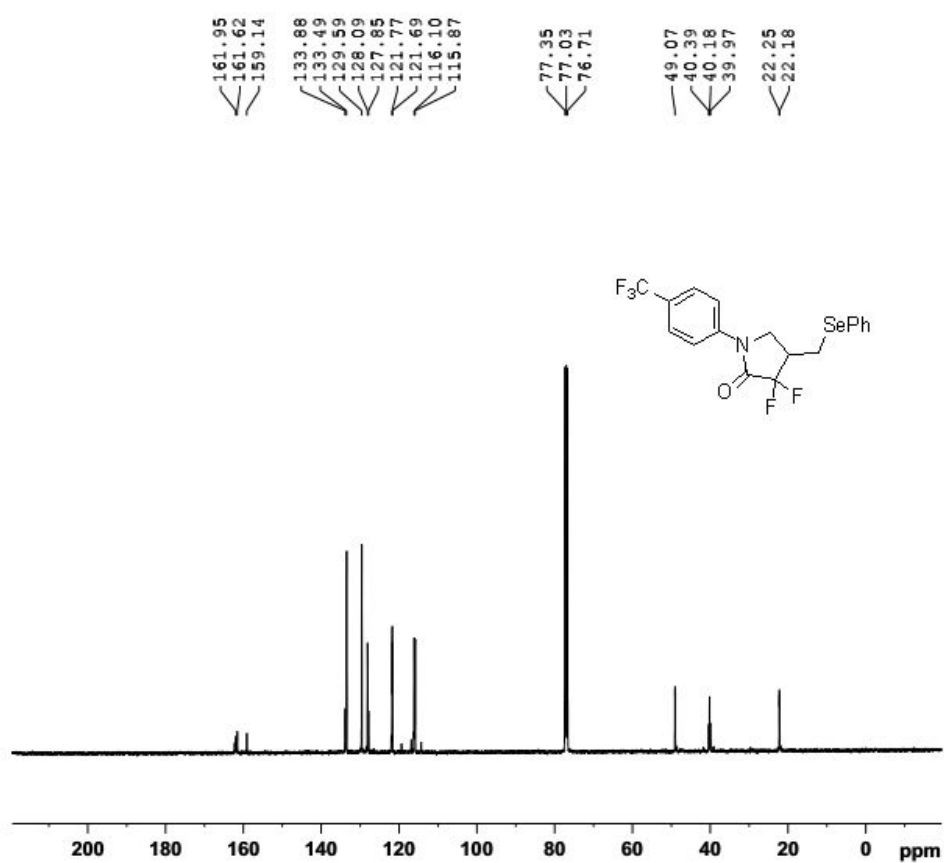
Compound 3i



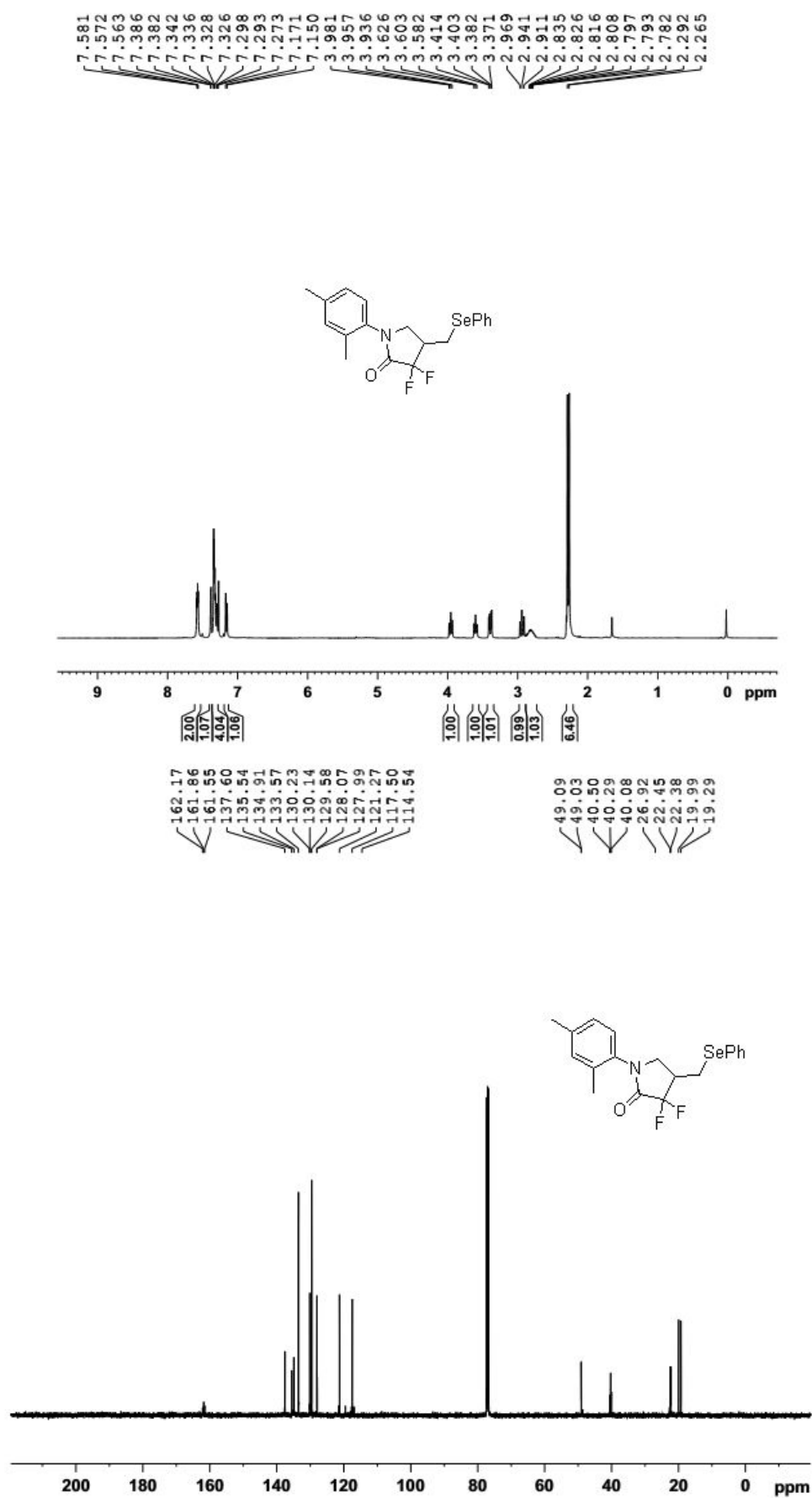


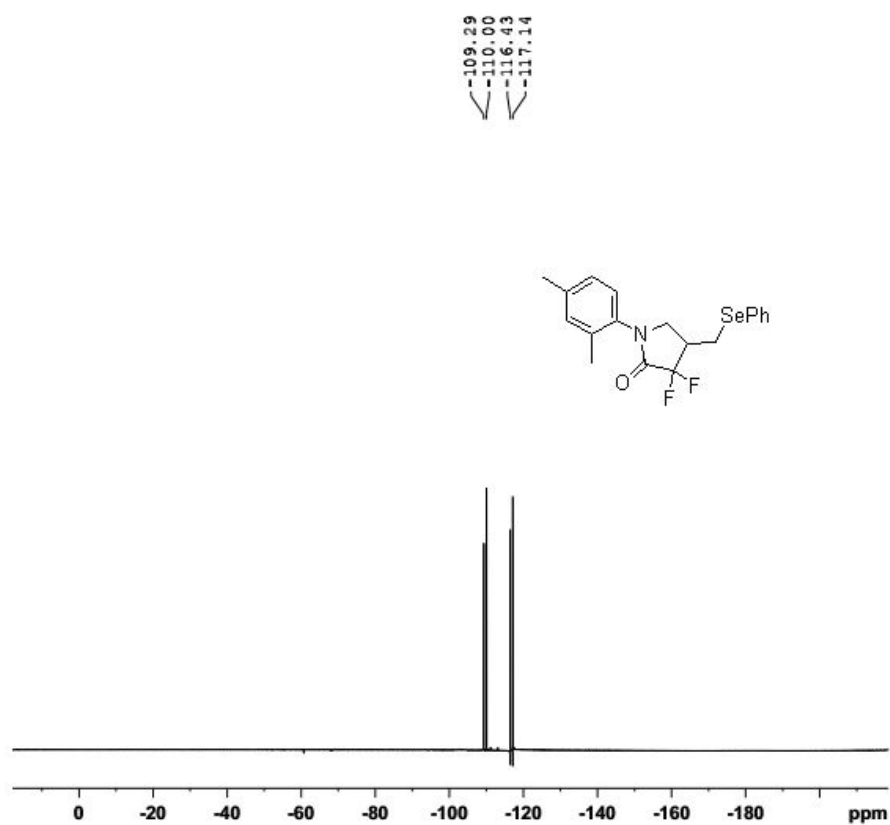
Compound 3j



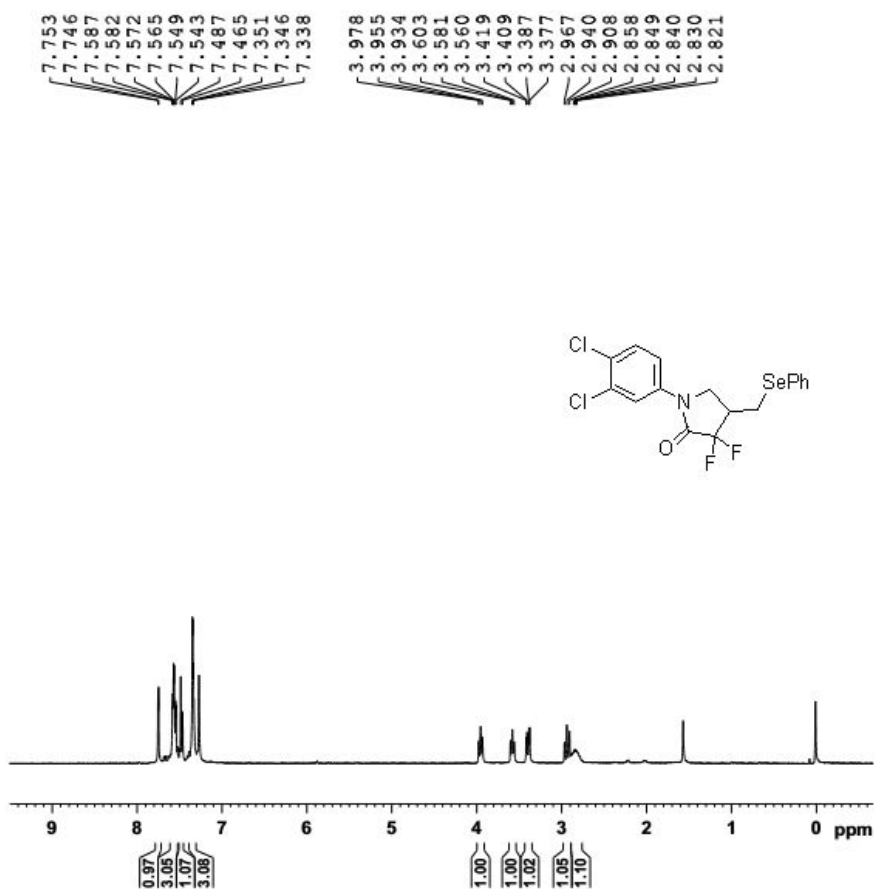


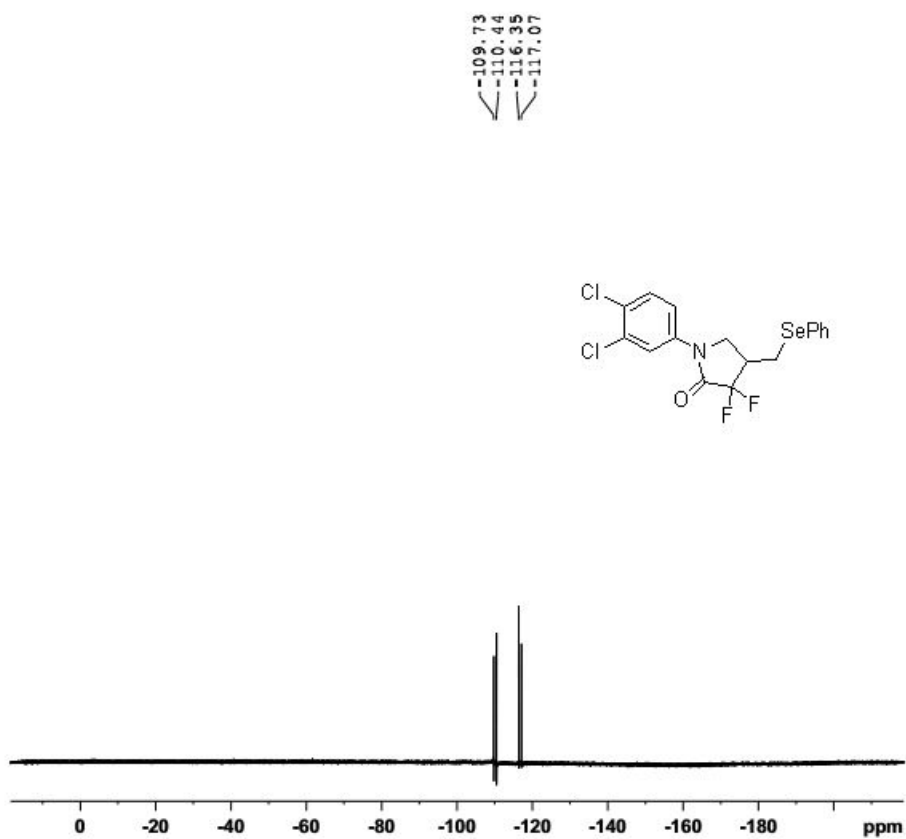
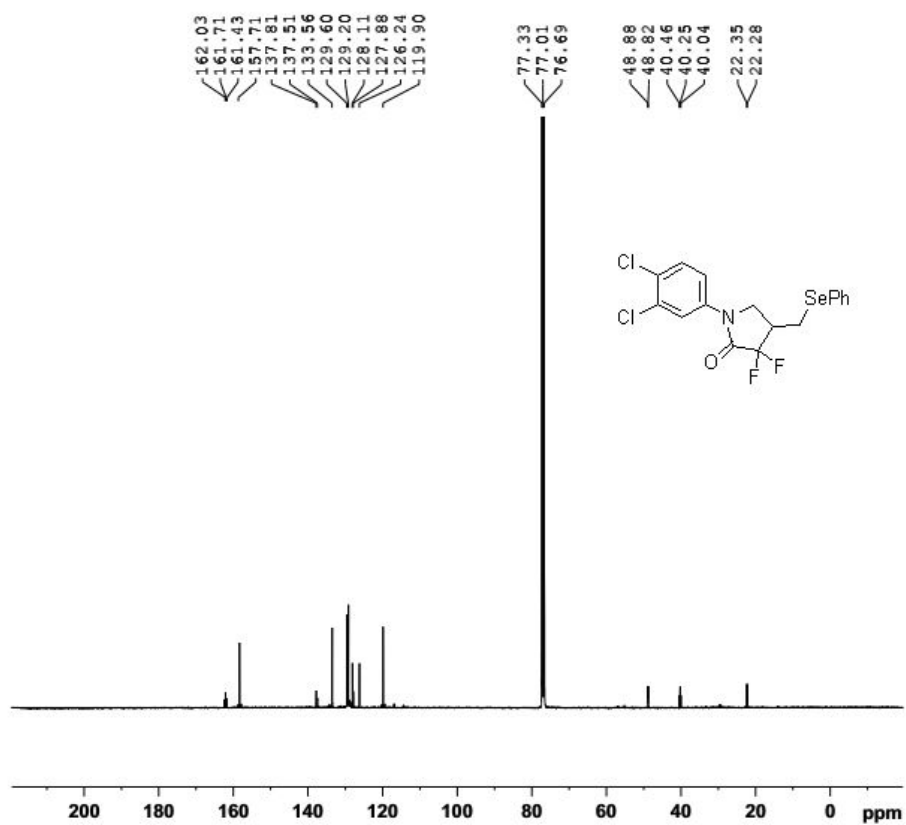
Compound 3k



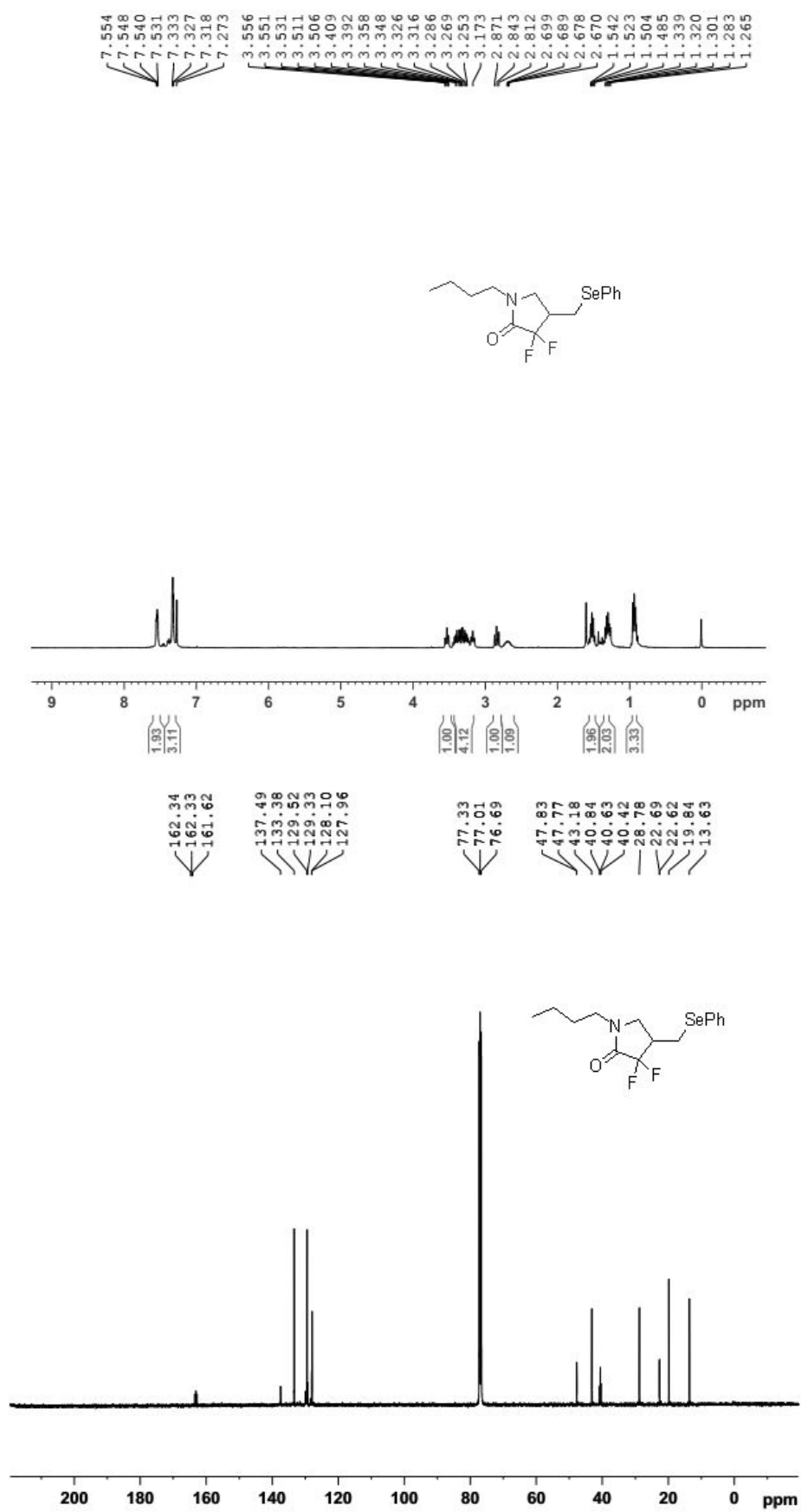


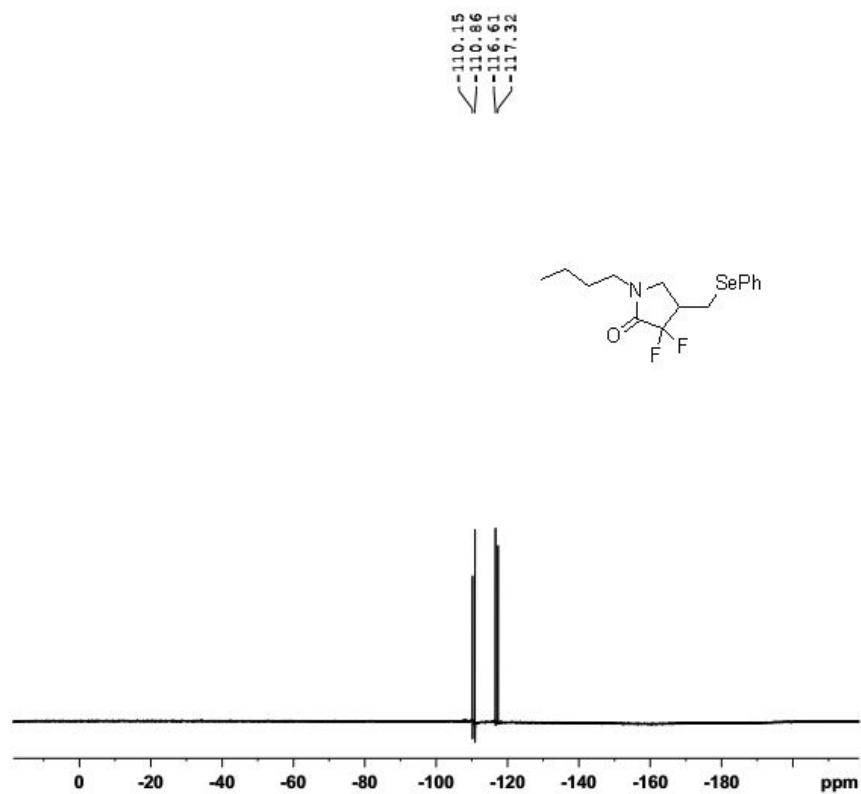
Compound 31



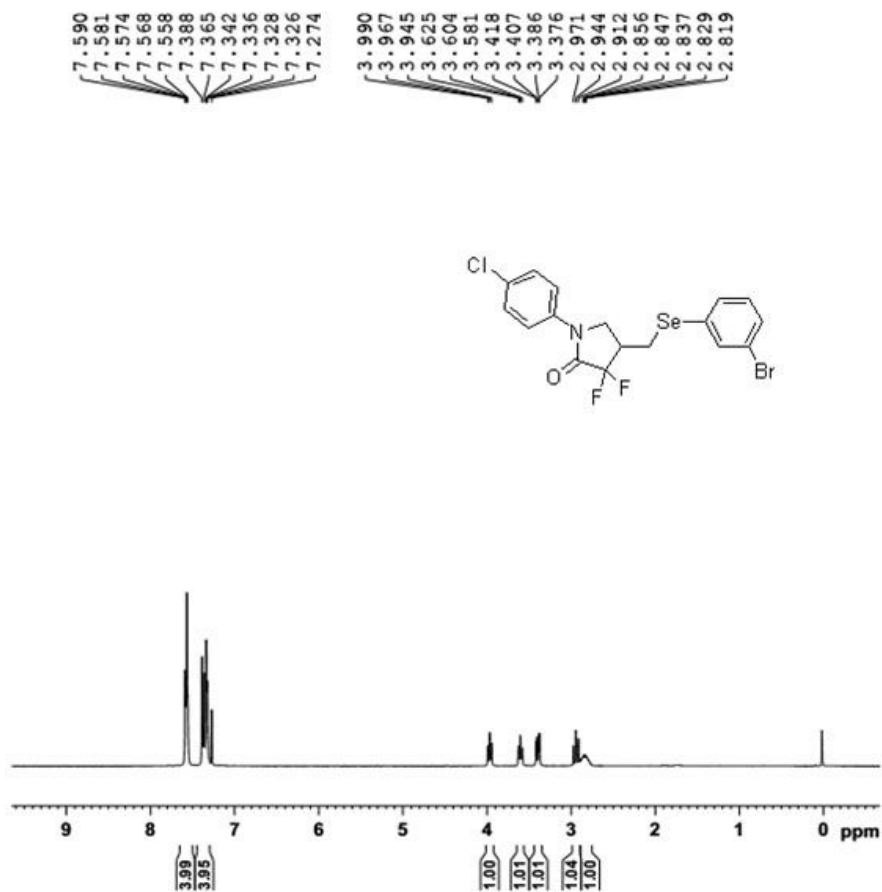


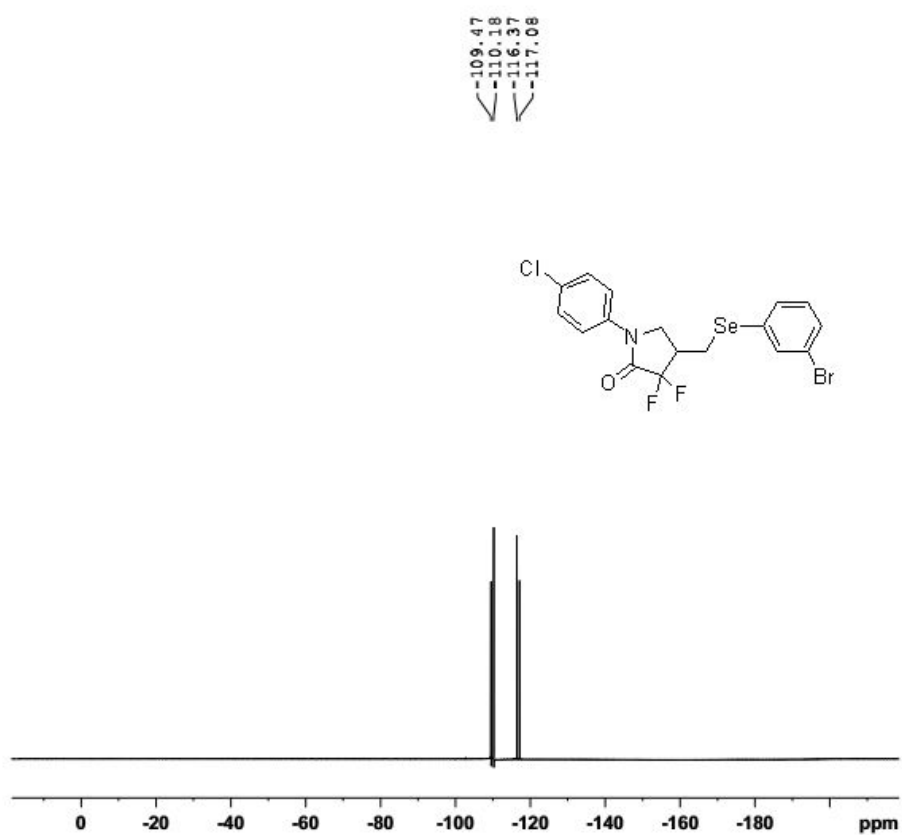
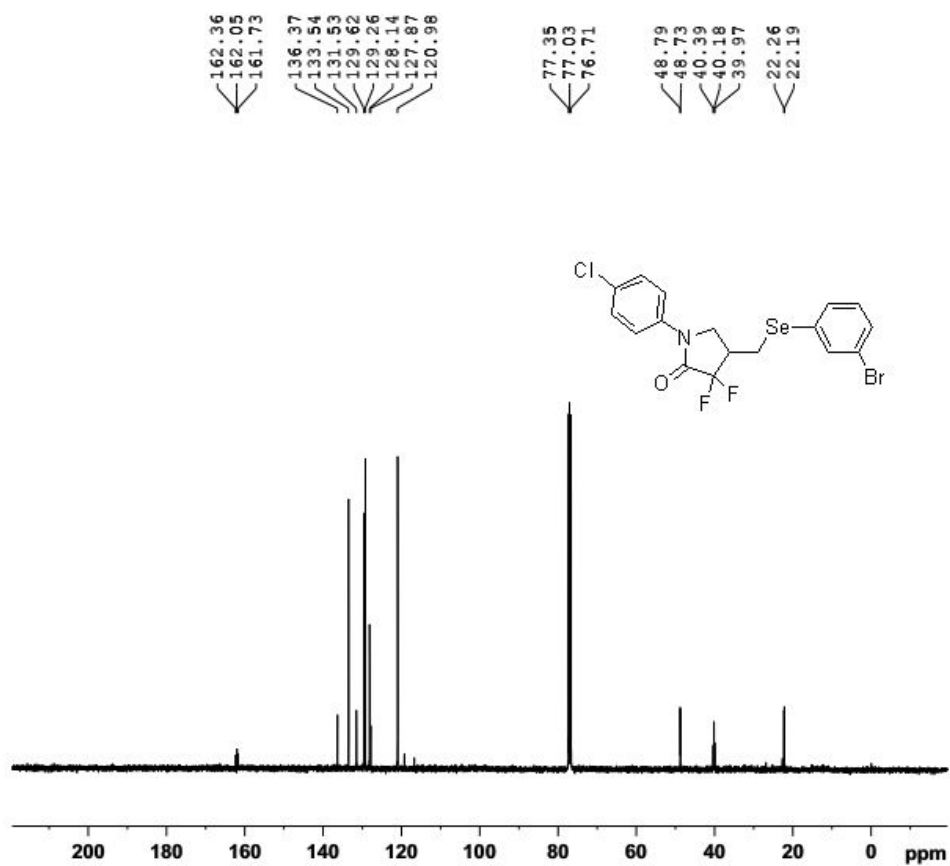
Compound 3m



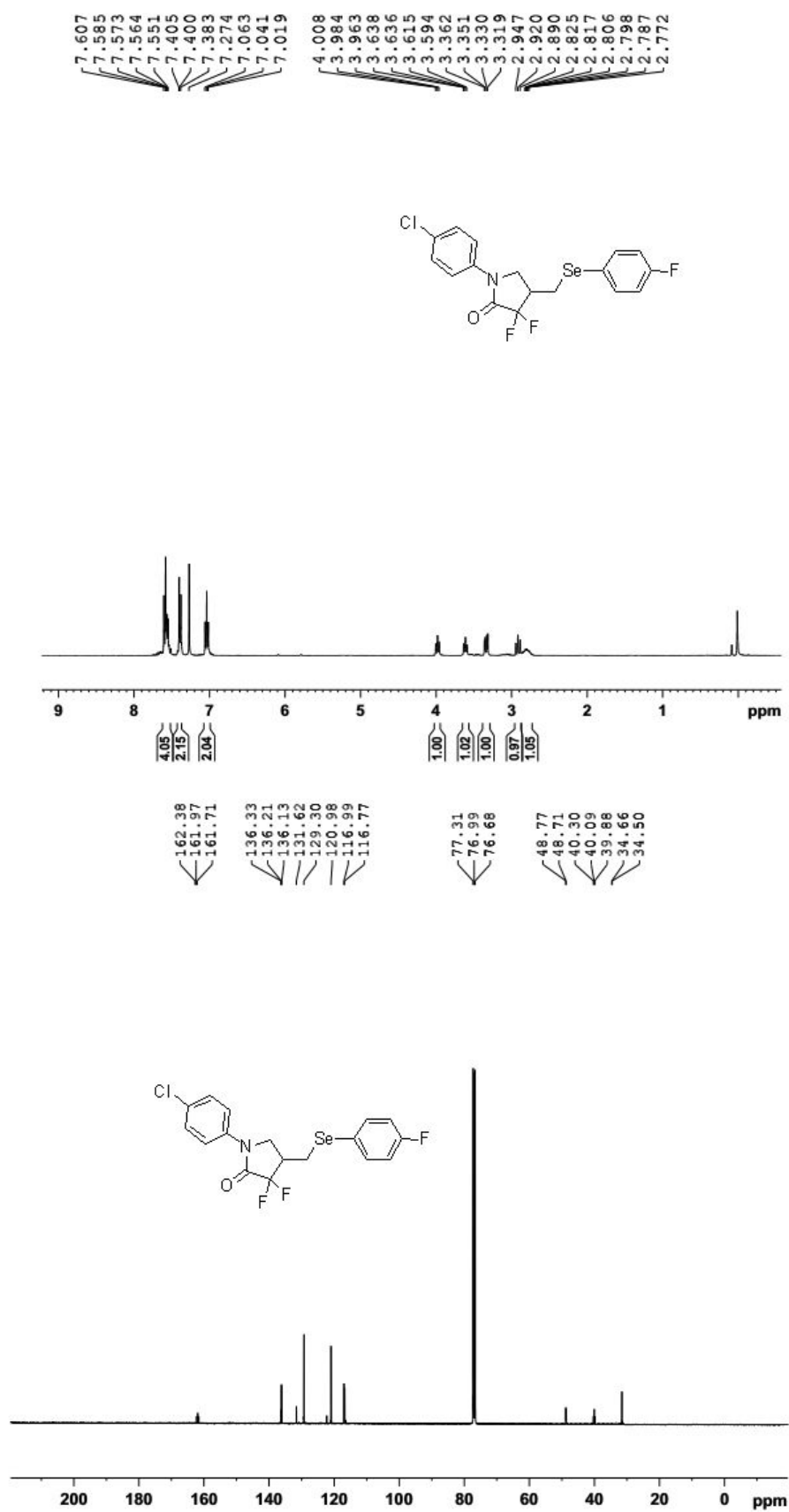


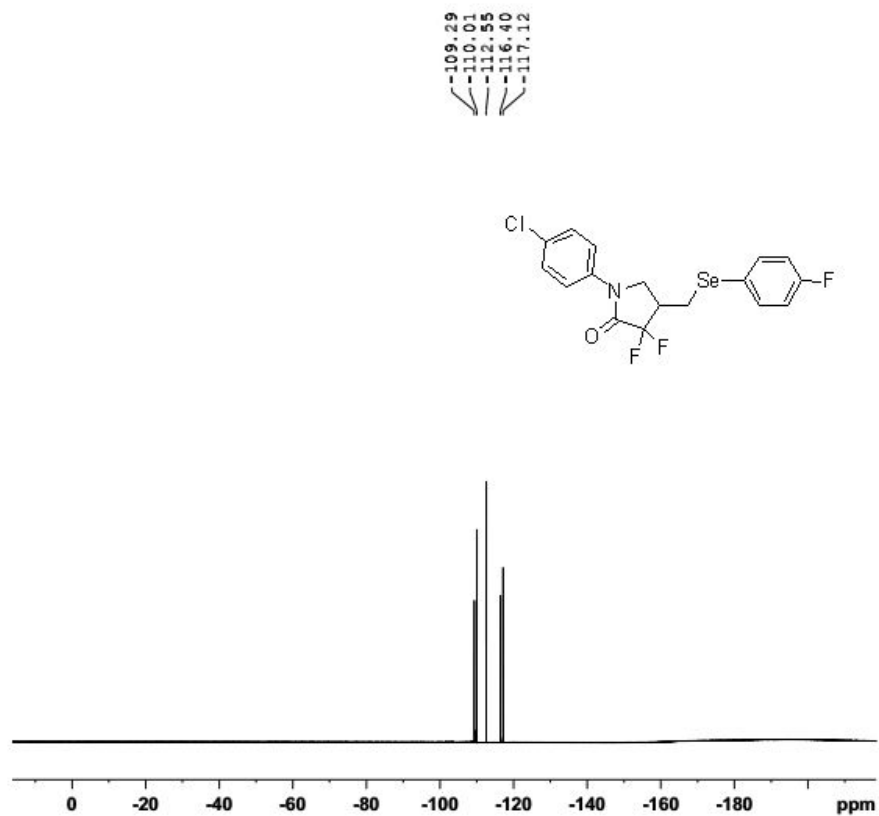
Compound 3n



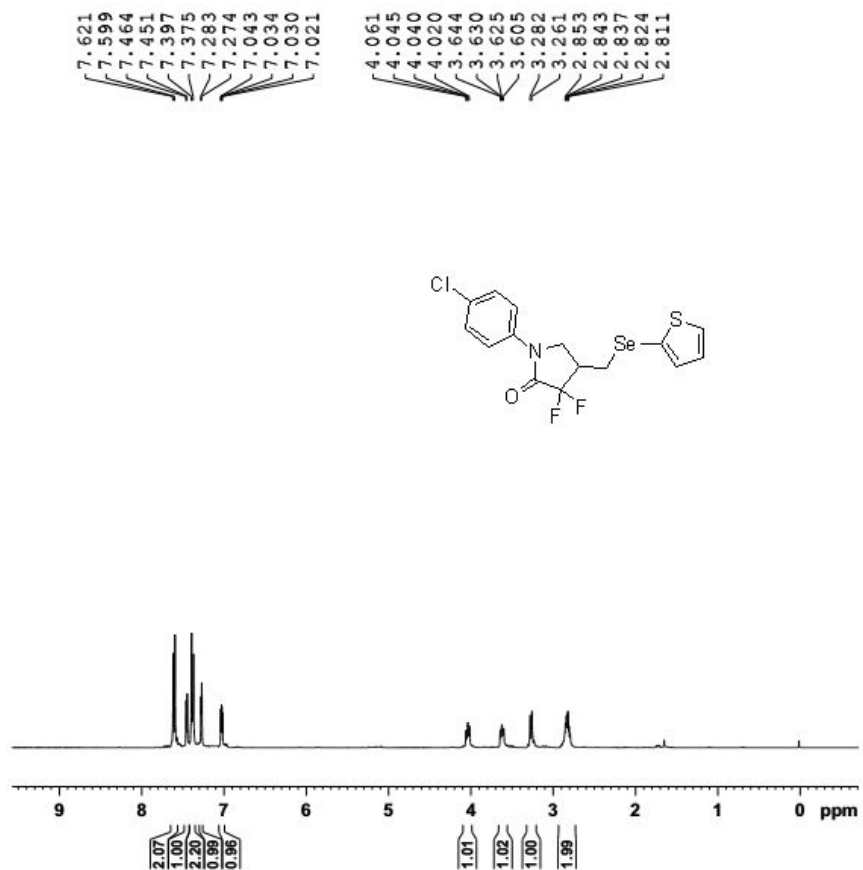


Compound 3o





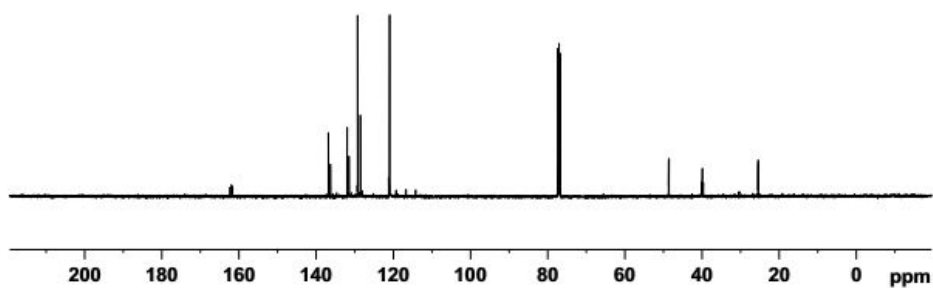
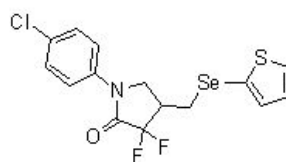
Compound 3p



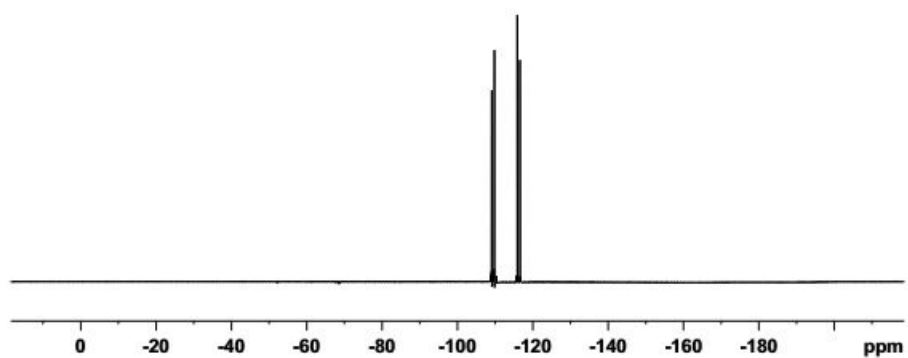
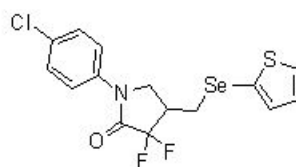
162.34
162.03
161.72
136.87
136.36
132.02
131.54
129.29
128.57
121.23
121.00

77.40
77.08
76.76

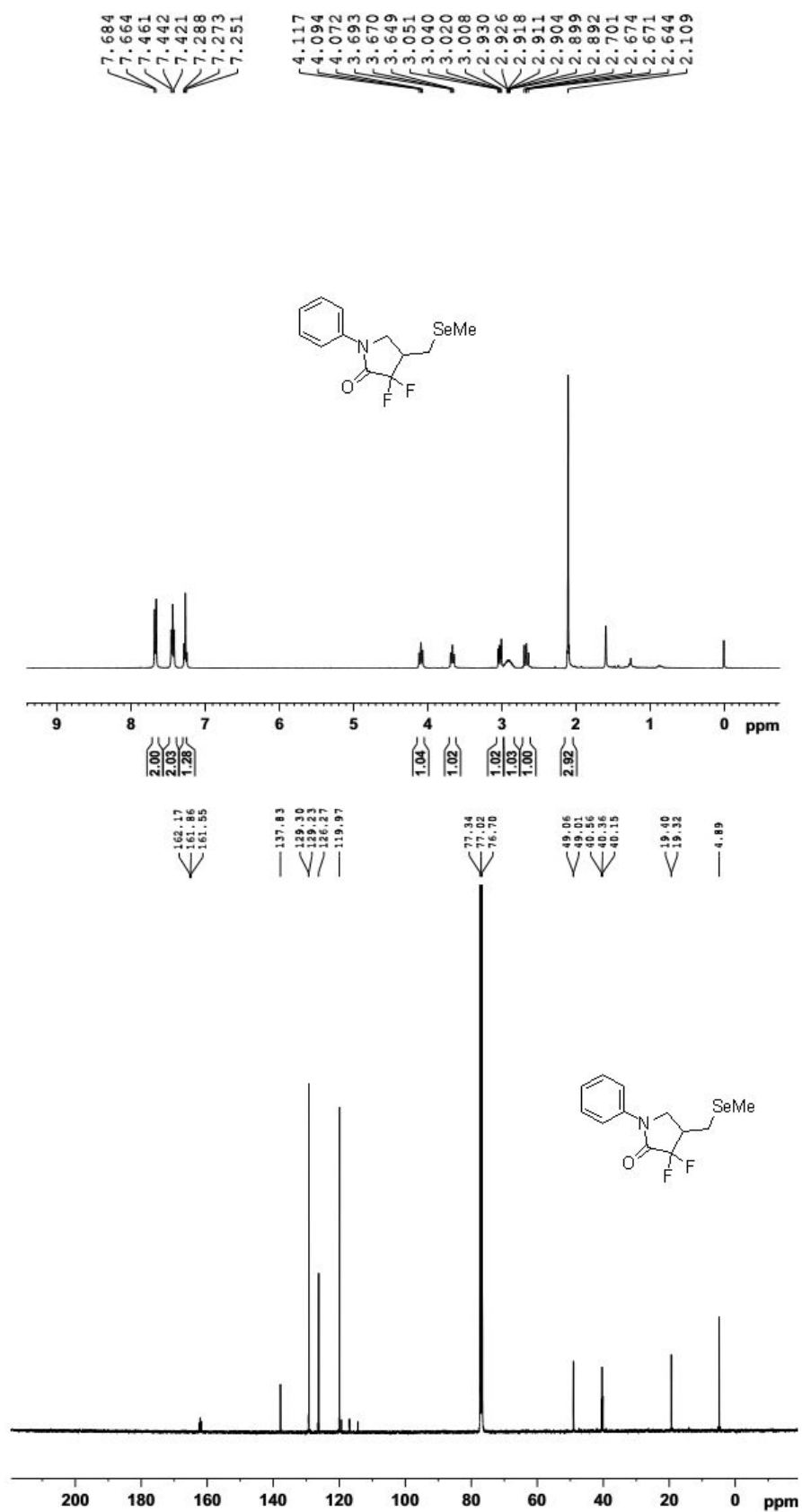
48.65
48.59
40.14
39.93
39.72
25.47
25.41

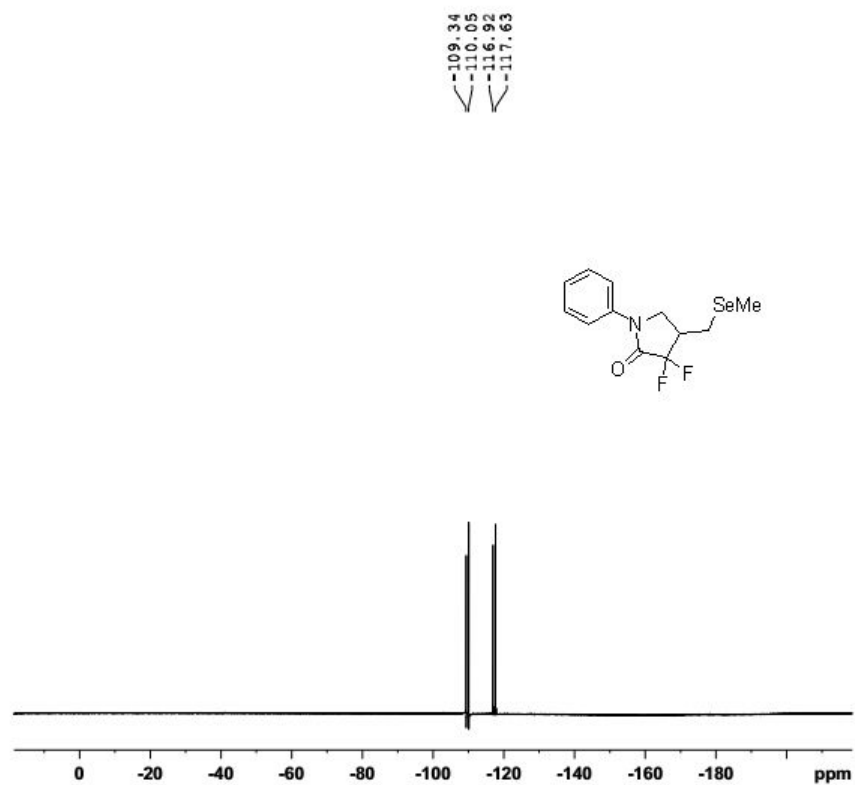


-109.07
-109.79
-115.87
-116.58

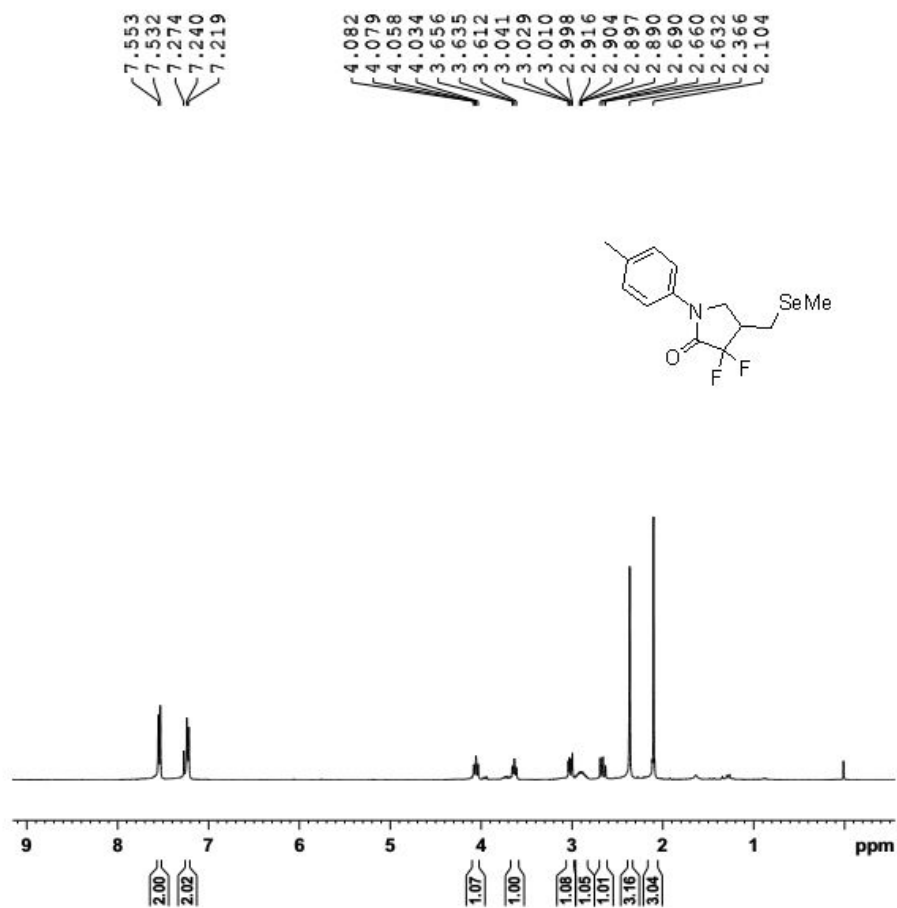


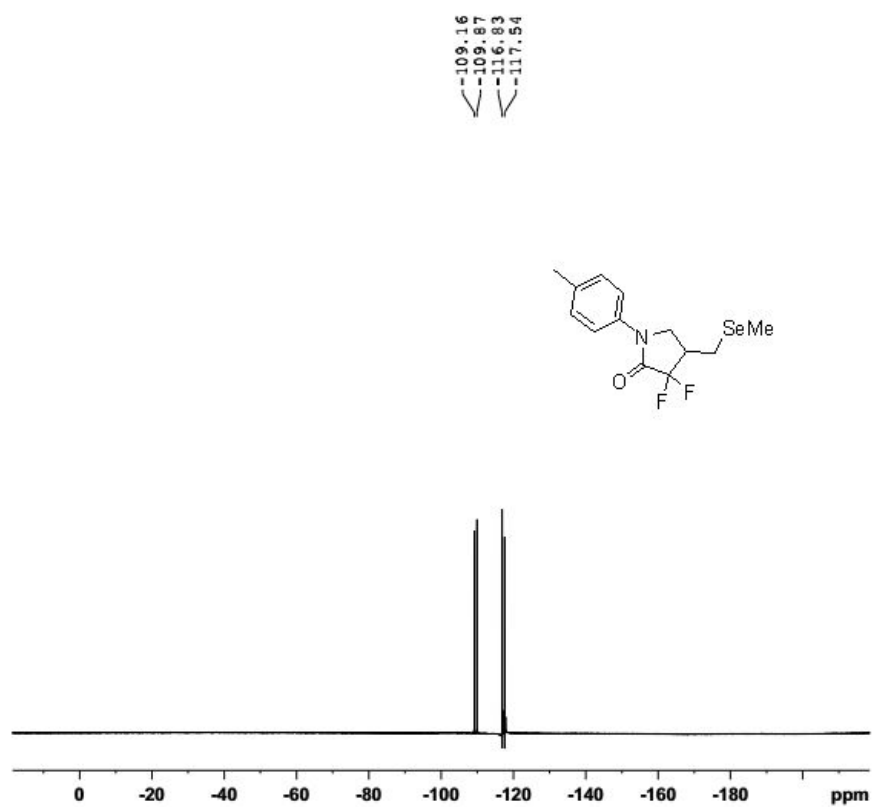
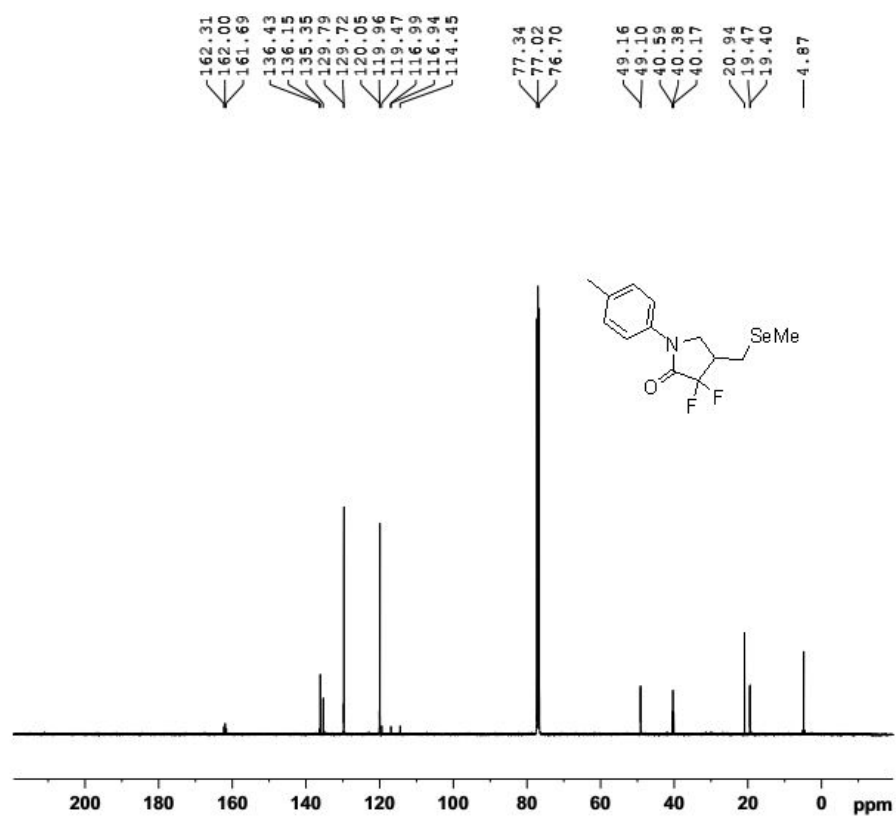
Compound 3q



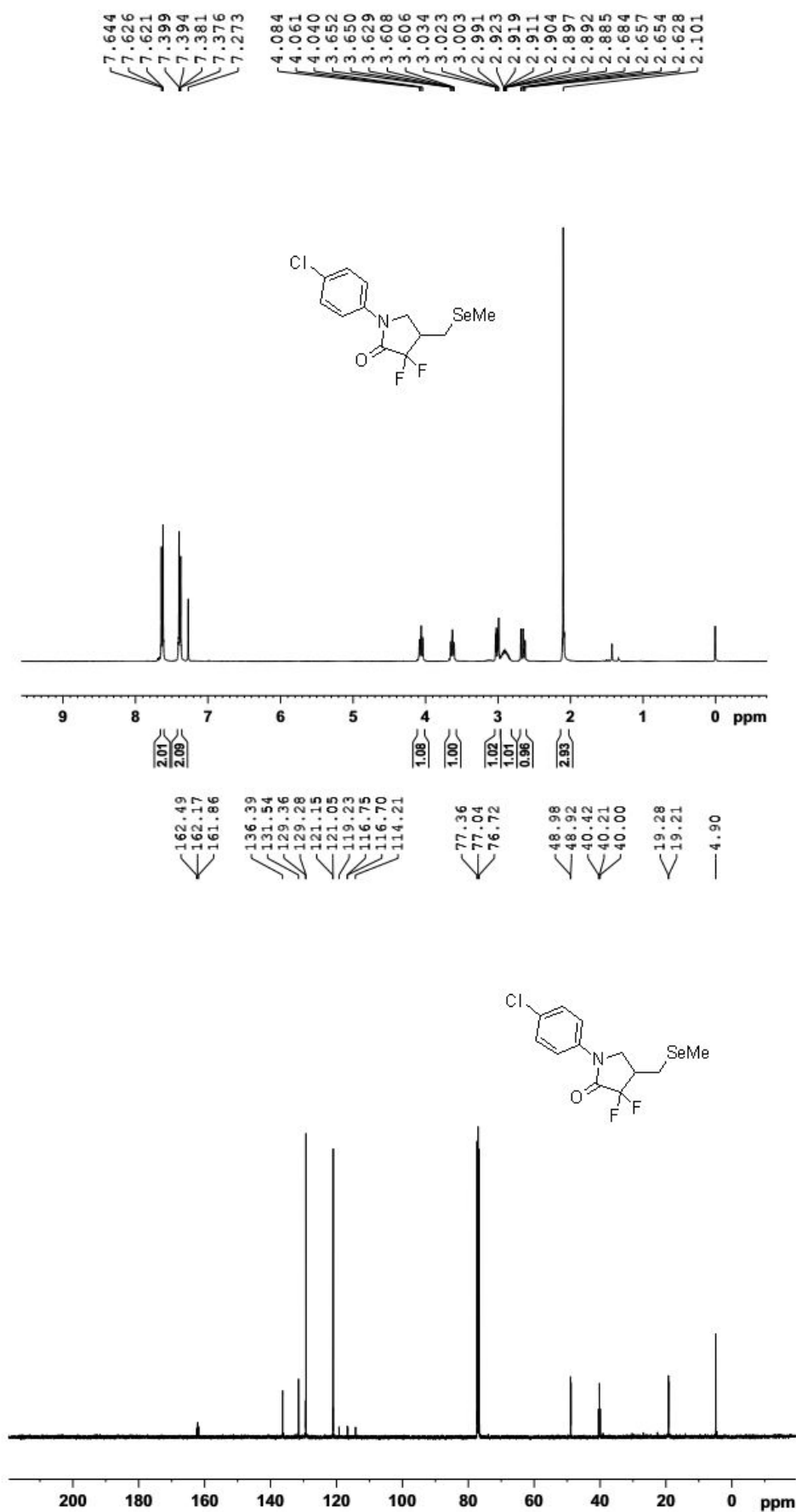


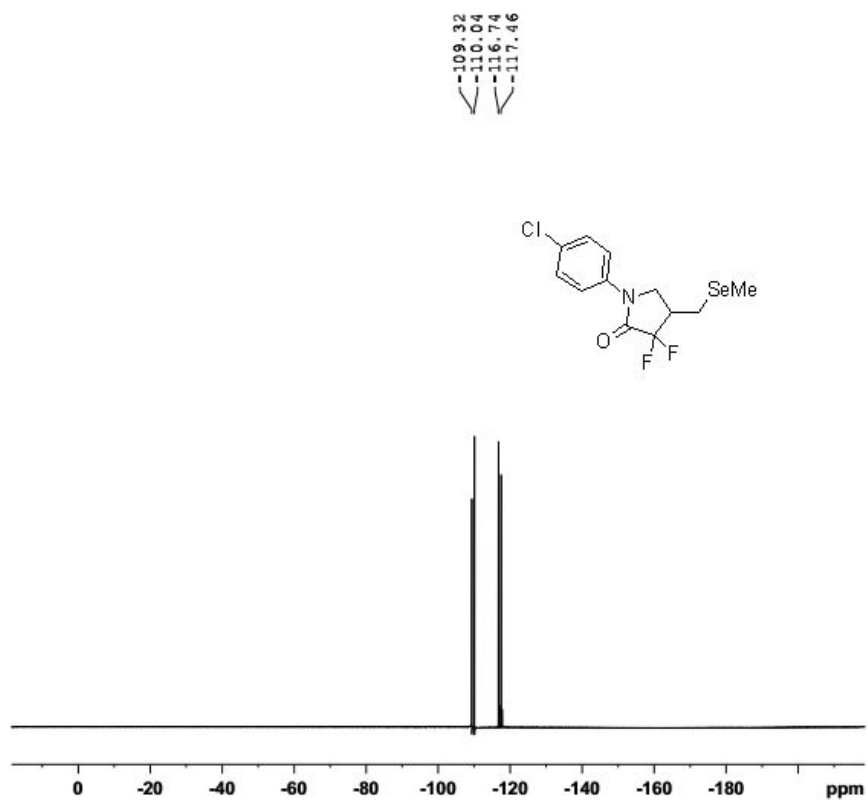
Compound 3r



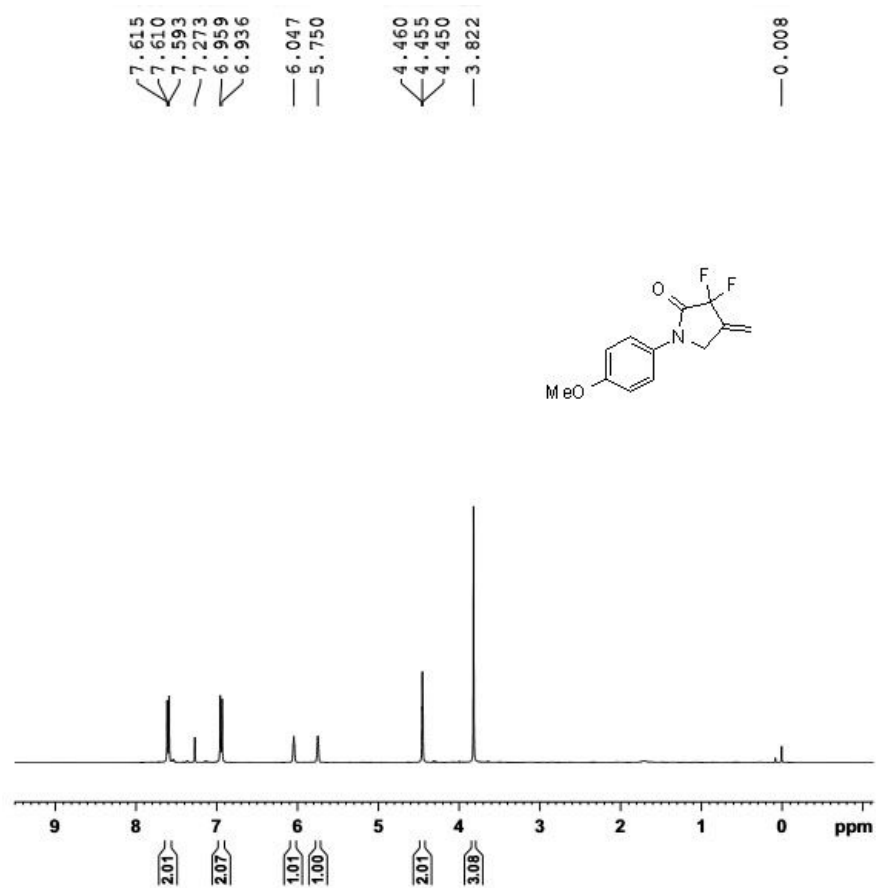


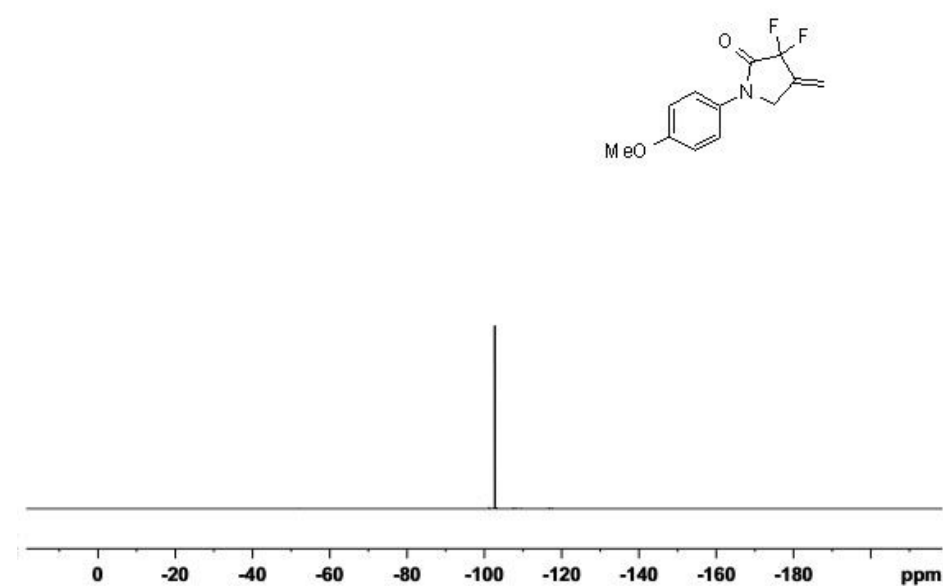
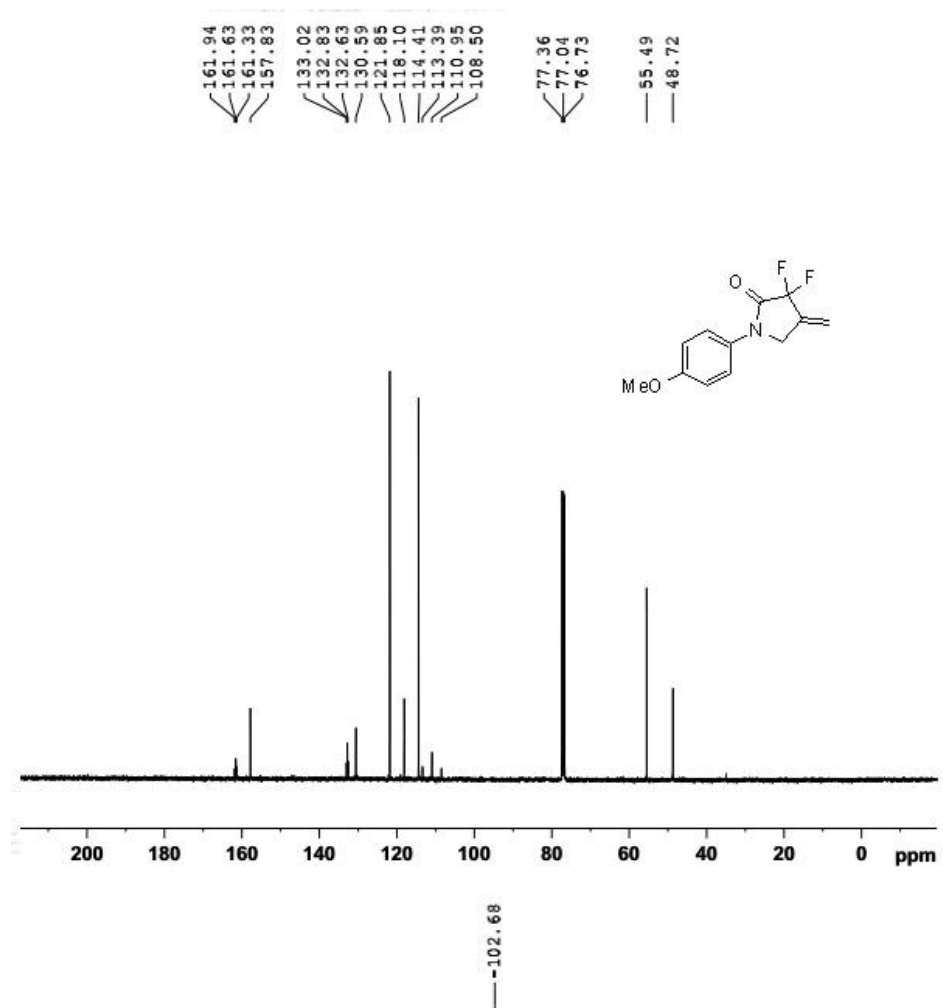
Compound 3s



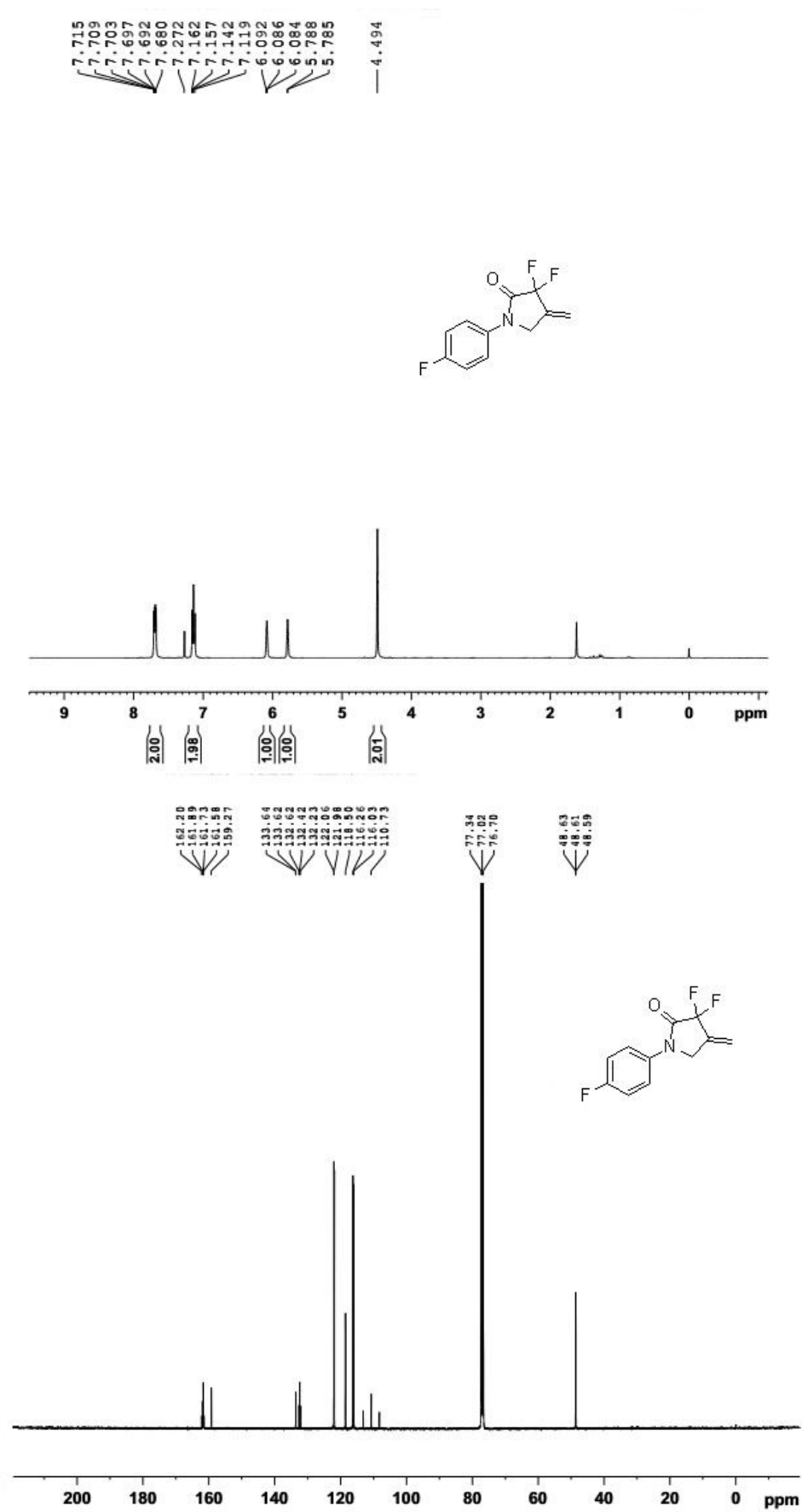


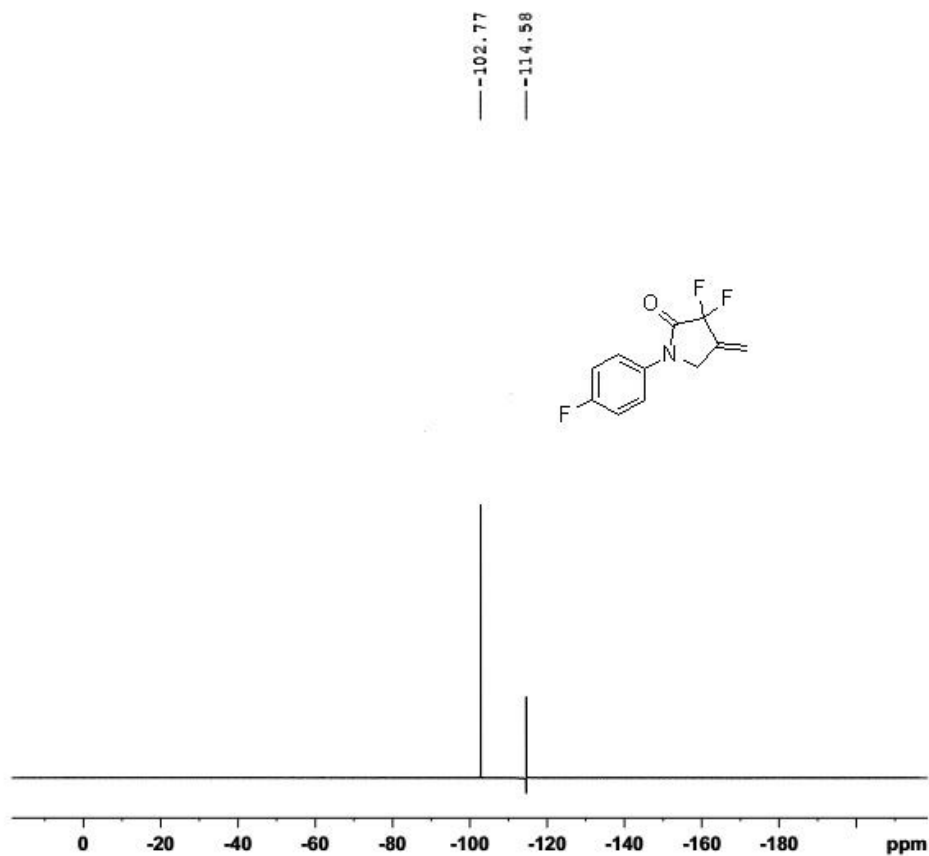
Compound 4





Compound 5





Compound 6

