Regioselective C-H chalcogenylation and halogenation of arenes and alkenes under metal-free conditions

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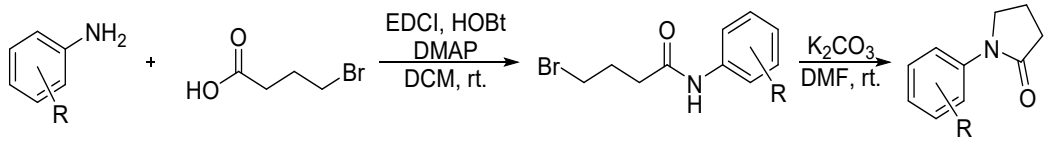
1. General Information

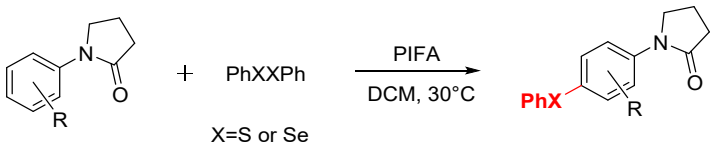
The Silica gel F254 plates were used for thin layer chromatography (TLC) in which the spots were examined under UV light at 254 nm. Flash chromatography was performed on silica gel (300-400 mesh). Anhydrous solvents were obtained according to standard procedures. Tetrahydrofuran (THF) was distilled from sodium-benzophenoneketyl. Methylene chloride (CH_2Cl_2) was distilled over P_2O_5. Methanol (MeOH) was distilled from magnesium. All other commercial reagents were purchased from commercial sources and used as received. NMR spectra were recorded on Varian Mercury spectrometer (400 MHz and 600 MHz). ^{1}H NMR spectra were recorded at ambient temperature at 400 MHz or 600 MHz. ^{13}C NMR spectra were recorded at ambient temperature at 100 MHz or 150 MHz. ^{1}H-NMR spectra were referenced to Chloroform-*d* (7.26 ppm) or DMSO-d_6 (2.50 ppm), and reported as follows: Chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m= multiplet). Chemical shifts of the ^{13}C-NMR spectra were measured relative to chloroform-*d* (77.23 ppm) or DMSO-d_6 (39.51 ppm). For ^{1}H NMR spectra acquired in CD_3OD, chemical shifts are reported as δ values in ppm and are calibrated according to internal CD_3OD (3.31 ppm). For ^{13}C NMR spectra, chemical shifts are reported as δ values in ppm relative to CD_3OD. The NMR data are reported as follows: chemical shift in ppm on the δ scale, multiplicity (app = apparent, br = broad, s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet), coupling constants (Hz), and integration. LCMS/ HRMS were recorded on a Bruker Daltonics Data analysis 3.4 mass spectrometer.

2. Typical Procedure for the Synthesis of Substrates



A flame-dried round-bottomed flask was charged with dry DCM (10 mL, 0.1 M), Aniline (1 mmol, 1 eq), 4-Bromobutyric acid (1.2 mmol, 1.2 eq), EDCI (1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, 1.2 mmol, 1.2 eq.), HOBt (1-hydroxybenzotriazole, 1.2 mmol, 1.2 eq) and DMAP (0.2 mmol, 20 mol%). The reaction mixture was stirring for 30 minutes at room temperature, and then the substituted aniline (1 mmol, 1 eq.) was added. After consumption of the starting material (monitored by TLC) the reaction mixture was concentrated under reduced pressure. Then diluted with ethyl acetate (40 mL) and the mixture was washed with 1 M HCl (20 mL) three times. The organic layer was washed with brine and dried with anhydrous Na_2SO_4. The crude product was concentrated for next step without further purified. A solution of the above crude product in dry DMF (5 mL) was added K_2CO_3 (2.0 mmol) and the mixture was stirred overnight. After completion of the reaction monitored with TLC, the reaction mixture was diluted with ethyl acetate (40 mL) and washed with saturated NaCl solution (3×20 mL).The combined organic layers were dried over $MgSO_4$ and filtered. The solvent was removed *in vacuo*.The resulting product was purified by flash silica gel column chromatography using PE / EA (2:1) as eluent.

3. Typical Procedure for the Preparation of 1-(4-(phenylselanyl) phenyl)pyrrolidin-2-ones

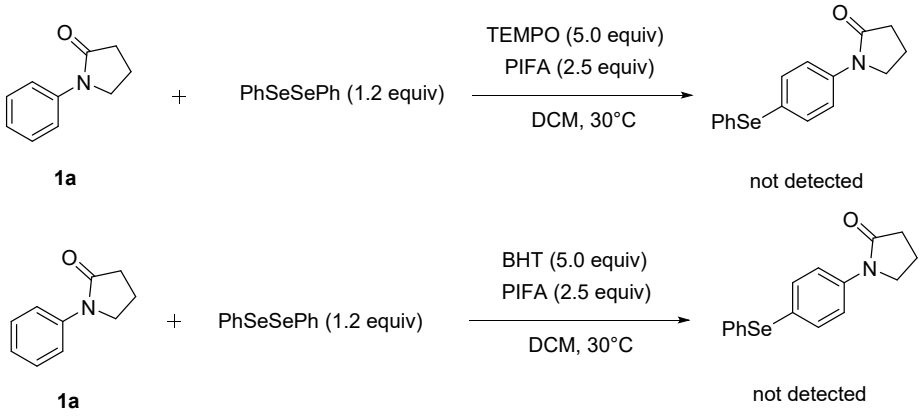


To a solution of 1-phenylpyrrolidin-2-one (0.1 mmol) in DCM (3 mL) was added PIFA (0.25 mmol), PhSeSePh or PhSSPh (0.12 mmol) at 30℃ and the solution was stirred for 1 h . The reaction mixture was concentrated under reduced pressure. The resulting product was purified by flash silica gel column chromatography using DCM / EA (60:1) as eluent.

4. Typical Procedure for the Preparation of 1-(4-halophenyl)-pyrrolidin-2-ones

To a solution of 1-phenylpyrrolidin-2-one (0.1 mmol) in DCM (3 mL) was added PIFA (0.25 mmol), PhSeCl or PhSeBr (0.12 mmol) at 60℃ and the solution was stirred for 2 h in sealing reaction tube. After consumption of the starting material (monitored by TLC) the reaction mixture was concentrated under reduced pressure. The resulting product was purified by flash silica gel column chromatography using DCM / EA (60:1) as eluent.

5. Mechanistic Experiments



To a solution of **1a** (0.1 mmol) in DCM (3 mL) was added PIFA (0.25 mmol), PhSeSePh (0.12 mmol), TEMPO or BHT (0.5 mmol) at 30 ℃ and the solution was stirred for 2 h . Sampling after 1 h for TLC detection and analysis. The expected compound was not detected.

6. Further applications

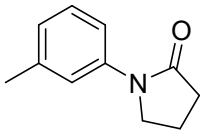
6.1 Anti-tumor activity

In Vitro Antiproliferative Assay: K562 cell line were initially purchased from the AmericanType

Culture Collection (ATCC, Manassas, VA, USA,). For growth assay in the presence of 1-(4-(phenylselanyl)phenyl)pyrrolidin-2-one derivatives, the cancer cells were plated in plates at a density of 50,000 each well in 5% FBS DMEM medium. The cells were then treated with 1-(4-(phenylselanyl)phenyl)pyrrolidin-2-one derivatives separately at 6 different doses for 4 days, while equal treatment volume of DMSO and adriamycin or mitoxantrone was employed as vehicle control and positive control, respectively. Cell numbers were counted with a Coulter instrument (Beckman-Coulter). The ratio of drug-treated cell numbers to vehicle-treated cell numbers was defined as the survival ratio. IC_{50} values were obtained from dose-response curves for each 1-(4-(phenylselanyl)phenyl)pyrrolidin-2-one derivatives.

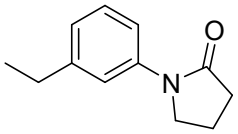
7. Analytic Data

1-(m-tolyl)pyrrolidin-2-one (1b)[1]:



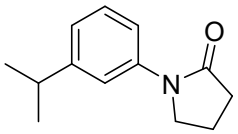
White solid, yield 86%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.40 (s, 1H), 7.35 (d, J = 8.3 Hz, 1H), 7.24 (t, J = 7.8 Hz, 1H), 7.00 (d, J = 7.3 Hz, 1H), 3.96 – 3.80 (m, 2H), 2.65 – 2.48 (m, 2H), 2.34 (s, 3H), 2.23 – 2.02 (m, 2H).

1-(3-ethylphenyl)pyrrolidin-2-one (1c)[1]:



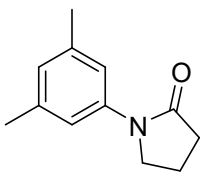
White solid, yield 95%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.44 (s, 1H), 7.35 (d, J = 8.2 Hz, 1H), 7.27 (t, J = 7.8 Hz, 1H), 7.03 (d, J = 7.4 Hz, 1H), 4.06 – 3.79 (m, 2H), 2.65 (q, J = 7.6 Hz, 2H), 2.61 – 2.52 (m, 2H), 2.27 – 1.99 (m, 2H), 1.23 (t, J = 7.6 Hz, 3H).

1-(3-isopropylphenyl)pyrrolidin-2-one (1d)[1]:



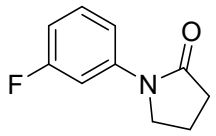
White oil, yield 54%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.51 – 7.45 (m, 1H), 7.37 – 7.31 (m, 1H), 7.28 (t, J = 7.8 Hz, 1H), 7.06 (d, J = 7.4 Hz, 1H), 3.90 (t, J = 7.1 Hz, 2H), 2.90 (hept, J = 6.9 Hz, 1H), 2.58 (t, J = 8.1 Hz, 2H), 2.16 (p, J = 7.5 Hz, 2H), 1.26 (s, 3H), 1.24 (s, 3H).

1-(3,5-dimethylphenyl)pyrrolidin-2-one (1e)[2]:



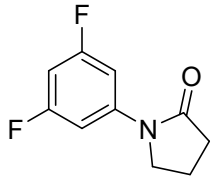
White solid, yield 79%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.17 (s, 2H), 6.84 (s, 1H), 3.95 – 3.81 (m, 2H), 2.57 (t, J = 8.1 Hz, 2H), 2.30 (s, 6H), 2.15 (p, J = 7.8 Hz, 2H).

1-(2-fluorophenyl)pyrrolidin-2-one (1f)[1]:



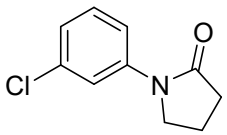
White solid, yield 98%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.48 – 7.28 (m, 2H), 7.27 – 7.12 (m, 2H), 3.84 (t, J = 7.0 Hz, 2H), 2.56 (t, J = 8.0 Hz, 2H), 2.24 (p, J = 7.4 Hz, 2H).

1-(3,5-difluorophenyl)pyrrolidin-2-one (1g)[3]



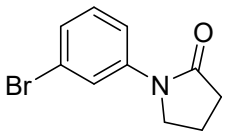
White solid, yield 61%. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.27 (d, J = 7.8 Hz, 2H), 6.58 (t, J = 8.8 Hz, 1H), 3.82 (t, J = 7.0 Hz, 2H), 2.63 (t, J = 8.1 Hz, 2H), 2.18 (p, J = 7.6 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-d) δ 174.5, 164.3 (d, J = 14.8 Hz), 161.9 (d, J = 14.7 Hz), 141.5 (t, J = 13.1 Hz), 102.4 (dd, J = 60.6, 9.0 Hz), 99.4 (t, J = 25.7 Hz), 48.5, 32.9, 17.7. HRMS(ESI) *m/z*: calculated for $C_{10}H_{10}F_2NO$ $[M+H]^+$ 198.0725, found 198.0729.

1-(3-chlorophenyl)pyrrolidin-2-one (1h)[1]:



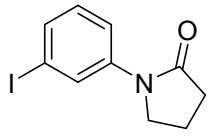
White solid, yield 87%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.82 (s, 1H), 7.50 (d, J = 8.1 Hz, 1H), 7.37 (t, J = 8.1 Hz, 1H), 7.18 (d, J = 7.3 Hz, 1H), 3.93 (t, J = 7.0 Hz, 2H), 2.62 (t, J = 8.1 Hz, 2H), 2.20 (p, J = 7.8 Hz, 2H).

1-(3-bromophenyl)pyrrolidin-2-one (1i)[2]:



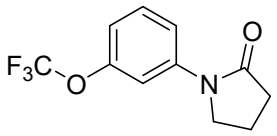
Light red solid, yield 76%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.97 – 7.92 (m, 1H), 7.55 – 7.47 (m, 1H), 7.35 – 7.22 (m, 2H), 3.89 (t, J = 7.1 Hz, 2H), 2.59 (t, J = 8.1 Hz, 2H), 2.16 (p, J = 7.5 Hz, 2H).

1-(3-iodophenyl)pyrrolidin-2-one (1j)[4]:



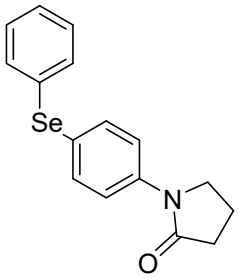
White solid, yield 52%. ^{1}H NMR (400 MHz, Methanol-d4) δ 8.10 (s, 1H), 7.63 – 7.43 (m, 2H), 7.22 – 7.02 (m, 1H), 3.96 – 3.80 (m, 2H), 2.58 (t, J = 7.3 Hz, 2H), 2.16 (p, J = 7.0 Hz, 2H).

1-(3-(trifluoromethoxy)phenyl)pyrrolidin-2-one(1k):



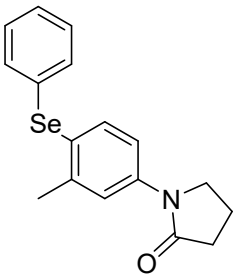
White solid, yield 29%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.80 (s, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.45 (t, J = 8.2 Hz, 1H), 7.07 (d, J = 8.0 Hz, 1H), 3.93 (t, J = 7.1 Hz, 2H), 2.61 (t, J = 8.1 Hz, 2H), 2.18 (p, J = 7.6 Hz, 2H).^{13}C NMR (101 MHz, Methanol-d_4) δ 175.8, 149.2, 140.9, 129.8, 120.5 (q, J = 255.8 Hz), 117.9, 116.3, 112.8, 48.8, 32.2, 17.4. HRMS(ESI) *m/z*: calculated for $C_{11}H_{11}F_3NO_2$ $[M+H]^+$ 246.0736, found 246.0732.

1-(4-(phenylselanyl)phenyl)pyrrolidin-2-one (3a):



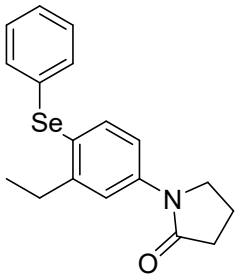
White solid. yield 91%. mp: 55℃-60℃. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.56 (d, J = 8.7 Hz, 2H), 7.48 (d, J = 8.7 Hz, 2H), 7.44 – 7.38 (m, 2H), 7.32 – 7.20 (m, 3H), 3.90 (t, J = 7.1 Hz, 2H), 2.58 (t, J = 8.1 Hz, 2H), 2.16 (p, J = 7.6 Hz, 2H).^{13}C NMR (151 MHz, DMSO-d_6) δ 174.5, 140.0, 134.8, 132.0, 131.8, 130.0, 127.6, 123.9, 120.7, 48.4, 32.8, 17.8. ^{77}Se NMR (76 MHz, DMSO) δ 401.29. HRMS(ESI) *m/z*: calculated for $C_{16}H_{16}NOSe$ $[M+H]^+$ 318.0392, found 318.0397.

1-(3-methyl-4-(phenylselanyl)phenyl)pyrrolidin-2-one (3b):



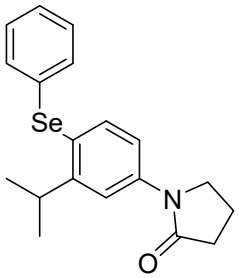
White solid. yield 85%. mp: 59℃-63℃. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.56 (s, 1H), 7.48 – 7.28 (m, 4H), 7.27 – 7.14 (m, 3H), 3.89 (t, J = 7.0 Hz, 2H), 2.58 (t, J = 8.1 Hz, 2H), 2.37 (s, 3H), 2.16 (p, J = 7.6 Hz, 2H).^{13}C NMR (101 MHz, Methanol-d_4) δ 175.6, 140.9, 139.3, 134.8, 131.6, 131.1, 129.1, 126.8, 126.7, 122.0, 118.7, 49.0, 32.2, 21.5, 17.5. HRMS(ESI) *m/z*: calculated for $C_{17}H_{18}NOSe$ $[M+H]^+$ 332.0548, found 332.0547.

1-(3-ethyl-4-(phenylselanyl)phenyl)pyrrolidin-2-one (3c):



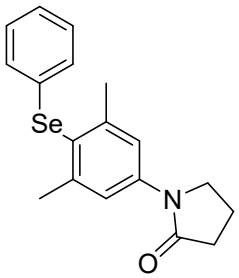
White solid. yield 87%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.61 (d, J = 2.1 Hz, 1H), 7.39 (d, J = 8.5 Hz, 1H), 7.35 – 7.27 (m, 3H), 7.27 – 7.17 (m, 3H), 3.90 (t, J = 7.0 Hz, 2H), 2.80 (q, J = 7.5 Hz, 2H), 2.58 (t, J = 8.1 Hz, 2H), 2.16 (p, J = 7.6 Hz, 2H), 1.17 (t, J = 7.5 Hz, 3H).^{13}C NMR (101 MHz, Methanol-d_4) δ 175.6, 146.9, 139.6, 135.5, 131.7, 131.5, 129.0, 126.7, 126.0, 120.7, 118.7, 49.0, 32.2, 29.1, 17.5, 14.3. HRMS(ESI) *m/z*: calculated for $C_{18}H_{20}NOSe$ $[M+H]^+$ 346.0705, found 346.0711.

1-(3-isopropyl-4-(phenylselanyl)phenyl)pyrrolidin-2-one (3d):



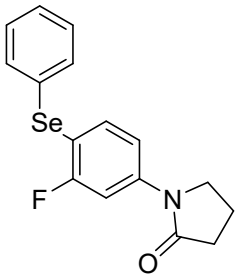
White solid. yield 98%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.71 (d, J = 1.7 Hz, 1H), 7.42 (d, J = 8.5 Hz, 1H), 7.35 – 7.14 (m, 6H), 3.90 (t, J = 7.0 Hz, 2H), 3.48 (hept, J = 6.6 Hz, 1H), 2.58 (t, J = 8.0 Hz, 2H), 2.16 (p, J = 7.5 Hz, 2H), 1.18 (s, 3H), 1.17 (s, 3H).^{13}C NMR (101 MHz, Methanol-d_4) δ 175.6, 151.3, 139.9, 135.7, 132.0, 131.5, 129.0, 126.6, 125.8, 118.6, 118.1, 49.0, 33.1, 32.2, 22.5, 17.5. HRMS(ESI) *m/z*: calculated for $C_{19}H_{22}NOSe$ $[M+H]^+$ 360.0861, found 360.0864.

1-(3,5-dimethyl-4-(phenylselanyl)phenyl)pyrrolidin-2-one (3e):



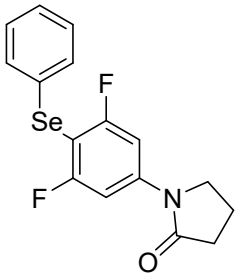
White solid. yield 97%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.48 (s, 2H), 7.26 – 7.09 (m, 3H), 7.05 (d, J = 7.0 Hz, 2H), 3.92 (t, J = 6.9 Hz, 2H), 2.59 (t, J = 8.0 Hz, 2H), 2.46 (s, 6H), 2.17 (p, J = 7.3 Hz, 2H).^{13}C NMR (151 MHz, Methanol-d_4) δ 175.7, 144.1, 139.9, 132.8, 128.9, 128.2, 125.9, 125.4, 119.5, 49.0, 32.2, 23.4, 17.5. HRMS(ESI) *m/z*: calculated for $C_{18}H_{20}NOSe$ $[M+H]^+$ 346.0705, found 346.0708.

1-(3-fluoro-4-(phenylselanyl)phenyl)pyrrolidin-2-one (3f):



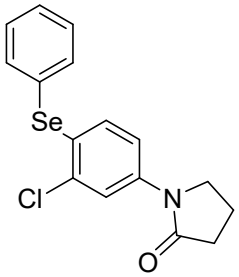
White solid. yield 78%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.67 (d, J = 11.1 Hz, 1H), 7.52 – 7.39 (m, 2H), 7.36 – 7.20 (m, 5H), 3.88 (t, J = 7.0 Hz, 2H), 2.59 (t, J = 8.1 Hz, 2H), 2.15 (p, J = 7.7 Hz, 2H).^{13}C NMR (151 MHz, DMSO-d_6) δ 175.0, 161.5 (d, J = 240.3 Hz), 142.3 (d, J = 10.5 Hz), 136.4 (d, J = 3.2 Hz), 131.9, 130.3, 130.1, 127.9, 116.2 (d, J = 2.8 Hz), 110.2 (d, J = 22.8 Hz), 106.8 (d, J = 28.9 Hz), 48.4, 32.8, 17.6. HRMS(ESI) *m/z*: calculated for $C_{16}H_{15}FNOSe$ $[M+H]^+$ 336.0297, found 336.0292.

1-(3,5-difluoro-4-(phenylselanyl)phenyl)pyrrolidin-2-one (3g):



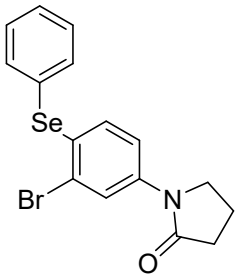
White solid. yield 77%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.53 – 7.45 (m, 2H), 7.40 – 7.32 (m, 2H), 7.31 – 7.25 (m, 1H), 7.24 – 7.19 (m, 2H), 3.89 (t, J = 7.1 Hz, 2H), 2.61 (t, J = 8.1 Hz, 2H), 2.17 (p, J = 8.0 Hz, 2H).^{13}C NMR (101 MHz, DMSO-d_6) δ 175.5, 163.1 (dd, J = 241.5, 8.3 Hz), 143.5 (t, J = 13.8 Hz), 131.0, 130.4, 130.1, 127.5, 102.7 (dd, J = 31.0, 2.3 Hz), 98.0 (t, J = 27.6 Hz), 48.5, 33.0, 17.5. HRMS(ESI) *m/z*: calculated for $C_{16}H_{14}F_2NOSe$ $[M+H]^+$ 354.0203, found 354.0189.

1-(3-chloro-4-(phenylselanyl)phenyl)pyrrolidin-2-one (3h):



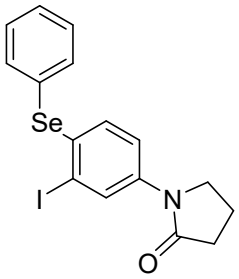
White solid. yield 58%. mp: 58℃-61℃. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.87 (d, J = 2.0 Hz, 1H), 7.62 – 7.51 (m, 2H), 7.47 – 7.34 (m, 3H), 7.31 (dd, J = 8.7, 2.0 Hz, 1H), 7.00 (d, J = 8.7 Hz, 1H), 3.85 (t, J = 7.1 Hz, 2H), 2.57 (t, J = 8.1 Hz, 2H), 2.14 (p, J = 7.6 Hz, 2H).^{13}C NMR (101 MHz, Methanol-d_4) δ 175.7, 139.1, 135.0, 133.9, 131.4, 129.5, 128.4, 128.3, 128.1, 120.8, 118.9, 48.7, 32.1, 17.3. HRMS(ESI) *m/z*: calculated for $C_{16}H_{15}ClNOSe$ $[M+H]^+$ 352.0002, found 351.9996.

1-(3-bromo-4-(phenylselanyl)phenyl)pyrrolidin-2-one (3i):



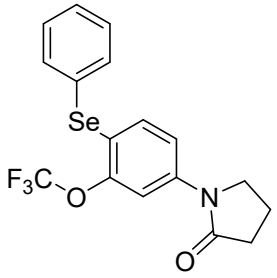
White solid. yield 58%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.02 (d, J = 2.3 Hz, 1H), 7.64 – 7.53 (m, 2H), 7.47 – 7.36 (m, 3H), 7.34 (m, 1H), 6.95 (d, J = 8.7 Hz, 1H), 3.85 (t, J = 7.1 Hz, 2H), 2.57 (t, J = 8.1 Hz, 2H), 2.21 – 2.09 (m, 2H).^{13}C NMR (101 MHz, Methanol-d_4) δ 174.1, 137.3, 133.6, 129.5, 129.3, 128.1, 127.3, 127.0, 122.6, 122.1, 117.9, 47.2, 30.6, 15.8. HRMS(ESI) *m/z*: calculated for $C_{16}H_{15}BrNOSe$ $[M+H]^+$ 395.9497, found 395.9493.

1-(3-iodo-4-(phenylselanyl)phenyl)pyrrolidin-2-one (3j):



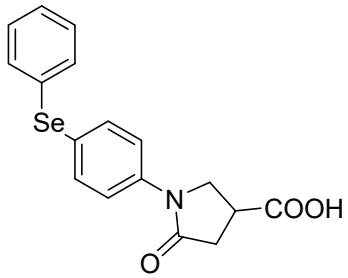
White solid. yield 84%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.22 (d,J = 2.0 Hz, 1H), 7.65 – 7.51 (m, 2H), 7.47 – 7.31 (m, 3H), 6.96 (d, J = 8.7 Hz, 2H), 3.84 (t, J = 7.0 Hz, 2H), 2.56 (t, J = 8.0 Hz, 2H), 2.19 – 2.11 (m, 2H).^{13}C NMR (101 MHz, DMSO-d_6) δ 174.7, 139.7, 134.4, 133.3, 131.9, 130.8, 130.6, 130.0, 129.0, 120.4, 102.6, 48.3, 32.7, 17.7. HRMS(ESI) *m/z*: calculated for $C_{16}H_{15}INOSe$ $[M+H]^+$ 443.9358, found 443.9355.

1-(4-(phenylselanyl)-3-(trifluoromethoxy)phenyl)pyrrolidin-2-one (3k):



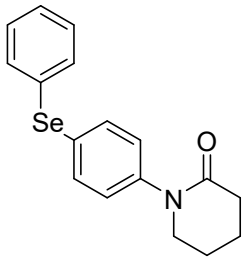
White solid. yield 56%. mp: 60℃-62℃. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.97 (s, 1H), 7.59 – 7.48 (m, 2H), 7.43 – 7.32 (m, 3H), 7.30 (m, 1H), 7.18 (d, J = 8.7 Hz, 1H), 3.87 (t, J = 7.1 Hz, 2H), 2.59 (t, J = 8.1 Hz, 2H), 2.16 (p, J = 7.6 Hz, 2H).^{13}C NMR (101 MHz, Methanol-d_4) δ 175.8, 147.4 (q, J = 1.6 Hz), 139.8, 134.5, 133.0, 129.4, 128.2, 128.1, 121.0,120.6 (q, J = 258.3 Hz), 118.5, 112.6 (q, J = 1.5 Hz), 48.6, 32.2, 17.3. HRMS(ESI) *m/z*: calculated for $C_{17}H_{15}F_3NO_2Se$ $[M+H]^+$ 402.0215, found 402.0215.

5-oxo-1-(4-(phenylselanyl)phenyl)pyrrolidine-3-carboxylic acid (3l):



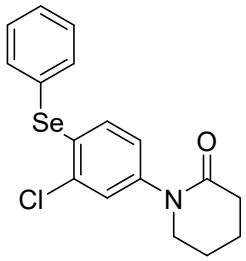
White solid. yield 56%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.46 (d, J = 8.3 Hz, 2H), 7.38 (d, J = 8.3 Hz, 2H), 7.36 – 7.26 (m, 2H), 7.25 – 7.08 (m, 3H), 4.21 – 3.85 (m, 2H), 3.45 – 3.27 (m, 1H), 2.77 (d, J = 7.9 Hz, 2H).^{13}C NMR (101 MHz, Methanol-d_4) δ 174.5, 173.3, 138.4, 133.6, 132.3, 131.2, 129.1, 127.0, 126.8, 121.3, 50.8, 35.5, 35.1. HRMS(ESI) *m/z*: calculated for $C_{17}H_{16}NO_3Se$ $[M+H]^+$ 362.0290, found 362.0292.

1-(4-(phenylselanyl)phenyl)piperidin-2-one (3m):



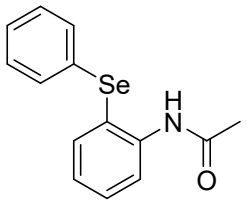
White solid. yield 44%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.58 – 7.41 (m, 4H), 7.40 – 7.24 (m, 3H), 7.24 – 7.13 (m, 2H), 3.65 (t, J = 5.3 Hz, 2H), 2.50 (t, J = 6.1 Hz, 2H), 2.10 – 1.76 (m, 4H).^{13}C NMR (101 MHz, Methanol-d_4) δ 171.5, 142.4, 133.3, 133.0, 130.6, 129.9, 129.2, 127.4, 127.2, 51.6, 32.0, 22.9, 20.7. HRMS(ESI) *m/z*: calculated for $C_{17}H_{18}NOSe$ $[M+H]^+$ 332.0548, found 332.0548.

1-(3-chloro-4-(phenylselanyl)phenyl)piperidin-2-one (3n):



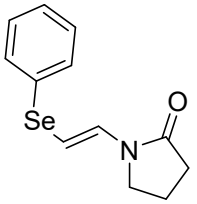
White solid. yield 36%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.68 – 7.56 (m, 2H), 7.50 – 7.31 (m, 4H), 7.05 – 6.98 (m, 1H), 6.98-6.92 (m, 1H), 3.62 (t, J = 5.3 Hz, 2H), 2.48 (t, J = 6.1 Hz, 2H), 2.10 – 1.75 (m, 4H).^{13}C NMR (151 MHz, Methanol-d_4) δ 171.5, 142.4, 135.7, 133.1, 132.0, 130.9, 129.6, 128.8, 127.6, 127.3, 125.3, 51.5, 32.0, 22.8, 20.6. HRMS(ESI) *m/z*: calculated for $C_{17}H_{17}ClNOSe$ $[M+H]^+$ 366.0158, found 366.0153.

N-(2-(phenylselanyl)phenyl)acetamide (3o):



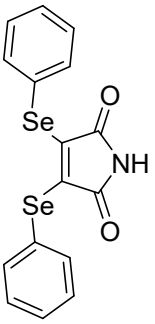
White solid. yield 34%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.58 (d, J = 7.6 Hz, 1H), 7.51 – 7.18 (m, 7H), 7.11 (t, J = 7.3 Hz, 1H), 2.02 (s, 3H).^{13}C NMR (101 MHz, Methanol-d_4) δ 170.7, 137.7, 134.5, 132.3, 130.4, 129.2, 128.4, 127.2, 126.4, 126.3, 125.4, 21.7. HRMS(ESI) *m/z*: calculated for $C_{14}H_{14}NOSe$ $[M+H]^+$ 292.0235, found 292.0232.

(E)-1-(2-(phenylselanyl)vinyl)pyrrolidin-2-one (3p):



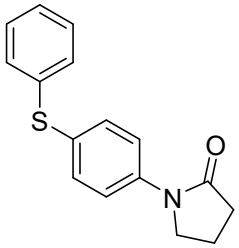
White solid. yield 19%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.43 (d, J = 6.6 Hz, 2H), 7.36 (d, J = 14.0 Hz, 1H), 7.31 – 7.15 (m, 3H), 6.06 (d, J = 14.0 Hz, 1H), 3.65 (t, J = 6.8 Hz, 2H), 2.50 (t, J = 7.9 Hz, 2H), 2.27 – 1.99 (m, 2H).^{13}C NMR (101 MHz, Methanol-d_4) δ 174.2, 132.1, 131.6, 130.2, 128.9, 126.3, 97.1, 45.1, 30.5, 17.0. HRMS(ESI) *m/z*: calculated for $C_{12}H_{14}NOSe$ $[M+H]^+$ 268.0235, found 268.0232.

3,4-bis(phenylselanyl)-1H-pyrrole-2,5-dione (3q):



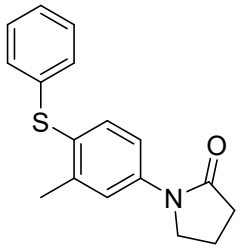
Yellow solid. yield 43%. mp: 117℃-120℃. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.45 – 7.38 (m, 4H), 7.35 – 7.30 (m, 2H), 7.30 – 7.23 (m, 4H).^{13}C NMR (151 MHz, Methanol-d_4) δ 168.4, 139.2, 133.8, 129.0, 128.1, 126.5. HRMS(ESI) *m/z*: calculated for $C_{16}H_{11}NO_2Se_2Na$ $[M+Na]^+$ 431.9012, found 431.9004.

1-(4-(phenylthio)phenyl)pyrrolidin-2-one (3r):



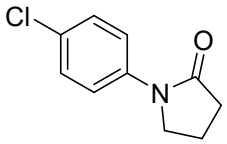
White oil. yield 40%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.66 – 7.56 (m, 2H), 7.41 – 7.33 (m, 2H), 7.32 – 7.17 (m, 5H), 3.91 (t, J = 7.1 Hz, 2H), 2.59 (t, J = 8.1 Hz, 2H), 2.17 (p, J = 7.5 Hz, 2H).^{13}C NMR (101 MHz, Methanol-d4) δ 175.6, 138.6, 136.3, 131.8, 131.2, 130.1, 128.9, 126.6, 121.1, 49.0, 32.2, 17.5. HRMS(ESI) *m/z*: calculated for $C_{16}H_{16}NOS$ $[M+H]^+$ 270.0947, found 270.0945.

1-(3-methyl-4-(phenylthio)phenyl)pyrrolidin-2-one (3s):



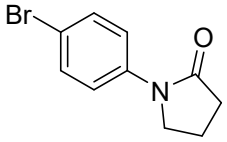
White oil. yield 66%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.64 – 7.55 (m, 1H), 7.48 – 7.41 (m, 1H), 7.37 – 7.31 (m, 1H), 7.29 – 7.22 (m, 2H), 7.20 – 7.14 (m, 1H), 7.13 – 7.07 (m, 2H), 3.91 (t, J = 7.1 Hz, 2H), 2.59 (t, J = 8.1 Hz, 2H), 2.34 (s, 3H), 2.17 (p, J = 7.6 Hz, 2H).^{13}C NMR (101 MHz, Methanol-d4) δ 175.7, 141.1, 139.5, 136.6, 134.1, 128.9, 128.8, 128.4, 125.9, 122.3, 118.6, 49.0, 32.2, 19.6, 17.5. HRMS(ESI) *m/z*: calculated for $C_{17}H_{18}NOS$ $[M+H]^+$ 284.1104, found 284.1102.

1-(4-chlorophenyl)pyrrolidin-2-one (5a)[1]



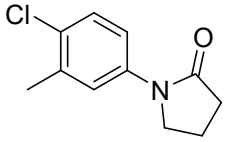
White solid. yield 69%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.61 (d, J = 8.9 Hz, 2H), 7.36 (d, J = 8.9 Hz, 2H), 3.90 (t, J = 7.1 Hz, 2H), 2.59 (t, J = 8.1 Hz, 2H), 2.17 (p, J = 7.5 Hz, 2H).^{13}C NMR (101 MHz, Methanol-d_4) δ 175.6, 138.0, 129.6, 128.4, 121.7, 49.0, 32.1, 17.5. HRMS(ESI) *m/z*: calculated for $C_{10}H_{11}ClNO$ $[M+H]^+$ 196.0524, found 196.0520.

1-(4-bromophenyl)pyrrolidin-2-one (5b)[5]



White solid. yield 96%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.74 – 7.28 (m, 4H), 4.01 – 3.71 (m, 2H), 2.69 – 2.43 (m, 2H), 2.27 – 2.00 (m, 2H).^{13}C NMR (101 MHz, Methanol-d_4) δ 175.6, 138.5, 131.4, 121.9, 117.1, 48.9, 32.1, 17.4. HRMS(ESI) *m/z*: calculated for $C_{10}H_{11}BrNO$ $[M+H]^+$ 240.0019, found 240.0018.

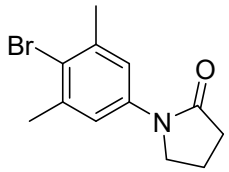
1-(4-chloro-3-methylphenyl)pyrrolidin-2-one (5c)



White solid. yield 62%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.56 (d, J = 2.6 Hz, 1H), 7.43 (dd, J = 8.7, 2.6 Hz, 1H), 7.33 (d, J = 8.7 Hz, 1H), 3.89 (t, J = 7.1 Hz, 2H), 2.58 (t, J = 8.1 Hz, 2H), 2.36 (s, 3H), 2.16 (p,

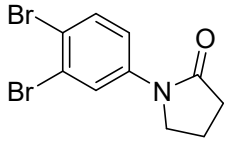
J = 7.6 Hz, 2H).[13]C NMR (101 MHz, Methanol-d_4) δ 175.6, 137.9, 136.1, 129.8, 128.7, 122.7, 119.3, 49.07, 32.1, 18.9, 17.5. HRMS(ESI) *m/z*: calculated for $C_{11}H_{13}ClNO$ $[M+H]^+$ 210.0680, found 210.0680.

1-(4-bromo-3,5-dimethylphenyl)pyrrolidin-2-one (5d)



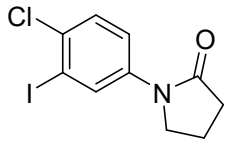
White solid. yield 81%. [1]H NMR (400 MHz, Methanol-d_4) δ 7.40 (s, 2H), 3.88 (t, *J* = 7.1 Hz, 2H), 2.57 (t, *J* = 8.1 Hz, 2H), 2.40 (s, 6H), 2.16 (p, *J* = 7.5 Hz, 2H). [13]C NMR (101 MHz, Methanol-d_4) δ 175.6, 138.3, 137.9, 122.4, 120.2, 49.1, 32.2, 22.7, 17.5. HRMS(ESI) *m/z*: calculated for $C_{12}H_{15}BrNO$ $[M+H]^+$ 268.0337, found 268.0332.

1-(3,4-dibromophenyl)pyrrolidin-2-one (5e)



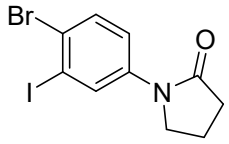
White solid. yield 76%. [1]H NMR (400 MHz, Methanol-d_4) δ 8.12 (d, *J* = 2.6 Hz, 1H), 7.65 (d, *J* = 8.8 Hz, 1H), 7.49 (dd, *J* = 8.8, 2.6 Hz, 1H), 3.88 (t, *J* = 7.0 Hz, 2H), 2.59 (t, *J* = 8.1 Hz, 2H), 2.17 (p, *J* = 7.6 Hz, 2H).[13]C NMR (101 MHz, Methanol-d_4) δ 175.8, 139.6, 133.2, 124.7, 124.1, 120.0, 118.9, 48.6, 32.1, 17.3. HRMS(ESI) *m/z*: calculated for $C_{10}H_{10}Br_2NO$ $[M+H]^+$ 317.9124, found 317.9124.

1-(4-chloro-3-iodophenyl)pyrrolidin-2-one (5f)



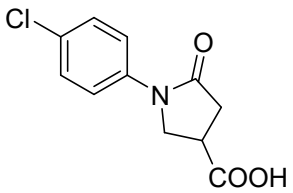
White solid. yield 50%. [1]H NMR (400 MHz, Methanol-d_4) δ 8.29 (d, *J* = 2.6 Hz, 1H), 7.59 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.47 (d, *J* = 8.8 Hz, 1H), 3.88 (t, *J* = 7.1 Hz, 2H), 2.59 (t, *J* = 8.1 Hz, 2H), 2.16 (p, *J* = 7.6 Hz, 2H).[13]C NMR (101 MHz, Chloroform-*d*) δ 174.3, 138.6, 133.8, 130.6, 129.0, 120.7, 97.8, 48.5, 32.6, 17.8. HRMS(ESI) *m/z*: calculated for $C_{10}H_{10}ClINO$ $[M+H]^+$ 321.9490, found 321.9492.

1-(4-bromo-3-iodophenyl)pyrrolidin-2-one (5g)



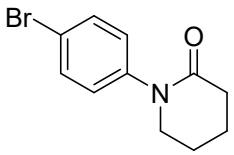
White solid. yield 84%. [1]H NMR (400 MHz, Methanol-d_4) δ 8.30 (d, *J* = 2.6 Hz, 1H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.51 (dd, *J* = 8.8, 2.6 Hz, 1H), 3.87 (t, *J* = 7.1 Hz, 2H), 2.58 (t, *J* = 8.1 Hz, 2H), 2.16 (p, *J* = 7.5 Hz, 2H).[13]C NMR (101 MHz, Chloroform-*d*) δ 174.3, 139.1, 132.4, 130.7, 124.4, 120.8, 101.0, 48.5, 32.7, 17.8. HRMS(ESI) *m/z*: calculated for $C_{10}H_{10}BrINO$ $[M+H]^+$ 365.8985, found 365.8980.

1-(4-chlorophenyl)-5-oxopyrrolidine-3-carboxylic acid (5h)



White solid. yield 67%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.56 (s, 1H), 7.69 (d, J = 9.0 Hz, 2H), 7.43 (d, J = 9.0 Hz, 2H), 4.13 – 3.84 (m, 2H), 2.92 – 2.61 (m, 2H), 1.91 (s, 1H).^{13}C NMR (101 MHz, DMSO-d_6) δ 174.6, 172.5, 138.5, 129.1, 128.3, 121.4, 50.3, 35.6, 35.5. HRMS(ESI) *m/z*: calculated for $C_{11}H_{11}ClNO_3$ $[M+H]^+$ 240.0422, found 240.0411.

1-(4-bromophenyl)piperidin-2-one (5i)



White solid. yield 63%. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.55 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 3.65 (t, J = 5.4 Hz, 2H), 2.50 (t, J = 6.1 Hz, 2H), 2.08 – 1.81 (m, 4H).^{13}C NMR (101 MHz, Methanol-d_4) δ 171.5, 142.3, 132.0, 128.2, 120.0, 51.6, 32.0, 22.8, 20.7. HRMS(ESI) *m/z*: calculated for $C_{11}H_{13}BrNO$ $[M+H]^+$ 254.0175, found 254.0171.

8. Crystallographic data for 3a

Table 1 Crystal data and structure refinement for 3a.

CCDC	2183282
Empirical formula	$C_{16}H_{15}NOSe$
Formula weight	316.25
Temperature/K	293.15
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	15.9417(14)
b/Å	7.4061(8)
c/Å	12.3726(14)
α/°	90
β/°	107.420(11)
γ/°	90
Volume/Å^3	1393.8(3)
Z	4
ρ_{calc}g/cm^3	1.507
μ/mm^{-1}	2.685
F(000)	640.0
Crystal size/mm^3	0.35 × 0.3 × 0.25
Radiation	MoKα (λ = 0.71073)

2Θ range for data collection/°	6.118 to 52.742
Index ranges	$-19 \le h \le 13$, $-8 \le k \le 9$, $-12 \le l \le 15$
Reflections collected	6701
Independent reflections	2839 [R_{int} = 0.0322, R_{sigma} = 0.0536]
Data/restraints/parameters	2839/0/172
Goodness-of-fit on F^2	1.013
Final R indexes [I>=2σ (I)]	R_1 = 0.0472, wR_2 = 0.0877
Final R indexes [all data]	R_1 = 0.0937, wR_2 = 0.1057
Largest diff. peak/hole / e Å^{-3}	0.30/-0.43

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 3a. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
Se1	1292.5(3)	8293.5(6)	4772.4(4)	81.9(2)
O1	5844.7(16)	8380(4)	6304(2)	72.1(8)
N1	5138.9(16)	8780(3)	7652.5(19)	39.3(6)
C1	1213(2)	10106(5)	3644(3)	59.7(10)
C2	902(2)	9650(7)	2518(4)	75.2(12)
C3	829(3)	10953(9)	1704(4)	90.4(15)
C4	1056(3)	12696(8)	1997(4)	89.5(15)
C5	1377(3)	13161(6)	3121(4)	80.5(13)
C6	1453(3)	11871(6)	3940(4)	69.7(11)
C7	2494(2)	8603(4)	5660(3)	50.7(9)
C8	3145(2)	9014(4)	5169(3)	47.5(8)
C9	4011(2)	9088(4)	5815(3)	44.0(8)
C10	4254(2)	8735(4)	6968(3)	38.9(7)
C11	3592(2)	8353(4)	7455(3)	48.9(9)
C12	2728(2)	8297(4)	6799(3)	55.6(9)
C13	5858(2)	8537(4)	7284(3)	45.6(8)
C14	6654(2)	8457(4)	8296(3)	49.1(8)
C15	6351(2)	9049(5)	9286(3)	55.9(9)
C16	5362(2)	8837(5)	8883(2)	52.0(9)

Table 3 Anisotropic Displacement Parameters (Å^2×10^3) for 3a. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Se1	53.0(3)	80.4(4)	97.8(4)	9.6(2)	0.7(2)	-19.1(2)
O1	57.7(16)	126(2)	37.5(15)	1.5(14)	21.2(12)	12.0(14)
N1	46.0(16)	45.3(15)	26.7(14)	1.9(12)	11.1(12)	1.4(12)
C1	33.9(19)	75(3)	64(3)	-4(2)	4.9(17)	2.4(18)
C2	44(2)	98(3)	75(3)	-19(3)	5(2)	4(2)
C3	60(3)	144(5)	61(3)	-10(4)	10(2)	20(3)
C4	61(3)	127(5)	80(4)	25(3)	20(3)	27(3)
C5	74(3)	79(3)	89(4)	11(3)	25(3)	7(2)
C6	66(3)	73(3)	62(3)	0(2)	8(2)	-2(2)
C7	46(2)	42(2)	60(2)	-3.0(18)	10.3(18)	-2.8(16)
C8	55(2)	45(2)	37.6(19)	-2.4(16)	7.0(16)	2.9(17)
C9	50(2)	47(2)	36.7(19)	3.9(16)	15.0(15)	0.8(16)
C10	47.2(19)	34.1(17)	37.6(19)	-1.1(15)	16.3(15)	-1.8(14)
C11	58(2)	52(2)	42(2)	9.4(17)	22.4(17)	2.0(17)
C12	49(2)	58(2)	66(3)	10(2)	26.7(19)	-2.4(18)
C13	45(2)	48(2)	43(2)	2.4(17)	12.4(16)	-0.1(15)
C14	49(2)	45(2)	49(2)	3.3(17)	8.9(16)	-2.5(16)
C15	66(2)	50(2)	43(2)	-2.2(17)	3.4(18)	-0.2(18)
C16	59(2)	64(2)	33.5(19)	1.9(17)	14.8(16)	9.7(18)

Table 4 Bond Lengths for 3a.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Se1	C1	1.914(4)	C5	C6	1.371(5)
Se1	C7	1.915(3)	C7	C8	1.384(4)
O1	C13	1.212(4)	C7	C12	1.365(5)
N1	C10	1.412(4)	C8	C9	1.374(4)
N1	C13	1.367(4)	C9	C10	1.386(4)
N1	C16	1.457(4)	C10	C11	1.392(4)
C1	C2	1.373(5)	C11	C12	1.374(5)
C1	C6	1.380(5)	C13	C14	1.494(4)
C2	C3	1.374(6)	C14	C15	1.510(4)
C3	C4	1.360(6)	C15	C16	1.512(4)
C4	C5	1.375(6)			

Table 5 Bond Angles for 3a.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C1	Se1	C7	99.84(14)	C12	C7	C8	118.8(3)
C10	N1	C16	121.0(2)	C9	C8	C7	120.5(3)
C13	N1	C10	125.8(3)	C8	C9	C10	120.9(3)
C13	N1	C16	112.7(3)	C9	C10	N1	122.3(3)
C2	C1	Se1	119.5(3)	C9	C10	C11	118.0(3)
C2	C1	C6	119.3(4)	C11	C10	N1	119.7(3)
C6	C1	Se1	121.2(3)	C12	C11	C10	120.4(3)
C1	C2	C3	119.8(4)	C7	C12	C11	121.3(3)
C4	C3	C2	120.9(4)	O1	C13	N1	125.5(3)
C3	C4	C5	119.7(5)	O1	C13	C14	126.3(3)
C6	C5	C4	119.8(5)	N1	C13	C14	108.2(3)
C5	C6	C1	120.5(4)	C13	C14	C15	105.7(3)
C8	C7	Se1	121.8(3)	C14	C15	C16	105.0(3)
C12	C7	Se1	119.2(3)	N1	C16	C15	104.6(2)

Table 6 Torsion Angles for 3a.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
Se1	C1	C2	C3	178.9(3)	C8	C9	C10	C11	-1.8(4)
Se1	C1	C6	C5	-178.8(3)	C9	C10	C11	C12	1.2(4)
Se1	C7	C8	C9	-174.9(2)	C10	N1	C13	O1	5.8(5)
Se1	C7	C12	C11	174.4(2)	C10	N1	C13	C14	-172.9(3)
O1	C13	C14	C15	170.3(3)	C10	N1	C16	C15	-174.8(3)
N1	C10	C11	C12	-179.7(3)	C10	C11	C12	C7	0.3(5)
N1	C13	C14	C15	-11.0(3)	C12	C7	C8	C9	0.9(5)
C1	C2	C3	C4	-0.4(6)	C13	N1	C10	C9	-24.1(4)
C2	C1	C6	C5	0.5(6)	C13	N1	C10	C11	156.9(3)
C2	C3	C4	C5	1.1(6)	C13	N1	C16	C15	13.2(4)
C3	C4	C5	C6	-1.0(7)	C13	C14	C15	C16	18.5(3)
C4	C5	C6	C1	0.2(6)	C14	C15	C16	N1	-19.1(3)
C6	C1	C2	C3	-0.4(5)	C16	N1	C10	C9	165.1(3)
C7	C8	C9	C10	0.7(5)	C16	N1	C10	C11	-13.9(4)
C8	C7	C12	C11	-1.4(5)	C16	N1	C13	O1	177.3(3)
C8	C9	C10	N1	179.2(3)	C16	N1	C13	C14	-1.4(3)

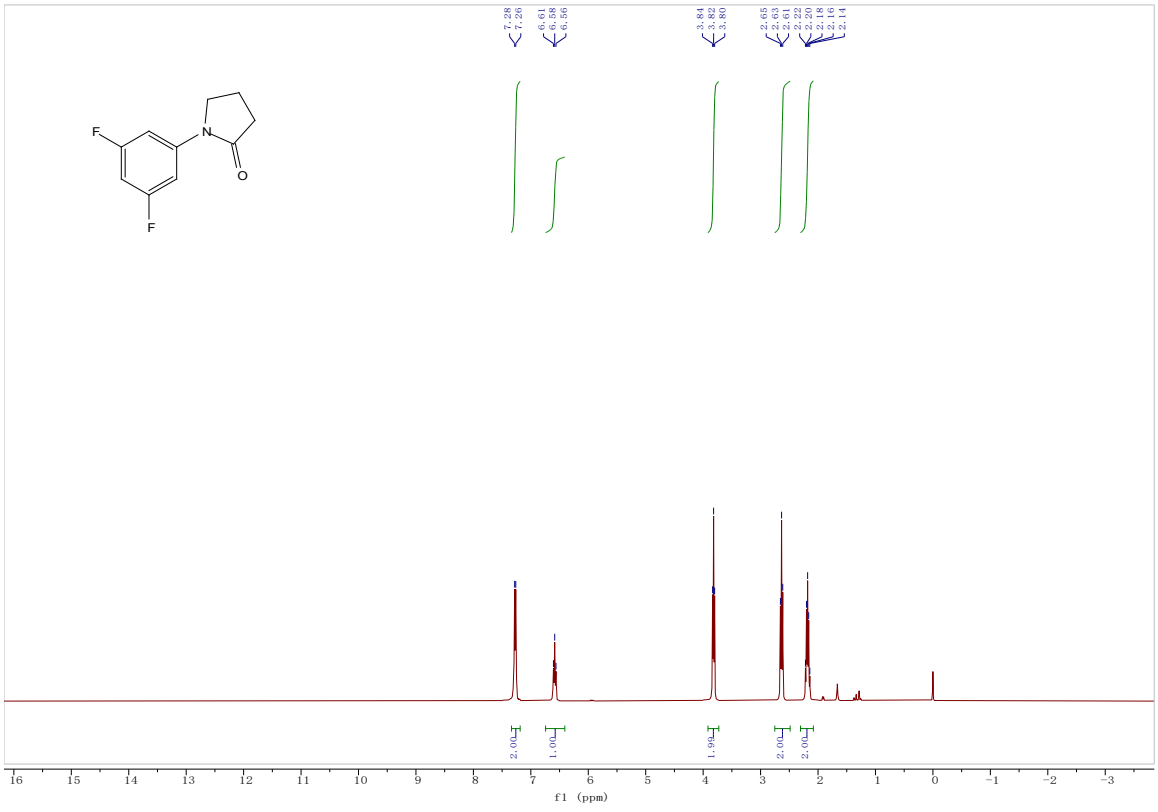
Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3)

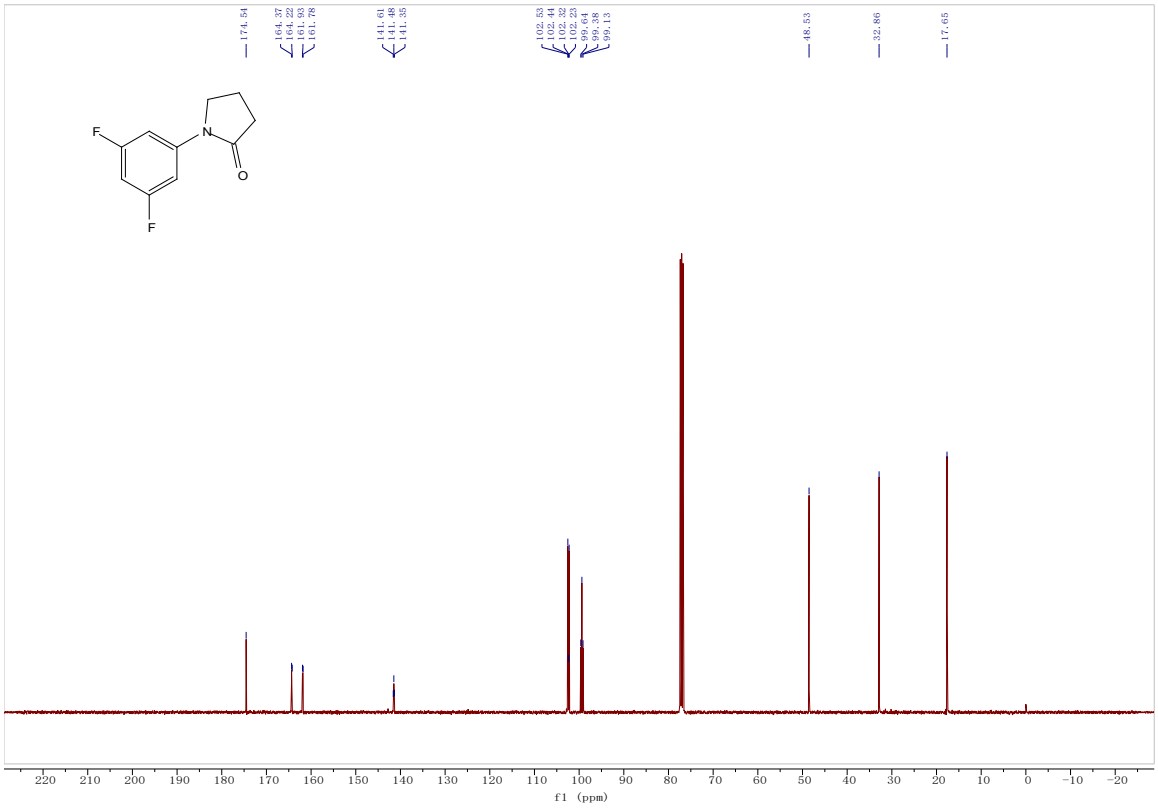
for 3a.

Atom	*x*	*y*	*z*	U(eq)
H2	741.58	8464.21	2307.29	90
H3	621.44	10638.32	942.42	108
H4	994.56	13569.36	1438.29	107
H5	1541.08	14346.92	3325.75	97
H6	1668.27	12187.53	4700.73	84
H8	2994.44	9241.08	4394.83	57
H9	4440.13	9379.36	5474.48	53
H11	3735.17	8133.27	8229.34	59
H12	2292.93	8046.48	7138.44	67
H14A	7108.47	9258.54	8201.72	59
H14B	6887.09	7238.02	8411.89	59
H15A	6512.83	10295.5	9482.78	67
H15B	6608.59	8295.48	9942.84	67
H16B	5185.61	7730.4	9174.15	62
H16A	5077.9	9849.9	9126.47	62

9. NMR Spectra

9.1 NMR spectra of compound **1**

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99.38
99.13
48.53
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17.65
F
N
O
F
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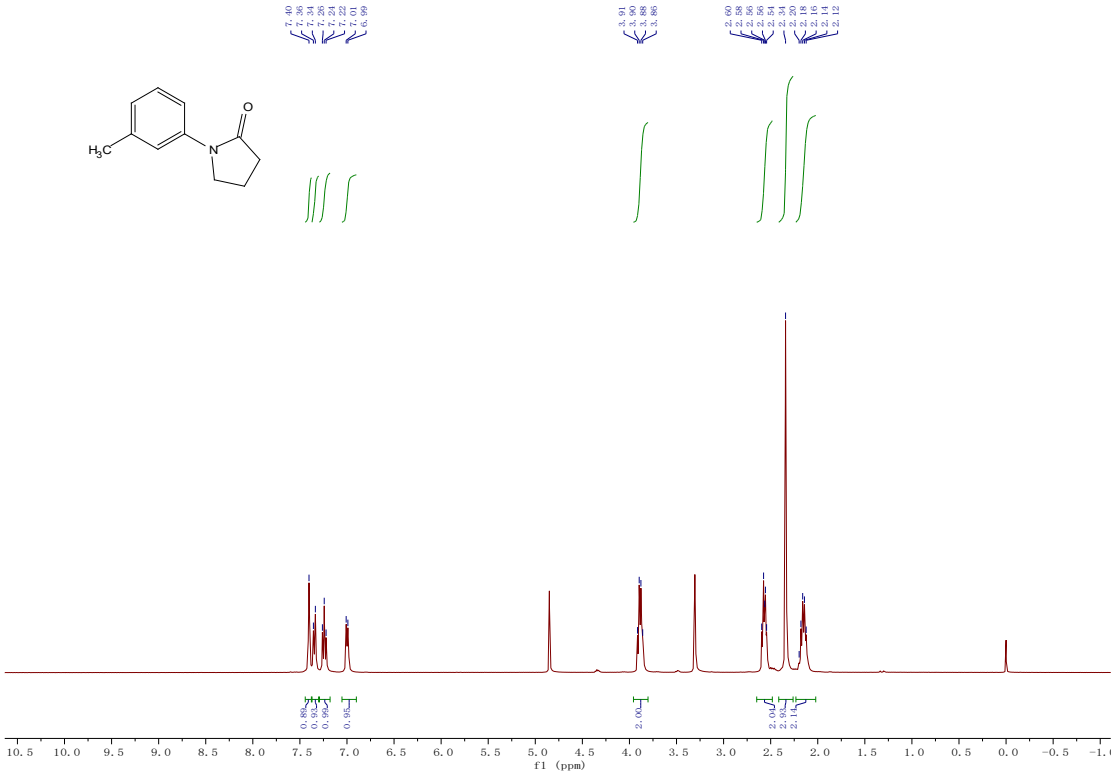
f1 (ppm)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7.34
7.26
7.24
7.22
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6.99
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3.90
3.88
3.86
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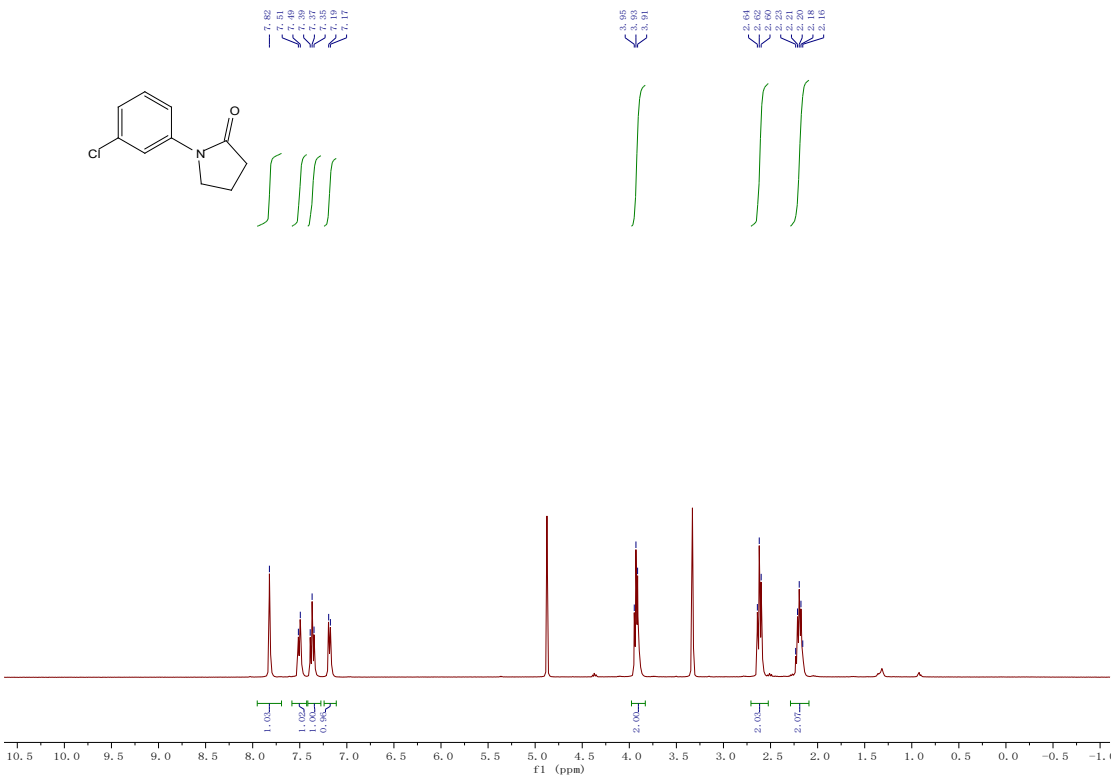
2.58
2.56
2.56
2.54
2.34
2.20
2.18
2.16
2.14
2.12
O
N
H3C
0.88
0.92
0.96
0.95
2.00
2.04
2.03
2.14
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


Cl
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N
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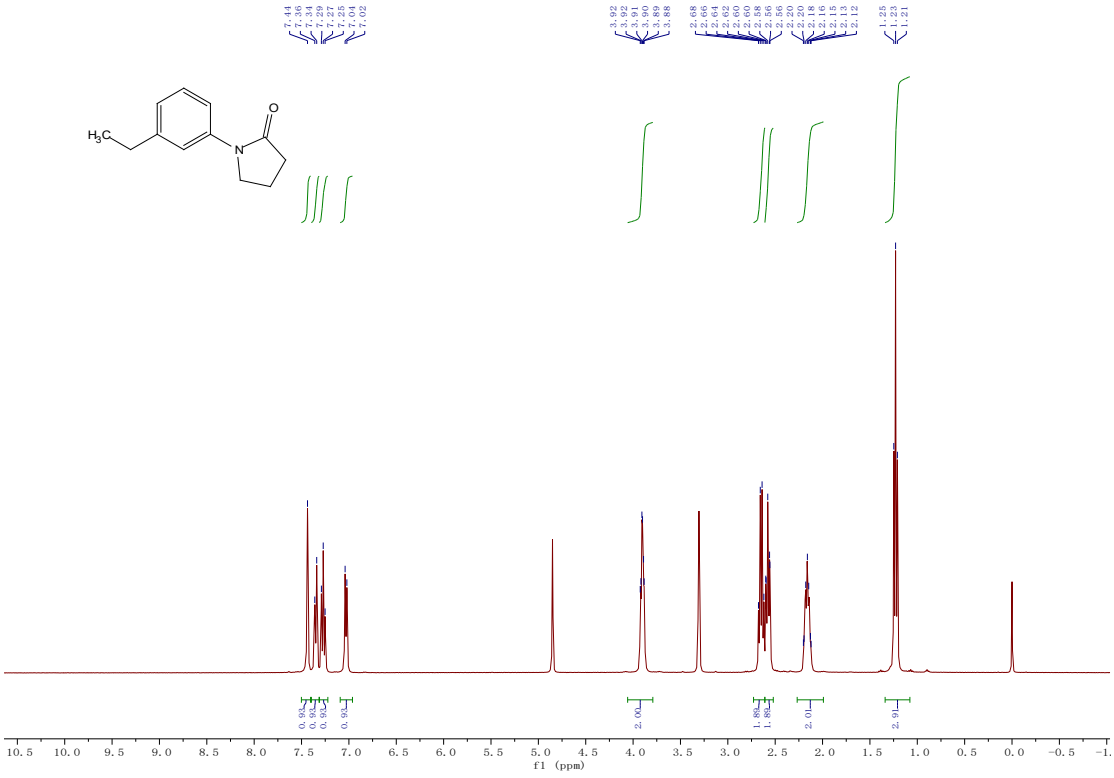
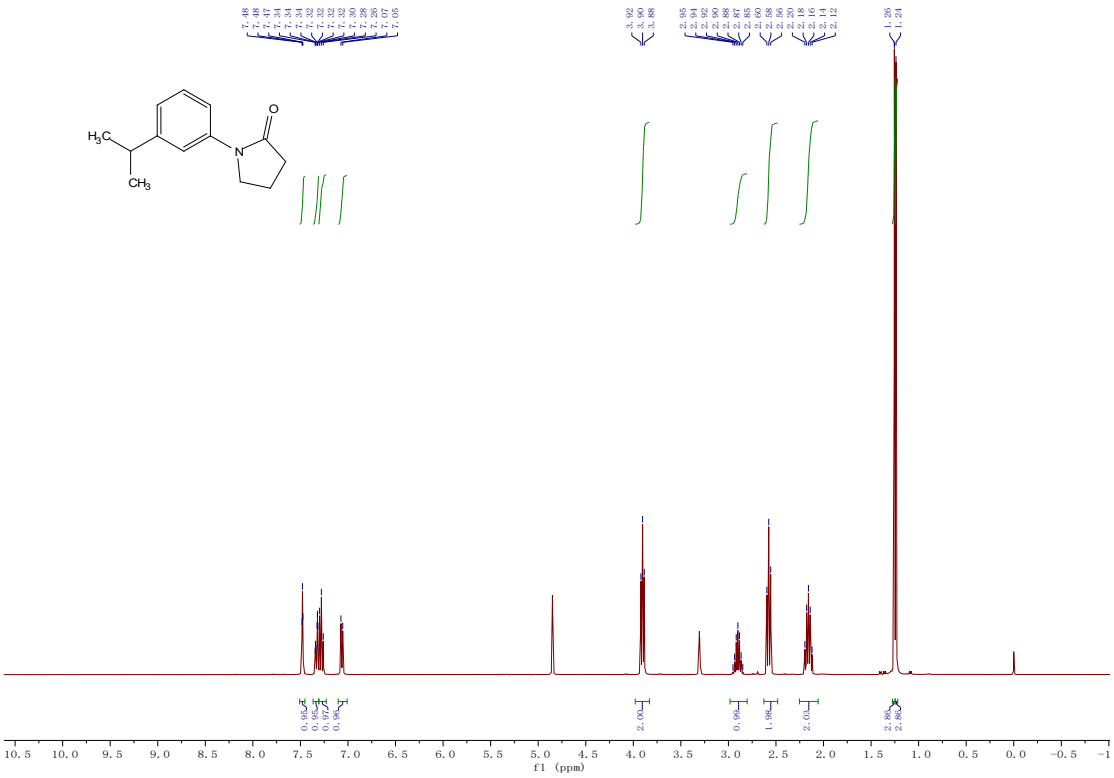

H3C
O
N
f1 (ppm)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7.28
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7.07
7.05
3.92
3.90
3.88
2.95
2.94
2.92
2.90
2.88
2.87
2.85
2.60
2.58
2.56
2.20
2.18
2.16
2.15
2.14
2.12
1.26
1.24
H3C
CH3
O
N
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0.95
0.97
0.98
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0.99
1.98
2.00
2.85
2.80
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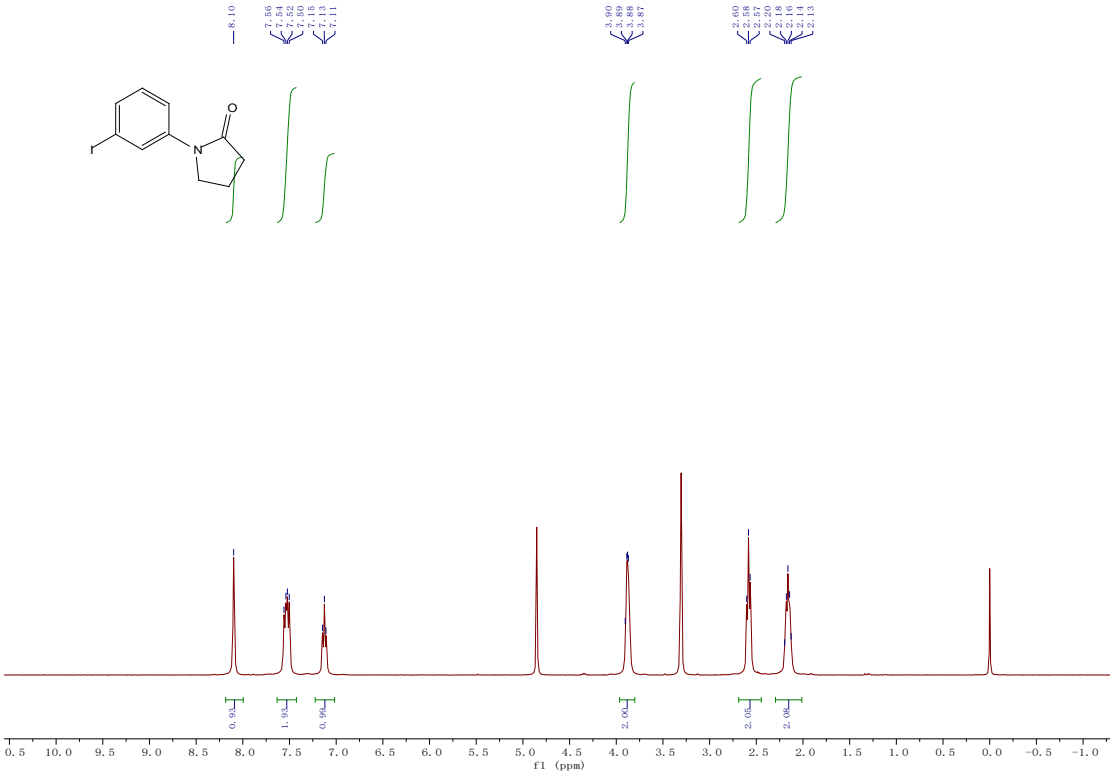
f1 (ppm)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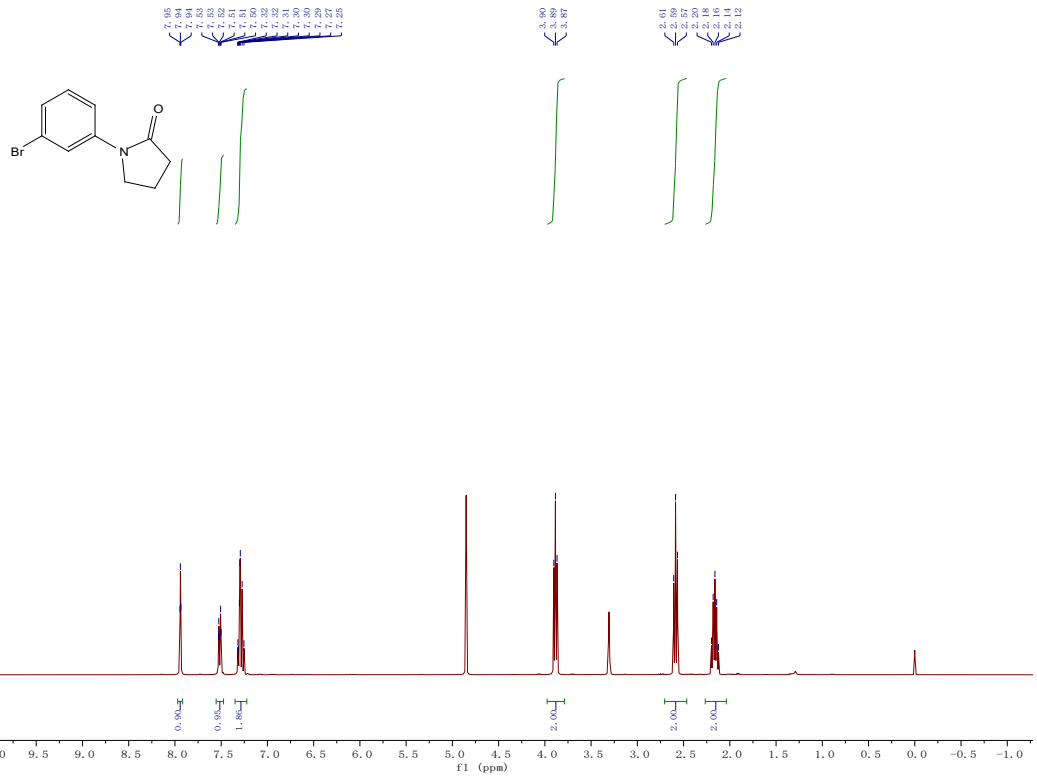
3.88
3.87
2.60
2.58
2.57
2.20
2.18
2.16
2.14
2.13
I
O
N
0.91
1.93
0.98
2.00
2.05
2.08
0.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
f1 (ppm)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7.50
7.32
7.32
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7.30
7.29
7.27
7.25
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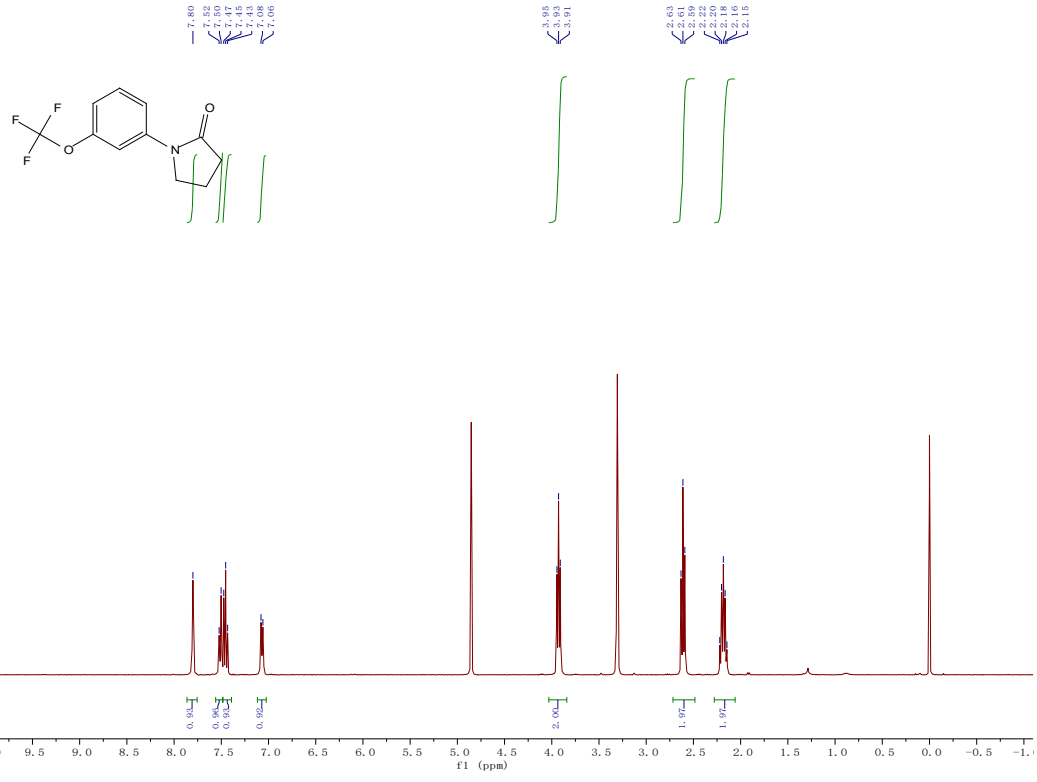
3.88
3.87
2.61
2.59
2.57
2.20
2.18
2.16
2.14
2.12
Br
O
N
0.90
0.96
1.84
2.00
2.00
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
f1 (ppm)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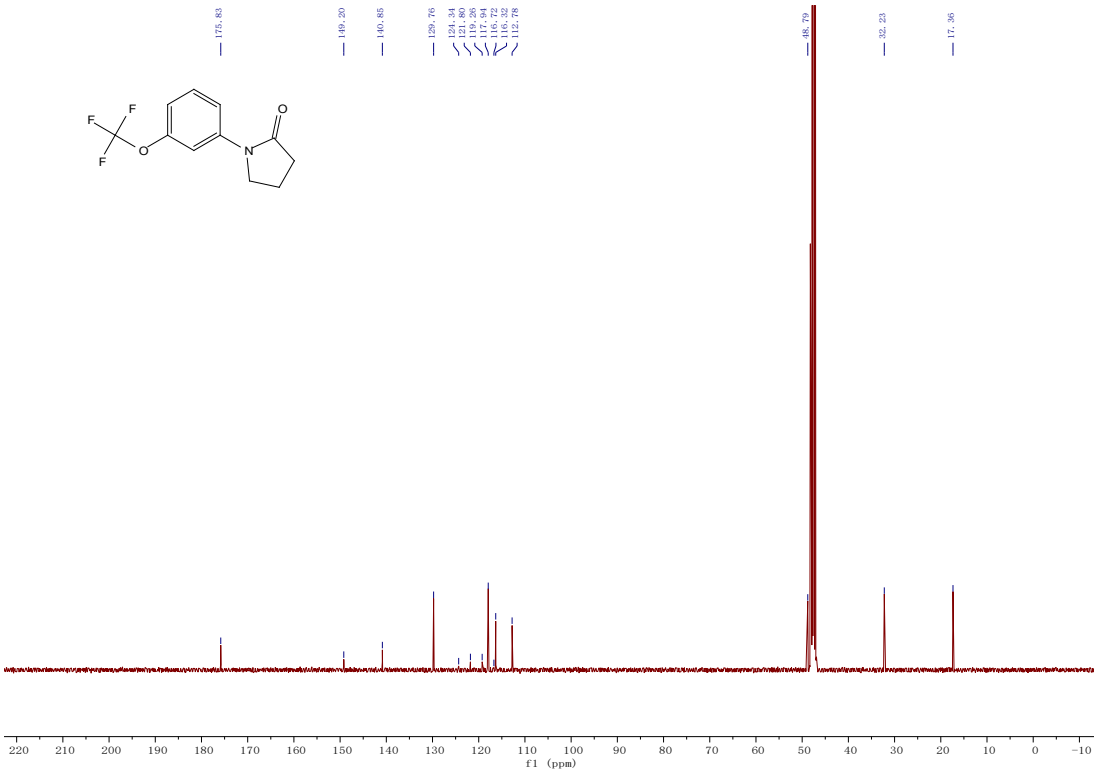
2.59
2.22
2.20
2.18
2.16
2.15
F
F
F
O
N
O
0.63
0.96
0.94
0.92
2.00
1.97
1.97
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.
f1 (ppm)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121.00
119.26
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116.52
112.78
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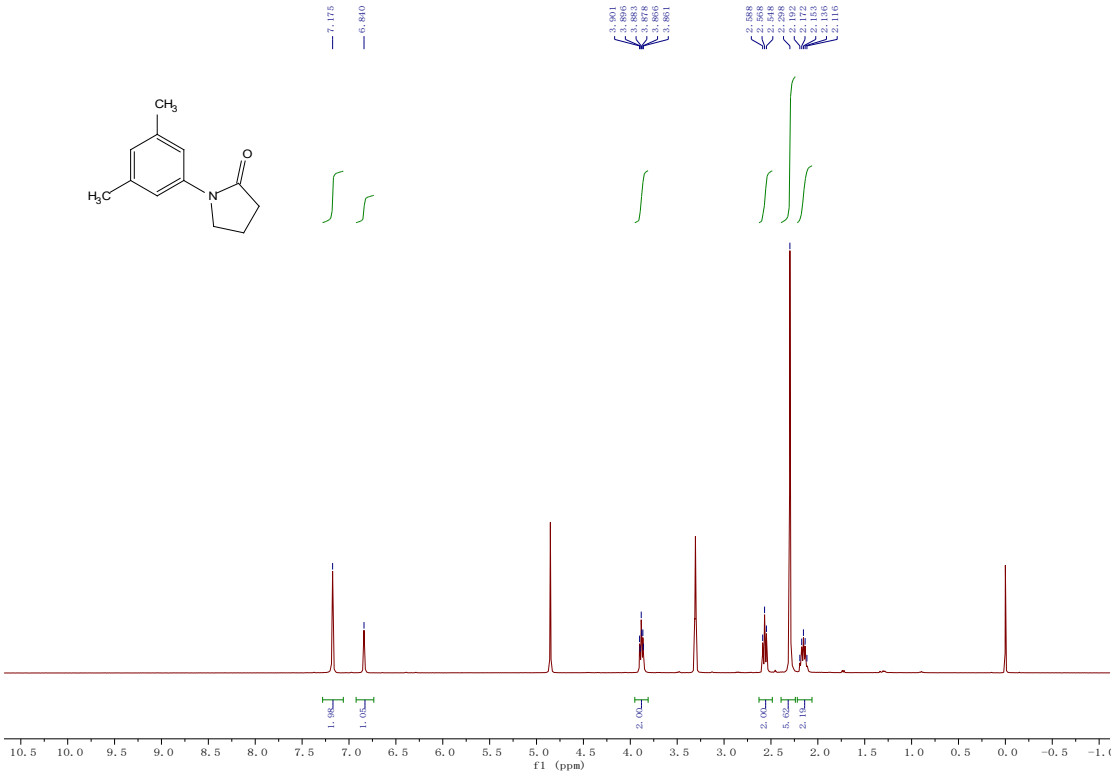
17.36
F
F
F
O
O
N
f1 (ppm)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2.192
2.172
2.153
2.135
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H3C
O
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2.00
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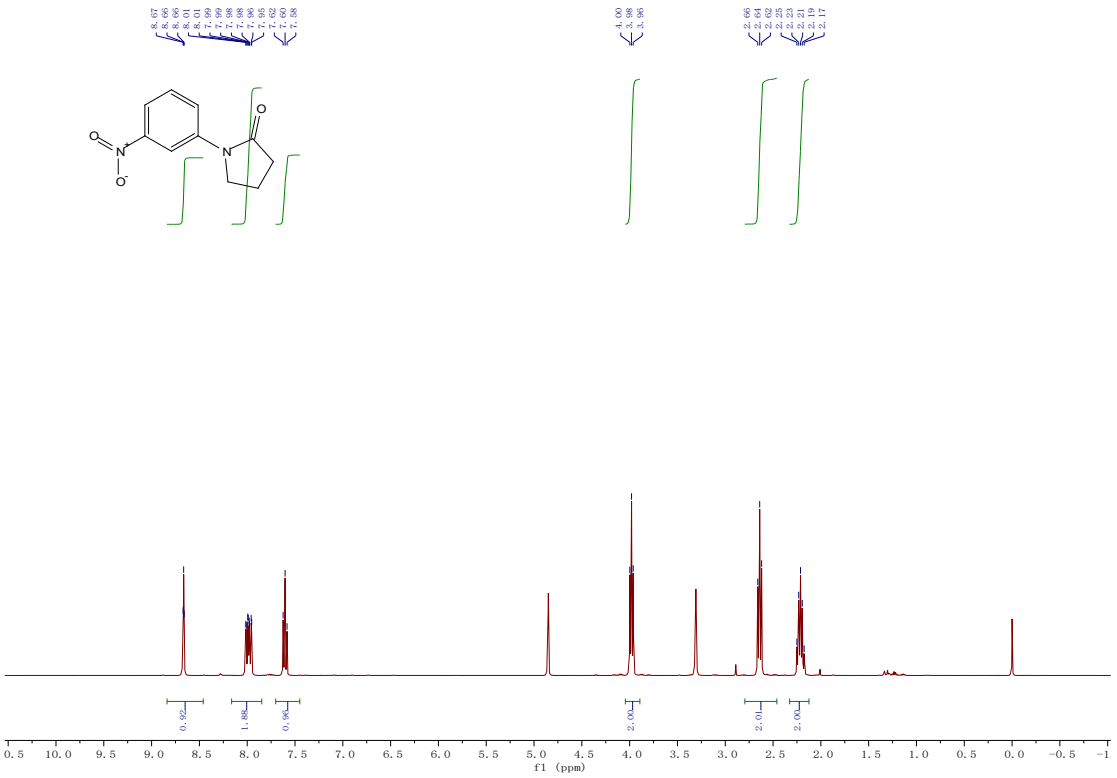
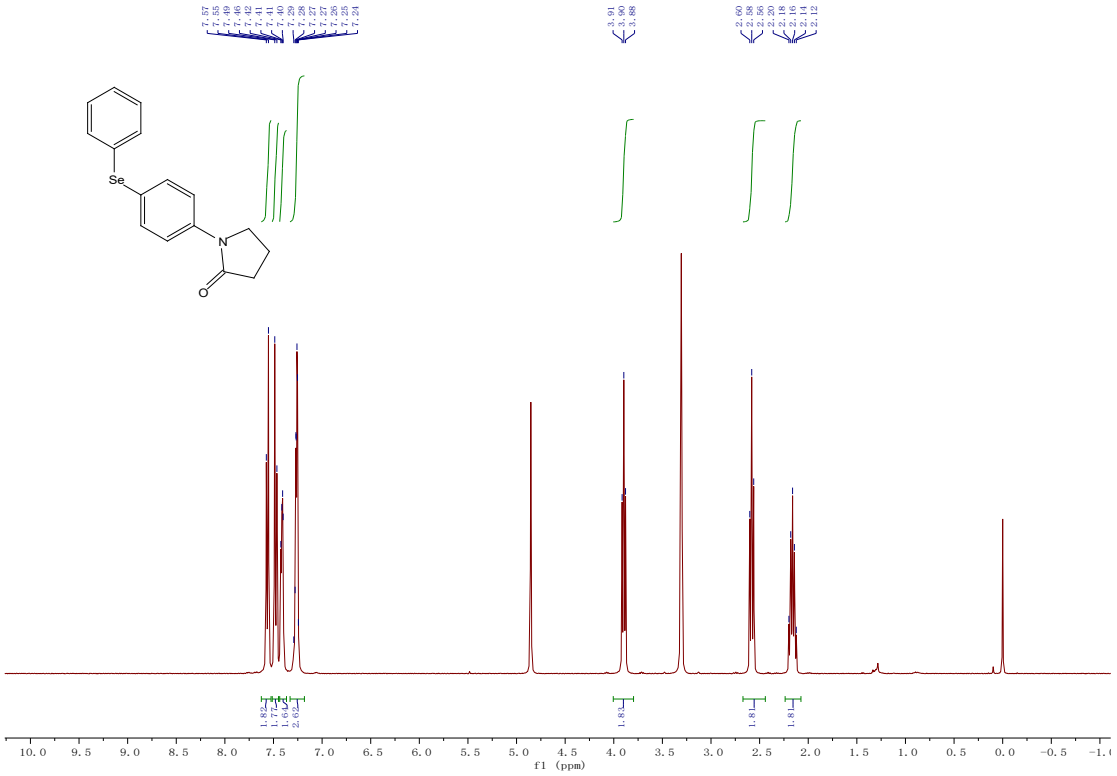
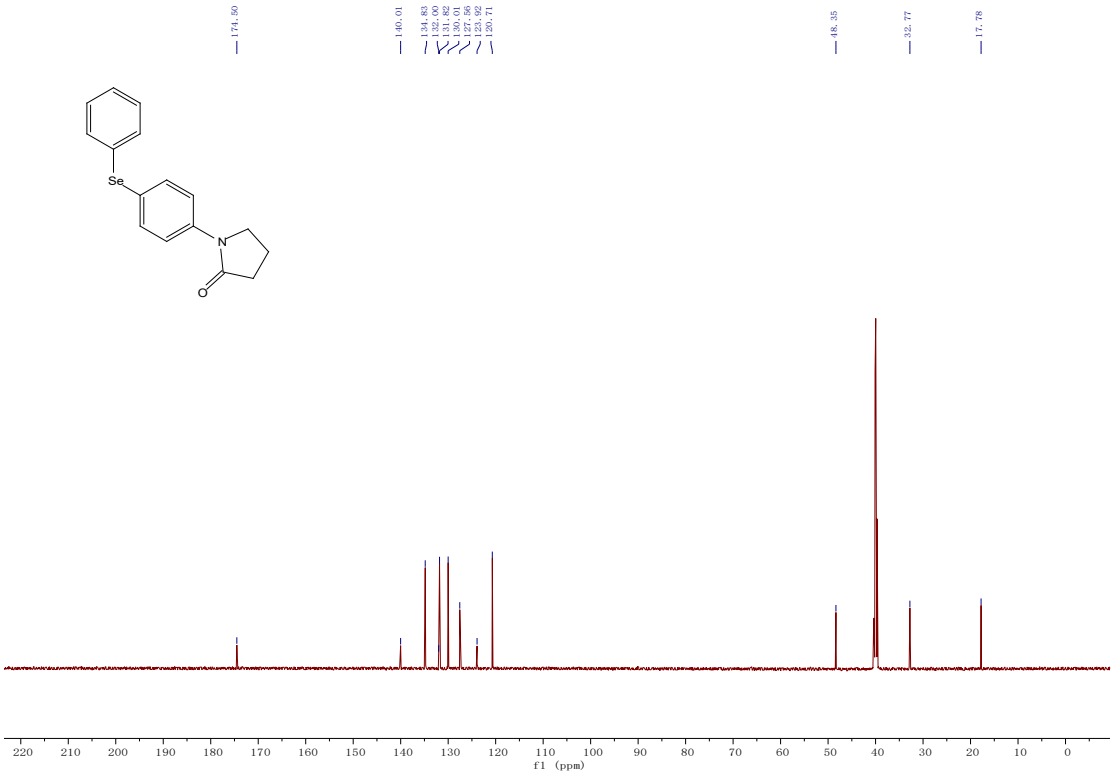
2.10
f1 (ppm)



9.2 NMR spectra of compound **3**

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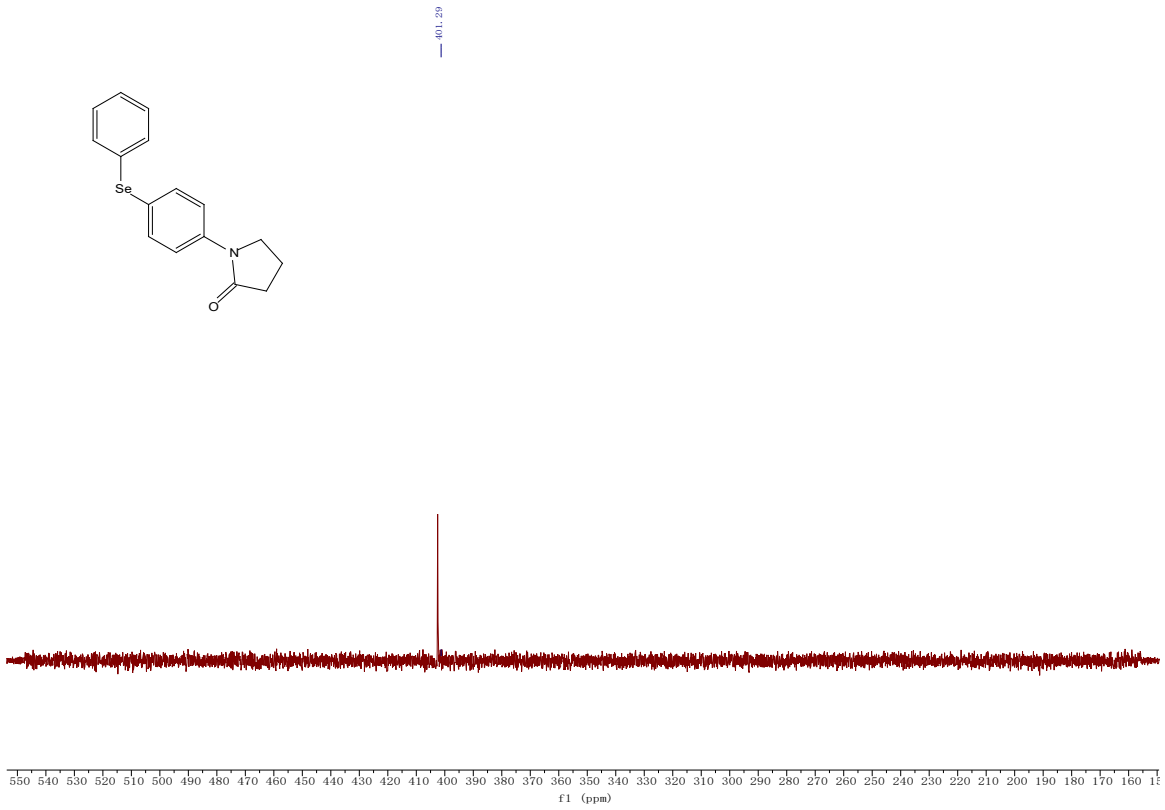
O
f1 (ppm)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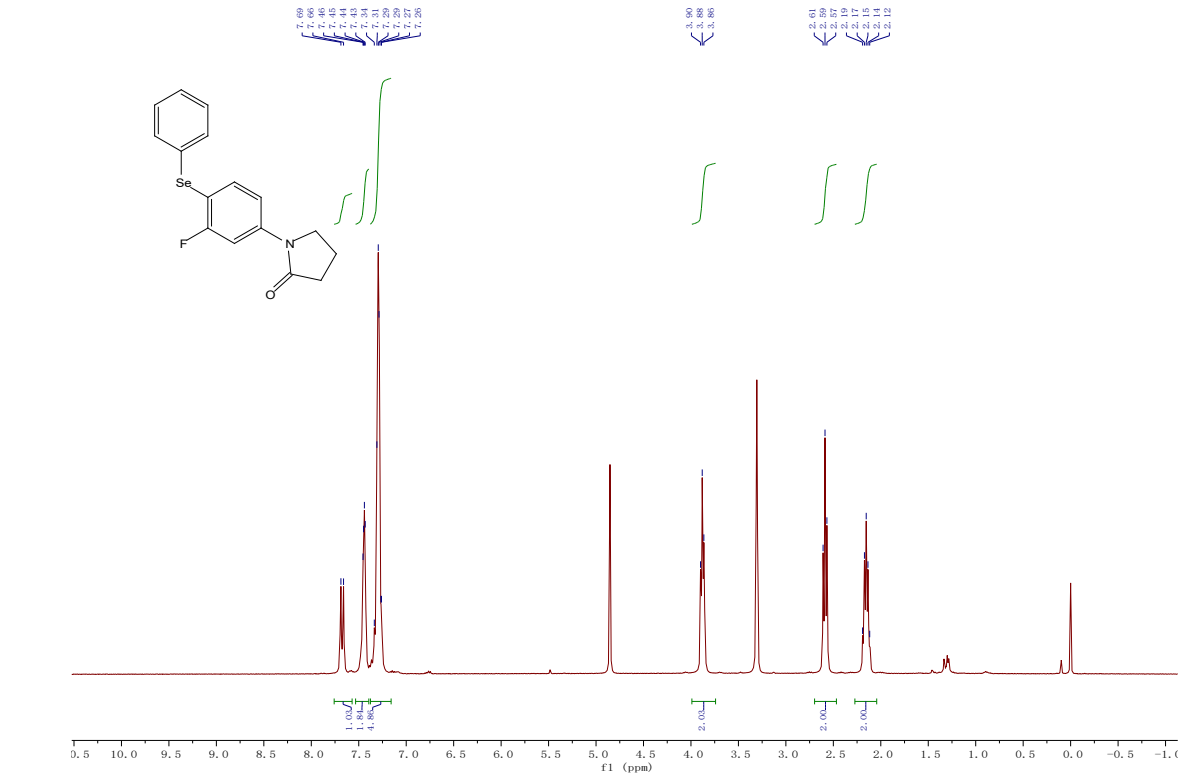
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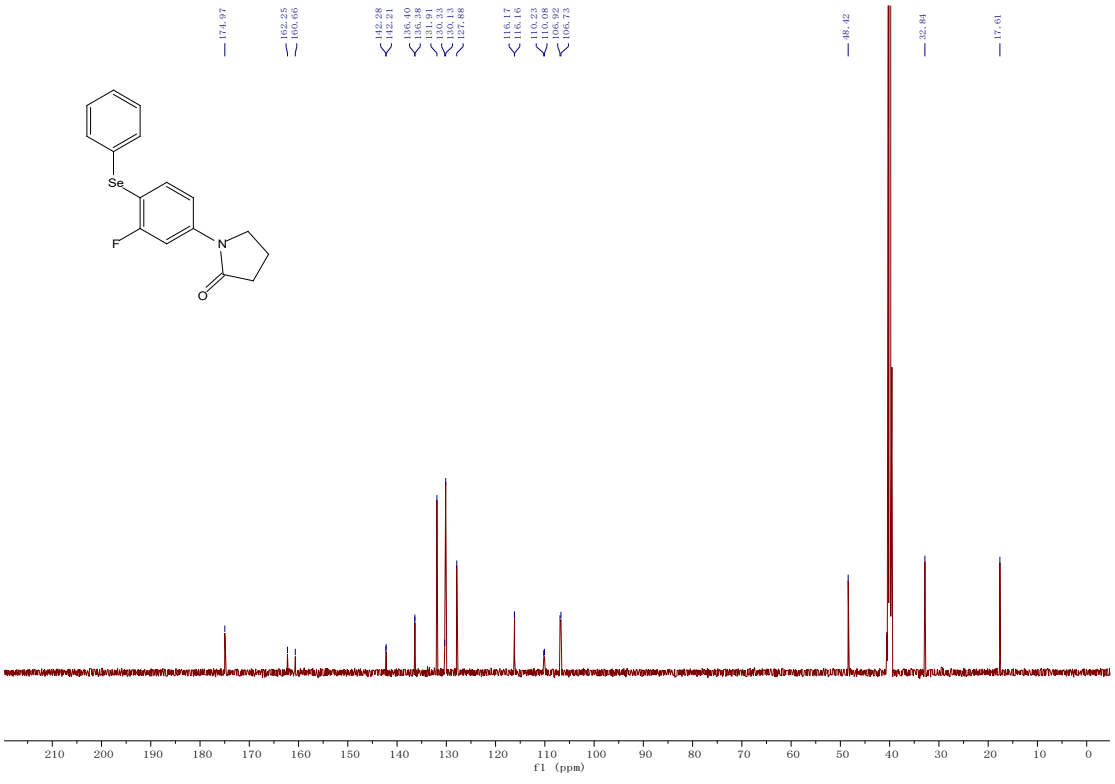
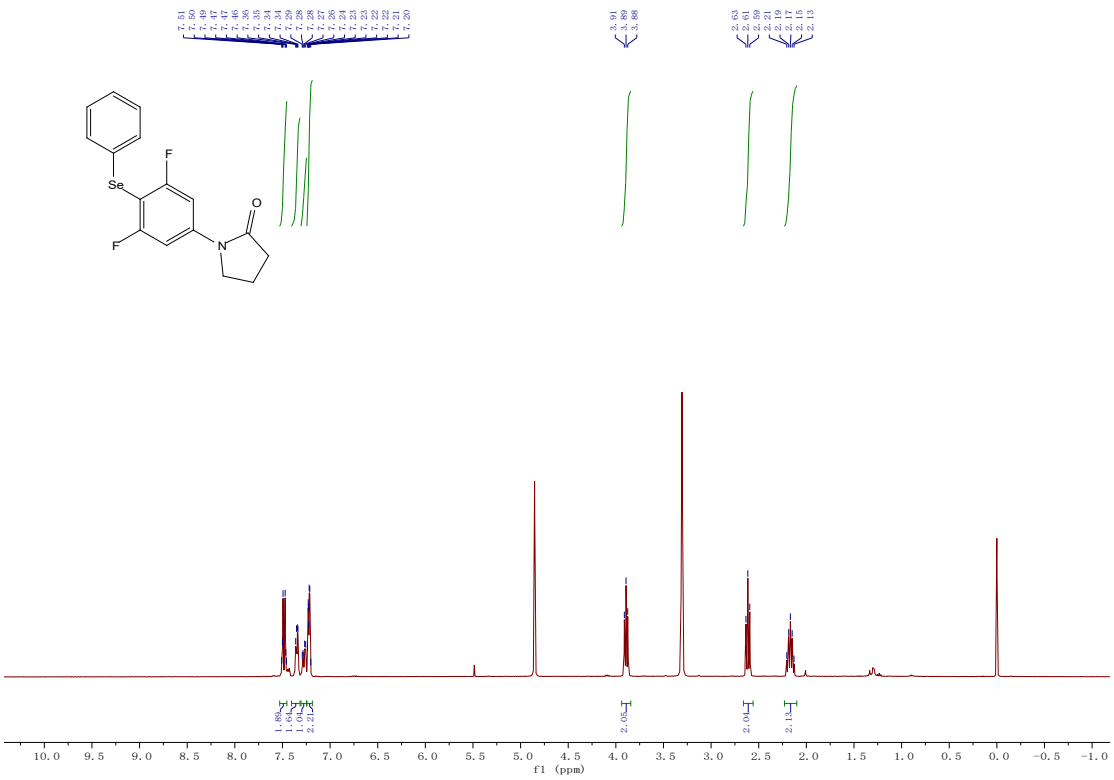
F
N
O
f1 (ppm)


Se
F
N
O
f1 (ppm)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7.20
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3.89
3.88
2.63
2.61
2.59
2.21
2.19
2.17
2.15
2.13
F
Se
F
O
N
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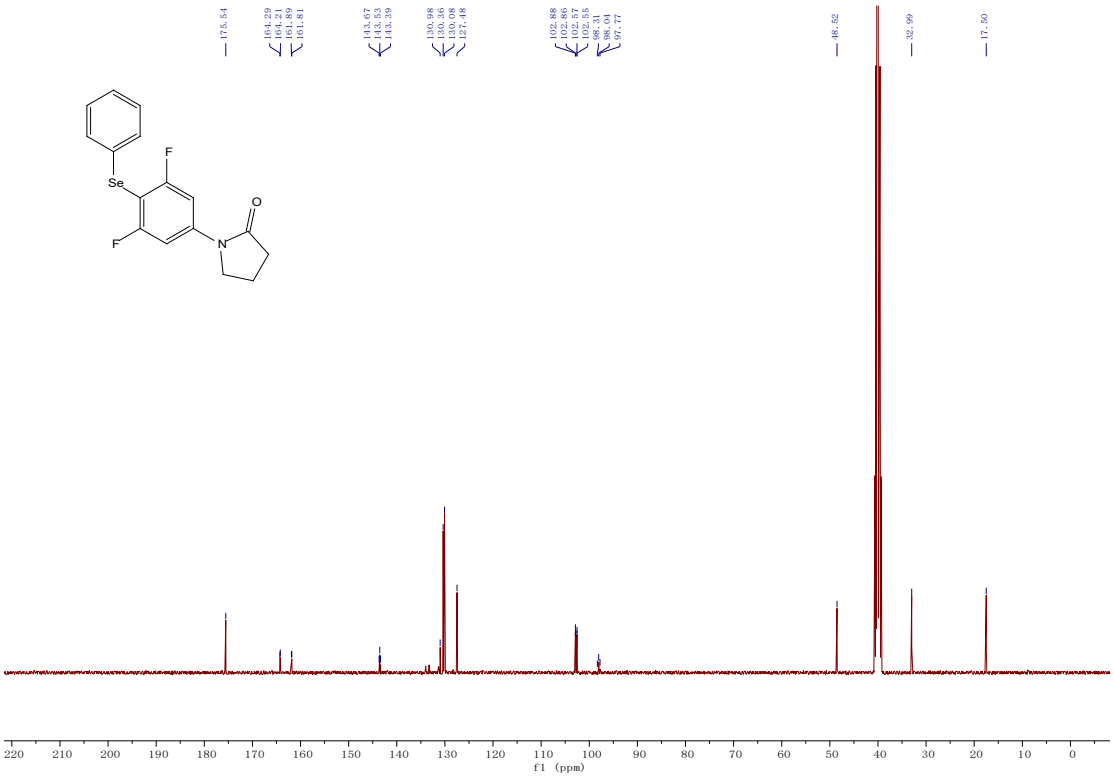
1.64
1.00
2.27
2.00
2.04
2.18
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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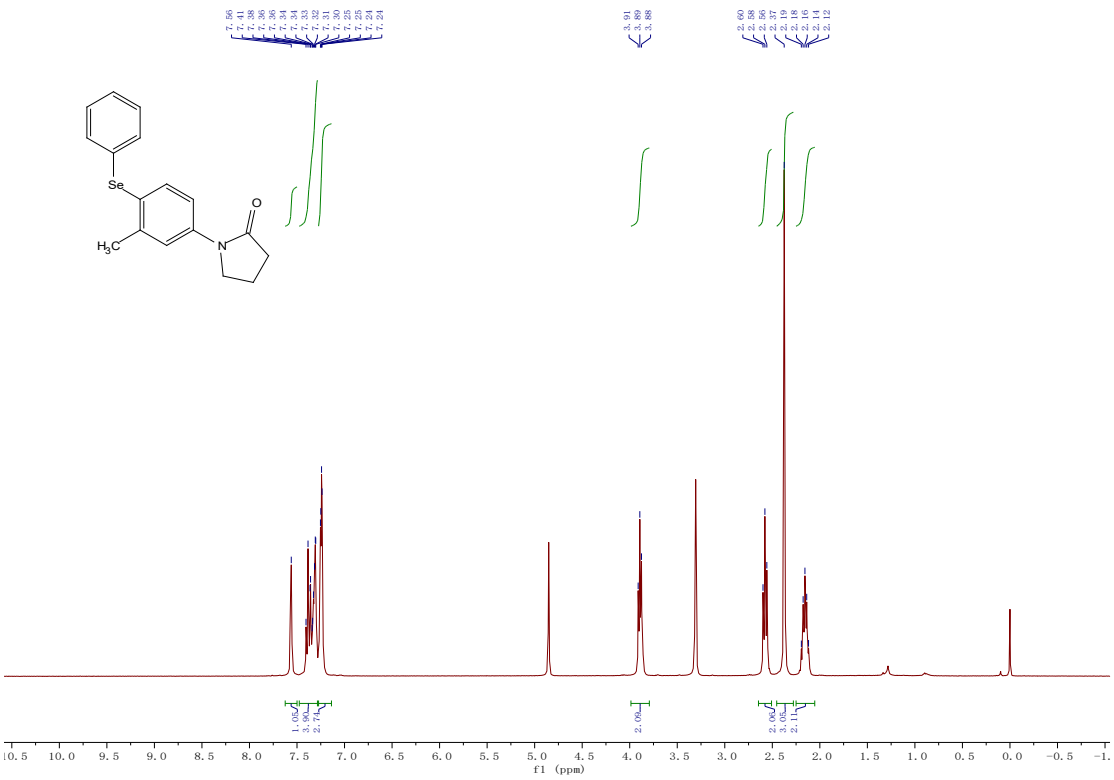
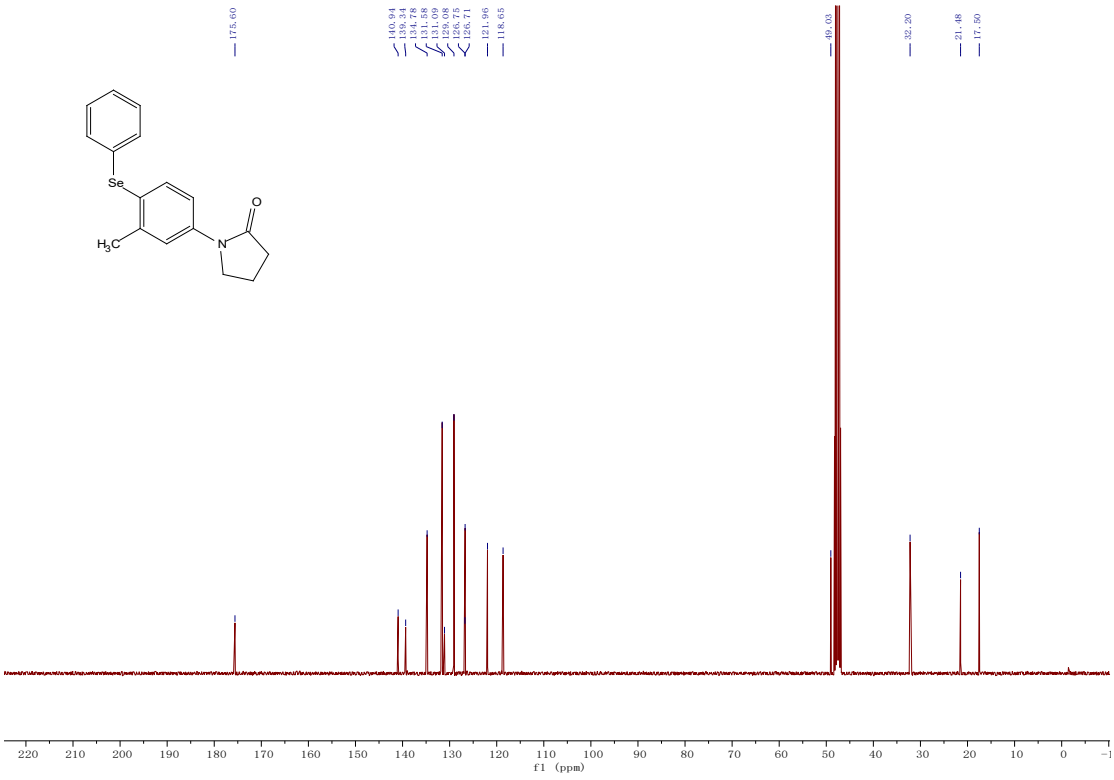
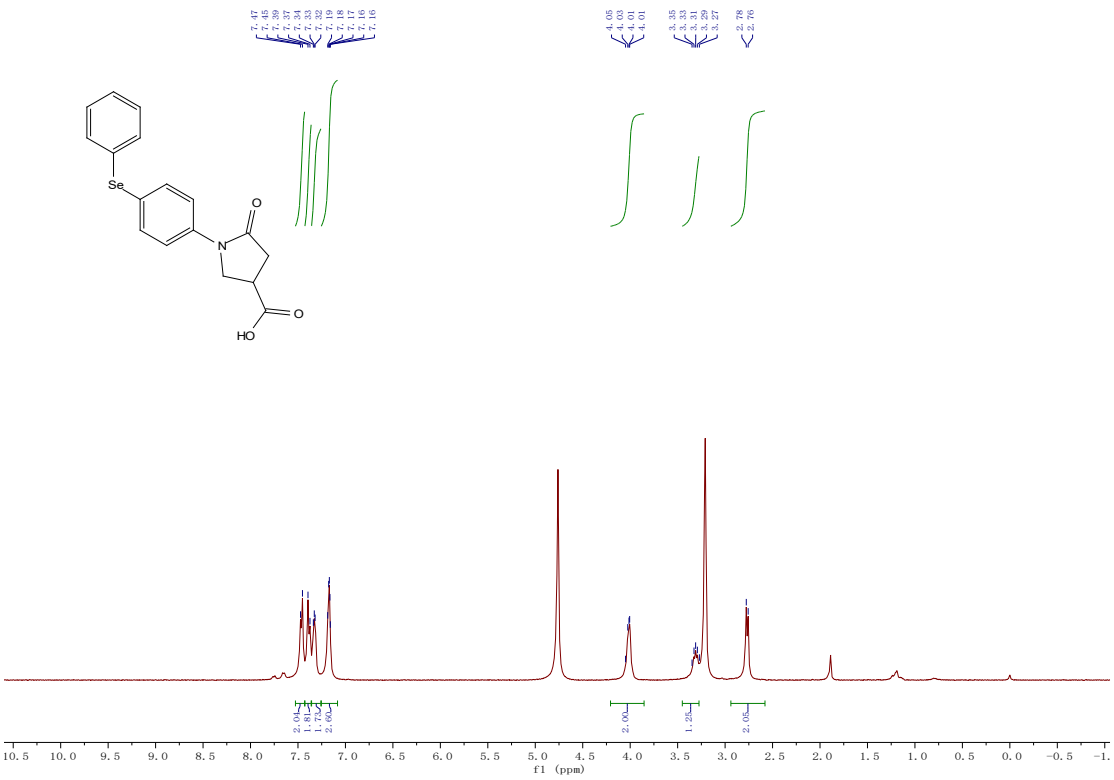
164.29
164.21
161.89
161.81
143.67
143.53
143.39
130.98
130.36
130.08
127.48
102.88
102.86
102.77
102.55
98.31
98.04
97.77
48.52
32.99
17.90
F
Se
F
O
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Se
O
N
H3C
f1 (ppm)


Se
O
N
H3C
f1 (ppm)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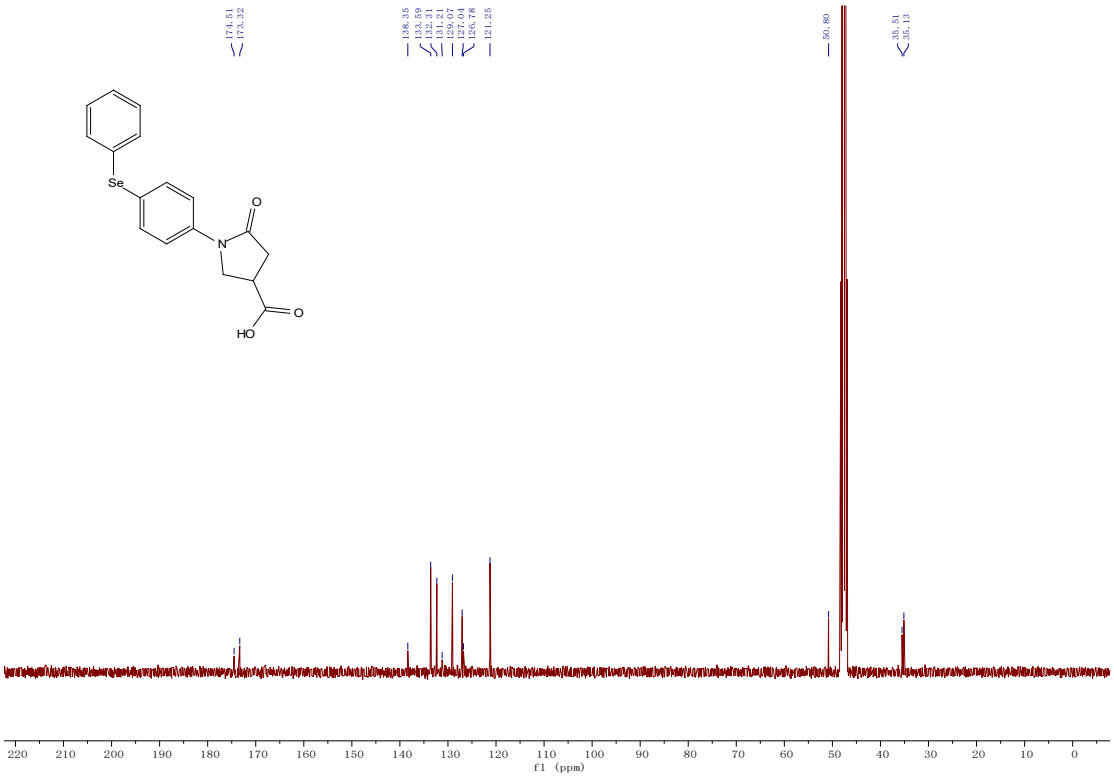
7.45
7.39
7.37
7.34
7.33
7.32
7.19
7.18
7.17
7.16
7.16
4.05
4.03
4.01
4.01
3.35
3.33
3.31
3.29
3.27
2.78
2.76
Se
O
N
O
HO
2.04
1.81
1.72
2.60
2.00
1.28
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.
f1 (ppm)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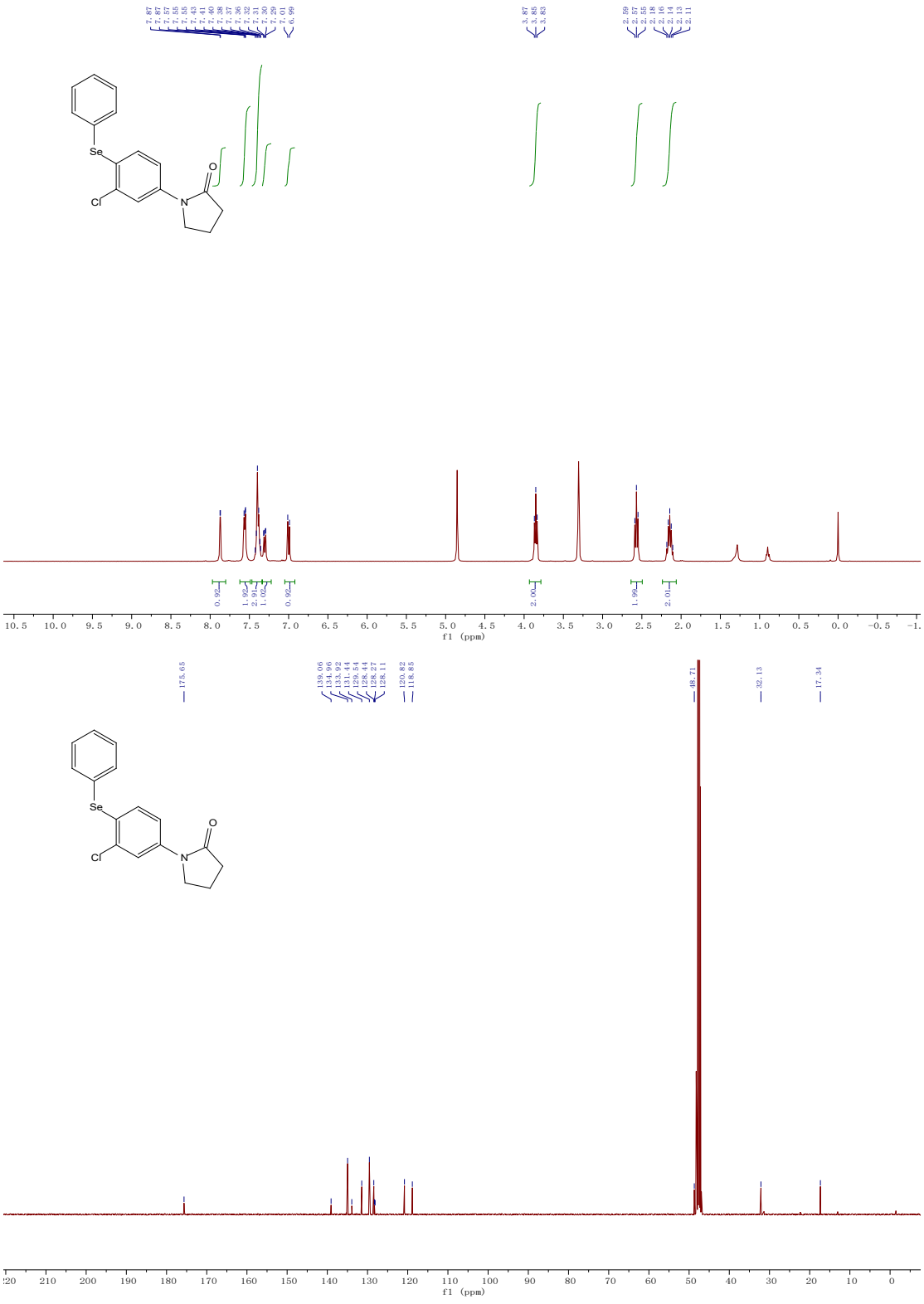
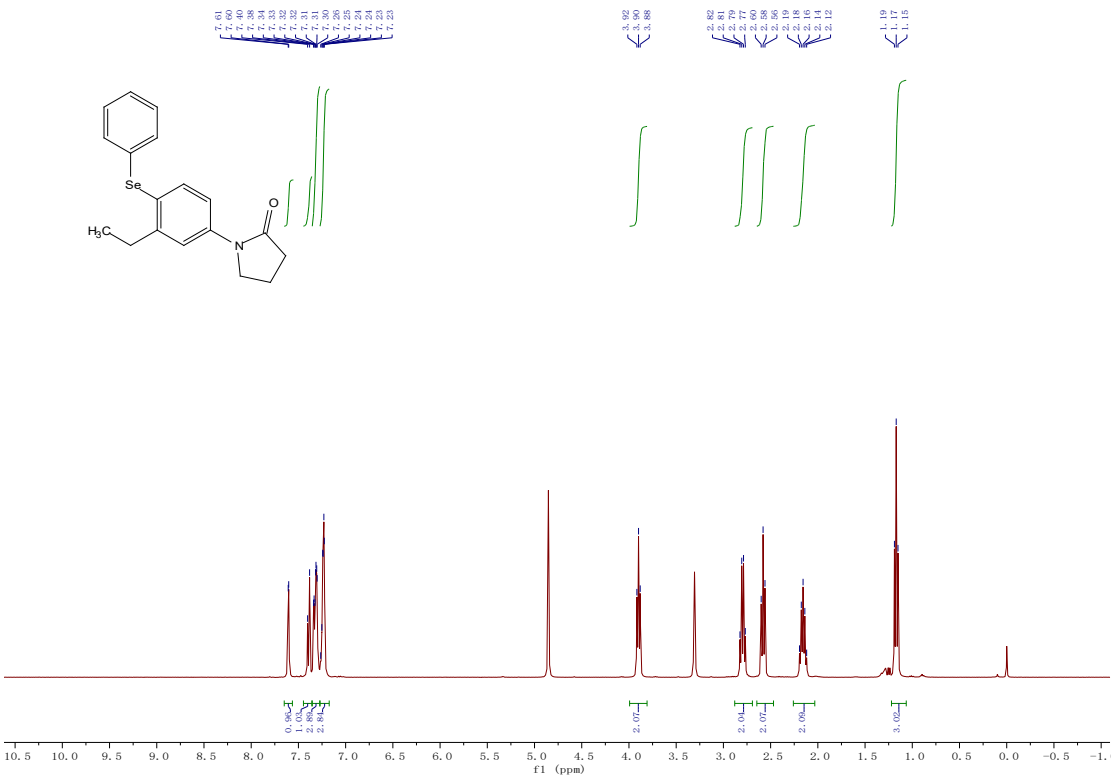
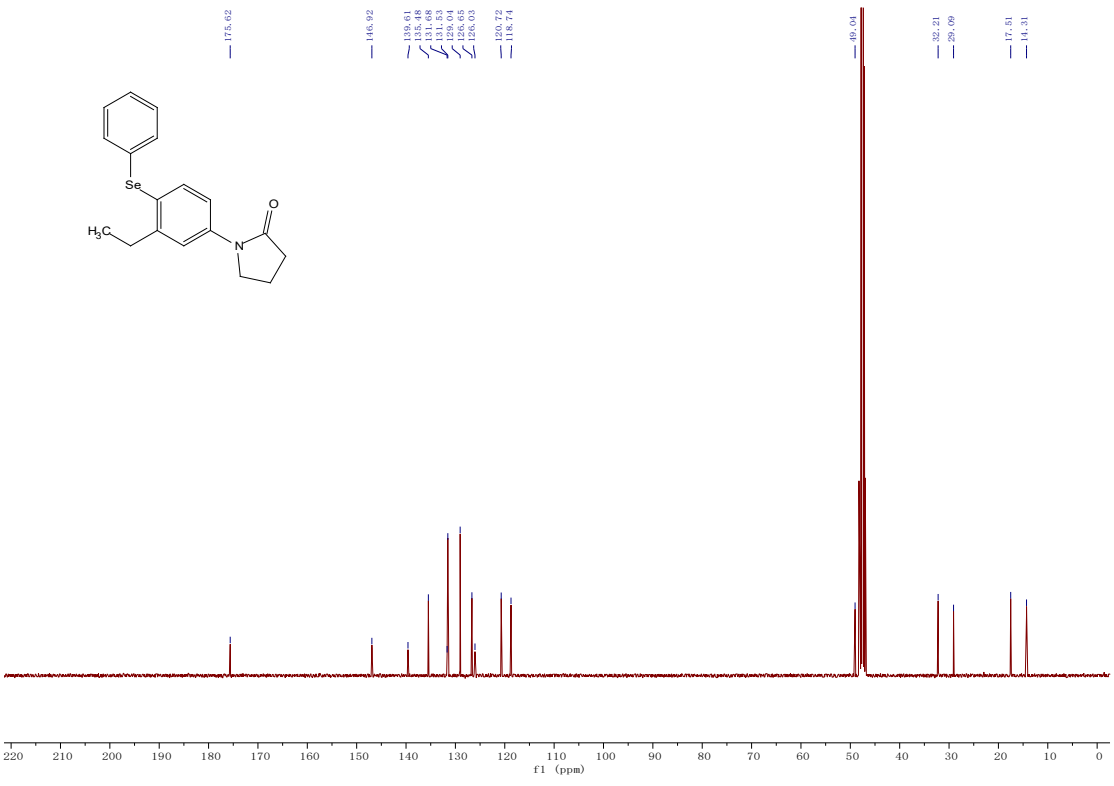
173.32
138.35
133.59
132.31
131.21
130.07
127.04
126.78
121.25
50.80
35.51
35.13
Se
O
N
O
HO
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.87
7.87
7.57
7.55
7.55
7.43
7.41
7.40
7.38
7.37
7.36
7.32
7.31
7.30
7.29
7.01
6.99
3.87
3.85
3.83
2.59
2.57
2.55
2.18
2.16
2.15
2.14
2.13
2.11
Se
Cl
O
N
0.92
1.99
2.91
1.02
0.92
2.00
1.99
2.01
f1 (ppm)
175.65
139.06
134.96
134.92
131.44
129.54
128.44
128.27
128.11
120.82
118.85
48.71
32.13
17.34
f1 (ppm)


7.61
7.60
7.49
7.48
7.34
7.33
7.32
7.32
7.31
7.30
7.26
7.25
7.24
7.24
7.23
7.23
3.92
3.90
3.88
2.82
2.81
2.79
2.77
2.60
2.38
2.36
2.19
2.18
2.16
2.14
2.12
1.19
1.17
1.15
Se
O
H3C
N
0.96
1.00
1.97
2.81
2.07
2.04
2.07
2.00
3.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)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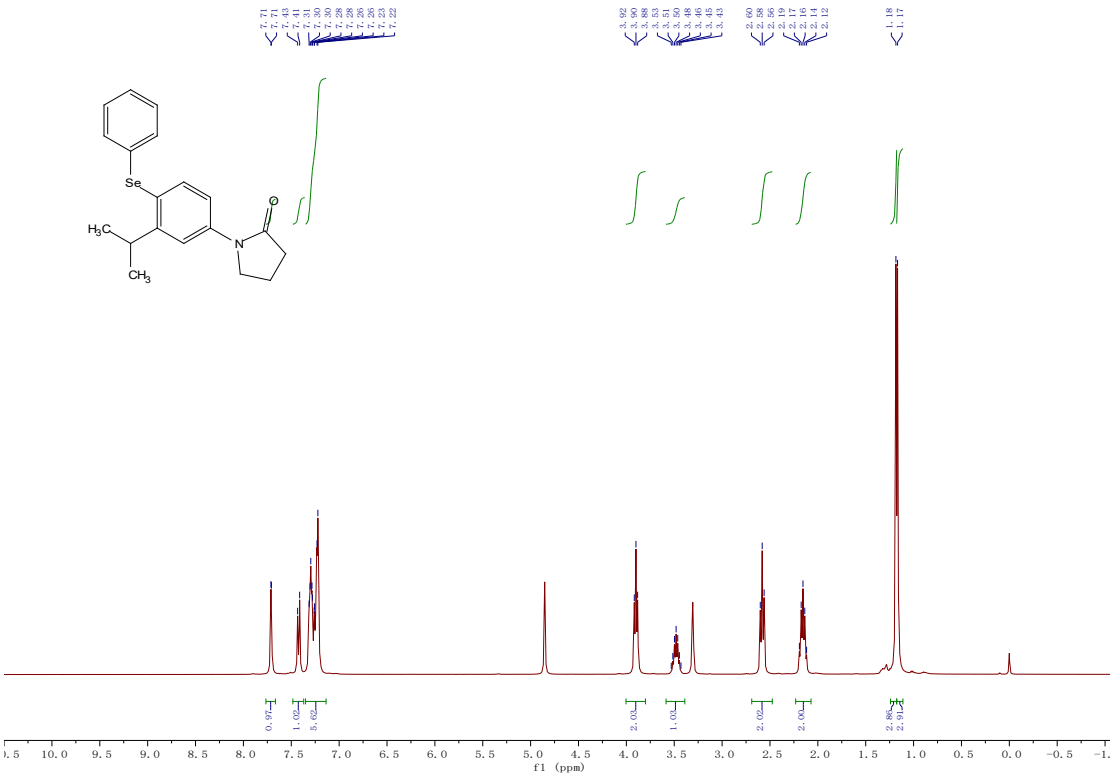
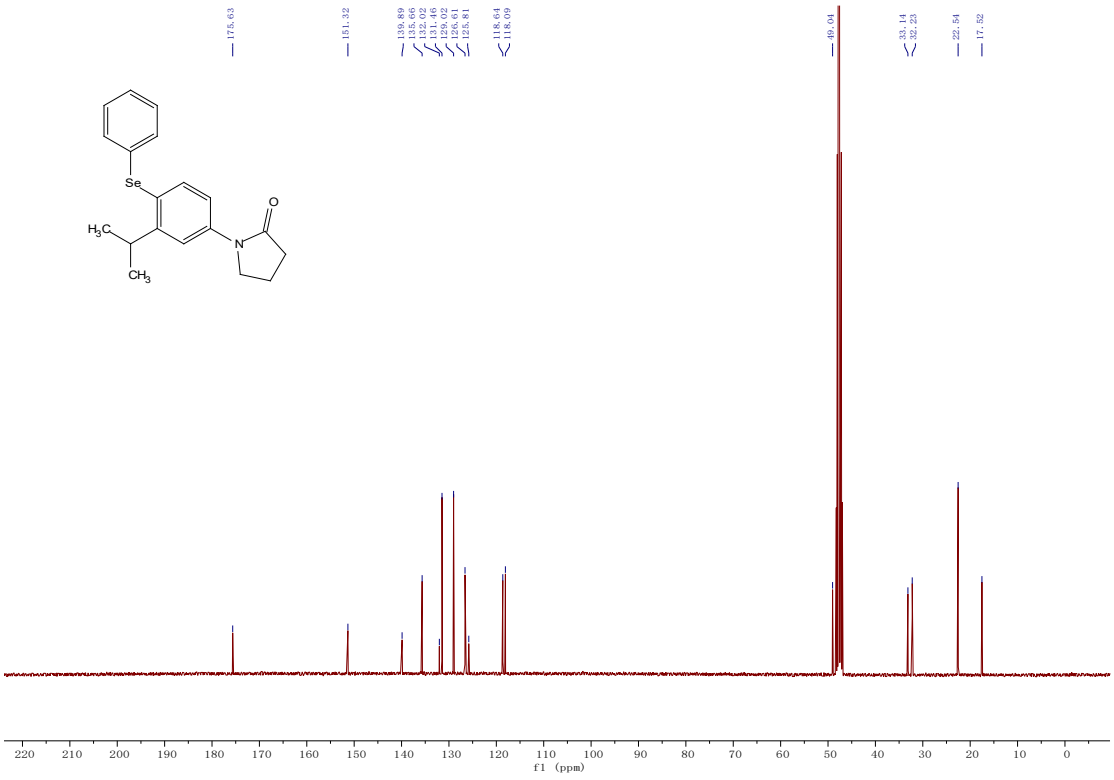
146.92
139.61
135.48
131.68
131.53
129.04
128.65
126.03
120.72
118.74
49.04
32.21
29.09
17.51
14.31
Se
O
H3C
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.71
7.71
7.43
7.41
7.31
7.30
7.28
7.28
7.26
7.26
7.23
7.22
3.92
3.90
3.88
3.53
3.51
3.50
3.48
3.46
3.45
3.43
2.60
2.58
2.56
2.19
2.17
2.16
2.14
2.12
1.18
1.17
Se
O
N
H3C
CH3
0.97
1.02
5.62
2.00
1.04
2.02
2.00
2.88
2.91
f1 (ppm)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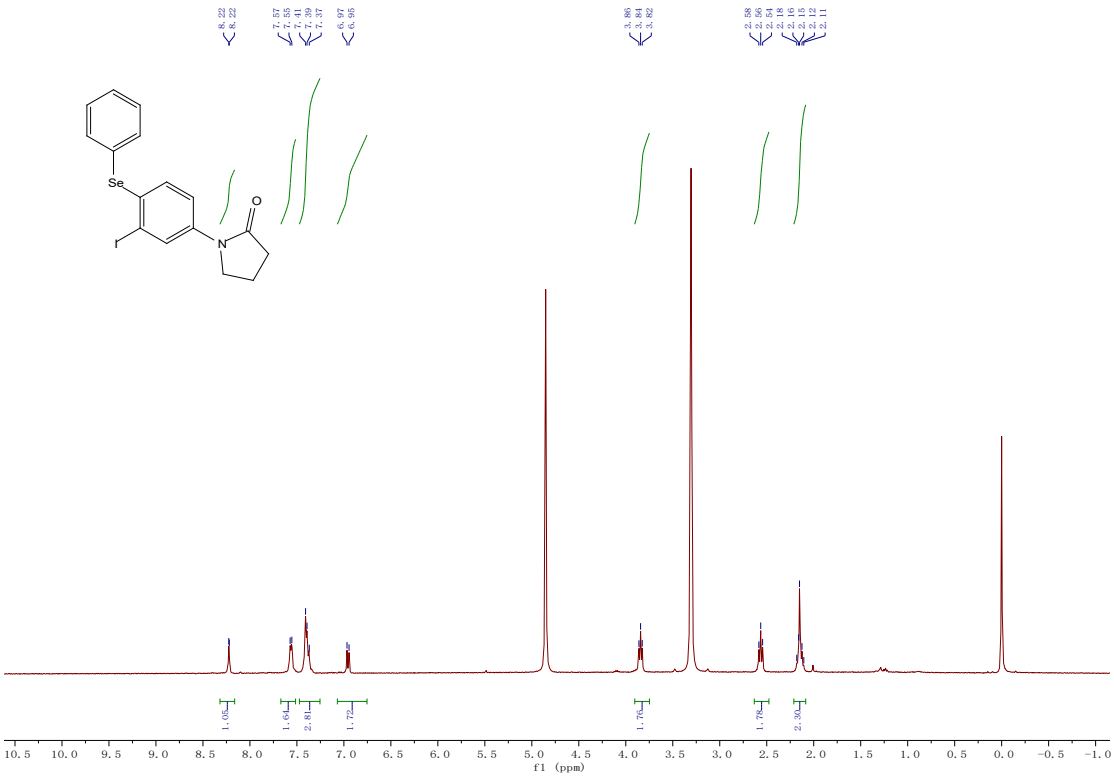
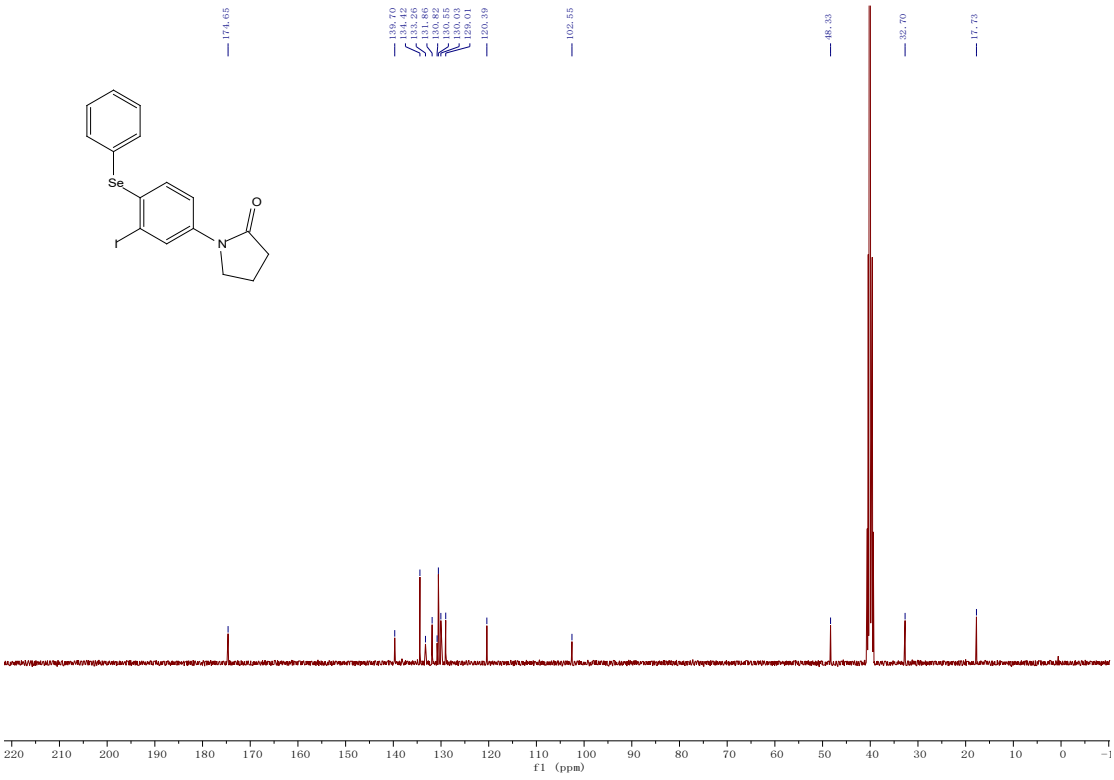
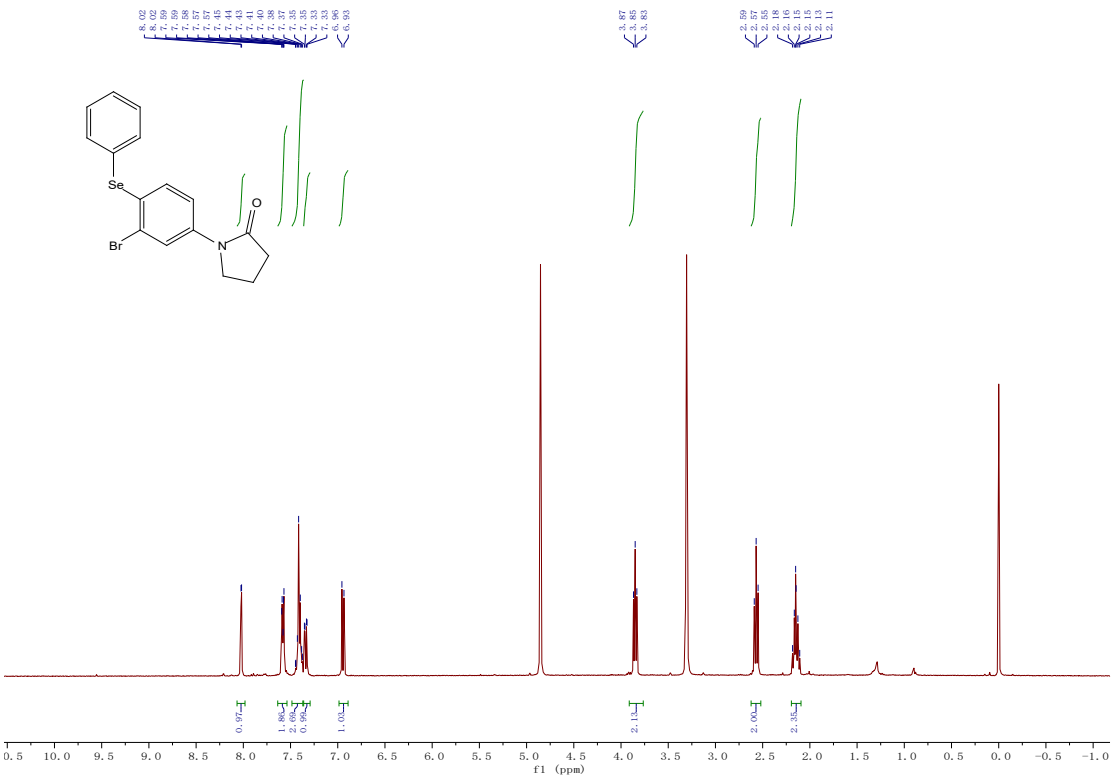
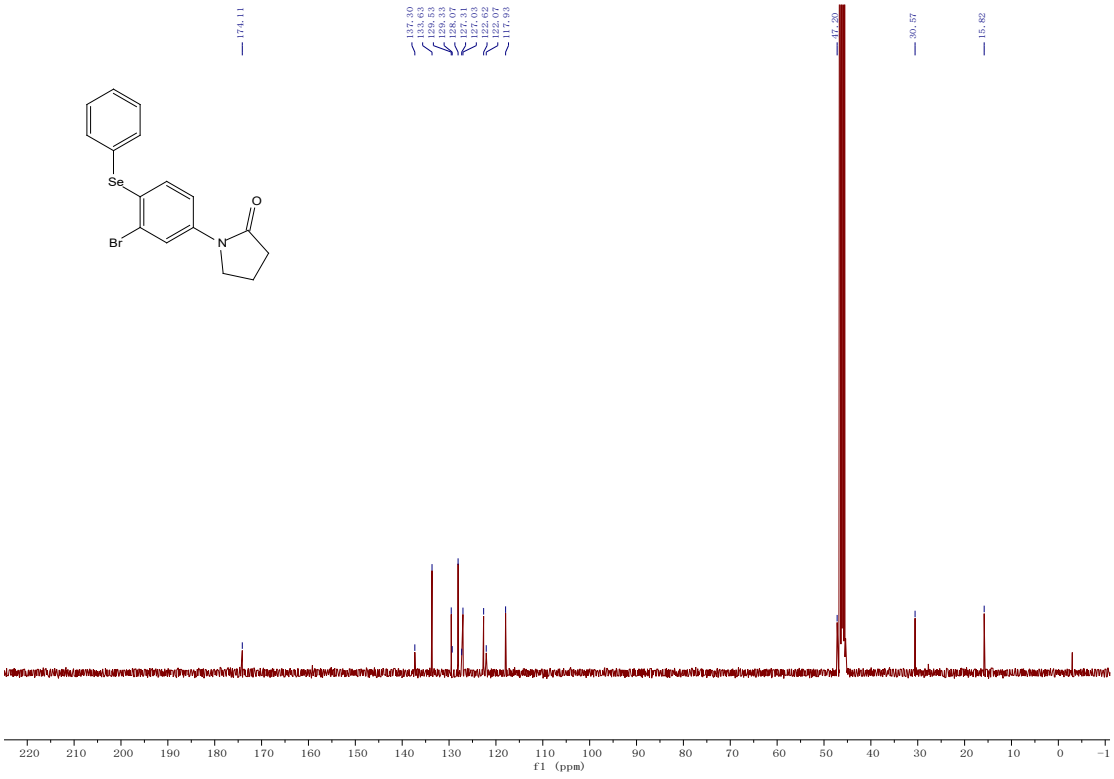
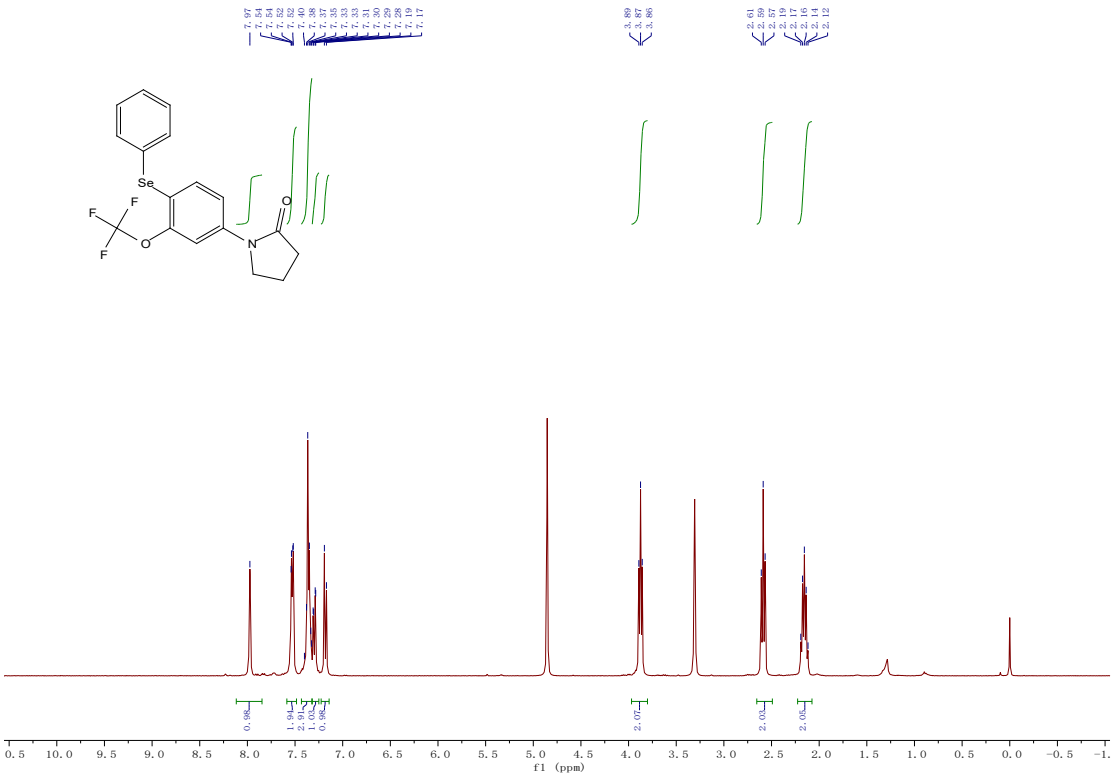
151.32
139.89
135.66
132.02
131.46
129.02
126.61
125.81
118.64
118.09
49.04
33.14
32.23
22.54
17.52
Se
O
N
H3C
CH3
f1 (ppm)

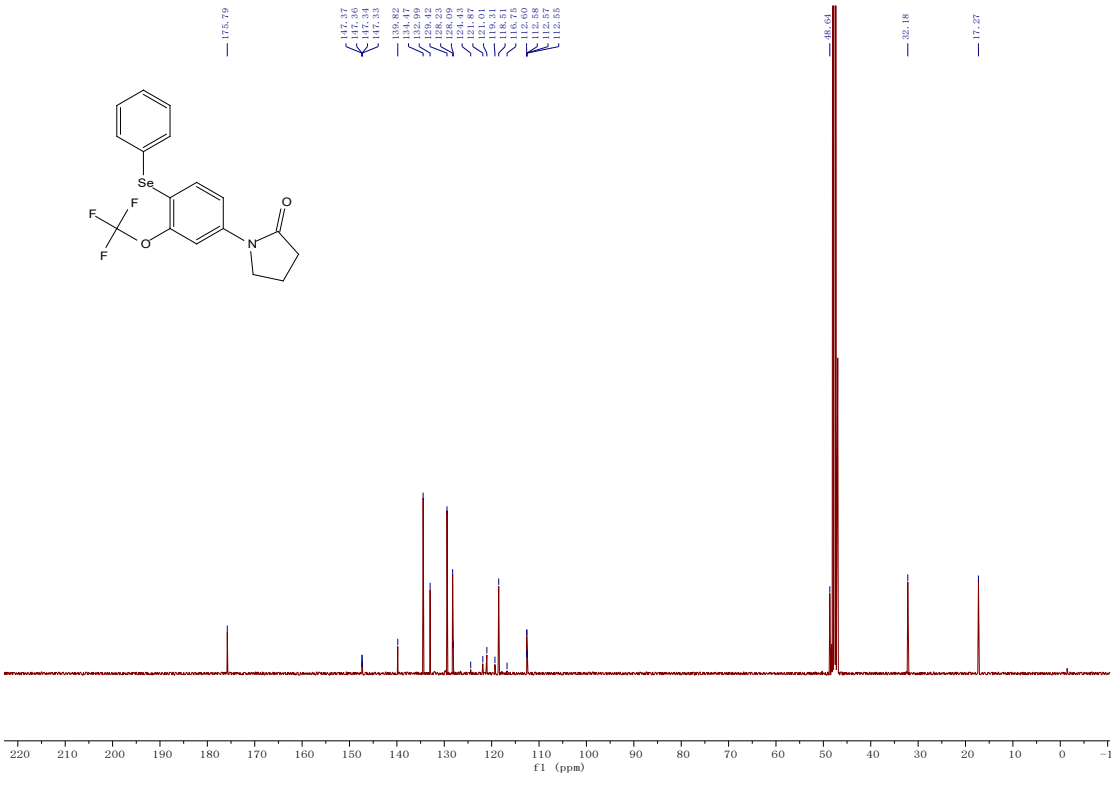

8.22
8.22
7.57
7.55
7.41
7.39
7.37
6.97
6.95
3.86
3.84
3.82
2.58
2.56
2.54
2.18
2.16
2.15
2.13
2.12
2.11
Se
I
O
N
1.05
1.64
2.81
1.72
1.70
1.78
2.30
f1 (ppm)


174.65
139.70
134.42
133.26
131.86
130.82
130.55
130.03
129.01
120.39
102.55
48.33
32.70
17.73
Se
I
O
N
f1 (ppm)


8.02
8.02
7.59
7.59
7.58
7.57
7.57
7.44
7.43
7.41
7.40
7.38
7.37
7.35
7.33
6.93
3.87
3.85
2.59
2.57
2.55
2.18
2.16
2.15
2.13
2.11
Se
Br
O
N
0.97
1.88
2.69
0.96
1.00
2.14
2.00
2.33
f1 (ppm)


174.11
137.30
133.65
129.53
129.33
128.07
127.71
127.03
122.62
122.07
117.93
47.20
30.57
15.82
Se
Br
O
N
f1 (ppm)


7.97
7.94
7.84
7.82
7.82
7.40
7.38
7.37
7.35
7.33
7.31
7.30
7.28
7.19
7.17
3.89
3.87
3.86
2.61
2.59
2.57
2.19
2.17
2.16
2.14
2.12
Se
F
F
F
O
O
N
0.98
1.94
2.91
1.00
0.98
2.07
2.03
2.00
f1 (ppm)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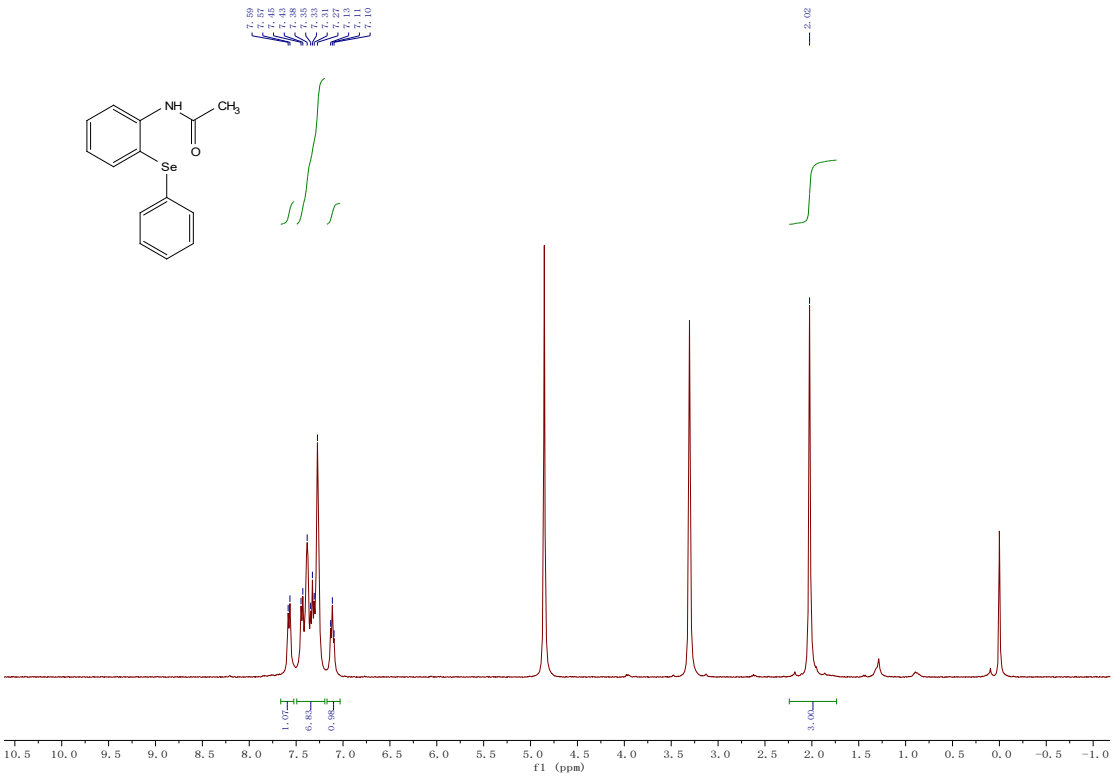
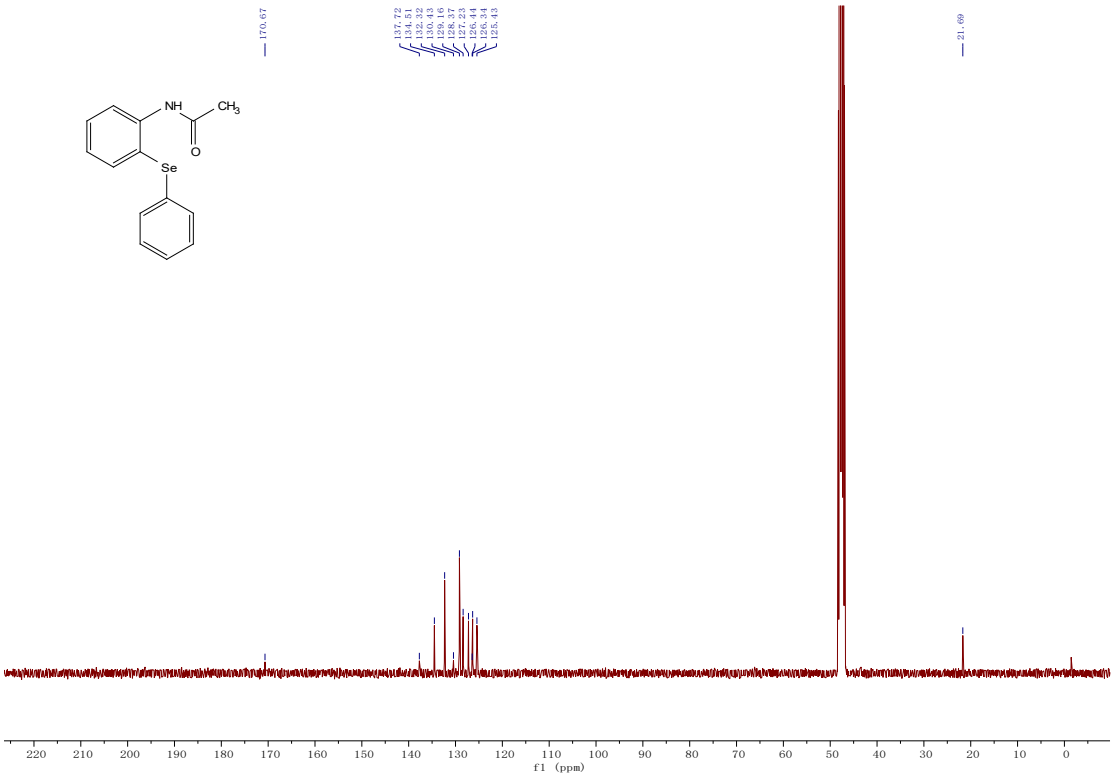
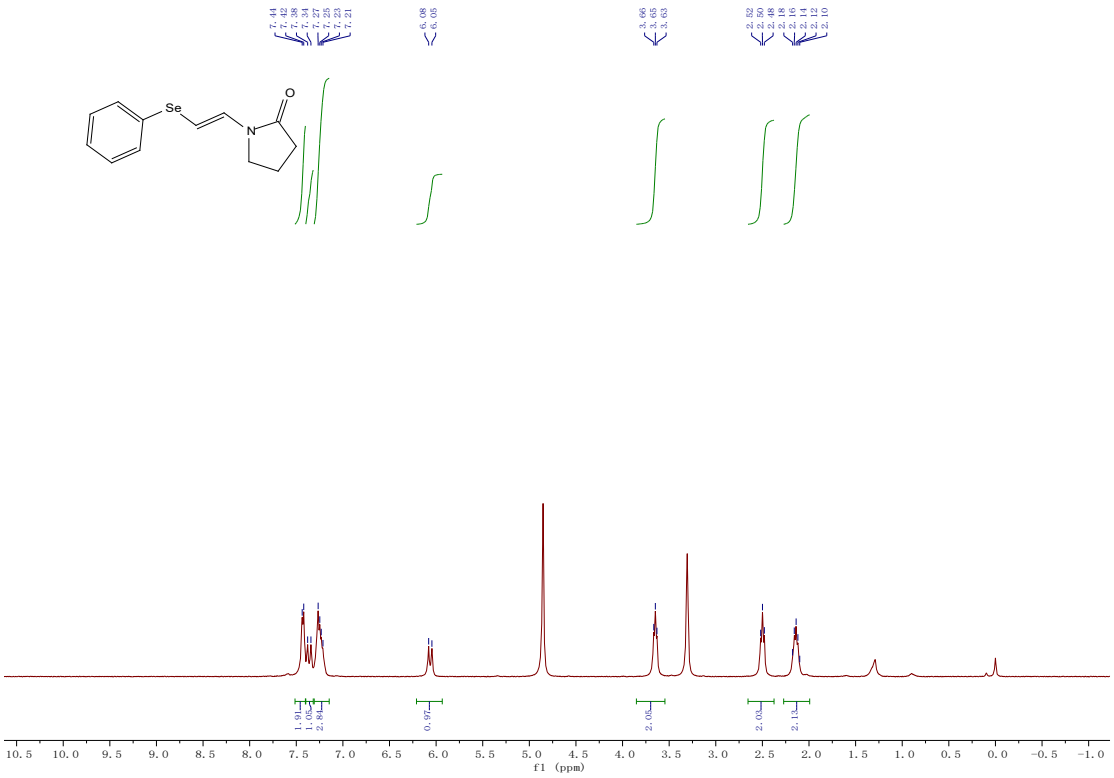
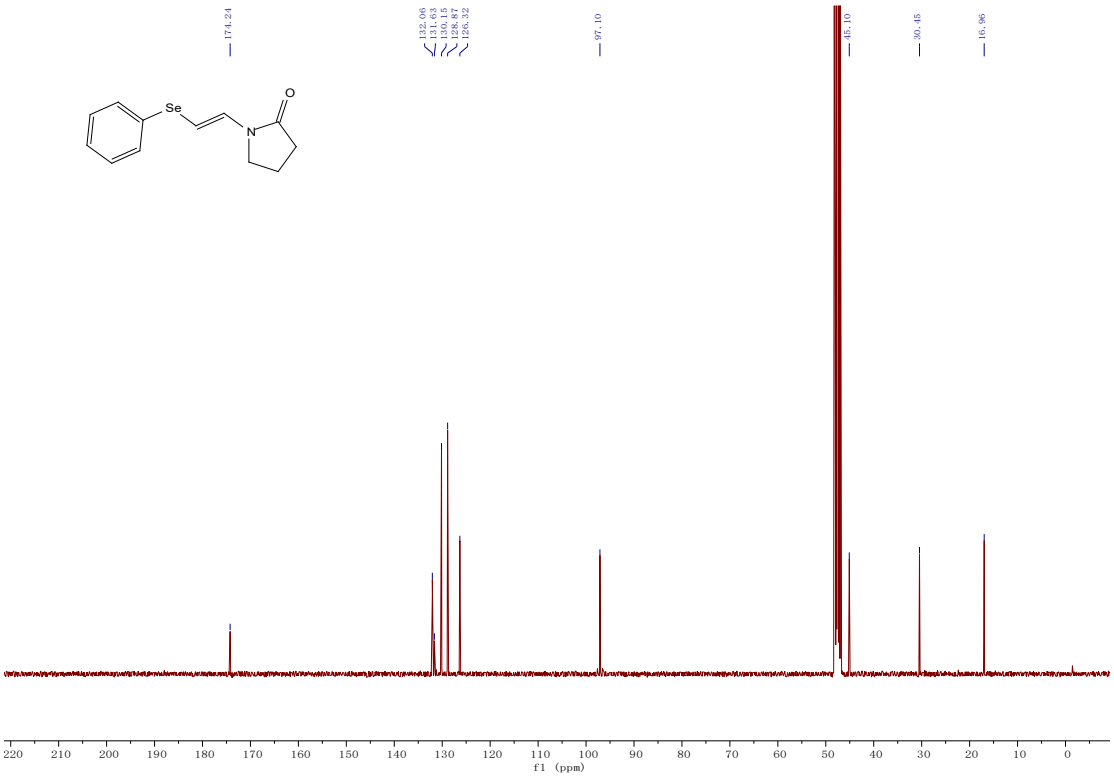
147.37
147.36
147.34
147.33
139.82
134.47
132.99
129.42
128.23
126.09
124.43
121.87
121.01
119.31
118.51
116.75
112.60
112.58
112.57
112.55
48.64
32.18
17.27
Se
F
F
F
O
O
N
f1 (ppm)


7.59
7.57
7.45
7.43
7.38
7.35
7.33
7.31
7.27
7.13
7.11
7.10
2.02
NH
CH3
O
Se
1.07
6.83
0.98
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


170.67
137.72
134.51
132.32
130.43
129.16
128.37
127.23
126.44
126.34
125.43
21.69
NH
CH3
O
Se
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.44
7.42
7.38
7.34
7.27
7.25
7.23
7.21
6.08
6.05
3.66
3.65
3.63
2.52
2.50
2.48
2.18
2.16
2.14
2.12
2.10
Se
O
N
1.91
1.00
1.04
2.84
0.97
2.00
2.00
2.13
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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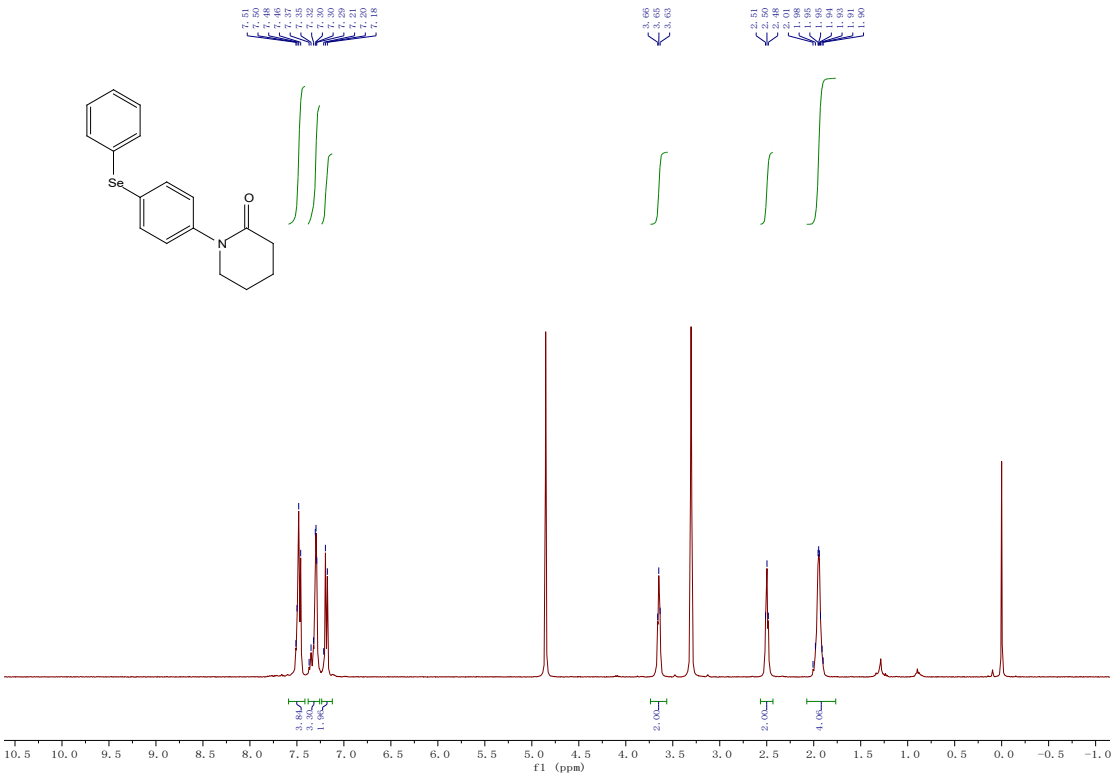
132.06
131.63
130.15
128.87
126.32
97.10
45.10
30.45
16.96
Se
O
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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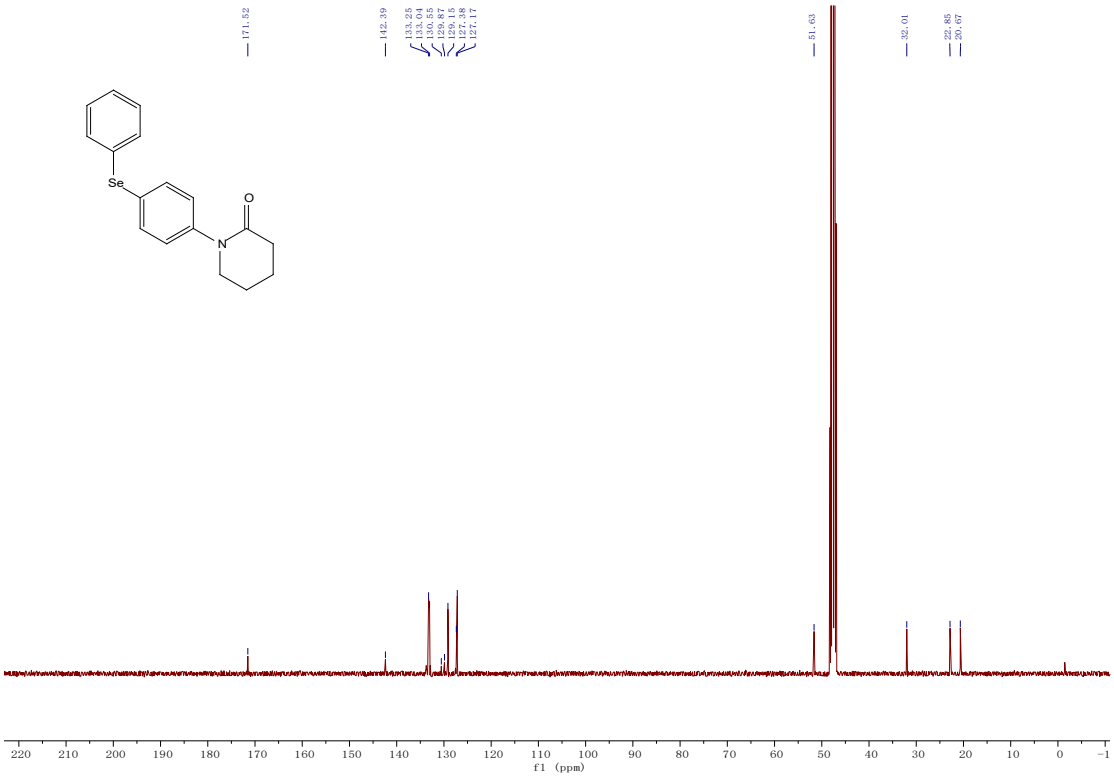
7.50
7.48
7.46
7.37
7.35
7.32
7.30
7.29
7.21
7.20
7.18
3.66
3.65
3.63
2.51
2.50
2.48
2.01
1.98
1.95
1.94
1.93
1.91
1.90
Se
O
N
3.84
3.82
1.96
2.00
2.00
4.06
f1 (ppm)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142.39
133.25
133.04
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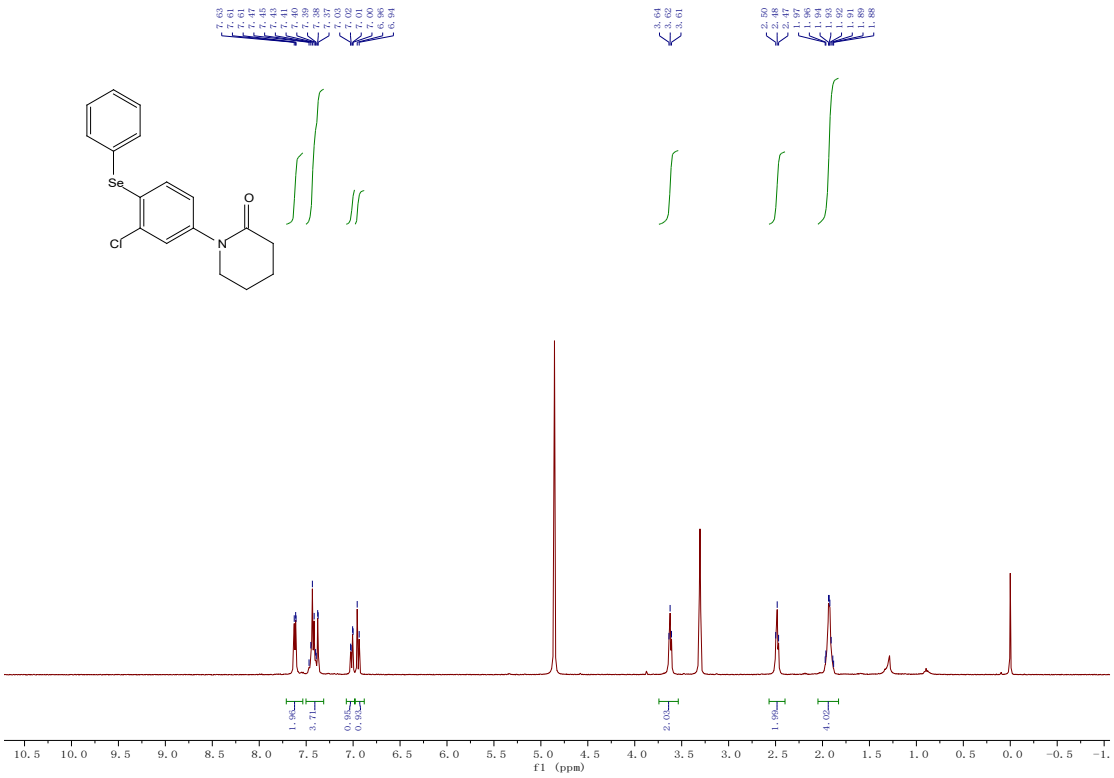
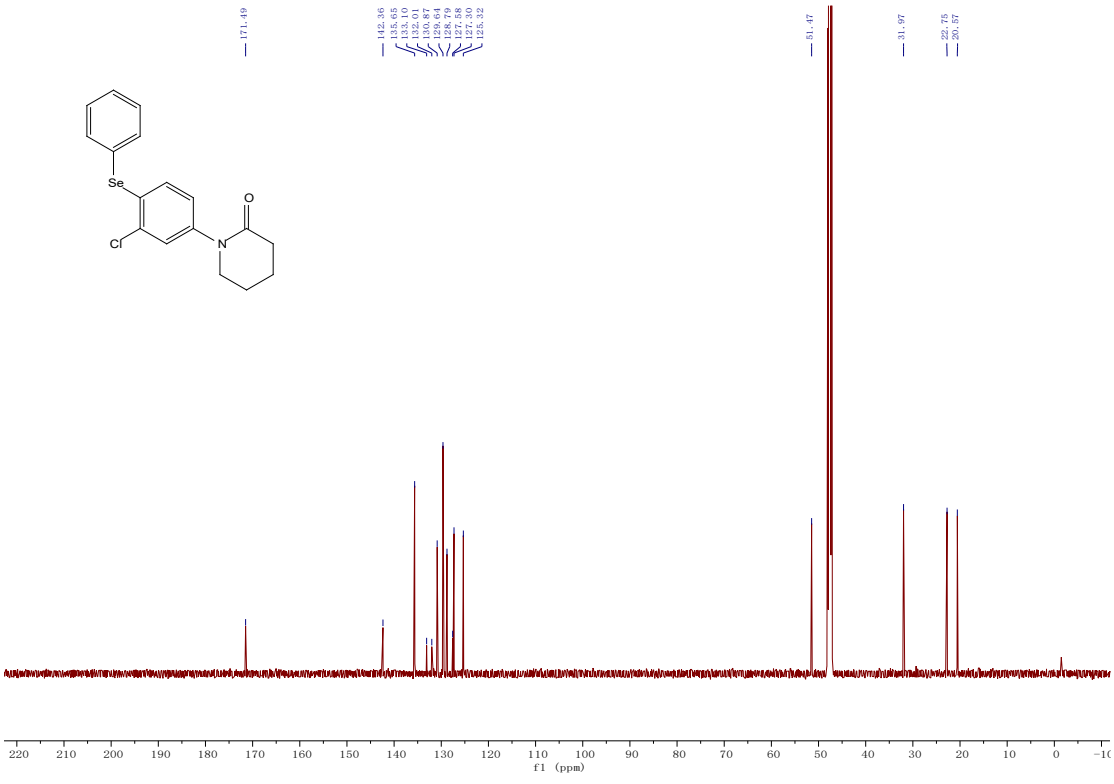
129.87
129.18
127.98
127.17
51.63
32.01
22.85
20.67
Se
O
N
f1 (ppm)


7.63
7.61
7.61
7.47
7.45
7.43
7.41
7.40
7.39
7.38
7.37
7.03
7.02
7.01
7.00
6.98
6.94
3.64
3.62
3.61
2.50
2.48
2.47
1.97
1.96
1.94
1.93
1.92
1.91
1.89
1.88
Se
Cl
O
N
1.96
3.71
0.96
0.93
2.00
1.98
4.02
f1 (ppm)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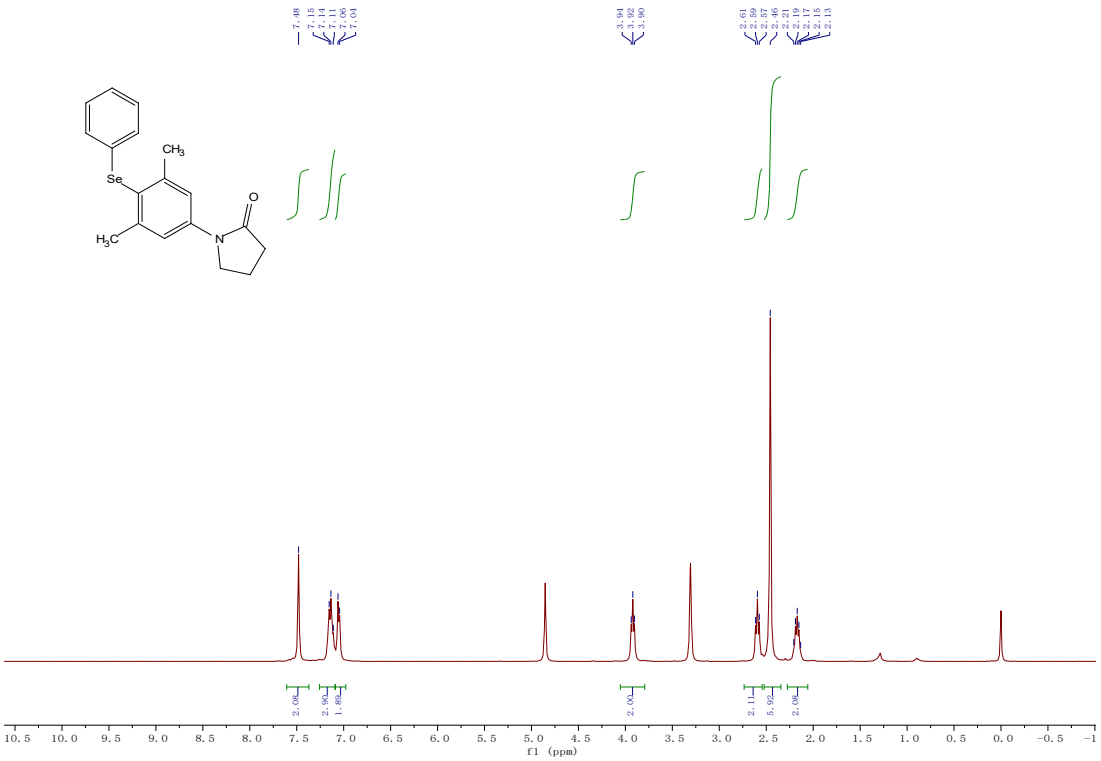
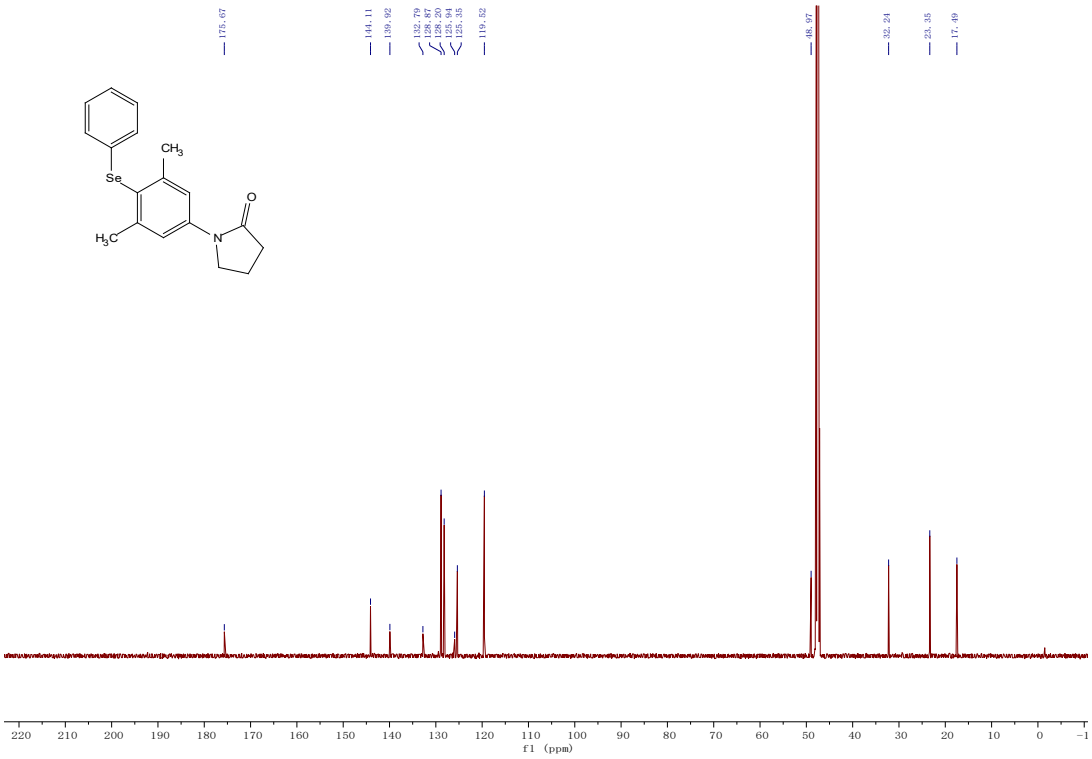
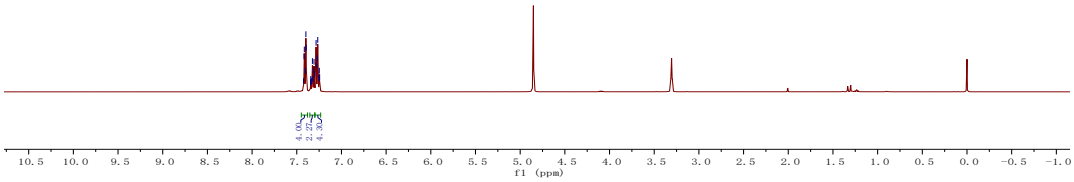
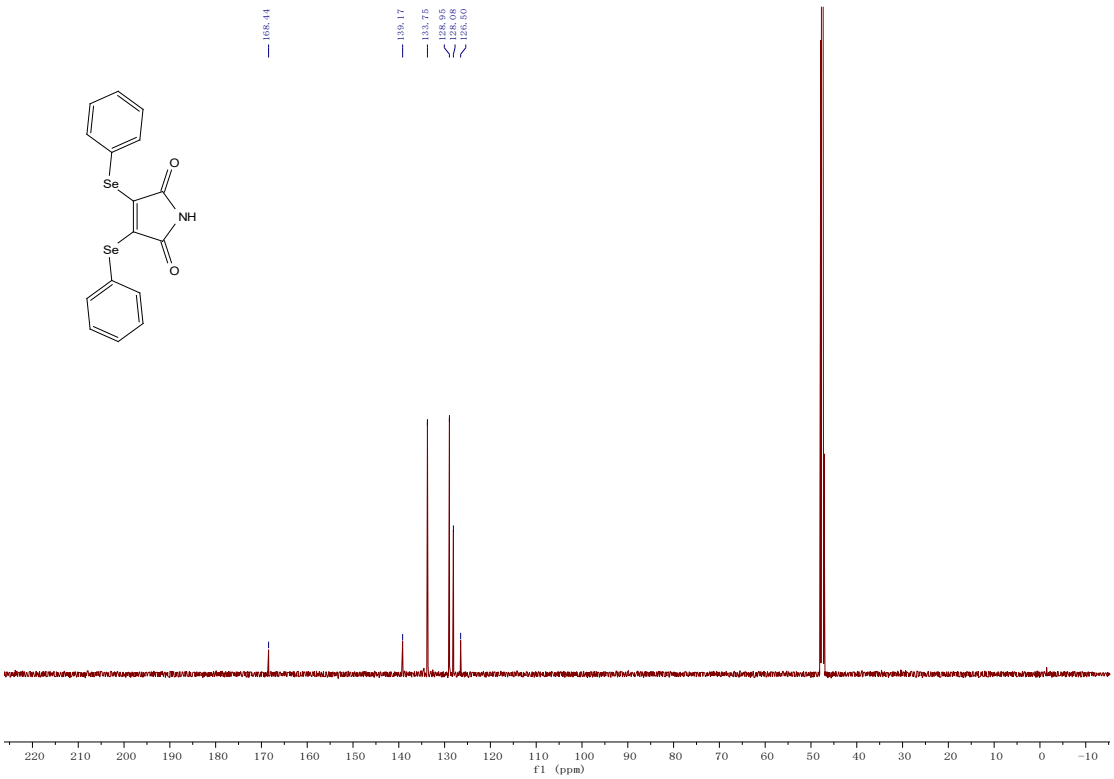
135.65
133.10
132.01
130.87
129.64
128.79
127.58
127.30
125.32
51.47
31.97
22.75
20.67
Se
Cl
O
N
f1 (ppm)

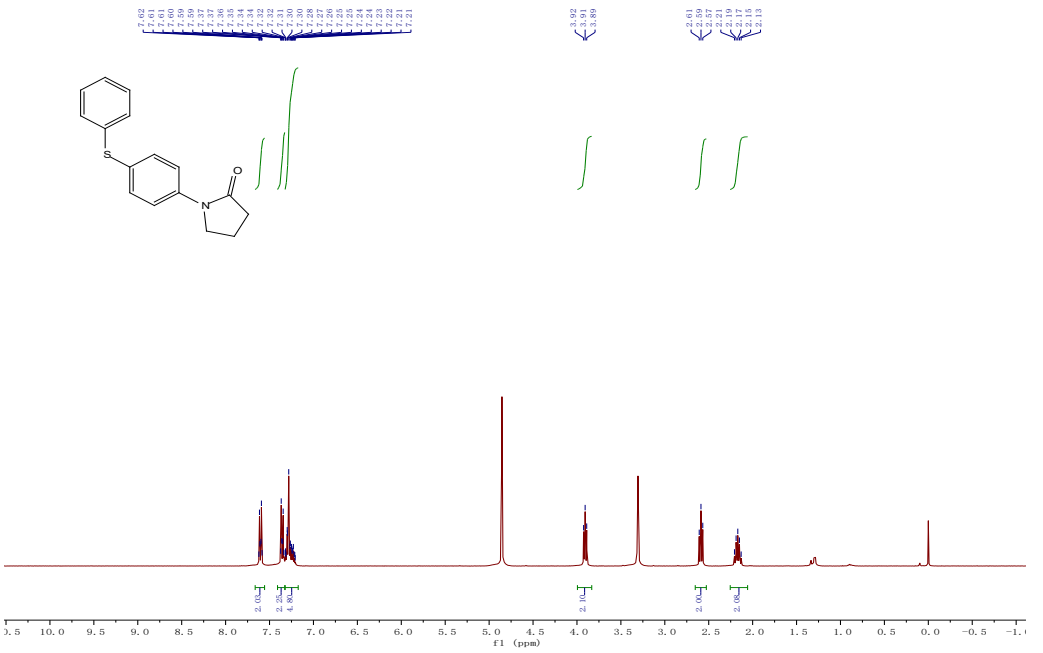

7.48
7.15
7.14
7.11
7.06
7.04
3.94
3.92
3.90
2.61
2.59
2.57
2.46
2.21
2.19
2.17
2.15
2.13
CH3
Se
H3C
N
O
2.08
2.80
1.80
2.00
2.11
5.92
2.08
f1 (ppm)


175.67
144.11
139.92
132.79
128.87
128.20
125.94
125.35
119.52
48.97
32.24
23.35
17.49
CH3
Se
H3C
N
O
f1 (ppm)


7.42
7.42
7.42
7.40
7.40
7.36
7.35
7.34
7.34
7.33
7.32
7.32
7.31
7.31
7.30
7.28
7.28
7.27
7.27
7.25
7.25
7.25
7.24
Se
O
NH
Se
O


4.00
2.27
4.30
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


168.44
139.17
133.75
128.95
128.08
126.50
Se
O
NH
Se
O
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.61
7.61
7.60
7.60
7.59
7.37
7.37
7.36
7.35
7.34
7.34
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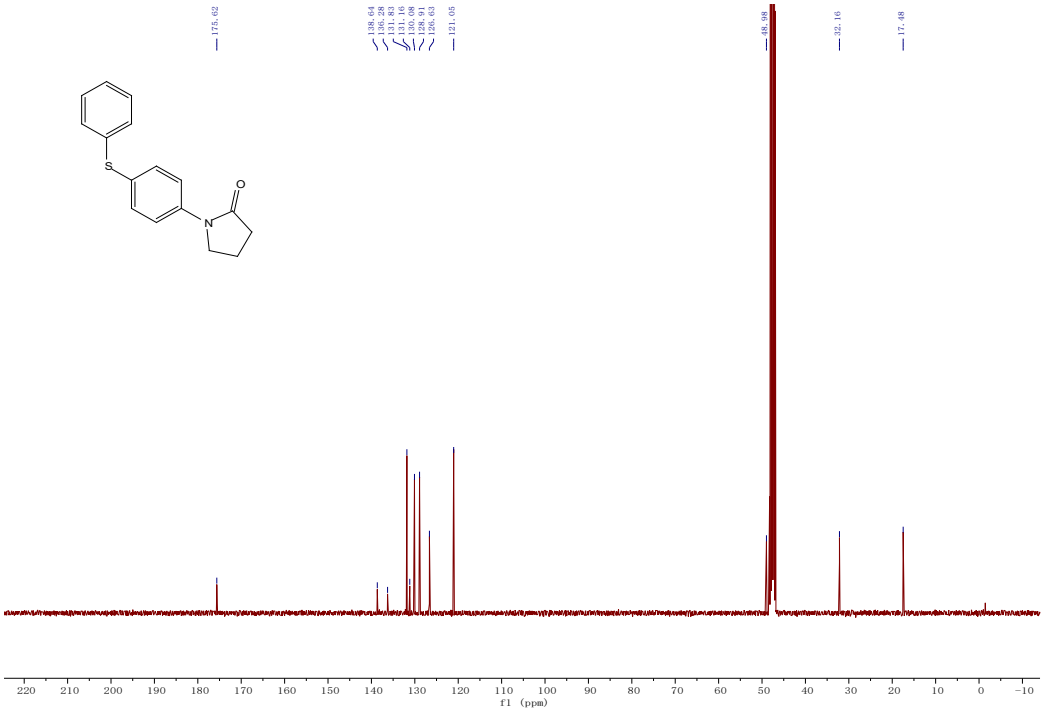
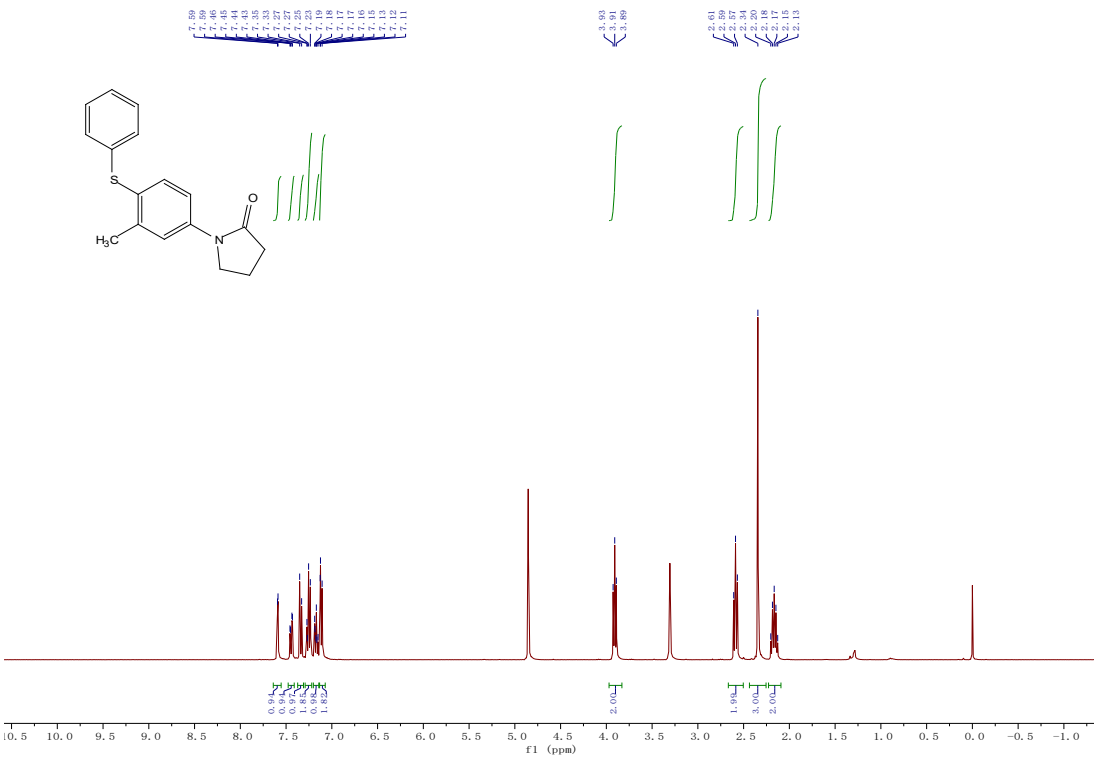
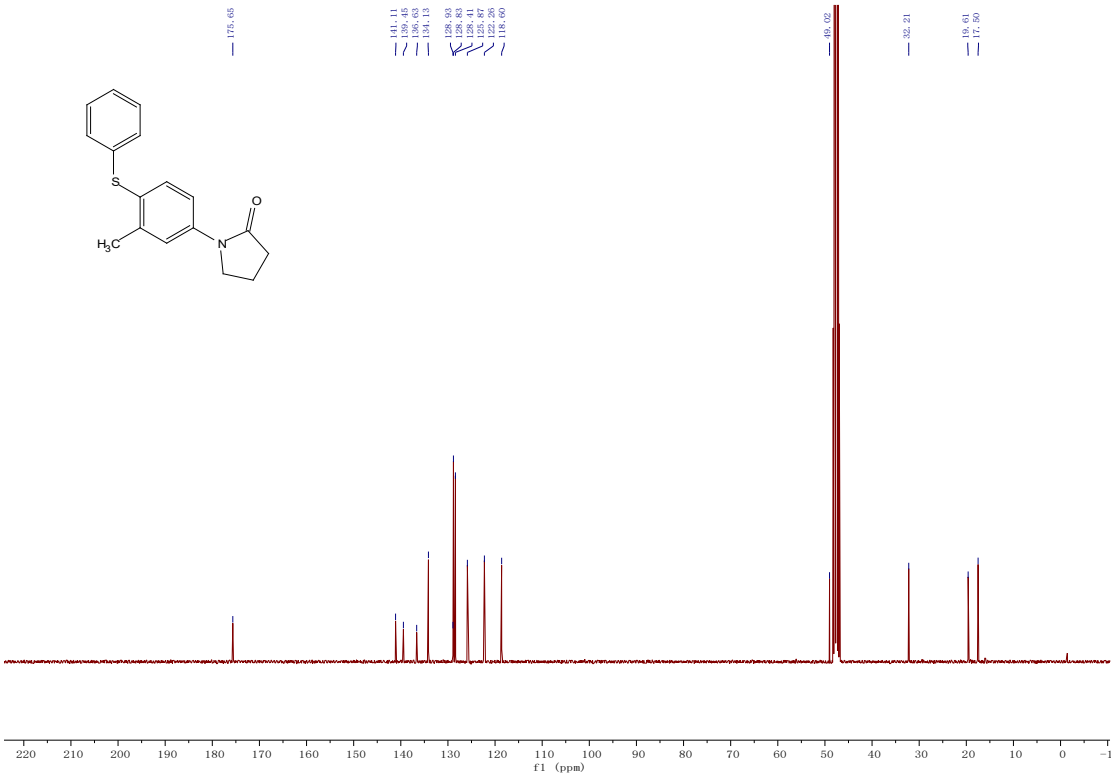
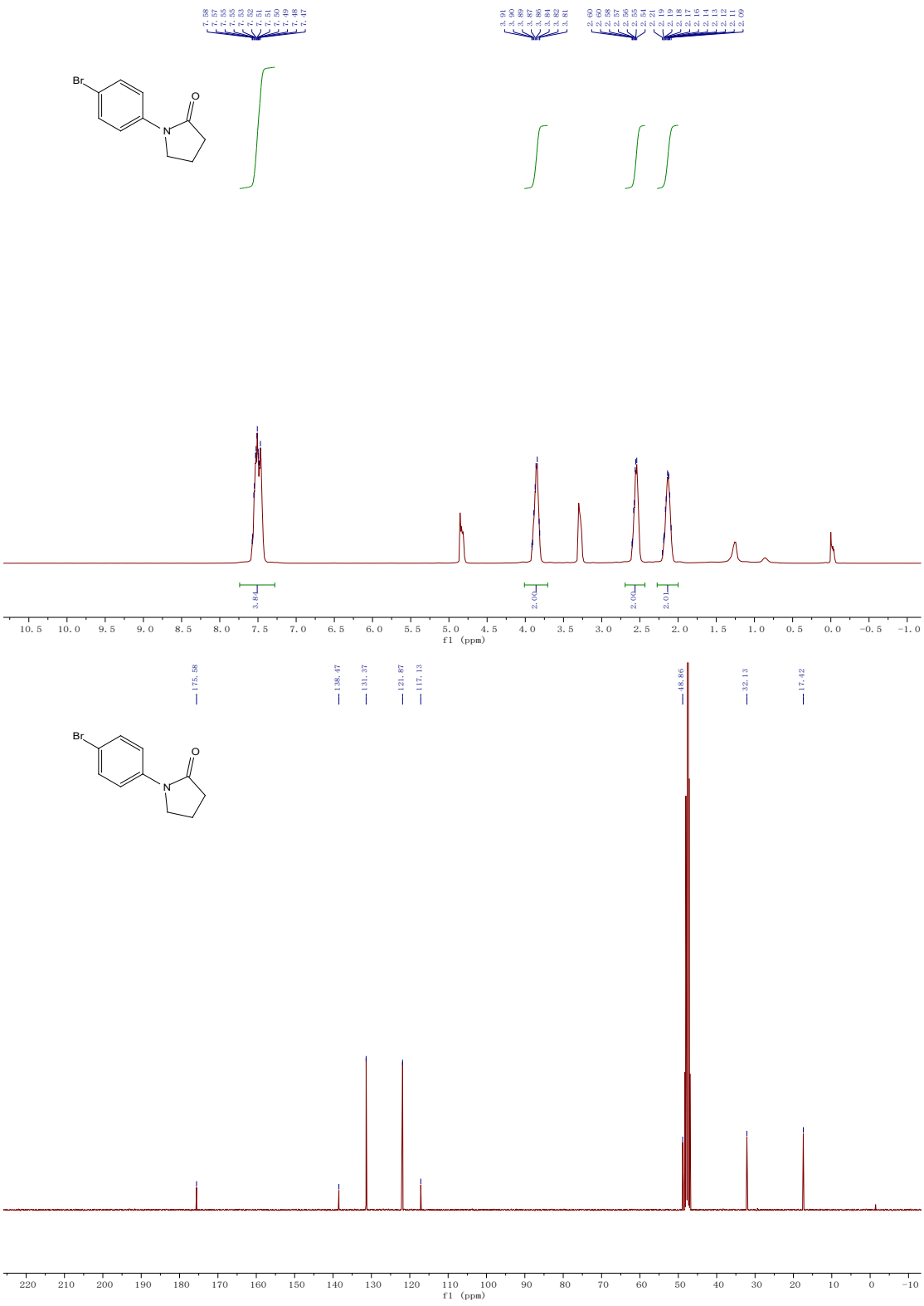
7.31
7.31
7.30
7.30
7.28
7.27
7.26
7.25
7.25
7.24
7.24
7.23
7.22
7.21
7.21
3.92
3.91
3.89
2.61
2.59
2.57
2.21
2.19
2.17
2.15
2.13
S
O
N
2.03
2.25
4.80
2.10
2.00
2.08
f1 (ppm)

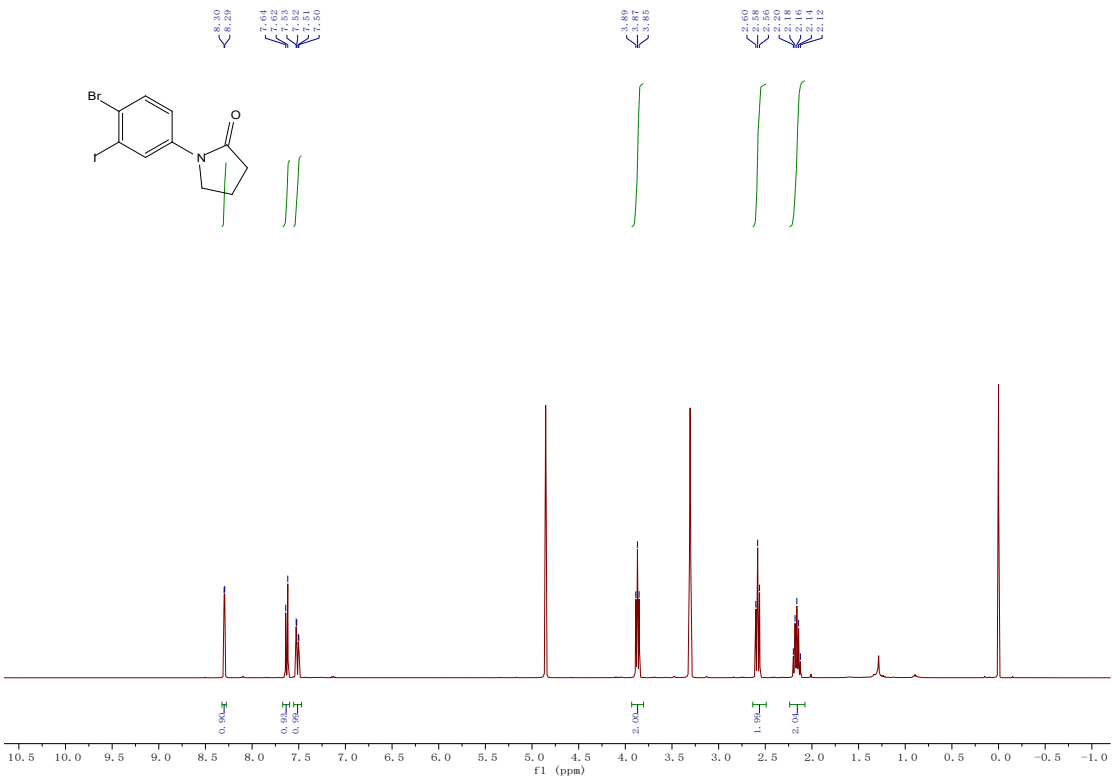

175.62
138.64
136.28
131.83
131.16
130.98
128.91
126.63
121.05
48.98
32.16
17.48
S
O
N
f1 (ppm)

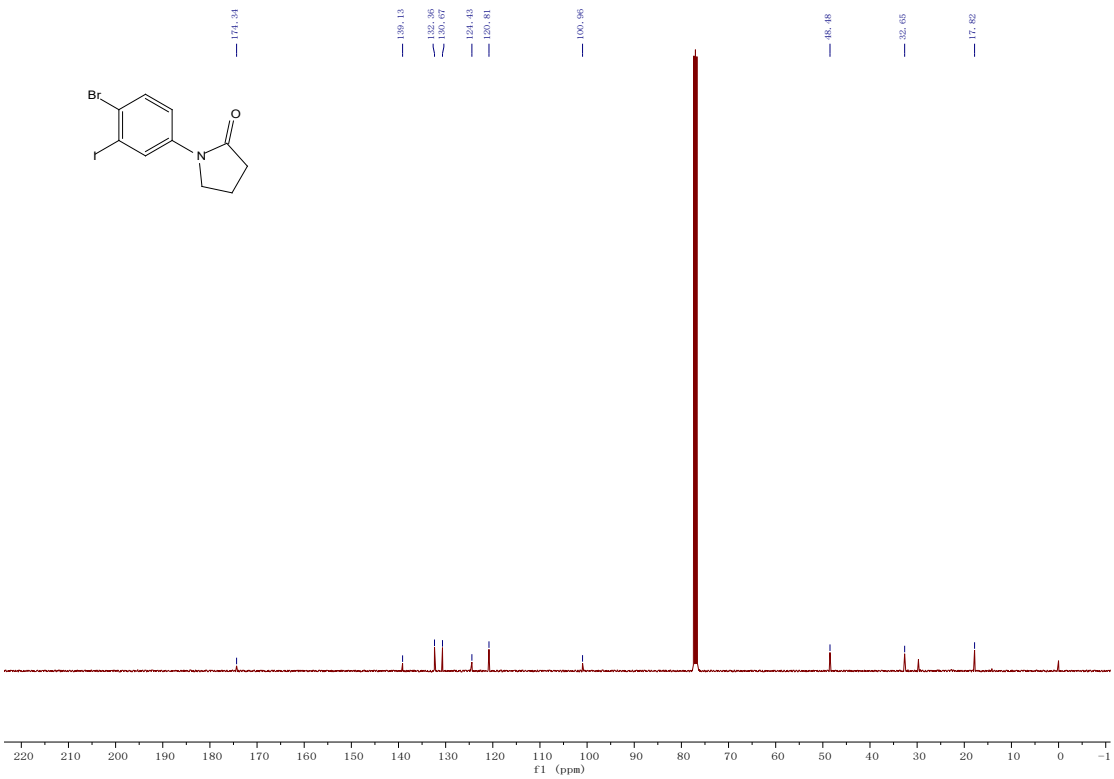

7.59
7.59
7.46
7.46
7.44
7.43
7.35
7.34
7.27
7.25
7.23
7.19
7.18
7.17
7.17
7.17
7.16
7.15
7.13
7.12
7.11
3.93
3.91
3.89
2.61
2.59
2.57
2.34
2.20
2.18
2.17
2.15
2.13
S
O
N
H3C
0.94
0.94
0.97
1.85
0.98
1.82
2.04
1.96
3.04
2.04
f1 (ppm)

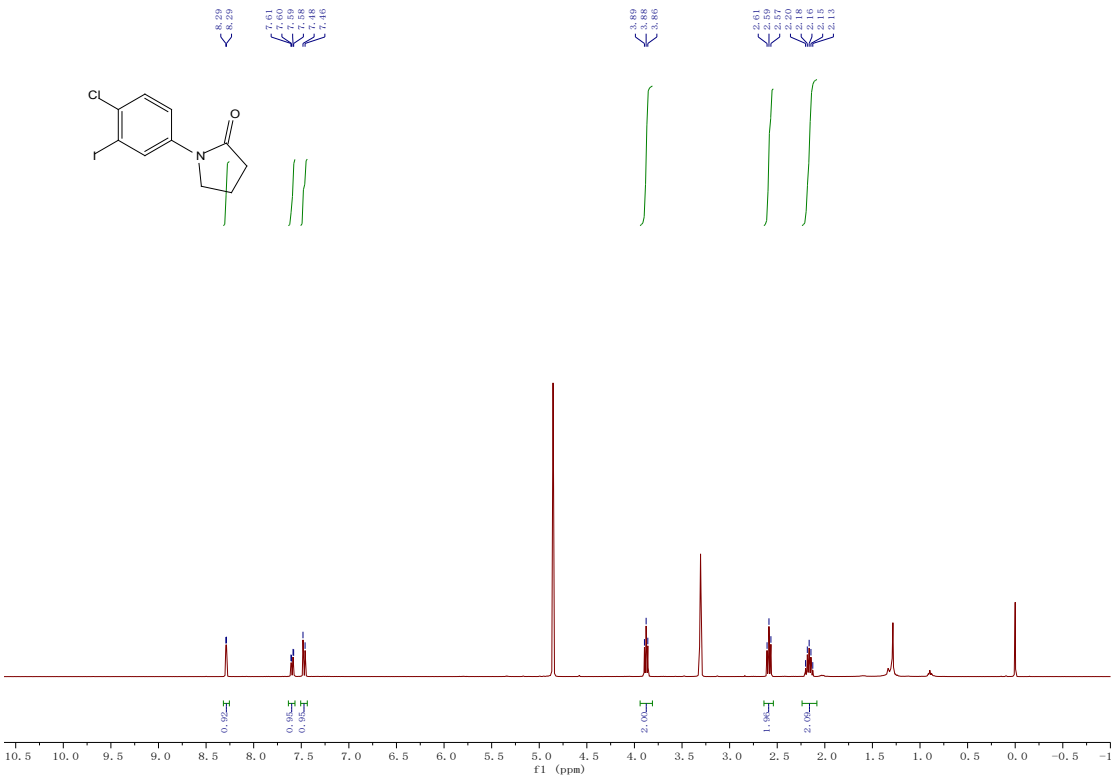

175.65
141.11
139.45
136.63
134.13
128.93
128.83
128.41
125.87
122.98
118.60
49.02
32.21
19.61
17.50
S
O
N
H3C
f1 (ppm)

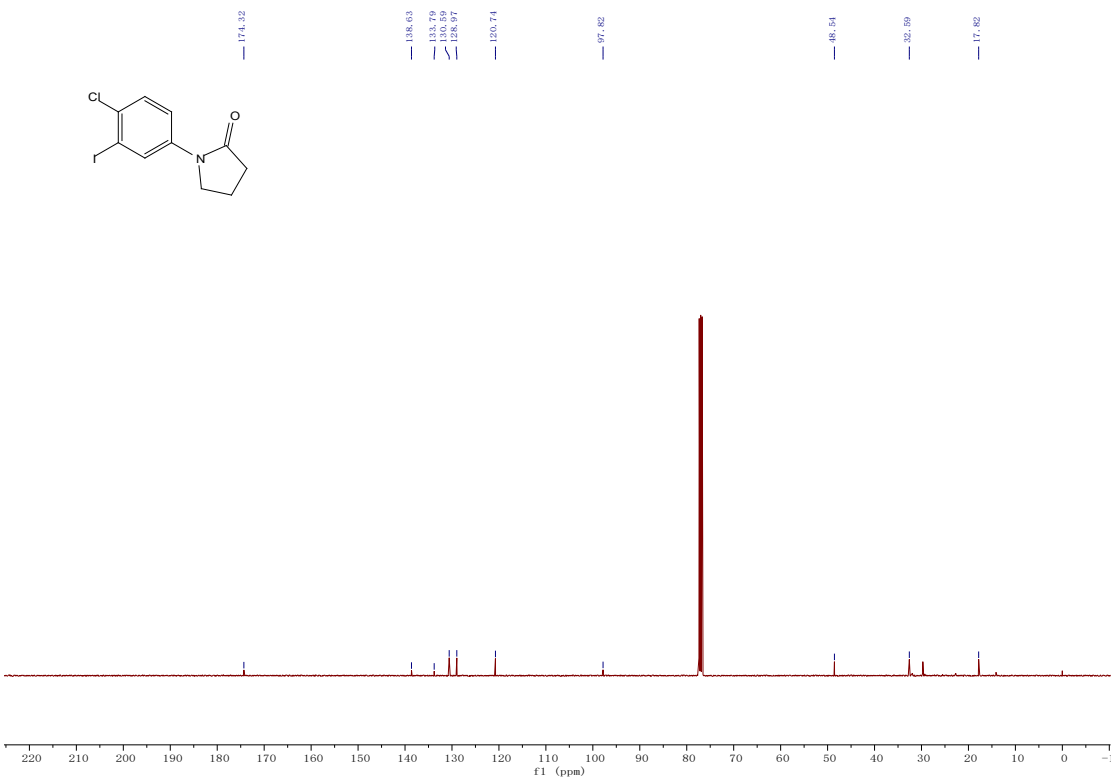
9.3 NMR spectra of compound **5**

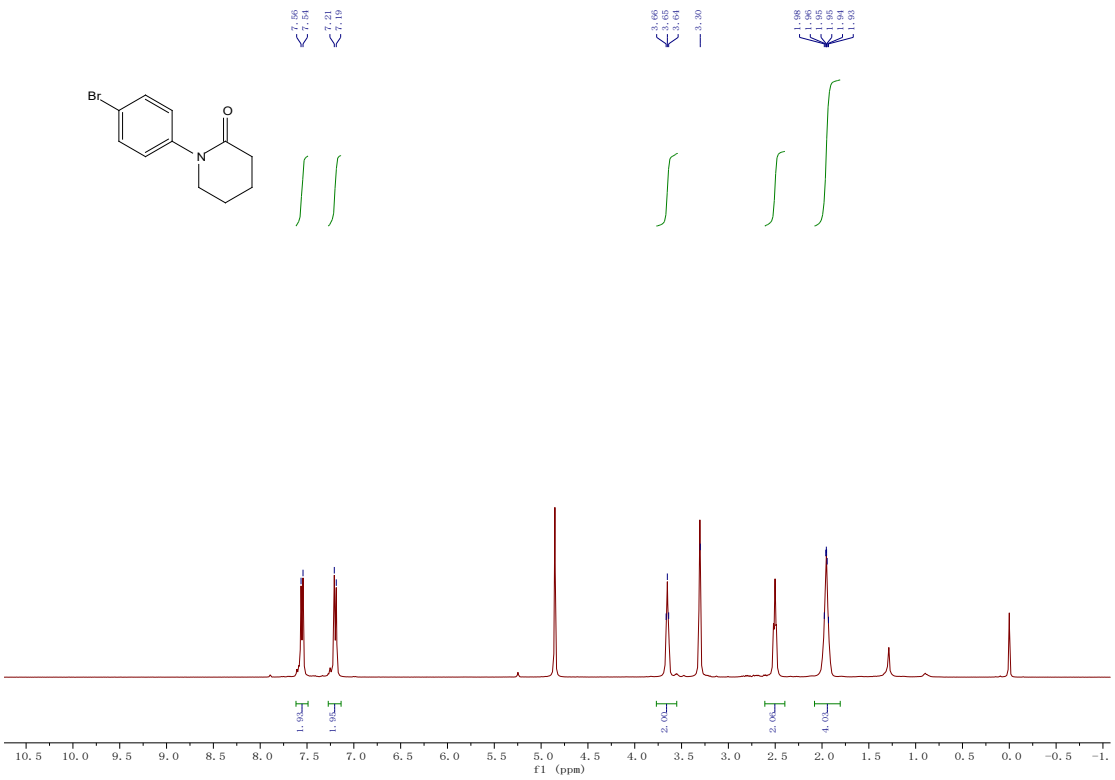


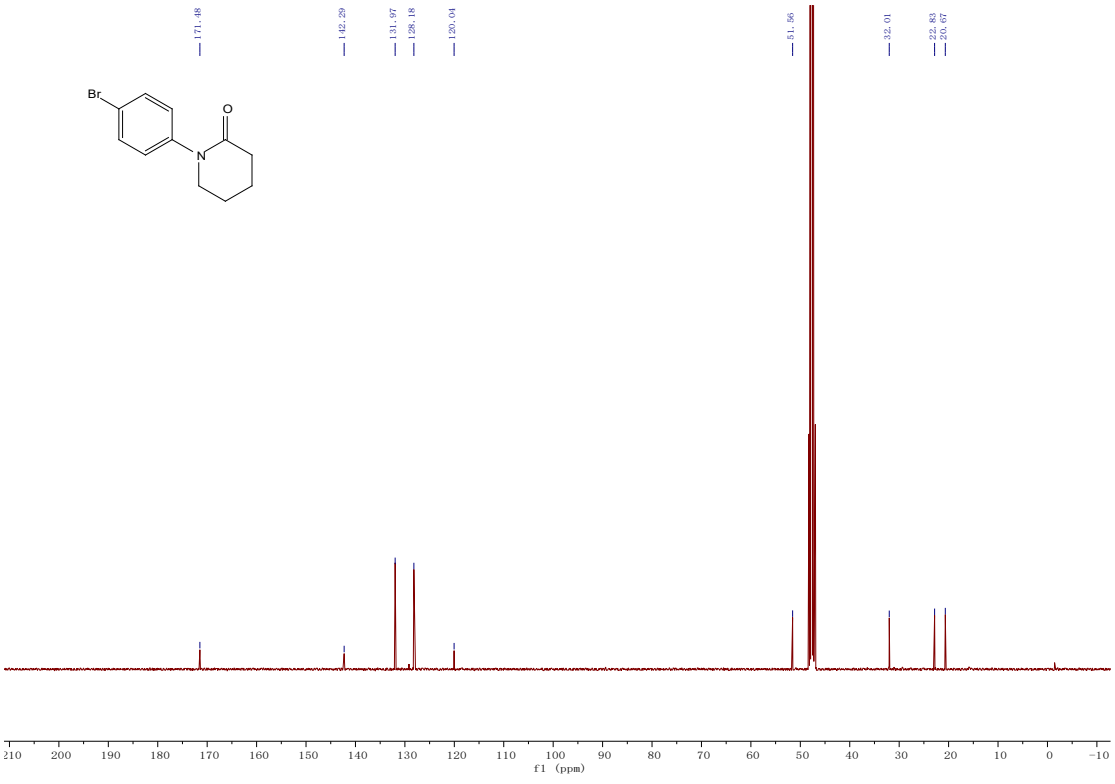

8.30
8.29
7.64
7.62
7.53
7.52
7.51
7.50
3.89
3.87
3.85
2.60
2.58
2.56
2.20
2.18
2.16
2.14
2.12
Br
I
O
N
0.90
0.93
0.98
2.00
1.98
2.04
f1 (ppm)

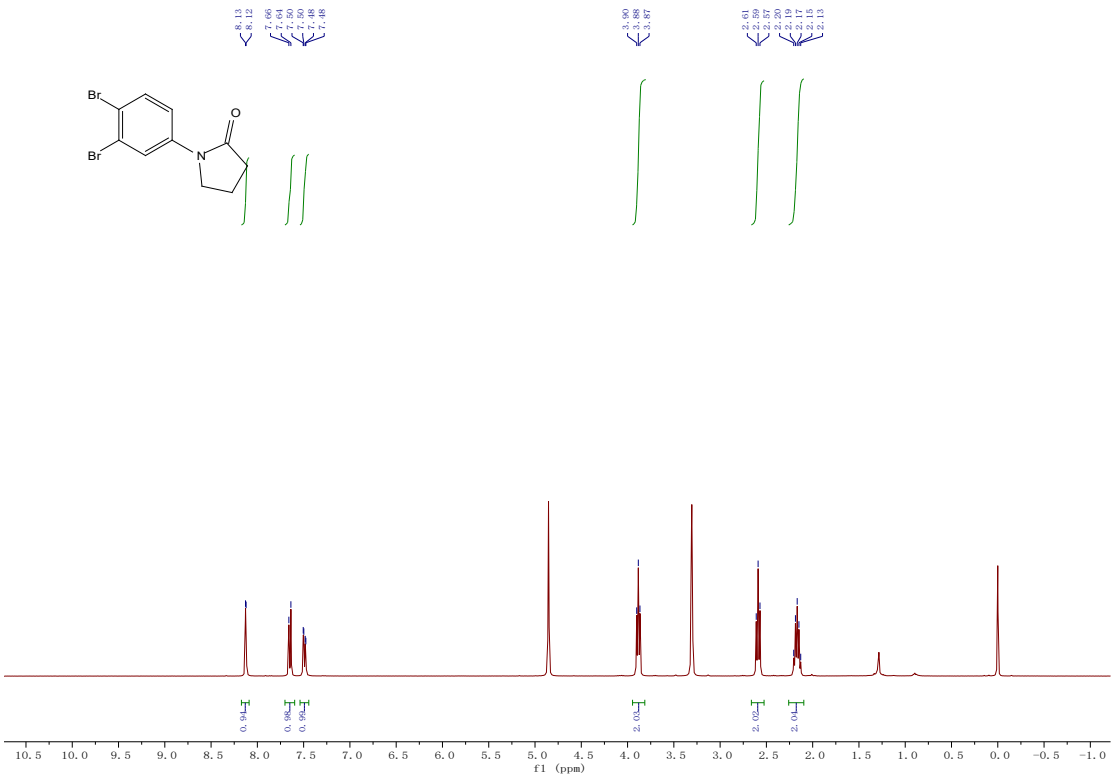

174.34
139.13
132.36
130.67
124.43
120.81
100.96
48.48
32.65
17.82
Br
I
O
N
f1 (ppm)

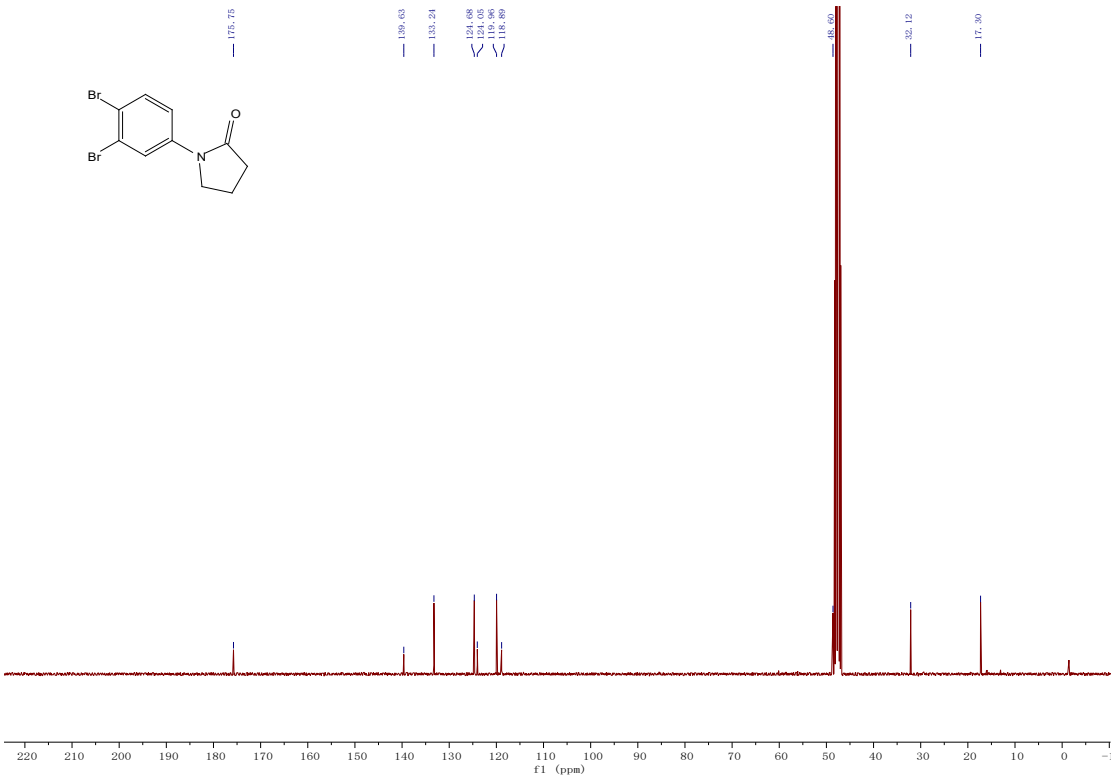

8.29
8.29
7.61
7.60
7.59
7.58
7.48
7.46
3.89
3.88
3.86
2.61
2.59
2.57
2.20
2.18
2.16
2.15
2.13
Cl
I
O
N
0.92
0.94
0.94
2.00
1.96
2.09
f1 (ppm)

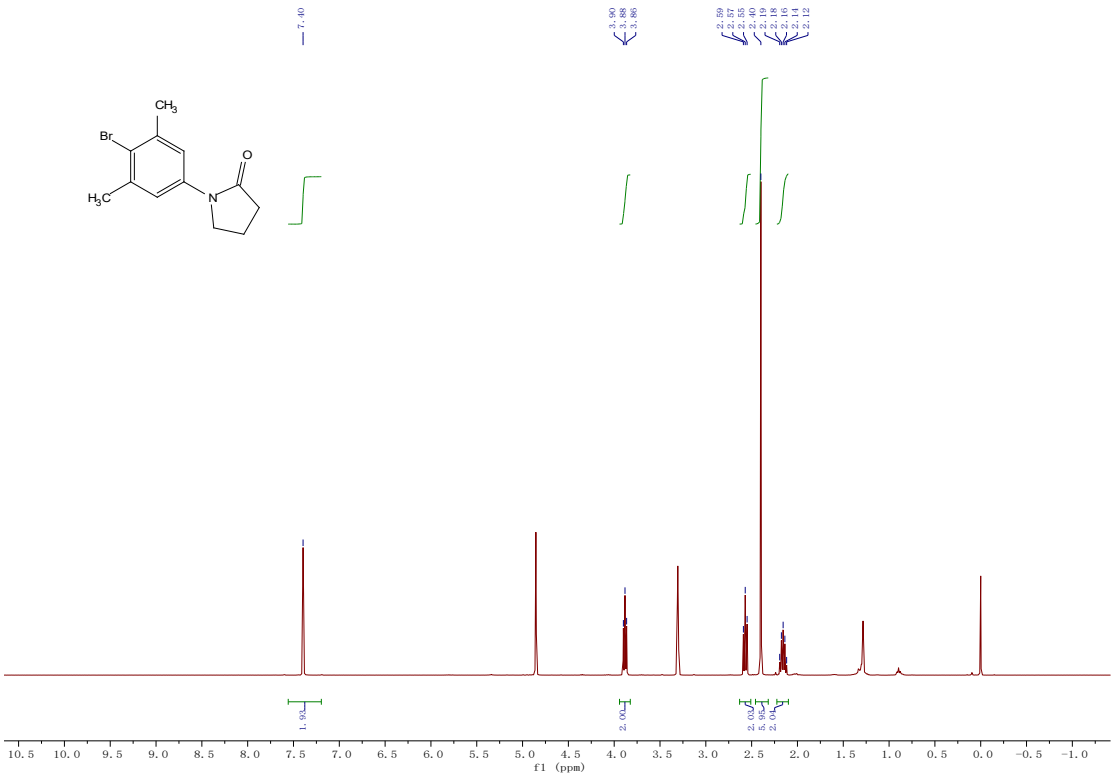

174.32
138.63
133.79
130.59
128.97
120.74
97.82
48.54
32.59
17.82
Cl
I
O
N
f1 (ppm)

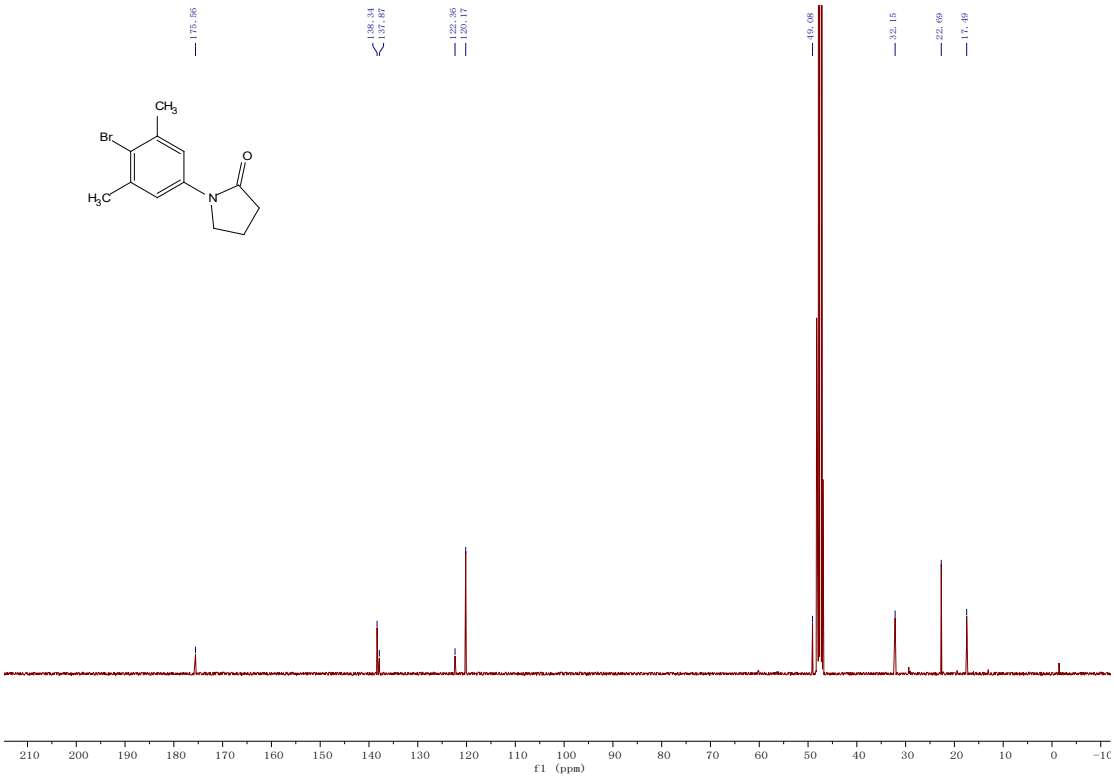

7.86
7.84
7.21
7.19
3.66
3.65
3.64
3.30
1.98
1.96
1.95
1.95
1.94
1.93
Br
O
N
1.90
1.90
2.00
2.00
4.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)

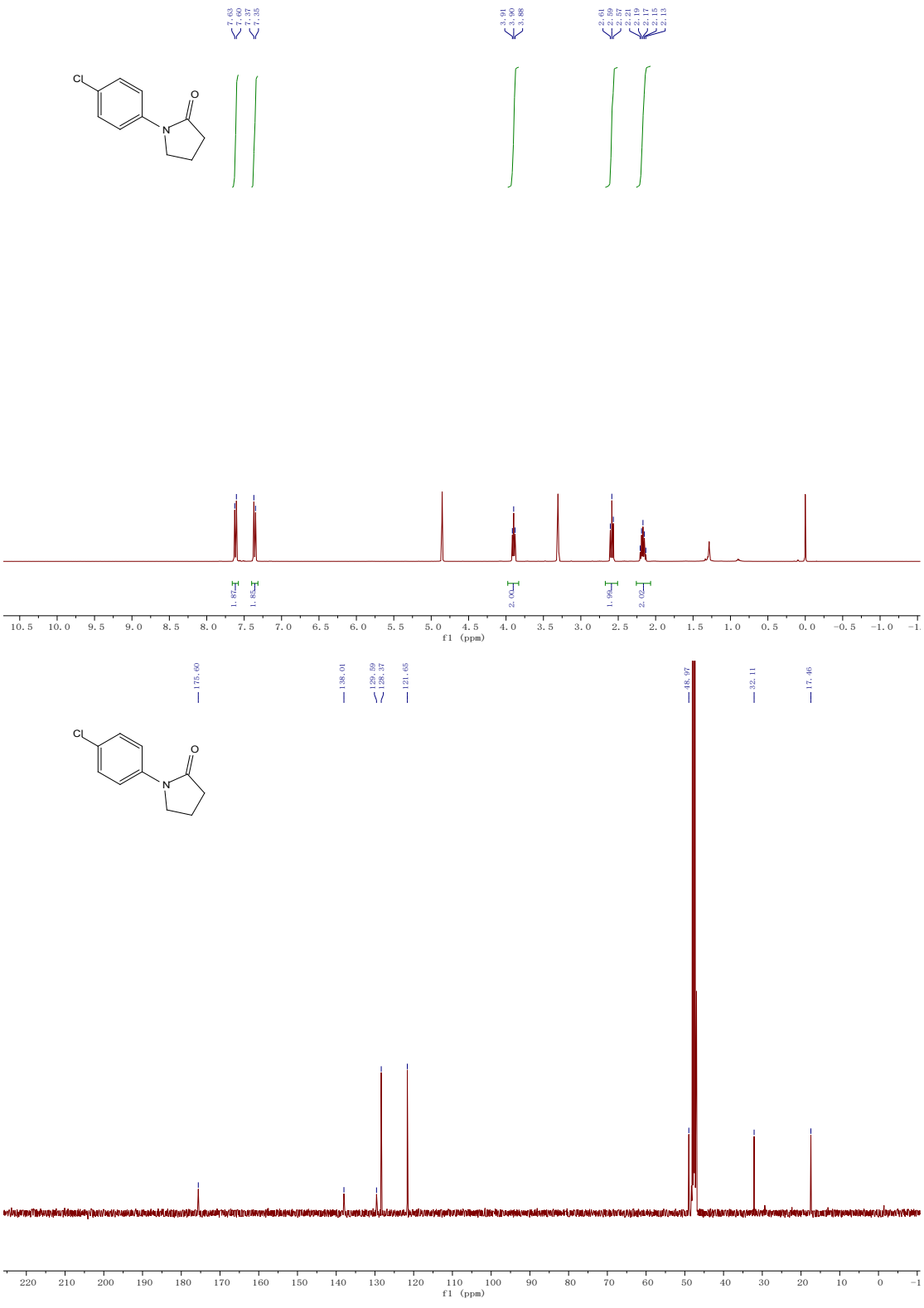

171.48
142.29
131.97
128.18
120.04
51.96
32.01
22.83
20.67
Br
O
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

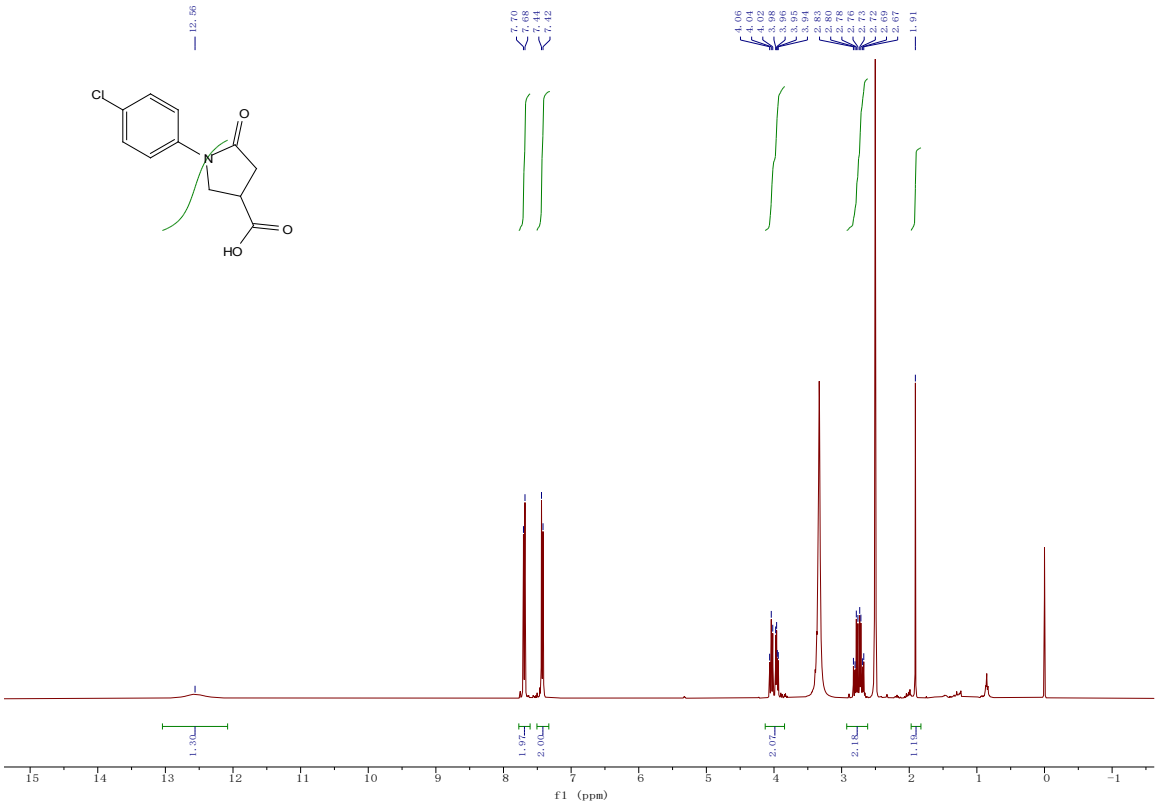

8.13
8.12
7.66
7.64
7.50
7.50
7.48
7.48
3.90
3.88
3.87
2.61
2.59
2.57
2.20
2.19
2.17
2.17
2.15
2.13
Br
Br
O
N
0.94
0.98
0.99
2.03
2.02
2.04
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

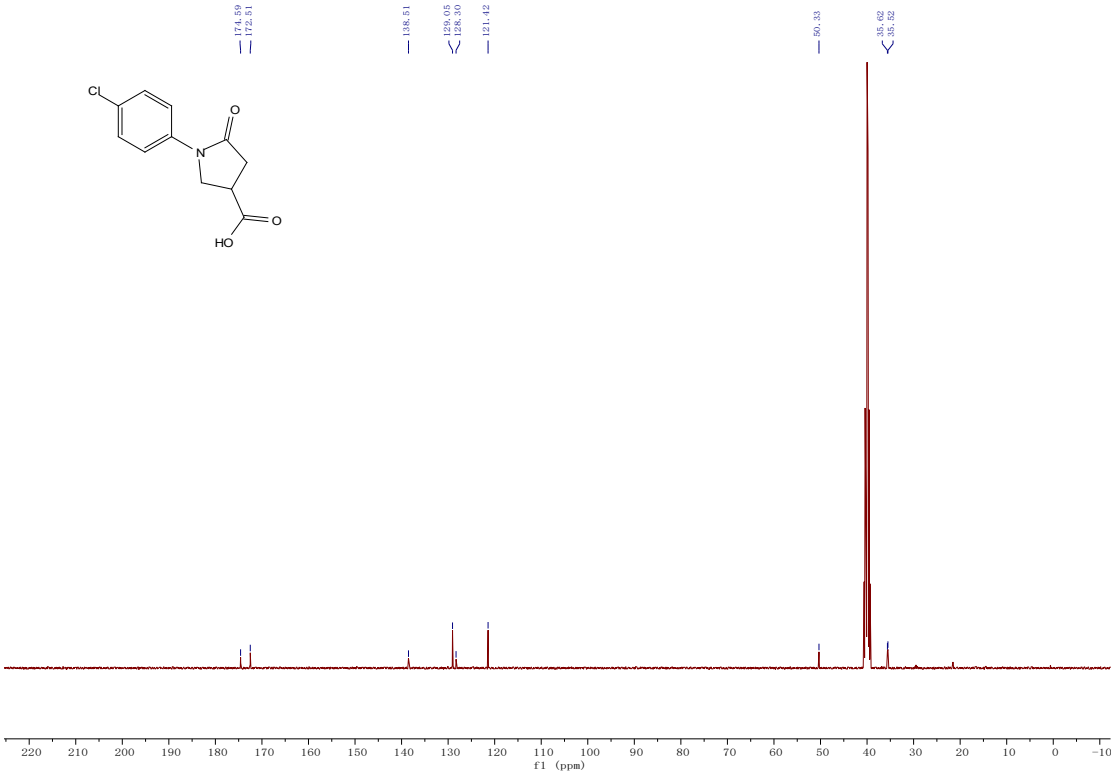

175.75
139.63
133.24
124.68
124.05
119.96
118.89
48.60
32.12
17.30
Br
Br
O
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

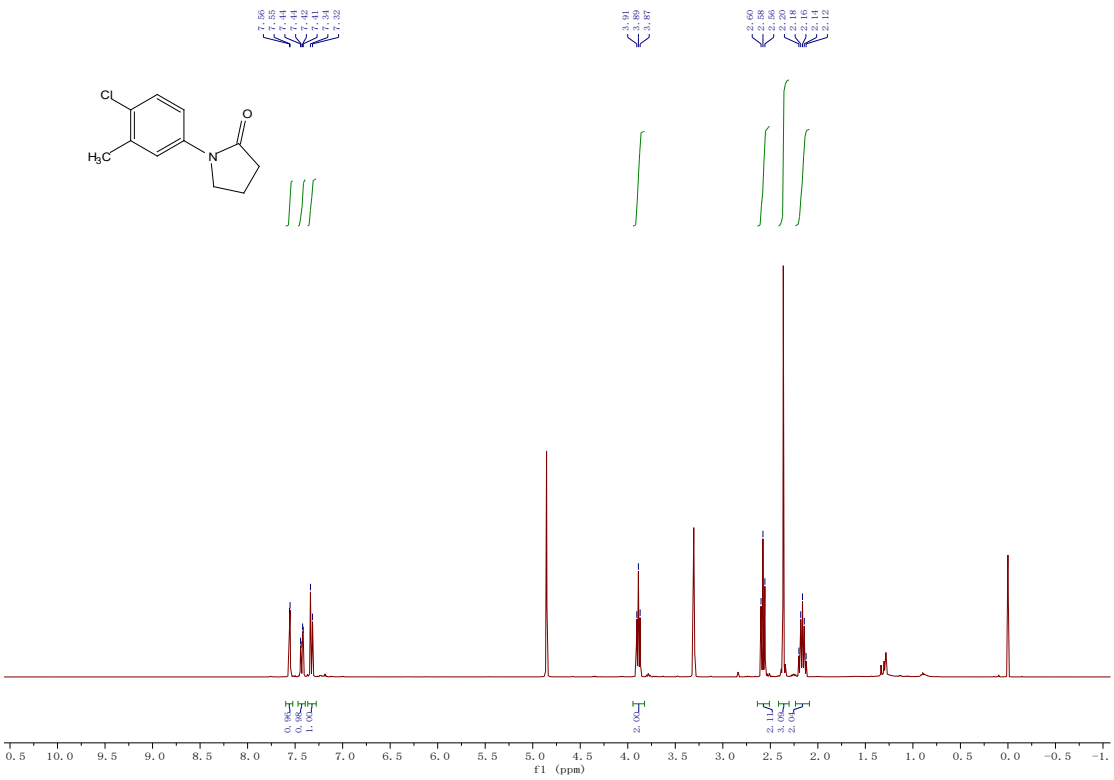

7.40
3.90
3.88
3.86
2.69
2.57
2.55
2.40
2.19
2.18
2.16
2.14
2.12
CH3
Br
H3C
N
O
1.90
2.00
2.03
5.90
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

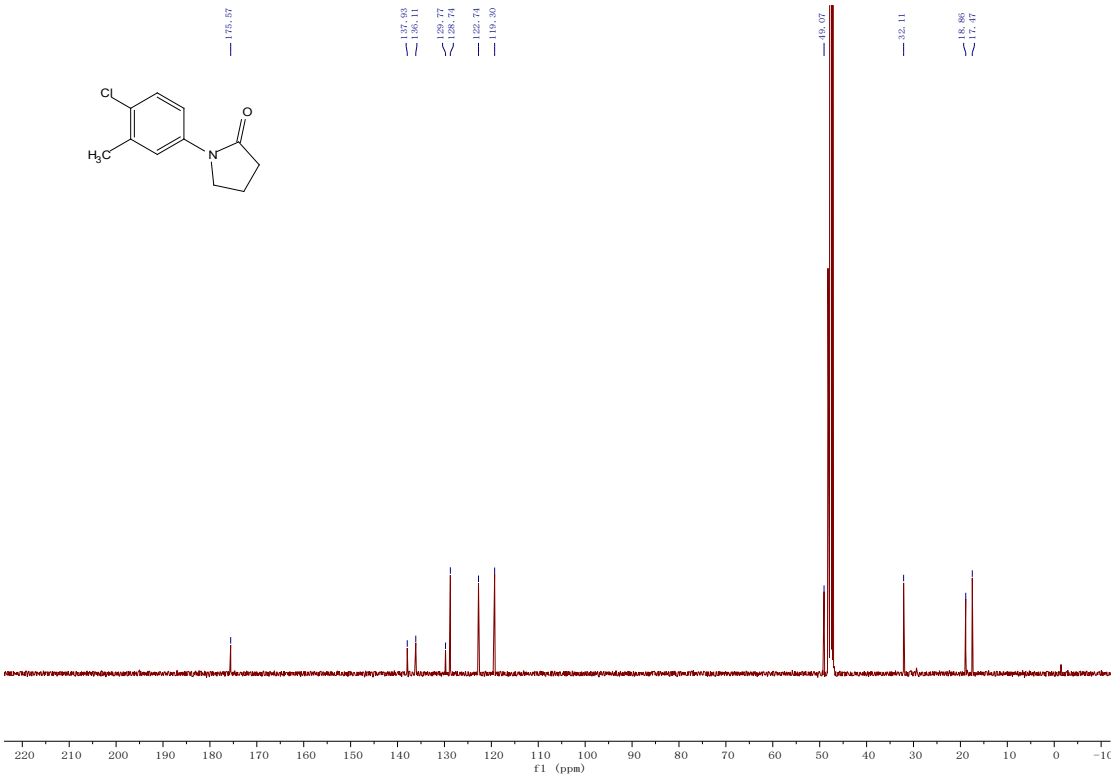

175.56
138.34
137.87
122.36
120.17
49.08
32.15
22.69
17.49
CH3
Br
H3C
N
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.63
7.60
7.37
7.35
3.91
3.90
3.88
2.61
2.59
2.57
2.21
2.19
2.17
2.15
2.13
Cl
O
N
1.87
1.85
2.00
1.99
2.02
f1 (ppm)
175.60
138.01
129.89
128.37
121.65
48.97
32.11
17.46
Cl
O
N
f1 (ppm)


12.56
7.70
7.68
7.44
7.42
4.06
4.04
4.02
3.98
3.96
3.95
3.94
2.83
2.80
2.78
2.76
2.73
2.72
2.69
2.67
1.91
Cl
O
N
O
HO
1.30
1.97
2.00
2.07
2.18
1.19
f1 (ppm)


174.59
172.51
138.51
129.05
128.30
121.42
60.33
35.62
35.52
Cl
O
N
O
HO
f1 (ppm)


7.56
7.55
7.44
7.44
7.42
7.41
7.34
7.32
3.91
3.89
3.87
2.60
2.58
2.56
2.20
2.18
2.16
2.14
2.12
Cl
O
H3C
N
0.96
0.98
1.00
2.00
2.11
3.08
2.04
f1 (ppm)


175.57
137.93
136.11
129.77
128.74
122.74
119.30
49.07
32.11
18.86
17.47
Cl
O
H3C
N
f1 (ppm)

10. References

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