Supporting Information for

Chemoselective (Hetero)Arene Electroreduction Enabled by Rapid Alternating Polarity

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Table of Contents

General experimental

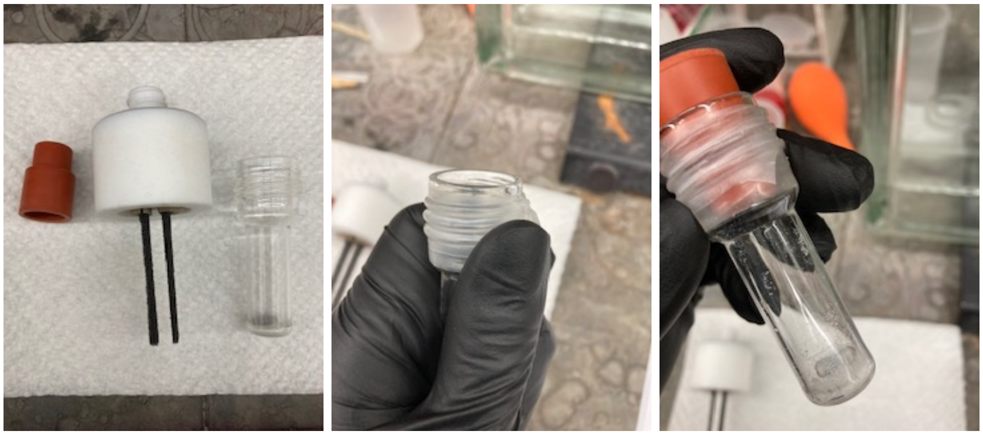
Tetrahydrofuran (THF), *N*,*N*-dimethylformamide (DMF), toluene, acetonitrile (CH_3CN), and dichloromethane (CH_2Cl_2) were obtained by passing the previously degassed solvents through an activated alumina column. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous material, unless otherwise stated. Reactions were monitored by LC/MS, GC/MS and thin layer chromatography (TLC). TLC was performed using 0.25 mm E. Merck silica plates (60F-254), using short-wave UV light for visualization, and phosphomolybdic acid and $Ce(SO_4)_2$, acidic ethanolic anisaldehyde, or $KMnO_4$ and heat as developing agents. NMR spectra were recorded on Bruker DRX-600, DRX-500, and AMX-400 instruments and are calibrated using residual undeuterated solvent ($CHCl_3$ at 7.26 ppm ^{1}H NMR, 77.16 ppm ^{13}C NMR; CH_3OH at 3.31 ppm ^{1}H NMR, 49.0 ppm ^{13}C NMR; DMSO at 2.5 ppm ^{1}H NMR, 39.5 ppm ^{13}C NMR). The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Column chromatography was performed using E. Merck silica (60, particle size 0.043–0.063 mm), and pTLC was performed on Merck silica plates (60F-254). High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer by electrospray ionization time of flight reflectron experiments. Gas chromatography-mass spectrometry (GC/MS) were recorded on an Agilent 5975 MSD Series spectrometer.

General procedures for (hetero)arene electroreduction

To an ElectraSyn reaction vial charged with an aromatic substrate (0.1 mmol), tetramethylammonium tetrafluoroborate ($\mathrm{Me_4N{\bullet}BF_4}$, 40 mg, 0.25 mmol) was added 1.5 mL of tetrahydrofuran (THF) and 1.5 mL of ethanol (EtOH) followed by addition of dimethyl sulfide (DMS, 22 μL, 0.3 mmol). After the resulting mixture was purged with argon balloon for roughly 10 seconds, an ElectraSyn vial cap equipped with anode (RVC) and cathode (RVC) was inserted into it. The mixture was electrolyzed at 0 °C or room temperature under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 10-20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with water, then brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. The resulting crude mixture was purified by preparative thin-layer chromatography (pTLC) or silica gel column chromatography. See the individual entries below for detailed conditions.

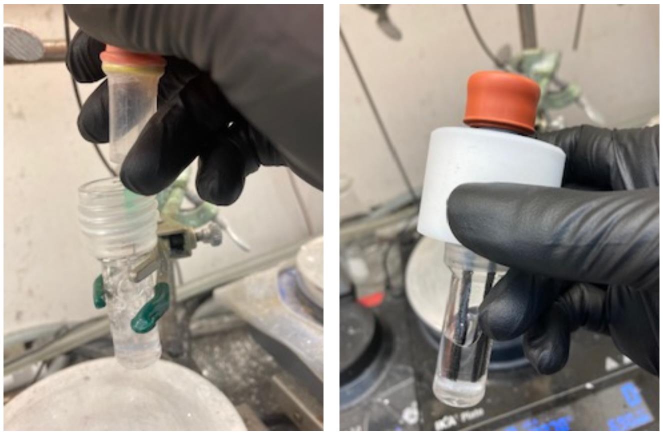
Note: It was found that solubility of $\mathrm{Me_4N{\bullet}BF_4}$ varies depending on a supplier. In a case 20 mA is unable to achieve, $\mathrm{Me_4N{\bullet}OPiv}$ (in situ generation) can be used as an alternative electrolyte. Additionally, THF/MeOH (1/2.5) gives better conductivity with $\mathrm{Me_4N{\bullet}BF_4}$, and this solvent system is effective for the reduction of heteroarene substrates. Detailed procedures for these modified reaction conditions are provided in FAQ in this supporting information.

Graphical guide for rAP arene electroreduction (reduction of compound 1)

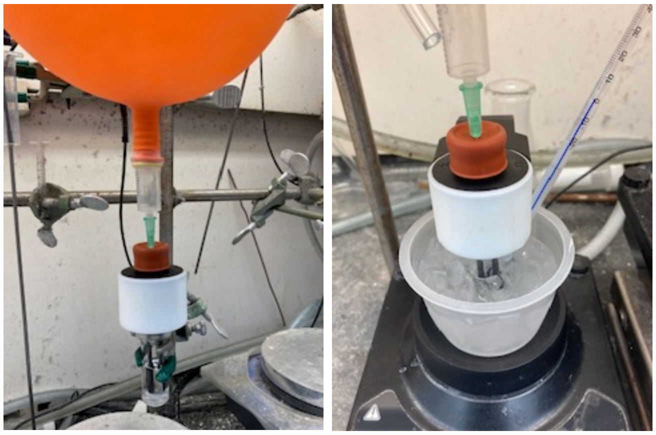


(Left) Septum, IKA ElectraSyn cap equipped with RVC electrodes and clean 5 mL ElectraSyn vial with a stir bar. **(Center)** Parafilm is wrapped a few times around Electrasyn vial to ensure a good seal. **(Right)** The vial is charged with $Me_4N{\bullet}BF_4$ (40 mg, 0.25 mmol) and substrate (14 mg, 0.1 mmol). No precaution to air and moisture is needed while charging the vial.

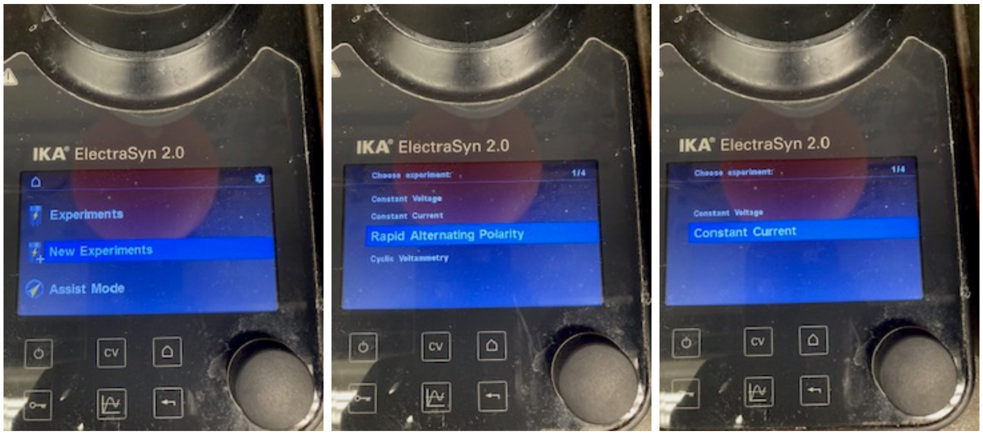
(Left) To the charged vial, THF (1.5 mL) is added. **(Center)** EtOH (1.5 mL) is added. **(Right)** Addition of DMS (22 μL, 0.3 mmol).



(Left) Be sure to bubble Ar through solvent as depicted for roughly 10 seconds. **(Right)** IKA ElectraSyn cap fitted with electrodes and septum is assembled together with the ElectraSyn vial. The septum is placed tightly over the top of the cap and folded over itself. (Ensure that electrodes are immersed in solvent.)

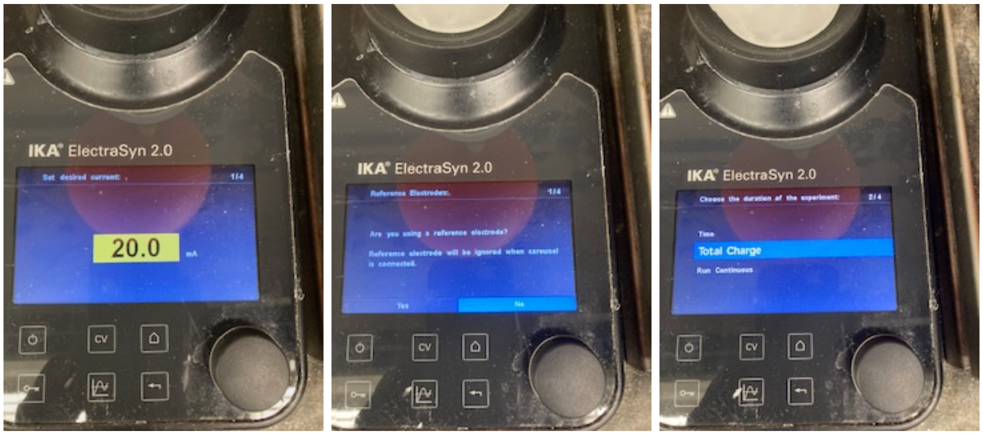


(Left) An argon balloon is attached. **(Right)** Entire reaction mixture prior to electrolysis in an ice bath (Ice bath is needed only when the reaction is performed at 0 ºC).



(Left) Select "*New Experiment*". **(Center)** Select "*Rapid Alternating Polarity*". **(Right)** Select "*Constant Current*". Permission for the usage of ElectraSyn2.0 for the pictures is granted by IKA.

Note: Software update is needed if there is no "Rapid Alternating Polarity" on the screen. Please visit https://www.ika.com/en/Services/Firmware-update-csrvf-8.html and follow the instruction.

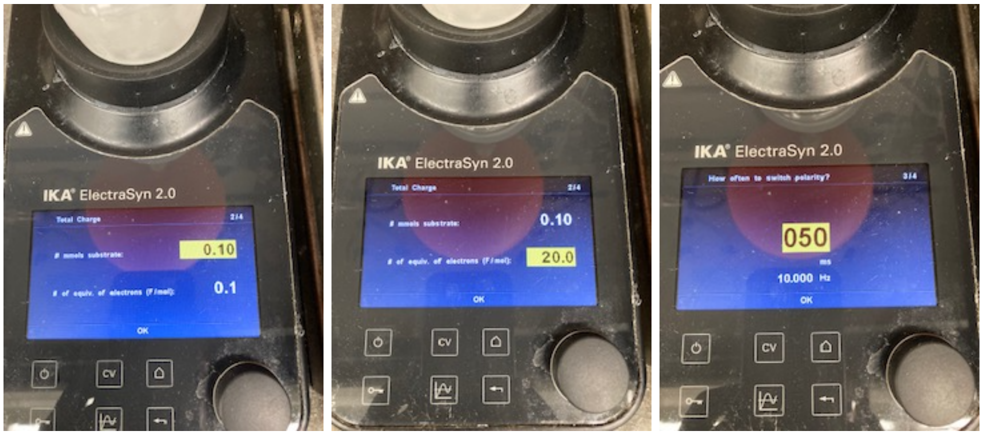


Set desired current: 1/4
20.0 mA

Reference Electrodes: 1/4
Are you using a reference electrode?
Reference electrode will be ignored when carousel is connected.

Choose the duration of the experiment: 2/4
Time
Total Charge
Run Continuous

(Left) Set desired current. **(Center)** Reference electrode is not necessary. **(Right)** Select "*Total Charge*". Permission for the usage of ElectraSyn2.0 for the pictures is granted by IKA.

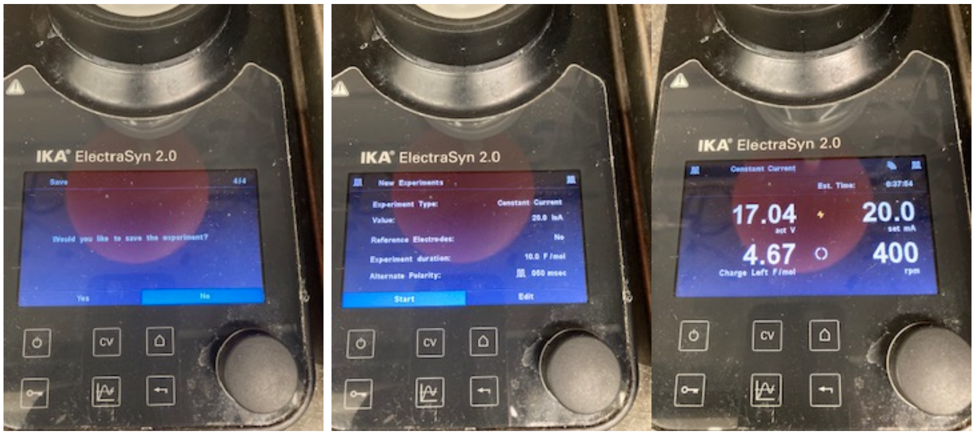


Total Charge 2/4
mmols substrate: 0.10
of equiv. of electrons (F/mol): 0.1

Total Charge 2/4
mmols substrate: 0.10
of equiv. of electrons (F/mol): 20.0

How often to switch polarity? 3/4
050 ms
10.000 Hz

(Left) Set the amount of substrate present (mmol) **(Center)** Set the electron amount (F/mol). **(Right)** Set frequency of alternating polarity. Permission for the usage of ElectraSyn2.0 for the pictures is granted by IKA.

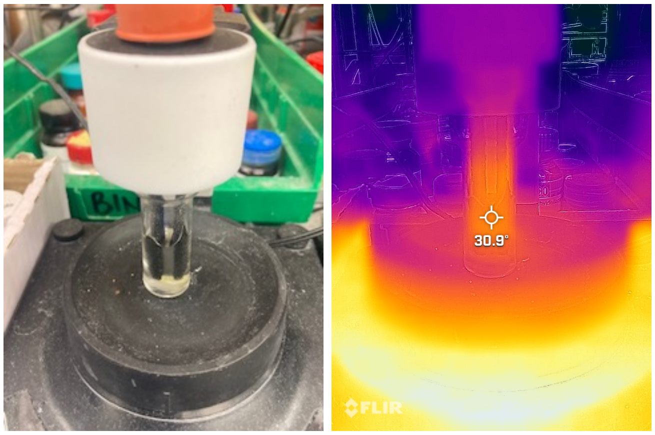


Save 4/4
Would you like to save the experiment?

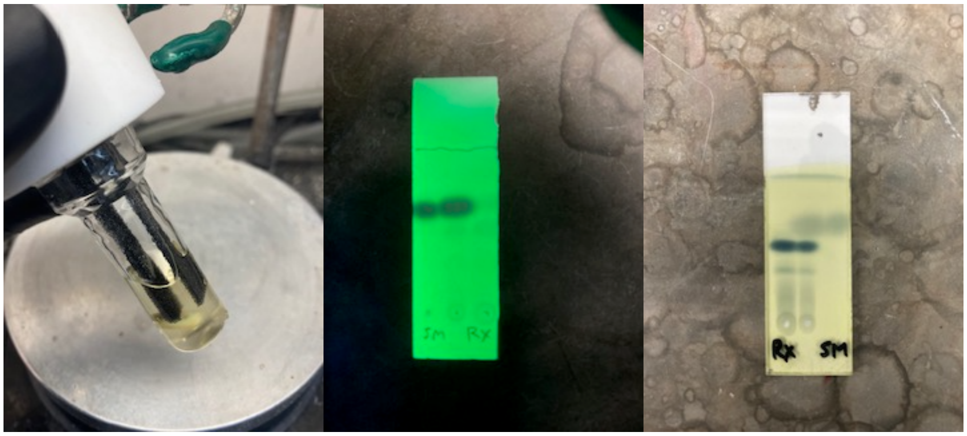
New Experiments
Experiment Type: Constant Current
Value: 20.0 mA
Reference Electrodes: No
Experiment duration: 10.0 F/mol
Alternate Polarity: 050 msec

Constant Current
Est. Time: 0:37:54
17.04 act V
20.0 set mA
4.67 Charge Left F/mol
400 rpm

(Left) Choose to save the experiment settings (optional). **(Center)** Confirm all the parameters and select "*Start*" if they look good. **(Right)** The home screen will display actual reaction voltage, rate of stirring, charge remaining, time of reaction, and the set current. Permission for the usage of ElectraSyn2.0 for the pictures is granted by IKA.



(Left and Right) Reaction temperature when the reaction was conducted without any cooling operation (FLIR ONE Gen 3 – iOS -Thermal Imaging Camera was used).

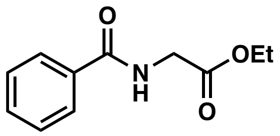


(Left) After the reaction. **(Center)** Crude TLC (Hexane/AcOEt = 5:1) under UV light (254 nm). **(Right)** Crude TLC (Hexane/AcOEt = 5:1) stained with PMA.

Synthesis of starting materials

Starting materials **1, 34**, **36** and 1-naphthonitrile (for **28**), were purchased and used without further purification.

Compound 3



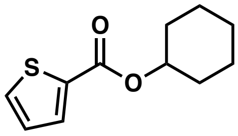
To a mixture of ethyl glycinate hydrochloride (1.0 g, 7.2 mmol), triethylamine (2.2 g, 21.5 mmol) and dichloromethane (15 mL) was added benzoyl chloride (1.0 g, 7.2 mmol) at 0 °C, and the reaction mixture was stirred at room temperature. After 2 h, the reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 2:1) to afford the desired product in 88% yield (1.3 g) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84 – 7.79 (m, 2H), 7.54 – 7.50 (m, 1H), 7.47 – 7.42 (m, 2H), 6.66 (s, 1H), 4.30 – 4.20 (m, 4H), 1.32 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 170.23, 167.52, 133.92, 131.94, 128.77, 127.20, 61.83, 42.05, 14.31.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 208.0974; Found 208.0977.

Compound 5s



To a mixture of 2-thiophenecarboxylic acid (300 mg, 2.34 mmol) and dichloromethane (3 mL) were added oxalyl chloride (380 mg, 3.04 mmol) and dimethylformamide (2 drops) at 0 °C, and the reaction mixture was stirred at room temperature. After 1 h, the solvent and remaining oxalyl chloride were removed, and the residue was dissolved in dichloromethane (3.0 mL). To the reaction mixture were added cyclohexanol (276 mg, 2.88 mmol), 4-dimethylaminopyridine (28 mg, 0.23 mmol) and triethylamine (349 mg, 3.51 mmol) in 1 mL of dichloromethane at 0 °C, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 20:1 to 10:1) to afford the desired product in 84% yield (406 mg) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.79 (dd, *J* = 3.7, 1.3 Hz, 1H), 7.53 (dd, *J* = 4.9, 1.3 Hz, 1H), 7.09 (dd, *J* = 5.0, 3.7 Hz, 1H), 5.01-4.97 (m, 1H), 1.98 – 1.88 (m, 2H), 1.79-1.75 (m, 2H), 1.63 – 1.51 (m, 3H), 1.47-1.40 (m, 2H), 1.37 – 1.31 (m, 1H).

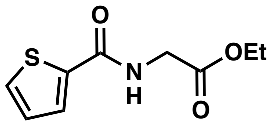
^{13}C NMR (151 MHz, CDCl$_3$) δ 161.86, 134.92, 133.18, 132.10, 127.76, 73.54, 31.75, 25.57, 23.76.

HRMS (ESI-TOF, m/z): Not found.

GC/MS (EI): 207 (7%), 129 (93%), 111 (100%).

The ^{1}H and ^{13}C NMR were consistent with the reported spectral data. *(1)*

Compound 6s



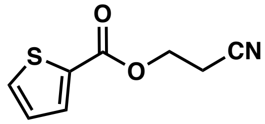
To a mixture of 2-thiophenecarboxylic acid (300 mg, 2.34 mmol), ethyl glycinate hydrochloride (392 mg, 2.80 mmol), 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (HATU, 978 mg, 2.57 mmol) and dimethylformamide (4.0 mL) was added triethylamine (592 mg, 5.85 mmol) at 0 °C, and the reaction mixture was stirred at room temperature. After 3 h, the reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. NaHCO$_3$ aq. and brine, then dried over Na$_2$SO$_4$ and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 2:1 to 1:1) to afford the desired product in 91% yield (453 mg) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.56 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.49 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.08 (dd, *J* = 5.0, 3.7 Hz, 1H), 6.55 (s, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.21 (d, *J* = 5.0 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 170.08, 161.97, 138.18, 130.52, 128.69, 127.82, 61.87, 41.87, 14.29.

HRMS (ESI-TOF, m/z): Calcd for [M+H]$^{+}$ 214.0538; Found 214.0545.

Compound 7s



To a mixture of 2-thiophenecarboxylic acid (400 mg, 3.12 mmol) and dichloromethane (5.0 mL) were added oxalyl chloride (515 mg, 4.06 mmol) and dimethylformamide (2 drops) at 0 °C, and the reaction mixture was stirred at room temperature. After 1 h, the solvent and remaining oxalyl chloride were removed, and the residue was dissolved in dichloromethane (5.0 mL). To the reaction mixture were added 3-hydroxypropionitrile (264 mg, 3.74 mmol), 4-dimethylaminopyridine (38 mg, 0.31 mmol) and triethylamine (473 mg, 4.68 mmol) in 1 mL of dichloromethane at 0 °C, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 5:1 to 2:1) to afford the desired product in 91% yield (509 mg) as a colorless oil.

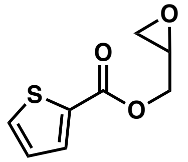
^{1}H NMR (600 MHz, CDCl$_3$) δ 7.85 (dd, *J* = 3.8, 1.3 Hz, 1H), 7.61 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.13 (dd, *J* = 5.0, 3.7 Hz, 1H), 4.50 (t, *J* = 6.3 Hz, 2H), 2.83 (t, *J* = 6.3 Hz, 2H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 161.63, 134.46, 133.52, 132.49, 128.11, 116.75, 59.32, 18.30.

HRMS (ESI-TOF, m/z): Not found.

GC/MS (EI): 181 (21%), 111 (100%).

Compound 8s



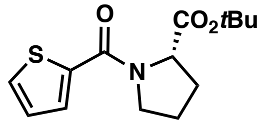
To a mixture of 2-thiophenecarboxylic acid (400 mg, 3.12 mmol), potassium carbonate (643 mg, 4.68 mmol), sodium iodide (46 mg, 0.31 mmol) and dimethylformamide (4.0 mL) was added epichlorohydrin (375 mg, 4.06 mmol) at room temperature, and the reaction mixture was stirred at 70 °C. After 2 days, the reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 5:1 to 2:1) to afford the desired product in 77% yield (438 mg) as a colorless oil.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.84 (dd, *J* = 3.7, 1.3 Hz, 1H), 7.58 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.11 (dd, *J* = 5.0, 3.8 Hz, 1H), 4.62 (dd, *J* = 12.3, 3.1 Hz, 1H), 4.16 (dd, *J* = 12.2, 6.1 Hz, 1H), 3.34-3.31 (m, 1H), 2.89 (dd, *J* = 4.9, 4.1 Hz, 1H), 2.72 (dd, *J* = 4.9, 2.6 Hz, 1H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 162.01, 134.05, 133.20, 132.98, 127.96, 65.59, 49.52, 44.86.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 185.0272; Found 185.0274.

Compound 9s



To a mixture of 2-thiophenecarboxylic acid (247 mg, 1.93 mmol), ethyl *tert*-butyl *L*-prolinate (300 mg, 1.75 mmol), 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (HATU, 732 mg, 1.93 mmol) and dimethylformamide (3.0 mL) was added triethylamine (354 mg, 3.50 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 2:1) to afford the desired product in 93% yield (459 mg) as a white solid.

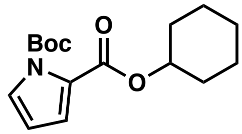
(observed as a mixture of rotamers)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 – 7.31 (m, 2H), 7.07-7.06 (m, 1H), 4.69 – 4.48 (m, 1H), 3.95 – 3.79 (m, 2H), 2.37 – 2.05 (m, 2H), 1.98 (br, 2H), 1.47 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.43, 161.95, 138.91, 130.20, 130.01, 127.18, 81.42, 61.13, 49.40, 29.05, 28.15, 25.59.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 282.1164; Found 282.1159.

Compound 10s



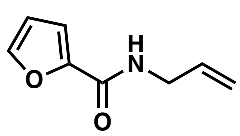
To a mixture of pyrrole-2-carboxylic acid (344 mg, 3.10 mmol) and dichloromethane (5.0 mL) were added oxalyl chloride (511 mg, 4.03 mmol) and dimethylformamide (2 drops) at 0 °C, and the reaction mixture was stirred at room temperature. After 2 h, the solvent and remaining oxalyl chloride were removed, and the residue was dissolved in dichloromethane (5.0 mL). To the reaction mixture were added cyclohexanol (402 mg, 3.72 mmol), 4-dimethylaminopyridine (38 mg, 0.31 mmol) and triethylamine (473 mg, 4.68 mmol) in 1 mL of dichloromethane at 0 °C, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. To the residue dissolved in acetonitrile (5.0 mL) were added 4-dimethylaminopyridine (454 mg, 3.72 mmol) and di-*tert*-butyl decarbonate (744 mg, 3.41 mmol), and the reaction mixture was stirred at room temperature for overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 0.5 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 10:1) to afford the desired product in 64% yield (579 mg) as a colorless amorphous.

^{1}H NMR (600 MHz, $CDCl_3$) (observed as a mixture of rotamers) δ 7.29 (dd, *J* = 3.1, 1.7 Hz, 1H), 6.81 (dd, *J* = 3.5, 1.8 Hz, 1H), 6.18 – 6.12 (m, 1H), 4.94 – 4.91 (m, 1H), 1.97 – 1.90 (m, 2H), 1.79 – 1.72 (m, 2H), 1.58 – 1.47 (m, 12H), 1.43 – 1.37 (m, 2H), 1.34 – 1.26 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) (observed as a mixture of rotamers) δ 160.39, 148.52, 126.57, 126.26, 120.59, 110.10, 84.75, 73.25, 31.76, 27.82, 25.58, 23.87.

HRMS (ESI-TOF, m/z): Calcd for $[M+Na]^+$ 316.1525; Found 316.1521.

Compound 11s



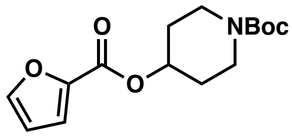
To a mixture of 2-furoic acid (300 mg, 2.68 mmol) and dichloromethane (5.0 mL) were added oxalyl chloride (442 mg, 3.48 mmol) and dimethylformamide (2 drops) at 0 °C, and the reaction mixture was stirred at room temperature. After 4 h, the solvent and remaining oxalyl chloride were removed, and the residue was dissolved in dichloromethane (5.0 mL). To the reaction mixture was added allylamine (459 mg, 8.04 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 15 min. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (CH_2Cl_2/AcOEt = 20:1) to afford the desired product in 96% yield (390 mg) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.11 (dd, *J* = 3.5, 0.9 Hz, 1H), 6.49 (dd, *J* = 3.5, 1.8 Hz, 1H), 6.43 (s, 1H), 5.91 (ddt, *J* = 17.2, 10.3, 5.7 Hz, 1H), 5.26 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.18 (dq, *J* = 10.2, 1.4 Hz, 1H), 4.06 – 4.04 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 158.31, 148.09, 143.96, 134.08, 116.84, 114.38, 112.28, 41.59.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 152.0721; Found 152.0708.

Compound 12s



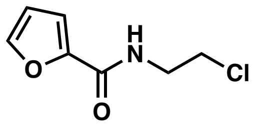
To a mixture of 2-furoic acid (400 mg, 3.57 mmol) and dichloromethane (5.0 mL) were added oxalyl chloride (589 mg, 4.64 mmol) and dimethylformamide (2 drops) at 0 °C, and the reaction mixture was stirred at room temperature. After 2 h, the solvent and remaining oxalyl chloride were removed, and the residue was dissolved in dichloromethane (5.0 mL). To the reaction mixture were added tert-butyl 4-hydroxy-1-piperidinecarboxylate (790 mg, 3.93 mmol), 4-dimethylaminopyridine (44 mg, 0.36 mmol) and triethylamine (542 mg, 5.36 mmol) in 1 mL of dichloromethane at 0 °C, and the reaction mixture was stirred at room temperature for overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 0.5 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (CH_2Cl_2/AcOEt = 5:1) to afford the desired product in 94% yield (994 mg) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (dd, J = 1.7, 0.9 Hz, 1H), 7.17 (dd, J = 3.5, 0.9 Hz, 1H), 6.51 (dd, J = 3.5, 1.7 Hz, 1H), 5.17 – 5.14 (m, 1H), 3.77 (br, 2H), 3.30 – 3.26 (m, 2H), 1.98 – 1.90 (m, 2H), 1.74 (br, 2H), 1.47 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 158.16, 154.88, 146.51, 144.90, 118.09, 111.98, 79.87, 70.64, 41.19 (br), 30.81, 28.57.

HRMS (ESI-TOF, m/z): Calcd for $[M+Na]^+$ 318.1317; Found 318.1314.

Compound 13s



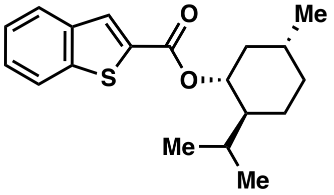
To a mixture of 2-furoic acid (300 mg, 2.68 mmol) and dichloromethane (5.0 mL) were added oxalyl chloride (442 mg, 3.48 mmol) and dimethylformamide (2 drops) at 0 °C, and the reaction mixture was stirred at room temperature. After 2 h, the solvent and remaining oxalyl chloride were removed, and the residue was dissolved in dichloromethane (5.0 mL). To the reaction mixture were added 2-chloroethylamine hydrochloride (342 mg, 2.95 mmol) and triethylamine (542 mg, 5.36 mmol) at 0 °C, and the reaction mixture was stirred at 0 °C for 10 min. The reaction mixture was poured into 1N HCl aq., followed by extraction with AcOEt. The organic layer was washed with sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4. The AcOEt solution of crude product was filtered through short pad of silica gel, then the filtrate was concentrated. The resulting solid was washed with hexane to afford the desired product in 80% yield (372 mg) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.46 (dd, *J* = 1.8, 0.9 Hz, 1H), 7.13 (dd, *J* = 3.5, 0.9 Hz, 1H), 6.75 (br, 1H), 6.51 (dd, *J* = 3.5, 1.8 Hz, 1H), 3.80 – 3.75 (m, 2H), 3.72 – 3.68 (m, 2H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 158.54, 147.74, 144.27, 114.79, 112.37, 44.11, 40.98.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 174.0322; Found 174.0322.

Compound 14s



To a mixture of benzothiazole-2-carboxylic acid (570 mg, 3.20 mmol) and dichloromethane (5.0 mL) were added oxalyl chloride (528 mg, 4.16 mmol) and dimethylformamide (2 drops) at 0 °C, and the reaction mixture was stirred at room temperature. After 2 h, the solvent and remaining oxalyl chloride were removed, and the residue was dissolved in dichloromethane (5.0 mL). To the reaction mixture were added *L*-menthol (550 mg, 3.52 mmol), 4-dimethylaminopyridine (39 mg, 0.32 mmol) and triethylamine (486 mg, 4.80 mmol) in 1 mL of dichloromethane at 0 °C, and the reaction mixture was stirred at room temperature for overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 0.5 N HCl aq., sat. NaHCO$_3$ aq. and brine, then dried over Na$_2$SO$_4$ and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 20:1 to 10:1) to afford the desired product in 98% yield (996 mg) as a white solid.

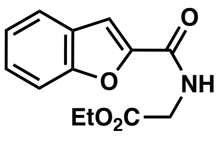
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.05 (d, *J* = 0.8 Hz, 1H), 7.88 – 7.85 (m, 2H), 7.46 – 7.43 (m, 1H), 7.41 – 7.39 (m, 1H), 4.93 (td, *J* = 10.9, 4.4 Hz, 1H), 2.18 – 2.15 (m, 1H), 2.01 – 1.98 (m, 1H), 1.77 – 1.69 (m, 2H), 1.59 – 1.54 (m, 2H), 1.18 – 1.12 (m, 2H), 0.95 – 0.93 (m, 6H), 0.82 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 162.57, 142.32, 138.94, 134.53, 130.28, 126.92, 125.60, 124.98, 122.87, 75.91, 47.35, 41.05, 34.41, 31.61, 26.76, 23.89, 22.18, 20.87, 16.79.

HRMS (ESI-TOF, m/z): Not found.

GC/MS (EI): 316 (11%), 178 (100%), 161 (71%), 138 (54%), 123 (29%), 95 (57%), 81 (31%).

Compound 15s



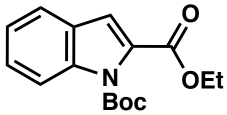
To a mixture of benzofuran-2-carboxylic acid (379 mg, 2.34 mmol), ethyl glycinate hydrochloride (392 mg, 2.80 mmol), 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (HATU, 978 mg, 2.57 mmol) and dimethylformamide (4.0 mL) was added triethylamine (592 mg, 5.85 mmol) at 0 °C, and the reaction mixture was stirred at room temperature. After 3 h, the reaction mixture was quenched with water. The resulting precipitate was dissolved in AcOEt and dried over Na_2SO_4, then concentrated. The resulting solid was washed with hexane to afford the desired product in 85% yield (492 mg) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68 (ddd, *J* = 7.8, 1.3, 0.7 Hz, 1H), 7.52 (dq, *J* = 8.4, 0.9 Hz, 1H), 7.49 (d, *J* = 1.0 Hz, 1H), 7.43 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H), 7.30 (ddd, *J* = 8.0, 7.2, 0.9 Hz, 1H), 7.13 (s, 1H), 4.31 – 4.25 (m, 4H), 1.33 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 169.73, 158.96, 155.00, 148.27, 127.65, 127.23, 123.90, 122.92, 112.04, 111.06, 61.93, 41.35, 14.31.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 248.0923; Found 248.0927.

Compound 16s



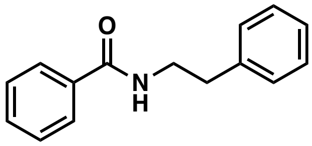
To a mixture of ethyl indole-2-carboxylate (1.0 g, 5.29 mmol), 4-dimethylaminopyridine (130 mg, 1.06 mmol) and acetonitrile (5.0 mL) was added di-*tert*-butyl decarbonate (1270 mg, 5.82 mmol), and the reaction mixture was stirred at room temperature for overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 0.5 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 10:1 to 5:1) to afford the desired product quantitatively (1590 mg) as a colorless amorphous.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 – 8.07 (m, 1H), 7.61 – 7.59 (m, 1H), 7.42 – 7.39 (m, 1H), 7.28 – 7.25 (m, 1H), 7.10 (d, *J* = 0.8 Hz, 1H), 4.40 –4.37 (m, 2H), 1.63 (s, 9H), 1.40 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.05, 149.43, 137.96, 130.98, 127.69, 126.86, 123.39, 122.28, 115.01, 114.87, 84.70, 61.52, 28.00, 14.39.

HRMS (ESI-TOF, m/z): Calcd for $[M+Na]^+$ 312.1212; Found 312.1206.

Compound 17s



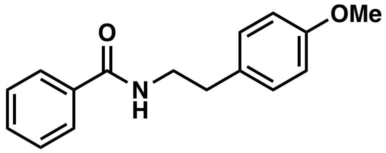
To a mixture of phenethylamine (475 mg, 3.92 mmol), triethylamine (720 mg, 7.12 mmol) and dichloromethane (10 mL) was added benzoyl chloride (500 mg, 3.56 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4. The AcOEt solution of crude product was filtered through short pad of silica gel, then the filtrate was concentrated. The resulting solid was washed with hexane to afford the desired product quantitatively (830 mg) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 – 7.66 (m, 2H), 7.50 – 7.46 (m, 1H), 7.43 – 7.37 (m, 2H), 7.36 – 7.30 (m, 2H), 7.28 – 7.22 (m, 3H), 6.16 (br, 1H), 3.77 – 3.67 (m, 2H), 2.94 (t, *J* = 6.9 Hz, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 167.58, 139.05, 134.81, 131.54, 128.96, 128.87, 128.70, 126.93, 126.75, 41.26, 35.85.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 226.1232; Found 226.1230.

Compound 18s



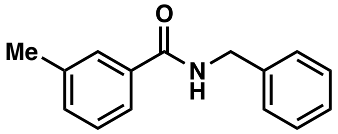
To a mixture of 4-methoxyphenylethylamine (592 mg, 3.92 mmol), triethylamine (720 mg, 7.12 mmol) and dichloromethane (10 mL) was added benzoyl chloride (500 mg, 3.56 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4. The AcOEt solution of crude product was filtered through short pad of silica gel, then the filtrate was concentrated. The resulting solid was washed with hexane to afford the desired product quantitatively (960 mg) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 – 7.66 (m, 2H), 7.50 – 7.46 (m, 1H), 7.43 – 7.37 (m, 2H), 7.19 – 7.13 (m, 2H), 6.90 – 6.83 (m, 2H), 6.10 (br, 1H), 3.80 (s, 3H), 3.71 – 3.67 (m, 2H), 2.88 (t, *J* = 6.9 Hz, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 167.55, 158.50, 134.85, 131.53, 130.99, 129.91, 128.71, 126.93, 114.29, 55.43, 41.43, 34.93.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 256.1338; Found 256.1335.

Compound 19s



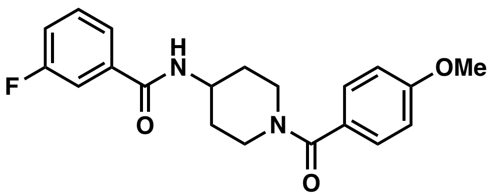
To a mixture of benzylamine (457 mg, 4.27 mmol) and dichloromethane (5 mL) was added *m*-toluoyl chloride (300 mg, 1.94 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 30 min. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 2:1) to afford the desired product quantitatively (464 mg) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63 – 7.62 (m, 1H), 7.57 – 7.56 (m, 1H), 7.36 – 7.35 (m, 4H), 7.33 – 7.27 (m, 3H), 6.41 (br, 1H), 4.65 (d, *J* = 5.6 Hz, 2H), 2.39 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 167.65, 138.61, 138.38, 134.51, 132.41, 128.92, 128.60, 128.07, 127.85, 127.75, 124.03, 44.26, 21.48.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 226.1232; Found 226.1229.

Compound 20s



To a mixture of 3-fluorobenzoic acid (500 mg, 3.15 mmol) and dichloromethane (6.0 mL) were added oxalyl chloride (520 mg, 4.10 mmol) and dimethylformamide (2 drops) at 0 °C, and the reaction mixture was stirred at room temperature. After 3 h, the solvent and remaining oxalyl chloride were removed, and the residue was dissolved in dichloromethane (6.0 mL). To the reaction mixture were added 4-amino-1-Boc-piperidine (757 mg, 3.78 mmol) and triethylamine (956 mg, 9.45 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 2:1) to afford the amide coupling product in 64% yield (651 mg) as a white solid. To a mixture of the obtained coupling product (100 mg, 0.310 mmol) and dichloromethane (1.0 mL) was added trifluoroacetic acid (0.5 mL), and the reaction mixture was stirred at room temperature. After 1 h, the solvent was removed under reduced pressure, and the residue was dissolved in dichloromethane (2.0 mL). To the reaction mixture were added 4-methoxybenzoyl chloride (63 mg, 0.372 mmol) and triethylamine (94 mg, 0.93 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 1:1 to 1:2, then AcOEt) to afford the desired product quantitatively (111 mg) as a white solid.

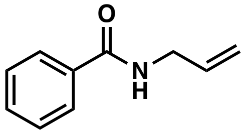
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 – 7.45 (m, 2H), 7.42 – 7.31 (m, 3H), 7.20 – 7.19 (m, 1H), 6.95 – 6.84 (m, 2H), 6.29 (d, *J* = 7.8 Hz, 1H), 4.64 (br, 2H), 4.25 – 4.22 (m, 1H), 3.83 (s, 3H), 3.08 (br, 2H), 2.10 – 2.08 (m, 2H), 1.50 (br, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 170.61, 165.71 (J_{CF} = 3.0 Hz), 162.89 (J_{CF} = 249 Hz), 161.00, 136.78 (J_{CF} = 6.0 Hz), 130.38 (J_{CF} = 7.6 Hz), 129.11, 127.90, 122.54 (J_{CF} = 4.5 Hz), 118.71 (J_{CF} = 21 Hz), 114.56 (J_{CF} = 23 Hz), 113.91, 55.50, 47.58, 32.52 (br).

^{19}F NMR (376 MHz, $CDCl_3$) δ -111.64.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 357.1614; Found 357.1603.

Compound 21s



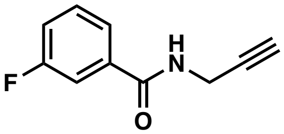
To a mixture of allylamine (304 mg, 5.33 mmol) and dichloromethane (5 mL) was added benzoyl chloride (300 mg, 2.13 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4. The AcOEt solution of crude product was filtered through short pad of silica gel, then the filtrate was concentrated to afford the desired product quantitatively (352 mg) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 – 7.74 (m, 2H), 7.53 – 7.47 (m, 1H), 7.46 – 7.39 (m, 2H), 6.23 (br, 1H), 6.00 – 5.89 (m, 1H), 5.30 – 5.23 (m, 1H), 5.20 – 5.18 (m, 1H), 4.11 – 4.08 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 167.46, 134.62, 134.29, 131.65, 128.73, 127.03, 116.86, 42.57.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 162.0919; Found 162.0918.

Compound 22s



To a mixture of 3-fluorobenzoic acid (300 mg, 1.89 mmol), 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (HATU, 795 mg, 2.08 mmol) and dimethylformamide (3.0 mL) was added propargylamine (312 mg, 5.67 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4. The AcOEt solution of crude product was filtered through short pad of silica gel, then the filtrate was concentrated. The resulting solid was washed with hexane to afford the desired product in 81% yield (274 mg) as a white solid.

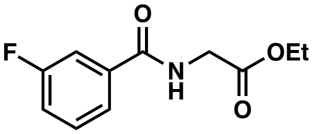
^{1}H NMR (600 MHz, CDCl$_3$) δ 7.57 – 7.46 (m, 2H), 7.45 – 7.38 (m, 1H), 7.24 – 7.20 (m, 1H), 6.27 (br, 1H), 4.26 – 4.25 (m, 2H), 2.30 – 2.29 (m, 1H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 165.92, 162.92 (J_{CF} = 248 Hz), 136.12 (J_{CF} = 6.0 Hz), 130.50 (J_{CF} = 9.1 Hz), 122.57 (J_{CF} = 3.0 Hz), 119.02 (J_{CF} = 21 Hz), 114.65 (J_{CF} = 23 Hz), 79.28, 72.32, 30.06.

^{19}F NMR (376 MHz, CDCl$_3$) δ -111.42.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 178.0668; Found 178.0663.

Compound 23s



To a mixture of 3-fluorobenzoic acid (500 mg, 3.15 mmol) and dichloromethane (10.0 mL) were added oxalyl chloride (520 mg, 4.10 mmol) and dimethylformamide (2 drops) at 0 °C, and the reaction mixture was stirred at room temperature. After 4 h, the solvent and remaining oxalyl chloride were removed, and the residue was dissolved in dichloromethane (10.0 mL). To the reaction mixture were added ethyl glycinate hydrochloride (528 mg, 3.78 mmol) and triethylamine (956 mg, 9.45 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4. The AcOEt solution of crude product was filtered through short pad of silica gel, then the filtrate was concentrated. The resulting solid was washed with hexane to afford the desired product in 96% yield (683 mg) as a white solid.

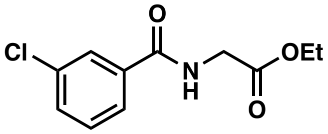
^{1}H NMR (600 MHz, CDCl$_3$) δ 7.58 – 7.56 (m, 1H), 7.55 – 7.52 (m, 1H), 7.44 – 7.41 (m, 1H), 7.24 – 7.22 (m, 1H), 6.64 (br, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 4.23 (d, *J* = 5.0 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 170.05, 166.23 (J_{CF} = 3.0 Hz), 162.93 (J_{CF} = 249 Hz), 136.16 (J_{CF} = 6.0 Hz), 130.44, 122.62, (J_{CF} = 3.0 Hz), 118.99 (J_{CF} = 21 Hz), 114.70 (J_{CF} = 23 Hz), 61.95, 42.08, 14.30.

^{19}F NMR (376 MHz, CDCl$_3$) δ -111.54.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 226.0879; Found 226.0874.

Compound 24s



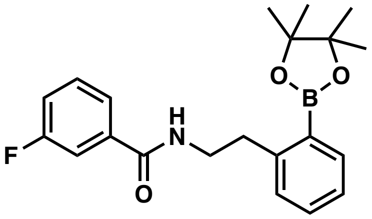
To a mixture of 3-chlorobenzoic acid (200 mg, 1.28 mmol), ethyl glycinate hydrochloride (214 mg, 1.54 mmol), 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (HATU, 633 mg, 1.66 mmol) and dimethylformamide (3.0 mL) was added triethylamine (389 mg, 3.84 mmol) at 0 °C, and the reaction mixture was stirred at room temperature. After 2 h, the reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. NaHCO$_3$ aq. and brine, then dried over Na$_2$SO$_4$. The AcOEt solution of crude product was filtered through short pad of silica gel, then the filtrate was concentrated. The resulting solid was washed with hexane to afford the desired product in 98% yield (303 mg) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.80 (t, *J* = 1.9 Hz, 1H), 7.68 – 7.66 (m, 1H), 7.50 – 7.48 (m, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 6.68 (br, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 4.22 (d, *J* = 5.0 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 170.05, 166.20, 135.65, 134.99, 131.98, 130.08, 127.63, 125.23, 61.94, 42.07, 14.29.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 242.0584; Found 242.0585.

Compound 25s



To a mixture of *N*-(2-bromophenethyl)-3-fluorobenzamide (483 mg, 1.50 mmol), potassium acetate (294 mg, 3.00 mmol), and bis(pinacolato)diboron (495 mg, 1.95 mmol) in dioxane (6.0 mL) was added $PdCl_2(PPh_3)_2$ (53 mg, 0.075 mmol) under inert atmosphere and the reaction mixture was stirred at 90 °C for overnight. The reaction mixture was diluted with AcOEt. The organic layer was washed with water and brine, then dried over Na_2SO_4. After concentration, the resulting residue was purified by flash column chromatography (hexane/AcOEt = 10:1 to 5:1, then 2:1) to furnish the desired product (456 mg, 82%) as a white solid.

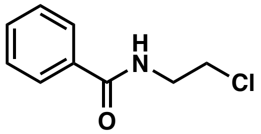
^{1}H NMR (600 MHz, CDCl$_3$) δ 7.78 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.47 – 7.37 (m, 3H), 7.35 – 7.32 (m, 1H), 7.26 – 7.23 (m, 2H), 7.15 – 7.12 (m, 1H), 6.72 (br, 1H), 3.77 – 3.71 (m, 2H), 3.19 – 3.11 (m, 2H), 1.35 (s, 12H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 166.38 (J_{CF} = 3.0 Hz), 162.75 (J_{CF} = 246 Hz), 145.59, 137.39 (J_{CF} = 6.0 Hz), 136.08, 131.58, 130.12 (J_{CF} = 7.6 Hz), 129.80, 128.92, 126.13, 122.70 (J_{CF} = 3.0 Hz), 118.22 (J_{CF} = 23 Hz), 114.35 (J_{CF} = 23 Hz), 84.33, 42.69, 34.49, 24.96.

^{19}F NMR (376 MHz, CDCl$_3$) δ -112.24.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 369.2026; Found 369.2013.

Compound 26s



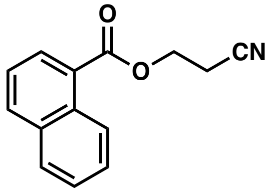
To a mixture of benzoyl chloride (300 mg, 2.13 mmol), 2-chloroethylamine hydrochloride (272 mg, 2.34 mmol) and dichloromethane (5.0 mL) were added triethylamine (431 mg, 4.26 mmol) at 0 °C, and the reaction mixture was stirred at 0 °C for 1.5 h. The reaction mixture was poured into 1N HCl aq., followed by extraction with AcOEt. The organic layer was washed with sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 2:1) to afford the desired product quantitatively (423 mg) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.82 – 7.74 (m, 2H), 7.55 – 7.49 (m, 1H), 7.48 – 7.40 (m, 2H), 6.59 (br, 1H), 3.83 – 3.80 (m, 2H), 3.76 – 3.71 (m, 2H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 167.75, 134.23, 131.90, 128.80, 127.11, 44.32, 41.80.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 184.0529; Found 184.0523.

Compound 27s



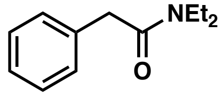
To a mixture of 1-naphthoic acid (534 mg, 3.10 mmol) and dichloromethane (5.0 mL) were added oxalyl chloride (512 mg, 4.03 mmol) and dimethylformamide (2 drops) at 0 °C, and the reaction mixture was stirred at room temperature. After 2 h, the solvent and remaining oxalyl chloride were removed, and the residue was dissolved in dichloromethane (5.0 mL). To the reaction mixture were added 3-Hydroxypropionitrile (331 mg, 4.65 mmol), 4-dimethylaminopyridine (38 mg, 0.31 mmol) and triethylamine (471 mg, 4.65 mmol) in 1 mL of dichloromethane at 0 °C, and the reaction mixture was stirred at room temperature for overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 10:1 to 5:1, then 2:1) to afford the desired product in 98% yield (681 mg) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.94 – 8.93 (m, 1H), 8.28 (dd, *J* = 7.3, 1.3 Hz, 1H), 8.08 – 8.06 (m, 1H), 7.91 – 7.90 (m, 1H), 7.66 – 7.63 (m, 1H), 7.58 – 7.49 (m, 2H), 4.62 (t, *J* = 6.3 Hz, 2H), 2.90 (t, *J* = 6.3 Hz, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.76, 134.33, 133.98, 131.55, 131.02, 128.82, 128.27, 126.54, 125.74, 125.68, 124.66, 117.05, 59.32, 18.36.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 226.0868; Found 226.0876.

Compound 43



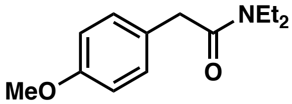
To a mixture of phenylacetic acid (500 mg, 3.67 mmol) and dichloromethane (10.0 mL) were added oxalyl chloride (606 mg, 4.77 mmol) and dimethylformamide (2 drops) at 0 °C, and the reaction mixture was stirred at room temperature. After 3.5 h, the solvent and remaining oxalyl chloride were removed, and the residue was dissolved in dichloromethane (10.0 mL). To the reaction mixture was added diethylamine (1074 mg, 14.7 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 5:1 to 2:1) to afford the desired product quantitatively (730 mg) as a pale yellow oil.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.34 – 7.27 (m, 2H), 7.27 – 7.21 (m, 3H), 3.70 (d, *J* = 0.7 Hz, 2H), 3.39 (q, *J* = 7.1 Hz, 2H), 3.30 (q, *J* = 7.2 Hz, 2H), 1.12 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 170.23, 135.68, 128.80, 128.75, 126.78, 42.48, 41.08, 40.26, 14.34, 13.07.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 192.1388; Found 192.1391.

Compound 30s



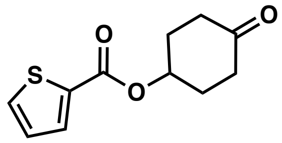
To a mixture of phenylacetic acid (500 mg, 3.01 mmol) and dichloromethane (10.0 mL) were added oxalyl chloride (497 mg, 3.91 mmol) and dimethylformamide (2 drops) at 0 °C, and the reaction mixture was stirred at room temperature. After 1 h, the solvent and remaining oxalyl chloride were removed, and the residue was dissolved in dichloromethane (10.0 mL). To the reaction mixture was added diethylamine (660 mg, 9.03 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 2.5 h. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. NaHCO$_3$ aq. and brine, then dried over Na$_2$SO$_4$ and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 2:1 to 1:1) to afford the desired product in 73% (485 mg) as a pale yellow oil.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.20 – 7.14 (m, 2H), 6.88 – 6.81 (m, 2H), 3.79 (s, 3H), 3.63 (s, 2H), 3.38 (q, *J* = 7.1 Hz, 2H), 3.29 (q, *J* = 7.1 Hz, 2H), 1.13 – 1.08 (m, 6H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 170.57, 158.50, 129.80, 127.69, 114.18, 55.40, 42.42, 40.25, 40.12, 14.38, 13.08.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 222.1494; Found 222.1499.

Compound 31s



To a mixture of 2-thiophenecarboxylic acid (400 mg, 3.12 mmol) and dichloromethane (5.0 mL) were added oxalyl chloride (515 mg, 4.06 mmol) and dimethylformamide (2 drops) at 0 °C, and the reaction mixture was stirred at room temperature. After 1 h, the solvent and remaining oxalyl chloride were removed, and the residue was dissolved in dichloromethane (5.0 mL). To the reaction mixture were added

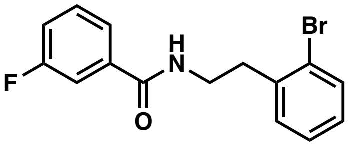
4-Hydroxycyclohexanone (425 mg, 3.74 mmol), 4-dimethylaminopyridine (38 mg, 0.31 mmol) and triethylamine (473 mg, 4.68 mmol) in 1 mL of dichloromethane at 0 °C, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 1 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 5:1 to 2:1) to afford the desired product in 79% yield (546 mg) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84 – 7.83 (m, 1H), 7.62 – 7.52 (m, 1H), 7.15 – 7.07 (m, 1H), 5.40 – 5.38 (m, 1H), 2.67 – 2.62 (m, 2H), 2.44 – 2.40 (m, 2H), 2.30 – 2.20 (m, 2H), 2.18 – 2.12 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 209.83, 161.56, 133.85, 133.77, 132.79, 128.04, 69.43, 37.37, 30.65.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 225.0585; Found 225.0593.

Compound 32s



To a mixture of 3-fluorobenzoic acid (1.0 g, 6.31 mmol), 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (HATU, 2633 mg, 6.94 mmol) and dimethylformamide (10.0 mL) were added triethylamine (1277 mg, 12.6 mmol) and 2-bromophenethylamine (1386 mg, 6.94 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for overnight. The reaction mixture was quenched with water. The resulting precipitate was dissolved in AcOEt and dried over Na_2SO_4, then concentrated. The resulting solid was washed with hexane to afford the desired product quantitatively (2061 mg) as a white brown solid.

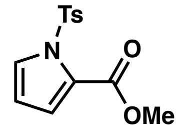
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 – 7.56 (m, 1H), 7.48 – 7.42 (m, 2H), 7.40 – 7.37 (m, 1H), 7.28 – 7.26 (m, 2H), 7.18 (m, 1H), 7.13 – 7.10 (m, 1H), 6.21 (br, 1H), 3.76 – 3.72 (m, 2H), 3.10 (t, J = 6.9 Hz, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.42 (J_{CF} = 3.0 Hz), 162.89 (J_{CF} = 248 Hz), 138.35, 136.97 (J_{CF} = 6.0 Hz), 133.19, 131.22, 130.37 (J_{CF} = 7.6 Hz), 128.62, 127.90, 124.73, 122.41 (J_{CF} = 1.5 Hz), 118.60 (J_{CF} = 21 Hz), 114.47 (J_{CF} = 24 Hz), 40.13, 35.76.

^{19}F NMR (376 MHz, $CDCl_3$) δ -111.65.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 322.0243; Found 322.0239.

Compound 33



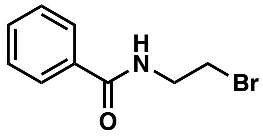
To a solution of methyl 1*H*-pyrrole-2-carboxylate (300 mg, 2.40 mmol) in THF (5.0 mL) were added sodium hydride (60% in mineral oil, 144 mg, 3.60 mmol) at 0 °C, and the reaction mixture was stirred at 0 °C. After 15 min, *p*-toluene sulfonyl chloride (503 mg, 2.64 mmol) was added to the reaction mixture. The resulting reaction mixture was stirred at room temperature for 5 h, then poured into 1N HCl aq., followed by extraction with AcOEt. The organic layer was washed with sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4. After concentration, the resulting residue was purified by flash column chromatography (hexane/AcOEt = 5:1 to 2:1) to furnish the desired product in 97% yield (652 mg) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.87 (d, *J* = 8.4 Hz, 2H), 7.72 (dd, *J* = 3.2, 1.9 Hz, 1H), 7.33 – 7.31 (m, 2H), 7.04 (dd, *J* = 3.7, 1.9 Hz, 1H), 6.30 (dd, *J* = 3.7, 3.2 Hz, 1H), 3.73 (s, 3H), 2.43 (s, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 159.29, 145.11, 135.98, 129.60, 129.32, 128.35, 124.99, 123.47, 110.46, 51.91, 21.85.

The ^{1}H and ^{13}C NMR were consistent with the reported spectral data. *(2)*

Compound 35



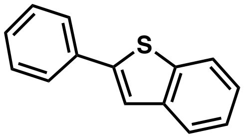
To a mixture of benzoyl chloride (300 mg, 2.13 mmol), 2-chloroethylamine hydrochloride (480 mg, 2.34 mmol) and dichloromethane (5.0 mL) were added triethylamine (431 mg, 4.26 mmol) at 0 °C, and the reaction mixture was stirred at 0 °C for 1.5 h. The reaction mixture was poured into 1N HCl aq., followed by extraction with AcOEt. The organic layer was washed with sat. $NaHCO_3$ aq. and brine, then dried over. The AcOEt solution of crude product was filtered through short pad of silica gel, then the filtrate was concentrated. The resulting solid was washed with hexane to afford the desired product quantitatively (522 mg) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.81 – 7.77 (m, 2H), 7.54 – 7.50 (m, 1H), 7.48 – 7.43 (m, 2H), 6.57 (br, 1H), 3.90 – 3.87 (m, 2H), 3.62 – 3.60 (m, 2H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 167.66, 134.22, 131.93, 128.82, 127.11, 41.68, 32.90.

The ^{1}H and ^{13}C NMR were consistent with the reported spectral data. *(3)*

Compound 37



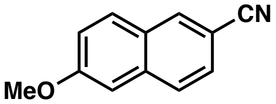
To a mixture of thianaphthene-2-boronic acid (300 mg, 1.69 mmol), sodium carbonate (537 mg, 5.07 mmol), iodobenzene (517 mg, 2.54 mmol) in dioxane (3.0 mL) / water (0.5 mL) was added 1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane (41 mg, 0.051 mmol) under inert atmosphere, and the reaction mixture was stirred at 80 °C for overnight. The reaction mixture was diluted with AcOEt. The organic layer was washed with water, sat. $Na_2S_2O_3$ aq. and brine, then dried over Na_2SO_4. After concentration, the resulting residue was purified by flash column chromatography (hexane/AcOEt = 10:1) to furnish the desired product in 60% yield (214 mg) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 – 7.81 (m, 1H), 7.79 – 7.77 (m, 1H), 7.75 – 7.69 (m, 2H), 7.56 – 7.55 (m, 1H), 7.47 – 7.40 (m, 2H), 7.38 – 7.28 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 144.40, 140.84, 139.66, 134.46, 129.10, 128.42, 126.65, 124.66, 124.46, 123.71, 122.42, 119.60.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 211.0581; Found 211.0586.

Compound 38



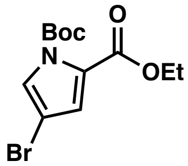
To a mixture of 2-bromo-6-methoxynaphthalene (474 mg, 2.00 mmol), potassium ferrocyanide (169 mg, 0.4 mmol), copper iodide (76 mg, 0.4 mmol), potassium iodide (132 mg, 0.8 mmol) and sodium carbonate (84 mg, 0.8 mmol) in *N*, *N*-dimethylacetamide (2.0 mL) was added 1,2-dimethylethylenediamine (353 mg, 4.00 mmol) under inert atmosphere, and the reaction mixture was stirred at 140 °C for overnight. The reaction mixture was diluted with diethyl ether. The organic layer was washed with water, 1 N HCl aq. and brine, then dried over Na_2SO_4. After concentration, the resulting residue was purified by flash column chromatography (hexane/AcOEt = 5:1) to furnish the desired product in 64% yield (214 mg) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 – 8.13 (m, 1H), 7.78 – 7.77 (m, 2H), 7.57 – 7.56 (m, 1H), 7.26 – 7.23 (m, 1H), 7.15 (d, *J* = 2.5 Hz, 1H), 3.95 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.17, 136.57, 133.91, 130.12, 127.95, 127.89, 127.24, 120.83, 119.73, 106.90, 106.04, 55.65.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 184.0762; Found 184.0761.

Compound 48



To a mixture of Ethyl 4-bromo-1H-pyrrole-2-carboxylate (1.0 g, 4.59 mmol), 4-dimethylaminopyridine (673 mg, 5.51 mmol) and acetonitrile (5.0 mL) was added di-*tert*-butyl decarbonate (1102 mg, 5.05 mmol), and the reaction mixture was stirred at room temperature for overnight. The reaction mixture was poured into water, followed by extraction with AcOEt. The organic layer was washed with 0.5 N HCl aq., sat. $NaHCO_3$ aq. and brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (CH_2Cl_2) to afford the desired product quantitatively (1511 mg) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (d, *J* = 1.9 Hz, 1H), 6.78 (d, *J* = 1.9 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 1.57 (s, 9H), 1.34 (t, *J* = 7.1 Hz, 3H).

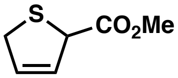
^{13}C NMR (151 MHz, $CDCl_3$) δ 159.99, 147.29, 126.18, 125.49, 122.03, 98.89, 85.72, 61.36, 27.76, 14.33.

HRMS (ESI-TOF, m/z): Not found.

The ^{1}H and ^{13}C NMR were consistent with the reported spectral data. *(4)*

Product characterization

Compound 2



The reaction was performed with **1** (14 mg, 0.1 mmol) and tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) in 1.5 mL of EtOH and 1.5 mL of THF (DMS was not used). The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 10 F/mol. The reaction mixture was diluted with diethyl ether and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **2** in 92% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 5:1) to furnish product **2** (12.0 mg, 83%) as a colorless oil.

^{1}H NMR (600 MHz, CDCl$_3$) δ 6.07 – 6.04 (m, 1H), 5.88 – 5.80 (m, 1H), 4.82 – 4.79 (m, 1H), 3.92 – 3.85 (m, 1H), 3.82 – 3.76 (m, 1H), 3.74 (s, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 172.44, 131.96, 127.34, 55.56, 52.83, 39.56.

HRMS (ESI-TOF, m/z): Not found.

GC/MS (EI): 144 (17%), 85 (100%).

The ^{1}H and ^{13}C NMR were consistent with the reported spectral data. *(5)*

Note:

The reaction carried out in the presence of DMS (22 μL, 0.3 mmol) gave the product **2** in 91% determined by ^{1}H NMR spectroscopic analysis (nitromethane was used as an internal standard).

The reaction carried out under open-air condition in the presence of DMS (22 μL, 0.3 mmol) gave the product **2** in 77% with trace amount of the starting material **1** determined by ^{1}H NMR spectroscopic analysis (nitromethane was used as an internal standard).

Conditions employing other AC waveforms

AC (sinusoidal, 10 Hz)

The reaction was performed with **1** (14 mg, 0.1 mmol) and tetramethylammonium tetrafluoroborate (80 mg, 0.5 mmol) in 1.5 mL of EtOH and 1.5 mL of THF (DMS was not added). The resulting reaction mixture was electrolyzed for 17 h at room temperature under constant potential of 10 V with alternating current (sinusoidal wave form, 10 Hz, the current reached around 20 mA). The waveform was generated from LabQuest 2 (Vernier) and amplified by Vernier Power Amplifier. The reaction mixture was diluted with diethyl ether and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **2** in 17% and the starting material **1** in 42% (nitromethane was used as an internal standard).

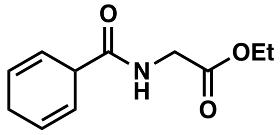
AC (sinusoidal, 1 Hz)

The reaction was performed with **1** (14 mg, 0.1 mmol) and tetramethylammonium tetrafluoroborate (80 mg, 0.5 mmol) in 1.5 mL of EtOH and 1.5 mL of THF (DMS was not used). The resulting reaction mixture was electrolyzed for 24 h at room temperature under a constant potential of 10 V with alternating current (sinusoidal wave form, 1 Hz, the current reached around 3 mA). The waveform was generated from LabQuest 2 (Vernier) and amplified by Vernier Power Amplifier. The reaction mixture was diluted with diethyl ether and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **2** in 9% and the starting material **1** in 79% (nitromethane was used as an internal standard).

Alternating polarity with every 5 seconds

The reaction was performed with **1** (14 mg, 0.1 mmol) and tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) in 1.5 mL of EtOH and 1.5 mL of THF (DMS was not used). The resulting reaction mixture was electrolyzed at room temperature, under a constant current (DC current) of 20 mA with alternating polarity every 5 seconds (ElectraSyn2.0 default alternating polarity function was used instead of rAP) for 10 F/mol. The reaction mixture was diluted with diethyl ether and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **2** in 12%, ethyl ester **46** (from trans esterification) in 29% and trace amount of the starting material **1** (nitromethane was used as an internal standard).

Compound 4



Following the general procedure, the reaction was performed with **3** (21 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **4** in 59% and benzyl alcohol in 23% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 1:1) to furnish product **4** (11.1 mg, 54%) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 6.21 (br, 1H), 5.97 – 5.93 (m, 2H), 5.83 – 5.80 (m, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 4.01 (d, *J* = 5.2 Hz, 2H), 3.69 – 3.65 (m, 1H), 2.77 – 2.74 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 172.73, 170.04, 127.40, 123.28, 61.67, 44.64, 41.61, 26.06, 14.26.

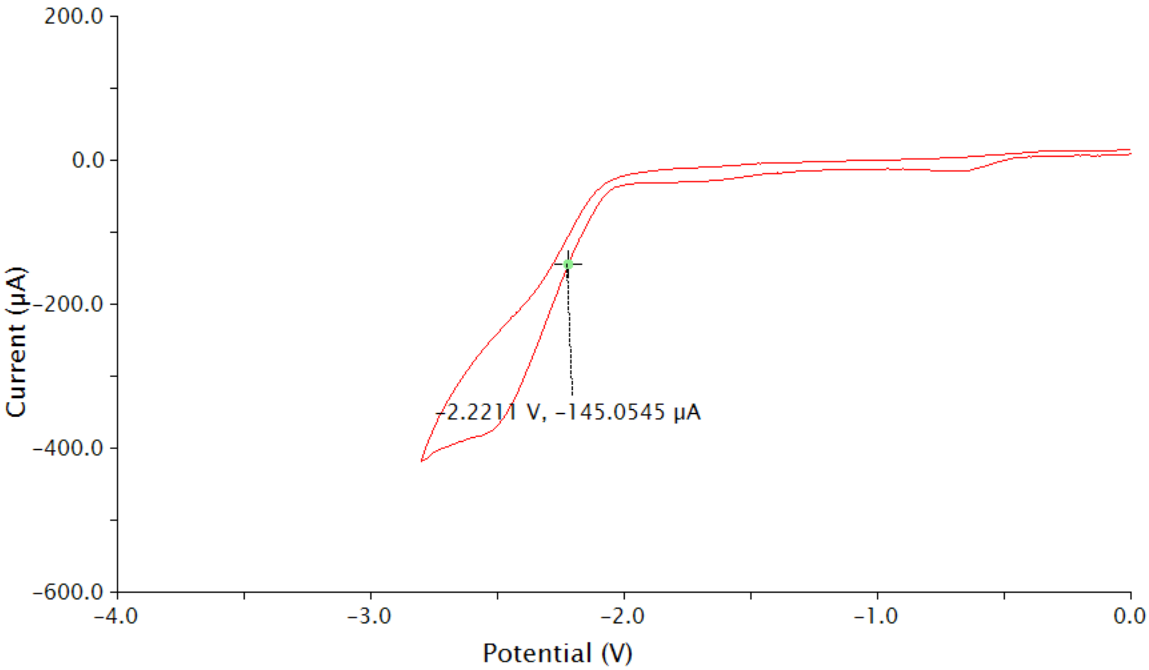
HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 210.1130; Found 210.1138.

Note:

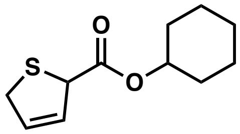
The reaction carried out under open-air condition for 40 F/mol gave the product **4** in 19% and benzyl alcohol in 9% with 37% recovery of the starting material **2** determined by ^{1}H NMR spectroscopic analysis (nitromethane was used as an internal standard).

Cyclic voltammogram of compound 3

A cyclic voltammogram of 15 mM of compound **3** and 0.2 M of TBA•BF$_4$ in 3 mL of THF/EtOH (1:1) is shown below. A 3mm GC disk electrode was used as a working electrode. Ag/AgCl was used as a reference. The CV was recorded under Ar atmosphere at 50 mV/s.



Compound 5



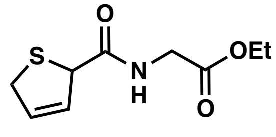
Following the general procedure, the reaction was performed with **5s** (63 mg, 0.3 mmol), tetramethylammonium tetrafluoroborate (120 mg, 0.75 mmol) and DMS (66 μL, 0.9 mmol) in 4.0 mL of EtOH and 4.0 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **5** in 98% (nitromethane was used as an internal standard). The crude reaction mixture was purified by flash column chromatography (hexane/AcOEt = 20:1 to 10:1) to furnish the desired product **5** (57 mg, 90%) as a colorless oil.

^{1}H NMR (600 MHz, CDCl$_3$) δ 6.05 – 6.02 (m, 1H), 5.85 – 5.83 (m, 1H), 4.84 – 4.68 (m, 2H), 3.88 – 3.84 (m, 1H), 3.79 – 3.76 (m, 1H), 1.85 – 1.81 (m, 2H), 1.77 – 1.64 (m, 2H), 1.57 – 1.42 (m, 3H), 1.42 – 1.21 (m, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 171.42, 131.70, 127.60, 73.84, 56.08, 39.45, 31.50, 31.40, 25.49, 23.66, 23.63.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 213.0949; Found 213.0956.

Compound 6



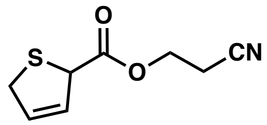
Following the general procedure, the reaction was performed with **6s** (21 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **6** in 67% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 1:1) to furnish product **6** (13.4 mg, 62%) as a colorless.

^{1}H NMR (600 MHz, CDCl$_3$) δ 5.97 – 5.96 (m, 2H), 4.83 – 4.78 (m, 1H), 4.24 – 4.19 (m, 2H), 4.01 (dd, J = 5.3, 1.6 Hz, 2H), 3.94 – 3.87 (m, 1H), 3.86 – 3.80 (m, 1H), 1.28 (t, J = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 170.46, 169.70, 130.15, 129.64, 61.72, 59.26, 41.76, 39.72, 14.26.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 216.0694; Found 216.0702.

Compound 7



Following the general procedure, the reaction was performed with **7s** (18 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **7** in 48% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 2:1) to furnish product **7** (6.8 mg, 37%) as a colorless oil.

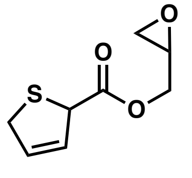
^{1}H NMR (600 MHz, CDCl$_3$) δ 6.11 – 6.08 (m, 1H), 5.86 – 5.84 (m, 1H), 4.85 – 4.78 (m, 1H), 4.36 – 4.33 (m, 2H), 3.91 – 3.87 (m, 1H), 3.82 – 3.78 (m, 1H), 2.73 (t, J = 6.3 Hz, 2H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 171.49, 132.67, 126.70, 116.62, 59.67, 55.24, 39.60, 18.03.

HRMS (ESI-TOF, m/z): Not found.

GC/MS (EI): 183 (10%), 128 (26%), 111 (42%), 85 (100%).

Compound 8 (Mixture of diastereomers)



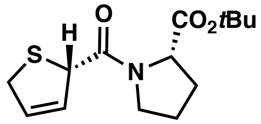
Following the general procedure, the reaction was performed with **8s** (18 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **8** in 54% (dr = 1:1, nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 1:1) to furnish product **8** (8.4 mg, 45%) as a colorless oil.

^{1}H NMR (600 MHz, CDCl$_3$) δ 6.08 – 6.06 (m, 1H), 5.88 – 5.82 (m, 1H), 4.84 – 4.83 (m, 1H), 4.47 – 4.44 (m, 1H), 4.05 – 3.99 (m, 1H), 3.92 – 3.85 (m, 1H), 3.83 – 3.76 (m, 1H), 3.26 – 3.20 (m, 1H), 2.86 – 2.84 (m, 1H), 2.70 – 2.66 (m, 1H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 171.78, 132.28, 132.27, 127.08, 66.06, 65.76, 55.47, 55.45, 49.35, 49.32, 44.79, 44.77, 39.58.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 187.0429; Found 187.0428.

Compound 9a



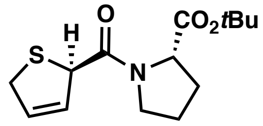
Following the general procedure, the reaction was performed with **9s** (28 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **9a** and **9b** in 84% (dr = 1:1, nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (diethyl ether) to furnish product **9a** (11.3 mg, 40%) as a colorless and product **9b** (9.5 mg, 34%) as a white solid. The stereochemistry was determined by X-ray analysis of product **9b**. A crystal suitable for the analysis was obtained by recrystallization from diethyl ether.

^{1}H NMR (600 MHz, CDCl$_3$) (observed as a mixture of rotamers) δ 6.06 – 6.01 (m, 1H), 5.88 – 5.73 (m, 1H), 4.92 – 4.91 (m, 1H), 4.52 – 4.34 (m, 1H), 3.87 – 3.80 (m, 1H), 3.79 – 3.78 (m, 1H), 3.71 – 3.53 (m, 2H), 2.22 – 1.88 (m, 4H), 1.45 (s, 9H).

^{13}C NMR (151 MHz, CDCl$_3$) (observed as a mixture of rotamers) δ 171.62, 170.12, 131.75, 131.15, 128.35, 128.24, 82.49, 81.43, 60.30, 60.10, 55.81, 54.79, 47.52, 47.37, 40.02, 39.65, 31.94, 29.32, 28.14, 24.95, 22.06.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 284.1320; Found 284.1317.

Compound 9b



^{1}H NMR (600 MHz, CDCl$_3$) (observed as a mixture of rotamers) δ 6.09 – 5.99 (m, 1H), 5.85 – 5.76 (m, 1H), 4.93 – 4.67 (m, 1H), 4.41 – 4.33 (m, 1H), 3.95 – 3.84 (m, 1H), 3.83 – 3.79 (m, 1H), 3.70 – 3.51 (m, 2H), 2.30 – 2.01 (m, 2H), 2.01 – 1.80 (m, 2H), 1.47 – 1.45 (m, 9H).

^{13}C NMR (151 MHz, CDCl$_3$) (observed as a mixture of rotamers) δ 171.35, 171.02, 170.68, 169.77, 131.41, 131.23, 128.53, 128.13, 82.49, 81.39, 60.38, 60.10, 55.07, 54.60, 47.29, 47.00, 39.96, 31.51, 29.19, 28.13, 28.10, 24.98, 22.47.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 284.1320; Found 284.1329 .

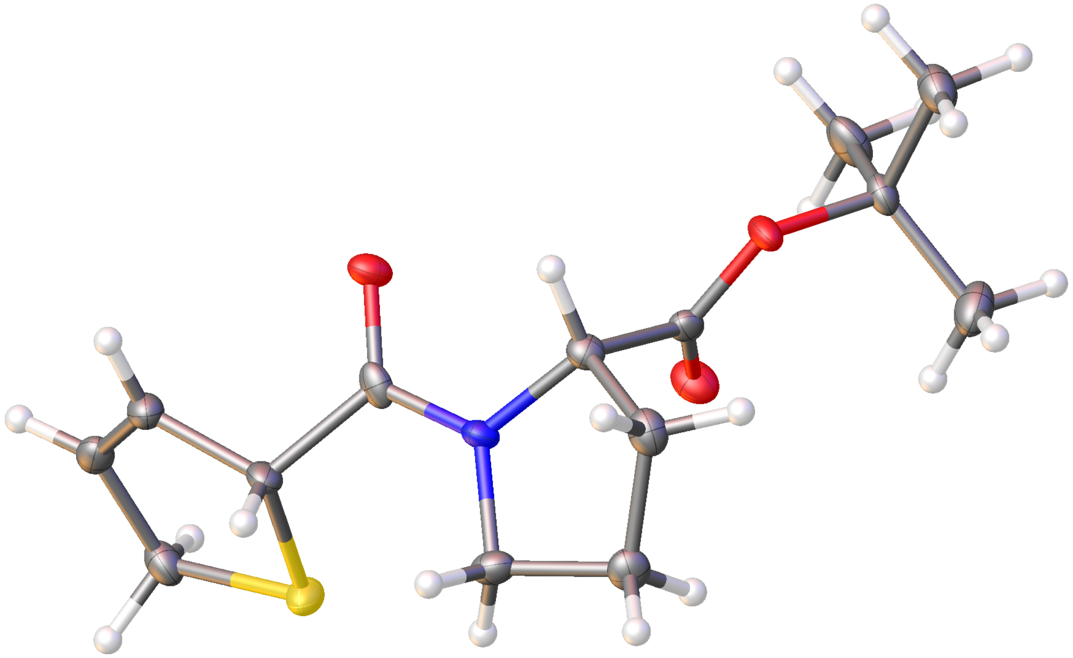
X-ray crystal structure of compound 9b

The single crystal X-ray diffraction studies were carried out on a Bruker SMART APEX II diffractometer equipped with Cu K_α radiation (λ=1.54178 Å).

Crystals of the subject compound were used as received (grow from Et2O).

A 0.120 x 0.120 x 0.020 mm colorless crystal was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using ϕ and ϖ scans. Crystal-to-detector distance was 45 mm and exposure time was 2.0, 6.0, 12.0 and 16.0 seconds (depending on the 2θ range) per frame using a scan width of 1.80°. Data collection was 99.9% complete to 67.500° in θ. A total of 7791 reflections were collected covering the indices, -7<=h<=7, -9<=k<=8, -19<=l<=19. 2726 reflections were found to be symmetry independent, with a R_{int} of 0.0473. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be *P2/₁*. The data were integrated using the Bruker SAINT Software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

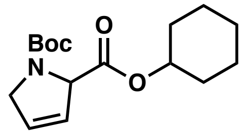
All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All carbon bonded hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Crystallographic data are summarized below. For further information, please see CIF file (CCDC deposition number: 2122303).



Empirical formula	C14 H21 N O3 S	
Molecular formula	C14 H21 N O3 S	
Formula weight	283.38	
Temperature	100.15 K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 6.1039(4) Å	α= 90°.
	b = 7.4036(5) Å	β= 99.084(4)°.
	c = 16.1833(10) Å	γ = 90°.
Volume	722.16(8) $Å^3$	

Z	2
Density (calculated)	1.303 Mg/m^3
Absorption coefficient	2.029 mm^{-1}
F(000)	304
Crystal size	0.12 x 0.12 x 0.02 mm^3
Crystal color, habit	colorless plate
Theta range for data collection	2.765 to 70.179°.
Index ranges	-7<=h<=7, -9<=k<=8, -19<=l<=19
Reflections collected	7791
Independent reflections	2726 [R(int) = 0.0473]
Completeness to theta = 67.500°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7533 and 0.5724
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2726 / 1 / 175
Goodness-of-fit on F^2	1.036
Final R indices [I>2sigma(I)]	R1 = 0.0395, wR2 = 0.0904
R indices (all data)	R1 = 0.0456, wR2 = 0.0934
Absolute structure parameter	0.014(19)
Largest diff. peak and hole	0.357 and -0.215 e.Å^{-3}

Compound 10



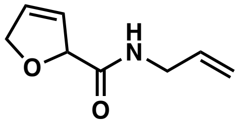
Following the general procedure, the reaction was performed with **10s** (29 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **10** in 59% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 5:1) to furnish product **10** (16.1 mg, 55%) as a colorless oil.

^{1}H NMR (600 MHz, CDCl$_3$) (observed as a mixture of rotamers) δ 6.00 – 5.89 (m, 1H), 5.78 – 5.66 (m, 1H), 5.01 – 4.90 (m, 1H), 4.82 – 4.78 (m, 1H), 4.30 – 4.12 (m, 2H), 1.82 (br, 2H), 1.73 – 1.70 (m, 2H), 1.59 – 1.09 (m, 15H).

^{13}C NMR (151 MHz, CDCl$_3$) (observed as a mixture of rotamers) δ 170.13, 169.79, 153.94, 153.64, 129.29, 129.19, 125.30, 125.18, 80.28, 80.26, 80.05, 73.59, 73.48, 66.95, 66.71, 53.67, 53.48, 31.66, 31.55, 31.47, 28.57, 28.48, 25.52, 25.45, 23.75, 23.72, 23.60.

HRMS (ESI-TOF, m/z): Calcd for $[M+Na]^+$ 318.1681; Found 318.1686.

Compound 11



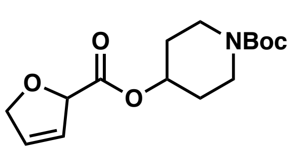
Following the general procedure, the reaction was performed with **11s** (15 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **11** in 91% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 1:2) to furnish product **11** (14.0 mg, 92%) as a colorless oil.

^{1}H NMR (600 MHz, CDCl$_3$) δ 6.69 (br, 1H), 6.04 – 6.02 (m, 1H), 5.97 – 5.95 (m, 1H), 5.86 – 5.80 (m, 1H), 5.21 – 5.14 (m, 2H), 5.13 – 5.12 (m, 1H), 4.83 – 4.73 (m, 2H), 3.93 – 3.82 (m, 2H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 171.01, 134.05, 127.13, 126.91, 116.49, 86.36, 76.73, 41.23.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 154.0868; Found 154.0870.

Compound 12



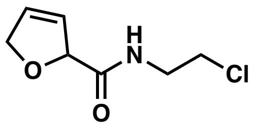
Following the general procedure, the reaction was performed with **12s** (90 mg, 0.3 mmol), tetramethylammonium tetrafluoroborate (150 mg, 0.9 mmol) and DMS (66 μL, 0.9 mmol) in 4.0 mL of EtOH and 4.0 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **12** in 67% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 2:1) to furnish product **12** (49.5 mg, 56%) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 6.08 – 6.06 (m, 1H), 5.86 – 5.84 (m, 1H), 5.26 – 5.24 (m, 1H), 5.00 – 4.97 (m, 1H), 4.88 – 4.84 (m, 1H), 4.76 – 4.73 (m, 1H), 3.69 – 3.66 (m, 2H), 3.27 – 3.23 (m, 2H), 1.87 – 1.83 (m, 2H), 1.65 – 1.60 (m, 2H), 1.45 (s, 9H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 170.69, 154.84, 129.56, 124.84, 84.60, 79.87, 76.87, 70.68, 40.97, 30.59, 28.54.

HRMS (ESI-TOF, m/z): Calcd for $[M+Na]^+$ 320.1474; Found 320.1474.

Compound 13



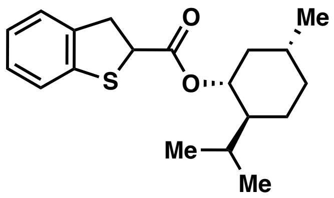
Following the general procedure, the reaction was performed with **13s** (17 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **13** in 61% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 1:1) to furnish product **13** (10.4 mg, 59%) as a colorless oil.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.02 (br, 1H), 6.02 – 6.00 (m, 1H), 5.98 – 5.96 (m, 1H), 5.21 – 5.14 (m, 1H), 4.84 – 4.80 (m, 1H), 4.78 – 4.75 (m, 1H), 3.64 – 3.57 (m, 4H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 171.46, 127.44, 126.55, 86.23, 76.78, 43.88, 40.63.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 176.0478; Found 176.0486.

Compound 14 (Mixture of diastereomers)



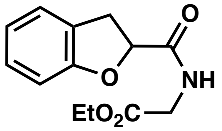
Following the general procedure, the reaction was performed with **14s** (32 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **14** in 79% (dr = 1:1, nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 30:1) to furnish product **14** (19.8 mg, 62%, dr = 1:0.9) as a colorless oil.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.20 – 7.10 (m, 3H), 7.04 – 7.01 (m, 1H), 4.70 – 4.66 (m, 1H), 4.47 – 4.38 (m, 1H), 3.71 – 3.63 (m, 1H), 3.47 – 3.43 (m, 1H), 2.02 – 2.00 (m, 1H), 1.96 – 1.94 (m, *J* = 7.0, 2.8 Hz, 1H), 1.75 –1.73 (m, *J* = 7.0, 2.8 Hz, 1H), 1.69 – 1.65 (m, 2H), 1.48 – 1.46 (m, 1H), 1.43 – 1.31 (m, 1H), 1.08 – 0.94 (m, 2H), 0.93 – 0.82 (m, 6H), 0.73 (dd, *J* = 8.5, 7.0 Hz, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 171.49, 171.39, 139.54, 139.37, 138.79, 138.65, 127.69, 127.65, 124.80, 124.76, 124.67, 124.64, 121.73, 121.71, 75.93, 75.81, 49.32, 49.17, 47.17, 47.04, 40.82, 40.59, 38.37, 38.18, 34.33, 31.53, 31.52, 26.21, 26.14, 23.45, 23.36, 22.14, 20.96, 20.90, 16.34, 16.25.

HRMS (ESI-TOF, m/z): Calcd for [M+H]$^+$ 319.1732; Found 319.1725.

Compound 15



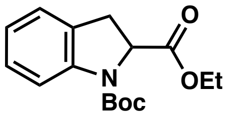
Following the general procedure, the reaction was performed with **15s** (25 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **15** in 81% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 1:1) to furnish product **15** (15.8 mg, 63%) as a colorless.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.22 – 7.09 (m, 3H), 6.95 – 6.84 (m, 2H), 5.17 (dd, *J* = 10.8, 6.5 Hz, 1H), 4.22 – 4.18 (m, 2H), 4.11 (dd, *J* = 18.3, 5.6 Hz, 1H), 3.99 (dd, *J* = 18.3, 5.2 Hz, 1H), 3.62 – 3.57 (m, 1H), 3.47 – 3.38 (m, 1H), 1.26 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 172.06, 169.45, 158.41, 128.42, 125.36, 125.26, 121.91, 109.90, 80.47, 61.74, 41.10, 34.05, 14.23.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 250.1079; Found 250.1084.

Compound 16



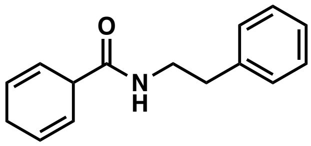
Following the general procedure, the reaction was performed with **16s** (29 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 10 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **16** in 84% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 10:1) to furnish product **16** (23.2 mg, 80%) as a colorless.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.89 – 7.49 (m, 1H), 7.19 (br, 1H), 7.13 – 7.05 (m, 1H), 6.95 – 6.93 (m, 1H), 4.97 – 4.76 (m, 1H), 4.21 (br, 2H), 3.53 – 3.48 (m, 1H), 3.12 – 3.08 (m, 1H), 1.61 – 1.50 (m, 9H), 1.28 – 1.25 (m, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 172.12, 151.78, 142.75, 128.02, 124.87, 124.43, 122.63, 114.77, 81.38, 61.42, 60.55, 32.87, 28.38, 14.34.

HRMS (ESI-TOF, m/z): Calcd for $[M+Na]^+$ 314.1368; Found 314.1363.

Compound 17



Following the general procedure, the reaction was performed with **17s** (23 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5

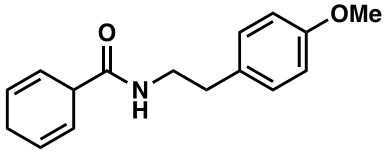
mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **17** in 59% and benzyl alcohol in 33% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 1:1) to furnish product **17** (13.0 mg, 57%) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.32 – 7.27 (m, 2H), 7.24 – 7.20 (m, 1H), 7.18 – 7.14 (m, 2H), 5.88 – 5.85 (m, 2H), 5.76 – 5.73 (m, 2H), 5.69 (br, 1H), 3.61 – 3.58 (m, 1H), 3.50 – 3.47 (m, 2H), 2.79 (t, J = 6.8 Hz, 2H), 2.75 – 2.58 (m, 2H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 172.47, 139.00, 129.02, 128.69, 126.99, 126.63, 123.74, 45.02, 40.82, 35.80, 26.03.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 228.1388; Found 228.1383.

Compound 18



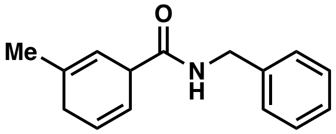
Following the general procedure, the reaction was performed with **18s** (26 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **18** in 44% and benzyl alcohol in 27% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 1:1) to furnish product **18** (10.1 mg, 39%) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.10 – 7.05 (m, 2H), 6.85 – 6.81 (m, 2H), 5.89 – 5.85 (m, 2H), 5.77 – 5.72 (m, 2H), 5.69 (br, 1H), 3.79 (s, 3H), 3.61 – 3.57 (m, 1H), 3.44 (td, J = 6.9, 6.0 Hz, 2H), 2.73 (t, J = 6.8 Hz, 2H), 2.71 – 2.59 (m, 2H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 172.45, 158.40, 131.01, 129.95, 126.97, 123.77, 114.09, 55.42, 45.02, 41.03, 34.90, 26.05.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 258.1494; Found 258.1501.

Compound 19



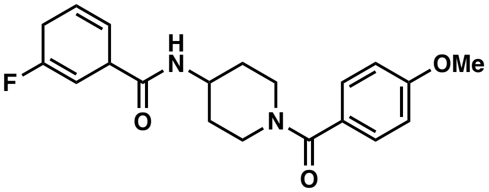
Following the general procedure, the reaction was performed with **19s** (23 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **19** in 43% and 3-methylbenzyl alcohol in 26% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 2:1) to furnish product **19** (9.5 mg, 42%) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.36 – 7.29 (m, 2H), 7.30 – 7.26 (m, 1H), 7.26 – 7.22 (m, 2H), 5.93 – 5.90 (m, 2H), 5.84 – 5.82 (m, 1H), 5.55 – 5.53 (m, 1H), 4.48 – 4.39 (m, 2H), 3.70 – 3.68 (m, 1H), 2.67 – 2.57 (m, 2H), 1.74 (s, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 173.00, 138.53, 134.85, 128.83, 127.66, 127.55, 127.08, 123.48, 117.86, 46.19, 43.61, 30.93, 23.52.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 228.1388; Found 228.1394.

Compound 20

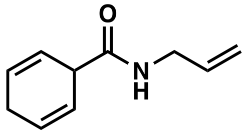


Following the general procedure, the reaction was performed with **20s** (18 mg, 0.05 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 10 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **20** in 48% and 3-fluorobenzyl alcohol in 34% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (AcOEt) to furnish product **20** (5.2 mg, 29%) as a white solid.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37 (d, *J* = 8.9 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 5.90 – 5.80 (m, 1H), 5.78 – 5.74 (m, 1H), 5.55 (d, *J* = 8.1 Hz, 1H), 5.33 – 5.28 (m, 1H), 4.02 – 3.98 (m, 1H), 3.83 (s, 3H), 3.79 – 3.73 (m, 1H), 3.02 – 2.98 (br, 2H), 2.95 – 2.86 (m, 2H), 1.94 (br, 2H), 1.71 (br, 2H), 1.35 (br, 2H).
^{13}C NMR (151 MHz, CDCl$_3$) δ 171.28 (J_{CF} = 1.5 Hz), 170.73, 161.05, 159.70 (260 Hz), 129.14, 127.65, 124.94 (J_{CF} = 11 Hz), 123.74 (J_{CF} = 3.0 Hz), 113.91, 99.58 (J_{CF} = 17 Hz), 55.51, 47.05, 46.15 (J_{CF} = 6.0 Hz), 32.96-31.60 (br), 26.95 (J_{CF} = 27 Hz).
^{19}F NMR (376 MHz, CDCl$_3$) δ -99.97.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 359.1771; Found 359.1766.

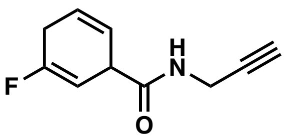
Compound 21



Following the general procedure, the reaction was performed with **21s** (16 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 µL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **21** in 44% and benzyl alcohol in 19% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 1:1) to furnish product **21** (6.1 mg, 37%) as a colorless.
^{1}H NMR (600 MHz, CDCl$_3$) δ 5.95 – 5.91 (m, 2H), 5.86 – 5.79 (m, 3H), 5.75 (br, 1H), 5.18 – 5.08 (m, 2H), 3.88 – 3.86 (m, 2H), 3.67 – 3.64 (m, 1H), 2.76 – 2.73 (m, 2H).
^{13}C NMR (151 MHz, CDCl$_3$) δ 172.45, 134.34, 127.14, 123.74, 116.20, 45.00, 41.97, 26.08.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 164.1075; Found 164.1080.

Compound 22



Following the general procedure, the reaction was performed with **22s** (18 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 µL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **22** in 62% and 3-fluorobenzyl alcohol in 12% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/Et_2O = 1:3) to furnish product **22** (10.8 mg, 60%) as white solid.

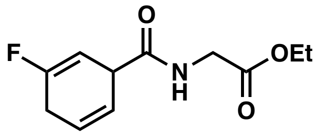
^{1}H NMR (600 MHz, $CDCl_3$) δ 5.92 – 5.73 (m, 3H), 5.35 – 5.31 (m, 1H), 4.04 – 4.01 (m, 2H), 3.85 – 3.81 (m, 1H), 2.94 – 2.91 (m, 2H), 2.25 – 2.23 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.32 (J_{CF} = 3.0 Hz), 159.81 (J_{CF} = 258 Hz), 125.04 (J_{CF} = 11 Hz), 123.50 (J_{CF} = 3.0 Hz), 99.37 (J_{CF} = 18 Hz), 79.32, 72.04, 45.88 (J_{CF} = 6.0 Hz), 29.63, 26.97 (J_{CF} = 26 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -102.68.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 180.0825; Found 180.0822.

Compound 23



Following the general procedure, the reaction was performed with **23s** (23 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **23** in 71% and 3-fluorobenzyl alcohol in 19% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 1:1) to furnish product **23** (15.5 mg, 69%) as a white solid.

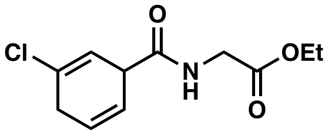
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.19 (br, 1H), 5.92 – 5.83 (m, 1H), 5.81 – 5.78 (m, 1H), 5.37 – 5.34 (m, 1H), 4.21 (q, J = 7.2 Hz, 2H), 4.00 (dd, J = 5.2, 1.6 Hz, 2H), 3.85 – 3.83 (m, 1H), 2.94 – 2.90 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.89 (J_{CF} = 1.5 Hz), 169.86, 159.71 (J_{CF} = 258 Hz), 125.08 (J_{CF} = 11 Hz), 123.50 (J_{CF} = 1.5 Hz), 99.44 (J_{CF} = 18 Hz), 61.75, 45.86 (J_{CF} = 7.6 Hz), 41.62, 26.95 (J_{CF} = 27 Hz), 14.25.

^{19}F NMR (376 MHz, CDCl$_3$) δ -102.98.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 228.1036; Found 228.1041.

Compound 24



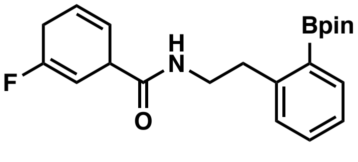
Following the general procedure, the reaction was performed with **24s** (24 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 10 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **24** in 71% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/Et$_2$O = 1:3, then toluene/AcOEt = 10:1) to furnish product **24** (13.0 mg, 54%) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 6.13 (br, 1H), 5.95 – 5.92 (m, 1H), 5.91 – 5.90 (m, 1H), 5.83 – 5.80 (m, 1H), 4.24 – 4.20 (m, 2H), 4.08 – 3.95 (m, 2H), 3.82 – 3.79 (m, 1H), 3.04 – 2.99 (m, 2H), 1.29 (t, J = 7.2 Hz, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 171.19, 169.83, 132.86, 126.61, 122.38, 120.50, 61.80, 47.10, 41.67, 33.48, 14.27.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 244.0740; Found 244.0734.

Compound 25



Following the general procedure, the reaction was performed with **25s** (37 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 10 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **25** in 40% and 3-fluorobenzyl alcohol in 22% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 1:1, then toluene/AcOEt = 5:1) to furnish product **25** (11.8 mg, 32%) as a colorless amorphous.

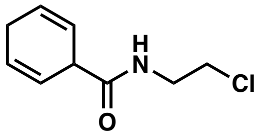
^{1}H NMR (600 MHz, CDCl$_3$) δ 7.80 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.36 (td, *J* = 7.5, 1.6 Hz, 1H), 7.25 – 7.21 (m, 1H), 7.13 – 7.11 (m, 1H), 5.78 – 5.75 (m, 2H), 5.73 – 5.68 (m, 1H), 5.26 – 5.22 (m, 1H), 3.73 – 3.71 (m, 1H), 3.53 – 3.46 (m, 2H), 3.05 (t, *J* = 6.6 Hz, 2H), 2.86 – 2.80 (m, 2H), 1.35 (s, 12H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 171.53 (J_{CF} = 3.0 Hz), 159.37 (J_{CF} = 257 Hz), 145.60, 136.58, 131.16, 130.01, 126.06, 124.40 (J_{CF} = 11 Hz), 124.11, 124.09, 99.83 (J_{CF} = 17 Hz), 83.93, 46.14 (J_{CF} = 7.6 Hz), 41.74, 35.20, 26.92 (J_{CF} = 26 Hz), 25.04.

^{19}F NMR (376 MHz, CDCl$_3$) δ -100.76.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 371.2183; Found 371.2177.

Compound 26



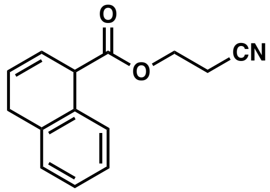
Following the general procedure, the reaction was performed with **26s** (18 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **26** in 33% and benzyl alcohol in 18% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 2:1) to furnish product **26** (6.0 mg, 33%) as a colorless oil.

^{1}H NMR (600 MHz, CDCl$_3$) δ 6.12 (br, 1H), 5.97 – 5.94 (m, 2H), 5.82 – 5.79 (m, 2H), 3.69 – 3.54 (m, 5H), 2.77 – 2.74 (m, 2H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 172.87, 127.42, 123.39, 44.88, 44.15, 41.38, 26.08.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 186.0686; Found 186.0687.

Compound 27



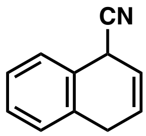
Following the general procedure, the reaction was performed with **27s** (23 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **27** in 42% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (toluene/AcOEt = 10:1) to furnish product **27** (6.7 mg, 30%) as a colorless oil.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.28 – 7.17 (m, 4H), 6.24 – 6.18 (m, 1H), 5.99 – 5.96 (m, 1H), 4.52 – 4.46 (m, 1H), 4.34 – 4.22 (m, 2H), 3.59 – 3.50 (m, 1H), 3.42 – 3.35 (m, 1H), 2.72 – 2.60 (m, 2H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 172.19, 134.45, 131.08, 128.89, 128.81, 128.58, 127.64, 126.57, 122.29, 116.70, 59.31, 46.59, 29.97, 18.07.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 228.1025; Found 228.1030.

Compound 28



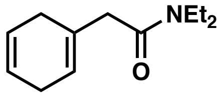
For 1-naphthonitrile, the procedure was adapted from our previous rAP imide reduction, *(6)* since the standard condition gave the overreduction. The reaction was performed with the corresponding aromatic substrate (15 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and pivalic acid (31 mg, 0.3 mmol) in 3.0 mL of MeOH. The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with rapid alternating polarity (100 ms, 5 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **28** in 95% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 5:1) to furnish product **28** (14.0 mg, 90%) as a colorless oil.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.46 – 7.41 (m, 1H), 7.32 – 7.27 (m, 2H), 7.22 – 7.16 (m, 1H), 6.23 – 6.20 (m, 1H), 5.95 – 5.92 (m, 1H), 4.64 – 4.61 (m, 1H), 3.54 – 3.45 (m, 1H), 3.45 – 3.36 (m, 1H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 133.37, 129.22, 128.97, 128.42, 128.40, 128.00, 127.27, 120.01, 119.79, 31.06, 29.34.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 156.0813; Found 156.0810.

Compound 29



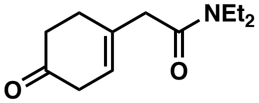
Following the general procedure, the reaction was performed with **43** (19 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with rapid alternating polarity (100 ms, 5 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **29** in 45% and the starting material in 42% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (CH_2Cl_2/AcOEt = 10:1, 2 times) to furnish product **29** (3.5 mg, 18%) as a colorless oil (significant loss in separation from the starting material due to the close Rf value).

^{1}H NMR (600 MHz, CDCl$_3$) δ 5.72 – 5.66 (m, 2H), 5.51 – 5.48 (m, 1H), 3.38 (q, J = 7.1 Hz, 2H), 3.30 (q, J = 7.1 Hz, 2H), 3.01 (s, 2H), 2.75 – 2.69 (m, 2H), 2.68 – 2.63 (m, 2H), 1.18 – 1.12 (m, 6H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 169.97, 129.96, 124.16, 123.92, 121.44, 43.01, 42.39, 40.13, 29.41, 26.99, 14.45, 13.19.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 194.1545; Found 194.1547.

Compound 30



Following the general procedure, the reaction was performed with **30s** (22 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at room temperature, under a constant current of

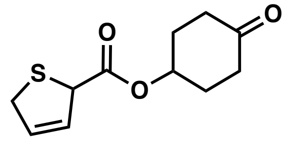
20 mA with rapid alternating polarity (100 ms, 5 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **30** in 30% and the starting material in 38% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (AcOEt) to furnish product **30** (5.5 mg, 25%) as an off-white solid.

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.55 – 5.53 (m, 1H), 3.38 (q, *J* = 7.2 Hz, 2H), 3.30 (q, *J* = 7.1 Hz, 2H), 3.13 – 3.12 (m, 2H), 2.91 – 2.89 (m, 2H), 2.59 – 2.44 (m, 4H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 210.39, 169.61, 133.78, 121.40, 42.38, 41.80, 40.32, 39.81, 38.68, 28.88, 14.49, 13.18.

HRMS (ESI-TOF, m/z): Calcd for [M+H]$^+$ 210.1494; Found 210.1497.

Compound 31



Following the general procedure, the reaction was performed with **31s** (22 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 *μ*L, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 10 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **31** in 50%, **31’** (alcohol) in 25% and the starting material in 17% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 1:1) to furnish product **31** (9.0 mg, 40%) as a colorless oil and product **31’** (alcohol) (1:1 cis-trans mixture, 5.3 mg, 23%) as a colorless oil.

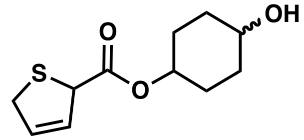
^{1}H NMR (600 MHz, CDCl$_3$) δ 6.09 – 6.07 (m, 1H), 5.88 – 5.85 (m, 1H), 5.20 – 5.18 (m, 1H), 4.83 – 4.81 (m, 1H), 3.89 – 3.85 (m, 1H), 3.82 – 3.79 (m, 1H), 2.61 – 2.56 (m, 2H), 2.38 – 2.33 (m, 2H), 2.19 – 2.14 (m, 2H), 2.07 – 2.02 (m, 2H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 209.90, 171.31, 132.28, 127.11, 69.63, 55.77, 39.54, 37.21, 37.18, 30.37, 30.24.

HRMS (ESI-TOF, m/z): Not found.

GC/MS (EI): 226 (4%), 130 (9%), 111 (13%), 96 (13%), 85 (100%).

Compound 31’ (1:1 cis-trans mixture)

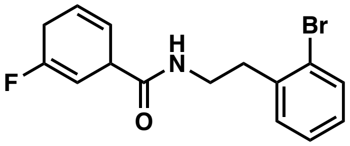


^{1}H NMR (600 MHz, $CDCl_3$) δ 6.06 – 6.03 (m, 1H), 5.86 – 5.82 (m, 1H), 4.92 – 4.73 (m, 2H), 3.91 – 3.81 (m, 1H), 3.81 – 3.69 (m, 2H), 2.07 – 1.85 (m, 3H), 1.80 – 1.32 (m, 7H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.48, 171.38, 131.90, 131.89, 127.45, 127.42, 72.87, 68.81, 56.04, 55.92, 39.49, 39.48, 31.95, 30.57, 28.21, 28.09, 27.53, 27.43.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 229.0898; Found 229.0902.

Compound 32



Following the general procedure, the reaction was performed with **32s** (32 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 10 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. After passing through a short silica gel pad, ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **32** in 31%, **32’** (deBr) in 13% and the starting material in 17% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 1:1) to furnish product **32** (9.0 mg, 28%) as a colorless oil and product **32’** (deBr) (3.5 mg, 11%) as a white solid.

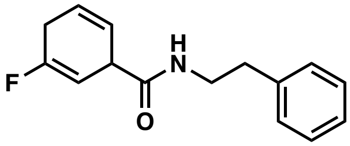
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (dd, J = 8.0, 1.3 Hz, 1H), 7.24 (td, J = 7.4, 1.3 Hz, 1H), 7.18 (dd, J = 7.6, 1.8 Hz, 1H), 7.11 – 7.09 (m, 1H), 5.82 – 5.79 (m, 1H), 5.76 – 5.63 (m, 2H), 5.29 – 5.25 (m, 1H), 3.77 – 3.74 (m, 1H), 3.56 – 3.49 (m, 2H), 2.97 (t, J = 6.8 Hz, 2H), 2.88 – 2.85 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.77, 159.53 (J_{CF} = 258 Hz), 138.22, 133.10, 131.34, 128.52, 127.66, 124.74, 124.68 (J_{CF} = 11 Hz), 123.94, 99.75 (J_{CF} = 18 Hz), 46.20 (J_{CF} = 7.6 Hz), 39.46, 35.65, 26.96 (J_{CF} = 27 Hz).

^{19}F NMR (376 MHz, CDCl$_3$) δ -103.22.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 324.0399; Found 324.0406.

Compound 32'



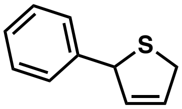
^{1}H NMR (600 MHz, CDCl$_3$) δ 7.32 – 7.29 (m, 2H), 7.25 – 7.21 (m, 1H), 7.19 – 7.13 (m, 2H), 5.82 – 5.78 (m, 1H), 5.75 – 5.72 (m, 1H), 5.64 (br, 1H), 5.28 – 5.24 (m, 1H), 3.77 – 3.73 (m, 1H), 3.52 – 3.44 (m, 2H), 2.92 – 2.81 (m, 2H), 2.80 (t, J = 6.9 Hz, 2H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 171.64 (J_{CF} = 3.0 Hz),159.51 (J_{CF} = 258 Hz), 138.81, 129.00, 128.75, 126.74, 124.63 (J_{CF} = 11 Hz), 124.00 (J_{CF} = 3.0 Hz), 99.77 (J_{CF} = 17 Hz), 46.24 (J_{CF} = 6.0 Hz), 40.88, 35.70, 26.91 (J_{CF} = 26 Hz).

^{19}F NMR (376 MHz, CDCl$_3$) δ -100.53.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 246.1294; Found 246.1292.

Compound 39



Following the general procedure, the reaction was performed with **36** (21 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **39** in 52% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 20:1) to furnish product **39** (7.0 mg, 43%) as a colorless oil.

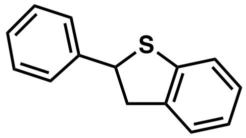
H NMR (600 MHz, CDCl$_3$) δ 7.35 – 7.26 (m, 4H), 7.25 – 7.22 (m, 1H), 6.01 – 5.99 (m, 1H), 5.84 – 5.82 (m, 1H), 5.38 – 5.35 (m, 1H), 4.01 – 3.96 (m, 1H), 3.89 – 3.85 (m, 1H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 143.62, 133.16, 128.84, 128.74, 127.73, 127.43, 58.89, 39.95.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 163.0581; Found 163.0573.

The ^{1}H and ^{13}C NMR were consistent with the reported spectral data. (*7*)

Compound 40



Following the general procedure, the reaction was performed with **37** (16 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (73 μL, 1.0 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with rapid alternating polarity (100 ms, 5 Hz) for 40 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **40** in 64% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/toluene = 5:1) to furnish product **40** (9.5 mg, 45%) as a colorless oil.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.46 – 7.40 (m, 2H), 7.34 – 7.29 (m, 2H), 7.29 – 7.26 (m, 1H), 7.23 – 7.14 (m, 3H), 7.07 – 7.04 (m, 1H), 5.07 (t, *J* = 8.2 Hz, 1H), 3.65 (dd, *J* = 15.6, 8.0 Hz, 1H), 3.51 – 3.46 (m, 1H).

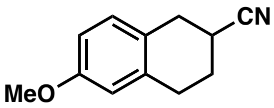
^{13}C NMR (151 MHz, CDCl$_3$) δ 141.95, 141.30, 139.12, 128.79, 127.81, 127.79, 127.29, 124.63, 124.49, 121.99, 54.13, 44.79.

HRMS (ESI-TOF, m/z): Not found.

GC/MS (EI): 212 (100%), 178 (36%), 134 (37%).

The ^{1}H and ^{13}C NMR were consistent with the reported spectral data. (*8*)

Compound 41



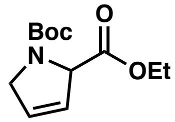
Following the general procedure, the reaction was performed with **38** (18 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **41** in 42% (nitromethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/toluene = 5:1) to furnish product **41** (7.0 mg, 39%) as a colorless oil.

^{1}H NMR (600 MHz, CDCl$_3$) δ 6.99 (d, *J* = 8.5 Hz, 1H), 6.72 (dd, *J* = 8.5, 2.7 Hz, 1H), 6.63 (d, *J* = 2.8 Hz, 1H), 3.78 (s, 3H), 3.11 – 3.03 (m, 1H), 3.02 – 2.92 (m, 3H), 2.86 – 2.80 (m, 1H), 2.22 – 2.14 (m, 1H), 2.09 – 2.01 (m, 1H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 158.41, 135.77, 130.05, 124.52, 122.26, 113.73, 112.86, 55.41, 31.81, 27.48, 26.36, 25.87.

HRMS (ESI-TOF, m/z): Calcd for $[M+H]^+$ 188.1075; Found 188.1080.

Compound 49



Following the general procedure, the reaction was performed with **48** (32 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.3 mmol) and DMS (22 *μ*L, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 10 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **49** in 43% (dibromomethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 5:1) to furnish product **49** (9.4 mg, 40%) as a colorless oil.

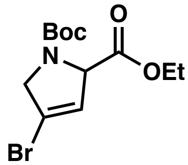
observed as a mixture of rotamers

H NMR (600 MHz, CDCl$_3$) δ 6.00 – 5.90 (m, 1H), 5.77 – 5.68 (m, 1H), 5.04 – 4.90 (m, 1H), 4.31 – 4.10 (m, 4H), 1.48 – 1.41 (m, 9H), 1.29 – 1.24 (m, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 170.79, 170.44, 154.00, 153.59, 129.44, 129.33, 125.05, 124.95, 80.31, 80.20, 66.82, 66.51, 61.37, 61.34, 53.66, 53.45, 28.56, 28.45, 14.41, 14.29.

HRMS (ESI-TOF, m/z): Calcd for $[M+Na]^+$ 264.1212; Found 264.1212.

Compound 50



Following the general procedure, the reaction was performed with **48** (32 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.3 mmol), DMS (22 *μ*L, 0.3 mmol) and acetic acid (60 mg, 1.0 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 10 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **50** in 73% (dibromomethane was used as an internal standard). The crude reaction mixture was purified by pTLC (hexane/AcOEt = 5:1) to furnish product **50** (20.8 mg, 65%) as a colorless oil.

observed as a mixture of rotamers

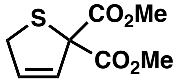
^{1}H NMR (600 MHz, $CDCl_3$) δ 5.93 – 5.86 (m, 1H), 4.96 – 4.87 (m, 1H), 4.35 – 4.31 (m, 1H), 4.29 – 4.15 (m, 3H), 1.48 – 1.42 (m, 9H), 1.30 – 1.26 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 169.48, 169.14, 153.24, 152.71, 124.92, 124.76, 119.12, 118.57, 80.96, 80.93, 67.04, 66.60, 61.74, 61.72, 57.88, 57.67, 28.49, 28.37, 14.40, 14.27.

HRMS (ESI-TOF, m/z): Calcd for $[M+Na]^+$ 342.0317; Found 342.0324.

Alkylation

Compound 42



To a mixture of diisopropylamine (40 mg, 0.40 mmol) and THF (2.0 mL) was added *n*-butyl lithium (2.5 M solution in hexane, 120 μL, 0.3 mmol) at –78 °C, and the reaction mixture was warmed up to 0 °C, then cooled to –78 °C again. To the reaction mixture was added **2** (28 mg, 0.2 mmol) in 0.5 mL of THF. After 1 h, methyl chloroformate (38 mg, 0.4 mmol) in 0.5 mL of THF was added, and the reaction mixture was stirred at –78 °C for 10 min. After warming the reaction to 0 °C, the reaction mixture was poured into sat. NH_4Cl aq., followed by extraction with AcOEt. The organic layer was washed with brine, then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/AcOEt = 5:1) to afford the desired product **42** in 64% yield (26 mg) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.12 – 6.10 (m, 1H), 5.99 – 5.97 (m, 1H), 3.88 (t, *J* = 2.4 Hz, 2H), 3.79 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 169.44, 132.74, 128.51, 73.15, 53.66, 39.83.

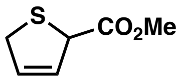
HRMS (ESI-TOF, m/z): Calcd for $[M+Na]^+$ 225.0197; Found 225.0192.

The ^{1}H and ^{13}C NMR were consistent with the reported spectral data. (*9*)

Comparisons with direct current electrolysis

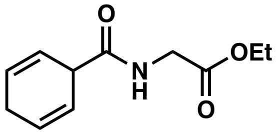
For comparisons with direct current (DC), the same current (mA) and electron amount (F/mol) as ones used in rAP reduction were applied to each substrate as the optimal DC condition, except for compound **48**. RVC electrodes were used for anode and cathode. The product yield was determined by NMR analysis of the crude reaction mixture. See the individual entries below for detailed conditions.

Compound 2



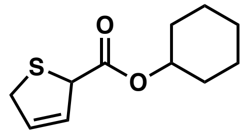
The reaction was performed with **1** (14 mg, 0.1 mmol) and tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) in 1.5 mL of EtOH and 1.5 mL of THF (DMS was not used). The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with direct current for 10 F/mol. The reaction mixture was diluted with diethyl ether and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found trace amount of **2** with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 4



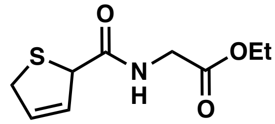
The reaction was performed with **3** (21 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **4** in 13% and benzyl alcohol in 33% with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 5



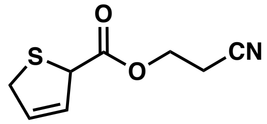
The reaction was performed with **5s** (21 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found no production of **5** with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 6



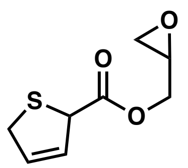
The reaction was performed with **6s** (21 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **6** in 7% with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 7



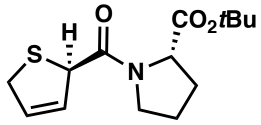
The reaction was performed with **7s** (18 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found no production of **7** with disappearance of the starting material (nitromethane was used as an internal standard).

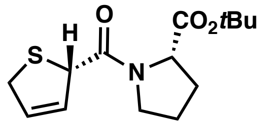
Compound 8 (Mixture of diastereomers)



The reaction was performed with **8s** (18 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found no production of **8** with disappearance of the starting material (nitromethane was used as an internal standard).

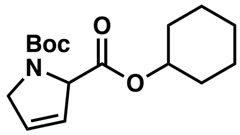
Compound 9a and 9b





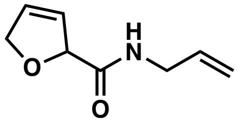
The reaction was performed with **9s** (28 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **9a** and **9b** in 48% with disappearance of the starting material (dr = 1:1, nitromethane was used as an internal standard).

Compound 10



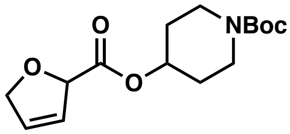
The reaction was performed with **10s** (29 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **10** in 31% with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 11



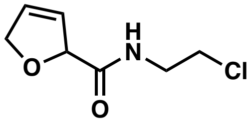
The reaction was performed with **11s** (15 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **11** in 52% with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 12



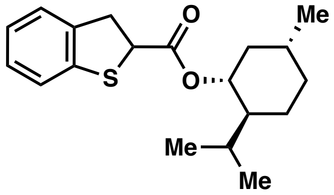
The reaction was performed with **12s** (30 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found trace amount of **12** with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 13



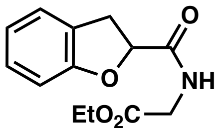
The reaction was performed with **13s** (17 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **13** in 37% with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 14 (Mixture of diastereomers)



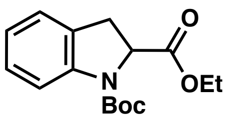
The reaction was performed **14s** (32 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found trace amount of **14** with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 15



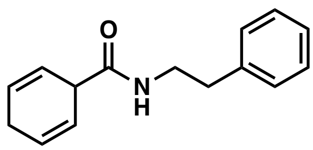
The reaction was performed **15s** (25 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA withdirect current for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **15** in 7% with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 16



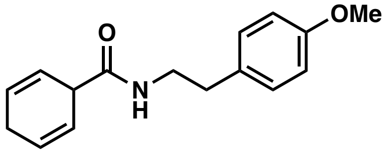
The reaction was performed with **16s** (29 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 10 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **16** in 40% with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 17



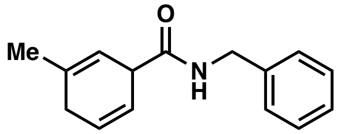
The reaction was performed with **17s** (23 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **17** in 14% and benzyl alcohol in 36% with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 18



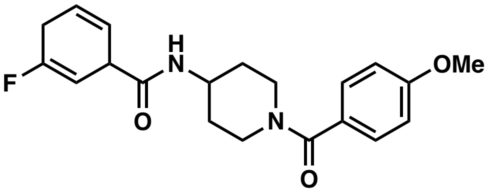
The reaction was performed with **18s** (26 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found trace amount of **18**, benzyl alcohol in 19% and trace amount of the starting material (nitromethane was used as an internal standard).

Compound 19



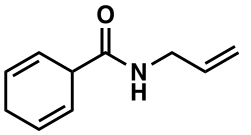
The reaction was performed with **19s** (23 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found trace amount of **19** and 3-methylbenzyl alcohol in 39% with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 20



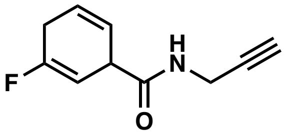
The reaction was performed with **20s** (18 mg, 0.05 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 10 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **20** in 19% with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 21



The reaction was performed with **21s** (16 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **21** in 17% and benzyl alcohol in 13% with disappearance of the starting material (nitromethane was used as an internal standard).

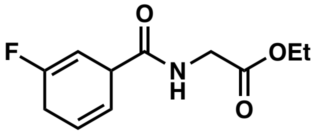
Compound 22



The reaction was performed with **22s** (18 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 15 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **22** in 31% and 3-

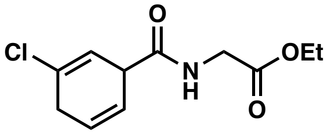
fluorobenzyl alcohol in 10% with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 23



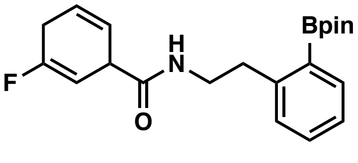
The reaction was performed with **23s** (23 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **23** in 23% and 3-fluorobenzyl alcohol in 8% with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 24



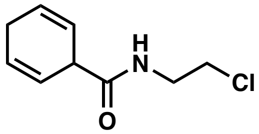
The reaction was performed with **24s** (24 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 10 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **24** in 32% with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 25



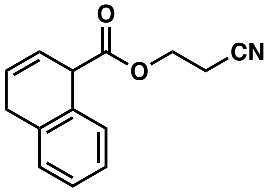
The reaction was performed with **25s** (37 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 10 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **25** in 27% and the starting material in 24% (nitromethane was used as an internal standard).

Compound 26



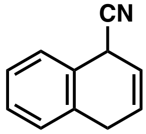
The reaction was performed with **26s** (18 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **26** in 18%, benzyl alcohol in 22% and trace amount of the starting material (nitromethane was used as an internal standard).

Compound 27



The reaction was performed with **27s** (23 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA withdirect current for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found trace amount of **27** with disappearance of the starting material (nitromethane was used as an internal standard).

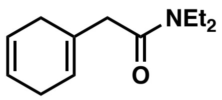
Compound 28



The reaction was performed with the corresponding aromatic substrate (15 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and pivalic acid (31 mg, 0.3 mmol) in 3.0 mL of MeOH. The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with direct current for 20

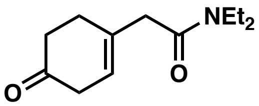
F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **28** in 24% and the starting material in 8% (nitromethane was used as an internal standard).

Compound 29



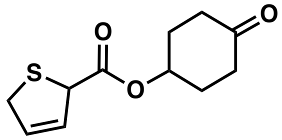
The reaction was performed with **43** (19 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with direct current for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found trace amount of **29** and the starting material in 75% (nitromethane was used as an internal standard).

Compound 30



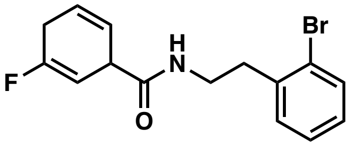
The reaction was performed with **30s** (22 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with direct current for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found no production of **30** and the starting material in 41% (nitromethane was used as an internal standard).

Compound 31



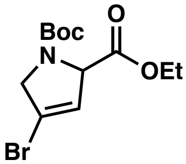
The reaction was performed with **31s** (22 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 10 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found no production of **31** and **31**' (alcohol) with disappearance of the starting material (nitromethane was used as an internal standard).

Compound 32



The reaction was performed with **32s** (32 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (50 mg, 0.3 mmol) and DMS (22 μL, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 10 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. After passing through a short silica gel pad, ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **32** in 16%, **32'** (deBr) in 13% (nitromethane was used as an internal standard).

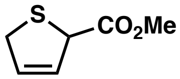
Compound 50



The reaction was performed with **48** (32 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.3 mmol), DMS (22 μL, 0.3 mmol) and acetic acid (60 mg, 1.0 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with direct current for 45 F/mol (6 h). The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **50** in 11% and the starting material in 17% (dibromomethane was used as an internal standard).

Comparisons with other Birch reduction conditions

For compound 2



Birch reduction using lithium and liquid ammonia *(10)*

To condensed liquid ammonia (~2 mL) in a round bottom flask at –78 °C was added lithium (15 mg, 5 mmol), then the resulting mixture was stirred at –78 °C. After complete dissolution of the lithium metal (deep blue color), a mixture of **1** (71 mg, 0.5 mmol), THF (0.5 mL) and *tert*-butanol (0.3 mL) was added, and the reaction mixture was stirred for 2 h. Saturated NH_4Cl aq. solution (5 mL) was added, then the resulting reaction mixture was left at ambient temperature to allow evaporation of the ammonia. The reaction mixture was diluted with diethyl ether and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^1H NMR spectroscopic analysis of the crude reaction mixture found no production of **2** with disappearance of the starting material.

Birch reduction using lithium and ethylenediamine

The procedure is adapted from K. Koide et al. (*11*) To a mixture of **1** (71 mg, 0.5 mmol) and ethylenediamine (180 mg, 3.0 mmol) and THF (3.0 mL) and *t*-BuOH (93 mg, 1.25 mmol) was added lithium (5 mg, 1.5 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h. The reaction mixture was carefully dropped into 1N HCl aq. and diluted with diethyl ether, then washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^1H NMR spectroscopic analysis of the crude reaction mixture found no production of **2** and the starting material in 8%.

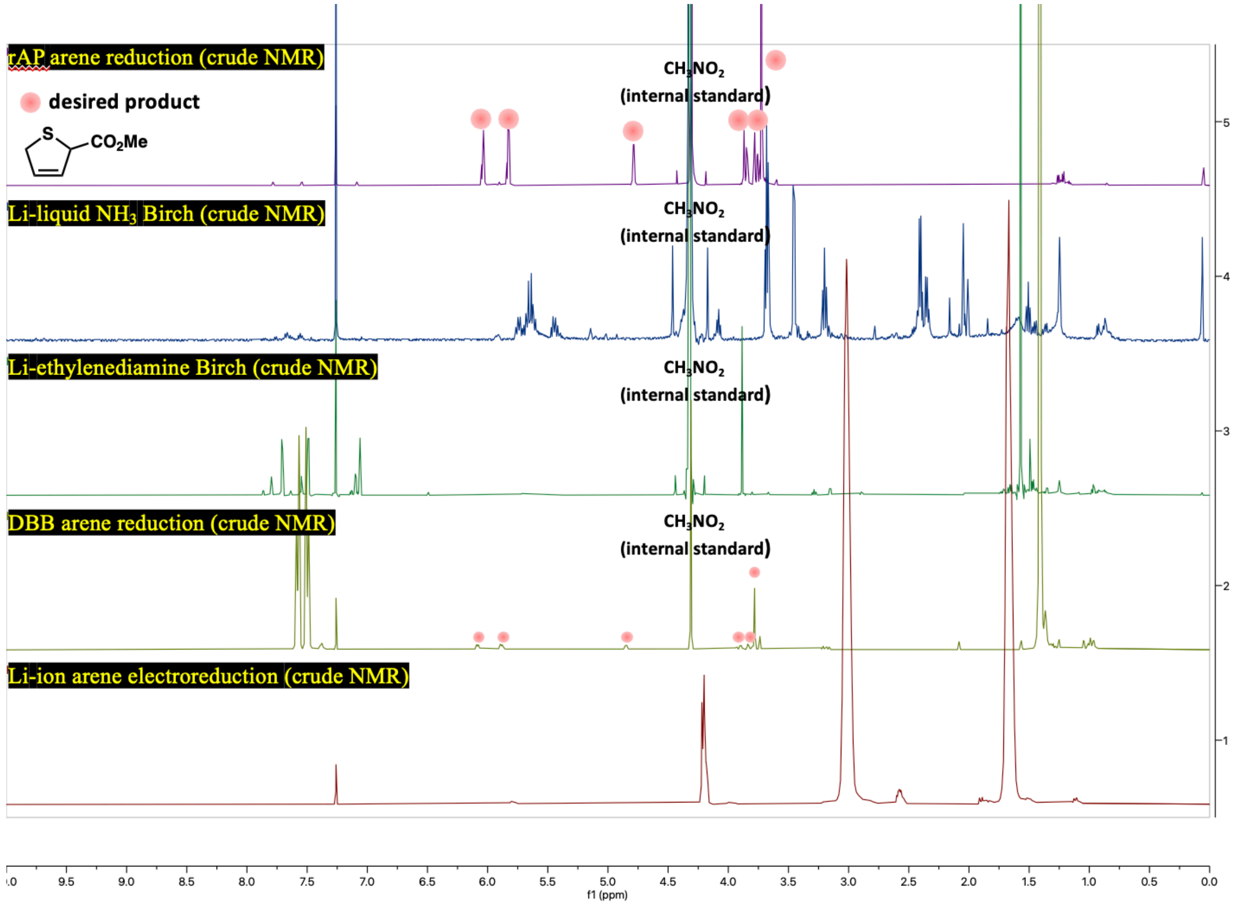
Arene reduction using lithium di-*tert*-butylbiphenyl (LiDBB)

The procedure is adapted from T. J. Donohoe et al. (*12*) Freshly cut lithium wire (6 mg, 2.0 mmol) was hammered out into a foil, cut into several small strips, and placed in a culture tube containing di-*tert*-butylbiphenyl (DBB, 533 mg, 2.0 mmol). The tube was evacuated and purged with argon several times. THF (5 mL) was added, and the contents of the tube was stirred vigorously at 0 °C for 2 h. The solution gradually became turquoise, characteristic of the DBB radical-anion. The resulting LiDBB solution was cooled to –78 °C and stirred vigorously. To the LiDBB solution was added a mixture of **1** (71 mg, 0.5 mmol), bis(methoxyethyl)amine (80 mg, 0.6 mmol) and THF (0.5 mL). The reaction mixture was stirred at –78 °C for 1 h, then carefully dropped into 1N HCl aq. The mixture was diluted with diethyl ether, then washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^1H

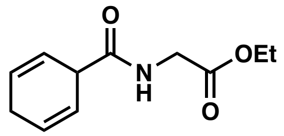
NMR spectroscopic analysis of the crude reaction mixture found **2** in 39% with disappearance of the starting material.

Li-ion arene electroreduction (LER)

The procedure is adapted from P. S. Baran et al. (*13*) The reaction was performed with **1** (14 mg, 0.1 mmol), 1,3-dimethylurea (DMU, 26 mg, 0.3 mmol), tris(pyrrolidinophosphine) oxide (257 mg, 1 mmol), 1.5 M THF solution of lithium bromide (500 μL, 0.75 mmol) and THF (2.5 mL). Using Mg for anode and galvanized steel wire for cathode, the resulting reaction mixture was electrolyzed at room temperature, under a constant current of 10 mA with direct current for 6 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found no production of **2** with disappearance of the starting material.



For compound 4



Birch reduction using lithium and liquid ammonia (*14*)

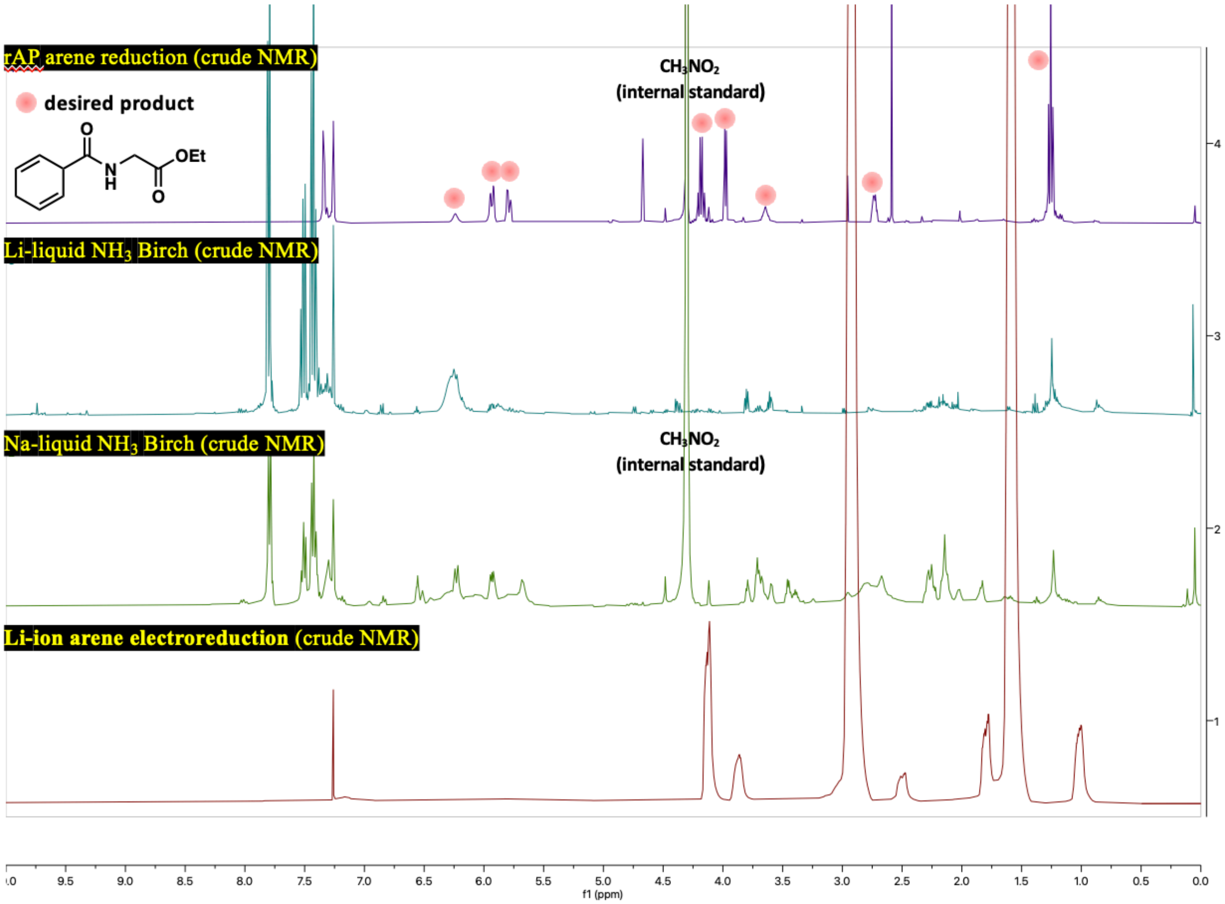
To a mixture of condensed liquid ammonia (~2 mL), **3** (105 mg, 0.5 mmol), THF (1.0 mL) and *tert*-butanol (0.3 mL) in a round bottom flask at –78 °C was added lithium (15 mg, 5 mmol). The resulting reaction mixture was stirred for 2 h. Saturated NH_4Cl solution (5 mL) was added, then the resulting reaction mixture was left at ambient temperature to allow evaporation of the ammonia. The reaction mixture was diluted with diethyl ether and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found no production of **4** with disappearance of the starting material.

Birch reduction using sodium and liquid ammonia (*14*)

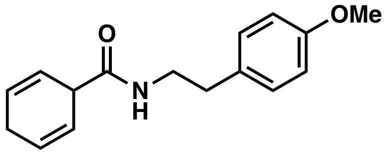
To condensed liquid ammonia (~2 mL), **3** (105 mg, 0.5 mmol), THF (1.0 mL) and *tert*-butanol (0.3 mL) in a round bottom flask at –78 °C was added sodium (57 mg, 2.5 mmol). The resulting reaction mixture was stirred for 2.5 h. Saturated NH_4Cl solution (5 mL) was added, then the resulting reaction mixture was left at ambient temperature to allow evaporation of the ammonia. The reaction mixture was diluted with diethyl ether and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found no production of **4** with disappearance of the starting material.

Li-ion arene electroreduction (LER)

The procedure is adapted from P. S. Baran et al. (*13*) The reaction was performed with **3** (21 mg, 0.1 mmol), 1,3-dimethylurea (DMU, 26 mg, 0.3 mmol), tris(pyrrolidinophosphine) oxide (257 mg, 1 mmol), 1.5 M THF solution of lithium bromide (500 μL, 0.75 mmol) and THF (2.5 mL). Using Mg for anode and galvanized steel wire for cathode, the resulting reaction mixture was electrolyzed at room temperature, under a constant current of 10 mA with direct current for 12 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found no production of **4** with disappearance of the starting material.

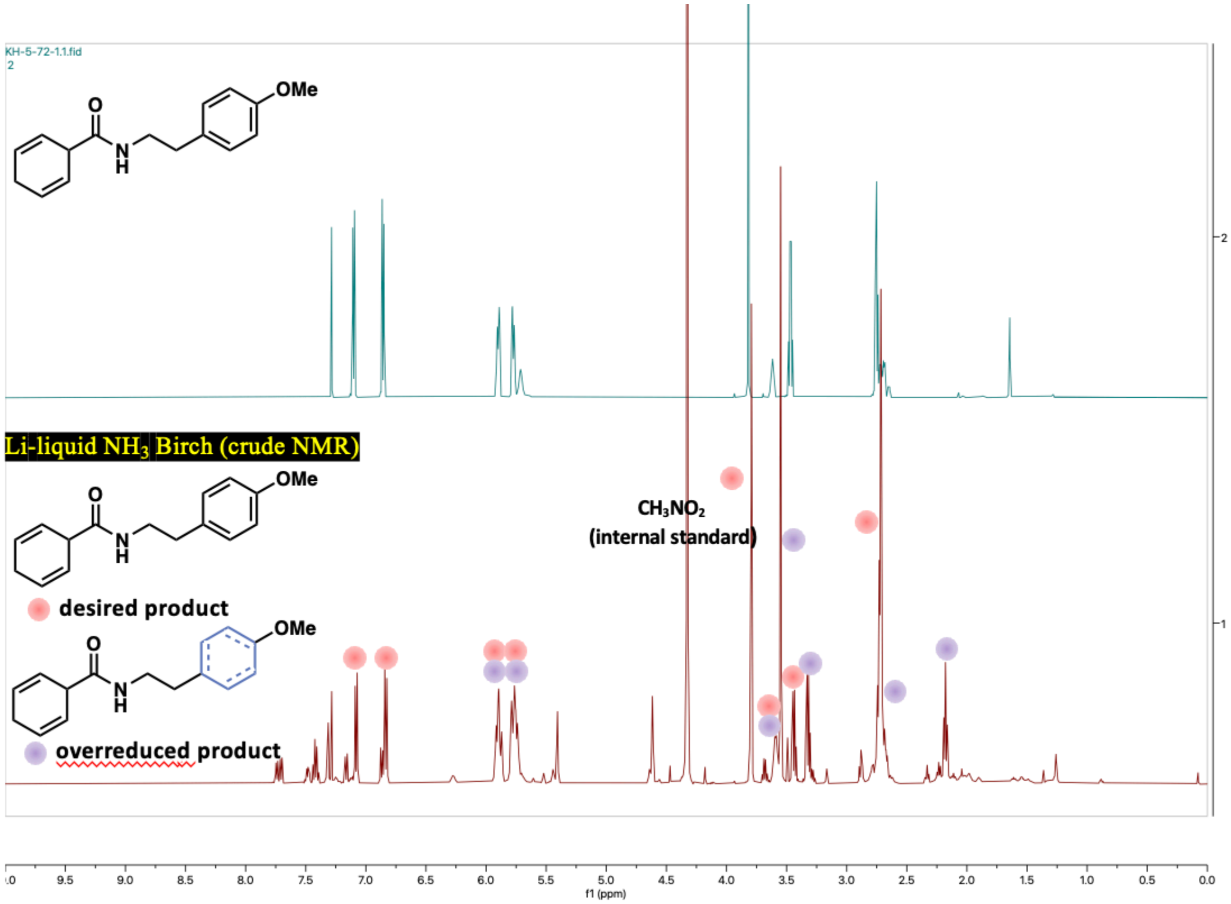


For compound 18

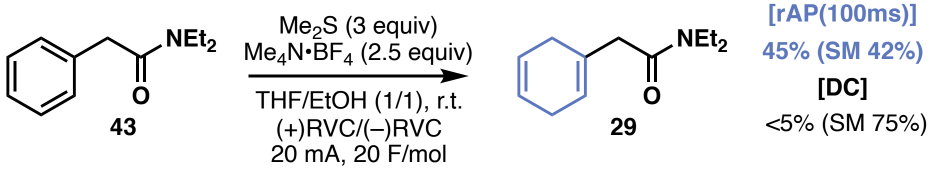


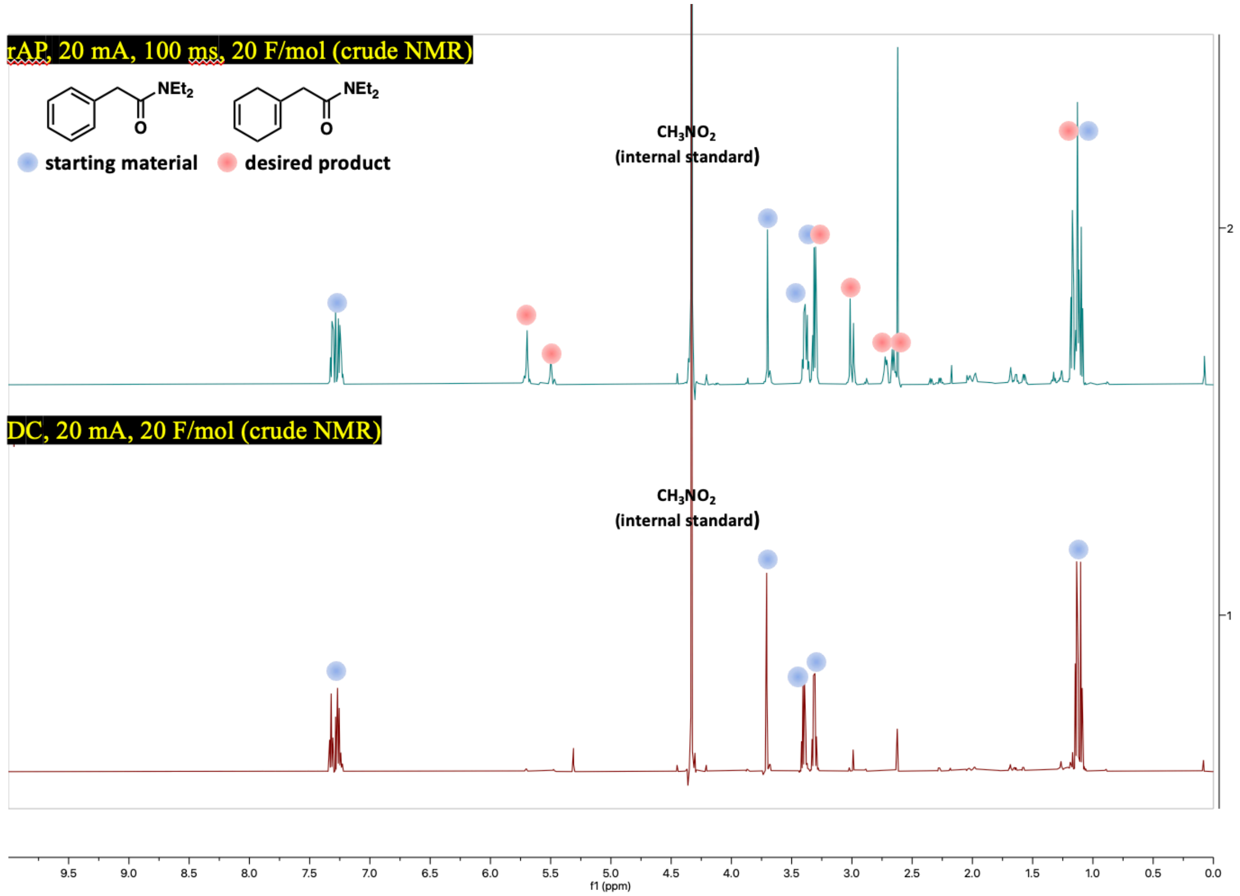
Birch reduction using lithium and liquid ammonia (*14*)

To condensed liquid ammonia (~1 mL) in a round bottom flask at –78 °C was added lithium (9 mg, 3 mmol), then the resulting mixture was stirred at –78 °C. After complete dissolution of the lithium metal (deep blue color), a mixture of **18s** (72 mg, 0.3 mmol), THF (1.0 mL) and *tert*-butanol (0.3 mL) was added, and the reaction mixture was stirred for 2 h. Saturated NH$_4$Cl solution (5 mL) was added, then the resulting reaction mixture was left at ambient temperature to allow evaporation of the ammonia. The reaction mixture was diluted with diethyl ether and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction found mixture of compound **18** in 30% and an overreduced product (inseparable from the desired product) in 38% with small amount of another reduced by-product and 9% recovery of the starting material. The Birch reduction using lithium and liquid ammonia gave non-chemoselective products.



NMR difference between rAP and DC (Figure 2A)





Direct detection of H_2 (Figure 2B)

rAP without Pd/C (20 mA, 50 ms, 10 F/mol)

The reaction was performed with *cis*-cyclooctene **44** (22 mg, 0.2 mmol) and tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 10 F/mol. To the reaction mixture was added dodecane (34 mg, 0.2 mmol) as an internal standard. GC/MS analysis of the crude reaction mixture found no cyclooctane with quantitative recovery of *cis*-cyclooctene **44**.

DC without Pd/C (20 mA, 50 ms, 10 F/mol)

The reaction was performed with *cis*-cyclooctene **44** (22 mg, 0.2 mmol) and tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with direct current for 10 F/mol. To the reaction mixture was added dodecane (34 mg, 0.2 mmol) as an internal standard. GC/MS analysis of the crude reaction mixture found no cyclooctane with 63% recovery of *cis*-cyclooctene **44**.

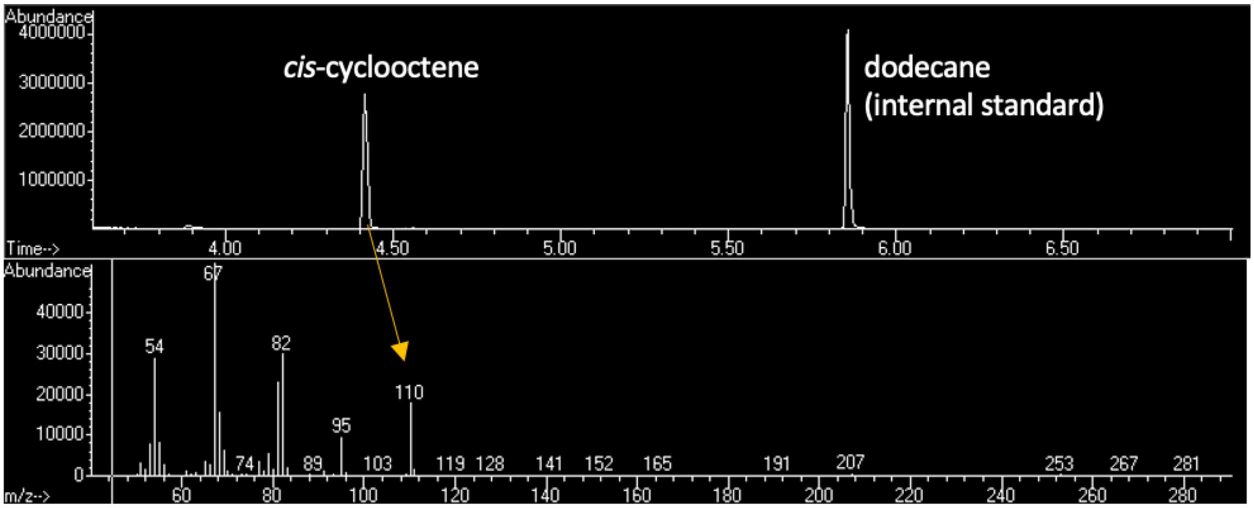
rAP with Pd/C (20 mA, 50 ms, 10 F/mol)

The reaction was performed with *cis*-cyclooctene **44** (22 mg, 0.2 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and palladium on carbon (Pd/C, 10 wt. % loading, matrix activated carbon support, 10 mg, 0.01 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 10 F/mol. To the reaction mixture was added dodecane (34 mg, 0.2 mmol) as an internal standard. GC/MS analysis of the crude reaction mixture found no cyclooctane with 97% recovery of *cis*-cyclooctene **44**.

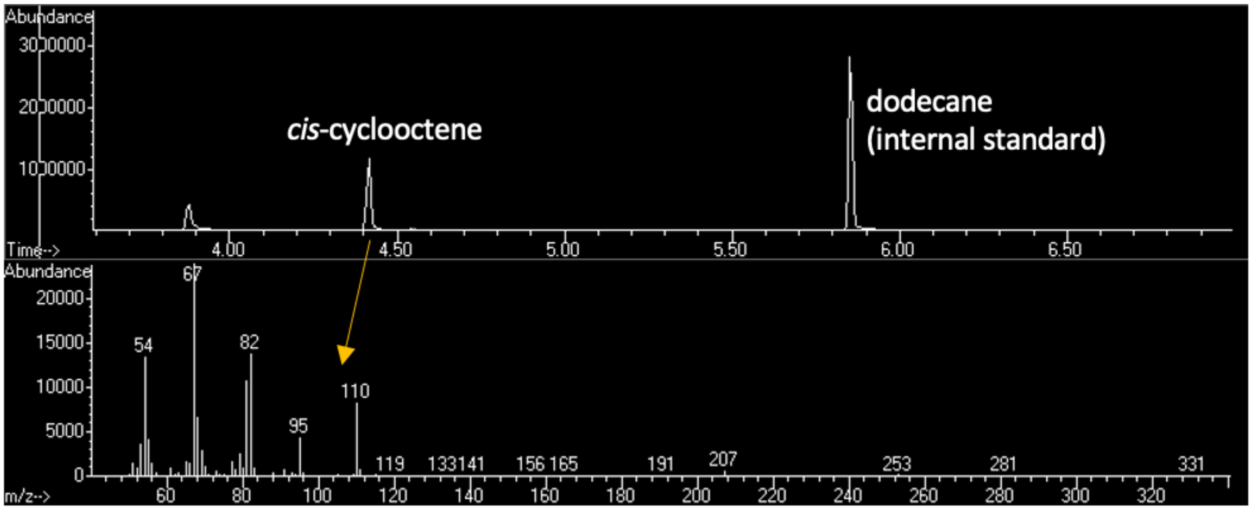
DC with Pd/C (20 mA, 50 ms, 10 F/mol)

The reaction was performed with *cis*-cyclooctene **44** (22 mg, 0.2 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and palladium on carbon (Pd/C, 10 wt. % loading, matrix activated carbon support, 10 mg, 0.01 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 10 F/mol. To the reaction mixture was added dodecane (34 mg, 0.2 mmol) as an internal standard. GC/MS analysis of the crude reaction mixture found cyclooctane **45** in 14% with 44% recovery of *cis*-cyclooctene **44**.

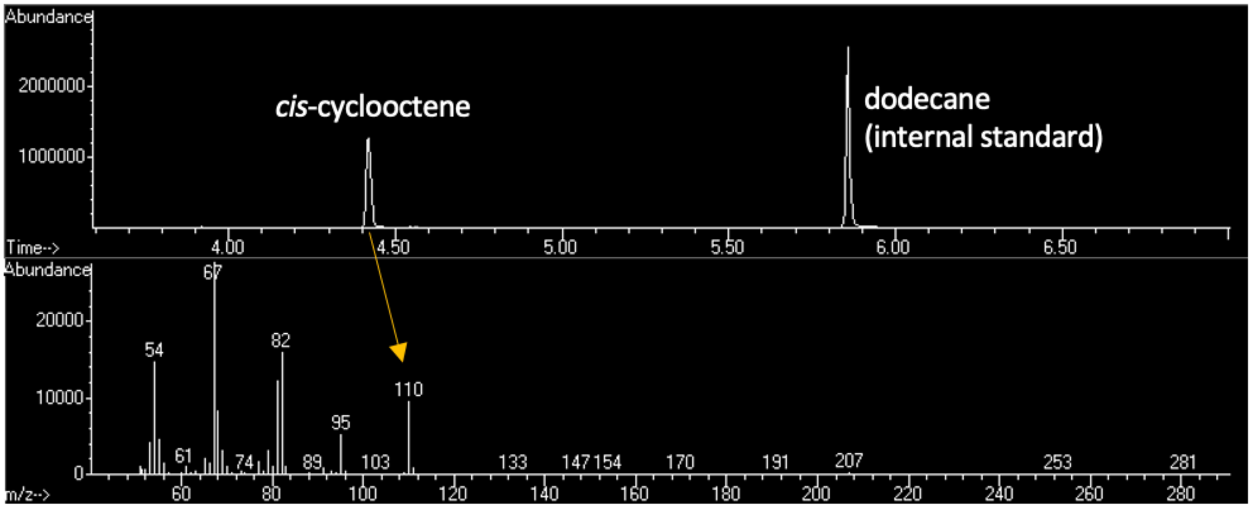
rAP without Pd/C (20 mA, 50 ms, 10 F/mol)



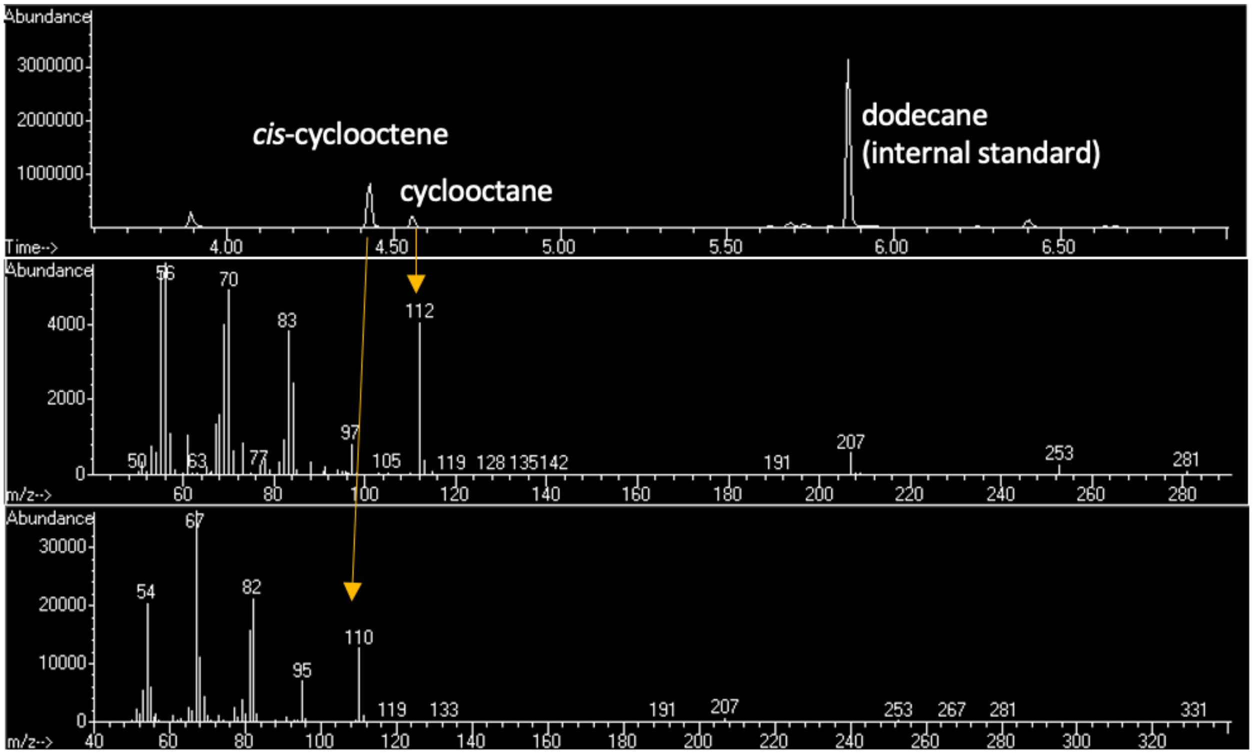
DC without Pd/C (20 mA, 10 F/mol)



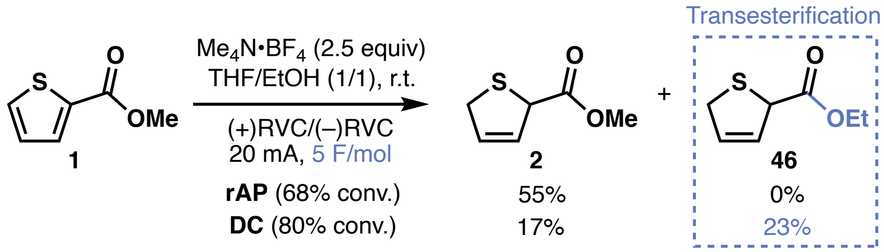
rAP with Pd/C (20 mA, 50 ms, 10 F/mol)



DC with Pd/C (20 mA, 10 F/mol)



Transesterification (Figure 2B)

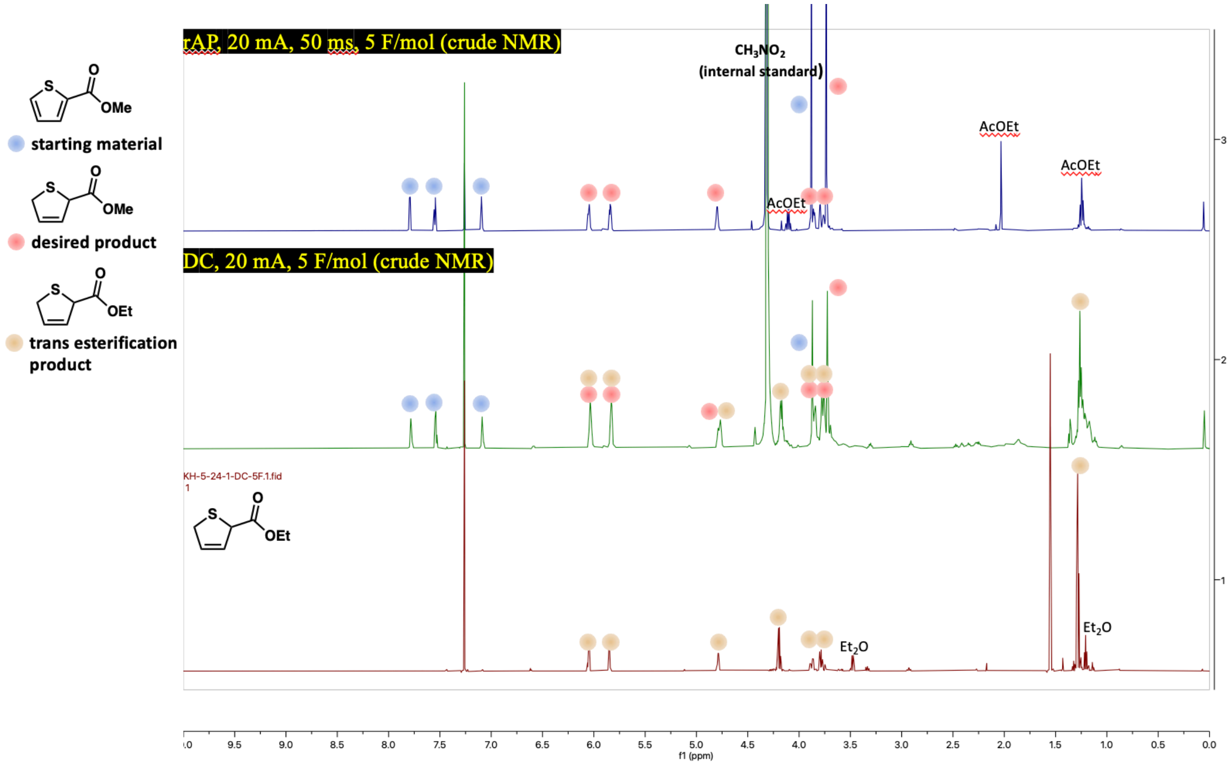


rAP (20 mA, 50 ms, 5 F/mol)

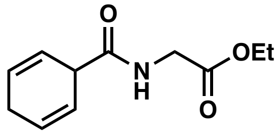
The reaction was performed with **1** (14 mg, 0.1 mmol) and tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) in 1.5 mL of EtOH and 1.5 mL of THF (DMS was not used). The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 5 F/mol. The reaction mixture was diluted with diethyl ether and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **2** in 55% and the starting material **1** in 32% (nitromethane was used as an internal standard).

DC (20 mA, 5 F/mol)

The reaction was performed with **1** (14 mg, 0.1 mmol) and tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) in 1.5 mL of EtOH and 1.5 mL of THF (DMS was not used). The resulting reaction mixture was electrolyzed at room temperature, under a constant current of 20 mA with direct current for 5 F/mol. The reaction mixture was diluted with diethyl ether and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **2** in 17%, ethyl ester **46** (from trans esterification) in 23% and the starting material **1** in 20% (nitromethane was used as an internal standard).

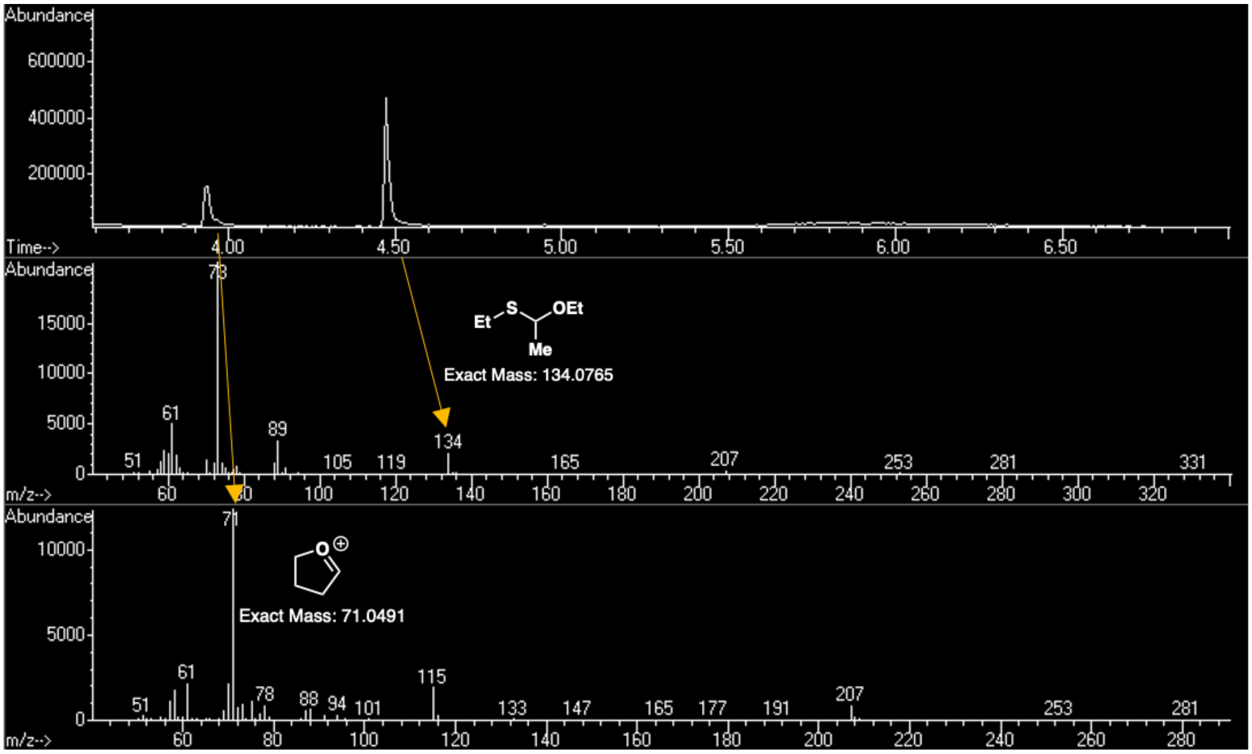

S
O
OMe
● starting material
S
O
OMe
● desired product
S
O
OEt
● trans esterification product
rAP, 20 mA, 50 ms, 5 F/mol (crude NMR)
CH_3NO_2 (internal standard)
AcOEt
AcOEt
AcOEt
DC, 20 mA, 5 F/mol (crude NMR)
KH-5-24-1-DC-5F.1.fid
1
S
O
OEt
Et_2O
Et_2O
3
2
1
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

Evidence for sulfide oxidation (Figure 2C)



Following the general procedure, the reaction was performed with **3** (21 mg, 0.1 mmol), tetramethylammonium tetrafluoroborate (40 mg, 0.25 mmol) and diethyl sulfide (32 *μ*L, 0.3 mmol) in 1.5 mL of EtOH and 1.5 mL of THF. The resulting reaction mixture was electrolyzed at 0 °C, under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 20 F/mol. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **4** in 43% and benzyl alcohol in 29% (nitromethane was used as an internal standard). GC/MS analysis of the crude reaction mixture found (1-ethoxyethyl)(ethyl)sulfide **47** and a fragmentation of THF oxidation product.

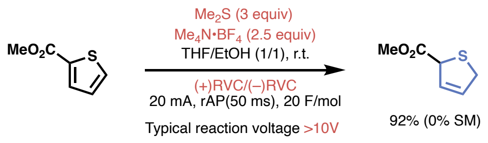
Note: When DMS was used as an electron donor (standard condition), the corresponding oxidized product, (ethoxymethyl)(methyl)sulfide, was not detected probably due to its low boiling point.



Scale-up reaction (Figure 2E)

Modification of reaction conditions for scale-up

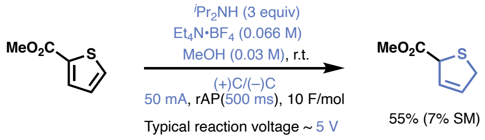
Optimal conditions on 0.1 mmol scale



Problems:

- Me$_2$S additive needs to be replaced (too smelly).
- Me$_4$N•BF$_4$ is not completely soluble; more soluble electrolyte is needed.
- Graphite is the only available electrode for rAP scaleup equipment.
- Reaction voltage is too high for scaleup equipment (Max output 10 V).

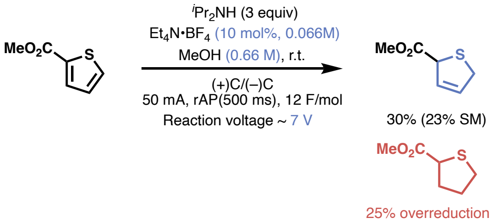
Modified conditions on 0.1 mmol scale



Modifications made for solving scaleup problems:

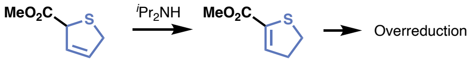
- Me$_2$S was replaced with ^{i}Pr$_2$NH (<$30/kg)
- Et$_4$N•BF$_4$ is completely soluble and decreased reaction voltage dramatically.
- Solvent is changed to MeOH to further reduce reaction voltage.
- Reaction worked with graphite electrodes with lower frequency (500 ms pulse, 0.5 Hz).
- Current is increased to 50 mA to shorten reaction time, yet reaction voltage is still less than 10 V.

2 mmol scale reaction

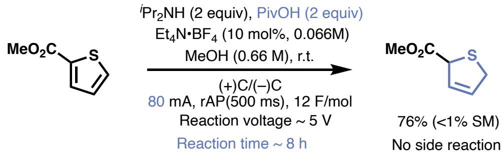


Note:

- Amount of electrolyte does not need to be scaled; only 10 mol% is enough for large scale.
- Reaction concentration x 10 to avoid using large amount of solvent.
- Since the concentration of ^{i}Pr$_2$NH increased, side reaction (base-mediated isomerization of the product. followed by second reduction) started to occur.



2 mmol scale reaction



DC instead of rAP: 100% SM recovery

Note:

- Reaction solution was buffered with pivalic acid (~ $30/kg) to attenuate basicity.
- Current was further increased to 80 mA to improve conversion.
- Crude product was very clean (short silica-plug is sufficient).
- Under these conditions, DC electrolysis resulted in only decomposition of ^{i}Pr$_2$NH and H$_2$ gas evolution (100% SM recovery by NMR)

Comments on the choice of graphite electrode and frequency

Since RVC electrodes cannot be used for our current scale-up reactor, the reaction was reoptimized using graphite electrode. While the desired product was not obtained by 50 ms rAP (SM recovery), it was found that much longer pulse (500 ms) effectively delivered the desired product. Although the exact reason is not clear at this moment, porous graphite electrode might consume more non-faradaic current (i.e., more capacitive current) than RVC electrode. Thus, at the higher frequency vast majority of the electric energy is used for charging and discharging the electrode surface, resulting in much lower reactivity. Accordungly, we think the optimal frequency rather depends on electrode material than reaction scale.

50 mmol scale reaction

Reactor Signal generator Amplifier

Left: Reactor assembly, **Middle:** rAP power supply constituted with a combination of a signal generator and an amplifier. **Right:** Reactor components. (Connection of electrodes is indicated by + and – sign in the picture)

As described in the middle picture, rAP waveform was generated from a signal generator (RIGOL, DG812) and the output was adjusted by an amplifier (Accel Instruments, TS250).

The reactor consisted of two parts, a glass beaker and an electrode head. The beaker was 100 mL EasyMax reactor. The electrode head was machined polypropylene with a 14 1/4 inch graphite rods arrayed in a circle. The gap between electrodes was 2 mm at the closest point. The reactor was sealed with a Viton O-ring and clamp. The graphite electrodes were obtained from Electron Microscopy Sciences (Cat#70212).

Procedure

To a reactor beaker equipped with a stir bar were added MeOH (50 mL) and pivalic acid (10.2 g, 100 mmol), followed by slow addition of diisopropylamine (14 mL, 100 mmol). This step is mildly exothermic. After completion of the addition, tetraethylammonium tetrafluoroborate (1.2 g, 6 mmol) and methyl thiophen-2-carboxylate **1** (7.1 g, 50 mmol) were added to the solution. Electrode assembly was inserted to the beaker, and the reactor was fastened by a chain clamp. Argon gas was bubbled through the solution, and then entire reactor was enclosed in a ziplock bag with two tiny holes from which wires were connected to rAP power supply. 10 Vpp (peak to peak, 5V from the offset) was applied to the reaction for 9 h. (During the reaction, the observed current value was around 2.0 A. Since the reaction solution was slowly warmed up due to Joule effect, the reactor was submerged to a water during the reaction.) After 9 hours of electrolysis, the crude mixture was poured into brine and crude products were extracted by organic solvent mixture (hexane/EtOAc =

3/1). The crude product was further purified by column chromatography (hexane/EtOAc = 5/1) to afford the desired product **2** in 84% yield (6.07 g).

Frequently asked questions

Question 1: Is this reaction sensitive to air and water?

Answer:

The reaction is not particularly air and water-sensitive. The yield and reaction rate were not affected even when considerably wet $Me_4N \cdot BF_4$ was used. However, for less reactive substrates (e.g. compound **3**), insufficient Ar purge potentially suppresses the reaction progress since oxygen reduction would prevent the desired reduction process (see the procedure sections of compound **2** and **4** for the results of open-air experiment). Bubbling with Ar before electrolysis and keeping Ar balloon on the top of the reaction vial while running a reaction are recommended to obtain the satisfactory conversion.

Question 2: Can I remove smelly DMS?

Answer:

Reaction can proceed without DMS since THF could work as an electron donor instead in some case. However, for relatively less reactive substrates such as benzamide derivatives, the condition without DMS may present lower conversion and lower yield. Also, DMS can play a role in avoiding undesired oxidative side reaction on the product. Other than DMS, a mixture of diisopropylamine and pivalic acid (1:1) can also be used as an alternative electron donor as demonstrated in our scale up reaction.

Question 3: Electrolysis can't be carried out due to too high voltage (>30V). Why and how can I fix this?

Answer:

$Me_4N \cdot BF_4$ shows the different conductivity attributed to its solubility depending on bottles, probably due to the difference of moisture content and/or crystal system. One solution is using $Me_4N \cdot OPiv$ prepared by neutralizing pivalic acid with TMA•OH (40% solution in H_2O, commercially available) in situ. The procedure is as follows;

To an EtOH (1.2 mL) solution of PivOH (0.2 mmol), aqueous TMA•OH (0.2 mmol) was added. After stirring for 10 sec, the solution was diluted with THF (1.2 mL) followed by the addition of substrate (0.1 or 0.2 mmol) and DMS (3 equiv to SM). The resulting mixture was electrolyzed under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz) for 10~20 F/mol.

In addition, 3.5 mL of MeOH/THF (2.5:1) is more conductive solvent system that afforded the product in acceptable yield for reactive substrates such as heteroaromatics. The procedure and results are as follows;

The reaction was performed with the corresponding aromatic substrate (0.1 mmol), tetramethylammonium tetrafluoroborate (low solubility one, 40 mg, 0.25 mmol) and DMS (22 μL, 0.3 mmol) in 2.5 mL of MeOH and 1.0 mL of THF. The resulting reaction mixture was electrolyzed under a constant current of 20 mA with rapid alternating polarity (50 ms, 10 Hz). The reaction mixture was diluted with diethyl ether and washed with brine. The organic layer was dried over sodium sulfate anhydrous, filtered and concentrated under the reduced pressure.

For compound **2**:

The resulting reaction mixture was electrolyzed for 10 F/mol. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **2** in 70% (nitromethane was used as an internal standard).

For compound **11**:

The resulting reaction mixture was electrolyzed for 15 F/mol. ^{1}H NMR spectroscopic analysis of the crude reaction mixture found **11** in 88% (nitromethane was used as an internal standard).

Question 4: Is there any appropriate reaction voltage?

Answer: This reaction can be run across a wide range of voltage. The typical reaction voltage under the conditions described above is between 10-25 V (no reference). Although no safety issue was observed during this study, this relatively high voltage can be reduced by modifying electrolyte and solvent as demonstrated in scale-up example (reaction voltage was ~5V).

Question 5: Do I need to conduct the reaction in an ice bath?

Answer: Ice-bath is not crucial for the success of the reaction, yet this operation gave slightly better yield for some substrates.

Question 6: How can I monitor the reaction?

We typically use TLC analysis to monitor the reaction. UV visualization (254 nm) is used to see the starting material, and phosphomolybdic acid in ethanol (PMA) or potassium permanganate in water ($KMnO_4$) is employed as a stain to visualize the product. In most cases, the product spot appears just below the starting material (lower R_f value) and is stained well with PMA or $KMnO_4$.

Question 7: Are those dearomatized products stable?

Some products are gradually rearomatized at room temperature. Even storing in a freezer cannot completely suppresses rearomatization in some cases (e.g. compound **4**, **6, 17**). Freezing them with the benzene under inert atmosphere or immediate use is recommended.

References

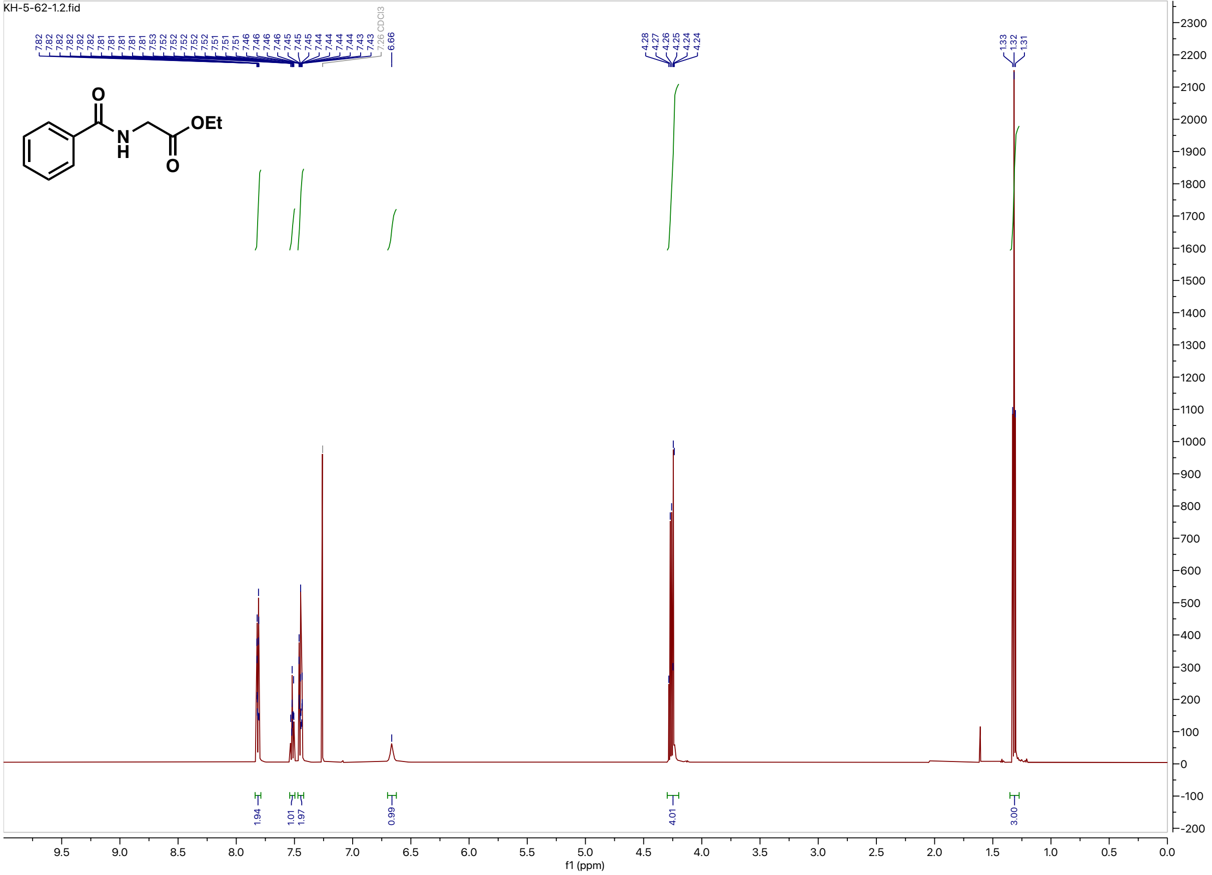
1. C. K. Lee, J. S. Yu, H.-J. Lee, Determination of aromaticity indices of thiopheneand furan by nuclear magnetic resonance spectroscopic analysis of their phenyl esters, *J. Heterocyclic Chem.*, **39**, 1207–1217 (2002).
2. J. Fu, N. Wurzer, V. Lehner, O. Reiser, H. M. L. Davies, Rh(II)-catalyzed monocyclopropanation of pyrroles and its application to the synthesis pharmaceutically relevant compounds, *Org. Lett.* **21**, 6102−6106 (2019).
3. T.-T. Chen, A.-E. Wang, P.-Q. Huang, Chemoselective synthesis of α-amino-α-cyanophosphonates by reductive *gem*-cyanation–phosphonylation of secondary amides, *Org. Lett.* **21***,* 3808-3812 (2019).
4. E Scott T. Handy, Yanan Zhang, Howard Bregman, A modular synthesis of the Lamellarins: total synthesis of Lamellarin G trimethyl ether, *J. Org. Chem.* **69**, 2362-2366 (2004).
5. H.-J. Altenbach, D. J. Brauer, G. F. Merhof, Synthesis of 1-Deoxy-4-thio-D-ribose starting from Thiophene-2-carboxylic acid, *Tetrahedron*, **53**, 6019–6026 (1997).
6. Y. Kawamata, K. Hayashi, E. Carlson, S. Shaji, D. Waldmann, B. J. Simmons, J. T. Edwards, C. W. Zapf, M. Saito, P. S. Baran, Chemoselective electrosynthesis using rapid alternating polarity, *J. Am. Chem. Soc.*, **143**, 16580–16588 (2021).
7. E. Rogers, H. Araki, L. A. Batory, C. E. McInnis, J. T. Njardarson, Highly selective copper-catalyzed ring expansion of vinyl thiiranes: application to synthesis of biotin and the heterocyclic core of Plavix, *J. Am. Chem. Soc.* **129**, 2768-2769 (2007).
8. Q. Liao, W. You, Z.-B. Lou, L.-R. Wen, C. Xi, Copper-catalyzed tandem S-alkylation and S-alkenylation of sodium sulfide: synthesis of 2,3-dihydrothiophenes and thiophenes, *Tetrahedron. Lett. Chem.* **54**, 1475–1477 (2013).
9. J. Nokami, M. Mae, S. Fukutake, T. Ubuka, M. Yamada, Synthesis of *2'-deoxy*-4'-*C*-hydroxymethyl-4'-thio- ribonucleosides and thier *2',3'-dideoxy* and *2',3'- didehydro-2',3'-dideoxy* analogues, *Heterocycles* 76, 1337–1360 (2008).
10. P. W. Rabideau, Z. Marcinow, The Birch reduction of aromatic compounds, *Organic Reactions* **42** (1992).
11. J. Burrows, S. Kamo, K. Koide, Scalable Birch reduction with lithium and ethylenediamine in tetrahydrofuran. *Science* **374**, 741–746 (2021).

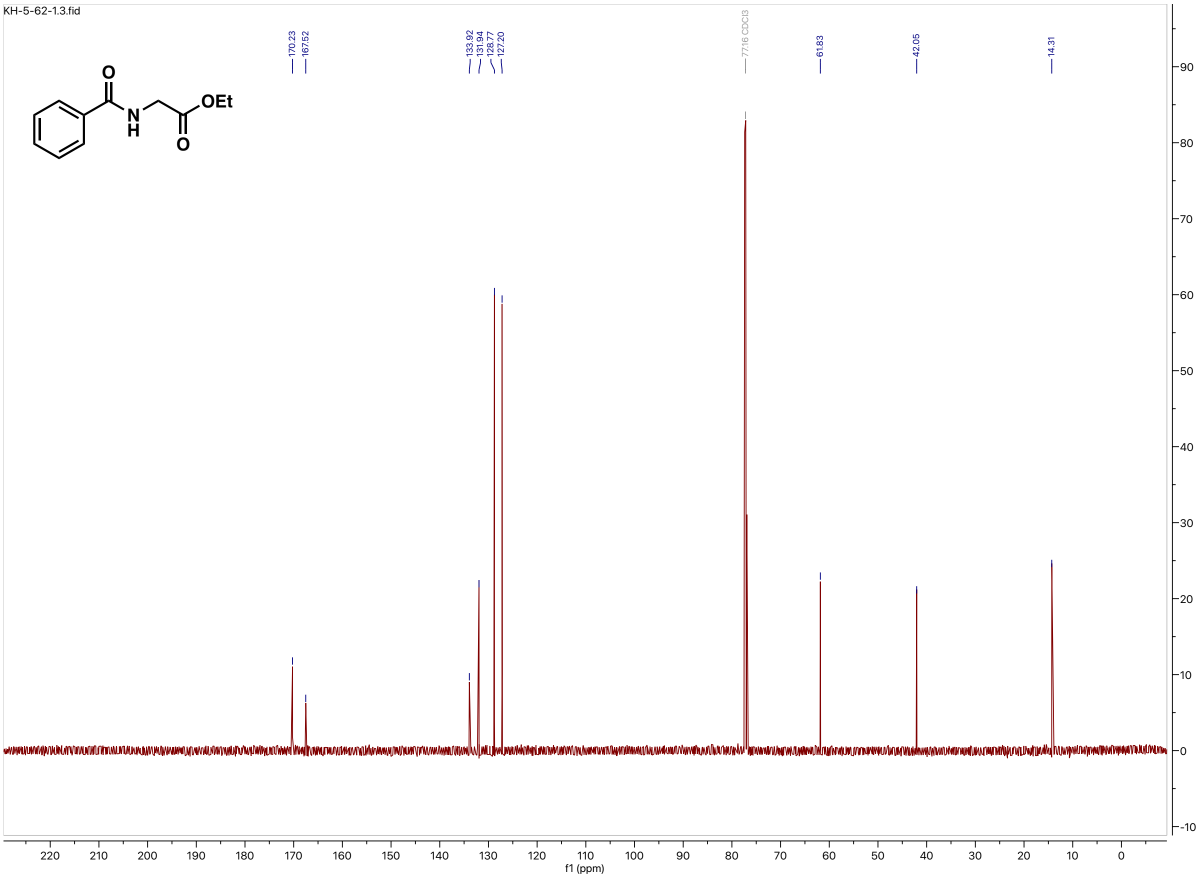
12. (a) T. J. Donohoe, D. House, Ammonia Free Partial Reduction of Aromatic Compounds Using Lithium Di-tert-butylbiphenyl (LiDBB), *J. Org. Chem.* **67**, 5015–5018 (2002). (b) T. J. Donohoe, R. E. Thomas, The partial reduction of electron-deficient pyrroles: procedures describing both Birch (Li/NH_3) and ammonia-free (Li/DBB) conditions, *Nature Protocol*, **2**, 1888-1895 (2007).

13. B. K. Peters, K. X. Rodriguez, S. H. Reisberg, S. B. Beil, D. P. Hickey, Y. Kawamata, M. Collins, J. Starr, L. Chen, S. Udyavara, K. Klunder, T. J. Gorey, S. L. Anderson, M. Neurock, S. D. Minteer, P. S. Baran, Scalable and safe synthetic organic electroreduction inspired by Li-ion battery chemistry, *Science.* **363**, 838–845 (2019).
14. E. Kuehne, B. F. Lambert, The Reduction of Aromatic Acids and Amides by Sodium in Liquid Ammonia, *J. Am. Chem. Soc.* **81**, 4278–4287 (1959).

NMR Spectra

Compound 3

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OEt
O
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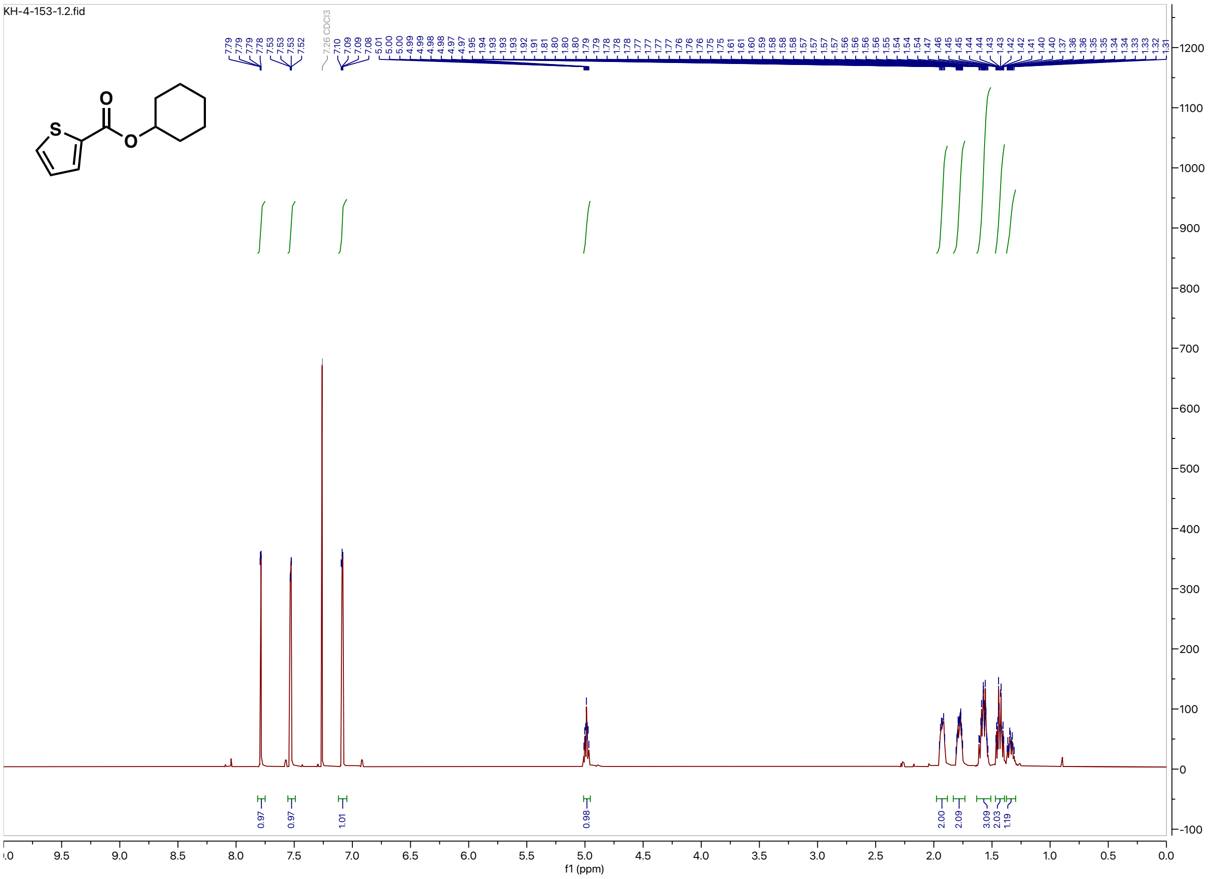
167.52
133.92
131.94
128.77
127.20
77.16 CDCl3
61.83
42.05
14.31
90
80
70
60
50
40
30
20
10
0
-10
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Compound 5s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7.52
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7.10
7.09
7.09
7.08
5.01
5.00
5.00
4.99
4.99
4.98
4.98
4.97
1.95
1.94
1.93
1.93
1.93
1.92
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1.80
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1.79
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1.77
1.77
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1.57
1.57
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1.57
1.56
1.56
1.56
1.55
1.54
1.54
1.54
1.47
1.46
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1.45
1.44
1.44
1.43
1.43
1.42
1.42
1.41
1.40
1.40
1.37
1.36
1.36
1.35
1.35
1.34
1.34
1.33
1.33
1.32
1.31
0.97
0.97
1.01
0.98
2.00
2.09
3.09
2.03
1.19
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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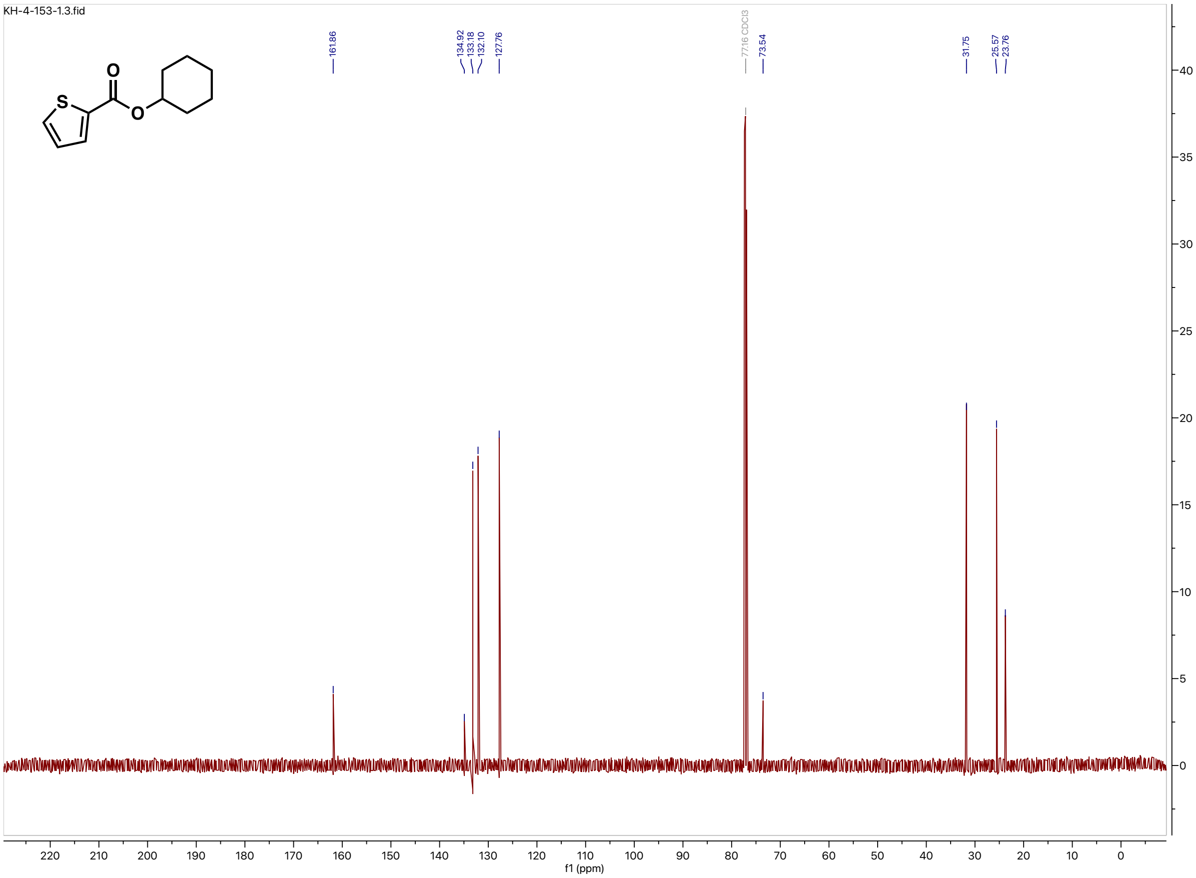
0.0
f1 (ppm)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23.76
40
35
30
25
20
15
10
5
0
220
210
200
190
180
170
160
150
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100
90
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70
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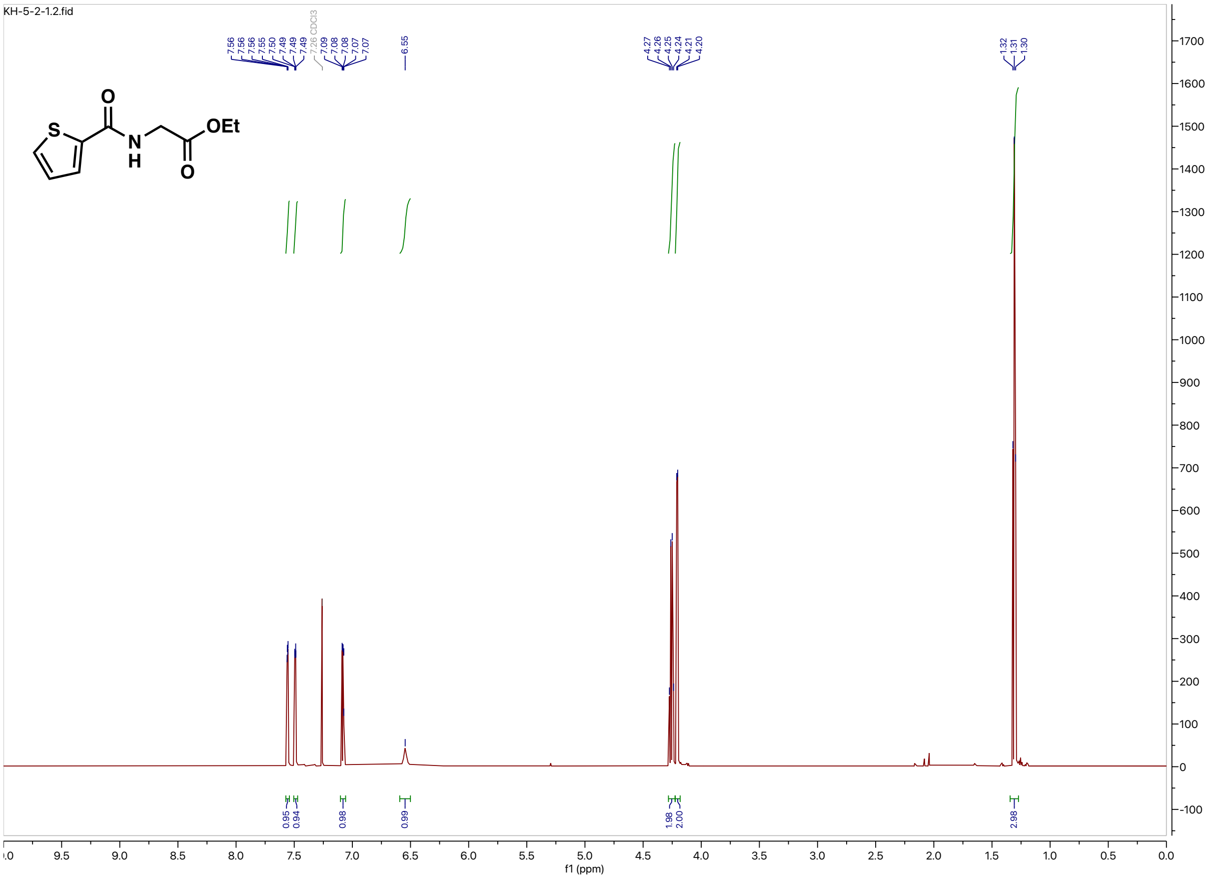
50
40
30
20
10
0
f1 (ppm)

Compound 6s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7.56
7.56
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7.49
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7.08
7.08
7.07
7.07
6.55
4.27
4.26
4.25
4.24
4.21
4.20
1.32
1.31
1.30
S
O
N
H
OEt
O
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0.94
0.98
0.99
1.98
2.00
2.98
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.5
3.0
2.5
2.0
1.5
1.0
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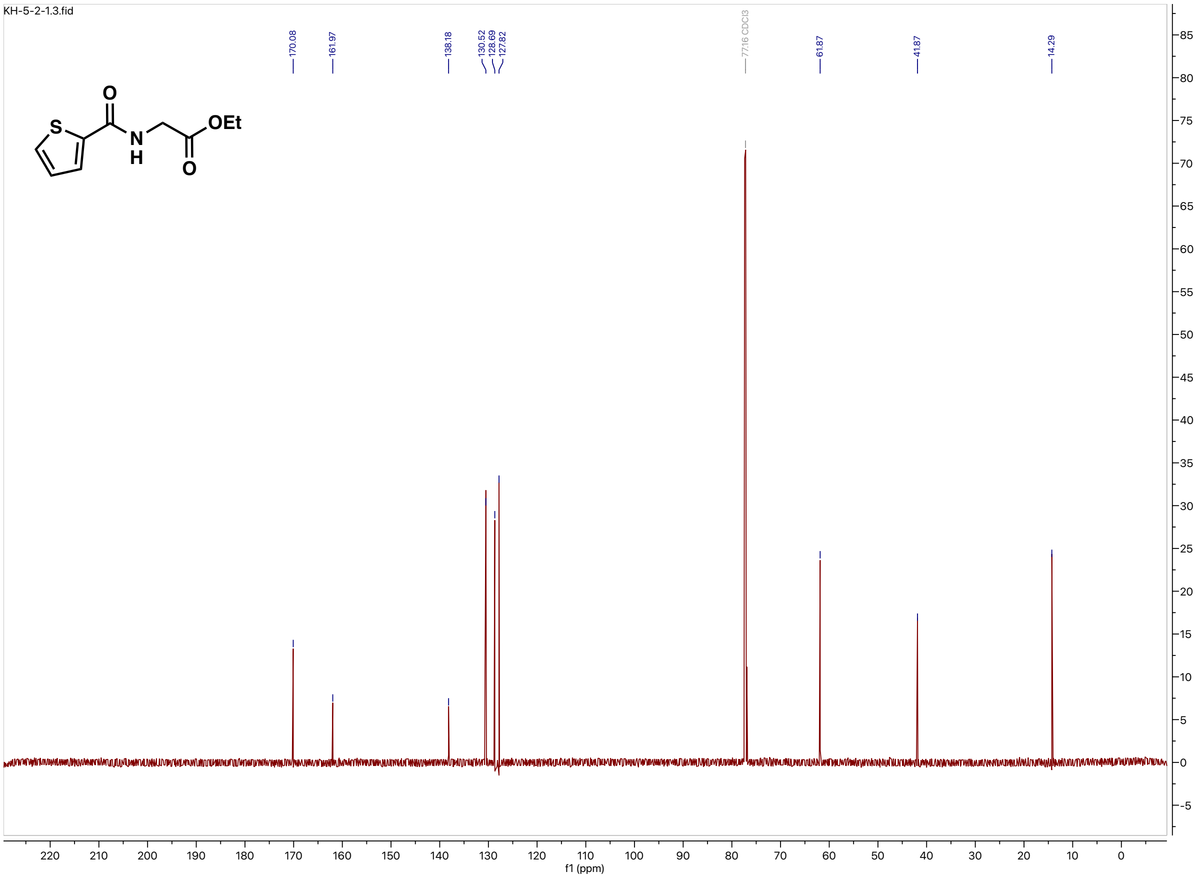
0.0
f1 (ppm)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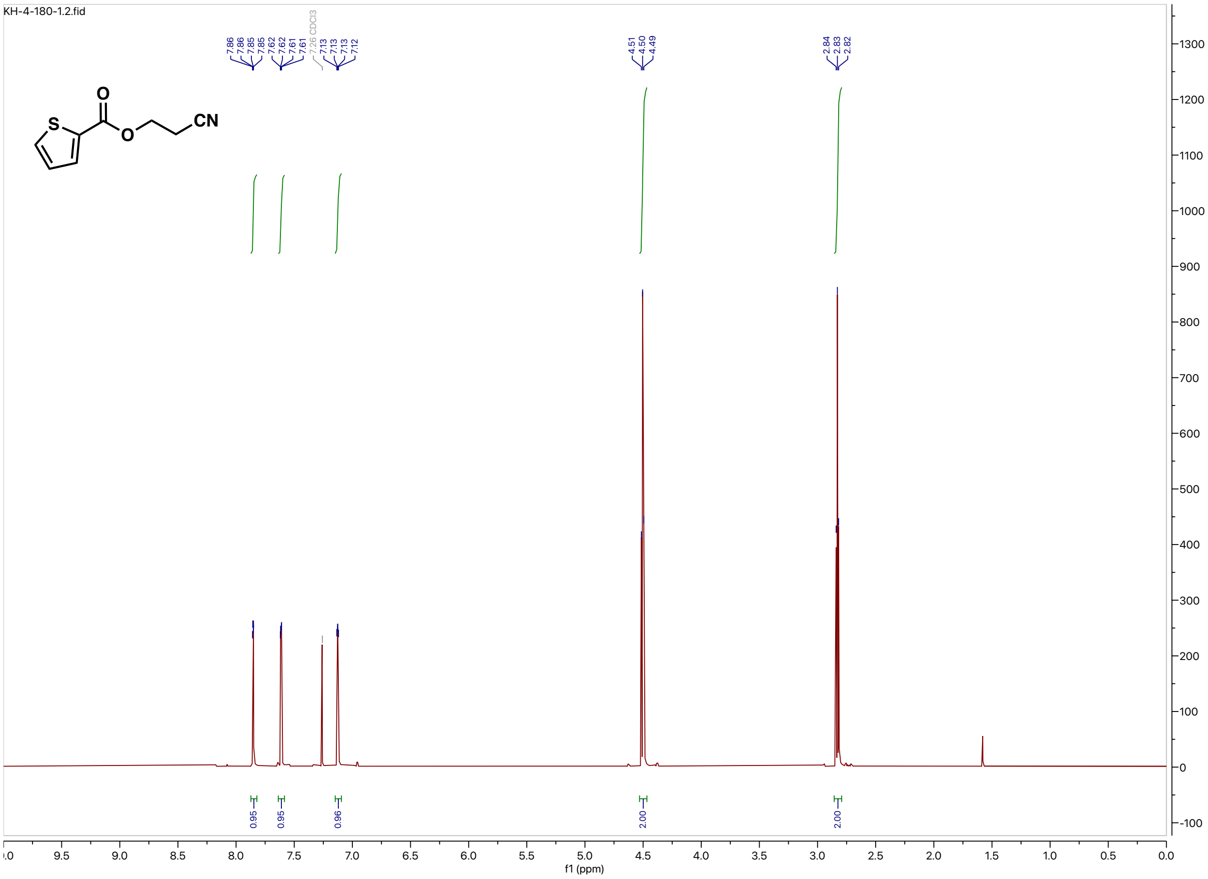
O
N
H
OEt
O
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Compound 7s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7.13
7.13
7.13
7.13
7.12
4.51
4.50
4.49
2.84
2.83
2.82
S
O
O
CN
0.95
0.95
0.96
2.00
2.00
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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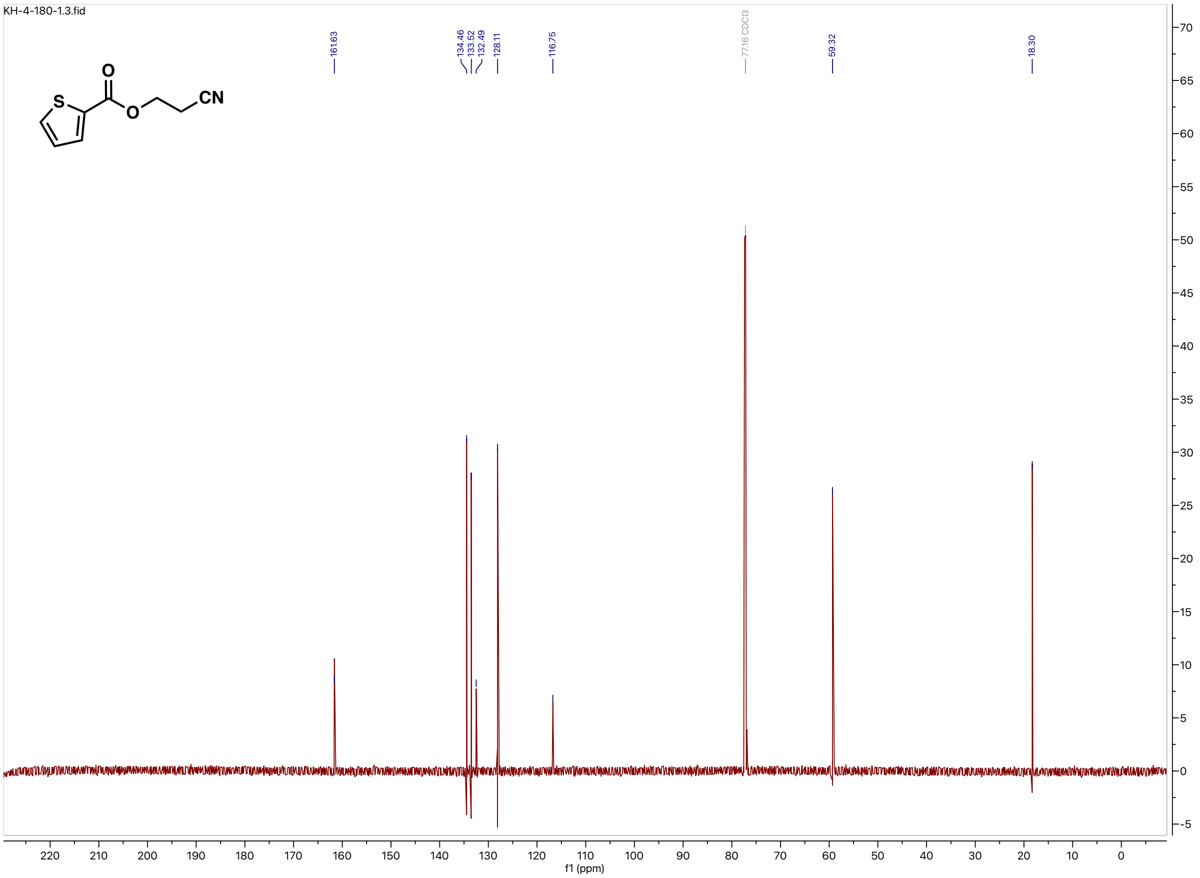
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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S
O
O
CN
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
220
210
200
190
180
170
160
150
140
130
120
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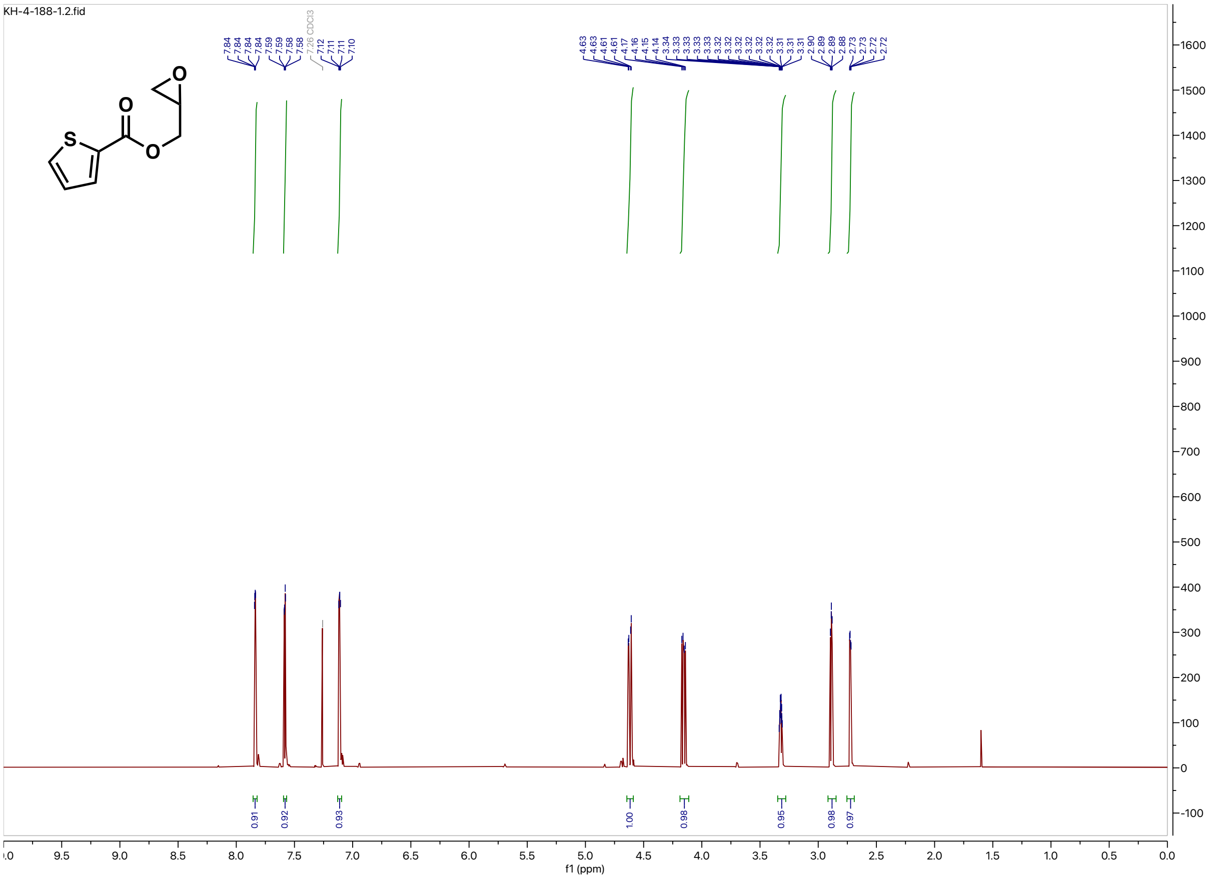
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Compound 8s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O
O
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7.84
7.84
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7.58
7.26 CDCl3
7.12
7.11
7.11
7.10
4.63
4.63
4.61
4.61
4.17
4.16
4.15
4.14
3.34
3.33
3.33
3.33
3.33
3.32
3.32
3.32
3.32
3.32
3.31
3.31
2.90
2.89
2.89
2.88
2.73
2.73
2.72
2.72
0.91
0.92
0.93
1.00
0.98
0.95
0.98
0.97
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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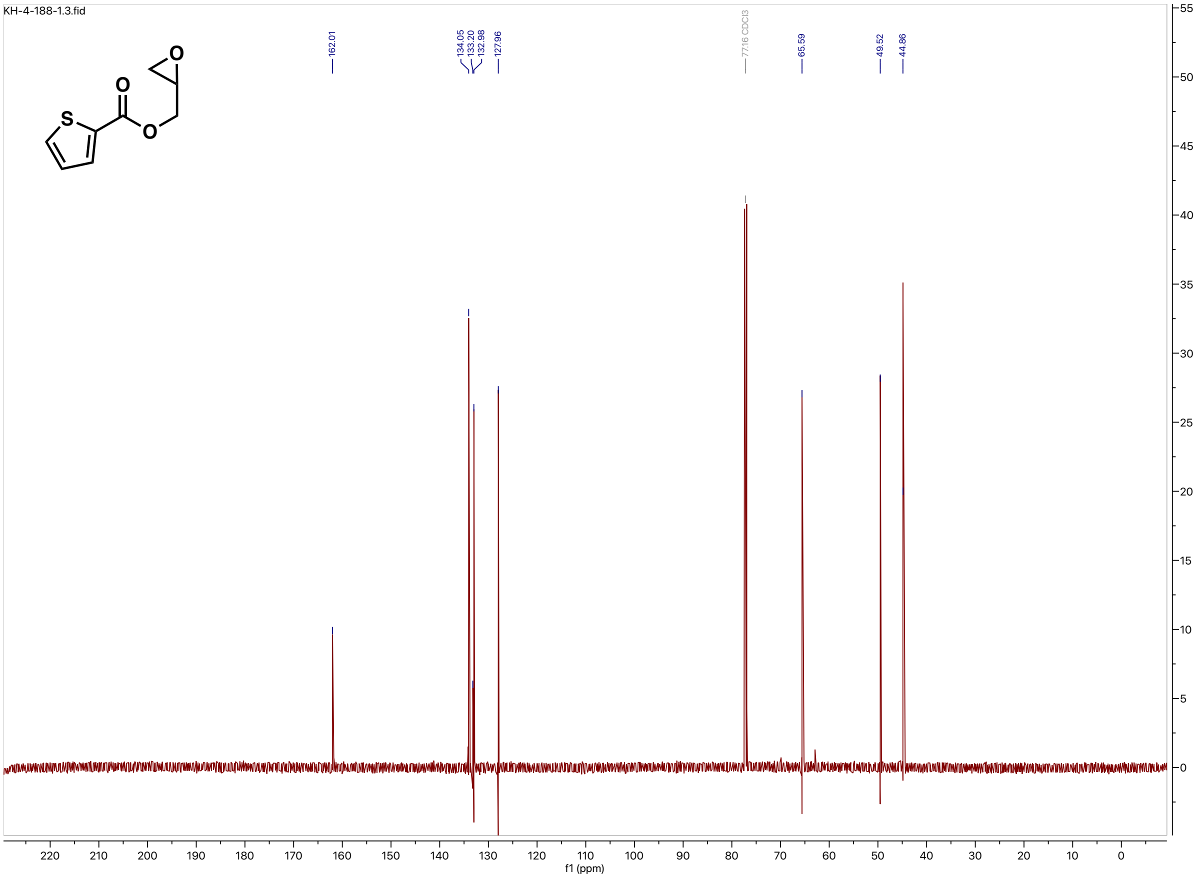
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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S
O
O
O
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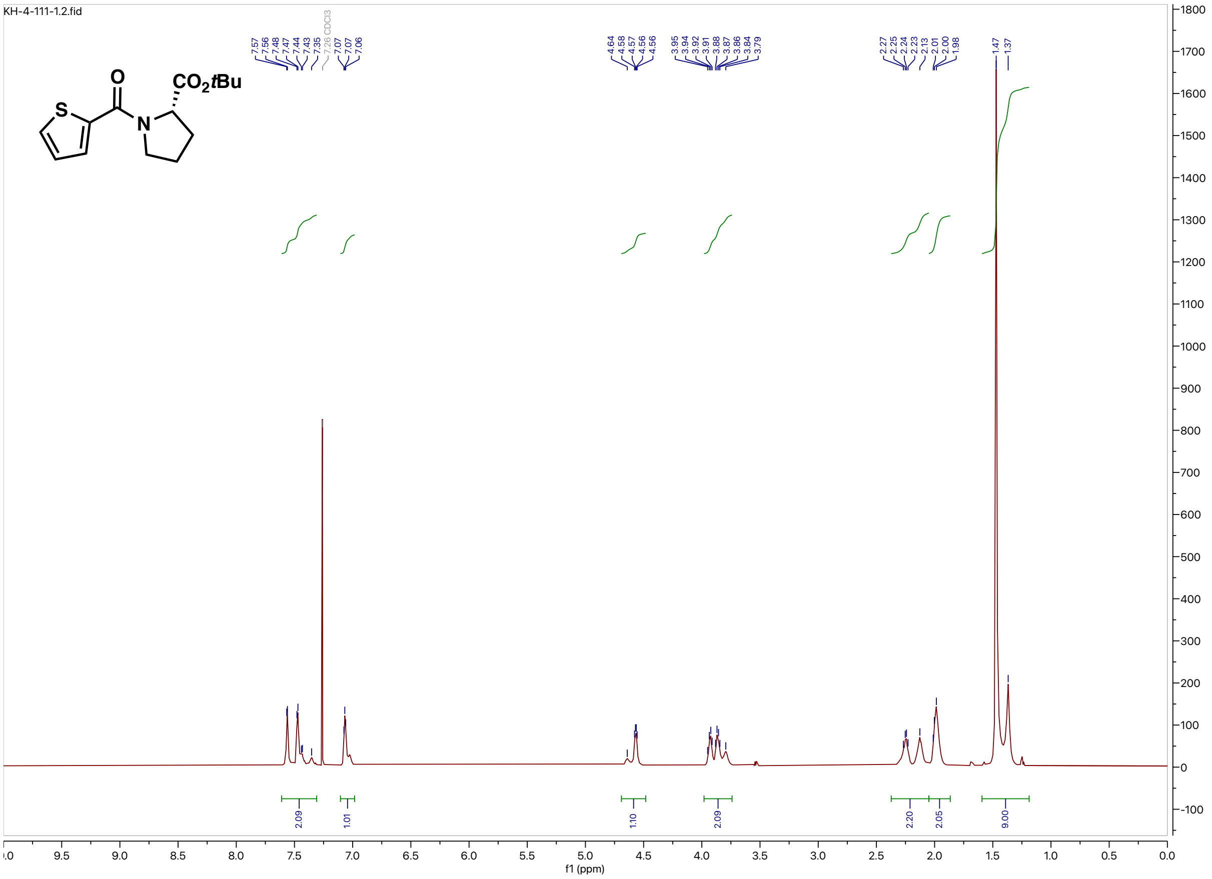
f1 (ppm)
55 50 45 40 35 30 25 20 15 10 5 0

Compound 9s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O
N
CO2tBu
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7.35
7.26 CDCl3
7.07
7.07
7.06
4.64
4.58
4.57
4.56
4.56
3.95
3.94
3.92
3.91
3.88
3.87
3.86
3.84
3.79
2.27
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2.24
2.23
2.13
2.01
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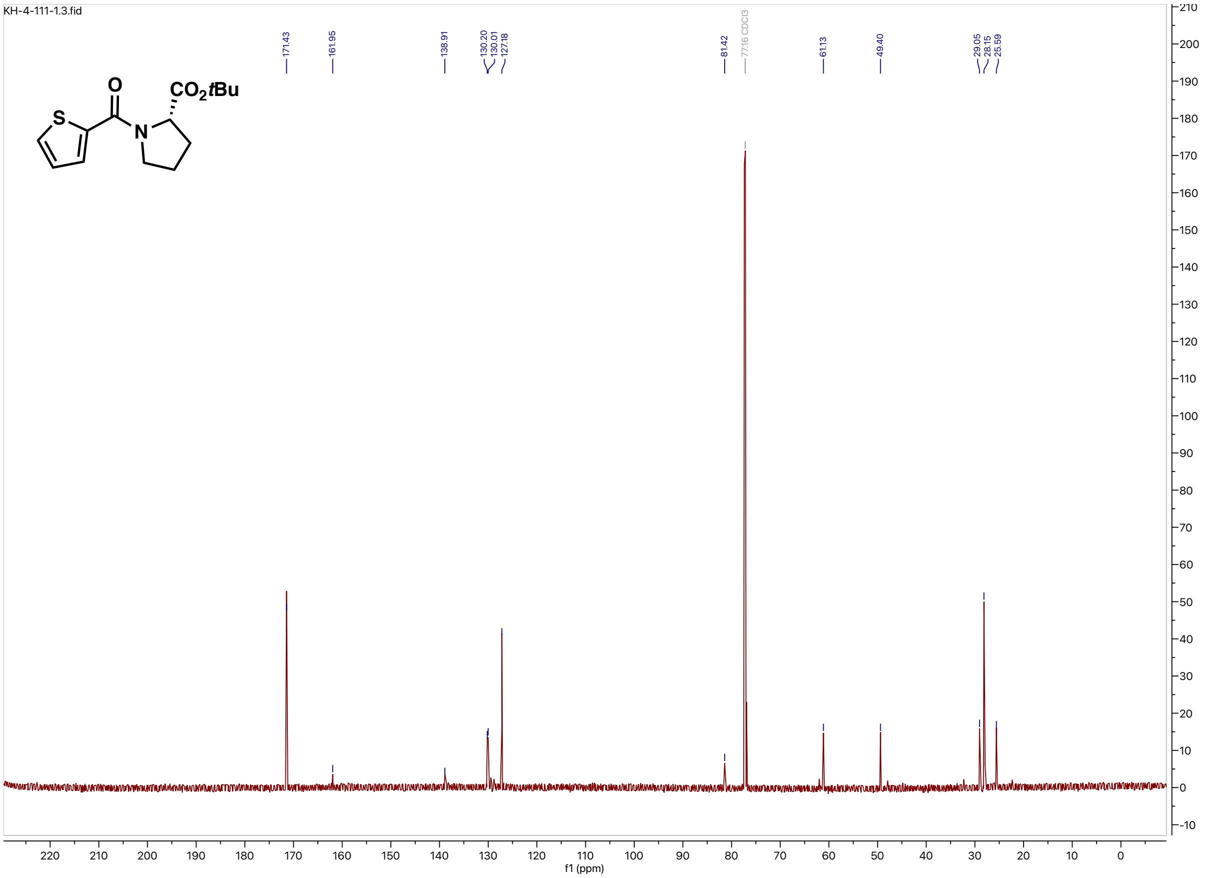
2.09
2.20
2.05
9.00
f1 (ppm)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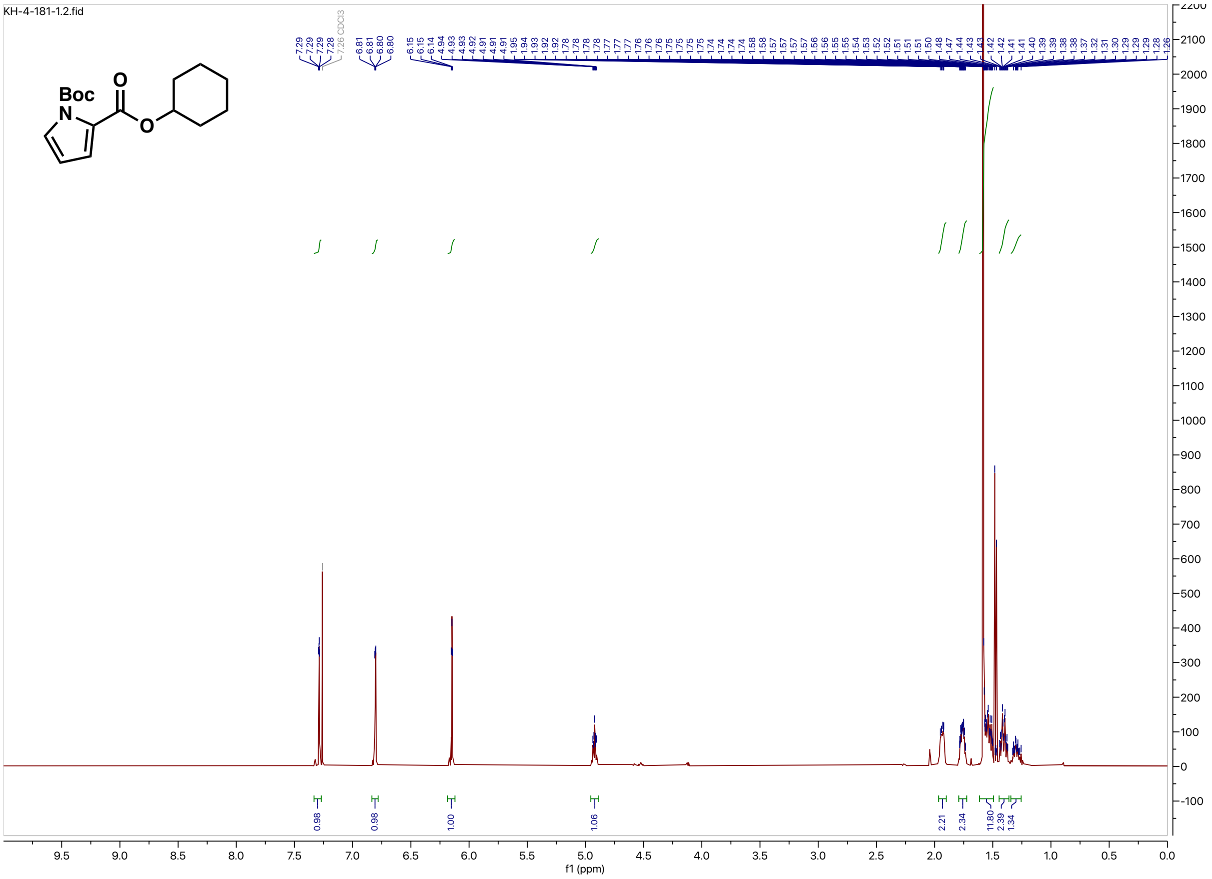
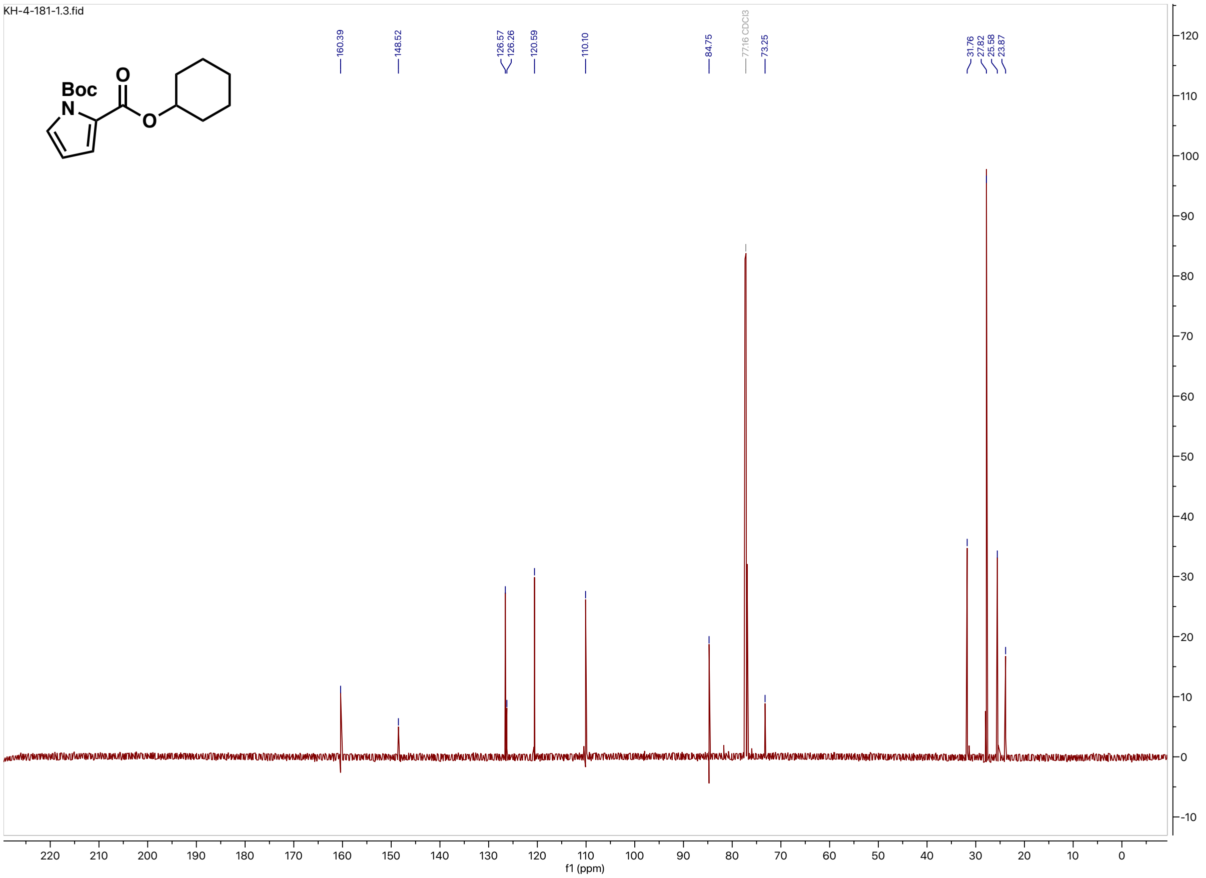
49.40
29.05
28.15
25.59
O
S
N
CO2tBu
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

Compound 10s

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Boc
N
O
O
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126.57
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110.10
84.75
77.16 CDCl3
73.25
31.76
27.82
25.58
23.87
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
220
210
200
190
180
170
160
150
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130
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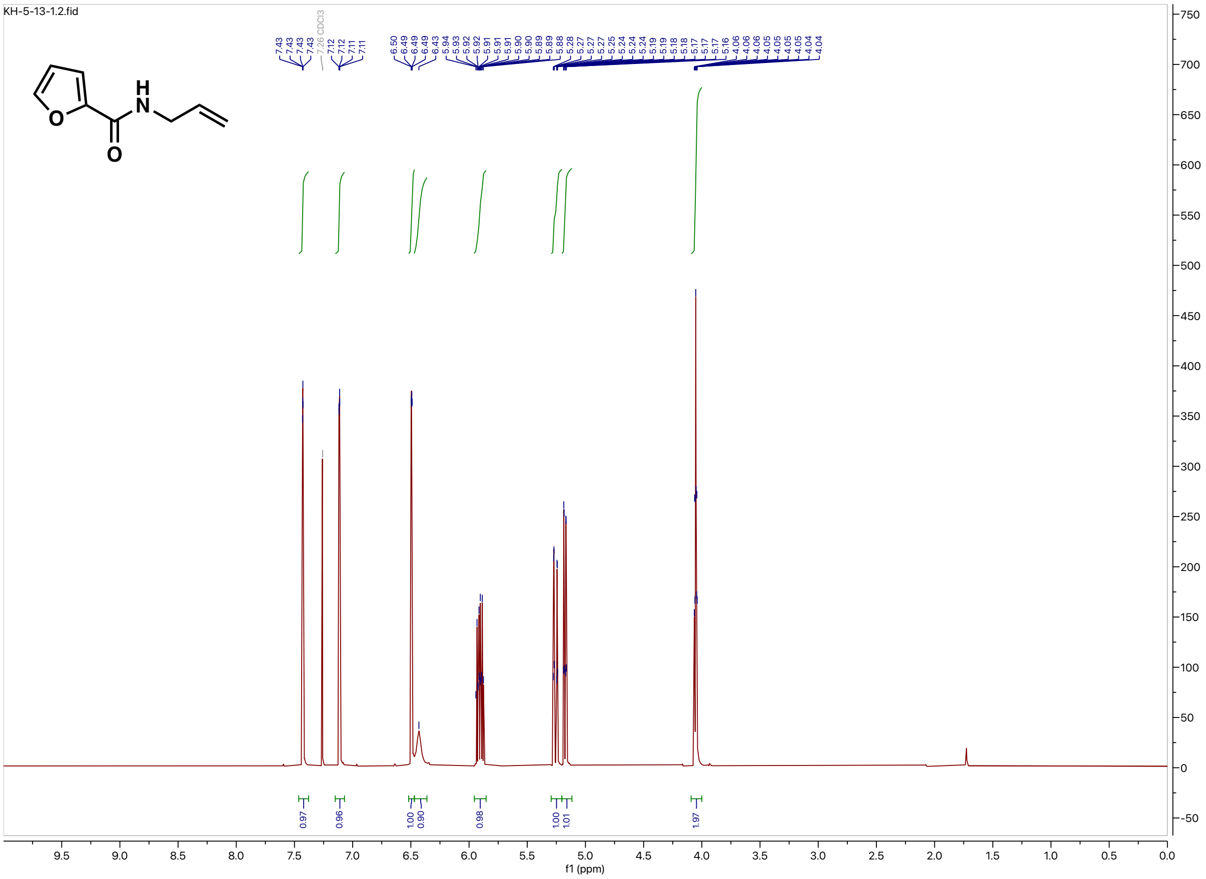
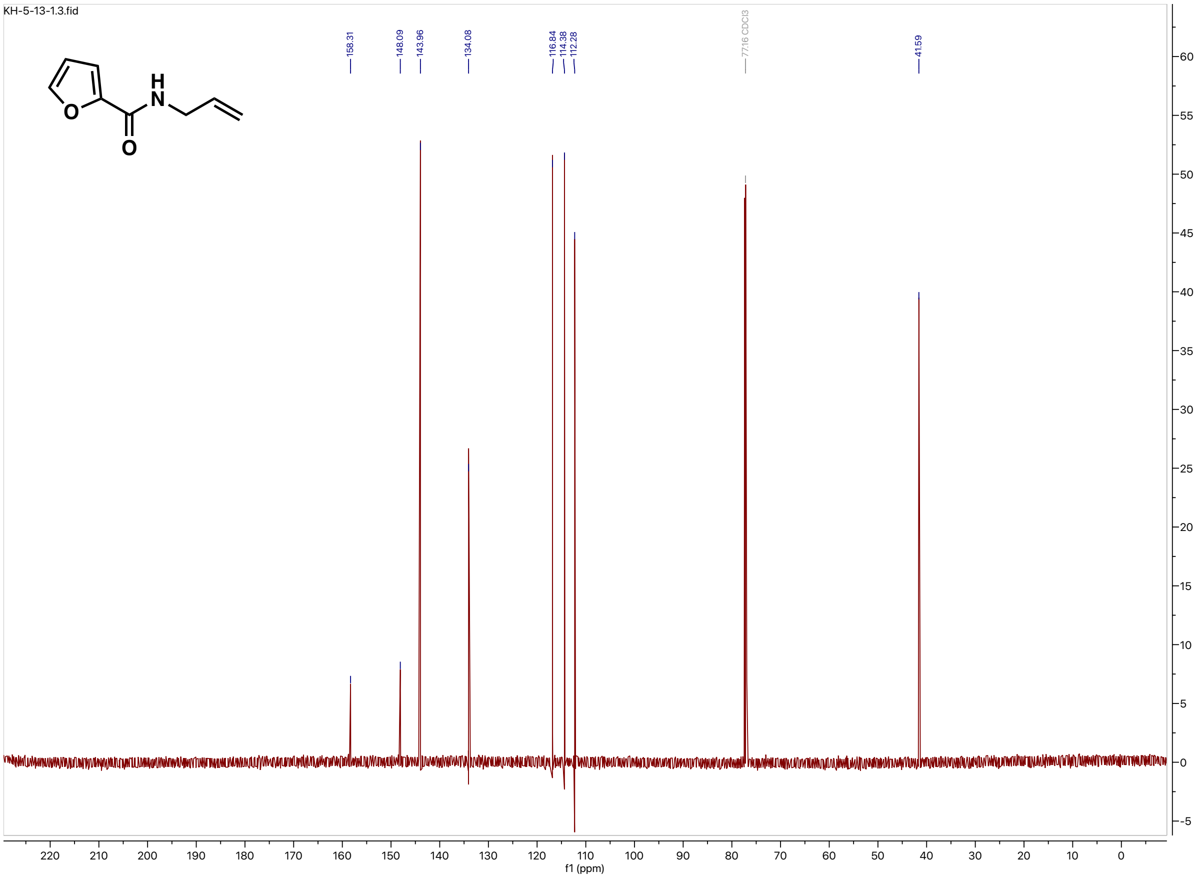
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Compound 11s

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114.38
112.28
77.16 CDCl3
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H
N
O
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210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
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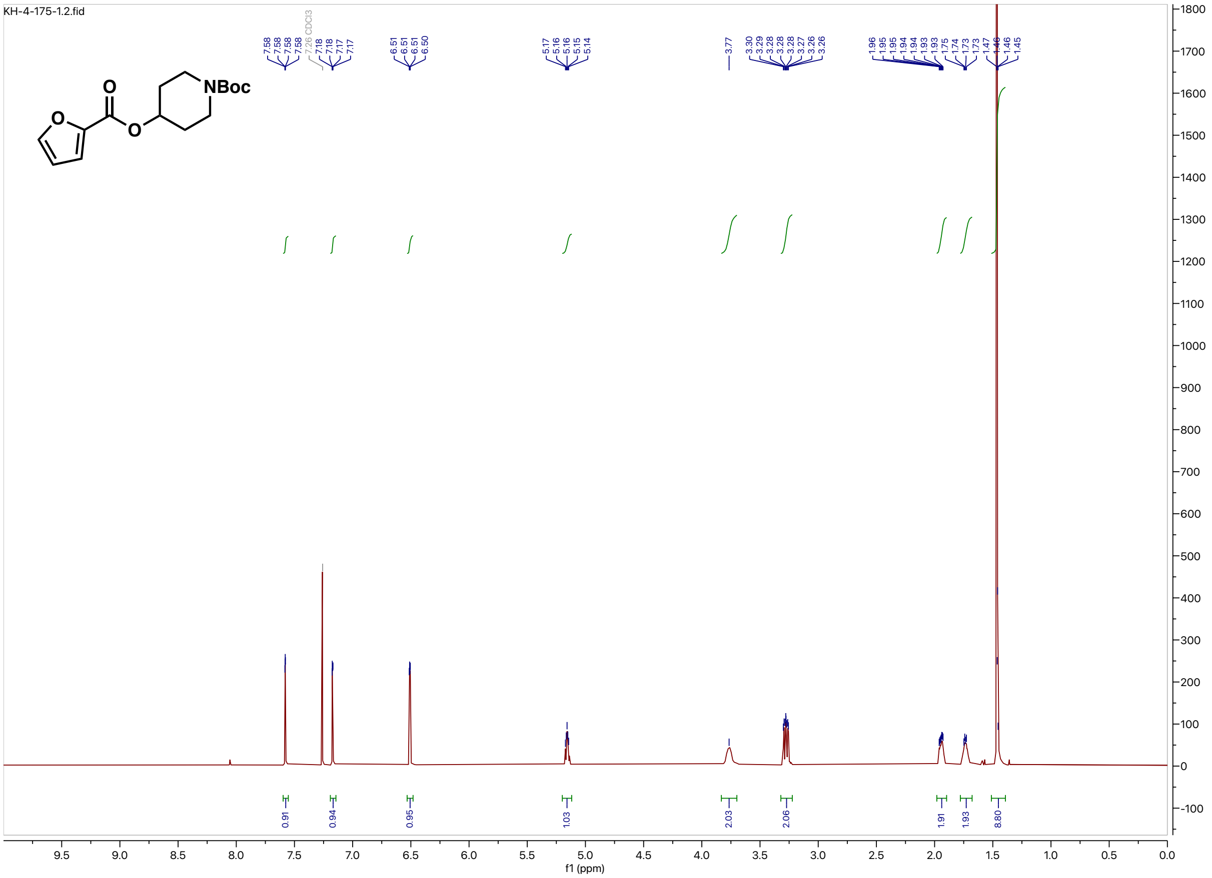
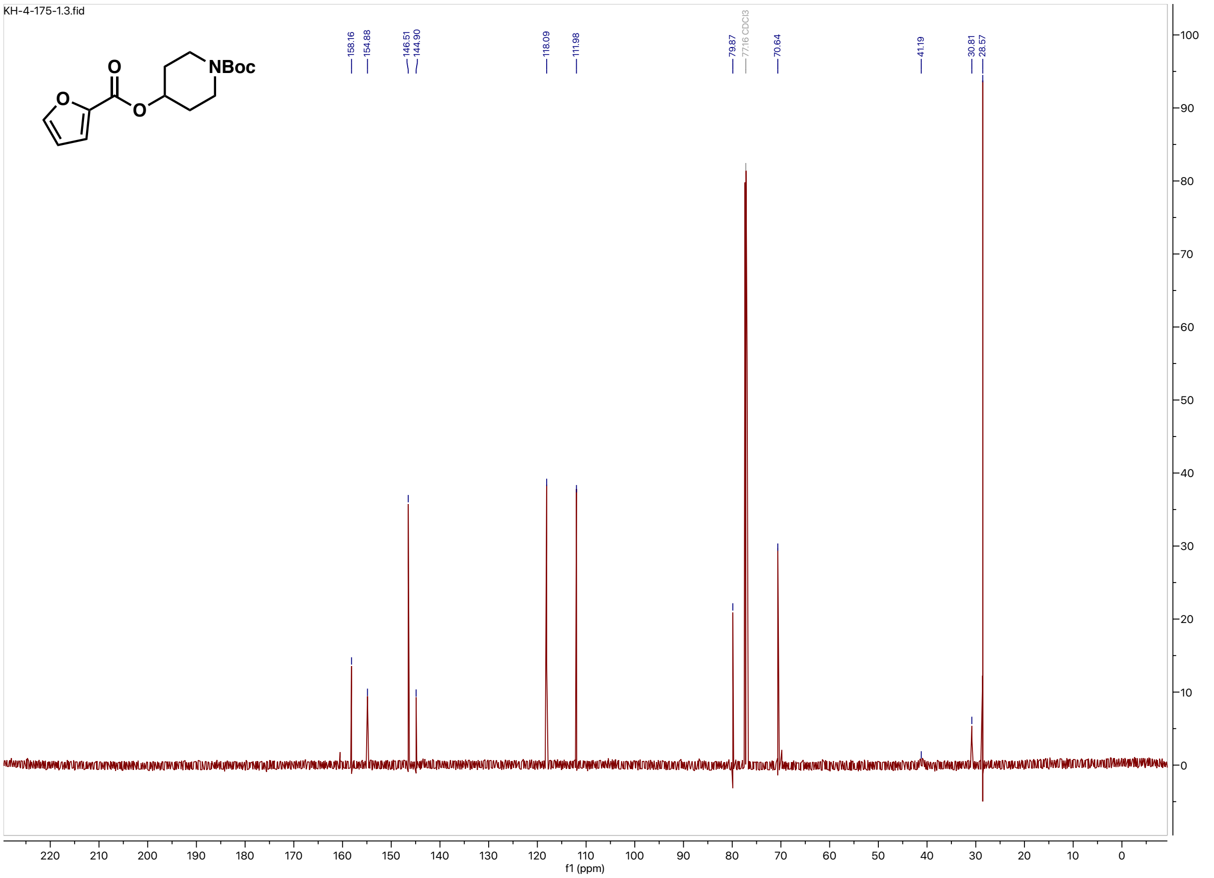
f1 (ppm)
60
55
50
45
40
35
30
25
20
15
10
5
0
-5

Compound 12s

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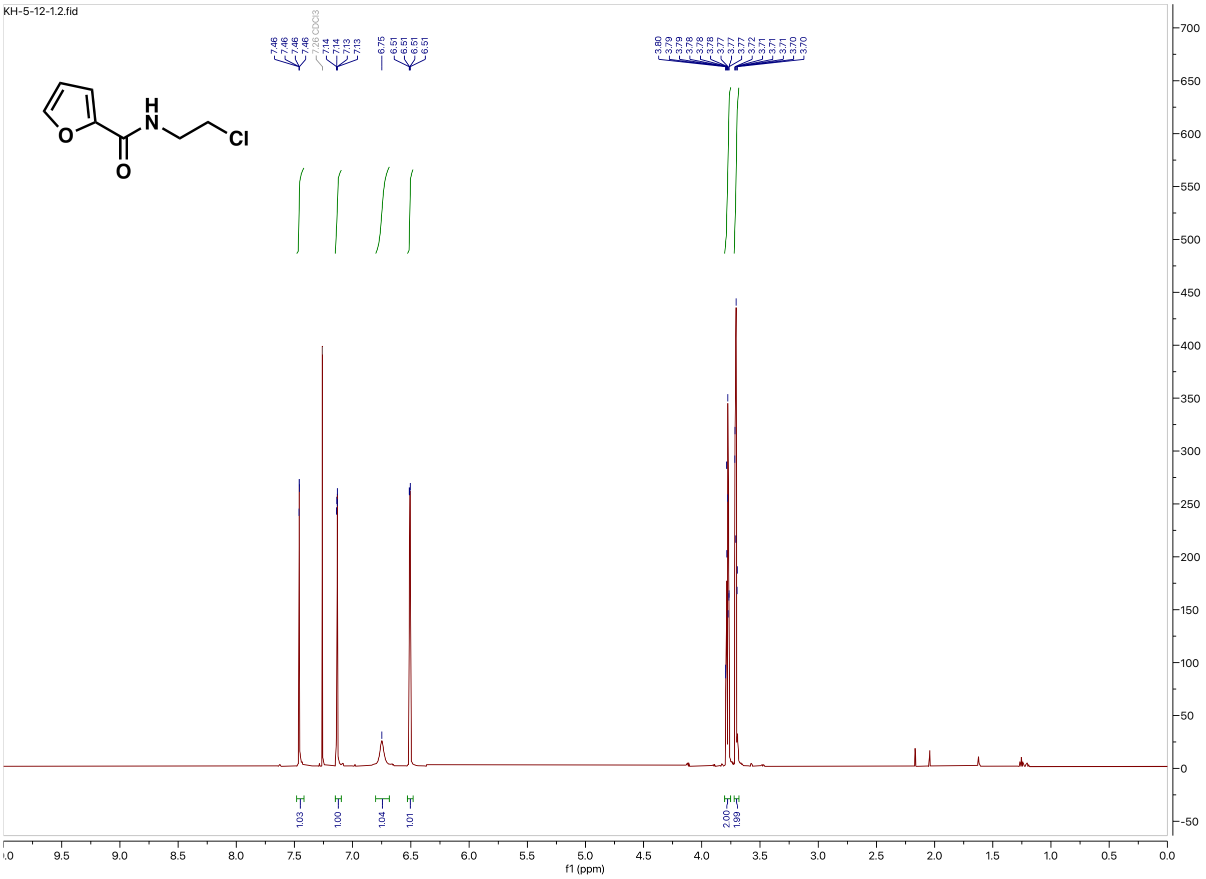
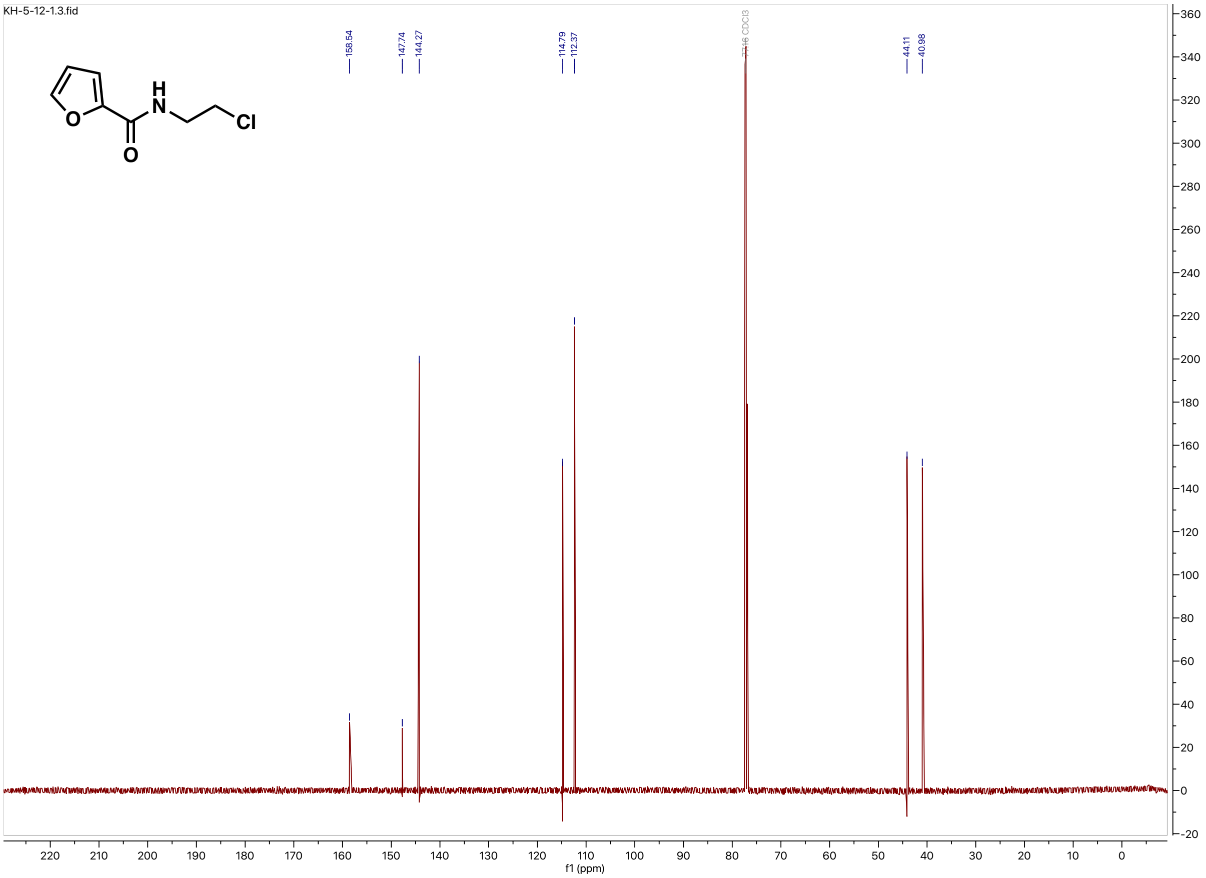
77.16 CDCl3
70.64
41.19
30.81
28.57
100
90
80
70
60
50
40
30
20
10
0
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Compound 13s

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H
N
Cl
O
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340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
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210
200
190
180
170
160
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100
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70
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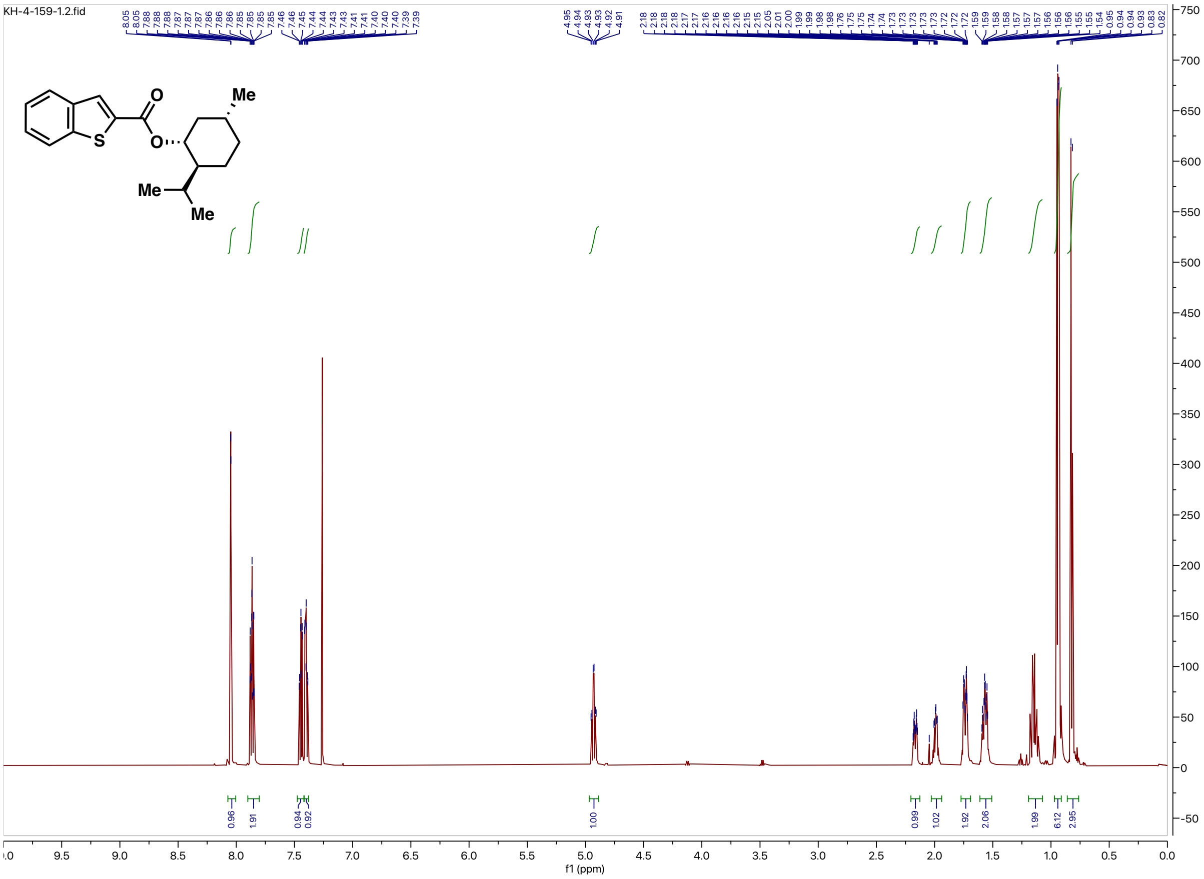
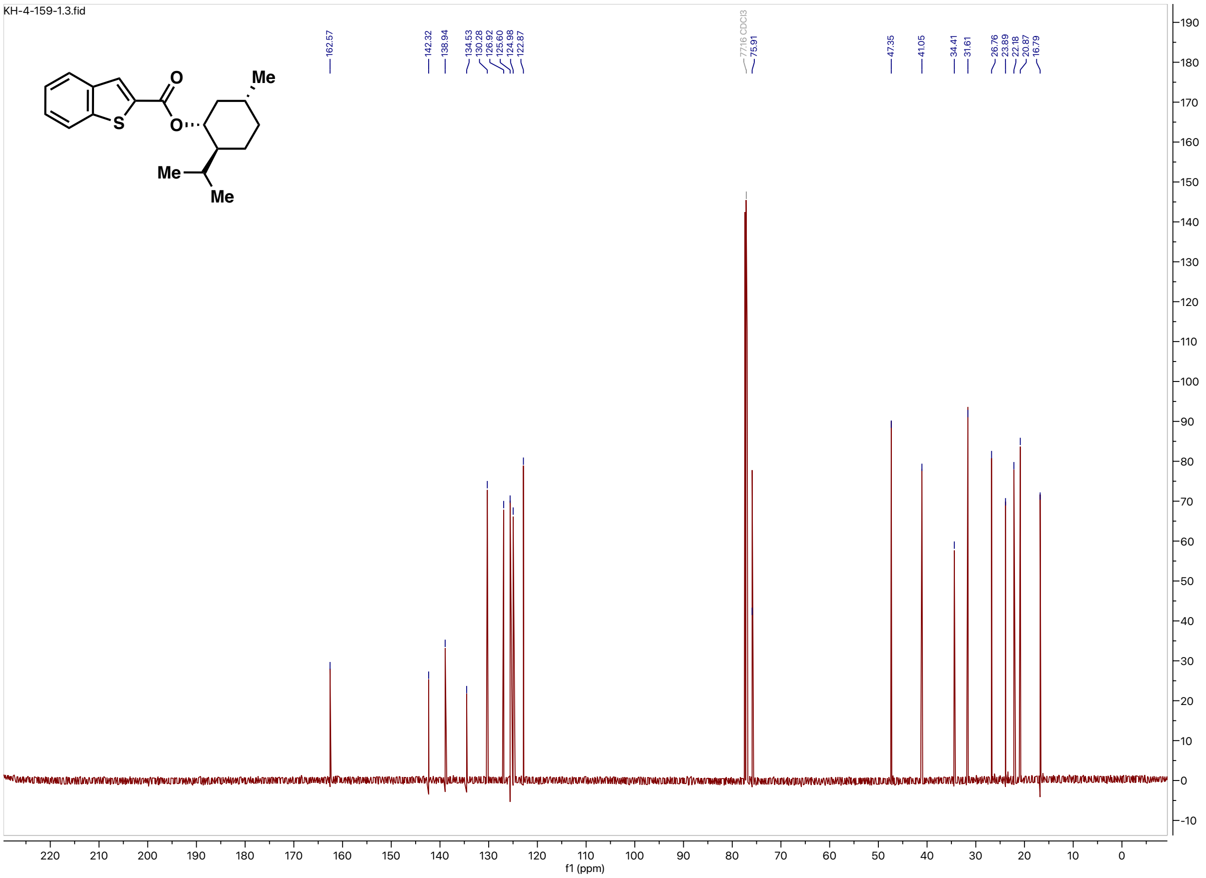
50
40
30
20
10
0
f1 (ppm)

Compound 14s

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124.98
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75.91
47.35
41.05
34.41
31.61
26.76
23.89
22.18
20.87
16.79
O
O
S
Me
Me
Me
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
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10
0
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180
170
160
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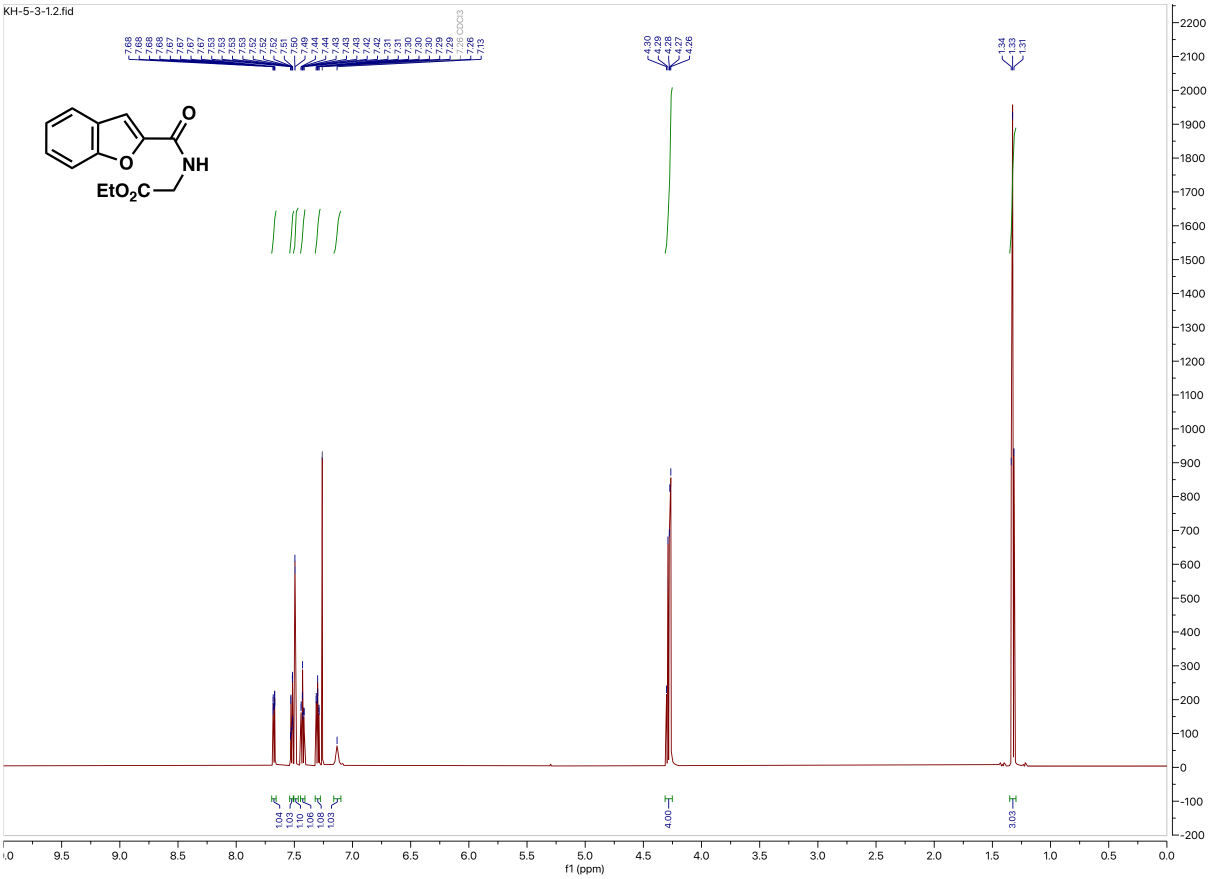
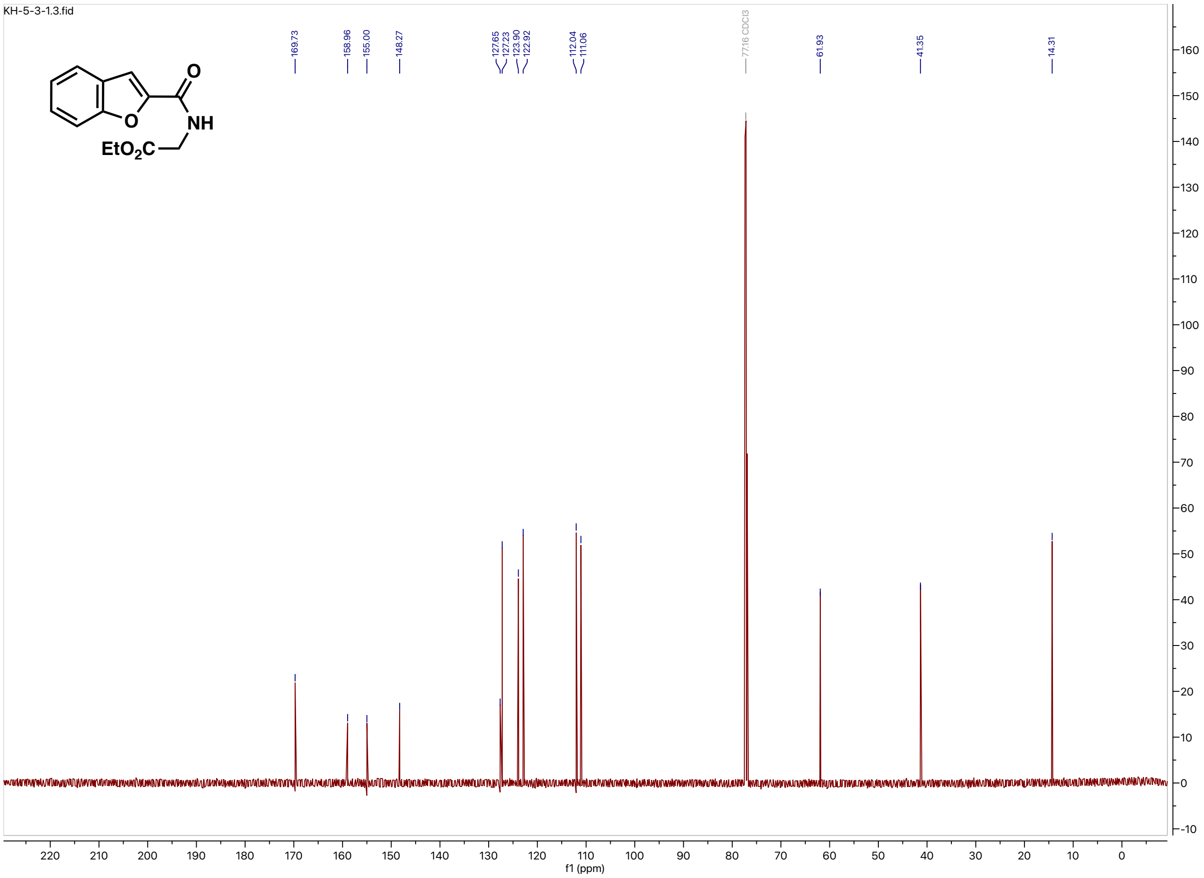
f1 (ppm)

Compound 15s

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123.90
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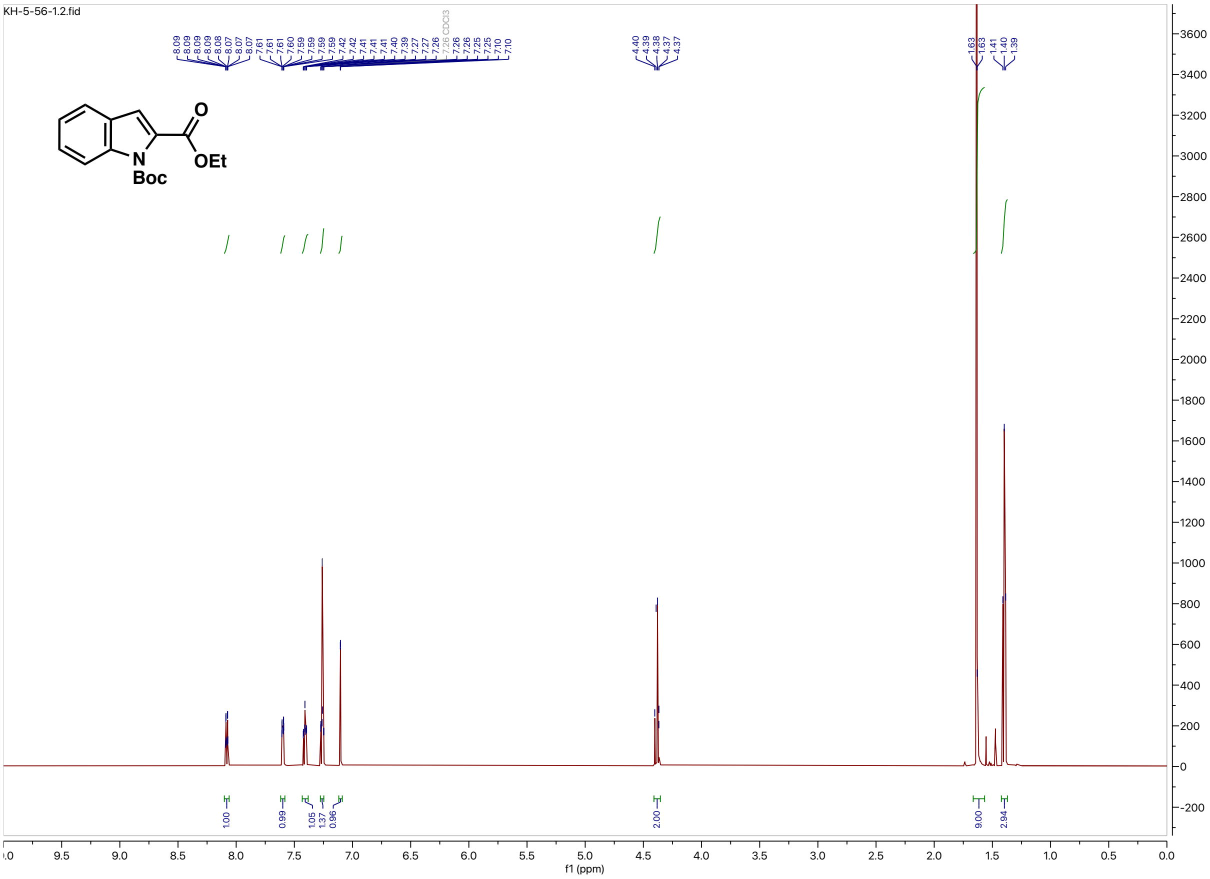
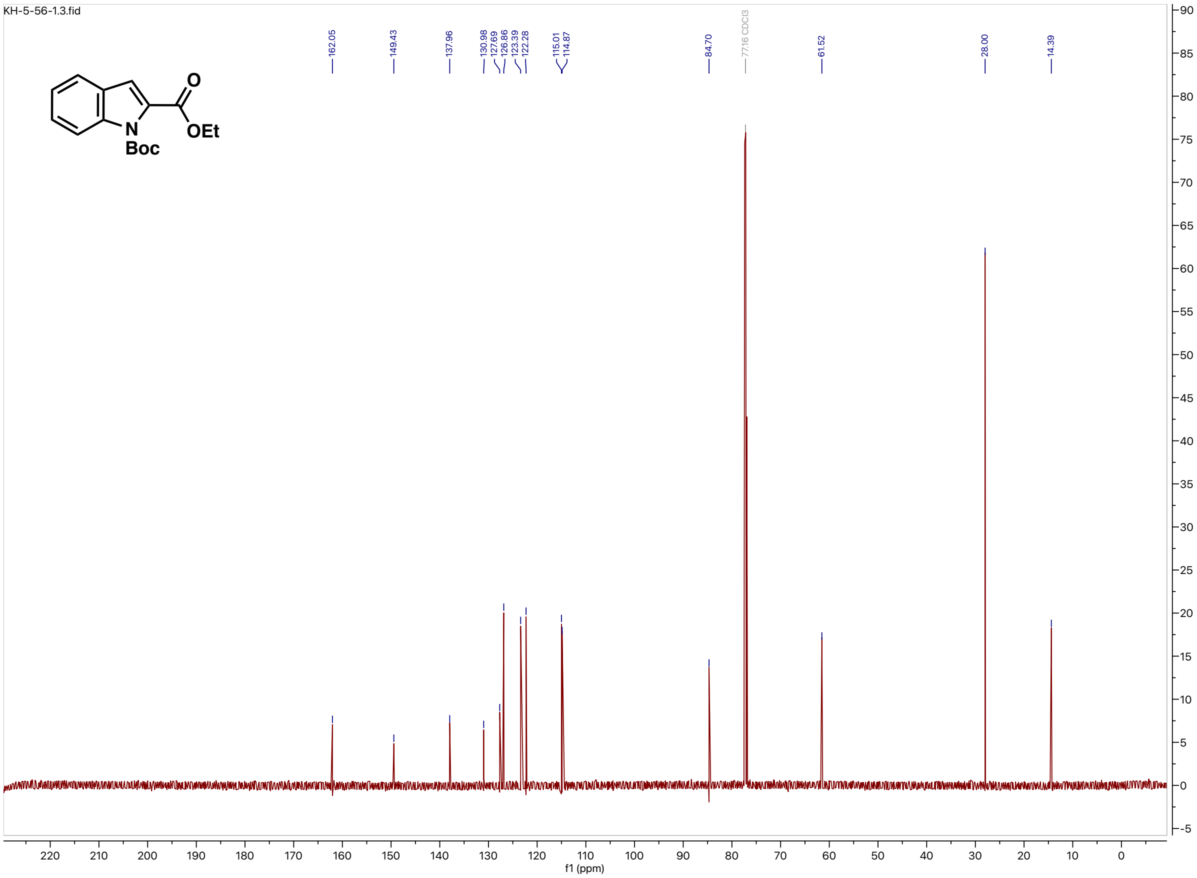
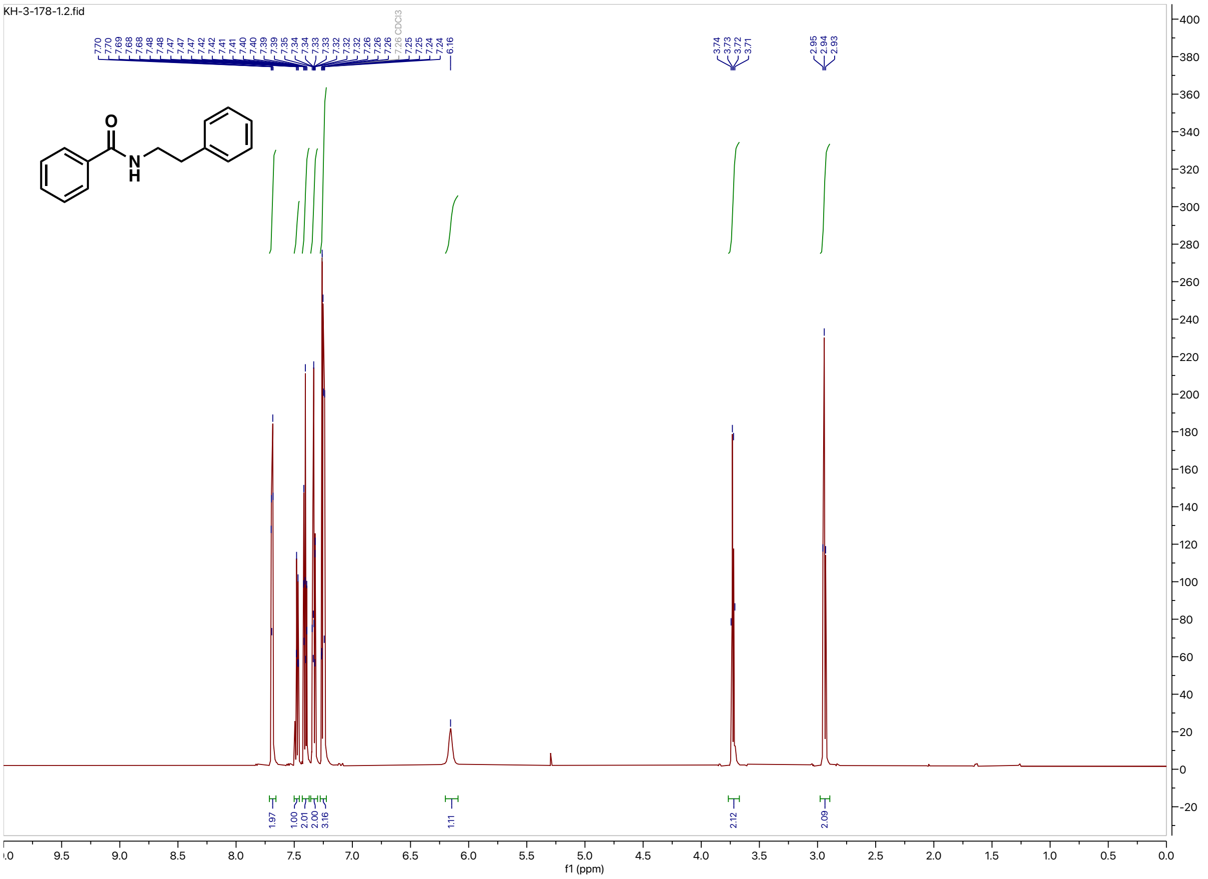
111.06
77.16 CDCl3
61.93
41.35
14.31
O
O
NH
EtO2C
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

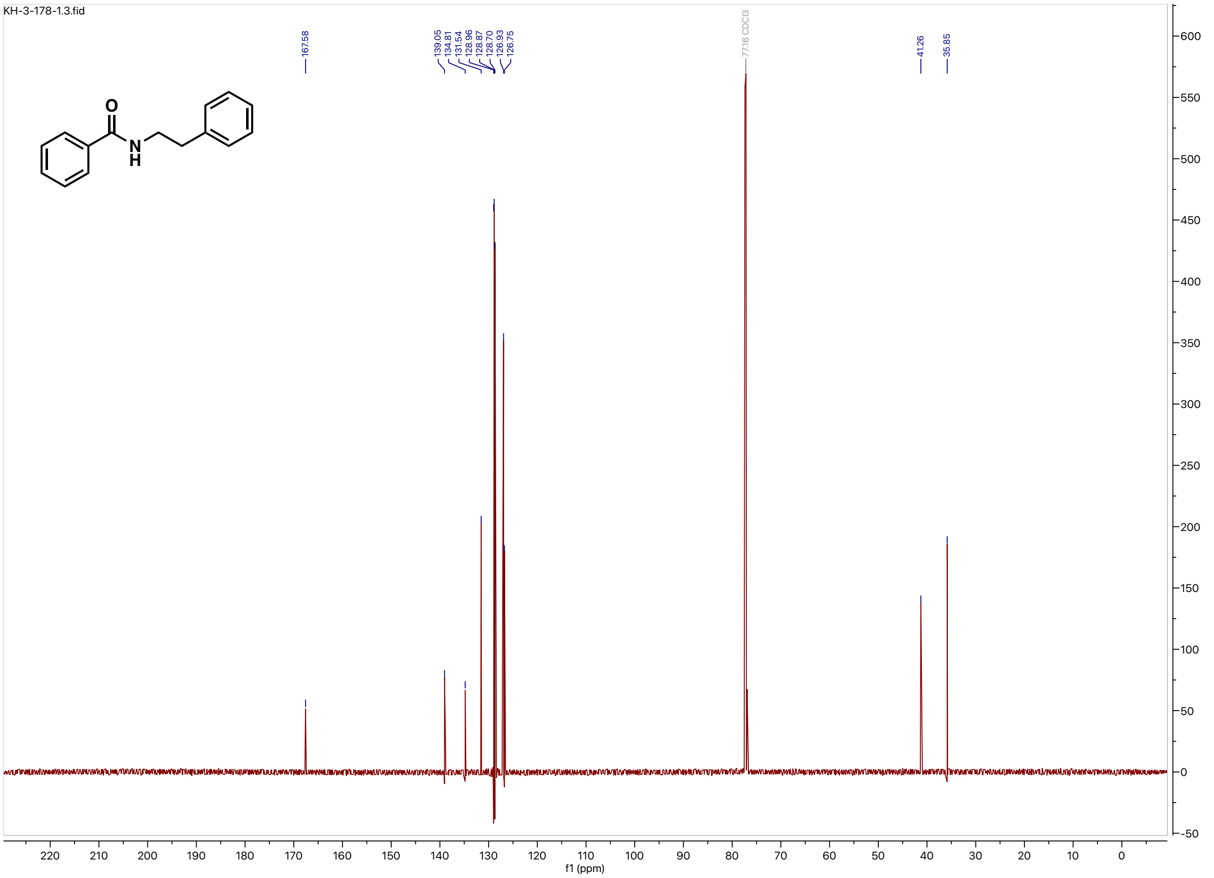
Compound 16s



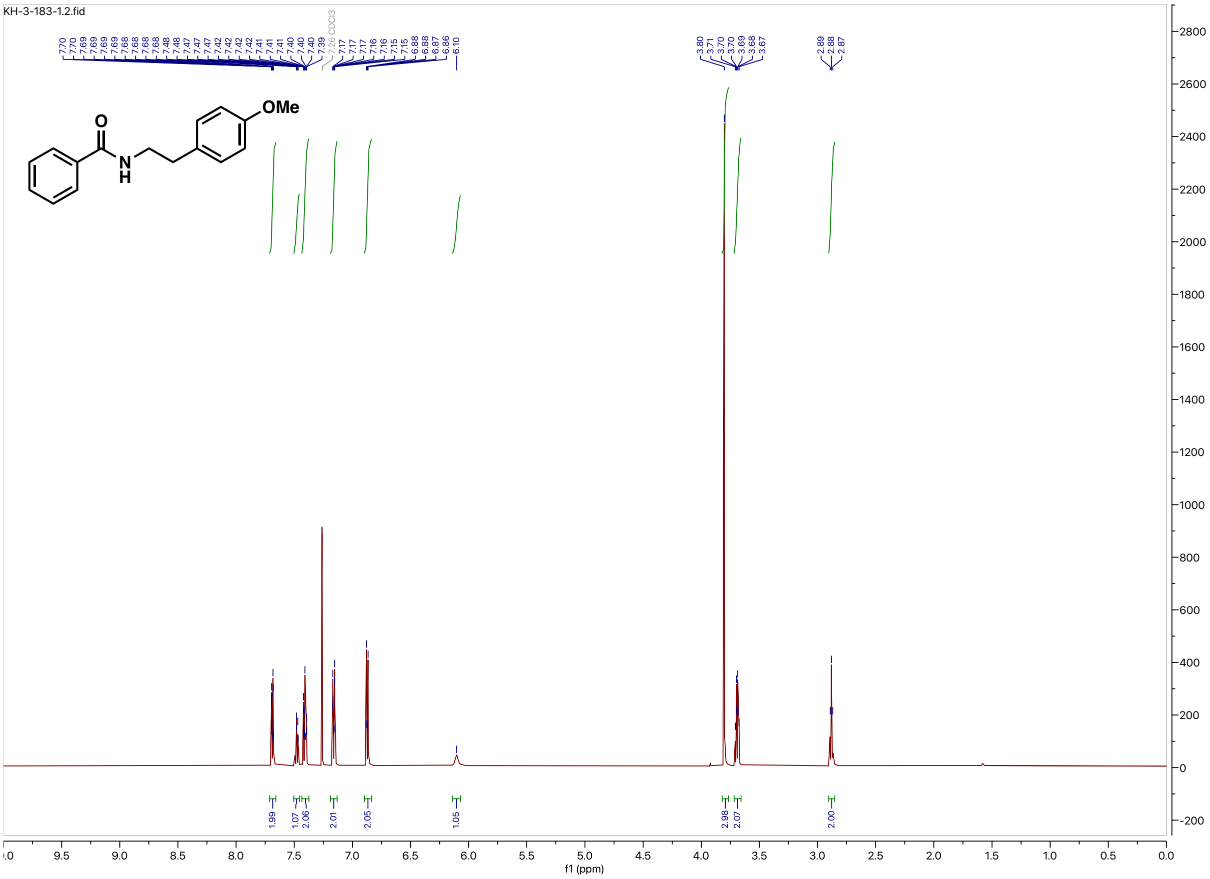

KH-5-56-1.3.fid
O
N
Boc
OEt
162.05
149.43
137.96
130.98
127.69
126.86
123.39
122.28
115.01
114.87
84.70
77.16 CDCl3
61.52
28.00
14.39
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

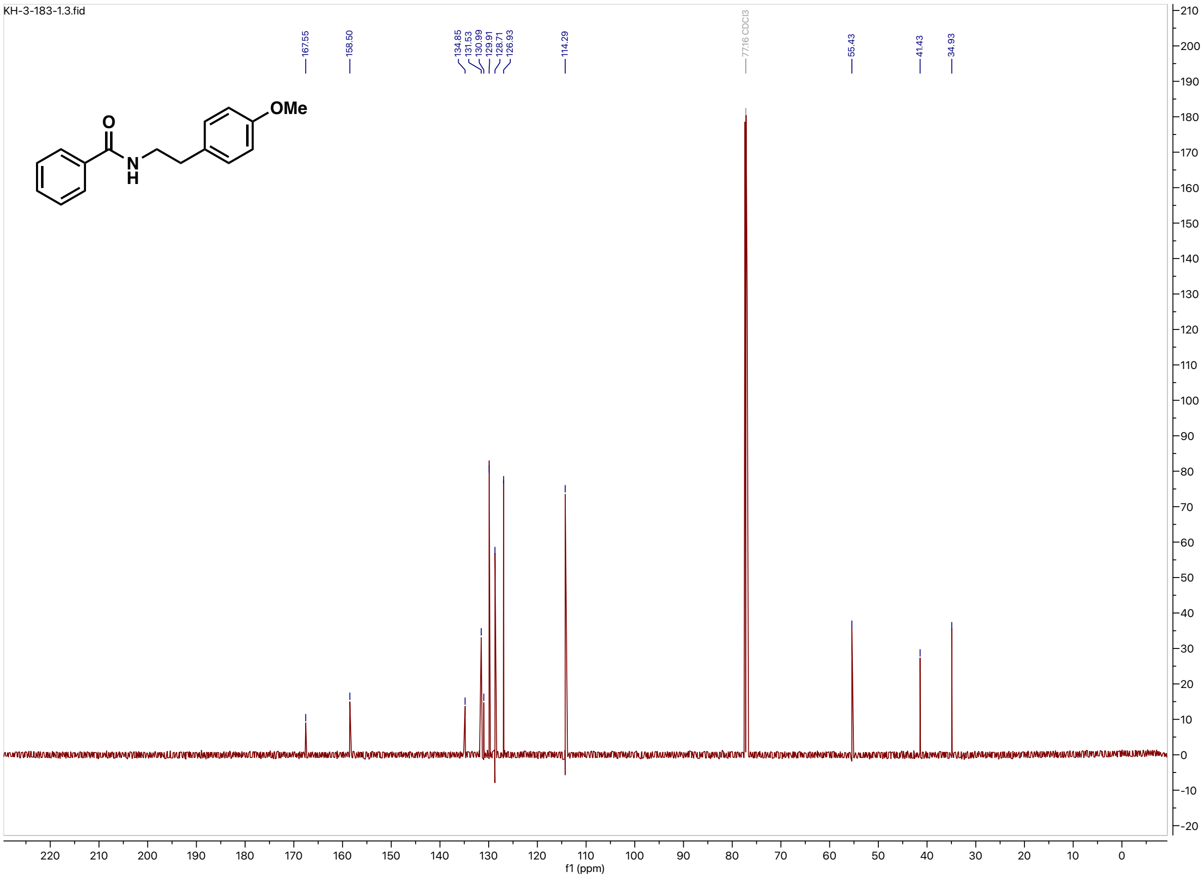
Compound 17s



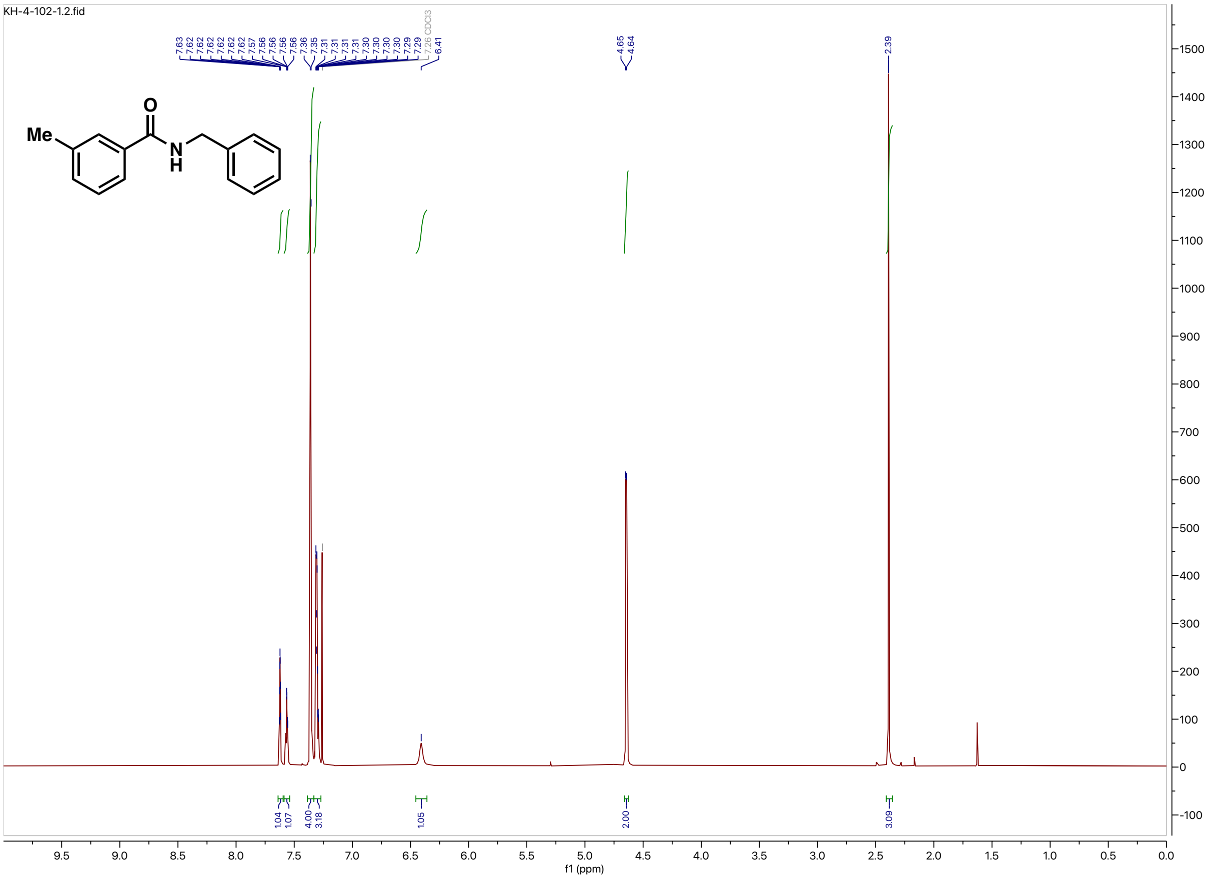

KH-3-178-1.3.fid
167.58
139.05
134.81
131.54
128.96
128.87
128.70
126.93
126.75
77.16 CDCl3
41.26
35.85
O
N
H
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

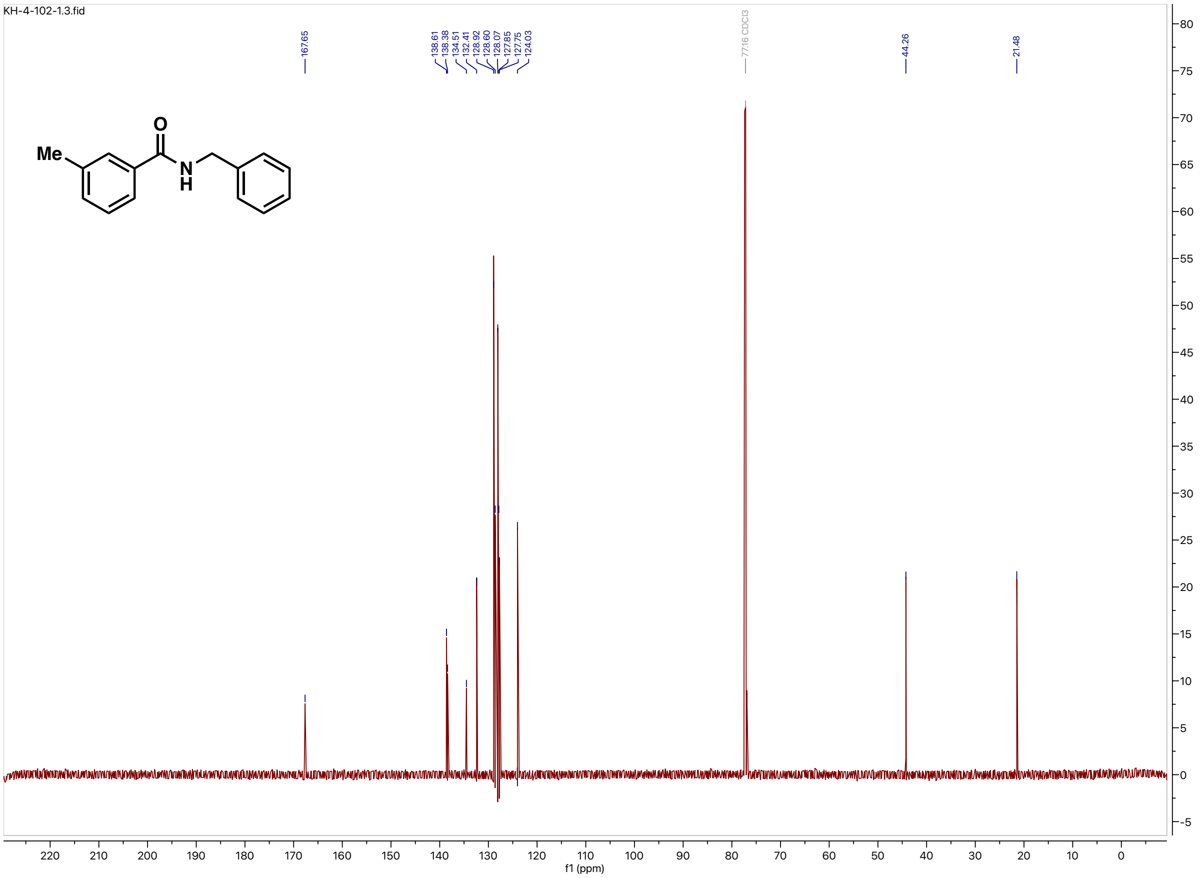
Compound 18s



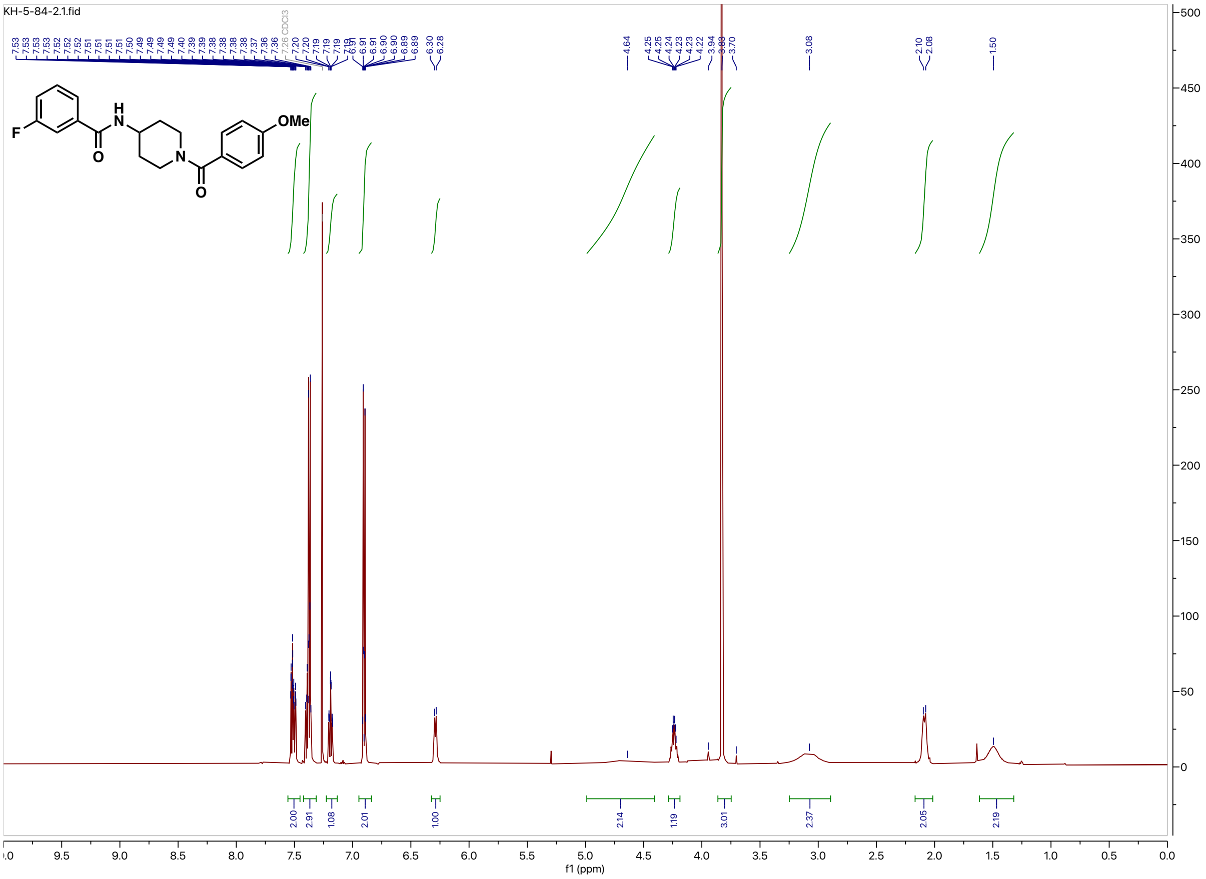

KH-3-183-1.3.fid
167.55
158.50
134.85
131.53
130.99
129.91
128.71
126.93
114.29
77.16 CDCl3
55.43
41.43
34.93
O
N
H
OMe
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20

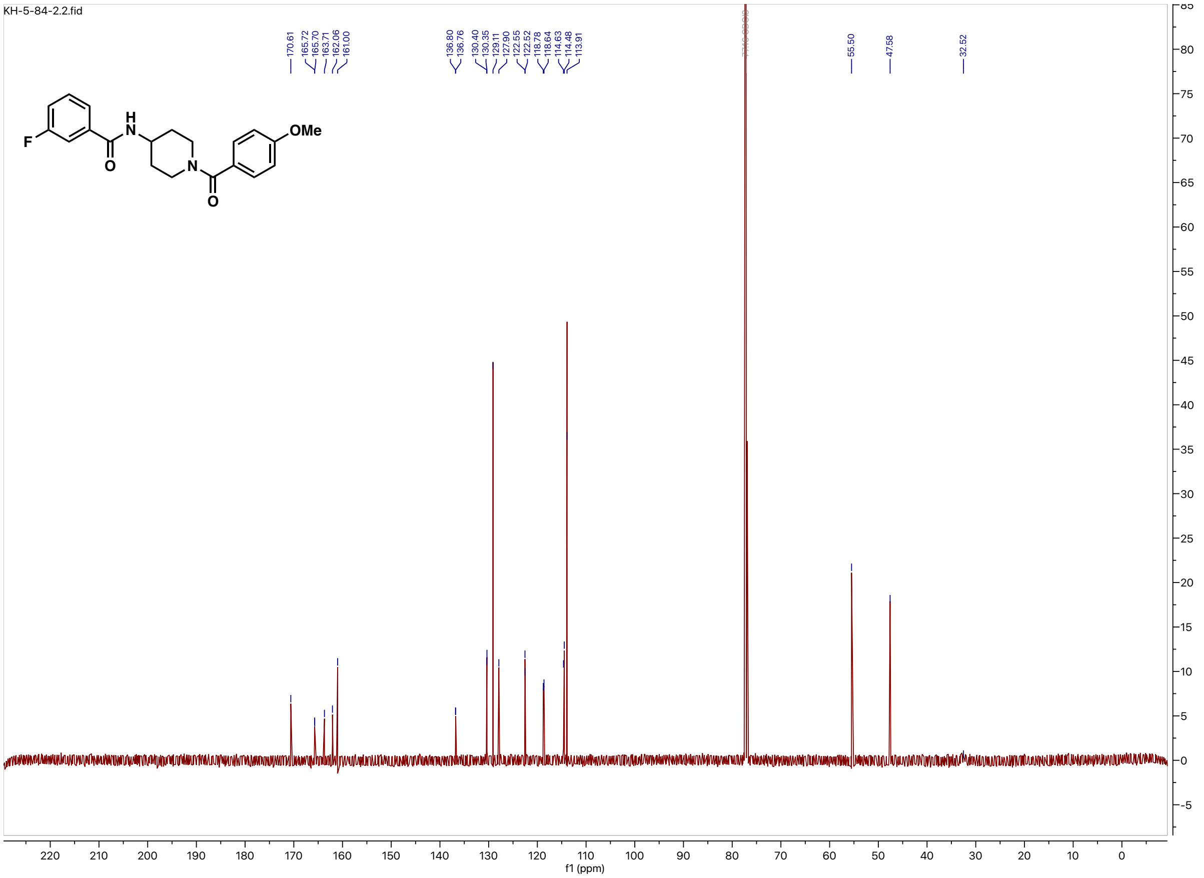
Compound 19s

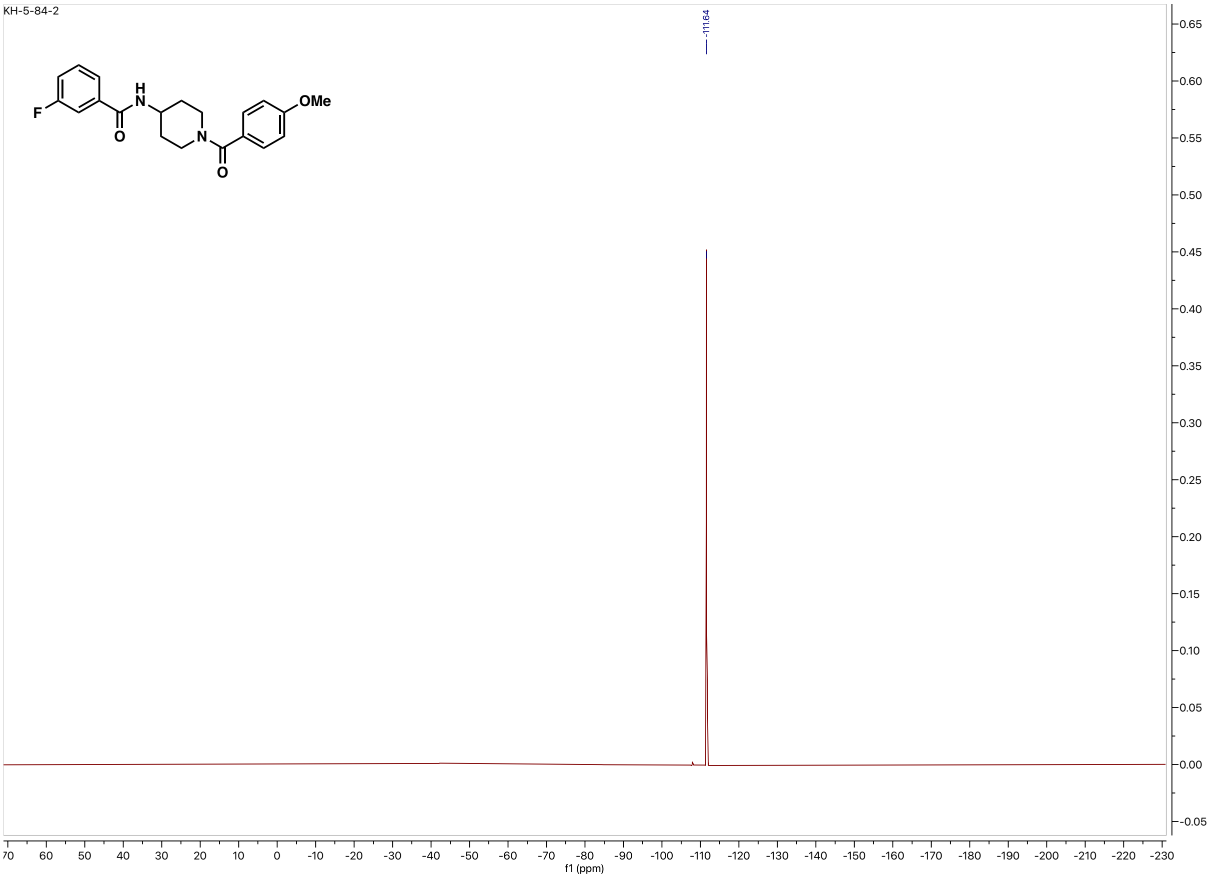



KH-4-102-1.3.fid
167.65
138.61
138.38
134.51
132.41
128.92
128.60
128.07
127.85
127.75
124.03
77.16 CDCl3
44.26
21.48
Me
O
N
H
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

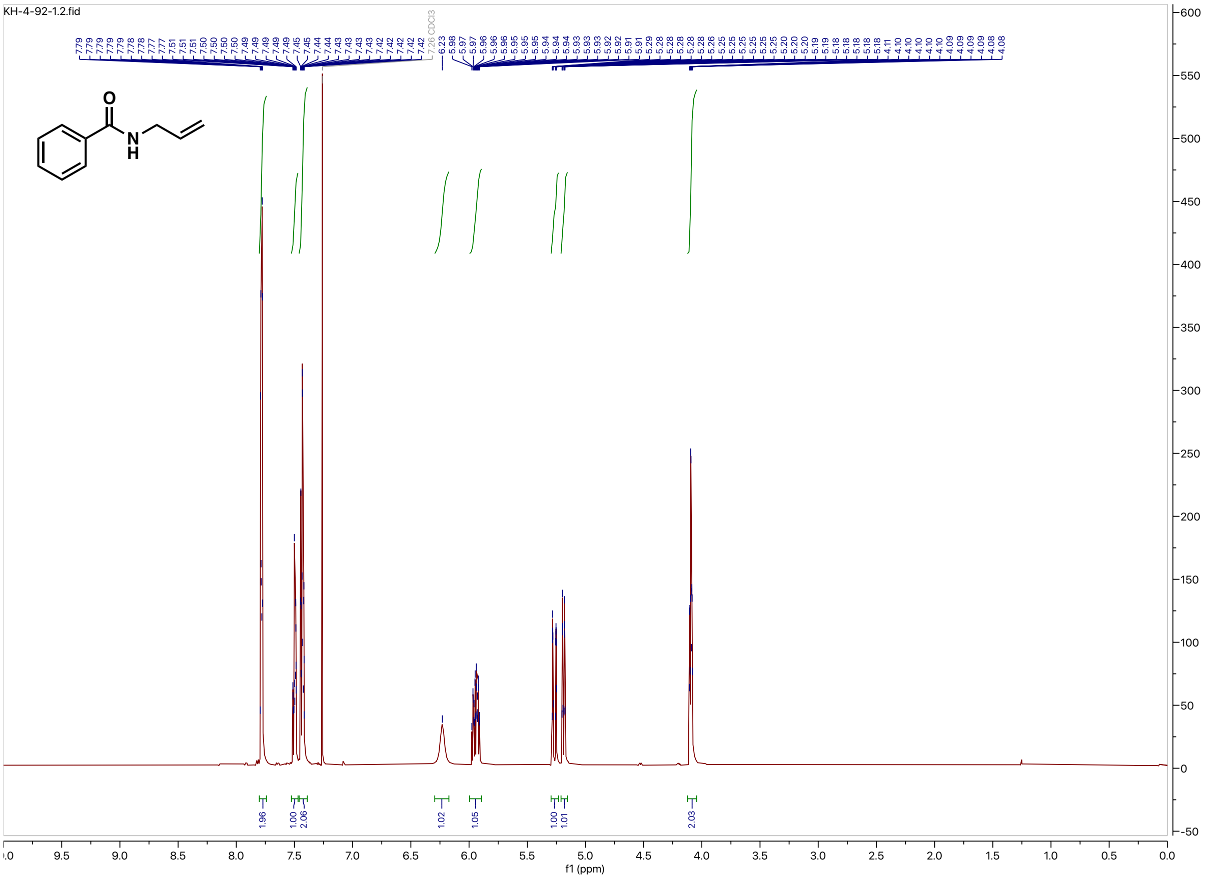
Compound 20s

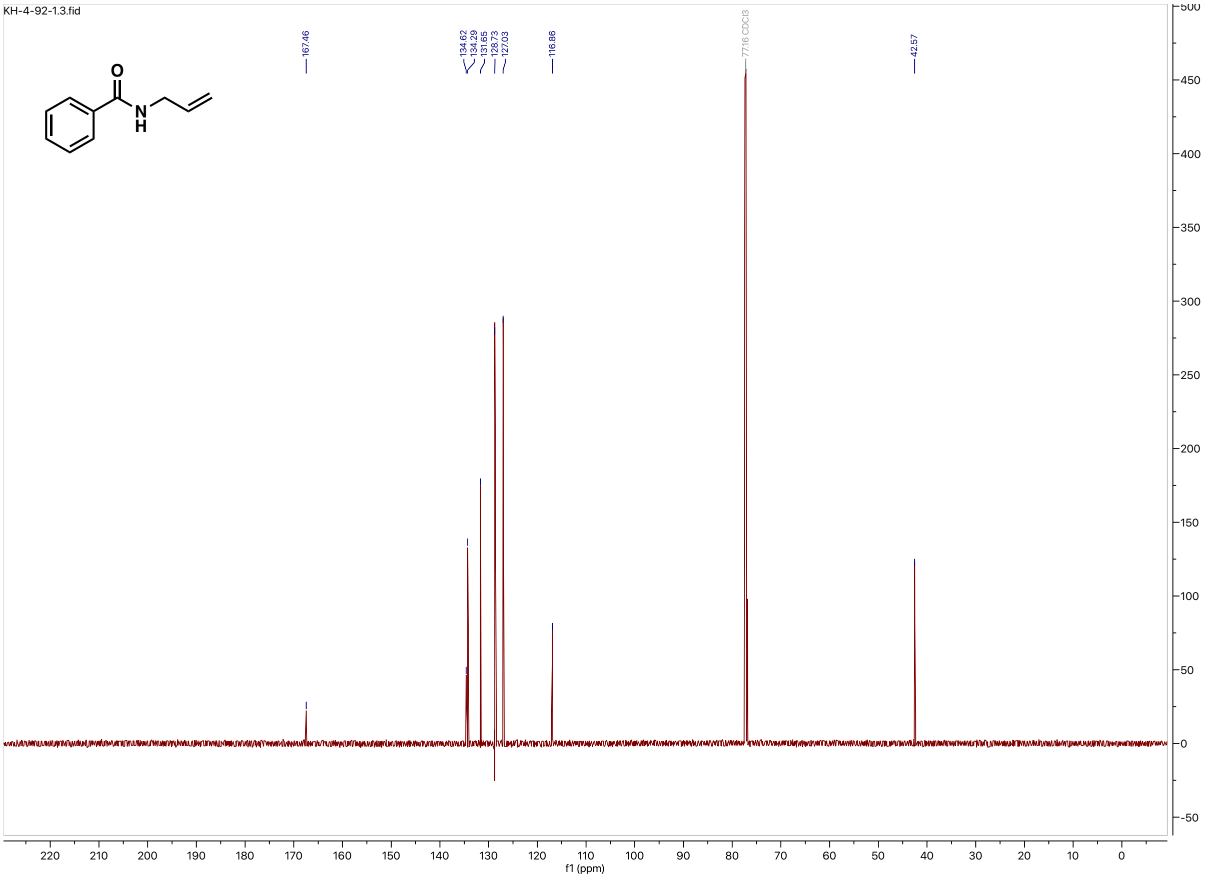



KH-5-84-2.2.fid
170.61
165.72
165.70
163.71
162.06
161.00
136.80
136.76
130.40
130.35
129.11
127.90
122.55
122.52
118.78
118.64
114.63
114.48
113.91
55.50
47.58
32.52
F
H
N
O
N
O
OMe
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

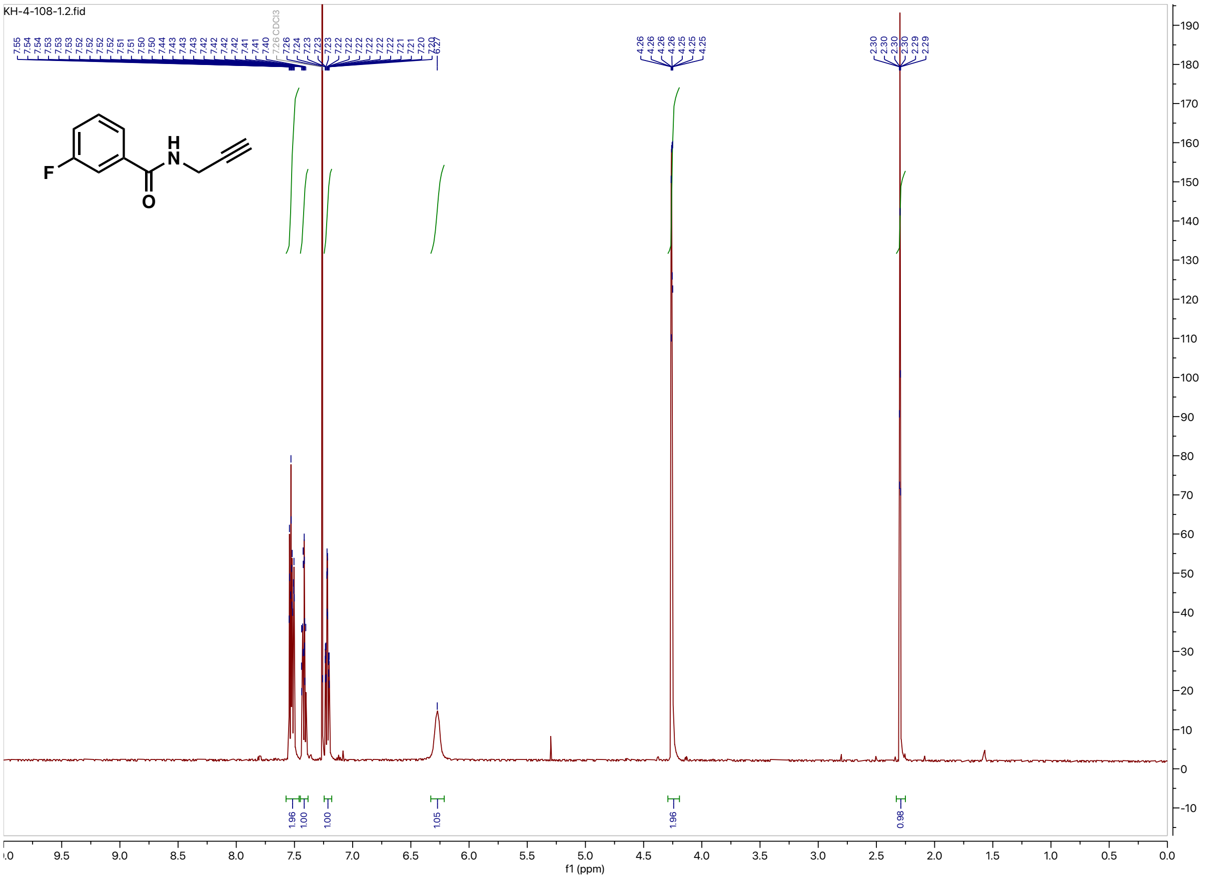

KH-5-84-2
F
H
N
O
N
O
OMe
-111.64
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
f1 (ppm)

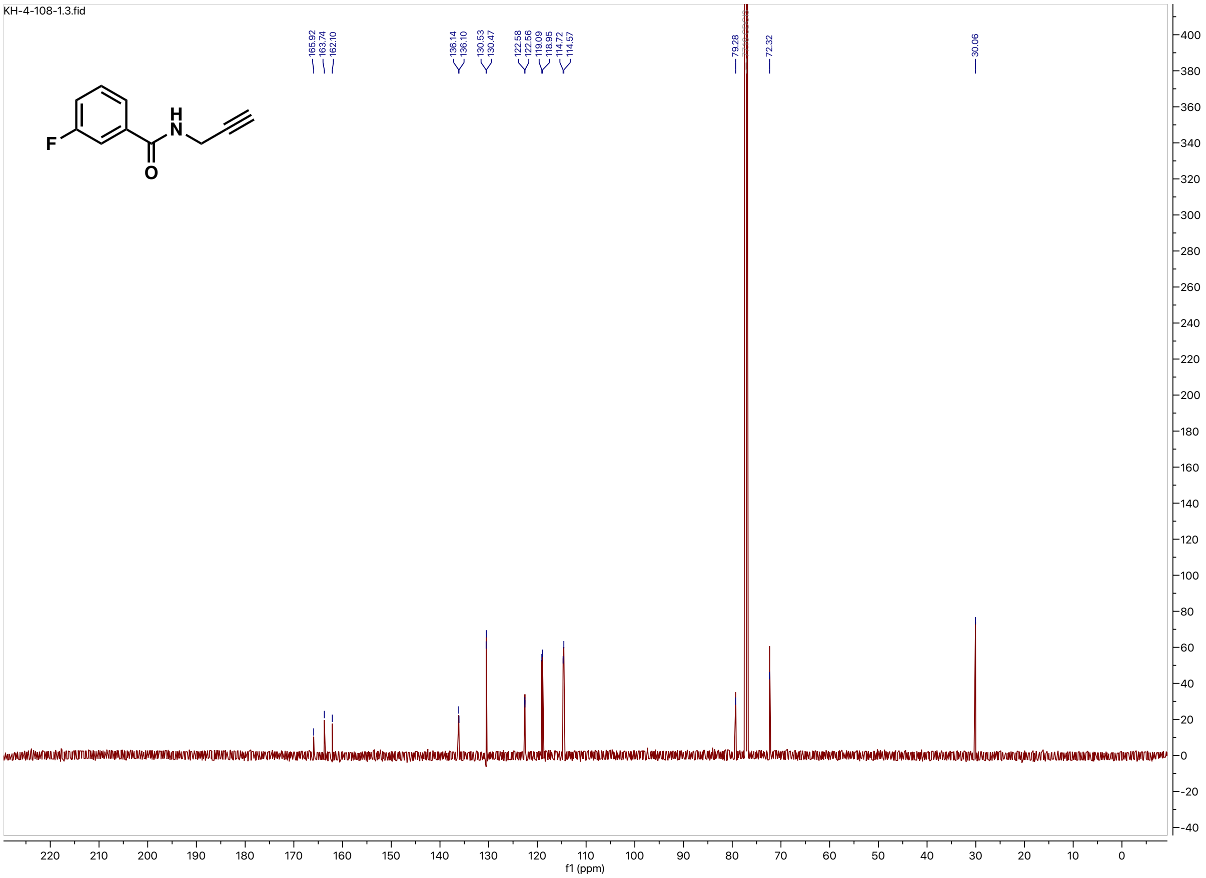
Compound 21s

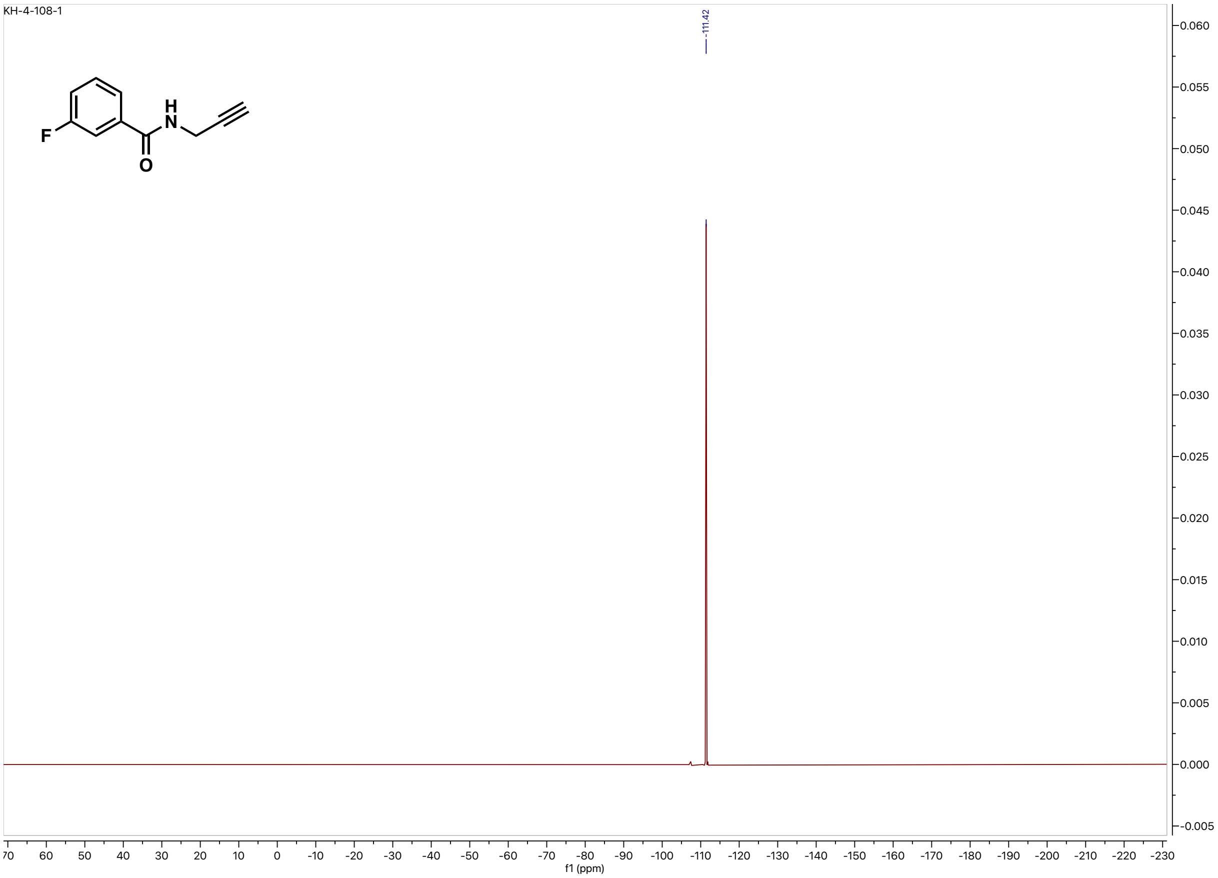



KH-4-92-1.3.fid
O
N
H
167.46
134.62
134.29
131.65
128.73
127.03
116.86
77.16 CDCl3
42.57
500
450
400
350
300
250
200
150
100
50
0
-50
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

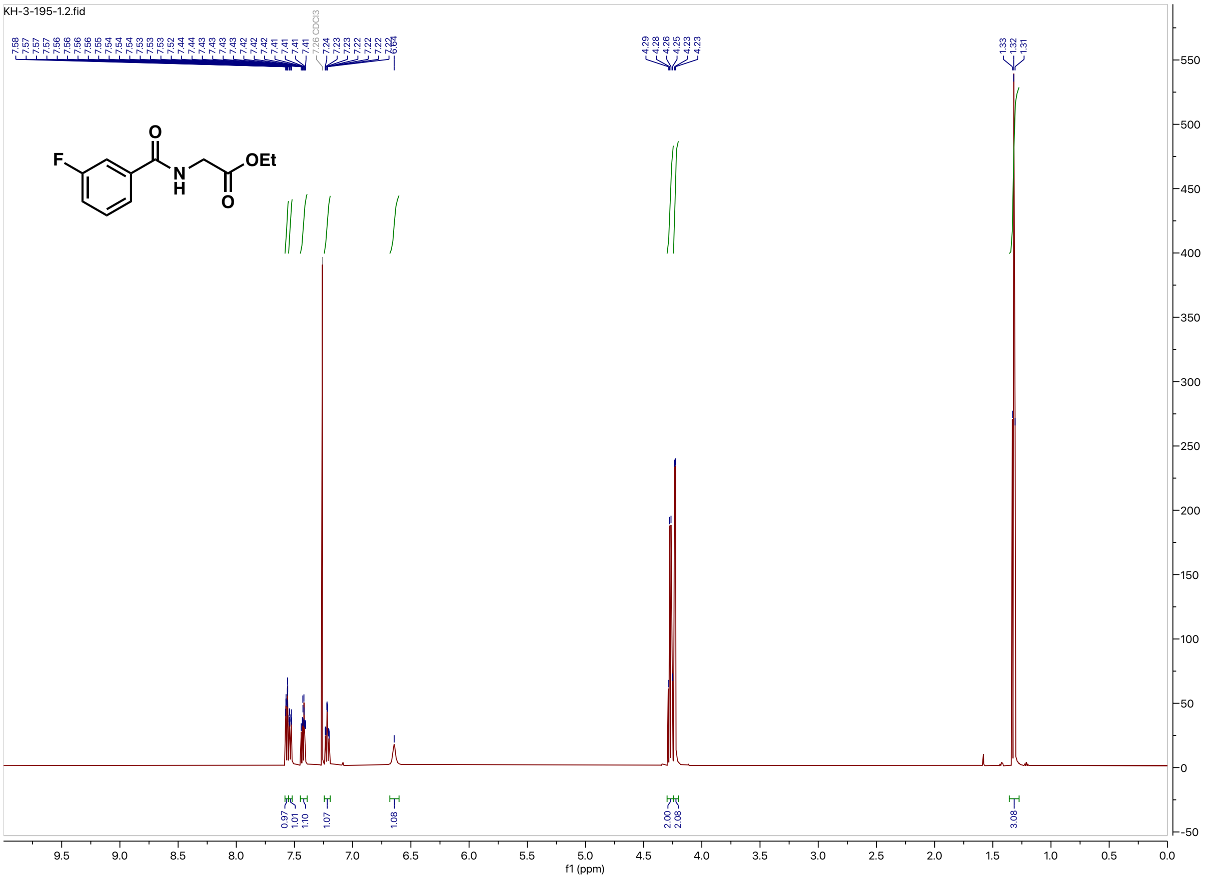
Compound 22s

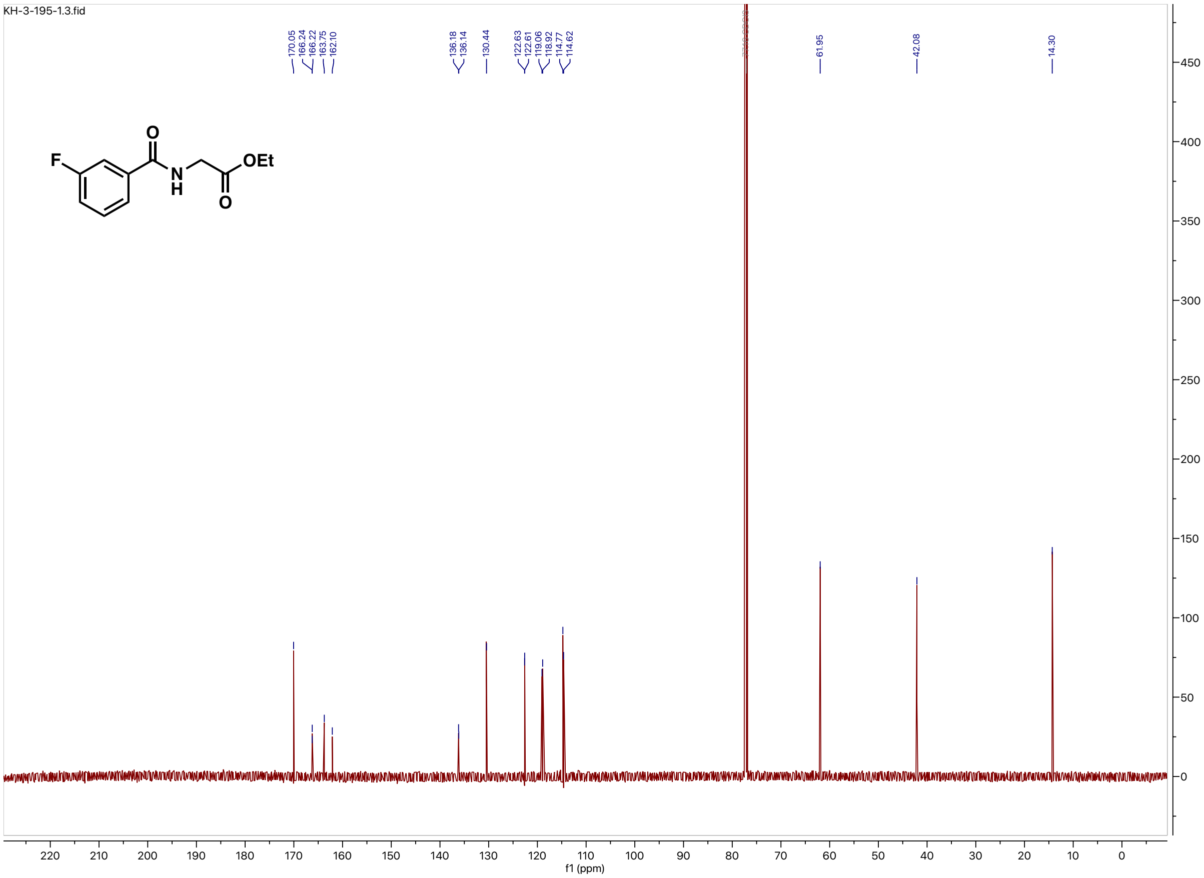


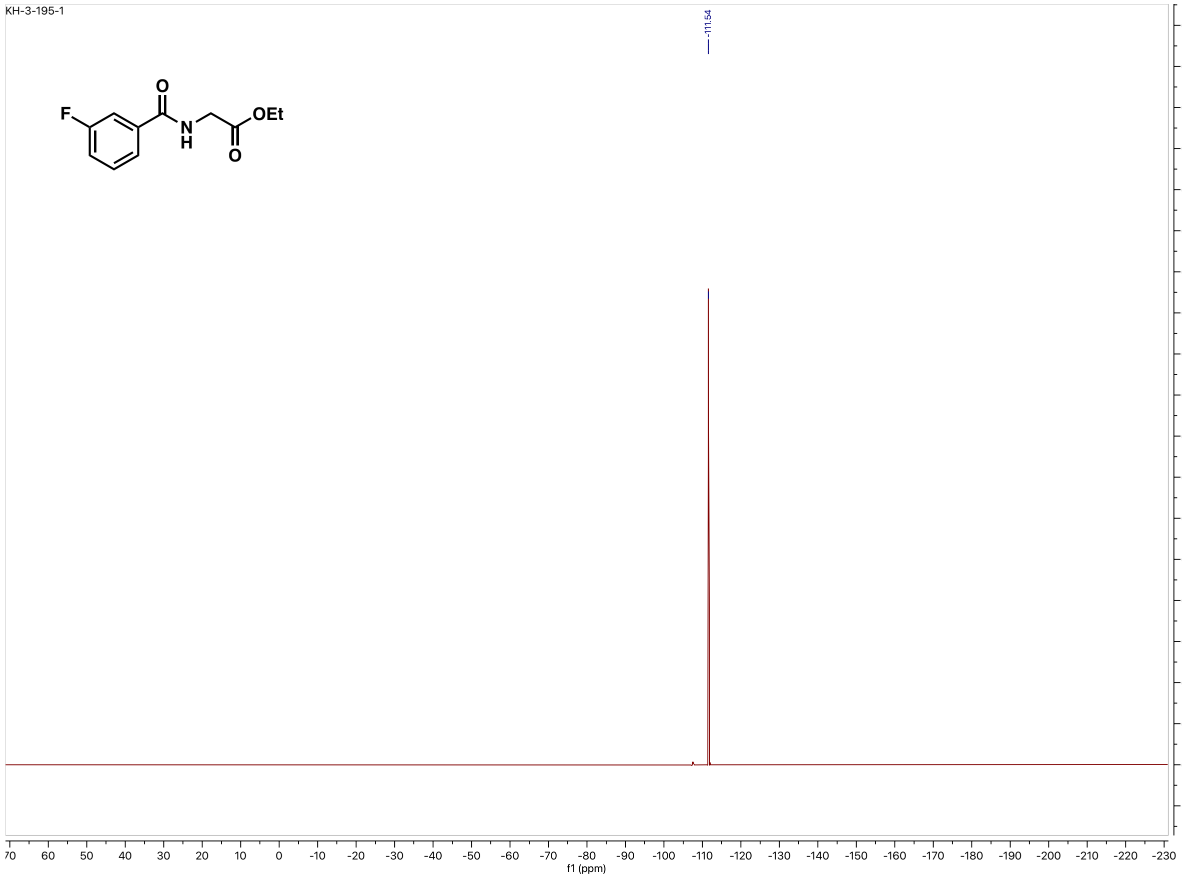

KH-4-108-1.3.fid
165.92
163.74
162.10
136.14
136.10
130.53
130.47
122.58
122.56
119.09
118.95
114.72
114.57
79.28
72.32
30.06
F
H
N
O
400
380
360
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
-40
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


KH-4-108-1
-111.42
F
H
N
O
0.060
0.055
0.050
0.045
0.040
0.035
0.030
0.025
0.020
0.015
0.010
0.005
0.000
-0.005
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230
f1 (ppm)

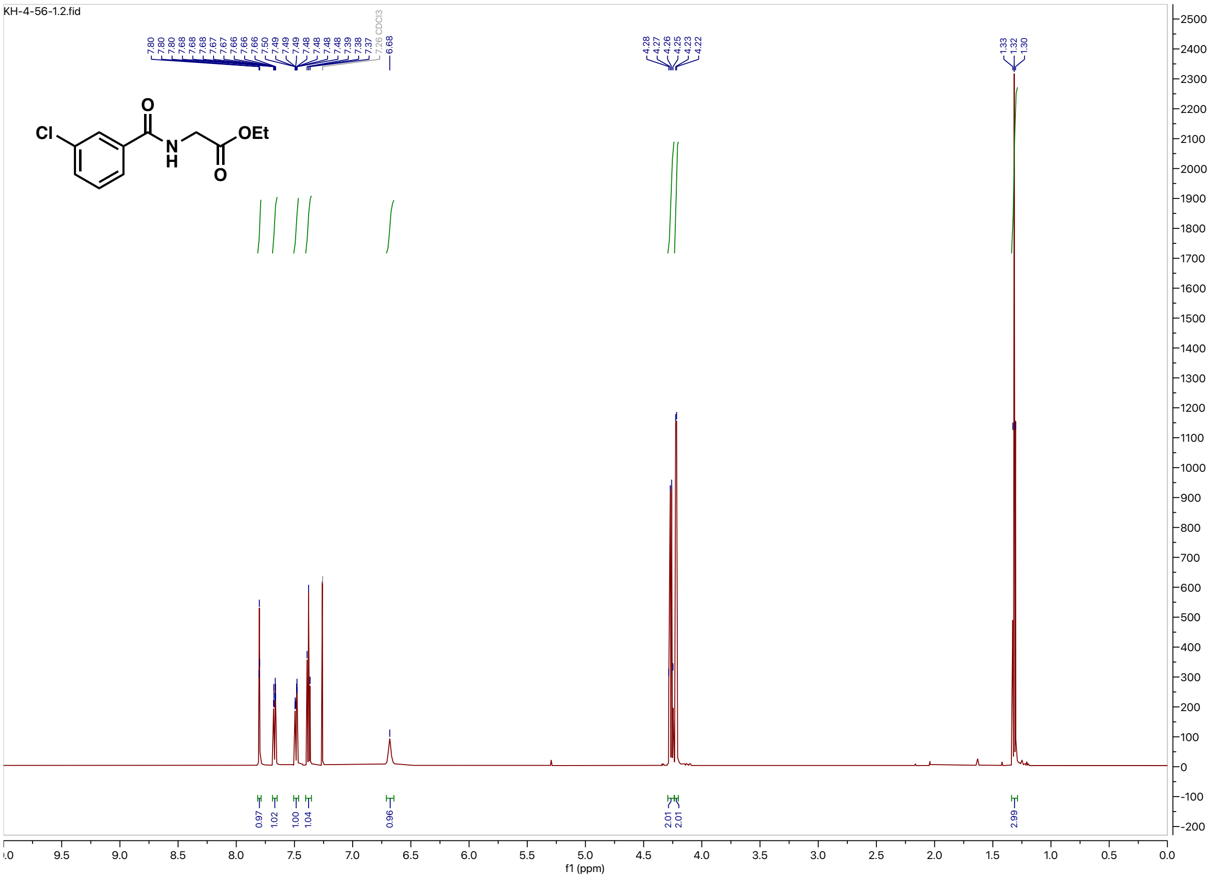
Compound 23s

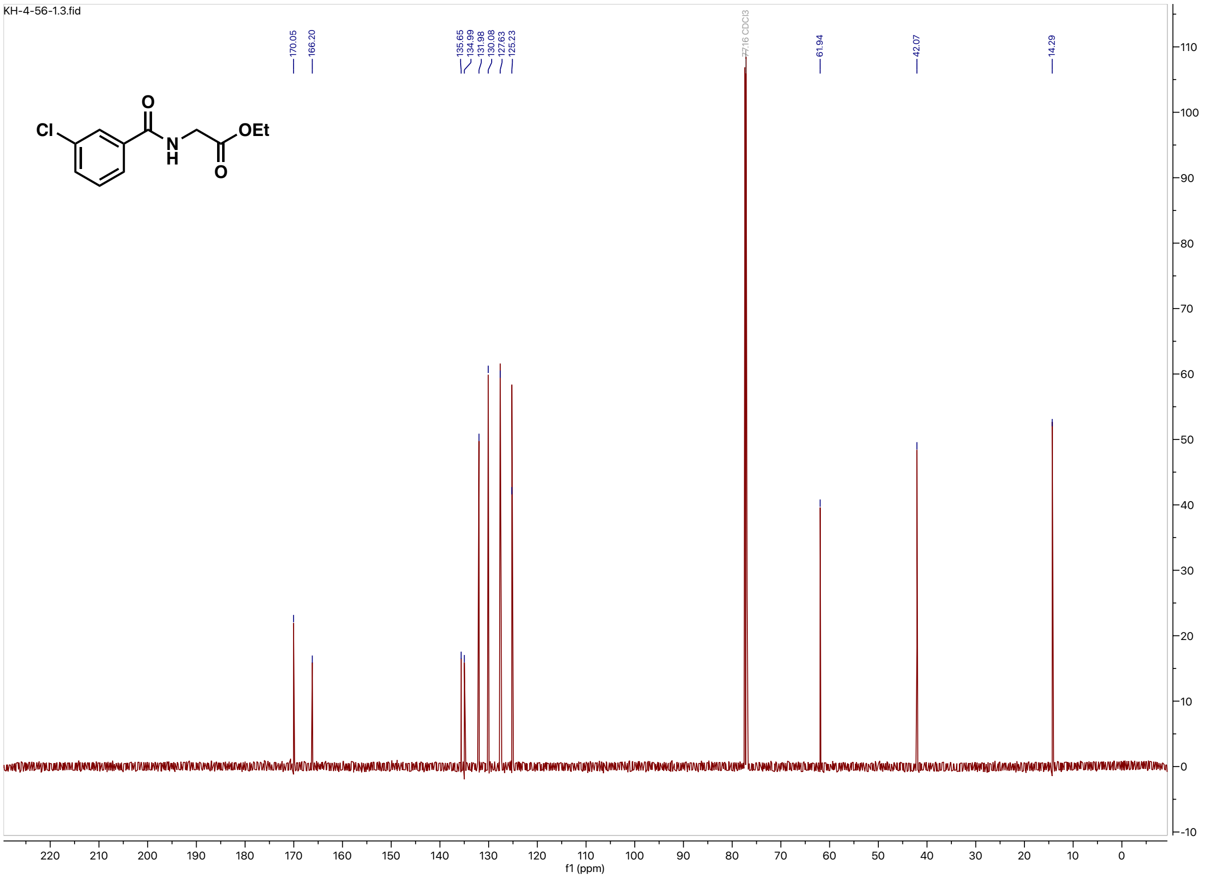



KH-3-195-1.3.fid
170.05
166.24
166.22
163.75
162.10
136.18
136.14
130.44
122.63
122.61
119.06
118.92
114.77
114.62
61.95
42.08
14.30
F
O
N
H
OEt
O
450
400
350
300
250
200
150
100
50
0
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

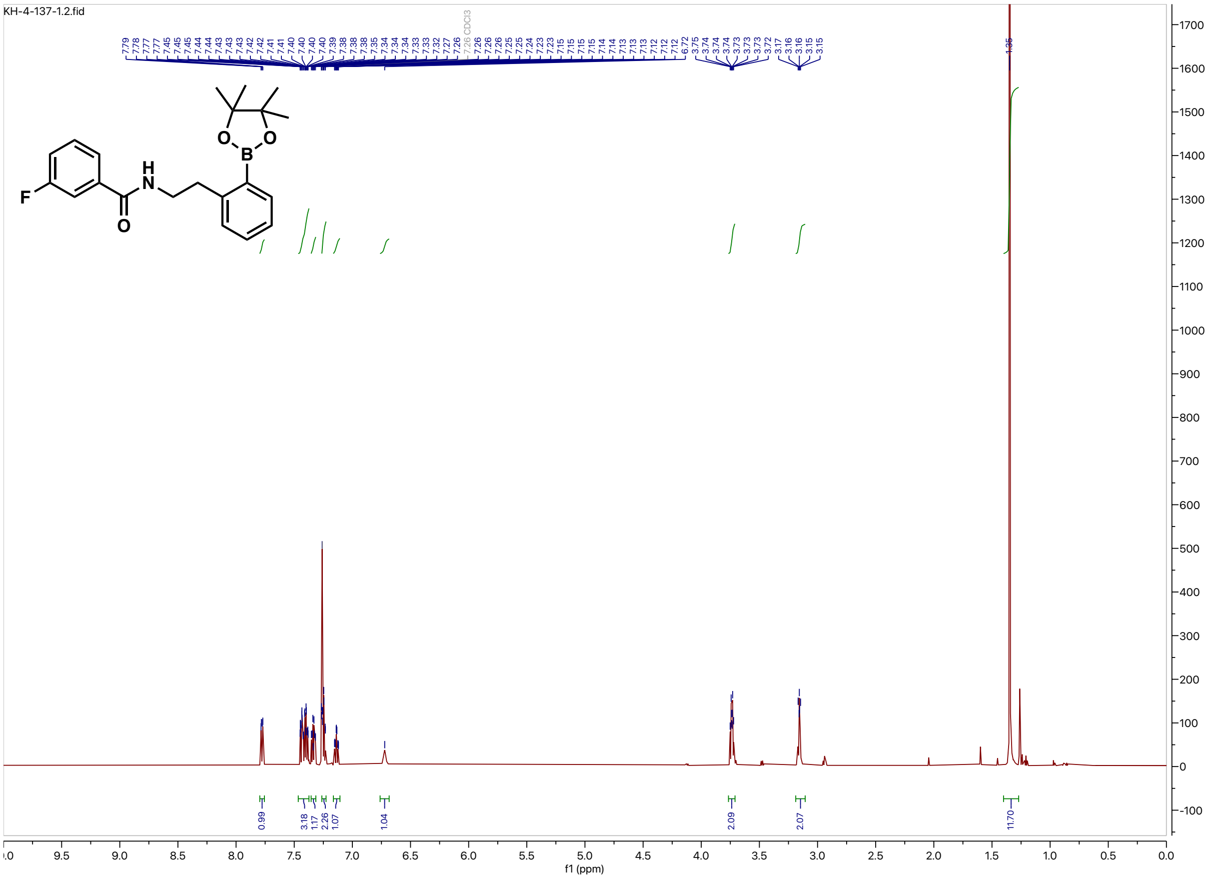

KH-3-195-1
F
O
N
H
OEt
O
-111.54
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
f1 (ppm)

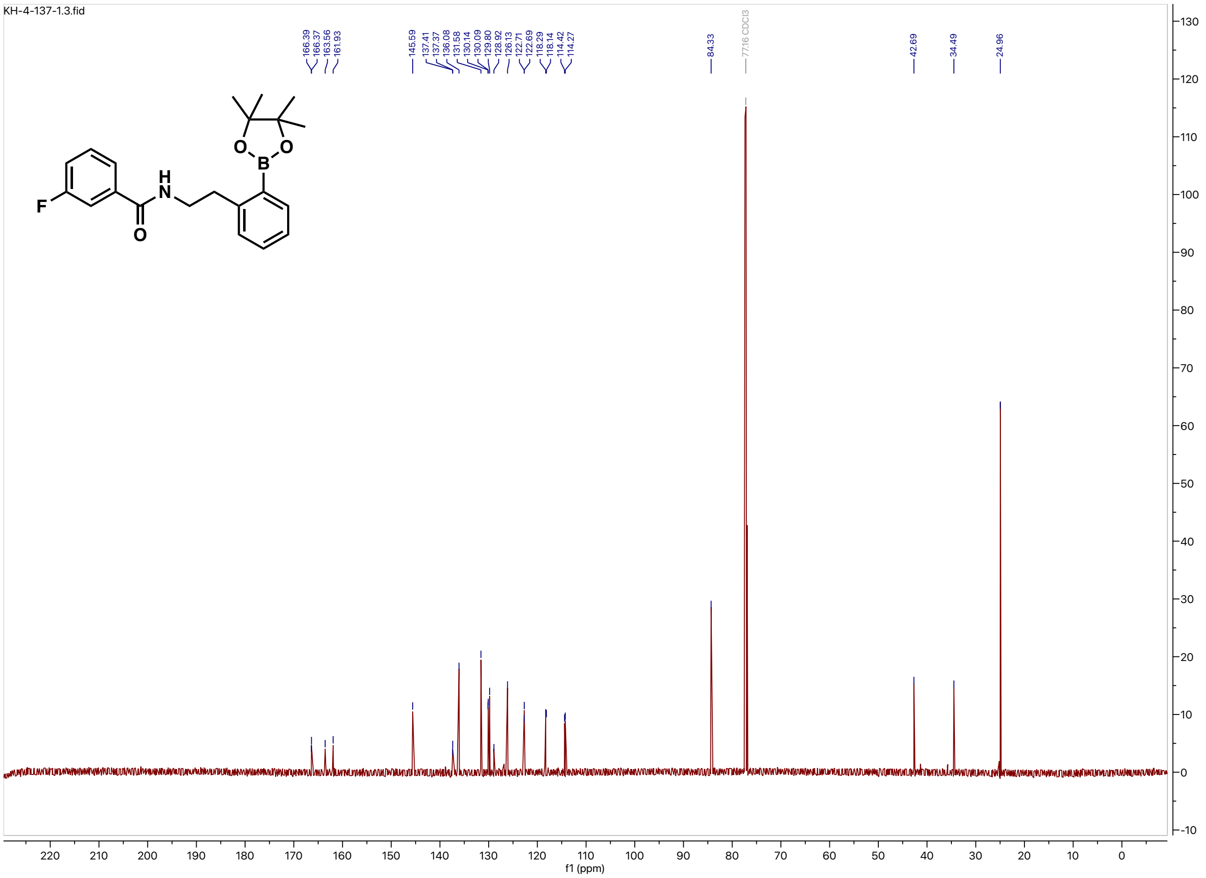
Compound 24s

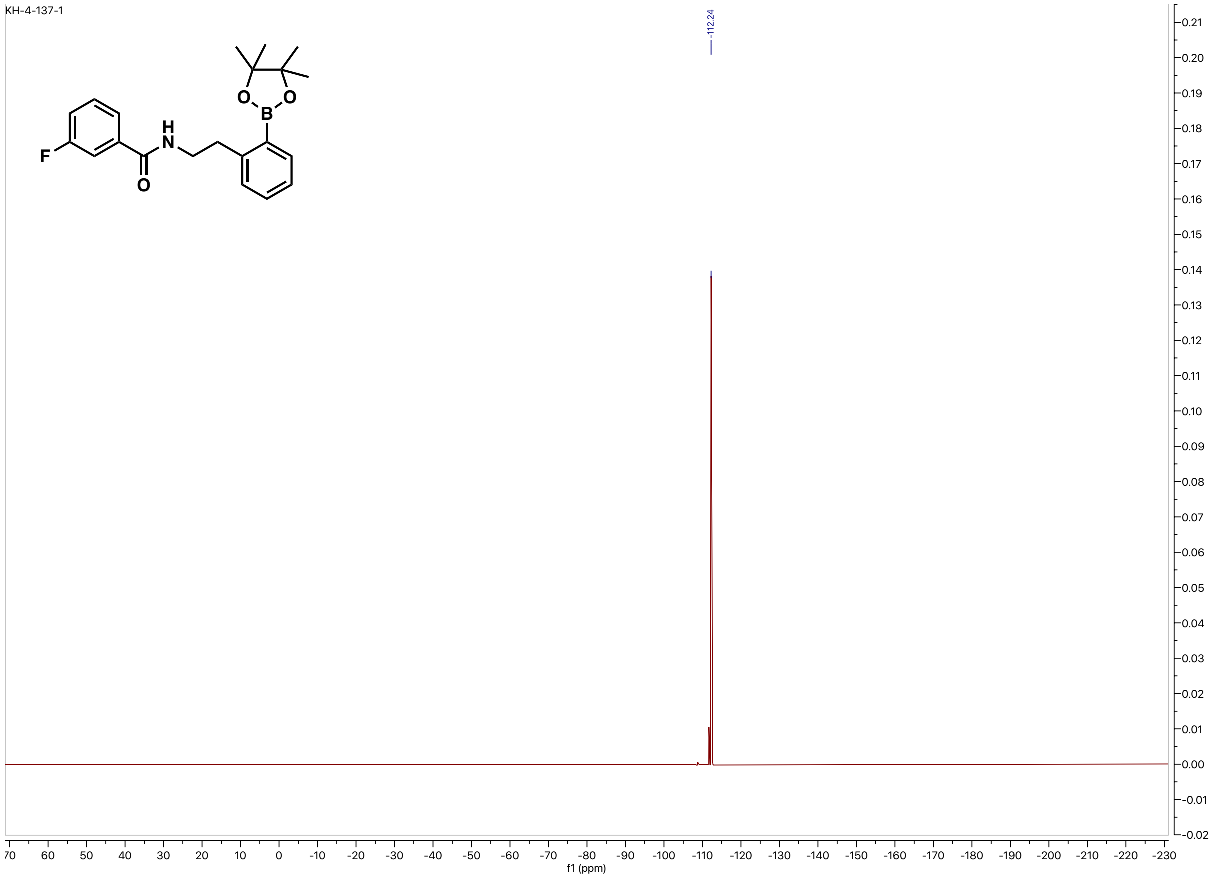



KH-4-56-1.3.fid
170.05
166.20
135.65
134.99
131.98
130.08
127.63
125.23
77.16 CDCl3
61.94
42.07
14.29
Cl
O
N
H
OEt
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
110
100
90
80
70
60
50
40
30
20
10
0
-10

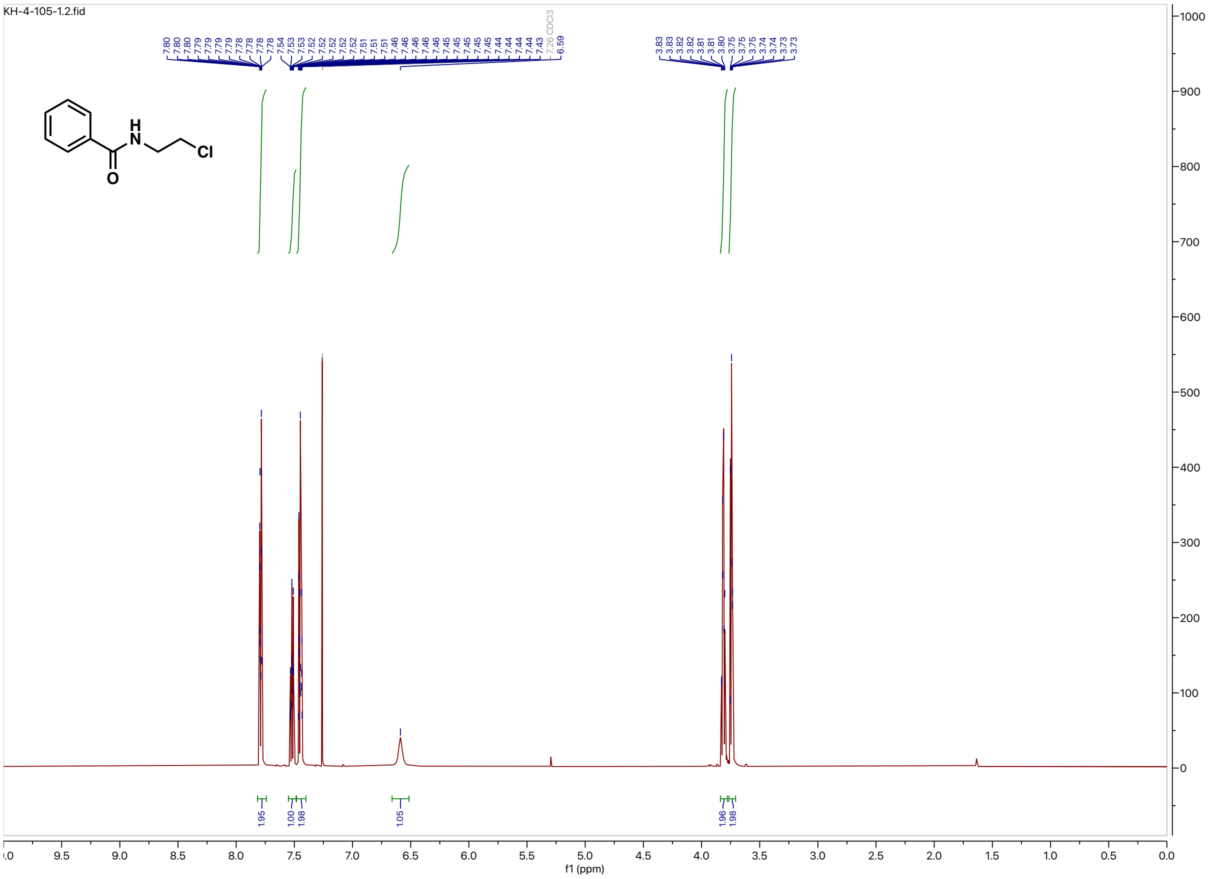
Compound 25s

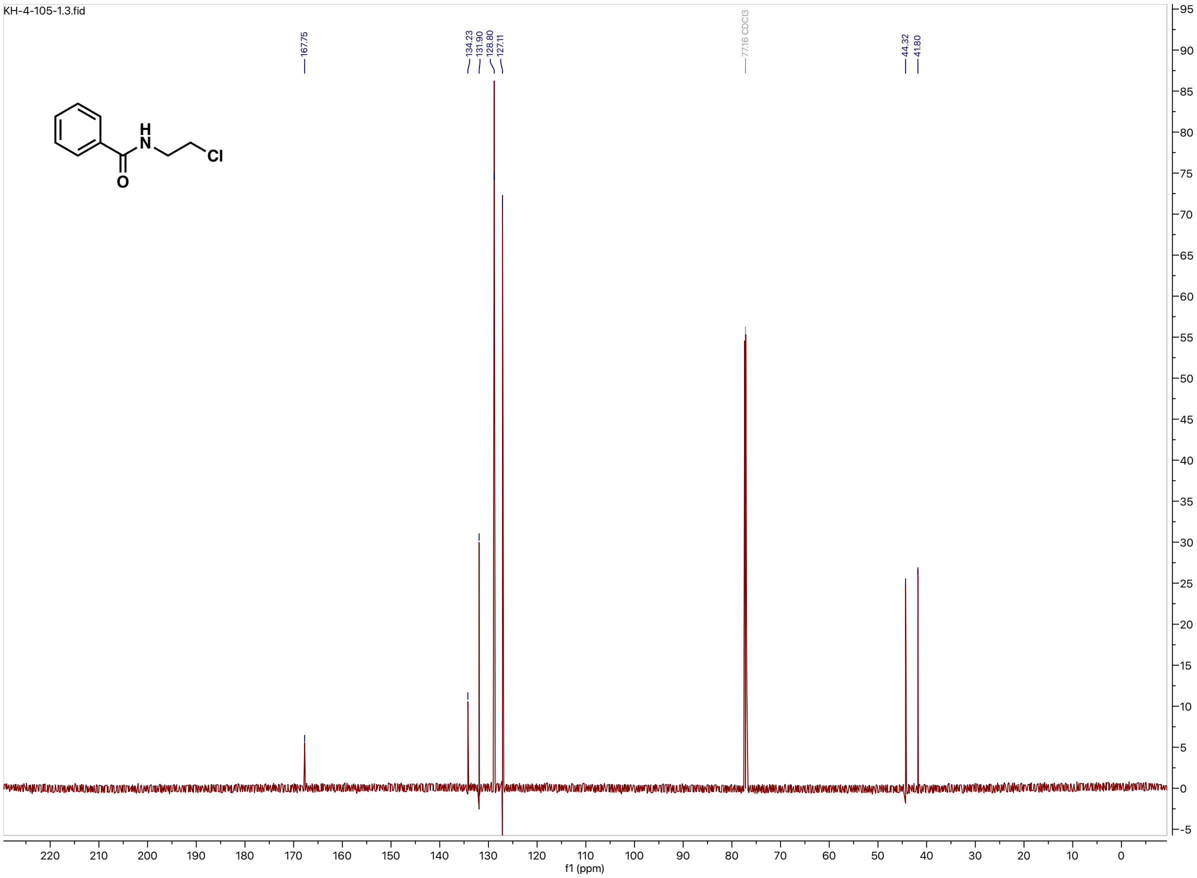



KH-4-137-1.3.fid
166.39
166.37
163.56
161.93
145.59
137.41
137.37
136.08
131.58
130.14
130.09
129.80
128.92
126.13
122.71
122.69
118.29
118.14
114.42
114.27
84.33
77.16 CDCl3
42.69
34.49
24.96
F
H
N
O
O
B
O
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

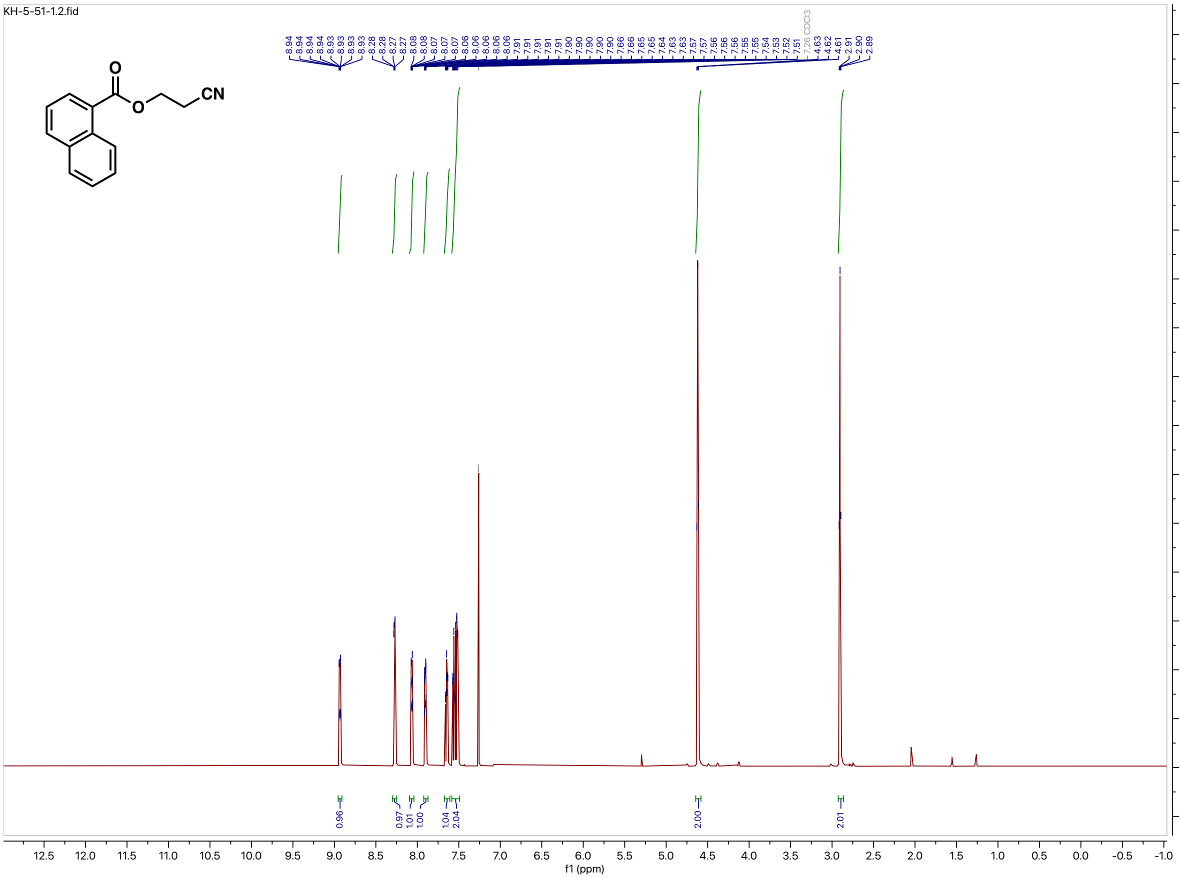

KH-4-137-1
-112.24
F
H
N
O
O
B
O
0.21
0.20
0.19
0.18
0.17
0.16
0.15
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
-0.01
-0.02
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
f1 (ppm)

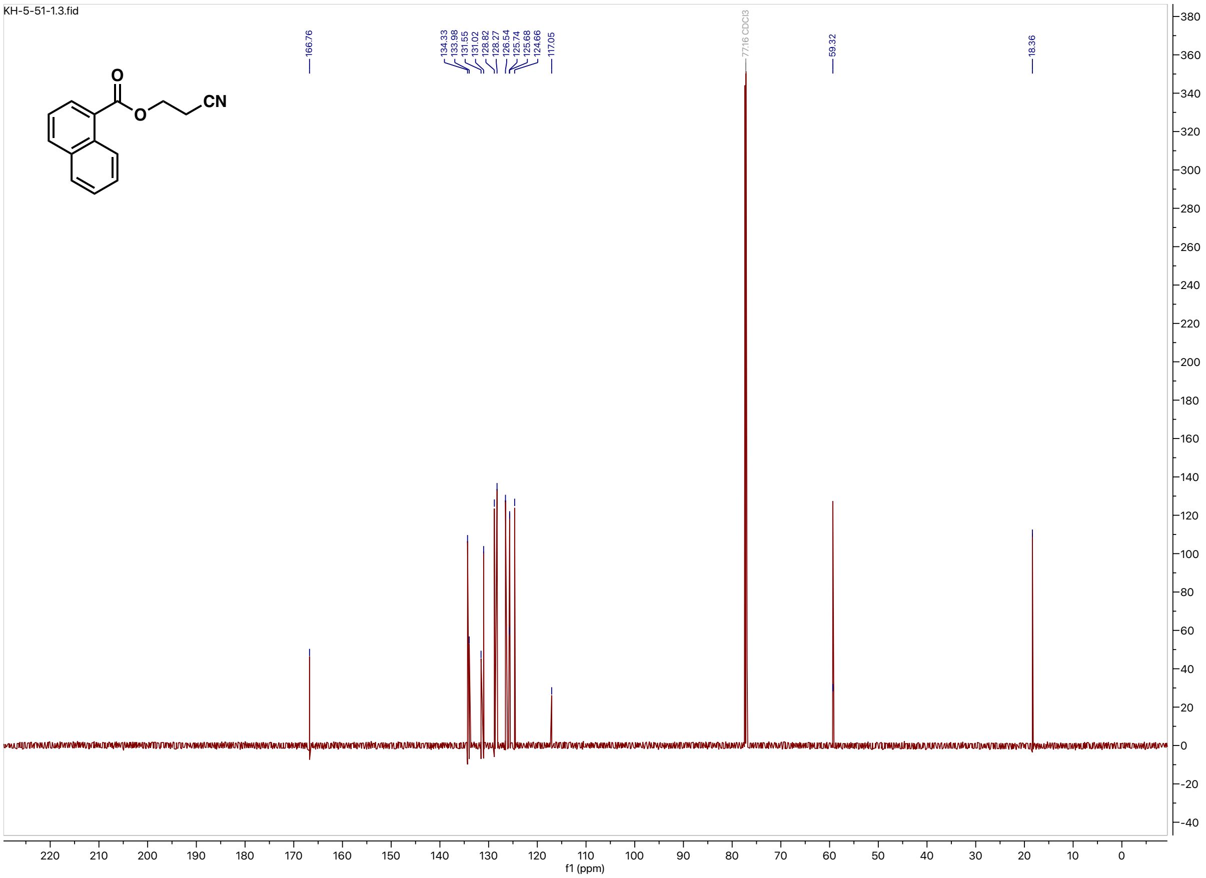
Compound 26s



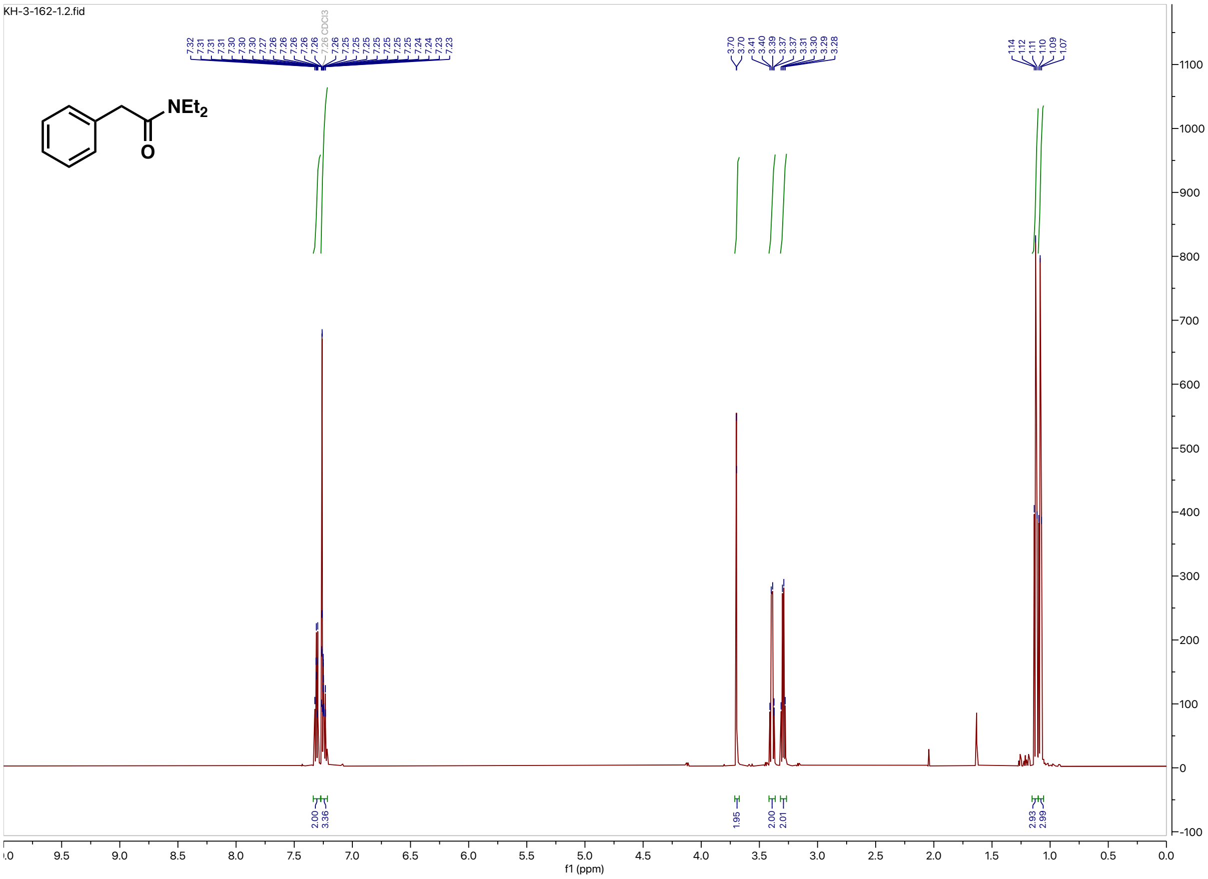

KH-4-105-1.3.fid
167.75
134.23
131.90
128.80
127.11
77.16 CDCl3
44.32
41.80
H
N
O
Cl
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

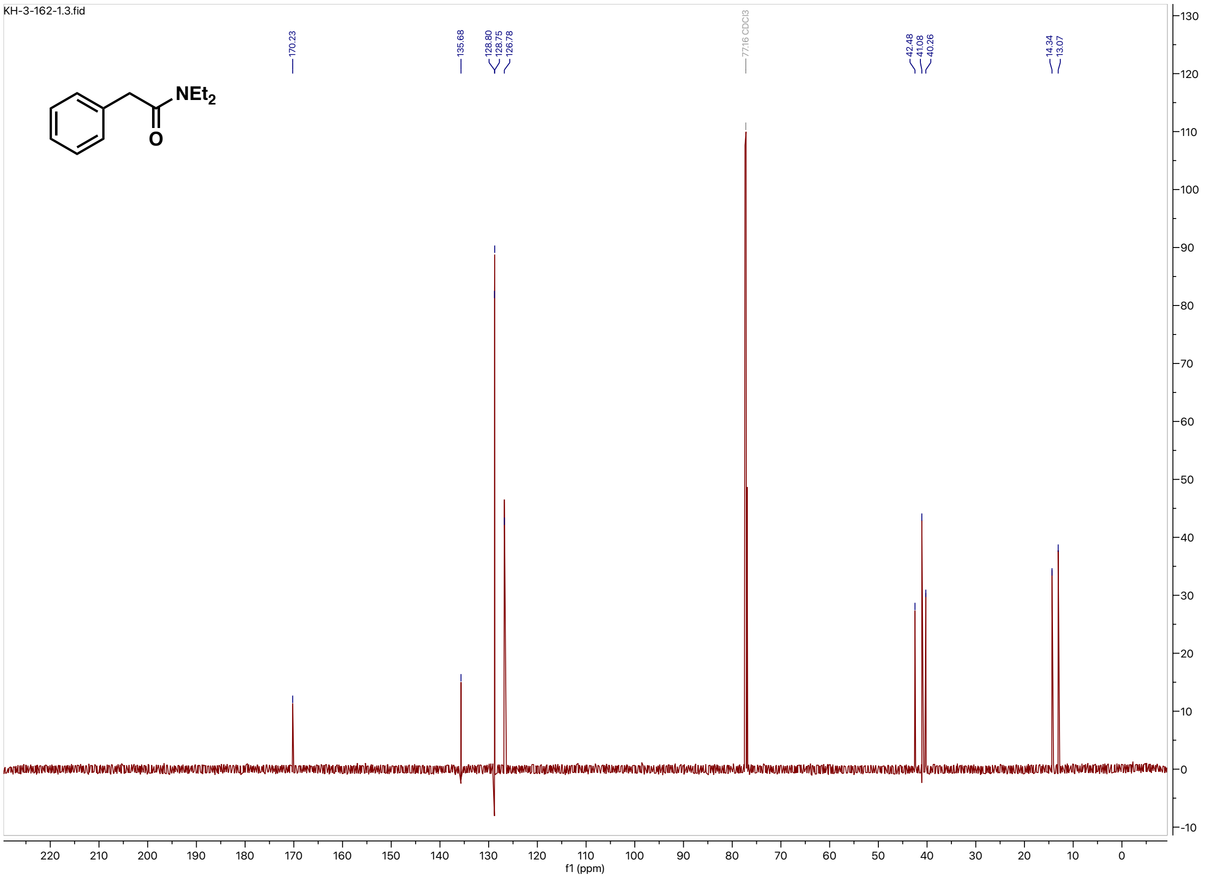
Compound 27s



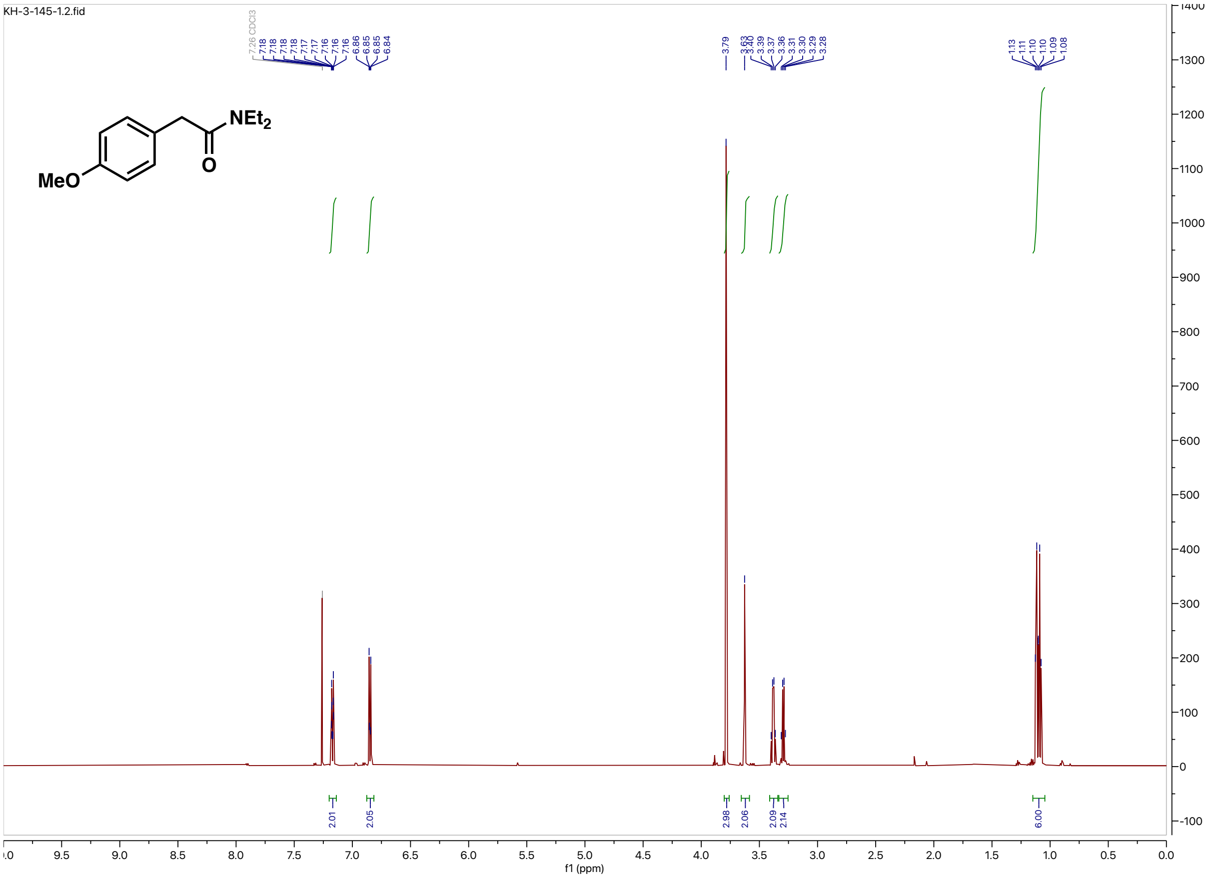

KH-5-51-1.3.fid
166.76
134.33
133.98
131.55
131.02
128.82
128.27
126.54
125.74
125.68
124.66
117.05
77.16 CDCl3
59.32
18.36
O
O
CN
380
360
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
-40
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

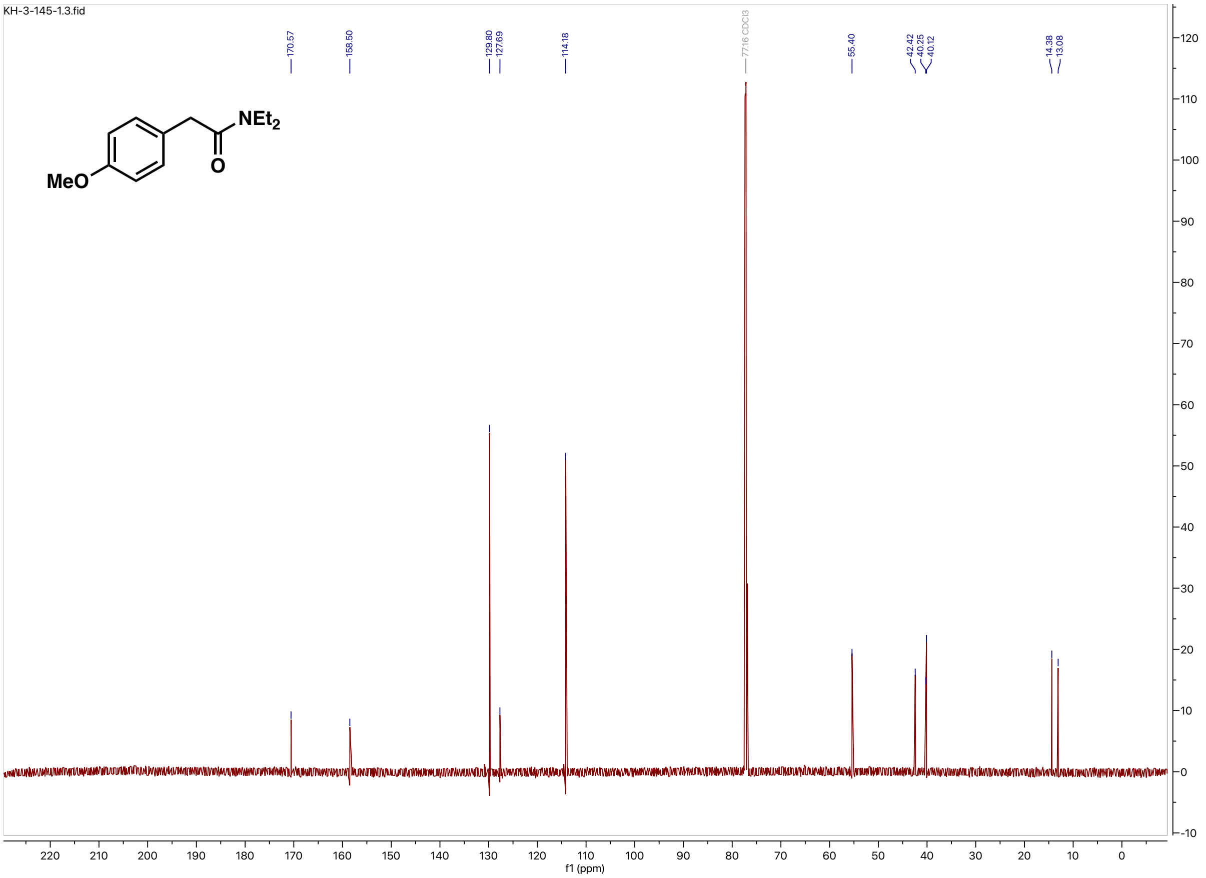
Compound 43


KH-3-162-1.2.fid
NEt2
O
7.32 7.31 7.31 7.30 7.30 7.30 7.27 7.26 7.26 7.26 7.26 7.26 CDCl3 7.26 7.25 7.25 7.25 7.25 7.25 7.25 7.25 7.24 7.24 7.23 7.23
3.70 3.70 3.41 3.40 3.39 3.37 3.37 3.31 3.30 3.29 3.28
1.14 1.12 1.11 1.10 1.09 1.07
2.00 3.36
1.95
2.00 2.01
2.93 2.99
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
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
f1 (ppm)

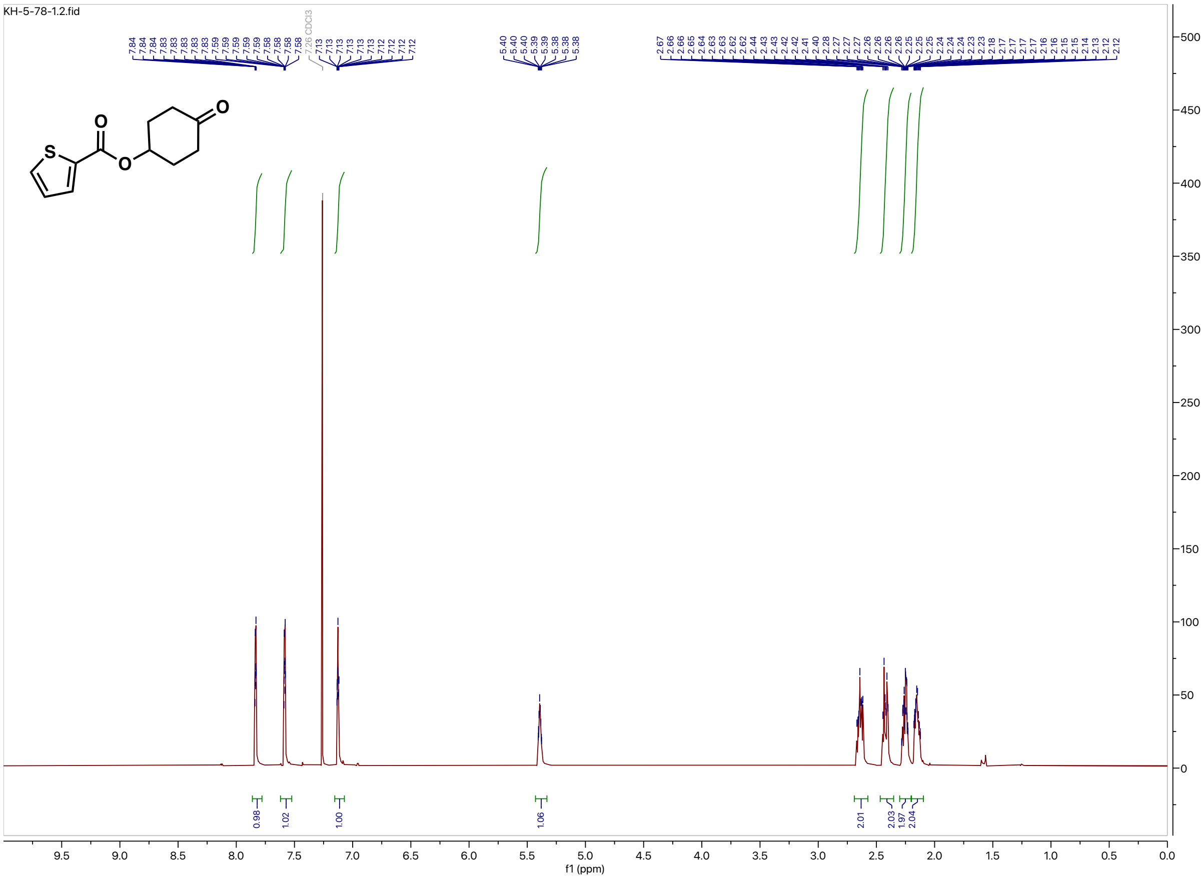

KH-3-162-1.3.fid
NEt$_2$
O
170.23
135.68
128.80
128.75
126.78
77.16 CDCl3
42.48
41.08
40.26
14.34
13.07
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

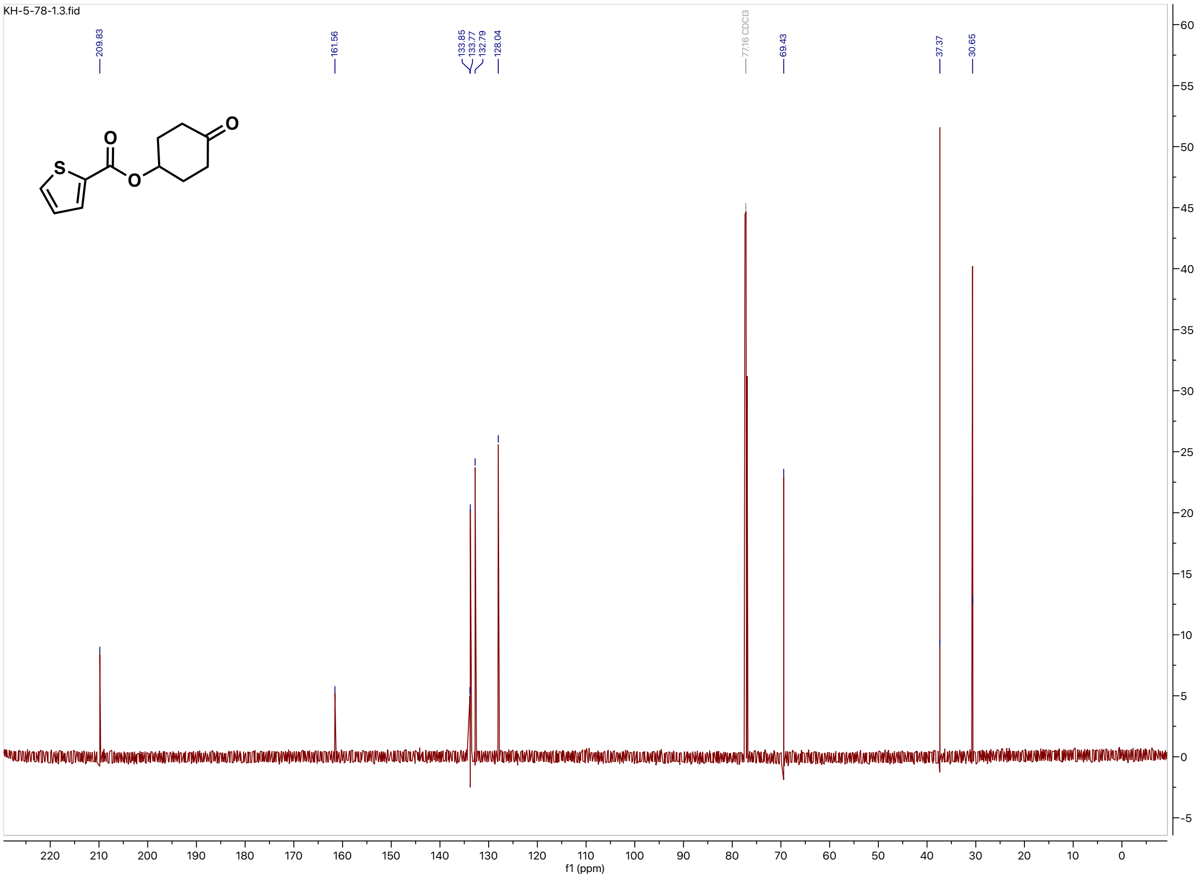
Compound 30s



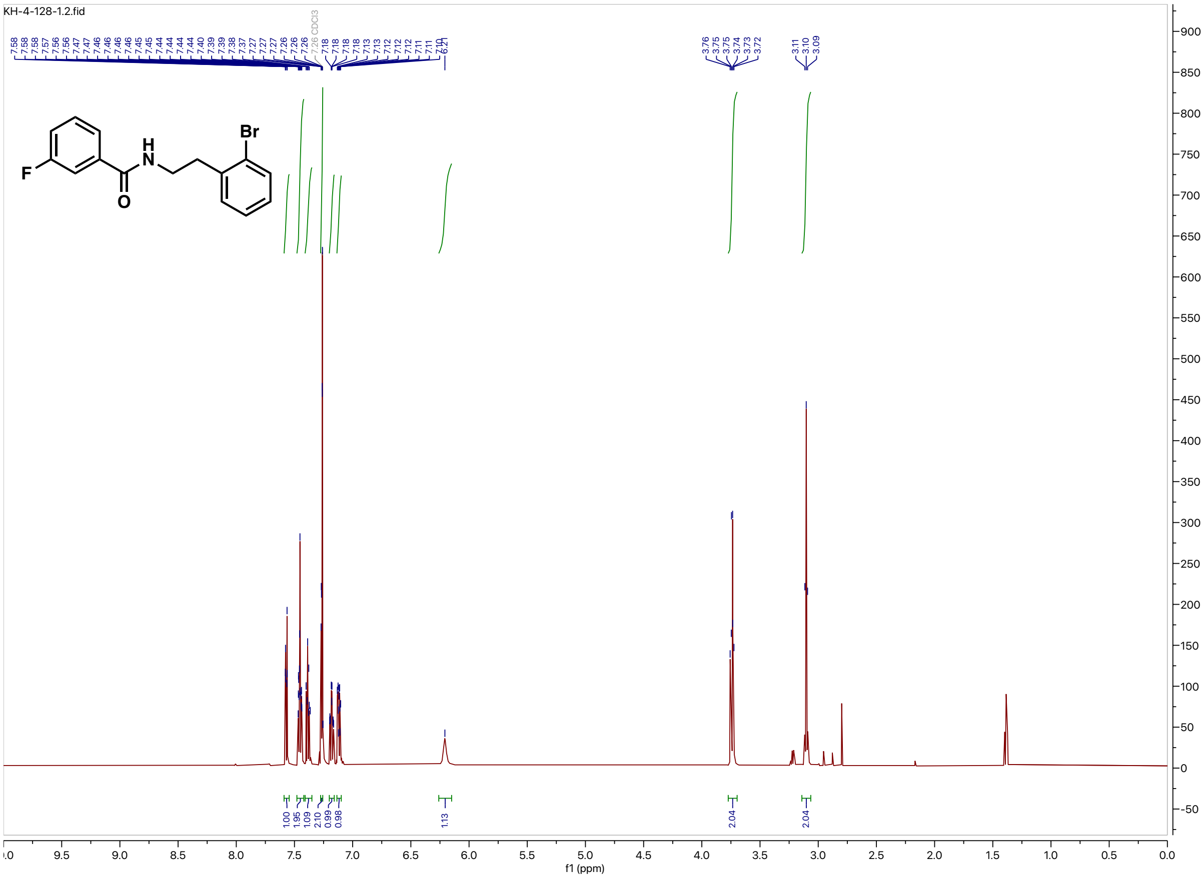

KH-3-145-1.3.fid
170.57
158.50
129.80
127.69
114.18
77.16 CDCl3
55.40
42.42
40.25
40.12
14.38
13.08
MeO
NEt$_2$
O
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
120 110 100 90 80 70 60 50 40 30 20 10 0 -10

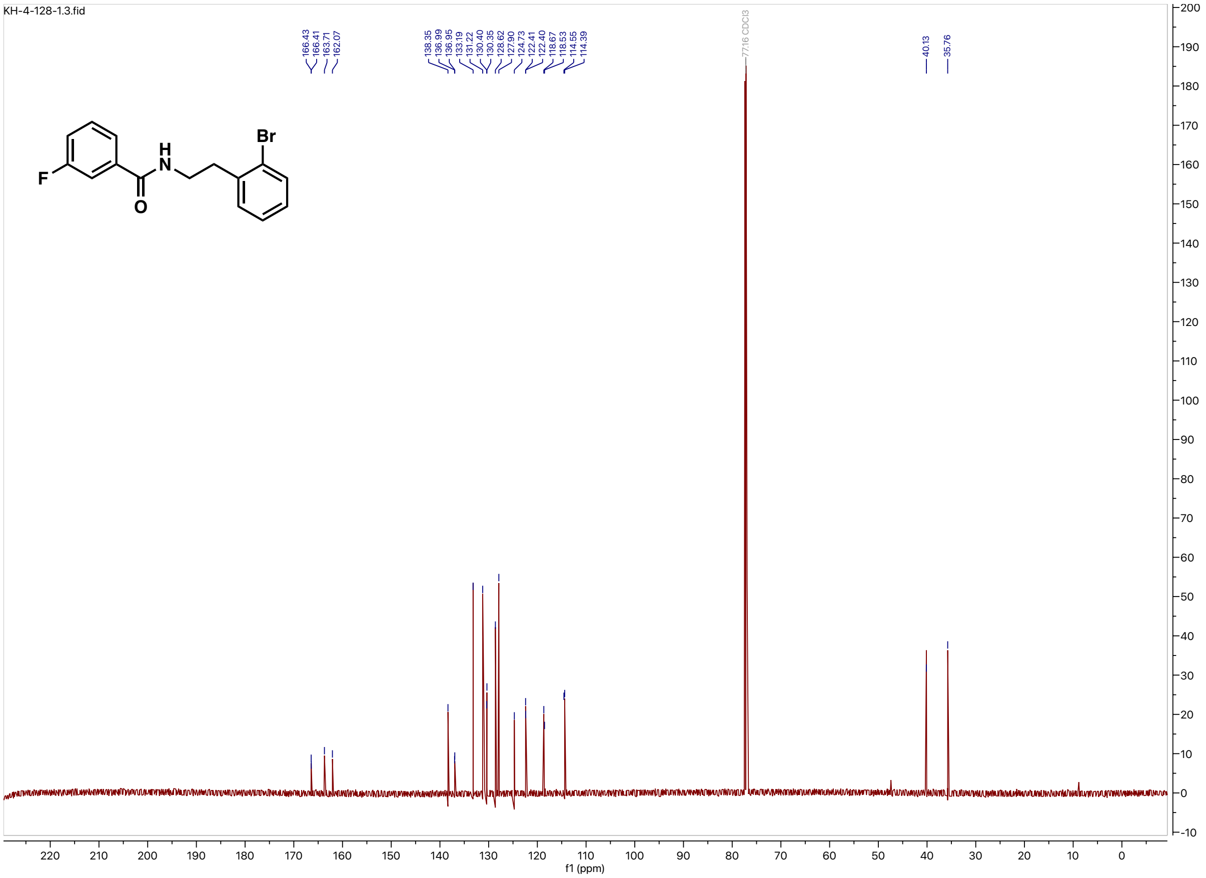
Compound 31s

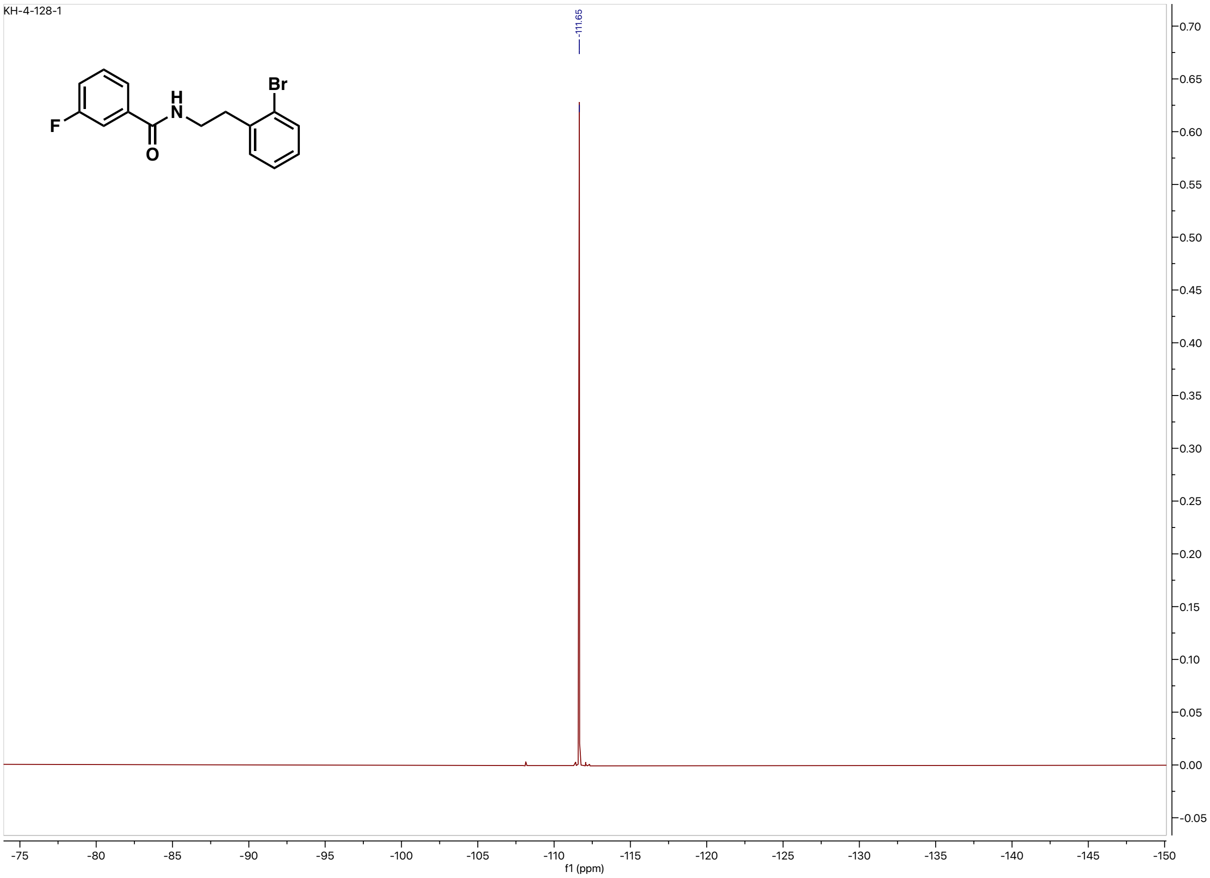



KH-5-78-1.3.fid
209.83
161.56
133.85
133.77
132.79
128.04
77.16 CDCl3
69.43
37.37
30.65
S
O
O
O
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

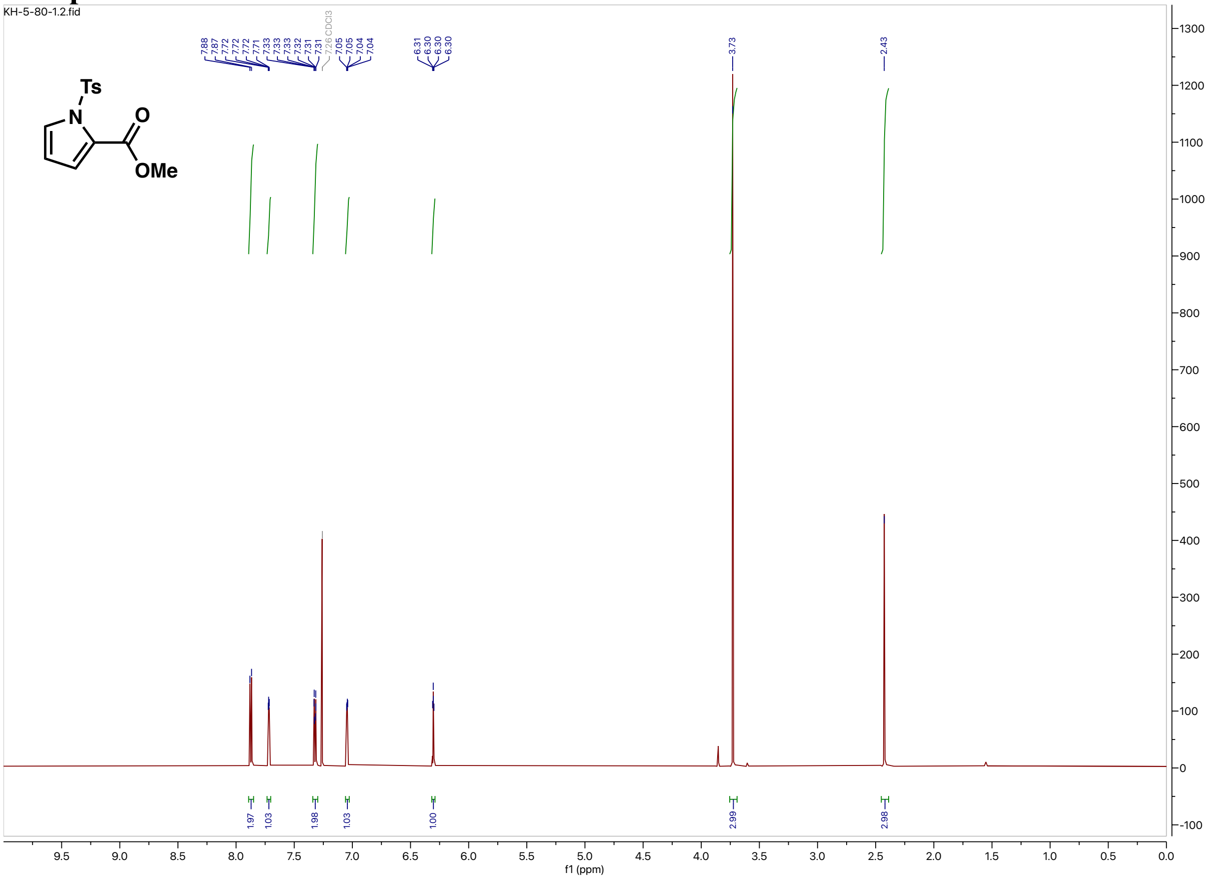
Compound 32s

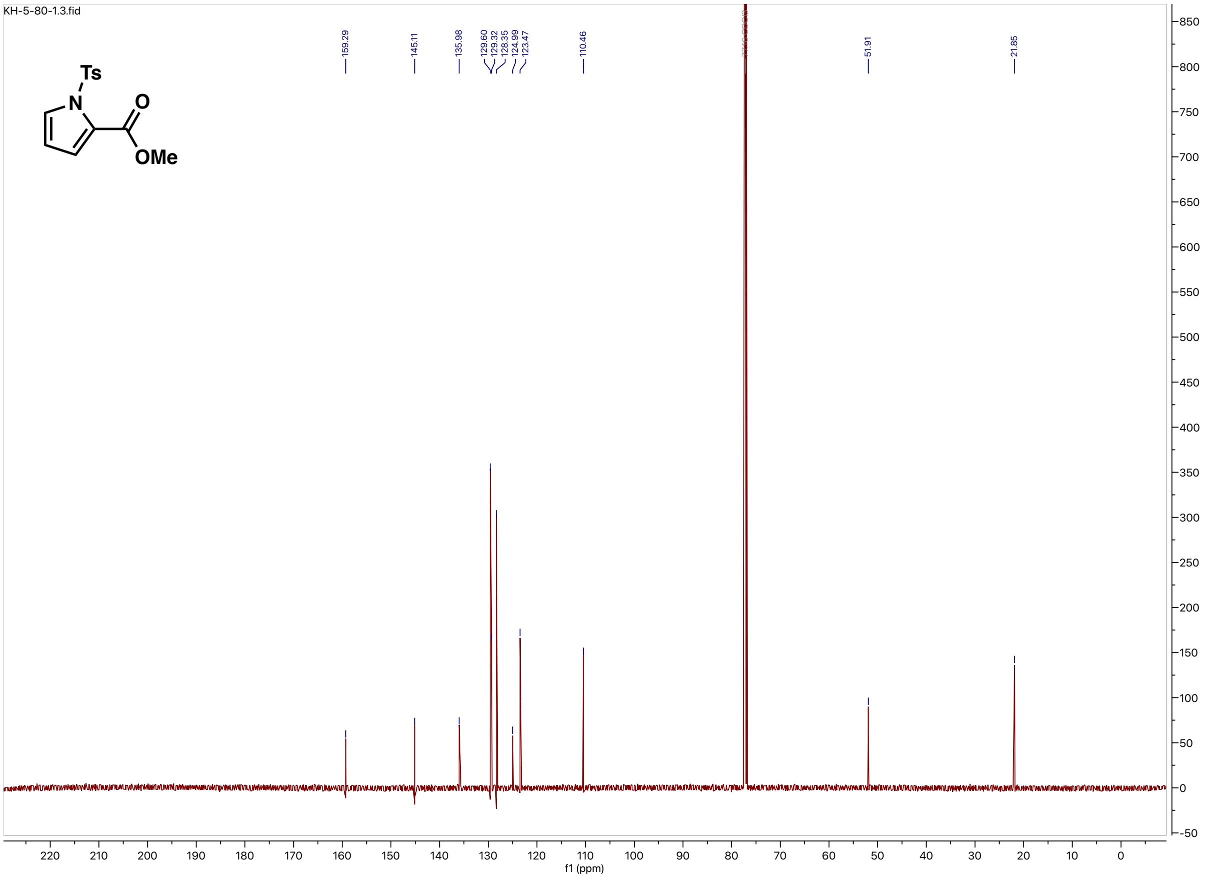



KH-4-128-1.3.fid
166.43
166.41
163.71
162.07
138.35
136.99
136.95
133.19
131.22
130.40
130.35
128.62
127.90
124.73
122.41
122.40
118.67
118.53
114.55
114.39
77.16 CDCl3
40.13
35.76
F
H
N
O
Br
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

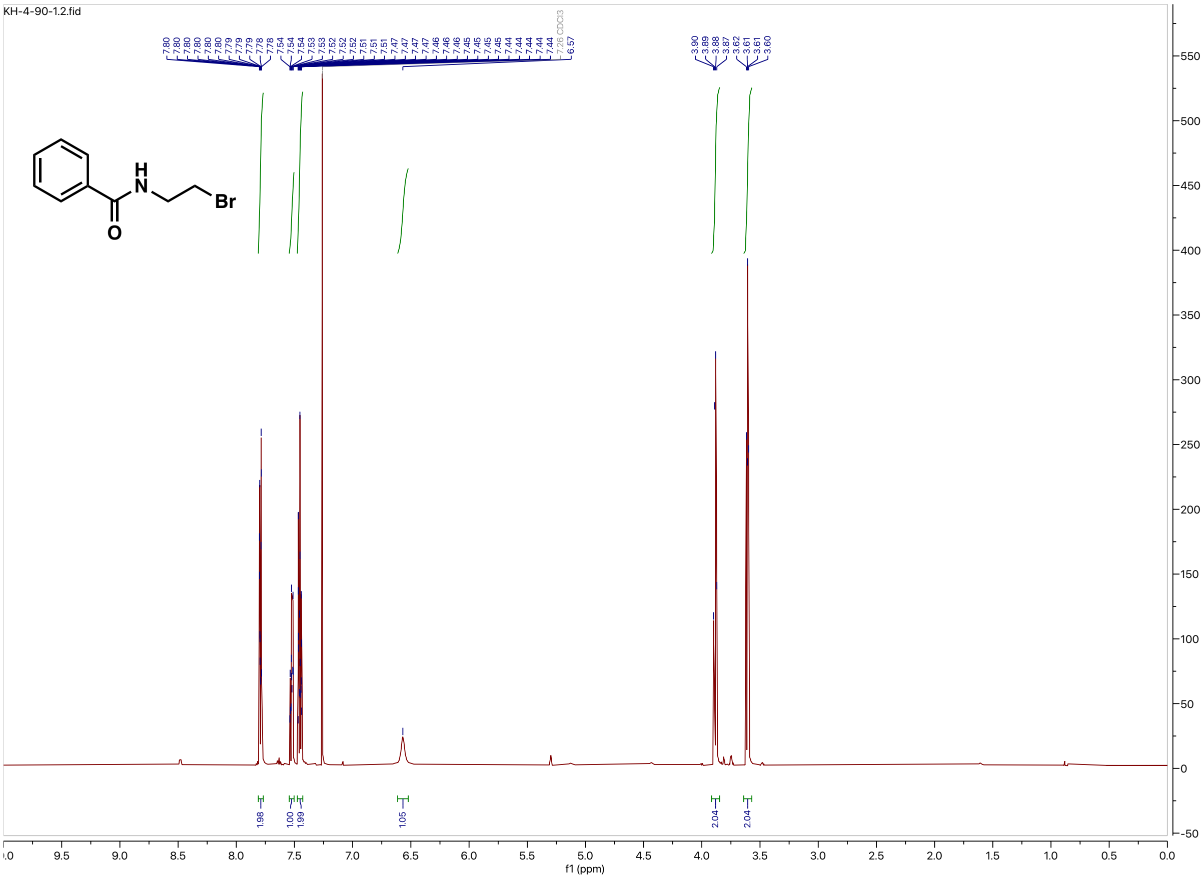

KH-4-128-1
-111.65
F
H
N
O
Br
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
f1 (ppm)

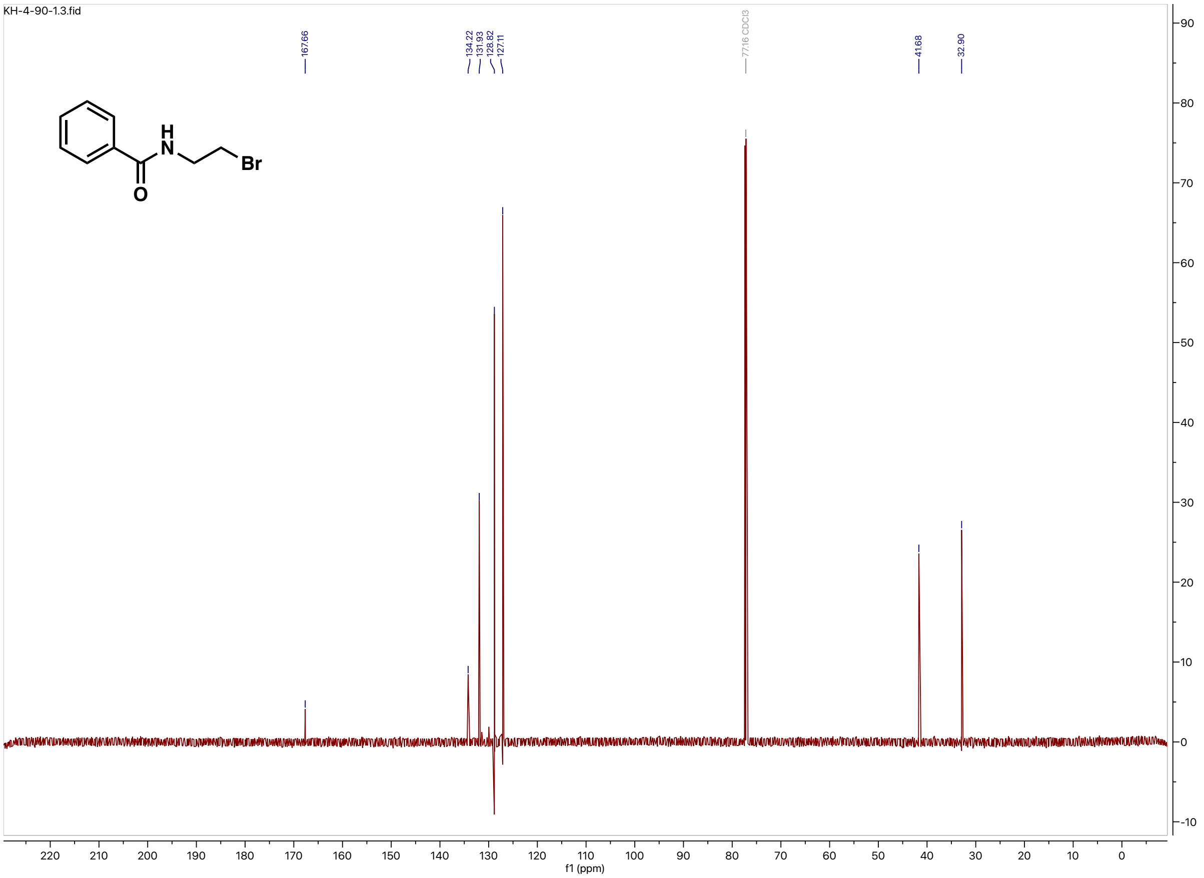
Compound 33


KH-5-80-1.2.fid
Ts
N
O
OMe
7.88
7.87
7.72
7.72
7.72
7.71
7.33
7.33
7.33
7.32
7.31
7.31
7.26 CDCl3
7.05
7.05
7.04
7.04
6.31
6.30
6.30
6.30
3.73
2.43
1.97
1.03
1.98
1.03
1.00
2.99
2.98
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
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
f1 (ppm)

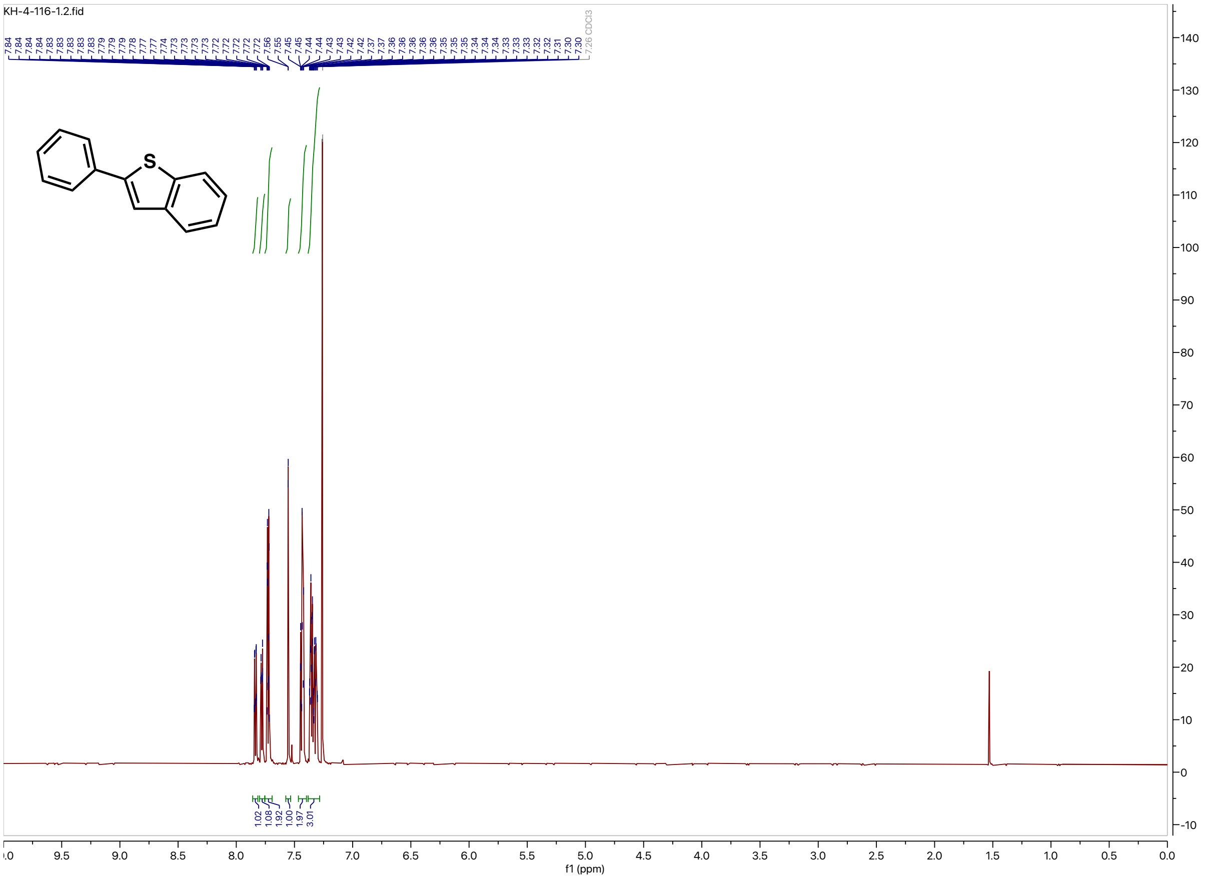

KH-5-80-1.3.fid
Ts
N
O
OMe
159.29
145.11
135.98
129.60
129.32
128.35
124.99
123.47
110.46
77.16 CDCl3
51.91
21.85
850
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

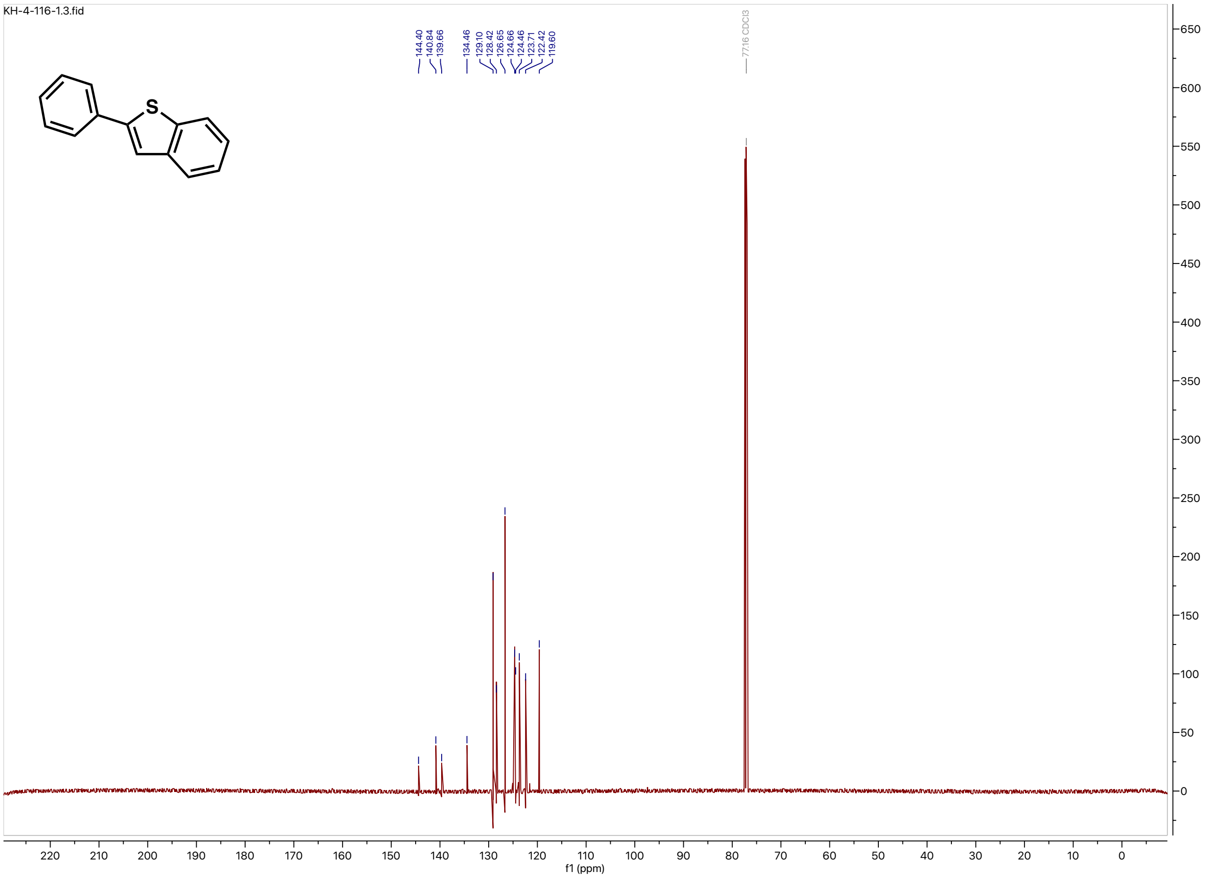
Compound 35


KH-4-90-1.2.fid
7.80 7.80 7.80 7.80 7.80 7.80 7.79 7.79 7.79 7.78 7.78 7.54 7.54 7.54 7.53 7.53 7.52 7.52 7.52 7.51 7.51 7.51 7.47 7.47 7.47 7.47 7.46 7.46 7.46 7.45 7.45 7.45 7.45 7.44 7.44 7.44 7.44 7.44
7.26 CDCl3
6.57
3.90 3.89 3.88 3.87 3.62 3.61 3.61 3.60
H
N
Br
O
1.98
1.00
1.99
1.05
2.04
2.04
550
500
450
400
350
300
250
200
150
100
50
0
-50
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
f1 (ppm)

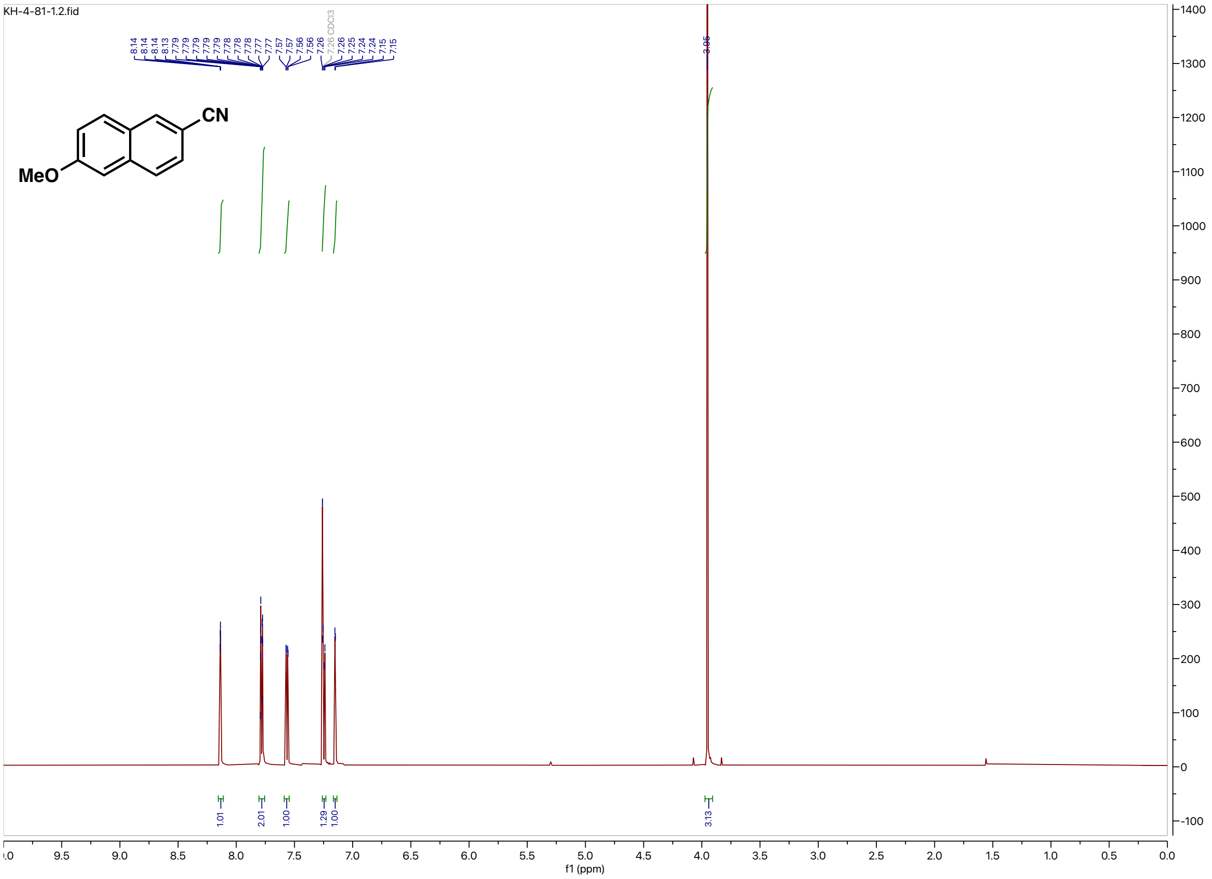

KH-4-90-1.3.fid
167.66
134.22
131.93
128.82
127.11
77.16 CDCl3
41.68
32.90
H
N
Br
O
90
80
70
60
50
40
30
20
10
0
-10
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

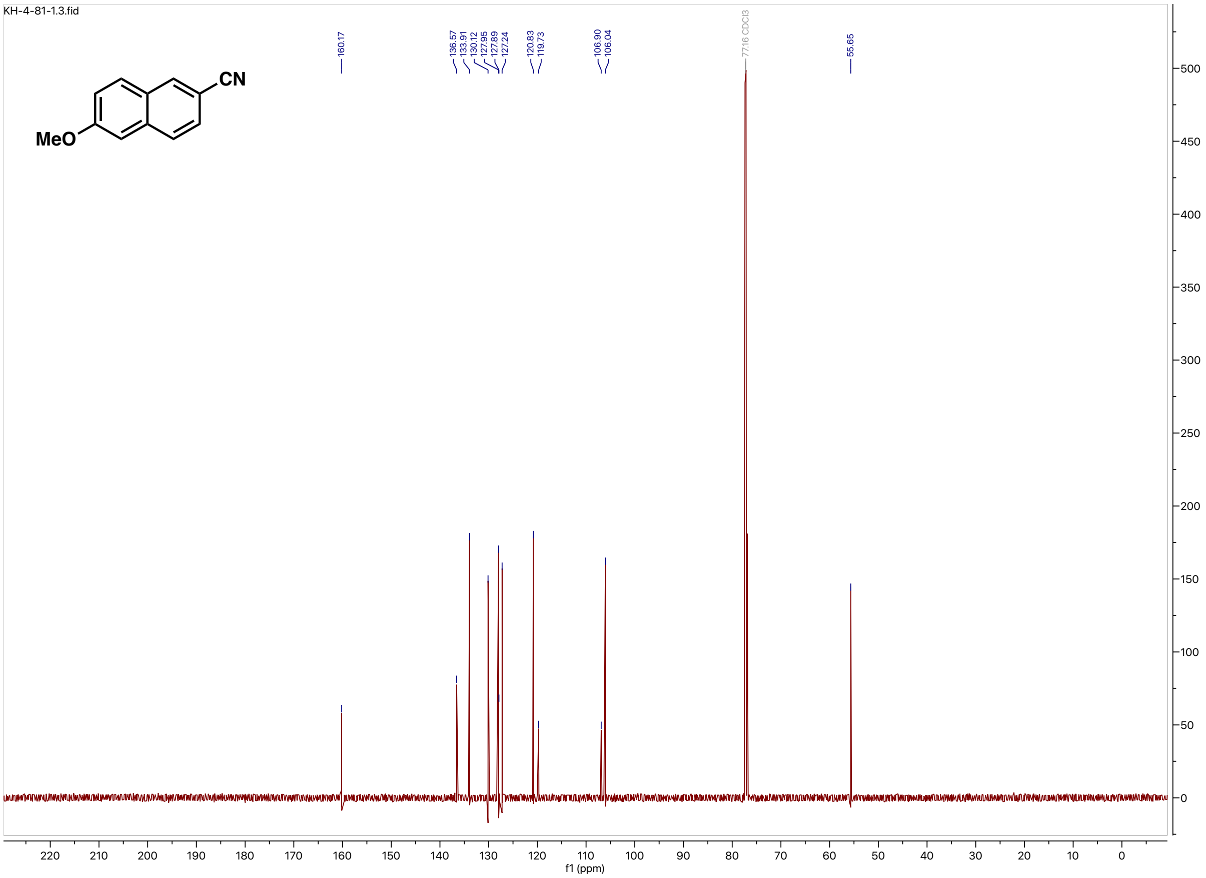
Compound 37


KH-4-116-1.2.fid
7.84
7.84
7.84
7.83
7.83
7.83
7.83
7.79
7.79
7.79
7.78
7.77
7.77
7.74
7.73
7.73
7.73
7.73
7.72
7.72
7.72
7.72
7.72
7.56
7.55
7.45
7.45
7.44
7.44
7.43
7.43
7.42
7.42
7.37
7.37
7.36
7.36
7.36
7.36
7.35
7.35
7.35
7.34
7.34
7.33
7.33
7.33
7.32
7.32
7.31
7.30
7.30
7.26 CDCl3
S
1.02
1.08
1.92
1.00
1.97
3.01
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
f1 (ppm)
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

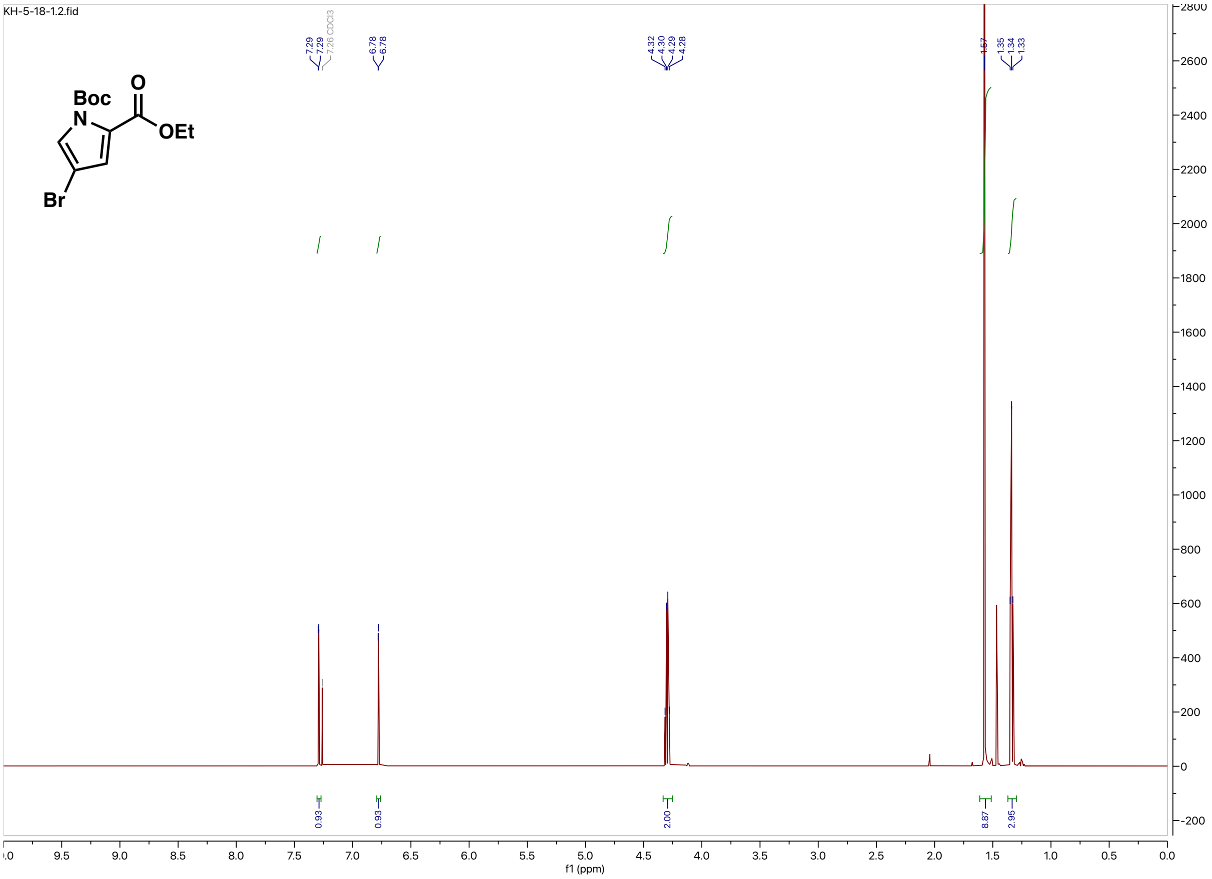

KH-4-116-1.3.fid
S
144.40
140.84
139.66
134.46
129.10
128.42
126.65
124.66
124.46
123.71
122.42
119.60
77.16 CDCl3
650
600
550
500
450
400
350
300
250
200
150
100
50
0
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

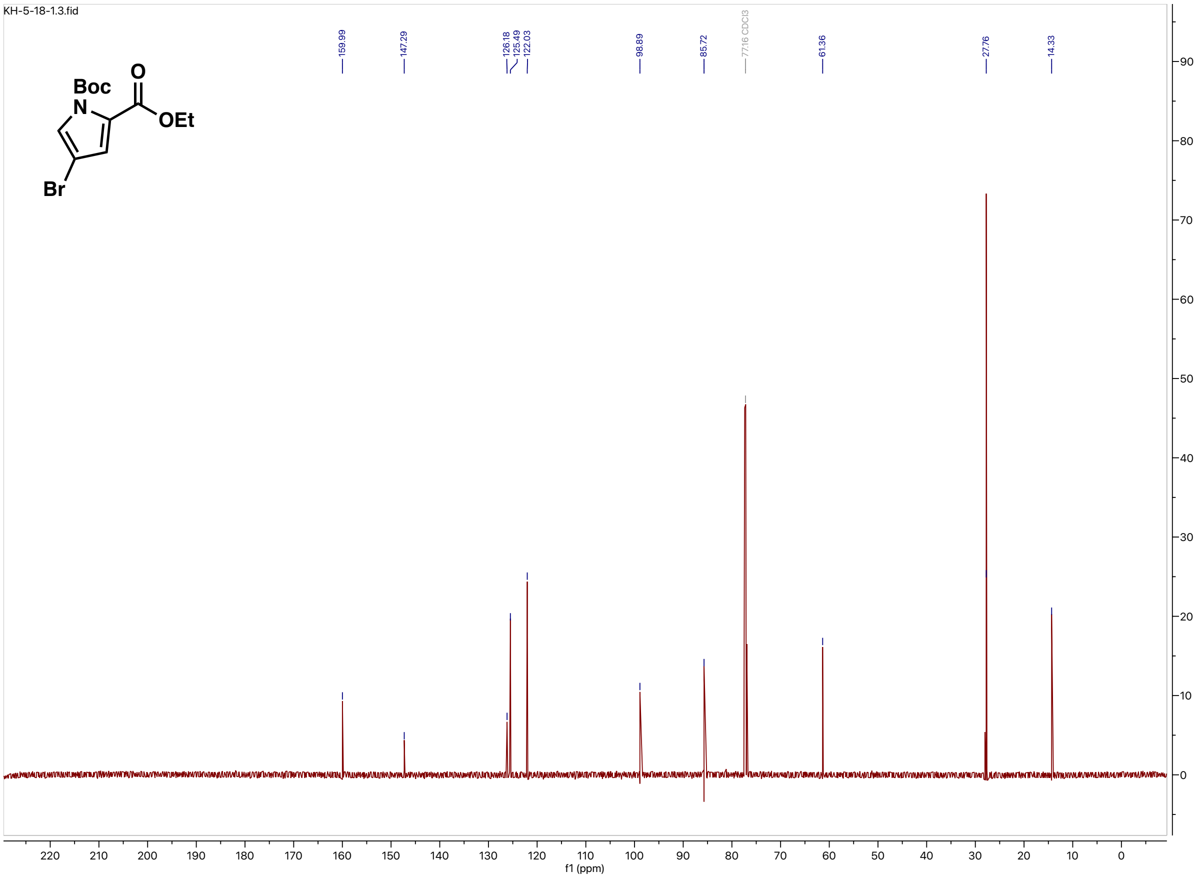
Compound 38


KH-4-81-1.2.fid
8.14
8.14
8.14
8.13
7.79
7.79
7.79
7.79
7.79
7.78
7.78
7.78
7.77
7.77
7.57
7.57
7.56
7.56
7.26
7.26 CDCl3
7.26
7.25
7.24
7.24
7.15
7.15
3.95
CN
MeO
1.01
2.01
1.00
1.29
1.00
3.13
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
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
f1 (ppm)

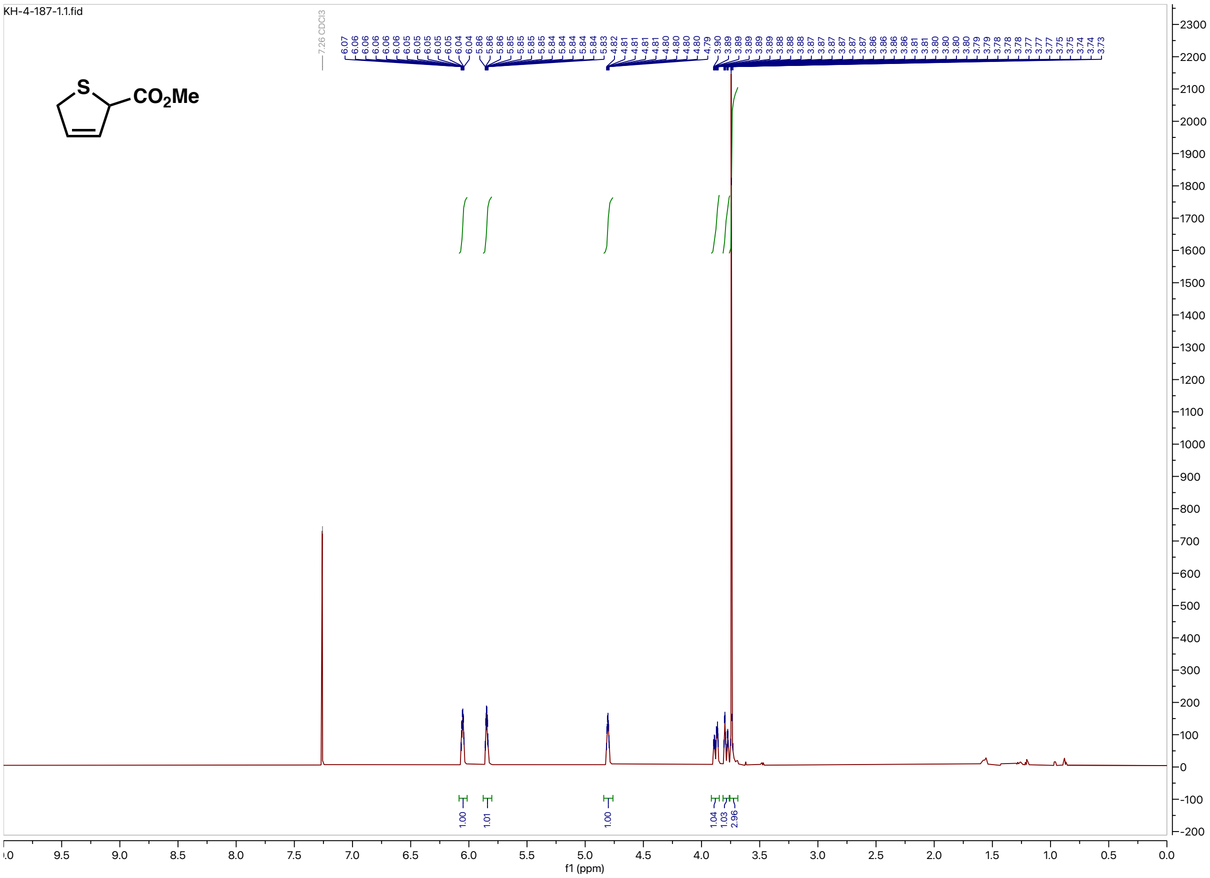

KH-4-81-1.3.fid
MeO
CN
160.17
136.57
133.91
130.12
127.95
127.89
127.24
120.83
119.73
106.90
106.04
77.16 CDCl3
55.65
500
450
400
350
300
250
200
150
100
50
0
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

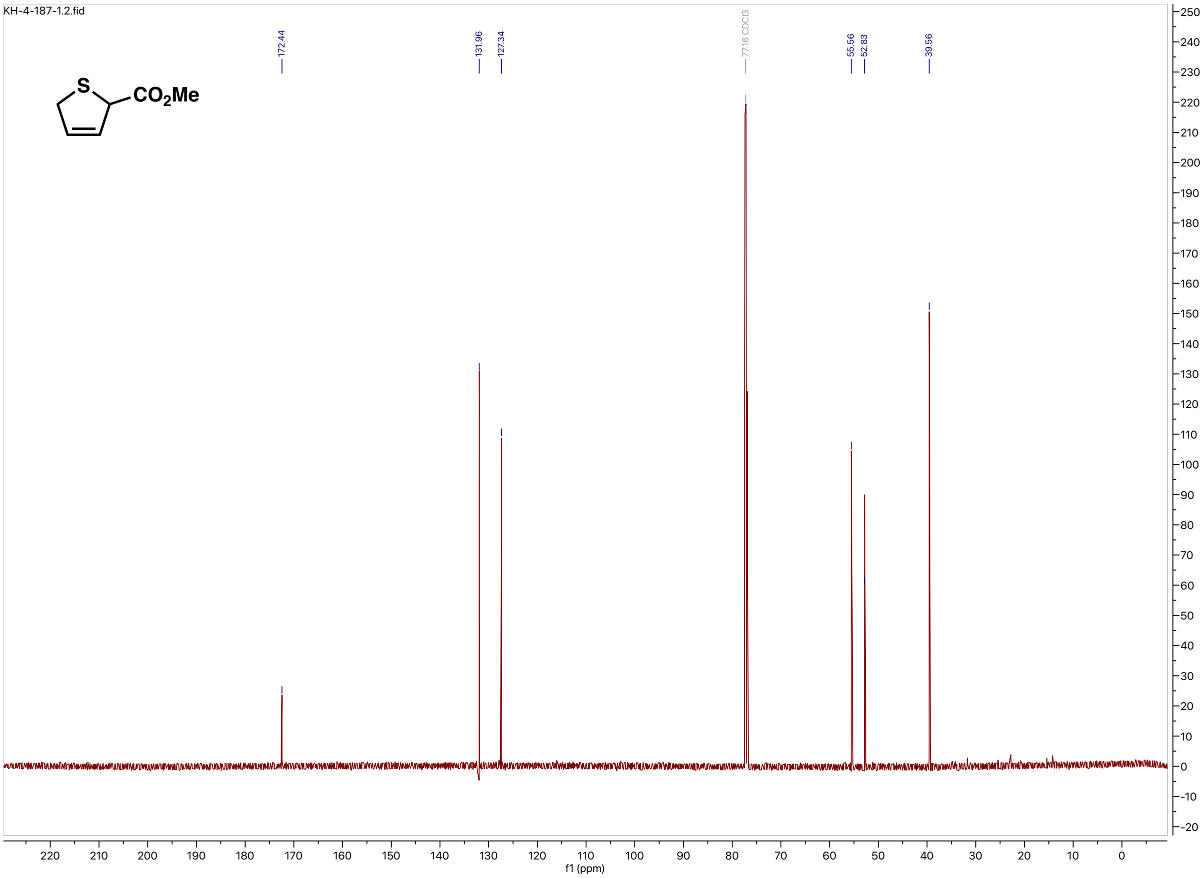
Compound 48


KH-5-18-1.2.fid
Boc
N
O
OEt
Br
7.29
7.29
7.26 CDCl3
6.78
6.78
4.32
4.30
4.29
4.28
1.57
1.35
1.34
1.33
0.93
0.93
2.00
8.87
2.95
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
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
f1 (ppm)

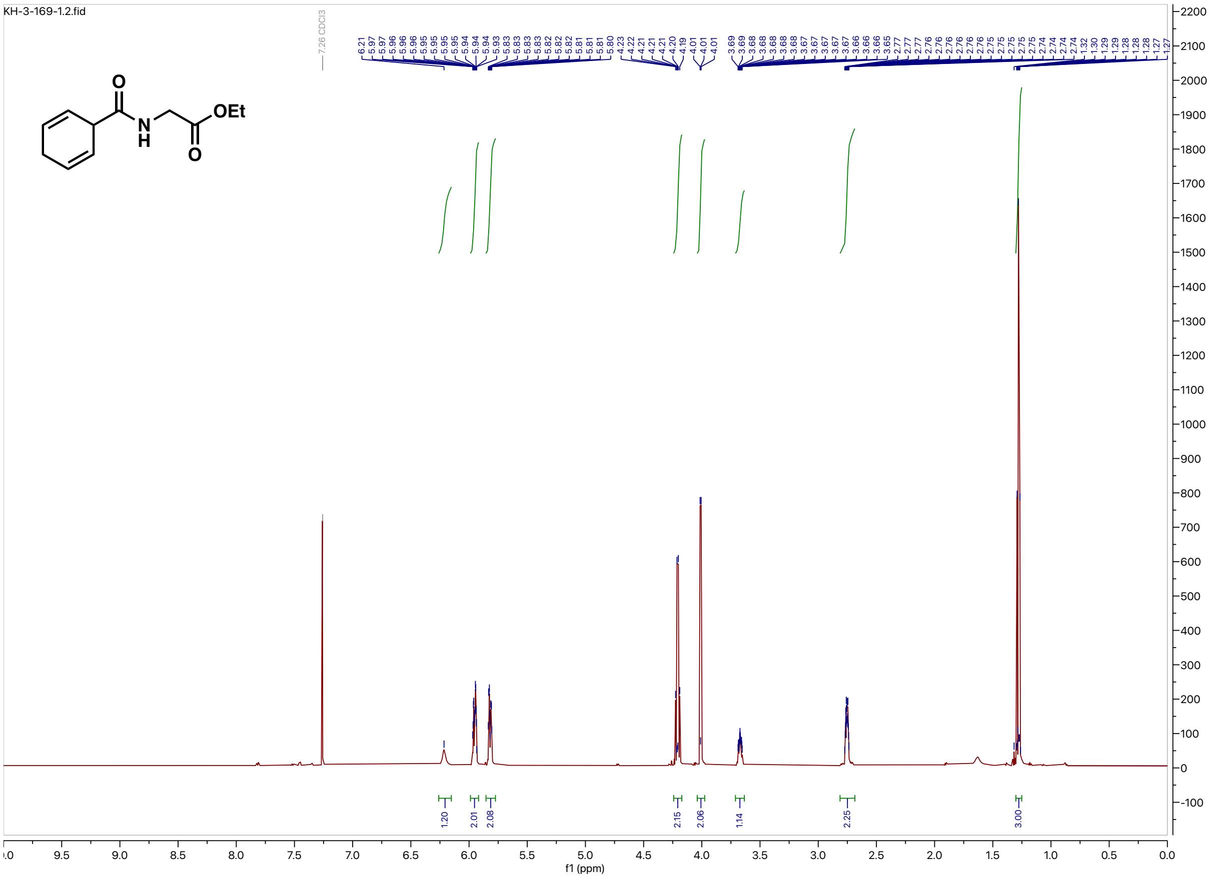

KH-5-18-1.3.fid
Boc
N
O
OEt
Br
159.99
147.29
126.18
125.49
122.03
98.89
85.72
77.16 CDCl3
61.36
27.76
14.33
90
80
70
60
50
40
30
20
10
0
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

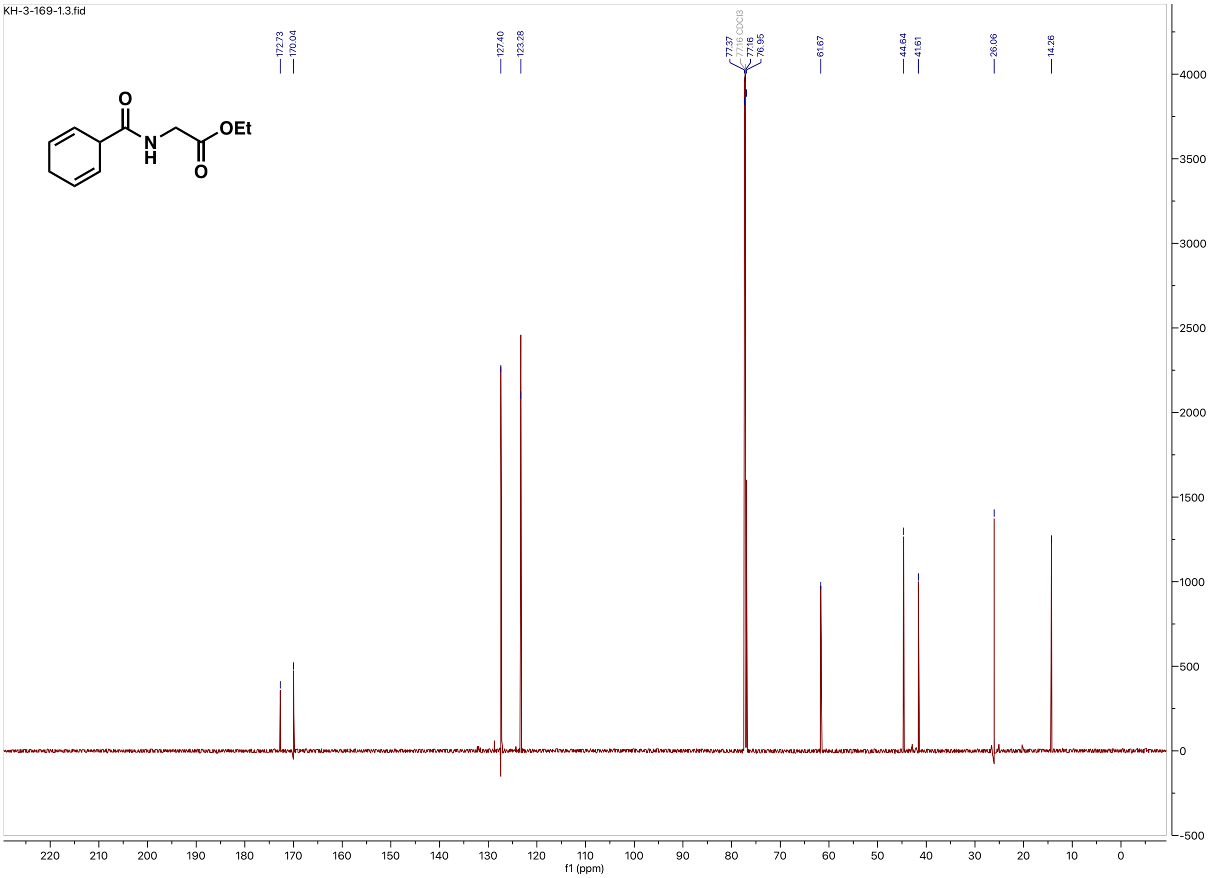
Compound 2


KH-4-187-1.1.fid
S
CO2Me
7.26 CDCl3
6.07
6.06
6.06
6.06
6.06
6.06
6.05
6.05
6.05
6.05
6.05
6.04
6.04
5.86
5.86
5.86
5.85
5.85
5.85
5.85
5.84
5.84
5.84
5.84
5.83
4.82
4.81
4.81
4.81
4.81
4.80
4.80
4.80
4.80
4.79
3.90
3.89
3.89
3.89
3.89
3.89
3.88
3.88
3.88
3.87
3.87
3.87
3.87
3.87
3.86
3.86
3.86
3.86
3.81
3.81
3.80
3.80
3.80
3.80
3.79
3.79
3.78
3.78
3.78
3.77
3.77
3.77
3.75
3.75
3.74
3.74
3.73
1.00
1.01
1.00
1.04
1.03
2.96
2300
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
.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
f1 (ppm)

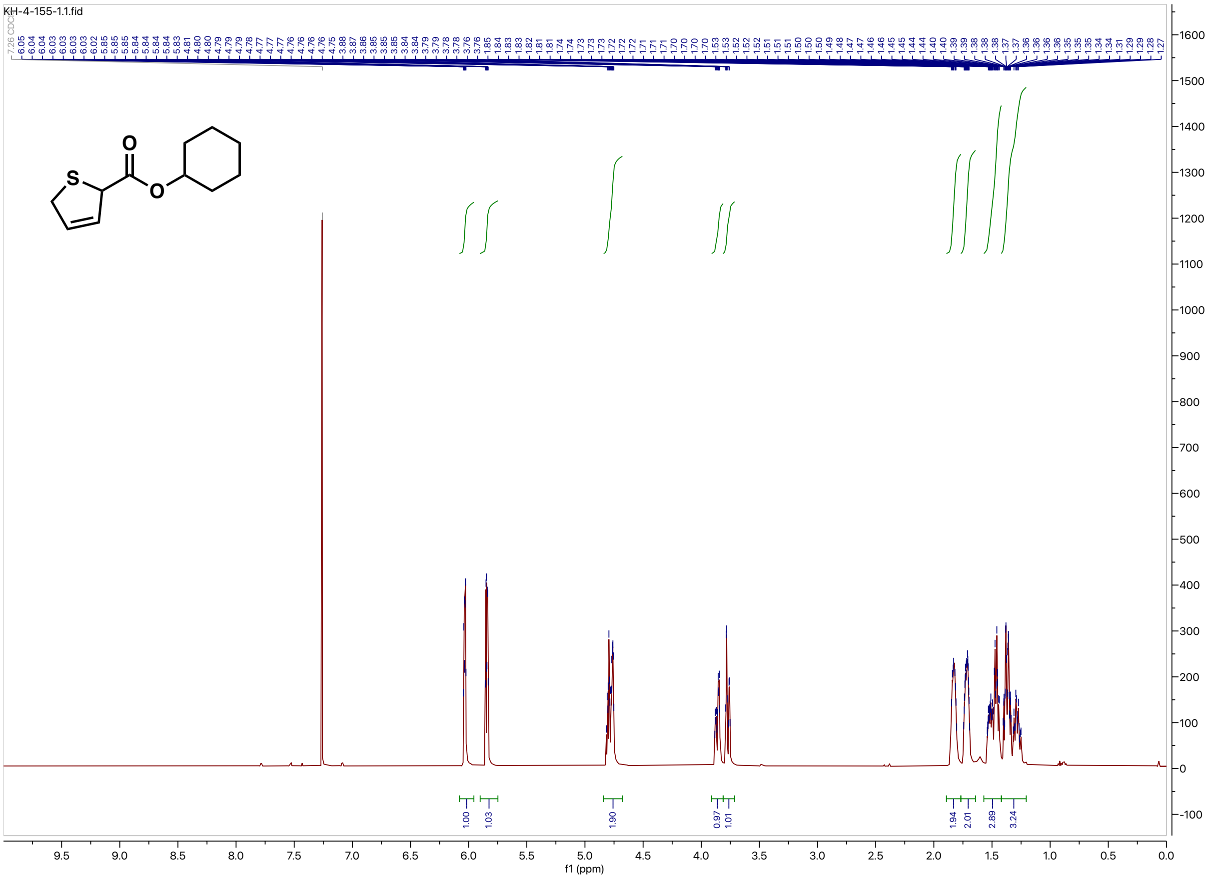

KH-4-187-1.2.fid
172.44
131.96
127.34
77.16 CDCl3
55.56
52.83
39.56
S
CO2Me
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

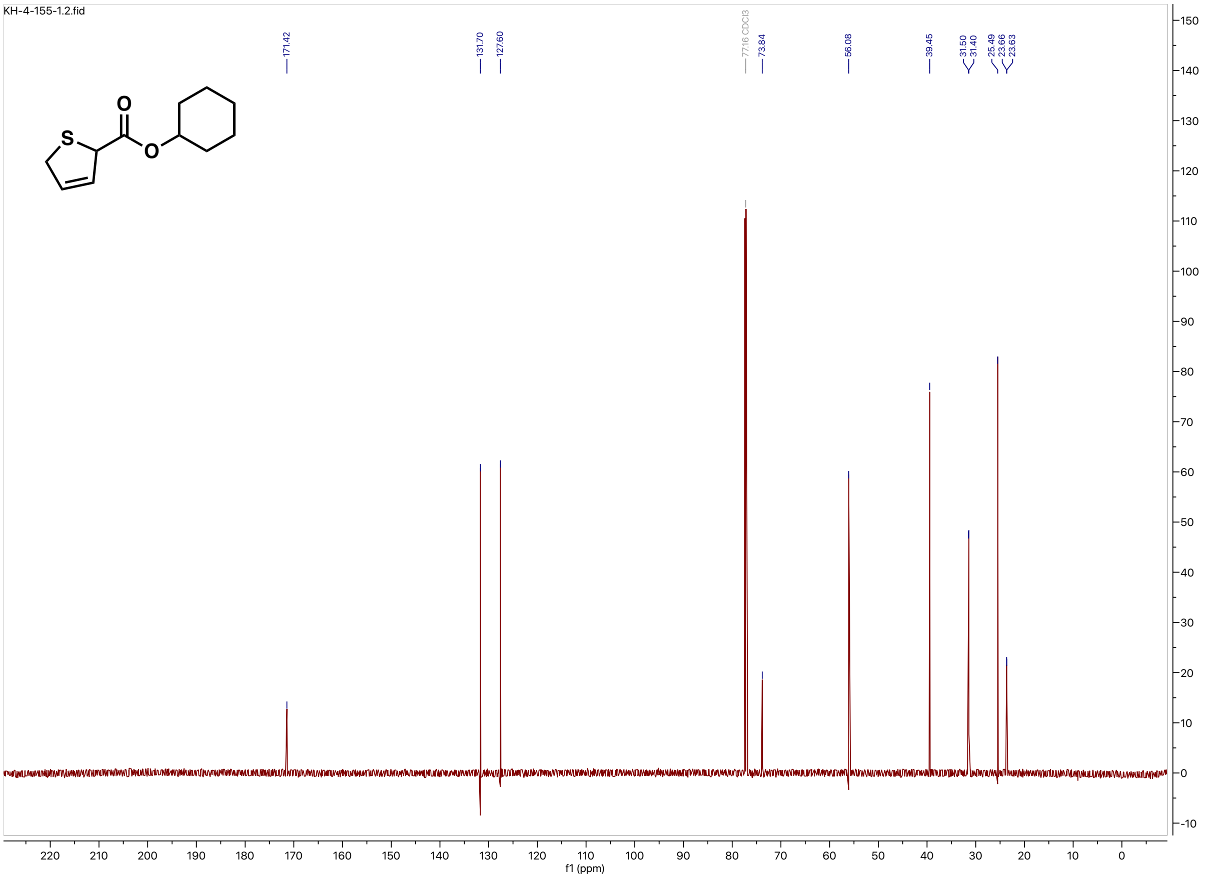
Compound 4


KH-3-169-1.2.fid
7.26 CDCl3
6.21
5.97
5.97
5.96
5.96
5.96
5.95
5.95
5.95
5.94
5.94
5.94
5.93
5.83
5.83
5.83
5.83
5.82
5.82
5.82
5.81
5.81
5.81
5.80
4.23
4.22
4.21
4.21
4.21
4.20
4.19
4.01
4.01
4.01
3.69
3.69
3.68
3.68
3.68
3.68
3.67
3.67
3.67
3.67
3.67
3.66
3.66
3.65
2.77
2.77
2.77
2.76
2.76
2.76
2.76
2.75
2.75
2.75
2.75
2.74
2.74
2.74
1.32
1.30
1.29
1.29
1.28
1.28
1.27
1.27
O
N
H
OEt
O
1.20
2.01
2.08
2.15
2.06
1.14
2.25
3.00
f1 (ppm)

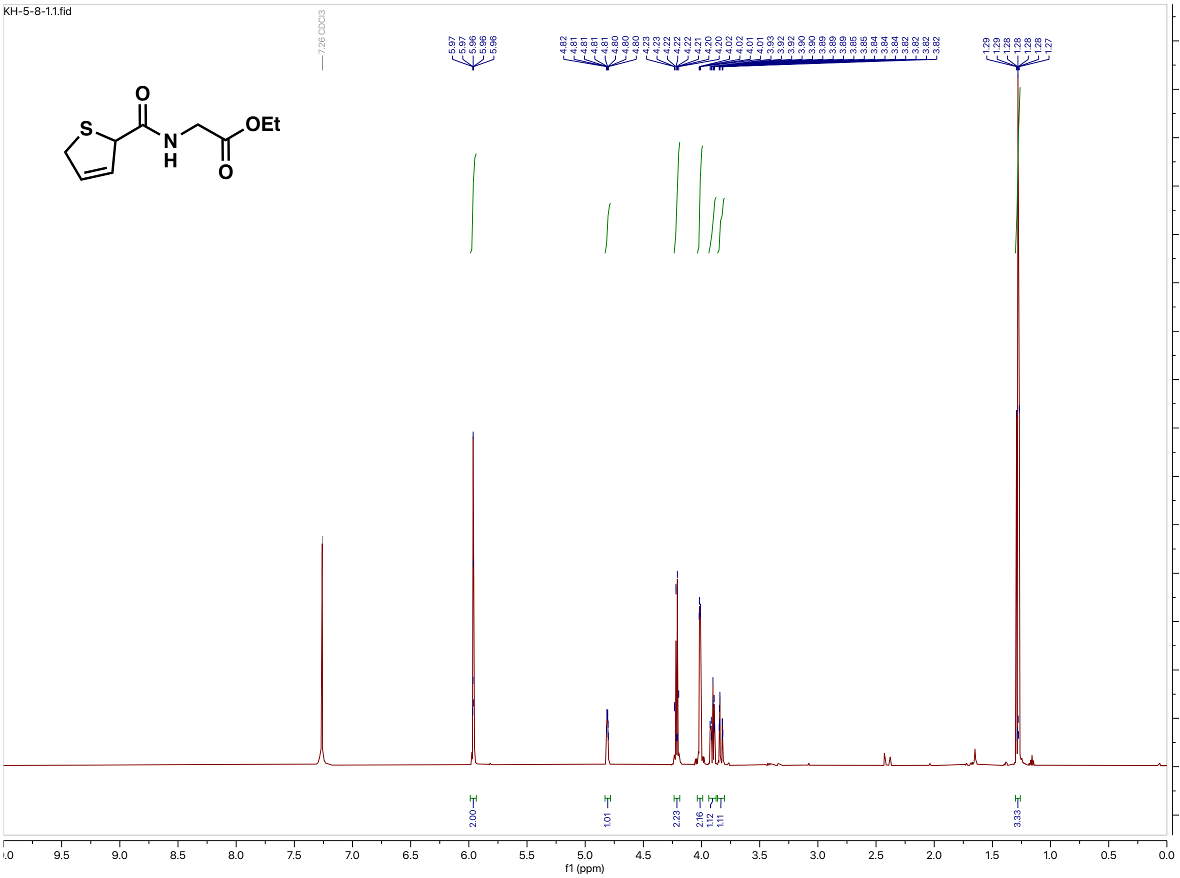

KH-3-169-1.3.fid
O
N
H
OEt
O
172.73
170.04
127.40
123.28
77.37
77.16 CDCl3
77.16
76.95
61.67
44.64
41.61
26.06
14.26
4000
3500
3000
2500
2000
1500
1000
500
0
-500
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

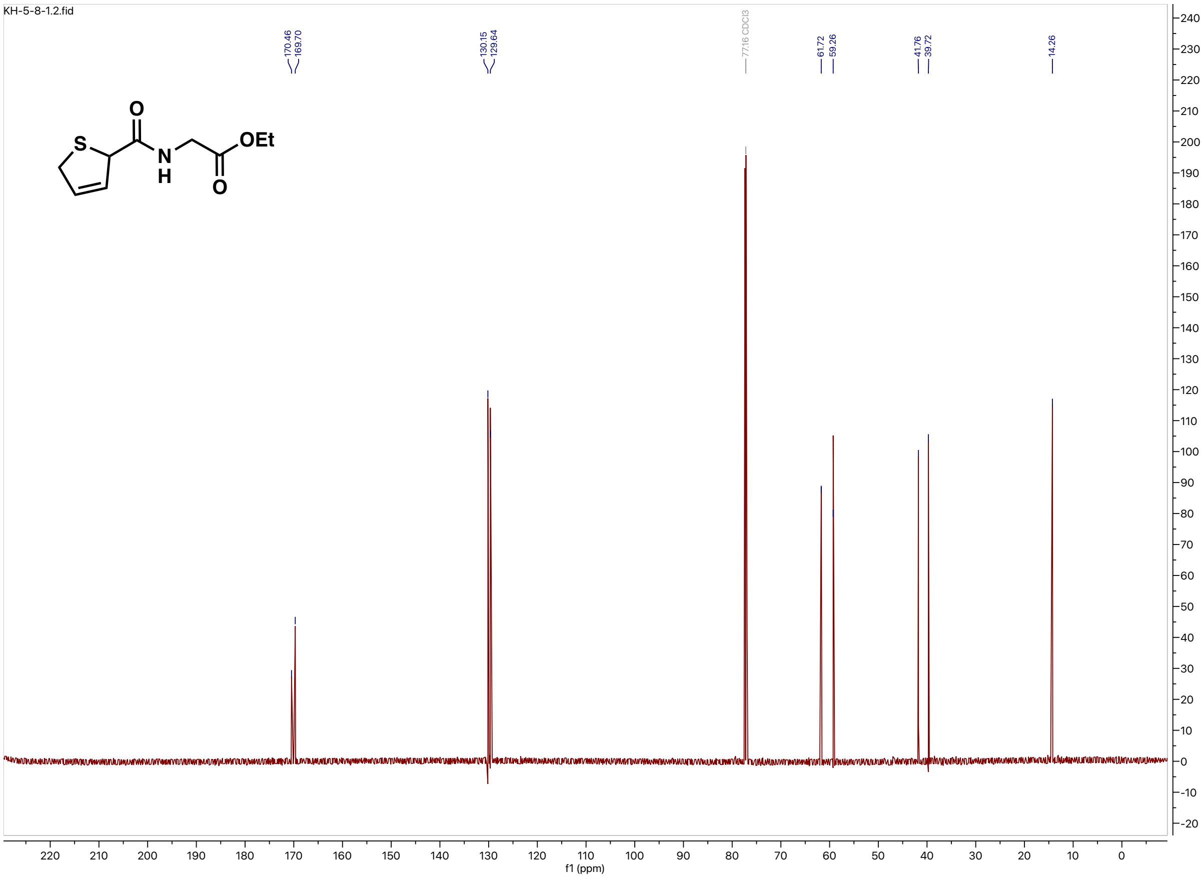
Compound 5


KH-4-155-1.1.fid
7.26 CDCl3
6.05 6.04 6.03 6.03 6.03 6.03 6.02 5.85 5.85 5.85 5.84 5.84 5.84 5.84 5.83 4.81 4.80 4.80 4.79 4.79 4.79 4.78 4.77 4.77 4.77 4.76 4.76 4.76 4.75 3.88 3.87 3.86 3.85 3.85 3.85 3.84 3.84 3.79 3.79 3.78 3.78 3.76 3.76 1.85 1.84 1.83 1.83 1.82 1.81 1.74 1.74 1.73 1.73 1.73 1.72 1.72 1.72 1.71 1.71 1.71 1.70 1.70 1.70 1.70 1.53 1.53 1.52 1.52 1.52 1.51 1.51 1.51 1.50 1.50 1.49 1.48 1.47 1.47 1.46 1.46 1.45 1.45 1.44 1.44 1.40 1.39 1.39 1.38 1.38 1.38 1.37 1.37 1.36 1.36 1.36 1.35 1.35 1.34 1.31 1.29 1.28 1.27
S
O
O
1.00
1.03
1.90
0.97
1.01
1.94
2.01
2.89
3.24
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
f1 (ppm)
1600 1500 1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0 -100

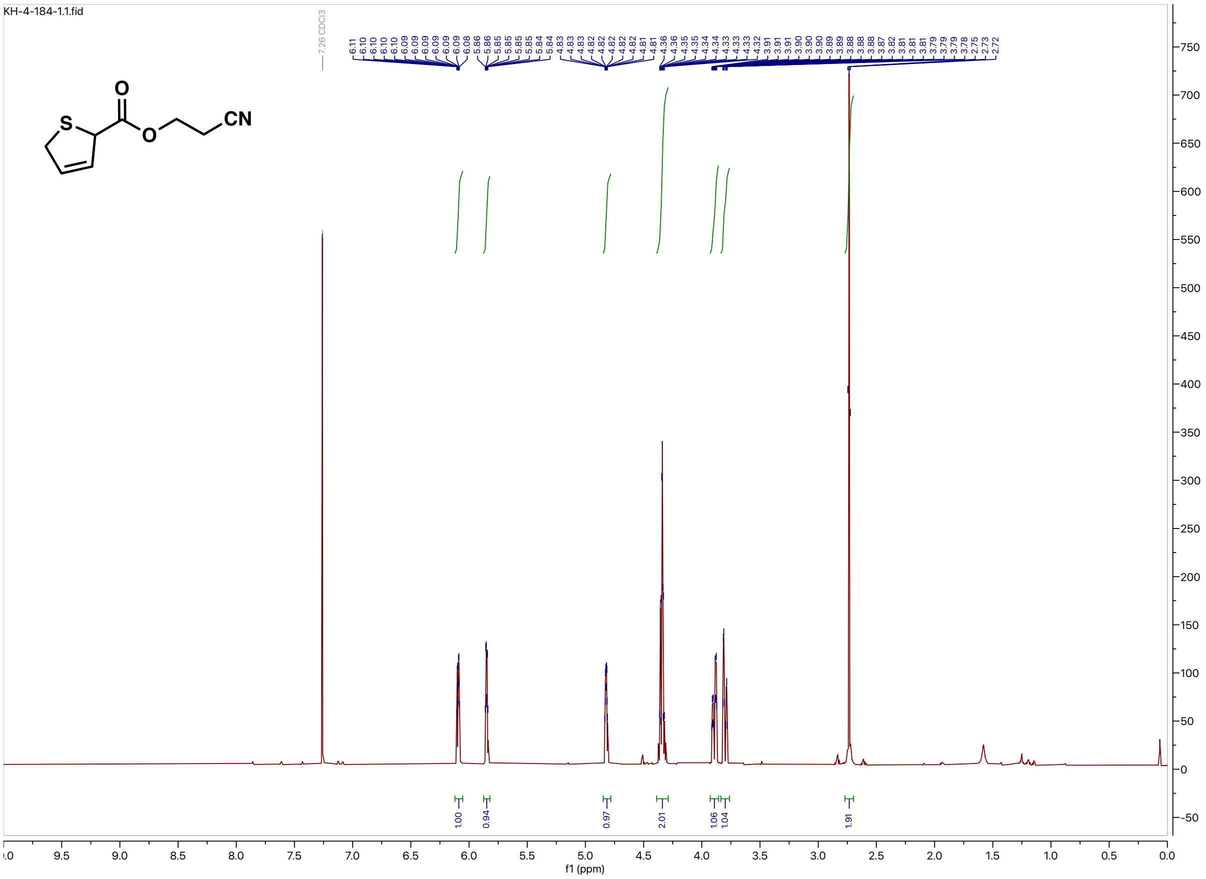

KH-4-155-1.2.fid
171.42
131.70
127.60
77.16 CDCl3
73.84
56.08
39.45
31.50
31.40
25.49
23.66
23.63
S
O
O
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

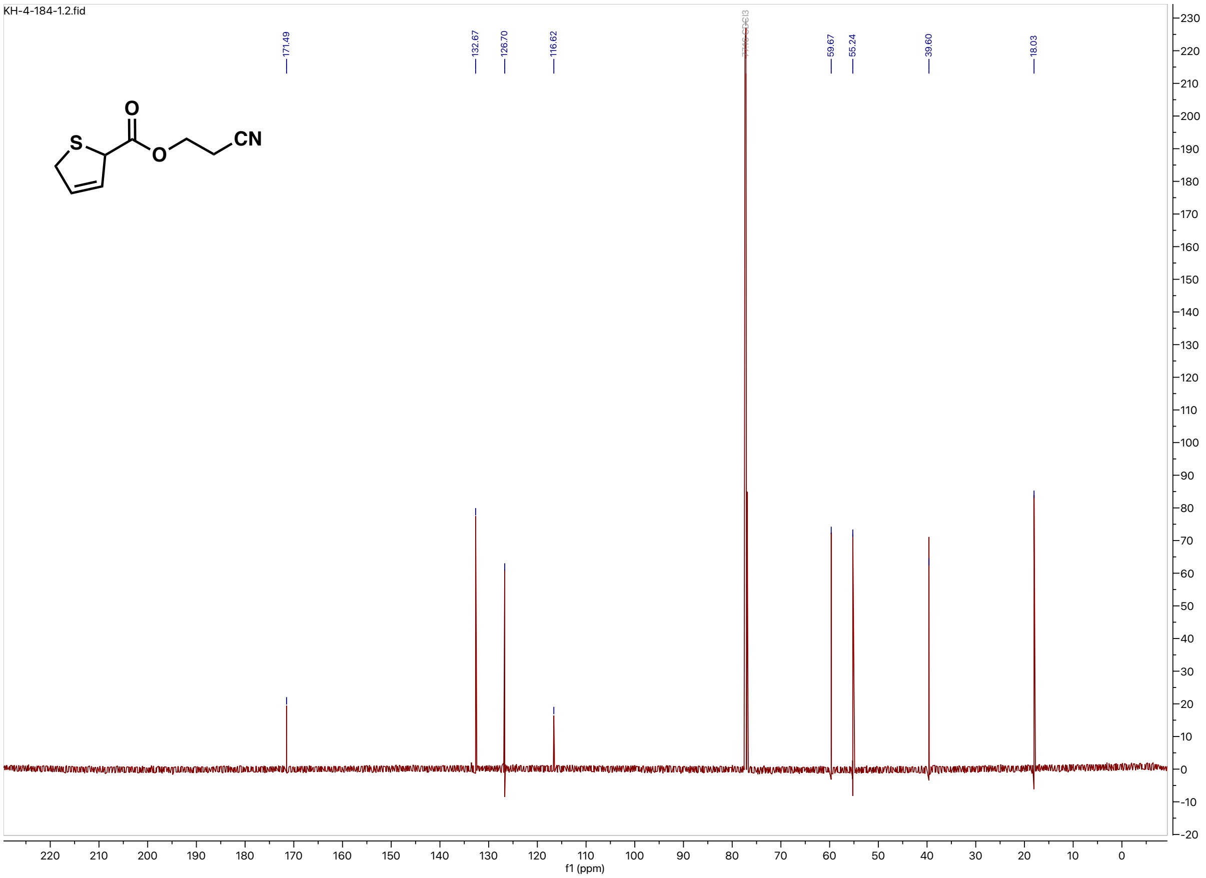
Compound 6


KH-5-8-1.1.fid
7.26 CDCl3
5.97 5.97 5.96 5.96 5.96
4.82 4.81 4.81 4.81 4.81 4.80 4.80 4.80
4.23 4.23 4.22 4.22 4.22 4.21 4.20 4.20 4.20 4.02 4.02 4.01 4.01 3.93 3.92 3.92 3.90 3.90 3.89 3.89 3.89 3.85 3.85 3.84 3.84 3.82 3.82 3.82 3.82
1.29 1.29 1.28 1.28 1.28 1.28 1.27
S
O
N
H
OEt
O
2.00
1.01
2.23
2.16
1.12
1.11
3.33
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
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
f1 (ppm)

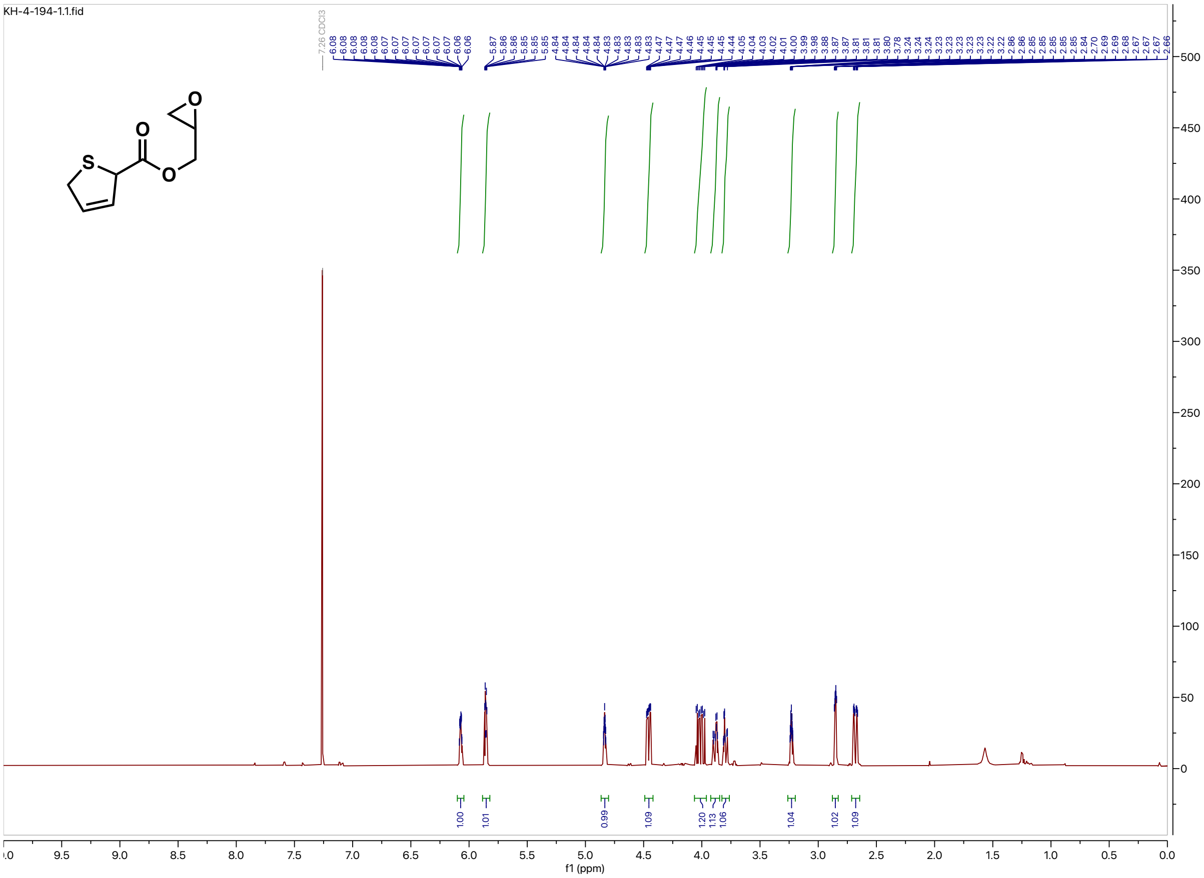

KH-5-8-1.2.fid
170.46
169.70
130.15
129.64
77.16 CDCl3
61.72
59.26
41.76
39.72
14.26
S
O
N
H
OEt
O
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
240
230
-10
-20

Compound 7

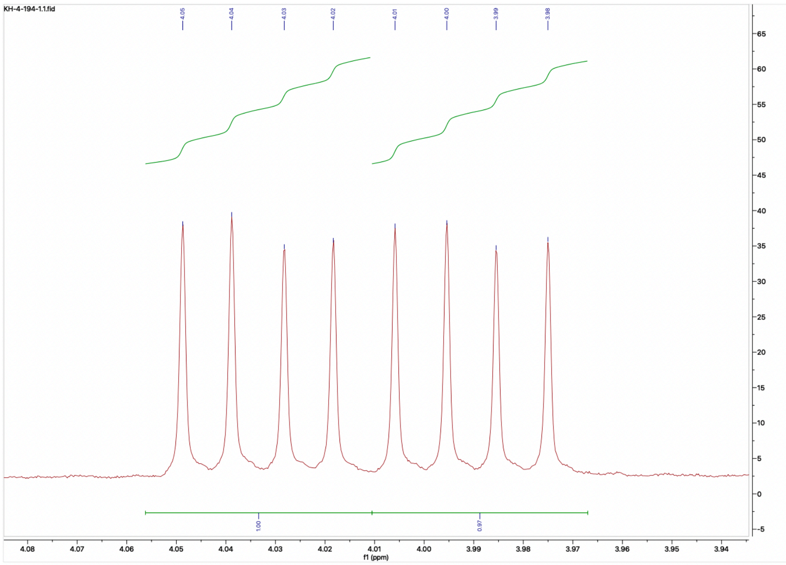

KH-4-184-1.1.fid
O
S
O
CN
7.26 CDCl3
6.11 6.10 6.10 6.10 6.09 6.09 6.09 6.09 6.09 6.08
5.86 5.86 5.85 5.85 5.85 5.85 5.84 5.84
4.83 4.83 4.83 4.82 4.82 4.82 4.82 4.81 4.81
4.36 4.36 4.35 4.35 4.34 4.34 4.33 4.33 4.33 4.32
3.91 3.91 3.91 3.90 3.90 3.90 3.89 3.89 3.88 3.88 3.88 3.87
3.82 3.81 3.81 3.79 3.79 3.79 3.78
2.75 2.73 2.72
1.00
0.94
0.97
2.01
1.06
1.04
1.91
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
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
f1 (ppm)

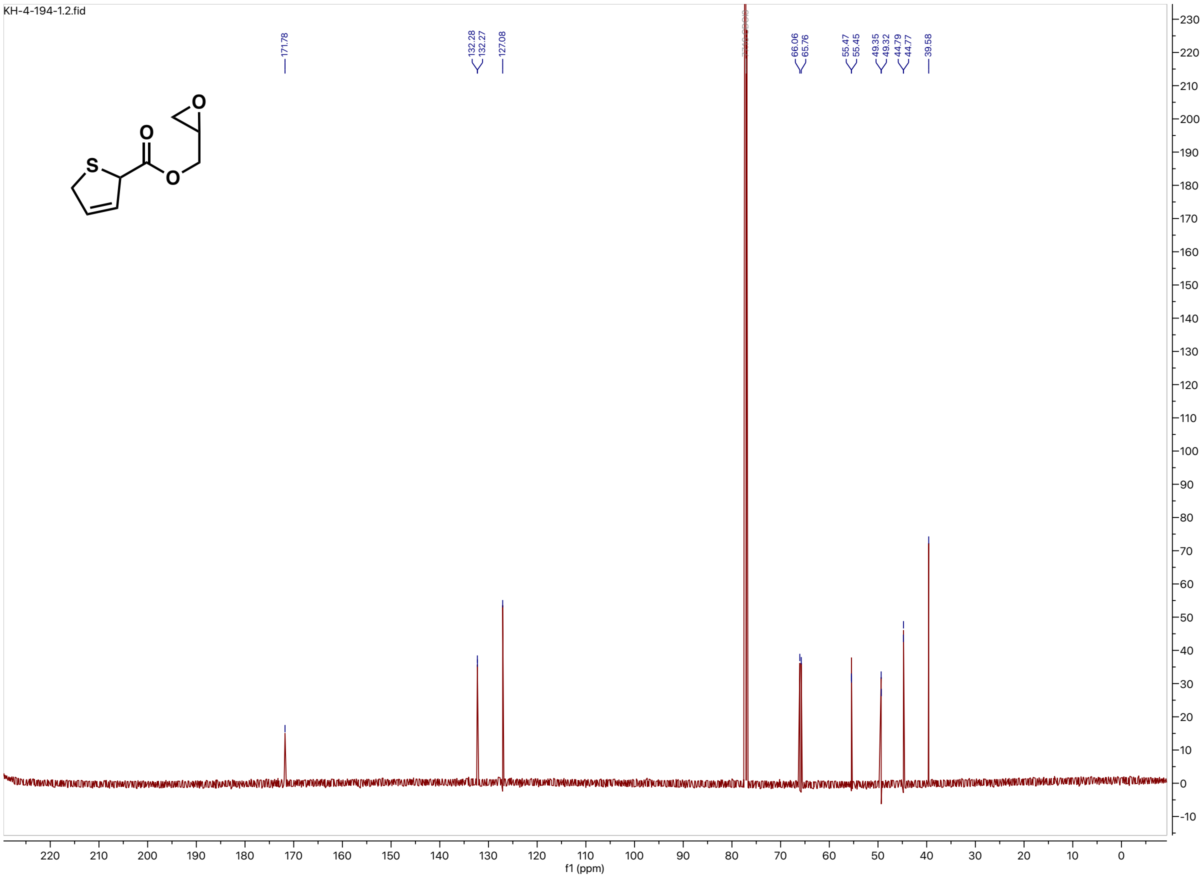

KH-4-184-1.2.fid
171.49
132.67
126.70
116.62
CDCl3
59.67
55.24
39.60
18.03
S
O
O
CN
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
230
-10
-20

Compound 8

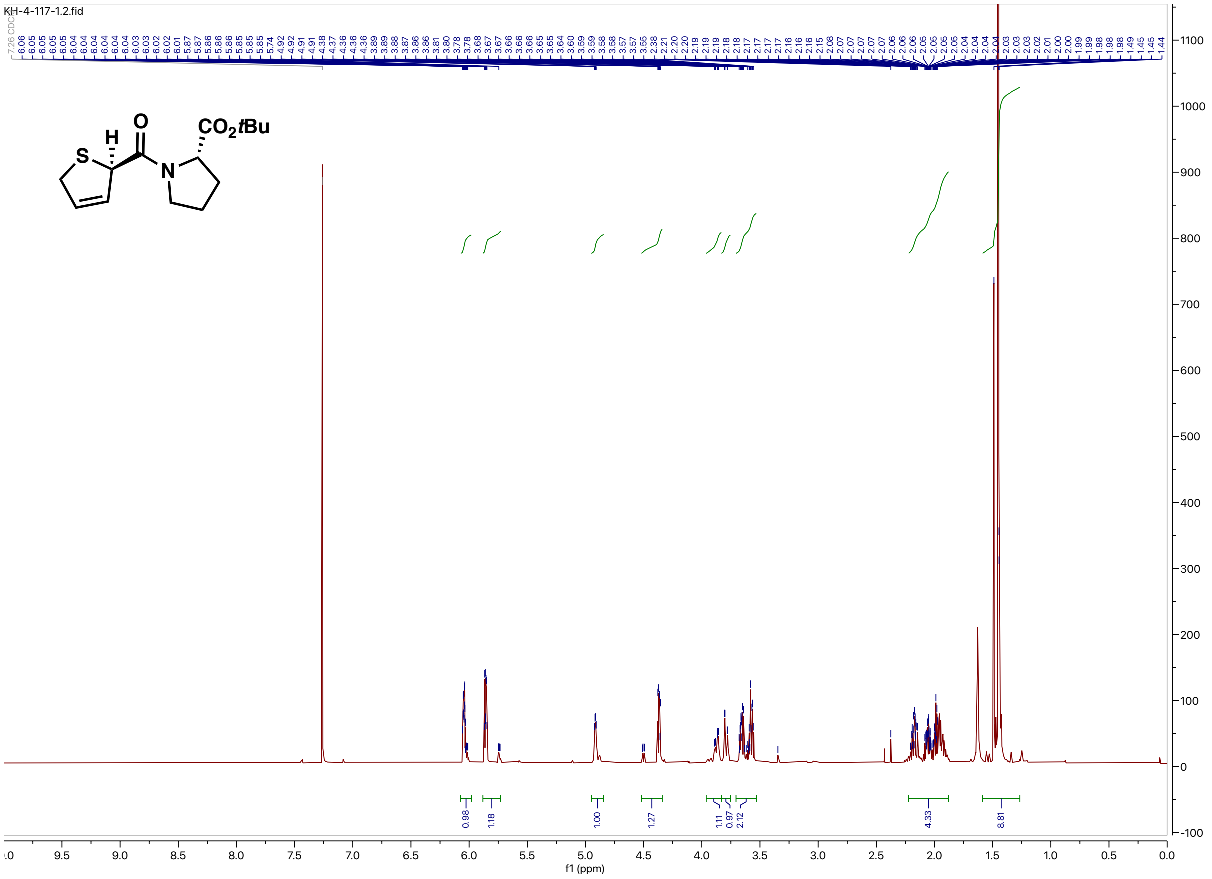


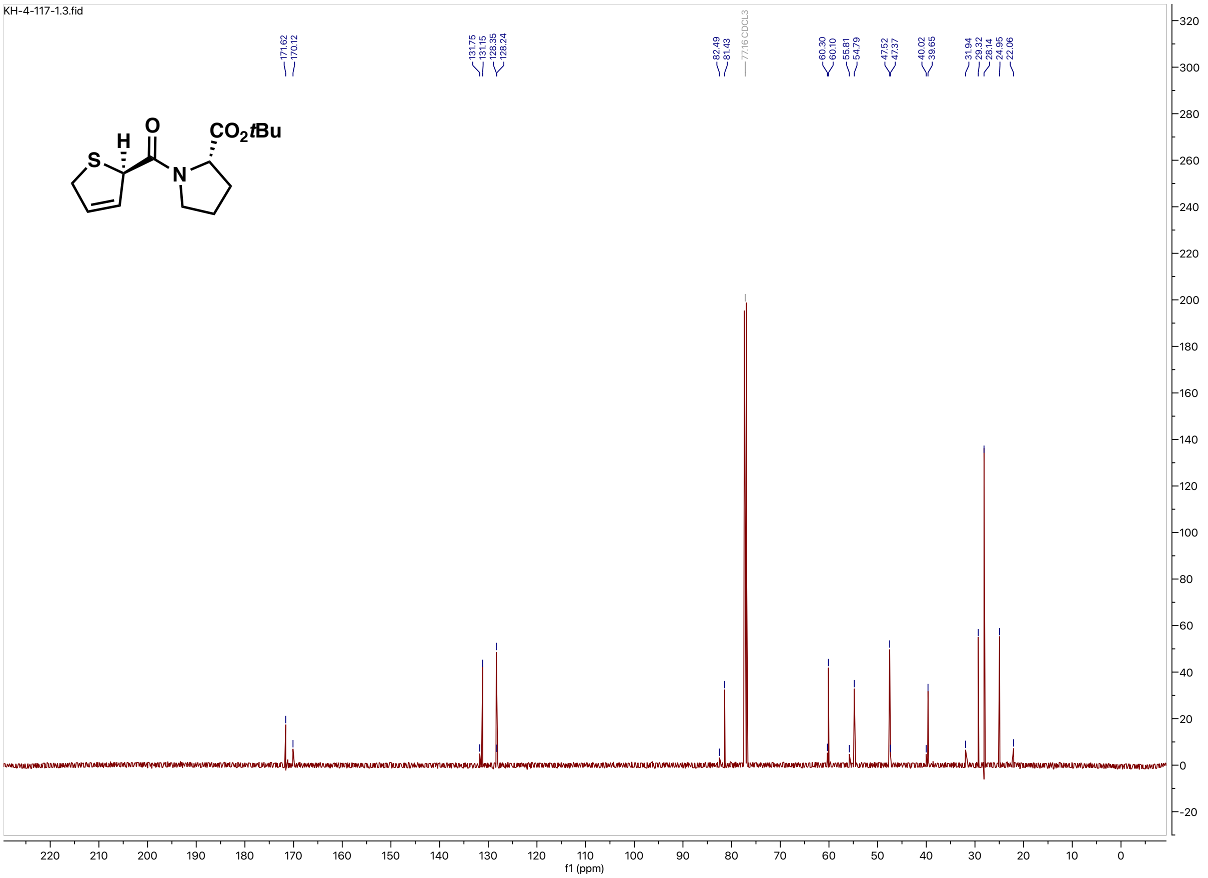
The dr was determined by integration of the following peaks.



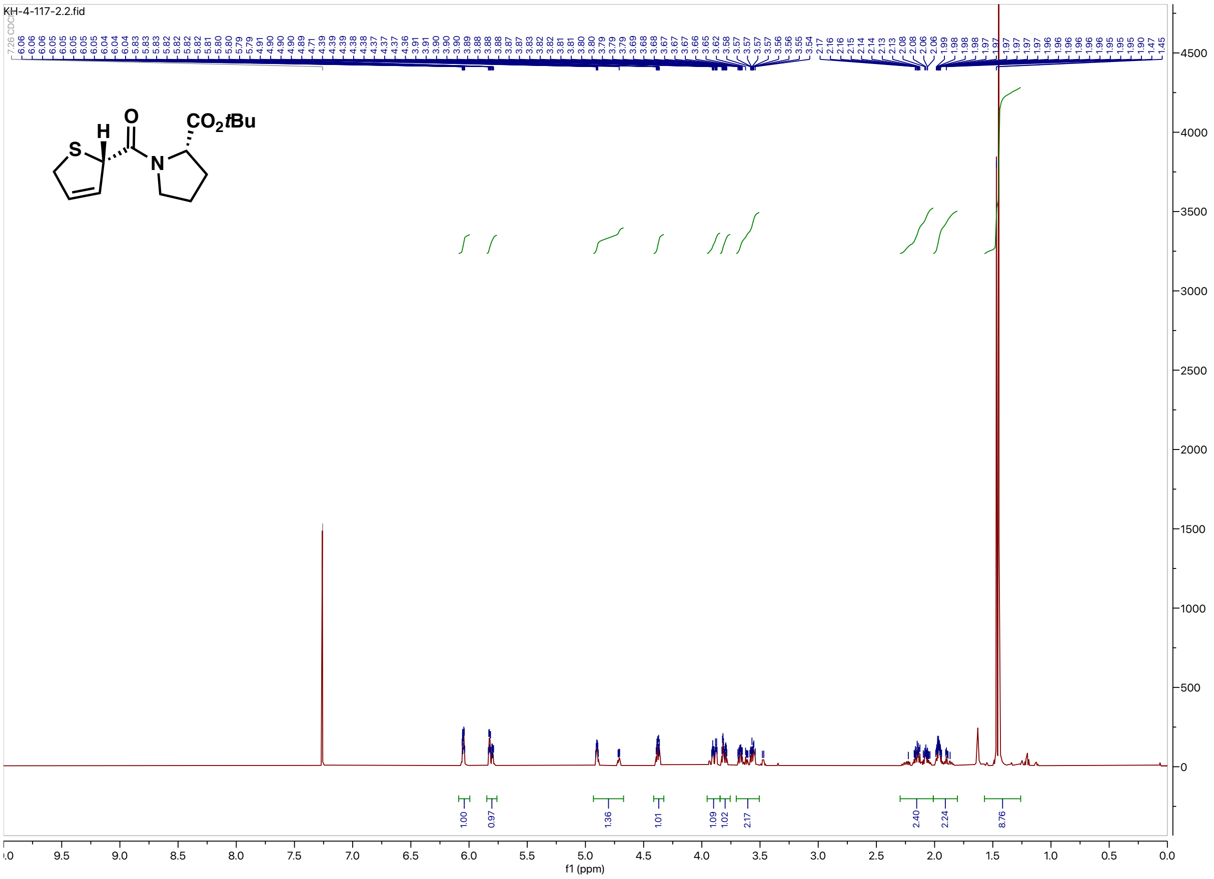

KH-4-194-1.2.fid
171.78
132.28
132.27
127.08
66.06
65.76
55.47
55.45
49.35
49.32
44.79
44.77
39.58
S
O
O
O
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

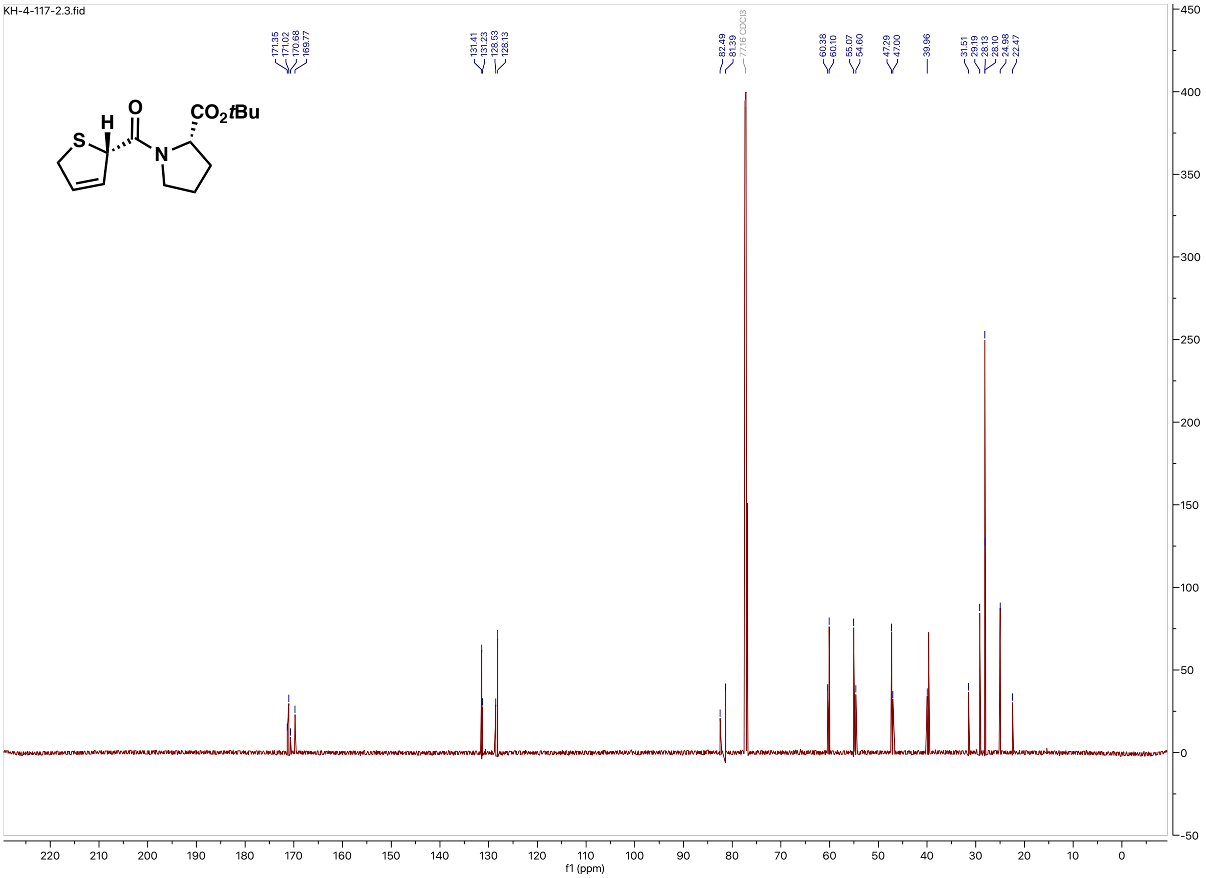
Compound 9a


KH-4-117-1.2.fid
7.26 CDCl3
6.06 6.05 6.05 6.05 6.05 6.04 6.04 6.04 6.04 6.04 6.04 6.03 6.03 6.02 6.02 6.01 5.87 5.87 5.86 5.86 5.86 5.85 5.85 5.85 5.74 4.92 4.92 4.91 4.91 4.38 4.37 4.36 4.36 4.36 3.89 3.89 3.88 3.87 3.86 3.86 3.81 3.80 3.78 3.78 3.68 3.67 3.67 3.66 3.66 3.66 3.65 3.65 3.64 3.60 3.59 3.59 3.58 3.58 3.57 3.57 3.55 2.38 2.21 2.20 2.20 2.19 2.19 2.19 2.18 2.18 2.17 2.17 2.17 2.17 2.16 2.16 2.16 2.15 2.08 2.07 2.07 2.07 2.07 2.07 2.06 2.06 2.06 2.05 2.05 2.05 2.05 2.04 2.04 2.04 2.04 2.03 2.03 2.03 2.02 2.01 2.00 2.00 1.99 1.99 1.98 1.98 1.98 1.49 1.45 1.45 1.44
H
O
S
N
CO2tBu
0.98
1.18
1.00
1.27
1.11
0.97
2.12
4.33
8.81
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
.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
f1 (ppm)

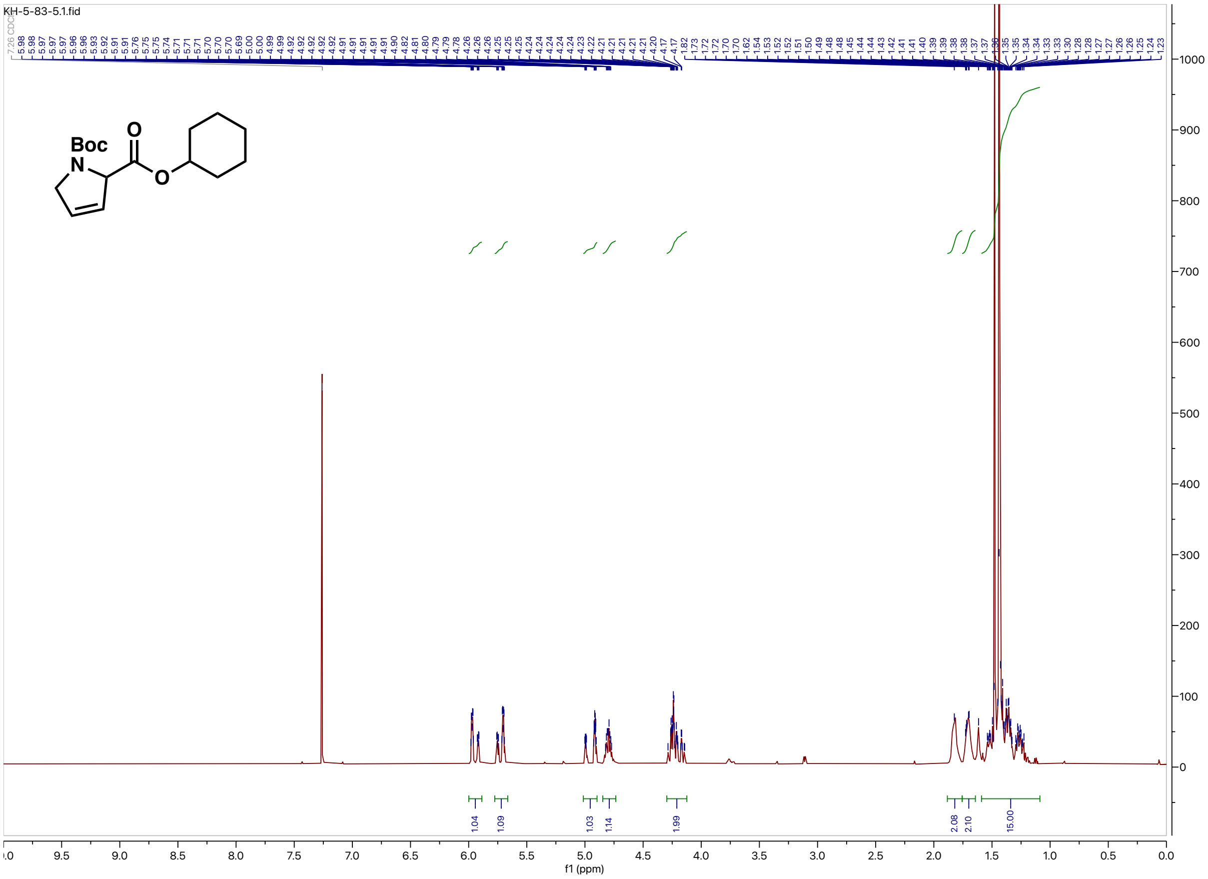

KH-4-117-1.3.fid
171.62
170.12
131.75
131.15
128.35
128.24
82.49
81.43
77.16 CDCL3
60.30
60.10
55.81
54.79
47.52
47.37
40.02
39.65
31.94
29.32
28.14
24.95
22.06
S
H
O
N
CO2tBu
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

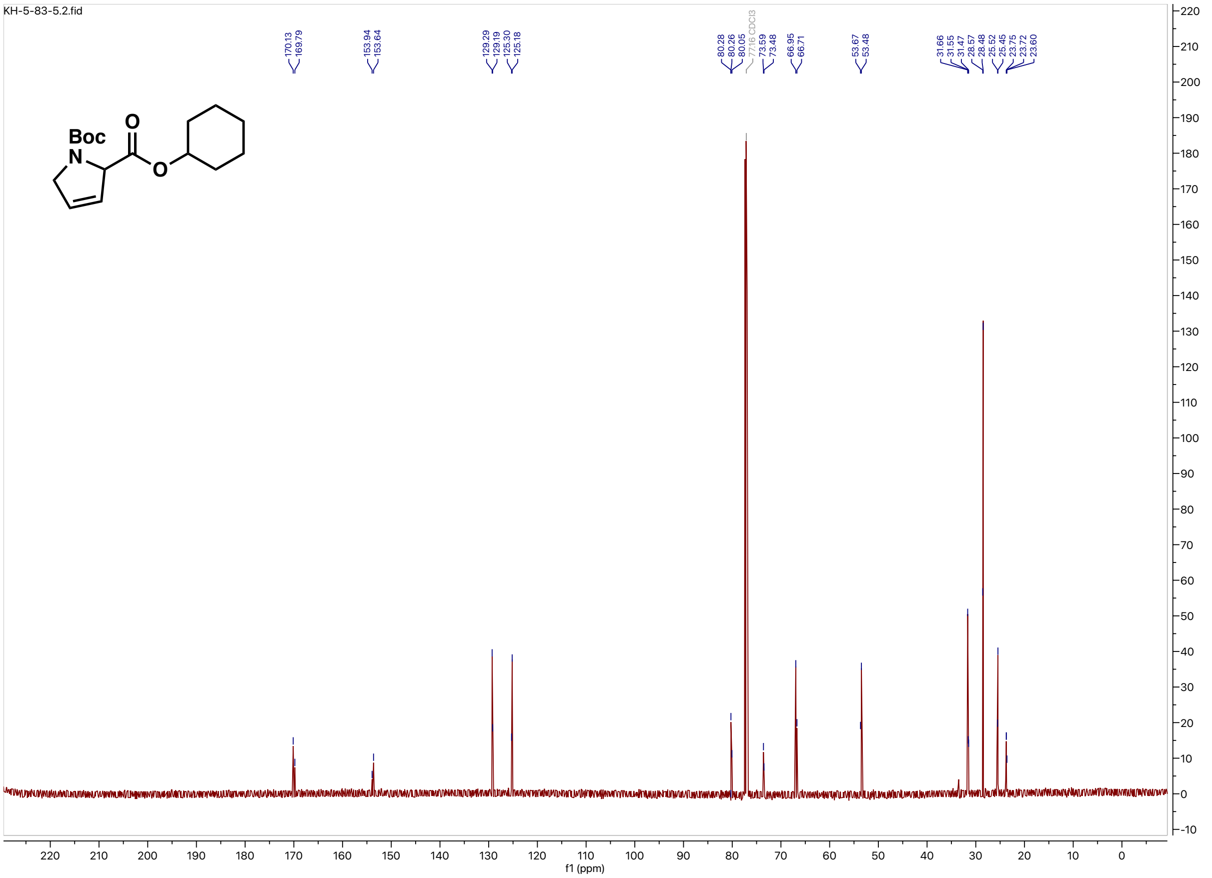
Compound 9b



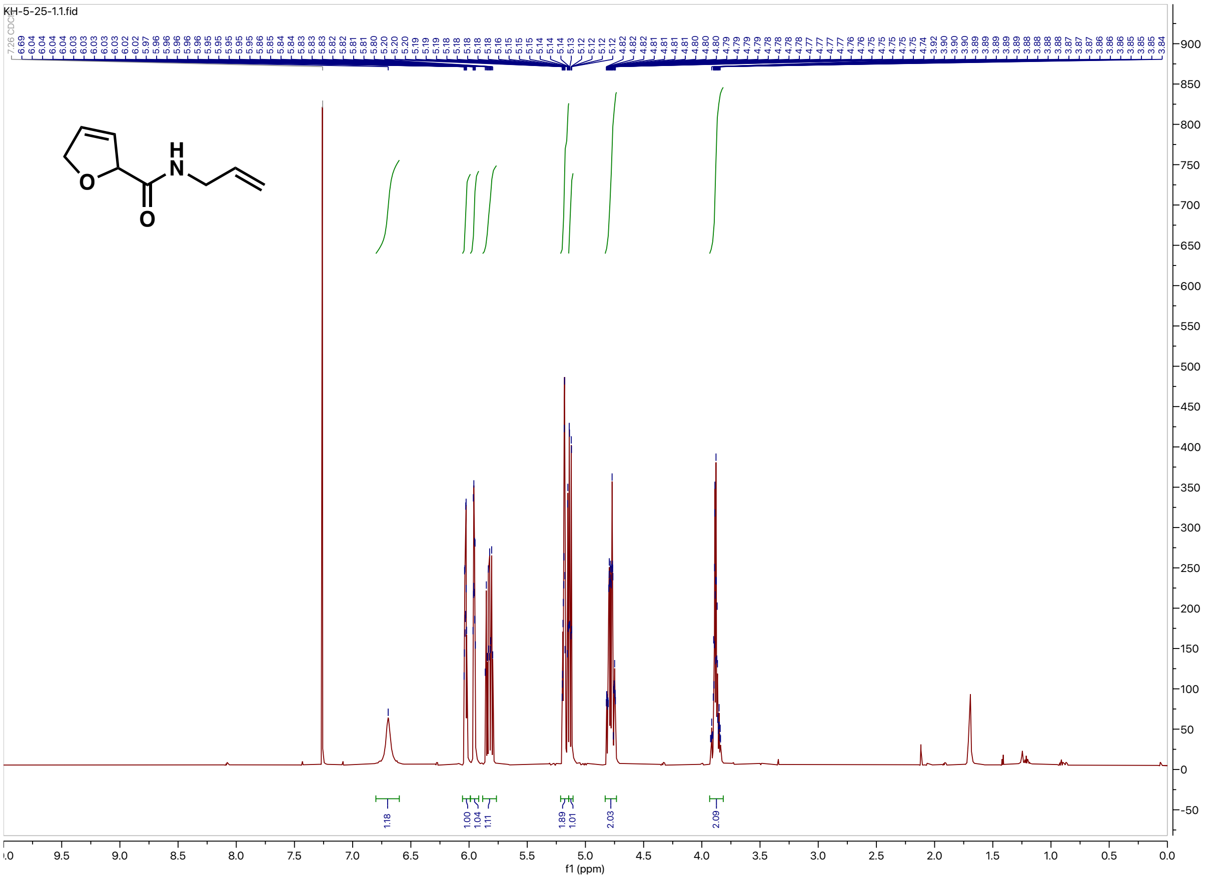

KH-4-117-2.3.fid
171.35
171.02
170.68
169.77
131.41
131.23
128.53
128.13
82.49
81.39
77.16 CDCl3
60.38
60.10
55.07
54.60
47.29
47.00
39.96
31.51
29.19
28.13
28.10
24.98
22.47
S
H
O
N
CO2tBu
450
400
350
300
250
200
150
100
50
0
-50
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

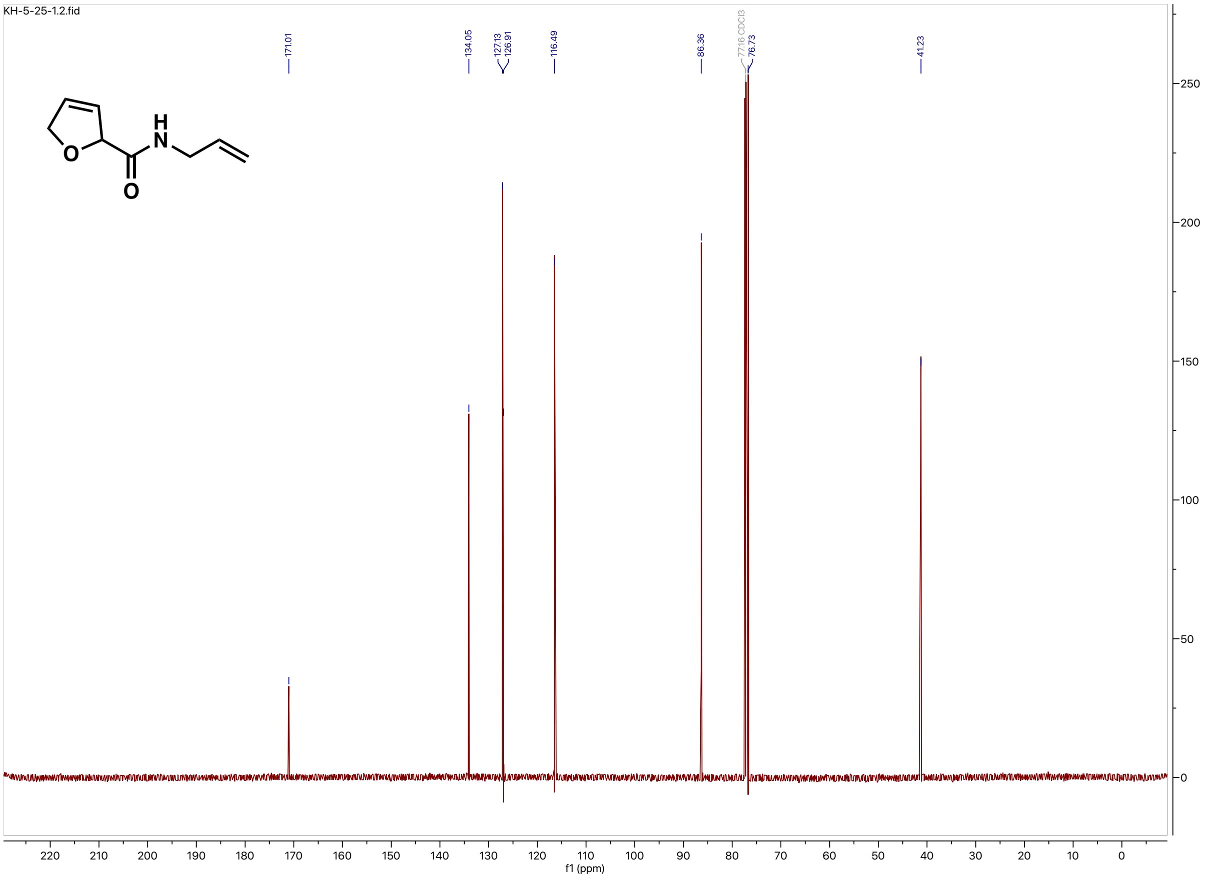
Compound 10


KH-5-83-5.1.fid
7.26 CDCl3
Boc
N
O
O
1.04
1.09
1.03
1.14
1.99
2.08
2.10
15.00
1000
900
800
700
600
500
400
300
200
100
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
f1 (ppm)

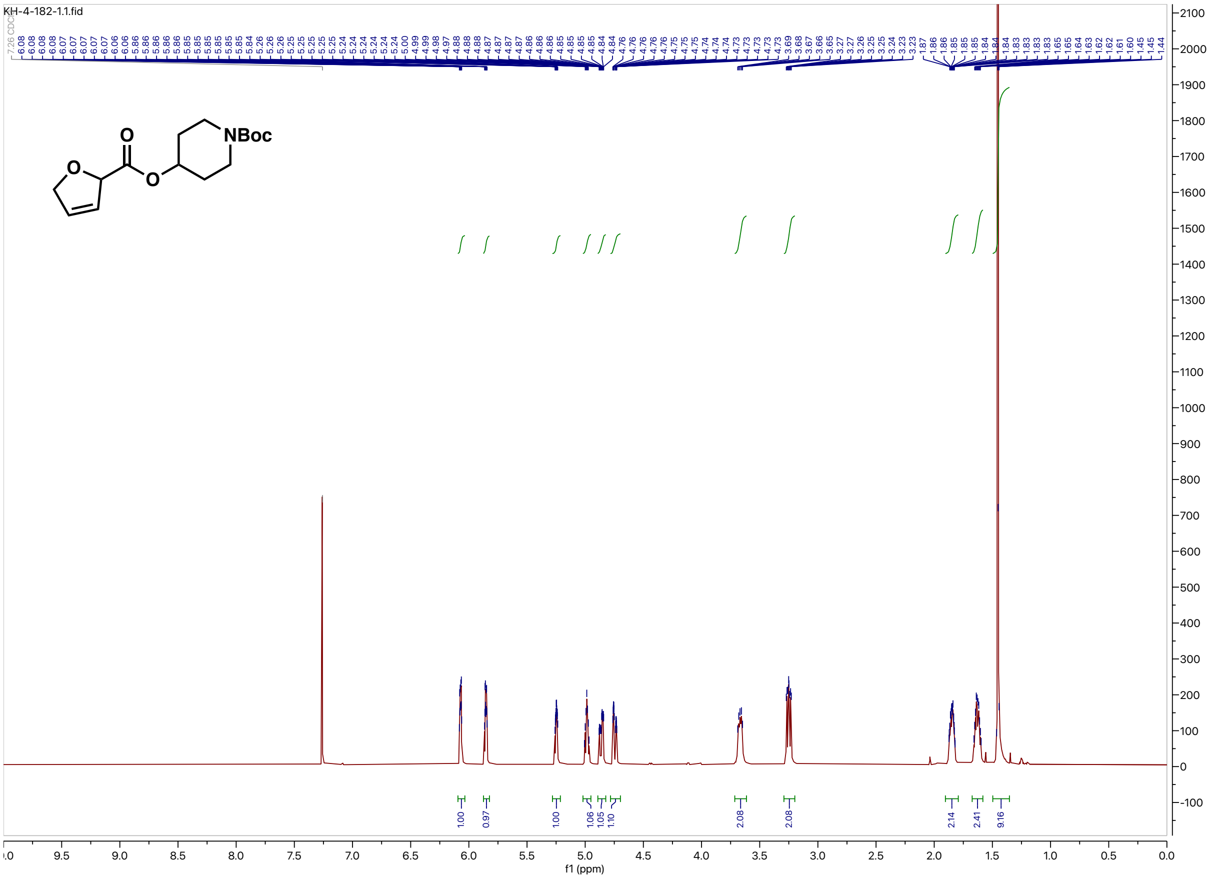

KH-5-83-5.2.fid
Boc
N
O
O
170.13
169.79
153.94
153.64
129.29
129.19
125.30
125.18
80.28
80.26
80.05
77.16 CDCl3
73.59
73.48
66.95
66.71
53.67
53.48
31.66
31.55
31.47
28.57
28.48
25.52
25.45
23.75
23.72
23.60
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

Compound 11

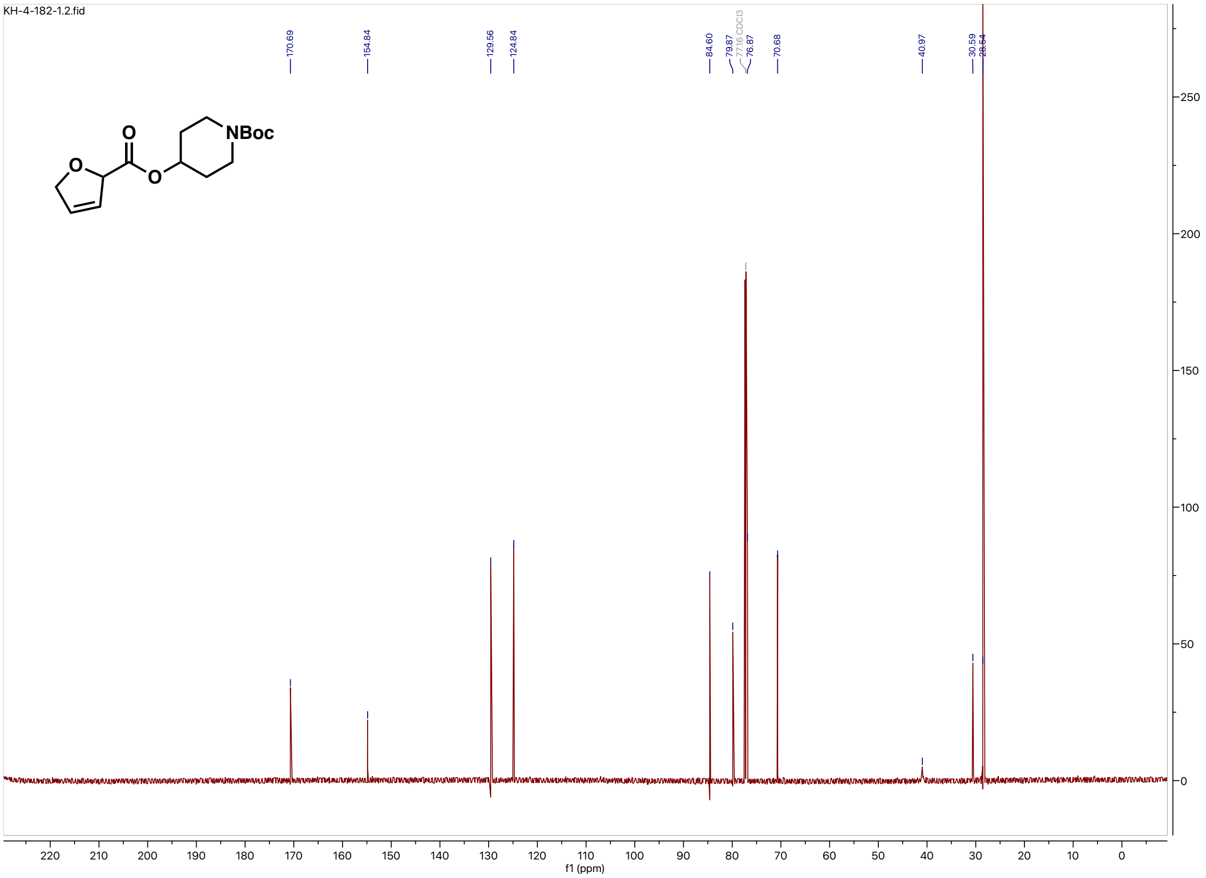

KH-5-25-1.1.fid
7.26 CDCl3
6.69
6.04
6.04
6.04
6.04
6.03
6.03
6.03
6.03
6.03
6.02
6.02
5.97
5.96
5.96
5.96
5.96
5.96
5.95
5.95
5.95
5.95
5.95
5.86
5.85
5.84
5.84
5.84
5.83
5.83
5.83
5.82
5.82
5.81
5.81
5.80
5.20
5.20
5.20
5.19
5.19
5.19
5.19
5.18
5.18
5.18
5.18
5.18
5.16
5.15
5.15
5.15
5.14
5.14
5.14
5.13
5.12
5.12
5.12
5.12
4.82
4.82
4.82
4.81
4.81
4.81
4.80
4.80
4.80
4.79
4.79
4.79
4.79
4.78
4.78
4.78
4.78
4.77
4.77
4.77
4.76
4.76
4.75
4.75
4.75
4.75
4.75
4.74
3.92
3.90
3.90
3.90
3.89
3.89
3.89
3.89
3.89
3.89
3.88
3.88
3.88
3.87
3.87
3.87
3.86
3.86
3.85
3.85
3.84
O
H
N
O
1.18
1.00
1.04
1.11
1.89
1.01
2.03
2.09
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
f1 (ppm)
900
850
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50


KH-5-25-1.2.fid
171.01
134.05
127.13
126.91
116.49
86.36
77.16 CDCl3
76.73
41.23
H
N
O
O
250
200
150
100
50
0
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)

Compound 12

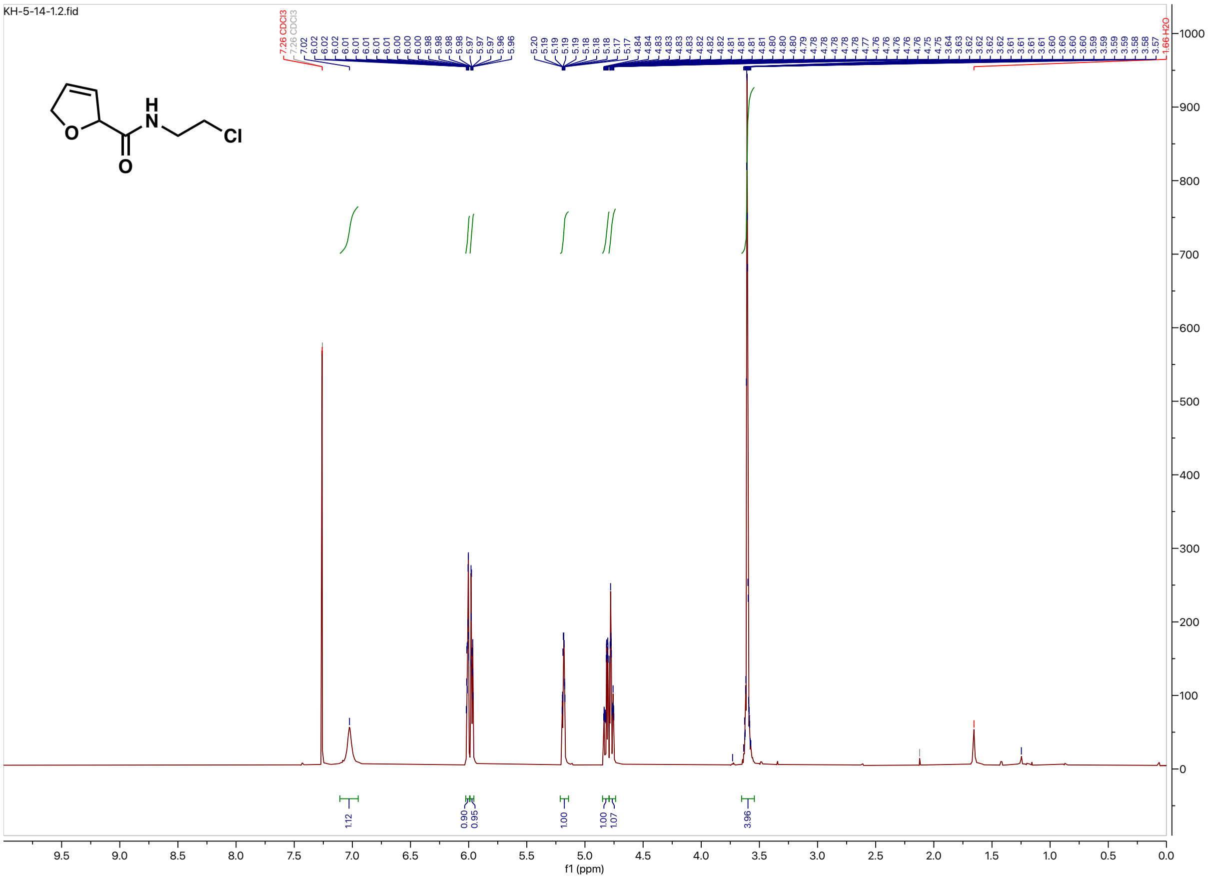


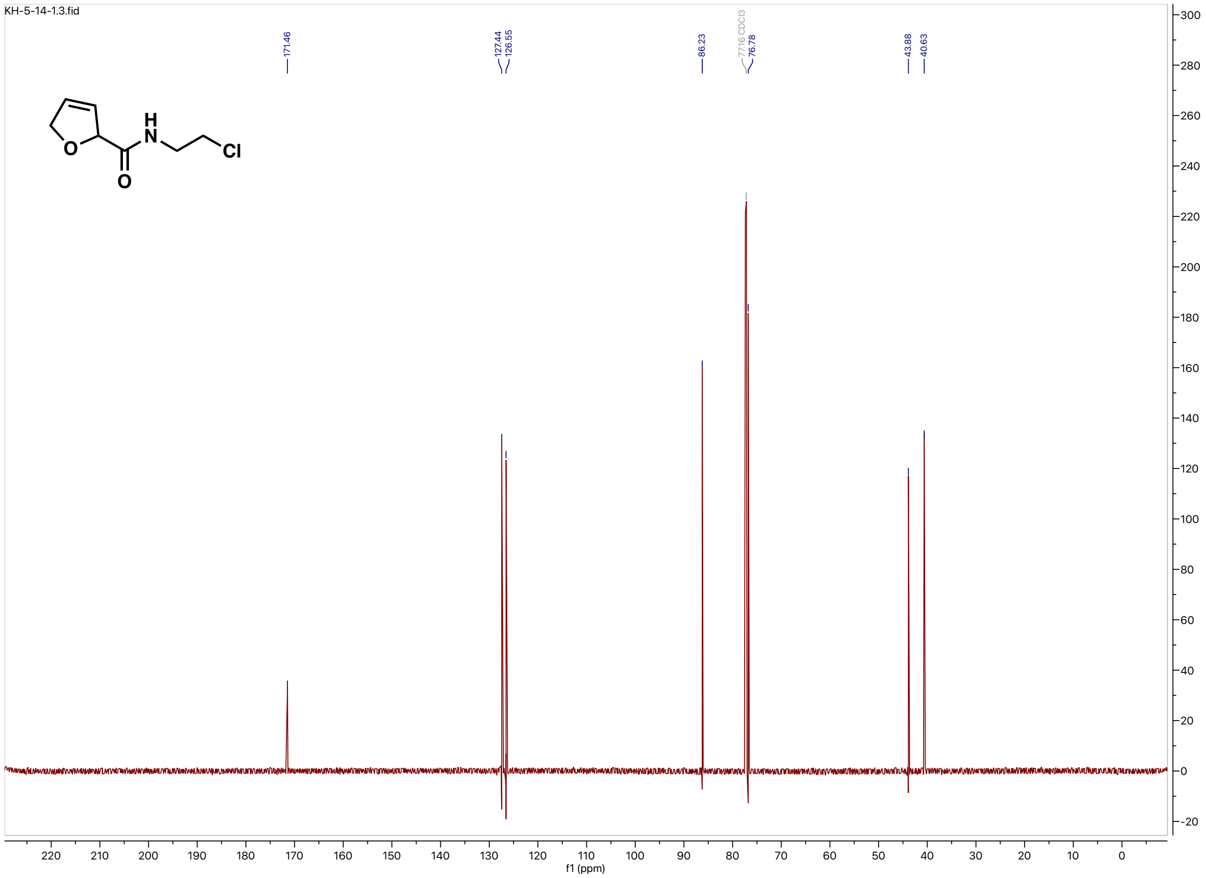
KH-4-182-1.1.fid
NBoc
O
O
O
1.00
0.97
1.00
1.06
1.05
1.10
2.08
2.08
2.14
2.41
9.16
f1 (ppm)



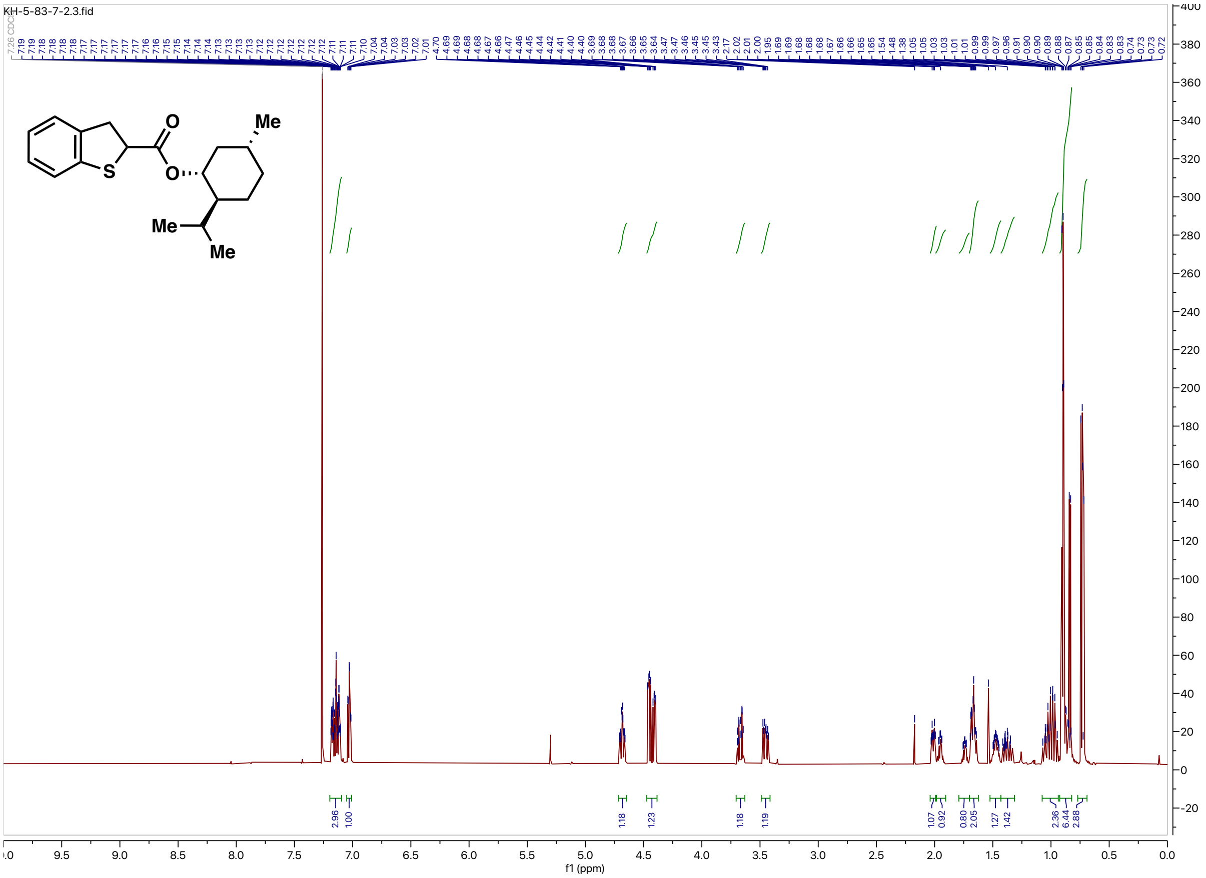
KH-4-182-1.2.fid
170.69
154.84
129.56
124.84
84.60
79.87
77.16 CDCl3
76.87
70.68
40.97
30.59
28.54
O
O
O
NBoc
250
200
150
100
50
0
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Compound 13

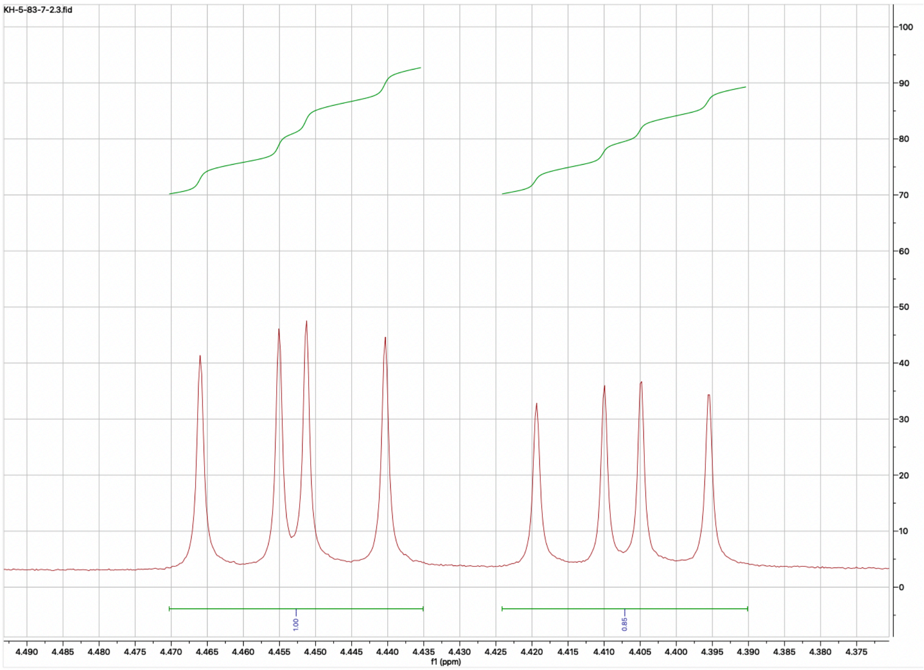

KH-5-14-1.2.fid
H
N
O
O
Cl
7.26 CDCl3
7.26 CDCl3
7.02
6.02
6.02
6.02
6.01
6.01
6.01
6.01
6.01
6.00
6.00
6.00
5.98
5.98
5.98
5.98
5.97
5.97
5.97
5.96
5.96
5.20
5.19
5.19
5.19
5.19
5.18
5.18
5.18
5.17
5.17
4.84
4.84
4.83
4.83
4.83
4.83
4.82
4.82
4.82
4.81
4.81
4.81
4.81
4.80
4.80
4.80
4.79
4.78
4.78
4.78
4.78
4.78
4.77
4.76
4.76
4.76
4.76
4.76
4.75
4.75
3.64
3.63
3.62
3.62
3.62
3.62
3.61
3.61
3.61
3.61
3.60
3.60
3.60
3.60
3.59
3.59
3.59
3.59
3.58
3.58
3.57
1.66 H2O
1000
900
800
700
600
500
400
300
200
100
0
1.12
0.90
0.95
1.00
1.00
1.07
3.96
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
f1 (ppm)

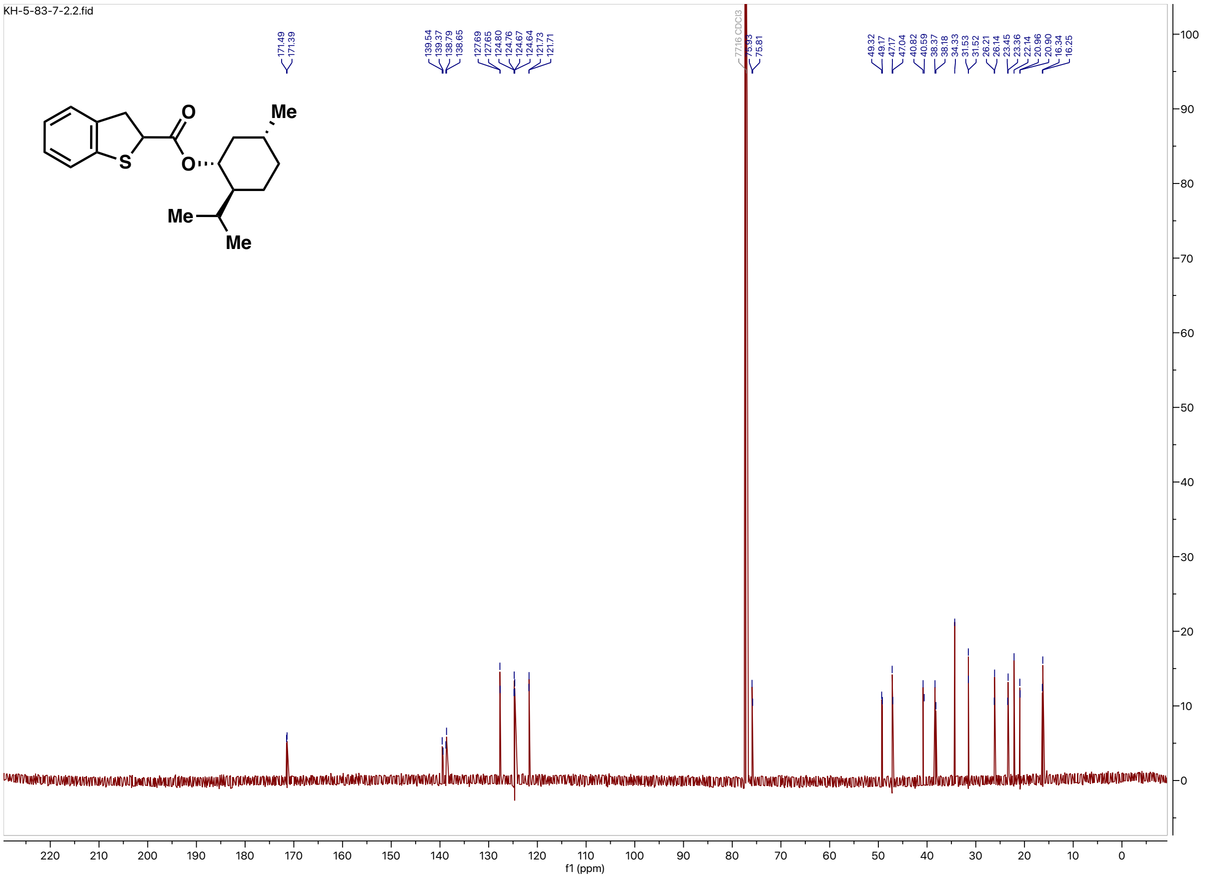

KH-5-14-1.3.fid
171.46
127.44
126.55
86.23
77.16 CDCl3
76.78
43.88
40.63
O
H
N
Cl
O
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Compound 14

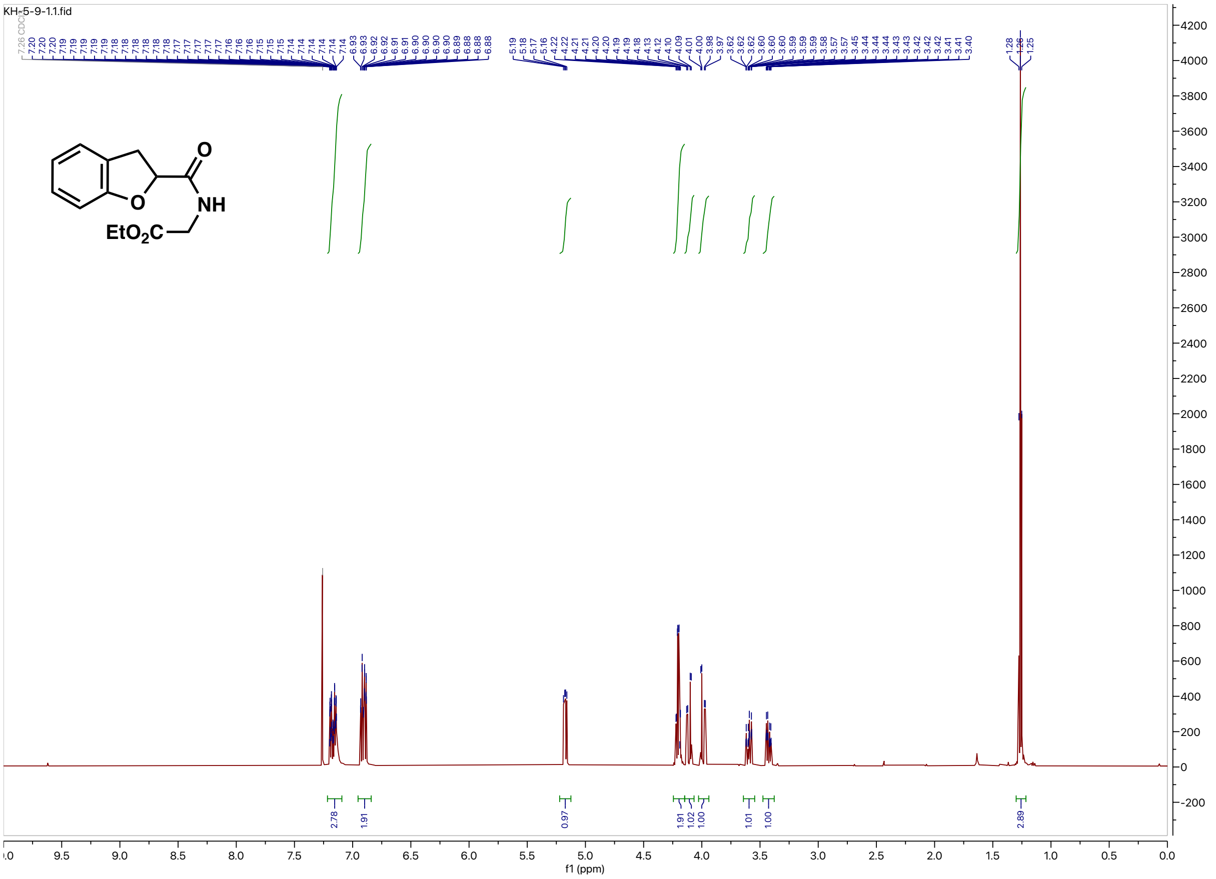


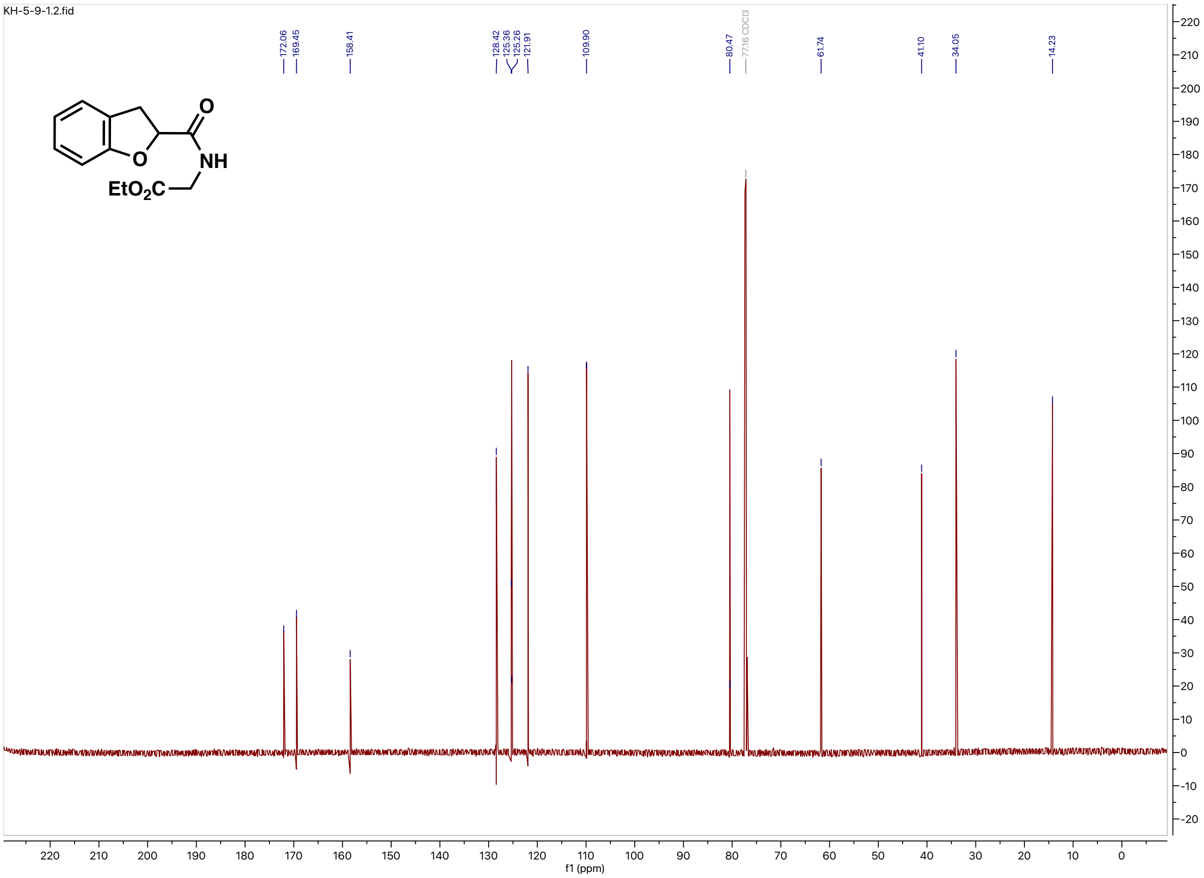
The dr was determined by integration of the following peaks.



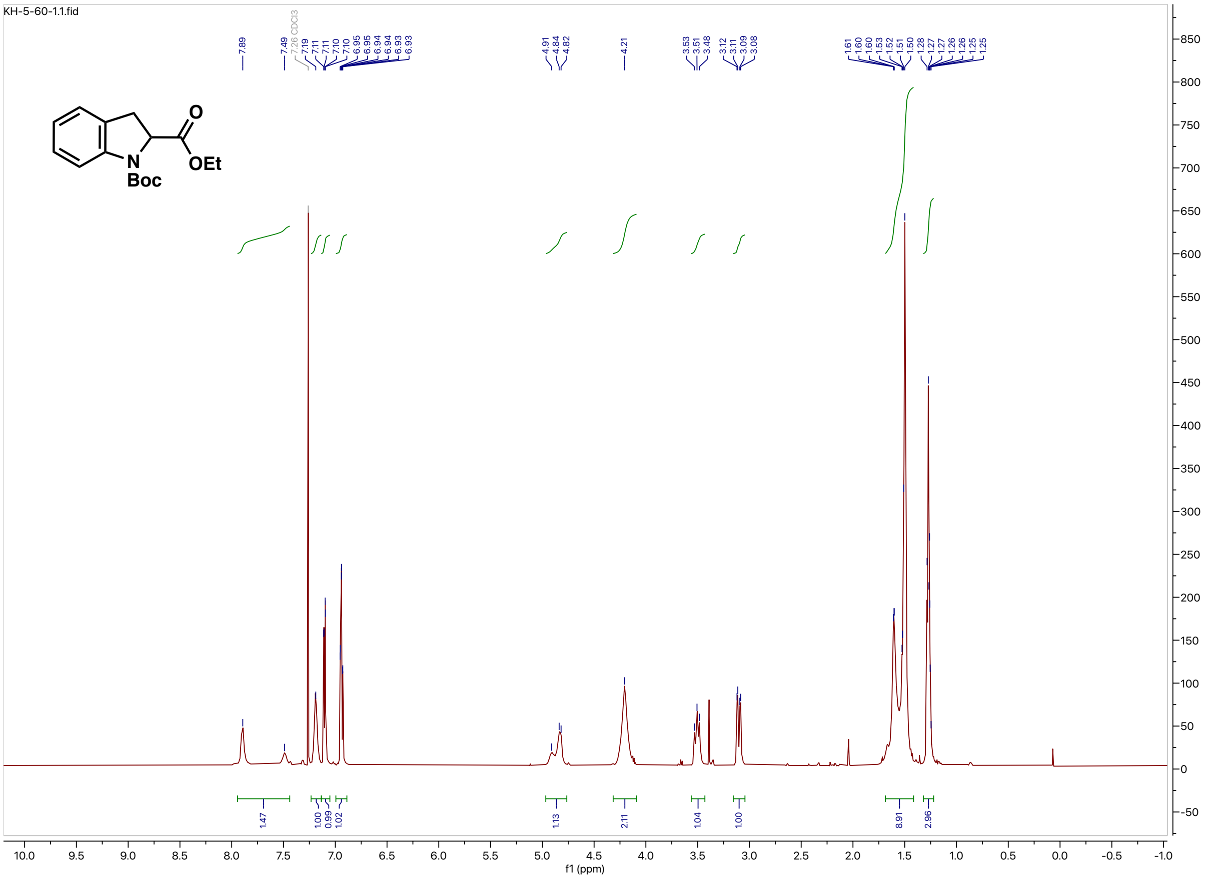

KH-5-83-7-2.2.fid
171.49
171.39
139.54
139.37
138.79
138.65
127.69
127.65
124.80
124.76
124.67
124.64
121.73
121.71
77.16 CDCl3
75.93
75.81
49.32
49.17
47.17
47.04
40.82
40.59
38.37
38.18
34.33
31.53
31.52
26.21
26.14
23.45
23.36
22.14
20.96
20.90
16.34
16.25
O
S
O
Me
Me
Me
100
90
80
70
60
50
40
30
20
10
0
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)

Compound 15

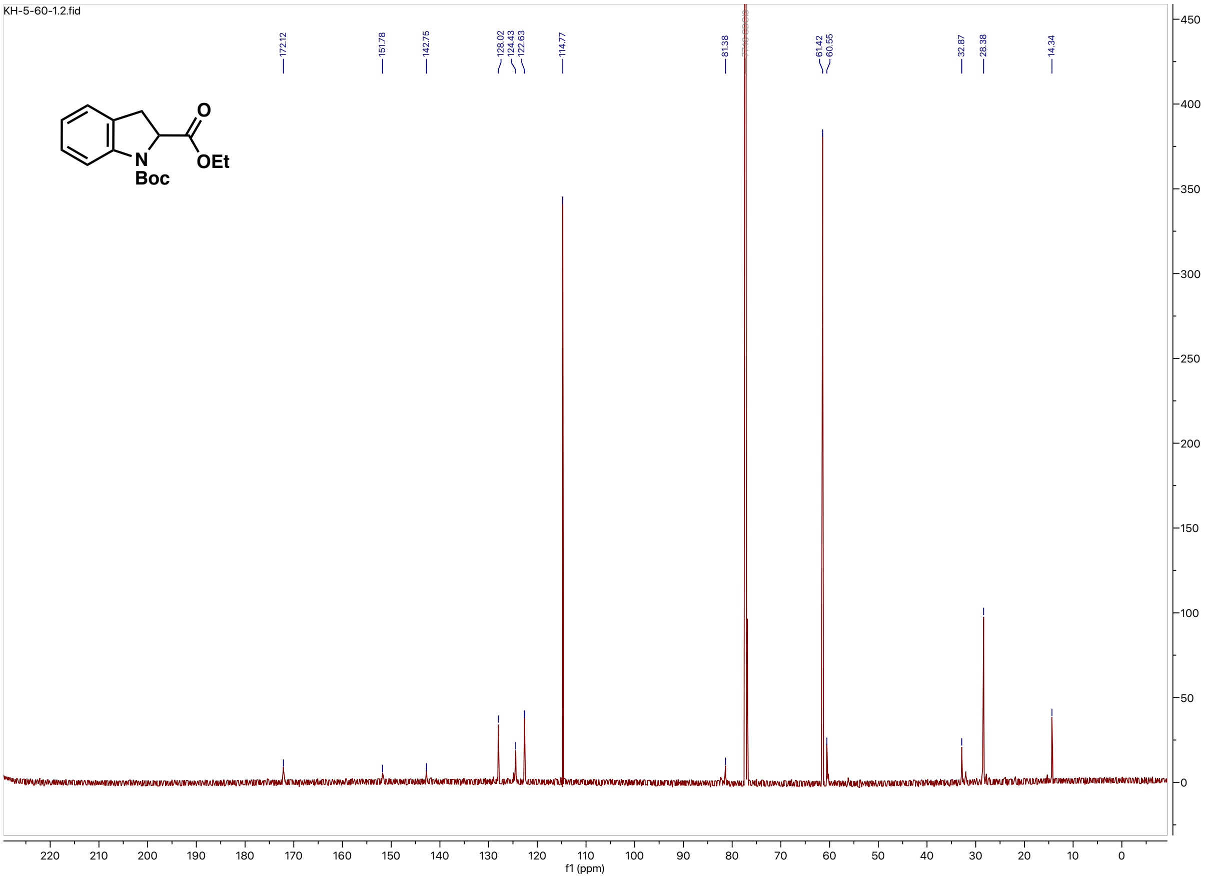

KH-5-9-1.1.fid
7.26 CDCl3
7.20
7.20
7.19
7.19
7.19
7.19
7.18
7.18
7.18
7.18
7.18
7.17
7.17
7.17
7.17
7.16
7.16
7.15
7.15
7.14
7.14
7.14
7.14
7.14
7.14
6.93
6.93
6.92
6.92
6.91
6.91
6.90
6.90
6.90
6.89
6.88
6.88
6.88
5.19
5.18
5.17
5.16
4.22
4.22
4.21
4.21
4.20
4.20
4.19
4.19
4.18
4.13
4.12
4.10
4.09
4.01
4.00
3.98
3.97
3.62
3.62
3.62
3.60
3.60
3.59
3.59
3.58
3.57
3.57
3.45
3.44
3.44
3.43
3.43
3.42
3.42
3.41
3.41
3.40
1.28
1.26
1.25
O
NH
O
EtO2C
2.78
1.91
0.97
1.91
1.02
1.00
1.01
1.00
2.89
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
f1 (ppm)
4200
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200


KH-5-9-1.2.fid
172.06
169.45
158.41
128.42
125.36
125.26
121.91
109.90
80.47
77.16 CDCl3
61.74
41.10
34.05
14.23
O
NH
O
EtO$_2$C
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20

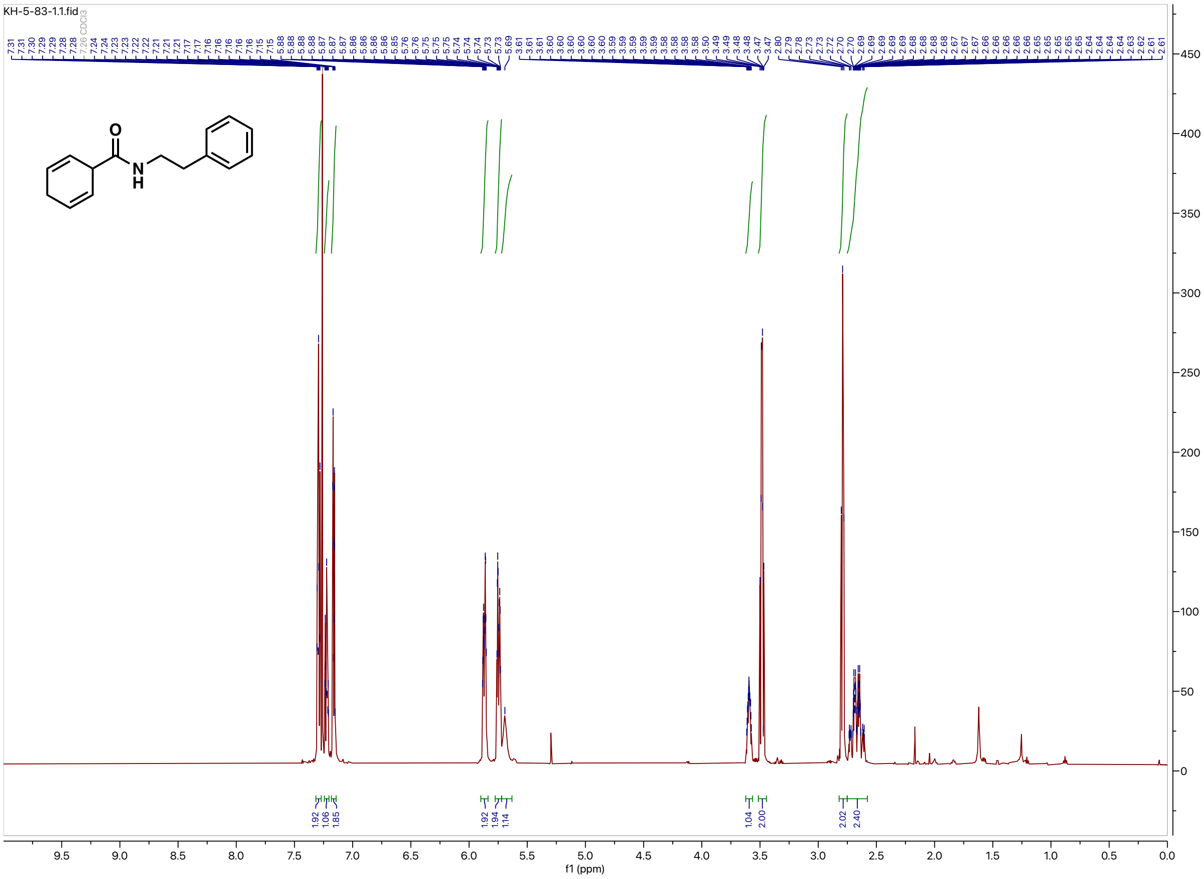
Compound 16

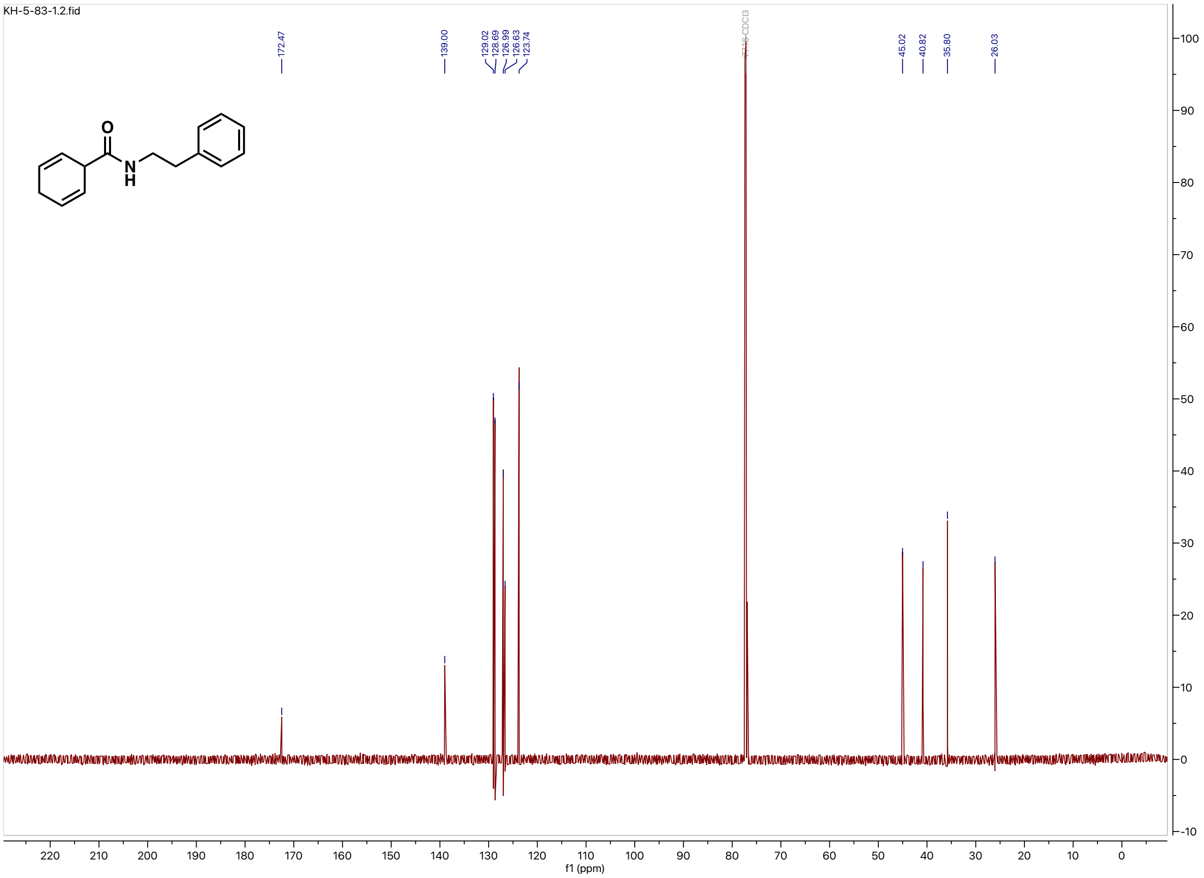


KH-5-60-1.1.fid
7.89
7.49
7.26 CDCl3
7.19
7.11
7.11
7.10
7.10
6.95
6.95
6.94
6.94
6.93
6.93
4.91
4.84
4.82
4.21
3.53
3.51
3.48
3.12
3.11
3.09
3.08
1.61
1.60
1.53
1.52
1.51
1.50
1.28
1.27
1.27
1.26
1.26
1.25
O
N
OEt
Boc
1.47
1.00
0.99
1.02
1.13
2.11
1.04
1.00
8.91
2.96
850
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
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)

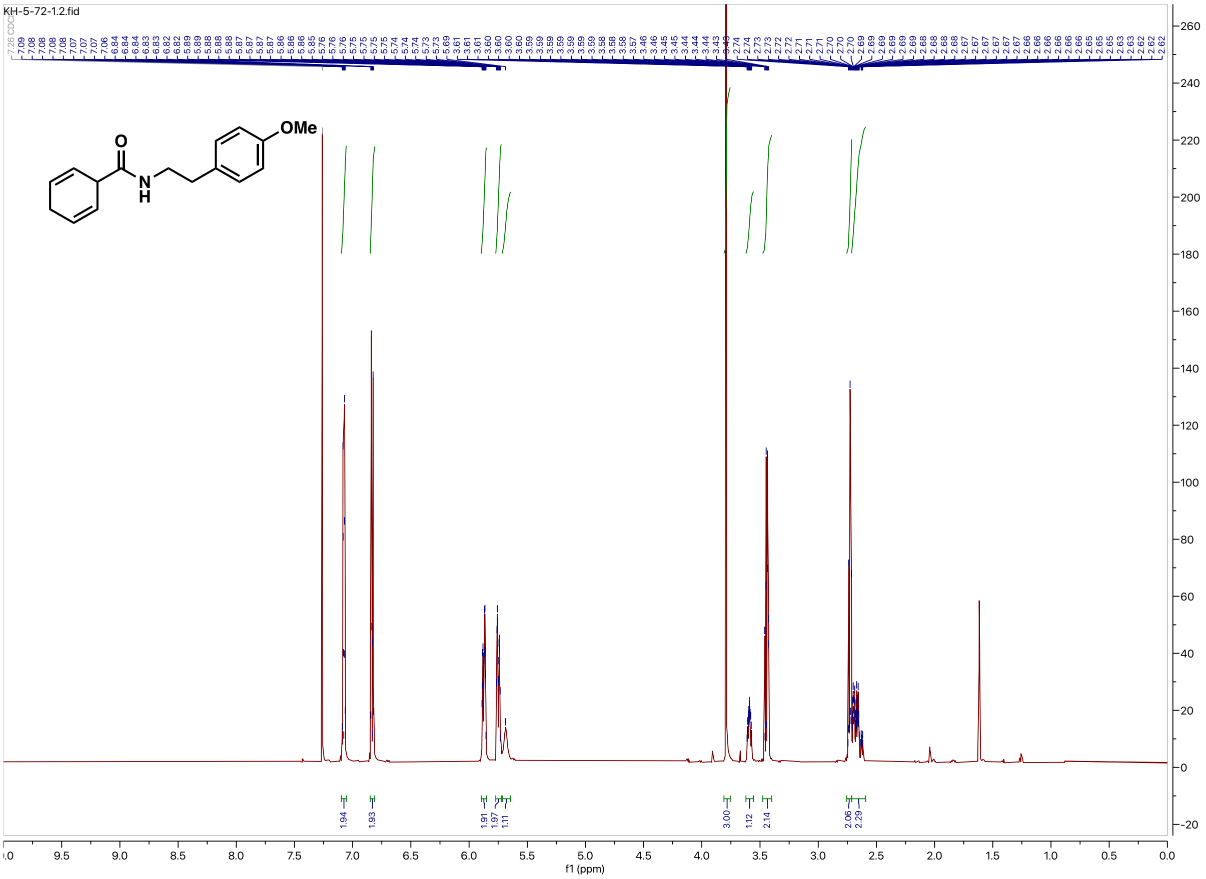

KH-5-60-1.2.fid
172.12
151.78
142.75
128.02
124.43
122.63
114.77
81.38
61.42
60.55
32.87
28.38
14.34
O
N
OEt
Boc
450
400
350
300
250
200
150
100
50
0
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

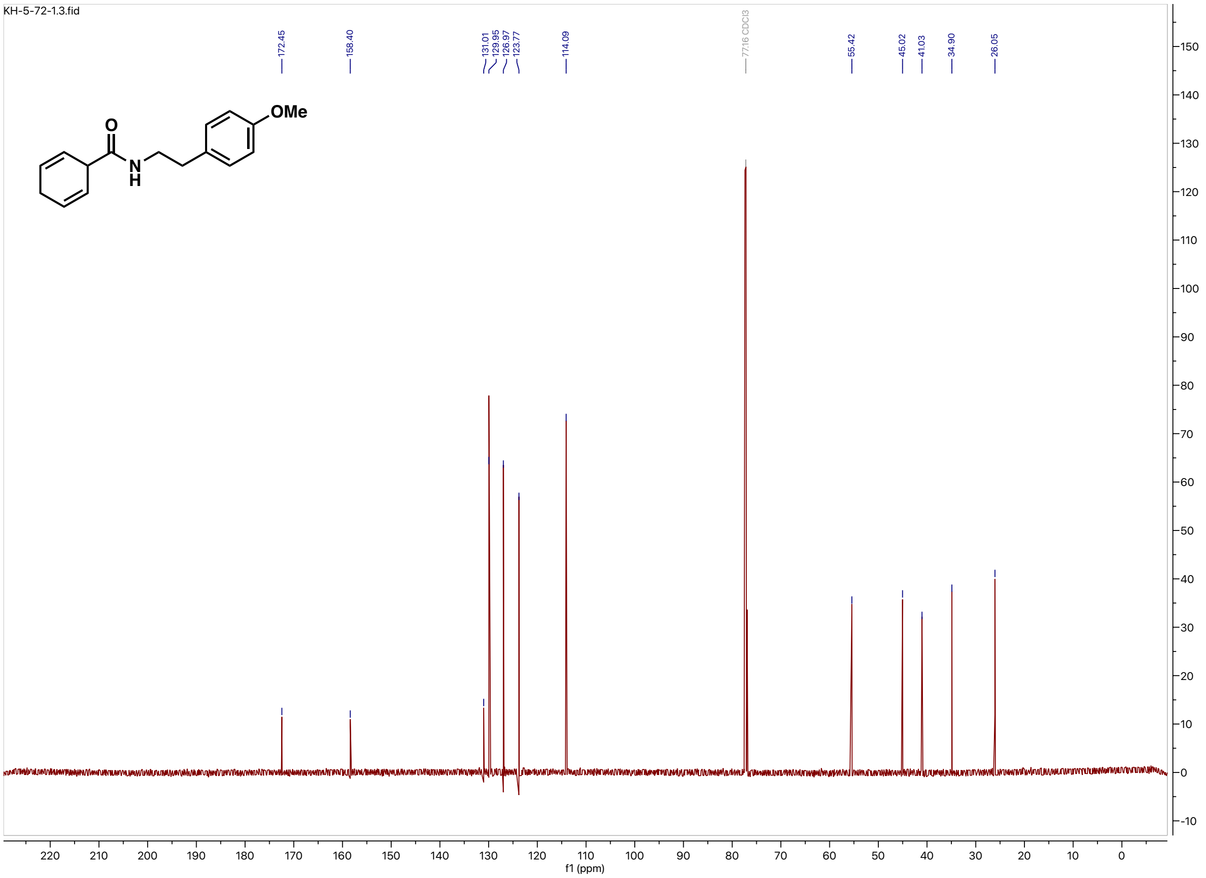
Compound 17


KH-5-83-1.1.fid
7.26 CDCl3
1.92
1.06
1.85
1.92
1.94
1.14
1.04
2.00
2.02
2.40
O
N
H
f1 (ppm)
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
450 400 350 300 250 200 150 100 50 0

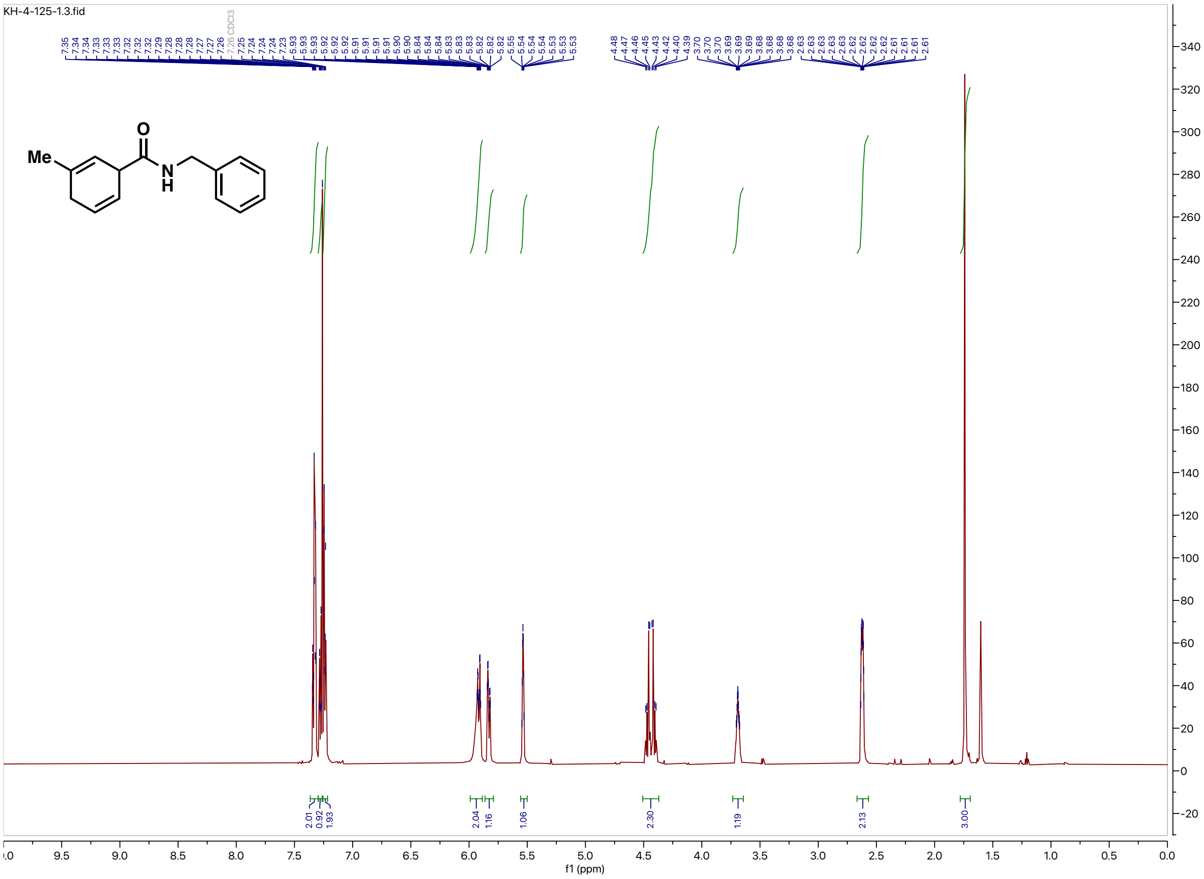

KH-5-83-1.2.fid
172.47
139.00
129.02
128.69
126.99
126.63
123.74
77.16 CDCl3
45.02
40.82
35.80
26.03
O
N
H
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
100
90
80
70
60
50
40
30
20
10
0
-10

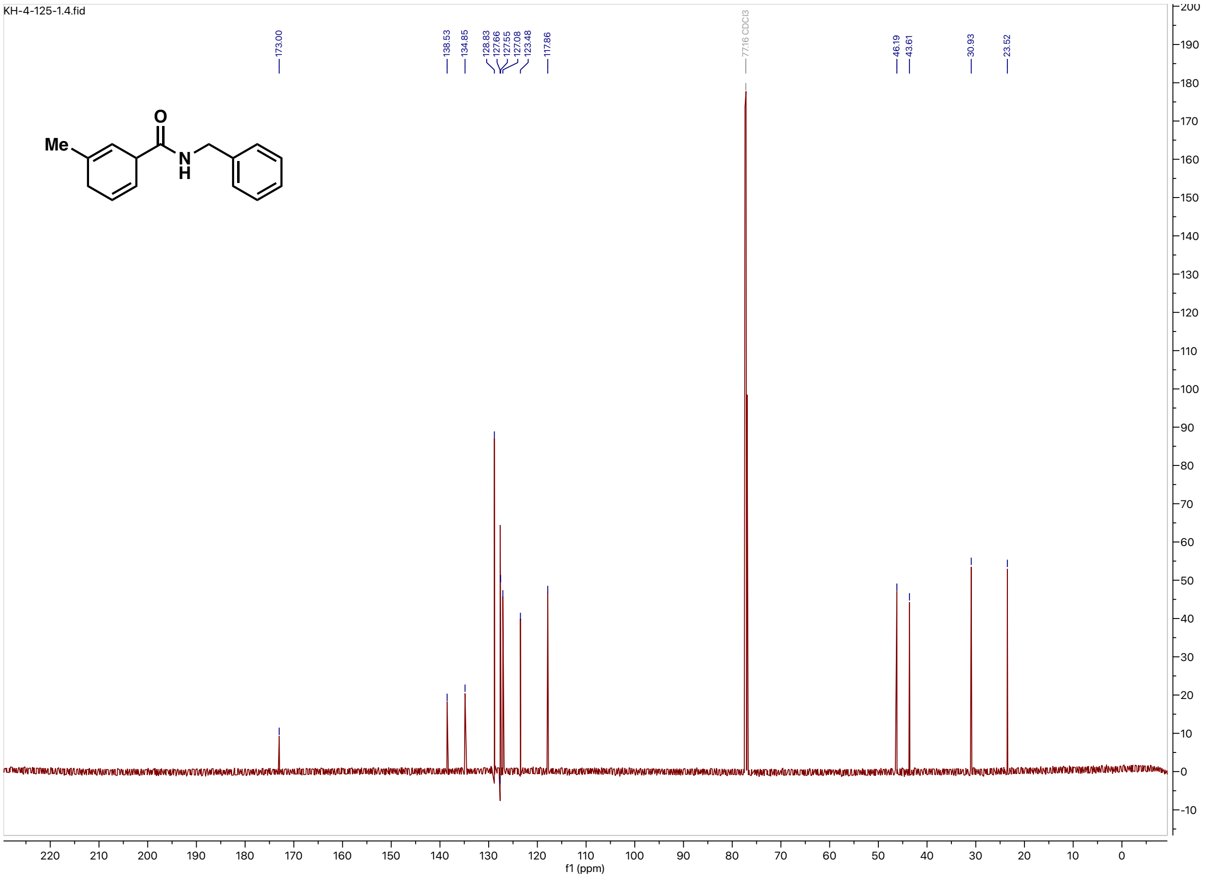
Compound 18


KH-5-72-1.2.fid
7.26 CDCl3
7.09 7.08 7.08 7.08 7.07 7.07 7.07 7.06 6.84 6.84 6.84 6.83 6.83 6.82 6.82 5.89 5.89 5.88 5.88 5.88 5.87 5.87 5.87 5.86 5.86 5.86 5.85 5.76 5.76 5.75 5.75 5.75 5.75 5.74 5.74 5.74 5.73 5.73 5.69 3.61 3.61 3.61 3.60 3.60 3.60 3.60 3.59 3.59 3.59 3.59 3.59 3.59 3.58 3.58 3.58 3.57 3.46 3.45 3.45 3.44 3.44 3.44 3.43 3.43 2.74 2.74 2.73 2.73 2.72 2.72 2.71 2.71 2.70 2.70 2.70 2.69 2.69 2.69 2.69 2.69 2.69 2.69 2.68 2.68 2.68 2.67 2.67 2.67 2.67 2.67 2.66 2.66 2.66 2.66 2.66 2.65 2.65 2.63 2.63 2.62 2.62 2.62
O
N
H
OMe
1.94
1.93
1.91
1.97
1.11
3.00
1.12
2.14
2.06
2.29
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
f1 (ppm)
260 240 220 200 180 160 140 120 100 80 60 40 20 0 -20

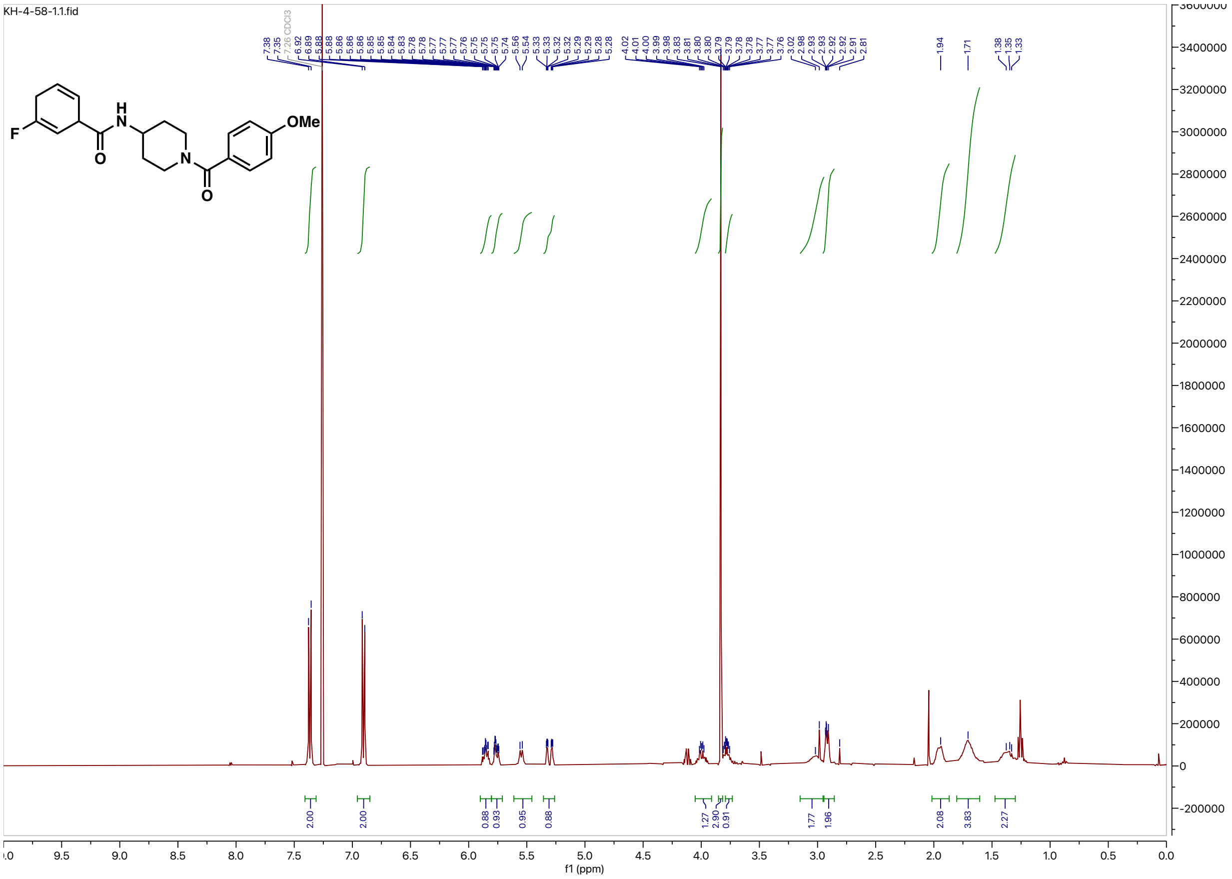

KH-5-72-1.3.fid
172.45
158.40
131.01
129.95
126.97
123.77
114.09
77.16 CDCl3
55.42
45.02
41.03
34.90
26.05
O
N
H
OMe
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

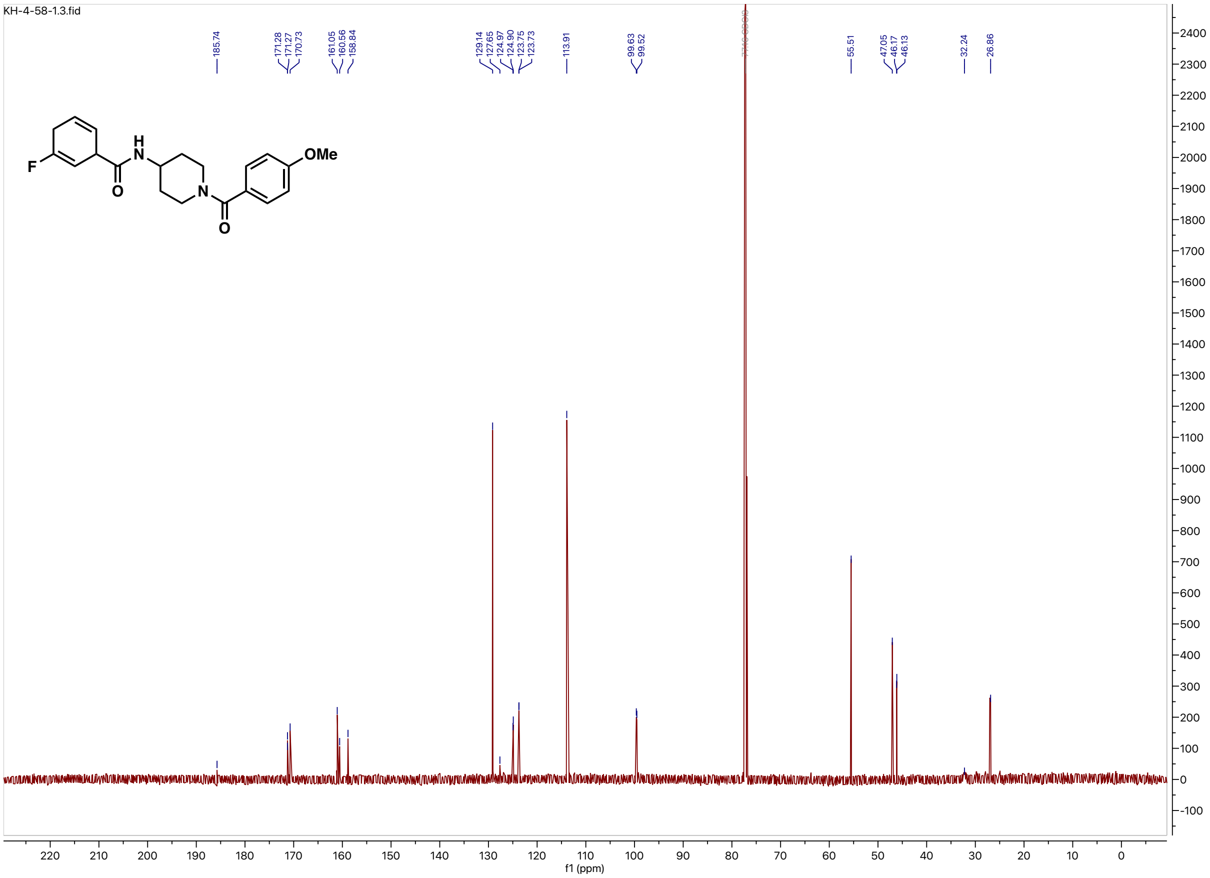
Compound 19

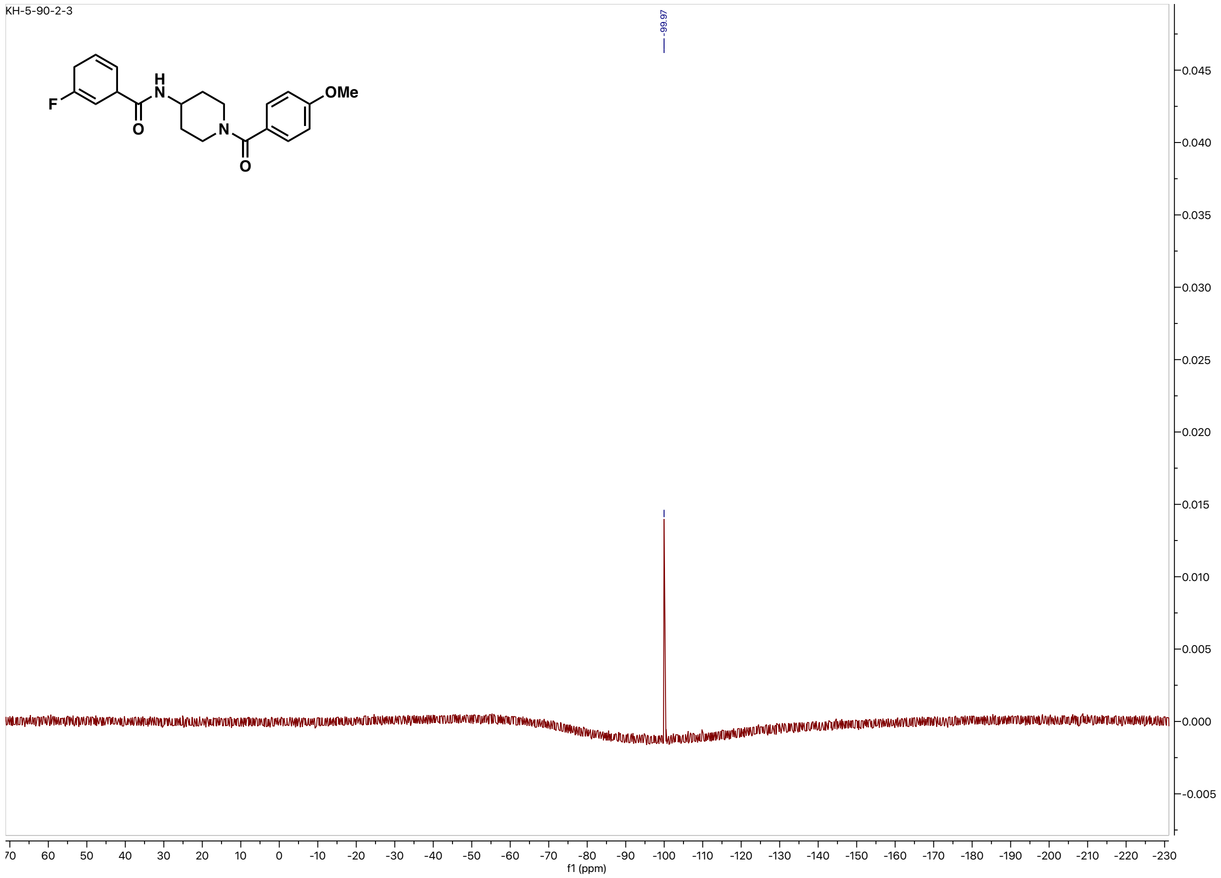

KH-4-125-1.3.fid
7.35 7.34 7.34 7.33 7.33 7.32 7.32 7.32 7.29 7.28 7.28 7.28 7.27 7.27 7.26 CDCl3 7.25 7.24 7.24 7.23 7.23 5.93 5.93 5.93 5.92 5.92 5.92 5.91 5.91 5.91 5.90 5.90 5.84 5.84 5.84 5.83 5.83 5.83 5.82 5.82 5.82 5.55 5.54 5.54 5.54 5.53 5.53 5.53
4.48 4.47 4.46 4.45 4.43 4.42 4.40 4.39 3.70 3.70 3.69 3.69 3.69 3.68 3.68 3.68 2.63 2.63 2.63 2.63 2.62 2.62 2.62 2.62 2.61 2.61 2.61 2.61
Me
O
N
H
2.01
0.92
1.93
2.04
1.16
1.06
2.30
1.19
2.13
3.00
f1 (ppm)


KH-4-125-1.4.fid
173.00
138.53
134.85
128.83
127.66
127.55
127.08
123.48
117.86
77.16 CDCl3
46.19
43.61
30.93
23.52
Me
O
N
H
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)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

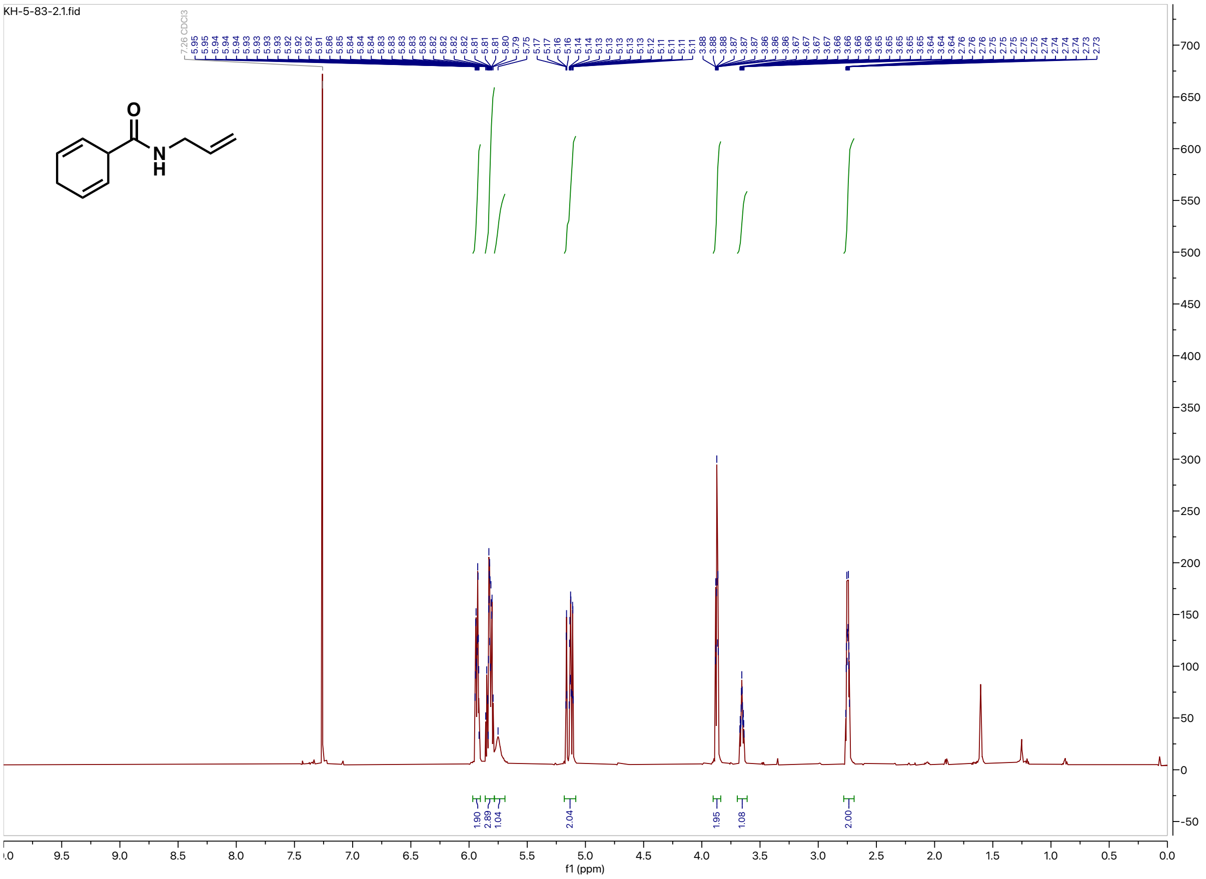
Compound 20

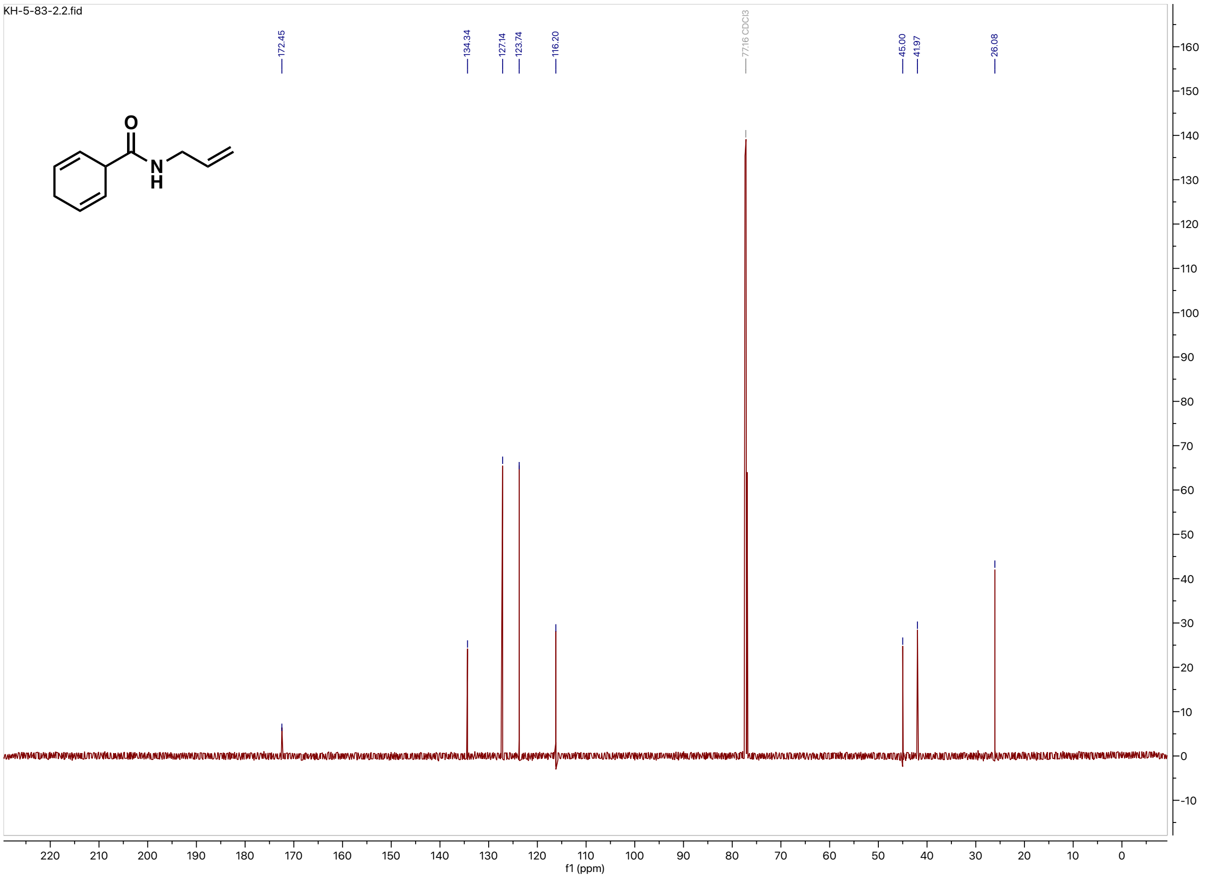



KH-4-58-1.3.fid
185.74
171.28
171.27
170.73
161.05
160.56
158.84
129.14
127.65
124.97
124.90
123.75
123.73
113.91
99.63
99.52
55.51
47.05
46.17
46.13
32.24
26.86
F
H
N
O
N
O
OMe
2400
2300
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

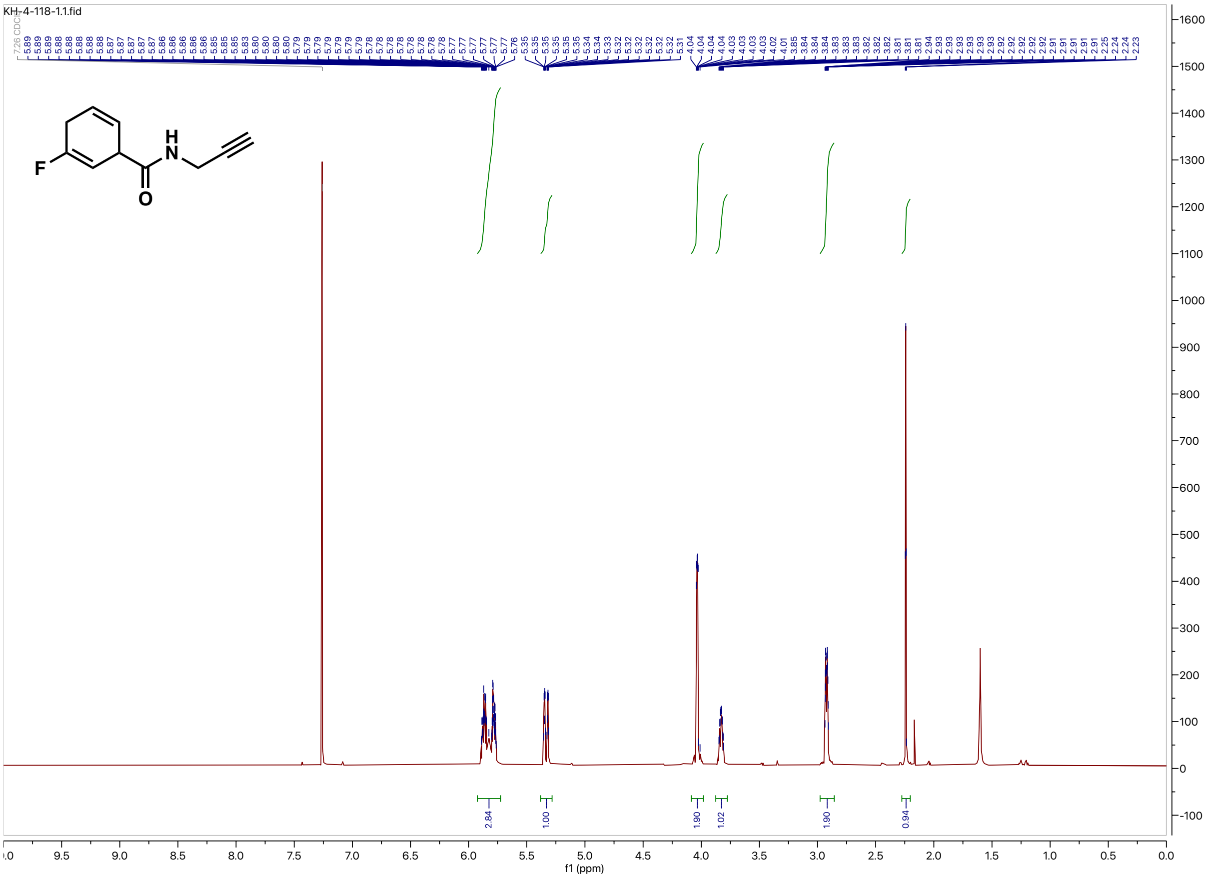

KH-5-90-2-3
-99.97
F
H
N
O
N
O
OMe
0.045
0.040
0.035
0.030
0.025
0.020
0.015
0.010
0.005
0.000
-0.005
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230
f1 (ppm)

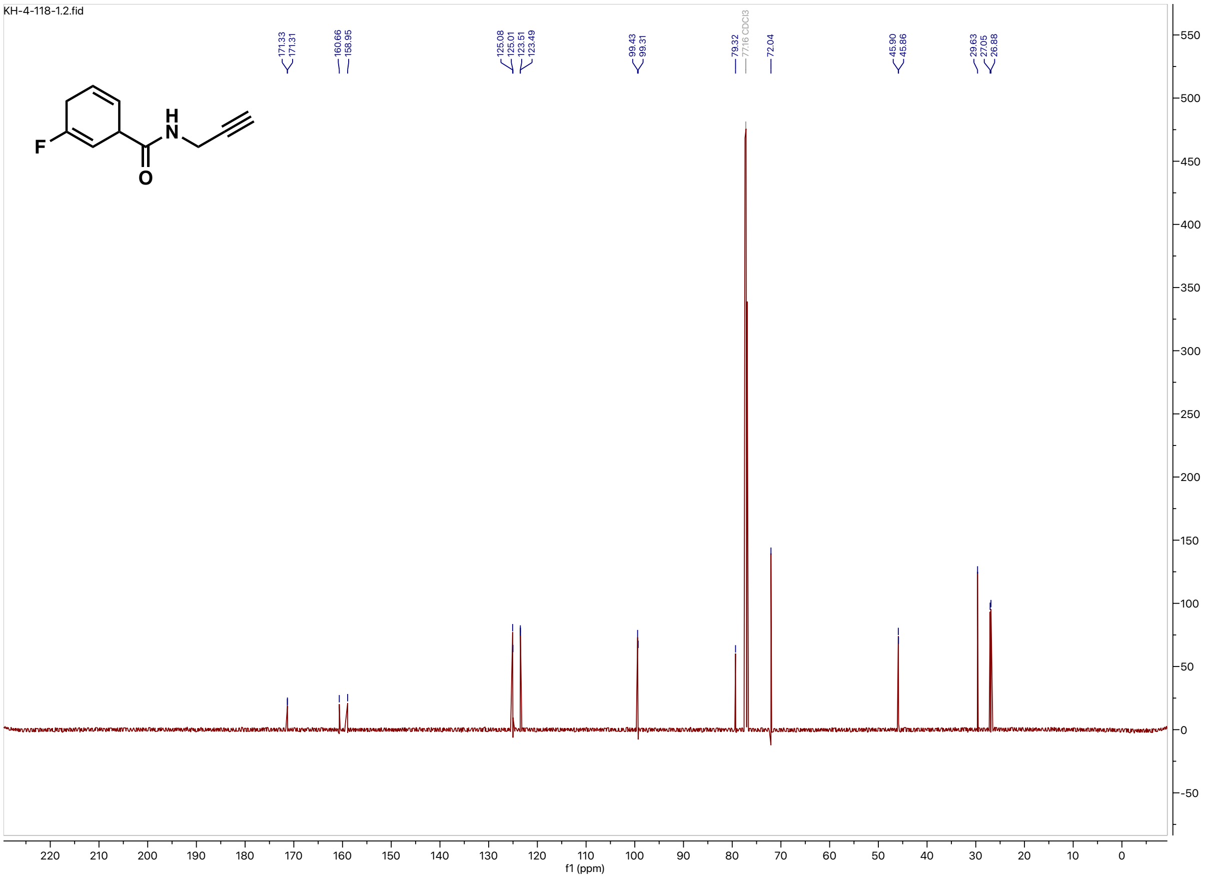
Compound 21

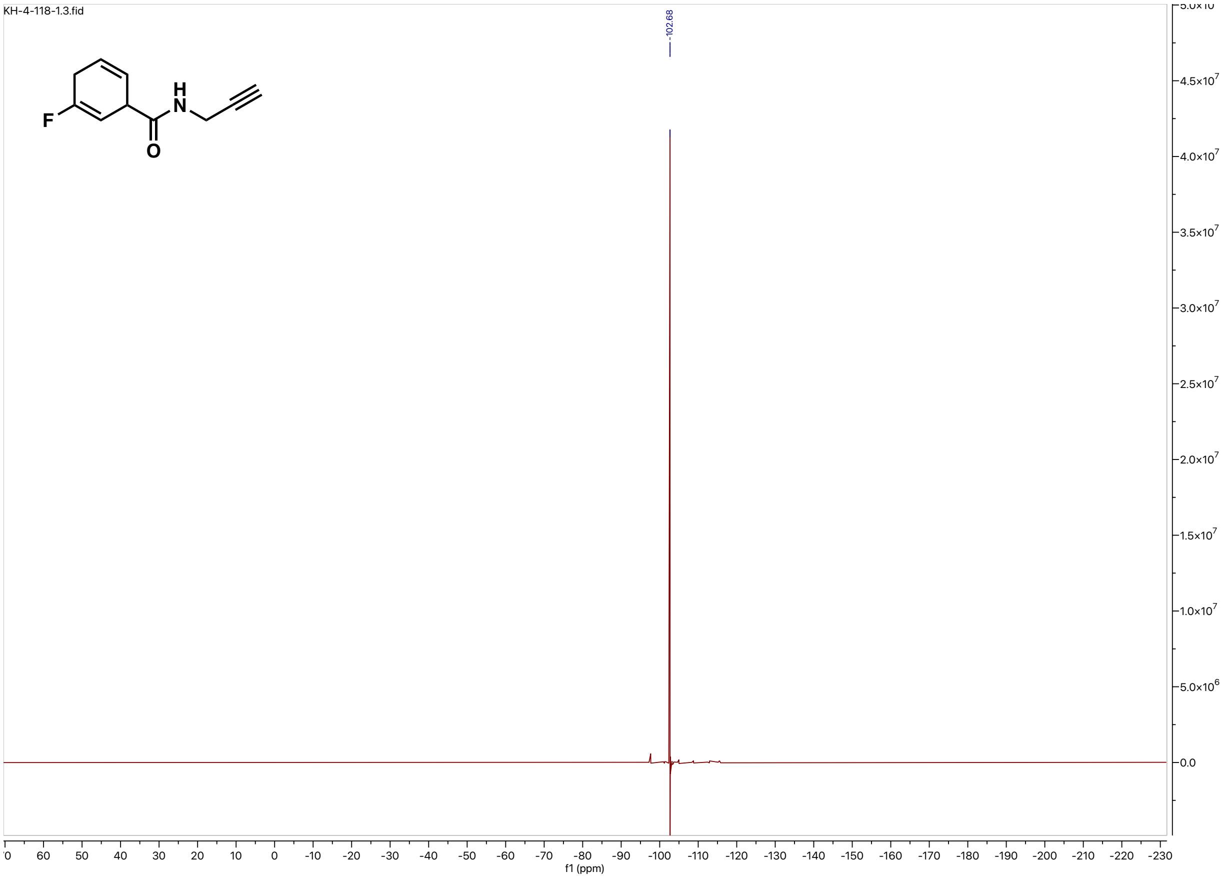

KH-5-83-2.1.fid
7.26 CDCl3
5.95 5.95 5.94 5.94 5.94 5.93 5.93 5.93 5.92 5.92 5.92 5.91 5.86 5.85 5.84 5.84 5.84 5.83 5.83 5.83 5.83 5.82 5.82 5.82 5.81 5.81 5.81 5.80 5.79 5.75
5.17 5.17 5.16 5.16 5.14 5.14 5.13 5.13 5.13 5.13 5.12 5.11 5.11 5.11 5.11
3.88 3.88 3.88 3.87 3.87 3.86 3.86 3.67 3.67 3.67 3.67 3.66 3.66 3.66 3.65 3.65 3.65 3.65 3.64 3.64
2.76 2.76 2.75 2.75 2.75 2.75 2.74 2.74 2.74 2.73 2.73
O
N
H
1.90
2.89
1.04
2.04
1.95
1.08
2.00
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
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
f1 (ppm)


KH-5-83-2.2.fid
172.45
134.34
127.14
123.74
116.20
77.16 CDCl3
45.00
41.97
26.08
O
N
H
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
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)

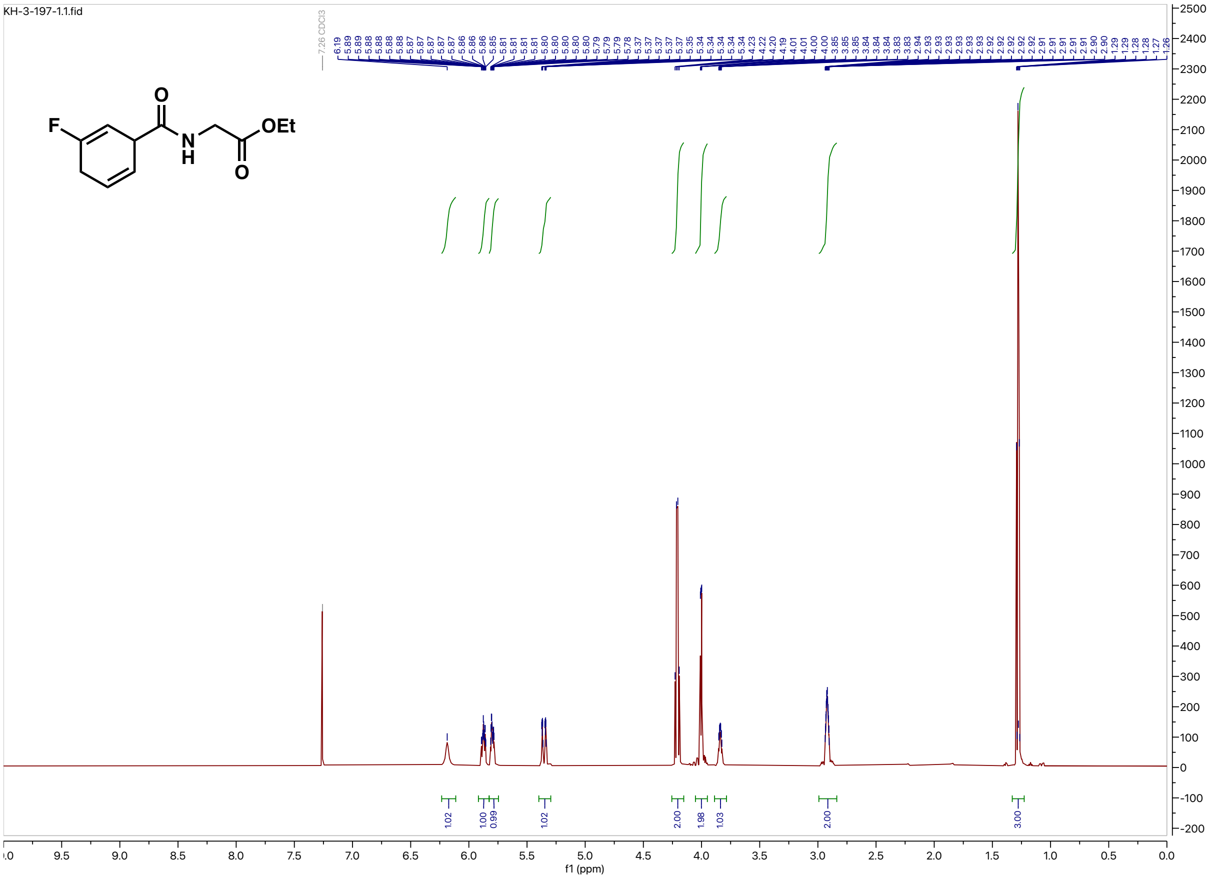
Compound 22

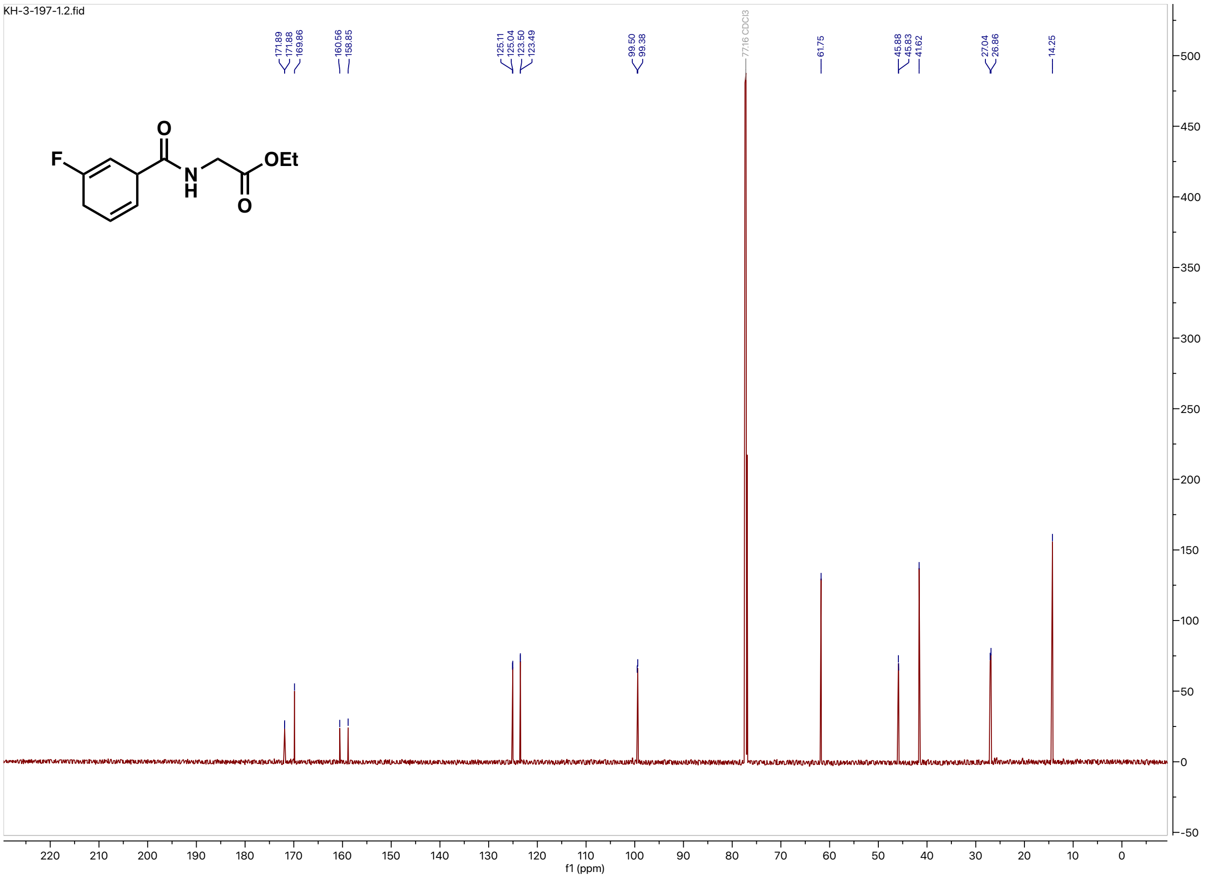


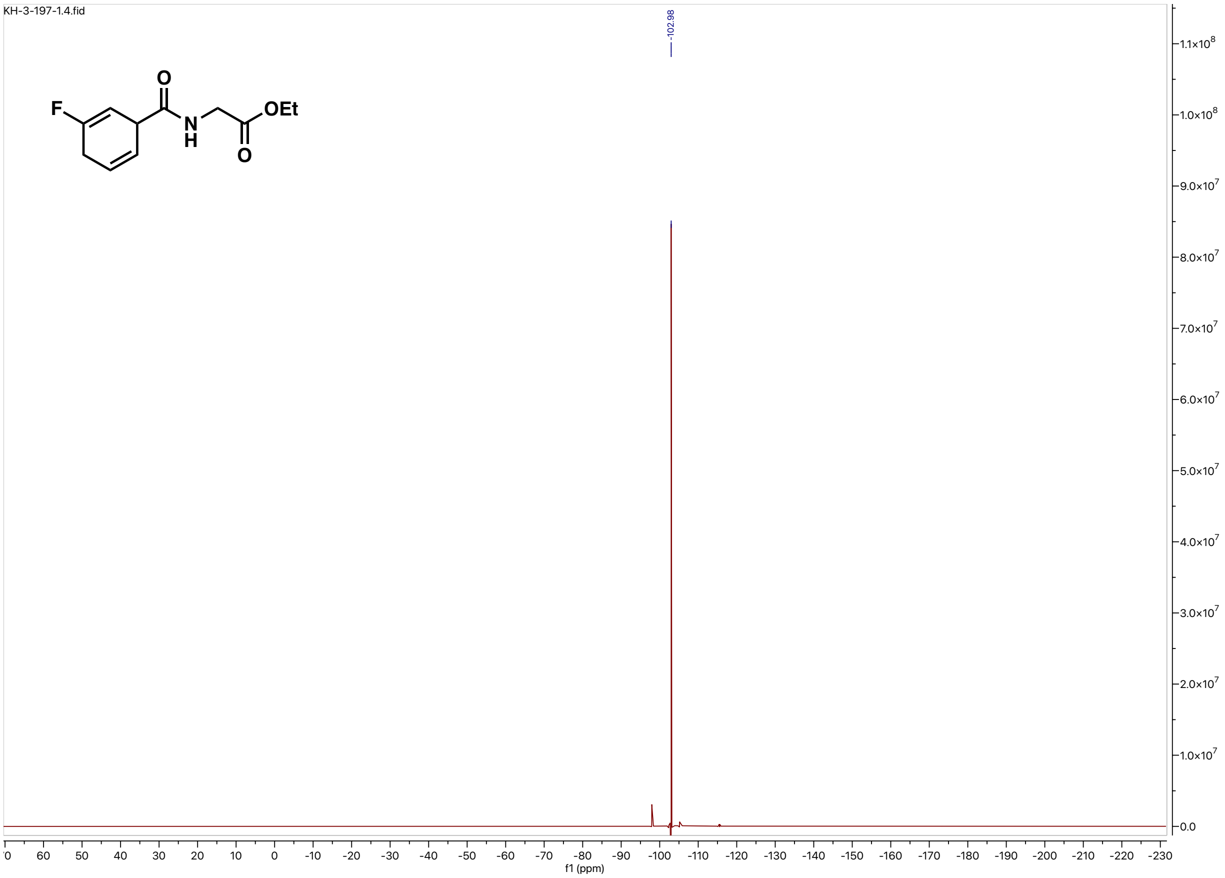

KH-4-118-1.2.fid
171.33
171.31
160.66
158.95
125.08
125.01
123.51
123.49
99.43
99.31
79.32
77.16 CDCl3
72.04
45.90
45.86
29.63
27.05
26.88
F
H
N
O
550
500
450
400
350
300
250
200
150
100
50
0
-50
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


KH-4-118-1.3.fid
F
H
N
O
-102.68
5.0×10
4.5×10^7
4.0×10^7
3.5×10^7
3.0×10^7
2.5×10^7
2.0×10^7
1.5×10^7
1.0×10^7
5.0×10^6
0.0
0 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230
f1 (ppm)

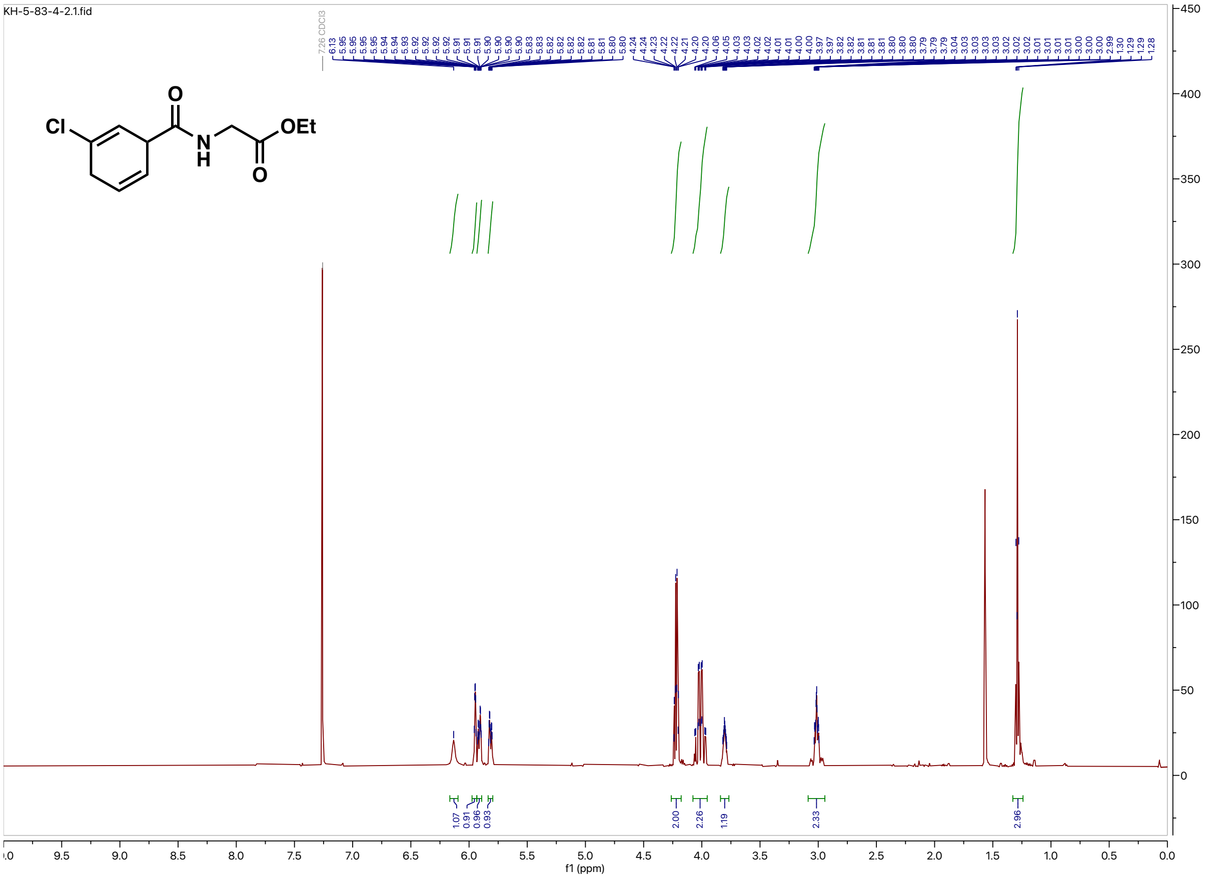
Compound 23

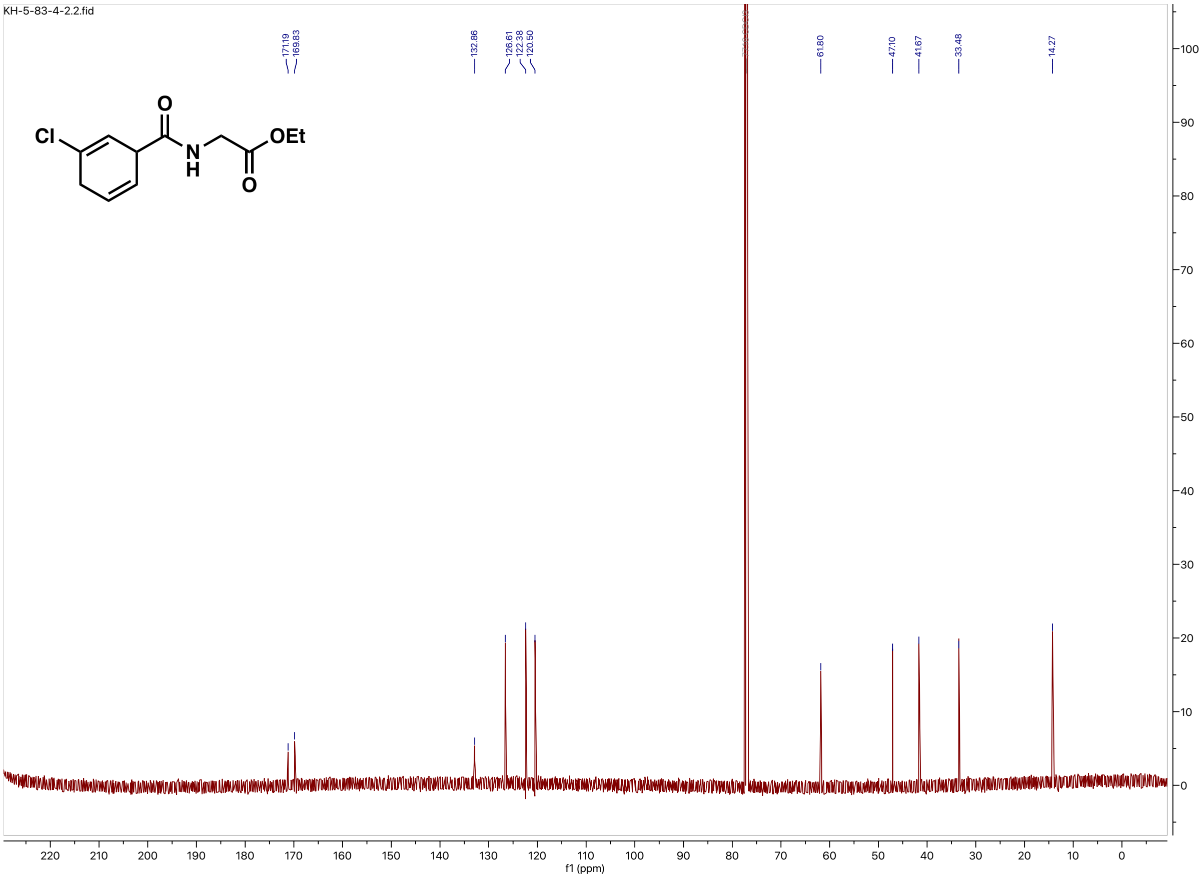

KH-3-197-1.1.fid
F
O
N
H
OEt
O
7.26 CDCl3
6.19 5.89 5.89 5.88 5.88 5.88 5.88 5.87 5.87 5.87 5.87 5.86 5.86 5.86 5.85 5.81 5.81 5.81 5.81 5.80 5.80 5.80 5.80 5.80 5.79 5.79 5.79 5.78 5.37 5.37 5.37 5.37 5.37 5.35 5.34 5.34 5.34 5.34 5.34 4.23 4.22 4.20 4.19 4.01 4.01 4.00 4.00 3.85 3.85 3.85 3.84 3.84 3.84 3.83 3.83 2.94 2.93 2.93 2.93 2.93 2.93 2.93 2.92 2.92 2.92 2.92 2.92 2.91 2.91 2.91 2.91 2.91 2.90 2.90 1.29 1.29 1.28 1.28 1.27 1.26
1.02
1.00
0.99
1.02
2.00
1.98
1.03
2.00
3.00
f1 (ppm)
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
2500 2400 2300 2200 2100 2000 1900 1800 1700 1600 1500 1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0 -100 -200


KH-3-197-1.2.fid
171.89
171.88
169.86
160.56
158.85
125.11
125.04
123.50
123.49
99.50
99.38
77.16 CDCl3
61.75
45.88
45.83
41.62
27.04
26.86
14.25
F
O
N
H
OEt
O
500
450
400
350
300
250
200
150
100
50
0
-50
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)

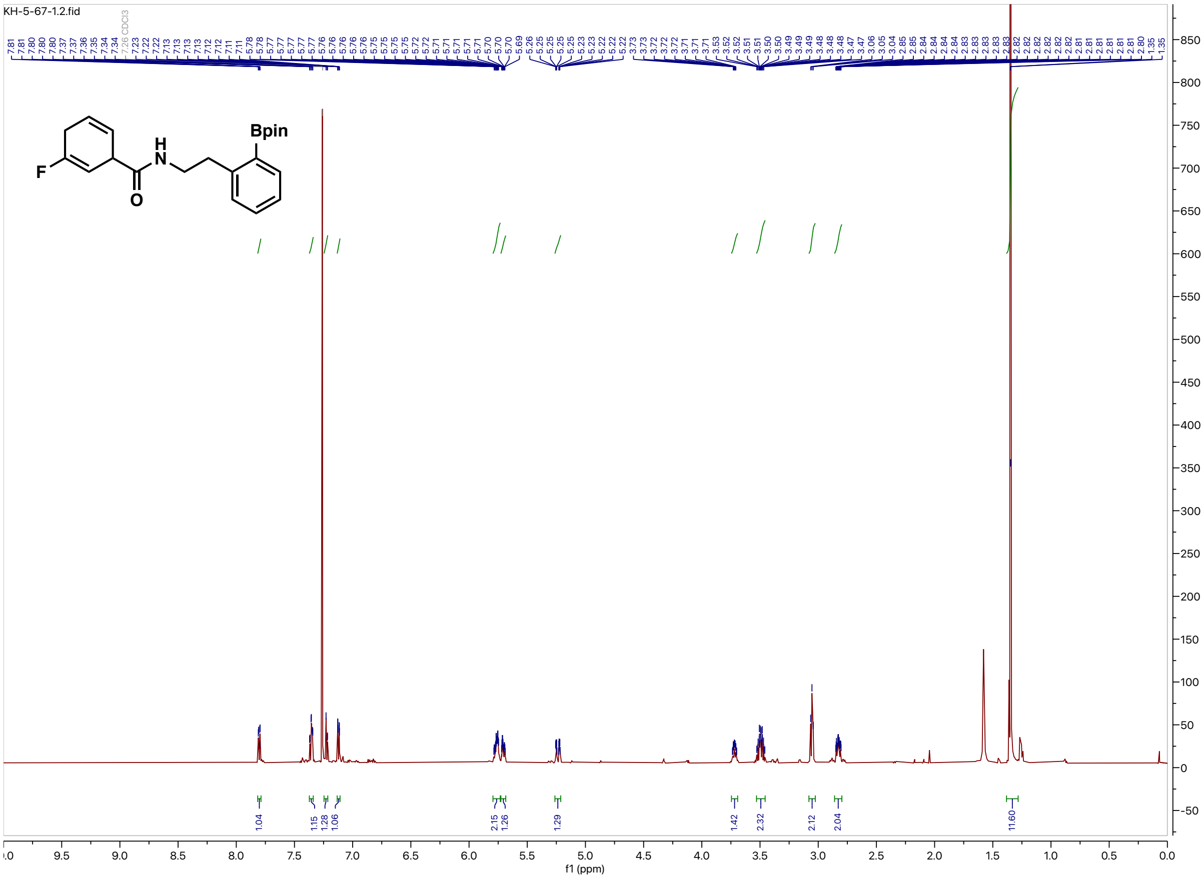

KH-3-197-1.4.fid
-102.98
F
O
N
H
OEt
O
1.1×10^8
1.0×10^8
9.0×10^7
8.0×10^7
7.0×10^7
6.0×10^7
5.0×10^7
4.0×10^7
3.0×10^7
2.0×10^7
1.0×10^7
0.0
0 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230
f1 (ppm)

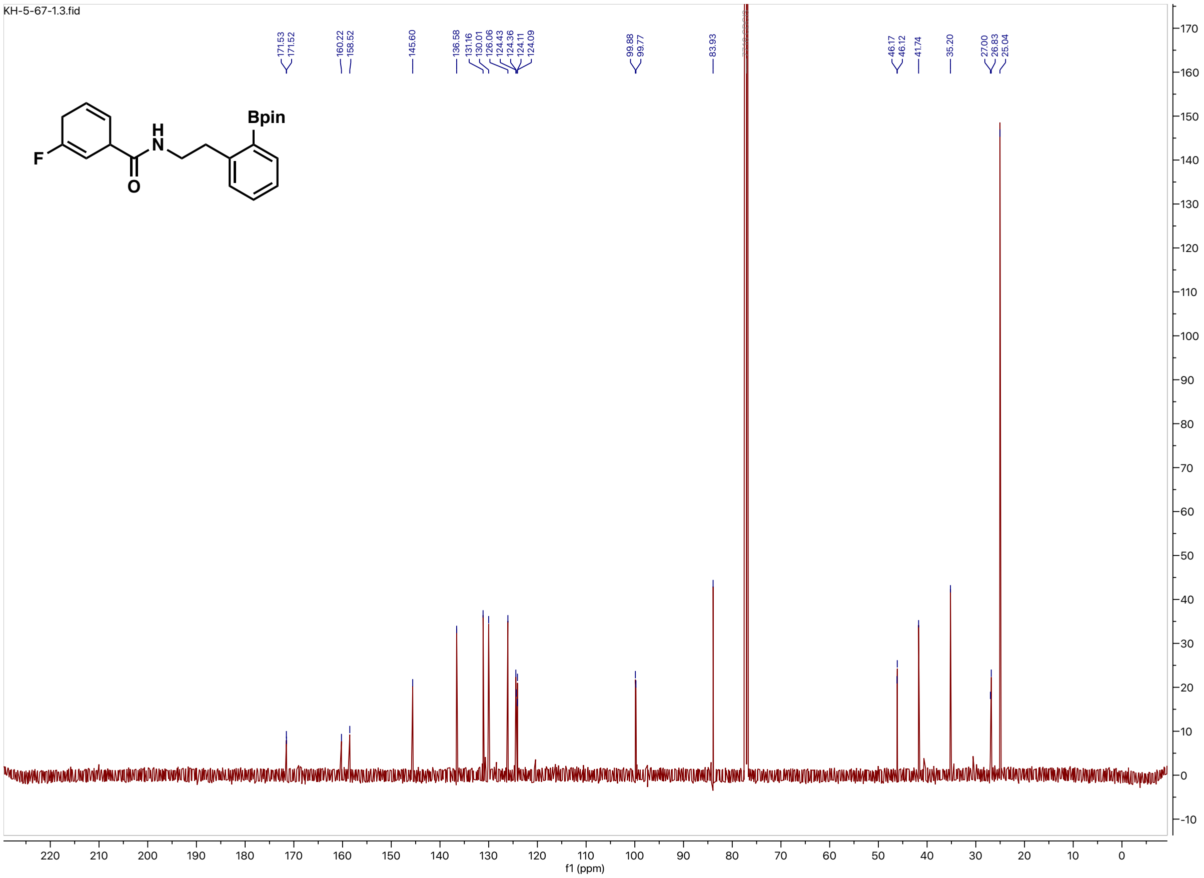
Compound 24

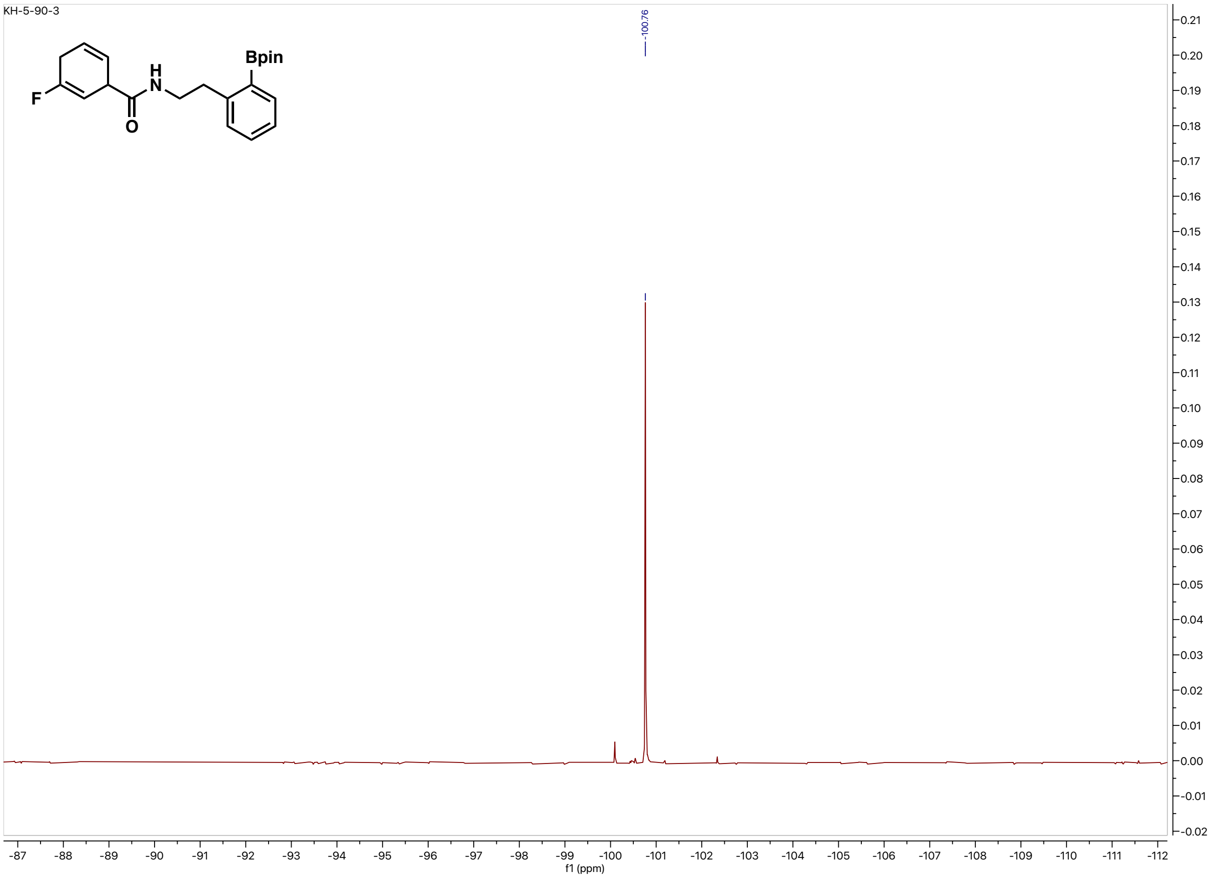

KH-5-83-4-2.1.fid
7.26 CDCl3
6.13
5.95
5.95
5.95
5.95
5.94
5.94
5.93
5.92
5.92
5.92
5.92
5.91
5.91
5.91
5.90
5.90
5.90
5.90
5.83
5.83
5.82
5.82
5.82
5.82
5.81
5.81
5.80
5.80
4.24
4.24
4.23
4.22
4.22
4.21
4.20
4.20
4.06
4.05
4.03
4.03
4.02
4.02
4.01
4.01
4.00
4.00
3.97
3.97
3.82
3.82
3.81
3.81
3.81
3.80
3.80
3.80
3.79
3.79
3.79
3.04
3.03
3.03
3.03
3.03
3.02
3.02
3.02
3.01
3.01
3.01
3.01
3.00
3.00
3.00
2.99
1.30
1.29
1.29
1.28
Cl
O
N
H
OEt
O
1.07
0.91
0.96
0.93
2.00
2.26
1.19
2.33
2.96
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
f1 (ppm)
450
400
350
300
250
200
150
100
50
0


KH-5-83-4-2.2.fid
171.19
169.83
132.86
126.61
122.38
120.50
61.80
47.10
41.67
33.48
14.27
Cl
O
N
H
OEt
O
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)
100
90
80
70
60
50
40
30
20
10
0

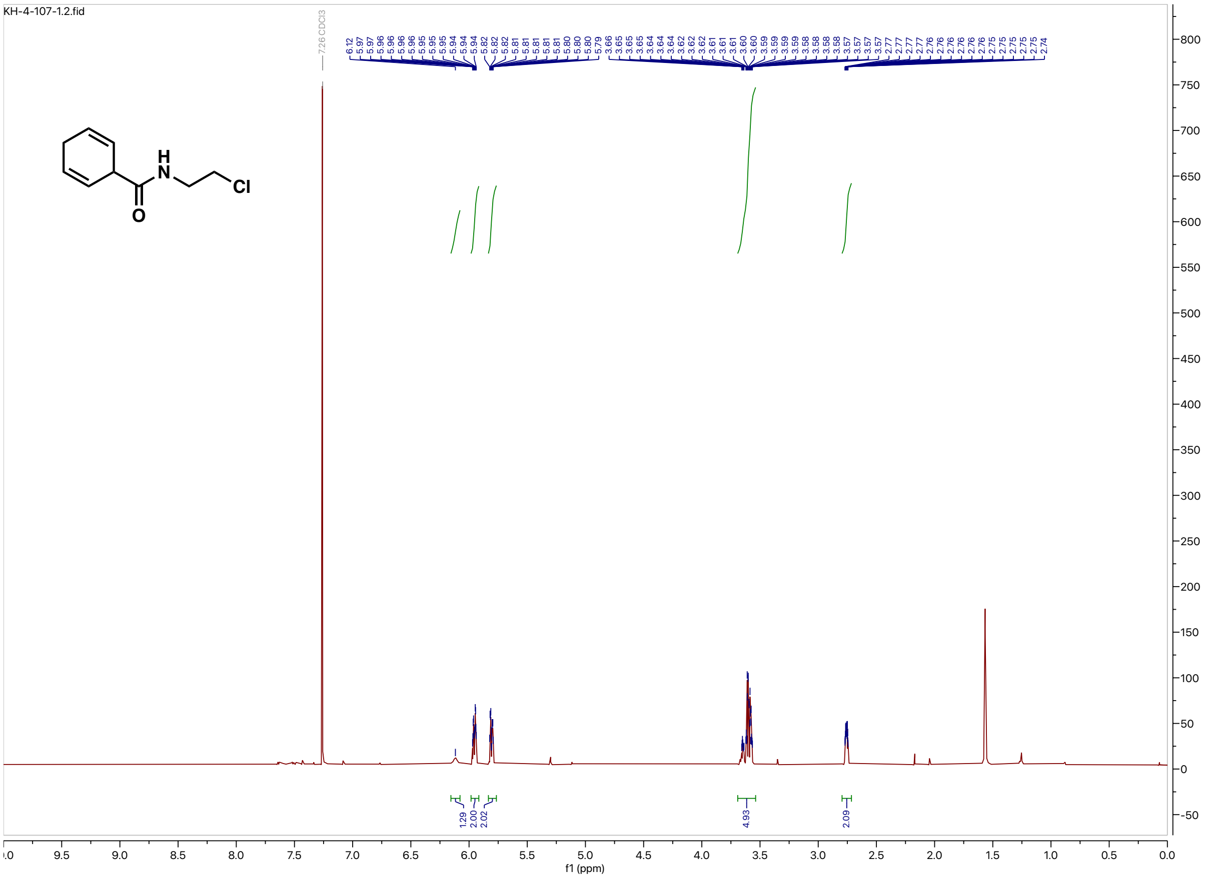
Compound 25

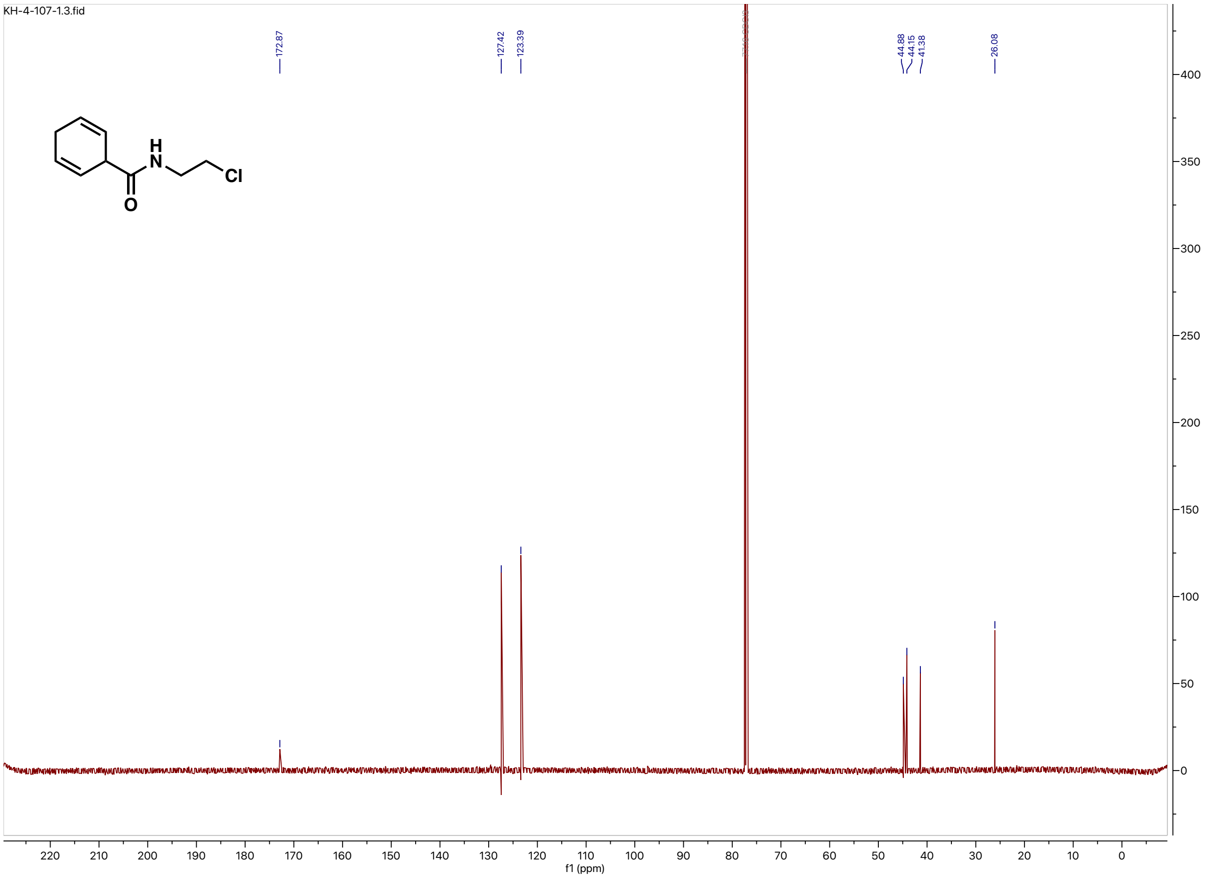

KH-5-67-1.2.fid
7.81 7.81 7.80 7.80 7.37 7.37 7.36 7.35 7.34 7.34 7.26 CDCl3 7.23 7.22 7.22 7.13 7.13 7.13 7.13 7.12 7.12 7.11 7.11 5.78 5.78 5.77 5.77 5.77 5.77 5.76 5.76 5.76 5.76 5.75 5.75 5.75 5.72 5.72 5.72 5.71 5.71 5.71 5.71 5.70 5.70 5.70 5.69 5.26 5.25 5.25 5.25 5.23 5.23 5.22 5.22 5.22 3.73 3.73 3.72 3.72 3.72 3.71 3.71 3.53 3.52 3.52 3.51 3.51 3.50 3.50 3.49 3.49 3.48 3.48 3.48 3.47 3.47 3.06 3.05 3.04 2.85 2.85 2.84 2.84 2.84 2.84 2.83 2.83 2.83 2.83 2.82 2.82 2.82 2.82 2.81 2.81 2.81 2.81 2.80 1.35 1.35
Bpin
F
H
N
O
1.04
1.15
1.28
1.06
2.15
1.26
1.29
1.42
2.32
2.12
2.04
11.60
850
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
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
f1 (ppm)


KH-5-67-1.3.fid
171.53
171.52
160.22
158.52
145.60
136.58
131.16
130.01
126.06
124.43
124.36
124.11
124.09
99.88
99.77
83.93
46.17
46.12
41.74
35.20
27.00
26.83
25.04
F
H
N
O
Bpin
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
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)

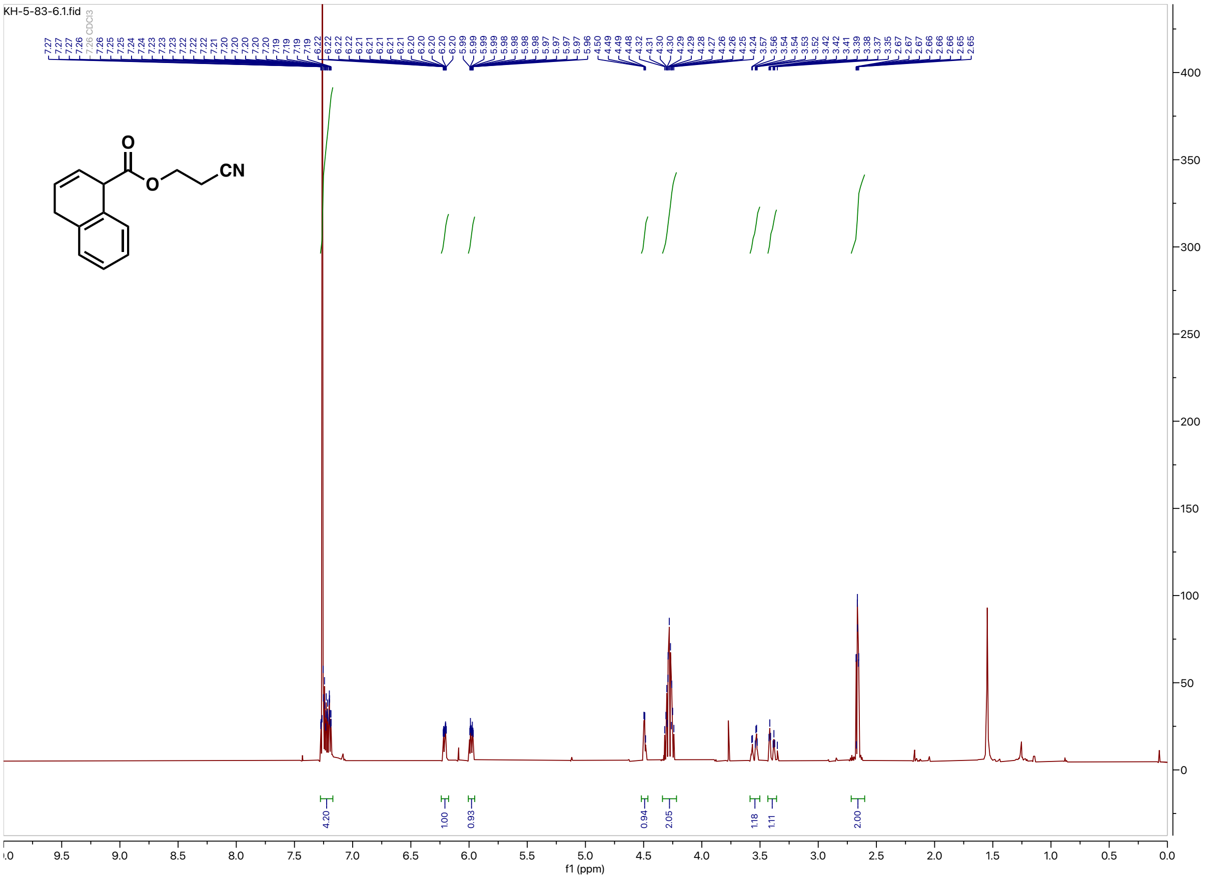

KH-5-90-3
-100.76
F
H
N
O
Bpin
0.21
0.20
0.19
0.18
0.17
0.16
0.15
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
-0.01
-0.02
-87
-88
-89
-90
-91
-92
-93
-94
-95
-96
-97
-98
-99
-100
-101
-102
-103
-104
-105
-106
-107
-108
-109
-110
-111
-112
f1 (ppm)

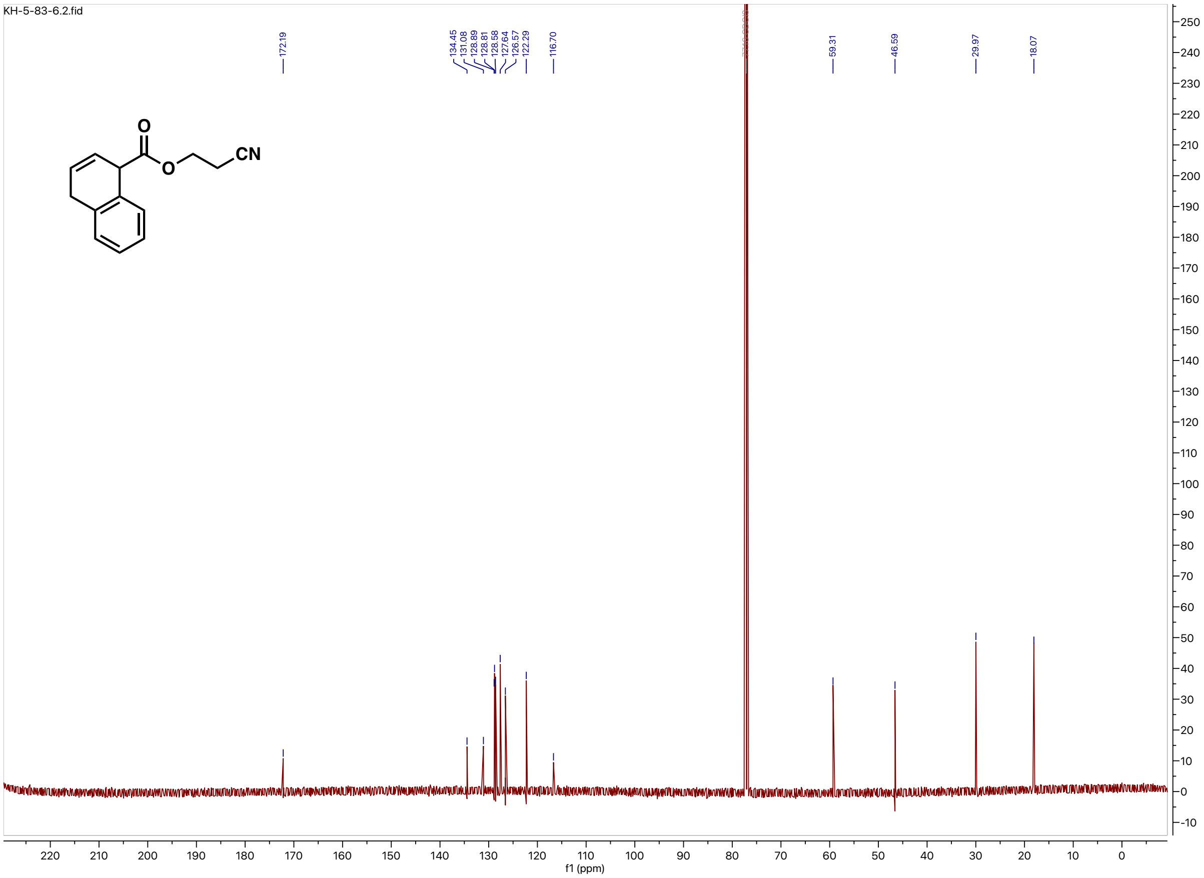
Compound 26


KH-4-107-1.2.fid
7.26 CDCl3
6.12 5.97 5.97 5.96 5.96 5.96 5.96 5.95 5.95 5.95 5.94 5.94 5.94 5.82 5.82 5.82 5.81 5.81 5.81 5.81 5.80 5.80 5.79
3.66 3.65 3.65 3.64 3.64 3.62 3.62 3.62 3.61 3.61 3.60 3.60 3.60 3.59 3.59 3.59 3.58 3.58 3.58 3.58 3.57 3.57 3.57 3.57
2.77 2.77 2.77 2.76 2.76 2.76 2.76 2.76 2.75 2.75 2.75 2.75 2.74
H
N
Cl
O
1.29
2.00
2.02
4.93
2.09
f1 (ppm)
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
800 750 700 650 600 550 500 450 400 350 300 250 200 150 100 50 0 -50

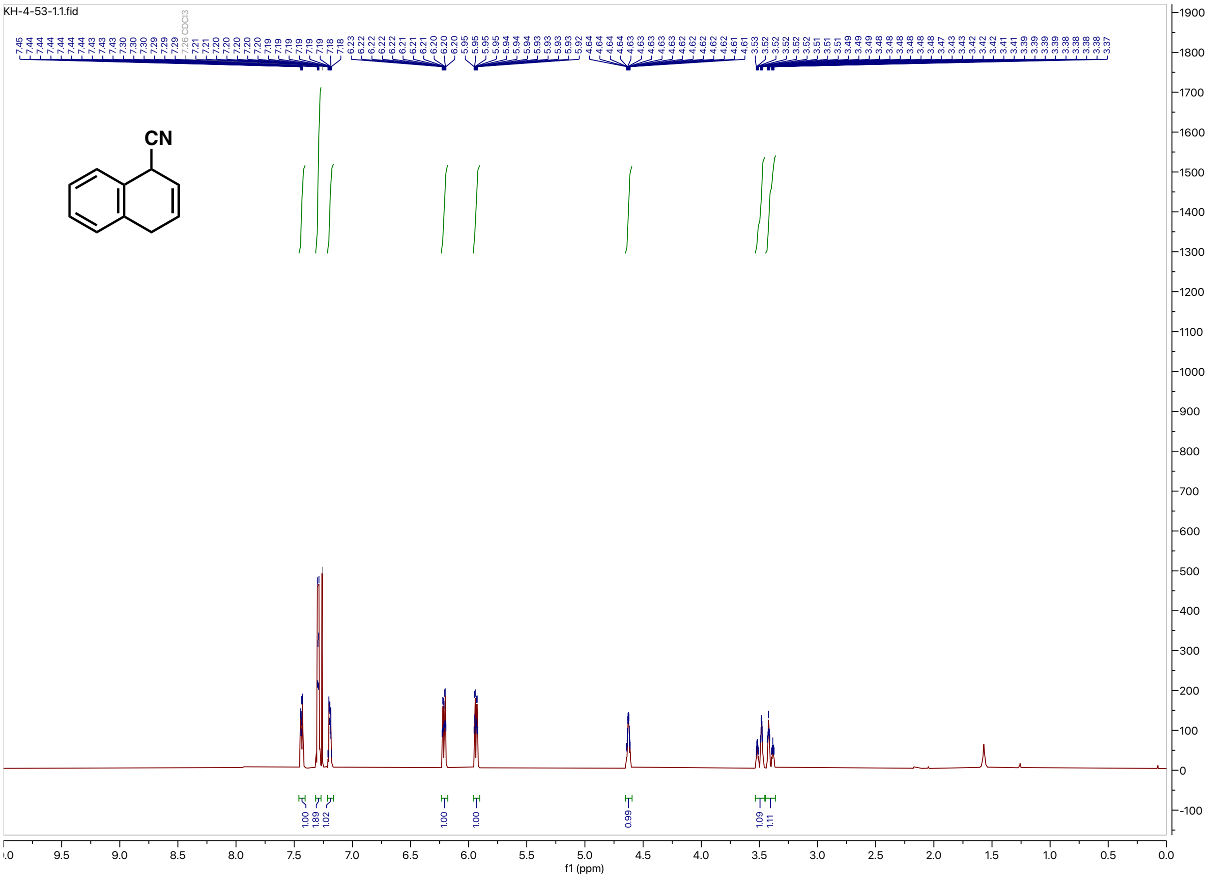

KH-4-107-1.3.fid
172.87
127.42
123.39
44.88
44.15
41.38
26.08
H
N
Cl
O
400
350
300
250
200
150
100
50
0
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Compound 27

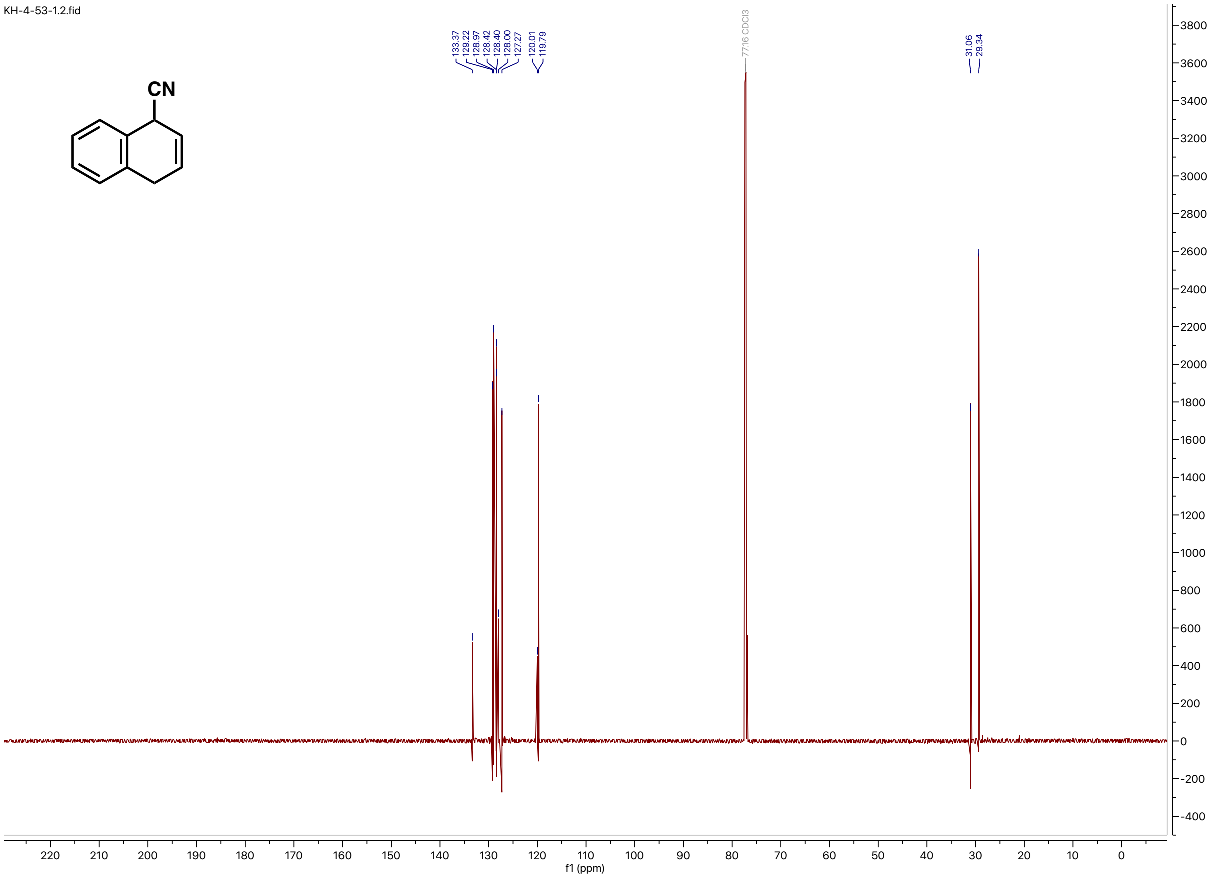

KH-5-83-6.1.fid
7.27 7.27 7.26 7.26 CDCl3 7.26 7.25 7.24 7.24 7.23 7.23 7.23 7.22 7.22 7.22 7.21 7.20 7.20 7.20 7.20 7.19 7.19 7.19 7.19 6.22 6.22 6.22 6.22 6.21 6.21 6.21 6.21 6.20 6.20 6.20 6.20 6.20 5.99 5.99 5.99 5.98 5.98 5.98 5.97 5.97 5.97 5.96 4.50 4.49 4.49 4.48 4.32 4.31 4.30 4.30 4.29 4.29 4.28 4.27 4.26 4.26 4.25 4.24 3.57 3.56 3.54 3.54 3.53 3.52 3.42 3.41 3.39 3.38 3.37 3.35 2.67 2.67 2.67 2.66 2.66 2.65 2.65
O
O
CN
4.20
1.00
0.93
0.94
2.05
1.18
1.11
2.00
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
f1 (ppm)
400
350
300
250
200
150
100
50
0


KH-5-83-6.2.fid
172.19
134.45
131.08
128.89
128.81
128.58
127.64
126.57
122.29
116.70
59.31
46.59
29.97
18.07
O
O
CN
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)
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

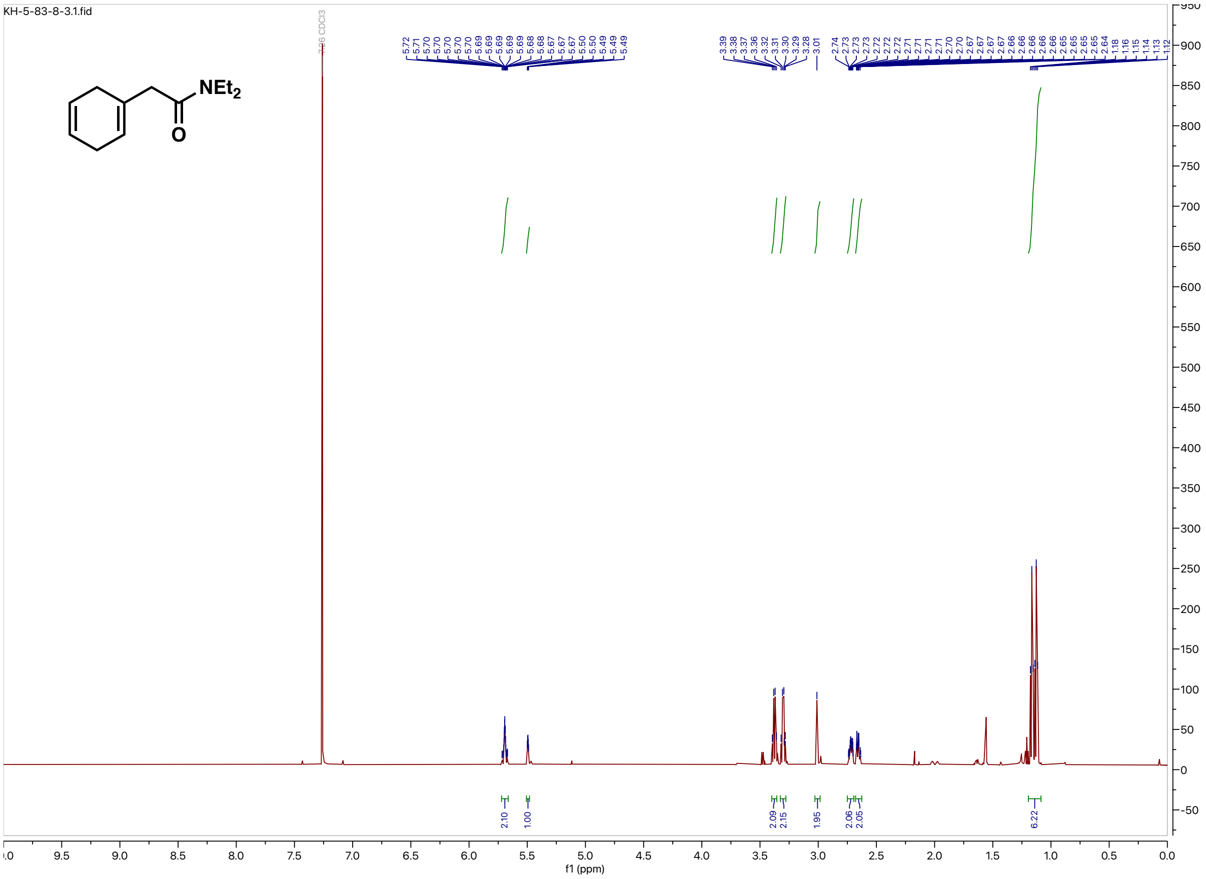
Compound 28

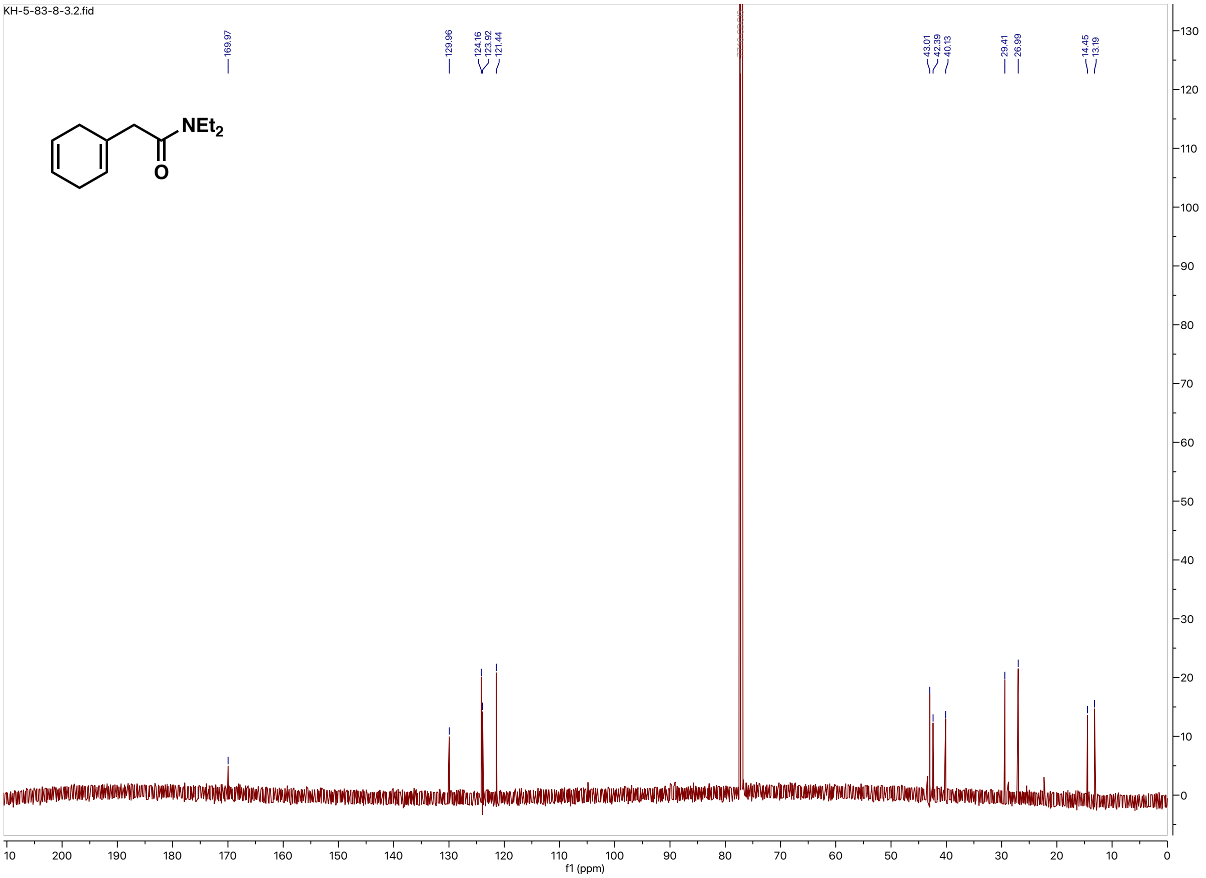


KH-4-53-1.1.fid
7.45 7.44 7.44 7.44 7.44 7.44 7.43 7.43 7.30 7.30 7.29 7.29 7.29
7.26 CDCl3
7.21 7.21 7.20 7.20 7.20 7.20 7.19 7.19 7.19 7.19 7.19 7.18 7.18
6.23 6.22 6.22 6.22 6.21 6.21 6.21 6.20 6.20
5.95 5.95 5.95 5.95 5.94 5.94 5.93 5.93 5.93 5.93 5.92
4.64 4.64 4.64 4.63 4.63 4.63 4.63 4.62 4.62 4.62 4.62 4.62 4.61 4.61
3.53 3.52 3.52 3.52 3.52 3.51 3.51 3.49 3.49 3.49 3.48 3.48 3.48 3.48 3.48 3.47 3.43 3.43 3.42 3.42 3.42 3.41 3.39 3.39 3.39 3.38 3.38 3.38 3.38 3.37
CN
1.00
1.89
1.02
1.00
1.00
0.99
1.09
1.11
1900 1800 1700 1600 1500 1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0 -100
.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
f1 (ppm)

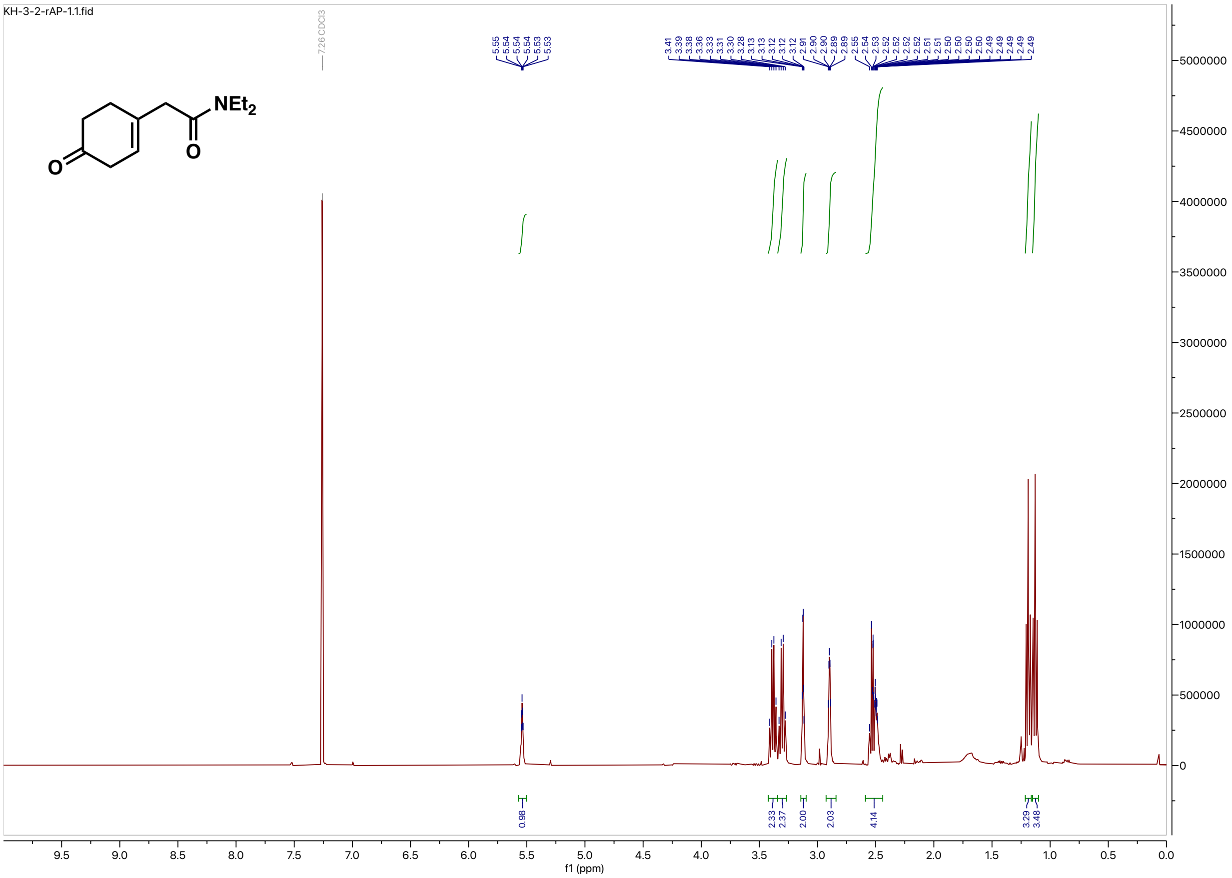

KH-4-53-1.2.fid
CN
133.37
129.22
128.97
128.42
128.40
128.00
127.27
120.01
119.79
77.16 CDCl3
31.06
29.34
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
-400
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

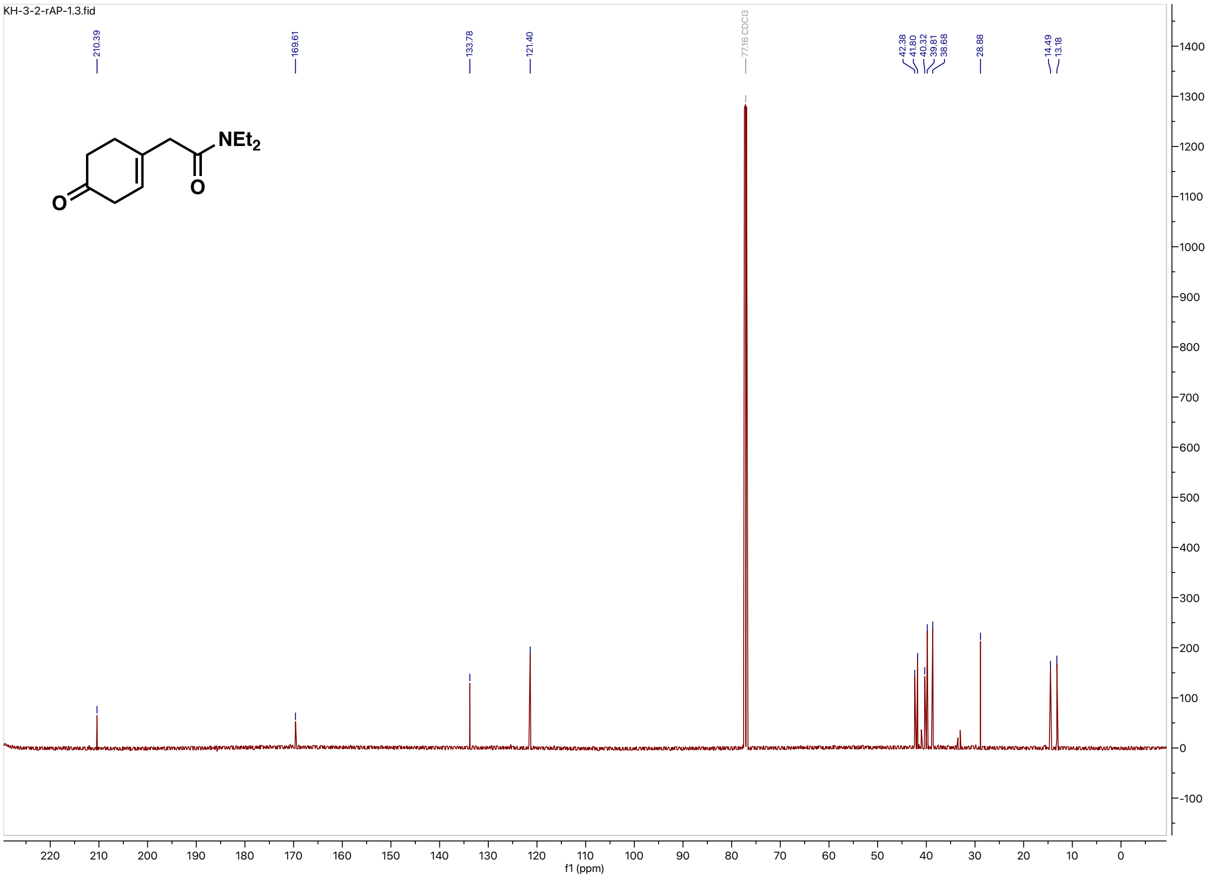
Compound 29


KH-5-83-8-3.1.fid
NEt$_2$
O
7.26 CDCl3
5.72 5.71 5.70 5.70 5.70 5.70 5.69 5.69 5.69 5.69 5.68 5.68 5.67 5.67 5.67 5.50 5.49 5.49 5.49
3.39 3.38 3.37 3.36 3.32 3.31 3.30 3.29 3.28 3.01
2.74 2.73 2.73 2.73 2.72 2.72 2.72 2.71 2.71 2.71 2.71 2.70 2.70 2.67 2.67 2.67 2.67 2.66 2.66 2.66 2.66 2.65 2.65 2.65 2.65 2.64 1.18 1.16 1.15 1.14 1.13 1.12
2.10
1.00
2.09
2.15
1.95
2.06
2.05
6.22
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
f1 (ppm)
950 900 850 800 750 700 650 600 550 500 450 400 350 300 250 200 150 100 50 0 -50

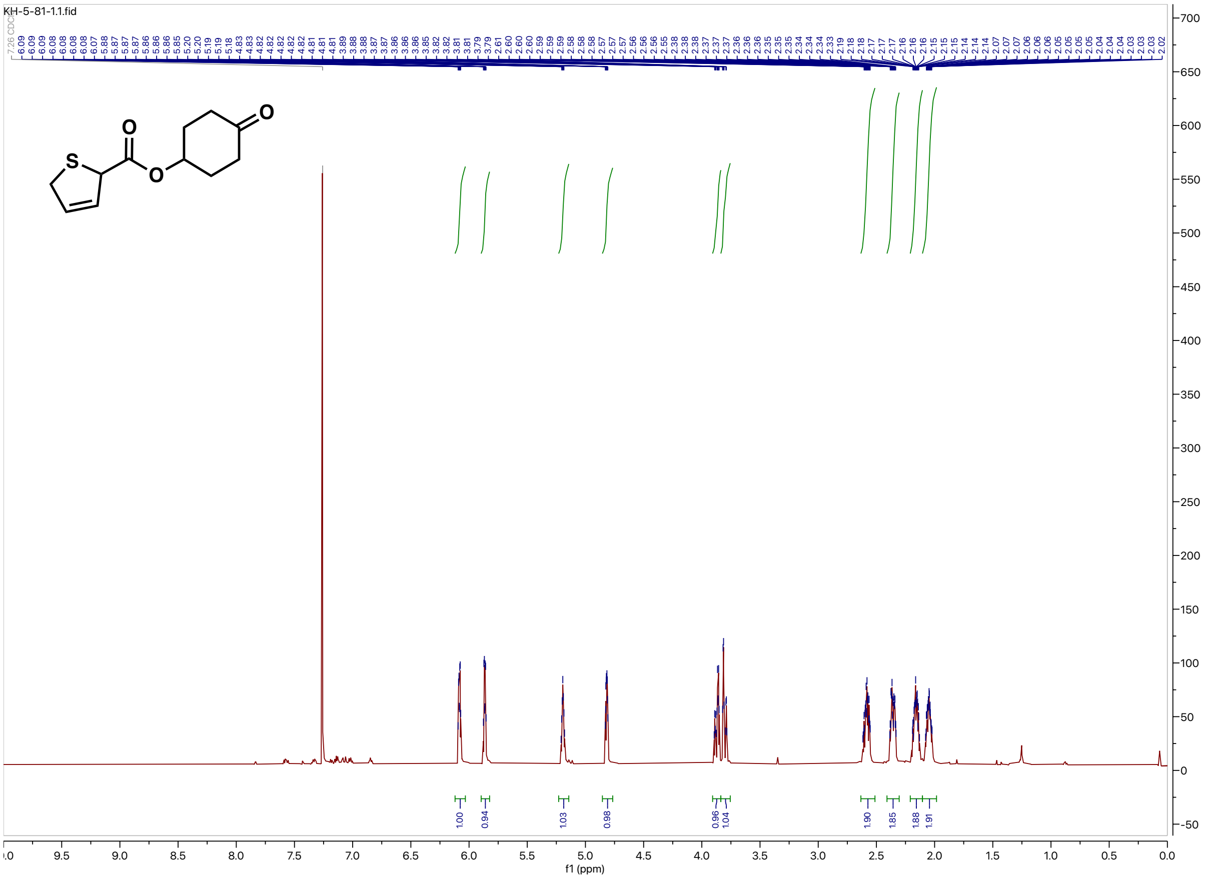

KH-5-83-8-3.2.fid
169.97
129.96
124.16
123.92
121.44
43.01
42.39
40.13
29.41
26.99
14.45
13.19
NEt2
O
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
130 120 110 100 90 80 70 60 50 40 30 20 10 0

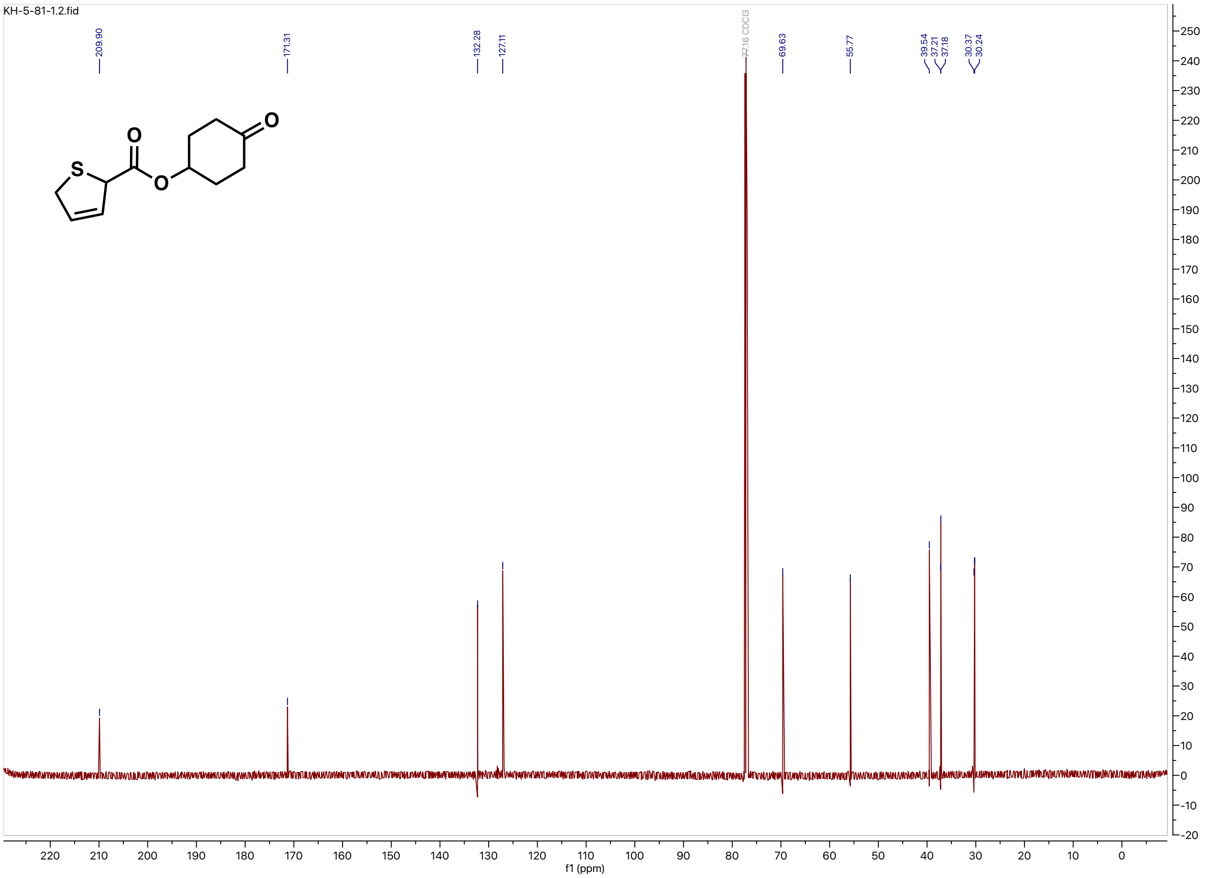
Compound 30


KH-3-2-rAP-1.1.fid
NEt2
O
O
7.26 CDCl3
5.55
5.54
5.54
5.54
5.53
5.53
3.41
3.39
3.38
3.36
3.33
3.31
3.30
3.28
3.13
3.13
3.12
3.12
3.12
2.91
2.90
2.90
2.89
2.89
2.55
2.54
2.53
2.52
2.52
2.52
2.52
2.51
2.51
2.50
2.50
2.50
2.50
2.49
2.49
2.49
2.49
2.49
0.98
2.33
2.37
2.00
2.03
4.14
3.29
3.48
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
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
f1 (ppm)

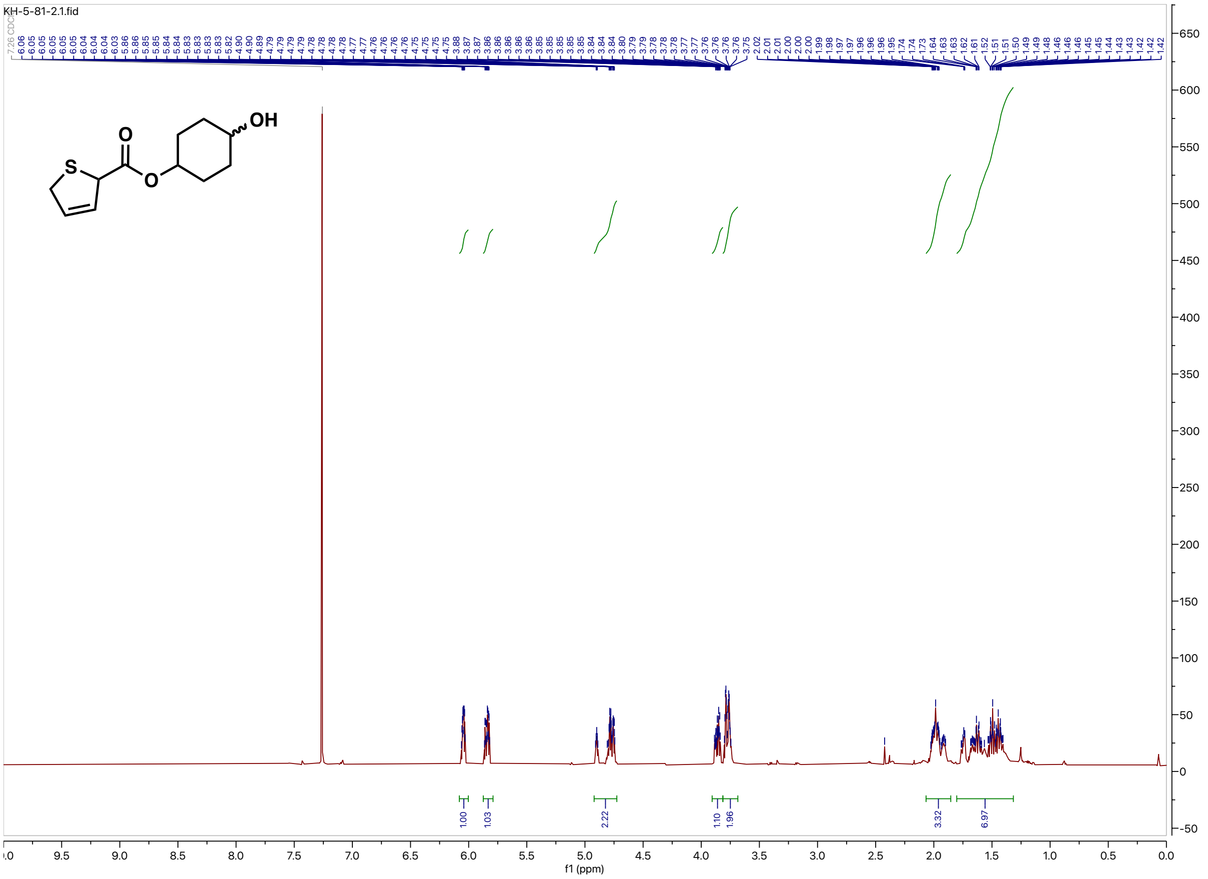

KH-3-2-rAP-1.3.fid
210.39
169.61
133.78
121.40
77.16 CDCl3
42.38
41.80
40.32
39.81
38.68
28.88
14.49
13.18
NEt2
O
O
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

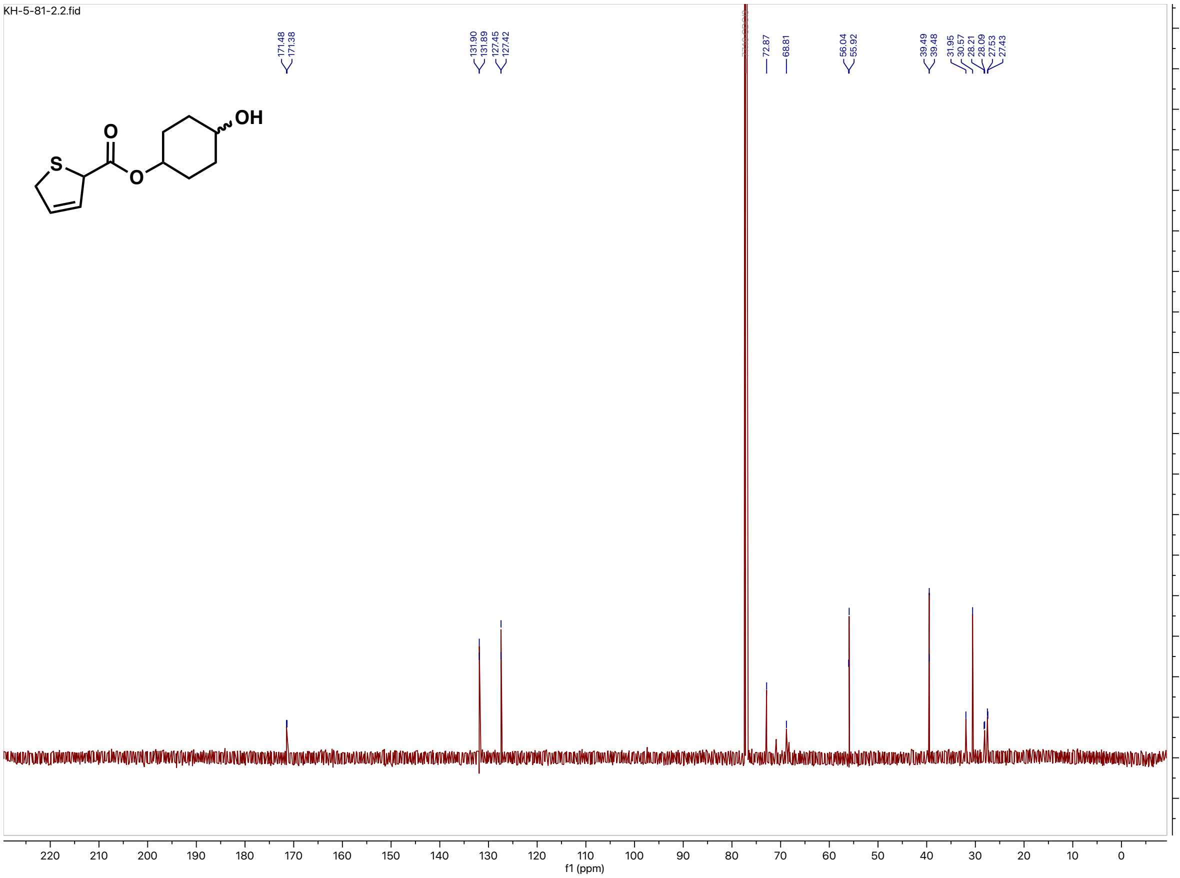
Compound 31


KH-5-81-1.1.fid
7.26 CDCl3
6.09
6.09
6.09
6.08
6.08
6.08
6.07
5.88
5.87
5.87
5.86
5.86
5.86
5.85
5.20
5.20
5.19
5.19
5.18
4.83
4.83
4.82
4.82
4.82
4.82
4.81
4.81
4.81
3.89
3.88
3.88
3.87
3.87
3.86
3.86
3.85
3.82
3.82
3.81
3.81
3.79
2.61
2.60
2.60
2.60
2.59
2.59
2.58
2.58
2.58
2.57
2.57
2.57
2.56
2.56
2.55
2.38
2.38
2.37
2.37
2.37
2.36
2.36
2.35
2.35
2.35
2.34
2.34
2.33
2.19
2.18
2.17
2.17
2.17
2.16
2.16
2.16
2.15
2.15
2.14
2.14
2.14
2.07
2.07
2.06
2.06
2.05
2.05
2.05
2.05
2.04
2.04
2.03
2.03
2.02
S
O
O
O
1.00
0.94
1.03
0.98
0.96
1.04
1.90
1.85
1.88
1.91
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
f1 (ppm)
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50

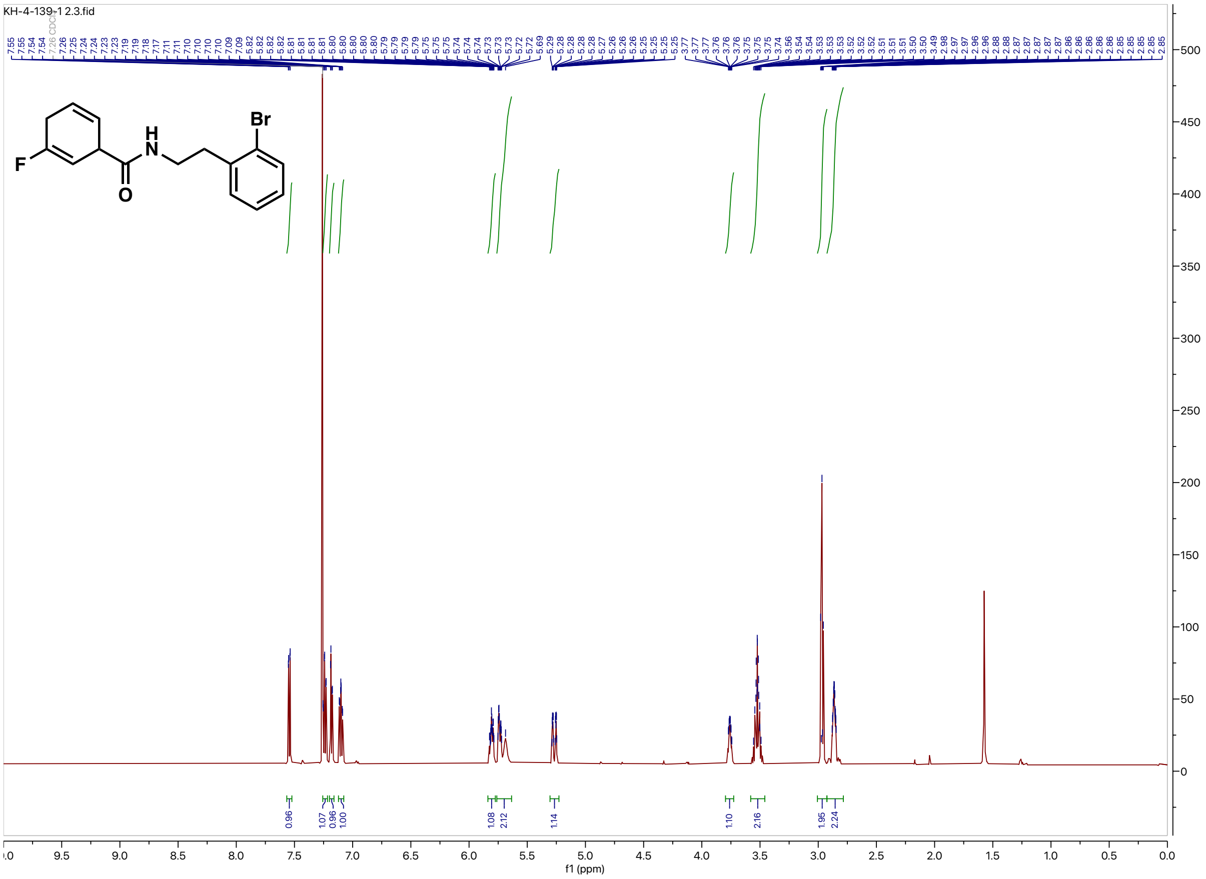

KH-5-81-1.2.fid
209.90
171.31
132.28
127.11
77.16 CDCl3
69.63
55.77
39.54
37.21
37.18
30.37
30.24
S
O
O
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20

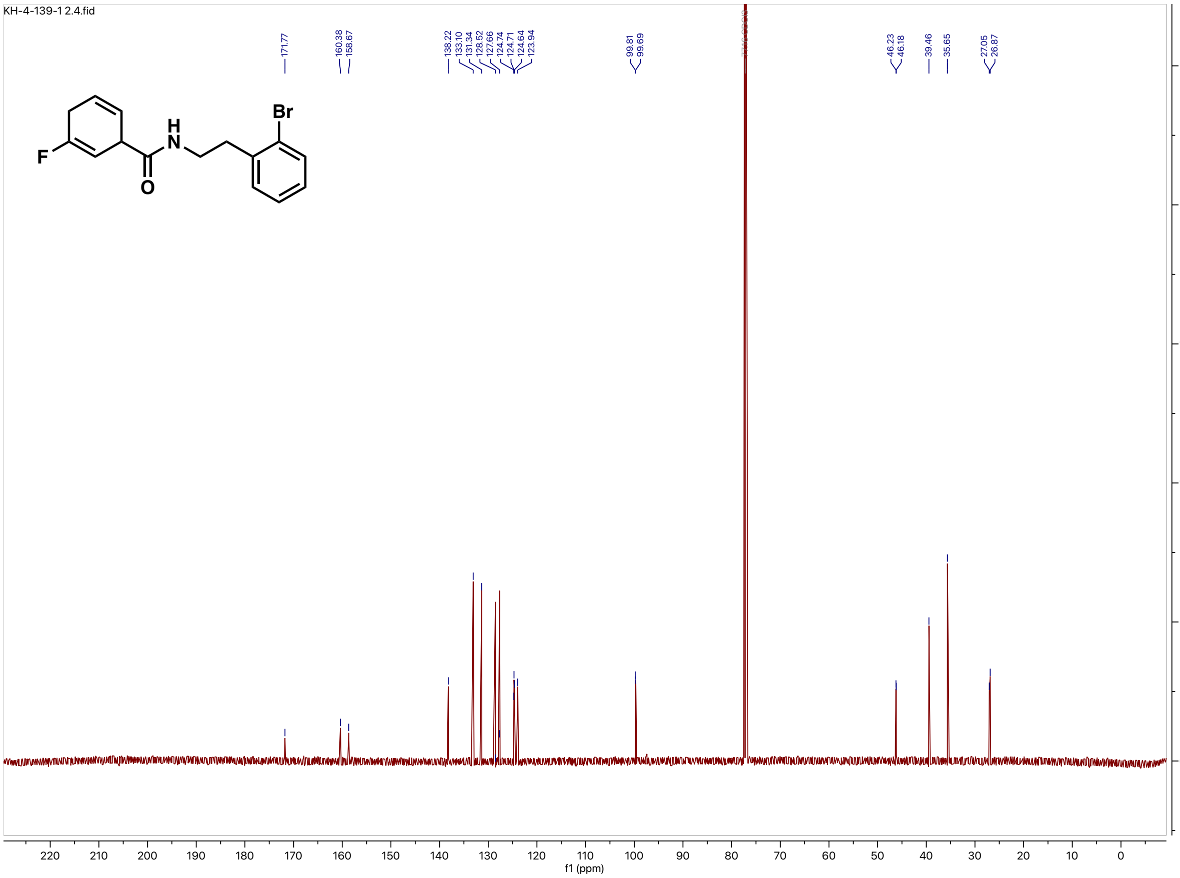
Compound 31’

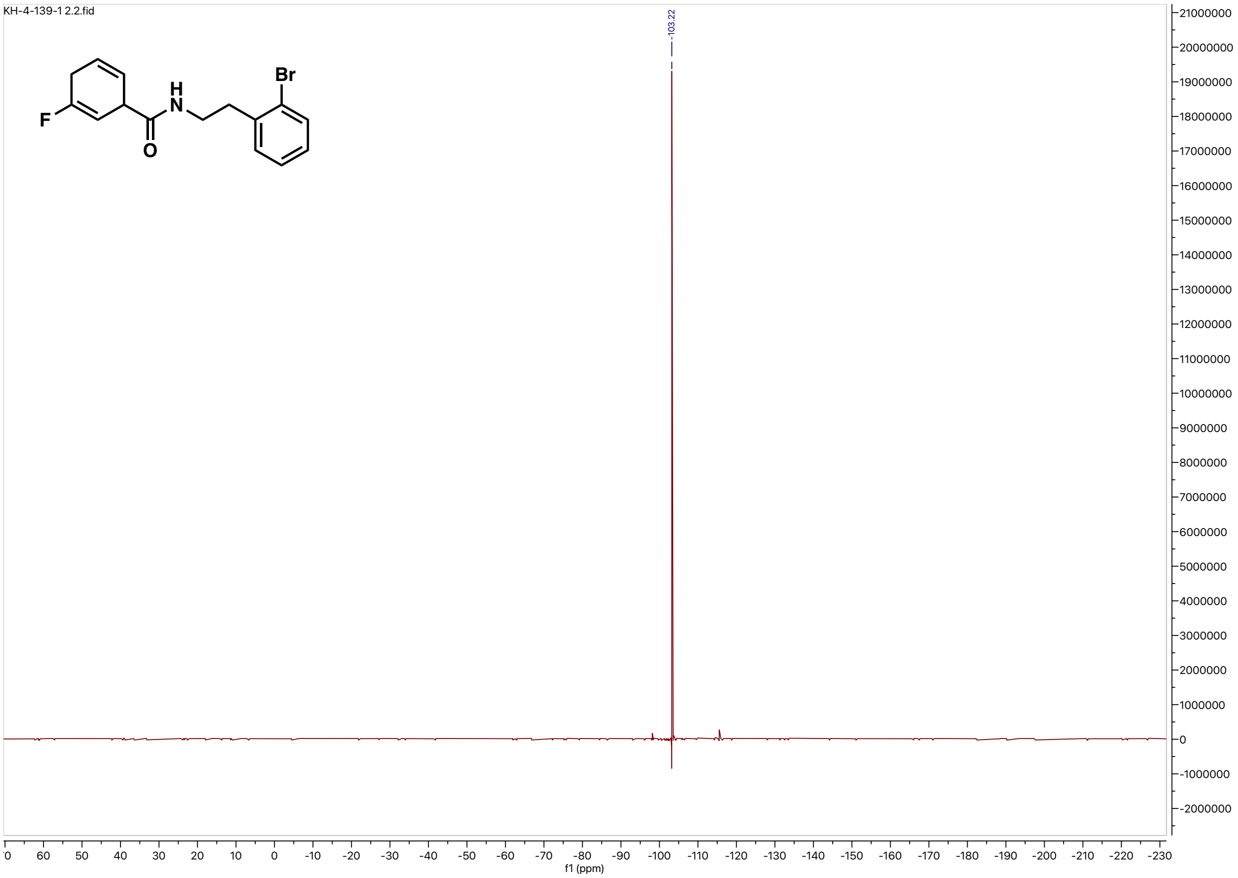

KH-5-81-2.1.fid
7.26 CDCl3
6.06 6.05 6.05 6.05 6.05 6.05 6.04 6.04 6.04 6.03 5.86 5.86 5.85 5.85 5.84 5.84 5.83 5.83 5.83 5.83 5.82 4.90 4.90 4.89 4.79 4.79 4.79 4.79 4.78 4.78 4.78 4.78 4.77 4.77 4.76 4.76 4.76 4.75 4.75 4.75 3.88 3.87 3.87 3.86 3.86 3.86 3.86 3.85 3.85 3.85 3.85 3.84 3.84 3.84 3.80 3.79 3.79 3.78 3.78 3.78 3.77 3.77 3.76 3.76 3.76 3.76 3.75 2.02 2.01 2.01 2.00 2.00 2.00 1.99 1.98 1.97 1.97 1.96 1.96 1.96 1.95 1.74 1.74 1.73 1.64 1.63 1.63 1.62 1.61 1.52 1.51 1.51 1.50 1.49 1.49 1.48 1.46 1.46 1.46 1.45 1.45 1.44 1.43 1.43 1.42 1.42
O
S
O
OH
1.00
1.03
2.22
1.10
1.96
3.32
6.97
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
f1 (ppm)
650 600 550 500 450 400 350 300 250 200 150 100 50 0 -50


KH-5-81-2.2.fid
S
O
O
OH
171.48
171.38
131.90
131.89
127.45
127.42
72.87
68.81
56.04
55.92
39.49
39.48
31.95
30.57
28.21
28.09
27.53
27.43
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)
90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5

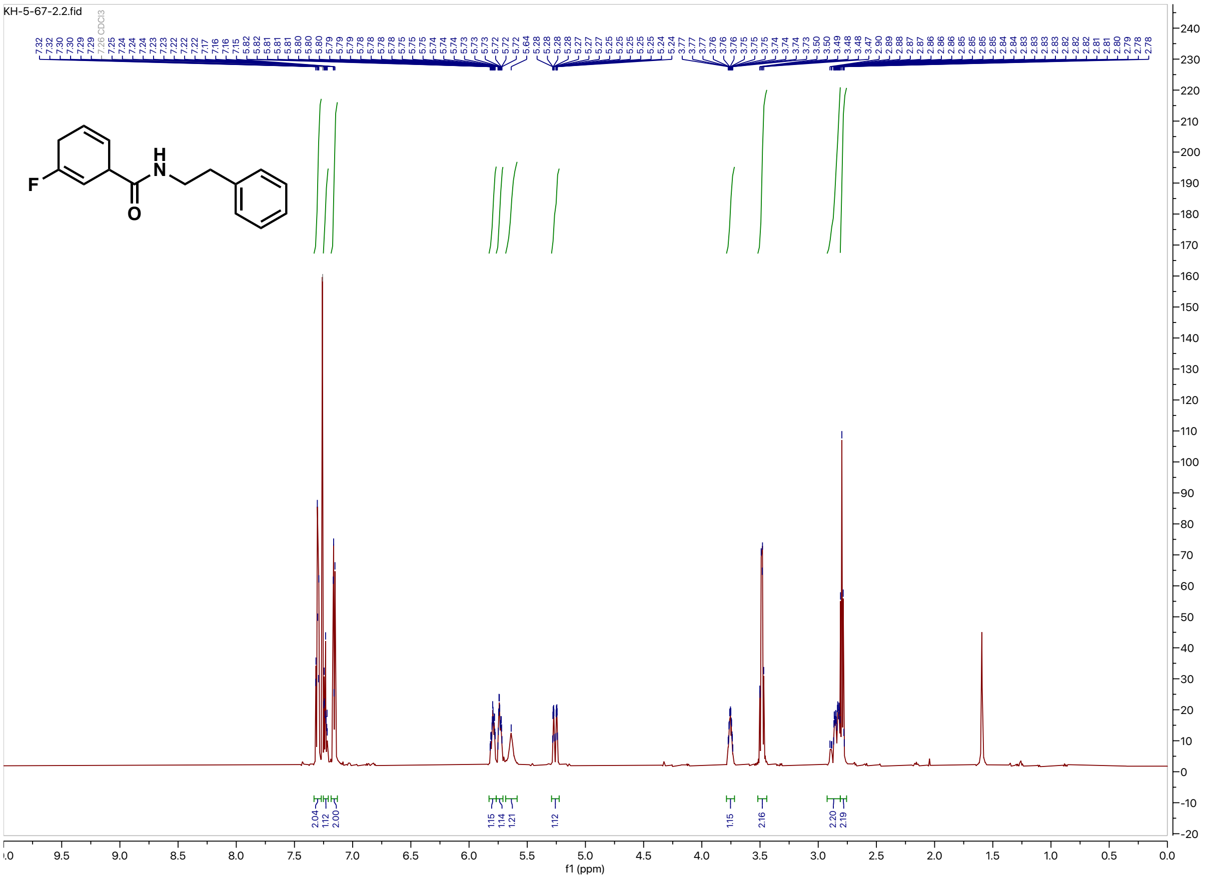
Compound 32

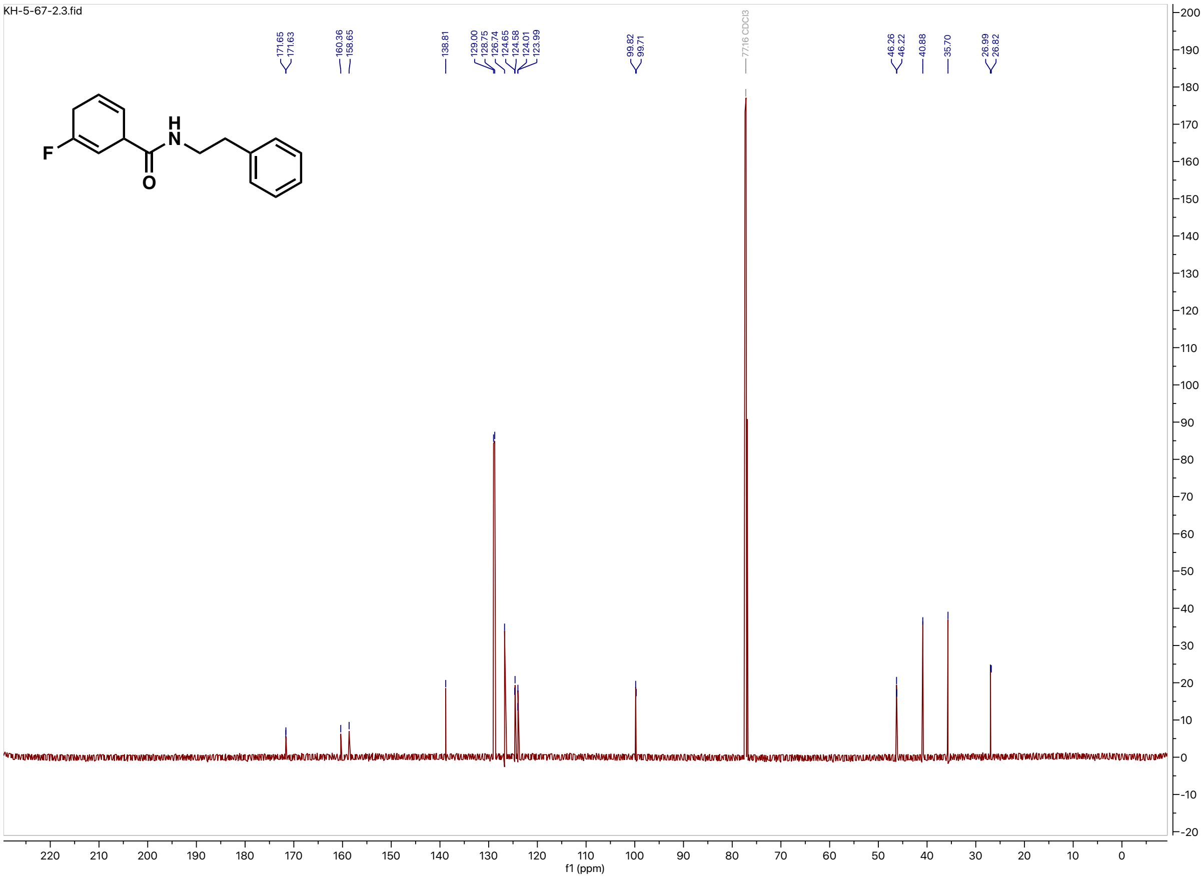

KH-4-139-1 2.3.fid
7.55 7.55 7.54 7.54 7.26 CDCl3 7.26 7.25 7.24 7.24 7.23 7.23 7.19 7.19 7.18 7.17 7.11 7.11 7.10 7.10 7.10 7.10 7.09 7.09 5.82 5.82 5.82 5.82 5.81 5.81 5.81 5.81 5.80 5.80 5.80 5.80 5.80 5.79 5.79 5.79 5.79 5.75 5.75 5.75 5.74 5.74 5.74 5.73 5.73 5.73 5.72 5.72 5.69 5.29 5.28 5.28 5.28 5.28 5.27 5.26 5.26 5.26 5.25 5.25 5.25 5.25 3.77 3.77 3.77 3.76 3.76 3.76 3.75 3.75 3.75 3.74 3.56 3.54 3.54 3.53 3.53 3.53 3.52 3.52 3.52 3.51 3.51 3.51 3.50 3.50 3.49 2.98 2.97 2.97 2.96 2.96 2.88 2.88 2.87 2.87 2.87 2.87 2.87 2.86 2.86 2.86 2.86 2.85 2.85 2.85 2.85 2.85
Br
H
N
F
O
0.96
1.07
0.96
1.00
1.08
2.12
1.14
1.10
2.16
1.95
2.24
500
450
400
350
300
250
200
150
100
50
0
.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
f1 (ppm)

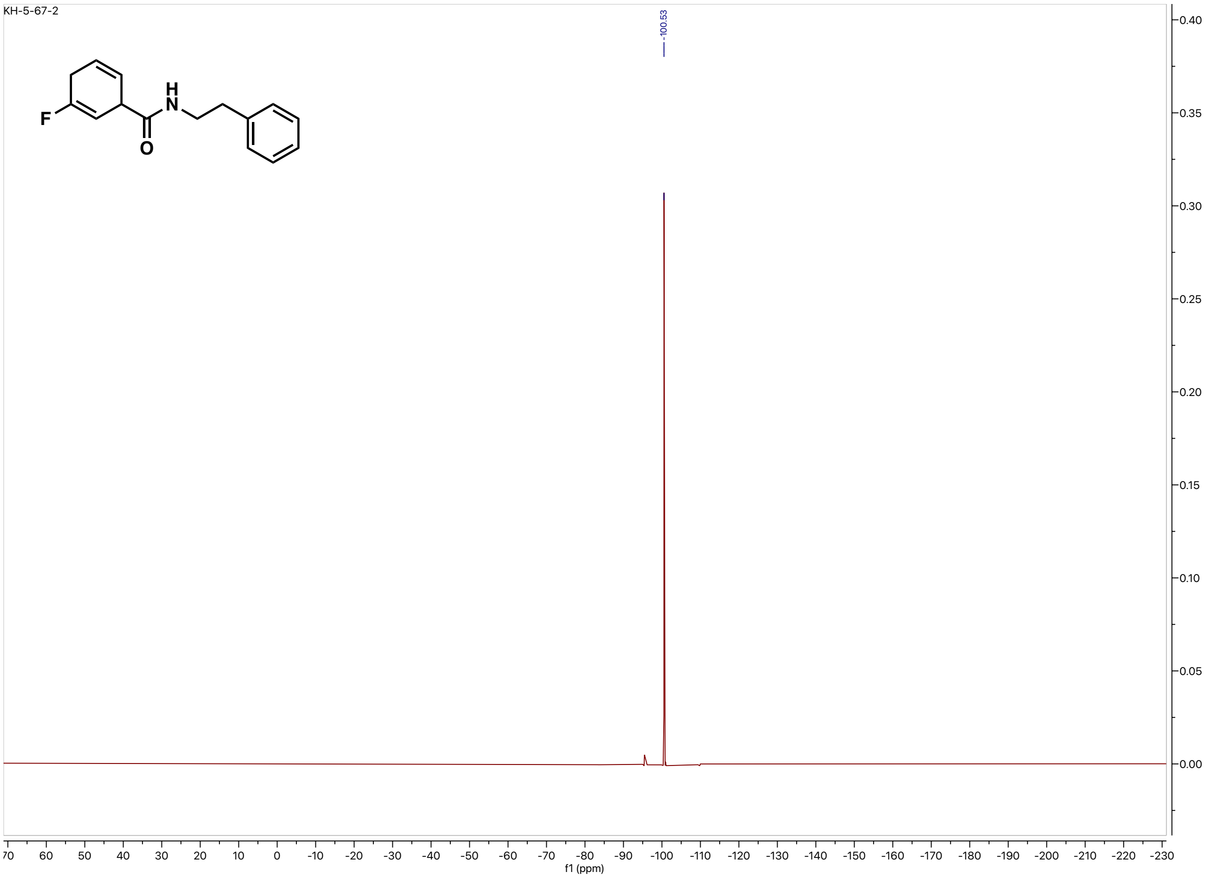

KH-4-139-1 2.4.fid
171.77
160.38
158.67
138.22
133.10
131.34
128.52
127.66
124.74
124.71
124.64
123.94
99.81
99.69
77.16 CDCl3
46.23
46.18
39.46
35.65
27.05
26.87
F
H
N
O
Br
250
200
150
100
50
0
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


KH-4-139-1 2.2.fid
-103.22
F
H
N
O
Br
21000000
20000000
19000000
18000000
17000000
16000000
15000000
14000000
13000000
12000000
11000000
10000000
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
-1000000
-2000000
0
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
f1 (ppm)

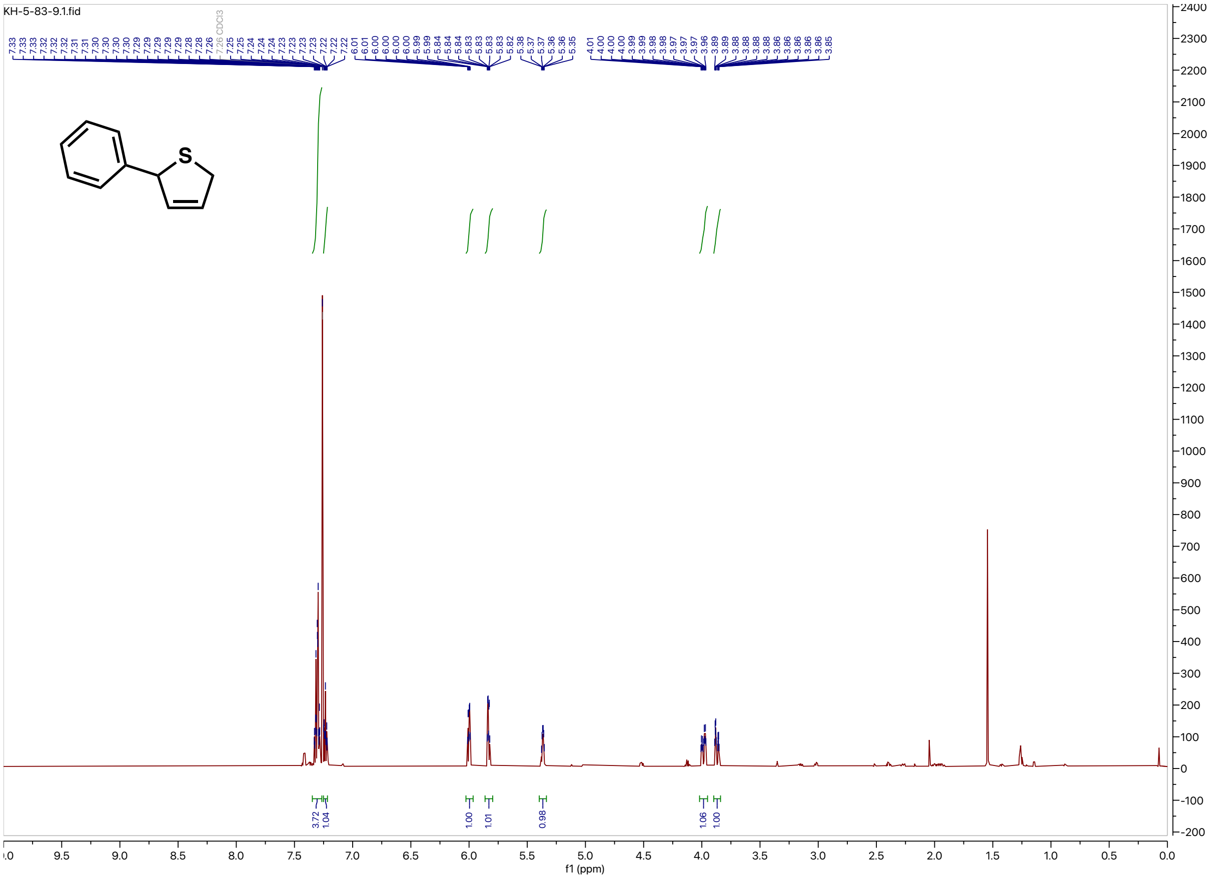
Compound 32’

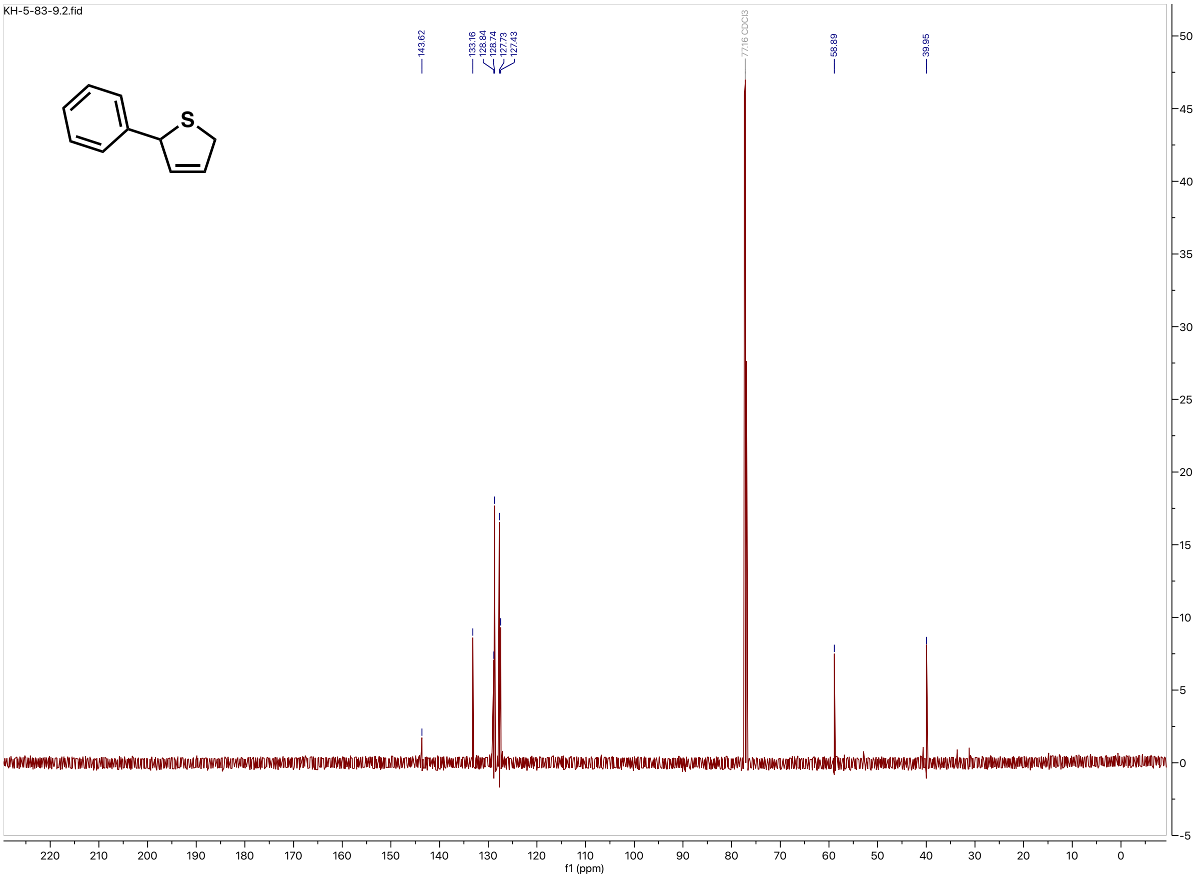

KH-5-67-2.2.fid
7.32 7.32 7.30 7.30 7.29 7.29 7.26 CDCl3 7.25 7.24 7.24 7.24 7.23 7.23 7.22 7.22 7.22 7.17 7.16 7.15 5.82 5.82 5.81 5.81 5.81 5.80 5.80 5.79 5.79 5.79 5.78 5.78 5.78 5.75 5.75 5.75 5.74 5.74 5.74 5.73 5.73 5.73 5.72 5.72 5.72 5.64 5.28 5.28 5.28 5.27 5.27 5.27 5.25 5.25 5.25 5.25 5.24 3.77 3.77 3.76 3.76 3.76 3.75 3.75 3.75 3.74 3.74 3.74 3.73 3.50 3.50 3.49 3.48 3.48 3.47 2.90 2.89 2.88 2.87 2.87 2.86 2.86 2.86 2.85 2.85 2.85 2.84 2.84 2.83 2.83 2.83 2.82 2.82 2.81 2.81 2.80 2.79 2.78 2.78
F
H
N
O
2.04
1.12
2.00
1.15
1.14
1.21
1.12
1.15
2.16
2.20
2.19
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
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
f1 (ppm)


KH-5-67-2.3.fid
171.65
171.63
160.36
158.65
138.81
129.00
128.75
126.74
124.65
124.58
124.01
123.99
99.82
99.71
77.16 CDCl3
46.26
46.22
40.88
35.70
26.99
26.82
F
H
N
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
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)

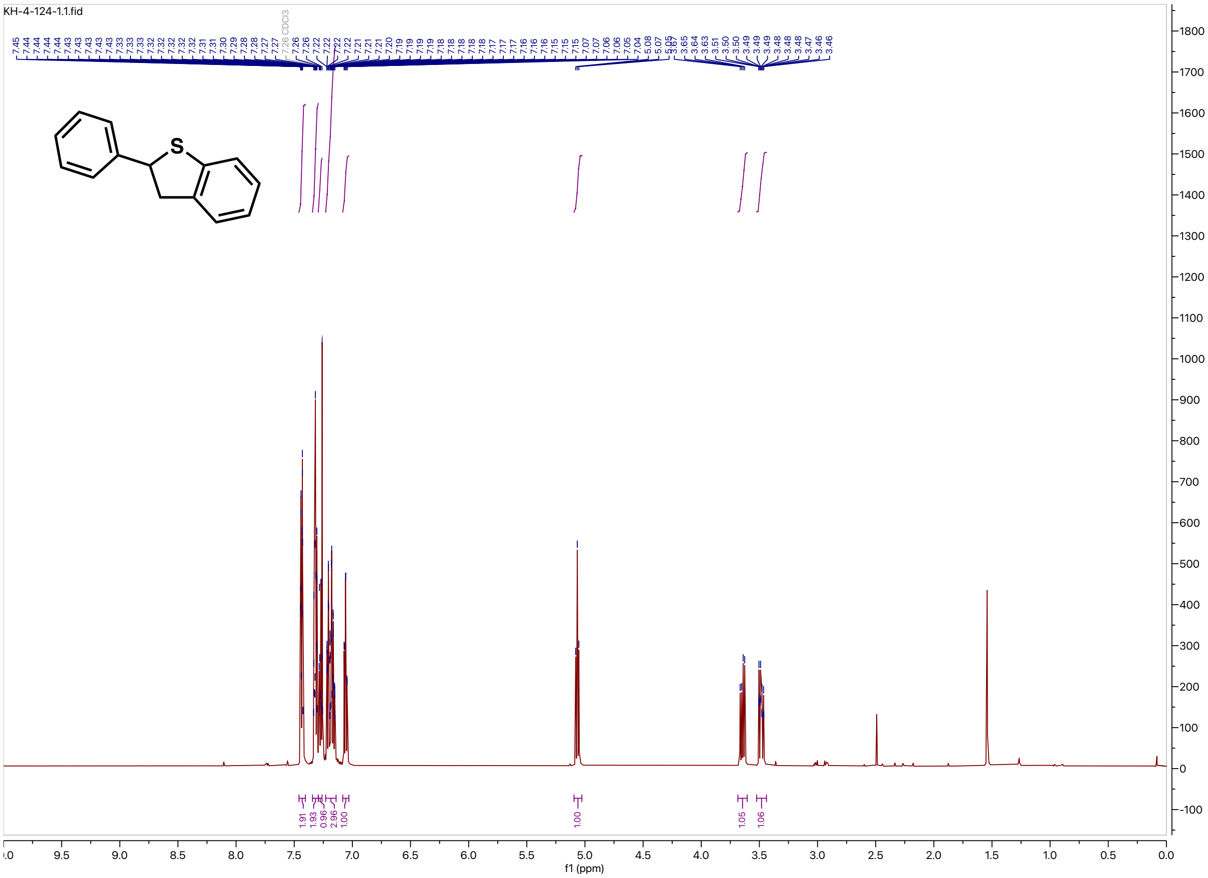

KH-5-67-2
-100.53
F
H
N
O
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
f1 (ppm)

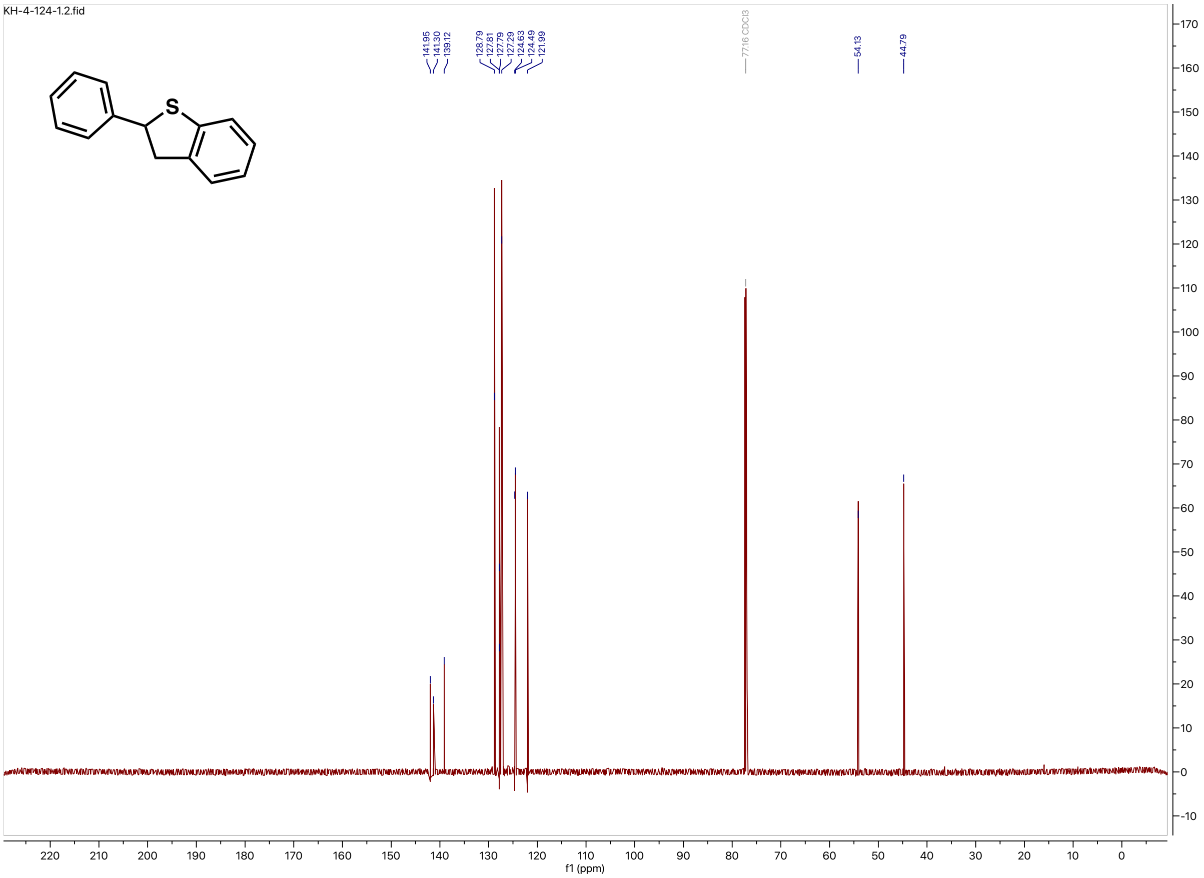
Compound 39


KH-5-83-9.1.fid
7.33 7.33 7.32 7.32 7.32 7.31 7.31 7.30 7.30 7.30 7.30 7.29 7.29 7.29 7.29 7.28 7.28 7.26
7.26 CDCl3
7.25 7.25 7.24 7.24 7.24 7.23 7.23 7.23 7.23 7.22 7.22 7.22
6.01 6.01 6.00 6.00 6.00 5.99 5.99 5.84 5.84 5.84 5.83 5.83 5.83 5.83 5.82
5.38 5.37 5.37 5.36 5.36 5.35
4.01 4.00 4.00 3.99 3.99 3.98 3.98 3.97 3.97 3.97 3.96 3.89 3.89 3.88 3.88 3.88 3.86 3.86 3.86 3.86 3.86 3.85
S
3.72
1.04
1.00
1.01
0.98
1.06
1.00
f1 (ppm)
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
2400 2300 2200 2100 2000 1900 1800 1700 1600 1500 1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0 -100 -200

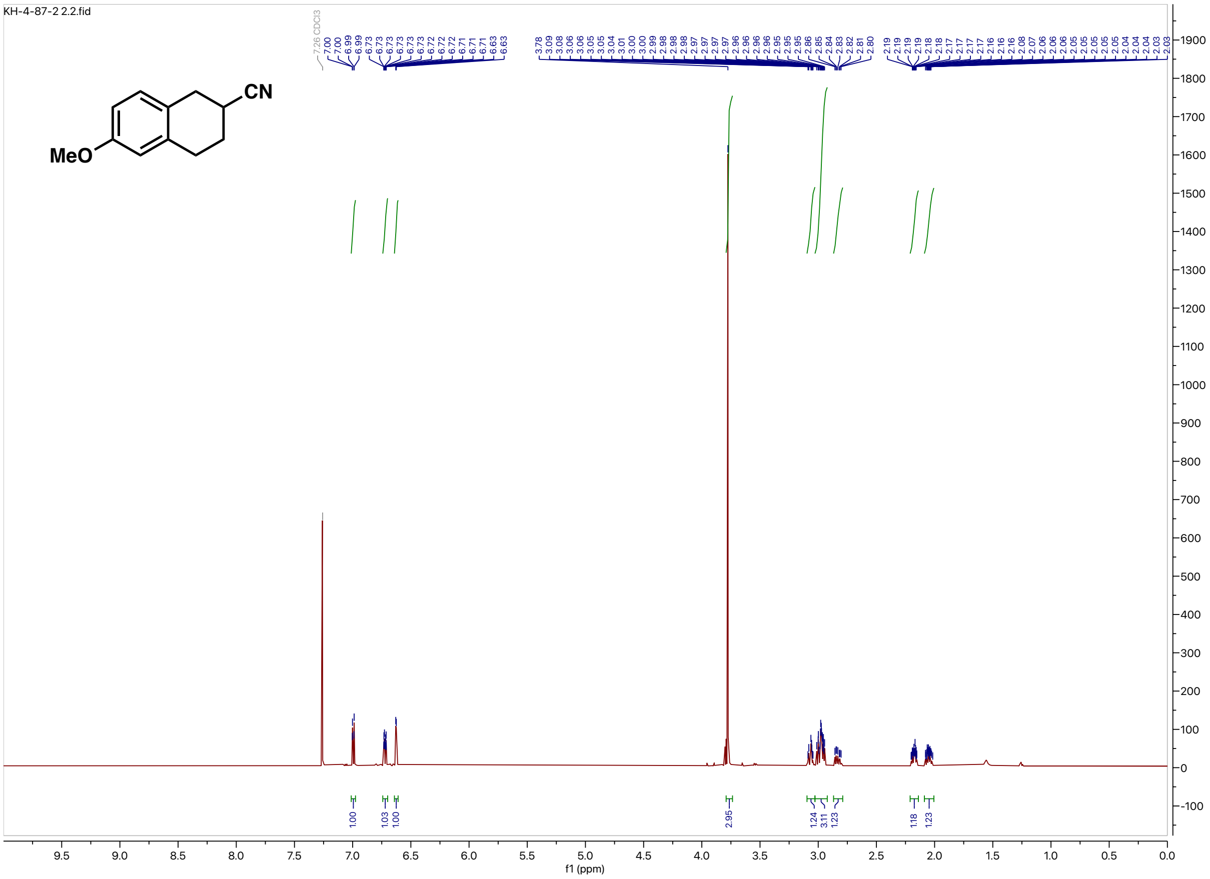

KH-5-83-9.2.fid
S
143.62
133.16
128.84
128.74
127.73
127.43
77.16 CDCl3
58.89
39.95
50
45
40
35
30
25
20
15
10
5
0
-5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

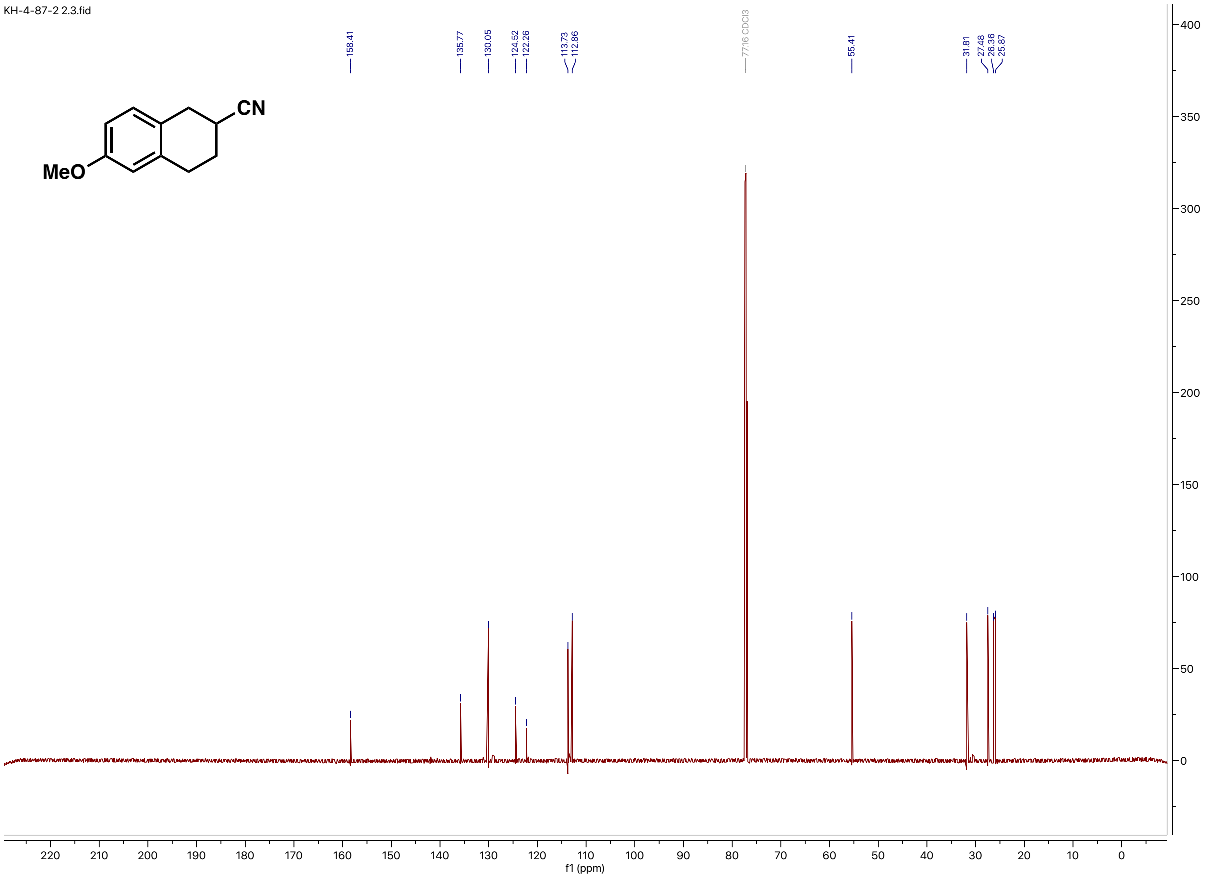
Compound 40


KH-4-124-1.1.fid
7.45
7.44
7.44
7.44
7.44
7.43
7.43
7.43
7.43
7.33
7.33
7.33
7.32
7.32
7.32
7.32
7.32
7.31
7.31
7.30
7.29
7.28
7.28
7.27
7.27
7.26 CDCl3
7.26
7.26
7.22
7.22
7.22
7.22
7.21
7.21
7.21
7.20
7.19
7.19
7.19
7.19
7.18
7.18
7.18
7.18
7.18
7.17
7.17
7.17
7.16
7.16
7.16
7.15
7.15
7.15
7.07
7.07
7.06
7.06
7.05
7.04
5.08
5.07
5.05
3.67
3.65
3.64
3.63
3.51
3.50
3.50
3.49
3.49
3.49
3.48
3.48
3.48
3.47
3.46
3.46
S
1.91
1.93
0.96
2.96
1.00
1.00
1.05
1.06
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
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
f1 (ppm)

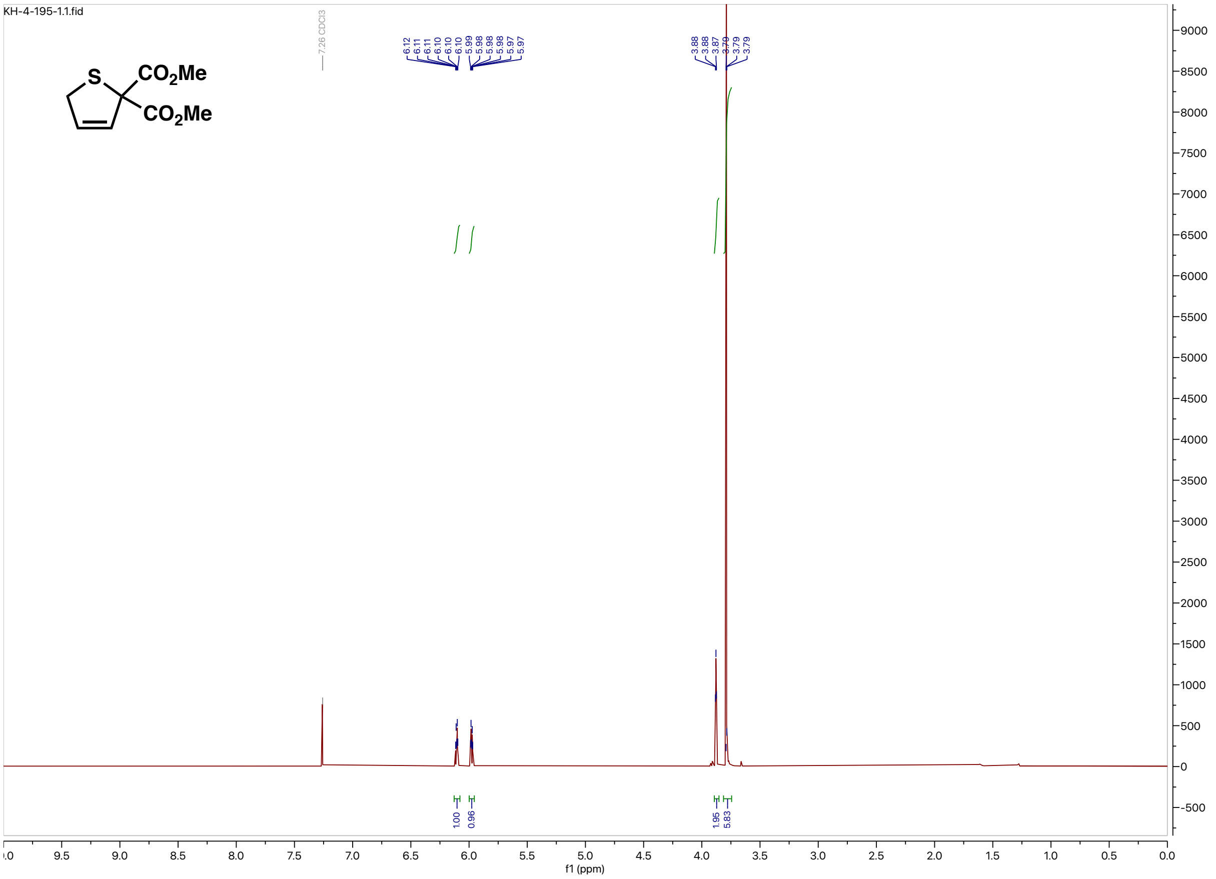

KH-4-124-1.2.fid
S
141.95
141.30
139.12
128.79
127.81
127.79
127.29
124.63
124.49
121.99
77.16 CDCl3
54.13
44.79
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

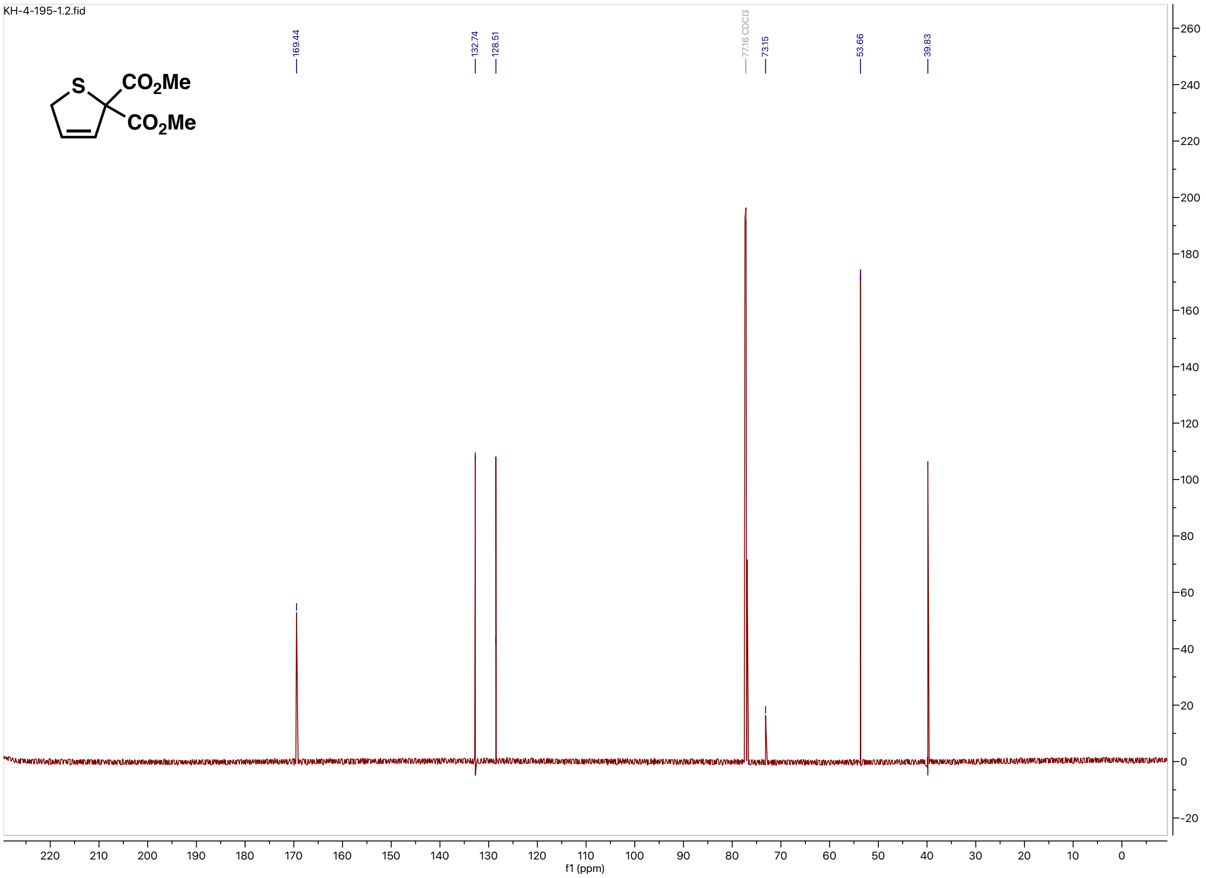
Compound 41


KH-4-87-2 2.2.fid
MeO
CN
7.26 CDCl3
7.00
7.00
6.99
6.99
6.73
6.73
6.73
6.73
6.73
6.72
6.72
6.71
6.71
6.71
6.63
6.63
3.78
3.09
3.08
3.06
3.06
3.05
3.05
3.04
3.01
3.00
3.00
2.99
2.98
2.98
2.98
2.97
2.97
2.97
2.97
2.96
2.96
2.96
2.96
2.95
2.95
2.95
2.86
2.85
2.84
2.83
2.82
2.81
2.80
2.19
2.19
2.19
2.19
2.18
2.18
2.17
2.17
2.17
2.17
2.16
2.16
2.16
2.08
2.07
2.06
2.06
2.06
2.05
2.05
2.05
2.05
2.04
2.04
2.03
2.03
1.00
1.03
1.00
2.95
1.24
3.11
1.23
1.18
1.23
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
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
f1 (ppm)

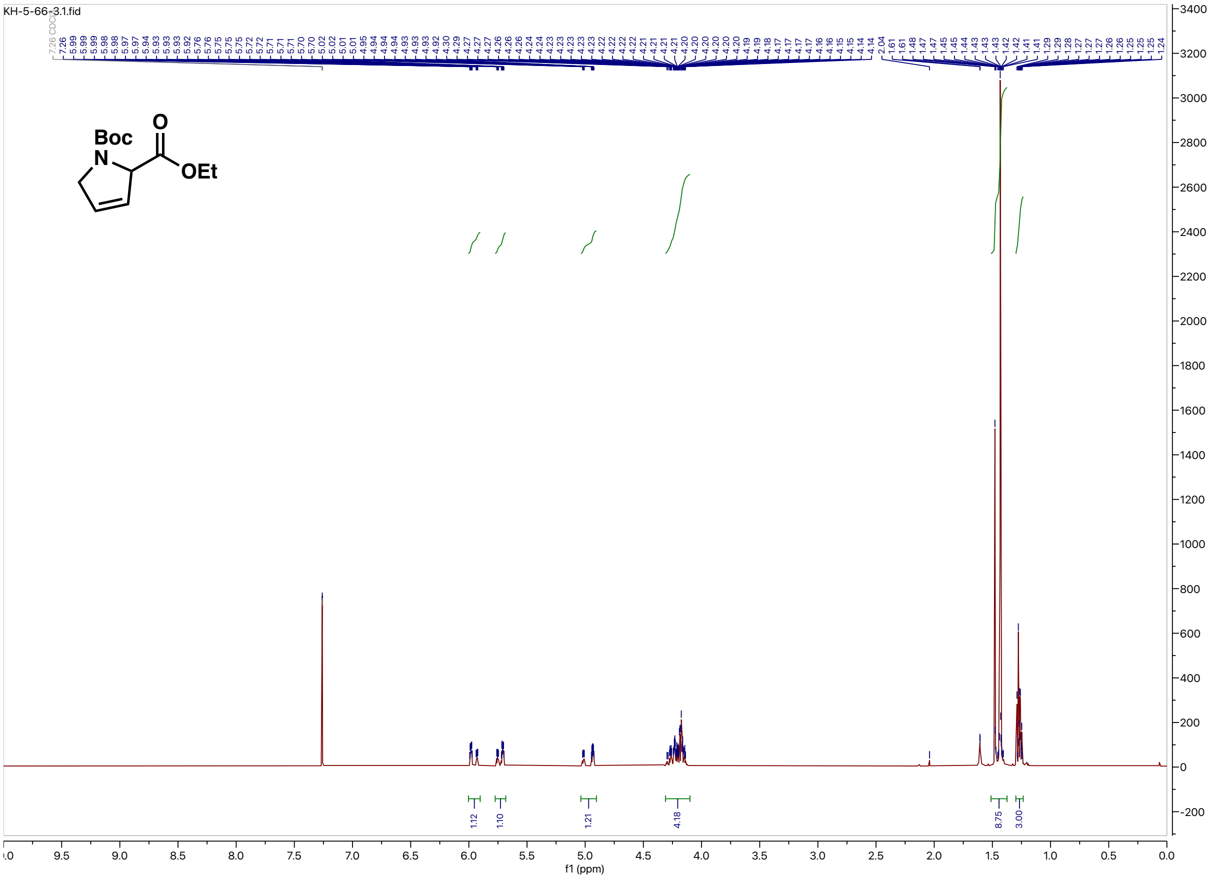

KH-4-87-2 2.3.fid
MeO
CN
158.41
135.77
130.05
124.52
122.26
113.73
112.86
77.16 CDCl3
55.41
31.81
27.48
26.36
25.87
400
350
300
250
200
150
100
50
0
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

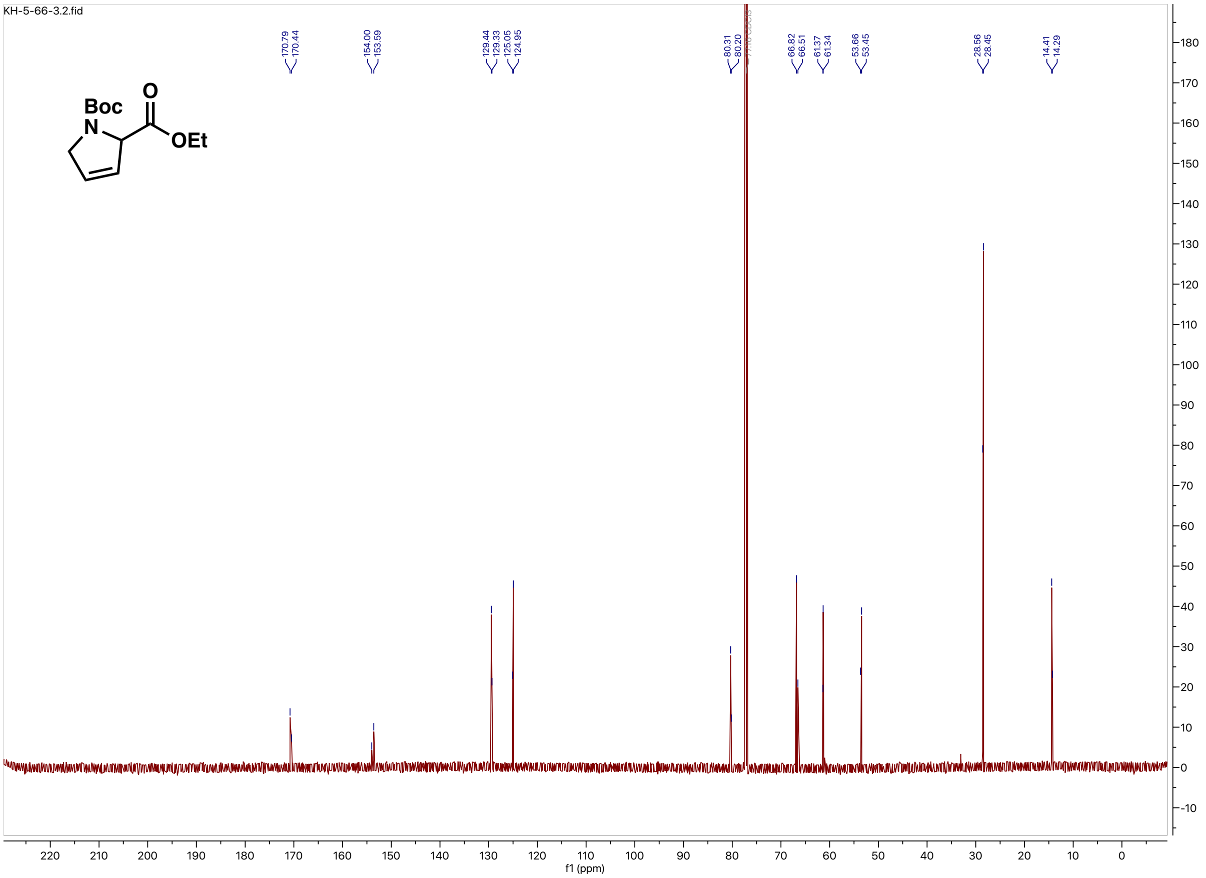
Compound 42


KH-4-195-1.1.fid
CO2Me
CO2Me
S
7.26 CDCl3
6.12
6.11
6.11
6.10
6.10
6.10
5.99
5.98
5.98
5.98
5.97
5.97
3.88
3.88
3.87
3.79
3.79
3.79
1.00
0.96
1.95
5.83
9000
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
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
f1 (ppm)

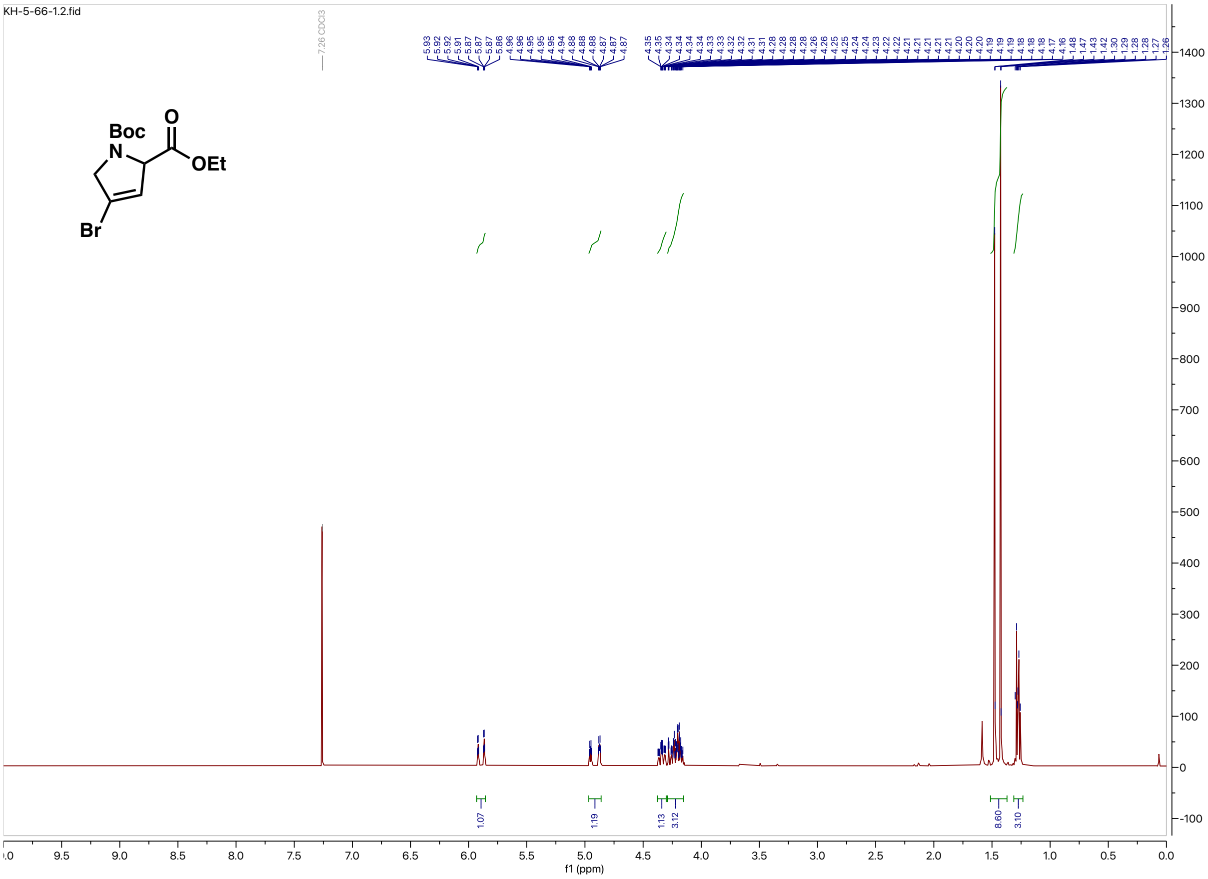

KH-4-195-1.2.fid
169.44
132.74
128.51
77.16 CDCl3
73.15
53.66
39.83
S
CO2Me
CO2Me
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

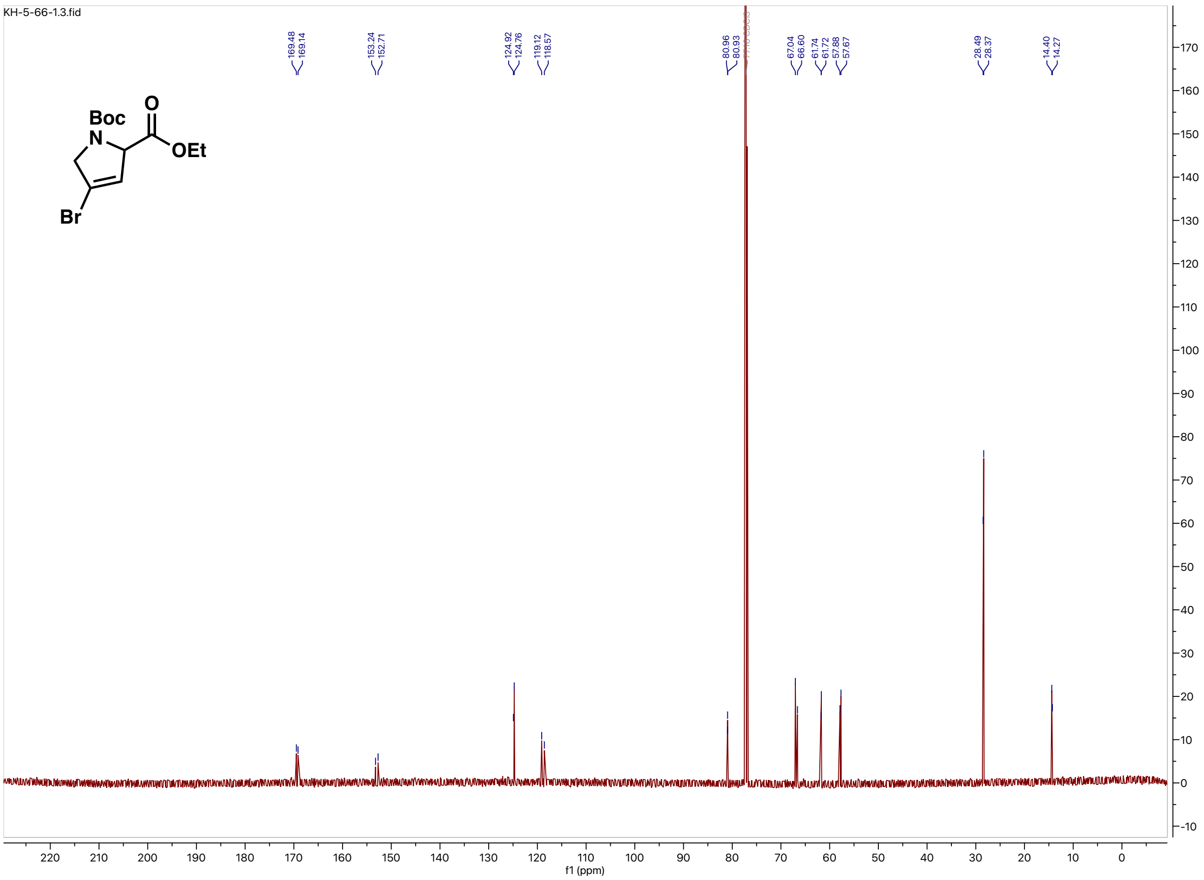
Compound 49


KH-5-66-3.1.fid
7.26 CDCl3
7.26
5.99
5.99
5.98
5.98
5.97
5.94
5.93
5.93
5.92
5.76
5.76
5.75
5.75
5.72
5.72
5.71
5.71
5.70
5.70
5.02
5.02
5.01
5.01
4.95
4.94
4.94
4.93
4.93
4.92
4.30
4.29
4.27
4.27
4.26
4.26
4.26
4.24
4.24
4.23
4.23
4.23
4.23
4.22
4.22
4.22
4.22
4.21
4.21
4.21
4.21
4.20
4.20
4.20
4.20
4.20
4.19
4.19
4.18
4.17
4.17
4.17
4.16
4.16
4.15
4.14
4.14
2.04
1.61
1.61
1.48
1.47
1.47
1.45
1.45
1.44
1.43
1.43
1.43
1.42
1.42
1.41
1.41
1.29
1.29
1.28
1.27
1.27
1.27
1.26
1.26
1.25
1.25
1.24
Boc
N
O
OEt
1.12
1.10
1.21
4.18
8.75
3.00
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
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
f1 (ppm)


KH-5-66-3.2.fid
Boc
N
O
OEt
170.79
170.44
154.00
153.59
129.44
129.33
125.05
124.95
80.31
80.20
77.16 CDCl3
66.82
66.51
61.37
61.34
53.66
53.45
28.56
28.45
14.41
14.29
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
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)

Compound 50


KH-5-66-1.2.fid
7.26 CDCl3
5.93
5.92
5.92
5.91
5.87
5.87
5.87
5.86
4.96
4.96
4.95
4.95
4.95
4.94
4.88
4.88
4.88
4.87
4.87
4.87
4.35
4.35
4.34
4.34
4.34
4.34
4.33
4.33
4.32
4.32
4.31
4.31
4.28
4.28
4.28
4.26
4.26
4.25
4.25
4.24
4.24
4.23
4.22
4.22
4.21
4.21
4.21
4.21
4.20
4.20
4.20
4.19
4.19
4.19
4.18
4.18
4.18
4.17
4.16
1.48
1.47
1.43
1.42
1.30
1.29
1.28
1.28
1.27
1.26
Boc
N
O
OEt
Br
1.07
1.19
1.13
3.12
8.60
3.10
f1 (ppm)


KH-5-66-1.3.fid
169.48
169.14
153.24
152.71
124.92
124.76
119.12
118.57
80.96
80.93
67.04
66.60
61.74
61.72
57.88
57.67
28.49
28.37
14.40
14.27
Boc
N
O
OEt
Br
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
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)