Electronic Supplementary Material (ESI) for Chemical Science.


# Supporting Information

# A Free-Radical Design Featuring an Intramolecular Migration for a Synthetically Versatile Alkyl–(Hetero)Arylation of Simple Olefins

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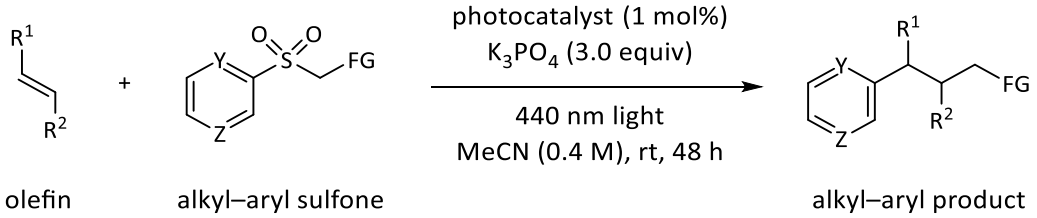
## TABLE OF CONTENTS

## I. General Information

All procedures were performed under air unless stated otherwise. Acetonitrile, dichloromethane, dimethyl sulfoxide, methanol, tetrahydrofuran, and toluene were dried using a solvent purification system. $[Ru(dMebpy)_3](PF_6)_2$ (**PC1**), $[Ir(dFCF_3ppy)_2(dtbbpy)]PF_6$ (**PC2**), and $[Ir(dFCF_3ppy)_2(4,4'–dCF_3bpy)]PF_6$ (**PC3**) were prepared according to literature procedures.[1,2] Styrene and 4-chlorostyene, which were used to prepare products **29** and **30**, were filtered a plug of silica gel before use. All other commercial reagents and solvents were used as received. Reactions were monitored by thin-layer chromatography (TLC) or liquid chromatography-mass spectrometry (LC-MS). TLC was performed on Silicycle 250-μm silica-gel F-254 plates and visualized by UV fluorescence (254 nm) or $KMnO_4$ stain. Organic or aqueous solutions were concentrated under reduced pressure on a Heidolph rotary evaporator. Chromatographic purification of products was accomplished by flash chromatography on Silicycle F60 silica gel or preparative thin-layer chromatography was performed on Silicycle 1000-μm silica-gel F-254 plates. 1D NOESY spectra were recorded on a Bruker AV-III 850 MHz spectrometer. All other NMR spectra were recorded on a Bruker NEO 400 MHz spectrometer. Chemical shifts were internally referenced to residual protic solvent signals of $CDCl_3$ (7.26 ppm for $^1H$, 77.16 ppm for $^{13}C$) or $CD_3CN$ (1.97 ppm for $^1H$, 118.26 and 1.32 ppm for $^{13}C$). Data for $^1H$ NMR are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, app = apparent), and coupling constant (Hz). Data for $^{13}C$ NMR are reported in terms of chemical shift and, if applicable, multiplicity and coupling constant (Hz). Cyclic voltammetry (CV) experiments were performed using a CH Instruments 600E electrochemical analyzer, a 3-mm glassy carbon disk working electrode (polished with 0.05- μm MicroPolish powder on a Microcloth polishing pad), a platinum-wire counter electrode, and a $Ag/AgNO_3$ reference electrode. Potentials were corrected to SCE by adding 0.31 V (we measured $E_{1/2}[Fc^+/Fc]$ = +0.09 V vs. $Ag/AgNO_3$, $Fc^+/Fc$ is at +0.40 V vs. SCE).[3] High-resolution mass spectra (ESI-HRMS) were obtained on a ThermoFisher Scientific UHPLC/QExactive HF-X mass spectrometer equipped with a C18 column. Low-resolution mass spectra (LRMS) and the yield for **41** were obtained by LC-MS on an Agilent 1290 Infinity II instrument equipped with a Zorbax SB-C18 column and an Infinity LC/MSD using electrospray ionization (ESI). Fluorescence-quenching experiments were performed on a LAMBDA 365 UV/vis spectrophotometer using 3.5 mL LAB4US quartz cuvettes with a 10 mm path length.

## II. General Procedure for Alkyl–Arylation of Olefins




Alkyl–aryl sulfone (0.8 mmol, 1.0 equiv), olefin (2.4 mmol, 3.0 equiv), finely ground potassium phosphate (509 mg, 2.4 mmol, 3.0 equiv), $Ru(dMebpy)_3(PF_6)_2$ (**PC1**, 7.5 mg, 8 μmol, 1 mol%), and acetonitrile (2 mL, 0.4 M in sulfone) were added to an 8-mL vial equipped with a magnetic stir bar and sealed with a septum cap. The resulting mixture was thoroughly shaken to disperse the insoluble potassium phosphate, cooled in an ice bath, and sparged with nitrogen for 15 minutes. The degassed mixture was stirred and irradiated with 440 nm light near room temperature (see "Section III. Photoreactor Setup") for 48 hours. The mixture was diluted with EtOAc and the resulting solution was washed with water (2 ×) and brine (1 ×), dried over sodium sulfate, and concentrated. The residue was purified by silica-gel chromatography to afford the desired alkyl–aryl product.

*Note: lower yields were obtained when the potassium phosphate was not ground or when it was dried in a 120 ºC oven.*

## III. Photoreactor Setup

Reaction mixtures were irradiated by suspending the 8-mL reaction vial ~1 cm above a 5-W LED chip, which was powered by a 4-V circuit supplied by a commercial power box. 12-Seat reactors that could be placed over a standard 8-inch stir plate were 3D-printed in-house and wired with one LED chip per vial seat to facilitate throughput. Fans were used to keep the reaction mixtures near room temperature. All alkyl–arylation products were obtained by irradiation with blue 440-nm LED chips, except for **43**, which required a 40-W tuna blue Kessil lamp, and **30** and **31**, which required green 510–575-nm LED chips. In the latter cases, blue-light irradiation led to lower yields and the formation of a white film on the vial surface, which we attribute to light-induced styrene polymerization.

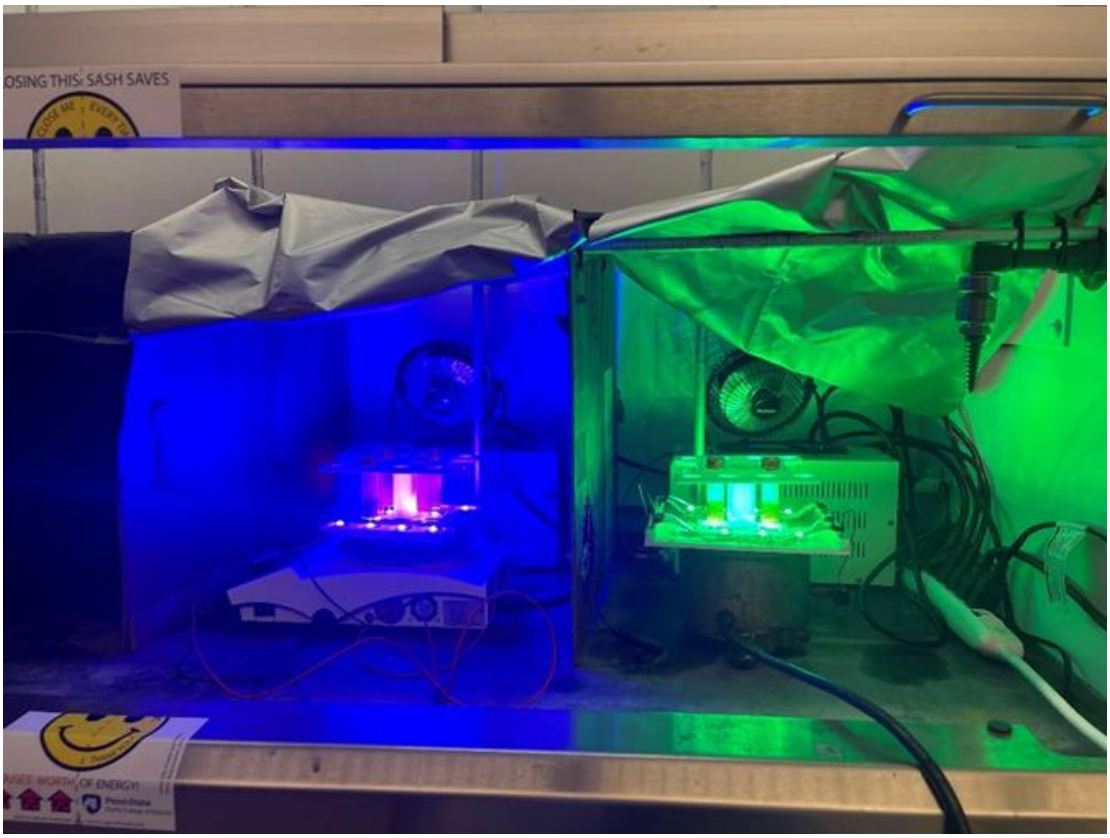
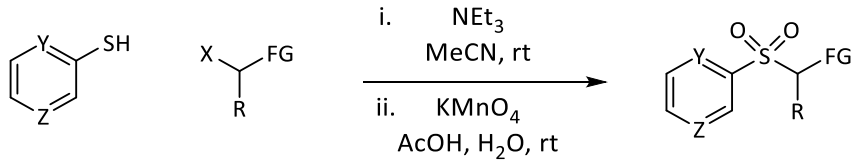



**Figure S1.** Photograph of 3D-printed photoreactors wired with blue 440-nm (left) and green 510–575-nm (right) LED chips.

## IV. Procedures for Substrate Preparation

### General Procedure A: Preparation of Alkyl–Aryl Sulfones from Aryl Thiols ($KMnO_4$ Oxidation)



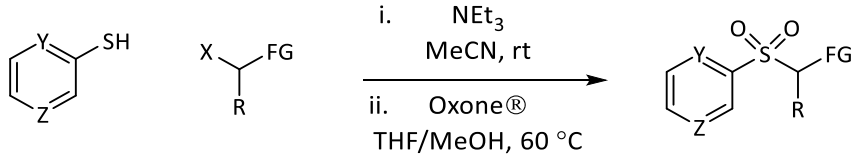

aryl thiol alkyl halide alkyl–aryl sulfone

Alkyl halide (18 mmol, 1.2 equiv) was added dropwise over ~5 minutes to a solution of aryl thiol (15 mmol, 1.0 equiv) and triethylamine (2.5 mL, 18 mmol, 1.2 equiv) in acetonitrile (75 mL, 0.2 M in aryl thiol) at 0 ºC, and the mixture was stirred while warming to room temperature. Upon consumption of the aryl thiol, the solvent was evaporated and the residue was dissolved in ethyl acetate (100 mL). The resulting solution was washed with water (2 ×) and brine (1 ×), and the organic layer was dried over sodium sulfate, and concentrated. The crude alkyl–aryl sulfide was used without further purification.

A solution of potassium permanganate (3.56 g, 22.5 mmol, 1.5 equiv) in water (150 mL) was added over ~5 min to a solution of alkyl–aryl sulfide (≤15 mmol, ≤1.0 equiv) in acetic acid (75 mL). Upon consumption of the alkyl–aryl sulfide and the corresponding sulfoxide (the intermediate formed before generation of the desired sulfone), saturated aqueous sodium bisulfite was added until the dark solution turned clear. The resulting aqueous solution was extracted with ethyl acetate (3 × 200 mL), and the combined organic layers were washed with sodium bicarbonate (1 ×), water (1 ×), and brine (1 ×), dried over sodium sulfate, and concentrated. The residue was purified by silica-gel chromatography to afford the alkyl–aryl sulfone.

*Note: some sulfones were obtained more conveniently by cooling the clear, aqueous solution obtained after quenching with sodium bisulfite to 0 ºC, collecting the solid by filtration, and purifying the resulting crude solid by recrystallization. Yields were modestly diminished in these cases because some of the sulfone remained dissolved in the aqueous filtrate. This material could be recovered by extraction and silica-gel chromatography as described in the preceding paragraph.*

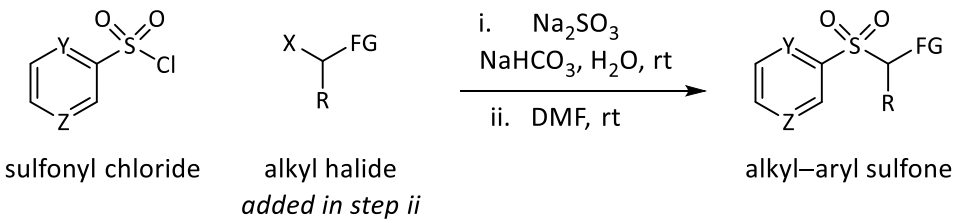
**General Procedure B: Preparation of Alkyl–Aryl Sulfones from Aryl Thiols (Oxone Oxidation)**




Alkyl halide (18 mmol, 1.2 equiv) was added dropwise over ~5 minutes to a solution of aryl thiol (15 mmol, 1.0 equiv) and triethylamine (2.5 mL, 18 mmol, 1.2 equiv) in acetonitrile (75 mL) at 0 °C, and the mixture was stirred while warming to room temperature. Upon consumption of the aryl thiol, the solvent was evaporated, and the residue was dissolved in ethyl acetate (100 mL). The resulting solution was washed with water (2 ×) and brine (1 ×), and the organic layer was dried over sodium sulfate, and concentrated. The crude alkyl–aryl sulfide was used without further purification.

A solution of Oxone® (15 g, 99 mmol, 6.6 equiv) in water (150 mL) was added over ~10 min to a solution of alkyl–aryl sulfide (≤15 mmol, ≤1.0 equiv) in 1:1 tetrahydrofuran/methanol (150 mL). The resulting mixture was heated to 60 ºC. Upon consumption of the alkyl–aryl sulfide and the corresponding sulfoxide, the intermediate formed before generation of the desired sulfone, the mixture was cooled to room temperature and filtered through Celite®. The filtrate was extracted with ethyl acetate (3 × 200 mL), and the combined organic layers were washed with sodium bicarbonate (1 ×), water (1 ×), and brine (1 ×), dried over sodium sulfate, and concentrated. The residue was purified by silica-gel chromatography or recrystallization to afford the alkyl–aryl sulfone.

**General Procedure C: Preparation of Alkyl–Aryl Sulfones from Aryl Sulfonyl Chlorides**

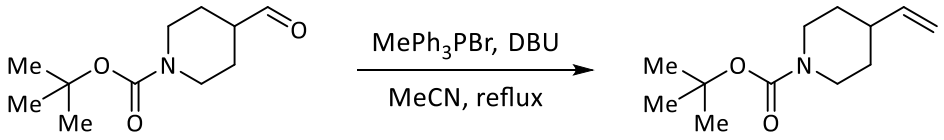



A mixture of aryl sulfonyl chloride (15 mmol, 1.0 equiv), sodium sulfite (3.78 g, 30 mmol, 2.0 equiv), and sodium bicarbonate (2.52 g, 30 mmol, 2.0 equiv) in water (15 mL) open to air was

stirred at room temperature until vigorous gas evolution was complete (typically after a few minutes), then heated to 80 °C. Upon consumption of the aryl sulfonyl chloride, water was evaporated. The residue was dissolved in boiling ethanol (50 mL), the hot suspension was filtered through Celite®, the filter cake was washed with further boiling ethanol (2 × 50 mL), and the filtrate was concentrated. The crude aryl sulfinate was used without further purification.

Alkyl halide (18 mmol, 1.2 equiv) was added dropwise over ~5 minutes to a solution of alkyl–aryl sulfinate (≤15 mmol, ≤1.0 equiv) in dimethylformamide (30 mL) at room temperature. Upon consumption of the aryl sulfinate, the mixture was poured over ice. The resulting cold suspension was filtered, and the filter cake was washed with ethyl acetate. The filtrate was washed water (3 ×) and brine (3 ×), dried over sodium sulfate, and concentrated. The residue was purified by silica-gel chromatography or recrystallization to afford the alkyl–aryl sulfone.

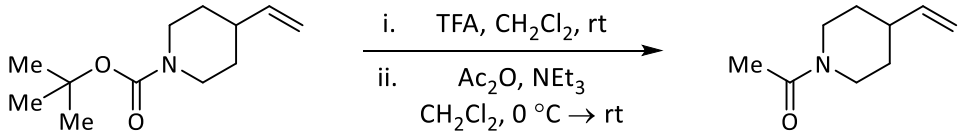
**Preparation of *tert*-butyl 4-vinylpiperidine-1-carboxylate (11)**




**11**

A mixture of *tert*-butyl 4-vinylpiperidine-1-carboxylate (4.27 g, 20.0 mmol, 1.0 equiv), methyltriphenyl phosphonium bromide (14.3 g, 40 mmol, 2.0 equiv), and 1,8-diazabicyclo-[5.4.0]undec-7-ene (6.0 mL, 40.0 mol, 2.0 equiv) in acetonitrile (350 mL) was refluxed overnight. After cooling to room temperature, the mixture was and diluted with ethyl acetate, washed with water (1 ×) and brine (1 ×), dried over sodium sulfate, and concentrated. The residual oil was purified by silica-gel chromatography (10% ethyl acetate/hexanes) to afford olefin **11** as a clear oil (3.4 g, 80%).

**Preparation of 1-(4-vinylpiperidin-1-yl)ethan-1-one (S26)**




**11** **S26**

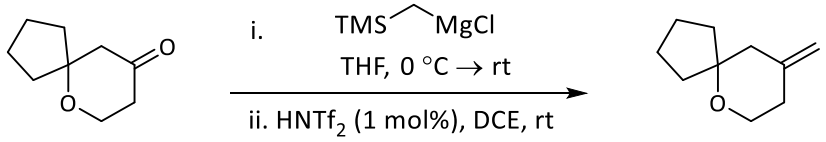
Trifluoroacetic acid (19 mL, 250 mmol, 5.0 equiv) was added dropwise to a solution of Boc amine **11** (5.56 g, 50 mmol, 1.0 equiv) in dichloromethane (250 mL) at room temperature. Upon consumption of **11**, the solution was concentrated to remove the excess trifluoroacetic acid and volatile byproducts, and the residue was redissolved in dichloromethane. The resulting solution was washed with saturated aqueous sodium bicarbonate (1 ×), water (1 ×), and brine (1 ×), dried over sodium sulfate, and concentrated. The crude secondary amine was used in the next step without further purification.

Acetic anhydride (5.2 mL, 55 mmol, 1.1 equiv) and triethylamine (10.5 mL, 75 mmol, 1.5 equiv) were added to a solution of the crude secondary amine (≤50 mmol, ≤1.0 equiv) in (170 mL) at 0 °C, and the mixture was stirred while warming to room temperature. Upon consumption of the free amine, the mixture was concentrated and purified by silica-gel chromatography to afford acetamide **S26** as a pale-orange oil (6.76 g, 88%).

## V. Synthesis of (±)-Oliceridine

6-Oxaspiro[4.5]decan-9-one (4.7 g, 30 mmol, 1.0 equiv) was prepared in two steps from but-3-en-1-ol and cyclopentanone as previously described[4] for use in the preparation of **57** (see below).

**Synthesis of 9-methylene-6-oxaspiro[4.5]decane[5] (57)**




*2 steps from commercial*

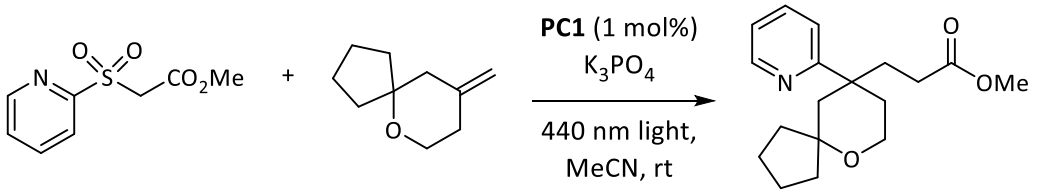
**57**

A solution of (trimethylsilyl)methylmagnesium chloride (1 M in tetrahydrofuran, 90 mL, 90 mmol, 3.0 equiv) was added dropwise to a solution of 6-oxaspiro[4.5]decan-9-one (4.7 g, 30 mmol, 1.0 equiv) in tetrahydrofuran (150 mL) under nitrogen at 0 °C. The reaction mixture was stirred overnight while warming to room temperature, quenched with saturated ammonium chloride, and extracted with dichloromethane (3 ×). The combined organic extracts were then washed with water (1 ×) and brine (1 ×), dried over sodium sulfate, and concentrated. The crude silane was used without further purification.

A solution of trifluoromethanesulfonimide (1 M in 1,2-dichloroethane, 0.3 mL, 0.3 mmol, 1 mol%) was added to a solution of the crude silane (≤15 mmol, ≤1.0 equiv) in 1,2-dichloroethane (60 mL) under nitrogen at room temperature. After 15 minutes, the mixture was washed with water (1 ×) and brine (1 ×), dried over sodium sulfate, and concentrated. The residual oil was purified by silica-gel chromatography (5% ethyl acetate/hexanes) to afford olefin **57** as a pale-yellow oil (1.54 g, 10.1 mmol, 34%).

*Note: This Peterson olefination procedure, which was adapted from a recent report,[6] proved significantly more effective than a range of Wittig protocols in our hands.*

**Synthesis of methyl 3-(9-(pyridin-2-yl)-6-oxaspiro[4.5]decan-9-yl)propanoate (58)**

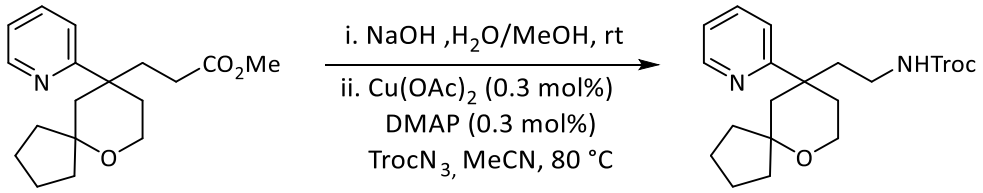



**12** **57** **58**

*1:1 stoichiometry* *95% yield*

Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1** using 0.69 mmol of the alkyl–aryl sulfone and only 1 equivalent of olefin **57**. Desired product **58** was obtained as a clear, colorless oil (199 mg, 95%). See "Section VI. Characterization Data" for isolation conditions and spectroscopic data.

**Synthesis of 2,2,2-trichloroethyl (2-(9-(pyridin-2-yl)-6-oxaspiro[4.5]decan-9-yl)ethyl)carbamate (59)**



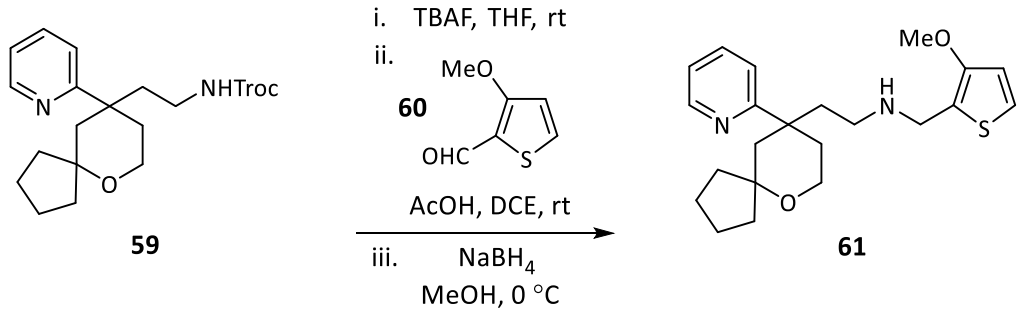

**58** **59**

A solution of sodium hydroxide (3 M in water, 2.9 mL, 8.7 mmol, 3.0 equiv) was added slowly to a solution of ester **58** (892 mg, 2.9 mmol, 1.0 equiv) 1:1 water/methanol (17 mL) at room temperature. Upon consumption of the ester (~3 hours), the reaction mixture was quenched and adjusted to pH 7 with 1 M hydrochloric acid. The resulting neutral solution was extracted with ethyl acetate (3 ×), and the combined organic extracts were washed with water (1 ×) and brine (1 ×), dried over sodium sulfate, and concentrated. The crude carboxylic acid was used without further purification.

Following a modified Curtius Rearrangement procedure,[7] a solution of the crude carboxylic acid (1.0 g, ≤3.5 mmol, ≤1.0 equiv) in acetonitrile (70 mL) was sparged with nitrogen for ~10 minutes. $Cu(OAc)_2$ (1 M in acetonitrile, 0.11 mL, 0.11 mmol, 0.3 mol%), 4-dimethylaminopyridine (1 M solution in acetonitrile 0.11 mL, 0.11 mmol, 0.3 mol%), and 2,2,2-trichloroethyl carbonazidate (0.92 g, 4.2 mmol, 1.2 equiv) were then added to the degassed solution of carboxylic acid under nitrogen. The resulting mixture was heated to 80 °C overnight. After cooling to room temperature,

the solvent was evaporated and the residual oil was purified by silica-gel chromatography (10–30% ethyl acetate/hexane) to afford Troc amine **59** as a white solid (1.05 g, 89%).

**Synthesis of N-((3-methoxythiophen-2-yl)methyl)-2-(9-(pyridin-2-yl)-6-oxaspiro[4.5]decan-9-yl)ethan-1-amine[5] (61)**




Tetra-*n*-butylammonium fluoride (1 M solution in tetrahydrofuran, 1.6 mL, 1.6 mmol, 4.0 equiv) was added slowly to a solution of Troc amine **59** (140 mg, 0.4 mmol, 1.0 equiv) in tetrahydrofuran (3.2 mL) under nitrogen, and the mixture was stirred overnight at room temperature. Upon confirming consumption of **59** (TLC, 40% ethyl acetate/hexanes), the solvent was evaporated to afford a crude primary amine, which was used without further purification.

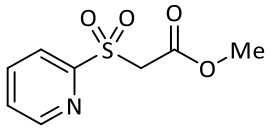
3-Methoxythiophene-2-carbaldehyde[8] (**60**, 171 mg, 1.2 mmol, 3.0 equiv) and acetic acid (23 µL, 0.4 mmol, 1.0 equiv) were added to a solution of the crude primary amine (≤0.4 mmol, ≤1.0 equiv) in 1,2-dichloroethane (1.4 mL) under nitrogen, and the mixture was stirred overnight at room temperature. Conversion to the corresponding imine was verified by removing an aliquot that was diluted with 1 M sodium hydroxide, extracted with dichloromethane, concentrated, dissolved in $CD_3CN$, and analyzed by $^1H$ NMR. The reaction mixture was cooled to 0 °C for the final step.

Sodium borohydride (76 mg, 2.0 mmol, 5.0 equiv, added in one portion) and methanol (2 mL, added carefully while venting the reaction vessel) were added to the reaction mixture containing the imine at 0 °C. The resulting solution was stirred under nitrogen overnight while warming to room temperature. The solvent was removed, and the residue was dissolved in ethyl acetate and washed with 1 M sodium hydroxide (1 ×). The desired secondary amine was extracted from the organic layer with 1 M hydrochloric acid (2 ×). The combined aqueous extracts were basified to ~pH 10 with saturated aqueous sodium bicarbonate and extracted with ethyl acetate (2 ×). The

combined organic layers were washed with water (1 ×) and brine (1 ×), dried over sodium sulfate, and concentrated. The residue was purified by silica-gel chromatography (1% triethylamine/ethyl acetate) to afford secondary amine **61** as a yellow oil (82 mg, 0.21 mmol, 53%).

## VI. Characterization Data

**Methyl 2-(pyridin-2-ylsulfonyl)acetate[9] (12)**



Prepared according to General Procedure A in "Section IV. Procedures for Substrate Preparation" using 50 mmol of the aryl thiol.

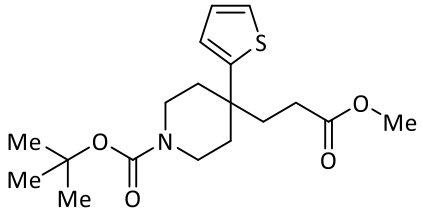
**Chromatography solvent:** 30-40% ethyl acetate/hexanes

**Physical characteristics:** white solid

**Yield:** 8.4 g (78%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.85 – 8.67 (m, 1H), 8.11 (dt, J = 7.9, 1.1 Hz, 1H), 8.00 (td, J = 7.8, 1.7 Hz, 1H), 7.59 (ddd, J = 7.7, 4.7, 1.2 Hz, 1H), 4.49 (s, 2H), 3.69 (s, 3H).

***Tert*-butyl 4-(3-methoxy-3-oxopropyl)-4-(thiophen-2-yl)piperidine-1-carboxylate (14)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 10-20% ethyl acetate/hexanes

**Physical characteristics:** pink solid

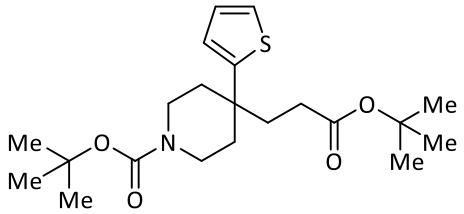
**Yield:** 270 mg (95%)

**ESI-HRMS:** m/z calculated for $C_{18}H_{27}NO_4S$ $[M+H]^+$ 354.1734, found 354.1730.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.21 (dd, *J* = 5.1, 1.1 Hz, 1H), 6.95 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.79 (dd, *J* = 3.5, 1.2 Hz, 1H), 3.84 – 3.69 (m, 2H), 3.59 (s, 3H), 3.15 – 3.00 (m, 2H), 2.14 – 1.99 (m, 4H), 1.96 – 1.87 (m, 2H), 1.76 – 1.62 (m, 2H), 1.43 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 174.03, 154.97, 149.44, 126.94, 124.40, 124.00, 79.56, 51.73, 40.78 (br), 40.00 (br), 39.78, 39.56, 36.94, 28.92, 28.55.

***Tert*-butyl 4-(3-(tert-butoxy)-3-oxopropyl)-4-(thiophen-2-yl)piperidine-1-carboxylate (15)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-20% ethyl acetate/hexanes

**Physical characteristics:** white solid

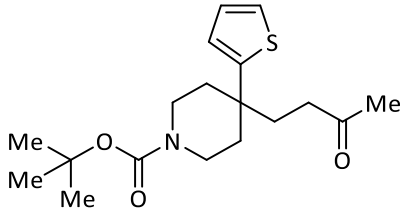
**Yield:** 294 mg (93%)

**ESI-HRMS:** m/z calculated for $C_{21}H_{33}NO_4S$ $[M+H]^+$ 396.2203, found 396.2198.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.21 (dd, *J* = 5.1, 1.1 Hz, 1H), 6.96 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.79 (dd, *J* = 3.5, 1.1 Hz, 1H), 3.87 – 3.64 (m, 2H), 3.16 – 3.02 (m, 2H), 2.09 – 1.96 (m, 4H), 1.91 – 1.82 (m, 2H), 1.76 – 1.63 (m, 2H), 1.44 (s, 9H), 1.39 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.02, 155.02, 149.83, 126.94, 124.26, 123.86, 80.41, 79.55, 40.28 (br), 39.75, 39.54, 37.08 (br), 30.29, 28.58, 28.19.

***Tert*-butyl 4-(3-oxobutyl)-4-(thiophen-2-yl)piperidine-1-carboxylate (16)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-35% ethyl acetate/hexanes

**Physical characteristics:** pink oil

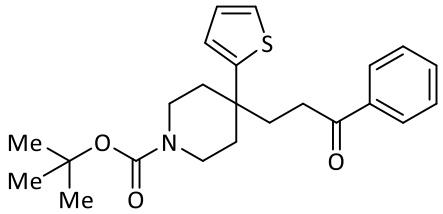
**Yield:** 227 mg (84%)

**ESI-HRMS:** m/z calculated for $C_{18}H_{27}NO_3S$ $[M+H]^+$ 338.1784, found 338.1785.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.21 (dd, *J* = 5.1, 1.1 Hz, 1H), 6.97 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.80 (dd, *J* = 3.5, 1.1 Hz, 1H), 3.88 – 3.58 (m, 2H), 3.16 – 2.99 (m, 2H), 2.30 – 2.15 (m, 2H), 2.10 – 1.96 (m, 5H), 1.85 (t, 2H), 1.74 – 1.63 (m, 2H), 1.43 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 208.10, 154.69, 149.67, 126.71, 124.00, 123.68, 79.24, 40.52 (br), 39.70 (br), 39.16, 38.09, 38.06, 37.05 (br), 36.72 (br), 29.81, 28.32.

***Tert*-butyl 4-(3-oxo-3-phenylpropyl)-4-(thiophen-2-yl)piperidine-1-carboxylate (17)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 10% ethyl acetate/hexanes

**Physical characteristics:** white solid

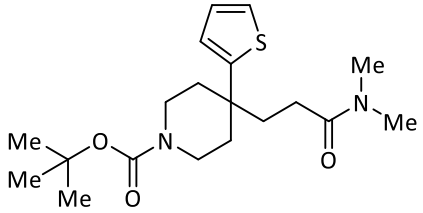
**Yield:** 165 mg (52%)

**ESI-HRMS:** m/z calculated for $C_{23}H_{29}NO_3S$ $[M+H]^+$ 400.1941, found 400.1944.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.81 – 7.75 (m, 2H), 7.54 – 7.48 (m, 1H), 7.43 – 7.36 (m, 2H), 7.25 – 7.21 (m, 1H), 7.02 – 6.96 (m, 1H), 6.89 – 6.84 (m, 1H), 3.88 – 3.69 (m, 2H), 3.21 – 3.08 (m, 2H), 2.81 – 2.66 (m, 2H), 2.20 – 2.06 (m, 2H), 2.02 (t, 2H), 1.83 – 1.70 (m, 2H), 1.44 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 200.06, 155.00, 150.05, 136.82, 133.12, 128.65, 128.11, 127.01, 124.31, 123.98, 79.59, 40.78 (br), 40.03 (br), 39.73, 39.12, 37.00 (br), 33.33, 28.56.

***Tert*-butyl-4-(3-(dimethylamino)-3-oxopropyl)-4-(thiophen-2-yl)piperidine-1-carboxylate (18)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 10-40% ethyl acetate/hexanes

**Physical characteristics:** white solid

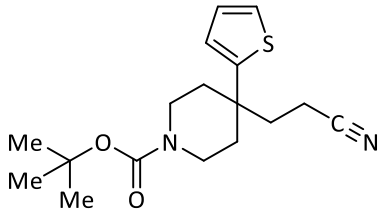
**Yield:** 202 mg (69%)

**ESI-HRMS:** m/z calculated for $C_{19}H_{30}N_2O_3S$ $[M+H]^+$ 367.2050, found 367.2044.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.20 (dd, $J$ = 5.1, 1.1 Hz, 1H), 6.96 (dd, $J$ = 5.1, 3.5 Hz, 1H), 6.81 (dd, $J$ = 3.5, 1.1 Hz, 1H), 3.87 – 3.60 (m, 2H), 3.16 – 3.06 (m, 2H), 2.86 (s, 3H), 2.79 (s, 3H), 2.15 – 2.00 (m, 4H), 1.96 – 1.87 (m, 2H), 1.80 – 1.66 (m, 2H), 1.43 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 172.79, 155.02, 150.26, 126.90, 124.16, 123.81, 79.55, 40.75 (br), 40.02 (br), 39.98, 39.67, 37.18, 36.93 (br), 35.52, 28.56, 28.02.

***Tert*-butyl 4-(2-cyanoethyl)-4-(thiophen-2-yl)piperidine-1-carboxylate (19)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-35% ethyl acetate/hexanes

**Physical characteristics:** white solid

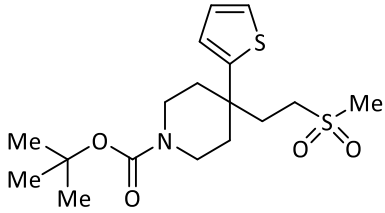
**Yield:** 210 mg (83%)

**ESI-HRMS:** m/z calculated for $C_{17}H_{24}N_2O_2S$ $[M+H]^+$ 321.1631, found 321.1626.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.30 – 7.23 (m, 1H), 7.00 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.84 (dd, *J* = 3.5, 1.1 Hz, 1H), 3.92 – 3.73 (m, 2H), 3.04 (t, *J* = 12.2 Hz, 2H), 2.17 – 2.02 (m, 4H), 1.98 – 1.89 (m, 2H), 1.78 – 1.65 (m, 2H), 1.44 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 154.86, 147.65, 127.32, 124.99, 124.76, 119.87, 79.79, 40.84, 40.34 (br), 39.95, 36.78, 28.55, 12.26.

***Tert*-butyl 4-(2-(methylsulfonyl)ethyl)-4-(thiophen-2-yl)piperidine-1-carboxylate (20)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 10-50% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

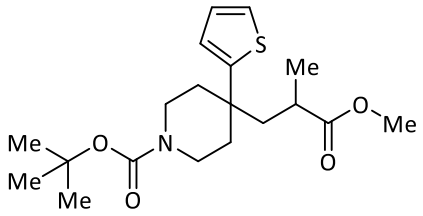
**Yield:** 240 mg (80%)

**LRMS:** m/z calculated for $C_{17}H_{27}NO_4S_2$ $[M+Na]^+$ 396.1, found 396.0.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.27 – 7.23 (m, 1H), 6.98 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.83 (dd, *J* = 3.5, 1.1 Hz, 1H), 3.92 – 3.69 (m, 2H), 3.09 (t, *J* = 11.1 Hz, 2H), 2.81 – 2.72 (m, 5H), 2.14 – 2.03 (m, 4H), 1.79 – 1.67 (m, 2H), 1.44 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 154.87, 148.13, 127.33, 124.74, 124.69, 79.81, 50.36, 40.52, 39.86, 39.43, 37.19, 36.92, 28.54.

***Tert*-butyl 4-(3-methoxy-2-methyl-3-oxopropyl)-4-(thiophen-2-yl)piperidine-1-carboxylate (21)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-15% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

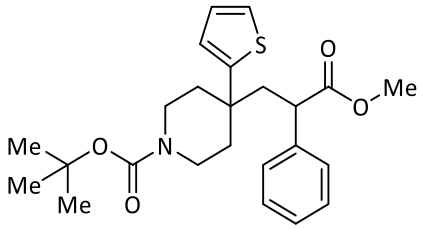
**Yield:** 258 mg (88%)

**ESI-HRMS:** m/z calculated for $C_{19}H_{29}N_2O_2S$ $[M+H]^+$ 368.1890, found 368.1884.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.21 (d, *J* = 5.1 Hz, 1H), 6.95 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.81 (d, *J* = 3.6 Hz, 1H), 3.77 (d, *J* = 13.7 Hz, 2H), 3.53 (s, 3H), 3.11 – 2.97 (m, 2H), 2.42 – 2.30 (m, 1H), 2.26 (dd, *J* = 13.9, 8.9 Hz, 1H), 2.12 – 1.95 (m, 2H), 1.74 – 1.61 (m, 2H), 1.52 – 1.47 (m, 1H), 1.43 (s, 9H), 0.99 (d, *J* = 6.9 Hz, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 177.37, 154.83, 149.41, 126.70, 124.59, 123.91, 79.40, 51.66, 49.04, 40.48 (br), 40.04, 39.72 (br), 37.96 (br), 36.10 (br), 35.25, 28.45, 20.03.

***Tert*-butyl 4-(3-methoxy-3-oxo-2-phenylpropyl)-4-(thiophen-2-yl)piperidine-1-carboxylate (22)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-25% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

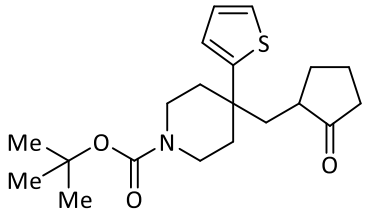
**Yield:** 209 mg (61%)

**ESI-HRMS:** m/z calculated for $C_{24}H_{31}NO_4S$ $[M+H]^+$ 430.2047, found 430.2050.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.27 – 7.21 (m, 4H), 7.15 – 7.09 (m, 2H), 6.99 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.84 (dd, *J* = 3.5, 1.1 Hz, 1H), 3.88 – 3.64 (m, 3H), 3.51 (s, 3H), 3.45 (dd, *J* = 8.6, 3.8 Hz, 1H), 3.13 – 2.93 (m, 2H), 2.66 (dd, *J* = 14.1, 8.7 Hz, 1H), 2.10 – 1.95 (m, 2H), 1.92 (dd, *J* = 14.1, 3.9 Hz, 1H), 1.80 – 1.69 (m, 1H), 1.65 – 1.55 (m, 1H), 1.43 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 174.40, 154.92, 149.23, 140.32, 128.82, 127.75, 127.30, 126.86, 124.93, 124.28, 79.54, 52.23, 48.93, 47.26, 40.88, 40.52, 39.91 (br), 37.51 (br), 37.02 (br), 28.56.

***Tert*-butyl 4-((2-oxocyclopentyl)methyl)-4-(thiophen-2-yl)piperidine-1-carboxylate (23)**




Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 10-30% ethyl acetate/hexanes

**Physical characteristics:** white solid

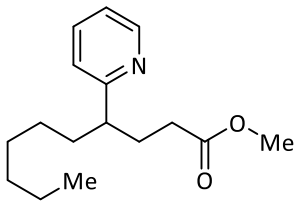
**Yield:** 201 mg (69%)

**ESI-HRMS:** m/z calculated for $C_{20}H_{29}NO_3S$ $[M+H]^+$ 364.1941, found 364.1945.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.21 (dd, *J* = 5.1, 1.1 Hz, 1H), 6.96 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.82 (dd, *J* = 3.6, 1.2 Hz, 1H), 3.87 – 3.67 (m, 2H), 3.20 – 3.02 (m, 2H), 2.34 – 2.16 (m, 2H), 2.15 – 2.03 (m, 2H), 2.03 – 1.67 (m, 6H), 1.65 – 1.52 (m, 1H), 1.50 – 1.39 (m, 10H), 1.32 – 1.13 (m, 1H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 221.08, 155.01, 150.47, 127.00, 124.15, 123.94, 79.55, 46.31, 45.81, 40.79 (br), 39.95, 39.89 (br), 38.24, 37.32 (br), 31.93, 28.58, 20.81.

**Methyl 4-(pyridin-2-yl)decanoate (24)**




Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-15% ethyl acetate/hexanes

**Physical characteristics:** yellow oil

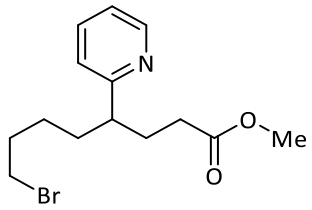
**Yield:** 167 mg (79%)

**ESI-HRMS:** m/z calculated for $C_{16}H_{25}NO_2$ $[M+H]^+$ 264.1958, found 264.1959.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.61 – 8.50 (m, 1H), 7.64 – 7.52 (m, 1H), 7.15 – 7.04 (m, 2H), 3.60 (s, 3H), 2.80 – 2.64 (m, 1H), 2.22 – 2.08 (m, 2H), 2.06 – 1.97 (m, 2H), 1.77 – 1.56 (m, 2H), 1.30 – 1.13 (m, 7H), 1.11 – 1.00 (m, 1H), 0.82 (t, J = 6.9 Hz, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 174.16, 164.29, 149.53, 136.35, 122.97, 121.43, 51.57, 47.31, 35.77, 32.24, 31.82, 30.61, 29.42, 27.53, 22.70, 14.16.

**Methyl 8-bromo-4-(pyridin-2-yl)octanoate (25)**




Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-50% dichloromethane/hexanes

**Physical characteristics:** clear, colorless oil

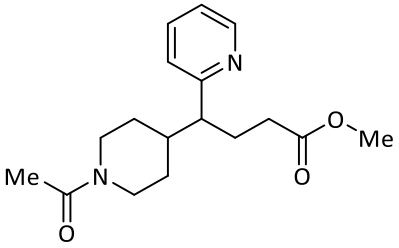
**NMR Yield:** 66% as judged by $^{1}$H NMR analysis of the crude mixture using mesitylene as an external standard

**ESI-HRMS:** m/z calculated for $C_{14}H_{20}BrNO_2$ $[M+H]^+$ 314.0750, found 314.0752.

**$^{1}$H NMR (400 MHz, $CDCl_3$):** δ 8.57 – 8.45 (m, 1H), 7.73 – 7.59 (m, 1H), 7.28 – 7.11 (m, 2H), 3.55 (s, 3H), 3.46 – 3.34 (m, 2H), 2.82 – 2.67 (m, 1H), 2.14 – 2.02 (m, 2H), 1.86 – 1.61 (m, 4H), 1.40 – 1.11 (m, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 174.51, 164.72, 150.30, 137.12, 124.14, 122.39, 51.83, 47.40, 35.21, 35.12, 33.45, 32.51, 31.29, 26.65.

**Methyl 4-(1-acetylpiperidin-4-yl)-4-(pyridin-2-yl)butanoate (26)**




Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-100% ethyl acetate/hexanes, then 1% methanol in ethyl acetate

**Physical characteristics:** yellow oil

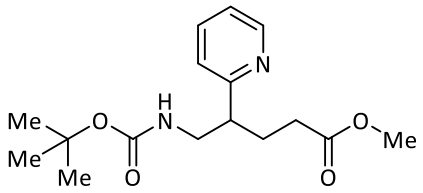
**Yield:** 183 mg (75%)

**ESI-HRMS:** m/z calculated for $C_{17}H_{24}N_2O_3$ $[M+H]^+$ 305.1860, found 305.1854.

**$^{1}$H NMR (400 MHz, $CDCl_3$):** (mixture of rotamers 1:1) δ 8.62 – 8.46 (m, 1H), 7.65 – 7.49 (m, 1H), 7.18 – 7.08 (m, 1H), 7.08 – 6.97 (m, 1H), 4.74 – 4.57 (m, 0.5 x 1H), 4.52 – 4.41 (m, 0.5 x 1H), 3.86 – 3.75 (m, 0.5 x 1H), 3.73 – 3.62 (m, 0.5 x 1H), 3.62 – 3.51 (m, 3H), 3.06 – 2.95 (m, 0.5 x 1H), 2.94 – 2.82 (m, 0.5 x 1H), 2.55 – 2.32 (m, 2H), 2.21 – 1.84 (m, 9H), 1.35 – 0.94 (m, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)**: (mixture of rotamers) δ 173.95, 173.88, 168.82, 162.18, 162.08, 149.80, 149.75, 136.34, 124.28, 124.18, 121.78, 121.76, 52.31, 52.28, 51.61, 46.81, 46.73, 41.90, 41.82, 40.82, 40.76, 32.13, 32.05, 30.97, 30.83, 30.15, 29.98, 26.90, 26.84, 21.53, 21.48.

**Methyl 5-((*tert*-butoxycarbonyl)amino)-4-(pyridin-2-yl)pentanoate (27)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 20% ethyl acetate/hexanes

**Physical characteristics:** pale-yellow oil

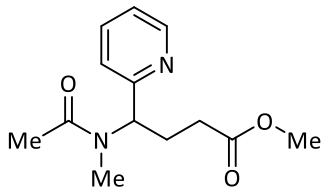
**Yield:** 228 mg (92%)

**ESI-HRMS:** m/z calculated for $C_{16}H_{24}N_2O_4$ $[M+H]^+$ 252.1594, found 252.1595.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.59 – 8.47 (m, 1H), 7.60 (td, J = 7.7, 1.9 Hz, 1H), 7.19 – 7.04 (m, 2H), 5.03 – 4.89 (m, 1H), 3.60 (s, 3H), 3.51 – 3.34 (m, 2H), 3.05 – 2.87 (m, 1H), 2.25 – 2.15 (m, 2H), 2.07 – 1.96 (m, 2H), 1.38 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.79, 161.91, 156.11, 149.67, 136.65, 123.77, 121.97, 79.20, 51.65, 46.47, 44.48, 31.81, 28.47, 27.67.

**Methyl 4-(N-methylacetamido)-4-(pyridin-2-yl)butanoate (28)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-40% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

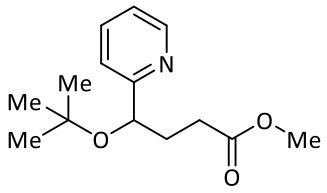
**Yield:** 198 mg (99%)

**ESI-HRMS:** m/z calculated for $C_{13}H_{18}N_2O_3$ $[M+H]^+$ 250.1317, found 251.1389.

**$^1$H NMR (400 MHz, $CDCl_3$):** (mixture of rotamers 7:3) δ 8.57 – 8.44 (m, 1H), 7.71 – 7.51 (m, 1H), 7.28 – 7.04 (m, 2H), 5.84 (dd, *J* = 9.1, 6.2 Hz, 0.7 × 1H), 5.01 (dd, *J* = 9.5, 5.7 Hz, 0.3 × 1H), 3.62 (s, 0.3 × 3H), 3.60 (s, 0.7 × 3H), 2.73 (s, 0.7 × 3H), 2.65 (s, 0.3 × 3H), 2.63 – 2.51 (m, 0.3 × 1H), 2.49 – 2.12 (m, 5H), 2.05 (s, 0.7 × 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** (mixture of rotamers) δ 173.57, 173.44, 171.44, 171.27, 158.65, 158.29, 149.54, 148.95, 136.88, 136.74, 123.69, 122.79, 122.58, 121.76, 61.33, 55.82, 51.85, 51.71, 31.16, 30.73, 30.51, 27.82, 25.61, 24.59, 22.21, 21.93.

**Methyl 4-(*tert*-butoxy)-4-(pyridin-2-yl)butanoate (29)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-20% ethyl acetate/hexanes

**Physical characteristics:** pale-yellow oil

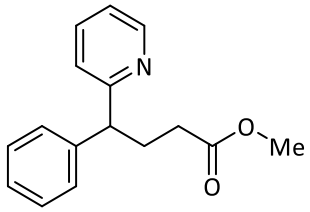
**Yield:** 194 mg (96%)

**ESI-HRMS:** m/z calculated for $C_{14}H_{21}NO_3$ $[M+H]^+$ 252.1594, found 252.1595.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.49 – 8.33 (m, 1H), 7.59 (td, J = 7.6, 1.8 Hz, 1H), 7.49 – 7.36 (m, 1H), 7.12 – 6.94 (m, 1H), 4.62 – 4.43 (m, 1H), 3.57 (s, 3H), 2.46 – 2.21 (m, 2H), 2.00 – 1.79 (m, 2H), 1.05 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 174.04, 165.27, 148.55, 136.52, 121.94, 120.84, 74.62, 74.40, 51.55, 33.35, 30.52, 28.51.

**Methyl 4-phenyl-4-(pyridin-2-yl)butanoate (30)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**, except that 1 equivalent of olefin (styrene) was employed and the reaction mixture was irradiated with green light (510–575 nm). Blue-light irradiation led to lower yields and the formation of a white film on the vial surface, which we attribute to light-induced styrene polymerization. Even with this change, a major byproduct corresponding to the addition of a second equivalent of styrene to the desired product (as judged by LC-MS) lowered the yield.

**Chromatography solvent:** 0-11% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

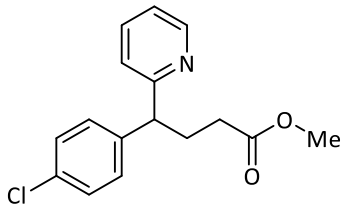
**Yield:** 35% as judged by calibrated $^1$H NMR analysis after attempted isolation (one impurity could not be fully removed; the cleanest fraction, ~90% pure, was characterized as below)

**ESI-HRMS:** m/z calculated for $C_{16}H_{17}NO_2$ $[M+H]^+$ 256.1332, found 256.1330.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.67 – 8.52 (m, 1H), 7.56 (td, *J* = 7.7, 1.9 Hz, 1H), 7.35 – 7.26 (m, 4H), 7.24 – 7.18 (m, 1H), 7.17 – 7.12 (m, 1H), 7.12 – 7.07 (m, 1H), 4.09 (t, *J* = 7.8 Hz, 1H), 3.63 (s, 3H), 2.66 – 2.48 (m, 1H), 2.49 – 2.36 (m, 1H), 2.29 (t, *J* = 7.8 Hz, 2H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.99, 163.09, 149.44, 143.13, 136.62, 128.73, 128.17, 126.79, 123.06, 121.60, 52.87, 51.67, 32.58, 30.14.

**Methyl 4-(4-chlorophenyl)-4-(pyridin-2-yl)butanoate (31)**




Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**, except that 1 equivalent of olefin (4-chlorostyrene) was employed and the reaction mixture was irradiated with green light (510–575 nm). Blue-light irradiation led to lower yields and the formation of a white film on the vial surface, which we attribute to light-induced styrene polymerization.

**Chromatography solvent:** 0-15% ethyl acetate/hexanes

**Physical characteristics:** pale yellow oil

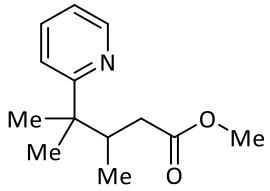
**Yield:** 147 mg (63%)

**ESI-HRMS:** m/z calculated for $C_{16}H_{16}ClNO_2$ $[M+H]^+$ 290.0942, found 290.0941.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.64 – 8.49 (m, 1H), 7.56 (td, J = 7.7, 1.9 Hz, 1H), 7.33 – 7.19 (m, 4H), 7.16 – 7.05 (m, 2H), 4.06 (t, J = 7.7 Hz, 1H), 3.63 (s, 3H), 2.64 – 2.50 (m, 1H), 2.44 – 2.31 (m, 1H), 2.27 (t, J = 7.7 Hz, 2H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.78, 162.45, 149.57, 141.65, 136.69, 132.54, 129.50, 128.80, 123.00, 121.77, 52.10, 51.68, 32.36, 30.12.

**Methyl 3,4-dimethyl-4-(pyridin-2-yl)pentanoate (32)**




Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-15% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

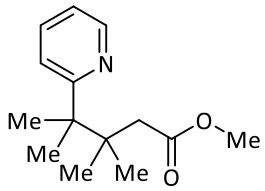
**Yield:** 116 mg (66%)

**ESI-HRMS:** m/z calculated for $C_{13}H_{19}NO_2$ $[M+H]^+$ 222.1489, found 222.1488.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.55 (ddd, J = 4.8, 2.0, 1.0 Hz, 1H), 7.59 (td, J = 7.7, 1.9 Hz, 1H), 7.29 (dt, J = 8.1, 1.1 Hz, 1H), 7.07 (ddd, J = 7.5, 4.8, 1.1 Hz, 1H), 3.59 (s, 3H), 2.61 – 2.50 (m, 1H), 2.25 (dd, J = 14.9, 3.3 Hz, 1H), 1.97 (dd, J = 14.8, 11.0 Hz, 1H), 1.29 (s, 6H), 0.82 (d, J = 6.8 Hz, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 174.24, 167.80, 148.71, 136.12, 120.93, 120.42, 51.54, 43.17, 39.53, 37.52, 24.99, 23.49, 15.14.

**Methyl 3,3,4-trimethyl-4-(pyridin-2-yl)pentanoate (33)**




Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-10% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

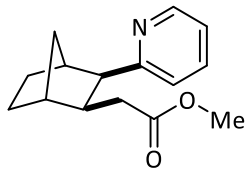
**Yield:** 67 mg (35%)

**ESI-HRMS:** m/z calculated for $C_{14}H_{21}NO_2$ $[M+H]^+$ 236.1645, found 236.1644.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.59 – 8.51 (m, 1H), 7.60 – 7.53 (m, 1H), 7.33 – 7.28 (m, 1H), 7.08 (ddd, J = 7.4, 4.8, 1.1 Hz, 1H), 3.57 (s, 3H), 2.31 (s, 2H), 1.38 (s, 6H), 0.97 (s, 6H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.88, 165.97, 147.85, 135.24, 122.66, 120.93, 51.23, 46.17, 42.36, 38.89, 23.63, 22.74.

**(±)-Methyl 2-(3-(pyridin-2-yl)bicyclo[2.2.1]heptan-2-yl)acetate (34)**




Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-15% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

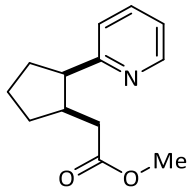
**Yield:** 128 mg (65%, isolated in >20:1 dr); crude 10:1 dr (minor isomer unknown, see "Section VII. Determination of Diastereochemical Outcomes (Products **34**–**39**)")

**ESI-HRMS:** m/z calculated for $C_{15}H_{19}NO_2$ $[M+H]^+$ 246.1489, found 246.1489.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.61 – 8.46 (m, 1H), 7.55 (td, J = 7.7, 1.9 Hz, 1H), 7.14 – 7.09 (m, 1H), 7.09 – 7.04 (m, 1H), 3.50 (s, 3H), 3.12 – 3.02 (m, 1H), 2.63 – 2.48 (m, 2H), 2.18 – 2.05 (m, 2H), 1.90 – 1.80 (m, 2H), 1.74 – 1.56 (m, 2H), 1.47 – 1.30 (m, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.97, 162.82, 149.13, 135.81, 123.51, 120.93, 53.01, 51.37, 44.82, 42.25, 41.48, 36.63, 35.32, 30.45, 29.45.

**(±)-Methyl 2-(2-(pyridin-2-yl)cyclopentyl)acetate (35)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-20% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

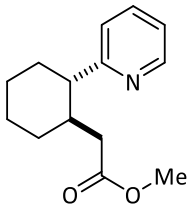
**Yield:** 147 mg (84%, isolated in >20:1 *cis*/*trans*); crude >20:1 *cis*/*trans* (see "Section VII. Determination of Diastereochemical Outcomes (Products **34**–**39**)")

**ESI-HRMS:** m/z calculated for $C_{13}H_{17}NO_2$ $[M+H]^+$ 220.1332, found 220.1326.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.59 – 8.49 (m, 1H), 7.54 (td, J = 7.7, 1.9 Hz, 1H), 7.13 – 6.99 (m, 2H), 3.52 (s, 3H), 3.41 (q, J = 7.9 Hz, 1H), 2.81 – 2.65 (m, 1H), 2.13 – 2.01 (m, 2H), 2.01 – 1.87 (m, 4H), 1.77 – 1.64 (m, 1H), 1.64 – 1.51 (m, 1H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.94, 163.07, 149.21, 135.94, 123.43, 121.17, 51.38, 49.78, 40.76, 35.93, 31.93, 30.11, 24.14.

**(±)-Methyl 2-(2-(pyridin-2-yl)cyclohexyl)acetate (36)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-20% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

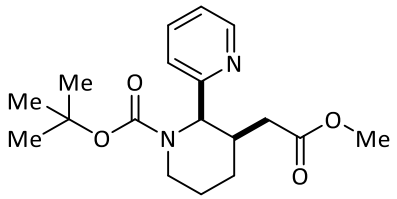
**Yield:** 130 mg (70%, isolated in 5:1 *trans*/*cis*); crude 5:1 *trans*/*cis* (see "Section VII. Determination of Diastereochemical Outcomes (Products **34**–**39**)")

**ESI-HRMS:** m/z calculated for $C_{14}H_{19}NO_2$ $[M+H]^+$ 234.1489, found 234.1488.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.58 – 8.45 (m, 1H), 7.62 – 7.47 (m, 1H), 7.19 – 6.98 (m, 2H), 3.49 (s, 0.8 × 3H), 3.46 (s, 0.2 × 3H), 3.05 – 2.96 (m, 0.2 × 1H), 2.70 – 2.61 (m, 0.2 × 1H), 2.44 (td, *J* = 11.5, 3.4 Hz, 0.8 × 1H), 2.38 – 2.15 (m, 1H), 2.11 – 1.70 (m, 6H), 1.63 – 1.05 (m, 5H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.87, 173.43, 164.59, 163.94, 149.31, 148.98, 136.53, 136.19, 122.40, 122.19, 121.43, 121.19, 51.96, 51.33, 51.28, 47.70, 39.50, 38.71, 36.00, 34.16, 32.54, 32.27, 30.33, 26.37, 26.03, 25.86, 25.10, 20.76.

**(±)-*Tert*-butyl 3-(2-methoxy-2-oxoethyl)-2-(pyridin-2-yl)piperidine-1-carboxylate (37)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-20% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

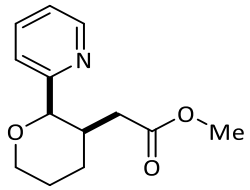
**Yield:** 247 mg (93%, isolated in >20:1 *cis*/*trans*); crude >20:1 *cis*/*trans* (see "Section VII. Determination of Diastereochemical Outcomes (Products **34**–**39**)")

**ESI-HRMS:** m/z calculated for $C_{18}H_{26}N_2O_4$ $[M+H]^+$ 335.1965, found 335.1963.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.63 – 8.40 (m, 1H), 7.81 – 7.58 (m, 1H), 7.39 – 7.06 (m, 2H), 5.55 – 5.12 (m, 1H), 4.02 – 3.80 (m, 1H), 3.59 (s, 3H), 3.37 (td, J = 12.8, 3.3 Hz, 1H), 2.47 – 2.25 (m, 1H), 2.25 – 1.98 (m, 3H), 1.91 – 1.73 (m, 1H), 1.63 – 1.50 (m, 2H), 1.36 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.53, 160.90, 155.83, 149.45, 137.26, 125.44, 123.19, 80.03, 58.86 (br), 57.53 (br), 51.97, 41.46 (br), 40.84 (br), 38.47, 37.12, 28.59.

**(±)-Methyl 2-(2-methyl-2-(pyridin-2-yl)cyclohexyl)acetate (38)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-20% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

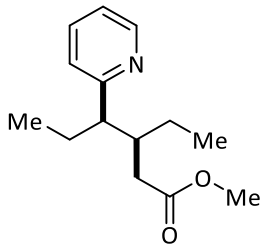
**Yield:** 178 mg (89%, isolated in >20:1 *cis*/*trans*); crude >20:1 *cis*/*trans* (see "Section VII. Determination of Diastereochemical Outcomes (Products **34**–**39**)")

**ESI-HRMS:** m/z calculated for $C_{13}H_{17}NO_3$ $[M+H]^+$ 236.1281, found 236.1281.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.59 – 8.48 (m, 1H), 7.72 – 7.60 (m, 1H), 7.42 – 7.33 (m, 1H), 7.19 – 7.08 (m, 1H), 4.67 (d, J = 2.5 Hz, 1H), 4.25 – 4.14 (m, 1H), 3.70 – 3.59 (m, 1H), 3.50 (s, 3H), 2.82 – 2.68 (m, 1H), 2.42 (dd, J = 15.6, 10.1 Hz, 1H), 1.98 – 1.79 (m, 3H), 1.50 – 1.36 (m, 1H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.54, 160.26, 148.84, 136.62, 122.17, 120.63, 81.95, 69.44, 51.50, 34.52, 31.18, 27.79, 20.73.

**(±)-*Tert*-butyl 3-(2-methoxy-2-oxoethyl)-2-(pyridin-2-yl)piperidine-1-carboxylate (39)**




Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-10% ethyl acetate/hexanes

**Physical characteristics:** pale-yellow oil

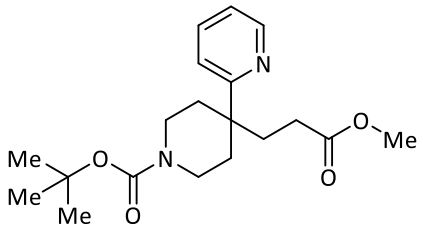
**Yield:** using *trans*-3-hexene: 168 mg (89%, isolated in 17:1 *syn*/*anti*); crude 17:1 *syn*/*anti* (see "Section VII. Determination of Diastereochemical Outcomes (Products **34**–**39**)"); using *cis*-3-hexene: 165 mg (88%, isolated in >20:1 *syn*/*anti*); crude 15:1 *syn*/*anti*

**ESI-HRMS:** m/z calculated for $C_{14}H_{21}NO_2$ $[M+H]^+$ 236.1645, found 236.1643.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.59 – 8.48 (m, 1H), 7.57 (td, *J* = 7.6, 1.9 Hz, 1H), 7.18 – 7.00 (m, 2H), 3.68 (s, 0.05 × 3H), 3.57 (s, 0.95 × 3H), 2.70 (q, *J* = 7.3 Hz, 1H), 2.34 – 2.17 (m, 2H), 2.06 (dd, *J* = 14.8, 7.8 Hz, 1H), 1.78 (p, *J* = 7.3 Hz, 2H), 1.51 – 1.32 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H), 0.70 (t, *J* = 7.3 Hz, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 174.25, 163.32, 149.27, 136.03, 124.11, 121.36, 51.54, 51.45, 41.00, 36.13, 24.89, 24.08, 12.41, 10.69.

***Tert*-butyl 4-(3-methoxy-3-oxopropyl)-4-(pyridin-2-yl)piperidine-1-carboxylate (40)**




Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 20-30% ethyl acetate/hexanes

**Physical characteristics:** pale-yellow oil

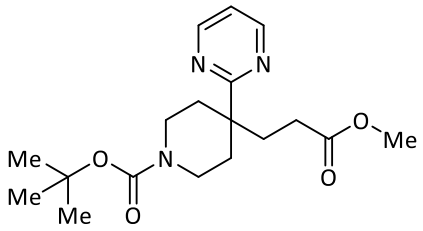
**Yield:** 253 mg (91%)

**ESI-HRMS:** m/z calculated for $C_{19}H_{28}N_2O_4$ $[M+H]^+$ 349.2122, found 349.2123.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.62 – 8.53 (m, 1H), 7.68 – 7.58 (m, 1H), 7.29 – 7.22 (m, 1H), 7.15 – 7.05 (m, 1H), 3.87 – 3.60 (m, 2H), 3.55 (s, 3H), 3.03 – 2.83 (m, 2H), 2.40 – 2.27 (m, 2H), 2.04 – 1.87 (m, 4H), 1.71 – 1.58 (m, 2H), 1.42 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 174.08, 163.30, 155.10, 149.26, 136.50, 121.37, 121.32, 79.37, 51.65, 42.27, 41.11 (br), 40.21 (br), 37.63, 34.55, 28.75, 28.55.

***Tert*-butyl 4-(3-methoxy-3-oxopropyl)-4-(pyrimidin-2-yl)piperidine-1-carboxylate (41)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC2**.

**Chromatography solvent:** 20-40% ethyl acetate/hexanes

**Physical characteristics:** yellow solid

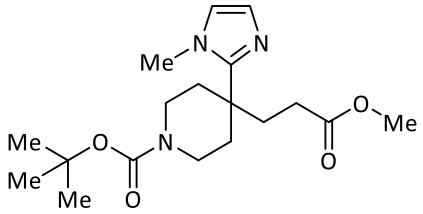
**Yield:** 209mg (75%)

**ESI-HRMS:** m/z calculated for $C_{18}H_{27}N_3O_4$ $[M+H]^+$ 350.20743, found 350.2077.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.70 (d, *J* = 4.8 Hz, 2H), 7.11 (t, *J* = 4.9 Hz, 1H), 3.93 – 3.73 (m, 2H), 3.55 (s, 3H), 2.78 (t, *J* = 11.3 Hz, 2H), 2.58 – 2.47 (m, 2H), 2.10 – 1.92 (m, 4H), 1.64 – 1.54 (m, 2H), 1.42 (s, 10H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.97, 172.73, 156.97, 155.14, 118.61, 79.32, 51.68, 44.39, 41.40 (br), 40.71 (br), 37.59, 34.28, 28.78, 28.57.

***Tert*-butyl 4-(3-methoxy-3-oxopropyl)-4-(1-methyl-1H-imidazol-2-yl)piperidine-1-carboxylate (42)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 1% triethylamine/ethyl acetate

**Physical characteristics:** pale-yellow oil

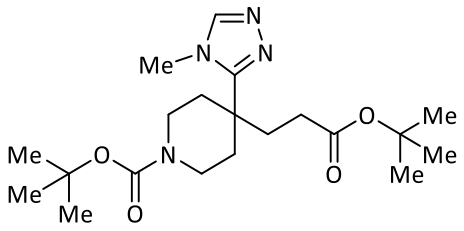
**NMR Yield:** 83% as judged by $^1$H NMR analysis of the crude mixture using mesitylene as an internal standard

**ESI-HRMS:** m/z calculated for $C_{18}H_{29}N_3O_4$ $[M+H]^+$ 366.2387, found 366.2390.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 6.87 (d, *J* = 1.2 Hz, 1H), 6.77 (d, *J* = 1.2 Hz, 1H), 3.74 (dt, *J* = 13.7, 4.1 Hz, 2H), 3.67 (s, 3H), 3.50 (s, 3H), 3.08 – 2.84 (m, 2H), 2.44 – 2.33 (m, 2H), 1.98 – 1.96 (m, 3H), 1.56 – 1.45 (m, 2H), 1.40 (s, 9H).

13C NMR (100 MHz, CDCl3): δ 174.29, 155.52, 148.85, 126.49, 124.70, 79.53, 51.95, 41.45, 40.10, 35.83, 35.52, 35.13, 29.22, 28.54.

***Tert*-butyl 4-(3-(tert-butoxy)-3-oxopropyl)-4-(4-methyl-4H-1,2,4-triazol-3-yl)piperidine-1-carboxylate (43)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC3**, expect that the reaction mixture was irradiated with a 40-W tuna blue Kessil lamp.

**Chromatography solvent:** 0-100% ethyl acetate/hexanes, then 1-5% methanol/ethyl acetate

**Physical characteristics:** yellow solid

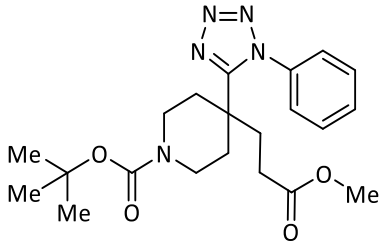
**Yield:** 209 mg (66%)

**ESI-HRMS:** m/z calculated for $C_{20}H_{34}N_4O_4$ $[M+H]^+$ 395.2653, found 395.2650.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.04 (s, 1H), 3.74 (dt, *J* = 14.1, 4.3 Hz, 2H), 3.67 (s, 3H), 3.09 – 2.80 (m, 2H), 2.41 – 2.30 (m, 2H), 2.01 – 1.81 (m, 4H), 1.60 – 1.50 (m, 2H), 1.39 (s, 10H), 1.32 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 172.37, 154.99, 80.79, 79.68, 41.04 (br), 40.25 (br), 38.47, 34.80 (br), 34.41, 33.94, 33.35, 29.63, 28.52, 28.12.

***Tert*-butyl 4-(3-methoxy-3-oxopropyl)-4-(1-phenyl-1H-tetrazol-5-yl)piperidine-1-carboxylate (44)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC2** and 1:1 DMSO/MeCN as the solvent.

**Chromatography solvent:** 30% ethyl acetate/hexanes

**Physical characteristics:** white solid

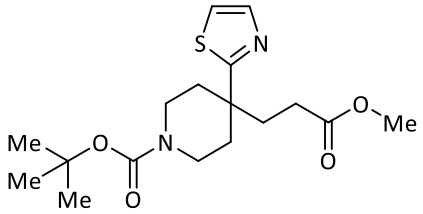
**Yield:** 122 mg (37%)

**ESI-HRMS:** m/z calculated for $C_{21}H_{29}N_5O_4$ $[M+H]^+$ 416.2292, found 416.2294.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.70 – 7.55 (m, 3H), 7.52 – 7.43 (m, 2H), 3.86 – 3.69 (m, 2H), 3.58 (s, 3H), 3.03 – 2.70 (m, 2H), 2.35 – 2.07 (m, 4H), 1.95 (t, *J* = 7.6 Hz, 2H), 1.51 – 1.36 (m, 11H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.06, 156.81, 154.65, 135.40, 131.36, 129.87, 126.93, 79.78, 51.95, 40.63 (br), 39.99 (br), 38.05, 35.58, 34.06, 28.38, 28.10.

***Tert*-butyl 4-(3-methoxy-3-oxopropyl)-4-(thiazol-2-yl)piperidine-1-carboxylate (45)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC2**.

**Chromatography solvent:** 10-50% ethyl acetate/hexanes

**Physical characteristics:** white solid

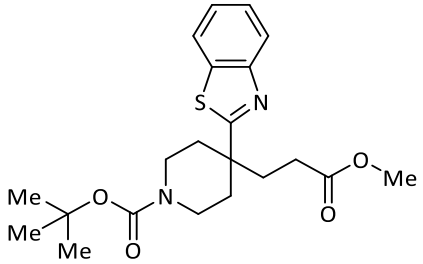
**Yield:** 275 mg (98%)

**ESI-HRMS:** m/z calculated for $C_{17}H_{26}N_2O_4S$ $[M+H]^+$ 355.1686, found 355.1686.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.67 (d, *J* = 3.3 Hz, 1H), 7.27 (d, *J* = 3.3 Hz, 1H), 3.95 – 3.65 (m, 2H), 3.55 (s, 3H), 2.97 (t, *J* = 12.1 Hz, 2H), 2.32 – 2.16 (m, 2H), 2.16 – 2.02 (m, 2H), 2.02 – 1.86 (m, 2H), 1.78 – 1.60 (m, 2H), 1.39 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 175.43, 173.62, 154.85, 142.21, 118.95, 79.52, 51.69, 42.64, 40.83 (br), 40.04 (br), 38.99, 36.13, 28.56, 28.46.

***Tert*-butyl 4-(benzo[d]thiazol-2-yl)-4-(3-methoxy-3-oxopropyl)piperidine-1-carboxylate (46)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC2** and DMSO as the solvent.

**Chromatography solvent:** 10-30% ethyl acetate/hexanes

**Physical characteristics:** white solid

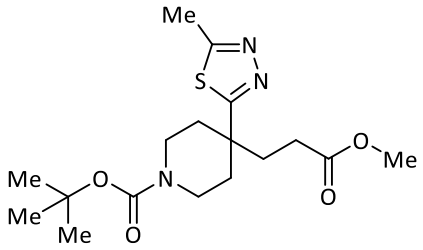
**Yield:** 320 mg (99%)

**ESI-HRMS:** m/z calculated for $C_{21}H_{28}N_2O_4S$ $[M+H]^+$ 405.1843, found 405.1839.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.96 (d, *J* = 8.1 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 4.04 – 3.77 (m, 2H), 3.52 (s, 3H), 3.20 – 2.89 (m, 2H), 2.46 – 2.27 (m, 2H), 2.27 – 2.13 (m, 2H), 2.12 – 1.97 (m, 2H), 1.83 – 1.65 (m, 2H), 1.42 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 175.89, 173.49, 154.86, 152.99, 135.07, 125.98, 125.11, 123.06, 121.66, 79.53, 51.65, 43.52, 41.03 (br), 40.19 (br), 38.70, 36.03, 28.59, 28.46.

***Tert*-butyl 4-(3-methoxy-3-oxopropyl)-4-(5-methyl-1,3,4-thiadiazol-2-yl)piperidine-1-carboxylate (47)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC2**.

**Chromatography solvent:** 0-50% ethyl acetate/hexanes

**Physical characteristics:** pale-yellow oil

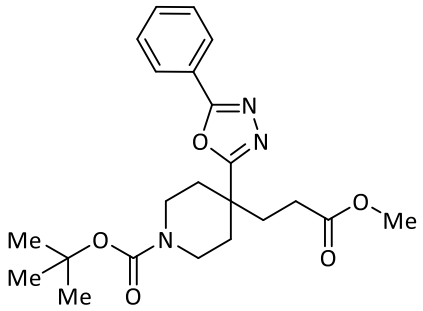
**Yield:** 199 mg (67%)

**ESI-HRMS:** m/z calculated for $C_{17}H_{27}N_3O_4S$ $[M+H]^+$ 370.1795, found 370.1797.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 3.97 – 3.73 (m, 2H), 3.60 (s, 3H), 3.12 – 2.88 (m, 2H), 2.76 (s, 3H), 2.32 – 2.10 (m, 4H), 2.06 – 1.92 (m, 2H), 1.84 – 1.62 (m, 2H), 1.43 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 175.34, 173.50, 165.84, 154.91, 79.79, 51.88, 41.68, 40.34 (br), 38.81, 36.46 (br), 28.54, 28.48, 15.87.

***Tert*-butyl 4-(3-methoxy-3-oxopropyl)-4-(5-phenyl-1,3,4-oxadiazol-2-yl)piperidine-1-carboxylate (48)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC2** using 0.4 mmol of the alkyl–aryl sulfone.

**Chromatography solvent:** 0-25% ethyl acetate/hexanes

**Physical characteristics:** off-white oil

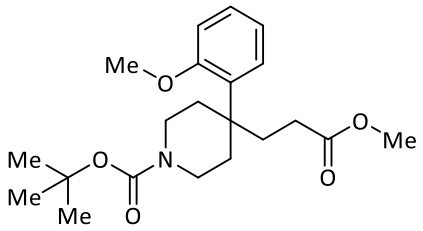
**Yield:** 129 mg (78%)

**ESI-HRMS:** m/z calculated for $C_{22}H_{29}N_3O_5$ $[M+H]^+$ 416.2180, found 416.2180.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.08 – 7.97 (m, 2H), 7.58 – 7.43 (m, 3H), 4.07 – 3.84 (m, 2H), 3.58 (s, 3H), 3.19 – 2.72 (m, 2H), 2.44 – 2.32 (m, 2H), 2.32 – 2.19 (m, 2H), 2.15 – 2.02 (m, 2H), 1.79 – 1.57 (m, 3H), 1.45 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.19, 168.54, 165.24, 154.85, 131.96, 129.22, 127.05, 123.90, 79.89, 51.97, 40.91 (br), 38.74, 36.03, 33.89, 28.65, 28.55.

***Tert*-butyl 4-(3-methoxy-3-oxopropyl)-4-(2-methoxyphenyl)piperidine-1-carboxylate (49)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-30% ethyl acetate/hexanes

**Physical characteristics:** pale-yellow oil

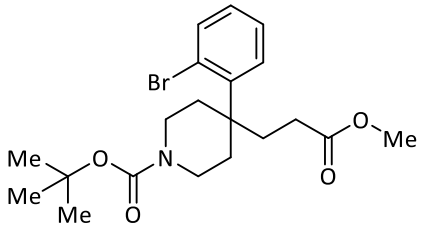
**Yield:** 269 mg (89%)

**ESI-HRMS:** m/z calculated for $C_{21}H_{31}NO_5$ $[M+H]^+$ 378.2275, found 378.2269.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 174.59, 158.78, 155.17, 131.13, 129.20, 127.95, 120.57, 112.08, 79.30, 55.16, 51.58, 40.95 (br), 40.11 (br), 39.99, 34.69, 32.24, 29.56, 28.60.

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 7.24 – 7.18 (m, 1H), 7.12 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.94 – 6.84 (m, 2H), 3.80 (s, 3H), 3.63 – 3.50 (m, 5H), 3.30 – 3.16 (m, 2H), 2.36 – 2.24 (m, 2H), 2.17 (t, *J* = 8.3 Hz, 2H), 1.97 – 1.87 (m, 2H), 1.83 – 1.71 (m, 2H), 1.43 (s, 9H).

***Tert*-butyl 4-(2-bromophenyl)-4-(3-methoxy-3-oxopropyl)piperidine-1-carboxylate (50)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 10% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

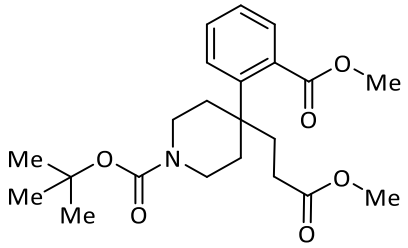
**Yield:** 314 mg (93%)

**ESI-HRMS:** m/z calculated for $C_{20}H_{28}NBrNO_4$ $[M+H]^+$ 426.1274, found 426.1280.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.59 (d, *J* = 14.9 Hz, 1H), 7.25 (d, *J* = 73.6 Hz, 2H), 7.11 – 6.99 (m, 1H), 3.60 – 3.47 (m, 5H), 3.39 – 3.25 (m, 2H), 2.52 – 2.29 (m, 4H), 2.02 – 1.83 (m, 4H), 1.42 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.95, 155.00, 141.55, 136.73, 130.59, 128.29, 127.41, 122.48, 79.51, 51.67, 41.44, 40.54 (br), 39.79 (br), 34.39, 30.32, 29.37, 28.53.

***Tert*-butyl 4-(3-methoxy-3-oxopropyl)-4-(2-(methoxycarbonyl)phenyl)piperidine-1-carboxylate (51)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-20% ethyl acetate/hexanes

**Physical characteristics:** white solid

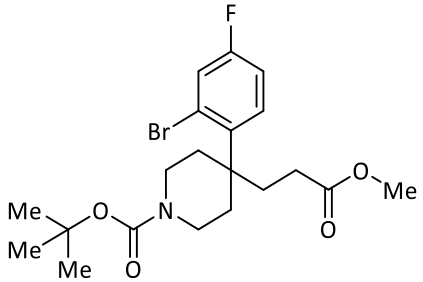
**Yield:** 190 mg (59%)

**ESI-HRMS:** m/z calculated for $C_{22}H_{31}NO_6$ $[M+H]^+$ 406.2224, found 406.2225.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.40 (ddd, *J* = 8.5, 7.1, 1.7 Hz, 1H), 7.35 – 7.23 (m, 4H), 3.88 (s, 3H), 3.66 – 3.53 (m, 5H), 3.21 – 3.04 (m, 2H), 2.29 – 1.95 (m, 6H), 1.80 – 1.66 (m, 2H), 1.42 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 174.16, 172.15, 155.00, 140.29, 133.87, 130.07, 129.68, 128.99, 126.43, 79.56, 52.75, 51.71, 41.11, 35.64 (br), 34.90, 29.40, 28.56.

***Tert*-butyl 4-(2-bromo-4-fluorophenyl)-4-(3-methoxy-3-oxopropyl)piperidine-1-carboxylate (52)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 10-30% ethyl acetate/hexanes

**Physical characteristics:** brown oil

**Yield:** 235 mg (66%)

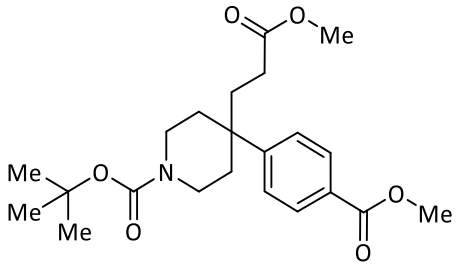
**ESI-HRMS:** m/z calculated for $C_{20}H_{27}BrFNO_4$ $[M+H]^+$ 444.11803, found 444.1183.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.37 (dd, *J* = 8.2, 2.8 Hz, 1H), 7.23 (dd, *J* = 9.0, 6.1 Hz, 1H), 7.04 – 6.97 (m, 1H), 3.58 (s, 3H), 3.57 – 3.46 (m, 2H), 3.45 – 3.25 (m, 2H), 2.58 – 2.20 (m, 4H), 2.06 – 1.85 (m, 4H), 1.44 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.87, 160.74 (d, *J* = 251.1 Hz), 155.02, 137.64 (d, *J* = 3.7 Hz), 131.40 (d, *J* = 7.9 Hz), 123.67 (d, *J* = 23.9 Hz), 122.36 (d, *J* = 8.7 Hz), 114.26 (d, *J* = 19.7 Hz), 79.70, 51.77, 41.18, 39.93 (br), 34.57, 30.16, 29.36, 28.57.

**$^{19}$F NMR (376 MHz, $CDCl_3$):** δ -115.01.

***Tert*-butyl 4-(3-methoxy-3-oxopropyl)-4-(4-(methoxycarbonyl)phenyl)piperidine-1-carboxylate (53)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-20% ethyl acetate/hexanes

**Physical characteristics:** pale-yellow oil

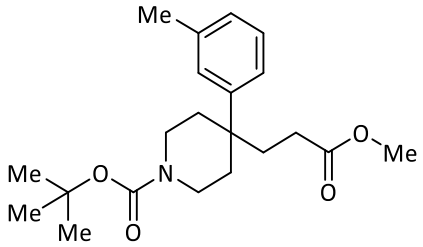
**Yield:** 152 mg (47%)

**ESI-HRMS:** m/z calculated for $C_{22}H_{31}NO_6$ $[M+H]^+$ 406.2224, found 406.2225.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.60 (d, J = 8.2 Hz, 1H), 7.55 – 7.43 (m, 2H), 7.39 (d, J = 8.2 Hz, 1H), 3.76 – 3.61 (m, 2H), 3.55 (s, 3H), 3.17 – 3.04 (m, 2H), 2.21 – 2.05 (m, 2H), 2.00 – 1.89 (m, 4H), 1.80 – 1.66 (m, 2H), 1.43 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 173.84, 166.93, 154.99, 149.35, 130.05, 128.42, 127.02, 79.64, 52.23, 51.74, 40.34 (br), 40.07, 37.48, 35.18, 28.73, 28.55.

***Tert*-butyl 4-(3-methoxy-3-oxopropyl)-4-(m-tolyl)piperidine-1-carboxylate (54)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-20% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

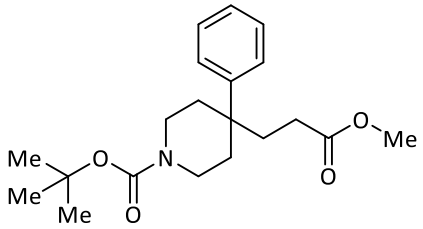
**NMR Yield:** 42% as judged by $^1$H NMR analysis of the crude mixture using mesitylene as an internal standard; isolated as a 3:2 mixture of *meta* and *para* isomers

**ESI-HRMS:** m/z calculated for $C_{21}H_{31}NO_4$ $[M+H]^+$ 362.2326, found 362.2327.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.25 – 6.98 (m, 4H), 3.73 – 3.61 (m, 2H), 3.61 – 3.49 (m, 3H), 3.16 – 3.01 (m, 2H), 2.34 (s, 0.6 × 3H), 2.32 (s, 0.4 × 3H), 2.14 – 2.08 (m, 1H), 2.04 – 1.94 (m, 2H), 1.94 – 1.83 (m, 2H), 1.74 – 1.60 (m, 3H), 1.47 – 1.38 (m, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 174.26, 155.12, 143.49, 140.35, 138.23, 135.87, 129.48, 128.62, 127.62, 127.11, 126.83, 124.01, 79.46, 51.65, 39.46, 39.27, 38.08, 37.92, 35.18 (br), 28.89, 28.63, 28.58, 21.89, 20.97.

***Tert*-butyl 4-(3-methoxy-3-oxopropyl)-4-phenylpiperidine-1-carboxylate[10] (55)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 0-20% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

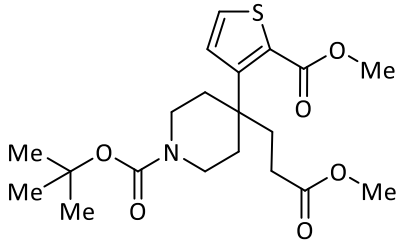
**NMR Yield:** 34% as judged by $^1$H NMR analysis of the crude mixture using mesitylene as an internal standard

**ESI-HRMS:** m/z calculated for $C_{20}H_{29}NO_4$ $[M+H]^+$ 348.2169, found 348.2172.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.39 – 7.33 (m, 2H), 7.30 – 7.20 (m, 3H), 3.78 – 3.63 (m, 2H), 3.57 (s, 3H), 3.11 (ddd, *J* = 13.3, 9.9, 3.1 Hz, 2H), 2.23 – 2.10 (m, 2H), 2.04 – 1.88 (m, 4H), 1.71 (ddd, *J* = 13.9, 9.9, 3.9 Hz, 2H), 1.45 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 174.15, 155.07, 143.52, 128.77, 126.91, 126.38, 79.46, 51.65, 40.72, 39.90, 39.58, 37.91, 28.83, 28.56.

***Tert*-butyl 4-(3-methoxy-3-oxopropyl)-4-(2-(methoxycarbonyl)thiophen-3-yl)piperidine-1-carboxylate (56)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1** using 0.4 mmol of the alkyl–aryl sulfone.

**Chromatography solvent:** 0-20% ethyl acetate/hexanes

**Physical characteristics:** pale-yellow oil

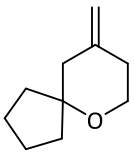
**Yield:** 68 mg (41%)

**ESI-HRMS:** m/z calculated for $C_{20}H_{29}NO_6S$ $[M+H]^+$ 412.1788, found 412.1788.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.42 (d, *J* = 5.3 Hz, 1H), 7.00 (d, *J* = 5.3 Hz, 1H), 3.82 (s, 3H), 3.55 (s, 5H), 3.25 – 3.07 (m, 2H), 2.46 – 2.17 (m, 4H), 1.97 (t, *J* = 8.4 Hz, 2H), 1.91 – 1.79 (m, 2H), 1.40 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 174.05, 162.65, 154.97, 152.05, 130.63, 129.91, 128.04, 79.42, 52.38, 51.63, 40.89 (br), 40.09, 39.97 (br), 35.23, 32.49, 29.58, 28.51.

**9-Methylene-6-oxaspiro[4.5]decanepropanoate[5] (57)**



Prepared as described in "Section V. Synthesis of (±)-Oliceridine."

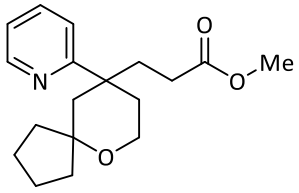
**Chromatography solvent:** 0-10% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

**Yield:** 1.54 g (34%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 4.79 – 4.60 (m, 2H), 3.67 (t, *J* = 5.7 Hz, 2H), 2.26 – 2.12 (m, 4H), 1.81 – 1.65 (m, 4H), 1.63 – 1.47 (m, 4H).

**Methyl 3-(9-(pyridin-2-yl)-6-oxaspiro[4.5]decan-9-yl)propanoate (58)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1** using 0.69 mmol of the alkyl–aryl sulfone and only 1 equivalent of olefin **56**.

**Chromatography solvent:** 0-30% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

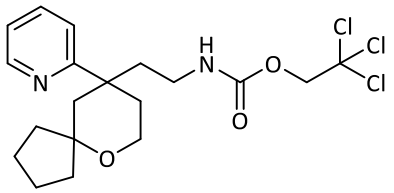
**Yield:** 199 mg (95%)

**ESI-HRMS:** m/z calculated for $C_{18}H_{25}NO_3$ $[M+H]^+$ 304.1907, found 304.1897.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.61 – 8.51 (m, 1H), 7.67 – 7.56 (m, 1H), 7.31 – 7.25 (m, 1H), 7.13 – 7.07 (m, 1H), 3.81 – 3.66 (m, 2H), 3.54 (s, 3H), 2.47 – 2.30 (m, 2H), 2.19 – 2.01 (m, 2H), 1.89 (d, J = 13.6 Hz, 1H), 1.86 – 1.68 (m, 3H), 1.68 – 1.56 (m, 2H), 1.56 – 1.32 (m, 4H), 1.14 – 1.04 (m, 1H), 0.74 – 0.61 (m, 1H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 174.15, 164.13, 149.00, 136.19, 121.39, 121.17, 83.04, 59.49, 51.62, 45.43, 41.70, 41.05, 40.36, 34.05, 33.06, 28.64, 24.14, 22.54.

**2,2,2-trichloroethyl (2-(9-(pyridin-2-yl)-6-oxaspiro[4.5]decan-9-yl)ethyl)carbamate (59)**



Prepared as described in "Section V. Synthesis of (±)-Oliceridine."

**Chromatography solvent:** 0-30% ethyl acetate/hexanes

**Physical characteristics:** white solid

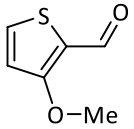
**Yield:** 1.05 g (89%)

**ESI-HRMS:** m/z calculated for $C_{19}H_{25}N_2O_3$ $[M+H]^+$ 435.1004, found 435.1008.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.61 – 8.48 (m, 1H), 7.73 (td, *J* = 7.8, 1.9 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.26 – 7.14 (m, 1H), 5.65 (s, 1H), 4.72 – 4.62 (m, 2H), 3.77 – 3.60 (m, 2H), 3.09 – 2.88 (m, 1H), 2.66 – 2.52 (m, 1H), 2.53 – 2.44 (m, 1H), 2.38 (dd, *J* = 13.7, 2.2 Hz, 1H), 2.03 – 1.98 (m, 1H), 1.87 (d, *J* = 13.6 Hz, 1H), 1.77 – 1.33 (m, 8H), 1.13 – 1.03 (m, 1H), 0.70 (dt, *J* = 13.3, 8.8 Hz, 1H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 165.30, 155.23, 149.59, 137.17, 122.50, 122.07, 96.95, 83.48, 74.71, 59.71, 46.04, 45.52, 42.10, 41.48, 37.26, 34.71, 34.02, 24.66, 23.19.

**3-Methoxythiophene-2-carbaldehyde[8] (60)**



Prepared from commercially available 3-methoxythiophene following a reported procedure.[8]

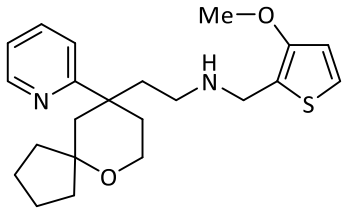
**Chromatography solvent:** 0-30% ethyl acetate/hexanes

**Physical characteristics:** yellow solid

**Yield:** 1.72 g (81%)

**$^1$H NMR (400 MHz, $CDCl_3$):** ) δ 9.92 (d, *J* = 1.2 Hz, 1H), 7.81 (dd, *J* = 5.5, 1.2 Hz, 1H), 7.03 (d, *J* = 5.5 Hz, 1H), 3.99 (s, 3H).

***N*-((3-Methoxythiophen-2-yl)methyl)-2-(9-(pyridin-2-yl)-6-oxaspiro[4.5]decan-9-yl)ethan-1-amine[5] (61)**




Prepared as described in "Section V. Synthesis of (±)-Oliceridine."

**Chromatography solvent:** 1% triethylamine/ethyl acetate

**Physical characteristics:** yellow oil

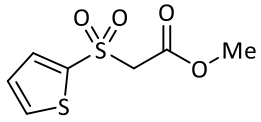
**Yield:** 82 mg (53%)

**ESI-HRMS:** m/z calculated for $C_{21}H_{19}NO_3S$ $[M+H]^+$ 387.2101, found 387.2100.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.55 – 8.43 (m, 1H), 7.70 – 7.60 (m, 1H), 7.37 (dt, *J* = 8.1, 1.1 Hz, 1H), 7.17 – 7.05 (m, 2H), 6.82 (d, *J* = 5.5 Hz, 1H), 3.73 (s, 3H), 3.68 – 3.61 (m, 2H), 3.58 (s, 2H), 2.47 – 2.28 (m, 3H), 1.92 – 1.79 (m, 4H), 1.71 – 1.30 (m, 9H), 1.09 – 1.00 (m, 1H), 0.66 (dt, *J* = 13.5, 8.9 Hz, 1H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 165.95, 154.98, 149.38, 136.91, 122.86, 122.47, 121.80, 121.12, 117.64, 83.51, 59.85, 59.36, 46.46, 46.28, 44.62, 42.27, 41.53, 34.70, 34.32, 24.68, 23.22.

**Methyl 2-(thiophen-2-ylsulfonyl)acetate[11] (62)**




Prepared according to General Procedure B in "Section IV. Procedures for Substrate Preparation."

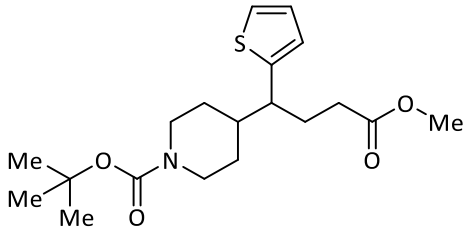
**Chromatography solvent:** 30% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil / clear, low-melting solid

**Yield:** 6.0 g (91%) on 30 mmol scale

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.84 – 7.70 (m, 2H), 7.18 (dd, *J* = 4.9, 3.9 Hz, 1H), 4.21 (s, 2H), 3.75 (s, 3H).

***Tert*-butyl 4-(4-methoxy-4-oxo-1-(thiophen-2-yl)butyl)piperidine-1-carboxylate (63)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**.

**Chromatography solvent:** 20-30% ethyl acetate/hexanes

**Physical characteristics:** clear colorless oil

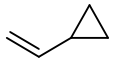
**Yield:** 230 mg (78%)

**LRMS:** m/z calculated for $C_{19}H_{29}NO_4S$ $[M+H]^+$ 368.2, found 368.1.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.15 (d, J = 5.0 Hz, 1H), 6.91 (dd, J = 5.0, 3.5 Hz, 1H), 6.73 (d, J = 3.0 Hz, 1H), 4.07 (d, J = 22.0 Hz, 2H), 3.62 (s, 3H), 2.75 – 2.50 (m, 3H), 2.28 – 2.08 (m, 3H), 1.84 (d, J = 13.1 Hz, 1H), 1.80 – 1.70 (m, 1H), 1.63 – 1.49 (m, 1H), 1.42 (s, 10H), 1.24 – 1.01 (m, 2H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)**: δ 173.99, 154.85, 146.22, 126.65, 125.33, 123.58, 79.38, 51.64, 46.21, 42.77, 32.22, 30.41, 30.04, 29.28, 28.56.

**Vinylcyclopropane[12] (64)**



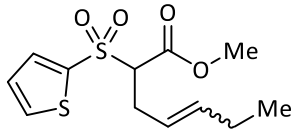
Prepared from cyclopropanecarbaldehyde according to a standard protocol and distilled directly from reaction mixture.[12]

**Physical characteristics:** clear, colorless oil

**Yield:** 157 mg (12%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 5.35 (ddd, *J* = 17.0, 10.2, 8.7 Hz, 1H), 5.07 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.85 (dd, *J* = 10.2, 1.8 Hz, 1H), 1.41 (dtd, *J* = 13.1, 8.5, 4.8 Hz, 1H), 0.74 – 0.68 (m, 2H), 0.42 – 0.35 (m, 2H).

**Methyl 2-(thiophen-2-ylsulfonyl)hept-4-enoate (68)**



Prepared according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1** using 0.4 mmol of the alkyl–aryl sulfone. Some impurities remained in the NMR spectra after isolation, but we are nonetheless confident in this structural assignment as almost every signal was adequately resolved. Many of the signals appear as major and minor partners, which we attribute to a mixture of *E*/*Z* isomers (major isomer unknown). The ratio was assigned as 2.5:1 by integration of the methyl ester $^{1}$H NMR signal.

**Chromatography solvent:** 10% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

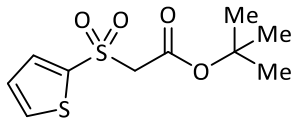
**NMR Yield:** 6% as judged by $^{1}$H NMR analysis of the crude mixture using mesitylene as an internal standard

**LRMS:** m/z calculated for $C_{12}H_{16}O_4S_2$ $[M+H]^+$ 289.1, found 289.0.

**$^{1}$H NMR (400 MHz, $CDCl_3$):** δ 7.74 – 7.70 (m, 1H), 7.66 – 7.61 (m, 1H), 7.15 – 7.09 (m, 1H), 5.58 – 5.41 (m, 1H), 5.22 – 5.07 (m, 1H), 4.01 – 3.91 (m, 1H), 2.76 – 2.50 (m, 2H), 2.01 – 1.81 (m, 2H), 0.91 – 0.59 (m, 3H overlapping with aliphatic impurities).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 166.07, 137.65, 137.65, 137.58, 137.58, 136.82, 136.82, 136.15, 136.15, 135.49, 135.44, 135.44, 128.95, 128.05, 128.05, 121.72, 121.72, 121.33, 71.66, 71.50, 68.31, 53.10, 38.88, 30.63, 29.86, 25.66, 25.44, 23.89, 20.70, 13.64, 11.11.

***Tert*-butyl 2-(thiophen-2-ylsulfonyl)acetate (S1)**



Prepared according to General Procedure B in "Section IV. Procedures for Substrate Preparation" using 10 mmol of the aryl thiol.

**Chromatography solvent:** 0-30% ethyl acetate/hexanes

**Physical characteristics:** pale-yellow oil

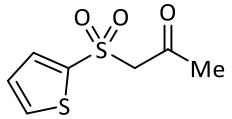
**Yield:** 2.0 g (76%)

**ESI-HRMS:** m/z calculated for $C_{10}H_{14}O_4S_2$ $[M+Na]^+$ 285.0226, found 285.0226.

**$^{1}$H NMR (400 MHz, $CDCl_3$):** δ 7.81 – 7.72 (m, 2H), 7.17 (dd, J = 4.7, 4.1 Hz, 1H), 4.11 (s, 2H), 1.42 (s, 10H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 161.32, 139.83, 135.35, 134.80, 127.94, 84.00, 63.32, 27.90.

**1-(Thiophen-2-ylsulfonyl)propan-2-one[13] (S2)**



Prepared according to General Procedure A in "Section IV. Procedures for Substrate Preparation" using 10 mmol of the aryl thiol. In addition, the requisite alkyl chloride was employed as the electrophile and the alkylation was setup at 0 °C.

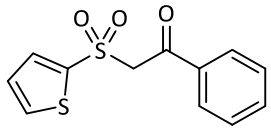
**Chromatography solvent:** 30% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil (note: decomposes at rt to a brown oil)

**Yield:** 1.5 g (73%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.90 – 7.75 (m, 1H), 7.74 – 7.66 (m, 1H), 7.18 (t, J = 4.3 Hz, 1H), 4.25 (s, 2H), 2.43 (s, 3H).

**1-Phenyl-2-(thiophen-2-ylsulfonyl)ethan-1-one[14] (S3)**



Prepared according to General Procedure B in "Section IV. Procedures for Substrate Preparation" using 10 mmol of the aryl thiol.

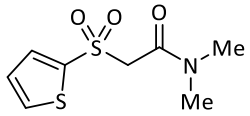
**Recrystallization solvent:** hexanes/ethyl acetate

**Physical characteristics:** brown crystalline solid

**Yield:** 1.4 g (52%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.01 – 7.88 (m, 2H), 7.78 – 7.67 (m, 2H), 7.67 – 7.57 (m, 1H), 7.55 – 7.41 (m, 2H), 7.14 (dd, J = 5.0, 3.8 Hz, 1H), 4.83 (s, 2H).

***N*,*N*-Dimethyl-2-(thiophen-2-ylsulfonyl)acetamide (S4)**



Prepared according to General Procedure B in "Section IV. Procedures for Substrate Preparation" using 10 mmol of the aryl thiol. In addition, the requisite alkyl chloride was employed as the electrophile and the alkylation was setup at 0 °C.

**Recrystallization solvent:** hexanes/ethyl acetate

**Physical characteristics:** white crystalline solid

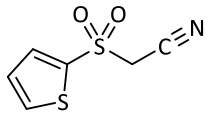
**Yield:** 2.0 g (42%)

**ESI-HRMS:** m/z calculated for $C_8H_{11}NO_3S_2$ $[M+H]^+$ 234.0253, found 234.0252.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.87 – 7.63 (m, 2H), 7.16 (dd, J = 4.9, 3.9 Hz, 1H), 4.32 (s, 2H), 3.15 (s, 3H), 2.97 (s, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 161.26, 139.52, 135.42, 134.98, 128.02, 61.01, 38.74, 36.17.

**2-(Thiophen-2-ylsulfonyl)acetonitrile[15] (S5)**



Prepared according to General Procedure A in "Section IV. Procedures for Substrate Preparation" using 10 mmol of the aryl thiol.

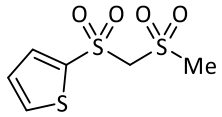
**Recrystallization solvent:** hexanes/ethyl acetate

**Physical characteristics:** white solid

**Yield:** 1.2 g (63%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.03 – 7.85 (m, 2H), 7.30 (dd, J = 4.9, 3.8 Hz, 1H), 4.19 (s, 2H).

**2-(((Methylsulfonyl)methyl)sulfonyl)thiophene (S6)**



Prepared according with modified General Procedure A in "Section IV. Procedures for Substrate Preparation" using 10 mmol of the aryl thiol with chloromethyl methyl sulfide as alkyl halide in step 1, and using 2.5 equivalents of potassium permanganate in step 2.

**Chromatography solvent:** 50-70% ethyl acetate/hexanes

**Physical characteristics:** white crystalline solid

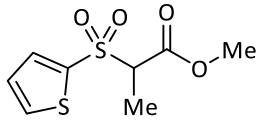
**Yield:** 1.6 g (64%)

**LRMS:** m/z calculated for $C_6H_8O_4S_3$ $[M+H]^+$ 241.0, found 240.9

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.88 (dd, J = 3.9, 1.3 Hz, 1H), 7.85 (dd, J = 5.0, 1.3 Hz, 1H), 7.22 (dd, J = 4.9, 4.0 Hz, 1H), 4.66 (s, 2H), 3.29 (s, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 138.08, 137.14, 136.49, 128.50, 74.24, 42.76.

**Methyl 2-(thiophen-2-ylsulfonyl)propanoate (S7)**



Prepared according to General Procedure B in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl thiol.

**Chromatography solvent:** 0-15% ethyl acetate in hexanes

**Physical characteristics:** clear, colorless oil

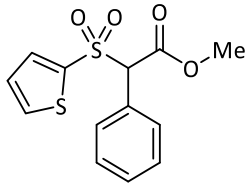
**Yield:** 2.6 g (75%)

**ESI-HRMS:** m/z calculated for $C_8H_{10}O_4S_2$ $[M+H]^+$ 235.0093, found 235.0095.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.79 (dd, J = 4.9, 1.4 Hz, 1H), 7.70 (dd, J = 3.8, 1.4 Hz, 1H), 7.19 (dd, J = 5.0, 3.8 Hz, 1H), 4.14 (q, J = 7.1 Hz, 1H), 3.74 (s, 3H), 1.61 (d, J = 7.1 Hz, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 166.78, 137.27, 136.17, 135.43, 128.04, 66.41, 53.28, 12.49.

**1-Phenyl-2-(thiophen-2-ylsulfonyl)ethan-1-one (S8)**




Prepared according to General Procedure C in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl sulfonyl chloride.

**Chromatography solvent:** 20-40% ethyl acetate/hexanes

**Physical characteristics:** white solid

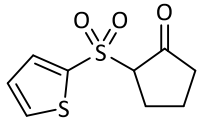
**Yield:** 4.6 g (100%)

**ESI-HRMS:** m/z calculated for $C_{13}H_{12}O_2S_2$ $[M+H]^+$ 297.0250, found 297.0252.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.69 (dd, J = 5.0, 1.4 Hz, 1H), 7.47 – 7.35 (m, 4H), 7.35 – 7.28 (m, 2H), 7.05 (dd, J = 5.0, 3.8 Hz, 1H), 5.19 (s, 1H), 3.80 (s, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 165.28, 136.74, 136.68, 135.69, 130.18, 129.93, 128.79, 128.01, 127.63, 75.94, 53.40.

**2-(Thiophen-2-ylsulfonyl)cyclopentan-1-one (S9)**




Prepared according to General Procedure B in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl thiol.

**Recrystallization solvent:** hexanes/ethyl acetate

**Physical characteristics:** white solid

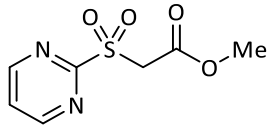
**Yield:** 2.6 g (75%)

**ESI-HRMS:** m/z calculated for $C_9H_{10}O_3S_2$ $[M+H]^+$ 231.0144, found 231.0146.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.77 (dd, J = 5.0, 1.4 Hz, 1H), 7.71 (dq, J = 3.8, 1.1 Hz, 1H), 7.18 (dd, J = 5.0, 3.8 Hz, 1H), 3.89 – 3.76 (m, 1H), 2.74 – 2.59 (m, 1H), 2.53 – 2.28 (m, 3H), 2.26 – 2.12 (m, 1H), 1.99 – 1.82 (m, 1H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 206.94, 138.66, 135.83, 135.10, 128.13, 70.57, 38.86, 25.54, 20.10.

**Methyl 2-(pyrimidin-2-ylsulfonyl)acetate (S10)**



Prepared according to General Procedure A in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl thiol.

**Recrystallization solvent:** hexanes/ethyl acetate

**Physical characteristics:** white solid

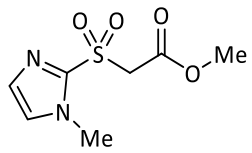
**Yield:** 1.92 g (60%)

**ESI-HRMS:** m/z calculated for $C_7H_8N_2O_4S$ $[M+H]^+$ 217.0278, found 217.0276.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.97 (d, J = 4.9 Hz, 2H), 7.60 (t, J = 4.9 Hz, 1H), 4.61 (s, 2H), 3.70 (s, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 165.19, 163.01, 158.81, 124.08, 55.31, 53.34.

**Methyl 2-((1-methyl-1H-imidazol-2-yl)sulfonyl)acetate[16] (S11)**



Prepared according to General Procedure B in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl thiol.

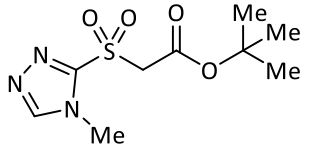
**Recrystallization solvent:** hexanes/ethyl acetate

**Physical characteristics:** white solid

**Yield:** 838 mg (26%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.17 (s, 1H), 7.03 (s, 1H), 4.42 (s, 2H), 3.97 (s, 3H), 3.71 (s, 3H).

***Tert*-butyl 2-((4-methyl-4H-1,2,4-triazol-3-yl)sulfonyl)acetate (S12)**



Prepared according to General Procedure A in "Section IV. Procedures for Substrate Preparation" using 10 mmol of the aryl thiol.

**Recrystallization solvent:** hexanes/ethyl acetate

**Physical characteristics:** white crystalline solid

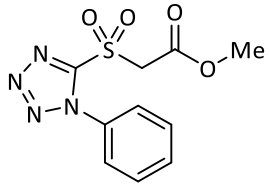
**Yield:** 1.1 g (42%)

**ESI-HRMS:** m/z calculated for $C_9H_{15}NO_4S$ $[M+H]^+$ 262.0856, found 262.0857.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.25 (s, 1H), 4.50 (s, 2H), 4.03 (s, 3H), 1.44 (s, 9H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 161.15, 146.67, 84.87, 60.55, 33.45, 27.93.

**Methyl 2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)acetate[17] (S13)**



Prepared according to General Procedure A in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl thiol.

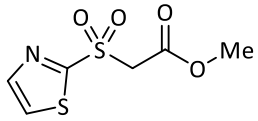
**Recrystallization solvent:** hexanes/ethyl acetate

**Physical characteristics:** white crystalline solid

**Yield:** 1.9 g (58%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.73 – 7.52 (m, 5H), 4.71 (s, 2H), 3.79 (s, 3H).

**Methyl 2-(thiazol-2-ylsulfonyl)acetate (S14)**



Prepared according to General Procedure A in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl thiol.

**Chromatography solvent:** 10-50% ethyl acetate/hexanes

**Physical characteristics:** pale-yellow oil

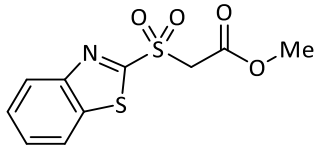
**Yield:** 3.3 g (98%)

**ESI-HRMS:** m/z calculated for $C_6H_7NO_4S_2$ $[M+H]^+$ 221.9889, found 221.9887.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.06 (d, J = 3.0 Hz, 1H), 7.80 (d, J = 3.0 Hz, 1H), 4.45 (s, 2H), 3.70 (s, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 164.23, 162.24, 145.23, 127.08, 58.82, 53.38.

**Methyl 2-(benzo[d]thiazol-2-ylsulfonyl)acetate[17] (S15)**



Prepared according to General Procedure A in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl thiol.

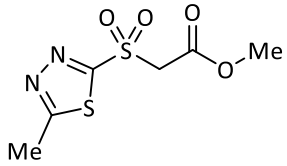
**Chromatography solvent:** 10% ethyl acetate/hexanes

**Physical characteristics:** white, crystalline solid

**Yield:** 2.4 g (70%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.23 (d, J = 8.0 Hz, 1H), 8.03 (d, J = 7.9 Hz, 1H), 7.73 – 7.55 (m, 2H), 4.58 (s, 2H), 3.74 (s, 3H).

**Methyl 2-((5-methyl-1,3,4-thiadiazol-2-yl)sulfonyl)acetate (S16)**



Prepared according to General Procedure A in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl thiol.

**Recrystallization solvent:** hexanes/ethyl acetate

**Physical characteristics:** white, crystalline solid

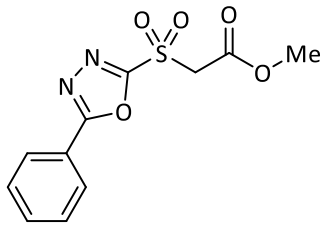
**Yield:** 2.2 g (63%)

**ESI-HRMS:** m/z calculated for $C_6H_8N_2O_4S_2$ $[M+H]^+$ 236.9998, found 236.9997.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 4.58 (s, 2H), 3.75 (s, 3H), 2.91 (s, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 171.25, 167.72, 162.17, 59.01, 53.58, 16.23.

**Methyl 2-((5-phenyl-1,3,4-oxadiazol-2-yl)sulfonyl)acetate (S17)**



Prepared according to General Procedure A in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl thiol.

**Chromatography solvent:** 10% ethyl acetate/hexanes

**Physical characteristics:** white, low-melting solid

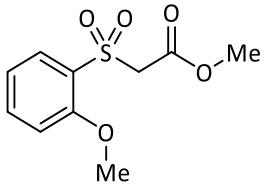
**Yield:** 1.3 g (31%)

**ESI-HRMS:** m/z calculated for $C_{11}H_{10}N_2O_5S$ $[M+H]^+$ 283.0383, found 283.0384.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.15 (d, J = 7.6 Hz, 2H), 7.71 – 7.41 (m, 3H), 4.58 (s, 2H), 3.79 (s, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 167.03, 161.52, 161.41, 133.54, 129.55, 127.97, 122.18, 59.42, 53.90.

**Methyl 2-((2-methoxyphenyl)sulfonyl)acetate[18,19] (S18)**



Prepared according to General Procedure A in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl thiol.

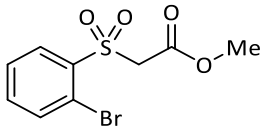
**Chromatography solvent:** 10% ethyl acetate/hexanes

**Physical characteristics:** white, low-melting solid

**Yield:** 2.8 g (84%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.95 (d, J = 7.8 Hz, 1H), 7.63 (t, J = 8.0 Hz, 1H), 7.21 – 6.94 (m, 2H), 4.39 (s, 2H), 4.01 (s, 3H), 3.67 (s, 3H).

**Methyl 2-((2-bromophenyl)sulfonyl)acetate[19] (S19)**



Prepared according to General Procedure A in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl thiol.

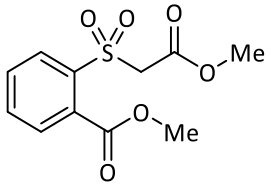
**Recrystallization solvent:** hexanes/ethyl acetate

**Physical characteristics:** white, crystalline solid

**Yield:** 3.0 g (67%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.21 – 8.14 (m, 1H), 7.83 – 7.76 (m, 1H), 7.58 – 7.48 (m, 2H), 4.49 (s, 2H), 3.69 (s, 3H).

**Methyl 2-((2-methoxy-2-oxoethyl)sulfonyl)benzoate[20] (S20)**



Prepared according to General Procedure A in "Section IV. Procedures for Substrate Preparation" using 10 mmol of the aryl thiol.

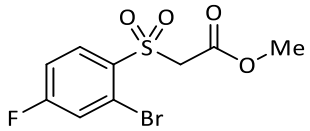
**Recrystallization solvent:** hexanes/ethyl acetate

**Physical characteristics:** white, crystalline solid

**Yield:** 2.1 g (79%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.24 – 8.07 (m, 1H), 7.86 – 7.60 (m, 3H), 4.66 (s, 2H), 3.98 (s, 3H), 3.73 (s, 3H).

**Methyl 2-((2-bromo-4-fluorophenyl)sulfonyl)acetate (S21)**



Prepared according to General Procedure C in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl thiol.

**Recrystallization solvent:** hexanes/ethyl acetate

**Physical characteristics:** white, crystalline solid

**Yield:** 3.1 g (67%)

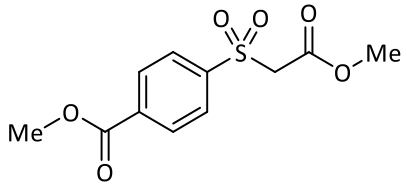
**ESI-HRMS:** m/z calculated for $C_9H_8BrFO_4S$ $[M+H]^+$ 310.9384, found 310.9387.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 165.34 (d, J = 261.4 Hz), 162.67, 135.00 (d, J = 10.0 Hz), 134.20 (d, J = 3.6 Hz), 123.06 (d, J = 25.4 Hz), 122.38 (d, J = 10.4 Hz), 115.47 (d, J = 21.6 Hz), 58.22, 53.30.

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 8.18 (dd, J = 8.9, 5.7 Hz, 1H), 7.52 (dd, J = 7.9, 2.5 Hz, 1H), 7.30 – 7.17 (m, 1H), 4.46 (s, 2H), 3.69 (s, 3H).

**$^{19}$F NMR (376 MHz, $CDCl_3$):** δ -101.18.

**Methyl 4-((2-methoxy-2-oxoethyl)sulfonyl)benzoate[21] (S22)**



Prepared according to General Procedure C in "Section IV. Procedures for Substrate Preparation" using 10 mmol of the aryl thiol.

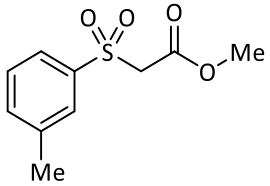
**Recrystallization solvent:** hexanes/ethyl acetate

**Physical characteristics:** white, crystalline solid

**Yield:** 1.1 g (39%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.27 – 8.20 (m, 2H), 8.05 – 7.99 (m, 2H), 4.15 (s, 2H), 3.97 (s, 3H), 3.70 (s, 3H).

**Methyl 2-(3-tolylsulfonyl)acetate[21] (S23)**



Prepared according to General Procedure C in "Section IV. Procedures for Substrate Preparation" using 20 mmol of the aryl thiol.

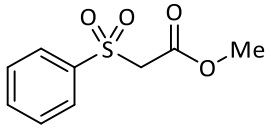
**Chromatography solvent:** 10-30% ethyl acetate/hexanes

**Physical characteristics:** yellow oil

**Yield:** 3.7 g (81%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.71 – 7.58 (m, 2H), 7.46 – 7.30 (m, 2H), 4.07 (s, 2H), 3.59 (s, 3H), 2.35 (s, 3H).

**Methyl 2-(phenylsulfonyl)acetate[19] (S24)**



Prepared according to General Procedure A in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl thiol.

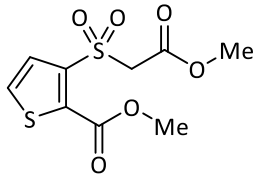
**Chromatography solvent:** 0-10% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

**Yield:** 2.6 g (79%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.00 – 7.90 (m, 2H), 7.75 – 7.64 (m, 1H), 7.65 – 7.51 (m, 2H), 4.13 (s, 2H), 3.71 (s, 3H).

**Methyl 3-((2-methoxy-2-oxoethyl)sulfonyl)thiophene-2-carboxylate (S25)**



Prepared according to General Procedure C in "Section IV. Procedures for Substrate Preparation" using 15 mmol of the aryl thiol.

**Recrystallization solvent:** hexanes/ethyl acetate

**Physical characteristics:** white, crystalline solid

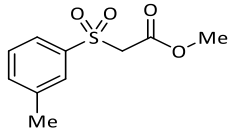
**Yield:** 850 mg (20%)

**ESI-HRMS:** m/z calculated for $C_9H_{10}O_6S_2$ $[M+H]^+$ 278.9993, found 278.9991.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.64 (d, J = 5.2 Hz, 1H), 7.56 (d, J = 5.3 Hz, 1H), 4.74 (s, 2H), 3.95 (s, 3H), 3.70 (s, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$):** δ 163.39, 160.33, 142.94, 134.72, 131.88, 129.91, 59.47, 53.41, 53.16.

**1-(4-Vinylpiperidin-1-yl)ethan-1-one[22] (S26)**



Prepared as a dedicated protocol in "Section IV. Procedures for Substrate Preparation."

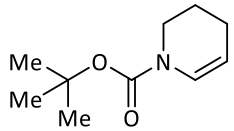
**Chromatography solvent:** 0-10% ethyl acetate/hexanes

**Physical characteristics:** pale-yellow oil

**Yield:** 3.7 g (81%)

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 5.76 (ddd, *J* = 17.0, 10.5, 6.3 Hz, 1H), 5.09 – 4.93 (m, 2H), 4.64 – 4.52 (m, 1H), 3.88 – 3.75 (m, 1H), 3.14 – 2.99 (m, 1H), 2.66 – 2.53 (m, 1H), 2.30 – 2.13 (m, 1H), 2.09 (s, 3H), 1.84 – 1.66 (m, 2H), 1.39 – 1.16 (m, 2H).

***Tert*-butyl 3,4-dihydropyridine-1(2H)-carboxylate[23] (S27)**



Prepared from *tert*-butyl 2-oxopiperidine-1-carboxylate according to a standard protocol.[23]

**Chromatography solvent:** 0-10% ethyl acetate/hexanes

**Physical characteristics:** clear, colorless oil

**Yield:** 2.6 g (79%)

**$^1$H NMR (400 MHz, $CDCl_3$):** $^1$H NMR (400 MHz, $CDCl_3$) δ 6.89 – 6.66 (m, 1H), 4.97 – 4.73 (m, 1H), 3.62 – 3.43 (m, 2H), 2.03 – 1.98 (m, 2H), 1.85 – 1.75 (m, 2H), 1.48 (s, 10H)

## VII. Determination of Diastereochemical Outcomes (Products 34–39)

**Product 34:**

The major diastereomer of **34** was assigned by 2D NOESY analysis of the purified material (>20:1 dr). The $^1$H NMR spectrum of this material (Figure S2) shows assignments for $H_a$, $H_b$, $H_c$, and $H_d$ that were the focus of the 2D NOESY analysis. The corresponding 2D NOESY spectrum (Figure S3) and the zoomed-in inset show that the three strongest nOE interactions for $H_a$ are with $H_b$, $H_c$, and $H_d$. This result is consistent with assignment of the major diastereomer of **34** as drawn since $H_b$, $H_c$, and $H_d$ are only the nearest neighbors of $H_a$ in space in this relative configuration. Finally, the $^1$H NMR spectrum of crude **34** (Figure S4) indicates a 10:1 mixture of the major diastereomer with a minor, unknown diastereomer by integration of the $CO_2CH_3$ signals.

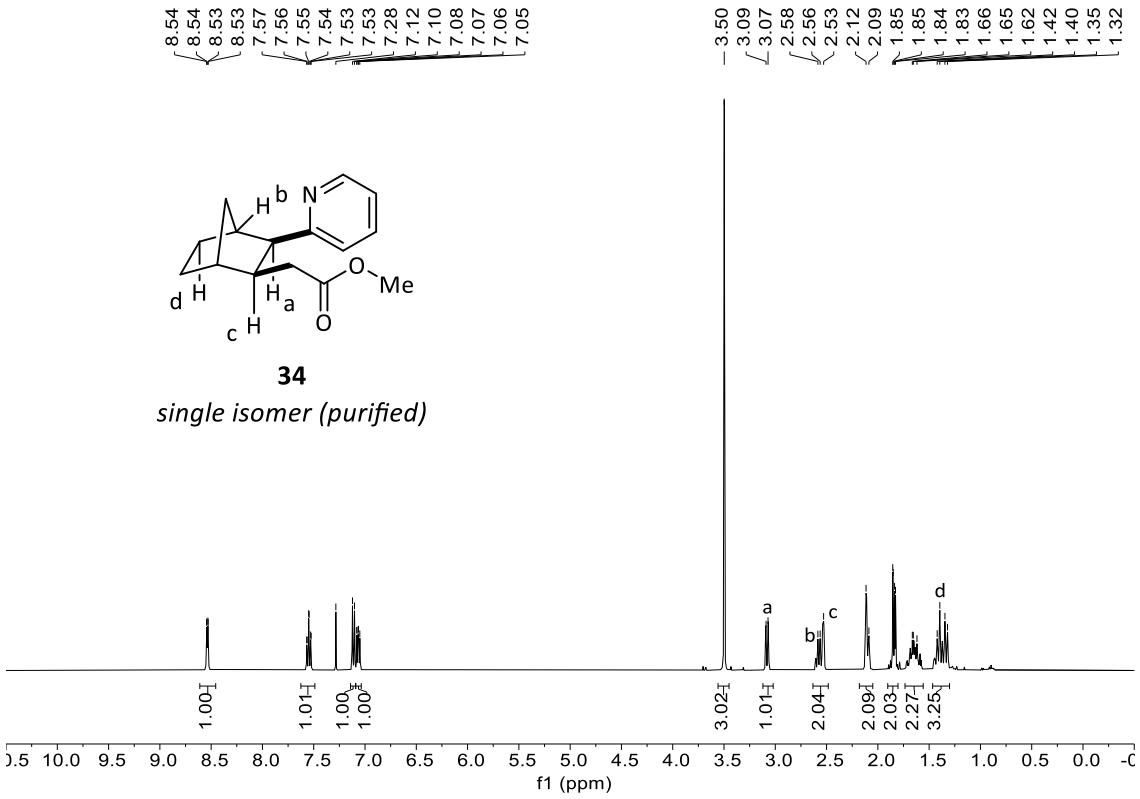



**Figure S2.** $^1$H NMR spectrum of purified **34** (major stereoisomer, >20:1 dr) with relevant signals labeled.

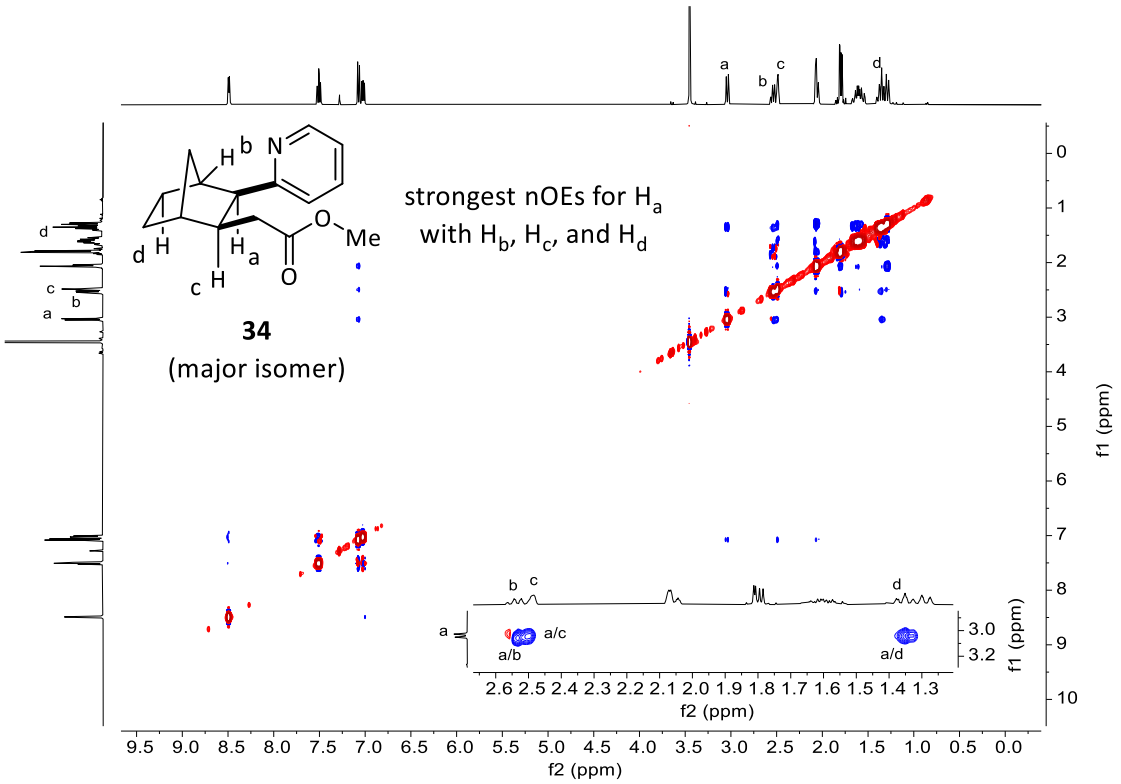



**Figure S3.** 2D NOESY spectrum of purified **34** (major stereoisomer, >20:1 dr). The strongest nOE interactions with $H_a$ are consistent with the relative stereochemistry as drawn.

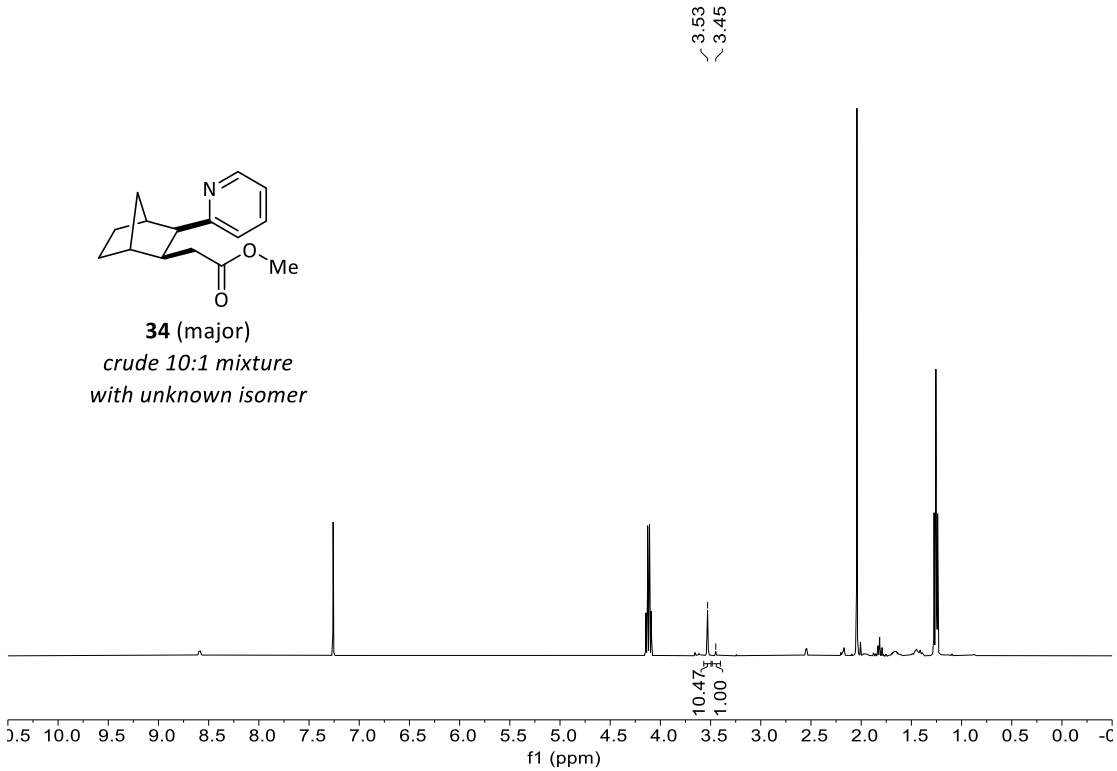



**Figure S4.** $^1$H NMR spectrum of crude **34** (10:1 dr by integration of the $CO_2CH_3$ signals).

**Product 35:**

The ethyl ester analog of **35** has previously been characterized.[24] Since the known ethyl ester was established as the *cis*-diastereomer and the signals in its $^1$H NMR spectrum align very well, except for the alkyl ester resonances, with those observed for purified **35** (see "Section XIV. NMR Spectra"), the major diastereomer of **35** was assigned as *cis* by analogy. The $^1$H NMR spectrum of crude **35** (Figure S5) indicates a >20:1 *cis*/*trans* mixture by integration of the major and minor benzylic resonances ($H_a$ and $H_b$, respectively). Although the *trans*-diastereomer of the known ethyl ester has not been described, the benzylic resonance in Figure S5 assigned to $H_b$ in the minor *trans*-diastereomer was also observed in the known $^1$H NMR spectrum of corresponding ethyl ester.

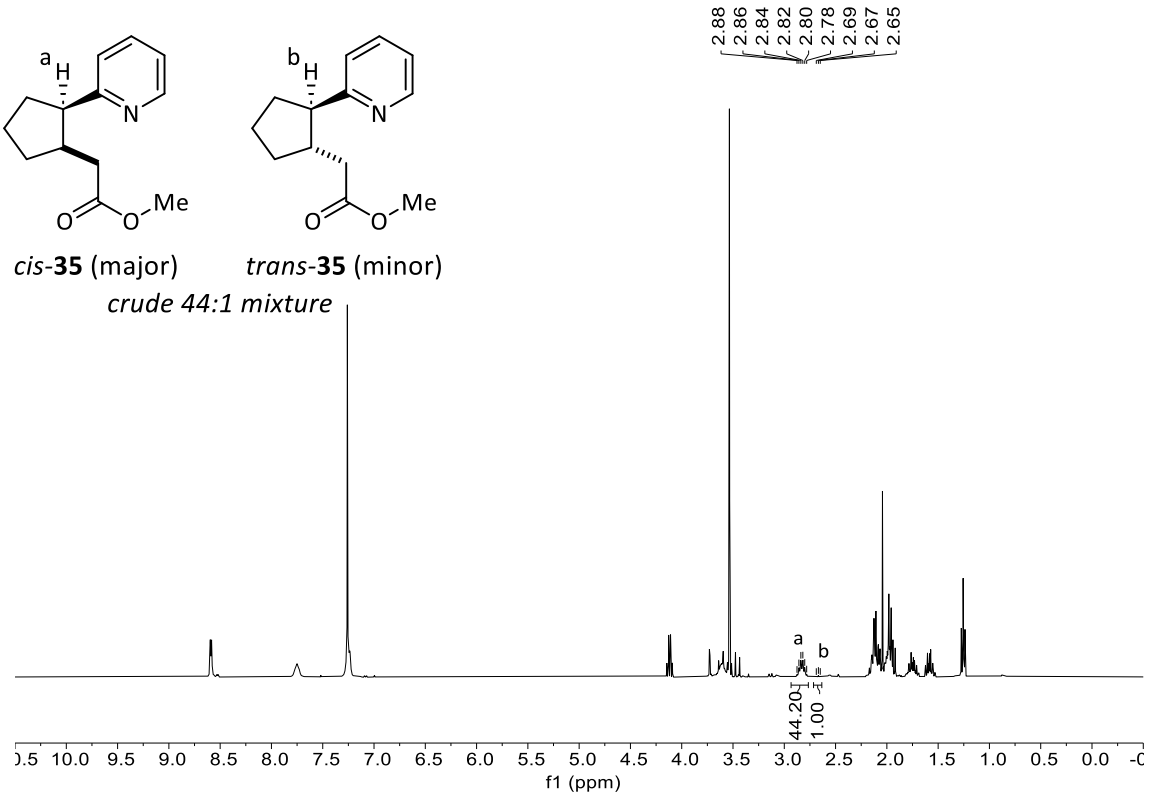



**Figure S5.** $^1$H NMR spectrum of crude **35** (>20:1 *cis*/*trans* by integration of benzylic resonances $H_a$ and $H_b$). The major diastereomer was assigned as *cis*-**35** by analogy to the known ethyl ester analog.[24]

**Product 36:**

Both diastereomers of the ethyl ester analog of **36** have previously been characterized.[24] Since the signals in the reported $^1$H NMR spectra of the known *cis*- and *trans*-ethyl esters align very well, except for the alkyl ester resonances, with those observed for the two diastereomers in purified **36**

(see "Section XIV. NMR Spectra"), the major diastereomer of **36** was assigned as *trans* and the minor diastereomer of **36** was assigned as *cis*. The $^1$H NMR spectrum of crude **36** (Figure S6) indicates a 5:1 *trans*/*cis* mixture by integration of one signal in the major and minor diastereomers ($H_a$ and $H_b$, respectively).

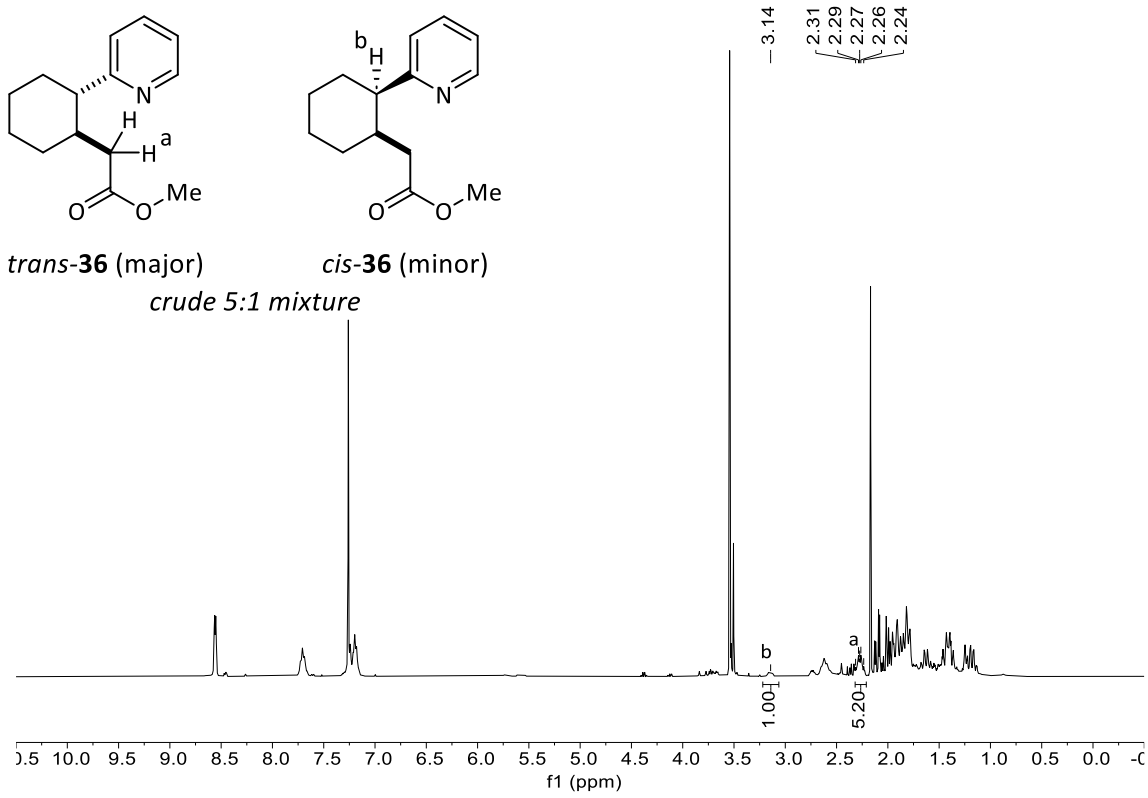



**Figure S6.** $^1$H NMR spectrum of crude **36** (5:1 *trans*/*cis* by integration of resonances $H_a$ and $H_b$). The relative stereochemistry was assigned by analogy to the ethyl ester analog of **36**.[24]

**Product 37:**

The major diastereomer of **37** was assigned as *cis* by 2D NOESY analysis of the purified material (>20:1 *cis*/*trans*). The $^1$H NMR spectrum of this material (Figure S**7**) shows assignments for $H_a$, $H_b$, and $H_c$ that were the focus of the 2D NOESY analysis. The corresponding 2D NOESY spectrum (Figure S8) shows a strong nOE interaction between $H_a$ and $H_c$, but not between $H_a$ and $H_b$. These results are consistent with the assignment of *cis*-**37** as the major diastereomer. Finally, the $^1$H NMR spectrum of crude **37** (Figure S9) indicates a >20:1 *cis*/*trans* mixture since no signals attributable to another diastereomer are observed.

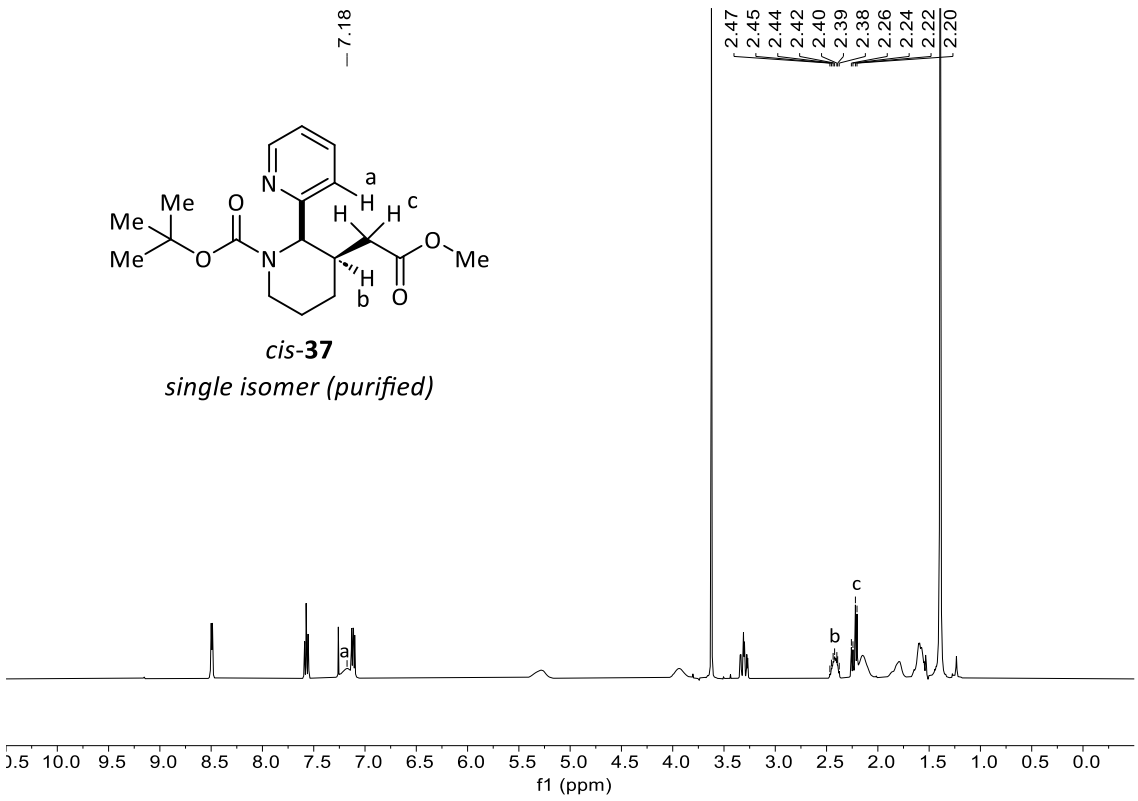



**Figure S7.** $^{1}$H NMR spectrum of purified **37** (>20:1 *cis*/*trans*) with relevant signals labeled.

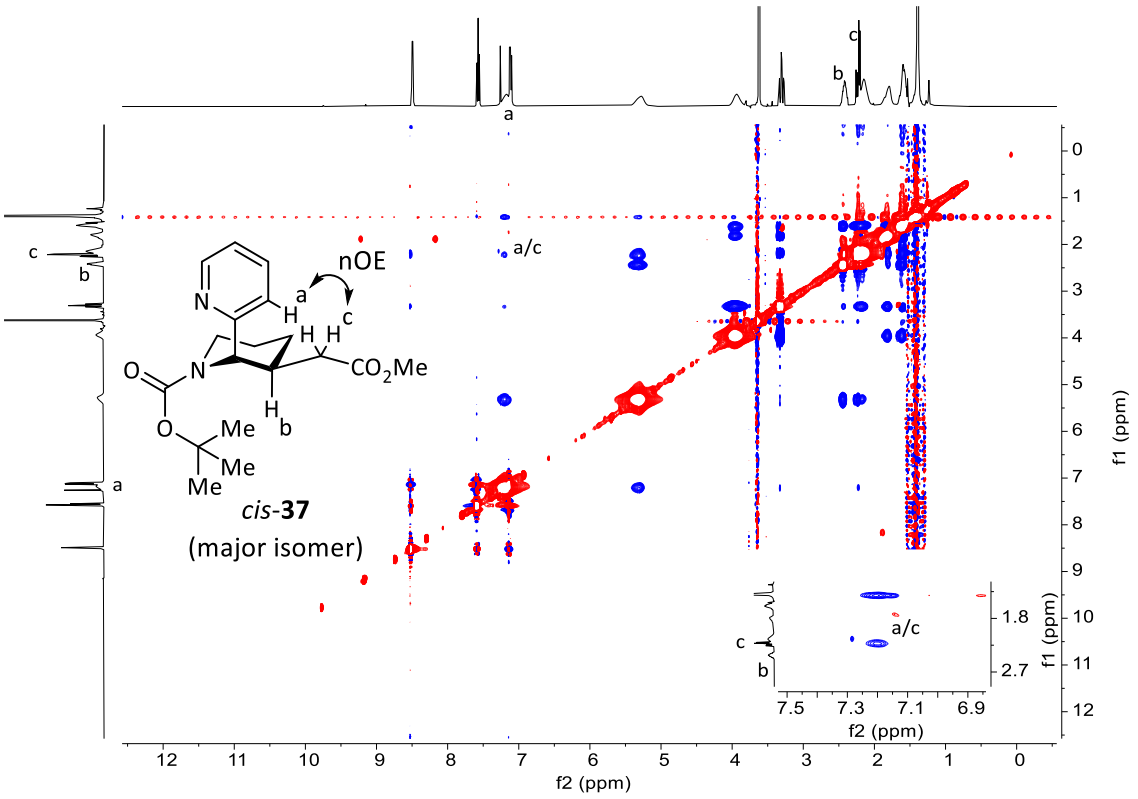



**Figure S8.** 2D NOESY spectrum of purified **37** (>20:1 *cis*/*trans*). The strong nOE interactions observed between $H_a$ and $H_c$ but not between $H_a$ and $H_b$ are consistent with *cis*-**37** as the major diastereomer.

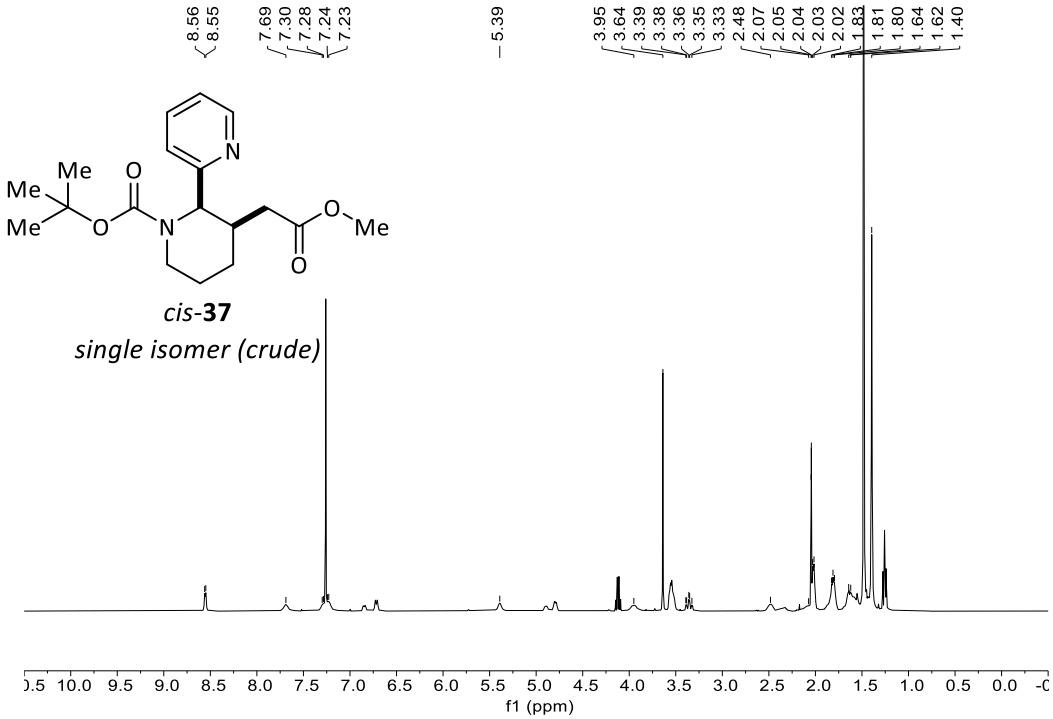



**Figure S9.** $^1$H NMR spectrum of crude **37** (>20:1 *cis*/*trans*, no minor diastereomer observed).

**Product 38:**

The major diastereomer of **38** was assigned as *cis* by measurement of the coupling constant between two vicinal diagnostic signals, $H_a$ and $H_b$, in $^1$H NMR spectrum of the purified material (Figure S10, >20:1 *cis*/*trans*). The measured value of $J$ = 2.5 Hz is consistent with the prediction from the Karplus equation when vicinal protons have a dihedral angle of ~60º, as expected for the depicted chair conformation of *cis*-**38** and the corresponding ring flip (not shown). A value of $J \cong$ 10 Hz would be expected for *trans*-**38**, which would predominantly adopt the greyed, all-equatorial conformation wherein the corresponding protons, $H_c$ and $H_d$, would have a dihedral angle of ~180º.[25,26] Finally, the $^1$H NMR spectrum of crude **38** (Figure S11) indicates a >20:1 *cis*/*trans* mixture since no signals attributable to another diastereomer are observed.

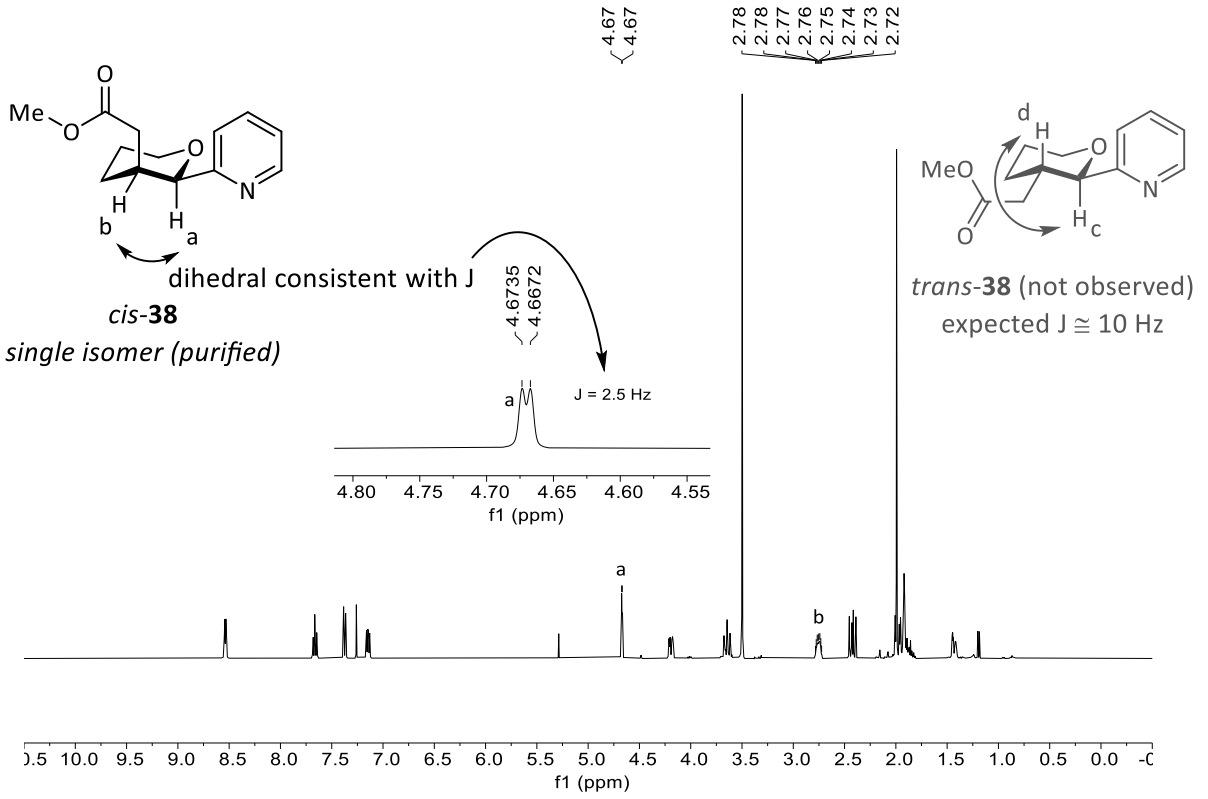



**Figure S10.** $^1$H NMR spectrum of purified **38** (>20:1 *cis*/*trans*) with relevant signals labeled and measurement of their coupling constant that is consistent with *cis*-**38** as the major diastereomer.

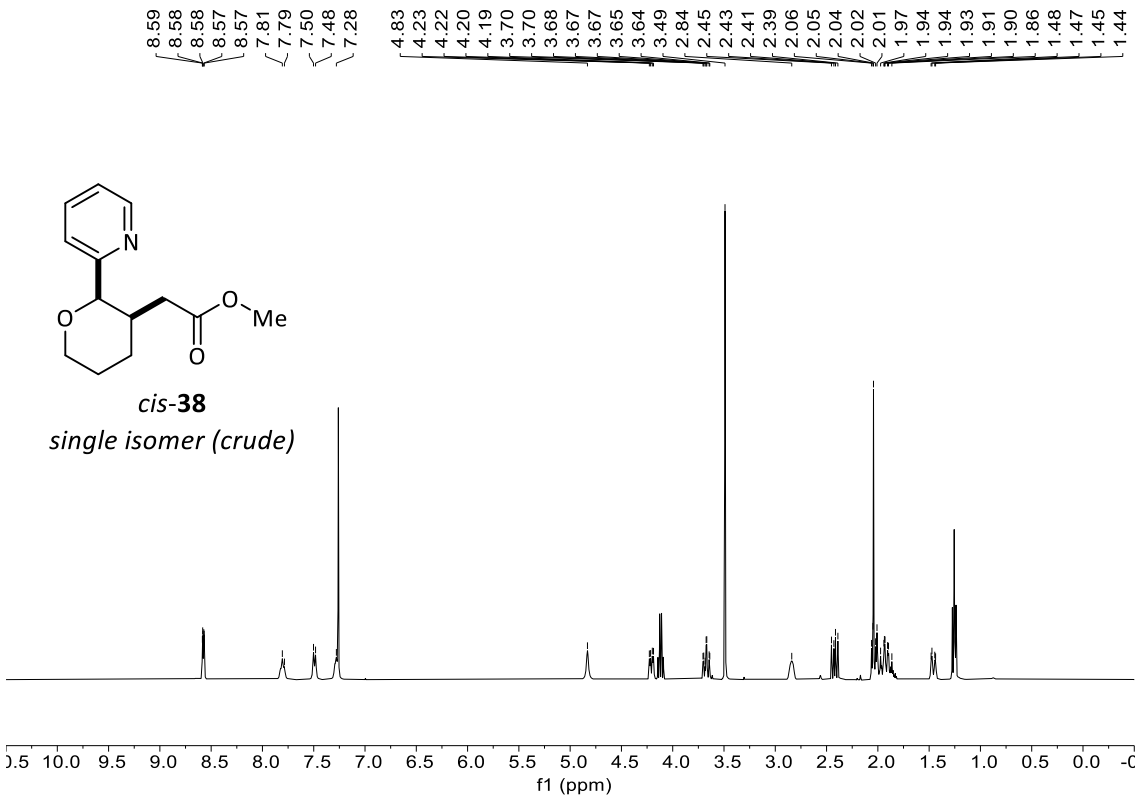
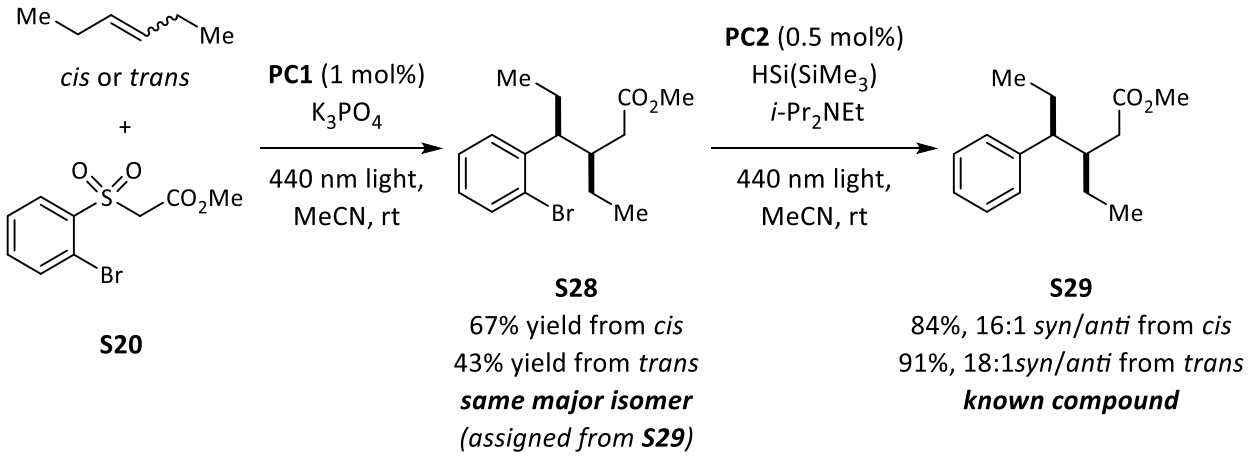



**Figure S11.** $^{1}$H NMR spectrum of crude **38** (>20:1 *cis*/*trans*, no minor diastereomer observed).

**Product 39:**

The major diastereomer of **39** was assigned as *syn* by preparing product **S28**, wherein the 2-pyridyl moiety in **39** was replaced with a 2-bromophenyl group, by the title alkyl–arylation. **S28** was subsequently converted to known phenyl analog **S29** by debromination for comparison to the reported NMR spectra of *syn*- and *anti*-**S29**.[27] Furthermore, since the same major diastereomer of **39** was obtained when using either *cis*- or *trans*-3-hexene as the olefin, each isomer of 3-hexene was employed in separate preparations of **S28** and **S29** to verify that this stereochemical convergence was not restricted to **39**.




Step 1: Alkyl–arylation of *cis*-3-hexene with **S19** (2.4 mmol) according to the general procedure in "Section II. General Procedure for Alkyl–Arylation of Olefins" afforded **S28** (523 mg, 67%). Similarly, alkyl–arylation of *trans*-3-hexene with **S19** (0.8 mmol) also afforded **S28** (108 mg, 0.34 mmol, 43%). In both cases, purity was prioritized over yield during isolation. The same major diastereomer was obtained in both cases, but the assignment and analysis were performed only after debromination, which was not expected to alter the stereochemical composition of the product mixture.

Step 2: Based on a reported procedure,[28] a mixture of **S28** (prepared in Step 1 from *cis*-3-hexene, 157 mg, 0.5 mmol, 1.0 equiv), diisipropylethylamine (174 µL, 1.0 mmol, 2.0 equiv), tris(trimethylsilyl)silane (309 µL, 1.0 mmol, 2.0 equiv), and $Ir(ppy)_2(dtbbpy)PF_6$ (2.4 mg, 2.5 µmol, 0.5 mol%) in acetonitrile (5 mL, 0.1 M) was irradiated overnight with a 440-nm blue light in a vented 8-mL vial at room temperature. After irradiation was stopped, potassium fluoride on alumina (3 g) was added directly to the mixture, which was stirred vigorously. After 15 minutes, the suspension was filtered through Celite® pad, and the filter cake was washed with ethyl acetate. The filtrate was concentrated, and the residue was purified by silica-gel chromatography to afford **S29** as a clear, colorless oil (98 mg, 84%). This procedure was also performed using **S28** prepared from *trans*-3-hexene (0.34 mmol) to afford a second sample of **S29** (72 mg, 91%). Spectroscopic data matched those previously reported.

The $^1$H NMR spectra of crude **S29** derived from *cis*-3-hexene (Figure S12) and *trans*-3-hexene (Figure S13) indicate 16:1 and 18:1 *syn*/*anti* mixtures, respectively, by integration of the $CO_2C\mathbf{H_3}$ signals.

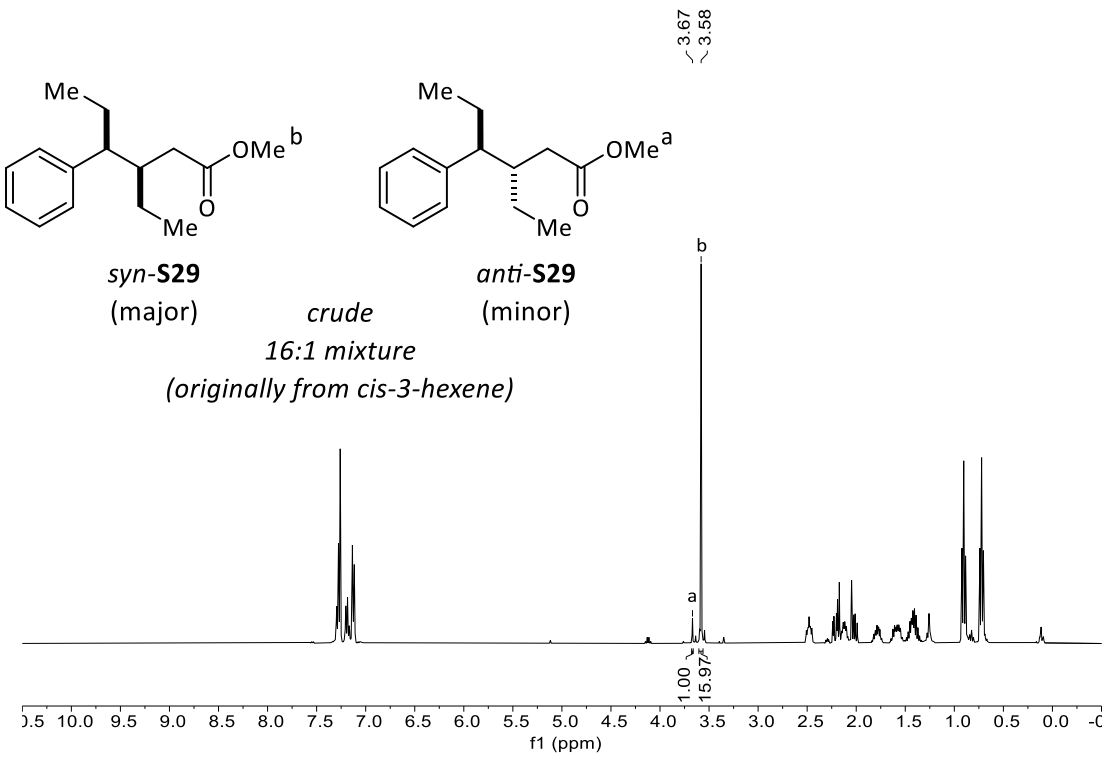



**Figure S12.** $^1$H NMR spectrum of crude **S29** derived from *cis*-3-hexene (16:1 *syn*/*anti* by integration of $CO_2CH_3$ signals). Both diastereomers of **S29** have previously been characterized.[27]

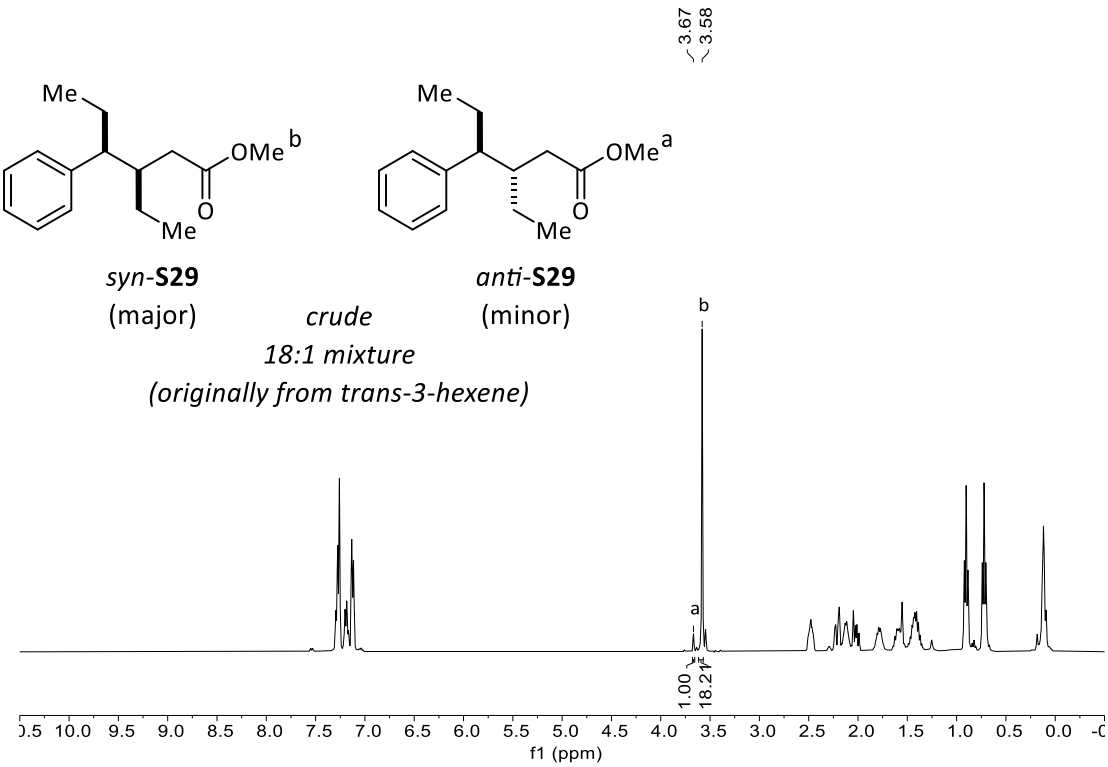



**Figure S13.** $^1$H NMR spectrum of crude **S29** derived from *trans*-3-hexene (18:1 *syn*/*anti* by integration of $CO_2CH_3$ signals). Both diastereomers of **S29** have previously been characterized.[27]

The major diastereomer of **39** was assigned as *syn* by analogy. The $^1$H NMR spectra of crude **39** derived from *trans*-3-hexene (Figure S14) and *cis*-3-hexene (Figure S15) indicate 17:1 and 15:1 *syn*/*anti* mixtures, respectively, by integration of the $CO_2CH_3$ signals.

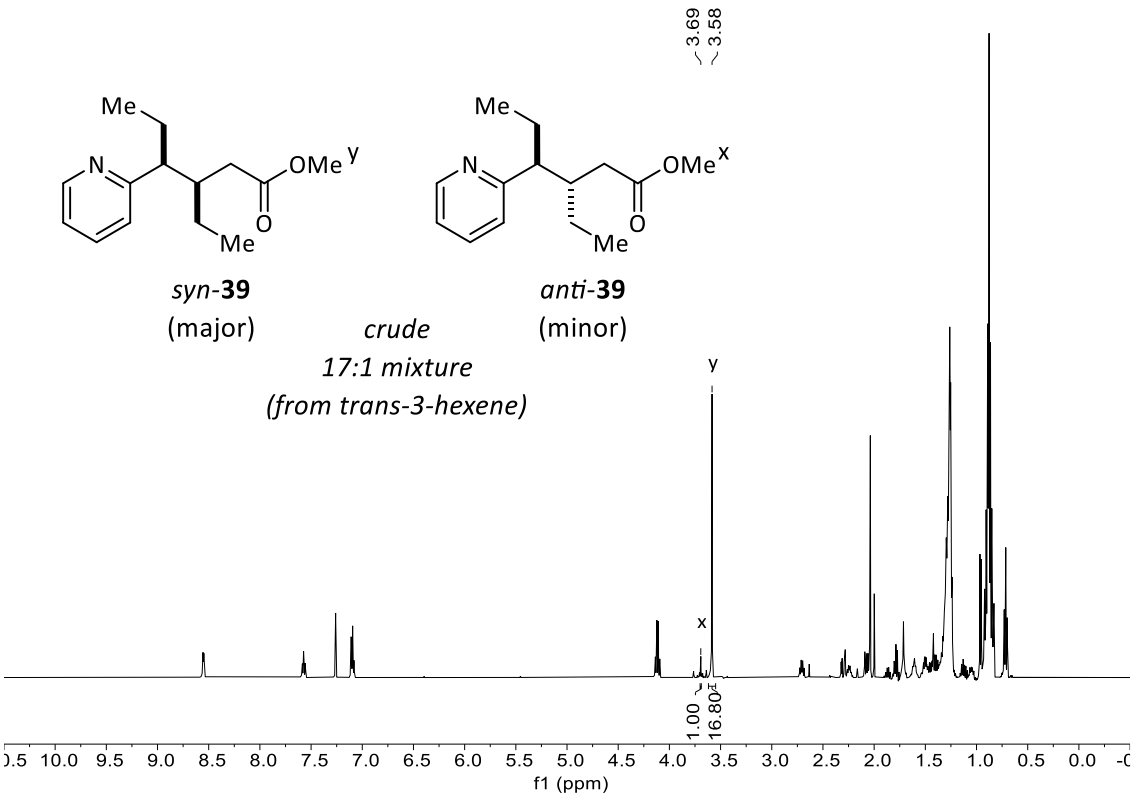



**Figure S14.** $^1$H NMR spectrum of crude **39** derived from *trans*-3-hexene (17:1 *syn*/*anti* by integration of $CO_2CH_3$ signals). The relative stereochemistry was assigned as discussed above.

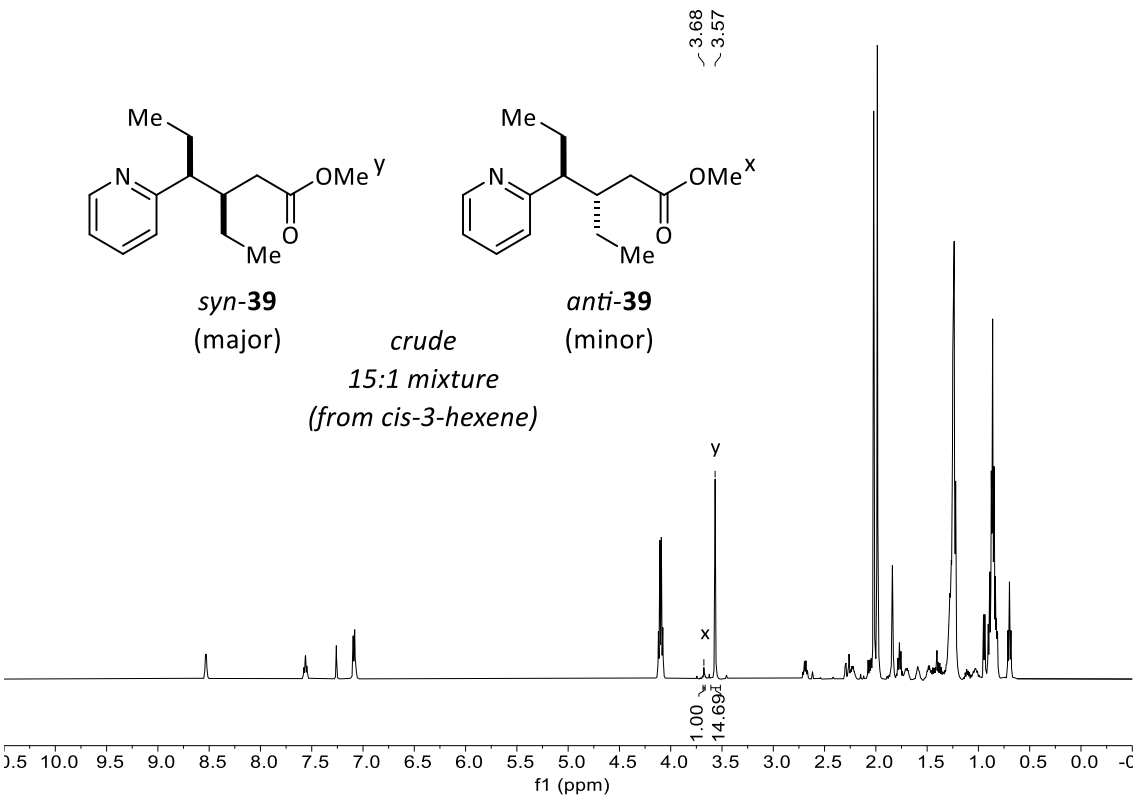



**Figure S15.** $^{1}$H NMR spectrum of crude **39** derived from *cis*-3-hexene (15:1 *syn*/*anti* by integration of $CO_2C\mathbf{H_3}$ signals). The relative stereochemistry was assigned as discussed above.

## VIII. Discussion of Diastereoselectivity (Products 34–39)

The good-to-excellent diastereoselectivities obtained for products **34**–**39** can be rationalized by relatively simple three-dimensional models. A more rigorous analysis of these results will be the subject of a forthcoming investigation, but the reasoning outlined in this section seeks to offer a digestible preliminary understanding. The range of diastereomer-forming reactions performed herein can be classified into four general olefin structures: (a) five-membered, cyclic olefins, (b) six-membered, carbocyclic olefins, (c) six-membered, heterocyclic olefins, and (d) acyclic olefins.

Across all alkene classes, however, we first postulate that the addition of the alkyl radical to the arylsulfonyl group (**8** → **9** in Figure 2) involves the highest-energy transition state in the radical cascade. The highest-energy intermediate should always be the spirocyclic, cyclohexadienyl radical (**9**) because it is the only intermediate wherein aromaticity is absent. Furthermore, we expect the formation of **9** to involve a higher-energy transition state than its decomposition because of the entropic cost needed for the alkyl radical and arylsulfonyl group (see **8** in Figure 2) to encounter each other in the appropriate orientation. The conversion of rigid intermediate **9** into **10** does not require such a significant reorientation. An elementary step analogous to **8** → **9** was also recently identified computationally by Stephenson as having the highest-energy transition of a radical Smiles-Truce mediated alkene aminoarylation with arylsulfonamides[29] that likely shares some general mechanistic elements to the present work. If this proposal holds throughout the following analysis, the formation of **9** would also be the diastereoselectivity-determining step. It then follows from the Hammond postulate that for each class of olefins, the most stable diastereomer of **9** will lead to the major product diastereomer.

Structures of starting materials, products, and relevant intermediates are all shown in Figure S16. Since each product in this section can form two diastereomers,[30] we simplified each analysis to a comparison between the two conformations of the above-mentioned intermediates that would best account for the formation of either product diastereomer. Furthermore, since the alkyl–aryl sulfone was identical in all cases herein, the olefin structure should fully account for differences in diastereoselectivity. The alkyl radicals (**8** in Figure 2 and **S30**, **S32**, **S34**, **S36**, **S38**, **S40**, **S42**, **S44**, and **S46** in Figure S16) are shown for clarity in each case, but the key comparisons will be limited to the spirocyclic, cyclohexadienyl radicals (**9** in Figure 2 and **S31**, **S33**, **S35**, **S37**, **S39**, **S41**, **S43**, **S45**, and **S47** in Figure S16).

Cyclopentene, afforded product **35** in excellent *cis*-selectivity (>20:1). We propose that this high diastereoselectivity originates primarily from the inherent stabilities of fused 5,5 ring systems. The *cis*-product would proceed via *cis*-fused 5,5 intermediate **S31**, whereas the *trans*-product would involve *trans*-fused 5,5 intermediate **S33**. We expect the *trans*-fused intermediate to suffer from significant ring strain, as established for bicyclo[3.3.0]octane.[31,32] Although the intermediates involved herein have different atoms and substituents, we hypothesize nonetheless that the greater strain in *trans*-bicyclo[3.3.0]octane (>6 kcal/mol less stable than the *cis*-isomer) is significant enough to translate to **S33** vs. **S31**. Five-membered, cyclic product **33**, derived from norbornene, would also involve a fused 5,5 intermediate. Its slightly lower dr (10:1) may result from destabilization of **S31** by the additional two-carbon bridge.

Cyclohexene afforded product **36** in modest *trans*-selectivity (5:1). This result could be explained by the relative stabilities of fused 5,6 intermediates **S35** and **S37**. Similarly to the inherent stabilities of fused 5,5 system previously discussed, *cis*-bicyclo[4.3.0]octane is more stable than the *trans*-isomer, but the energy difference is only ~1 kcal/mol. We therefore propose that the destabilizing diaxial-type interaction in *cis*-fused intermediate **S35** between the highlighted S=O and axial C–H moieties is the primary source of energy differences between **S35** and **S37**. Since **S37** represents an all-equatorial conformation with respect to the six-membered ring, it can completely avoid this steric clash and generates the major *trans*-diastereomer, albeit in modest selectivity.

In contrast to *trans*-selective cyclohexene, heterocyclic six-membered olefins afforded products **37** and **38** in excellent *cis*-selectivities (>20:1). For this class of olefins, a variety of factors may conspire to strongly favor *cis*-fused intermediate **S41** over *trans*-fused **S43**. One clear difference owing to the replacement of a $CH_2$ unit in cyclohexene with a heteroatom adjacent to the C=C bond is the loss of the previously mentioned diaxial-type interaction highlighted in **S35**. This effect, alone, may not fully account for the excellent diastereoselectivities observed for **37** and **38**, but it nonetheless likely plays a key role. The above-mentioned preference for *cis*-bicyclo[4.3.0]octanes is also consistent with these observed selectivities.

For both the carbocyclic and heterocyclic six-membered olefins, we also assumed that the most-relevant *cis*-fused intermediates, **S35** and **S41**, would place the new ‘alkyl’ group (blue bond) in a pseudo-axial position with respect to the six-membered ring and the ‘transferring aryl’ group (red

bond) in a pseudo-equatorial position. In principle, *cis*-products could also form via the corresponding ring-flipped, *cis*-fused intermediates (**S39**). Because such structures would suffer from severe diaxial interactions between the cyclohexadienyl-radical moiety and the two highlighted H atoms in all cases, however, this conformation was discounted.

Finally, acyclic olefin 3-hexene generated product **39** in good *syn*-selectivity irrespective of the isomer subjected to alkyl–arylation (17:1 and 15:1 *syn*/*anti* from *trans*- and *cis*-3-hexene, respectively). We expect that after the formation of the first C–C bond between electrophilic alkyl radical **4** and an acyclic olefin (see Figure 2), free rotation about the former C=C bond occurs. Conformers **S44** and **S46** can therefore equilibrate before the radical-migration step, and the geometry of the starting olefin does not have a significant impact on the stereochemical outcome. Furthermore, destabilizing steric interactions would clearly favor both **S44** and **S45** over **S46** and **S47**, leading to the *syn*-product in good selectivity. A similar model was proposed by Stephenson for their aminoarylation.[29,33]

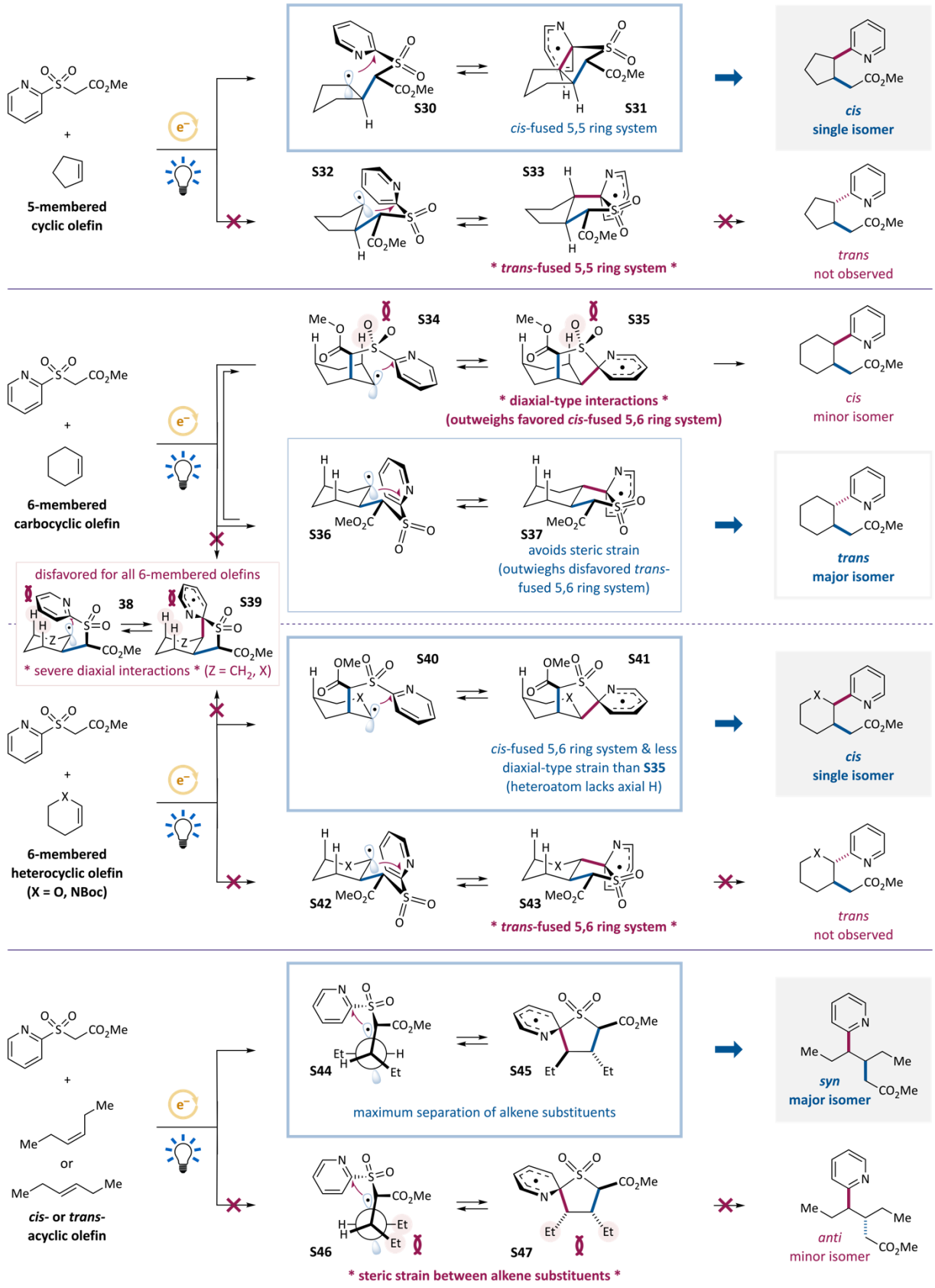



**Figure S16.** Rationale for diastereoselectivity.

## IX. Stern-Volmer Analysis for Fluorescence Quenching of PC1

### General Procedure

A series of five acetonitrile solutions containing photocatalyst **PC1** and quencher in in quartz cuvettes were prepared in a nitrogen-filled glove box by adding stock solutions of **PC1** (0.01 M, 30 μL per sample) and quencher (0.25 M: 0 μL, 30 μL, 60 μL, 90 μL, 120 μL). The total volume of each sample was adjusted to 3.0 mL by adding acetonitrile, affording a 0.1-mM concentration of **PC1** in all samples and 0-mM, 2.5-mM, 5.0-mM, 7.5-mM, and 10-mM concentrations of quencher. Samples were excited with 459 nm light, and emission was measured at 619 nm.

### Analysis

Figure S17 below indicates that the anionic conjugate base of sulfone **S1** (deprotonated with DBU) quenches excited-state photoredox catalyst **PC1**, consistent with the proposed mechanism (see Figure 2). In contrast, no quenching is observed in the presence of either neutral sulfone **62** (Figure S18) or olefin **S48** (Figure S19). Figure S20 also indicates that the DBU•HCl also affords no quenching, implying that the anionic conjugate base of sulfone **S1** and not the cationic conjugate acid of DBU is responsible for the quenching observed in Figure S17.

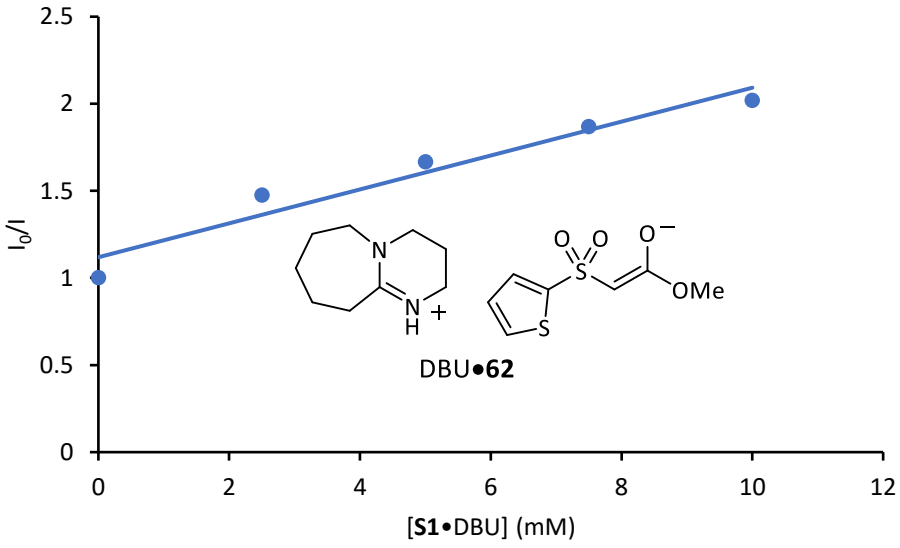



**Figure S17.** Fluorescence quenching of **PC1** (0. 1 mM) with a 1:1 mixture of **62**, deprotonated by DBU, suggests that the deprotonated sulfone quenches the excited-state photoredox catalyst.

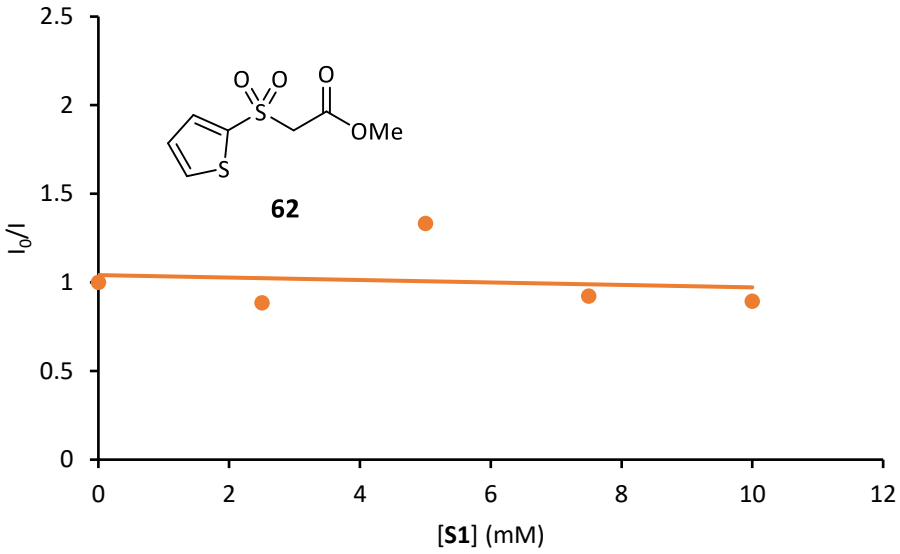



**Figure S18.** Fluorescence quenching of **PC1** (0.1 mM) with **62** suggests that the neutral sulfone does not quench the excited-state photoredox catalyst.

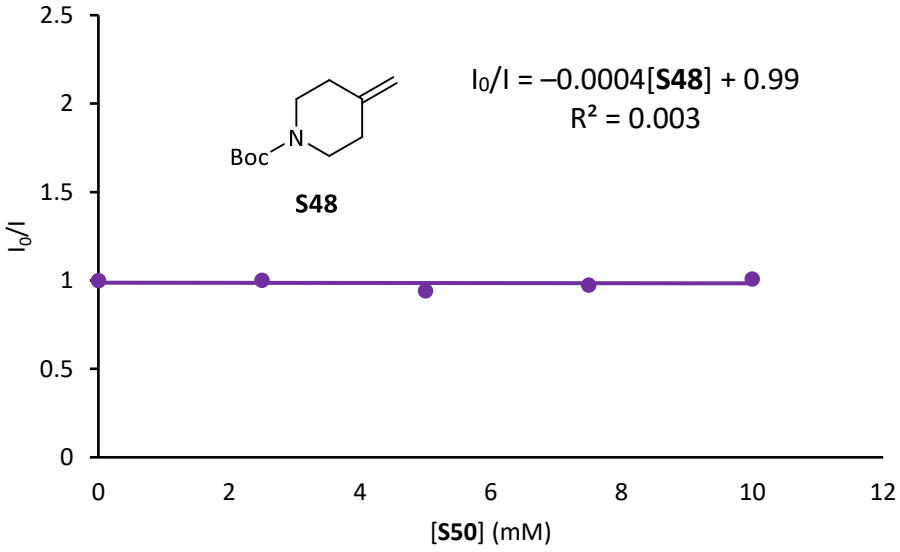



**Figure S19.** Fluorescence quenching of **PC1** (0.1 mM) with **S48** suggests that the olefin does not quench the excited-state photoredox catalyst.

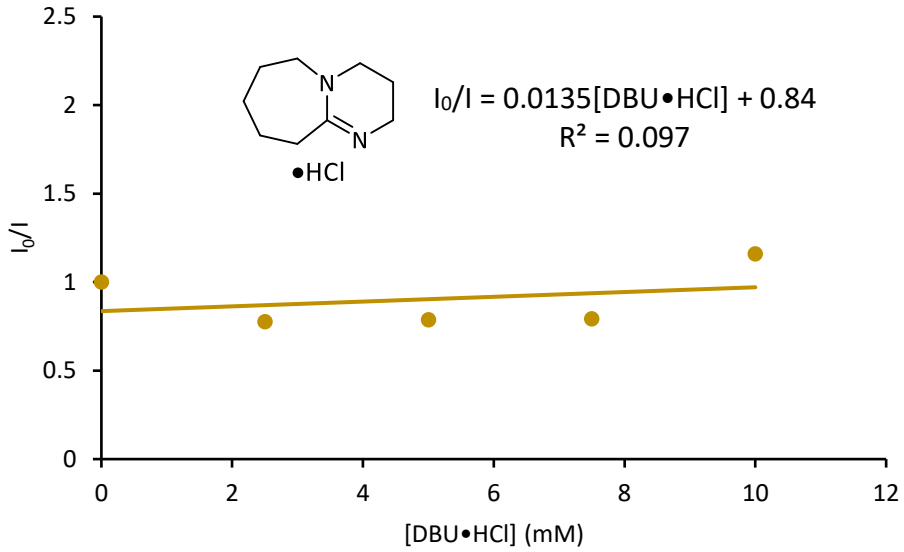



**Figure S20.** Fluorescence quenching of **PC1** (0.1 mM) with DBU•HCl suggests that the conjugate acid of DBU is not responsible for the quenching of excited-state **PC1** observed in Figure S21.

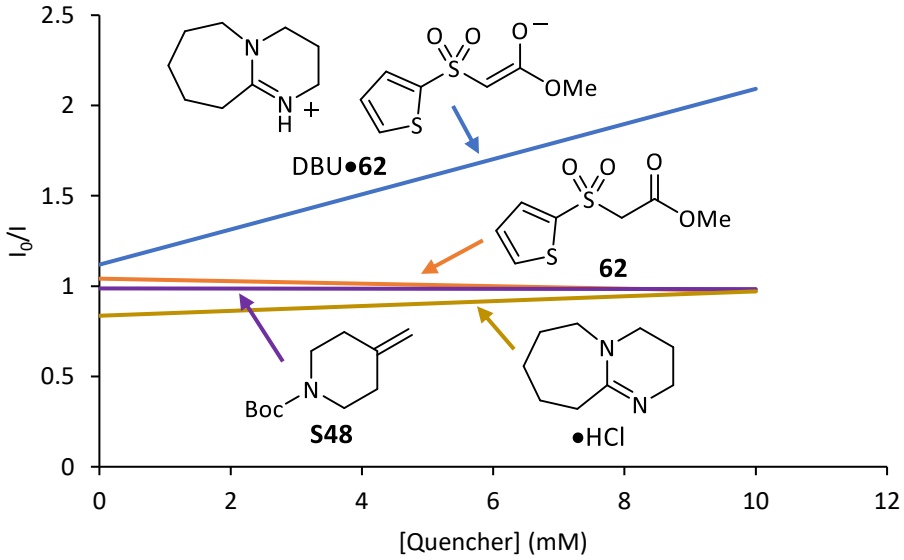



**Figure S21.** Superimposed fluorescence-quenching plots.

## X. Cyclic Voltammetry

### General Procedure

A mixture of sulfone (0.003 M), potassium phosphate (0.003 M) and tetrabutylammonium hexafluorophosphate (0.1 M) in acetonitrile (5 mL) was prepared in a 10-mL three-neck flask (undivided cell) at room temperature and stirred for 10 minutes. All measurements were scanned oxidatively, from 0 V vs. $Ag/AgNO_3$ to +0.6 V or +0.8 V vs. $Ag/AgNO_3$, and then reductively, to 0 V vs. $Ag/AgNO_3$, at 500 mV/s. Cyclic voltammograms are shown in Figures S23–S28.

### Analysis

Some products in Table 1 required Ir-based photoredox catalysts **PC2** or **PC3** instead of standard Ru-based **PC1** to obtain optimal yields. By studying the electrochemical properties of the sulfone substrates, a general trend was observed that can be used as a rough guideline to aid in the selection of the optimal photoredox catalyst.

Since the excited-state photoredox catalyst oxidizes the anionic conjugate base of the sulfone (see "IX. Stern-Volmer Analysis for Fluorescence Quenching of PC1"), the peak oxidation potentials for a selection a selection of sulfones (deprotonated by $K_3PO_4$) requiring different photoredox catalysts were measured. As summarized in Figure S22, sulfones with conjugate bases that have $E^{ox} \lesssim +0.6–0.7$ V vs. SCE react efficiently with standard photoredox catalyst **PC1**. In contrast, sulfones with conjugate bases that have $E^{ox} \gtrsim +0.8–0.9$ V vs. SCE require more-oxidizing photoredox catalysts **PC2** or **PC3**. The only sulfone that required **PC3**, the most-oxidizing photoredox catalyst, was also the most difficult to oxidize.

Products **53** and **54** were also obtained in superior yields using **PC2**, although their corresponding sulfones are easily oxidized and these results fall outside of this rough guideline.

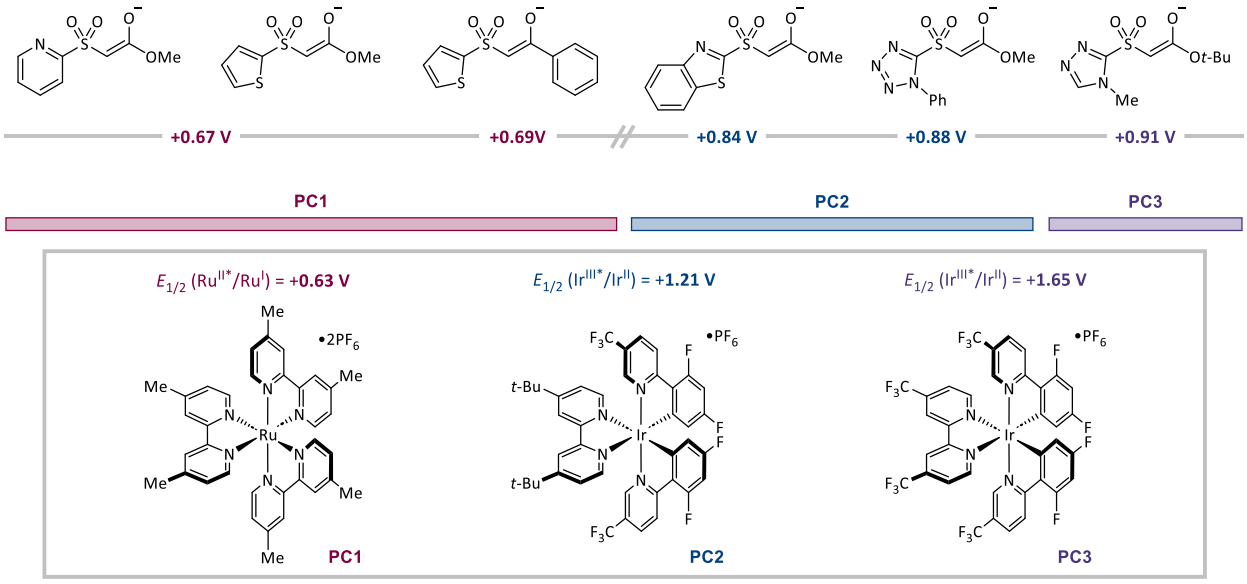



**Figure S22.** Guide for photoredox catalyst selection based on the electrochemical potentials of the photoredox catalysts[34,35] and the conjugate bases of the alkyl–aryl sulfones (vs. SCE in MeCN).

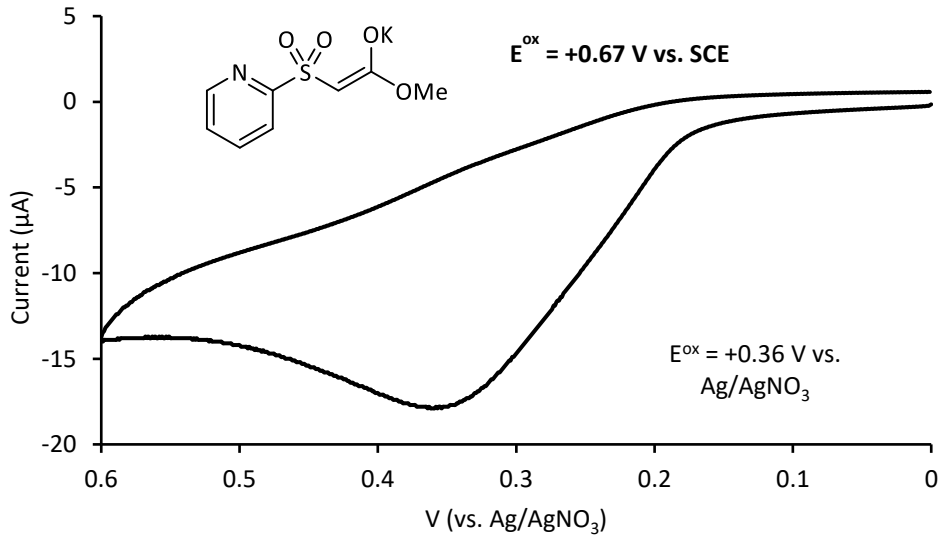



**Figure S23.** Cyclic voltammogram of sulfone **12**, deprotonated by $K_3PO_4$, at 500 mV/s.

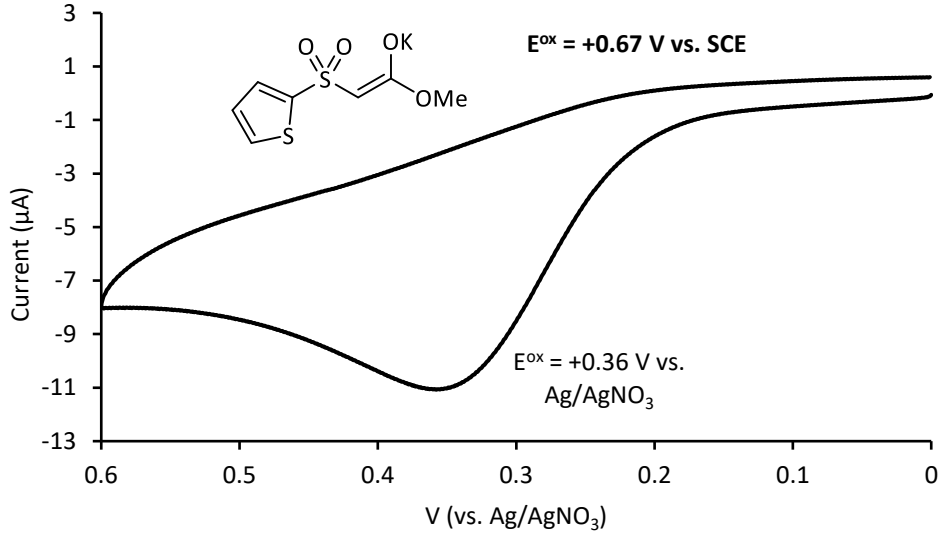



**Figure S24.** Cyclic voltammogram of sulfone **62**, deprotonated by $K_3PO_4$, at 500 mV/s.

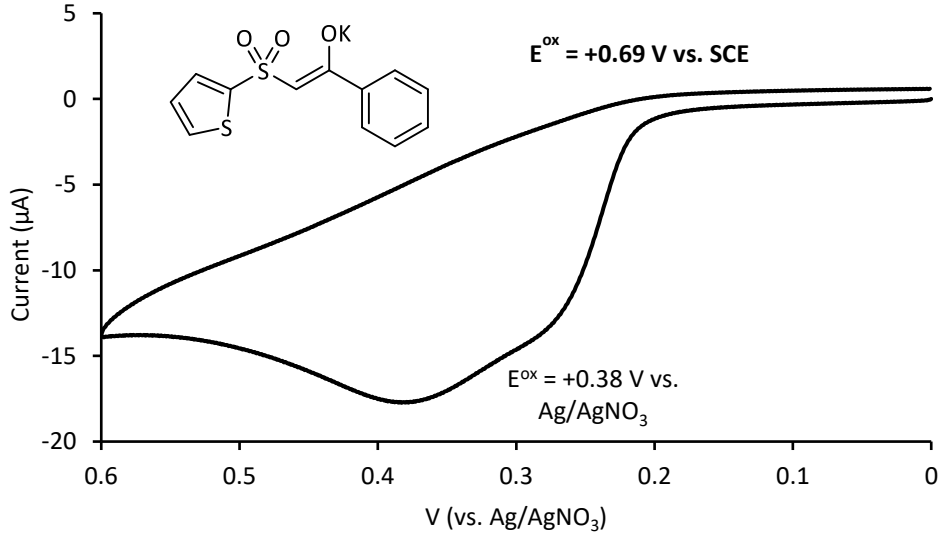



**Figure S25.** Cyclic voltammogram of sulfone **S3**, deprotonated by $K_3PO_4$, at 500 mV/s.

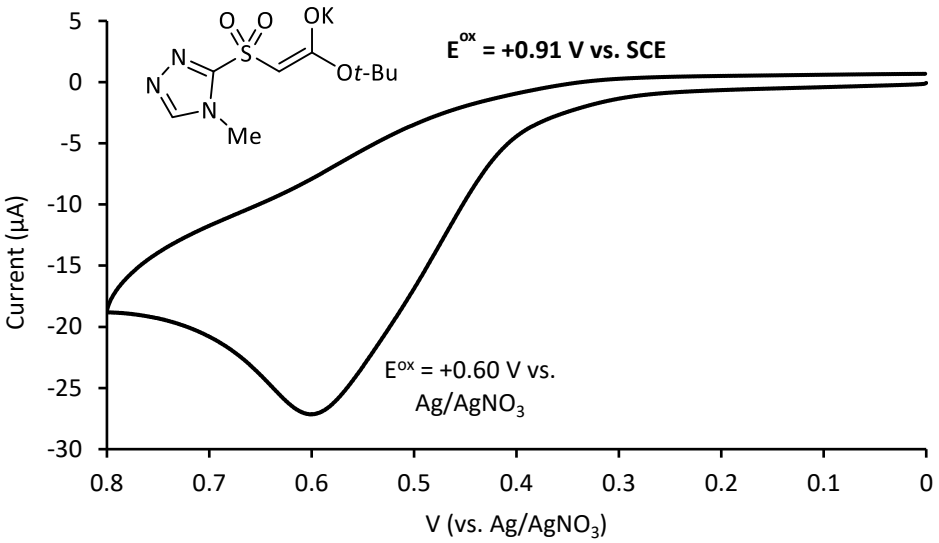



**Figure S26.** Cyclic voltammogram of sulfone **S12**, deprotonated by $K_3PO_4$, at 500 mV/s.

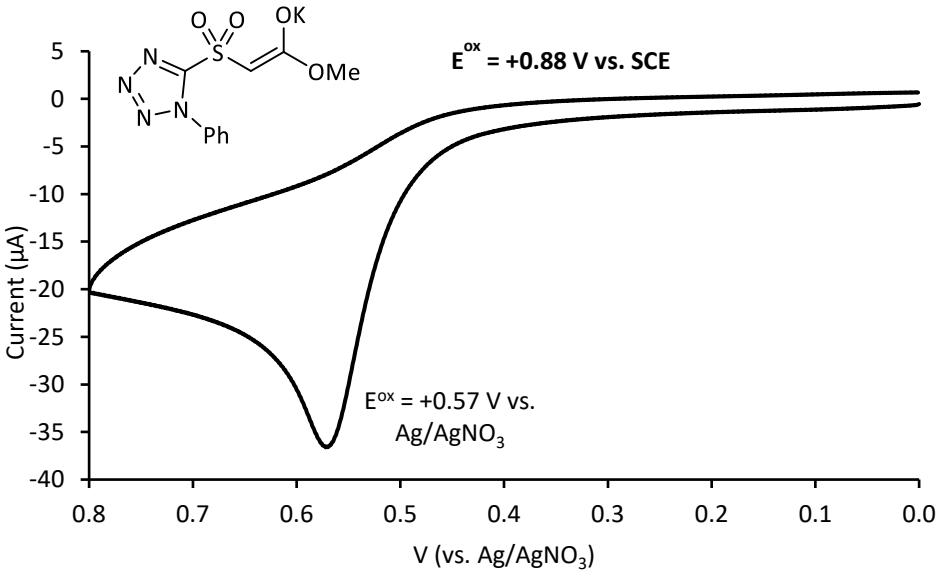



**Figure S27.** Cyclic voltammogram of sulfone **S13**, deprotonated by $K_3PO_4$, at 500 mV/s.

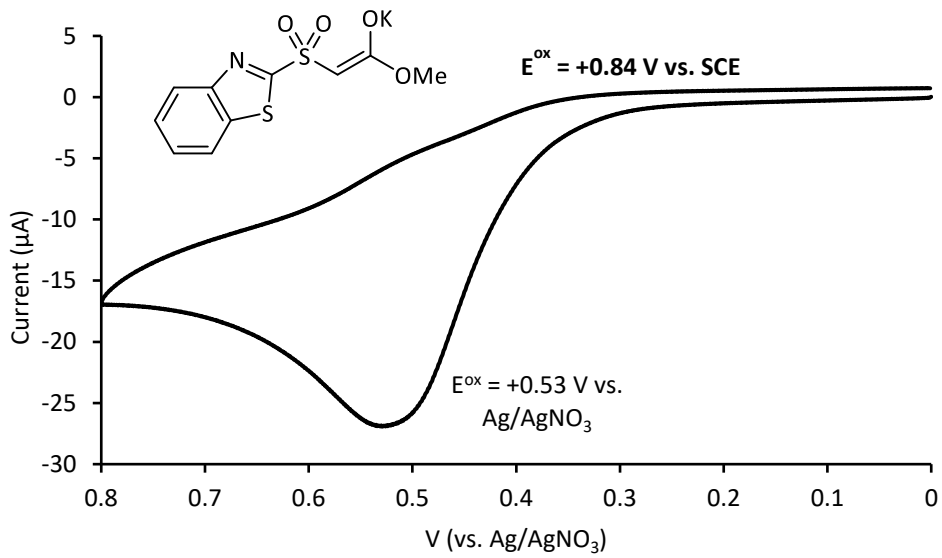
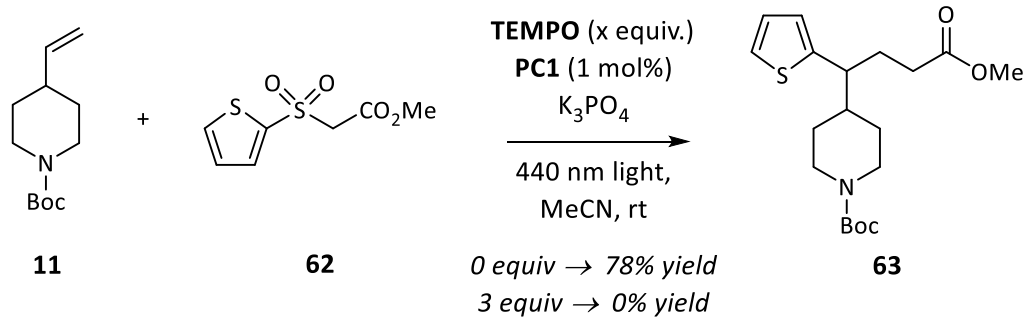



**Figure S28.** Cyclic voltammogram of sulfone **S15**, deprotonated by $K_3PO_4$, at 500 mV/s.

## XI. Experiments to Test for the Presence of Radicals (Scheme 2a–b)

### TEMPO Inhibition (Scheme 2a)

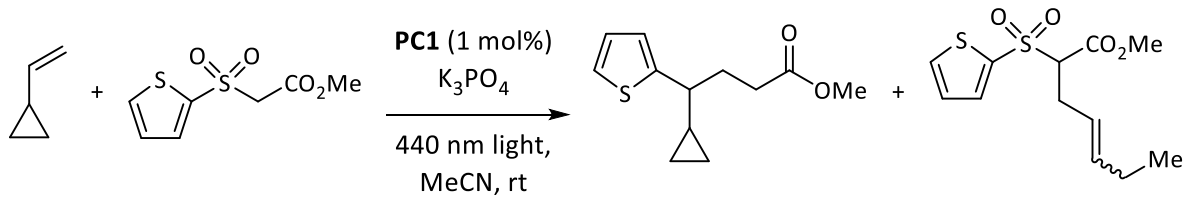



**11** **62** **63**

*0 equiv → 78% yield*
*3 equiv → 0% yield*

Olefin **11** and alkyl–aryl sulfone **62** were converted to product **63** according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1** in the absence or presence of TEMPO. Without TEMPO, **63** was obtained in 78% yield. See "Section VI. Characterization Data" for isolation conditions and spectroscopic data. With TEMPO (3 equiv), no product was detected by $^1$H NMR or LC-MS analysis of the crude reaction mixture.

### Cyclopropane Opening (Scheme 2b)

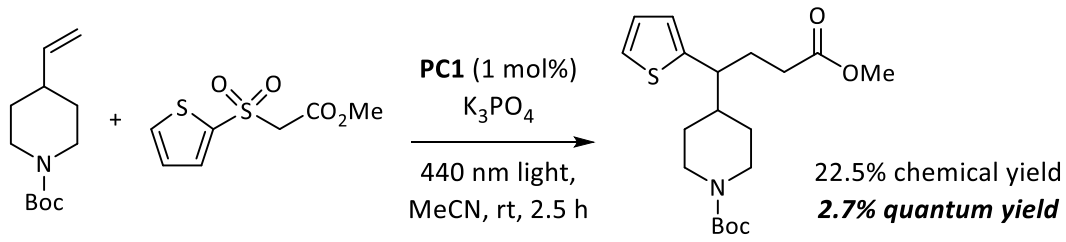



**64** **62** **65** **68**

*0% yield* *6% yield*

Olefin **64** and alkyl–aryl sulfone **62** were subjected to conditions outlined in "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1**. Product **65** was not detected by $^1$H NMR or LC-MS analysis of the crude reaction mixture. The vast majority of the starting materials remained intact, but a new product was detected in 6% yield by $^1$H NMR analysis. Partial purification of this material allowed its structure to be assigned as compound **68** (see "Section VI. Characterization Data" for isolation conditions and spectroscopic data).

## XII. Quantum Yield Measurement (Scheme 2c)




**11** **62** **63**

### Chemical Yield Measurement

Olefin **11** (1.2 mmol) and alkyl–aryl sulfone **62** (0.4 mmol) were converted to product **63** according to "Section II. General Procedure for Alkyl–Arylation of Olefins" with **PC1** and with mesitylene as an internal standard. After 2.5 hours (9000 s), $^1$H NMR analysis of the reaction mixture revealed a chemical yield of 22.5% (0.0900 mmol) of **63**.

### Actinometry

Following a previously described procedure,[36] we measured the photon flux of the 440-nm photoreactor seat used in the chemical yield measurement described immediately above to be $3.765 \times 10^{-7}$ mol/s.

### Quantum Yield Calculation

After 2.5 hours (9000 s), 3.39 mmol of photons are estimated to have passed through the reaction mixture.

We measured that **PC1** absorbs 98.8% of 440-nm light (A = 1.92) for the path length and concentration used in the chemical yield measurement. Therefore, 3.35 mmol of photons are estimated to have been absorbed by **PC1**. The quantum yield is therefore estimated as

$$\phi = \frac{0.0900 \text{ mmol } \mathbf{63}}{3.37 \text{ mmol photons}} = 2.7\%$$

## XIII. References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30. Norbornene-derived **53** could form up to 4 diastereomers, although (a) the first addition of the alkyl radical to this olefin is expected to selectively add to the less-hindered C=C face, *syn* to the $CH_2$ bridge, and (b) the focus of this discussion is the diastereoselectivity of the aryl migration step. Therefore, these additional considerations for **53** are not discussed herein.

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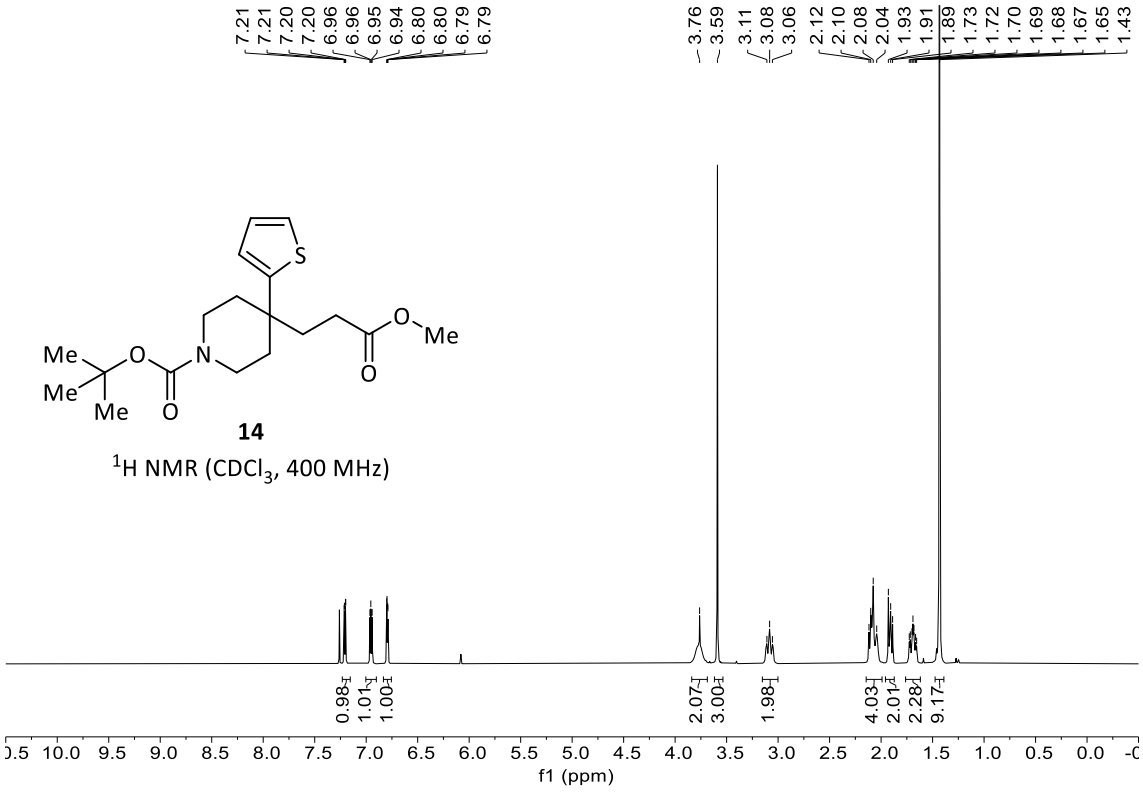
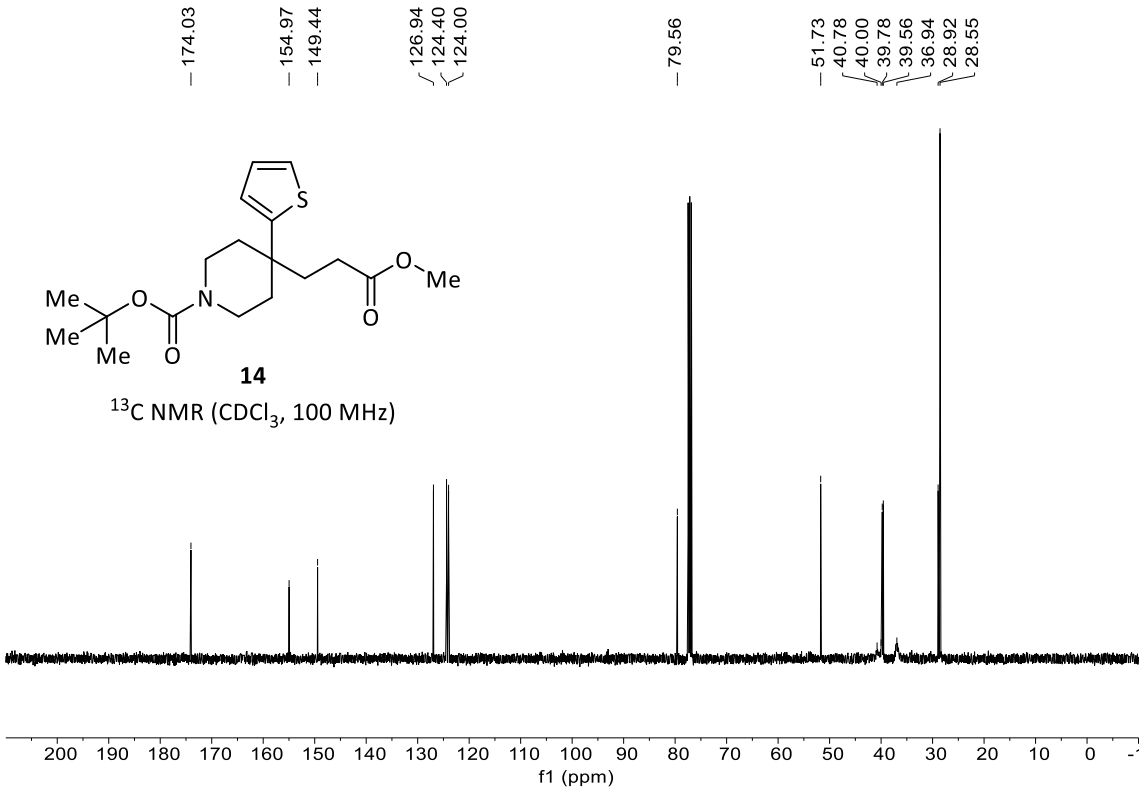
# XIV. NMR Spectra




**14**

$^{1}$H NMR ($CDCl_3$, 400 MHz)




**14**

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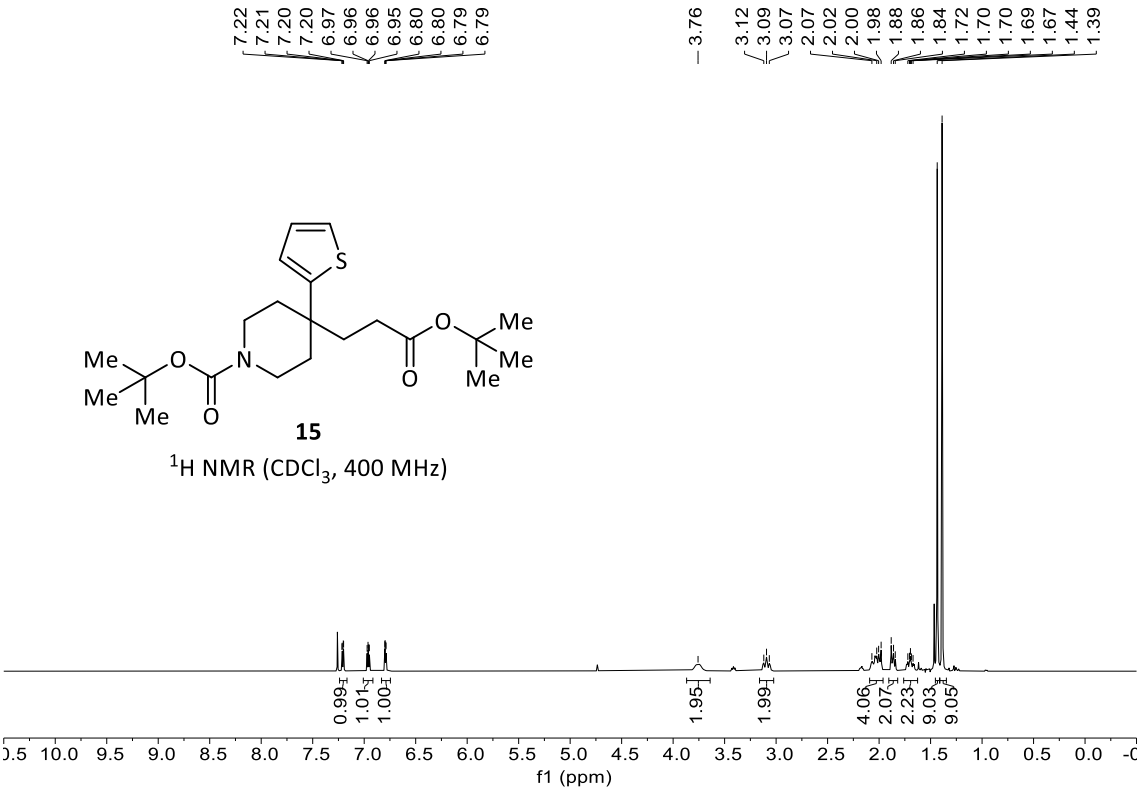


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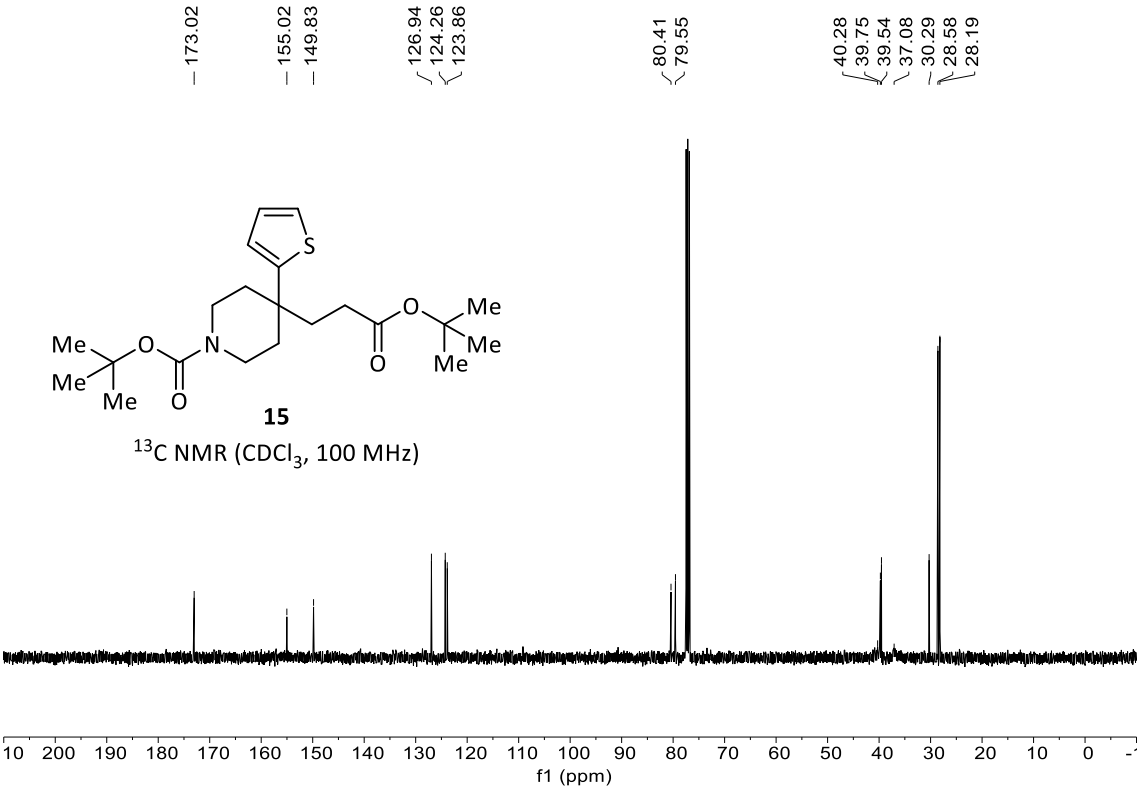


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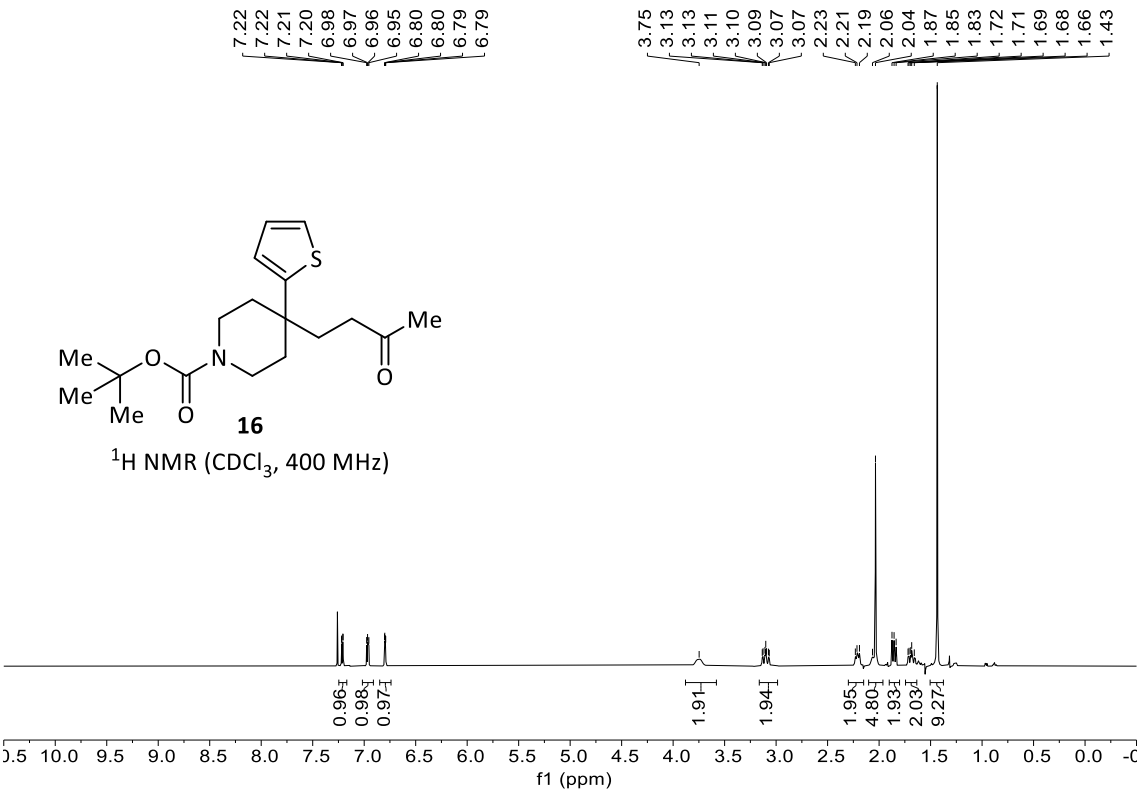


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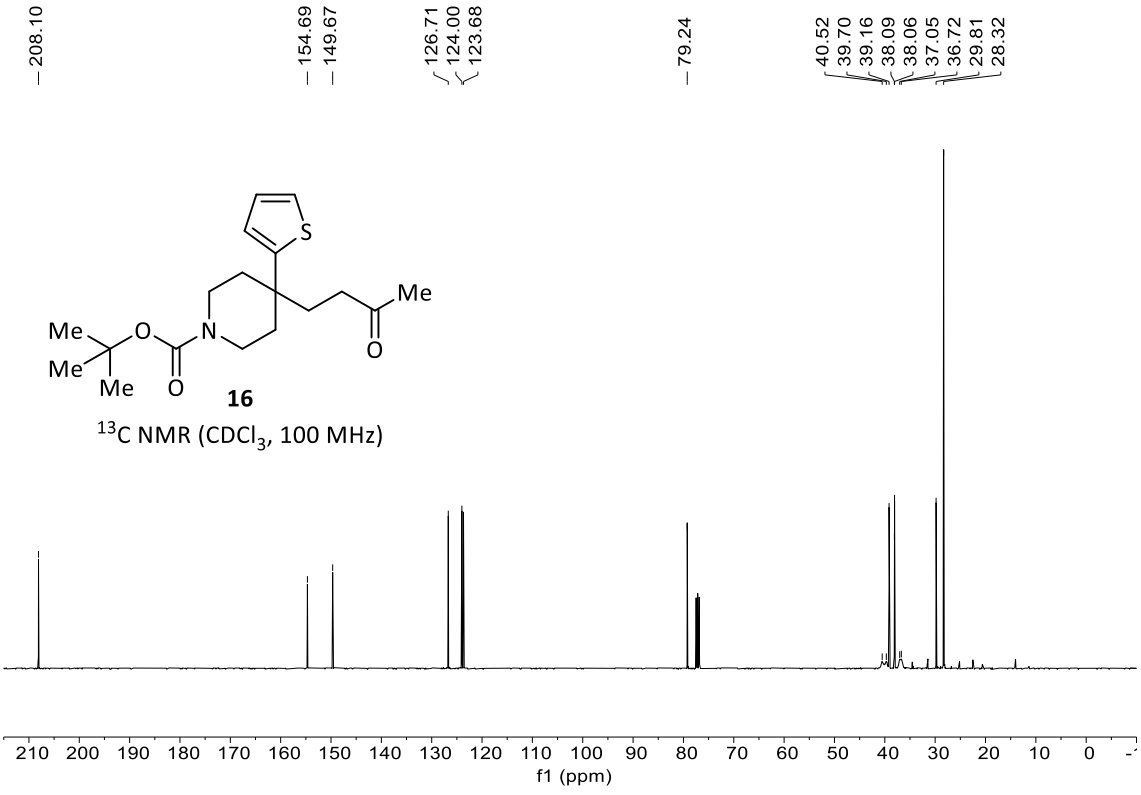


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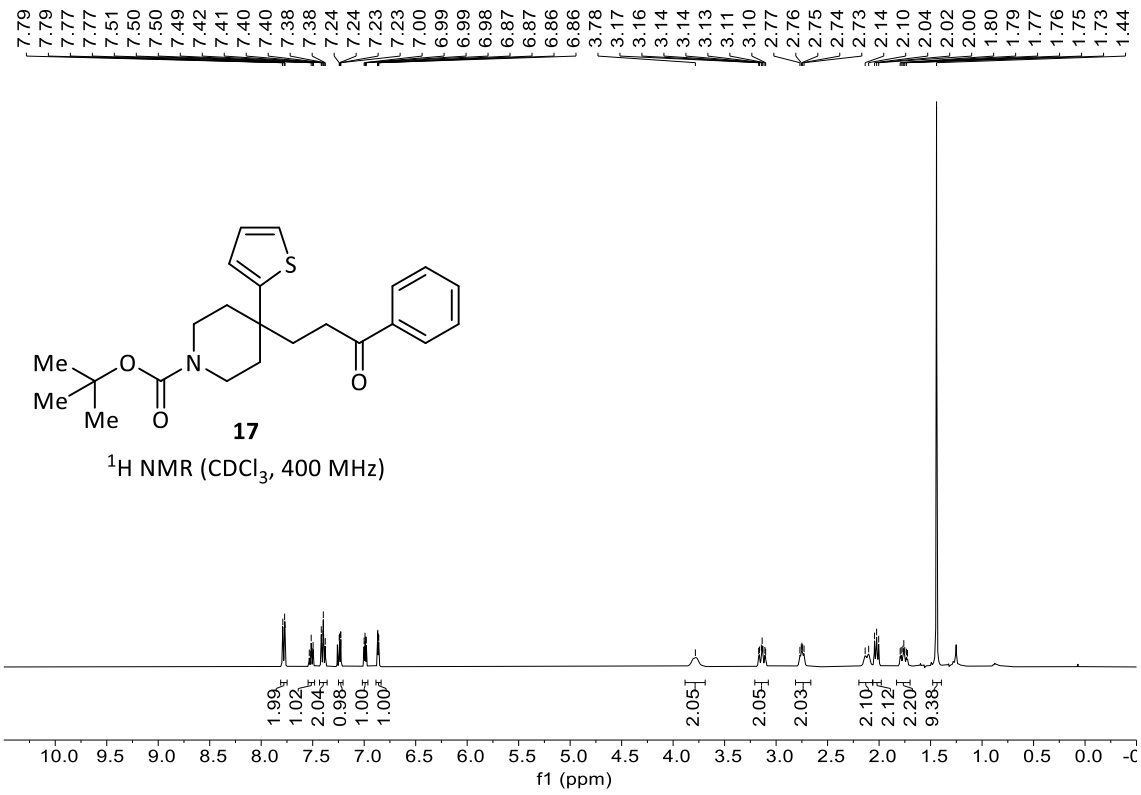


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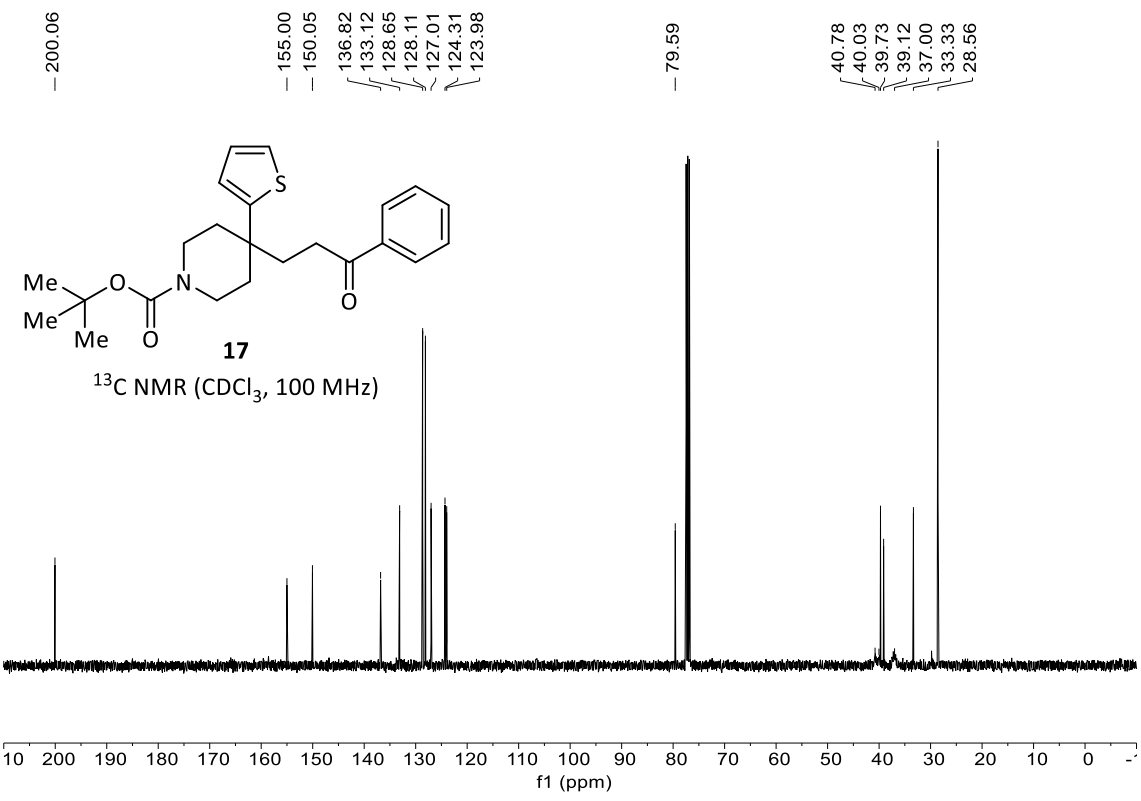


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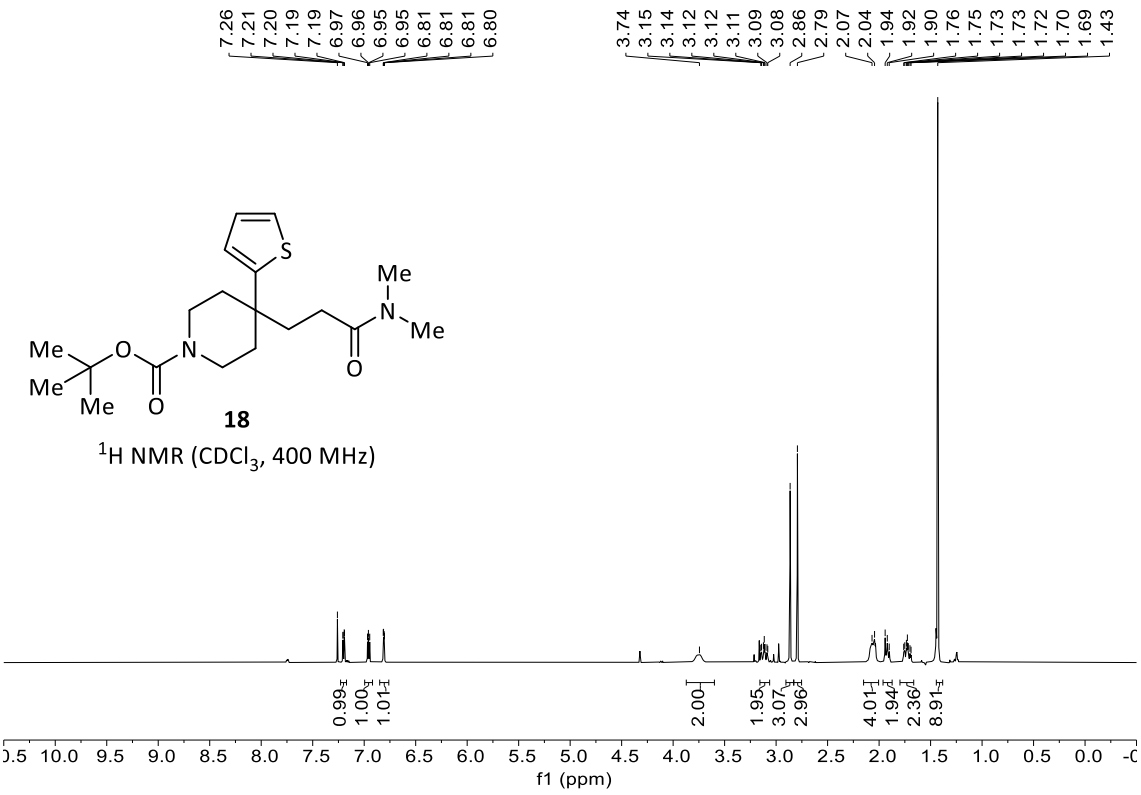


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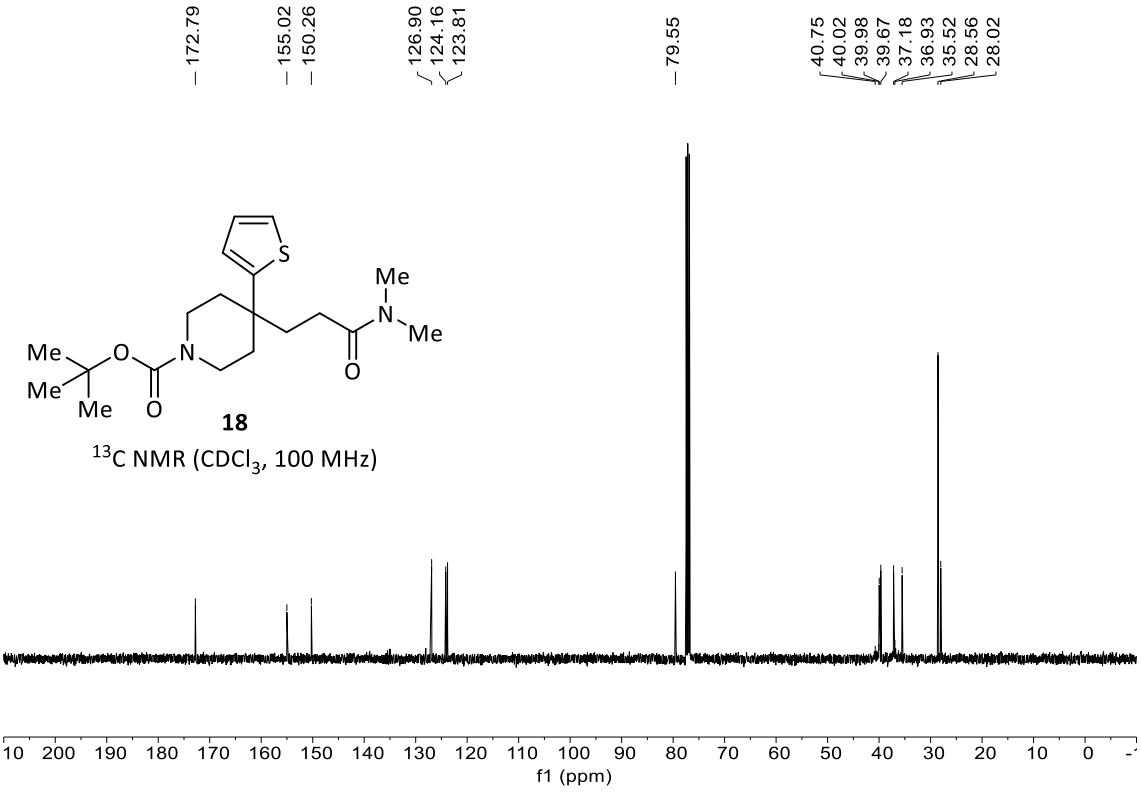


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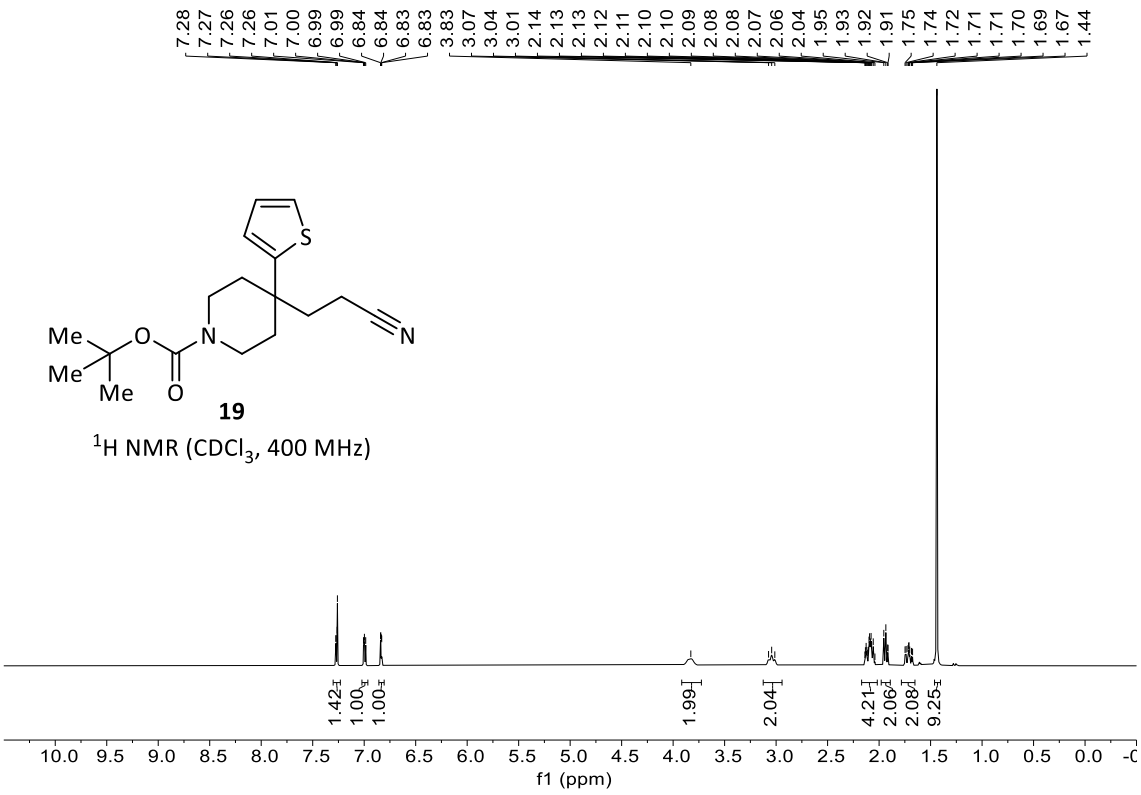


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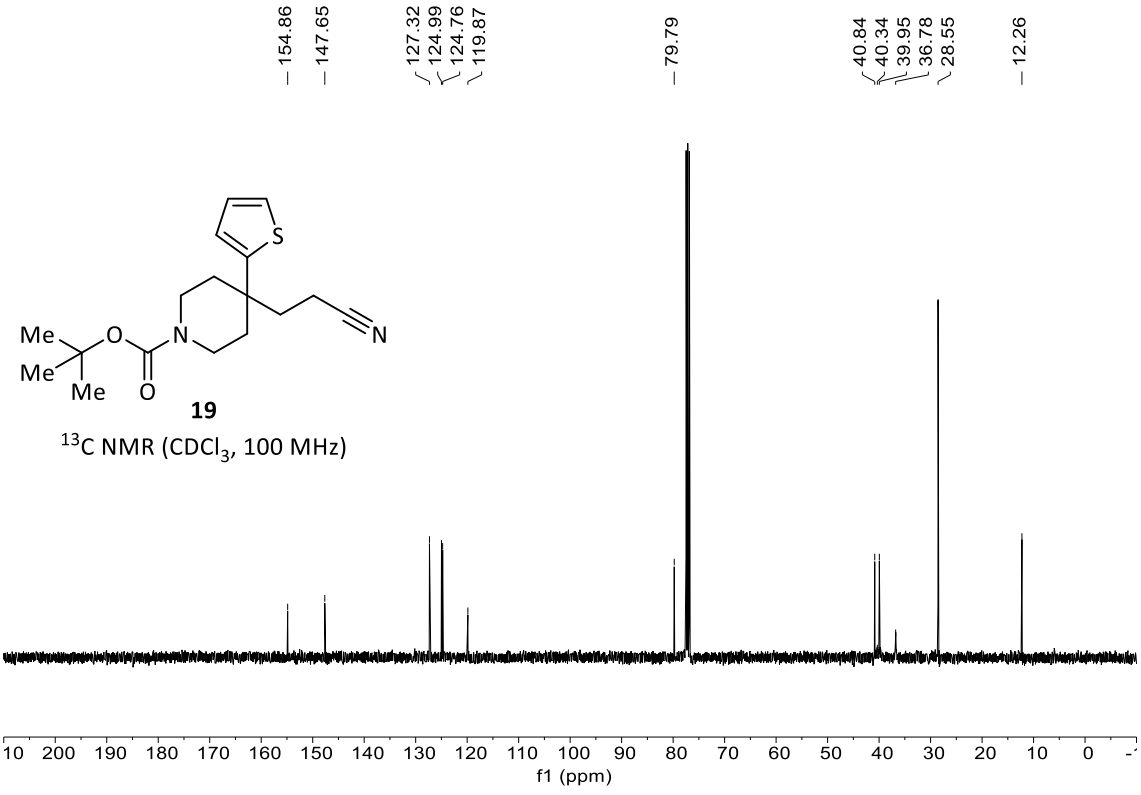


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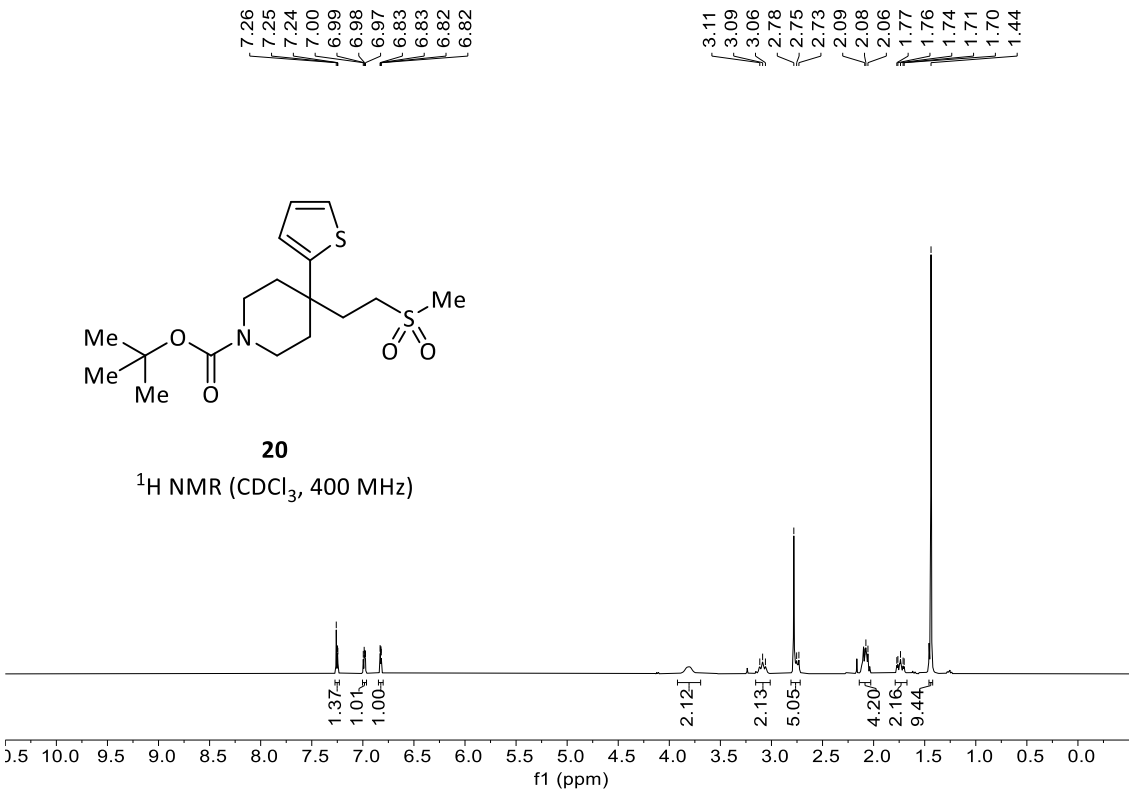


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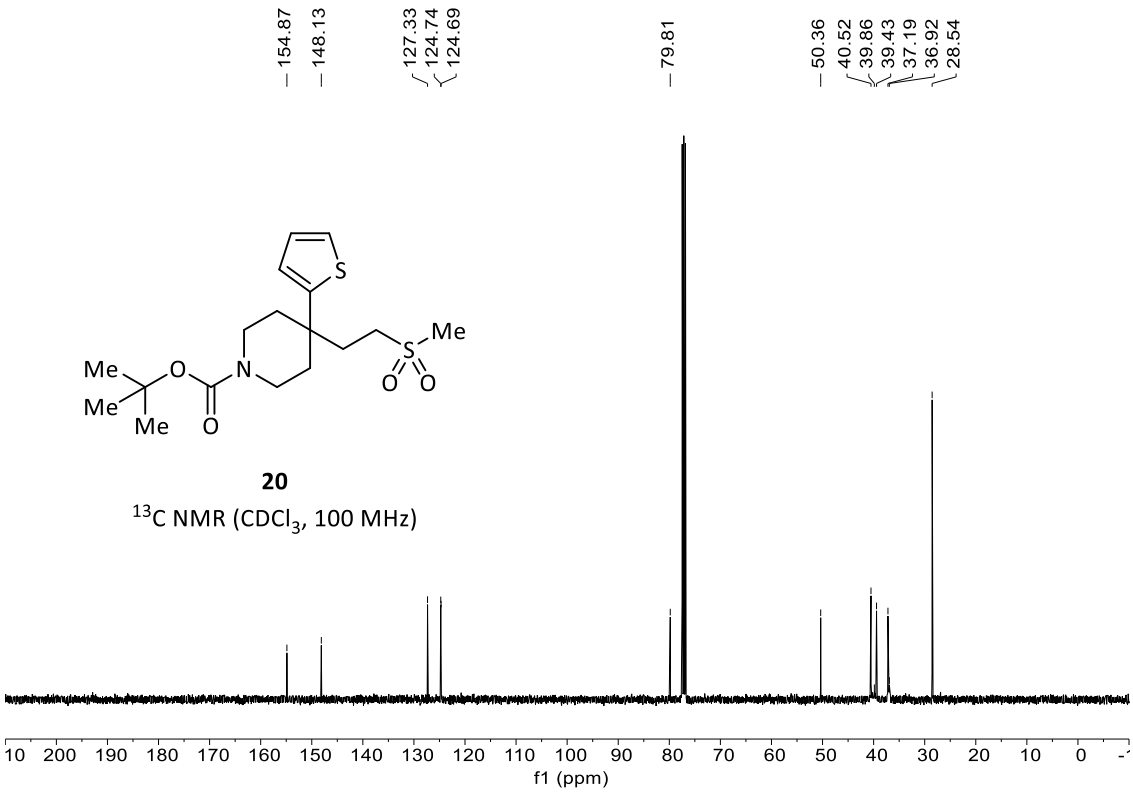


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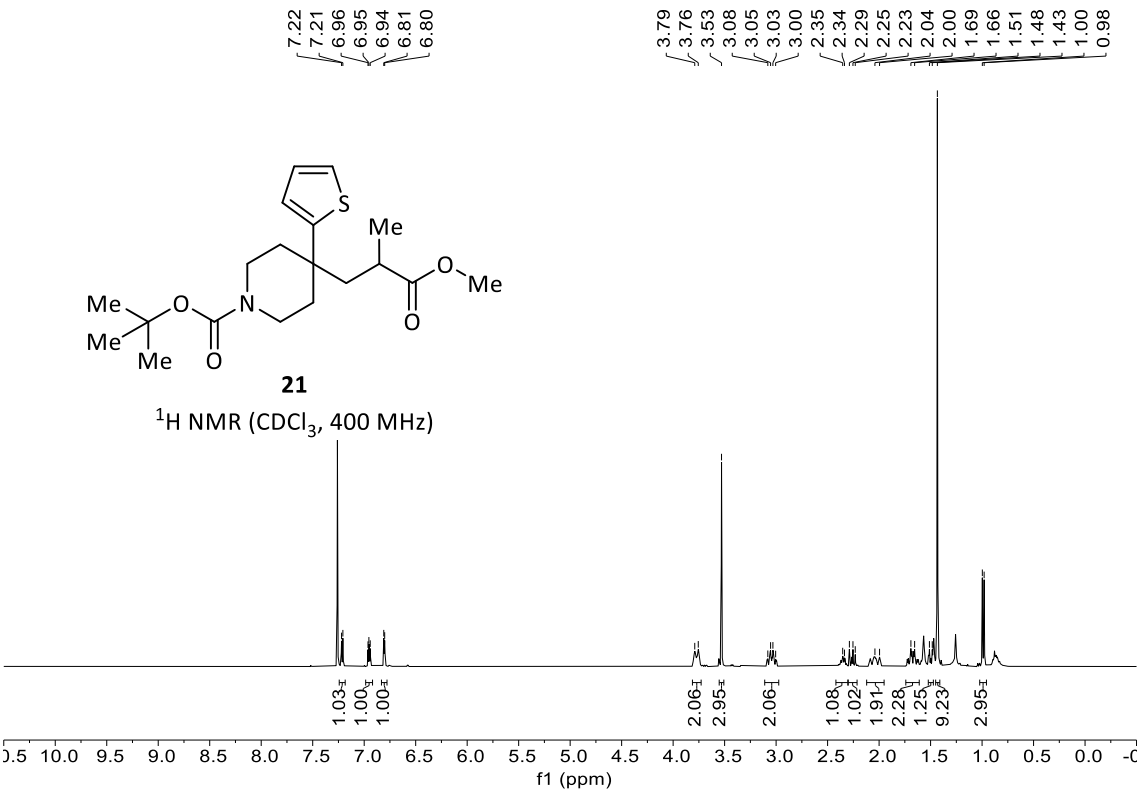


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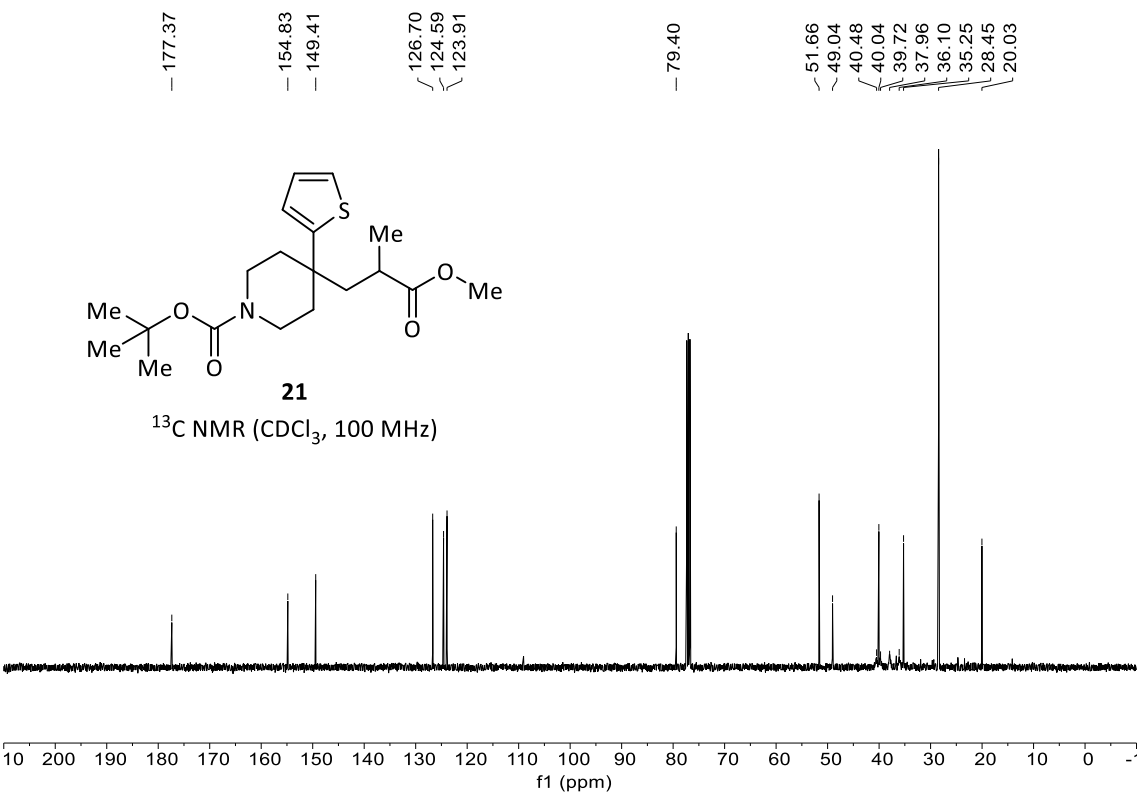


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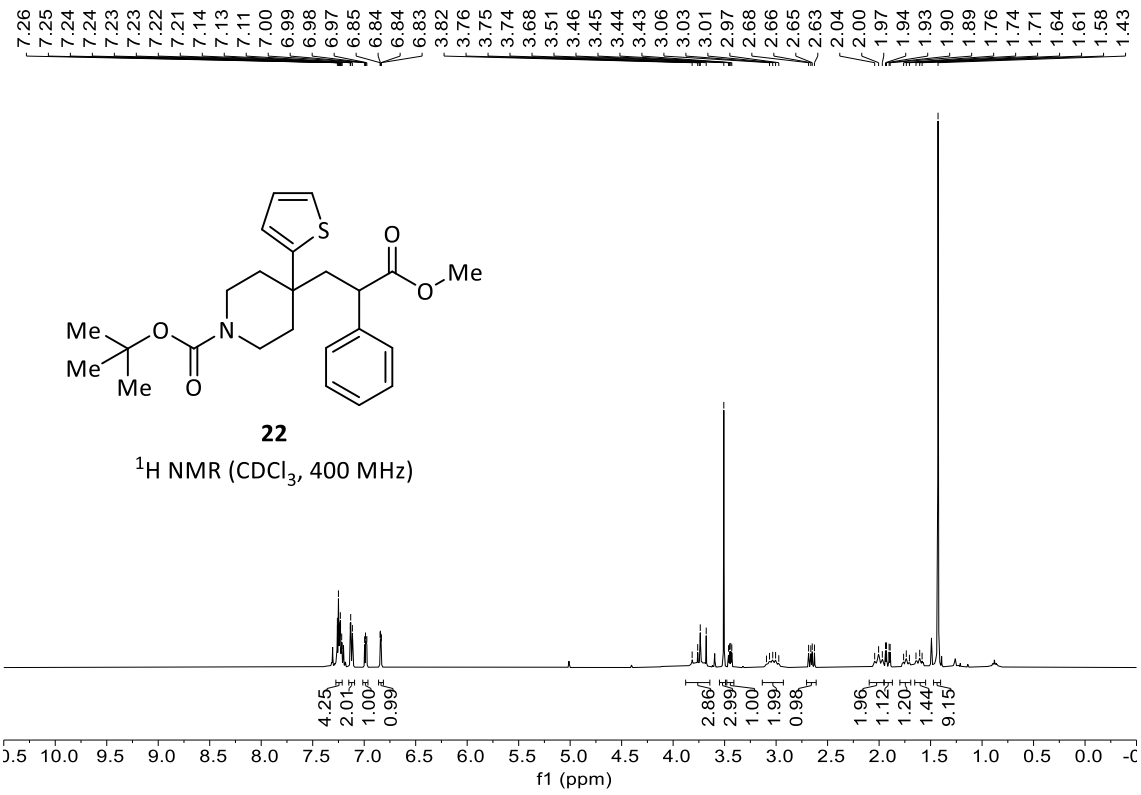


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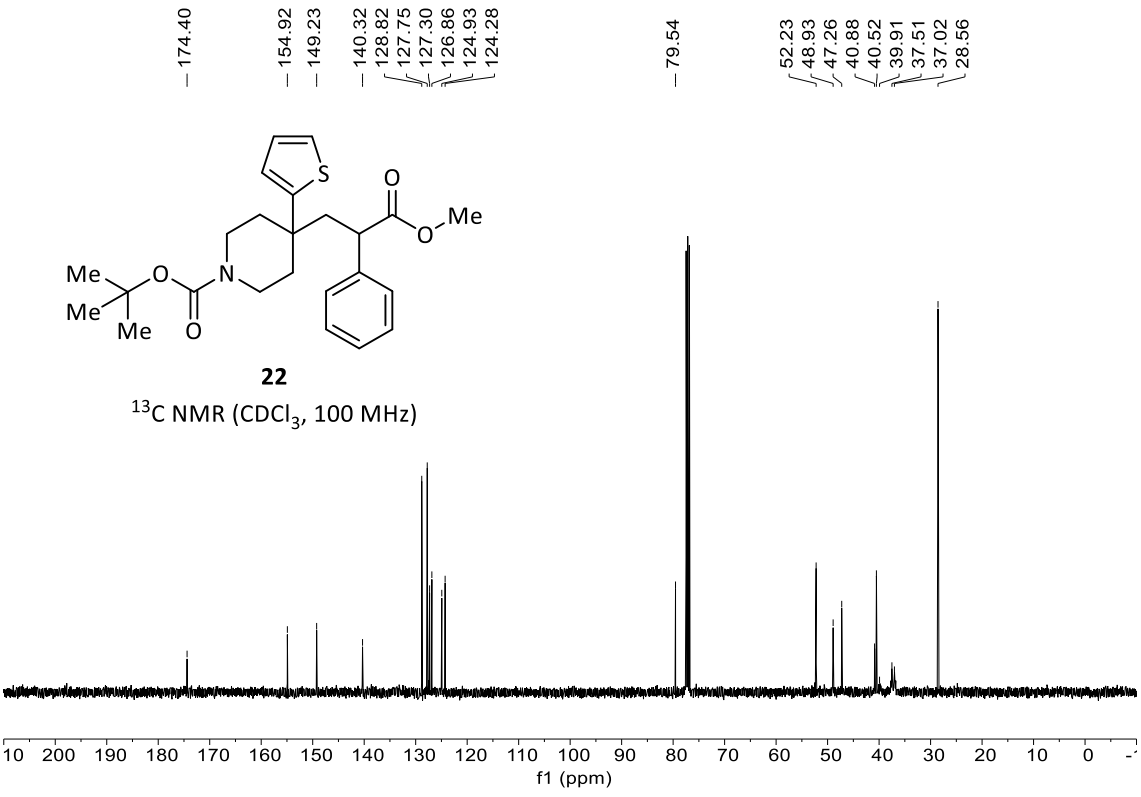


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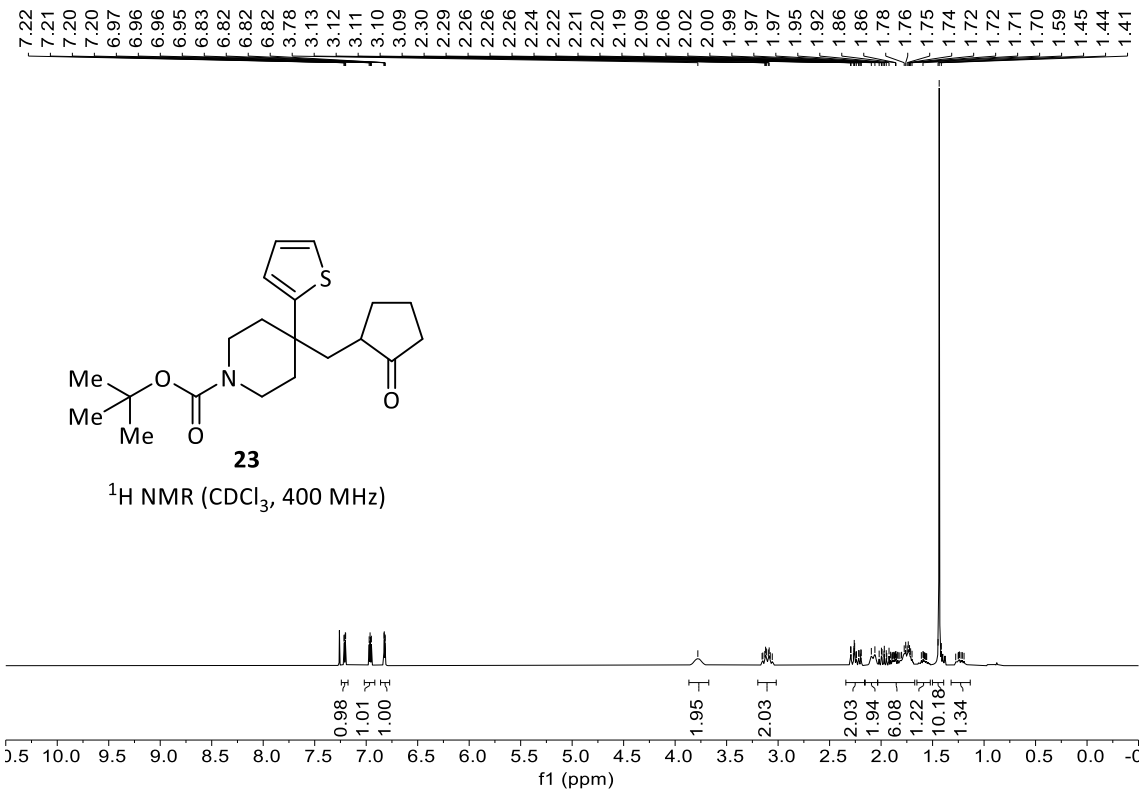


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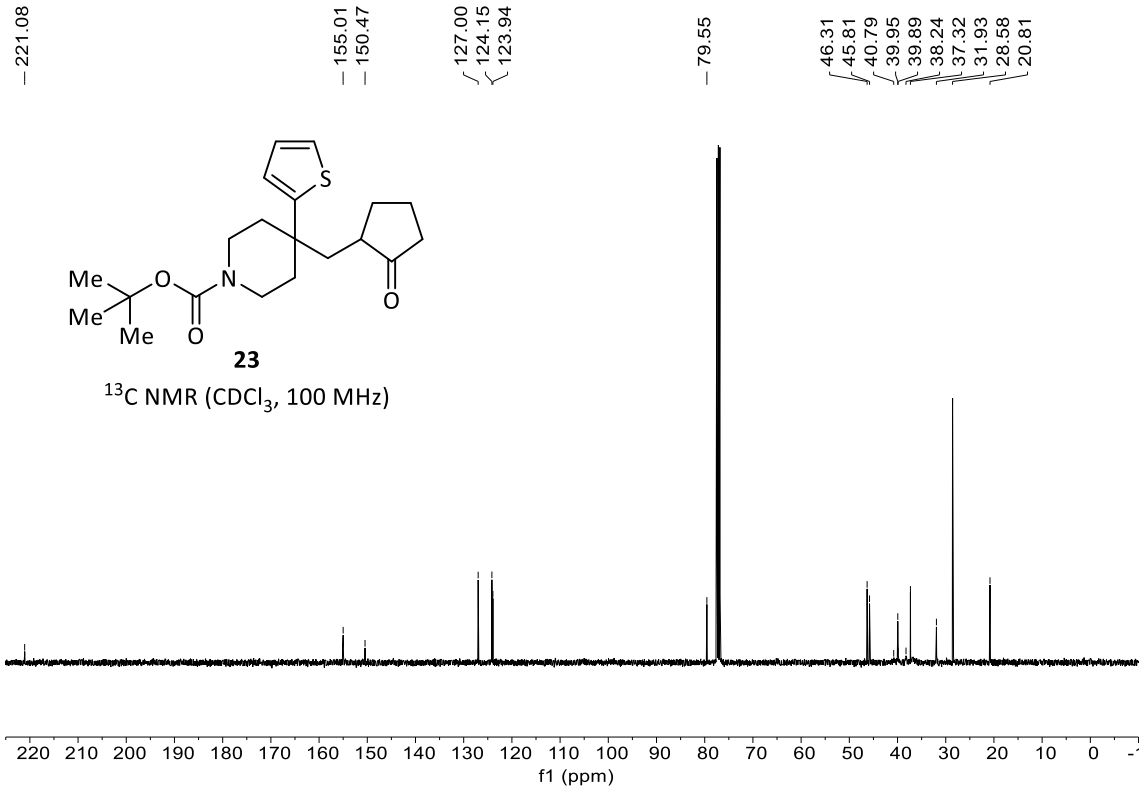


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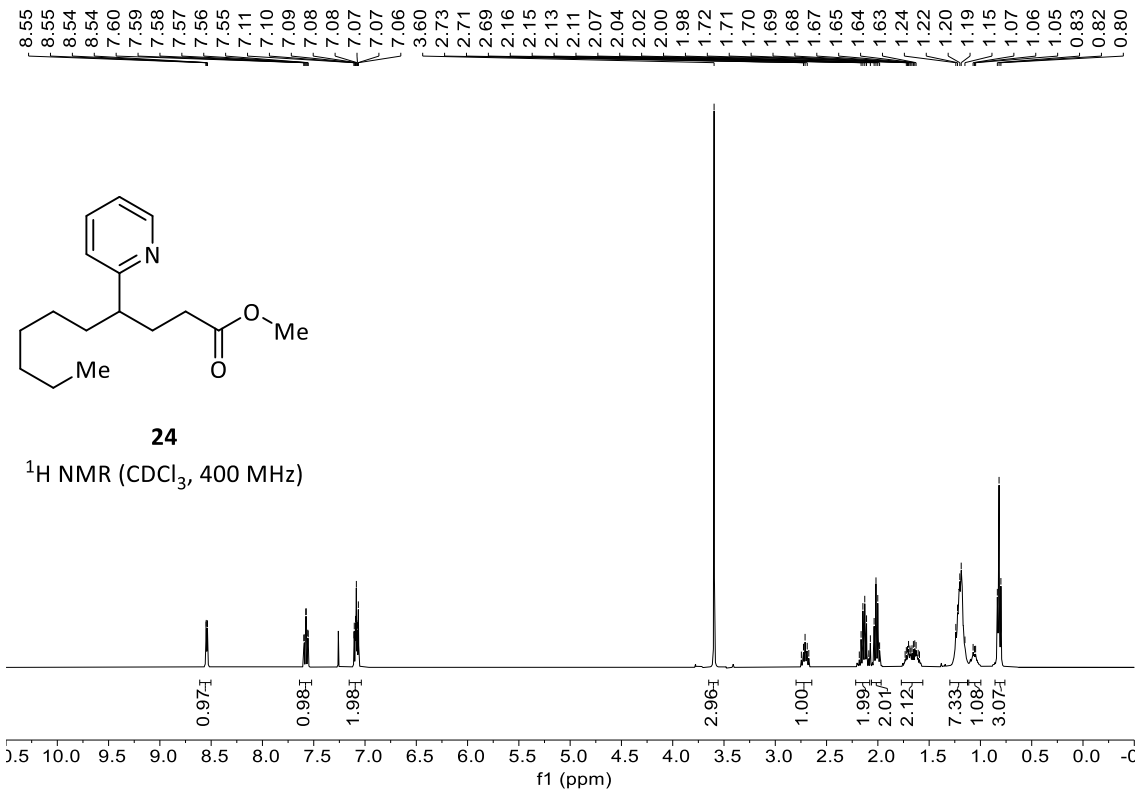


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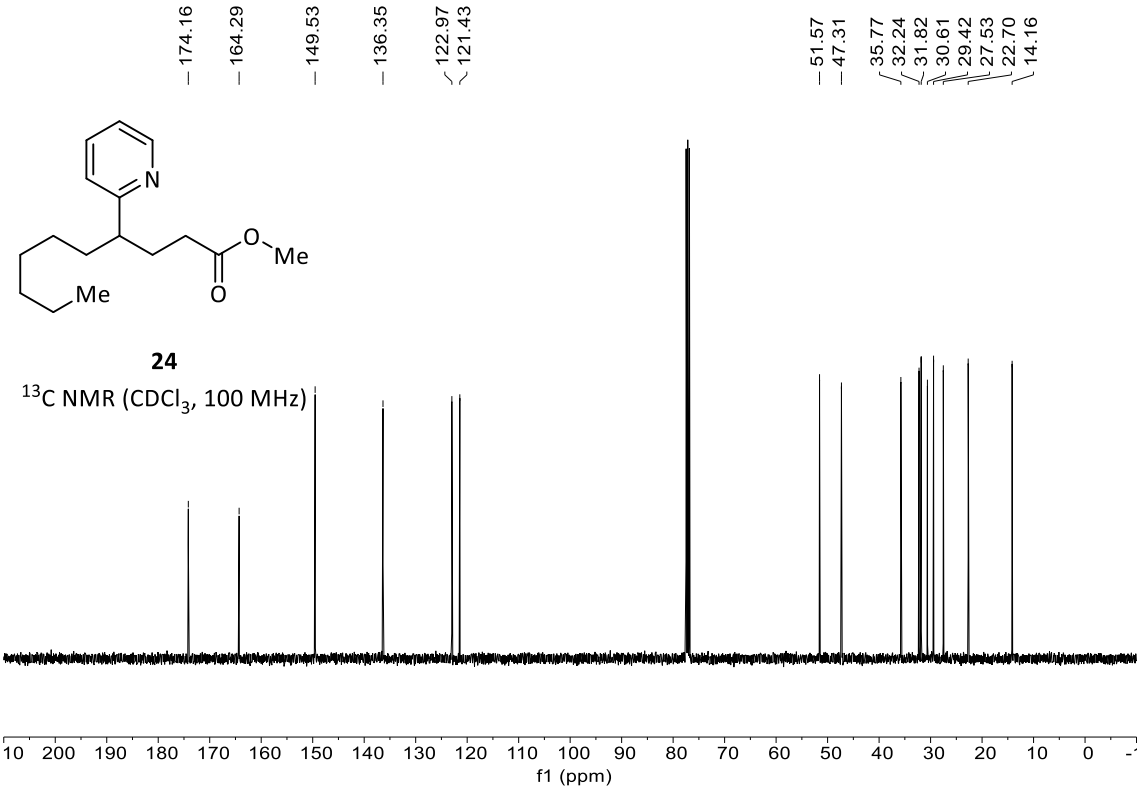


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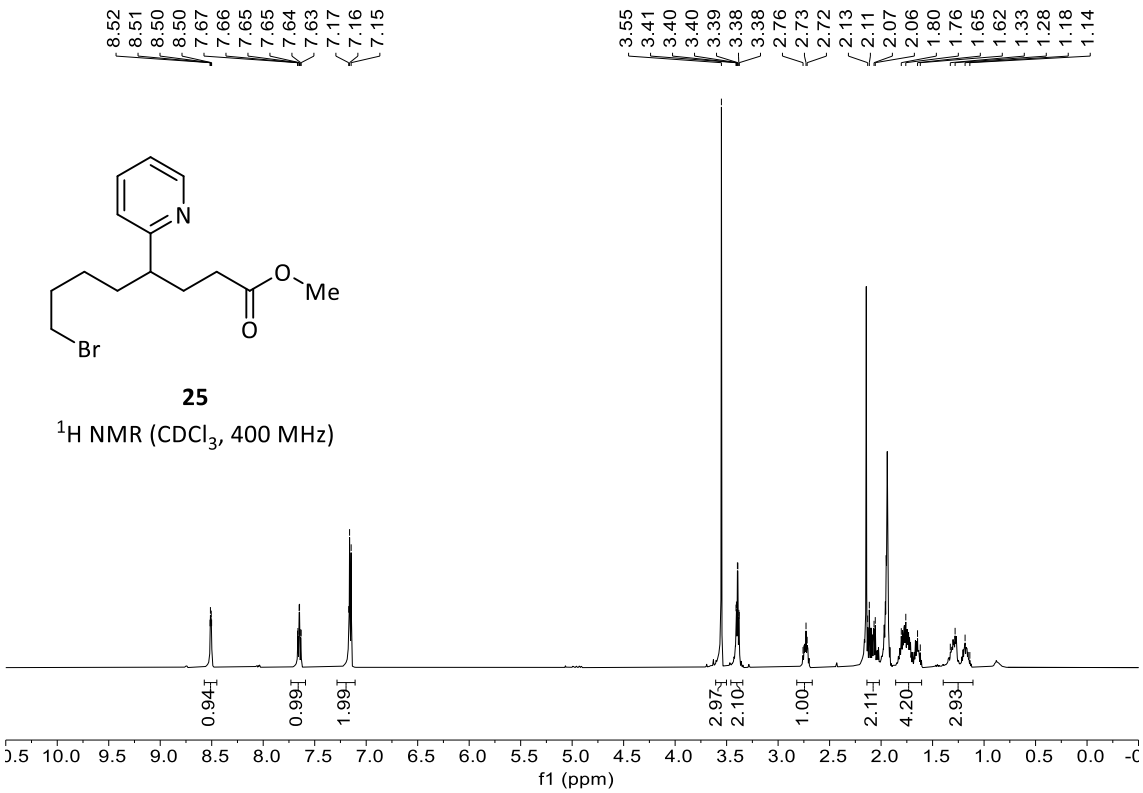


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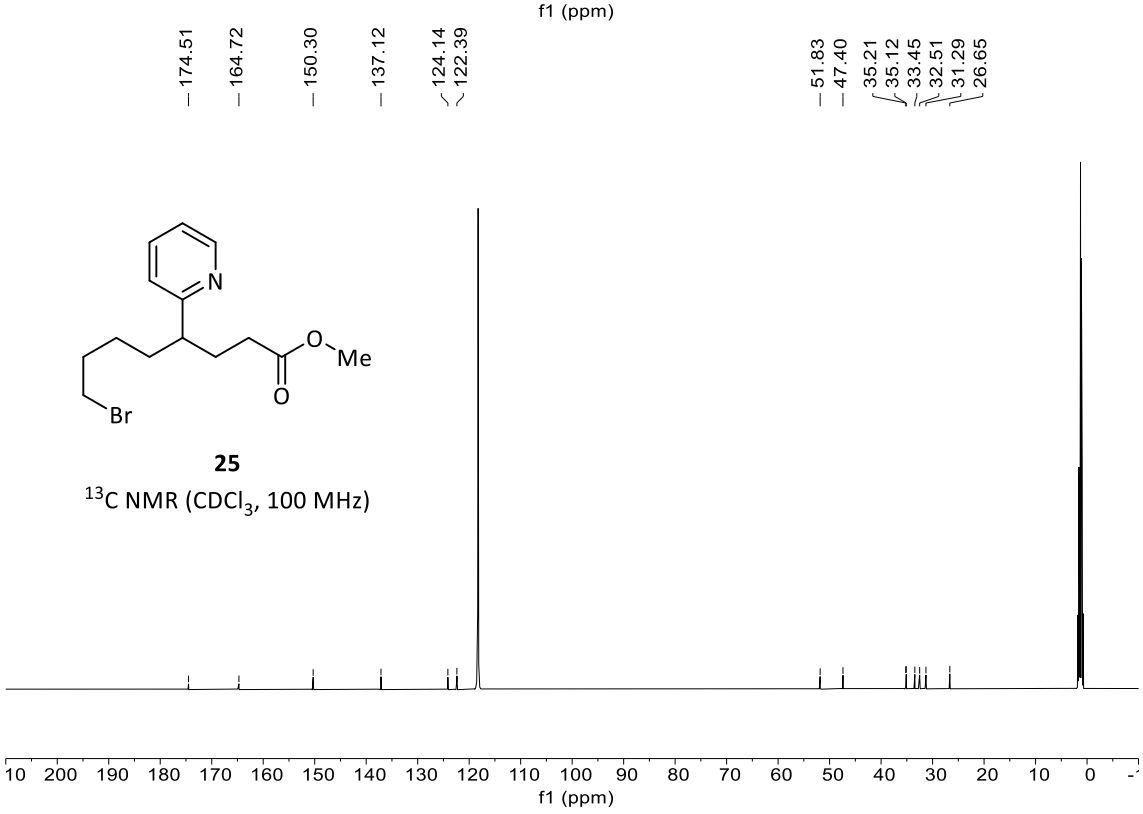


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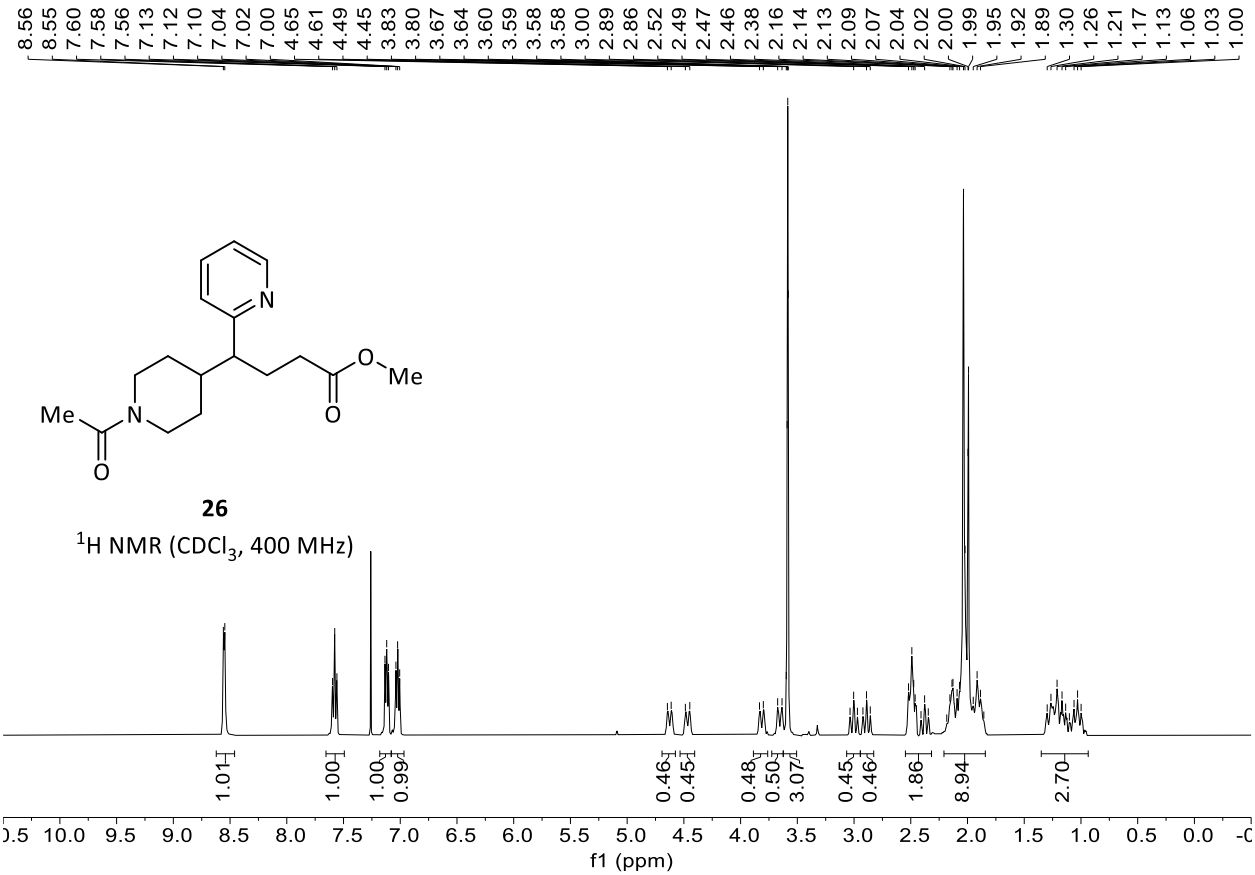


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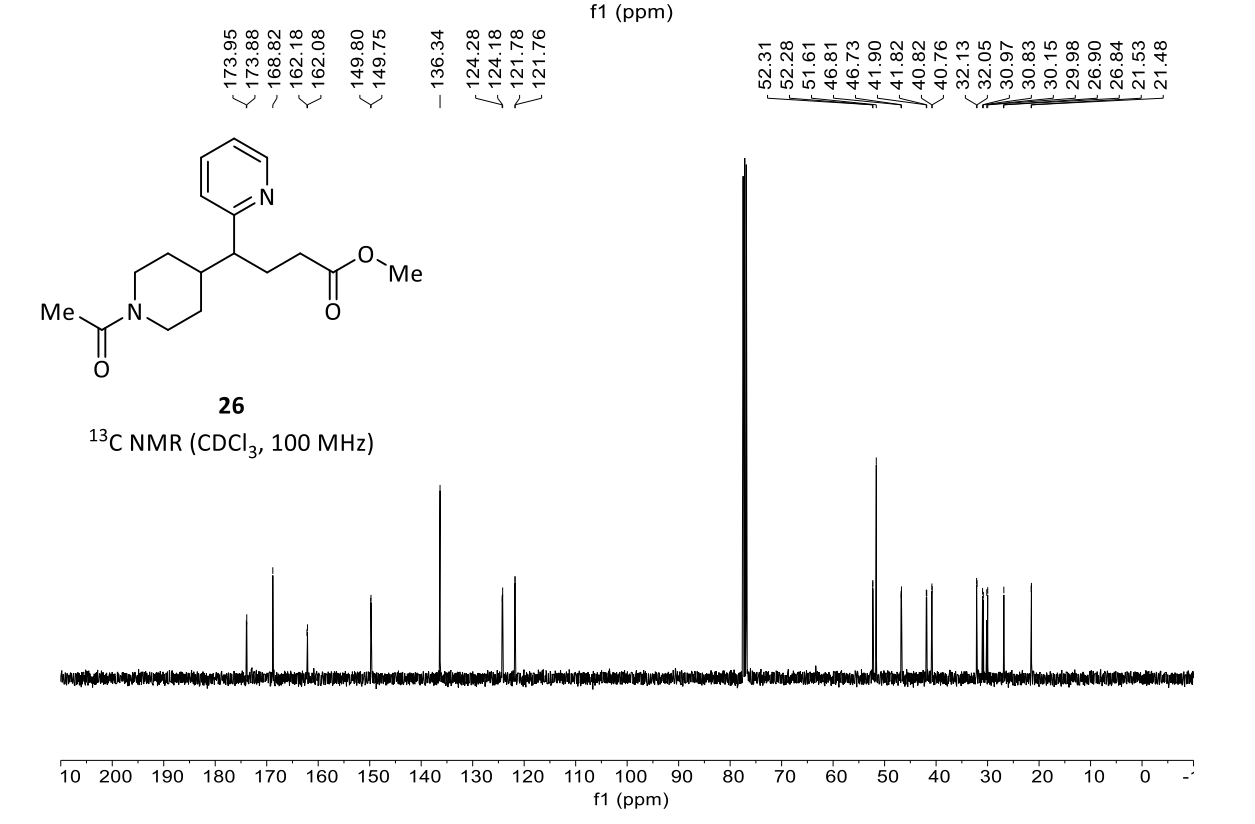


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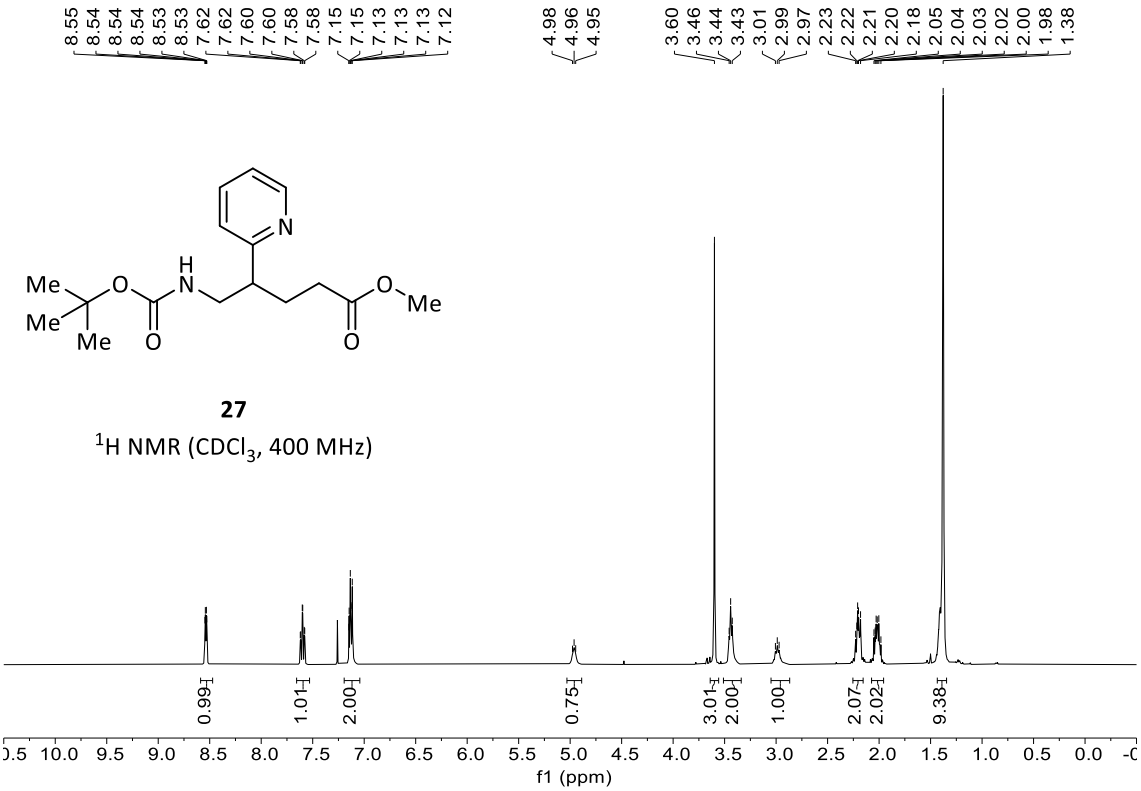


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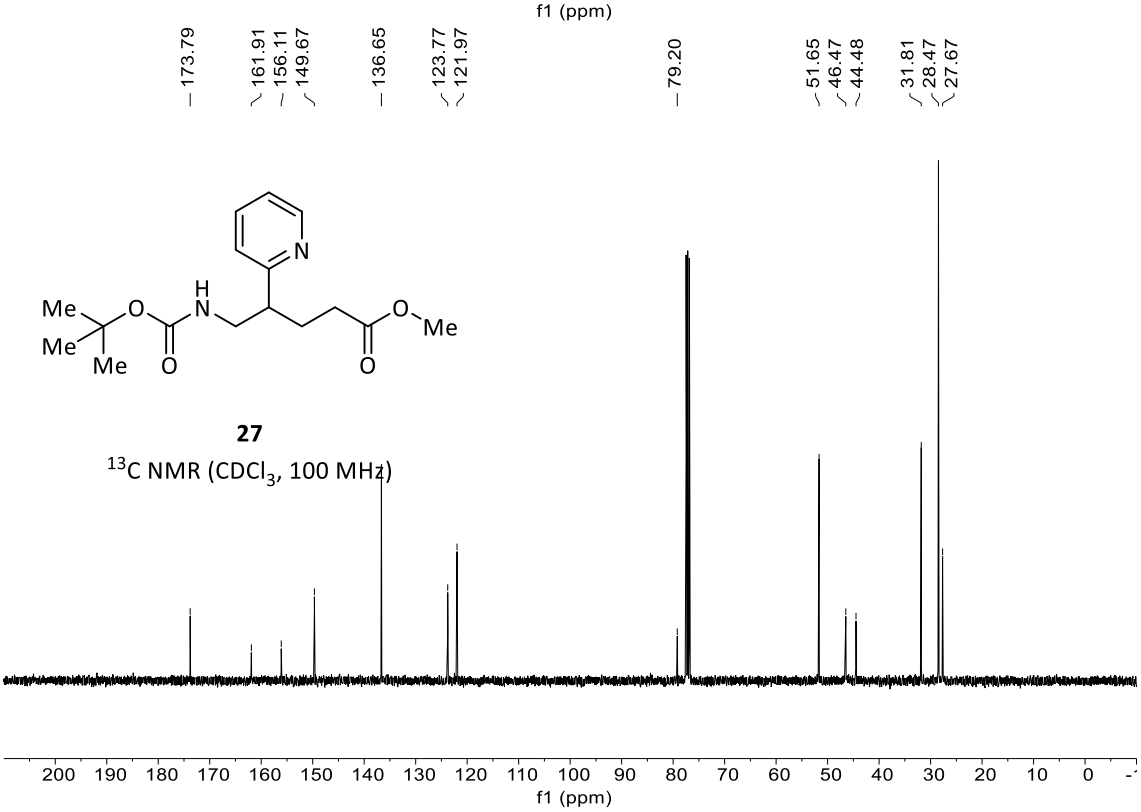


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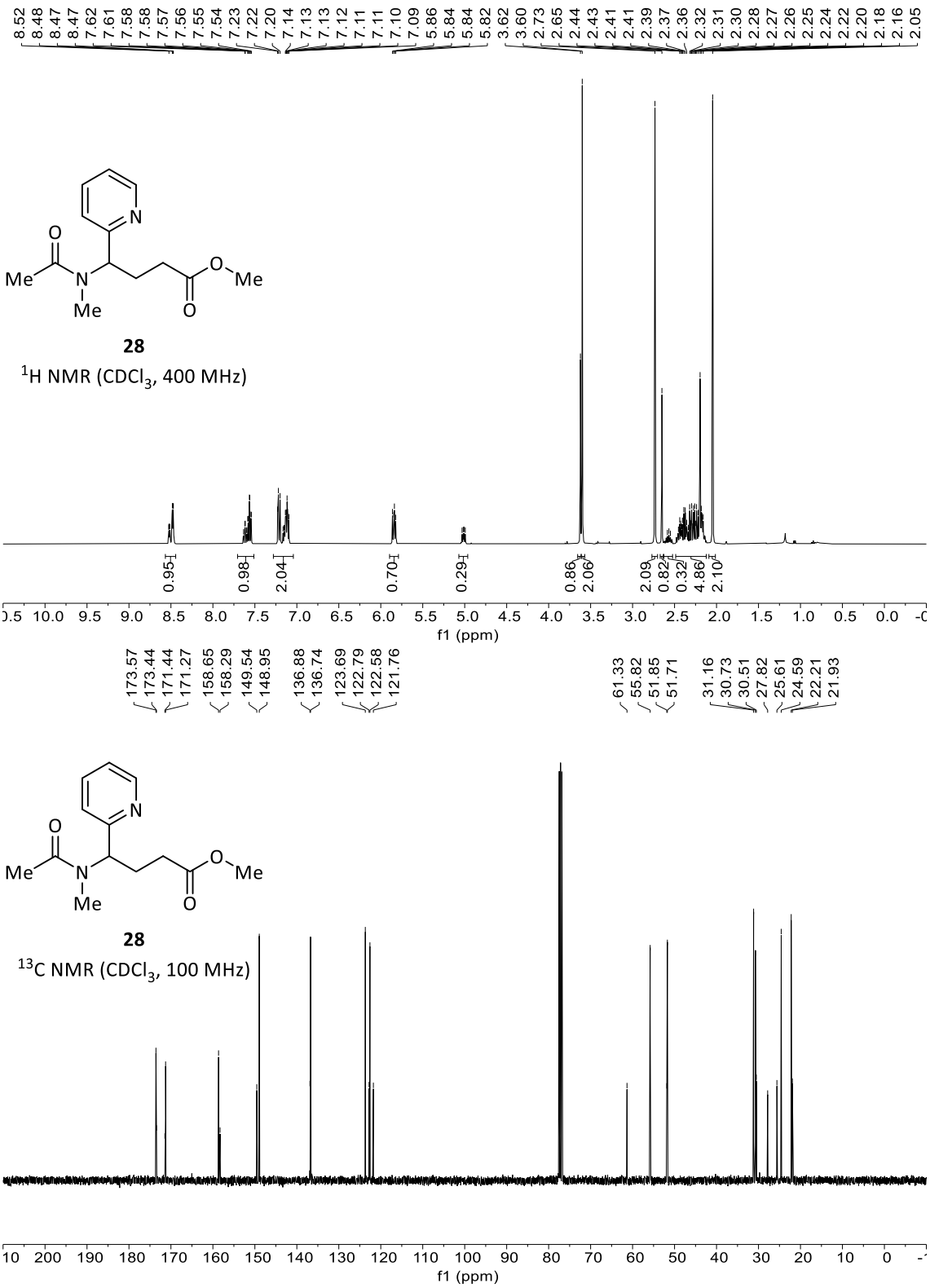
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N
O
Me
N
Me
O
O
Me
28
1H NMR (CDCl3, 400 MHz)
0.95 0.98 2.04 0.70 0.29 0.86 2.06 2.09 0.82 0.32 4.86 2.10
f1 (ppm)
173.57 173.44 171.44 171.27 158.65 158.29 149.54 148.95 136.88 136.74 123.69 122.79 122.58 121.76 61.33 55.82 51.85 51.71 31.16 30.73 30.51 27.82 25.61 24.59 22.21 21.93
N
O
Me
N
Me
O
O
Me
28
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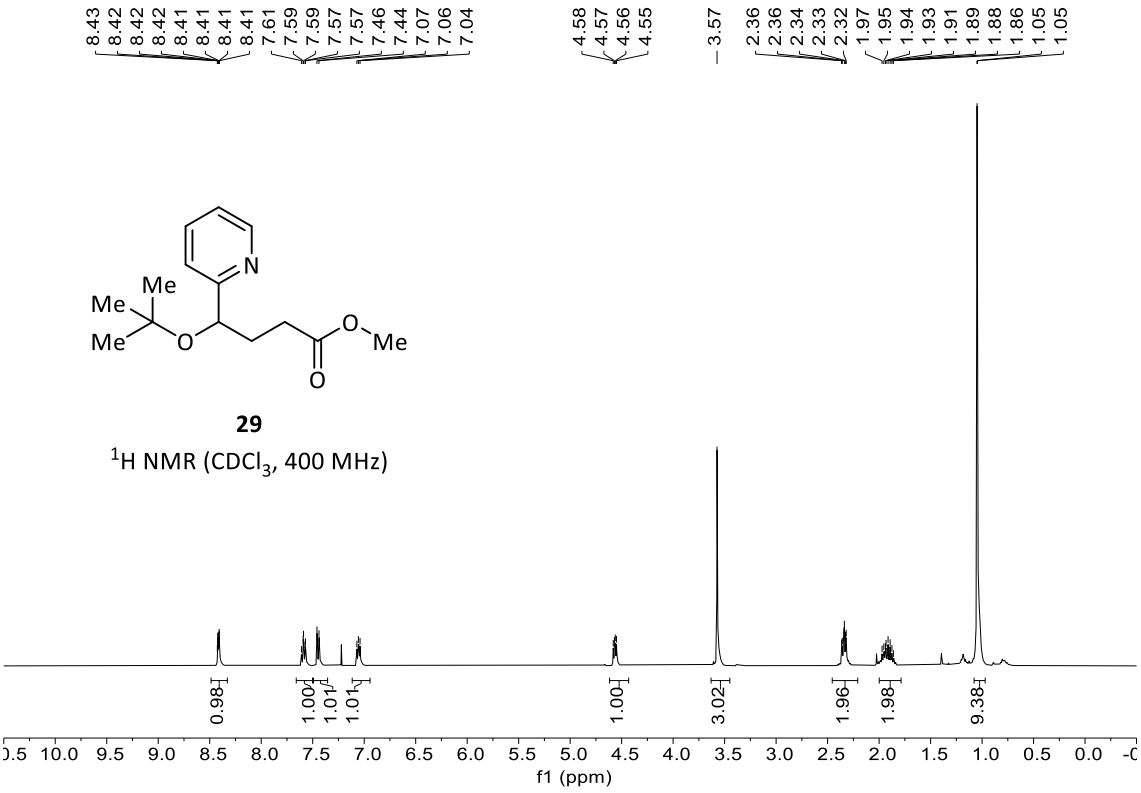
f1 (ppm)

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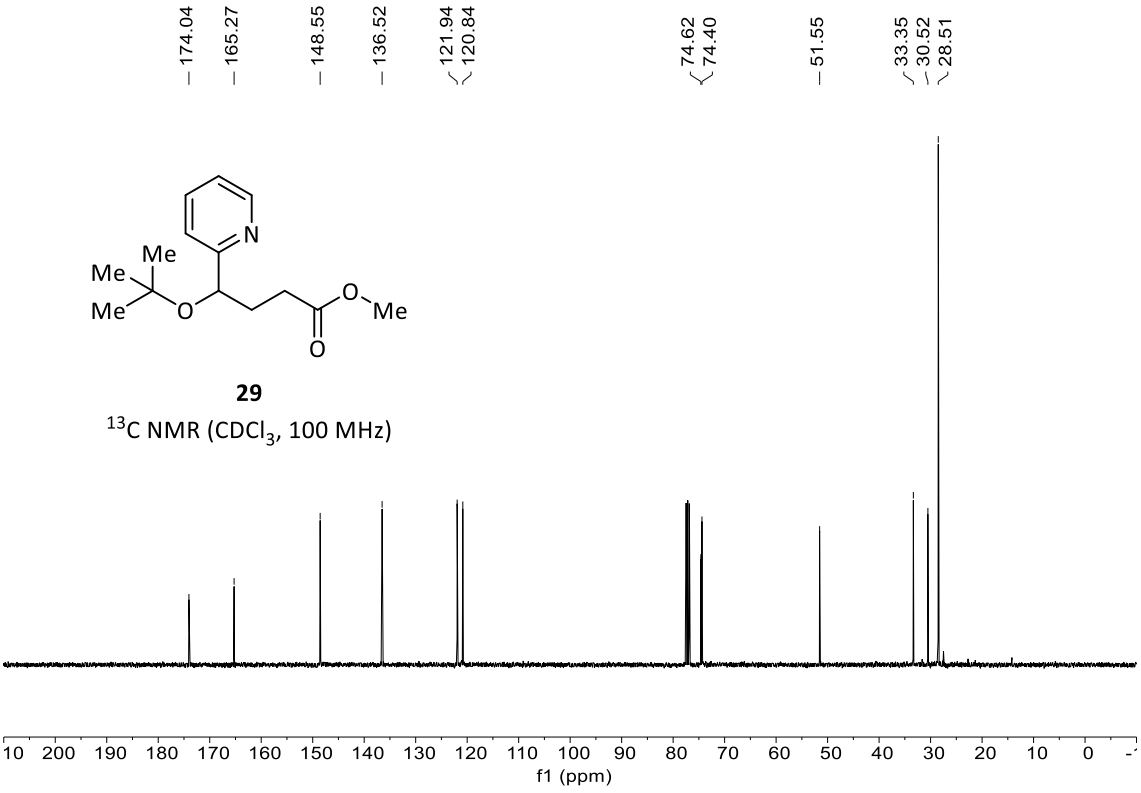


**29**

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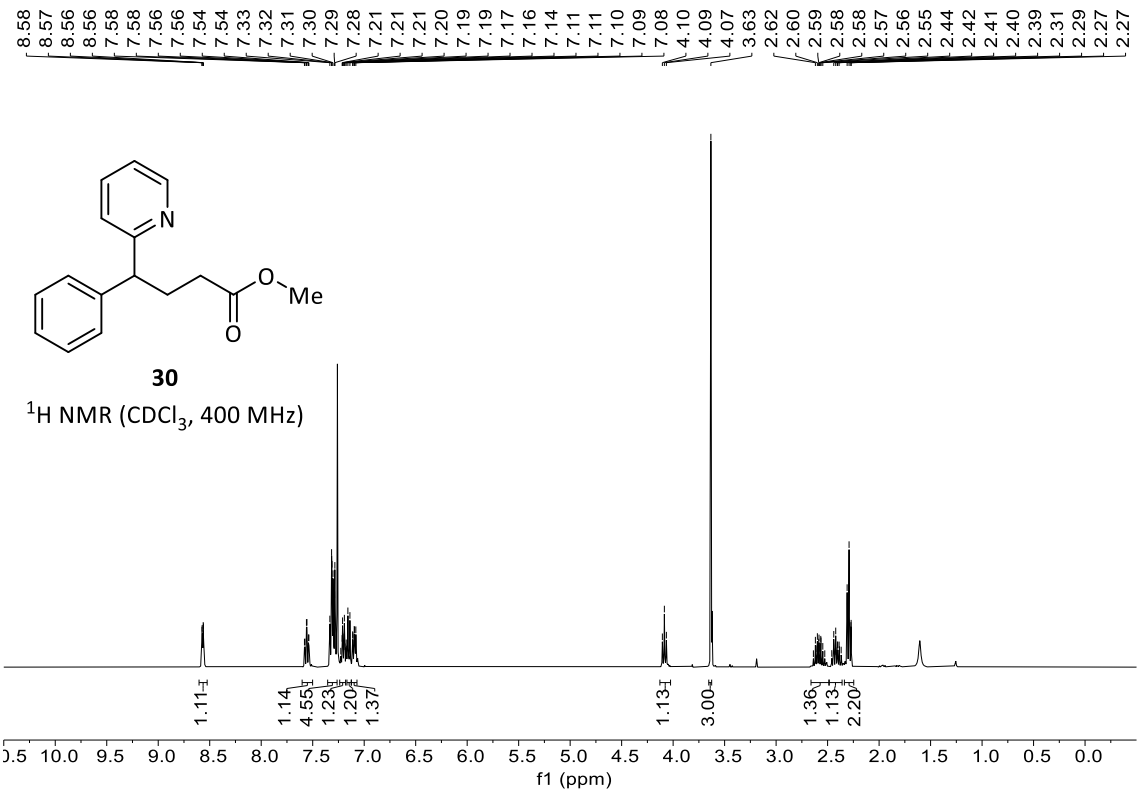
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N
O
Me
O
30
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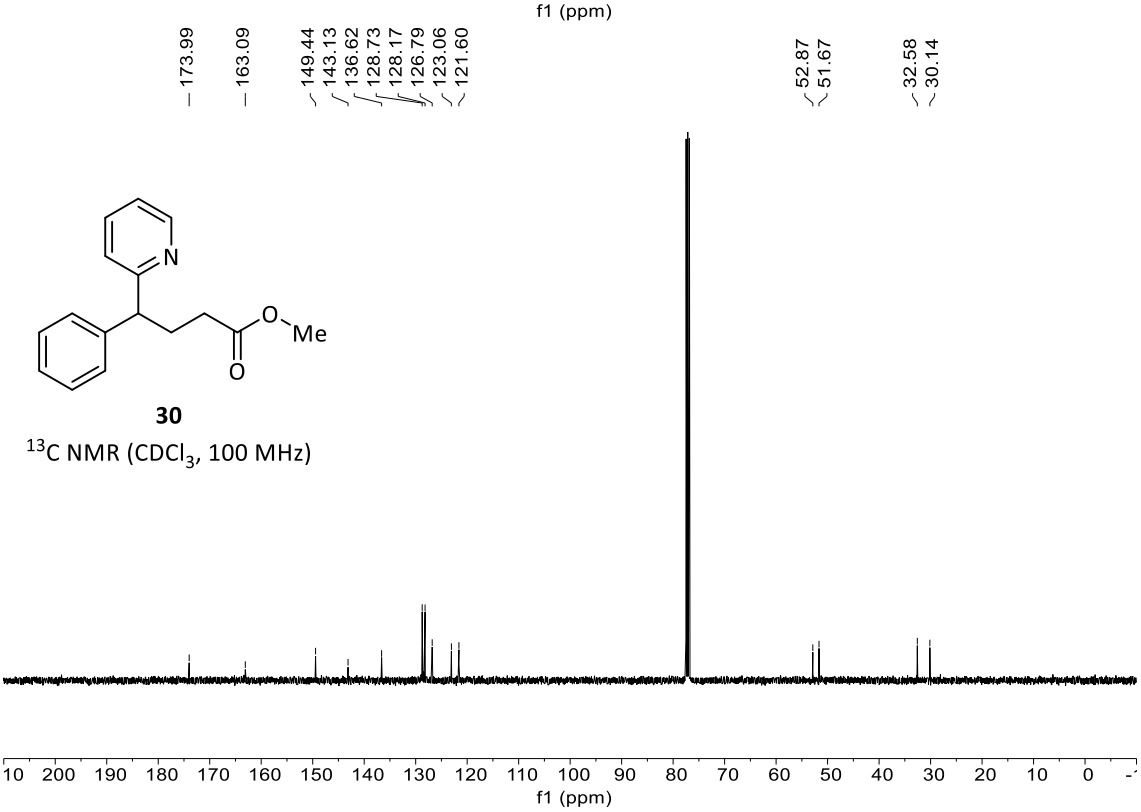
f1 (ppm)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N
O
Me
O
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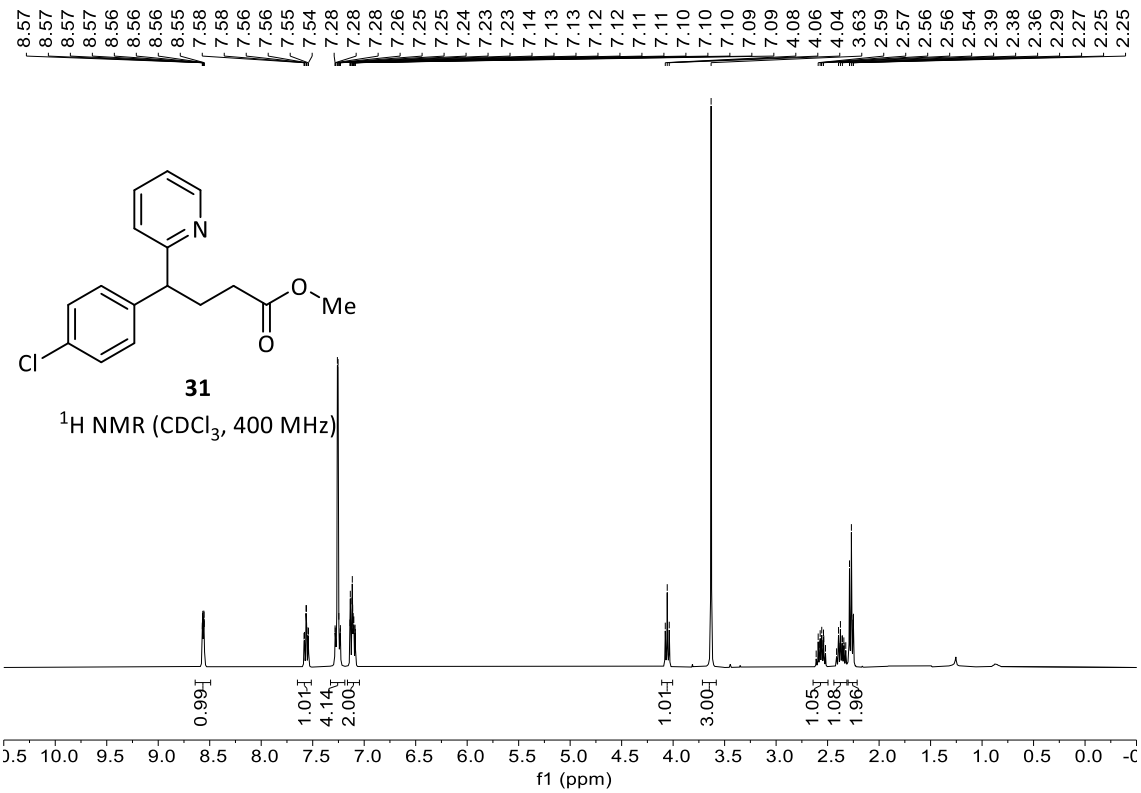
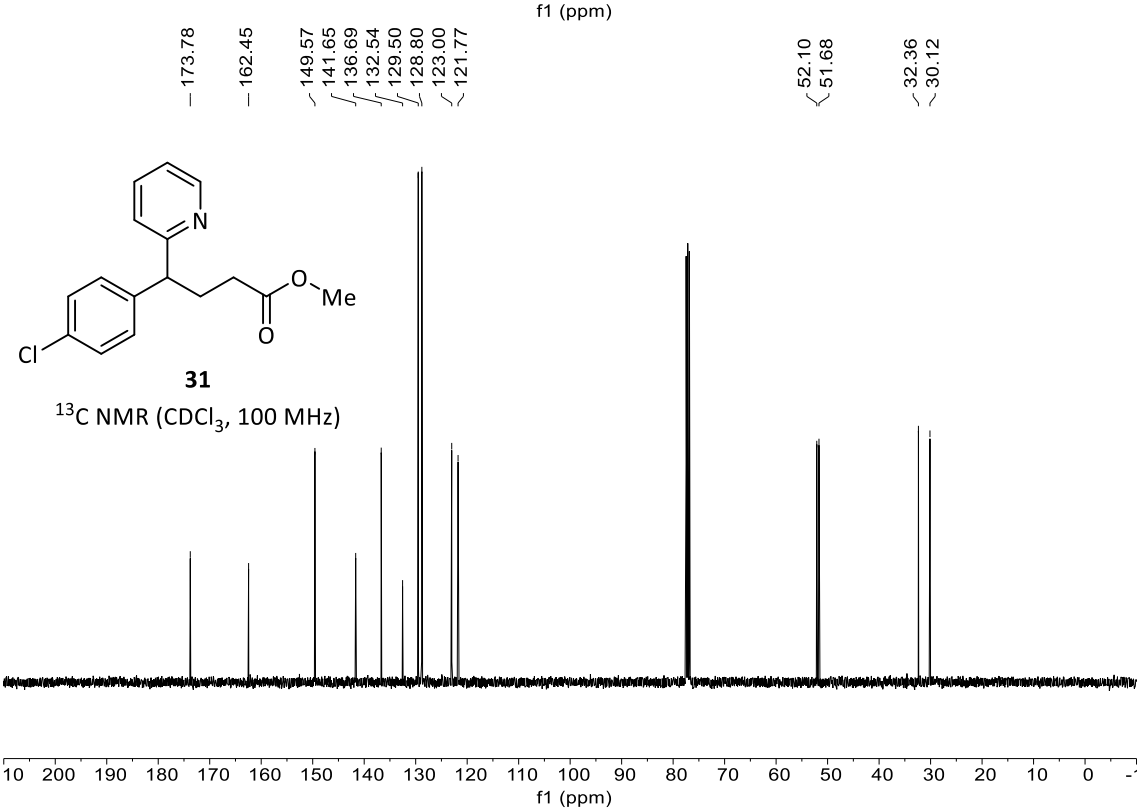
13C NMR (CDCl3, 100 MHz)
f1 (ppm)



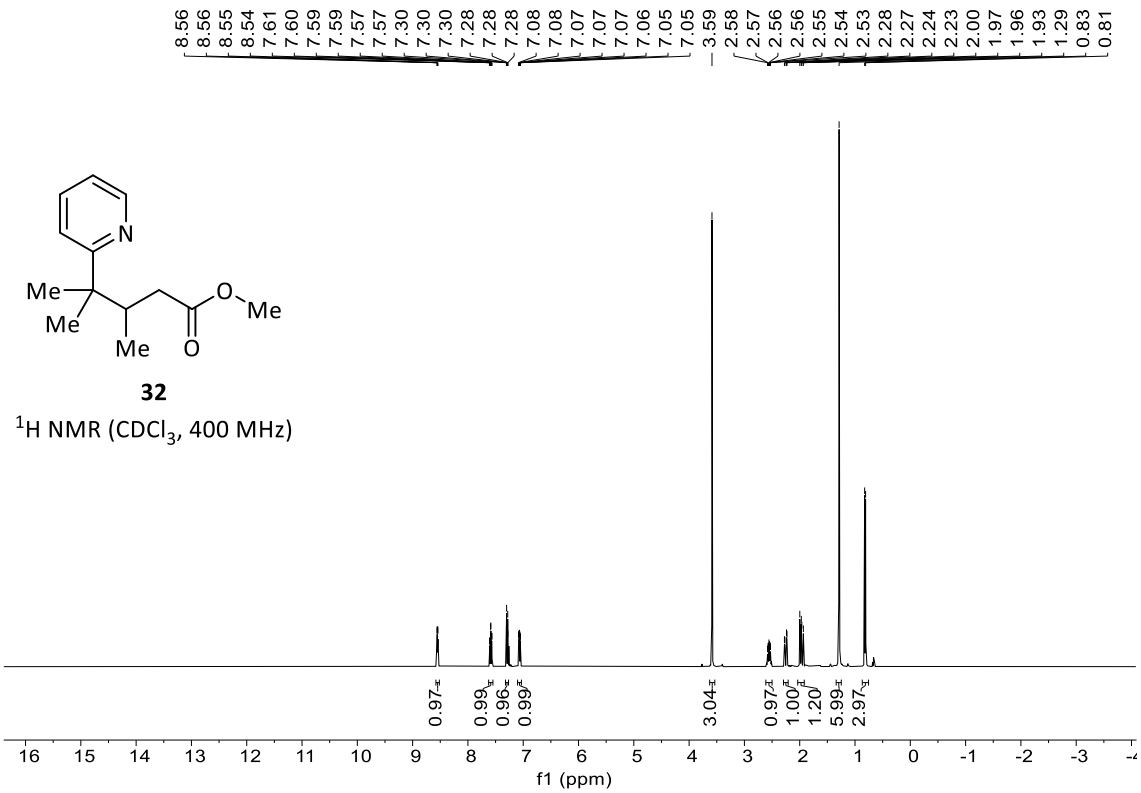

**31**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



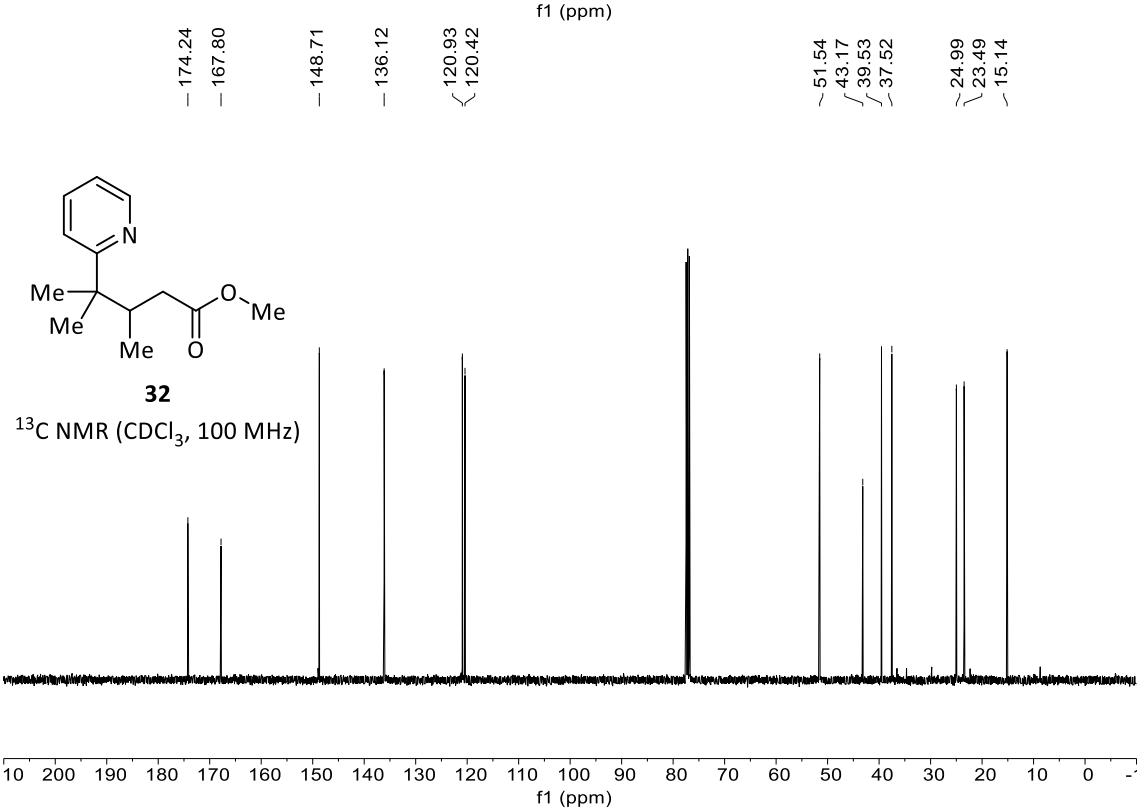

**31**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



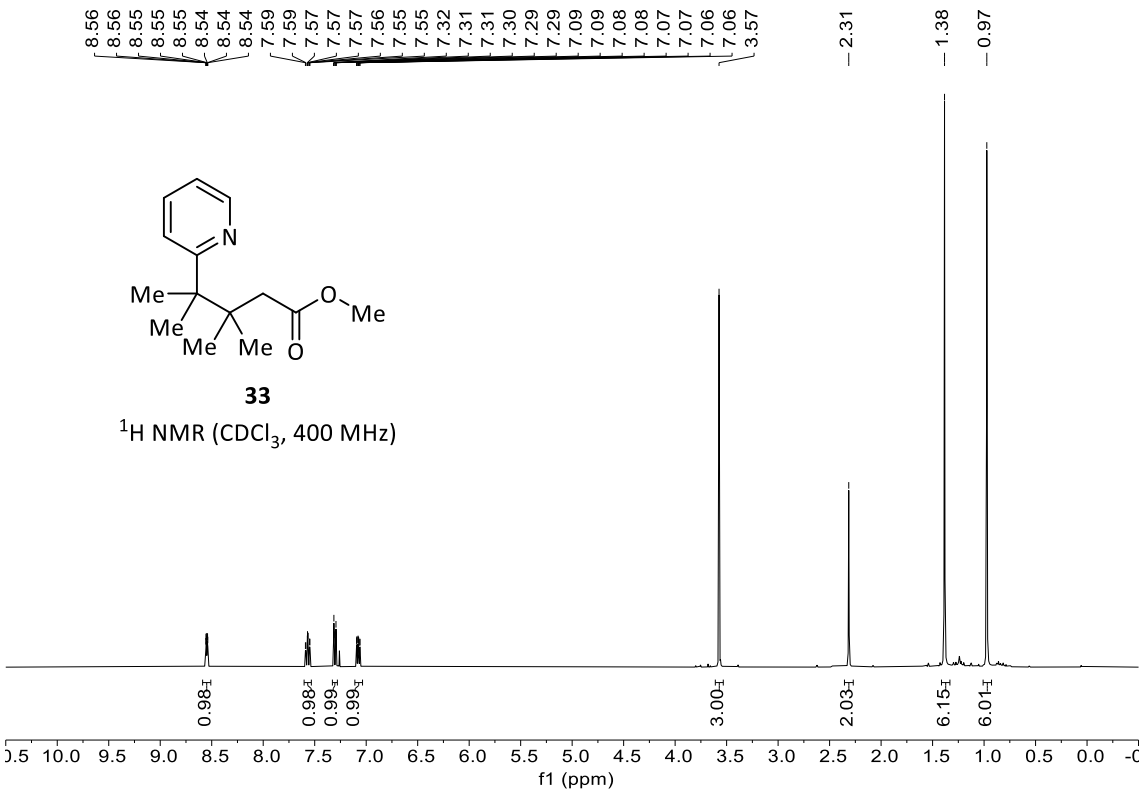

**32**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



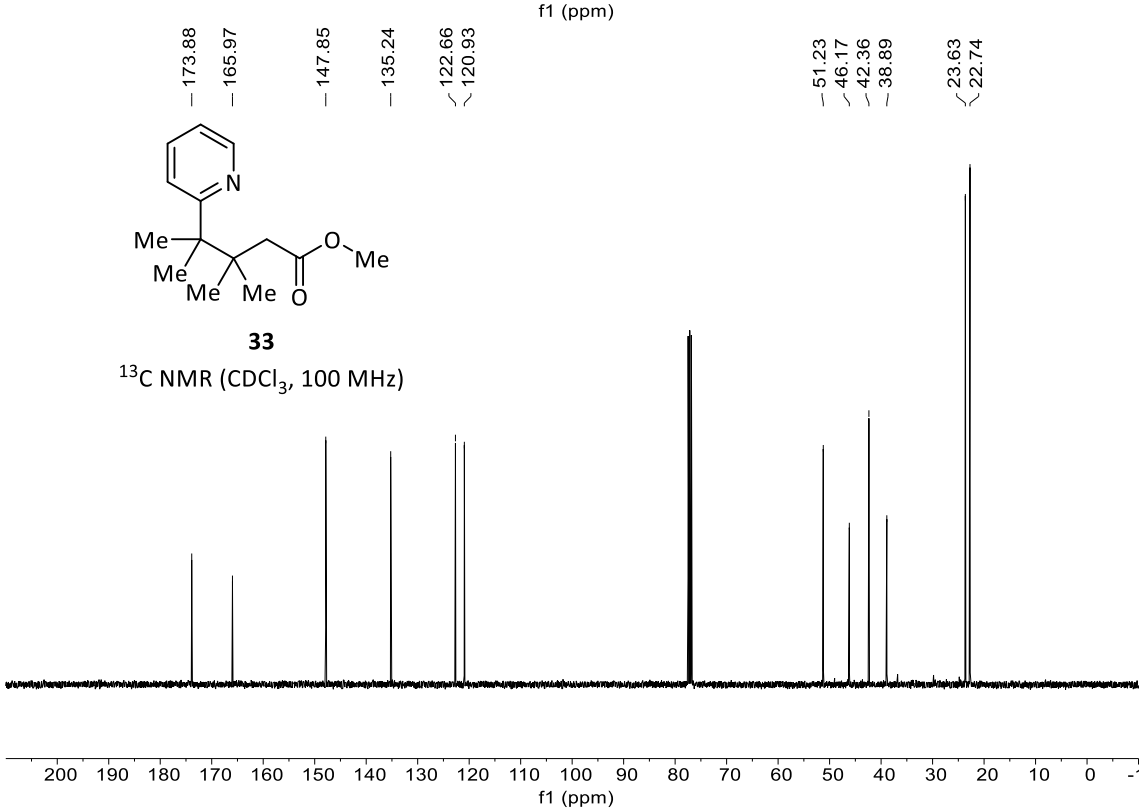

**32**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



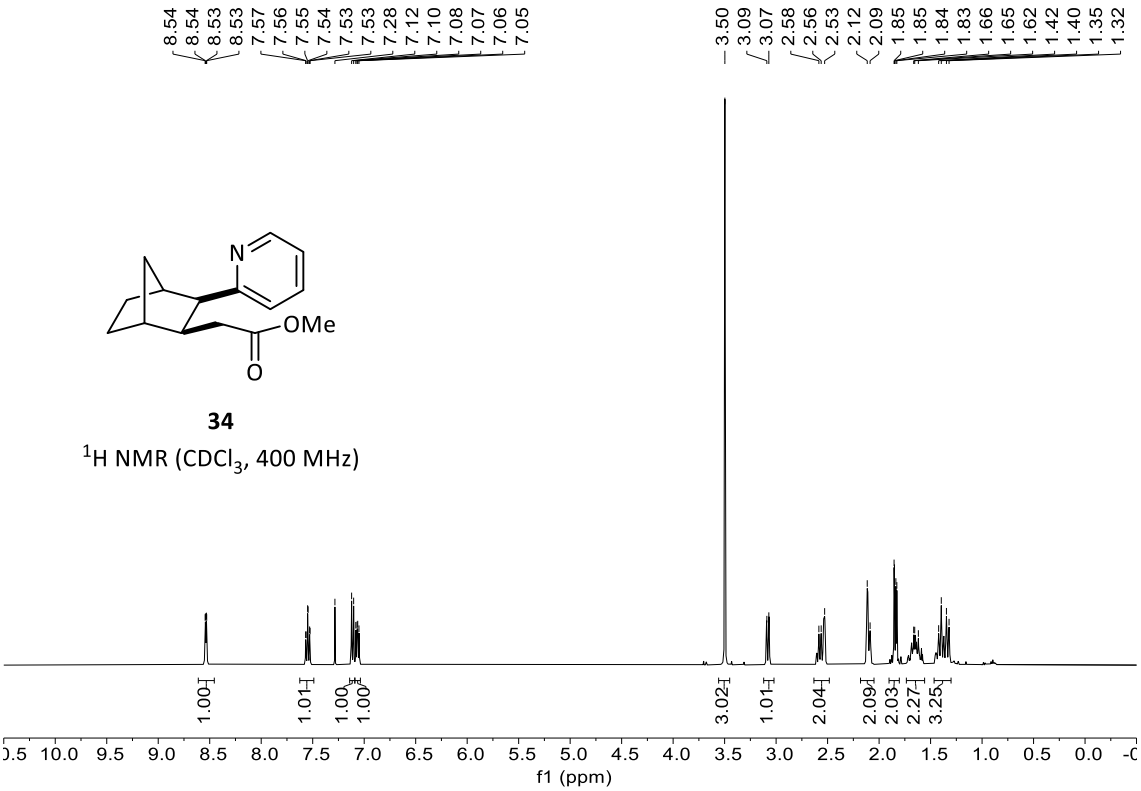

**33**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



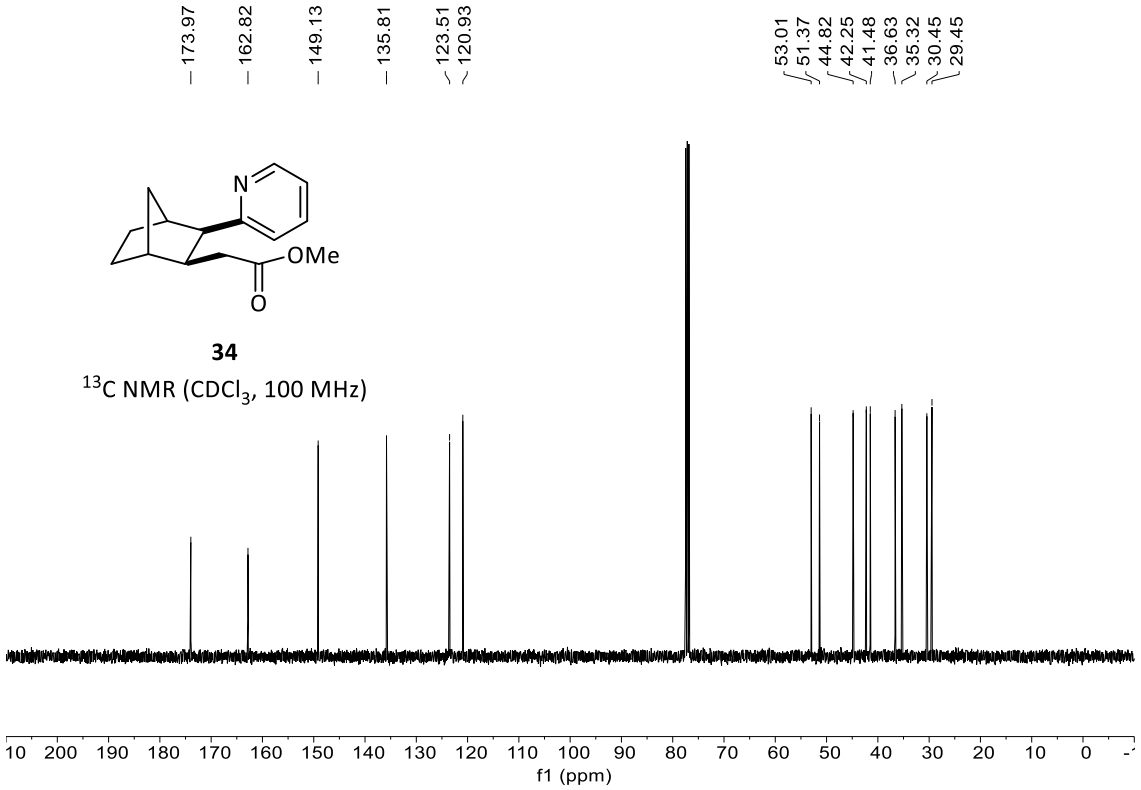

**33**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



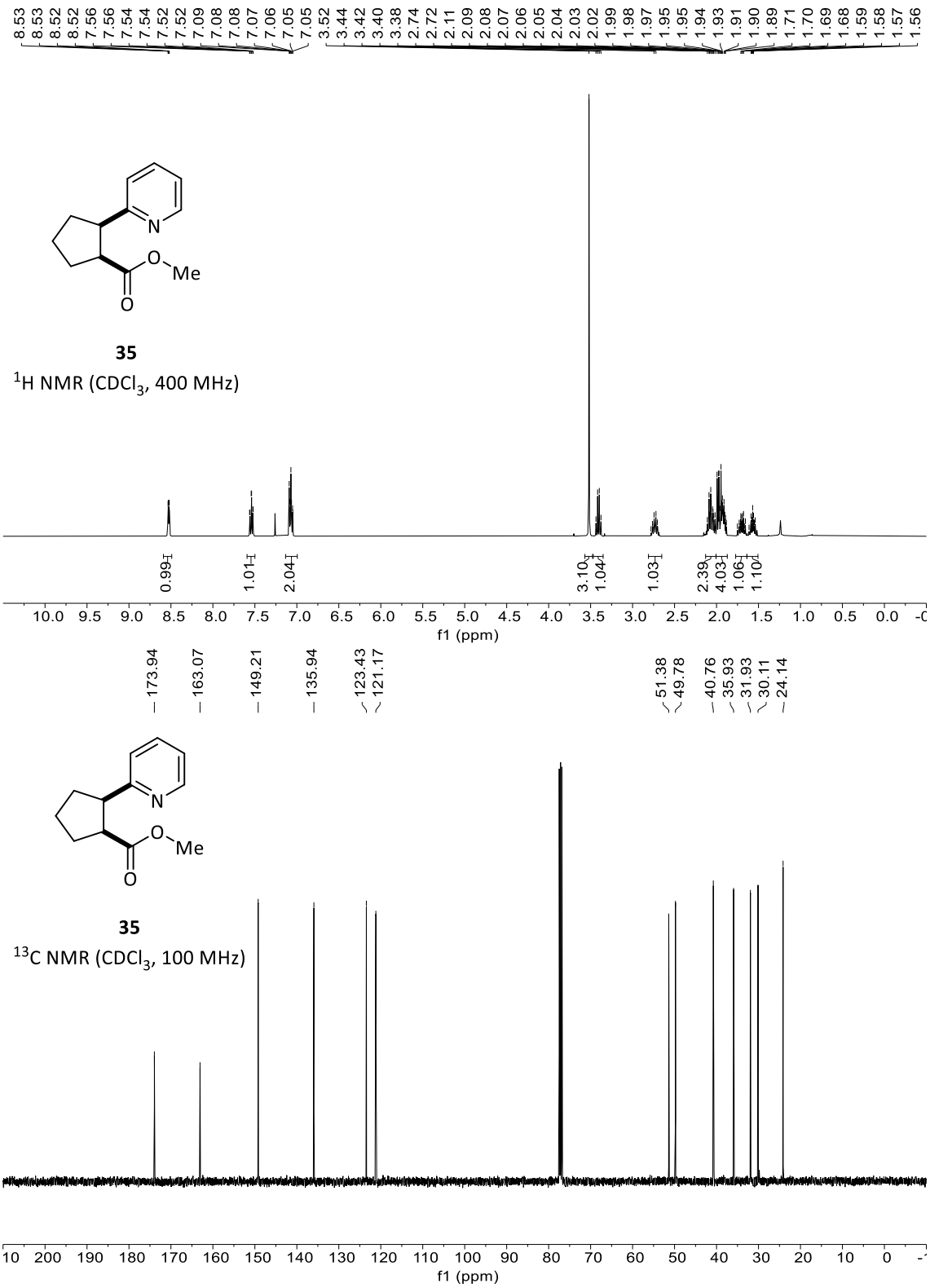

**34**

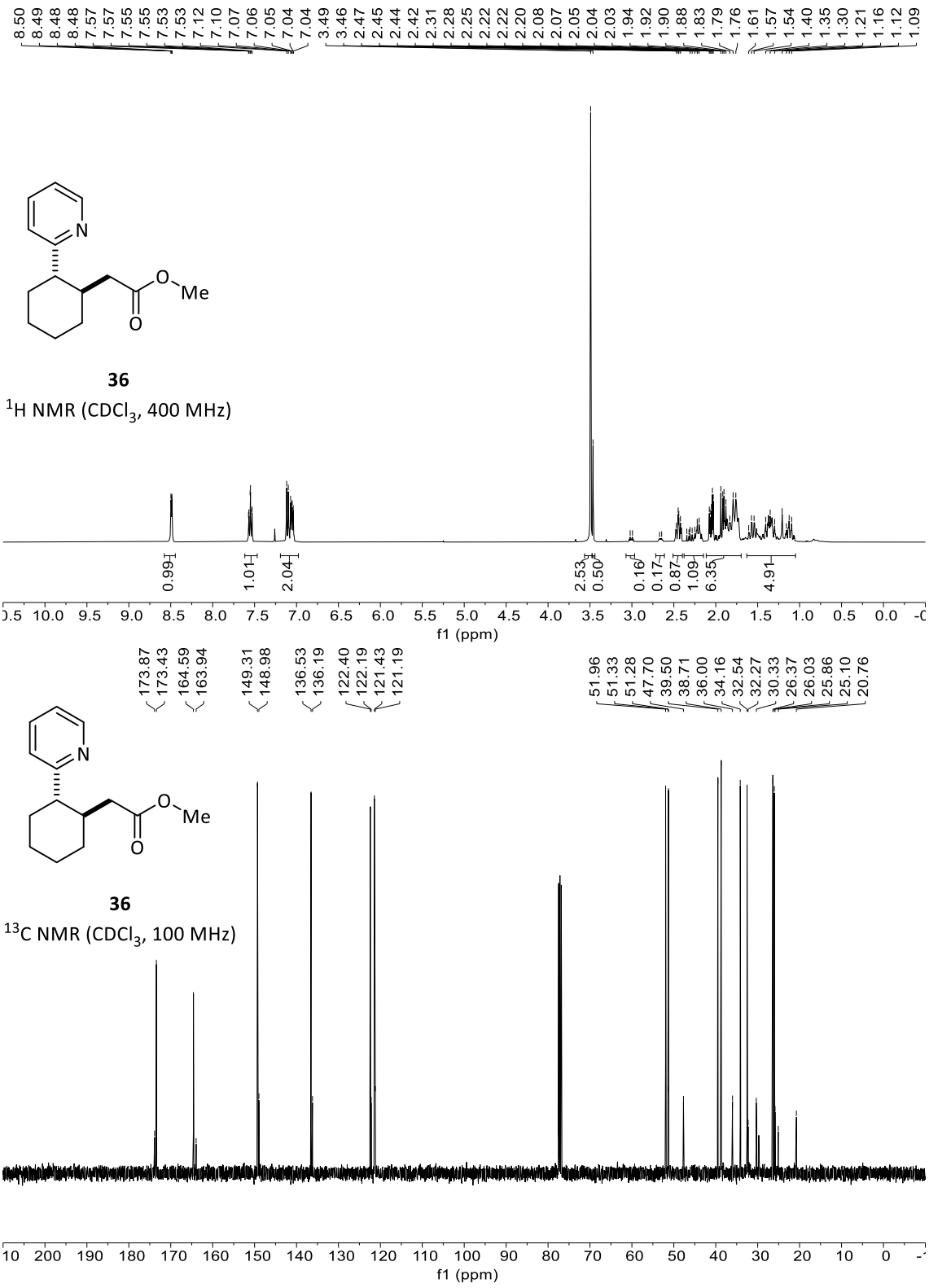
$^{1}$H NMR ($CDCl_3$, 400 MHz)

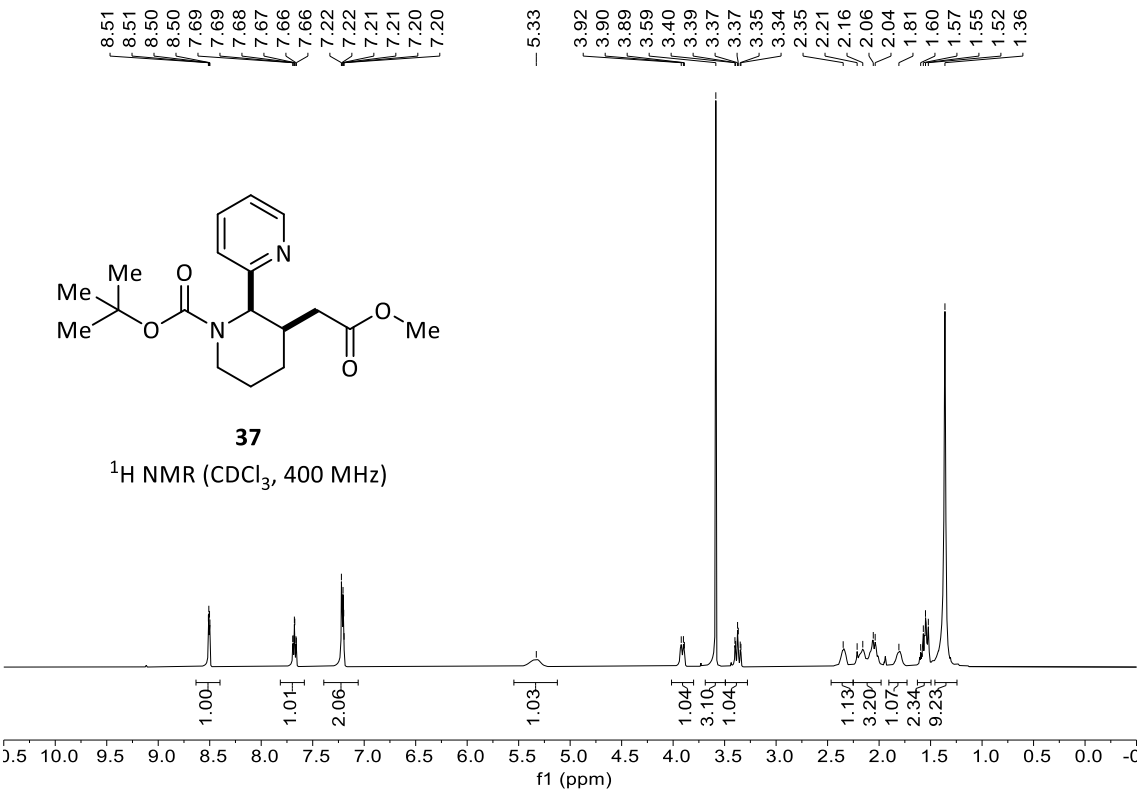



**34**

$^{13}$C NMR ($CDCl_3$, 100 MHz)

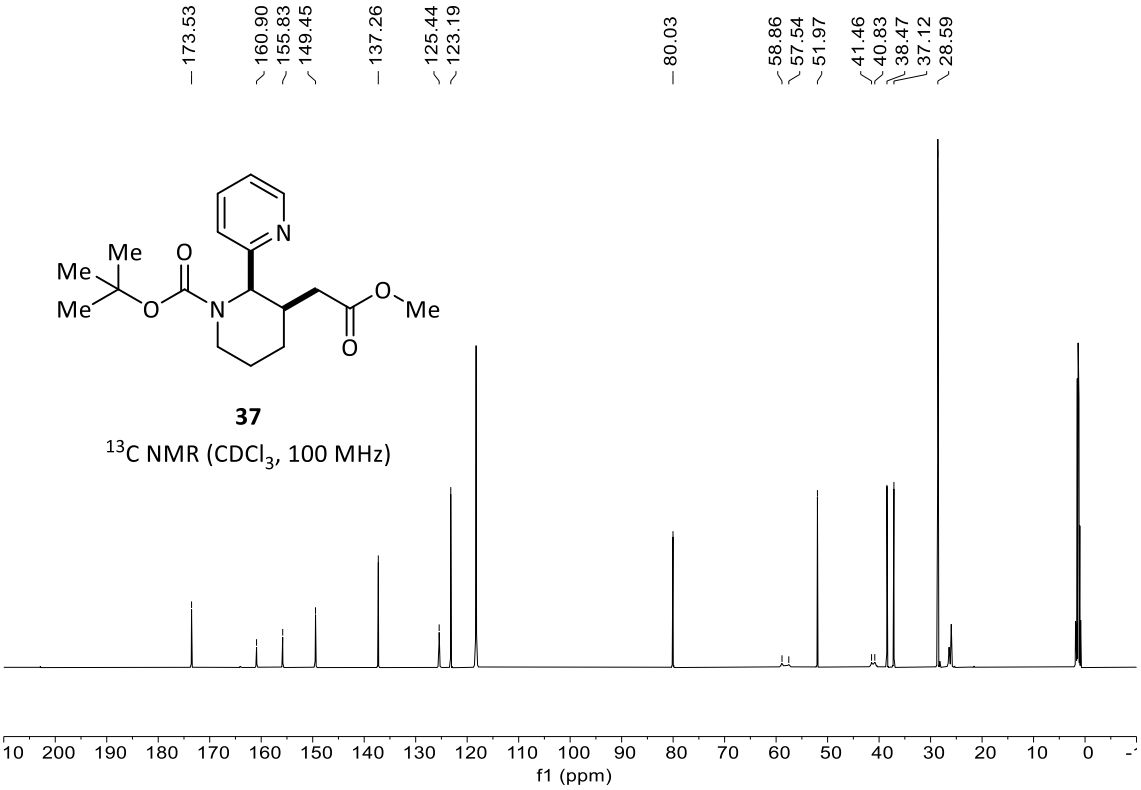

8.53 8.53 8.52 8.52 7.56 7.56 7.54 7.54 7.52 7.52 7.09 7.08 7.08 7.07 7.06 7.05 7.05 3.52 3.44 3.42 3.40 3.38 2.74 2.72 2.11 2.09 2.08 2.07 2.06 2.05 2.04 2.03 2.02 1.99 1.98 1.97 1.95 1.95 1.94 1.93 1.91 1.90 1.89 1.71 1.70 1.69 1.68 1.59 1.58 1.57 1.56
N
O
Me
O
35
1H NMR (CDCl3, 400 MHz)
0.99 1.01 2.04 3.10 1.04 1.03 2.39 4.03 1.06 1.10
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)
173.94 163.07 149.21 135.94 123.43 121.17 51.38 49.78 40.76 35.93 31.93 30.11 24.14
N
O
Me
O
35
13C NMR (CDCl3, 100 MHz)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.50 8.49 8.48 8.48 7.57 7.57 7.55 7.55 7.53 7.53 7.12 7.10 7.07 7.06 7.05 7.04 7.04
3.49 3.46 2.47 2.45 2.44 2.42 2.31 2.28 2.25 2.22 2.22 2.20 2.08 2.07 2.05 2.04 2.03 1.94 1.92 1.90 1.88 1.83 1.79 1.76 1.61 1.57 1.54 1.40 1.35 1.30 1.21 1.16 1.12 1.09
N
O
Me
O
36
1H NMR (CDCl3, 400 MHz)
0.99 1.01 2.04 2.53 0.50 0.16 0.17 0.87 1.09 6.35 4.91
f1 (ppm)
173.87 173.43 164.59 163.94 149.31 148.98 136.53 136.19 122.40 122.19 121.43 121.19
51.96 51.33 51.28 47.70 39.50 38.71 36.00 34.16 32.54 32.27 30.33 26.37 26.03 25.86 25.10 20.76
N
O
Me
O
36
13C NMR (CDCl3, 100 MHz)
f1 (ppm)



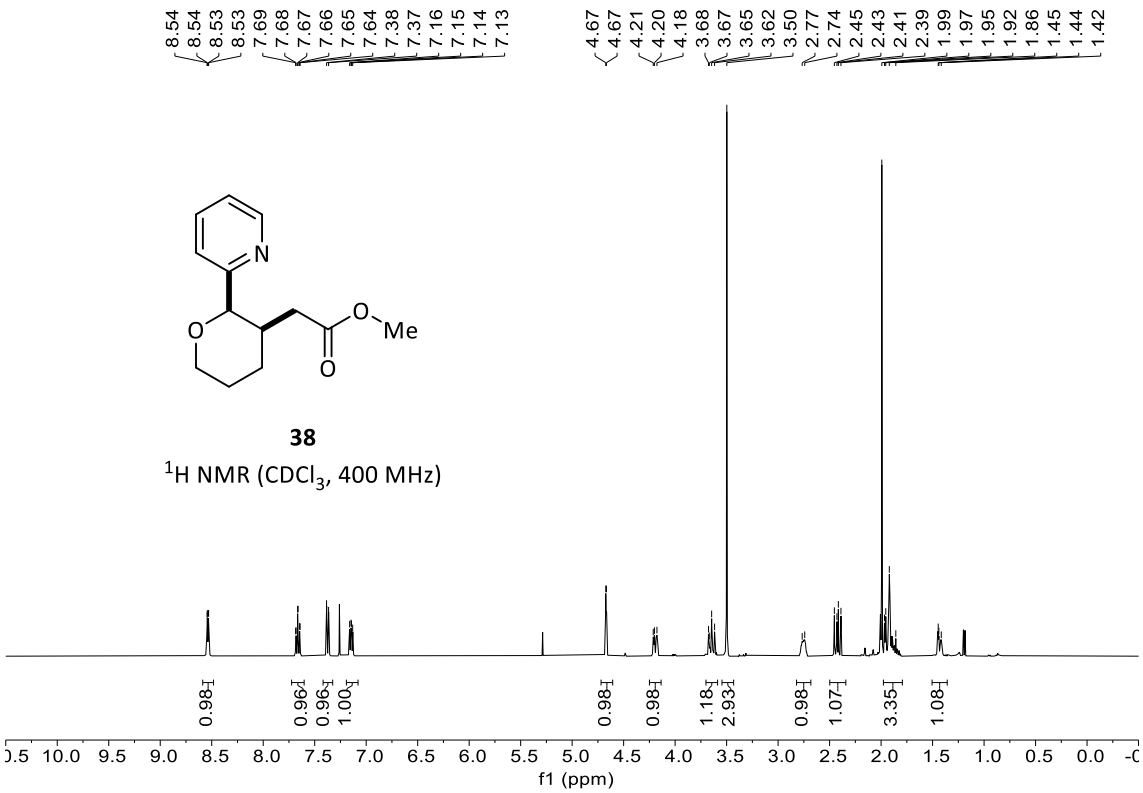

**37**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



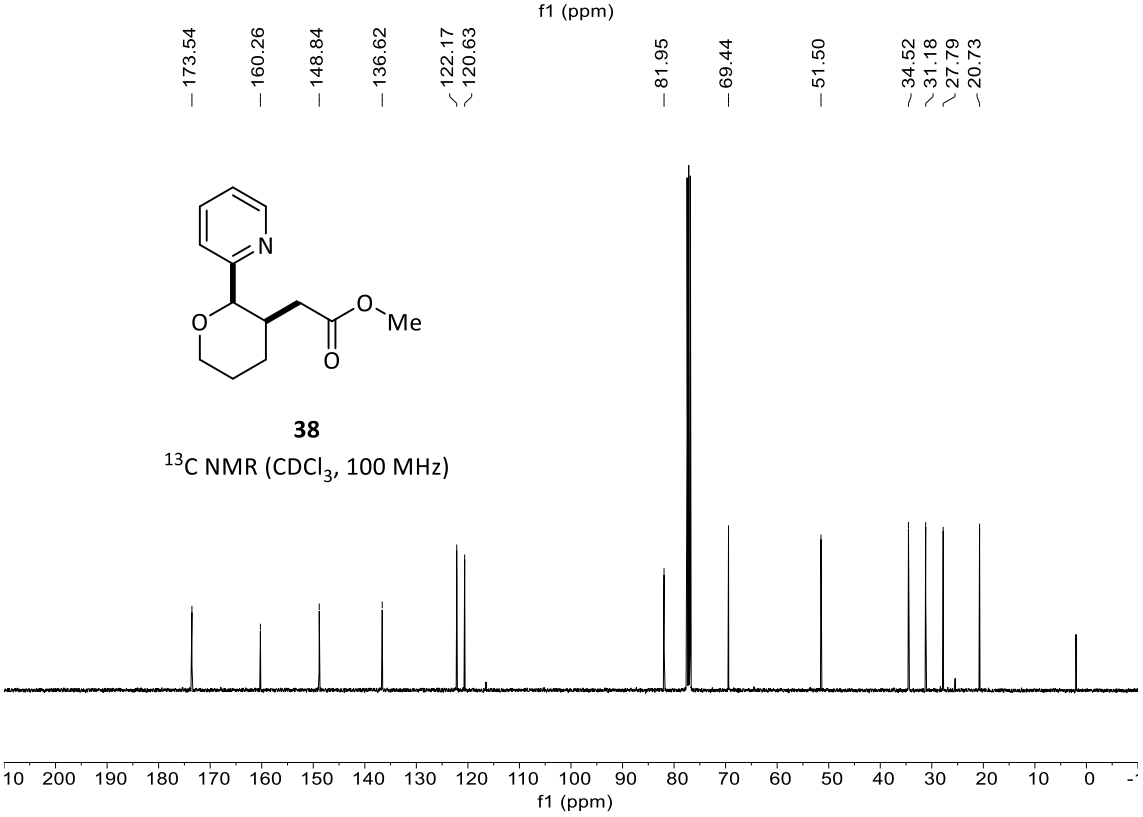

**37**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



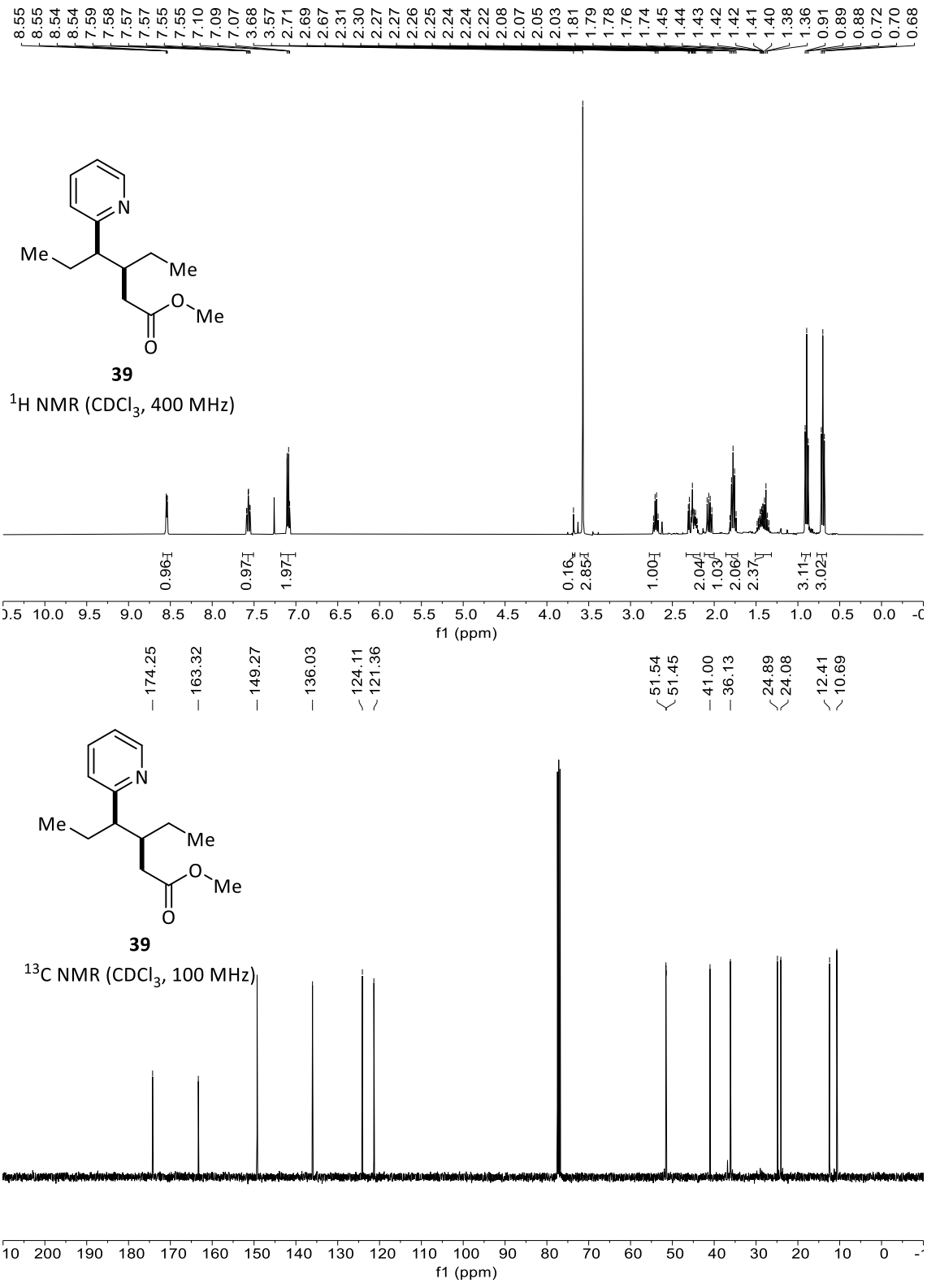

**38**

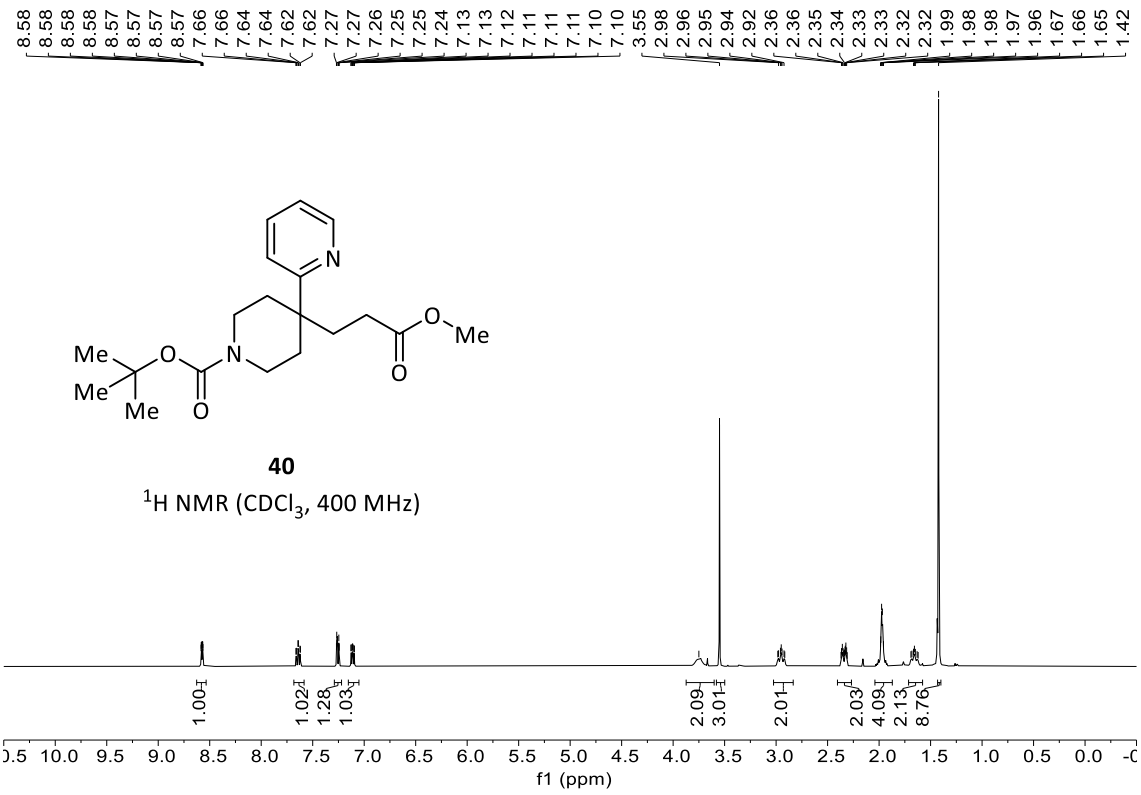
$^{1}$H NMR ($CDCl_3$, 400 MHz)




**38**

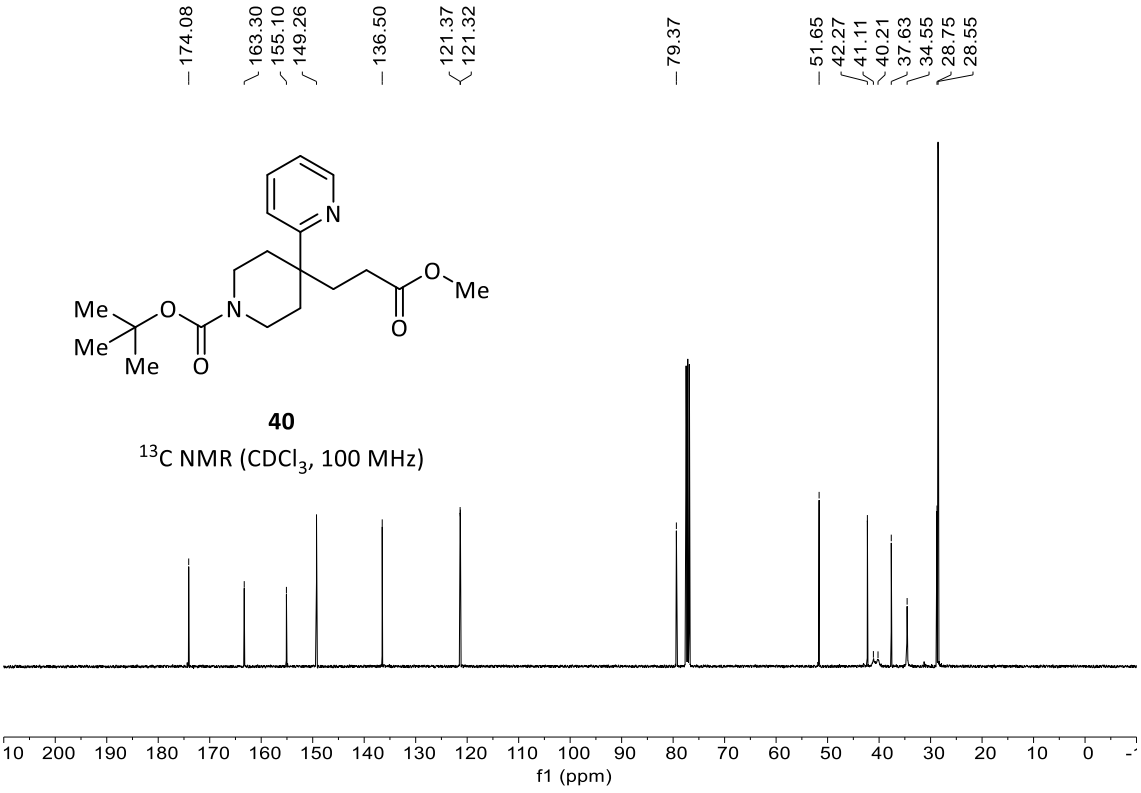
$^{13}$C NMR ($CDCl_3$, 100 MHz)


8.55 8.55 8.54 8.54 7.59 7.58 7.57 7.57 7.55 7.55 7.10 7.09 7.07 3.68 3.57 2.71 2.69 2.67 2.31 2.30 2.27 2.27 2.26 2.25 2.24 2.24 2.22 2.08 2.07 2.05 2.03 1.81 1.79 1.78 1.76 1.74 1.45 1.44 1.43 1.42 1.42 1.41 1.40 1.38 1.36 0.91 0.89 0.88 0.72 0.70 0.68
N
Me
Me
O
Me
O
39
1H NMR (CDCl3, 400 MHz)
0.96 0.97 1.97 0.16 2.85 1.00 2.04 1.03 2.06 2.37 3.11 3.02
f1 (ppm)
174.25 163.32 149.27 136.03 124.11 121.36 51.54 51.45 41.00 36.13 24.89 24.08 12.41 10.69
N
Me
Me
O
Me
O
39
13C NMR (CDCl3, 100 MHz)
f1 (ppm)



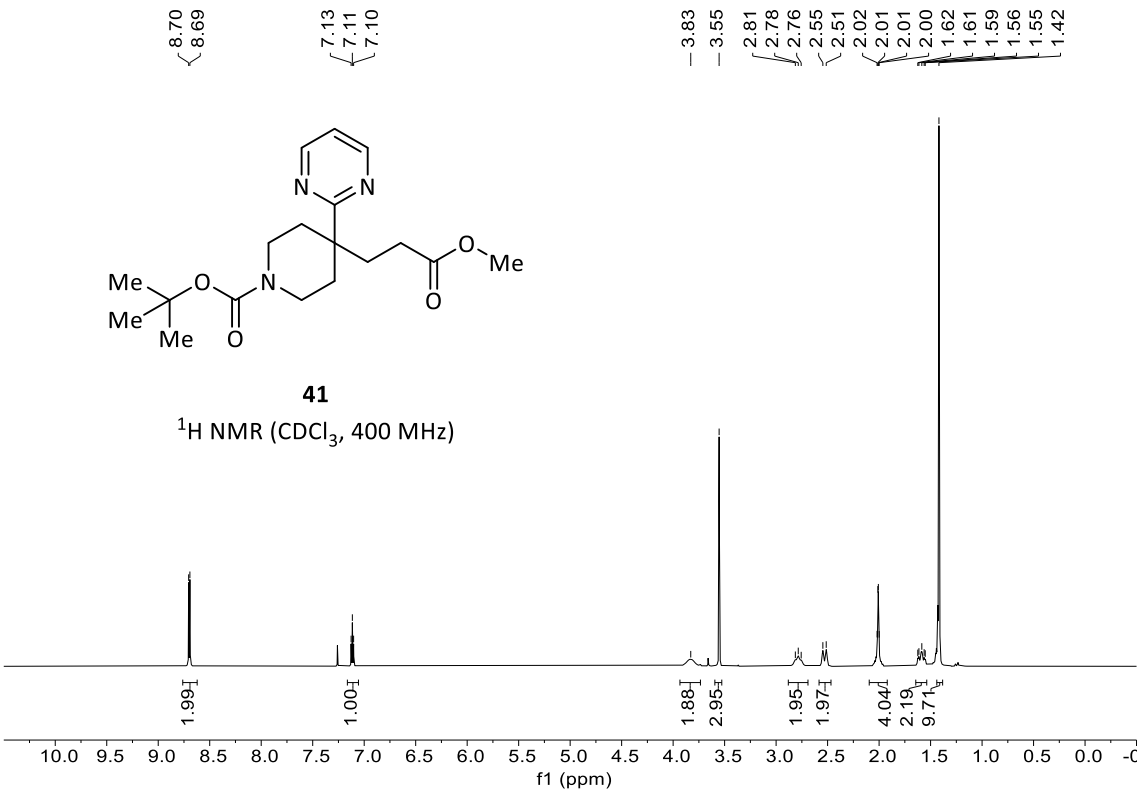

**40**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



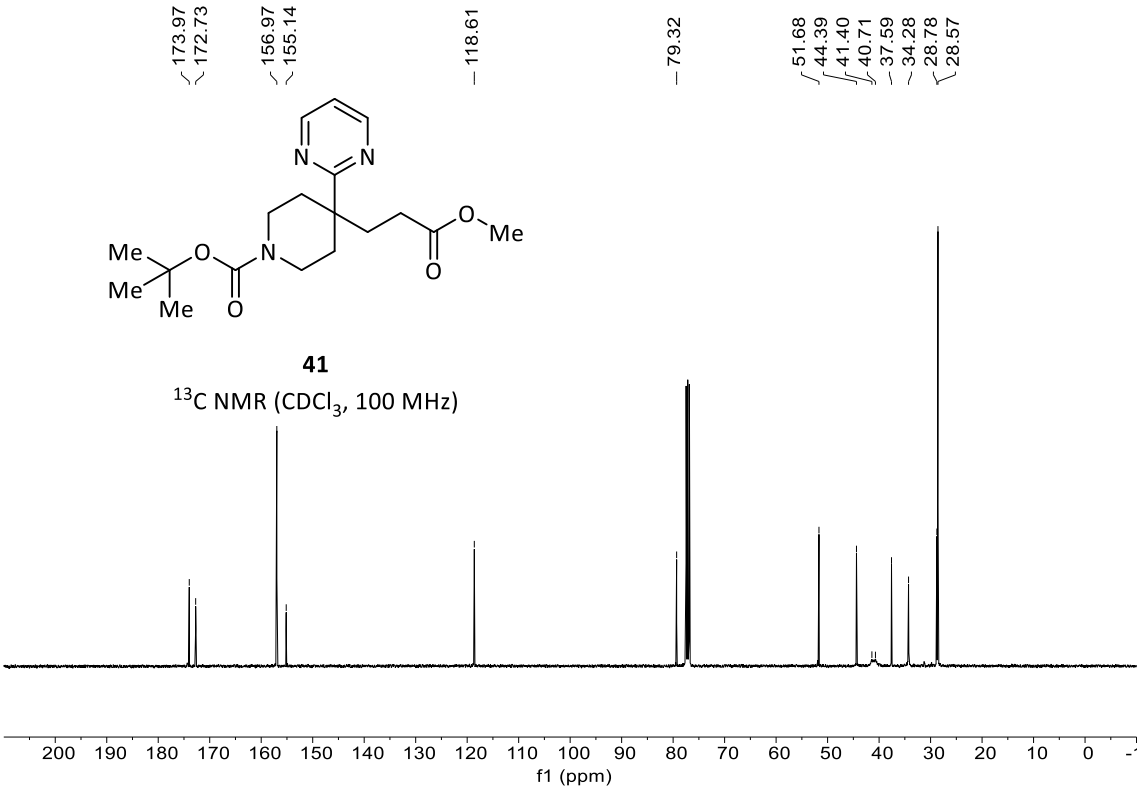

**40**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



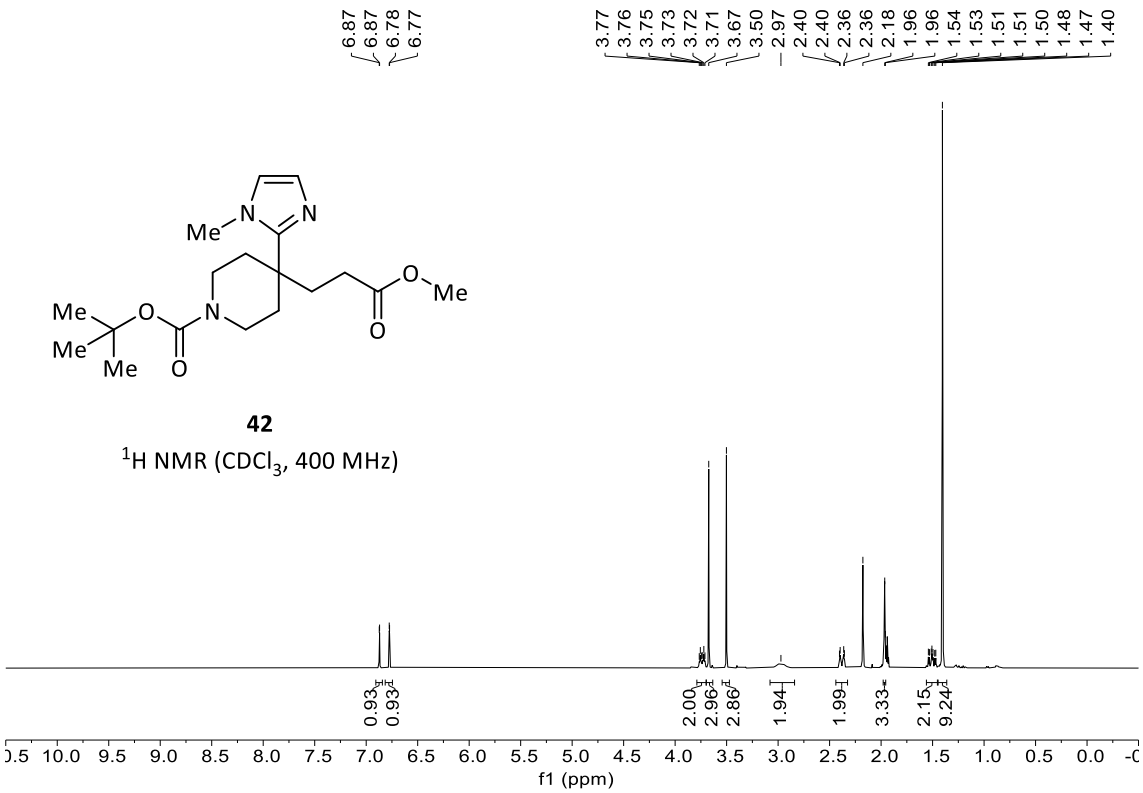

**41**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



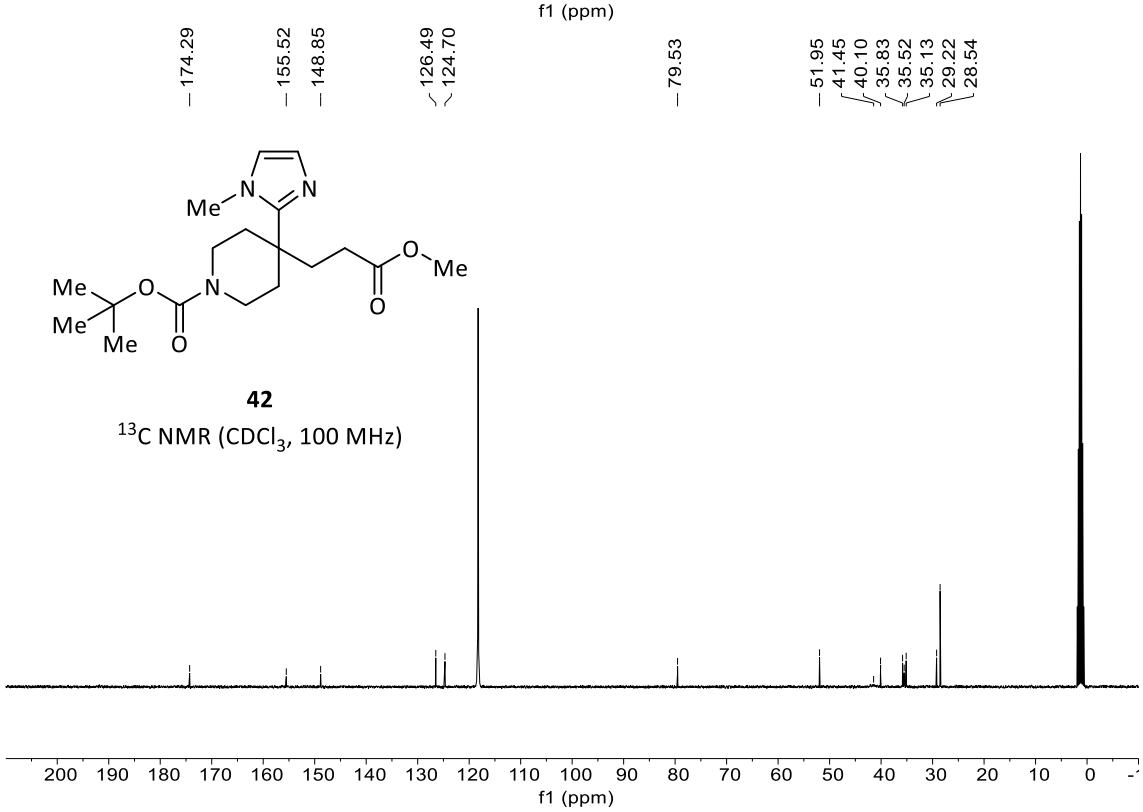

**41**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



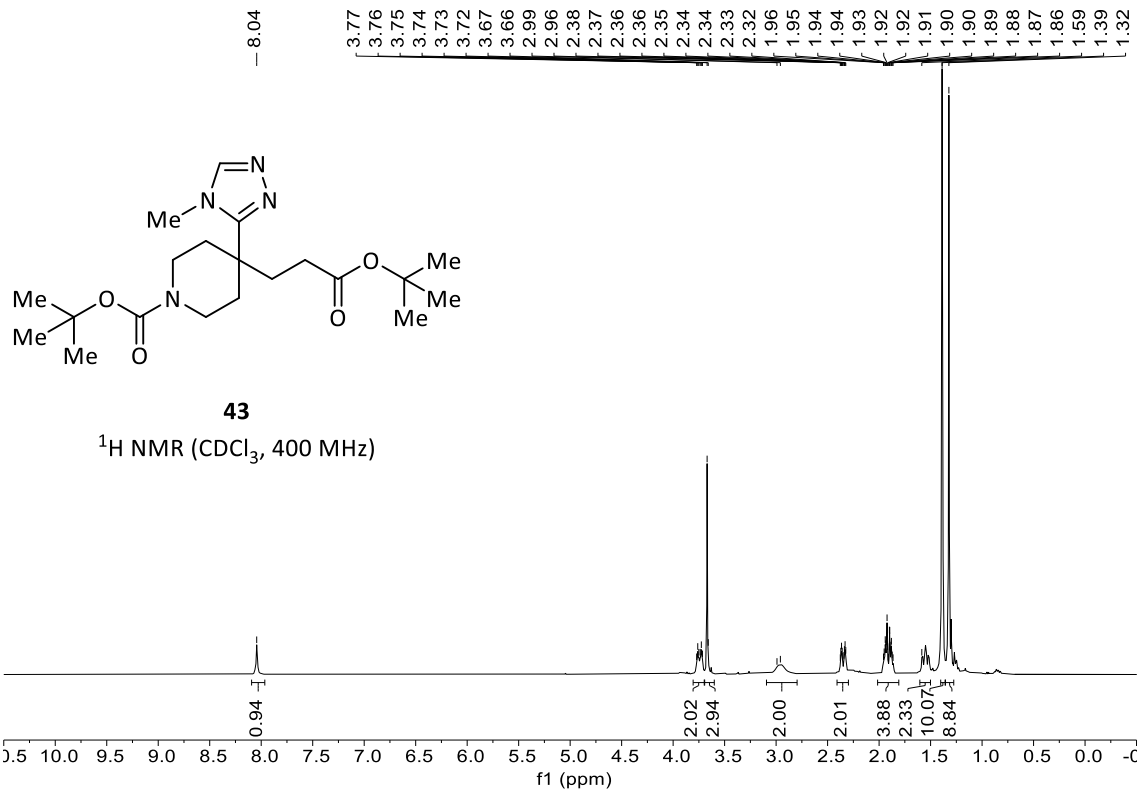

**42**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



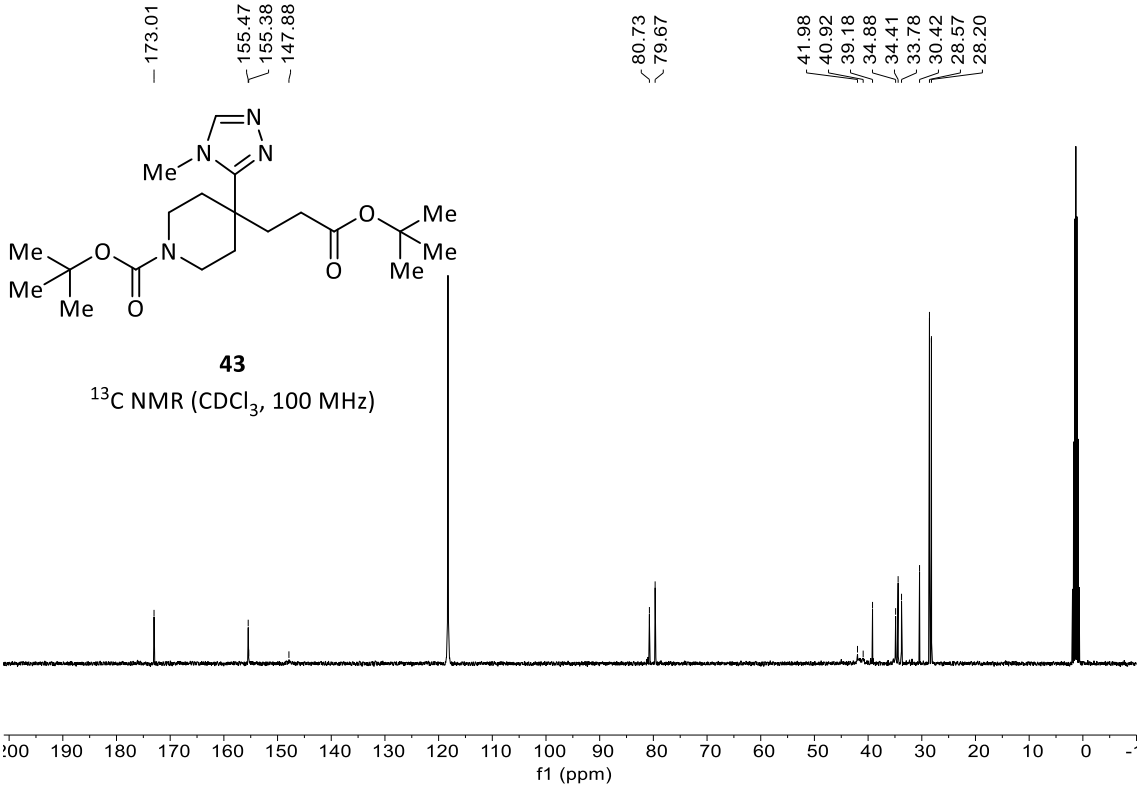

**42**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



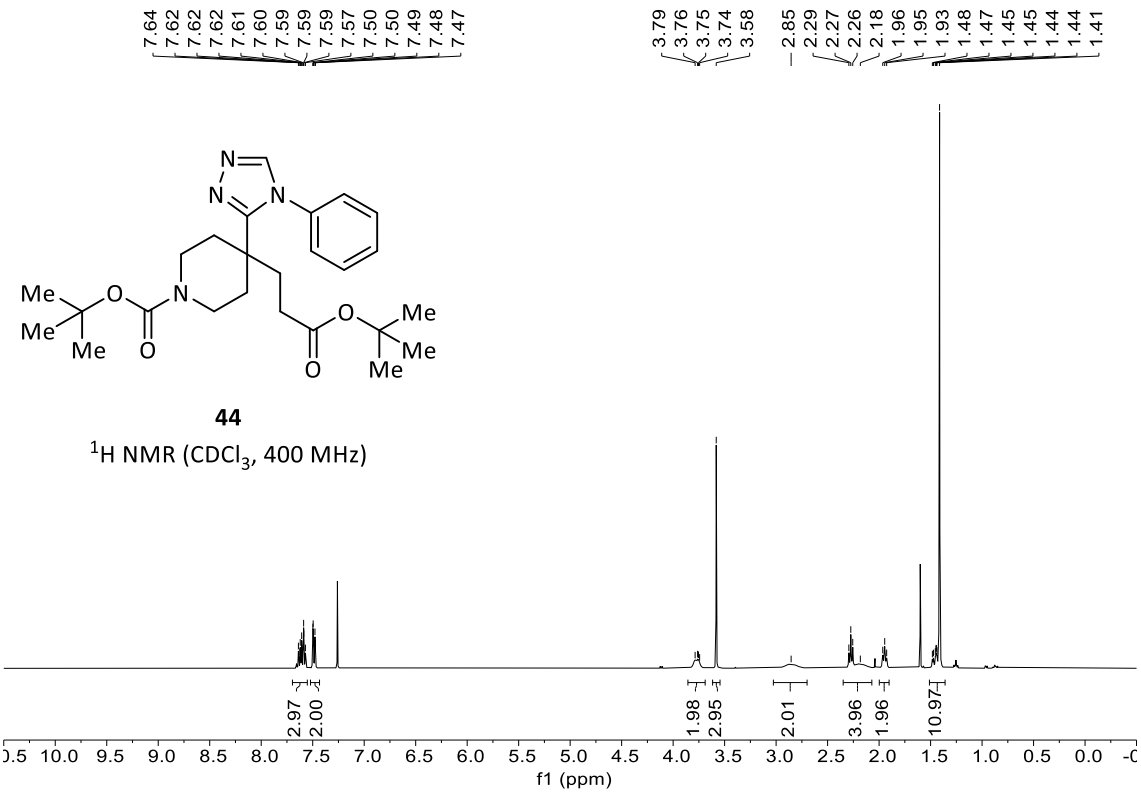

**43**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



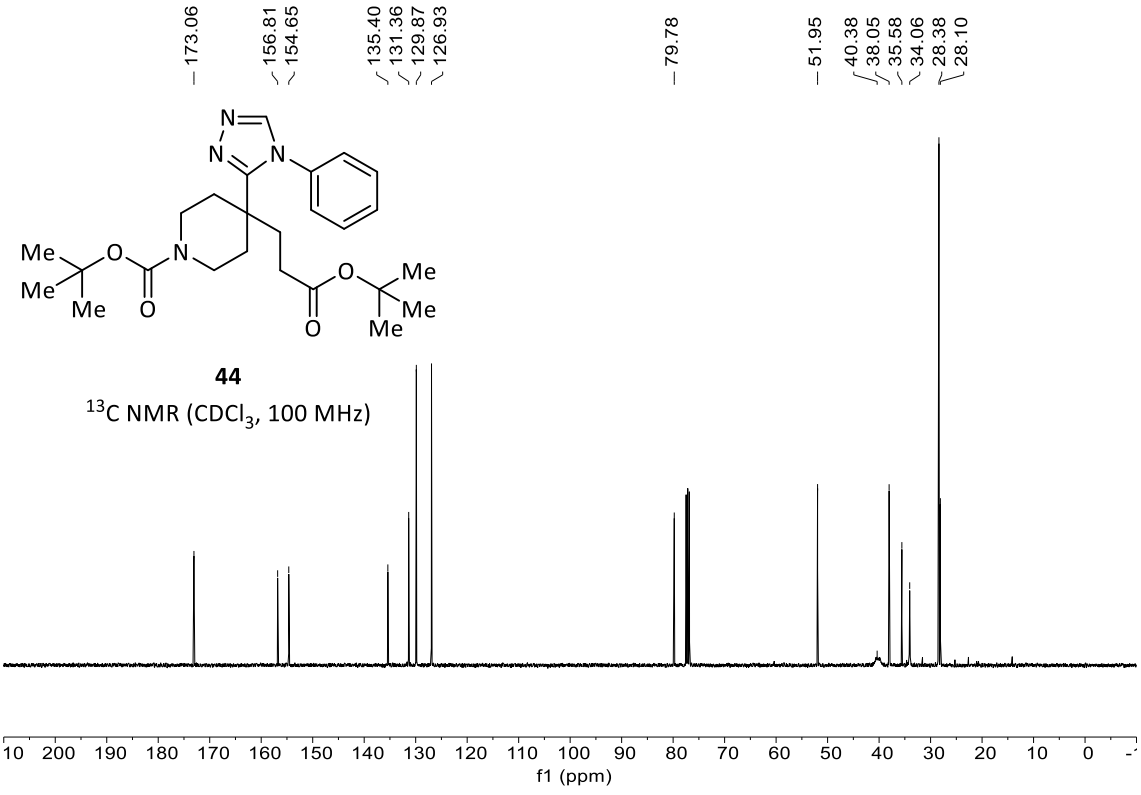

**43**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



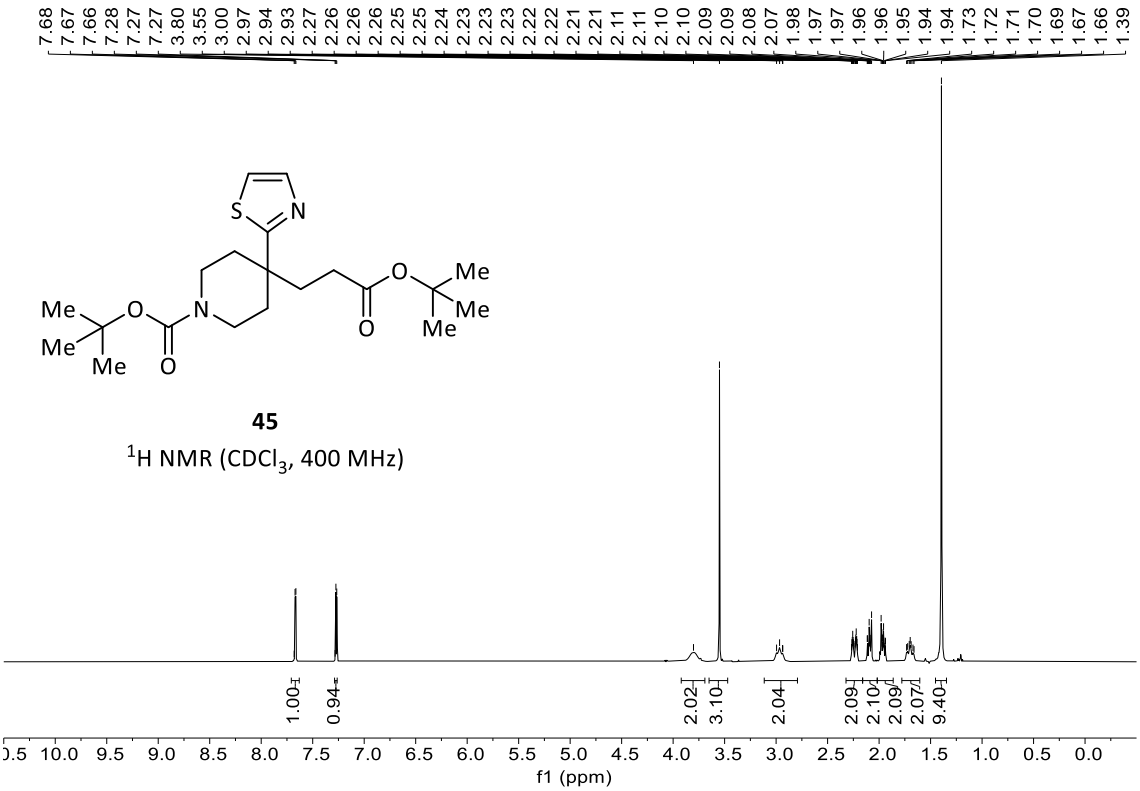

**44**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



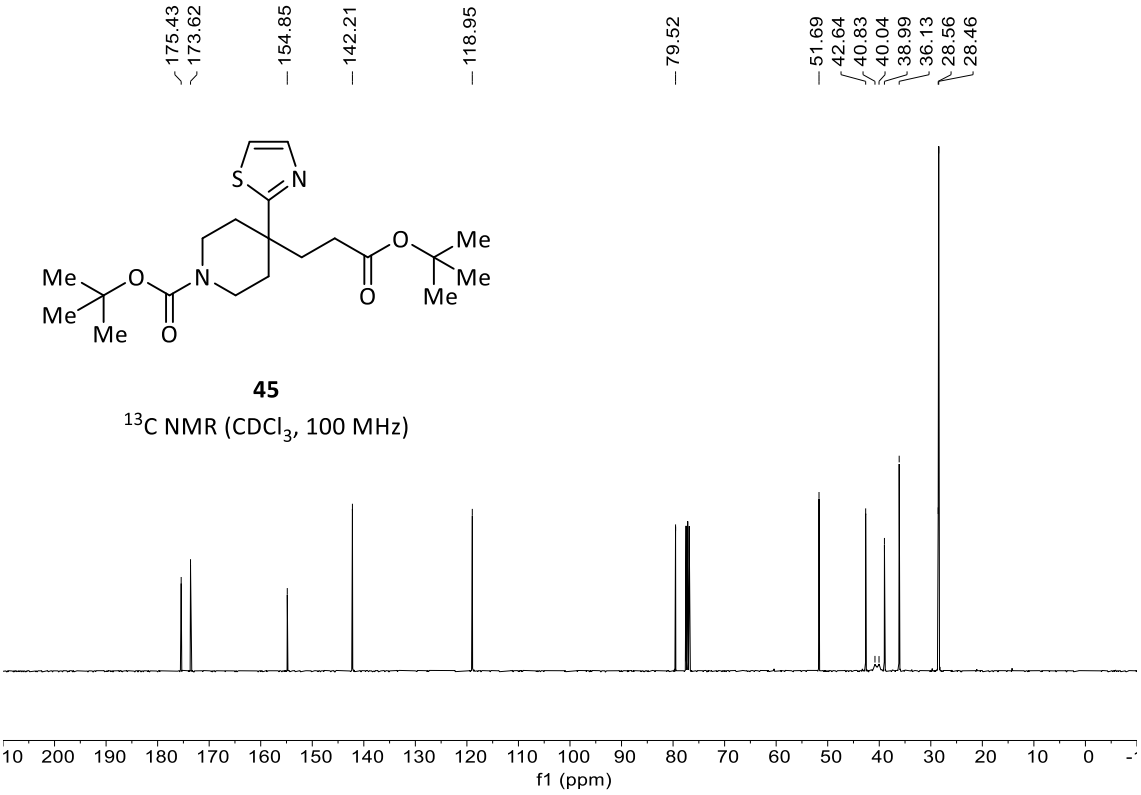

**44**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



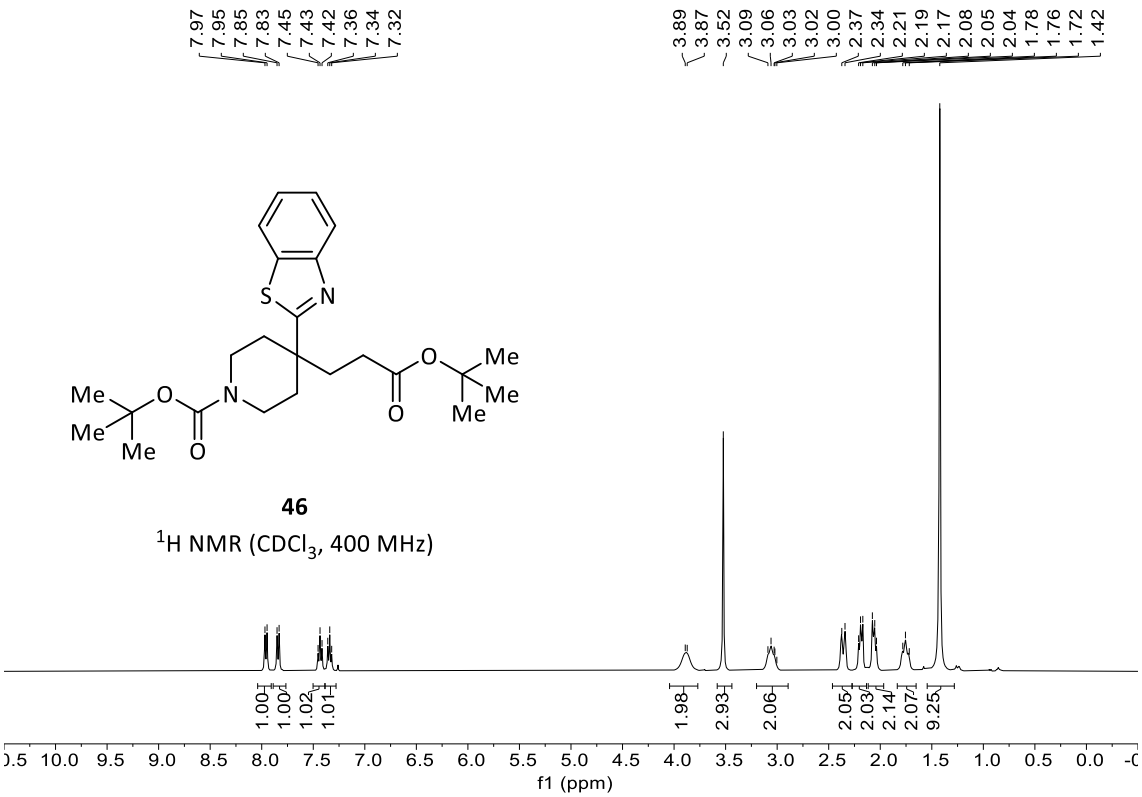

**45**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



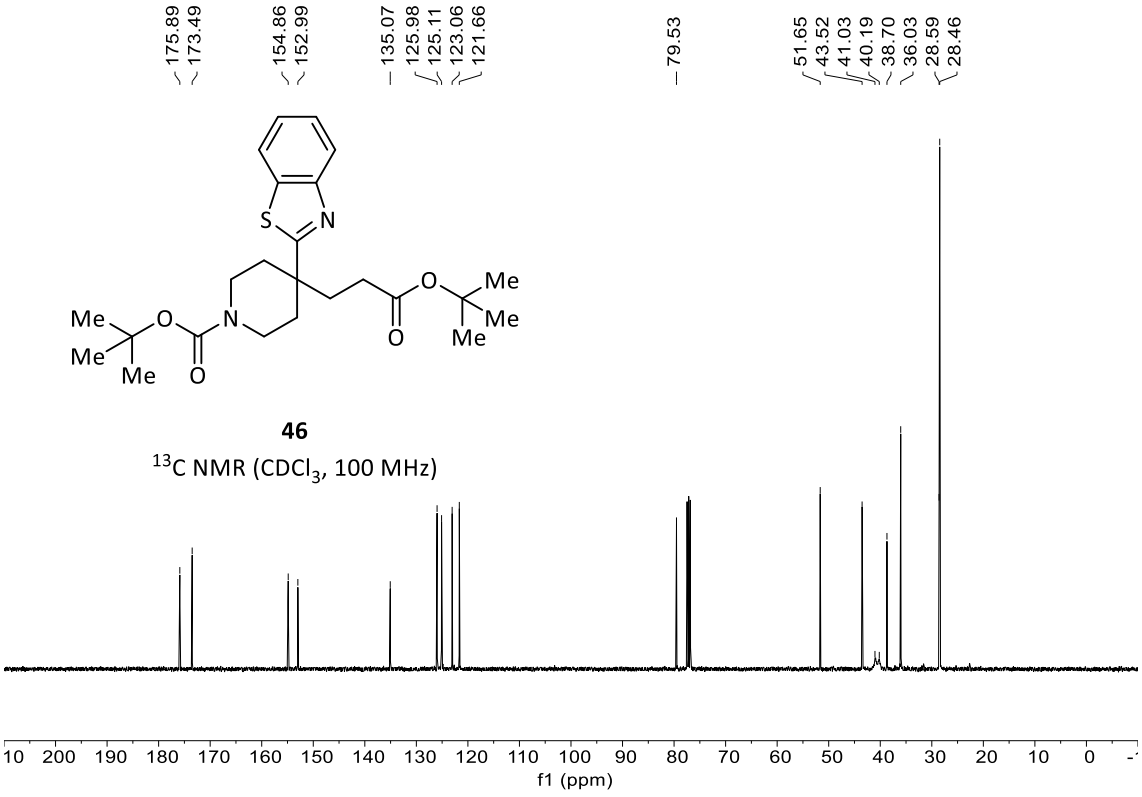

**45**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



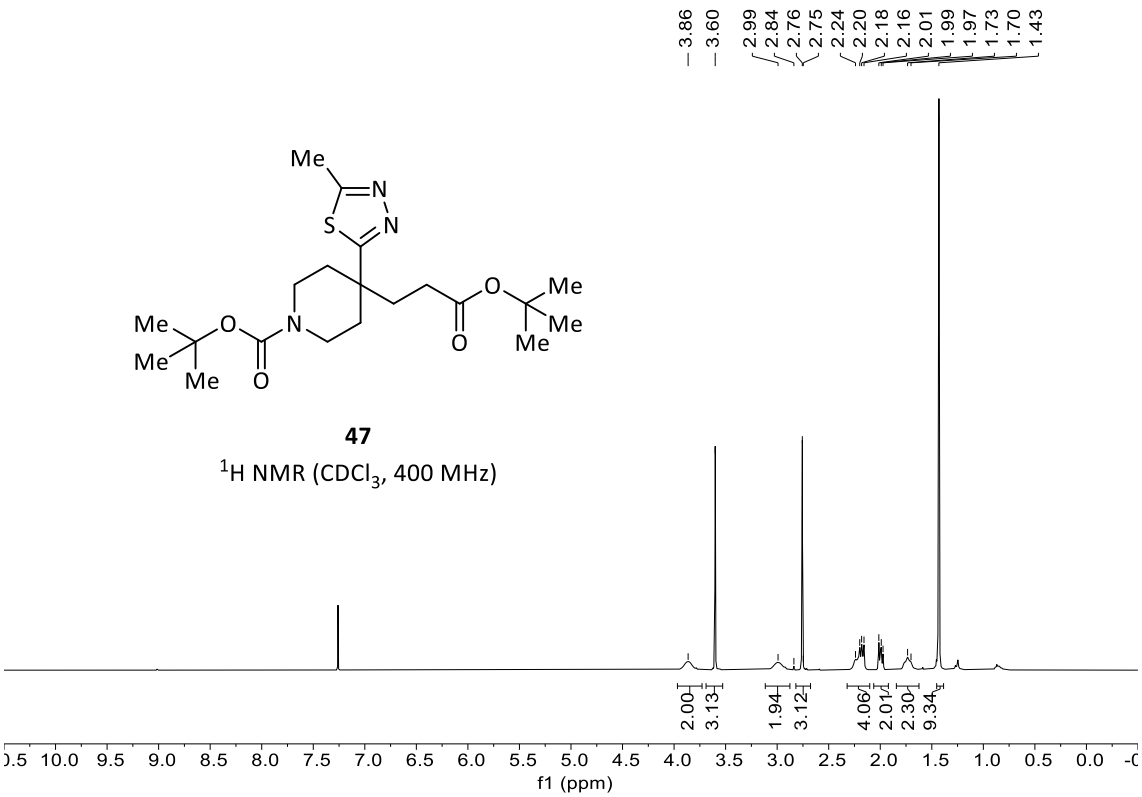

**46**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



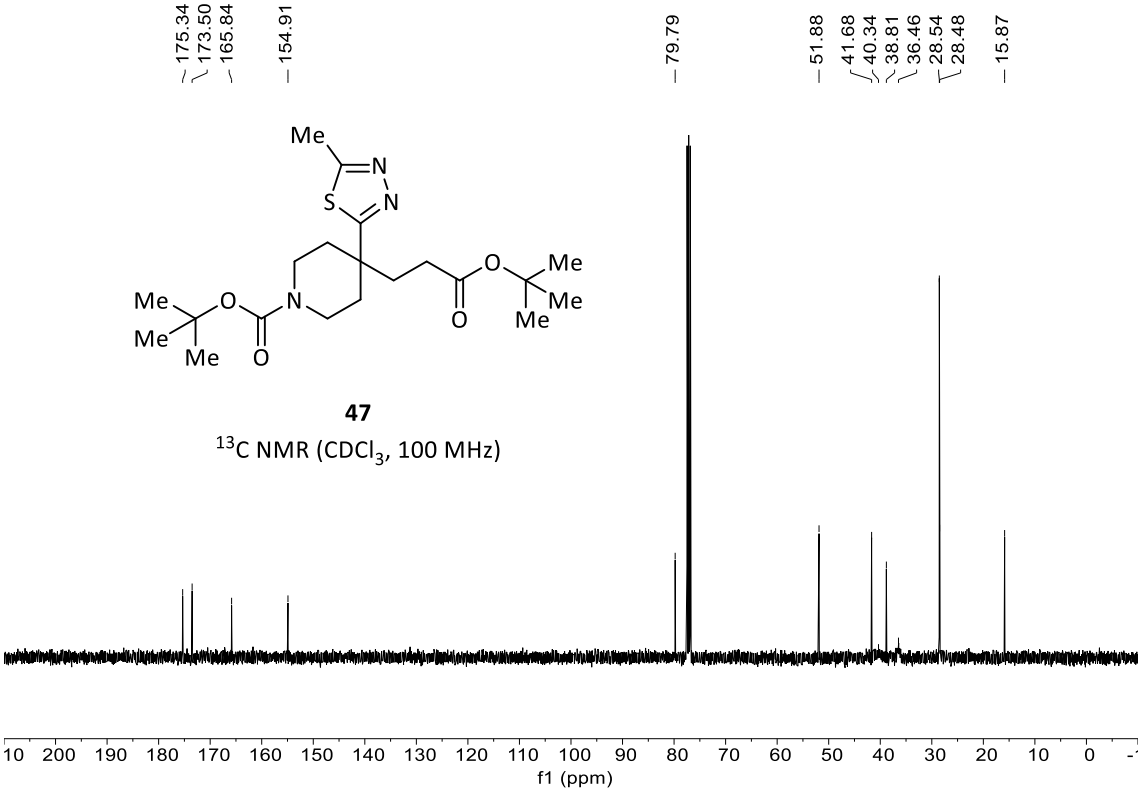

**46**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



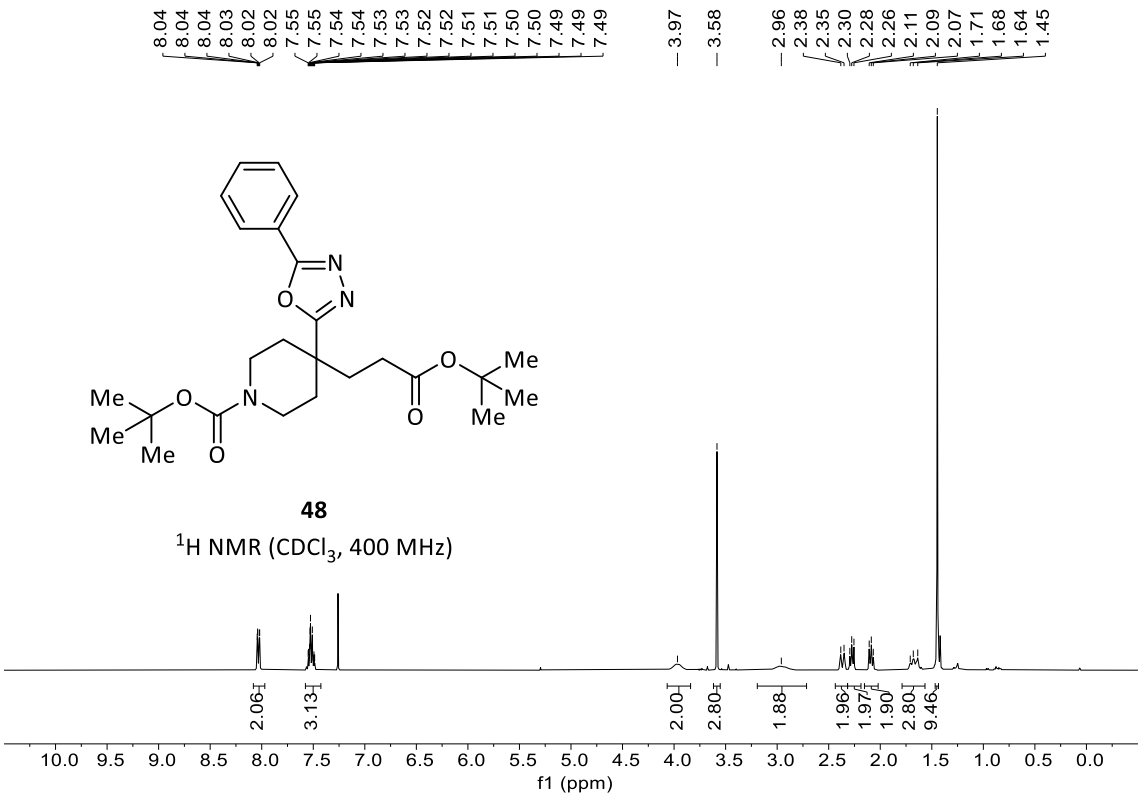

**47**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



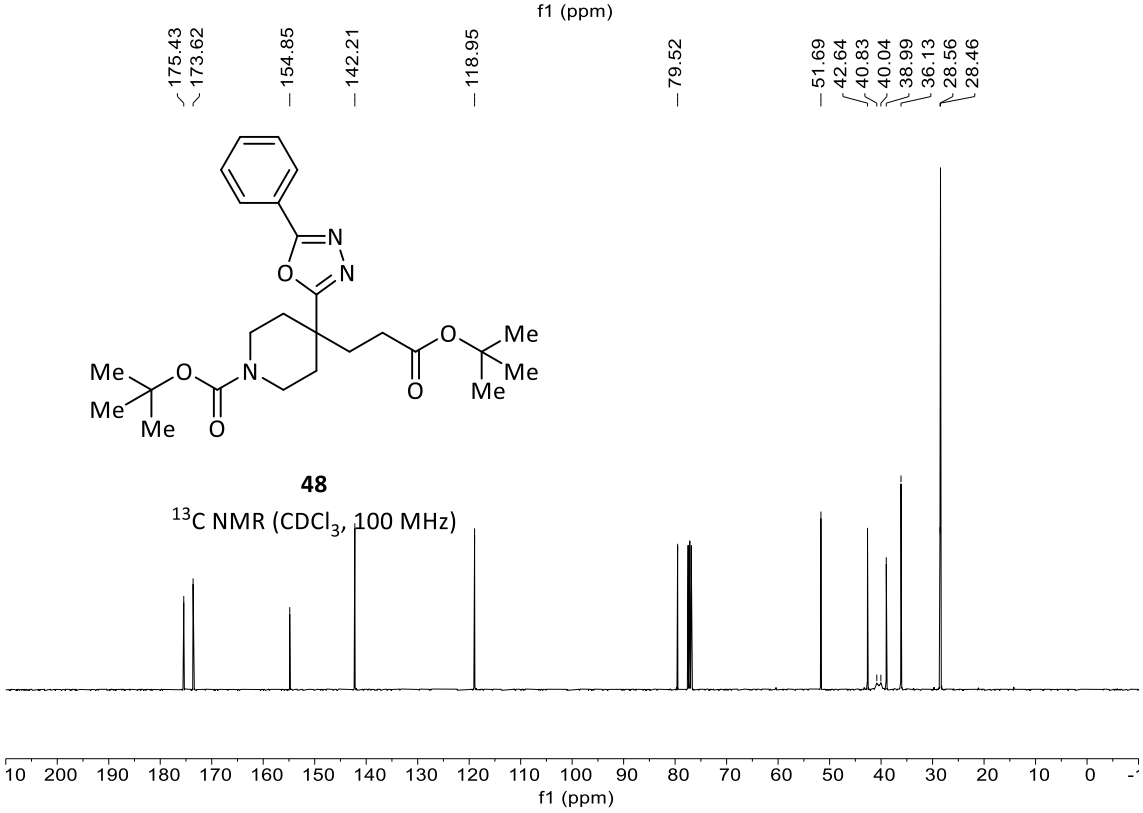

**47**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



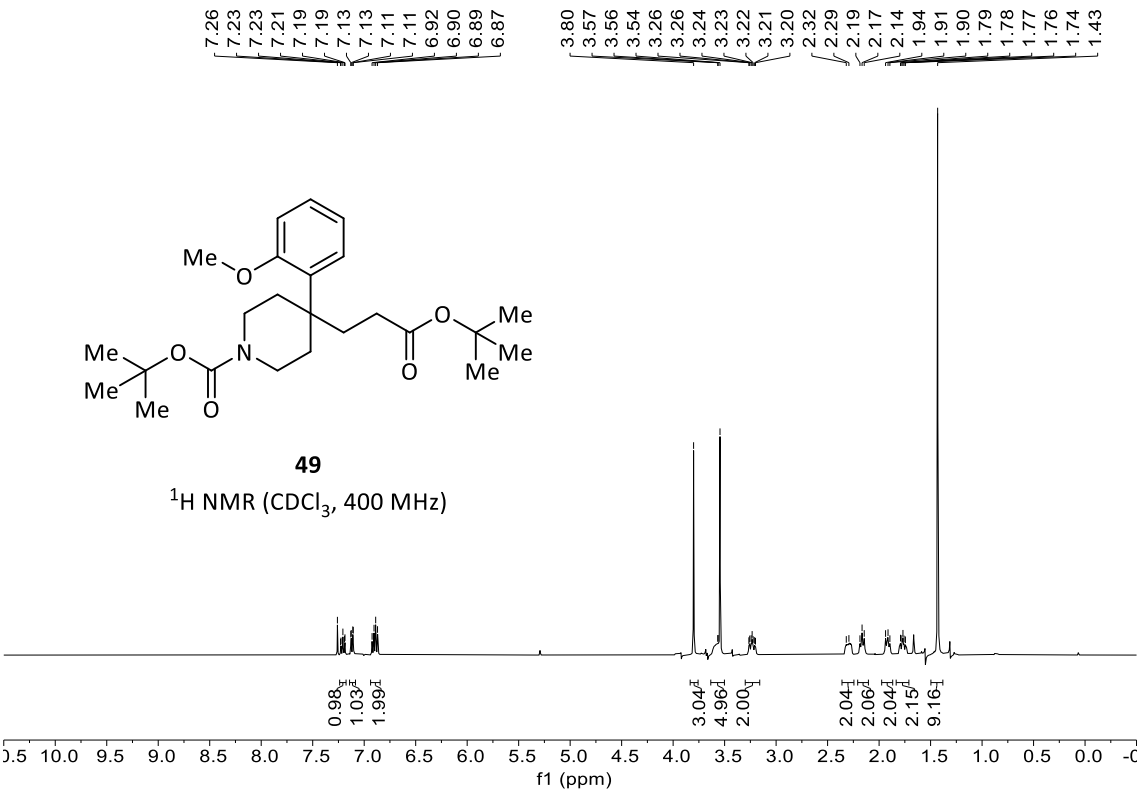

**48**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



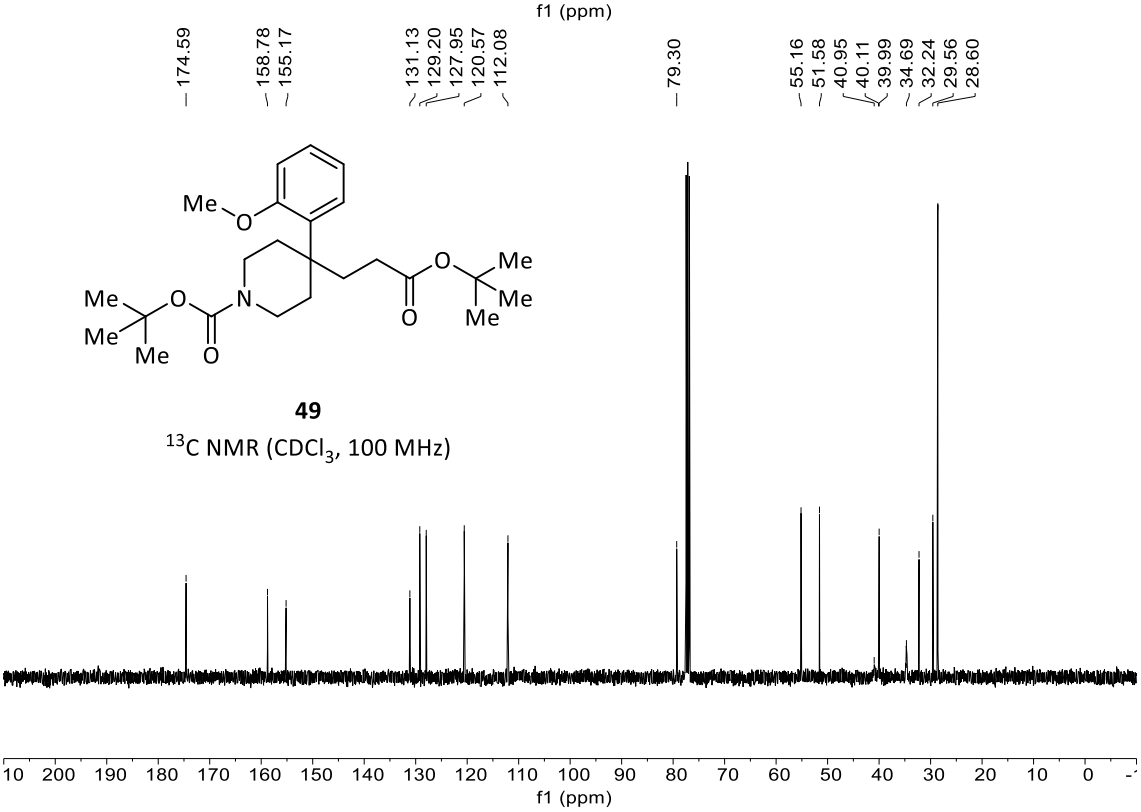

**48**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



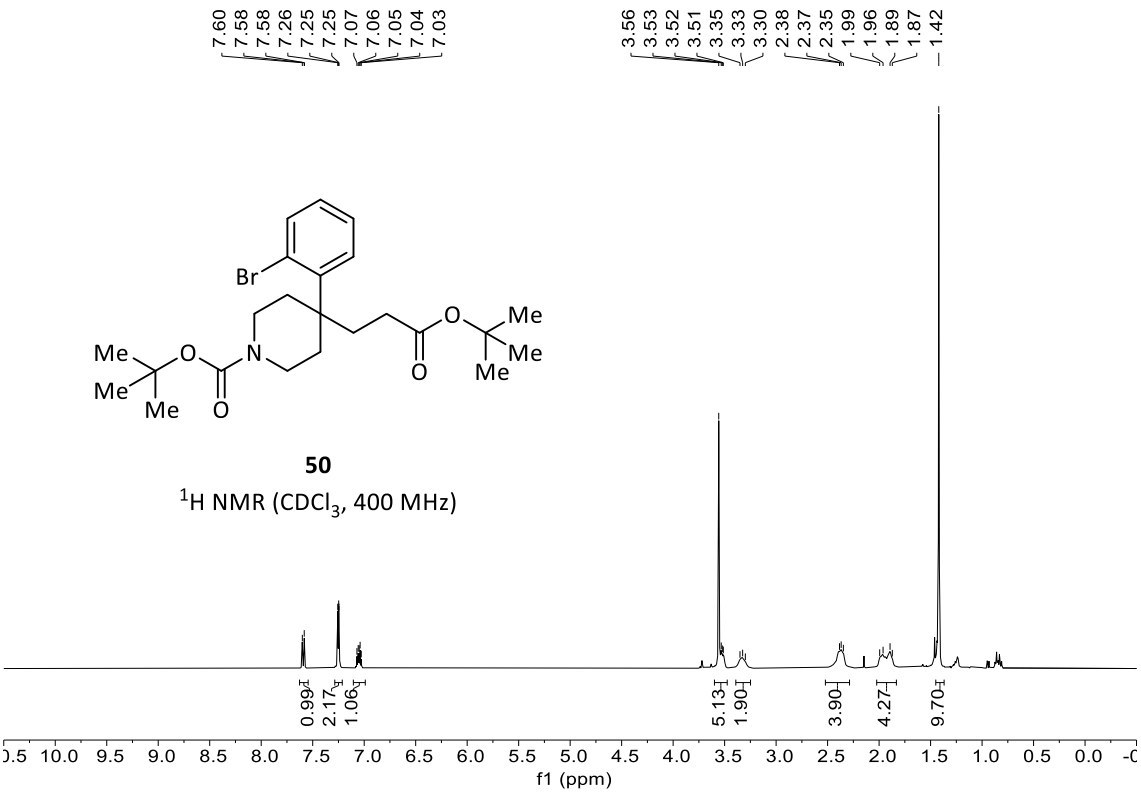

**49**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



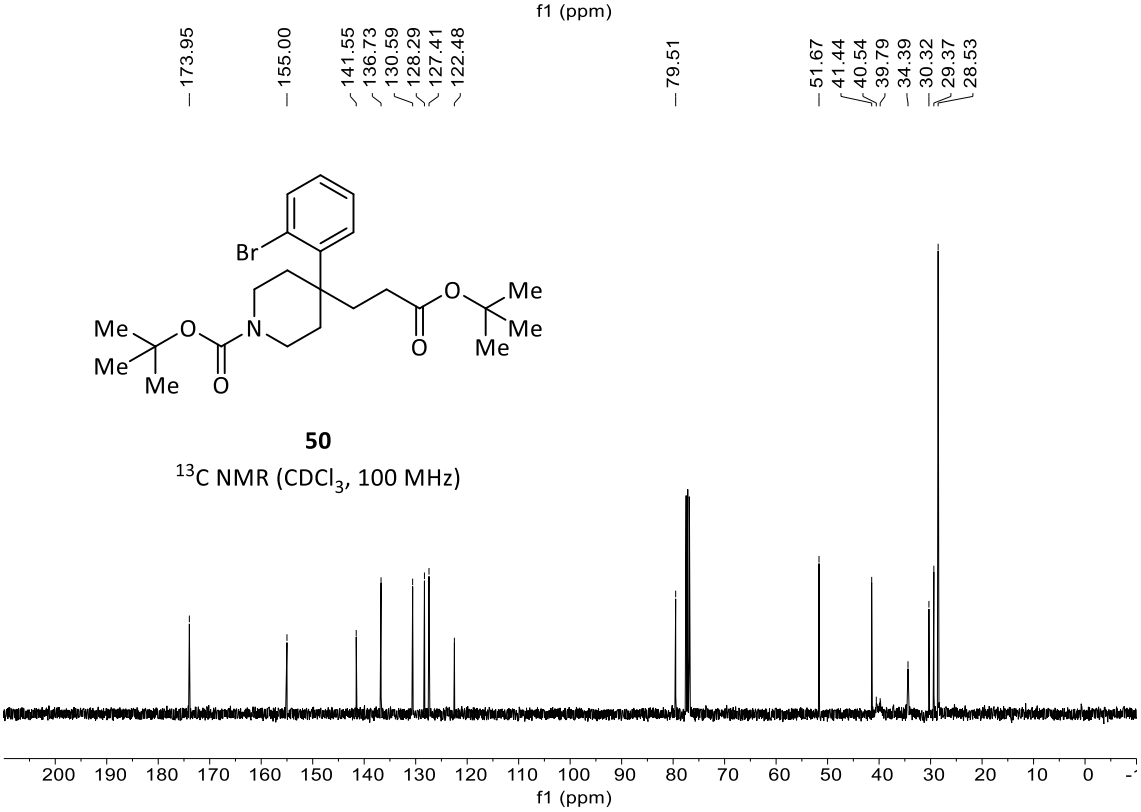

**49**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



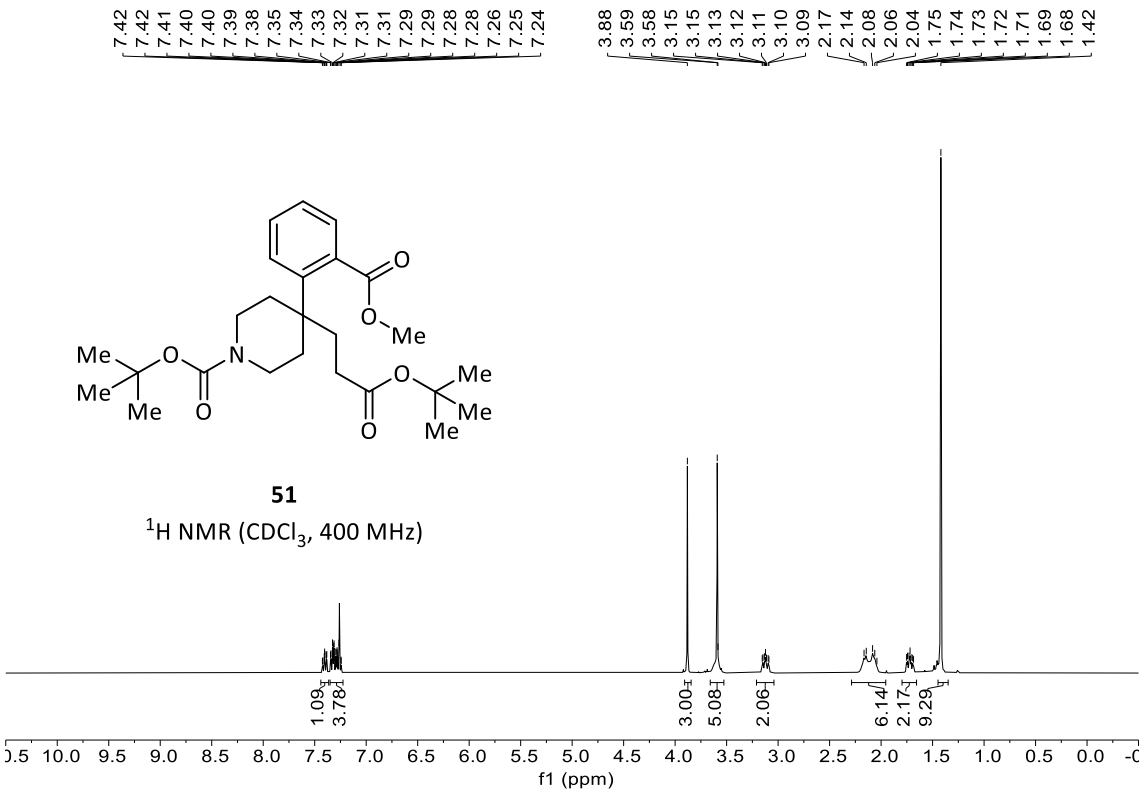

**50**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



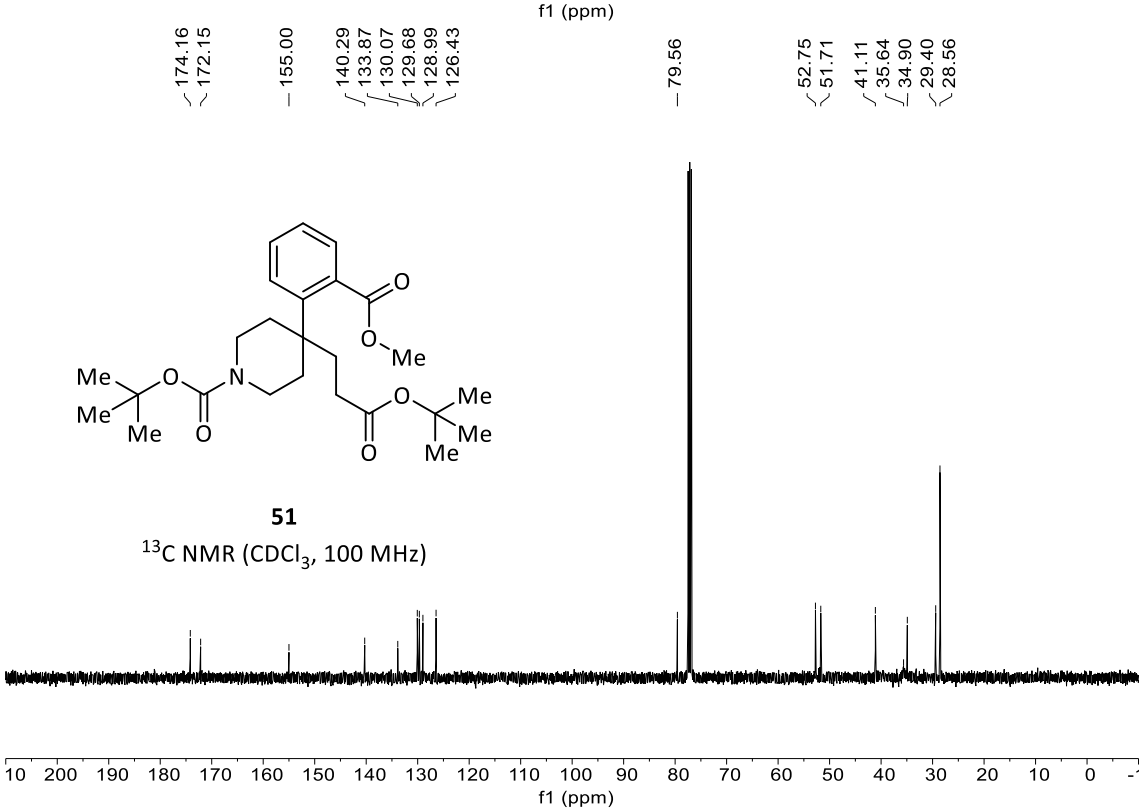

**50**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



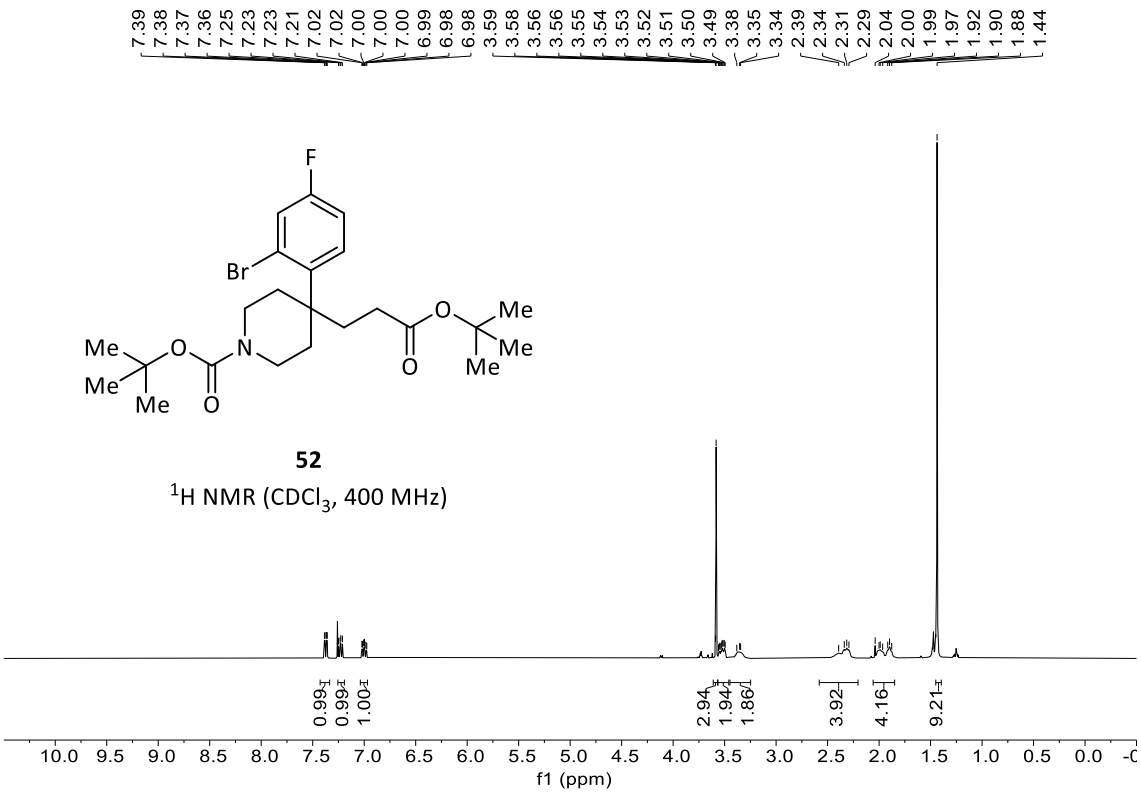

**51**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



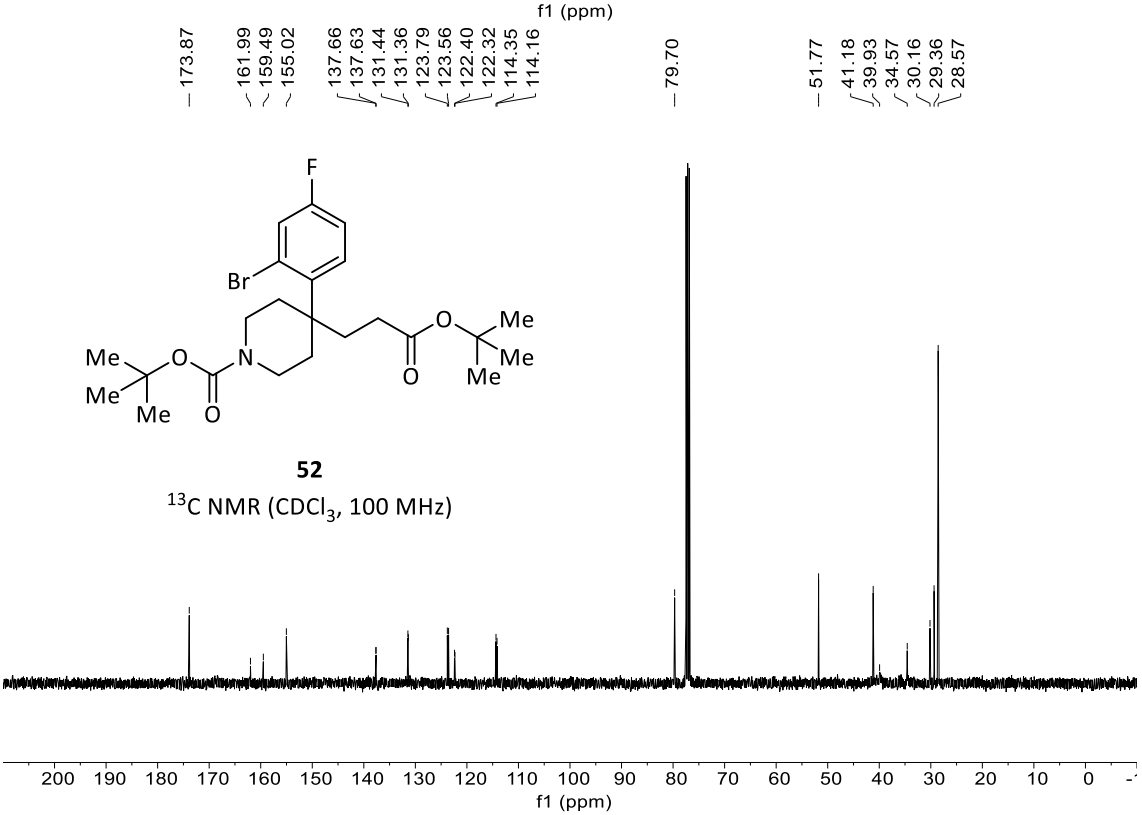

**51**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



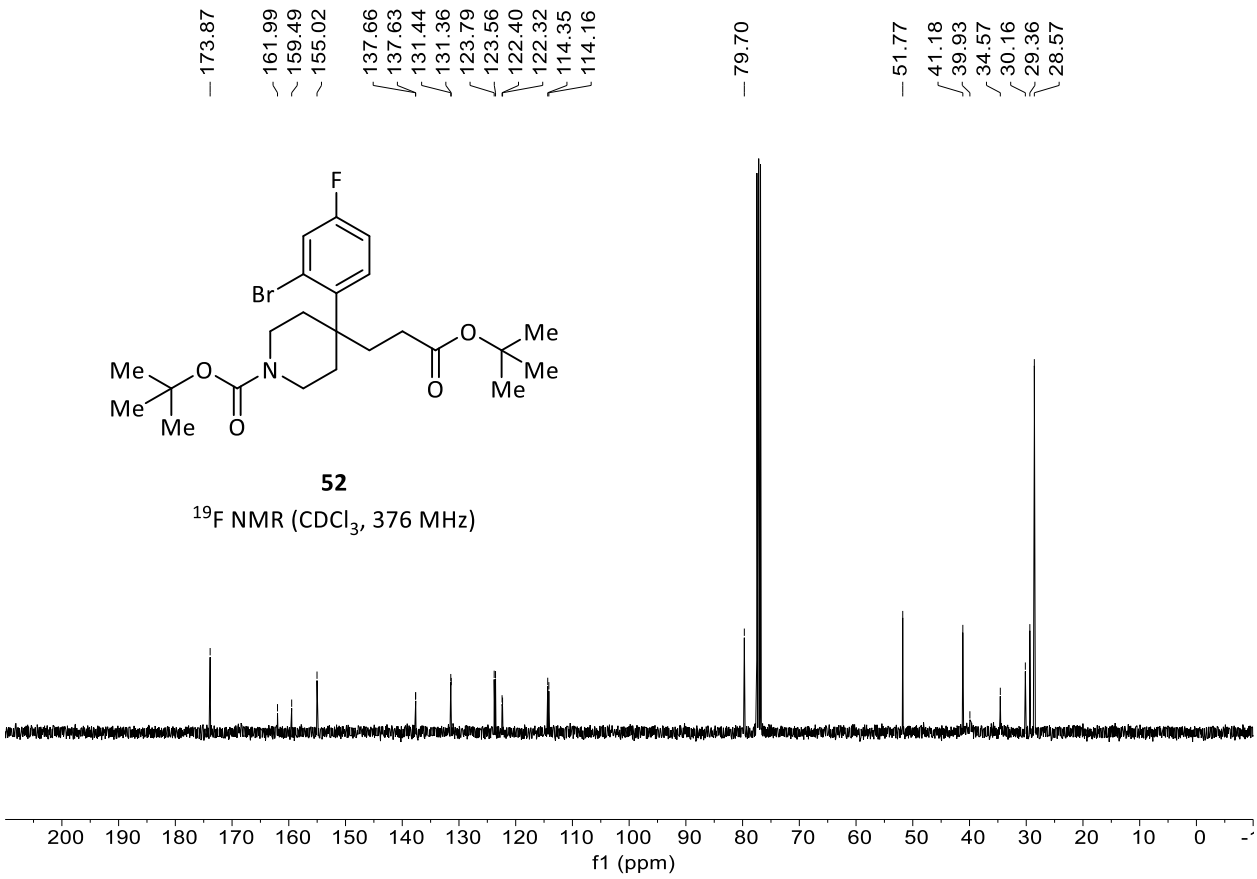

**52**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



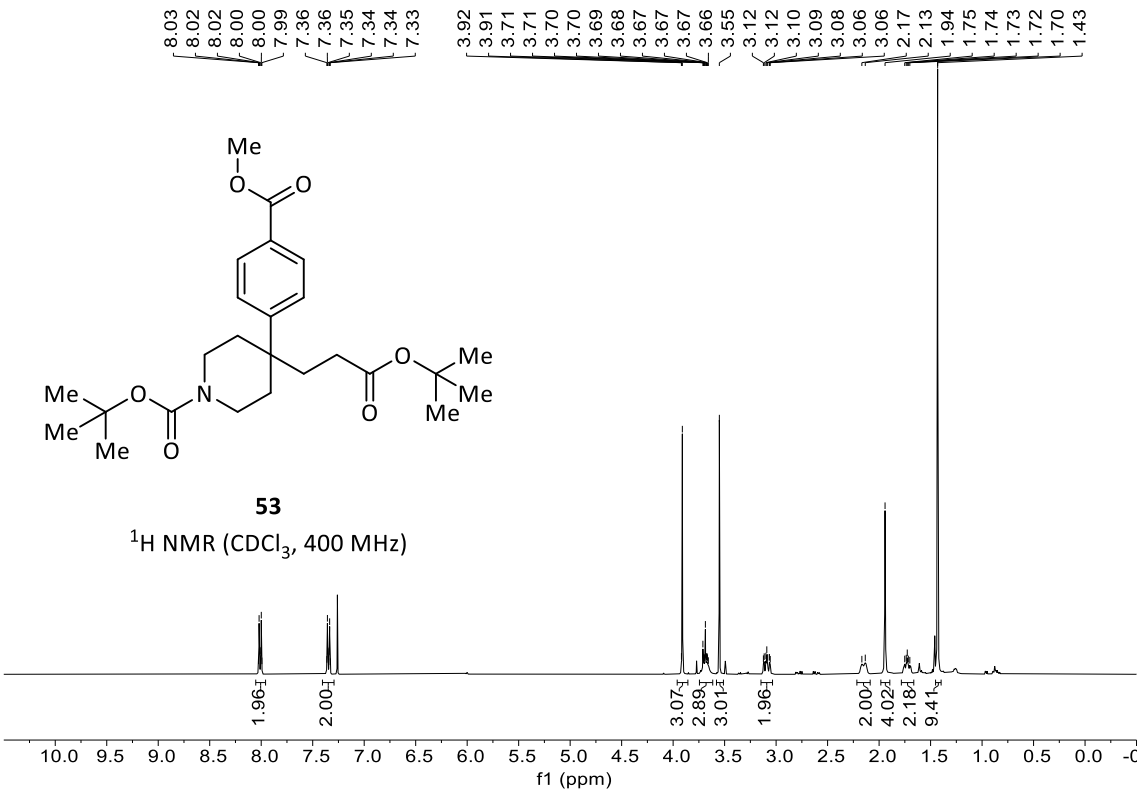

**52**

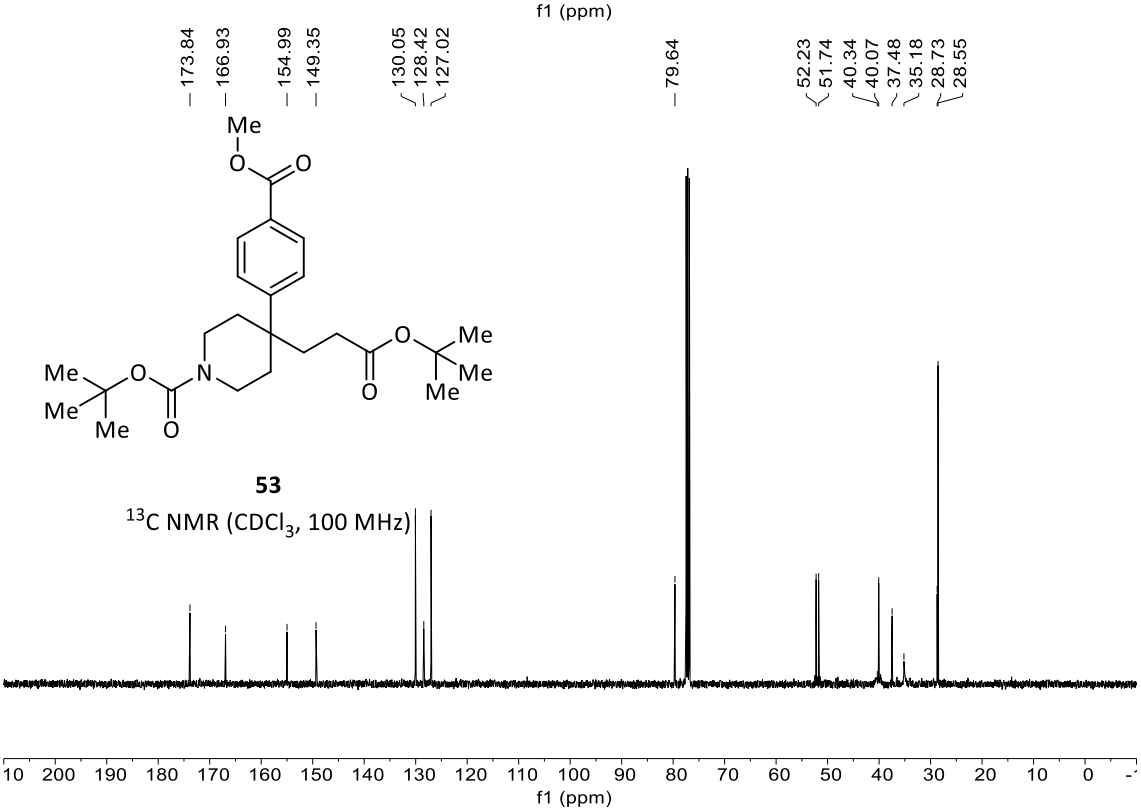
$^{13}$C NMR ($CDCl_3$, 100 MHz)

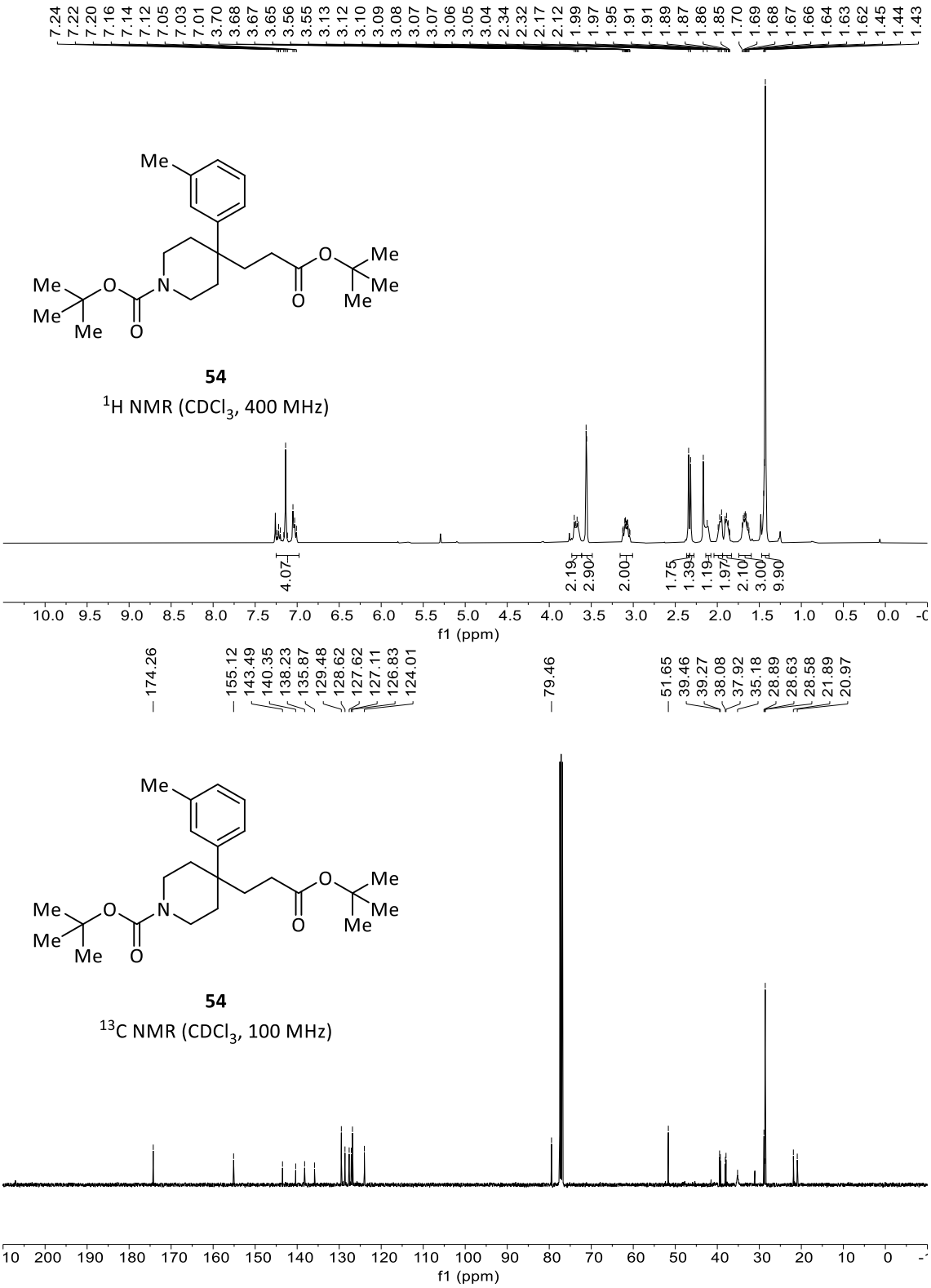


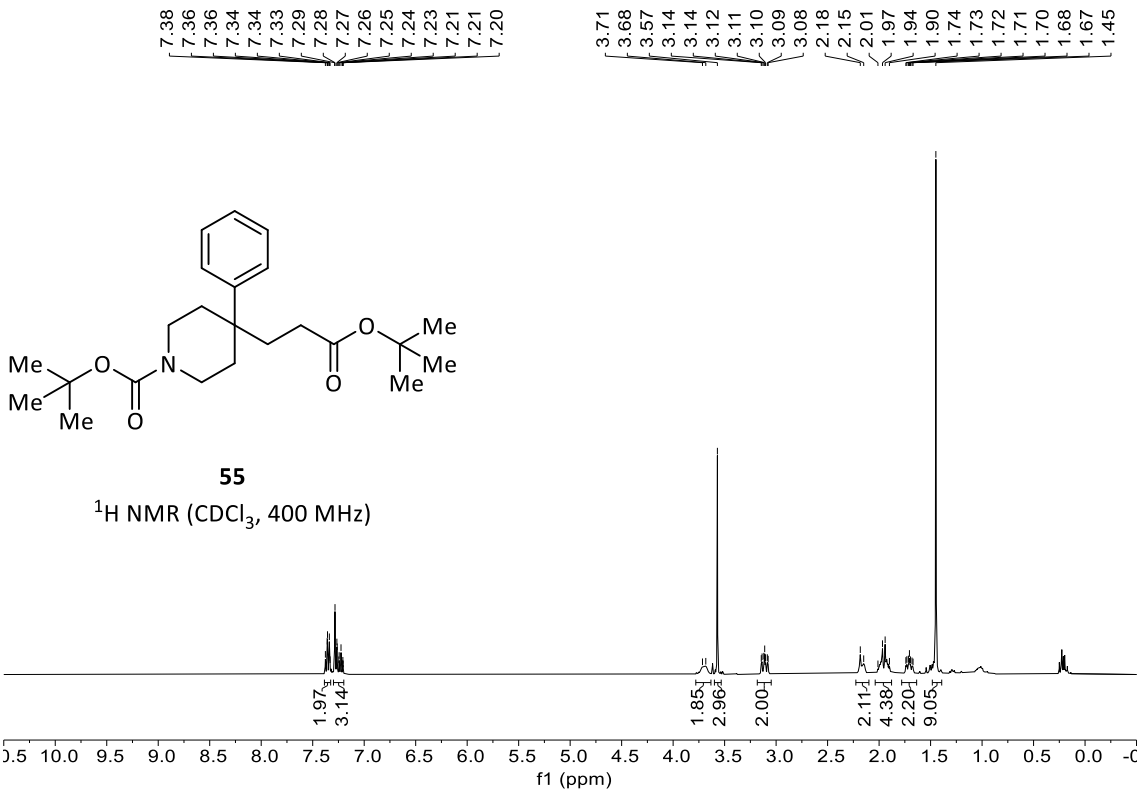

**52**

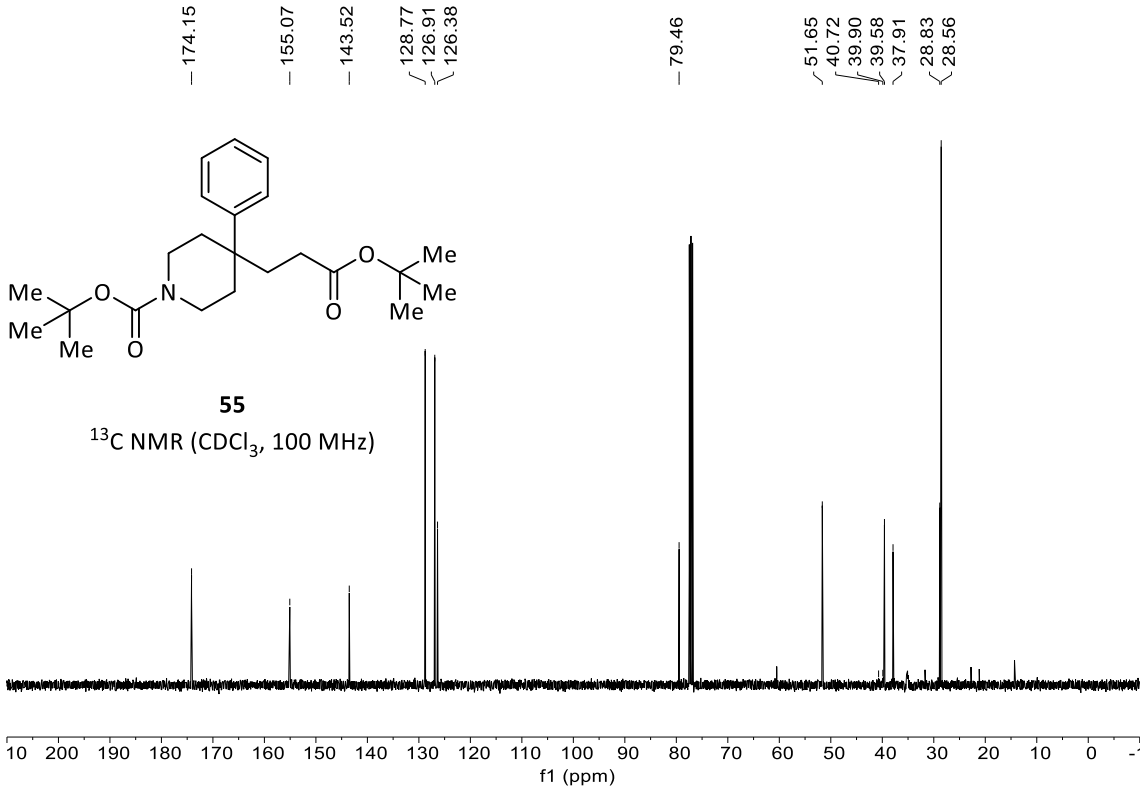
$^{19}$F NMR ($CDCl_3$, 376 MHz)

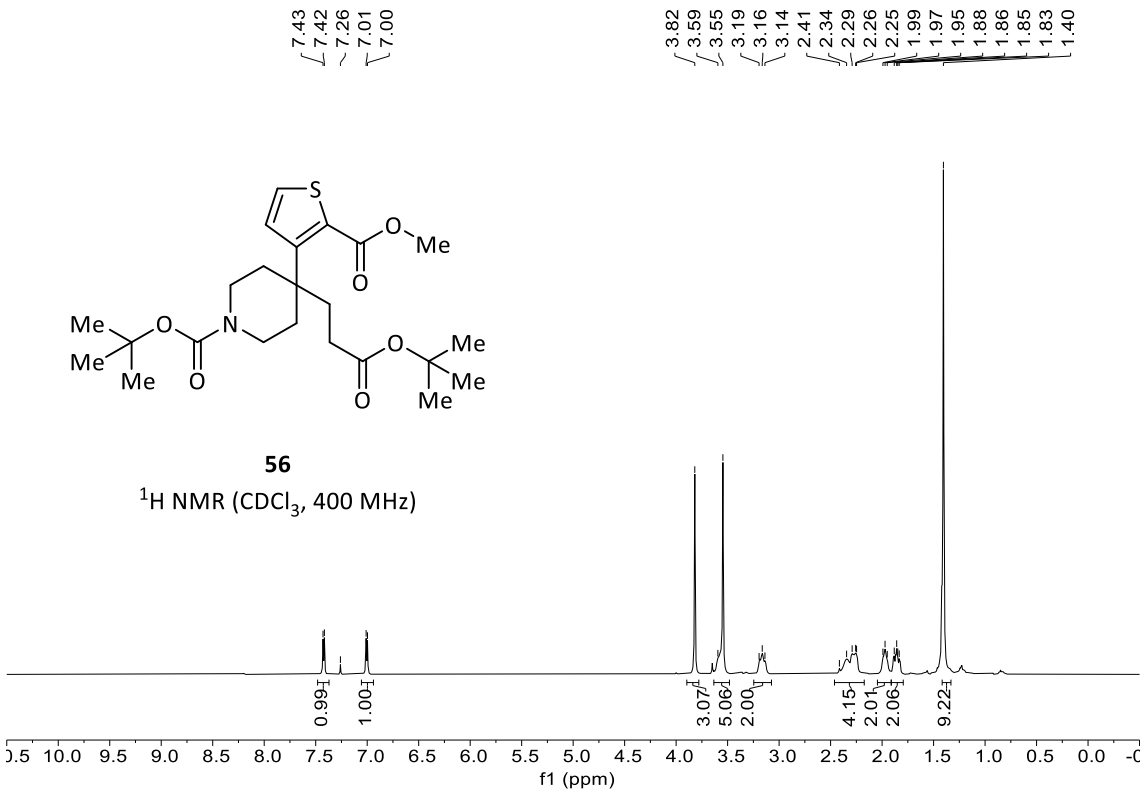

8.03 8.02 8.02 8.00 8.00 7.99 7.36 7.36 7.35 7.34 7.34 7.33
3.92 3.91 3.71 3.71 3.70 3.70 3.69 3.68 3.67 3.67 3.67 3.66 3.55 3.12 3.12 3.10 3.09 3.08 3.06 3.06 2.17 2.13 1.94 1.75 1.74 1.73 1.72 1.70 1.43
Me
O
O
Me
O
N
O
Me
Me
Me
O
O
Me
Me
Me
O
53
1H NMR (CDCl3, 400 MHz)
1.96 2.00 3.07 2.89 3.01 1.96 2.00 4.02 2.18 9.41
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)


173.84 166.93 154.99 149.35 130.05 128.42 127.02 79.64 52.23 51.74 40.34 40.07 37.48 35.18 28.73 28.55
Me
O
O
Me
O
N
O
Me
Me
Me
O
O
Me
Me
Me
O
53
13C NMR (CDCl3, 100 MHz)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.24 7.22 7.20 7.16 7.14 7.12 7.05 7.03 7.01 3.70 3.68 3.67 3.65 3.56 3.55 3.13 3.12 3.10 3.09 3.08 3.07 3.07 3.06 3.05 3.04 2.34 2.32 2.17 2.12 1.99 1.97 1.95 1.91 1.91 1.89 1.87 1.86 1.85 1.70 1.69 1.68 1.67 1.66 1.64 1.63 1.62 1.45 1.44 1.43
Me
Me
O
N
O
Me
Me
Me
O
O
Me
Me
Me
O
54
1H NMR (CDCl3, 400 MHz)
4.07
2.19
2.90
2.00
1.75
1.39
1.19
1.97
2.10
3.00
9.90
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)
174.26
155.12
143.49
140.35
138.23
135.87
129.48
128.62
127.62
127.11
126.83
124.01
79.46
51.65
39.46
39.27
38.08
37.92
35.18
28.89
28.63
28.58
21.89
20.97
Me
Me
O
N
O
Me
Me
Me
O
O
Me
Me
Me
O
54
13C NMR (CDCl3, 100 MHz)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

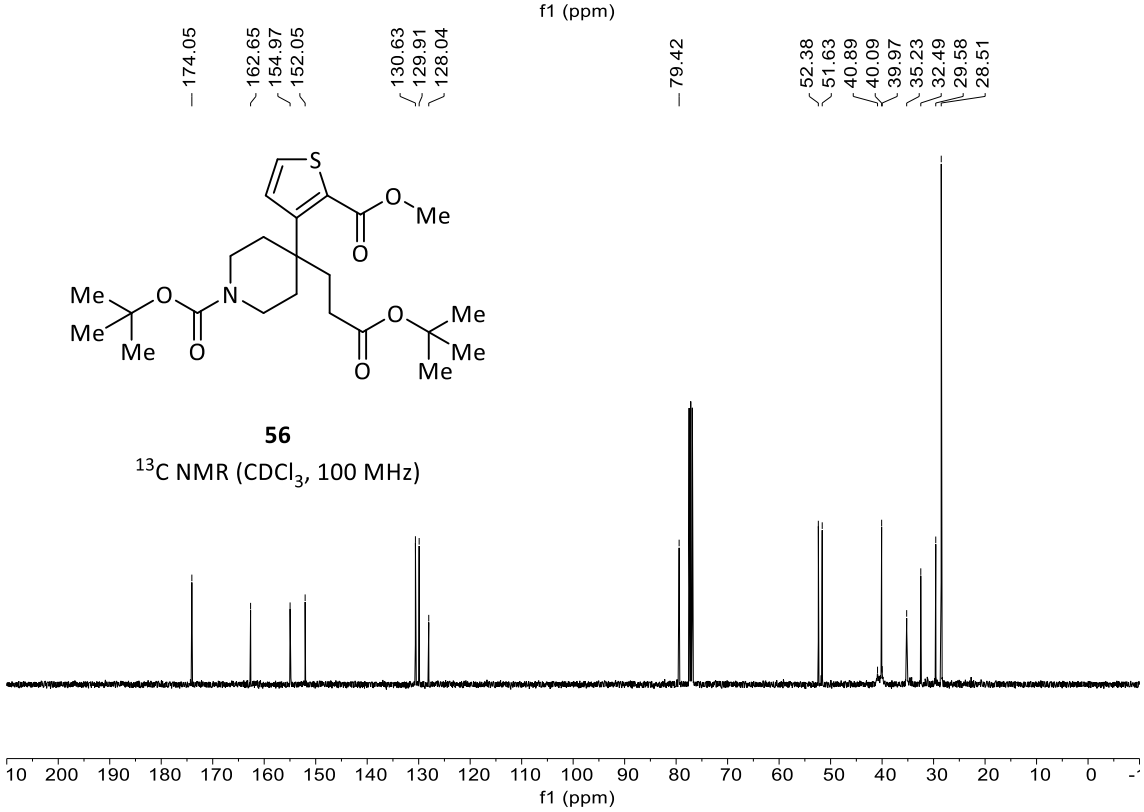

7.38 7.36 7.36 7.34 7.34 7.33 7.29 7.28 7.27 7.26 7.25 7.24 7.23 7.21 7.21 7.20
3.71 3.68 3.57 3.14 3.14 3.12 3.11 3.10 3.09 3.08 2.18 2.15 2.01 1.97 1.94 1.90 1.74 1.73 1.72 1.71 1.70 1.68 1.67 1.45
Me Me Me O N O O O Me Me Me
55
1H NMR (CDCl3, 400 MHz)
1.97 3.14 1.85 2.96 2.00 2.11 4.38 2.20 9.05
f1 (ppm)


174.15 155.07 143.52 128.77 126.91 126.38 79.46 51.65 40.72 39.90 39.58 37.91 28.83 28.56
Me Me Me O N O O O Me Me Me
55
13C NMR (CDCl3, 100 MHz)
f1 (ppm)



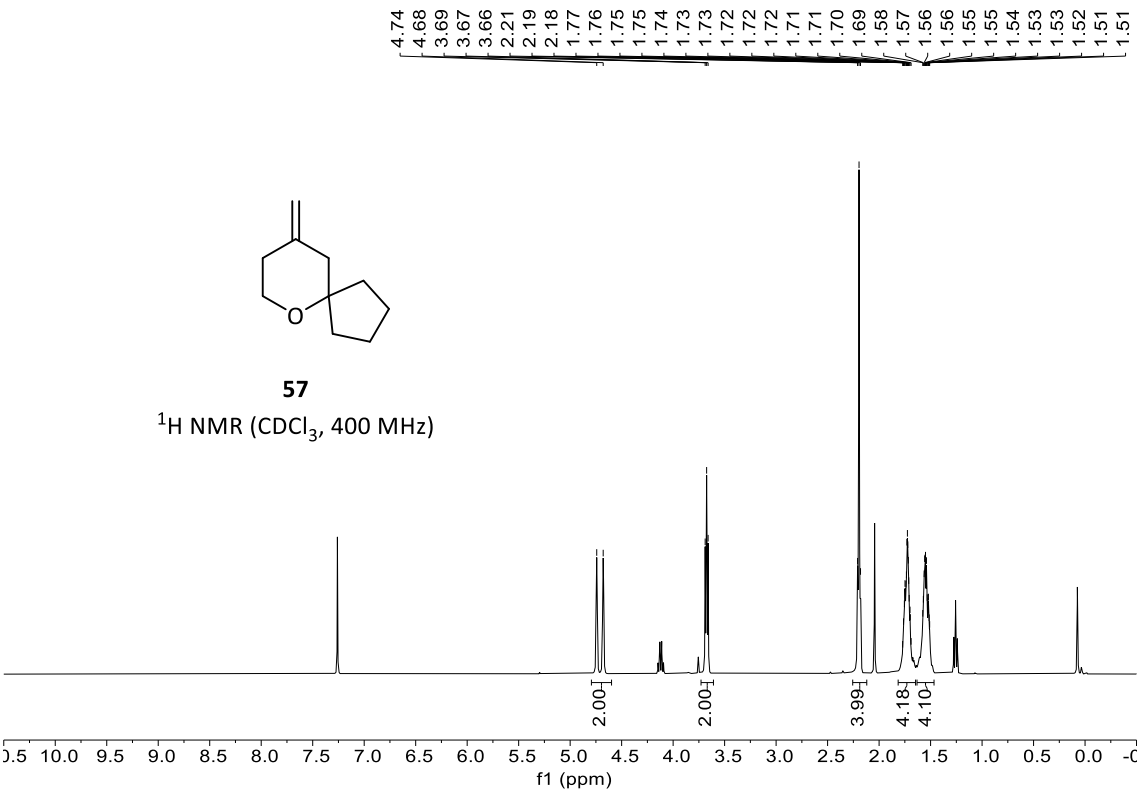

**56**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



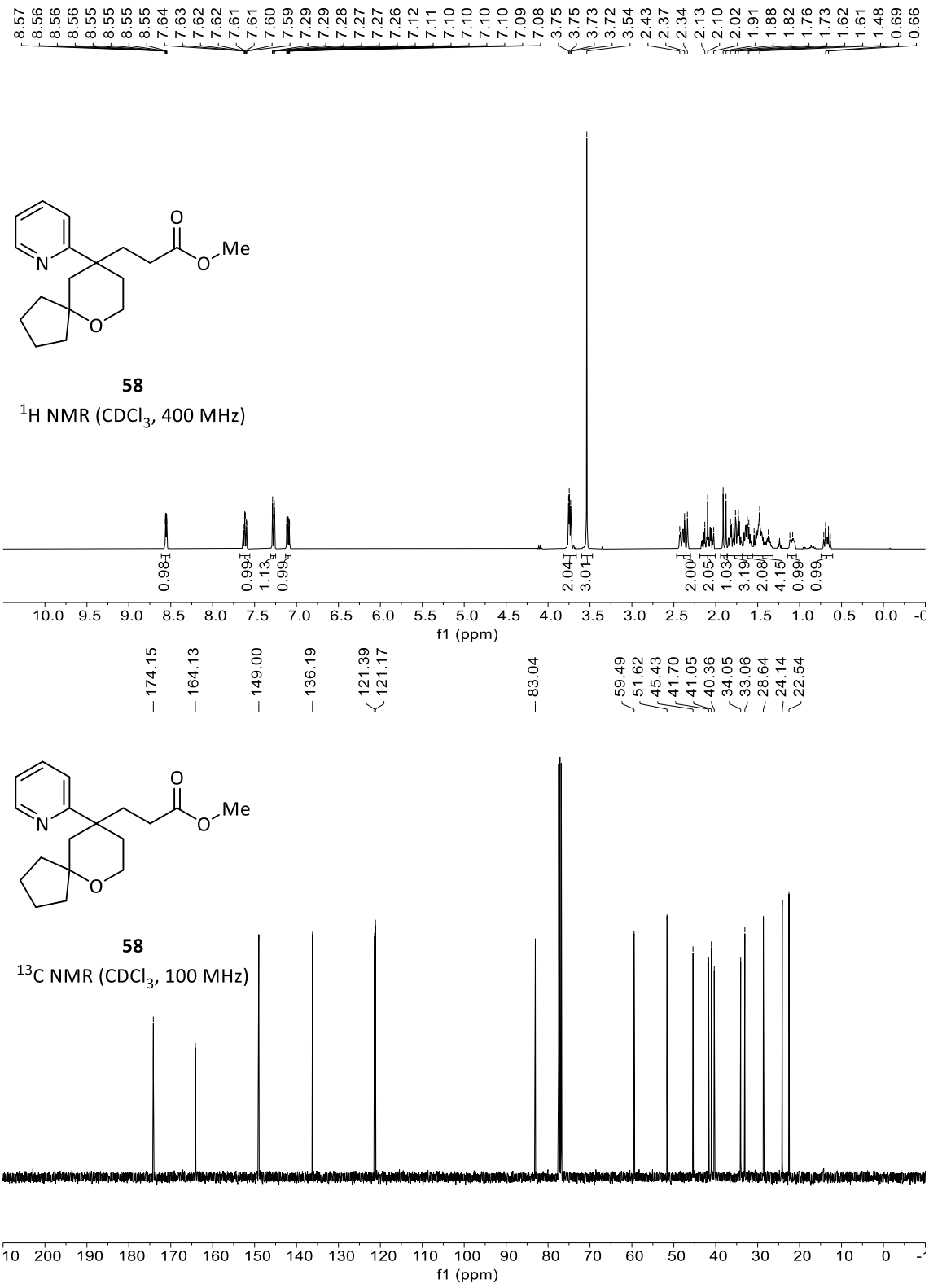

**56**

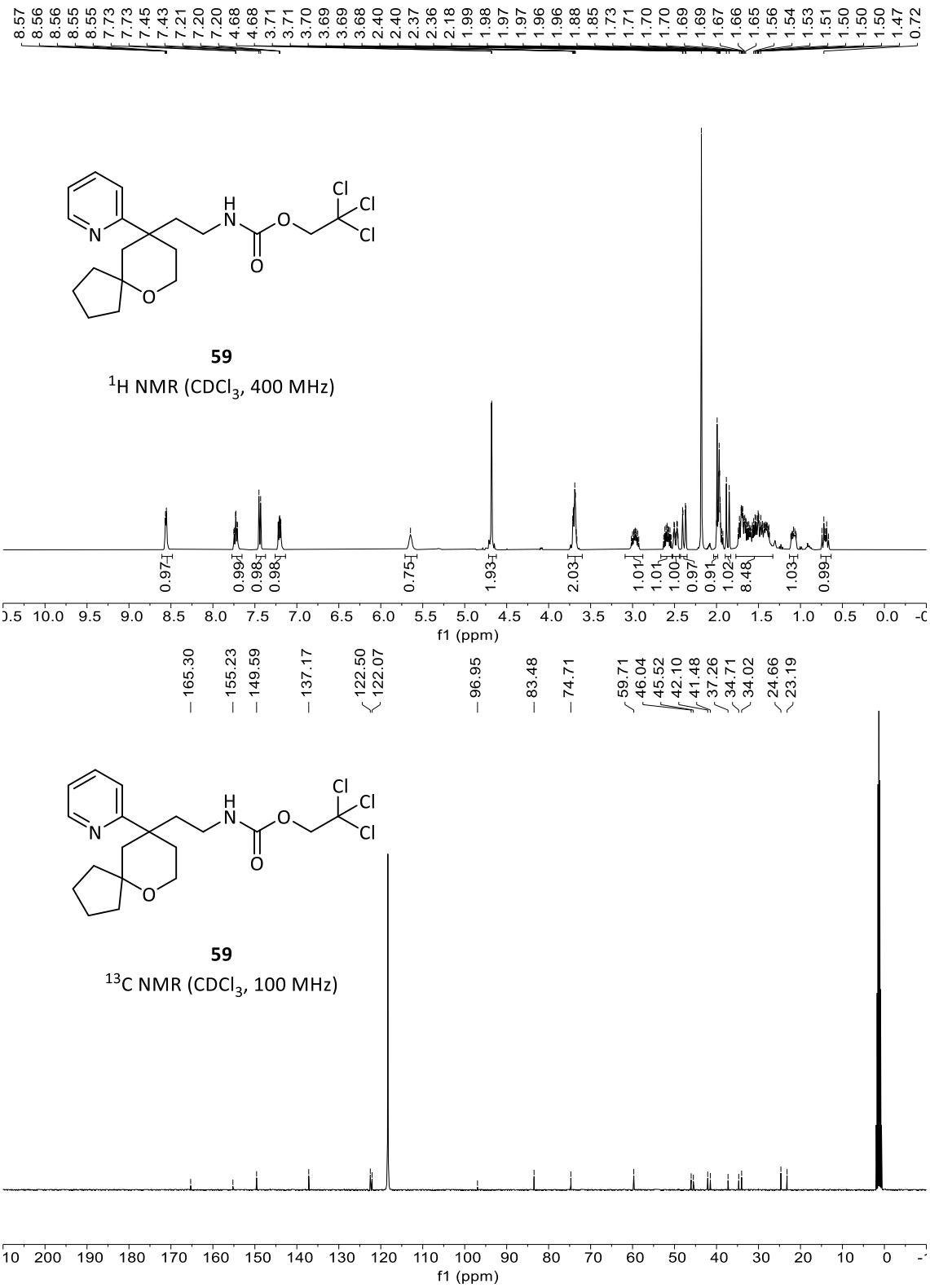
$^{13}$C NMR ($CDCl_3$, 100 MHz)

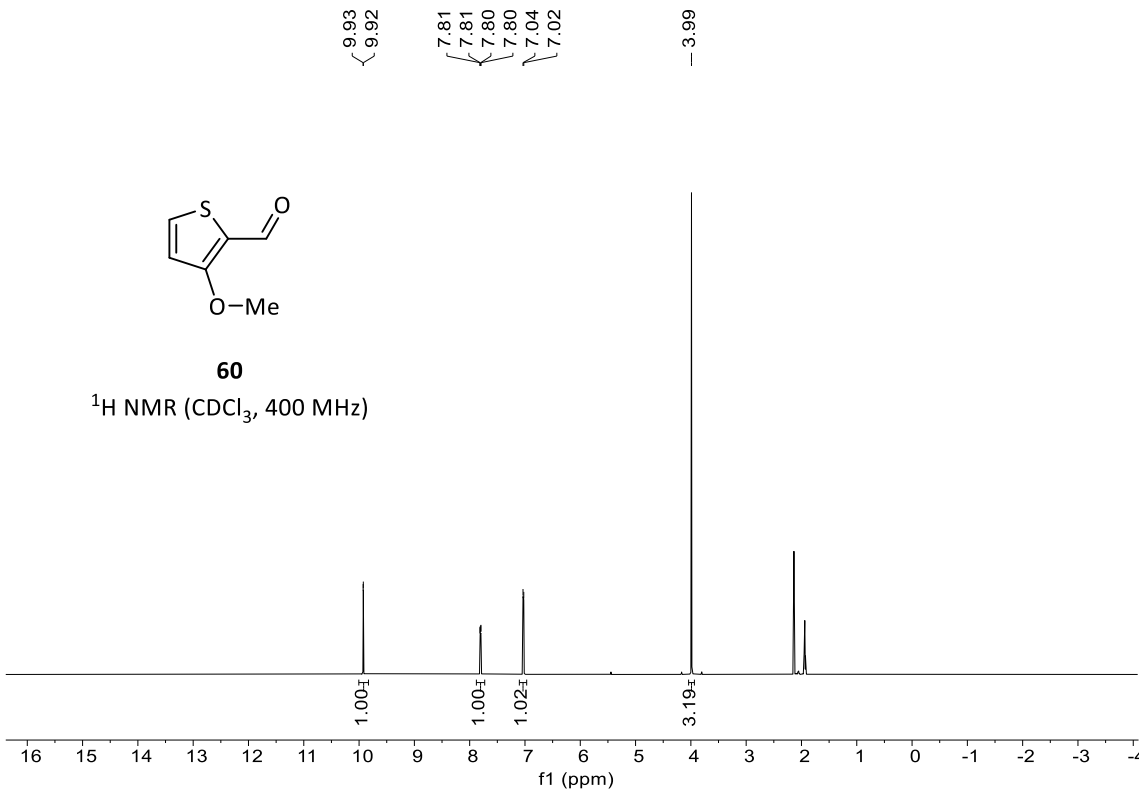



**57**

$^1$H NMR ($CDCl_3$, 400 MHz)

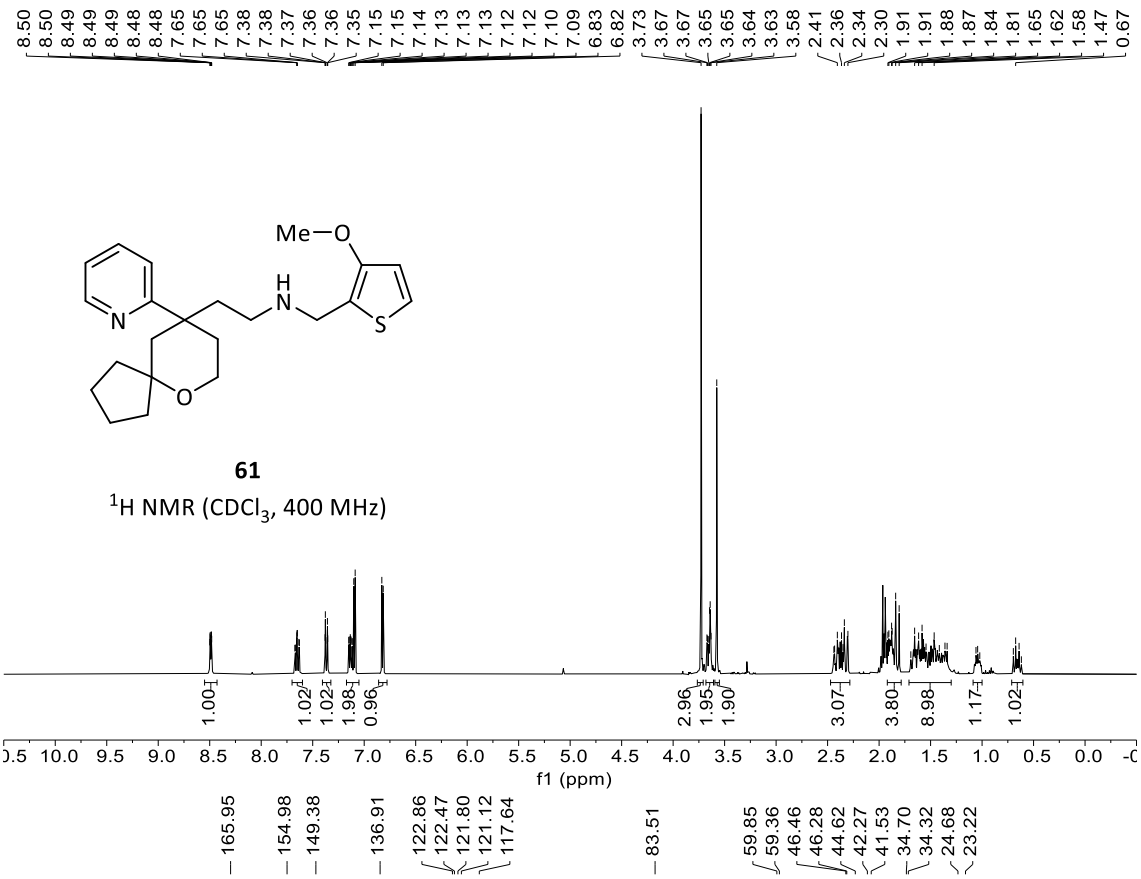

8.57 8.56 8.56 8.56 8.55 8.55 8.55 8.55 8.55 7.64 7.63 7.62 7.62 7.61 7.61 7.60 7.59 7.29 7.29 7.28 7.27 7.27 7.26 7.12 7.11 7.10 7.10 7.10 7.10 7.09 7.08 3.75 3.75 3.73 3.72 3.54 2.43 2.37 2.34 2.13 2.10 2.02 1.91 1.88 1.82 1.76 1.73 1.62 1.61 1.48 0.69 0.66
O
N
O
Me
O
58
1H NMR (CDCl3, 400 MHz)
0.98 0.99 1.13 0.99 2.04 3.01 2.00 2.05 1.03 3.19 2.08 4.15 0.99 0.99
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)
174.15 164.13 149.00 136.19 121.39 121.17 83.04 59.49 51.62 45.43 41.70 41.05 40.36 34.05 33.06 28.64 24.14 22.54
O
N
O
Me
O
58
13C NMR (CDCl3, 100 MHz)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.57 8.56 8.56 8.55 8.55 7.73 7.73 7.45 7.43 7.21 7.20 7.20 4.68 4.68 3.71 3.71 3.70 3.69 3.69 3.68 2.40 2.40 2.37 2.36 2.18 1.99 1.98 1.97 1.97 1.96 1.96 1.88 1.85 1.73 1.71 1.70 1.70 1.69 1.69 1.67 1.66 1.65 1.56 1.54 1.53 1.51 1.50 1.50 1.50 1.47 0.72
59
1H NMR (CDCl3, 400 MHz)
0.97 0.99 0.98 0.98 0.75 1.93 2.03 1.01 1.01 1.00 0.97 0.91 1.02 8.48 1.03 0.99
f1 (ppm)
165.30 155.23 149.59 137.17 122.50 122.07 96.95 83.48 74.71 59.71 46.04 45.52 42.10 41.48 37.26 34.71 34.02 24.66 23.19
59
13C NMR (CDCl3, 100 MHz)
f1 (ppm)



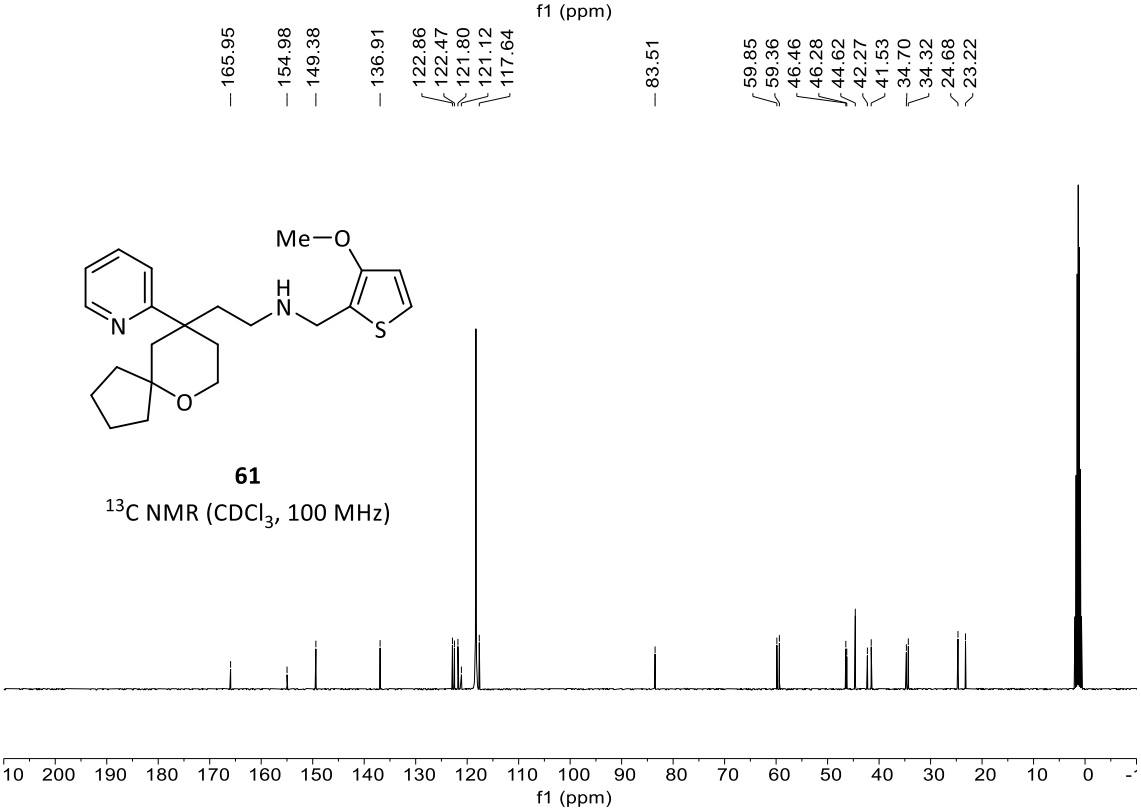

**60**

$^1$H NMR ($CDCl_3$, 400 MHz)



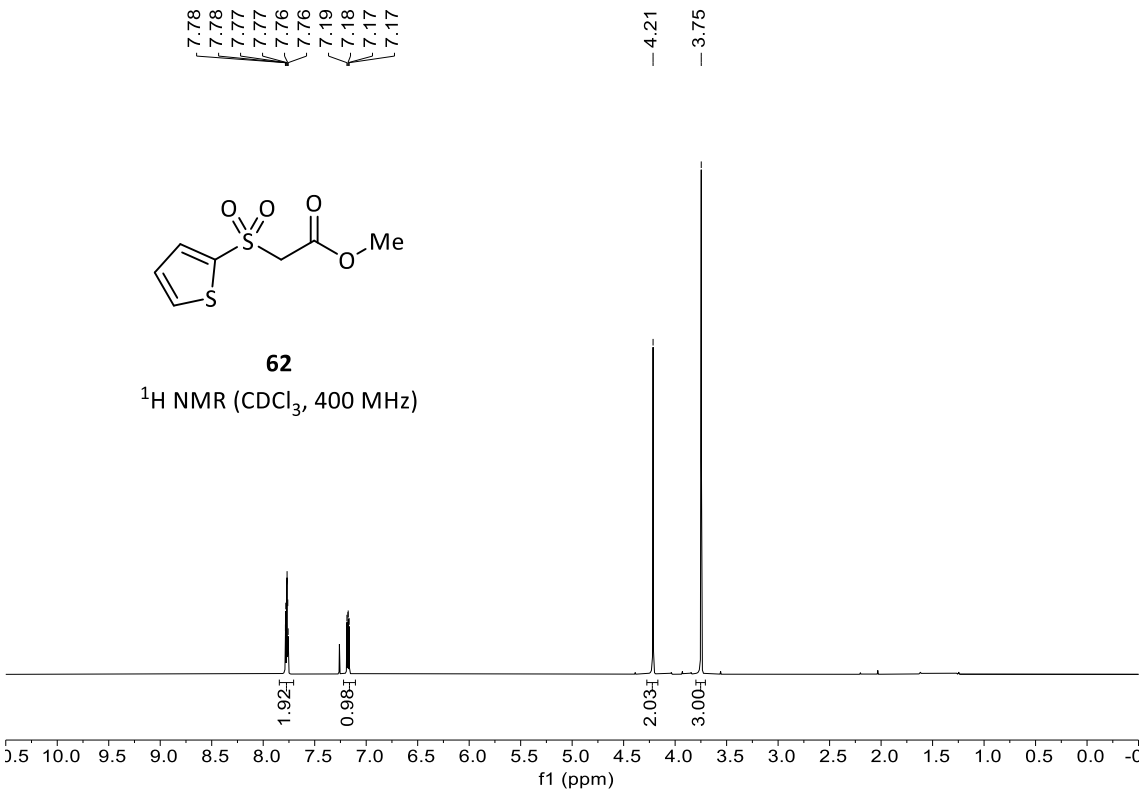

**61**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



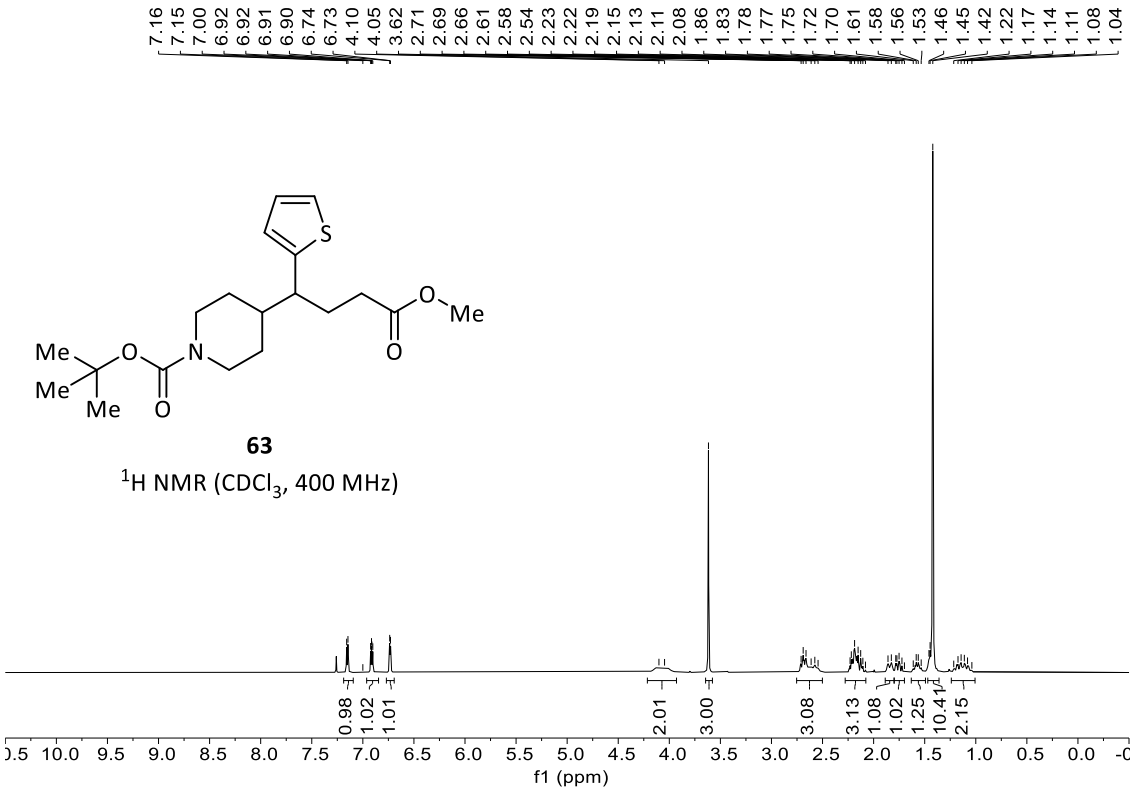

**61**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



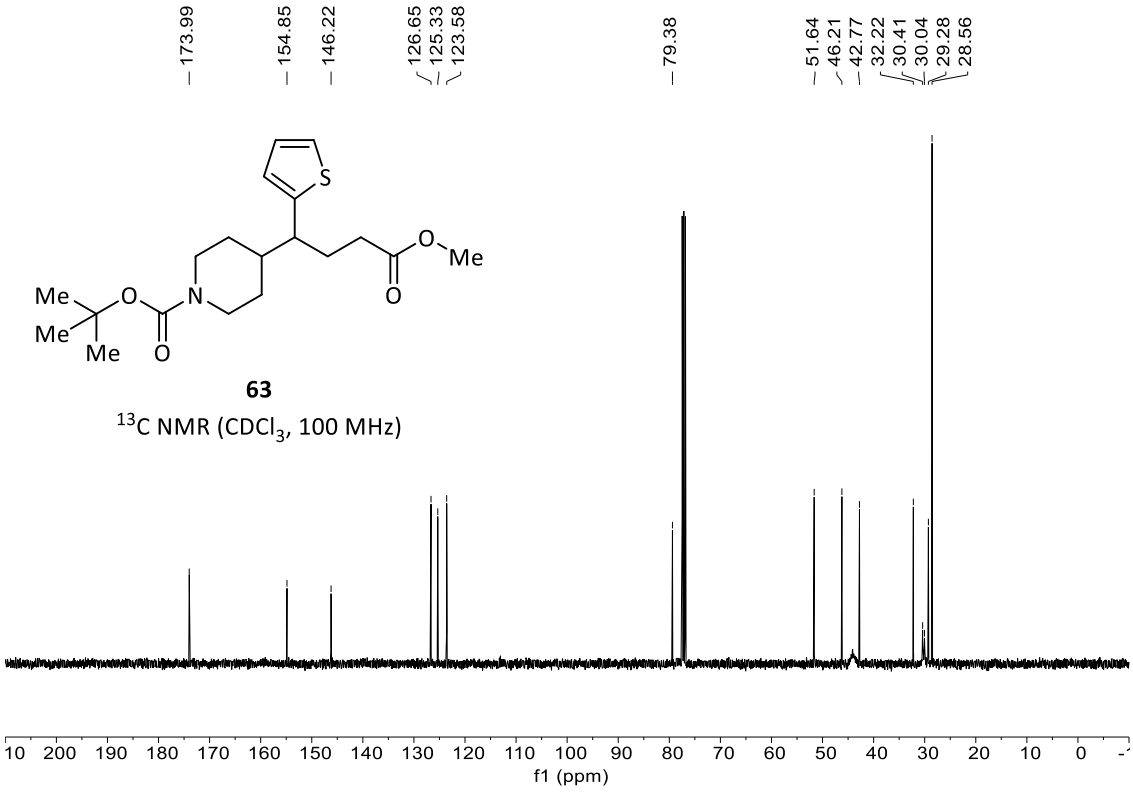

**62**

$^1$H NMR ($CDCl_3$, 400 MHz)



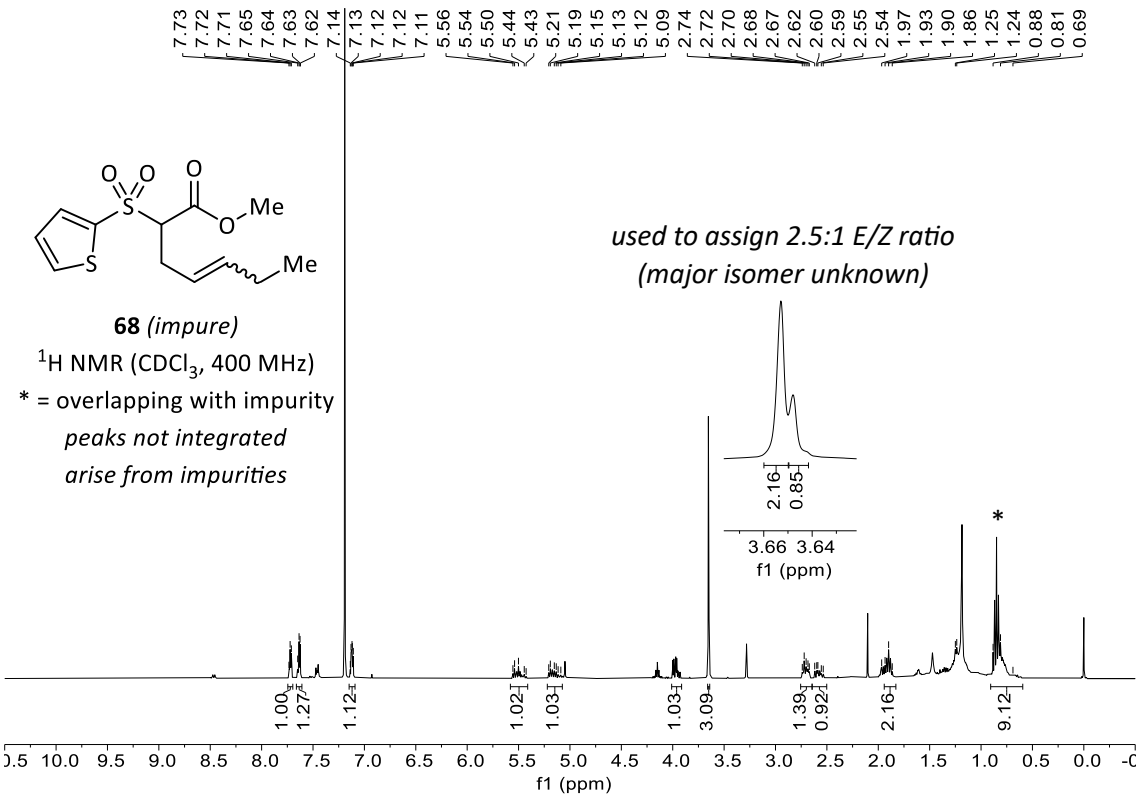

**63**

$^{1}$H NMR ($CDCl_3$, 400 MHz)




**63**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



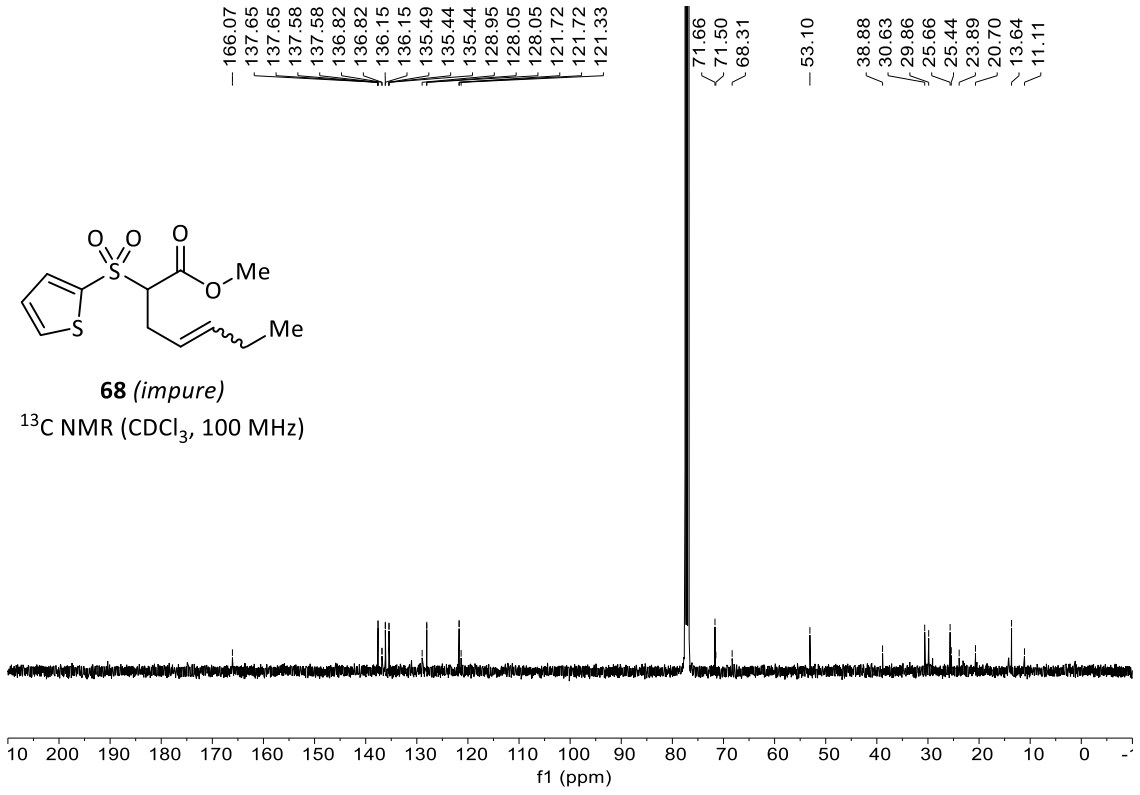

**68** *(impure)*

$^{1}$H NMR ($CDCl_3$, 400 MHz)

* = overlapping with impurity

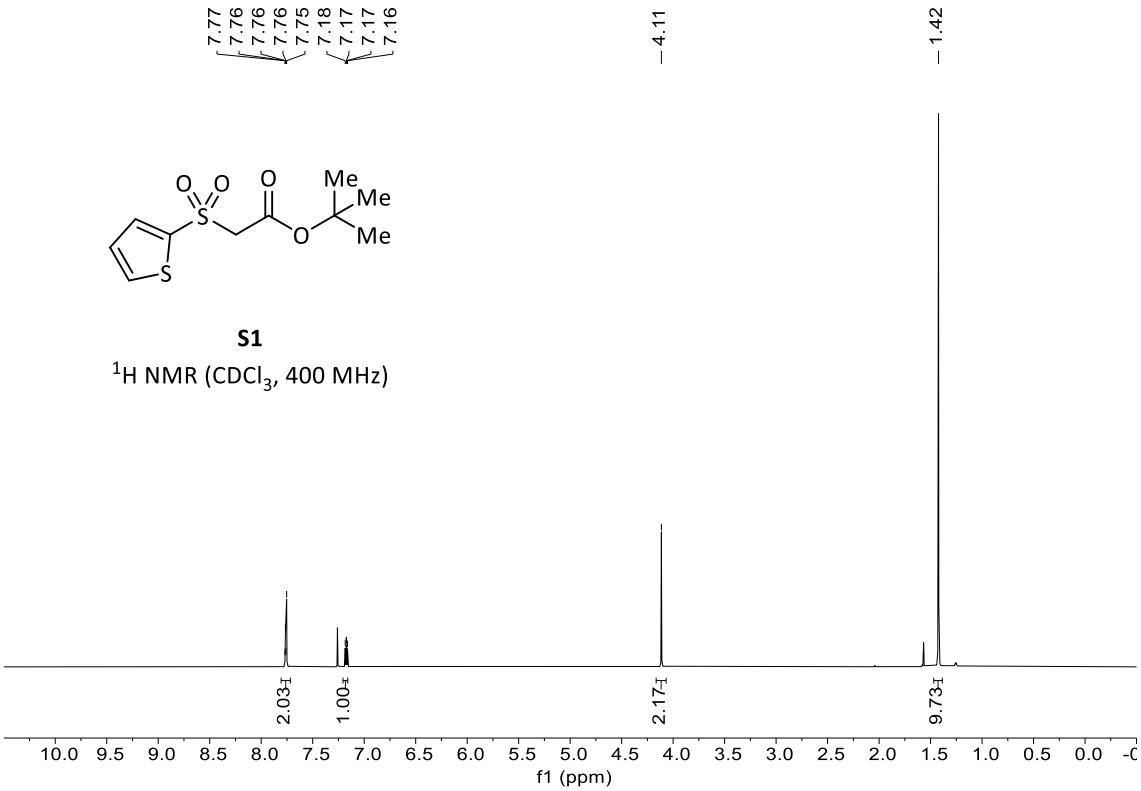
*peaks not integrated*

*arise from impurities*



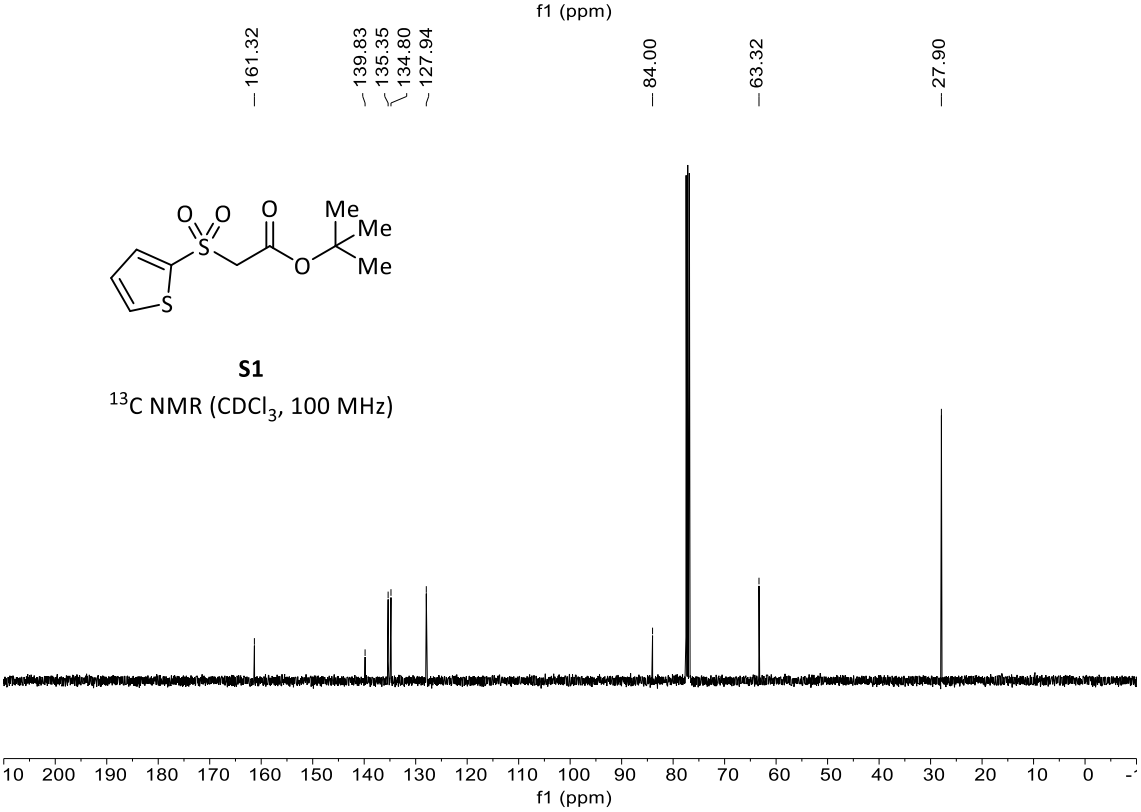

**68** *(impure)*

$^{13}$C NMR ($CDCl_3$, 100 MHz)



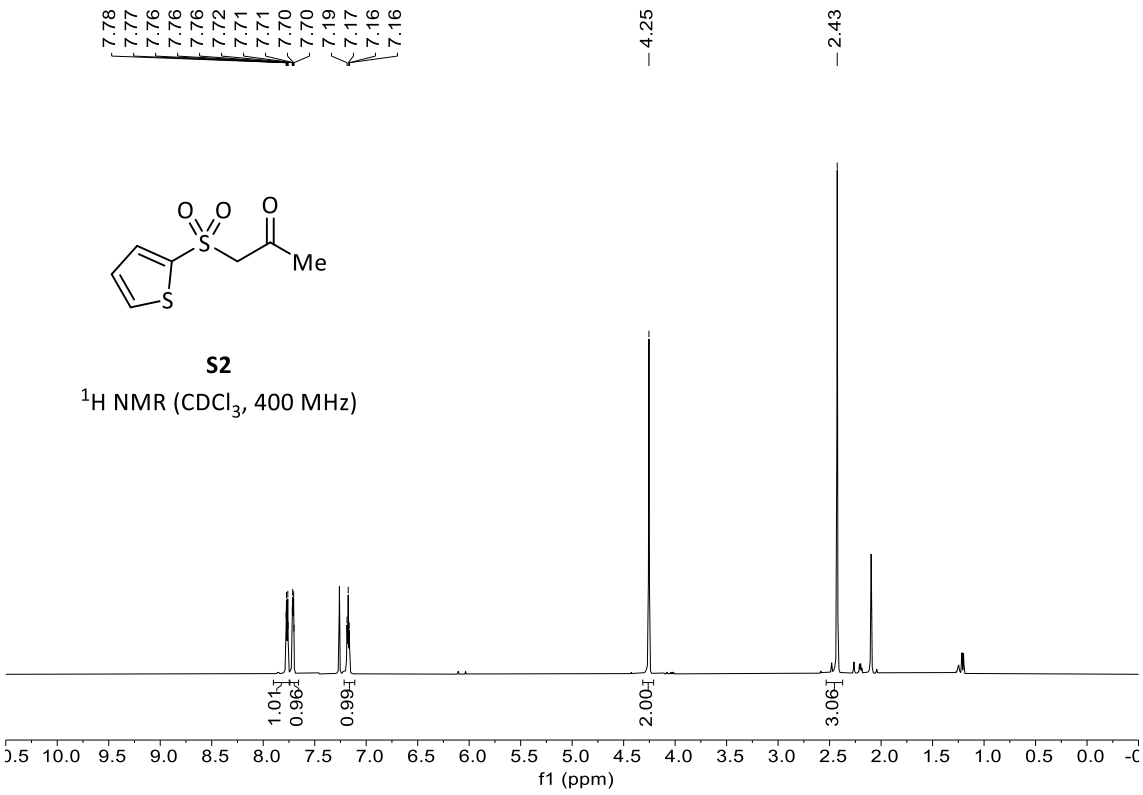

**S1**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



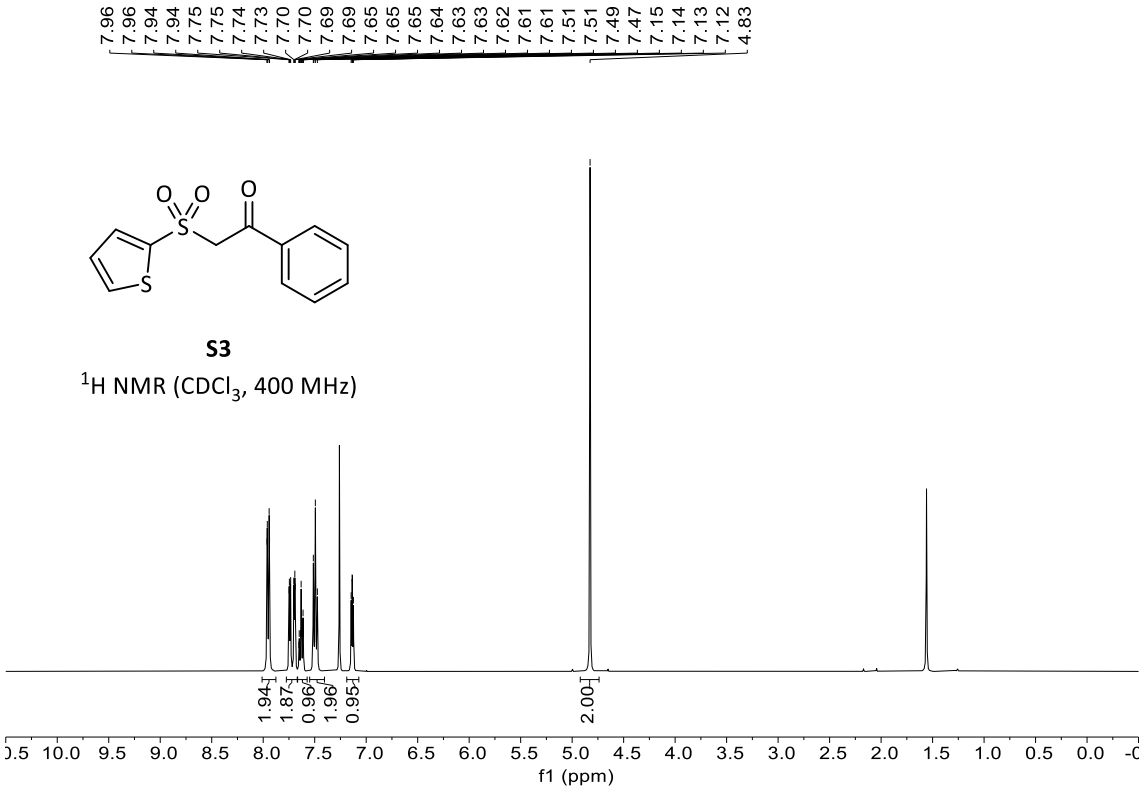

**S1**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



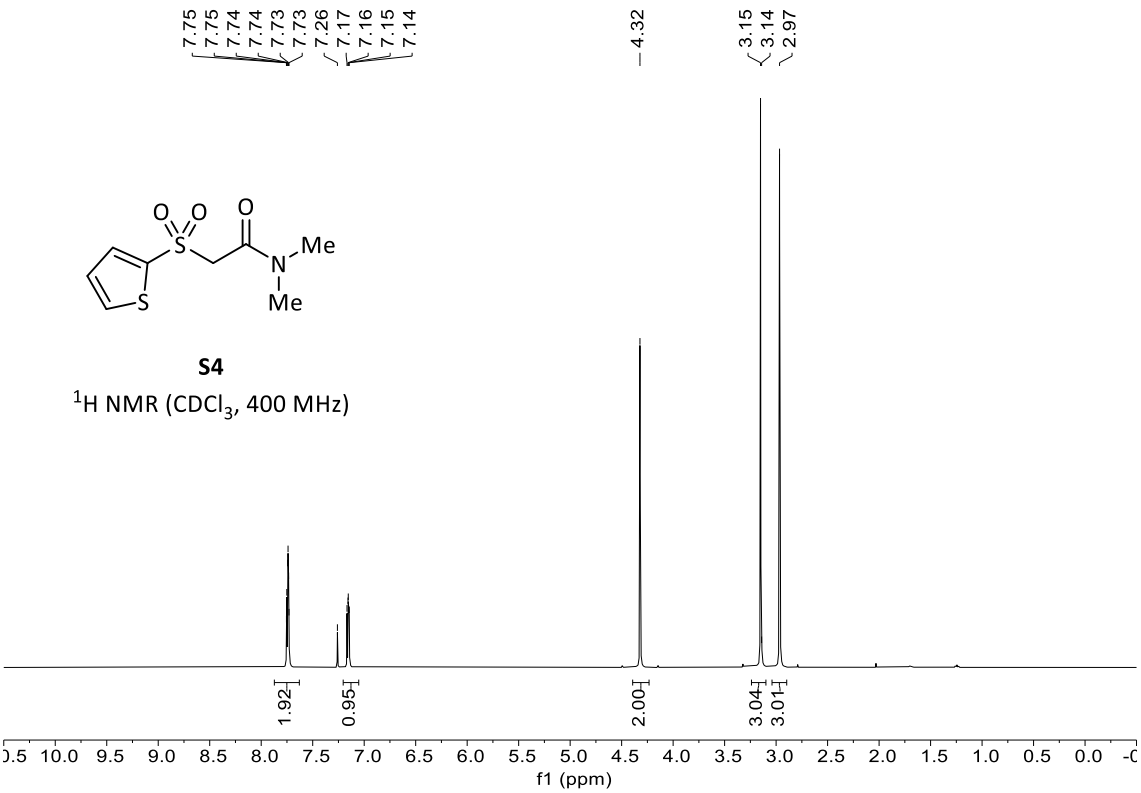

**S2**

$^1$H NMR ($CDCl_3$, 400 MHz)



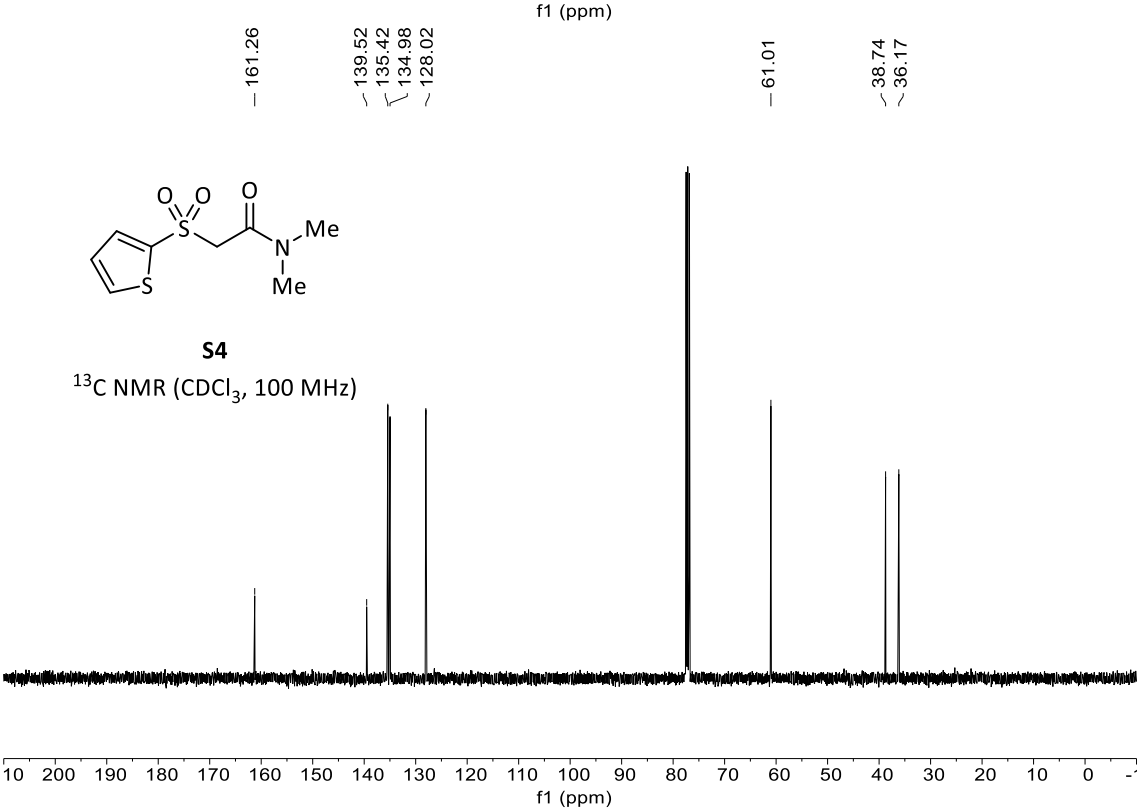

**S3**

$^1$H NMR ($CDCl_3$, 400 MHz)



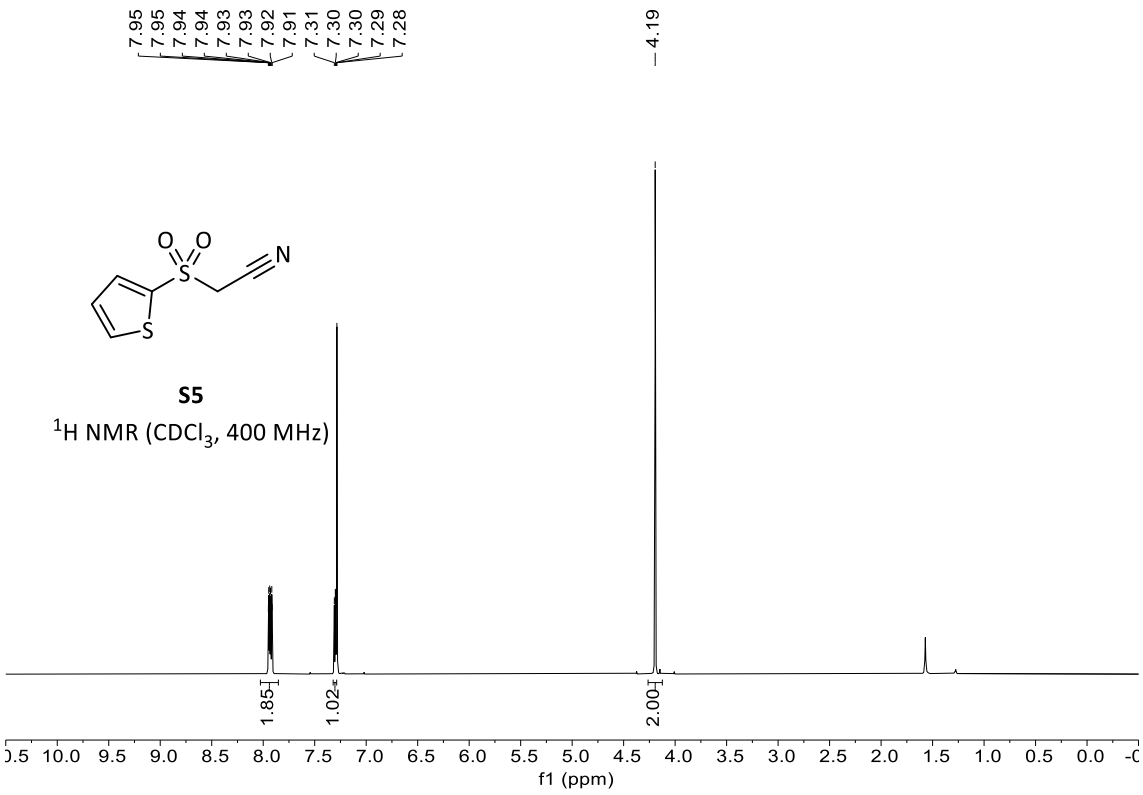

**S4**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



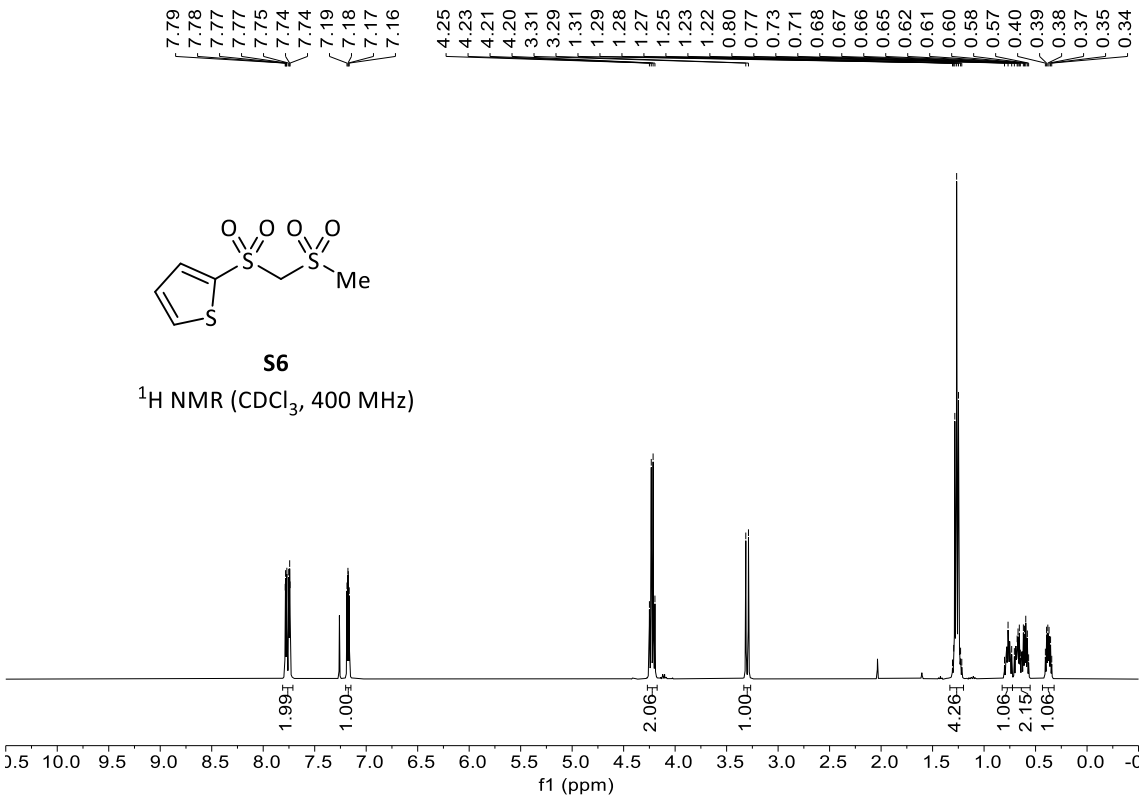

**S4**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



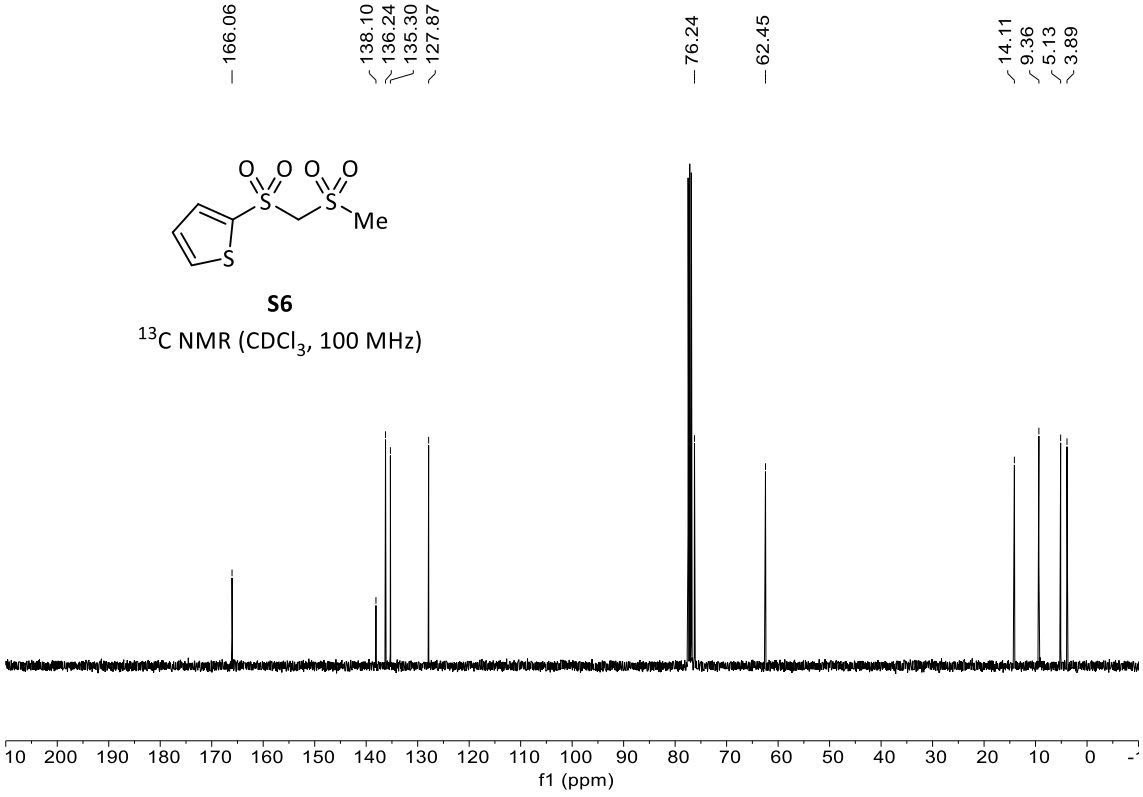

**S5**

$^1$H NMR ($CDCl_3$, 400 MHz)



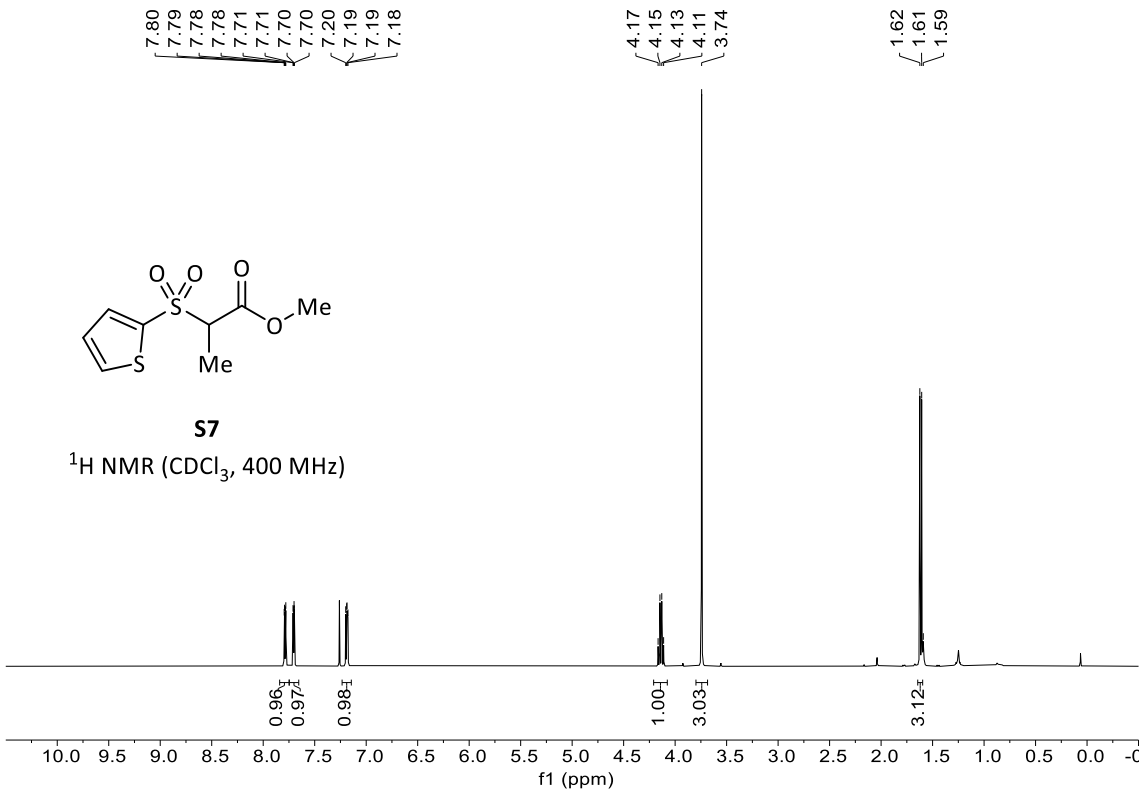

**S6**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



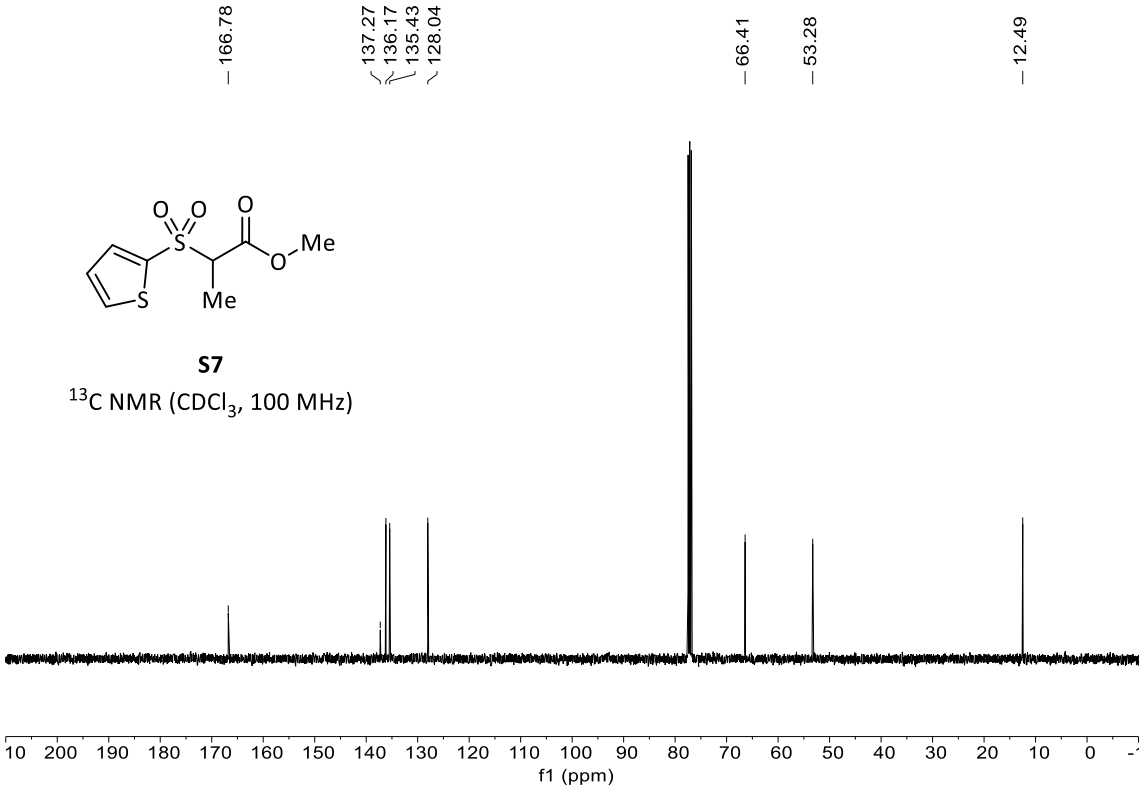

**S6**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



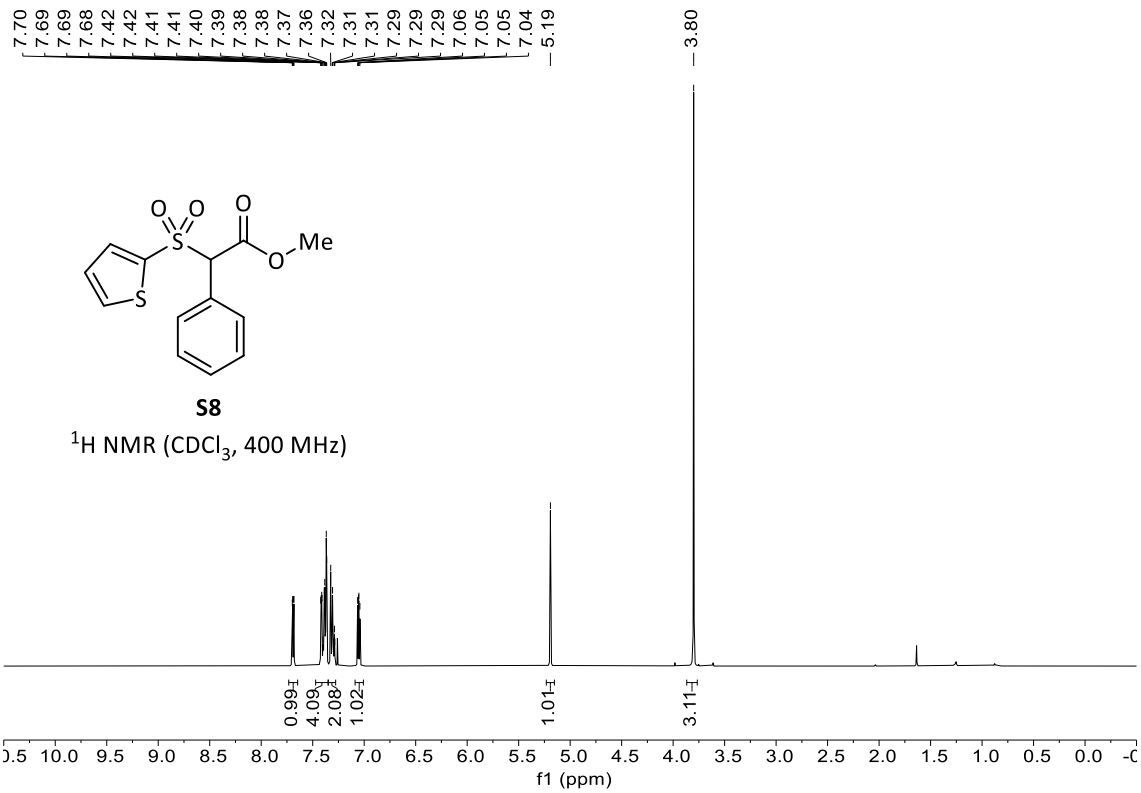

**S7**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



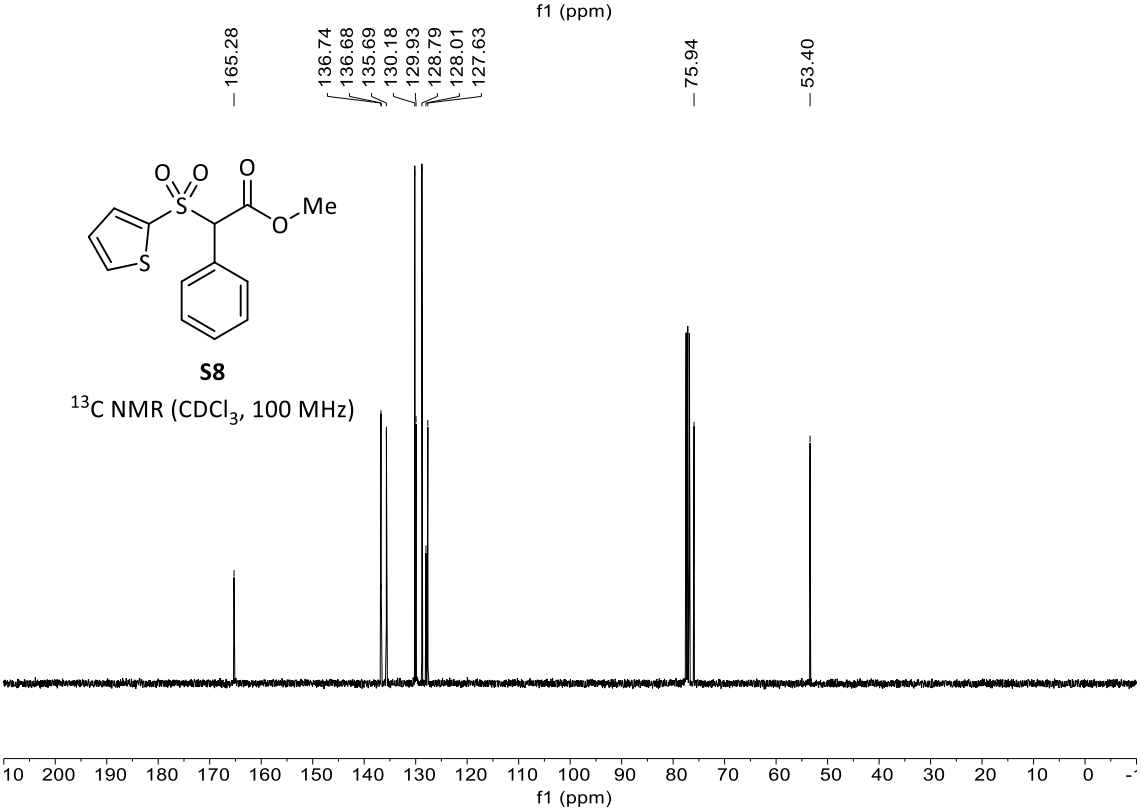

**S7**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



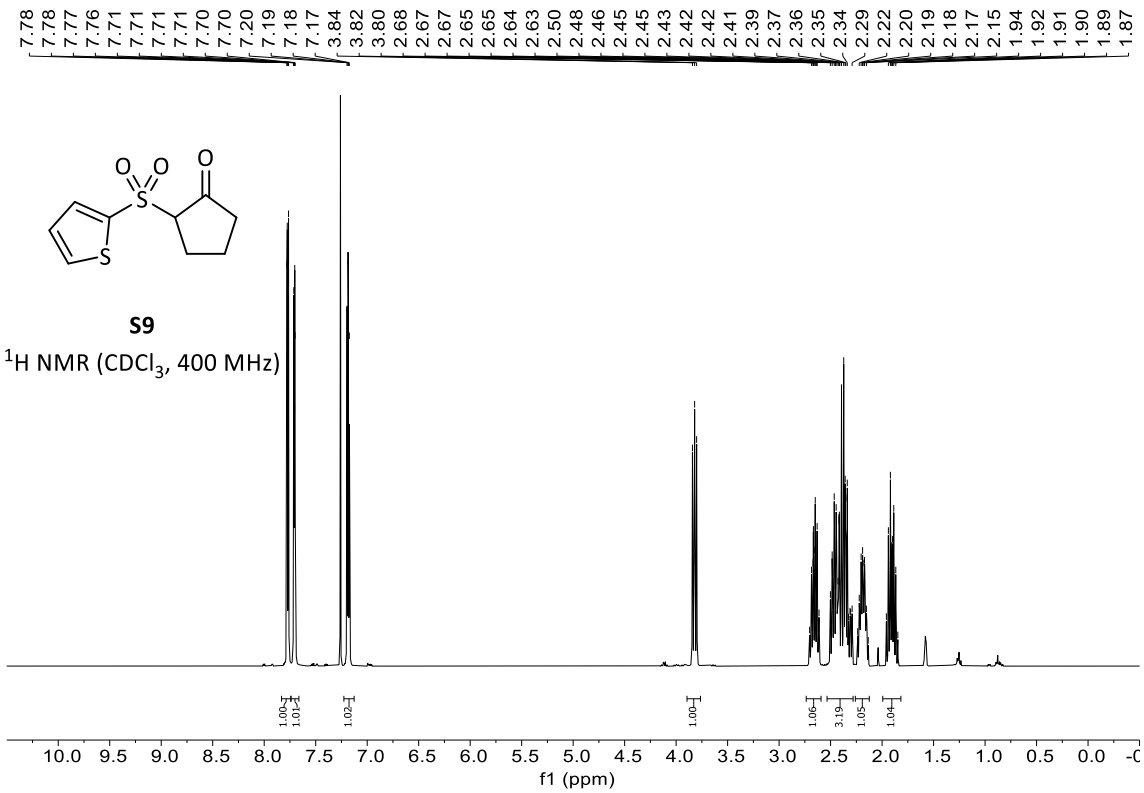

**S8**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



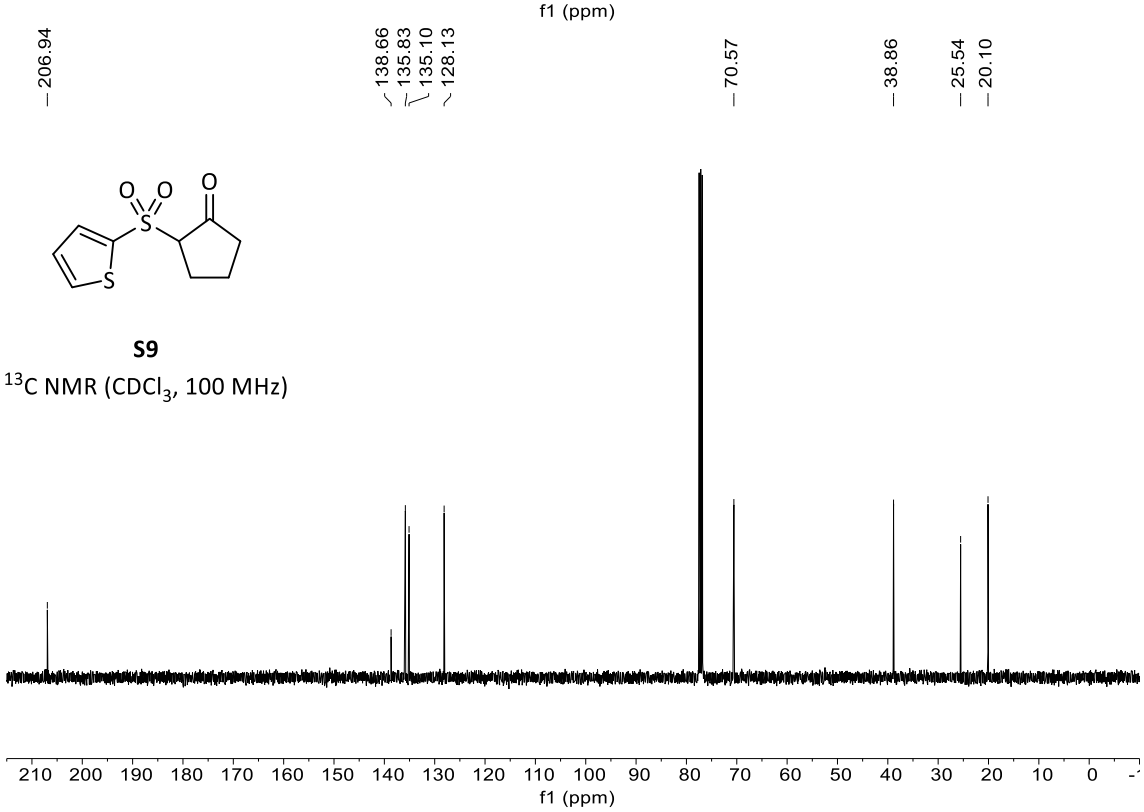

**S8**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



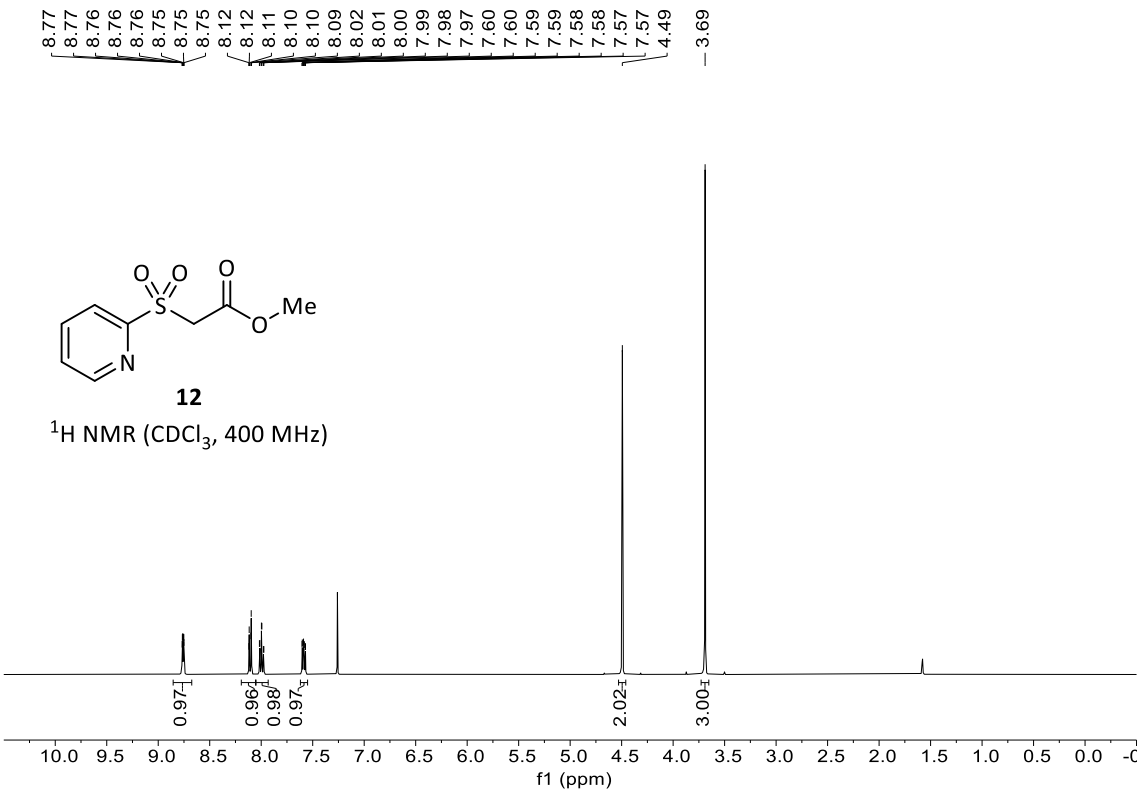

**S9**

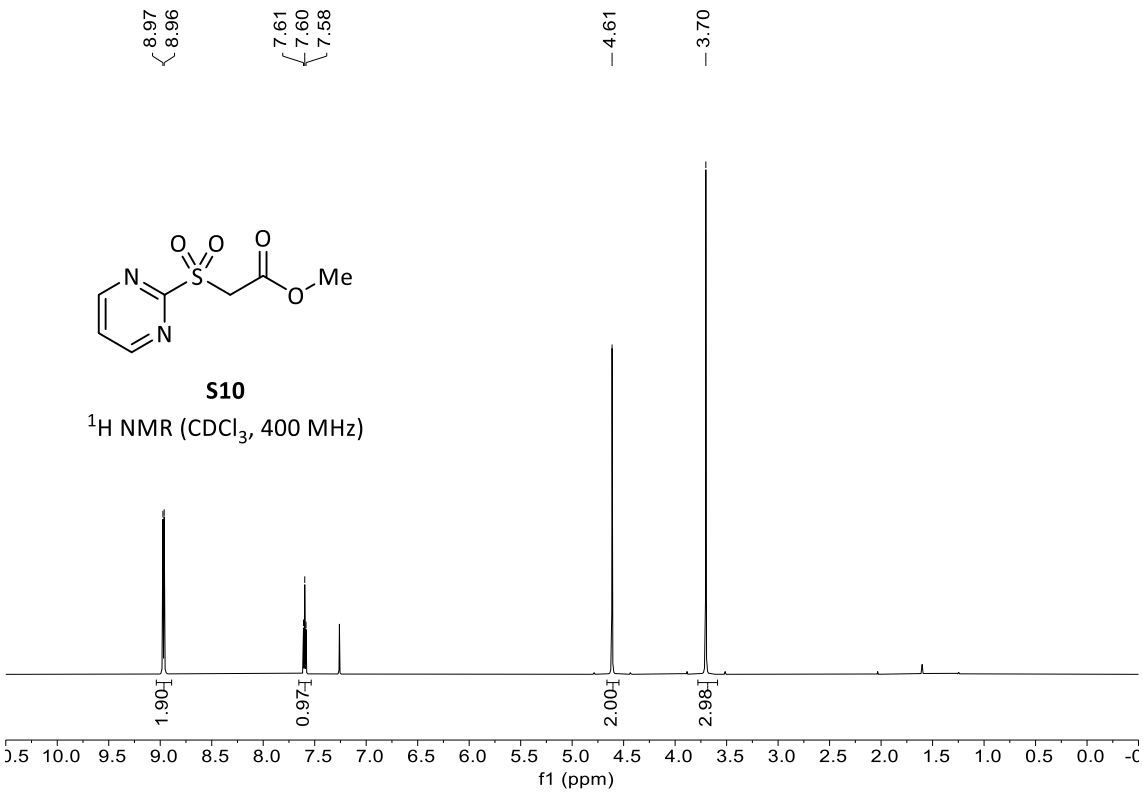
$^{1}$H NMR ($CDCl_3$, 400 MHz)




**S9**

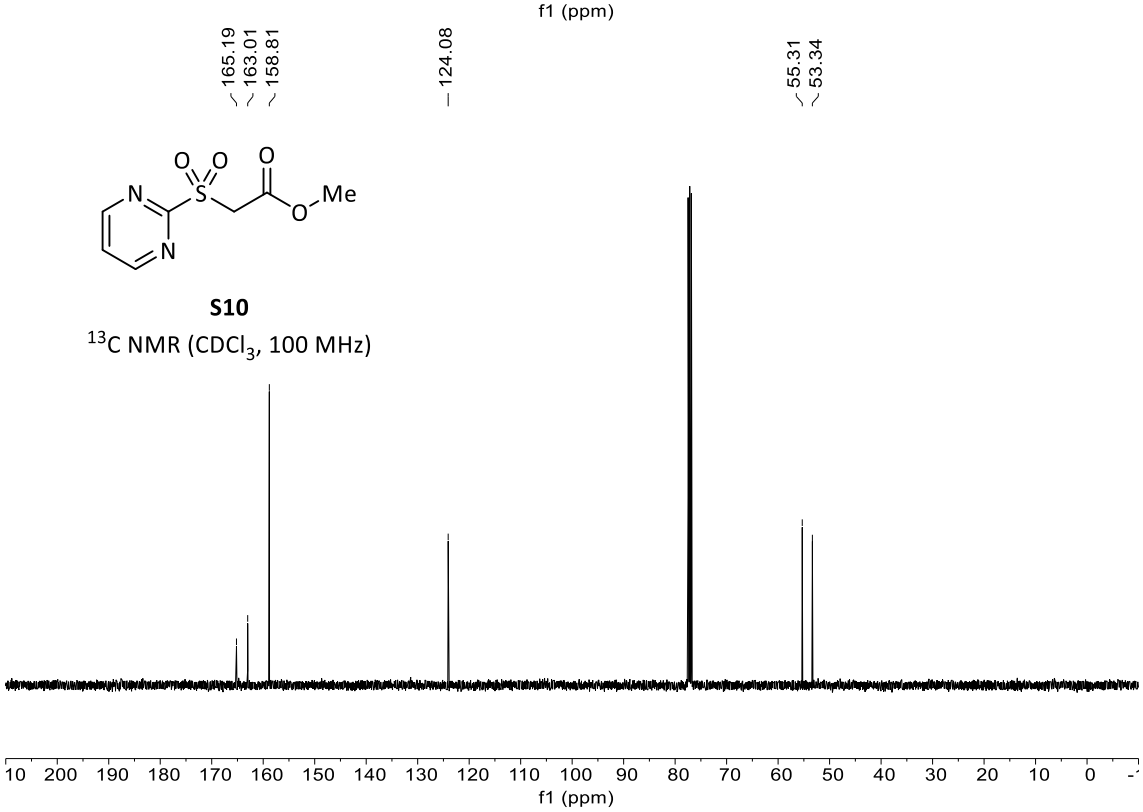
$^{13}$C NMR ($CDCl_3$, 100 MHz)


8.77
8.77
8.76
8.76
8.76
8.75
8.75
8.12
8.12
8.11
8.10
8.10
8.09
8.02
8.01
8.00
7.99
7.98
7.97
7.60
7.59
7.59
7.58
7.58
7.57
7.57
4.49
3.69
O
O
O
S
O
Me
N
12
1H NMR (CDCl3, 400 MHz)
0.97
0.96
0.98
0.97
2.02
3.00
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)



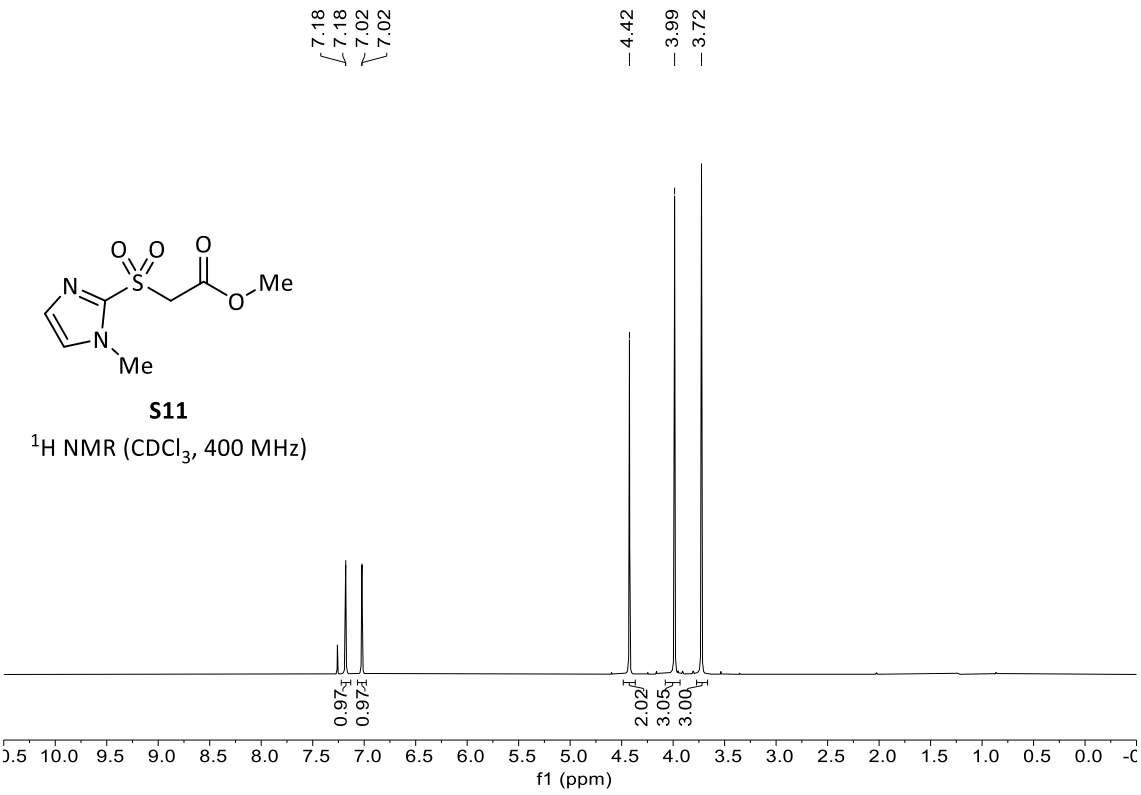

**S10**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



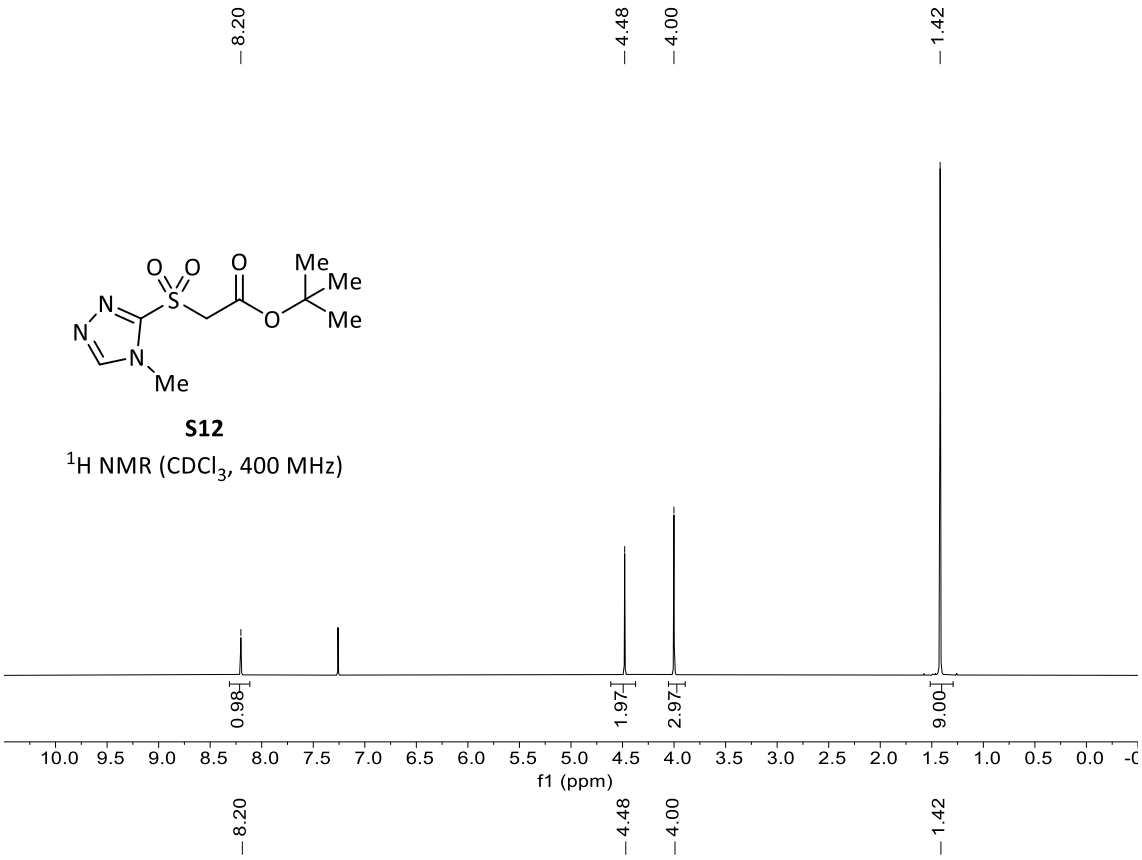

**S10**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



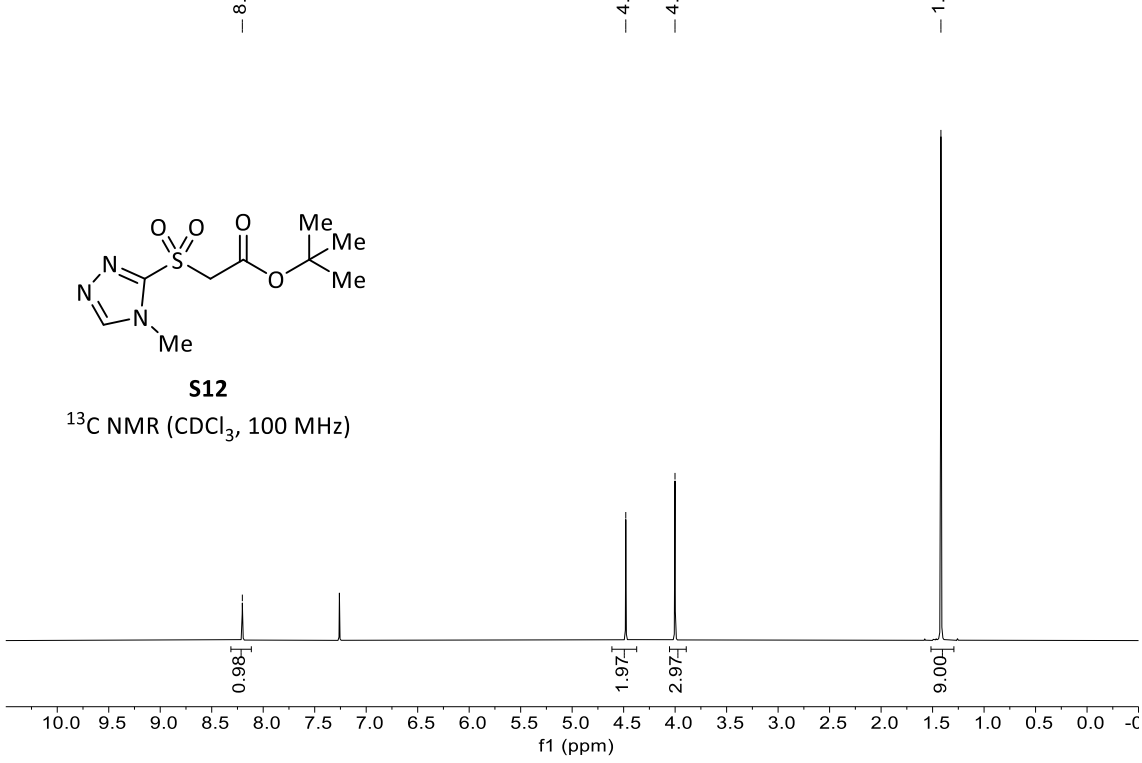

**S11**

$^1$H NMR ($CDCl_3$, 400 MHz)



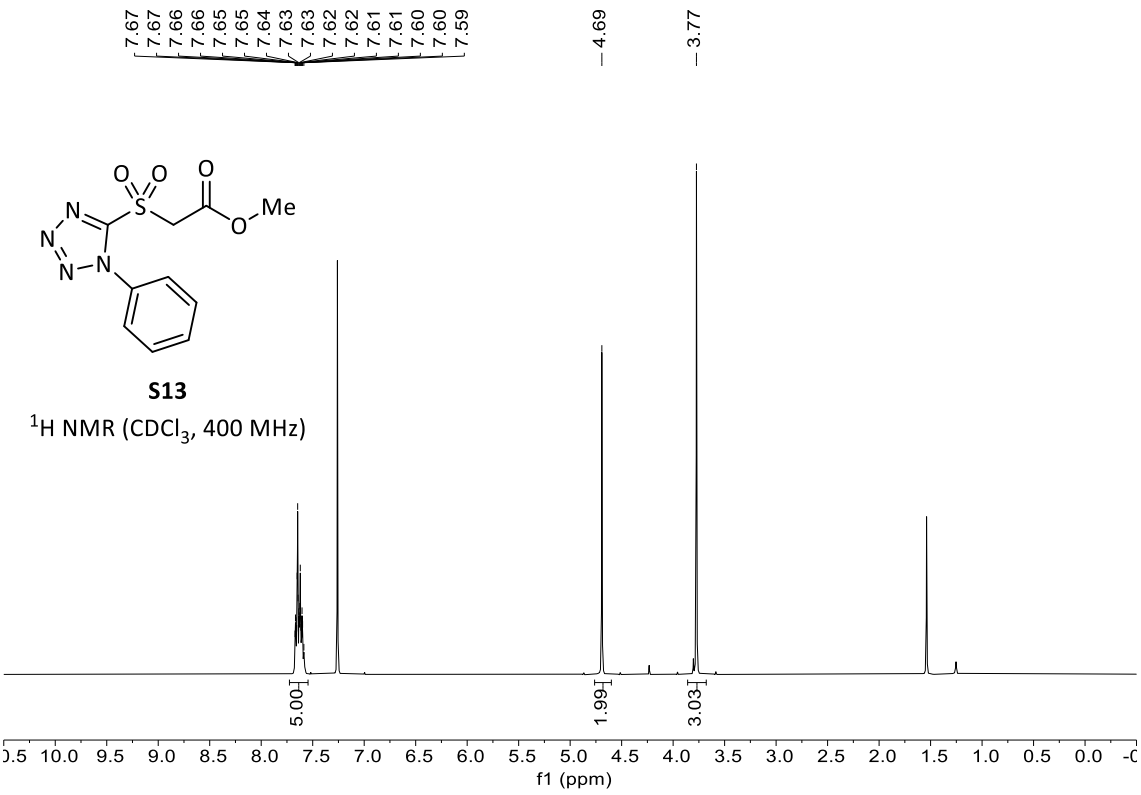

**S12**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



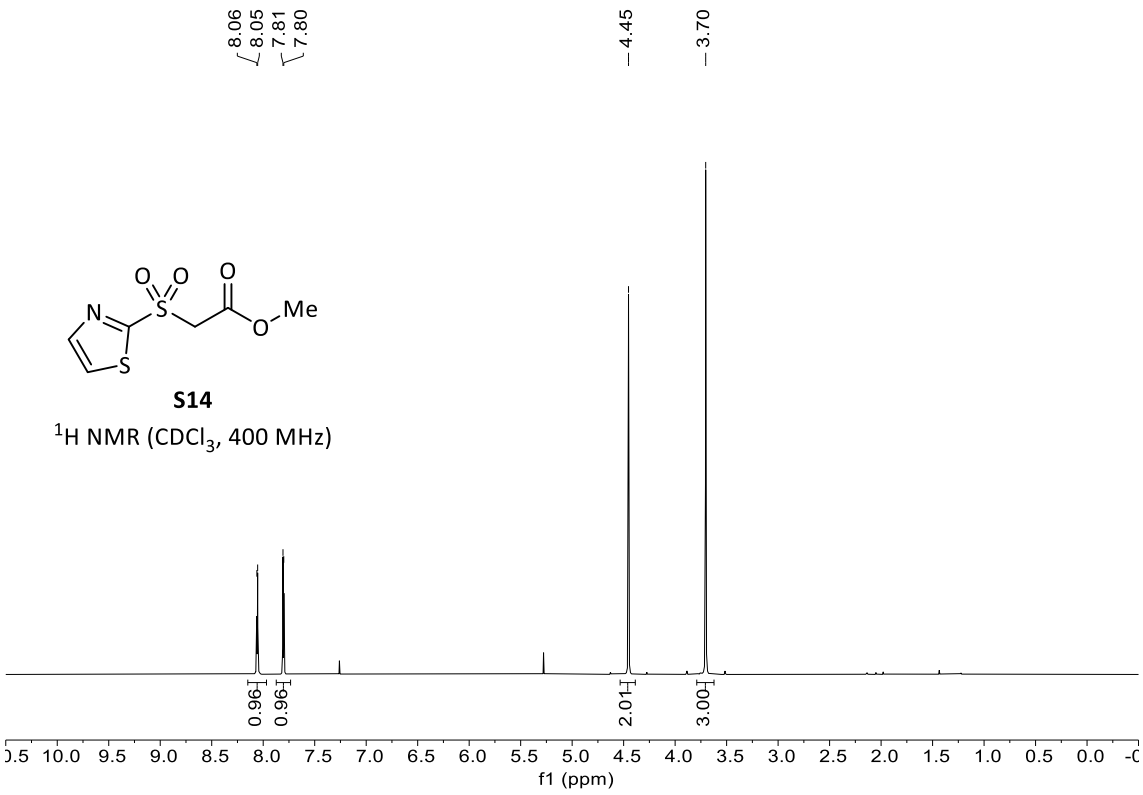

**S12**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



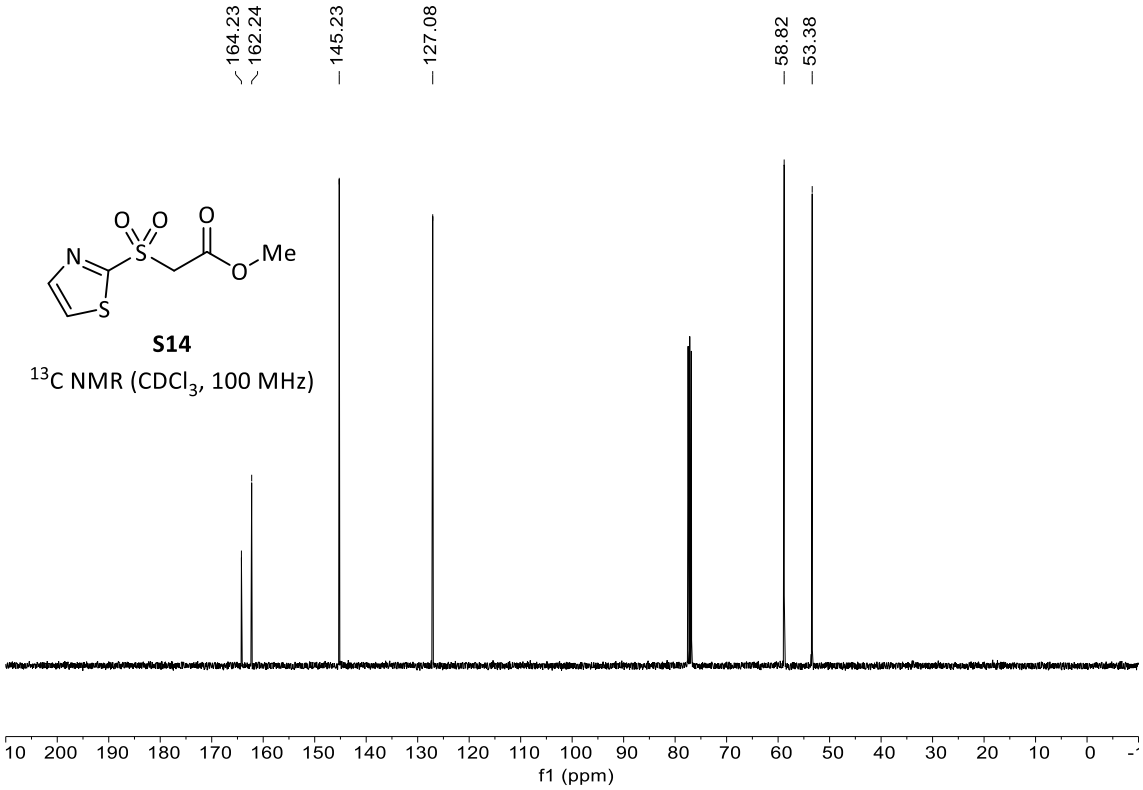

**S13**

$^1$H NMR ($CDCl_3$, 400 MHz)



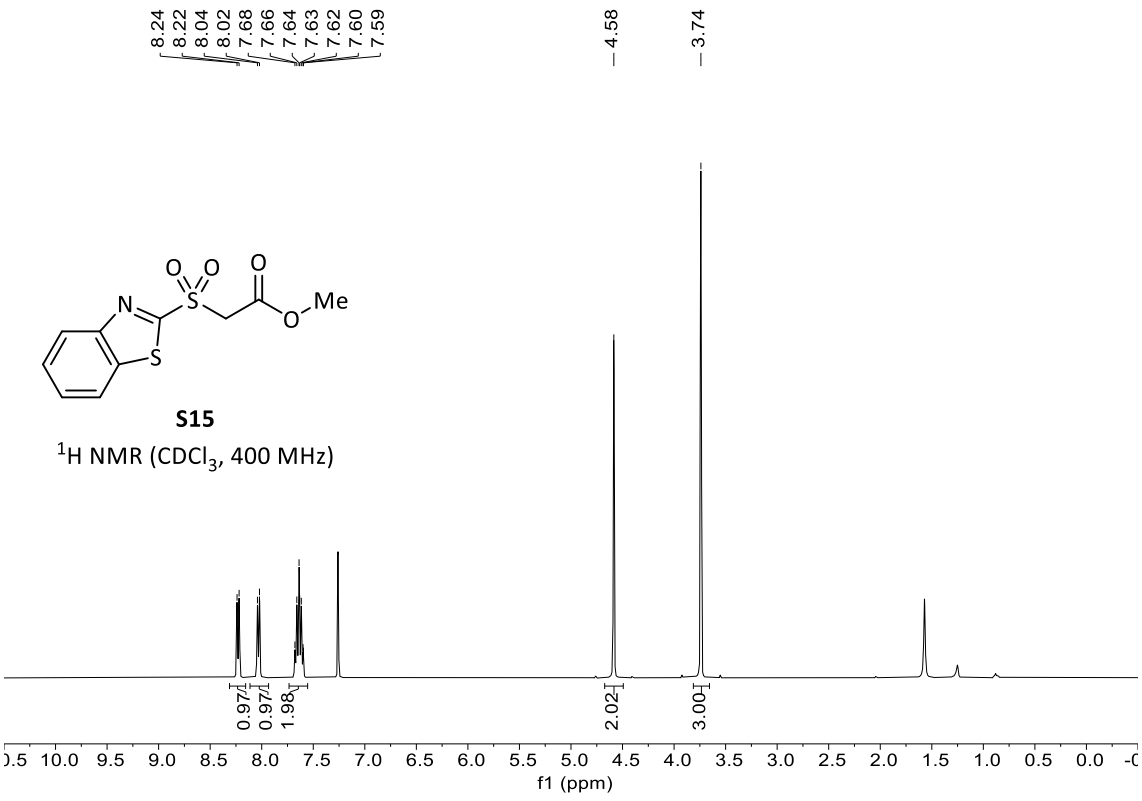

**S14**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



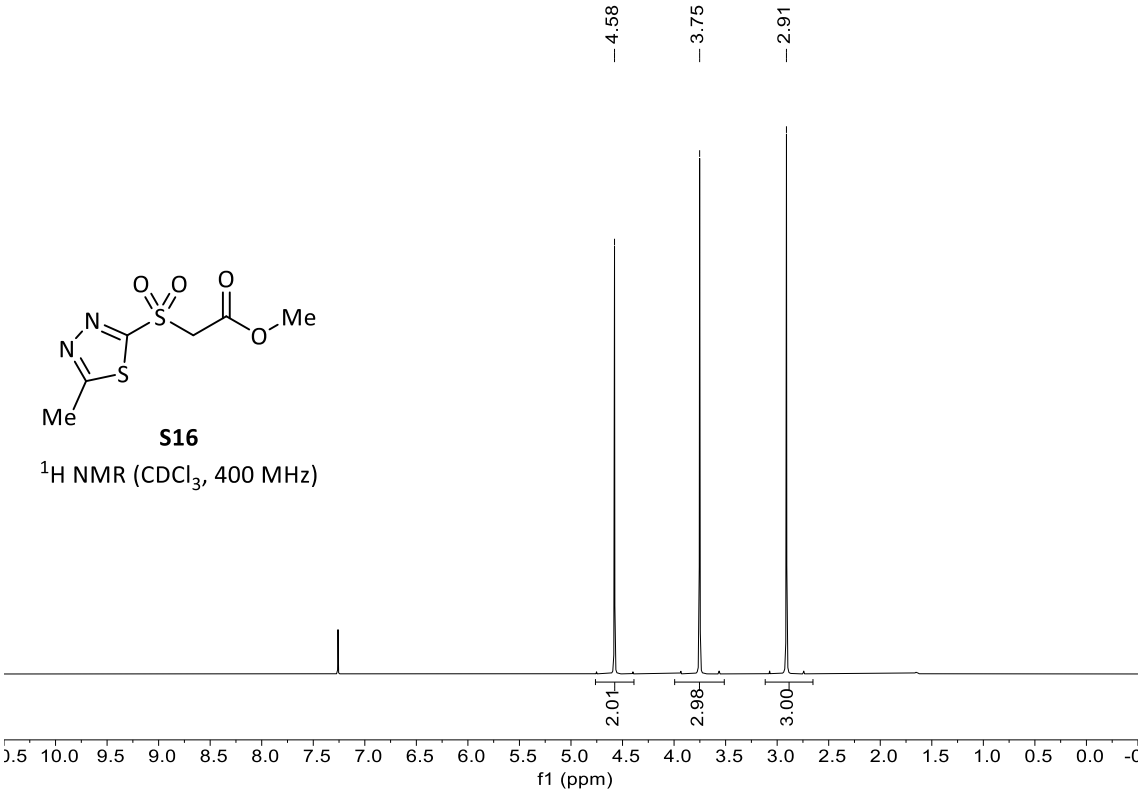

**S14**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



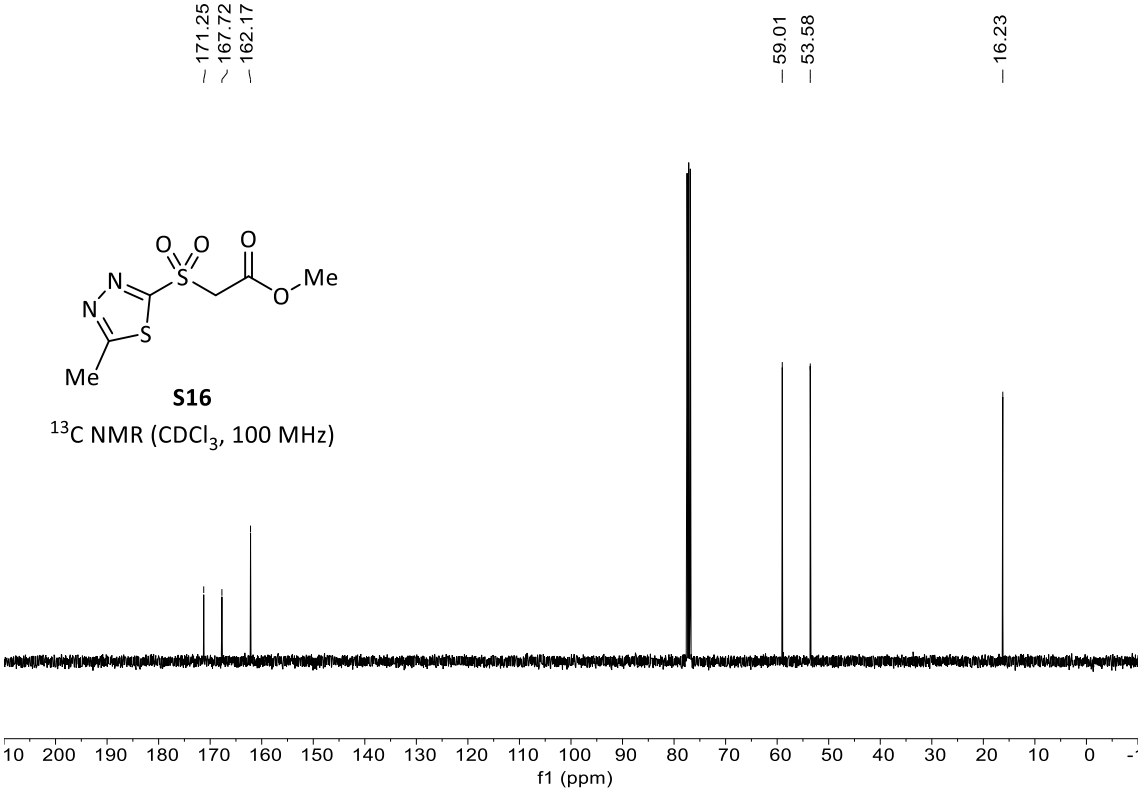

**S15**

$^1$H NMR ($CDCl_3$, 400 MHz)



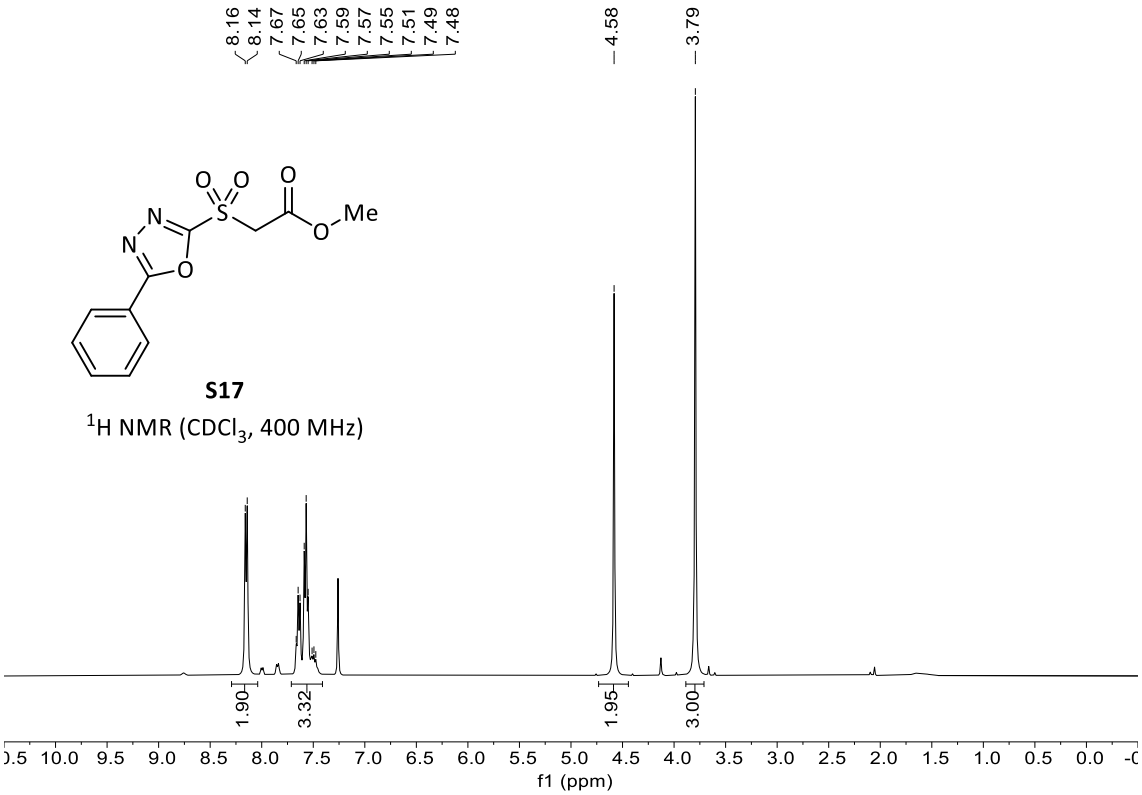

**S16**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



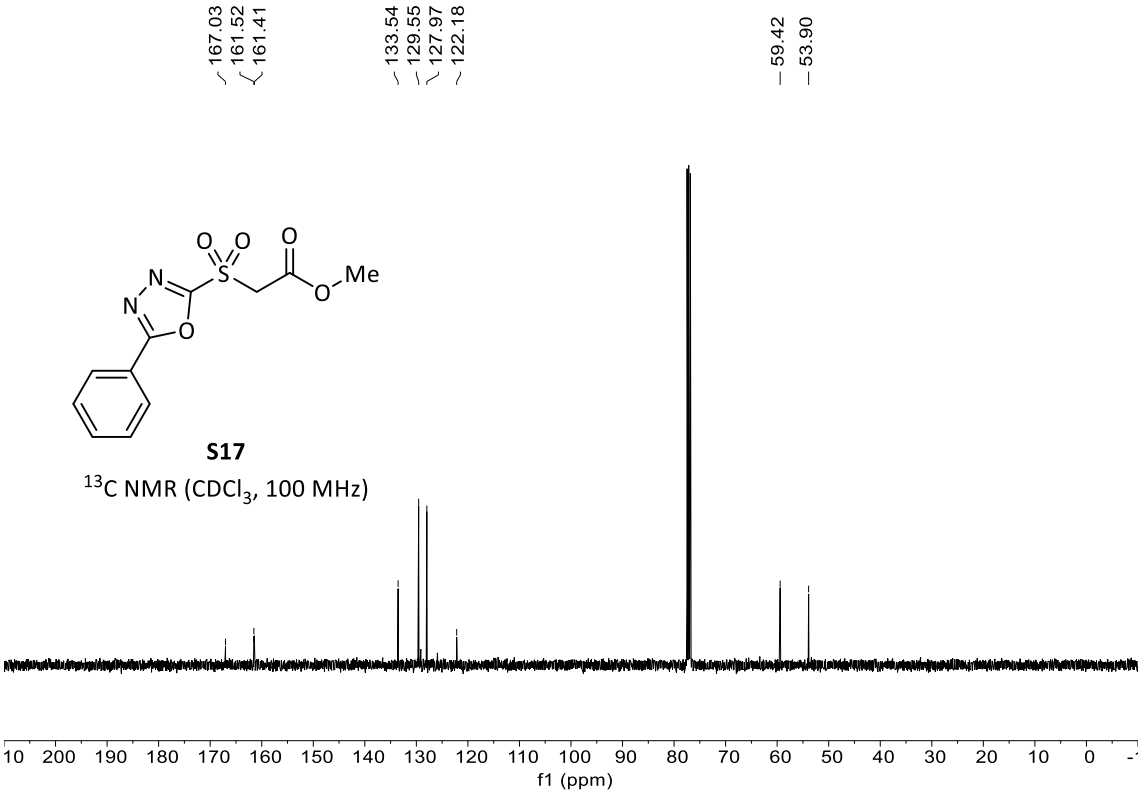

**S16**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



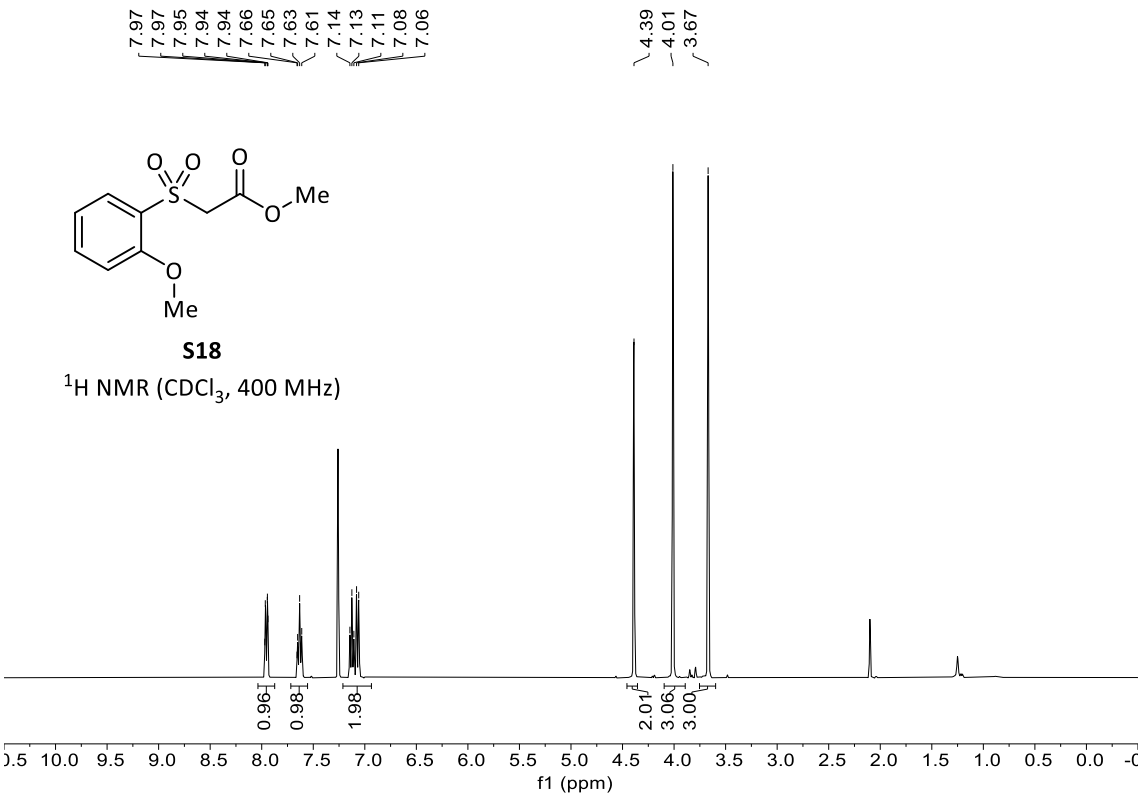

**S17**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



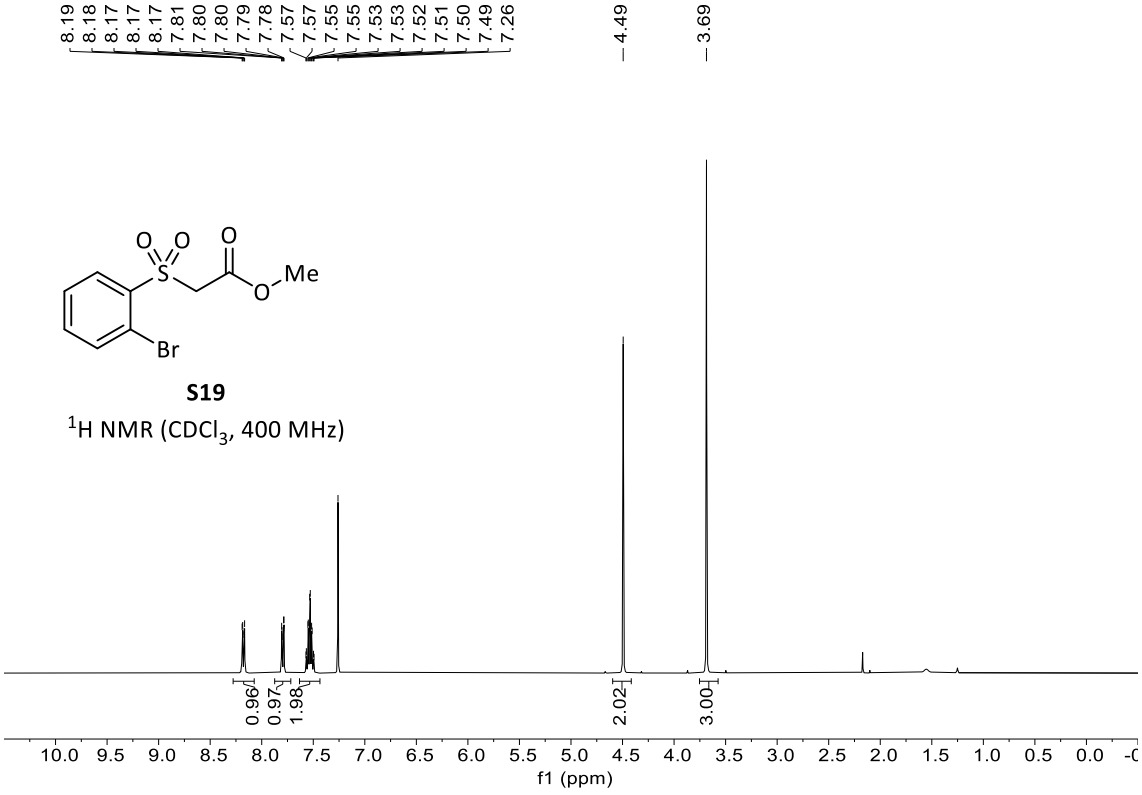

**S17**

$^{13}$C NMR ($CDCl_3$, 100 MHz)



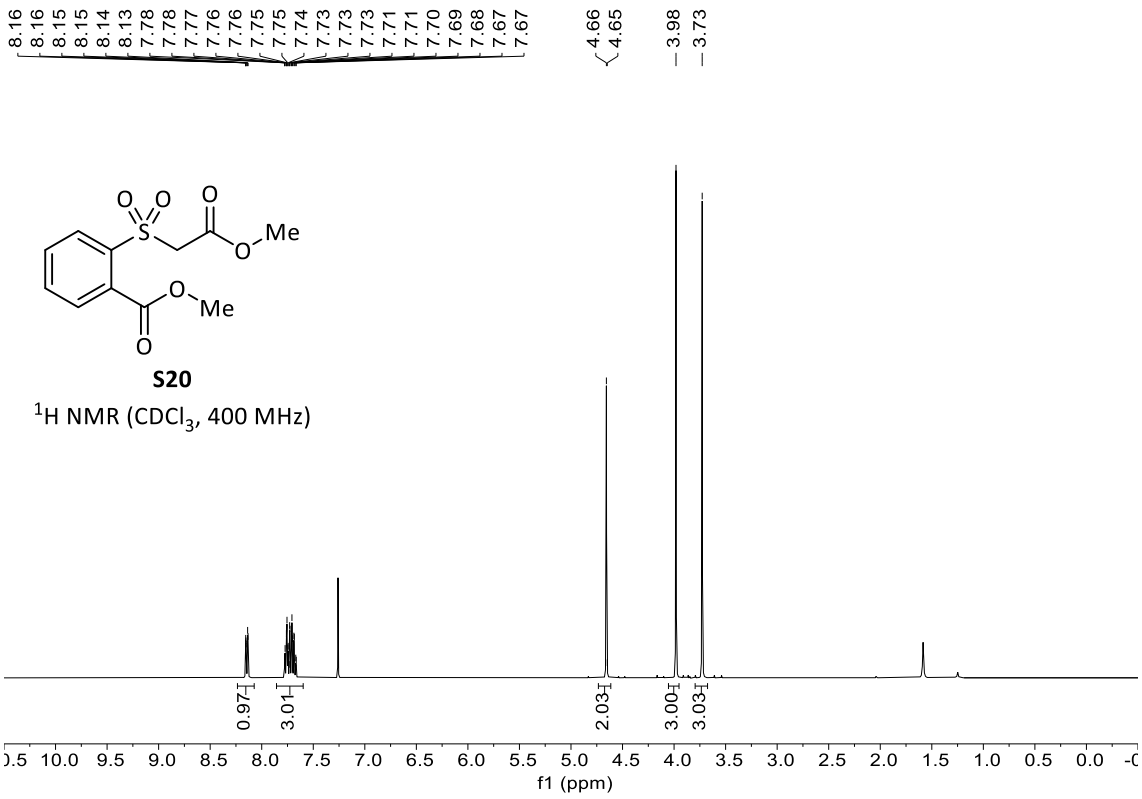

**S18**

$^1$H NMR ($CDCl_3$, 400 MHz)



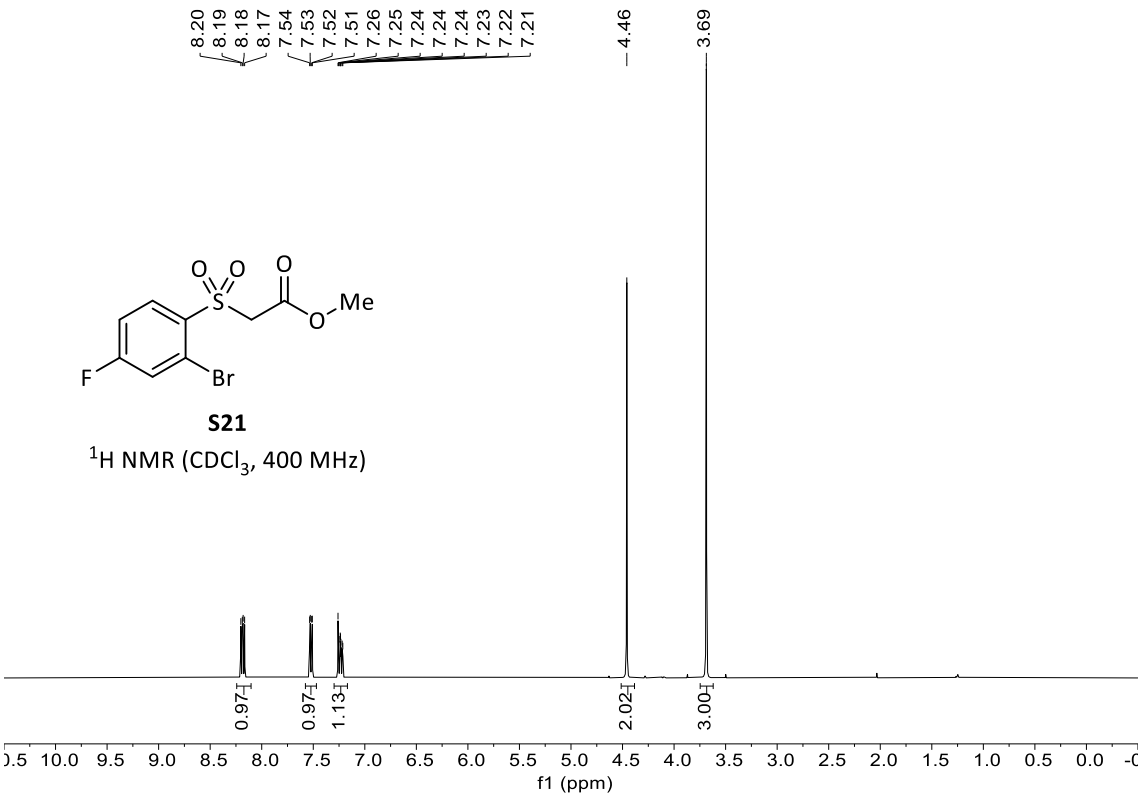

**S19**

$^1$H NMR ($CDCl_3$, 400 MHz)



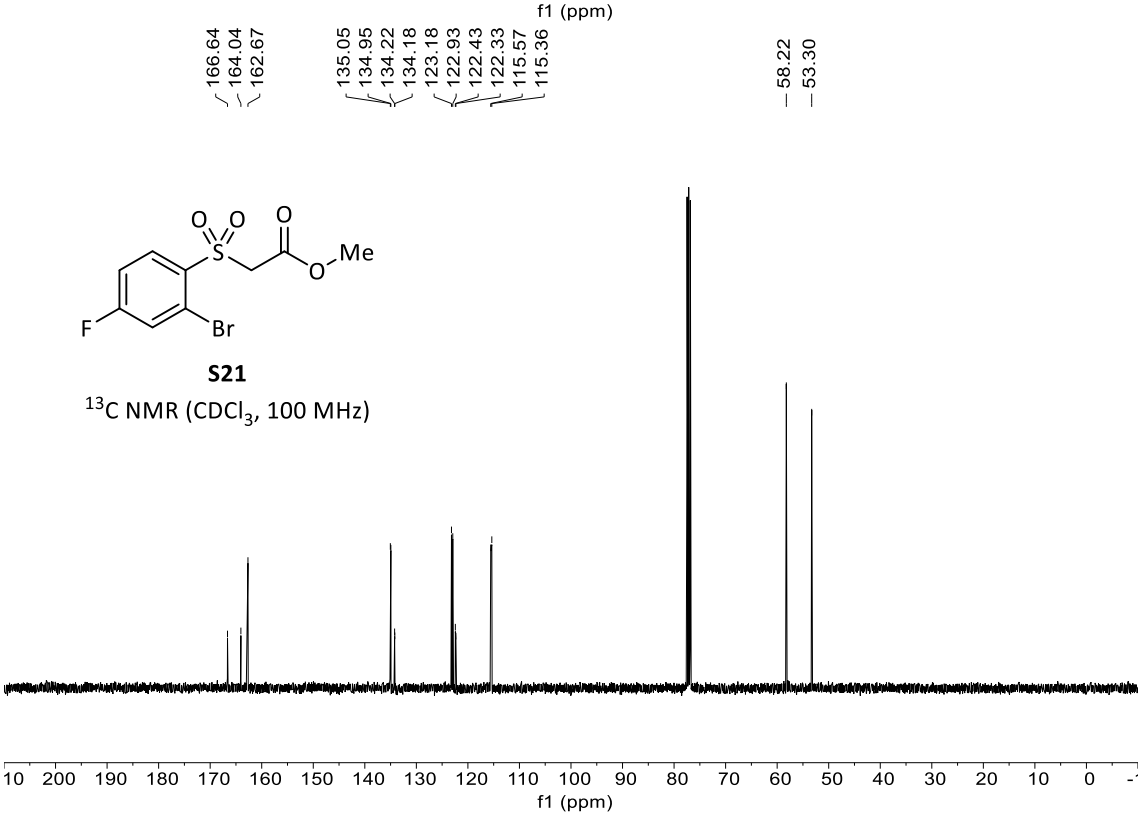

**S20**

$^1$H NMR ($CDCl_3$, 400 MHz)



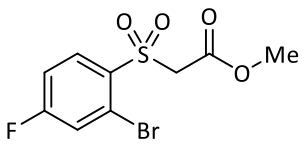

**S21**

$^{1}$H NMR ($CDCl_3$, 400 MHz)




**S21**

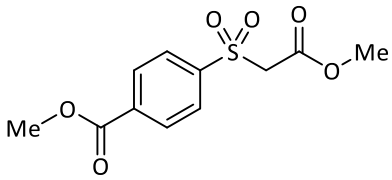
$^{13}$C NMR ($CDCl_3$, 100 MHz)



**S21**

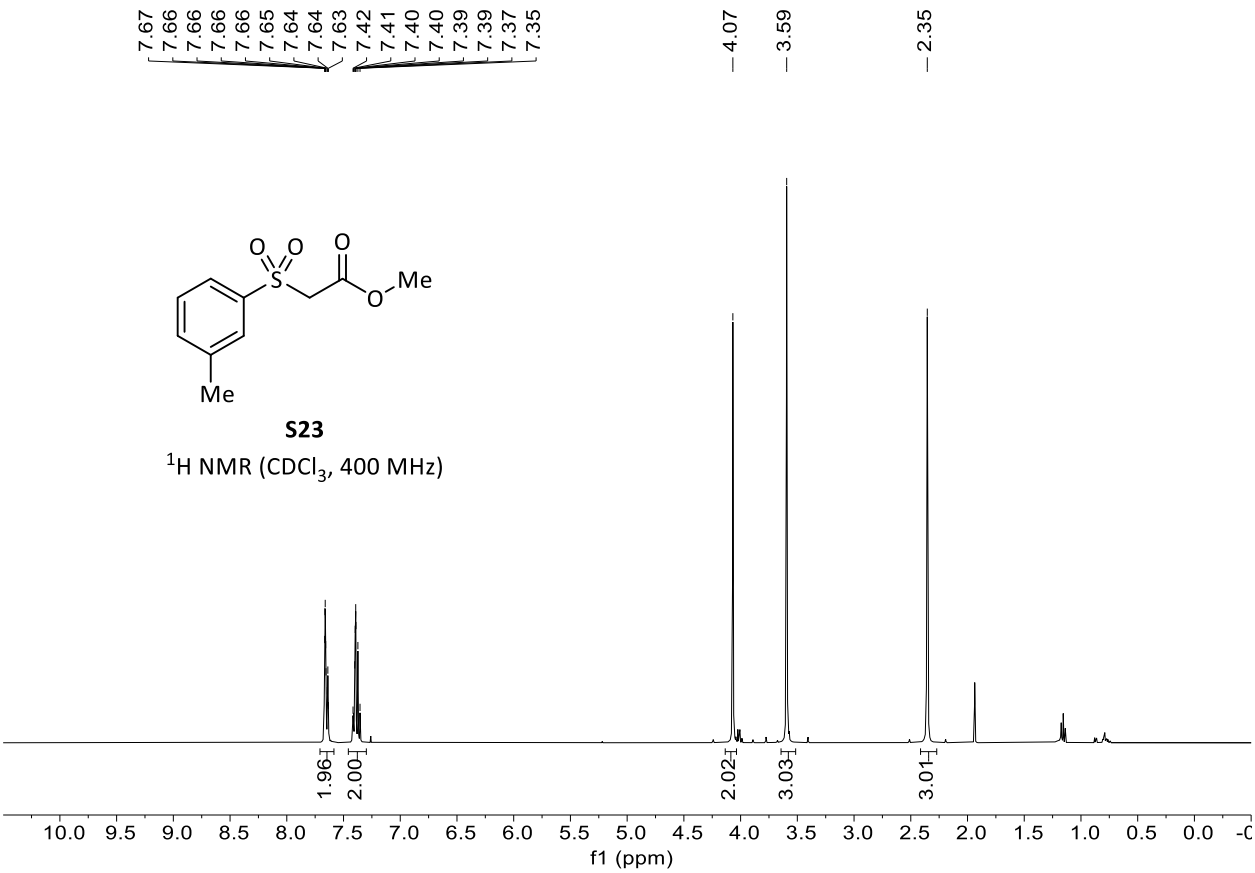
$^{19}$F NMR ($CDCl_3$, 376 MHz)



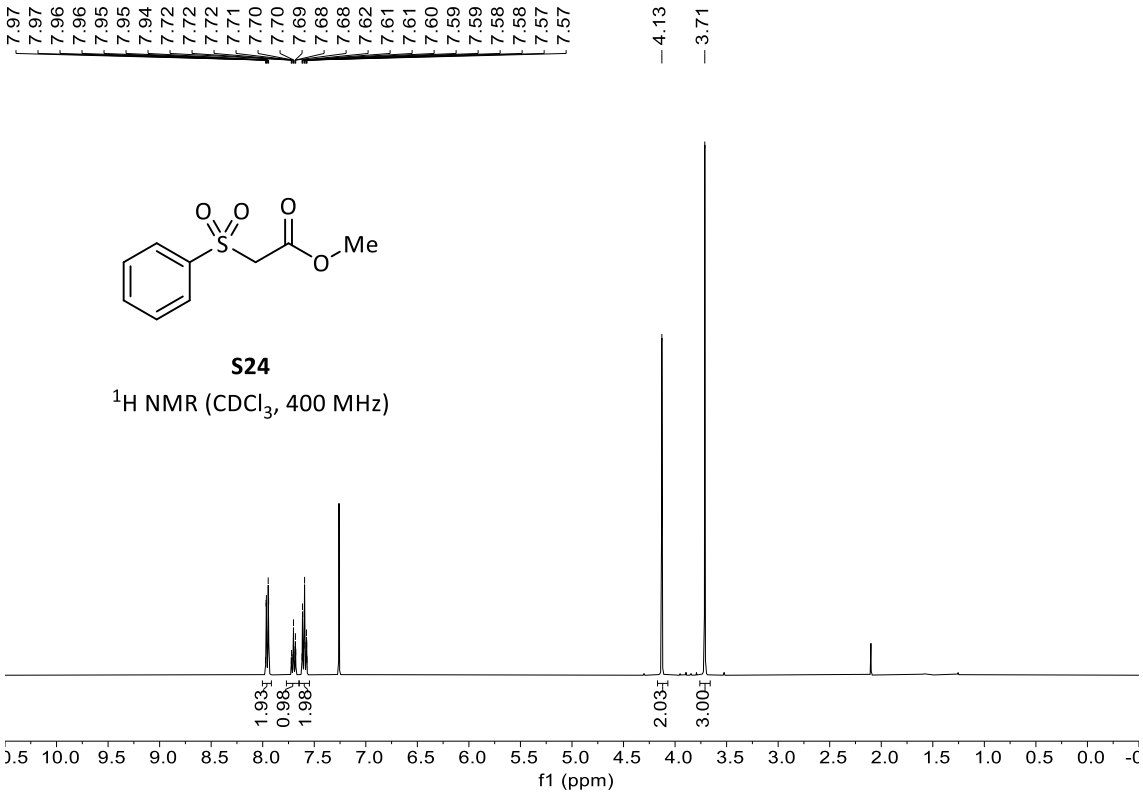
**S22**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



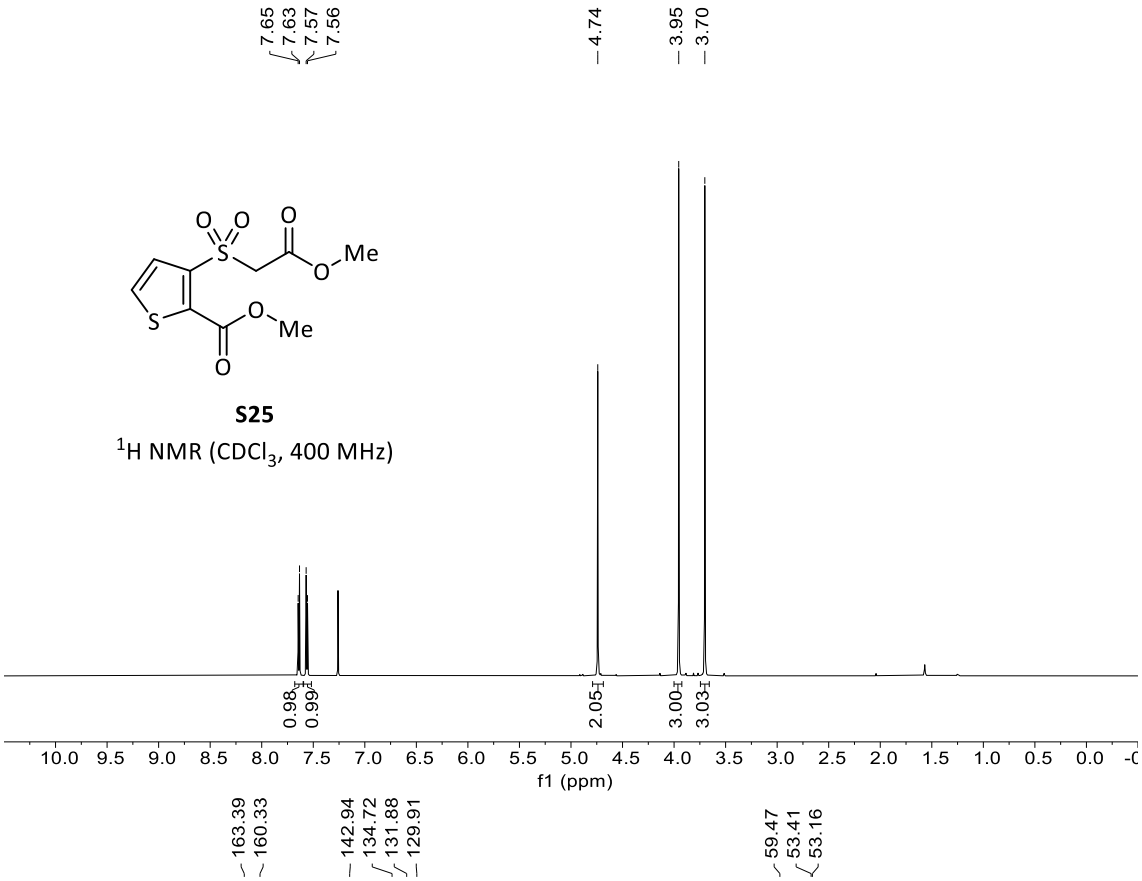

**S23**

$^1$H NMR ($CDCl_3$, 400 MHz)



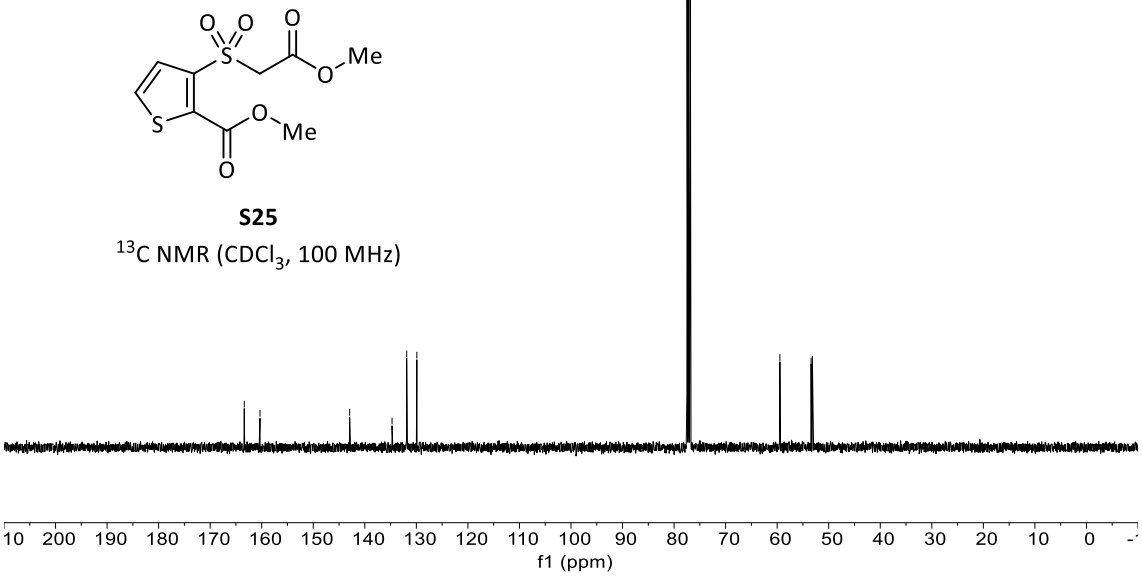

**S24**

$^1$H NMR ($CDCl_3$, 400 MHz)



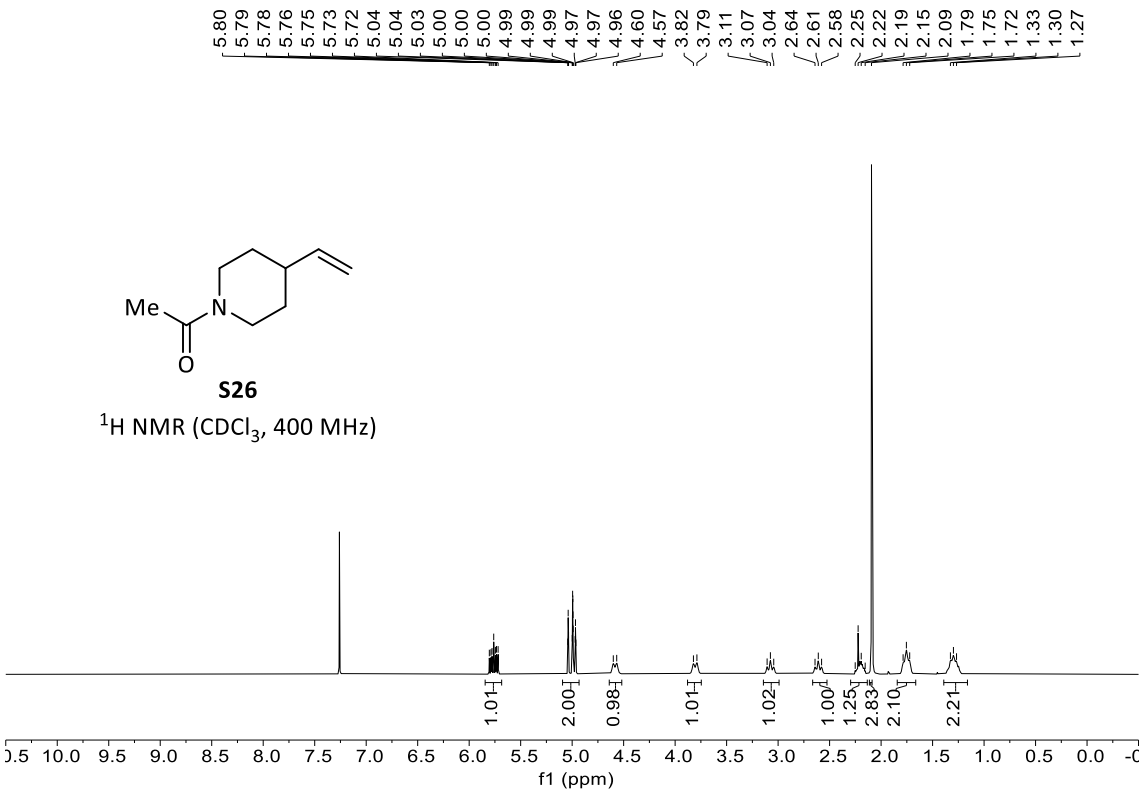

**S25**

$^{1}$H NMR ($CDCl_3$, 400 MHz)



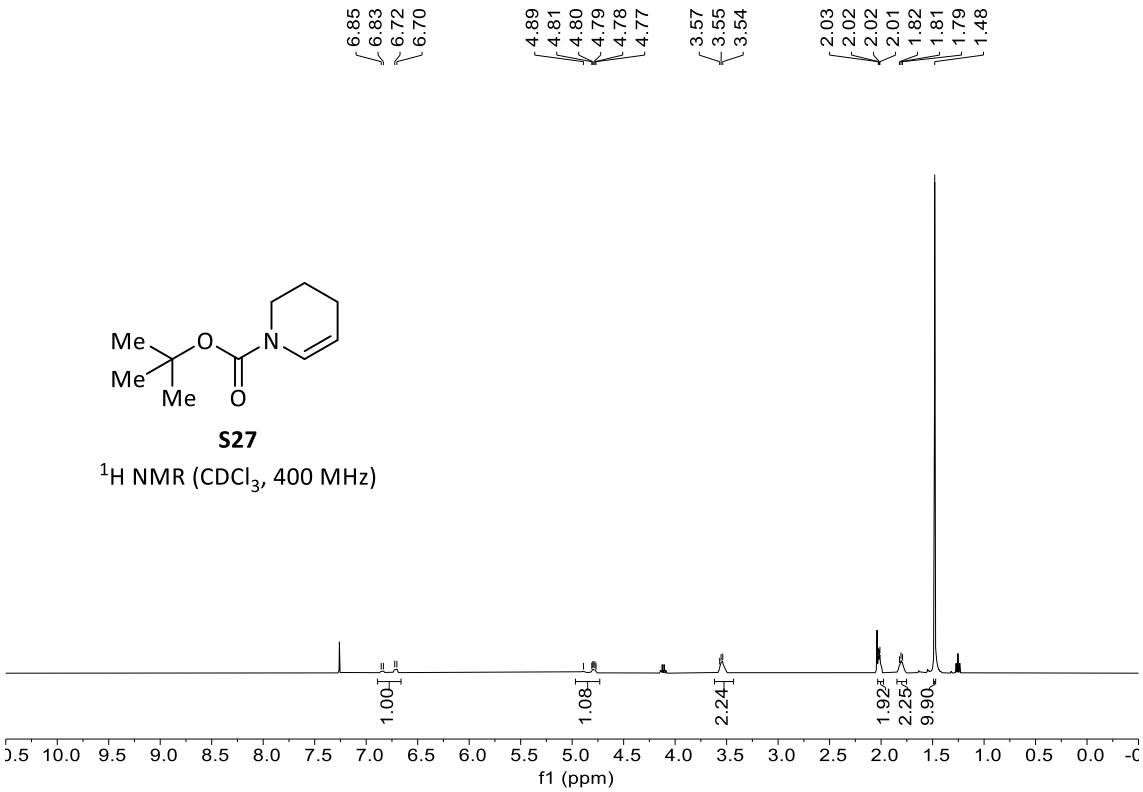

**S25**

$^{13}$C NMR ($CDCl_3$, 100 MHz)




**S26**

$^1$H NMR ($CDCl_3$, 400 MHz)




**S27**

$^1$H NMR ($CDCl_3$, 400 MHz)