.

SUPPLEMENTARY INFORMATION

A Chromatographic Relay Conjugated Photoredox Strategy: *S*, *Se*-Pharmacophore from Alkenes via Formal [2+2+1] Heteroannulation

Injamam Ul Hoque,[a] Saradindu Debnath,[a] Rabindranath Lo[b] and Soumitra Maity*[a]

[a] Department of Chemistry and Chemical Biology, Indian Institute of Technology (ISM) Dhanbad, JH 826004, India.

[b] Institute of Organic Chemistry and Biochemistry, Czech Academy of Sciences, Flemingovo náměstí 542/2, 160 00 Prague, Czech Republic.

Email: smaity@iitism.ac.in

1. General Considerations:

All commercially available chemicals and reagents were used without further purification unless otherwise stated. Solvents for extraction or column chromatography were of technical quality. All water used was purified via a Merck Millipore reverse osmosis purification system prior to use. All reactions were performed in oven-dried glassware under a positive pressure of argon with freshly distilled anhydrous solvents.[1] Solvents were transferred via syringe and were introduced into the reaction vessels through a rubber septum. Solvents were removed under reduced pressure using the Büchi Rotavapor apparatus. All reactions conducted at rt refer to the temperature range of 30-35 °C.

Thin-layer chromatography (TLC): The progress of the reaction was monitored by thin-layer chromatography (TLC) using SiO_2-60 UV254 coated aluminium sheets (Merck, TLC Silica gel 60 F_{254}). Visualization was achieved using UV light, iodine, and/or chemical staining with vanillin, basic potassium permanganate solutions or Seebach's "magic" stain as appropriate.

Flash column chromatography (FC): Purification of the reaction mixture was carried out with flash column chromatography on silica gel 230-400 mesh (Merck, 37-63 µm). Solvents for extraction and chromatography were of technical quality. Eluting solvent mixtures are individually reported in parenthesis.

Alumina for column chromatography: The alumina used in these reactions was column chromatographic grade (60- 325- mesh particle size) purchased from Sisco Research Laboratories Pvt. Ltd. The acidic, neutral, and basic alumina (Brockmann grade-I) used were approximate of pH ~4.5, 6.8-7.5 and 9.5-10.5 respectively (10% aq. suspension).

NMR spectra: Proton, Carbon, and Fluorine nuclear magnetic resonance (^{1}H, ^{13}C, and ^{19}F NMR) spectra were recorded on a Bruker Avance III HD (400, 101, and 377 MHz) spectrometer at 25 °C. Chemical shifts (δ) are given in ppm and reported as follows: multiplicity [s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), m (multiplet), and brs (broad singlet)], coupling constants (*J*) in Hz, number of protons; suggested assignment. The residual deuterated solvent was used as internal standard ($CDCl_3$: δ_H = 7.26 ppm; δ_C = 77.16 ppm; DMSO-d_6: δ_H = 2.50 ppm; δ_C = 39.52 ppm).

Melting point (Mp): Melting points were measured using open glass capillaries in 'Tempstar' (model: KMP-207A) and Remco-Kolkata apparatus and are reported uncorrected.

High-resolution mass spectrometry (HRMS): HRMS were recorded using Waters XEVO G2-XS QTOF and Agilent Technologies 6530 Accurate-Mass QTOF by ESI technique.

Photoreactions: Photoreactions were carried out in borosilicate made VWR®, Culture tube (16×125 mm) using PAR38 12 W blue LEDs placed at a distance of approximately 5 cm. The maximum light intensity is centered at 450 nm.

UV-Vis Spectrophotometer: UV-Vis absorption spectra were recorded using Shimadzu UV Spectrophotometer (model: UV-1800).

Luminescence spectrometer: Fluorescence quenching studies were carried out using a PerkinElmer LS 55 Fluorescence Spectrometer.

2. Preparation of Starting Materials:

2.1. Preparation of Alkene Substrates:

Most of the alkenes were purchased from commercial sources and used as received. Some of the alkenes are prepared and characterized accordingly.

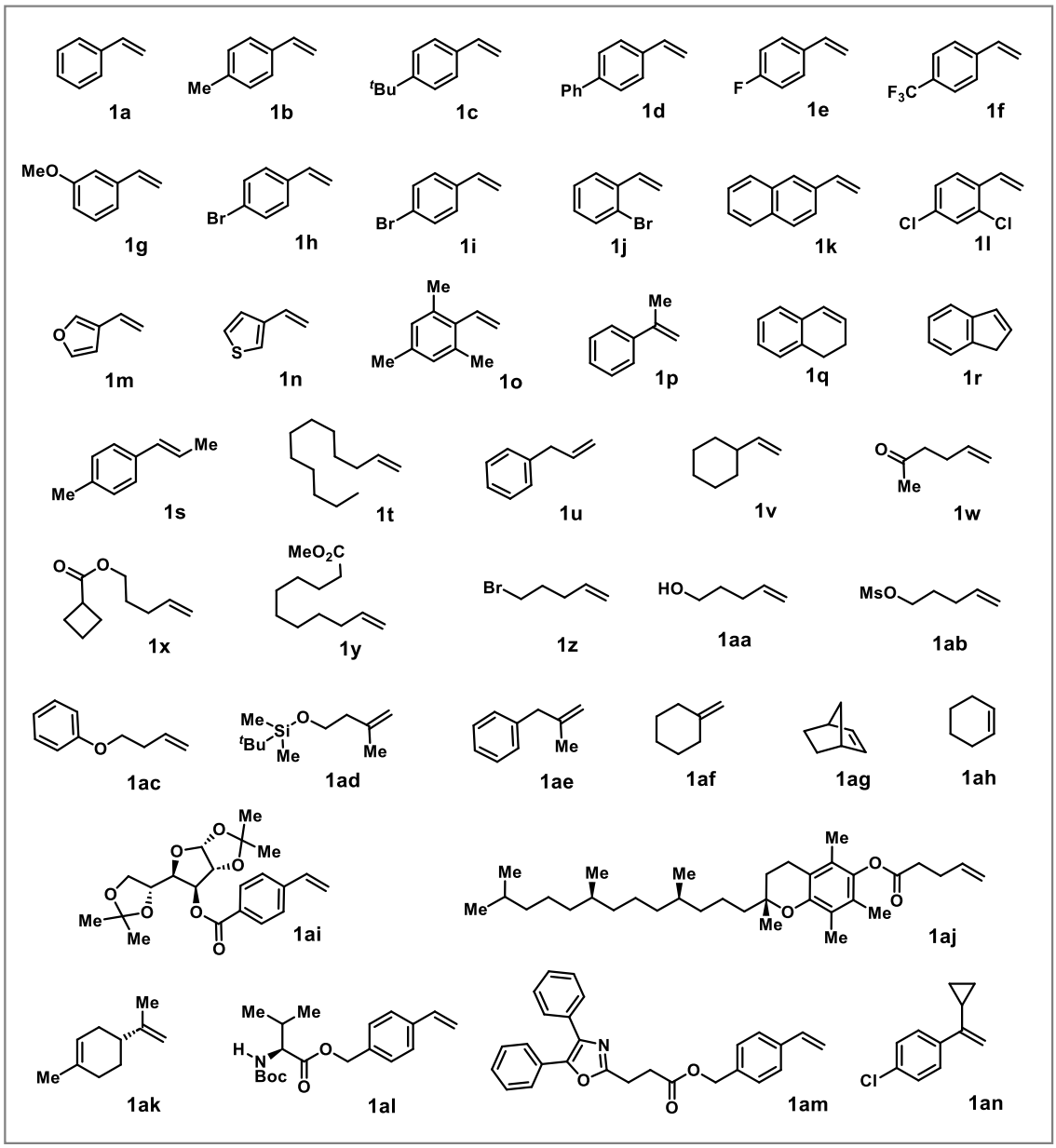


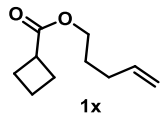
Figure S1: Alkenes included in the manuscript.

Pent-4-en-1-yl cyclobutanecarboxylate (1x):

To the ice-cooled solution of cyclobutane carboxylic acid (1.15 mL, 12 mmol) in dry DCM (45 mL), catalytic amount of DMAP (244 mg, 2 mmol) and 4-Penten-1-ol (1.03 mL, 10 mmol) were added. Then, the mixture was allowed to stir for 15 minutes to get a homogenous reaction mixture, and DCC (4.13 g, 20 mmol) was added at once under the same condition. Then cooling conditions were removed off, and the reaction mixture was allowed to stir for 6 h at room temperature. Conversion into ester was checked with TLC and filtered through a short pad of celite to remove the solid particles. Then the filtrate was concentrated under *vacuo* and purified by flash column chromatography on silica gel (EtOAc/ petroleum ether) to afford the corresponding alkenes.

Pent-4-en-1-yl cyclobutanecarboxylate (1x):

Yield: 76% (1.28 g).



1x

Nature: Colourless oil.

R_f value = 0.38 [EtOAc/petroleum ether=1:19(v/v)]

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.85 – 5.75 (m, 1H), 5.06 – 4.96 (m, 2H), 4.07 (t, *J* = 6.6 Hz, 2H), 3.17 – 3.08 (m, 1H), 2.33 – 2.23 (m, 2H), 2.23 – 2.15 (m, 2H), 2.14 – 2.08 (m, 2H), 2.02 – 1.86 (m, 2H), 1.76 – 1.69 (m, 2H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 175.7, 137.7, 115.4, 63.8, 38.3, 30.2, 28.0, 25.4, 18.5.

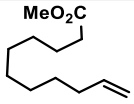
HRMS (ESI) *m/z* calcd for $C_{10}H_{16}O_2K$ $[M+K]^+$: 207.0787; found: 207.0766.

Methyl undec-10-enoate (1y):[2]

A solution of 10-undecenoic acid (1.84 g, 10 mmol) in 2% H_2SO_4/MeOH (20 mL) was refluxed for 4 h. After the completion of the reaction (monitored by TLC), the reaction mixture was cooled to rt and concentrated under vacuo. Then the reaction crude was diluted with ethyl acetate (20 mL) and saturated $NaHCO_3$ solution (10 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (2×15mL). The combined organic layers were washed with brine (30 mL) and dried over Na_2SO_4. The solution was concentrated and purified via silica gel column chromatography (230−400 mesh) using EtOAc/petroleum ether as eluent to afford the corresponding product **1v**.

Methyl undec-10-enoate (1y):[2]

Yield: 91% (1.8 g).



1y

Nature: Colourless oil.

R_f value = 0.41 [EtOAc:Petroleum ether = 1:19 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.82 – 5.72 (m, 1H), 4.98 – 4.88 (m, 2H), 3.63 (s, 3H), 2.27 (t, *J* = 7.5 Hz, 2H), 2.01 (q, *J* = 7.1 Hz, 2H), 1.61 – 1.55 (m, 2H), 1.36 – 1.31 (m, 2H), 1.26 – 1.21 (m, 8H).

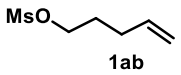
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 174.2, 139.1, 114.1, 51.4, 34.0, 33.7, 29.3, 29.2, 29.1, 29.0, 28.8, 24.9.

Pent-4-en-1-yl methanesulfonate (1ab):[3]

A 100 mL RB flask fitted with a stir bar was charged with a solution of 4-penten-1-ol (1.03 mL, 10 mmol) and triethylamine (1.53 mL, 11 mmol) in 40 mL dichloromethane. The mixture was cooled to 0 °C, and methanesulfonyl chloride (0.85 mL, 11 mmol) was added dropwise. The mixture was stirred for 2 h and quenched with 1(N) HCl (4 mL), and the solution was washed with saturated $NaHCO_3$ solution (2×30 mL) and brine (20 mL). The organic layer was dried over Na_2SO_4 and concentrated under vacuo. Then, the crude mass was purified via silica gel column chromatography (230−400 mesh) using EtOAc/petroleum ether as eluent to afford the corresponding product.

Pent-4-en-1-yl methanesulfonate (1ab):[3]

Yield: 88% (1.44 g).



1ab

Nature: Colourless oil.

R_f value = 0.40 [EtOAc:Petroleum ether = 1:19 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.80 – 5.69 (m, 1H), 5.05 – 4.97 (m, 2H), 4.18 (t, *J* = 6.5 Hz, 2H), 2.96 (s, 3H), 2.14 (q, *J* = 7.2 Hz, 2H), 1.84 – 1.77 (m, 2H).

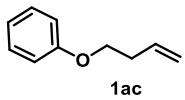
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 136.6, 116.0, 69.4, 37.2, 29.4, 28.1.

(But-3-en-1-yloxy)benzene (1ac):[4]

To a solution of phenol (941 mg, 10 mmol) and K_2CO_3 (3.46 g, 25 mmol) in CH_3CN (40 mL) was added 4-bromo-1-butene (2 mL, 20 mmol) and the mixture was refluxed for 12 h. After the completion of the reaction (monitored by TLC), the reaction mixture was cooled to rt and concentrated under vacuo. The residue was partitioned between CH_2Cl_2 (40 mL) and water (20 mL), and the aqueous layer was extracted with CH_2Cl_2 (2×30 mL). The combined organic layers were washed with brine (30 mL) and dried over Na_2SO_4. The solution was concentrated and purified via silica gel column chromatography (230−400 mesh) using EtOAc/petroleum ether as eluent to afford the corresponding product.

(But-3-en-1-yloxy)benzene (1ac):[4]

Yield: 64% (0.95 g).



1ac

Nature: Colourless oil.

R_f value = 0.43 [EtOAc:Petroleum ether = 1:19 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.30 – 7.26 (m, 2H), 6.98 – 6.89 (m, 3H), 5.98 – 5.88 (m, 1H), 5.20 – 5.10 (m, 2H), 4.03 (t, *J* = 6.7 Hz, 2H), 2.58 – 2.52 (m, 2H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 159.0, 134.6, 129.6, 120.8, 117.1, 114.7, 67.2, 33.8.

***tert*-Butyldimethyl((3-methylbut-3-en-1-yl)oxy)silane (1ad):**[5]

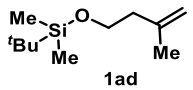
To a solution of 3-methylbut-3-en-1-ol (1 mL, 10 mmol) and imidazole (1.4 g, 20 mmol) in dry CH_2Cl_2 (20 mL) was added TBDMSCl (1.9 g, 12.5 mmol) and the resulting mixture was stirred at rt for 18 h. After the completion of the reaction, the reaction crude was diluted with CH_2Cl_2 (10 mL) and H_2O (10 mL) was added. The mixture was extracted with CH_2Cl_2 (2×20 mL), and the combined organic layers were washed with brine and dried over Na_2SO_4. The solution was concentrated and purified via silica

gel column chromatography (230−400 mesh) using EtOAc/petroleum ether as eluent to afford the corresponding product.

***tert*-Butyldimethyl((3-methylbut-3-en-1-yl)oxy)silane (1ad):**[5]

Yield: 90% (1.8 g).

Nature: Colourless oil.



1ad

R_f value = 0.39 [EtOAc:Petroleum ether = 1:19 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 4.75 – 4.69 (m, 2H), 3.71 (t, *J* = 7.1 Hz, 2H), 2.24 (t, *J* = 7.1 Hz, 2H), 1.74 (s, 3H), 0.89 (s, 9H), 0.05 (s, 6H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 143.2, 111.6, 62.3, 41.3, 26.1, 23.0, 18.5, -5.2.

(3a*R*,5*R*,6*S*,6a*R*)-5-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl 4-vinylbenzoate (1ai):

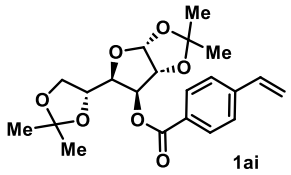
To the ice-cooled solution of 4-Vinylbenzoic acid (889 mg, 6 mmol) in dry DCM (25 mL), catalytic amounts of DMAP (122 mg, 1 mmol) and 1,2:5,6-Di-O-isopropylidene-*α*-D-glucofuranose (1.3 g, 5 mmol) were added. Then, the mixture was allowed to stir for 15 minutes to get a homogenous reaction mixture, and DCC (2.06 g, 10 mmol) was added at once under the same condition. Then cooling conditions were removed off, and the reaction mixture was allowed to stir for 6 h at room temperature. Conversion into ester was checked with TLC and filtered through a short pad of celite to remove the solid particles. Then the filtrate was concentrated under *vacuo* and purified by flash column chromatography on silica gel (EtOAc/ petroleum ether) to afford the corresponding alkene.

(3a*R*,5*R*,6*S*,6a*R*)-5-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl 4-vinylbenzoate (1ai):[6]

Yield: 81% (1.58 g).

Nature: Colourless viscous liquid.

R_f value = 0.32 [EtOAc/petroleum ether=1:4(v/v)]



1ai

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.97 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.3 Hz, 2H), 6.75 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.95 (d, *J* = 3.7 Hz, 1H), 5.87 (d, *J* = 17.6 Hz, 1H), 5.49 (d, *J* = 2.7 Hz, 1H), 5.40 (d, *J* = 11.0 Hz, 1H), 4.63 (d, *J* = 3.7 Hz, 1H), 4.38 – 4.31 (m, 2H), 4.13 – 4.06 (m, 2H), 1.55 (s, 3H), 1.41 (s, 3H), 1.31 (s, 3H), 1.26 (s, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 165.1, 142.6, 136.0, 130.1, 128.7, 126.4, 117.1, 112.5, 109.5, 105.3, 83.5, 80.1, 76.7, 72.7, 67.4, 26.9, 26.8, 26.3, 25.3.

(*R*)-2,5,7,8-Tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl pent-4-enoate (1aj):

To the ice-cooled solution of 4-pentenoic acid (0.61 mL, 6 mmol) in dry DCM (25 mL), catalytic amounts of DMAP (122 mg, 1 mmol) and DL-α-tocopherol (2.26 mL, 5 mmol) were added. Then, the mixture was allowed to stir for 15 minutes to get a homogenous reaction mixture, and DCC (2.06 g, 10 mmol) was added at once under the same condition. Then cooling conditions were removed off, and the reaction mixture was allowed to stir for 6 h at room temperature. Conversion into ester was checked with TLC

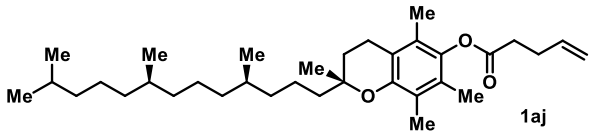
and filtered through a short pad of celite to remove the solid particles. Then the filtrate was concentrated under *vacuo* and purified by flash column chromatography on silica gel (EtOAc/ petroleum ether) to afford the corresponding alkene.

(*R*)-2,5,7,8-Tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl pent-4-enoate (1aj):

Yield: 77% (1.97 g).

Nature: Colourless gel.

R_f value = 0.37 [EtOAc/petroleum ether=1:9(v/v)].



^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.98 – 5.88 (m, 1H), 5.19 – 5.06 (, 2H), 2.72 (t, *J* = 7.3 Hz, 2H), 2.61 – 2.54 (m, 4H), 2.10 (s, 3H), 2.02 (s, 3H), 1.97 (s, 3H), 1.86 – 1.73 (m, 2H), 1.59 – 1.48 (m, 3H), 1.40 – 1.36 (m, 4H), 1.29 – 1.19 (m, 11H), 1.19 – 1.04 (m, 6H), 0.89 – 0.85 (m, 12H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 171.8, 149.5, 140.6, 136.7, 126.8, 125.0, 123.2, 117.5, 116.0, 75.2, 39.5, 37.7, 37.6, 37.5, 37.4, 33.5, 32.9, 32.8, 31.2, 29.1, 28.1, 25.0, 24.6, 22.9, 22.8, 21.2, 20.7, 19.9, 19.8, 19.7, 19.6, 13.2, 12.3, 12.0.

HRMS (ESI) *m/z* calcd for $C_{34}H_{56}O_3Na$ $[M+Na]^+$: 535.4127; found: 535.4109.

4-Vinylbenzyl (*tert*-butoxycarbonyl)-*L*-valinate (1al):[7]

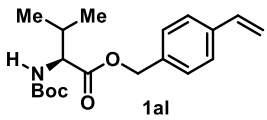
To a solution of Boc-*L*-valine (869 mg, 4.0 mmol) in 30 mL wet DMF (containing 1% water, 0.3 mL), 4-vinylbenzyl chloride (0.68 mL, 4.8 mmol) and Na_2CO_3 (508 mg, 4.8 mmol) were successively added. Then, the reaction mixture was stirred at 60 °C for 6 h. After completion of the reaction (as monitored by TLC), 30 mL of distilled water was added to the reaction mixture. The aqueous layer was extracted with ethyl acetate (3×30 mL), washed with brine, dried over Na_2SO_4, and concentrated under vacuo. The reaction crude was purified by silica gel column chromatography using EtOAc/petroleum ether as eluent to afford the corresponding product.

4-Vinylbenzyl (*tert*-butoxycarbonyl)-*L*-valinate (1al):[7]

Yield: 61% (814 mg).

Nature: Colourless gel.

R_f value = 0.41 [EtOAc/petroleum ether = 1:4 (v/v)]



^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.39 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 6.70 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.75 (d, *J* = 17.6 Hz, 1H), 5.26 (d, *J* = 11.4 Hz, 1H), 5.18 (d, *J* = 12.3 Hz, 1H), 5.10 (d, *J* = 12.4 Hz, 1H), 5.05 (d, *J* = 9.1 Hz, 1H), 4.27 (dd, *J* = 9.1, 4.6 Hz, 1H), 2.18 – 2.10 (m, 1H), 1.43 (s, 9H), 0.93 (d, *J* = 6.9 Hz, 3H), 0.84 (d, *J* = 6.9 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 172.4, 155.8, 137.8, 136.4, 135.0, 128.7, 126.5, 114.5, 79.8, 66.7, 58.6, 31.4, 28.4, 19.1, 17.6.

4-Vinylbenzyl 3-(4,5-diphenyloxazol-2-yl)propanoate (1am):

To a solution of Oxaprozin (1.17 g, 4.0 mmol) in 30 mL wet DMF (containing 1% water, 0.3 mL), 4-vinylbenzyl chloride (0.68 mL, 4.8 mmol) and Na_2CO_3 (508 mg, 4.8 mmol) were successively added. Then, the reaction mixture was stirred at 60 °C for 8 h. After completion of the reaction (as monitored

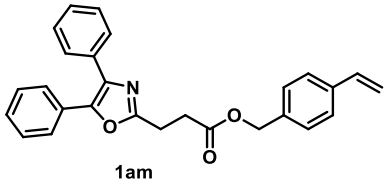
by TLC), 30 mL of distilled water was added to the reaction mixture. The aqueous layer was extracted with ethyl acetate (3×30 mL), dried with dried Na_2SO_4, and concentrated under reduced pressure. Purification of the crude mixture with silica gel chromatography (EtOAc/petroleum ether) provided the title compound.

4-Vinylbenzyl 3-(4,5-diphenyloxazol-2-yl)propanoate (1am):[8]

Yield: 73% (1.2 mg).

Nature: Colourless oil.

R_f value = 0.35 [EtOAc:Petroleum ether = 1:9 (v/v)].



1am

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.66 (dd, *J* = 8.1, 1.5 Hz, 2H), 7.59 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.41 – 7.31 (m, 10H), 6.71 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.75 (dd, *J* = 17.6, 0.7 Hz, 1H), 5.27 (dd, *J* = 10.9, 0.6 Hz, 1H), 5.18 (s, 2H), 3.23 (t, *J* = 7.4 Hz, 2H), 3.00 (t, *J* = 7.4 Hz, 2H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 171.9, 161.7, 145.5, 137.6, 136.4, 135.3, 135.1, 132.5, 129.0, 128.7, 128.6, 128.5, 128.4, 128.1, 127.9, 126.5, 126.4, 114.3, 66.3, 31.1, 23.5.

2.2. Preparation of Bromomalonates Substrates:

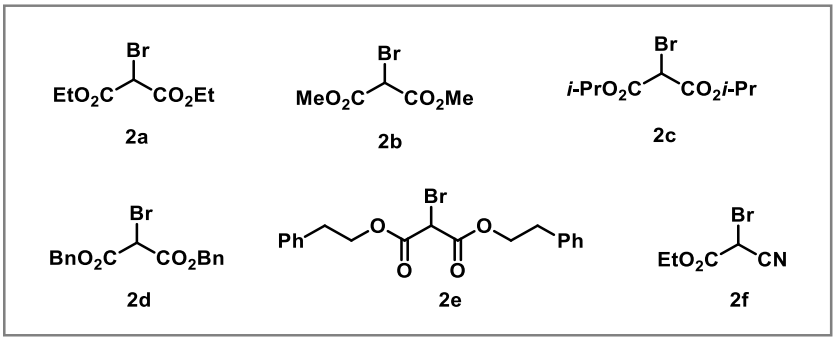
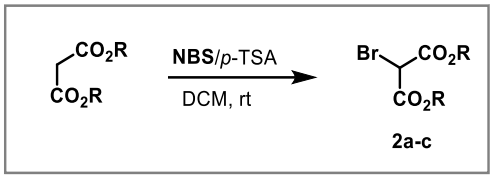
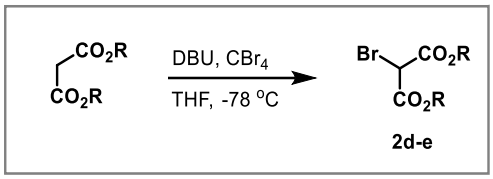


Figure S2: Bromomalonates included in the manuscript.



General Procedure A (GP-A):[9] To a solution of the malonate compound (5.0 mmol) in dichloromethane (50 mL), *N*-bromosuccinimide (1.07 g, 6.0 mmol) and *p*-toluensulphonic acid (172 mg, 1.0 mmol) were added, and the mixture was stirred at room temperature for 6 h. After the reaction was completed (monitored by TLC), the reaction mixture was filtered, washed with water (2×40 mL), and extracted with Et_2O (3×50 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under vacuo. The residue was purified by silica gel column chromatography using EtOAc/petroleum ether as eluent to afford the corresponding bromo product.

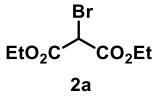


General Procedure B (GP-B):[10] DBU (748 µL, 5.0 mmol) was slowly added to malonate compound (5.0 mmol) in dry THF (40 mL) at 0 °C. The reaction mixture was stirred at this temperature for 30 min and was then cooled to -78 °C. CBr_4 (1.66 g, 5.0 mmol) was then added in one portion. Then, The reaction mixture was stirred at -78 °C for 6 h and was quenched by the slow addition of the saturated solution of NH_4Cl (15 mL) and water (5 mL). The mixture was warmed to rt, and the organic layer was separated and washed with brine (15 mL). The combined aqueous layer was then extracted with dichloromethane (2×25 mL). The combined organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography using EtOAc/petroleum ether as eluent to afford the corresponding bromo product.

Diethyl 2-bromomalonate (2a):[11]

Prepared according to GP-A.

Yield: 91% (1.09 g).



2a

Nature: Colourless oil.

R_f value = 0.31 [EtOAc/petroleum ether=1:19 (v/v)].

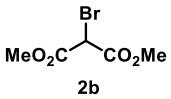
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 4.82 (s, 1H), 4.28 (q, *J* = 7.1 Hz, 4H), 1.30 (t, *J* = 7.1 Hz, 6H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 164.7, 63.4, 42.6, 14.0.

Dimethyl 2-bromomalonate (2b):

Prepared according to GP-A.

Yield: 90% (950 mg).



2b

Nature: Colourless oil.

R_f value = 0.43 [EtOAc/petroleum ether=1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 4.9 (s, 1H), 3.8 (s, 6H).

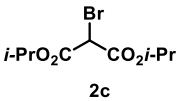
$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 165.2, 54.2, 41.7.

HRMS (ESI) *m/z* calcd for $C_5H_8BrO_4$ $[M+H]^+$: 210.9606; found: 210.9632.

Diisopropyl 2-bromomalonate (2c):

Prepared according to GP-A.

Yield: 82% (1.10 g).



2c

Nature: Colourless oil.

R_f value = 0.32 [EtOAc/petroleum ether=1:19 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.14 – 5.05 (m, 2H), 4.76 (s, 1H), 1.27 (d, *J* = 6.3 Hz, 12H).

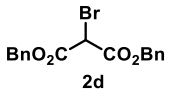
$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 164.2, 71.3, 43.5, 21.5, 21.4.

HRMS (ESI) *m/z* calcd for $C_9H_{15}BrO_4Na$ $[M+Na]^+$: 289.0051; found: 289.0070.

Dibenzyl 2-bromomalonate (2d):[10]

Prepared according to GP-B.

Yield: 72% (1.31 g).



2d

Nature: Colourless oil.

R_f value = 0.31 [EtOAc/petroleum ether=1:19 (v/v)].

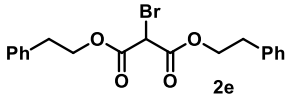
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.36 – 7.34 (m, 6H), 7.32 – 7.29 (m, 4H), 5.22 (s, 4H), 4.92 (s, 1H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 164.5, 134.6, 128.9, 128.8, 128.5, 68.9, 42.4.

Diphenethyl 2-bromomalonate (2e):

Prepared according to GP-B.

Yield: 66% (1.29 g).



2e

Nature: Colourless oil.

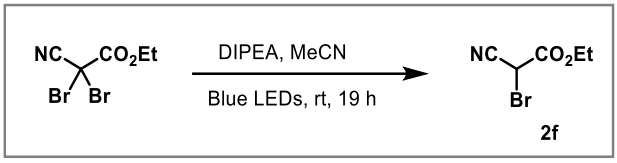
R_f value = 0.33 [EtOAc/petroleum ether=1:19 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.33 – 7.29 (m, 4H), 7.26 – 7.19 (m, 6H), 4.81 (s, 1H), 4.38 (t, *J* = 7.0 Hz, 4H), 2.94 (t, *J* = 7.0 Hz, 4H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 164.5, 137.1, 129.1, 128.7, 126.9, 67.6, 42.3, 34.8.

HRMS (ESI) *m/z* calcd for $C_{19}H_{19}BrO_4Na$ $[M+Na]^+$: 413.0364; found: 413.0356.

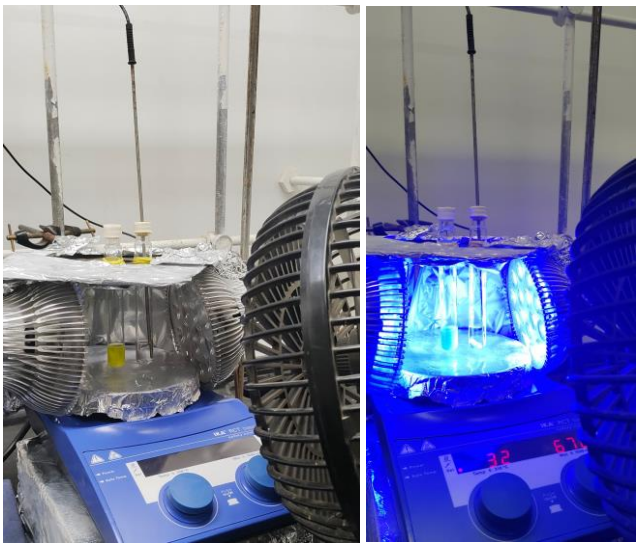
Preparation of ethyl 2-bromo-2-cyanoacetate (2f):[12]



A borosilicate culture tube fitted with a rubber septum was charged with ethyl 2,2-dibromo-2-cyanoacetate (136 mg, 0.5 mmol), *N*, *N*-diisopropylethylamine (174 µL, 1.0 mmol) and MeCN (4 mL). The reaction tube was covered with a piece of aluminum foil to avoid ambient light, degassed via argon bubbling for 10 min, and then left under positive argon pressure by removing the exit needle. Then, the piece of aluminum foil was removed, and the tube was irradiated at rt with 12 W blue LEDs at a distance of approximately 5 cm for 19 h. After the completion of the reaction (monitored by TLC), the reaction crude was concentrated, and the residue was treated with saturated $NaHCO_3$ solution (8 mL) and extracted with DCM (3×10 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The organic portion was concentrated under vacuo, and the residue was quickly passed through a short pad of silica gel and immediately used for the photochemical reaction.

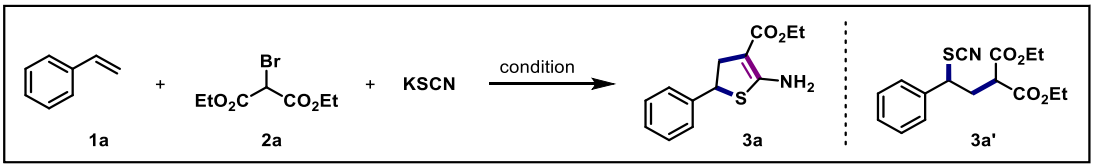
3. Reaction Optimization:

General Procedure for Reaction Optimization: An oven-dried culture tube equipped with a stir bar was charged with catalyst (x mol%), diethyl 2-bromomalonate **2a** (34 µL, 0.2 mmol) and potassium thiocyanate (39 mg, 0.4 mmol). The tube was sealed with a Teflon screw cap, evacuated, and backfilled with argon, before styrene **1a** (46 µL, 0.4 mmol) and dry solvent (2 mL) were added to it. Then, the reaction mixture was degassed by Freeze-Pump-Thaw cycles and irradiated at rt with LEDs at a distance of approximately 5 cm for a specific time. After the completion of the carbothiocyanation reaction (confirmed by TLC), the reaction mixture was concentrated in vacuo and directly purified by neutral alumina column chromatography using EtOAc/petroleum ether as eluent (slow elution) to afford the corresponding 2-amino-dihydrothiophene product **3a**.



Experimental set-up

Table S1: Optimization of the reaction condition:[a]



entry	catalyst (mol%)	solvent	3a (%)[b]
1	*fac*-Ir(ppy)$_3$ (1)	CH_3CN	78
2	Ir(dFCF$_3$ppy)(dtbpy)PF$_6$ (1)	CH_3CN	trace
3	Ru(bpy)$_3$(PF$_6$)$_2$ (2)	CH_3CN	trace
4	eosin Y (5)	CH_3CN	trace
5	rose bengal (5)	CH_3CN	trace
6	4CzIPN (5)	CH_3CN	trace
7	*fac*-Ir(ppy)$_3$ (1)	CH_3NO_2	67
8	*fac*-Ir(ppy)$_3$ (1)	Toluene	68
9	*fac*-Ir(ppy)$_3$ (1)	DCE	47
10	*fac*-Ir(ppy)$_3$ (1)	THF	31

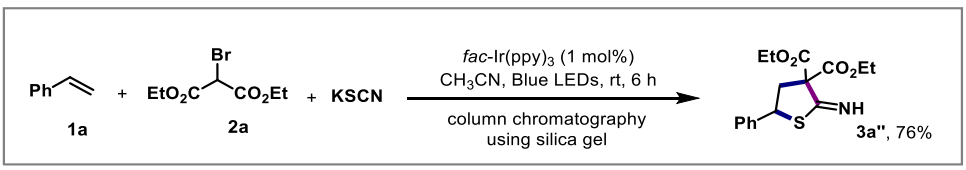
11	*fac*-Ir(ppy)$_3$ (1)	DMF	35
12	*fac*-Ir(ppy)$_3$ (1)	DMSO	39
13[c]	*fac*-Ir(ppy)$_3$ (1)	CH_3CN	0
14	-	CH_3CN	0
15[d]	*fac*-Ir(ppy)$_3$ (1)	CH_3CN	53
16[e]	*fac*-Ir(ppy)$_3$ (1)	CH_3CN	63
17[f]	*fac*-Ir(ppy)$_3$ (1)	CH_3CN	57
18[g]	-	CH_3CN	trace
19[h]	*fac*-Ir(ppy)$_3$ (1)	CH_3CN	69
20[i]	*fac*-Ir(ppy)$_3$ (1)	CH_3CN	71
Efforts to direct annulation (domino carbothiocyanation-cyclization-hydrolysis-decarboxylation-isomerization)			
21[j]	*fac*-Ir(ppy)$_3$ (1)	CH_3CN	0 (0)[k]
22[l]	*fac*-Ir(ppy)$_3$ (1)	CH_3CN	trace (33)[k]
23[m]	*fac*-Ir(ppy)$_3$ (1)	CH_3CN	11 (54)[k]
24[n]	*fac*-Ir(ppy)$_3$ (1)	CH_3CN	0 (trace)[k]
25[o]	*fac*-Ir(ppy)$_3$ (1)	CH_3CN	16 (59)[k]

[a]Unless otherwise noted, all reactions were carried out with **1a** (0.4 mmol), **2a** (0.2 mmol), **KSCN** (0.4 mmol) catalyst (x mol%), solvent (2 mL), degassed condition, irradiation with blue LEDs for 6 h, column chromatography using neutral alumina; [b]isolated yield; [c]reaction in dark; [d]reaction under open air; [e]CH_3CN (1 mL); [f]CH_3CN (3 mL); [g]reaction performed at 60 °C; [h]column chromatography using acidic alumina; [i]column chromatography using basic alumina; [j]1 equiv. *p*-toluenesulfonic acid was used as additive; [k]crude ^{1}H NMR yield (%) of **3a** (**3a'**) using 1,1,2,2-tetrachloroethane as internal standard; [l]20 mol% $Yb(OTf)_3$ was used as additive; [m]100 mg neutral alumina was used as additive; [n]20 mol% $FeCl_3$ was used as additive; [o]neutral alumina (3 equiv.) was added after the photoreaction and stirred at rt for 5 h.

Discussion:

Adsorption on alumina is important for the success of the reaction. As reported by Posner et.al, that adsorption of organic electrophiles (malonate esters) to water-contained alumina might bring electrophile (ester) and nucleophile(water) into proximity and the enhanced electrophilicity of ester carbonyl through Al-centered coordination might work synergistically to hydrolyze ester to acid, and thereby decarboxylation. For discussion, see: Posner, G. H.; Rogers, D. Z.; Kinzig, C. M.; Gurria, G. M. Tetrahedron Lett., 1975, **16**, 3597-3600.

Silica gel column chromatography after three-component photo-catalytic reaction:



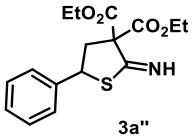
An oven-dried culture tube equipped with a magnetic stir bar was charged with *fac*-Ir(ppy)$_3$ (1.3 mg, 0.002 mmol, 1 mol%), diethyl 2-bromomalonate **2a** (34 µg, 0.2 mmol), potassium thiocyanate (39 mg, 0.4 mmol) and dry acetonitrile (2 mL). The tube was sealed with a Teflon screw cap before styrene **1a** (46 µL, 0.4 mmol) was added to it. Then, the yellow reaction mixture was degassed by Freeze-Pump-Thaw cycles with argon and irradiated at rt with 12 W blue LEDs at a distance of approximately 5 cm for 6 h. A high-speed fan was used to maintain the temperature. After the completion of the photocatalytic reaction (confirmed by TLC), reaction crude was concentrated and residue was purified by silica gel column chromatography using EtOAc/petroleum ether as eluent (slow elution for the complete cyclization) to afford the corresponding 2-imino-tetrahydrothiophene product **3a''**.

Diethyl 2-imino-5-phenyldihydrothiophene-3,3(2*H*)-dicarboxylate (3a''):

Yield: 76% (49 mg).

Nature: Colourless oil.

R_f value = 0.37 [EtOAc:Petroleum ether = 1:4 (v/v)].



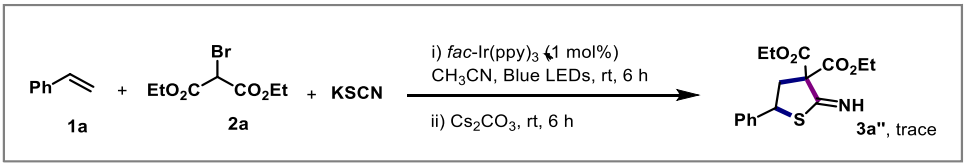
3a''

^{1}H NMR (400 MHz, DMSO-d$_6$) δ (ppm): 10.90 (brs, 1H), 7.46 (d, *J* = 7.2 Hz, 2H), 7.40 – 7.36 (m, 2H), 7.34 – 7.30 (m, 1H), 4.85 (dd, *J* = 11.2, 5.0 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 2.98 (dd, *J* = 13.0, 5.0 Hz, 1H), 2.83 (dd, *J* = 12.9, 11.3 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, DMSO-d$_6$) δ (ppm): 166.8, 166.7, 138.2, 128.8, 128.1, 127.6, 70.4, 62.1, 61.9, 49.6, 44.2, 13.8, 13.7.

HRMS (ESI) *m/z* calcd for $C_{16}H_{20}NO_4S$ $[M+H]^+$: 322.1113; found: 322.1114.

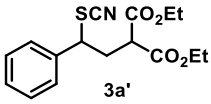
Effort to cyclize carbothiocyanation intermediate using base after three-component photo-catalytic reaction:



An oven-dried culture tube equipped with a magnetic stir bar was charged with *fac*-Ir(ppy)$_3$ (2.6 mg, 0.004 mmol, 1 mol%), diethyl 2-bromomalonate **2a** (68 µg, 0.4 mmol), potassium thiocyanate (78 mg, 0.8 mmol) and dry acetonitrile (4 mL). The tube was sealed with a Teflon screw cap before styrene **1a** (92 µL, 0.8 mmol) was added to it. Then, the yellow reaction mixture was degassed by Freeze-Pump-Thaw cycles with argon and irradiated at rt with 12 W blue LEDs at a distance of approximately 5 cm for 6 h. A high-speed fan was used to maintain the temperature. After the completion of the photocatalytic reaction (confirmed by TLC), Cs_2CO_3 (65 mg, 0.2 mmol) was added and stirred at rt for 6 h. Then reaction crude was concentrated and the crude ^{1}H NMR was recorded using 1,1,2,2-tetrachloroethane as internal standard but only trace amount of **3a''** was observed.

Diethyl 2-(2-phenyl-2-thiocyanatoethyl)malonate (3a'):

*Isolation of this compound in pure form is difficult due to the cyclization (**3a''**) in silica gel column chromatography. Hence to prove the carbo-thiocyanation product in three-component photo-catalytic reaction, NMR spectra and HRMS was collected from crude residue.*



R_f value = 0.38 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.40 – 7.37 (m, 3H), 7.35 – 7.32 (m, 2H), 4.46 (dd, *J* = 9.3, 6.5 Hz, 1H), 4.25 – 4.10 (m, 4H), 3.31 (dd, *J* = 8.4, 6.3 Hz, 1H), 2.82 – 2.66 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 168.2, 136.9, 129.5, 129.4, 127.6, 110.9, 62.1, 50.9, 49.8, 34.5, 14.1, 14.0.

HRMS (ESI) *m/z* calcd for $C_{16}H_{20}NO_4S$ $[M+H]^+$: 322.1113; found: 322.1111.

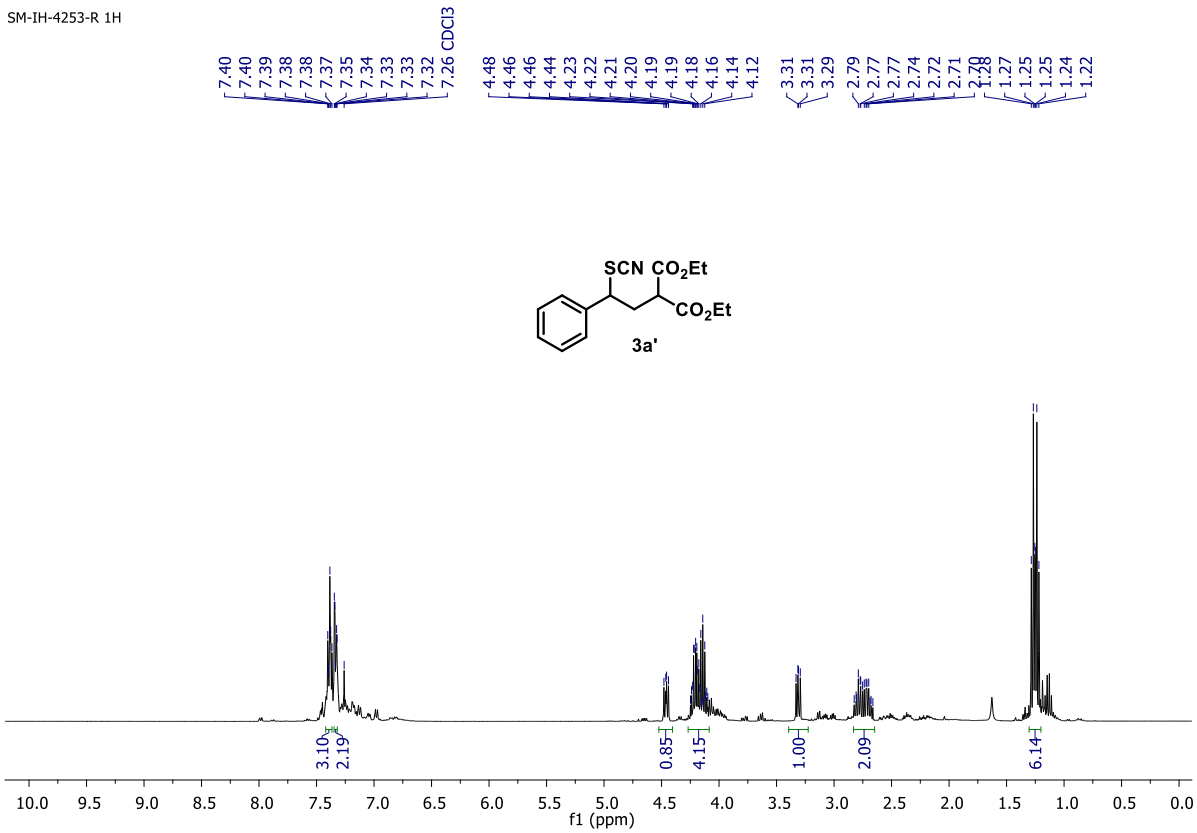


Figure S3: Crude ^{1}H NMR of carbothiocyanation product **3a'** (400 MHz, $CDCl_3$):

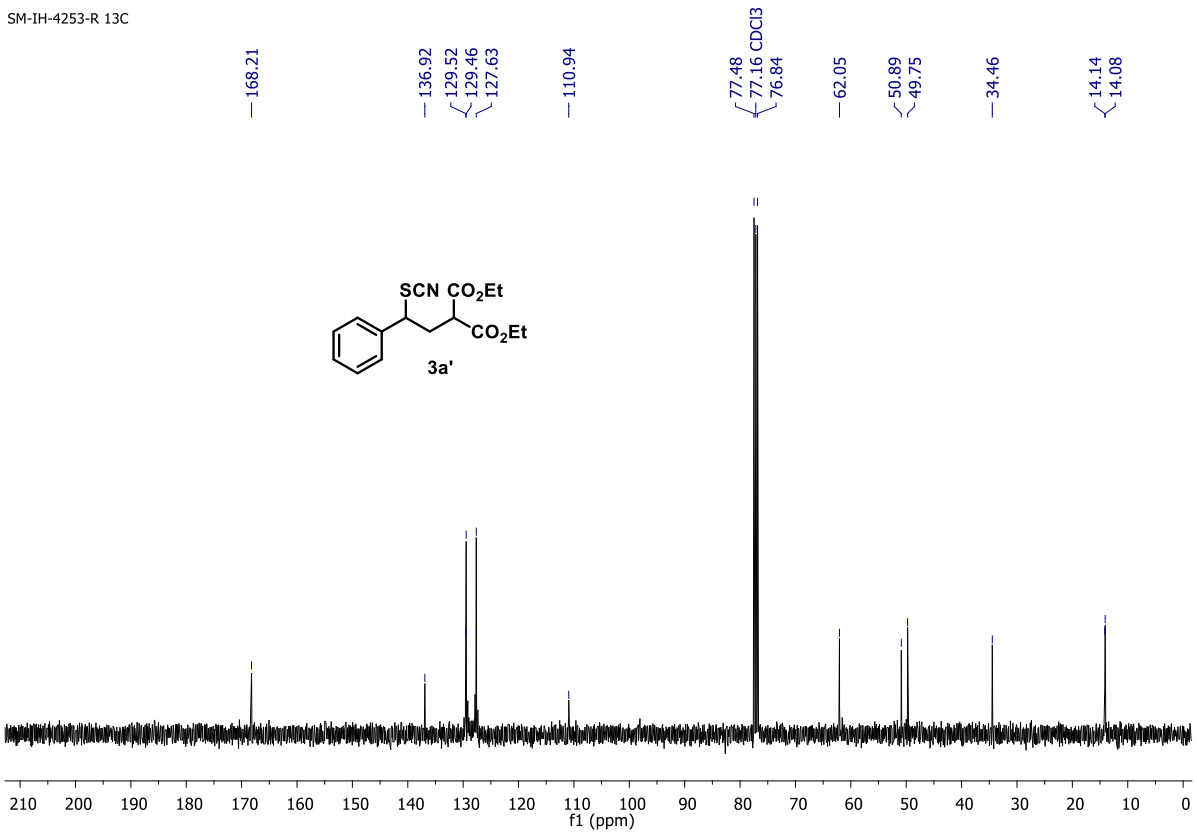


Figure S4: Crude $^{13}C\{^{1}H\}$ NMR of carbothiocyanation product **3a'** (101 MHz, $CDCl_3$):

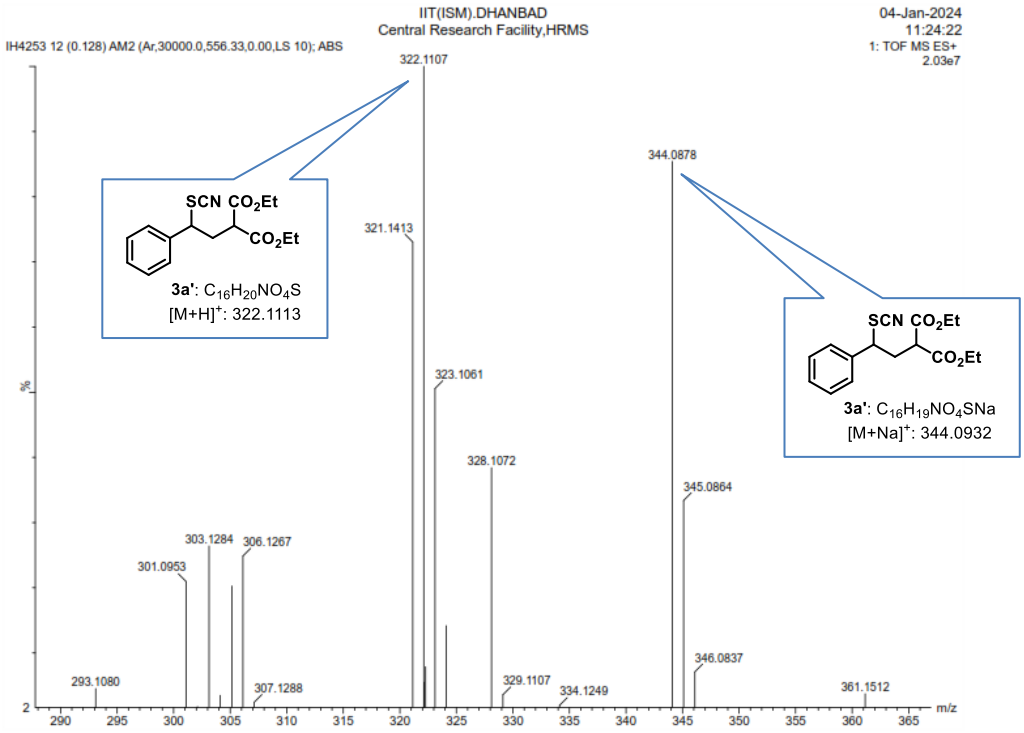
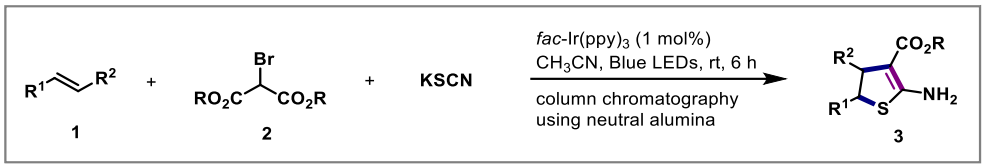


Figure S5: Crude HRMS of carbothiocyanation product **3a'**

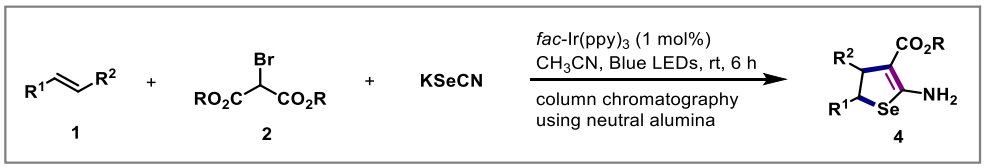
4. Synthetic Procedures:

General procedure for photocatalytic 2-amino-dihydrothiophene synthesis (GP1):



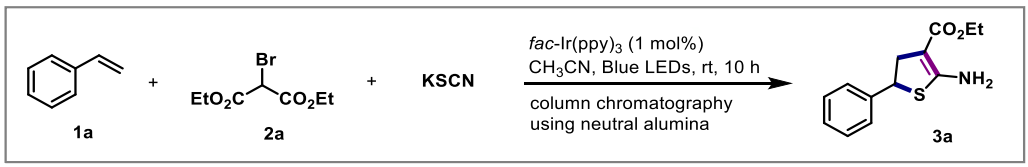
An oven-dried culture tube equipped with a magnetic stir bar was charged with *fac*-Ir(ppy)$_3$ (1.3 mg, 0.002 mmol, 1 mol%), bromomalonate **2** (0.2 mmol), potassium thiocyanate (39 mg, 0.4 mmol) and dry acetonitrile (2 mL). The tube was sealed with a Teflon screw cap before olefin **1** (aromatic olefin, 0.4 mmol & aliphatic olefin, 0.8 mmol) was added to it. Then, the yellow reaction mixture was degassed by Freeze-Pump-Thaw cycles with argon and irradiated at rt with 12 W blue LEDs at a distance of approximately 5 cm for 6 h (10 h for aliphatic olefin). A high-speed fan was used to maintain the temperature. After completion of the reaction (confirmed by TLC), the reaction mixture was concentrated in vacuo and directly purified by activated neutral alumina column chromatography using EtOAc/petroleum ether as eluent to afford the corresponding 2-amino-dihydrothiophene product **3**.

General procedure for photocatalytic 2-amino-dihydroselenophene synthesis (GP2):



An oven-dried culture tube equipped with a magnetic stir bar was charged with *fac*-Ir(ppy)$_3$ (1.3 mg, 0.002 mmol, 1 mol%), bromomalonate **2** (0.2 mmol), potassium selenocyanate (58 mg, 0.4 mmol) and dry acetonitrile (2 mL). The tube was sealed with a Teflon screw cap before olefin **1** (0.4 mmol) was added to it. Then, the yellow reaction mixture was degassed by Freeze-Pump-Thaw cycles with argon and irradiated at rt with 12 W blue LEDs at a distance of approximately 5 cm for 6 h. A high-speed fan was used to maintain the temperature. After completion of the reaction (confirmed by TLC), the reaction mixture was concentrated in vacuo and directly purified by activated neutral alumina column chromatography using EtOAc/petroleum ether as eluent to afford the corresponding 2-amino-dihydroselenophene product **4**.

Procedure of gram scale reaction of 3a:

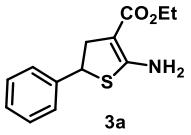


Following **GP-1**, a 250 mL round bottom flask equipped with a magnetic stir bar was charged with *fac*-Ir(ppy)$_3$ (39 mg, 0.06 mmol, 1 mol%), diethyl bromomalonate **2a** (1.02 mL, 6 mmol), potassium thiocyanate (1.17 g, 12 mmol), and dry acetonitrile (60 mL). The RB flask was sealed with a septum, evacuated, and backfilled with argon before styrene **1a** (1.38 mL, 12 mmol) was added to it. Then, the

yellow reaction mixture was degassed by Freeze-Pump-Thaw cycles and irradiated at rt with 12 W blue LEDs at a distance of approximately 5 cm for 10 h. A high-speed fan was used to maintain the temperature. After the completion of the reaction (confirmed by TLC), the reaction mixture was concentrated in vacuo and directly purified by activated neutral alumina column chromatography using EtOAc/petroleum ether as eluent to afford the corresponding 2-amino-dihydrothiophene product **3a** with 71% yield, 1.06 g.

5. Compound Characterization Data:

Ethyl 2-amino-5-phenyl-4,5-dihydrothiophene-3-carboxylate (3a):[13]



3a

Yield: 78% (39 mg).

Nature: White solid.

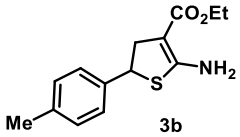
Mp: 84-86 °C

R_f value = 0.30 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.44 – 7.42 (m, 2H), 7.35 – 7.31 (m, 2H), 7.29 – 7.27 (m, 1H), 6.05 (brs, 2H), 4.86 (t, *J* = 8.1 Hz, 1H), 4.18 – 4.12 (m, 2H), 3.40 (dd, *J* = 14.3, 8.5 Hz, 1H), 3.15 (dd, *J* = 14.3, 7.7 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.5, 162.1, 141.7, 128.8, 127.9, 127.4, 91.2, 59.2, 51.6, 41.8, 14.8.

Ethyl 2-amino-5-(*p*-tolyl)-4,5-dihydrothiophene-3-carboxylate (3b):



3b

Yield: 82% (43 mg).

Nature: White solid.

Mp: 101-103 °C

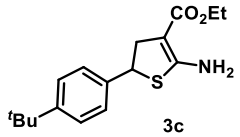
R_f value = 0.35 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.31 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 6.05 (brs, 2H), 4.84 (t, *J* = 8.1 Hz, 1H), 4.18 – 4.12 (m, 2H), 3.38 (dd, *J* = 14.3, 8.5 Hz, 1H), 3.14 (dd, *J* = 14.3, 7.8 Hz, 1H), 2.33 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.5, 162.2, 138.6, 137.7, 129.5, 127.3, 91.3, 59.2, 51.4, 41.8, 21.2, 14.8.

HRMS (ESI) *m/z* calcd for $C_{14}H_{18}NO_2S$ $[M+H]^+$: 264.1058; found: 264.1060.

Ethyl 2-amino-5-(4-(*tert*-butyl)phenyl)-4,5-dihydrothiophene-3-carboxylate (3c):



3c

Yield: 80% (49 mg).

Nature: White solid.

Mp: 110-112 °C

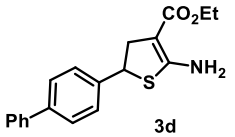
R_f value = 0.33 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.37 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 6.08 (brs, 2H), 4.85 (t, *J* = 8.1 Hz, 1H), 4.18 – 4.12 (m, 2H), 3.38 (dd, *J* = 14.3, 8.5 Hz, 1H), 3.16 (dd, *J* = 14.3, 7.9 Hz, 1H), 1.31 (s, 9H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.5, 162.3, 150.9, 138.5, 127.0, 125.7, 91.3, 59.1, 51.3, 41.7, 34.7, 31.4, 14.8.

HRMS (ESI) *m/z* calcd for $C_{17}H_{24}NO_2S$ $[M+H]^+$: 306.1528; found: 306.1518.

Ethyl 5-([1,1'-biphenyl]-4-yl)-2-amino-4,5-dihydrothiophene-3-carboxylate (3d):



3d

Yield: 74% (48 mg).

Nature: White solid.

Mp: 101-103 °C

R_f value = 0.36 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.59 – 7.55 (m, 4H), 7.50 (d, *J* = 8.3 Hz, 2H), 7.46 – 7.42 (m, 2H), 7.39 – 7.31 (m, 1H), 6.08 (brs, 2H), 4.90 (t, *J* = 8.0 Hz, 1H), 4.20 – 4.14 (m, 2H), 3.44 (dd, *J* = 14.3, 8.5 Hz, 1H), 3.20 (dd, *J* = 14.3, 7.5 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.5, 162.2, 140.7, 128.9, 127.8, 127.5, 127.2, 91.2, 59.2, 51.2, 41.8, 14.8.

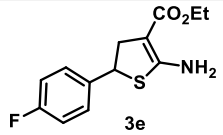
HRMS (ESI) *m/z* calcd for $C_{19}H_{20}NO_2S$ $[M+H]^+$: 326.1215; found: 326.1221.

Ethyl 2-amino-5-(4-fluorophenyl)-4,5-dihydrothiophene-3-carboxylate (3e):

Yield: 82% (44 mg).

Nature: Colourless gummy solid.

R_f value = 0.41 [EtOAc:Petroleum ether = 1:9 (v/v)].



3e

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.39 (dd, *J* = 8.5, 1.4 Hz, 2H), 7.03 – 6.98 (m, 2H), 6.06 (brs, 2H), 4.83 (t, *J* = 8.0 Hz, 1H), 4.18 – 4.12 (m, 2H), 3.39 (dd, *J* = 14.3, 8.5 Hz, 1H), 3.10 (dd, *J* = 14.3, 7.4 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.4, 162.3 (d, *J* = 247.6 Hz), 161.9, 137.5 (d, *J* = 3.3 Hz), 129.0 (d, *J* = 8.1 Hz), 115.7 (d, *J* = 21.5 Hz), 91.0, 59.2, 50.7, 41.9, 14.8.

^{19}F NMR (377 MHz, $CDCl_3$) δ (ppm): -114.44 (s).

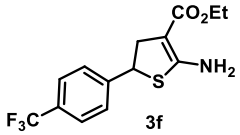
HRMS (ESI) *m/z* calcd for $C_{13}H_{15}FNO_2S$ $[M+H]^+$: 268.0808; found: 268.0800.

Ethyl 2-amino-5-(4-(trifluoromethyl)phenyl)-4,5-dihydrothiophene-3-carboxylate (3f):

Yield: 71% (45 mg).

Nature: Colourless gummy solid.

R_f value = 0.38 [EtOAc:Petroleum ether = 1:9 (v/v)].



3f

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.58 (d, *J* = 8.3 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 6.08 (brs, 2H), 4.85 (dd, *J* = 8.4, 7.0 Hz, 1H), 4.18 – 4.12 (m, 2H), 3.45 (dd, *J* = 14.4, 8.6 Hz, 1H), 3.13 (dd, *J* = 14.4, 6.8 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.3, 161.5, 146.0, 130.0, 127.7, 126.8 (q, *J* = 273.0 Hz), 125.8 (q, *J* = 3.8 Hz), 90.9, 59.3, 50.5, 41.7, 14.7.

^{19}F NMR (377 MHz, $CDCl_3$) δ (ppm): -62.59 (s, 3F).

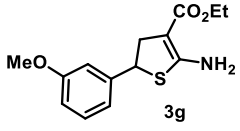
HRMS (ESI) *m/z* calcd for $C_{14}H_{15}F_3NO_2S$ $[M+H]^+$: 318.0776; found: 318.0774.

Ethyl 2-amino-5-(3-methoxyphenyl)-4,5-dihydrothiophene-3-carboxylate (3g):

Yield: 82% (46 mg).

Nature: Colourless gummy solid.

R_f value = 0.30 [EtOAc:Petroleum ether = 1:9 (v/v)].



3g

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.26 – 7.24 (m, 1H), 7.01 – 6.97 (m, 2H), 6.83 – 6.80 (m, 1H), 6.08 (brs, 2H), 4.83 (t, *J* = 8.2 Hz, 1H), 4.17 – 4.11 (m, 2H), 3.80 (s, 3H), 3.39 (dd, *J* = 14.3, 8.5 Hz, 1H), 3.14 (dd, *J* = 14.3, 7.8 Hz, 1H), 1.25 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.4, 162.1, 159.9, 143.2, 129.8, 119.7, 113.2, 113.1, 91.1, 59.2, 55.4, 51.5, 41.7, 14.7.

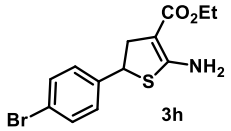
HRMS (ESI) *m/z* calcd for $C_{14}H_{18}NO_3S$ $[M+H]^+$: 280.1007; found: 280.1008.

Ethyl 2-amino-5-(4-bromophenyl)-4,5-dihydrothiophene-3-carboxylate (3h):

Yield: 70% (46 mg).

Nature: Colourless gummy solid.

R_f value = 0.32 [EtOAc:Petroleum ether = 1:9 (v/v)].



3h

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.44 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 6.08 (brs, 2H), 4.77 (t, *J* = 8.2 Hz, 1H), 4.18 – 4.10 (m, 2H), 3.40 (dd, *J* = 14.3, 8.5 Hz, 1H), 3.09 (dd, *J* = 14.3, 7.1 Hz, 1H), 1.25 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.4, 161.8, 140.9, 131.9, 129.0, 121.7, 90.9, 59.3, 50.6, 41.7, 14.7.

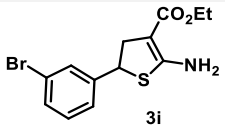
HRMS (ESI) *m/z* calcd for $C_{13}H_{15}BrNO_2S$ $[M+H]^+$: 328.0007; found: 328.0013.

Ethyl 2-amino-5-(3-bromophenyl)-4,5-dihydrothiophene-3-carboxylate (3i):

Yield: 67% (44 mg).

Nature: Colourless gummy solid.

R_f value = 0.34 [EtOAc:Petroleum ether = 1:9 (v/v)].



3i

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.56 (t, *J* = 1.8 Hz, 1H), 7.42 – 7.39 (m, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.21 – 7.18 (m, 1H), 6.07 (brs, 2H), 4.78 (dd, *J* = 8.4, 7.4 Hz, 1H), 4.19 – 4.11 (m, 2H), 3.41 (dd, *J* = 14.4, 8.6 Hz, 1H), 3.11 (dd, *J* = 14.4, 7.2 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.4, 161.7, 144.1, 131.0, 130.4, 130.3, 126.0, 122.7, 90.8, 59.3, 50.5, 41.7, 14.7.

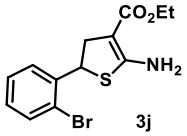
HRMS (ESI) *m/z* calcd for $C_{13}H_{15}BrNO_2S$ $[M+H]^+$: 328.0007; found: 328.0002.

Ethyl 2-amino-5-(2-bromophenyl)-4,5-dihydrothiophene-3-carboxylate (3j):

Yield: 64% (42 mg).

Nature: Colourless gummy solid.

R_f value = 0.33 [EtOAc:Petroleum ether = 1:9 (v/v)].



3j

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.62 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.33 – 7.29 (m, 1H), 7.15 – 7.11 (m, 1H), 6.06 (brs, 2H), 5.14 (dd, *J* = 8.5, 4.7 Hz, 1H), 4.18 – 4.15 (m, 2H), 3.46 (dd, *J* = 14.5, 8.5 Hz, 1H), 3.13 (dd, *J* = 14.6, 4.6 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.4, 161.8, 141.2, 133.0, 129.2, 128.1, 123.9, 91.0, 59.3, 49.5, 39.6, 14.8.

HRMS (ESI) *m/z* calcd for $C_{13}H_{15}BrNO_2S$ $[M+H]^+$: 328.0007; found: 328.0009.

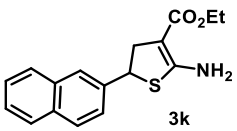
Ethyl 2-amino-5-(naphthalen-2-yl)-4,5-dihydrothiophene-3-carboxylate (3k):

Yield: 57% (34 mg).

Nature: White solid.

Mp: 134 – 136 °C

R_f value = 0.42 [EtOAc:Petroleum ether = 1:9 (v/v)].



3k

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.84 – 7.80 (m, 4H), 7.60 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.51 – 7.45 (m, 2H), 6.13 (brs, 2H), 5.03 (t, *J* = 8.2 Hz, 1H), 4.21 – 4.13 (m, 2H), 3.48 (dd, *J* = 14.3, 8.6 Hz, 1H), 3.26 (dd, *J* = 14.3, 7.5 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.5, 162.2, 138.9, 133.3, 133.0, 128.8, 128.0, 127.8, 126.5, 126.2, 126.0, 125.3, 91.2, 59.2, 51.7, 41.6, 14.8.

HRMS (ESI) *m/z* calcd for $C_{17}H_{18}NO_2S$ $[M+H]^+$: 300.1058; found: 300.1052.

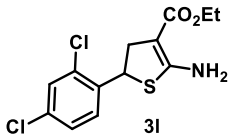
Ethyl 2-amino-5-(2,4-dichlorophenyl)-4,5-dihydrothiophene-3-carboxylate (3l):

Yield: 66% (42 mg).

Nature: White solid.

Mp: 133 – 135 °C

R_f value = 0.32 [EtOAc:Petroleum ether = 1:9 (v/v)].



3l

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.53 (d, *J* = 8.5 Hz, 1H), 7.37 (d, *J* = 2.2 Hz, 1H), 7.22 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.11 (brs, 2H), 5.08 (dd, *J* = 8.5, 4.5 Hz, 1H), 4.19 – 4.11 (m, 2H), 3.44 (dd, *J* = 14.6, 8.5 Hz, 1H), 3.07 (dd, *J* = 14.6, 4.5 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.4, 161.5, 138.3, 133.9, 133.8, 129.3, 128.8, 127.7, 90.6, 59.3, 46.1, 39.5, 14.8.

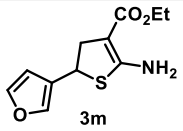
HRMS (ESI) *m/z* calcd for $C_{13}H_{14}Cl_2NO_2S$ $[M+H]^+$: 318.0122; found: 318.0117.

Ethyl 2-amino-5-(furan-3-yl)-4,5-dihydrothiophene-3-carboxylate (3m):

Yield: 71% (34 mg).

Nature: Colourless gummy solid.

R_f value = 0.39 [EtOAc:Petroleum ether = 1:9 (v/v)].



3m

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.40 – 7.39 (m, 1H), 7.38 – 7.37 (m, 1H), 6.45 (s, 1H), 6.05 (brs, 2H), 4.77 (t, *J* = 7.8 Hz, 1H), 4.18 – 4.12 (m, 2H), 3.29 (dd, *J* = 14.0, 8.1 Hz, 1H), 3.05 (dd, *J* = 14.1, 7.7 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.5, 162.1, 143.7, 139.5, 126.0, 109.6, 91.4, 59.2, 42.8, 40.7, 14.8.

HRMS (ESI) *m/z* calcd for $C_{11}H_{14}NO_3S$ $[M+H]^+$: 240.0694; found: 240.0694.

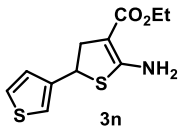
Ethyl 5-amino-2,3-dihydro-[2,3'-bithiophene]-4-carboxylate (3n):

Yield: 74% (38 mg).

Nature: White solid.

Mp: 79 – 81 °C.

R_f value = 0.40 [EtOAc:Petroleum ether = 1:9 (v/v)].



3n

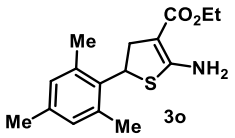
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.30 – 7.28 (m, 1H), 7.20 (s, 1H), 7.14 (dd, *J* = 5.0, 1.2 Hz, 1H), 6.07 (brs, 2H), 4.92 (t, *J* = 7.8 Hz, 1H), 4.18 – 4.12 (m, 2H), 3.36 (dd, *J* = 14.2, 8.2 Hz, 1H), 3.14 (dd, *J* = 14.2, 7.5 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.5, 162.1, 142.2, 126.8, 126.6, 121.8, 91.3, 59.2, 46.8, 41.1, 14.8.

HRMS (ESI) *m/z* calcd for $C_{11}H_{14}NO_2S_2$ $[M+H]^+$: 256.0466; found: 256.0472.

Ethyl 2-amino-5-mesityl-4,5-dihydrothiophene-3-carboxylate (3o):

Yield: 77% (45 mg).



Nature: White solid.

Mp: 131 – 133 °C

R_f value = 0.37 [EtOAc:Petroleum ether = 1:9 (v/v)].

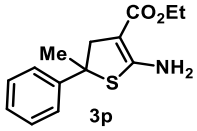
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.85 (s, 2H), 6.07 (brs, 2H), 5.62 (t, *J* = 10.2 Hz, 1H), 4.19 – 4.10 (m, 2H), 3.27 (d, *J* = 4.7 Hz, 1H), 3.24 (d, *J* = 4.5 Hz, 1H), 2.44 (s, 6H), 2.25 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.6, 162.7, 137.7, 137.3, 132.5, 130.4, 91.9, 59.1, 45.7, 38.7, 21.3, 20.9, 14.7.

HRMS (ESI) *m/z* calcd for $C_{16}H_{22}NO_2S$ $[M+H]^+$: 292.1371; found: 292.1371.

Ethyl 2-amino-5-methyl-5-phenyl-4,5-dihydrothiophene-3-carboxylate (3p):

Yield: 51% (27 mg).



Nature: Colourless gummy solid.

R_f value = 0.31 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.47 – 7.44 (m, 2H), 7.36 – 7.32 (m, 2H), 7.27 – 7.23 (m, 1H), 6.00 (brs, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.43 (d, *J* = 14.1 Hz, 1H), 3.12 (d, *J* = 14.1 Hz, 1H), 1.89 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H).

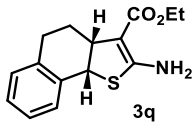
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.8, 162.0, 145.6, 128.5, 127.2, 126.1, 91.3, 60.8, 59.2, 47.6, 31.6, 14.8.

HRMS (ESI) *m/z* calcd for $C_{14}H_{18}NO_2S$ $[M+H]^+$: 264.1058; found: 264.1048.

Ethyl (3a*R*,9b*S*)-2-amino-3a,4,5,9b-tetrahydronaphtho[1,2-*b*]thiophene-3-carboxylate (3q):

Yield: 78% (73 mg, combined yield as a 2:1 mixture of diastereomers).

Characterization data was obtained for the major diastereomer by flash-column chromatography.



Nature: Colourless gummy solid.

R_f value = 0.32 [EtOAc:Petroleum ether = 1:9 (v/v)].

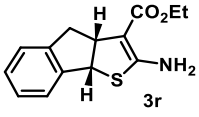
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.21 – 7.14 (m, 4H), 6.04 (brs, 2H), 5.24 (d, *J* = 7.1 Hz, 1H), 4.25 – 4.15 (m, 2H), 3.35 – 3.30 (m, 1H), 3.06 – 3.01 (m, 1H), 2.88 – 2.74 (m, 2H), 1.98 – 1.90 (m, 1H), 1.30 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.5, 162.8, 137.6, 133.4, 129.5, 129.4, 127.7, 126.3, 97.9, 59.1, 50.9, 44.5, 29.4, 23.8, 14.9.

HRMS (ESI) *m/z* calcd for $C_{15}H_{18}NO_2S$ $[M+H]^+$: 276.1058; found: 276.1053.

Ethyl (3a*R*,8b*S*)-2-amino-3a,8b-dihydro-4*H*-indeno[1,2-*b*]thiophene-3-carboxylate (3r):

Yield: 82% (43 mg).



Nature: Colourless gummy solid.

R_f value = 0.30 [EtOAc:Petroleum ether = 1:9 (v/v)].

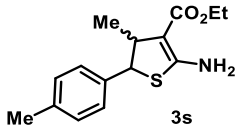
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.28 – 7.20 (m, 4H), 6.02 (brs, 2H), 5.24 (d, *J* = 8.8 Hz, 1H), 4.32 – 4.17 (m, 3H), 3.43 (dd, *J* = 16.7, 8.2 Hz, 1H), 3.19 (dd, *J* = 16.7, 4.8 Hz, 1H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.6, 162.5, 143.0, 142.7, 128.2, 127.0, 125.2, 124.9, 95.9, 59.1, 54.6, 50.8, 40.3, 14.8.

HRMS (ESI) *m/z* calcd for $C_{14}H_{16}NO_2S$ $[M+H]^+$: 262.0902; found: 262.0902.

Ethyl 2-amino-4-methyl-5-(*p*-tolyl)-4,5-dihydrothiophene-3-carboxylate (3s):

Yield: 63% (34 mg, combined yield as a 3.2:1 mixture of diastereomers).



3s

Nature: Colourless gummy solid.

R_f value = 0.41 [EtOAc:Petroleum ether = 1:9 (v/v)].

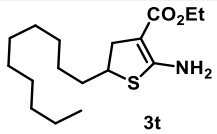
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): (for the mixture) 7.28 – 7.22 (m, 2H), 7.20 – 7.12 (m, 2H), 6.06 (brs, 2H), 4.76 – 4.07 (m, 3H), 3.67 – 3.41 (m, 1H), (2.35 (s) + 2.34 (s), 3H), 1.36 – 0.96 (m, 6H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): (for the major isomer) 166.5, 161.5, 140.7, 137.5, 129.5, 126.7, 96.6, 59.0, 57.6, 49.3, 21.2, 20.4, 14.7; (for the minor isomer) 166.6, 161.6, 140.4, 137.1, 129.7, 128.0, 96.7, 64.4, 63.3, 53.6, 21.3, 20.3, 15.2.

HRMS (ESI) *m/z* calcd for $C_{15}H_{20}NO_2S$ $[M+H]^+$: 278.1215; found: 278.1222.

Ethyl 2-amino-5-decyl-4,5-dihydrothiophene-3-carboxylate (3t):

Yield: 75% (47 mg).



3t

Nature: Colourless oil.

R_f value = 0.42 [EtOAc:Petroleum ether = 1:9 (v/v)].

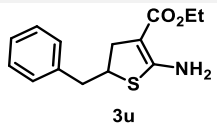
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.98 (brs, 2H), 4.16 – 4.10 (m, 2H), 3.72 – 3.64 (m, 1H), 3.09 (dd, *J* = 14.0, 8.1 Hz, 1H), 2.68 (dd, *J* = 14.0, 6.8 Hz, 1H), 1.72 – 1.67 (m, 3H), 1.34 – 1.24 (m, 19H), 0.87 (t, *J* = 6.8 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.7, 162.6, 91.6, 59.1, 49.2, 39.3, 36.6, 32.0, 29.7, 29.7, 29.6, 29.5, 28.3, 22.8, 14.8, 14.3.

HRMS (ESI) *m/z* calcd for $C_{17}H_{32}NO_2S$ $[M+H]^+$: 314.2148; found: 314.2145.

Ethyl 2-amino-5-benzyl-4,5-dihydrothiophene-3-carboxylate (3u):

Yield: 74% (39 mg).



3u

Nature: Colourless oil.

R_f value = 0.33 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.33 – 7.29 (m, 2H), 7.26 – 7.22 (m, 1H), 7.21 – 7.19 (m, 2H), 5.97 (brs, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.95 – 3.88 (m, 1H), 3.10 – 2.94 (m, 3H), 2.82 (dd, *J* = 14.1, 5.9 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.7, 162.7, 139.2, 129.1, 128.7, 126.9, 91.3, 59.1, 50.1, 42.5, 38.7, 14.8.

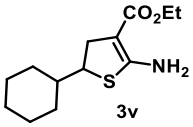
HRMS (ESI) *m/z* calcd for $C_{14}H_{18}NO_2S$ $[M+H]^+$: 264.1058; found: 264.1055.

Ethyl 2-amino-5-cyclohexyl-4,5-dihydrothiophene-3-carboxylate (3v):

Yield: 73% (37 mg).

Nature: Colourless oil.

R_f value = 0.36 [EtOAc:Petroleum ether = 1:9 (v/v)].



3v

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.98 (brs, 2H), 4.16 – 4.10 (m, 2H), 3.59 (q, *J* = 8.4 Hz, 1H), 3.03 (dd, *J* = 14.0, 8.3 Hz, 1H), 2.72 (dd, *J* = 14.0, 8.8 Hz, 1H), 1.82 – 1.72 (m, 4H), 1.66 – 1.64 (m, 1H), 1.58 – 1.48 (m, 1H), 1.29 – 0.93 (m, 5H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.5, 162.7, 92.1, 59.0, 55.7, 43.4, 37.0, 31.8, 30.8, 26.3, 26.2, 26.1, 14.8.

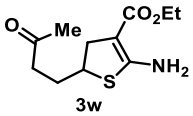
HRMS (ESI) *m/z* calcd for $C_{13}H_{22}NO_2S$ $[M+H]^+$: 256.1371; found: 256.1369.

Ethyl 2-amino-5-(3-oxobutyl)-4,5-dihydrothiophene-3-carboxylate (3w):

Yield: 64% (31 mg).

Nature: Colourless oil.

R_f value = 0.32 [EtOAc:Petroleum ether = 1:4 (v/v)].



3w

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.97 (brs, 2H), 4.14 (q, *J* = 7.0 Hz, 2H), 3.71 – 3.65 (m, 1H), 3.11 (dd, *J* = 14.1, 8.2 Hz, 1H), 2.70 (dd, *J* = 14.0, 3.9 Hz, 1H), 2.55 (t, *J* = 7.4 Hz, 2H), 2.16 (s, 3H), 2.00 – 1.91 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 207.8, 166.6, 161.7, 91.4, 59.2, 47.7, 41.4, 39.1, 30.3, 30.2, 14.8.

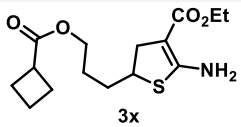
HRMS (ESI) *m/z* calcd for $C_{11}H_{17}NO_3SNa$ $[M+Na]^+$: 266.0827; found: 266.0819.

Ethyl 2-amino-5-(3-((cyclobutanecarbonyl)oxy)propyl)-4,5-dihydrothiophene-3-carboxylate (3x):

Yield: 75% (47 mg).

Nature: Colourless oil.

R_f value = 0.36 [EtOAc:Petroleum ether = 1:4 (v/v)].



3x

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.97 (brs, 2H), 4.27 – 4.10 (m, 2H), 4.07 (t, *J* = 5.8 Hz, 2H), 3.71 – 3.67 (m, 1H), 3.17 – 3.08 (m, 2H), 2.70 (dd, *J* = 14.0, 6.0 Hz, 1H), 2.32 – 2.14 (m, 4H), 2.03 – 1.85 (m, 2H), 1.80 – 1.67 (m, 4H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 175.6, 165.4, 162.1, 91.5, 63.9, 59.1, 48.3, 39.3, 38.2, 33.1, 27.2, 25.4, 18.6, 14.8.

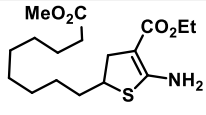
HRMS (ESI) *m/z* calcd for $C_{15}H_{24}NO_4S$ $[M+H]^+$: 314.1426; found: 314.1421.

Ethyl 2-amino-5-(9-methoxy-9-oxononyl)-4,5-dihydrothiophene-3-carboxylate (3y):

Yield: 71% (49 mg).

Nature: Colourless oil.

R_f value = 0.32 [EtOAc:Petroleum ether = 1:9 (v/v)].



3y

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.00 (brs, 2H), 4.16 – 4.10 (m, 2H), 3.69 – 3.63 (m, 1H), 3.66 (s, 3H), 3.08 (dd, *J* = 14.0, 8.1 Hz, 1H), 2.67 (dd, *J* = 14.0, 6.7 Hz, 1H), 2.29 (t, *J* = 7.5 Hz, 2H), 1.71 – 1.66 (m, 2H), 1.62 – 1.58 (m, 2H), 1.32 – 1.24 (m, 10H), 1.26 (t, *J* = 7.1 Hz, 3H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 174.5, 166.7, 162.4, 91.5, 59.1, 51.6, 49.1, 39.3, 36.6, 34.2, 29.5, 29.4, 29.3, 29.2, 28.2, 25.0, 14.8.

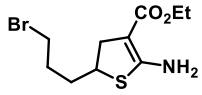
HRMS (ESI) *m/z* calcd for $C_{17}H_{30}NO_4S$ $[M+H]^+$: 344.1896; found: 344.1892.

Ethyl 2-amino-5-(3-bromopropyl)-4,5-dihydrothiophene-3-carboxylate (3z):

Yield: 53% (31 mg).

Nature: Colourless oil.

R_f value = 0.43 [EtOAc:Petroleum ether = 1:4 (v/v)].



3z

^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.98 (brs, 2H), 4.14 (q, *J* = 6.9 Hz, 2H), 3.72 – 3.65 (m, 1H), 3.41 (t, *J* = 6.4 Hz, 2H), 3.13 (dd, *J* = 14.0, 8.1 Hz, 1H), 2.72 (dd, *J* = 13.9, 5.8 Hz, 1H), 1.96 – 1.85 (m, 4H), 1.27 (t, *J* = 7.1 Hz, 3H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 166.6, 161.9, 91.4, 59.2, 47.8, 39.2, 35.2, 33.2, 31.0, 14.8.

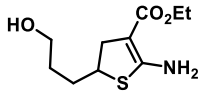
HRMS (ESI) *m/z* calcd for $C_{10}H_{16}NO_2S$ $[M-Br]^+$: 214.0902; found: 214.0898.

Ethyl 2-amino-5-(3-hydroxypropyl)-4,5-dihydrothiophene-3-carboxylate (3aa):

Yield: 65% (30 mg).

Nature: Colourless oil.

R_f value = 0.37 [EtOAc:Petroleum ether = 2:3 (v/v)].



3aa

^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.99 (brs, 2H), 4.30 – 4.11 (m, 2H), 3.72 – 3.65 (m, 3H), 3.12 (dd, *J* = 14.0, 8.1 Hz, 1H), 2.72 (dd, *J* = 14.0, 6.1 Hz, 1H), 1.82 – 1.77 (m, 2H), 1.68 – 1.61 (m, 2H), 1.34 – 1.24 (m, 3H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 166.7, 162.3, 91.5, 62.6, 59.1, 48.6, 39.3, 33.0, 31.1, 14.8.

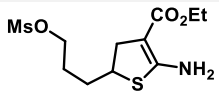
HRMS (ESI) *m/z* calcd for $C_{10}H_{18}NO_3S$ $[M+H]^+$: 232.1007; found: 232.1007.

Ethyl 2-amino-5-(3-((methylsulfonyl)oxy)propyl)-4,5-dihydrothiophene-3-carboxylate (3ab):

Yield: 63% (39 mg).

Nature: Colourless oil.

R_f value = 0.42 [EtOAc:Petroleum ether = 1:4 (v/v)].



3ab

^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.33 (brs, 2H), 4.23 – 4.18 (m, 2H), 4.04 – 3.98 (m, 2H), 3.69 – 3.66 (m, 1H), 3.17 (s, 3H), 2.99 (dd, *J* = 13.8, 8.1 Hz, 1H), 2.56 (dd, *J* = 13.8, 5.7 Hz, 1H), 1.74 – 1.68 (m, 4H), 1.17 (t, *J* = 7.1 Hz, 3H).

$^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ (ppm): 165.4, 163.0, 87.7, 70.1, 58.1, 46.5, 38.5, 36.6, 32.3, 27.0, 14.8.

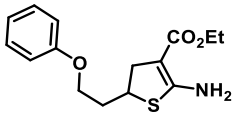
HRMS (ESI) *m/z* calcd for $C_{11}H_{19}NO_5S_2Na$ $[M+Na]^+$: 332.0602; found: 332.0610.

Ethyl 2-amino-5-(2-phenoxyethyl)-4,5-dihydrothiophene-3-carboxylate (3ac):

Yield: 70% (41 mg).

Nature: Colourless oil.

R_f value = 0.32 [EtOAc:Petroleum ether = 1:9 (v/v)].



3ac

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.31 – 7.27 (m, 2H), 6.97 – 6.93 (m, 1H), 6.90 – 6.88 (m, 2H), 5.99 (brs, 2H), 4.33 – 4.12 (m, 2H), 4.04 (t, *J* = 6.0 Hz, 2H), 3.98 – 3.91 (m, 1H), 3.18 (dd, *J* = 14.0, 8.0 Hz, 1H), 2.79 (dd, *J* = 14.0, 5.5 Hz, 1H), 2.24 – 2.13 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.7, 162.2, 158.7, 129.6, 121.0, 114.6, 91.3, 65.6, 59.2, 45.3, 39.2, 36.1, 14.8.

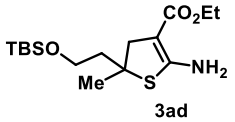
HRMS (ESI) *m/z* calcd for $C_{15}H_{20}NO_3S$ $[M+H]^+$: 294.1164; found: 294.1161.

Ethyl 2-amino-5-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-5-methyl-4,5-dihydrothiophene-3-carboxylate (3ad):

Yield: 62% (43 mg).

Nature: Colourless oil.

R_f value = 0.43 [EtOAc:Petroleum ether = 1:4 (v/v)].



3ad

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.94 (brs, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.77 – 3.73 (m, 2H), 2.93 (d, *J* = 14.0 Hz, 1H), 2.77 (d, *J* = 14.0 Hz, 1H), 2.10 – 2.03 (m, 1H), 1.95 – 1.89 (m, 1H), 1.50 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.90 (s, 9H), 0.06 (s, 6H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.9, 163.0, 90.7, 60.4, 59.0, 57.1, 47.4, 44.7, 28.3, 26.1, 18.4, 14.8, -5.2.

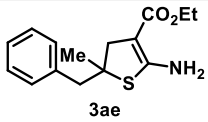
HRMS (ESI) *m/z* calcd for $C_{16}H_{32}NO_3SSi$ $[M+H]^+$: 346.1872; found: 346.1867.

Ethyl 2-amino-5-benzyl-5-methyl-4,5-dihydrothiophene-3-carboxylate (3ae):

Yield: 65% (36 mg).

Nature: Colourless oil.

R_f value = 0.33 [EtOAc:Petroleum ether = 1:9 (v/v)].



3ae

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.32 – 7.22 (m, 5H), 6.00 (brs, 2H), 4.19 – 4.11 (m, 2H), 3.10 (d, *J* = 13.4 Hz, 1H), 3.03 (d, *J* = 14.0 Hz, 1H), 2.98 (d, *J* = 13.4 Hz, 1H), 2.77 (d, *J* = 14.0 Hz, 1H), 1.45 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.8, 162.4, 137.7, 130.5, 128.1, 126.9, 91.2, 59.7, 59.0, 48.1, 46.1, 27.6, 14.8.

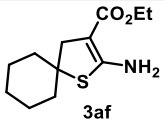
HRMS (ESI) *m/z* calcd for $C_{15}H_{20}NO_2S$ $[M+H]^+$: 278.1215; found: 278.1212.

Ethyl 2-amino-1-thiaspiro[4.5]dec-2-ene-3-carboxylate (3af):

Yield: 58% (28 mg).

Nature: Colourless oil.

R_f value = 0.32 [EtOAc:Petroleum ether = 1:9 (v/v)].



3af

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.93 (brs, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.82 (s, 2H), 2.01 – 1.97 (m, 2H), 1.67 – 1.56 (m, 6H), 1.50 – 1.40 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.9, 162.2, 91.0, 61.7, 59.1, 46.4, 39.6, 25.6, 24.4, 14.8.

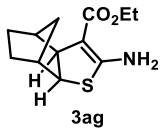
HRMS (ESI) *m/z* calcd for $C_{12}H_{20}NO_2S$ $[M+H]^+$: 242.1215; found: 242.1206.

Ethyl (3a*R*,4*S*,7*R*,7a*S*)-2-amino-3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[*b*]thiophene-3-carboxylate (3ag):

Yield: 63% (30 mg).

Nature: Colourless oil.

R_f value = 0.39 [EtOAc:Petroleum ether = 1:9 (v/v)].



3ag

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.00 (brs, 2H), 4.22 – 4.07 (m, 2H), 3.58 (dd, *J* = 8.7, 1.5 Hz, 1H), 3.29 (dd, *J* = 8.7, 1.0 Hz, 1H), 2.39 (d, *J* = 3.2 Hz, 1H), 2.19 (d, *J* = 3.6 Hz, 1H), 1.84 – 1.81 (m, 1H), 1.62 – 1.58 (m, 1H), 1.57 – 1.49 (m, 1H), 1.32 – 1.24 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.24 – 1.17 (m, 2H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.6, 164.2, 94.8, 58.9, 56.8, 52.4, 44.7, 43.1, 32.4, 28.5, 28.2, 14.8.

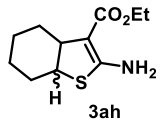
HRMS (ESI) *m/z* calcd for $C_{12}H_{18}NO_2S$ $[M+H]^+$: 240.1053; found: 240.1048.

Ethyl 2-amino-3a,4,5,6,7,7a-hexahydrobenzo[*b*]thiophene-3-carboxylate (3ah):

Yield: 62% (28 mg, combined yield as a 1.3:1 mixture of diastereomers).

Nature: Colourless oil.

R_f value = 0.37 [EtOAc:Petroleum ether = 1:9 (v/v)].



3ah

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): (for the mixture) 5.99 (brs, 2H), 4.32 – 4.22 (m, 2H), 4.17 – 3.86 (m, 1H), 3.65 – 3.25 (m, 1H), 2.48 – 2.21 (m, 1H), 2.04 – 1.93 (m, 1H), 1.85 – 1.72 (m, 2H), 1.70 – 1.43 (m, 4H), 1.33 – 1.29 (m, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 170.2, 169.1, 166.0, 165.4, 115.0, 64.2, 63.1, 47.4, 47.0, 42.4, 42.0, 34.8, 33.4, 29.1, 26.8, 26.3, 25.0, 23.7, 21.7, 14.4, 14.2.

HRMS (ESI) *m/z* calcd for $C_{11}H_{18}NO_2S$ $[M+H]^+$: 228.1058; found: 228.1055.

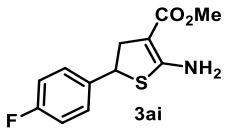
Methyl 2-amino-5-(4-fluorophenyl)-4,5-dihydrothiophene-3-carboxylate (3ai):[13]

Yield: 79% (40 mg).

Nature: White solid.

Mp: 95 – 97 °C

R_f value = 0.37 [EtOAc:Petroleum ether = 1:9 (v/v)].



3ai

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.38 (dd, *J* = 8.7, 1.3 Hz, 2H), 7.02 – 6.98 (m, 2H), 6.09 (brs, 2H), 4.82 (dd, *J* = 8.3, 7.4 Hz, 1H), 3.68 (s, 3H), 3.39 (dd, *J* = 14.3, 8.5 Hz, 1H), 3.10 (dd, *J* = 14.3, 7.2 Hz, 1H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.7, 162.3 (d, *J* = 247.4 Hz) 162.2, 137.6 (d, *J* = 3.3 Hz), 128.9 (d, *J* = 8.1 Hz), 115.7 (d, *J* = 21.6 Hz), 90.6, 50.7 (d, *J* = 2.6 Hz), 41.8.

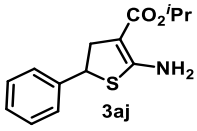
^{19}F NMR (377 MHz, $CDCl_3$) δ (ppm): -114.39 (s).

Isopropyl 2-amino-5-phenyl-4,5-dihydrothiophene-3-carboxylate (3aj):

Yield: 76% (40 mg).

Nature: Colourless gummy solid.

R_f value = 0.35 [EtOAc:Petroleum ether = 1:9 (v/v)].



3aj

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.43 (d, *J* = 7.1 Hz, 2H), 7.35 – 7.31 (m, 2H), 7.29 – 7.27 (m, 1H), 6.05 (brs, 2H), 5.07 – 5.00 (m, 1H), 4.87 (t, *J* = 8.3 Hz, 1H), 3.39 (dd, *J* = 14.3, 8.5 Hz, 1H), 3.14 (dd, *J* = 14.3, 8.0 Hz, 1H), 1.24 (d, *J* = 5.8 Hz, 3H), 1.23 (d, *J* = 5.7 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 167.1, 161.7, 141.6, 128.8, 127.9, 127.4, 91.6, 66.2, 51.6, 41.9, 22.4.

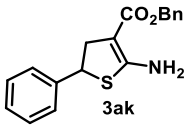
HRMS (ESI) *m/z* calcd for $C_{14}H_{18}NO_2S$ $[M+H]^+$: 264.1058; found: 264.1053.

Benzyl 2-amino-5-phenyl-4,5-dihydrothiophene-3-carboxylate (3ak):

Yield: 72% (45 mg).

Nature: White solid.

Mp: 58 – 59 °C



3ak

R_f value = 0.32 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.44 – 7.42 (m, 2H), 7.37 – 7.26 (m, 8H), 6.12 (brs, 2H), 5.21 – 5.13 (m, 2H), 4.88 (t, *J* = 8.2 Hz, 1H), 3.45 (dd, *J* = 14.3, 8.6 Hz, 1H), 3.21 (dd, *J* = 14.3, 7.9 Hz, 1H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.0, 163.0, 141.5, 137.2, 128.8, 128.6, 128.0, 127.9, 127.8, 127.4, 90.8, 64.9, 51.7, 41.7.

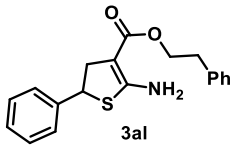
HRMS (ESI) *m/z* calcd for $C_{18}H_{18}NO_2S$ $[M+H]^+$: 312.1053; found: 312.1049.

Phenethyl 2-amino-5-phenyl-4,5-dihydrothiophene-3-carboxylate (3al):

Yield: 74% (48 mg).

Nature: White solid.

Mp: 82 – 84 °C



3al

R_f value = 0.31 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.43 – 7.41 (m, 2H), 7.36 – 7.27 (m, 5H), 7.24 – 7.20 (, 3H), 6.04 (brs, 2H), 4.85 (t, *J* = 8.0 Hz, 1H), 4.32 (t, *J* = 6.8 Hz, 2H), 3.38 (dd, *J* = 14.3, 8.5 Hz, 1H), 3.15 (dd, *J* = 14.3, 7.5 Hz, 1H), 2.95 (t, *J* = 6.9 Hz, 2H).

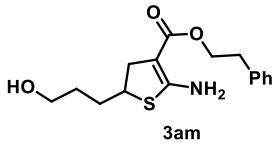
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.2, 162.4, 141.6, 138.5, 129.1, 128.8, 128.5, 127.9, 127.3, 126.5, 90.9, 63.9, 51.5, 41.5, 35.6.

HRMS (ESI) *m/z* calcd for $C_{19}H_{19}NO_2SNa$ $[M+Na]^+$: 348.1034; found: 348.1025.

Phenethyl 2-amino-5-(3-hydroxypropyl)-4,5-dihydrothiophene-3-carboxylate (3am):

Yield: 63% (39 mg).

Nature: Colourless oil.



3am

R_f value = 0.38 [EtOAc:Petroleum ether = 2:3 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.32 – 7.28 (m, 2H), 7.24 – 7.20 (m, 3H), 5.92 (brs, 2H), 4.30 (t, *J* = 7.0 Hz, 2H), 3.73 – 3.67 (m, 1H), 3.66 (d, *J* = 6.3 Hz, 2H), 3.10 (dd, *J* = 14.0, 8.1 Hz, 1H), 2.95 (t, *J* = 7.0 Hz, 2H), 2.70 (dd, *J* = 14.0, 6.0 Hz, 1H), 1.82 – 1.76 (m, 2H), 1.67 – 1.60 (m, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.3, 162.5, 138.6, 129.1, 128.6, 126.5, 91.4, 63.8, 62.6, 48.7, 39.2, 35.7, 33.0, 31.0.

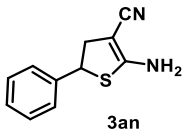
HRMS (ESI) *m/z* calcd for $C_{16}H_{22}NO_3S$ $[M+H]^+$: 308.1320; found: 308.1321.

2-Amino-5-phenyl-4,5-dihydrothiophene-3-carbonitrile (3an):[13]

Yield: 52% (21 mg).

Nature: White solid.

Mp: 79 – 81 °C



3an

R_f value = 0.43 [EtOAc:Petroleum ether = 1:4 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.43– 7.40 (m, 2H), 7.37 – 7.29 (m, 3H), 4.97 (t, *J* = 8.2 Hz, 1H), 4.76 (brs, 2H), 3.29 (dd, *J* = 13.9, 8.3 Hz, 1H), 3.11 (dd, *J* = 13.9, 8.0 Hz, 1H).

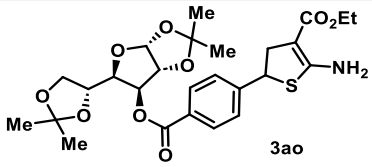
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 162.3, 140.1, 129.0, 128.4, 127.3, 117.8, 69.9, 53.6, 42.2.

Ethyl 2-amino-5-(4-((((3a*R*,5*R*,6*S*,6a*R*)-5-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl)oxy)carbonyl)phenyl)-4,5-dihydrothiophene-3-carboxylate (3ao):

Yield: 56% (60 mg)

Nature: Colourless gummy solid.

R_f value = 0.35 [EtOAc:Petroleum ether = 1:4 (v/v)].



3ao

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.99 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 8.3 Hz, 2H), 6.08 (brs, 2H), 5.94 (d, *J* = 3.7 Hz, 1H), 5.49 (d, *J* = 2.6 Hz, 1H), 4.85 (dd, *J* = 8.5, 6.8 Hz, 1H), 4.62 (d, *J* = 3.7 Hz, 1H), 4.37 – 4.31 (m, 2H), 4.19 – 4.07 (m, 4H), 3.45 (dd, *J* = 14.3, 8.6 Hz, 1H), 3.16 – 3.10 (m, 1H), 1.56 (s, 3H), 1.42 (s, 3H), 1.32 (s, 3H), 1.28 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.3, 164.9, 161.5, 147.8, 130.3, 129.1, 127.5, 112.5, 109.6, 105.3, 90.9, 83.5, 80.1, 76.8, 72.7, 67.4, 59.3, 50.6, 41.5, 27.0, 26.9, 26.3, 25.4, 14.8.

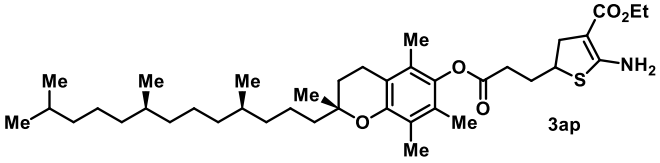
HRMS (ESI) *m/z* calcd for $C_{26}H_{34}NO_9S$ $[M+H]^+$: 536.1954; found: 536.1963.

Ethyl 2-amino-5-(3-oxo-3-(((*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl) chroman-6-yl)oxy)propyl)-4,5-dihydrothiophene-3-carboxylate (3ap):

Yield: 53% (70 mg).

Nature: Colourless oil.

R_f value = 0.38 [EtOAc:Petroleum ether = 1:4 (v/v)].



3ap

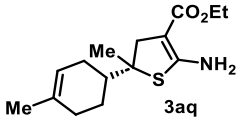
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.01 (brs, 2H), 4.33 – 4.12 (m, 2H), 3.82 – 3.76 (m, 1H), 3.19 (dd, *J* = 14.1, 8.1 Hz, 1H), 2.80 (dd, *J* = 14.2, 5.1 Hz, 1H), 2.72 (t, *J* = 7.4 Hz, 2H), 2.58 (t, *J* = 6.7 Hz, 2H), 2.21 – 2.14 (m, 2H), 2.08 (s, 3H), 2.00 (s, 3H), 1.96 (s, 3H), 1.85 – 1.72 (m, 2H), 1.62 – 1.33 (m, 9H), 1.30 – 1.23 (m, 12H), 1.16 – 1.03 (m, 6H), 0.87 – 0.83 (m, 12H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 171.5, 166.6, 161.8, 149.6, 140.5, 126.7, 124.9, 123.2, 117.5, 91.4, 75.2, 59.2, 47.5, 39.5, 39.1, 37.7, 37.6, 37.5, 37.4, 32.9, 32.8, 32.0, 31.8, 31.1, 28.1, 24.9, 24.6, 22.9, 22.8, 21.2, 20.7, 19.9, 19.8, 19.7, 19.6, 14.8, 13.2, 12.3, 12.0.

HRMS (ESI) *m/z* calcd for $C_{39}H_{64}NO_5S$ $[M+H]^+$: 658.4505; found: 658.4508.

Ethyl (*S*)-2-amino-5-methyl-5-((*S*)-4-methylcyclohex-3-en-1-yl)-4,5-dihydrothiophene-3-carboxylate (3aq):

Yield: 52% (29 mg, combined yield as a 1.1:1 mixture of diastereomers).



Nature: Colourless oil.

R_f value = 0.33 [EtOAc:Petroleum ether = 1:9 (v/v)].

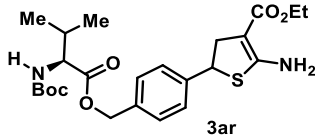
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): (for the mixture) 5.93 (brs, 2H), 5.37 – 5.36 (m, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 2.97 – 2.93 (m, 1H), 2.75 – 2.66 (m, 1H), 2.10 – 1.69 (m, 7H), 1.65 (s, 3H), {1.46 (s) + 1.45 (s), 3H}, 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): (for the mixture) 166.9, 166.8, 162.1, 162.0, 134.3, 134.1, 120.3, 120.1, 91.5, 91.4, 59.1, 59.0, 44.7, 44.6, 31.0, 30.9, 29.9, 28.7, 27.7, 26.7, 25.6, 25.5, 25.2, 23.4, 14.8.

HRMS (ESI) *m/z* calcd for $C_{15}H_{27}N_2O_2S$ $[M+NH_4]^+$: 299.1793; found: 299.1785.

Ethyl 2-amino-5-(4-((((*tert*-butoxycarbonyl)-*L*-valyl)oxy)methyl)phenyl)-4,5-dihydrothiophene-3-carboxylate (3ar):

Yield: 62% (59 mg).



Nature: Colourless gummy solid.

R_f value = 0.30 [EtOAc:Petroleum ether = 1:4 (v/v)].

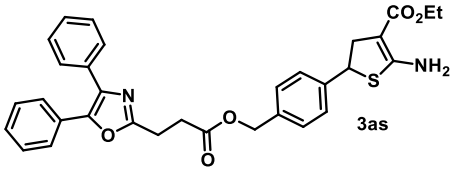
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.40 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 6.14 (brs, 2H), 5.12 (q, *J* = 12.5 Hz, 2H), 5.03 (d, *J* = 9.0 Hz, 1H), 4.82 (t, *J* = 8.0 Hz, 1H), 4.27 – 4.20 (m, 1H), 4.17 – 4.08 (m, 2H), 3.38 (dd, *J* = 14.3, 8.5 Hz, 2H), 3.11 (dd, *J* = 14.3, 7.4 Hz, 1H), 2.19 – 2.08 (m, 1H), 1.42 (s, 9H), 1.24 (t, *J* = 7.1 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H), 0.83 (d, *J* = 6.9 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 172.4, 166.4, 162.0, 155.8, 142.0, 135.1, 128.7, 127.5, 90.9, 79.9, 66.6, 59.1, 58.6, 51.0, 41.7, 31.3, 28.4, 19.1, 17.6, 14.7.

HRMS (ESI) *m/z* calcd for $C_{24}H_{35}N_2O_6S$ $[M+H]^+$: 479.2216; found: 479.2210.

Ethyl 2-amino-5-(4-(((3-(4,5-diphenyloxazol-2-yl)propanoyl)oxy)methyl)phenyl)-4,5-dihydrothiophene-3-carboxylate (3as):

Yield: 66% (73 mg).



Nature: Colourless gummy solid.

R_f value = 0.37 [EtOAc:Petroleum ether = 1:4 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.63 – 7.61 (m, 2H), 7.57 – 7.54 (m, 2H), 7.39 – 7.28 (m, 10H), 6.08 (brs, 2H), 5.15 (s, 2H), 4.80 (t, *J* = 8.0 Hz, 1H), 4.18 – 4.12 (m, 2H), 3.37 (dd, *J* = 14.3, 8.5 Hz, 1H), 3.21 (t, *J* = 7.4 Hz, 2H), 3.10 (dd, *J* = 14.3, 7.5 Hz, 1H), 2.97 (t, *J* = 7.4 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).

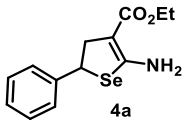
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 172.0, 166.4, 162.0, 161.8, 145.5, 141.8, 135.4, 135.2, 132.5, 129.0, 128.8, 128.7, 128.6, 128.2, 128.0, 127.6, 126.6, 91.0, 66.3, 59.2, 51.1, 41.7, 31.2, 23.6, 14.8.

HRMS (ESI) *m/z* calcd for $C_{32}H_{31}N_2O_5S$ $[M+H]^+$: 555.1954; found: 555.1953.

Ethyl 2-amino-5-phenyl-4,5-dihydroselenophene-3-carboxylate (4a):[14]

Yield: 66% (39 mg).

Nature: White solid.



4a

Mp: 122 – 124 °C

R_f value = 0.35 [EtOAc:Petroleum ether = 1:9 (v/v)].

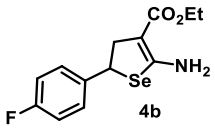
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.44 (d, *J* = 7.9 Hz, 2H), 7.33 – 7.29 (m, 2H), 7.27 – 7.23 (m, 1H), 6.24 (brs, 2H), 5.10 (t, *J* = 7.9 Hz, 1H), 4.18 – 4.12 (m, 2H), 3.46 (dd, *J* = 14.7, 7.7 Hz, 1H), 3.32 (dd, *J* = 14.7, 8.2 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.7, 160.7, 142.2, 128.8, 127.8, 127.5, 95.7, 59.3, 48.6, 43.0, 14.7.

Ethyl 2-amino-5-(4-fluorophenyl)-4,5-dihydroselenophene-3-carboxylate (4b):

Yield: 67% (42 mg).

Nature: White solid.



4b

Mp: 61 – 63 °C

R_f value = 0.38 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.41 (dd, *J* = 8.6, 1.3 Hz, 2H), 7.01 – 6.96 (m, 2H), 6.25 (brs, 2H), 5.06 (t, *J* = 7.7 Hz, 1H), 4.18 – 4.12 (m, 2H), 3.44 (dd, *J* = 14.7, 7.7 Hz, 1H), 3.27 (dd, *J* = 14.7, 7.9 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.6, 162.2 (d, *J* = 246.4 Hz), 160.5, 138.2 (d, *J* = 3.3 Hz), 129.1 (d, *J* = 8.2 Hz), 115.6 (d, *J* = 21.4 Hz), 95.4, 59.4, 47.6, 43.2, 14.7.

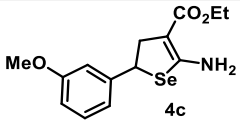
^{19}F NMR (377 MHz, $CDCl_3$) δ (ppm): -114.56 (s).

HRMS (ESI) *m/z* calcd for $C_{13}H_{15}FNO_2Se$ $[M+H]^+$: 316.0252; found: 316.0252.

Ethyl 2-amino-5-(3-methoxyphenyl)-4,5-dihydroselenophene-3-carboxylate (4c):

Yield: 69% (45 mg).

Nature: Colourless oil.



4c

R_f value = 0.33 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.24 – 7.20 (m, 1H), 7.03 – 7.00 (m, 2H), 6.80 – 6.78 (m, 1H), 6.26 (brs, 2H), 5.07 (t, *J* = 8.0 Hz, 1H), 4.18 – 4.12 (m, 2H), 3.80 (s, 3H), 3.44 (dd, *J* = 14.7, 7.7 Hz, 1H), 3.31 (dd, *J* = 14.7, 8.3 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H).

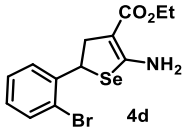
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.6, 160.7, 159.8, 143.7, 129.8, 119.9, 113.2, 113.1, 95.6, 59.3, 55.4, 48.5, 42.8, 14.7.

HRMS (ESI) *m/z* calcd for $C_{14}H_{18}NO_3Se$ $[M+H]^+$: 328.0452; found: 328.0445.

Ethyl 2-amino-5-(2-bromophenyl)-4,5-dihydroselenophene-3-carboxylate (4d):

Yield: 56% (42 mg).

Nature: White solid.



4d

Mp: 74 – 76 °C

R_f value = 0.34 [EtOAc:Petroleum ether = 1:9 (v/v)].

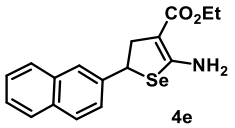
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.57 – 7.53 (m, 2H), 7.30 – 7.26 (m, 1H), 7.12 – 7.08 (m, 1H), 6.23 (brs, 2H), 5.20 (t, *J* = 5.9 Hz, 1H), 4.22 – 4.17 (m, 2H), 3.42 (d, *J* = 6.5 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.7, 160.5, 142.3, 132.9, 128.9, 128.1, 127.5, 124.3, 95.6, 59.4, 46.2, 40.0, 14.8.

HRMS (ESI) *m/z* calcd for $C_{13}H_{15}BrNO_2Se$ $[M+H]^+$: 375.9451; found: 375.9458.

Ethyl 2-amino-5-(naphthalen-2-yl)-4,5-dihydroselenophene-3-carboxylate (4e):

Yield: 52% (36 mg).



4e

Nature: White solid.

Mp: 92 – 94 °C

R_f value = 0.38 [EtOAc:Petroleum ether = 1:9 (v/v)].

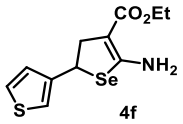
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.82 – 7.78 (m, 4H), 7.63 – 7.61 (m, 1H), 7.49 – 7.44 (m, 2H), 6.27 (brs, 2H), 5.28 (t, *J* = 7.8 Hz, 1H), 4.18 (q, *J* = 7.0 Hz, 2H), 3.53 (dd, *J* = 14.7, 7.7 Hz, 1H), 3.44 (dd, *J* = 14.7, 7.8 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.7, 160.7, 139.5, 133.3, 133.0, 128.8, 128.0, 127.8, 126.5, 126.2, 125.9, 125.7, 95.7, 59.3, 48.8, 42.8, 14.8.

HRMS (ESI) *m/z* calcd for $C_{17}H_{18}NO_2Se$ $[M+H]^+$: 348.0503; found: 348.0503.

Ethyl 2-amino-5-(thiophen-3-yl)-4,5-dihydroselenophene-3-carboxylate (4f):

Yield: 61% (37 mg).



4f

Nature: White solid.

Mp: 75 – 77 °C

R_f value = 0.36 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.29 – 7.27 (m, 1H), 7.19 – 7.15 (m, 2H), 6.23 (brs, 2H), 5.16 (t, *J* = 7.6 Hz, 1H), 4.18 – 4.13 (m, 2H), 3.43 (dd, *J* = 14.5, 7.4 Hz, 1H), 3.29 (dd, *J* = 14.5, 7.9 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 166.7, 160.8, 142.8, 127.1, 126.5, 121.5, 95.7, 59.3, 43.4, 42.6, 14.8.

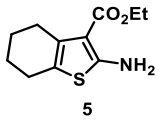
HRMS (ESI) *m/z* calcd for $C_{11}H_{14}NO_2SSe$ $[M+H]^+$: 303.9910; found: 303.9916.

6. Synthetic Transformations of Photo-Annulation Products:

Aromatization to 2-aminothiophenes 5:

A 100 mL round bottom flask equipped with a magnetic stir bar was charged with 2-amino-dihydrothiophene **3ah** (455 mg, 2.0 mmol), DDQ (681 mg, 3.0 mmol) and benzene (40 mL). The reaction mixture was refluxed for 2 h. After the completion of the reaction, the mixture was quenched with saturated sodium sulfite and extracted with ethyl acetate (2×25 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The solution was concentrated, and the residue was purified by silica gel column chromatography (230−400 mesh) using EtOAc/petroleum ether as eluent to afford the corresponding 2-amino-thiophenes product **5**.

Ethyl 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (5):[15]



Yield: 66% (297 mg).

Nature: Yellow solid.

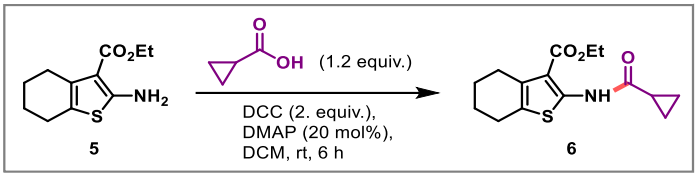
Mp: 114 – 116 °C

R_f value = 0.51 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.22 (brs, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.60 – 2.58 (m, 2H), 2.40 – 2.39 (m, 2H), 1.69 – 1.63 (m, 4H), 1.23 (t, *J* = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 165.1, 163.0, 131.3, 115.5, 102.6, 58.7, 26.6, 24.0, 22.9, 22.5, 14.4.

Amine to cyclopropane amide 6:

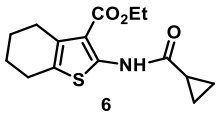


To the ice-cooled solution of cyclopropane carboxylic acid (48 mg, 0.6 mmol) in dry DCM (5 mL), catalytic amount of DMAP (12 mg, 0.1 mmol) and amine compound **5** (113 mg, 0.5 mmol) were added. Then, the mixture was allowed to stir for 15 minutes to get a homogenous reaction mixture, and DCC (206 mg, 1.0 mmol) was added at once under the same condition. Then cooling conditions were removed off, and the reaction mixture was allowed to stir for 6 h at room temperature. Conversion into amide was checked with TLC and filtered through a short pad of celite to remove the solid particles. Then the filtrate was concentrated under vacuo and purified by flash column chromatography on silica gel (EtOAc/ petroleum ether) to afford the corresponding product **6**.

Ethyl 2-(cyclopropanecarboxamido)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (6):

Yield: 73% (107 mg).

Nature: Pale-yellow solid.



6

Mp: 122 – 124 °C

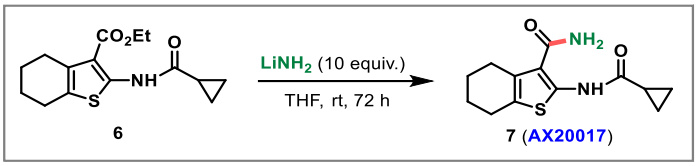
R_f value = 0.42 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 11.47 (brs, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 2.76 (t, *J* = 4.8 Hz, 2H), 2.62 (t, *J* = 4.7 Hz, 2H), 1.78 – 1.77 (m, 4H), 1.69 – 1.64 (m, 1H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.15 – 1.11 (m, 2H), 0.94 – 0.89 (m, 2H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 170.9, 166.9, 148.1, 130.7, 126.5, 111.0, 60.5, 26.5, 24.5, 23.1, 23.0, 15.6, 14.5, 8.8.

HRMS (ESI) *m/z* calcd for $C_{15}H_{20}NO_3S$ $[M+H]^+$: 294.1164; found: 294.1172.

Synthesis of AX20017: Ester to amide 7:[16]

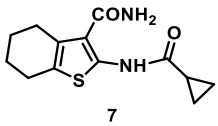


Lithium amide (46 mg, 2.0 mmol) was added in one portion to the solution of ester compound **6** (59 mg, 0.2 mmol) in dry THF (2 mL) in a dry culture tube. The air-tight closed reaction mixture was stirred at rt for 72 h. After the completion of the reaction (monitored by TLC), the reaction crude was poured onto crushed ice with continuous stirring in a fume hood. The pH of the solution was adjusted to between 4 and 5 with 1 M aqueous HCl. The precipitated product was filtered out, washed with water (2 mL) and hexane (2 mL), and dried. The crude product was then recrystallized from ethanol.

2-(cyclopropanecarboxamido)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide (7):[16]

Yield: 72% (38 mg).

Nature: Yellow solid.



7

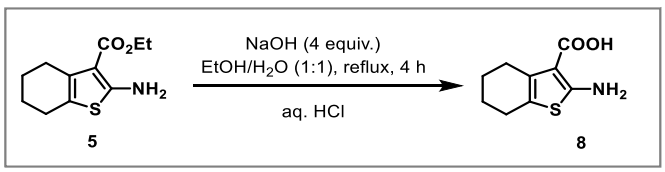
Mp: 217 – 219 °C

R_f value = 0.33 [EtOAc:Petroleum ether = 2:3 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 12.22 (brs, 1H), 5.94 (brs, 2H), 2.71 (t, *J* = 4.9 Hz, 2H), 2.65 (t, *J* = 5.1 Hz, 2H), 1.85 – 1.79 (m, 4H), 1.69 – 1.63 (m, 1H), 1.12 – 1.08 (m, 2H), 0.92 – 0.87 (m, 2H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 171.0, 168.6, 147.1, 127.4, 127.2, 112.5, 26.6, 24.4, 23.0, 22.7, 15.6, 8.7.

Ester hydrolysis to Acid 8:[17]



A 10 mL round bottom flask equipped with a magnetic stir bar was charged with 2-amino-thiophene **5** (113 mg, 0.5 mmol), NaOH (80 mg, 2 mmol) and ethanol/water (1:1) (2 mL). The reaction mixture was refluxed for 4 h. After the completion of the reaction, ethanol was evaporated and the aqueous phase

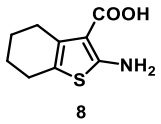
was acidified by 2M HCl. The precipitated solid was collected by filtration and washed with water to afford the corresponding acid product **8**.

2-Amino-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic acid (8):[18]

Yield: 82% (81 mg).

Nature: White solid.

Mp: 155 – 157 °C



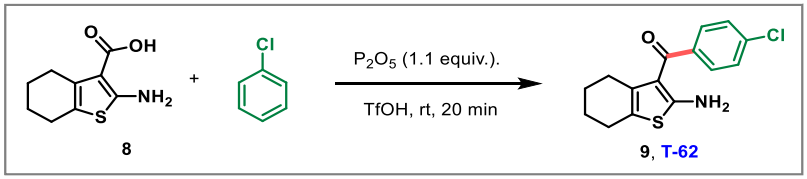
8

R_f value = 0.32 [EtOAc:Petroleum ether = 3:7 (v/v)].

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.75 (brs, 1H), 7.18 (brs, 2H), 2.57 (t, *J* = 5.5 Hz, 2H), 2.40 (t, *J* = 5.4 Hz, 2H), 1.69 – 1.62 (m, 4H).

^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 166.9, 162.8, 131.8, 115.1, 103.2, 26.6, 24.0, 22.9, 22.5.

Synthesis of T-62: Acid to Ketone 9:[19]



8 **9**, **T-62**

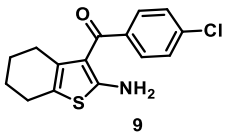
A 25 mL round bottom flask equipped with a magnetic stir bar was charged with acid compound **5** (39 mg, 0.2 mmol), chlorobenzene (26 µL, 0.22 mmol), P_2O_5 (31 mg, 0.22 mmol) and TfOH (2 mL). The reaction mixture was stirred at rt for 30 minutes. After the completion of the reaction, the reaction crude was quenched with 6 mL of ice water, and the whole was basified by 2 M aqueous NaOH to pH 12. The solution was extracted with dichloromethane (3×10 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The solution was concentrated and residue was purified by silica gel column chromatography (230−400 mesh) using acetone/petroleum ether as eluent to afford the corresponding product **9**.

(2-Amino-4,5,6,7-tetrahydrobenzo[*b*]thiophen-3-yl)(4-chlorophenyl)methanone (9):[20]

Yield: 79% (46 mg).

Nature: Yellow solid.

Mp: 123 – 125 °C



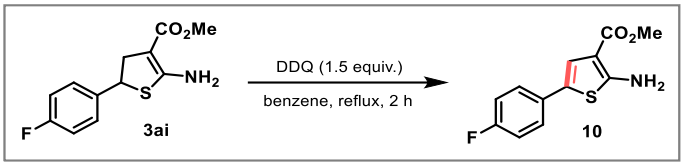
9

R_f value = 0.41 [EtOAc:Petroleum ether = 1:4 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.43 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 8.5 Hz, 2H), 6.73 (brs, 2H), 2.51 (t, *J* = 6.3 Hz, 2H), 1.80 (t, *J* = 6.1 Hz, 2H), 1.76 – 1.70 (m, 2H), 1.52 – 1.46 (m, 2H).

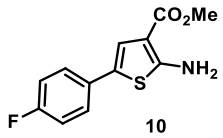
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 191.4, 165.0, 140.7, 136.4, 131.0, 129.1, 128.4, 118.7, 115.7, 28.2, 24.8, 23.2, 22.9.

Aromatization to 2-aminothiophenes 10:



A culture tube equipped with a magnetic stir bar was charged with 2-amino-dihydrothiophene **3ai** (51 mg, 0.2 mmol), DDQ (68 mg, 0.3 mmol) and benzene (4 mL). The reaction mixture was refluxed for 2 h. After the completion of the reaction, the mixture was quenched with saturated sodium sulfite and extracted with ethyl acetate (2×5 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The solution was concentrated and residue was purified by silica gel column chromatography (230−400 mesh) using EtOAc/petroleum ether as eluent to afford the corresponding 2-aminothiophenes product **10**.

Methyl 2-amino-5-(4-fluorophenyl)thiophene-3-carboxylate (10):[13]



Yield: 74% (37 mg).

Nature: White solid

Mp: 193 – 195 °C

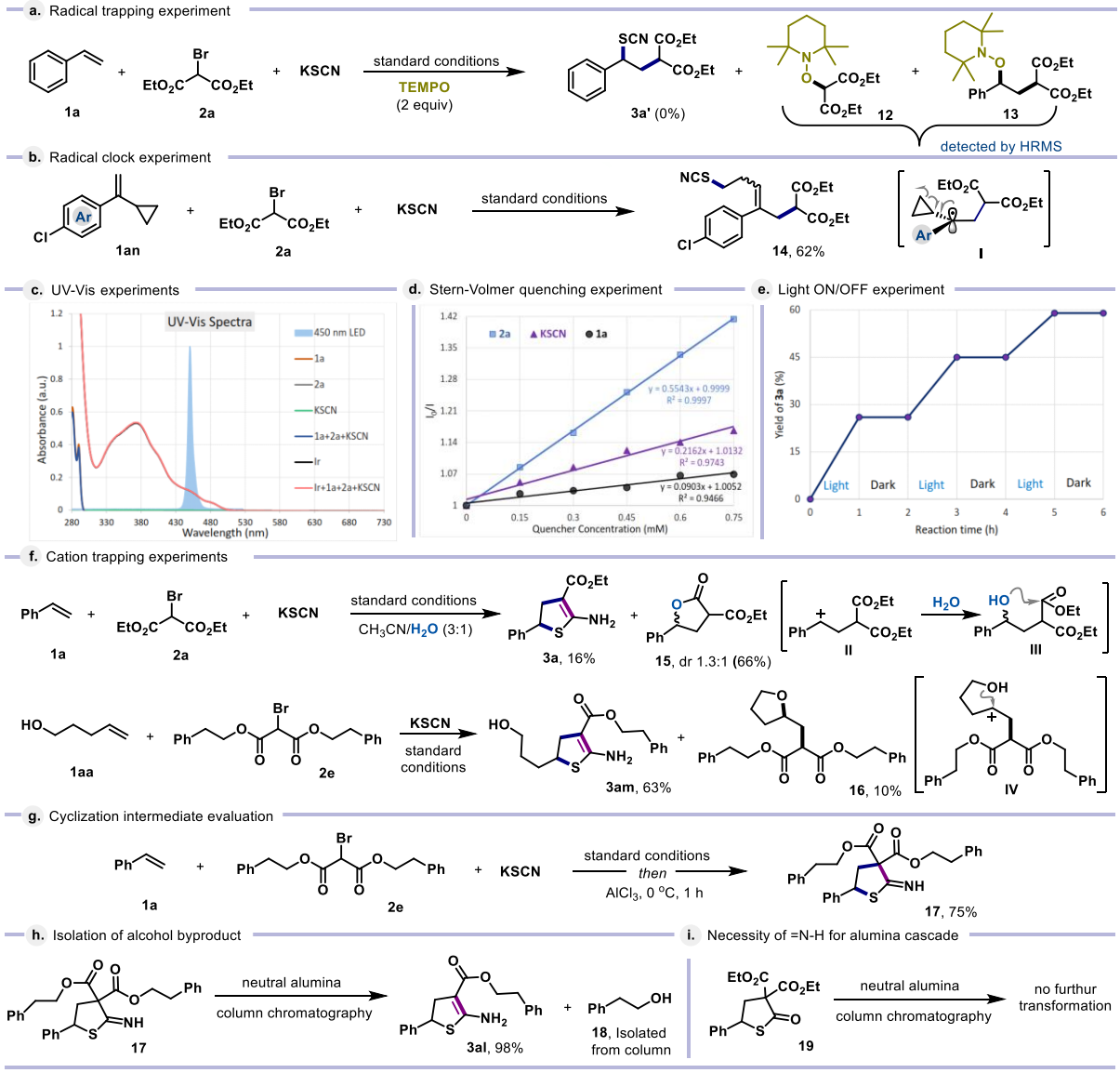
R_f value = 0.32 [EtOAc:Petroleum ether = 1:19 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.38 (dd, *J* = 8.9, 1.5 Hz, 2H), 7.14 (s, 1H), 7.05 – 7.00 (m, 2H), 6.00 (brs, 2H), 3.83 (s, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 165.9, 162.2, 161.9 (d, *J* = 247.4 Hz), 130.3 (d, *J* = 3.0 Hz), 126.5 (d, *J* = 7.9 Hz), 124.0, 121.2, 115.9 (d, *J* = 21.8 Hz), 107.7, 51.3.

^{19}F NMR (377 MHz, $CDCl_3$) δ (ppm): -115.56 (s).

7. Mechanistic Studies:



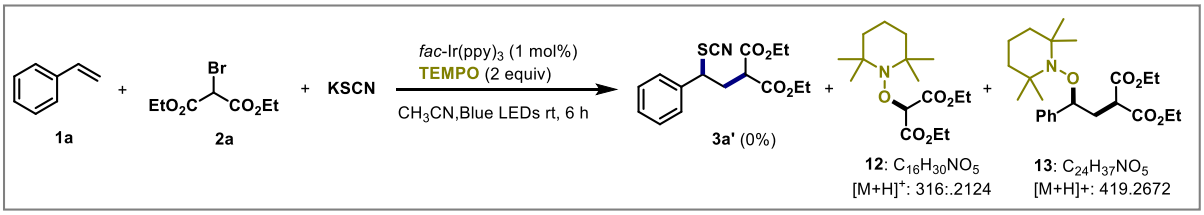
Scheme S1: Mechanistic Studies.

Disscussion: To gain insight into the mechanism of this photo-annulation process, several experiments were conducted (Scheme S1). The addition of TEMPO (a radical-trapping reagent) to the reaction resulted in complete inhibition with concomitant detection of malonyl-TEMPO **12** and benzyl-TEMPO **13** adducts (Scheme S1a), supporting the formation of a malonyl radical and its subsequent addition to styrene. Moreover, the reaction of *α*-cyclopropyl-4-chlorostyrene **1an** with **2a** generated the ring-opened product **14**, again confirming the initial formation of the malonyl radical in this process (Scheme S1b). UV-Vis studies of the reaction components and their combination with the normalized emission spectrum of blue LEDs eliminates the formation of EDA complex as well as the possibility of direct excitation of reacting compounds in this current protocol (Scheme S1c).[21] Stern-Volmer fluorescence quenching experiment reveals bromomalonates to be effective quenchers of the excited state photocatalyst, with malonyl radicals being the initiators of the reaction (Scheme S1d). Light on/off used

in experiment confirmed that continuous light irradiation is essential for the carbothiocyanation step to proceed (Scheme S1e). The formation of carbocation intermediate was supported by conducting the reaction in a mix of acetonitrile and water, during which trapping of carbocation **II** with more nucleophilic water occurred to give *γ*–lactone **15** via formation of *γ*–hydroxymalonate intermediate **III** (Scheme S1f).[22] When unactivated alkene (4-penten-1-ol, **1aa**) reacted under standard condition, desired 2-amino-dihydrothiophene derivative **3am** and tetrahydrofuran **17** was observed. The isolated byproduct tetrahydrofuran **17** (10%), providing direct proof of intramolecular trapping of the aliphatic carbocation.[23] When 2-imino-hydrothiophene product (Scheme S1g) was passed through alumina column, phenethyl alcohol **18** was isolated along with **3al**, indicating one of the ester was hydrolyzed in alumina before its decarboxylation (Scheme S1h). Interestingly, a similar gem-ester containing thiolactone **19** during alumina column-chromatography did not show any reactivity, illustrating that imino-H (=N-H) might have a key role in the hydrolysis event (Scheme S1i). The quantum yield of the three-component reaction to **3a** was calculated to be $\Phi = 0.11 < 1$ (*vide infra*). This, along with the above carbocation trapping experiments, suggests a radical-polar crossover pathway for the photocatalytic carbothiocyanation reaction.

7.1. Radical Trapping Experiment:

A radical trapping experiment was performed under the standard reaction condition to explore the reaction mechanism. In the presence of TEMPO (2 equiv.) free radical, the reaction of styrene **1a** (2 equiv.), diethyl 2-bromomalonate **2a** (1 equiv.), and potassium thiocyanate (2 equiv.) were fully suppressed and no desired product **3a'** was formed. Very importantly, a trace amount of TEMPO adducts **12** and **13** were detected in HRMS analysis from the crude reaction mixture, implying that the mechanism of this photo-reaction involves the generation of malonyl radicals from **2a**. This newly generated malonyl radical coupled with TEMPO to provide **12**. Additionally, the existence of **13** suggests that the benzyl radical species is also the intermediate of this reaction.



An oven-dried culture tube equipped with a magnetic stir bar was charged with *fac*-Ir(ppy)$_3$ (1.3 mg, 0.002 mmol, 1 mol%), diethyl 2-bromomalonate **2a** (34 mg, 0.2 mmol), potassium thiocyanate (39 mg, 0.4 mmol) and dry acetonitrile (2 mL). The tube was sealed with a Teflon screw cap before styrene **1a** (46 µL, 0.4 mmol) and TEMPO free radical (63 mg, 0.4 mmol) were added to it. Then, the reaction mixture was degassed by Freeze-Pump-Thaw cycles with argon and irradiated at rt with 12 W blue LEDs at a distance of approximately 5 cm for 6 h. A high-speed fan was used to maintain the temperature. After 6 h, no desired carbo-thiocyanation product **3a'** was formed. A trace amount of the TEMPO adducts **12** and **13** were detected in HRMS analysis from the crude reaction mixture. These results suggested that the reaction passes through the radical pathway.

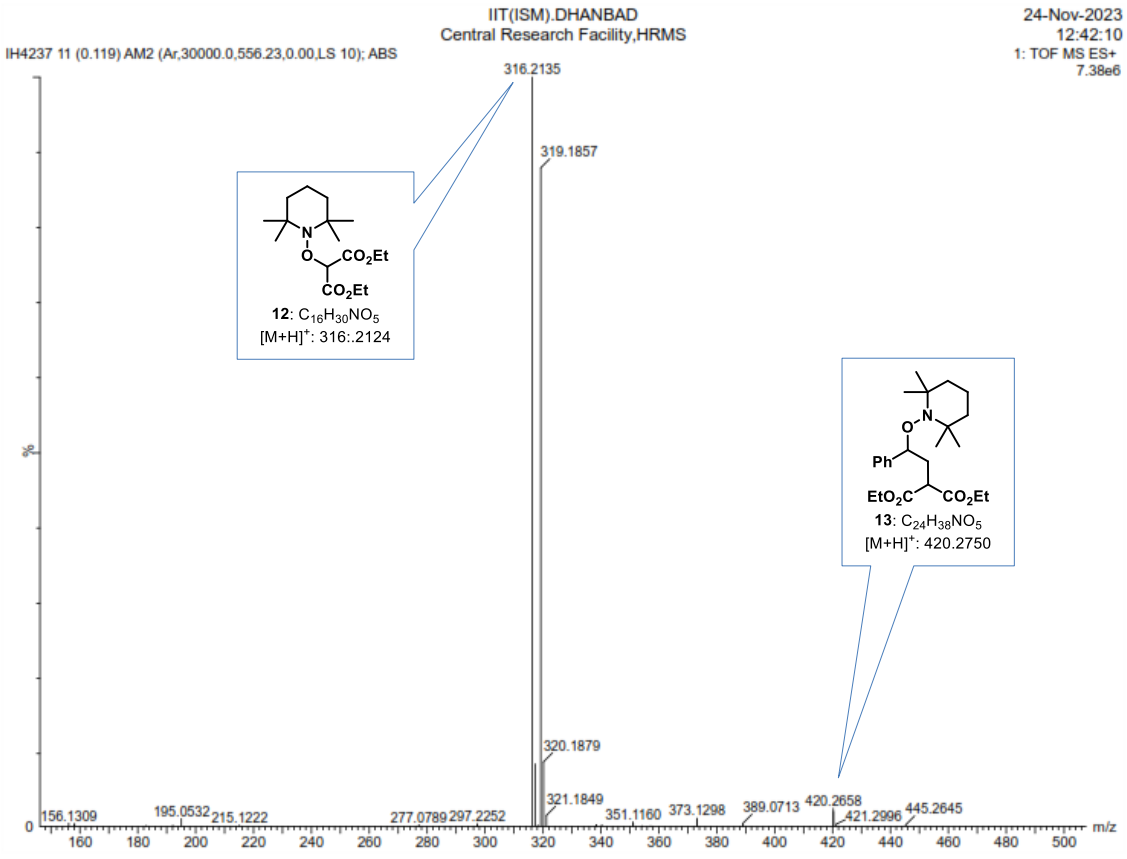
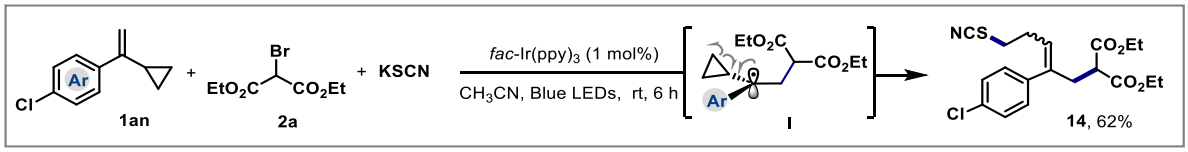


Figure S6: HRMS of the crude reaction mixture (compounds **12** and **13**).

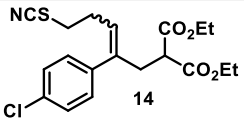
7.2. Radical Clock Experiment:

Next, a radical clock experiment was conducted to gain a better insight into the reaction mechanism. Here, *α*-cyclopropyl-4-chlorostyrene **1an** reacts with diethyl 2-bromomalonate **2a** and potassium thiocyanate under standard reaction conditions, producing ring-opening product **14** in good yield. The rearrangement product **14** resulted from oxidative addition with thiocyanate, which is generated from the rapid ring opening process of cyclopropyl methyl radical **I**, itself generated upon the addition of the malonyl radical to the alkene. This experiment discloses strong support for the participation of malonyl radicals in this protocol via SET-type mechanism.



A culture tube equipped with a magnetic stir bar was charged with *fac*-Ir(ppy)$_3$ (1.3 mg, 0.002 mmol, 1 mol%), diethyl 2-bromomalonate **2a** (34 mg, 0.2 mmol), potassium thiocyanate (39 mg, 0.4 mmol), and dry acetonitrile (2 mL). The tube was sealed with a Teflon screw cap before *α*-cyclopropyl-4-chlorostyrene **1an** (62 µL, 0.4 mmol) was added to it. Then, the yellow reaction mixture was degassed by Freeze-Pump-Thaw cycles with argon and irradiated at rt with 12 W blue LEDs at a distance of approximately 5 cm for 6 h. A high-speed fan was used to maintain the temperature. After completion of the reaction (confirmed by TLC), the crude was concentrated under vacuo and purified by silica gel column chromatography using EtOAc/petroleum ether as eluent to afford the corresponding product **14**.

Diethyl 2-(2-(4-chlorophenyl)-5-thiocyanatopent-2-en-1-yl)malonate (14):



Yield: 62% (49 mg).

Nature: Colourless oil.

R_f value = 0.39 [EtOAc:Petroleum ether = 1:4 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm): 7.34 (d, *J* = 8.5 Hz, 2H), 7.07 (d, *J* = 8.4 Hz, 2H), 5.53 (t, *J* = 7.3 Hz, 1H), 4.17 – 4.11 (m, 4H), 3.28 (t, *J* = 7.8 Hz, 1H), 2.93 (d, *J* = 7.7 Hz, 2H), 2.88 (t, *J* = 7.1 Hz, 2H), 2.40 (q, *J* = 7.1 Hz, 2H), 1.23 (t, *J* = 7.1 Hz, 6H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) *δ* (ppm): 168.8, 140.4, 136.8, 133.7, 129.9, 129.0, 125.8, 112.0, 61.7, 50.6, 38.4, 33.8, 29.2, 14.2.

HRMS (ESI) *m/z* calcd for $C_{19}H_{23}ClNO_4S$ $[M+H]^+$: 396.1036; found: 396.1040.

7.3. UV-Vis Experiments:

The UV-Vis absorption spectroscopic experiments were recorded using a quartz cuvette of 1.0 cm path length by Shimadzu UV-1800 Spectrophotometer. Initially, 5.0×10^{-5} M solution of ***fac*-Ir(ppy)$_3$** photocatalyst, and 1 mM solution of **1a**, **2a**, and **KSCN** in acetonitrile were prepared and then absorbance of individual reacting components and their combinations were measured with the wavelength range from 280 to 730 nm. The emission spectrum of PAR38 12 W blue LEDs was also measured using an Ocean Optics HR4000 High-Resolution Fiber Optic Spectrometer. Here, the λ_{max} value of the PAR38 12 W blue LEDS is 450 nm and presented in the below graph with the normalized value.

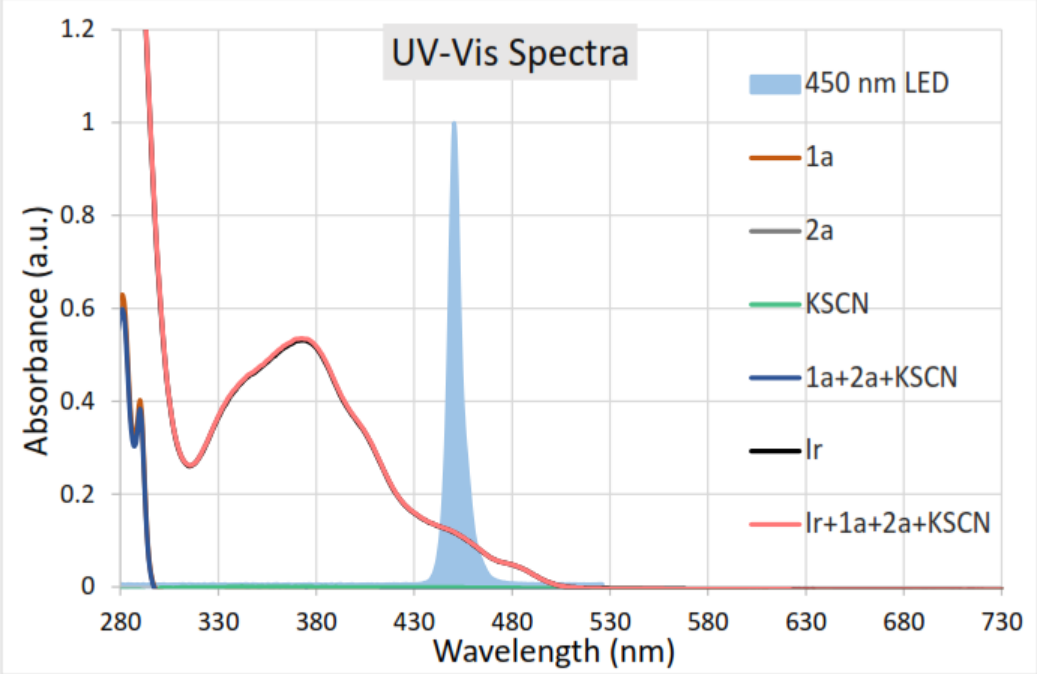


Figure S7: UV-Vis spectra of ***fac*-Ir(ppy)$_3$** individual reactants, **1a**, **2a**, **KSCN** and their combined mixtures along with normalized emission spectrum of PAR38 12 W blue LEDs.

Comments: These spectra clearly indicate that the ***fac*-Ir(ppy)$_3$** photocatalyst shows absorption exclusively at λ_{max} = 373 nm, and there is no new peak in the absorption spectra of the mixture of starting materials and also with/without photocatalyst. Hence, the formation of any electron donor-acceptor (EDA) complex is being ruled out. Also, the absorption spectra of reacting components didn't absorb light in the visible light region, especially the 450 nm emission region. Hence, the product formation from the reacting components under the direct irradiation of light (450 nm LEDs) without photocatalyst is being ruled out.

7.4. Stern-Volmer Fluorescence Quenching Experiments:

Fluorescence quenching studies were carried out using a PerkinElmer LS 55 Fluorescence Spectrometer. Photocatalyst and varying concentrations of quencher were combined in dry and degassed acetonitrile in quartz cuvettes. For the quenching experiments, the concentration of the *fac*-Ir(ppy)$_3$ was 5.0 x 10^{-5} M. The solution was irradiated at 373 nm, and the intensity of emission maxima was observed at 521 nm. Plots were derived according to the Stern-Volmer equation, and K_{sv} was calculated.

$$\text{Stern-Volmer equation: } I_0/I = 1 + K_{sv}[Q]$$

Where I_0 is the luminescence intensity without the quencher, I is the intensity with the quencher, [Q] is the concentration of added quencher, and K_{sv} is the Stern-Volmer quenching constant.

All the emission spectra were recorded after each addition of the quencher. The result shows a significant change in emission intensity was observed for diethyl 2-bromomalonate **2a** than the **KSCN** and styrene **1a**.

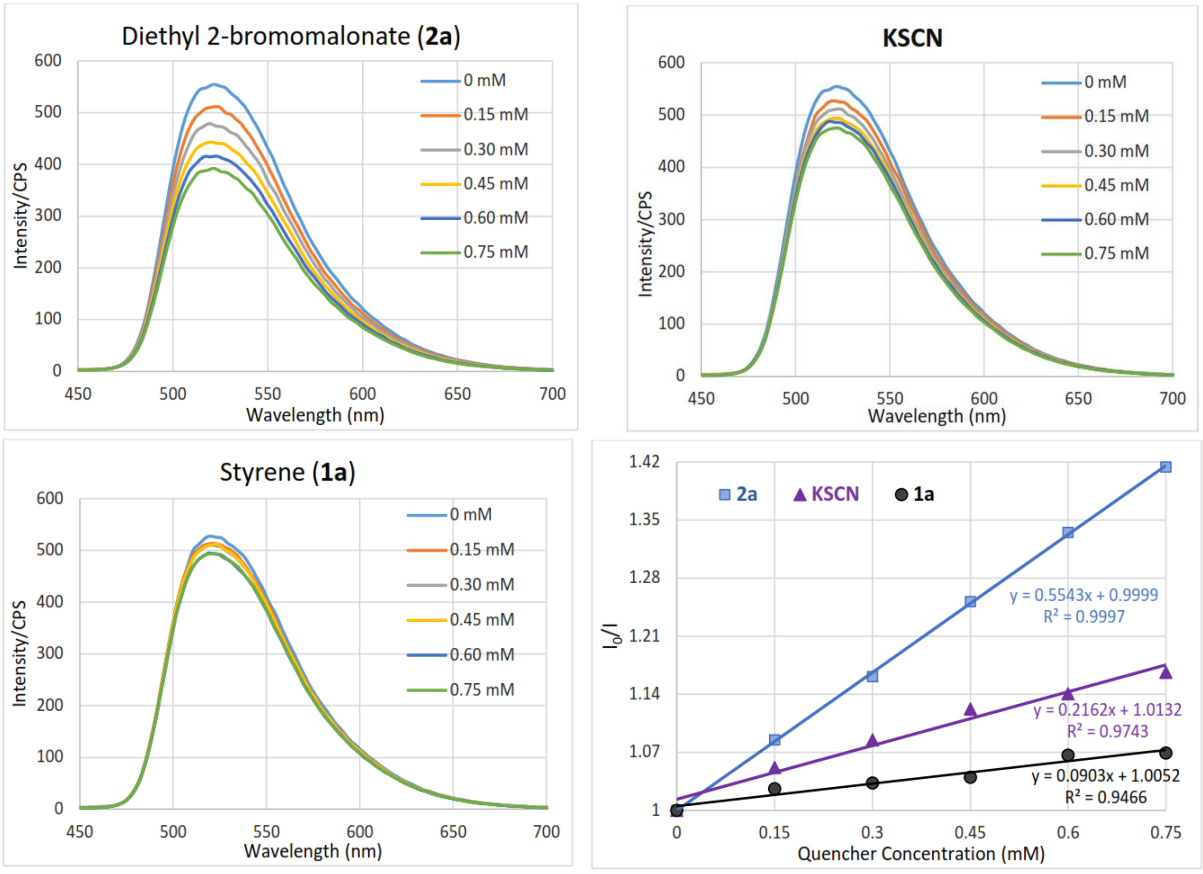


Figure S8: Emission spectra of *fac*-Ir(ppy)$_3$ with varying concentrations of quencher and Stern-Volmer plots of *fac*-Ir(ppy)$_3$, quenching with varying concentrations of **2a**, **KSCN**, and **1a**.

Comments: This result shows that the photocatalyst is more readily quenched with bromomalonate or thiocyanatomalonate than potassium thiocyanate or styrene. Hence, this photocatalytic reaction was passed through the radical initiation of bromomalonate **2a**.

7.5. Light ON/OFF Experiments:

Six reactions were set up in 0.2 mmol scale in the reaction tube with diethyl 2-bromomalonate **2a**, styrene **1a**, potassium thiocyanate, and *fac*-Ir(ppy)$_3$ as mentioned in the standard reaction condition (GP1). The resulting mixture was irradiated with 12 W blue LEDs for 1 h. After 1 h, the blue LEDs irradiation was put off, and one reaction tube was removed from the irradiation setup for product isolation. The remaining five tubes were stirred in the absence of light for an additional 1 h. Then, one tube was removed for analysis, and the irradiation source was turned on to irradiate the remaining four reaction mixtures. Like this way, the alternately switch on and switch off of the irradiation source for 6 h. The isolated yields of desired product **3a** were measured by simply purifying the reaction crude by column chromatography using neutral alumina.

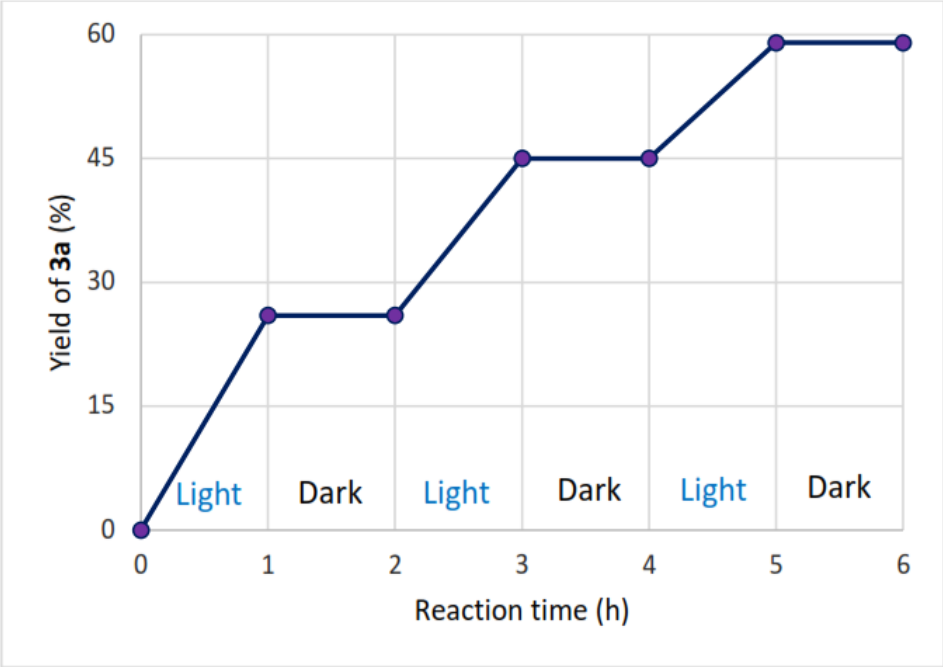
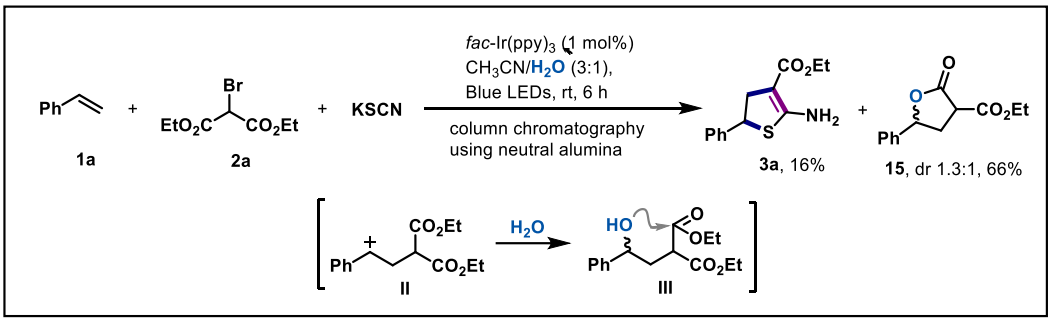


Figure S9: Light ON/OFF experiments

Comments: The light ON/OFF experiment shows that continuous light irradiation was essential for the photo-catalytic three-component carbo-thiocyanation reaction of alkenes.

7.6. Cation Trapping Experiments:

When we carried out the reaction between styrene **1a**, diethyl 2-bromomalonate **2a**, and potassium thiocyanate in the presence of water under the standard condition, we found the formation of lactones **15** in good yield along with a minor amount of 2-amino-dihydrothiophene **3a**. The lactone product **15** was resulted from hydroxy trapping from water to the cationic intermediate **II**,[22] which is generated from the oxidative transformation of radical to cation, itself generated upon addition of the malonyl radical to the alkene **1a**. This reveals strong support for the presence of the cationic intermediate in this reaction.



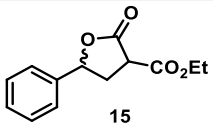
A culture tube equipped with a magnetic stir bar was charged with *fac*-Ir(ppy)$_3$ (1.3 mg, 0.002 mmol, 1 mol%), diethyl 2-bromomalonate **2a** (34 mg, 0.2 mmol), potassium thiocyanate (39 mg, 0.4 mmol), acetonitrile (1.5 mL) and water (0.5 mL). The tube was sealed with a Teflon screw cap before styrene **1a** (46 µL, 0.4 mmol) was added to it. Then, the yellow reaction mixture was degassed by Freeze-Pump-Thaw cycles with argon and irradiated at rt with 12 W blue LEDs at a distance of approximately 5 cm for 6 h. After completion of the reaction (confirmed by TLC), the crude reaction mixture was extracted with ethyl acetate (2×2 mL), washed with brine, and dried over anhydrous Na_2SO_4. The organic solution was concentrated, and the residue was purified by activated neutral alumina column chromatography using EtOAc/petroleum ether as eluent to afford the corresponding product **3a** with lactone **15**.

Ethyl 2-oxo-5-phenyltetrahydrofuran-3-carboxylate (15):[22]

Yield: 66% (31 mg, combined yield as a 1.3:1 mixture of diastereomers).

Nature: Colourless oil.

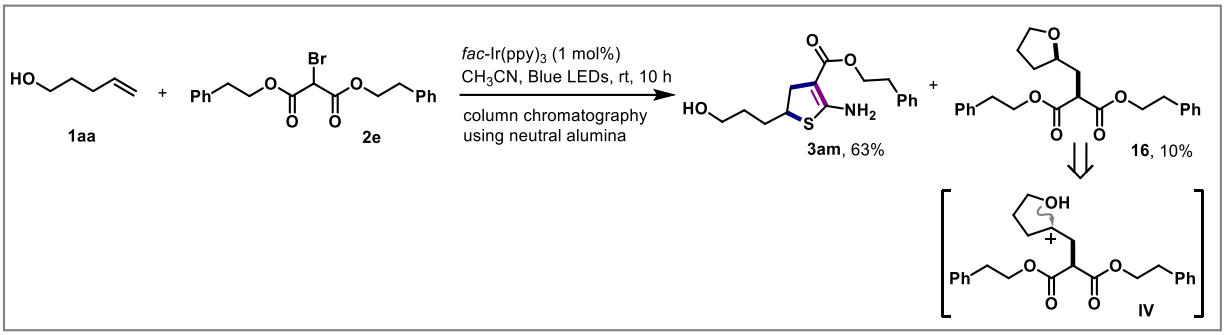
R_f value = 0.43 [EtOAc:Petroleum ether = 1:4 (v/v)].



^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): (for the major isomer) 7.42 – 7.32 (m, 5H), 5.45 (dd, *J* = 10.2, 6.2 Hz, 1H), 4.31 – 4.24 (m, 2H), 3.77 (dd, *J* = 11.7, 8.9 Hz, 1H), 2.91 – 2.84 (m, 1H), 2.73 – 2.64 (m, 1H), 1.31 (t, *J* = 7.2 Hz, 3H); (for the major isomer) 7.42 – 7.32 (m, 5H), 5.72 (t, *J* = 7.2 Hz, 1H), 4.31 – 4.24 (m, 2H), 3.70 (dd, *J* = 9.2, 4.9 Hz, 1H), 3.06 – 3.00 (m, 1H), 2.47 – 2.39 (m, 1H), 1.34 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): (for the major isomer) 171.7, 167.6, 138.1, 129.1, 129.0, 125.9, 80.1, 62.4, 47.9, 35.0, 14.2; (for the major isomer) 171.9, 167.8, 138.7, 129.0, 128.8, 125.3, 80.6, 62.6, 47.1, 35.0, 14.2.

After styrene **1a**, we performed the same reaction with aliphatic alkenes (pent-4-en-1-ol, **1aa**). We have isolated tetrahydrofuran **16** (10%) along with the desired 2-amino-dihydrothiophene product **3am**. The isolated byproduct, providing direct proof of intramolecular trapping of the aliphatic carbocation.



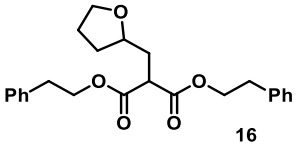
A culture tube equipped with a magnetic stir bar was charged with *fac*-Ir(ppy)$_3$ (1.3 mg, 0.002 mmol, 1 mol%), diphenethyl 2-bromomalonate **2e** (58 mg, 0.2 mmol), potassium thiocyanate (39 mg, 0.4 mmol), acetonitrile (1.5 mL) and water (0.5 mL). The tube was sealed with a Teflon screw cap before pent-4-en-1-ol **1aa** (83 µL, 0.8 mmol) was added to it. Then, the yellow reaction mixture was degassed by Freeze-Pump-Thaw cycles with argon and irradiated at rt with 12 W blue LEDs at a distance of approximately 5 cm for 10 h. After completion of the reaction (confirmed by TLC), the crude reaction mixture was purified by activated neutral alumina column chromatography using EtOAc/petroleum ether as eluent to afford the corresponding product.

Diphenethyl 2-((tetrahydrofuran-2-yl)methyl)malonate (16):

Yield: 10% (8 g).

Nature: Colourless oil.

R$_f$ value = 0.35 [EtOAc:Petroleum ether = 2:3 (v/v)].

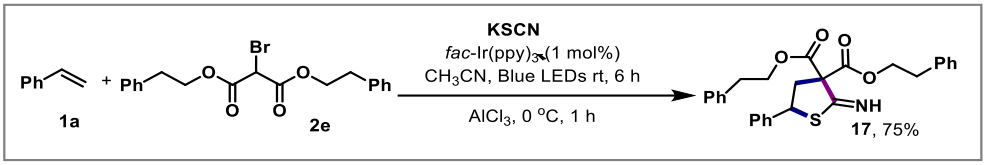


^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm): 7.31 – 7.27 (m, 4H), 7.24 – 7.19 (m, 6H), 4.33 – 4.28 (m, 4H), 3.79 – 3.73 (m, 2H), 3.69 – 3.63 (m, 1H), 3.56 (dd, *J* = 8.8, 5.9 Hz, 1H), 2.92 – 2.88 (m, 4H), 2.10 – 2.04 (m, 1H), 2.01 – 1.88 (m, 2H), 1.86 – 1.76 (m, 2H), 1.48 – 1.41 (m, 1H).

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ (ppm): 169.6, 169.4, 137.7, 129.1, 128.6, 126.7, 76.5, 67.8, 65.9, 49.5, 35.0, 34.7, 31.5, 25.7.

HRMS (ESI) *m/z* calcd for $C_{24}H_{28}O_5Na$ [M+Na]$^+$: 419.1834; found: 419.1836.

7.7. Cyclization Intermediate Evaluation:



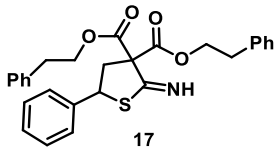
An oven-dried culture tube equipped with a magnetic stir bar was charged with *fac*-Ir(ppy)$_3$ (2.6 mg, 0.004 mmol, 1 mol%), diphenethyl 2-bromomalonate **2e** (117 mg, 0.4 mmol), potassium thiocyanate (78 mg, 0.8 mmol) and dry acetonitrile (4 mL). The tube was sealed with a Teflon screw cap before styrene **1a** (92 µL, 0.8 mmol) was added to it. Then, the yellow reaction mixture was degassed by Freeze-Pump-Thaw cycles with argon and irradiated at rt with 12 W blue LEDs at a distance of approximately 5 cm for 6 h. A high-speed fan was used to maintain the temperature. After the completion of the reaction (confirmed by TLC), Aluminum chloride (54 mg, 0.4 mmol) was added to the ice-cold reaction mixture. After 1 h, 4 mL of ethyl acetate was added and quenched with saturated ammonium chloride (4 mL). The crude reaction mixture was extracted with ethyl acetate (2×4 mL), washed with brine (5 mL), and dried over anhydrous Na_2SO_4. The organic portion was concentrated, and the residue was quickly purified by silica gel column chromatography using EtOAc/petroleum ether as eluent to afford the corresponding 2-imino-tetrahydrothiophene product.

Diphenethyl 2-imino-5-phenyldihydrothiophene-3,3(2*H*)-dicarboxylate (17):

Yield: 75% (142 mg).

Nature: Colourless oil.

R_f value = 0.33 [EtOAc:Petroleum ether = 1:4 (v/v)].



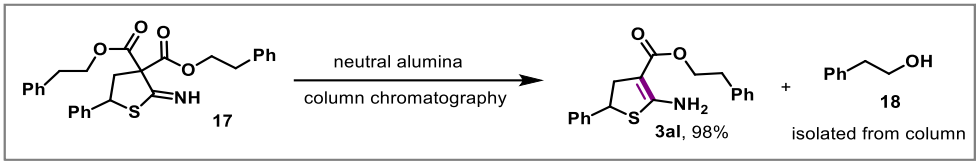
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.35 – 7.28 (m, 9H), 7.25 – 7.18 (m, 6H), 4.62 (dd, *J* = 11.5, 5.0 Hz, 1H), 4.44 (t, *J* = 6.8 Hz, 2H), 4.40 – 4.36 (m, 2H), 3.01 – 2.90 (m, 5H), 2.84 – 2.78 (m, 1H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 177.3, 166.7, 166.6, 137.8, 137.3, 137.2, 129.1, 129.0, 128.9, 128.8, 128.7, 128.5, 127.8, 126.9, 126.8, 70.3, 67.2, 67.1, 50.6, 45.3, 34.9, 34.8.

HRMS (ESI) *m/z* calcd for $C_{28}H_{28}NO_4S$ $[M+H]^+$: 474.1739; found: 474.1729.

7.8. Isolation of Alcohol Byproduct:

To recognize the reaction pathway by identifying the byproduct, we conducted column chromatography of pure compound **17** using neutral alumina. The decarboxylative isomerization product **3al** was isolated in quantitative yield. After getting **3al**, the column was washed with a high polar solvent (ethylacetate), and the eluate, after evaporation in the rotary evaporator, was sent for NMR. The crude NMR shows the presence of 2-phenethyl alcohol as a major component.



0.2 mmol (95 mg) of compound **17** was charged in a medium-sized column packed with neural alumina. 10% ethyl acetate/petroleum ether was used for the elution of 2-amino-dihydrothiophene product **3al** with 98% yield (64 mg). Then, ethyl acetate was used to wash the column. The eluate was concentrated in vacuo, and phenethyl alcohol **18** was detected in NMR spectroscopy.

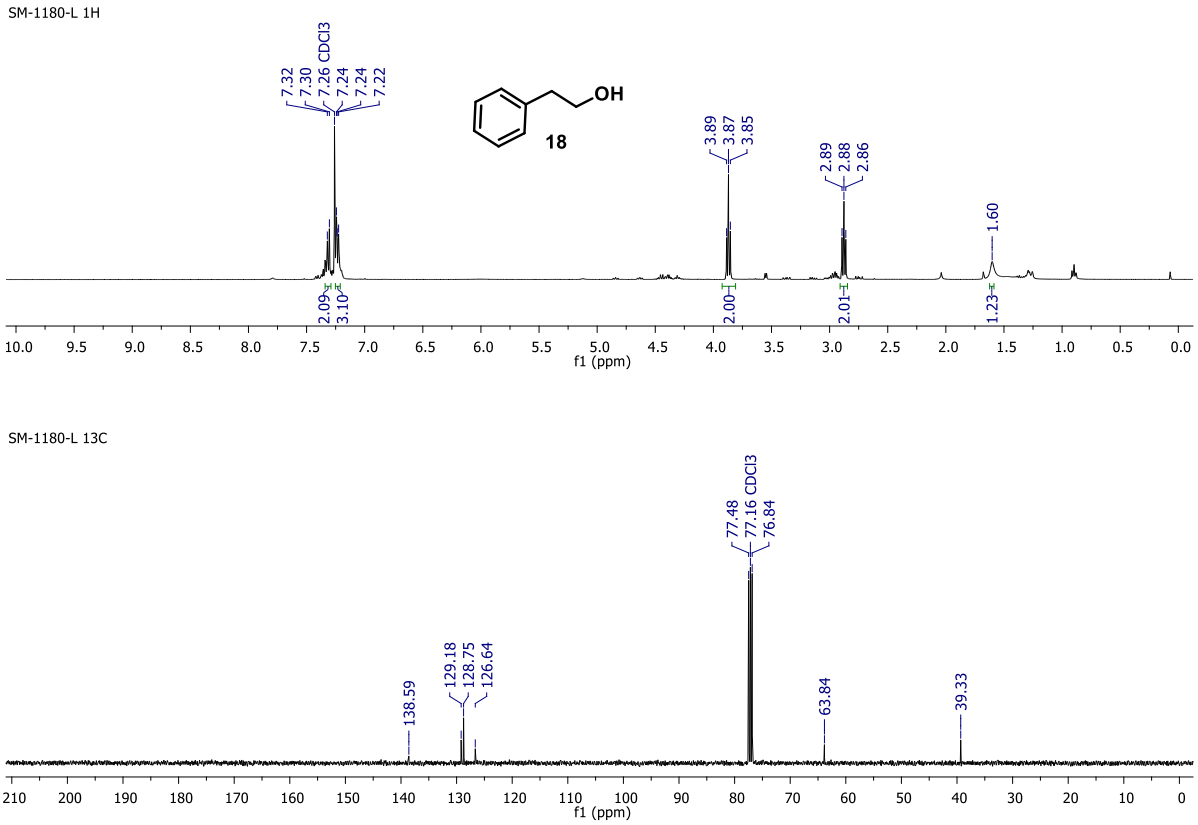
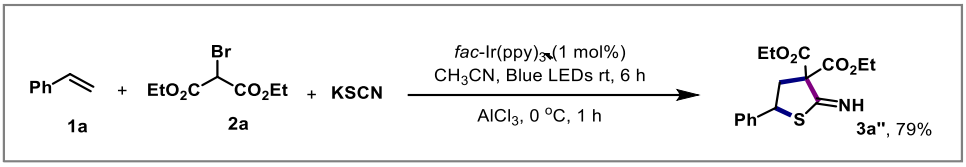
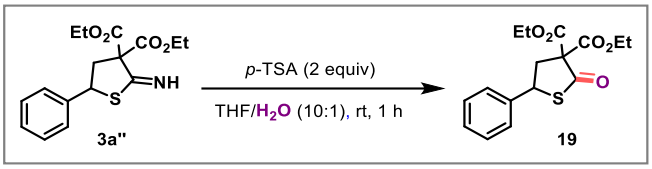


Figure S10: ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of crude product **18**.

7.9. Necessity of =N-H for Alumina Cascade:

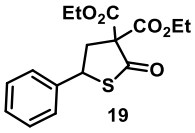


An oven-dried culture tube equipped with a magnetic stir bar was charged with *fac*-Ir(ppy)$_3$ (2.6 mg, 0.004 mmol, 1 mol%), diethyl 2-bromomalonate **2a** (68 µg, 0.4 mmol), potassium thiocyanate (78 mg, 0.8 mmol) and dry acetonitrile (4 mL). The tube was sealed with a Teflon screw cap before styrene **1a** (92 µL, 0.8 mmol) was added to it. Then, the yellow reaction mixture was degassed by Freeze-Pump-Thaw cycles with argon and irradiated at rt with 12 W blue LEDs at a distance of approximately 5 cm for 6 h. A high-speed fan was used to maintain the temperature. After the completion of the reaction (confirmed by TLC), Aluminum chloride (54 mg, 0.4 mmol) was added to the ice-cold reaction mixture. After 1 h, 4 mL of ethyl acetate was added and quenched with saturated ammonium chloride (4 mL). The crude reaction mixture was extracted with ethyl acetate (2×4 mL), washed with brine (5 mL), and dried over anhydrous Na_2SO_4. The organic portion was concentrated, and the residue was quickly purified by silica gel column chromatography using EtOAc/petroleum ether as eluent to afford the corresponding 2-imino-tetrahydroselenophene product **3a''** with 79% yield.



Compound **3a''** (64 mg, 0.2 mmol) was added to a mixture of THF–H_2O (2 mL, 10:1) and *p*-toluenesulfonic acid (69 mg, 0.4 mmol) and the reaction mixture was vigorously stirred at rt for 1 h. After completion of the reaction, the crude was concentrated under vacuo, and the residue was purified by silica gel column chromatography using EtOAc/petroleum ether as eluent to afford the corresponding product **19**.

Diethyl 2-oxo-5-phenyldihydrothiophene-3,3(2*H*)-dicarboxylate (19):



Yield: 87% (56 mg).

Nature: Colourless oil.

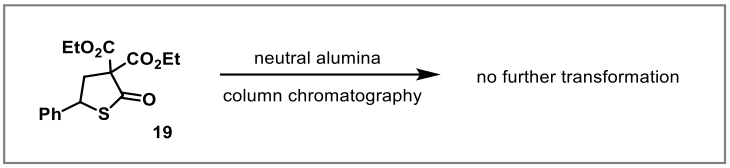
R_f value = 0.33 [EtOAc:Petroleum ether = 1:9 (v/v)].

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.44 (d, *J* = 7.6 Hz, 2H), 7.41 – 7.32 (m, 3H), 4.90 (dd, *J* = 11.4, 5.1 Hz, 1H), 4.41 – 4.32 (m, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 3.19 (dd, *J* = 13.3, 5.1 Hz, 1H), 2.93 (dd, *J* = 13.3, 11.4 Hz, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 197.5, 165.8, 165.4, 137.6, 129.2, 128.8, 127.8, 73.8, 63.4, 63.1, 50.4, 43.5, 14.1, 14.0.

HRMS (ESI) *m/z* calcd for $C_{16}H_{18}O_5SNa$ $[M+Na]^+$: 345.0773; found: 345.0765.

Necessity of =N-H for Alumina Cascade:



0.1 mmol (32 mg) of compound **19** was charged in a medium-sized column packed with neural alumina. 20% ethyl acetate/petroleum ether was used for the elution of the compound. The eluate was concentrated under vacuo, and recorded the crude ^{1}H NMR. ^{1}H NMR spectrum suggests that no further transformation occurred, and only compound **19** was found.

7.10. Determination of the Reaction Quantum Yield:

Emission spectrum of blue LEDs for quantum yield experiment was recorded using an Ocean Optics HR4000 High-Resolution Fiber Optic Spectrometer. Here, λ_{max} value of PAR38 12 W blue LED is 450 nm.

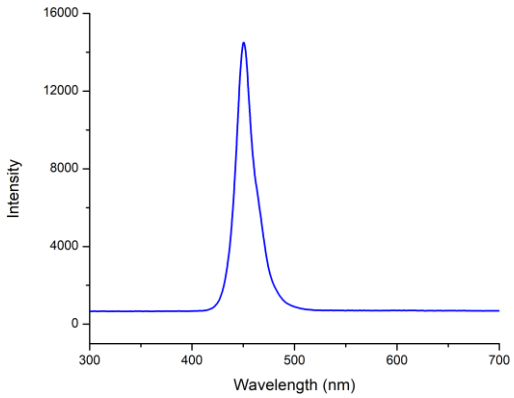


Figure S11: Emission spectrum of blue LEDs (PAR38)

Determination of the Light Intensity at 450 nm:

Following a modified procedure reported by Melchiorre and co-workers,[24] an aq. ferrioxalate actinometer solution was prepared and stored in the dark. The actinometer solution measures the photo decomposition of ferric oxalate anions to ferrous oxalate anions, which are then reacted with 1,10-phenanthroline to form $[Fe(Phen)_3]^{2+}$. Its concentration is then estimated by UV-Vis absorbance at 510 nm. The number of moles of $[Fe(Phen)_3]^{2+}$complex formed is related to the numbers of photons absorbed by the actinometer solution.

Preparation of the solutions used for the studies:

1. Potassium ferrioxalate solution: Potassium ferrioxalate trihydrate (148 mg) and 95- 98% H_2SO_4 (70 µL) were added to a 25 mL volumetric flask and filled to the mark with distilled water.
2. Buffer solution: Sodium acetate (1.235 g) and 95-98% H_2SO_4 (0.25 mL) were added to a 25 mL volumetric flask and filled to the mark with distilled water.

The actinometry measurements:

a. 1 mL of the actinometer solution was taken in a quartz cuvette (l = 1 cm). Both the cuvettes of actinometer solution and reaction solution were placed next to each other at a distance of 8 cm away from a 12 W blue LED (λ_{max} = 450 nm) and irradiated for 15 s. The same process was repeated for different time intervals: 30 and 45 s.
b. After irradiation, the actinometer solution was transferred to a 20 mL flask containing 1.0 mg of 1,10-phenanthroline in 2 mL of buffer solution. The flask was filled to the mark with distilled water. In a similar manner, a blank solution (20 mL) was also prepared using the actinometer solution stored in dark.

c. Absorbance of the actinometer solution after complexation with 1,10-phenanthroline at λ = 510 nm was measured by UV-Vis spectrophotometry.

d. According to Beer's law, the number of moles of Fe^{2+} formed (x) for each sample was determined by Equation 1:

$$mol\ Fe^{2+} = \frac{v1.v3.\Delta A\ (510\ nm)}{1000.v2.l.\varepsilon\ (510\ nm)} \qquad (1)$$

Where:

v1 = Irradiated volume (1 mL).

v2 = The aliquot of the irradiated solution taken for the estimation of Fe^{2+} ions (1 mL).

v3 = Final volume of the solution after complexation with 1,10-phenanthroline (20 mL).

ε (510 nm) = Molar extinction coefficient of $[Fe(Phen)_3]^{2+}$ complex (11100 L mol^{-1} cm^{-1}).

l = Optical path-length of the cuvette (1 cm).

ΔA (510 nm) = Difference in absorbance between the irradiated solution and the solution stored in dark (blank).

e. The number of moles of Fe^{2+} formed (x) was plotted as a function of time (t). The slope ($\frac{dx}{dt}$) of the line is equal to the number of moles of Fe^{2+} formed per unit time.

f. This slope ($\frac{dx}{dt}$) was correlated to the number of moles of incident photons per unit time (F = photon flux) by using the Equation 2:

$$\Phi(\lambda) = \frac{\frac{dx}{dt}}{F.(1-10^{-A(\lambda)})} \qquad (2)$$

Φ(λ) = The quantum yield for Fe^{2+} formation at 450 nm is 0.9 [25]

g. A(λ) = Absorbance of the ferrioxalate actinometer solution at a wavelength of 450 nm, which was measured placing 1 mL of the solution in a cuvette of pathlength 1 cm by UV/Vis spectrophotometry.

Sample calculation according to the Equation 1:

$A^0 = 0.014$	$A^1_{15s} = 0.842$	$A^1_{30s} = 1.657$	$A^1_{45s} = 2.500$
	$\Delta A^1_{15s} = 0.828$	$\Delta A^1_{30s} = 1.643$	$\Delta A^1_{45s} = 2.486$

mol Fe^{2+} (15 S) = (1 mL×20 mL×0.828)/(1000 mL×1 cm×11100 L mol^{-1} cm^{-1}) = 1.491×10^{-6} mol

mol Fe^{2+} (30 S) = (1 mL×20 mL×1.643)/(1000 mL×1 cm×11100 L mol^{-1} cm^{-1}) = 2.960×10^{-6} mol

mol Fe^{2+} (45 S) = (1 mL×20 mL×2.486)/(1000 mL×1 cm×11100 L mol^{-1} cm^{-1}) = 4.479×10^{-6} mol

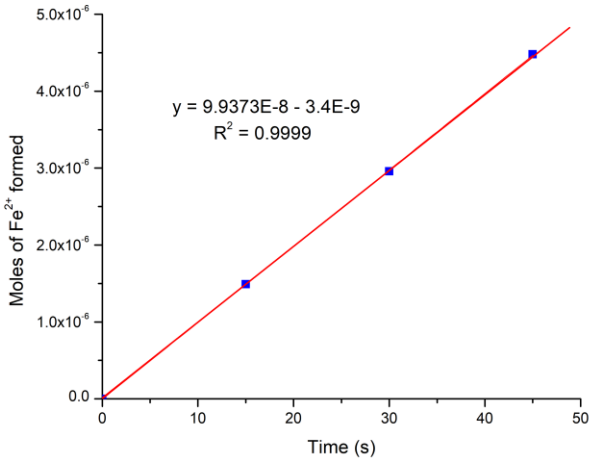


Figure S12: Moles of Fe^{2+} formed being plotted as a function of time

Moles of $[Fe(Phen)_3]^{2+}$ per unit of time formed due to decomposition of the actinometer solution at 450 nm blue LED irradiation as shown in the Equation 3:

$$F = \frac{\frac{dx}{dt}}{\Phi(\lambda).(1-10^{-A(\lambda)})} \qquad (3)$$

$A(\lambda)_{15s} = 0.633$ $A(\lambda)_{30s} = 1.230$ $A(\lambda)_{45s} = 1.853$

$F_{15s} = (9.9373\times10^{-8})/(0.9\times(1-10^{-0.633})) = 1.4392\times10^{-7}$

$F_{30s} = (9.9373\times10^{-8})/(0.9\times(1-10^{-1.230})) = 1.1732\times10^{-7}$

$F_{45s} = (9.9373\times10^{-8})/(0.9\times(1-10^{-1.853})) = 1.1195\times10^{-7}$

$F_{average} = (F_{15s} + F_{30s} + F_{45s})/3 = 1.2439\times10^{-7}$

h. The determined incident photons per unit time (F) is 1.2439×10^{-7} einsteins/s.

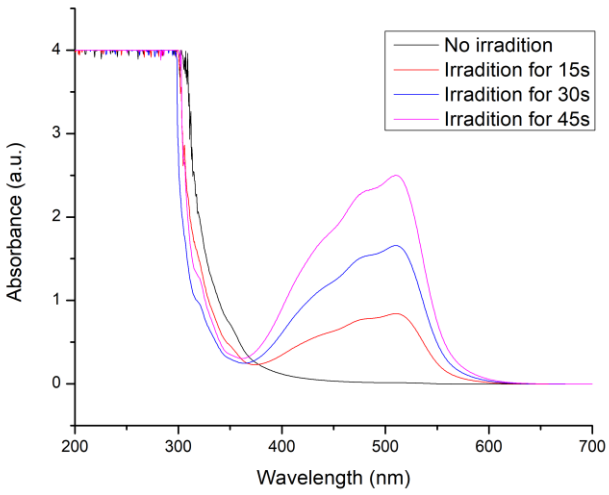
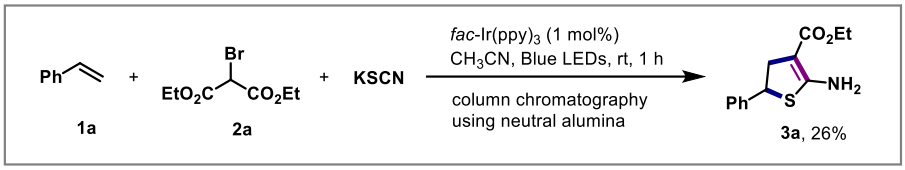


Figure S13: UV-Vis spectra of three irradiated and one non-irradiated ferrioxalate actinometer solutions.

Determination of the Reaction Quantum Yield:



A quartz cuvette with two sides taped over with electrical tape equipped with a magnetic stir bar was charged with *fac*-Ir(ppy)$_3$ (0.7 mg, 0.001 mmol, 1 mol%), diethyl 2-bromomalonate **2a** (17 µL, 0.1 mmol), potassium thiocyanate (19 mg, 0.2 mmol) and dry acetonitrile (1 mL). The quartz cuvette was capped before styrene **1a** (23 µL, 0.2 mmol) was added to it. Then, the yellow reaction mixture was degassed with argon and irradiated at rt with 12 W blue LEDs at a distance of approximately 5 cm for 1 h. A high-speed fan was used to maintain the temperature. After 1 h, the reaction mixture was concentrated in vacuo and directly purified by activated neutral alumina column chromatography using EtOAc/petroleum ether as eluent (slow elution) to afford the corresponding 2-amino-dihydrothiophene product **3a** (6.5 mg, 26%).

Yield of the product is 26% (5.2×10^{-5} mol), where the photon flux is 1.2439×10^{-7} einstein s^{-1} (described above), t is the reaction time (3600 s) and f is the fraction of incident light absorbed by the reaction mixture. An absorbance of the reaction mixture at 450 nm was measured to be 1.723 nm.

$$\Phi = \frac{mol\ of\ product\ formed}{photon\ flux \cdot t \cdot f} \qquad (4)$$

Sample quantum yield calculation according to the Equation 4:

$f = 1-10^{(-1.723)} = 0.9810$

$\Phi = 5.2\times10^{-5}$ mol/(1.2439×10^{-7} einstein s^{-1} ×3600 s×0.9810) = 0.11

The reaction quantum yield (Φ) was thus determined to be 0.11

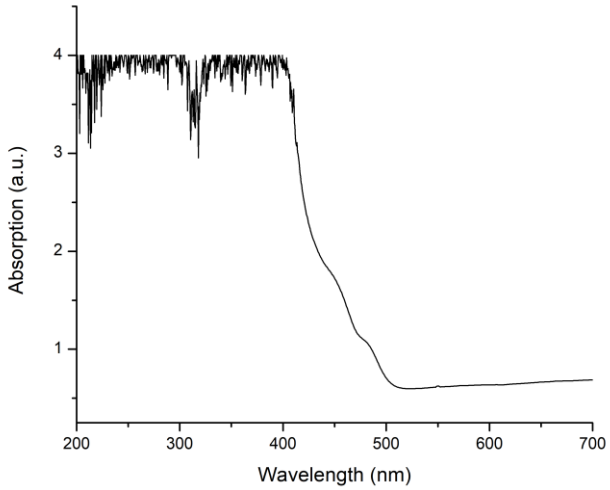


Figure S14: UV-Vis spectra of reaction mixture solution.

8. X-ray Crystal Structure and Data:

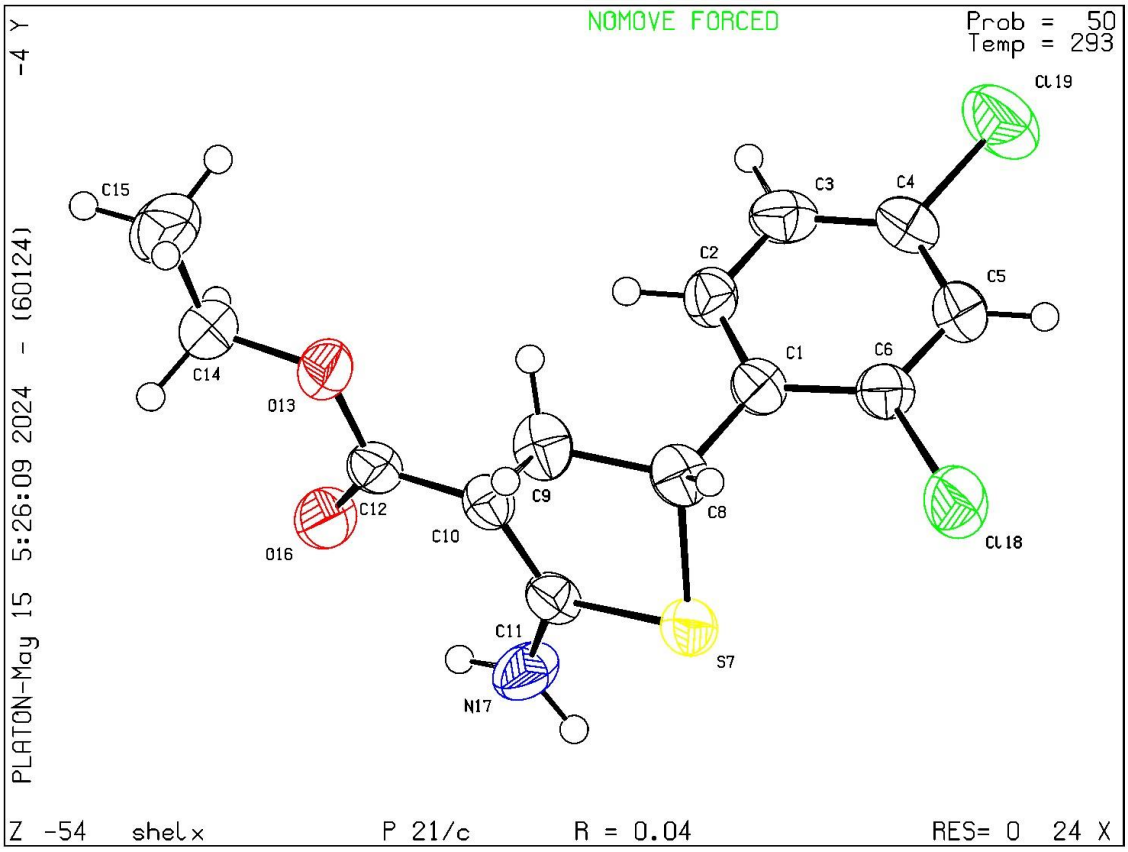


Figure S15: ORTEP plot of compound **3l** with 50% ellipsoid probability.

Preparation of the Crystal Sample: In a 5 mL glass vial with **3l** (20 mg) dissolved in acetonitrile (0.5 mL) and pentane (4 mL) was slowly added to the top of the solution. The vial was capped and allowed to slowly evaporate at room temperature for 5 days to obtain good-quality crystal.

Crystal data for 3l: X-ray single crystal data were collected using MoKα (λ = 0.71073 Å) radiation on a Rigaku SuperNova diffractometer equipped with an Eos S2 detector. Structure solution/refinement were carried out using Shelx-2013. The structure was solved by direct method and refined in a routine manner. Non-hydrogen atoms were treated anisotropically. All hydrogen atoms were geometrically fixed. CCDC (**CCDC No: 2132622**) contains the supplementary crystallographic data of **3l**. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

Datablock: shelx

Bond precision:	C-C = 0.0030 A		Wavelength=0.71073
Cell:	a=14.9528(13)	b=9.7498(8)	c=10.4550(11)
	alpha=90	beta=108.082(11)	gamma=90

Temperature: 293 K

	Calculated	Reported
Volume	1448.9(2)	1448.9(2)
Space group	P 21/c	P 21/c
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C13 H13 Cl2 N O2 S	?
Sum formula	C13 H13 Cl2 N O2 S	C13 H13 Cl2 N O2 S
Mr	318.20	318.21
Dx,g cm^{-3}	1.459	1.449
Z	4	4
Mu (mm-1)	0.588	0.588
F000	656.0	648.0
F000'	657.90	
h,k,lmax	19,12,13	19,12,13
Nref	3171	3123
Tmin,Tmax	0.919,0.943	
Tmin'	0.916	

Correction method= Not given

Data completeness= 0.985 Theta(max)= 27.000

R(reflections)= 0.0392(1774) wR2(reflections)= 0.0519(3123)

S = 1.015 Npar= 173

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

PLAT052_ALERT_1_C Info on Absorption Correction Method Not Given Please Do !
PLAT068_ALERT_1_C Reported F000 Differs from Calcd (or Missing)... Please Check
PLAT230_ALERT_2_C Hirshfeld Test Diff for O16 --C12 . 6.6 s.u.
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ..... 13.146 Check
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ..... 2.781 Check
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L= 0.600 2 Report
3 11 0, 6 0 0,

Alert level G

PLAT007_ALERT_5_G Number of Unrefined Donor-H Atoms ..... 2 Report
H17A H17B
PLAT199_ALERT_1_G Reported _cell_measurement_temperature ..... (K) 293 Check
PLAT200_ALERT_1_G Reported _diffrn_ambient_temperature ..... (K) 293 Check
PLAT793_ALERT_4_G Model has Chirality at C8 (Centro SpGr) R Verify
PLAT883_ALERT_1_G No Info/Value for _atom_sites_solution_primary . Please Do !
PLAT899_ALERT_4_G SHELXL2018 is Deprecated and Succeeded by SHELXL 2019/3 Note
PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min). 1 Note
1 0 0,
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L= 0.600 45 Note
PLAT941_ALERT_3_G Average HKL Measurement Multiplicity ..... 2.2 Low
PLAT961_ALERT_5_G Dataset Contains no Negative Intensities ..... Please Check
PLAT965_ALERT_2_G The SHELXL WEIGHT Optimisation has not Converged Please Check
PLAT967_ALERT_5_G Note: Two-Theta Cutoff Value in Embedded .res .. 54.0 Degree
PLAT969_ALERT_5_G The 'Henn et al.' R-Factor-gap value ..... 1.597 Note
Predicted wR2: Based on SigI**2 3.25 or SHELX Weight 5.11
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 0 Info

---

0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
6 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
14 **ALERT level G** = General information/check it is not something unexpected

5 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
3 ALERT type 2 Indicator that the structure model may be wrong or deficient
5 ALERT type 3 Indicator that the structure quality may be low
3 ALERT type 4 Improvement, methodology, query or suggestion
4 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

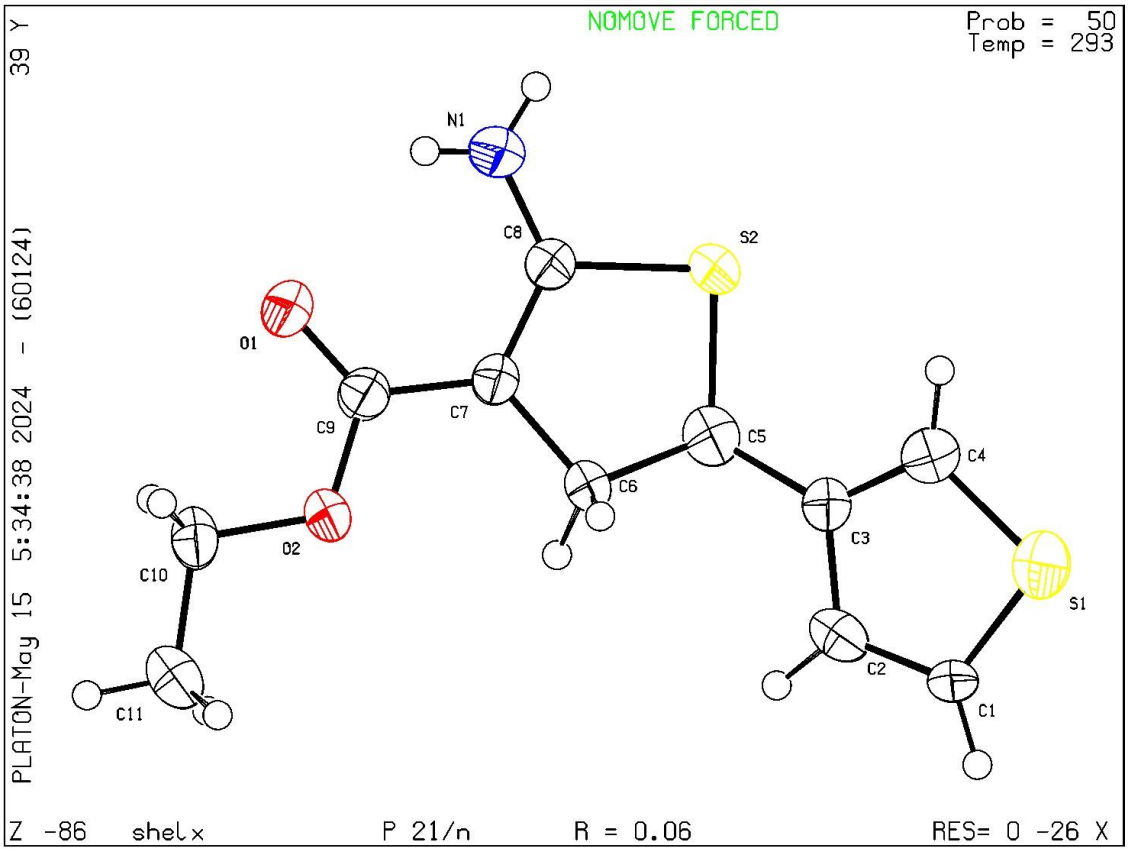


Figure S16: ORTEP plot of compound **3n** with 50% ellipsoid probability.

Preparation of the Crystal Sample: In a 5 mL glass vial with **3n** (20 mg) dissolved in acetonitrile (0.5 mL) and pentane (4 mL) was slowly added to the top of the solution. The vial was capped and allowed to slowly evaporate at room temperature for 5 days to obtain good-quality crystal.

Crystal data for 3n: X-ray single crystal data were collected using MoKα (λ = 0.71073 Å) radiation on a Rigaku SuperNova diffractometer equipped with an Eos S2 detector. Structure solution/refinement were carried out using Shelx-2013. The structure was solved by direct method and refined in a routine manner. Non-hydrogen atoms were treated anisotropically. All hydrogen atoms were geometrically fixed. CCDC (**CCDC No: 1980566**) contains the supplementary crystallographic data of **3n**. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

Datablock: shelx

Bond precision:	C-C = 0.0048 A		Wavelength=0.71073
Cell:	a=5.7014(5)	b=9.6716(8)	c=21.860(2)
	alpha=90	beta=92.246(7)	gamma=90
Temperature:	293 K		
	Calculated		Reported
Volume	1204.47(18)		1204.48(19)

Space group	P 21/n	P 21/n
Hall group	-P 2yn	-P 2yn
Moiety formula	C11 H13 N O2 S2	?
Sum formula	C11 H13 N O2 S2	C11 H13 N O2 S2
Mr	255.34	255.34
Dx,g cm^{-3}	1.408	1.408
Z	4	4
Mu (mm-1)	0.426	0.426
F000	536.0	536.0
F000'	537.19	
h,k,lmax	7,12,27	7,12,27
Nref	2630	2576
Tmin,Tmax	0.934,0.950	
Tmin'	0.934	

Correction method= Not given

Data completeness= 0.979 Theta(max)= 26.996

R(reflections)= 0.0637(1665) wR2(reflections)= 0.1648(2576)

S = 1.093 Npar= 153

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level B

PLAT230_ALERT_2_B Hirshfeld Test Diff for S1 --C1 . 7.5 s.u.

Alert level C

And 2 other PLAT230 Alerts

More ...

PLAT250_ALERT_2_C Large U3/U1 Ratio for <U(i,j)> Tensor(Resd 1) 2.2 Note

PLAT340_ALERT_3_C Low Bond Precision on C-C Bonds ..... 0.00478 Ang.

PLAT767_ALERT_4_C INS Embedded LIST 6 Instruction Should be LIST 4 Please Check

PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ..... 12.940 Check

PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ..... 2.621 Check

PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L= 0.600 4 Report
5 0 17, 3 3 19, 2 4 22, 2 4 23,

Alert level G

PLAT199_ALERT_1_G Reported _cell_measurement_temperature ..... (K) 293 Check

PLAT200_ALERT_1_G Reported _diffrn_ambient_temperature ..... (K) 293 Check

PLAT793_ALERT_4_G Model has Chirality at C5 (Centro SpGr) R Verify

PLAT883_ALERT_1_G No Info/Value for _atom_sites_solution_primary . Please Do !

PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L= 0.600 50 Note

PLAT941_ALERT_3_G Average HKL Measurement Multiplicity ..... 2.0 Low

PLAT961_ALERT_5_G Dataset Contains no Negative Intensities ..... Please Check

PLAT965_ALERT_2_G The SHELXL WEIGHT Optimisation has not Converged Please Check

PLAT967_ALERT_5_G Note: Two-Theta Cutoff Value in Embedded .res .. 54.0 Degree

PLAT969_ALERT_5_G The 'Henn et al.' R-Factor-gap value ..... 2.793 Note
Predicted wR2: Based on SigI**2 5.90 or SHELX Weight 15.08

PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 1 Info

---

0 **ALERT level A** = Most likely a serious problem - resolve or explain
1 **ALERT level B** = A potentially serious problem, consider carefully
8 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight

11 **ALERT level G** = General information/check it is not something unexpected

3 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
6 ALERT type 2 Indicator that the structure model may be wrong or deficient
5 ALERT type 3 Indicator that the structure quality may be low
3 ALERT type 4 Improvement, methodology, query or suggestion
3 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

9. Computational Details:

The structures of all the geometries in this study have been fully optimized using the dispersion-corrected PBE0-D3[26] functional with zero damping coupled with the def2-TZVPP[27] basis set. We utilized the COSMO solvation model[28] with an ethyl acetate solvent medium to consider the solvent effects. After that, we calculated the vibrational frequencies of each stationary point using the same level of theory. This helped us categorize the stationary points as either true minima (with no imaginary frequencies) or transition states (with only one imaginary frequency). Atoms in molecules (AIM) were calculated using Gaussian files with the Multiwfn 3.8 software.[29] The NBO calculations have been performed using the NBO 3.1 program[30] as implemented in Gaussian 16. All the calculations were executed using Gaussian 16.[31]

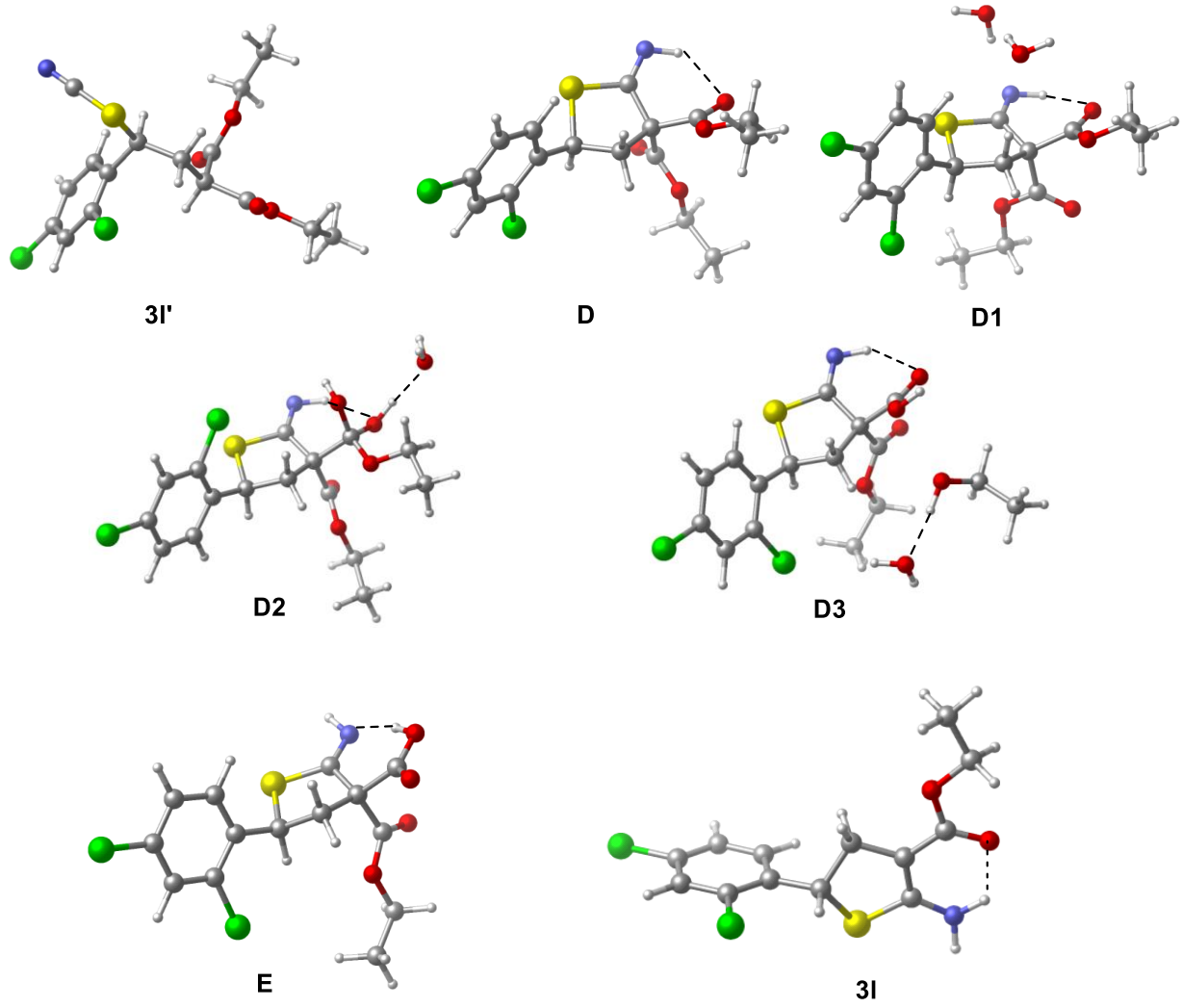


Figure S17: The optimized geometries of various intermediates and transition states are mentioned in Scheme 3. [C: grey, O: red, S: yellow, Cl: green, H: white, N: blue]

Table S2: The results of natural bond order (NBO) analysis and topological parameters calculated by the AIM approach.

Compound	Bond type	Wiberg bond index	Second-order perturbation stabilization energy $E^{(2)}$ (kcal/mol) $\mathrm{LP(O)} \rightarrow \sigma^{*}_{(N-H)}$	AIM parameters (a.u.) of the BCP		
				ρ_{BCP}	$\nabla^2\rho_{BCP}$	H_{BCP}
3l	N-H…O	0.018	4.17	0.024	0.091	0.0017
D	N-H…O	0.008	0.85	0.017	0.066	0.0023
E	O-H…N	0.138	37.46	0.067	0.075	-0.0230

Discussion: The nature of the hydrogen bonding interaction present in **3l** was investigated using the Natural Bond Orbital (NBO) and Quantum Theory of Atoms in Molecules (QTAIM) (Scheme 3d). The hydrogen bonding interaction occurs from a lone pair of electrons above the O atom to an anti-bonding orbital $\sigma^{*}_{(N-H)}$. Significant values in both the second-order perturbation energy $E^{(2)}$ and the Wiberg bond index can be used as an index to evaluate the strength of the intramolecular H-bonding interaction. To obtain further information about the characteristics of the hydrogen bonding interactions, the topological parameters were calculated by AIM (Table S2). The AIM calculations show the existence of a bond critical point (BCP) associated with the H-bond. The positive sign of the Laplacian ($\nabla^2\rho$) and H indicates the weak H-bond of electrostatic character present in **D** and **3l**. On the other hand, the O-H...N H-bond present in **E** is classified as a moderate H-bond specified by $\nabla^2\rho_{BCP} > 0$ and $H_{BCP} < 0$, which facilitates the decarboxylation process.[32]

Cartesian coordinates in xyz format

3l’

C	1.822749000	0.092021000	-1.047107000
O	1.484516000	-0.451789000	-2.067474000
O	2.613026000	1.154671000	-0.989232000
C	2.577254000	-0.880154000	1.117244000
O	2.775922000	-0.681313000	2.287736000
O	3.349046000	-1.622007000	0.338108000
C	3.100571000	1.671025000	-2.243805000
H	2.241662000	1.925342000	-2.867332000
H	3.664073000	0.881005000	-2.743437000
C	3.953540000	2.870731000	-1.939128000
H	4.339467000	3.286264000	-2.871219000
H	3.373105000	3.643497000	-1.432816000
H	4.800319000	2.597265000	-1.307895000
C	4.513750000	-2.215607000	0.948141000
H	5.116215000	-1.417545000	1.385193000
H	4.181653000	-2.874449000	1.752287000
C	5.255343000	-2.961404000	-0.125944000
H	5.569750000	-2.285915000	-0.922971000
H	6.145078000	-3.423971000	0.303976000
H	4.633027000	-3.747047000	-0.556745000
C	-1.891833000	0.222540000	-1.366360000
C	-2.818265000	-0.676972000	-1.862325000
C	-1.568689000	0.296218000	-0.011894000
C	-3.450910000	-1.531611000	-0.976522000
H	-3.044881000	-0.712435000	-2.919294000
C	-2.238288000	-0.578815000	0.847736000
C	-3.171581000	-1.489394000	0.378955000
H	-3.673800000	-2.154947000	1.067365000
H	-1.391393000	0.891713000	-2.056218000
C	1.388301000	-0.337340000	0.341490000
H	0.705909000	-1.179547000	0.198677000
C	0.704480000	0.777285000	1.124410000
H	0.454484000	0.394365000	2.111336000
H	1.403004000	1.603973000	1.261841000
C	-0.532733000	1.302956000	0.397299000
S	-1.226689000	2.642347000	1.473127000
C	-2.270393000	3.344341000	0.366338000
N	-3.000543000	3.843414000	-0.379213000
H	-0.205541000	1.825958000	-0.501971000
Cl	-1.958665000	-0.569718000	2.555395000
Cl	-4.611991000	-2.669482000	-1.558959000

D

C	0.561113000	0.421619000	-0.732868000
C	-0.475704000	-0.295430000	0.125500000
H	-0.218405000	-1.351351000	0.204246000
H	-0.508881000	0.125398000	1.130640000
C	-1.817708000	-0.166251000	-0.592277000
C	-1.530651000	-0.410616000	-2.085056000
C	-2.904292000	-1.117208000	-0.113766000
C	-3.454166000	-2.927740000	1.279632000
H	-3.830400000	-3.502113000	0.431793000
H	-4.284857000	-2.367848000	1.711991000
C	-2.762553000	-3.794872000	2.293517000
H	-2.385579000	-3.198187000	3.125354000
H	-1.929691000	-4.335615000	1.841786000
H	-3.472468000	-4.523818000	2.687200000

N	-2.325688000	-0.785821000	-2.986249000
H	-3.261118000	-0.933659000	-2.609182000
O	-2.481661000	-1.979665000	0.785412000
O	-4.030905000	-1.069141000	-0.547689000
S	0.156331000	-0.076123000	-2.441562000
C	-2.351953000	1.262560000	-0.423038000
O	-2.365111000	2.097877000	-1.286940000
O	-2.753925000	1.449696000	0.821853000
C	-3.258692000	2.762450000	1.150630000
C	-3.665750000	2.739540000	2.597040000
H	-4.098431000	2.979631000	0.488685000
H	-2.468730000	3.489545000	0.955582000
H	-4.053488000	3.720022000	2.877542000
H	-4.447161000	1.998235000	2.770291000
H	-2.813824000	2.510294000	3.238845000
C	1.974741000	0.087716000	-0.357687000
C	2.461504000	-1.208726000	-0.518195000
C	2.842187000	1.029439000	0.194221000
C	3.746084000	-1.564576000	-0.154388000
H	1.810610000	-1.958824000	-0.952840000
C	4.138616000	0.702765000	0.567791000
C	4.577407000	-0.595876000	0.387519000
H	4.101000000	-2.577255000	-0.291125000
H	4.790053000	1.453940000	0.992376000
Cl	2.338726000	2.667167000	0.455879000
Cl	6.191074000	-1.011135000	0.846823000
H	0.415011000	1.498873000	-0.672922000

D1

C	-0.525730000	0.677990000	0.206787000
C	0.478074000	-0.093170000	-0.644704000
H	0.257209000	-1.157553000	-0.593135000
H	0.413892000	0.220286000	-1.687236000
C	1.885380000	0.107232000	-0.067399000
C	1.723173000	0.140446000	1.458955000
C	2.869304000	-0.981943000	-0.491808000
C	3.326502000	-2.665919000	-2.062530000
H	3.480506000	-3.390773000	-1.261164000
H	4.290536000	-2.219796000	-2.312137000
C	2.653455000	-3.277442000	-3.259045000
H	2.498542000	-2.533678000	-4.041922000
H	1.688554000	-3.707092000	-2.985767000
H	3.283423000	-4.072860000	-3.660030000
N	2.604938000	-0.077515000	2.338596000
H	3.494936000	-0.312569000	1.901195000
O	2.461065000	-1.623752000	-1.565407000
O	3.912455000	-1.194058000	0.076009000
S	0.077931000	0.506232000	1.918473000
C	2.470652000	1.428497000	-0.578946000
O	3.320016000	1.492455000	-1.429809000
O	1.886012000	2.465140000	-0.012195000
C	2.273807000	3.776351000	-0.478209000
C	1.411740000	4.775938000	0.240566000
H	2.131972000	3.810050000	-1.559453000
H	3.334841000	3.913401000	-0.264053000
H	1.677427000	5.782627000	-0.085332000
H	0.356338000	4.609001000	0.019076000
H	1.558486000	4.712643000	1.319626000
O	1.563547000	-2.318751000	3.706443000
H	0.776471000	-2.096344000	4.209004000

H	1.960259000	-1.459985000	3.462557000
O	0.949869000	-2.973758000	1.038412000
H	1.140211000	-2.799216000	1.978674000
H	1.618554000	-3.606109000	0.767901000
C	-1.931208000	0.171937000	0.064931000
C	-2.236427000	-1.152387000	0.379449000
C	-2.973877000	0.976201000	-0.391260000
C	-3.512773000	-1.663906000	0.246525000
H	-1.444622000	-1.797946000	0.744776000
C	-4.266734000	0.490629000	-0.534524000
C	-4.521450000	-0.829379000	-0.212270000
H	-3.725834000	-2.694588000	0.496642000
H	-5.056803000	1.136664000	-0.891324000
Cl	-2.707808000	2.637346000	-0.812608000
Cl	-6.128319000	-1.442912000	-0.384888000
H	-0.489246000	1.736680000	-0.032936000

TS1

C	0.941140000	0.444997000	-0.887679000
C	-0.144221000	0.192935000	0.154301000
H	0.082767000	-0.699490000	0.732574000
H	-0.207259000	1.033341000	0.840954000
C	-1.456785000	-0.028739000	-0.589356000
C	-1.125347000	-0.881260000	-1.816974000
C	-2.539760000	-0.710569000	0.296951000
C	-3.586263000	-0.354353000	2.407043000
H	-3.558646000	-1.405692000	2.710820000
H	-4.532919000	-0.170916000	1.894578000
C	-3.421982000	0.554044000	3.597123000
H	-3.448406000	1.600568000	3.287733000
H	-2.474195000	0.365349000	4.104162000
H	-4.232692000	0.383679000	4.307478000
N	-1.891696000	-1.647053000	-2.466601000
H	-2.829473000	-1.602070000	-2.064666000
O	-2.504709000	-0.088360000	1.515273000
O	-3.689420000	-0.891088000	-0.263243000
S	0.556596000	-0.678456000	-2.278307000
C	-2.083004000	1.281073000	-1.093676000
O	-2.634182000	1.398556000	-2.157709000
O	-1.955286000	2.256974000	-0.211289000
C	-2.561032000	3.519088000	-0.552936000
C	-2.342611000	4.449574000	0.607674000
H	-3.620824000	3.349244000	-0.750265000
H	-2.097512000	3.887169000	-1.470005000
H	-2.791953000	5.418618000	0.385243000
H	-2.805101000	4.055196000	1.513895000
H	-1.277917000	4.598703000	0.793893000
O	-4.088373000	-3.129302000	0.509878000
H	-4.173735000	-2.134854000	0.093870000
O	-1.915488000	-2.182348000	0.657890000
H	-4.201186000	-3.770832000	-0.199579000
H	-1.402346000	-2.492585000	-0.098273000
H	-2.952174000	-2.879506000	0.643656000
C	2.357450000	0.329690000	-0.400112000
C	3.161580000	1.465837000	-0.493929000
C	2.945110000	-0.810100000	0.157758000
C	4.474262000	1.494108000	-0.058215000
H	2.735321000	2.363933000	-0.926042000
C	4.259597000	-0.811844000	0.600556000
C	5.013348000	0.343168000	0.489549000

H	5.068486000	2.393874000	-0.144759000
H	4.685595000	-1.709461000	1.027253000
Cl	2.084849000	-2.303945000	0.332570000
Cl	6.650269000	0.336986000	1.043847000
H	0.824280000	1.457343000	-1.277348000

D2

C	1.001419000	0.421162000	-0.877735000
C	-0.095755000	0.146160000	0.143643000
H	0.096339000	-0.789151000	0.664534000
H	-0.135429000	0.946721000	0.877748000
C	-1.412396000	0.004027000	-0.612917000
C	-1.094669000	-0.798371000	-1.880192000
C	-2.457893000	-0.745776000	0.273108000
C	-3.474295000	-0.473665000	2.417203000
H	-3.335307000	-1.532748000	2.652058000
H	-4.473920000	-0.342493000	1.992297000
C	-3.303209000	0.378999000	3.647275000
H	-3.435649000	1.435015000	3.404748000
H	-2.309508000	0.243257000	4.077521000
H	-4.045511000	0.101806000	4.397630000
N	-1.873206000	-1.491909000	-2.593759000
H	-2.823272000	-1.433088000	-2.229505000
O	-2.494071000	-0.055889000	1.469935000
O	-3.666313000	-0.755002000	-0.393687000
S	0.600472000	-0.639460000	-2.310568000
C	-2.001401000	1.351825000	-1.050768000
O	-2.596996000	1.524605000	-2.083716000
O	-1.781051000	2.302350000	-0.157521000
C	-2.337955000	3.598867000	-0.445937000
C	-2.002029000	4.498731000	0.710923000
H	-3.415226000	3.488333000	-0.581508000
H	-1.911346000	3.957429000	-1.384490000
H	-2.411294000	5.493451000	0.527912000
H	-2.430096000	4.115243000	1.638449000
H	-0.921672000	4.588753000	0.834615000
O	-5.336628000	-2.681405000	0.542307000
H	-4.248449000	-1.455791000	-0.022124000
O	-2.033003000	-2.047795000	0.562247000
H	-5.594095000	-3.277030000	-0.166682000
H	-2.053373000	-2.568231000	-0.247644000
H	-4.875364000	-3.235669000	1.177947000
C	2.412283000	0.263287000	-0.385536000
C	3.233491000	1.390405000	-0.427039000
C	2.979543000	-0.906564000	0.129623000
C	4.543216000	1.382144000	0.018324000
H	2.823097000	2.311472000	-0.824697000
C	4.290803000	-0.945162000	0.580763000
C	5.061820000	0.202131000	0.522137000
H	5.150654000	2.276078000	-0.027358000
H	4.700625000	-1.865537000	0.973497000
Cl	2.096861000	-2.392792000	0.238122000
Cl	6.694608000	0.149423000	1.086852000
H	0.905372000	1.450070000	-1.227882000

TS2

C	0.827065000	0.137357000	-0.913767000
C	-0.212184000	-0.103998000	0.176518000
H	0.102415000	-0.927532000	0.811358000

H	-0.319942000	0.787900000	0.790237000
C	-1.518628000	-0.491905000	-0.505932000
C	-1.134738000	-1.459886000	-1.634813000
C	-2.523259000	-1.188624000	0.464756000
C	-2.394172000	-0.056292000	2.825172000
H	-1.324860000	-0.263266000	2.808880000
H	-2.891112000	-0.880853000	3.343162000
C	-2.682580000	1.266580000	3.490065000
H	-3.753978000	1.476604000	3.501271000
H	-2.174735000	2.078587000	2.966861000
H	-2.328631000	1.242887000	4.522193000
N	-1.840859000	-2.344333000	-2.187896000
H	-2.767209000	-2.352729000	-1.757969000
O	-2.857823000	0.011495000	1.473073000
O	-3.643435000	-1.597246000	-0.041363000
S	0.518344000	-1.160172000	-2.164222000
C	-2.237130000	0.696261000	-1.157435000
O	-3.098379000	0.581937000	-1.991143000
O	-1.809829000	1.862366000	-0.696075000
C	-2.457341000	3.036546000	-1.219804000
C	-1.826774000	4.229687000	-0.556592000
H	-3.525434000	2.964072000	-1.006566000
H	-2.326539000	3.049983000	-2.303327000
H	-2.292651000	5.142308000	-0.931383000
H	-1.964985000	4.192038000	0.525206000
H	-0.758009000	4.275872000	-0.771976000
O	-5.153711000	0.006507000	0.905641000
H	-4.691099000	-0.800666000	0.353932000
O	-1.839005000	-2.133822000	1.189117000
H	-5.740855000	-0.375784000	1.565695000
H	-2.484435000	-2.812147000	1.417144000
H	-4.072938000	0.153249000	1.360892000
C	2.256639000	0.206399000	-0.456993000
C	2.945569000	1.395887000	-0.696453000
C	2.962891000	-0.804117000	0.203172000
C	4.257310000	1.596362000	-0.305284000
H	2.425543000	2.195958000	-1.210738000
C	4.279621000	-0.632413000	0.604988000
C	4.915631000	0.569100000	0.347900000
H	4.759714000	2.532977000	-0.506536000
H	4.798330000	-1.433649000	1.113200000
Cl	2.255035000	-2.343205000	0.562586000
Cl	6.555903000	0.778955000	0.851794000
H	0.607919000	1.087962000	-1.400150000

D3

C	0.830130000	0.739444000	0.696689000
C	-0.153550000	0.603369000	-0.463717000
H	0.272951000	1.111000000	-1.327343000
H	-0.303658000	-0.442089000	-0.725685000
C	-1.460052000	1.289187000	-0.092666000
C	-1.066970000	2.563619000	0.699906000
C	-2.295066000	1.723501000	-1.295425000
C	-4.347175000	-1.408584000	-1.279456000
H	-4.927695000	-0.485074000	-1.340474000
H	-4.498499000	-1.814600000	-0.271107000
C	-4.824208000	-2.402277000	-2.317417000
H	-4.251258000	-3.331077000	-2.256533000
H	-4.706713000	-1.993126000	-3.323081000
H	-5.878839000	-2.643053000	-2.163077000

N	-1.774899000	3.575745000	0.937817000
H	-2.694960000	3.484288000	0.506911000
O	-2.994569000	-1.037986000	-1.466218000
O	-3.372865000	2.251604000	-1.208149000
S	0.571514000	2.429409000	1.320103000
C	-2.352083000	0.481069000	0.870695000
O	-3.444600000	0.831541000	1.224426000
O	-1.728994000	-0.593070000	1.326876000
C	-2.439189000	-1.373064000	2.309218000
C	-1.501441000	-2.432664000	2.816778000
H	-3.322593000	-1.800098000	1.831744000
H	-2.770748000	-0.704942000	3.105316000
H	-2.014325000	-3.037941000	3.565773000
H	-1.174541000	-3.089295000	2.009467000
H	-0.620698000	-1.985168000	3.279378000
O	-1.257019000	-3.200169000	-0.952780000
H	-0.479061000	-2.896247000	-0.475667000
H	-1.647843000	-3.866479000	-0.381756000
O	-1.672064000	1.529521000	-2.451172000
H	-2.250697000	1.848222000	-3.158109000
H	-2.429792000	-1.808215000	-1.286960000
C	2.241232000	0.452217000	0.269538000
C	3.057288000	1.425719000	-0.300374000
C	2.766900000	-0.836827000	0.365753000
C	4.338744000	1.147285000	-0.741924000
H	2.675369000	2.435261000	-0.396482000
C	4.046959000	-1.147841000	-0.065525000
C	4.824579000	-0.143870000	-0.615226000
H	4.953978000	1.923613000	-1.176837000
H	4.425692000	-2.156502000	0.025133000
Cl	1.818147000	-2.132590000	1.024886000
Cl	6.424856000	-0.517065000	-1.151553000
H	0.557235000	0.061665000	1.501410000

E

C	0.098557000	-0.106052000	-0.440124000
C	-0.740518000	-0.487555000	0.775658000
H	-0.350171000	-1.404835000	1.220065000
H	-0.702989000	0.296926000	1.527643000
C	-2.158243000	-0.754688000	0.292647000
C	-2.019352000	-1.539134000	-1.008629000
C	-2.995964000	-1.476734000	1.371813000
N	-2.946672000	-2.301469000	-1.410651000
H	-2.775439000	-2.782017000	-2.287640000
O	-2.803986000	-1.243416000	2.538823000
O	-3.923158000	-2.296759000	0.948728000
S	-0.487698000	-1.217143000	-1.775572000
C	-2.969819000	0.516737000	-0.041065000
O	-4.065106000	0.474719000	-0.536251000
O	-2.328469000	1.616955000	0.291796000
C	-3.003554000	2.867294000	0.024524000
C	-2.069242000	3.974508000	0.423267000
H	-3.931555000	2.880097000	0.598077000
H	-3.253178000	2.897994000	-1.037085000
H	-2.550266000	4.935691000	0.236109000
H	-1.822157000	3.913910000	1.484042000
H	-1.145505000	3.932596000	-0.155741000
H	-3.813555000	-2.422743000	-0.051939000
C	1.576900000	-0.222733000	-0.218063000
C	2.165364000	-1.464379000	0.016251000

C	2.413062000	0.893116000	-0.198333000
C	3.518606000	-1.604768000	0.257185000
H	1.539477000	-2.349536000	0.000729000
C	3.775933000	0.783752000	0.040070000
C	4.315204000	-0.469566000	0.264776000
H	3.952294000	-2.579721000	0.434506000
H	4.401021000	1.665908000	0.050106000
Cl	1.785593000	2.487621000	-0.458227000
Cl	6.011500000	-0.615666000	0.558957000
H	-0.144524000	0.906277000	-0.752203000

TS3

C	0.116360000	-0.163138000	-0.441709000
C	-0.733850000	-0.451547000	0.792128000
H	-0.355434000	-1.334403000	1.310355000
H	-0.704178000	0.388801000	1.480787000
C	-2.140290000	-0.740329000	0.294700000
C	-1.957280000	-1.637698000	-0.909223000
C	-3.074886000	-1.375452000	1.380689000
N	-2.883783000	-2.460868000	-1.204904000
H	-2.783001000	-3.088459000	-1.991351000
O	-2.915272000	-1.024811000	2.534840000
O	-3.955657000	-2.189284000	0.938605000
S	-0.444380000	-1.396582000	-1.690668000
C	-2.901495000	0.509970000	-0.182553000
O	-3.842620000	0.463176000	-0.931528000
O	-2.412470000	1.610035000	0.352430000
C	-3.064116000	2.850063000	-0.001112000
C	-2.291400000	3.961699000	0.651276000
H	-4.097055000	2.802084000	0.347117000
H	-3.069950000	2.933945000	-1.088901000
H	-2.755055000	4.917436000	0.402470000
H	-2.290245000	3.851489000	1.736525000
H	-1.259045000	3.976920000	0.298003000
H	-3.636022000	-2.459701000	-0.239284000
C	1.593955000	-0.240453000	-0.206996000
C	2.195426000	-1.446389000	0.149102000
C	2.415594000	0.883435000	-0.291733000
C	3.548887000	-1.545204000	0.408651000
H	1.581450000	-2.337222000	0.218462000
C	3.777734000	0.814895000	-0.035967000
C	4.330992000	-0.404122000	0.311257000
H	3.993498000	-2.492696000	0.681801000
H	4.391824000	1.701919000	-0.107147000
Cl	1.769678000	2.436022000	-0.708793000
Cl	6.026455000	-0.498919000	0.627501000
H	-0.140116000	0.813220000	-0.847687000

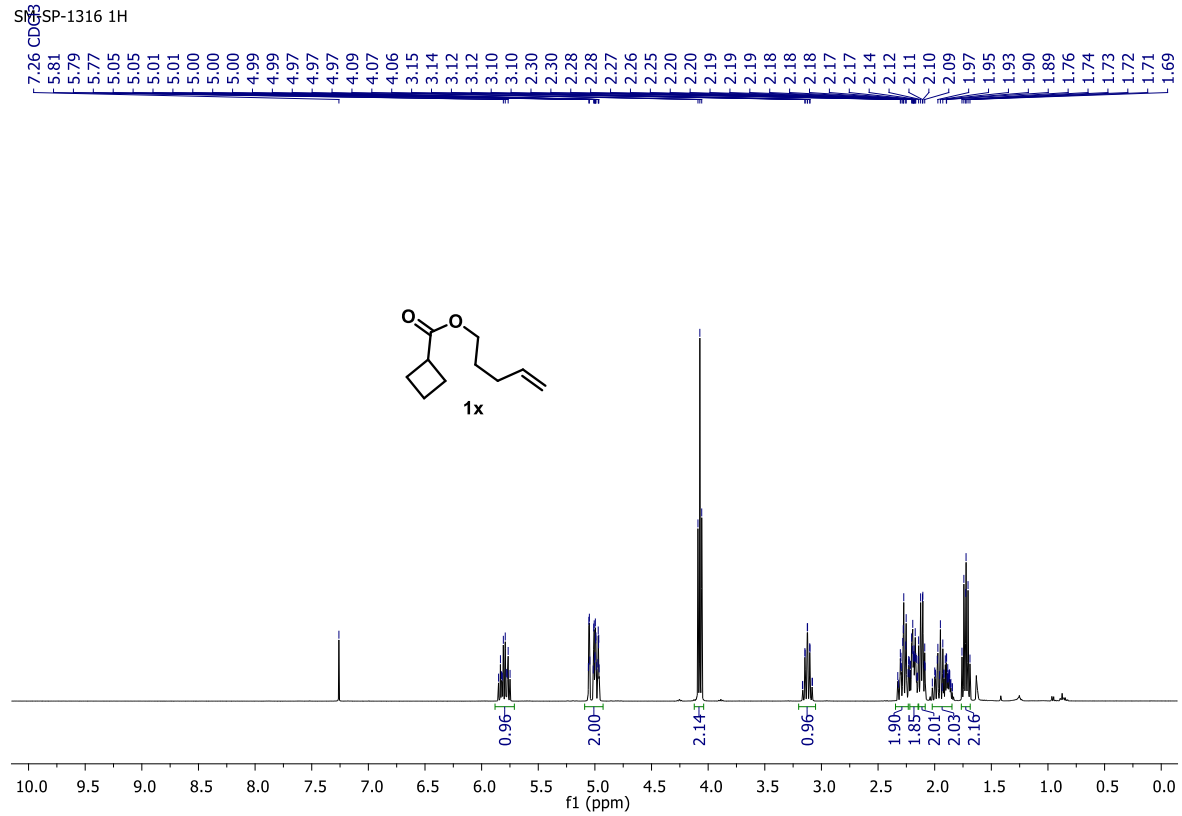
3l

C	0.053883000	0.642071000	0.459286000
C	-1.039676000	-0.297599000	-0.057335000
H	-0.761801000	-0.699678000	-1.038295000
H	-1.129789000	-1.145894000	0.623186000
C	-2.297270000	0.515429000	-0.140570000
C	-2.079317000	1.864489000	-0.267890000
C	-3.619616000	-0.028172000	-0.203492000
C	-4.915937000	-2.004292000	-0.164858000
H	-5.405951000	-1.738899000	-1.104290000
H	-5.533817000	-1.626386000	0.652772000

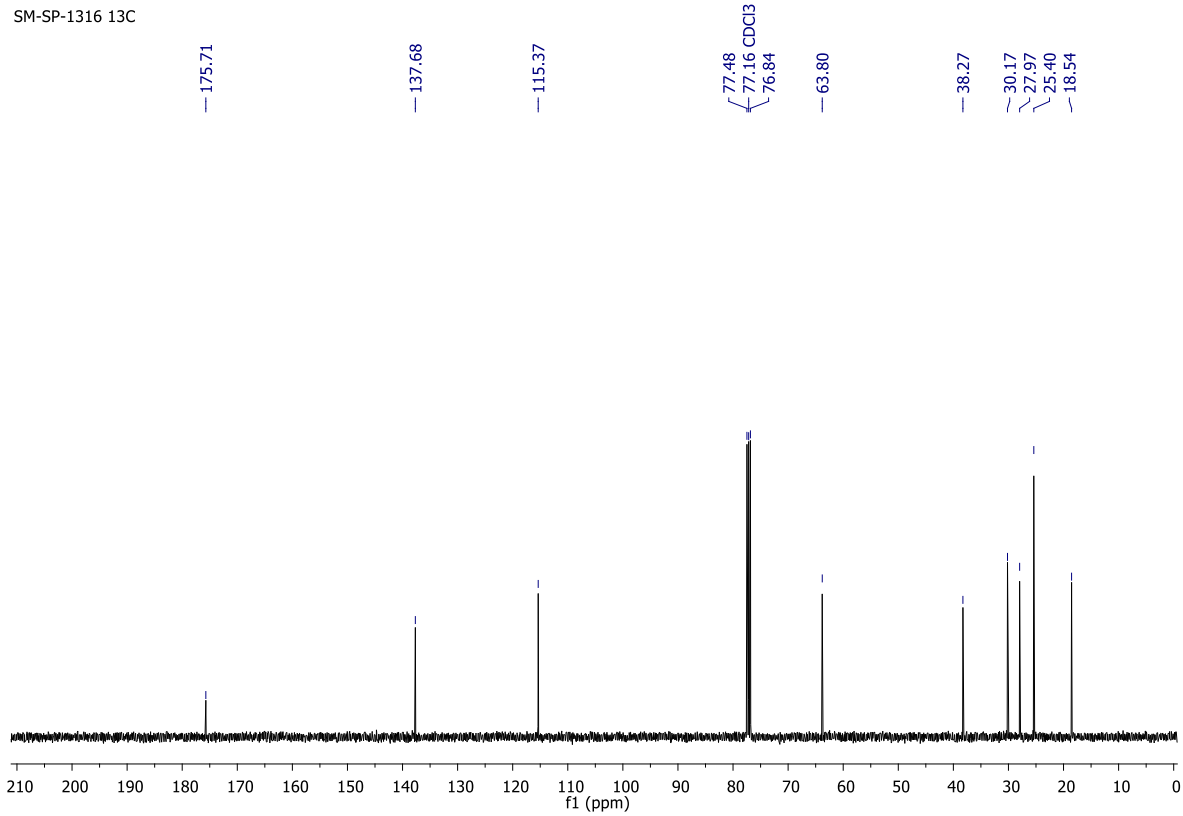
C	-4.694339000	-3.489128000	-0.053479000
H	-4.204588000	-3.740768000	0.888786000
H	-4.076199000	-3.853816000	-0.875633000
H	-5.654550000	-4.006366000	-0.090235000
N	-2.990223000	2.814890000	-0.496590000
H	-3.956701000	2.518218000	-0.500099000
H	-2.768063000	3.786190000	-0.371795000
O	-3.632515000	-1.370498000	-0.111952000
O	-4.655913000	0.621108000	-0.327062000
S	-0.387850000	2.306852000	-0.179769000
C	1.451316000	0.251114000	0.082470000
C	2.415645000	-0.095208000	1.028232000
C	1.829939000	0.191300000	-1.258739000
C	3.697108000	-0.486218000	0.663620000
C	3.096916000	-0.193352000	-1.653171000
H	1.103996000	0.464693000	-2.015558000
C	4.024193000	-0.530745000	-0.678647000
H	4.423071000	-0.750590000	1.419932000
H	3.364960000	-0.229738000	-2.700596000
Cl	2.060569000	-0.065438000	2.724909000
Cl	5.617991000	-1.014140000	-1.142422000
H	-0.028567000	0.718981000	1.541537000

10. NMR Spectra:

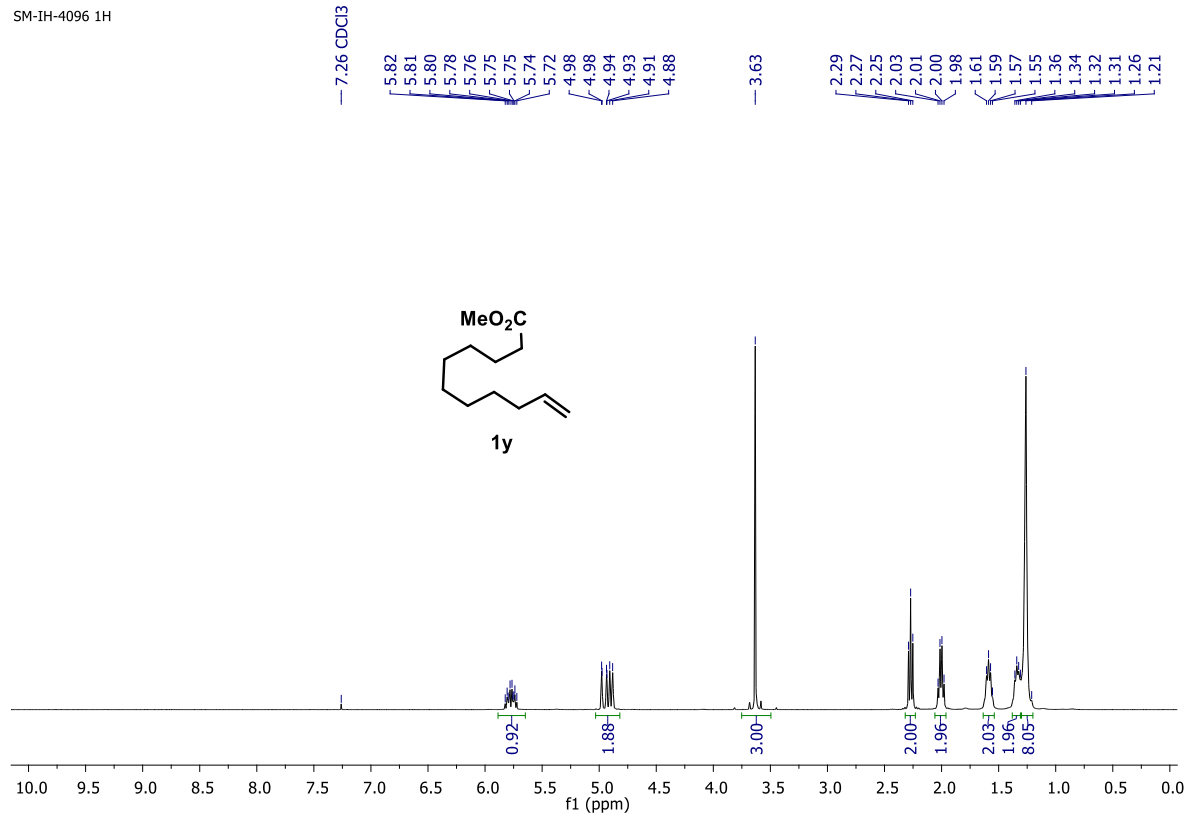
^{1}H NMR of **1x** (400 MHz, $CDCl_3$):



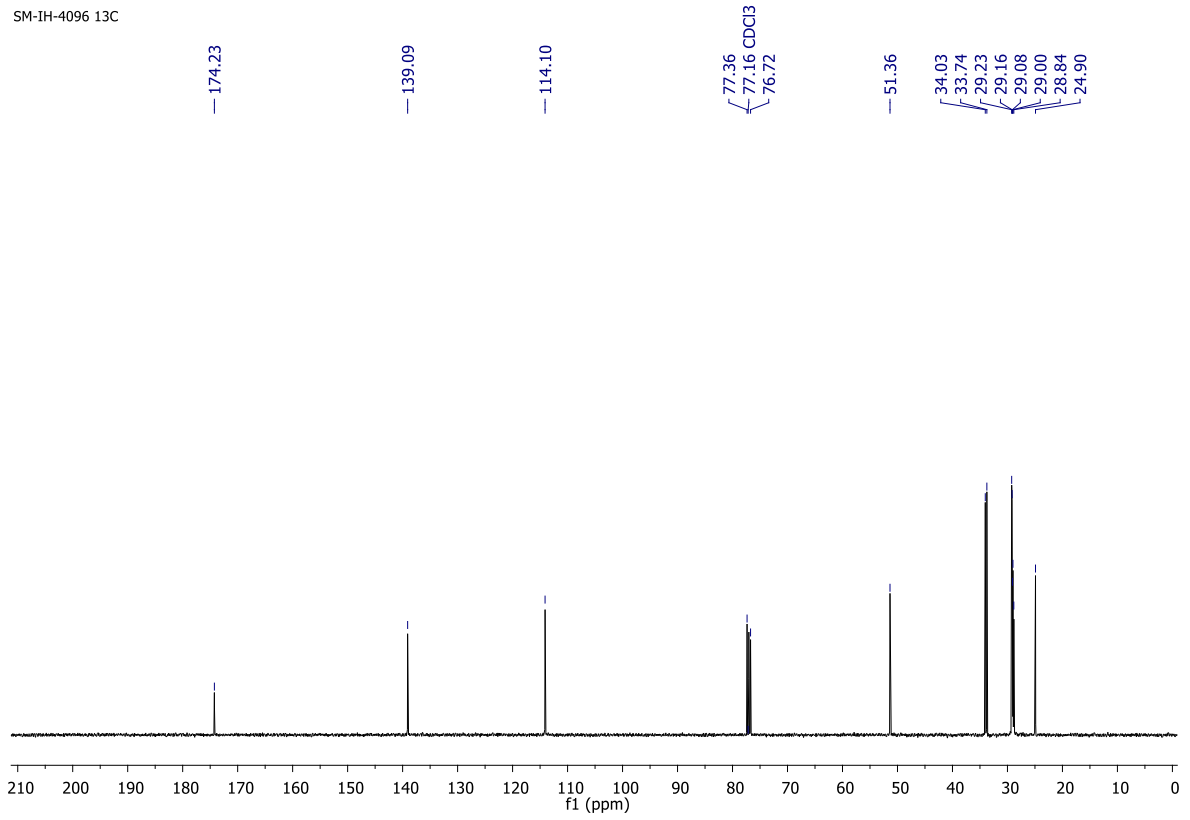
^{13}C{^{1}H} NMR of **1x** (101 MHz, $CDCl_3$):



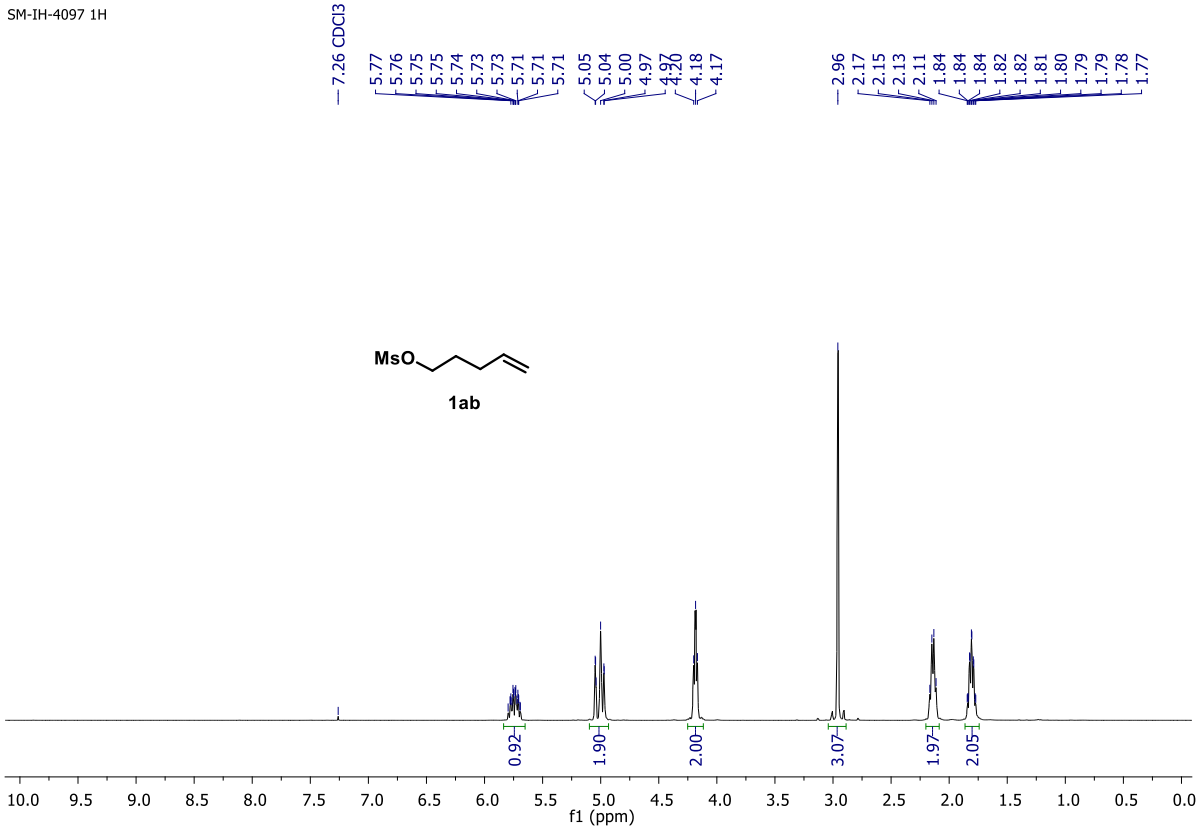
^{1}H NMR of **1y** (400 MHz, $CDCl_3$):



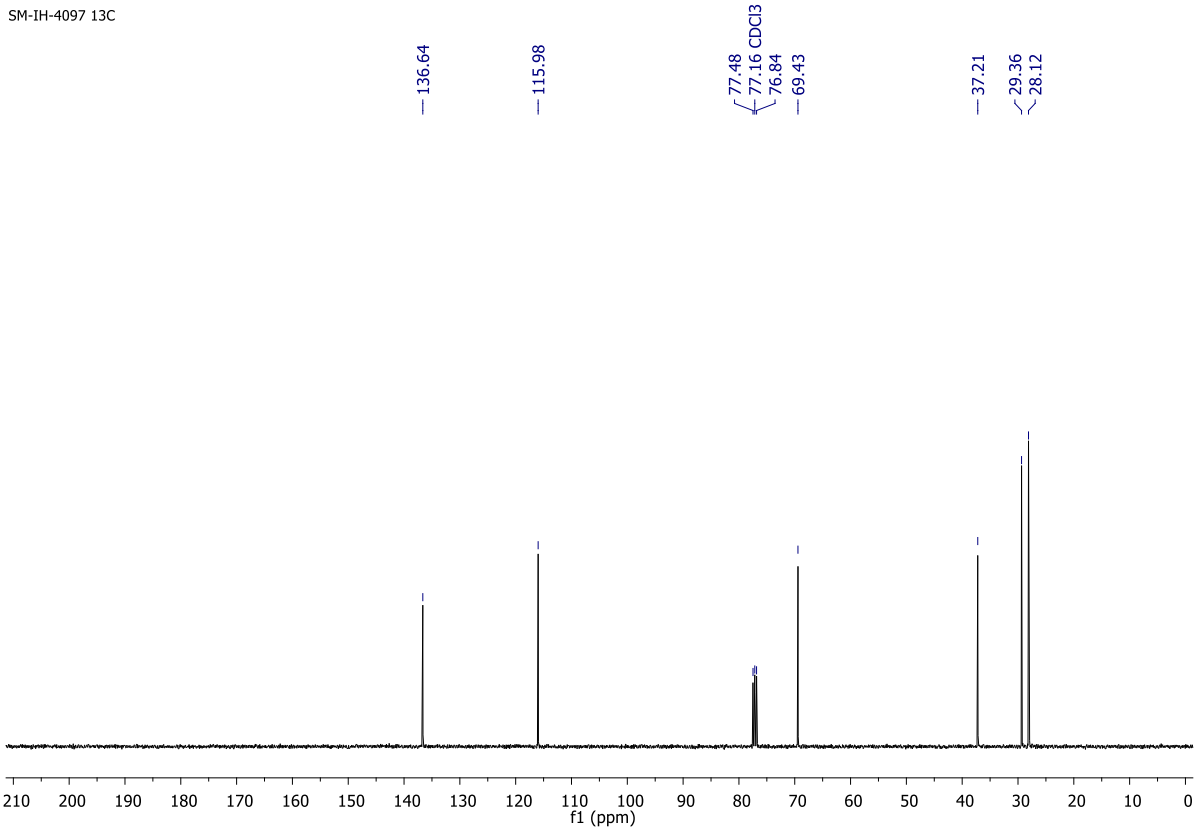
^{13}C{^{1}H} NMR of **1y** (101 MHz, $CDCl_3$):



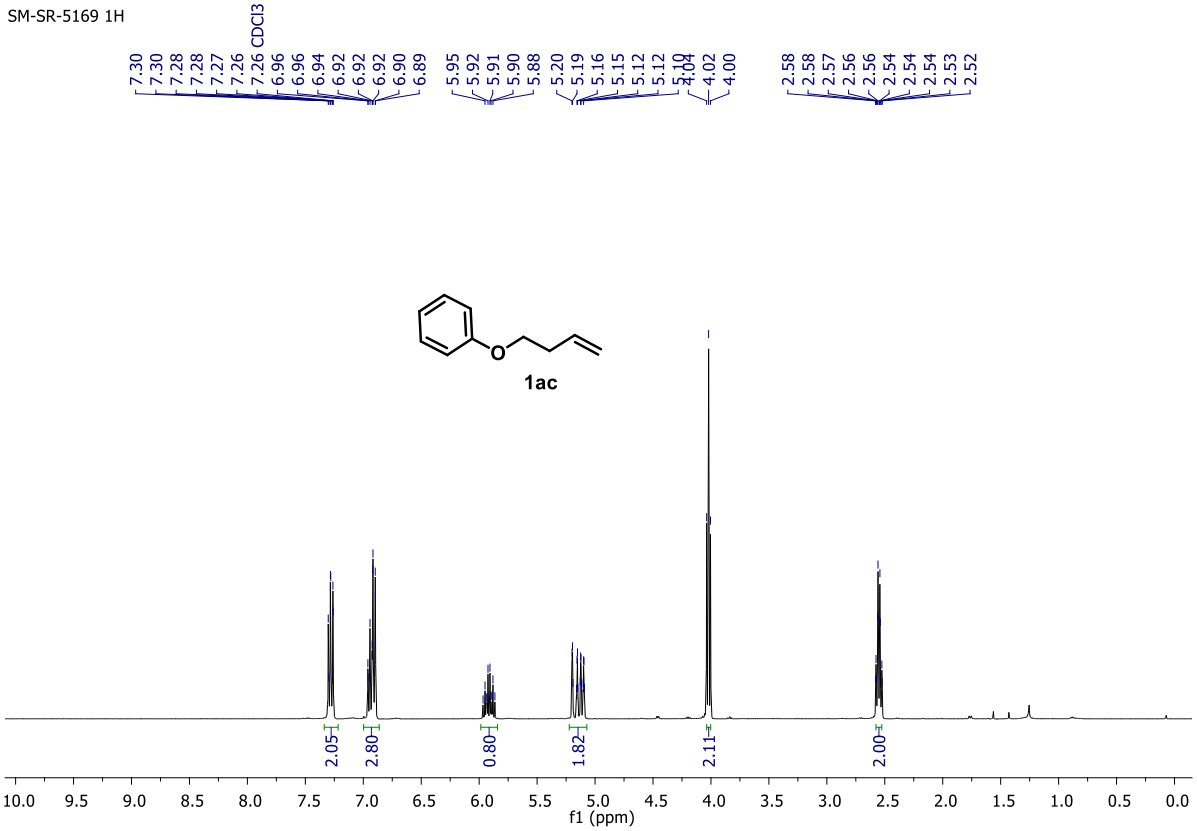
^{1}H NMR of **1ab** (400 MHz, $CDCl_3$):



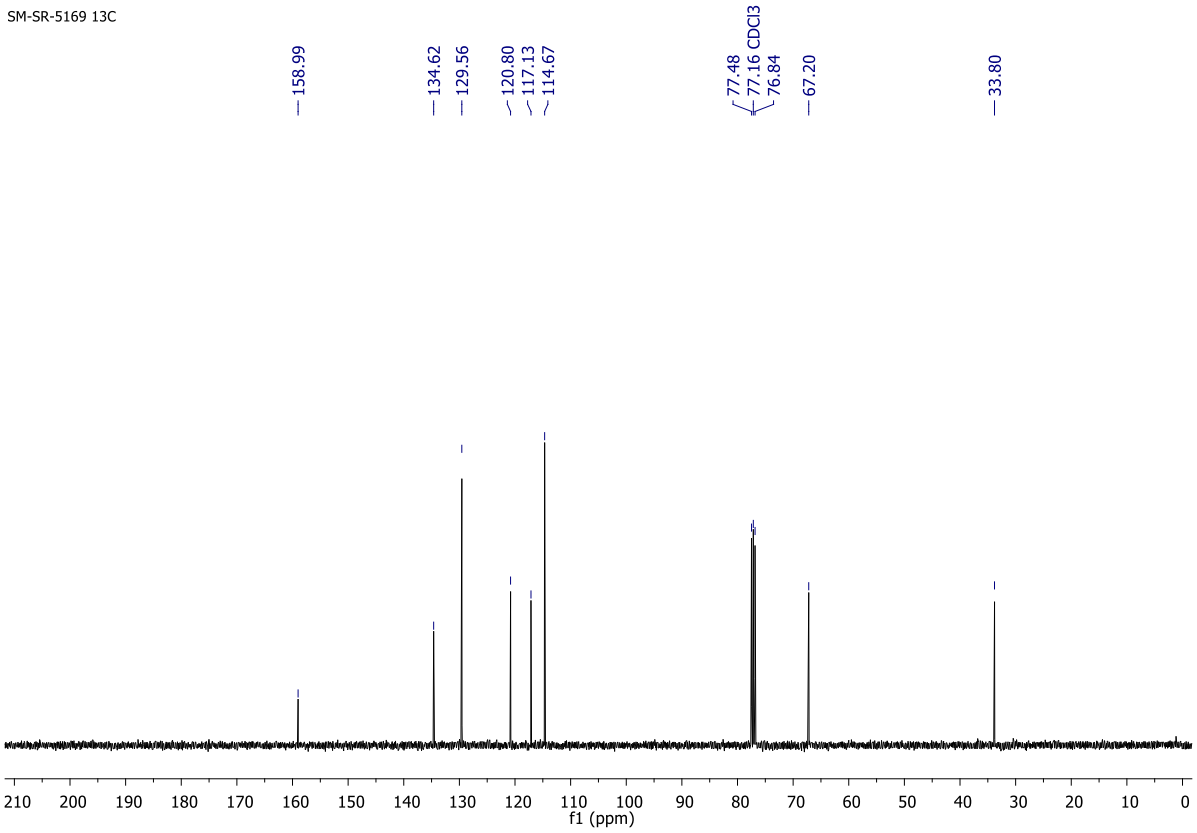
^{13}C{^{1}H} NMR of **1ab** (101 MHz, $CDCl_3$):



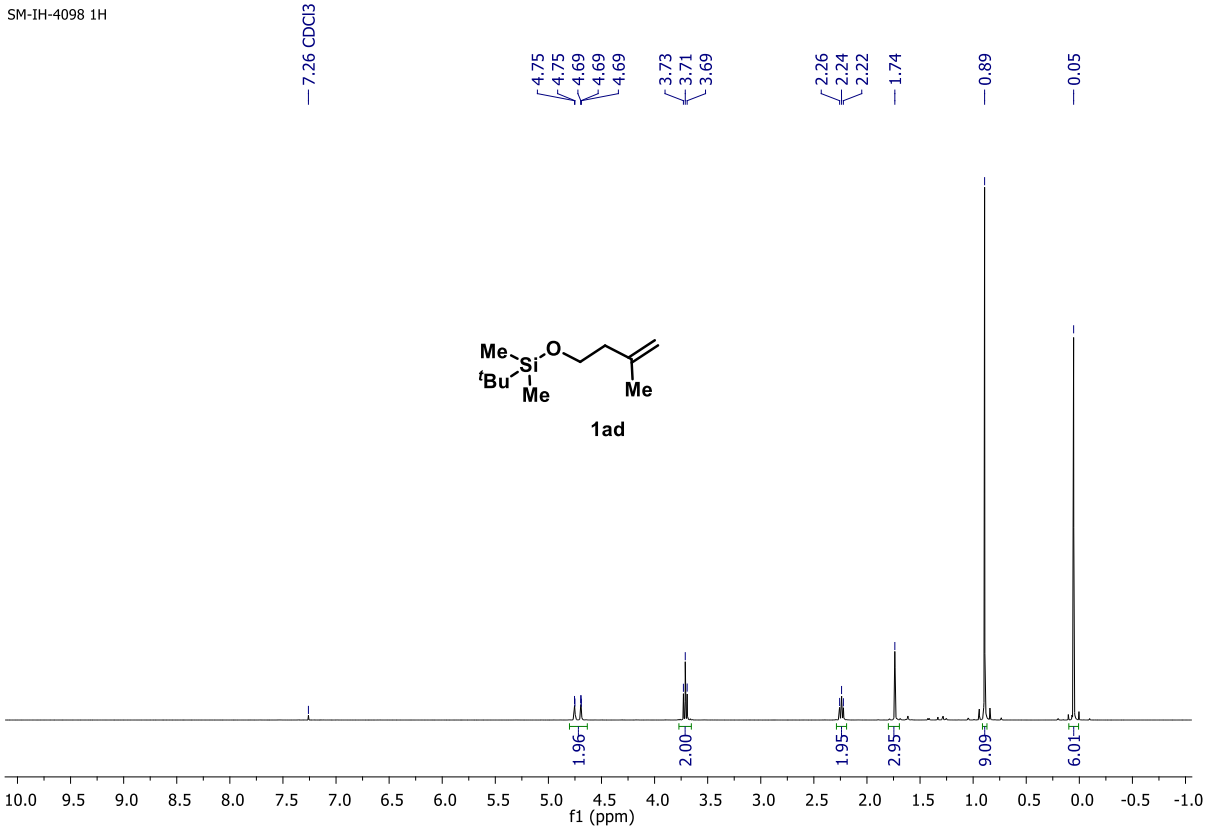
^{1}H NMR of **1ac** (400 MHz, $CDCl_3$):



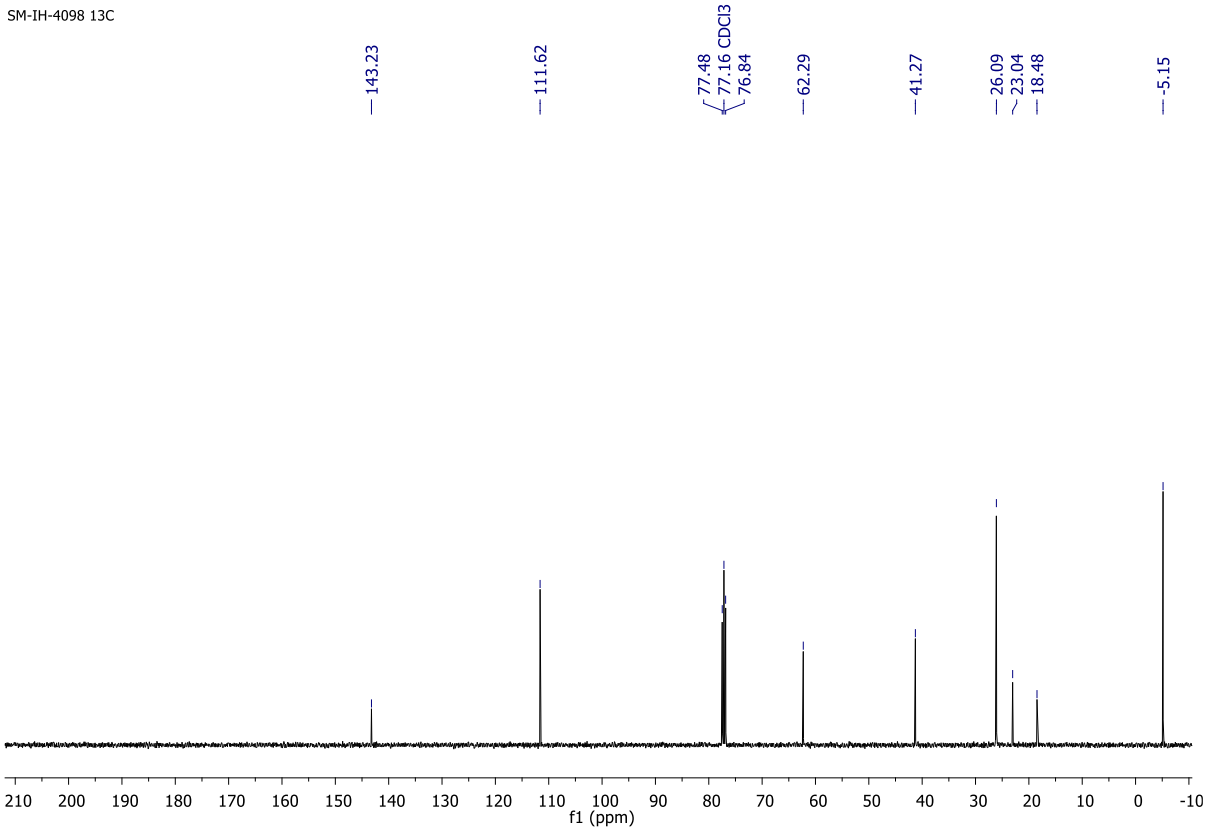
^{13}C{^{1}H} NMR of **1ac** (101 MHz, $CDCl_3$):



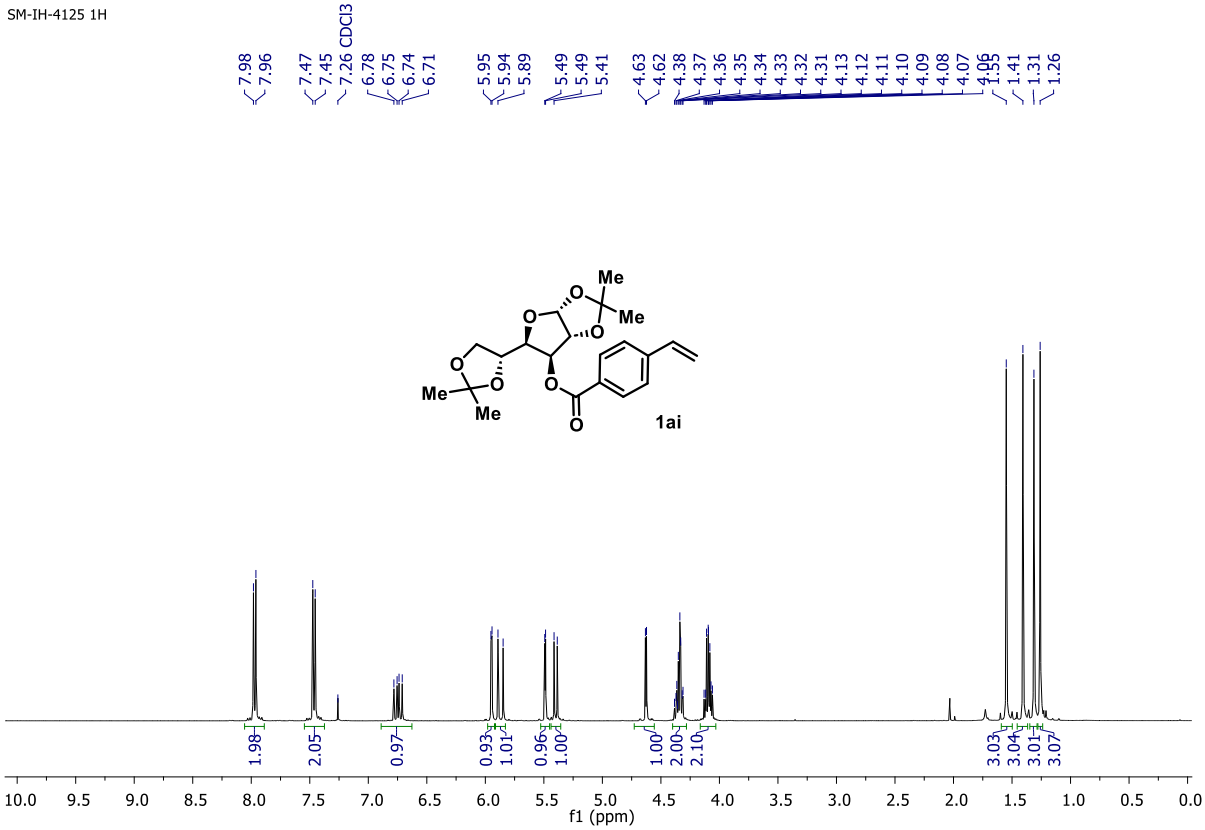
^{1}H NMR of **1ad** (400 MHz, $CDCl_3$):



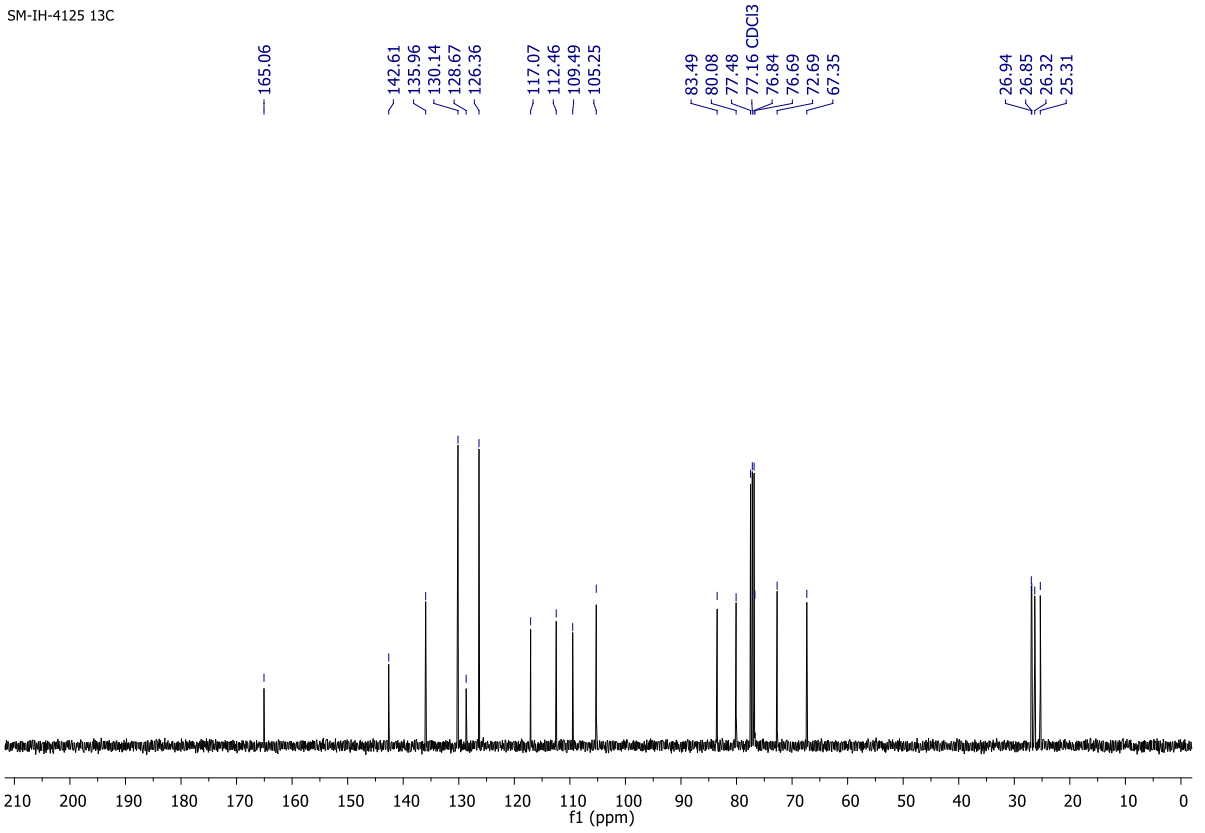
^{13}C{^{1}H} NMR of **1ad** (101 MHz, $CDCl_3$):



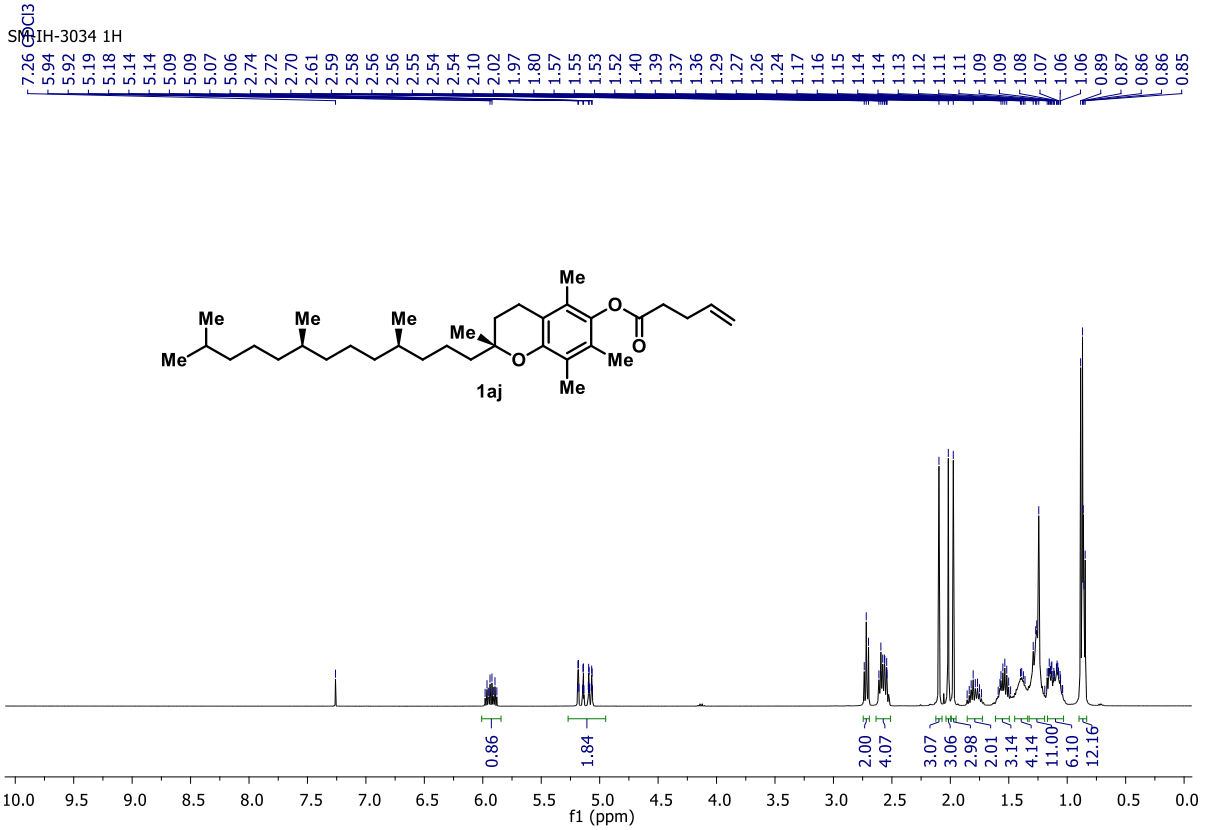
^{1}H NMR of **1ai** (400 MHz, $CDCl_3$):



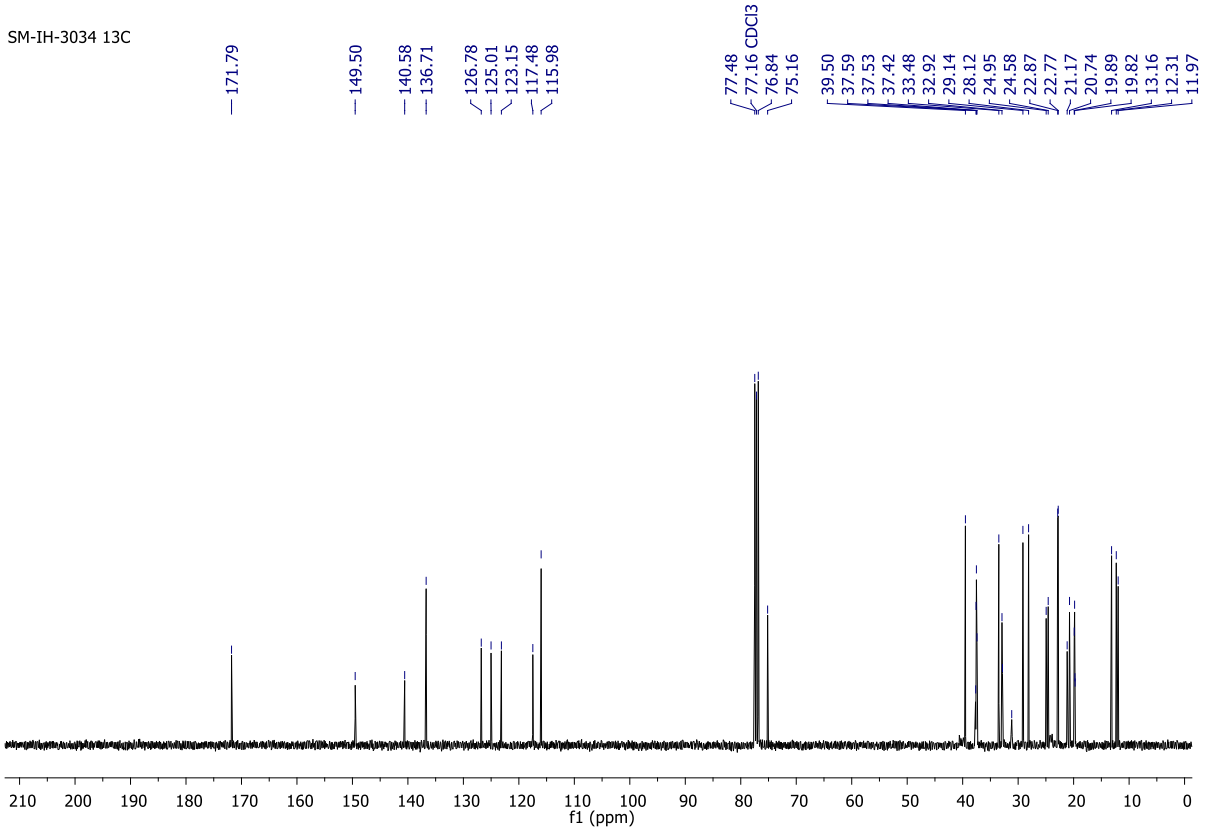
^{13}C{^{1}H} NMR of **1ai** (101 MHz, $CDCl_3$):



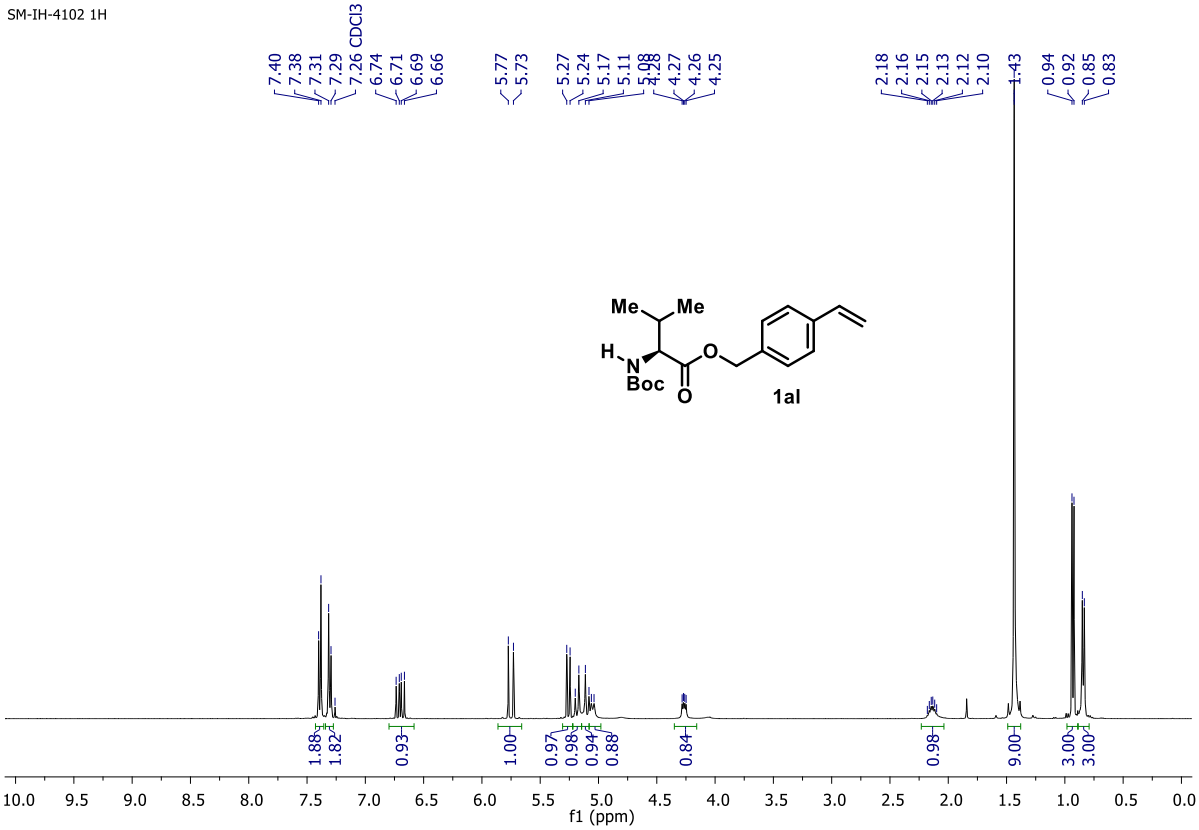
^{1}H NMR of **1aj** (400 MHz, $CDCl_3$):



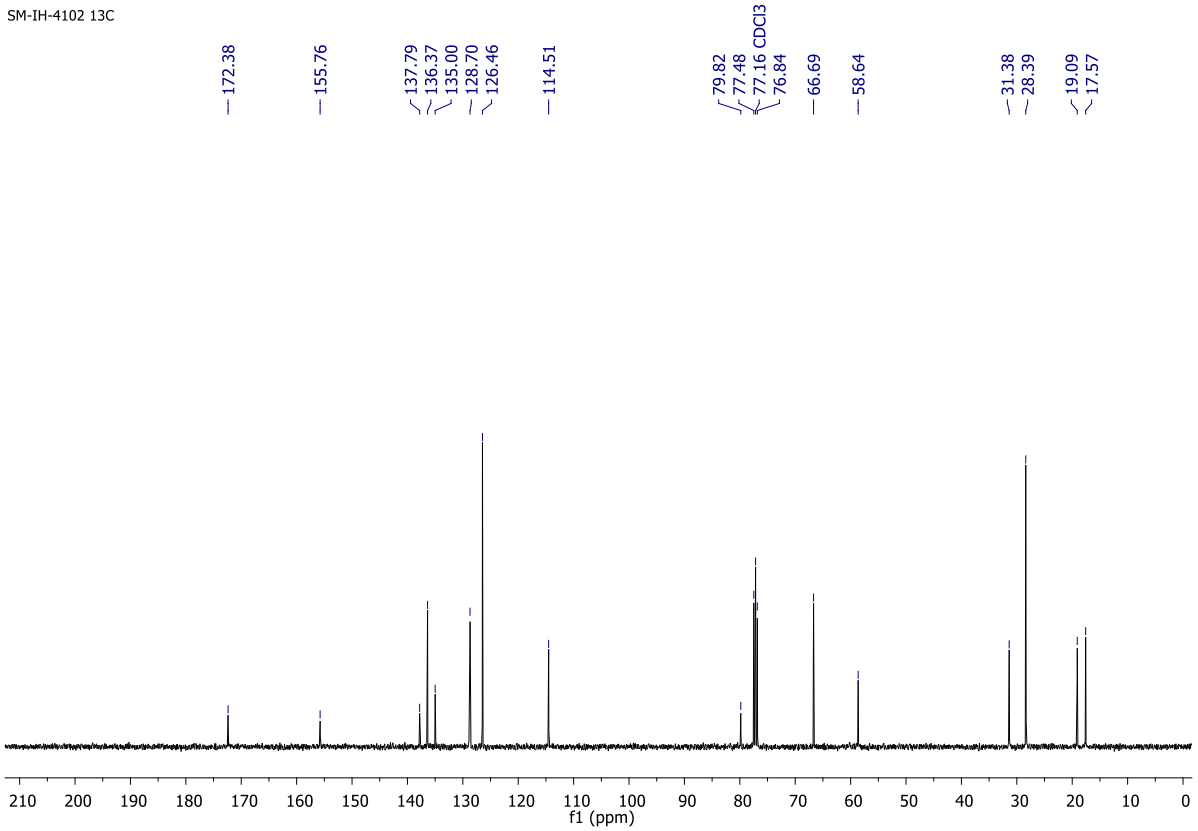
^{13}C{^{1}H} NMR of **1aj** (101 MHz, $CDCl_3$):



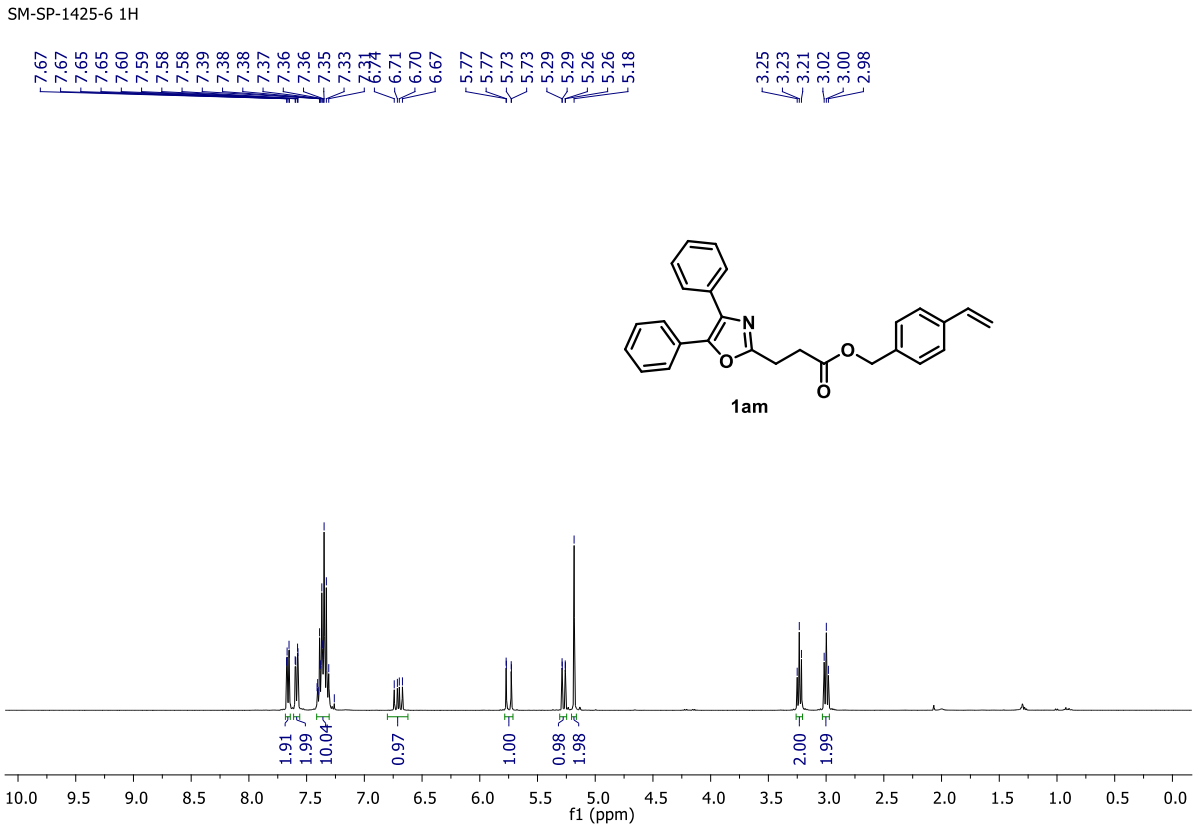
^{1}H NMR of **1al** (400 MHz, $CDCl_3$):



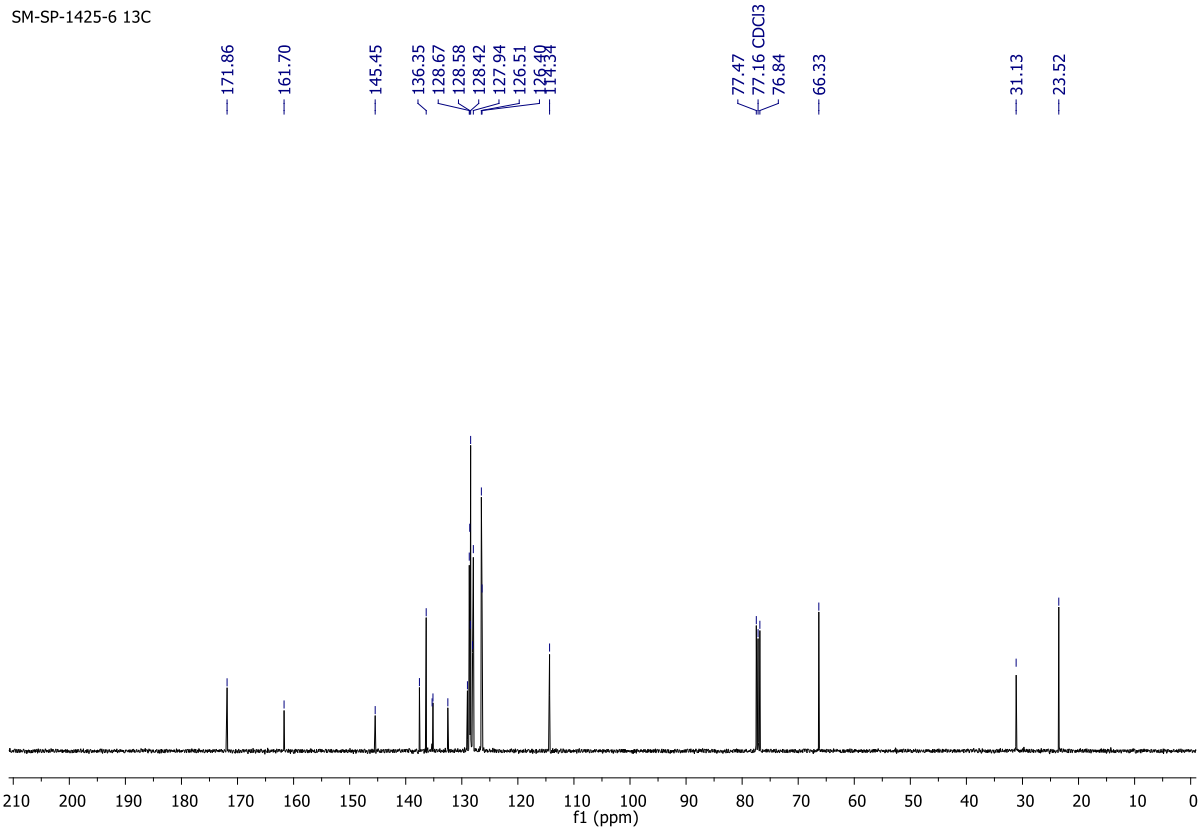
^{13}C{^{1}H} NMR of **1al** (101 MHz, $CDCl_3$):



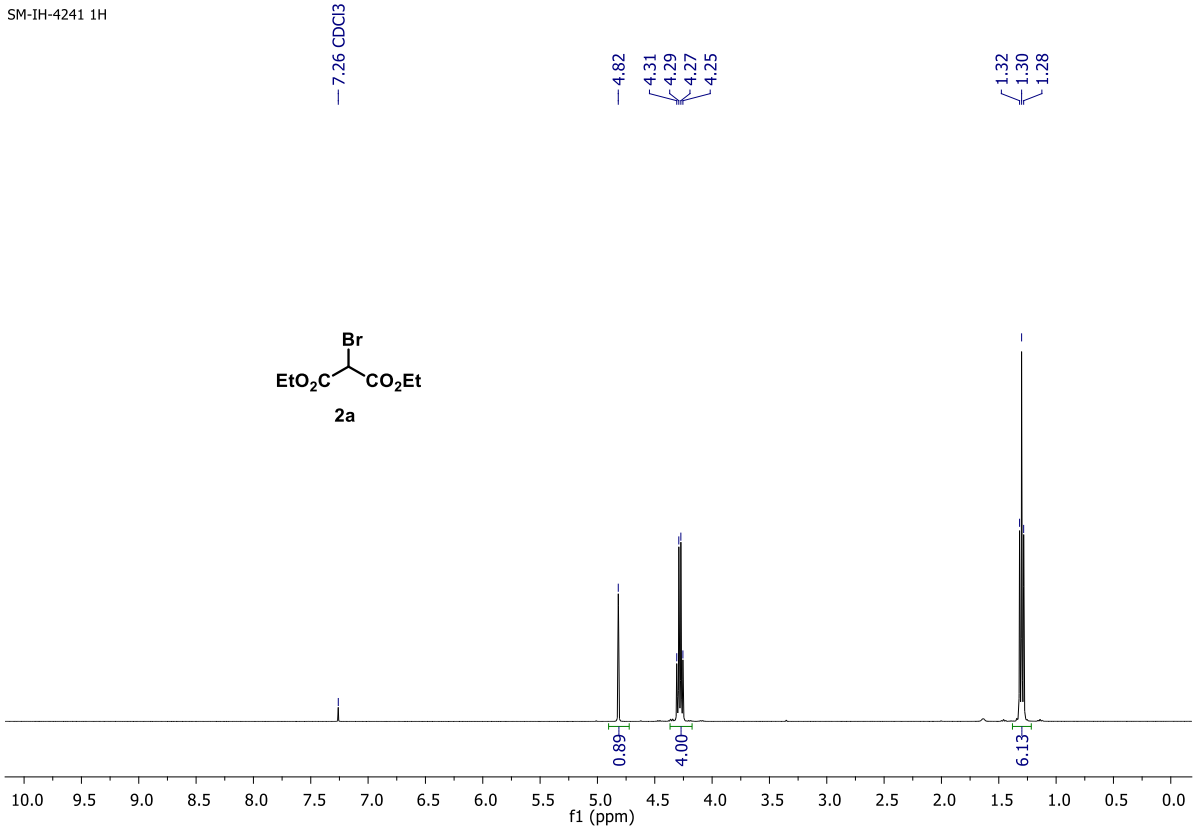
^{1}H NMR of **1am** (400 MHz, $CDCl_3$):



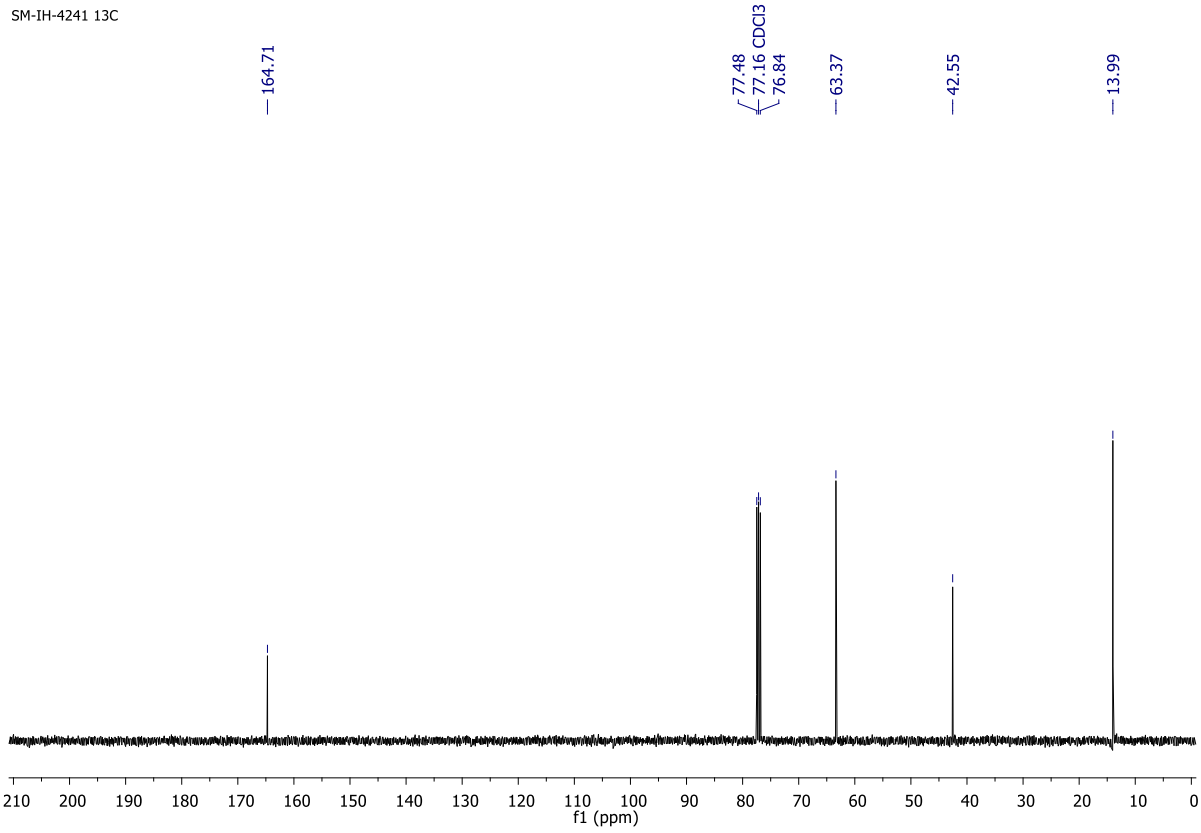
^{13}C{^{1}H} NMR of **1am** (101 MHz, $CDCl_3$):



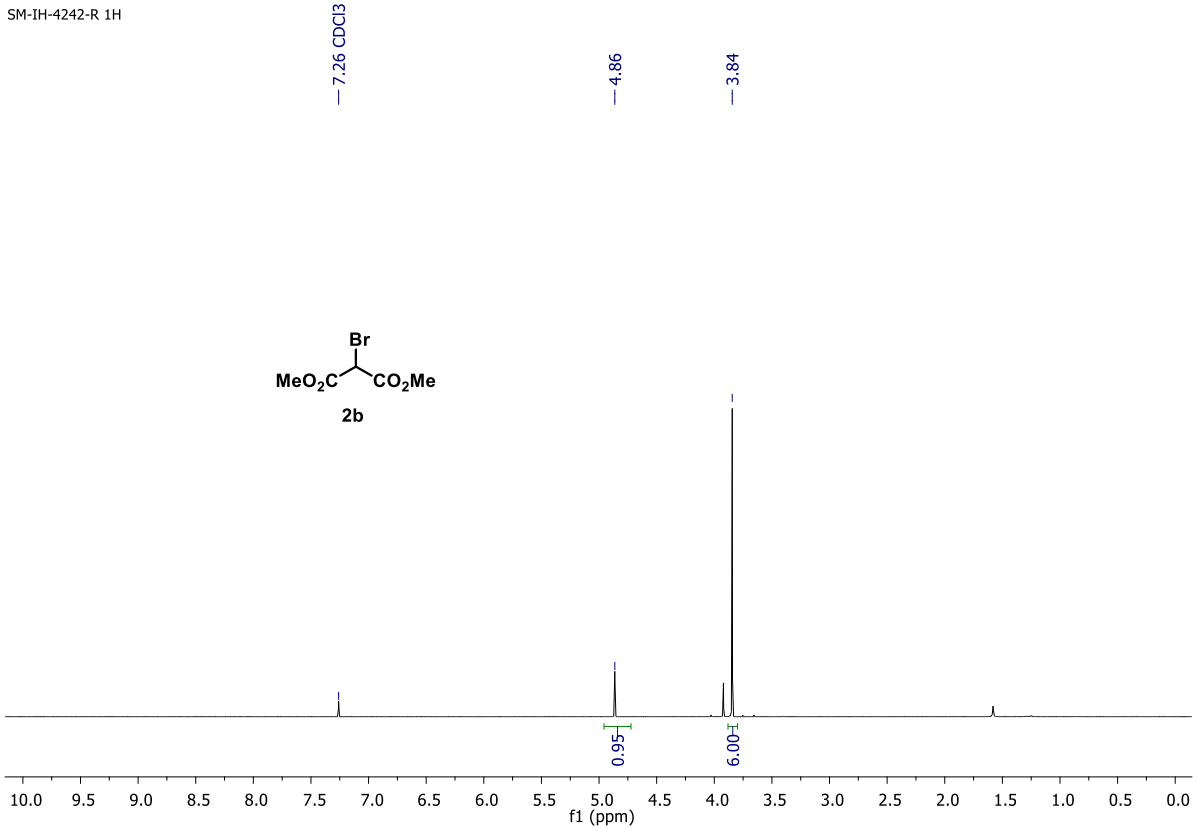
^{1}H NMR of **2a** (400 MHz, $CDCl_3$):



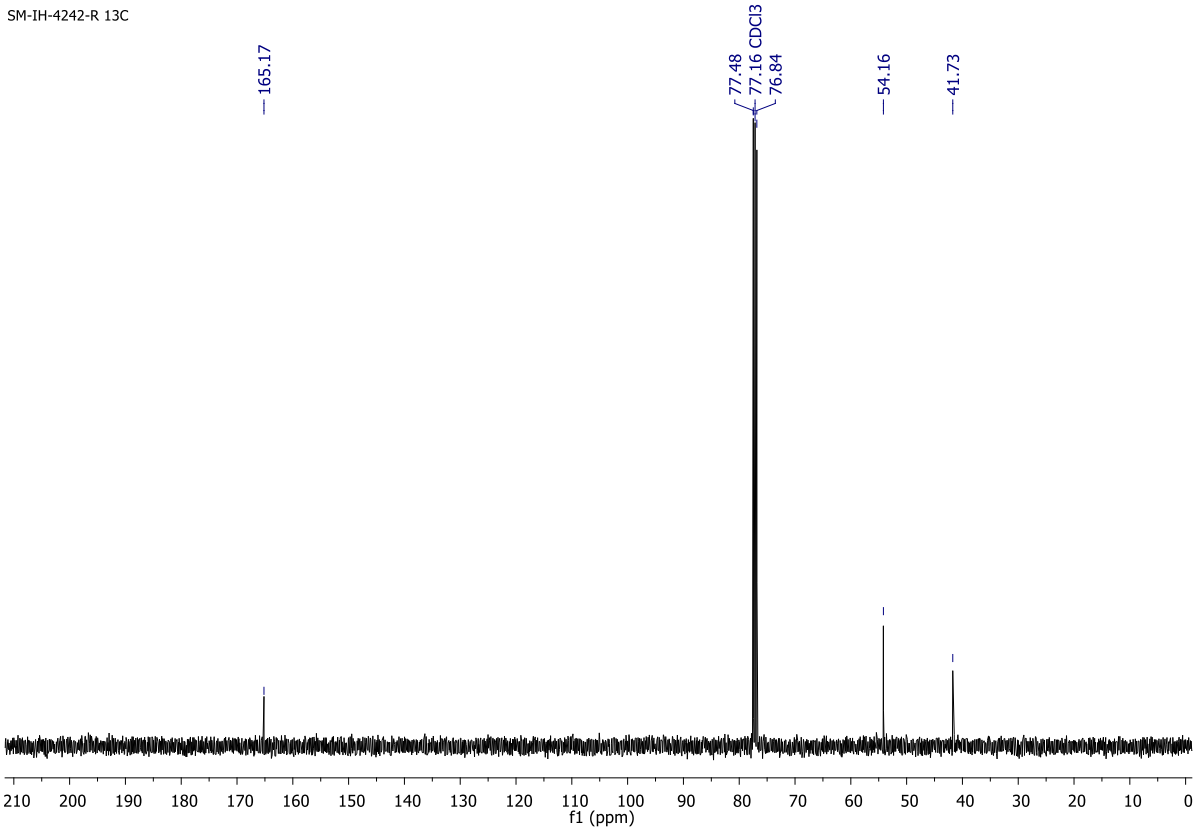
^{13}C{^{1}H} NMR of **2a** (101 MHz, $CDCl_3$):



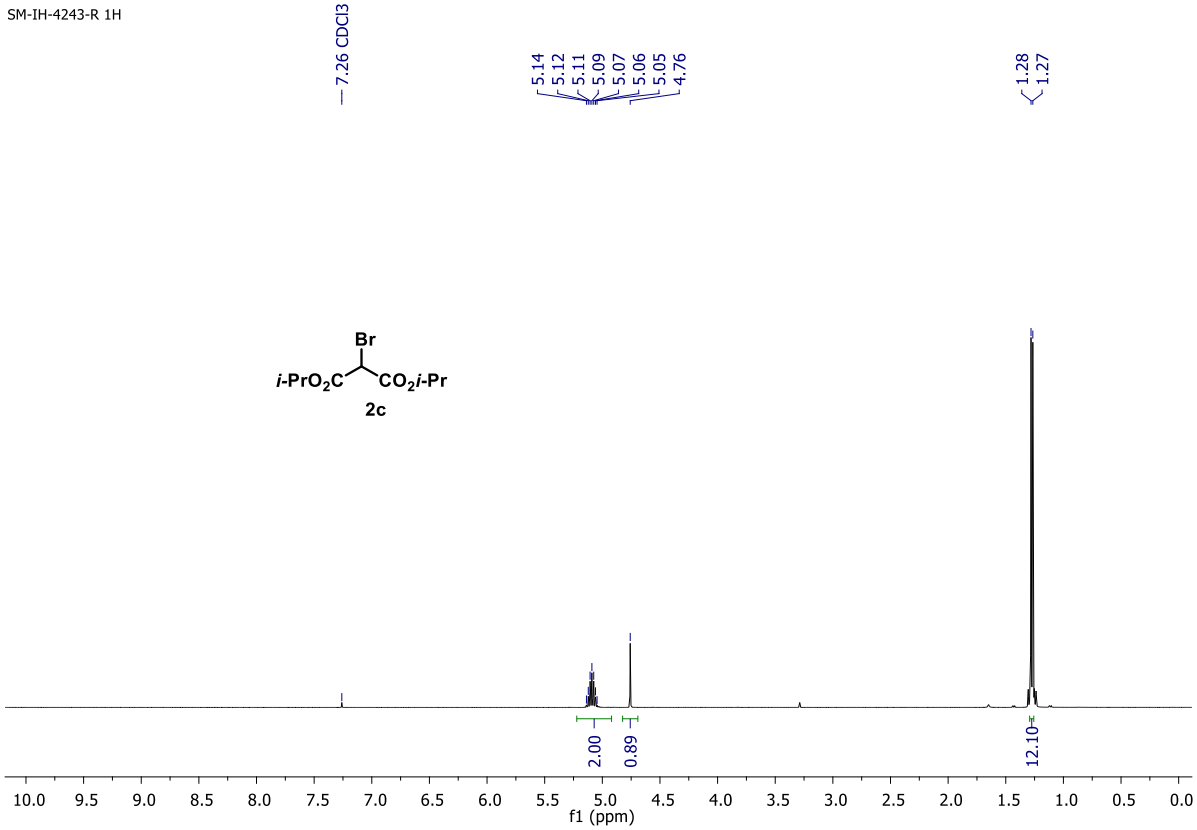
^{1}H NMR of **2b** (400 MHz, $CDCl_3$):



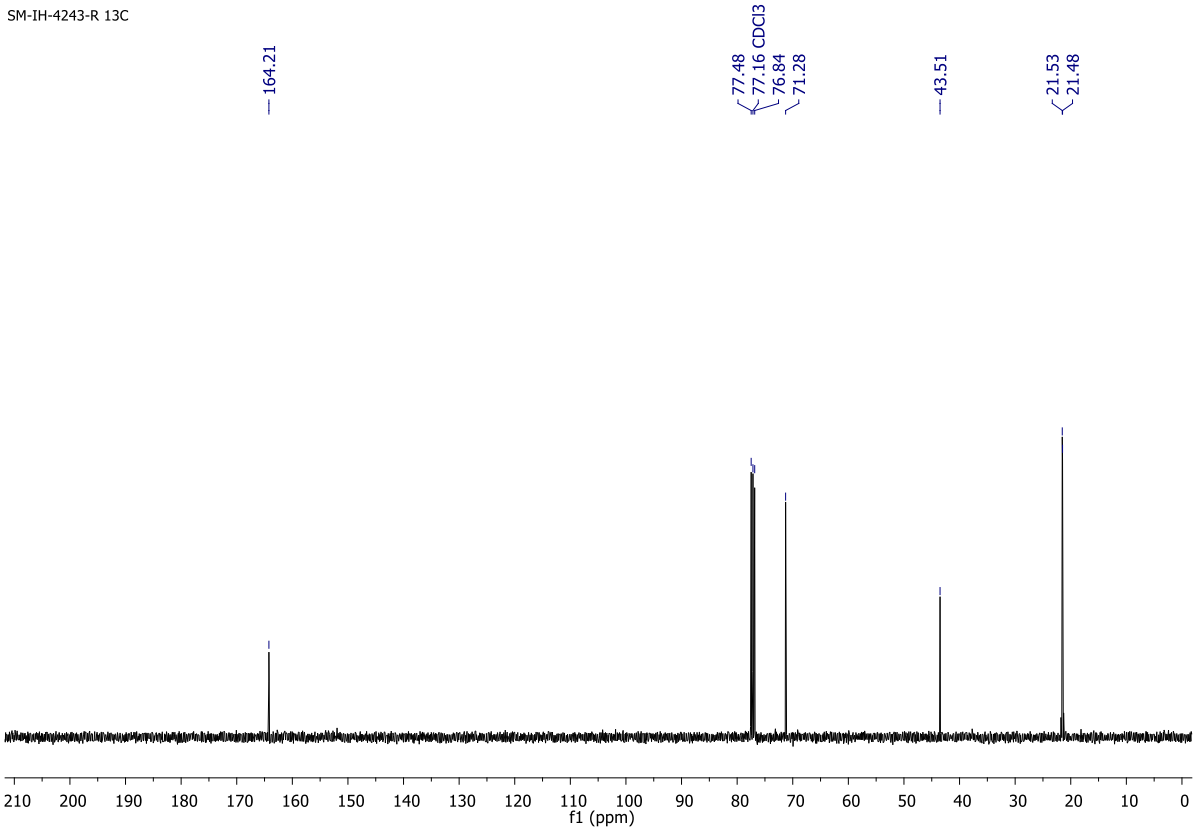
^{13}C{^{1}H} NMR of **2b** (101 MHz, $CDCl_3$):



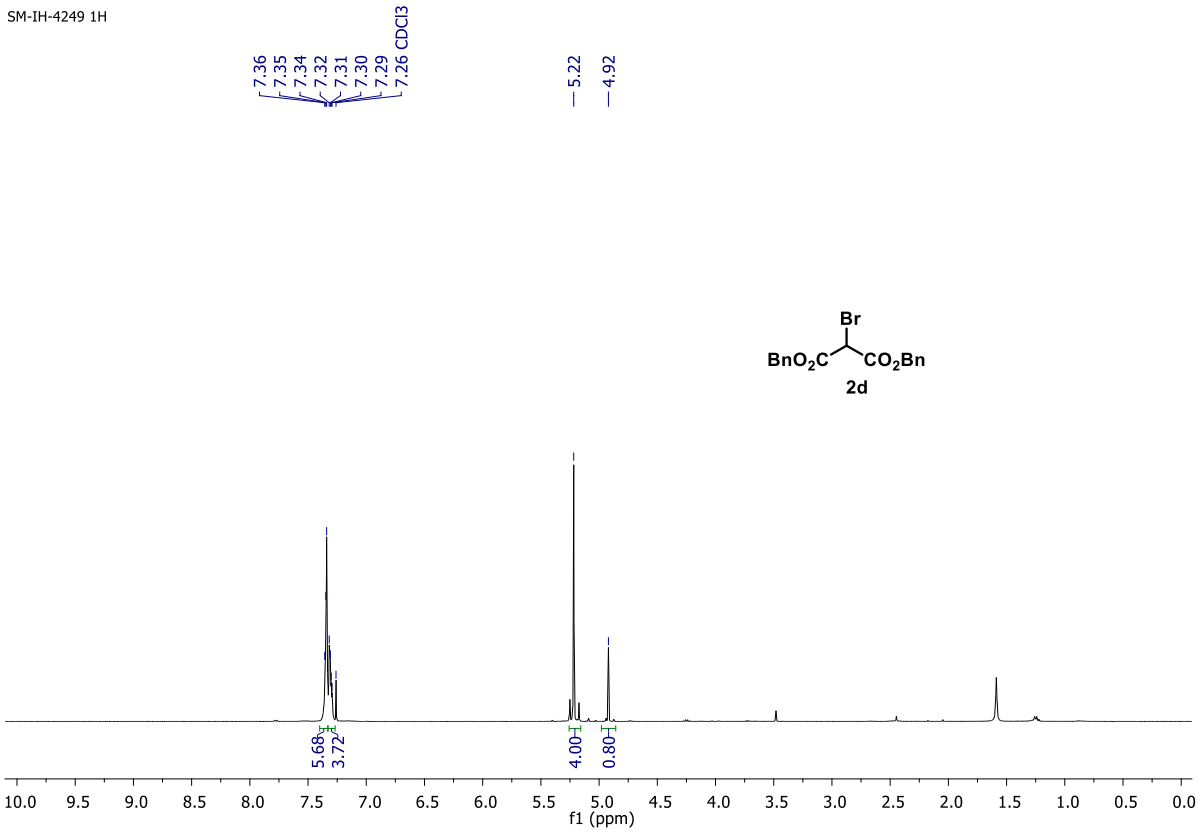
^{1}H NMR of **2c** (400 MHz, $CDCl_3$):



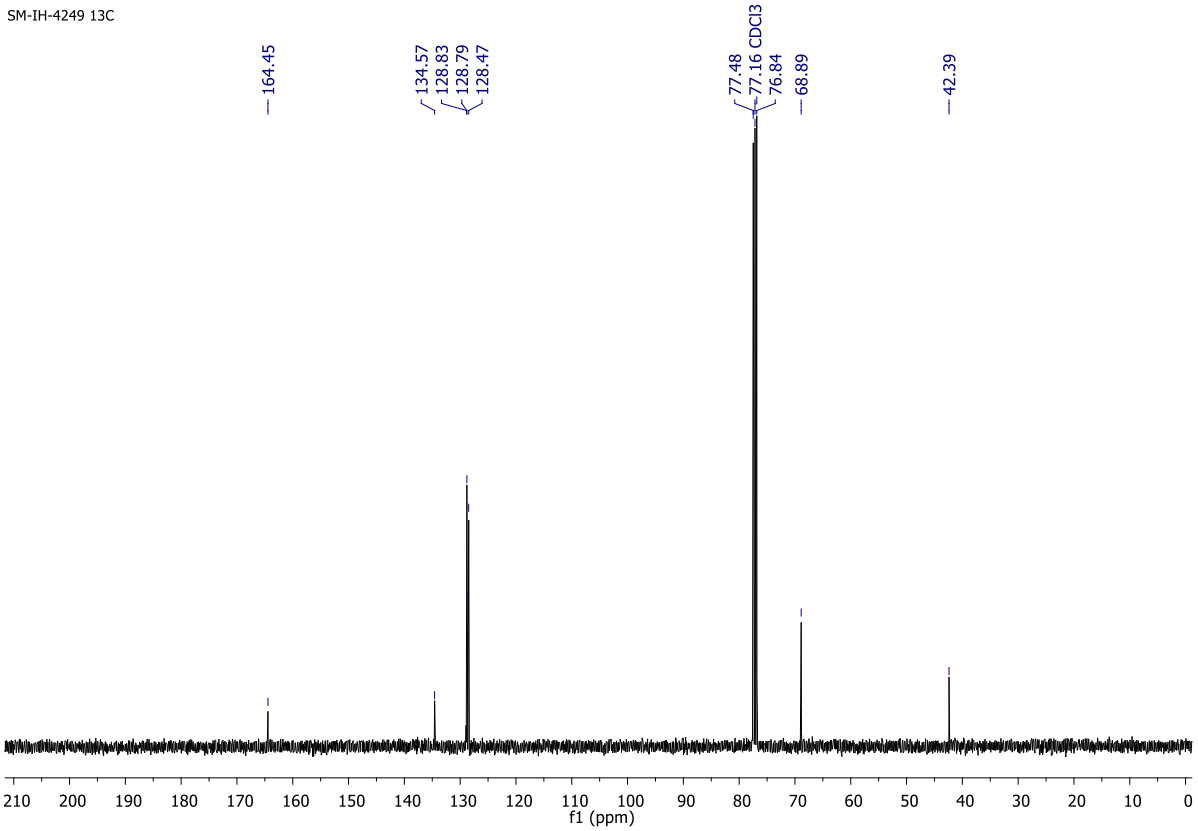
^{13}C{^{1}H} NMR of **2c** (101 MHz, $CDCl_3$):



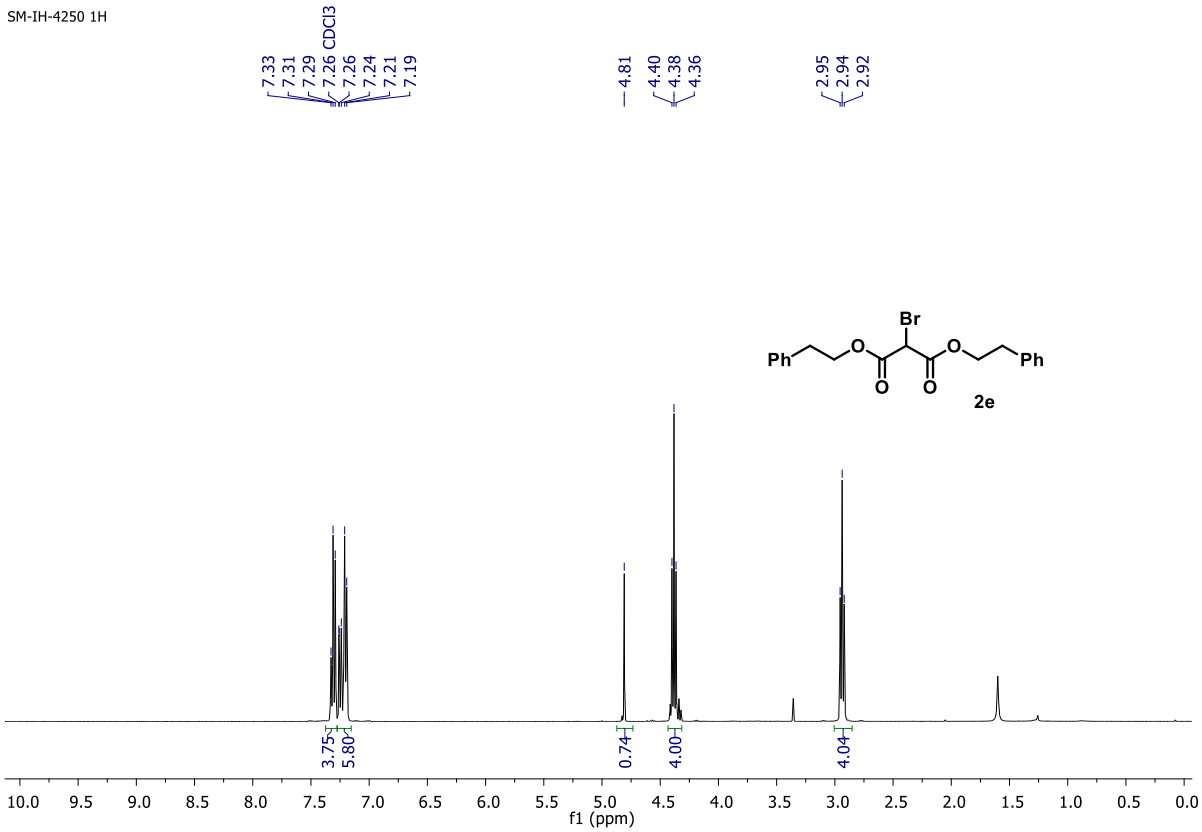
^{1}H NMR of **2d** (400 MHz, $CDCl_3$):



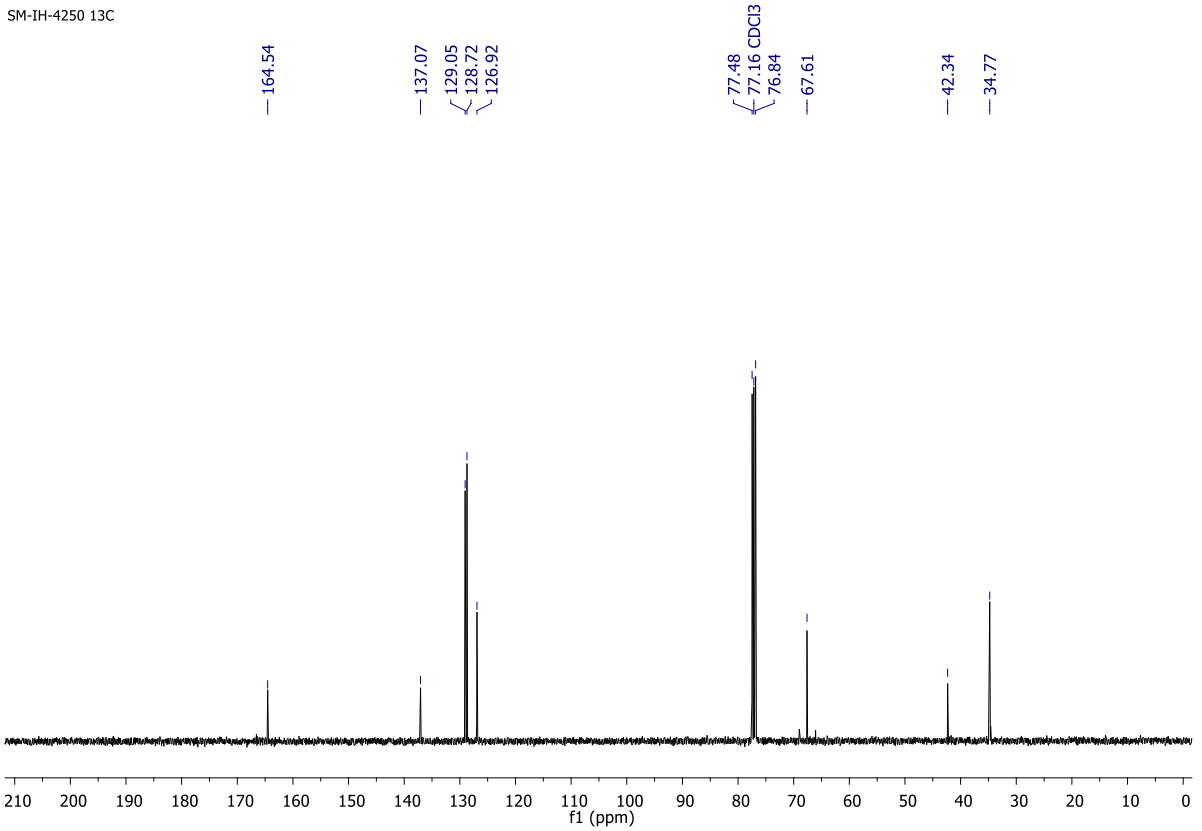
^{13}C{^{1}H} NMR of **2d** (101 MHz, $CDCl_3$):



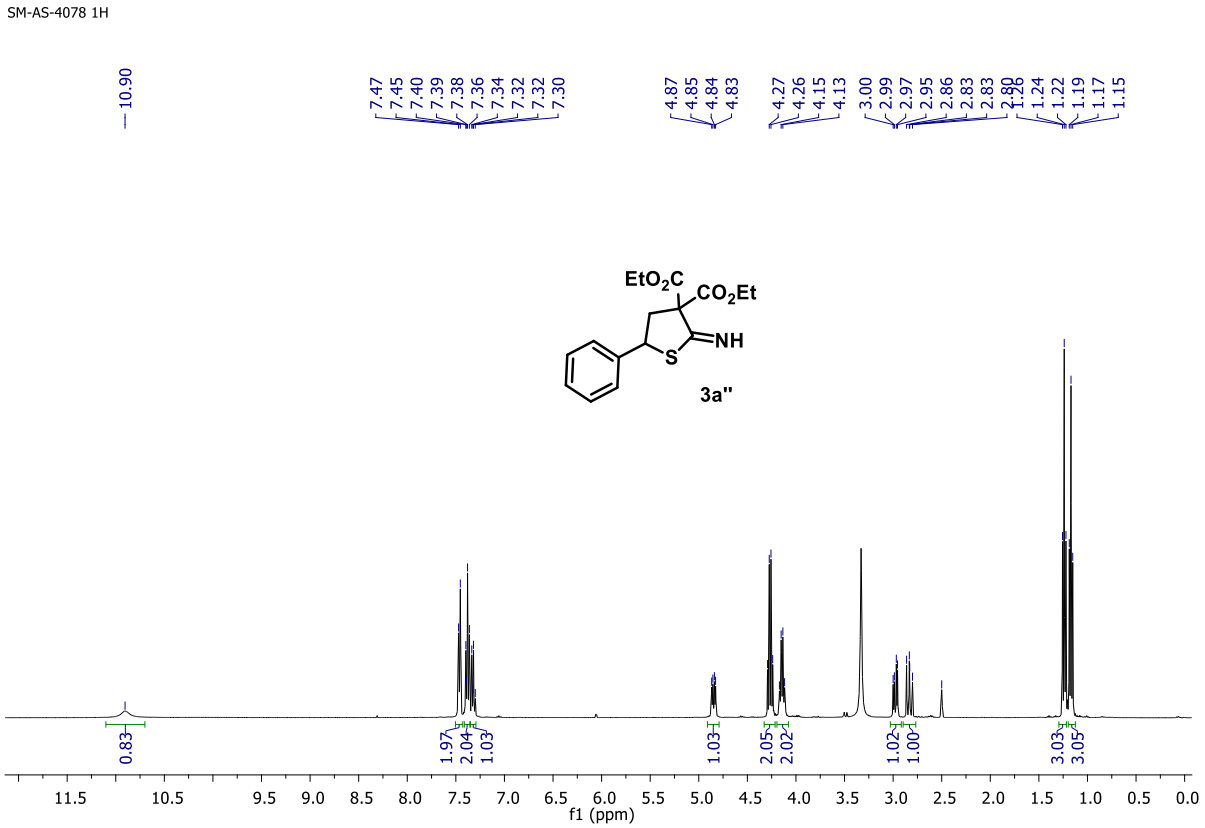
^{1}H NMR of **2e** (400 MHz, $CDCl_3$):



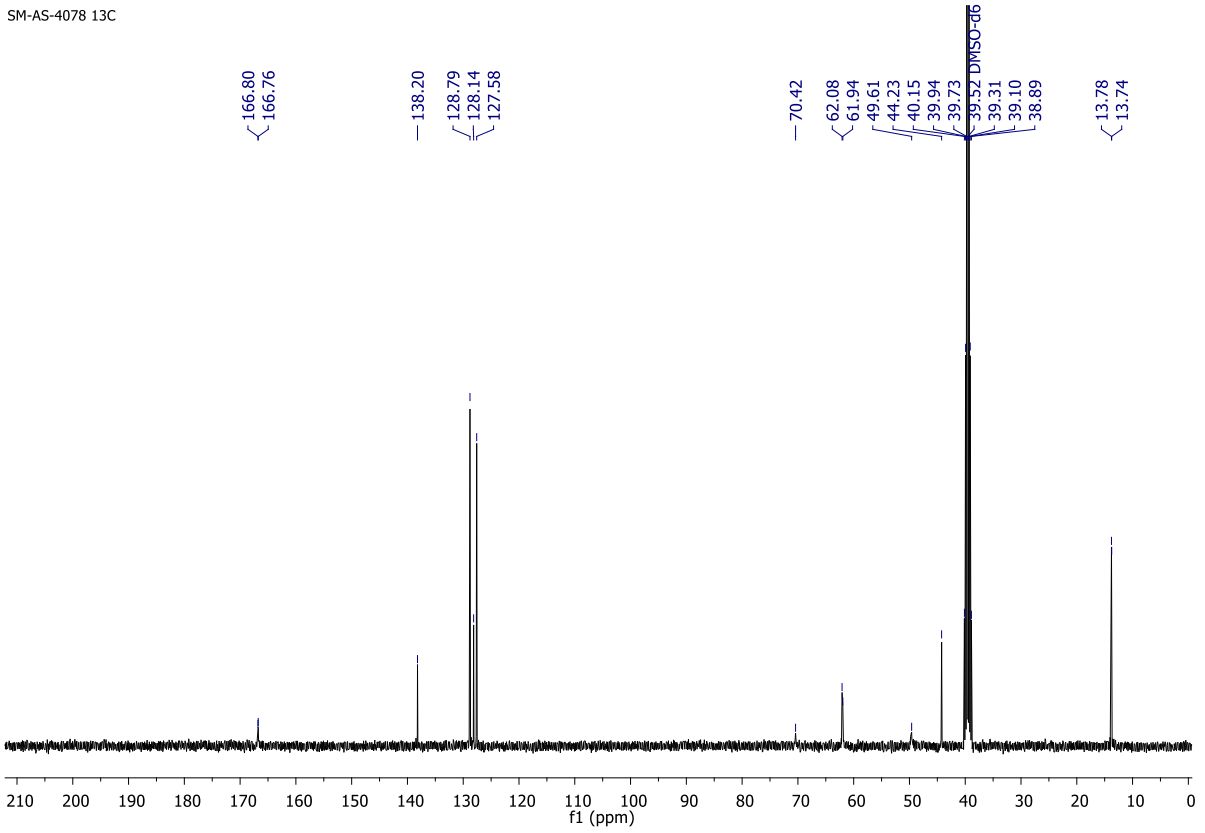
^{13}C{^{1}H} NMR of **2e** (101 MHz, $CDCl_3$):



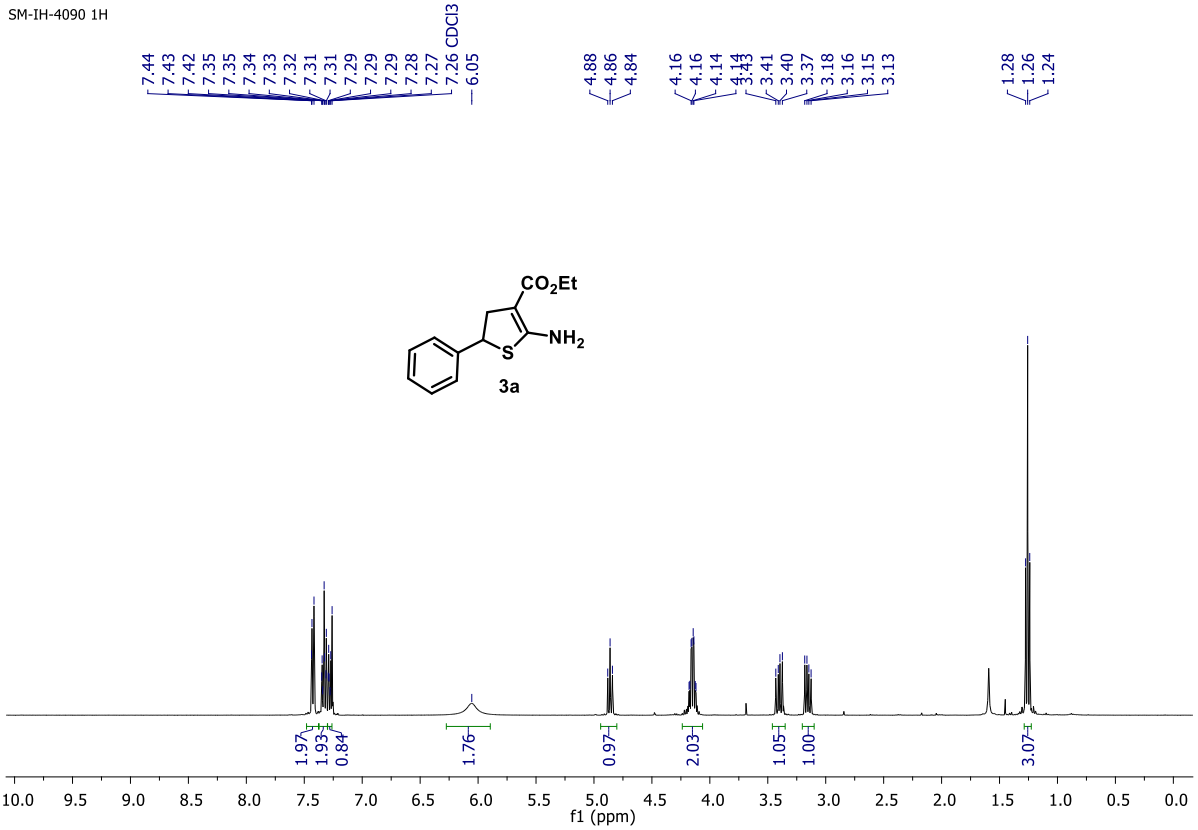
^{1}H NMR of **3a"** (400 MHz, DMSO-d_6):



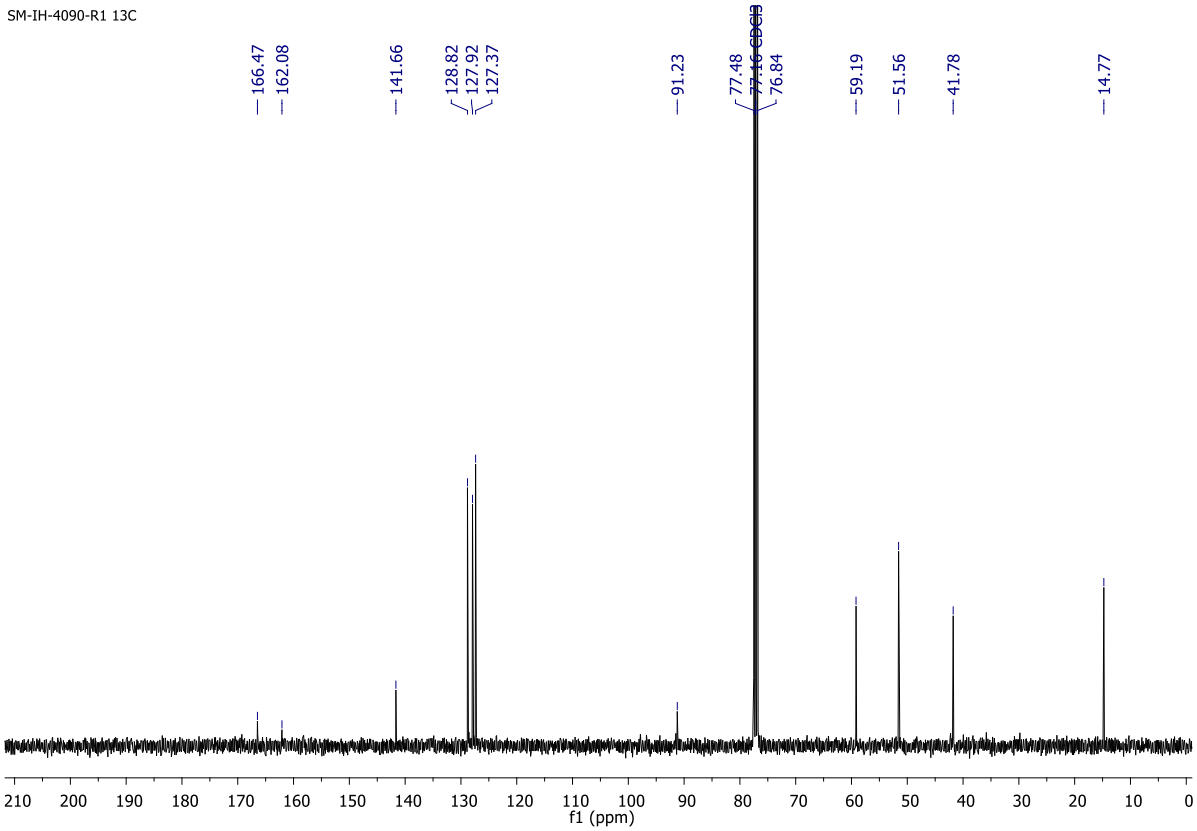
^{13}C{^{1}H} NMR of **3a"** (101 MHz, DMSO-d_6):



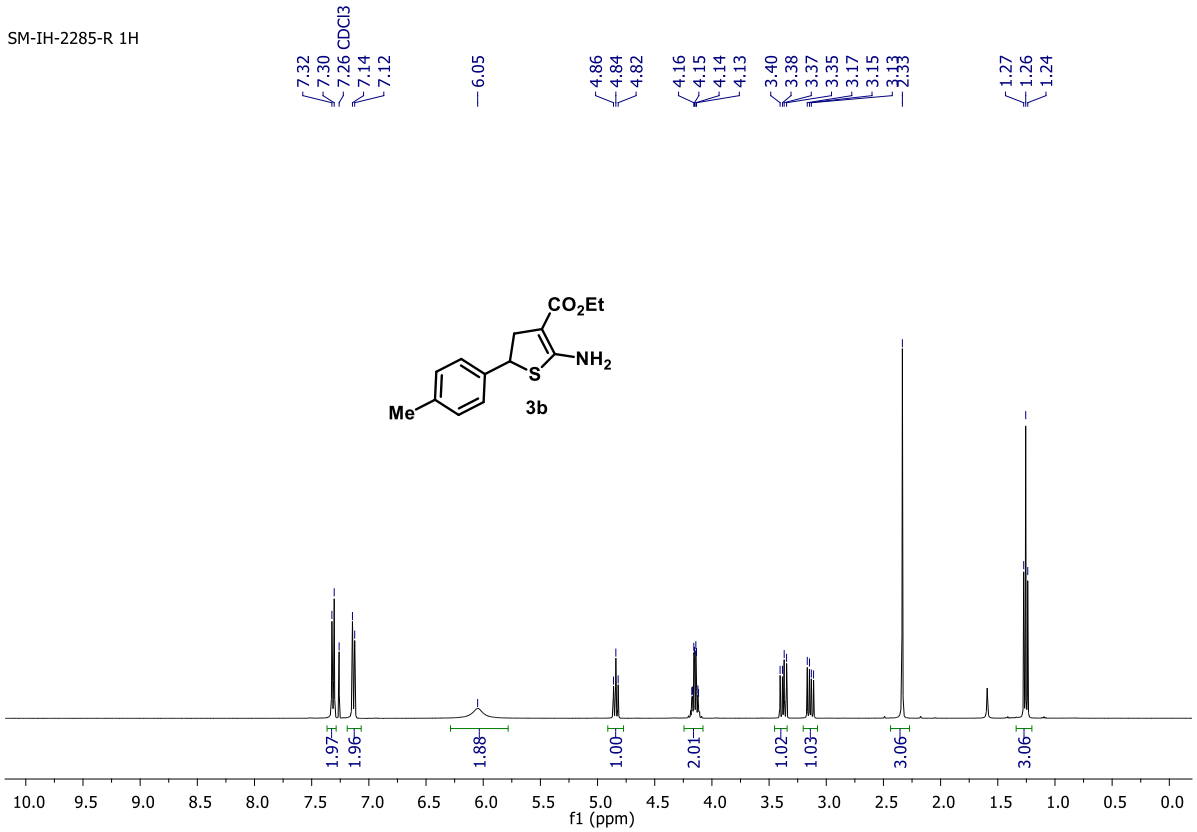
^{1}H NMR of **3a** (400 MHz, $CDCl_3$):



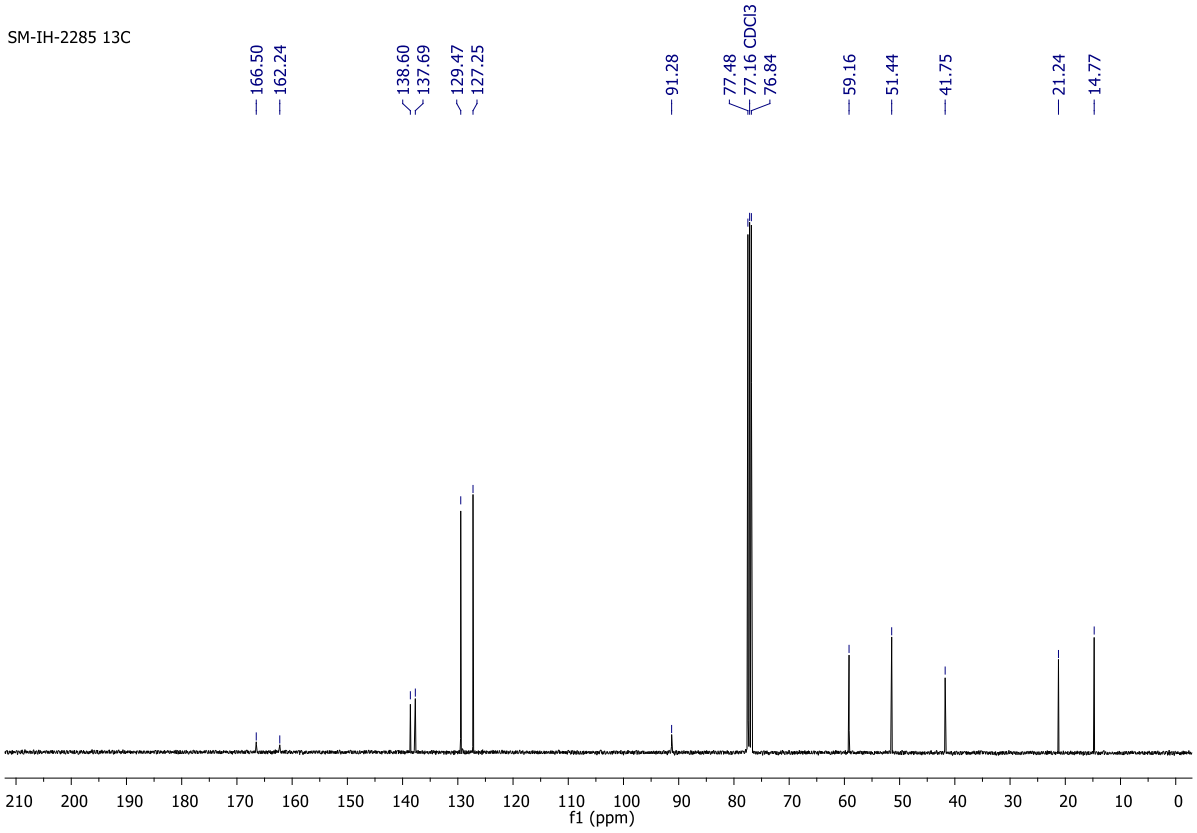
^{13}C{^{1}H} NMR of **3a** (101 MHz, $CDCl_3$):



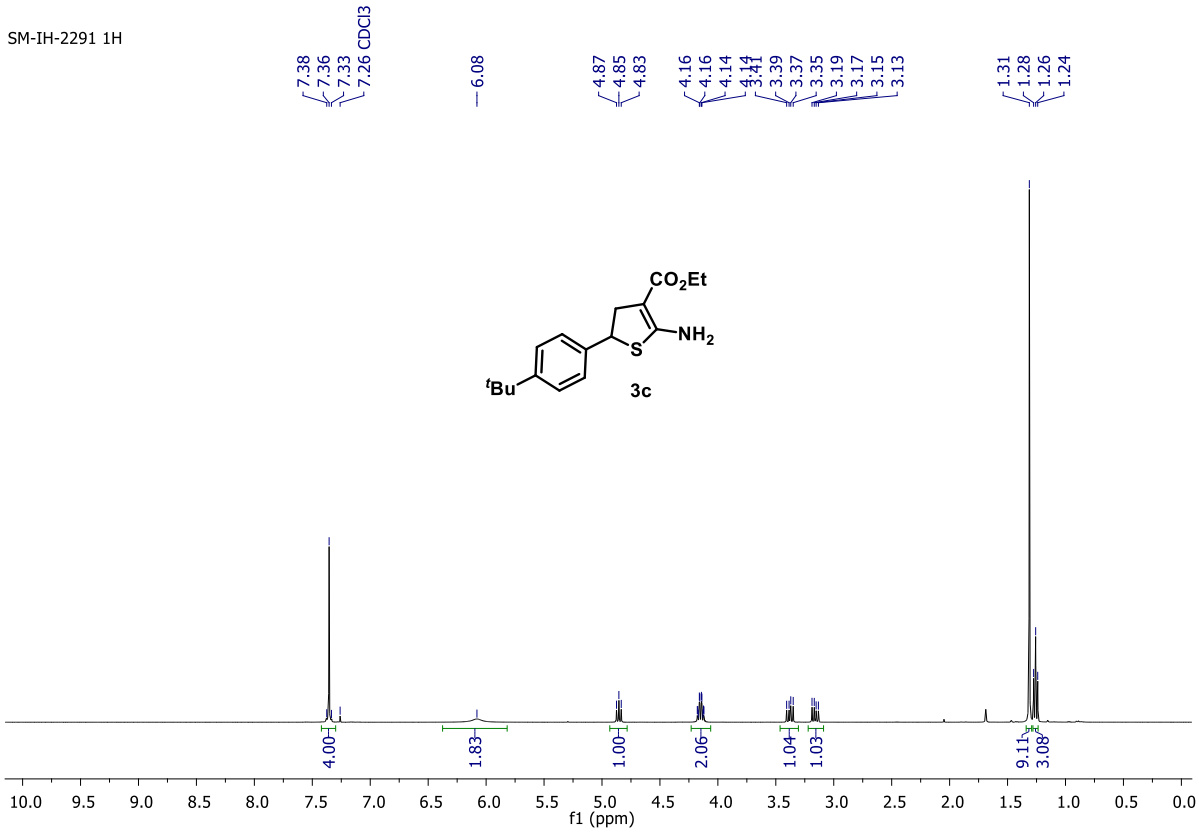
^{1}H NMR of **3b** (400 MHz, $CDCl_3$):



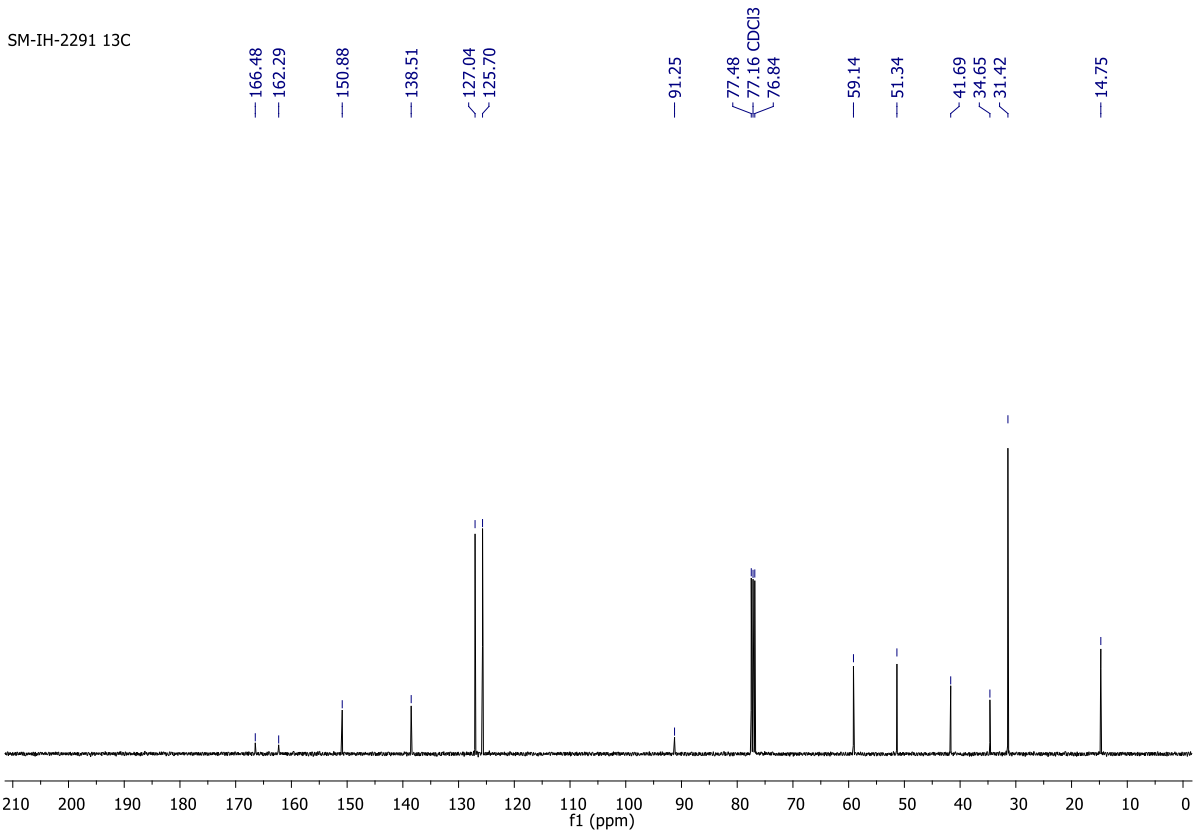
^{13}C{^{1}H} NMR of **3b** (101 MHz, $CDCl_3$):



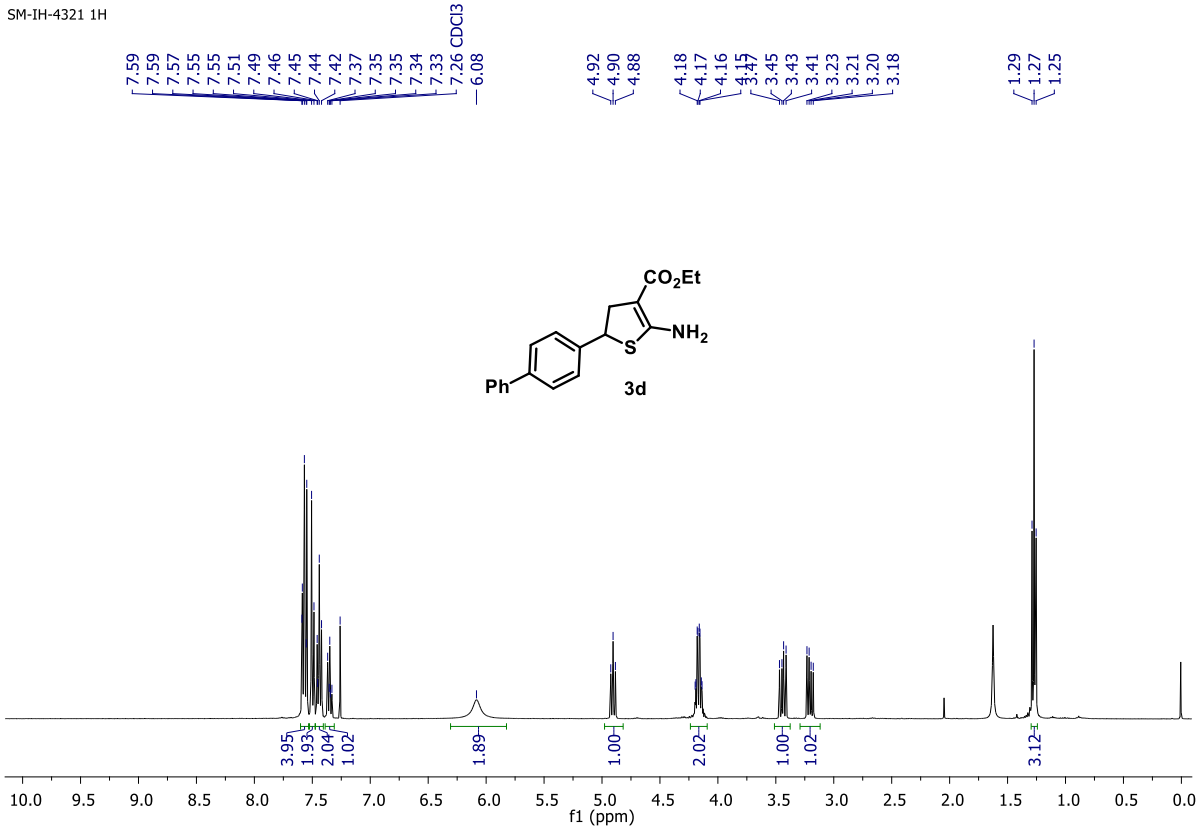
^{1}H NMR of **3c** (400 MHz, $CDCl_3$):



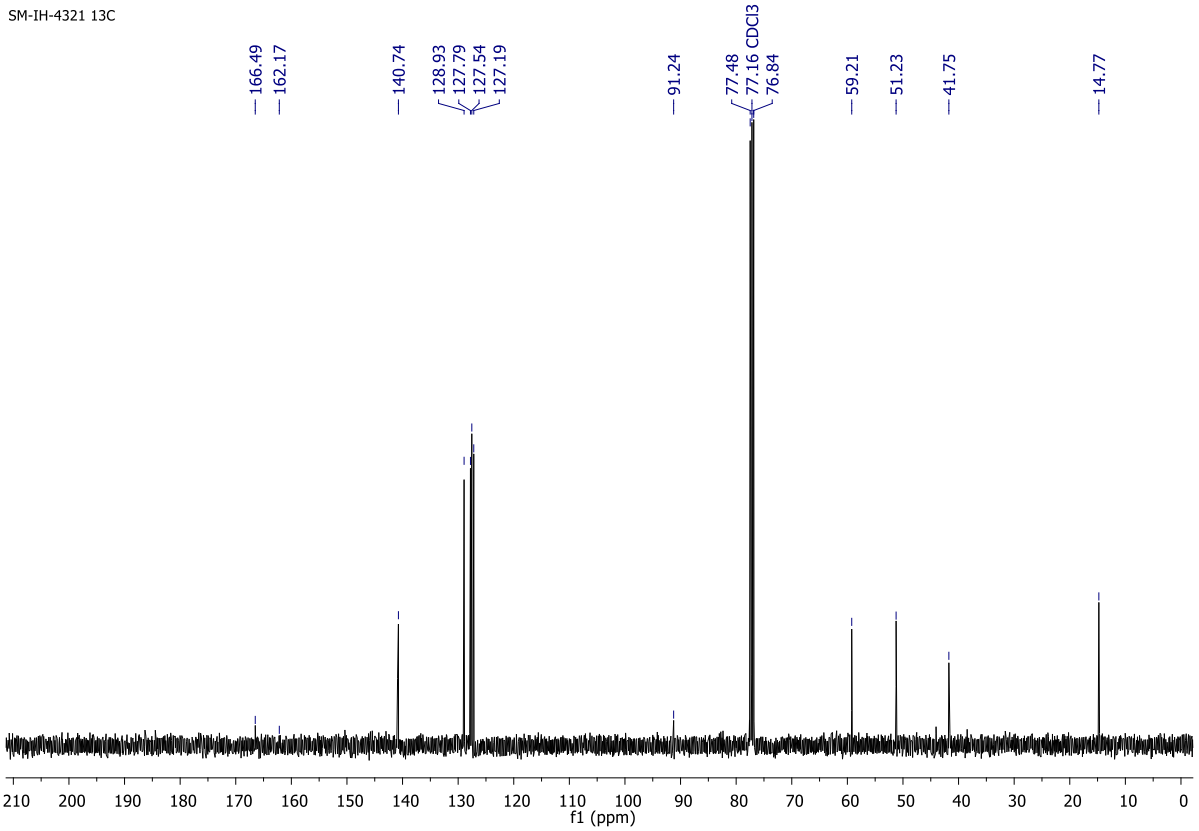
^{13}C{^{1}H} NMR of **3c** (101 MHz, $CDCl_3$):



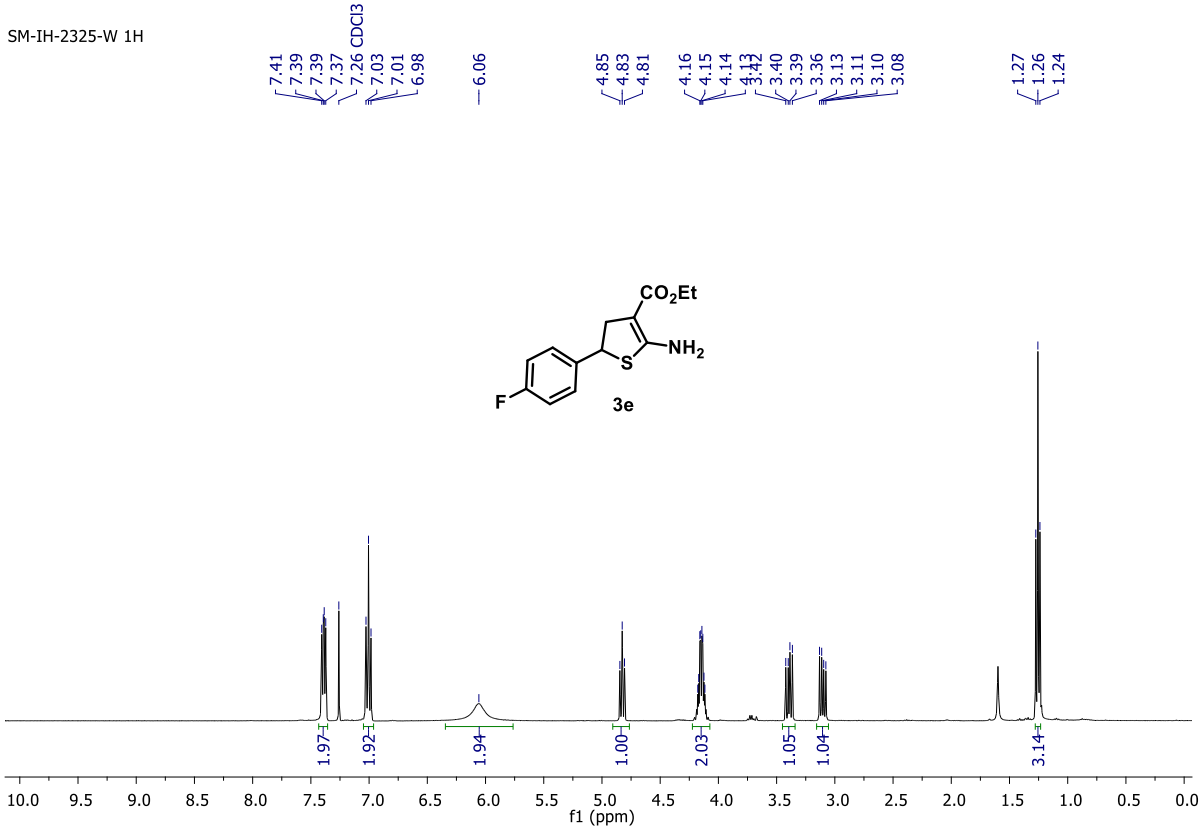
^{1}H NMR of **3d** (400 MHz, $CDCl_3$):



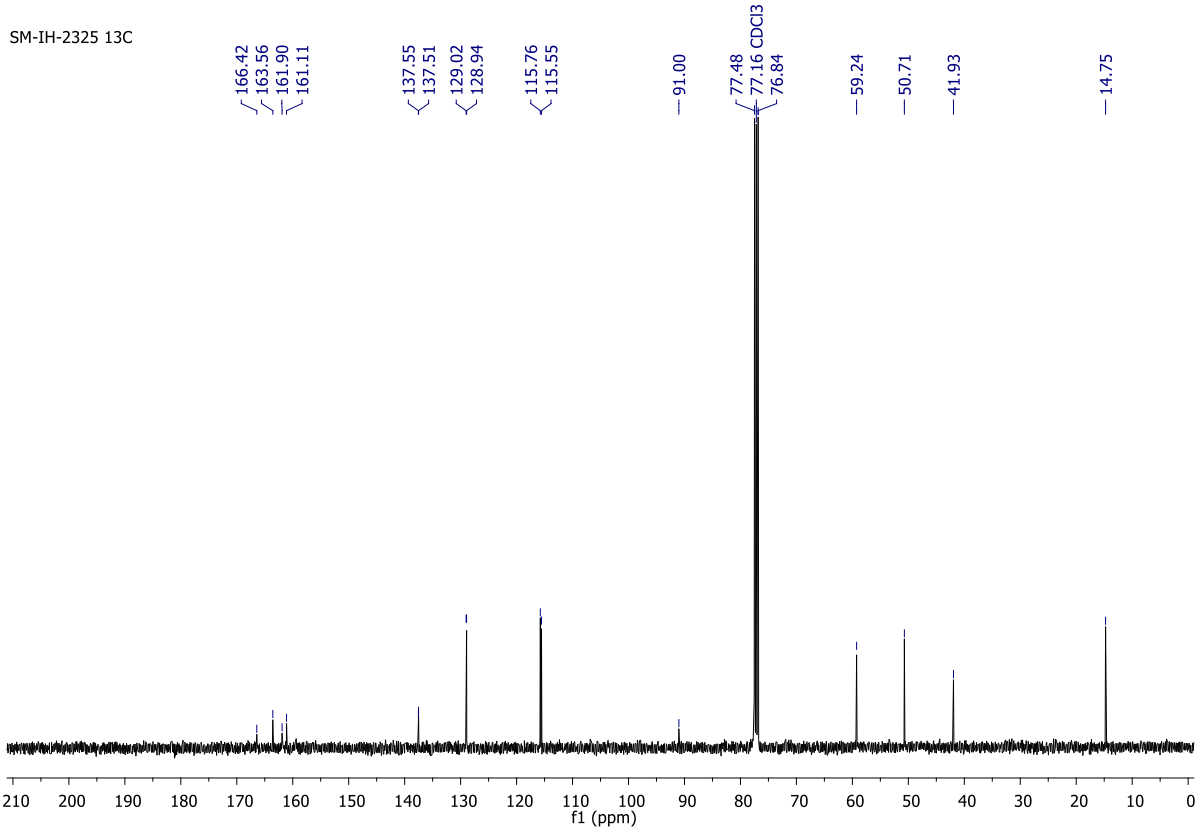
^{13}C{^{1}H} NMR of **3d** (101 MHz, $CDCl_3$):



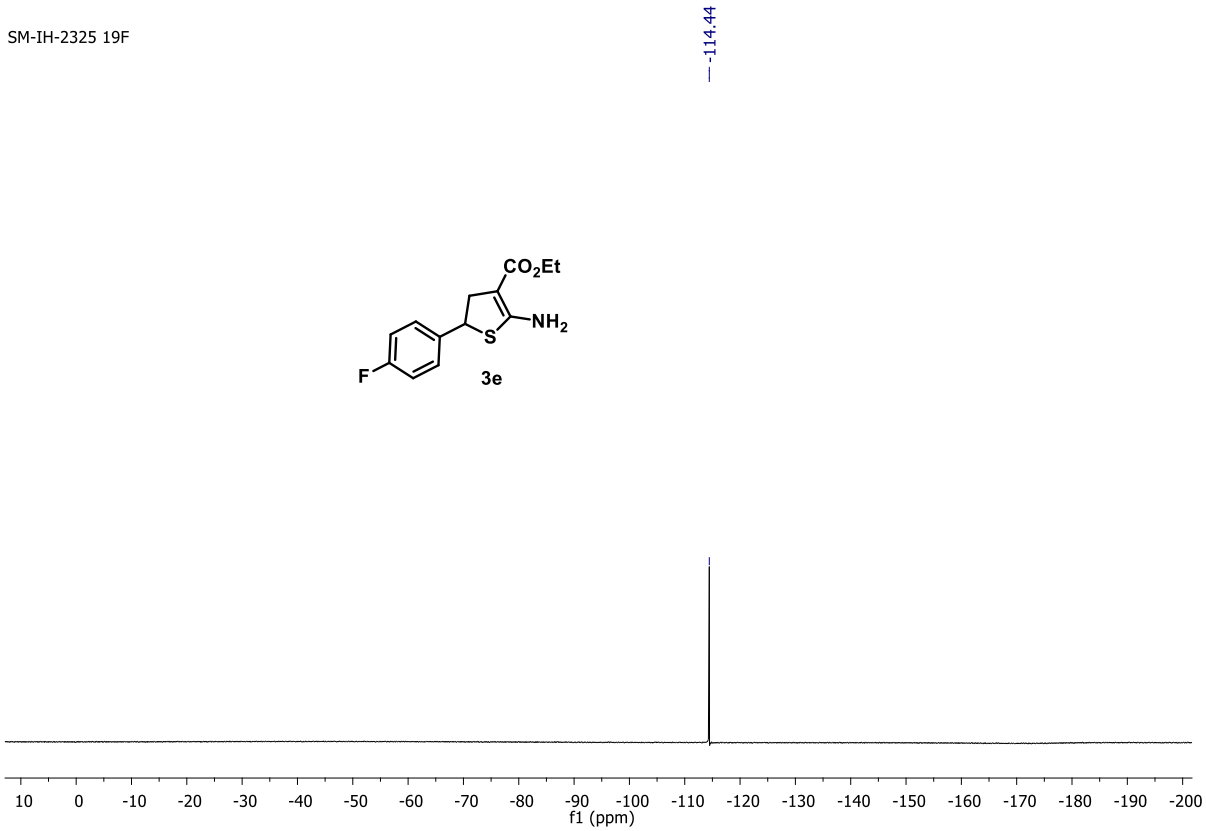
^{1}H NMR of **3e** (400 MHz, $CDCl_3$):



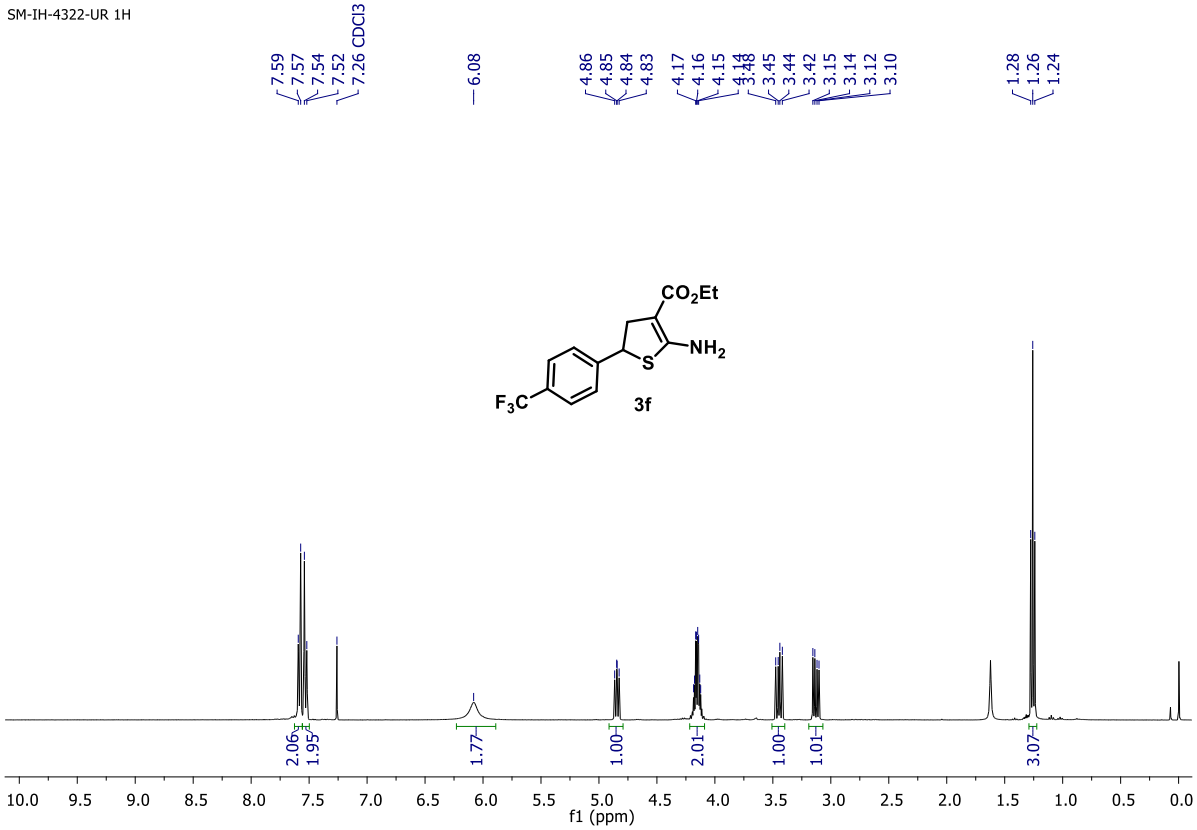
^{13}C{^{1}H} NMR of **3e** (101 MHz, $CDCl_3$):



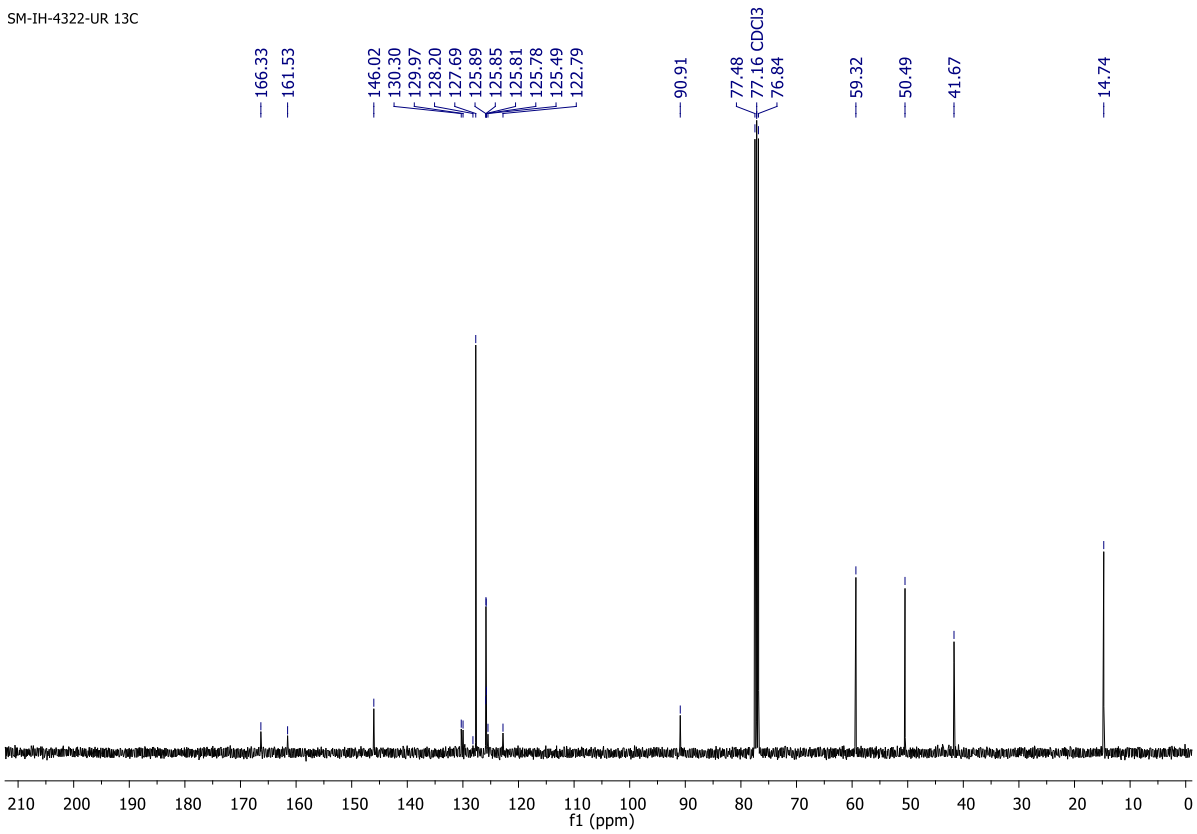
^{19}F NMR of **3e** (377 MHz, $CDCl_3$):



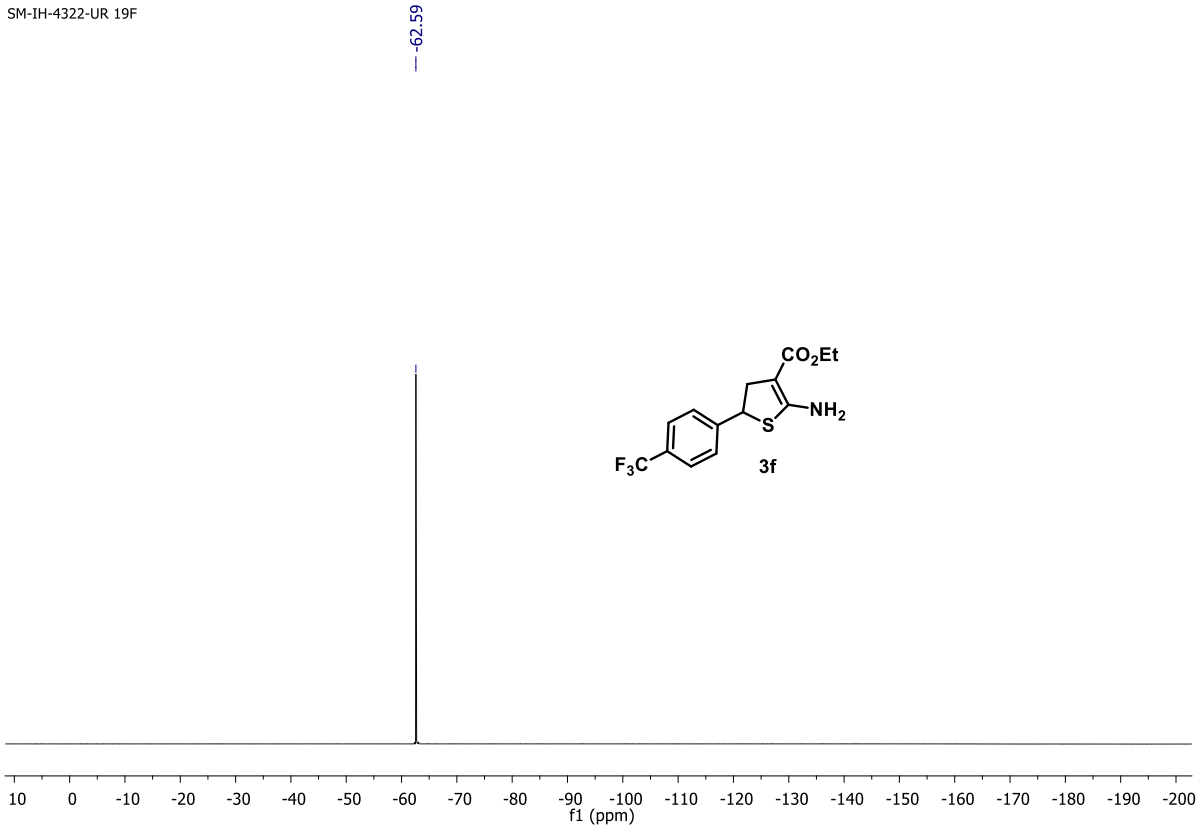
^{1}H NMR of **3f** (400 MHz, $CDCl_3$):



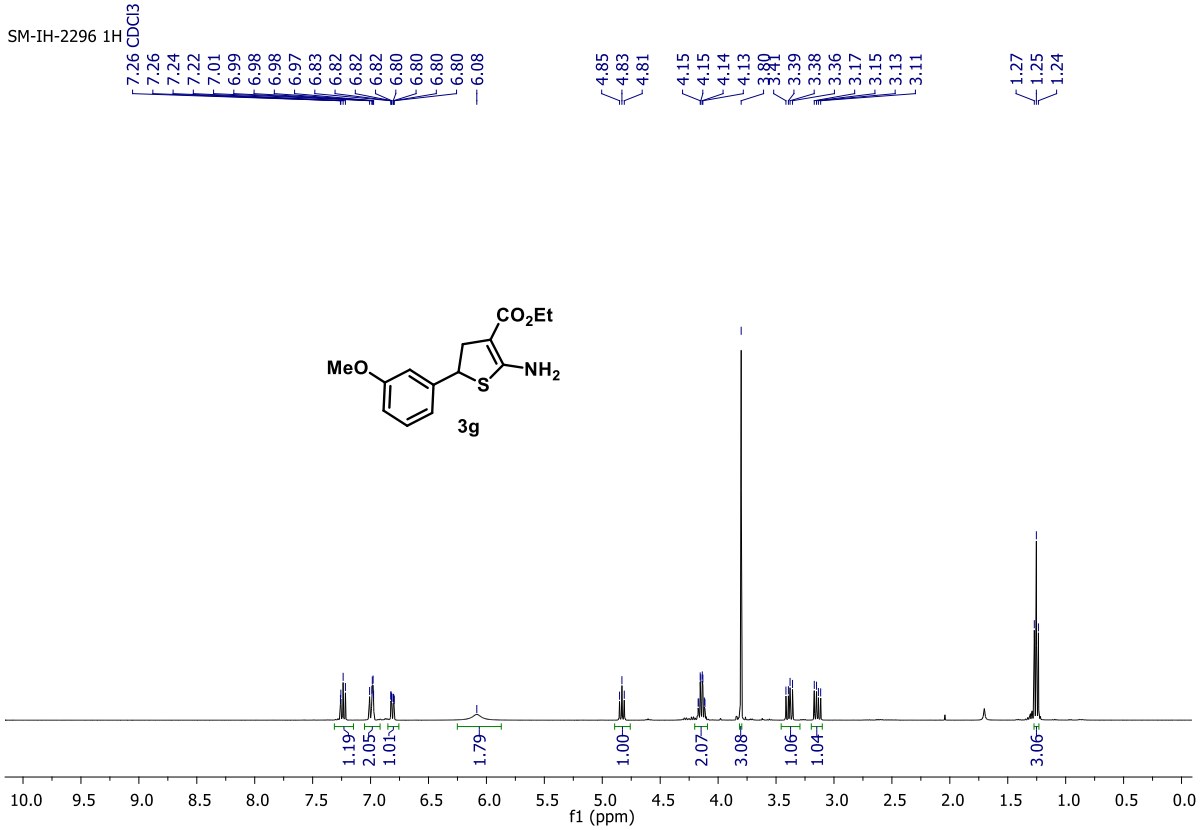
^{13}C{^{1}H} NMR of **3f** (101 MHz, $CDCl_3$):



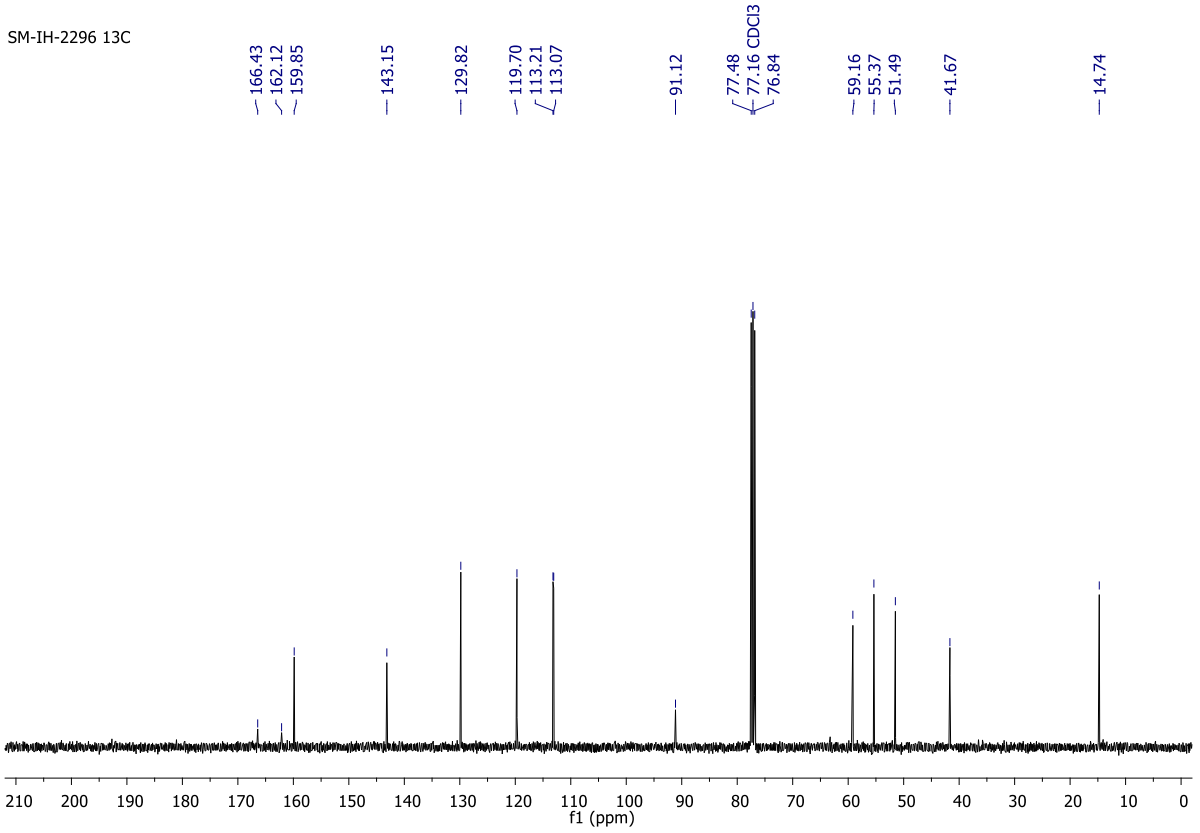
^{19}F NMR of **3f** (377 MHz, $CDCl_3$):



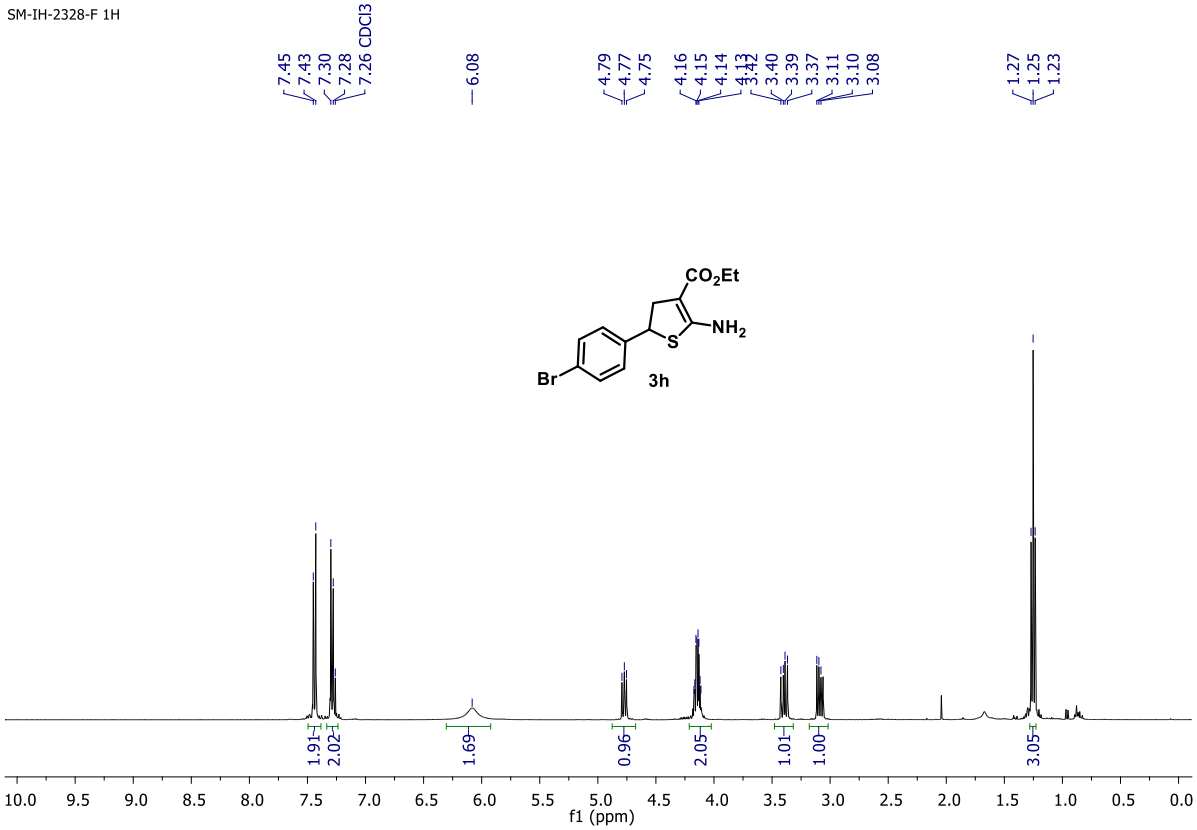
^{1}H NMR of **3g** (400 MHz, $CDCl_3$):



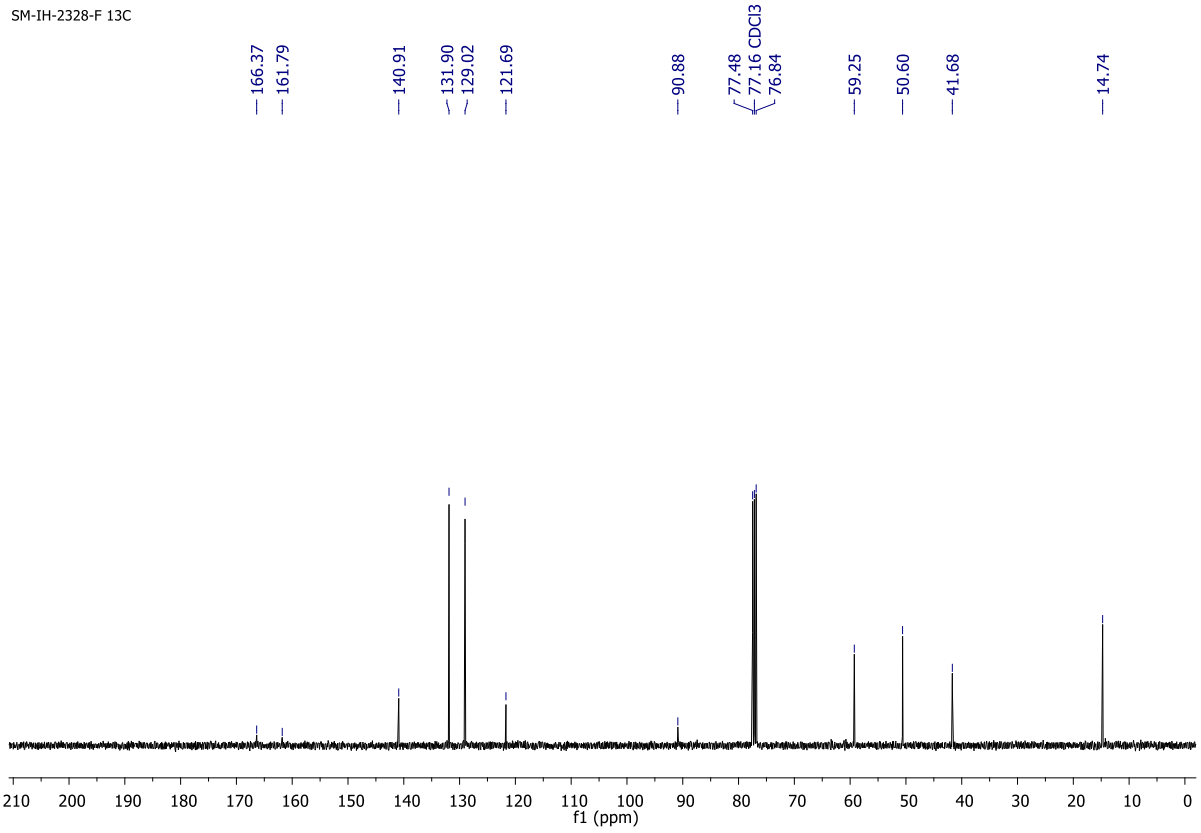
^{13}C{^{1}H} NMR of **3g** (101 MHz, $CDCl_3$):



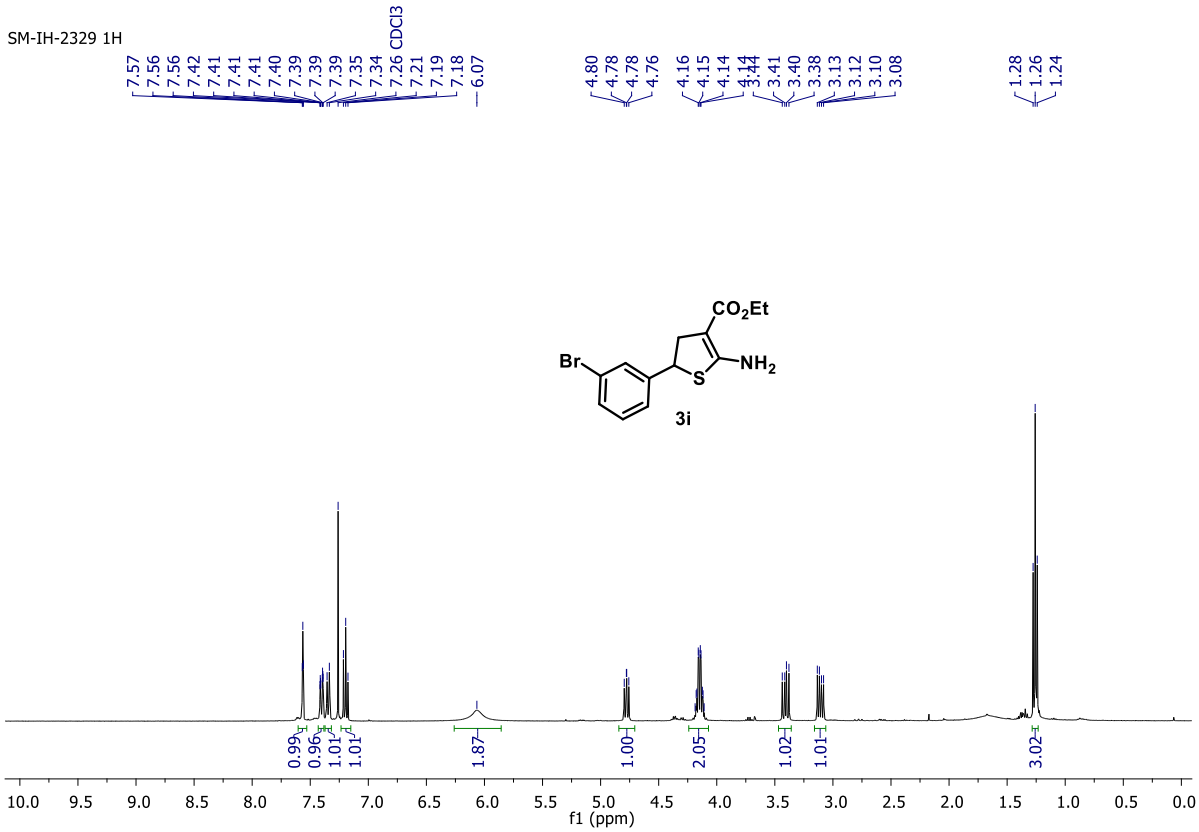
^{1}H NMR of **3h** (400 MHz, $CDCl_3$):



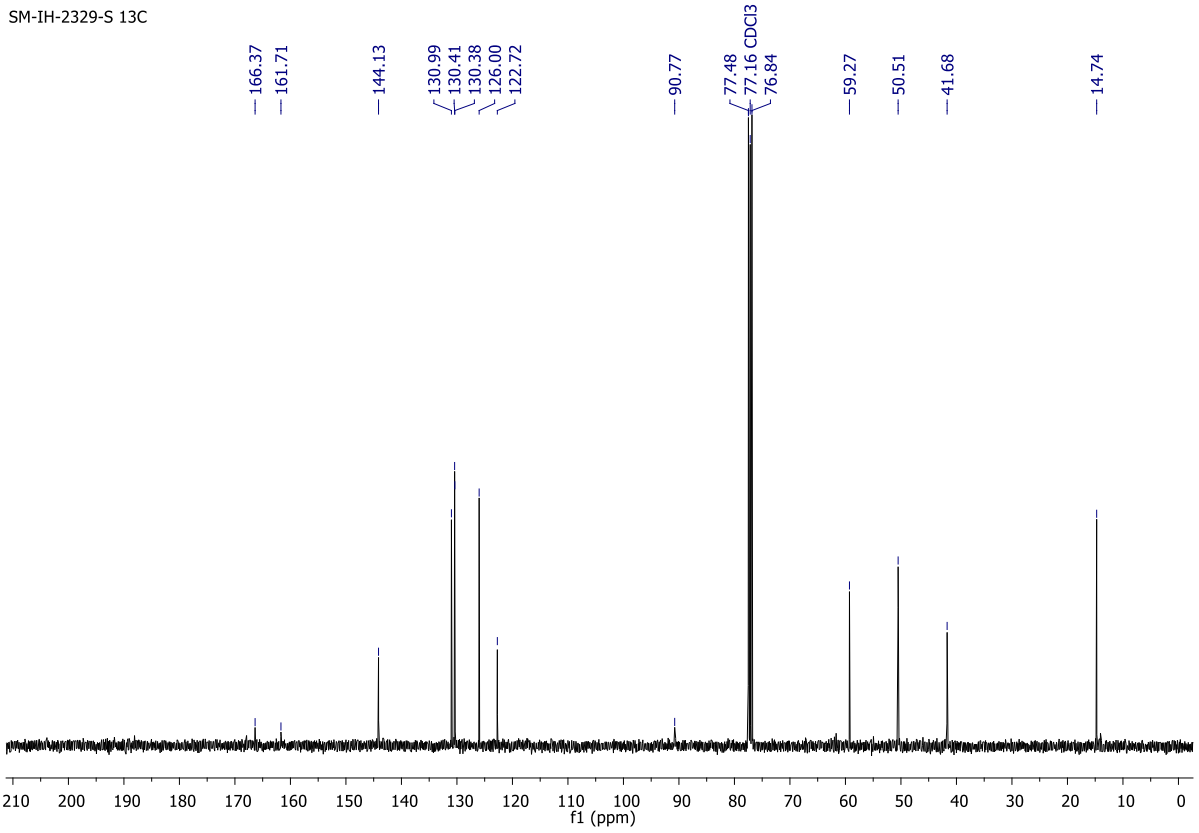
^{13}C{^{1}H} NMR of **3h** (101 MHz, $CDCl_3$):



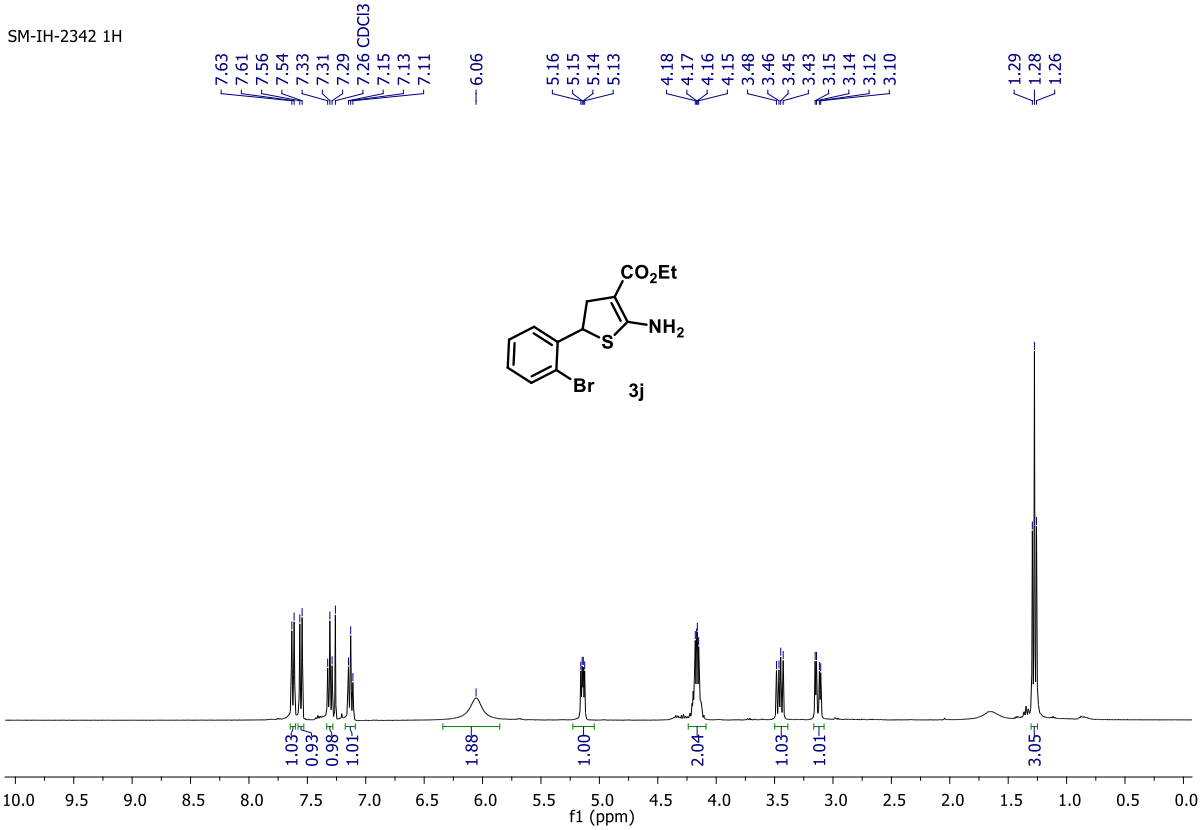
^{1}H NMR of **3i** (400 MHz, $CDCl_3$):



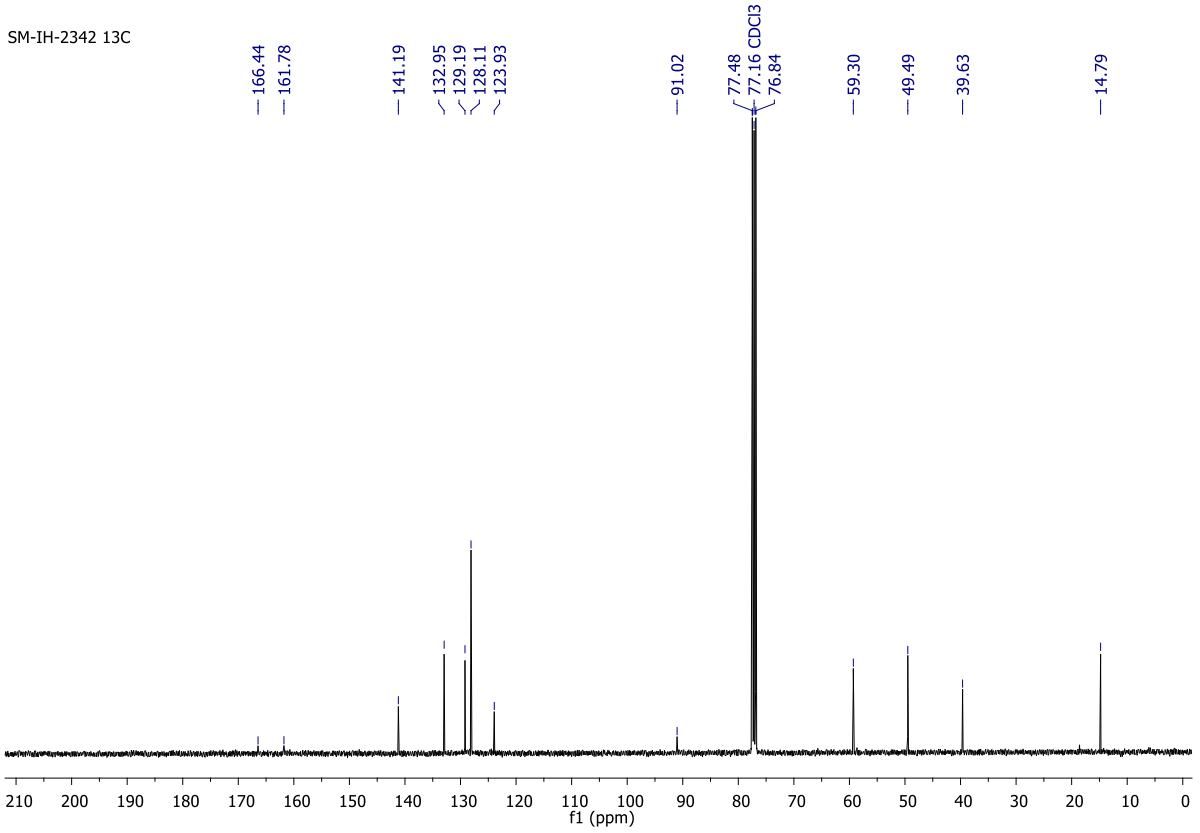
^{13}C{^{1}H} NMR of **3i** (101 MHz, $CDCl_3$):



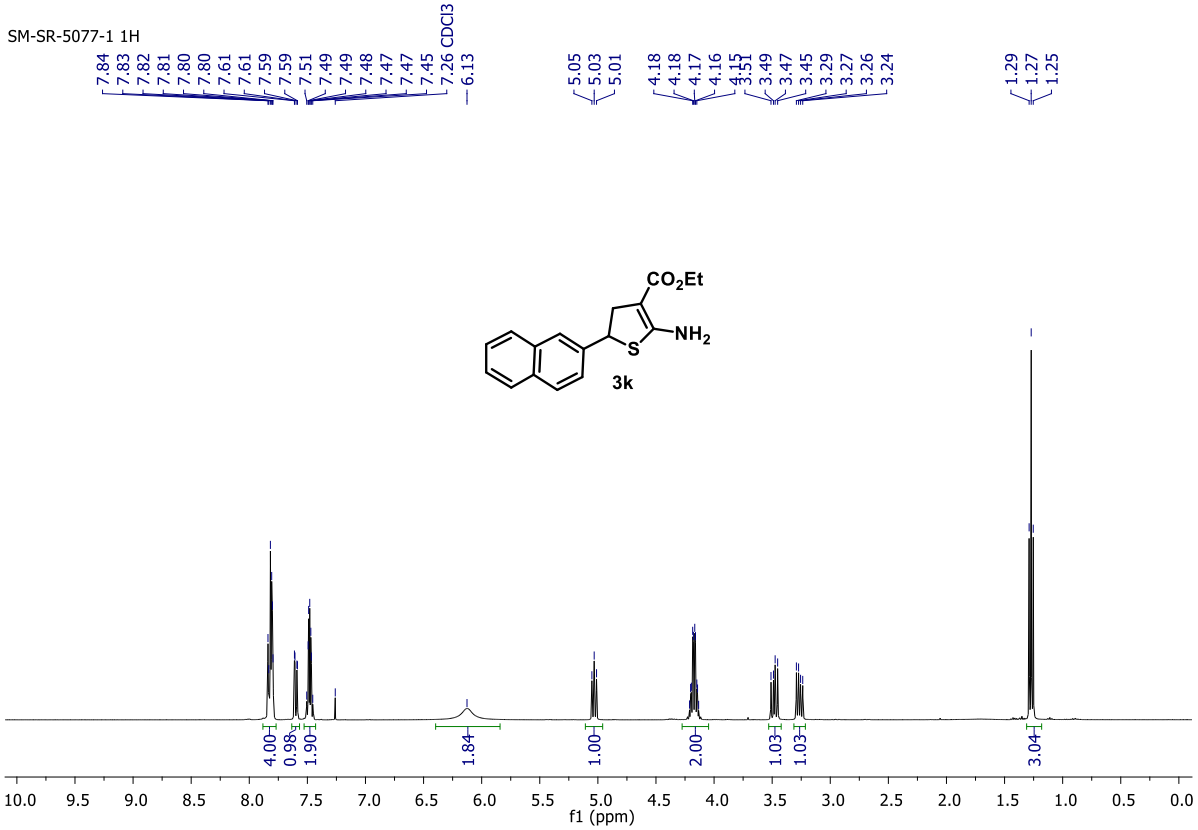
^{1}H NMR of **3j** (400 MHz, $CDCl_3$):



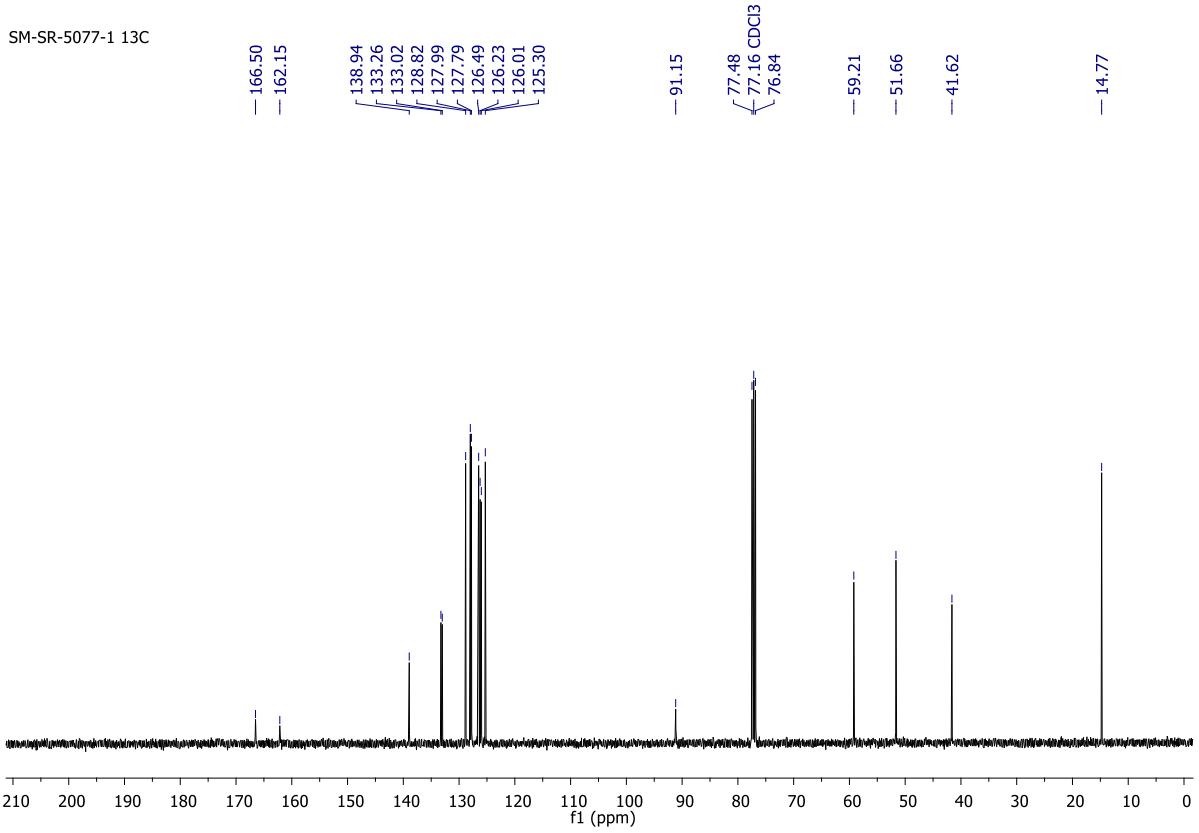
^{13}C{^{1}H} NMR of **3j** (101 MHz, $CDCl_3$):



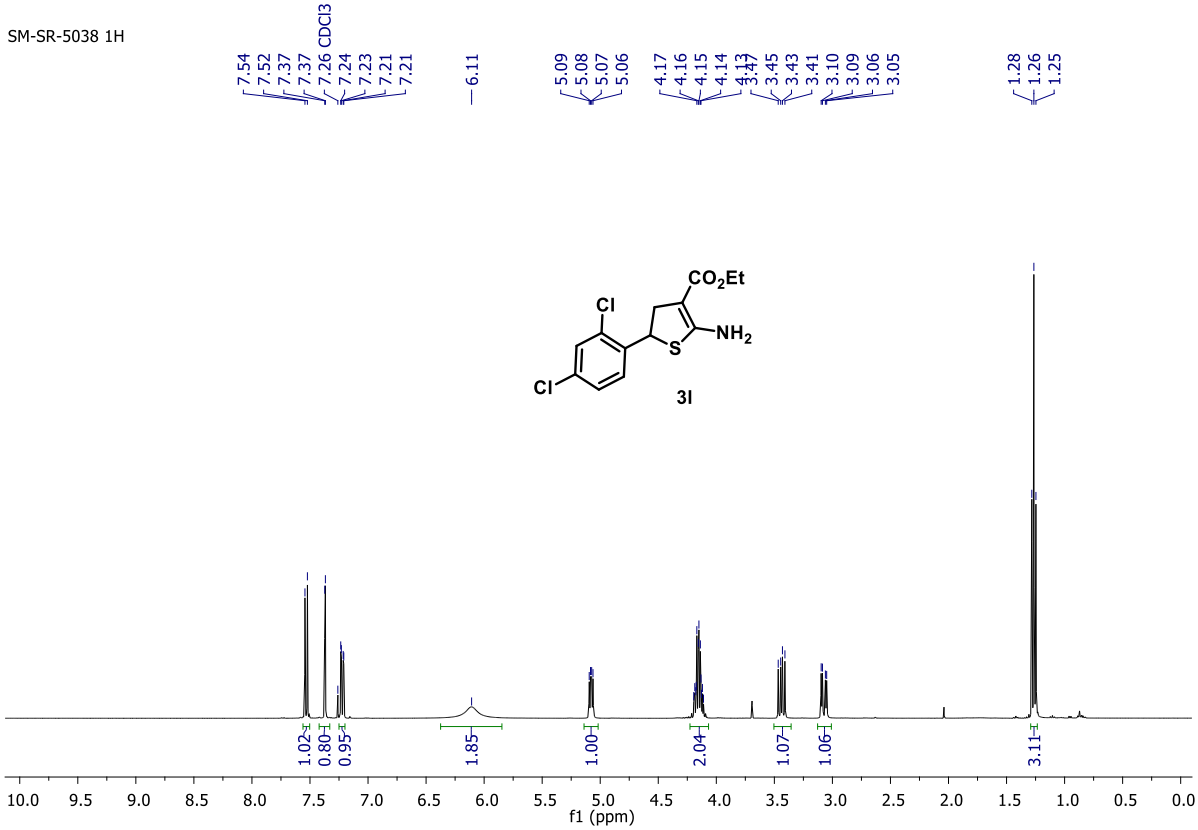
^{1}H NMR of **3k** (400 MHz, $CDCl_3$):



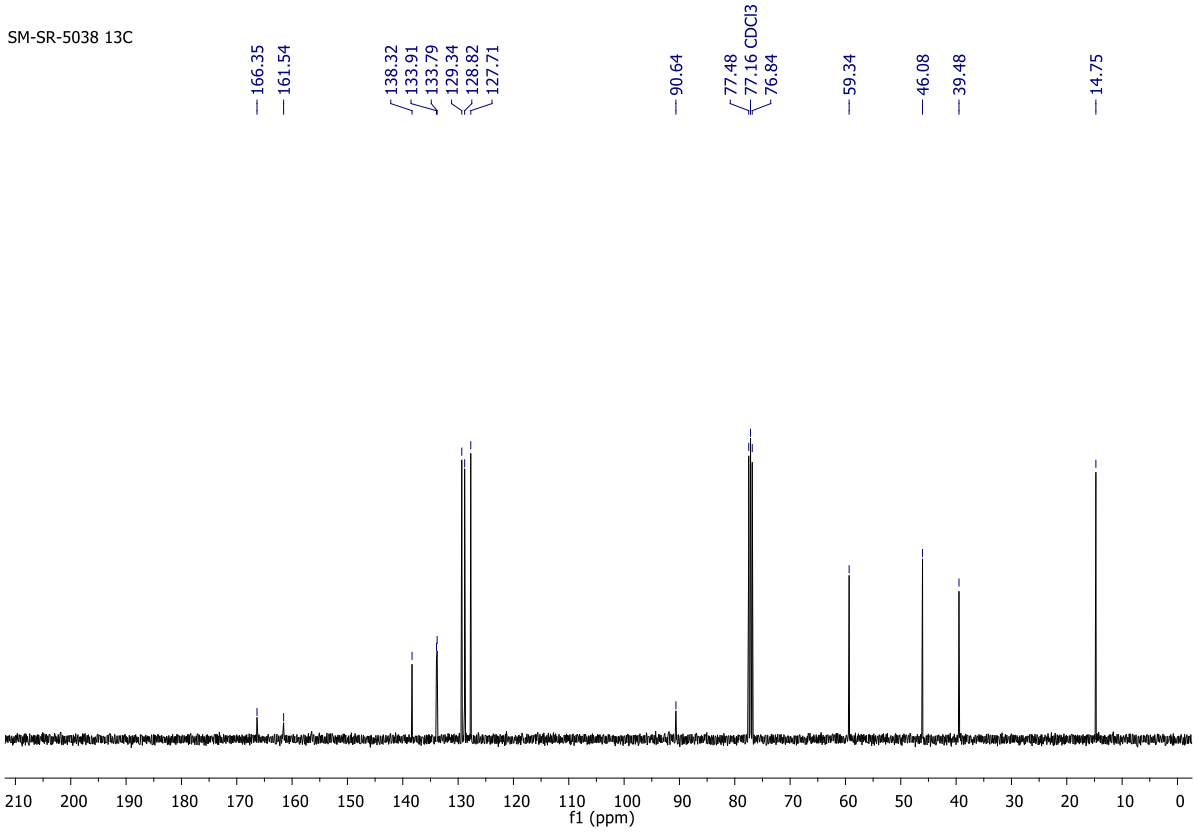
^{13}C{^{1}H} NMR of **3k** (101 MHz, $CDCl_3$):



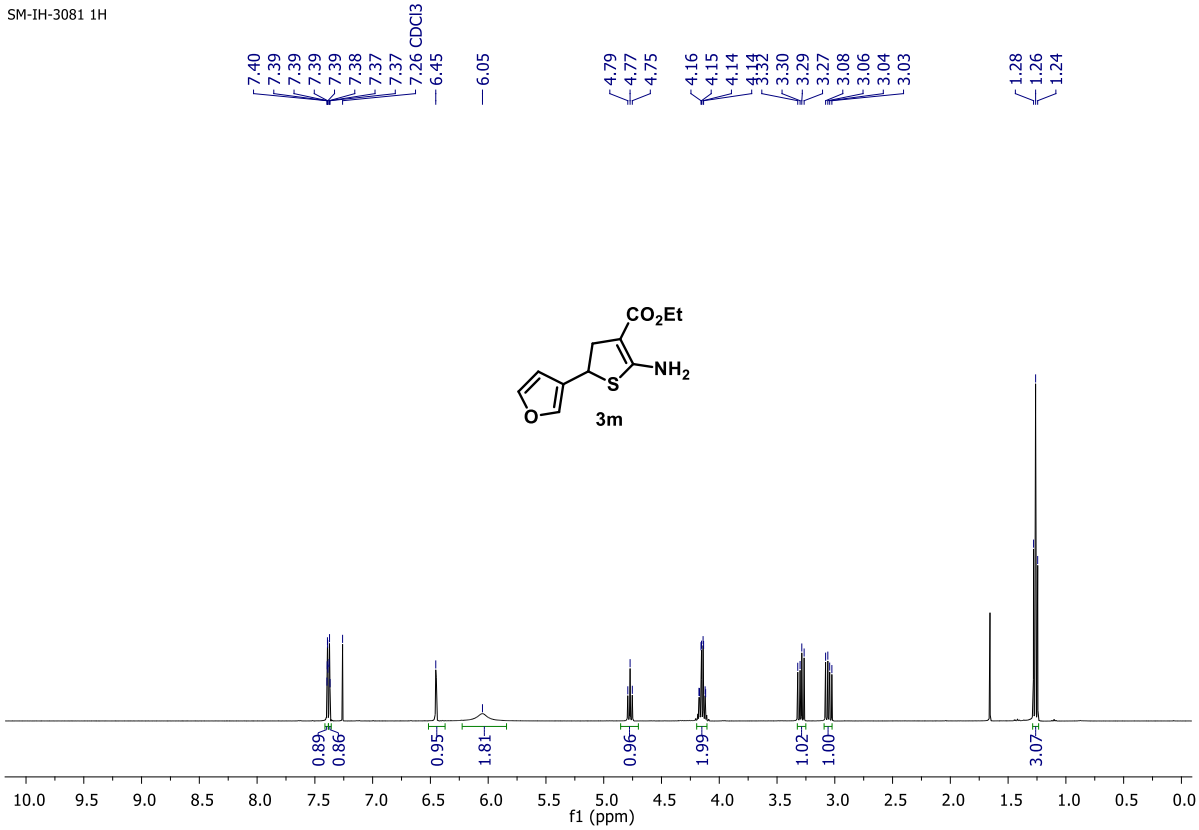
^{1}H NMR of **3l** (400 MHz, $CDCl_3$):



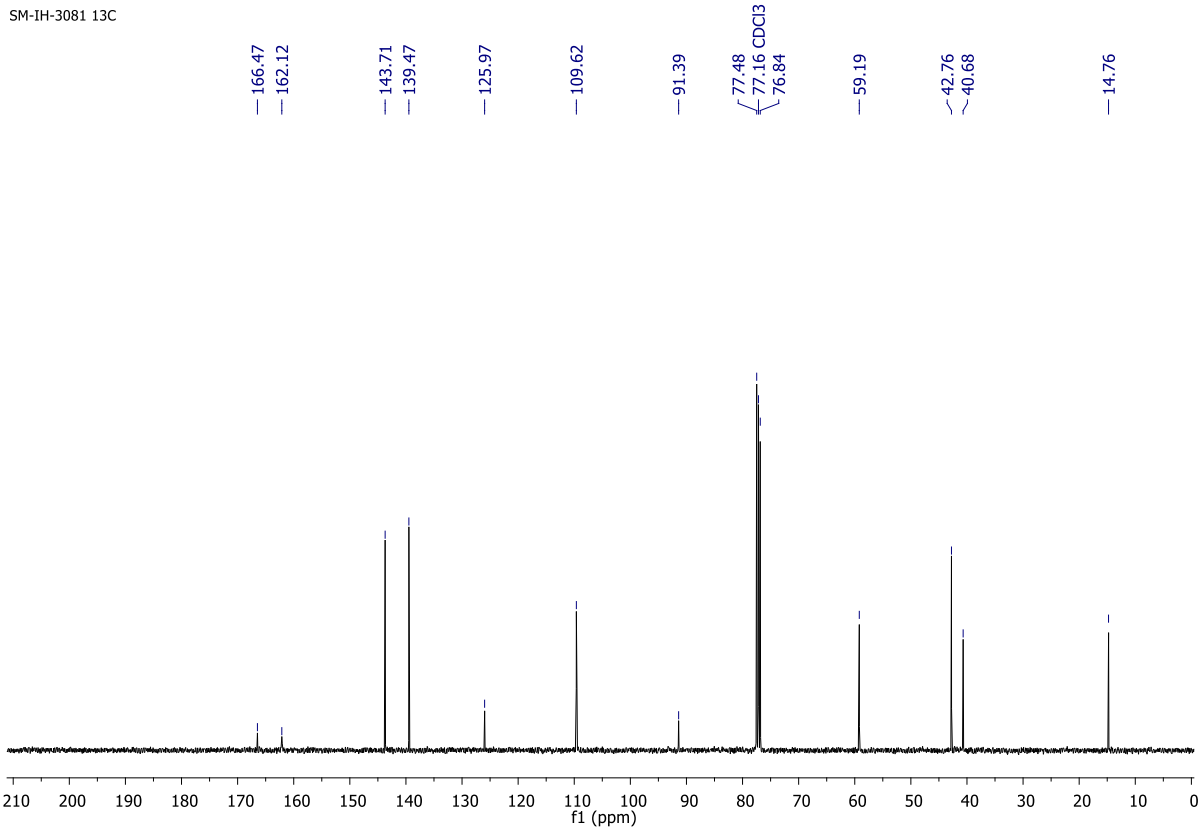
^{13}C{^{1}H} NMR of **3l** (101 MHz, $CDCl_3$):



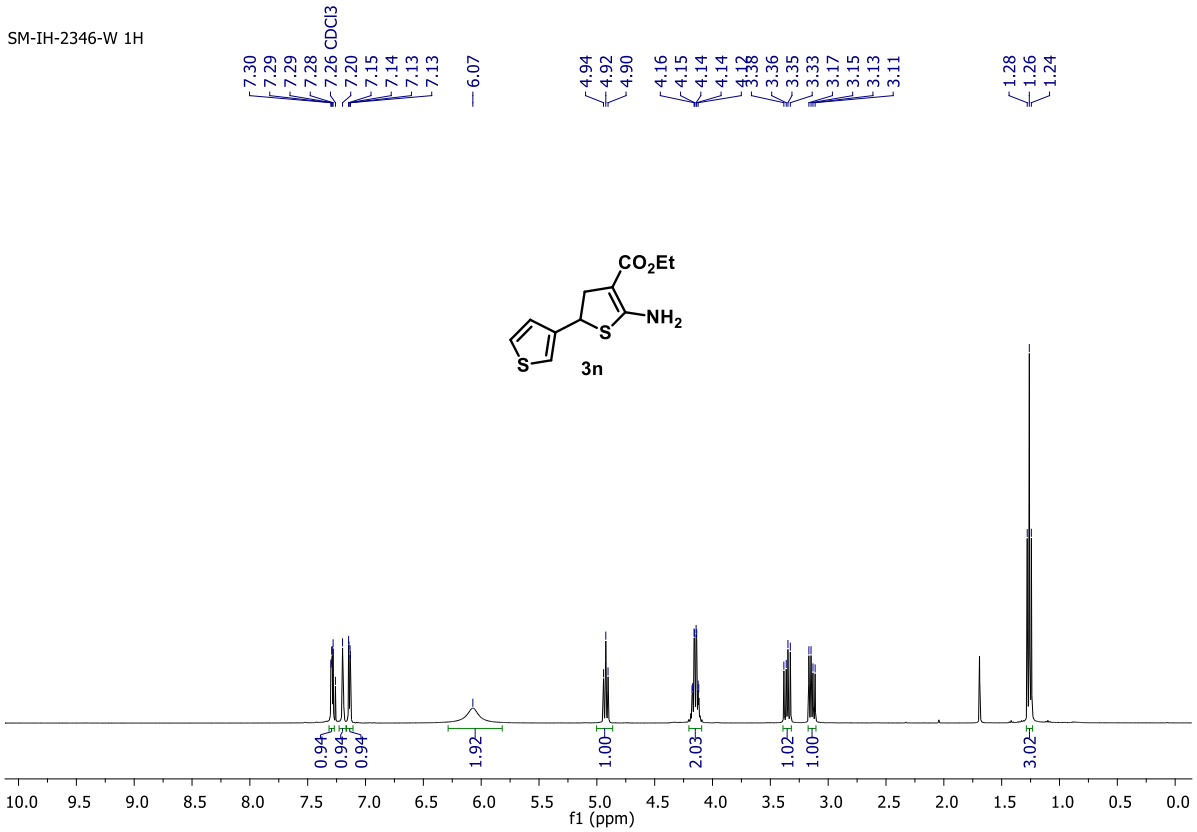
^{1}H NMR of **4m** (400 MHz, $CDCl_3$):



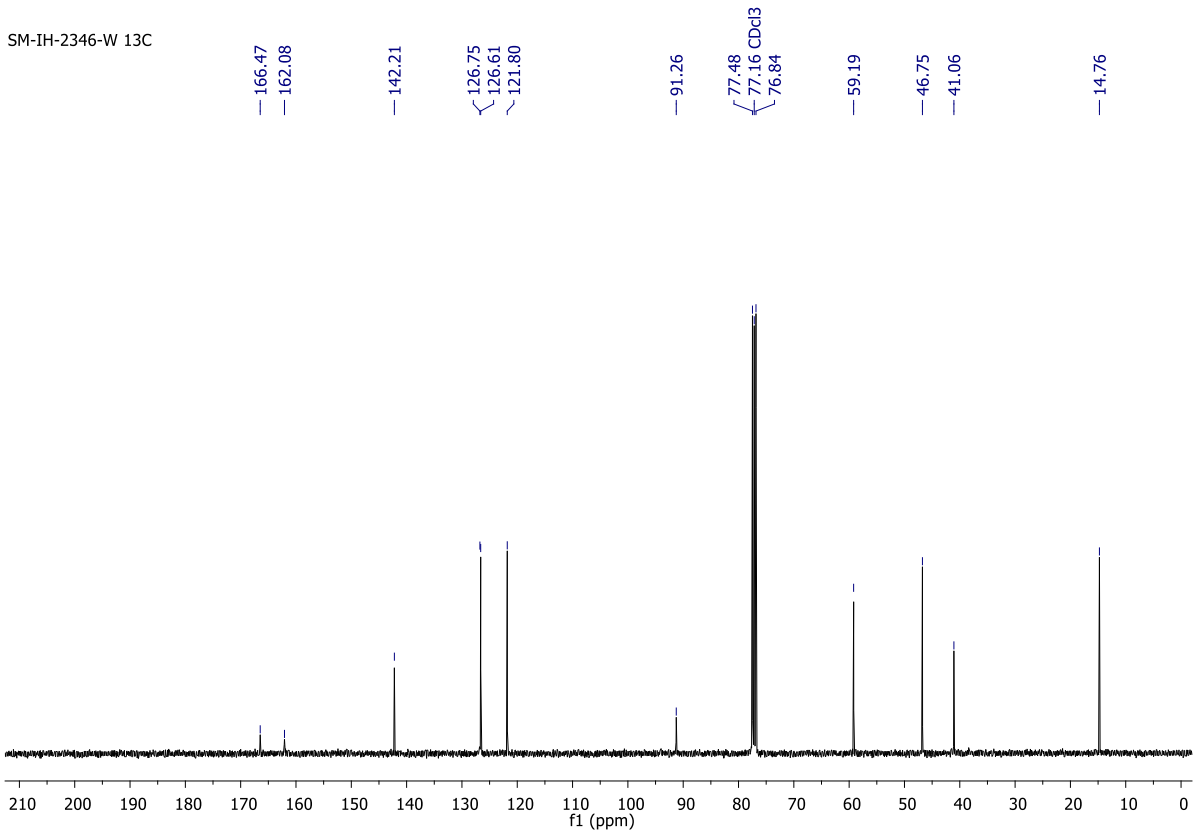
^{13}C{^{1}H} NMR of **3m** (101 MHz, $CDCl_3$):



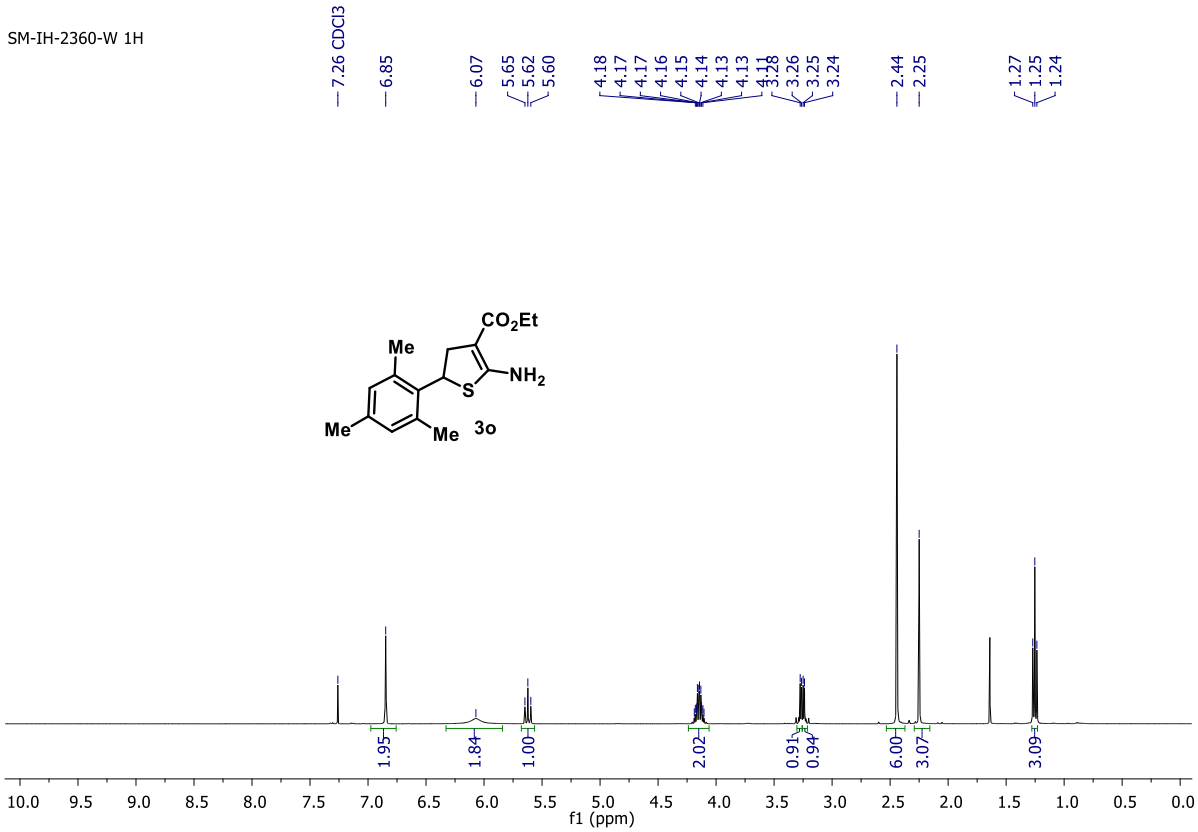
^{1}H NMR of **3n** (400 MHz, $CDCl_3$):



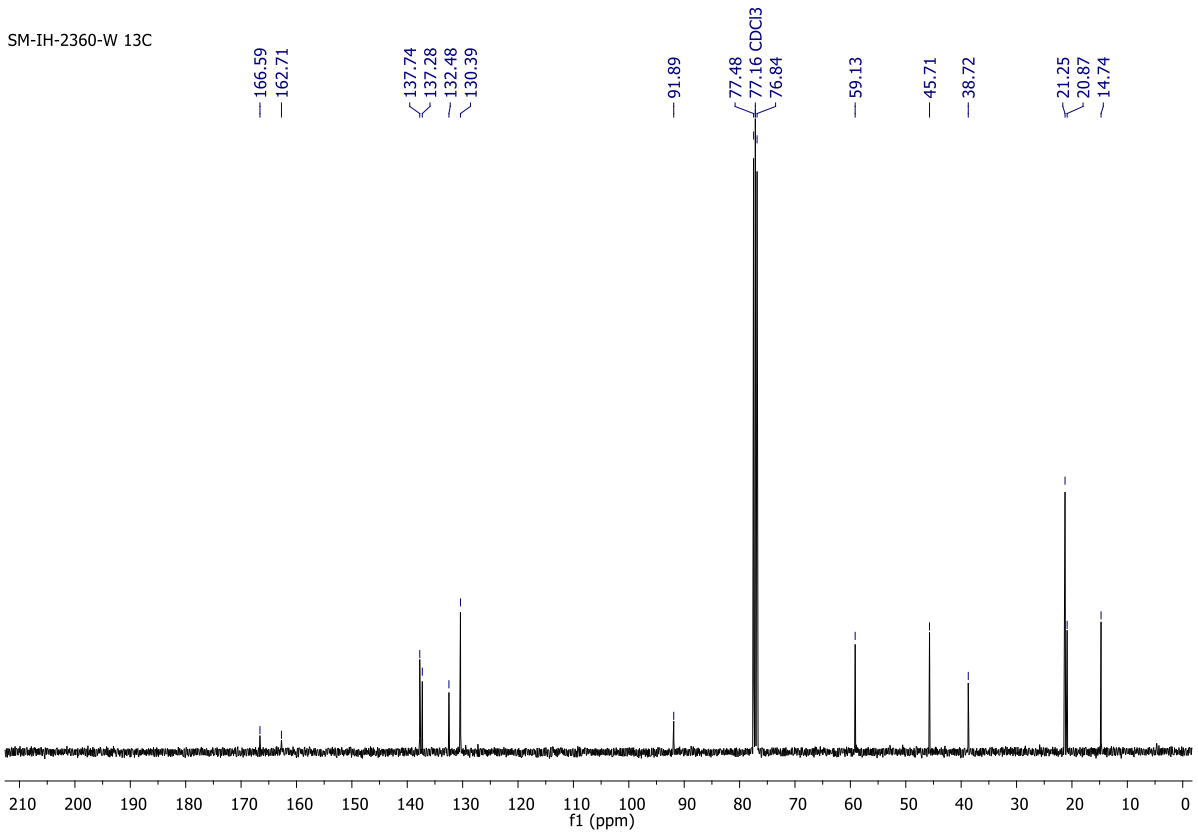
^{13}C{^{1}H} NMR of **3n** (101 MHz, $CDCl_3$):



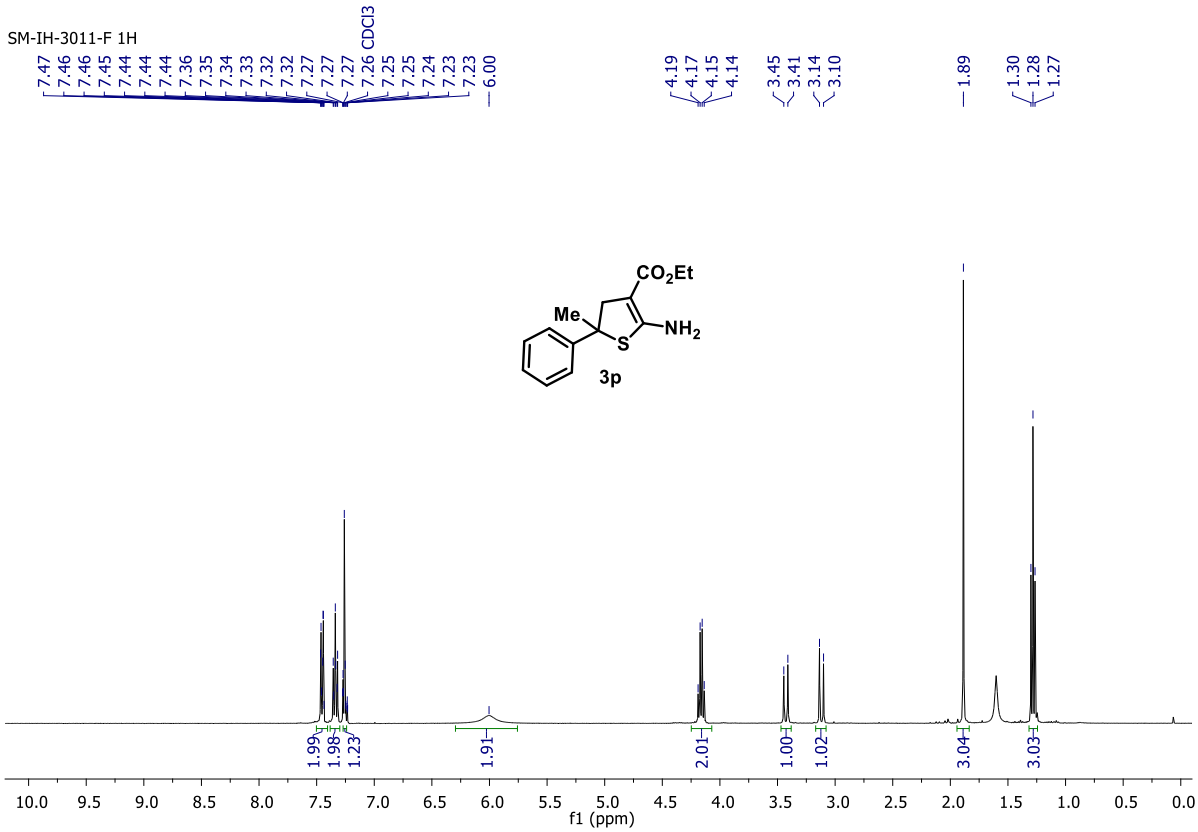
^{1}H NMR of **3o** (400 MHz, $CDCl_3$):



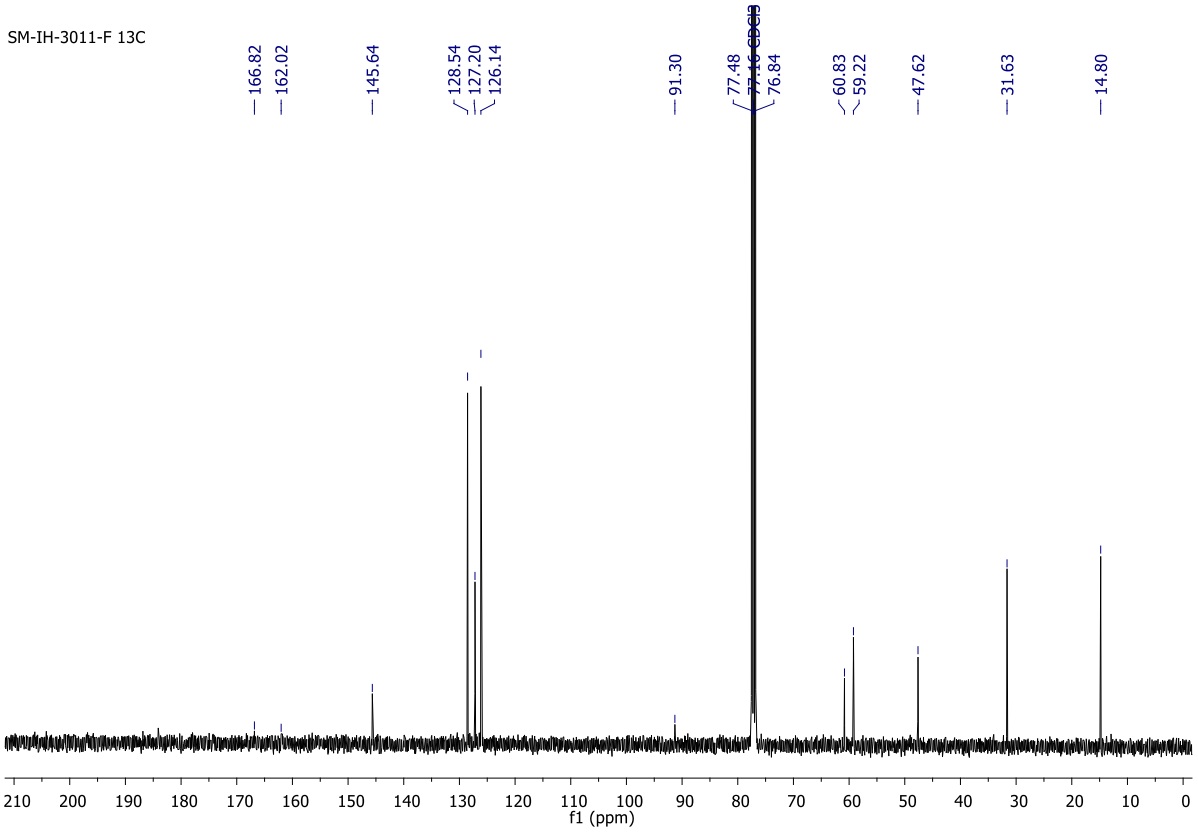
^{13}C{^{1}H} NMR of **3o** (101 MHz, $CDCl_3$):



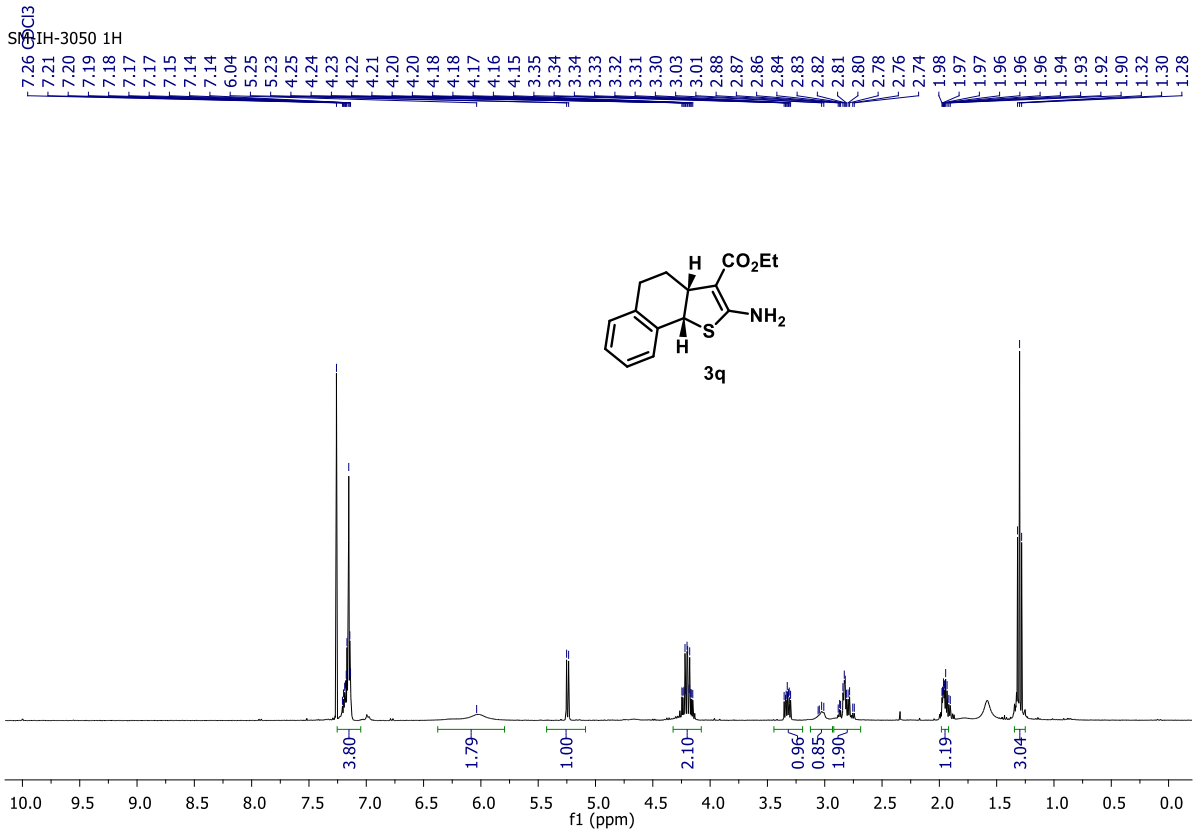
^{1}H NMR of **3p** (400 MHz, $CDCl_3$):



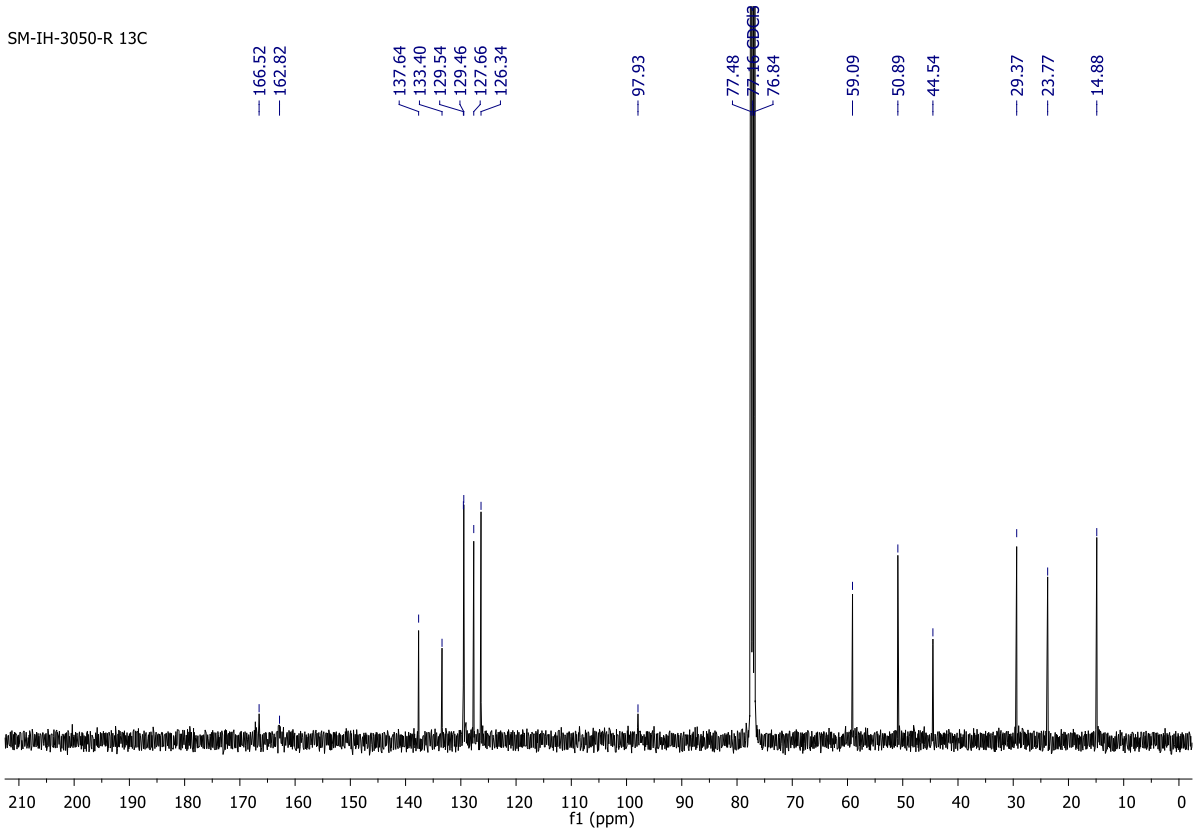
^{13}C{^{1}H} NMR of **3p** (101 MHz, $CDCl_3$):



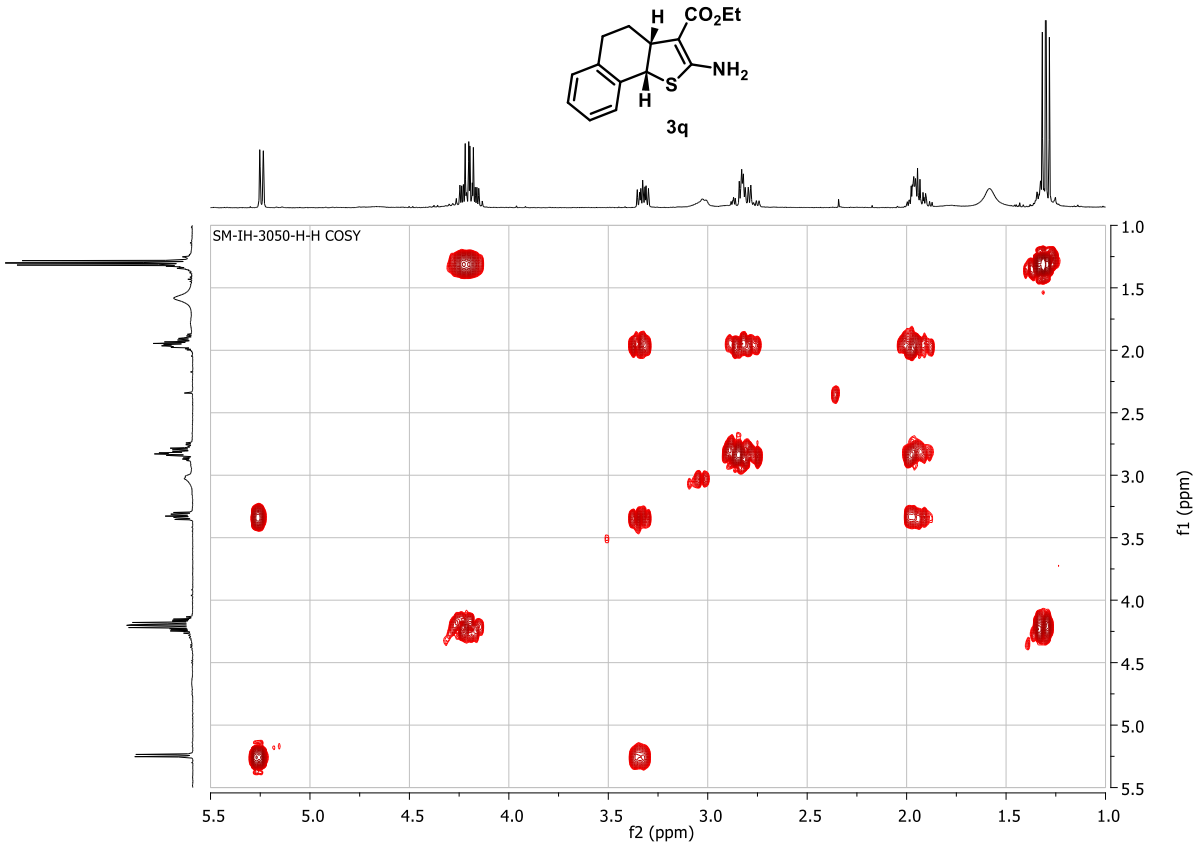
^{1}H NMR of **3q** (400 MHz, $CDCl_3$):



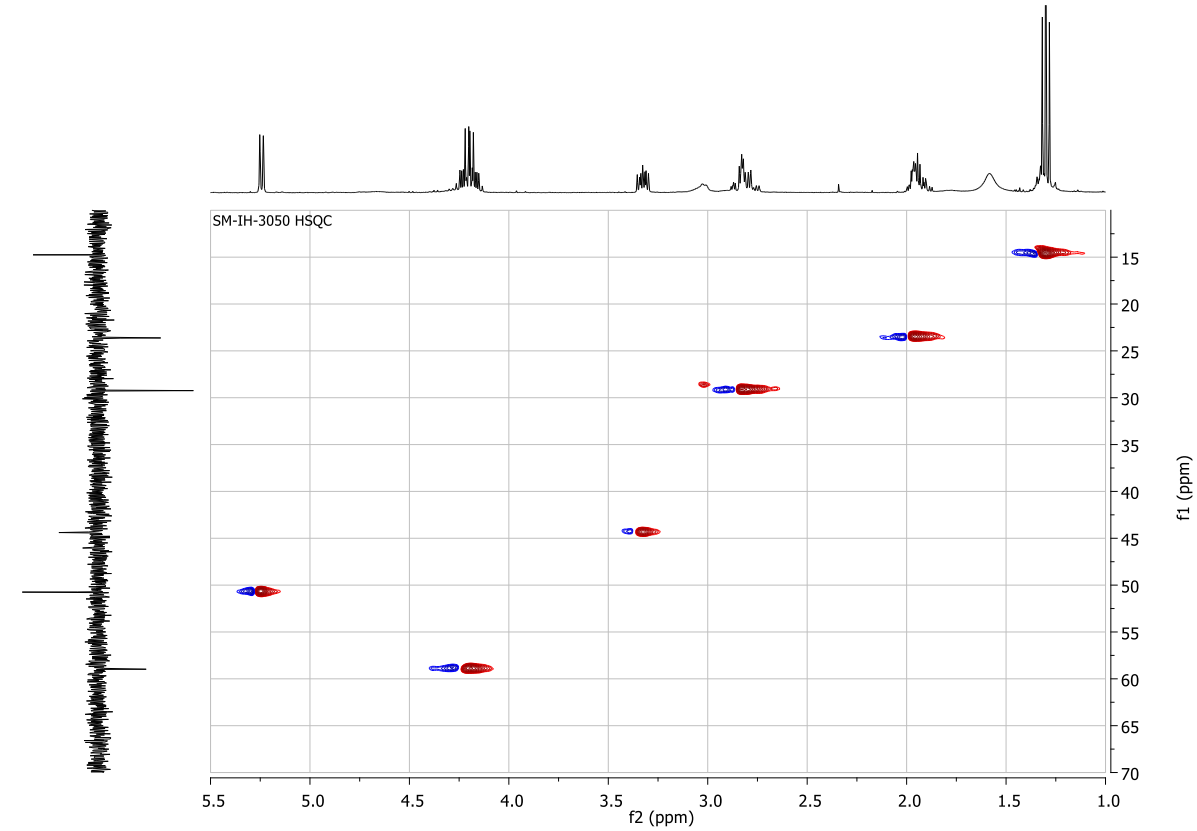
^{13}C{^{1}H} NMR of **3q** (101 MHz, $CDCl_3$):



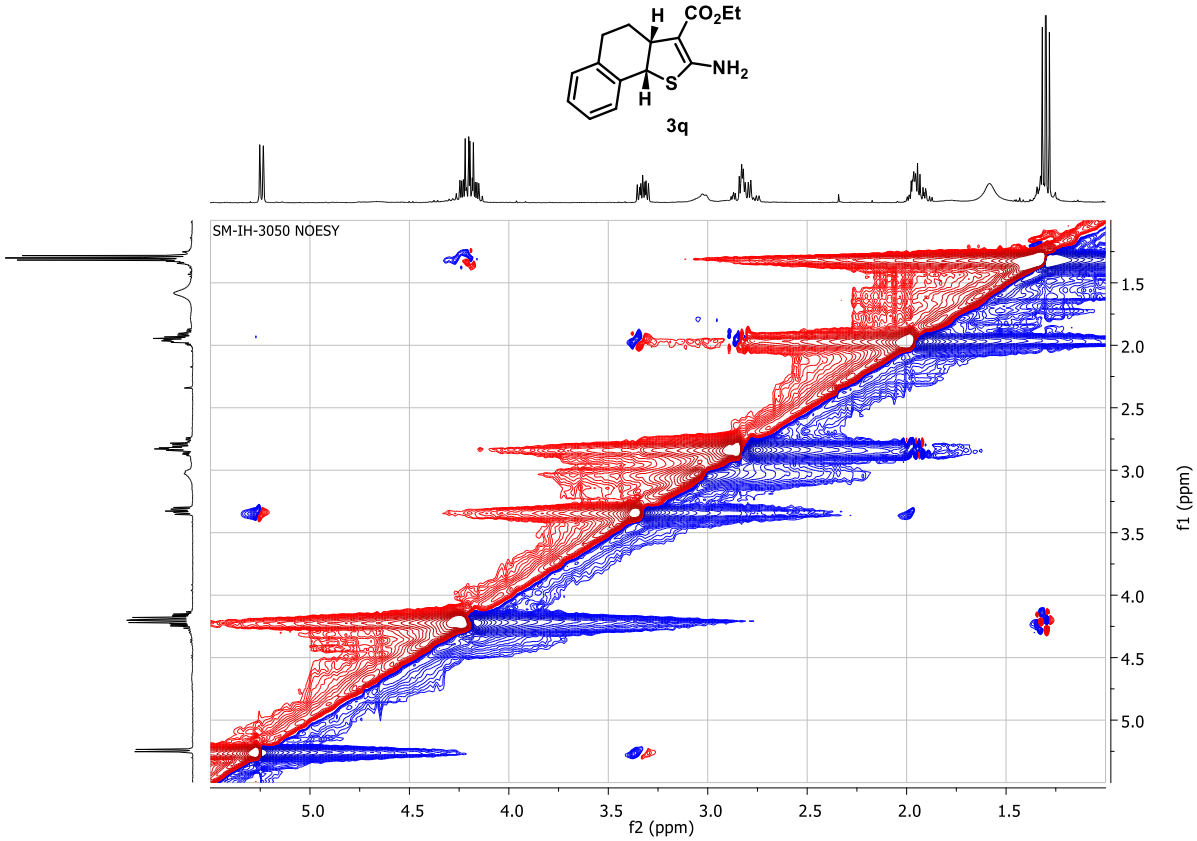
^{1}H-^{1}H COSY NMR of **3q**:



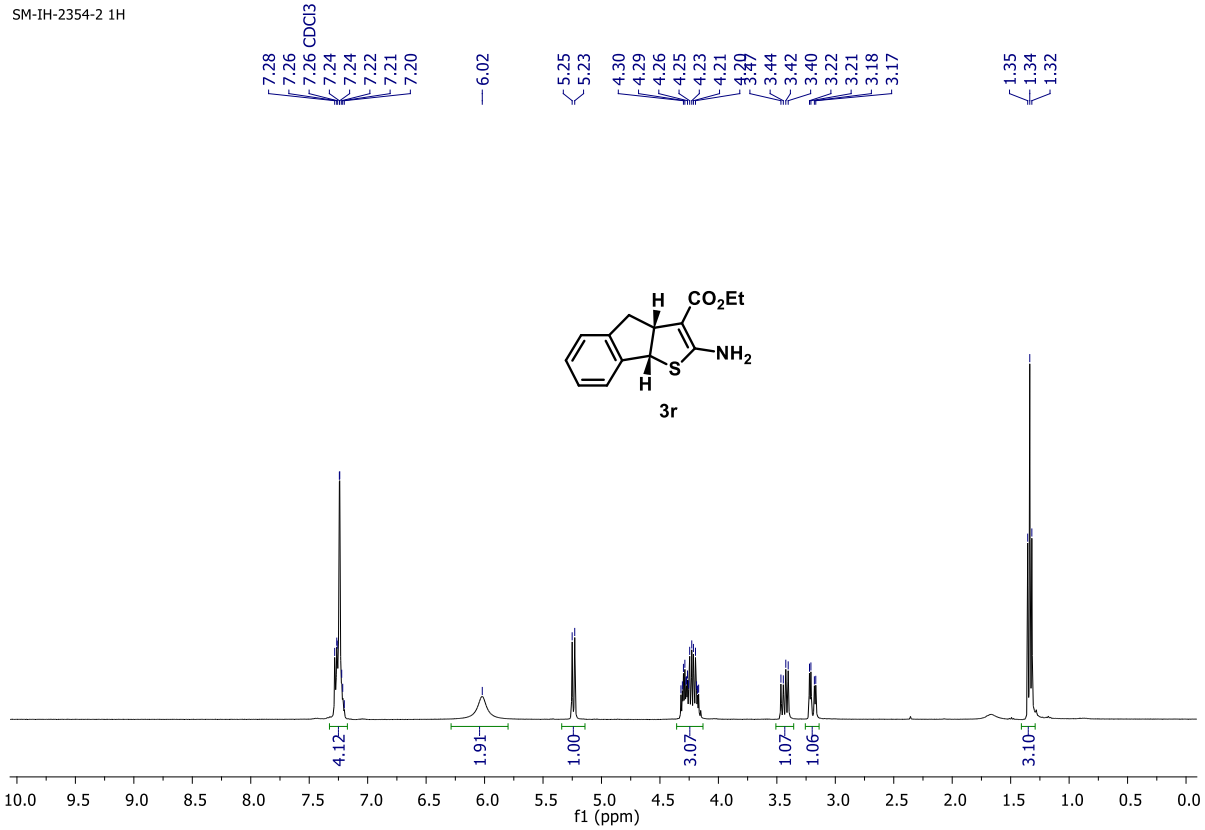
^{1}H-^{13}C HSQC NMR of **3q**:



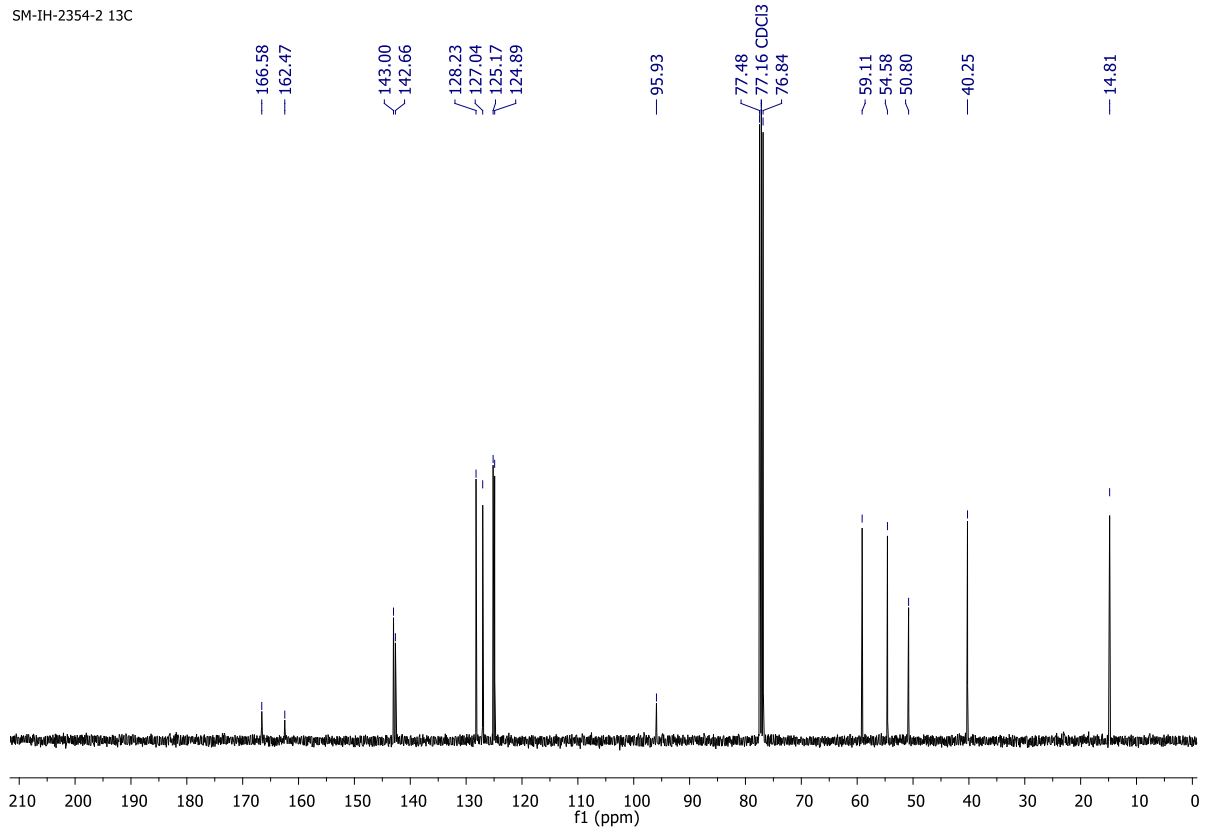
^{1}H-^{1}H NOESY NMR of **3q**:



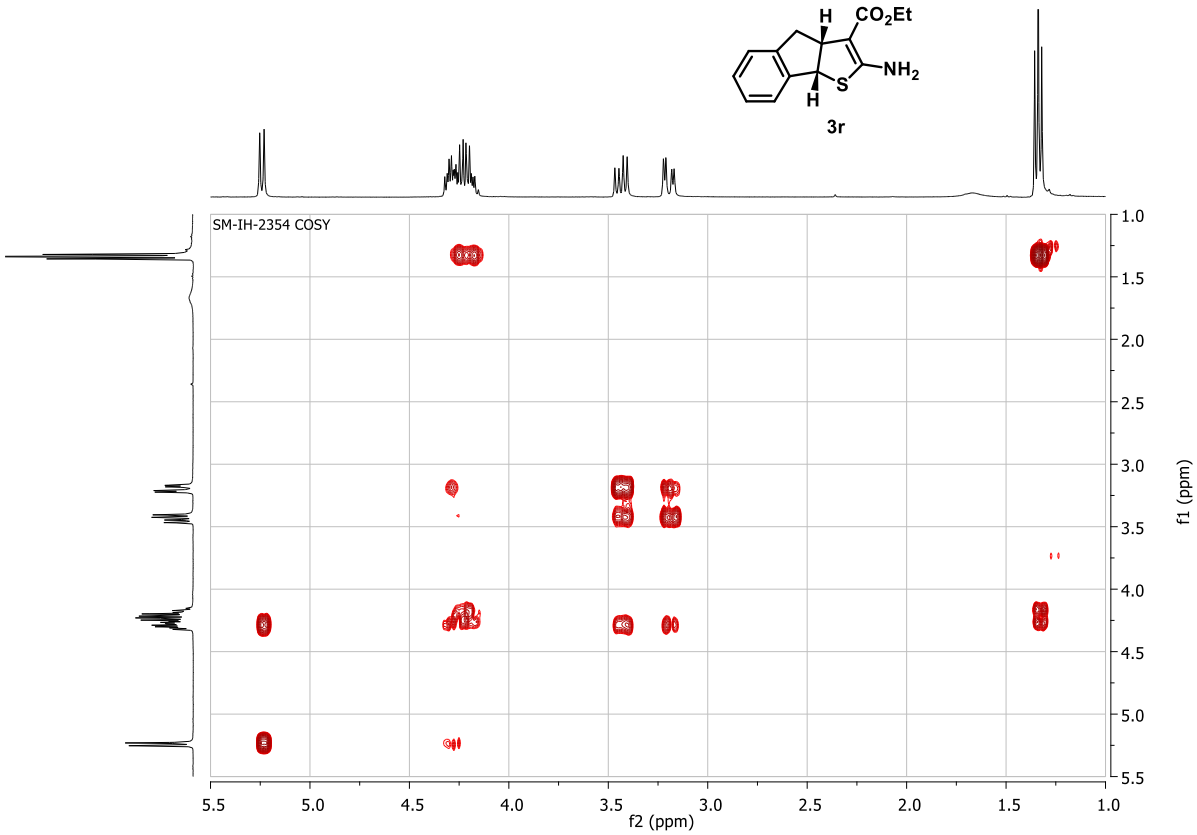
^{1}H NMR of **3r** (400 MHz, $CDCl_3$):



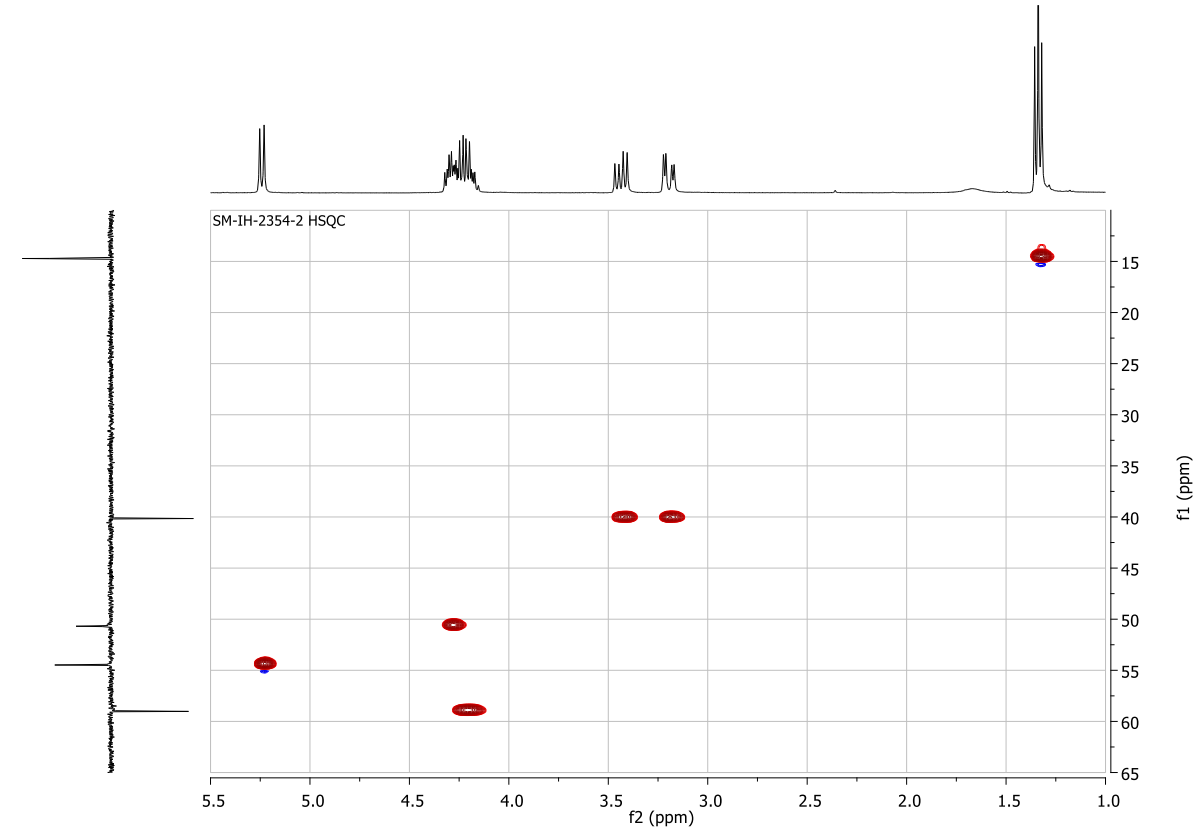
^{13}C{^{1}H} NMR of **3r** (101 MHz, $CDCl_3$):



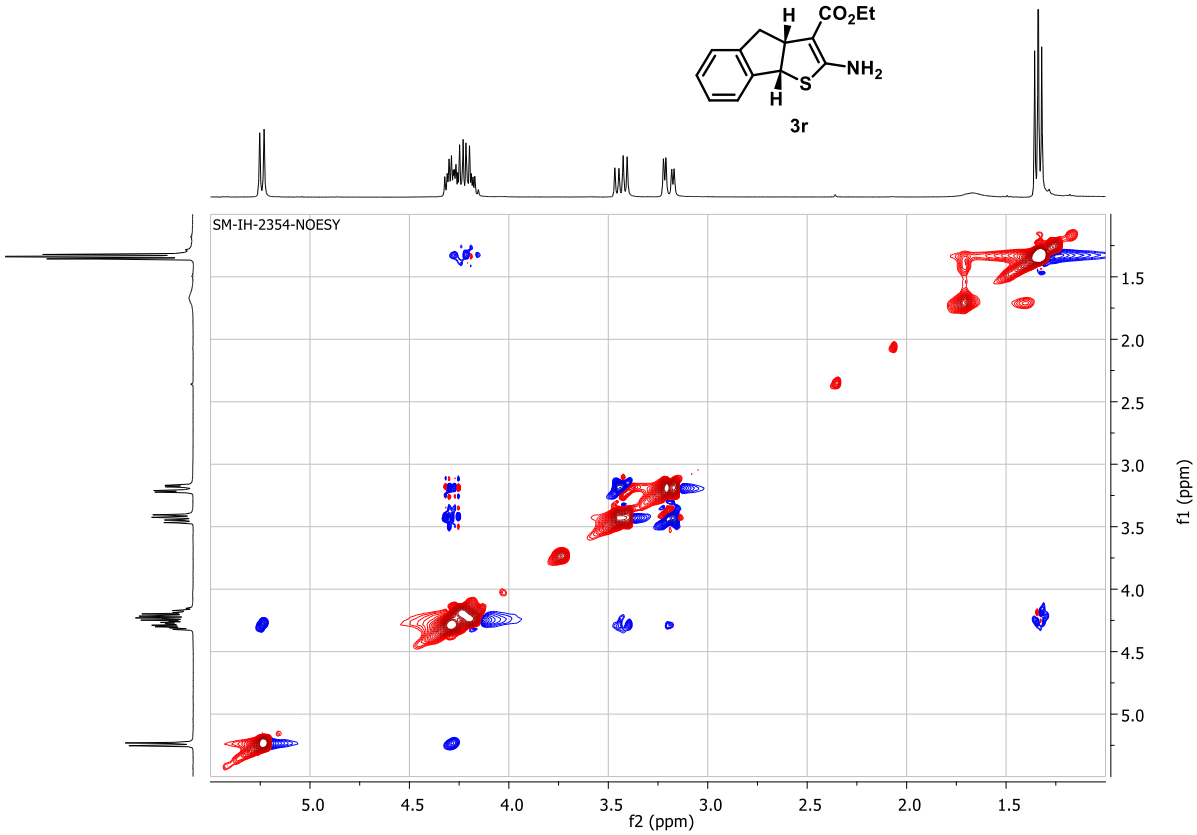
^{1}H-^{1}H COSY NMR of **3r**:



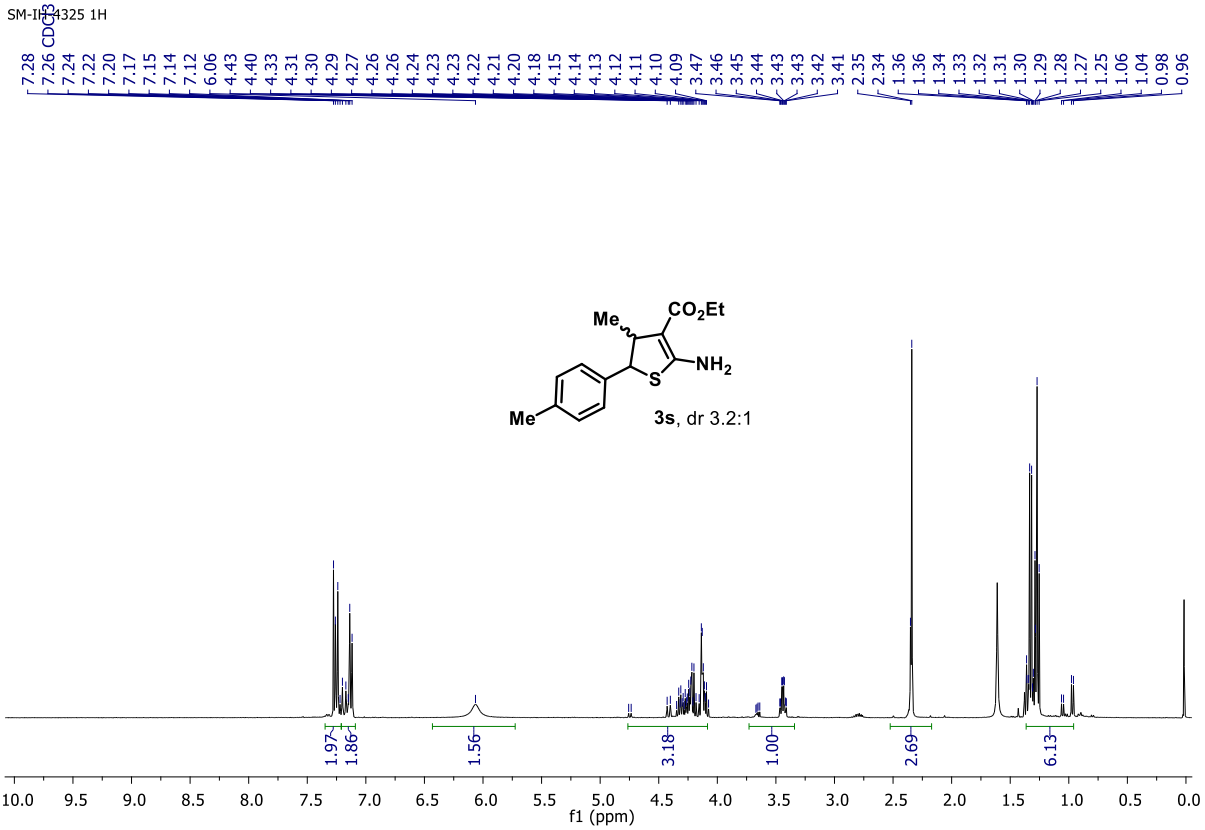
^{1}H-^{13}C HSQC NMR of **3r**:



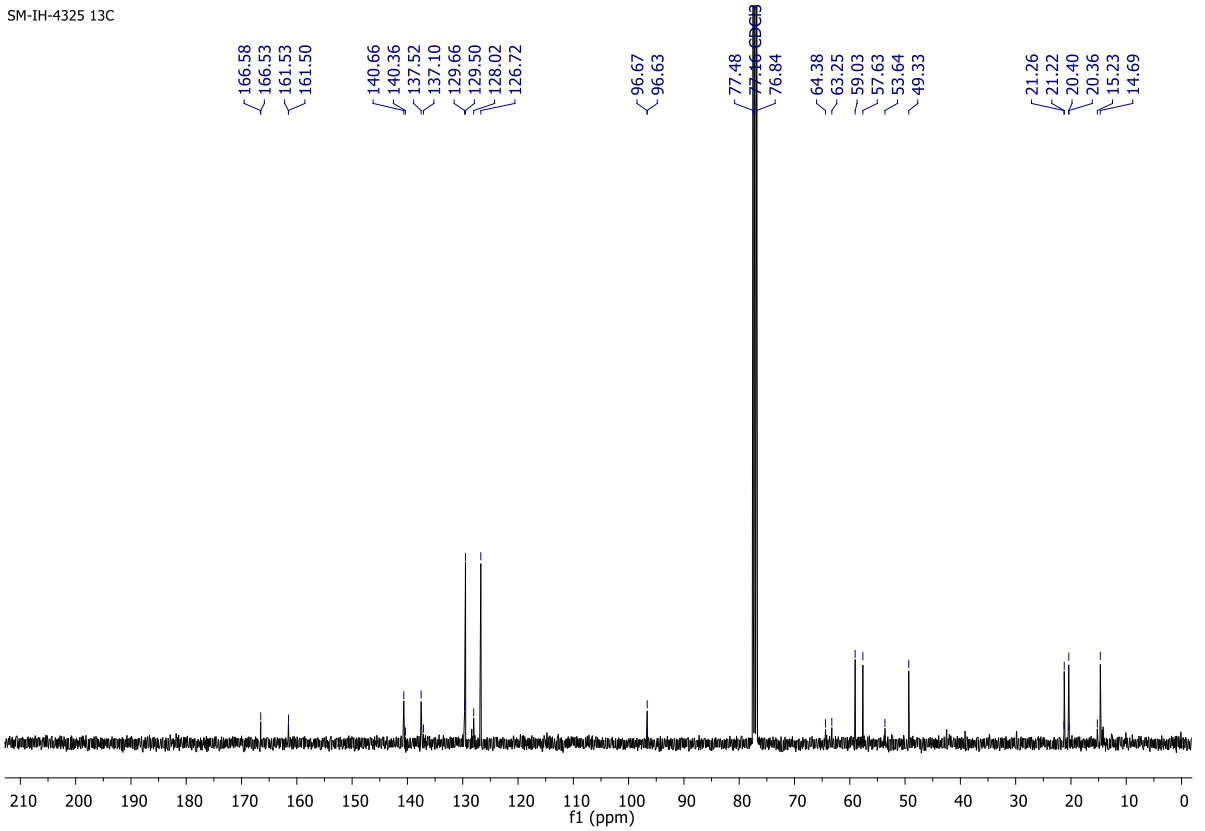
^{1}H-^{1}H NOESY NMR of **3r**:



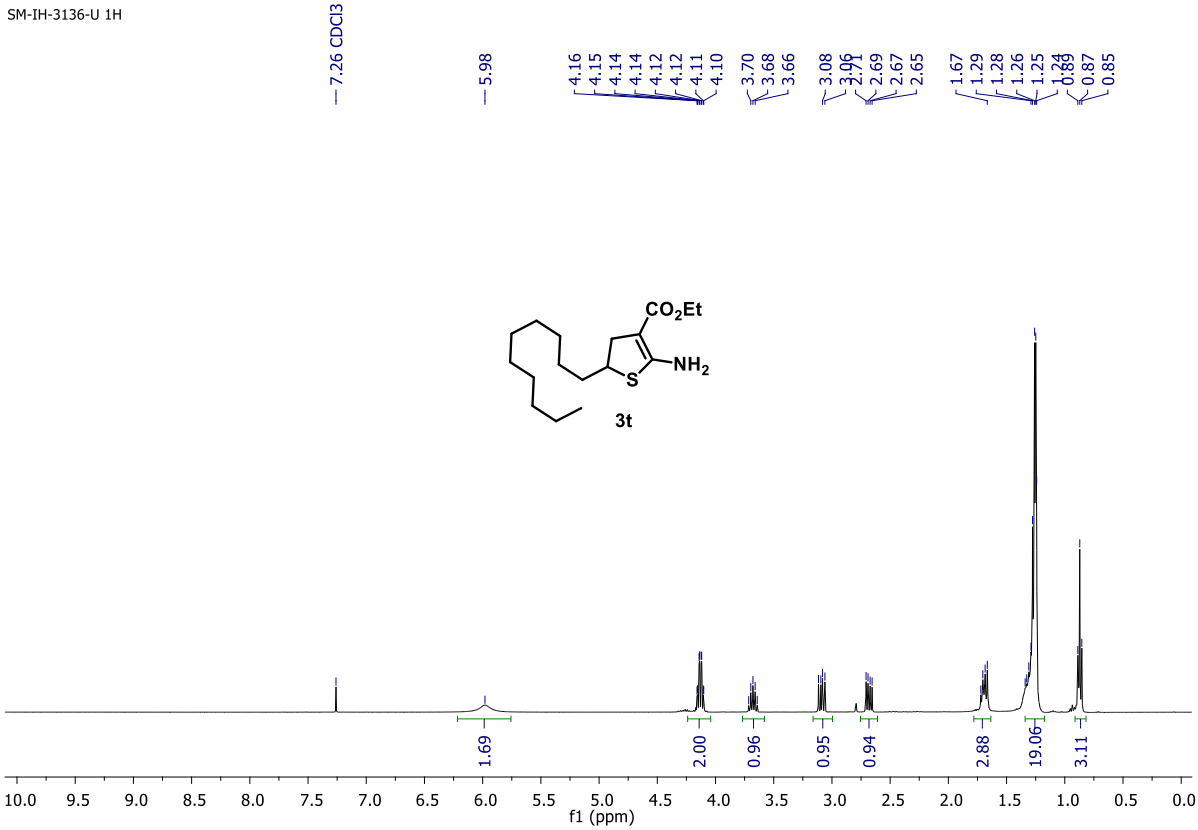
^{1}H NMR of **3s** (400 MHz, $CDCl_3$):



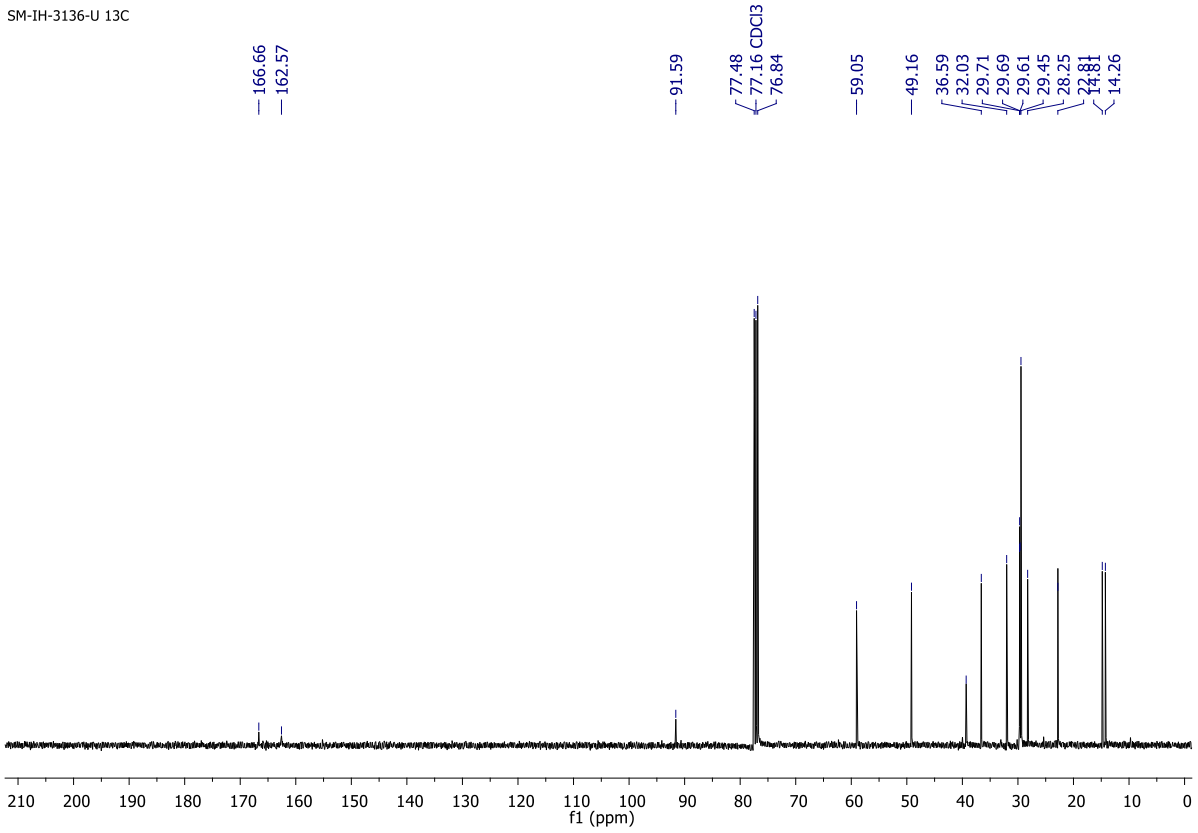
^{13}C{^{1}H} NMR of **3s** (101 MHz, $CDCl_3$):



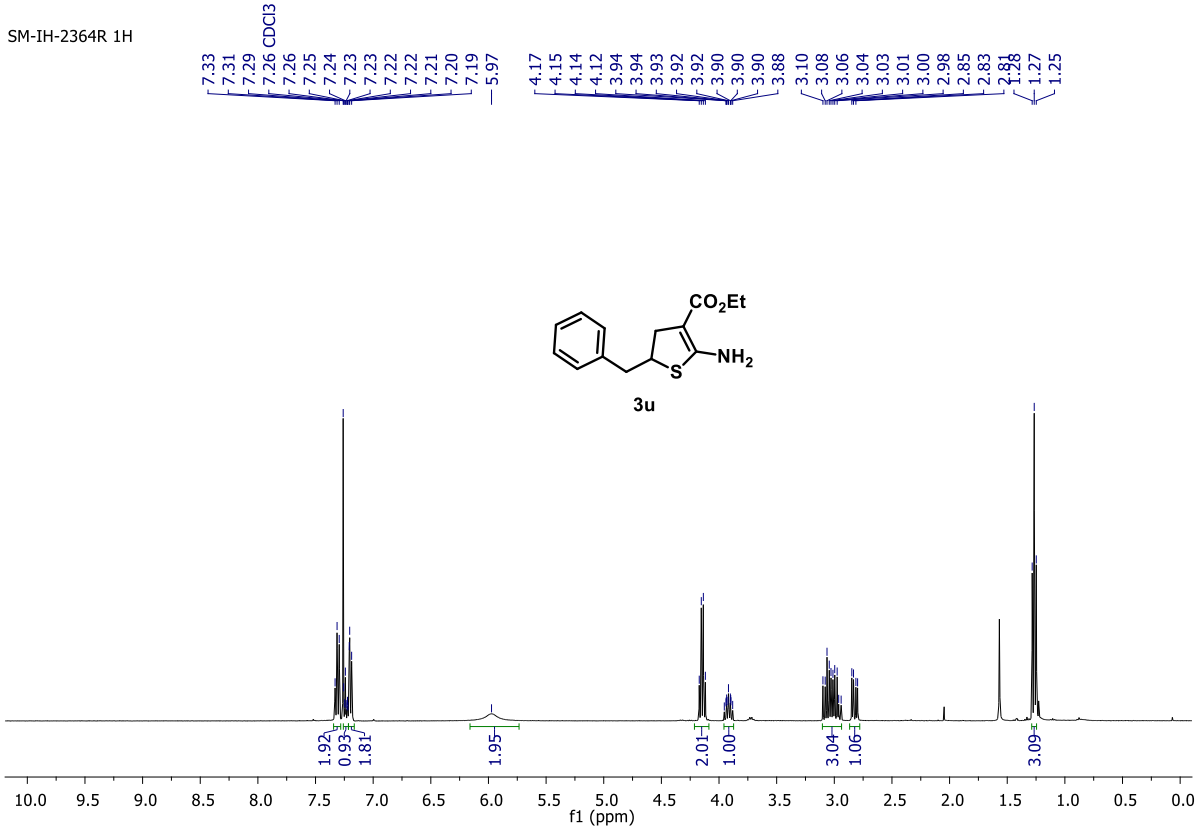
^{1}H NMR of **3t** (400 MHz, $CDCl_3$):



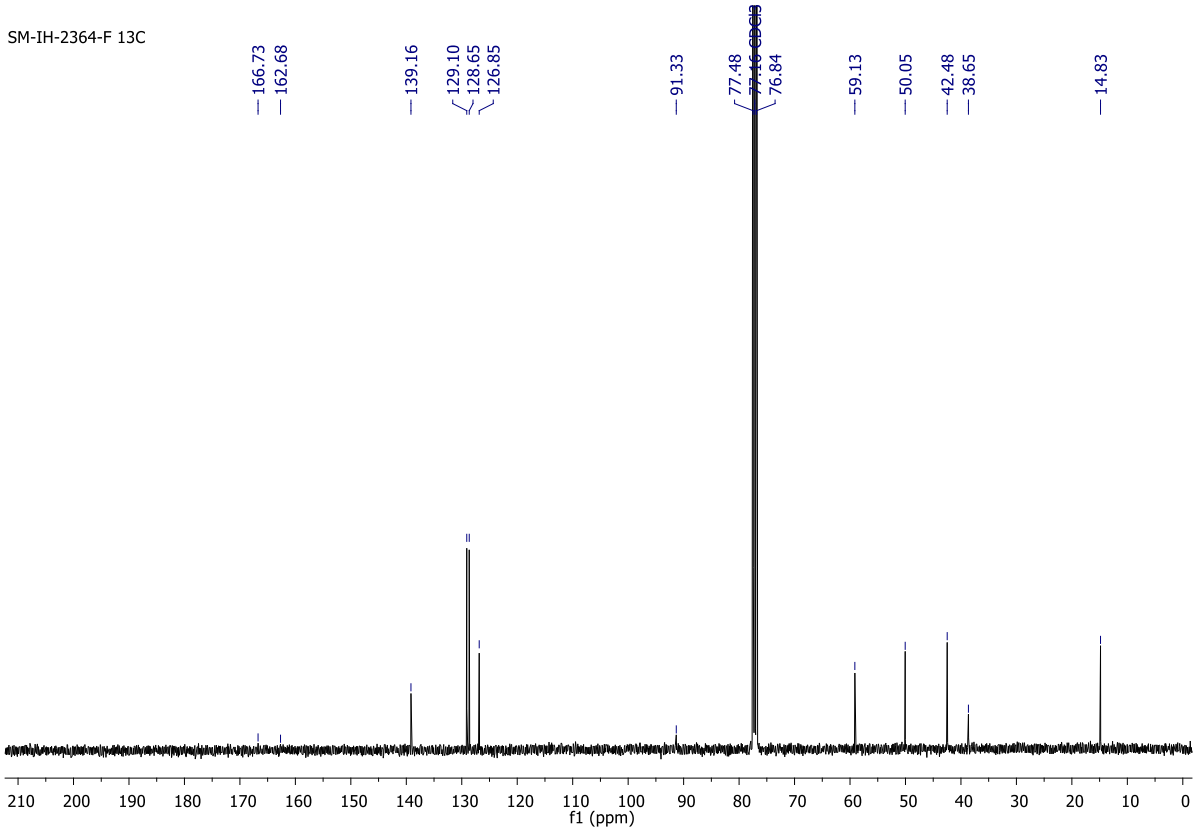
^{13}C{^{1}H} NMR of **3t** (101 MHz, $CDCl_3$):



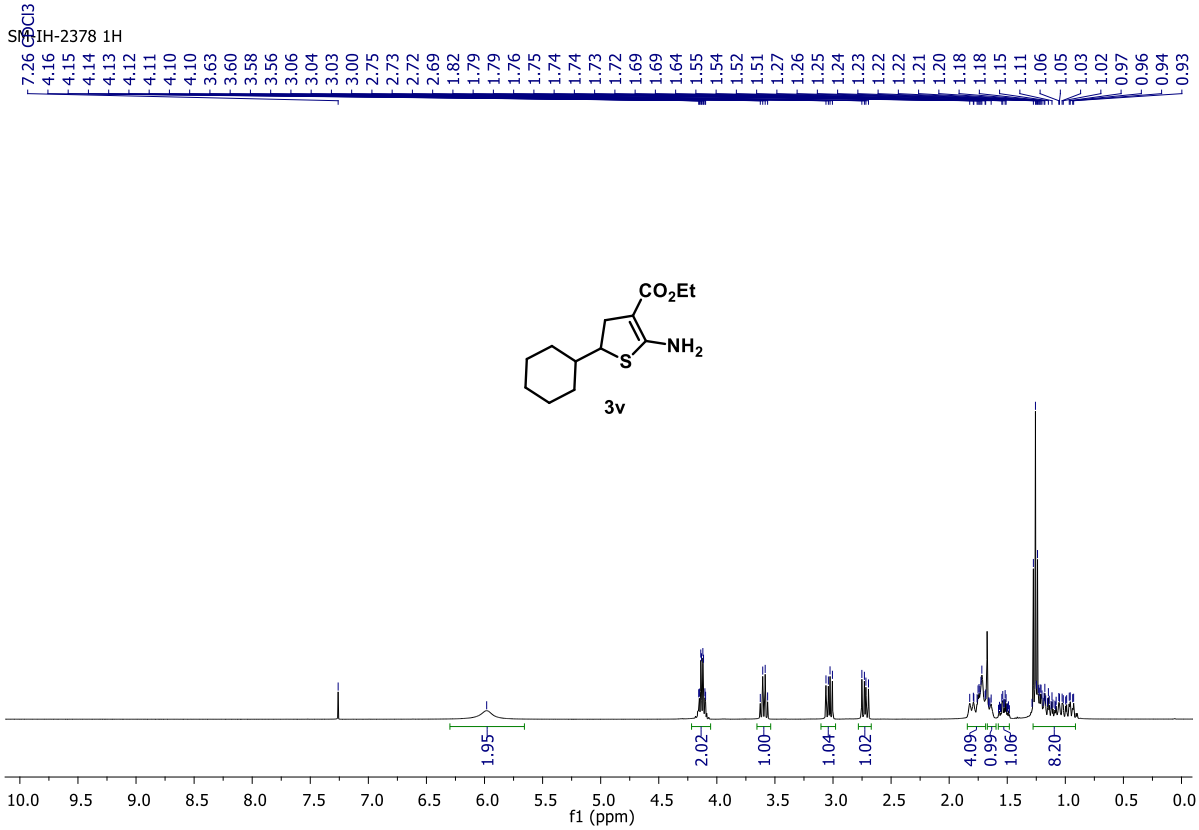
^{1}H NMR of **3u** (400 MHz, $CDCl_3$):



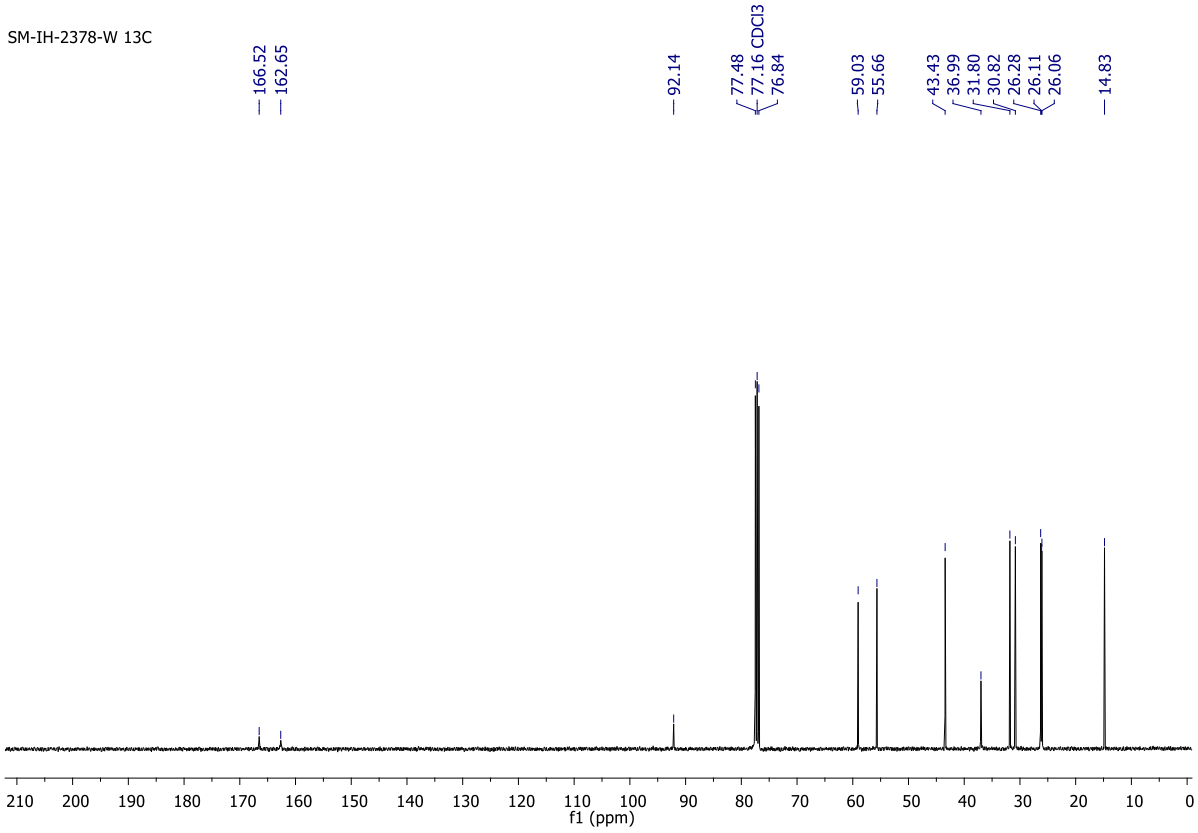
^{13}C{^{1}H} NMR of **3u** (101 MHz, $CDCl_3$):



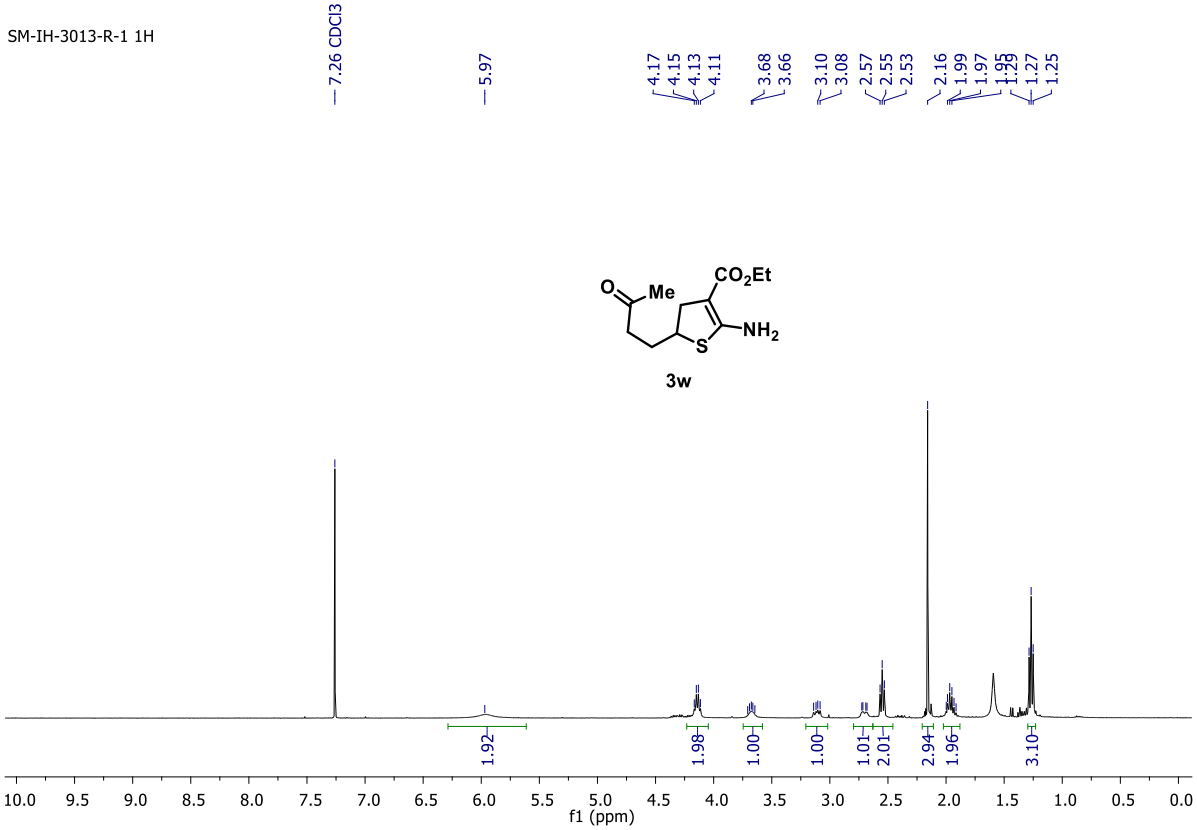
^{1}H NMR of **3v** (400 MHz, $CDCl_3$):



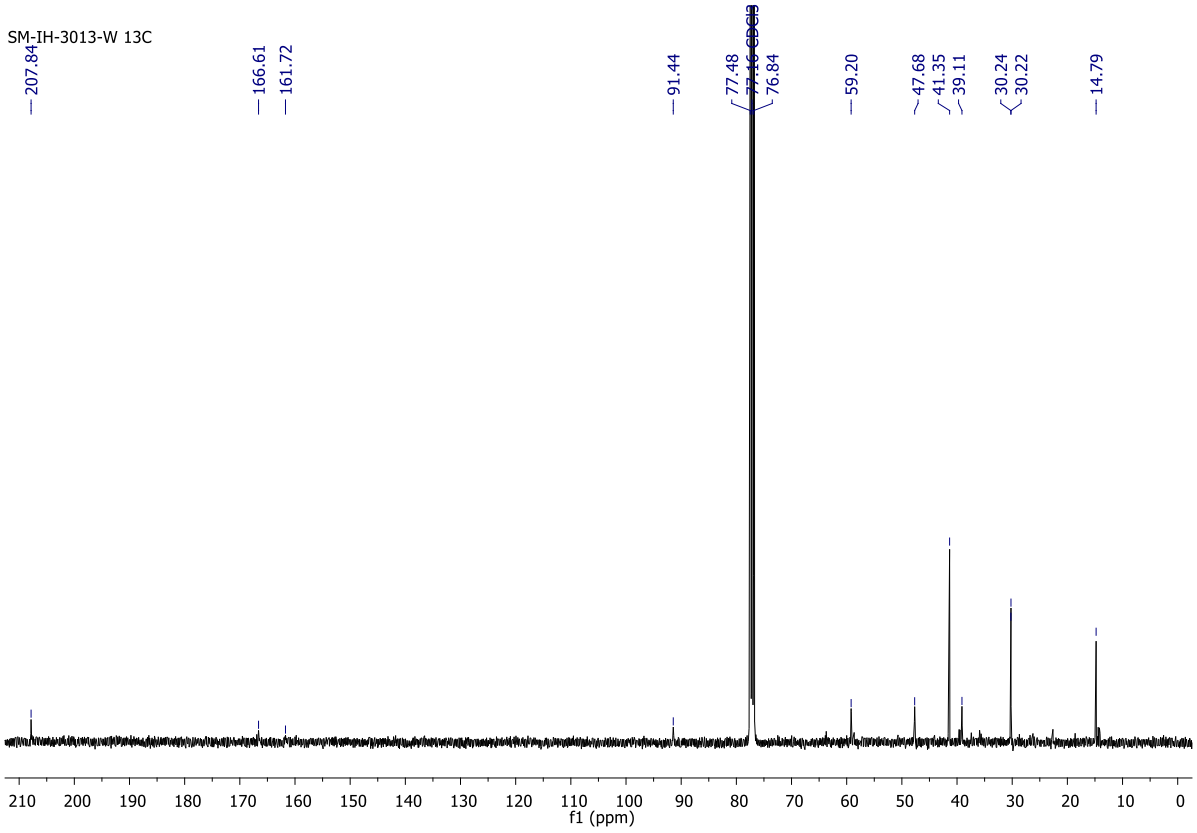
^{13}C{^{1}H} NMR of **3v** (101 MHz, $CDCl_3$):



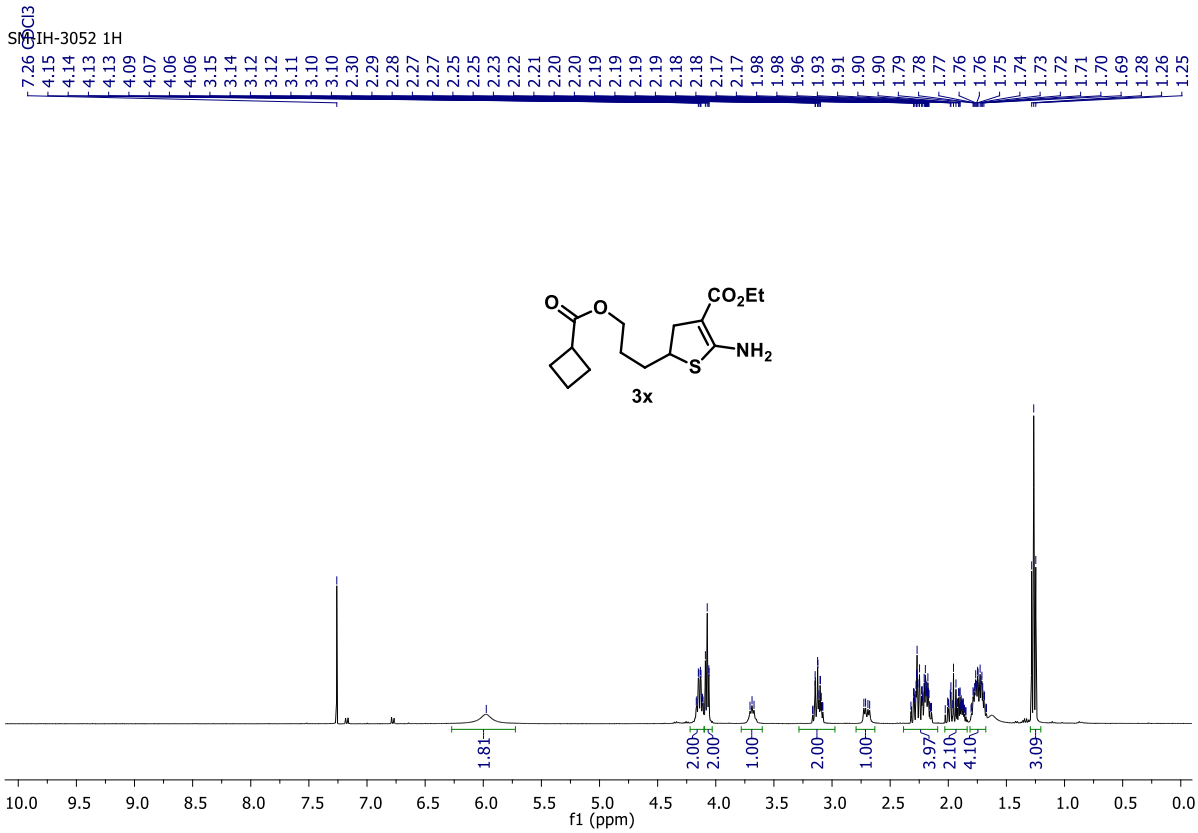
^{1}H NMR of **3w** (400 MHz, $CDCl_3$):



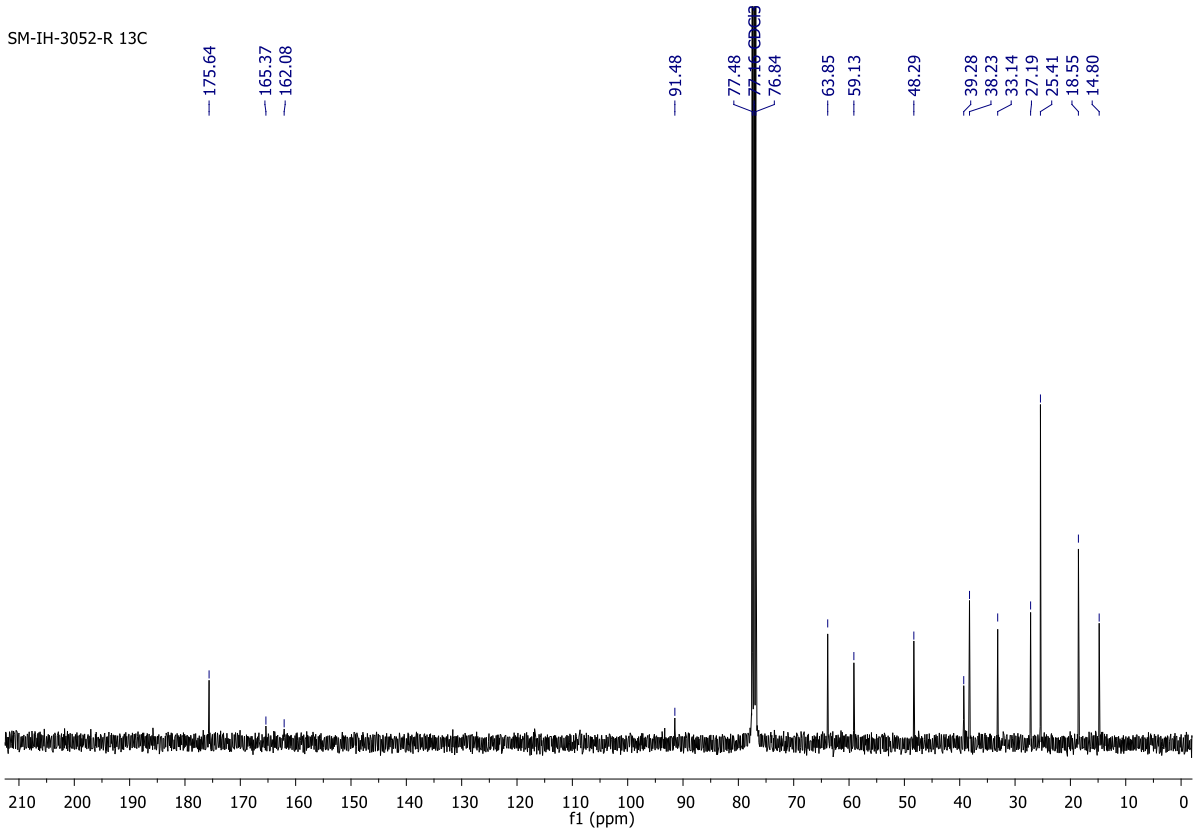
^{13}C{^{1}H} NMR of **3w** (101 MHz, $CDCl_3$):



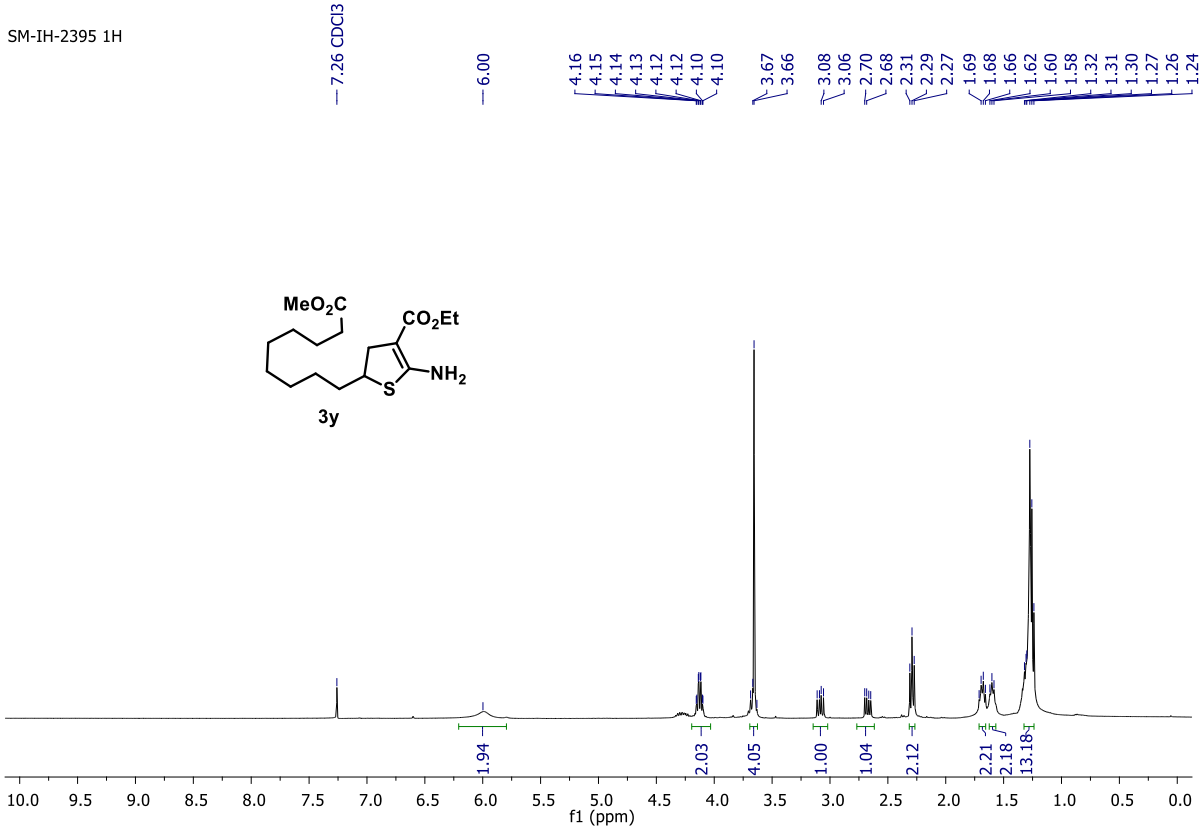
^{1}H NMR of **3x** (400 MHz, $CDCl_3$):



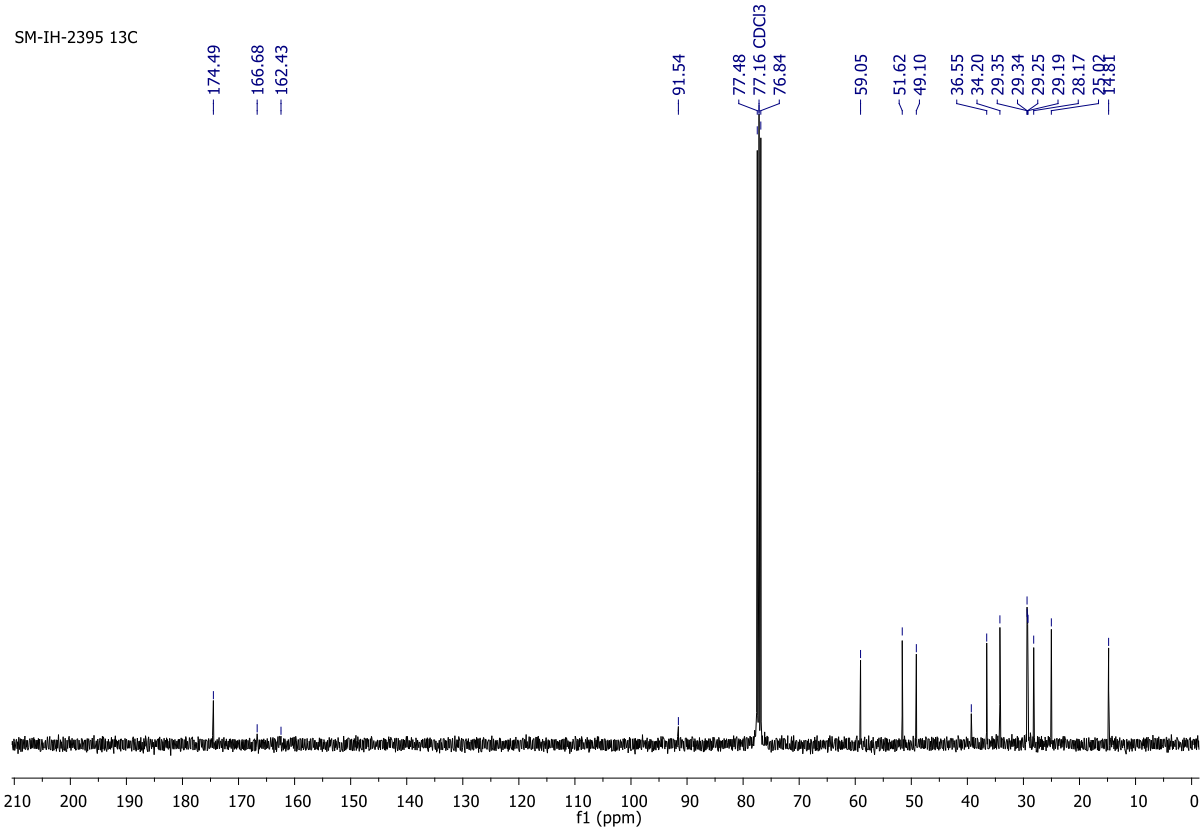
^{13}C{^{1}H} NMR of **3x** (101 MHz, $CDCl_3$):



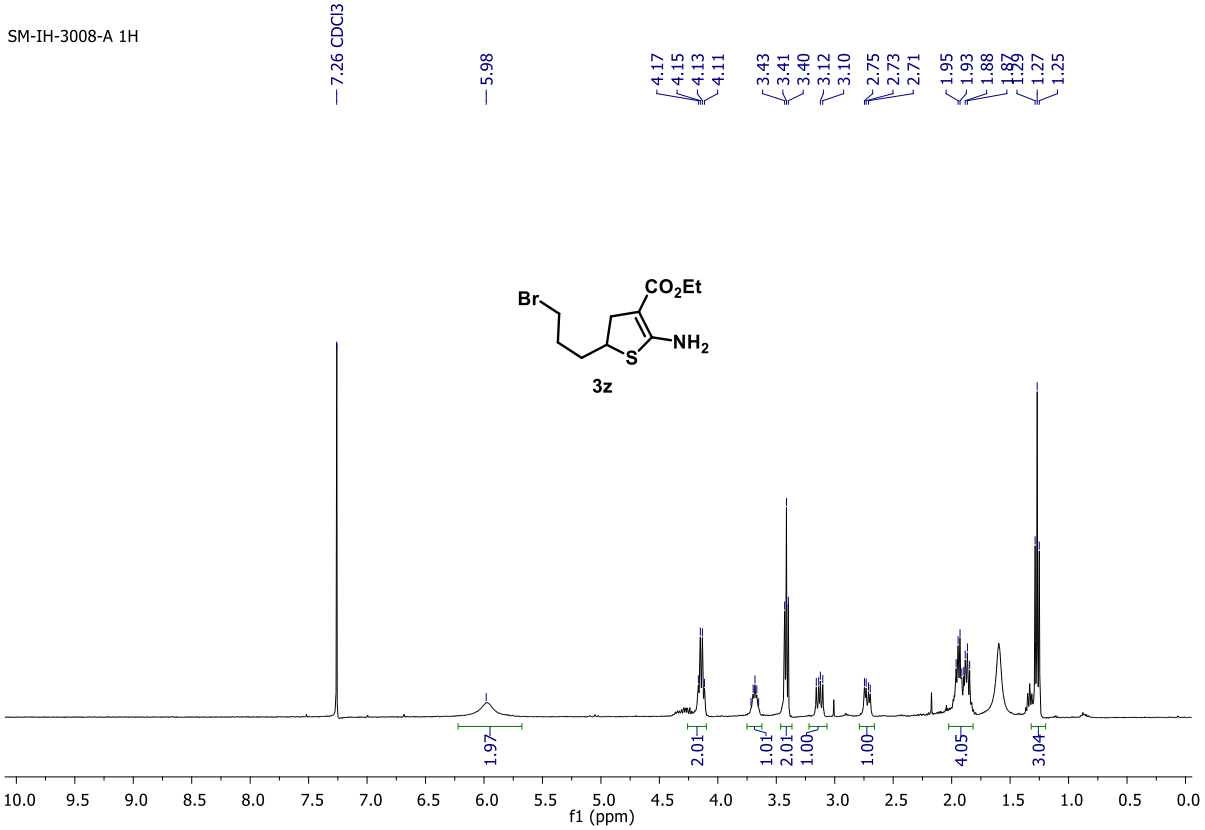
^{1}H NMR of **3y** (400 MHz, $CDCl_3$):



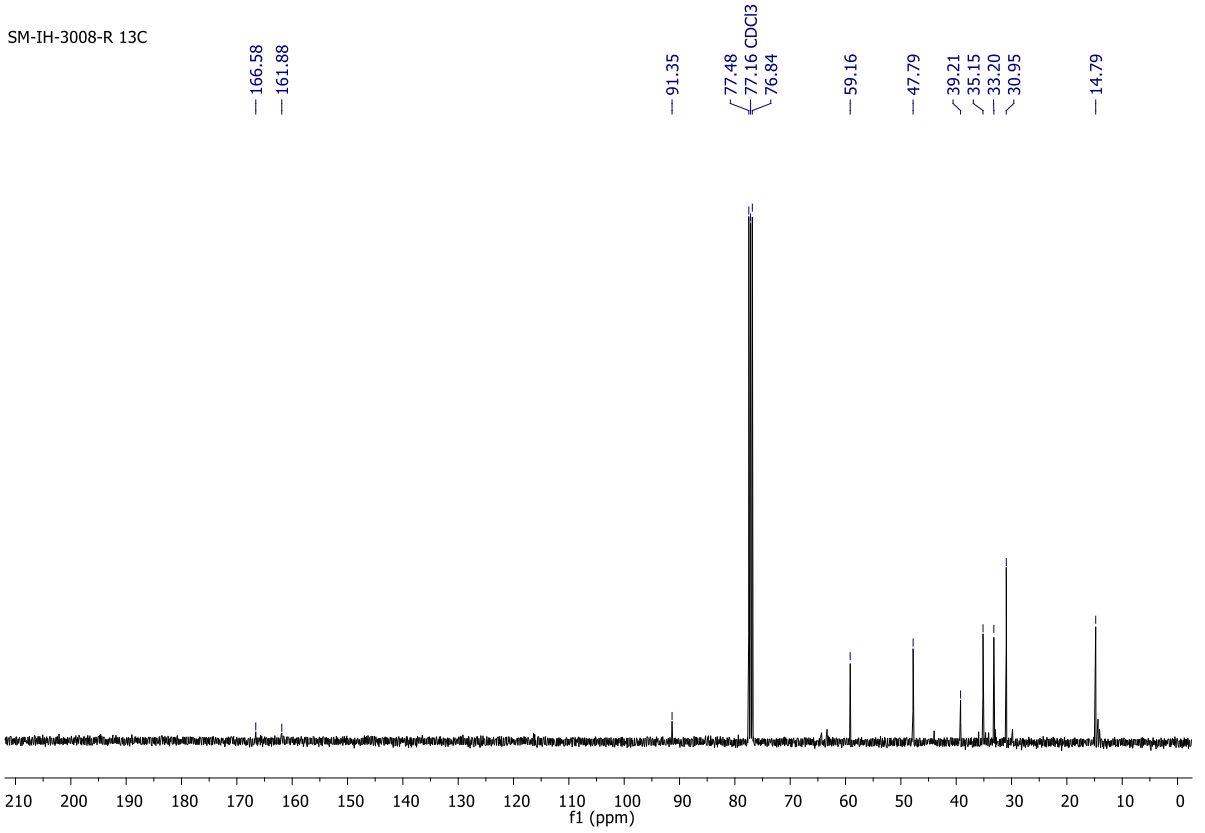
^{13}C{^{1}H} NMR of **3y** (101 MHz, $CDCl_3$):



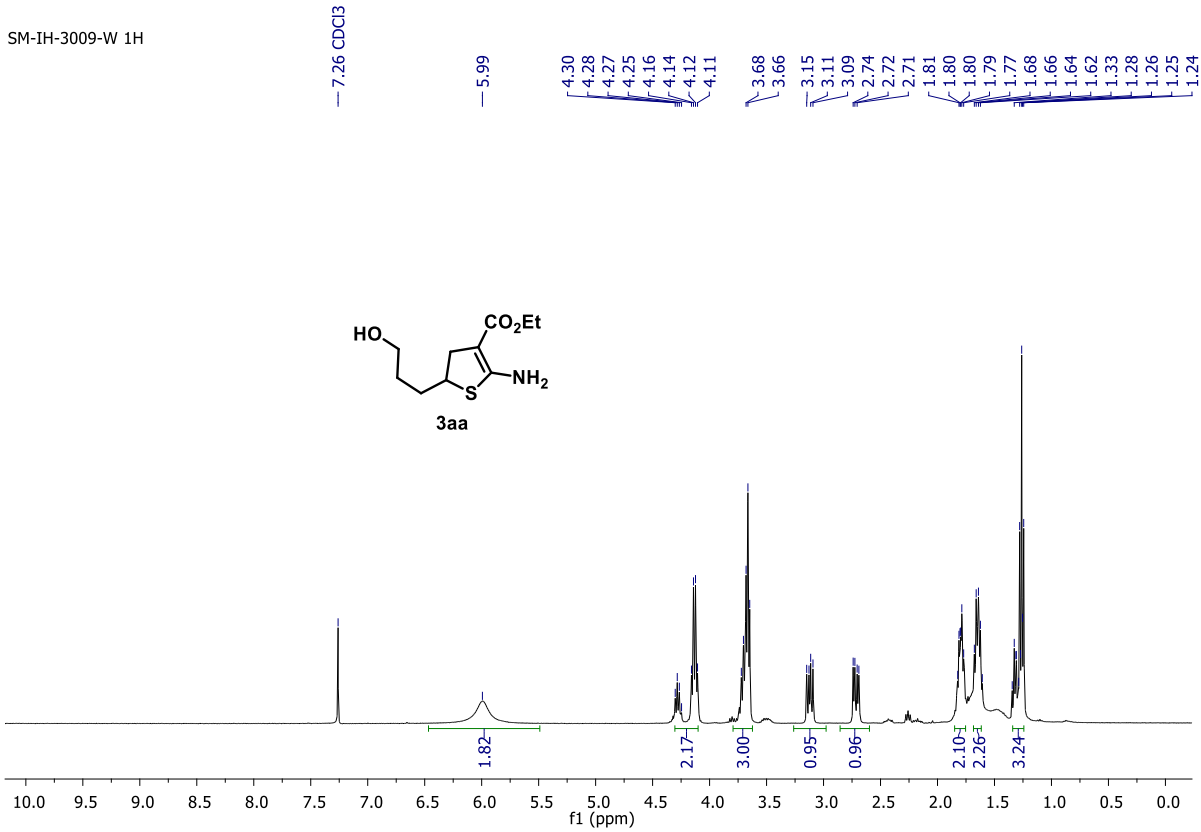
^{1}H NMR of **3z** (400 MHz, $CDCl_3$):



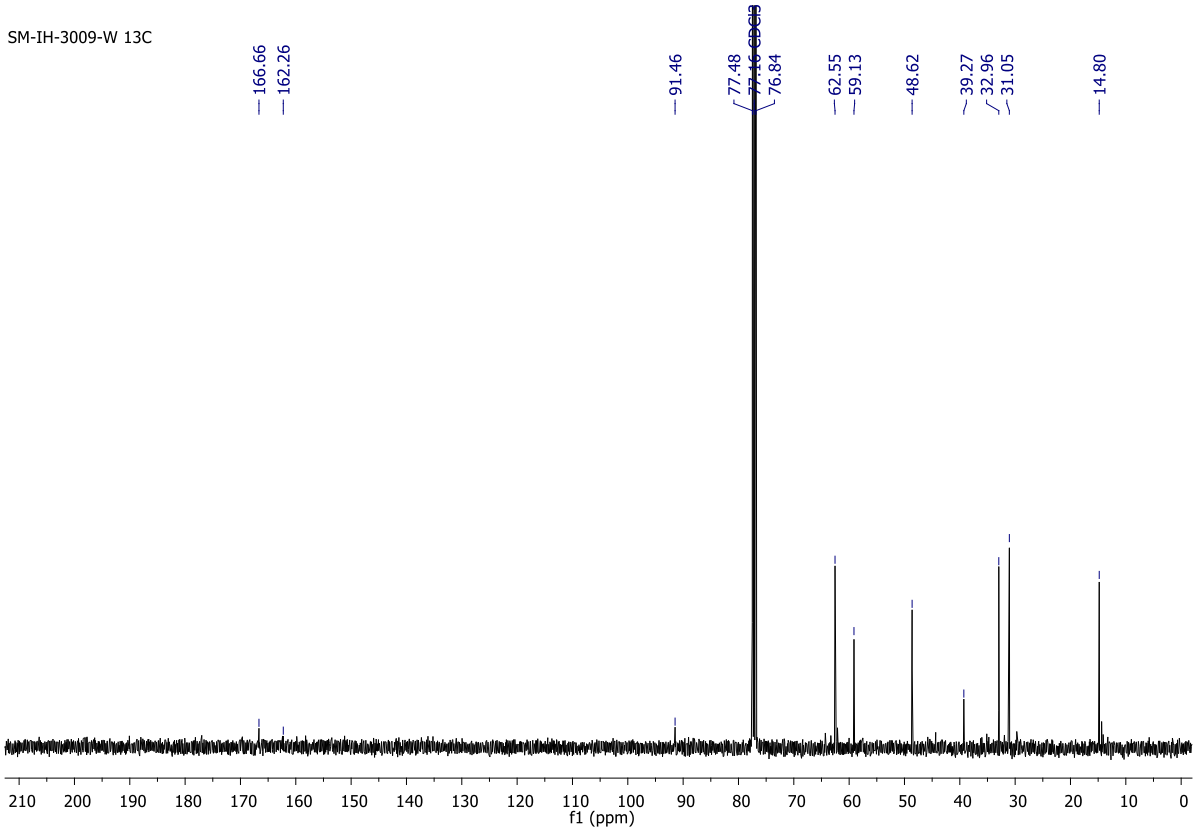
^{13}C{^{1}H} NMR of **3z** (101 MHz, $CDCl_3$):



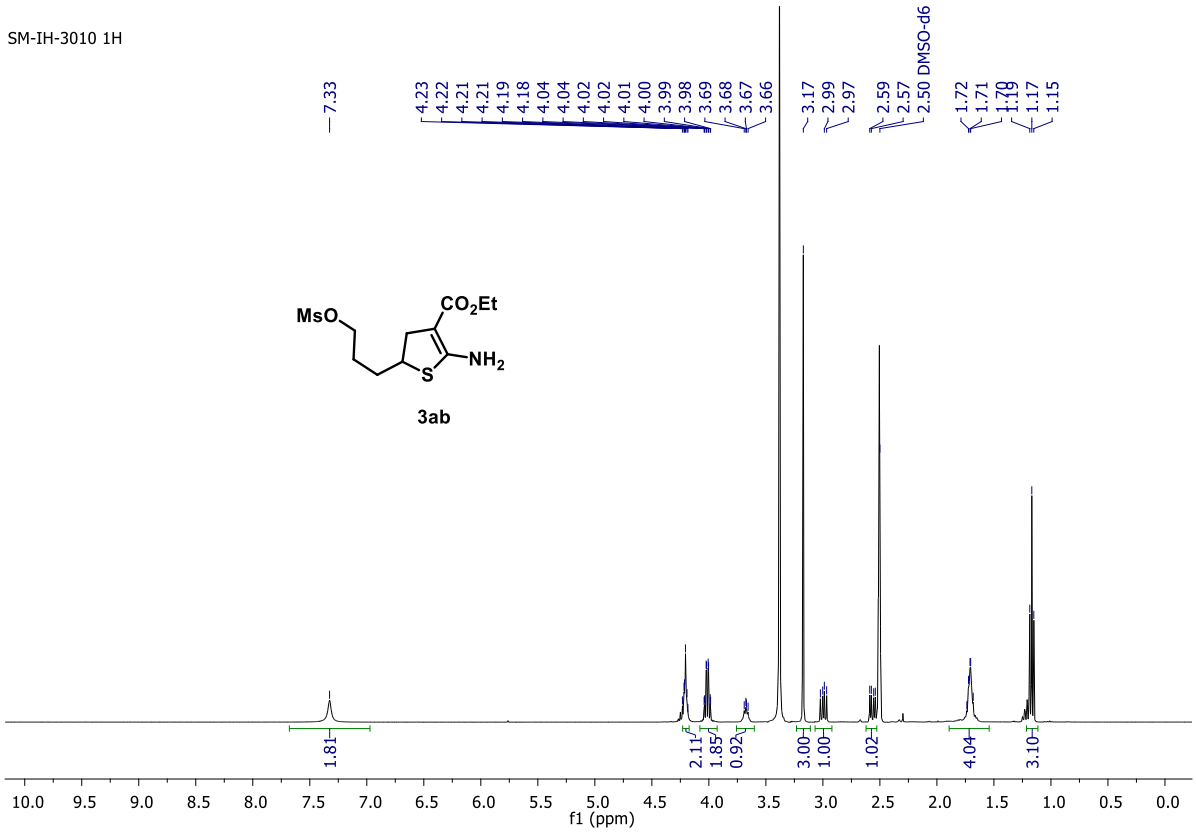
^{1}H NMR of **3aa** (400 MHz, $CDCl_3$):



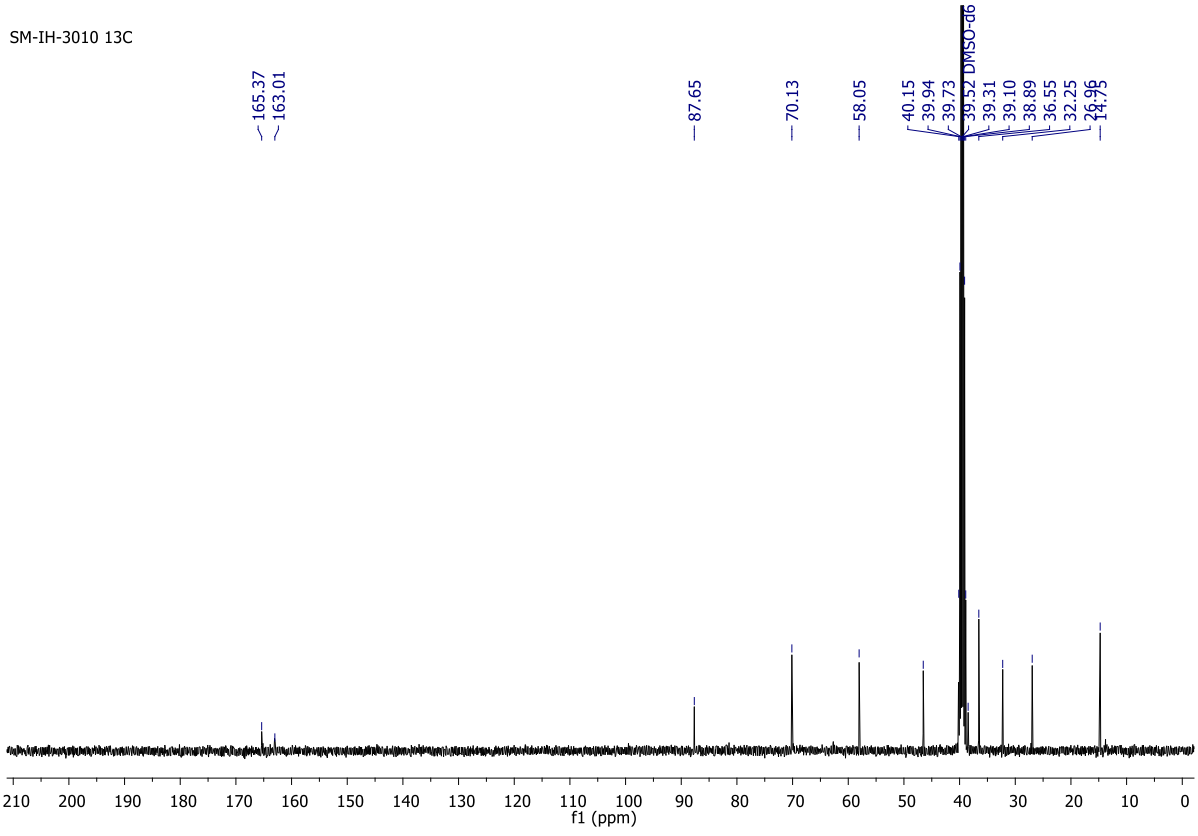
^{13}C{^{1}H} NMR of **3aa** (101 MHz, $CDCl_3$):



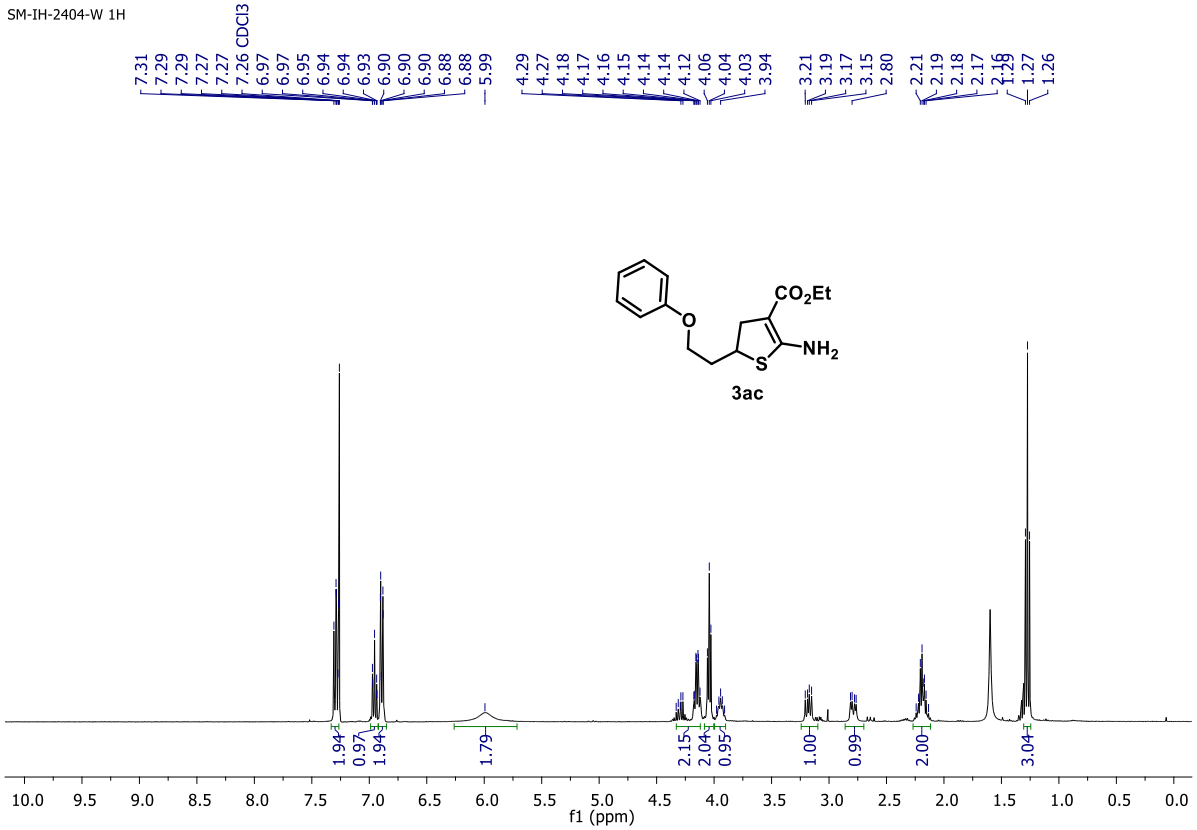
^{1}H NMR of **3ab** (400 MHz, DMSO-d_6):



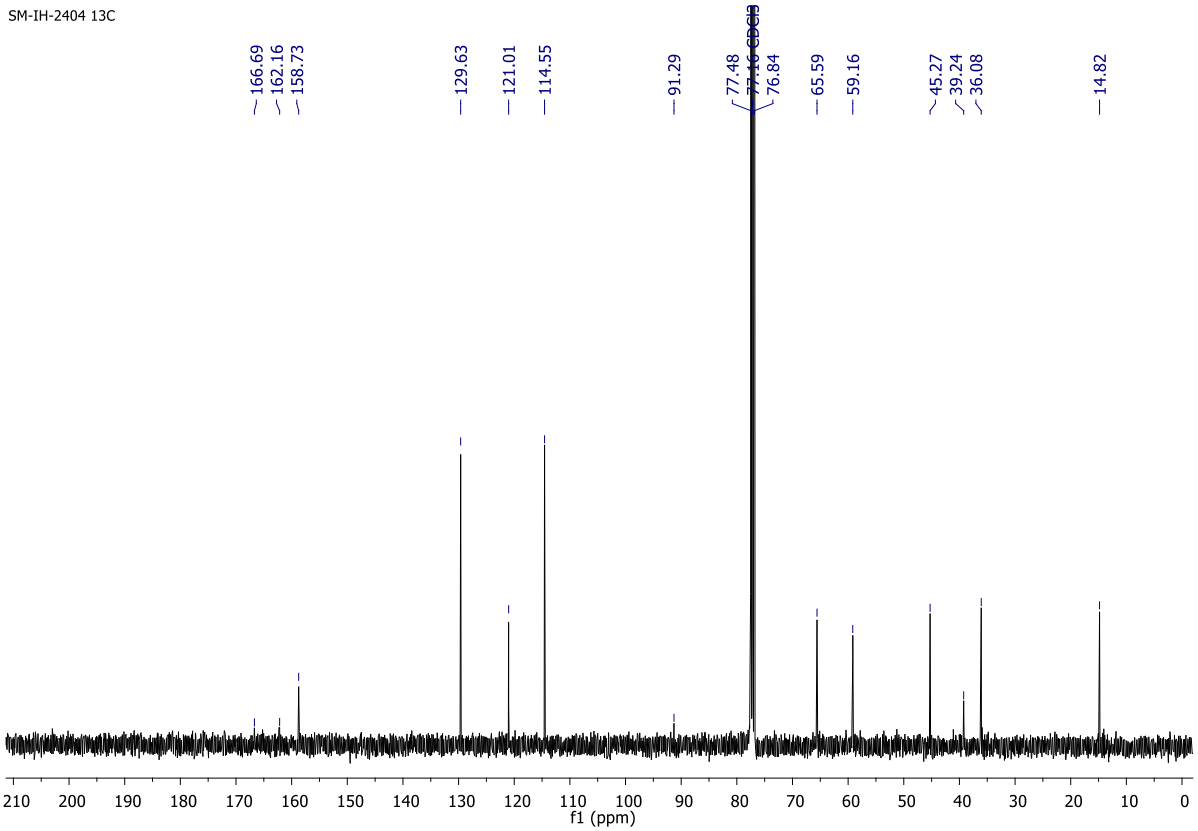
^{13}C{^{1}H} NMR of **3ab** (101 MHz, DMSO-d_6):



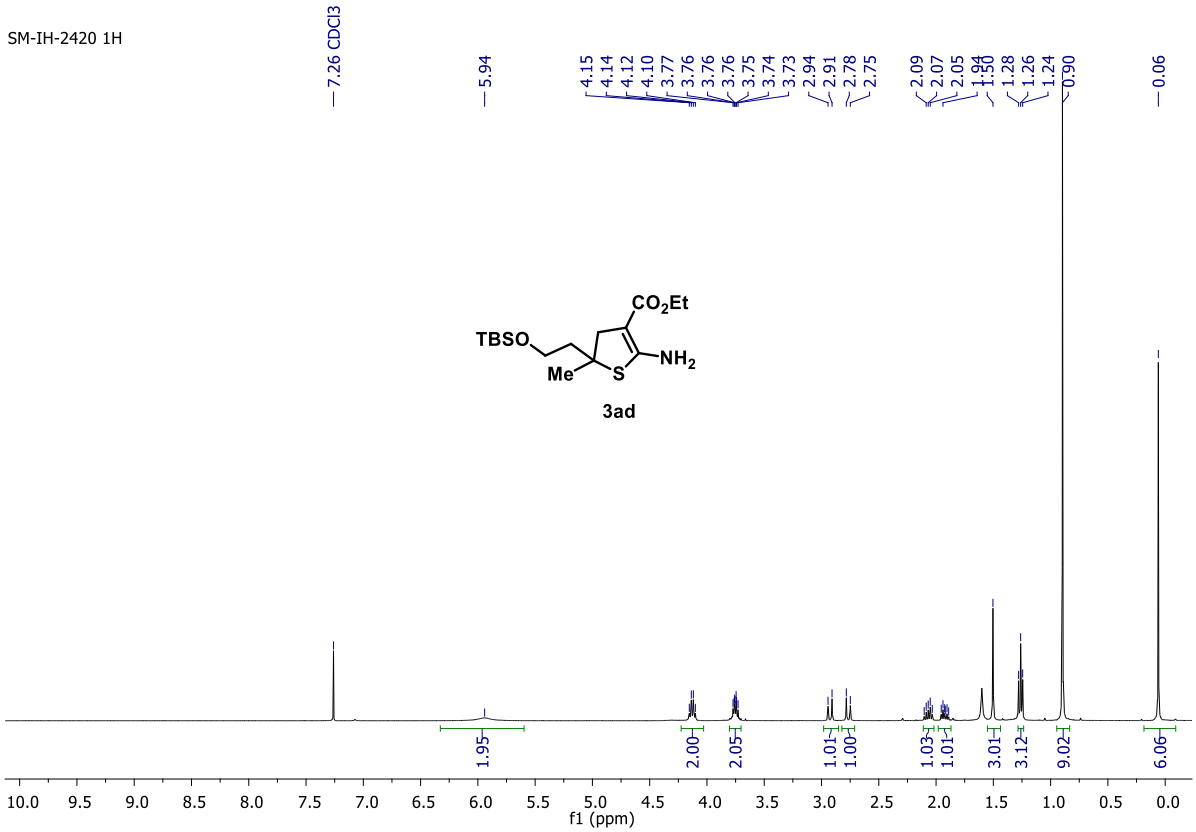
^{1}H NMR of **3ac** (400 MHz, $CDCl_3$):



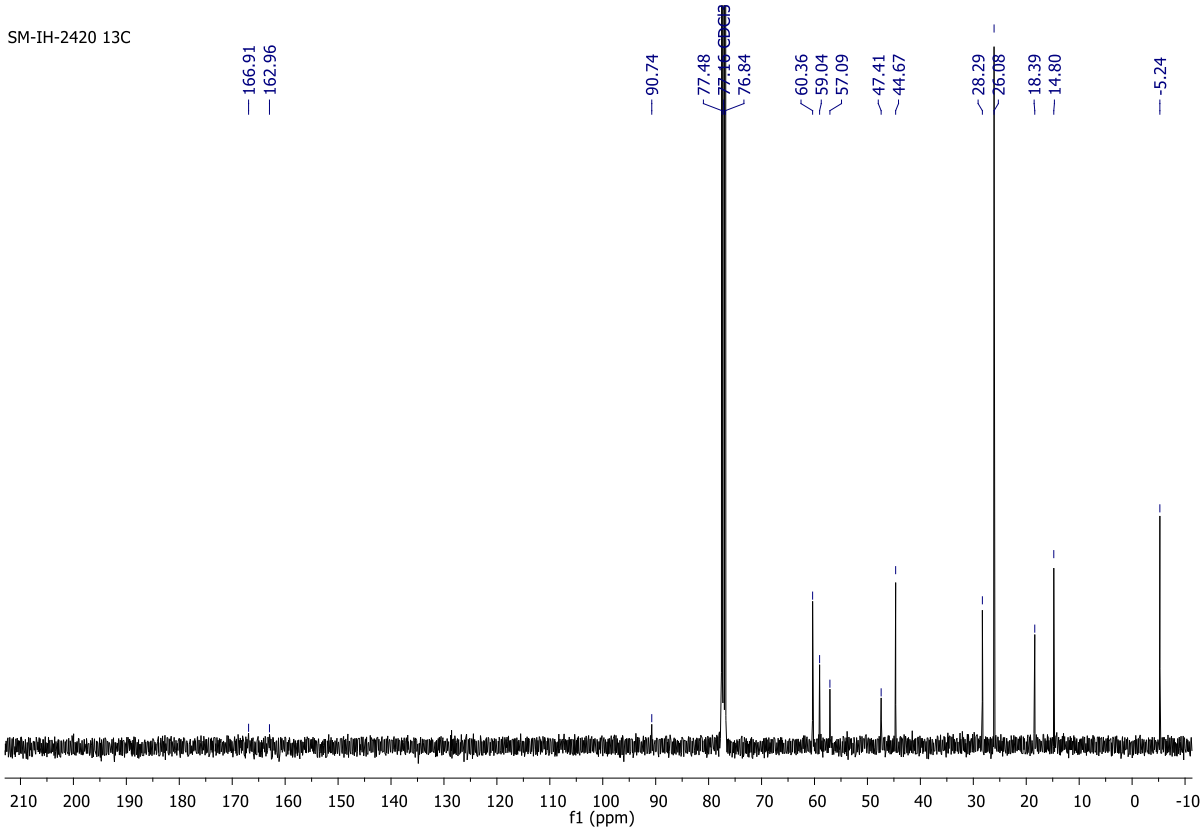
^{13}C{^{1}H} NMR of **3ac** (101 MHz, $CDCl_3$):



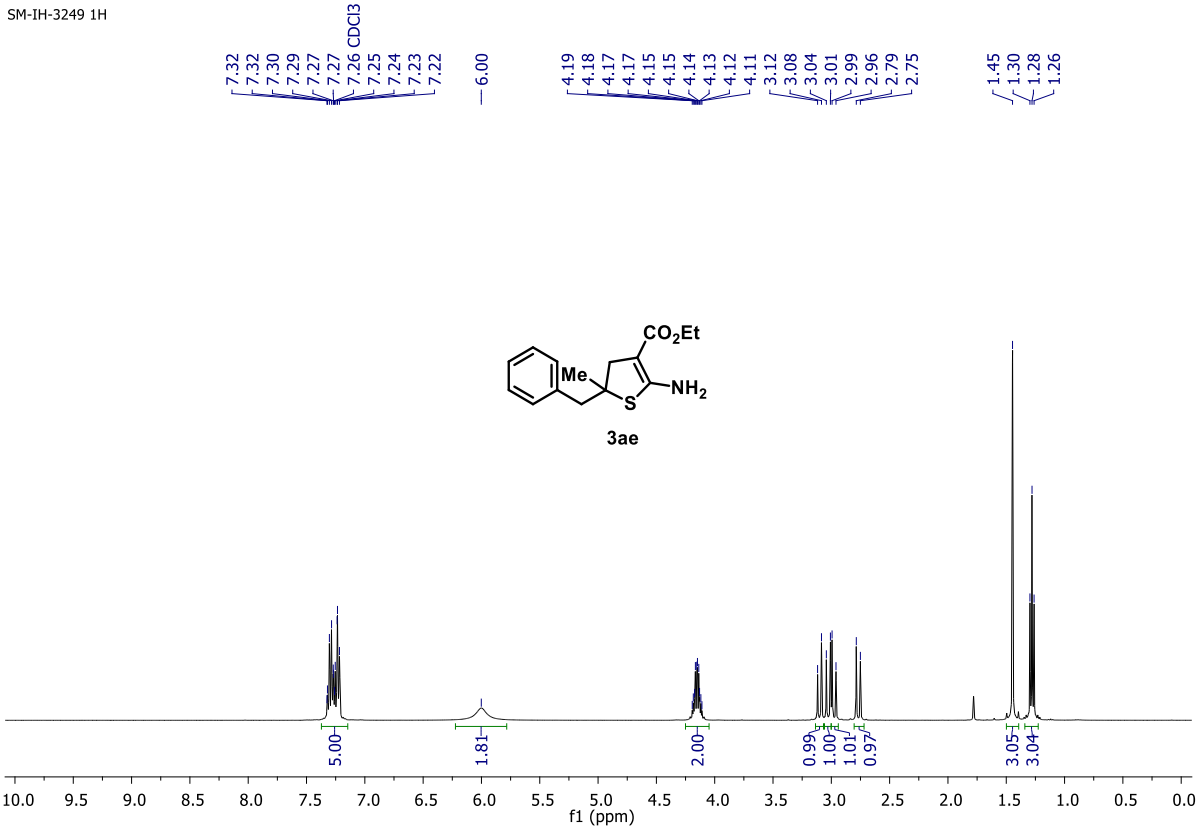
^{1}H NMR of **3ad** (400 MHz, $CDCl_3$):



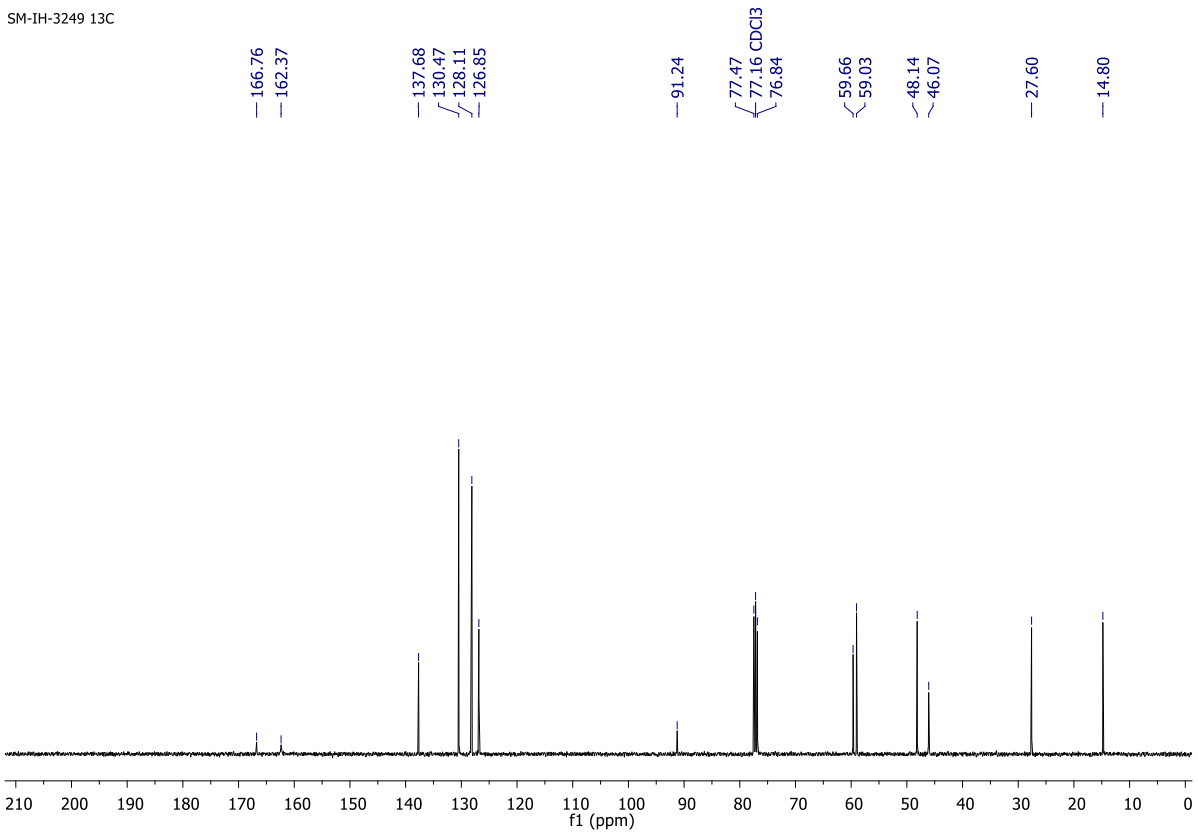
^{13}C{^{1}H} NMR of **3ad** (101 MHz, $CDCl_3$):



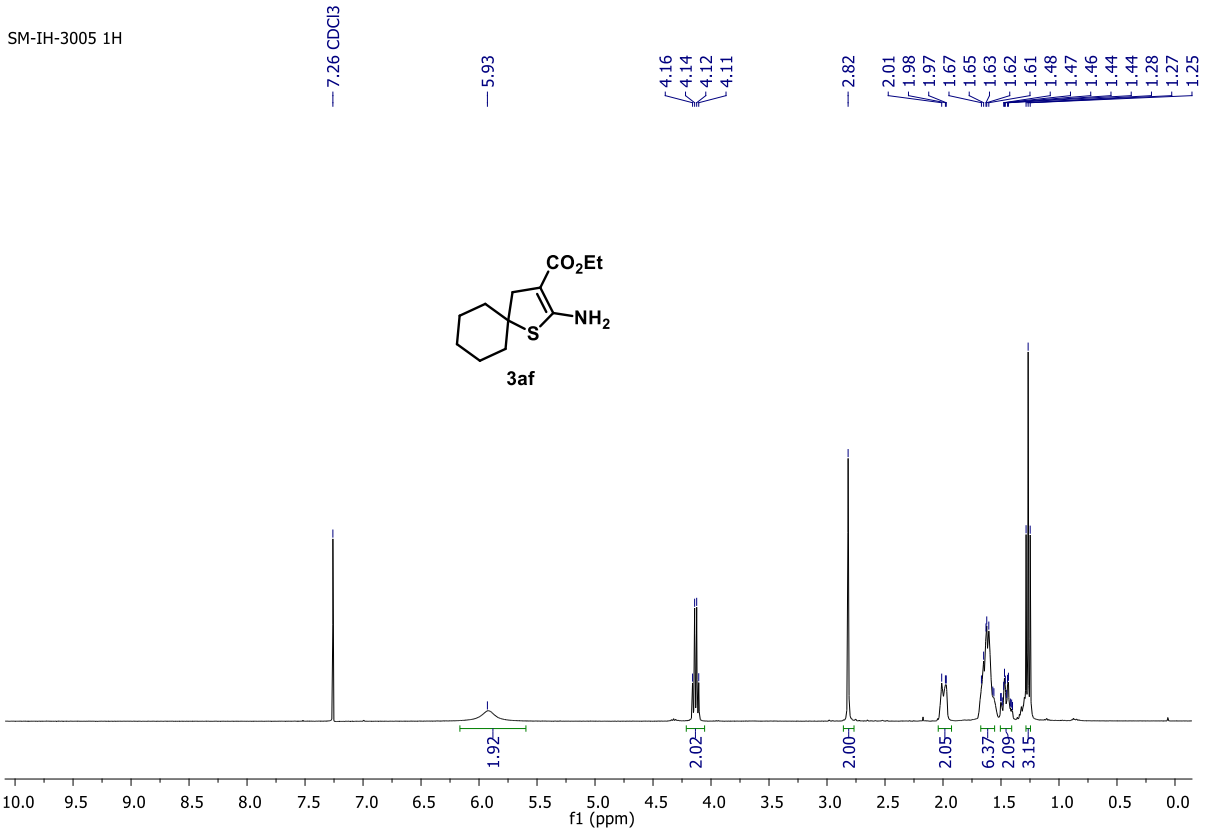
^{1}H NMR of **3ae** (400 MHz, $CDCl_3$):



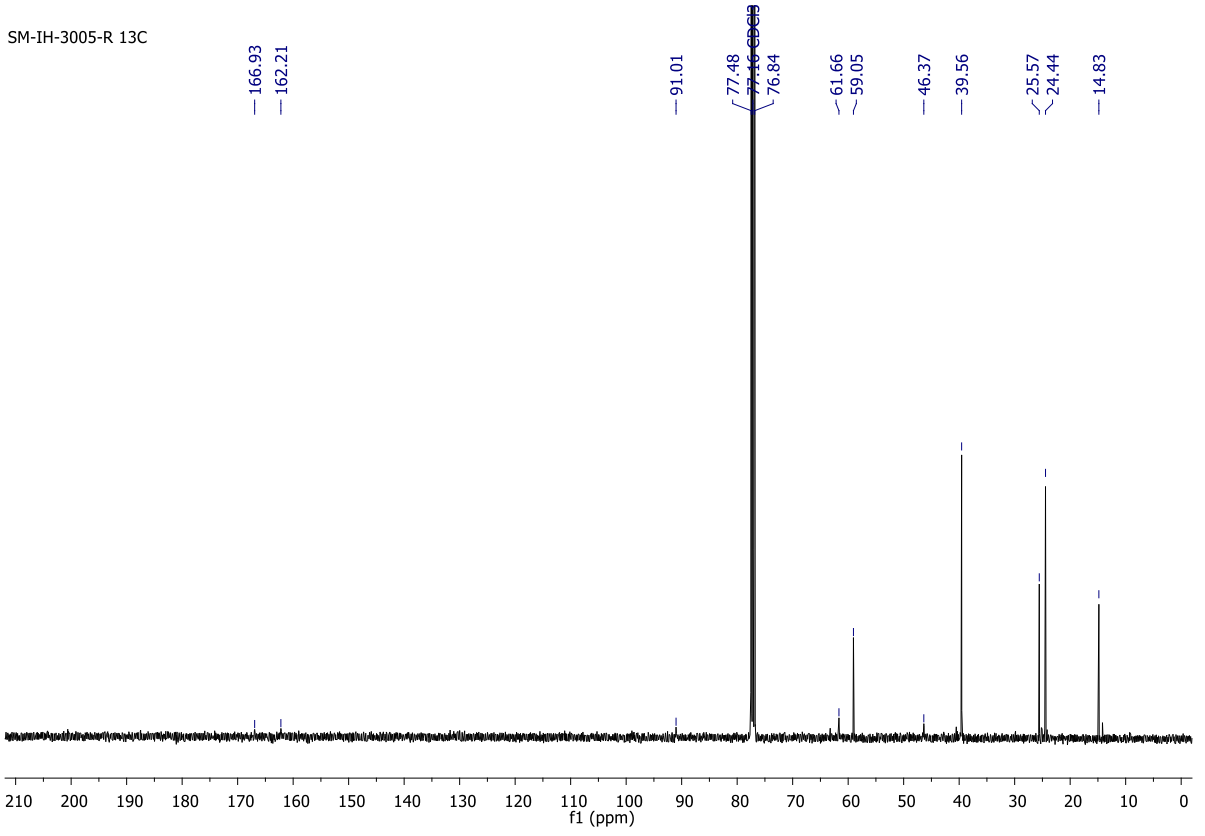
^{13}C{^{1}H} NMR of **3ae** (101 MHz, $CDCl_3$):



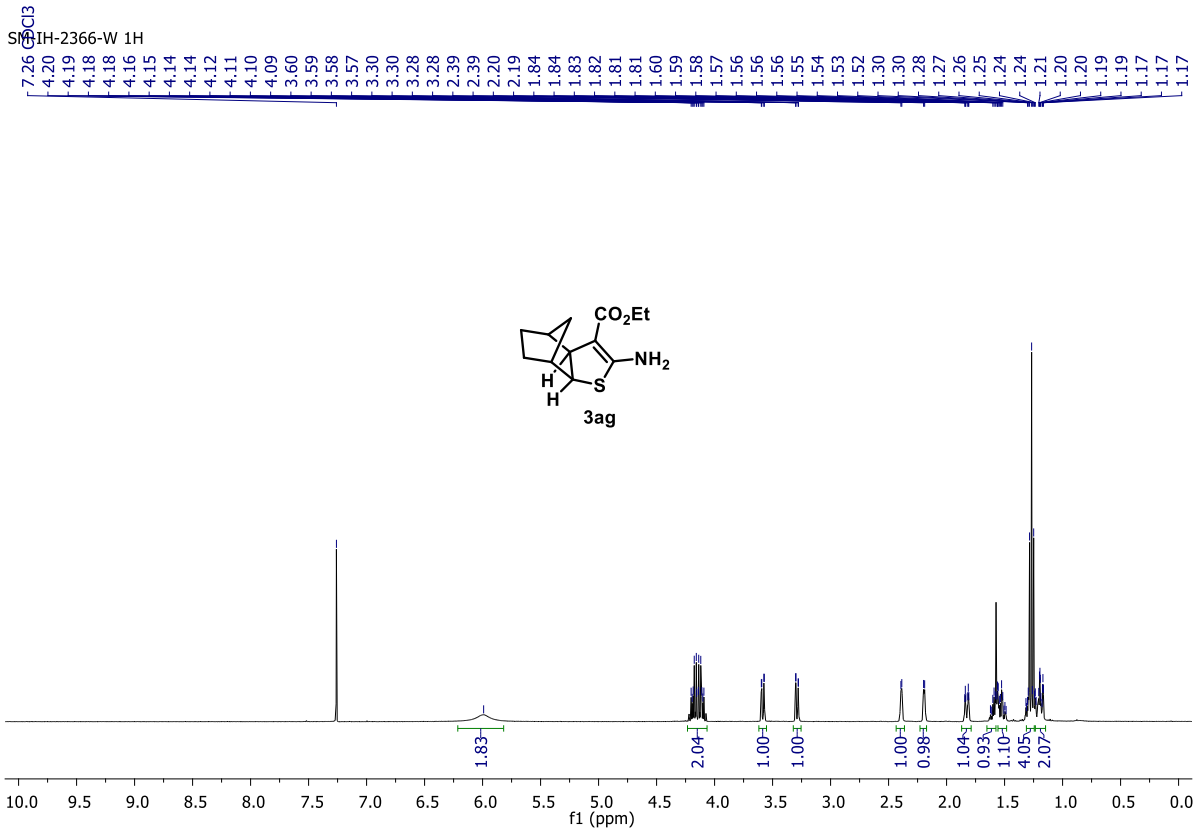
^{1}H NMR of **3af** (400 MHz, $CDCl_3$):



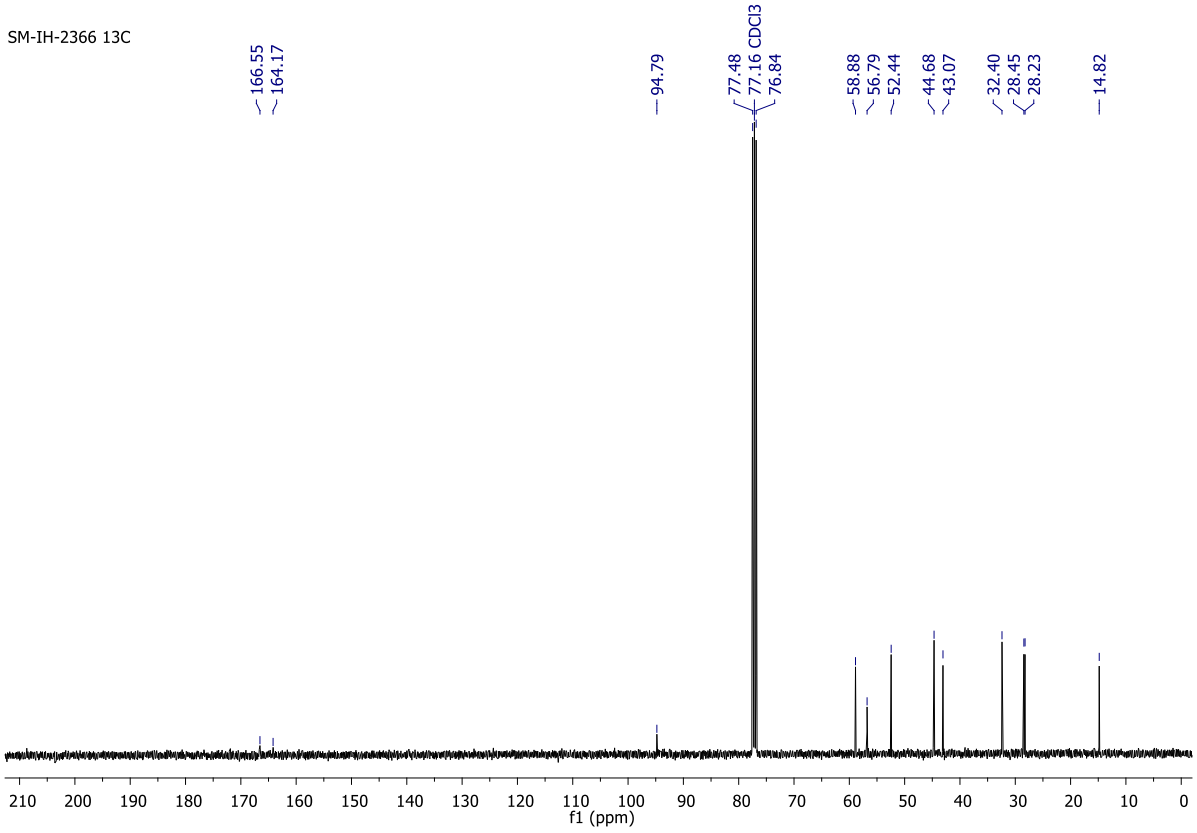
^{13}C{^{1}H} NMR of **3af** (101 MHz, $CDCl_3$):



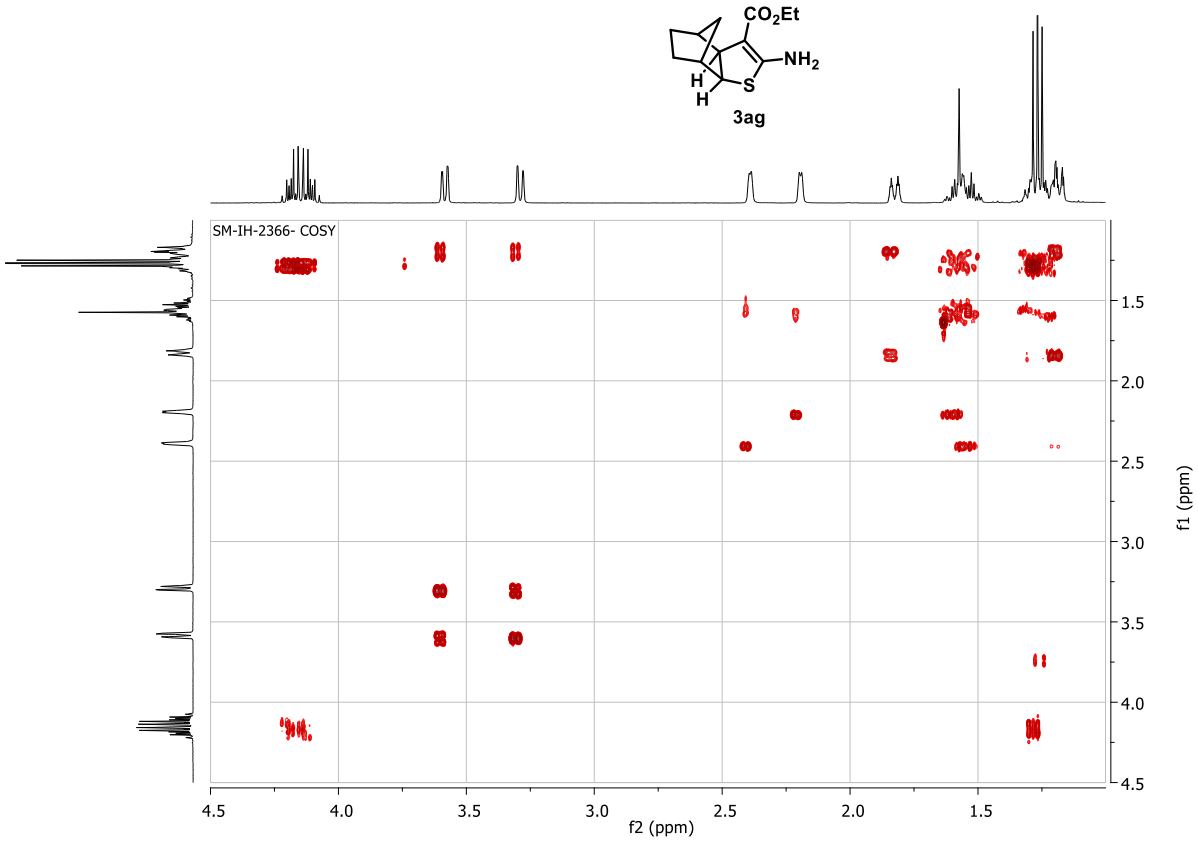
^{1}H NMR of **3ag** (400 MHz, $CDCl_3$):



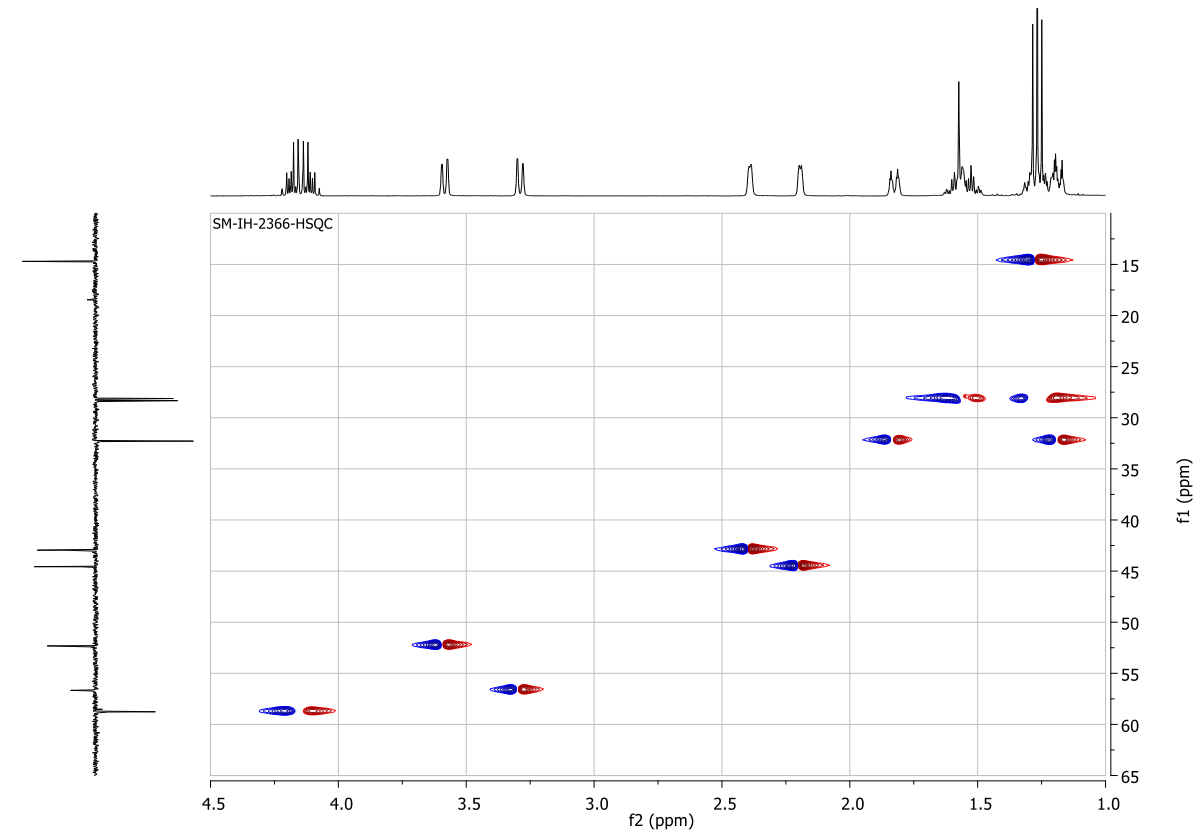
^{13}C{^{1}H} NMR of **3ag** (101 MHz, $CDCl_3$):



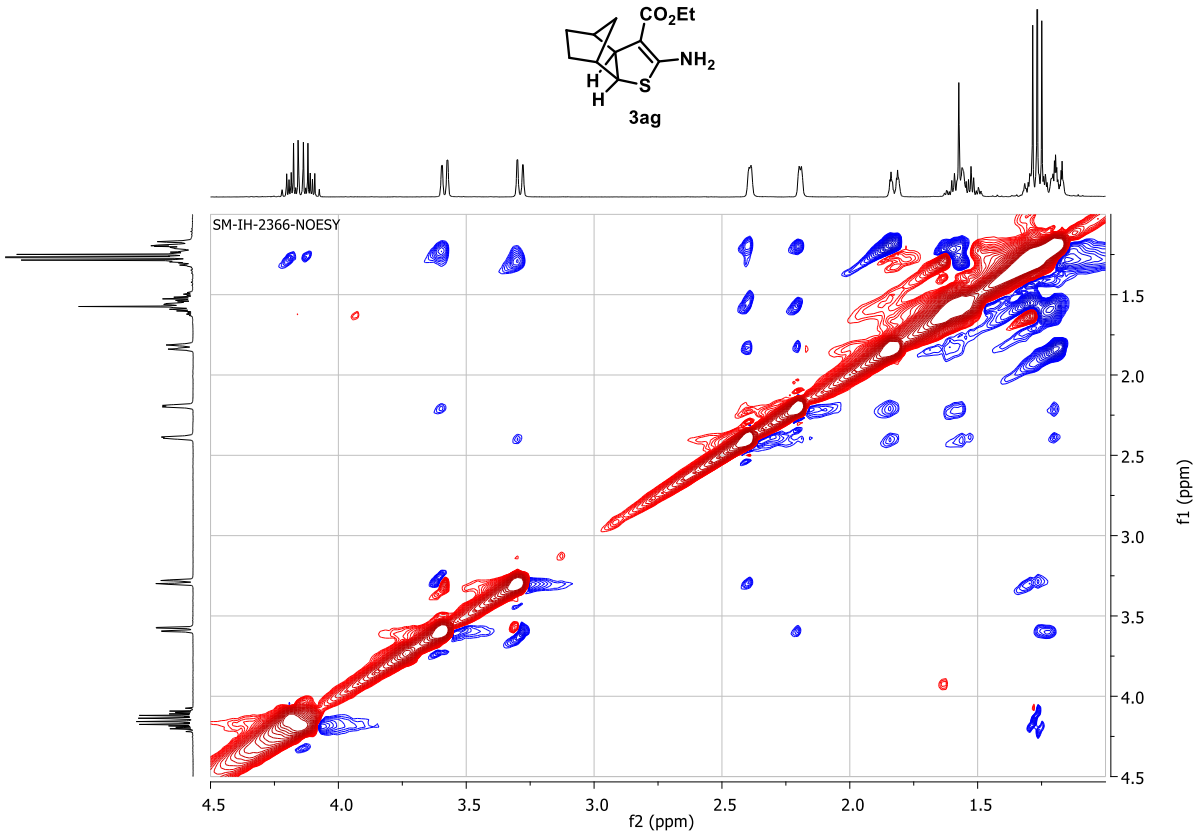
^{1}H-^{1}H COSY NMR of **3ag**:



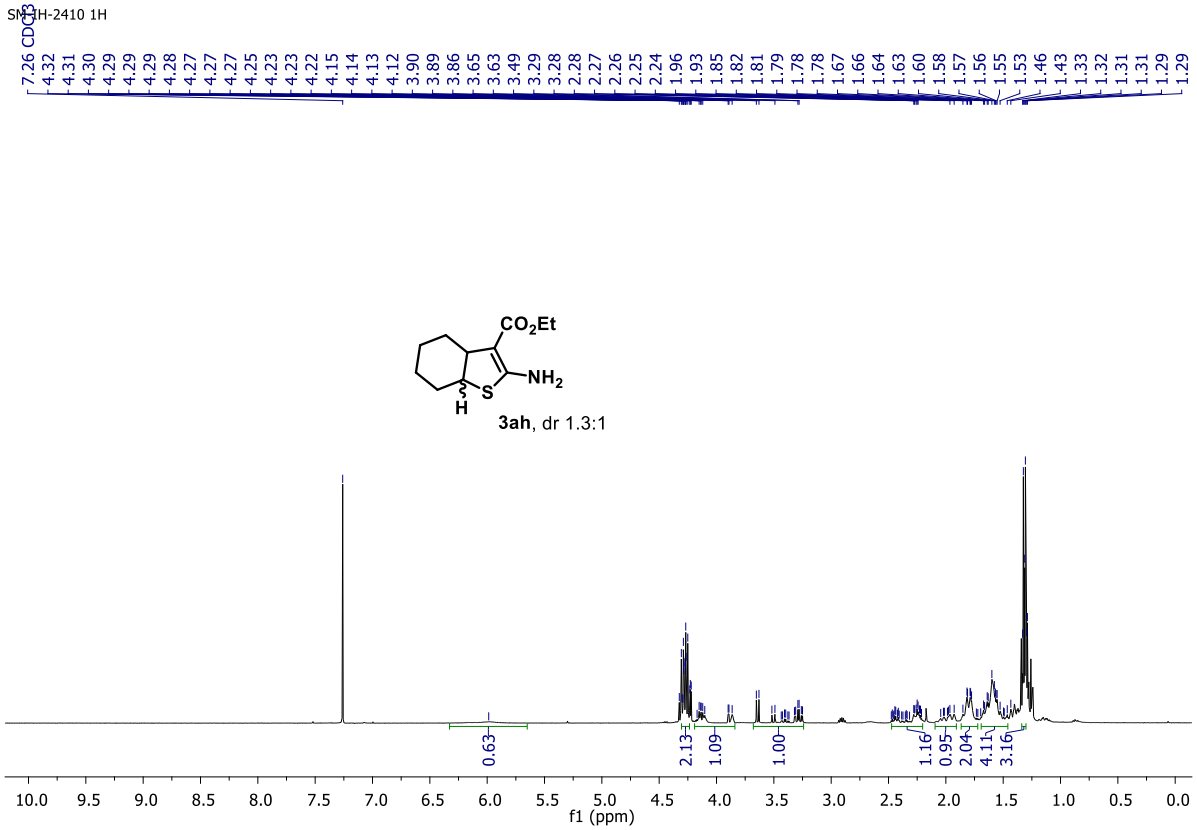
^{1}H-^{13}C HSQC NMR of **3ag**:



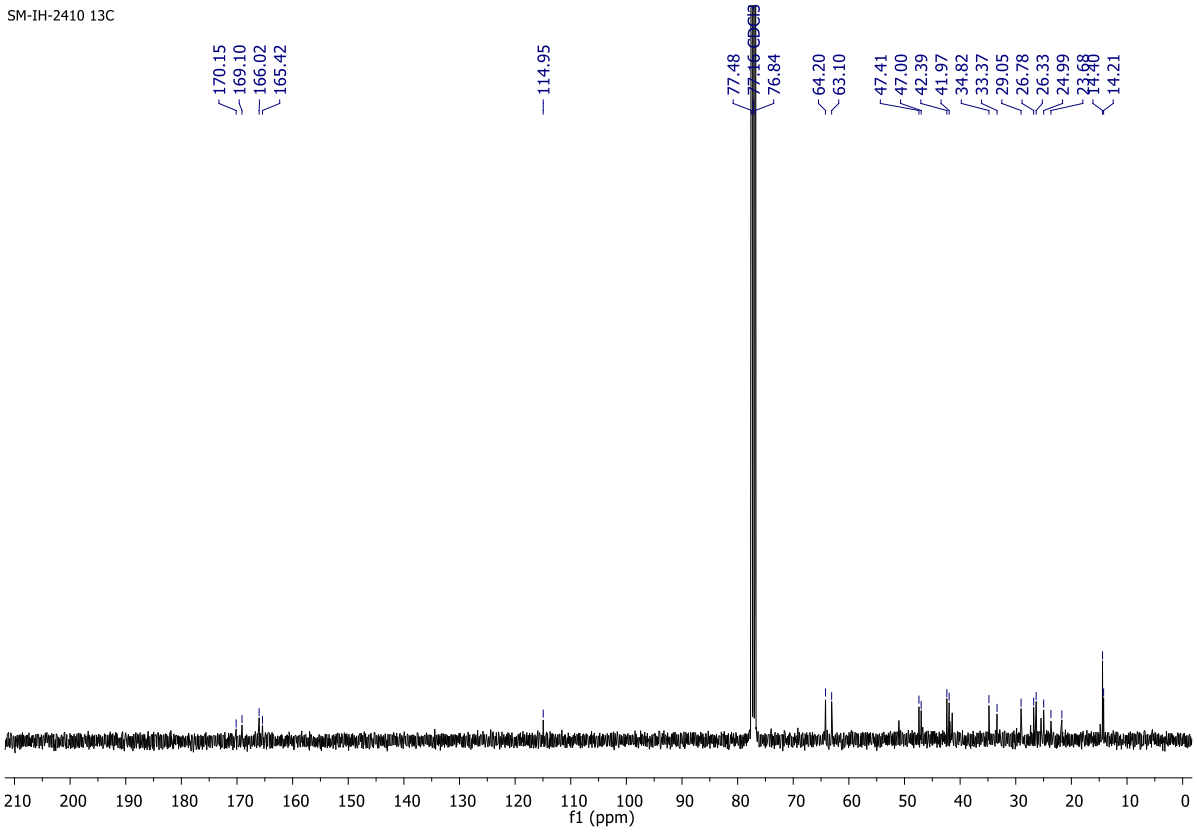
^{1}H-^{1}H NOESY NMR of **3ag**:



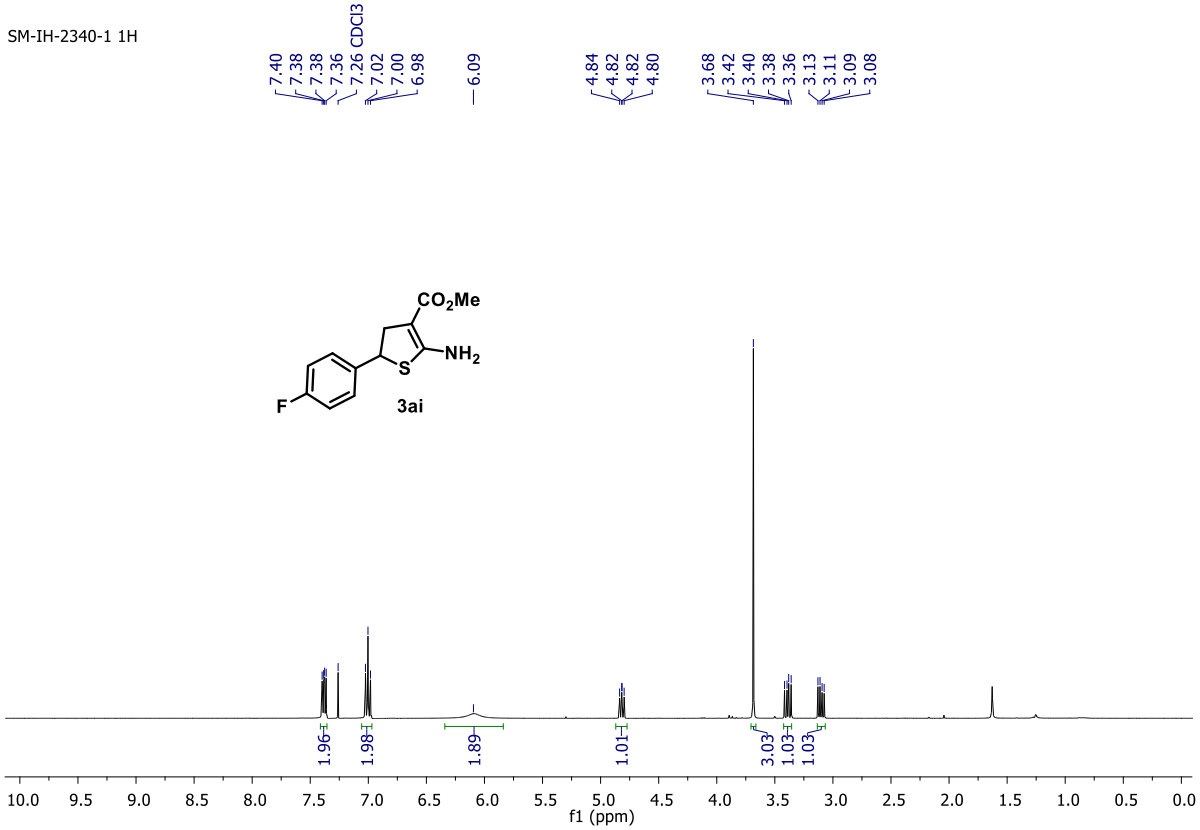
^{1}H NMR of **3ah** (400 MHz, $CDCl_3$):



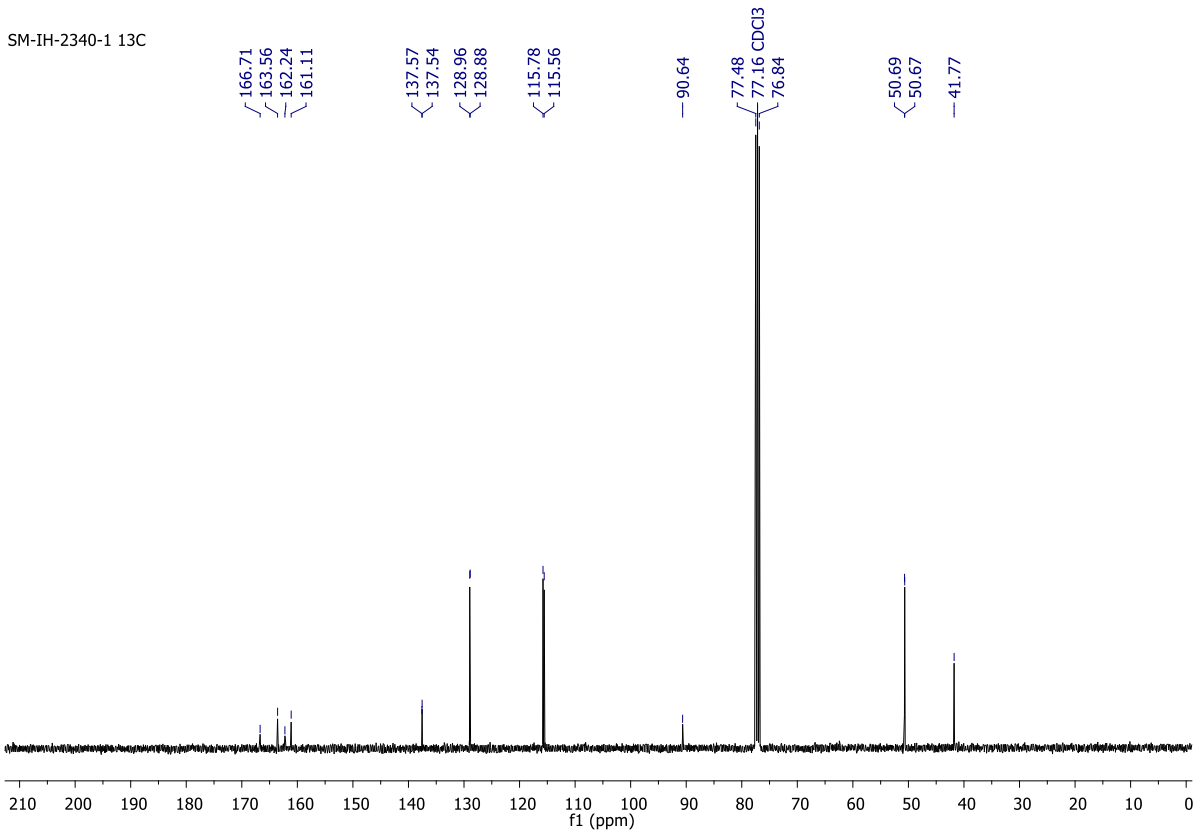
^{13}C{^{1}H} NMR of **3ah** (101 MHz, $CDCl_3$):



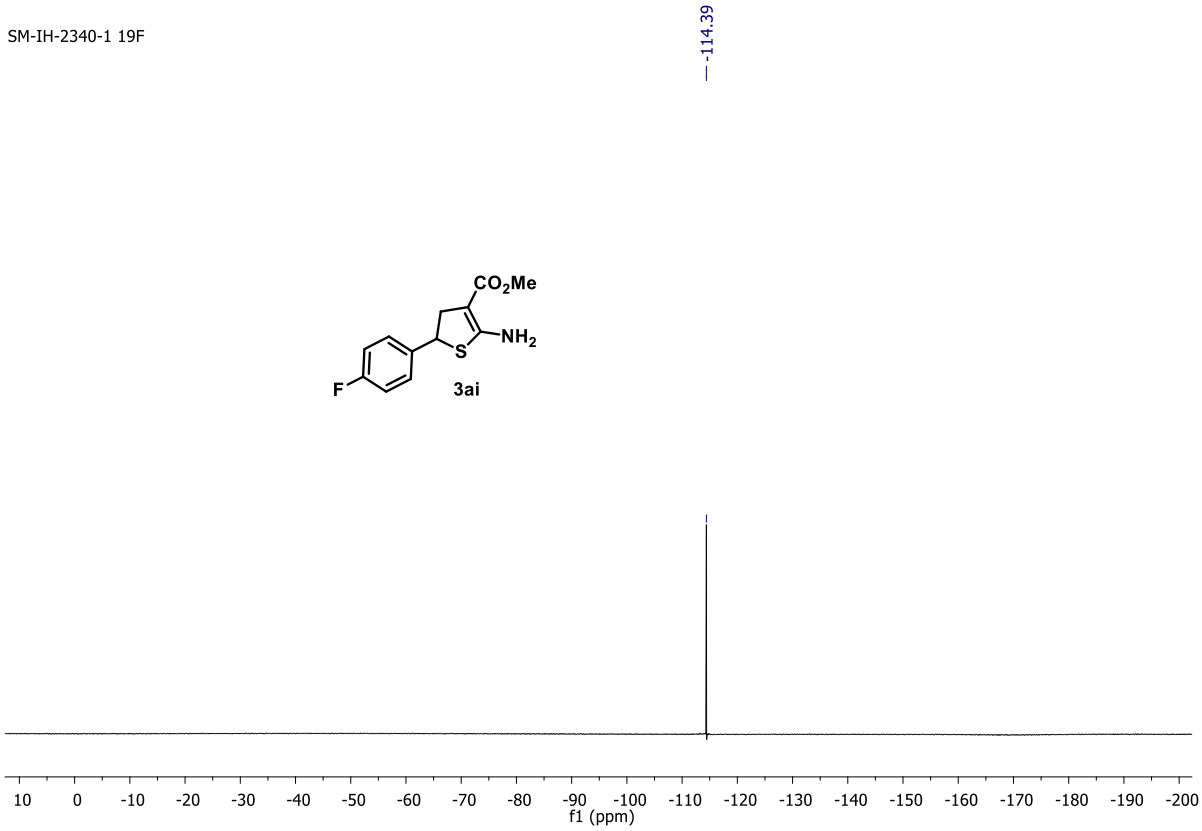
^{1}H NMR of **3ai** (400 MHz, $CDCl_3$):



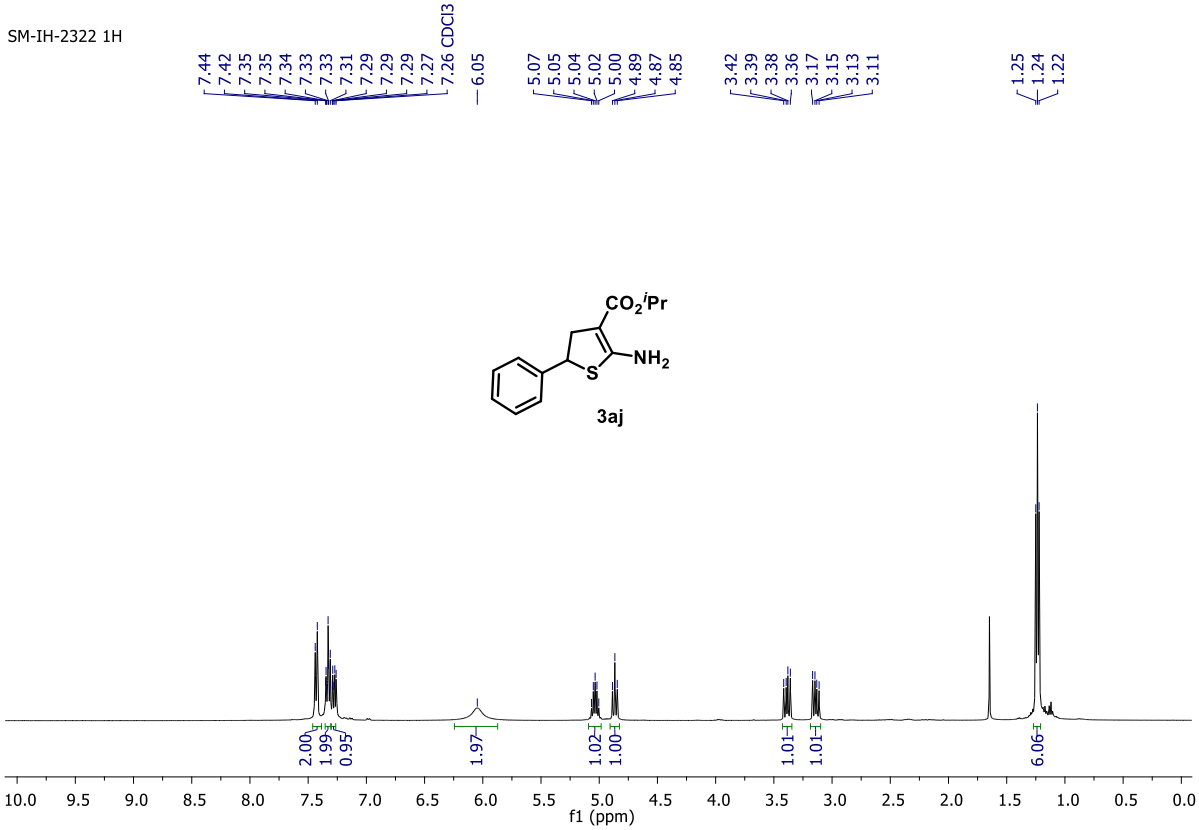
^{13}C{^{1}H} NMR of **3ai** (101 MHz, $CDCl_3$):



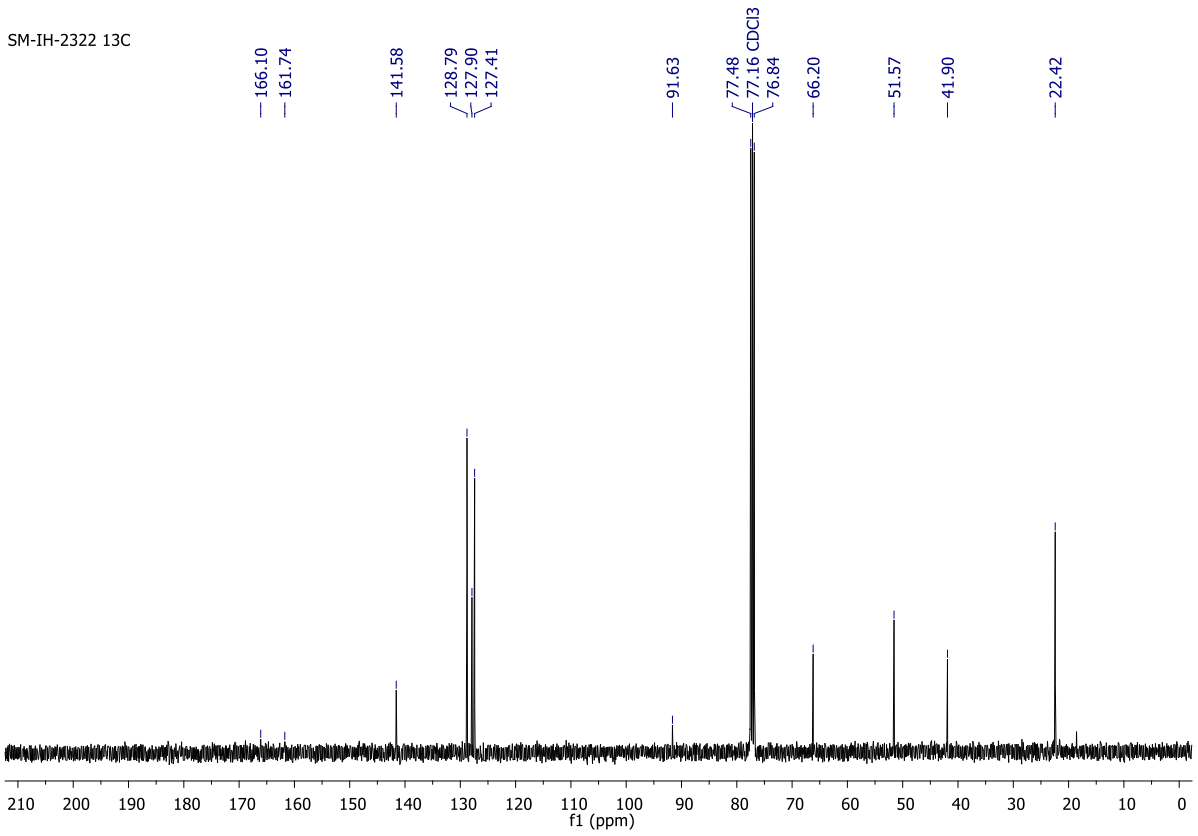
^{19}F NMR of **3ai** (377 MHz, $CDCl_3$):



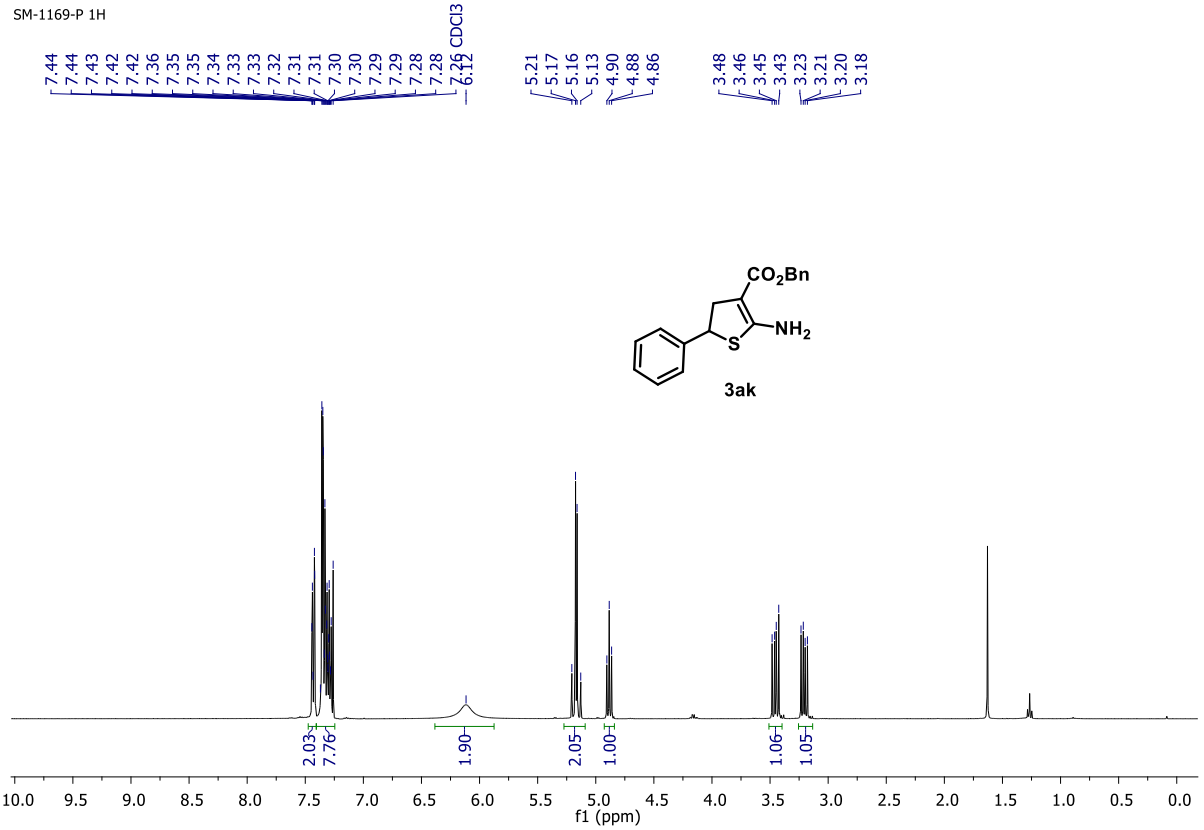
^{1}H NMR of **3aj** (400 MHz, $CDCl_3$):



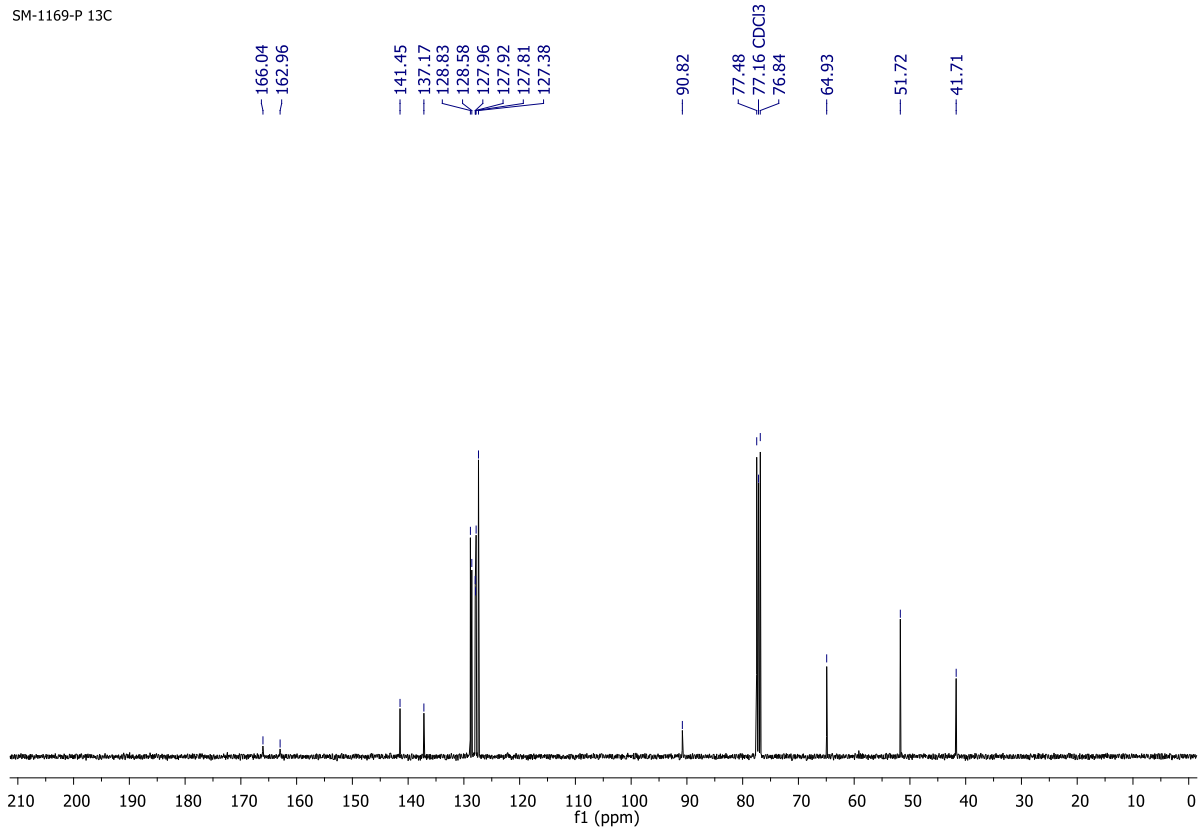
^{13}C{^{1}H} NMR of **3aj** (101 MHz, $CDCl_3$):



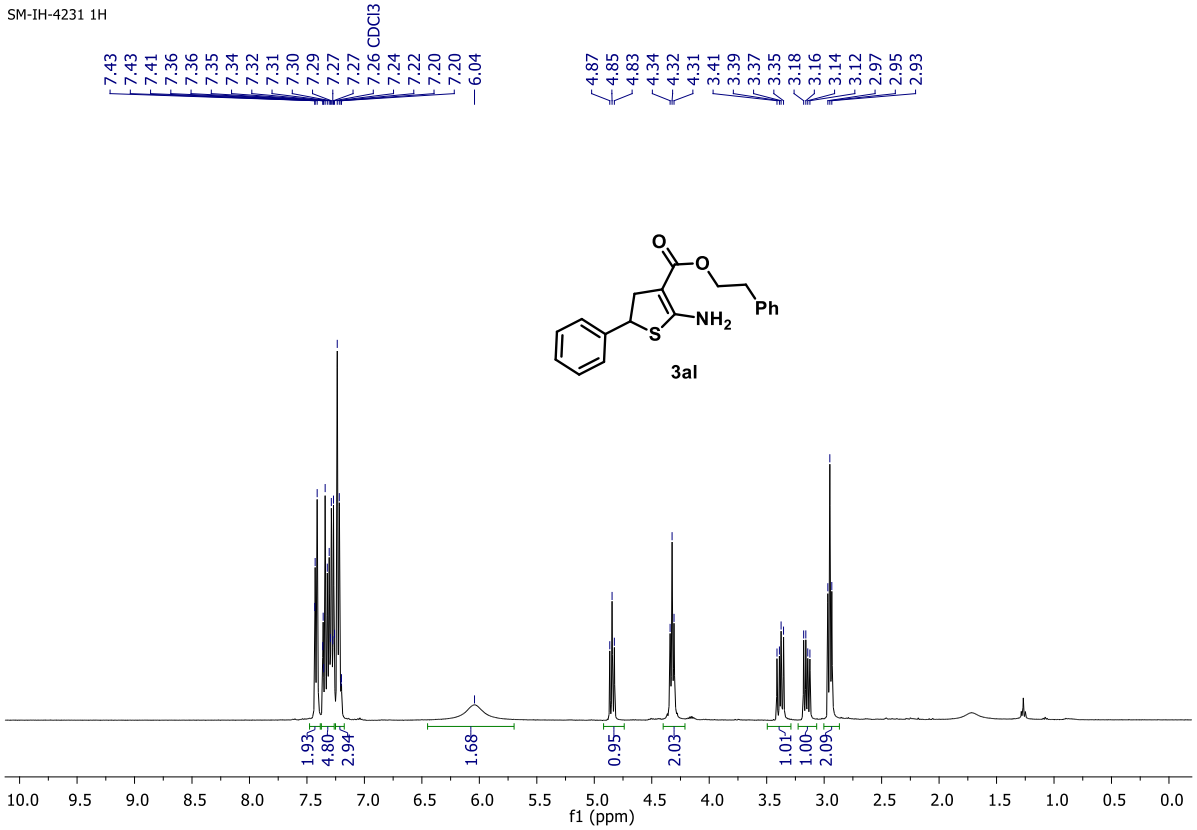
^{1}H NMR of **3ak** (400 MHz, $CDCl_3$):



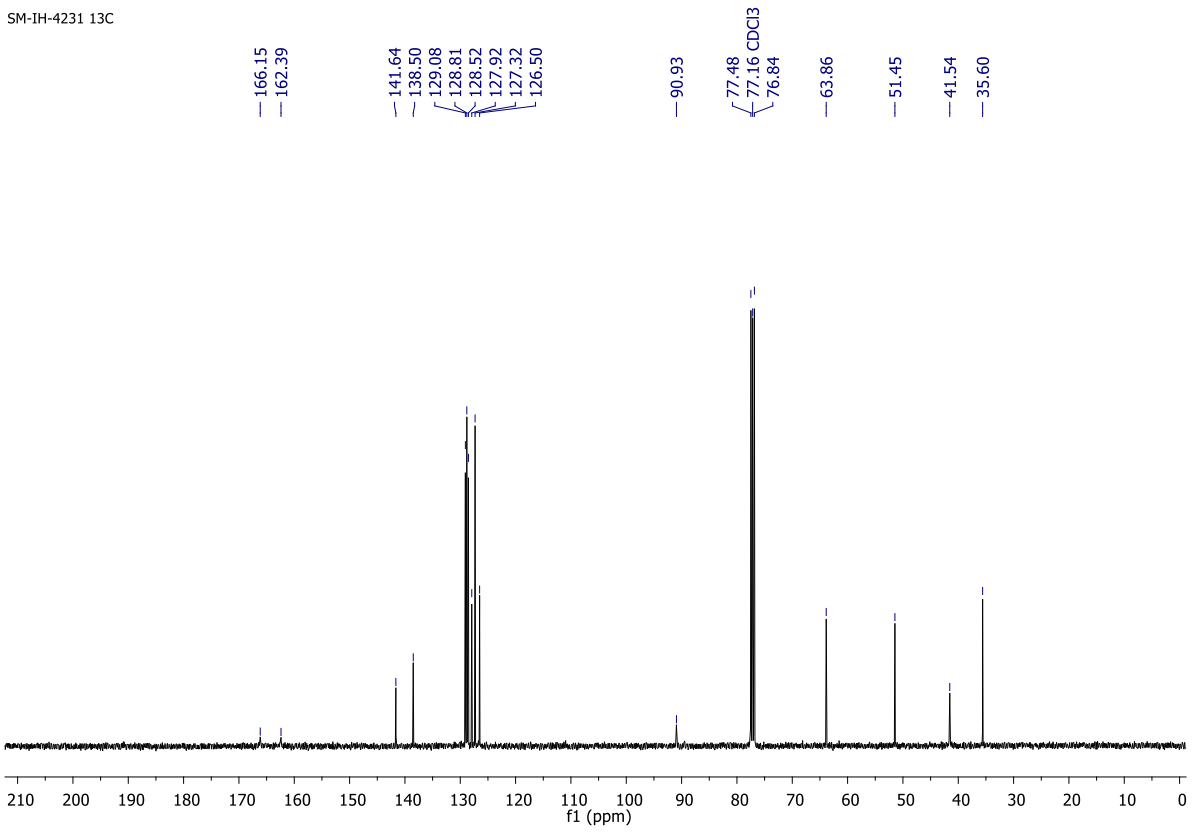
^{13}C{^{1}H} NMR of **3ak** (101 MHz, $CDCl_3$):



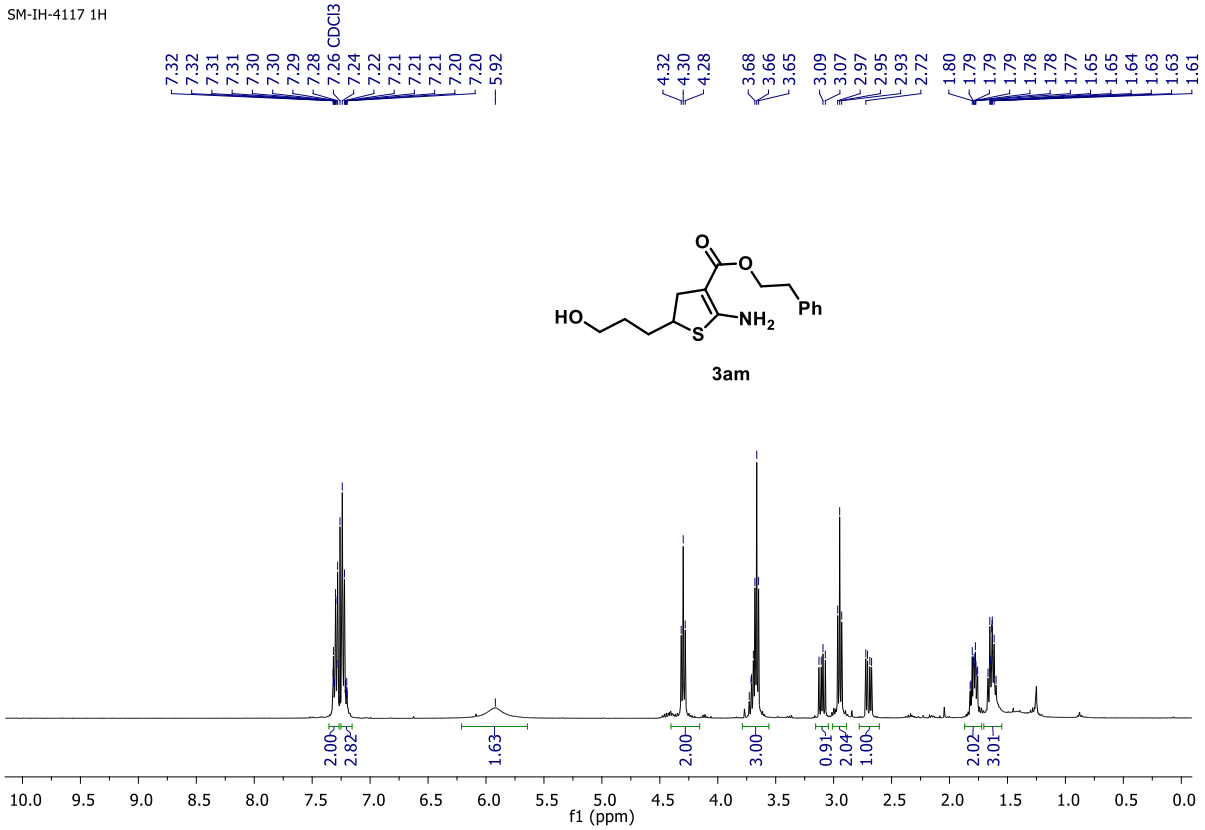
^{1}H NMR of **3al** (400 MHz, $CDCl_3$):



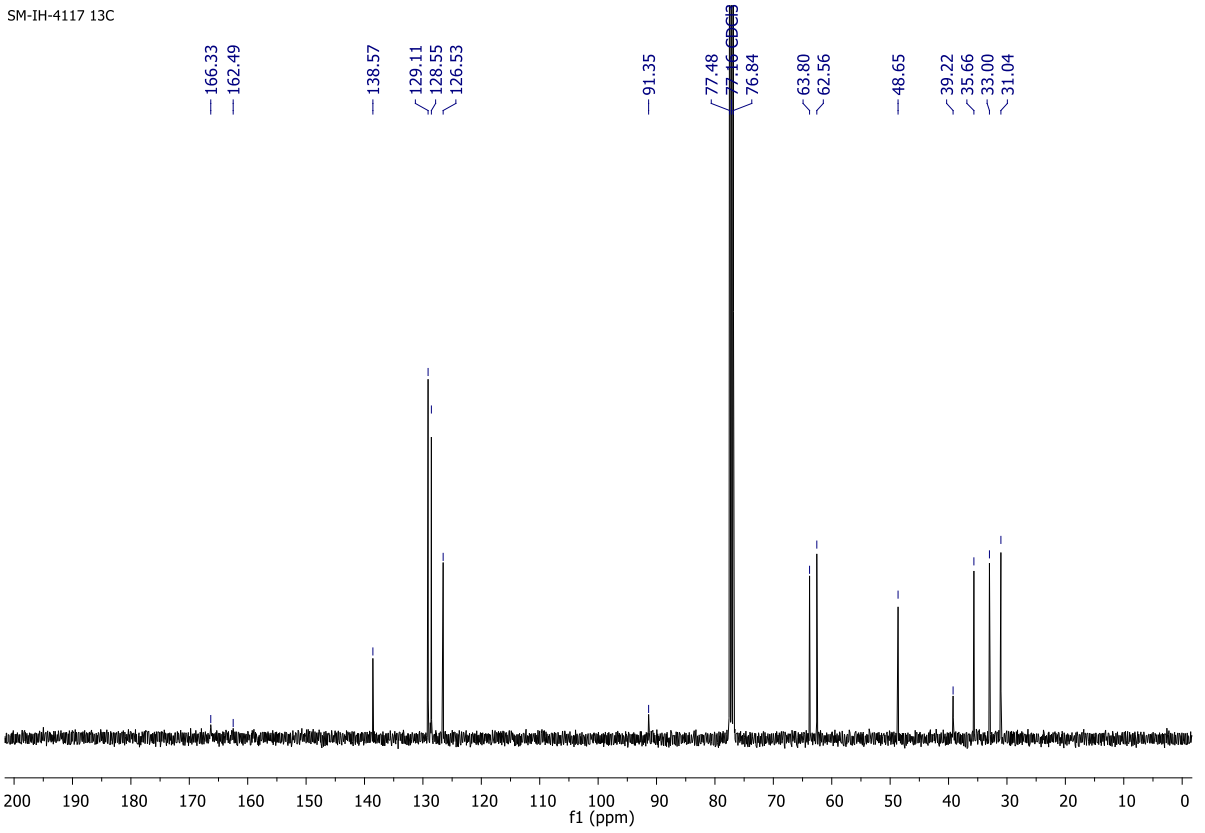
^{13}C{^{1}H} NMR of **3al** (101 MHz, $CDCl_3$):



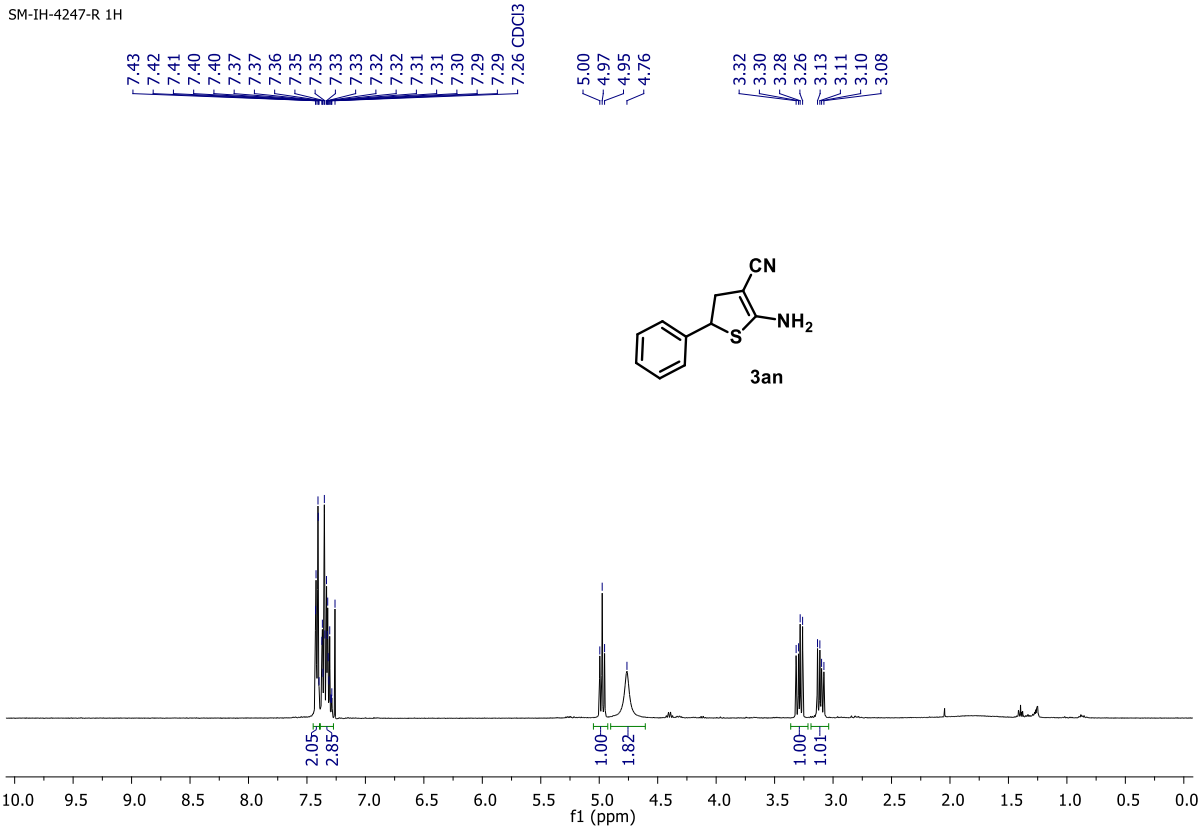
^{1}H NMR of **3am** (400 MHz, $CDCl_3$):



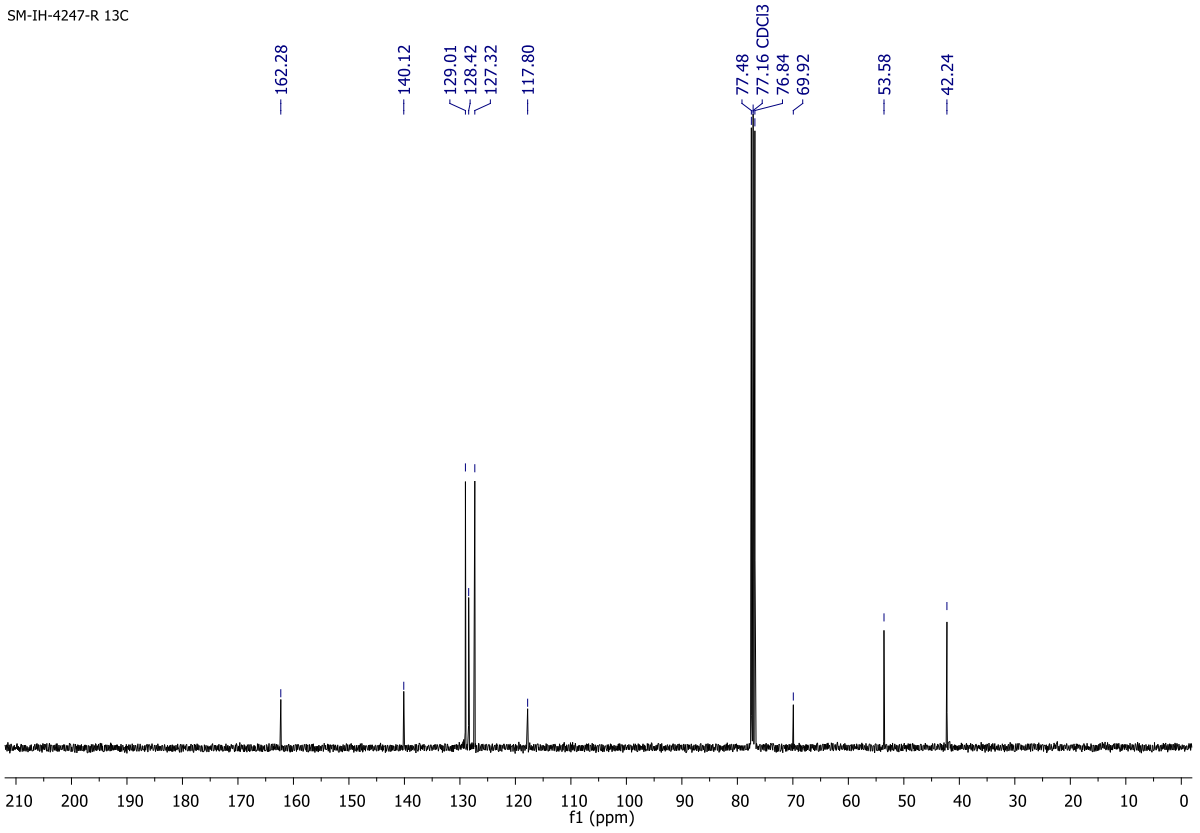
^{13}C{^{1}H} NMR of **3am** (101 MHz, $CDCl_3$):



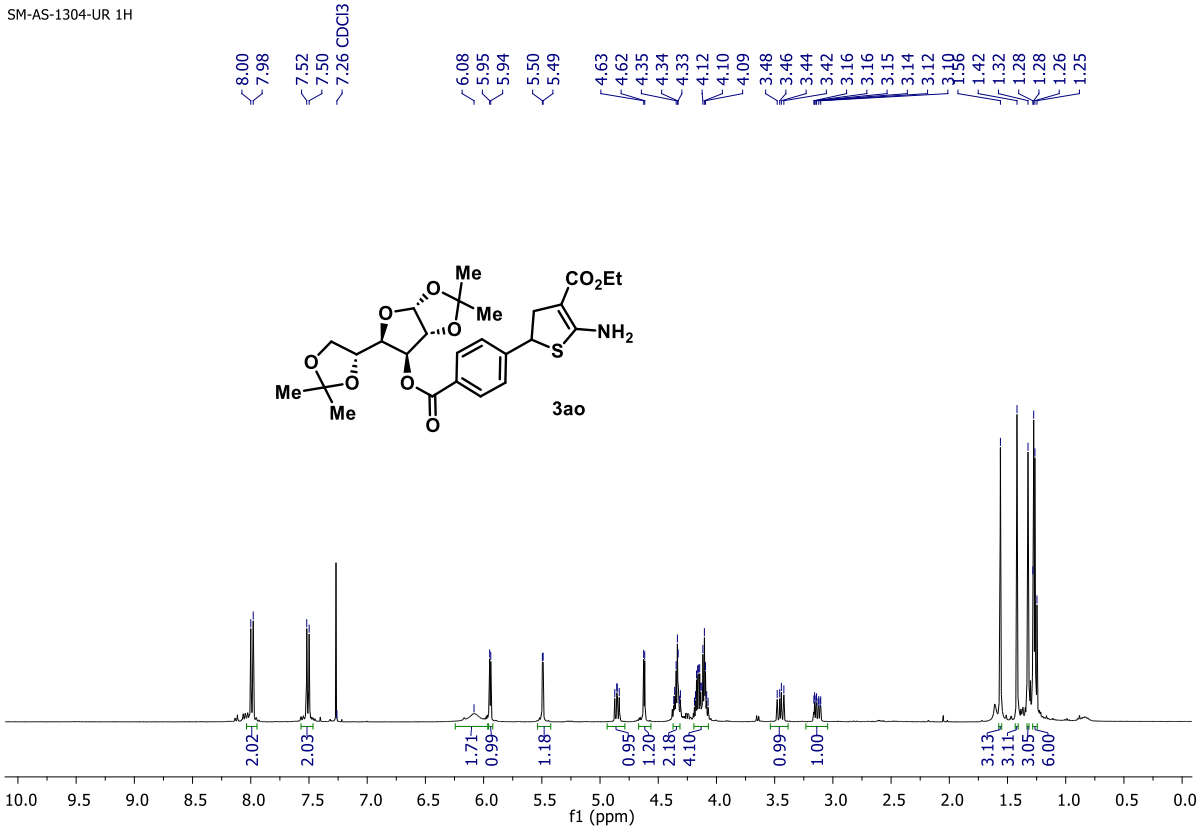
^{1}H NMR of **3an** (400 MHz, $CDCl_3$):



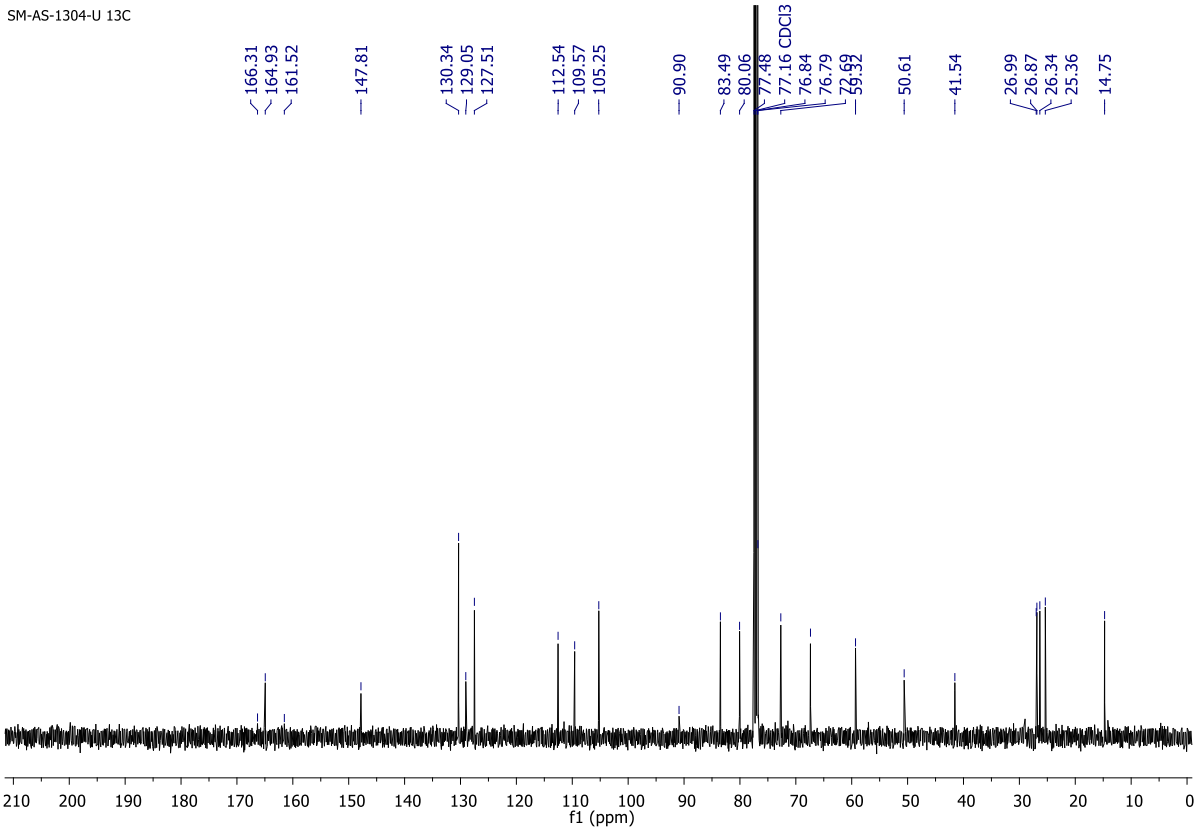
^{13}C{^{1}H} NMR of **3an** (101 MHz, $CDCl_3$):



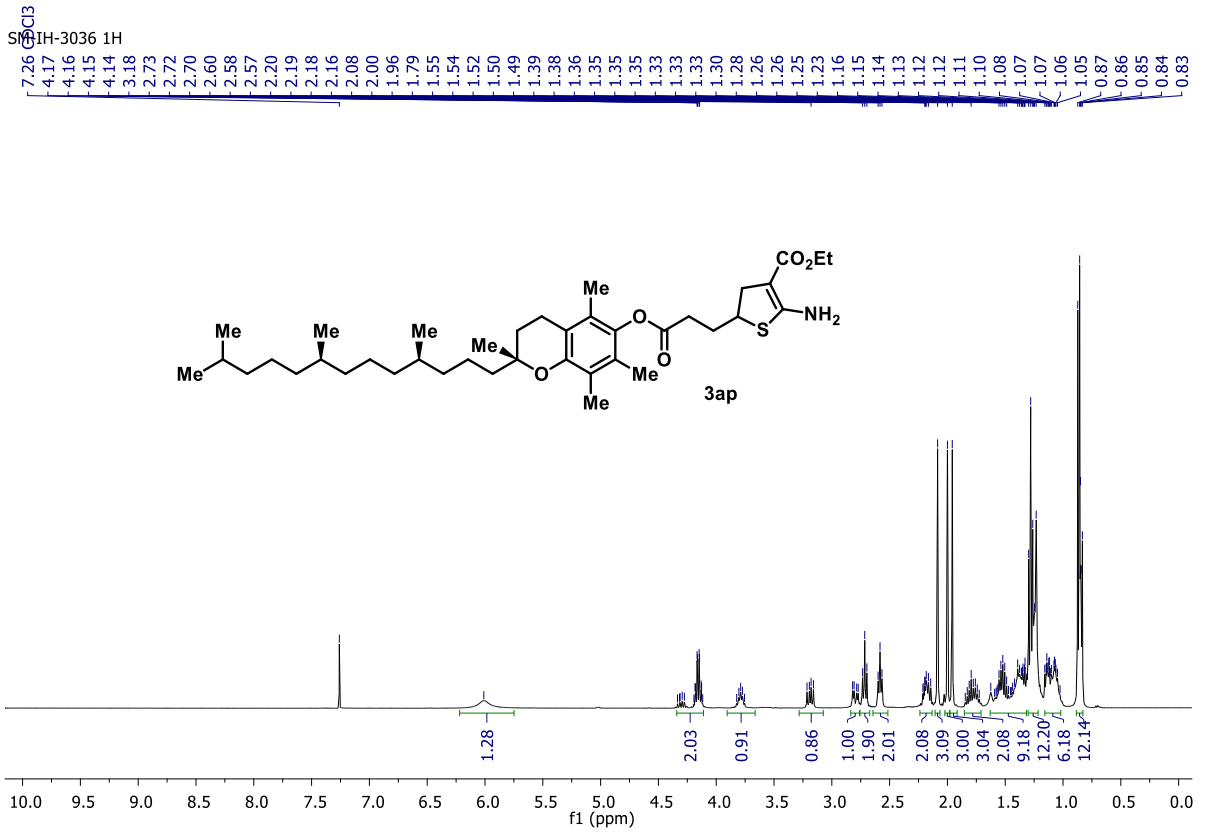
^{1}H NMR of **3ao** (400 MHz, $CDCl_3$):



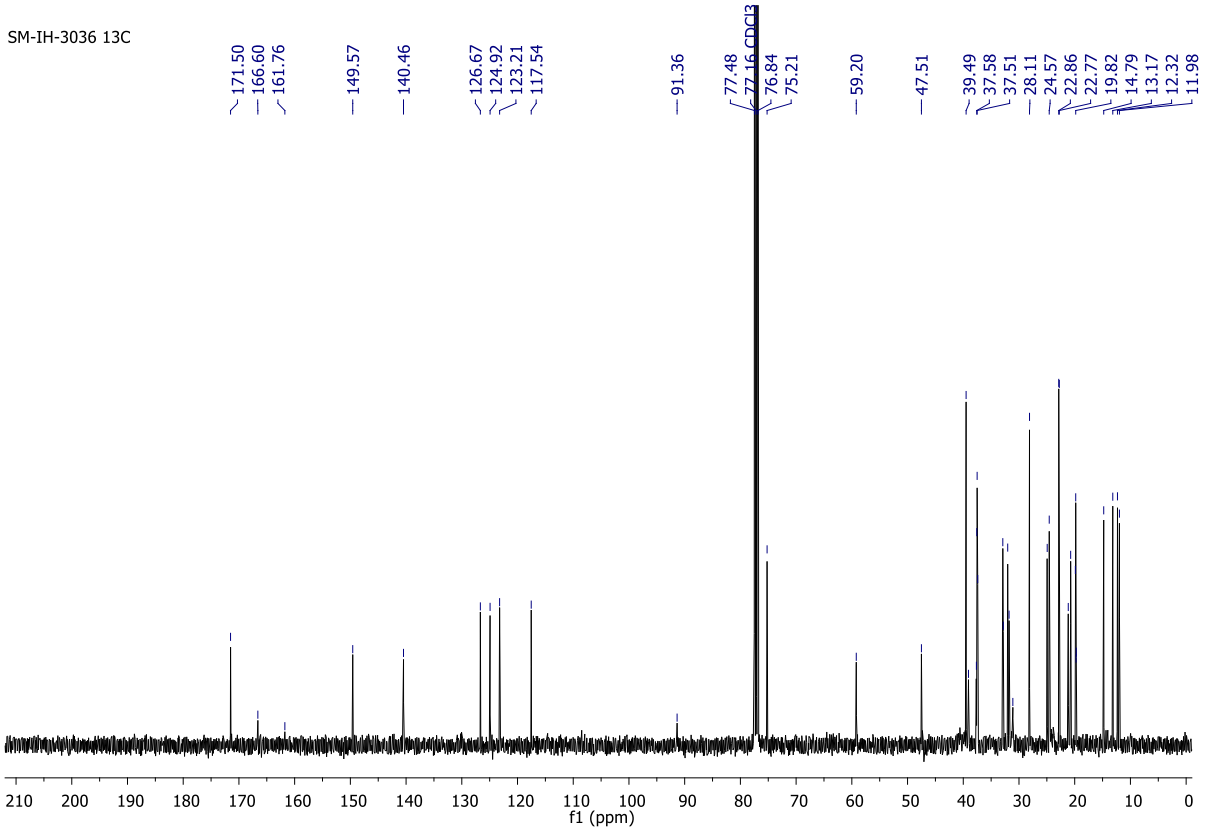
^{13}C{^{1}H} NMR of **3ao** (101 MHz, $CDCl_3$):



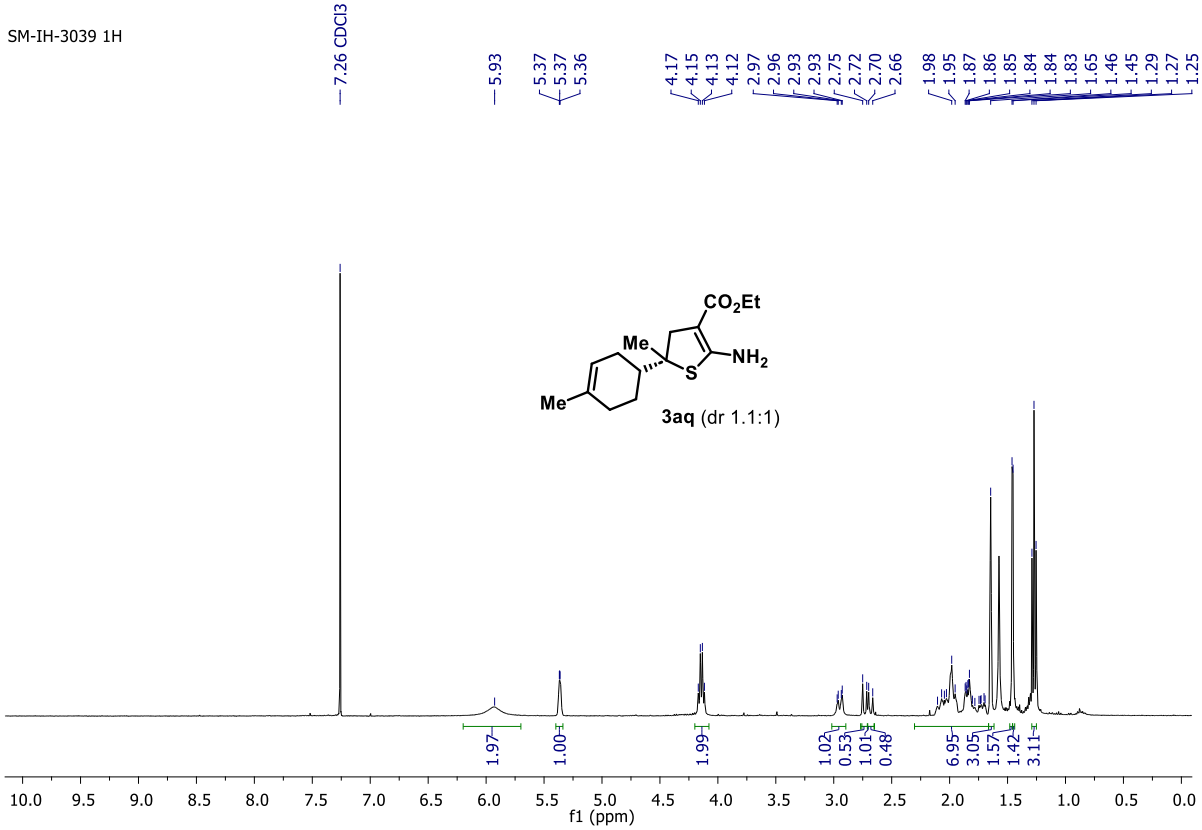
^{1}H NMR of **3ap** (400 MHz, $CDCl_3$):



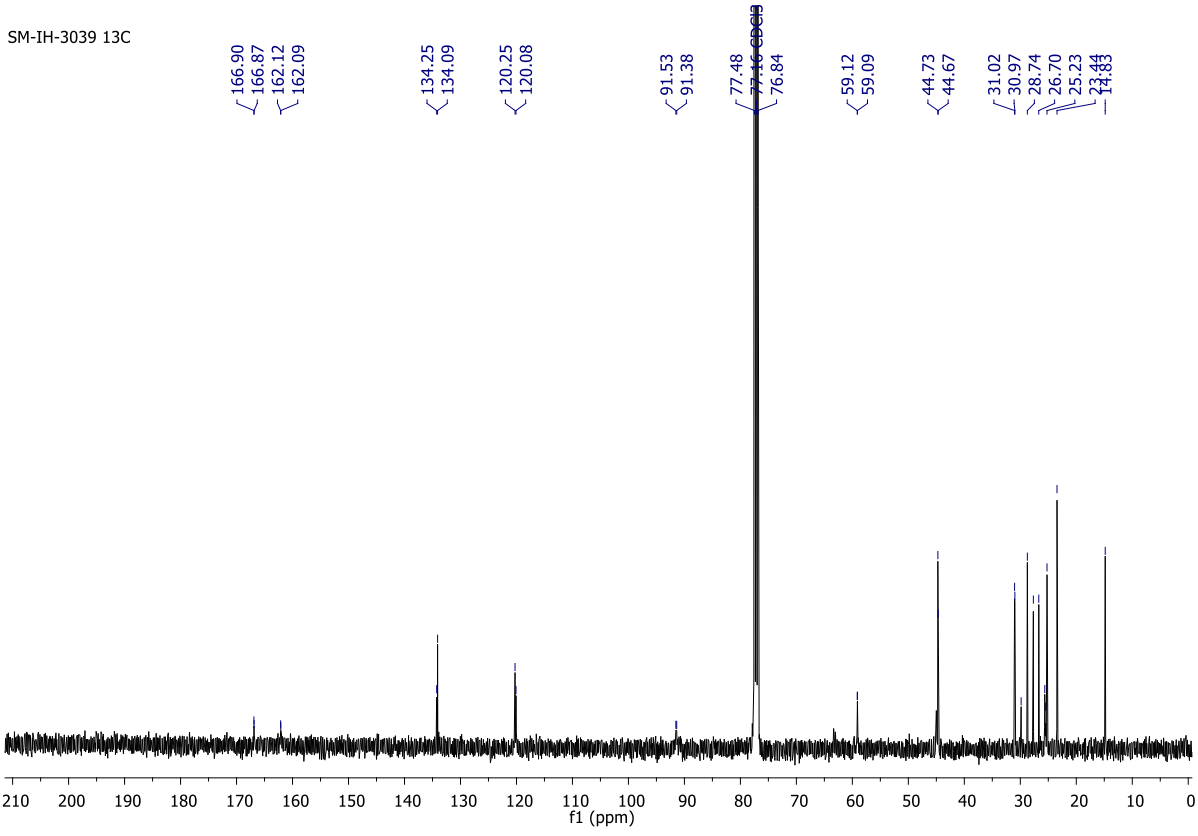
^{13}C{^{1}H} NMR of **3ap** (101 MHz, $CDCl_3$):



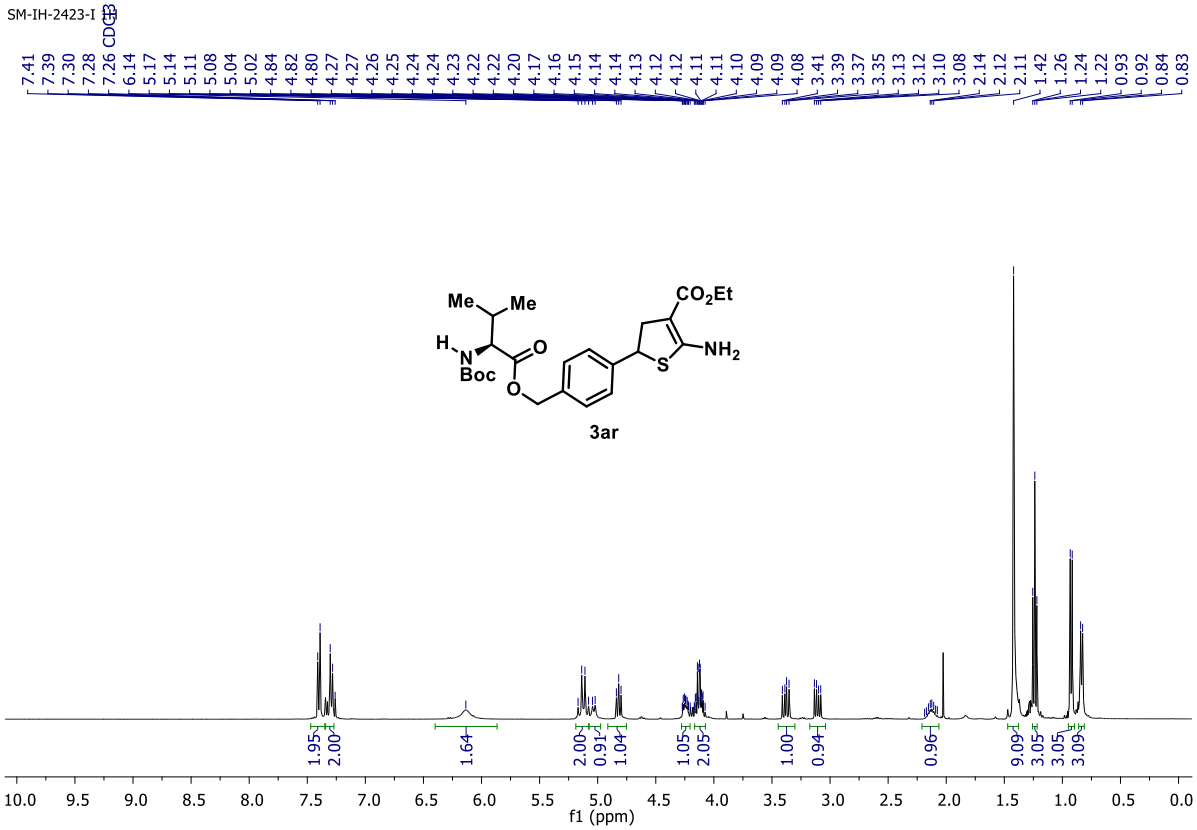
^{1}H NMR of **3aq** (400 MHz, $CDCl_3$):



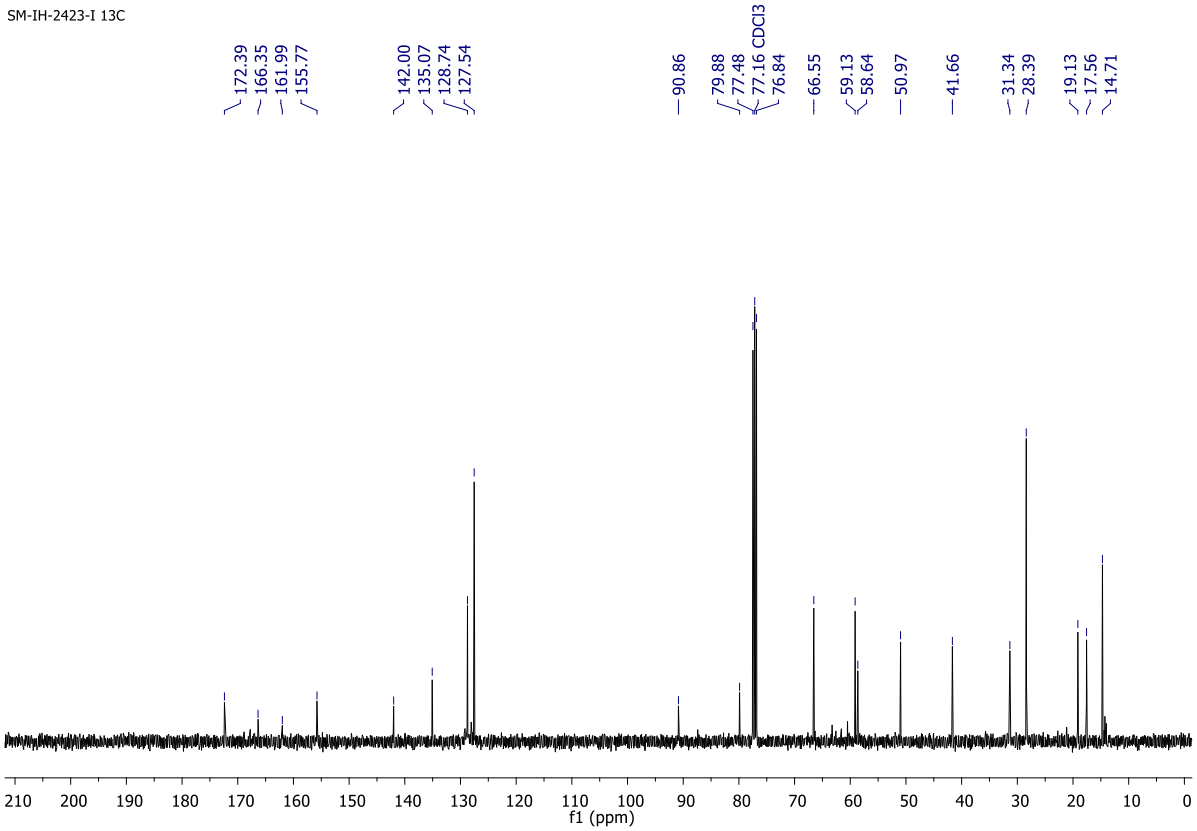
^{13}C{^{1}H} NMR of **3aq** (101 MHz, $CDCl_3$):



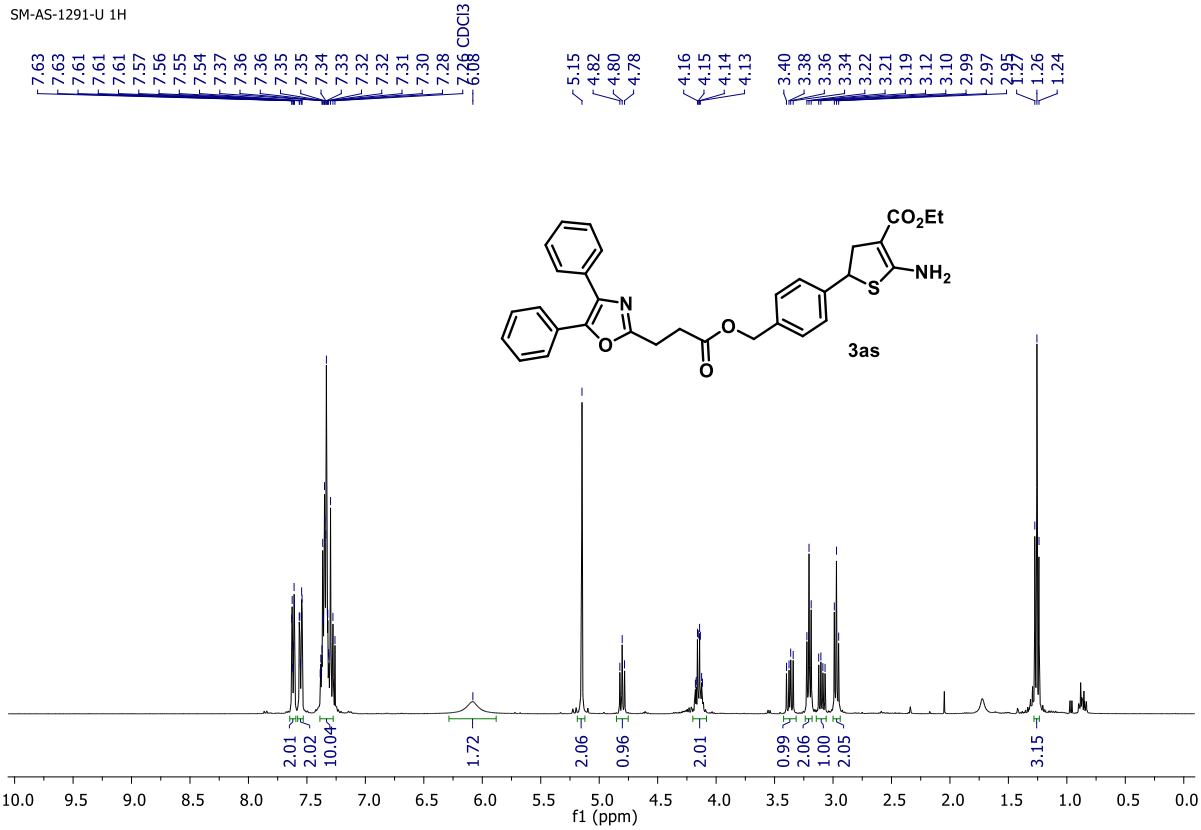
^{1}H NMR of **3ar** (400 MHz, $CDCl_3$):



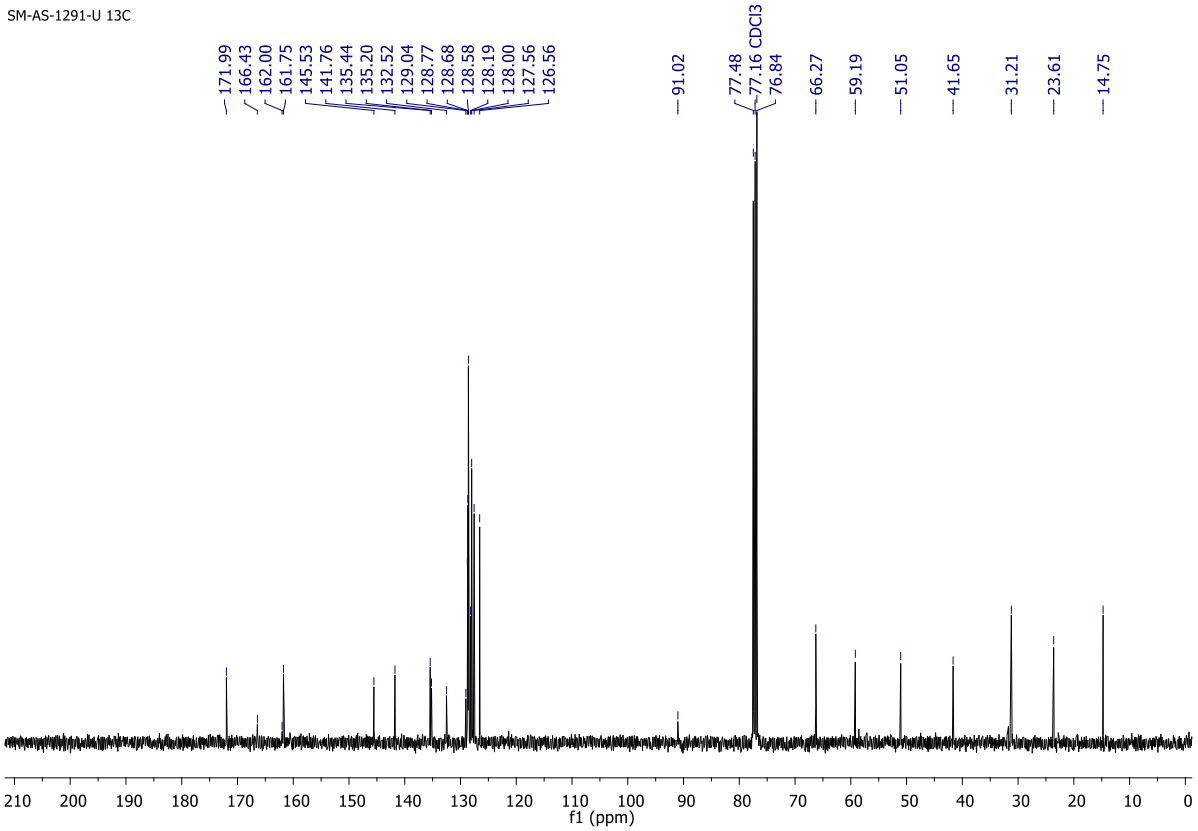
^{13}C{^{1}H} NMR of **3ar** (101 MHz, $CDCl_3$):



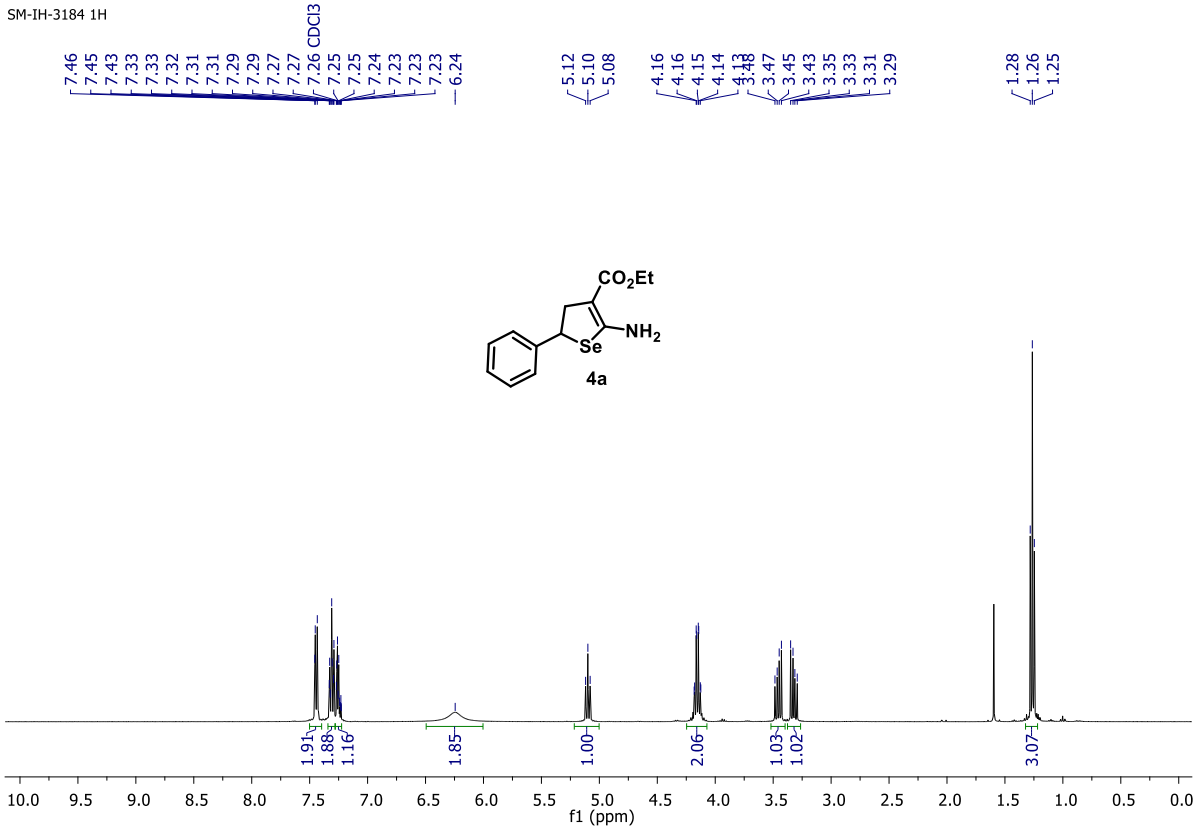
^{1}H NMR of **3as** (400 MHz, $CDCl_3$):



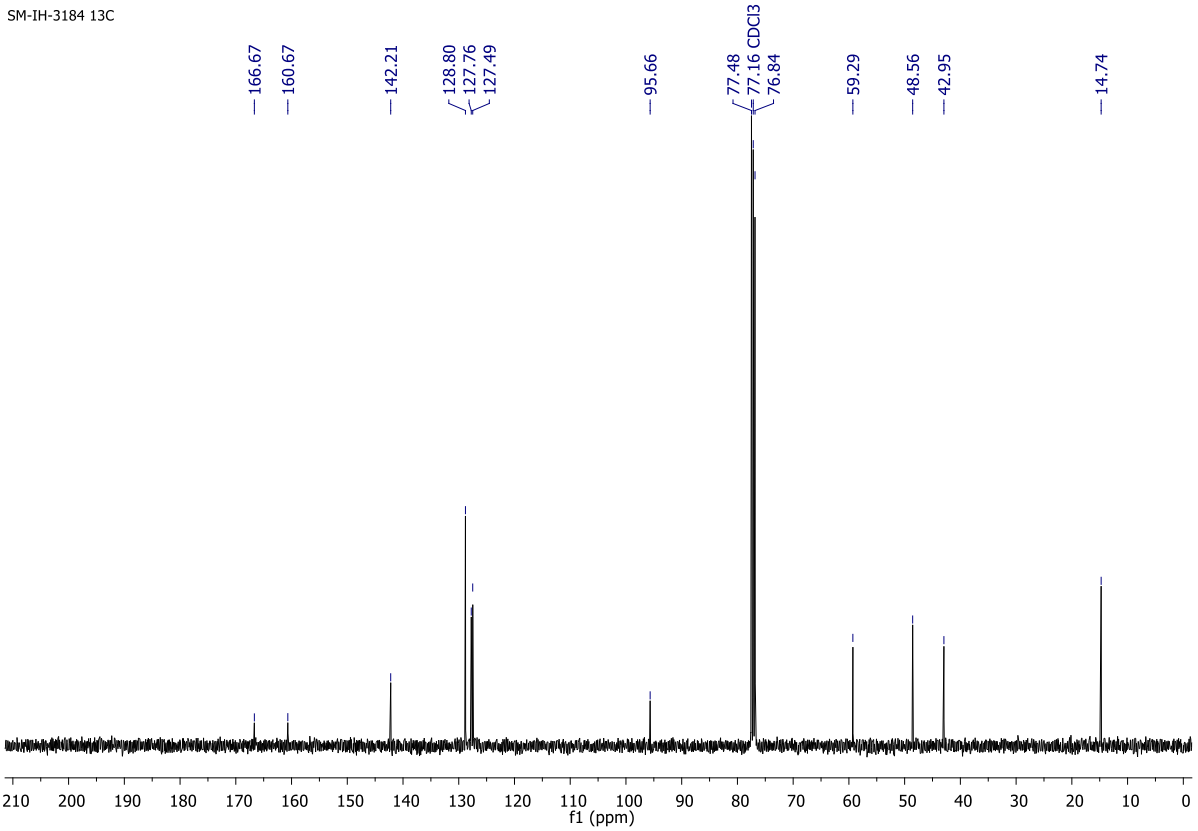
^{13}C{^{1}H} NMR of **3as** (101 MHz, $CDCl_3$):



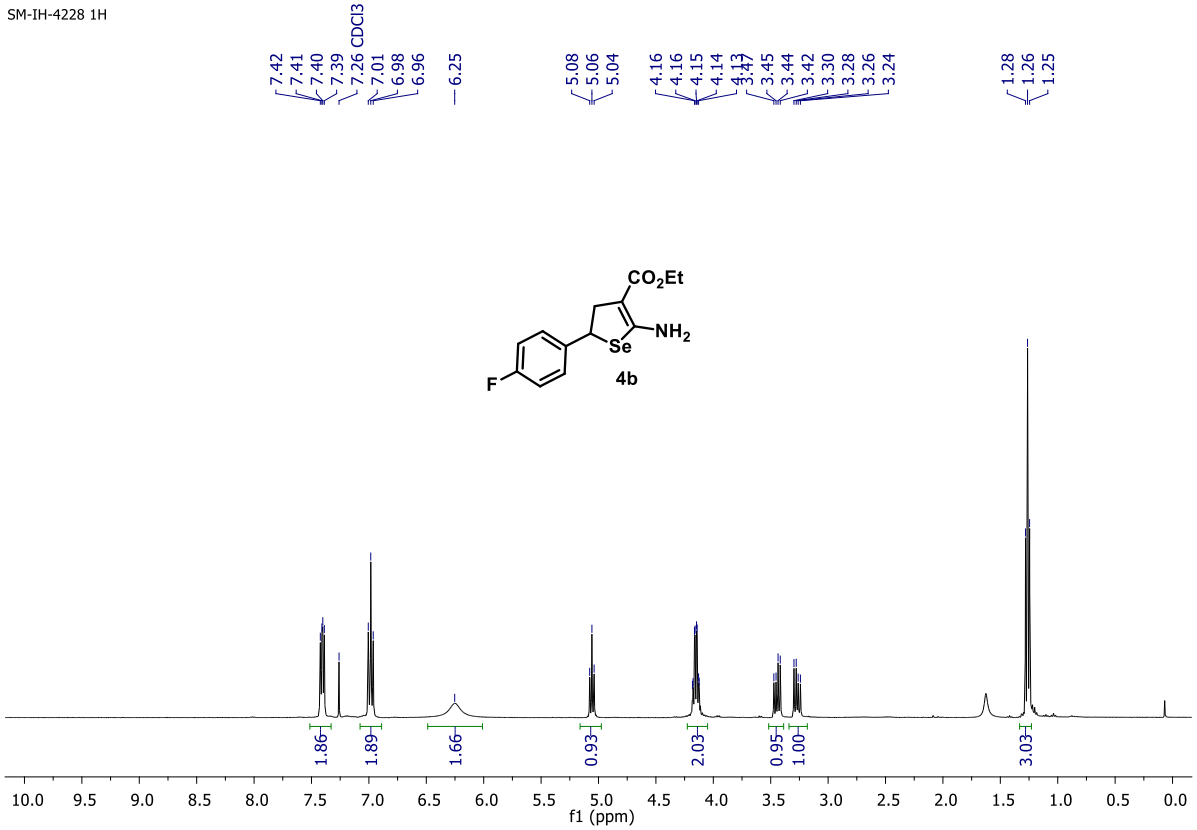
^{1}H NMR of **4a** (400 MHz, $CDCl_3$):



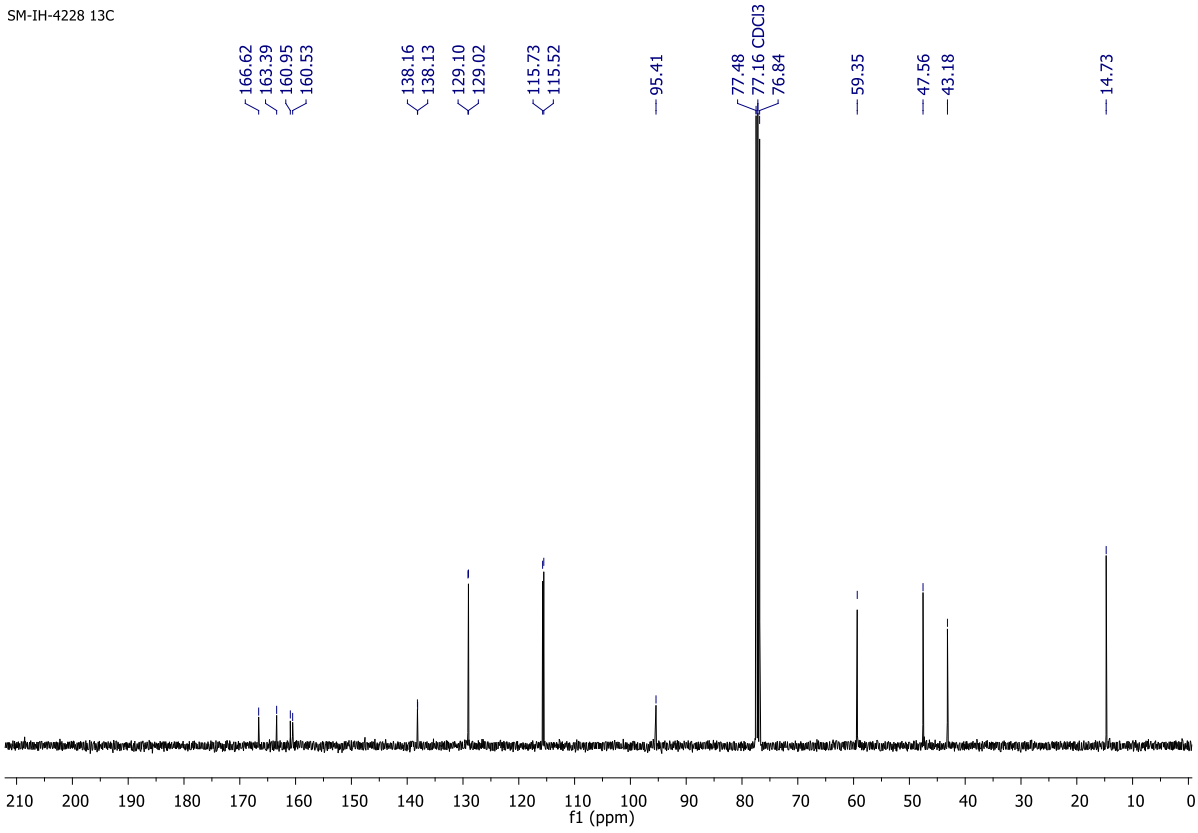
^{13}C{^{1}H} NMR of **4a** (101 MHz, $CDCl_3$):



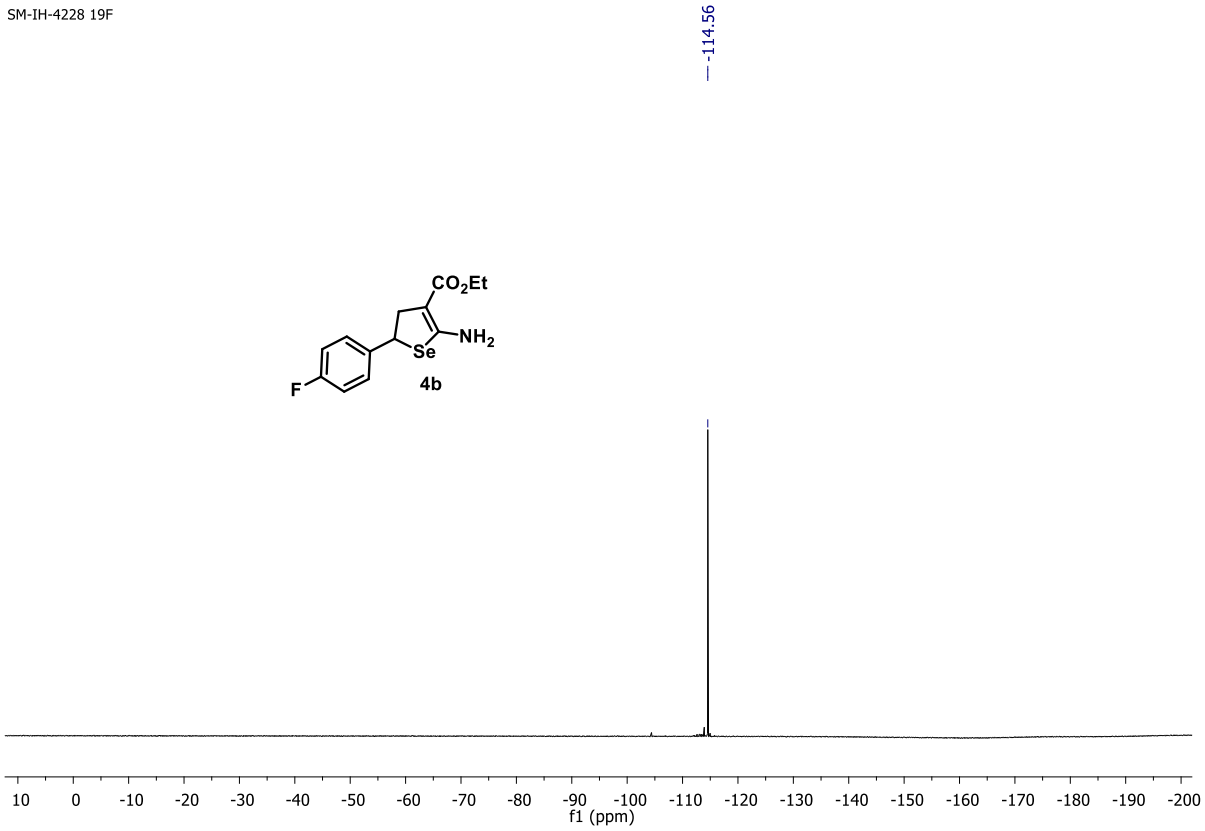
^{1}H NMR of **4b** (400 MHz, $CDCl_3$):



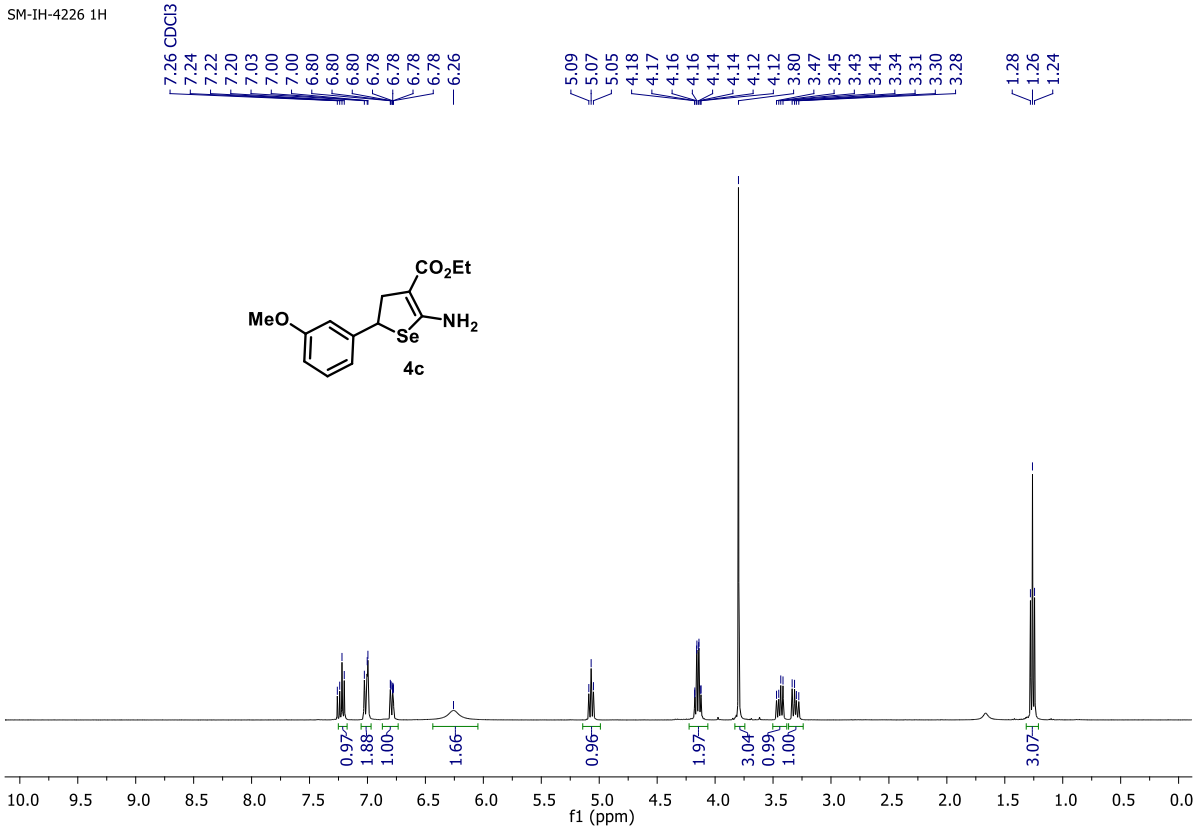
^{13}C{^{1}H} NMR of **4b** (101 MHz, $CDCl_3$):



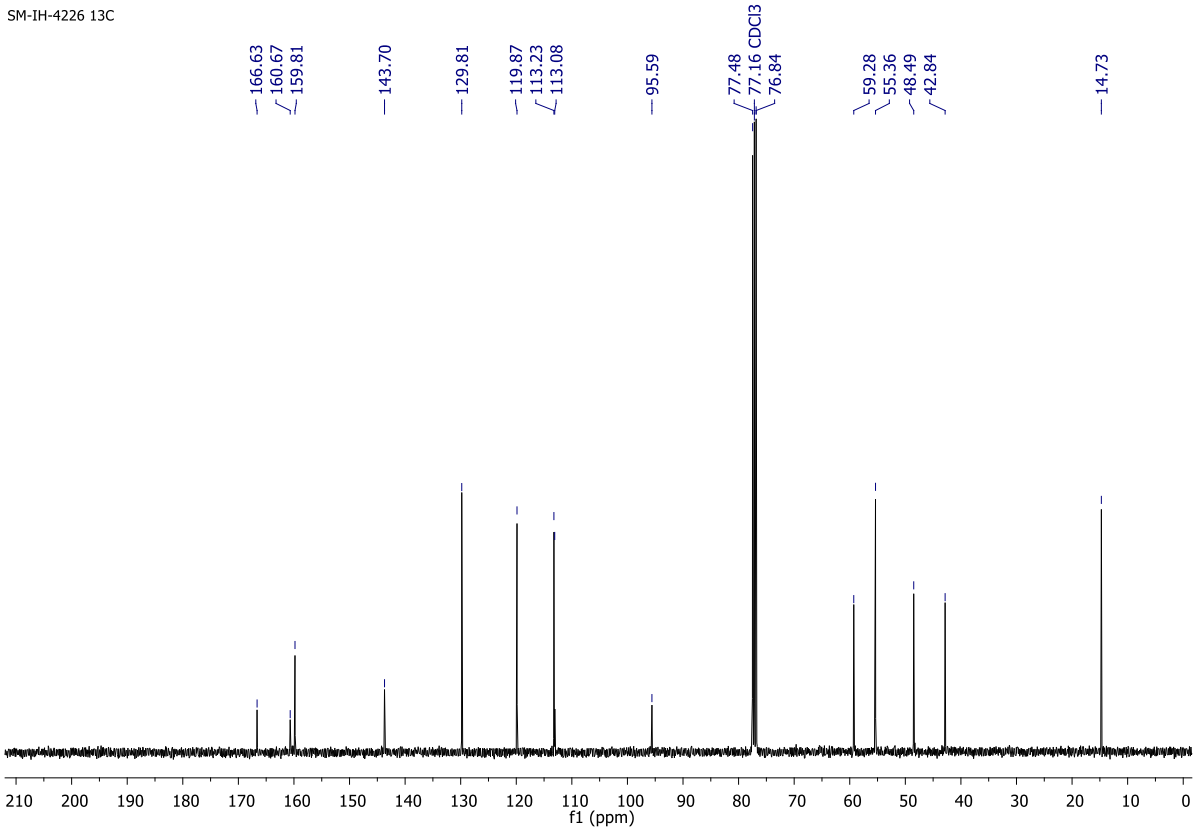
^{19}F NMR of **4b** (377 MHz, $CDCl_3$):



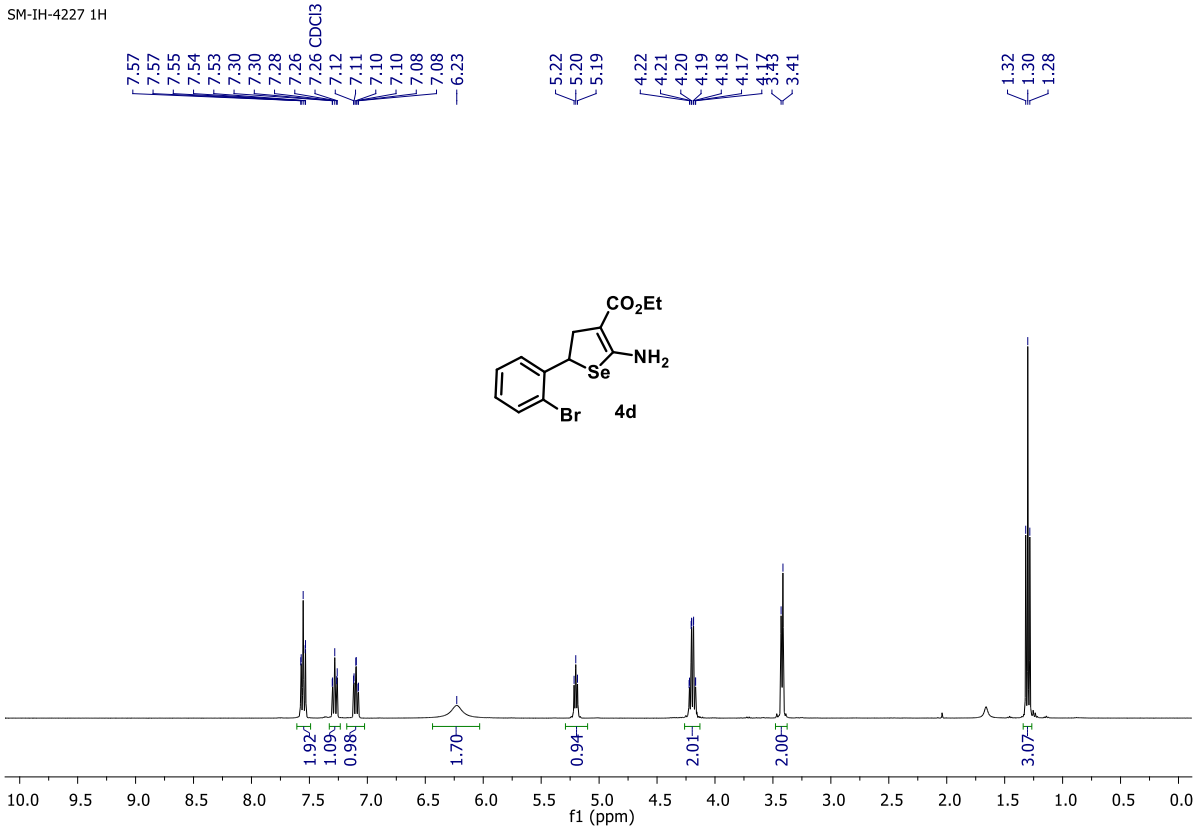
^{1}H NMR of **4c** (400 MHz, $CDCl_3$):



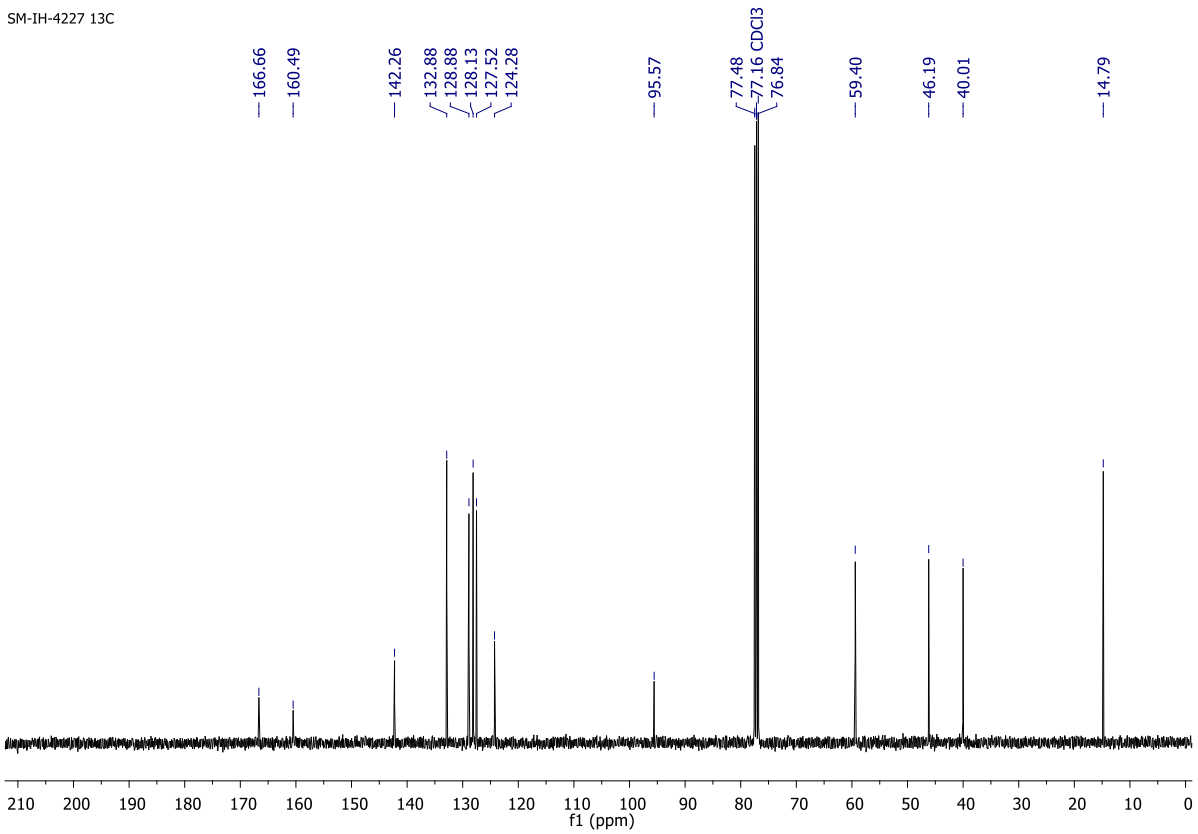
^{13}C{^{1}H} NMR of **4c** (101 MHz, $CDCl_3$):



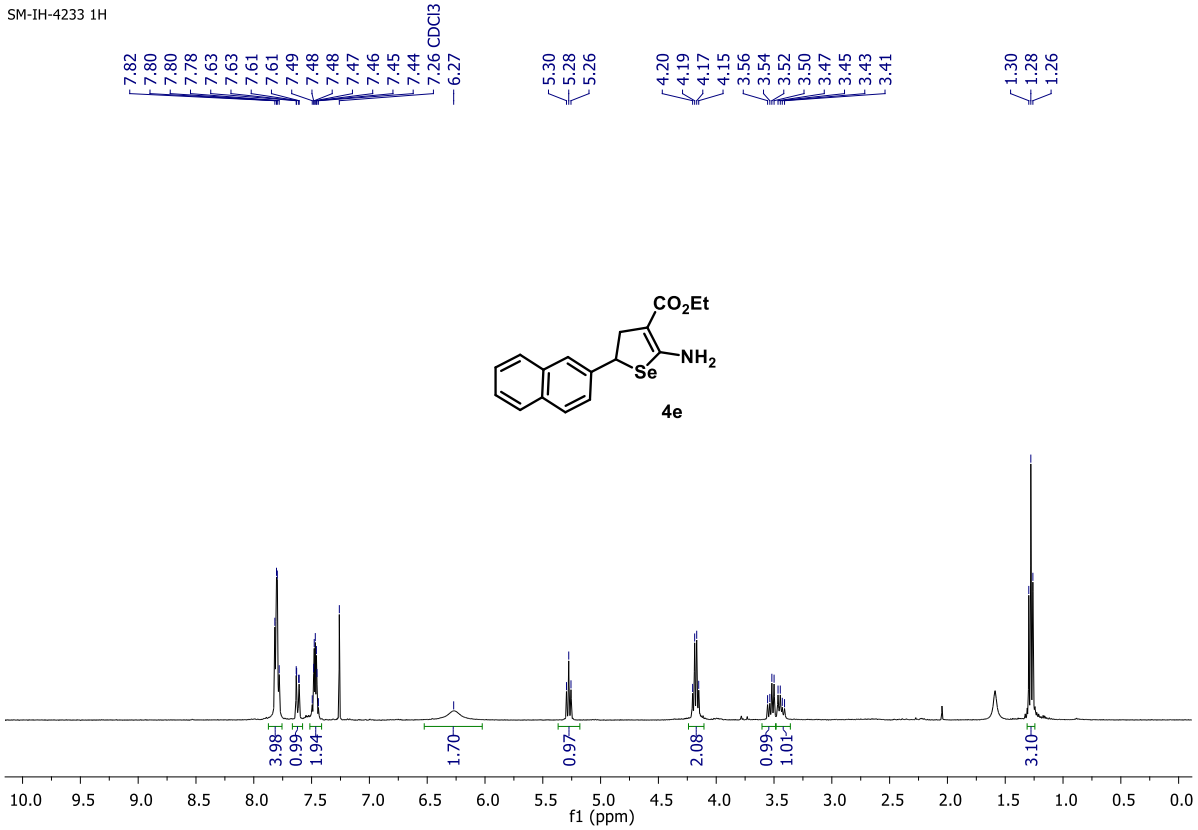
^{1}H NMR of **4d** (400 MHz, $CDCl_3$):



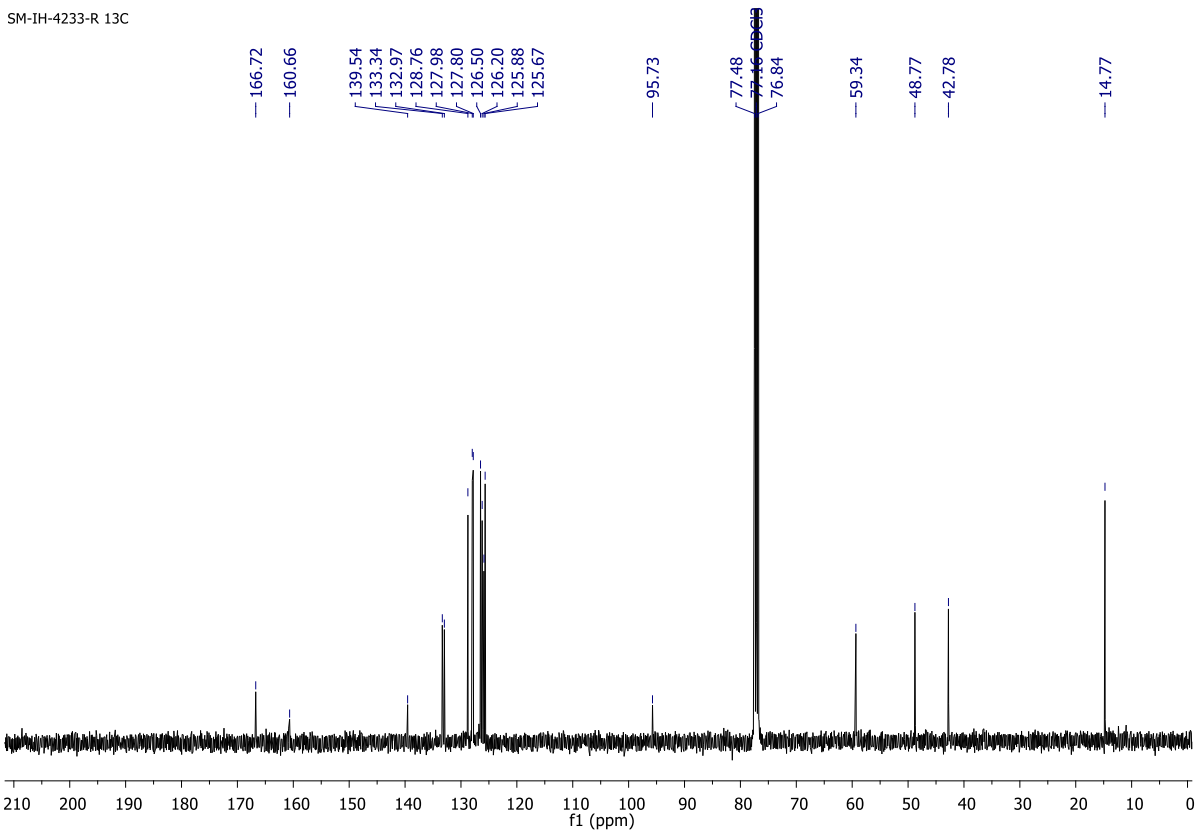
^{13}C{^{1}H} NMR of **4d** (101 MHz, $CDCl_3$):



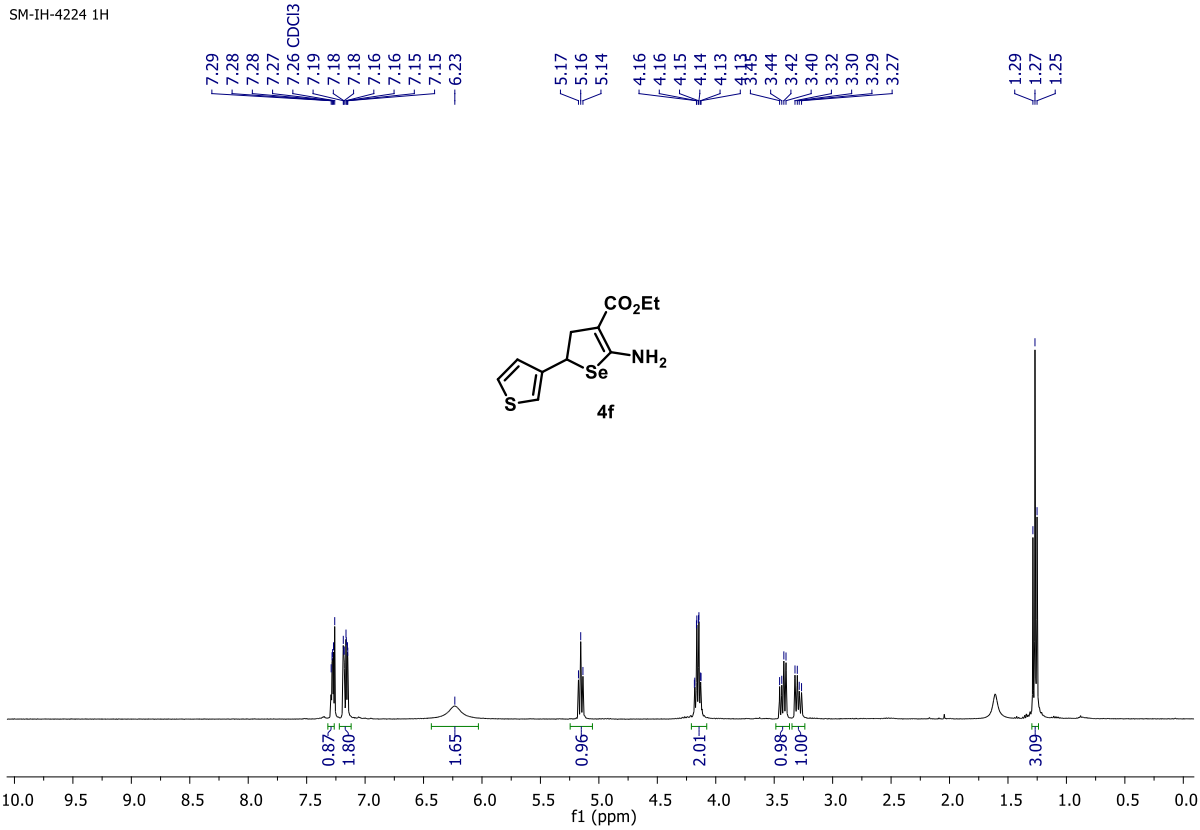
^{1}H NMR of **4e** (400 MHz, $CDCl_3$):



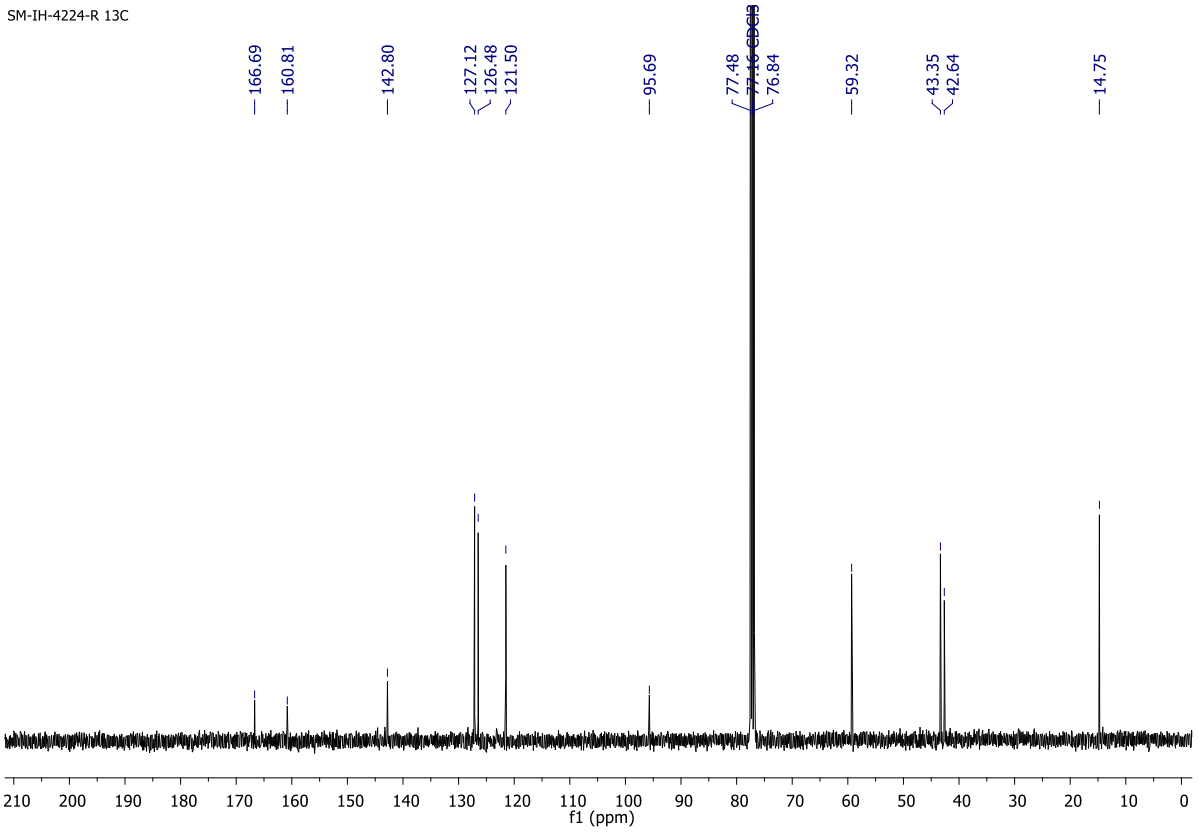
^{13}C{^{1}H} NMR of **4e** (101 MHz, $CDCl_3$):



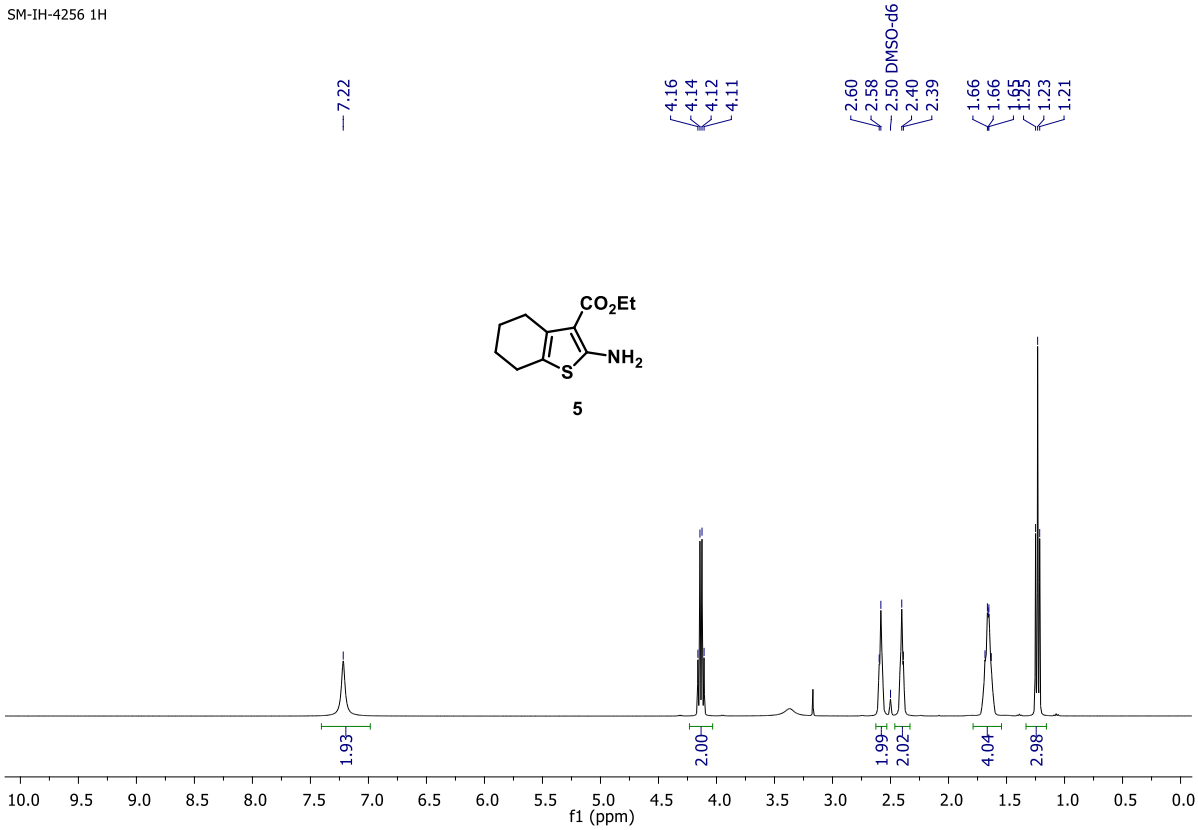
^{1}H NMR of **4f** (400 MHz, $CDCl_3$):



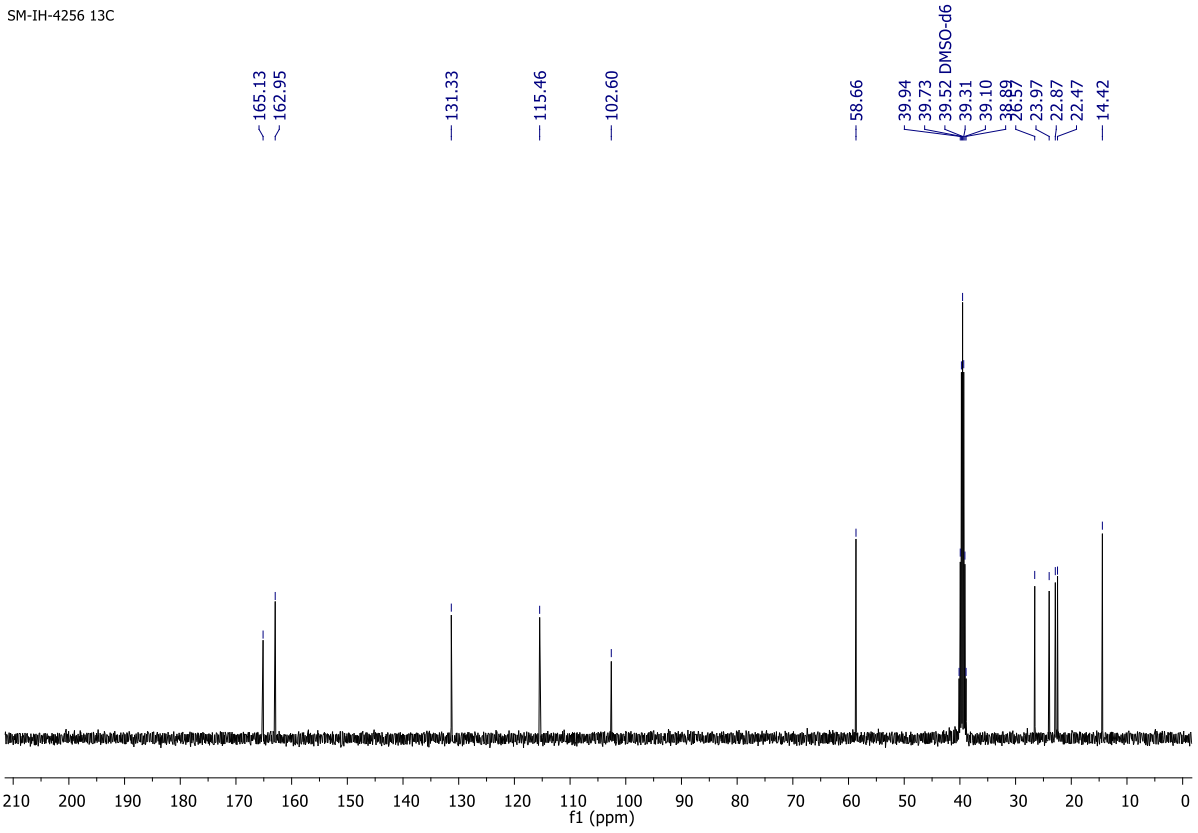
^{13}C{^{1}H} NMR of **4f** (101 MHz, $CDCl_3$):



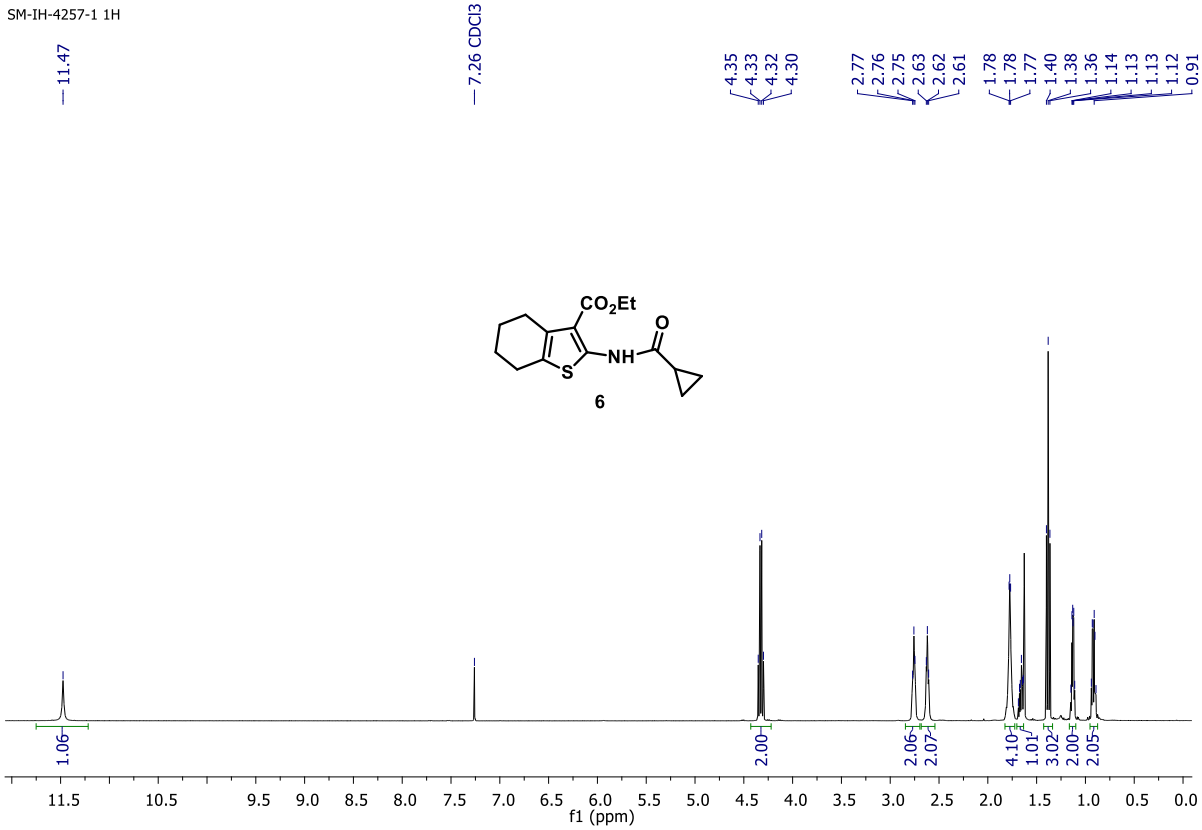
^{1}H NMR of **5** (400 MHz, DMSO-d_6):



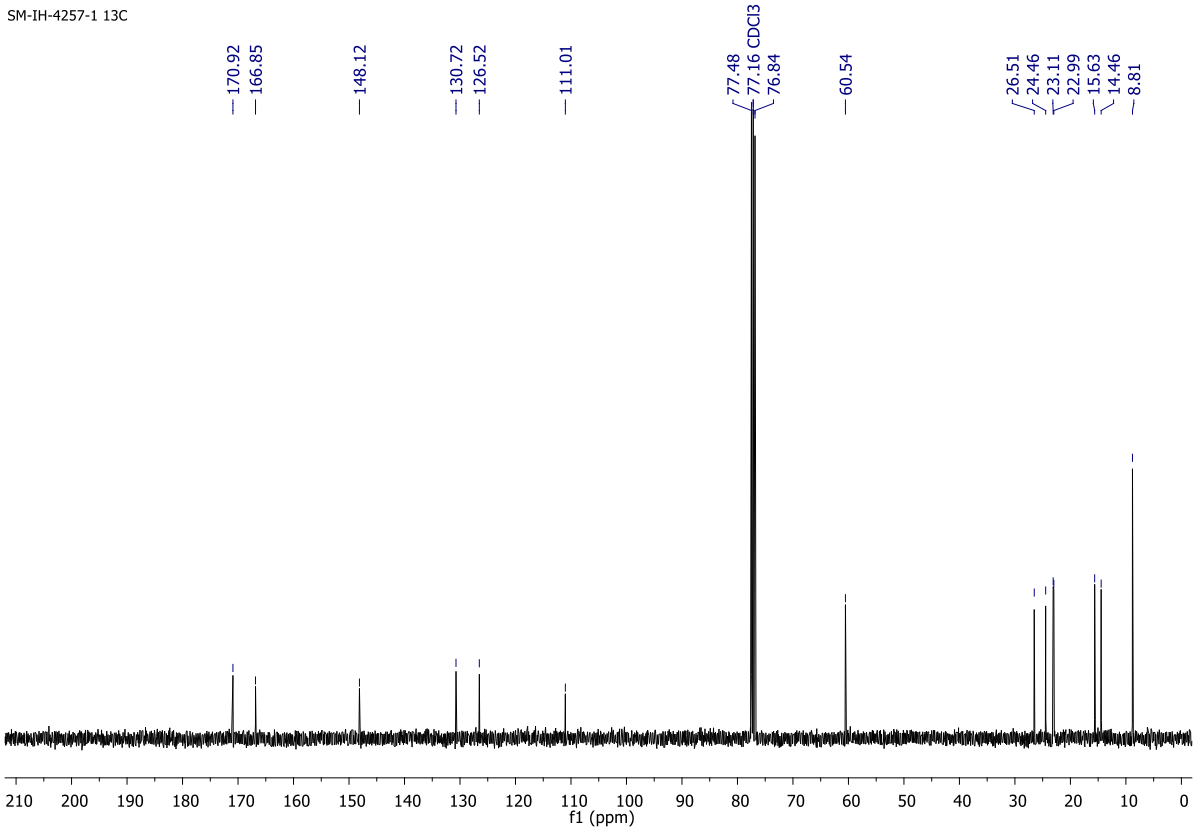
^{13}C{^{1}H} NMR of **5** (101 MHz, DMSO-d_6):



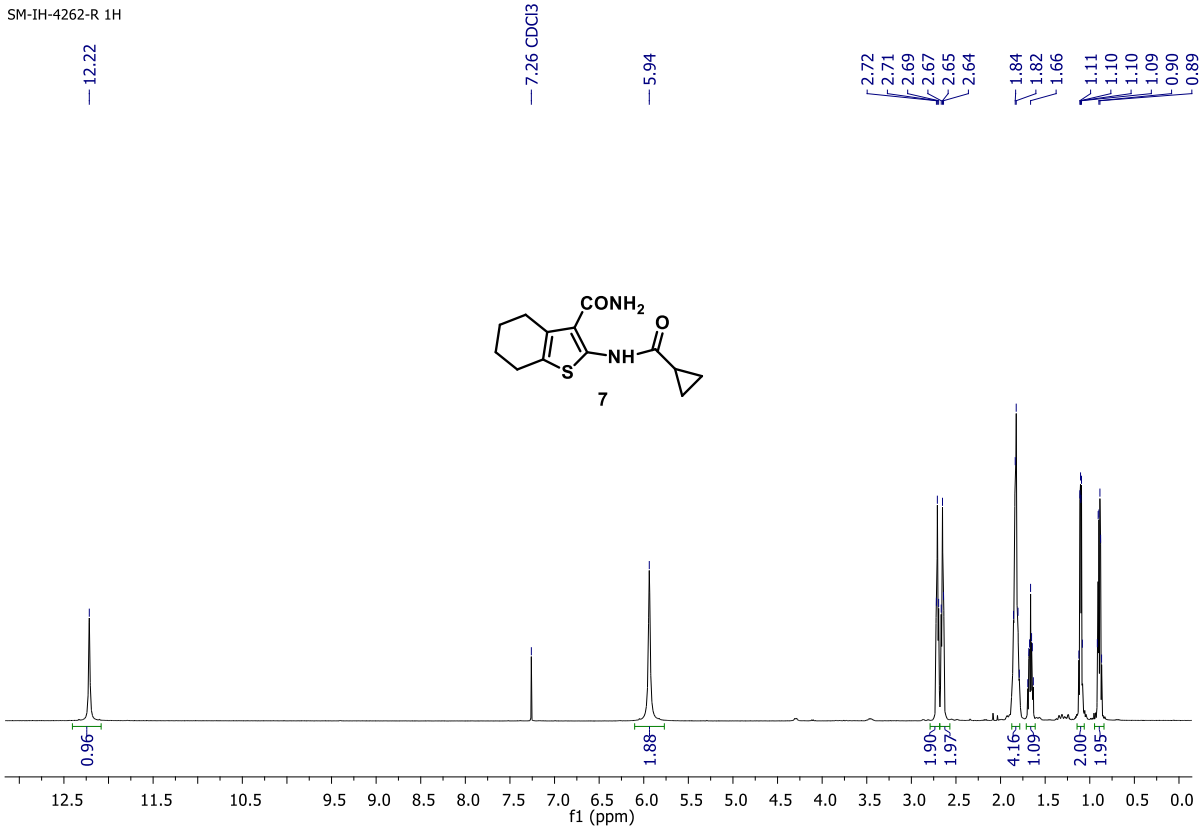
^{1}H NMR of **6** (400 MHz, $CDCl_3$):



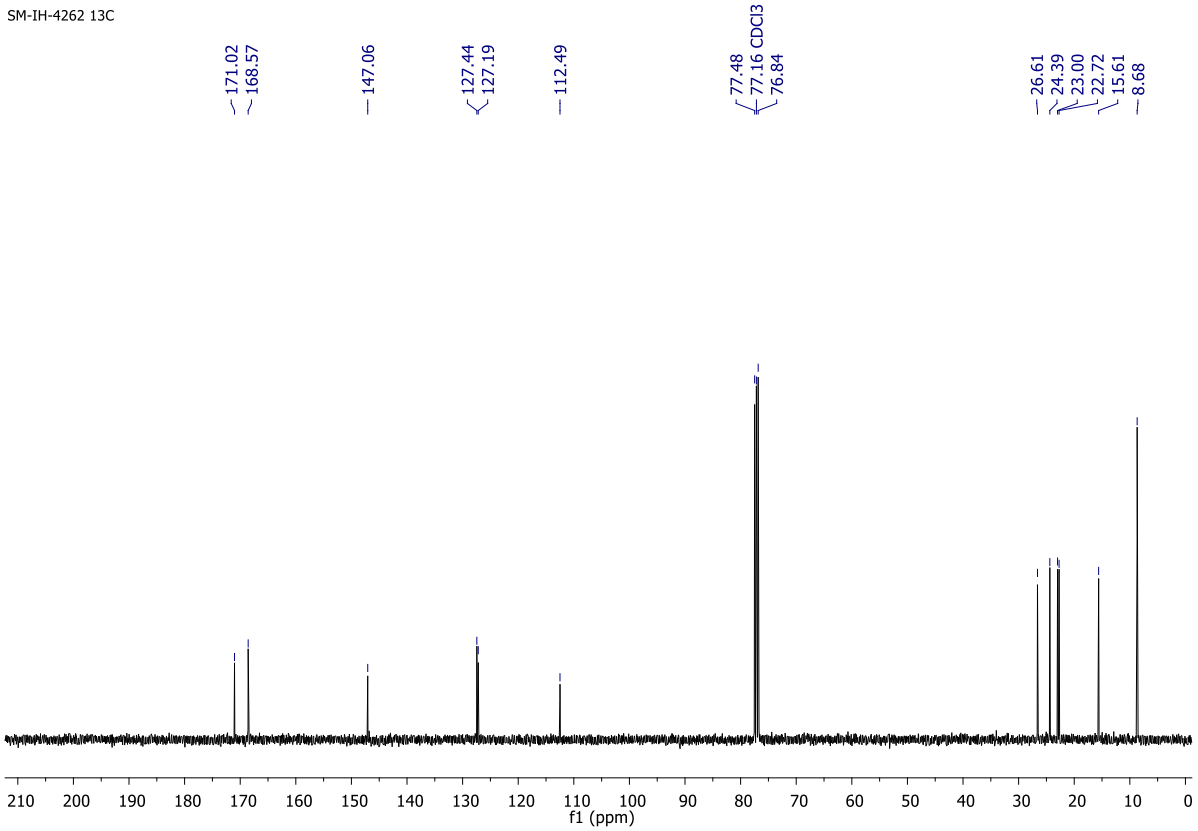
^{13}C{^{1}H} NMR of **6** (101 MHz, $CDCl_3$):



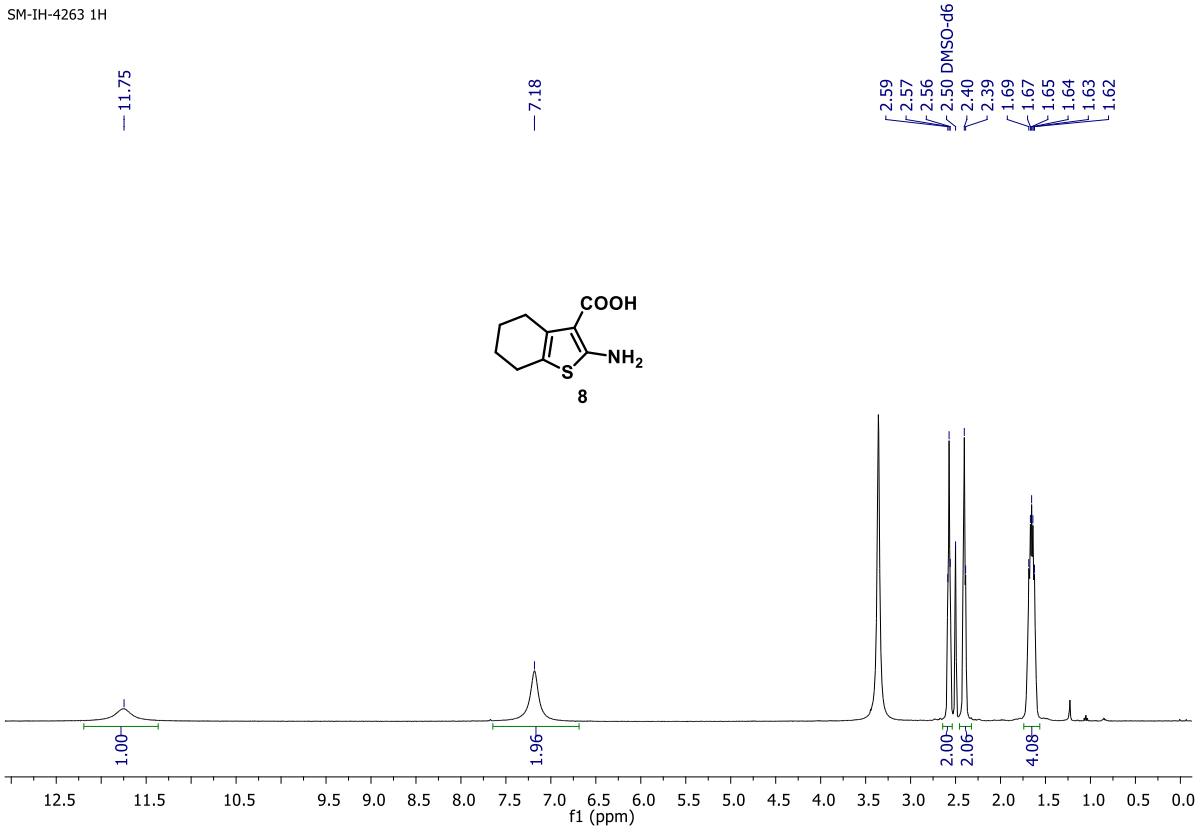
^{1}H NMR of **7** (400 MHz, $CDCl_3$):



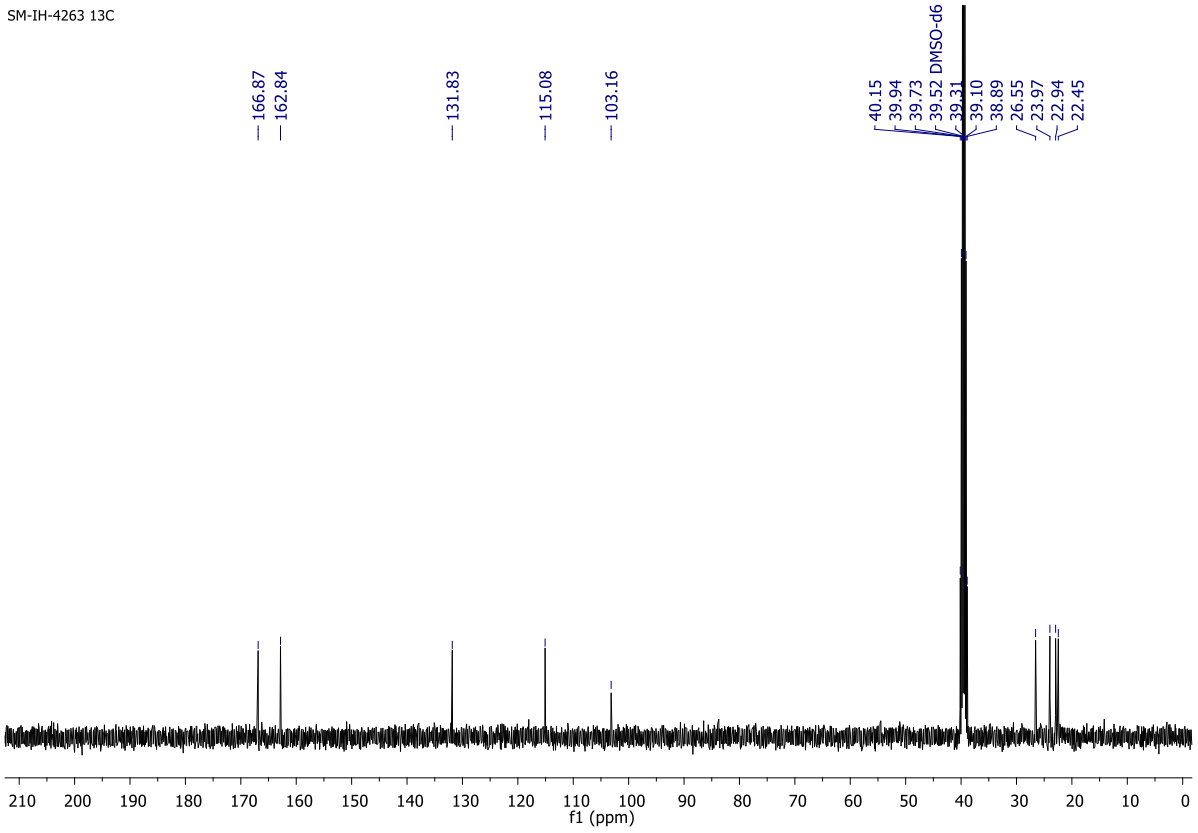
^{13}C{^{1}H} NMR of **7** (101 MHz, $CDCl_3$):



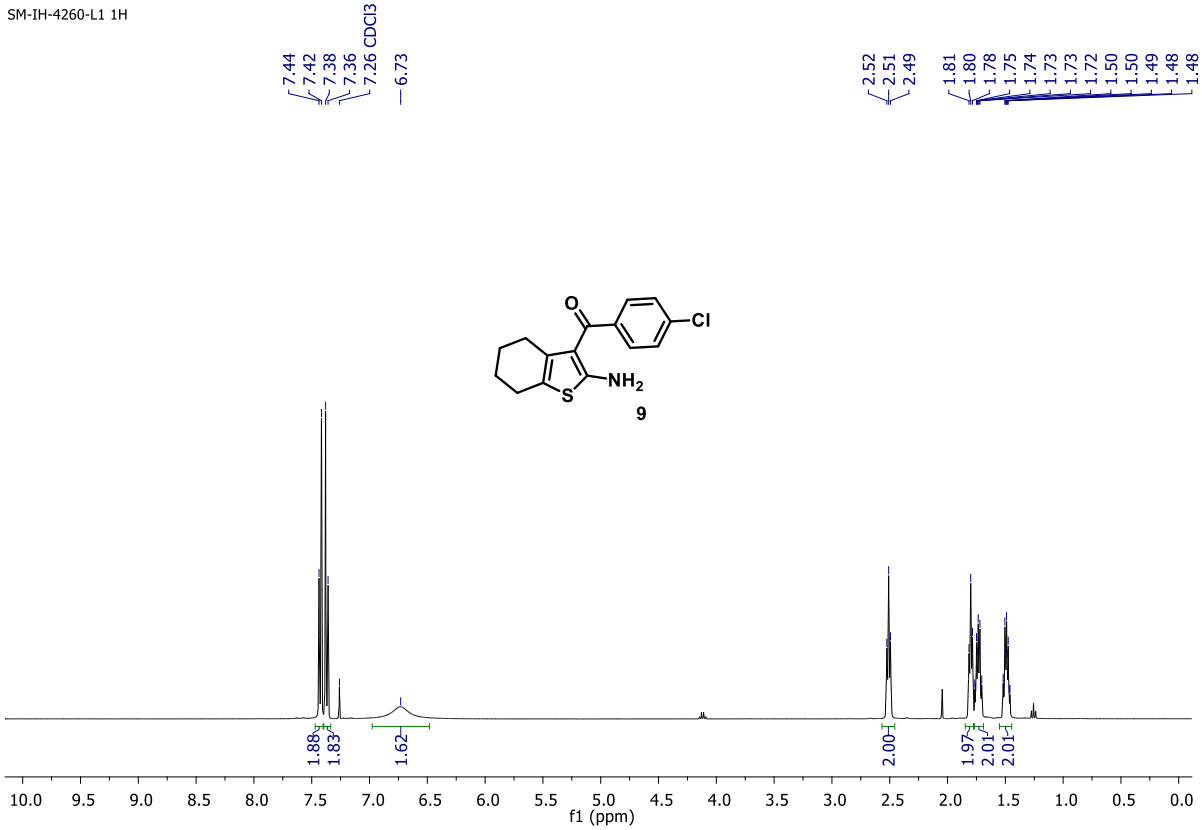
^{1}H NMR of **8** (400 MHz, DMSO-d_6):



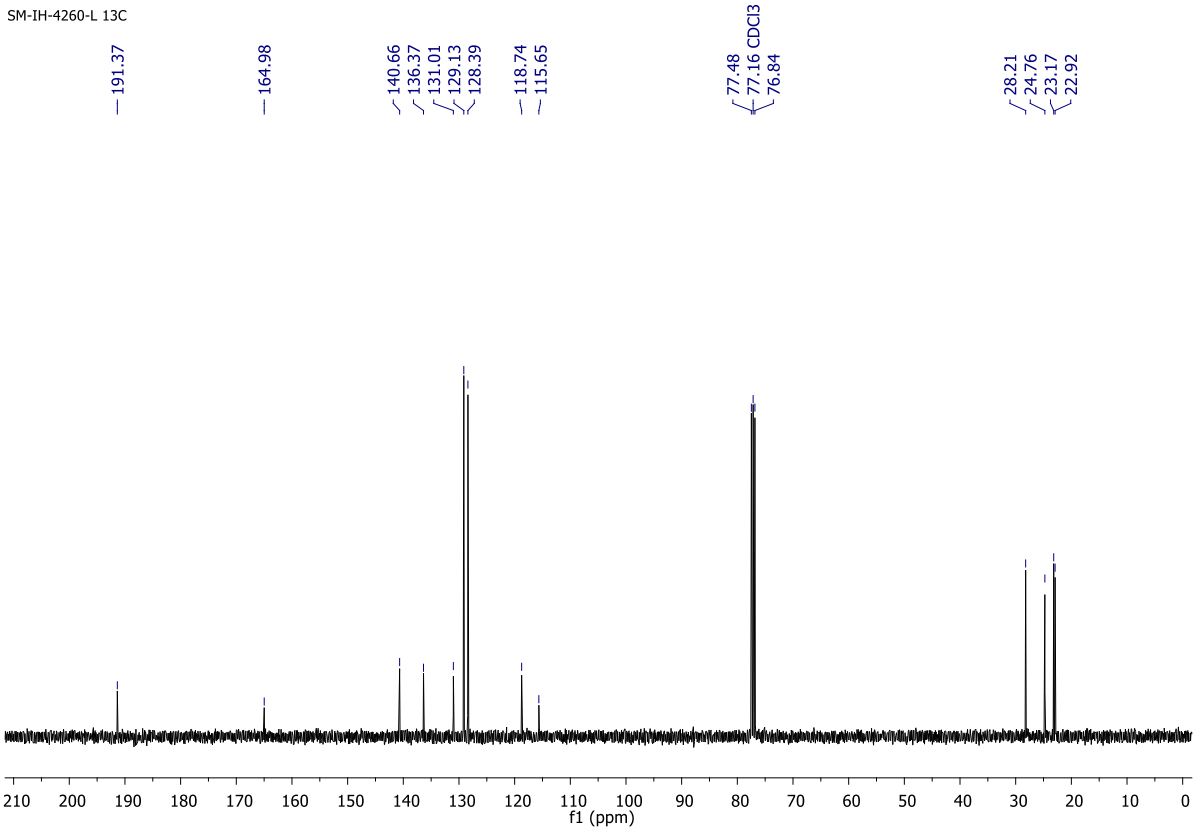
^{13}C{^{1}H} NMR of **8** (101 MHz, DMSO-d_6):



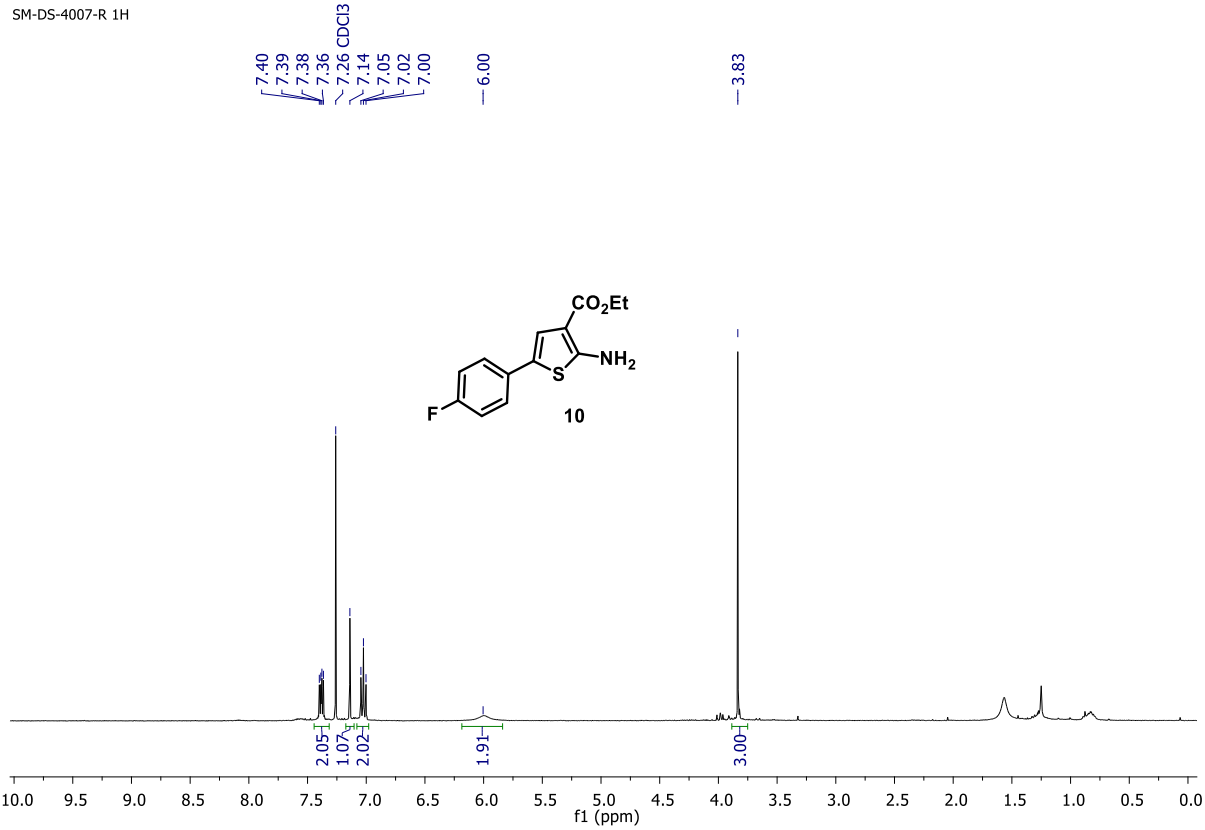
^{1}H NMR of **9** (400 MHz, $CDCl_3$):



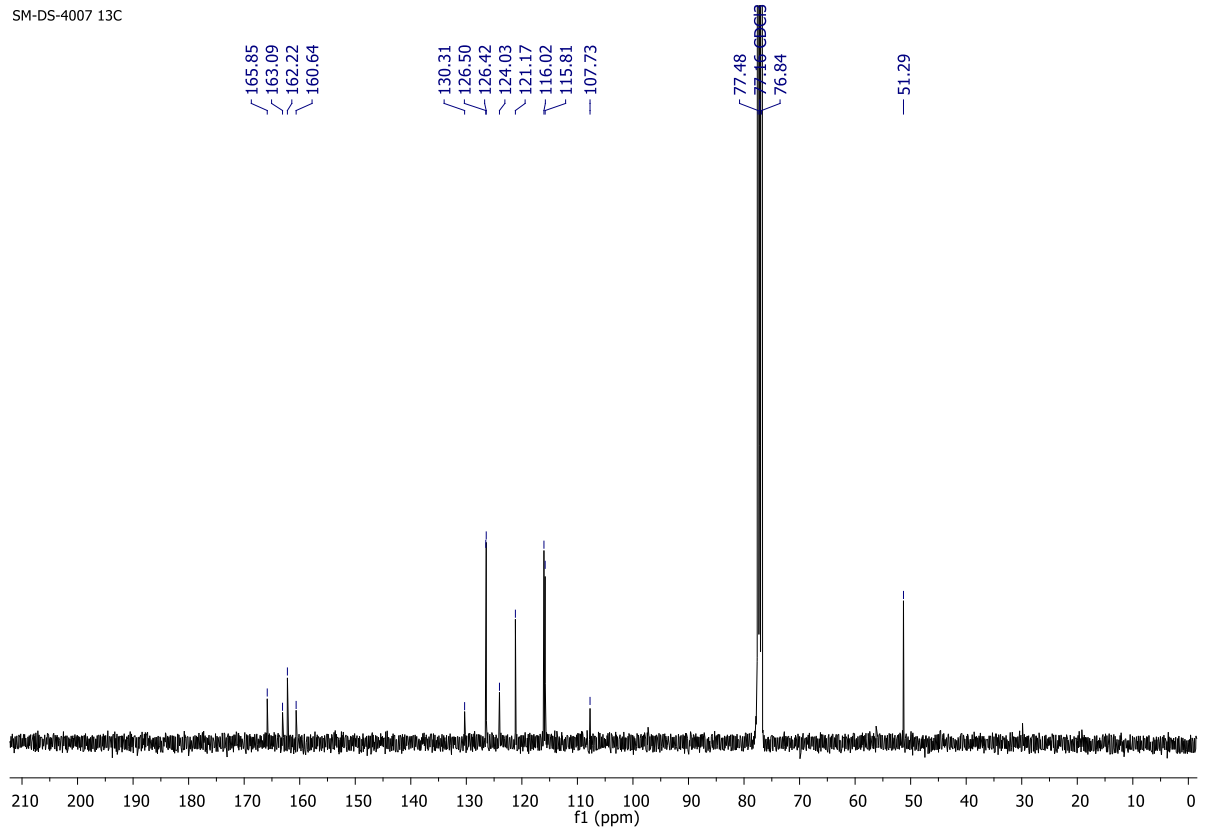
^{13}C{^{1}H} NMR of **9** (101 MHz, $CDCl_3$):



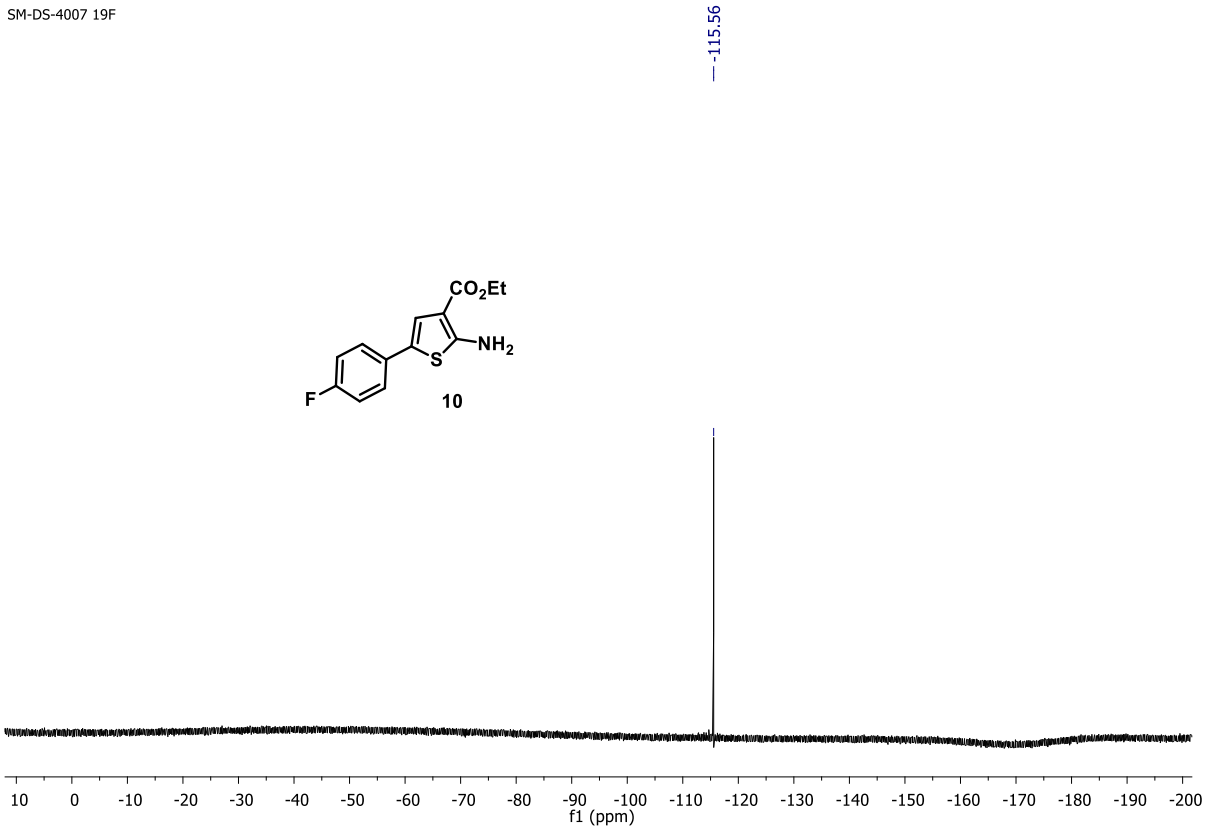
^{1}H NMR of **10** (400 MHz, $CDCl_3$):



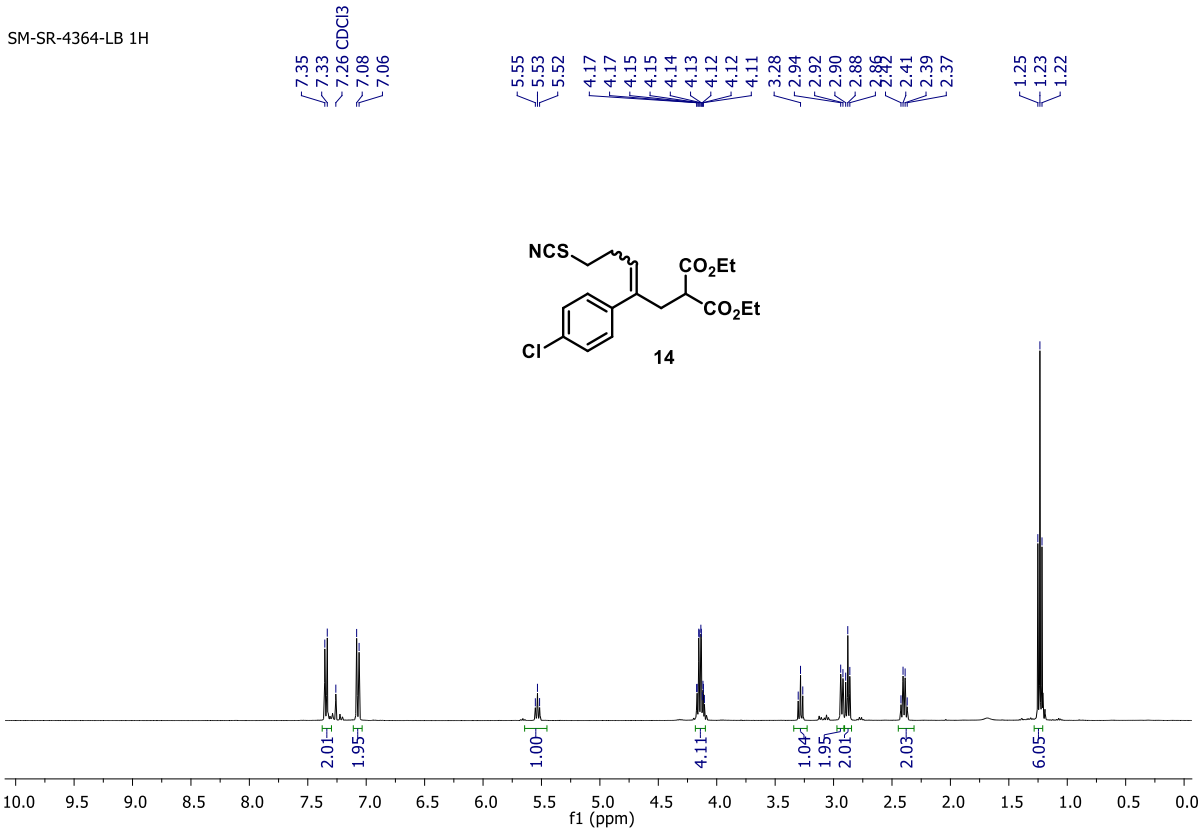
^{13}C{^{1}H} NMR of **10** (101 MHz, $CDCl_3$):



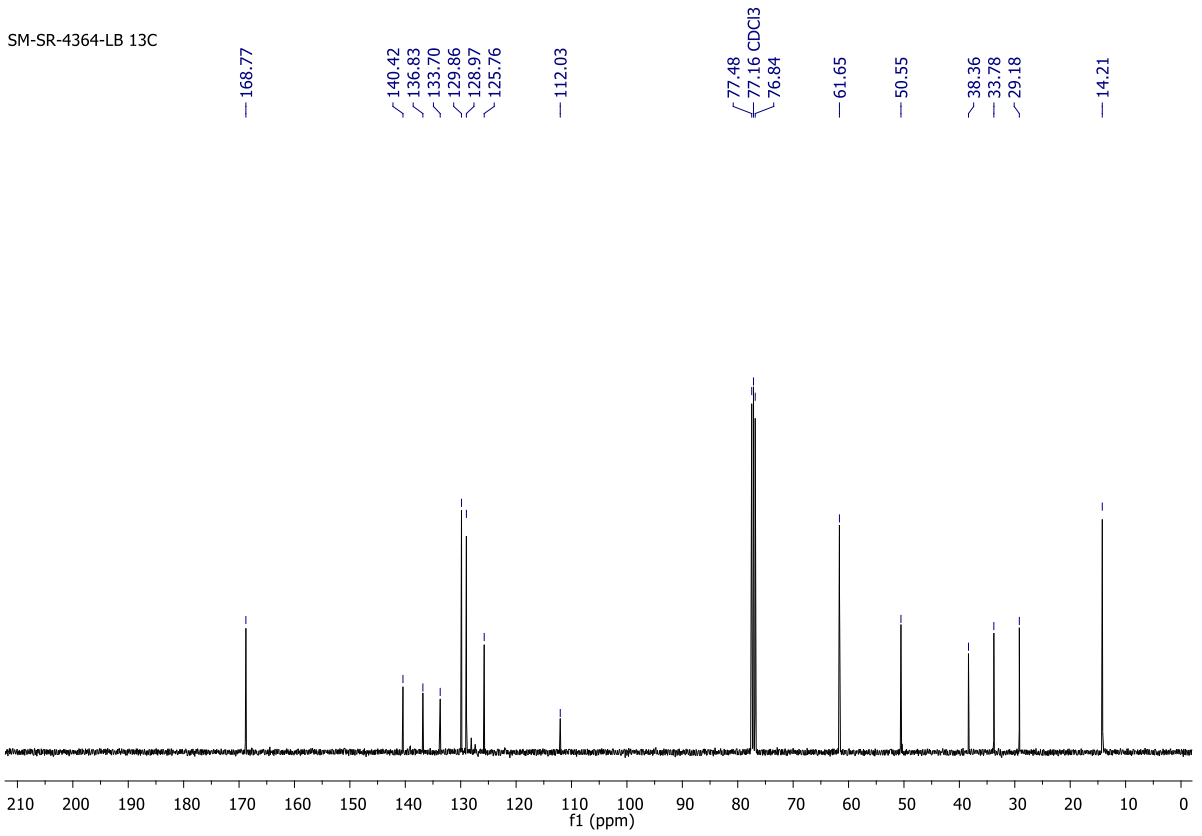
^{19}F NMR of **10** (377 MHz, $CDCl_3$):



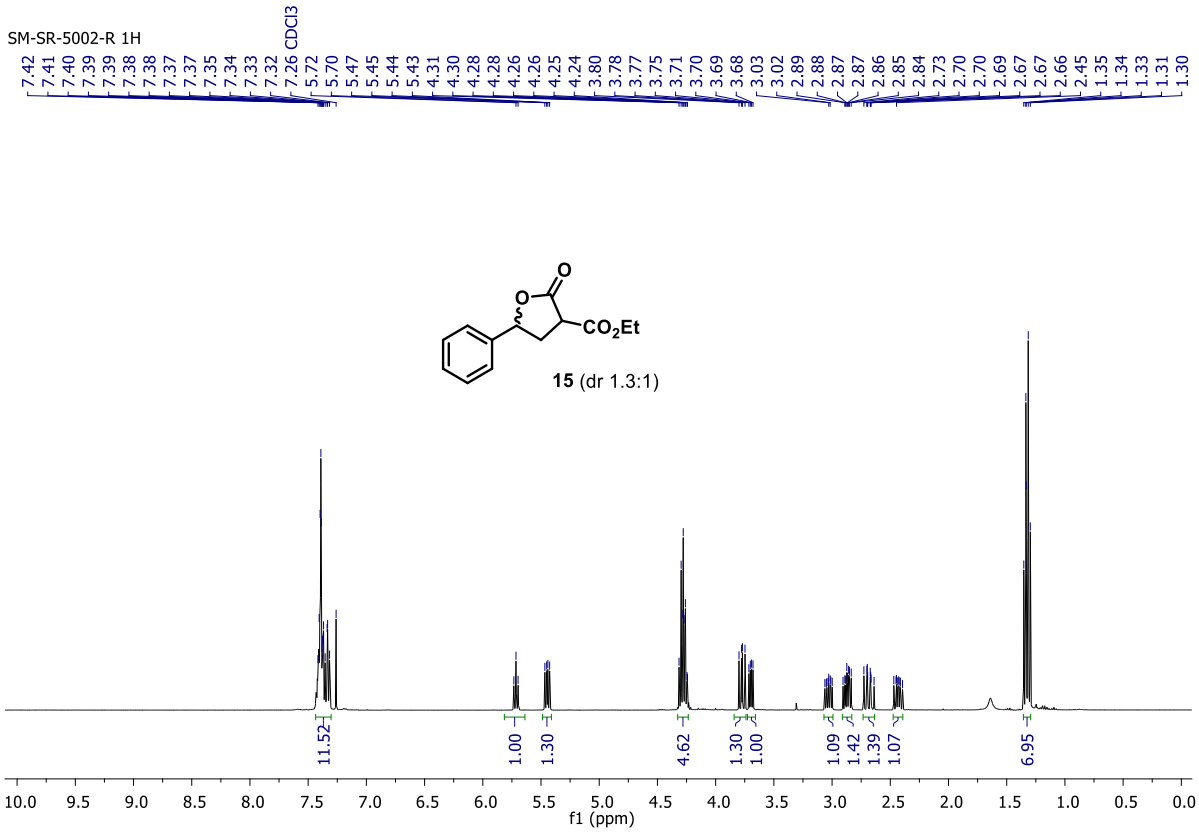
^{1}H NMR of **14** (400 MHz, $CDCl_3$):



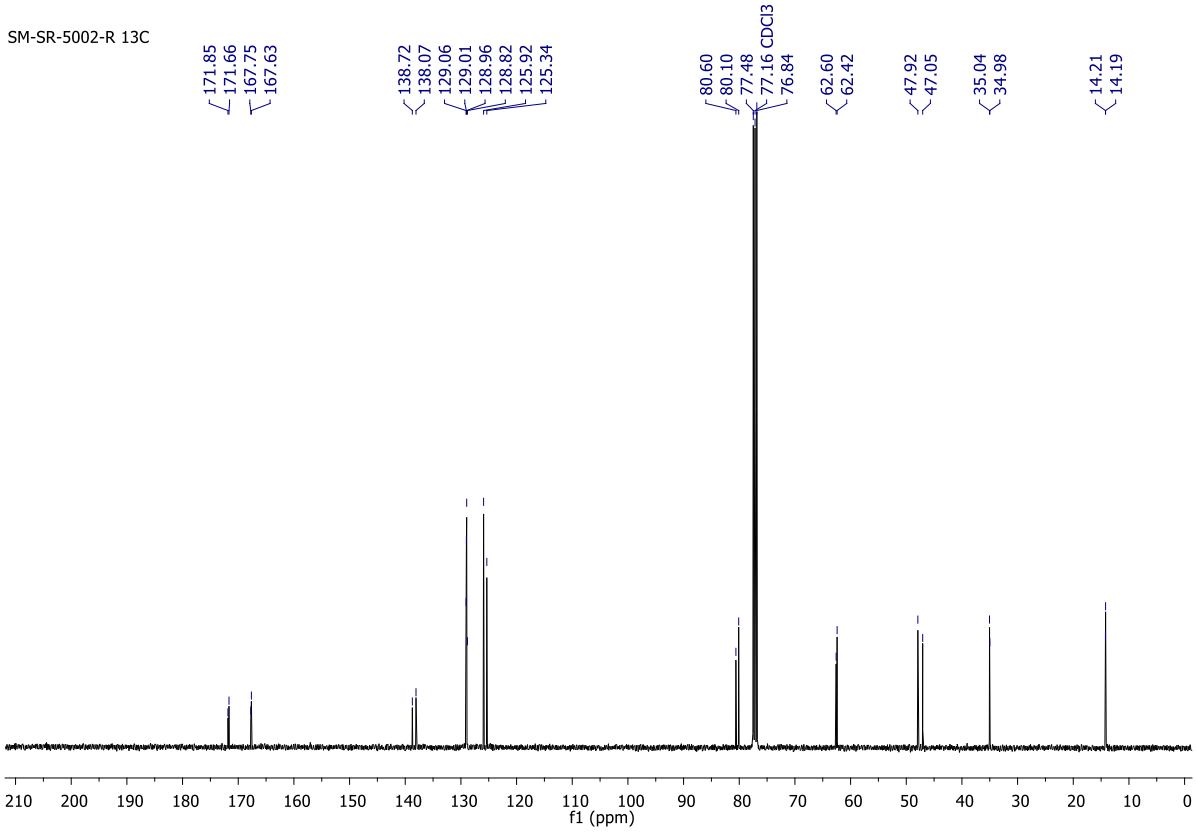
^{13}C{^{1}H} NMR of **14** (101 MHz, $CDCl_3$):



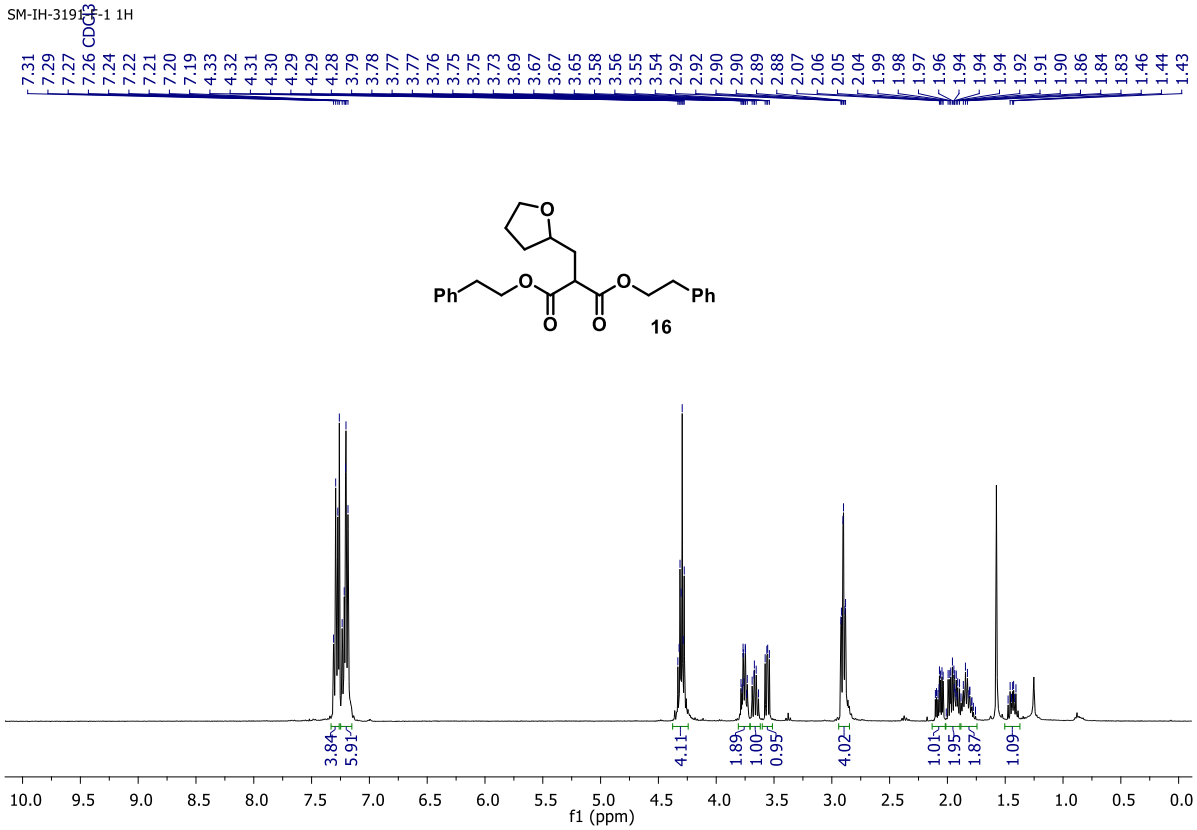
^{1}H NMR of **15** (400 MHz, $CDCl_3$):



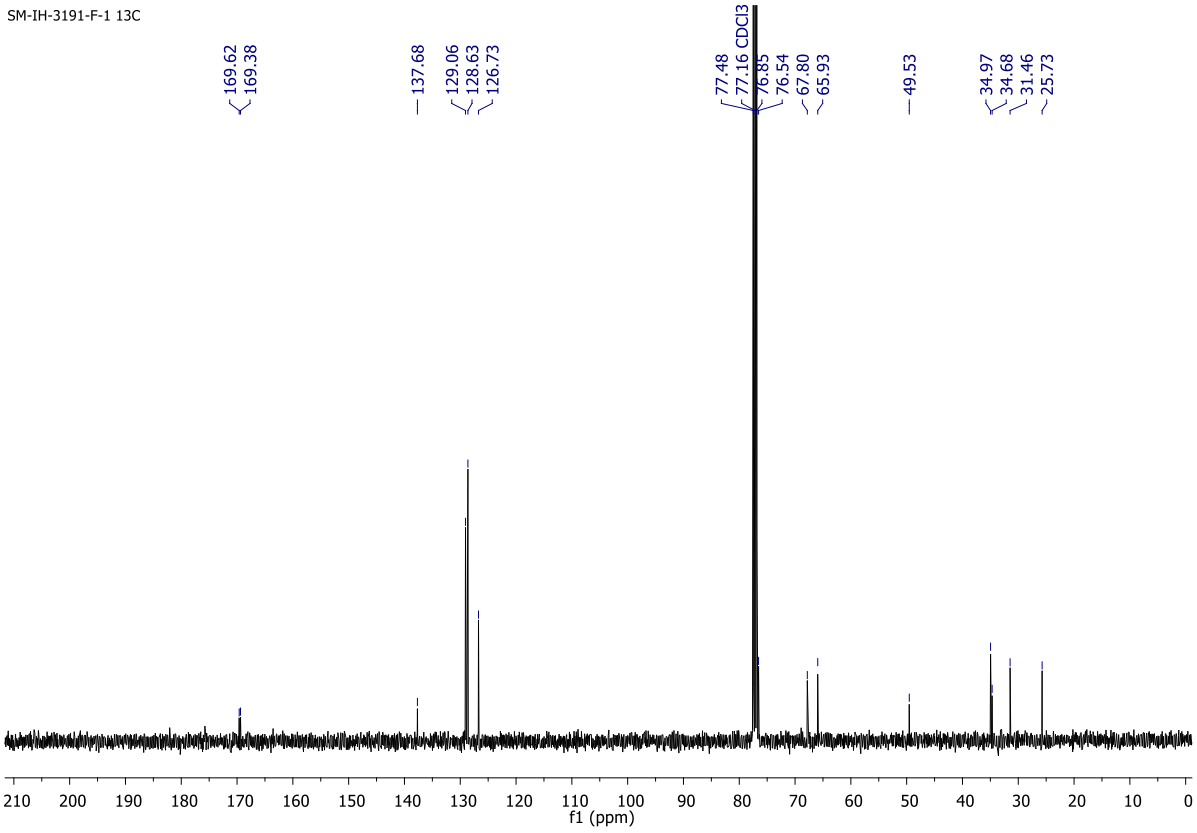
^{13}C{^{1}H} NMR of **15** (101 MHz, $CDCl_3$):



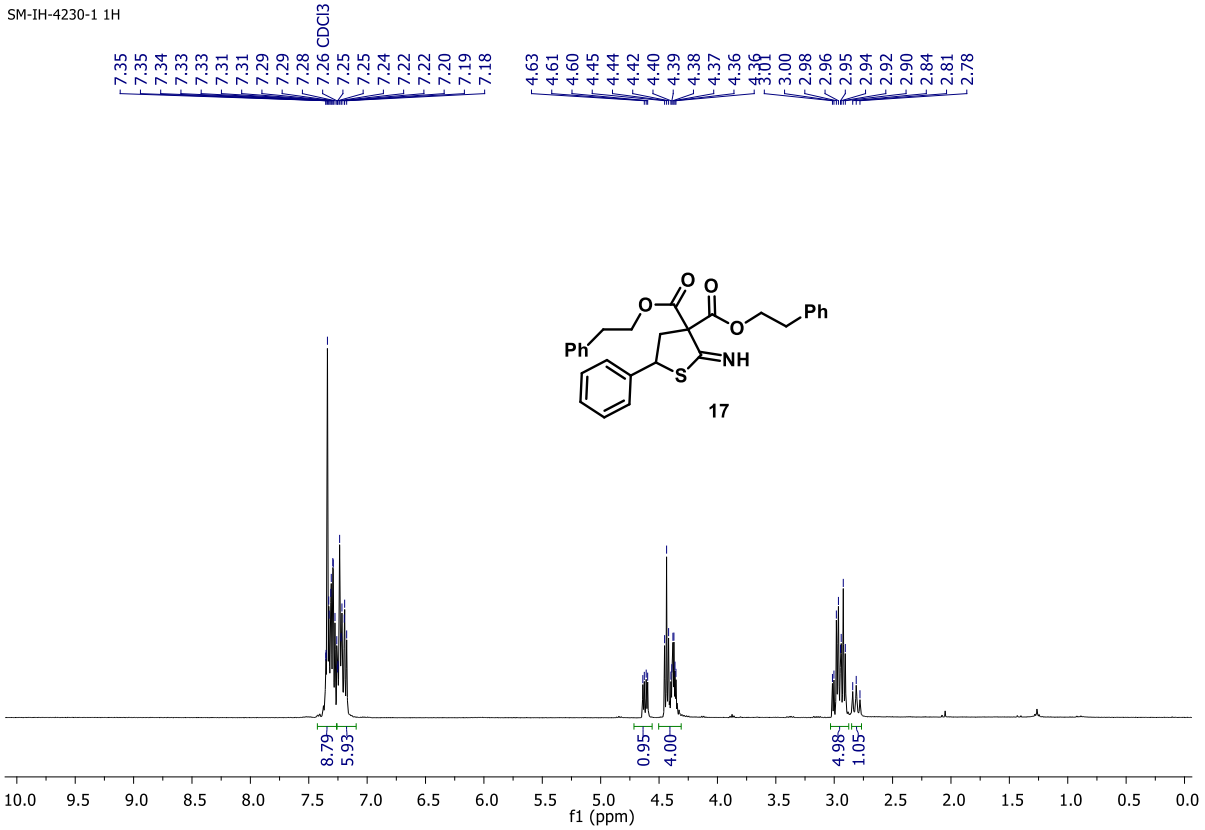
^{1}H NMR of **16** (400 MHz, $CDCl_3$):



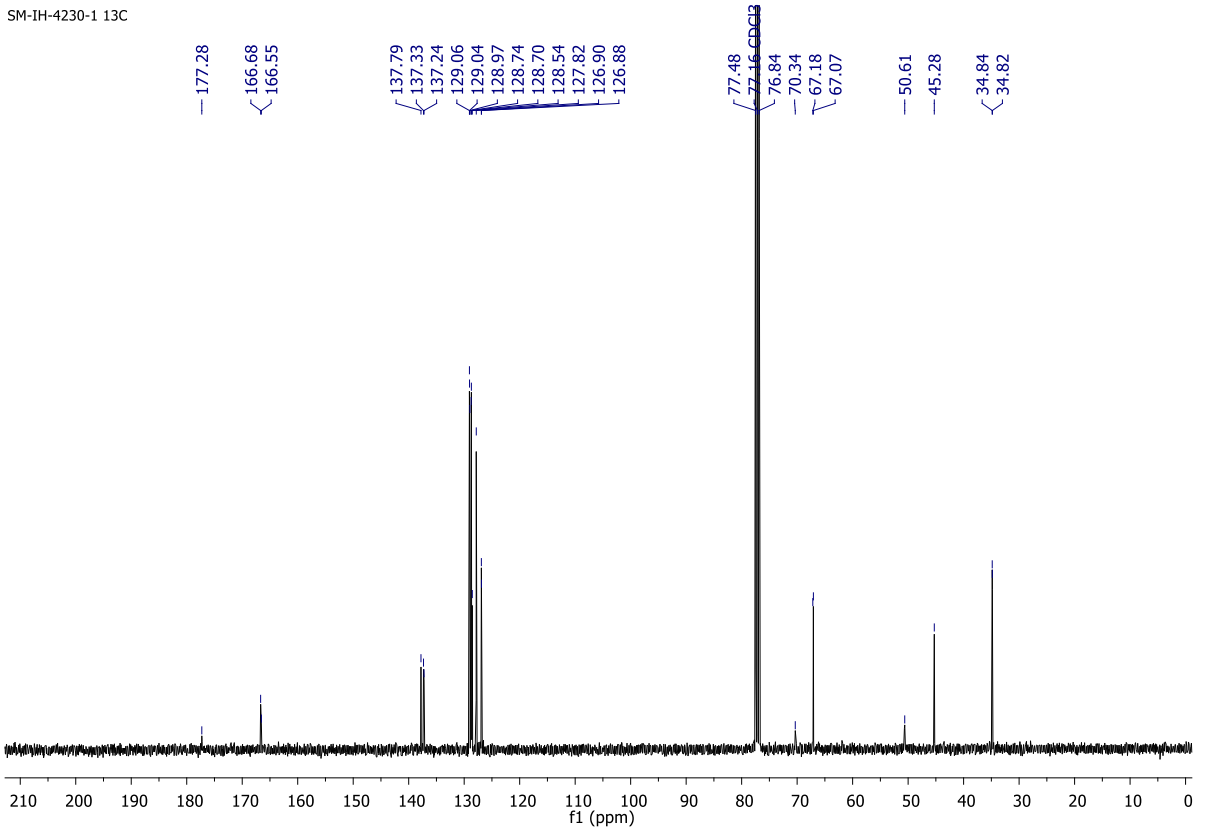
^{13}C{^{1}H} NMR of **16** (101 MHz, $CDCl_3$):



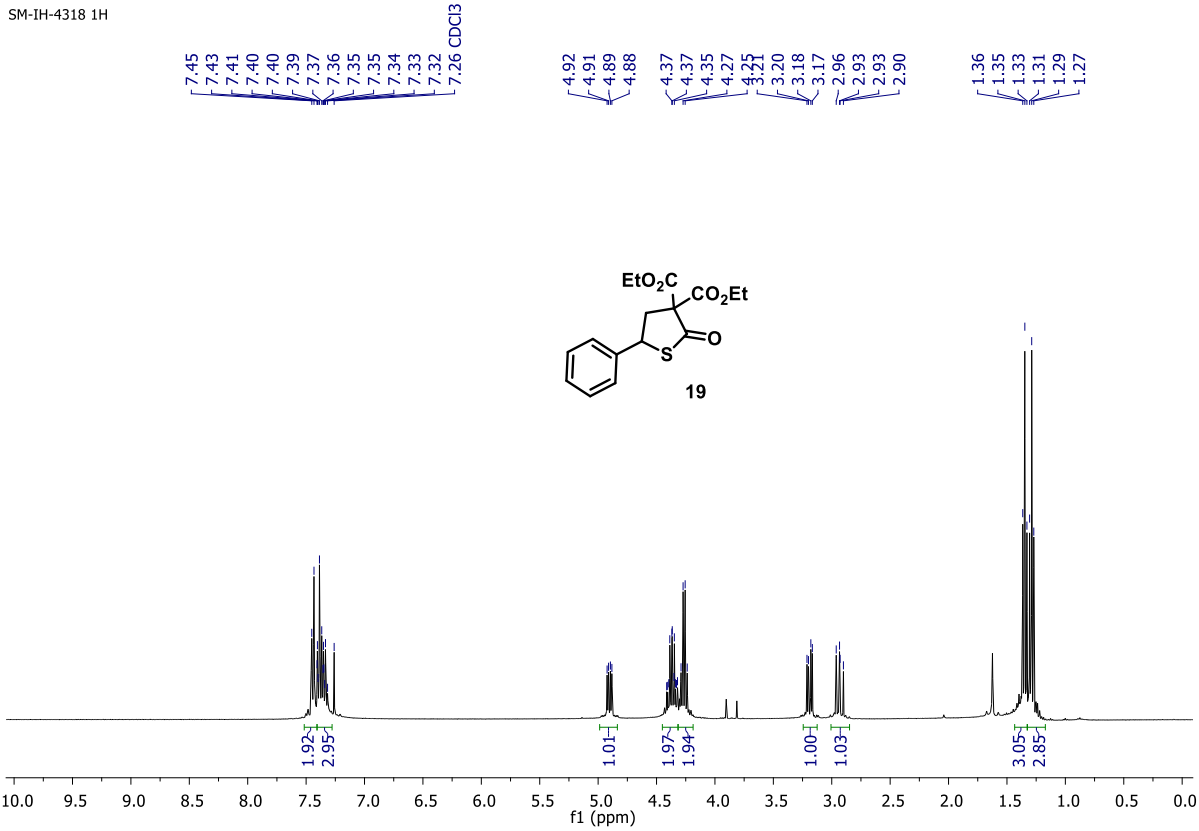
^{1}H NMR of **17** (400 MHz, $CDCl_3$):



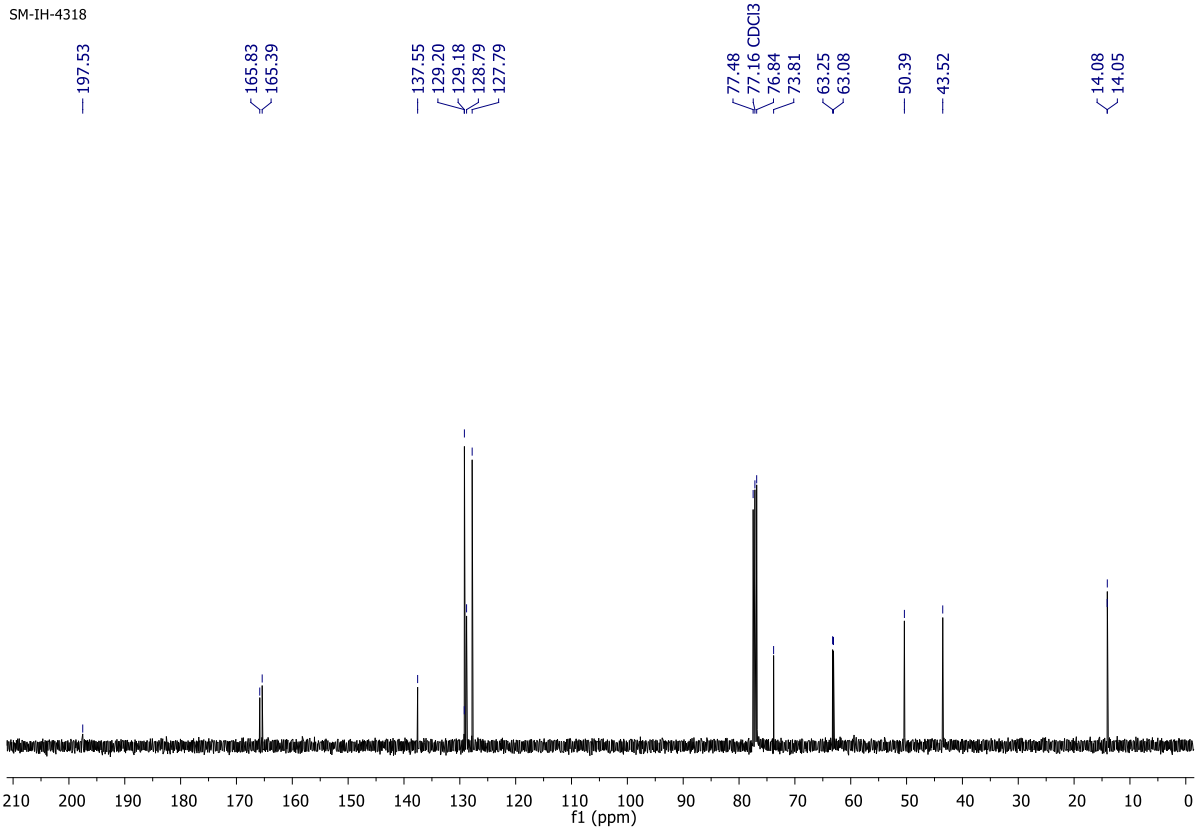
^{13}C{^{1}H} NMR of **17** (101 MHz, $CDCl_3$):



^{1}H NMR of **19** (400 MHz, $CDCl_3$):



^{13}C{^{1}H} NMR of **19** (101 MHz, $CDCl_3$):



11. References:

1. W. L. F. Armarego, *Purification of Laboratory Chemicals*, Butterworth-Heinemann, Oxford, Oxford, 2012.
2. T. V. K. Reddy, B. L. A. P. Devi, R. B. N. Prasad, P. Sujitha and C. G. Kumar, *Eur. J. Med. Chem.*, 2013, **67**, 384-389.
3. A. Yazici and S. G. Pyne, *Org. Lett.*, 2013, **15**, 5878-5881.
4. J. Niu, H. Zhou, Z. Li, J. Xu and S. Hu, *J. Org. Chem.*, 2008, **73**, 7814-7817.
5. J. C. Siu, J. B. Parry and S. Lin, *J. Am. Chem. Soc.*, 2019, **141**, 2825-2831.
6. W. Yao, G. Zhao, Y. Wu, L. Zhou, U. Mukherjee, P. Liu and M.-Y. Ngai, *J. Am. Chem. Soc.*, 2022, **144**, 3353-3359.
7. K. Matsubara, A. Kurimaru, M. Yamanaka, T. Hirashima, Y. Onishi, E. Murakami, E. Kawachi, Y. Koga and S. Ando, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 5593-5602.
8. F. Chen, Y. T. Tang, X. R. Li, Y. Y. Duan, C. X. Chen and Y. Zheng, *Adv. Synth. Catal.*, 2021, **363**, 5079-5084.
9. L.-Z. Fang, J.-M. Shen, Q.-H. Lv and F.-l. Yan, *Asian J. Chem.*, 2011, **23**, 3425.
10. L. B. Marx and J. W. Burton, *Chem. –Eur. J.*, 2018, **24**, 6747-6754.
11. M. R. Mazenauer, S. Manov, V. M. Galati, P. Kappeler and J. Stohner, *RSC Adv.*, 2017, **7**, 55434-55440.
12. M. D. Rathnayake and J. D. Weaver Iii, *Org. Lett.*, 2019, **21**, 9681-9687.
13. M.-S. Xie, G.-F. Zhao, T. Qin, Y.-B. Suo, G.-R. Qu and H.-M. Guo, *Chem. Commun.*, 2019, **55**, 1580-1583.
14. A. Jacob, P. G. Jones and D. B. Werz, *Org. Lett.*, 2020, **22**, 8720-8724.
15. K.-M. Wang, Y.-X. Ge, J. Zhang, Y.-T. Chen, N.-Y. Zhang, J.-S. Gu, L. Fang, X.-L. Zhang, J. Zhang and C.-S. Jiang, *Bioorg. Med. Chem. Lett.*, 2023, **79**, 129069.
16. P. Banhegyi, F. Waczek, Z. Szekelyhidi, B. Hegymegi-Barakonyi, G. Kéri and L. Őrfi, *Synth. Commun.*, 2008, **38**, 3270-3276.
17. F. Liu, X. Hou, L. F. Nie, K. Bozorov, M. Decker and G. Huang, *SynOpen*, 2018, **2**, 207-212.
18. S. Thanna, S. E. Knudson, A. Grzegorzewicz, S. Kapil, C. M. Goins, D. R. Ronning, M. Jackson, R. A. Slayden and S. J. Sucheck, *Org. Biomol. Chem.*, 2016, **14**, 6119-6133.
19. H. Wu, A. Sumita, Y. Otani and T. Ohwada, *J. Org. Chem.*, 2022, **87**, 15224-15249.
20. C.-J. Zhang, C. Y. J. Tan, J. Ge, Z. Na, G. Y. J. Chen, M. Uttamchandani, H. Sun and S. Q. Yao, *Angew. Chem. Int. Ed.*, 2013, **52**, 14060-14064.
21. (a) G. E. M. Crisenza, D. Mazzarella and P. Melchiorre, *J. Am. Chem. Soc.*, 2020, **142**, 5461-5476; (b) W. Sun, M. Zhao, Y. Meng, C. Zheng, K. Yang, S. Wang, C. Ke and Z. Zhang, *Org. Lett.*, 2024, **26**, 3762–3766; (c) M. R. Mutra and J. J. Wang, *Nat. Commun.*, 2022, **13**, 2345.
22. X.-J. Wei, D.-T. Yang, L. Wang, T. Song, L.-Z. Wu and Q. Liu, *Org. Lett.*, 2013, **15**, 6054-6057.
23. C.-J. Wallentin, J. D. Nguyen, P. Finkbeiner and C. R. J. Stephenson, *J. Am. Chem. Soc.*, 2012, **134**, 8875-8884.
24. Ł. Woźniak, J. J. Murphy and P. Melchiorre, *J. Am. Chem. Soc.*, 2015, **137**, 5678-5681.

25. S. R. Kandukuri, A. Bahamonde, I. Chatterjee, I. D. Jurberg, E. C. Escudero-Adán and P. Melchiorre, *Angew. Chem. Int. Ed.*, 2015, **54**, 1485-1489.
26. (a) C. Adamo and V. Barone, *J. Chem. Phys.*, 1999, **110**, 6158-6170; (b) S. Grimme, *J. Comput. Chem.*, 2004, **25**, 1463-1473; (c) S. Grimme, J. Antony, S. Ehrlich and H. Krieg, *J. Chem. Phys.*, 2010, **132**, 154104; (d) S. Grimme, *Wiley Interdiscip. Rev. Comput. Mol. Sci.*, 2011, **1**, 211-228; (e) S. Ehrlich, J. Moellmann and S. Grimme, *Acc. Chem. Res.*, 2013, **46**, 916-926.
27. (a) F. Weigend and R. Ahlrichs, *Phys. Chem. Chem. Phys.*, 2005, 3297-3305; (b) F. Weigend, *Phys. Chem. Chem. Phys.*, 2006, **8**, 1057-1065.
28. A. Klamt and G. Schüürmann, *J. Chem. Soc. Perkin Trans. 2.*, 1993, 799-805.
29. T. Lu and F. Chen, *J. Comput. Chem.*, 2012, **33**, 580-592.
30. A. E. Reed, L. A. Curtiss and F. Weinhold, *Chem. Rev.*, 1988, **88**, 899-926.
31. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson and H. Nakatsuji, *Gaussian16, Revision A. 03*, 2016.
32. I. Rozas, I. Alkorta and J. Elguero, *J. Am. Chem. Soc.*, 2000, **122**, 11154-11161.