Deoxyfluorinated Amidation and Esterification of Carboxylic Acid by Pyridinesulfonyl Fluoride

Anootha Neeliveettil,[†a,c] Soumyadip Dey,[†b] Vishnu Nomula,[a,c] Swati Thakur,[b] Debabrata Giri,[b] Abhishek Santra,[a,c] Abhijit Sau*[a,b]

Table of Contents	Page No.
Experimental Procedures	S1
General procedures for one pot coupling reactions	S2
Amide substrate scope	S2
Ester substrate scope	S13
NMR Studies for understanding reaction mechanism	S17
Synthesis of sulfonyl fluorides	S18
References	S19
Spectra	S22

Experimental Procedures:

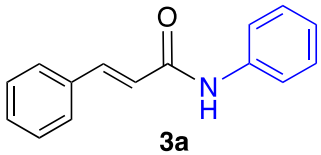
General. Chemicals were purchased and used without further purification. Dry solvents were obtained by distillation using standard procedures. Reactions requiring anhydrous conditions were performed under nitrogen; glassware and needles were either flame dried immediately prior to use or placed in an oven (150 °C) for at least 2 hours and allowed to cool either in a desiccator or under reduced pressure; liquid reagents, solutions or solvents were added *via* syringe through rubber septa; solid reagents were added *via* Schlenk type adapters. Teflon rings were used between the joints of the condensers and round bottom flasks. Reactions were monitored by TLC on Kieselgel 60 F254 (Merck). Detection was by examination under UV light (254 nm) and by charring with 10% sulfuric acid in ethanol. Flash column chromatography was performed using silica gel [Merck, 230−400 mesh (40−63 μm)]. Extracts were concentrated *in vacuo* using both a rotary evaporator (bath temperatures up to 40 °C) at a pressure of either 15 mmHg (diaphragm pump) or 0.1 mmHg (oil pump), as appropriate, and a high vacuum line at room temperature. ^{1}H NMR and ^{13}C NMR spectra were measured in the solvent stated at 400, 500, or 600 MHz. Chemical shifts are quoted in parts per million from

residual solvent peak ($CDCl_3$: ^1H - 7.26 ppm and ^{13}C - 77.16 ppm) and coupling constants (*J*) given in Hertz. Multiplicities are abbreviated as: b (broad), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or combinations thereof. The units of the specific rotation, (deg·mL)/(g·dm), are implicit and are not included in the reported value. Concentration *c* is given in g/100 mL.

General procedures for one-pot coupling reactions:

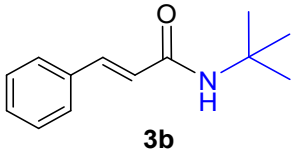
The carboxylic acid (1.0 equiv.) and 2-pyridinesulfonyl fluoride (1.2 equiv.) were weighed into an oven-dried round bottom flask. Then, the flask was filled with N_2, followed by the addition of ~ 1.0 ml anhydrous CH_3CN. The reaction solutions were stirred at rt for 30 min then desired amine or alcohol (1.2 equiv.) was added, and the reaction was stirred for 17 h. Completion of the reaction was determined by either TLC or NMR analysis of the crude material. The reaction mixture was concentrated *in vacuo* and directly purified by column chromatography to yield the respective amides or esters.

Amide substrate scope:



3a

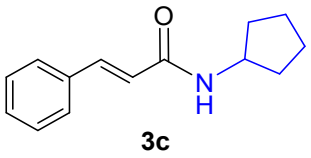
***N*-Phenylcinnamamide (3a):** Following the general procedure coupling reaction between cinnamic acid (50 mg, 0.34 mmol) and aniline (0.04 ml, 0.41 mmol) afforded compound **3a** as a white solid (68 mg, 90%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.99 (s, 1H), 7.74 (d, *J* = 15.5 Hz, 1H), 7.65 (d, *J* = 6.8 Hz, 2H), 7.45 (dd, *J* = 7.1, 1.9 Hz, 2H), 7.32 (dt, *J* = 10.6, 5.4 Hz, 5H), 7.11 (t, *J* = 7.3 Hz, 1H), 6.63 (dd, *J* = 15.5, 1.9 Hz, 1H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.1, 142.4, 138.1, 134.6, 129.9, 129.1, 128.9, 127.9, 124.5, 120.9, 120.0. **ESI-HRMS** for $C_{15}H_{14}NO$ $[M+H]^+$ calculated: 224.1070 found: 224.1067. Spectroscopic data was in agreement with previously reported data.[1]



3b

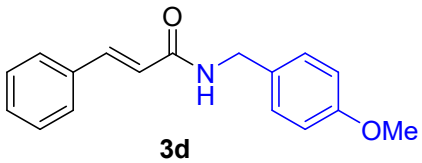
N-(Tert-butyl) cinnamamide (3b): Following the general procedure coupling reaction between cinnamic acid (50 mg, 0.34 mmol) and tertiary-butylamine (0.04 ml, 0.41 mmol)

afforded compound **3b** as a white solid (56 mg, 82%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.57 (d, *J* = 15.5 Hz, 1H), 7.47 (d, *J* = 1.4 Hz, 2H), 7.34 (dd, *J*= 7.5, 6.3 Hz, 3H), 6.33 (d, *J* = 15.5 Hz, 1H), 5.48 (s, 1H), 1.43 (s, 9H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 165.2, 140.3, 135.1, 129.5, 128.8, 127.7, 121.9, 51.6, 28.9. **ESI-HRMS** for $C_{13}H_{18}NO$ $[M+H]^+$ calculated: 204.1317, found: 204.1390. Spectroscopic data was in agreement with previously reported data.[2]



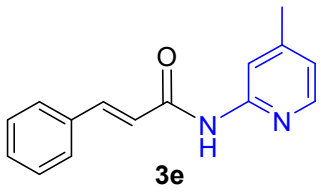
3c

N-Cyclopentylcinnamamide (3c): Following the general procedure coupling reaction between cinnamic acid (50 mg, 0.34 mmol) and cyclopentylamine (0.04 ml, 0.41 mmol) afforded compound **3c** as a white solid (62 mg, 85%) after purification by column chromatography (Hexane: EtOAc, 5:1 to 2:1).^{1}H **NMR (400 MHz, $CDCl_3$)** δ 7.61 (d, *J* = 15.6 Hz, 1H), 7.49 (dd, *J* = 7.5, 1.8 Hz, 2H), 7.36 (d, *J* = 6.6 Hz, 3H), 6.36 (dd, *J* = 15.6, 1.4 Hz, 1H), 5.58 (s, 1H), 4.35 (dd, *J* = 13.9, 7.0 Hz, 1H), 2.06 (dd, *J* = 12.4, 5.6 Hz, 2H), 1.77 – 1.66 (m, 4H), 1.45 (dd, *J* = 12.3, 6.3 Hz, 2H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 165.4, 140.8, 134.9, 129.6, 128.8, 127.8, 120.9, 51.4, 33.3, 23.8. **ESI-HRMS** for $C_{14}H_{18}NO$ $[M+H]^+$ calculated: 216.1318, found: 216.1391. Spectroscopic data was in agreement with previously reported data.[3]



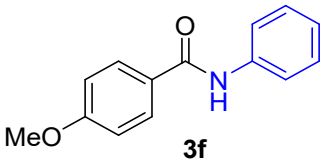
3d

N-(4-Methoxybenzyl)cinnamamide (3d): Following the general procedure coupling reaction between cinnamic acid (50 mg, 0.34 mmol) and 4-methoxybenzylamine (0.05 ml, 0.41 mmol) afforded compound **3d** as a white solid (78 mg, 86%)after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 (d, *J* = 15.6 Hz, 1H), 7.48 (dd, *J* = 6.5, 3.1 Hz, 2H), 7.39 – 7.31 (m, 3H), 7.25 (d, *J* = 8.4 Hz, 2H), 6.91 – 6.84 (m, 2H), 6.40 (d, *J* = 15.6 Hz, 1H), 5.98 (s, 1H), 4.49 (d, *J* = 5.7 Hz, 2H), 3.79 (s, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.7, 159.1, 141.3, 134.8, 130.3, 129.7, 129.4, 128.8, 127.8, 120.5, 114.2, 55.4, 43.4. **ESI-HRMS** for $C_{17}H_{18}NO_2$ $[M+H]^+$ calculated: 268.1262, found: 268.1335. Spectroscopic data was in agreement with previously reported data [4].



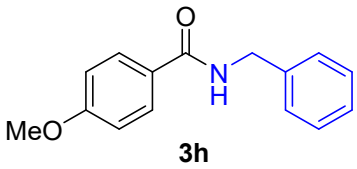
3e

N-(4-Methylpyridin-2-yl) cinnamamide (3e): Following the general procedure coupling reaction between cinnamic acid (50 mg, 0.34 mmol) and 2-amino-4-methylpyridine (44 mg, 0.41 mmol) afforded compound **3e** as a white solid (70 mg, 86%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.30 (s, 1H), 8.31 (s, 1H), 8.15 (d, *J* = 5.2 Hz, 1H), 7.82 (d, *J* = 15.6 Hz, 1H), 7.58 (dd, *J* = 6.5, 2.8 Hz, 2H), 7.47 – 7.38 (m, 3H), 6.96 (d, *J* = 5.0 Hz, 1H), 6.66 (d, *J* = 15.6 Hz, 1H), 2.46 (s, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.147, 151.7, 150.1, 147.4, 142.9, 134.4, 130.2, 128.9, 128.1, 121.1, 120.7, 114.9, 21.5. **ESI-HRMS** for $C_{15}H_{15}N_2O$ $[M+H]^+$ calculated: 239.1119, found: 239.1191. **mp:** 138-141°C.



3f

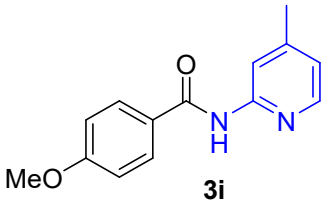
4-Methoxy-*N*-phenylbenzamide (3f): Following the general procedure coupling reaction between 4-methoxybenzoicacid (50 mg, 0.33 mmol) and aniline (0.03 ml, 0.39 mmol) at 50°C afforded compound **3f** as a white solid (66 mg, 88%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.88 – 7.82 (m, 2H), 7.75 (s, 1H), 7.63 (dd, *J* = 8.5, 0.9 Hz, 2H), 7.37 (t, *J* = 7.9 Hz, 2H), 7.14 (t, *J* = 7.4 Hz, 1H), 6.98 (d, *J* = 8.7 Hz, 2H), 3.88 (s, 3H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 165.3,162.5, 138.1, 129.1, 128.9, 127.2, 124.4, 120.2, 114.0, 55.5. **ESI-HRMS** for $[M+H]^+$ $C_{14}H_{14}NO_2$ calculated: 228.0958, found: 228.1031. Spectroscopic data was in agreement with previously reported data.[5]



3h

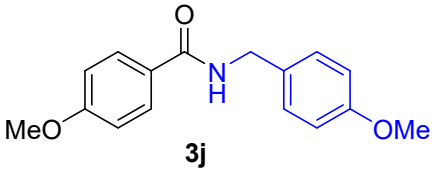
N-Benzyl-4-methoxybenzamide (3h): Following the general procedure coupling reaction between 4-methoxybenzoicacid (50 mg, 0.33 mmol), and benzylamine (0.04 ml, 0.39 mmol)

at 50 °C afforded compound **3h** as a white solid (73 mg, 92%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.79 – 7.72 (m, 2H), 7.35 (d, *J* = 4.4 Hz, 4H), 7.30 (d, *J* = 4.7 Hz, 1H), 6.95 – 6.89 (m, 2H), 6.37 (s, 1H), 4.63 (d, *J* = 5.7 Hz, 2H), 3.84 (s, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 166.9, 162.2, 138.5, 128.8, 128.7, 127.9, 127.6, 126.7, 113.8, 55.4, 44.1. **ESI-HRMS** for $C_{15}H_{16}NO_2$ $[M+H]^+$ calculated: 242.1174, found: 242.1176. Spectroscopic data was in agreement with previously reported data.[6]



3i

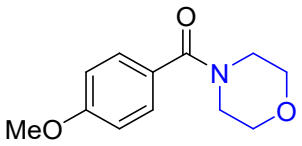
4-Methoxy-*N*-(4-methylpyridin-2-yl) benzamide (3i): Following the general procedure coupling reaction between 4-methoxybenzoicacid (50 mg, 0.33 mmol) and 2-amino-4-methylpyridine (42 mg, 0.39 mmol) at 50 °C afforded compound **3i** as a white solid (69mg, 86%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.55 (s, 1H), 8.23 (s, 1H), 8.13 (d, *J* = 4.8 Hz, 1H), 7.94 – 7.86 (m, 2H), 6.98 (dd, *J* = 9.3, 2.4 Hz, 2H), 6.89 (d, *J* = 5.0 Hz, 1H), 3.88 (s, 3H), 2.40 (s, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.2, 162.8, 151.7, 150.1, 147.3, 129.2, 126.5, 120.9, 114.7, 114.1, 55.5, 21.5. **ESI-HRMS** for $[M+H]^+$ $C_{14}H_{15}N_2O_2$ calculated: 243.1068, found: 243.1141. Spectroscopic data was in agreement with previously reported data.[7]



3j

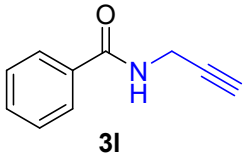
4-Methoxy-*N*-(4-methoxybenzyl) benzamide (3j): Following the general procedure coupling reaction between 4-methoxybenzoic acid (50 mg, 0.33 mmol) and 4-methoxybenzylamine (0.04 ml, 0.39 mmol) at 50 °C afforded compound **3j** as a white solid (80 mg, 89%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.77 – 7.72 (m, 2H), 7.30 – 7.26 (m, 2H), 6.95 – 6.85 (m, 4H), 6.26 (s, 1H), 4.56 (d, J = 5.5 Hz, 2H), 3.84 (s, 3H), 3.80 (s, 3H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.8, 162.2, 159.1, 130.5, 129.3, 128.8, 126.7, 114.2, 113.8, 55.4, 55.4, 43.6. **ESI-HRMS** for $[M+H]^+$ $C_{16}H_{18}NO_3$

calculated: 272.1209, found: 272.1282. Spectroscopic data was in agreement with previously reported data.[6]



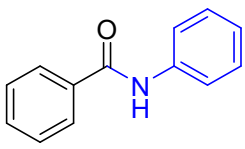
3k

(4-Methoxyphenyl) (morpholino)methanone (3k): Following the general procedure coupling reaction between 4-methoxybenzoic acid (50 mg, 0.33 mmol) and morpholine (0.03 ml, 0.39 mmol) at 50 °C afforded compound **3k** as a pale-yellow oil (52 mg, 71%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.41 – 7.36 (m, 2H), 6.94 – 6.89 (m, 2H), 3.83 (s, 3H), 3.67 (d, *J* = 18.0 Hz, 8H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.44, 160.92, 129.21, 127.32, 113.81, 66.93, 55.38, 29.71. **ESI-HRMS** for $[M+H]^+$ $C_{12}H_{16}NO_3$ calculated: 222.1122, found: 222.1125. Spectroscopic data was in agreement with previously reported data.[6]



3l

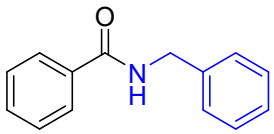
N-(Prop-2-yn-1-yl) benzamide (3l): Following the general procedure coupling reaction between benzoic acid (50 mg, 0.41 mmol) and propargylamine (0.03 ml, 0.50 mmol) at 50 °C afforded compound **3l** as a white solid (50 mg, 77%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.72 (d, *J* = 7.4 Hz, 2H), 7.45 (t, *J* = 7.1 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 2H), 6.24 (s, 1H), 4.19 (d, *J* = 2.4 Hz, 2H), 2.22 (s, 1H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 167.1, 133.8, 131.8, 128.7, 127.0, 79.5, 71.9, 29.8. **ESI-HRMS** for $[M+H]^+$ $C_{10}H_{10}NO$ calculated: 160.0682, found: 160.0755. Spectroscopic data was in agreement with previously reported data. [5,9]



3m

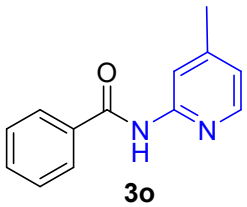
***N*-Phenylbenzamide (3m):** Following the general procedure coupling reaction between benzoic acid (50 mg, 0.41 mmol), and aniline (0.04 ml, 0.50 mmol) at 50°C afforded compound

3m as a white solid (68 mg, 84%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.87 (d, *J* = 7.8 Hz, 3H), 7.64 (dd, *J* = 8.5, 1.0 Hz, 2H), 7.55 (dd, *J* = 10.5, 4.1 Hz, 1H), 7.48 (t, *J* = 7.3 Hz, 2H), 7.37 (t, *J* = 7.9 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.8, 137.9, 135.0, 131.9, 129.1, 128.8, 127.0, 124.6, 120.2.**ESI-HRMS** for $[M+H]^+$ $C_{13}H_{12}NO$ calculated: 198.0852, found: 198.0925. Spectroscopic data was in agreement with previously reported data.[5]



3n

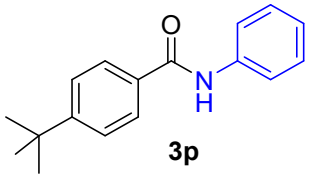
N-Benzylbenzamide (3n): Following the general procedure coupling reaction between benzoic acid (50 mg, 0.41 mmol) and benzylamine (0.04 ml, 0.50 mmol) afforded compound **3n** as a white solid (74 mg, 85%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.82 – 7.76 (m, 2H), 7.52 – 7.47 (m, 1H), 7.42 (ddd, *J* = 8.1, 6.6, 1.2 Hz, 2H), 7.36 (d, *J* = 4.4 Hz, 4H), 7.30 (d, *J* = 4.2 Hz, 1H), 6.45 (s, 1H), 4.65 (d, *J* = 5.7 Hz, 2H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 167.4, 138.2, 134.4, 131.6, 128.8, 128.6, 127.9, 127.6, 127.0, 44.2. **ESI-HRMS** for $[M+H]^+$ $C_{14}H_{14}NO$ calculated: 212.0992, found: 212.1065. Spectroscopic data was in agreement with previously reported data.[8]



3o

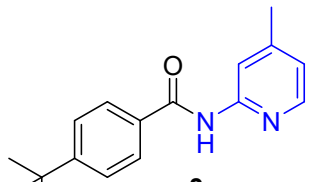
N-(4-Methylpyridin-2-yl) benzamide (3o): Following the general procedure coupling reaction between benzoic acid (50 mg, 0.41 mmol) and 2-amino-4-methoxypyridine (54 mg, 0.74 mmol) at 50 °C afforded compound **3o** as a white solid (73 mg, 84%) after purification by column chromatography (Hexane: EtOAc, 5:1 to 2:1).**^{1}H NMR (500 MHz, CDCl3)** δ 8.98 – 8.83 (m, 1H), 8.27 (s, 1H), 8.12 (t, J = 6.7 Hz, 1H), 7.95 (d, J = 7.3 Hz, 2H), 7.53 (dt, J = 15.1, 7.3 Hz, 3H), 6.90 (d, J = 4.7 Hz, 1H), 2.41 (s, 3H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 165.73, 151.6, 150.1, 147.5, 134.4, 132.2, 128.9, 127.2, 121.2, 114.7, 21.5. **ESI-HRMS** for $[M+H]^+$

$C_{13}H_{13}N_2O$ calculated: 213.0954, found: 213.1027. Spectroscopic data was in agreement with previously reported data.[7]



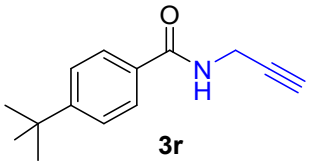
3p

4-(Tert-butyl)-N-phenylbenzamide (3p): Following the general procedure coupling reaction between 4-tert-butylbenzoic acid (50 mg, 0.28 mmol) and aniline (0.03 ml, 0.34 mmol) at 50 °C afforded compound **3p** as a white solid (63 mg, 89%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.81 (d, J = 8.5 Hz, 3H), 7.64 (dd, J = 8.5, 1.0 Hz, 2H), 7.51 (d, J = 8.6 Hz, 2H), 7.41 – 7.34 (m, 2H), 7.18 – 7.12 (m, 1H), 1.36 (s, 9H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.7, 155.5, 138.1, 132.1, 129.1, 126.9, 125.8, 124.5, 120.1, 35.0, 31.2. **ESI-HRMS** for $[M+H]^+$ $C_{17}H_{20}NO$ calculated: 254.1465, found: 254.1538. Spectroscopic data was in agreement with previously reported data.[5]



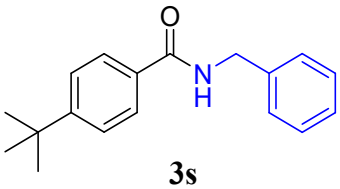
3q

4-(Tert-butyl)-*N*-(4-methylpyridin-2-yl) benzamide (3q): Following the general procedure coupling reaction between 4-tert-butylbenzoicacid (50 mg, 0.28 mmol) and 2-amino-4-methylpyridine (37 mg, 0.34 mmol) afforded compound **3q** as a white solid (62 mg, 83%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.60 (s, 1H), 8.26 (s, 1H), 8.15 (d, *J* = 4.7 Hz, 1H), 7.92 – 7.84 (m, 2H), 7.56 – 7.48 (m, 2H), 6.90 (d, *J* = 4.7 Hz, 1H), 2.41 (s, 3H), 1.36 (s, 9H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.6, 156.1, 151.4, 150.9, 146.4, 131.1, 127.2, 125.9, 121.0, 114.9, 35.1, 31.2, 21.0. **ESI-HRMS** for $[M+H]^+$ $C_{17}H_{21}N_2O$ calculated: 269.1581, found: 269.1654. Spectroscopic data was in agreement with previously reported data.[7]



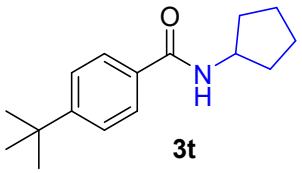
3r

4-(Tert-butyl)-N-(prop-2-yn-1-yl) benzamide (3r): Following the general procedure coupling reaction between 4-tert-butylbenzoicacid (50 mg, 0.28 mmol) and propargylamine (0.02 ml, 0.34 mmol) at 50 ℃ afforded compound **3r** as a white solid (48 mg, 80%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.75 – 7.70 (m, 2H), 7.48 – 7.43 (m, 2H), 6.28 (s, 1H), 4.25 (dd, *J* = 5.2, 2.6 Hz, 2H), 2.28 (t, *J* = 2.6 Hz, 1H), 1.33 (s, 9H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 167.1, 155.4, 130.9, 126.9, 125.6, 79.7, 71.8, 34.9, 31.2, 29.8. **ESI-HRMS** for $[M+H]^+$ $C_{14}H_{18}NO$ calculated: 216.1381, found: 216.1383. Spectroscopic data was in agreement with previously reported data.[9]



3s

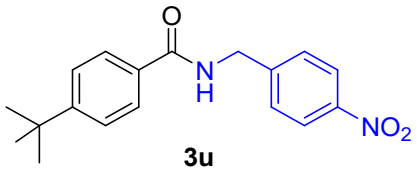
***N*-Benzyl-4-(tert-butyl) benzamide (3s):** Following the general procedure coupling reaction between 4-tert-butylbenzoicacid (50 mg, 0.28 mmol) and benzylamine (0.04 ml, 0.34 mmol) afforded compound **3s** as a white solid (66 mg, 88%) after purification by column chromatography (Hexane: EtOAc, 5:1 to 2:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.73 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 8.5 Hz, 2H), 7.35 (d, J = 4.3 Hz, 4H), 7.30 (d, J = 4.5 Hz, 1H), 6.38 (s, 1H), 4.65 (d, J = 5.7 Hz, 2H), 1.33 (s, 9H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 167.3, 155.1, 138.4, 131.5, 128.8, 127.9, 127.6, 126.8, 125.6, 44.1, 34.9, 31.2. **ESI-HRMS** for $[M+H]^+$ $C_{18}H_{22}NO$ calculated: 268.1693, found: 268.1696. Spectroscopic data was in agreement with previously reported data.[10]



3t

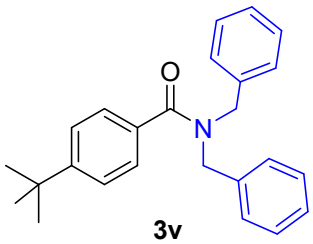
4-(Tert-butyl)-*N*-cyclopentylbenzamide (3t): Following the general procedure coupling reaction between 4-tert-butylbenzoicacid (50 mg, 0.28 mmol) and cyclopentylamine (0.03 ml,

0.34 mmol) afforded compound **3t** as a white solid (58 mg, 84%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.71 – 7.65 (m, 2H), 7.47 – 7.40 (m, 2H), 6.01 (s, 1H), 4.40 (d, *J* = 7.0 Hz, 1H), 2.14 – 2.04 (m, 2H), 1.76 – 1.66 (m, 4H), 1.53 – 1.43 (m, 2H), 1.33 (s, 9H).**^{13}C NMR (75 MHz, $CDCl_3$)** δ 167.1, 154.7, 132.1, 126.6, 125.5, 51.6, 34.9, 33.3, 31.2, 23.8. **ESI-HRMS** for $[M+H]^+$ $C_{16}H_{24}NO$ calculated: 246.1788, found: 246.1861. **mp:** 94-97 ℃.



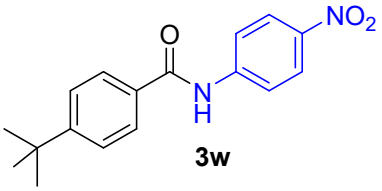
3u

4-(Tert-butyl)-*N*-(4-nitrobenzyl) benzamide (3u): Following the general procedure coupling reaction between 4-tert-butylbenzoicacid (50 mg, 0.28 mmol) and 4-nitrobenzylamine (65 mg, 0.34 mmol) at 50 ℃ afforded compound **3u** as a white solid (78 mg, 89%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.17 (d, *J* = 8.8 Hz, 2H), 7.76 (d, *J* = 8.5 Hz, 2H), 7.52 – 7.44 (m, 4H), 6.70 (s, 1H), 4.74 (d, *J* = 6.1 Hz, 2H), 1.34 (s, 9H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 167.6, 155.6, 147.2, 146.2, 130.8, 128.2, 126.9, 125.7, 123.9, 43.2, 35.0, 31.2. **ESI-HRMS** for $[M+H]^+$ $C_{18}H_{21}N_2O_3$ calculated: 313.1474, found: 313.1547. **mp:**149-153℃.



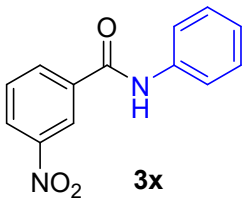
3v

***N, N*-Bibenzyl-4-(tert-butyl) benzamide (3v):** Following the general procedure coupling reaction between 4-tert-butylbenzoicacid (50 mg, 0.28 mmol) and dibenzyl amine (0.07 ml, 0.34 mmol) at 50 ℃ afforded compound **3v** as a white solid (89 mg, 89%) after purification by column chromatography (Hexane: EtOAc, 5:1 to 2:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.45 (d, *J* = 8.5 Hz, 2H), 7.41 – 7.27 (m, 10H), 7.17 (s, 2H), 4.69 (s, 2H), 4.44 (s, 2H), 1.30 (s, 9H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.5, 152.9, 137.1, 136.7, 133.1, 128.9, 128.7, 128.4, 127.6, 127.5, 127.1, 126.7, 125.5, 51.7, 46.9, 34.8, 31.2. **ESI-HRMS** for $[M+H]^+$ $C_{25}H_{28}NO$ calculated: 358.2092, found: 358.2165. **mp:** 100-103℃.



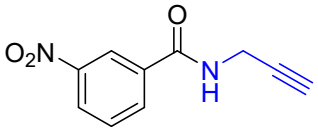
3w

4-(Tert-butyl)-*N*-(4-nitrophenyl) benzamide (3w): Following the general procedure coupling reaction between 4-tertbutylbenzoicacid (50 mg, 0.28 mmol) and 4-nitroaniline (47 mg, 0.34 mmol) at 50 °C afforded compound **3w** as a white solid (74 mg, 89%) after purification by column chromatography (Hexane: EtOAc, 5:1 to 2:1).**^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.49 (t, *J* = 2.1 Hz, 1H), 8.16 – 8.09 (m, 2H), 7.99 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.85 – 7.81 (m, 2H), 7.53 (t, *J* = 8.5 Hz, 3H), 1.36 (s, 9H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.9, 156.2, 148.6, 139.3, 131.1, 129.9, 127.0, 125.9, 118.9, 114.9, 35.1, 31.2. **ESI-HRMS** for $[M+H]^+$ $C_{17}H_{19}N_2O_3$ calculated: 299.1318, found: 299.1392. Spectroscopic data was in agreement with previously reported data.[11]



3x

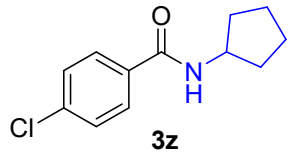
3-Nitro-*N*-phenylbenzamide (3x): Following the general procedure coupling reaction between 3-nitrobenzoicacid (50 mg, 0.30 mmol) and aniline (0.03 ml, 0.36 mmol) at 50 °C afforded compound **3x** as a pale yellow solid (62 mg, 85 after purification by column chromatography (Hexane: EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.70 (s, 1H), 8.43 – 8.38 (m, 1H), 8.26 (d, *J* = 7.7 Hz, 1H), 7.98 (s, 1H), 7.74 – 7.62 (m, 3H), 7.40 (t, *J* = 7.9 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 163.4, 148.3, 137.3, 136.6, 133.4, 130.1, 129.3, 126.4, 125.3, 121.9, 120.6. **ESI-HRMS** for $[M+H]^+$ $C_{13}H_{11}N_2O_3$ calculated: 243.0697, found: 243.0770. Spectroscopic data was in agreement with previously reported data.[12]



3y

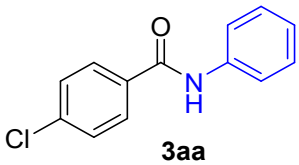
3-Nitro-*N*-(prop-2-yn-1-yl) benzamide (3y): Following the general procedure coupling reaction between 3-nitrobenzoicacid (50 mg, 0.30 mmol) and propargylamine (0.02 ml, 0.36 mmol) at 50 °C afforded compound **3y** as a yellow solid (51 mg, 83%) after purification by

column chromatography (Hexane: EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.62 (s, 1H), 8.39 (d, *J* = 8.2 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 7.68 (t, *J* = 8.0 Hz, 1H), 6.45 (s, 1H), 4.30 (dd, *J* = 5.1, 2.5 Hz, 2H), 2.33 (t, *J* = 2.5 Hz, 1H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 164.7, 148.3, 135.4, 133.3, 130.0, 126.5, 121.87, 78.8, 72.6, 30.1. **ESI-HRMS** for $[M+H]^+$ $C_{10}H_9N_2O_3$ calculated: 205.0540, found: 205.0613. Spectroscopic data was in agreement with previously reported data.[13]



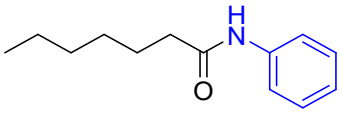
3z

4-Chloro-*N*-cyclopentylbenzamide (3z): Following the general procedure coupling reaction between 4-chlorobenzoicacid (50 mg, 0.32 mmol) and cyclopentylamine (0.04 ml, 0.38 mmol) at 50 °C afforded compound **3z** as a white solid (58 mg, 81%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.71 – 7.66 (m, 2H), 7.40 (d, *J* = 8.6 Hz, 2H), 5.99 (s, 1H), 4.39 (dd, *J* = 13.9, 6.9 Hz, 1H), 2.16 – 2.05 (m, 2H), 1.69 (ddt, *J* = 13.3, 9.8, 7.0 Hz, 4H), 1.55 – 1.43 (m, 2H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 166.1, 137.5, 133.3, 128.8, 128.3, 51.9, 33.2, 23.8. **ESI-HRMS** for $[M+H]^+$ $C_{12}H_{15}ClNO$ calculated: 224.0765, found: 224.0838. Spectroscopic data was in agreement with previously reported data.[14]



3aa

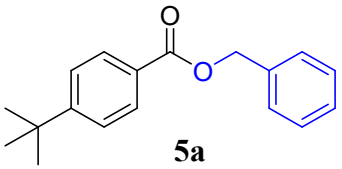
4-Chloro-*N*-phenylbenzamide (3aa): Following the general procedure coupling reaction between 4-chlorobenzoicacid (50 mg, 0.32 mmol) and aniline (0.03 ml, 0.38 mmol) at 50 °C afforded compound **3aa** as a white solid (62 mg, 84%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.84 (d, *J* = 8.6 Hz, 2H), 7.76 (s, 1H), 7.67 – 7.62 (m, 2H), 7.53 – 7.47 (m, 2H), 7.44 – 7.37 (m, 2H), 7.23 – 7.16 (m, 1H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.6, 138.2, 137.7, 133.4, 129.1, 129.1, 128.5, 124.8, 120.3. **ESI-HRMS** for $[M+H]^+$ $C_{13}H_{11}ClNO$ calculated: 232.0453, found: 232.0526. Spectroscopic data was in agreement with previously reported data.[5]



3ab

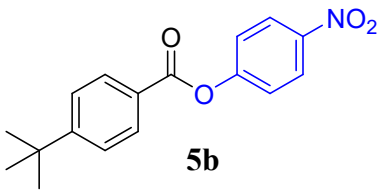
***N*-Phenylheptanamide (3ab):** Following the general procedure coupling reaction between heptanoic acid (50 mg, 0.38 mmol) and aniline (0.04 ml, 0.46 mmol) at 50 °C afforded compound **3ab** as a light-brown oil (57.6 mg, 74%) after purification by column chromatography (Hexane: EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.51 (d, *J* = 7.8 Hz, 1H), 7.31 (t, *J* = 7.9 Hz, 1H), 7.25 – 7.06 (m, 2H), 6.76 (tt, *J* = 7.5, 1.0 Hz, 1H), 6.71 – 6.67 (m, 1H), 2.34 (td, *J* = 7.6, 3.0 Hz, 2H), 1.77 – 1.58 (m, 2H), 1.43 – 1.23 (m, 6H), 0.89 (dd, *J* = 7.1, 6.1 Hz, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 171.9, 138.1, 128.9, 124.2, 119.9, 37.8, 31.6, 28.9, 25.7, 22.5, 14.1. **ESI-HRMS** for $[M+H]^+$ $C_{13}H_{20}NO$ calculated: 206.1466, found: 206.1539. Spectroscopic data was in agreement with previously reported data.[1]

Ester substrate Scope:



5a

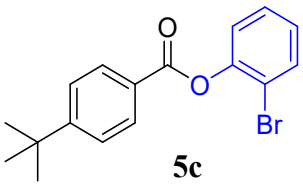
Benzyl 4-(tert-butyl) benzoate (5a): Following the general procedure coupling reaction between 4-tert-butylbenzoic acid (50 mg, 0.28 mmol) and benzyl alcohol (0.03 ml, 0.33 mmol) at 50 °C afford compound **5a** as a clear oil (49 mg, 65%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.03 – 7.99 (m, 2H), 7.47 – 7.41 (m, 4H), 7.40 – 7.30 (m, 3H), 5.36 (s, 2H), 1.33 (s, 9H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 166.5, 156.7, 136.3, 129.6, 128.6, 128.2, 128.1, 127.4, 125.38, 66.5, 35.1, 31.2. **ESI-HRMS** for $[M+Na]^+$ $C_{18}H_{20}NaO_2$ calculated: 291.1275, found: 291.1348. Spectroscopic data was in agreement with previously reported data.[15]



5b

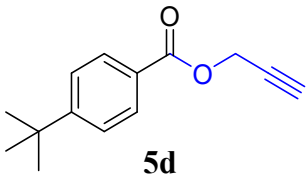
4-Nitrophenyl 4-(tert-butyl) benzoate (5b): Following the general procedure coupling reaction between 4-tert-butylbenzoic acid (50 mg, 0.28 mmol) and 4-nitro phenol (47 mg, 0.33 mmol) at 50 °C afford compound **5b** as a white solid (48 mg, 57%) after purification by column

chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.32 (d, *J* = 9.2 Hz, 2H), 8.13 (d, *J* = 8.7 Hz, 2H), 7.56 (d, *J* = 8.7 Hz, 2H), 7.41 (d, *J* = 9.2 Hz, 2H), 1.38 (s, 9H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.3, 158.3, 155.9, 145.4, 130.3, 125.8, 125.7, 125.3, 122.7, 35.3, 31.1. **ESI-HRMS** for $[M+H]^+$ $C_{17}H_{18}NO_4$ calculated: 300.1156, found: 300.1229. Spectroscopic data was in agreement with previously reported data.[16]



5c

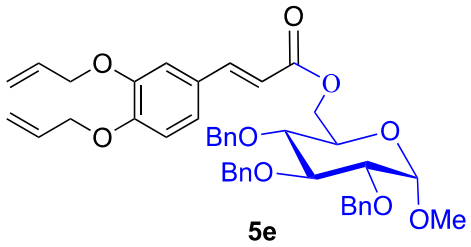
2-Bromophenyl 4-(tert-butyl) benzoate (5c): Following the general procedure coupling reaction between 4-tert-butylbenzoic acid (50 mg, 0.28 mmol) and 2-bromo phenol (0.04 ml, 0.33 mmol) at 50 °C afford compound **5c** as a light-yellow solid (48 mg, 51%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.22 – 8.16 (m, 2H), 7.65 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.58 – 7.52 (m, 2H), 7.37 (td, *J* = 8.1, 1.5 Hz, 1H), 7.29 – 7.24 (m, 1H), 7.15 (td, *J* = 8.0, 1.5 Hz, 1H), 1.37 (s, 9H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 164.3, 157.7, 148.6, 133.4, 130.4, 128.5, 127.3, 126.2, 125.7, 124.0, 116.4, 35.3, 31.2. **ESI-HRMS** for $[M+H]^+$ $C_{17}H_{18}BrO_2$ calculated: 333.0406, found: 333.0479. **mp:** 61-64°C.



5d

Prop-2-yn-1-yl-4-(tert-butyl) benzoate (5d): Following the general procedure coupling reaction between 4-tert-butylbenzoic acid (50 mg, 0.28 mmol) and propargyl alcohol (0.02 ml, 0.33 mmol) at 50 °C afford compound **5d** as a light-yellow oil (36 mg, 59%) after purification by column chromatography (Hexane:EtOAc, 5:1 to 2:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.00 (d, *J* = 8.6 Hz, 2H), 7.46 (d, *J* = 8.6 Hz, 2H), 4.91 (d, *J* = 2.5 Hz, 2H), 2.50 (t, *J* = 2.5 Hz, 1H), 1.34 (s, 9H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 161.1, 152.3, 124.9, 121.9, 120.7, 73.2, 70.1, 47.5, 30.4, 26.4. **ESI-HRMS** for $[M+H]^+$ $C_{14}H_{17}O_2$ calculated: 217.1131, found: 217.1203. Spectroscopic data was in agreement with previously reported data.[17]

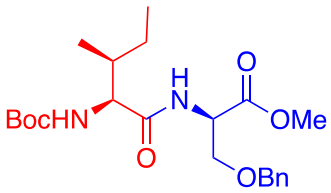
((2R,3R,4S,5R,6S)-3,4,5-tris(benzyloxy)-6-Methoxytetrahydro-2H-pyran-2-yl)methyl 3-(3,4-bis(allyloxy)phenyl)propanoate (5e):



5e

Following the general procedure allylated caffeic acid derivative (50 mg, 0.19 mmol) and α-methoxy-6-hydroxy-2,3,4-tribenzylglucopyranoside (160 mg, 0.34 mmol) afforded compound **5e** as a white solid (75 mg, 56%) purifying through column chromatography (Hexane:EtOAc, 7:1 to 3:1). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.51 (d, *J* = 15.9 Hz, 1H), 7.33 – 7.15 (m, 15H), 6.99 (d, *J* = 5.1 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 1H), 6.18 (d, *J* = 15.9 Hz, 1H), 6.01 (dtd, *J* = 22.2, 10.3, 5.2 Hz, 2H), 5.40 – 5.30 (m, 2H), 5.23 (d, *J* = 10.5 Hz, 2H), 4.94 (d, *J* = 10.7 Hz, 1H), 4.83 – 4.71 (m, 3H), 4.62 – 4.49 (m, 7H), 4.37 (dd, *J* = 12.0, 4.3 Hz, 1H), 4.30 (dd, *J* = 12.0, 1.9 Hz, 1H), 3.96 (t, *J* = 9.2 Hz, 1H), 3.81 (dd, *J* = 10.0, 1.8 Hz, 1H), 3.54 – 3.45 (m, 2H), 3.32 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 166.9, 150.8, 148.6, 145.2, 138.6, 138.1, 137.9, 133.1, 132.9, 128.5, 128.1, 128.1, 128.0, 128.0, 127.8, 127.5, 122.9, 118.0, 118.0, 115.3, 113.4, 112.6, 98.1, 82.1, 79.9, 77.5, 75.9, 75.2, 73.4, 70.0, 69.8, 68.8, 62.9, 55.3. **ESI-HRMS** for $[M+Na]^+$ $C_{43}H_{46}O_9Na^+$ calculated: 729.3040, found: 730.3016.

Methyl-*O*-benzyl-*N*-((tert-butoxycarbonyl)-*L*-isoleucyl)-*D*-serinate (8):

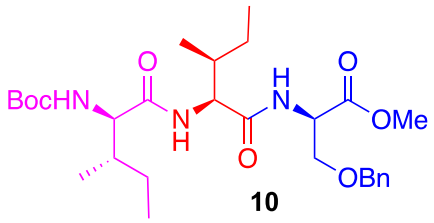


8

Following the general procedure coupling reaction between carboxylic acid **6** (1.0 g, 4.32 mmol) and corresponding amine **7** (0.904 mg, 4.32 mmol) afforded compound **8** as a white solid (1.6 g, 76%) after purifying through column chromatography (Hexane:EtOAc, 4:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.39 – 7.20 (m, 5H), 6.68 (d, *J* = 8.2 Hz, 1H), 5.10 (d, *J* = 8.6 Hz, 1H), 4.78 – 4.70 (m, 1H), 4.61 – 4.39 (m, 2H), 4.05 (t, *J* = 7.4 Hz, 1H), 3.89 (ddd, *J* = 9.5, 3.3, 1.7 Hz, 1H), 3.81 – 3.58 (m, 4H), 1.88 (d, *J* = 8.8 Hz, 1H), 1.44 (d, *J* = 1.8 Hz, 10H), 1.21 –

1.08 (m, 1H), 1.01 – 0.84 (m, 6H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 171.3, 170.4, 155.6, 137.4, 128.9, 128.5, 127.9, 127.7, 125.3, 120.4, 109.3, 73.3, 69.5, 59.1, 52.5, 37.7, 28.3, 24.7, 15.5, 11.6. Spectroscopic data was in agreement with previously reported data.[18]

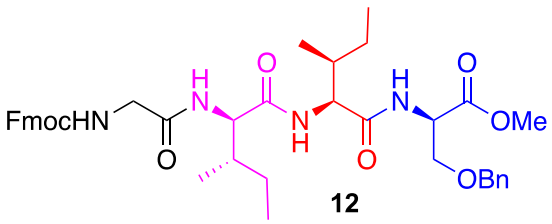
Methyl-*O*-benzyl-*N*-(tert-butoxycarbonyl)-*D*-alloisoleucyl-*L*-isoleucyl-*D*-serinate (10):



10

Compound **8** (1004 mg 3.11 mmol) was treated with 20 ml CH_2Cl_2/TFA (1:1) in room temperature for 1 hour resulting Boc deprotected amine after workup with sodium bicarbonate solution. Following the general procedure coupling reaction between carboxylic acid **9** (600 mg, 2.59 mmol), and crude amine afforded compound **10** as a white solid (0.92 g, 65%) purifying through column chromatography (Hexane:EtOAc, 3:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.38 – 7.23 (m, 5H), 6.72 – 6.63 (m, 2H), 4.99 (s, 1H), 4.72 (dt, *J* = 8.1, 3.3 Hz, 1H), 4.58 – 4.35 (m, 3H), 4.23 – 4.06 (m, 1H), 3.90 (dd, *J* = 9.5, 3.2 Hz, 1H), 3.73 (s, 3H), 3.64 (dd, *J* = 9.5, 3.2 Hz, 1H), 2.04 – 1.85 (m, 3H), 1.44 (s, 9H), 1.29 – 1.12 (m, 2H), 0.93 (dt, *J* = 14.1, 7.1 Hz, 9H), 0.82 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 171.74, 170.74, 170.29, 155.74, 137.35, 128.50, 127.97, 127.74, 125.28, 120.36, 109.34, 104.91, 73.33, 69.37, 58.17, 57.38, 52.55, 37.64, 37.16, 28.29, 26.46, 24.77, 15.33, 14.22, 11.74, 11.38. **ESI-HRMS:** $C_{28}H_{45}N_3O_7$ (M+H): calculated: 536.3336, found: 536.3336. Spectroscopic data was in agreement with previously reported data.[18]

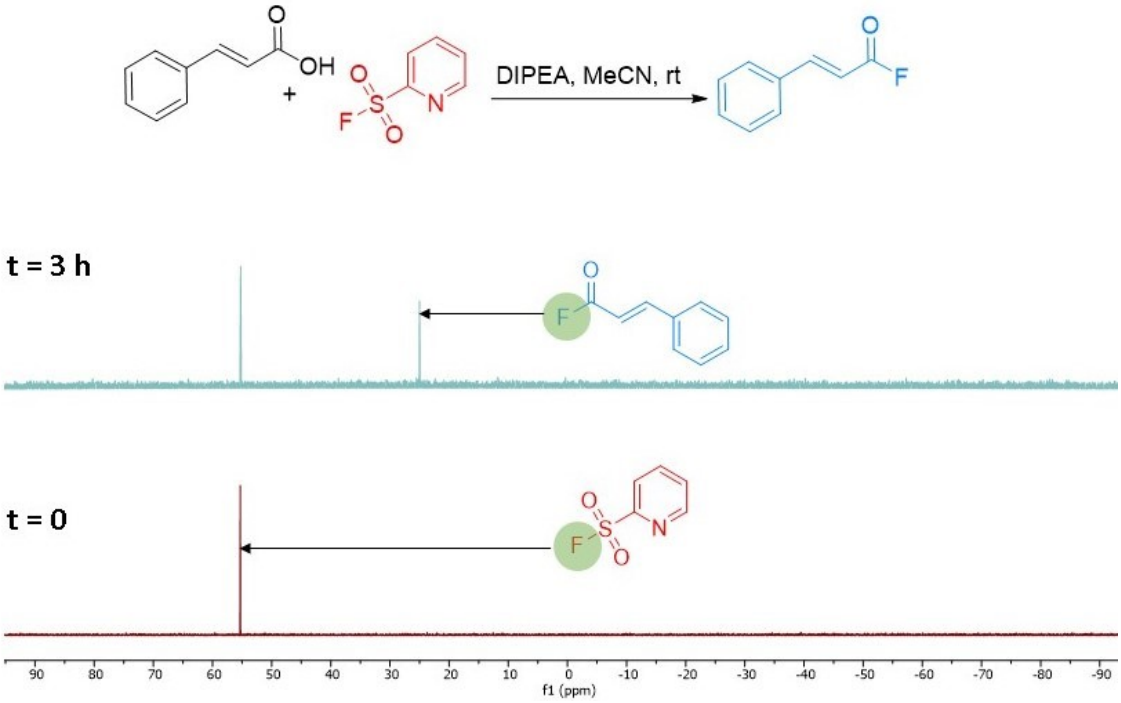
Methyl-*N*-(((9H-fluoren-9-yl) methoxy) carbonyl) glycyl-*D*-alloisoleucyl-*L*-isoleucyl-*O*-benzyl-*D*-serinate (12):



12

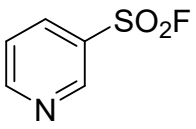
Compound **10** (352 mg, 0.807 mmol) was treated with 10 ml CH_2Cl_2/TFA (1:1) in room temperature for 1 hour resulting Boc deprotected amine after workup with sodium bicarbonate solution. Following the general procedure coupling between carboxylic acid **11** (200 mg, 0.673 mmol), and crude amine afford compound **12** as a colorless oil (262 mg, 54%) purifying through column chromatography (Hexane:EtOAc, 1:3). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.75 (d, *J* = 7.4 Hz, 2H), 7.57 (d, *J* = 6.8 Hz, 2H), 7.39 (td, *J* = 7.5, 2.7 Hz, 2H), 7.30 (d, *J* = 7.6 Hz, 4H), 7.24 (s, 1H), 7.23 – 7.17 (m, 2H), 6.74 (d, *J* = 8.8 Hz, 1H), 5.71 (s, 1H), 4.80 – 4.72 (m, 1H), 4.60 – 4.49 (m, 2H), 4.38 (ddq, *J* = 24.1, 17.5, 8.3 Hz, 5H), 4.17 (t, *J* = 6.9 Hz, 1H), 3.96 (d, *J* = 4.5 Hz, 1H), 3.84 (dd, *J* = 9.5, 3.5 Hz, 1H), 3.73 (d, *J* = 3.7 Hz, 1H), 3.65 (d, *J* = 4.6 Hz, 3H), 3.60 (dd, *J* = 9.6, 3.2 Hz, 1H), 1.97 – 1.88 (m, 2H), 1.47 (dd, *J* = 13.0, 5.5 Hz, 2H), 1.42 (d, *J* = 4.5 Hz, 1H), 1.20 – 1.14 (m, 2H), 0.97 – 0.94 (m, 5H), 0.90 (dt, *J* = 6.3, 3.6 Hz, 7H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 171.1, 170.9, 170.6, 169.3, 156.6, 143.8, 141.3, 137.3, 128.5, 127.9, 127.7, 127.1, 125.1, 119.9, 73.2, 69.6, 67.3, 57.6, 56.9, 52.5, 47.1, 44.5, 37.7, 31.9, 29.7, 29.4, 26.3, 24.8, 22.7, 15.5, 14.5, 14.2, 11.7, 11.4. **ESI-HRMS** for $C_{40}H_{51}N_4O_8$ (M+H): calculated: 715.3701, found: 715.3709.

NMR studies for understanding reaction mechanisms:



Scheme S1: ^{19}F NMR of reaction mixture without amine

Synthesis of sulfonyl fluorides:



P-2

3-Pyridinesulfonyl Fluoride: 3-Pyridinesulfonyl Chloride (500 mg, 2.82 mmol) was treated with 2equiv. KHF_2 (440 mg, 5.63 mmol) by dissolving in a biphasic solution of H_2O and acetonitrile. The reaction mixture was stirred at room temperature for 3 hours, followed by the reaction mixture was transferred to a separating funnel, and the organic layer was extracted with ethyl acetate, and dried over sodium sulphate. Next, the organic part was concentrated by rotary evaporation to give the desired 3-pyridinesulfonyl fluoride as a white solid. Spectroscopic data was in agreement with previously reported data.[19]

P-3

8-Quinolinesulfonyl Fluoride: 8-Puinolinesulfonyl Chloride (500 mg, 2.19 mmol) was treated with 2 equiv. KHF_2 (343 mg, 4.39 mmol) by dissolving in a biphasic solution of H_2O and acetonitrile. The reaction mixture was stirred at room temperature for 3 hours, followed by the reaction mixture was transferred to a separating funnel, and organic layer was extracted with ethyl acetate, and dried over sodium sulphate. Next, the organic part was concentrated by rotary evaporation to give the desired 8-quinolinesulfonyl fluoride as a white solid. Spectroscopic data was in agreement with previously reported data.[20]

References:

[1] Ling, L.; Chen, C.; Luo, M.; Zeng, X. Chromium-Catalyzed Activation of Acyl C-O Bonds with Magnesium for Amidation of Esters with Nitroarenes. *Org. Lett.* **2019**, 21, 1912−1916. https://doi.org/10.1021/acs.orglett.9b00554.

[2] Jiang, H.; Liu, B.; Li, Y.; Wang, A.; Huang, H. Synthesis of Amides via Palladium-CatalyzedAmidation of Aryl Halides. *Org. Lett.* **2011**, 13, 1028–1031, https://doi.org/10.1021/ol103081y.

[3] Santanu Ghosh, Chandan K.; Jana. Rapid access to cinnamamides and piper amides *via* three component coupling of arylaldehydes, amines, and Meldrum's acid. *Green Chem*., **2019**, 21, 5803–5807. https://doi.org/10.1039/C9GC02937K.

[4] Iqbal, N.; Cho, E. J. Formation of Carbonyl Compounds from Amines through Oxidative C-N Bond Cleavage Using Visible Light Photocatalysis and Applications to N-PMB-Amide Deprotection. *Adv. Synth. Catal.* **2015**, 357, 2187-2192. https://doi.org/10.1002/adsc.201500257.

[5] Wang, S.-M.; Zhao, C.; Zhang, X.; Qin, H.-L. Clickable coupling of carboxylic acids and amines at room temperature mediated by SO_2F_2: a significant breakthrough for the construction of amides and peptide linkages. *Org. Biomol. Chem*. **2019**, 17, 4087–4101. https://doi.org/10.1039/C9OB00699K.

[6] Tu, Y.; Yuan, L.; Wang, T.; Wang, C.; Ke, J.; Zhao, J. Palladium-Catalyzed Oxidative Carbonylation of Aryl Hydrazines with CO and O_2 at Atmospheric Pressure. *J. Org. Chem.* **2017**, *82*, 4970– 4976,https://doi.org/10.1021/acs.joc.7b00499.

[7] Kumar, M.; Verma, S.; Verma, A. K. Ru(II)-Catalyzed Oxidative Olefination of Benzamides: Switchable Aza-Michael and Aza-Wacker Reaction for Synthesis of Isoindolinones. *Org. Lett*. **2020**, 22, 4620− 4626. https://doi.org/10.1021/acs.orglett.0c01237.

[8] Dev, D.; Palakurthy, N. B.; Thalluri, K.; Chandra, J.; Mandal, B. Ethyl 2-Cyano-2-(2-nitrobenzenesulfonyloxyimino) acetate (*o*-NosylOXY): A Recyclable Coupling Reagent for Racemization-Free Synthesis of Peptide, Amide, Hydroxamate, and Ester. *J. Org. Chem.* **2014**, *79*, 5420– 5431.https://doi.org/10.1021/jo500292m.

[9] Herszman, J. D.; Berger, M.; Waldvogel, S. R. Fluorocyclization of *N*-Propargylamides to Oxazoles by Electrochemically Generated $ArIF_2$. *Org. Lett.* **2019**, *21*, 7893– 7896, https://doi.org/10.1021/acs.orglett.9b02884.

[10] Kunishima, M.; Yoshimura, K.; Morigaki, H.; Kawamata, R.; Terao, K.; Tani, S. Cyclodextrin-Based Artificial Acyltransferase: Substrate-Specific Catalytic Amidation of Carboxylic Acids in Aqueous Solvent. *J. Am. Chem. Soc.* **2001**, 123, 10760−10761.https://doi.org/10.1021/ja011660m.

[11] Wang, R.; Liu, H.; You, Y.-Y.; Wang, X.-Y.; Lv, B.-B.; Cao, L.-Q.; Xue, J.-Y.; Xu, Y.-G.; Shi, L. Discovery of novel VEGFR-2 inhibitors embedding 6,7-dimethoxyquinazoline and diarylamide fragments. *Bioorganic Med. Chem. Lett.* **2021**, 36, 127788.https://doi.org/10.1016/j.bmcl.2021.127788.

[12] Nordeman, P.; Odell, L. R.; Larhed, M. Aminocarbonylations employing Mo(CO)6 and a bridged two-vial system: Allowing the use of nitro group substituted aryl iodides and aryl bromides. *J. Org. Chem.* **2012**, *77*, 11393−11398. https://doi.org/10.1021/jo302322w.

[13] Nalivela, K. S.; Rudolph, M.; Baeissa, E. S.; Alhogbi, B. G.; Mkhalid, I. A. I.; Hashmi, A. S. K. Sequential Au/Cu Catalysis: A Two Catalyst One-Pot Protocol for the Enantioselective Synthesis of Oxazole α-Hydroxy Esters via Intramolecular Cyclization/Intermolecular Alder- Ene Reaction. *Adv. Synth. Catal*. **2018**, 360, 2183−2190.https://doi.org/10.1002/adsc.201800246.

[14] P.; Yu, Y.; Wang, Z.; Zeng, Y.; Chen. Metal-Free C−N or C−C Bond Cleavages of α-Azido Ketones: An Oxidative-Amidation Strategy for the Synthesis of α-Ketothioamides and Amides. J. Org. Chem. **2019**, 84, 14883– 14891.https://doi.org/10.1021/acs.joc.9b01777.

[15] Lu, B.; Zhu, F.; Sun, H. M.; Shen, Q. Esterification of the Primary Benzylic C–H Bonds with Carboxylic Acids Catalyzed by Ionic Iron (III) Complexes Containing an Imidazolinium Cation. *Org. Lett*. **2017**, 19, 1132– 1135. https://doi.org/10.1021/acs.orglett.7b00148.

[16] N.; Fattahi, M.; Ayubi, A.; Ramazani.Amidation and esterification of carboxylic acids with amines and phenols by N, N′-diisopropylcarbodiimide: A new approach for amide and ester bond formation in water. Tetrahedron **2018**, 74, 4351–4356. https://doi.org/10.1016/j.tet.2018.06.064.

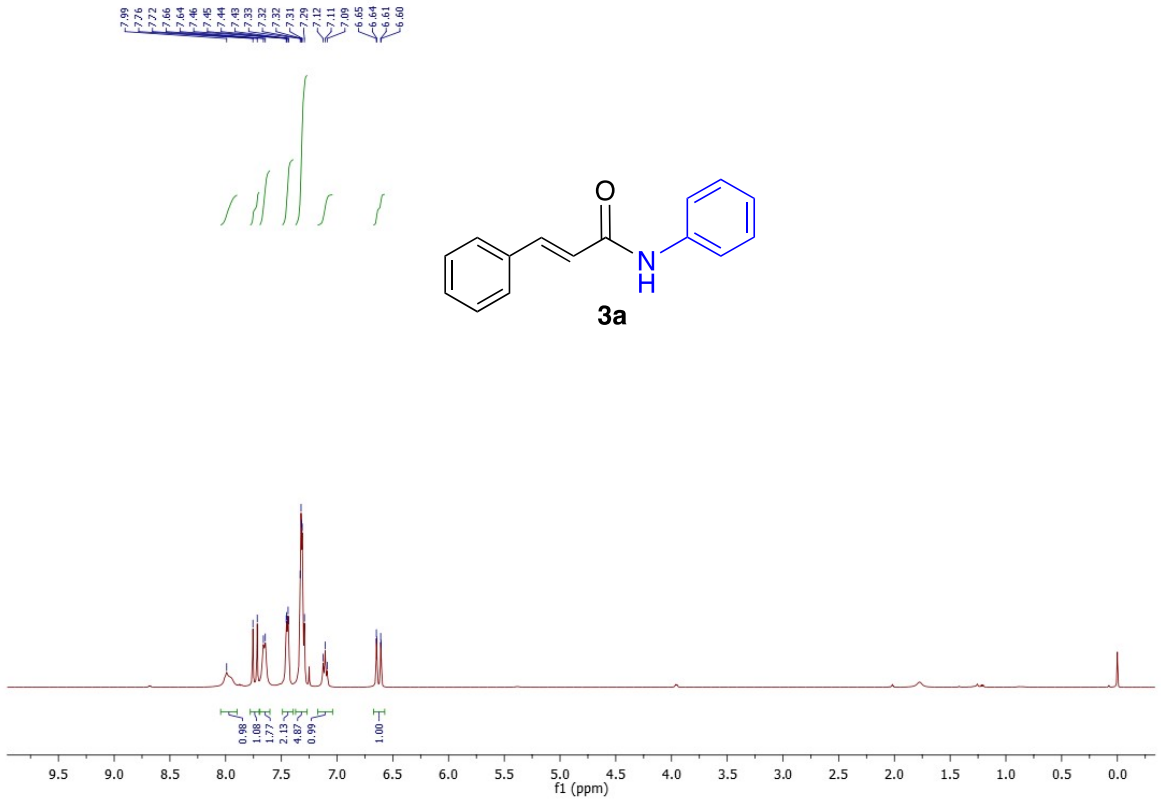
[17] G.R.; Pereira, G.C.; Brandao, L.M.; Arantes, H.A.; Oliveira, R.C.; Paula, M.F.; Nascimento, F.M.; Santos, R.K.; Rocha, J.C.; Lopes, A.B.; Oliveira. 7-Chloroquinolinotriazoles: Synthesis by the azide–alkyne cycloaddition click chemistry, antimalarial activity, cytotoxicity and SAR studies. *Eur. J. Med. Chem*. **2014**, 73, 295-309. https://doi.org/10.1016/j.ejmech.2013.11.022.

[18] D. Sangeetha, K. Nayani, V. Nomula, P. S. Mainkar and S. Chandrasekhar, Gram-scale solutionphase synthesis of heptapeptide side chain of teixobactin, Synlett, 2019, 30, 2268–2272. https://doi.org/10.1055/s-0039-1690232.

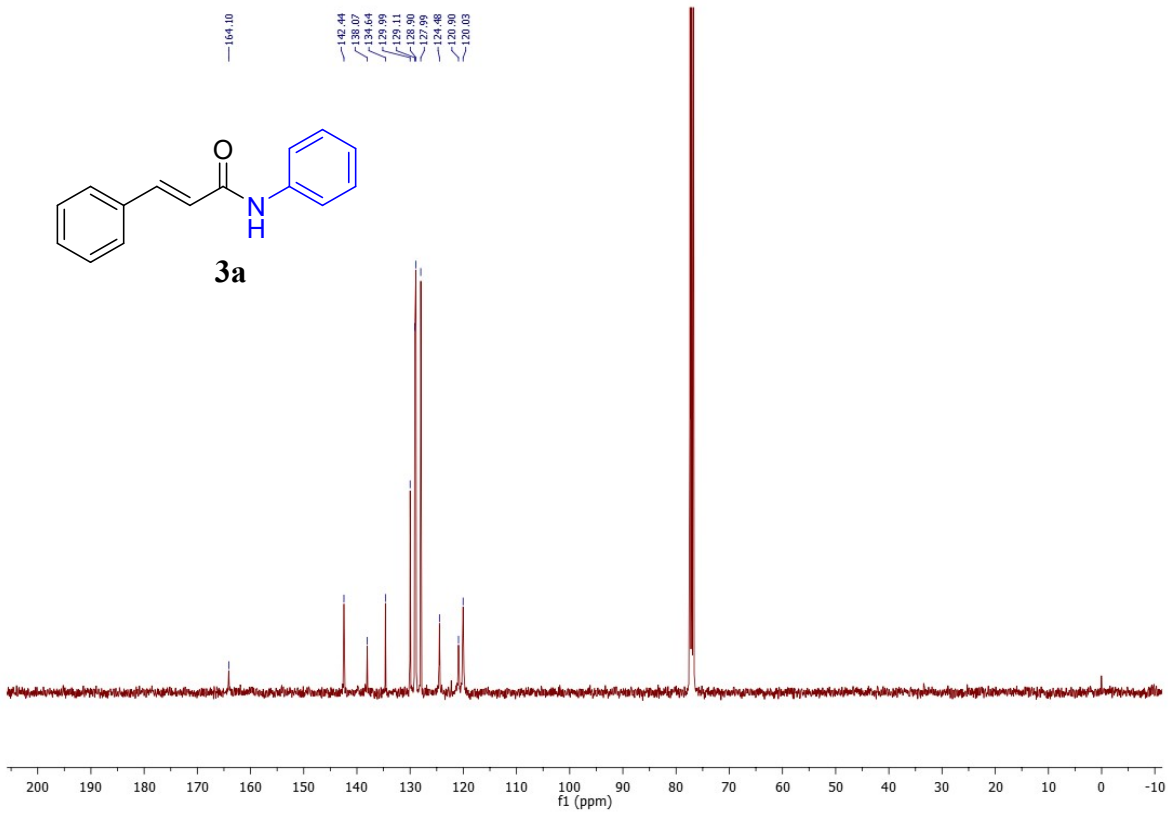
[19] Dong, Jiajia, Larissa Krasnova, M. G. Finn, and K. Barry Sharpless. "Sulfur (VI) fluoride exchange (SuFEx): another good reaction for click chemistry." *Angewandte Chemie International Edition* 53, no. 36 (**2014**): 9430-9448. https://doi.org/10.1002/anie.201309399.

[20] Li, Shaohua, Laura T. Beringer, Siyuan Chen, and Saadyah Averick. "Combination of AGET ATRP and SuFEx for post-polymerization chain-end modifications." *Polymer* 78 (**2015**): 37-41. https://doi.org/10.1016/j.polymer.2015.09.055.

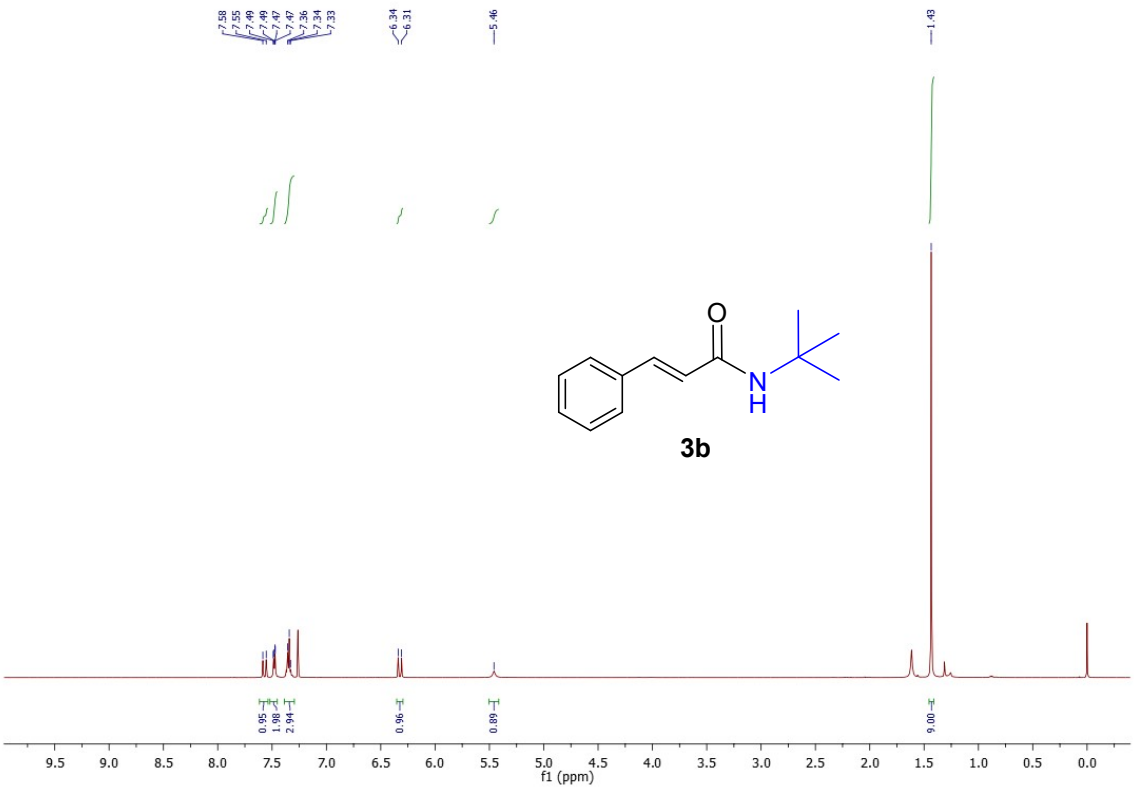
Spectra:



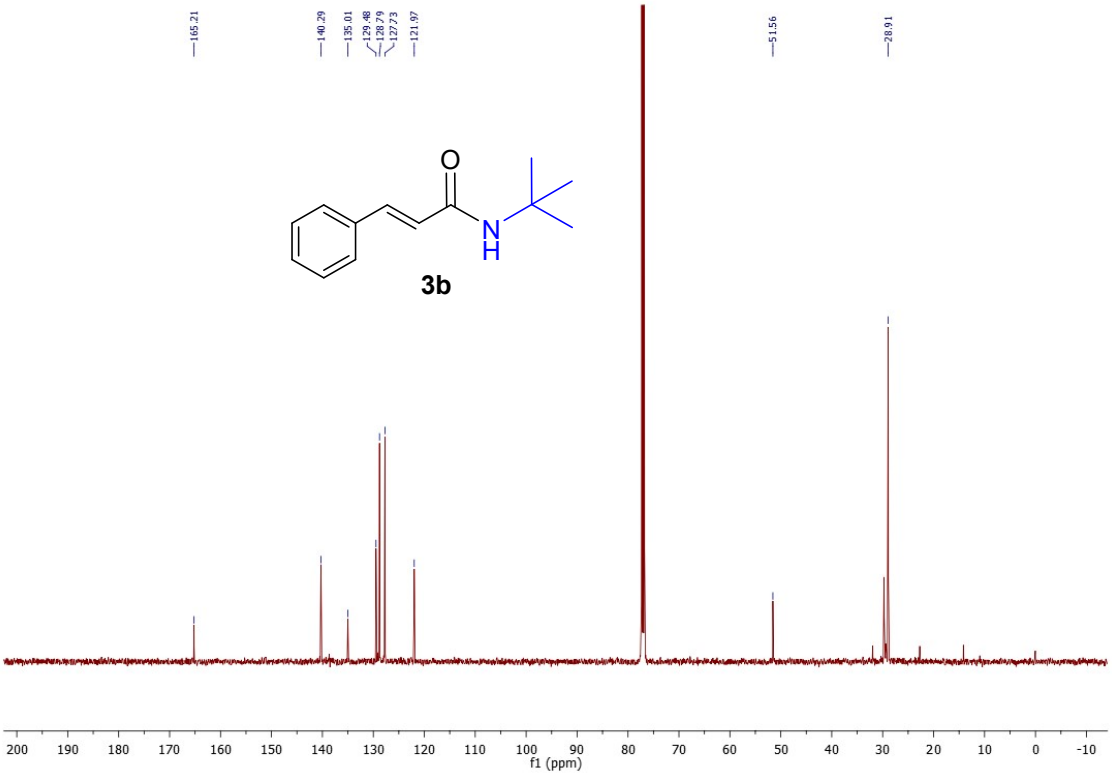
^{1}H NMR of Compound **3a (400 MHz, $CDCl_3$)**



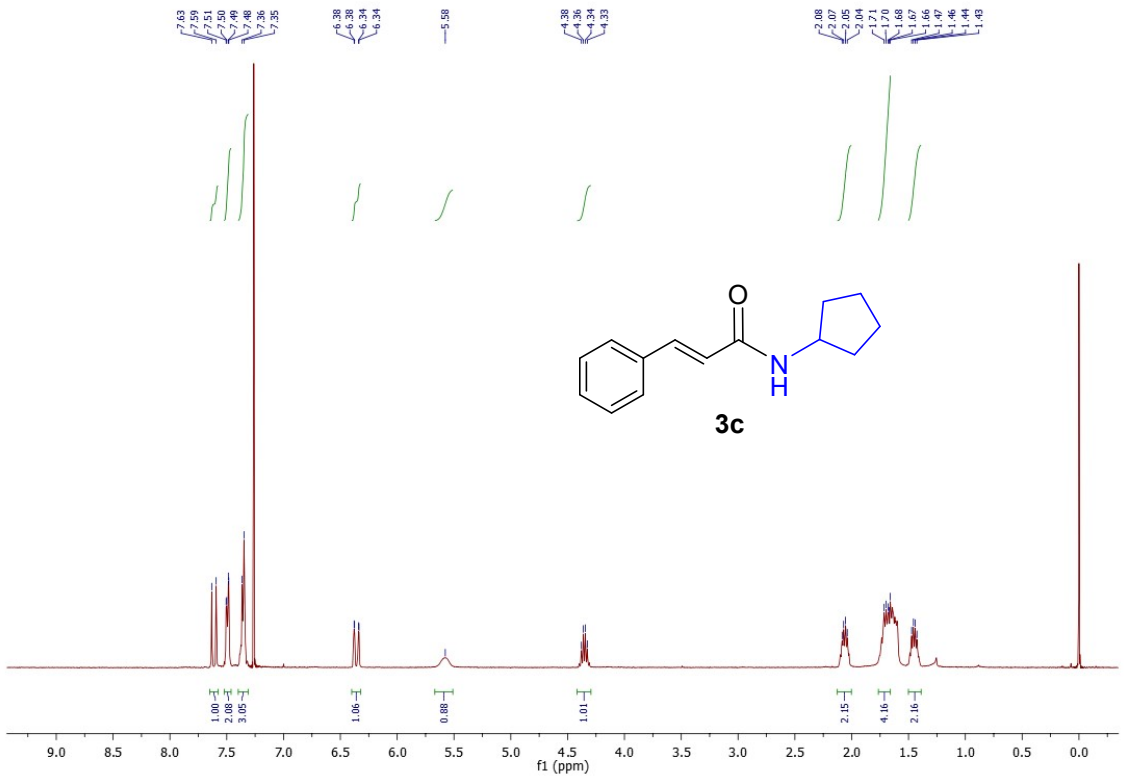
^{13}C NMR of Compound **3a (101 MHz, $CDCl_3$)**



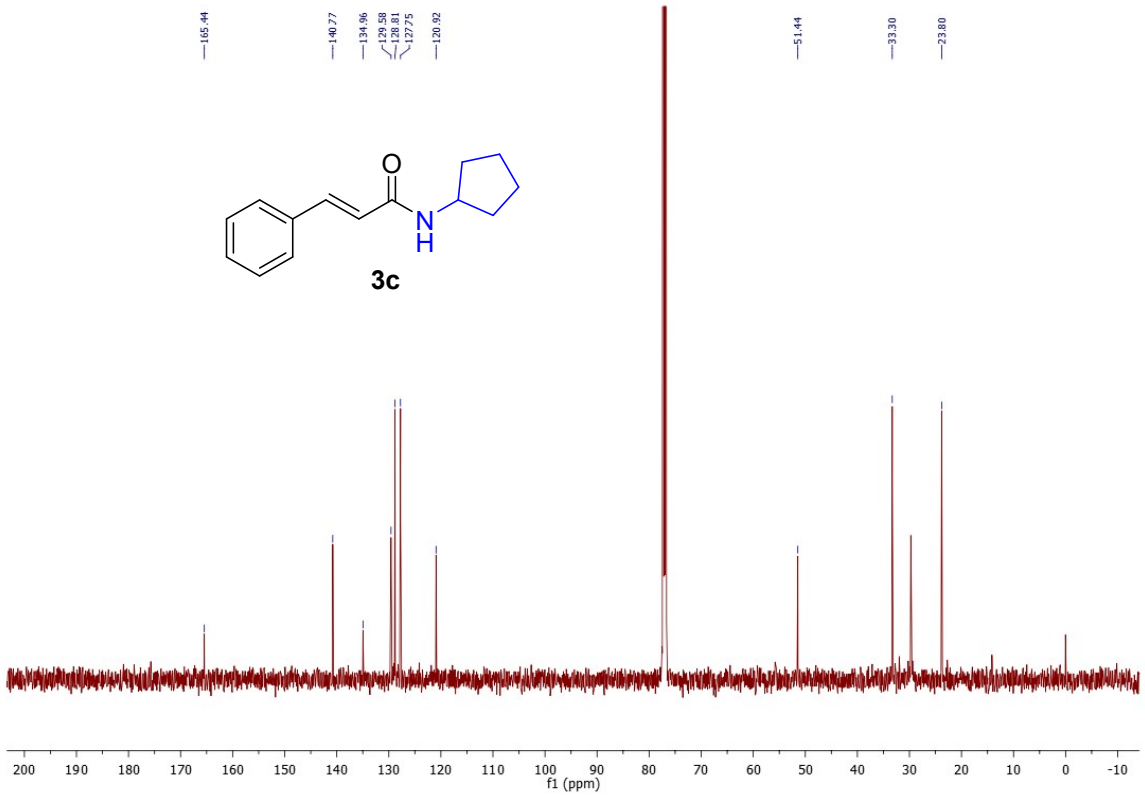
^{1}H NMR of Compound **3b (500 MHz, $CDCl_3$)**



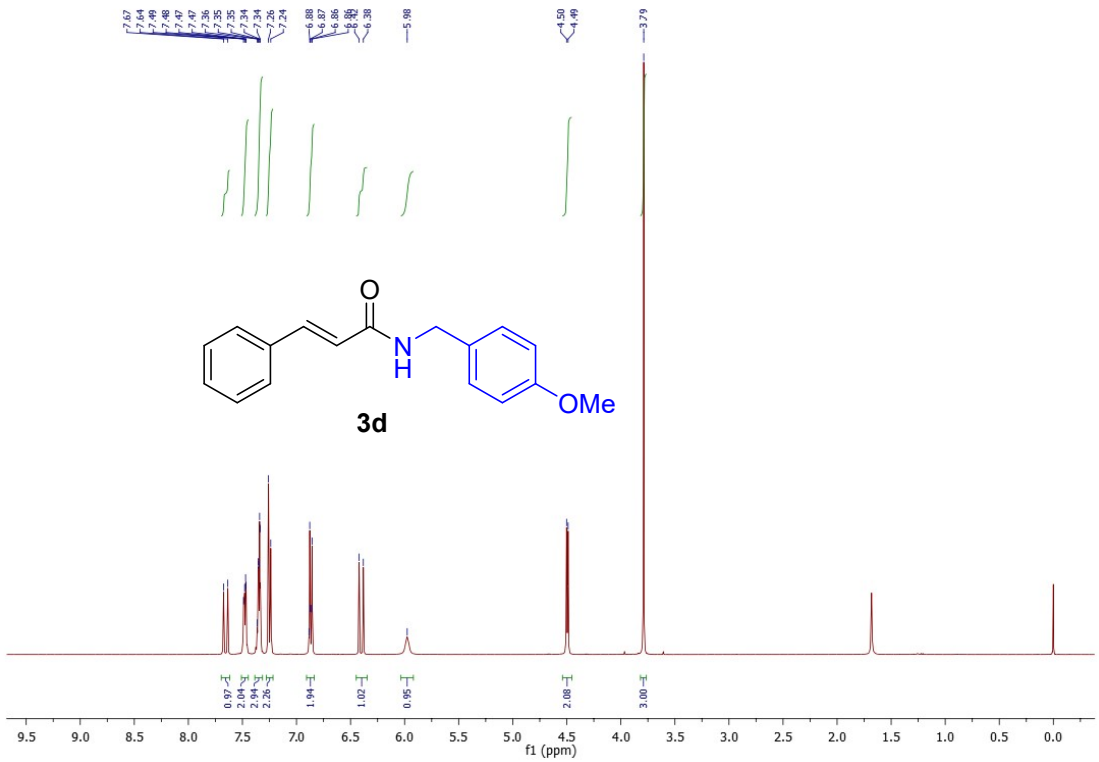
^{13}C NMR of Compound **3b (126 MHz, $CDCl_3$)**



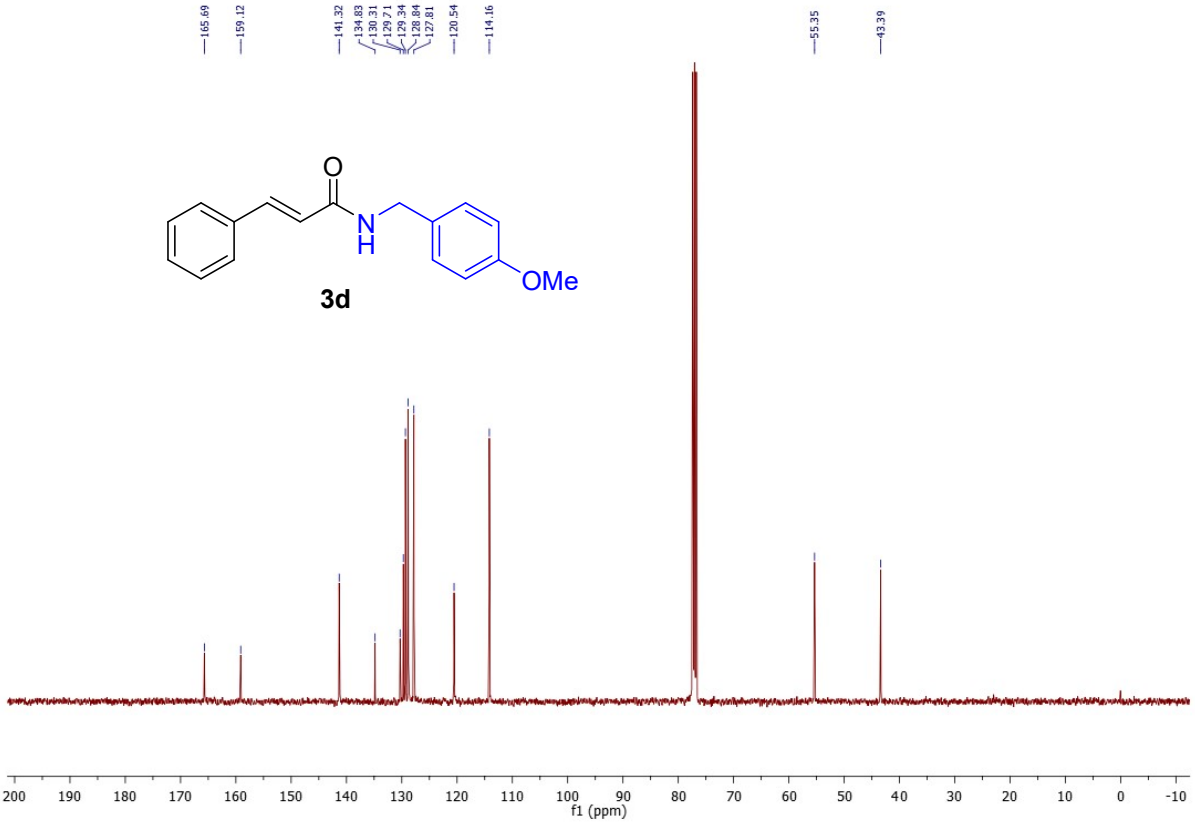
^{1}H NMR of Compound **3c (400 MHz, CDCl3)**



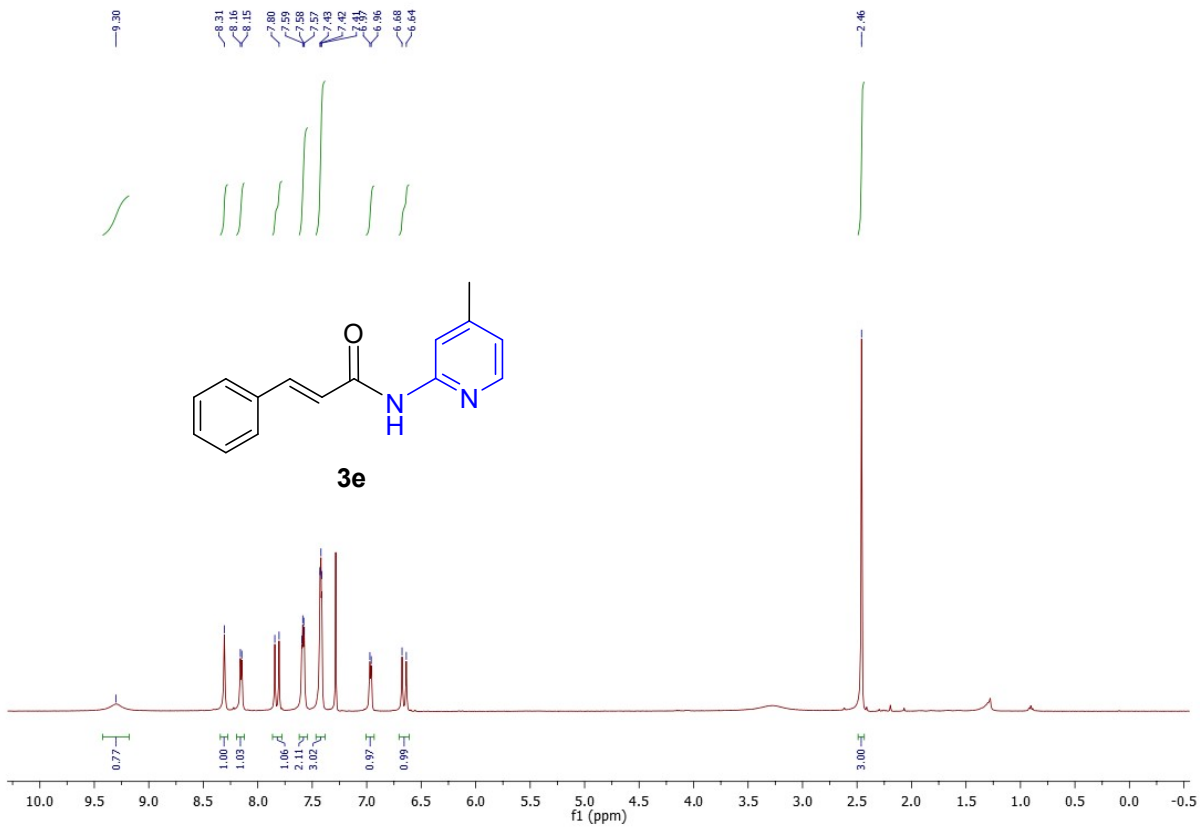
^{13}C NMR of Compound **3c (126 MHz, $CDCl_3$)**



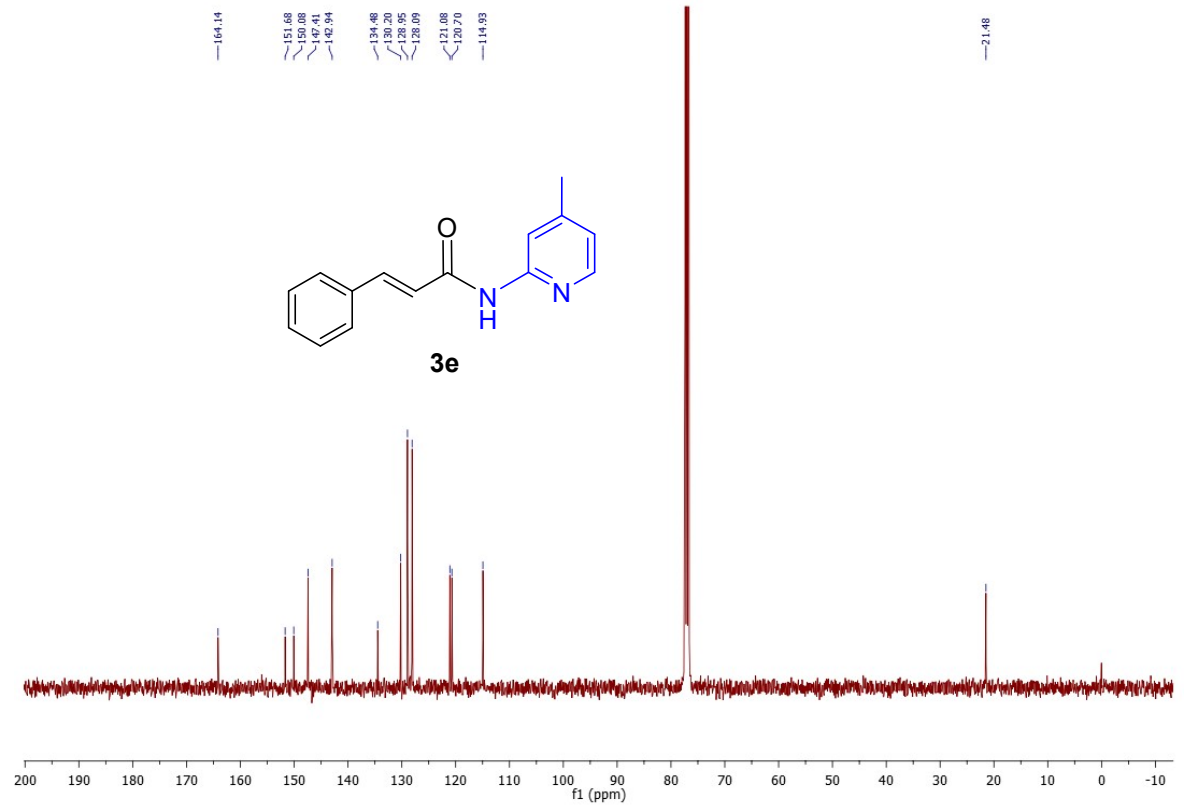
^{1}H NMR of Compound **3d (400 MHz, CDCl3)**



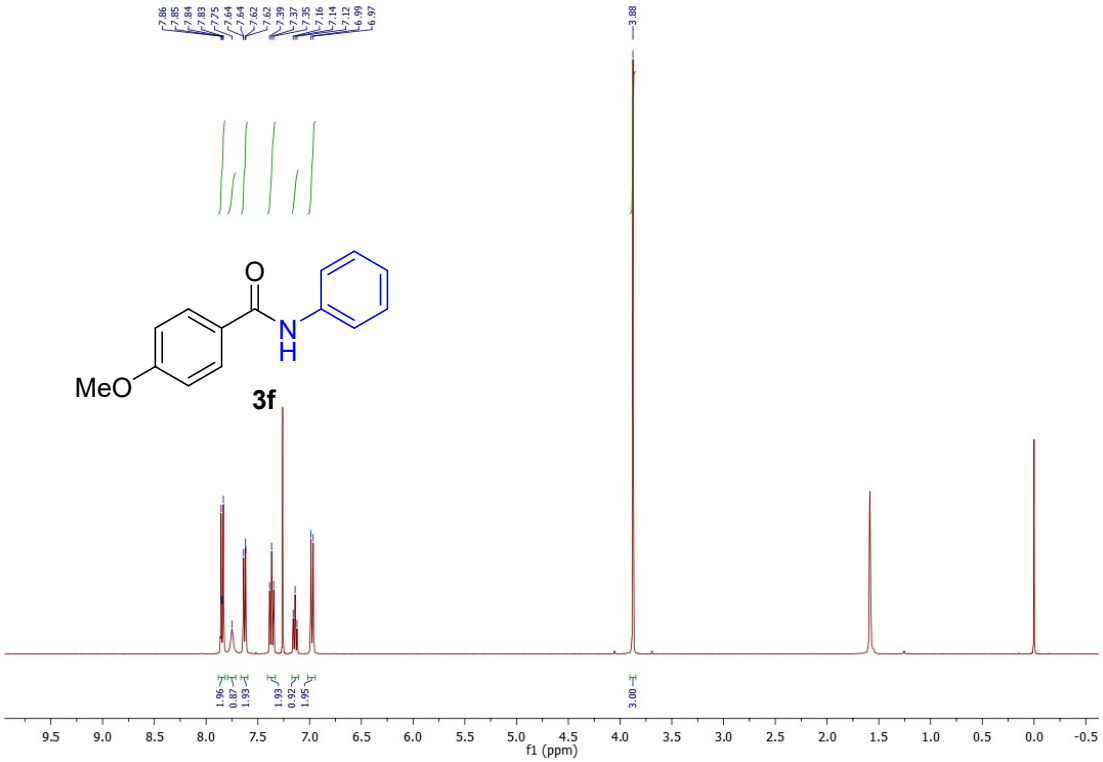
^{13}C NMR of Compound **3d (101 MHz, $CDCl_3$)**



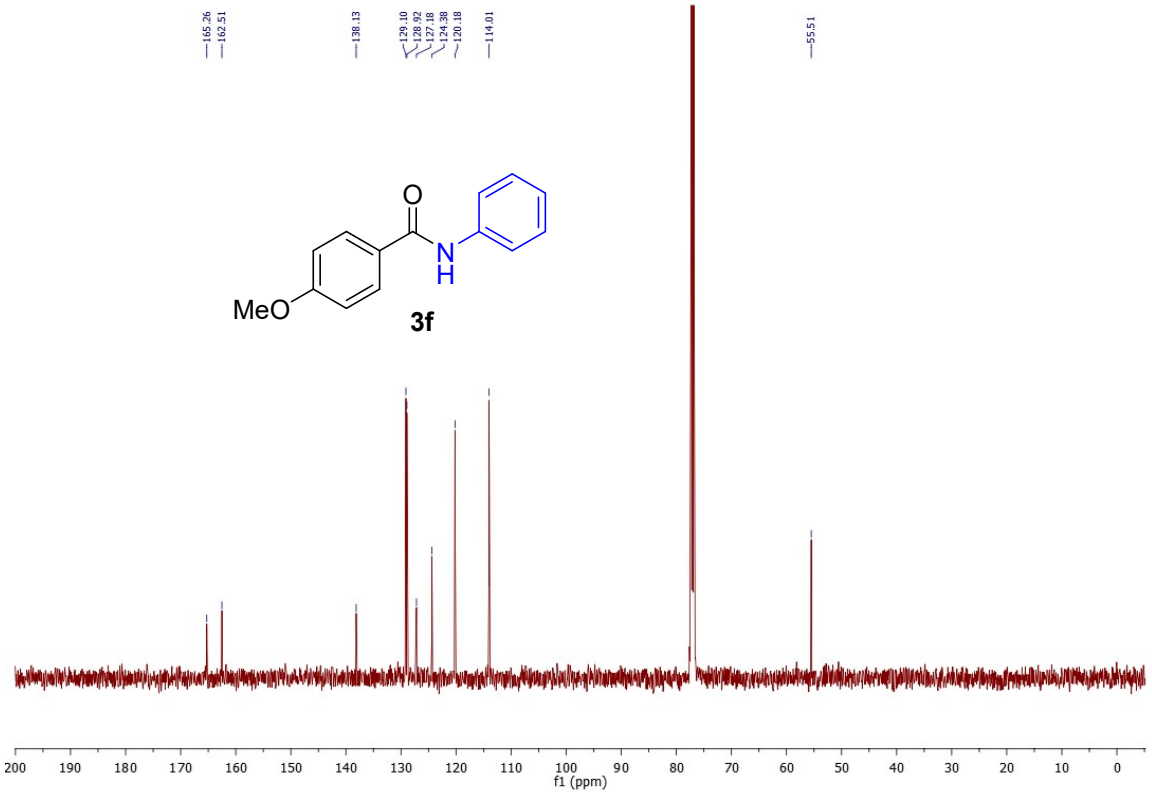
^{1}H NMR of Compound **3e (400 MHz, $CDCl_3$)**



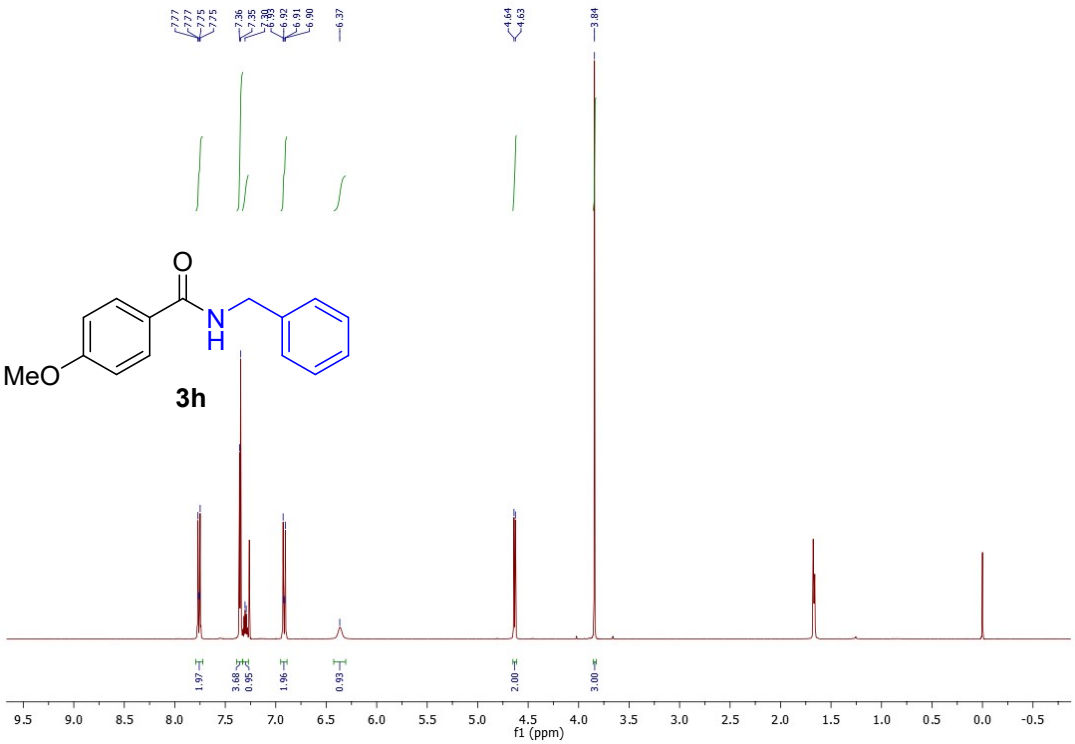
^{13}C NMR of Compound **3e (101 MHz, $CDCl_3$)**



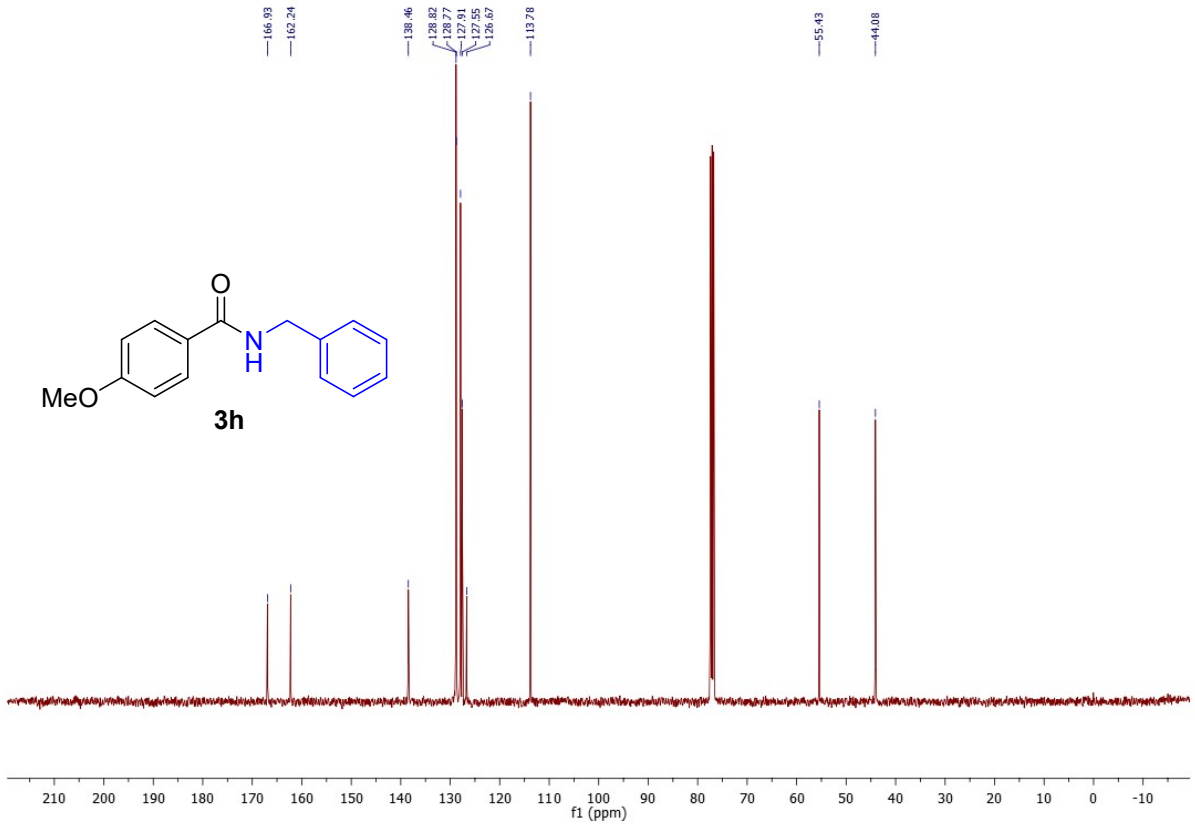
^{1}H NMR of Compound **3f (400 MHz, $CDCl_3$)**



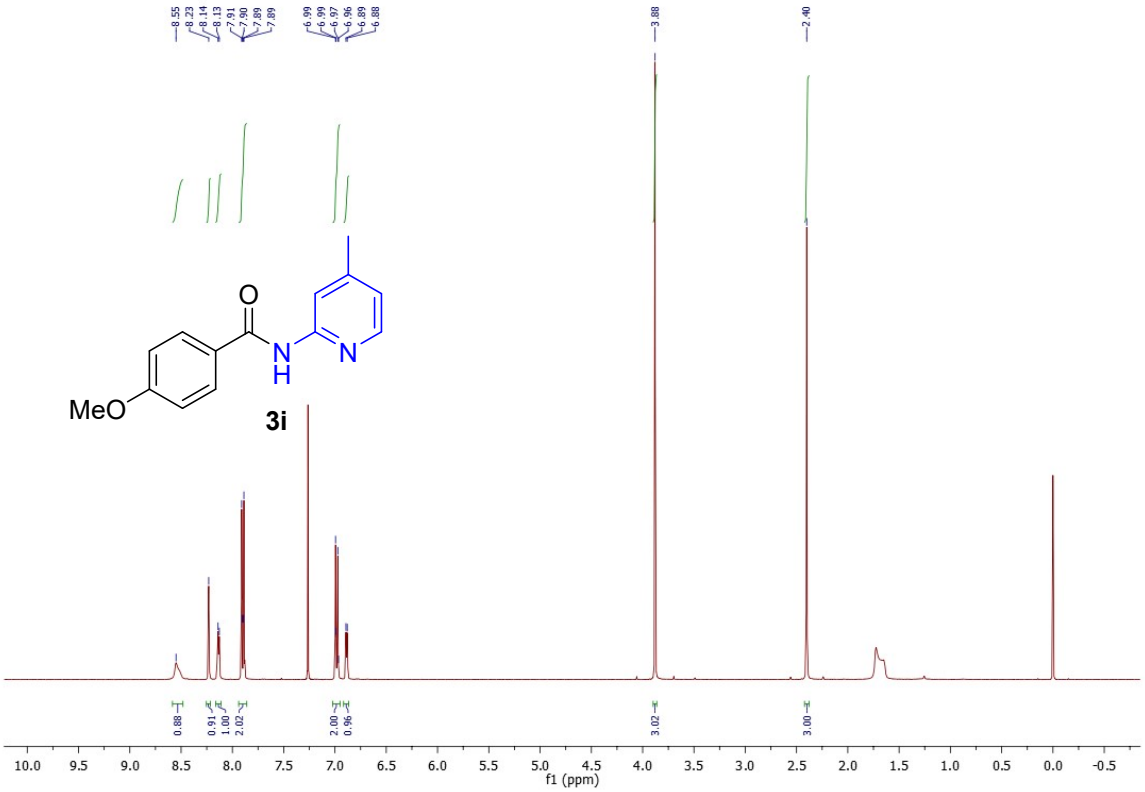
^{13}C NMR of Compound **3f (126 MHz, $CDCl_3$)**



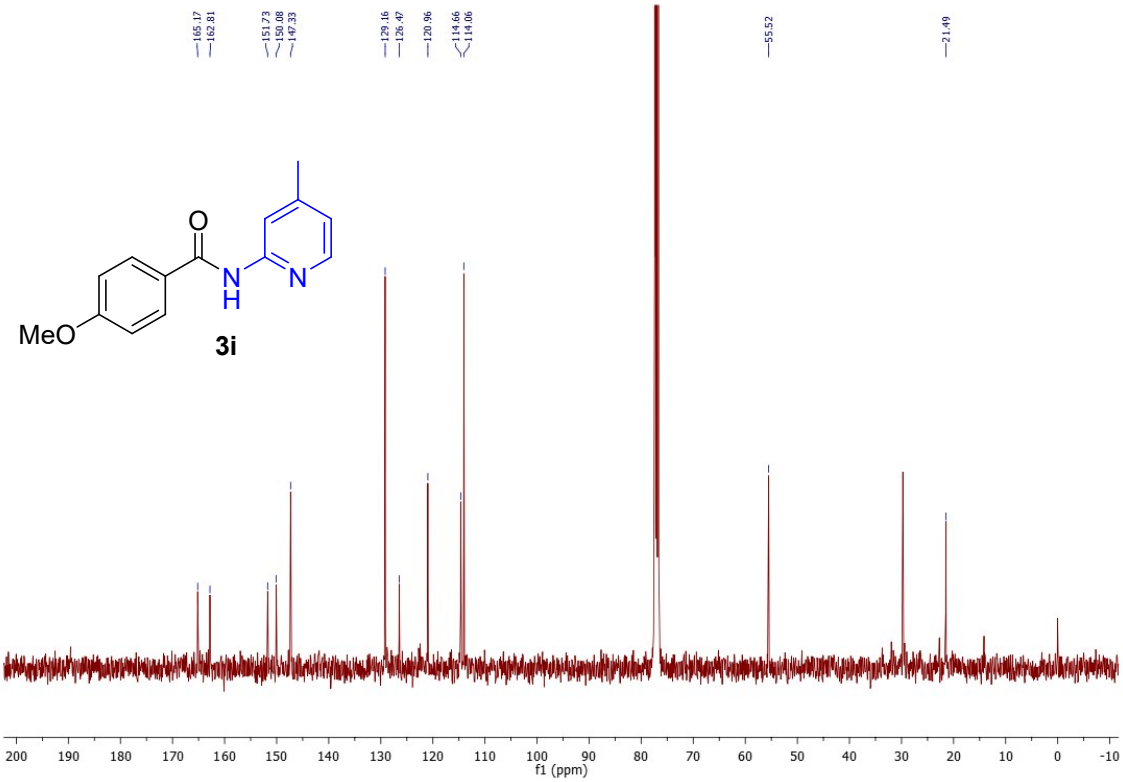
^{1}H NMR of Compound **3h (400 MHz, $CDCl_3$)**



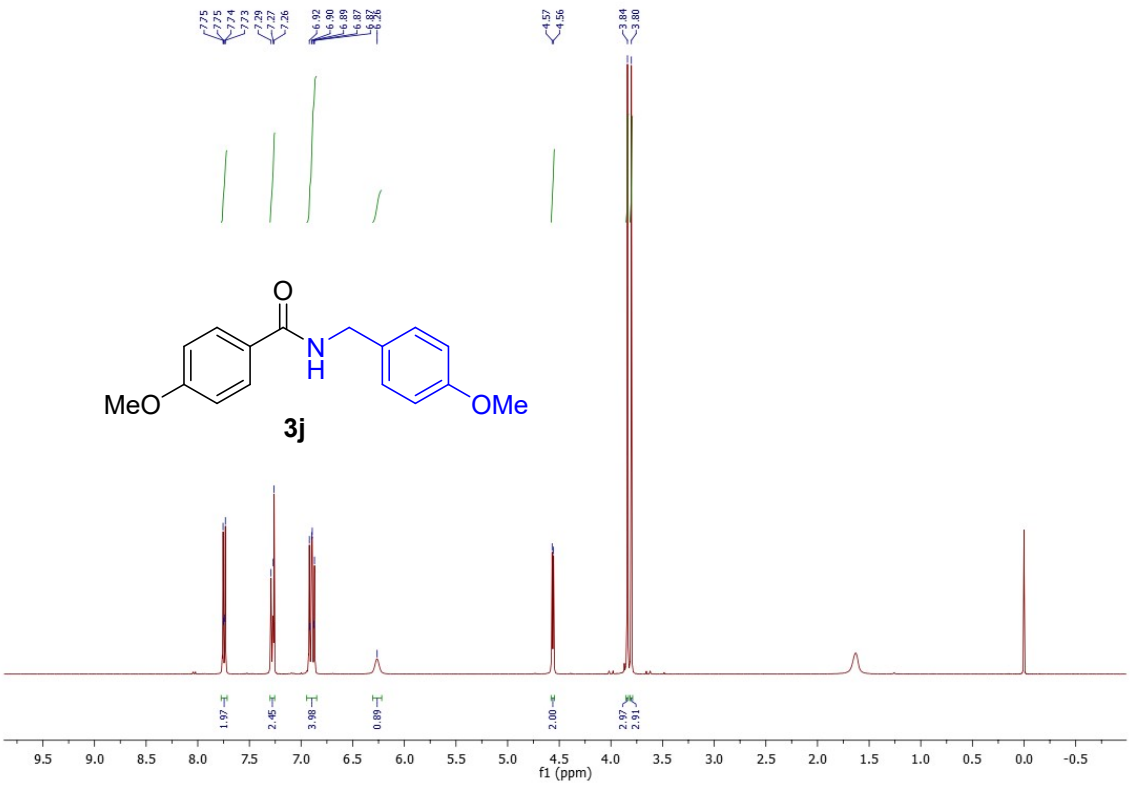
^{13}C NMR of Compound **3h (101 MHz, $CDCl_3$)**



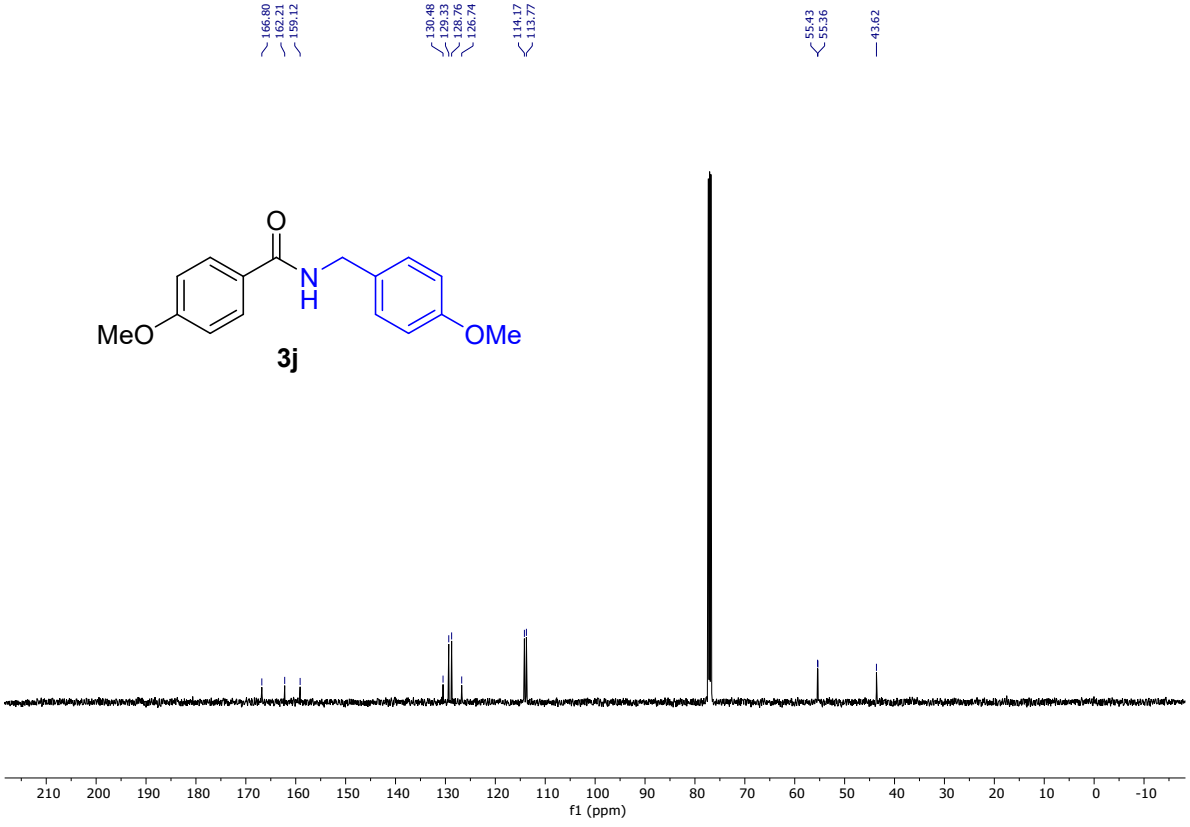
^{1}H NMR of Compound **3i (400 MHz, $CDCl_3$)**



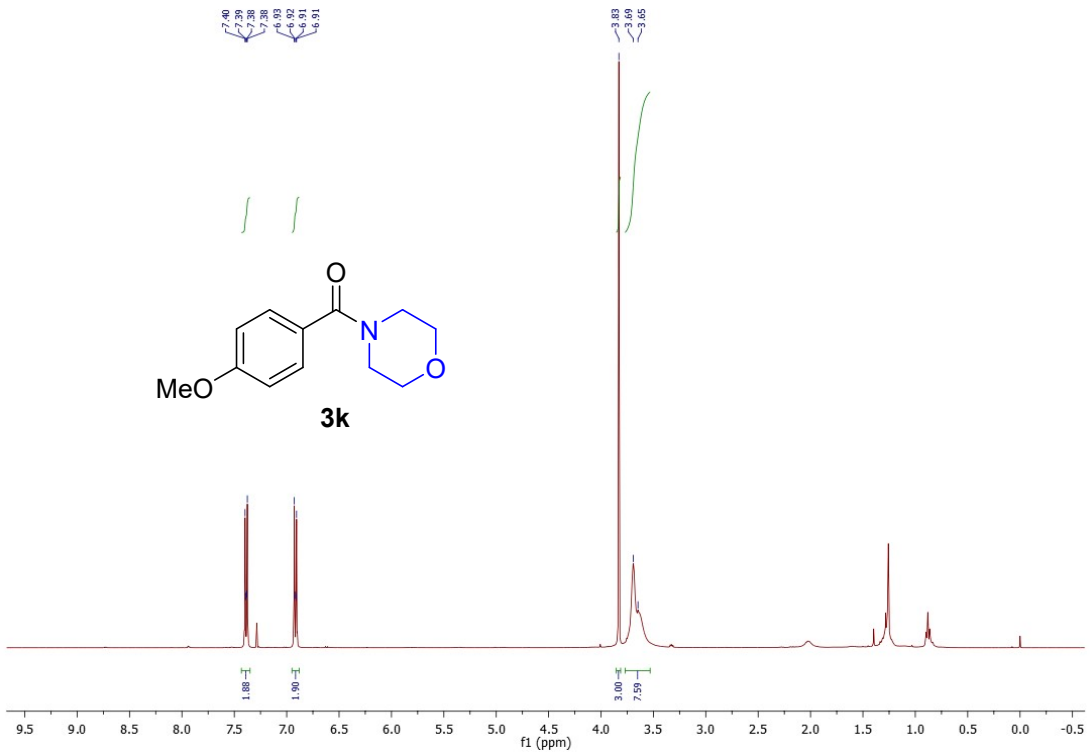
^{13}C NMR of Compound **3i (101 MHz, $CDCl_3$)**



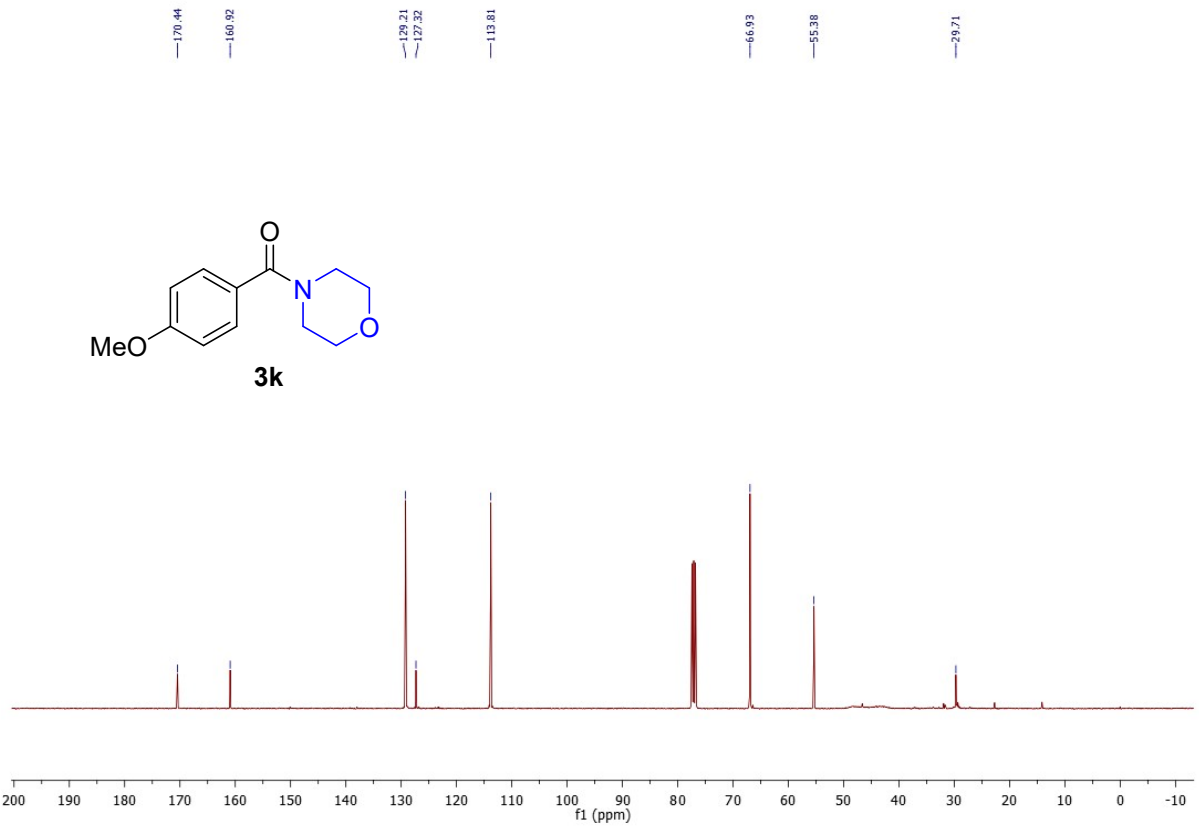
^{1}H NMR of Compound **3j (400 MHz, $CDCl_3$)**



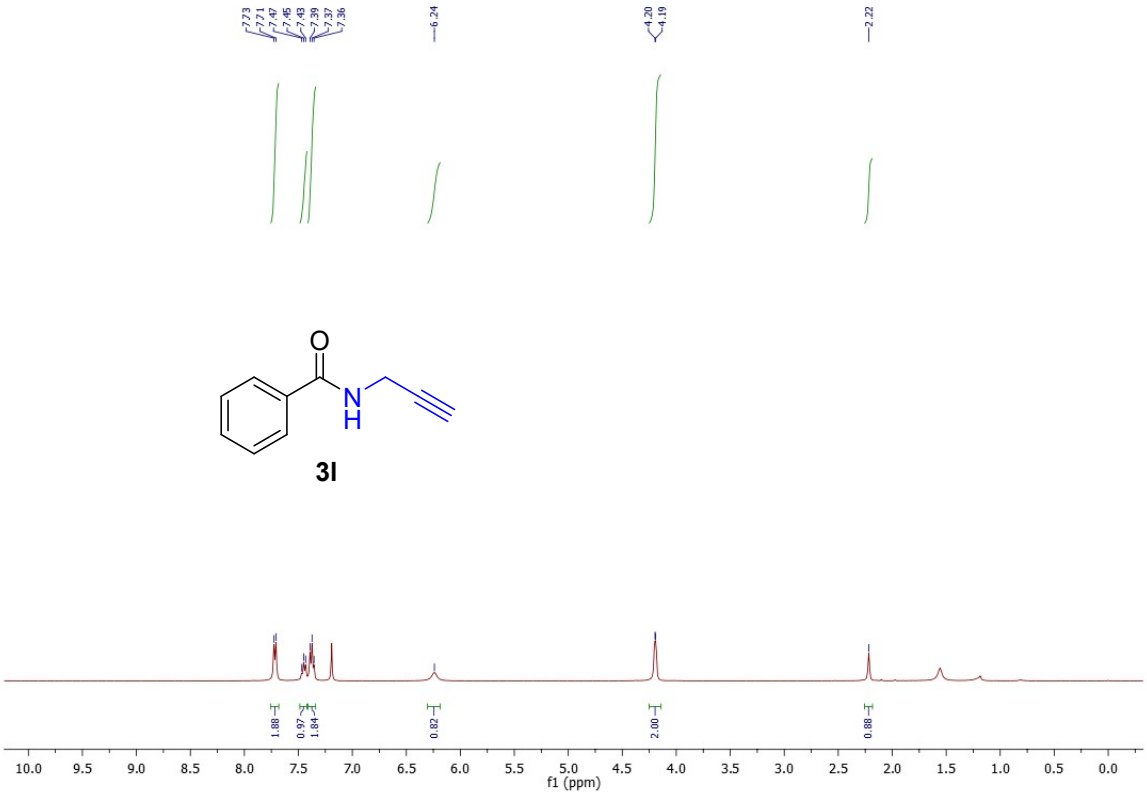
^{13}C NMR of Compound **3j (101 MHz, $CDCl_3$)**



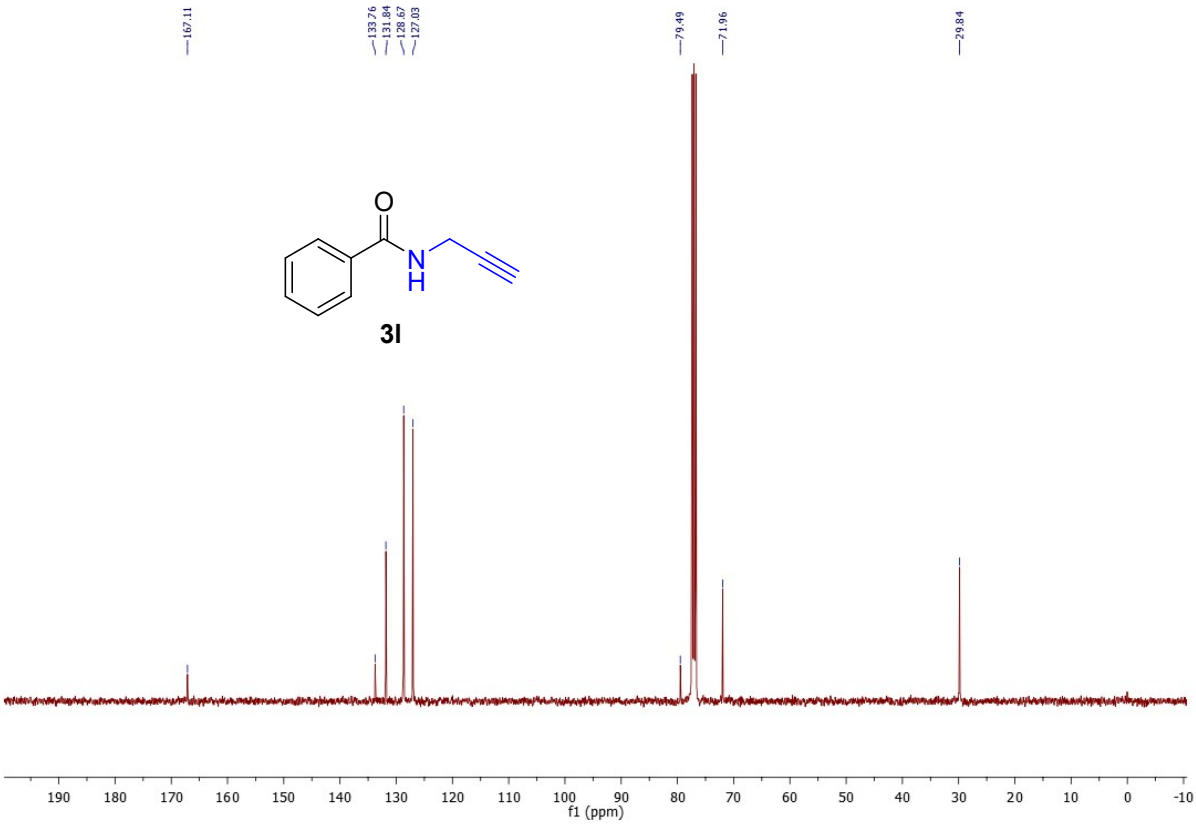
^{1}H NMR of Compound **3k (400 MHz, $CDCl_3$)**



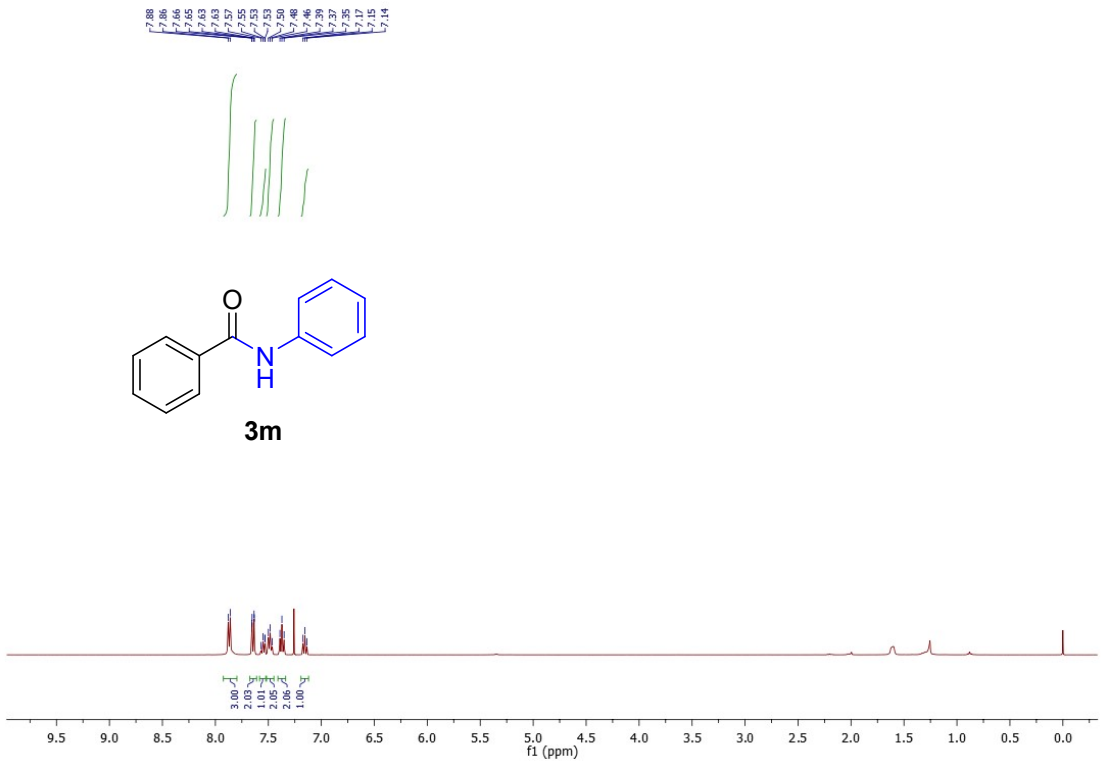
^{13}C NMR of Compound **3k (101 MHz, $CDCl_3$)**



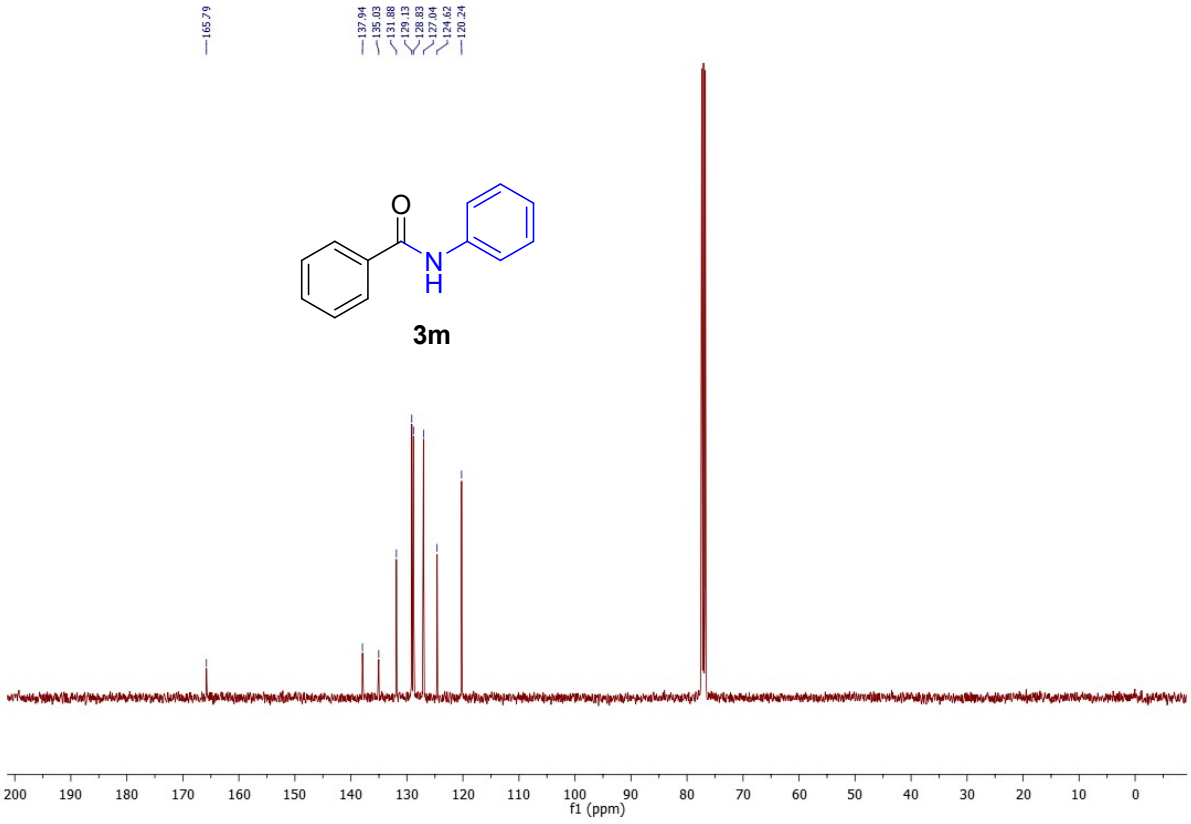
^{1}H NMR of Compound **3l (500 MHz, $CDCl_3$)**



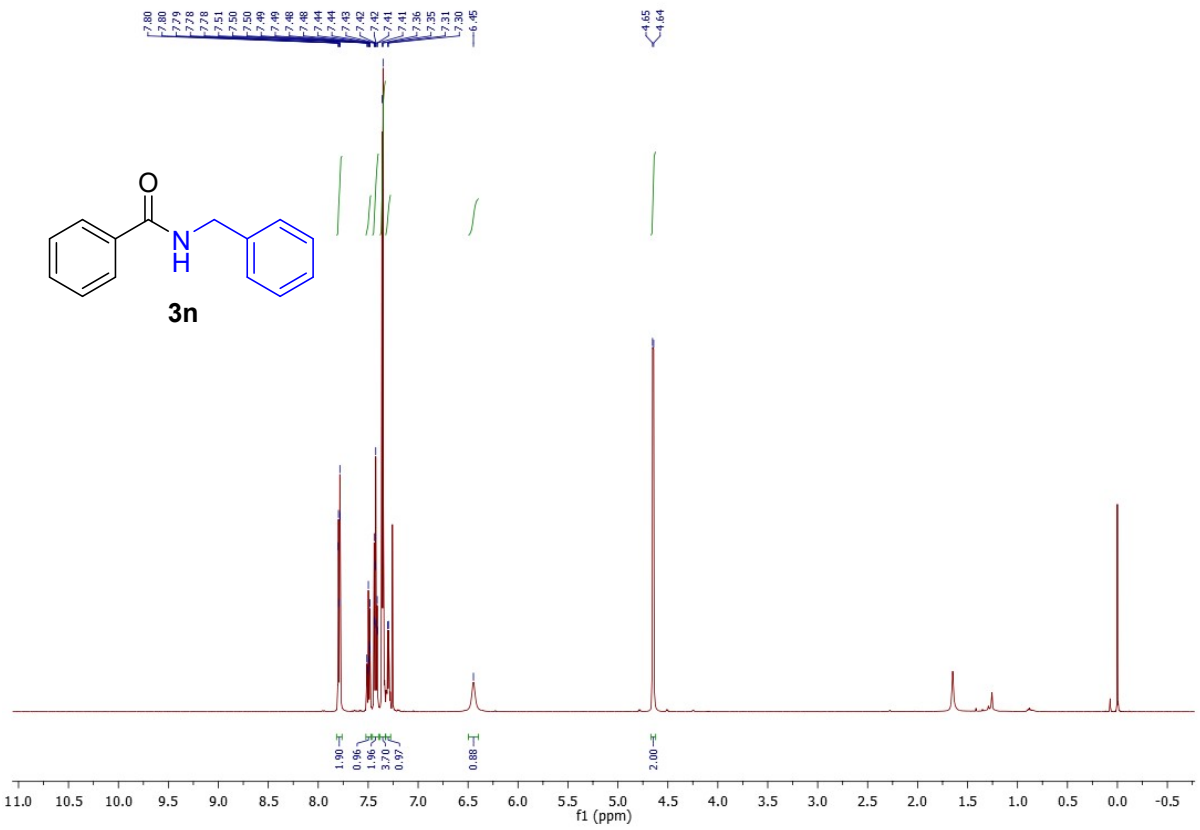
^{13}C NMR of Compound **3l (101 MHz, $CDCl_3$)**



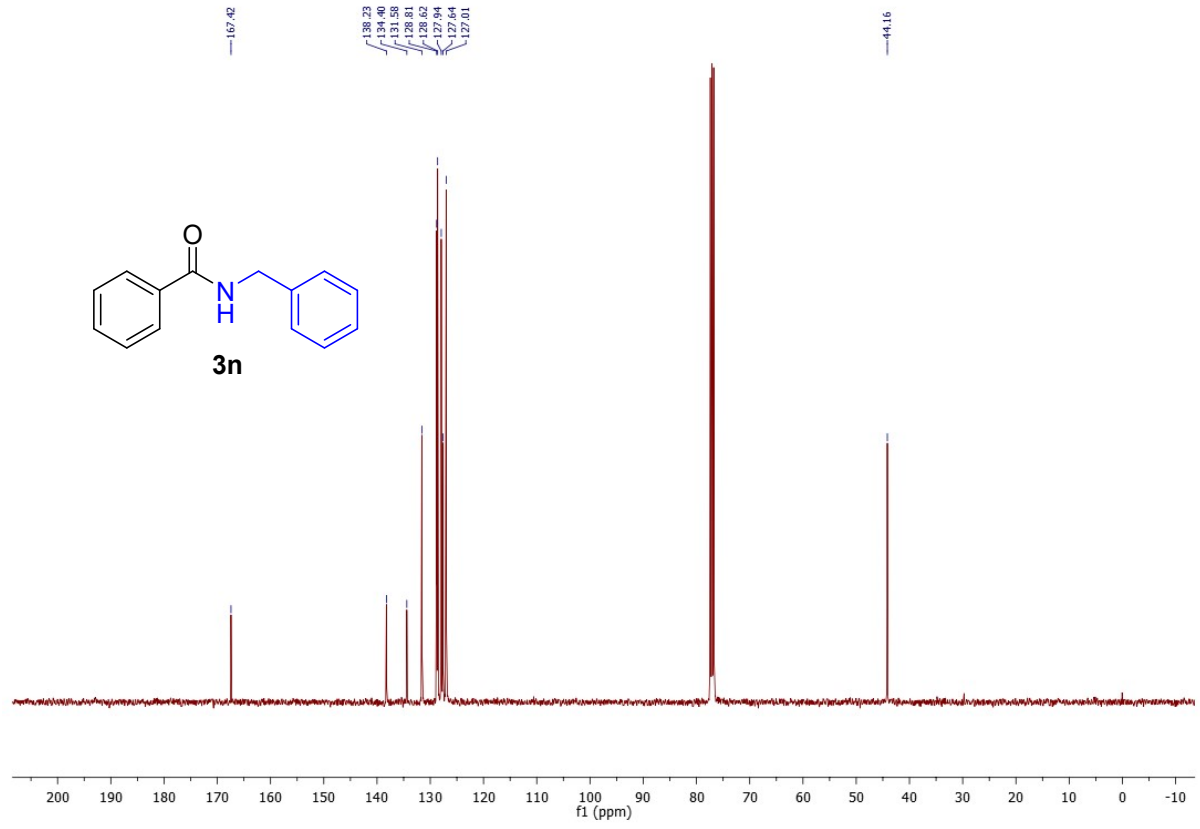
^{1}H NMR of Compound **3m (400 MHz, $CDCl_3$)**



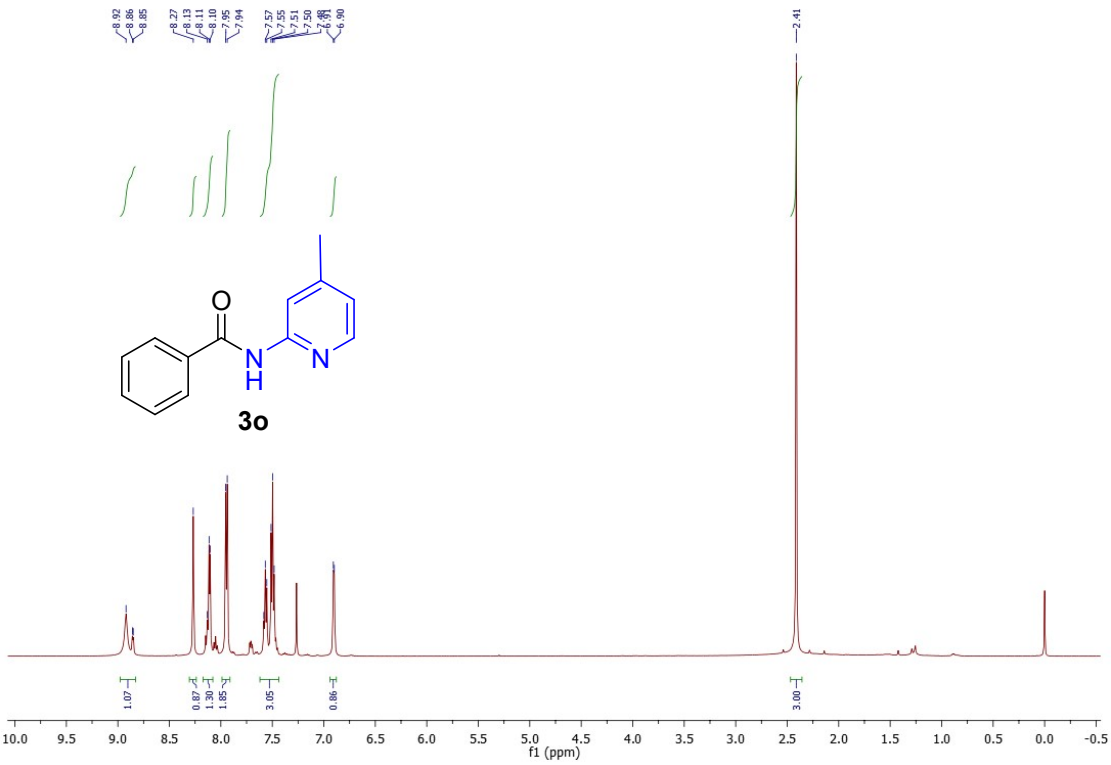
^{13}C NMR of Compound **3m (101 MHz, $CDCl_3$)**



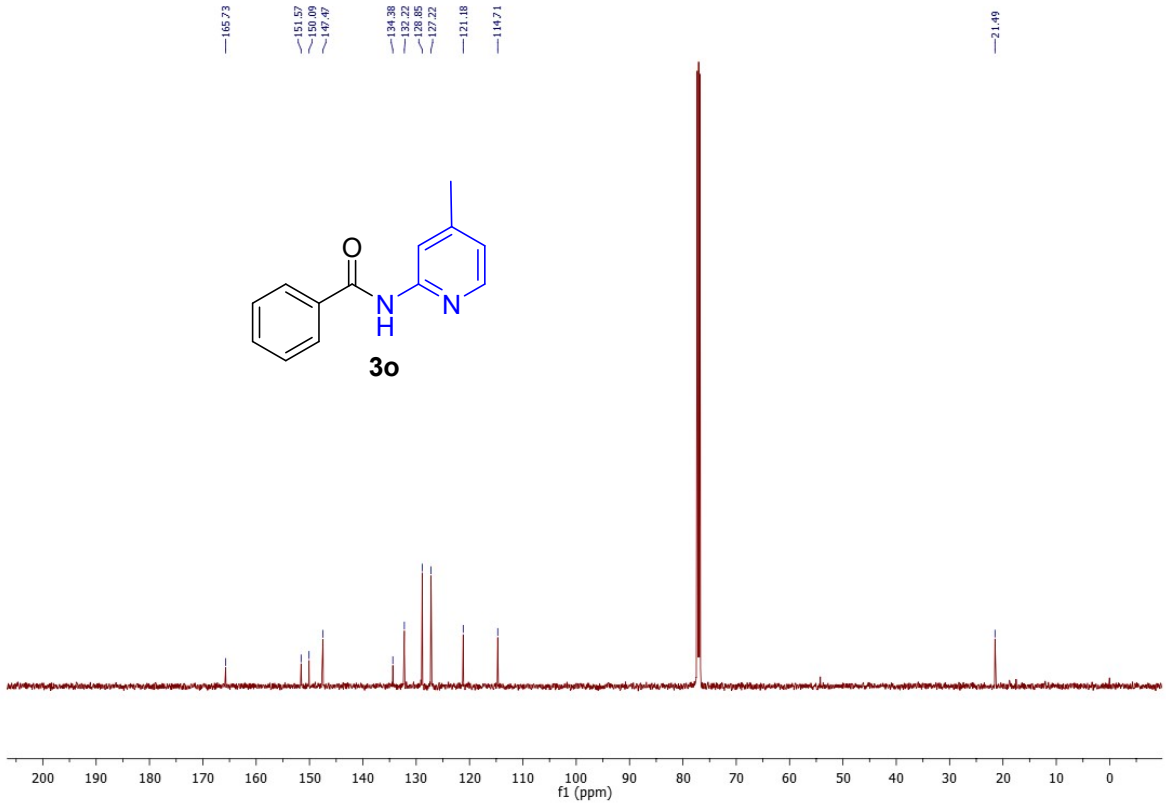
^{1}H NMR of Compound **3n (500 MHz, $CDCl_3$)**



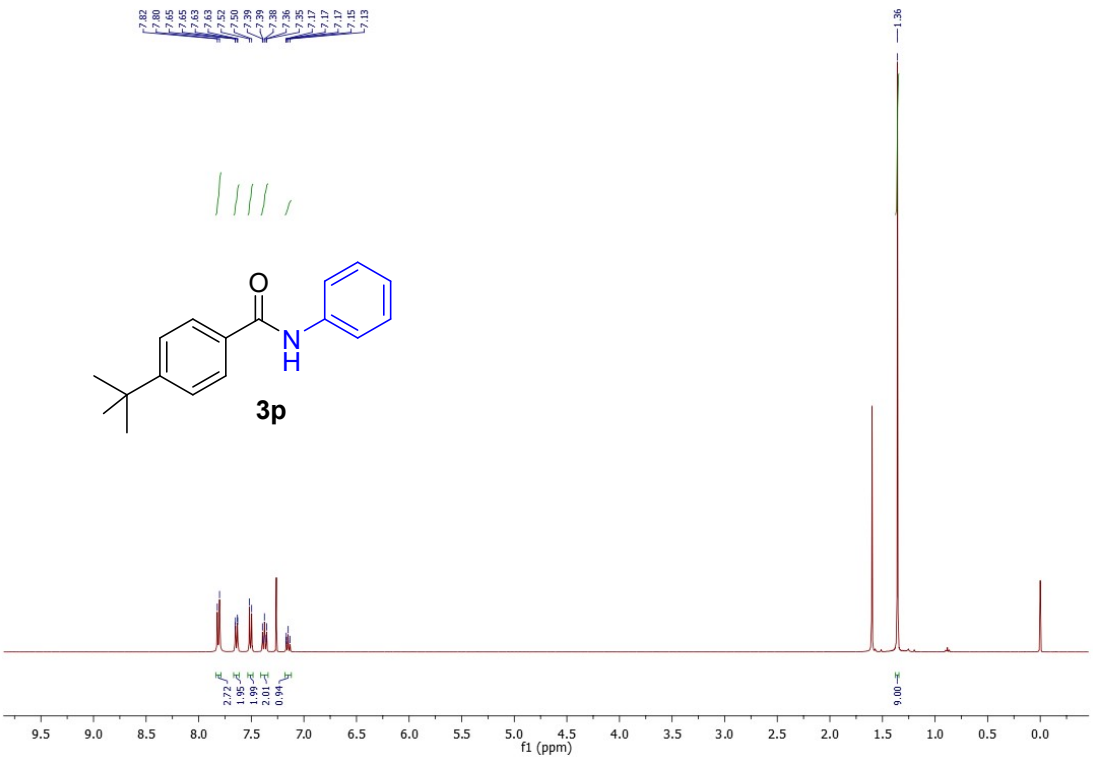
^{13}C NMR of Compound **3n (101 MHz, $CDCl_3$)**



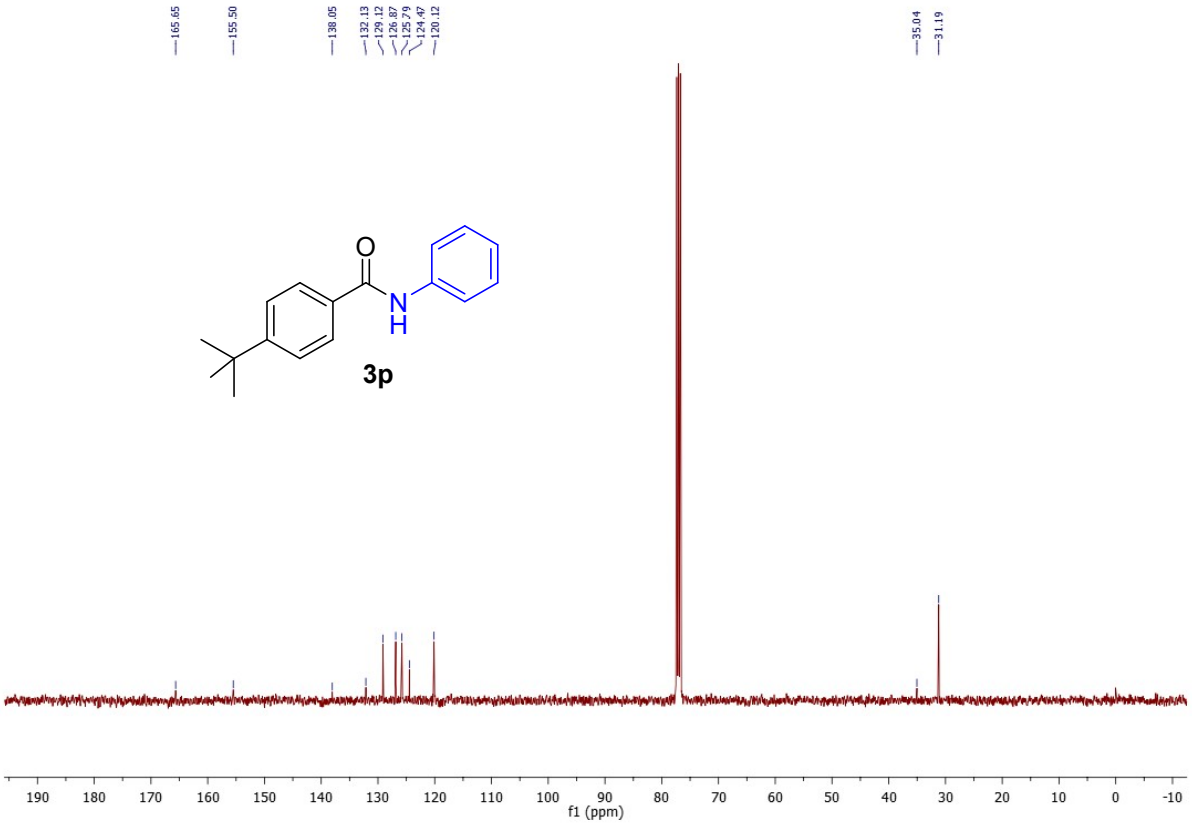
^{1}H NMR of Compound **3o (500 MHz, $CDCl_3$)**



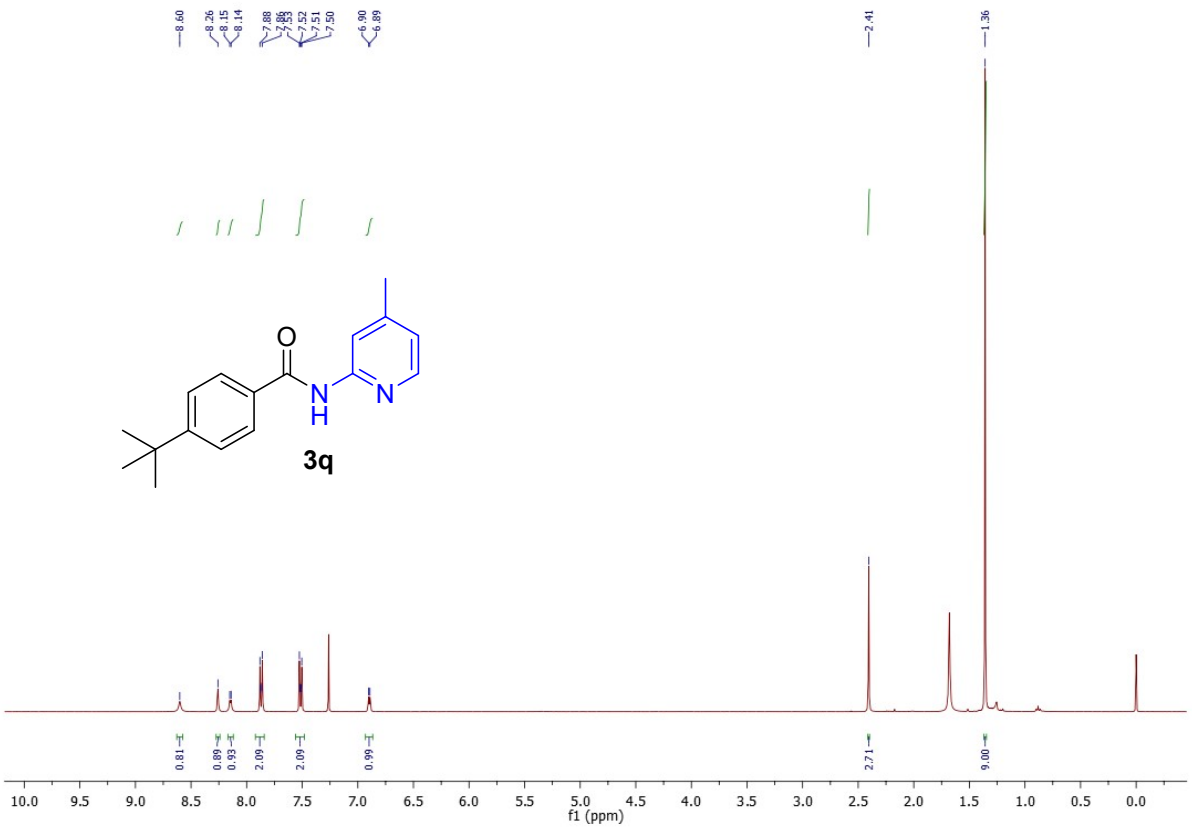
^{13}C NMR of Compound **3o (126 MHz, $CDCl_3$)**



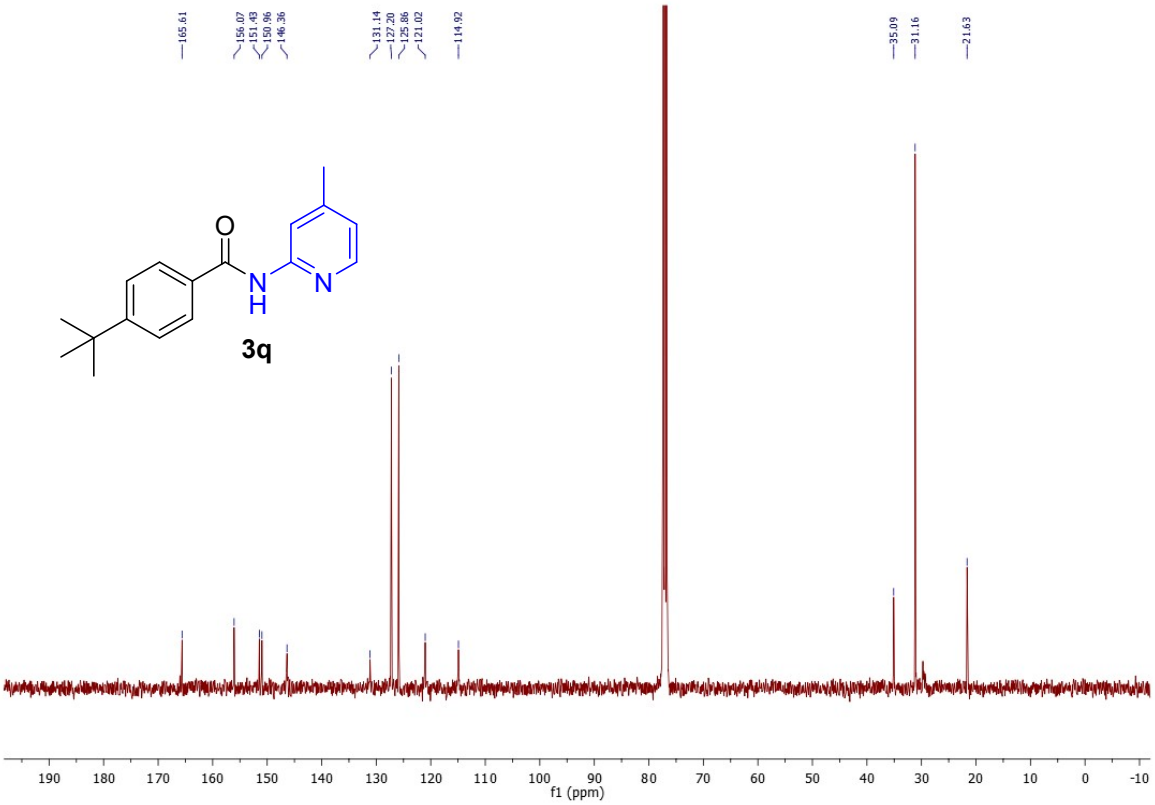
^{1}H NMR of Compound **3p (400 MHz, $CDCl_3$)**



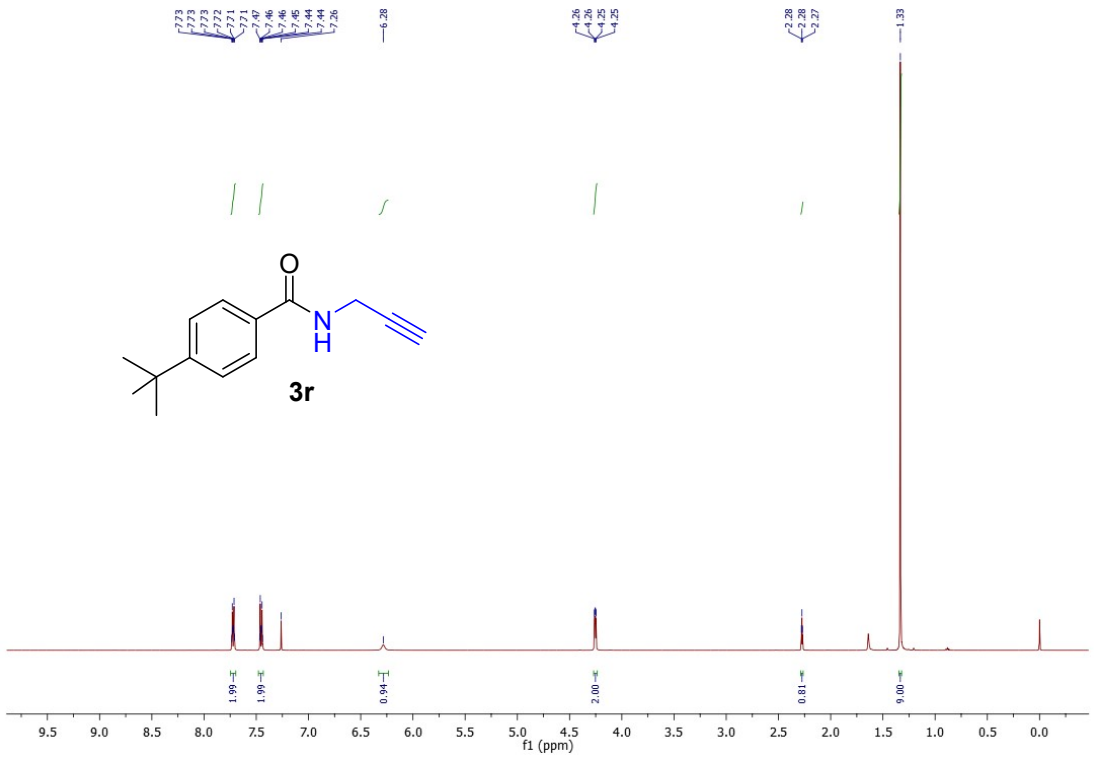
^{13}C NMR of Compound **3p (101 MHz, $CDCl_3$)**



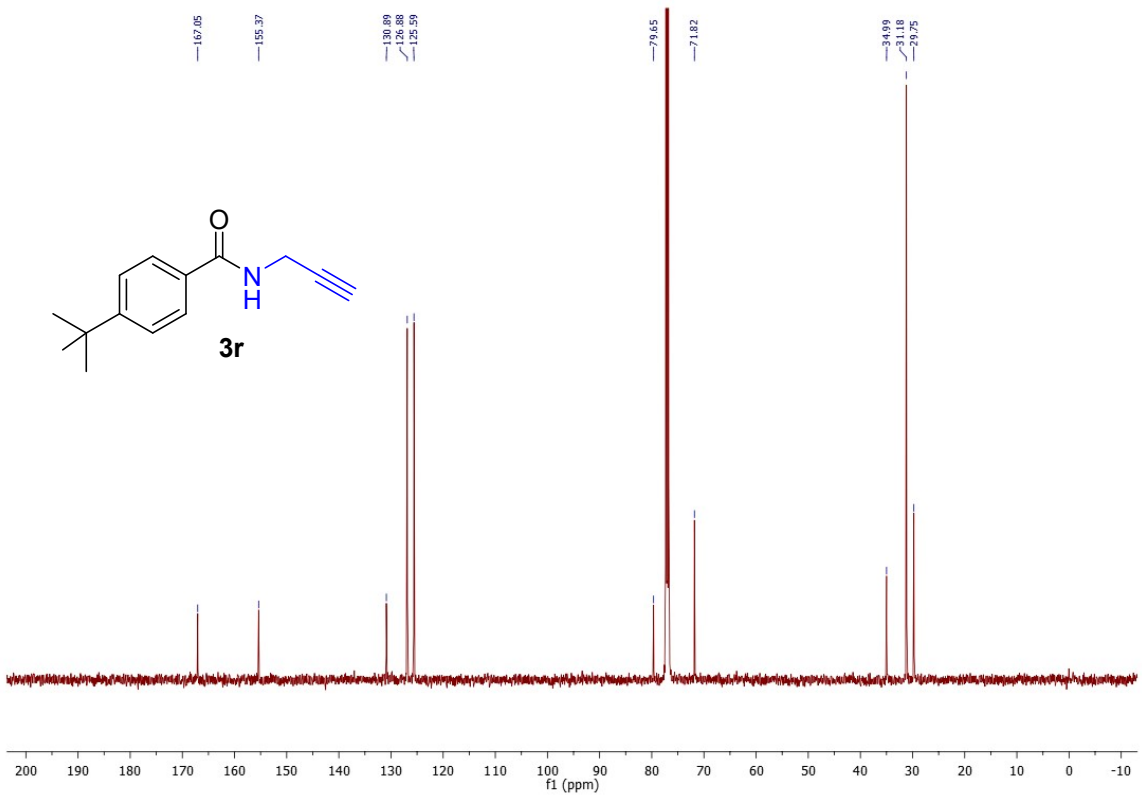
^{1}H NMR of Compound **3q (400 MHz, $CDCl_3$)**



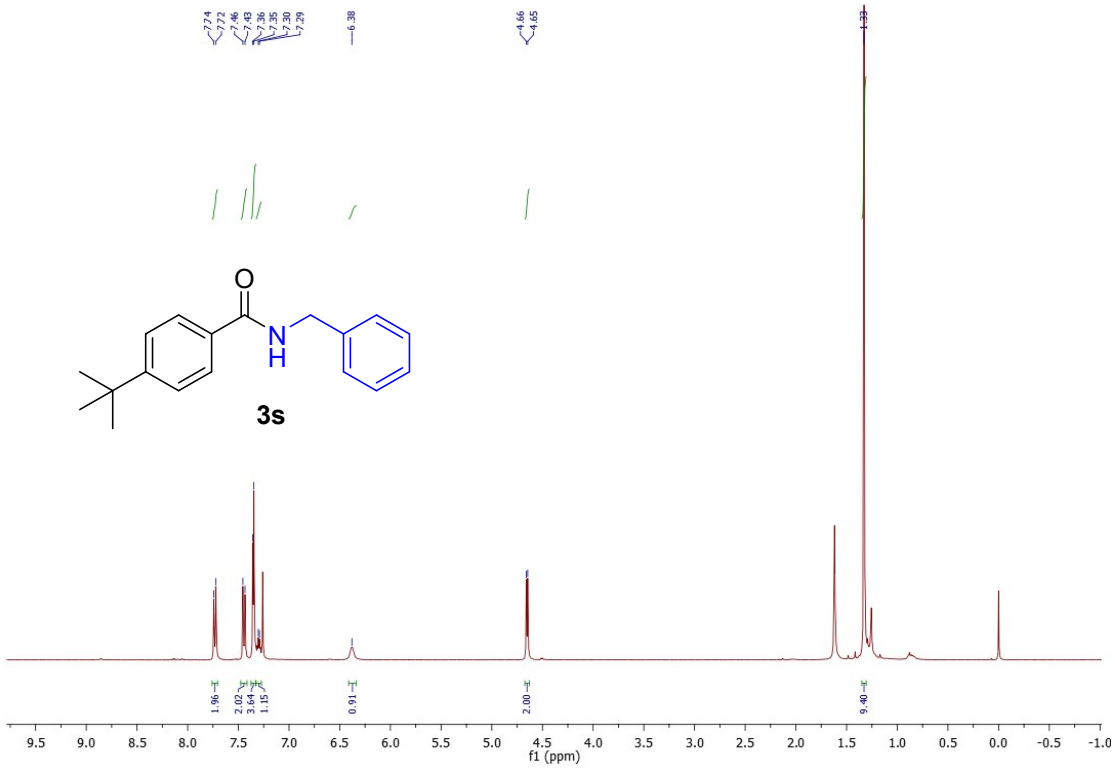
^{13}C NMR of Compound **3q (101 MHz, $CDCl_3$)**



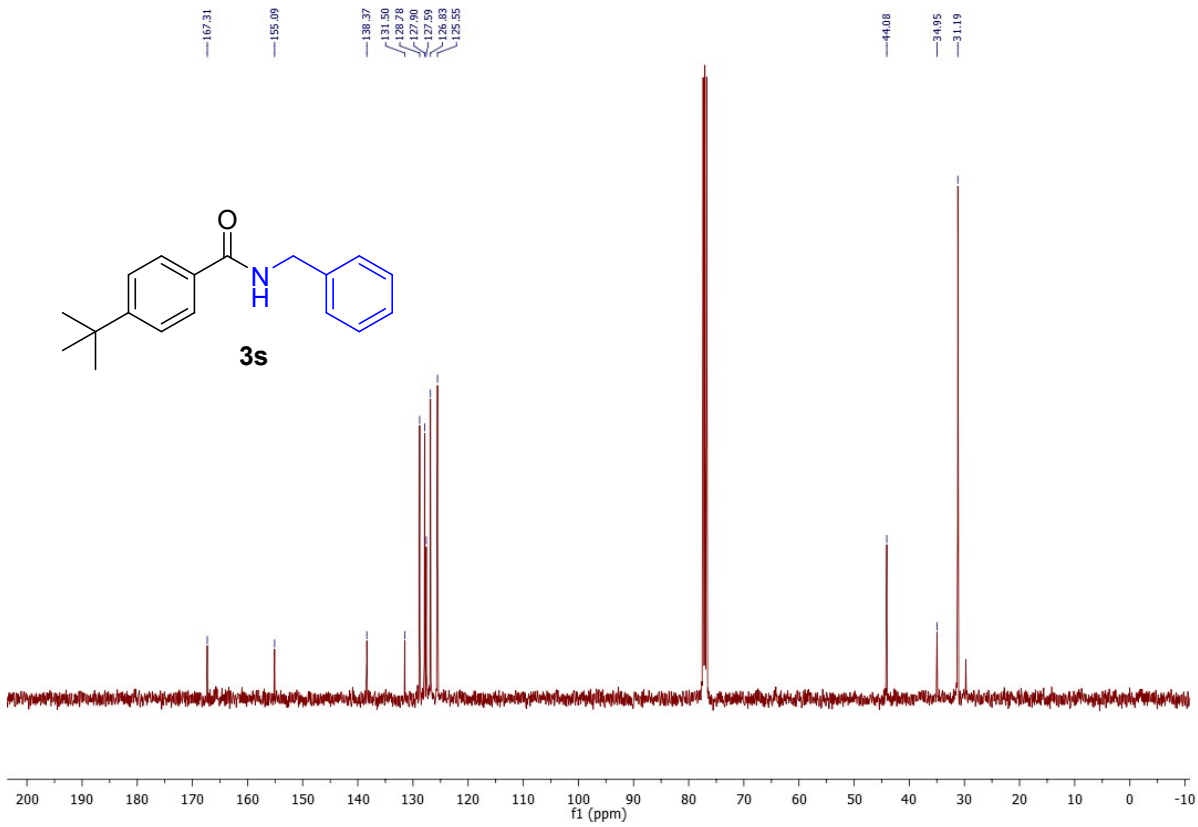
^{1}H NMR of Compound **3r (500 MHz, $CDCl_3$)**



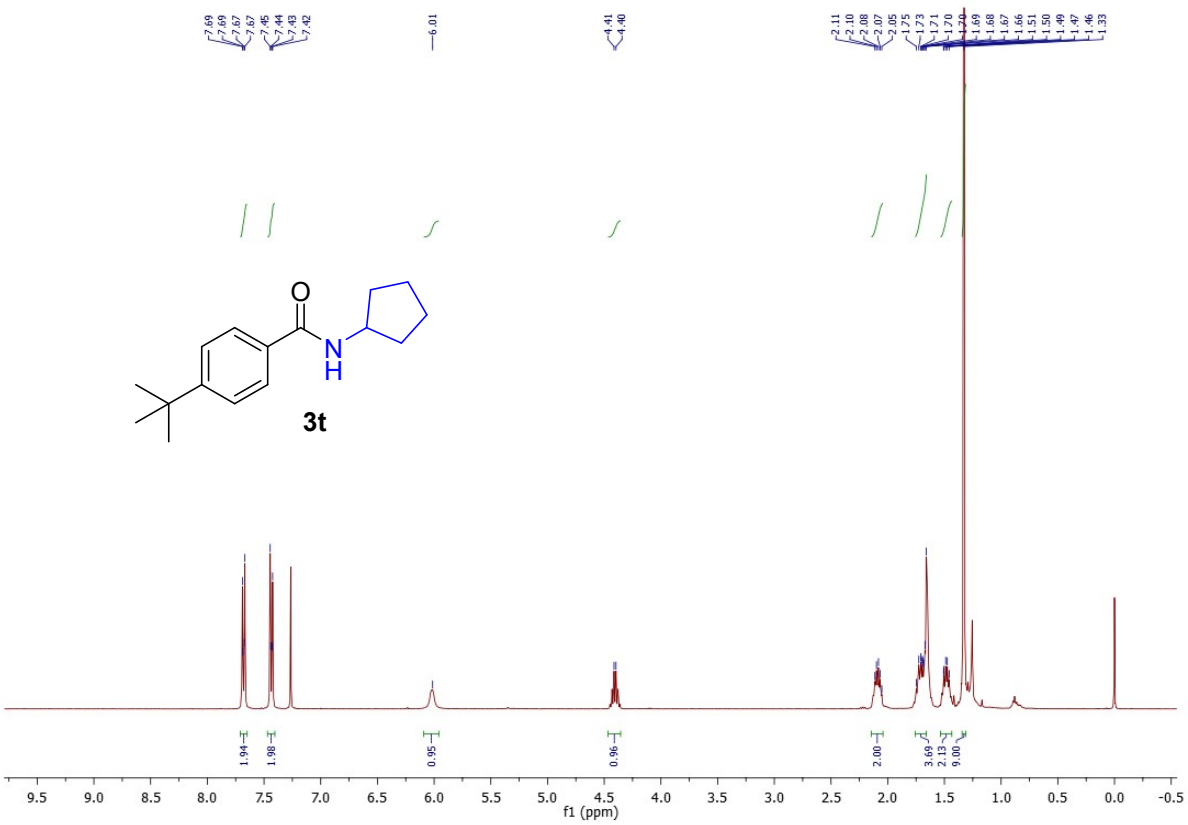
^{13}C NMR of Compound **3r (101 MHz, $CDCl_3$)**



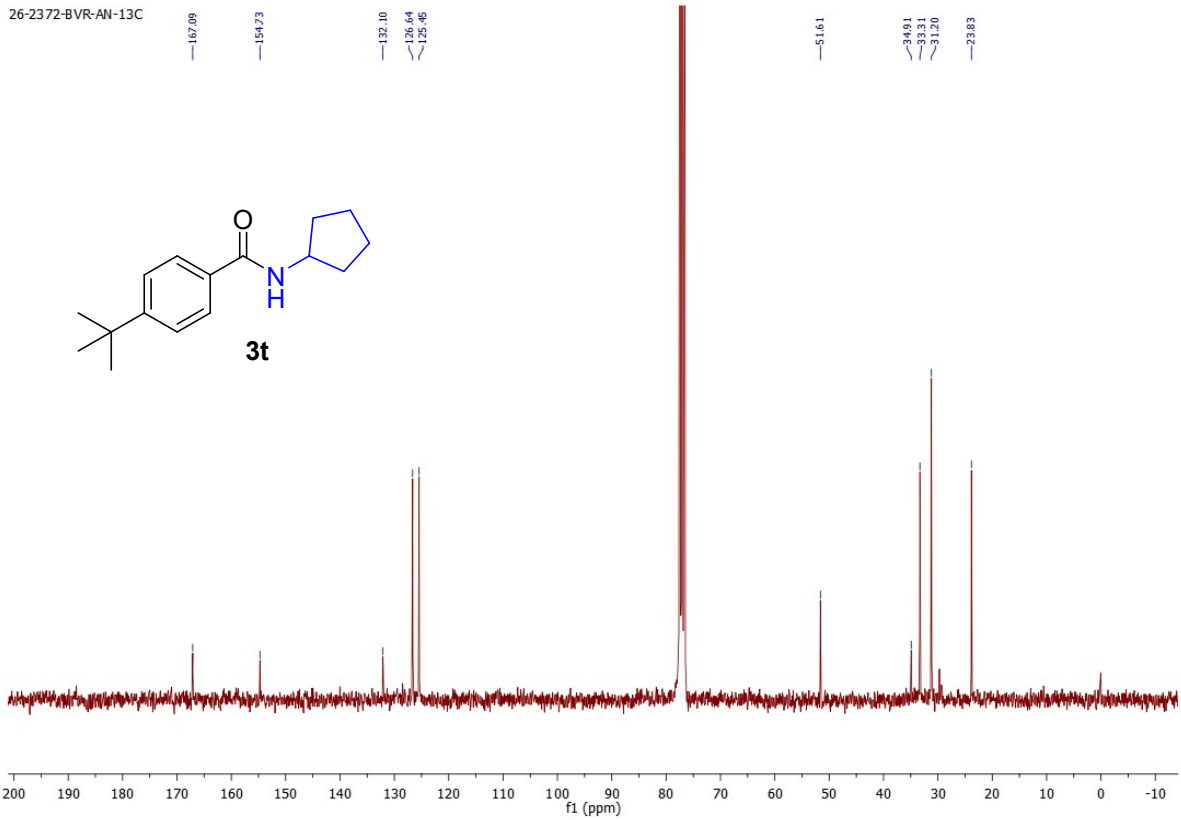
^{1}H NMR of Compound **3s (400 MHz, $CDCl_3$)**



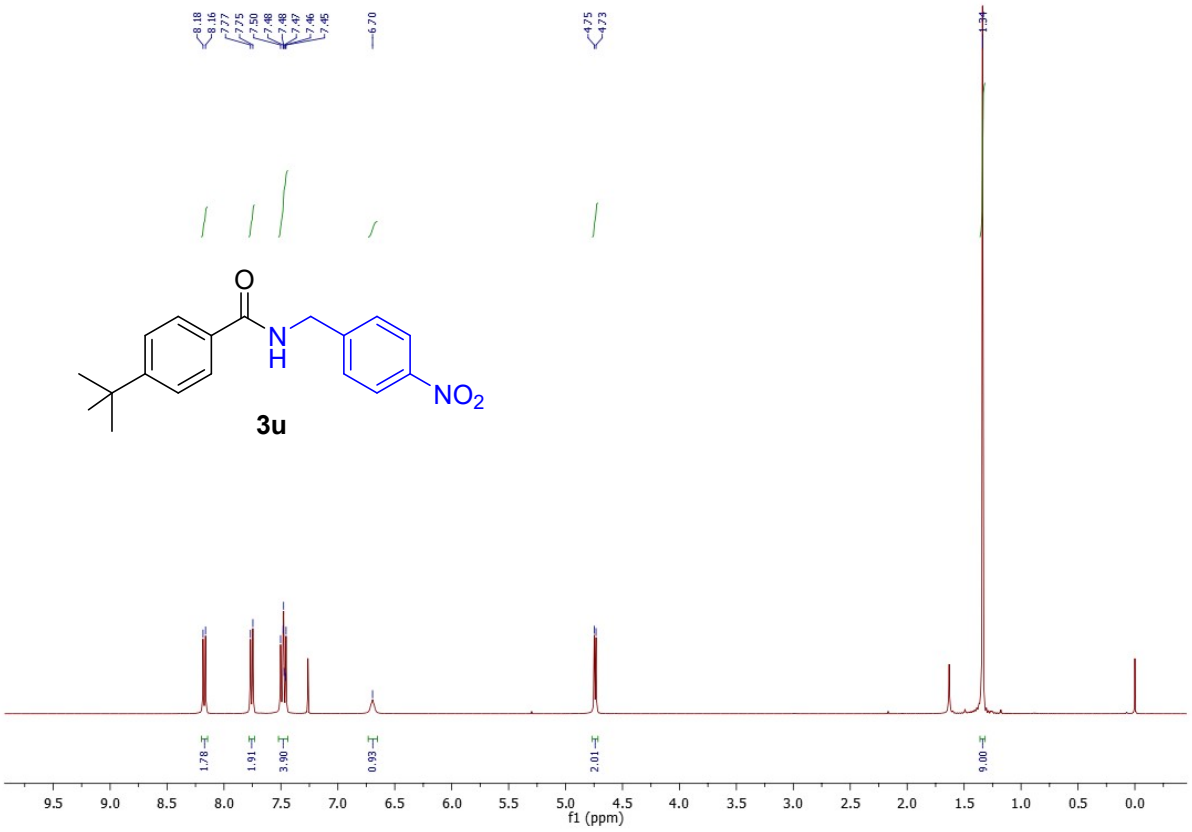
^{13}C NMR of Compound **3s (101 MHz, $CDCl_3$)**



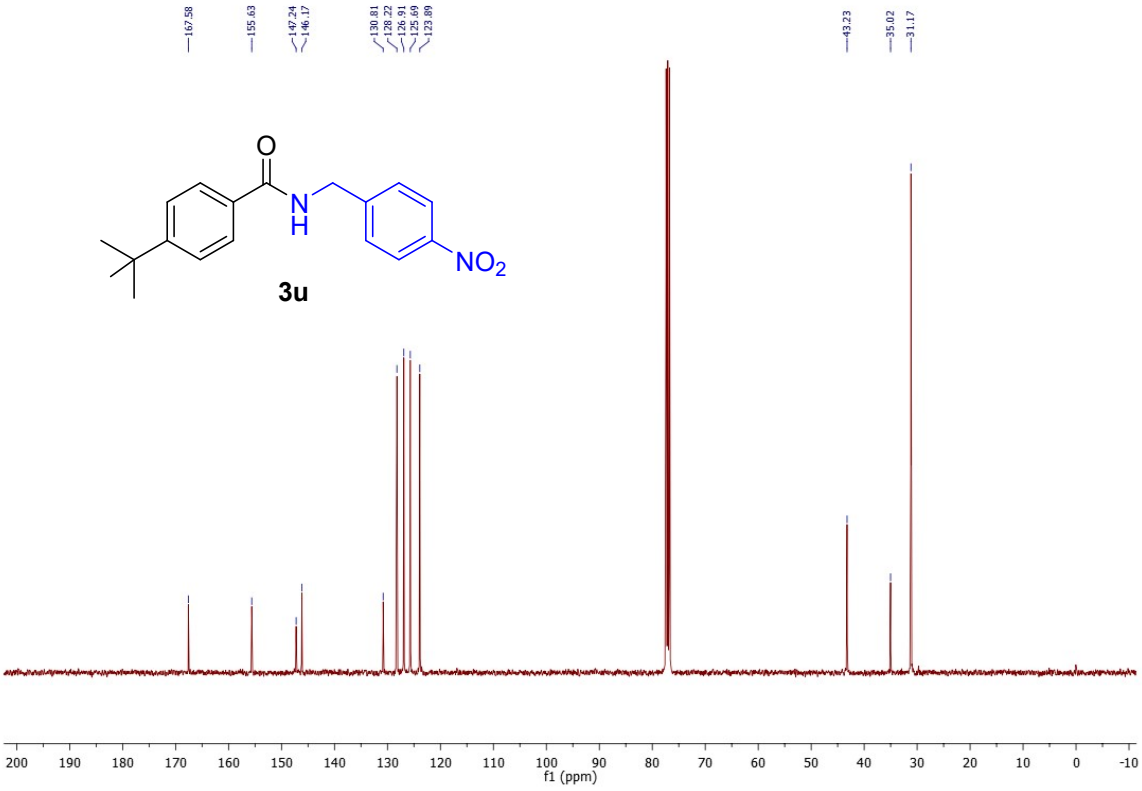
^{1}H NMR of Compound **3t (400 MHz, $CDCl_3$)**



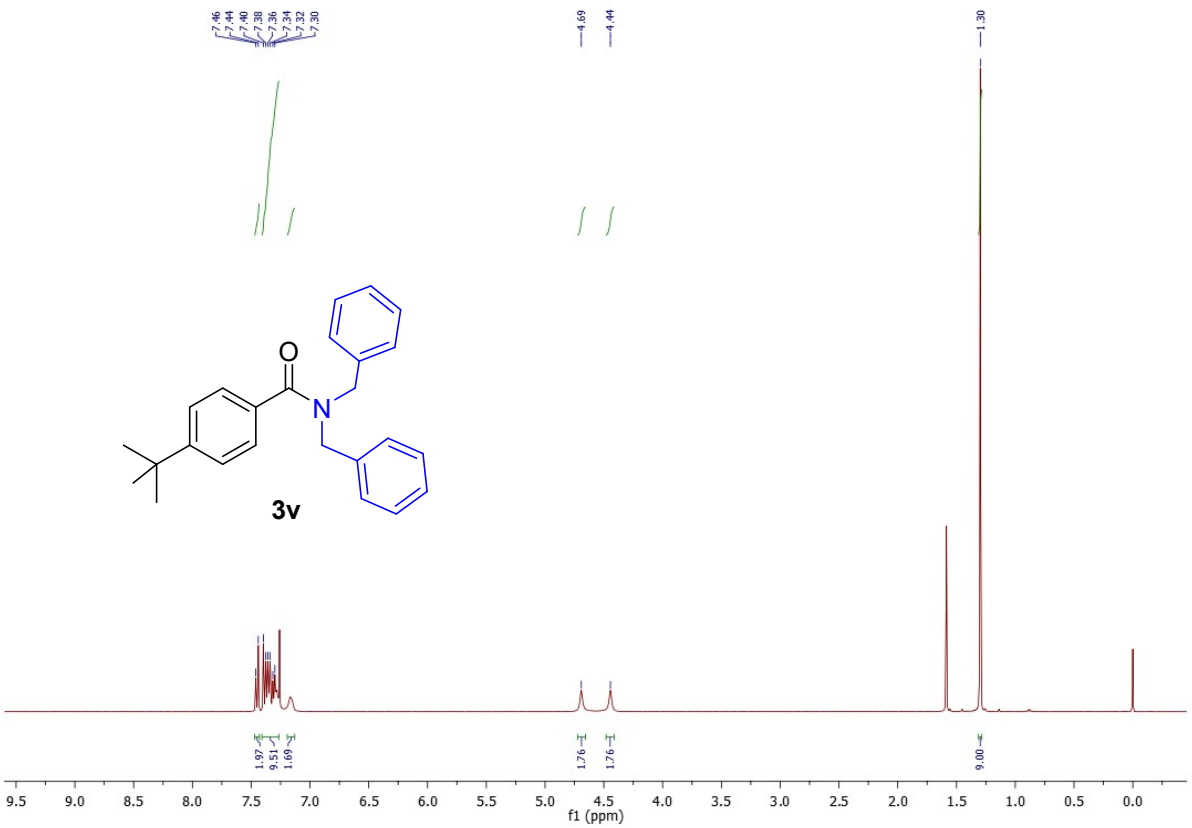
^{13}C NMR of Compound **3t (75 MHz, $CDCl_3$)**



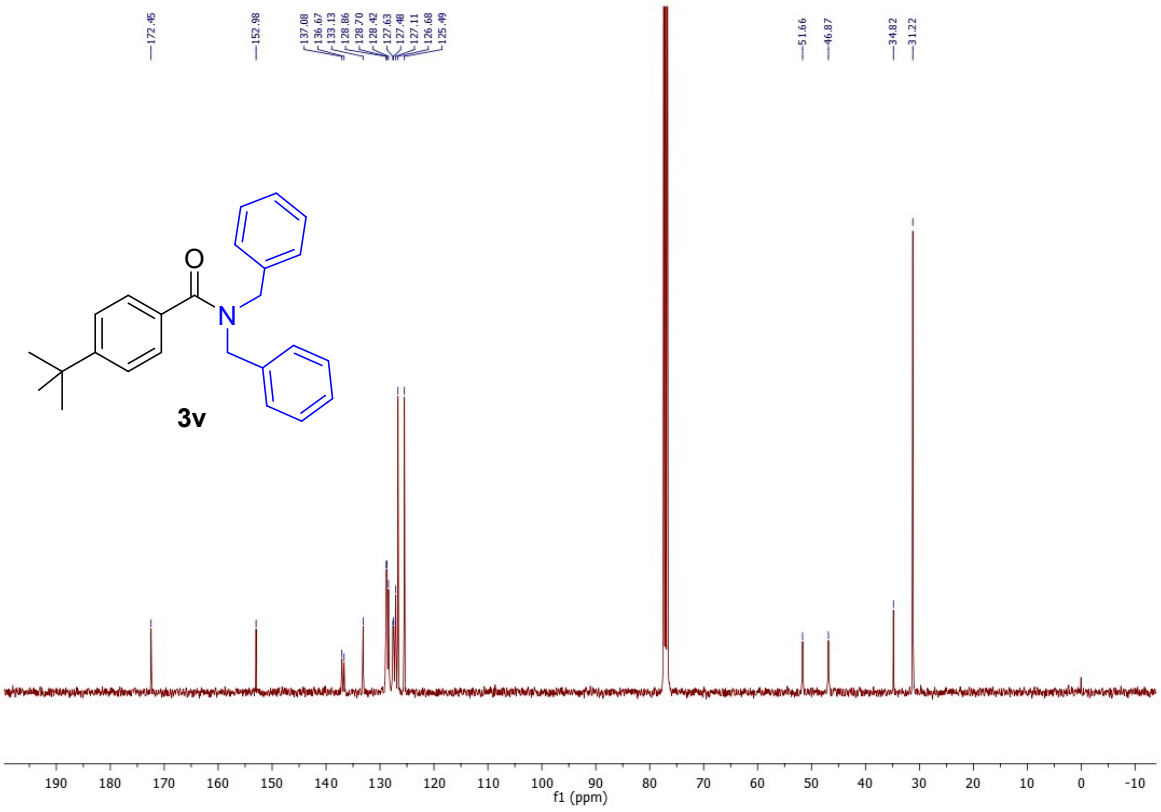
[1]H NMR of Compound **3u (400 MHz, $CDCl_3$)**



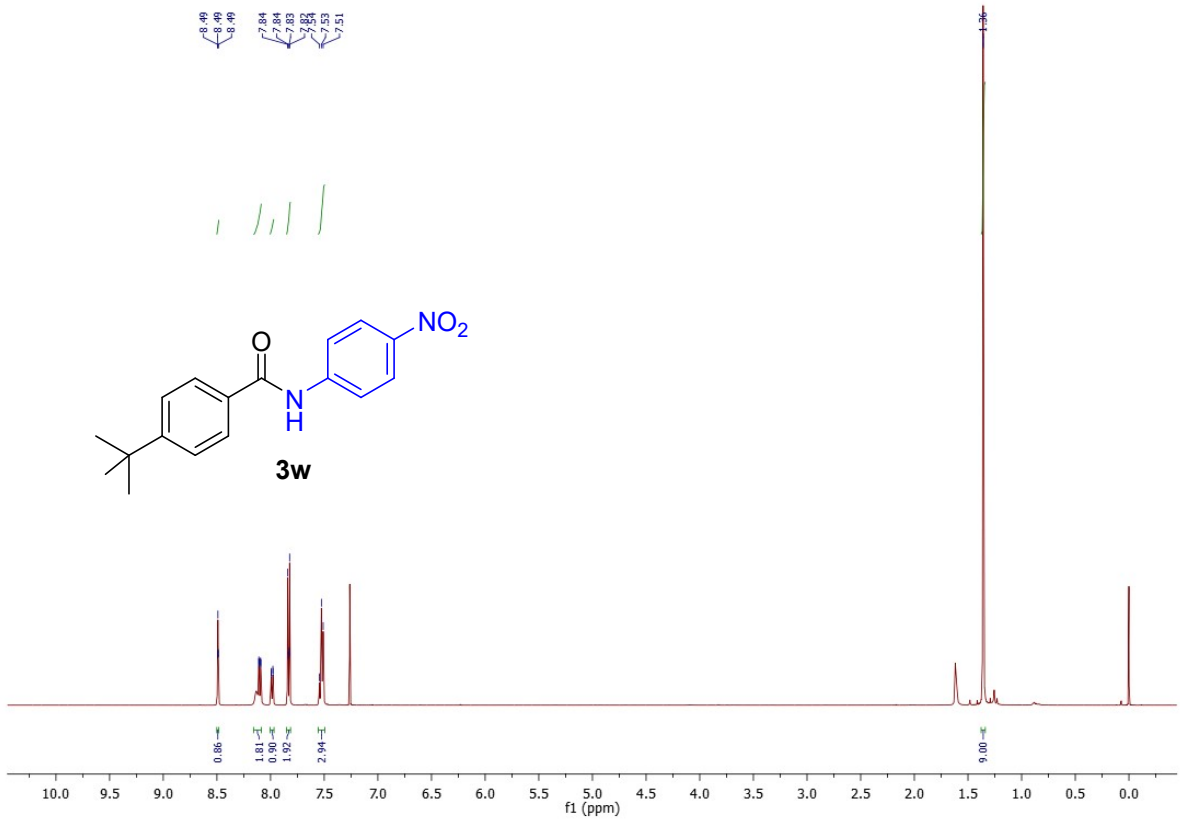
[13]C NMR of Compound **3u (101 MHz, $CDCl_3$)**



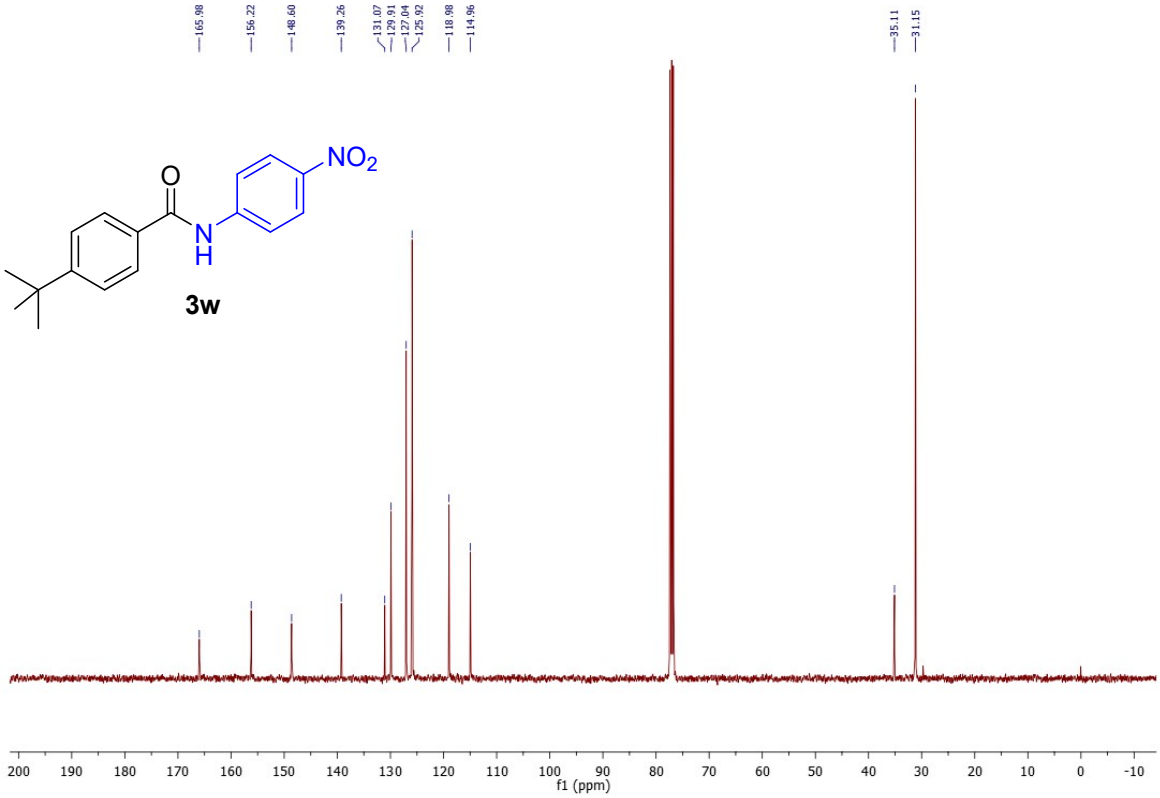
^{1}H NMR of Compound **3v (400 MHz, $CDCl_3$)**



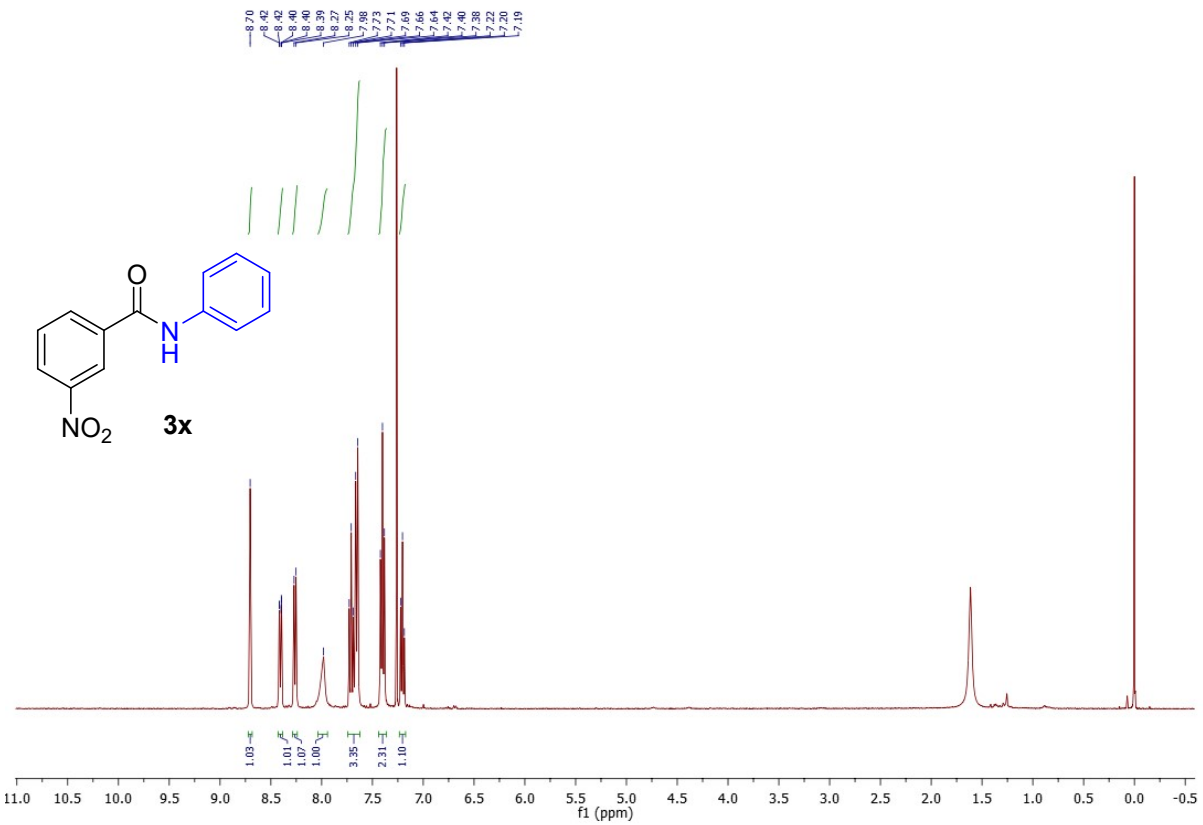
^{13}C NMR of Compound **3v (101 MHz, $CDCl_3$)**



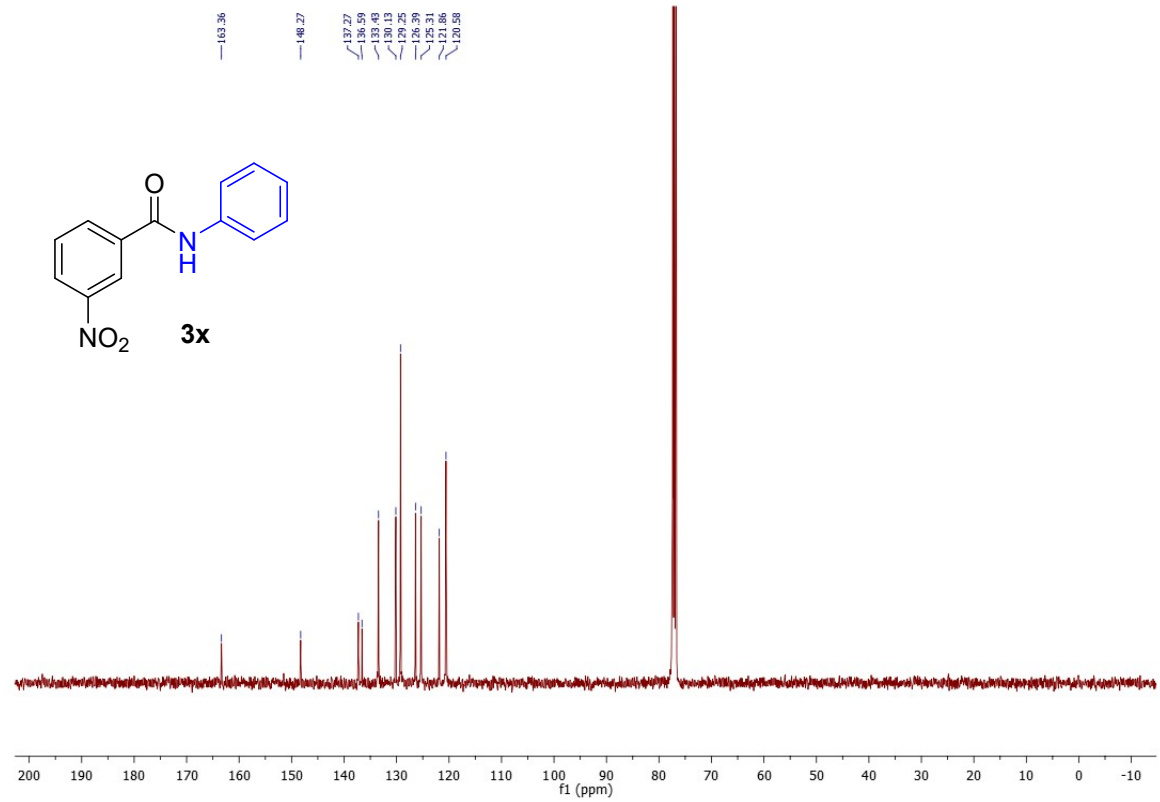
^{1}H NMR of Compound **3w (500 MHz, $CDCl_3$)**



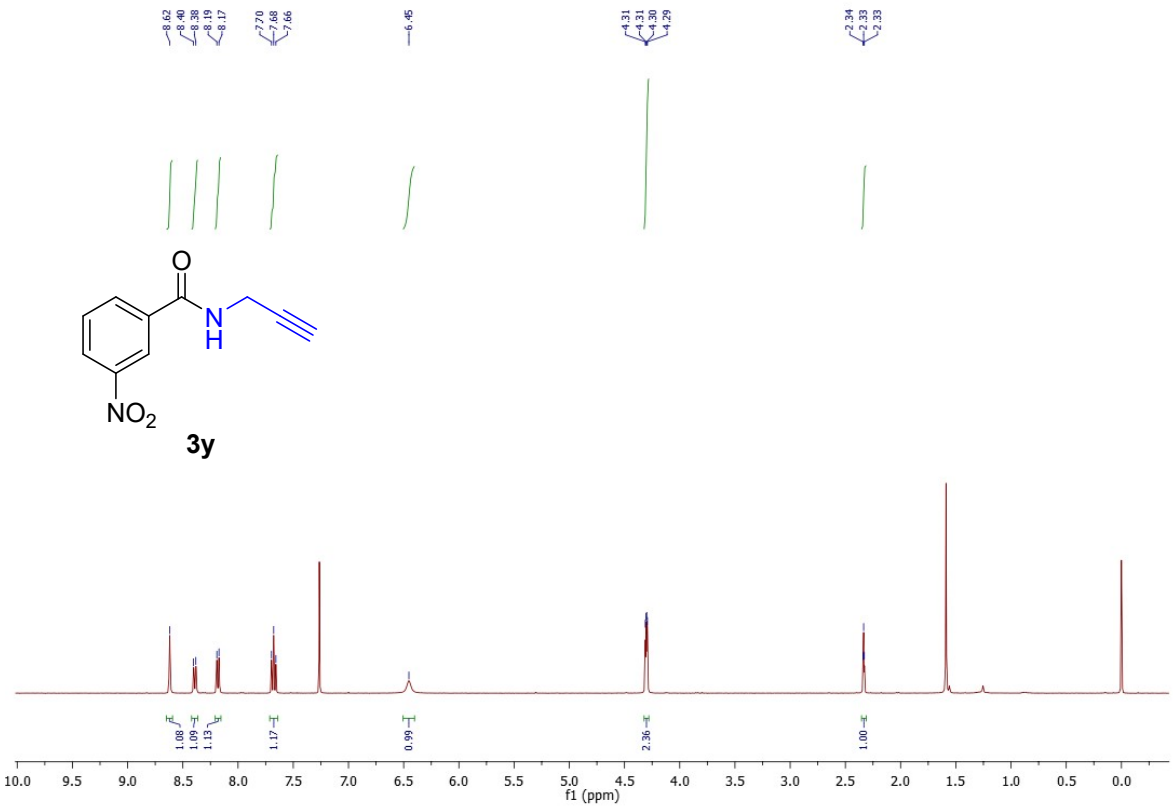
^{13}C NMR of Compound **3w (101 MHz, $CDCl_3$)**



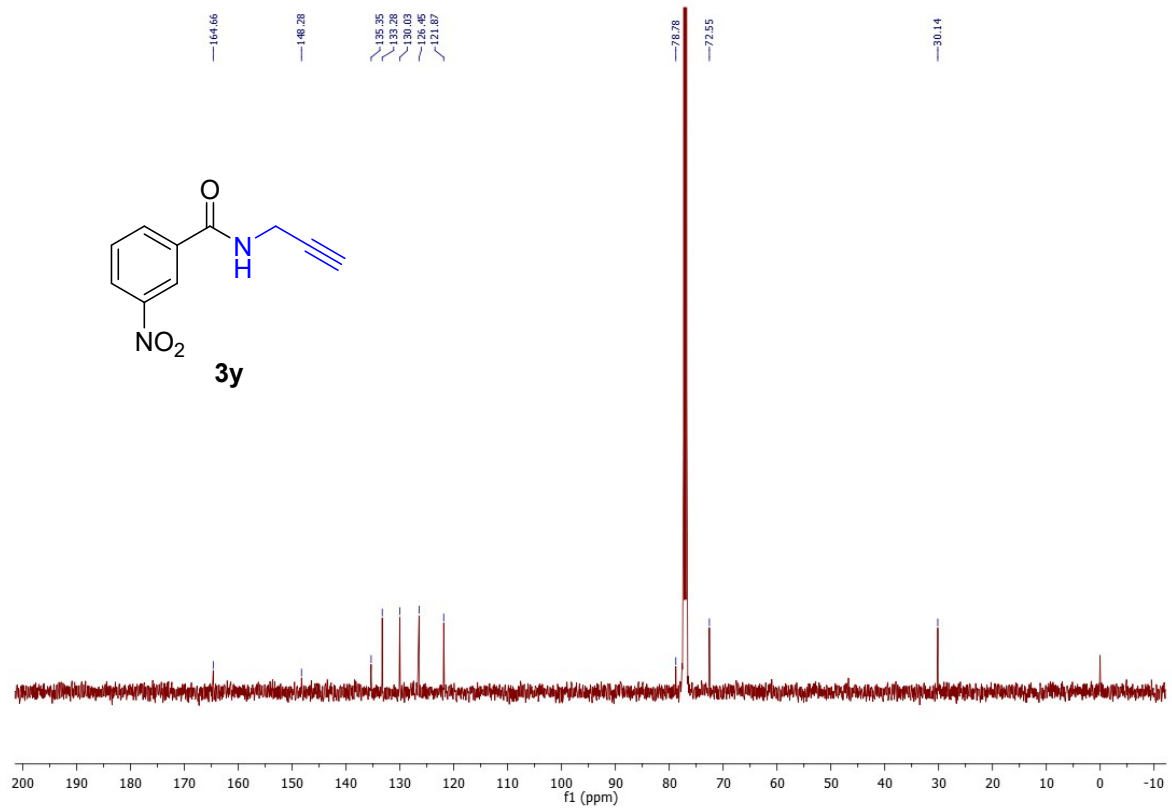
^{1}H NMR of Compound **3x (400 MHz, $CDCl_3$)**



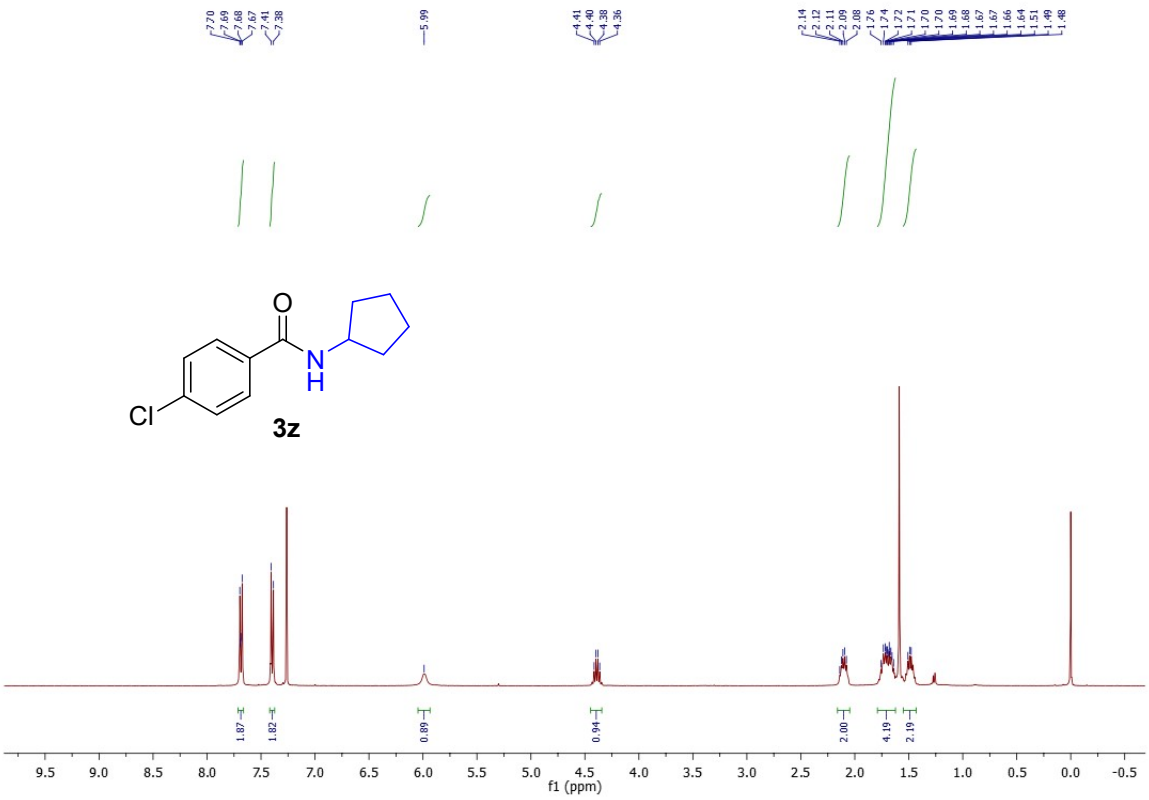
^{13}C NMR of Compound **3x (101 MHz, $CDCl_3$)**



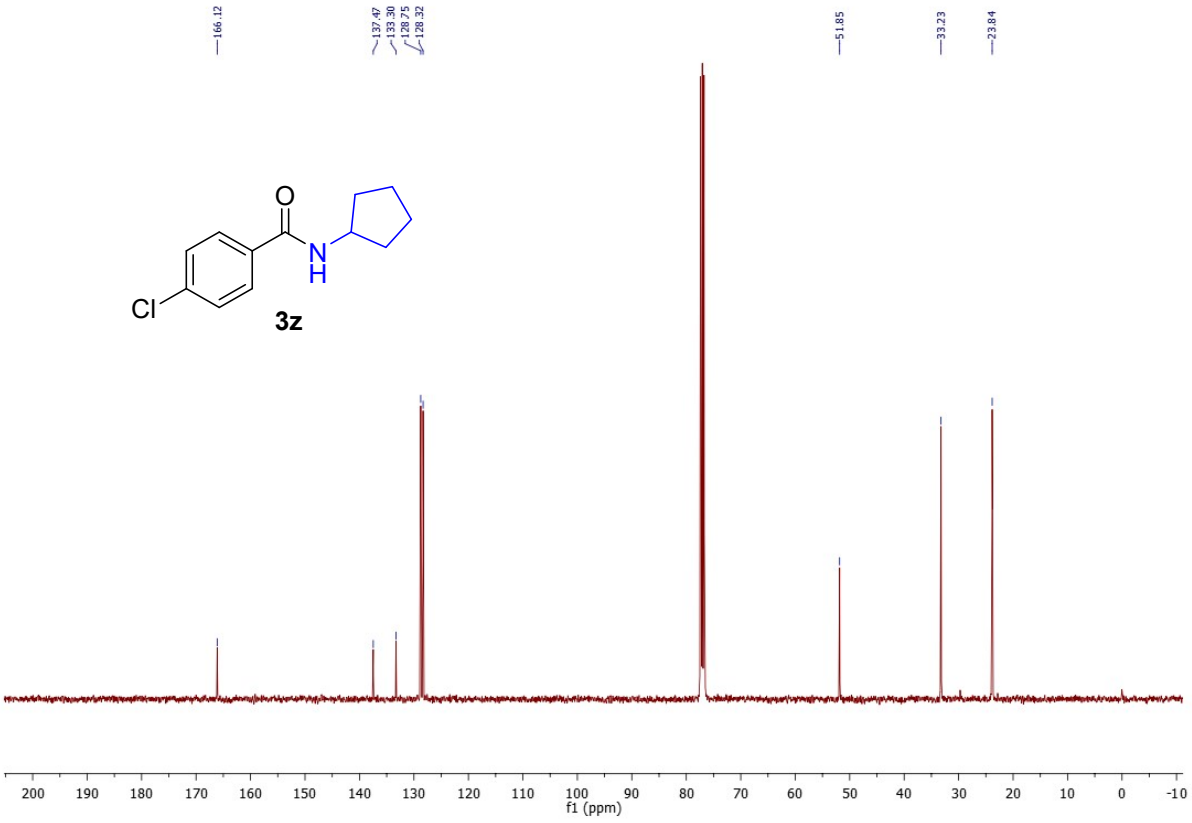
^{1}H NMR of Compound **3y (400 MHz, $CDCl_3$)**



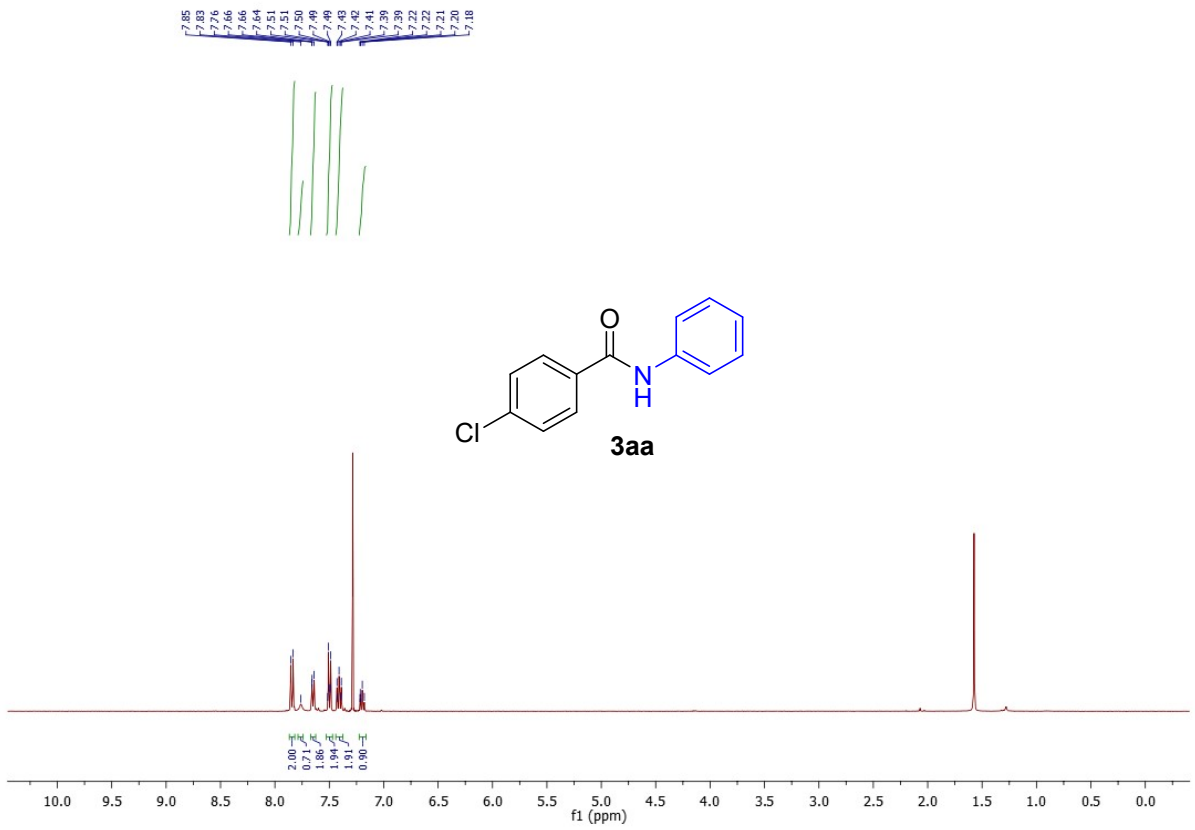
^{13}C NMR of Compound **3y (126 MHz, $CDCl_3$)**



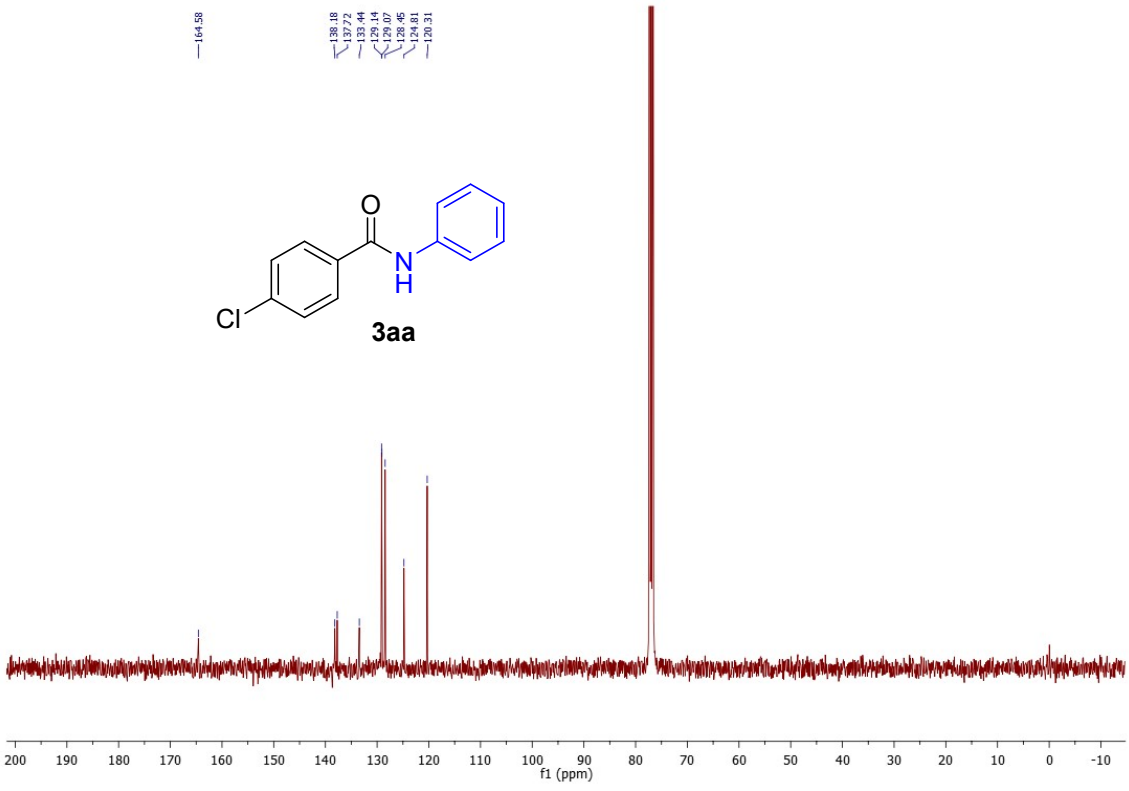
^{1}H NMR of Compound **3z (400 MHz, $CDCl_3$)**



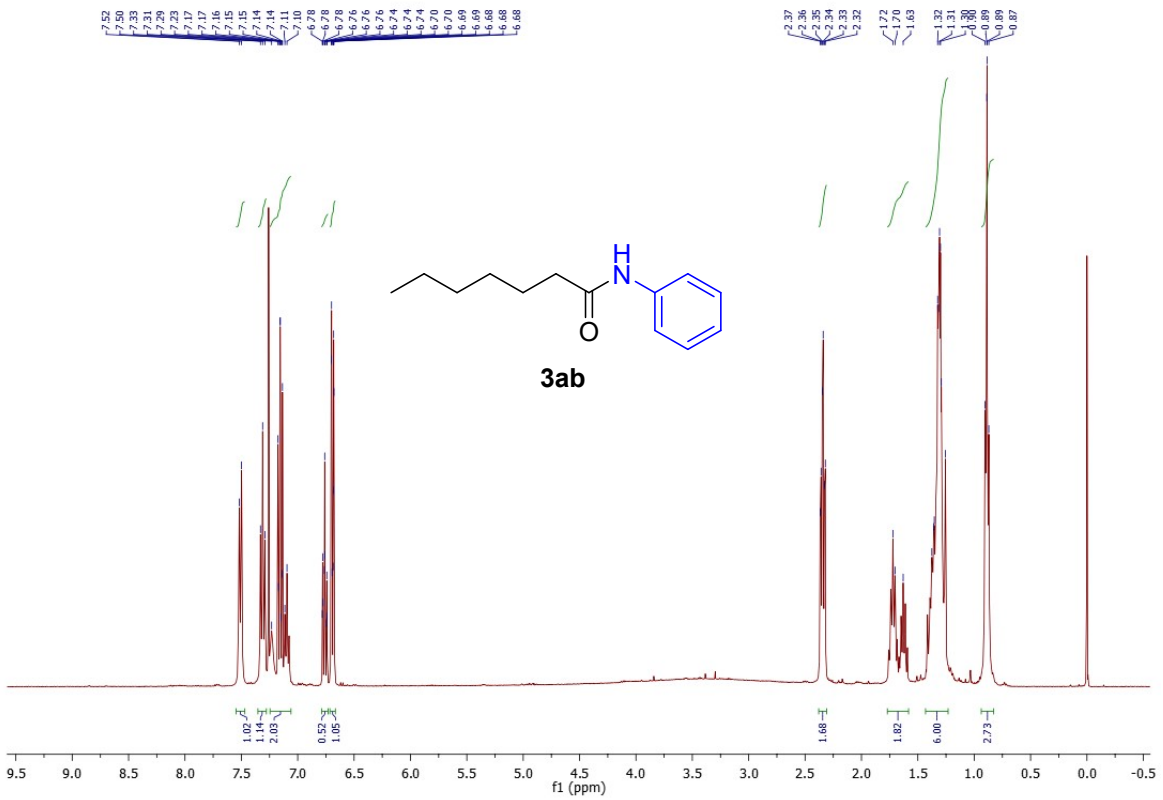
^{13}C NMR of Compound **3z (101 MHz, $CDCl_3$)**



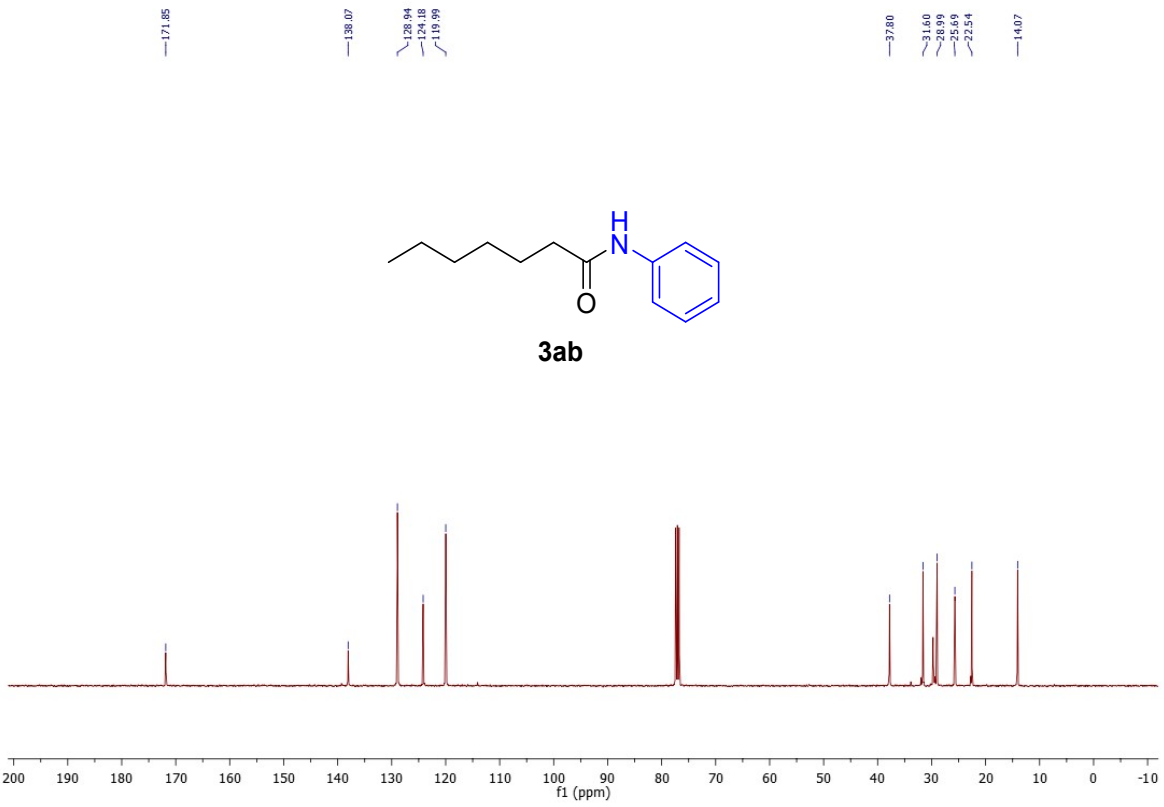
^{1}H NMR of Compound **3aa (400 MHz, $CDCl_3$)**



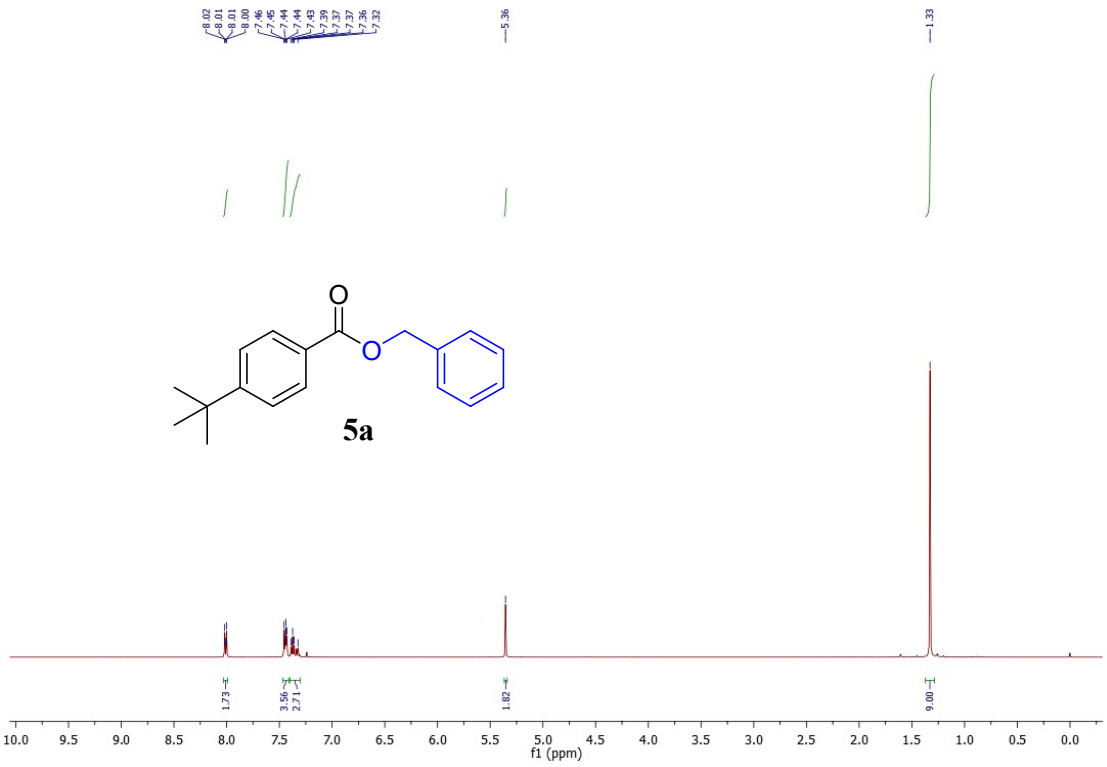
^{13}C NMR of Compound **3aa (101 MHz, $CDCl_3$)**



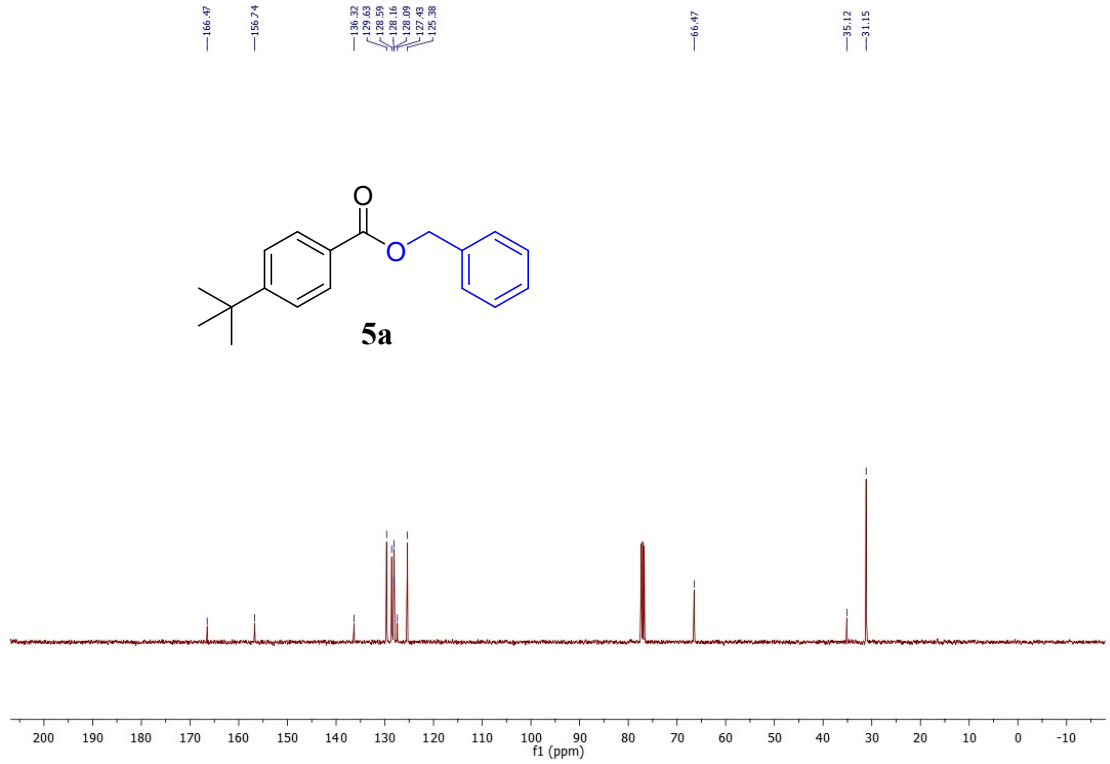
^{1}H NMR of Compound **3ab (400 MHz, $CDCl_3$)**



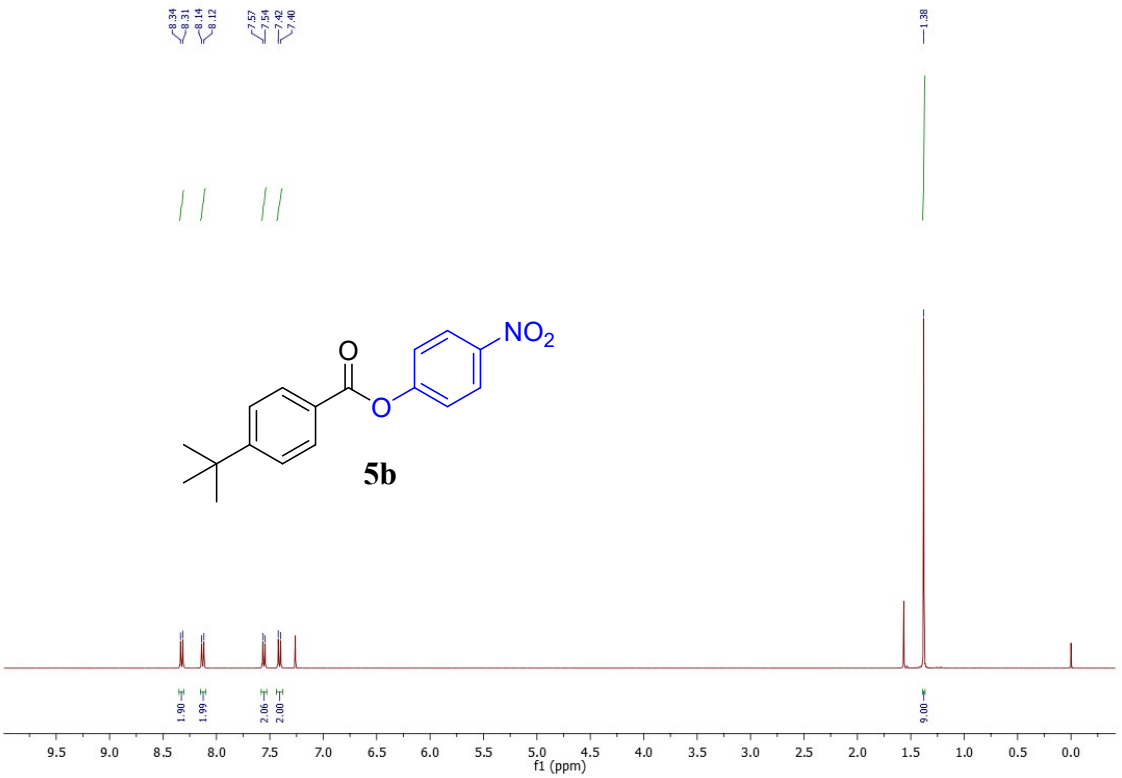
^{13}C NMR of Compound **3ab (101 MHz, $CDCl_3$)**



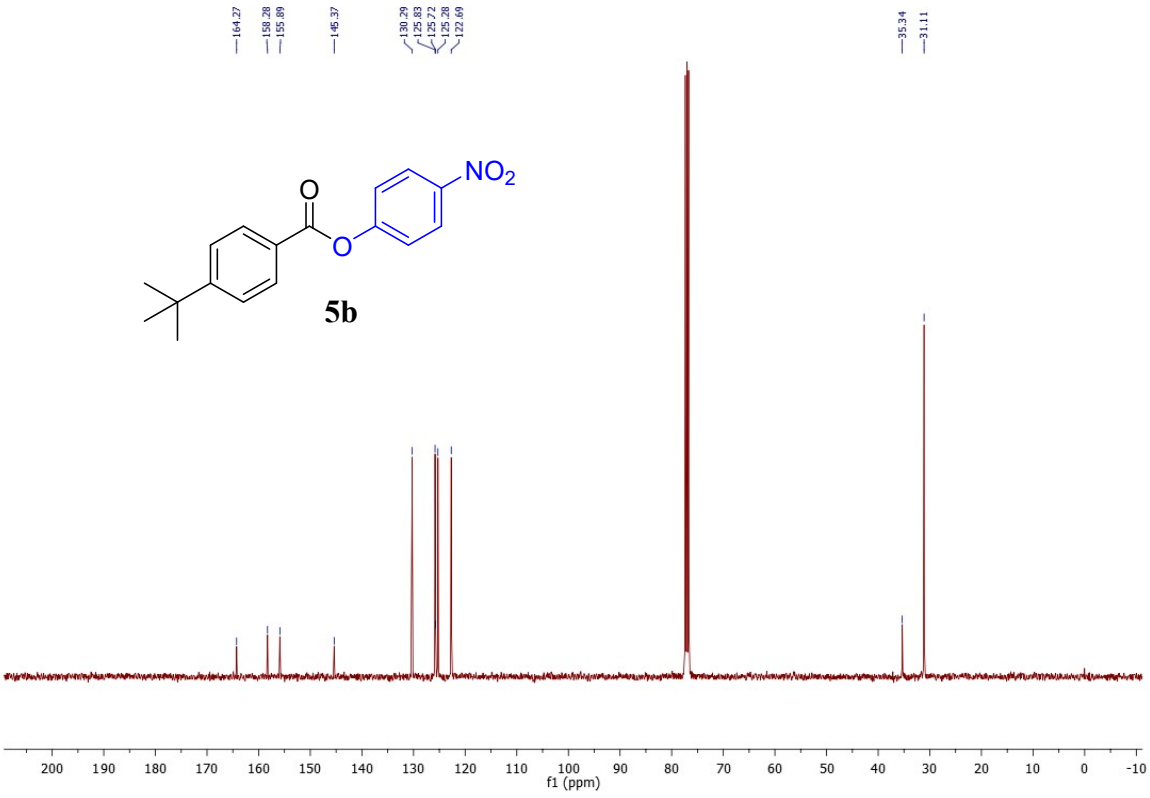
^{1}H NMR of Compound **5a (500 MHz, $CDCl_3$)**



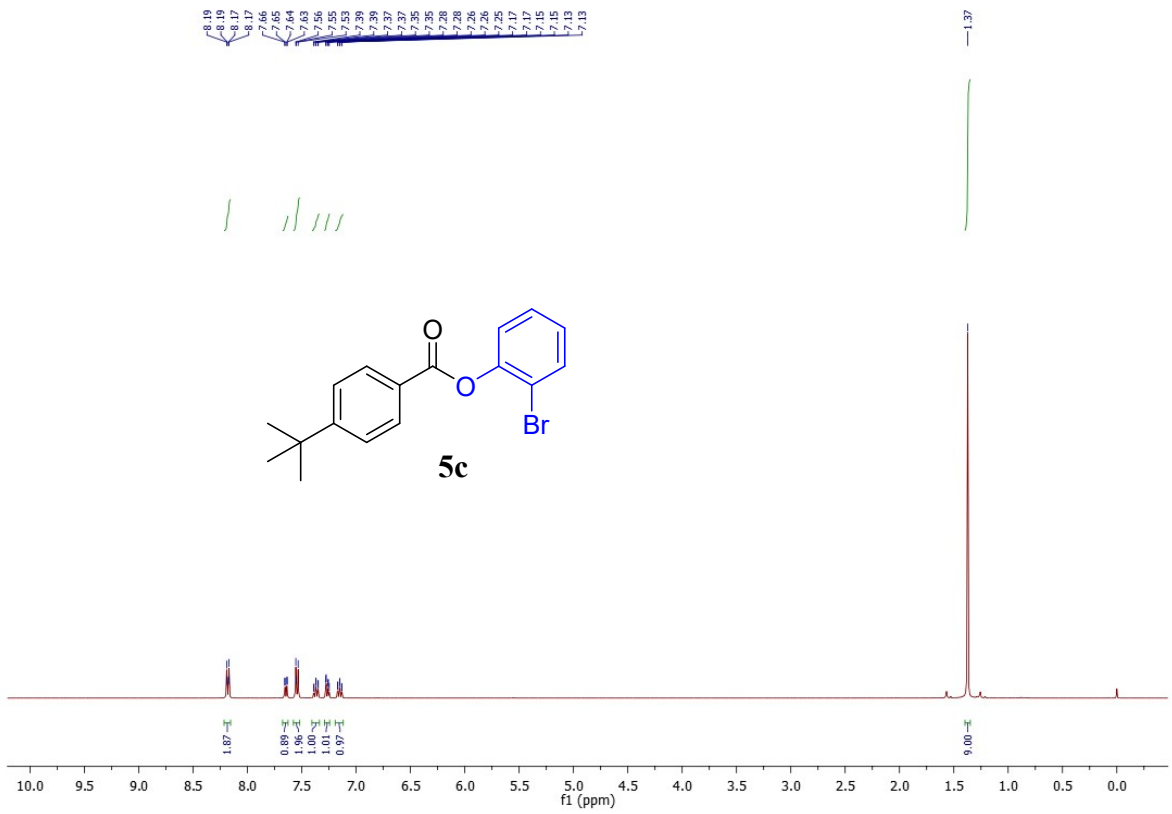
^{13}C NMR of Compound **5a (101 MHz, $CDCl_3$)**



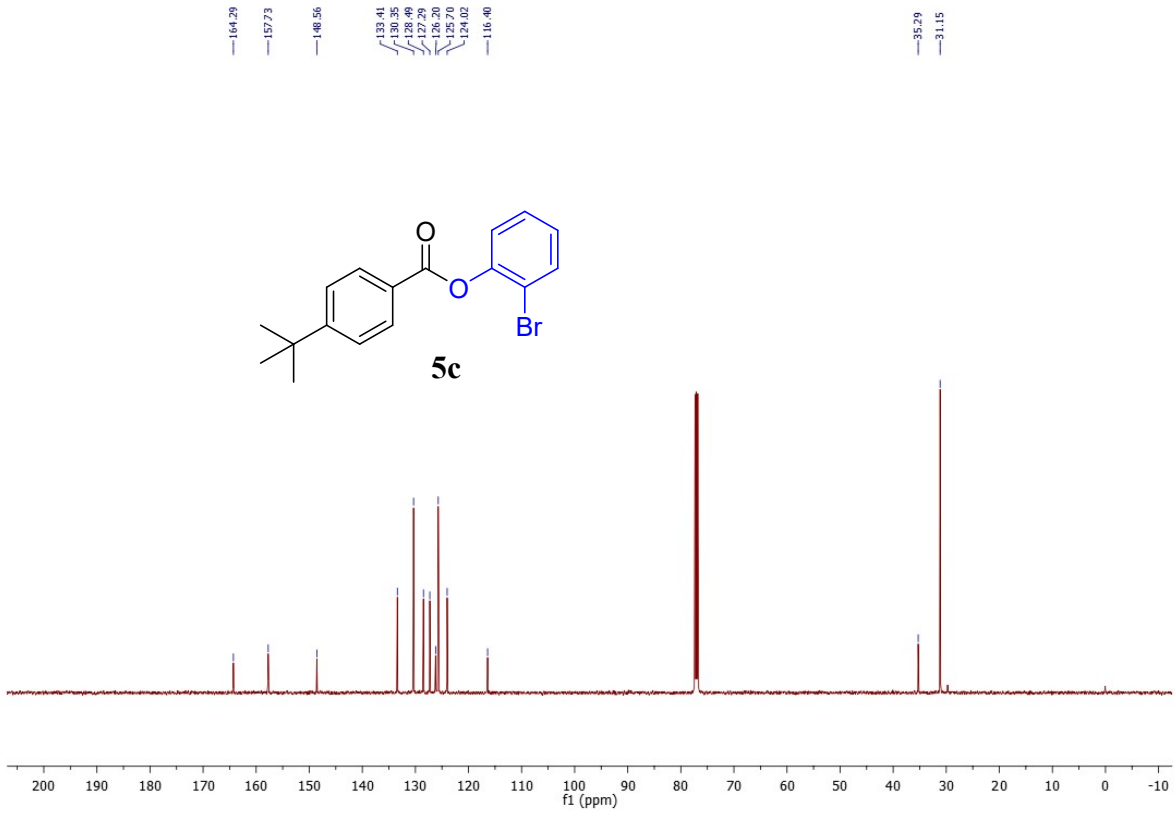
^{1}H NMR of Compound **5b (400 MHz, $CDCl_3$)**



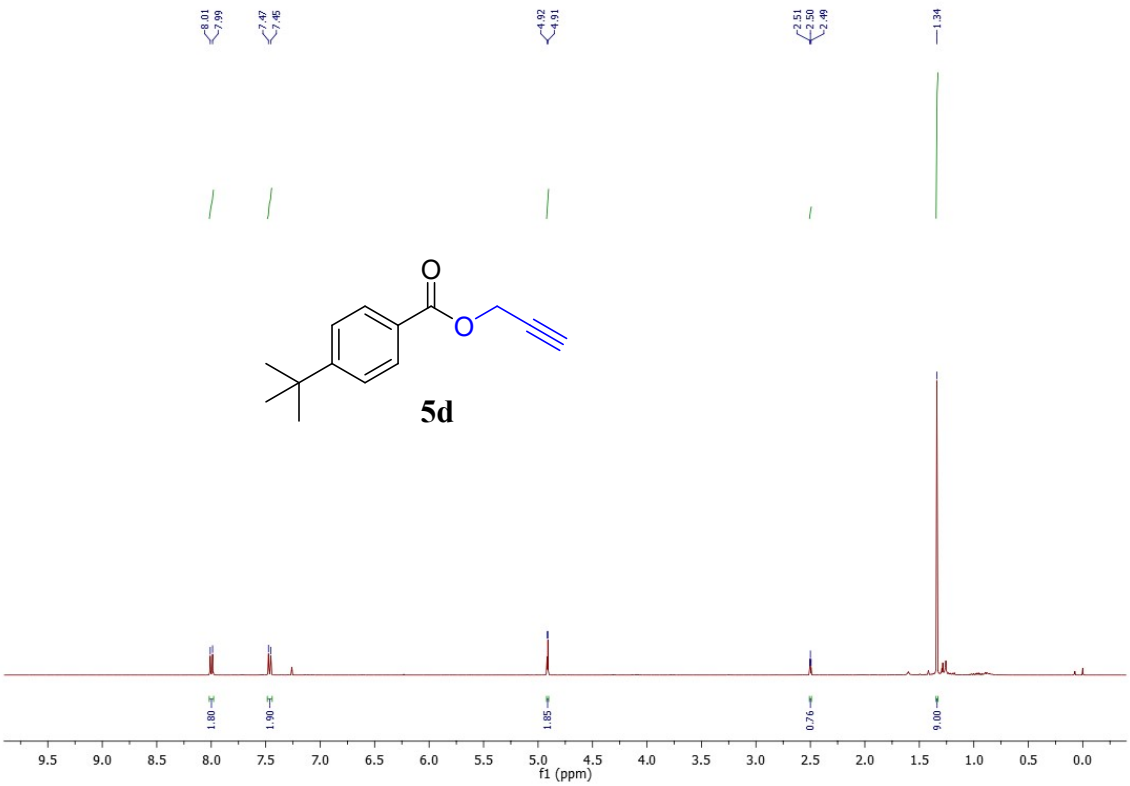
^{13}C NMR of Compound **5b (101 MHz, $CDCl_3$)**



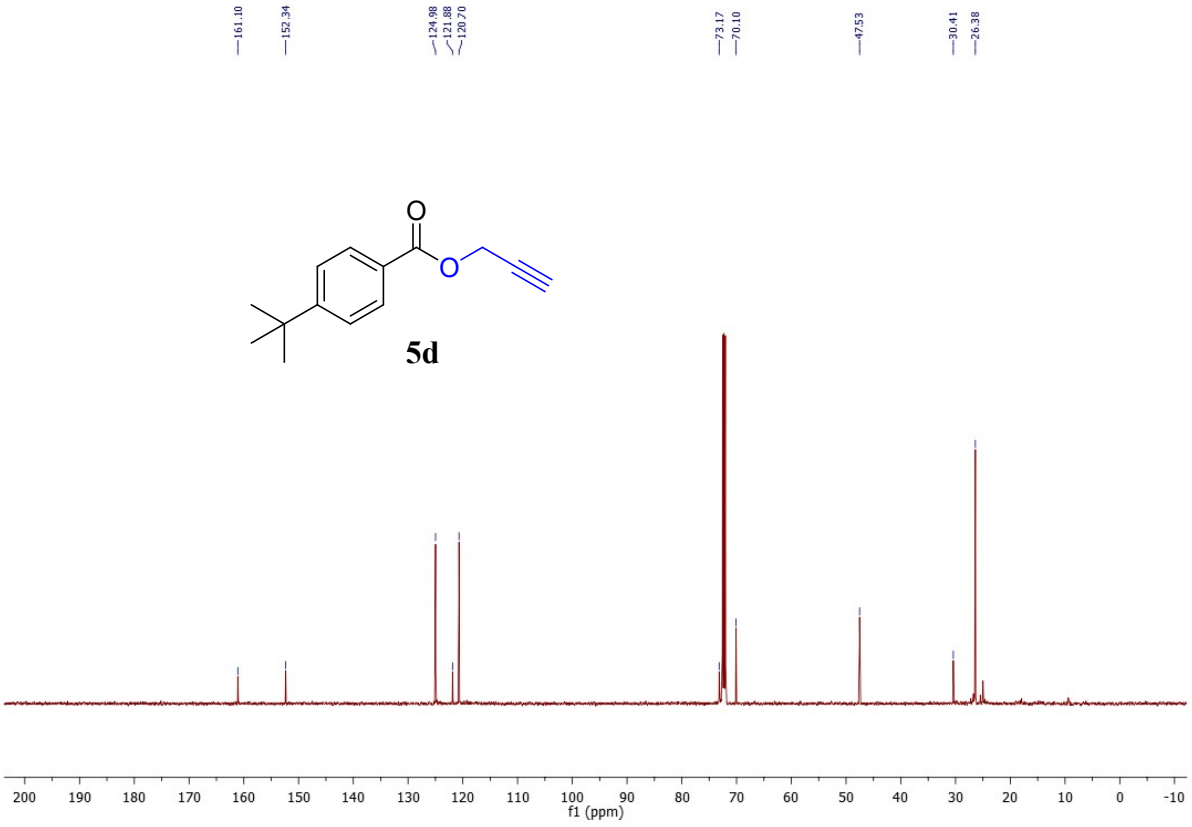
^{1}H NMR of Compound **5c (400 MHz, $CDCl_3$)**



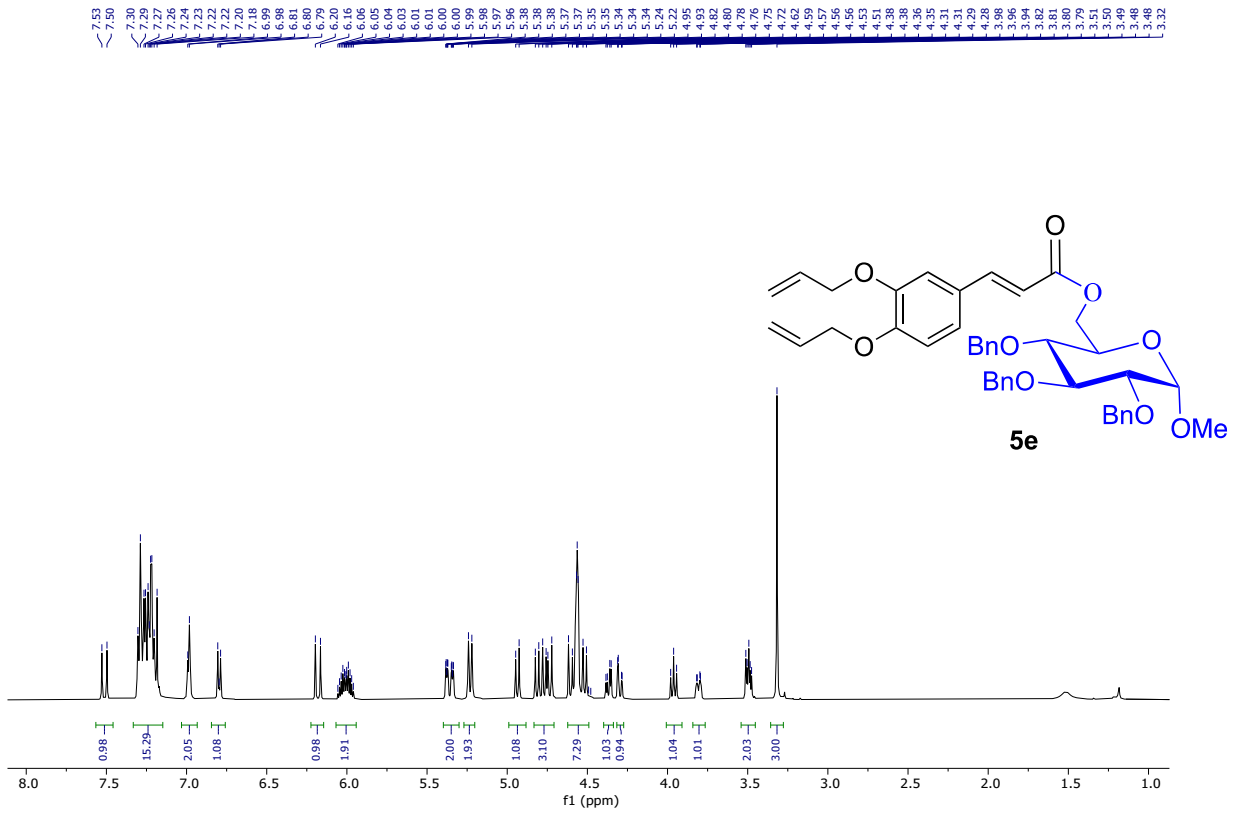
^{13}C NMR of Compound **5c (126 MHz, $CDCl_3$)**



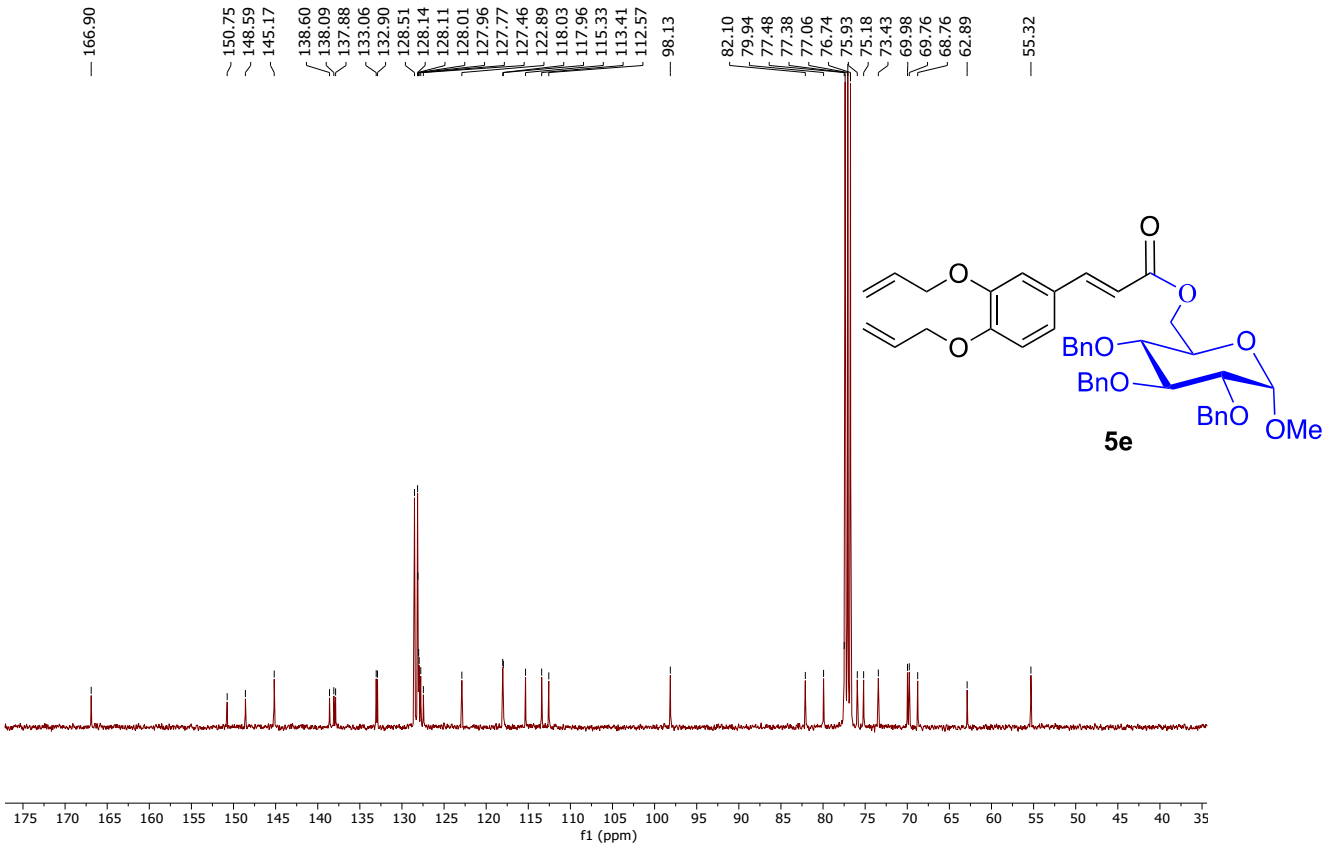
^{1}H NMR of Compound **5d (400 MHz, $CDCl_3$)**



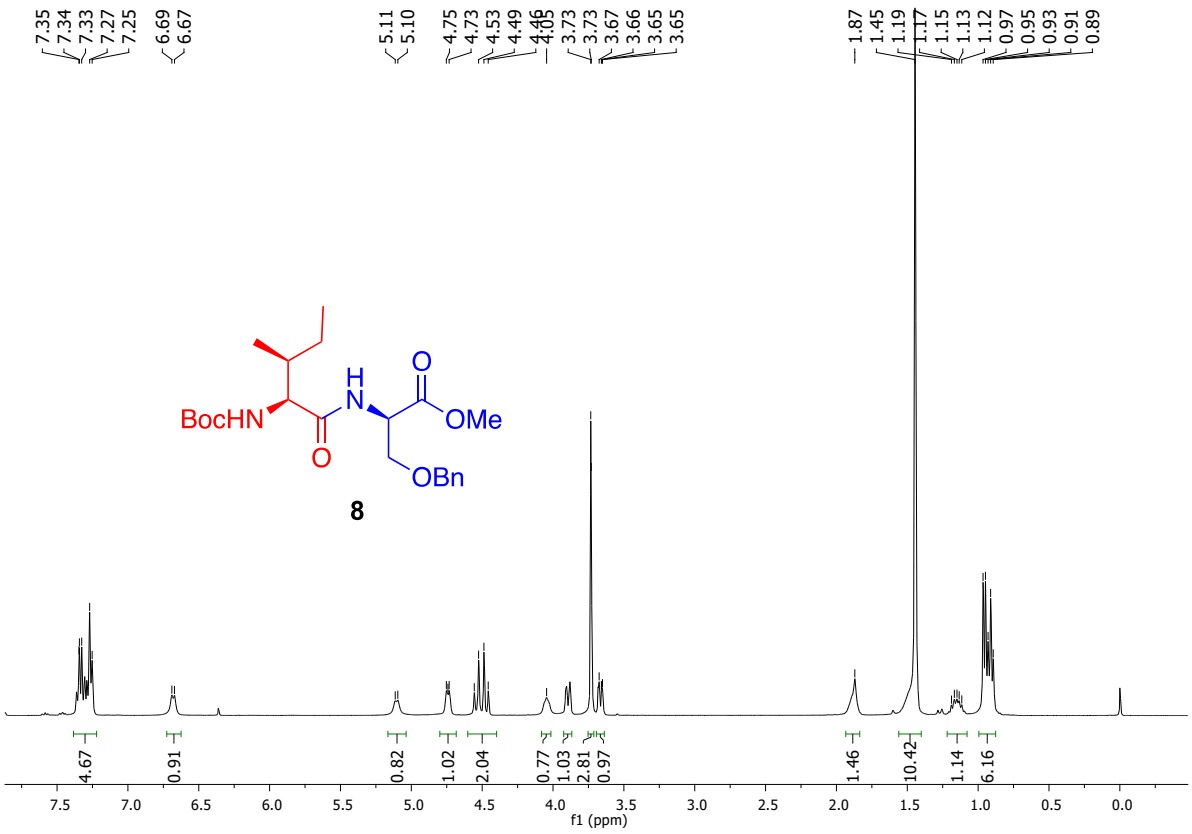
^{13}C NMR of Compound **5d (126 MHz, $CDCl_3$)**



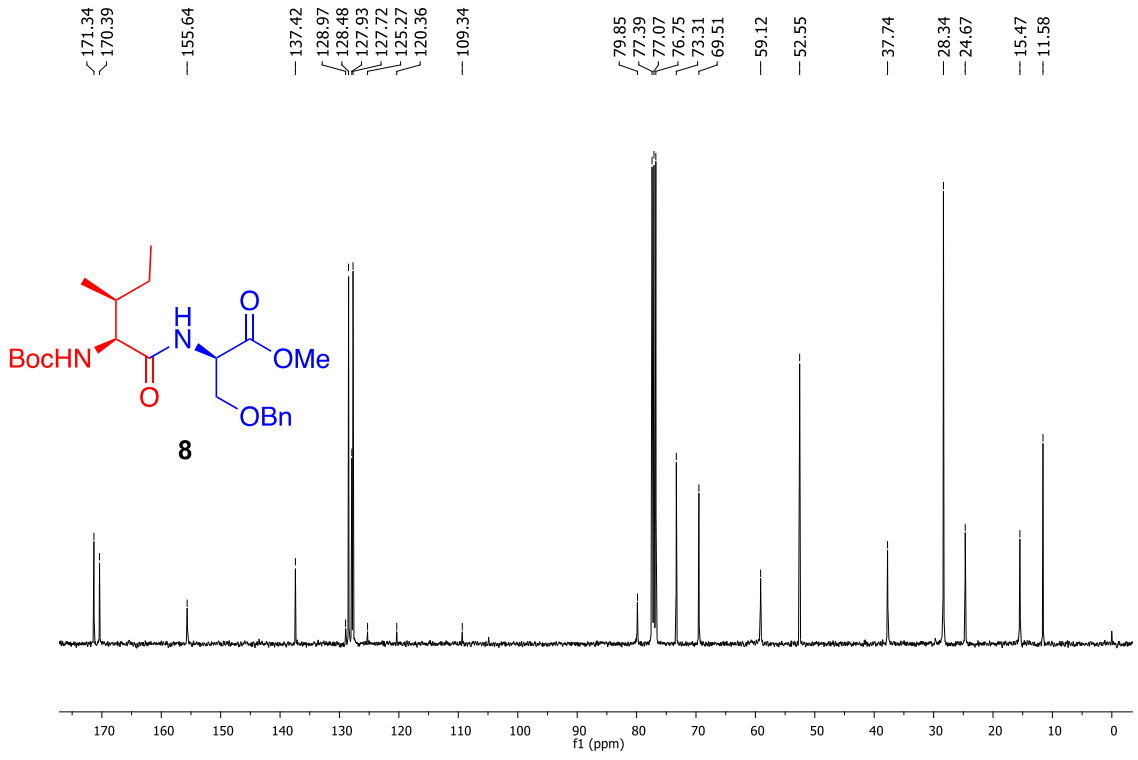
^{1}H NMR of Compound **5e (400 MHz, $CDCl_3$)**



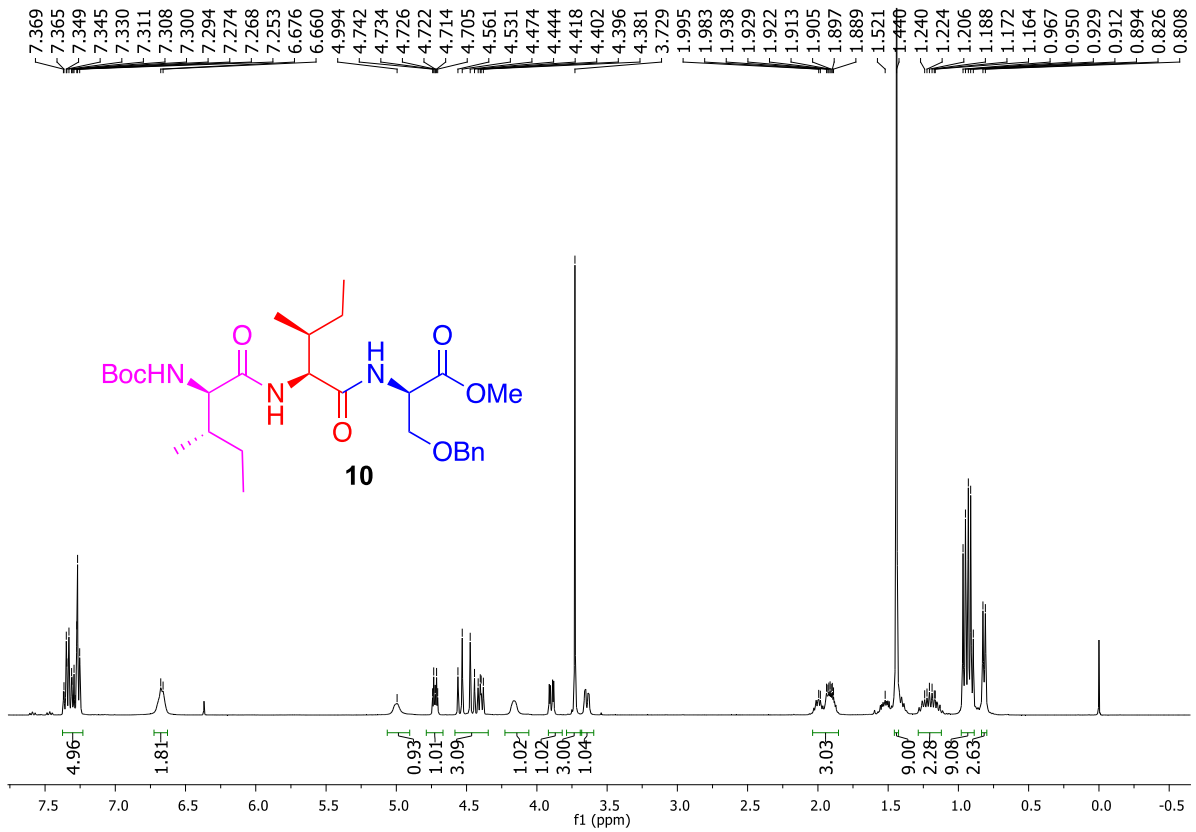
^{13}C NMR of Compound **5e (101 MHz, $CDCl_3$)**



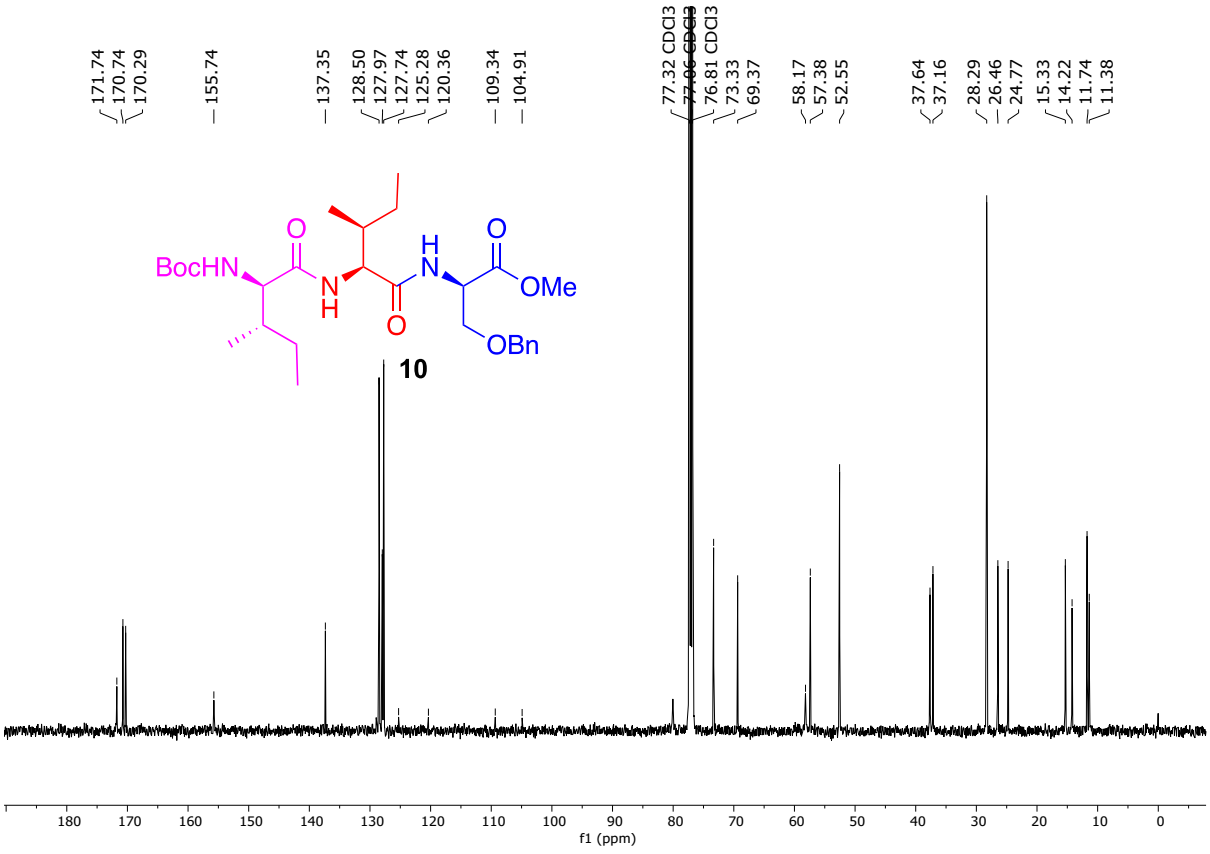
^{1}H NMR of Compound **8 (400 MHz, $CDCl_3$)**



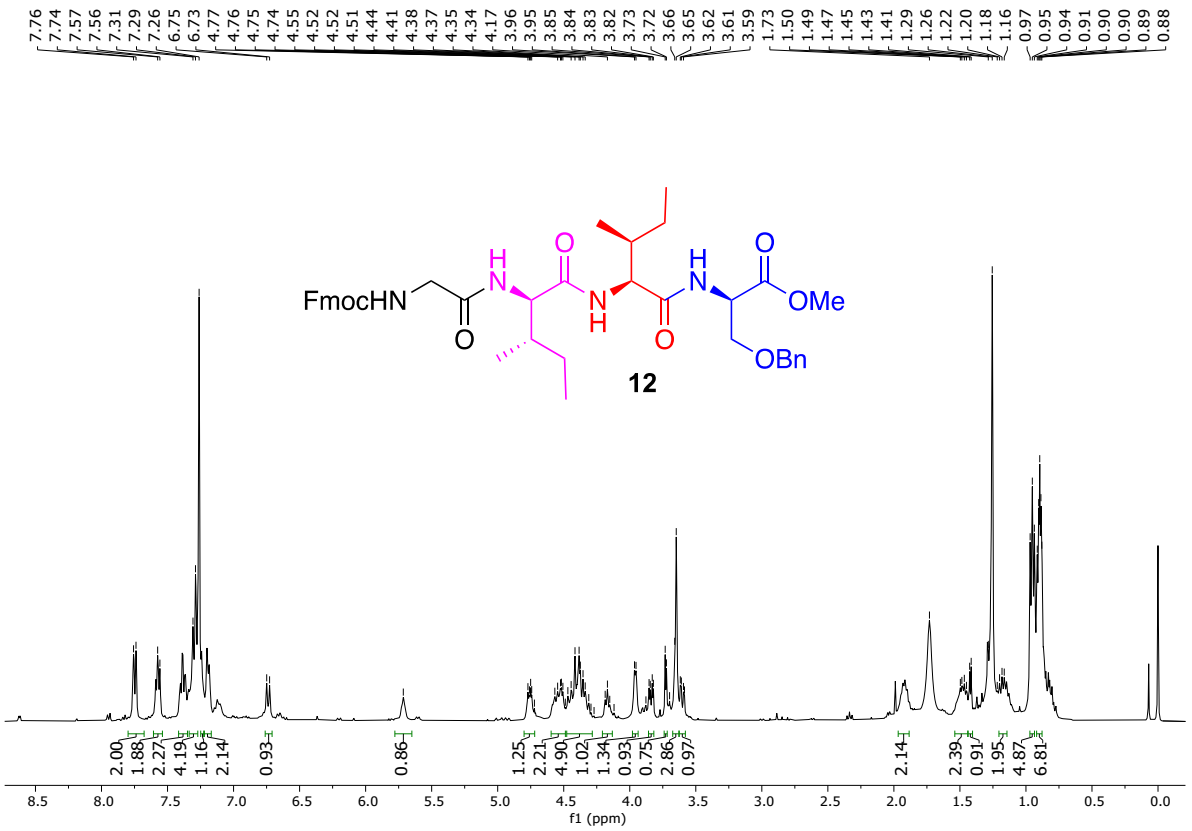
^{13}C NMR of Compound **8 (101 MHz, $CDCl_3$)**



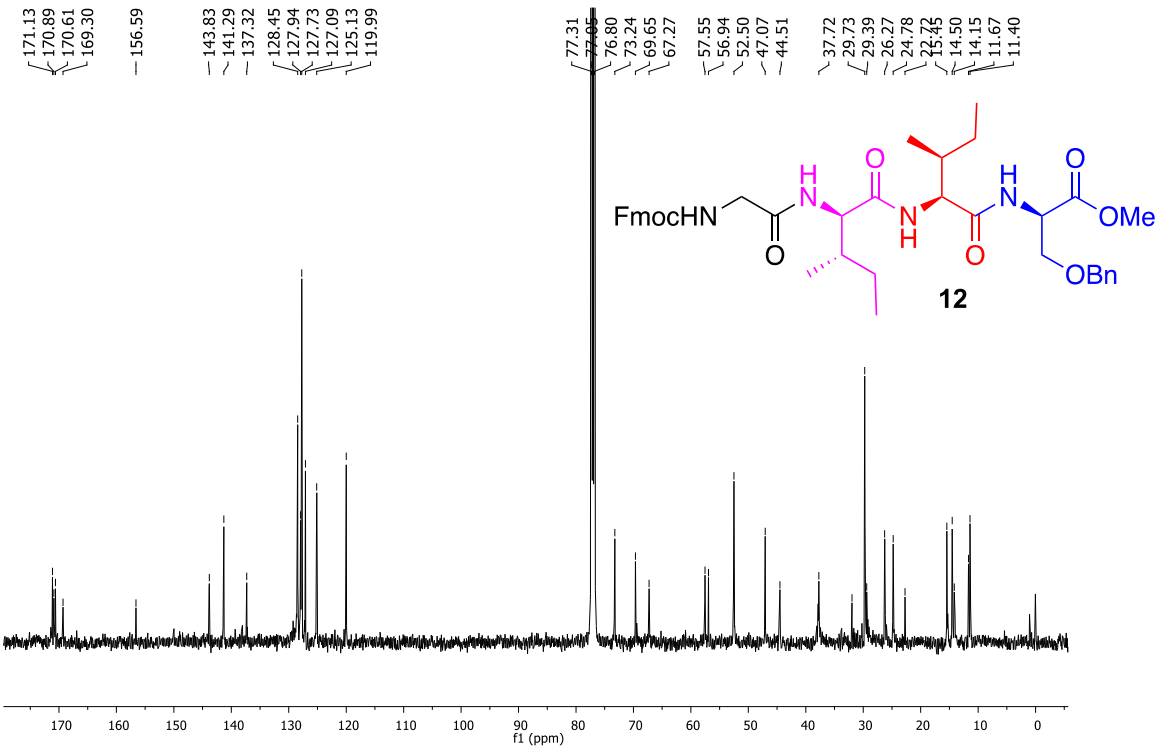
^{1}H NMR of Compound **10 (400 MHz, $CDCl_3$)**



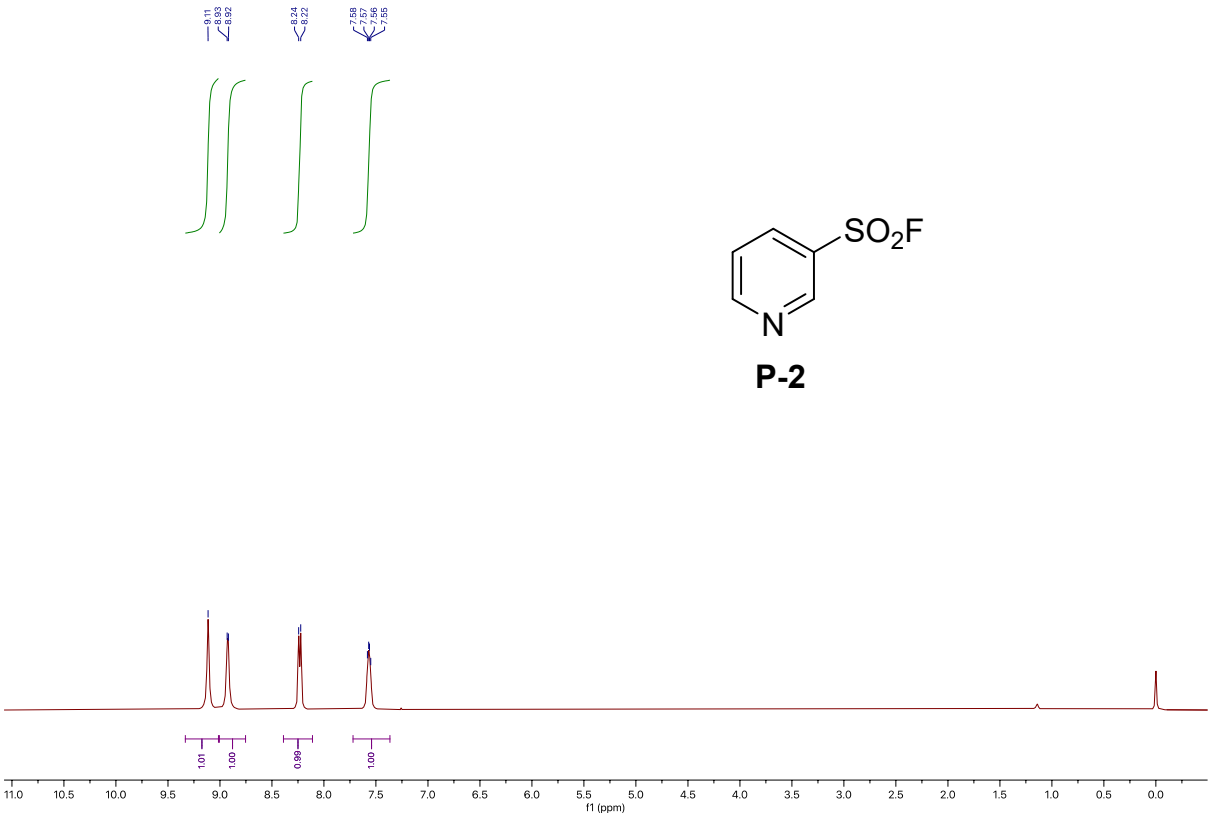
^{13}C NMR of Compound **10 (101 MHz, $CDCl_3$)**



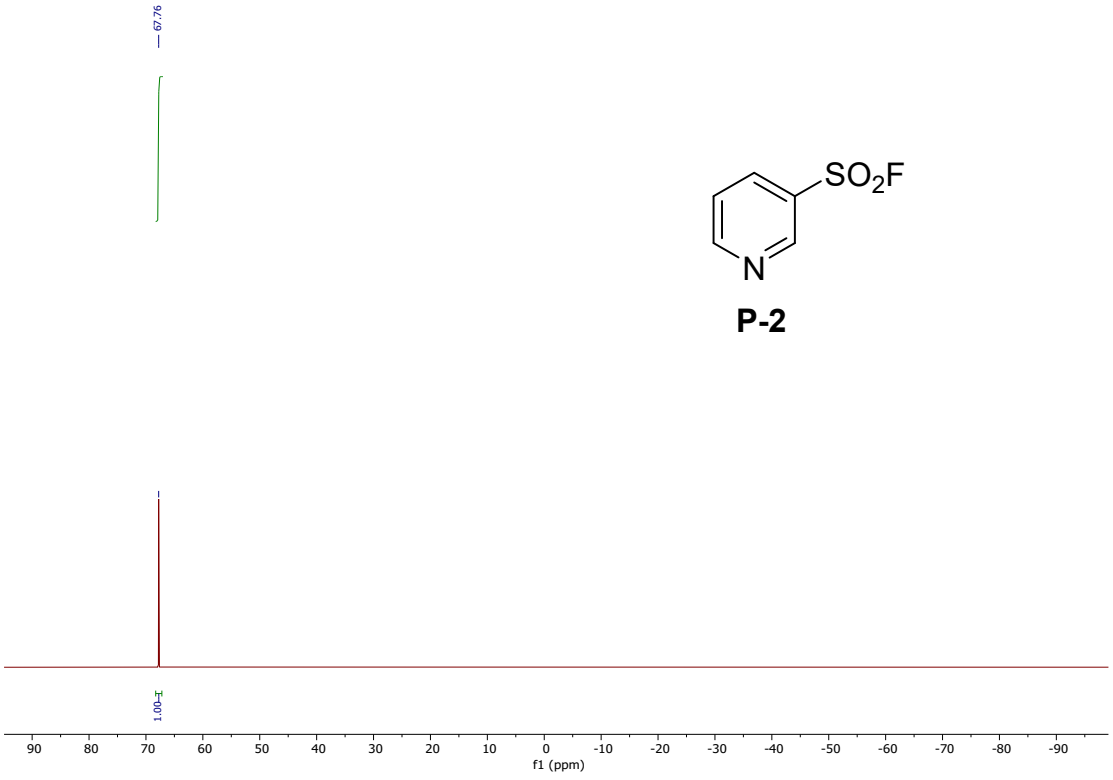
^{1}H NMR of Compound **12 (400 MHz, $CDCl_3$)**



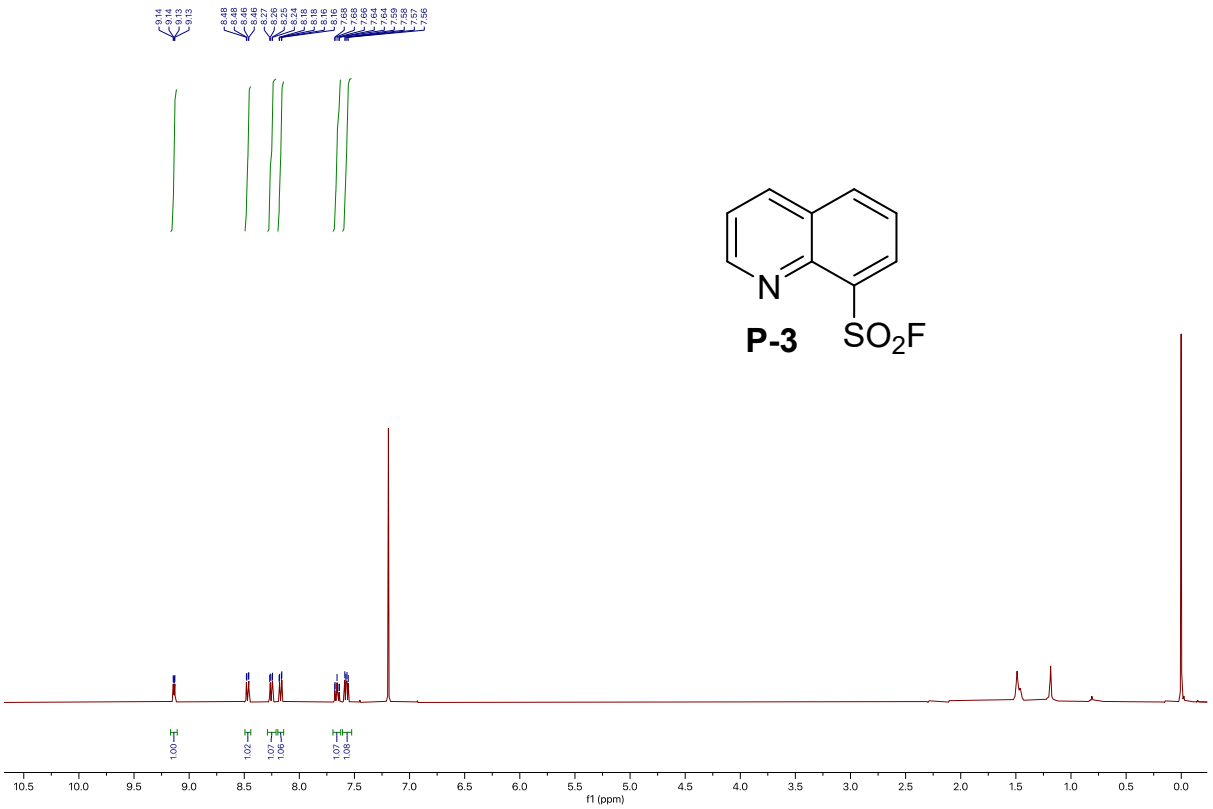
^{13}C NMR of Compound **12 (126 MHz, $CDCl_3$)**



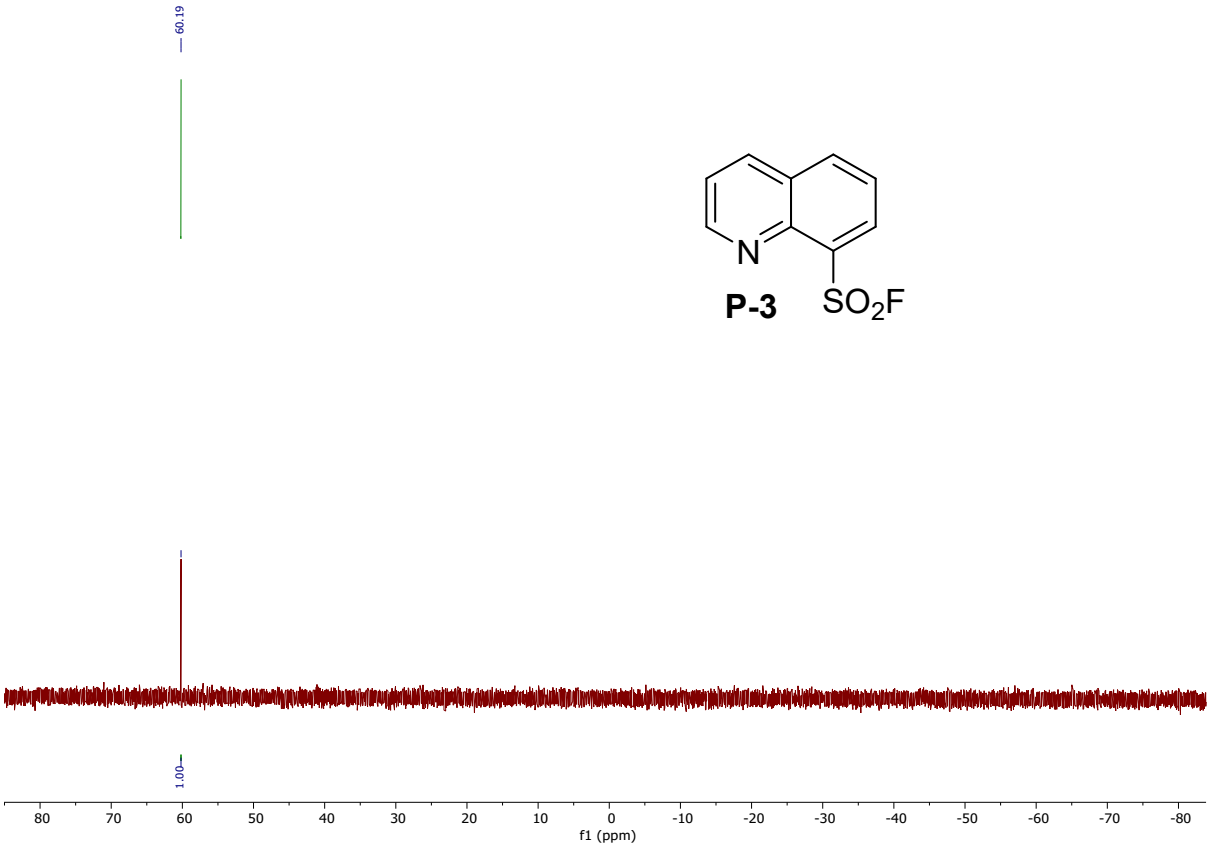
^{1}H NMR of 3-pyridinesulfonyl fluoride **P-2 (400 MHz, $CDCl_3$)**



^{19}F NMR of 3-pyridinesulfonyl fluoride **P-2 (377 MHz, $CDCl_3$)**



^{1}H NMR of 8-quinolinesulfonyl fluoride **P-3 (400 MHz, $CDCl_3$)**



^{19}F NMR of 8-quinolinesulfonyl fluoride **P-3 (377 MHz, $CDCl_3$)**