Supporting Information

Direct *N*-Methyl C−H Esterification of *O*-Tosyl Hydroxamates to Enable Facile Synthesis of Hemiaminal Esters†

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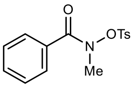
1. General Information

Unless otherwise noted, all glassware was oven-dried before use, and all reactions were performed under an air atmosphere. All reagents were used as received from commercial sources unless otherwise stated. Acetonitrile (MeCN) and methylene chloride (CH_2Cl_2) were distilled from calcium hydride (CaH_2) under a nitrogen atmosphere prior to use. Toluene and tetrahydrofuran (THF) were distilled from sodium metal under a nitrogen atmosphere before use. Anhydrous *N*,*N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), and triethylamine (Et_3N) were purchased from Energy Chemical or Adamas-beta and were used without further purification. Analytical thin-layer chromatography (TLC) was performed on pre-coated silica gel GF 254 plates, visualized by fluorescence quenching under UV light at 254 nm, or by staining with phosphomolybdic acid or potassium permanganate. Organic solutions were concentrated under reduced pressure using an IKA rotary evaporator. Product purification was performed by flash column chromatography using silica gel (400 mesh) with the indicated solvent system. Nuclear magnetic resonance (NMR) spectra were recorded with an Agilent 600 MHz instrument. Chemical shifts are reported in parts per million (ppm) and calibrated using the residual proton signal in the deuterated solvent ($CDCl_3$ at δ 7.26 ppm (^1H NMR) & 77.16 ppm (^{13}C NMR); DMSO-d_6 at δ 2.50 ppm (^1H NMR) & 39.52 ppm (^{13}C NMR)). Data are reported in the following format: chemical shift in ppm, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br s = broad singlet, m = multiplet, dd = doublet of doublets, etc.), coupling constant *J* in Hz, and integration. Infrared spectra were recorded on a PerkinElmer Frontier FTIR spectrometer and are reported in terms of frequency of absorption (cm^{-1}). High-resolution mass spectra (HRMS) were obtained using electrospray ionization (ESI) on a time of flight (TOF) mass spectrometer.

2. General Procedures for the Preparation and Characterization of Starting Materials

The following *O*-tosyl hydroxamates **1a**–**1g**, **1j**, **1l**, **1m**, **1o**, **1v**, **1w**, and compounds **1-I**–**1-III** were prepared according to our previous reported procedures.[1]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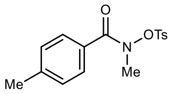
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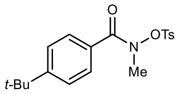
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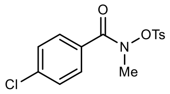
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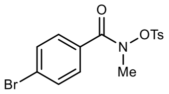
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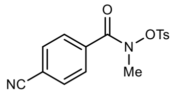
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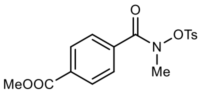
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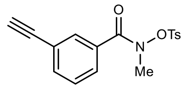
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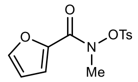
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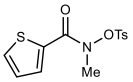
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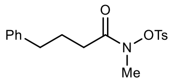
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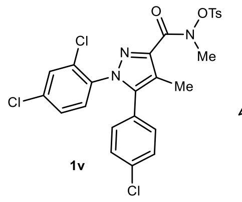
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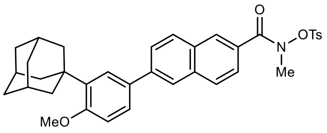
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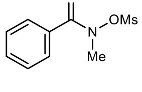
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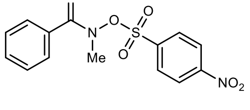
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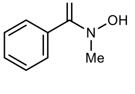
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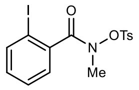
The following new *O*-tosyl hydroxamates, **1h**–**1i**, **1k**, **1n**, **1p**–**1u**, **1x**–**1y**, were synthesized according following **General Procedure 1A** are outlined below.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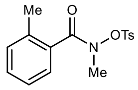
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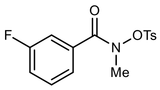
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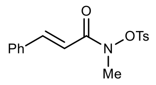
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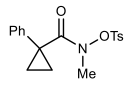
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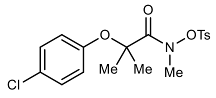
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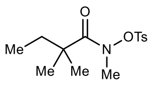
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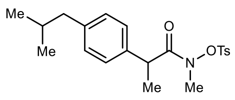
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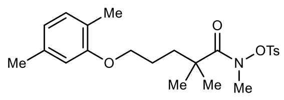
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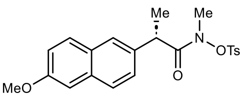
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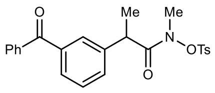
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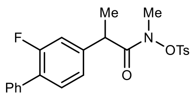
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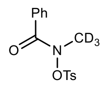
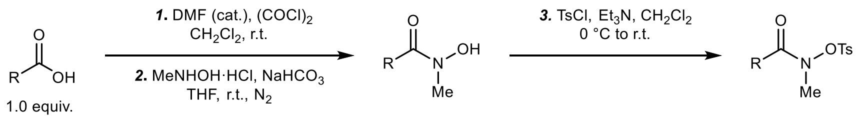

1a-*d*₃

General Procedure 1A (GP1A)



Step 1: *Preparation of acyl chlorides*

To a stirring solution of carboxylic acid (1.0 equiv.) in dry CH$_2$Cl$_2$ (0.5 M) was added DMF drops and oxalyl chloride (3.0 equiv.) dropwise using a syringe. An oil bubbler was connected to the reaction vial for releasing the pressure. The reaction mixture was stirred at room temperature (r.t.) for 17 h. The solvent and unreacted oxalyl chloride were removed under reduced pressure. The obtained acyl chlorides were used directly in the next part of the procedure.

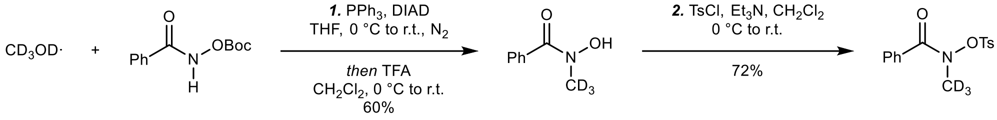
Step 2: *Preparation of N-hydroxy-N-methylamides*

To a stirring suspension of *N*-methylhydroxylamine hydrochloride (1.1 equiv.) and NaHCO$_3$ (2.2 equiv.) in THF under a nitrogen atmosphere was added THF solution of acyl chloride (1.0 equiv.) dropwise over 10 min. The reaction mixture was stirred overnight and was then diluted with H$_2$O. The mixture was extracted with CH_2Cl_2 (× 3). The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by recrystallization or flash column chromatography. This material was used directly in the next part of the procedure.

Step 3: *Preparation of O-tosyl hydroxamates*

To a solution of *N*-hydroxy-*N*-methylamide (1.0 equiv.) in dry CH_2Cl_2 was added Et_3N (1.1 equiv.) with magnetic stirring. The resulting clear solution was cooled in an ice bath and treated slowly with TsCl (1.1 equiv.). The reaction mixture was stirred at 0 °C for 30 min and then at r.t. for 4 h. After dilution with CH_2Cl_2, the organic phase was washed with brine, dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by recrystallization or flash column chromatography.

General Procedure 1B (GP1B) *for the preparation of O-tosyl hydroxamates* **1a-*d*3**



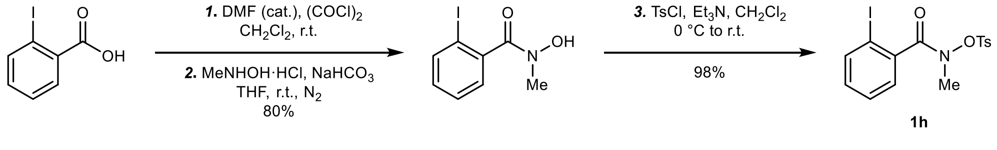
Step 1: *Mintsunobu reaction for the preparation of N-hydroxy-N-alkylbenzamide*

To an oven-dried round-bottom flask equipped with a magnetic stir bar was added *N*-((*tert*-butoxycarbonyl)oxy)benzamide (4.74 g, 20 mmol, 1.0 equiv.), methanol-*d*4 (0.86 g, 24 mmol, 1.2 equiv.), PPh_3 (7.34 g, 28 mmol, 1.4 equiv.) in dry THF (60 mL) at 0 °C under a nitrogen atmosphere. Then, DIAD (5.66 g, 28 mmol, 1.4 equiv.) was added slowly to the reaction mixture and stirred at 0 °C to r.t. for 4 h. The crude residue was purified by flash column chromatography on silica gel (eluted with PE/EA = 20:1) to obtain *N*-((*tert*-butoxycarbonyl)oxy)-*N*-(methyl-*d*3)benzamide as a colorless oil (4.37 g, 86%). Using the preceding *N*-((*tert*-butoxycarbonyl)oxy)-*N*-(methyl-*d*3)benzamide (4.37 g, 17.2 mmol, 1.0 equiv.) in CH_2Cl_2 (34 mL) was added TFA (6.6 mL, 86 mmol, 5.0 equiv.). After 2 h, the reaction mixture was quenched, and the crude *N*-hydroxy-*N*-(methyl-*d*3)benzamide (1.86 g, 70%) was used directly in the next part.

Step 2: *Preparation of O-tosyl hydroxamates*

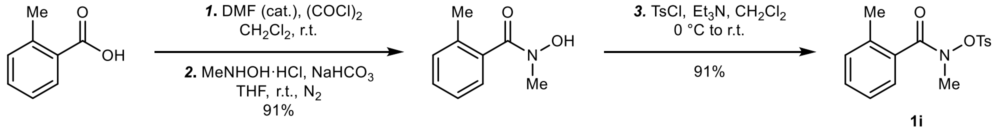
Then, using crude *N*-hydroxy-*N*-(methyl-*d*3)benzamide (1.86 g, 12 mmol, 1.0 equiv.), TsCl (2.52 g, 13.2 mmol, 1.1 equiv.), Et_3N (1.8 mL, 13.2 mmol, 1.1 equiv.) in CH_2Cl_2 (24 mL). The crude residue was purified by recrystallization (CH_2Cl_2/PE) to obtain **1a-*d*3** as a white solid (2.66 g, 72%). **M.P.** 98–101 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.1 Hz, 2H), 7.42–7.38 (m, 1H), 7.34–7.31 (m, 2H), 7.27 (t, *J* = 7.8 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 2.38 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.2, 146.2, 132.5, 131.4, 130.2, 129.8, 129.2, 128.5, 128.1, 21.8; **IR** (neat) $\tilde{\nu}_{max}$ 1692, 1379, 1194, 817, 701 cm^{-1}; **HRMS** (ESI/$[M + H]^+$) *m/z* calcd. for $C_{15}H_{13}D_3NO_4S^+$: 309.0983, found: 309.0988.

2-Iodo-*N*-methyl-*N*-(tosyloxy)benzamide (1h)



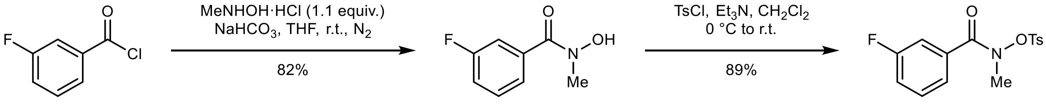
Prepared following the **GP1A** with slight modifications, using 2-iodobenzoic acid (2.48 g, 10 mmol, 1.0 equiv.), oxalyl chloride (3.82 g, 30 mmol, 3.0 equiv.), DMF (2 drops) in CH_2Cl_2 (20 mL). The reaction mixture was concentrated *in vacuo*, and the resulting acyl chloride was used directly in the next step. Using the preceding acyl chloride, *N*-methylhydroxylamine hydrochloride (0.67 g, 8 mmol, 1.0 equiv.), $NaHCO_3$ (2.02 g, 24 mmol, 3.0 equiv.) in THF (20 mL). The crude residue was purified by recrystallization (CH_2Cl_2/PE) to obtain *N*-hydroxy-2-iodo-*N*-methylbenzamide as a light-yellow oil (1.77 g, 80%). Then, using *N*-hydroxy-2-iodo-*N*-methylbenzamide (1.77 g, 6.4 mmol, 1.0 equiv.), TsCl (1.28 g, 6.7 mmol, 1.05 equiv.), Et_3N (0.98 mL, 7 mmol, 1.1 equiv.) in CH_2Cl_2 (14 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with PE/EA = 10:1 → 5:1) to obtain **1h** as a white solid (2.69 g, 98%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.68–7.59 (m, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.06–7.03 (m, 1H), 6.89–6.85 (m, 1H), 3.47 (s, 3H), 2.45 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 146.5, 139.5, 139.1, 131.0, 130.7, 130.1, 129.4, 128.4, 127.8, 92.3, 39.9, 22.0; **IR** (neat) $\tilde{\nu}_{max}$ 1681, 1596, 1432, 1380, 1192, 1178, 1015, 736 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{15}H_{14}INO_2Na^+$: 453.9580, found: 453.9581.

N,2-Dimethyl-*N*-(tosyloxy)benzamide (1i)



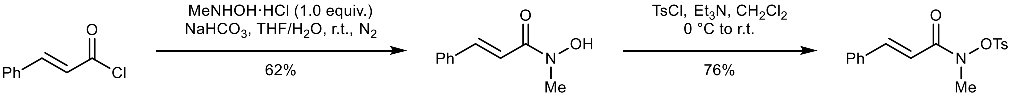
Prepared following the **GP1A** with slight modifications, using 2-methylbenzoic acid (2.72 g, 20 mmol, 1.0 equiv.), oxalyl chloride (3.82 g, 30 mmol, 3.0 equiv.), DMF (5 drops) in CH_2Cl_2 (40 mL). The reaction mixture was concentrated *in vacuo*, and the resulting acyl chloride was used directly in the next step. Using the preceding acyl chloride, *N*-methylhydroxylamine hydrochloride (1.36 g, 16.4 mmol, 1.0 equiv.), $NaHCO_3$ (4.13 g, 49.2 mmol, 3.0 equiv.) in THF (40 mL). The crude residue was purified by recrystallization (PE/EA) to obtain *N*-hydroxy-*N*,2-dimethylbenzamide as a light-yellow oil (2.46 g, 91%). Then, using *N*-hydroxy-2-iodo-*N*-methylbenzamide (2.46 g, 15 mmol, 1.0 equiv.), TsCl (2.99 g, 15.7 mmol, 1.05 equiv.), Et_3N (2.3 mL, 16.5 mmol, 1.1 equiv.) in CH_2Cl_2 (28 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with PE/EA = 10:1) to obtain **1i** as a white solid (4.35 g, 91%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.9 Hz, 2H), 7.24 (t, *J* = 8.2 Hz, 3H), 7.11–7.06 (m, 2H), 6.99 (d, *J* = 7.6 Hz, 1H), 3.44 (s, 3H), 2.42 (s, 3H), 2.14 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.8, 146.2, 136.1, 133.0, 130.7, 130.6, 130.1, 129.9, 129.3, 127.2, 125.5, 39.8, 21.9, 19.4; **IR** (neat) $\tilde{\nu}_{max}$ 2927, 1678, 1492, 1378, 1191, 1178, 1090, 735 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{16}H_{18}NO_2Na^+$: 320.0951, found: 320.0944.

3-Fluoro-*N*-methyl-*N*-(tosyloxy)benzamide (1k)



Prepared following the **GP1A** with slight modifications, using 3-fluorobenzoyl chloride (1.58 g, 10 mmol, 1.0 equiv.), *N*-methylhydroxylamine hydrochloride (0.91 g, 11 mmol, 1.1 equiv.), $NaHCO_3$ (1.85 g, 22 mmol, 2.2 equiv.) in THF (20 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to obtain 3-fluoro-*N*-hydroxy-*N*-methylbenzamide as a light-yellow oil (1.39 g, 82%). Then, using 3-fluoro-*N*-hydroxy-*N*-methylbenzamide (1.39 g, 8.2 mmol, 1.0 equiv.), TsCl (1.72 g, 9.02 mmol, 1.1 equiv.), Et_3N (1.25 mL, 9.02 mmol, 1.1 equiv.) in CH_2Cl_2 (16 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with PE/EA = 10:1) to obtain **1k** as a colorless oil (2.36 g, 89%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.53 (d, J = 8.2 Hz, 2H), 7.25–7.22 (m, 1H), 7.17–7.12 (m, 3H), 7.07 (tdd, J = 8.3, 2.6, 1.0 Hz, 1H), 6.86 (ddd, J = 9.1, 2.7, 1.5 Hz, 1H), 3.57 (d, J = 0.9 Hz, 3H), 2.40 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 169.6 (d, $J_{C–F}$ = 2.4 Hz), 162.2 (d, $J_{C–F}$ = 247.8 Hz), 146.6, 134.4 (d, $J_{C–F}$ = 7.4 Hz), 130.0, 129.9, 129.6 (d, $J_{C–F}$ = 8.0 Hz), 129.2, 124.1 (d, $J_{C–F}$ = 3.0 Hz), 118.2 (d, $J_{C–F}$ = 21.2 Hz), 115.6 (d, $J_{C–F}$ = 23.2 Hz), 39.9, 21.8; **^{19}F NMR** (565 MHz, $CDCl_3$) δ −112.1; **IR** (neat) $\tilde{\nu}_{max}$ 2989, 1698, 1380, 1179, 1190, 819, 743, 659 cm^{-1}; **HRMS** (ESI/[M + H]$^+$) *m/z* calcd. for $C_{15}H_{15}FNO_4S^+$: 324.0700, found: 324.0707.

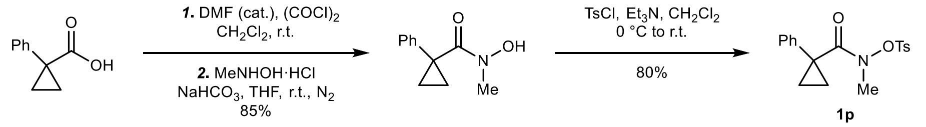
N-Methyl-*N*-(tosyloxy)cinnamamide (1n)



1n

Prepared following the **GP1A** with slight modifications, using cinnamoyl chloride (4.7 mL, 33 mmol, 1.1 equiv.), *N*-methylhydroxylamine hydrochloride (2.5 g, 30 mmol, 1.0 equiv.), $NaHCO_3$ (5.54 g, 66 mmol, 2.2 equiv.) in THF/H_2O (60/6 mL). The crude reaction mixture was purified by column chromatography on silica gel (eluted with PE/EA = 5:1 → EA) to obtain *N*-hydroxy-*N*-methylcinnamamide as a yellow oil (3.3 g, 62%). Then, using *N*-hydroxy-*N*-methylbenzamide (3.3 g, 18.6 mmol, 1.0 equiv.), TsCl (3.9 g, 20.5 mmol, 1.1 equiv.), Et_3N (2.8 mL, 20.5 mmol, 1.1 equiv.) in CH_2Cl_2 (40 mL). The crude residue was purified by recrystallization (CH_2Cl_2/PE) to obtain **1n** as a white solid (4.70 g, 76%). **M.P.** 58–59 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 15.7 Hz, 1H), 7.40–7.30 (m, 5H), 7.27 (d, J = 8.3 Hz, 2H), 6.46 (d, J = 15.7 Hz, 1H), 3.39 (s, 3H), 2.27 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.0, 147.0, 144.7, 134.4, 130.5, 130.4, 129.4, 128.8, 128.3, 114.9, 38.4, 21.7; **IR** (neat) $\tilde{\nu}_{max}$ 3057, 1712, 1667, 1377, 1088, 810, 680 cm^{-1}; **HRMS** (ESI/[M + H]$^+$) *m/z* calcd. for $C_{17}H_{18}NO_4S^+$: 332.0951, found: 332.0949.

N-Methyl-1-phenyl-*N*-(tosyloxy)cyclopropane-1-carboxamide (1p)

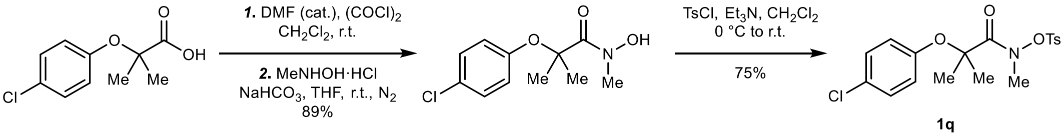


1p

Prepared following the **GP1A** using 1-phenylcyclopropane-1-carboxylic acid (0.81 g, 5 mmol, 1.0 equiv.), oxalyl chloride (1.3 mL, 15 mmol, 3.0 equiv.), DMF (2 drops) in CH_2Cl_2 (10 mL). The reaction mixture was concentrated *in vacuo*, and the resulting acyl chloride was used directly in the next step. Using the preceding acyl chloride, *N*-methylhydroxylamine hydrochloride (0.46 g, 5.5 mmol, 1.1 equiv.), $NaHCO_3$ (0.92 g, 11 mmol, 2.2 equiv.) in THF (11 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with EA) to obtain *N*-hydroxy-*N*-methyl-1-phenylcyclopropane-1-carboxamide as a colorless oil (0.81 g, 85%). Then, using *N*-hydroxy-*N*,2,2,3,3-pentamethylcyclopropane-1-carboxamide (0.81 g, 4.25 mmol, 1.0 equiv.), TsCl (0.89 g, 4.68 mmol, 1.1 equiv.), Et_3N (0.65 mL, 4.68 mmol, 1.1 equiv.) in CH_2Cl_2 (10 mL). The crude residue was purified by recrystallization (CH_2Cl_2/PE) to obtain **1p** as a white solid (1.17 g, 80%). **M.P.** 70–71 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.81 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.29 (t, J = 7.4 Hz, 2H), 7.26–7.21 (m, 1H), 7.06–7.01 (m, 2H), 3.16 (s, 3H), 2.47 (s, 3H), 1.37–1.32 (m, 2H), 1.12 (q, J = 3.6 Hz, 2H); **^{13}C**

NMR (151 MHz, $CDCl_3$) δ 173.6, 146.2, 138.6, 131.5, 129.8, 129.6, 128.8, 127.1(127.14), 127.1(127.09), 40.6, 29.6, 22.0, 14.9; **IR** (neat) $\tilde{\nu}_{max}$ 2989, 1695, 1366, 1178, 1068, 809, 770, 695 cm^{-1}; **HRMS** (ESI/[M + H]$^+$) *m/z* calcd. for $C_{18}H_{20}NO_4S^+$: 346.1108, found: 346.1117.

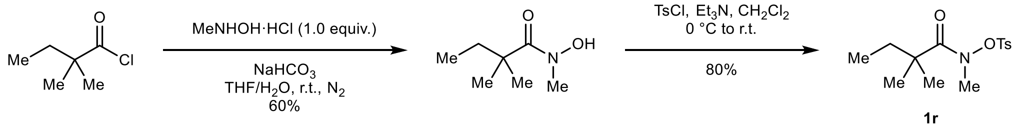
2-(4-Chlorophenoxy)-*N*,2-dimethyl-*N*-(tosyloxy)propanamide (1q)



1q

Prepared following the **GP1A** with slight modifications, using 2-(4-chlorophenoxy)-2-methylpropanoic acid (0.77 g, 3.6 mmol, 1.2 equiv.), oxalyl chloride (0.91 mL, 10.8 mmol, 3.6 equiv.), DMF (2 drops) in CH_2Cl_2 (10 mL). The reaction mixture was concentrated *in vacuo*, and the resulting acyl chloride was used directly in the next step. Using the preceding acyl chloride, *N*-methylhydroxylamine hydrochloride (0.25 g, 3 mmol, 1.0 equiv.), $NaHCO_3$ (0.84 g, 10 mmol, 3.0 equiv.) in THF (10 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with EA) to obtain 2-(4-chlorophenoxy)-*N*-hydroxy-*N*,2-dimethylpropanamide as a colorless oil (0.65 g, 89%). Then, using 2-(4-chlorophenoxy)-*N*-hydroxy-*N*,2-dimethylpropanamide (0.65 g, 2.7 mmol, 1.0 equiv.), TsCl (0.56 g, 3 mmol, 1.1 equiv.), Et_3N (0.41 mL, 3 mmol, 1.1 equiv.) in CH_2Cl_2 (10 mL). The crude residue was purified by recrystallization (CH_2Cl_2/PE) to obtain **1q** as a white solid (0.8 g, 75%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.85–7.80 (m, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.24–7.20 (m, 2H), 6.81–6.74 (m, 2H), 3.52 (s, 3H), 2.45 (s, 3H), 1.51 (s, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.1, 153.2, 146.3, 131.8, 129.8, 129.6, 129.4, 127.7, 119.9, 80.5, 41.7, 25.6, 21.9; **IR** (neat) $\tilde{\nu}_{max}$ 2994, 1703, 1596, 1489, 1387, 1192, 1179, 706 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{18}H_{20}ClNO_5SNa^+$: 420.0643, found: 420.0645.

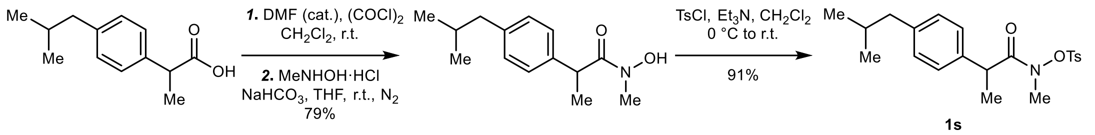
***N*,2,2-Trimethyl-*N*-(tosyloxy)butanamide (1r)**



1r

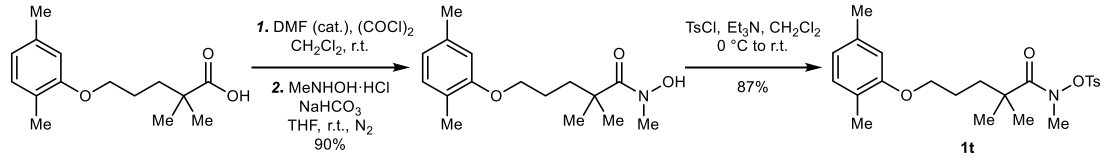
Prepared following the **GP1A** with slight modifications, using 2,2-dimethylbutanoyl chloride (3.23 g, 24 mmol, 1.2 equiv.), *N*-methylhydroxylamine hydrochloride (1.67 g, 20 mmol, 1.0 equiv.), $NaHCO_3$ (3.69 g, 44 mmol, 2.2 equiv.) in THF/H_2O (60/6 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with PE/EA = 1:1) to obtain *N*-hydroxy-*N*,2,2-trimethylbutanamide as a white solid (1.74 g, 60%). Then, using *N*-hydroxy-*N*,2,2-trimethylbutanamide (1.74 g, 12 mmol, 1.0 equiv.), TsCl (2.52 g, 13.2 mmol, 1.1 equiv.), Et_3N (1.83 mL, 13.2 mmol, 1.1 equiv.) in CH_2Cl_2 (30 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with PE/EA = 5:1) to obtain **1r** as a colorless oil (2.87 g, 80%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.86–7.82 (m, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 3.30 (s, 3H), 2.43 (s, 3H), 1.51 (t, *J* = 7.5 Hz, 2H), 1.09 (s, 6H), 0.67 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 179.9, 146.2, 131.8, 129.8, 129.4, 43.7, 41.6, 33.2, 25.5, 21.8, 9.2; **IR** (neat) $\tilde{\nu}_{max}$ 2929, 1663, 1473, 1379, 1192, 1179, 1032, 737 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{14}H_{21}NO_4SNa^+$: 322.1083, found: 322.1082.

2-(4-Isobutylphenyl)-*N*-methyl-*N*-(tosyloxy)propenamide (1s)



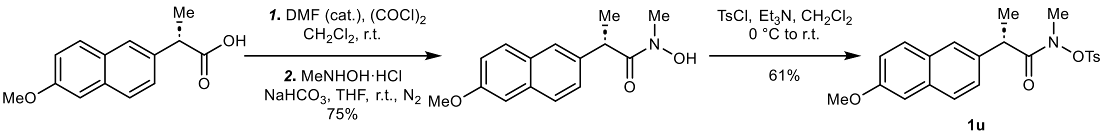
Prepared following the **GP1A** using 2-(4-isobutylphenyl)propanoic acid (2.06 g, 10 mmol, 1.0 equiv.), oxalyl chloride (2.5 mL, 30 mmol, 3.0 equiv.), DMF (2 drops) in CH_2Cl_2 (20 mL). The reaction mixture was concentrated *in vacuo*, and the resulting acyl chloride was used directly in the next step. Using the preceding acyl chloride, *N*-methylhydroxylamine hydrochloride (0.92 g, 11 mmol, 1.1 equiv.), $NaHCO_3$ (1.85 g, 22 mmol, 2.2 equiv.) in THF (22 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with EA) to obtain *N*-hydroxy-2-(4-isobutylphenyl)-*N*-methylpropanamide as a light-yellow oil (1.86 g, 79%). Then, using *N*-hydroxy-2-(4-isobutylphenyl)-*N*-methylpropanamide (1.86 g, 7.9 mmol, 1.0 equiv.), TsCl (1.67 g, 8.7 mmol, 1.1 equiv.), Et_3N (1.2 mL, 8.7 mmol, 1.1 equiv.) in CH_2Cl_2 (16 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with PE/EA = 10:1 → 5:1) to obtain **1s** as a colorless oil (2.8 g, 91%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.88 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H), 7.08–7.03 (m, 4H), 3.84 (q, J = 6.9 Hz, 1H), 3.10 (s, 3H), 2.48 (s, 3H), 2.42 (d, J = 7.2 Hz, 2H), 1.82 (dh, J = 13.4, 6.7 Hz, 1H), 1.24 (d, J = 7.0 Hz, 3H), 0.88 (d, J = 6.6 Hz, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.3, 146.8, 140.6, 136.7, 130.9, 130.2, 129.5, 129.4, 127.4, 45.1, 42.0, 38.8, 30.2, 22.5, 21.9, 19.1; **IR** (neat) $\tilde{\nu}_{max}$ 2970, 1693, 1383, 1194, 1180, 815, 734 cm^{-1}; **HRMS** (ESI/[M + H]$^+$) *m/z* calcd. for $C_{21}H_{28}NO_4S^+$: 390.1734, found: 390.1740.

5-(2,5-Dimethylphenoxy)-*N*,2,2-trimethyl-*N*-(tosyloxy)pentanamide (1t)



Prepared following the **GP1A** using 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoic acid (5.0 g, 20 mmol, 1.0 equiv.), oxalyl chloride (5 mL, 60 mmol, 3.0 equiv.), DMF (2 drops) in CH_2Cl_2 (45 mL). The reaction mixture was concentrated *in vacuo*, and the resulting acyl chloride was used directly in the next step. Using the preceding acyl chloride, *N*-methylhydroxylamine hydrochloride (1.84 g, 22 mmol, 1.1 equiv.), $NaHCO_3$ (3.7 g, 44 mmol, 2.2 equiv.) in THF (40 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with EA) to obtain 5-(2,5-dimethylphenoxy)-*N*-hydroxy-*N*,2,2-trimethylpentanamide as a colorless oil (5.0 g, 90%). Then, using 5-(2,5-dimethylphenoxy)-*N*-hydroxy-*N*,2,2-trimethylpentanamide (5.0 g, 18 mmol, 1.0 equiv.), TsCl (3.8 g, 19.8 mmol, 1.1 equiv.), Et_3N (2.7 mL, 19.8 mmol, 1.1 equiv.) in CH_2Cl_2 (18 mL). The crude residue was purified by recrystallization (CH_2Cl_2/PE) to obtain **1t** as a white solid (6.7 g, 87%). **M.P.** 106–107 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.87 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 8.1 Hz, 2H), 7.01 (d, J = 7.4 Hz, 1H), 6.67 (d, J = 7.4 Hz, 1H), 6.61 (d, J = 1.6 Hz, 1H), 3.87 (t, J = 6.1 Hz, 2H), 3.32 (s, 3H), 2.44 (s, 3H), 2.32 (s, 3H), 2.17 (s, 3H), 1.74–1.70 (m, 2H), 1.60–1.54 (m, 2H), 1.20 (s, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 179.6, 156.9, 146.2, 136.6, 131.9, 130.4, 129.9, 129.3, 123.5, 120.8, 111.9, 67.7, 43.2, 41.5, 37.2, 26.0, 25.0, 21.8, 21.5, 15.9.; **IR** (neat) $\tilde{\nu}_{max}$ 2989, 1706, 1370, 1181, 1038, 816, 759, 708, 659 cm^{-1}; **HRMS** (ESI/[M + H]$^+$) *m/z* calcd. for $C_{23}H_{32}NO_5S^+$: 434.1996, found: 434.1999.

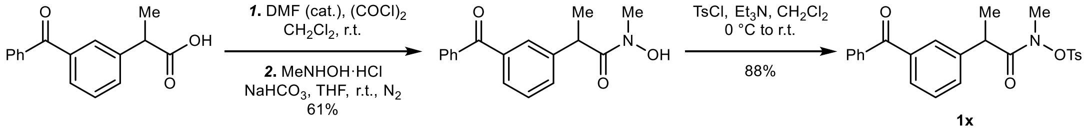
(*S*)-2-(6-Methoxynaphthalen-2-yl)-*N*-methyl-*N*-(tosyloxy)propenamide (1u)



1u

Prepared following the **GP1A** using naproxen (11.5 g, 50 mmol, 1.0 equiv.), oxalyl chloride (12.6 mL, 150 mmol, 3.0 equiv.), DMF (4 drops) in CH_2Cl_2 (100 mL). The reaction mixture was concentrated *in vacuo*, and the resulting acyl chloride was used directly in the next step. Using the preceding acyl chloride, *N*-methylhydroxylamine hydrochloride (4.5 g, 55 mmol, 1.1 equiv.), $NaHCO_3$ (9.2 g, 110 mmol, 2.2 equiv.) in THF (110 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with EA) to obtain (*S*)-*N*-hydroxy-2-(6-methoxynaphthalen-2-yl)-*N*-methylpropanamide as a light-yellow oil (9.7 g, 75%). Then, using (*S*)-*N*-hydroxy-2-(6-methoxynaphthalen-2-yl)-*N*-methylpropanamide (2.0 g, 7.7 mmol, 1.0 equiv.), TsCl (1.61 g, 8.5 mmol, 1.1 equiv.), Et_3N (1.2 mL, 8.5 mmol, 1.1 equiv.) in CH_2Cl_2 (16 mL). The crude residue was purified by recrystallization (CH_2Cl_2/PE) to obtain **1u** as a white solid (1.94 g, 61%). **M.P.** 83–84 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.88 (d, J = 8.1 Hz, 2H), 7.66 (d, J = 8.6 Hz, 2H), 7.52 (s, 1H), 7.37 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 6.6 Hz, 1H), 7.13 (dd, J = 8.9, 2.6 Hz, 1H), 7.09 (d, J = 2.5 Hz, 1H), 4.03 (q, J = 6.9 Hz, 1H), 3.90 (s, 3H), 3.11 (s, 3H), 2.45 (s, 3H), 1.34 (d, J = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.8, 146.8, 134.7, 133.8, 130.9, 130.3, 129.5, 129.4, 129.0, 127.3, 126.6, 126.3, 119.1, 105.6, 55.4, 42.4, 38.9, 21.9, 19.2; **IR** (neat) $\tilde{\nu}_{max}$ 2989, 1715, 1382, 1180, 1051, 812, 760, 661 cm^{-1}; **HRMS** (ESI/$[M + H]^+$) *m/z* calcd. for $C_{22}H_{24}NO_5S^+$: 414.1370, found: 414.1377.

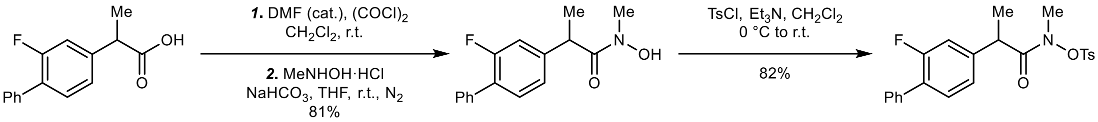
2-(3-Benzoylphenyl)-*N*-methyl-*N*-(tosyloxy)propenamide (1x)



1x

Prepared following the **GP1A** using ketoprofen (1.52 g, 6 mmol, 1.0 equiv.), oxalyl chloride (1.52 mL, 18 mmol, 3.0 equiv.), DMF (2 drops) in CH_2Cl_2 (12 mL). The reaction mixture was concentrated *in vacuo*, and the resulting acyl chloride was used directly in the next step. Using the preceding acyl chloride, *N*-methylhydroxylamine hydrochloride (0.55 g, 6.6 mmol, 1.1 equiv.), $NaHCO_3$ (1.1 g, 13.2 mmol, 2.2 equiv.) in THF (12 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with EA) to obtain 2-(3-benzoylphenyl)-*N*-hydroxy-*N*-methylpropanamide as a light-yellow oil (1.03 g, 61%). Then, using 2-(3-benzoylphenyl)-*N*-hydroxy-*N*-methylpropanamide (1.03 g, 3.67 mmol, 1.0 equiv.), TsCl (0.77 g, 4.03 mmol, 1.1 equiv.), Et_3N (0.55 mL, 4.03 mmol, 1.1 equiv.) in CH_2Cl_2 (7 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with PE/EA = 25:1) to obtain **1x** as a colorless oil (1.42 g, 88%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.85 (d, J = 8.1 Hz, 2H), 7.79 (d, J = 8.3 Hz, 2H), 7.67–7.61 (m, 1H), 7.61–7.55 (m, 2H), 7.48 (t, J = 7.6 Hz, 2H), 7.42–7.35 (m, 4H), 3.96 (q, J = 7.0 Hz, 1H), 3.11 (s, 3H), 2.43 (s, 3H), 1.30 (d, J = 7.0 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 196.4, 177.9, 147.1, 140.0, 138.0, 137.4, 132.6, 131.6, 130.7, 130.4, 130.2, 129.5, 129.4, 129.0, 128.7, 128.4, 42.4, 38.8, 21.9, 19.1; **IR** (neat) $\tilde{\nu}_{max}$ 2988, 1693, 1659, 1383, 1194, 801, 733 cm^{-1}; **HRMS** (ESI/$[M + H]^+$) *m/z* calcd. for $C_{24}H_{24}NO_5S^+$: 438.1370, found: 438.1377.

2-(2-Fluoro-[1,1'-biphenyl]-4-yl)-*N*-methyl-*N*-(tosyloxy)propenamide (1y)



1y

Prepared following the **GP1A** using 2-(2-fluoro-[1,1'-biphenyl]-4-yl)propanoic acid (1.22 g, 5 mmol, 1.0 equiv.), oxalyl chloride (1.3 mL, 15 mmol, 3.0 equiv.), DMF (2 drops) in CH_2Cl_2 (50 mL). The reaction mixture was concentrated *in vacuo*, and the resulting acyl chloride was used directly in the next step. Using the preceding acyl chloride, *N*-methylhydroxylamine hydrochloride (0.54 g, 5.5 mmol, 1.1 equiv.), $NaHCO_3$ (1.26 g, 15 mmol, 3.0 equiv.) in THF (50 mL). The crude residue was purified by flash column chromatography on silica gel (eluted with EA) to obtain 2-(2-fluoro-[1,1'-biphenyl]-4-yl)-*N*-hydroxy-*N*-methylpropanamide as a colorless oil (1.11 g, 81%). Then, using 2-(2-fluoro-[1,1'-biphenyl]-4-yl)-*N*-hydroxy-*N*-methylpropanamide (1.11 g, 4.0 mmol, 1.0 equiv.), TsCl (0.77 g, 4.4 mmol, 1.1 equiv.), Et_3N (0.61 mL, 4.4 mmol, 1.1 equiv.) in CH_2Cl_2 (10 mL). The crude residue was purified by recrystallization (eluted with PE/EA = 30:1) to obtain **1y** as a colorless oil (1.40 g, 82%); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.9 Hz, 2H), 7.52 (d, *J* = 7.3 Hz, 2H), 7.46–7.41 (m, 4H), 7.36 (t, *J* = 8.2 Hz, 2H), 7.05 (d, *J* = 7.4 Hz, 1H), 6.95 (d, *J* = 11.5 Hz, 1H), 3.99 (q, *J* = 6.9 Hz, 1H), 3.15 (s, 3H), 2.48 (s, 3H), 1.34 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 177.7, δ 159.7 (d, *J* = 248.3 Hz), 147.1, 141.0 (d, *J* = 7.6 Hz), 135.5, 130.9 (d, *J* = 3.9 Hz), 130.8, 130.4, 129.5, 129.0 (d, *J* = 2.9 Hz), 128.5, δ 127.9 (d, *J* = 13.4 Hz), 127.7, 123.9 (d, *J* = 3.4 Hz), 115.4 (d, *J* = 23.7 Hz), 41.8, 38.7, 21.9, 18.9; **^{19}F NMR** (564 MHz, $CDCl_3$) δ −117.49; **IR** (neat) $\tilde{\nu}_{max}$ 2983, 1694, 1659, 1383, 1192, 801, 734 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{23}H_{22}FNaNO_4SNa^+$: 450.1146, found: 450.1156.

3. General Procedures for the *N*-methyl C−H esterification of *O*-tosyl hydroxamates

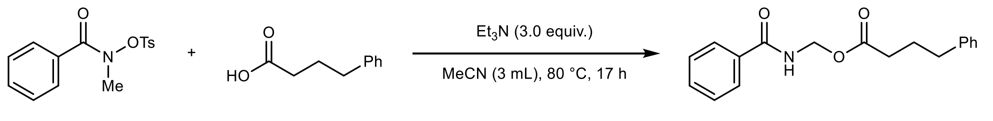
General Procedure 2A (GP2A)

To a 15 mL oven-dried vial equipped with a magnetic stir bar was added *O*-tosyl hydroxamate **1a**–**1y** (0.3 mmol, 1.0 equiv.), *n*-Bu_4NOAc (0.6 mmol, 2.0 equiv.), and MeCN (3.0 mL) under air atmosphere. The vial was then tightly capped and placed in a hotplate pre-heated to 80 °C with vigorous stirring for 12–24 h (TLC monitored the conversion of *O*-tosyl hydroxamates). After the time indicated for each reaction, the solvent was removed *in vacuo*, and the crude material was purified by flash column chromatography.

General Procedure 2B (GP2B)

To a 15 mL oven-dried vial equipped with a magnetic stir bar was added *O*-tosyl hydroxamate **1a** (0.3 mmol, 1.0 equiv.), carboxylic acid (0.6 mmol, 2.0 equiv.), Et_3N (0.9 mmol, 3.0 equiv.), and MeCN (3.0 mL) under air atmosphere. The vial was then tightly capped and placed in a hotplate pre-heated to 80 °C with vigorous stirring for 12–24 h (TLC monitored the conversion of *O*-tosyl hydroxamates). After the time indicated for each reaction, the solvent was removed *in vacuo*, and the crude material was purified by flash column chromatography.

Table S1. Optimization of carboxylic acid as the esterification reagent[a]

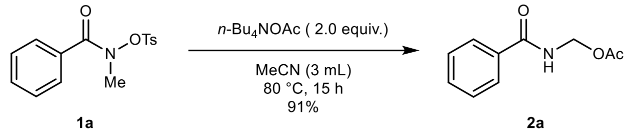


1a **3a**

Entry	Variations from above conditions	Yield **3a** (%)
1	**None**	**72**
2	*n*-Bu_4NOH (40% wt% in MeOH) instead of Et_3N	N.D.
3	*n*-Bu_4NOH (40% wt% in H_2O) instead of Et_3N	N.D.
4	Cs_2CO_3 instead of Et_3N	N.D.
5	Na_2CO_3 instead of Et_3N	N.D.
6	$NaHCO_3$ instead of Et_3N	N.D.
7	*t*-BuONa instead of Et_3N	Trace
8	Pyridine instead of Et_3N	N.D.
9	DBU instead of Et_3N	N.D.
10	*i*-Pr_2NEt instead of Et_3N	Trace
11	2,4,6-Collidine instead of Et_3N	N.D.
12	w/o Et_3N	N.D.

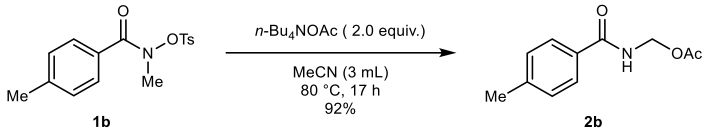
[a] Reaction conditions: **1a** (0.3 mmol, 1.0 equiv.), 4-phenylbutanoic acid (0.6 mmol, 2.0 equiv.), base (0.9 mmol, 3.0 equiv.), MeCN (3 mL), 80 °C, 17 h, air atmosphere, isolated yields. N.D.: not detected.

Benzamidomethyl acetate (2a)



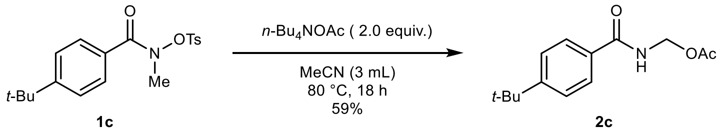
Prepared following the **GP2A** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.5 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 15 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2a** as a colorless oil (52.5 mg, 91%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.80 (d, *J* = 7.7 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 5.44 (d, *J* = 7.2 Hz, 2H), 2.06 (s, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 172.2, 167.7, 133.2, 132.4, 128.7, 127.4, 64.83, 21.0; **IR** (neat) $\tilde{\nu}_{max}$ 1728, 1662, 1531, 1228, 1016, 951, 750, 714 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{10}H_{11}NO_3Na^+$: 216.0631, found: 216.0632.

(4-Methylbenzamido)methyl acetate (2b)



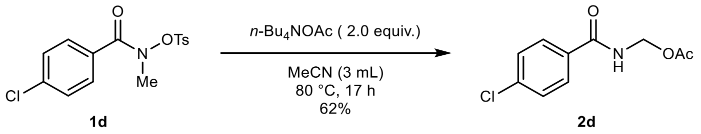
Prepared following the **GP2A** using *N*,4-dimethyl-*N*-(tosyloxy)benzamide **1b** (95.7 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 17 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 2:1) to afford the title compound **2b** as a colorless oil (57.1 mg, 92%). Rotamers present at room temperature. **M.P.** 175.2–176.6 °C;**^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.50 (t, *J* = 7.1 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 5.43 (d, *J* = 7.1 Hz, 2H), 2.38 (s, 3H), 2.05 (s, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 172.4, 167.9, 143.2, 130.59, 129.6 (129.62, major), 129.6 (129.58, minor), 127.6 (major), 127.5 (minor), 65.1, 21.8, 21.3; **IR** (neat) $\tilde{\nu}_{max}$ 1738, 1657, 1534, 1504, 1230, 1017, 950, 754 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{11}H_{13}NO_3Na^+$: 230.0788, found: 230.0782.

(4-(*tert*-Butyl)benzamido)methyl acetate (2c)



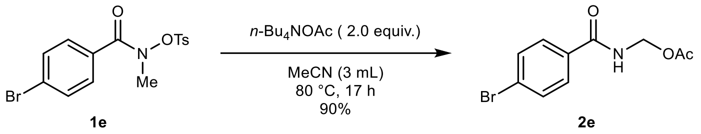
Prepared following the **GP2A** using 4-(*tert*-butyl)-*N*-methyl-*N*-(tosyloxy)benzamide **1c** (108.3 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 18 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2c** as a colorless oil (43.9 mg, 59%). **M.P.** 143.7–145.2 °C; **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.75 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.48 (t, *J* = 7.3 Hz, 1H), 7.45–7.43 (m, 2H), 5.44 (dd, *J* = 7.2, 1.2 Hz, 2H), 2.05 (t, *J* = 1.1 Hz, 3H), 1.31 (t, *J* = 1.2 Hz, 9H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 172.2, 167.6, 156.0, 130.3, 127.3, 125.7, 64.9, 35.1, 31.2, 21.0; **IR** (neat) $\tilde{\nu}_{max}$ 1740, 1660, 1535, 1502, 1233, 1017 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{14}H_{19}NO_3Na^+$: 272.1257, found: 272.1258.

(4-Chlorobenzamido)methyl acetate (2d)



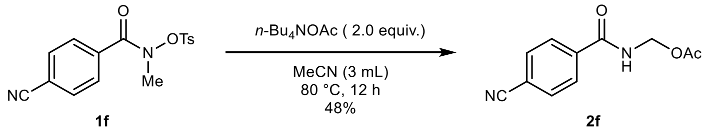
Prepared following the **GP2A** using 4-chloro-*N*-methyl-*N*-(tosyloxy)benzamide **1d** (101.7 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 17 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 2:1) to afford the title compound **2d** as a white solid (48.0 mg, 70%). **M.P.** 123.4–125.1 °C; **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 2H), 5.42 (d, *J* = 7.1 Hz, 2H), 2.07 (s, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 172.2, 166.7, 138.7, 131.6, 129.1, 128.9, 64.8, 21.1; **IR** (neat) $\tilde{\nu}_{max}$ 1740, 1659, 1597, 1535, 1487, 1231, 1094, 1015 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{10}H_{10}ClNO_3Na^+$: 250.0241, found: 250.0242.

(4-Bromobenzamido)methyl acetate (2e)



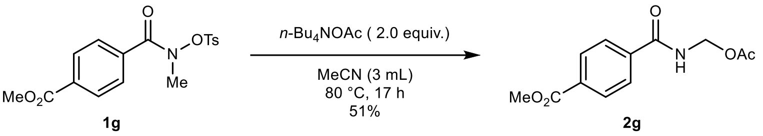
Prepared following the **GP2A** using 4-bromo-*N*-methyl-*N*-(tosyloxy)benzamide **1e** (114.9 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 17 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 2:1) to afford the title compound **2e** as a white solid (73.5 mg, 90%). **M.P.** 113.4–115.2 °C; **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.67 (dd, *J* = 8.7, 0.8 Hz, 2H), 7.58–7.52 (m, 3H), 5.42 (d, *J* = 7.2 Hz, 2H), 2.07 (s, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 172.2, 166.9, 132.0, 132.0, 129.0, 127.2, 64.8, 21.1; **IR** (neat) $\tilde{\nu}_{max}$ 1739, 1660, 1591, 1536, 1483, 1229, 1011, 954 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{10}H_{10}BrNO_3Na^+$: 293.9736, found: 293.9738.

(4-Cyanobenzamido)methyl acetate (2f)



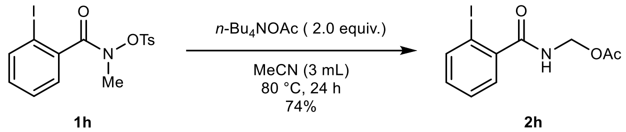
Prepared following the **GP2A** using 4-cyano-*N*-methyl-*N*-(tosyloxy)benzamide **1f** (99.1 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 12 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 2:1) to afford the title compound **2f** as a white solid (31.5 mg, 48%). **M.P.** 115.2–116.3 °C; **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.93–7.90 (m, 2H), 7.76–7.73 (m, 2H), 7.63 (t, *J* = 7.1 Hz, 1H), 5.43 (d, *J* = 7.1 Hz, 2H), 2.07 (s, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 172.1, 166.0, 137.1, 132.6, 128.2, 117.9, 115.8, 64.6, 21.0; **IR** (neat) $\tilde{\nu}_{max}$ 2233, 1737, 1666, 1535, 1227, 1018, 909, 727 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{11}H_{10}N_2O_3Na^+$: 241.0584, found: 241.0592.

Methyl 4-((acetoxymethyl)carbamoyl)benzoate (2g)



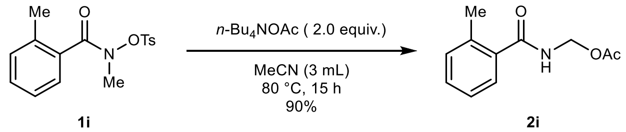
Prepared following the **GP2A** using 4-(methyl(tosyloxy)carbamoyl)benzoate **1g** (108.9 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 17 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 2:1) to afford the title compound **2g** as a white solid (38.7 mg, 51%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 8.07 (dd, *J* = 8.2, 1.5 Hz, 2H), 7.88–7.83 (m, 2H), 7.59 (t, *J* = 6.9 Hz, 1H), 5.44 (d, *J* = 7.2 Hz, 2H), 3.92 (s, 3H), 2.07 (s, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 172.2, 166.9, 166.2, 137.1, 133.4, 123.0, 127.5, 64.7, 52.6, 21.0; **IR** (neat) $\tilde{\nu}_{\max}$ 1727, 1684, 1535, 1373, 1278, 1236, 1046, 732 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{12}H_{13}NO_5Na^+$: 274.0686: 274.0670.

(2-Iodobenzamido)methyl acetate (2h)



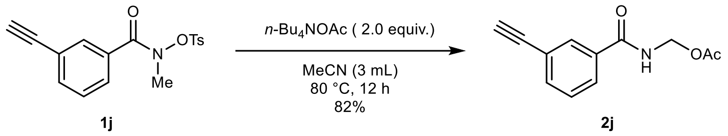
Prepared following the **GP2A** using 2-iodo-*N*-methyl-*N*-(tosyloxy)benzamide **1h** (129.4 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2h** as a white solid (73.0 mg, 74%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.88–7.79 (m, 1H), 7.38 (d, *J* = 4.3 Hz, 2H), 7.16–7.10 (m, 1H), 7.01 (t, *J* = 7.2 Hz, 1H), 5.40 (d, *J* = 7.3 Hz, 2H), 2.10 (s, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 172.1, 169.5, 140.8, 140.2, 131.8, 128.4, 128.3, 92.1, 64.4, 21.0; **IR** (neat) $\tilde{\nu}_{\max}$ 1659, 1514, 1511, 1394, 1251, 1056, 892 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{10}H_{10}INO_3Na^+$: 341.9598, found: 341.9893.

(2-Methylbenzamido)methyl acetate (2i)



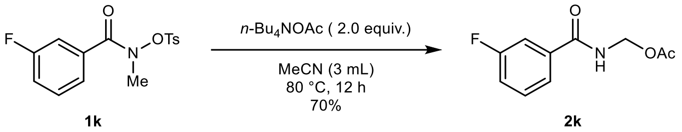
Prepared following the **GP2A** using *N*,2-dimethyl-*N*-(tosyloxy)benzamide **1i** (95.8 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 15 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2i** as a white solid (55.9 mg, 90%). Rotamers present at room temperature. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.36–7.28 (m, 2H), 7.17 (ddd, *J* = 20.7, 12.2, 7.9 Hz, 3H), 5.36 (d, *J* = 7.3 Hz, 2H), 2.41 (s, 3H), 2.05 (s, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 175.4 (minor), 172.0 (major), 171.4 (major), 170.1 (minor), 136.7 (minor), 136.5 (major), 135.1 (major), 134.8 (minor), 131.3 (major), 131.2 (minor), 130.6 (minor), 130.5 (major), 127.0 (minor), 126.9 (major), 125.9 (minor), 125.8 (major), 64.5, 21.0 (major), 20.7 (minor), 19.9; **IR** (neat) $\tilde{\nu}_{\max}$ 1655, 1516, 1394, 1305, 1065, 1044, 736, 702 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{11}H_{13}NO_3Na^+$: 230.0788, found: 230.0785.

(3-Ethynylbenzamido)methyl acetate (2j)



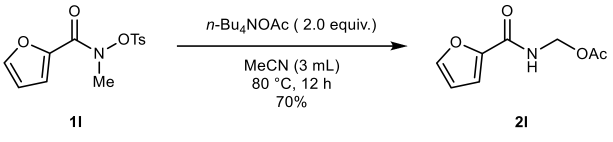
Prepared following the **GP2A** using 3-ethynyl-*N*-methyl-*N*-(tosyloxy)benzamide **1j** (98.8 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 12 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2j** as a white solid (53.7 mg, 82%). **M.P.** 95.4–97.2 °C; **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.90 (t, *J* = 1.8 Hz, 1H), 7.79 (dt, *J* = 7.9, 1.5 Hz, 1H), 7.64–7.57 (m, 2H), 7.39 (t, *J* = 7.8 Hz, 1H), 5.43 (d, *J* = 7.1 Hz, 2H), 3.12 (s, 1H), 2.07 (s, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 172.2, 166.9, 135.7, 133.5, 131.0, 128.9, 127.9, 122.9, 82.5, 78.6, 64.8, 21.1; **IR** (neat) $\tilde{\nu}_{max}$ 1737, 1663, 1530, 1236, 1200, 1019, 955 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{12}H_{11}NO_3Na^+$: 204.0631, found: 204.0636.

(3-Fluorobenzamido)methylz acetate (2k)



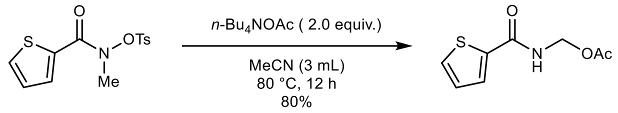
Prepared following the **GP2A** using 3-fluoro-*N*-methyl-*N*-(tosyloxy)benzamide **1k** (97.0 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 12 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2k** as a white solid (44.0 mg, 70%). Rotamers present at room temperature. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.58–7.50 (m, 3H), 7.43–7.39 (m, 1H), 7.22 (tdd, *J* = 8.2, 2.6, 1.0 Hz, 1H), 5.44 (d, *J* = 7.2 Hz, 2H), 2.08 (s, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 176.4 (minor), 172.3 (major), 167.6 (minor), 166.6 (major), 162.9 (d, $J_{C\text{–}F}$ = 248.0 Hz, minor), 162.8 (d, $J_{C\text{–}F}$ = 248.0 Hz, major), 135.5 (d, $J_{C\text{–}F}$ = 6.7 Hz), 130.5 (d, $J_{C\text{–}F}$ = 7.7 Hz), 122.9 (d, $J_{C\text{–}F}$ = 3.0 Hz, major), 122.8 (d, $J_{C\text{–}F}$ = 3.0 Hz, minor), 119.5 (d, $J_{C\text{–}F}$ = 21.3 Hz, major), 119.4 (d, $J_{C\text{–}F}$ = 21.3 Hz, minor), 114.9 (d, $J_{C\text{–}F}$ = 23.1 Hz, major), 114.8 (d, $J_{C\text{–}F}$ = 23.0, Hz, minor), 68.0 (minor), 64.8 (major), 21.0 (minor), 20.8 (major); **^{19}F NMR** (565 MHz, CDCl$_3$) δ −111.43, −111.47; **IR** (neat) $\tilde{\nu}_{max}$ 1659, 1536, 1484, 1223, 1270, 1066, 899, 737 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{10}H_{10}FNO_3Na^+$: 234.0537, found: 234.0539.

(Furan-2-carboxamido)methyl acetate (2l)



Prepared following the **GP2A** using *N*-methyl-*N*-(tosyloxy)furan-2-carboxamide **1l** (88.6 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 12 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2l** as a colorless oil (38.8 mg, 70%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.50–7.42 (m, 2H), 7.19 (dd, *J* = 3.5, 0.8 Hz, 1H), 6.51 (dd, *J* = 3.6, 1.8 Hz, 1H), 5.40 (d, *J* = 7.4 Hz, 2H), 2.06 (s, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 172.0, 158.4, 147.0, 144.8, 116.0, 112.5, 63.9, 21.0; **IR** (neat) $\tilde{\nu}_{max}$ 1659, 1593, 1524, 1473, 1047, 914, 771 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_8H_9NO_4Na^+$: 206.0424, found: 206.0424.

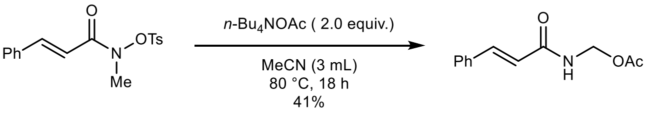
(Thiophene-2-carboxamido)methyl acetate (2m)



1m **2m**

Prepared following the **GP2A** using *N*-methyl-*N*-(tosyloxy)thiophene-2-carboxamide **1m** (93.4 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu_4NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 12 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2m** as a colorless oil (47.8 mg, 80%). Rotamers present in a 1:2 ratio at room temperature. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.65 (d, J = 3.7 Hz, 0.3H, minor), 7.58 (d, J = 3.7 Hz, 0.7H, major), 7.53 (d, J = 4.9 Hz, 0.7H, major), 7.51 (d, J = 4.9 Hz, 0.3H, minor), 7.34 (d, J = 7.5 Hz, 1H), 7.10–7.06 (m, 1H), 5.41 (d, J = 7.2 Hz, 1.4H, major), 4.98 (d, J = 6.8 Hz, 0.6H, minor), 2.09 (s, 1H, minor), 2.07 (s, 2H, major); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.1 (minor), 172.3 (major), 163.4 (minor), 162.2 (major), 138.1 (minor), 137.7 (major), 131.5 (major), 131.4 (minor), 129.4 (major), 129.3 (minor), 128.0 (128.02, minor), 128.0 (127.95, major), 67.7 (minor), 64.7 (major), 21.1 (major), 20.8 (minor); **IR** (neat) $\tilde{\nu}_{max}$ 1645, 1536, 1510, 1296, 1032, 753, 719 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_8H_9NO_3SNa^+$: 222.0195, found: 222.0192.

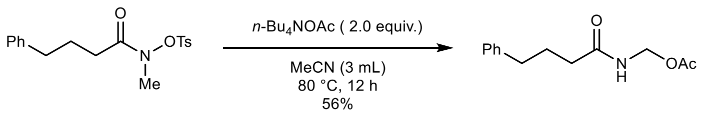
Cinnamamidomethyl acetate (2n)



1n **2n**

Prepared following the **GP2A** using *N*-methyl-*N*-(tosyloxy)cinnamamide **1n** (99.4 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu_4NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 18 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2n** as a colorless oil (26.9 mg, 41%). Rotamers present in a 1:2 ratio at room temperature. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.70 (dd, J = 15.7, 10.8 Hz, 1H), 7.52–7.47 (m, 2H), 7.39–7.31 (m, 4H), 6.50 (d, J = 15.7 Hz, 0.5H, major), 6.41 (d, J = 15.7 Hz, 0.5H, minor), 5.38 (d, J = 7.3 Hz, 0.8H, minor), 4.92 (d, J = 7.0 Hz, 1.2H, major), 2.10 (s, 2H, major), 2.08 (s, 1H, minor); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.2 (minor), 172.4 (major), 167.6 (major), 166.3 (minor), 143.4 (minor), 142.9 (major), 134.5 (major), 134.5 (minor), 130.3 (minor), 130.2 (major), 129.0 (129.02, minor), 129.0 (128.98, major), 128.1, 120.1 (minor), 119.50 (major), 67.3 (minor), 64.6 (major), 21.1 (minor), 20.9 (major); **IR** (neat) $\tilde{\nu}_{max}$ 1660, 1624, 1538, 1450, 1338, 1212, 1028, 766 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{12}H_{13}NO_3Na^+$: 242.0788, found: 242.0782.

(4-Phenylbutanamido)methyl acetate (2o)

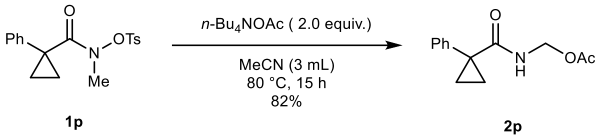


1o **2o**

Prepared following the **GP2A** using *N*-methyl-4-phenyl-*N*-(tosyloxy)butanamide **1o** (104.2 mg, 0.3

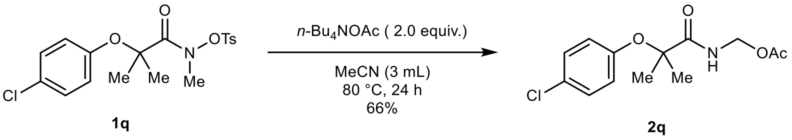
mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 12 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2o** as a colorless oil (39.3 mg, 56%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.28 (d, *J* = 7.7 Hz, 2H), 7.19–7.15 (m, 3H), 6.82 (t, *J* = 7.1 Hz, 1H), 5.21 (d, *J* = 7.3 Hz, 2H), 2.63 (d, *J* = 7.5 Hz, 2H), 2.21–2.19 (m, 2H), 2.04 (s, 3H), 1.98–1.95 (m, 2H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 173.4, 172.1, 141.3, 128.5, 128.5, 126.1, 64.2, 35.5, 35.1, 26.6, 21.0; **IR** (neat) $\tilde{\nu}_{max}$ 1740, 1662, 1535, 1227, 1017 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{13}H_{17}NO_3Na^+$: 258.1101, found: 258.1103.

(1-Phenylcyclopropane-1-carboxamido)methyl acetate (2p)



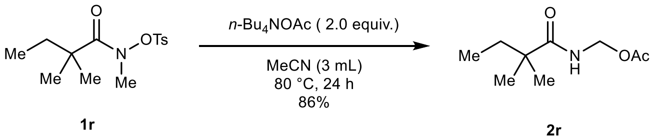
Prepared following the **GP2A** using *N*-methyl-1-phenyl-*N*-(tosyloxy)cyclopropane-1-carboxamide **1p** (103.5 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3.0 mL) at 80 °C for 15 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2p** as a colorless oil (57.0 mg, 82%). **M.P.** 151.9–152.9 °C; **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.37 (d, *J* = 4.3 Hz, 4H), 7.33 (dt, *J* = 9.1, 4.4 Hz, 1H), 6.40 (t, *J* = 7.3 Hz, 1H), 5.11 (d, *J* = 7.3 Hz, 2H), 2.02 (s, 3H), 1.66–1.64 (m, 2H), 1.12 (q, *J* = 3.8 Hz, 2H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 174.8, 171.6, 138.9, 131.1, 129.3, 128.4, 64.6, 30.5, 21.0, 16.6; **IR** (neat) $\tilde{\nu}_{max}$ 1651, 1515, 1445, 1201, 1067, 938, 699 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{13}H_{15}NO_3Na^+$: 256.0944, found :256.0948.

(2-(4-Chlorophenoxy)-2-methylpropanamido)methyl acetate (2q)



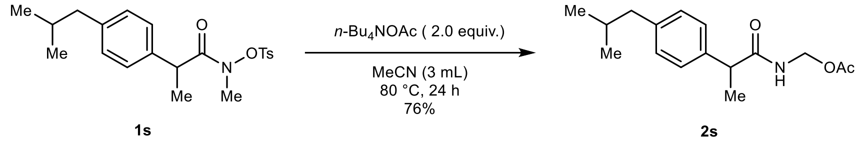
Prepared following the **GP2A** using 2-(4-chlorophenoxy)-*N*,2-dimethyl-*N*-(tosyloxy)propanamide **1q** (104.2 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2q** as a colorless oil (56.9 mg, 66%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.68 (d, *J* = 7.7 Hz, 1H), 7.20 (dd, *J* = 8.7, 2.0 Hz, 2H), 6.82–6.78 (m, 2H), 5.27 (d, *J* = 7.4 Hz, 2H), 2.00 (s, 3H), 1.48 (s, 6H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 175.4, 171.6, 152.7, 129.3, 128.6, 122.2, 81.5, 64.1, 24.8, 20.8; **IR** (neat) $\tilde{\nu}_{max}$ 1737, 1687, 1487, 1380, 1231, 1151, 958, 735 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{13}H_{16}ClNO_4Na^+$: 308.0660, found: 308.0669.

(2,2-Dimethylbutanamido)methyl acetate (2r)



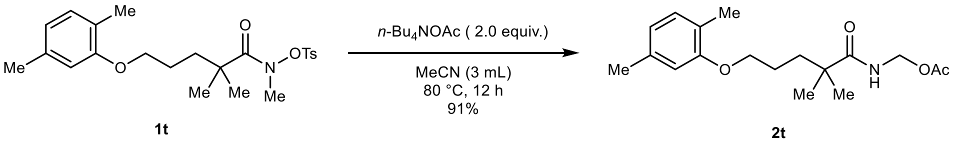
Prepared following the **GP2A** using *N*,2,2-trimethyl-*N*-(tosyloxy) butanamide **1r** (89.8 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2r** as a colorless oil (48.0 mg, 86%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 6.84 (d, *J* = 7.8 Hz, 1H), 5.21 (d, *J* = 6.3 Hz, 2H), 2.01 (s, 3H), 1.52–1.47 (m, 2H), 1.11 (s, 6H), 0.78 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 178.5, 172.1, 64.7, 42.6, 33.7, 24.7, 21.0, 9.0; **IR** (neat) $\tilde{\nu}_{max}$ 1654, 1519, 1477, 1382, 1251, 1190, 1066, 737 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_9H_{17}NO_3Na^+$: 210.1101, found: 210.1097.

(2-(4-Isobutylphenyl)propanamido)methyl acetate (2s)



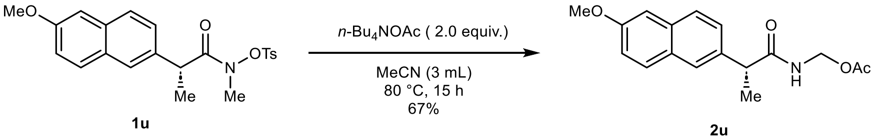
Prepared following the **GP2A** using 2-(4-isobutylphenyl)-*N*-methyl-*N*-(tosyloxy) propanamide **1s** (116.8 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2s** as a colorless oil (56.7 mg, 76%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.16–7.13 (m, 2H), 7.10–7.09 (m, 2H), 6.60 (t, *J* = 7.3 Hz, 1H), 5.19–5.11 (m, 2H), 3.53 (q, *J* = 7.1 Hz, 1H), 2.44 (d, *J* = 7.2 Hz, 2H), 1.98 (s, 3H), 1.85–1.81 (m, 1H), 1.48 (d, *J* = 7.2 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 6H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 175.3, 172.0, 141.2, 138.1, 123.0, 127.5, 64.7, 46.9, 45.3, 30.4, 22.6, 21.1, 18.5; **IR** (neat) $\tilde{\nu}_{max}$ 1740, 1670, 1512, 1366, 1211, 1187, 1016, 952 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{16}H_{23}NO_3Na^+$: 300.1570, found: 300.1572.

(5-(2,5-Dimethylphenoxy)-2,2-dimethylpentanamido)methyl acetate (2t)

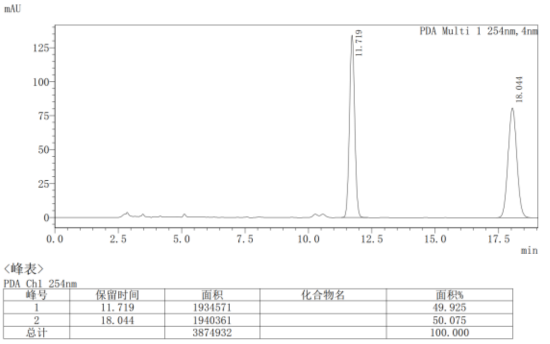


Prepared following the **GP2A** using 5-(2,5-dimethylphenoxy)-*N*,2,2-trimethyl-*N*-(tosyloxy)pentanamide **1t** (130.0 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3.0 mL) at 80 °C for 12 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2t** as a colorless oil (87.6 mg, 91%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.00 (d, *J* = 7.4 Hz, 1H), 6.92 (t, *J* = 7.1 Hz, 1H), 6.66 (d, *J* = 7.4 Hz, 1H), 6.60 (d, *J* = 1.8 Hz, 1H), 5.26 (d, *J* = 7.1 Hz, 2H), 3.92–3.88 (m, 2H), 2.30 (s, 3H), 2.17 (s, 3H), 2.04 (s, 3H), 1.71 (ttd, *J* = 10.9, 8.0, 6.9, 3.7 Hz, 4H), 1.22 (s, 6H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 178.2, 172.0, 156.9, 136.5, 130.3, 123.5, 120.8, 112.0, 67.8, 64.6, 42.1, 37.4, 25.2, 25.0, 21.4, 20.9, 15.8; **IR** (neat) $\tilde{\nu}_{max}$ 1728, 1667, 1509, 1264, 1202, 1130, 1017, 730 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{18}H_{27}NO_4Na^+$: 344.1832, found: 344.1839.

(*S*)-(2-(6-Methoxynaphthalen-2-yl)propanamido)methyl acetate (2u)



Prepared following the **GP2A** using (*S*)-2-(6-methoxynaphthalen-2-yl)-*N*-methyl-*N*-(tosyloxy)propanamide **1u** (124.0 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 15 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2u** as a white solid (60.7 mg, 67%, 99% ee). Rotamers present at room temperature. **M.P.** 129.3–131.5 °C; **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.70 (dd, *J* = 13.6, 8.7 Hz, 2H), 7.63 (d, *J* = 1.8 Hz, 1H), 7.33 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.15 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.11 (d, *J* = 2.6 Hz, 1H), 6.63 (t, *J* = 7.3 Hz, 1H), 5.25–5.06 (m, 2H), 3.90 (s, 3H), 3.68 (q, *J* = 7.1 Hz, 1H), 1.96 (s, 3H), 1.57 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 175.0, 171.8, 157.9 (major), 157.8 (minor), 136.0 (minor), 135.7 (major), 133.9 (major), 133.8 (minor), 129.3 (129.33, minor), 129.3 (129.28, major), 129.0, 127.8 (major), 127.7 (minor), 126.3 (major), 126.2 (minor), 126.1 (minor), 126.0 (major), 119.3 (major), 119.2 (minor), 105.7 (105.70, major), 105.7 (105.67, minor), 64.5, 55.4 (55.40, major), 55.4 (55.39, minor), 47.0 (47.05, minor), 47.0 (46.98, major), 20.9 (major), δ 20.7 (minor), 18.38 (major), 18.37 (minor); **IR** (neat) $\tilde{\nu}_{max}$ 1664, 1504, 1462, 1264, 1209, 1030, 925, 732 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{17}H_{19}NO_4Na^+$: 324.1206, found: 324.1207. Ee value were determined by chiral HPLC analysis. HPLC retention times (ID, eluent: hexanes/*i*-PrOH = 90/10, 254 nm, flow rate: 1.0 mL/min, T = 40 ºC): t$_1$ = 11.7 min (major), t$_2$ = 18.0 min (minor).



<峰表>
PDA Ch1 254nm

峰号	保留时间	面积	化合物名	面积%
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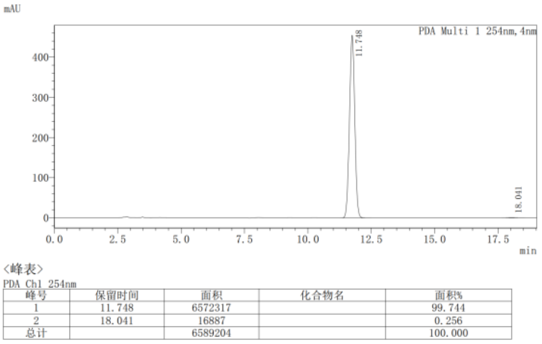
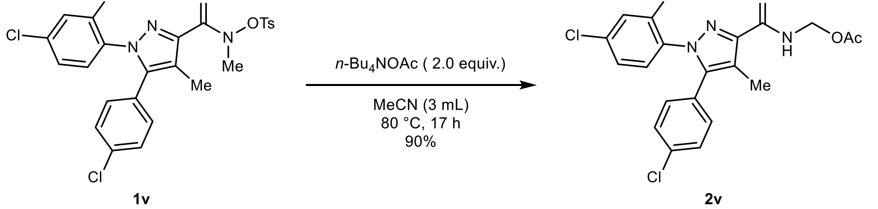
2	18.044	1940361		50.075
总计		3874932		100.000



<峰表>
PDA Ch1 254nm

峰号	保留时间	面积	化合物名	面积%
1	11.748	6572317		99.744
2	18.041	16887		0.256
总计		6589204		100.000

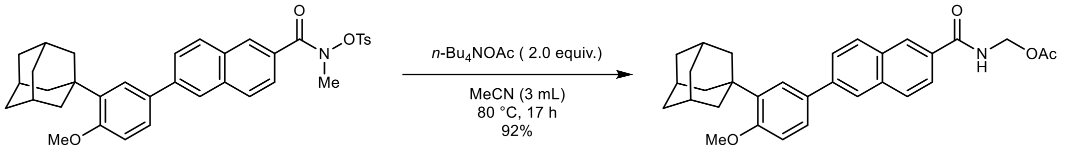
(5-(4-Chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1*H*-pyrazole-3-carboxamido)methyl acetate (2v)



Prepared following the **GP2A** using 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-*N*,4-dimethyl-*N*-(tosyloxy)-1*H*-pyrazole-3-carboxamidee **1v** (169.4 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu$_4$NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3 mL) at 80 °C for 17 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2v** as a white solid (122.2 mg, 90%). **M.P.** 125.0–127.3 °C; **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.96 (s, 1H), 7.41 (d, *J* = 2.1 Hz, 1H), 7.30–7.26 (m, 4H), 7.06–7.03 (m, 2H), 5.42 (d, *J* = 7.5 Hz, 2H), 2.36 (s, 3H), 2.06

(s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.7, 163.0, 144.0, 143.3, 136.2, 135.8, 135.1, 132.9, 130.9, 130.6, 130.4, 129.0, 128.0, 127.1, 118.4, 63.9, 21.1, 9.5; **IR** (neat) $\tilde{\nu}_{max}$ 1737, 1681, 1528, 1498, 1485, 1206, 1094, 1012 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{20}H_{16}Cl_3N_3O_3Na^+$: 474.0149, found: 474.0150.

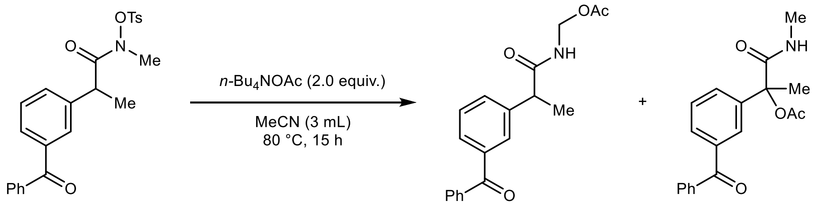
(6-(3-((3*r*,5*r*,7*r*)-Adamantan-1-yl)-4-methoxyphenyl)-2-naphthamido)methyl acetate (2w)



1w **2w**

Prepared following the **GP2A** using 6-(3-((3*r*,5*r*,7*r*)-adamantan-1-yl)-4-methoxyphenyl)-*N*-methyl-*N*-(tosyloxy)-2-naphthamide **1w** (178.7 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu_4NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3.0 mL) at 80 °C for 17 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **2w** as a white solid (133.5 mg, 92%). Rotamers present in a 1:1 ratio at room temperature. **M.P.** 119.3–121.5 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.35 (dd, *J* = 17.2, 1.8 Hz, 1H), 8.22 (t, *J* = 6.9 Hz, 0.4H, minor), 8.01–7.77 (m, 5.6H, major), 7.72–7.66 (m, 1H), 7.61–7.57 (m, 1H), 7.52 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.96 (dd, *J* = 23.8, 8.5 Hz, 1H), 5.54 (d, *J* = 7.1 Hz, 1H, major), 5.16 (d, *J* = 6.8 Hz, 1H, minor), 3.89 (d, *J* = 4.5 Hz, 3H), 2.20–2.18 (m, 6H), 2.11 (d, *J* = 5.1 Hz, 6H), 1.81 (s, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.2 (minor), 172.4 (major), 169.0 (minor), 167.8 (major), 156.0 (major), 158.9 (minor), 141.3 (major), 141.1 (minor), 139.1 (major), 139.0 (minor), 135.6 (major), 135.5 (minor), 132.6 (minor), 132.5 (major), 131.3 (131.31, minor), 131.3 (131.29, major), 130.0 (minor), 129.8 (major), 129.5 (129.54, minor), 129.5 (129.51, major), 128.8 (major), 128.7 (minor), 128.1 (minor), 128.0 (major), 126.8 (major), 126.6 (minor), 126.0 (126.01, major), 126.0 (125.97, minor)), 125.8, 124.8 (major), 124.7 (minor), 124.0 (124.01, major), 124.0 (123.95, minor), 112.2 (major), 112.1 (minor), 65.0, 55.2 (major, 55.23), 55.2 (55.20, minor), 40.7, 37.3 (37.27, major), 37.3 (37.26, minor), 37.2, 29.2, 21.1 (major), 20.9 (minor); **IR** (neat) $\tilde{\nu}_{max}$ 2903, 1628, 1530, 1491, 1281, 1235, 1030, 808, 754 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{31}H_{33}NO_4Na^+$: 506.2302, found: 506.2306.

(2-(3-Benzoylphenyl)propanamido)methyl acetate (2x) and (2-(3-benzoylphenyl)propanamido)methyl acetate (2x')



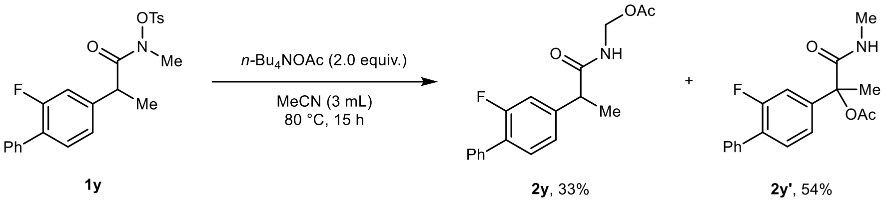
1x **2x**, 53% **2x'**, 43%

Prepared following the **GP2A** using 2-(3-benzoylphenyl)-*N*-methyl-*N*-(tosyloxy)propanamide **1x** (131.1 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu_4NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3.0 mL) at 80 °C for 15 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 5:1 → 3:1) to afford the title compounds **2x** (51.9 mg, 53%) and **2x’** (42.9 mg, 43%) as a colorless oil, respectively.

Data for **2x**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.72 (s, 1H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.60–7.57 (m, 1H), 7.53 (d, J = 7.8 Hz, 1H), 7.46 (dt, J = 23.5, 7.6 Hz, 3H), 6.78 (s, 1H), 5.22–5.13 (m, 2H), 3.64 (q, J = 7.1 Hz, 1H), 1.99 (s, 3H), 1.53 (d, J = 7.1 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 196.6, 174.2, 171.9, 141.2, 138.2, 137.4, 132.7, 131.6, 130.1, 129.4, 129.2, 128.9, 128.4, 64.5, 46.8, 21.0, 18.6; **IR** (neat) $\tilde{\nu}_{max}$ 3317, 1655, 1526, 1447, 1282, 1026, 820, 720 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{19}H_{19}NO_4Na^+$: 348.1206 found: 348.1209.

Data for **2x’**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.78–7.74 (m, 2H), 7.69–7.65 (m, 2H), 7.59–7.56 (m, 1H), 7.46 (q, J = 7.7 Hz, 3H), 6.56–6.51 (m, 1H), 2.79 (d, J = 4.9 Hz, 3H), 2.14 (s, 3H), 2.07 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 196.4, 171.4, 168.5, 141.1, 137.5, 137.4, 132.7, 130.2, 129.8, 129.3, 128.6, 128.4, 126.4, 83.9, 26.6, 22.9, 22.1; **IR** (neat) $\tilde{\nu}_{max}$ 1744, 1659, 1532, 1447, 1369, 1218, 732, 699 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{19}H_{19}NO_4Na^+$: 348.1206 found: 348.1212.

(2-(2-Fluoro-[1,1'-biphenyl]-4-yl)propanamido)methyl acetate (2y) and 2-(2-fluoro-[1,1'-biphenyl]-4-yl)-1-(methylamino)-1-oxopropan-2-yl acetate (2y')

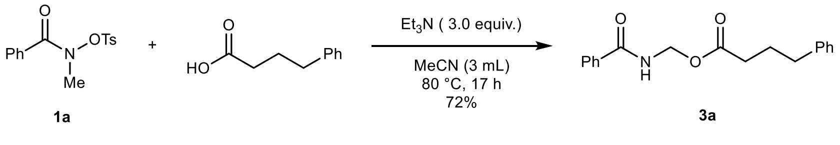


Prepared following the **GP2A** using 2-(2-fluoro-[1,1'-biphenyl]-4-yl)-*N*-methyl-*N*-(tosyloxy)propanamide **1y** (128.1 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu_4NOAc (180.9 mg, 0.6 mmol, 2.0 equiv.) in MeCN (3.0 mL) at 80 °C for 15 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 5:1 → 2:1) to afford the title compounds **2y** (30.9 mg, 33%) and **2y’** (51.4 mg, 54%) as a colorless oil, respectively.

Data for **2y**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.53 (d, J = 7.9 Hz, 2H), 7.46–7.36 (m, 4H), 7.15–7.08 (m, 2H), 6.74–6.64 (m, 1H), 5.29–5.13 (m, 2H), 3.59 (p, J = 7.1, 6.6 Hz, 1H), 2.03 (s, 3H), 1.54 (d, J = 7.1 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.1, 172.0, δ 159.9 (d, $J_{C\text{–}F}$ = 249.2 Hz), δ 142.0 (d, $J_{C\text{–}F}$ = 7.5 Hz), δ 135.4, δ 131.3 (d, $J_{C\text{–}F}$ = 4.0 Hz), δ 129.0 (d, $J_{C\text{–}F}$ = 2.9 Hz), 129.0, 128.6, 127.9, δ 123.7 (d, $J_{C\text{–}F}$ = 3.4 Hz), 115.4 (d, $J_{C\text{–}F}$ = 23.7 Hz), 64.5, 46.6, 21.0, 18.4; **^{19}F NMR** (565 MHz, $CDCl_3$) δ −117.16; **IR** (neat) $\tilde{\nu}_{max}$ 2984, 1661, 1531, 1284, 1021, 698 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{18}H_{18}FNO_3Na^+$: 338.1163 found: 338.1165.

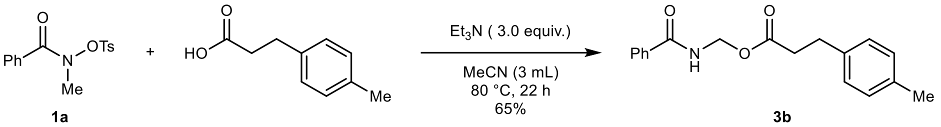
Data for **2y’**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.52 (d, J = 7.9 Hz, 2H), 7.42 (dt, J = 11.7, 7.8 Hz, 3H), 7.36 (t, J = 7.4 Hz, 1H), 7.29–7.21 (m, 2H), 6.46 (d, J = 4.6 Hz, 1H), 2.84 (d, J = 4.9 Hz, 3H), 2.19 (s, 3H), 2.08 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.4, 168.4, δ 159.6 (d, $J_{C\text{–}F}$ = 248.2 Hz), 142.0 (d, $J_{C\text{–}F}$ = 7.3 Hz), 135.2, 130.9 (d, $J_{C\text{–}F}$ = 3.9 Hz), 129.0 (d, $J_{C\text{–}F}$ = 2.8 Hz), 128.7 (d, $J_{C\text{–}F}$ = 13.7 Hz), 128.5, 127.9, 121.0, 113.1 (d, $J_{C\text{–}F}$ = 25.3 Hz), 83.5, 26.6, 22.9, 22.0; **^{19}F NMR** (565 MHz, $CDCl_3$) δ −117.16; **IR** (neat) $\tilde{\nu}_{max}$ 1743, 1665, 1484, 1409, 1224, 1010, 734, 767 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{18}H_{18}FNO_3Na^+$: 338.1163 found: 338.1166.

Benzamidomethyl 4-phenylbutanoate (3a)



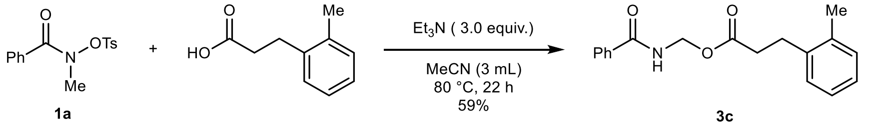
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 4-phenylbutanoic acid (98.5 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 17 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3a** as a colorless oil (64.3 mg, 72%). Rotamers present in a 1:3 ratio at room temperature. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.84–7.80 (m, 2H), 7.56–7.51 (m, 2H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.30–7.26 (m, 2H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.17–7.13 (m, 2H), 5.46 (d, *J* = 7.2 Hz, 2H), 2.68 (t, *J* = 7.6 Hz, 0.5H, minor), 2.64 (t, *J* = 7.6 Hz, 1.5H, major), 2.39–2.35 (m, 2H), 1.98–1.94 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.7, 167.7, 141.4 (minor), 141.2 (major), 133.2, 132.4, 128.8, 128.6 (128.56, minor), 128.6 (128.55, major), 128.5, 127.4, 126.1 (126.12, major), 126.1 (126.09, minor), 64.7, 35.1 (35.09, major), 35.1 (35.08, minor), 33.5 (major), 33.4 (minor), 26.4 (minor), 26.3 (major); **IR** (neat) $\tilde{\nu}_{max}$ 1707, 1658, 1531, 1291, 1138, 1030, 699 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{18}H_{19}NO_3Na^+$: 320.1257, found: 320.1258.

Benzamidomethyl 3-(*p*-tolyl)propanoate (3b)



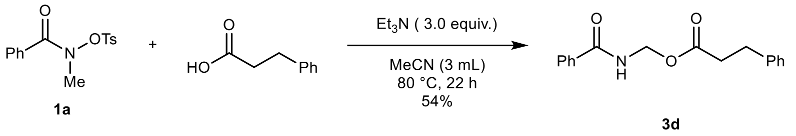
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 3-(*p*-tolyl)propanoic acid (98.5 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 22 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3b** as a colorless oil (57.6 mg, 65%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.80–7.76 (m, 2H), 7.56–7.53 (m, 1H), 7.45 (d, *J* = 7.9 Hz, 2H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.09–7.00 (m, 4H), 5.46 (d, *J* = 7.2 Hz, 2H), 2.90 (d, *J* = 7.8 Hz, 2H), 2.64 (d, *J* = 7.7 Hz, 2H), 2.25 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.4, 167.8, 137.2, 136.1, 133.4, 132.6, 129.5, 129.0, 128.4, 127.6, 65.0, 36.1, 30.6, 21.3; **IR** (neat) $\tilde{\nu}_{max}$ 1733, 1659, 1532, 1291, 1140, 1042, 812, 715 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{18}H_{19}NO_3Na^+$: 320.1257, found: 320.1253.

Benzamidomethyl 3-(*o*-tolyl)propanoate (3c)



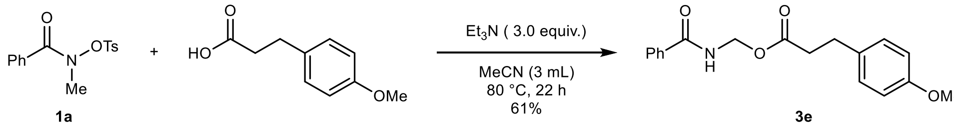
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 3-(*o*-tolyl)propanoic acid (98.5 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 22 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3c** as a colorless oil (52.7 mg, 59%). Rotamers present in a 1:6 ratio at room temperature. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.83–7.77 (m, 2H), 7.57–7.52 (m, 1H), 7.48–7.42 (m, 3H), 7.12–7.07 (m, 3H), 5.48 (d, *J* = 7.2 Hz, 2H), 2.96–2.93 (m, 2H), 2.64 (d, *J* = 8.1 Hz, 2H), 2.33 6 (s, 0.4H, minor), 2.31 (s, 2.6H, major); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.2, 167.6, 138.5 (minor), 138.2 (major), 136.1 (minor), 136.0 (major), 133.2 (minor), 132.4 (major), 130.4, 128.8, 128.5 (128.54, major), 128.5 (128.51, minor), 127.4, 126.6 (126.59, major), 126.6 (126.57, minor), 126.25 (major), 126.20 (major), 64.9, 34.4 (major), 34.2 (minor), 28.1, 19.3; **IR** (neat) $\tilde{\nu}_{max}$ 1657, 1531, 1490, 1282, 1051, 1042, 742, 693 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{18}H_{19}NO_3Na^+$: 320.1257, found: 320.1260.

Benzamidomethyl 3-phenylpropanoate (3d)



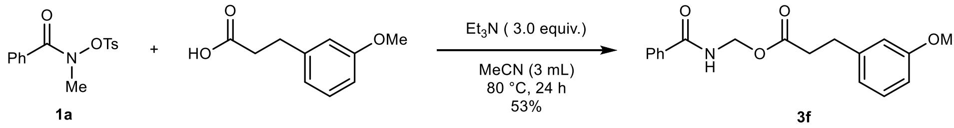
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 3-phenylpropanoic acid (90.1 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 22 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3d** as a colorless oil (45.0 mg, 53%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.57–7.51 (m, 1H), 7.51–7.41 (m, 3H), 7.32–7.11 (m, 5H), 5.46 (d, *J* = 7.2 Hz, 2H), 2.94 (t, *J* = 7.7 Hz, 2H), 2.67 (t, *J* = 7.8 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.0, 167.6, 140.1, 133.2, 132.4, 128.8, 128.6, 128.3, 127.4, 126.4, 64.8, 35.8, 30.8.; **IR** (neat) $\tilde{\nu}_{max}$ 1712, 1658, 1532, 1290, 1141, 1030, 698 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{17}H_{17}NO_3Na^+$: 306.1101, found: 306.1102.

Benzamidomethyl 3-(4-methoxyphenyl)propanoate (3e)



Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 3-(4-methoxyphenyl)propanoic acid (108.1 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 22 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3e** as a colorless oil (61.6 mg, 61%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.77 (dt, *J* = 7.0, 1.3 Hz, 2H), 7.56–7.52 (m, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 1H), 7.10–7.04 (m, 2H), 6.77–6.71 (m, 2H), 5.45 (d, *J* = 7.2 Hz, 2H), 3.70 (s, 3H), 2.88 (t, *J* = 7.6 Hz, 2H), 2.63 (t, *J* = 7.6 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.1, 167.6, 158.1, 133.2, 132.4, 132.1, 129.3, 128.8, 127.4, 114.0, 64.7, 55.2, 36.1, 29.9; **IR** (neat) $\tilde{\nu}_{max}$ 1711, 1656, 1513, 1247, 1032, 830, 715 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{18}H_{19}NO_4Na^+$: 336.1206, found: 336.1206.

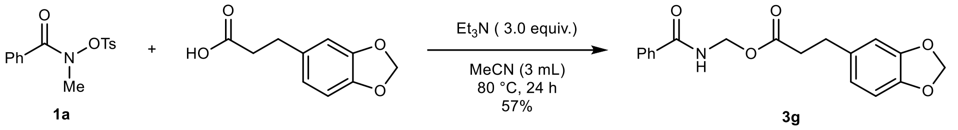
Benzamidomethyl 3-(3-methoxyphenyl)propanoate (3f)



Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 3-(3-methoxyphenyl)propanoic acid (108.1 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3f** as a colorless oil (50.0 mg, 53%). Rotamers present at room temperature. **M.P.**106.3–108.8 °C; **^{1}H NMR**

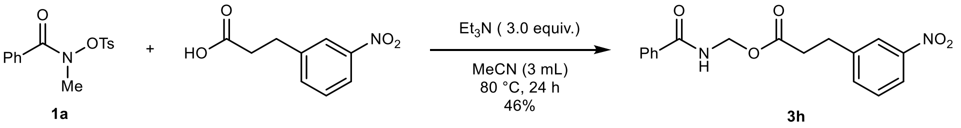
(600 MHz, CDCl$_3$) δ 7.81–7.76 (m, 2H), 7.53 (td, *J* = 7.2, 6.8, 1.1 Hz, 1H), 7.47–7.40 (m, 3H), 7.13 (t, *J* = 7.8 Hz, 1H), 6.77–6.68 (m, 3H), 5.46 (d, *J* = 7.1 Hz, 2H), 3.74 (s, 3H), 2.91 (t, *J* = 7.8 Hz, 2H), 2.66 (t, *J* = 7.8 Hz, 2H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 174.1, 167.6, 159.8, 141.8, 133.2, 132.4, 129.6 (129.64, minor), 129.6 (129.61, major), 128.8, 127.4 (major), 127.2 (minor), 120.7 (120.71, minor), 120.7 (120.67, major), 114.2 (minor), 114.1 (major), 111.8 (major), 111.7 (minor), 64.8, 55.25 (minor), 55.21 (major), 35.7 (major), 35.4 (minor), 30.85 (minor), 30.81 (major); **IR** (neat) $\tilde{\nu}_{\max}$ 1710, 1602, 1530, 1489, 1263, 1043, 734, 694 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $\mathrm{C_{18}H_{19}NO_4Na^+}$:336.1206, found: 336.1206.

Benzamidomethyl 3-(benzo[*d*][1,3]dioxol-5-yl)propanoate (3g)



Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 3-(benzo[*d*][1,3]dioxol-5-yl)propanoic acid (116.5 mg, 0.6 mmol, 2.0 equiv.), and Et$_3$N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3g** as a colorless oil (55.6 mg, 57%). Rotamers present at room temperature. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.78 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.54–7.51 (m, 1H), 7.43 (dd, *J* = 9.6, 5.8 Hz, 3H), 6.65–6.58 (m, 3H), 5.84 (s, 2H), 5.45 (d, *J* = 7.2 Hz, 2H), 2.84 (t, *J* = 7.6 Hz, 2H), 2.60 (t, *J* = 7.7 Hz, 2H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 177.2 (minor), 173.9 (major), 168.8 (minor), 167.7 (major), 147.7 (147.71, minor), 147.7 (147.69, major), 146.0, 134.2 (minor), 133.9 (major), 133.3 (minor), 133.2 (major), 132.4 (major), 132.3 (minor), 128.8, 127.4 (127.40, major), 127.4 (127.38, minor), 121.2, 108.9 (minor), 108.8 (major), 108.4 (minor), 108.3 (major), 100.9 (100.93, minor), 100.9 (100.89, major), 64.8, 36.1 (major), 35.9 (minor), 30.5 (30.52, major), 30.5 (30.50, minor); **IR** (neat) $\tilde{\nu}_{\max}$ 1710, 1657, 1530, 1490, 1246, 1040, 736, 694 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $\mathrm{C_{18}H_{17}NO_5Na^+}$: 350.0999, found: 350.0989.

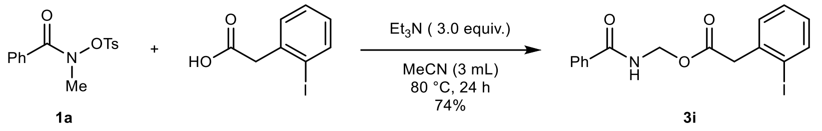
Benzamidomethyl 3-(3-nitrophenyl)propanoate (3h)



Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 3-(3-nitrophenyl)propanoic acid (117 mg, 0.6 mmol, 2.0 equiv.), and Et$_3$N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 2:1) to afford the title compound **3h** as a colorless oil (47.1 mg, 46%). Rotamers present at room temperature. **M.P.** 137.2–139.5 °C; **^{1}H NMR** (600 MHz, CDCl$_3$) δ 8.04 (t, *J* = 2.0 Hz, 1H), 7.99 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.77–7.74 (m, 2H), 7.55–7.50 (m, 2H), 7.44 (d, *J* = 7.8 Hz, 2H), 7.36 (d, *J* = 7.9 Hz, 1H), 5.45 (d, *J* = 7.3 Hz, 2H), 3.04 (t, *J* = 7.5 Hz, 2H), 2.71 (t, *J* = 7.5 Hz, 2H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 173.5, 167.8, 142.6 (minor), 142.3 (major), 135.1 (minor), 135.0 (major), 132.8 (major), 132.6 (minor), 129.8, 129.1, 129.0 (129.03, major), 129.0 (129.00, minor), 127.60 (127.60, minor), 127.6 (127.57, major), 127.5 (major), 127.4 (minor), 123.6, 121.9

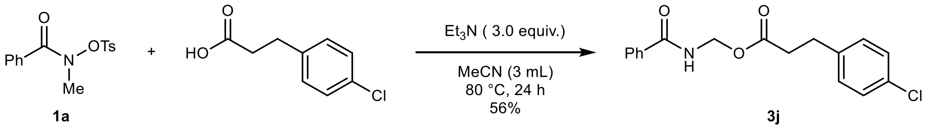
(121.92, major), 121.9 (121.91, minor), 65.3, 35.4 (major), 35.1 (minor), 30.5 (30.52, minor), 30.5 (30.50, major); **IR** (neat) $\tilde{\nu}_{max}$ 1711, 1654, 1534, 1408, 1230, 1066, 734 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{17}H_{16}N_2O_5Na^+$:351.0951, found: 351.0955.

Benzamidomethyl 2-(2-iodophenyl)acetate (3i)



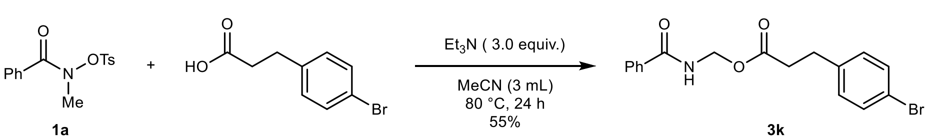
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 2-(2-iodophenyl)acetic acid (157.2 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 μL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3i** as a colorless oil (73.0 mg, 74%). Rotamers present in a 1:3 ratio at room temperature. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.81–7.77 (m, 2H), 7.51 (dt, *J* = 16.0, 7.4 Hz, 2H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.29–7.24 (m, 2H), 6.95 (td, *J* = 7.6, 1.8 Hz, 1H), 5.51 (d, *J* = 7.2 Hz, 2H), 3.83 (s, 0.2H, minor), 3.82 (s, 1.8H, major); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.9, 167.6, 139.6, 137.3, 133.2, 132.4, 130.9, 129.2, 128.8, 128.6, 127.4, 101.1, 65.4, 46.1; **IR** (neat) $\tilde{\nu}_{max}$ 1711, 1651, 1532, 1408, 1231, 1066, 736 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{16}H_{14}INO_3Na^+$: 432.0067, found: 432.0064.

Benzamidomethyl 3-(4-chlorophenyl)propanoate (3j)



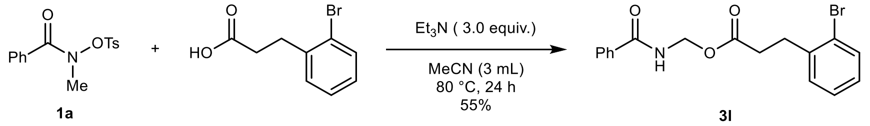
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 3-(4-chlorophenyl)propanoic acid (110.8 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 μL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3j** as a colorless oil (53.4 mg, 56%). Rotamers present at room temperature. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.7 Hz, 2H), 7.56–7.53 (m, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 2H), 7.08 (d, *J* = 8.1 Hz, 2H), 5.45 (d, *J* = 7.2 Hz, 2H), 2.90 (d, *J* = 7.6 Hz, 2H), 2.64 (d, *J* = 7.3 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.8, 167.7, 138.8 (minor), 138.5 (major), 133.1, 132.5, 132.2, 129.8 (major), 129.7 (minor), 128.8 (128.83, major), 128.8 (128.80, minor), 128.7 (128.73, minor), 128.71 (128.7, major), 127.4, 64.9, 35.6 (major), 35.4 (minor), 30.1 (major), 30.0 (minor); **IR** (neat) $\tilde{\nu}_{max}$ 1733, 1662, 1532, 1492, 1291, 1139, 820, 715 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{17}H_{16}ClNO_3Na^+$: 340.0711, found: 340.0719.

Benzamidomethyl 3-(4-bromophenyl)propanoate (3k)



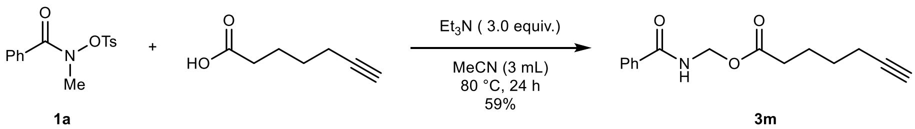
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 3-(4-bromophenyl)propanoic acid (137.4 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 μL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3k** as a colorless oil (59.9 mg, 55%). Rotamers present at room temperature. **M.P.** 137.5–139.3 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.78–7.74 (m, 2H), 7.57–7.53 (m, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.33 (dd, *J* = 10.0, 5.4 Hz, 3H), 7.05–7.01 (m, 2H), 5.45 (d, *J* = 7.2 Hz, 2H), 2.89 (t, *J* = 7.6 Hz, 2H), 2.66–2.63 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.8, 167.6, 139.1, 133.1, 132.5, 131.7 (131.71, minor), 131.7 (131.69, major), 130.19 (minor), 130.16 (major), 128.9, 127.4, 120.3, 64.9, 35.5 (major), 35.2 (minor), 30.2 (major), 30.1 (minor); **IR** (neat) $\tilde{\nu}_{max}$ 1739, 1660, 1591, 1536, 1483, 1229, 1010, 954 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{17}H_{16}BrNO_3Na^+$: 384.0206, found: 384.0212.

Benzamidomethyl 3-(2-bromophenyl)propanoate (3l)



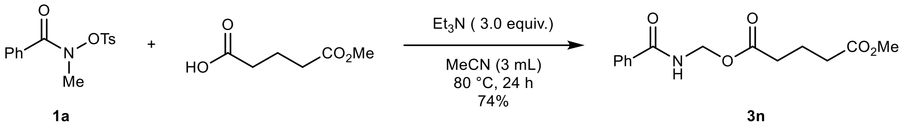
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 3-(2-bromophenyl)propanoic acid (137.4 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 μL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3l** as a colorless oil (59.4 mg, 55%). Rotamers present at room temperature. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.81–7.78 (m, 2H), 7.55–7.52 (m, 1H), 7.49 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 3H), 7.20 (dt, *J* = 7.7, 1.2 Hz, 1H), 7.15–7.11 (m, 1H), 7.03 (dd, *J* = 7.3, 1.6 Hz, 1H), 5.47 (d, *J* = 7.2 Hz, 2H), 3.05 (t, *J* = 7.7 Hz, 2H), 2.68 (t, *J* = 7.7 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.9, 167.6, 139.6 (minor), 139.4 (major), 133.2, 133.0, 132.5, 130.6 (minor), 130.5 (major), 128.8, 128.3, 127.7 (127.73, minor), 127.7 (127.67, major), 127.4, 124.5 (minor), 124.4 (major), 64.9, 34.0 (major), 33.8 (minor), 31.3; **IR** (neat) $\tilde{\nu}_{max}$ 1710, 1656, 1530, 1292, 1265, 1049, 1027, 737 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{17}H_{16}BrNO_3Na^+$: 384.0206, found: 384.0209.

Benzamidomethyl hept-6-ynoate (3m)



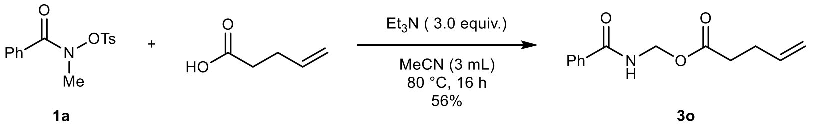
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), hept-6-ynoic acid (75.7 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 μL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3m** as a colorless oil (45.6 mg, 59%). Rotamers present at room temperature. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.6 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.44 (q, *J* = 8.7, 7.5 Hz, 3H), 5.45 (d, *J* = 7.1 Hz, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.18 (td, *J* = 7.4, 2.7 Hz, 2H), 1.93 (q, *J* = 2.6, 2.2 Hz, 1H), 1.73 (q, *J* = 7.5 Hz, 2H), 1.56–1.50 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.6, 167.7, 133.2, 132.4, 128.8, 127.4, 84.0 (minor), 83.9 (major), 68.8 (68.82, major), 68.8 (68.79, minor), 64.8, 33.7 (major), 33.3 (minor), 27.8, 23.8 (23.85, minor), 23.8 (23.79, major), 18.2 (18.22, minor), 18.2 (18.18, major); **IR** (neat) $\tilde{\nu}_{max}$ 1710, 1657, 1531, 1289, 1140, 1026, 715, 693 cm^{-1}; **HRMS** (ESI/[M + H]$^+$) *m/z* calcd. for $C_{15}H_{18}NO_3^+$: 260.1281, found: 260.1277.

Benzamidomethyl methyl glutarate (3n)



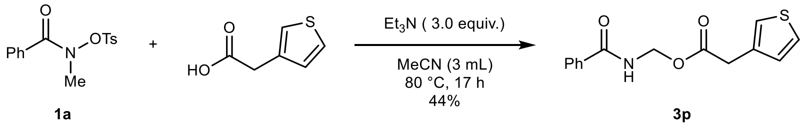
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 5-methoxy-5-oxopentanoic acid (87.7 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3n** as a colorless oil (62.4 mg, 74%). Rotamers present with a ratio of 1:5 at room temperature. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.6 Hz, 2H), 7.57–7.51 (m, 1H), 7.48–7.36 (m, 3H), 5.46 (d, *J* = 7.2 Hz, 2H), 3.67 (s, 0.5H, minor), 3.64 (s, 2.5H, major), 2.40 (t, *J* = 7.5 Hz, 2H), 2.36 (t, *J* = 7.3 Hz, 2H), 1.94 (q, *J* = 7.5 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.1, 173.4, 167.6, 133.2, 132.4, 128.8, 127.4, 64.9, 51.8, 33.2 (major), 33.0 (33.05, minor), 33.0 (33.04, major), 32.8 (minor), 20.0 (minor), 19.9 (major); **IR** (neat) $\tilde{\nu}_{max}$ 1729, 1657, 1533, 1286, 1201, 1147, 1029, 715 cm^{-1}; **HRMS** (ESI/[M + H]$^+$) *m/z* calcd. for $C_{14}H_{18}NO_5^+$: 280.1179, found: 280.1181.

Benzamidomethyl pent-4-enoate (3o)



Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), pent-4-enoic acid (60.0 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 16 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3o** as a colorless oil (38.8 mg, 56%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.81–7.77 (m, 2H), 7.55–7.49 (m, 2H), 7.42 (t, *J* = 7.8 Hz, 2H), 5.77 (ddt, *J* = 16.7, 10.2, 6.4 Hz, 1H), 5.45 (d, *J* = 7.2 Hz, 2H), 5.04–4.98 (m, 1H), 4.98–4.93 (m, 1H), 2.42 (td, *J* = 7.4, 1.1 Hz, 2H), 2.37–2.33 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.2, 167.7, 136.3, 133.2, 132.4, 128.8, 127.4, 115.8, 64.8, 33.4, 28.7; **IR** (neat) $\tilde{\nu}_{max}$ 1733, 1659, 1522, 1294, 1147, 914, 714, 693 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{13}H_{15}NO_3Na^+$: 256.0944, found: 256.0947.

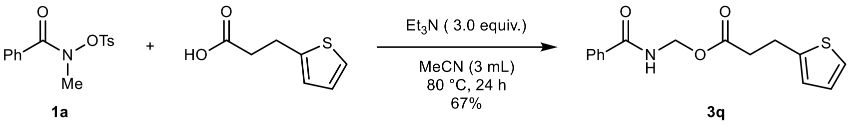
Benzamidomethyl 2-(thiophen-3-yl)acetate (3p)



Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0

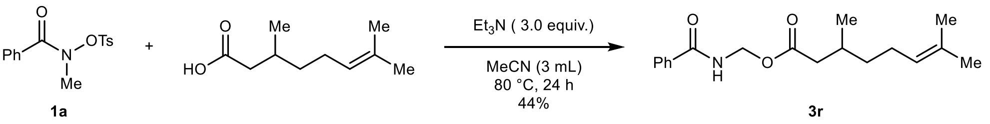
equiv.), 2-(thiophen-3-yl)acetic acid (85.3 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 μL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 17 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3p** as a colorless oil (36.7 mg, 44%). Rotamers present in a 1:4 ratio at room temperature. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.88–7.84 (m, 0.3H, minor), 7.81–7.76 (m, 1.7H, major), 7.52 (d, *J* = 7.4 Hz, 1H), 7.44 (q, *J* = 7.8 Hz, 3H), 7.28–7.24 (m, 1H), 7.16 (dd, *J* = 3.1, 1.2 Hz, 0.2H, minor), 7.14 (dd, *J* = 2.9, 1.2 Hz, 0.8H, major), 7.05 (dd, *J* = 4.9, 1.3 Hz, 0.2H, minor), 7.02 (dd, *J* = 4.9, 1.3 Hz, 0.8H, major), 5.49 (d, *J* = 7.2 Hz, 1.6H, major), 5.00 (d, *J* = 7.0 Hz, 0.4H, minor), 3.69 (s, 0.4H, minor), 3.68 (s, 1.6H, major); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.3 (minor), 172.3 (major), 168.8 (minor), 167.7 (major), 133.4 (minor), 133.3 (minor), 133.2 (major), 132.9 (major), 132.4 (major), 132.3 (minor), 128.8 (128.79, major), 128.8 (128.77, minor), 128.6 (minor), 128.5 (major), 127.4 (127.40, major), 127.4 (127.38, minor), 126.0 (major), 125.9 (minor), 123.3 (major), 123.2 (minor), 67.4 (minor), 65.3 (major), 35.7 (major), 35.52 (minor); **IR** (neat) $\tilde{\nu}_{max}$ 1715, 1656, 1532, 1490, 1295, 1143, 715 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{14}H_{13}NO_3SNa^+$: 298.0508, found: 298.0516.

Benzamidomethyl 3-(thiophen-2-yl)propanoate (3q)



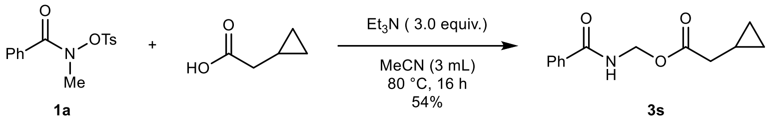
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 3-(thiophen-2-yl)propanoic acid (93.7 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 μL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3q** as a colorless oil (59.0 mg, 68%). Rotamers present in a 1:4 ratio at room temperature. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.84–7.74 (m, 2H), 7.58–7.50 (m, 1H), 7.45 (td, *J* = 7.8, 2.3 Hz, 2H), 7.39 (d, *J* = 7.4 Hz, 1H), 7.16–7.11 (m, 0.2H, minor), 7.09– 7.03 (m, 0.8H, major), 6.92 (dt, *J* = 5.3, 2.8 Hz, 0.2H, minor), 6.84 (dt, *J* = 5.3, 2.8 Hz, 1H), 6.81–6.77 (m, 0.8H, major), 5.48 (dd, *J* = 7.2, 2.3 Hz, 2H), 3.16 (td, *J* = 7.5, 2.2 Hz, 2H), 2.73 (qd, *J* = 7.8, 3.9 Hz, 2H); **^{13}C NMR** δ 173.6, 167.7, 142.6, 133.2, 132.4, 128.8, 127.4, 127.0 (minor), 126.9 (major), 124.9 (major), 124.8 (minor), 123.7 (123.73, major), 123.7 (123.70, minor), 64.9, 36.1 (major), 35.8 (minor), 25.1 (major), 25.0 (minor); **IR** (neat) $\tilde{\nu}_{max}$ 1702, 1658, 1394, 1264, 1036, 735, 704 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{15}H_{15}NO_3SNa^+$: 312.0665, found:312.0661.

Benzamidomethyl 3,7-dimethyloct-6-enoate (3r)



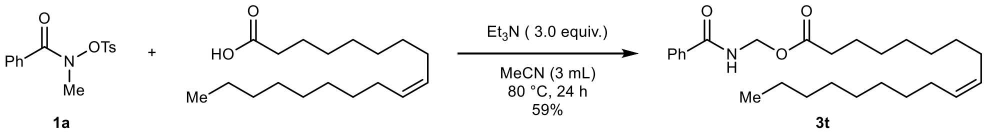
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 3,7-dimethyloct-6-enoic acid (102.1 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 μL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3r** as a colorless oil (40.4 mg, 44%). Rotamers present in a 1:2 ratio at room temperature. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.6 Hz, 2H), 7.55–7.51 (m, 1H), 7.46–7.40 (m, 3H), 5.46 (d, *J* = 7.1 Hz, 2H), 5.05–5.00 (m, 1H), 2.34 (dd, *J* = 15.0, 5.8 Hz, 1H, major), 2.14 (dd, *J* = 14.9, 8.3 Hz, 1H, minor), 1.96 (ddt, *J* = 21.9, 14.7, 7.2 Hz, 4H), 1.67 (s, 1H), 1.64 (s, 2H), 1.59 (s, 1H, minor), 1.56 (s, 2H, major), 1.34–1.29 (m, 1H, minor), 1.23–1.18 (m, 1H, major), 0.97 (d, *J* = 6.6 Hz, 0.6H, minor), 0.92 (d, *J* = 6.7 Hz, 2.4H, major); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.6, 167.6, 133.3, 132.4, 131.8, 128.8, 127.4, 124.2, 64.6, 41.7 (major), 41.5 (minor), 36.8, 30.1 (major), 30.0 (minor), 25.8 (25.83, minor), 25.8 (25.8, major), 25.5 (25.52, minor), 25.5 (25.46, major), 19.7 (minor), 19.6 (major), 17.8 (minor), 17.7 (major); **IR** (neat) $\tilde{\nu}_{max}$ 1707, 1660, 1532, 1265, 1027, 736, 704 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{18}H_{25}NO_3Na^+$: 326.1727, found: 326.1727.

Benzamidomethyl 2-cyclopropylacetate (3s)



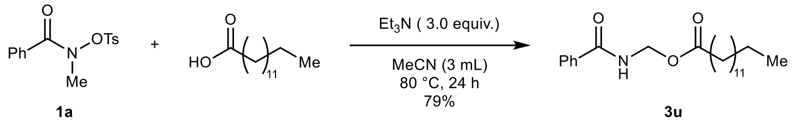
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 2-cyclopropylacetic acid (60 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 16 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3s** as a colorless oil (38.0 mg, 54%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.83–7.77 (m, 2H), 7.56–7.49 (m, 2H), 7.43 (t, *J* = 7.6 Hz, 2H), 5.47 (d, *J* = 7.1 Hz, 2H), 2.22 (d, *J* = 7.2 Hz, 2H), 1.04–0.97 (m, 1H), 0.54–0.48 (m, 2H), 0.16–0.11 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.7, 167.9, 133.5, 132.6, 129.0, 127.6, 65.0, 39.4, 6.9, 4.6; **IR** (neat) $\tilde{\nu}_{max}$ 1733, 1661, 1632, 1294, 1152, 1118, 966, 693 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{13}H_{15}NO_3Na^+$: 256.0944, found: 256.0950.

Benzamidomethyl oleate (3t)



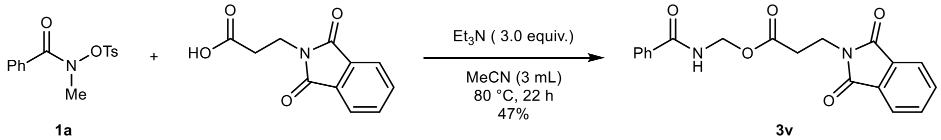
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), oleic acid (169.3 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3t** as a colorless oil (73.4 mg, 59%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.8 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 3H), 5.45 (d, *J* = 7.3 Hz, 2H), 5.32 (q, *J* = 6.4 Hz, 2H), 2.32 (t, *J* = 7.6 Hz, 2H), 1.99 (q, *J* = 6.6 Hz, 4H), 1.62–1.58 (m, 2H), 1.30–1.25 (m, 20H), 0.87 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.1, 167.6, 133.3, 132.4, 130.1, 129.8, 128.8, 127.4, 64.7, 34.2, 32.0, 29.9, 29.8, 29.6, 29.4, 29.2 (29.23), 29.2 (29.17), 29.1, 27.3, 27.2, 24.8 (24.81), 22.8 (22.79), 14.2; **IR** (neat) $\tilde{\nu}_{max}$ 1710, 1663, 1534, 1279, 1066, 713, 691 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{25}H_{41}NO_3Na^+$: 438.2979, found: 438.2973.

Benzamidomethyl tetradecanoate (3u)



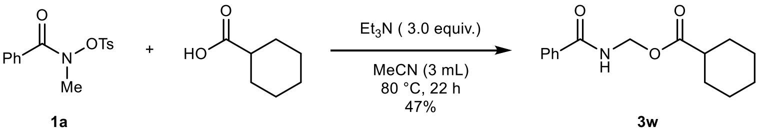
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), tetradecanoic acid (136.9 mg, 0.6 mmol, 2.0 equiv.), and Et$_3$N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 5:1) to afford the title compound **3u** as a white solid (67.3 mg, 79%). **M.P.** 156.2–157.7 °C; **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.80 (d, *J* = 7.7 Hz, 2H), 7.53 (s, 1H), 7.48 (t, *J* = 7.2 Hz, 1H), 7.44 (d, *J* = 7.5 Hz, 2H), 5.45 (d, *J* = 7.1 Hz, 2H), 2.32 (t, *J* = 7.9 Hz, 2H), 1.61–1.58 (m, 2H), 1.26–1.22 (m, 20H), 0.87 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 175.2, 167.7, 133.3, 132.4, 128.8, 127.4, 64.7, 34.3 (major), 34.0 (minor), 32.0, 29.8 (29.78, minor), 29.8 (29.76, major), 29.8 (29.75, major), 29.7 (29.74, minor), 29.7 (29.71, minor), 29.7 (29.68, major), 29.6 (minor), 29.5 (29.54, major), 29.5 (29.46), 29.4 (minor), 29.3 (major), 29.2 (29.19, minor), 29.2 (29.16, major), 24.8 (24.83, minor), 24.8 (24.82, major), 22.8 (22.80), 14.2; **IR** (neat) $\tilde{\nu}_{max}$ 2917, 2849, 1737, 1659, 1536, 1304, 1169, 692 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{22}H_{35}NO_3Na^+$: 384.2509, found: 384.2514.

Benzamidomethyl 3-(1,3-dioxoisoindolin-2-yl)propanoate (3v)



Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 3-(1,3-dioxoisoindolin-2-yl)propanoic acid (131.5 mg, 0.6 mmol, 2.0 equiv.), and Et$_3$N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3.0 mL) at 80 °C for 22 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3v** as a colorless oil (49.7 mg, 47%). Rotamers present in a 1:2 ratio at room temperature. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.86 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.81 (ddd, *J* = 9.5, 6.2, 2.0 Hz, 2H), 7.76–7.75 (m, 1H), 7.69 (ddd, *J* = 18.4, 5.4, 3.0 Hz, 2H), 7.55–7.50 (m, 1H), 7.44 (q, *J* = 7.9 Hz, 2H), 5.47 (d, *J* = 7.2 Hz, 1.4H, major), 5.02 (d, *J* = 6.9 Hz, 0.6H, minor), 4.00–3.97 (m, 2H), 2.78 (d, *J* = 7.4 Hz, 0.6H, minor), 2.73 (t, *J* = 6.9 Hz, 1.4H, major); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 174.8 (minor), 172.1 (major), 168.7 (minor), 168.1 (major), 167.6, 134.2, 133.3 (minor), 133.2 (major), 132.4 (major), 132.3 (minor), 132.1 (minor), 132.0 (major), 128.8 (128.79, minor), 128.8 (128.76, major), 127.5 (major), 127.4 (minor), 123.5, 67.4 (minor), 65.1 (major), 33.8 (major), 33.6 (minor), 33.2 (major), 32.6 (minor); **IR** (neat) $\tilde{\nu}_{max}$ 1773, 1712, 1468, 1397, 1298, 1192, 1030, 717 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{19}H_{16}N_2O_5Na^+$: 375.0951, found: 375.0957.

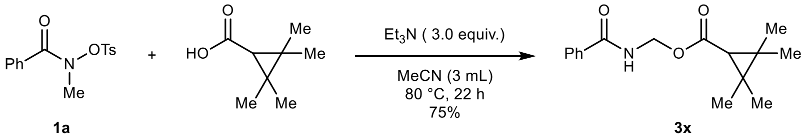
Benzamidomethyl cyclohexanecarboxylate (3w)



Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0

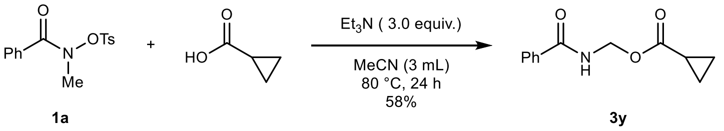
equiv.), cyclohexanecarboxylic acid (76.9 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3w** as a colorless oil (36.9 mg, 47%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.6 Hz, 2H), 7.51 (d, *J* = 7.4 Hz, 1H), 7.44 (q, *J* = 8.9, 7.7 Hz, 3H), 5.45 (d, *J* = 7.2 Hz, 2H), 2.34–2.28 (m, 1H), 1.88 (dd, *J* = 13.2, 3.8 Hz, 2H), 1.73–1.69 (m, 2H), 1.42–1.36 (m, 2H), 1.27–1.17 (m, 4H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 177.3, 167.6, 133.4, 132.3, 128.8, 127.4, 64.6, 43.0, 28.9, 25.7, 25.4; **IR** (neat) $\tilde{\nu}_{max}$ 1703, 1658, 1532, 1451, 1394, 1051, 738 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{15}H_{19}NO_3Na^+$: 284.1257, found: 284.1258.

Benzamidomethyl 2,2,3,3-tetramethylcyclopropane-1-carboxylate (3x)



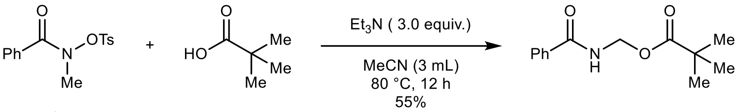
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 2,2,3,3-tetramethylcyclopropane-1-carboxylic acid (85.3 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 22 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3x** as a colorless oil (62.0 mg, 75%). Rotamers present at room temperature. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.56 (s, 1H), 7.49 (s, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 5.41 (d, *J* = 7.2 Hz, 2H), 1.24 (s, 1H), 1.20 (d, *J* = 2.3 Hz, 6H), 1.14 (s, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.2, 167.7, 133.4, 132.2, 128.6, 127.4, 64.1, 35.5, 31.1 (minor), 30.9 (major), 23.6 (minor), 23.5 (major), 16.6 (minor), 16.5 (major); **IR** (neat) $\tilde{\nu}_{max}$ 1659, 1532, 1489, 1307, 1187, 1136, 1112, 713 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{16}H_{21}NO_3Na^+$: 298.1414, found: 298.1421.

Benzamidomethyl cyclopropanecarboxylate (3y)



Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), cyclopropanecarboxylic acid (51.7 mg, 0.6 mmol, 2.0 equiv.), and Et_3N (125 µL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3y** as a colorless oil (38.2 mg, 58%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.55–7.50 (m, 1H), 7.49–7.40 (m, 3H), 5.45 (d, *J* = 7.2 Hz, 2H), 1.62 (dd, *J* = 8.6, 3.9 Hz, 1H), 1.02–0.98 (m, 2H), 0.90–0.86 (m, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 205.5, 176.1, 167.7, 133.3, 132.3, 128.8, 127.4, 64.8, 13.0, 9.1; **IR** (neat) $\tilde{\nu}_{max}$ 1724, 1656, 1532, 1490, 1295, 1145, 1030, 693 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{12}H_{13}NO_3Na^+$: 242.0788, found: 242.0788.

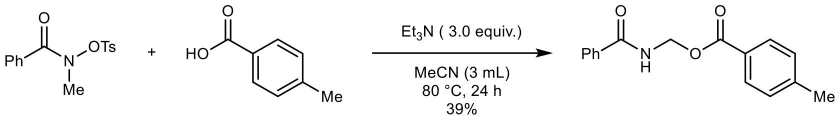
Benzamidomethyl pivalate (3z)



1a **3z**

Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (61.3 mg, 0.6 mmol, 2.0 equiv.), and Et$_3$N (125 μL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 12 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3z** as a colorless oil (39.0 mg, 55%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.81–7.77 (m, 2H), 7.54–7.50 (m, 1H), 7.43 (t, *J* = 7.6 Hz, 3H), 5.45 (d, *J* = 7.2 Hz, 2H), 1.18 (s, 9H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 179.9, 167.5, 133.4, 132.3, 128.8, 127.4, 64.8, 38.9, 27.1; **IR** (neat) $\tilde{\nu}_{\max}$ 1700, 1659, 1483, 1180, 1031, 739, 693 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{13}H_{17}NO_3Na^+$: 258.1101 found: 258.1103.

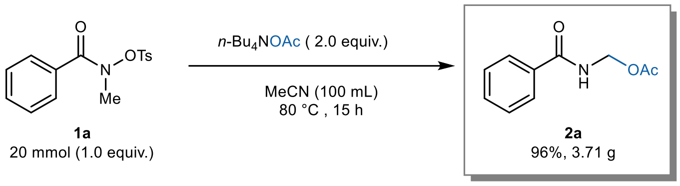
Benzamidomethyl 4-methylbenzoate (3aa)



1a **3aa**

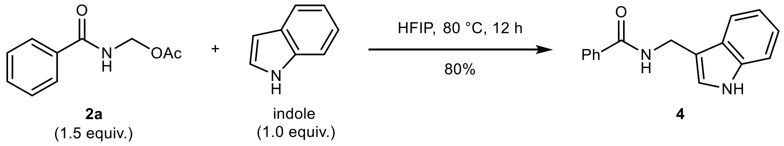
Prepared following the **GP2B** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (91.6 mg, 0.3 mmol, 1.0 equiv.), 4-methylbenzoic acid (81.7 mg, 0.6 mmol, 2.0 equiv.), and Et$_3$N (125 μL, 0.9 mmol, 3.0 equiv.) in MeCN (3 mL) at 80 °C for 24 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound **3aa** as a colorless oil (31.3 mg, 39%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.94 (d, *J* = 8.3 Hz, 2H), 7.84–7.81 (m, 2H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.53–7.50 (m, 1H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.22 (d, *J* = 7.9 Hz, 2H), 5.70 (d, *J* = 7.2 Hz, 2H), 2.39 (s, 3H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 167.7 (167.74), 167.7 (167.68), 144.4, 133.4, 132.3, 130.0, 129.3, 128.8, 127.4, 126.7, 65.2, 21.8; **IR** (neat) $\tilde{\nu}_{\max}$ 1659, 1530, 1416, 1286, 1029, 735, 691 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{16}H_{15}NO_3Na^+$: 320.1251 found: 320.1264.

4. Gram-scale Synthesis of Product 2a and Its Derivatizations



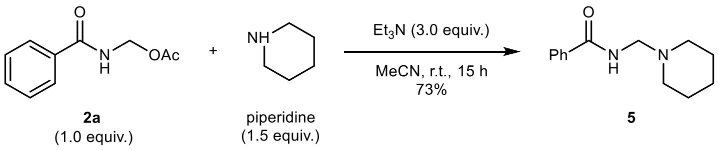
Prepared following the **GP2A** using *N*-methyl-*N*-(tosyloxy)benzamide **1a** (6.1 g, 20 mmol, 1.0 equiv.), *n*-Bu_4NOAc (12.1 g, 40 mmol, 2.0 equiv.) in MeCN (100 mL) at 80 °C for 15 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 3:1) to afford the title compound as a colorless oil (3.71 g, 96%).

N-((1*H*-indol-3-yl)methyl)benzamide (4)[2]



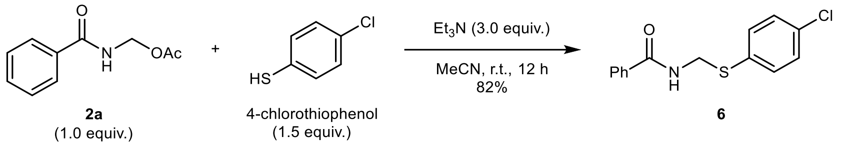
To a 15 mL oven-dried vial equipped with a magnetic stir bar was added benzamidomethyl acetate **2a** (86.9 mg, 0.45 mmol, 1.5 equiv.), indole (35.1 mg, 0.3 mmol, 1.0 equiv.) in HFIP (2 mL) at 80 °C for 12 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 2:1) to afford the title compound **4** as a colorless oil (60 mg, 80%). **^{1}H NMR** (600 MHz, DMSO-d_6) δ 10.96 (s, 1H), 8.86 (t, J = 5.7 Hz, 1H), 7.91–7.87 (m, 2H), 7.67 (d, J = 7.9 Hz, 1H), 7.52–7.48 (m, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.37 (d, J = 8.1 Hz, 1H), 7.31 (d, J = 2.4 Hz, 1H), 7.11–7.06 (m, 1H), 6.99 (t, J = 7.4 Hz, 1H), 4.66 (d, J = 5.7 Hz, 2H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 166.0, 136.4, 134.7, 131.1, 128.3, 127.3, 126.6, 124.0, 121.1, 118.9, 118.6, 112.6, 111.5, 34.7; **IR** (neat) $\tilde{\nu}_{max}$ 1643, 1536, 1457, 1290, 1066, 745, 698 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{16}H_{14}N_2ONa^+$: 273.0998, found: 273.0998.

N-(piperidin-1-ylmethyl)benzamide (5)[3]



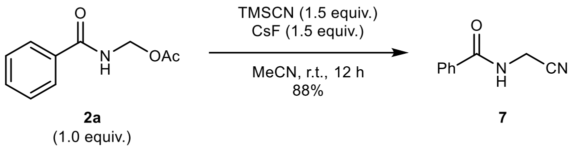
To a 15 mL oven-dried vial equipped with a magnetic stir bar was added benzamidomethyl acetate **2a** (116.0 mg, 0.6 mmol, 1.0 equiv.), piperidine (88 µL, 0.9 mmol, 1.5 equiv.), Et_3N (250 µL, 1.8 mmol, 3.0 equiv.) in MeCN (6 mL) at room temperature for 15 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with EA) to afford the title compound **5** as a white solid (96.1 mg, 73%). **M.P.** 125.3–126.1 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.80–7.76 (m, 2H), 7.52–7.45 (m, 1H), 7.40 (dd, J = 8.4, 7.0 Hz, 2H), 6.66 (d, J = 6.5 Hz, 1H), 4.25 (d, J = 6.3 Hz, 2H), 2.55 (t, J = 5.3 Hz, 4H), 1.56 (q, J = 5.6 Hz, 4H), 1.41 (t, J = 6.1 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 168.0, 134.4, 131.8, 128.7, 127.1, 62.6, 51.6, 25.8, 24.1; **IR** (neat) $\tilde{\nu}_{max}$ 1642, 1533, 1307, 1289, 1111, 1029, 693 cm^{-1}; **HRMS** (ESI/[M + Na]$^+$) *m/z* calcd. for $C_{13}H_{18}N_2NaO^+$: 241.1311, found: 241.1305.

N-(((4-chlorophenyl)thio)methyl)benzamide (6)[4]



To a 15 mL oven-dried vial equipped with a magnetic stir bar was added benzamidomethyl acetate **2a** (116.0 mg, 0.6 mmol, 1.0 equiv.), 4-chlorothiophenol (130.1 mg, 0.9 mmol, 1.5 equiv.), Et$_3$N (250 µL, 1.8 mmol, 3.0 equiv.) in MeCN (6 mL) at room temperature for 12 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 5:1) to afford the title compound **6** as a white solid (136.3 mg, 82%). **M.P.** 143.5–147.1 °C; **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.70–7.66 (m, 2H), 7.49 (td, *J* = 7.3, 6.8, 1.3 Hz, 1H), 7.41–7.37 (m, 4H), 7.26–7.23 (m, 2H), 6.70 (d, *J* = 6.5 Hz, 1H), 4.85 (d, *J* = 6.1 Hz, 2H); **^{13}C NMR** (151 MHz, CDCl$_3$) δ 167.2, 133.8, 133.8, 132.8, 132.3, 132.1, 129.5, 128.8, 127.1, 44.6; **IR** (neat) $\tilde{\nu}_{max}$ 1645, 1540, 1474, 1270, 1087, 1012, 823, 691 cm^{-1}; **HRMS** (ESI/[M + H]$^+$) *m/z* calcd. for $C_{14}H_{13}ClNOS^+$: 278.0401, found: 278.0402.

N-(cyanomethyl)benzamide (7)[5]

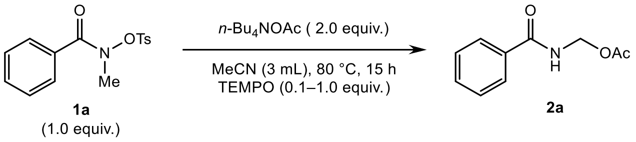


To a 15 mL oven-dried vial with a stir bar was added benzamidomethyl acetate **2a** (116.0 mg, 0.6 mmol, 1.0 equiv.), CsF (136.7 mg, 0.9 mmol, 1.5 equiv.), TMSCN (113 µL, 0.9 mmol, 1.5 equiv.) in MeCN (6 mL) at room temperature for 12 h. The crude reaction mixture was purified by flash column chromatography on silica gel (eluted with PE/EA = 2:1) to afford the title compound **7** as a white solid (84.5 mg, 88%). **M.P.** 113.2–115.4 °C; **^{1}H NMR** (600 MHz, DMSO-*d*$_6$) δ 9.21 (t, *J* = 5.5 Hz, 1H), 7.90–7.87 (m, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 4.33 (d, *J* = 5.5 Hz, 2H); **^{13}C NMR** (151 MHz, DMSO-*d*$_6$) δ 166.7, 132.9, 132.0, 128.6, 127.4, 117.7, 27.8; **IR** (neat) $\tilde{\nu}_{max}$ 1695, 1644, 1535, 1301, 1230, 1028, 696 cm^{-1}; **HRMS** (ESI/[M + H]$^+$) *m/z* calcd. for $C_9H_9N_2O^+$: 161.0709, found: 161.0705.

5. Mechanistic Experiments

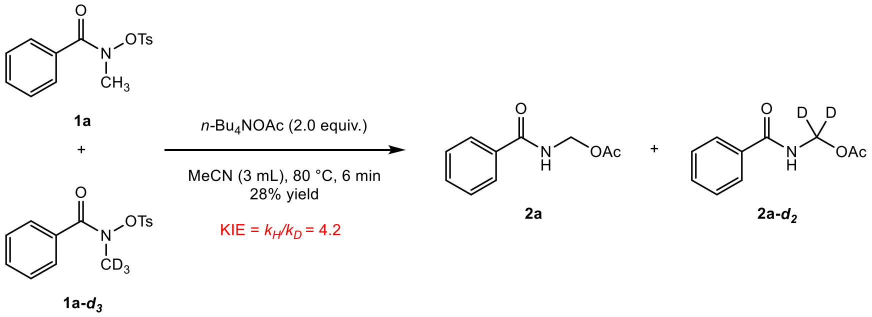
Radical Trapping Experiments

To a 15 mL oven-dried vial equipped with a magnetic stir bar was added *O*-tosyl hydroxamate **1a** (91.5 mg, 0.3 mmol, 1.0 equiv.), *n*-Bu4NOAc (180.9 mg, 0.6 mmol, 2 equiv.), TEMPO in varying amounts (1.6 mg, 0.1 equiv., 7.8 mg, 0.5 equiv., and 15.6 mg 1.0 equiv.), and MeCN (3.0 mL) under air atmosphere. The vial was then tightly capped and placed in an oil bath (80 °C) with vigorous stirring for 15 h. The yields of product **2a** (90% yield, 0.1 equiv. TEMPO; 92% yield, 0.5 equiv. TEMPO; and 89% yield, 1.0 equiv. TEMPO) were determined by flash column chromatography.

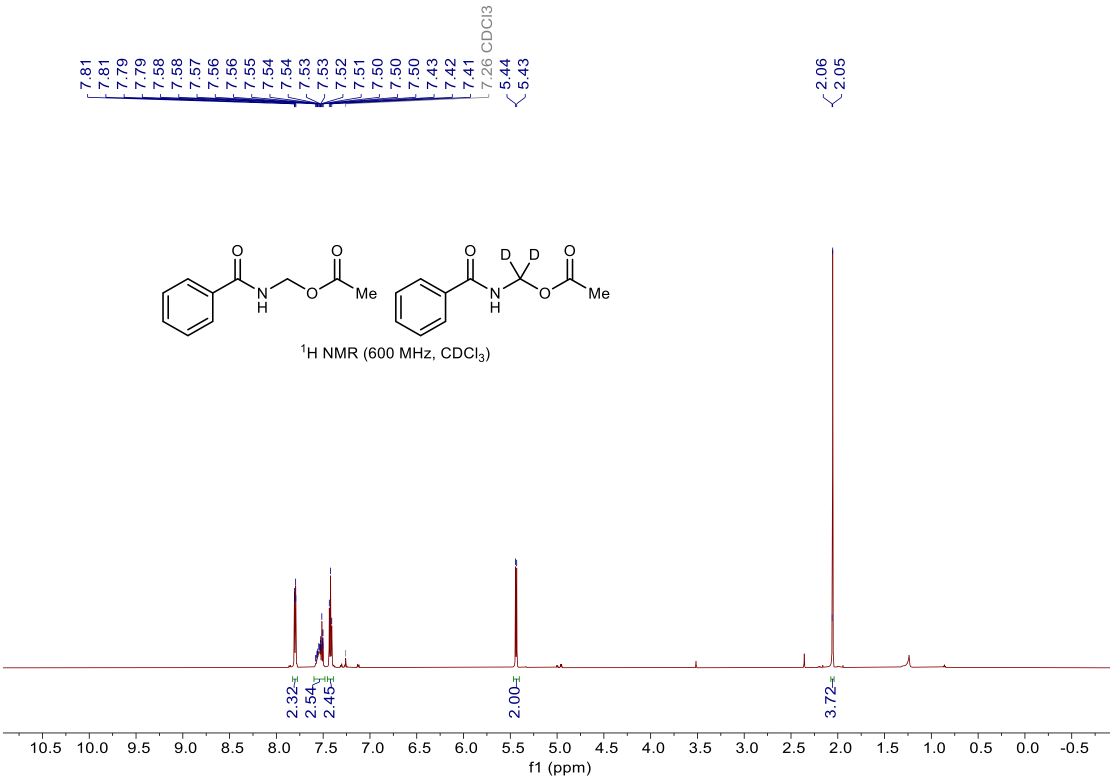


Entry	TEMPO (equiv.)	Yield of **2a** (%)
1	0.1 equiv.	90
2	0.5 equiv.	92
3	1.0 equiv.	89

Intermolecular Kinetic Isotope Effect



To a 15 mL oven-dried vial equipped with a magnetic stir bar was added **1a** (45.6 mg, 0.15 mmol, 1.0 equiv), **1a-*d*3** (46.2 mg, 0.15 mmol, 1.0 equiv.), **2** (180.9 mg, 0.6 mmol, 4.0 equiv.) in MeCN (3 mL) at 80 °C for 6 min. Then, the reaction mixture was purified by column chromatography to obtain **2a** and **2a-*d*2** (16.3 mg, 28%). The ratio of **2a** to **2a-*d*2** was measured as k_H/k_D = 4.2 (through the integration of the ^{1}H NMR spectrum).


7.81
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7.41
7.26 CDCl3
5.44
5.43
2.06
2.05
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N
H
O
O
Me
O
D
D
N
H
O
O
Me
1H NMR (600 MHz, CDCl3)
2.32
2.54
2.45
2.00
3.72
10.5
10.0
9.5
9.0
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2.5
2.0
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1.0
0.5
0.0
-0.5
f1 (ppm)

6. References

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(2) K. Nakamura and H. Togo, *Eur. J. Org. Chem.*, 2020, **2020**, 4713−4722.

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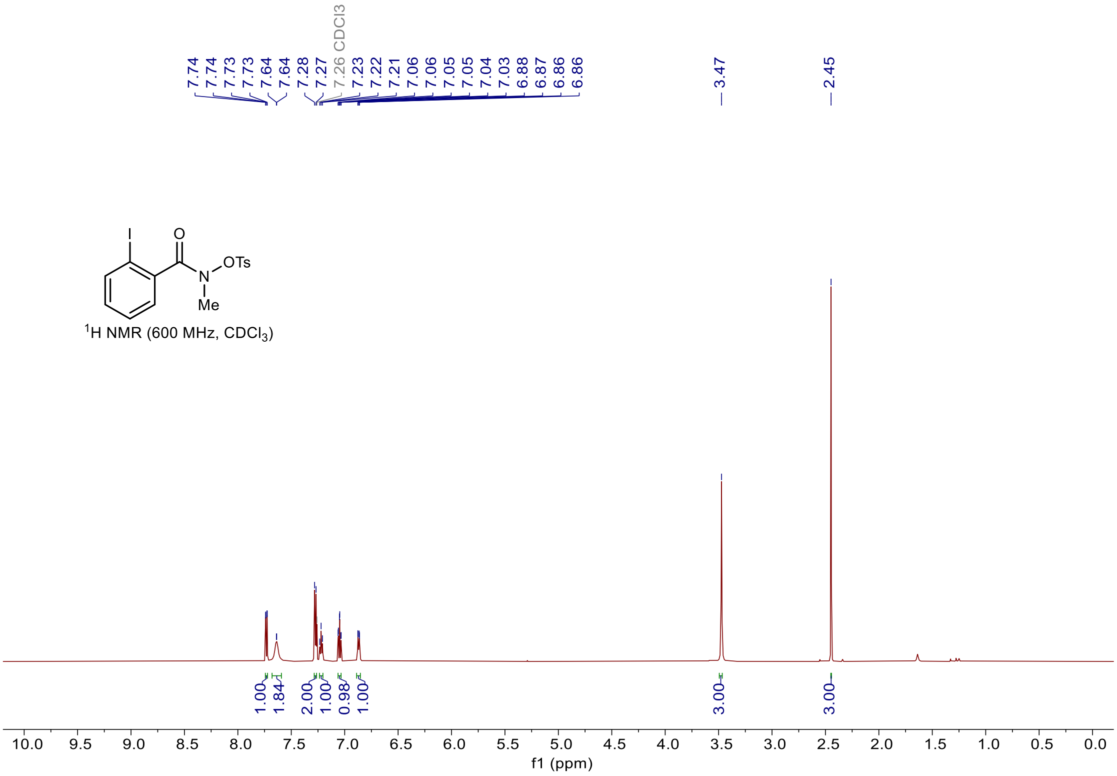
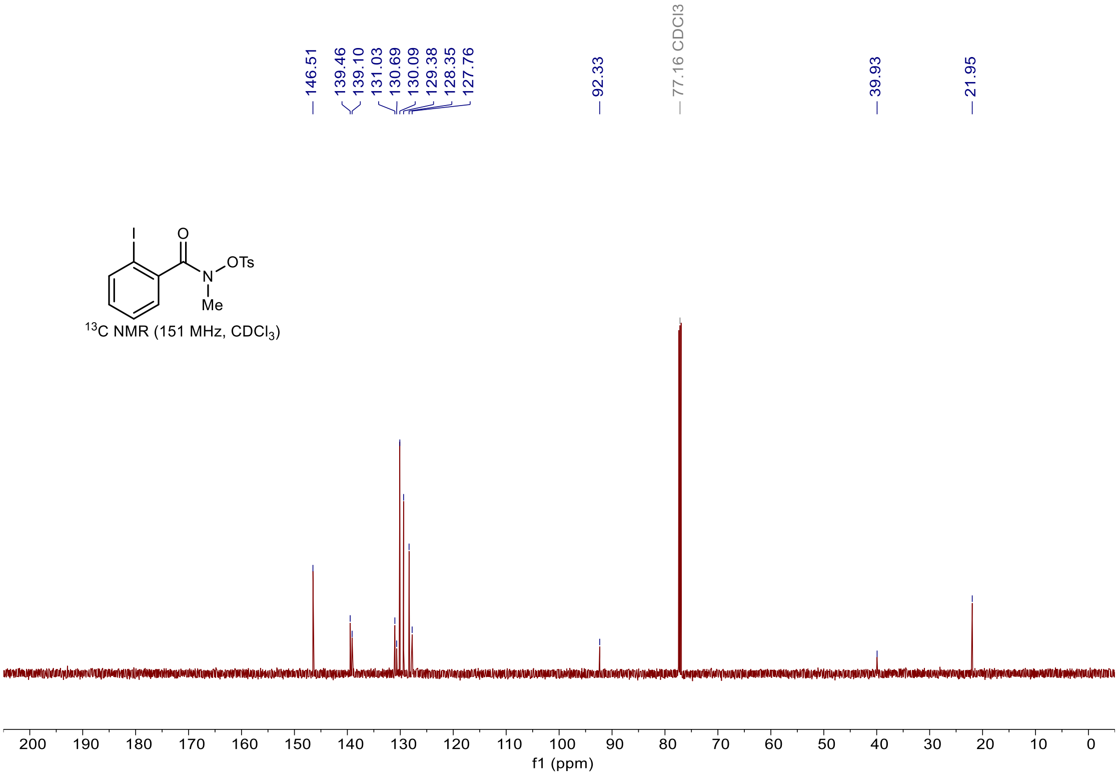
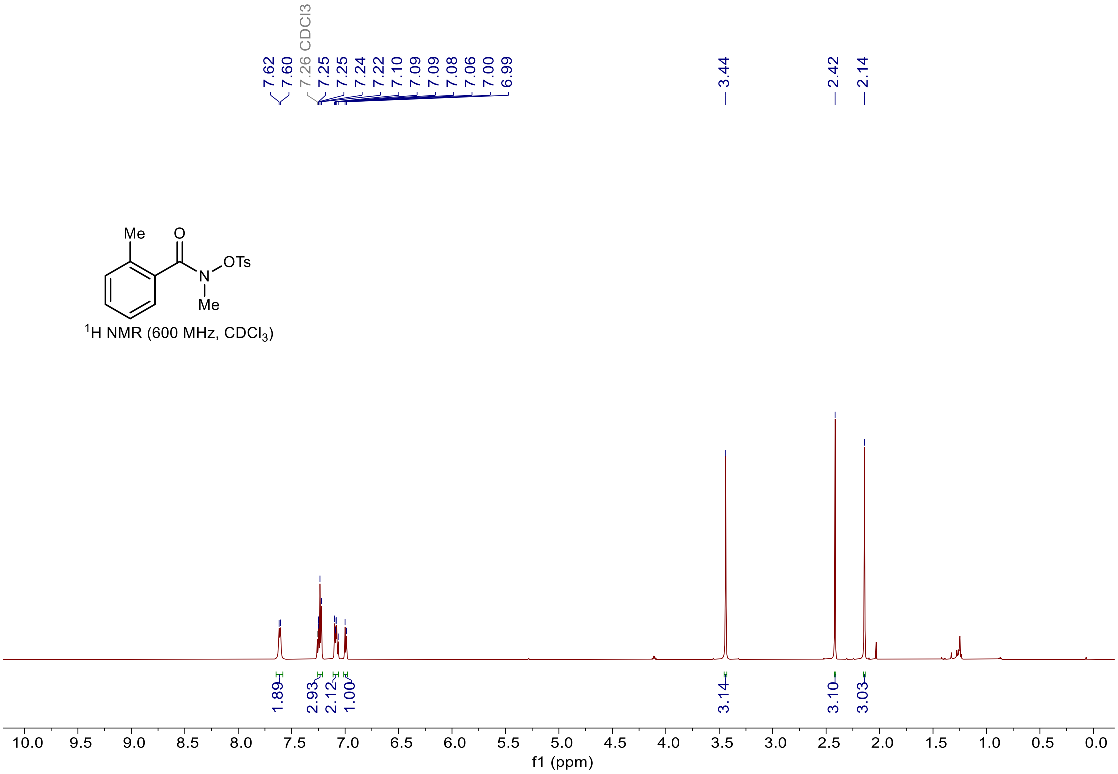
7. Copies of NMR Spectra

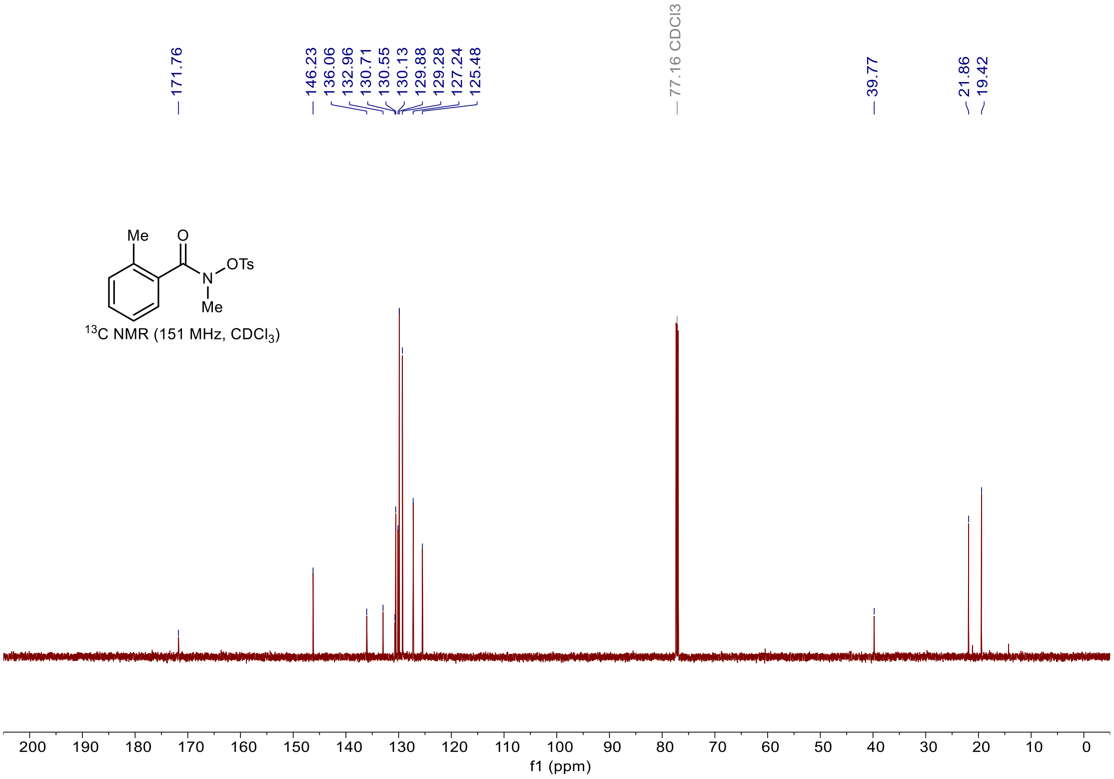
^{1}H and ^{13}C NMR spectra of compound 1h



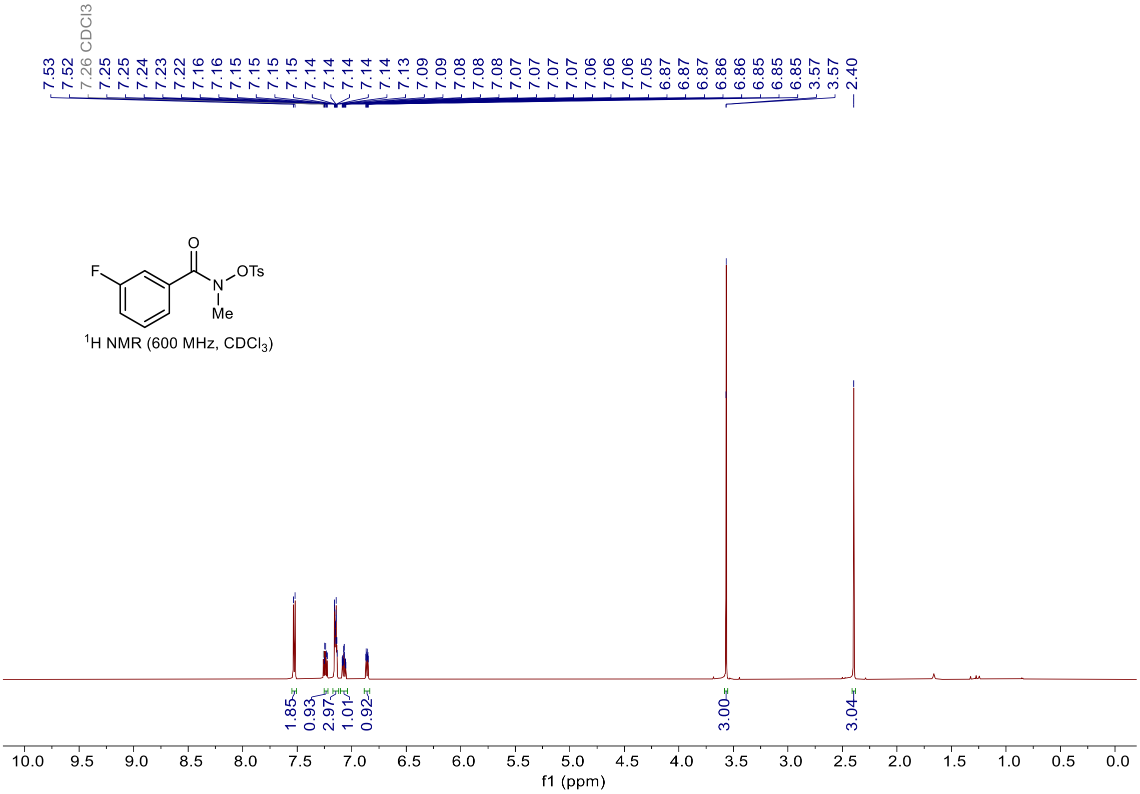


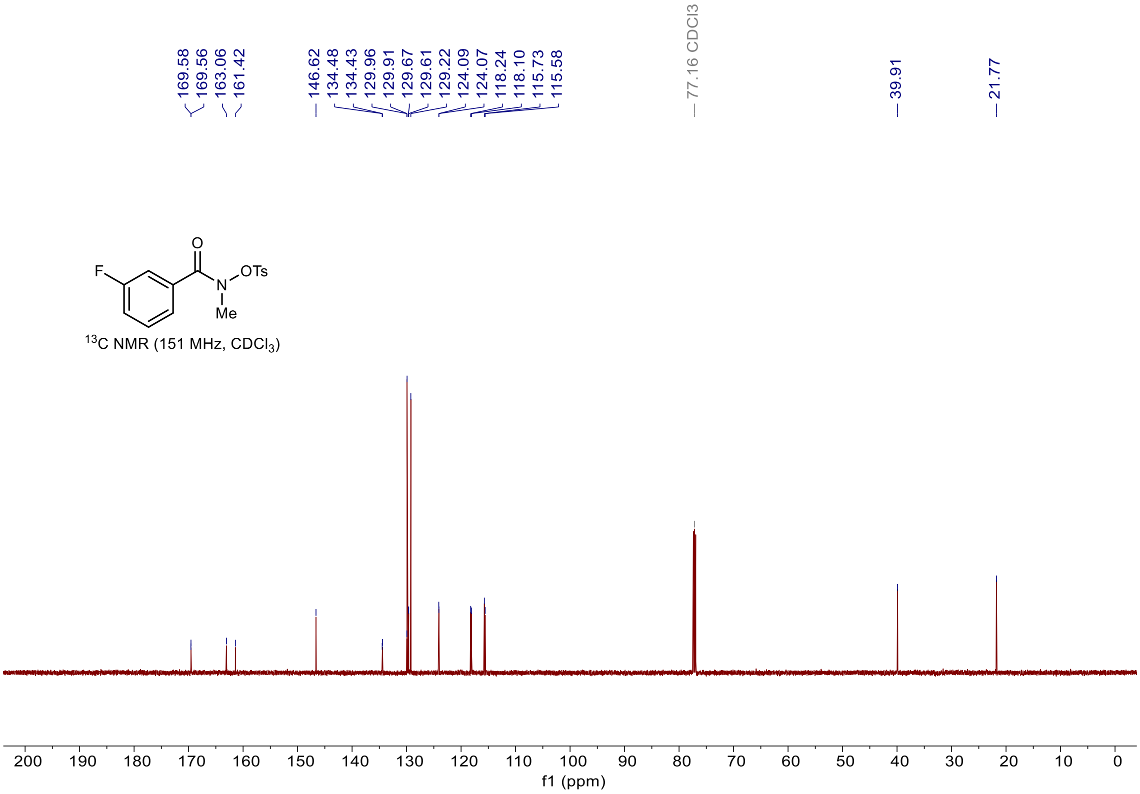
^{1}H and ^{13}C NMR spectra of compound 1i

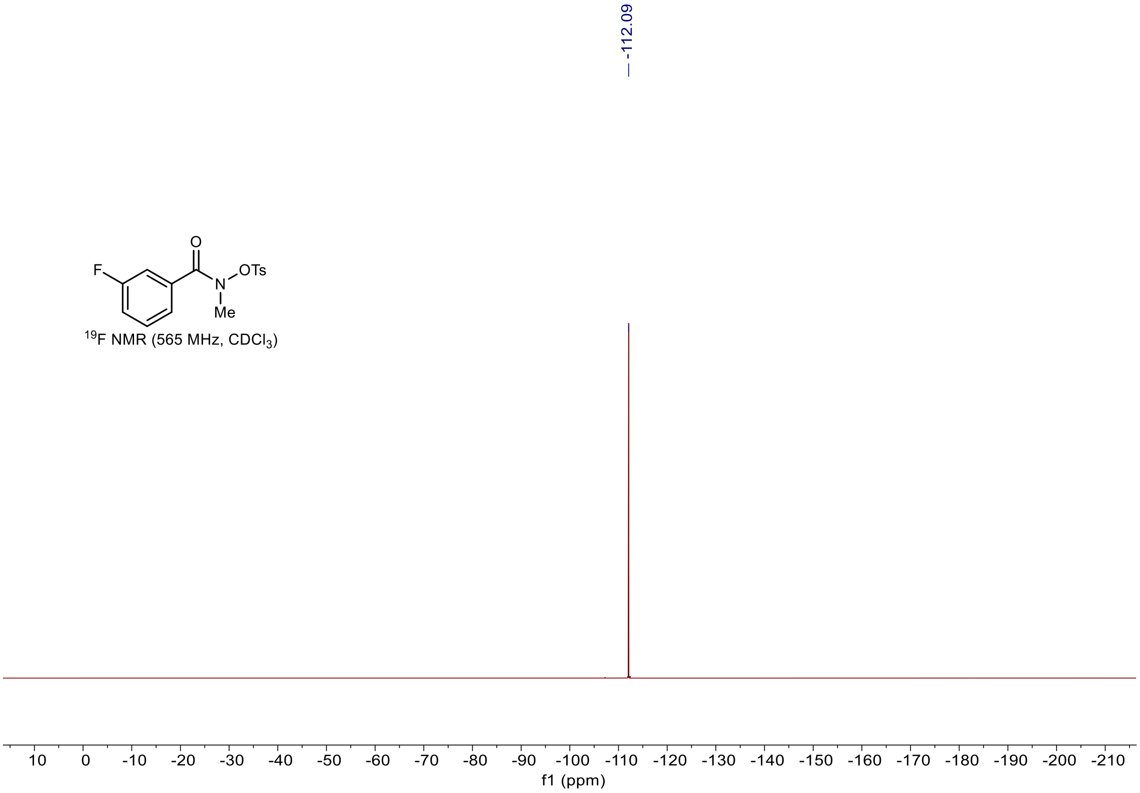




^{1}H, ^{13}C and ^{19}F NMR spectra of compound 1k

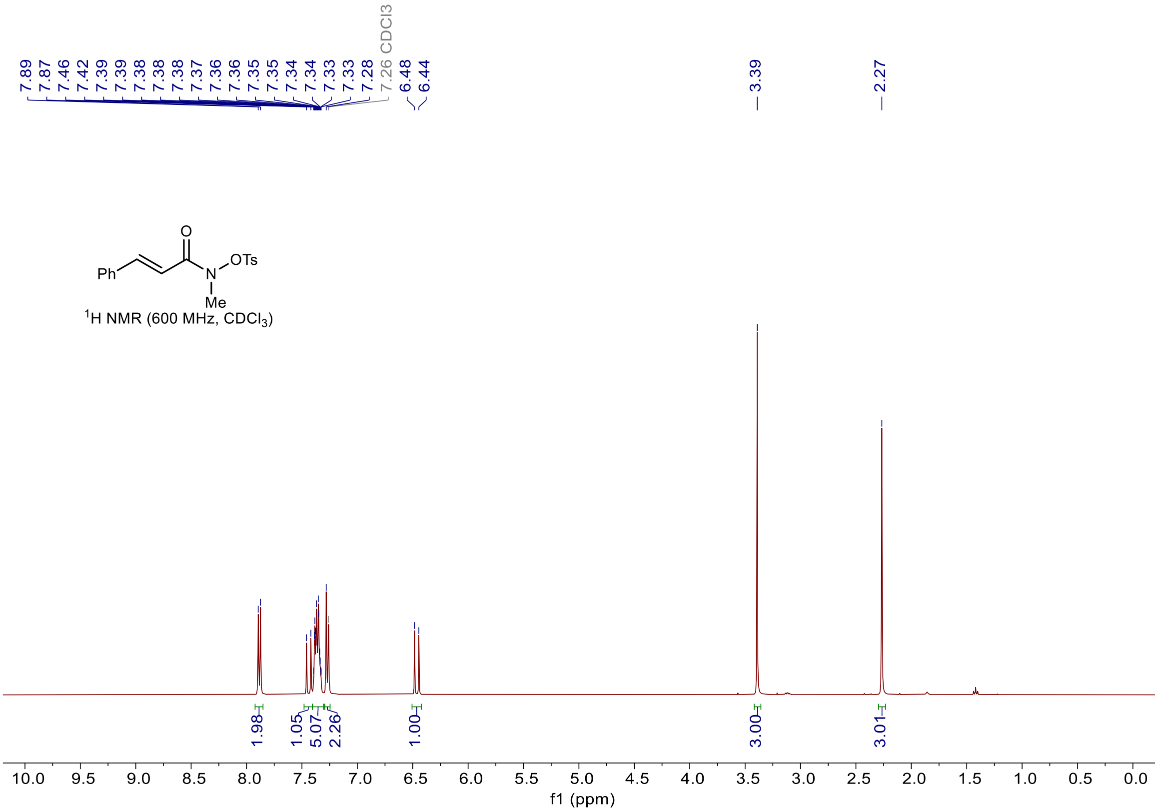


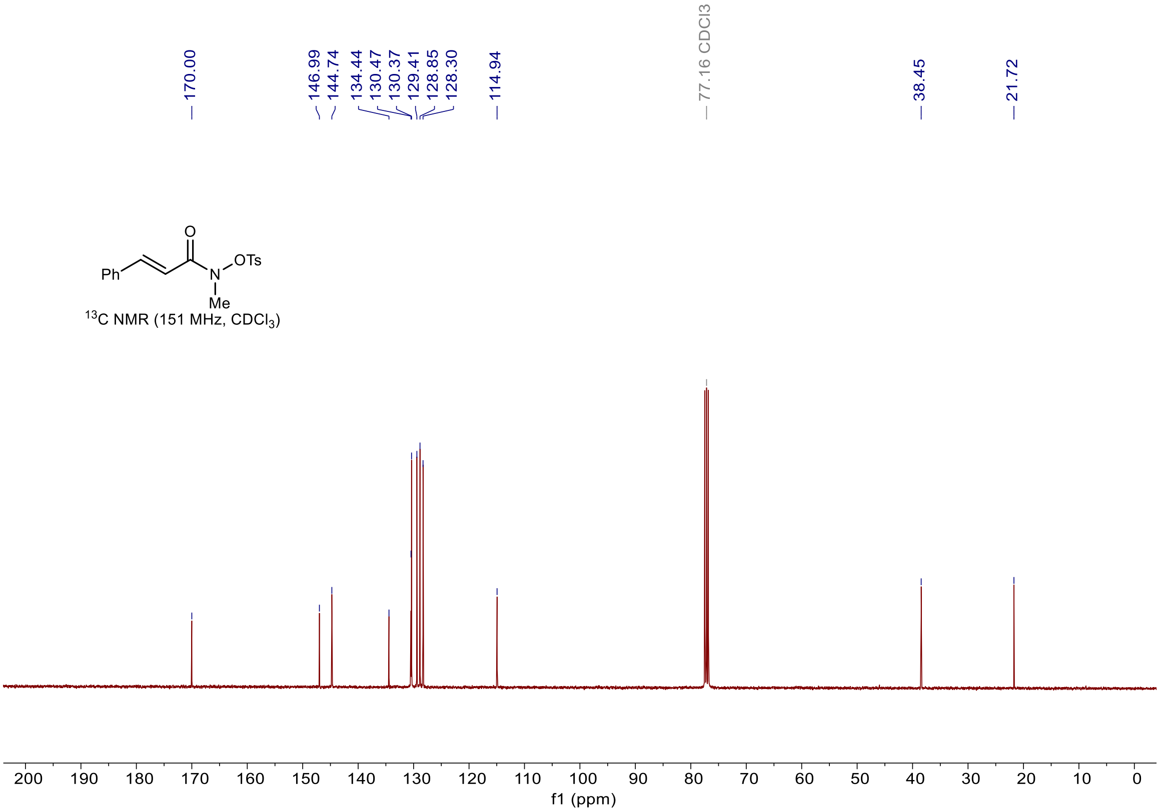




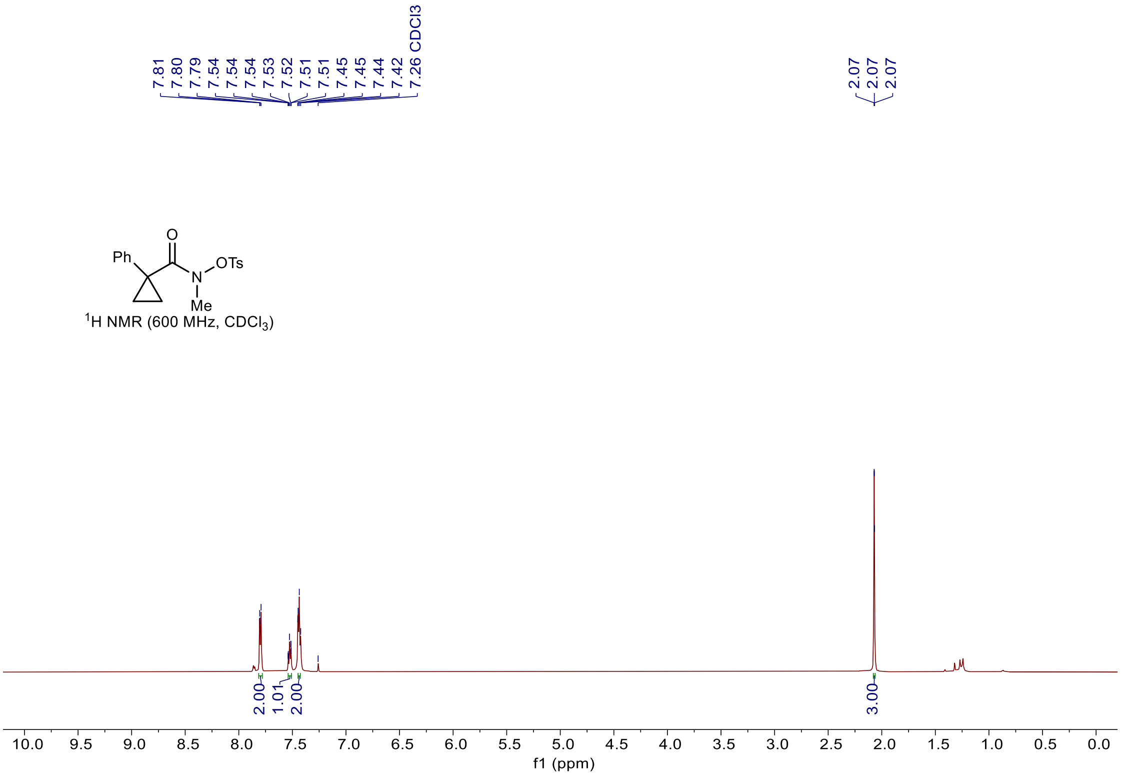
^{19}F NMR (565 MHz, $CDCl_3$)

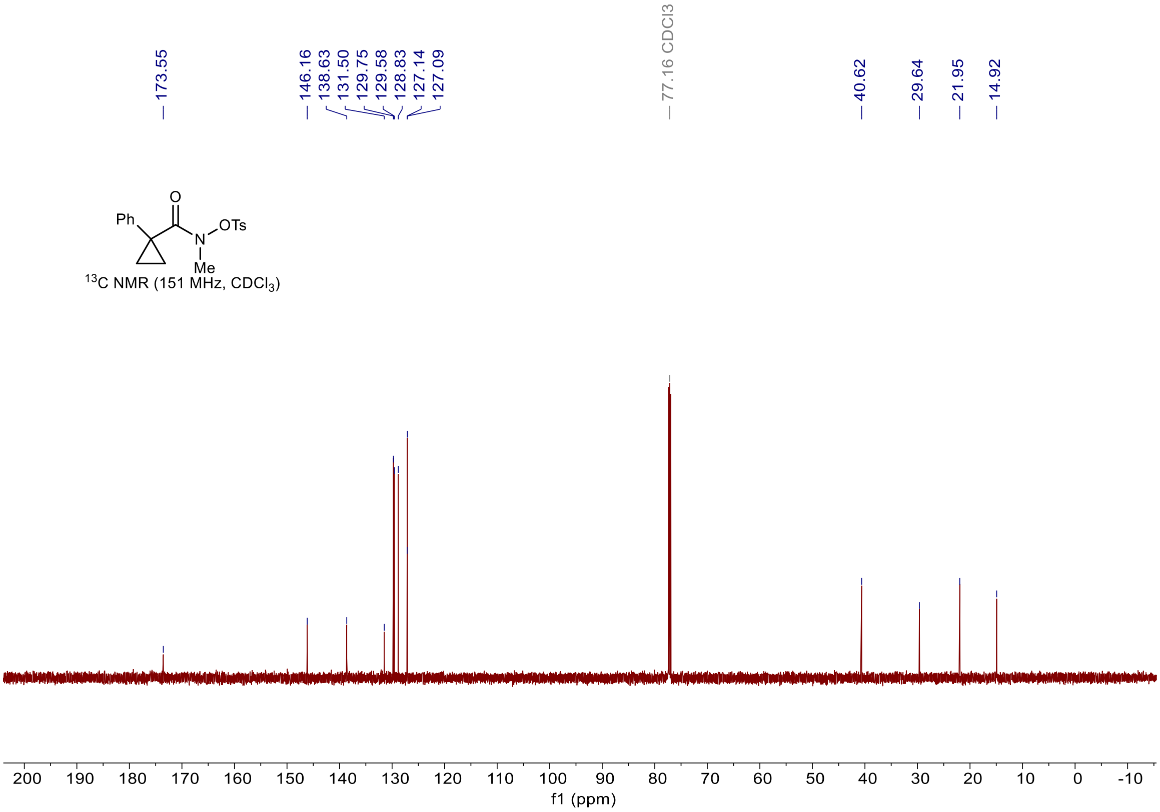
^{1}H and ^{13}C NMR spectra of compound 1n



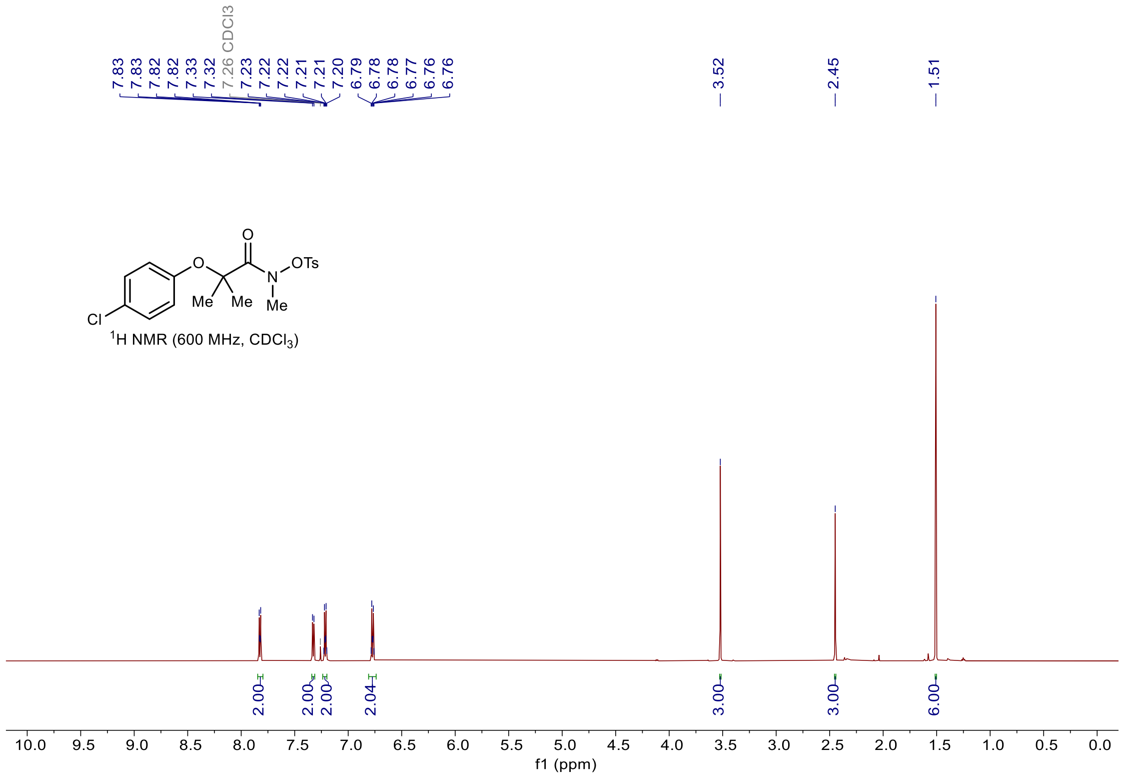


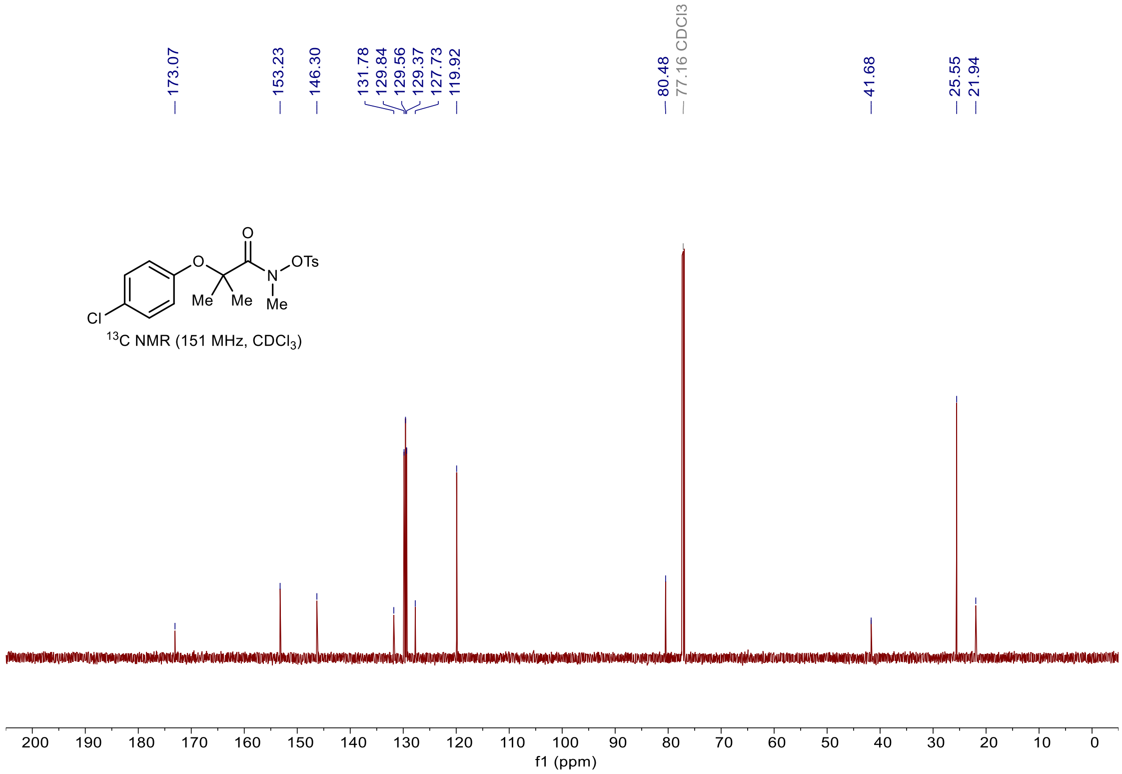
^{1}H and ^{13}C NMR spectra of compound 1p



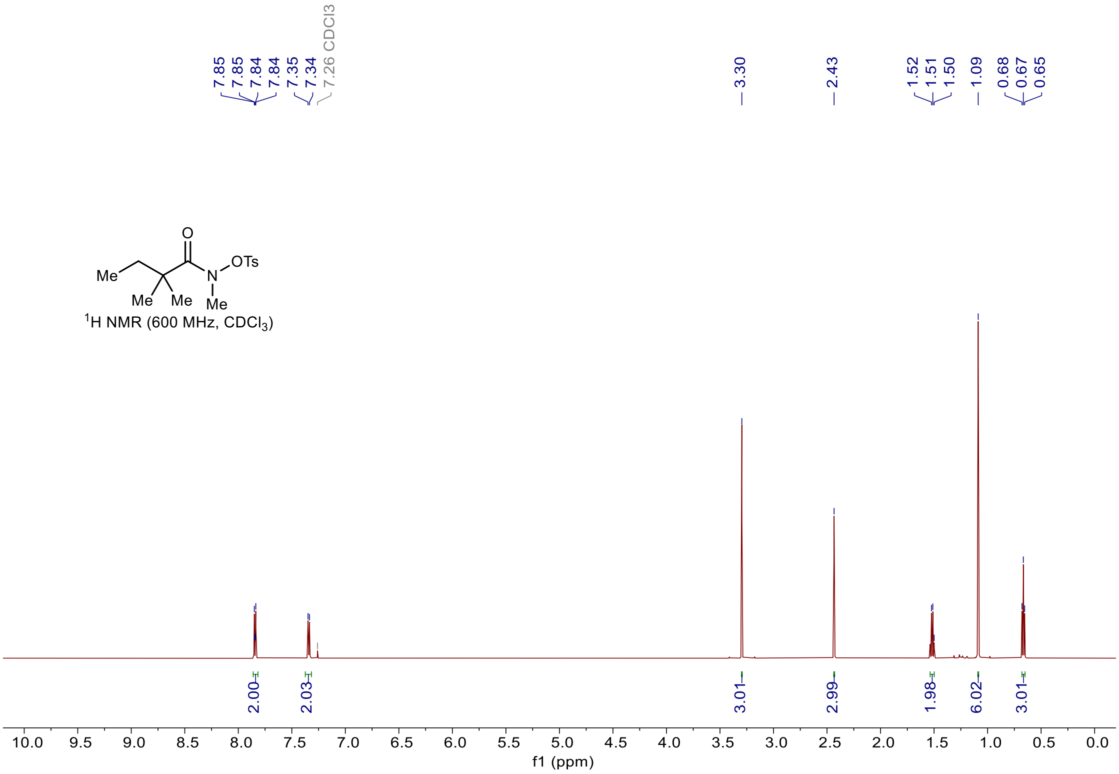


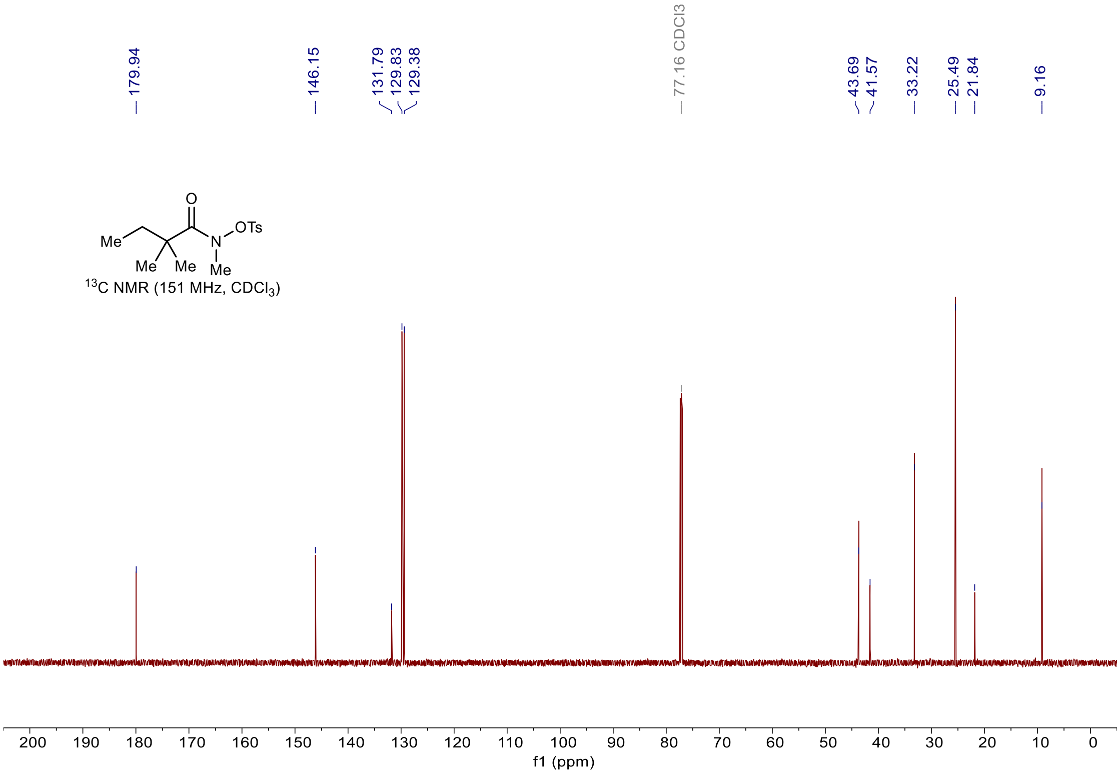
^{1}H and ^{13}C NMR spectra of compound 1q



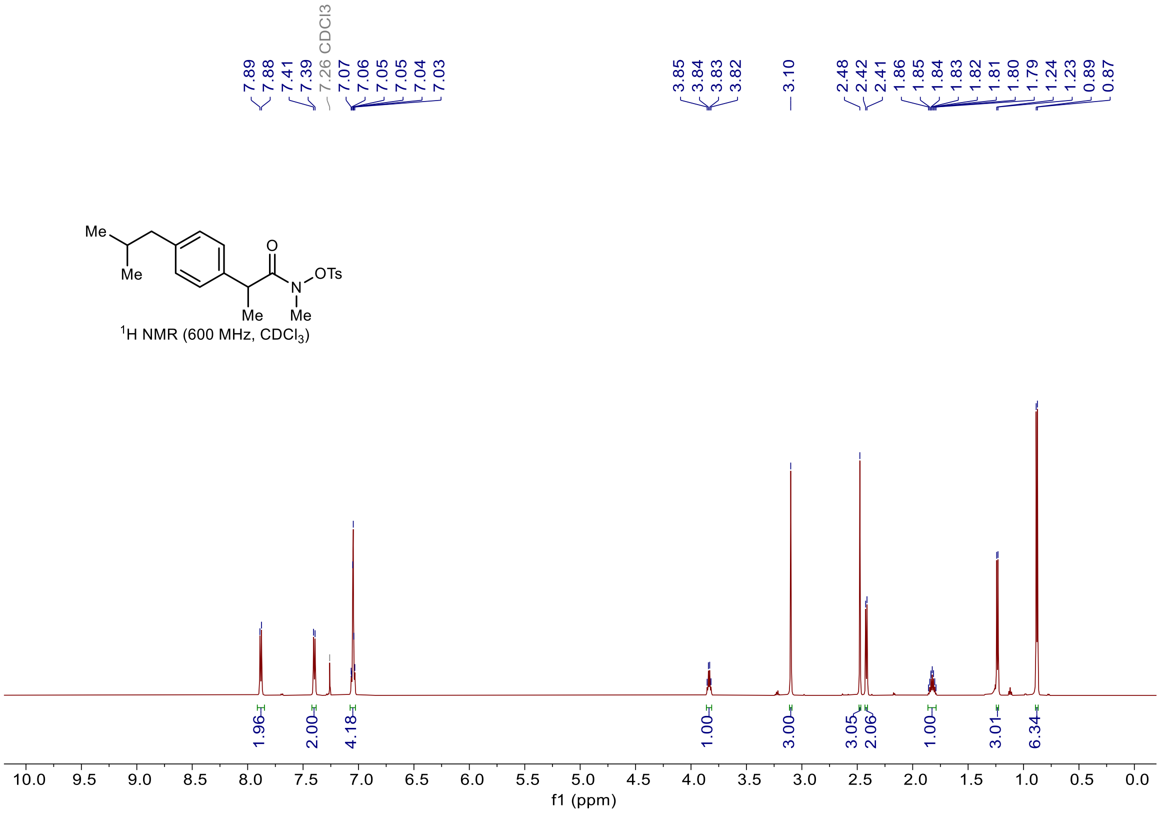


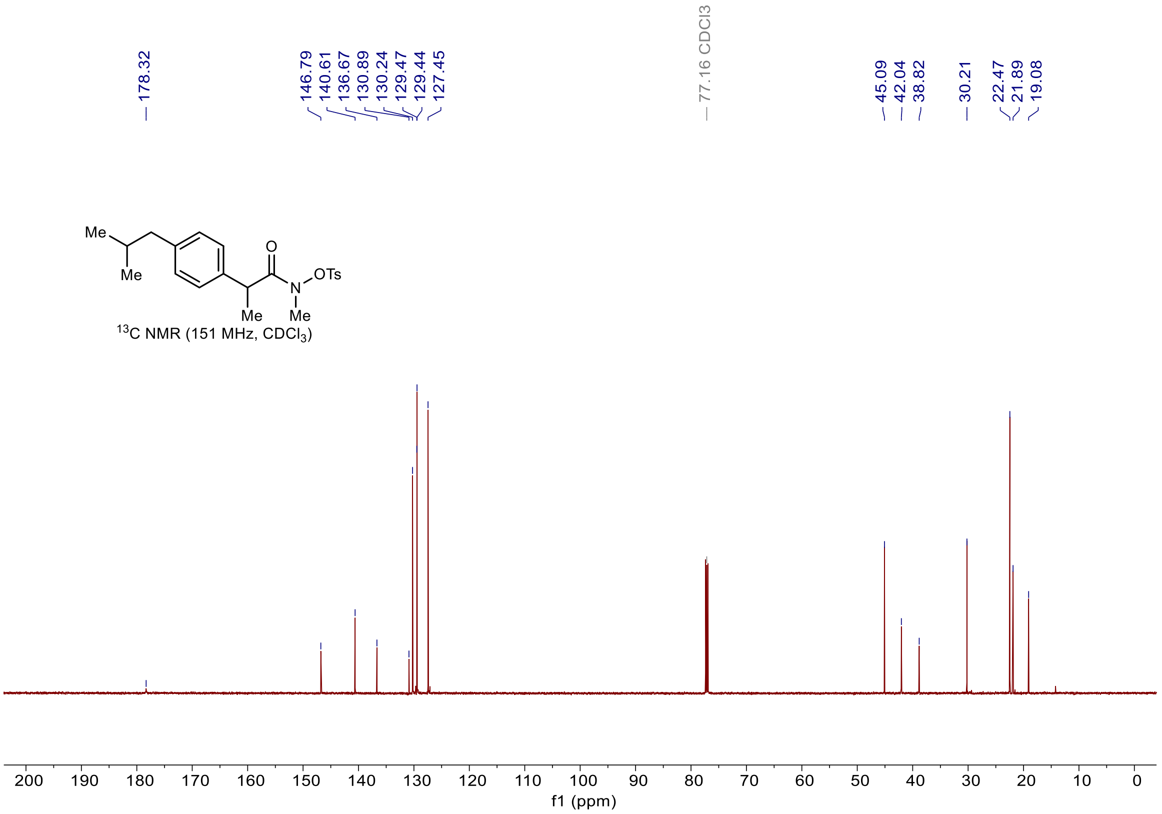
^{1}H and ^{13}C NMR spectra of compound 1r



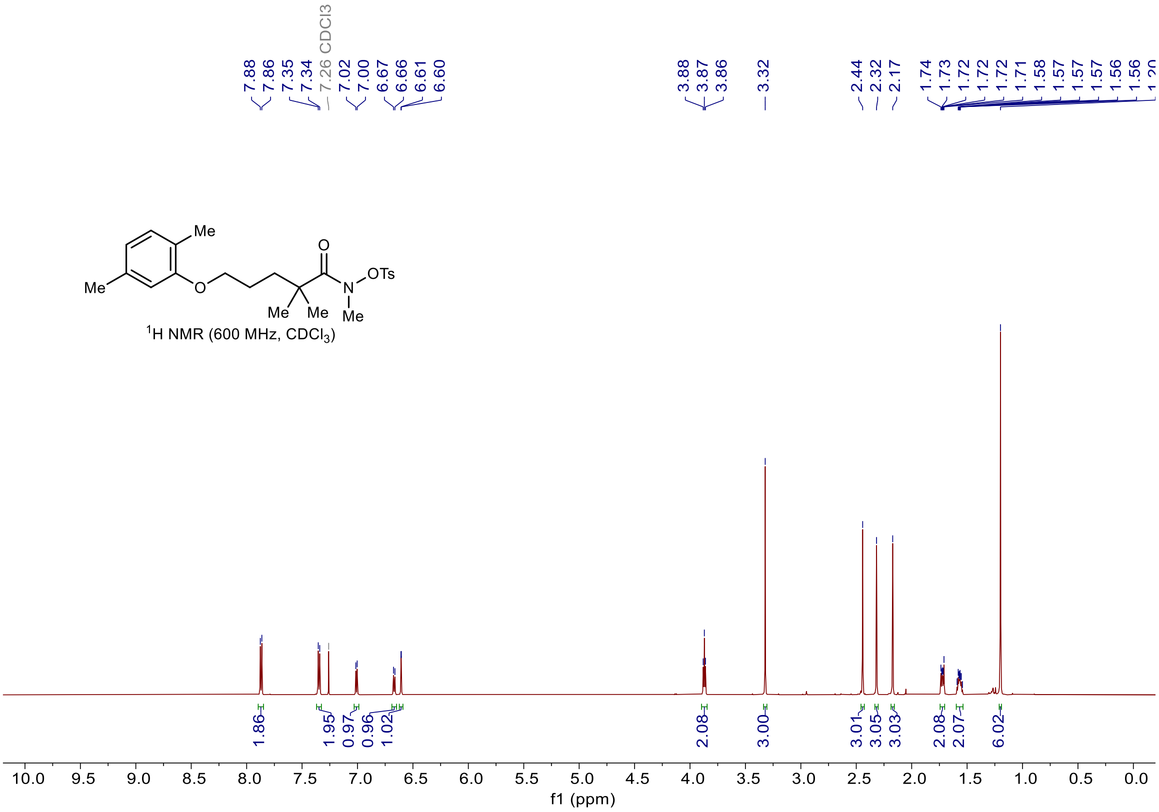


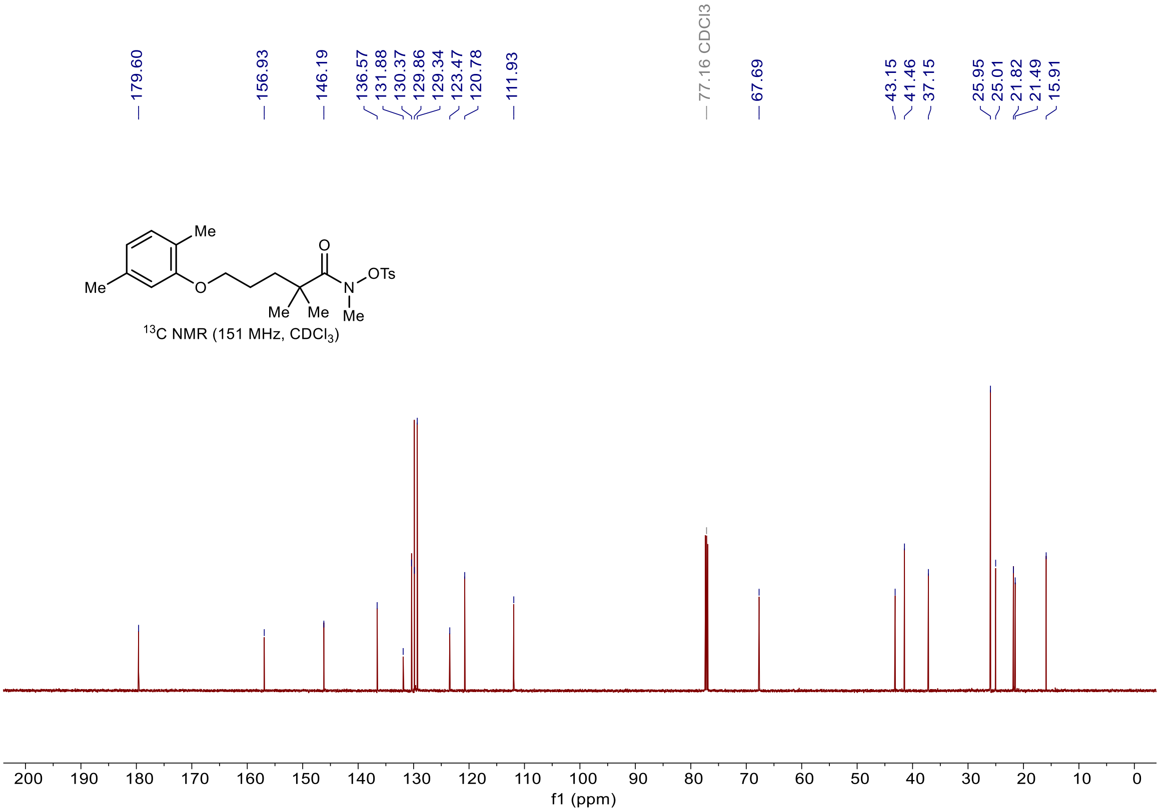
^{1}H and ^{13}C NMR spectra of compound 1s



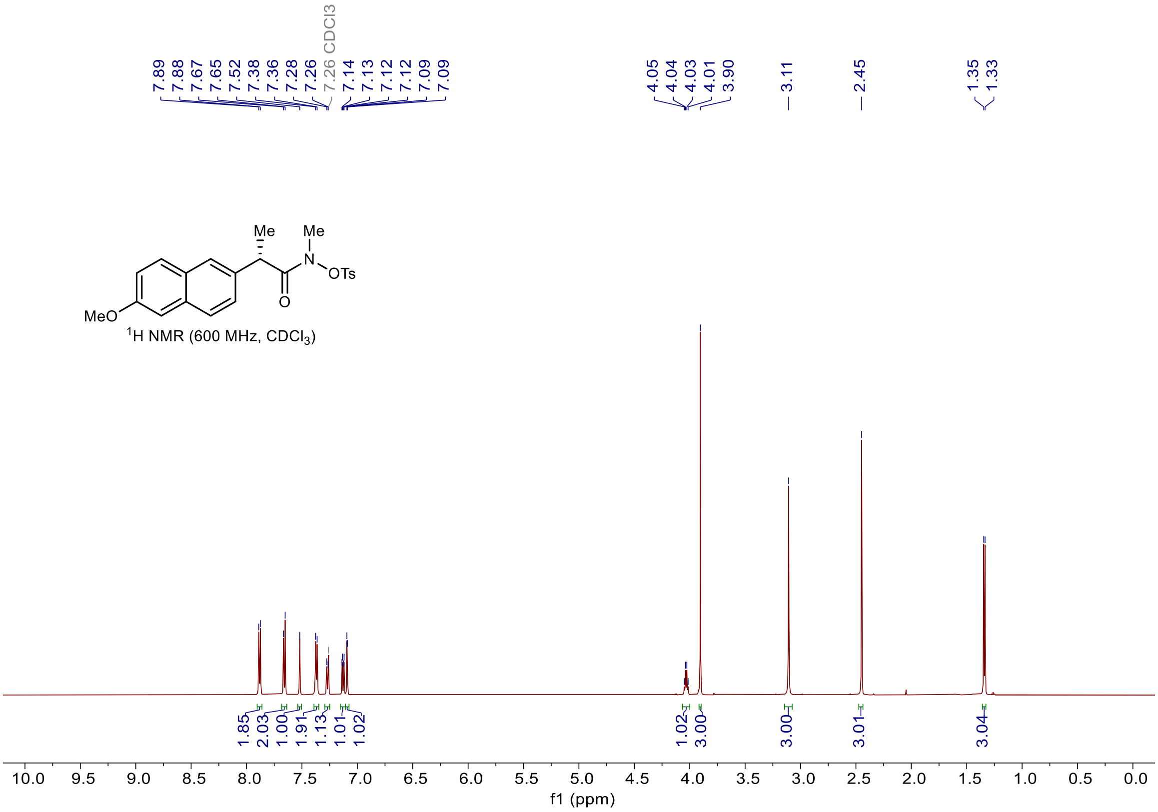


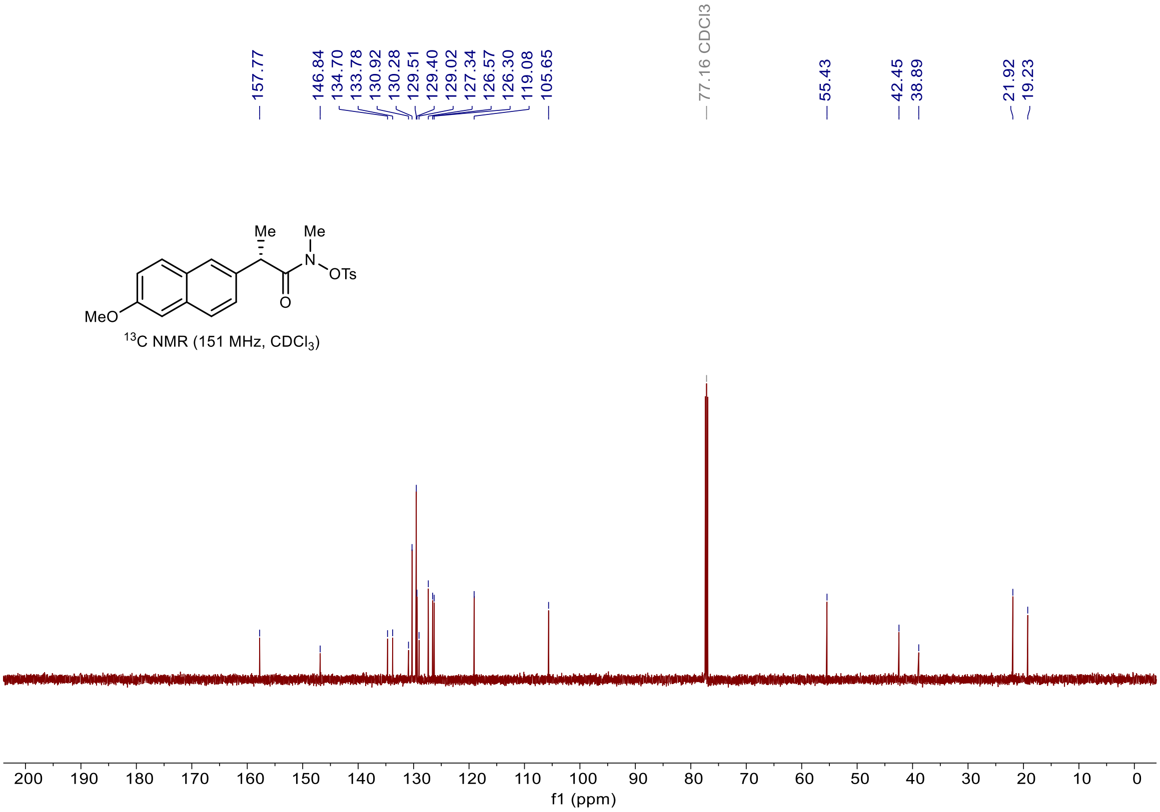
^{1}H and ^{13}C NMR spectra of compound 1t



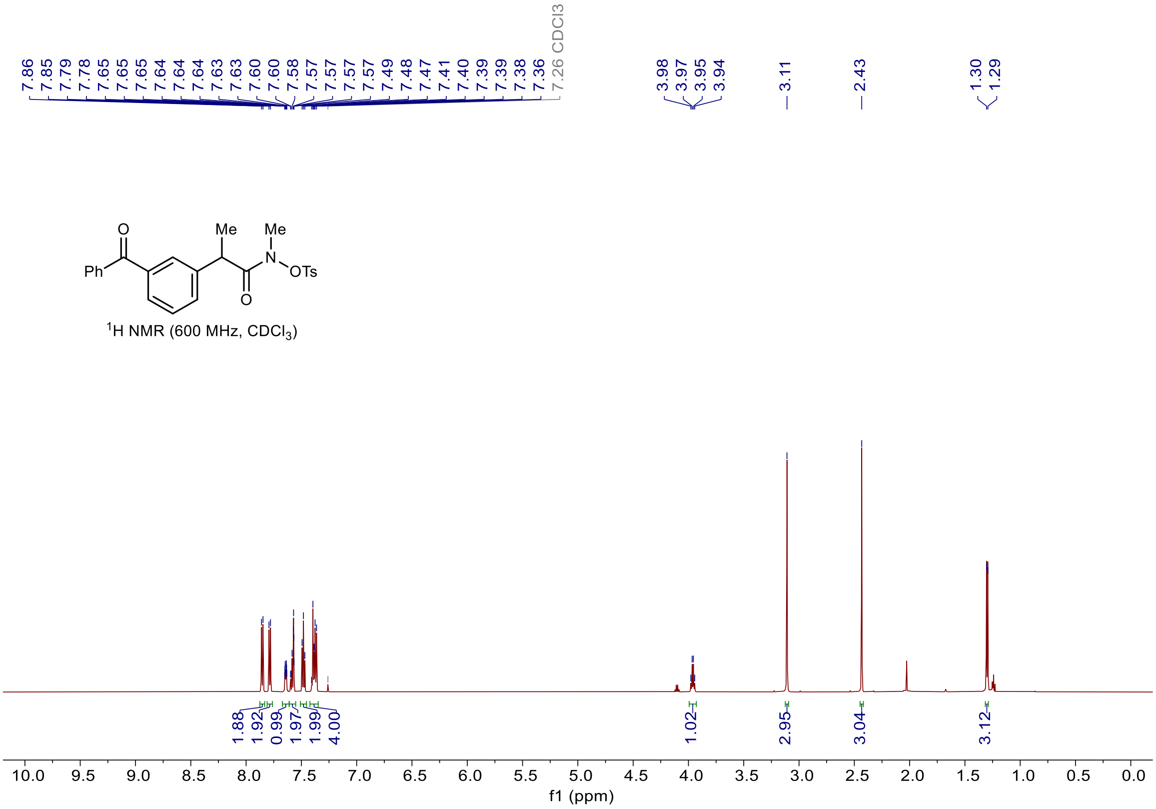


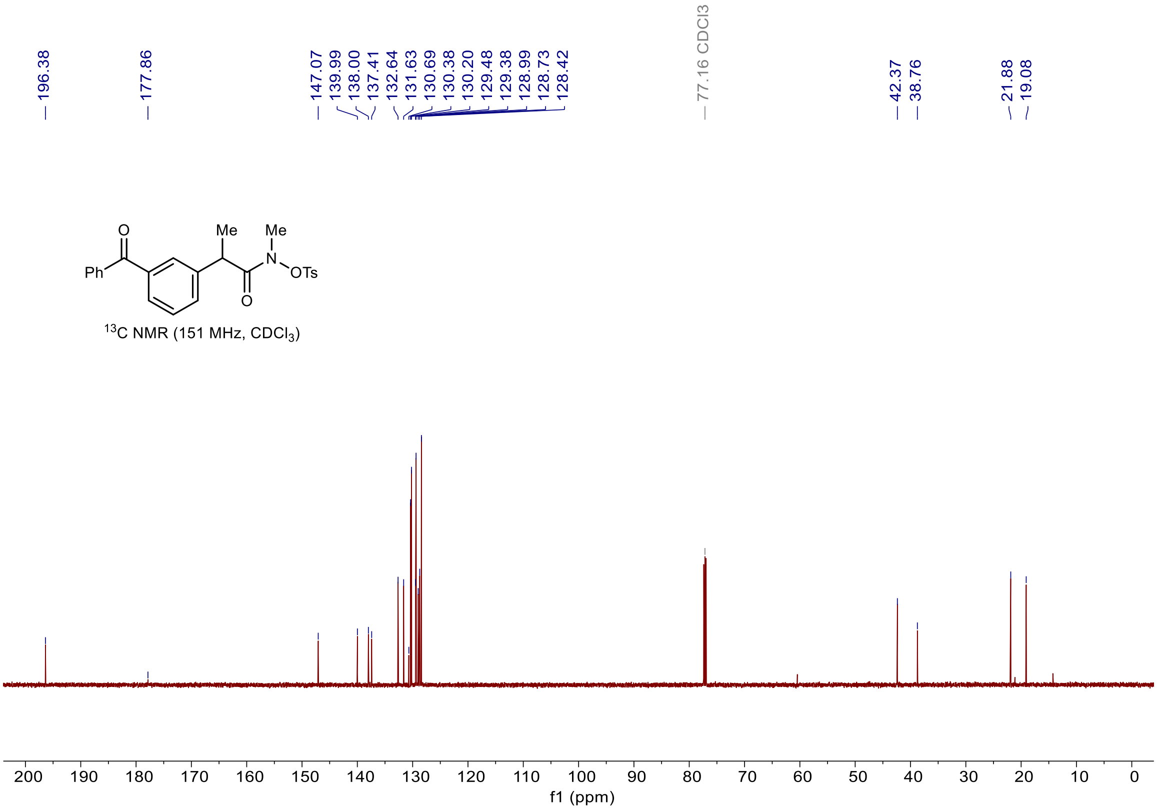
^{1}H and ^{13}C NMR spectra of compound 1u



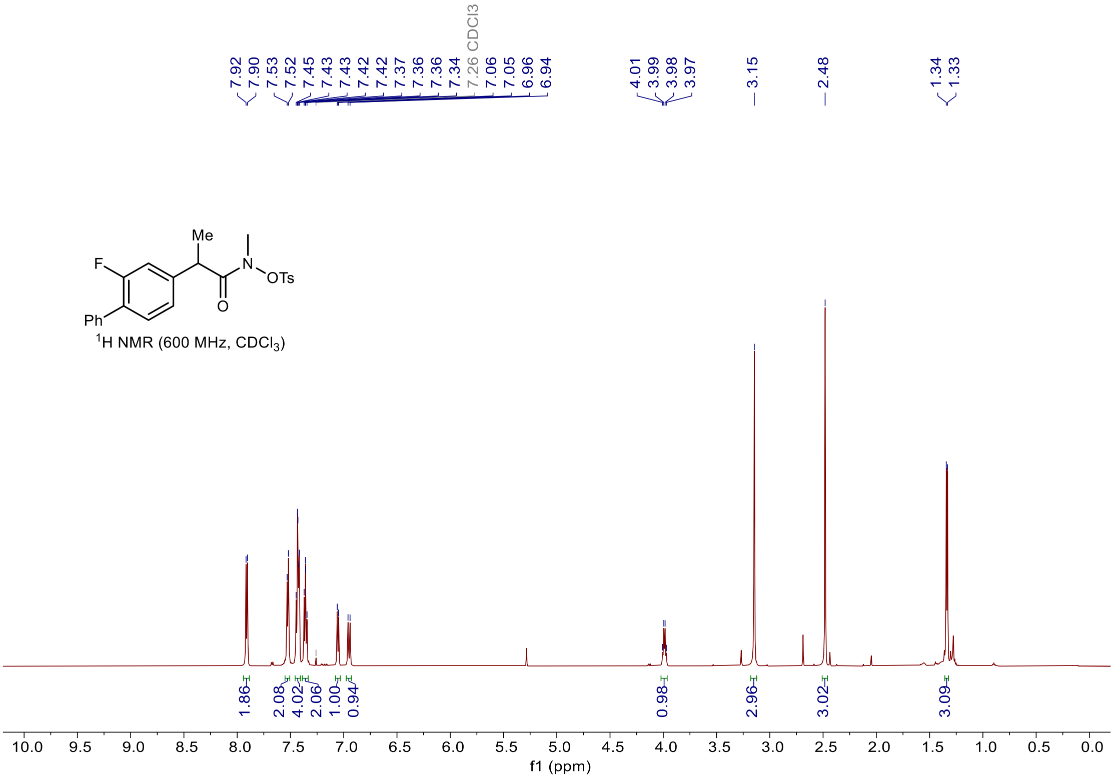


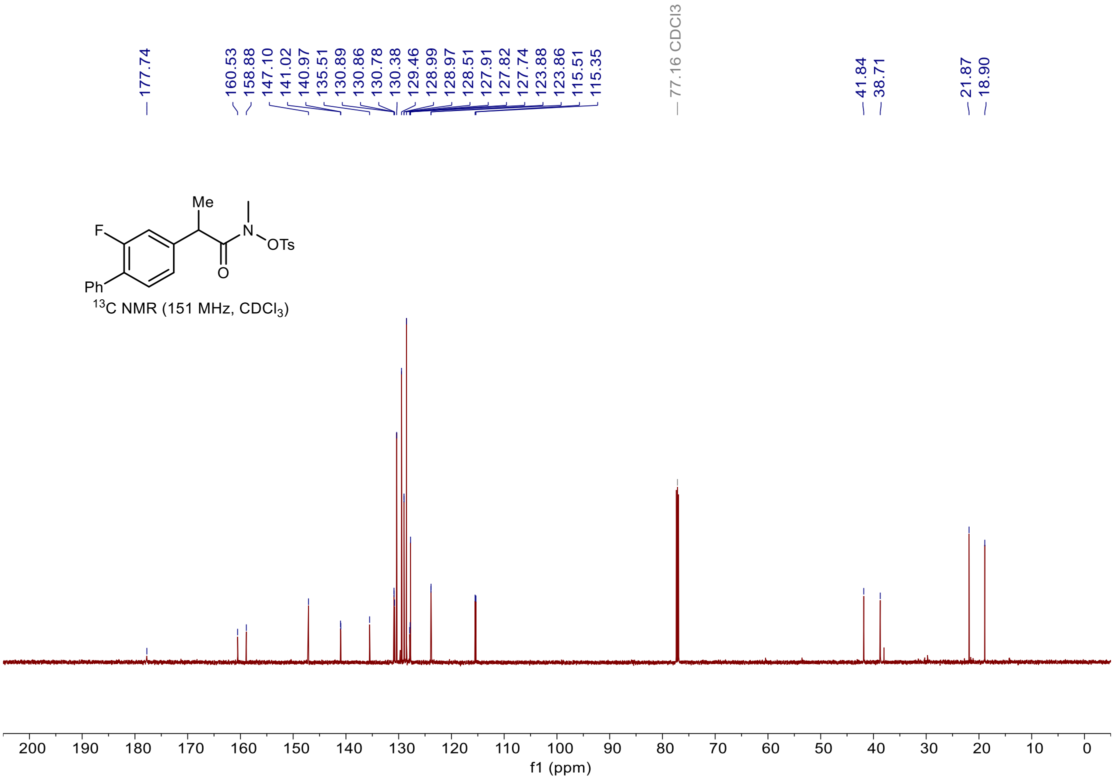
^{1}H and ^{13}C NMR spectra of compound 1x

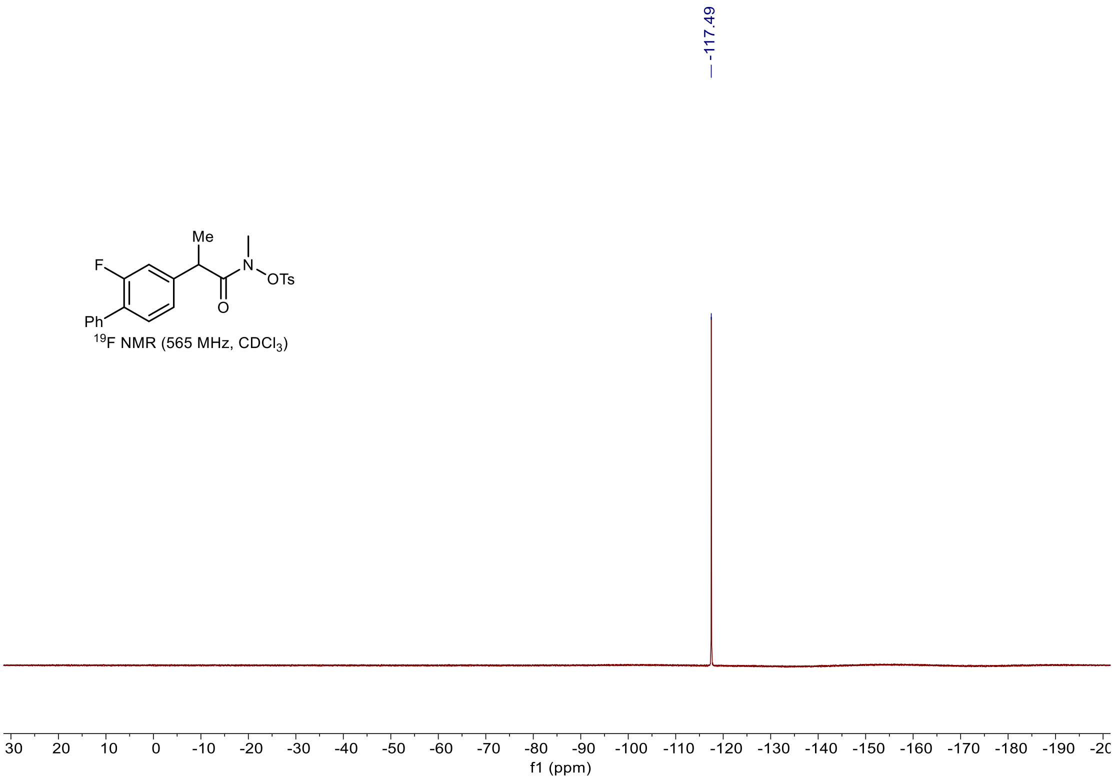




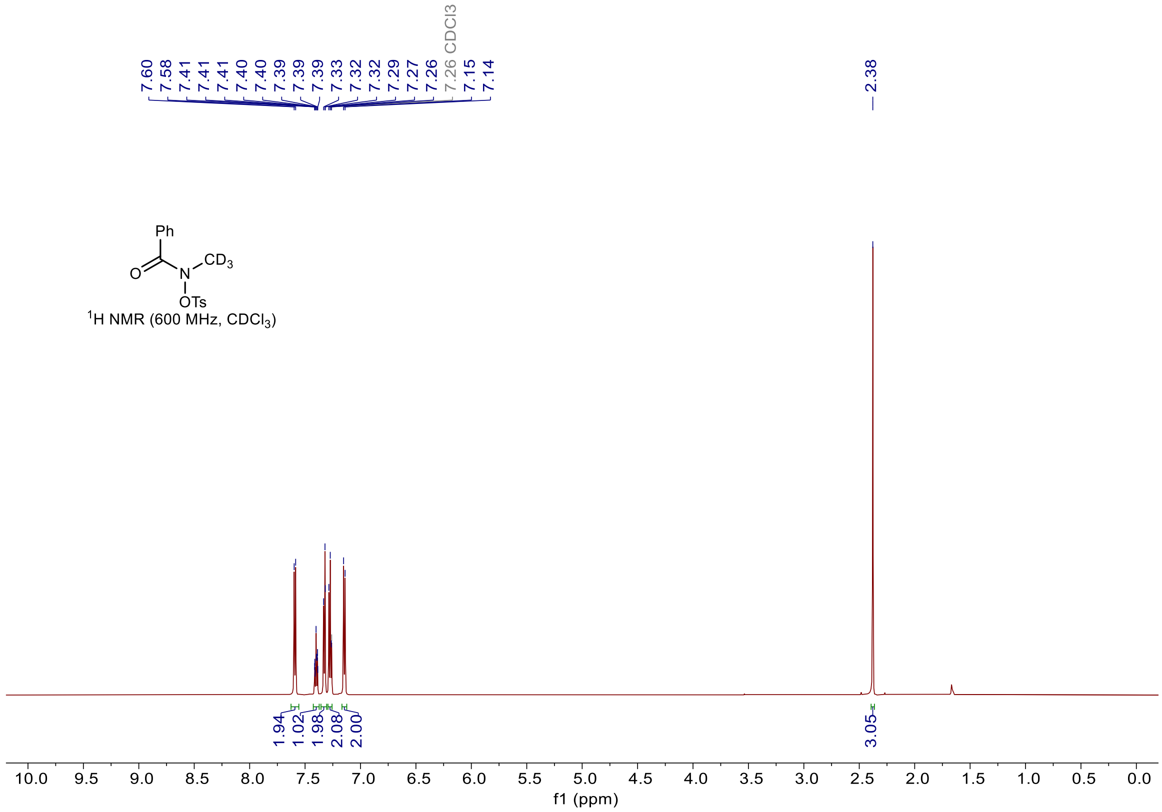
^{1}H and ^{13}C NMR spectra of compound 1y

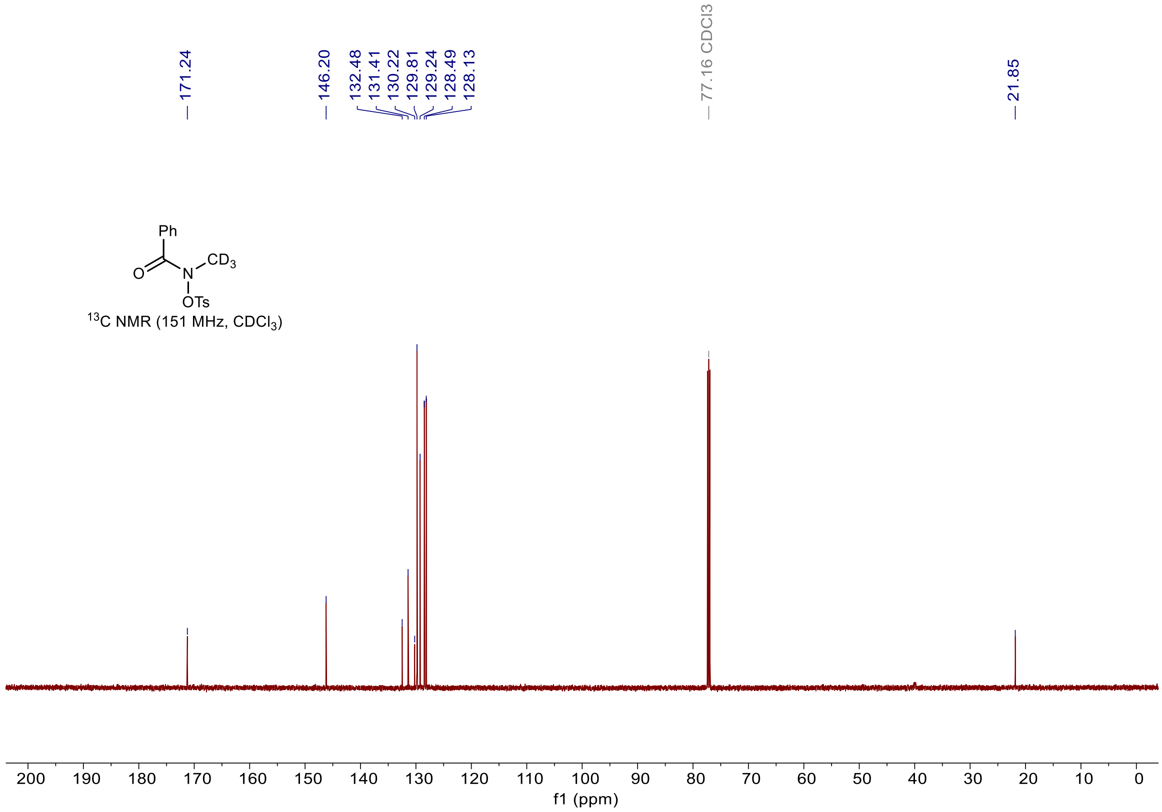




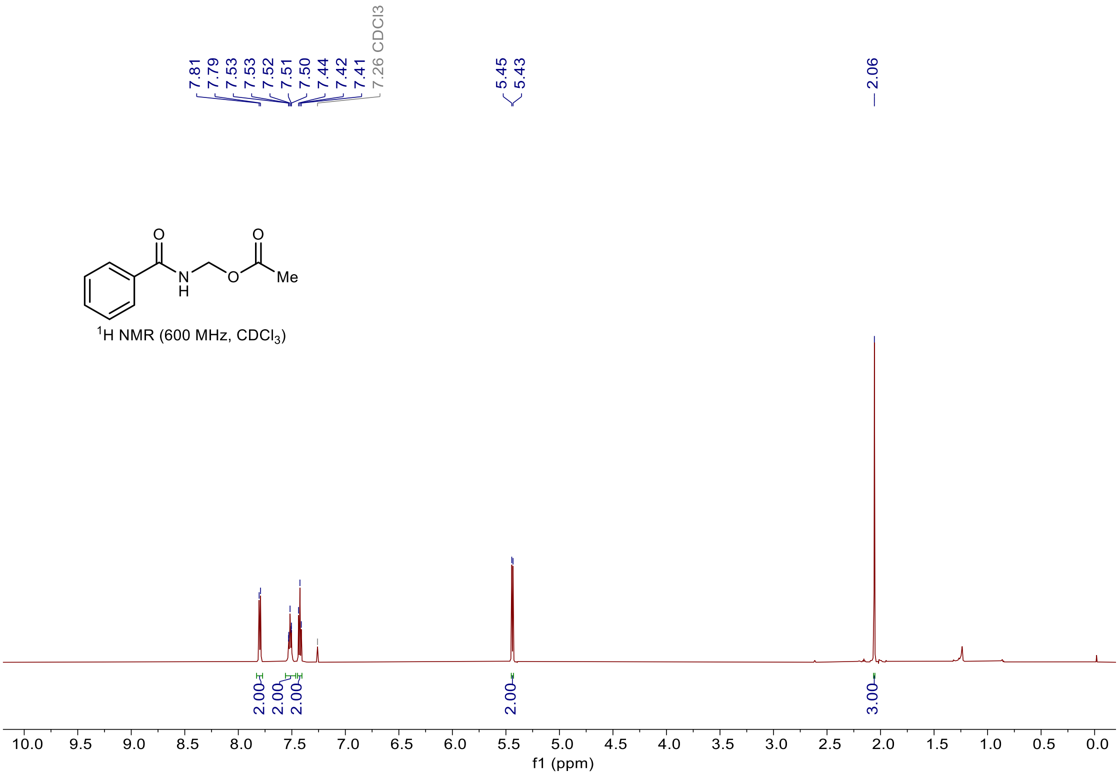

-117.49
Me
F
N
OTs
O
Ph
^{19}F NMR (565 MHz, CDCl$_3$)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)

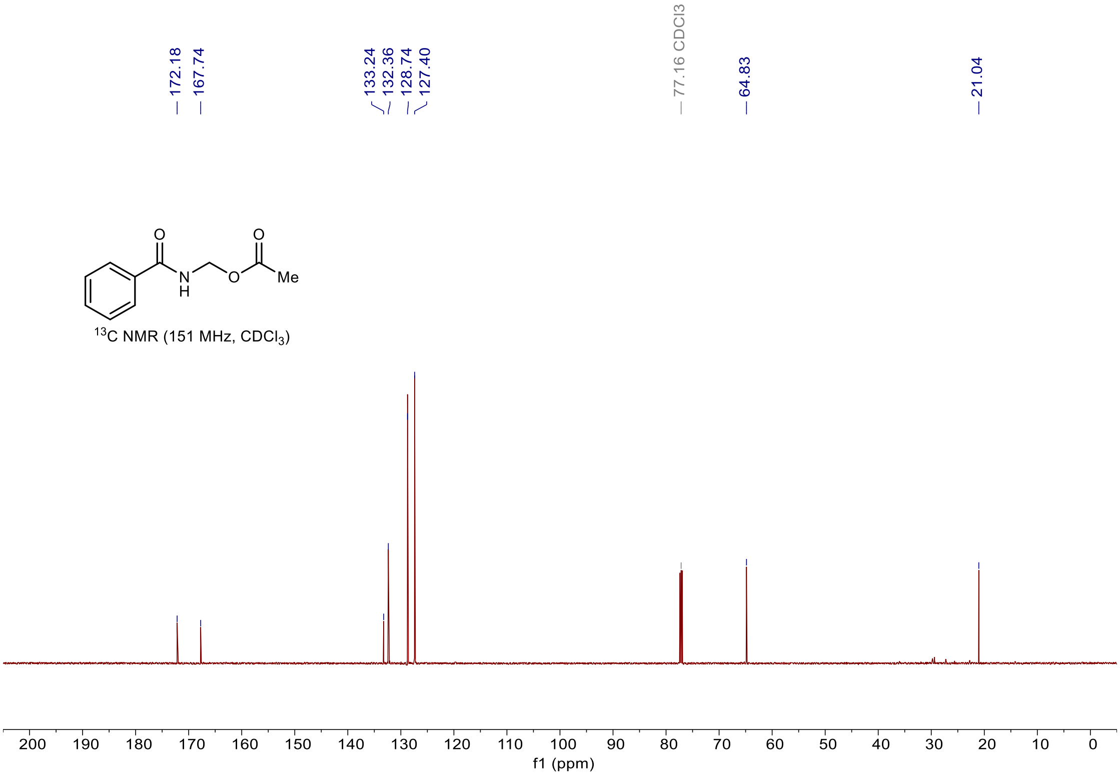
^{1}H and ^{13}C NMR spectra of compound 1a-*d*$_3$



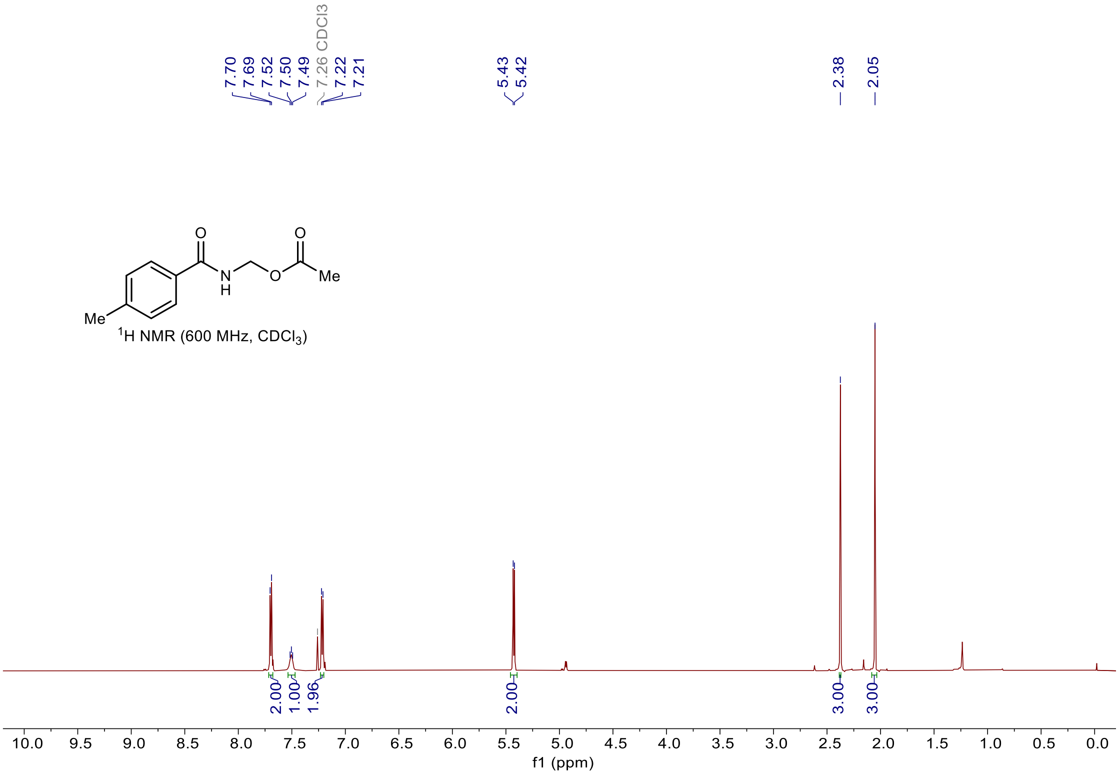


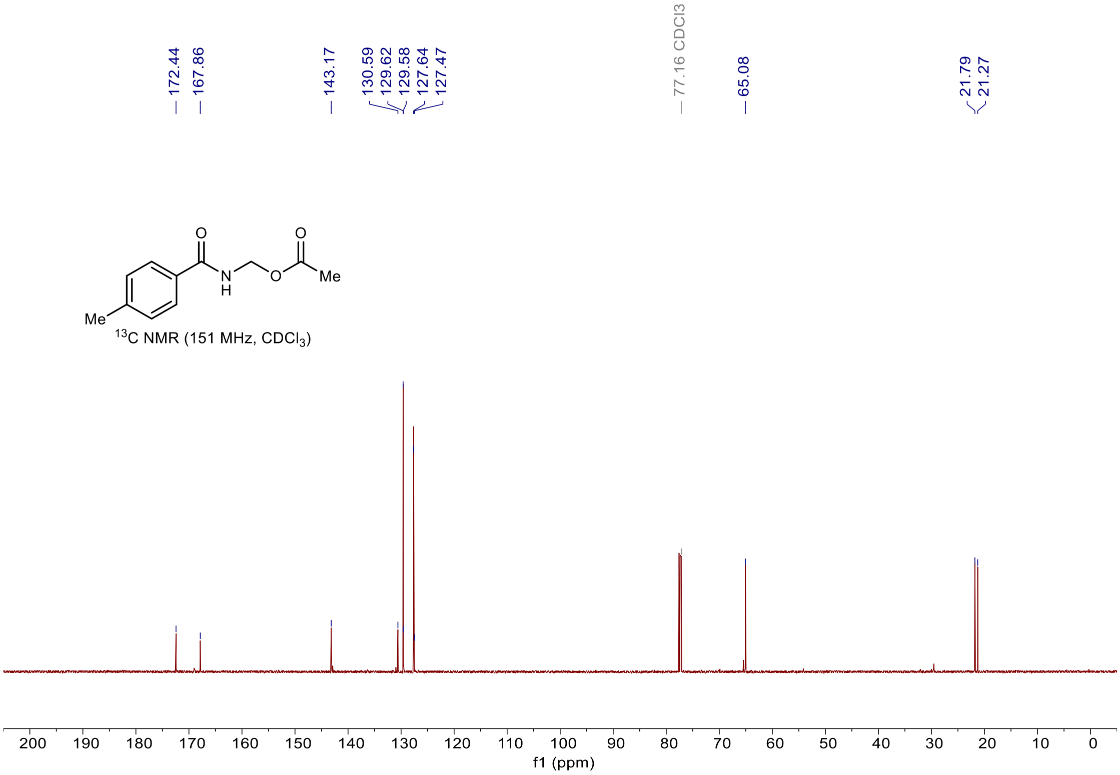
^{1}H and ^{13}C NMR spectra of compound 2a



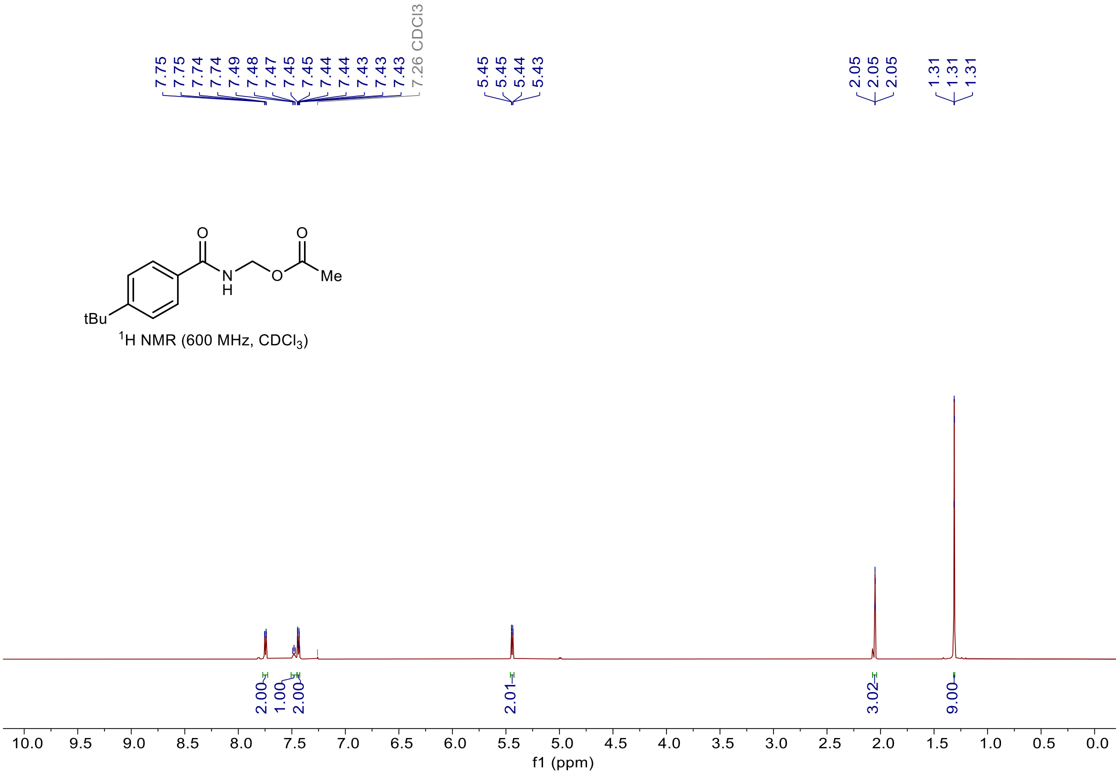


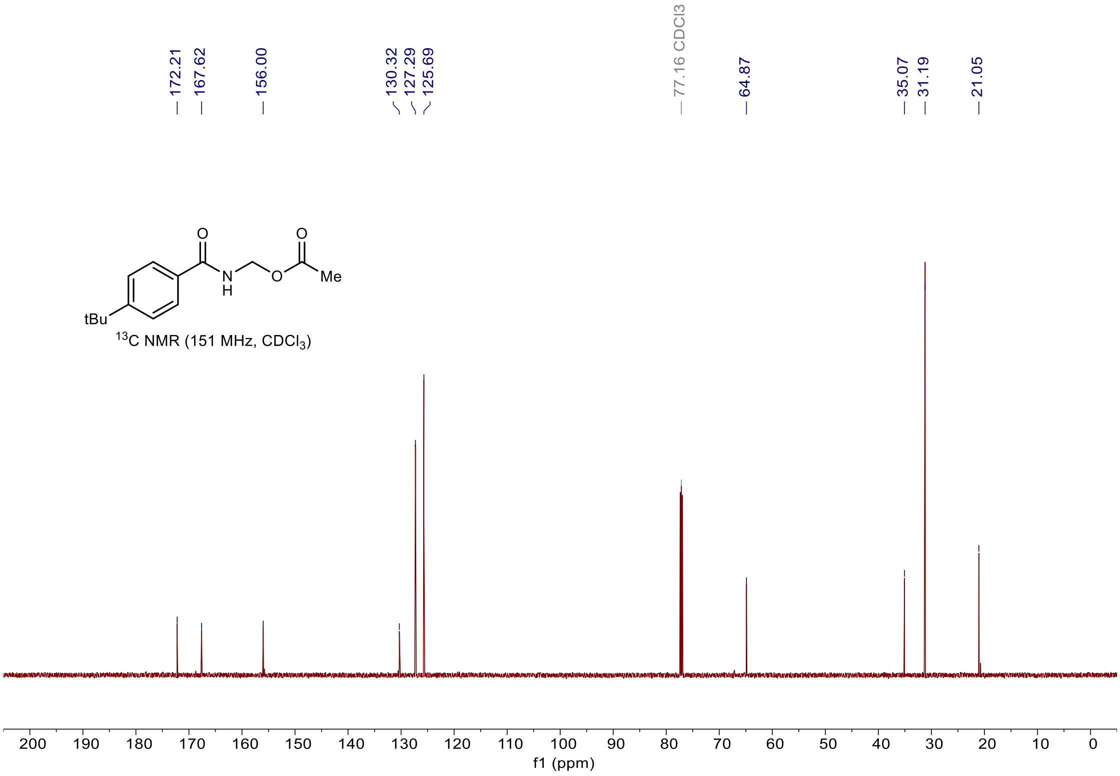
^{1}H and ^{13}C NMR spectra of compound 2b



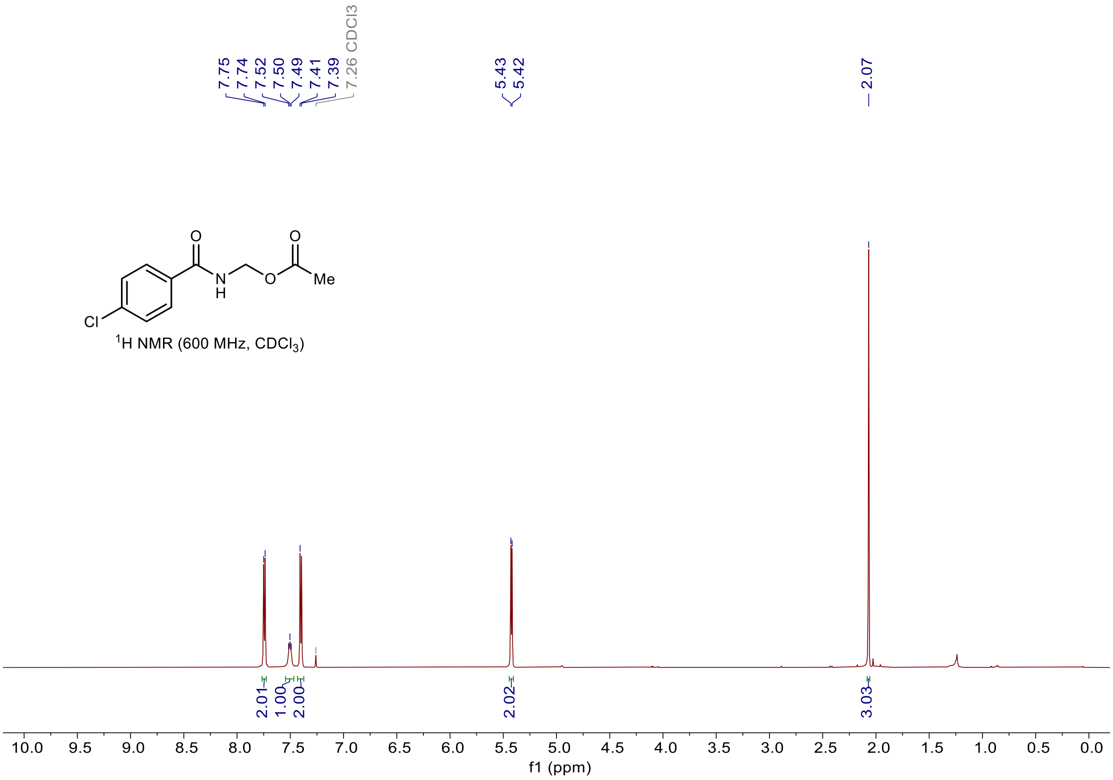


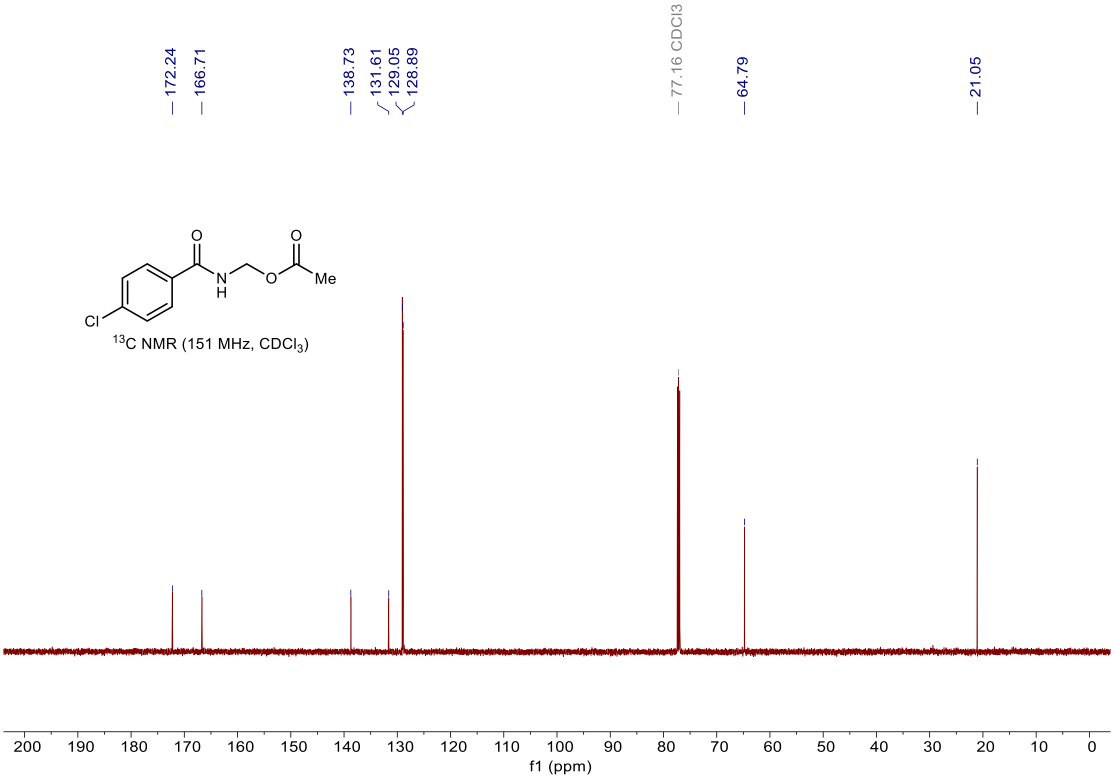
^{1}H and ^{13}C NMR spectra of compound 2c



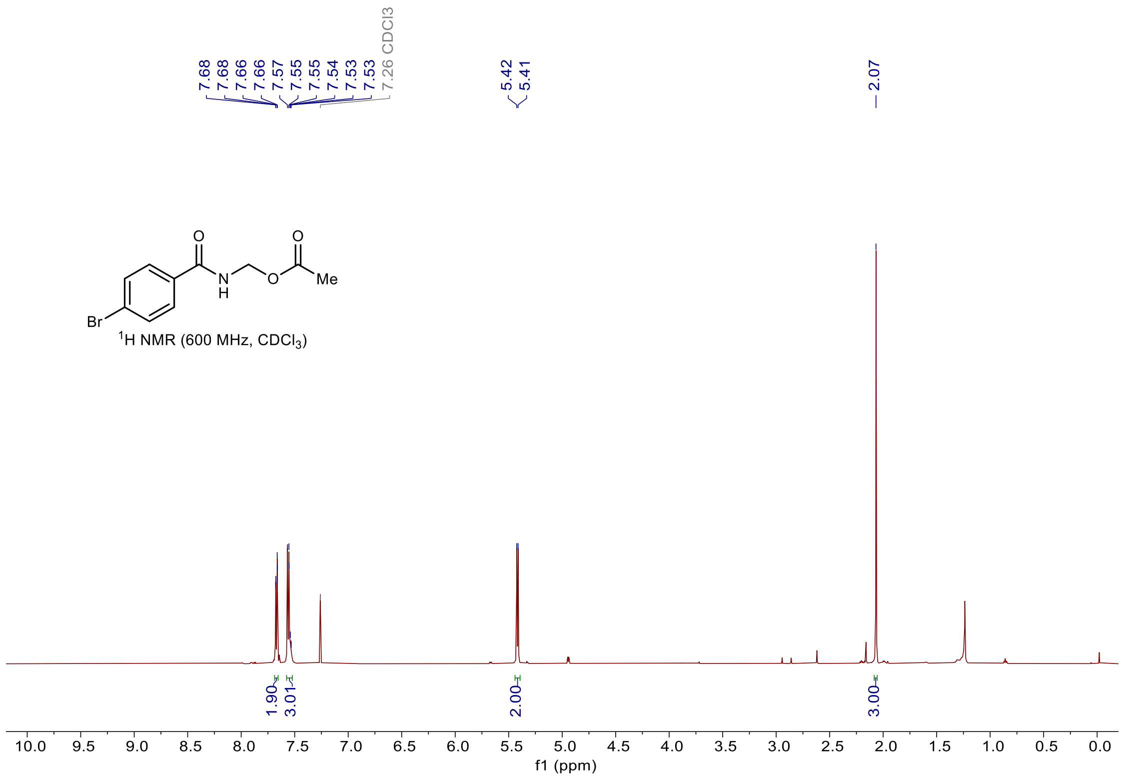


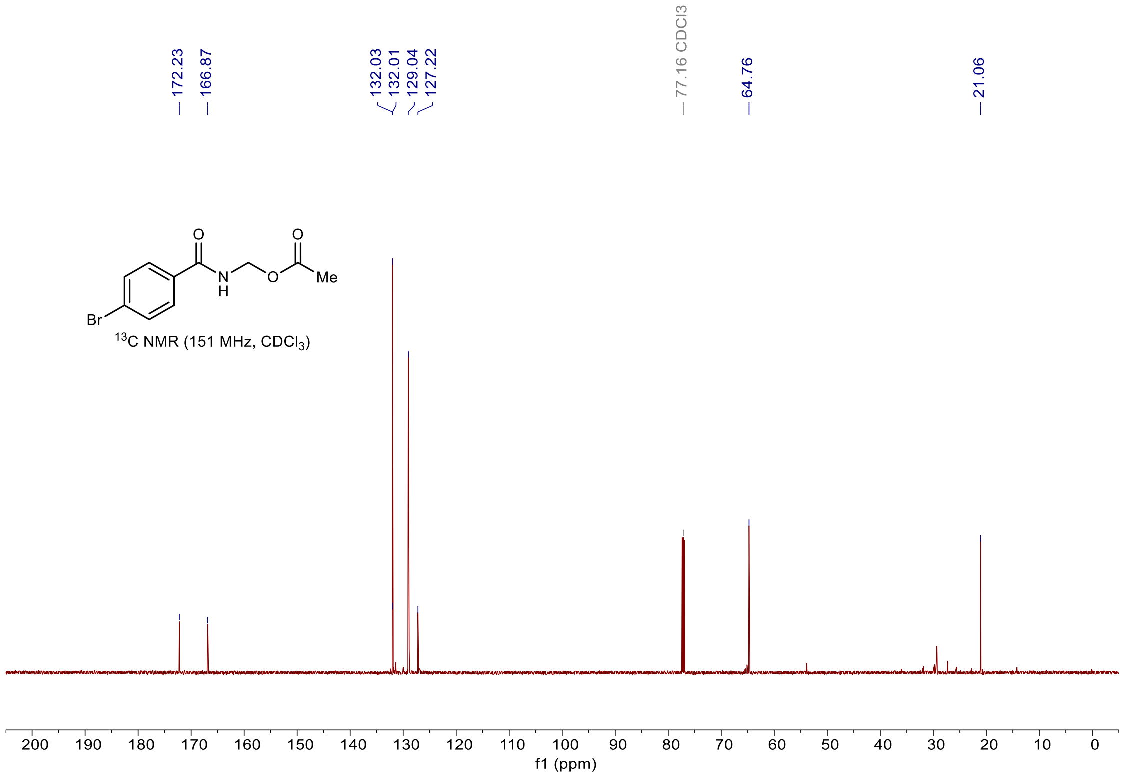
^{1}H and ^{13}C NMR spectra of compound 2d



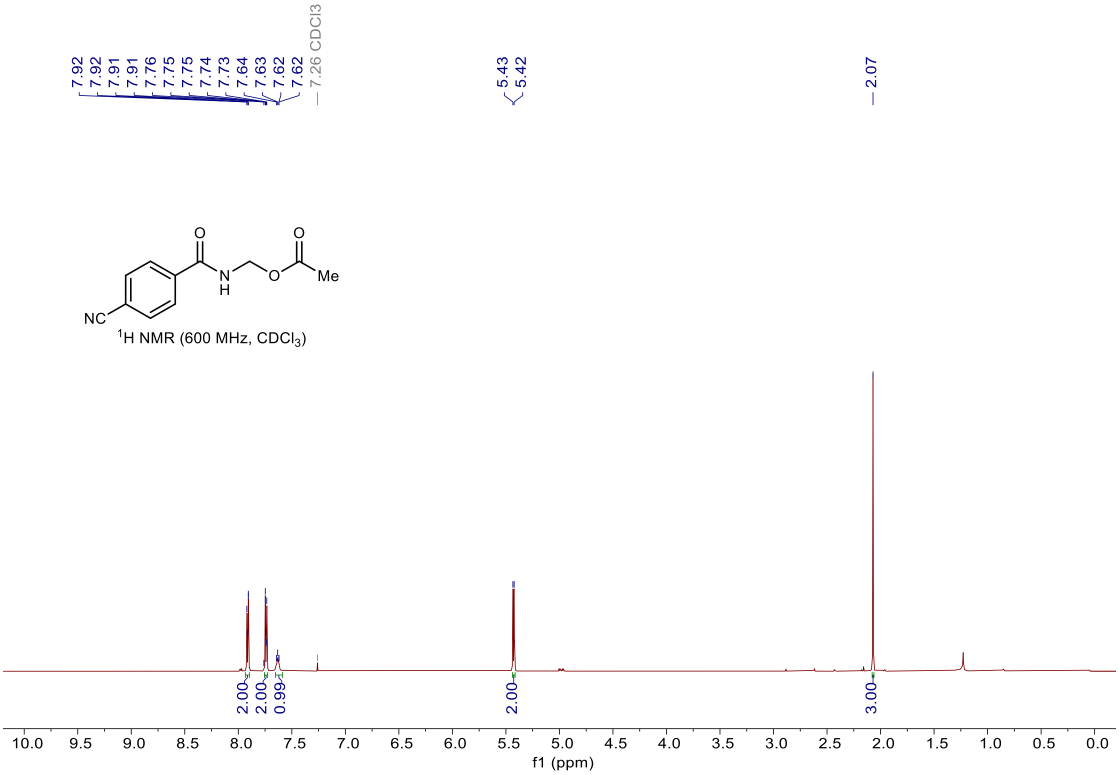


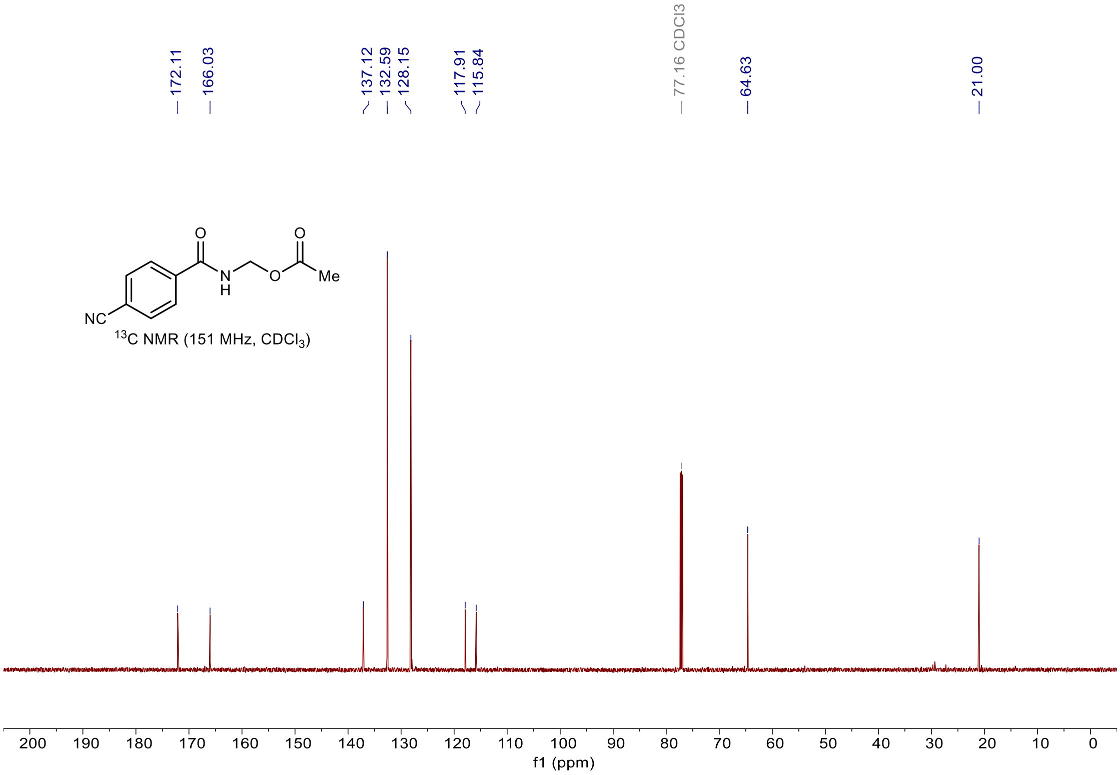
^{1}H and ^{13}C NMR spectra of compound 2e



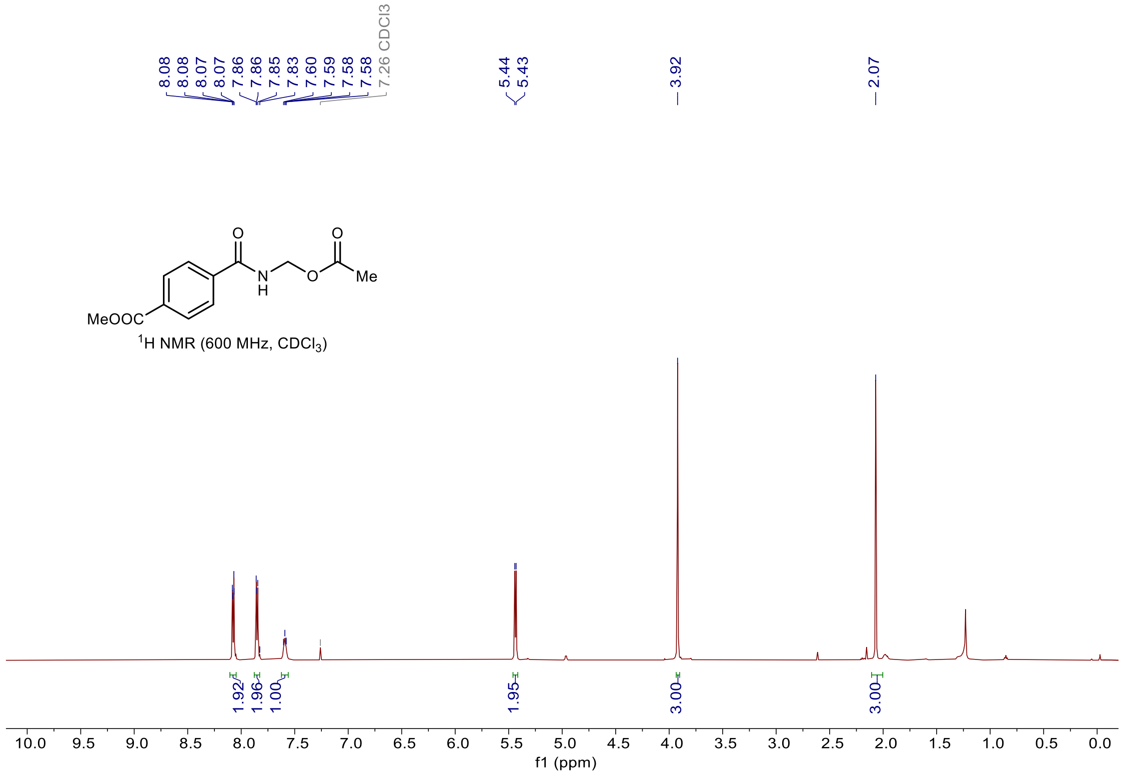


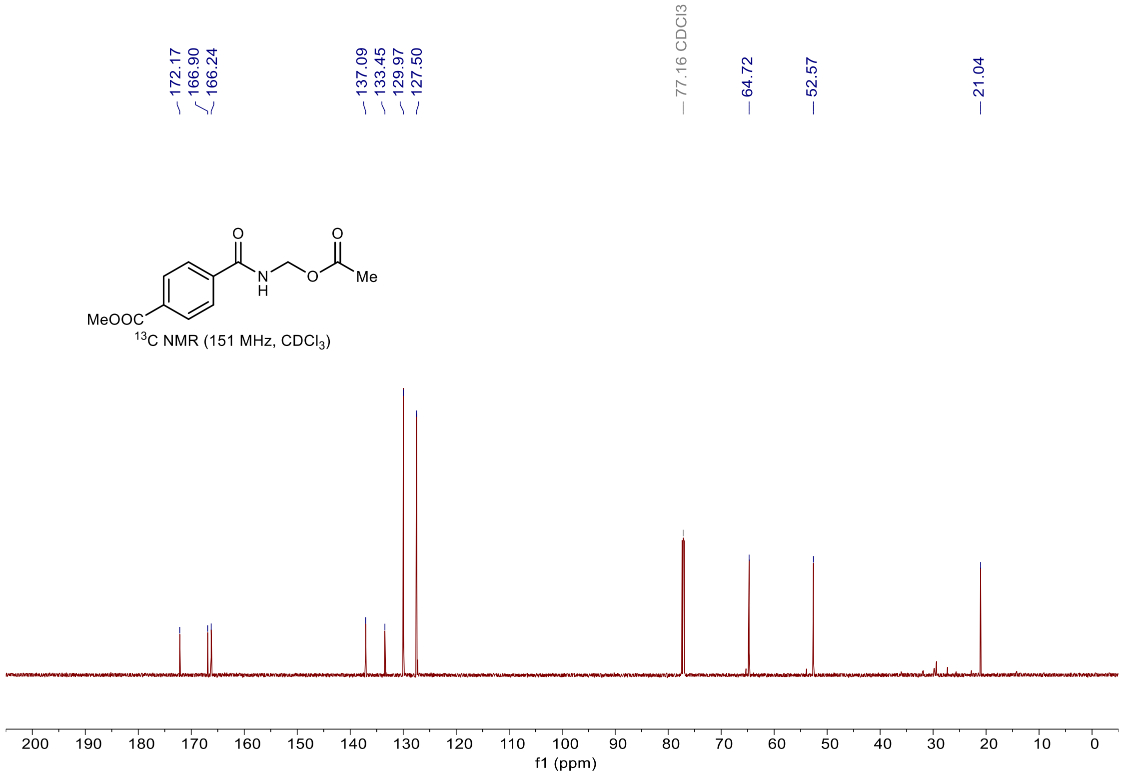
^{1}H and ^{13}C NMR spectra of compound 2f



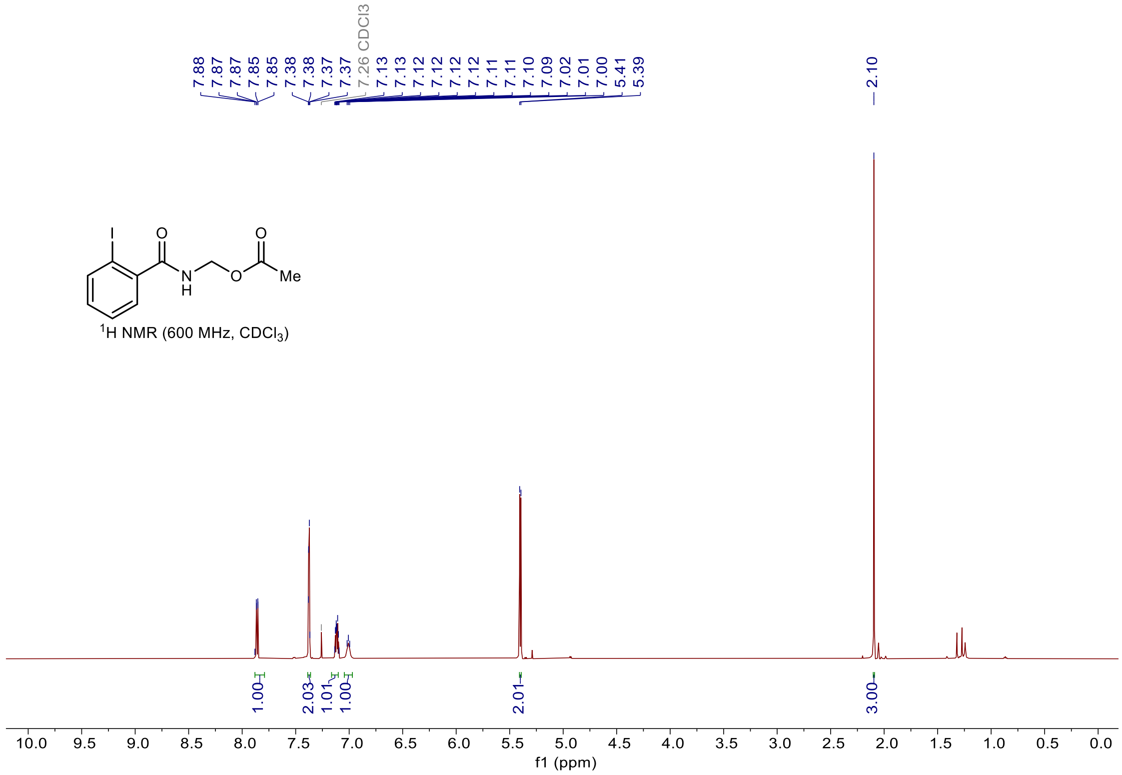


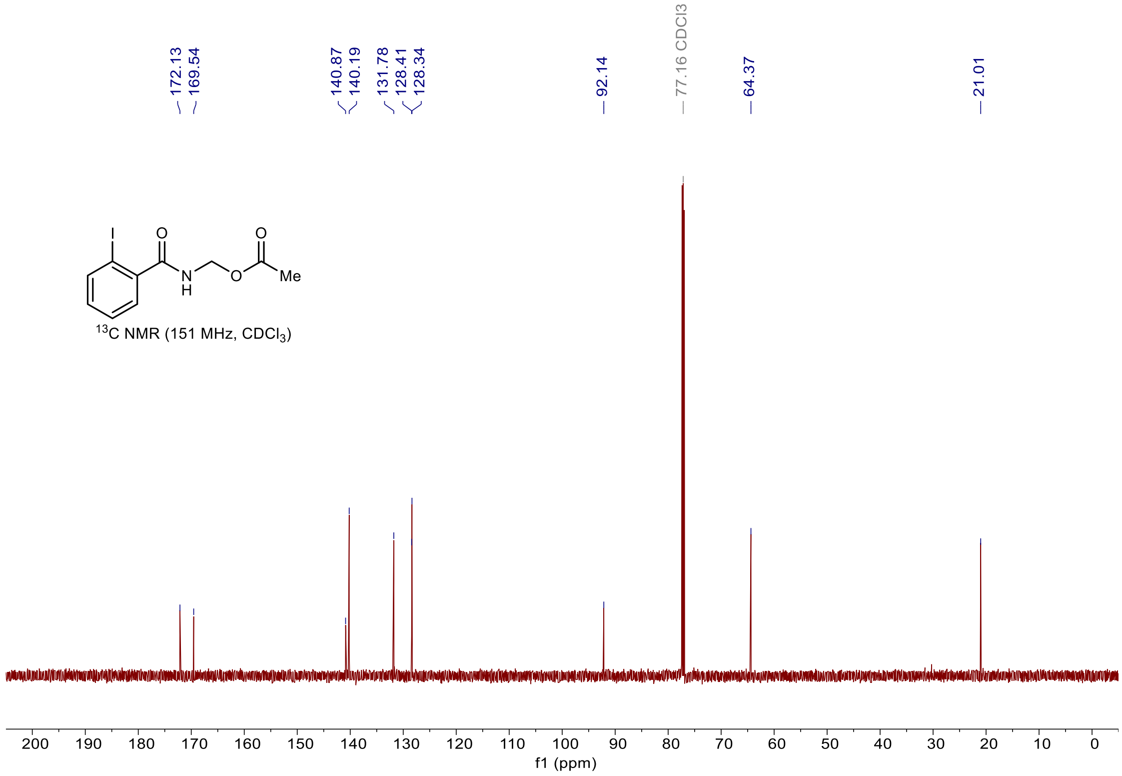
^{1}H and ^{13}C NMR spectra of compound 2g



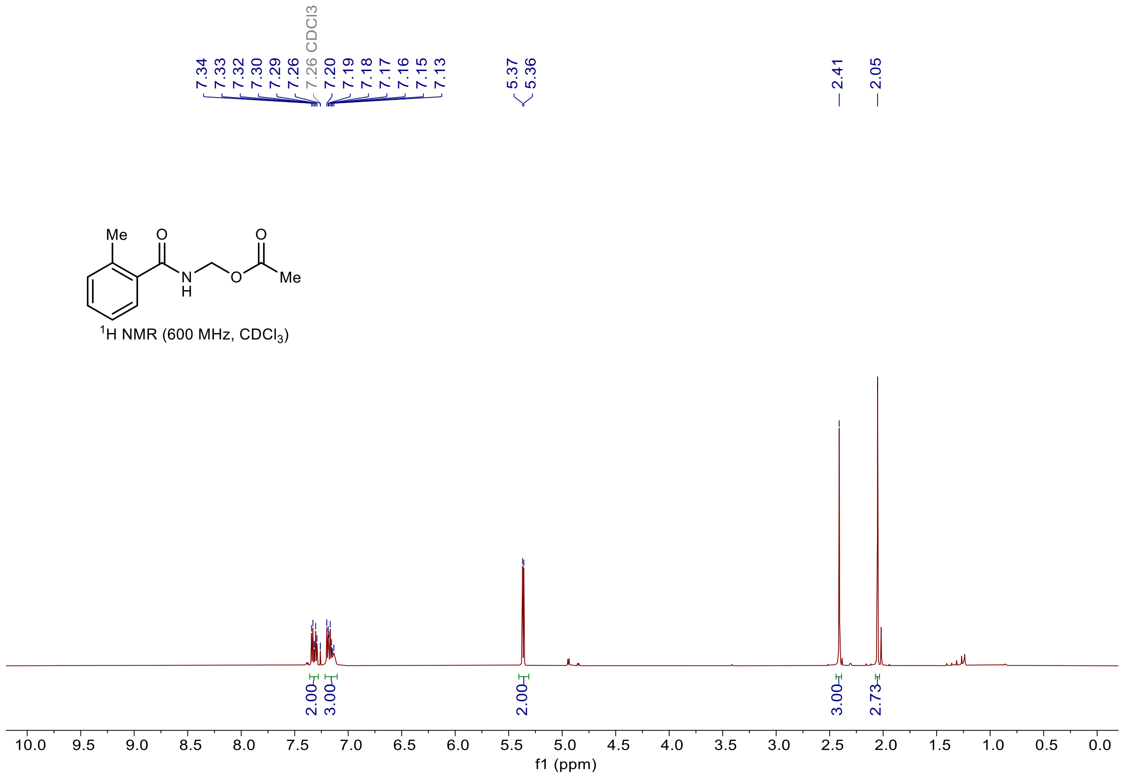


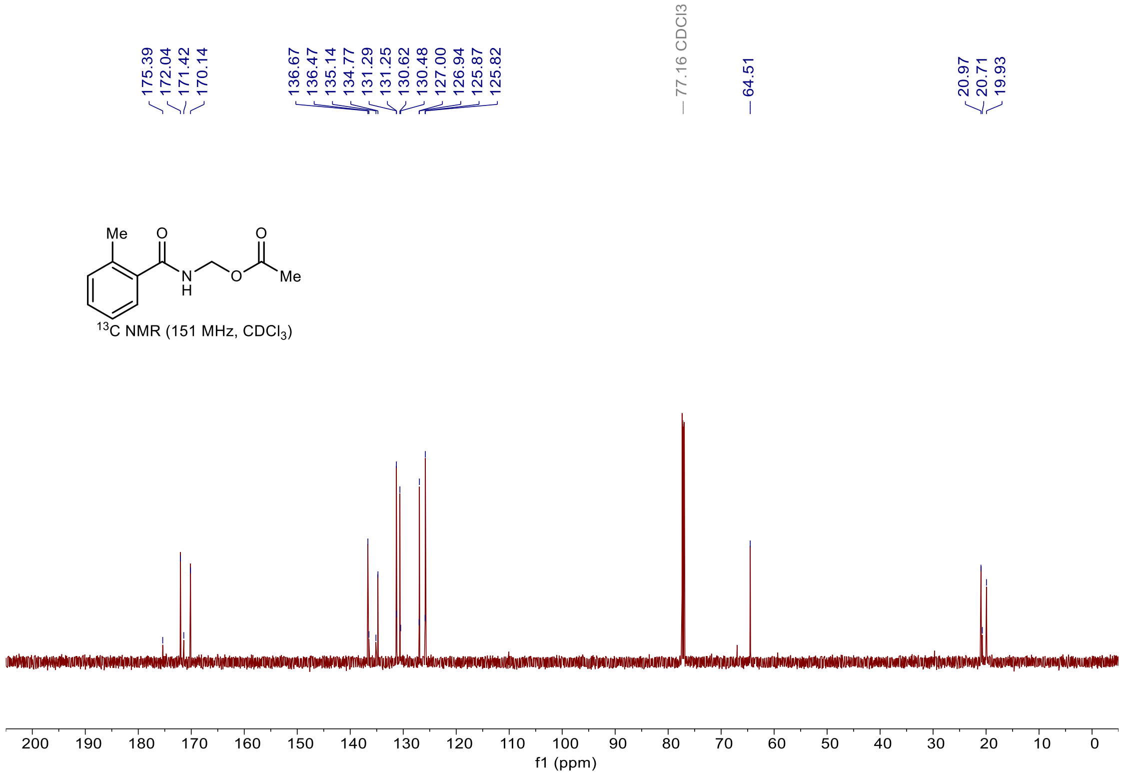
^{1}H and ^{13}C NMR spectra of compound 2h



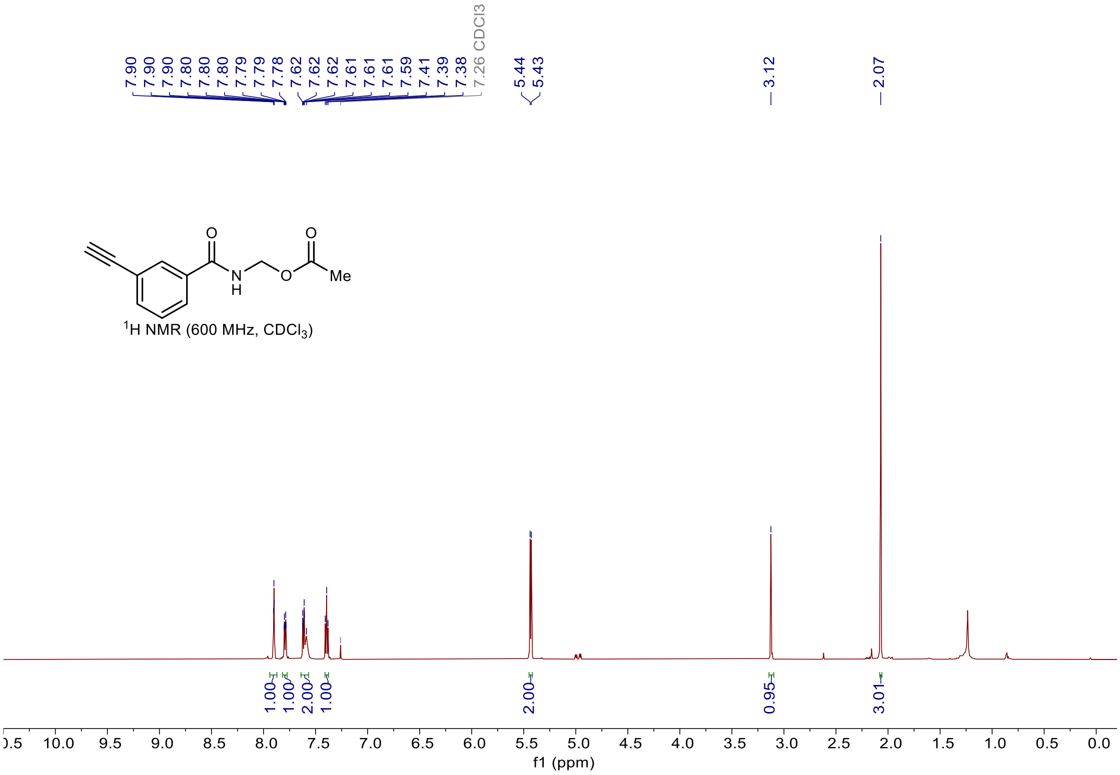


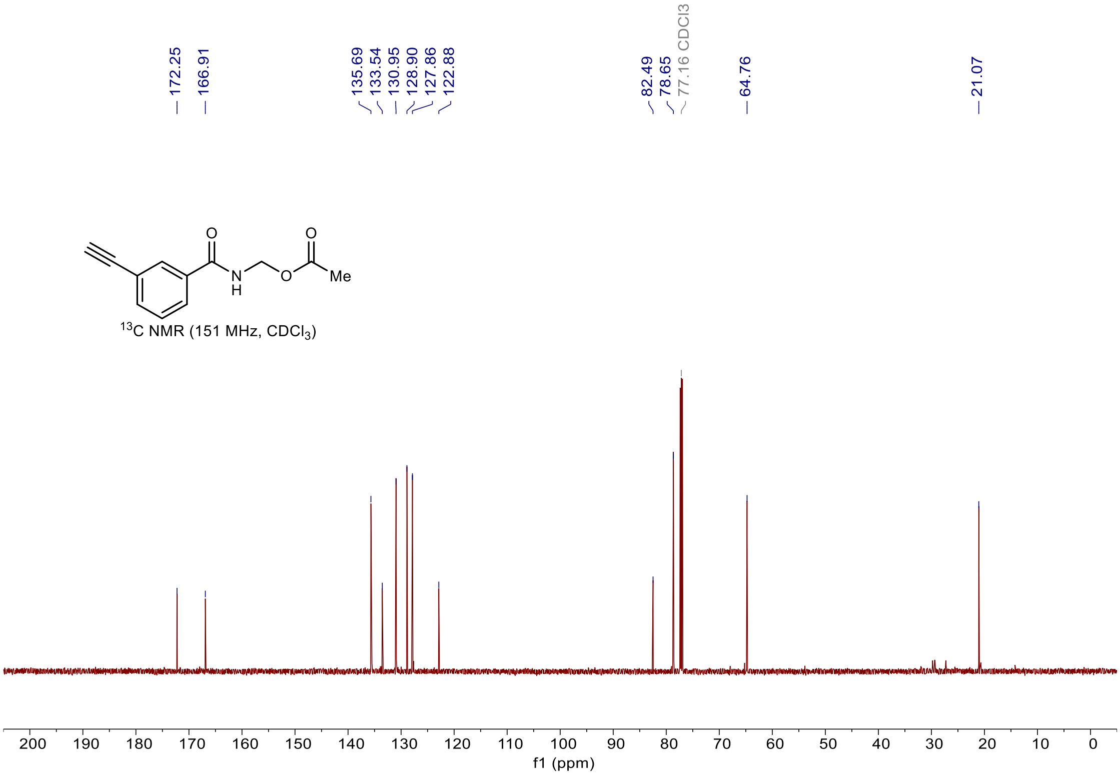
^{1}H and ^{13}C NMR spectra of compound 2i



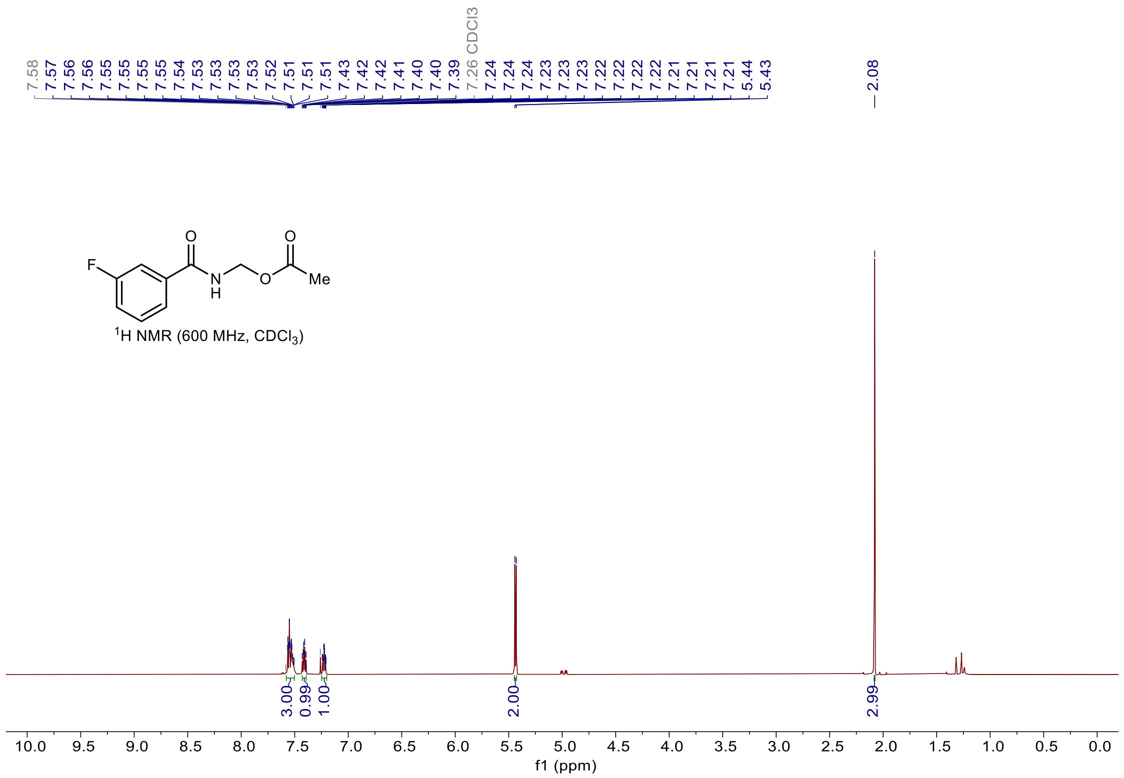


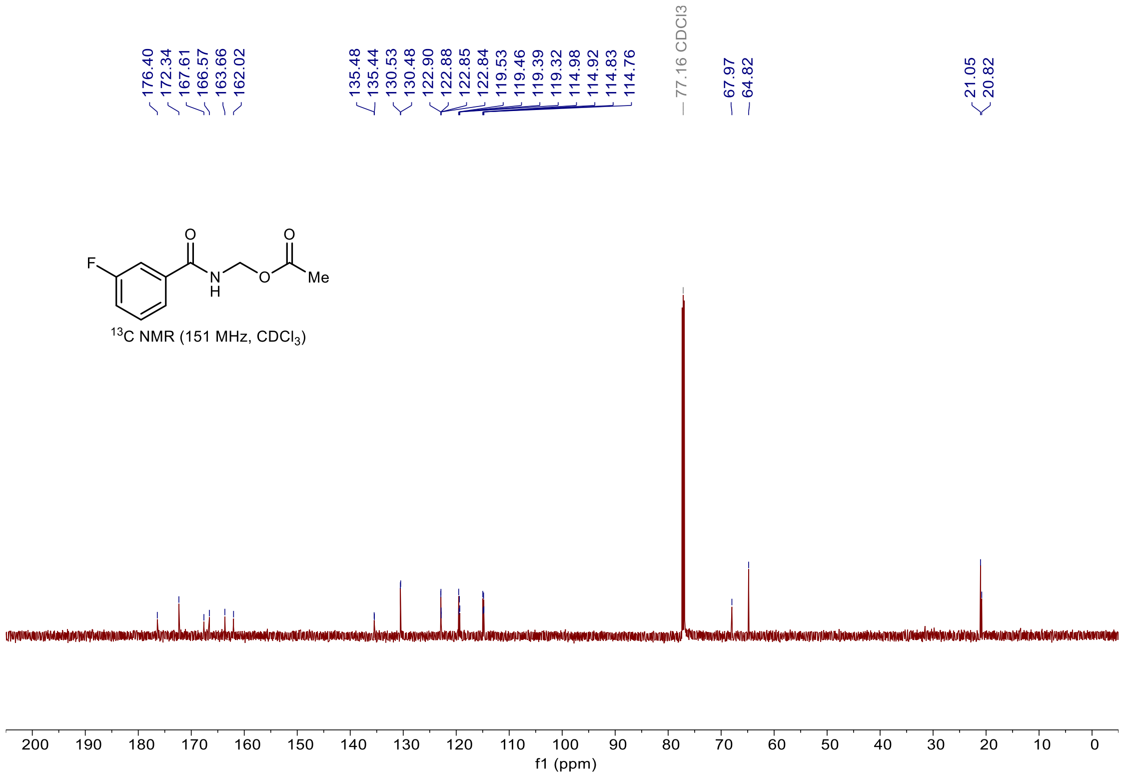
^{1}H and ^{13}C NMR spectra of compound 2j

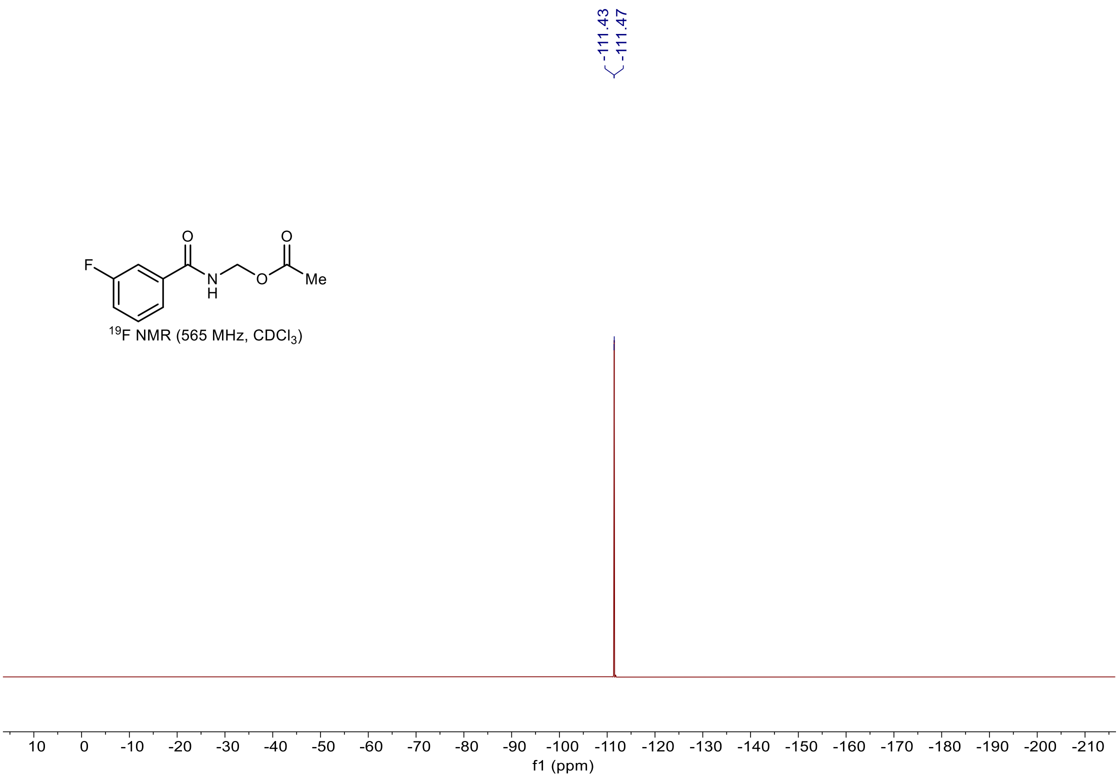




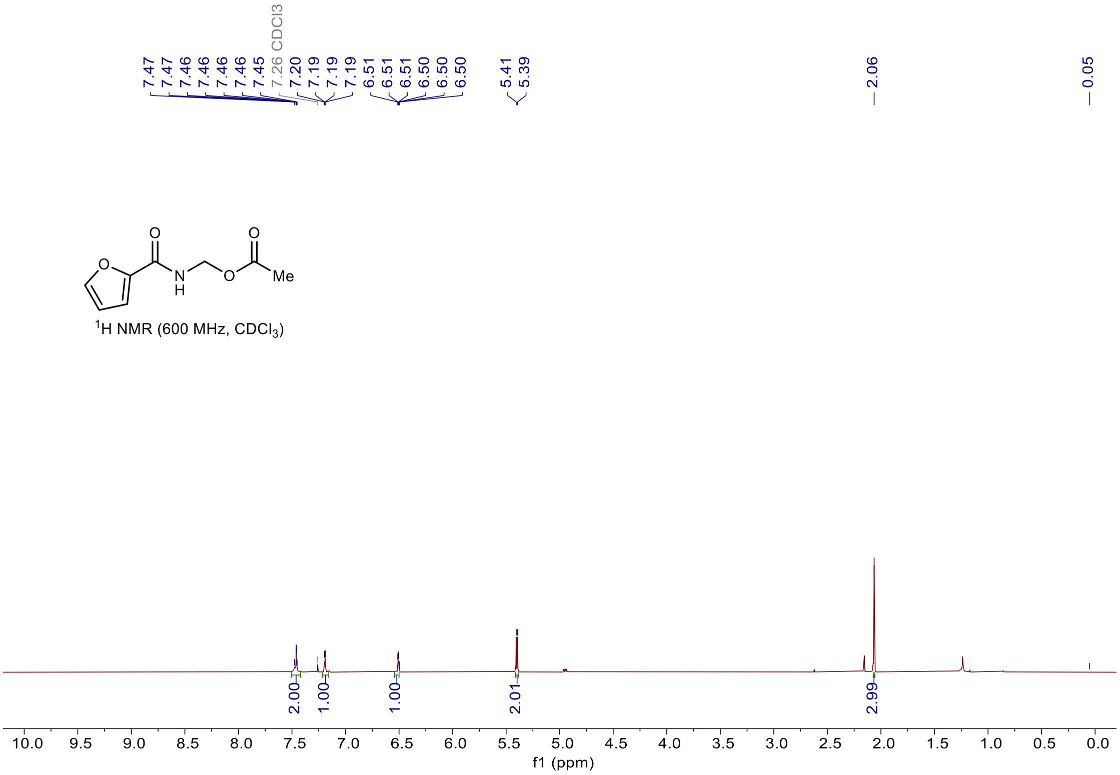
^{1}H and ^{13}C NMR spectra of compound 2k

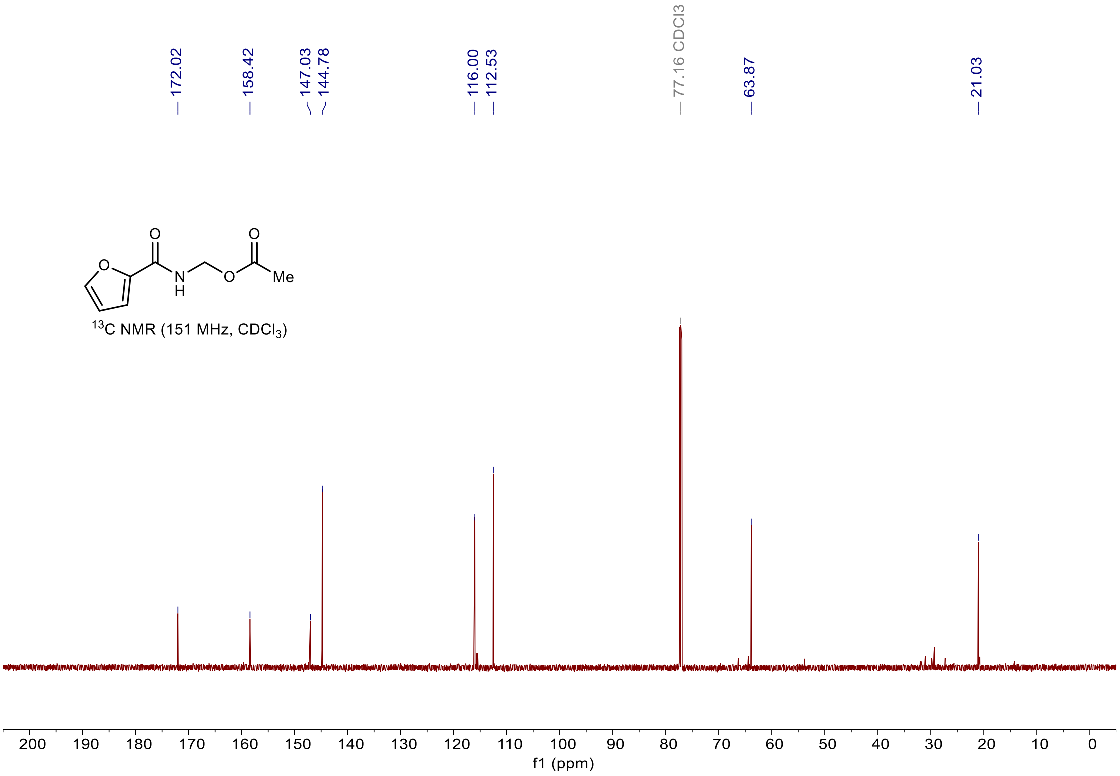




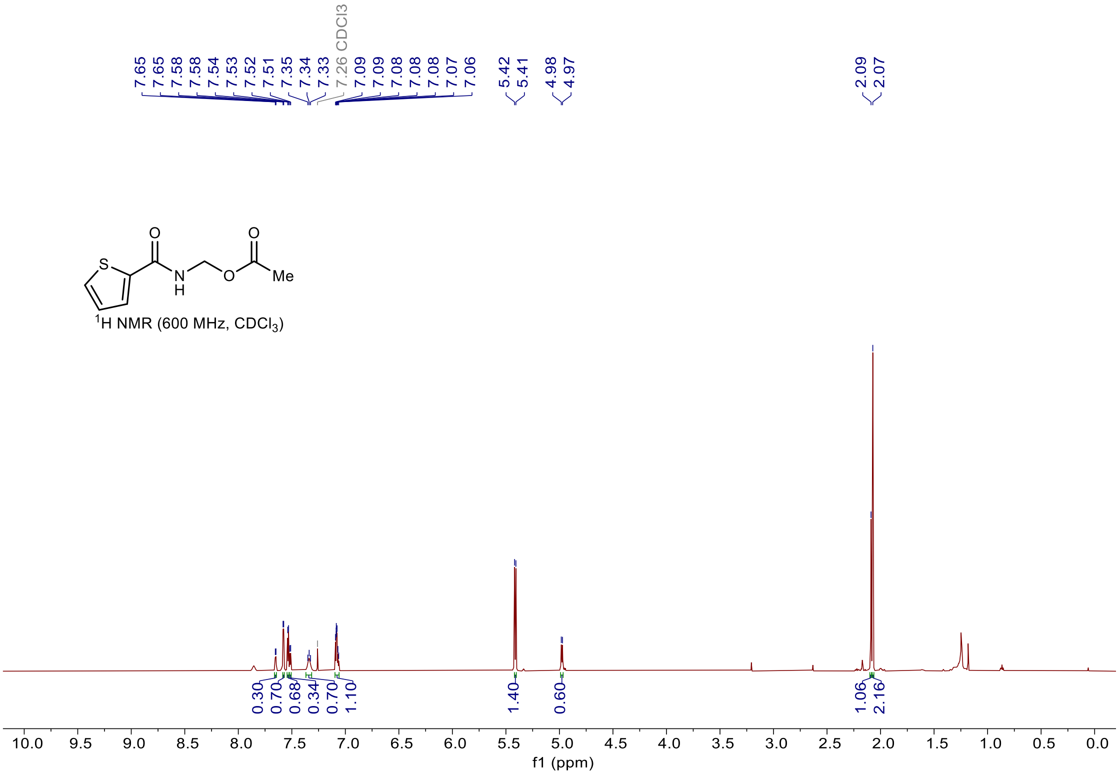

-111.43
-111.47
F
O
N
H
O
O
Me
^{19}F NMR (565 MHz, CDCl$_3$)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

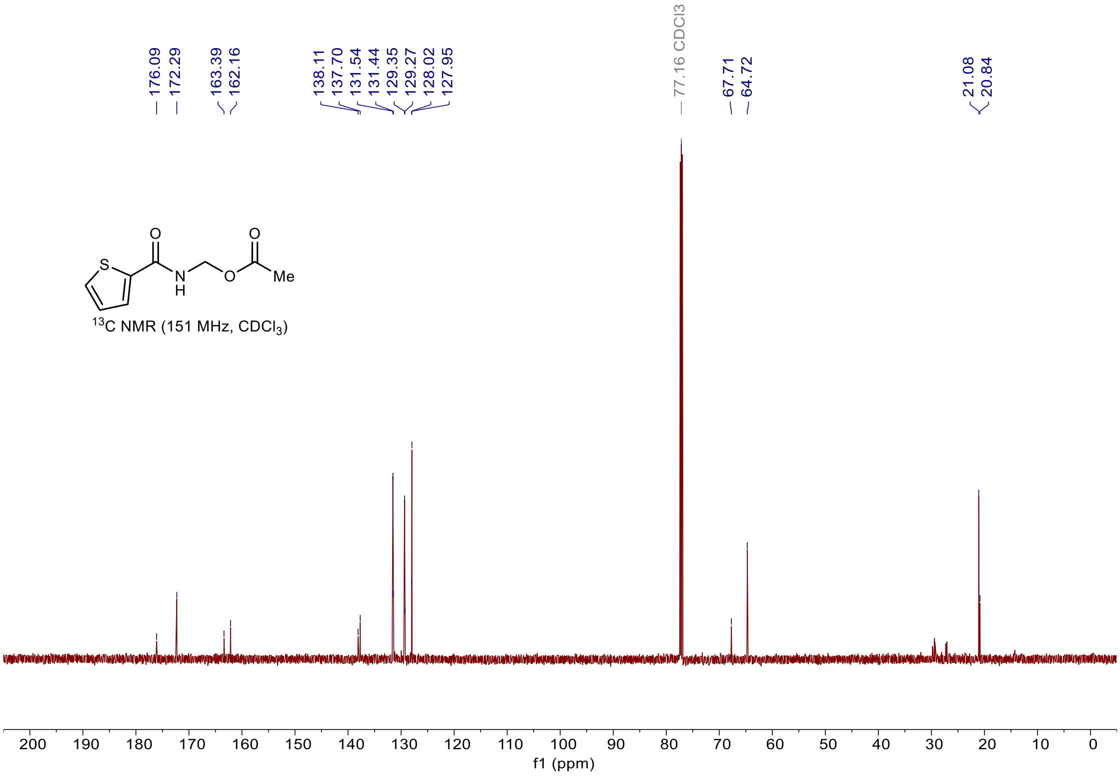
^{1}H and ^{13}C NMR spectra of compound 2l



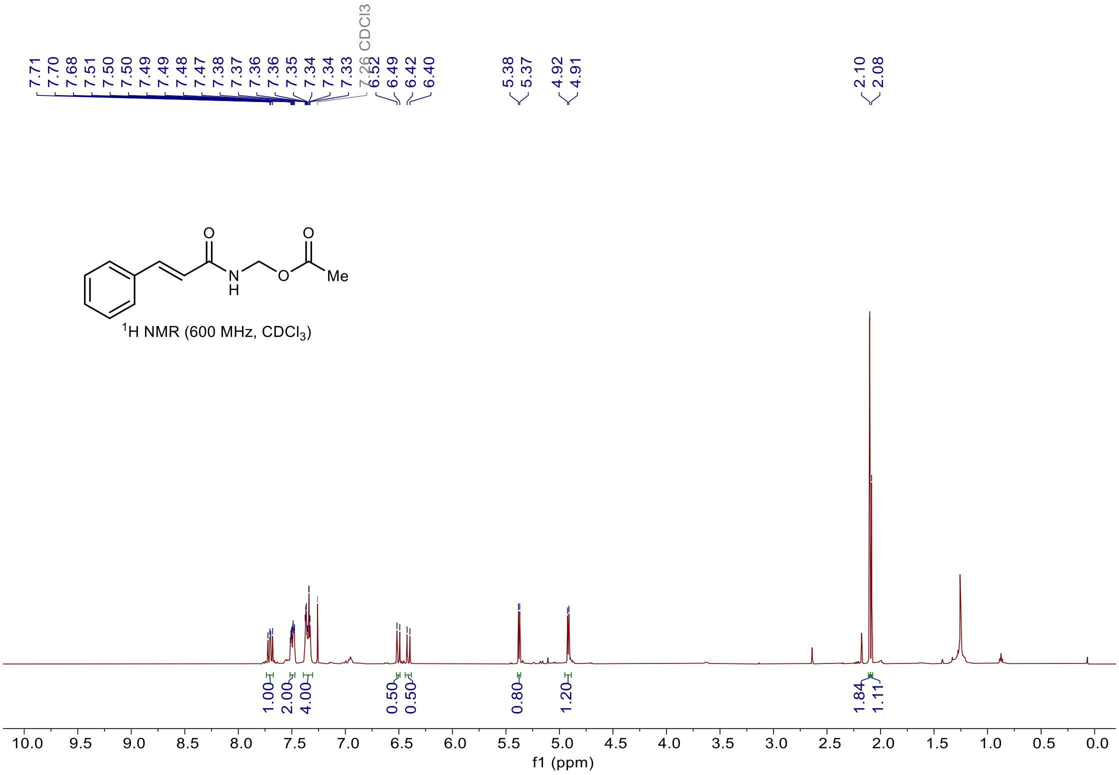


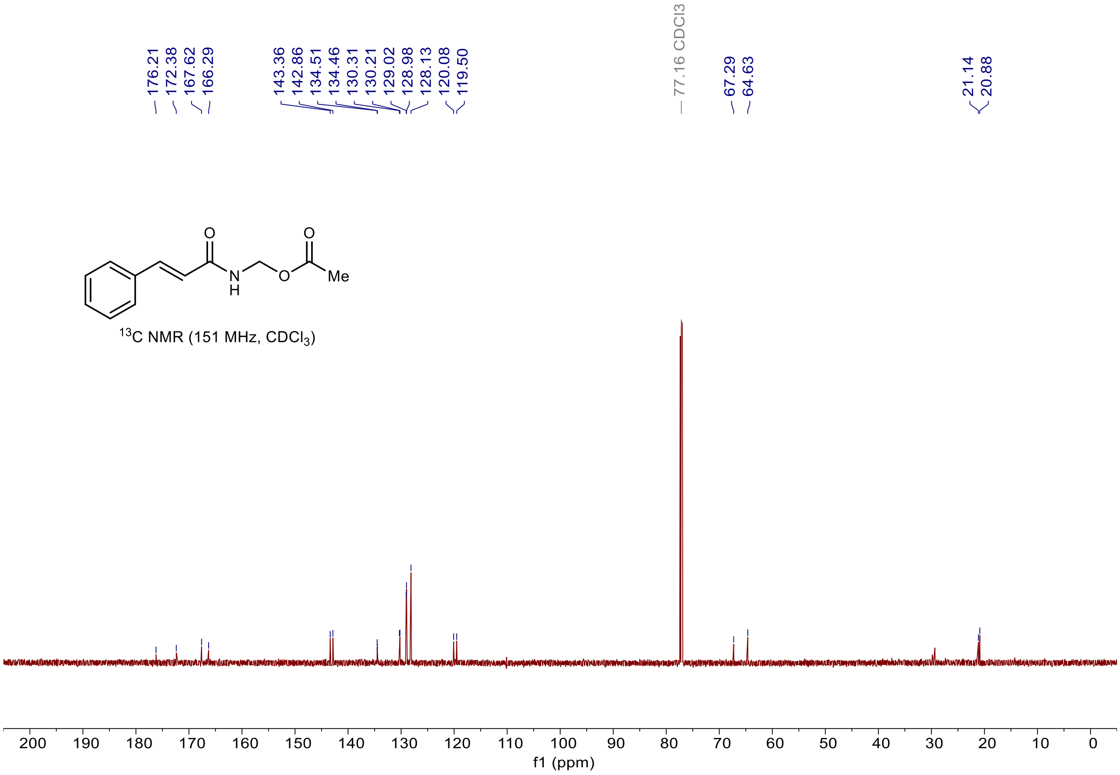
^{1}H and ^{13}C NMR spectra of compound 2m



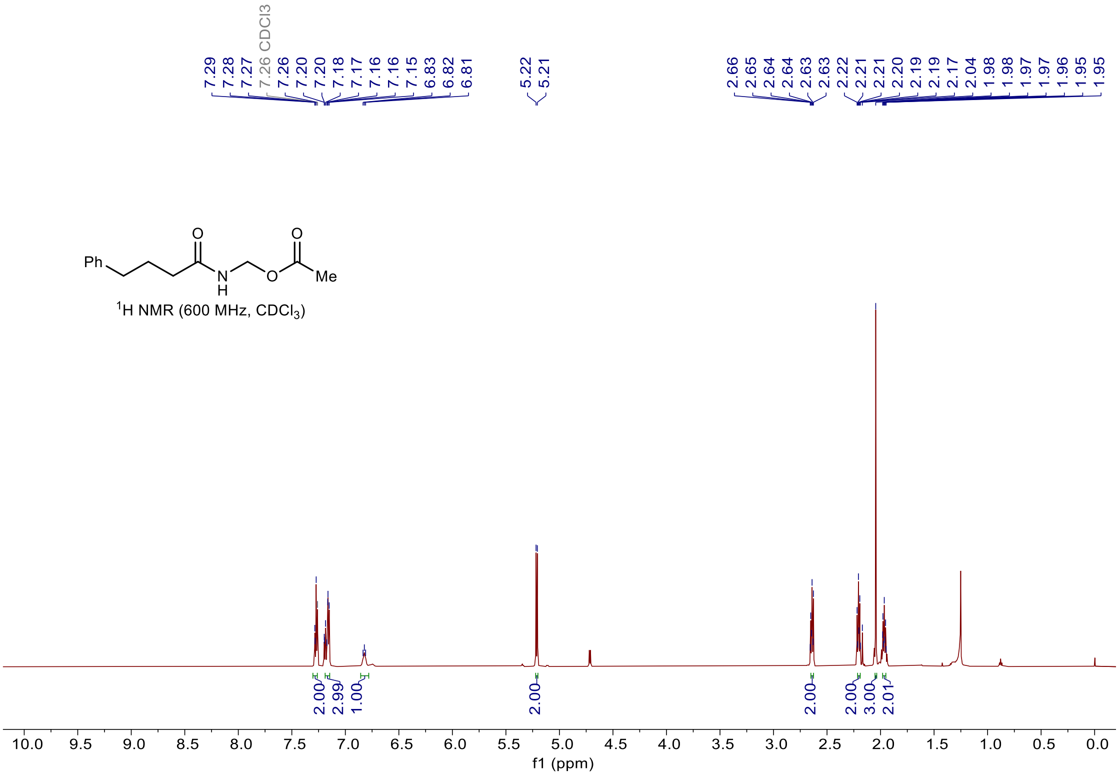


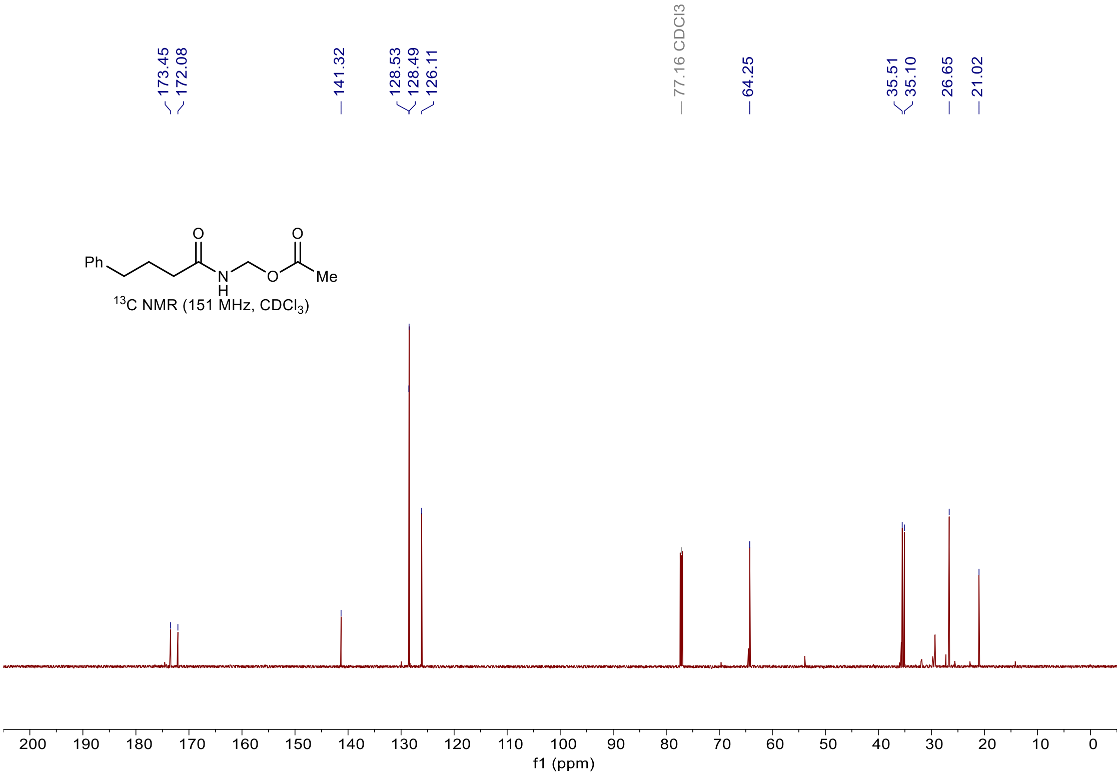
^{1}H and ^{13}C NMR spectra of compound 2n



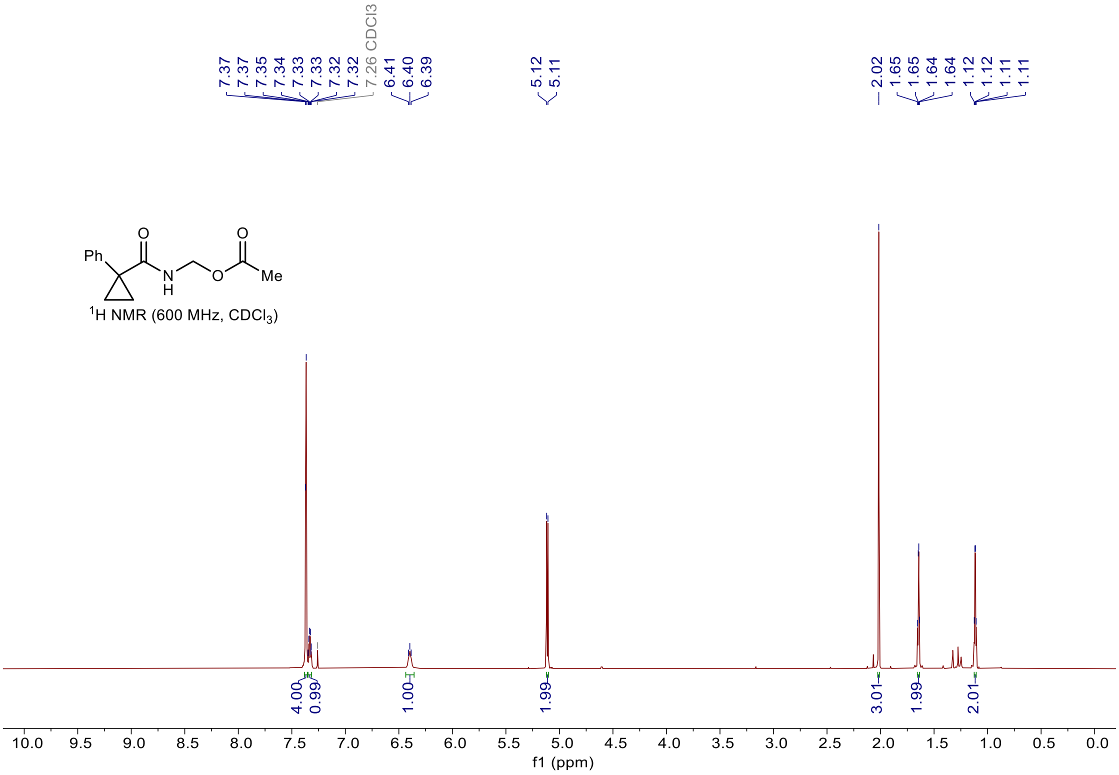


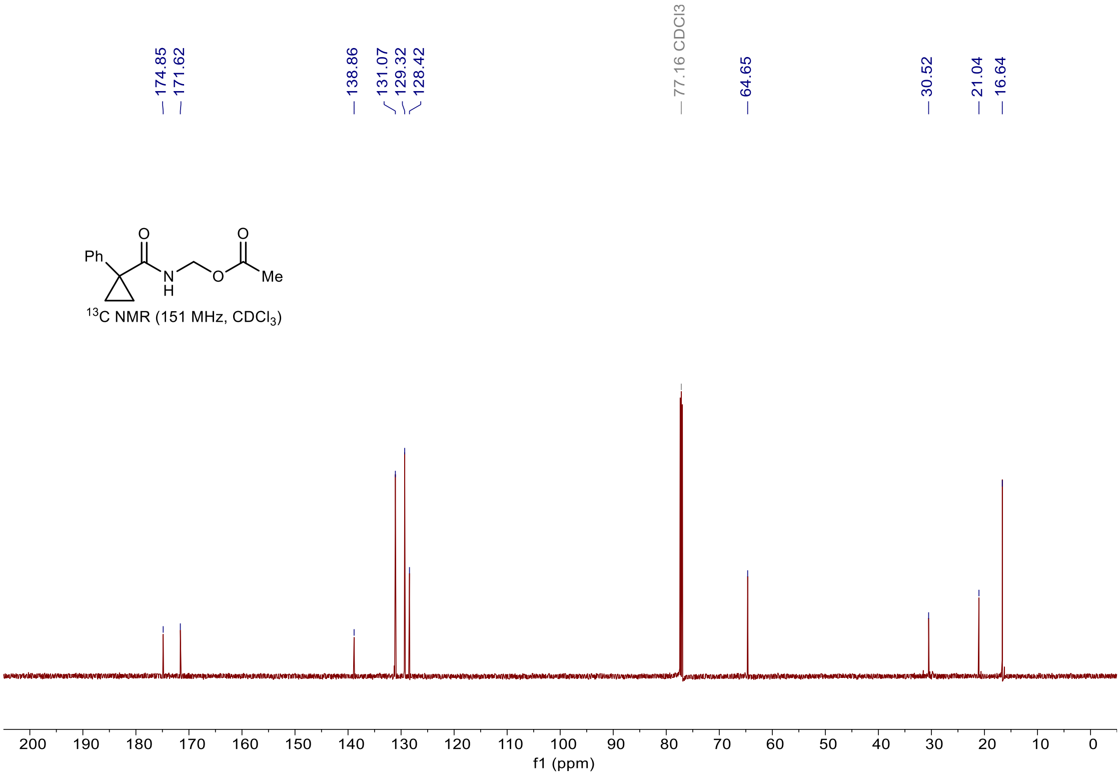
^{1}H and ^{13}C NMR spectra of compound 2o



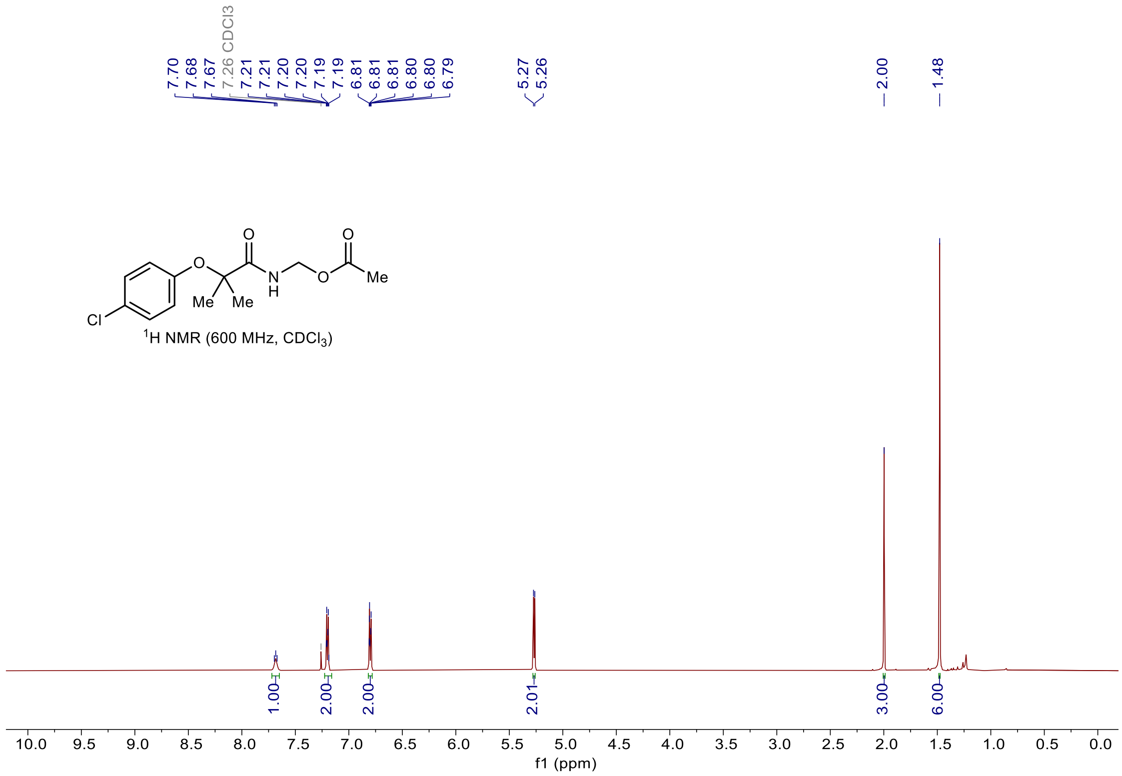


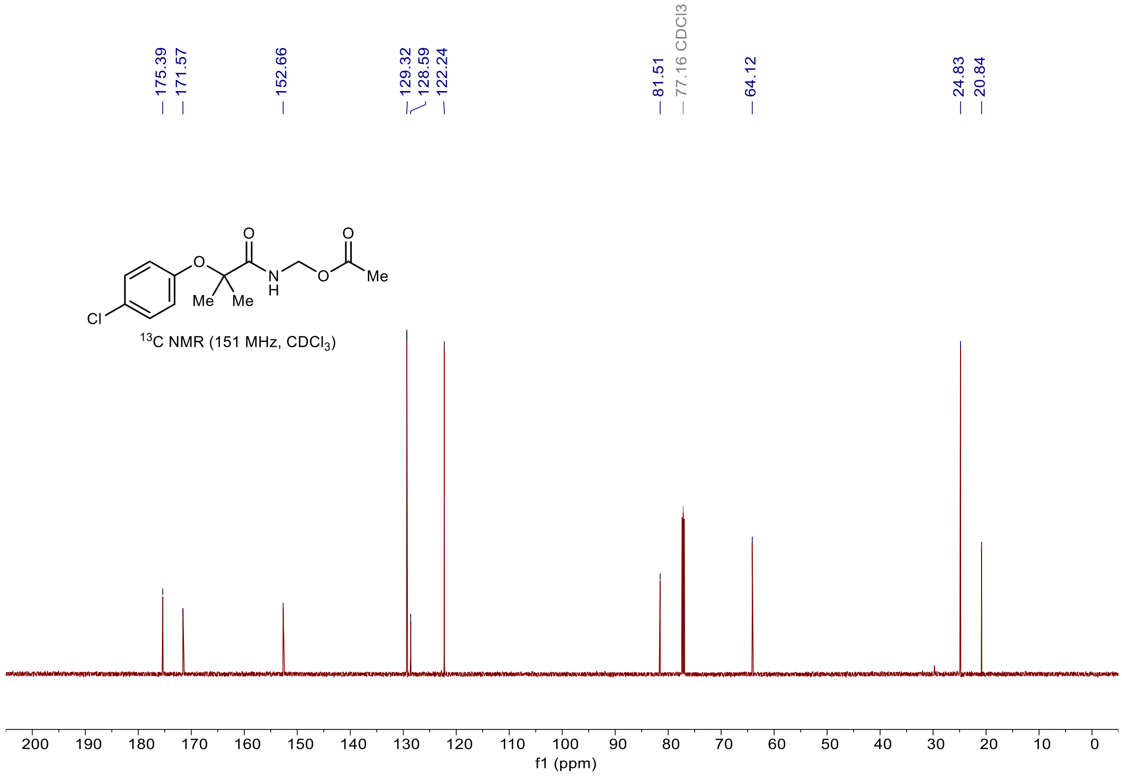
^{1}H and ^{13}C NMR spectra of compound 2p



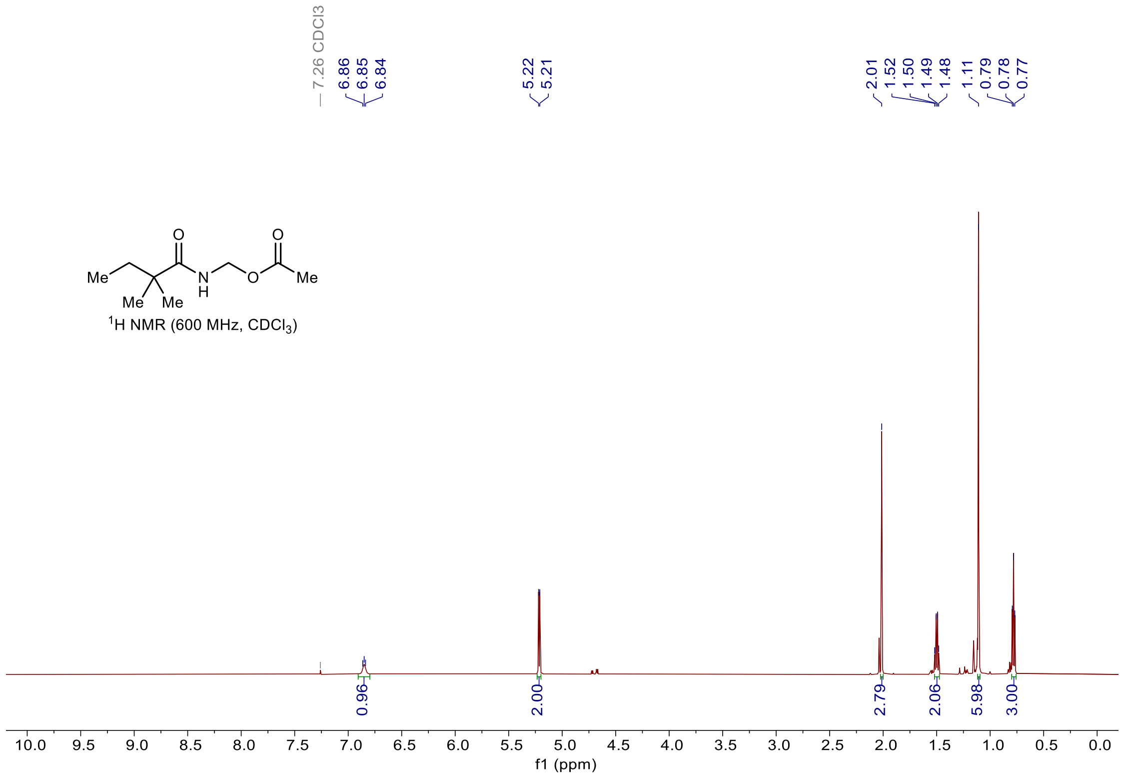


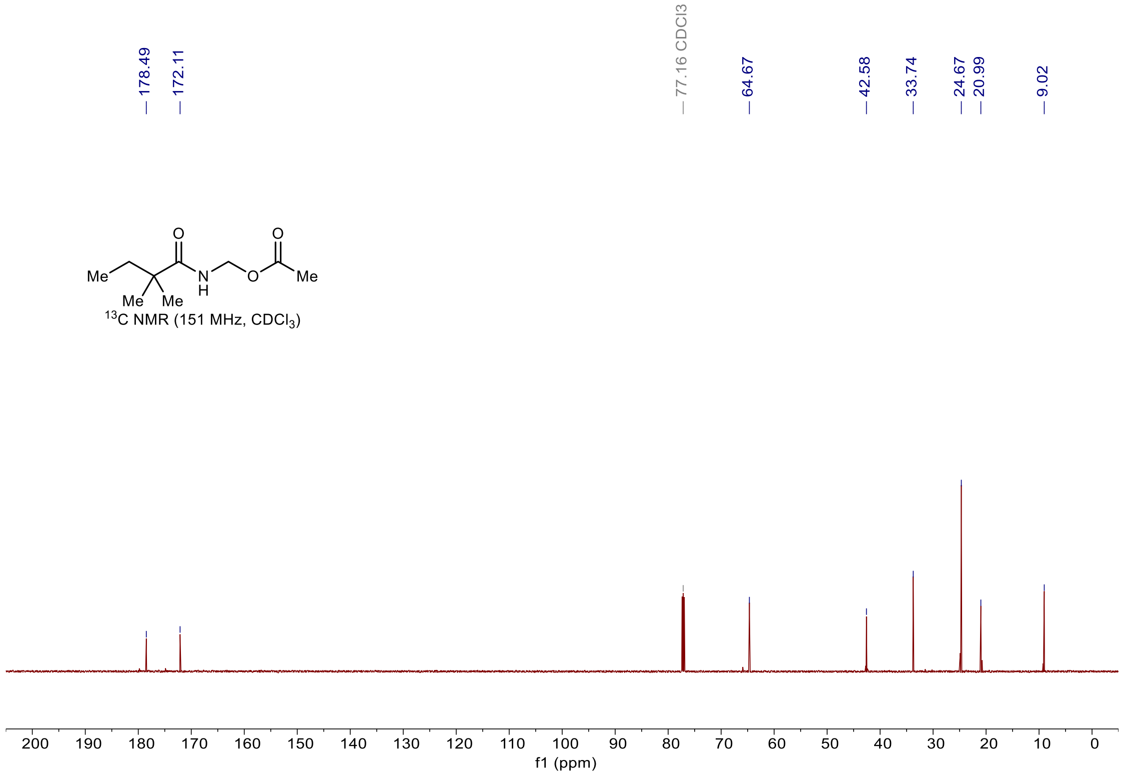
^{1}H and ^{13}C NMR spectra of compound 2q



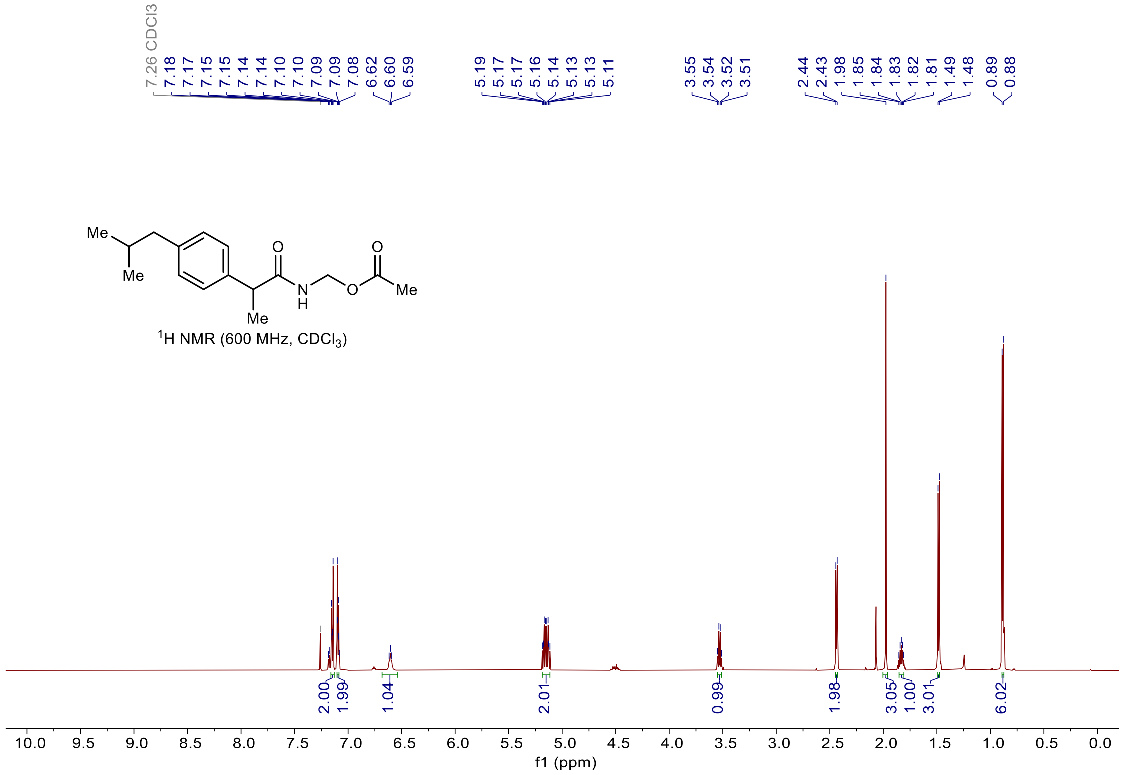


^{1}H and ^{13}C NMR spectra of compound 2r

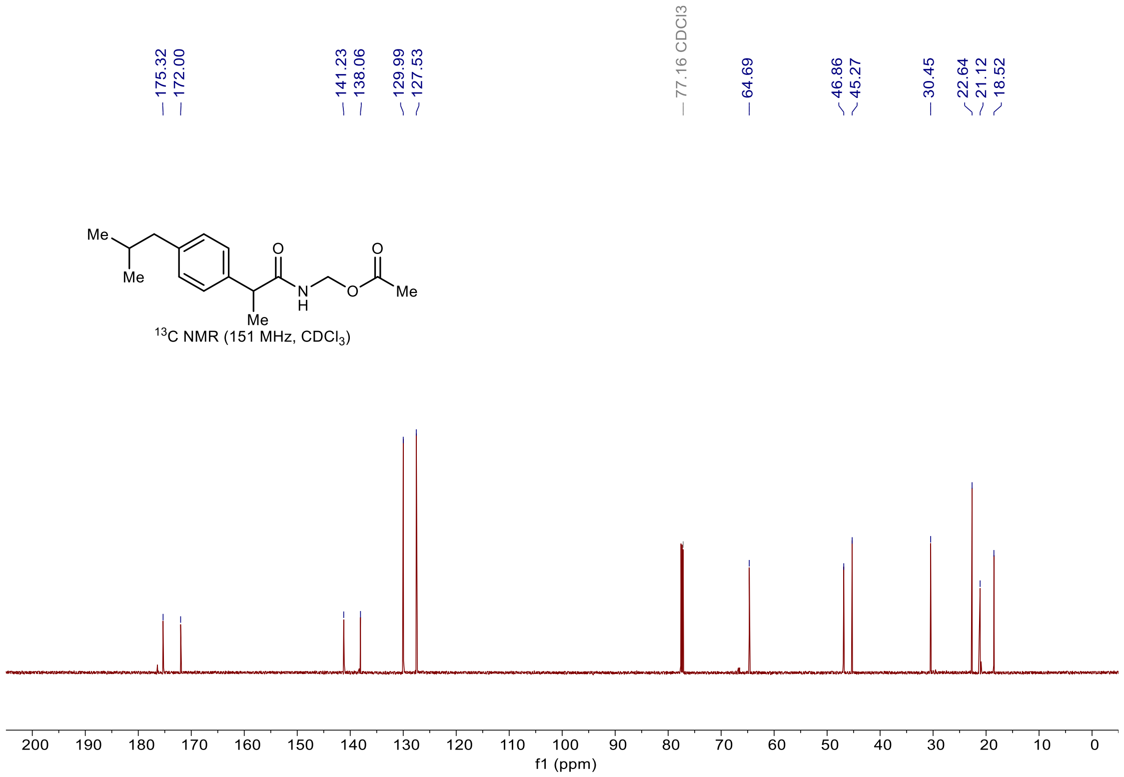




^{1}H and ^{13}C NMR spectra of compound 2s

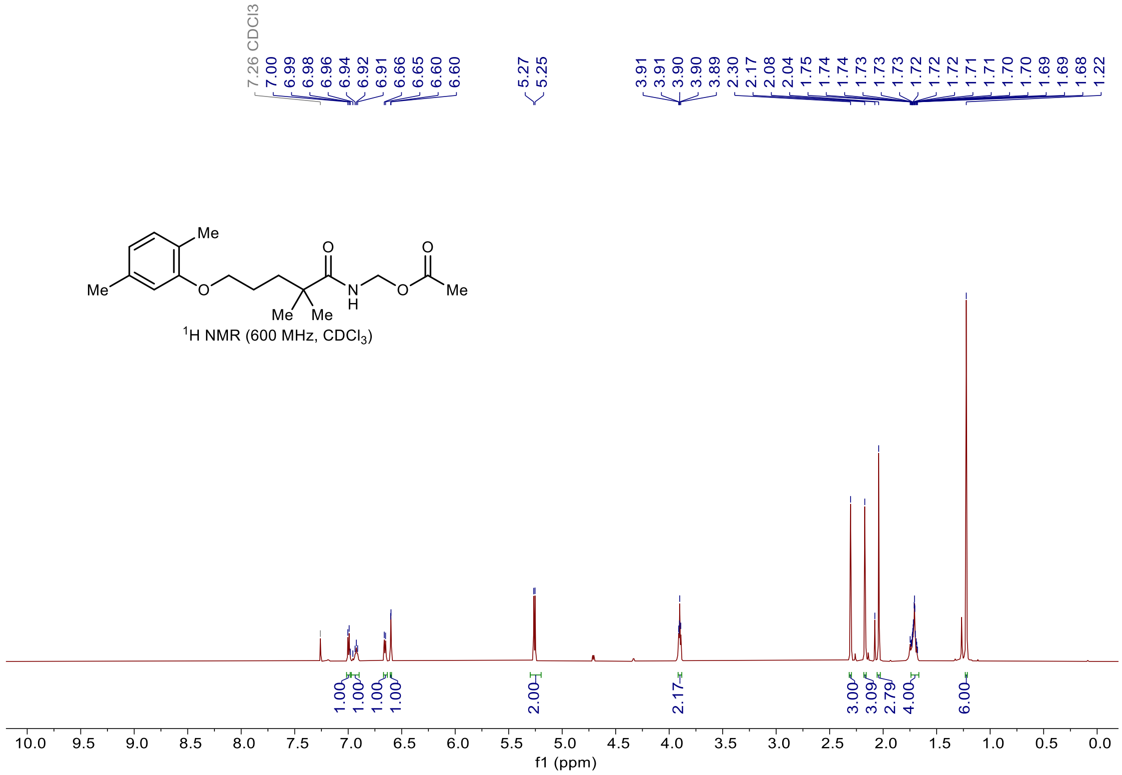


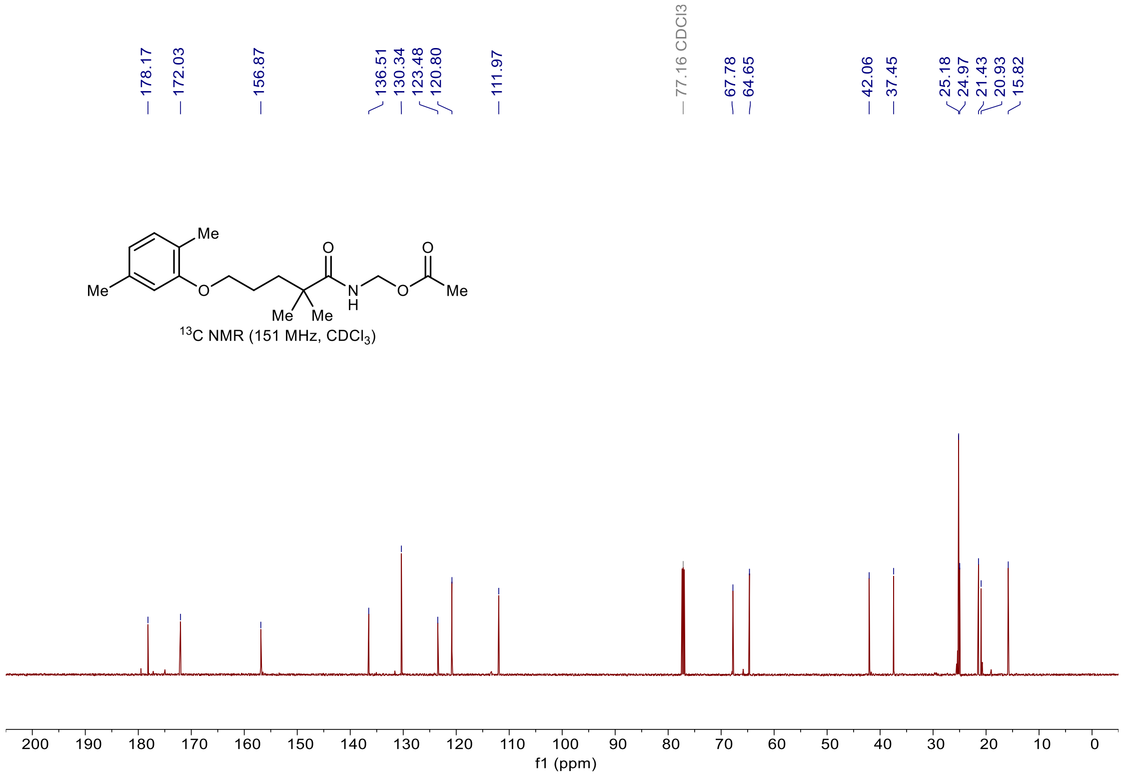
^{1}H NMR (600 MHz, CDCl$_3$)



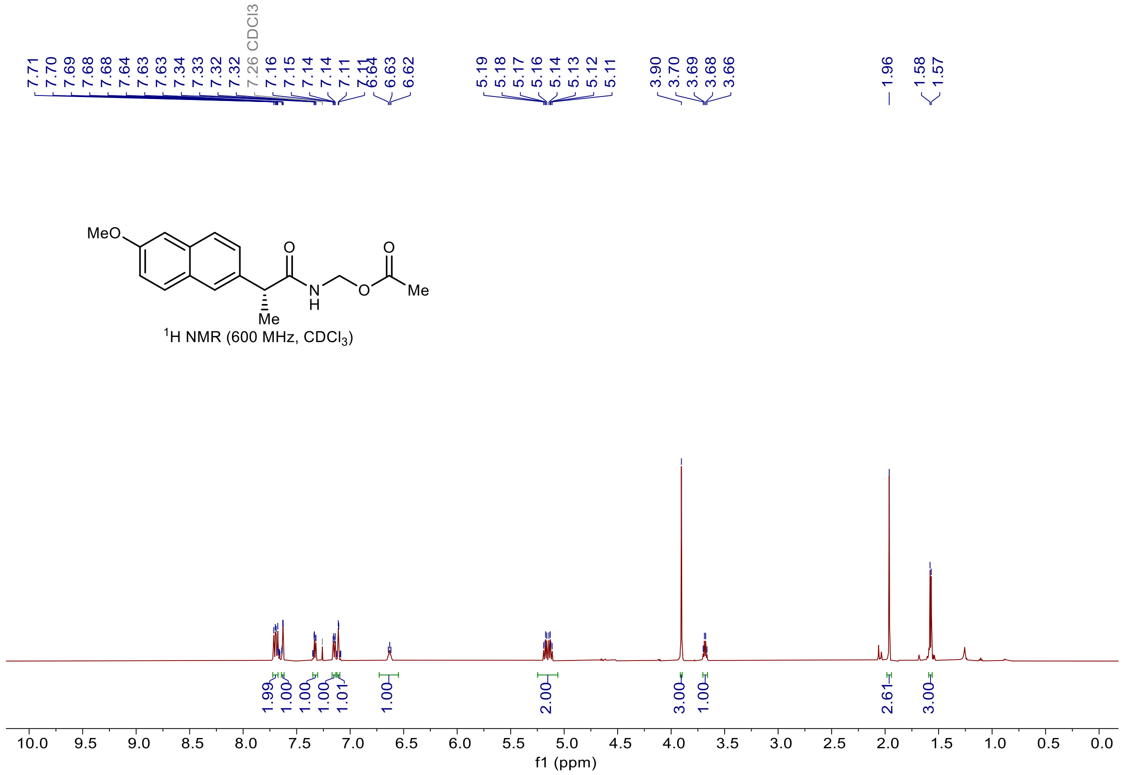
^{13}C NMR (151 MHz, CDCl$_3$)

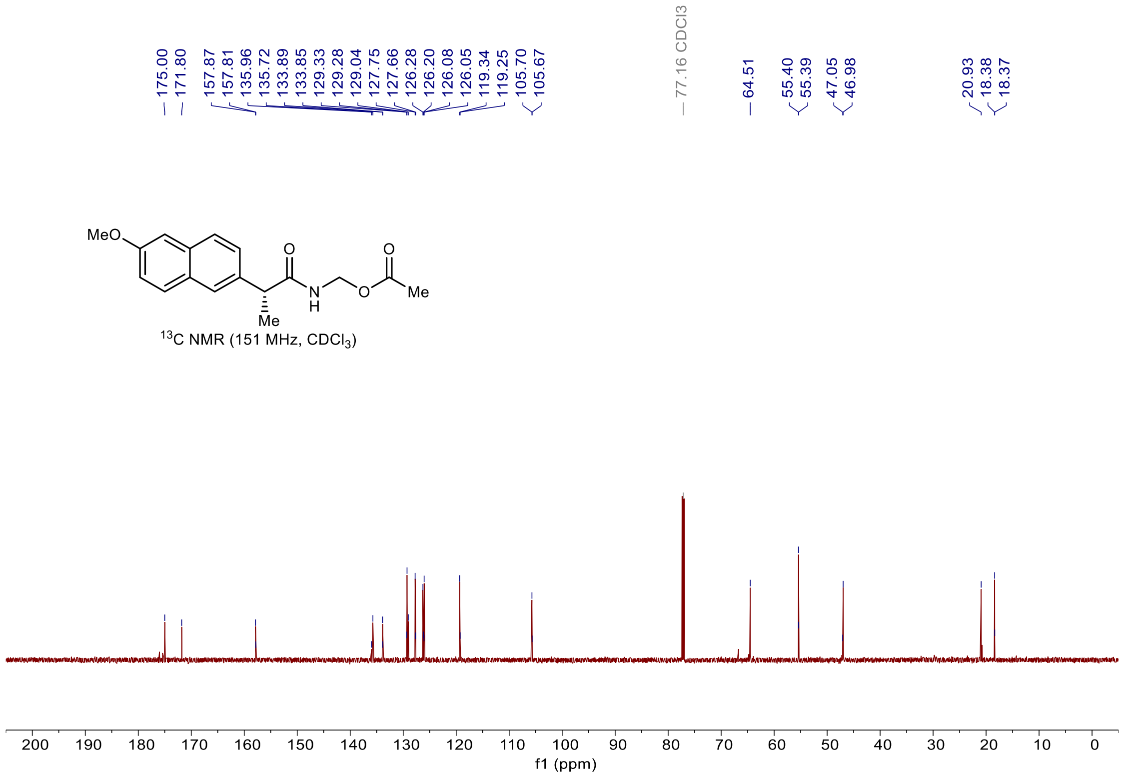
^{1}H and ^{13}C NMR spectra of compound 2t



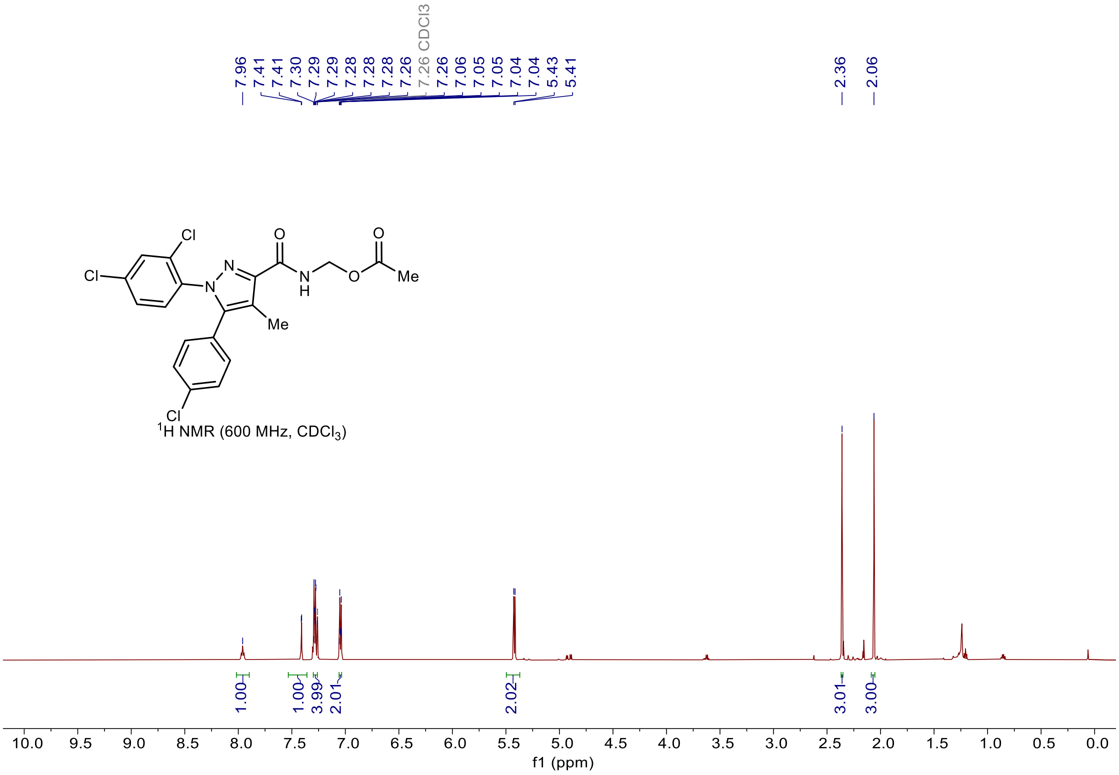


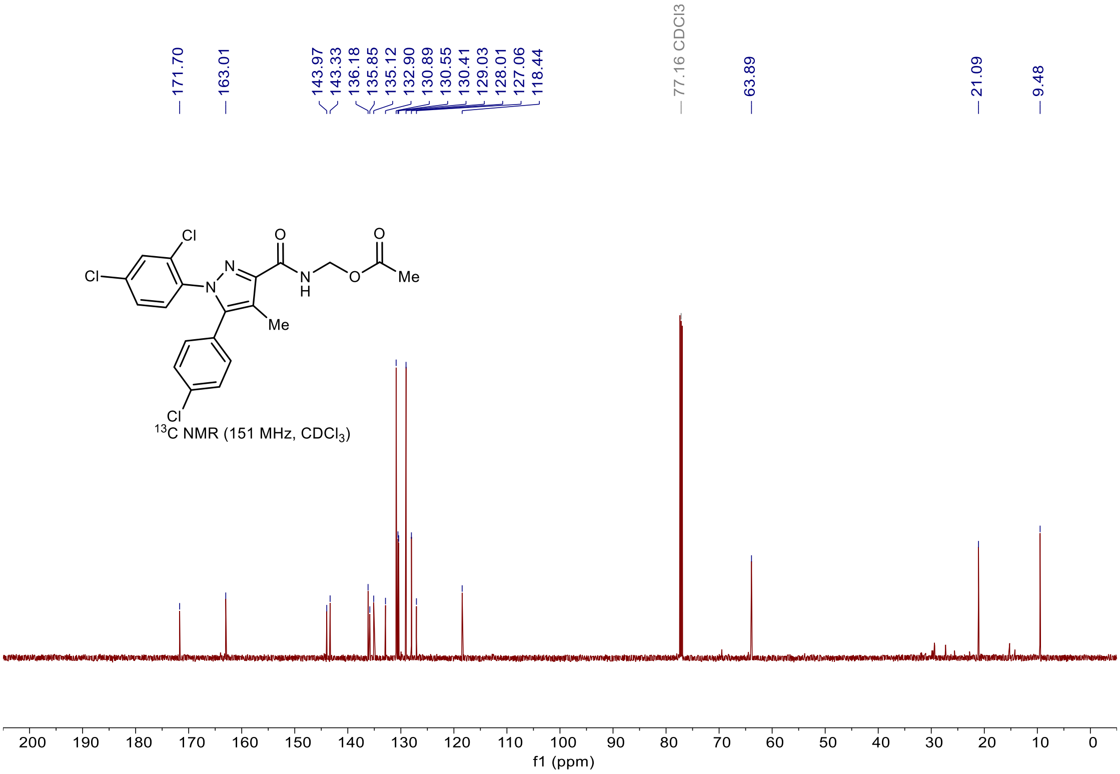
^{1}H and ^{13}C NMR spectra of compound 2u



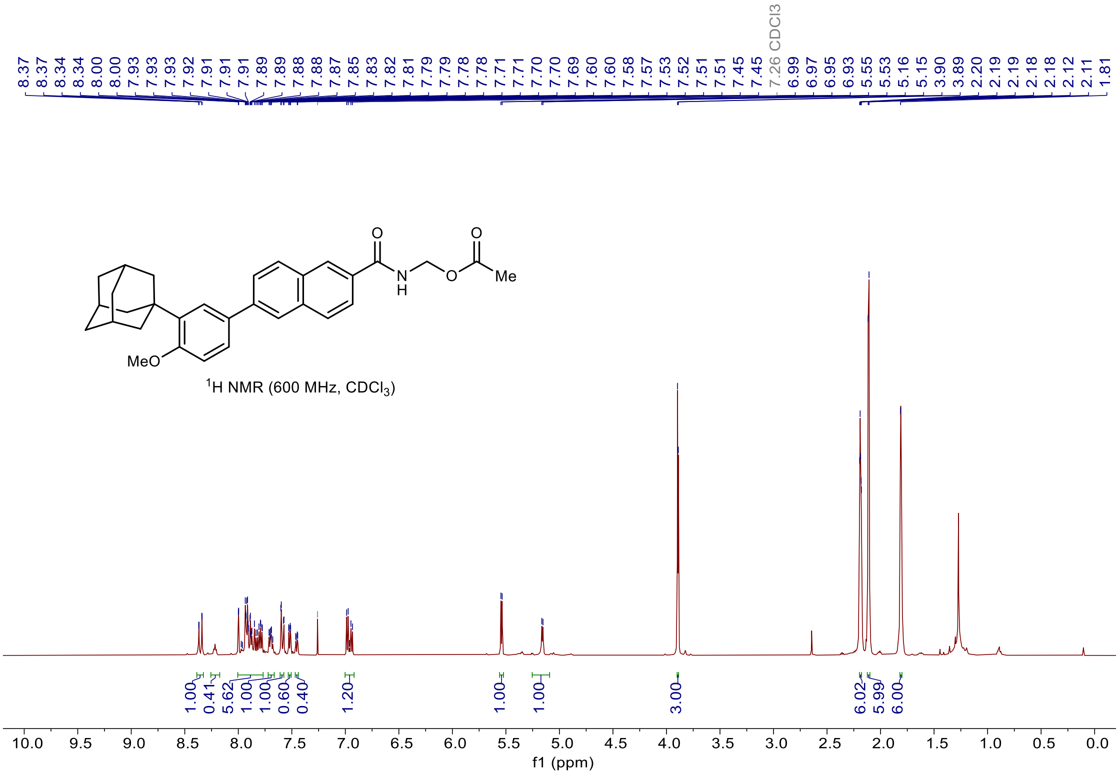


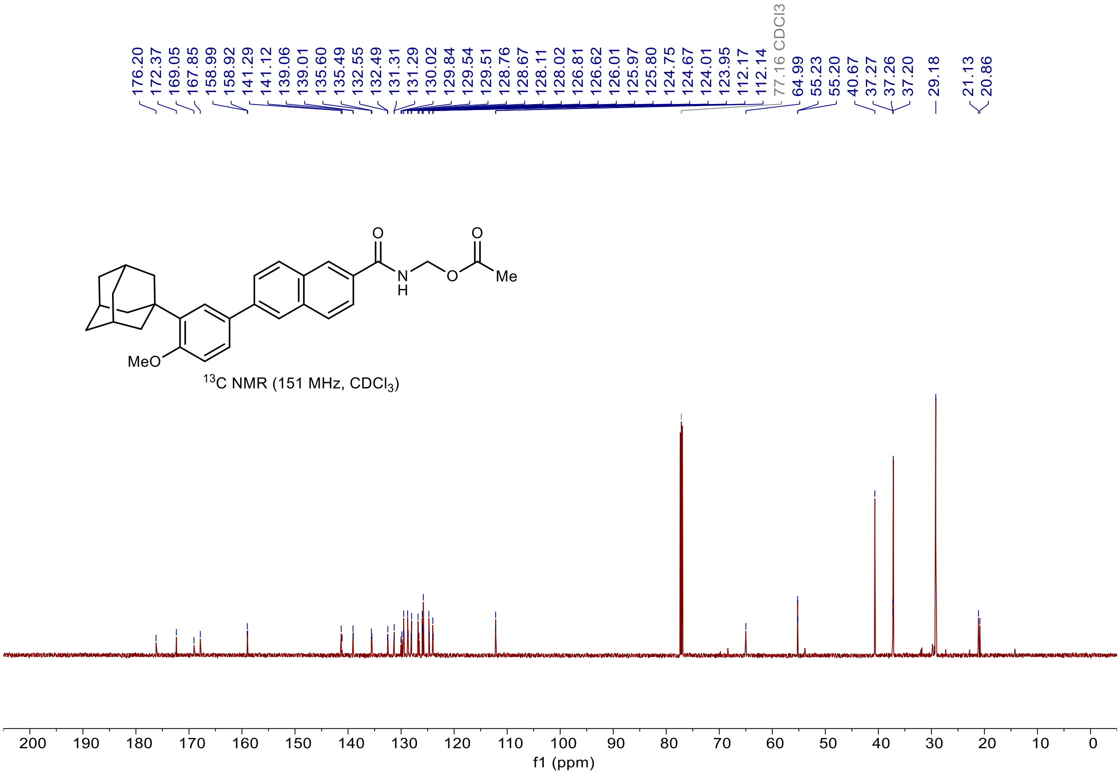
^{1}H and ^{13}C NMR spectra of compound 2v



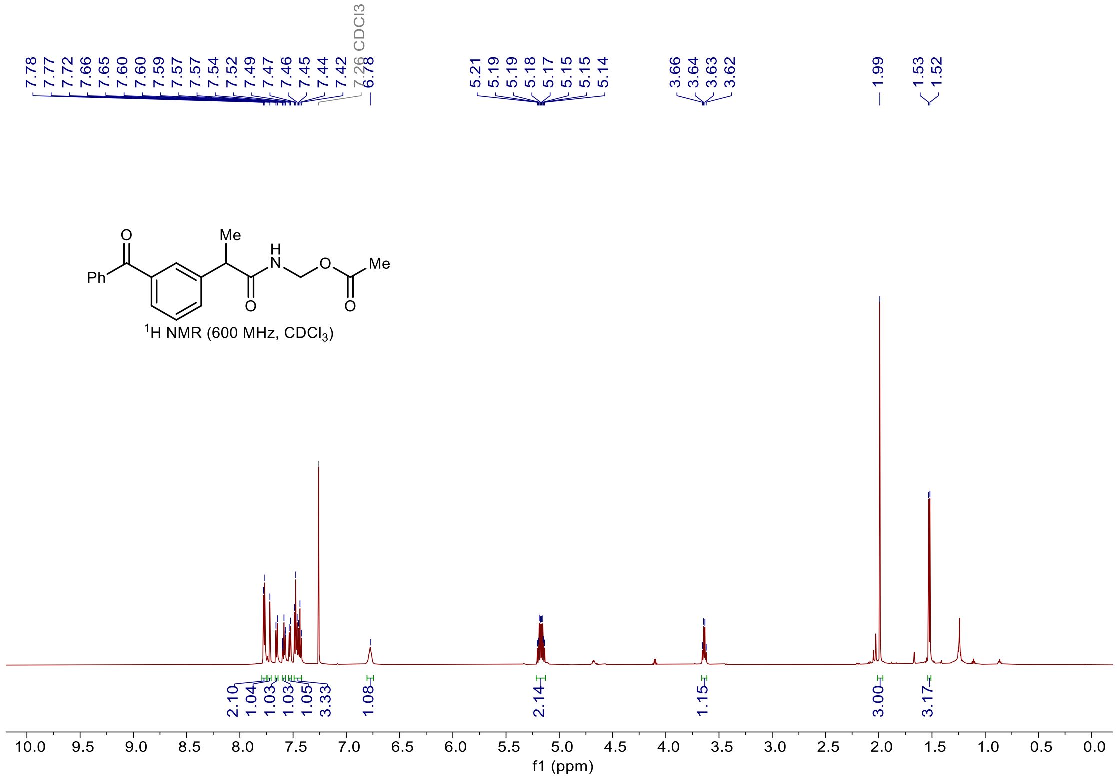


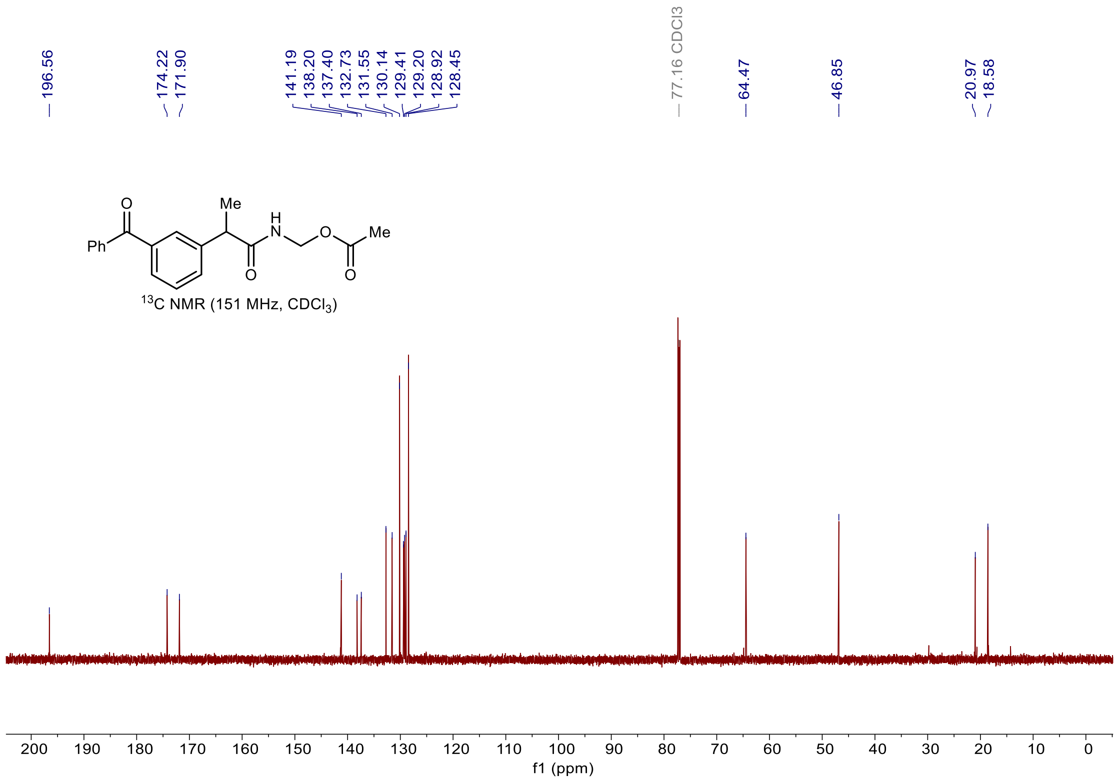
^{1}H and ^{13}C NMR spectra of compound 2w



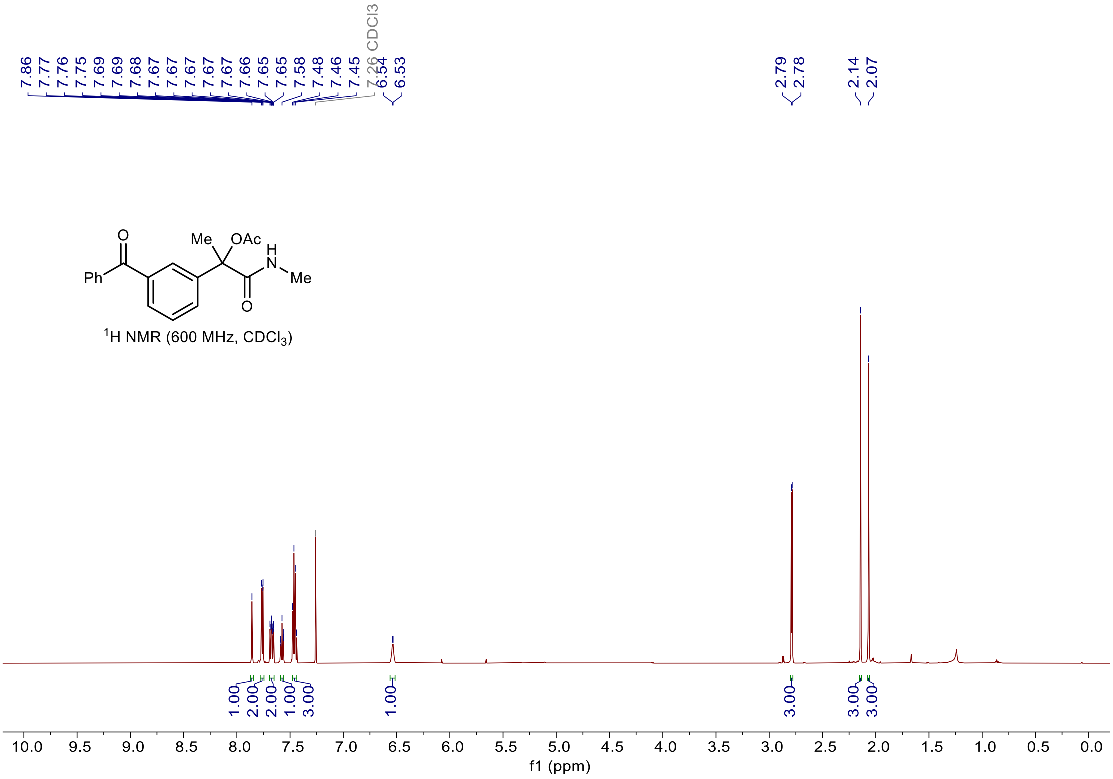


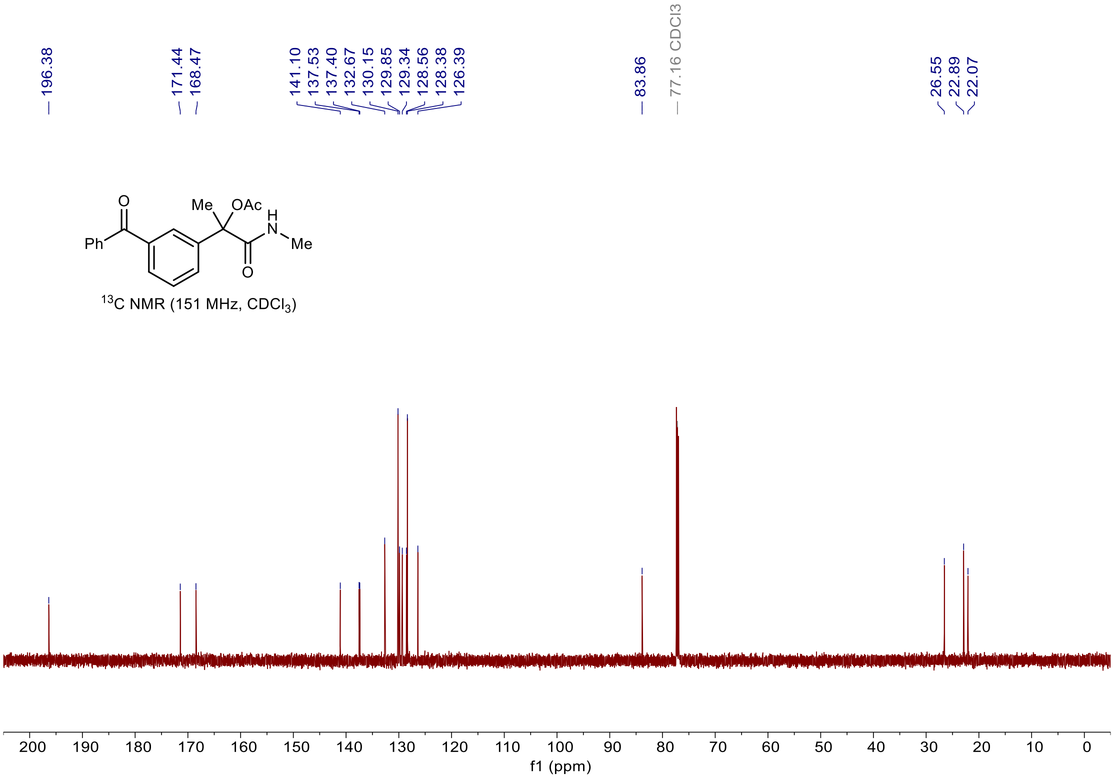
^{1}H and ^{13}C NMR spectra of compound 2x



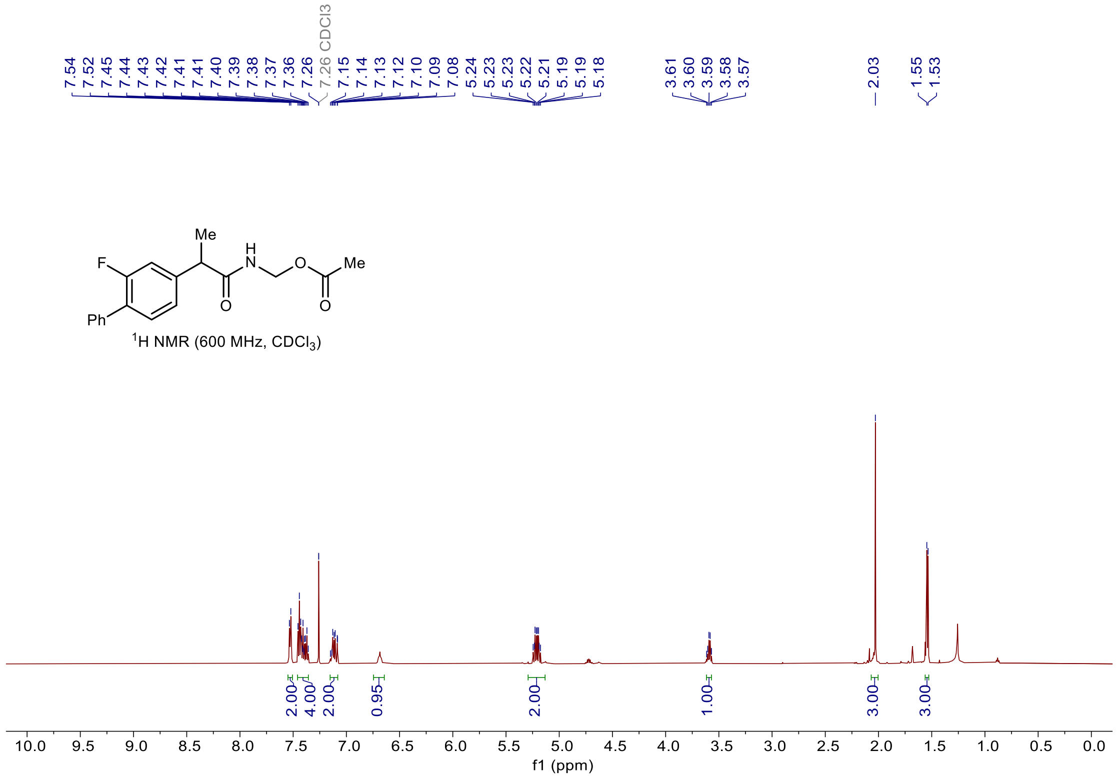


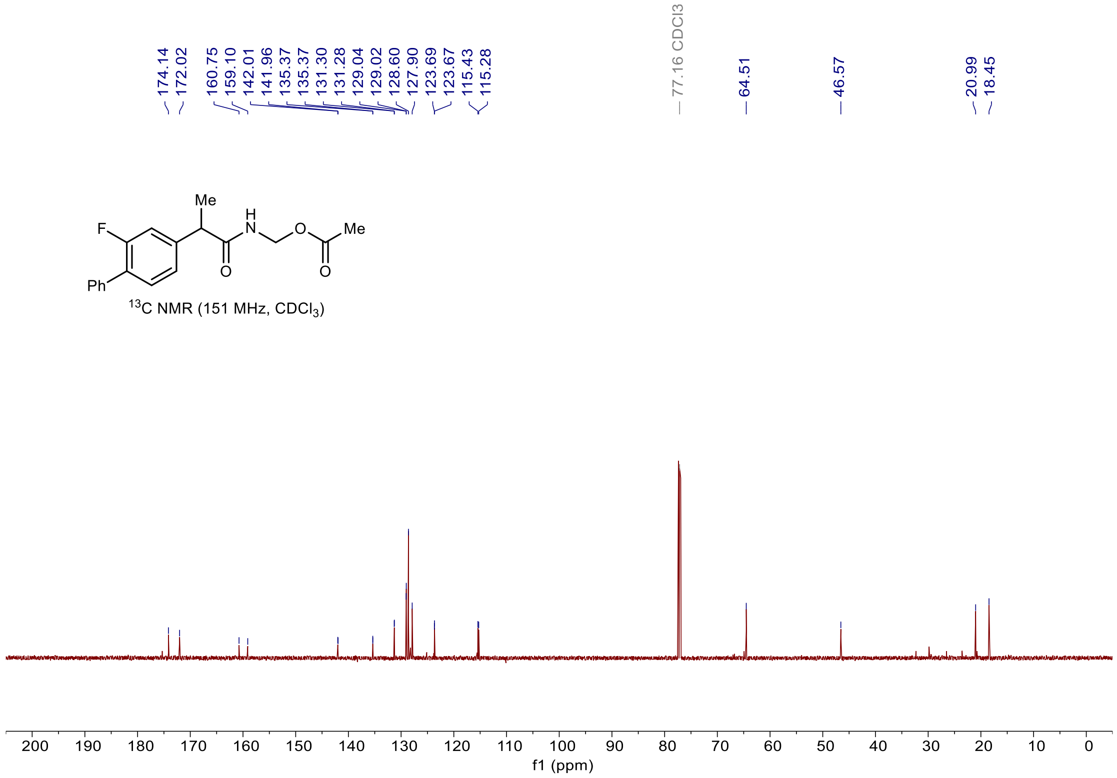
^{1}H and ^{13}C NMR spectra of compound 2x'

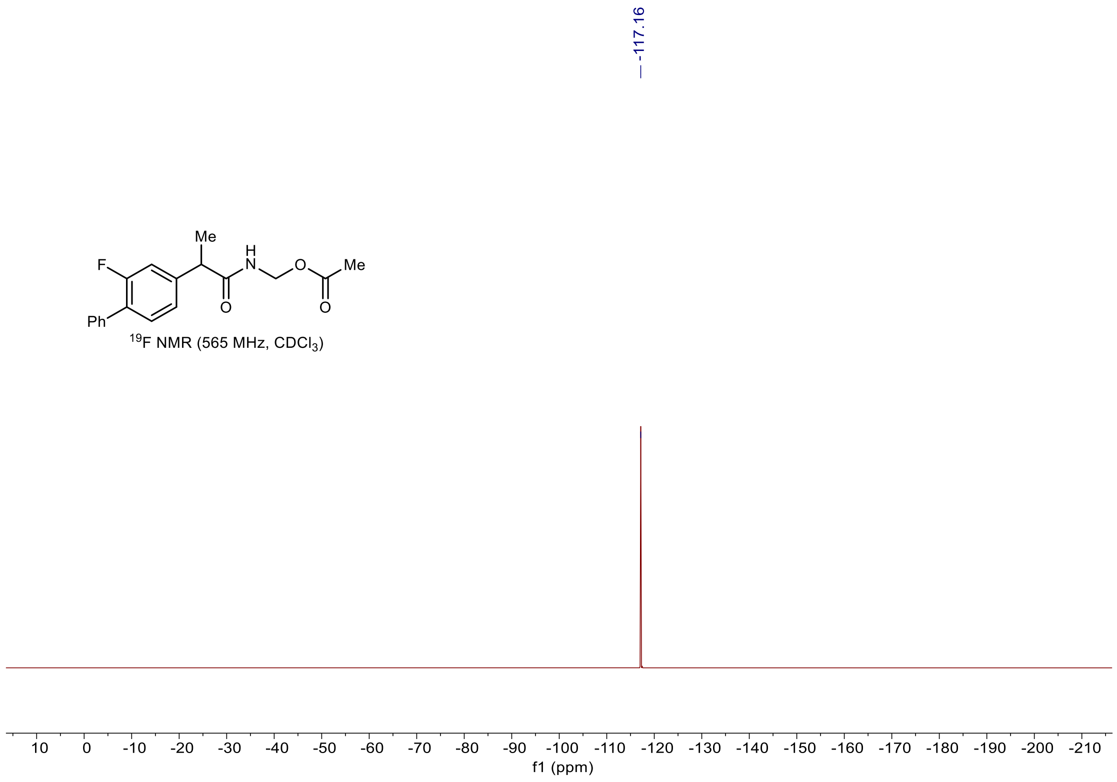




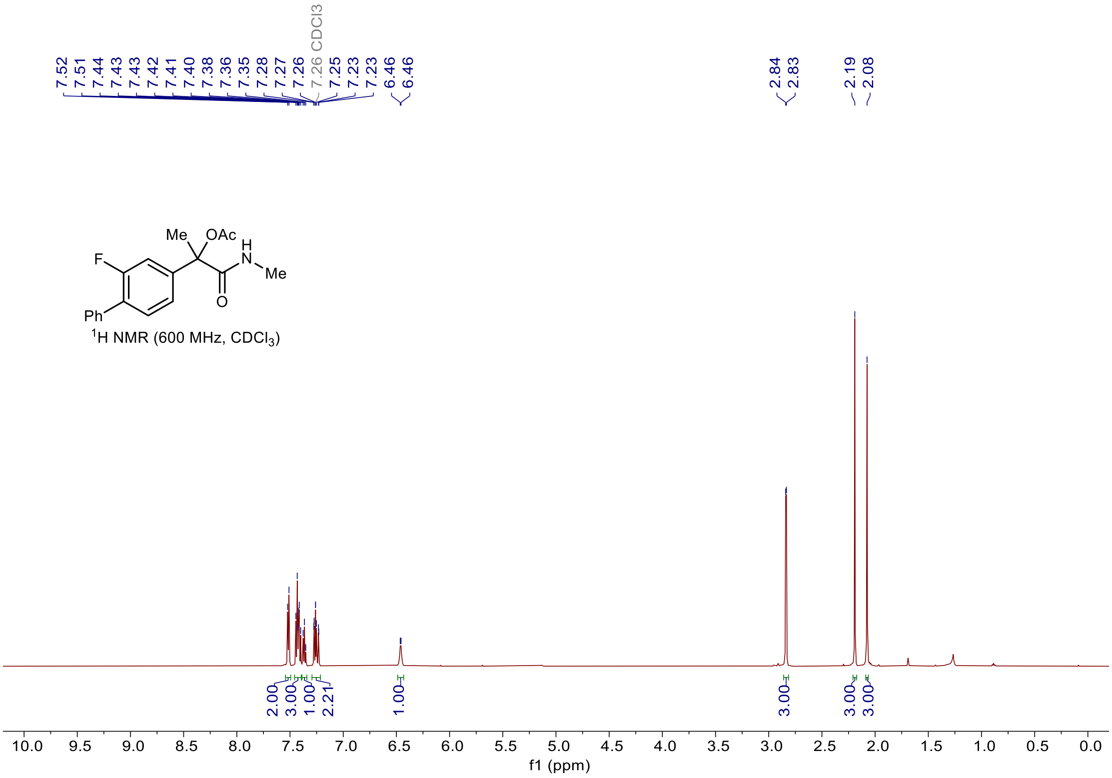
^{1}H, ^{13}C and ^{19}F NMR spectra of compound 2y

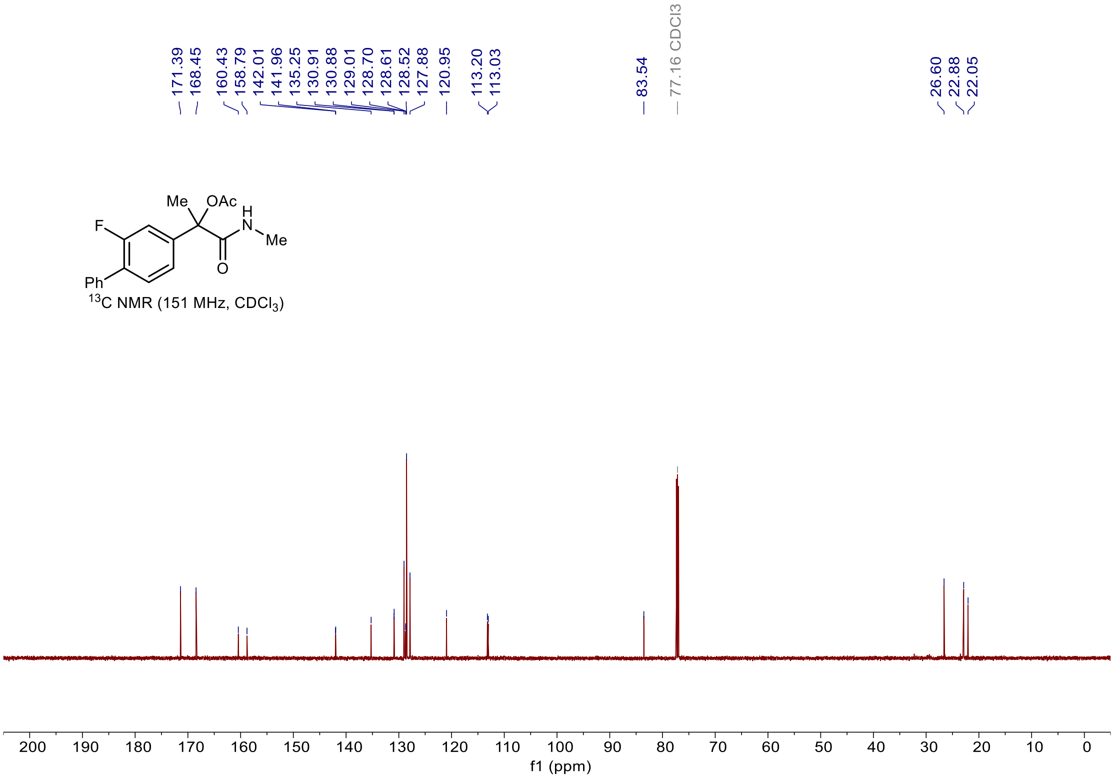


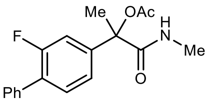



-117.16
Me
F
H
N
O
Me
Ph
O
O
^{19}F NMR (565 MHz, CDCl$_3$)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

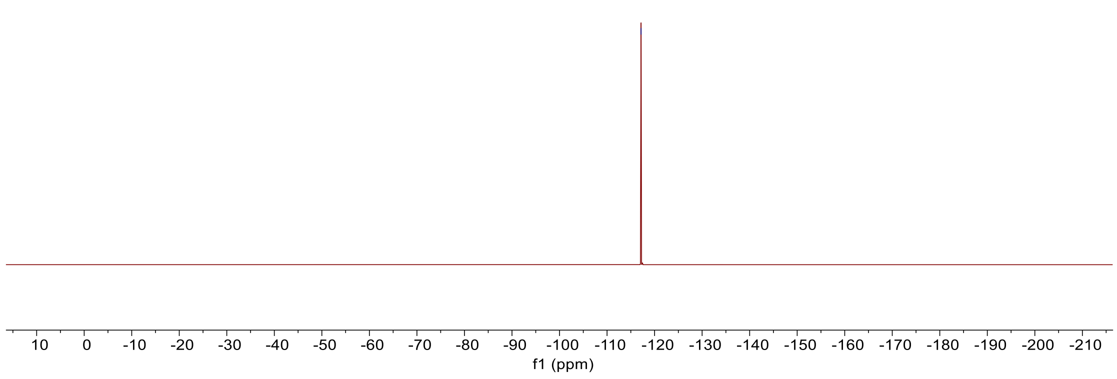
^{1}H, ^{13}C and ^{19}F NMR spectra of compound 2y'



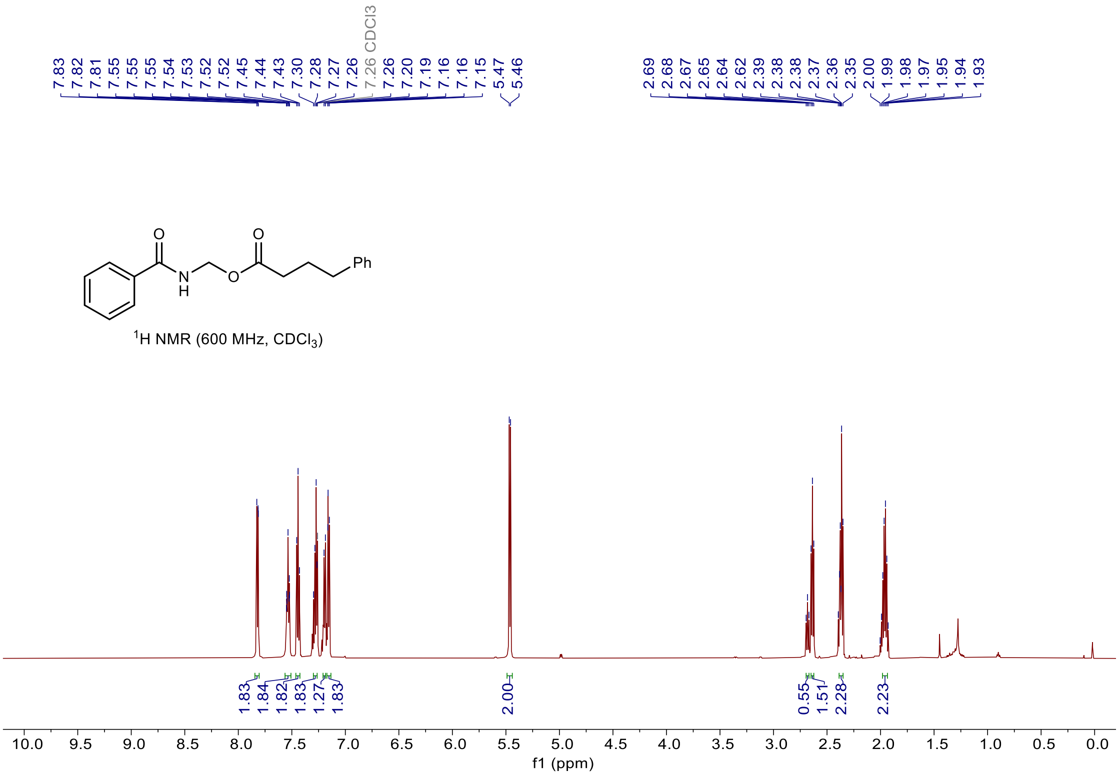


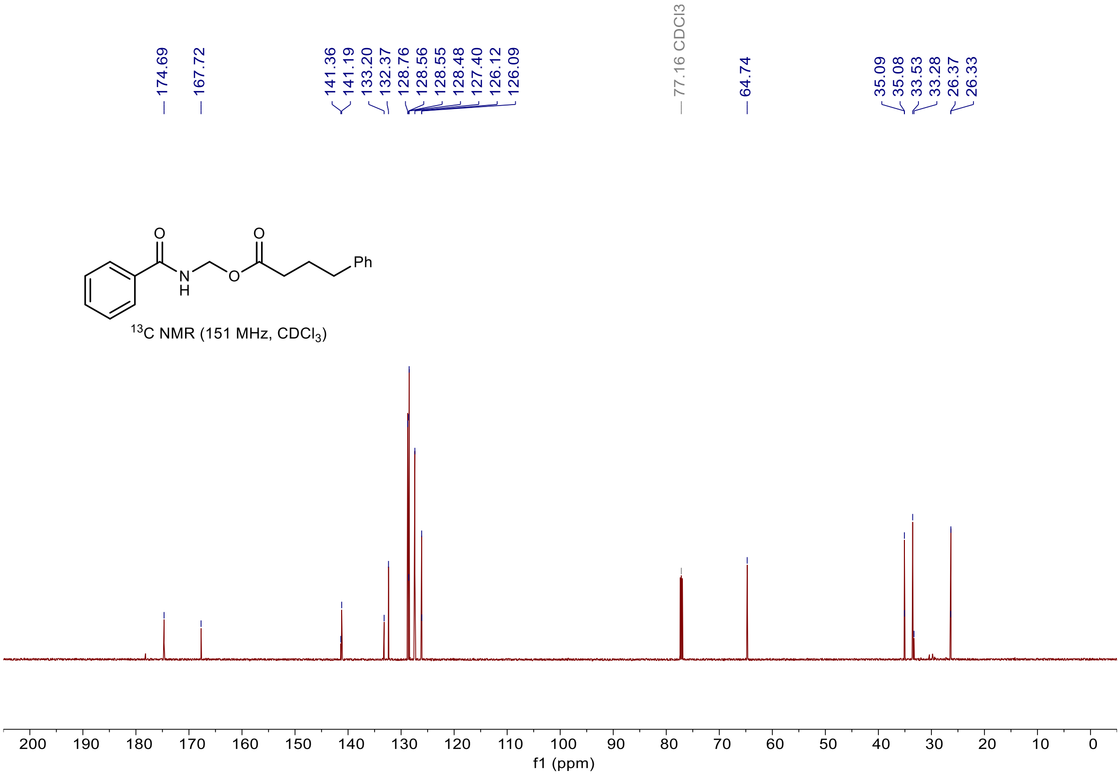


^{19}F NMR (565 MHz, CDCl$_3$)

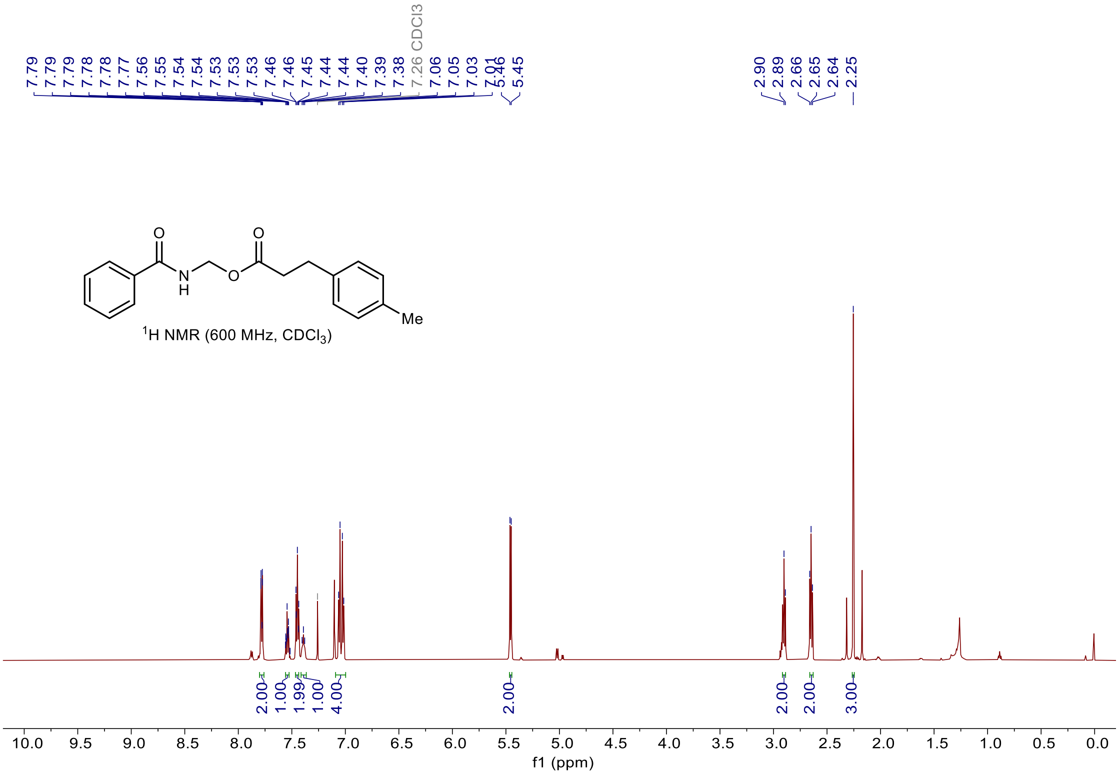


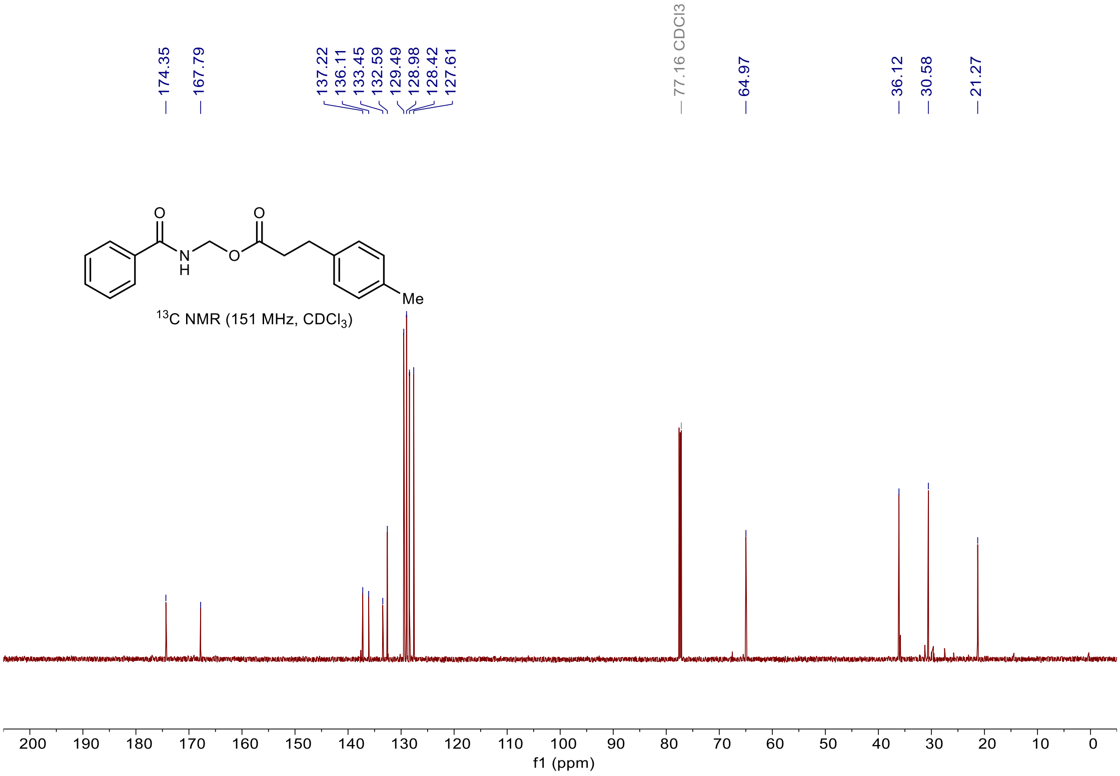
^{1}H and ^{13}C NMR spectra of compound 3a



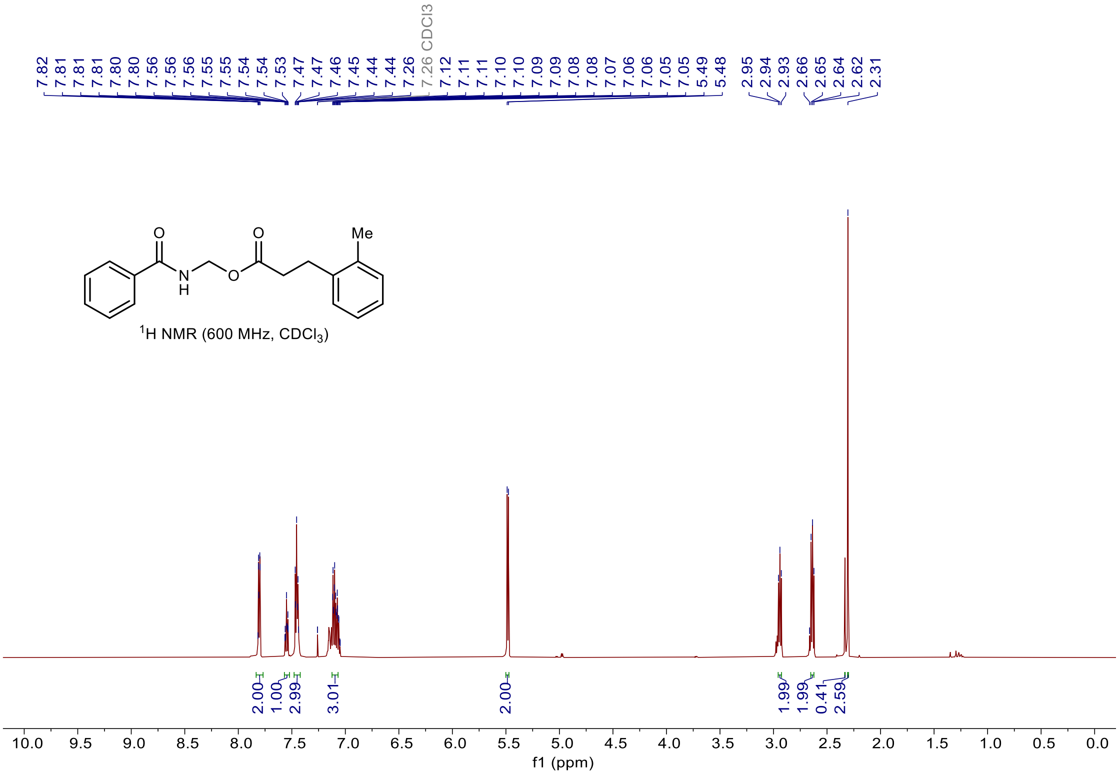


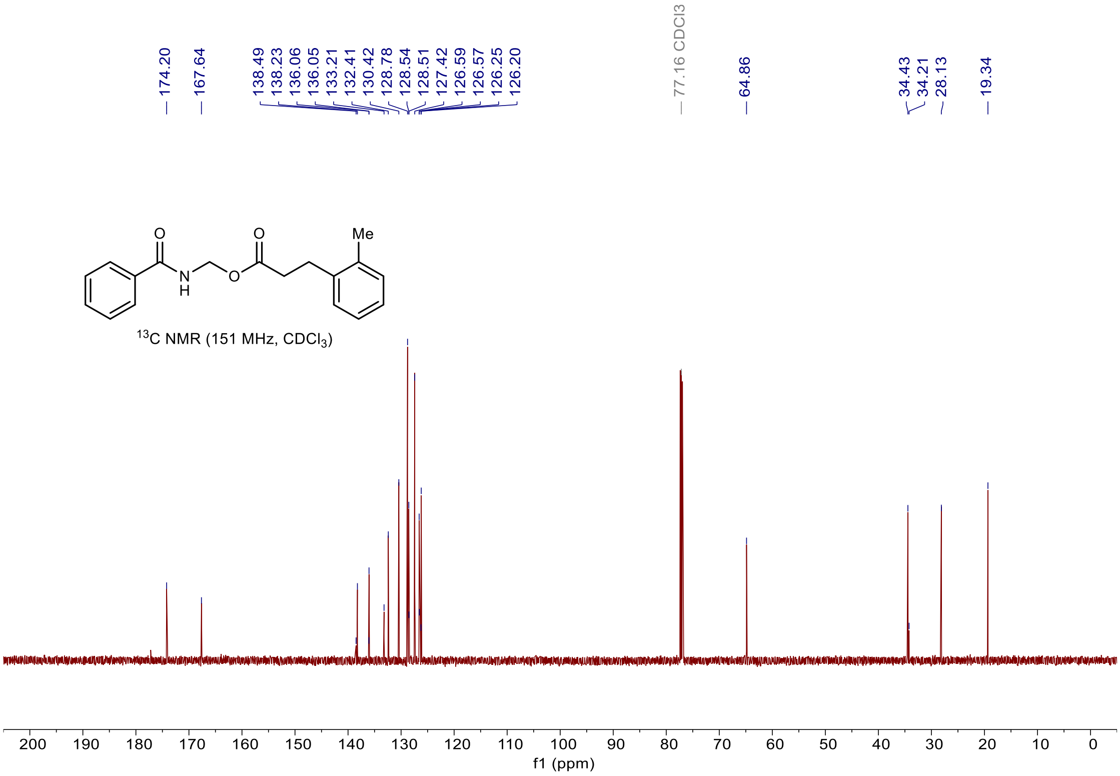
^{1}H and ^{13}C NMR spectra of compound 3b



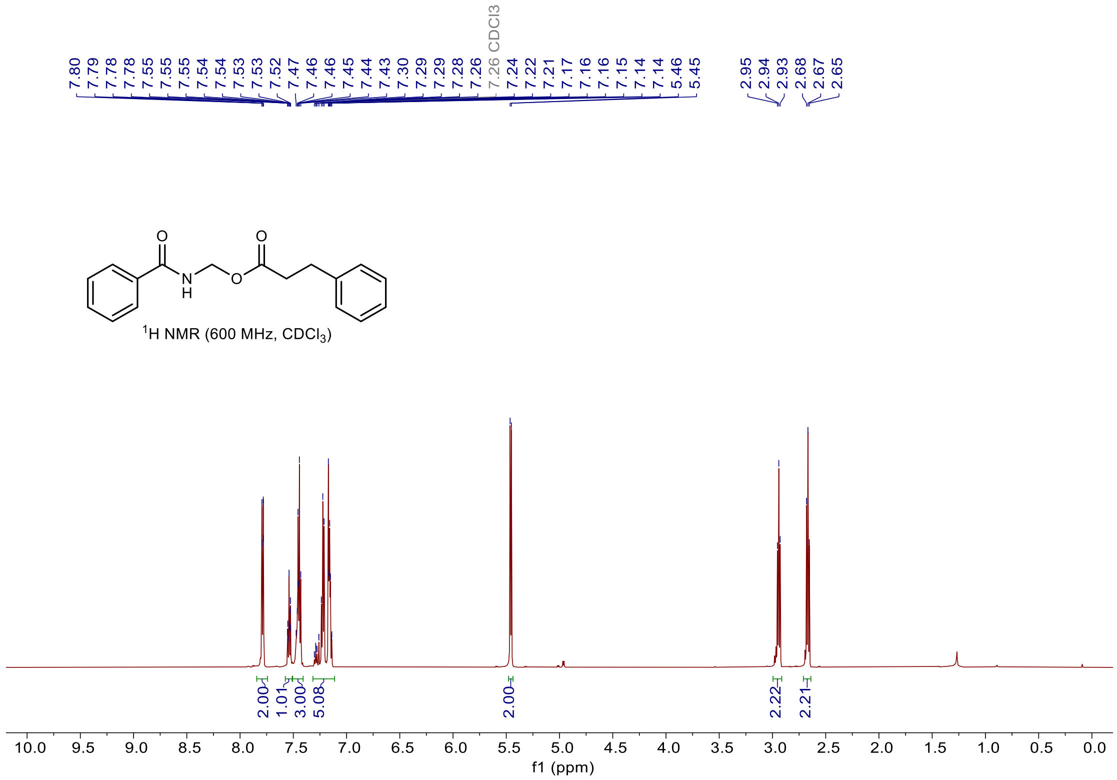


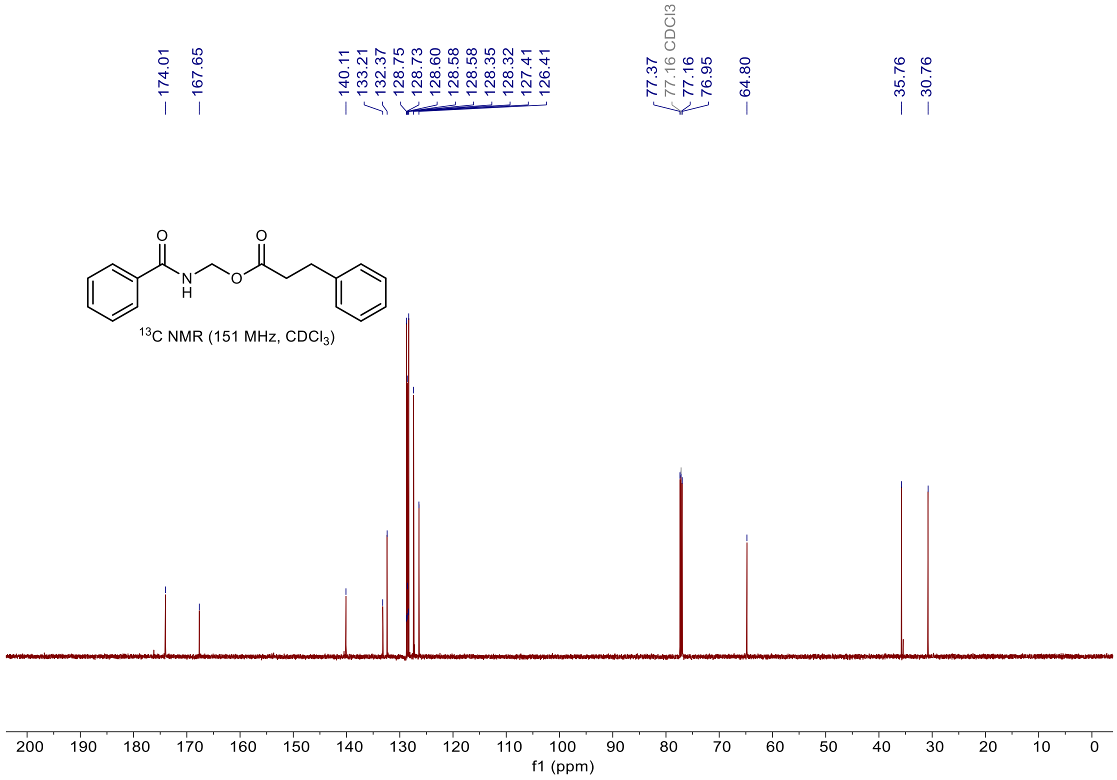
^{1}H and ^{13}C NMR spectra of compound 3c



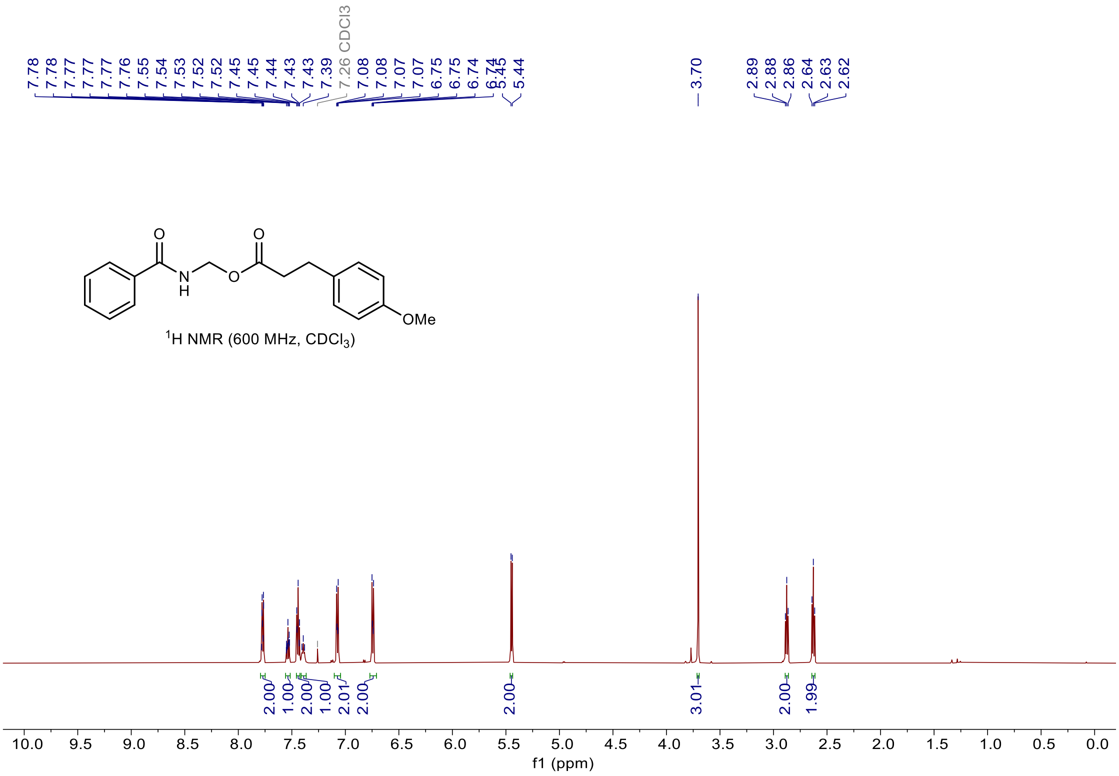


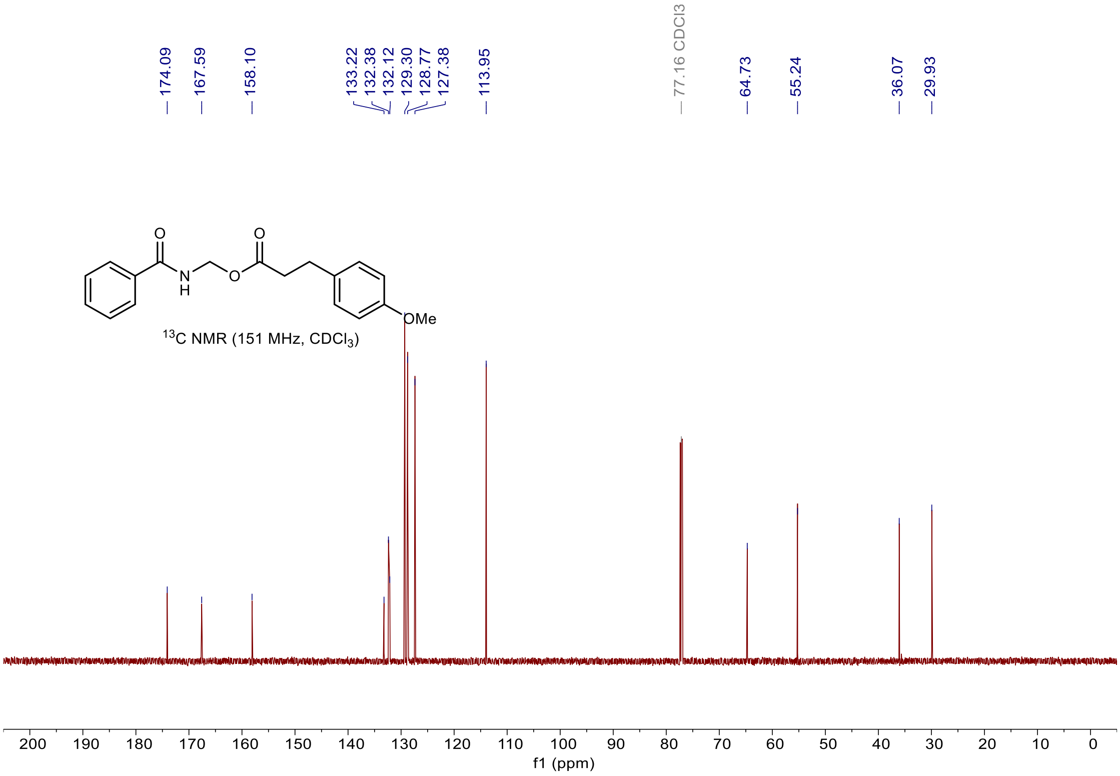
^{1}H and ^{13}C NMR spectra of compound 3d



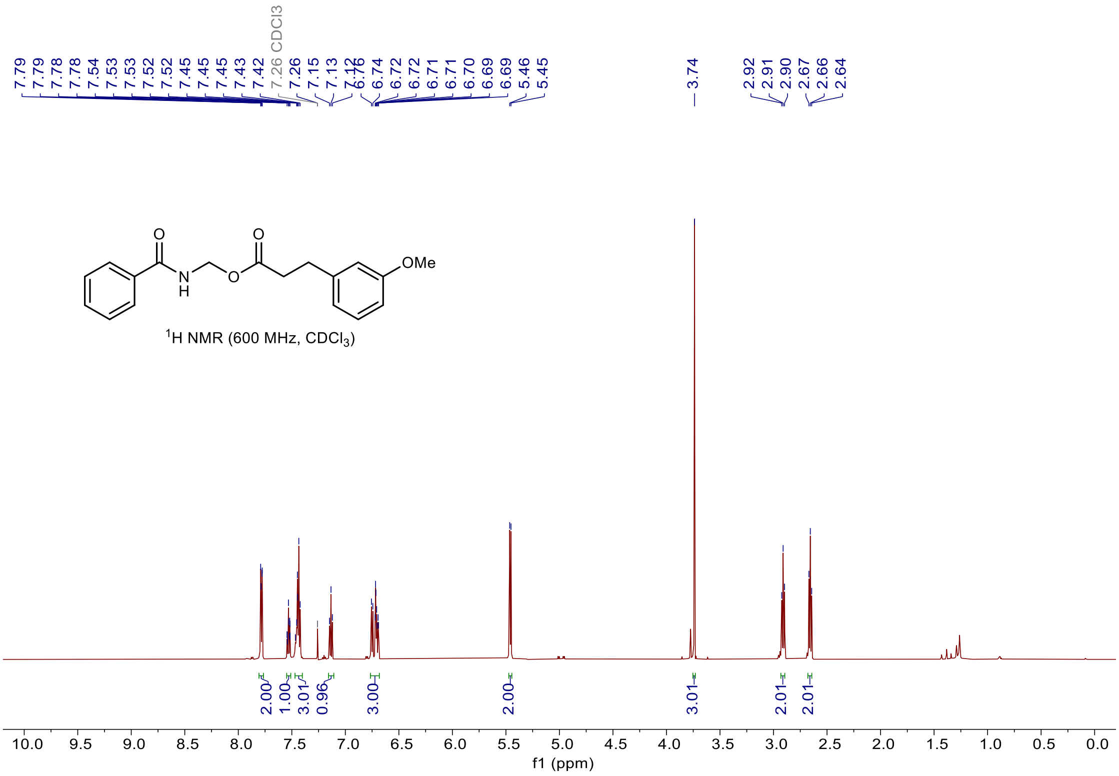


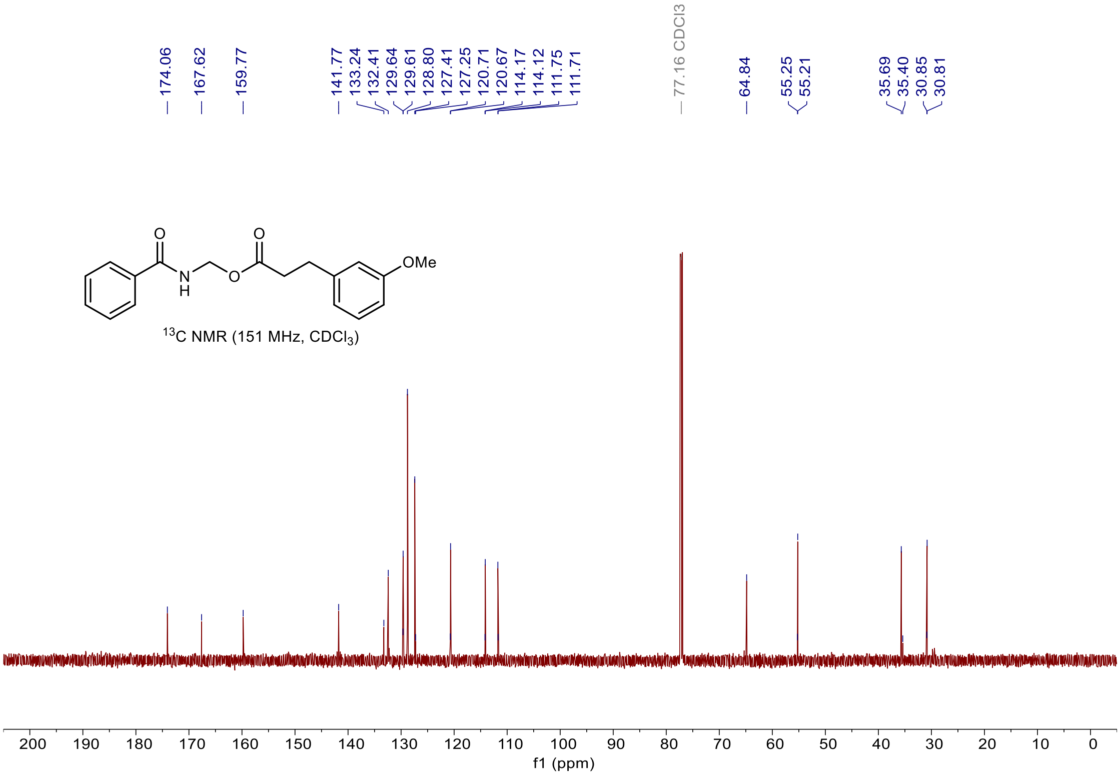
^{1}H and ^{13}C NMR spectra of compound 3e



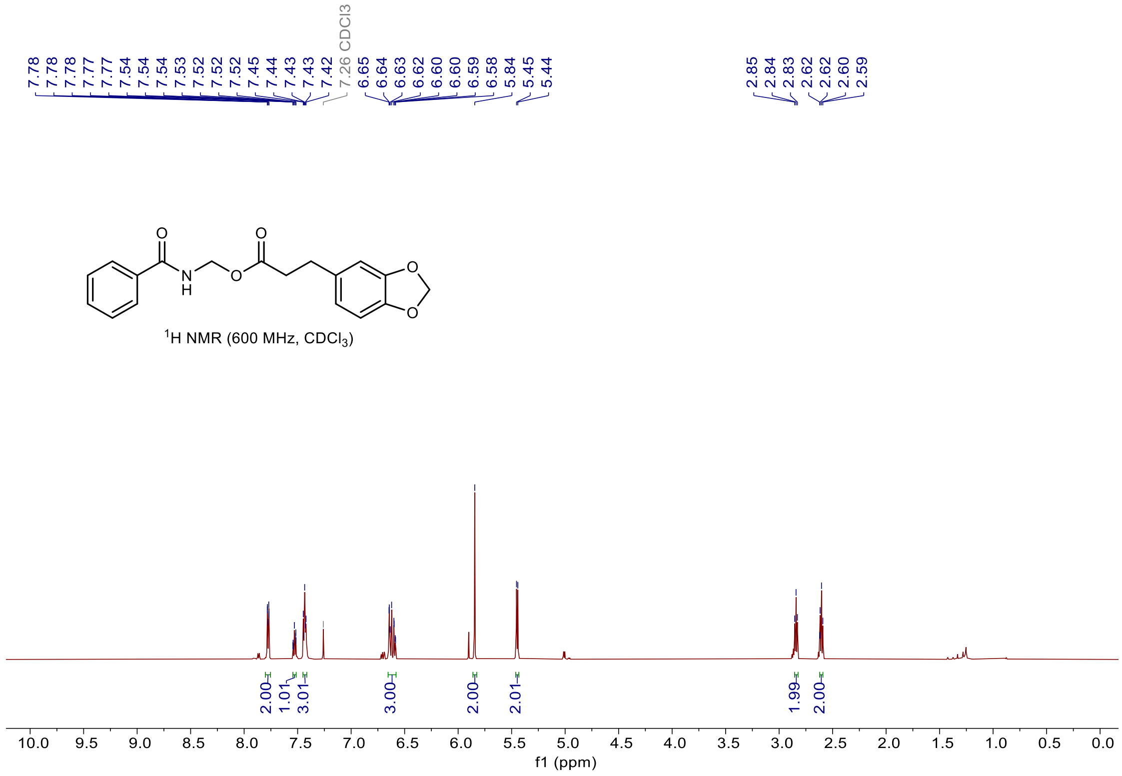


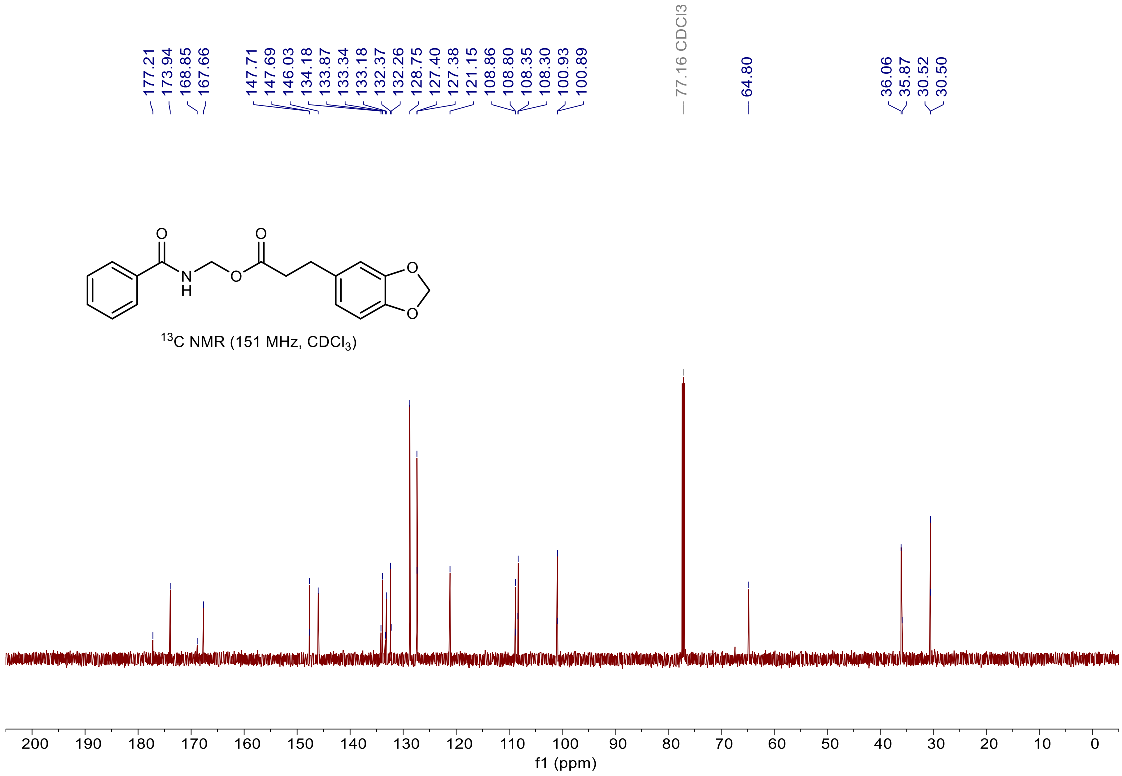
^{1}H and ^{13}C NMR spectra of compound 3f



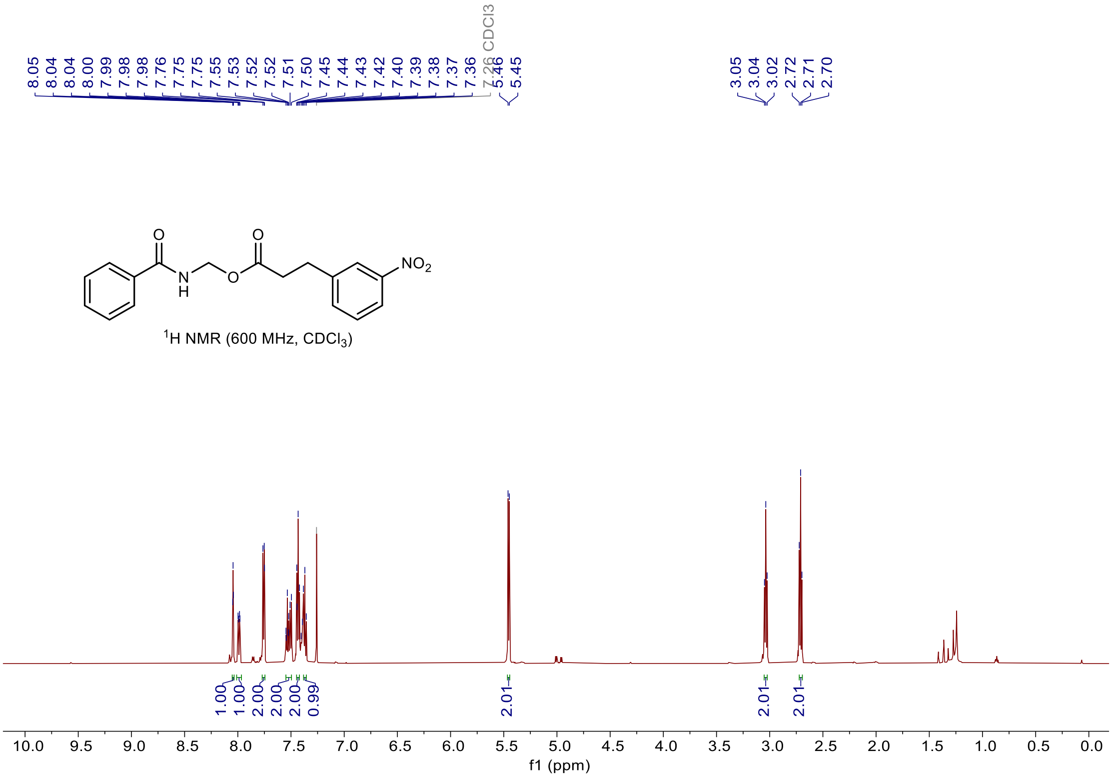


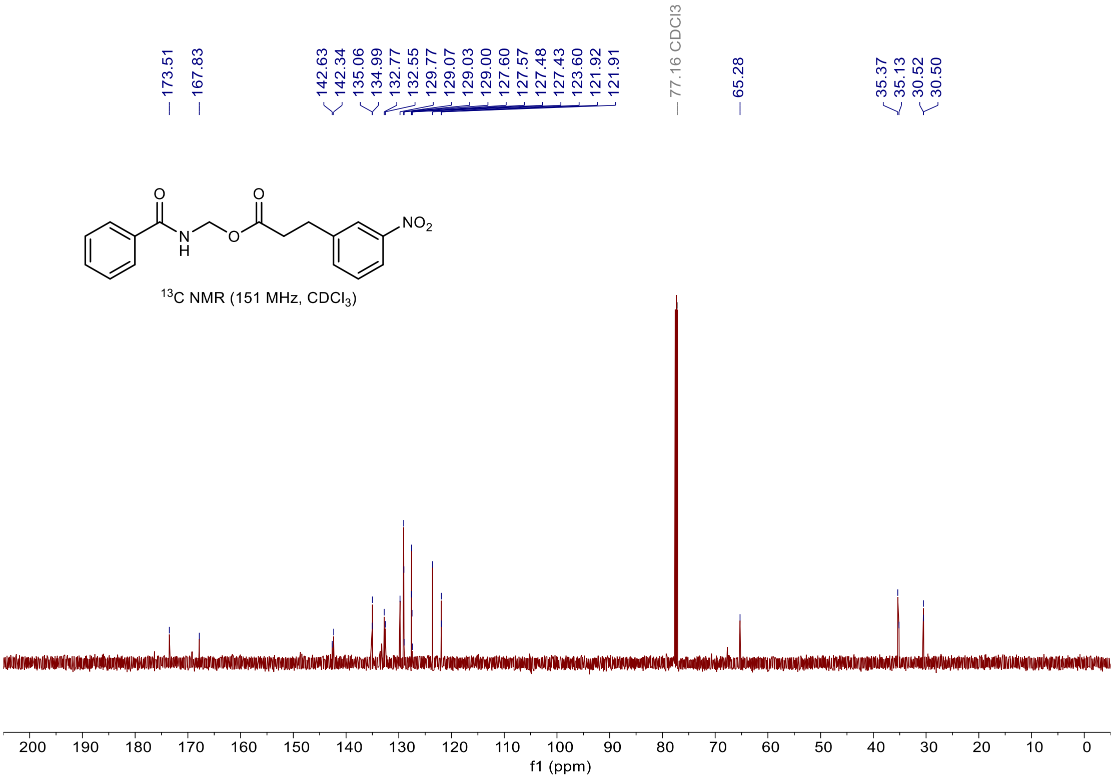
^{1}H and ^{13}C NMR spectra of compound 3g



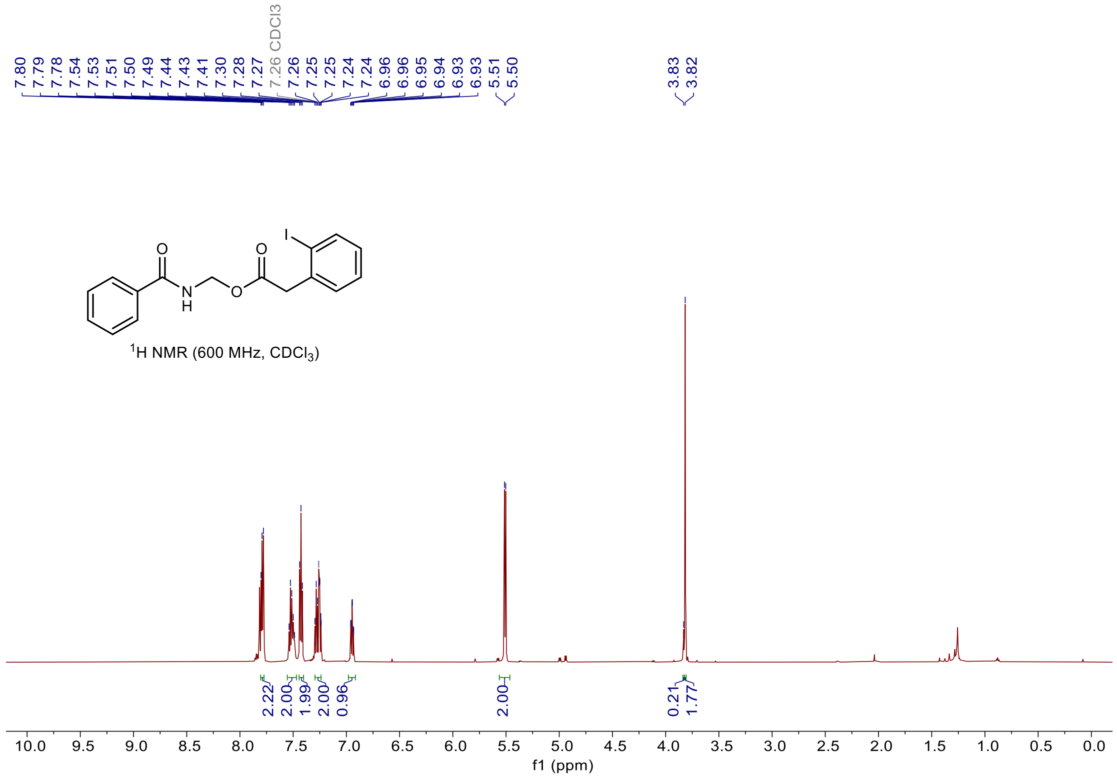


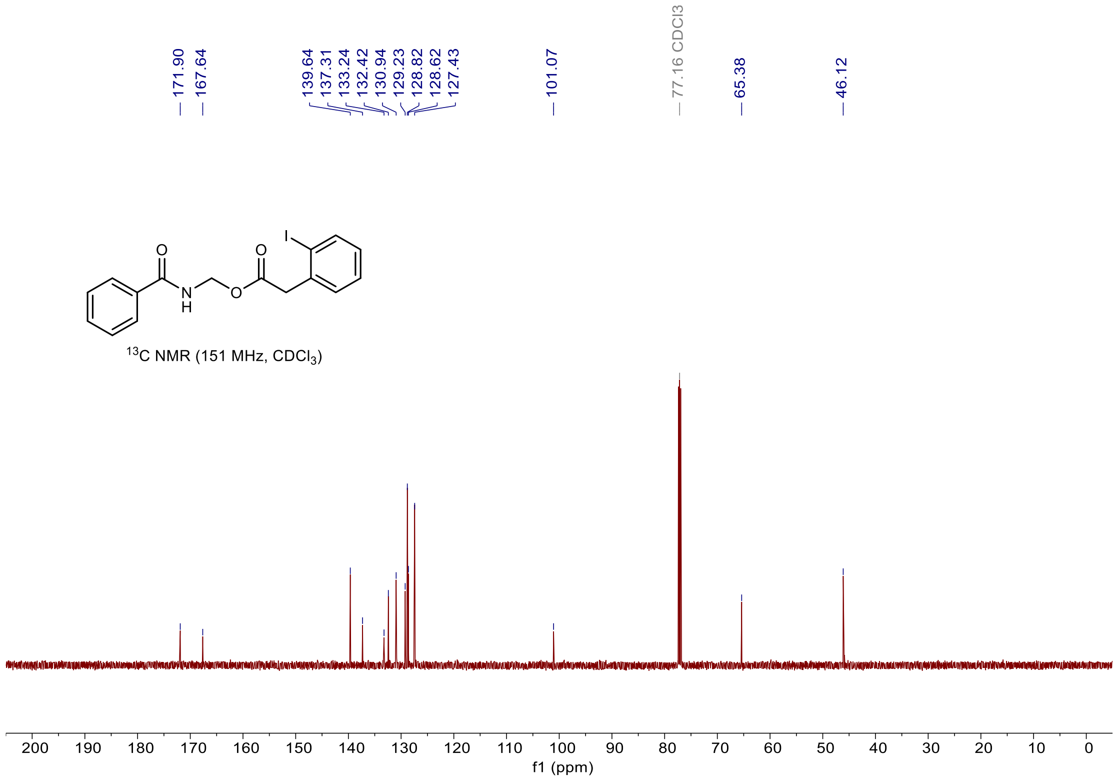
^{1}H and ^{13}C NMR spectra of compound 3h



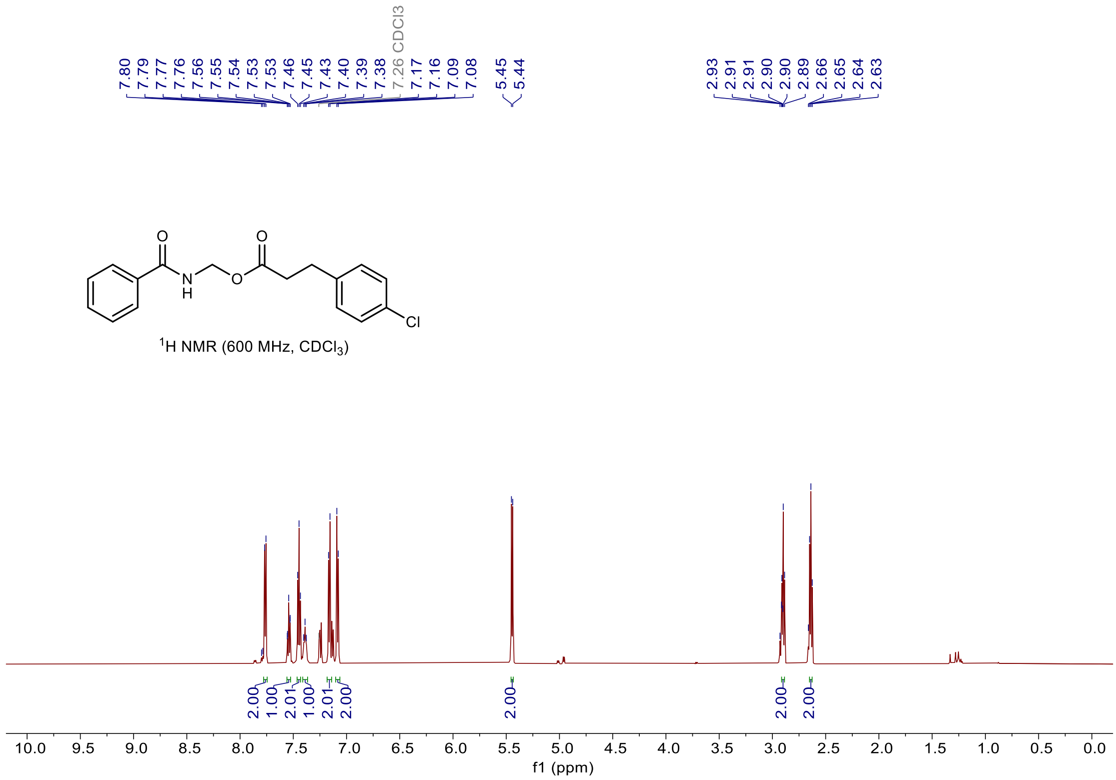


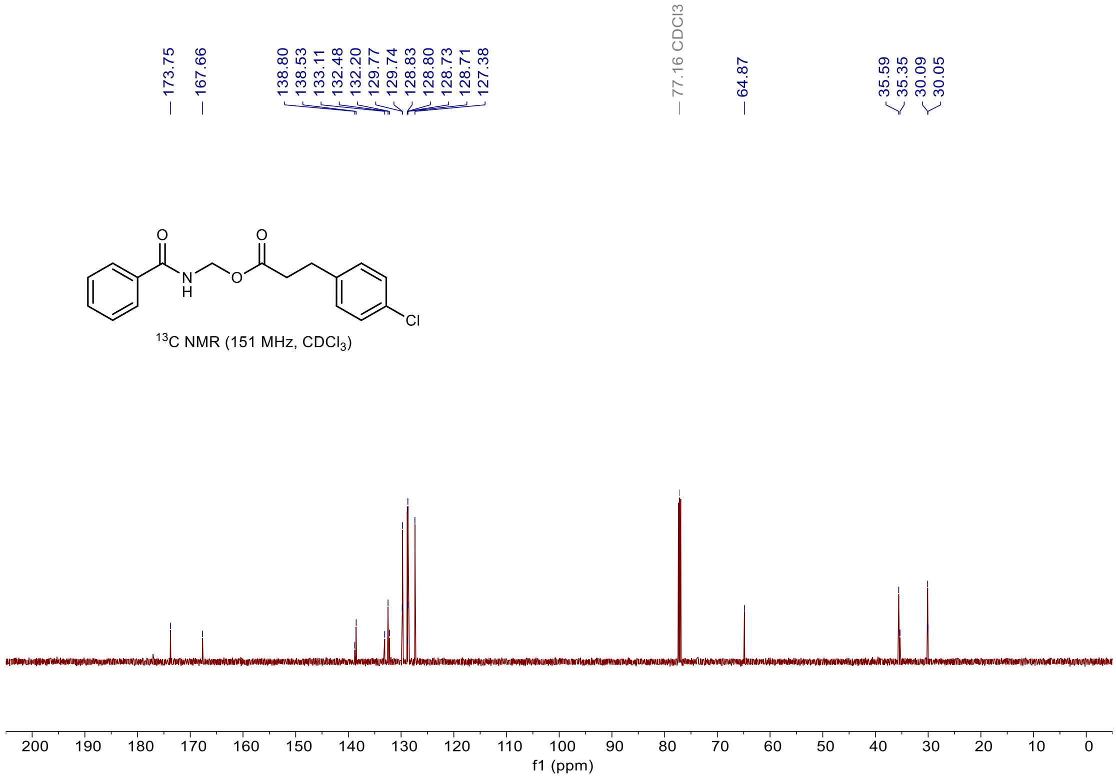
^{1}H and ^{13}C NMR spectra of compound 3i



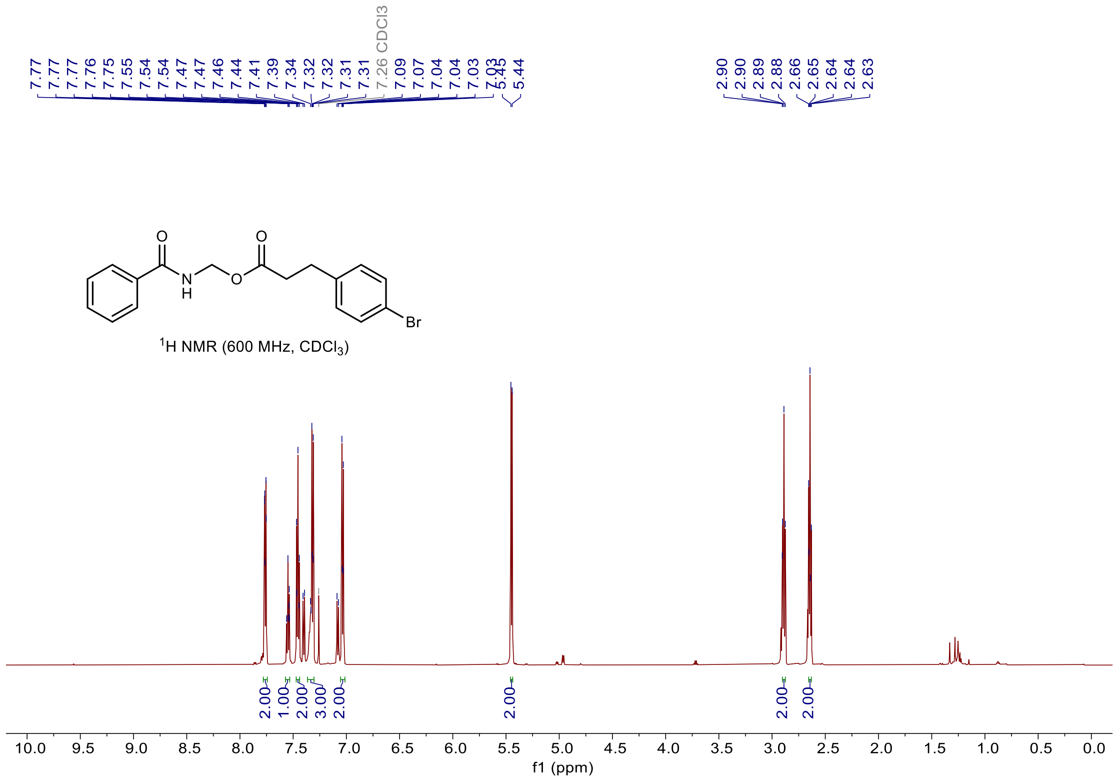


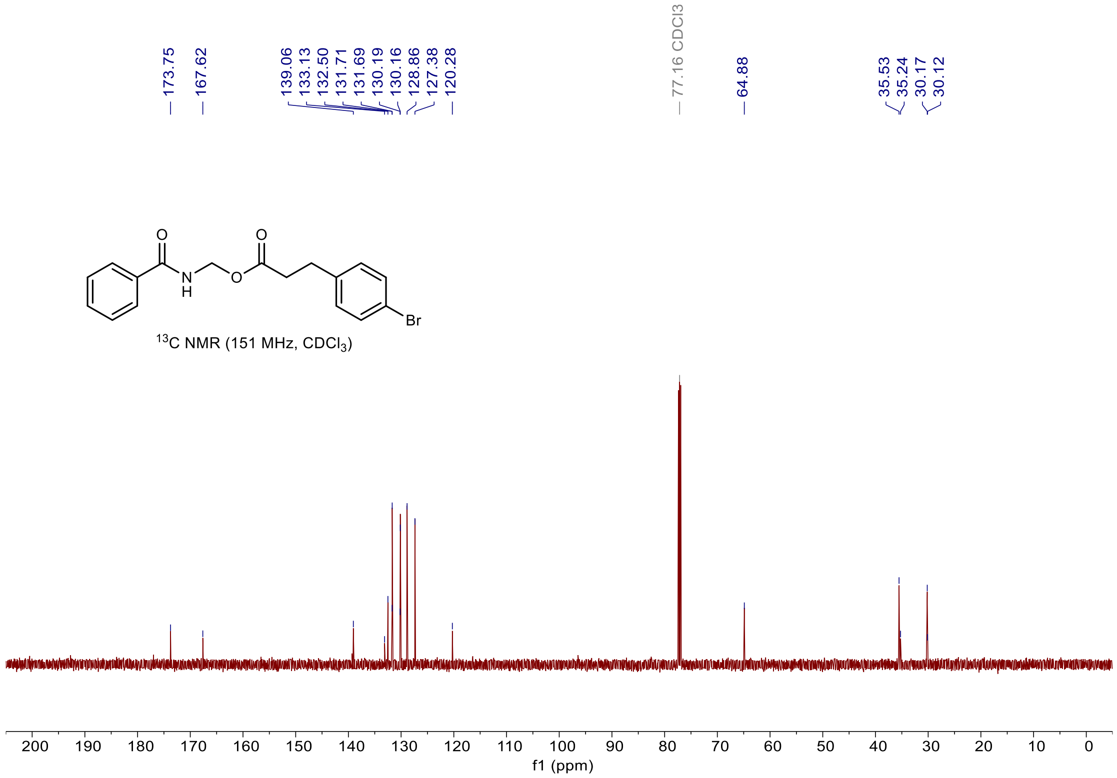
^{1}H and ^{13}C NMR spectra of compound 3j



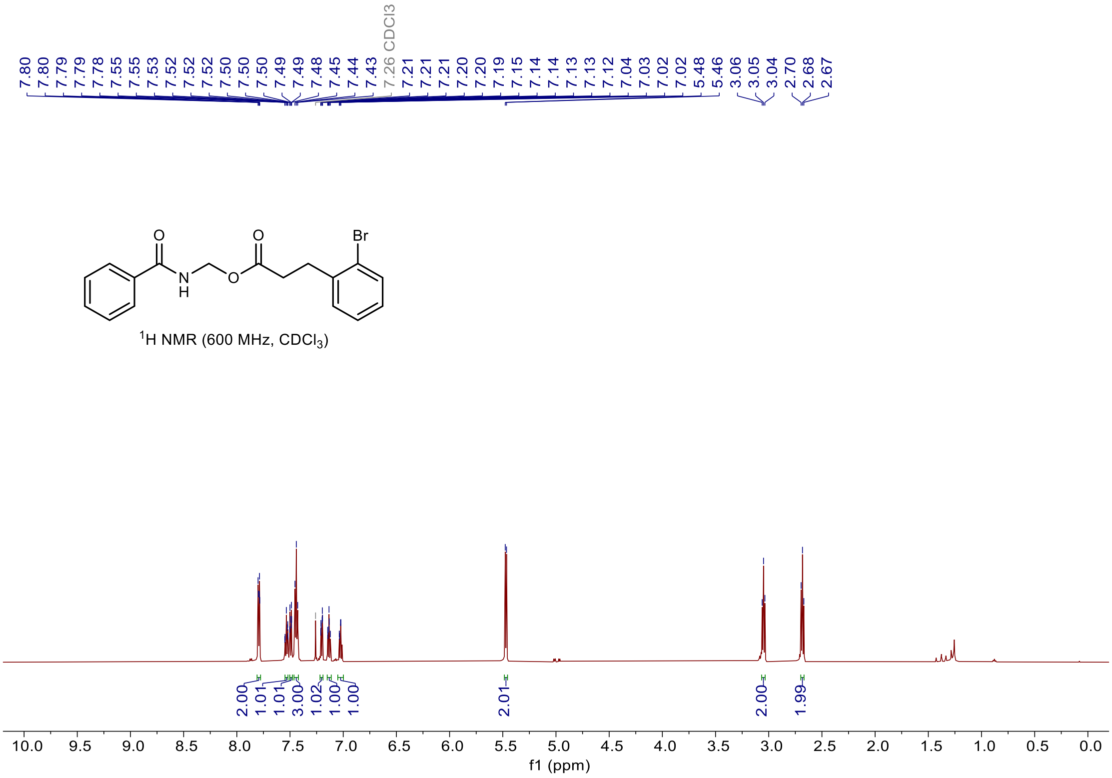


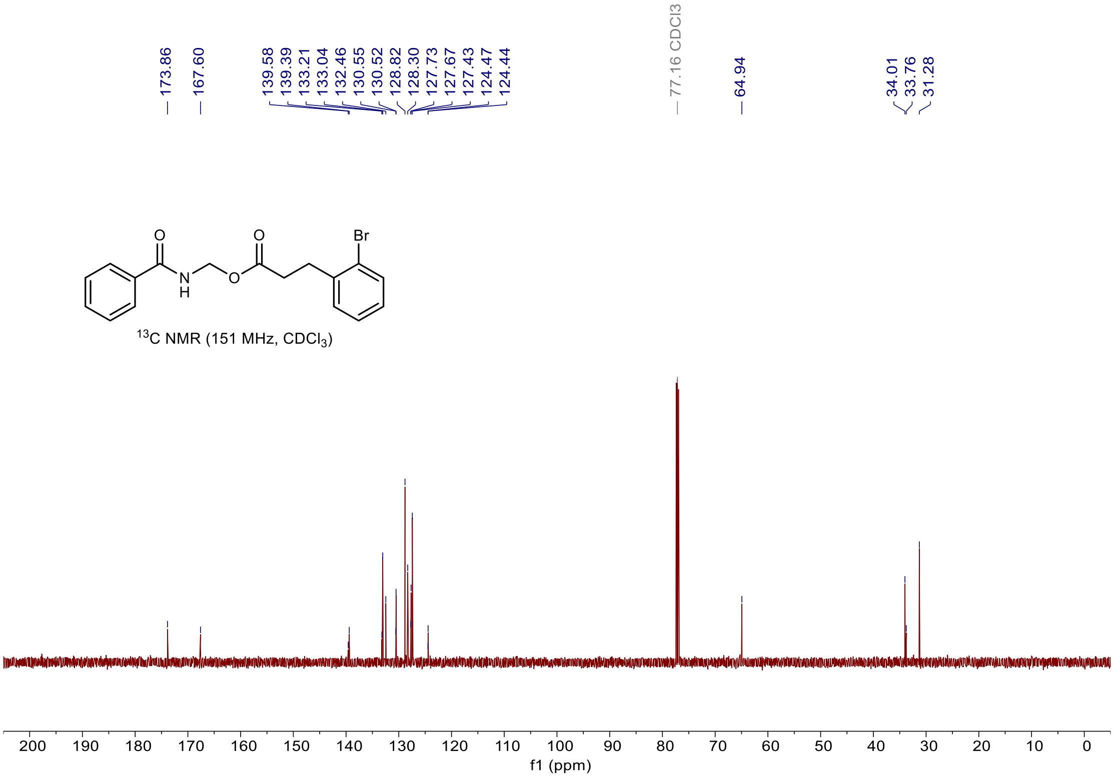
^{1}H and ^{13}C NMR spectra of compound 3k



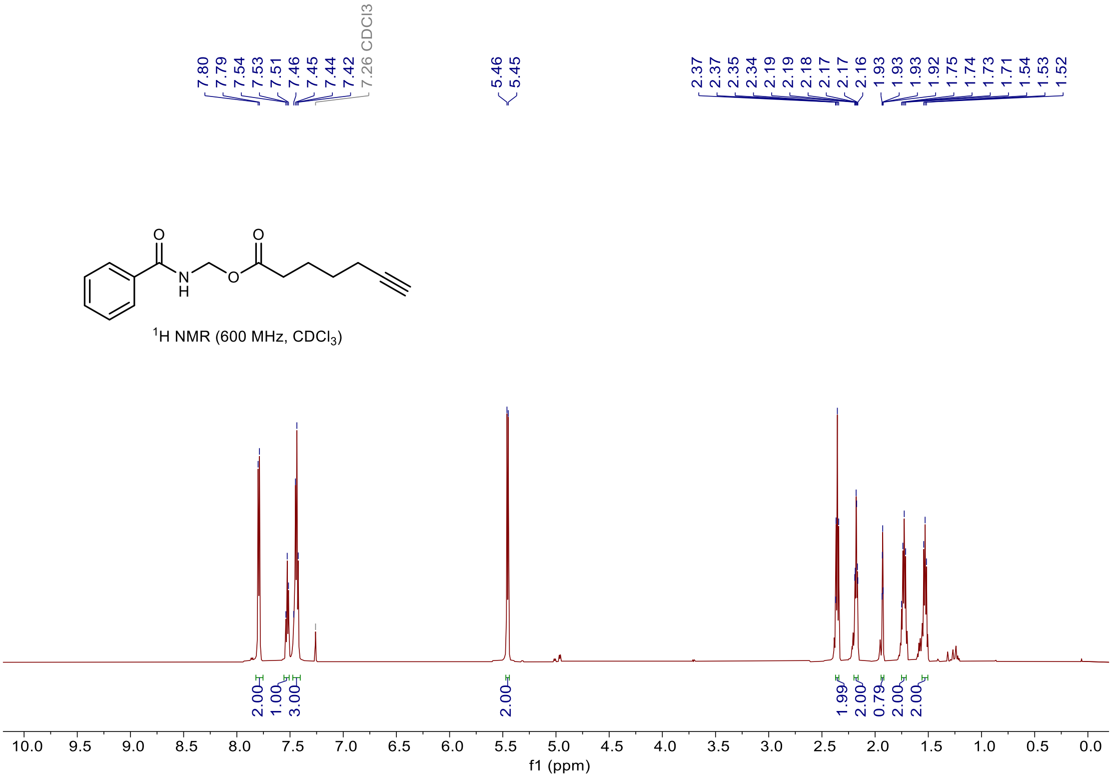


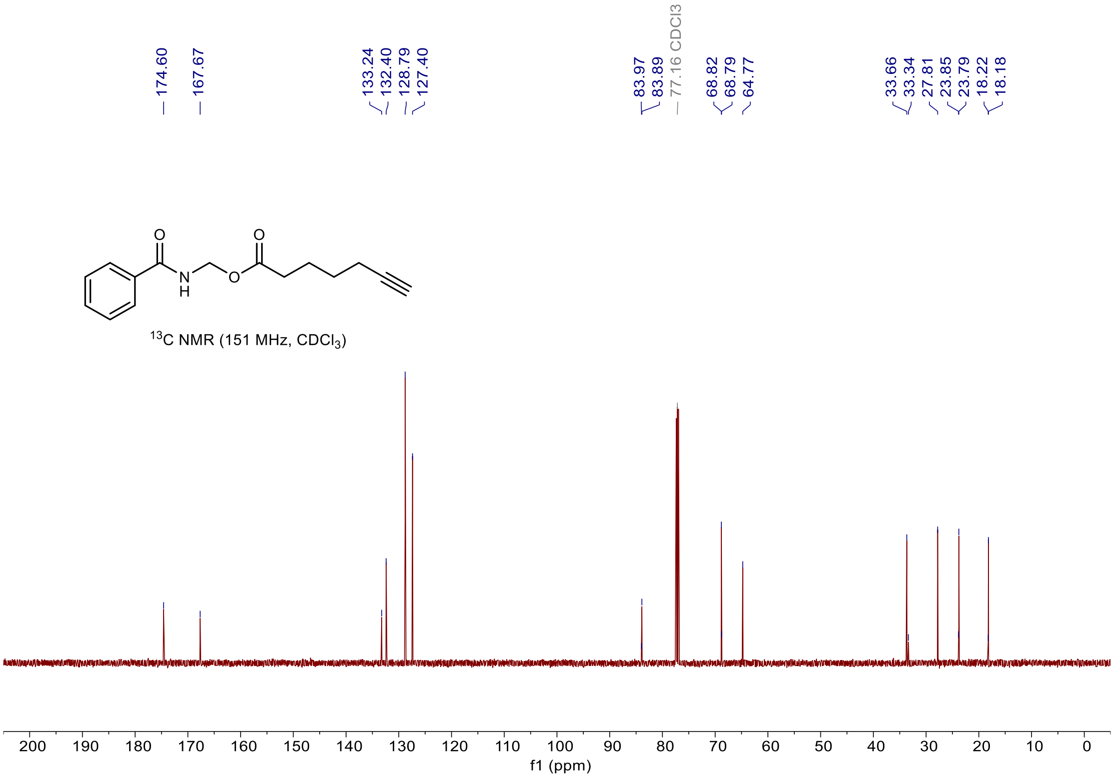
^{1}H and ^{13}C NMR spectra of compound 3l



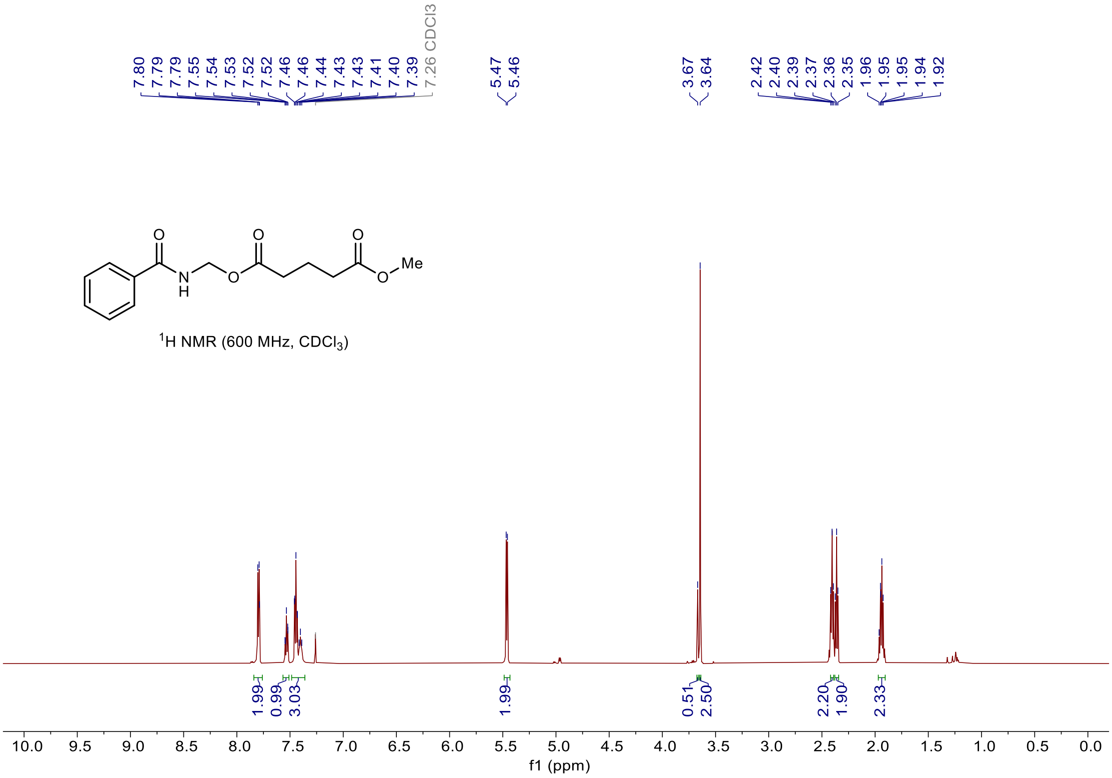


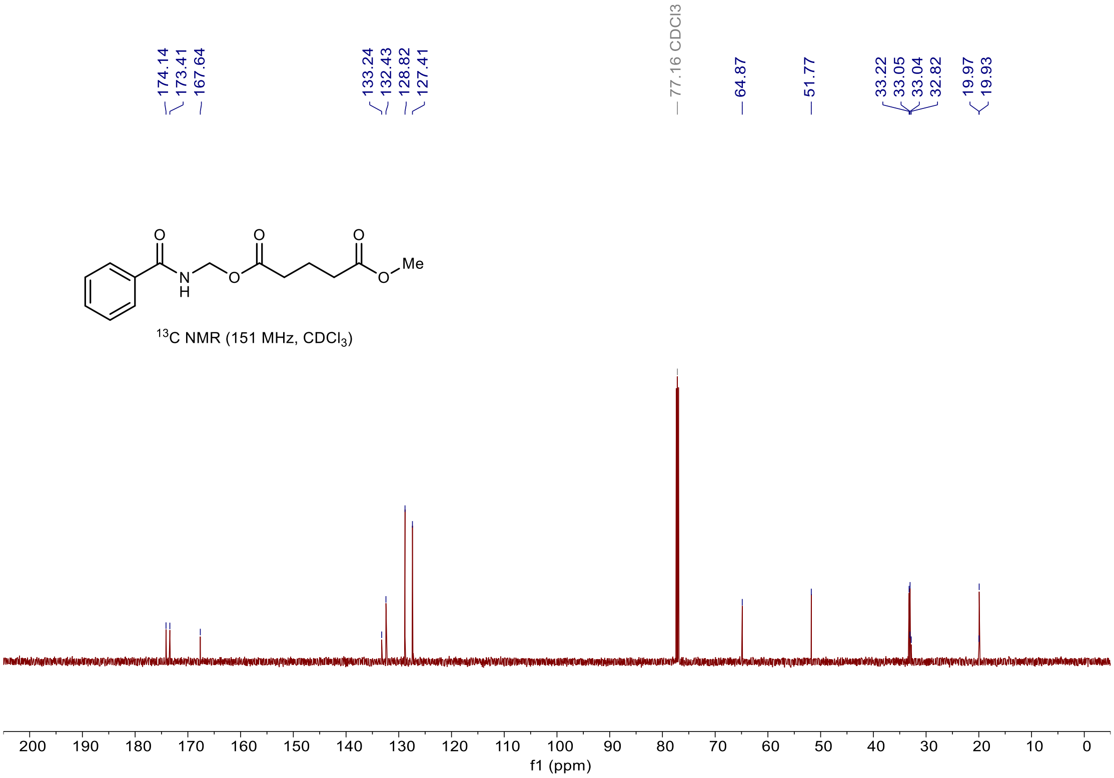
^{1}H and ^{13}C NMR spectra of compound 3m



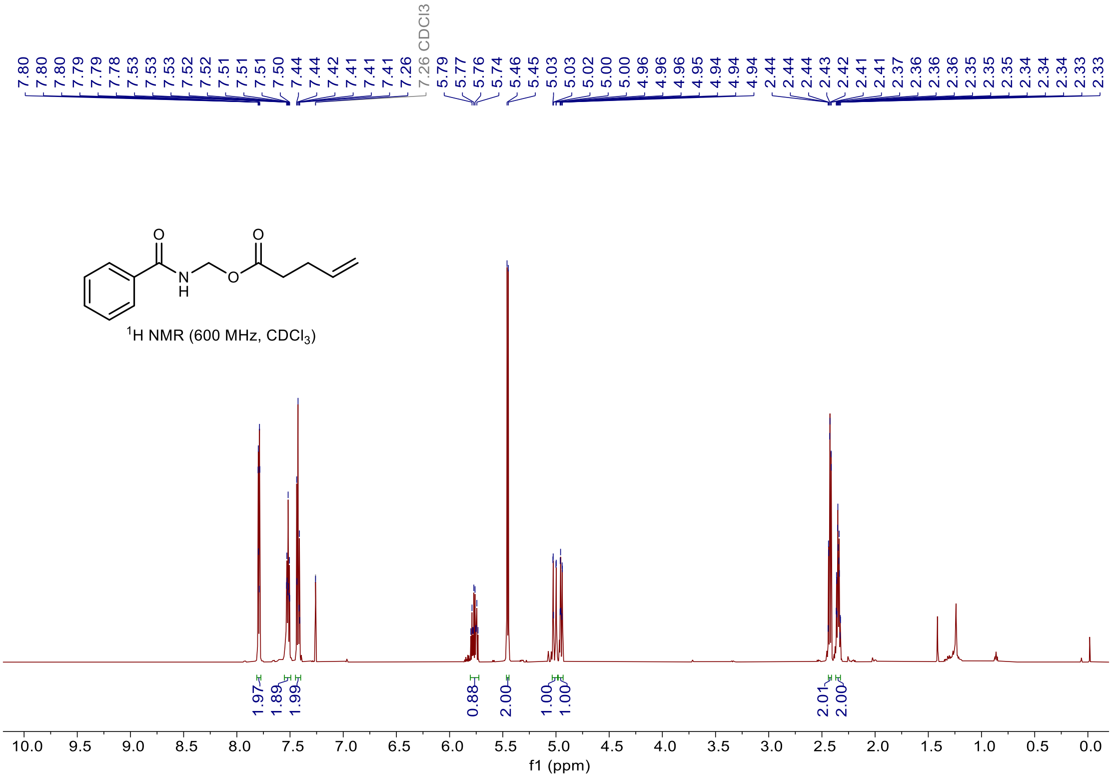


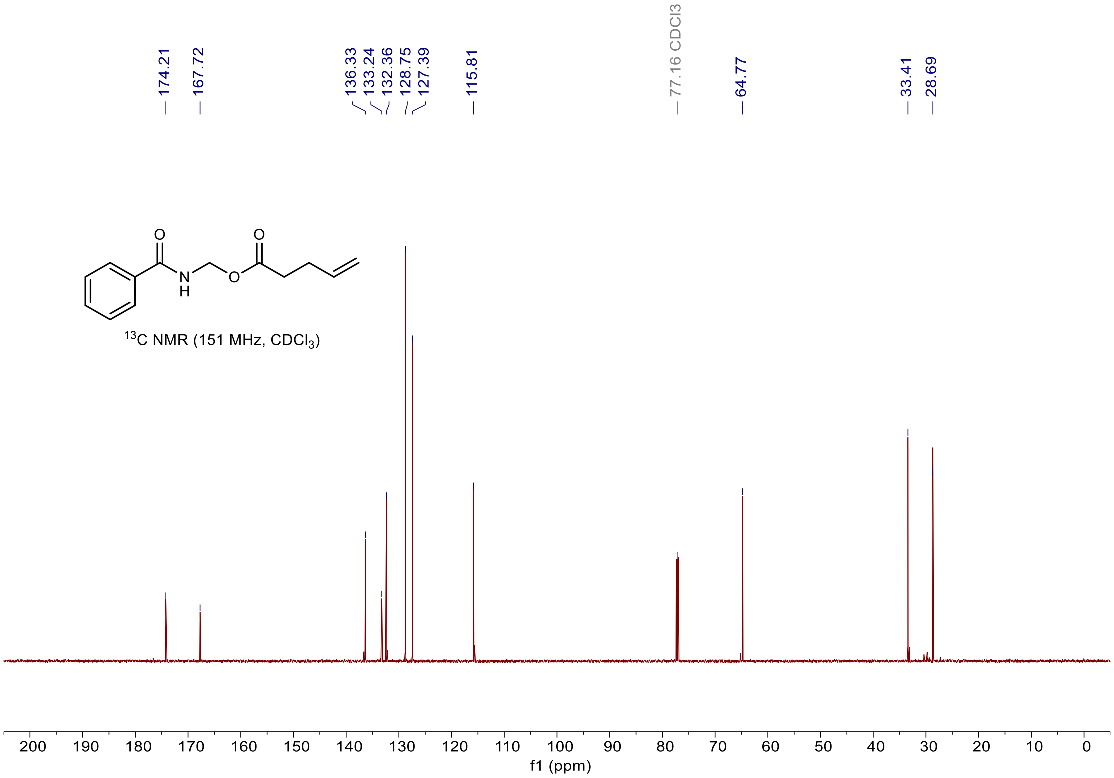
^{1}H and ^{13}C NMR spectra of compound 3n



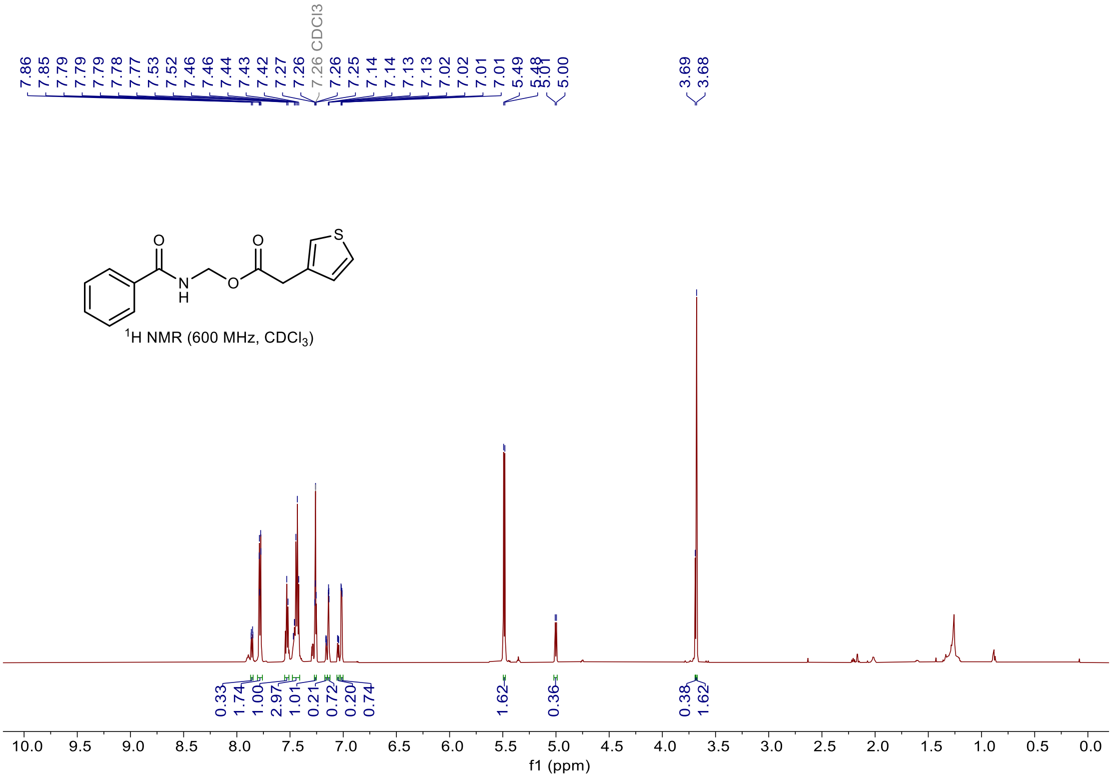


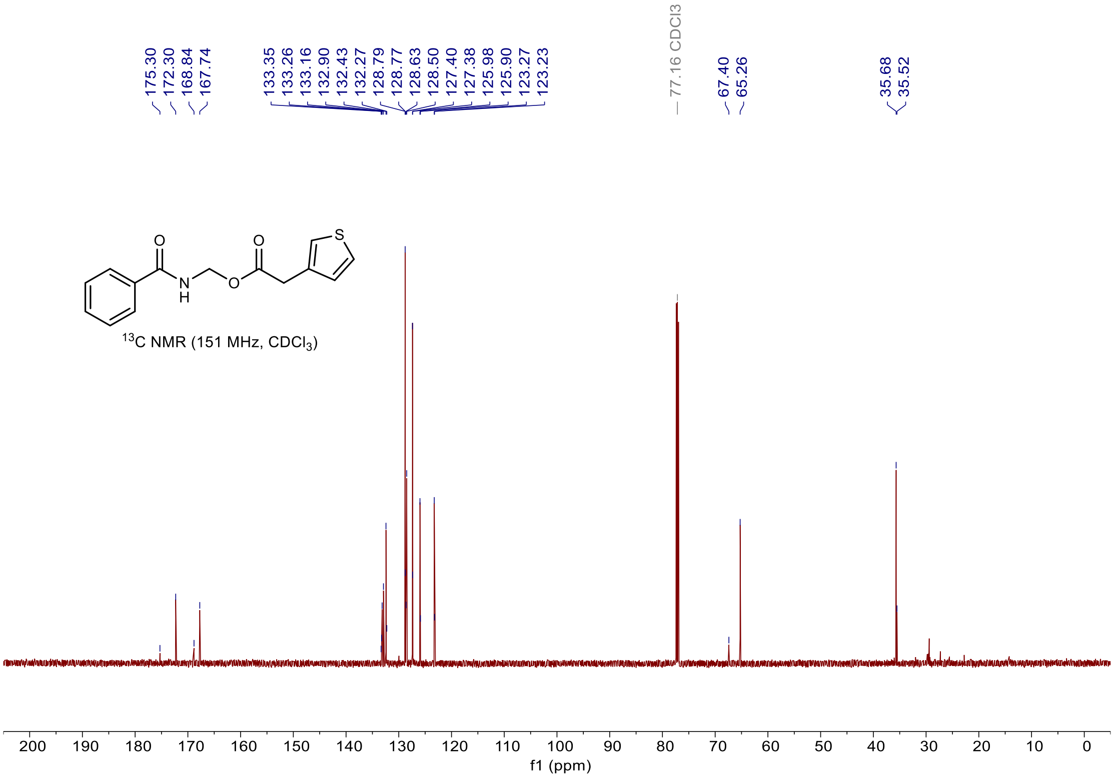
^{1}H and ^{13}C NMR spectra of compound 3o



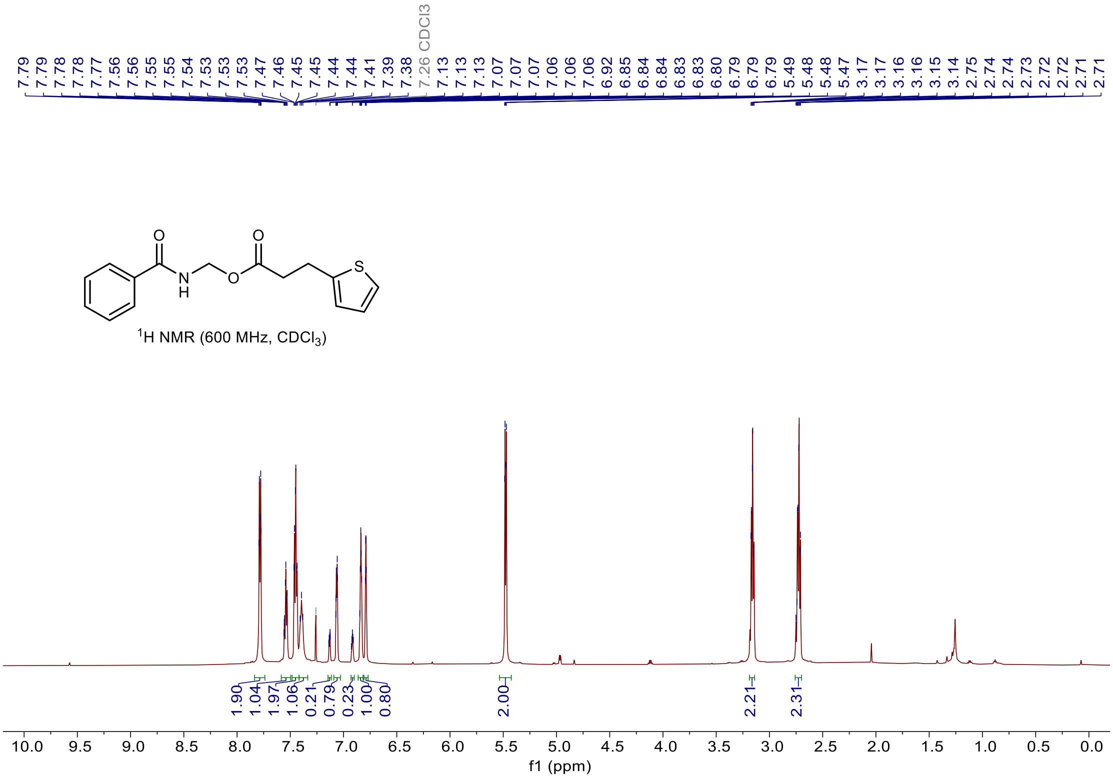


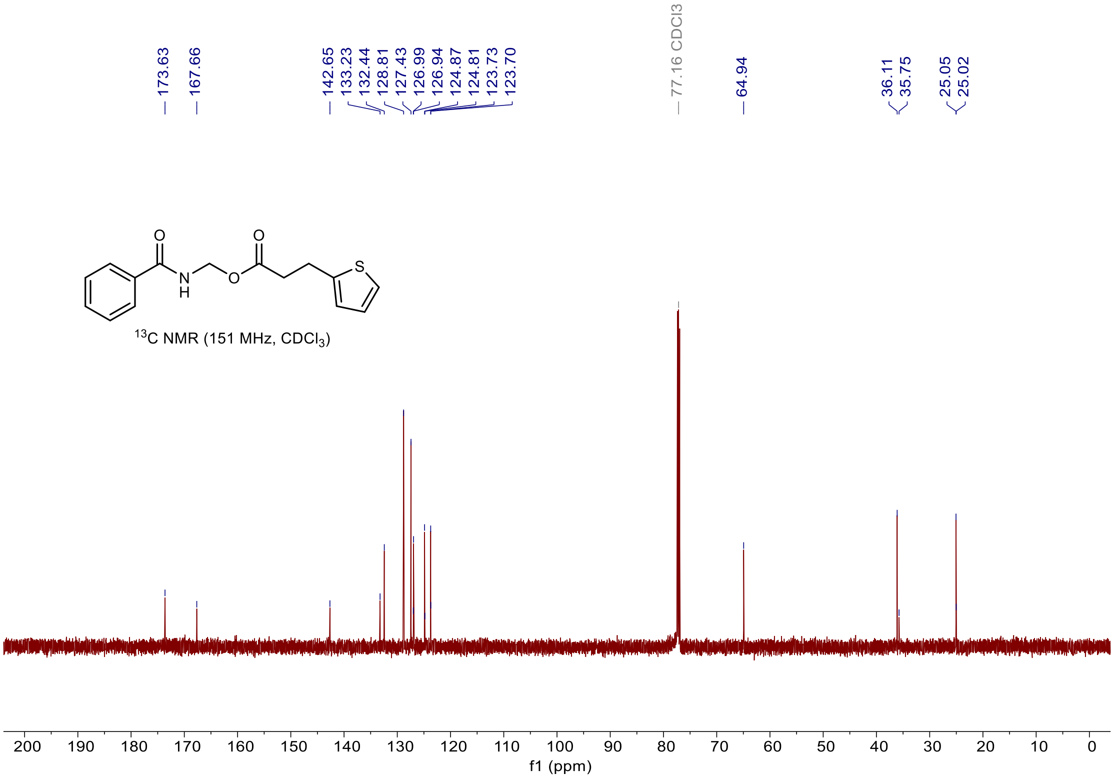
^{1}H and ^{13}C NMR spectra of compound 3p



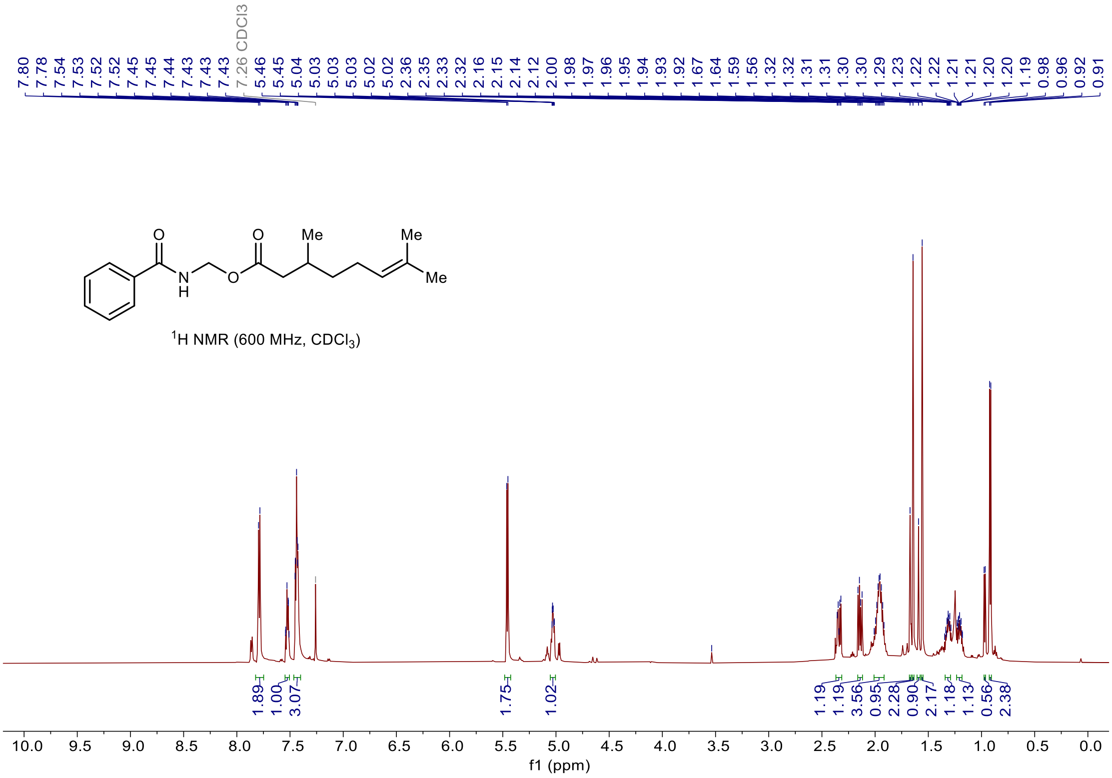


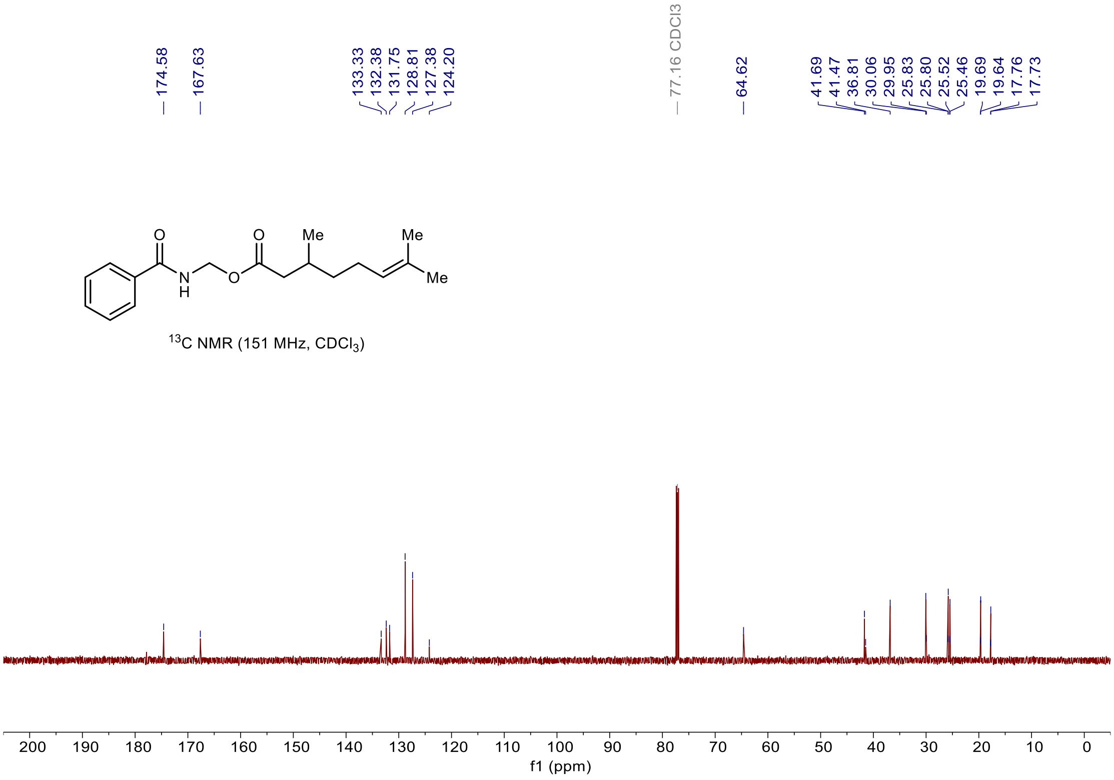
^{1}H and ^{13}C NMR spectra of compound 3q



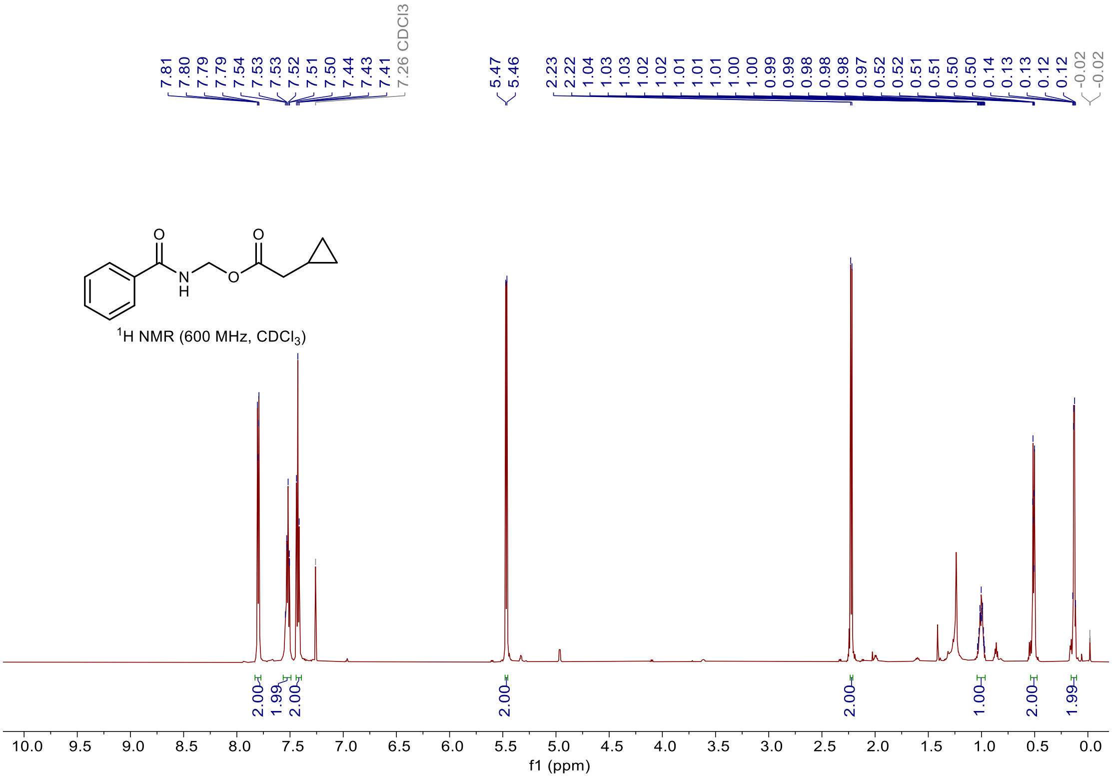


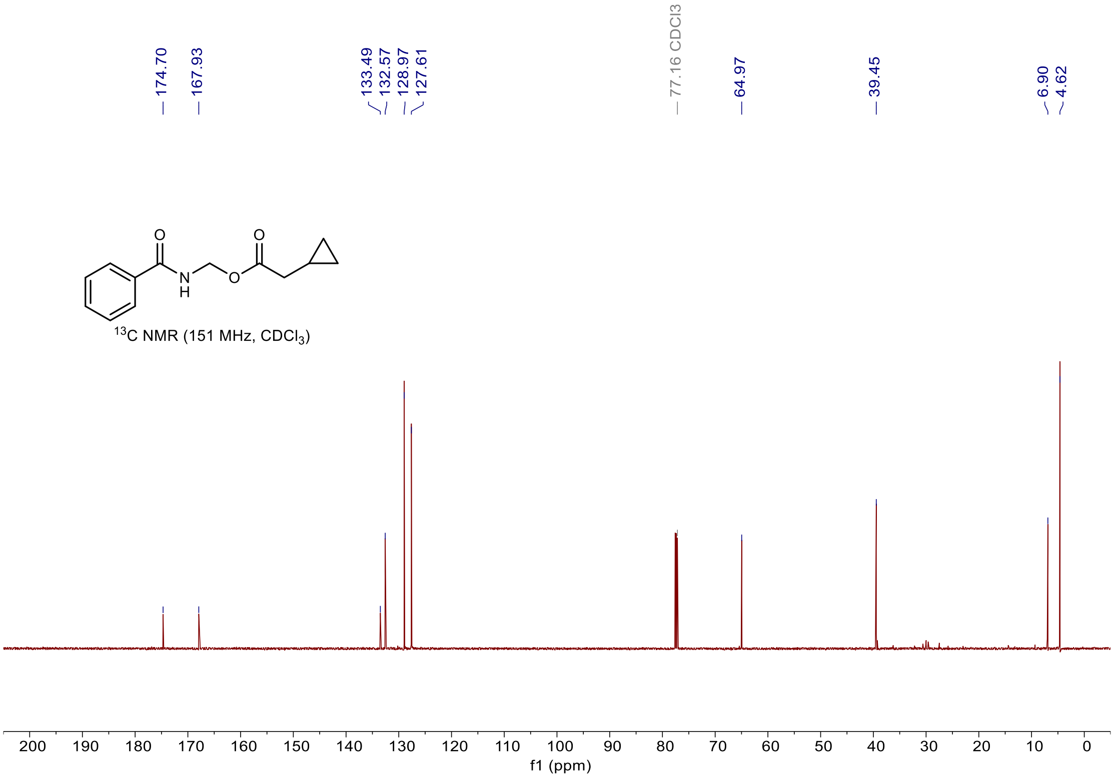
^{1}H and ^{13}C NMR spectra of compound 3r



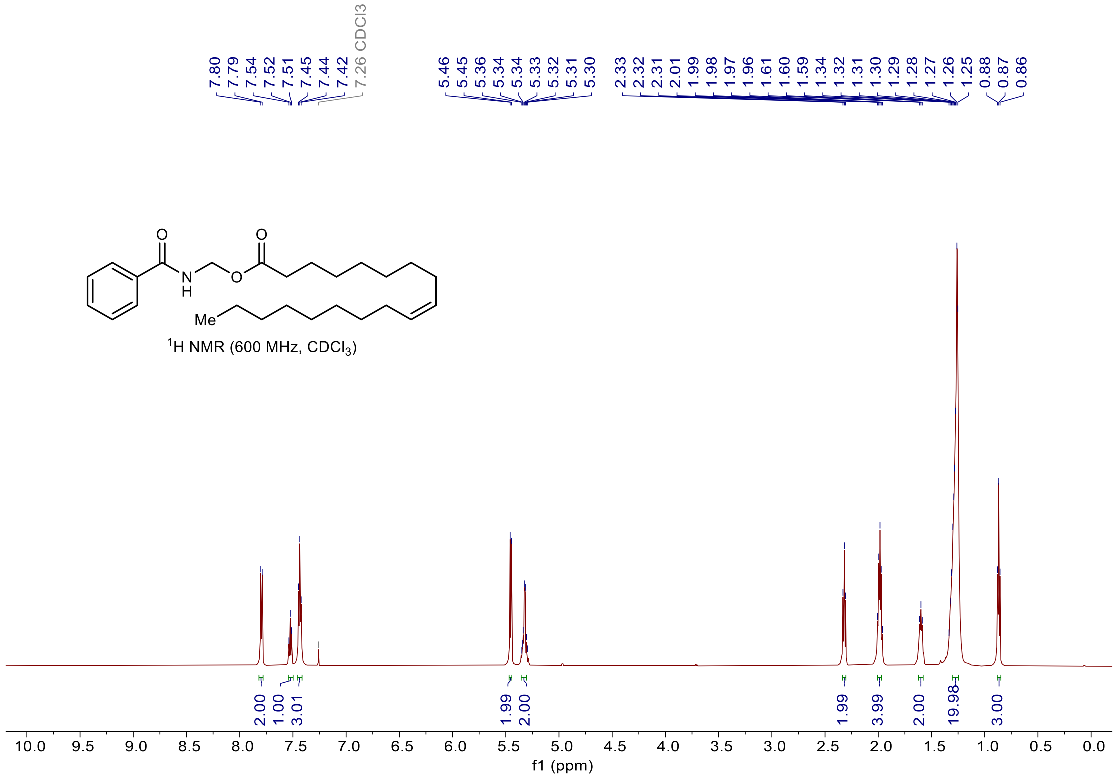


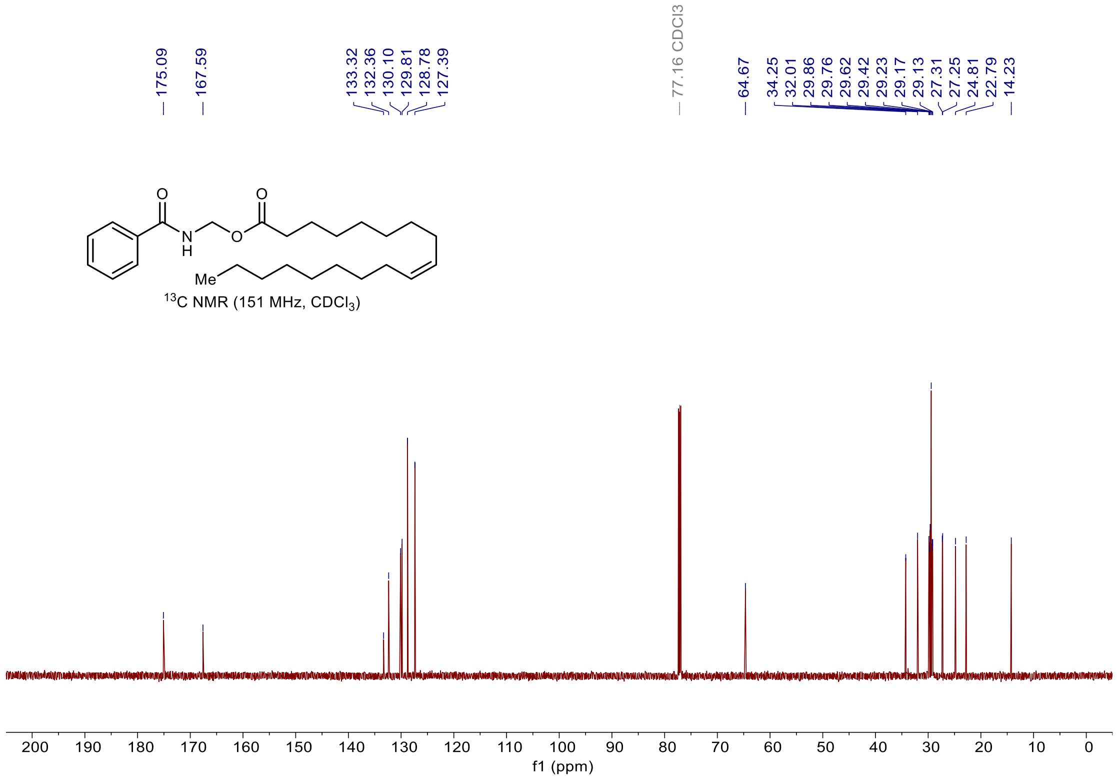
^1H and ^{13}C NMR spectra of compound 3s



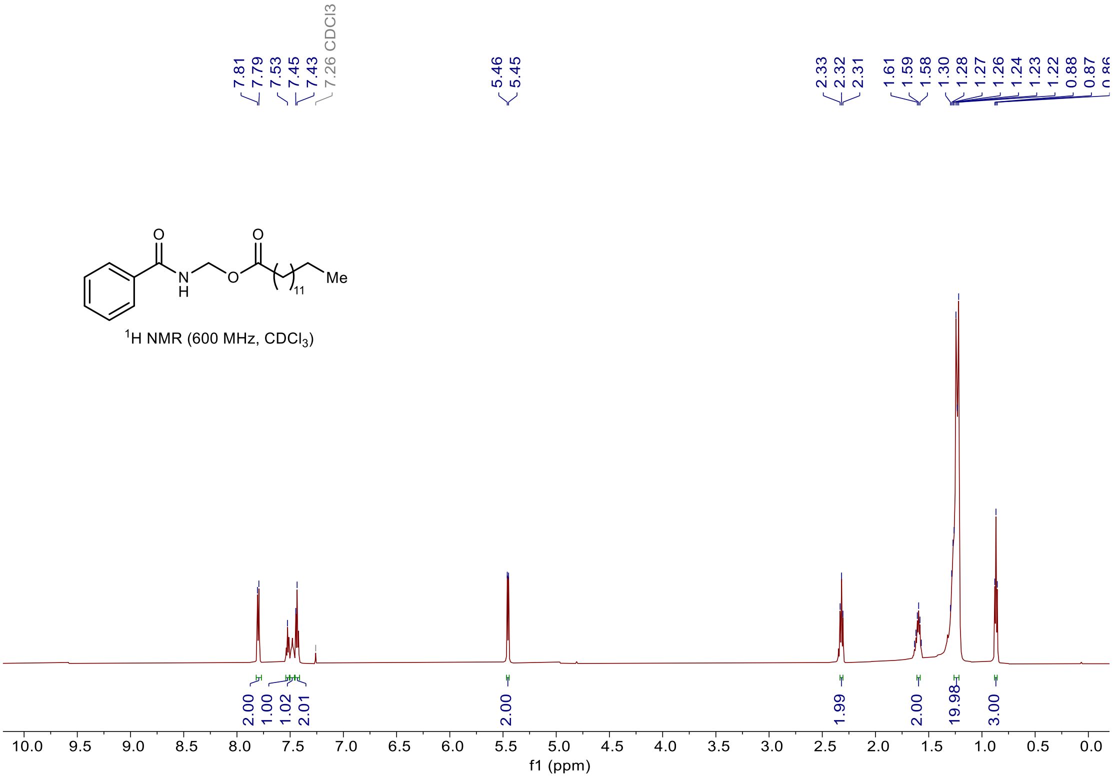


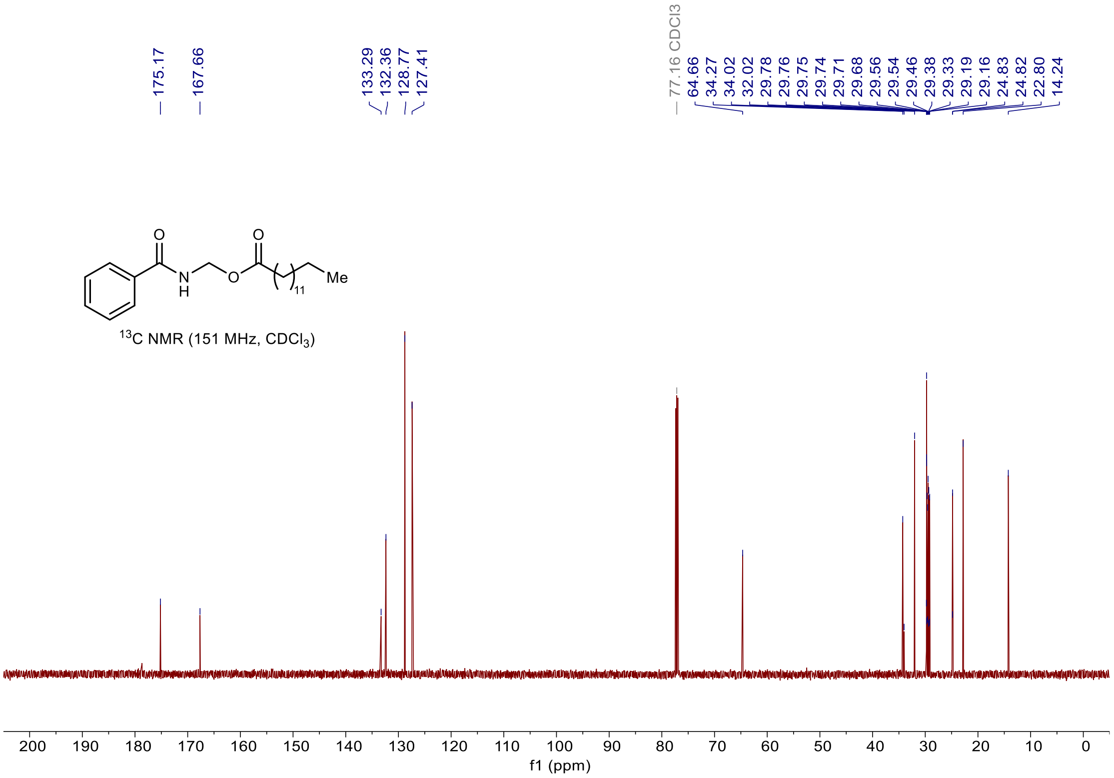
^{1}H and ^{13}C NMR spectra of compound 3t



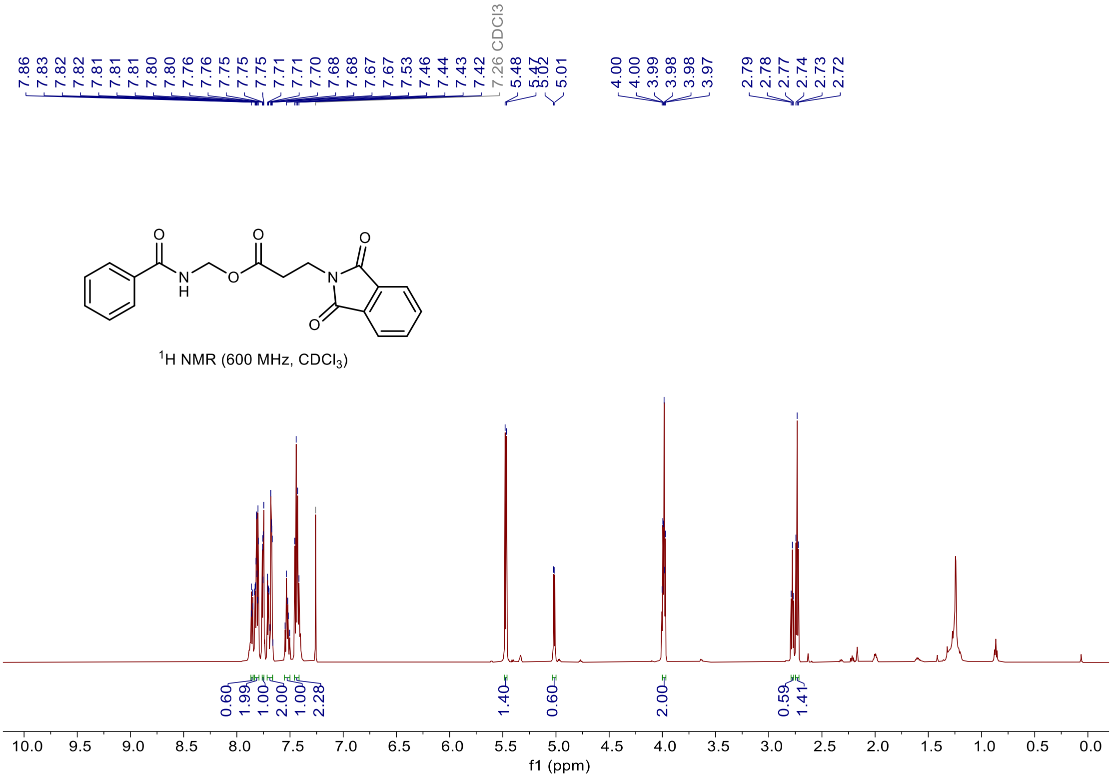


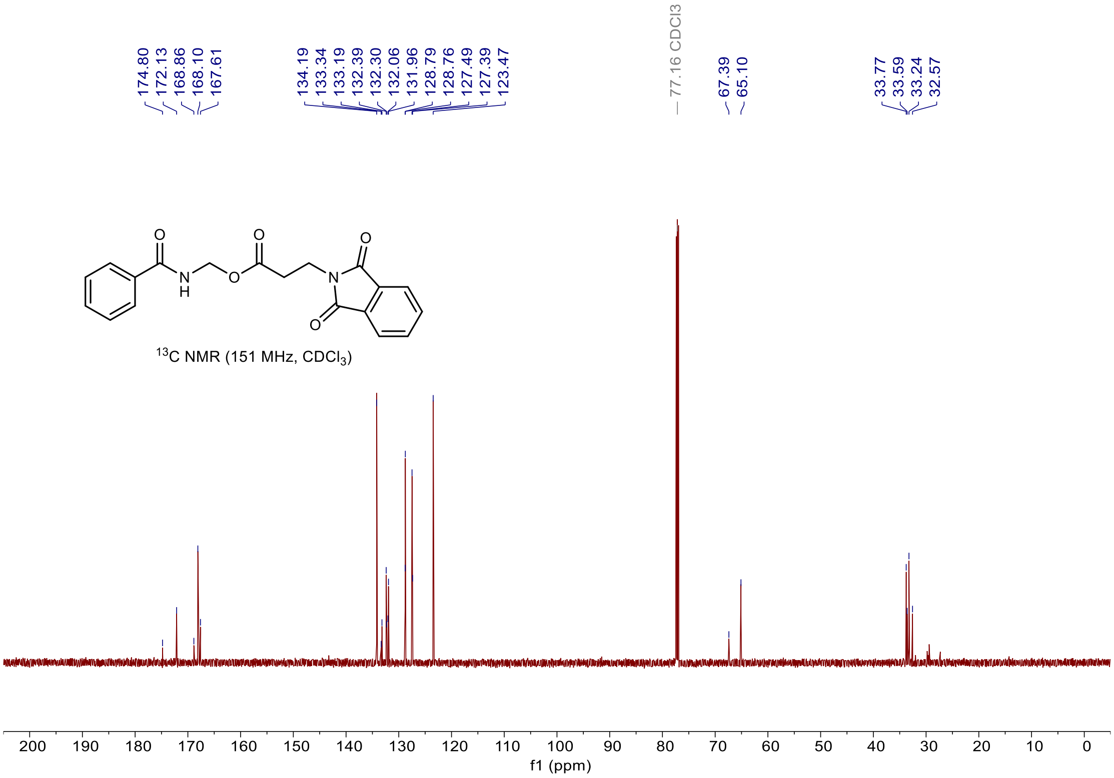
^{1}H and ^{13}C NMR spectra of compound 3u



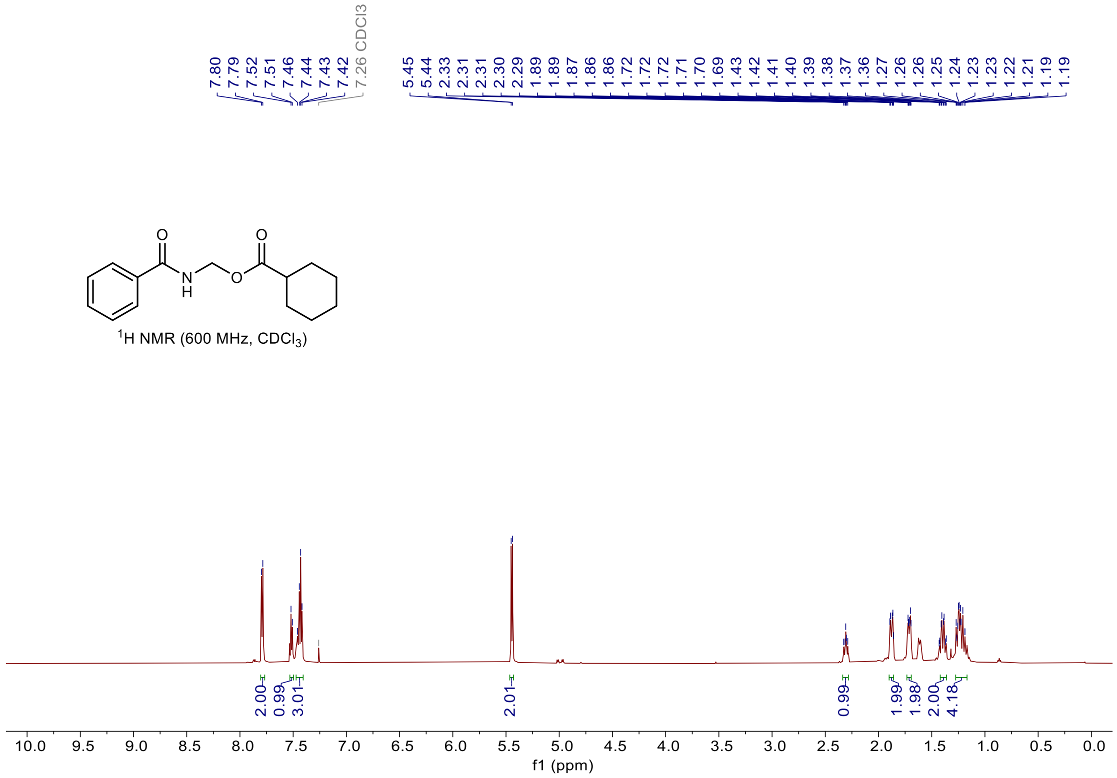


^{1}H and ^{13}C NMR spectra of compound 3v

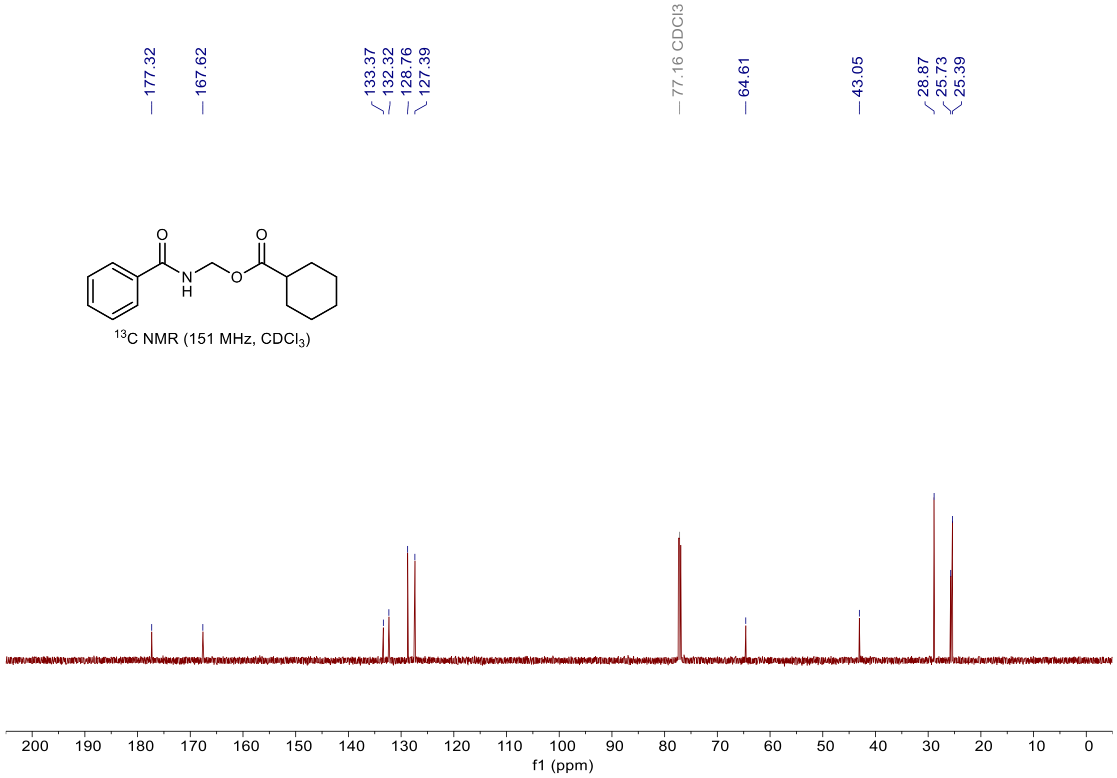




^{1}H and ^{13}C NMR spectra of compound 3w

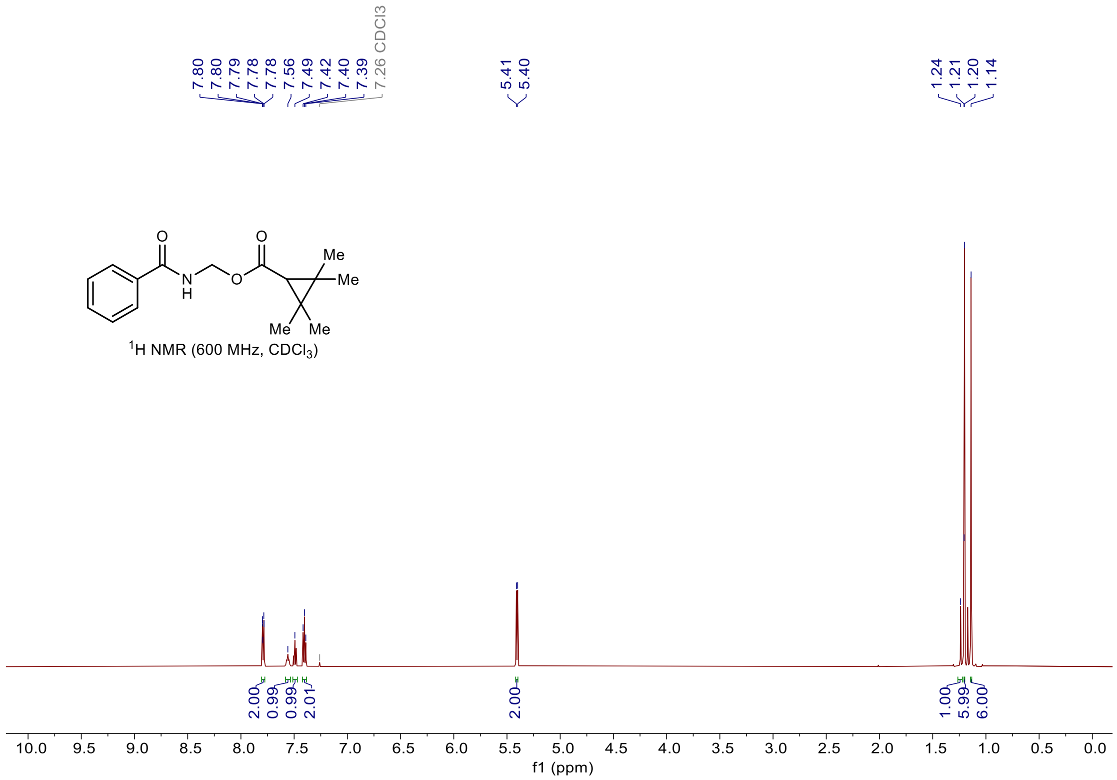


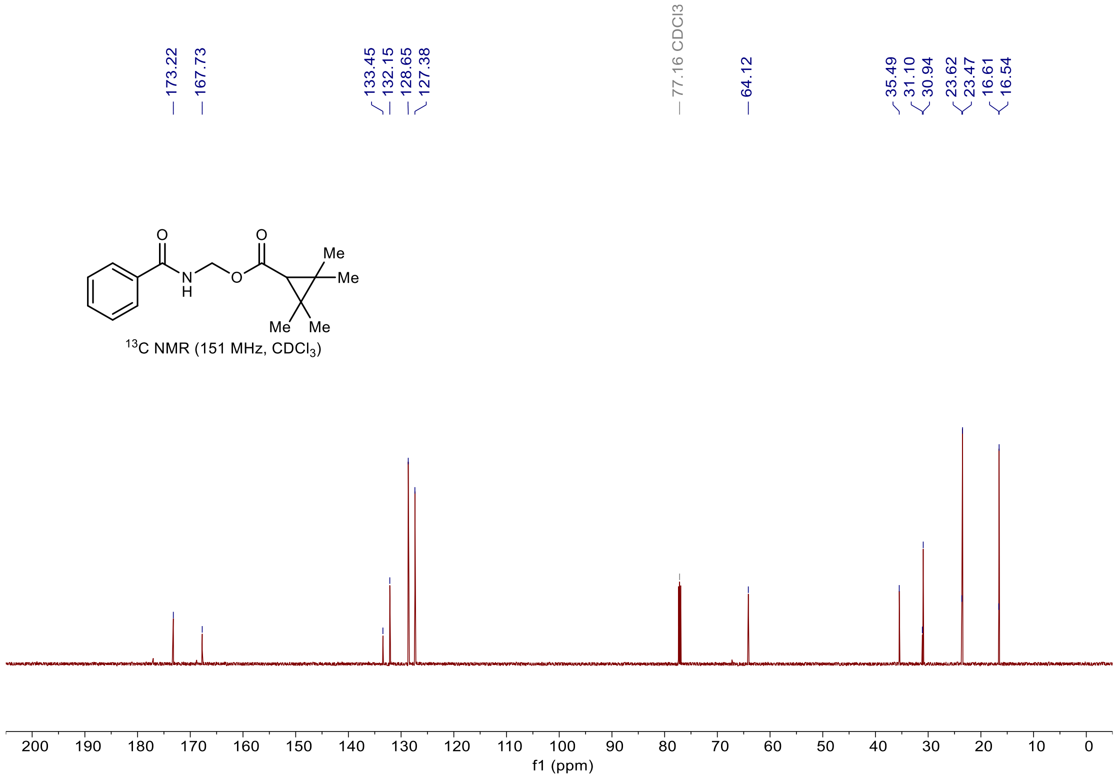
^{1}H NMR (600 MHz, CDCl$_3$)



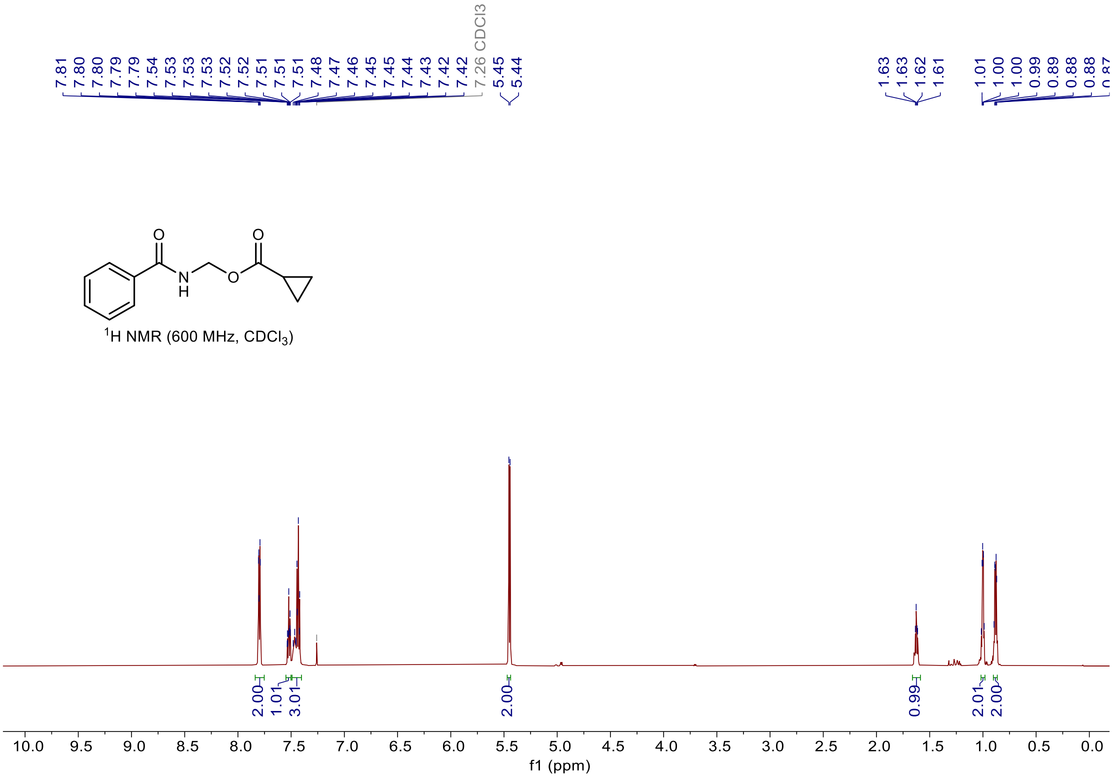
^{13}C NMR (151 MHz, CDCl$_3$)

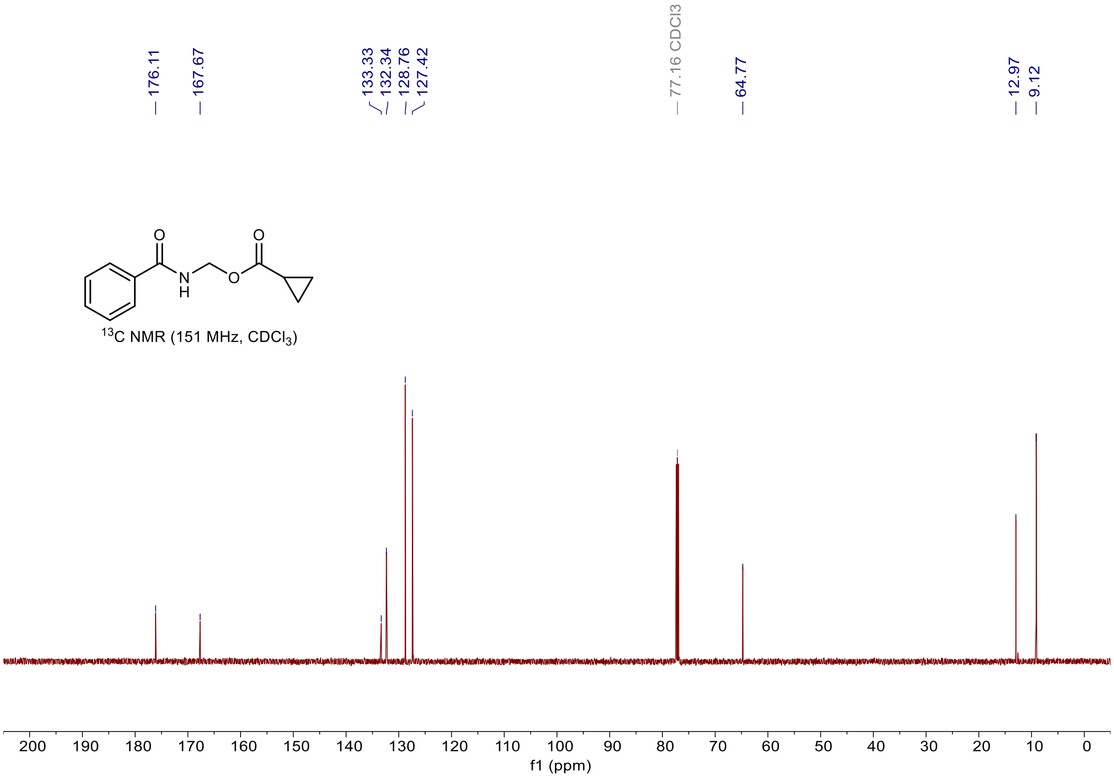
^{1}H and ^{13}C NMR spectra of compound 3x



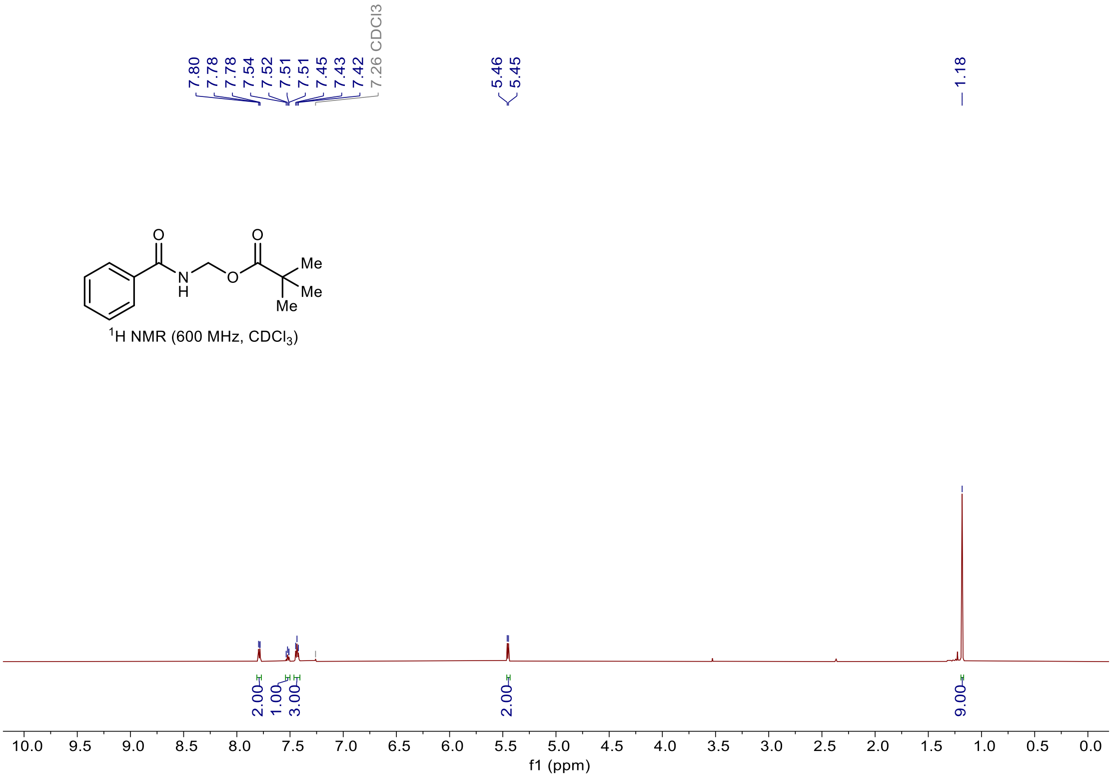


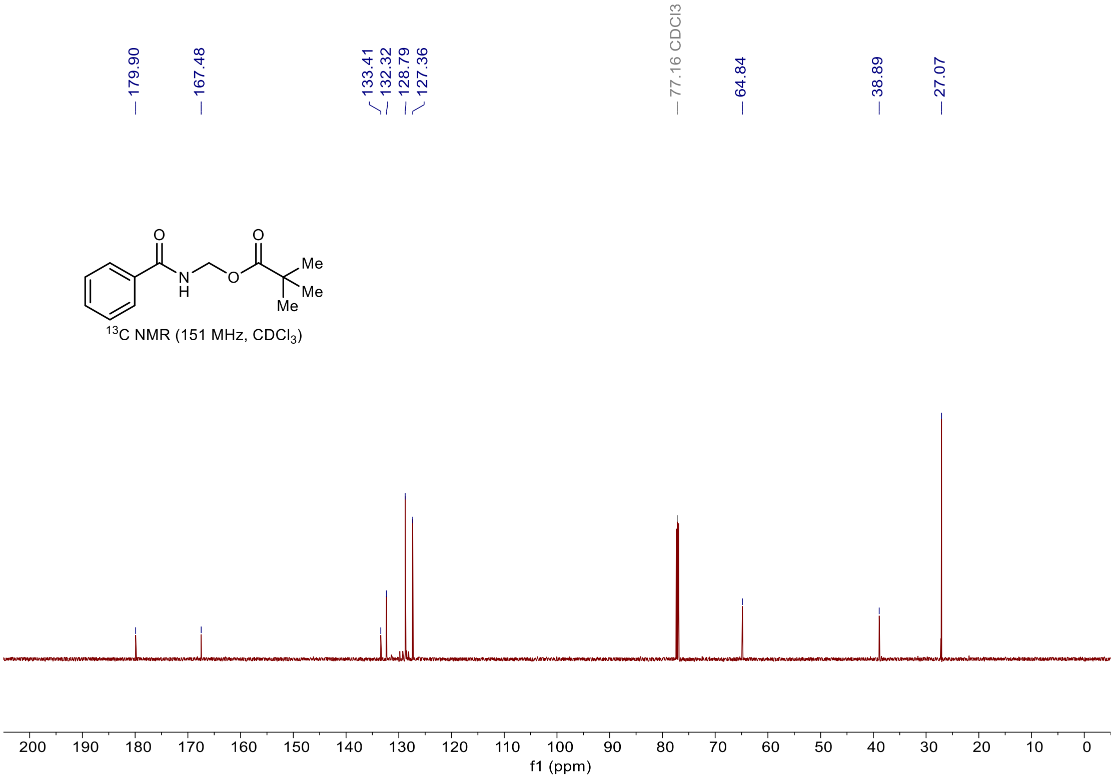
^{1}H and ^{13}C NMR spectra of compound 3y



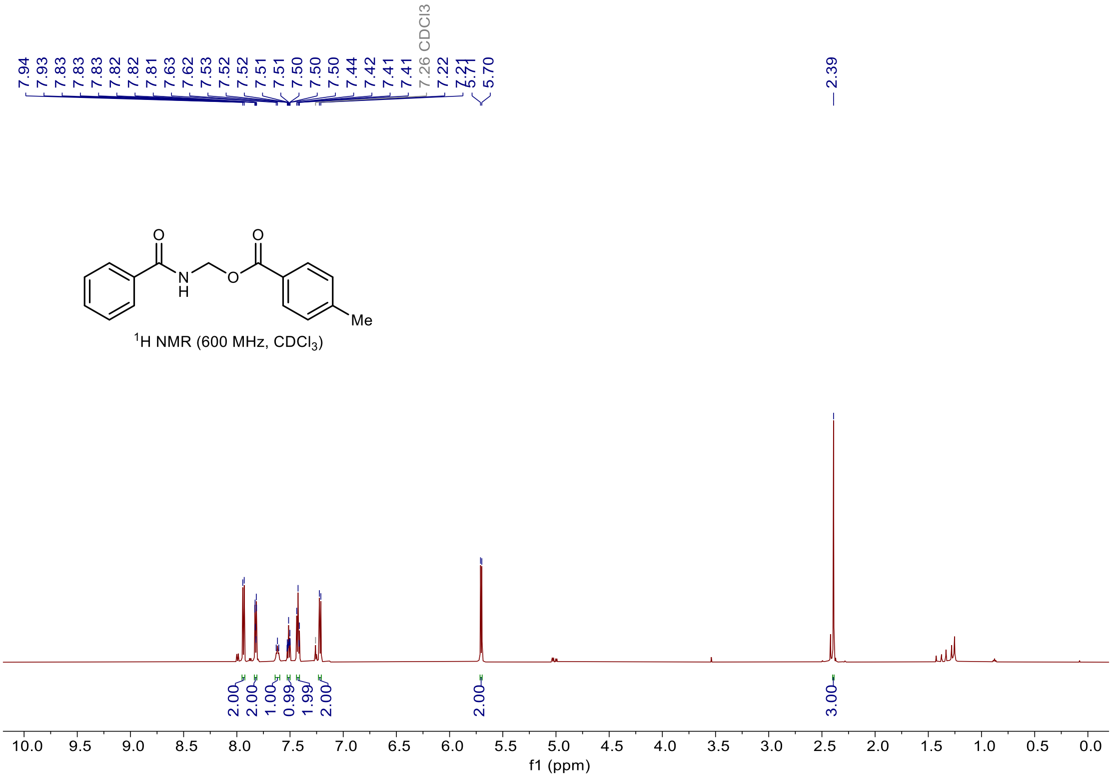


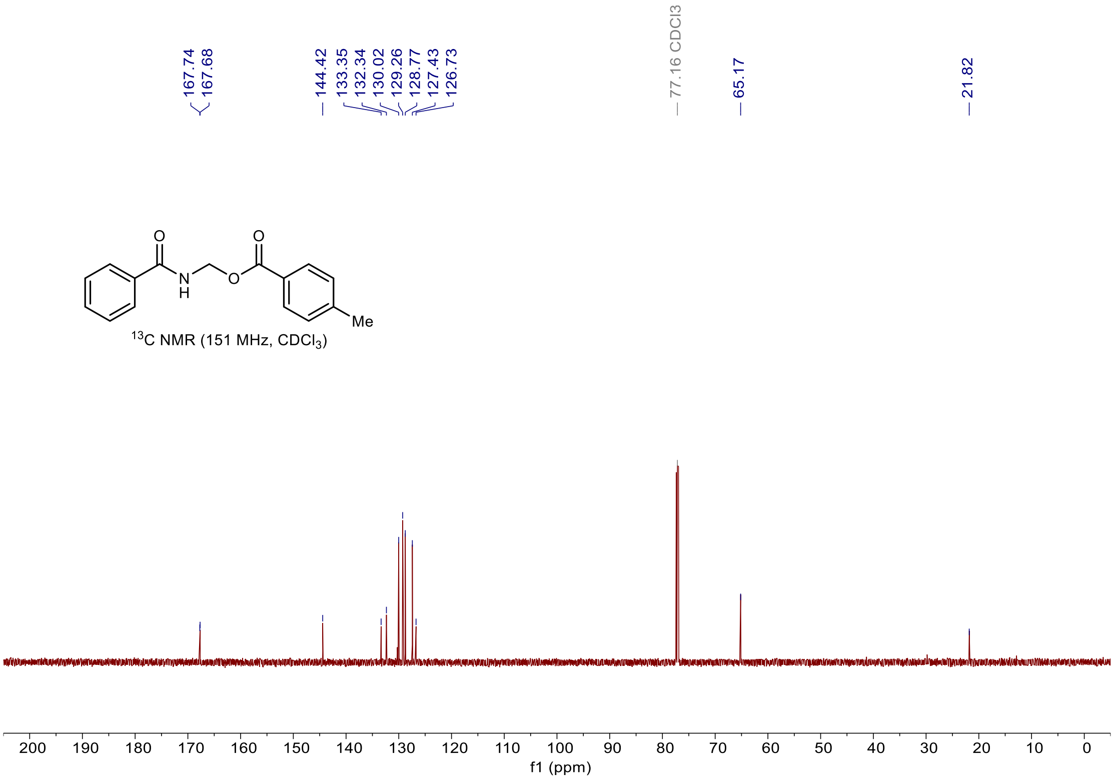
^{1}H and ^{13}C NMR spectra of compound 3z



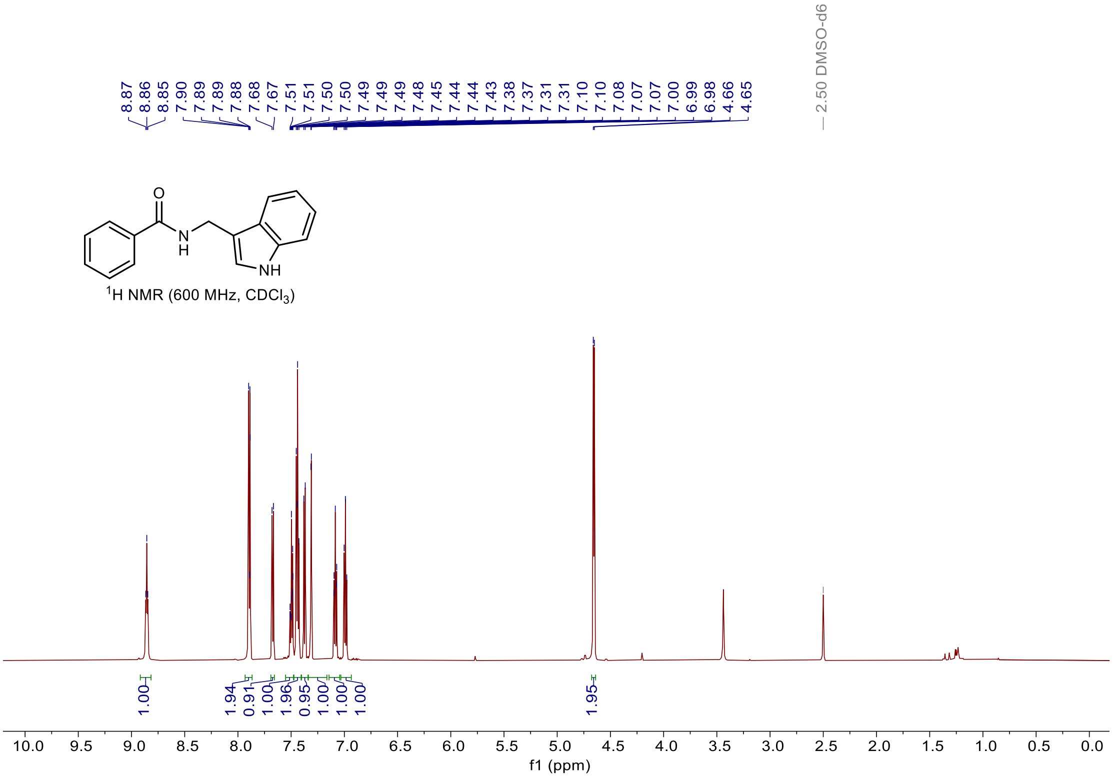


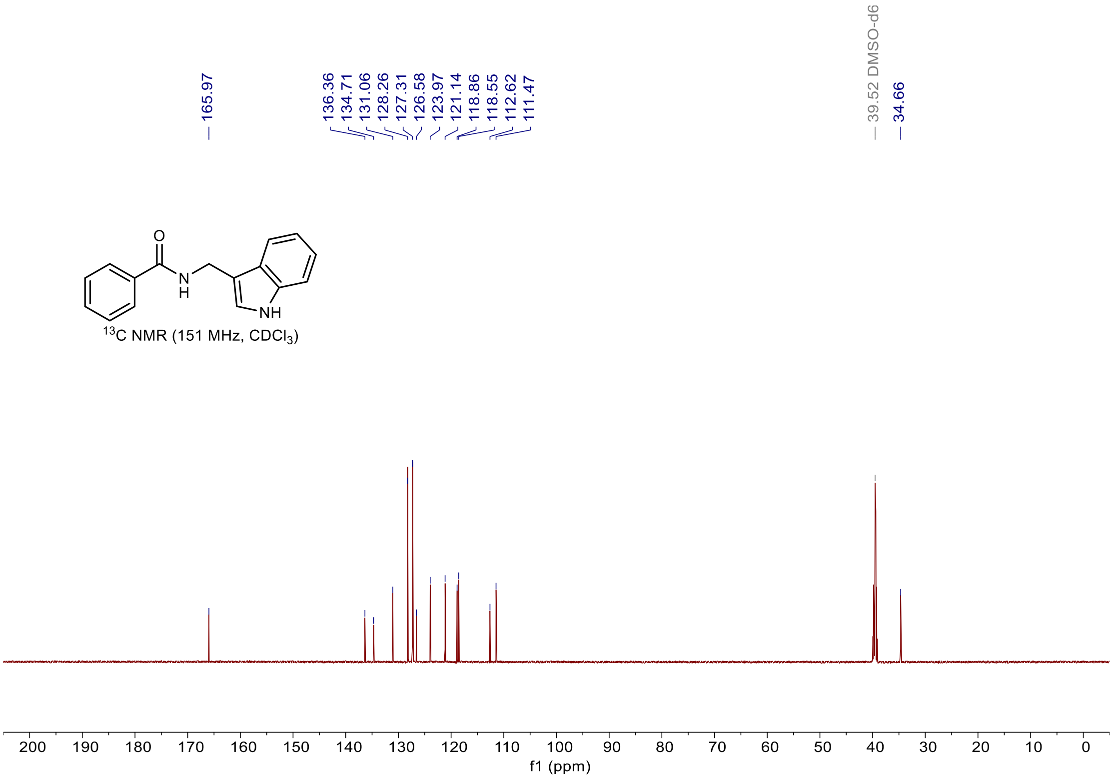
^{1}H and ^{13}C NMR spectra of compound 3aa



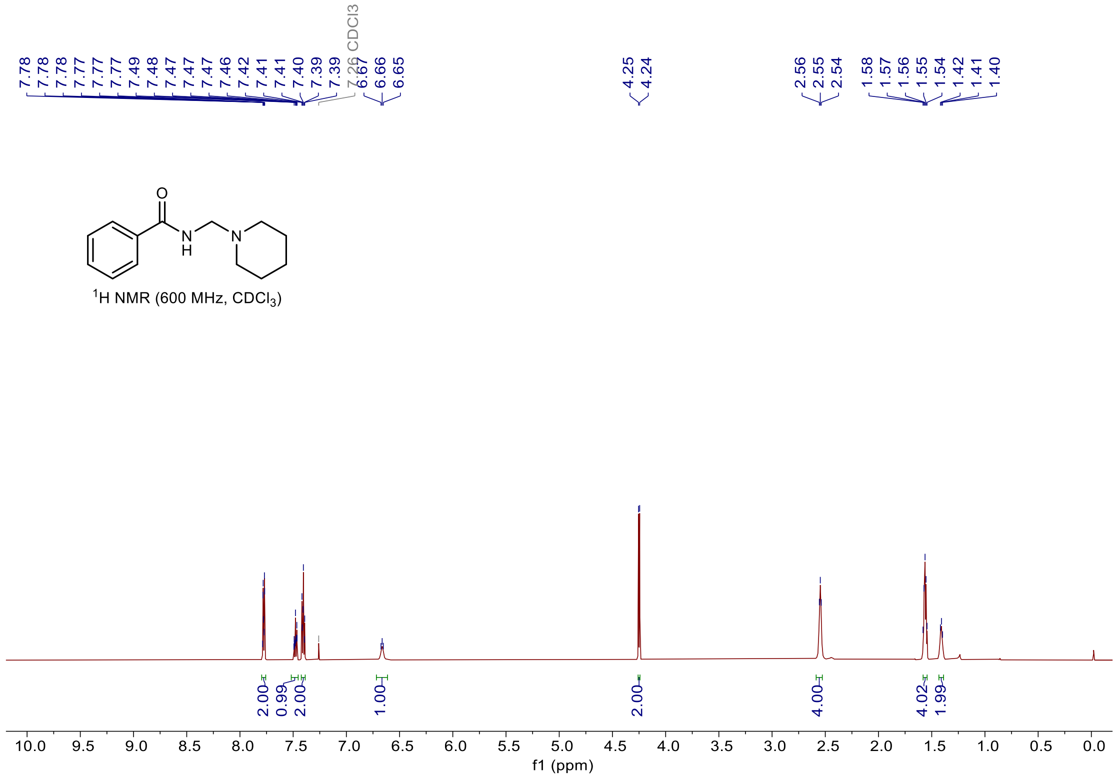


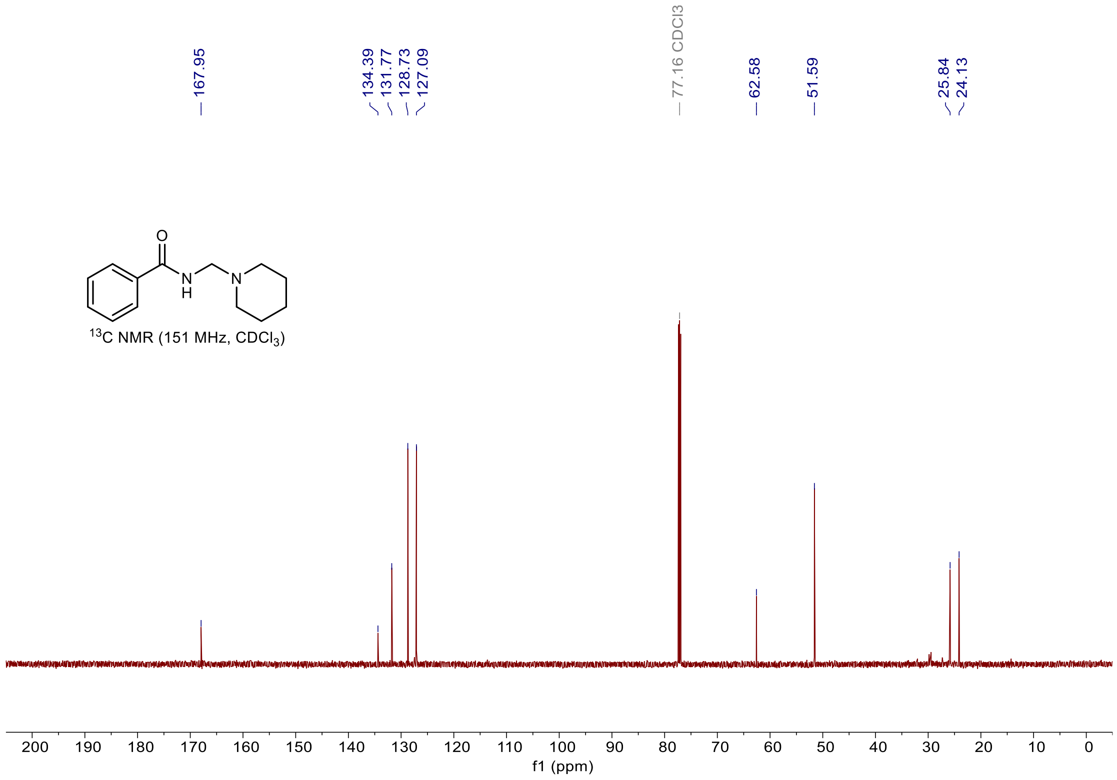
^{1}H and ^{13}C NMR spectra of compound 5



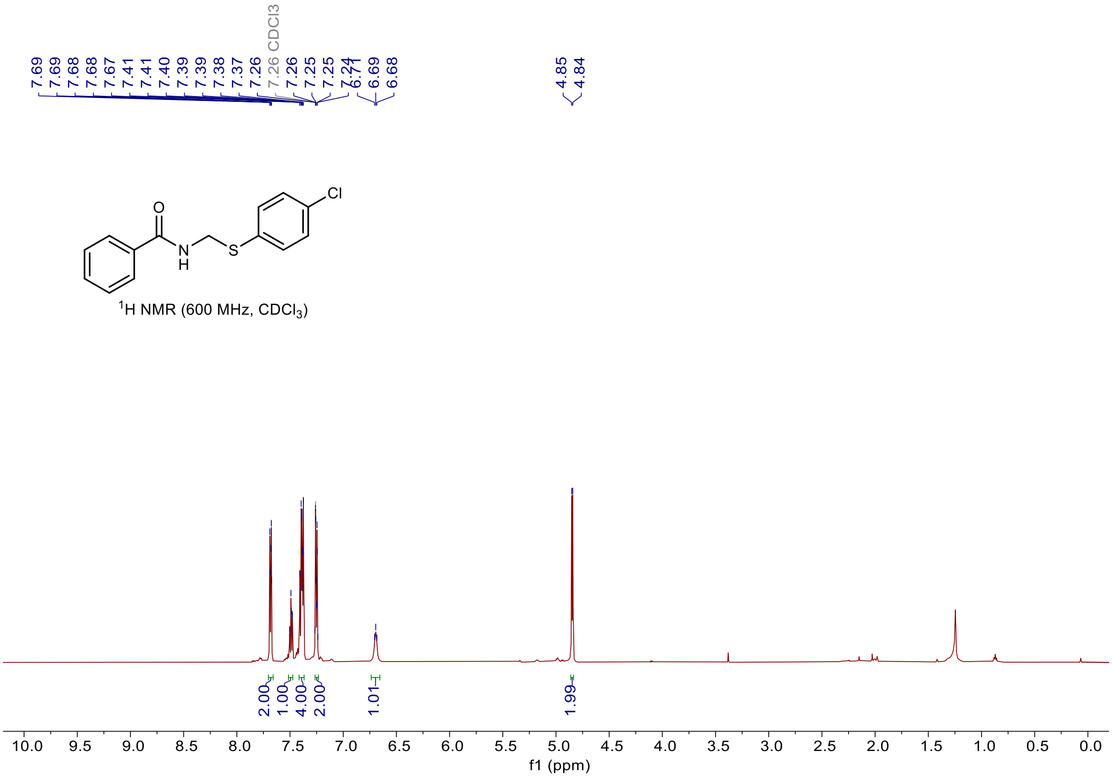


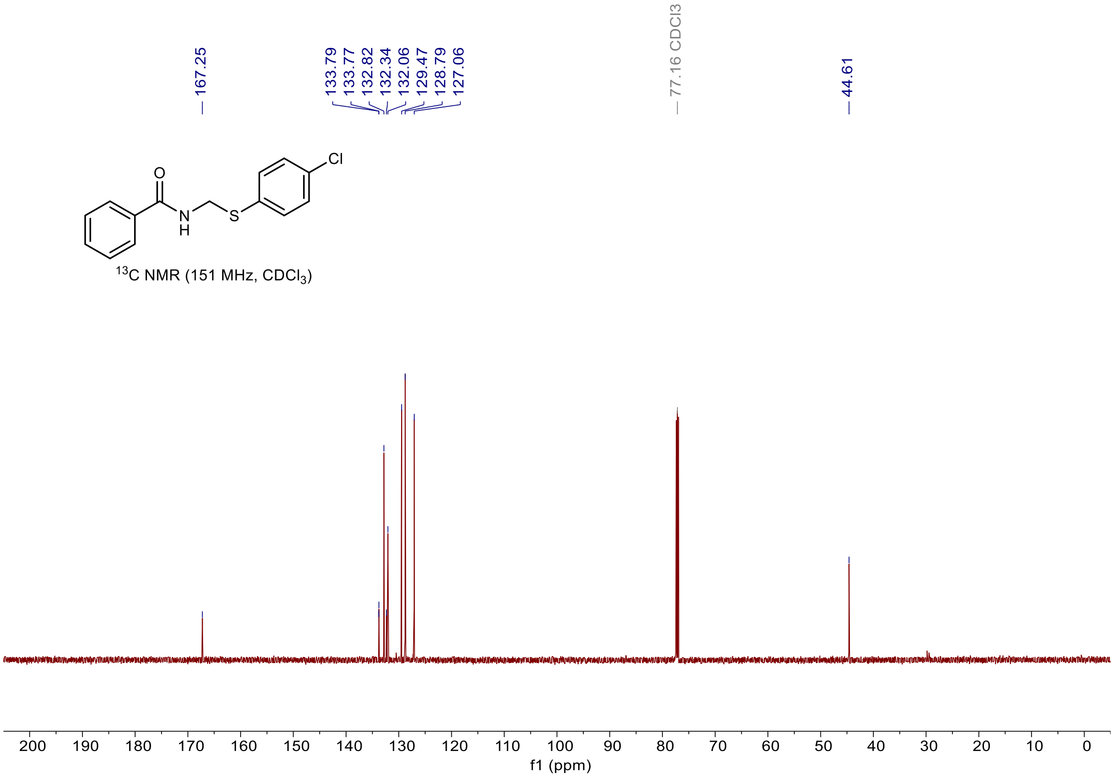
^{1}H and ^{13}C NMR spectra of compound 6





^{1}H and ^{13}C NMR spectra of compound 7





^{1}H and ^{13}C NMR spectra of compound 8