Electroreductive deconstruction and oxygenation of cyclic amines

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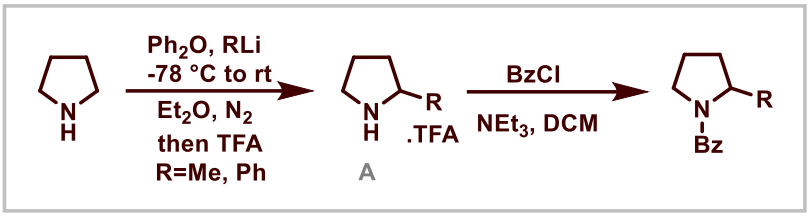
Contents

A. General Information

Unless noted otherwise, all reagents and solvents were purchased from commercial sources and used as received. All reactions were performed in oven-dried round-bottom flasks. Electrochemical reactions were performed at room temperature using a DC power supply of Keysight Technologies (25 V, 5A) and GW INSTEK GPP-4323 (32 V, 3A). Electrodes were commercially available from IKA. Cyclic voltammetry analysis was carried out in CH instrument electrochemical analyzer (CHI1210C). The developed chromatogram was analyzed by UV lamp (254 nm) or p-anisaldehyde solution. Column chromatography was performed on silica gel mesh size 230-400. The proton (^{1}H) and carbon $^{13}C\{^{1}H\}$ and ^{19}F NMR spectra were recorded in a 400 MHz JEOL JNM ECS400 spectrometer in the $CDCl_3$ solvent (unless otherwise mentioned) and are reported in δ units. Chemical shifts of NMR spectra are expressed in parts per million (ppm). Coupling constants (J values) are reported in Hz. High-resolution mass spectra (HRMS) were obtained using the electron spray ionization (ESI) technique and a TOF mass analyzer. Yields refer to isolated compounds. The description of the signals includes the following: s = singlet, d = doublet, dd = doublet of doublet, ddd = doublet of doublet of doublets, ddt = doublet of doublet of Triplets, dtd = doublet of triplet of doublets, tdd = triplet of doublet of doublets, t = triplet, dt = doublet of triplet, q = quartet, br = broad, and m = multiplet.

B. Preparation of the starting materials[1-6]

1. The synthesis of substrate 1a[1]

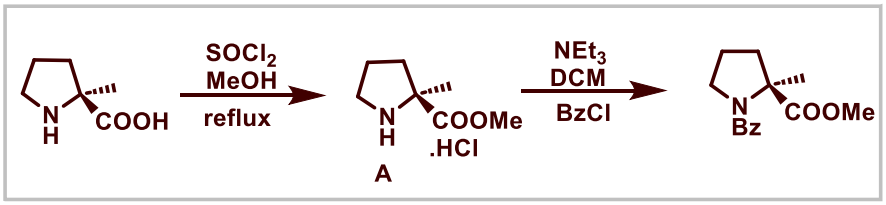


C2 substituted pyrrolidine TFA salt (**A**) was synthesized according to the reported procedure.[2] To a solution of pyrrolidine (821 μL, 10 mmol, 1.0 equiv) and benzophenone (2.19 g, 12 mmol, 1.2 equiv) in Et_2O (20 mL, 0.50 M) was added RLi (1.0 M in Et_2O, 25 mL, 25 mmol, 2.5 equiv) dropwise at -78 °C under an atmosphere of N_2. After being stirred at the same temperature for 10 min, the reaction mixture was allowed to warm to room temperature and stirred for 7 h. The reaction was quenched with MeOH at 0 °C, and the mixture was diluted with water and extracted with 6.0 M HCl aq. (pH = 1). The aqueous layer was basified to pH = 13 with 6.0 M NaOH *aq.* The mixture was extracted three times with CH_2Cl_2. The combined organic layer was acidified to pH = 1 with TFA, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was used for the next step without further purification.
To a solution of the crude product obtained above (1.0 equiv) and Et_3N (3.0 equiv) in CH_2Cl_2 (25 mL, 0.40 M) was added BzCl (1.2 equiv), Ac_2O (1.5 equiv), or TFAA (1.5 equiv) dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 1 h, which was then quenched with a saturated $NaHCO_3$ aqueous solution and extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (10-20% EtOAc in Hexane) to afford *N*-acyl pyrrolidine **1a**.

2. The synthesis of substrates 1b-1c and 6[1]

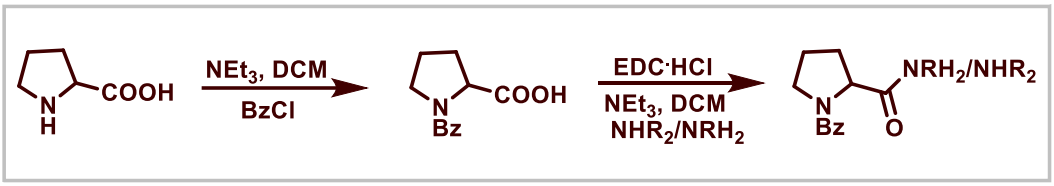
To a solution of pyrrolidine salt (1.0 equiv) and Et_3N (3.0 equiv-4.0 equiv) in CH_2Cl_2 (0.40 M) was added benzoyl chloride (1.2 equiv) dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 30 min, which was then quenched with a saturated $NaHCO_3$ aqueous solution. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (10-20% EtOAc in Hexane) to afford pyrrolidine **1b-1c**.

3. The synthesis of substrate 1d[1]



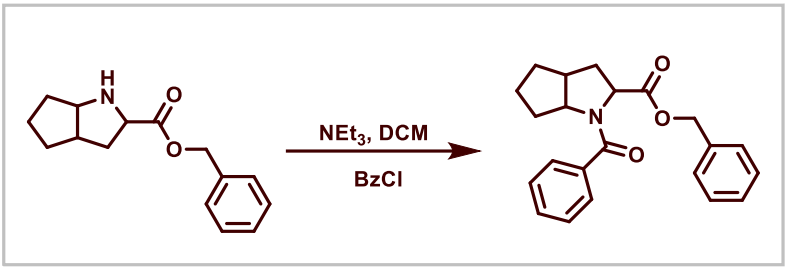
To a solution of pyrrolidine (2.0 mmol, 1.0 equiv) in MeOH (4.0 mL, 0.50 M) was added thionyl chloride (4.0 mmol, 2.0 equiv) dropwise at 0 °C. The reaction mixture was refluxed for 3 h. After the reaction mixture had been cooled to room temperature, the mixture was concentrated *in vacuo*. The crude product was used for the next step without further purification.
To a solution of the crude product obtained above (1.0 equiv) and Et_3N (836 μL, 6.0 mmol, 3.0 equiv) in CH_2Cl_2 (5.0 mL, 0.40 M) was added BzCl (279 μL, 2.4 mmol, 1.2 equiv) dropwise at 0 °C. After the mixture was allowed to warm to room temperature and stirred for 1 h, the reaction was quenched with a saturated $NaHCO_3$ aqueous solution. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (30-40% EtOAc in Hexane) to afford pyrrolidine **1d**.

4. The synthesis of substrate 1e[1-3]



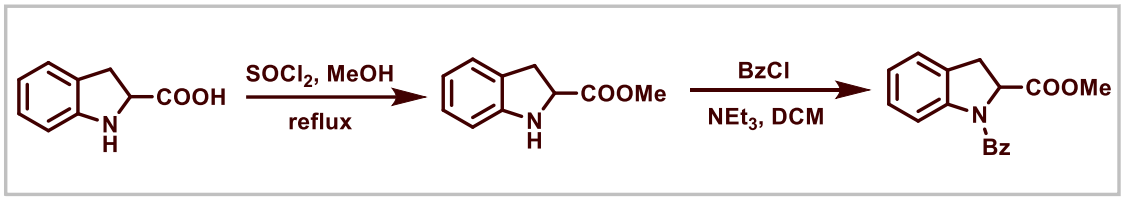
To a solution of proline (1.0 equiv) and Et_3N (3.0 equiv) in CH_2Cl_2 (0.50 M) was added BzCl (1.2 equiv) dropwise and stirred at room temperature for 30 min, which was then quenched with water. The mixture was extracted with 6.0 M NaOH *aq*. The aqueous layer was acidified to pH = 1 with 6.0 M HCl aq. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was concentrated *in vacuo*. The crude product was used for the next step without further purification.
To a solution of the crude product obtained above (1.0 equiv) in CH_2Cl_2 (0.50 M) was added EDC·HCl (1.2 equiv). After the mixture had been stirred at room temperature for 30 min, to this mixture were added Et_3N (1.5 equiv) and amine (1.2 equiv). The solution was stirred for several hours while the reaction progress was being monitored by TLC. After the starting material had been completely consumed, the reaction was quenched with water. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (50% EtOAc in Hexane) to afford pyrrolidine **1e**.

5. The synthesis of substrate 1f[1]



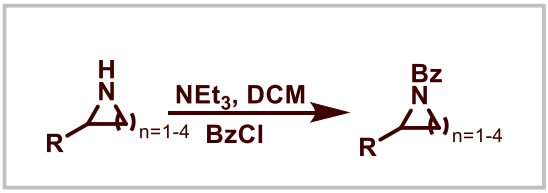
To a solution of pyrrolidine (1.0 equiv) and Et_3N (3.0 equiv-4.0 equiv) in CH_2Cl_2 (0.40 M) was added benzoyl chloride (1.2 equiv) dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 30 min, which was then quenched with a saturated $NaHCO_3$ aqueous solution. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (10-20% EtOAc in Hexane) to afford pyrrolidine **1f**.

6. The synthesis of substrates 1g-1h[1-2]



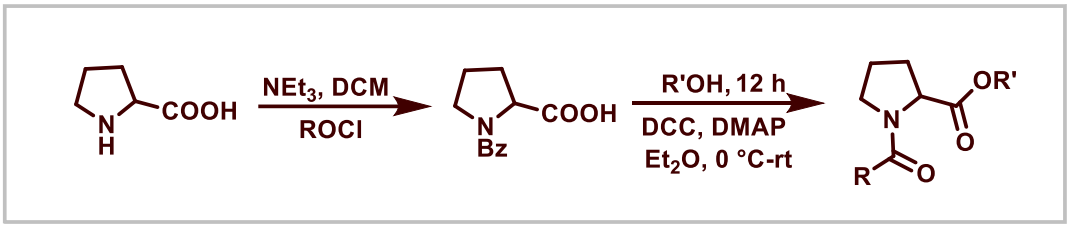
To a solution of indoline-2-carboxylic acid (1.5 mmol, 1.0 equiv) in MeOH (3.0 mL, 0.50 M) was added $SOCl_2$ (3.0 mmol, 2.0 equiv). After being heated at 70 °C for 3 h, the reaction mixture was concentrated *in vacuo*. To the residue were added CH_2Cl_2 (5.0 mL, 0.40 M), Et_3N (1.1 mL, 8.0 mmol, 4.0 equiv), and BzCl (3.0 mmol, 1.5 equiv). After being stirred for 2 h, the reaction was quenched with a saturated $NaHCO_3$ *aq*. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (30% EtOAc in Hexane) to afford **1g-1h**.

7. The synthesis of substrates 1i-1l[1-5]



To a solution of pyrrolidine (1.0 equiv) and Et_3N (3.0 equiv-4.0 equiv) in CH_2Cl_2 (0.40 M) was added benzoyl chloride (1.2 equiv) dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 30 min, which was then quenched with a saturated $NaHCO_3$ aqueous solution. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (10-20% EtOAc in Hexane) to afford pyrrolidine **1i-1l**.

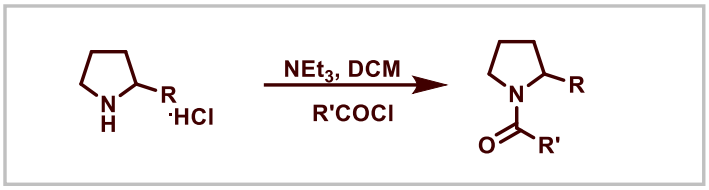
8. The synthesis of substrates 1aa-1af[1-3]



First, the proline was protected with a benzoyl group, following the reported procedure.[1-3] Then, DCC (6 mmol, 2 equiv) was added portion-wise to the alcohol (3 mmol, 1 equiv), proline derivative (4.5 mmol, 1.5 equiv), and DMAP (0.6 mmol, 20 mol%) in Et_2O (14 mL) at 0 °C. Once added, the reaction was stirred at room temperature. After completion, the mixture was filtered and washed with Et_2O. The

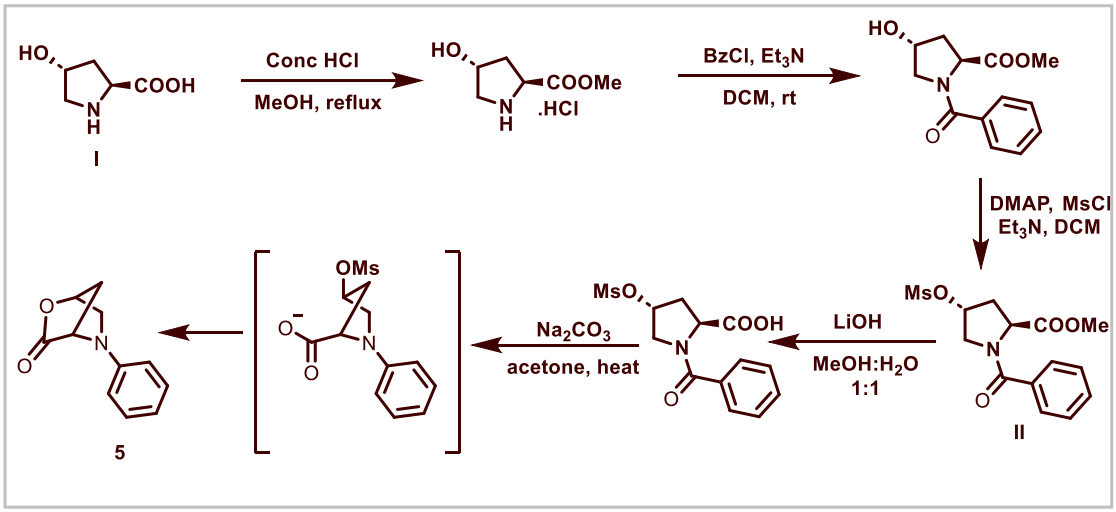
filtrate was evaporated, and the residue was purified by silica gel column chromatography (40-50% EtOAc in Hexane) to afford the desired products **1aa-1af.**

9. The synthesis of substrates 1m-1r and 3a-3i[1]



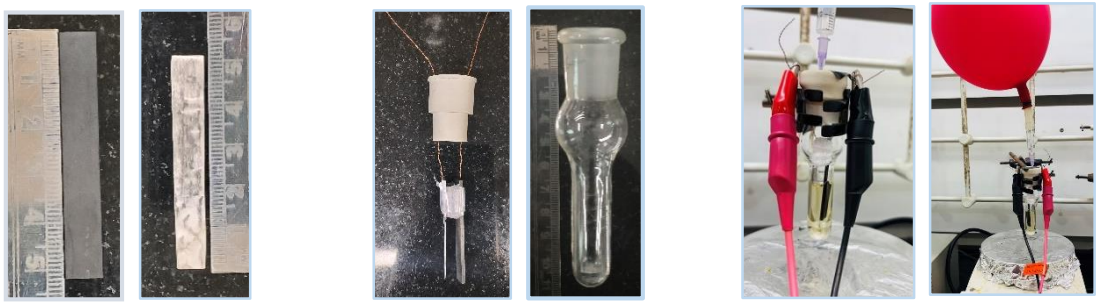
To a solution of pyrrolidine (1.0 equiv) in CH_2Cl_2 (0.40 M) were added Et_3N (3 equiv) and acyl chloride (1.2 equiv) at 0 °C. The reaction was allowed to warm to room temperature and stirred for 8 h. The reaction was quenched with water and extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (20-30% EtOAc in Hexane) to afford pyrrolidine **1m-1r** and **3a-3i**.

10. The synthesis of substrate 5[1]



Firstly, **II** is synthesised by using the reported procedure.[1] To a solution of **II** (1.7 mmol, 1.0 equiv) in MeOH/H_2O (3.3 mL/3.3 mL, 0.25 M) was added lithium hydroxide anhydrous (5.0 mmol, 3.0 equiv). After being stirred at room temperature for 5 min, the reaction was quenched with a 3.0 M HCl *aq.* (pH = 1) and extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was used for the next step without further purification.
To a solution of the crude product obtained above in acetone (0.10 M) was added sodium carbonate (1.22 mmol, 1.5 equiv). The mixture was stirred at 60 °C for 7 h while the reaction progress was being monitored by TLC. The solvent was removed under reduced pressure. The residue was diluted with water and extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (50% EtOAc in hexane) to afford **5** as a white solid.

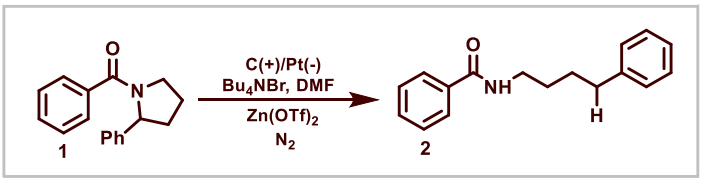
C. General setup and procedure for electrochemical reaction



Electrodes Undivided Cell Electrolysis

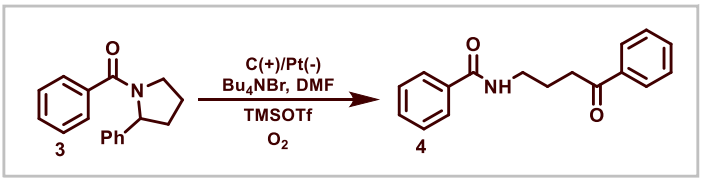
Figure: A

➢ **Synthesis of *δ*-substituted amides**



To an undivided cell equipped with a magnetic stirring bar and graphite as anode and platinum as cathode, having dimensions (W×H×D) 8×52.5×2 mm, were added pyrrolidine **1** (0.15 mmol, 1.0 equiv), Bu_4NBr (0.15 mmol), and zinc trifluoromethanesulfonate ($Zn(OTf)_2$: 10 mol%). After being sealed with a septum, the vial was evacuated and backfilled three times with N_2 gas. To this vial were added DMF (3.0 mL). After being electrolyzed at a constant current of 10 mA at room temperature for 12 h, the reaction mixture was diluted with water and extracted three times with EtOAc. The combined organic layer was concentrated *in vacuo*, and the residue was purified to afford the corresponding product **2.**

➢ **Synthesis of *δ*-ketoamides**



To an undivided cell equipped with a magnetic stirring bar and graphite as anode and platinum as cathode, having dimensions (W×H×D) 8×52.5×2 mm, were added pyrrolidine **3** (0.15 mmol, 1.0 equiv), and Bu_4NBr (0.15 mmol). After being sealed with a septum, the vial was evacuated and backfilled three times with O_2 gas. To the vial were added 3.0 mL of DMF and trimethylsilyl trifluoromethanesulfonate (TMSOTf: 10 mol%); the vial was kept under a continuous oxygen atmosphere using a balloon. Being electrolyzed at a constant current of 20 mA at room temperature for 12 h, the reaction mixture was

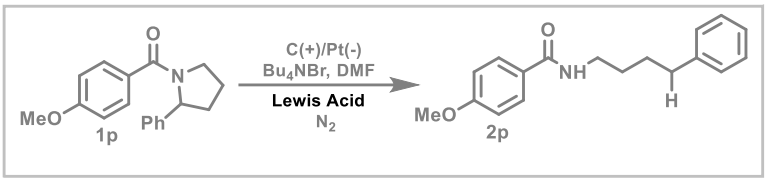
diluted with water and extracted three times with EtOAc. The combined organic layer was concentrated *in vacuo*, and the residue was purified to afford the corresponding product **4**.

D. Optimization studies

a. Synthesis of *δ*-substituted amides

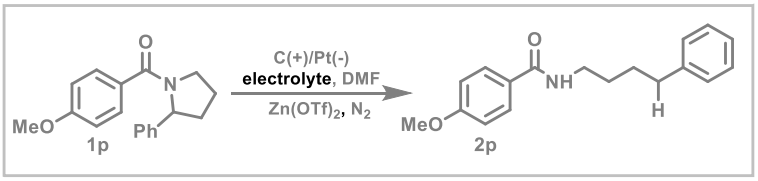
To an undivided cell equipped with a magnetic stirring bar and electrodes (anode & cathode) were added pyrrolidine **1p** (0.15 mmol, 1.0 equiv), electrolyte (0.15 mmol), and Lewis acid (10 mol%). After being sealed with a plastic septum, the cell was evacuated and backfilled three times with N_2 gas. To this vial, DMF (3 mL) was added. After being electrolyzed at a constant current of 10 mA at room temperature for 12 h, the reaction mixture was diluted with water and extracted three times with EtOAc. The combined organic layer was concentrated *in vacuo*, and the residue was purified to afford the corresponding product **2.**

I. Lewis acid



S.No.	**Lewis Acid**	Yield of 2p (%)
1	none	n.r.
2	$Cu(OTf)_2$	n.r.
3	TMSOTf	40
4	$BF_3{\cdot}Et_2O$	trace
5	$Sc(OTf)_3$	20
6	$Sn(OTf)_2$	n.r.
7	TMSCl	n.r.

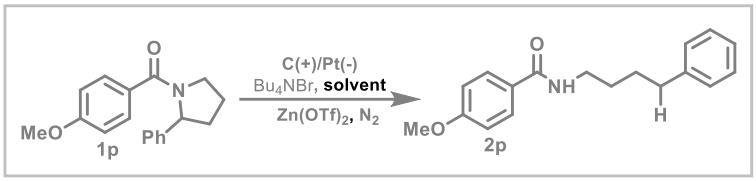
II. Electrolyte



S.No.	**Electrolyte**	Yield of 2p (%)
1	none	n.r.(High resistance)
2	Bu_4NI	30
3	Bu_4NOTf	n.r.
4	Bu_4NOAc	n.r.

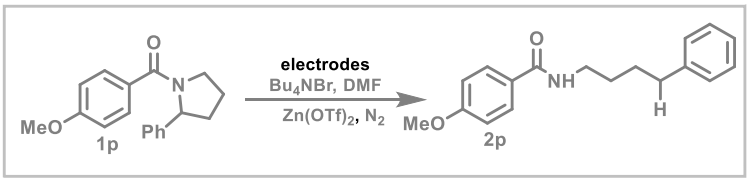
5	Bu_4NBF_4	trace
6	$LiClO_4$	n.r.

III. Solvent



S.No.	**Solvent**	Yield of 2p (%)
1	DMA	70
2	DCE	n.r.
3	DMSO	40
4	ACN	55
5	DCM	n.r.
6	THF	n.r.

IV. Electrode



S.No.	**Electrode**	Yield of 2p (%)
1	C(+)/C(-)	10
2	Al(+)/Pt(-)	60
3	Zn(+)/Pt(-)	42
4	Pt(+)/Pt(-)	15
5	C(+)/Ni(-)	40
6	Mg(+)/Pt(-)	n.r.

b. Synthesis of *δ*-ketoamides

To an undivided cell equipped with a magnetic stirring bar and electrodes (anode & cathode) were added pyrrolidine **3g** (0.15 mmol, 1.0 equiv), electrolyte (0.15 mmol), and Lewis acid (10 mol%). After being sealed with a plastic septum, the cell was evacuated and backfilled three times with O_2 gas. After adding 3.0 mL of DMF, the vial was kept under a continuous oxygen atmosphere using a balloon. After being electrolyzed at a constant current of 20 mA at room temperature for 12 h, the reaction mixture was diluted with water and extracted three times with EtOAc. The combined organic layer was concentrated *in vacuo*, and the residue was purified to afford the corresponding product **4g**.

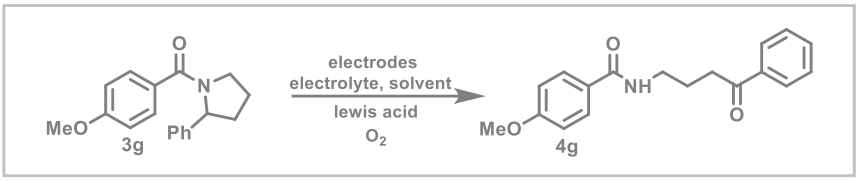


Table:1

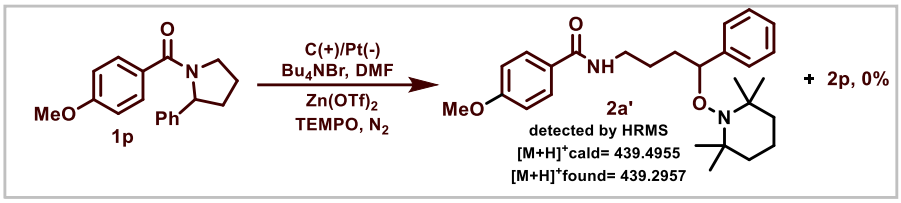
Entry[a]	Electrode	Supporting Electrolyte	Solvent	Lewis Acid	Yield(%)[b]
1	C(+)/Pt(-)	Bu_4NBF_4	DMF	$Zn(OTf)_2$	10
2	C(+)/Ni(-)	Bu_4NBF_4	DMF	$Zn(OTf)_2$	trace
3	Pt(+)/Pt(-)	Bu_4NBF_4	DMF	$Zn(OTf)_2$	n.r.
4	C(+)/Pt(-)	Bu_4NBr	DMF	$Zn(OTf)_2$	15
5	C(+)/Pt(-)	Bu_4NI	DMF	$Zn(OTf)_2$	n.r.
6	C(+)/Pt(-)	Bu_4NBr	DMF	$Sc(OTf)_3$	n.r.
7	C(+)/Pt(-)	Bu_4NBr	DMF	TMSCl	30
8	**C(+)/Pt(-)**	**Bu_4NBr**	**DMF**	**TMSOTf**	**75**
9	C(+)/Pt(-)	Bu_4NBr	ACN	TMSOTf	20
10[c]	C(+)/Pt(-)	Bu_4NBr	DMF	TMSOTf	50
11[d]	C(+)/Pt(-)	Bu_4NBr	DMF	TMSOTf	68
12[e]	C(+)/Pt(-)	Bu_4NBr	DMF	TMSOTf	25
13[f]	C(+)/Pt(-)	Bu_4NBr	DMF	TMSOTf	n.r.

[a] Reaction conditions: **3g** (0.15), electrolyte (0.15 mmol), solvent (3 mL), Lewis acid (10 mol%), 20 mA constant current, graphite anode and platinum cathode, dimensions (W×H×D) 8×52.5×2 mm, the distance between two electrodes is 5 mm and dipped 20 mm in solution, undivided cell, 25 °C, under contant pressure of oxygen balloon. [b] Isolated yield, n.r. = no

reaction. [c] 10 mA current instead of 20 mA. [d] 25 mA current instead of 20 mA. [e] In the open air atmosphere. [f] In the absence of electricity.

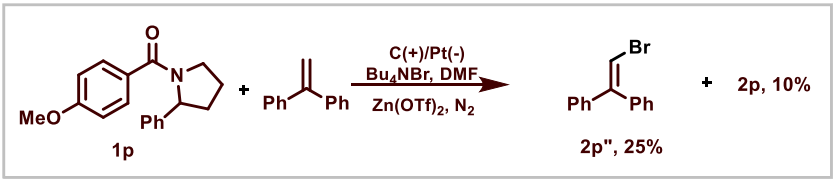
E. Mechanistic studies

i) Radical scavenging experiment with 2,2,6,6-tetramethyl-1-piperidinyloxy radical (TEMPO)



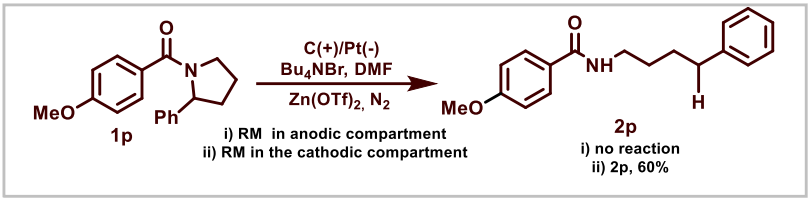
To an undivided cell equipped with a magnetic stirring bar and graphite as anode and platinum as cathode, pyrrolidine **1p** (0.15 mmol, 1.0 equiv), Bu_4NBr (0.15 mmol), and zinc trifluoromethanesulfonate ($Zn(OTf)_2$: 10 mol%) and TEMPO (2.0 equiv). After being sealed with a septum, the vial was evacuated and backfilled three times with N_2 gas. To this vial were added DMF (3.0 mL). After being electrolyzed at a constant current of 10 mA at room temperature for up to 18 h, the progress of the reaction was monitored by TLC, which shows that the starting material was consumed and a complex reaction mixture was observed. The TEMPO adduct was detected by HRMS analysis, which confirms that the reaction follows a radical pathway.

ii) Radical scavenging experiment with 1,1-diphenylethylene



To an undivided cell equipped with a magnetic stirring bar and graphite as anode and platinum as cathode, pyrrolidine **1p** (0.15 mmol, 1.0 equiv), Bu_4NBr (0.15 mmol), and zinc trifluoromethanesulfonate ($Zn(OTf)_2$: 10 mol%) and 1,1-diphenylethylene (1.0 equiv). After being sealed with a septum, the vial was evacuated and backfilled three times with N_2 gas. To this vial were added DMF (3.0 mL). After being electrolyzed at a constant current of 10 mA at room temperature the progress of the reaction was monitored by TLC. After 6h of reaction time, the starting material was consumed. Further, the reaction mixture was purified through column chromatography, 10% desired product **2p** and 25% of the (2-bromoethene-1,1-diyl)dibenzene **2p"** was obtained.

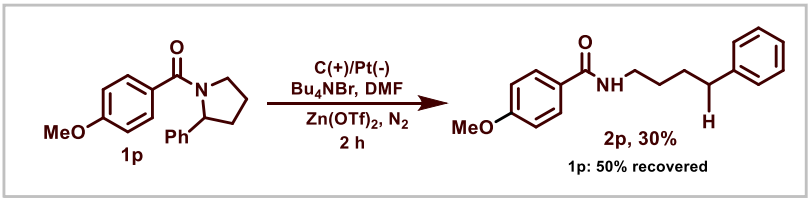
iii) Divided cell experiment



Case 1: In anodic chamber: A divided cell was equipped with two magnetic stir bars in the anodic and cathodic chambers, respectively. Further, the anodic chamber was filled with corresponding pyrrolidine **1p** (1.0 equiv, 0.15 mmol), Bu_4NBr (3.0 equiv., 0.45 mmol), and $Zn(OTf)_2$ (10 mol%) in DMF solvent under a nitrogen atmosphere. The cathodic chamber was filled only with supporting electrolyte Bu_4NBr (3.0 equiv, 0.45 mmol), and the solution was electrolyzed with a carbon anode (in the anodic chamber) and a platinum cathode (in the cathodic chamber) at a constant current of 10 mA for 24 h at room temperature (25-30 °C). The progress of the reaction was monitored by TLC, which showed the starting material remains unconsumed.

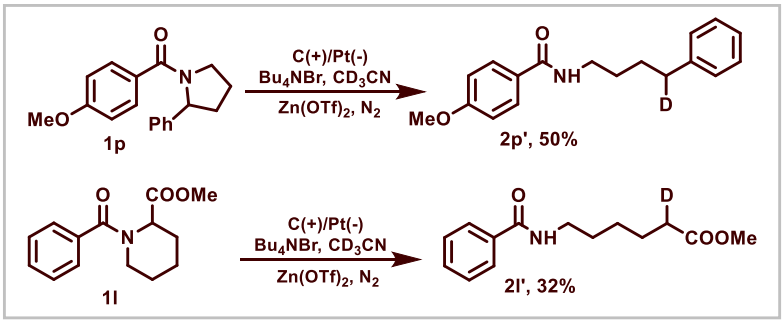
Case 2: In the cathodic chamber, a divided cell was equipped with two magnetic stir bars in the anodic and cathodic chambers, respectively. Further, the cathodic chamber was filled with corresponding pyrrolidine **1p** (1.0 equiv, 0.15 mmol), Bu_4NBr (3.0 equiv, 0.45 mmol), and $Zn(OTf)_2$ (10 mol%) in DMF solvent under a nitrogen atmosphere. The anodic chamber was filled with supporting electrolyte Bu_4NBr (3.0 equiv, 0.45 mmol), and the solution was electrolyzed with a carbon anode (in the anodic chamber) and a platinum cathode (in the cathodic chamber) at a constant current of 10 mA for 15 h at room temperature. The progress of the reaction was monitored by TLC. After total consumption of pyrrolidine, the reaction mixture was diluted with water and extracted three times with EtOAc. The combined organic layer was concentrated *in vacuo*, and the residue was purified to afford the corresponding product **2p** in a slightly lower yield, i.e., 60%. This implies that the reaction takes place by the cathodic reduction.

iv) Time-based electrolysis



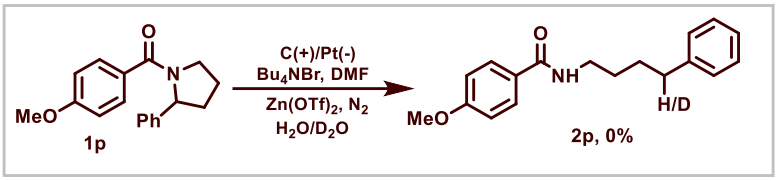
To an undivided cell equipped with a magnetic stirring bar and graphite as anode and platinum as cathode, pyrrolidine **1p** (0.15 mmol, 1.0 equiv), Bu_4NBr (0.15 mmol), and zinc trifluoromethanesulfonate ($Zn(OTf)_2$: 10 mol%). After being sealed with a septum, the vial was evacuated and backfilled three times with N_2 gas. To this vial was added DMF (3.0 mL). Reaction was electrolyzed at a constant current of 10 mA at room temperature for up to 2 h, the progress of the reaction was monitored by TLC, which shows that starting material remains with small amount of product formation. After, that the reaction was stirred overnight without electricity. Again, the progress of the reaction was monitored by TLC, similar TLC was observed. Further, the reaction mixture was purified through column chromatography, 30% desired product **2p** and approx. 50% of the starting material **1p** was recovered. This indicates that the chain propagation step is absent in this case.

v) Electrolysis in deuterated solvent (CD_3CN)



To an undivided cell equipped with a magnetic stirring bar and graphite as anode and platinum as cathode, **1** (0.15 mmol, 1.0 equiv), Bu_4NBr (0.15 mmol), and zinc trifluoromethanesulfonate ($Zn(OTf)_2$: 10 mol%). After being sealed with a septum, the vial was evacuated and backfilled three times with N_2 gas. To this vial were added CD_3CN (3.0 mL). After being electrolyzed at a constant current of 10 mA at room temperature for 12 h, the reaction mixture was diluted with water and extracted three times with EtOAc. The combined organic layer was concentrated *in vacuo*, and the residue was purified to afford the corresponding product **2.**

vi) Electrolysis in H_2O/D_2O



To an undivided cell equipped with a magnetic stirring bar and graphite as anode and platinum as cathode, pyrrolidine **1p** (0.15 mmol, 1.0 equiv), Bu_4NBr (0.15 mmol), and zinc trifluoromethanesulfonate ($Zn(OTf)_2$: 10 mol%). After being sealed with a septum, the vial was evacuated and backfilled three times with N_2 gas. To this vial were added DMF (3.0 mL) and H_2O/D_2O (equiv). After being electrolyzed at a constant current of 10 mA at room temperature for 12 h.

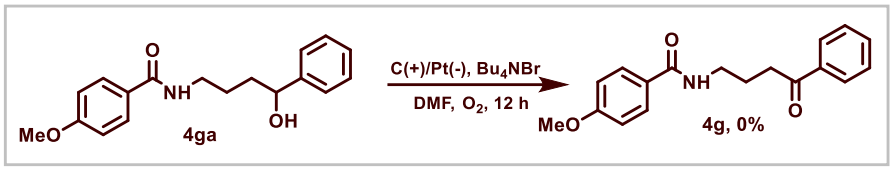
Table: 2

S.No.	H_2O (equiv.)	Yield 2p (%)
1	1	complex mixture
2	5	no reaction
3	10	no reaction

Table: 3

S.No.	D_2O (equiv.)	Yield 2p (%)
1	1	no reaction
2	5	no reaction
3	10	no reaction

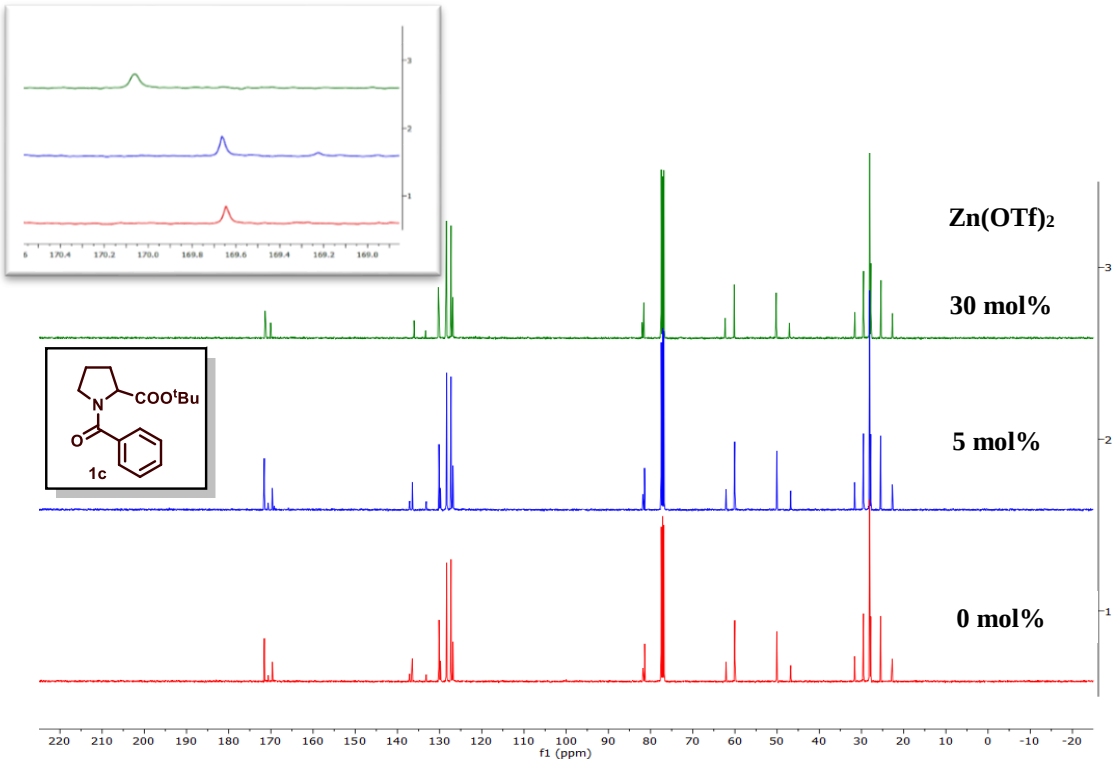
vii) Electrolysis of *δ*-Hydroxy benzamide



To an undivided cell equipped with a magnetic stirring bar and graphite as anode and platinum as cathode, δ-hydroxy benzamide **4ga** (0.15 mmol, 1.0 equiv), Bu_4NBr (0.15 mmol). After being sealed with a septum, the vial was evacuated and backfilled three times with O_2 gas. To this vial were added DMF (3.0 mL). After being electrolyzed at a constant current of 20 mA at room temperature for 12 h under oxygen atmosphere, the starting material **4ga** remains unconsumed as no desired product formed which excludes the possibility of its intermediancy or the participation of water in formation of *δ*-ketobenzamide **4g**.

viii) NMR studies

$^{13}C\{^1H\}$ NMR spectra of *N*-acyl pyrrolidines **1c** (0.20 mmol for (*N*-COPh), in the presence of $Zn(OTf)_2$ (0 mol%, 5 mol%, and 30 mol%) were measured in $CDCl_3$ (0.6 mL).



ix) Cyclic Voltammetry (CV) studies

Cyclic voltammetry analysis was performed using a CH Instrument electrochemical analyzer (CHI1210C). Samples were prepared in a 10 ml vial with 0.01 M of substrate (**1p**), and 0.1 M of tetrabutylammonium tetrafluoroborate (Bu_4NBF_4) in 6 mL dry acetonitrile (CH_3CN). All the cyclic voltammetry investigations were carried out using a three-electrode cell consisting of a glassy carbon working electrode (Disk electrode), a platinum wire (Pt) counter electrode, and a silver wire (Ag) as a pseudo-reference electrode, and ferrocene (Fc/Fc^+) as a reference or internal standard. The surface area of glassy carbon is 7.06 sq. mm. The working electrode was polished with 0.05 µm alumina slurry on a polishing pad and rinsed with deionized water before use. All the solutions used for the voltammetric experiments were deoxygenated by purging with high-purity argon gas (unless mentioned) for up to 5 minutes, and measurements were performed at room temperature. The scan rate applied was 50 mV/s, ranging from 0 V to -3V. CV experiment was measured in the negative or reductive direction. Graphs were plotted using the IUPAC convention.

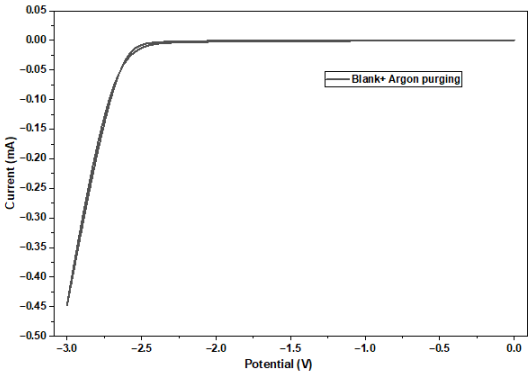


***Figure 1**: Bu_4NBF_4 (0.06 mmol) + ACN (6 mL) + Argon purging*

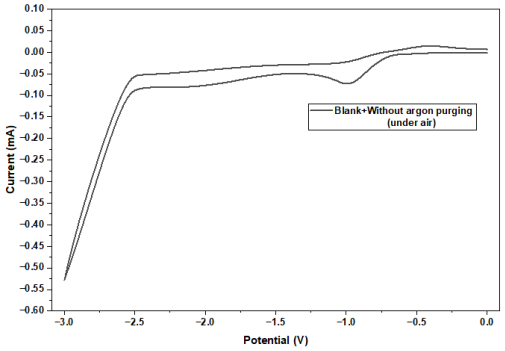


***Figure 2**: Bu_4NBF_4 (0.06 mmol) + ACN (6 mL) +without argon purging (open air)*

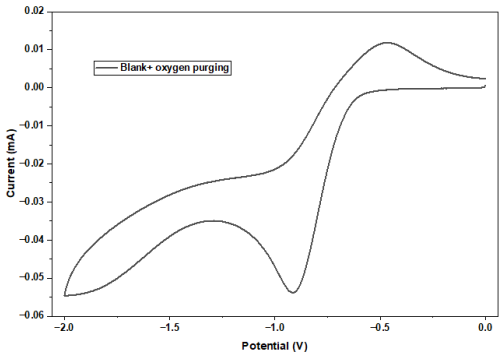


***Figure 3**: Bu_4NBF_4 (0.06 mmol) + ACN (6 mL) + Oxygen purging*

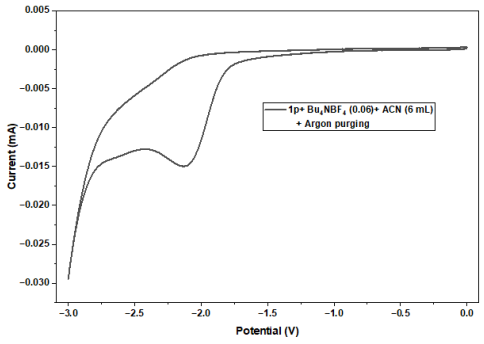


***Figure 4**: 1p+Bu_4NBF_4 (0.06 mmol) + ACN (6 mL) + Argon purging*

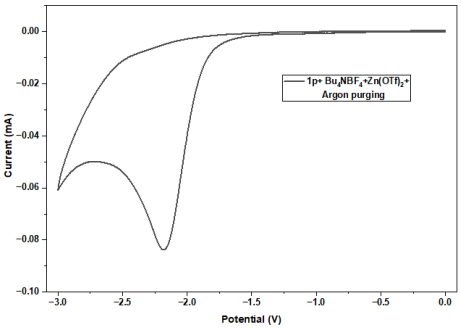


***Figure 5**:1p+Bu_4NBF_4 (0.06 mmol) + ACN (6 mL) + $Zn(OTf)_2$ + Argon purging*

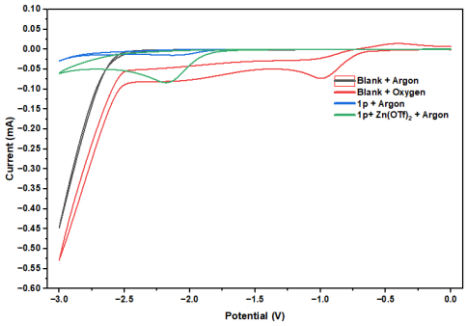
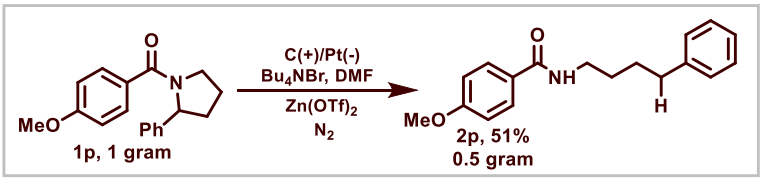


Figure 6

F. Synthetic applications

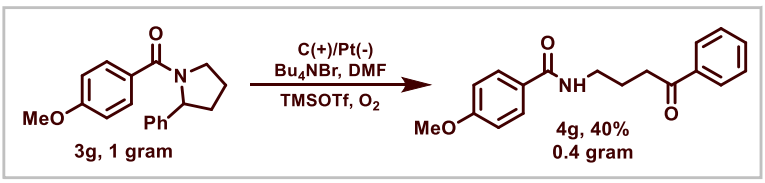
a) Electrochemical scale-up synthesis

➢ Synthesis of *δ*-substituted amide (2p)



To an undivided cell (20 mL) equipped with a magnetic stirring bar and graphite as anode and platinum as cathode were added pyrrolidine **1p** (3.5 mmol, 1.0 equiv), Bu_4NBr (7.1 mmol), and zinc trifluoromethanesulfonate ($Zn(OTf)_2$: 1.06 mmol). After being sealed with a septum, the vial was evacuated and backfilled three times with N_2 gas. To this vial were added DMF (12.0 mL). After being electrolyzed at a constant current of 10 mA at room temperature for 48 h, the reaction mixture was diluted with water and extracted three times with EtOAc. The combined organic layer was concentrated *in vacuo*, and the residue was purified to afford the corresponding product **2p** in 51% (0.5 gram) yield**.**

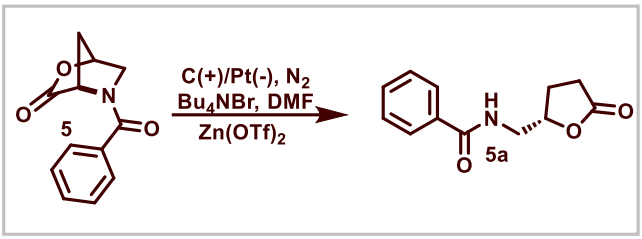
➢ Synthesis of *δ*-ketoamides (4g)



To an undivided cell (20 mL) equipped with a magnetic stirring bar and graphite as anode and platinum as cathode, were added pyrrolidine **3g (**3.5 mmol, 1.0 equiv) and Bu_4NBr (7.1 mmol). After being sealed with a septum, the vial was evacuated and backfilled three times with O_2 gas. To the vial were added 12.0 mL of DMF and trimethylsilyl trifluoromethanesulfonate (TMSOTf: 1.06 mmol), and kept under a continuous oxygen atmosphere using a balloon. After being electrolyzed at a constant current of 20 mA at room temperature for 60 h, the reaction mixture was diluted with water and extracted three times

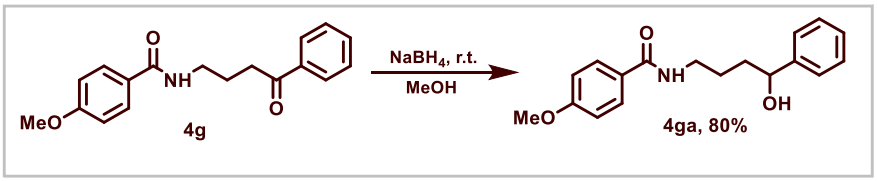
with EtOAc. The combined organic layer was concentrated *in vacuo*, and the residue was purified to afford the corresponding product **4g** in 40% yield.

b) Procedure for the electrochemical scaffold hopping



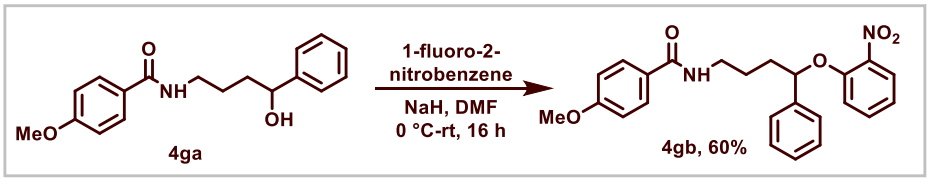
To an undivided cell equipped with a magnetic stirring bar and graphite as anode and platinum as cathode, having dimensions (W×H×D) 8×52.5×2 mm were added bicyclic compound **5** (0.15 mmol, 1.0 equiv), Bu_4NBr (0.15 mmol), and zinc trifluoromethanesulfonate ($Zn(OTf)_2$: 10 mol%). After being sealed with a septum, the vial was evacuated and backfilled three times with N_2 gas. To this vial were added DMF (3.0 mL). After being electrolyzed at a constant current of 10 mA at room temperature for 12 h, the reaction mixture was diluted with water and extracted three times with EtOAc. The combined organic layer was concentrated *in vacuo*, and the residue was purified to afford the corresponding product **5a** in **75%** yield**.**

c) Reduction of the keto-group in *δ*-ketoamides[7]



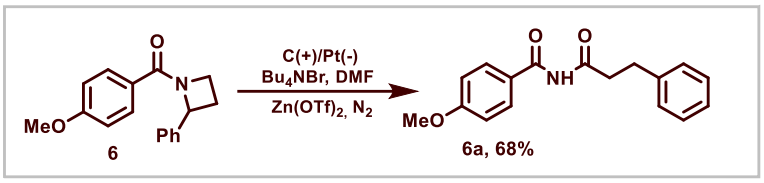
Dissolve *δ*-ketoamides **4g** (0.13 mmol) in methanol (0.8 mL) in a vial. Add $NaBH_4$ (0.19 mmol) portion-wise to the mixture. Observe the vigorous bubbling. Allow the reaction mixture to stand at room temperature until the bubbling ceases. Monitor the completion of the reaction. Extract the mixture *via* workup with CH_2Cl_2 and H_2O. Dry the organic layer over $MgSO_4$. Filter the mixture. Remove the solvent under vacuum to obtain *δ*-hydroxyamides **4ga** in 80% yield.

d) S_NAr reaction of *δ*-hydroxybenzamide[8]



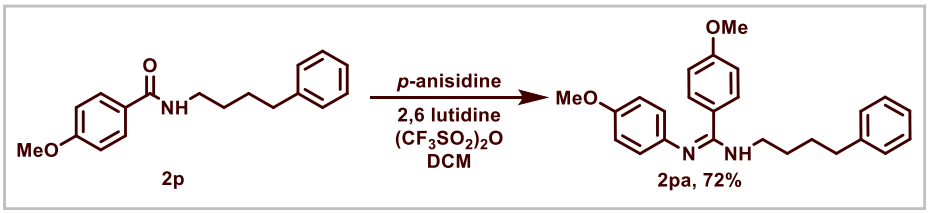
An oven-dried Schlenk tube was charged with sodium hydride (5 mg as 60% w/w dispersion in mineral oil, 0.10 mmol, 1.2 equiv.). After sealing the tube, it was evacuated and back-filled with N_2 three times. Then, a solution of *δ*-hydroxyamide **4ga** (28 mg, 0.09 mmol, 1.1 equiv) in dry DMF (1 mL) was added via syringe under N_2 atmosphere at 0 °C. The reaction was stirred at room temperature for 15 minutes. 1-Fluoro-2-nitrobenzene (9 µL, 0.08 mmol, 1.0 equiv) was subsequently added, and the reaction mixture was stirred at room temperature for 16 h. Upon completion, the reaction was quenched by the addition of sat. aqueous NH_4Cl (2 mL). The aqueous layer was extracted with ethyl acetate (3 x 5 mL), and the combined organic phase was washed with sat. aqueous NaCl (5 mL) and dried over anhydrous Na_2SO_4. The crude reaction mixture was then concentrated under reduced pressure and purified *via* column chromatography on silica gel to afford **4gb** in 60% yield.

e) Synthesis of diacyl amine derivative



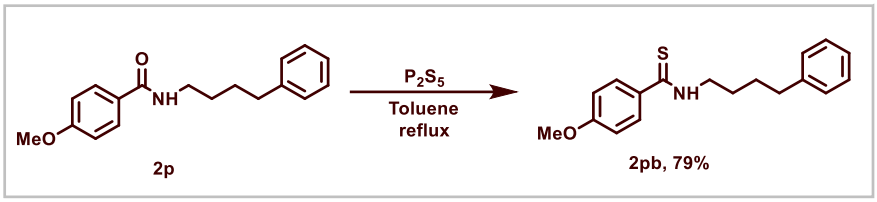
To an undivided cell equipped with a magnetic stirring bar and graphite as anode and platinum as cathode, were added azetidine **6** (0.15 mmol, 1.0 equiv), Bu_4NBr (0.15 mmol), and zinc trifluoromethanesulfonate ($Zn(OTf)_2$: 10 mol%). After being sealed with a septum, the vial was evacuated and backfilled three times with N_2 gas. To this vial were added DMF (3.0 mL). After being electrolyzed at a constant current of 10 mA at room temperature for 12 h, the reaction mixture was diluted with water and extracted three times with EtOAc. The combined organic layer was concentrated *in vacuo*, and the residue was purified to afford the corresponding product **6a** in 68**%** yield**.**

f) Synthesis of an amidine derivative[10]



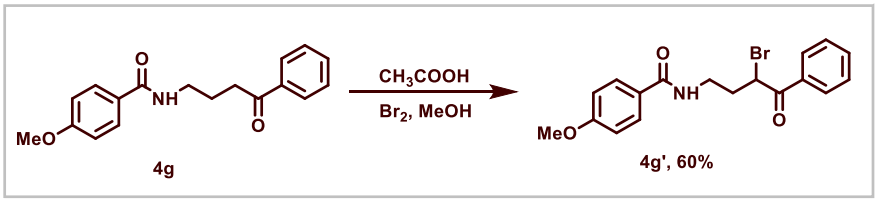
4-methoxy-N-(4-phenylbutyl) benzamide **2p** (30 mg, 0.105mmol, 1.0 equiv) was dissolved in 1 mL dry dichloromethane in a 10 mL round-bottom flask. 2,6-lutidine (0.026 mL, 0.231 mmol, 2.2 equiv) was then added at 23 °C, under nitrogen. The reaction flask was then cooled in an ice-water bath, and trifluoromethanesulfonic anhydride (0.02 mL, 0.11 mmol, 1.1 equiv) was added. The solution was stirred under nitrogen and gradually warmed to room temperature over 2.5 h. A solution of 4-methoxyaniline (16 mg, 0.127 mmol, 1.2 equiv) in 1 mL dry dichloromethane was then added to the reaction flask, and the contents were stirred overnight at 23 °C. The Reaction was quenched by adding 5 mL of water. The organic layer was separated, and the aqueous layer was extracted with 2x5 mL of ethyl acetate. Combined organic layers were then dried over sodium sulfate, concentrated, and purified using silica gel to get amidine **2pa** in 72% yield.

g) Synthesis of a thioamide derivative [11]



Reflux a solution of substituted benzamide **2p** (0.1 mmol) in toluene (5 mL) containing P_2S_5 (0.2 mmol) under a nitrogen atmosphere, allow the reaction to proceed for 2 h with continuous stirring. After completion, remove the solvent by concentrating the reaction mixture under reduced pressure. Purify the resulting compound silica gel column chromatography using a hexane/ethyl acetate mixture to obtain the desired product **2pb** in 79% yield.

h) *α*-Bromination of *δ*-ketoamide[7]



Add *δ*-ketoamide **4g** (0.1 mmol) to a 10 mL three-necked flask. Add 2 mL of anhydrous methanol and glacial acetic acid (0.03 mmol) to the reaction mixture. Add Br_2 (0.1 mmol) dropwise under stirring to the reaction mixture. Monitor the completion of the reaction. Perform the extraction with ethyl acetate. Purify the residue by column chromatography to obtain N-(3-bromo-4-oxo-4-phenylbutyl)-4-methoxybenzamide **4g'** in 60% yield.

G. Single-crystal X-Ray data for compound 2p

Sample preparation:

Solvent used - LR grade $CHCl_3$

Method used - Recrystallization from $CHCl_3$ by slow evaporation at room temperature.

For the determination of X-ray crystal structures of **2p,** a single crystal was selected and mounted with paratone oil on a glass fiber using gum. The data were collected at 298K on a CMOS-based Bruker D8 Venture PHOTON 100 diffractometer equipped with an INCOATEC micro-focus source with graphite monochromatic Mo Kα radiation (λ = 0.71073 Å) operating at 50 kV and 30 mA. For the integration of diffraction profiles SAINT program was used. Absorption correction was done by applying the SADABS HRMS of 4aSI-155 program. The crystal structure was solved by SIR 92 and refined by the full matrix least squares method using the SHELXL-97 WinGX system, Ver 1.70.01. All the non-hydrogen atoms in the structure were located in the Fourier map and refined anisotropically. The hydrogen atoms were fixed by HFIX in their ideal positions and refined using a riding model with

isotropic thermal parameters. The crystal structure (excluding structure factor) has been deposited at the Cambridge Crystallographic Data Centre and allocated deposition number: **CCDC 2420501**.

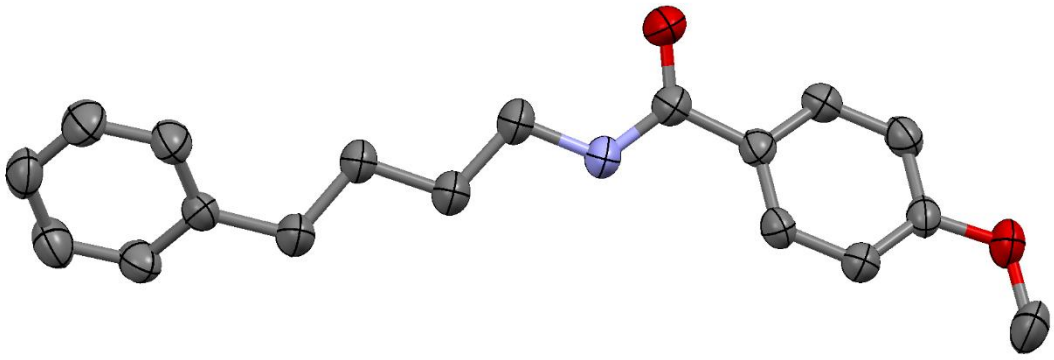


Figure B. ORTEP for compound **2p** with ellipsoid probability at 30%

Table 4. Crystal data and structure refinement for 2p	
Ccdc no.	2420501
Empirical formula	$C_{18}H_{21}NO_2$
Formula weight	283.36
Temperature/K	298
Crystal system	triclinic
Space group	P-1
a/Å	5.3594(4)
b/Å	7.8751(5)
c/Å	18.3484(14)
α/°	85.295(2)
β/°	87.694(3)
γ/°	88.454(2)
Volume/Å^3	770.96(10)
Z	2
ρ_{calc}g/cm^3	1.221
μ/mm^{-1}	0.079
F(000)	304.0
Crystal size/mm^3	0.235 × 0.156 × 0.123
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.192 to 53.316
Index ranges	$-6 \leq h \leq 6$, $-9 \leq k \leq 9$, $-22 \leq l \leq 22$
Reflections collected	12309

Independent reflections	3205 [R_{int} = 0.0452, R_{sigma} = 0.0359]
Data/restraints/parameters	3205/0/195
Goodness-of-fit on F^2	1.083
Final R indexes [I>=2σ (I)]	R_1 = 0.0588, wR_2 = 0.1598
Final R indexes [all data]	R_1 = 0.0699, wR_2 = 0.1683
Largest diff. peak/hole / e $Å^{-3}$	0.60/-0.19

Table 5. Bond Lengths for 340467_0m_a.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C15	1.370(2)	C7	C8	1.507(3)
O1	C16	1.417(3)	C8	C9	1.518(2)
O2	C11	1.232(2)	C9	C10	1.499(3)
N1	C10	1.464(2)	C11	C12	1.494(2)
N1	C11	1.337(2)	C12	C13	1.391(2)
C3	C4	1.373(3)	C12	C18	1.386(2)
C3	C2	1.376(3)	C13	C14	1.376(2)
C4	C5	1.374(3)	C14	C15	1.389(3)
C5	C6	1.382(3)	C15	C17	1.385(2)
C6	C7	1.513(2)	C18	C17	1.388(2)
C6	C1	1.384(3)	C2	C1	1.380(3)

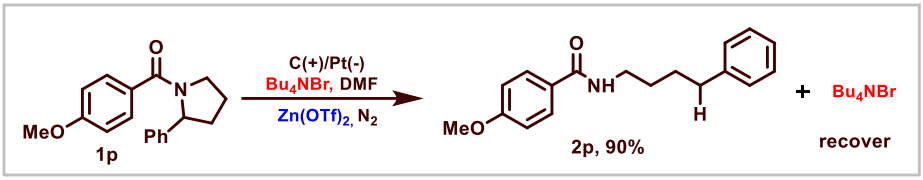
Table 6. Bond Angles for 340467_0m_a.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C15	O1	C16	118.04(15)	N1	C11	C12	117.30(16)
C11	N1	C10	121.35(16)	C13	C12	C11	117.96(16)
C4	C3	C2	118.92(18)	C18	C12	C11	123.76(16)
C3	C4	C5	120.67(18)	C18	C12	C13	118.24(16)
C4	C5	C6	121.31(18)	C14	C13	C12	121.05(16)
C5	C6	C7	119.37(17)	C13	C14	C15	119.91(16)
C5	C6	C1	117.56(17)	O1	C15	C14	115.22(15)
C1	C6	C7	123.08(17)	O1	C15	C17	124.69(17)
C8	C7	C6	117.02(16)	C17	C15	C14	120.09(16)
C7	C8	C9	112.19(16)	C12	C18	C17	121.51(16)
C10	C9	C8	113.85(16)	C15	C17	C18	119.14(17)
N1	C10	C9	110.67(16)	C3	C2	C1	120.34(19)
O2	C11	N1	121.79(17)	C2	C1	C6	121.20(18)
O2	C11	C12	120.91(16)				

H. Calculations of green chemistry metrics[12-13]

Synthesis of δ-substituted amide (2p)

To an undivided cell equipped with a magnetic stirring bar and graphite as anode and platinum as cathode, having dimensions (W×H×D) 8×52.5×2 mm, were added pyrrolidine **1p** (0.15 mmol, 1.0 equiv), Bu_4NBr (0.15 mmol), and zinc trifluoromethanesulfonate ($Zn(OTf)_2$: 10 mol%). After being sealed with a septum, the vial was evacuated and backfilled three times with N_2 gas. To this vial was added DMF (3.0 mL). After being electrolyzed at a constant current of 10 mA at room temperature for 12 h, the reaction mixture was diluted with water and extracted with EtOAc. The combined organic layer was concentrated in vacuo, and the residue was purified using silica gel chromatography (neutralized with triethylamine) to afford the corresponding product **2p**. After that, the electrolyte (**Bu_4NBr**) was recovered from the column using DCM: MeOH (95:5), the organic layer was concentrated in vacuo and washed with diethyl ether and hexane to afford **Bu_4NBr**.[13]



1p	$Zn(OTf)_2$	Bu_4NBr	2p	Bu_4NBr (recovered)	DMF
40 mg, 0.15 mmol MW = 281.1416 g/mol	5.45 mg, 10 mol% 0.015 mmol MW = 363.5 g/mol	50 mg, 1.0 equiv 0.15mmol MW = 322.37 g/mol	38 mg 0.13 mmol MW = 283.371 g/mol	20 mg	10 mg 0.15 mmol MW = 73.09 g/mol

1. **Reaction yield** = 0.13/0.15×100 = 90%

2. **Atom Economy (AE):** (Catalyst excluded)

   Molecular Weight of 1p = 281.1416 g/mol
   Molecular Weight of Bu_4NBr = 322.37 g/mol
   Molecular Weight of DMF = 73.09 g/mol
   Molecular Weight of 2p = 283.371 g/mol
   AE = 283.371/(281.1416+322.37+73.09)×100 = 41.88%

3. **Reaction Mass Efficiency:**

   Effective reactant mass = (40+50+10+5.45)-20 =85.45 mg
   Mass of product = 38 mg
   RME = 38/85.45×100 = 44.4%

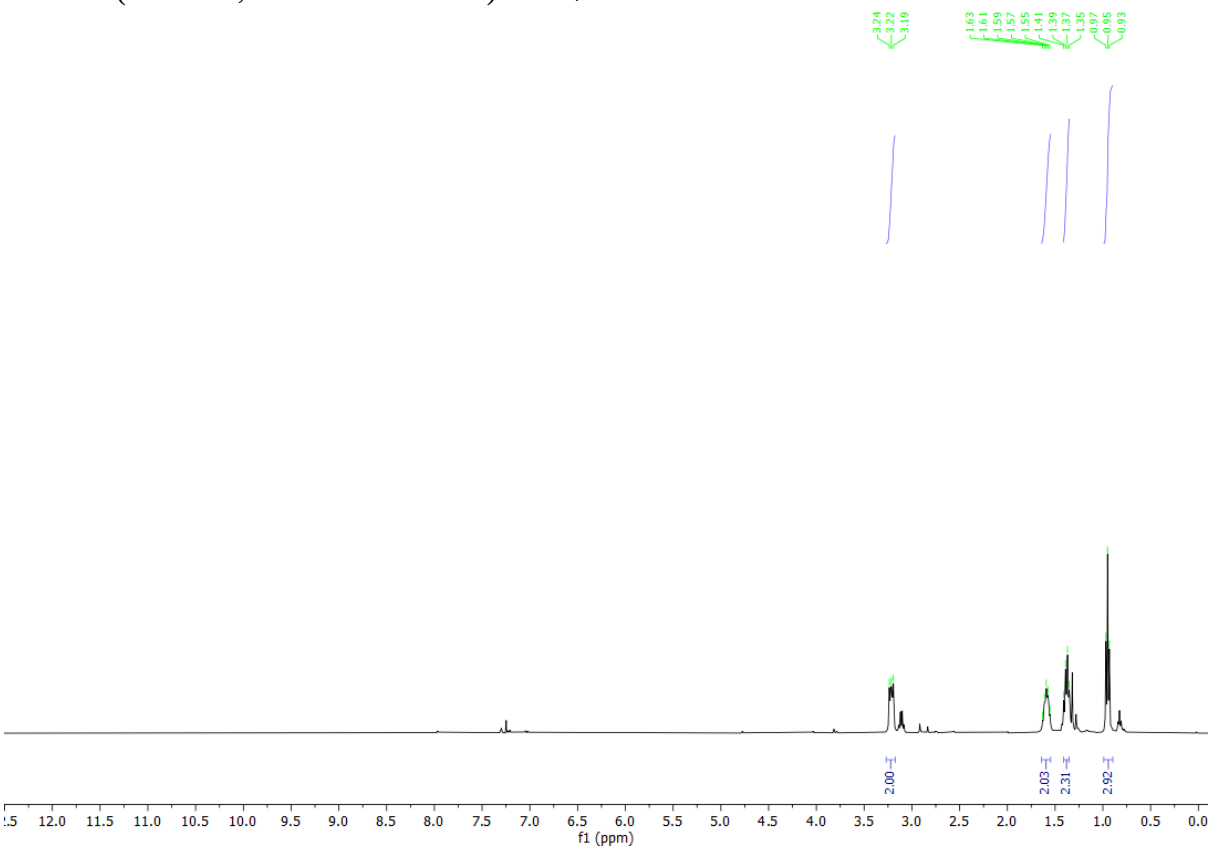
4. **Process Mass Intensity:**

   Effective input mass = (40+50+5.45+10)-20=85.45 mg
   Mass of product = 38 mg
   PMI = 85.45/38 =2.24

5. **E-Factor:** Total amount of reactant = 40+5.45+50+10 = 105.45 mg

   Final compound (2p) = 38 mg
   Waste = 105.45−38−20 = 47.45
   E-factor = 47.45/38 = 1.24

^{1}H NMR (400 MHz, CHLOROFORM-D) of Bu_4NBr:



I. Calculations of faradaic efficiency[14]

The faradaic efficiency of the reaction was calculated using the following formula:

$$n = \frac{Q_{\text{theo}}}{Q_{\text{exp}}} \times 100\%$$

$$Q_{\text{theo}} = z_{\text{P}} \cdot N_{\text{P}} \cdot F = z \cdot N \cdot Y \cdot F$$

$$Q_{\text{exp}} = I \cdot t = z \cdot N \cdot F \cdot \text{equiv.}$$

$$n = \frac{z \cdot N \cdot F \cdot Y}{z \cdot N \cdot F \cdot \text{equiv.}} = \frac{Y}{\text{equiv.}}$$

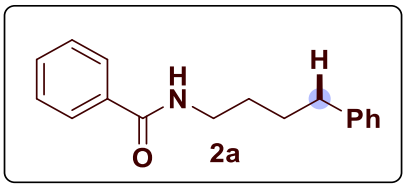
n: Faradaic efficiency in percent [%], Q_{theo}: theoretical charge in Coulomb [C], Q_{exp}: experimental charge in Coulomb [C], equiv.: electron equivalents (F mol^{-1} or equiv.), z_P: Number of electrons per product [−], N_P: Number of mols of the product [mol], Y: yield in percent [%].

Here, Y = 90 % yield, equiv.= 5.90 F mol^{-1}, For 2 electrons system

$$n = 2 \text{ x} \frac{90}{5.90} = 30.50\%$$

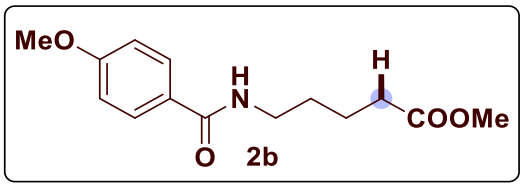
J. Characterization data of final compounds & intermediates

N-(4-phenylbutyl)benzamide (2a)



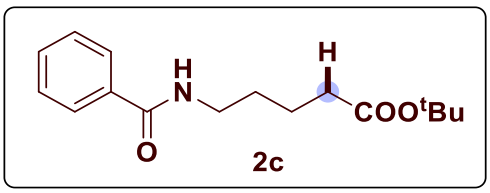
Overall yield: 84%, 32 mg**;** Nature: white solid**;** R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.74-7.71 (m, 2H), 7.50 – 7.45 (m, 1H), 7.42 – 7.38 (m, 2H), 7.29-7.25 (m, 2H), 7.20 - 7.16 (m, 3H), 6.15 (s, 1H), 3.46 (q, *J* = 6.6 Hz, 2H), 2.65 (t, *J* = 7.3 Hz, 2H), 1.73 - 1.61 (m, 4H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D); δ 167.7, 142.2, 134.8, 131.5, 128.7, 128.5, 128.5, 126.9, 126.0, 40.0, 35.6, 29.3, 28.8; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{17}H_{20}NO$ 254.1545, found $[M+H]^+$ 254.1556.

4-methoxy-N-(4-phenylbutyl)benzamide (2b)



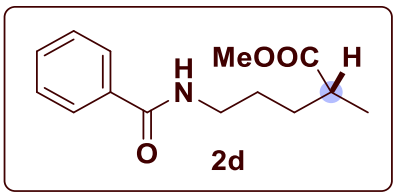
Overall yield: 82%, 32 mg**;** Nature: white solid**;** R_f = 0.4 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.75 – 7.71 (m, 2H), 6.90 – 6.87 (m, 2H), 6.37 (s, 1H), 3.82 (s, 3H), 3.65 (s, 3H), 3.42 (q, *J* = 6.9 Hz, 2H), 2.35 (t, *J* = 7.1 Hz, 2H), 1.72 – 1.60 (m, 4H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 174.2, 167.2, 162.2, 128.8, 126.9, 113.8, 55.5, 51.7, 39.5, 33.6, 29.1, 22.1; **HRMS** (ESI, Q-TOF) m/z $[M+Na]^+$ Calcd for $C_{14}H_{19}NO_4Na$ 288.1212, found $[M+Na]^+$ 288.1223.

tert-butyl 5-benzamidopentanoate (2c)



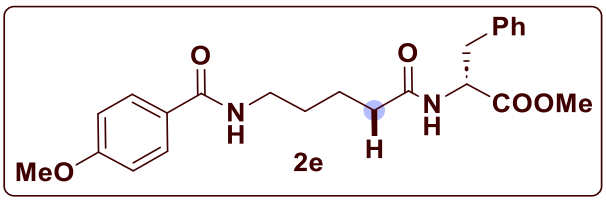
Overall yield: 87%, 36 mg**;** Nature: colorless oil; R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.78 – 7.74 (m, 2H), 7.46 – 7.36 (m, 3H), 6.57 (s, 1H), 3.41 (td, *J* = 6.4, 6.0 Hz, 2H), 2.24 (t, *J* = 6.8 Hz 2H), 1.66 – 1.58 (m, 4H), 1.41 (s, 9H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 173.2, 167.7, 134.8, 131.4, 128.5, 127.0, 80.4, 39.6, 35.0, 28.9, 28.2, 22.2; **HRMS** (ESI, Q-TOF) m/z $[M+Na]^+$ Calcd for $C_{16}H_{23}NO_3Na$ 300.1576, found $[M+Na]^+$ 300.1585.

methyl (R)-5-benzamido-2-methylpentanoate (2d)



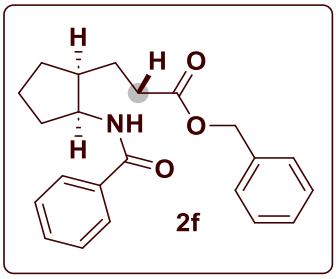
Overall yield: 77%, 28 mg**;** Nature: colorless oil; R_f = 0.4 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.77 – 7.74 (m, 2H), 7.50 – 7.45 (m, 1H), 7.44-7.41 (m, 2H), 6.29 (s, 1H), 3.66 (s, 3H), 3.46 – 3.39 (m, 2H), 2.53 – 2.46 (m, 1H), 1.67 – 1.46 (m, 4H), 1.16 (d, *J* = 7.3 Hz, 3H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 177.2, 167.6, 134.8, 131.5, 128.7, 126.9, 51.7, 39.9, 39.3, 31.0, 27.4, 17.4; **HRMS** (ESI, Q-TOF) m/z $[M+Na]^+$ Calcd for $C_{14}H_{19}NO_3Na$ 272.1263, found $[M+Na]^+$ 272.1278.

methyl (5-(4-methoxybenzamido) pentanoyl)-D-phenylalaninate (2e)



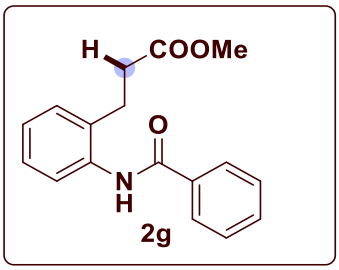
Overall yield: 67%, 38 mg**;** Nature: yellow solid**;** R_f = 0.5 (Hexane/ethyl acetate = 20:80); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.77 – 7.73 (m, 2H), 7.28 – 7.25 (m, 1H), 7.24 – 7.20 (m, 2H), 7.10 – 7.06 (m, 2H), 6.93 – 6.89 (m, 2H), 6.47 (s, 1H), 6.05 (d, *J* = 7.8 Hz, 1H), 4.88 (dt, *J* = 7.8, 6.0 Hz, 1H), 3.83 (s, 3H), 3.71 (s, 3H), 3.42 – 3.36 (m, 2H), 3.14 (dd, J = 14.0, 5.7 Hz, 1H), 3.04 (dd, *J* = 14.0, 6.6 Hz, 1H), 2.26-2.21 (m, 2H), 1.71-1.64 (m, 2H), 1.61 – 1.52 (m, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 172.8, 172.3, 167.2, 162.2, 135.9, 129.3, 128.9, 128.8, 127.3, 126.9, 113.8, 55.5, 53.1, 52.5, 39.2, 38.0, 35.5, 28.7, 22.4; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{23}H_{29}N_2O_5$ 413.2076, found $[M+H]^+$ 413.2074.

benzyl 3-((1S,2S)-2-benzamidocyclopentyl)propanoate (2f)



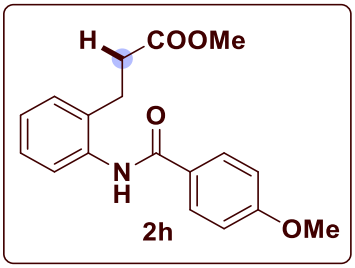
Overall yield: 74%, 39 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.73-7.70 (m, 2H), 7.51 – 7.46 (m, 1H), 7.44-7.41 (m, 2H), 7.33-7.28 (m, 5H), 5.94 (d, *J* = 8.2 Hz, 1H), 5.07 (s, 2H), 4.58 – 4.49 (m, 1H), 2.43 (t, *J* = 7.8 Hz, 2H), 2.08-2.00 (m, 2H), 1.93 – 1.65 (m, 6H), 1.34 – 1.29 (m, 1H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 173.7, 167.4, 136.1, 135.0, 131.5, 128.7, 128.6, 128.3, 126.9, 66.3, 53.0, 42.6, 33.2, 32.4, 29.6, 25.1, 21.7; **HRMS** (ESI, Q-TOF) m/z $[M+Na]^+$ Calcd for $C_{22}H_{25}NO_3Na$ 374.1732, found $[M+Na]^+$ 374.1745.

methyl 3-(2-benzamidophenyl)propanoate (2g)



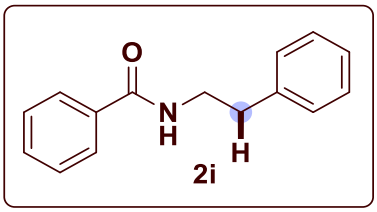
Overall yield: 38%, 16 mg**;** Nature: colorless oil; R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 9.63 (s, 1H), 8.12-8.09 (m, 2H), 7.83 (d, *J* = 6.9 Hz, 1H), 7.55 – 7.50 (m, 3H), 7.28 (dd, *J* = 6.9, 1.8 Hz, 1H), 7.21-7.15 (m, 2H), 3.66 (s, 3H), 2.92 (dd, *J* = 7.6, 4.8 Hz, 2H), 2.77 (dd, *J* = 7.3, 5.0 Hz, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 175.4, 166.0, 135.7, 134.9, 133.3, 131.8, 130.0, 128.9, 127.6, 127.2, 125.8, 125.7, 52.3, 35.6, 25.1; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{17}H_{18}NO_3$ 284.1287, found $[M+H]^+$ 284.1261.

methyl 3-(2-(4-methoxybenzamido)phenyl)propanoate (2h)



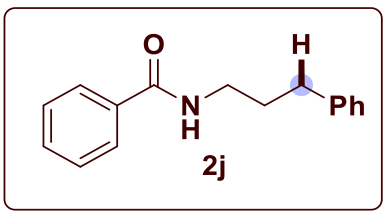
Overall yield: 81%, 38 mg**;** Nature: colorless oil; R_f = 0.45 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 9.51 (s, 1H), 8.08 – 8.04 (m, 2H), 7.81 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.28 – 7.25 (m, 1H), 7.20 – 7.11 (m, 2H), 7.01 – 6.97 (m, 2H), 3.87 (s, 3H), 3.66 (s, 3H), 2.94 – 2.89 (m, 2H), 2.77 (dd, *J* = 7.6, 4.8 Hz, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 175.5, 165.5, 162.4, 135.9, 133.2, 130.0, 129.4, 127.2, 127.2, 125.7, 125.6, 113.9, 55.5, 52.3, 35.6, 25.1; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{20}NO_4$ 314.1392, found $[M+H]^+$ 314.1386.

N-phenethylbenzamide (2i)



Overall yield: 85%, 28 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.68 (dd, *J* = 7.6, 2.1 Hz, 2H), 7.49 – 7.44 (m, 1H), 7.39 (dd, *J* = 8.7, 6.4 Hz, 2H), 7.34 – 7.30 (m, 2H), 7.23 (td, *J* = 6.2, 2.3 Hz, 3H), 6.22 (s, 1H), 3.71 (q, *J* = 6.6 Hz, 2H), 2.92 (t, *J* = 7.1 Hz, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 167.6, 139.0, 134.7, 131.5, 128.9, 128.8, 128.7, 126.9, 126.7, 41.3, 35.8; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{15}H_{16}NO$ 226.1232, found $[M+H]^+$ 226.1216.

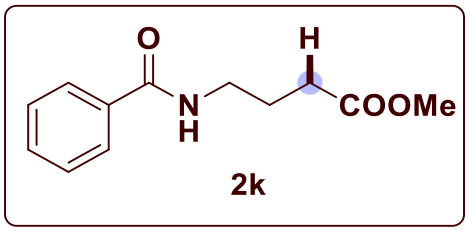
N-(3-phenylpropyl)benzamide (2j)



Overall yield: 70%, 25 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.67-7.64 (m, 2H), 7.49-7.44 (m, 1H), 7.41 – 7.35 (m, 3H), 7.31 – 7.26 (m, 2H), 7.20 (d, *J* = 4.6 Hz, 2H), 6.14 (s, 1H), 3.49 (q, *J* = 6.9 Hz, 2H), 2.72 (t, *J* = 7.6 Hz, 2H), 1.99-1.92 (m, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 167.6, 141.6,

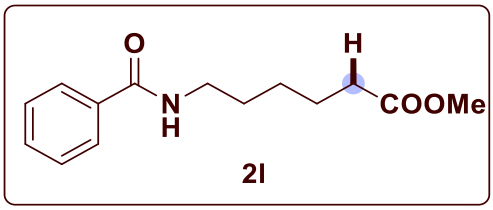
134.7, 131.5, 128.7, 128.6, 128.5, 126.9, 126.2, 39.9, 33.6, 31.2; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{16}H_{18}NO$ 240.1388, found $[M+H]^+$ 240.1372.

methyl 4-benzamidobutanoate (2k)



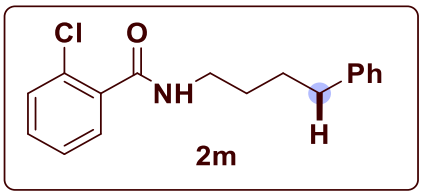
Overall yield: 82%, 27 mg**;** Nature: colorless oil; R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.77-7.74 (m, 2H), 7.50 – 7.43 (m, 1H), 7.41-7.38 (m, 2H), 6.74 (s, 1H), 3.63 (s, 3H), 3.49-3.44 (m, 2H), 2.41 (t, *J* = 7.1 Hz, 2H), 1.96-1.89 (m, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 174.3, 167.7, 134.8, 131.2, 128.6, 127.2, 51.9, 39.7, 31.8, 24.5; **HRMS** (ESI, Q-TOF) m/z $[M+Na]^+$ Calcd for $C_{12}H_{15}NO_3Na$ 244.0950, found $[M+Na]^+$ 244.0953.

methyl 6-benzamidohexanoate (2l)



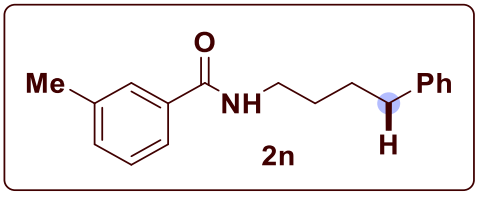
Overall yield: 47%, 17 mg**;** Nature: colorless oil; R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.77-7.74 (m, 2H), 7.50 – 7.46 (m, 1H), 7.43 – 7.39 (m, 2H), 6.19 (s, 1H), 3.65 (s, 3H), 3.48 – 3.43 (m, 2H), 2.32 (t, *J* = 7.3 Hz, 2H), 1.69 – 1.61 (m, 4H), 1.46 – 1.36 (m, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 174.2, 167.6, 134.8, 131.5, 128.7, 126.9, 51.6, 39.8, 33.9, 29.4, 26.5, 24.5; **HRMS** (ESI, Q-TOF) m/z $[M+Na]^+$ Calcd for $C_{14}H_{19}NO_3Na$ 272.1263, found $[M+Na]^+$ 272.1282.

2-chloro-N-(4-phenylbutyl)benzamide (2m)



Overall yield: 57%, 27 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.74-7.71 (m, 2H), 7.50 – 7.45 (m, 1H), 7.44 – 7.39 (m, 2H), 7.29 – 7.26 (m, 1H), 7.20 – 7.16 (m, 3H), 6.09 (s, 1H), 3.50 – 3.44 (m, 2H), 2.66 (t, *J* = 7.3 Hz, 2H), 1.74 – 1.63 (m, 4H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 167.6, 142.1, 134.8, 131.4, 128.6, 128.5, 128.4, 128.3, 126.8, 125.9, 39.9, 35.5, 29.3, 28.8; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{17}H_{19}NOCl$ 288.1155, found $[M+H]^+$ 288.1166.

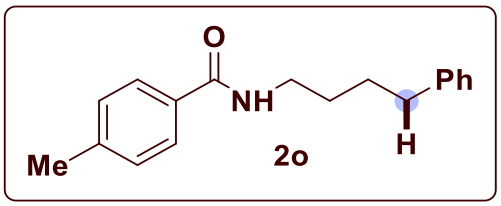
3-methyl-N-(4-phenylbutyl)benzamide (2n)



Overall yield: 70%, 28 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.56-7.54 (m, 1H), 7.51 – 7.47 (m, 1H), 7.30 – 7.27 (m, 2H), 7.24-7.23 (m, 2H), 7.18-7.16 (m,

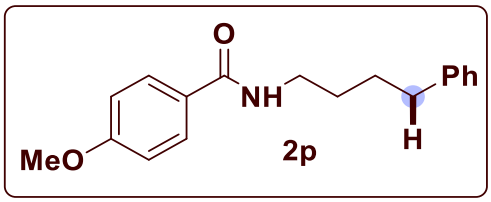
3H), 6.04 (s, 1H), 3.46 (td, *J* =6.4, 6.0 Hz, 2H), 2.65 (t, *J* = 6.0 Hz, 2H), 2.37 (s, 3H), 1.73 – 1.62 (m, 4H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 167.8, 142.1, 138.5, 134.8, 132.1, 128.5, 128.4, 127.6, 127.1, 125.9, 123.8, 39.9, 35.5, 29.3, 28.8, 21.4; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{22}NO$ 268.1701, found $[M+H]^+$ 268.1703.

4-methyl-N-(4-phenylbutyl)benzamide (2o)



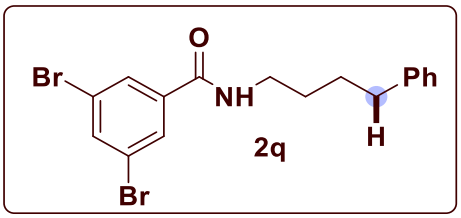
Overall yield: 77%, 30 mg**;** Nature: white solid**;** R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.65 – 7.61 (m, 2H), 7.28 – 7.24 (m, 2H), 7.18 (m, 5H), 6.15 (s, 1H), 3.47-3.41 (m, 2H), 2.64 (t, *J* = 5.7 Hz, 2H), 2.36 (s, 3H), 1.71 – 1.61 (m, 4H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 167.6, 142.2, 141.8, 132.0, 129.3, 128.5, 128.5, 126.9, 125.9, 39.9, 35.6, 29.4, 28.9, 21.5; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{22}NO$ 268.1701, found $[M+H]^+$ 268.1715.

4-methoxy-N-(4-phenylbutyl)benzamide (2p)



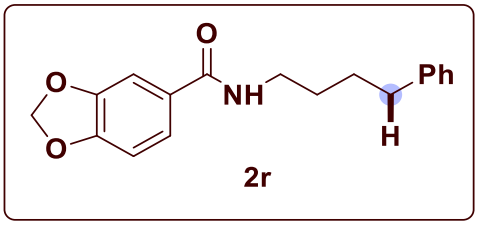
Overall yield: 90%, 38 mg**;** Nature: white solid**;** R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.71 – 7.67 (m, 2H), 7.29 – 7.24 (m, 2H), 7.17-7.14 (m, 3H), 6.91 – 6.87 (m, 2H), 6.09 (s, 1H), 3.82 (s, 3H), 3.47 – 3.41 (m, 2H), 2.64 (t, *J* = 7.3 Hz, 2H), 1.71-1.60 (m, 4H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 167.2, 162.1, 142.2, 128.7, 128.5, 128.5, 127.1, 125.9, 113.8, 55.5, 39.9, 35.6, 29.4, 28.9; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{22}NO_2$ 284.1651, found $[M+H]^+$ 284.1664.

3,5-dibromo-N-(4-phenylbutyl)benzamide (2q)



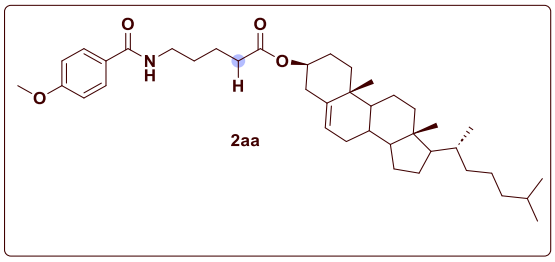
Overall yield: 55%, 33 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.73 (dd, *J* = 7.1, 2.1 Hz, 2H), 7.50 – 7.45 (m, 1H), 7.42 – 7.40 (m, 1H), 7.29 – 7.25 (m, 2H), 7.18 – 7.15 (m, 2H), 6.18 (s, 1H), 3.48 – 3.43 (m, 2H), 2.65 (t, *J* = 7.3 Hz, 2H), 1.72-1.62 (m, 4H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 167.6, 142.2, 134.8, 131.5, 128.7, 128.5, 128.5, 126.9, 126.0, 40.0, 35.6, 29.3, 28.8; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{17}H_{18}Br_2NO$ 409.9755, found $[M+H]^+$ 409.9760.

N-(4-phenylbutyl)benzo[d][1,3]dioxole-5-carboxamide (2r)



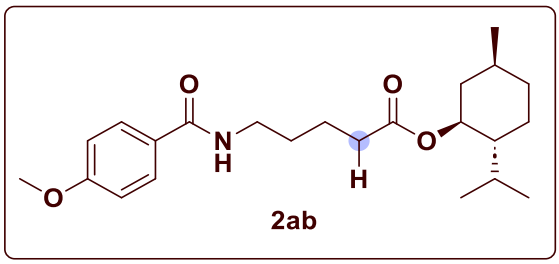
Overall yield: 74%, 33 mg**;** Nature: white solid; R_f = 0.4 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.27 (dd, *J* = 7.3, 5.5 Hz, 2H), 7.24 (d, *J* = 1.4 Hz, 2H), 7.17 (td, *J* = 6.9, 1.8 Hz, 3H), 6.80 – 6.77 (m, 1H), 6.12 (s, 1H), 5.99 (s, 2H), 3.44 – 3.39 (m, 2H), 2.64 (t, *J* = 7.3 Hz, 2H), 1.69 – 1.59 (m, 4H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 166.9, 150.3, 148.0, 142.2, 129.0, 128.5, 128.4, 125.9, 121.5, 108.0, 107.7, 101.7, 40.1, 35.6, 29.3, 28.8; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{20}NO_3$ 298.1443, found $[M+H]^+$ 298.1433.

(3S,10R,13R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)2,3,4,7,8,9,10, 11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 5-(4-methoxybenzamido) pentanoate (2aa)



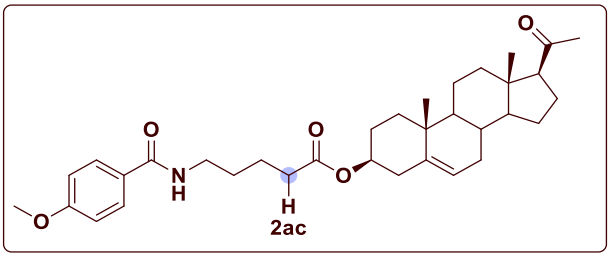
Overall yield: 55%, 51 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 50:50); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.73 (dd, *J* = 9.6, 2.7 Hz, 2H), 6.93 – 6.89 (m, 2H), 6.25 (s, 1H), 5.47 – 5.38 (m, 1H), 3.83 (s, 3H), 3.82 (br s, 1H), 3.43 (td, *J* = 6.0, 5.9 Hz, 2H), 2.35 – 2.28 (m, 2H), 2.25 – 2.05 (m, 2H), 1.99 – 1.68 (m, 6H), 1.57 – 1.26 (m, 16H), 1.20 – 0.97 (m, 13H), 0.85 (s, 3H), 0.84 (d, *J* = 1.8 Hz, 3H), 0.71 – 0.58 (m, 5H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 173.0, 167.1, 162.2, 159.9, 128.7, 127.0, 113.8, 83.1, 71.7, 63.7, 62.6, 56.2, 47.2, 42.8, 42.4, 40.5, 39.6, 38.2, 36.7, 36.2, 35.8, 35.1, 34.8, 34.0, 32.0, 31.7, 31.0, 29.8, 28.1, 26.4, 24.1, 23.9, 22.9, 22.7, 22.2, 22.0, 21.3, 18.7, 17.4, 17.1, 14.2, 13.9, 12.3, 11.8; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{40}H_{62}NO_4$ 620.4679, found $[M+H]^+$ 620.4689.

(1S,2R,5S)-2-isopropyl-5-methylcyclohexyl5-(4-methoxybenzamido) pentanoate (2ab)



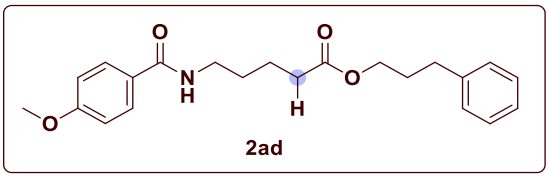
Overall yield: 62%, 36 mg**;** Nature: viscous oil; R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.75 – 7.72 (m, 2H), 6.92 – 6.88 (m, 2H), 6.30 (s, 1H), 4.67 (td, *J* = 11.0, 4.4 Hz, 1H), 3.83 (s, 3H), 3.43 (q, *J* = 6.6 Hz, 2H), 2.33 (t, *J* = 7.1 Hz, 2H), 2.00 – 1.92 (m, 2H), 1.68-1.62 (m, 5H), 1.50 – 1.42 (m, 2H), 1.39 – 1.30 (m, 2H), 1.08-0.97 (m, 2H), 0.87 (d, *J* = 2.3 Hz, 6H), 0.73 (d, *J* = 6.9 Hz, 3H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 173.4, 167.1, 162.1, 128.7, 127.0, 113.8, 74.3, 55.5, 47.1, 41.0, 39.5, 34.3, 34.2, 31.5, 29.1, 26.4, 23.5, 22.2, 22.1, 20.8, 16.4; **HRMS** (ESI, Q-TOF) m/z [M+H]$^+$ Calcd for $C_{23}H_{36}NO_4$ 390.2644, found [M+H]$^+$ 390.2639.

(3S,10R,13S,17S)-17-acetyl-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14, 15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl5-(4-methoxybenzamido)pentanoate (2ac)



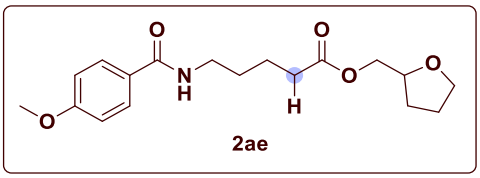
Overall yield: 37%, 30 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 50:50); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.74-7.71 (m, 2H), 6.92 – 6.90 (m, 2H), 6.22 (br s, 1H), 5.43 (br s, 1H), 4.57 (br s, 1H), 3.83 (s, 3H), 3.44-3.42 (m, 2H), 2.58 – 2.45 (m, 2H), 2.33-2.31 (m, 2H), 2.11 (s, 3H), 2.09 (s, 2H), 2.01-1.95 (m, 5H), 1.69-1.64 (s, 8H), 1.45-1.41 (m, 5H), 0.65 – 0.53 (m, 7H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 209.6, 167.1, 162.2, 159.8, 129.5, 128.7, 127.0, 113.8, 113.5, 82.9, 71.6, 63.5, 56.4, 55.8, 50.9, 47.1, 46.0, 44.3, 40.6, 39.5, 38.9, 34.8, 34.0, 31.7, 29.8, 26.3, 24.3, 22.9, 22.2, 21.3, 17.4, 13.7, 8.7; **HRMS** (ESI, Q-TOF) m/z [M+H]$^+$ Calcd for $C_{34}H_{48}NO_5$ 550.3532, found [M+H]$^+$ 550.3505.

3-phenylpropyl 5-(4-methoxybenzamido) pentanoate (2ad)



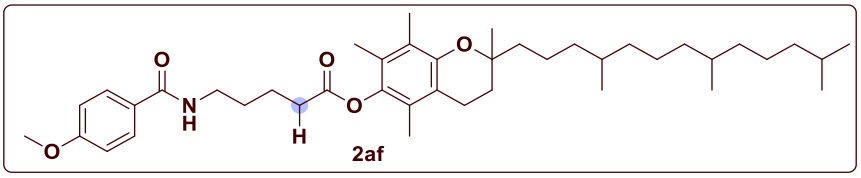
Overall yield: 55%, 30 mg**;** Nature: viscous oil; R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.76 – 7.71 (m, 2H), 7.29 – 7.25 (m, 2H), 7.20 – 7.14 (m, 3H), 6.92 – 6.88 (m, 2H), 6.27 (s, 1H), 4.09 (t, *J* = 6.4 Hz, 2H), 3.83 (s, 3H), 3.44 (q, *J* = 6.4 Hz, 2H), 2.69 – 2.65 (m, 2H), 2.36 (t, *J* = 7.1 Hz, 2H), 1.98 – 1.90 (m, 2H), 1.70 – 1.60 (m, 4H).; **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 173.8, 167.1, 162.1, 141.2, 128.7, 128.5, 128.4, 126.9, 126.1, 113.8, 63.9, 55.5, 39.5, 33.7, 32.2, 30.2, 29.1, 22.1; **HRMS** (ESI, Q-TOF) m/z [M+H]$^+$ Calcd for $C_{22}H_{28}NO_4$ 370.2018, found [M+H]$^+$ 370.2013.

(tetrahydrofuran-2-yl) methyl 5-(4-methoxybenzamido)pentanoate (2ae)



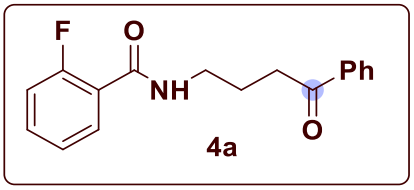
Overall yield: 68%, 34 mg**;** Nature: colorless oil; R_f = 0.4 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) 1H NMR (400 MHz,) δ 7.75 – 7.71 (m, 2H), 6.93 – 6.88 (m, 2H), 6.30 (s, 1H), 4.18 – 4.09 (m, 2H), 4.01-3.96 (m, 1H), 3.88-3.84 (m, 1H), 3.83 (s, 3H), 3.80 – 3.74 (m, 1H), 3.43 (q, *J* = 6.4 Hz, 2H), 2.41 (t, *J* = 7.1 Hz, 2H), 2.03 – 1.84 (m, 4H), 1.76-1.68 (m, 2H), 1.63 – 1.53 (m, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 173.7, 167.2, 162.1, 128.8, 127.1, 113.8, 68.5, 66.6, 55.5, 39.5, 33.7, 29.8, 29.0, 28.0, 25.8, 22.1; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{26}NO_5$ 336.1811, found $[M+H]^+$ 336.1805.

2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6-yl5-(4-methoxy benzamido) pentanoate (2af)



Overall yield: 27%, 26 mg**;** Nature: white solid**;** R_f = 0.5 (Hexane/ethyl acetate = 50:50); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.73 – 7.71 (m, 2H), 6.91-6.86 (m, 2H), 6.24 (s, 1H), 3.83 (s, 3H), 3.51 – 3.47 (m, 2H), 2.66 (t, *J* = 7.1 Hz, 2H), 2.57 (t, *J* = 6.6 Hz, 2H), 2.07 (s, 4H), 1.99 (s, 3H), 1.94 (s, 3H), 1.91 – 1.82 (m, 4H), 1.80-1.73 (m, 5H), 1.54 – 1.47 (m, 4H), 1.40 – 1.31 (m, 8H), 1.12 – 1.06 (m, 7H), 0.86 (s, 3H), 0.84 (s, 3H), 0.83 (s, 3H), 0.82 (s, 3H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 172.4, 167.2, 162.2, 149.5, 140.5, 128.8, 127.0, 126.7, 124.9, 123.2, 117.5, 113.8, 75.2, 55.5, 49.2, 39.5, 37.5, 34.0, 33.5, 32.9, 29.8, 28.1, 25.7, 25.0, 24.9, 24.5, 22.8, 22.7, 22.2, 21.1, 20.7, 19.8, 13.1, 12.3, 12.0; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{42}H_{66}NO_5$ 664.4941, found $[M+H]^+$ 664.4933.

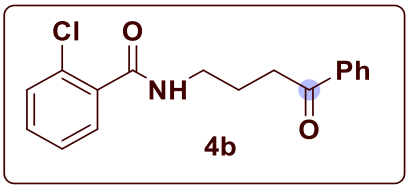
2-fluoro-N-(4-oxo-4-phenylbutyl)benzamide (4a)



Overall yield: 40%, 17 mg**;** Nature: yellow solid; R_f = 0.5 (Hexane/ethyl acetate = 40:60); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 8.06 – 8.02 (m, 1H), 7.95 (dt, *J* = 8.7, 1.6 Hz, 2H), 7.57 – 7.52 (m, 1H), 7.46 – 7.41 (m, 3H), 7.22 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.13 – 7.07 (m, 1H), 6.90 (s, 1H), 3.61 – 3.55 (m, 2H), 3.10 (t, *J* = 7.1 Hz, 2H), 2.09 (p, *J* = 7.1 Hz, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 199.8, 163.6, 161.9, 159.4, 136.7, 133.3 (d, *J* = 5.3 Hz), 132.0, 128.7, 128.1, 124.8 (d, *J* = 3.8 Hz), 121.2 (d, *J* = 11.5 Hz), 116.2, 115.9, 39.7, 36.0, 23.9; **^{19}F{^{1}H}**

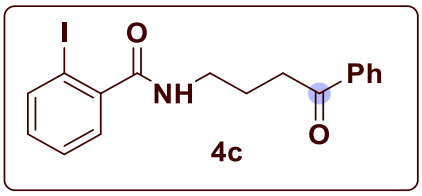
NMR (376 MHz, CHLOROFORM-D) δ -113.55. **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{17}H_{17}NO_2F$ 286.1243, found $[M+H]^+$ 286.1241.

2-chloro-N-(4-oxo-4-phenylbutyl)benzamide (4b)



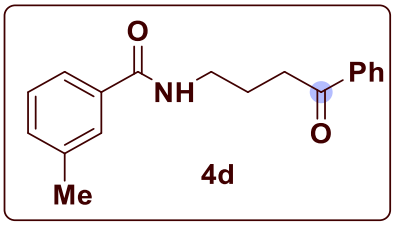
Overall yield: 47%, 21 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 40:60); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.97 – 7.94 (m, 2H), 7.57 – 7.55 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.39 – 7.27 (m, 3H), 6.40 (s, 1H), 3.57 (q, *J* = 6.9 Hz, 2H), 3.13 (d, *J* = 6.9 Hz, 2H), 2.09 (p, *J* = 6.9 Hz, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 199.9, 166.9, 136.7, 135.4, 133.4, 131.3, 130.6, 130.3, 130.1, 128.8, 128.2, 127.2, 39.8, 36.1, 23.8; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{17}H_{17}NO_2F$ 302.0948, found $[M+H]^+$ 302.0926.

2-iodo-N-(4-oxo-4-phenylbutyl)benzamide (4c)



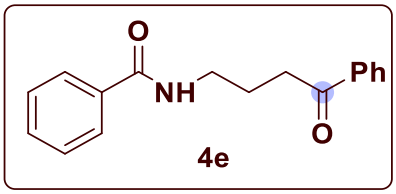
Overall yield: 45%, 26 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 40:60); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.97 – 7.94 (m, 2H), 7.57 – 7.55 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.39 – 7.27 (m, 3H), 6.40 (s, 1H), 3.57 (q, *J* = 6.9 Hz, 2H), 3.13 (d, *J* = 6.9 Hz, 2H), 2.09 (p, *J* = 6.9 Hz, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 199.9, 166.9, 136.7, 135.4, 133.4, 131.3, 130.6, 130.3, 130.1, 128.8, 128.2, 127.2, 39.8, 36.1, 23.8; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{17}H_{17}NO_2I$ 394.0304, found $[M+H]^+$ 394.0297.

3-methyl-N-(4-oxo-4-phenylbutyl)benzamide (4d)



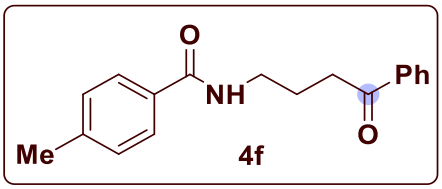
Overall yield: 68%, 28 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 40:60); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.96-7.94 (m, 2H), 7.58 – 7.51 (m, 3H), 7.46-7.42 (m, 2H), 7.31-7.26 (m, 2H), 6.58 (s, 1H), 3.54 (td, *J* = 7.2, 5.6 Hz, 2H), 3.12 (t, *J* = 6.9 Hz, 2H), 2.37 (s, 3H), 2.12 – 2.06 (m, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 200.5, 167.9, 138.5, 136.7, 134.6, 133.4, 132.2, 128.8, 128.5, 128.2, 127.8, 123.9, 40.0, 36.4, 23.6, 21.5; **HRMS** (ESI, Q-TOF) m/z $[M+Na]^+$ Calcd for $C_{18}H_{19}NO_2Na$ 304.1313, found $[M+Na]^+$ 304.1319.

N-(4-oxo-4-phenylbutyl)benzamide (4e)



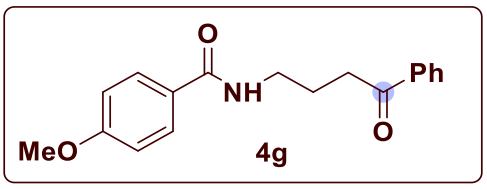
Overall yield: 62%, 24 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 40:60); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.98 – 7.94 (m, 2H), 7.77-7.75 (m, 2H), 7.59-7.54 (m, 1H), 7.48 – 7.41 (m, 5H), 6.67 (s, 1H), 3.59 – 3.52 (m, 2H), 3.14 (t, *J* = 6.6 Hz, 2H), 2.14-2.07 (m, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 200.7, 167.7, 136.7, 134.5, 133.5, 131.5, 130.2, 128.8, 128.2, 127.0, 40.1, 36.5, 23.5; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{17}H_{18}NO_2$ 268.1338, found $[M+H]^+$ 268.1335.

4-methyl-N-(4-oxo-4-phenylbutyl)benzamide (4f)



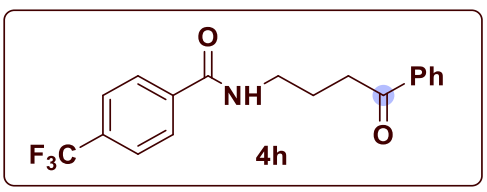
Overall yield: 72%, 30 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 40:60); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.97 – 7.94 (m, 2H), 7.67 – 7.64 (m, 2H), 7.58-7.53 (m, 1H), 7.47-7.43 (m, 2H), 7.23 – 7.19 (m, 2H), 6.54 (s, 1H), 3.54 (td, *J* = 7.2, 6.0 Hz, 2H), 3.13 (t, *J* = 6.6 Hz, 2H), 2.38 (s, 3H), 2.13-2.06(m, *J* = 6.4 Hz, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 200.6, 167.6, 141.8, 136.8, 133.4, 131.7, 129.3, 128.8, 128.2, 126.9, 40.0, 36.5, 23.6, 21.5; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{20}NO_2$ 282.1494, found $[M+H]^+$ 282.1500.

4-methoxy-N-(4-oxo-4-phenylbutyl)benzamide (4g)



Overall yield: 75%, 33 mg**;** Nature: white solid; R_f = 0.45 (Hexane/ethyl acetate = 40:60); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.97-7.94 (m, 2H), 7.75 – 7.71 (m, 2H), 7.58 – 7.53 (m, 1H), 7.46-7.42 (m, 2H), 6.92 – 6.88 (m, 2H), 6.56 (s, 1H), 3.83 (s, 3H), 3.53 (td, *J*= 6.4, 6.0 Hz, 2H), 3.13 (t, *J* = 6.6 Hz, 2H), 2.12-2.05 (m, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 200.7, 165.9, 158.3, 136.7, 133.5, 132.3, 128.8, 128.2, 127.7, 111.3, 56.5, 40.2, 36.6, 23.4; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{20}NO_3$ 298.1443, found $[M+H]^+$ 298.1429.

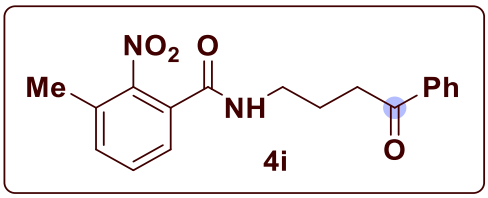
N-(4-oxo-4-phenylbutyl)-4-(trifluoromethyl)benzamide (4h)



Overall yield: 20%, 10 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 40:60); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.96 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.88 (d, *J* = 8.7 Hz, 2H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.59 – 7.55 (m, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 6.92 (s, 1H), 3.56 (td, *J* = 6.0, 5.5 Hz, 2H), 3.17 (t, *J* = 6.4 Hz, 2H), 2.16-2.09 (m, *J* = 6.6 Hz, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 200.9, 166.3, 137.8, 136.6, 133.6, 133.3(q, *J*=32.5 Hz),

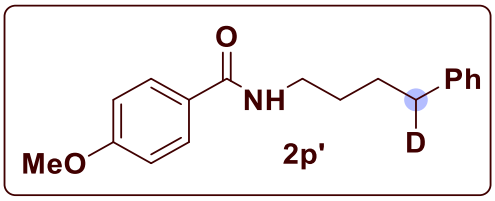
128.8, 128.2, 127.5, 125.7, 125.7, 122.5(q, *J*=274 Hz), 40.5, 36.7, 23.1;**^{19}F{^{1}H} NMR** (376 MHz, CHLOROFORM-D) δ -63.38. **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{17}NO_2F_3$ 336.1211, found $[M+H]^+$ 336.1216.

3-methyl-2-nitro-N-(4-oxo-4-phenylbutyl)benzamide (4i)



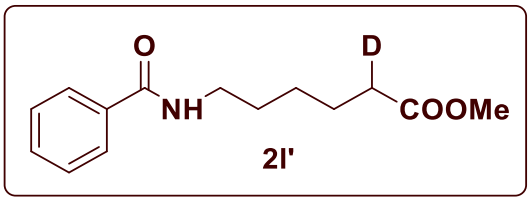
Overall yield: 40%, 19 mg**;** Nature: white solid; R_f = 0.4 (Hexane/ethyl acetate = 40:60); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.99-7.96 (m, *J* = 7.3, 1.6 Hz, 2H), 7.58 – 7.53 (m, 1H), 7.47-7.42 (m, 2H), 7.41 – 7.34 (m, 3H), 6.46 (s, 1H), 3.51 (q, *J* = 6.2 Hz, 2H), 3.13 (t, *J* = 6.9 Hz, 2H), 2.35 (s, 3H), 2.05 (p, *J* = 6.9 Hz, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 200.5, 165.5, 149.5, 136.7, 133.6, 133.4, 131.3, 130.6, 130.3, 128.8, 128.2, 125.6, 40.0, 36.1, 23.5, 17.8; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{19}N_2O_4$ 327.1345, found $[M+H]^+$ 327.1324.

4-methoxy-N-(4-phenylbutyl-4-d)benzamide (2p')



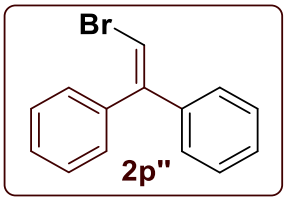
Overall yield: 50%, 21 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.71 – 7.68 (m, 2H), 7.29 – 7.25 (m, 2H), 7.19-7.16 (m, 3H), 6.91 – 6.88 (m, 2H), 6.05 (s, 1H), 3.83 (s, 3H), 3.44 (q, *J* = 6.9 Hz, 2H), 2.63 (t, *J* = 7.3 Hz, 1H), 1.68 – 1.61 (m, 4H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 167.1, 162.1, 142.2, 128.7, 128.5, 128.5, 127.1, 125.9, 113.8, 55.5, 39.9, 29.4, 28.8; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{21}DNO_2$ 285.1708, found $[M+H]^+$ 285.1701.

methyl 6-benzamidohexanoate-2-d (2l')



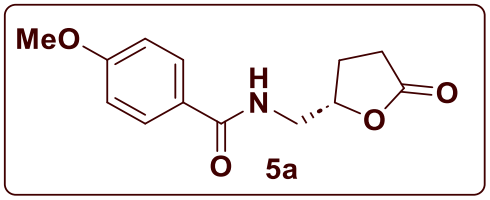
Overall yield: 32%, 12 mg**;** Nature: colorless oil; R_f = 0.5 (Hexane/ethyl acetate = 50:50); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.76-7.73 (m, 2H), 7.50-7.46 (m, 1H), 7.44 – 7.41 (m, 2H), 6.19 (s, 1H), 3.65 (s, 3H), 3.47 – 3.44 (m, 2H), 2.31 (t, *J* = 7.3 Hz, 1H), 1.69 – 1.64 (m, 4H), 1.43 – 1.39 (m, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 174.3, 167.6, 134.8, 131.5, 128.7, 126.9, 51.7, 39.8, 29.4, 26.4, 24.4; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{14}H_{19}DNO_3$ 251.1506, found $[M+H]^+$ 251.1516.

(2-bromoethene-1,1-diyl)dibenzene (2p'')



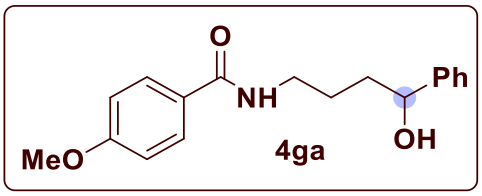
Overall yield: 25%, 9 mg**;** Nature: colorless oil; R_f = 0.5 (Hexane); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.41 – 7.36 (m, 3H), 7.31 – 7.27 (m, 5H), 7.21– 7.19 (m, 2H), 6.77 (s, 1H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 146.9, 140.8, 139.1, 129.7, 128.3, 128.2, 128.0, 127.7, 105.2; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{14}H_{12}Br$ 259.0122, found $[M+H]^+$ 259.0117.

(S)-5-((phenylamino)methyl)dihydrofuran-2(3H)-one (5a)



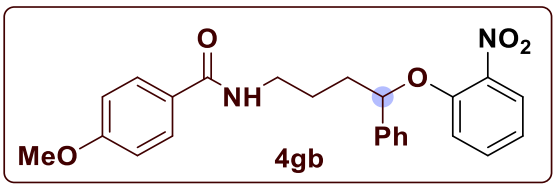
Overall yield: 75%, 21 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 20:80); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.74 (d, *J* = 9.2 Hz, 2H), 6.92 (d, *J* = 8.7 Hz, 2H), 6.51 (s, 1H), 4.72 (tt, *J* = 7.3, 3.7 Hz, 1H), 3.93 (ddd, *J* = 14.7, 6.9, 3.2 Hz, 1H), 3.84 (s, 3H), 3.51 (ddd, *J* = 14.7, 7.1, 5.3 Hz, 1H), 2.59 – 2.54 (m, 2H), 2.40-2.31 (m, 1H), 2.06-1.96 (m, 1H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 177.0, 167.4, 162.6, 129.0, 114.0, 79.8, 55.6, 43.4, 28.7, 24.9; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{12}H_{16}NO_3$ 222.1130, found $[M+H]^+$ 222.1117.

N-(4-hydroxy-4-phenylbutyl)-4-methoxybenzamide (4ga)



Overall yield: 80%, 31 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 40:60); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.71 – 7.67 (m, 2H), 7.31 (d, *J* = 4.1 Hz, 4H), 7.25 – 7.22 (m, 1H), 6.87 – 6.84 (m, 2H), 6.55 (t, *J* = 5.7 Hz, 1H), 4.70 (dd, *J* = 7.8, 5.0 Hz, 1H), 3.80 (s, 3H), 3.47 – 3.35 (m, 2H), 1.82 – 1.63 (m, 4H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 167.4, 162.1, 144.8, 128.8, 128.6, 127.6, 126.9, 125.9, 113.8, 74.2, 55.5, 39.9, 36.3, 26.1; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{22}NO_3$ 300.1600, found $[M+H]^+$ 300.1582.

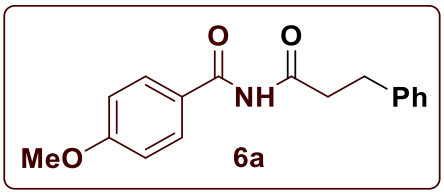
4-methoxy-N-(4-(2-nitrophenoxy)-4-phenylbutyl)benzamide (4gb)



Overall yield: 60%, 22 mg**;** Nature: yellow oil; R_f = 0.5 (Hexane/ethyl acetate = 60:40); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.76 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.73 – 7.70 (m, 2H), 7.33 (d, *J* = 3.2 Hz, 3H), 7.30 – 7.27 (m, 2H), 7.26 (d, *J* = 1.8 Hz, 1H), 6.91 – 6.88 (m, 3H), 6.83 (d, *J* = 8.7 Hz, 1H), 6.24 (t, *J* = 6.0 Hz, 1H), 5.34 (dd, *J* = 8.0, 4.4 Hz, 1H), 3.83 (s, 3H), 3.55 – 3.43 (m, 2H), 2.10 (dd, *J* = 14.2, 6.9 Hz, 1H), 2.00 – 1.92 (m, 1H), 1.86 – 1.79 (m, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 167.3, 162.2, 151.3, 140.3, 133.9, 129.0, 128.8, 128.2, 126.9, 125.9, 125.5,

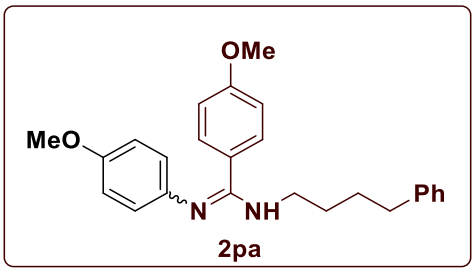
120.3, 116.1, 113.8, 81.2, 55.5, 39.4, 35.6, 25.7; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{24}H_{25}N_2O_5$ 421.1763, found $[M+H]^+$ 421.1741.

4-methoxy-N-(3-phenylpropanoyl)benzamide (6a)



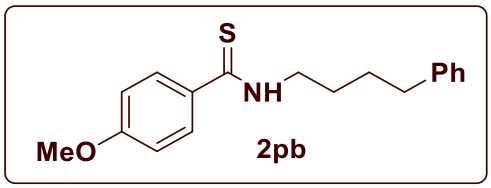
Overall yield: 68%, 38 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 50:50); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 8.72 (s, 1H), 7.82 – 7.79 (m, 2H), 7.30 – 7.25 (m, 4H), 7.22-7.17 (m, 1H), 6.97 – 6.94 (m, 2H), 3.86 (s, 3H), 3.32 (t, *J* = 7.6 Hz, 2H), 3.03 (t, *J* = 7.8 Hz, 2H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 175.6, 164.9, 163.7, 140.8, 129.9, 128.6, 128.6, 126.3, 124.8, 114.3, 55.7, 39.3, 30.2; **HRMS** (ESI, Q-TOF) m/z $[M+Na]^+$ Calcd for $C_{17}H_{17}NO_3Na$ 306.1106, found $[M+Na]^+$ 306.1095.

4-methoxy-N'-(4-methoxyphenyl)-N-(4-phenylbutyl)benzimidamide (2pa)



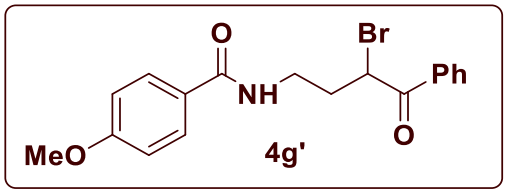
Overall yield: 72%, 29 mg**;** Nature: yellow oil; R_f = 0.5 (Hexane/ethyl acetate = 20:80); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.30 – 7.25 (m, 3H), 7.19 (d, *J* = 7.3 Hz, 2H), 7.11 (d, *J* = 8.7 Hz, 2H), 6.72 (d, *J* = 8.2 Hz, 2H), 6.62 (d, *J* = 8.2 Hz, 2H), 6.54 (d, *J* = 8.7 Hz, 2H), 4.39 (br s, 1H), 3.74 (s, 3H), 3.68 (s, 3H), 3.53 – 3.44 (m, 2H), 2.68 (t, *J* = 7.3 Hz, 3H), 1.78-1.66 (m, *J* = 14.7, 7.6 Hz, 4H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 159.9, 157.5, 154.3, 144.7, 142.4, 130.2, 128.5, 128.4, 128.2, 125.9, 123.9, 113.8, 113.7, 55.4, 55.3, 41.8, 35.7, 29.8, 29.0; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{25}H_{29}N_2O_2$ 389.2229, found $[M+H]^+$ 389.2250.

4-methoxy-N-(4-phenylbutyl)benzothioamide (2pb)



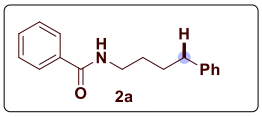
Overall yield: 79%, 26 mg**;** Nature: yellow solid; R_f = 0.5 (Hexane/ethyl acetate = 70:30); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.72 – 7.69 (m, 2H), 7.47 (s, 1H), 7.30 – 7.25 (m, 2H), 7.21 – 7.17 (m, 3H), 6.87 – 6.82 (m, 2H), 3.84-3.80 (d, *J* = 7.3 Hz, 2H), 3.82 (s, 3H), 2.70 – 2.66 (m, 2H), 1.77-174 (m, 4H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 198.1, 162.2, 141.9, 134.3, 128.5, 126.1, 113.7, 55.6, 46.7, 35.5, 28.9, 27.9; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{22}NOS$ 300.1422, found $[M+H]^+$ 300.1420.

N-(3-bromo-4-oxo-4-phenylbutyl)-4-methoxybenzamide (4g')

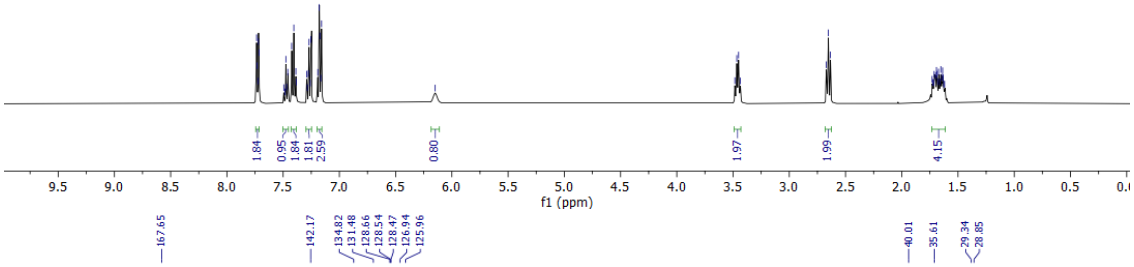


Overall yield: 60%, 22 mg**;** Nature: white solid; R_f = 0.5 (Hexane/ethyl acetate = 70:30); **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 7.99 (dd, *J* = 6.6, 1.6 Hz, 2H), 7.86 – 7.81 (m, 2H), 7.65 – 7.60 (m, 1H), 7.54 – 7.50 (m, 2H), 6.85 (dd, *J* = 8.9, 2.5 Hz, 2H), 5.67 (dd, *J* = 7.1, 4.4 Hz, 1H), 3.90 (s, 3H), 3.65 – 3.56 (m, 2H), 2.32 – 2.26 (m, 1H), 2.17-2.11 (m, 1H); **^{13}C{^{1}H} NMR** (100 MHz, CHLOROFORM-D) δ 195.5, 157.7, 153.3, 134.0, 132.3, 129.0, 128.8, 127.7, 113.4, 111.0, 56.3, 40.9, 29.7, 23.8; **HRMS** (ESI, Q-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{19}NO_3Br$ 376.0548, found $[M+H]^+$ 376.0546.

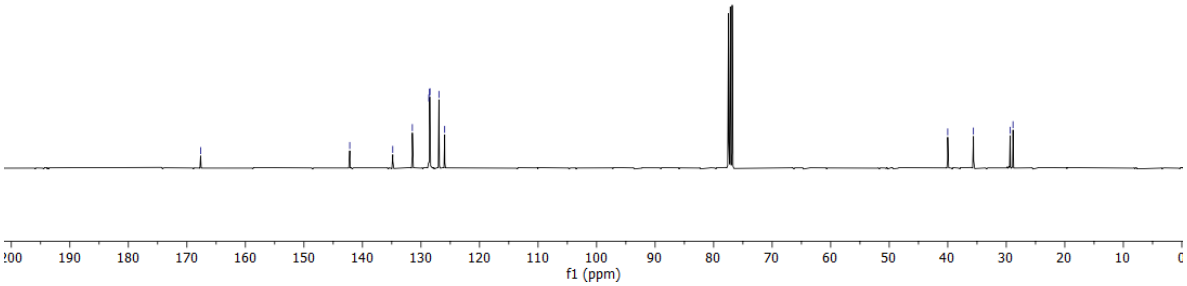
K. Copies of NMR spectra of compounds and HRMS of intermediates

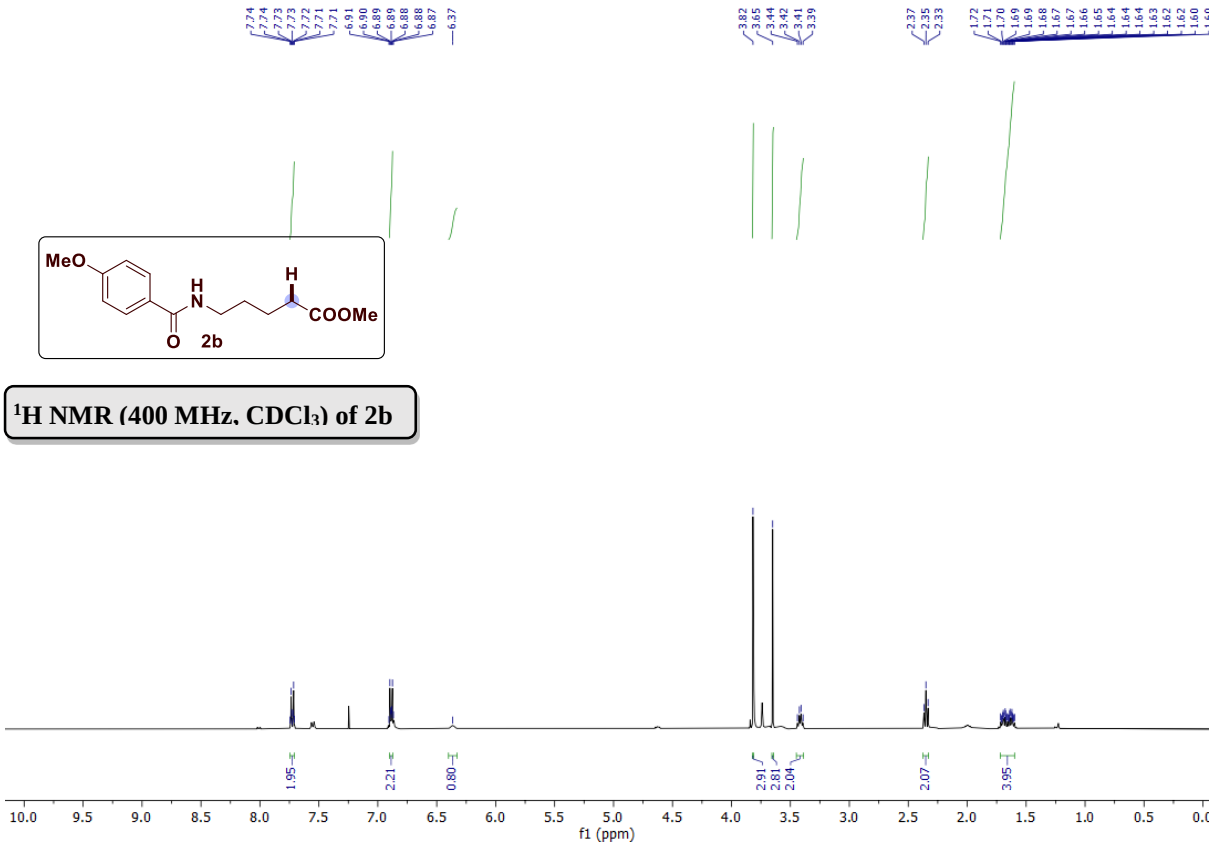


^{1}H NMR (400 MHz, $CDCl_3$) of 2a

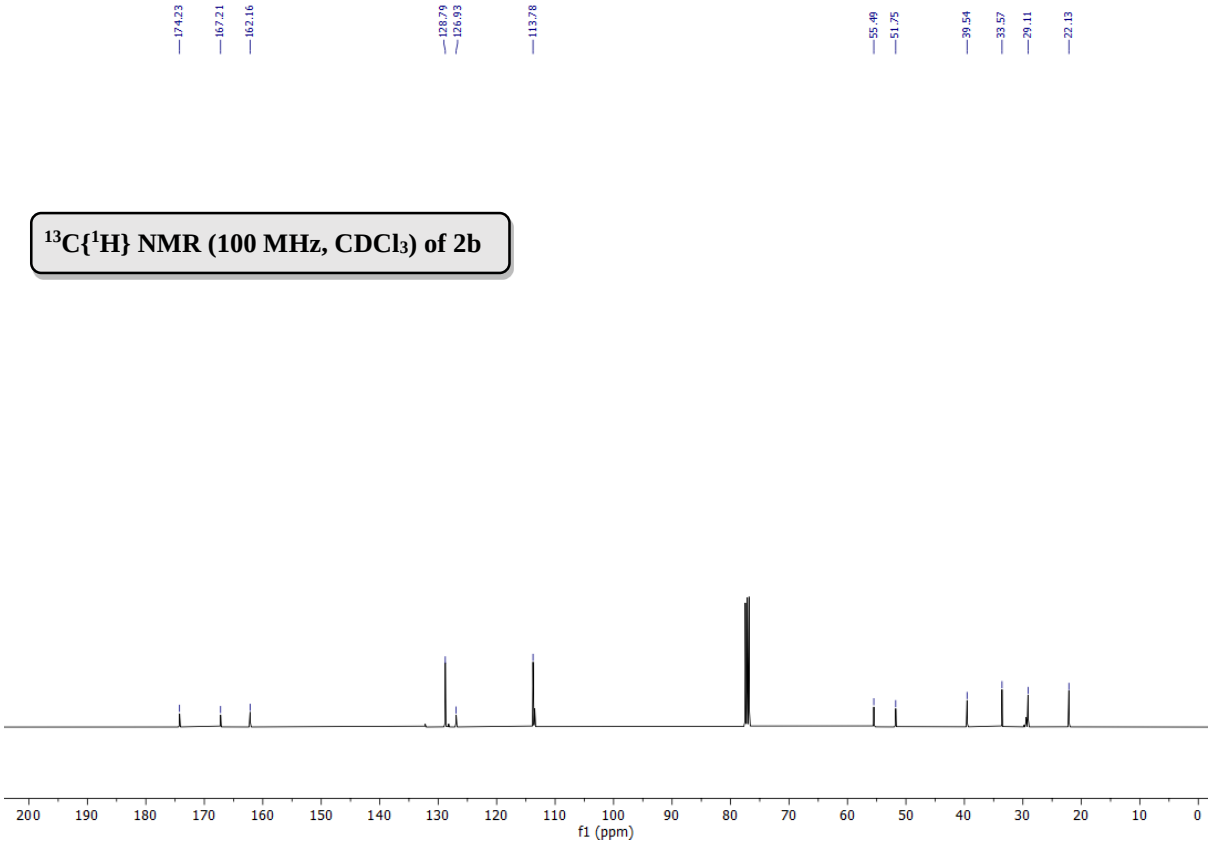


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2a

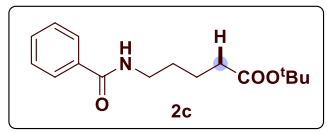




^{1}H NMR (400 MHz, $CDCl_3$) of 2b



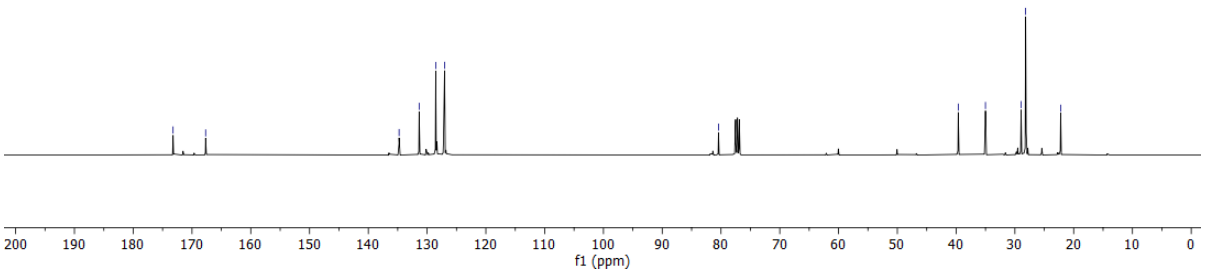
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of 2b

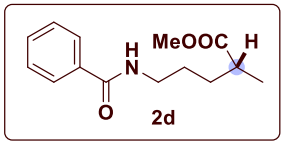


2c

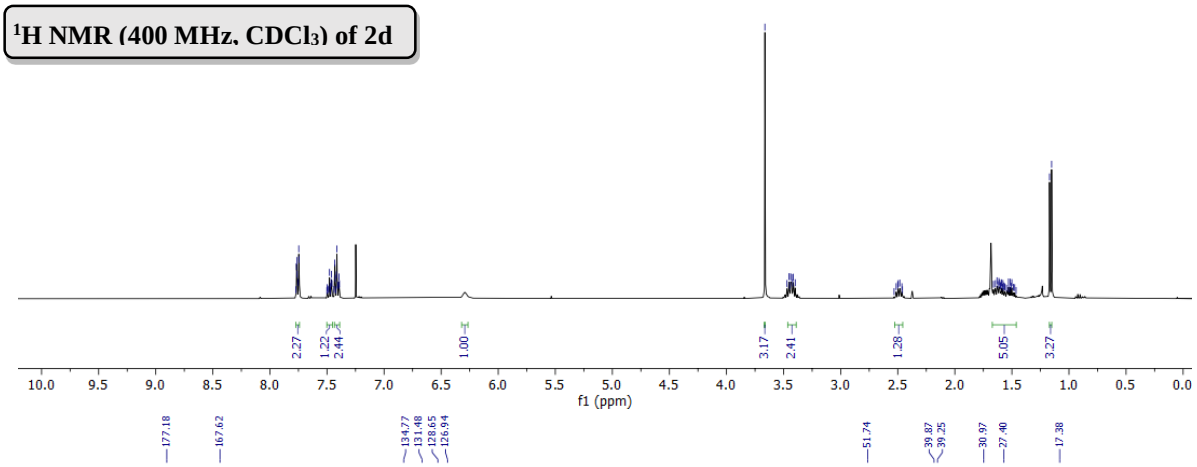
^{1}H NMR (400 MHz, $CDCl_3$) of 2c

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2c

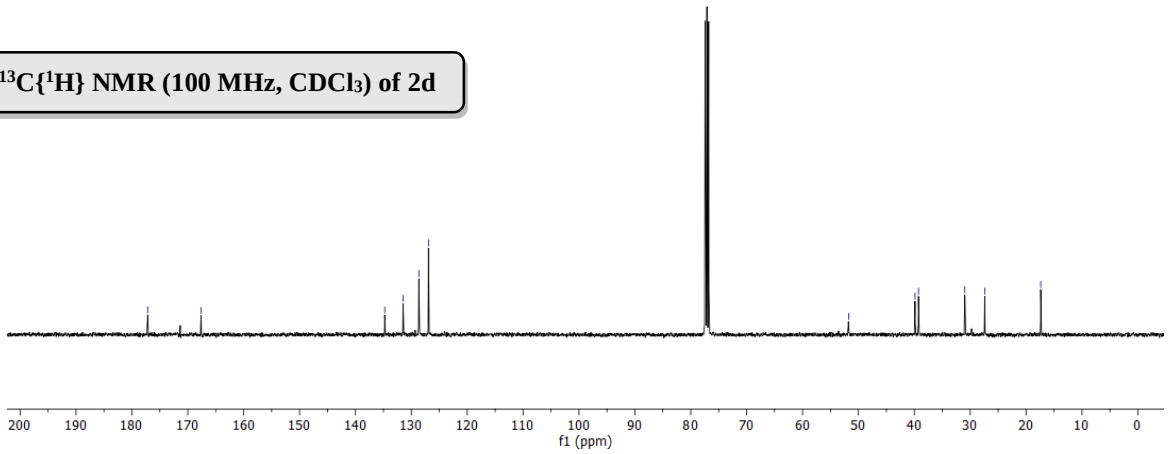


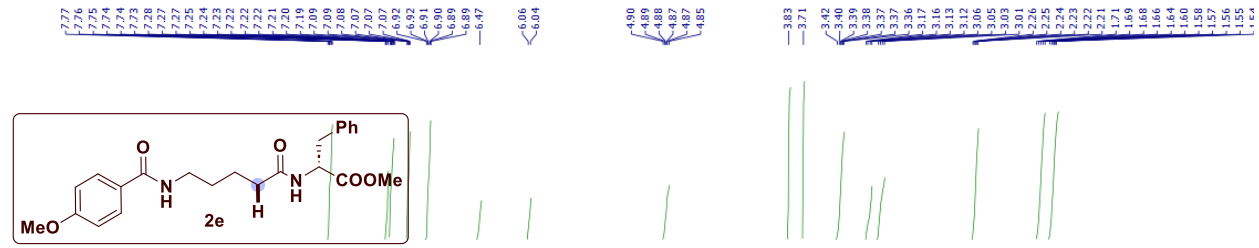


^{1}H NMR (400 MHz, $CDCl_3$) of 2d

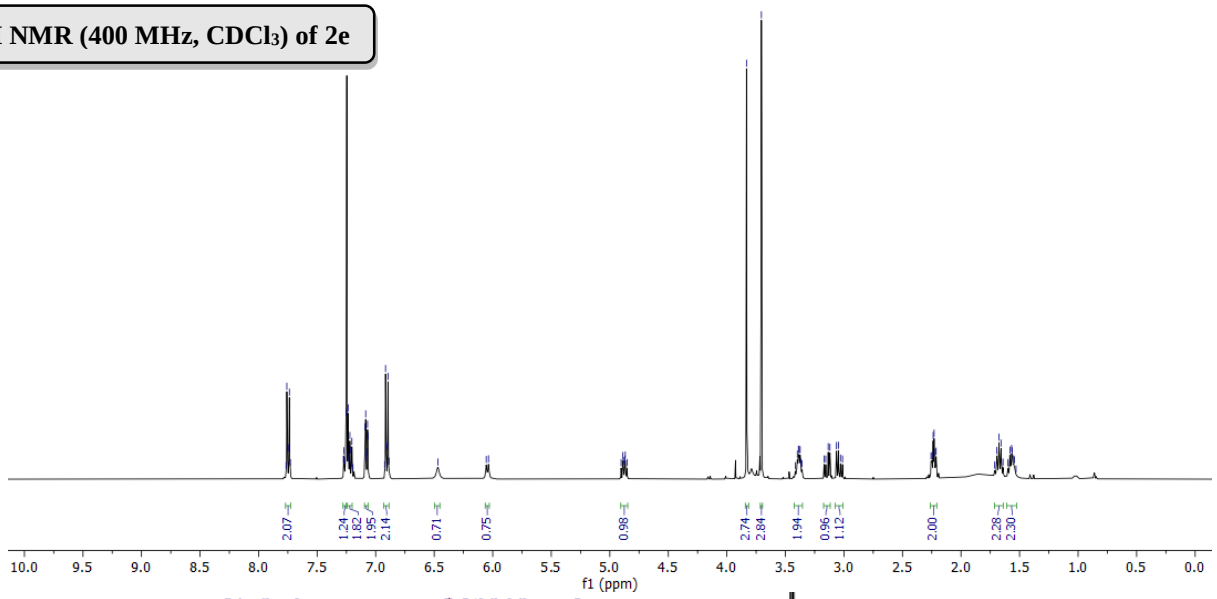


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2d

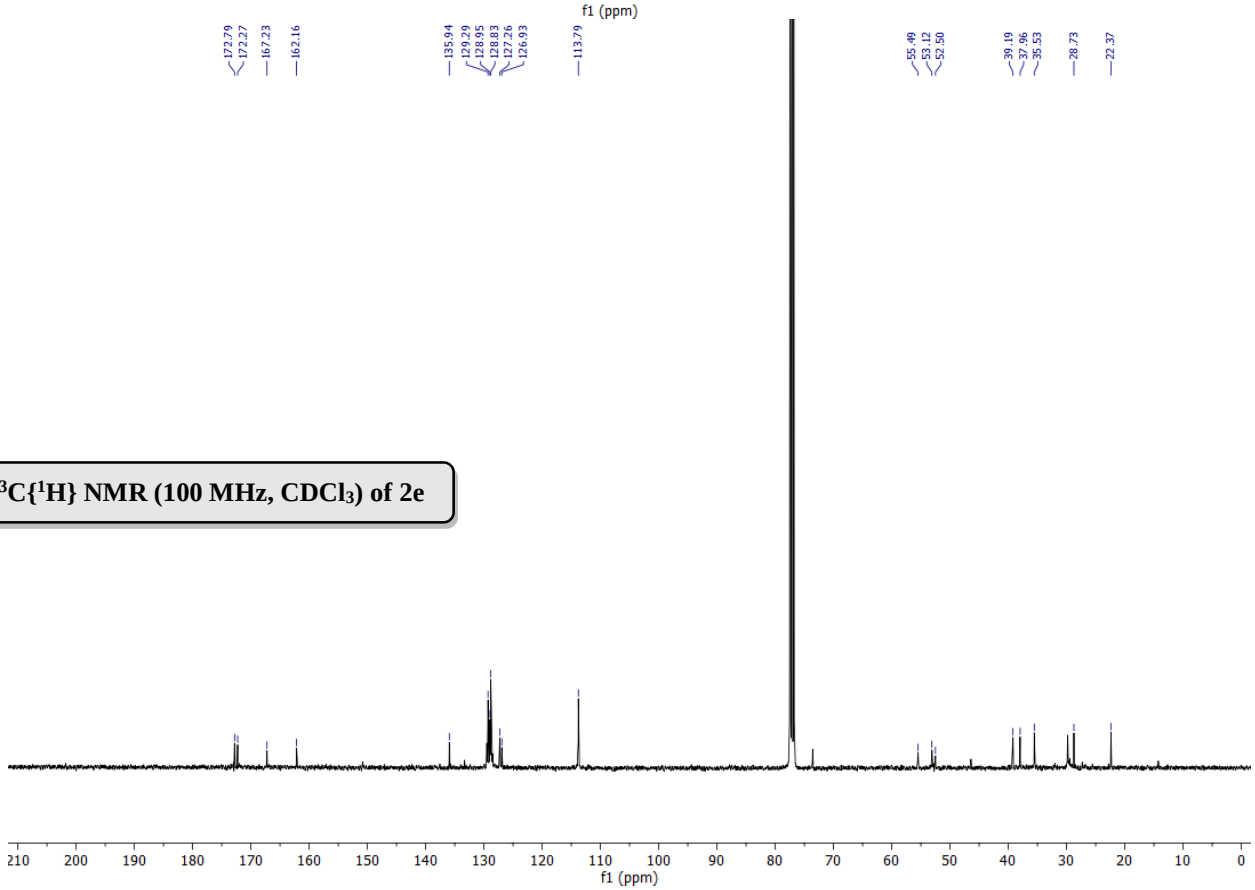


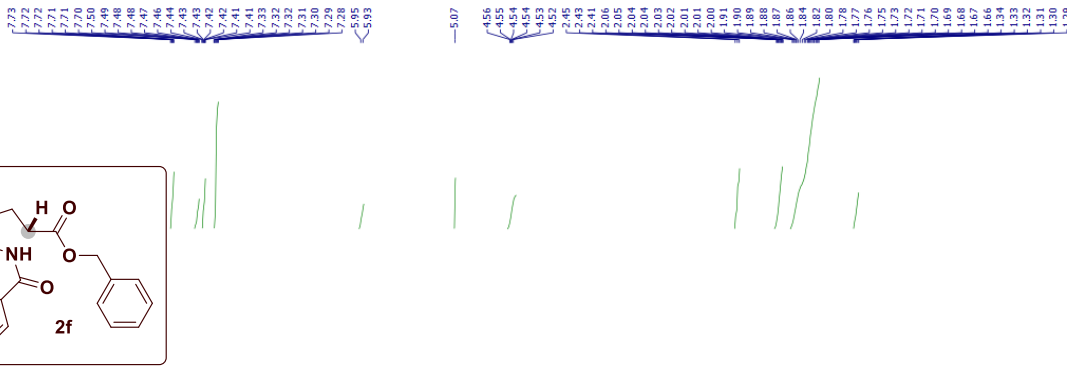


^{1}H NMR (400 MHz, $CDCl_3$) of 2e

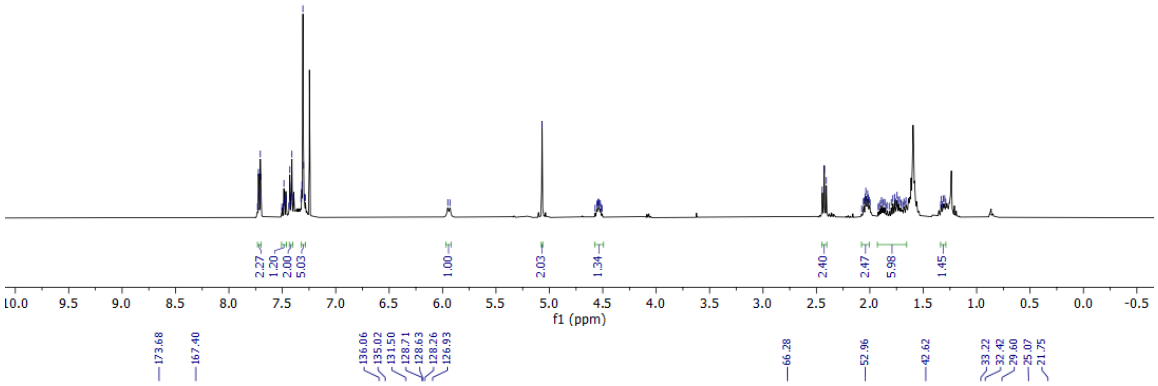


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2e

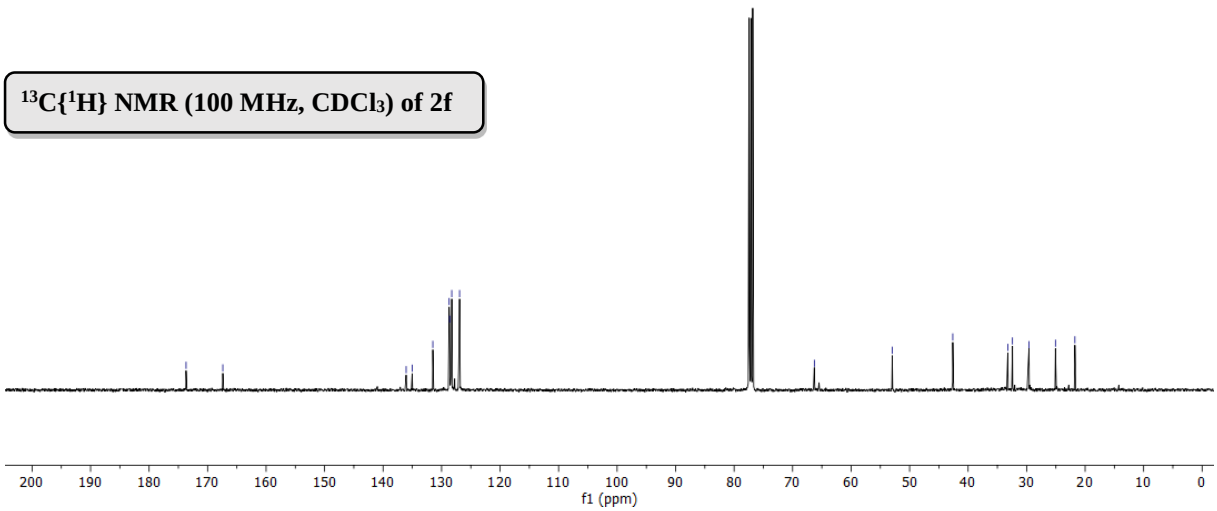


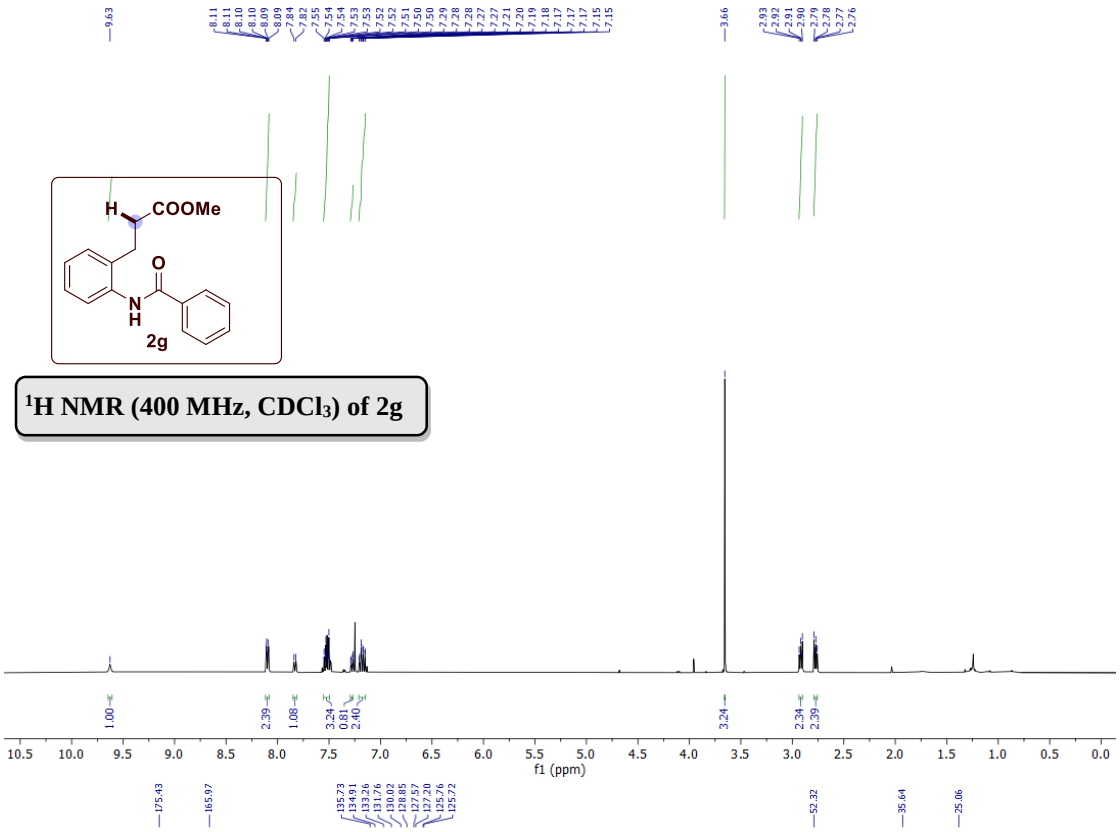


^{1}H NMR (400 MHz, $CDCl_3$) of 2f

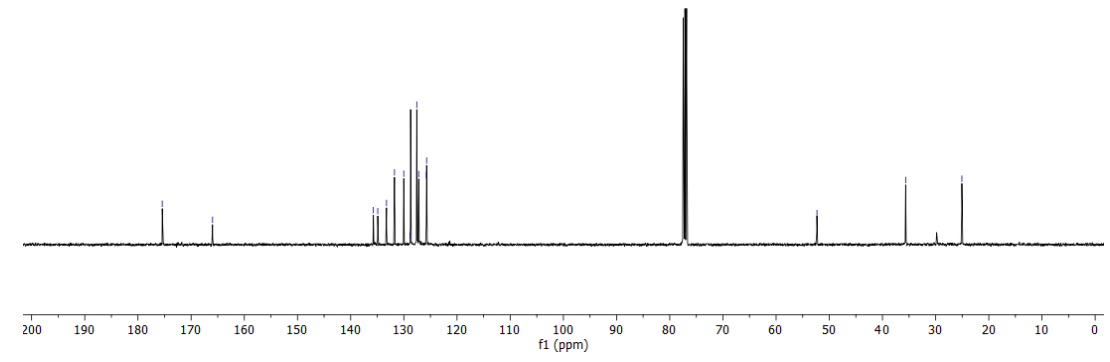


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2f

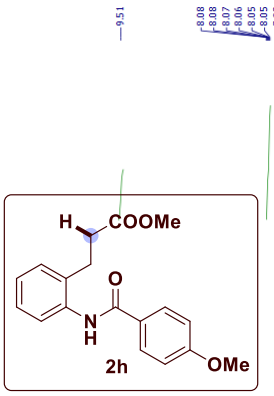




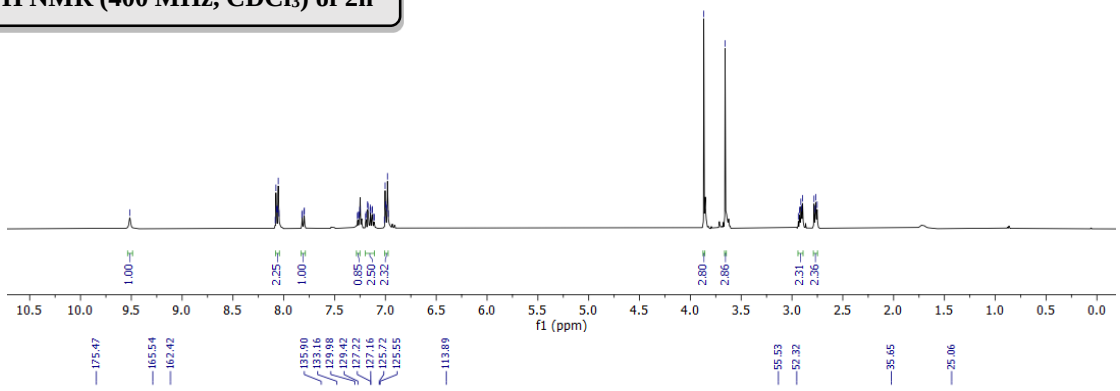
^{1}H NMR (400 MHz, $CDCl_3$) of 2g



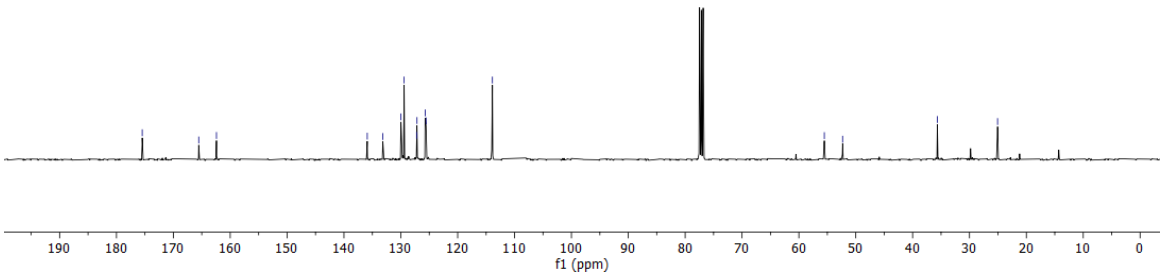
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2g

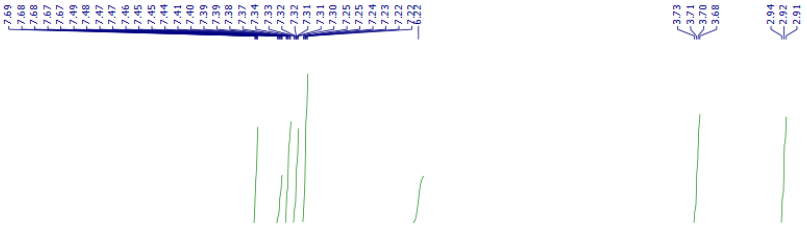


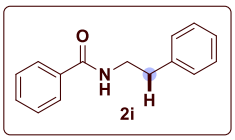
^{1}H NMR (400 MHz, $CDCl_3$) of 2h



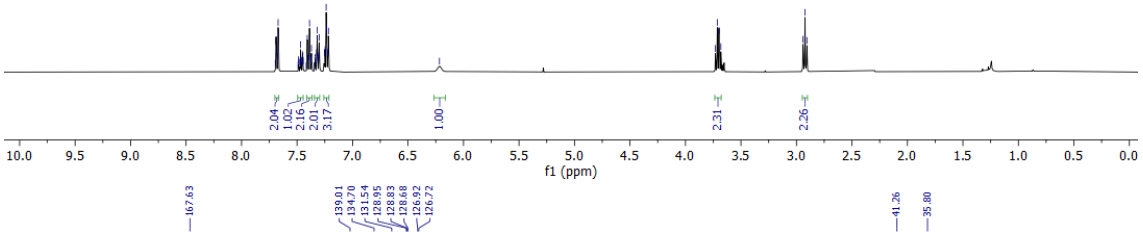
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2h



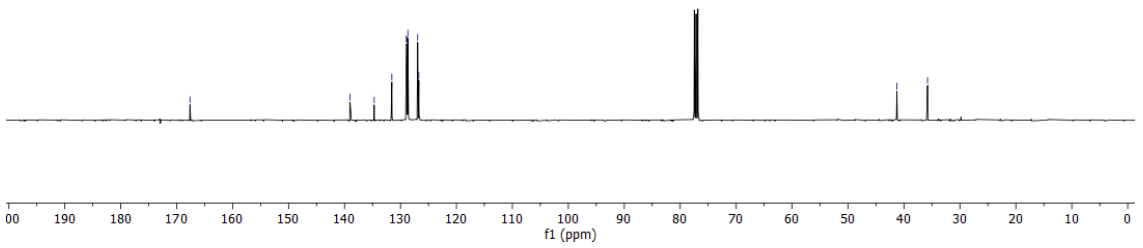


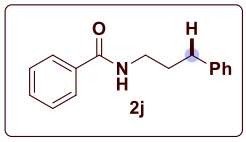


^{1}H NMR (400 MHz, $CDCl_3$) of 2i

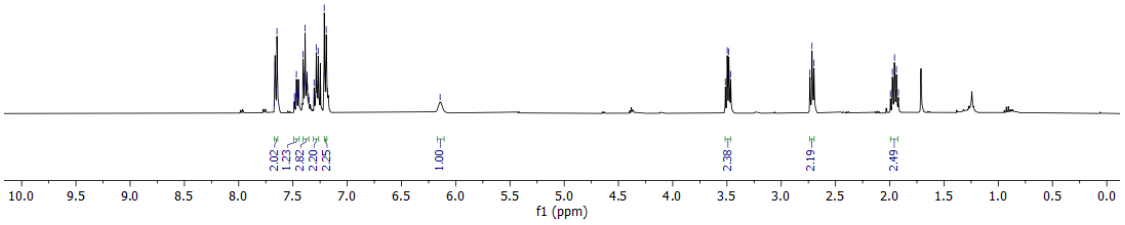


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2i

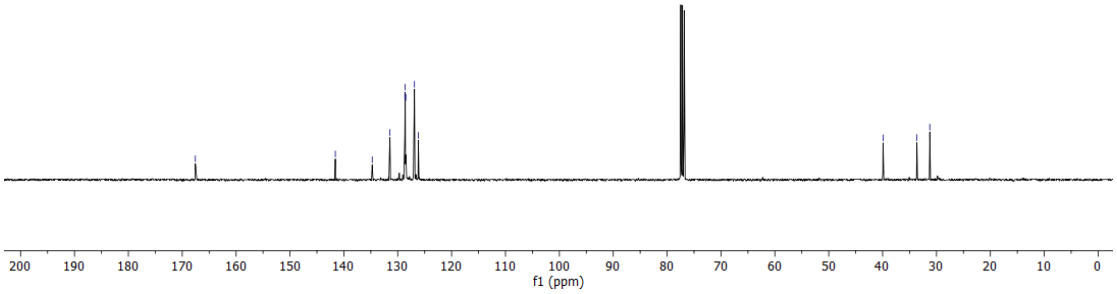


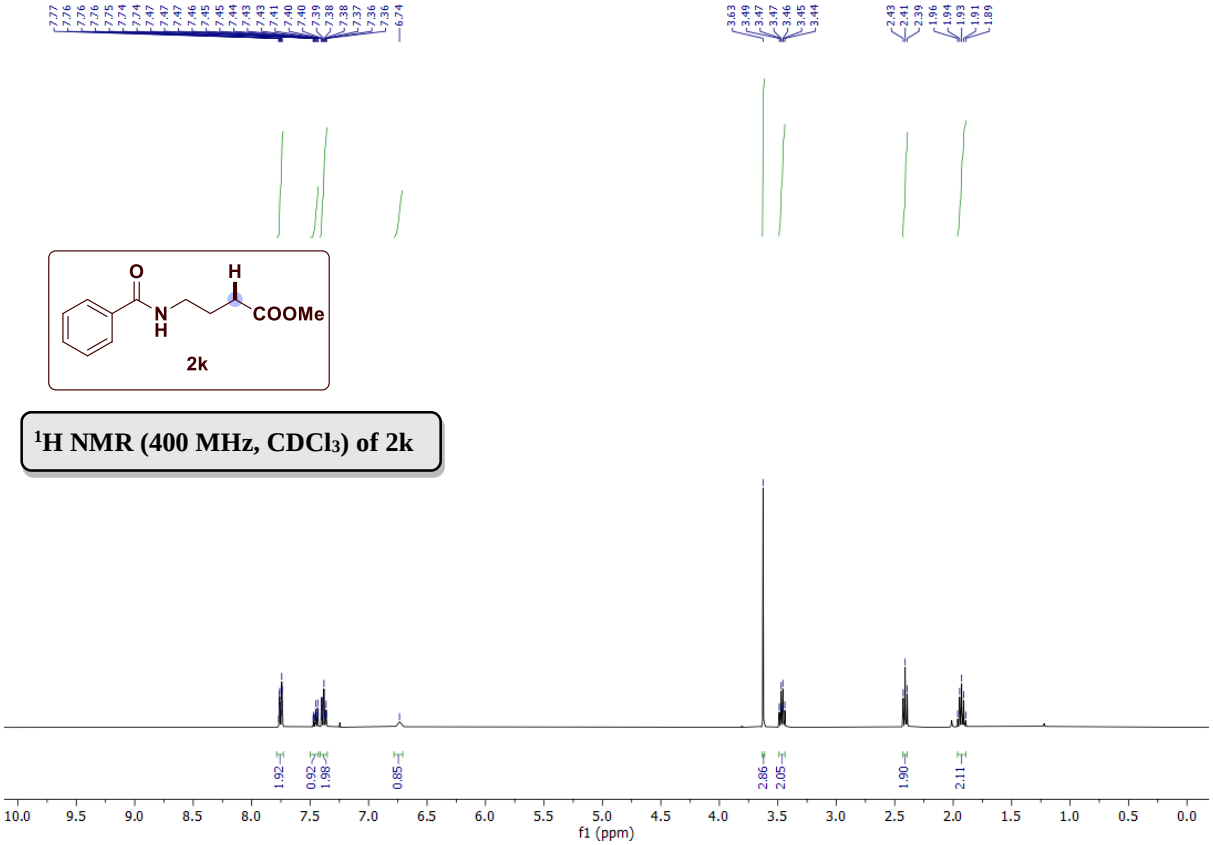


^{1}H NMR (400 MHz, $CDCl_3$) of 2j

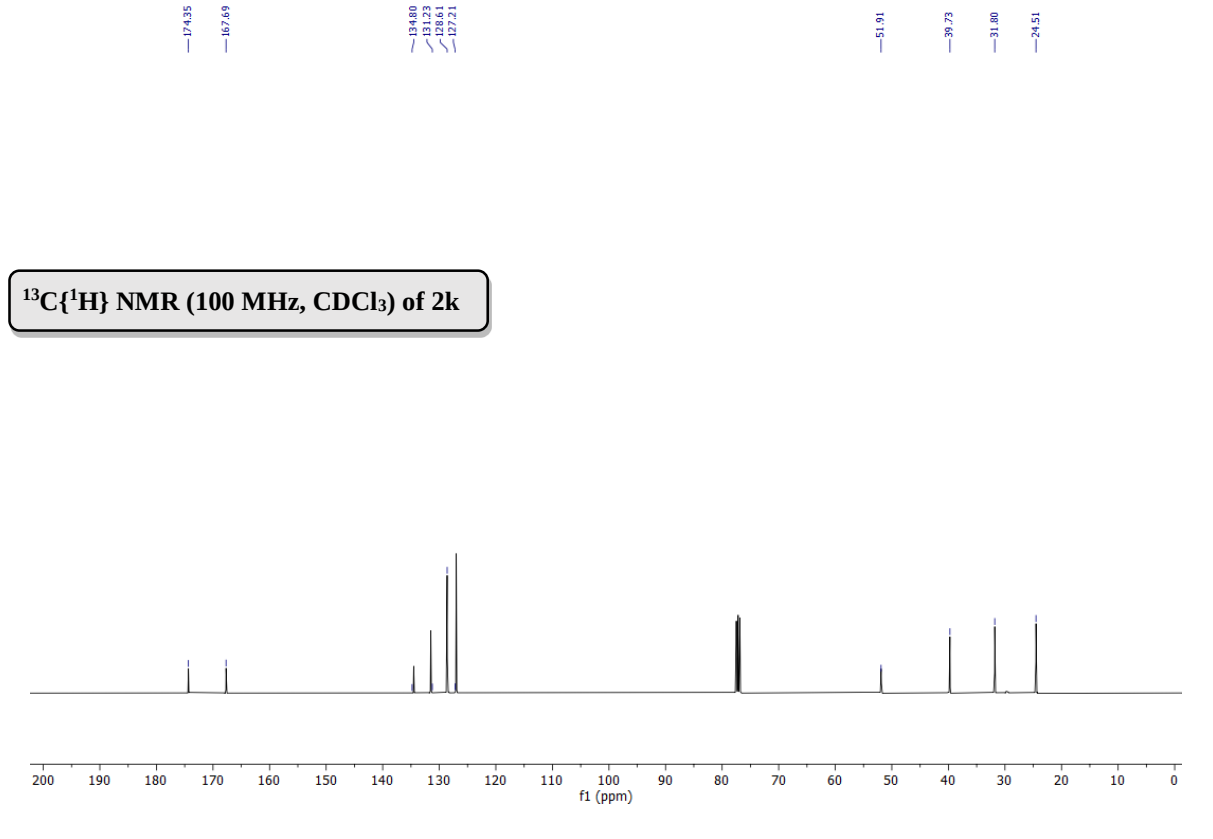


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2j

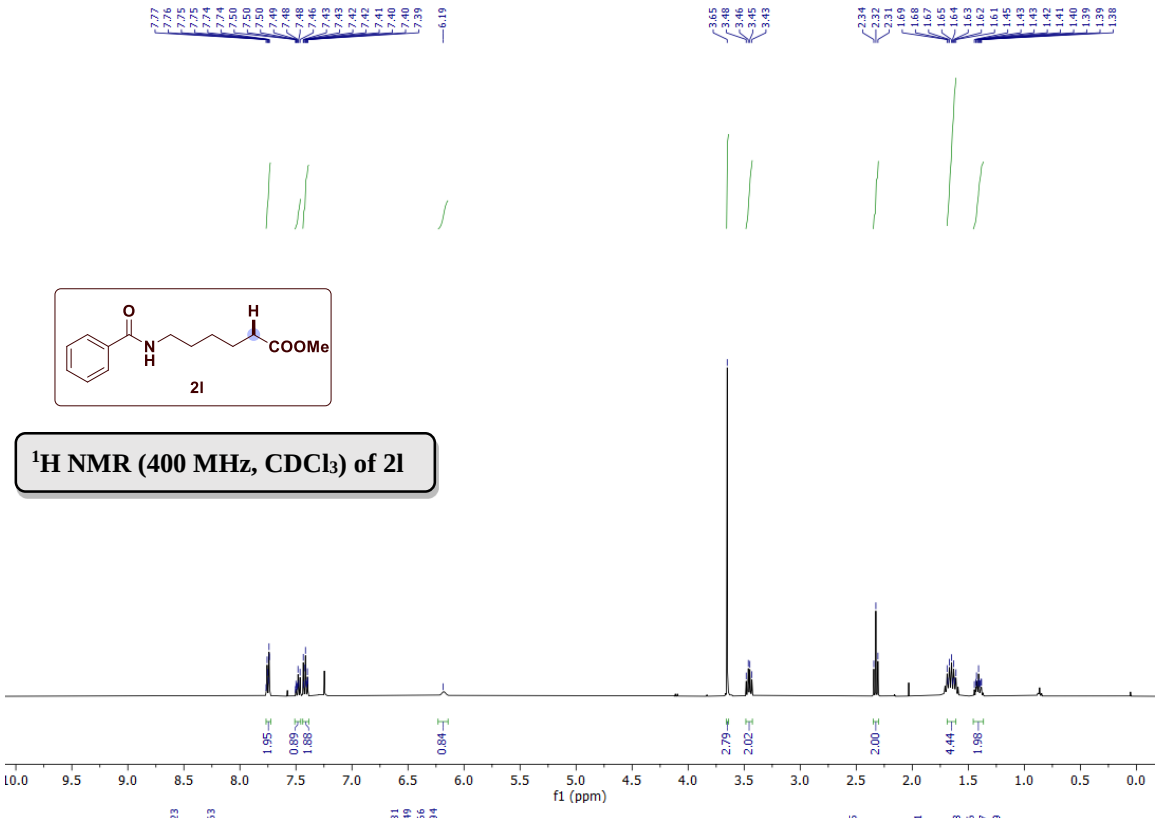




^{1}H NMR (400 MHz, $CDCl_3$) of 2k

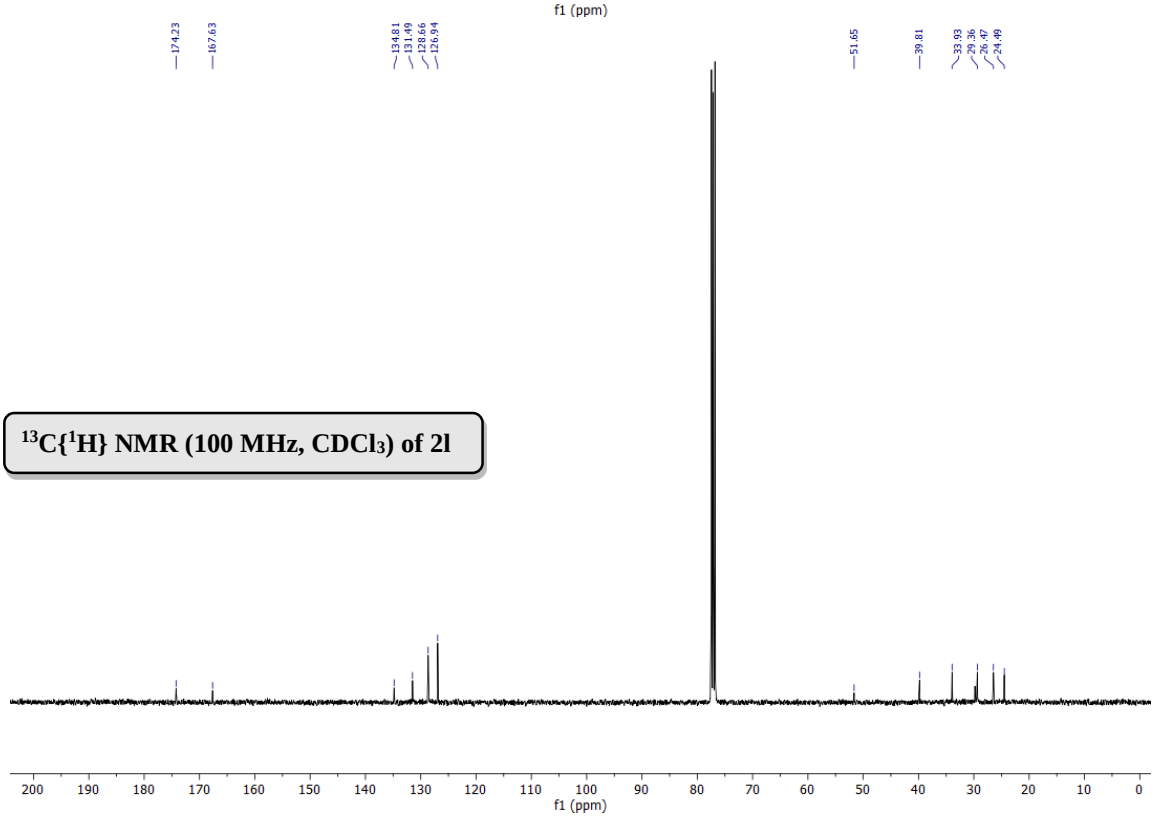


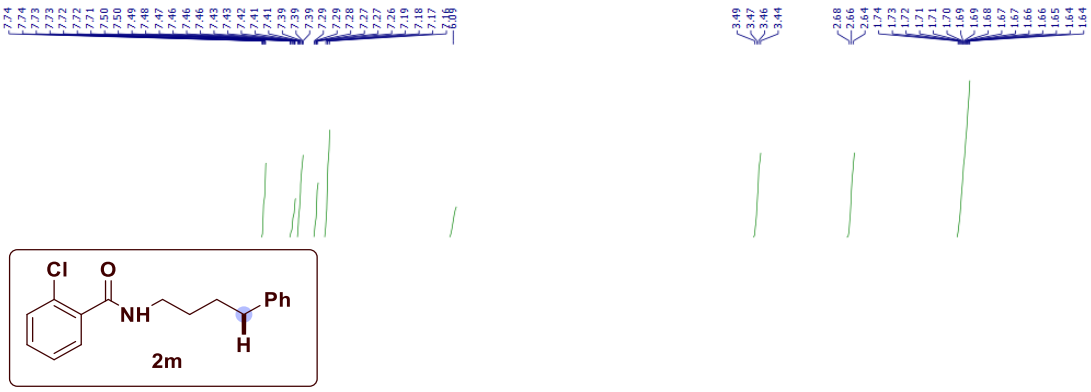
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2k



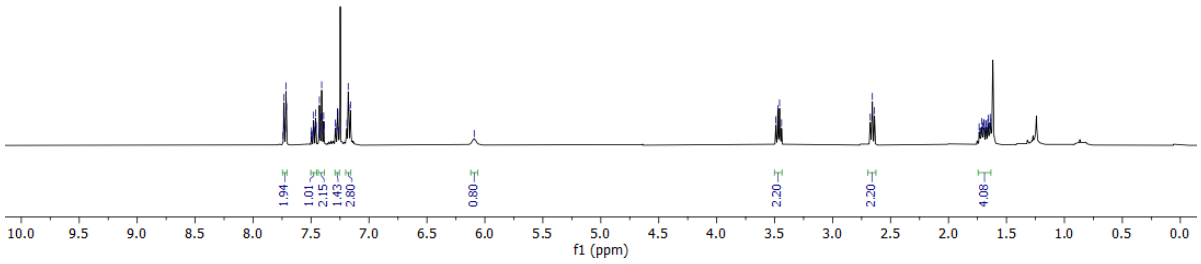
^{1}H NMR (400 MHz, $CDCl_3$) of 2l

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2l

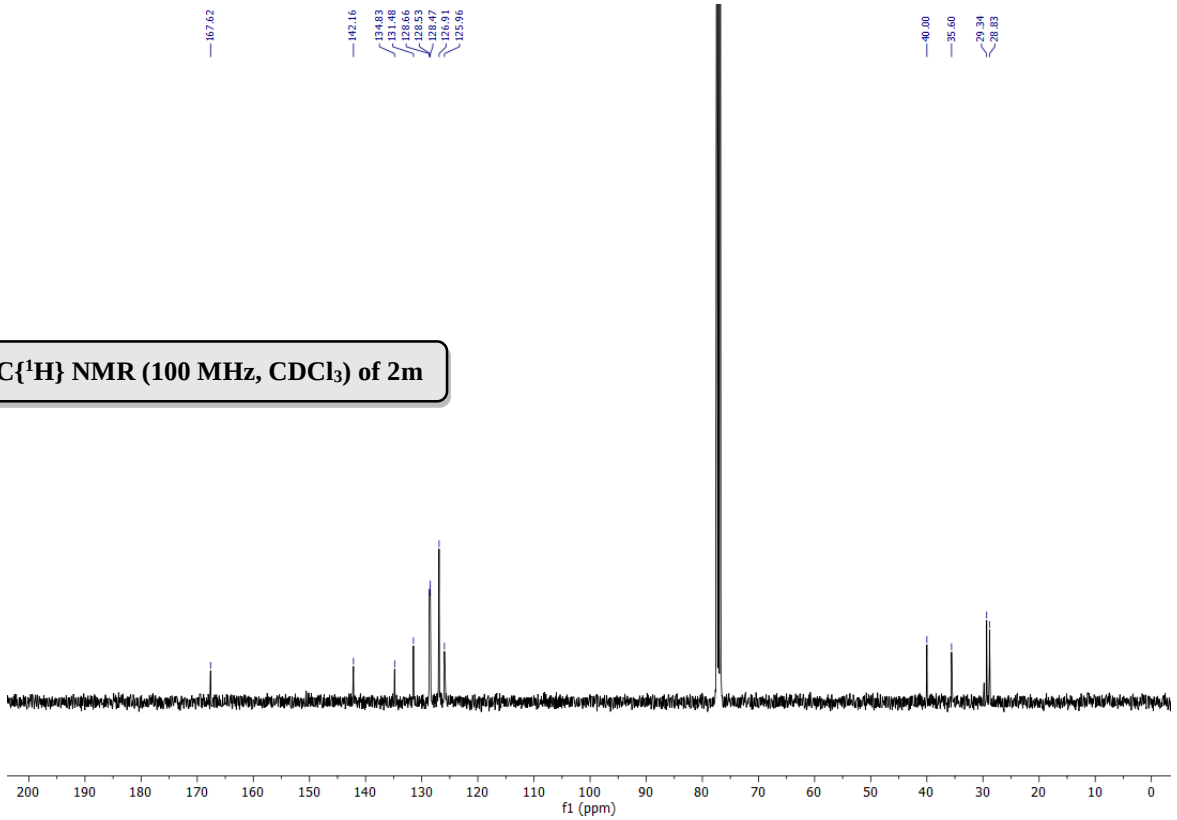


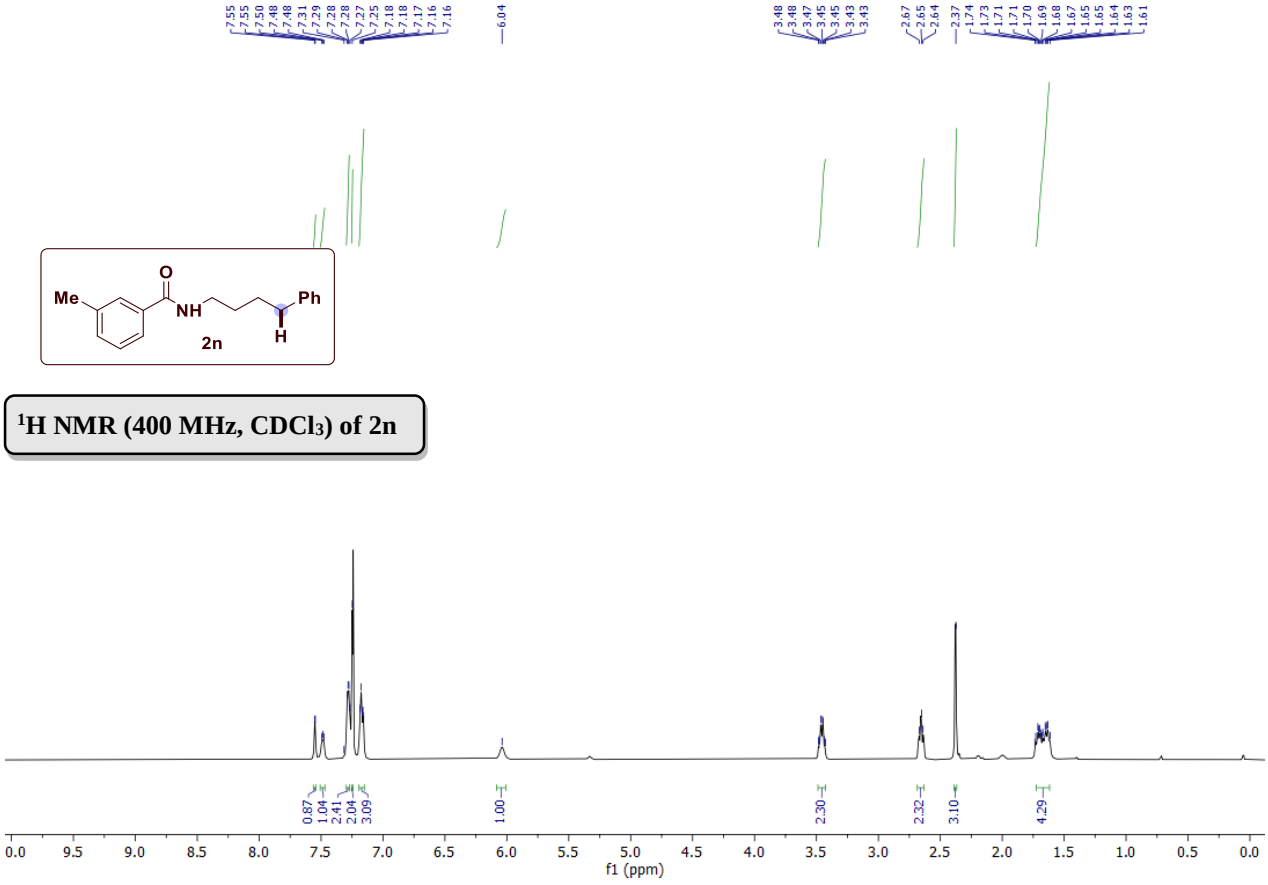


^{1}H NMR (400 MHz, $CDCl_3$) of 2m

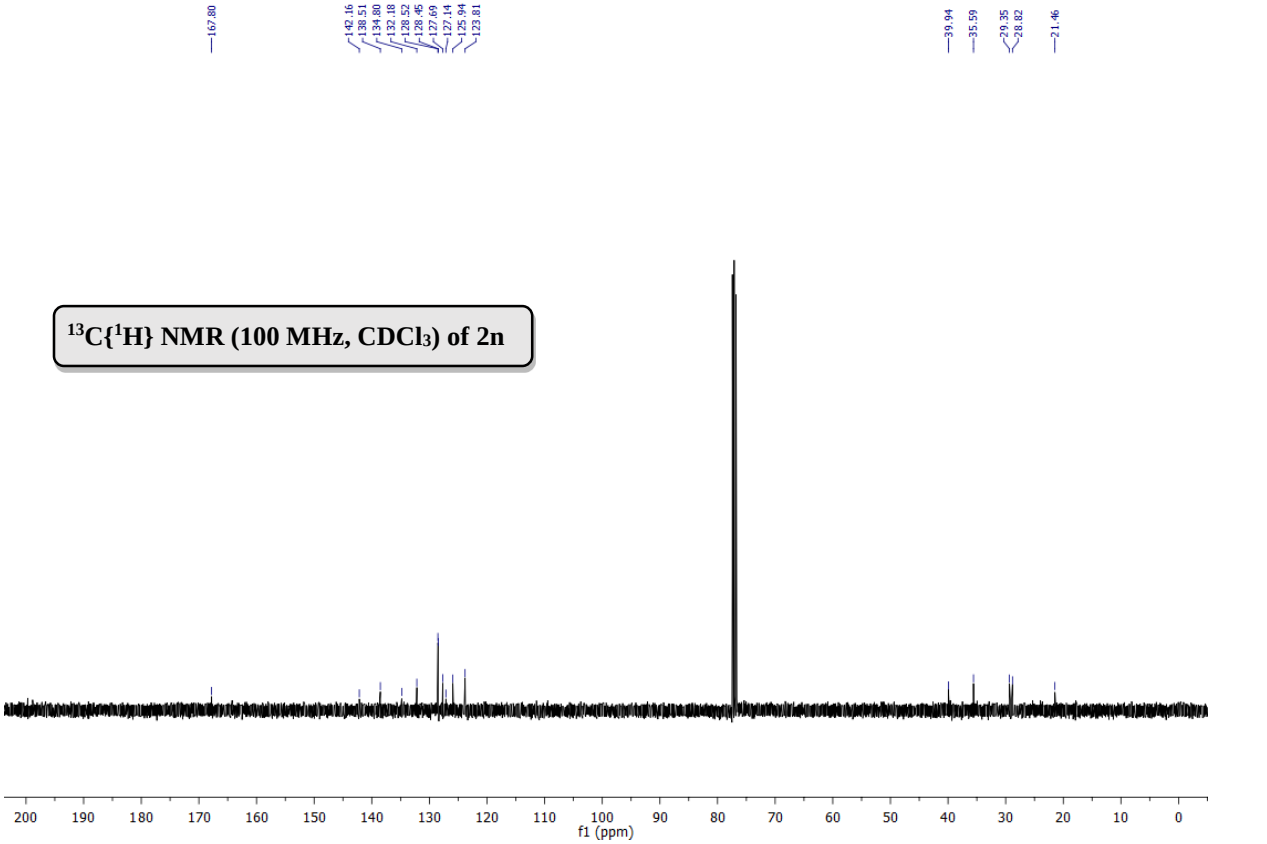


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2m

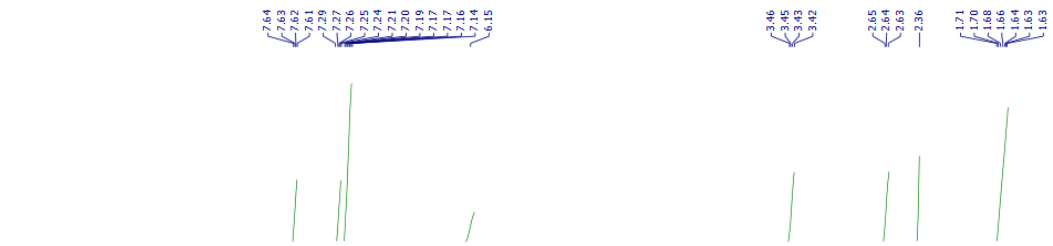


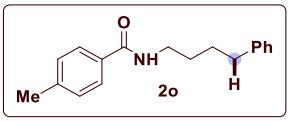


^{1}H NMR (400 MHz, $CDCl_3$) of 2n

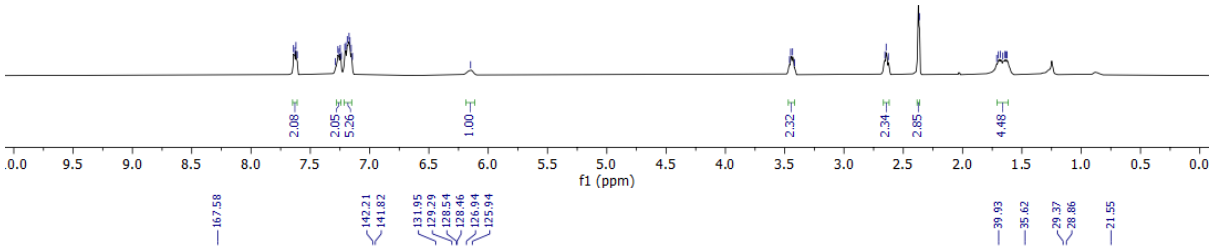


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2n

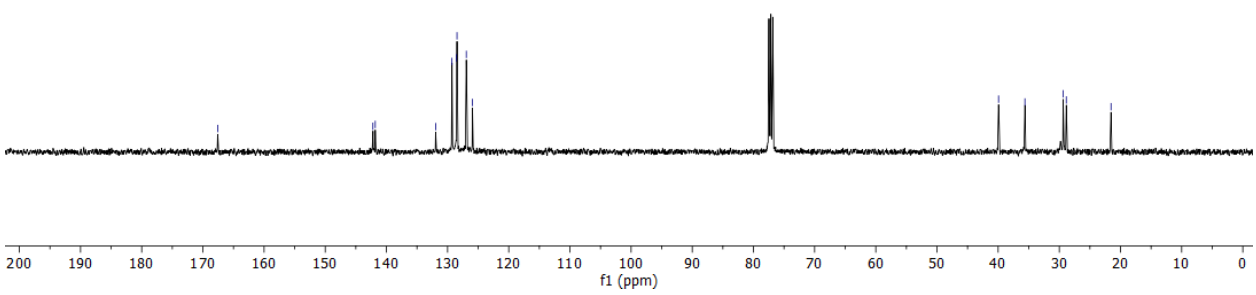


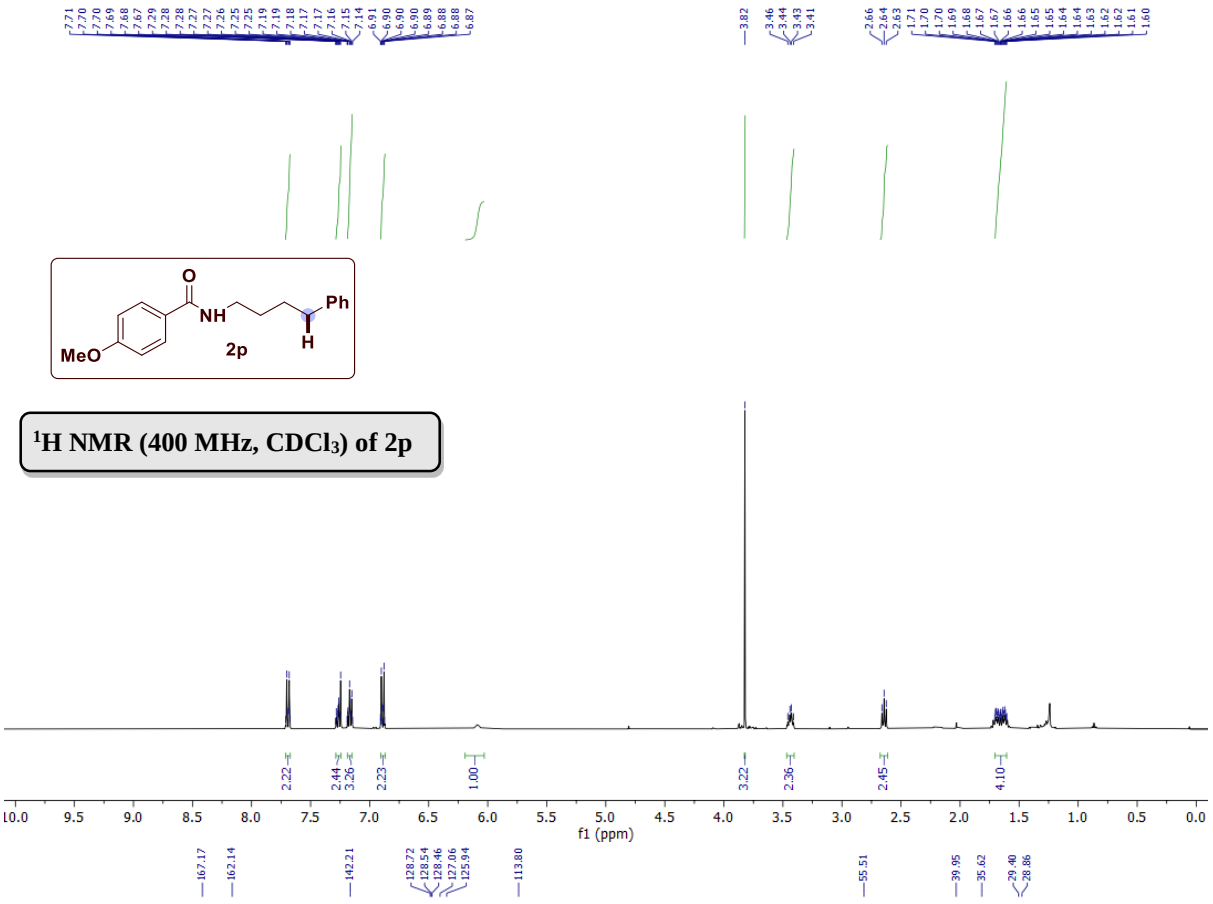


^{1}H NMR (400 MHz, $CDCl_3$) of 2o

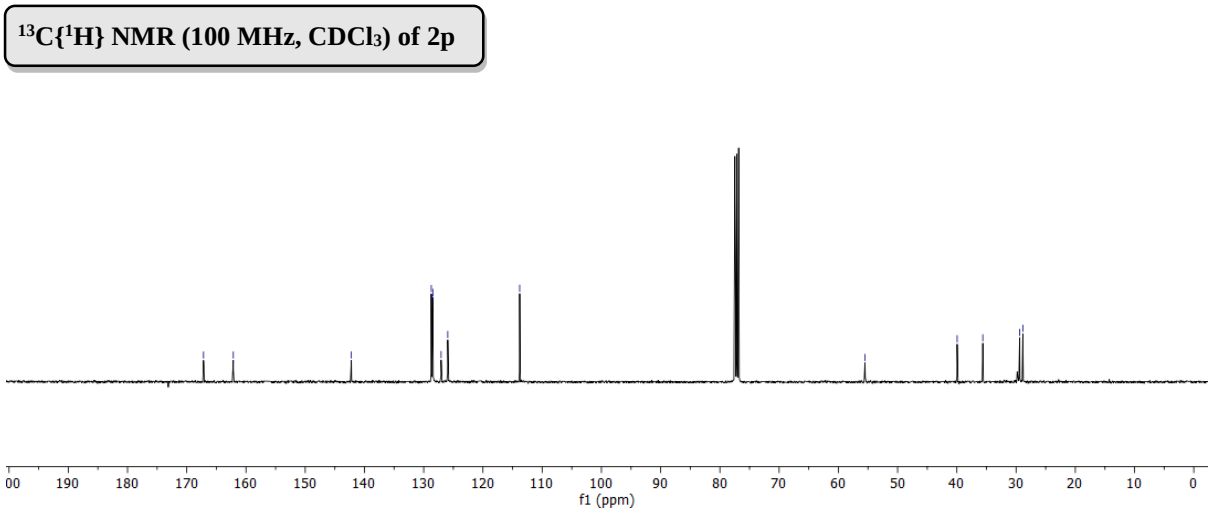


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2o

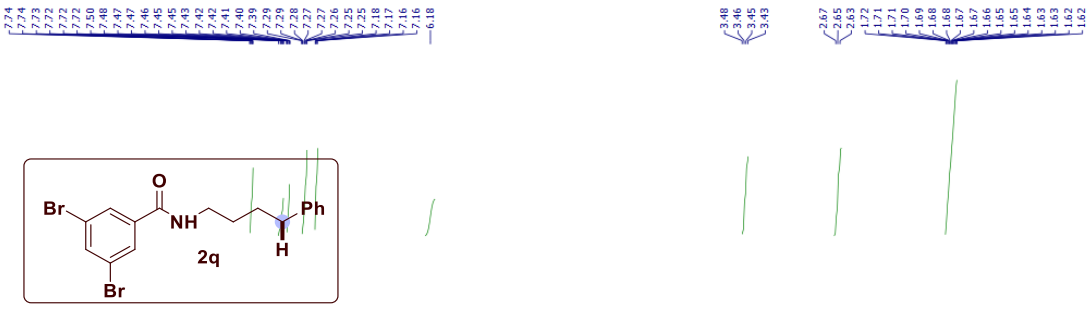




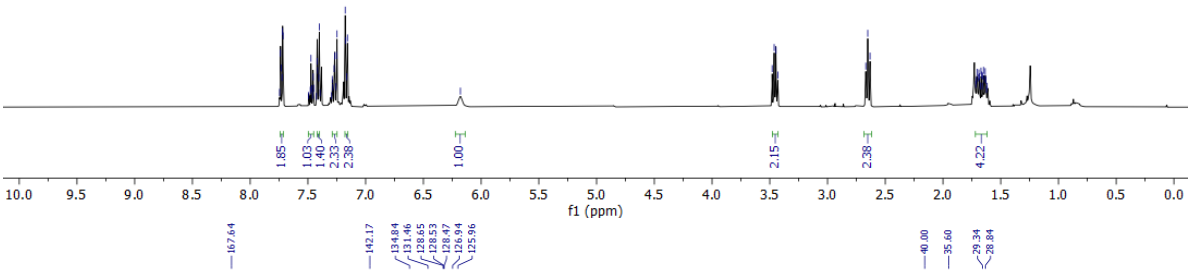
^{1}H NMR (400 MHz, $CDCl_3$) of 2p



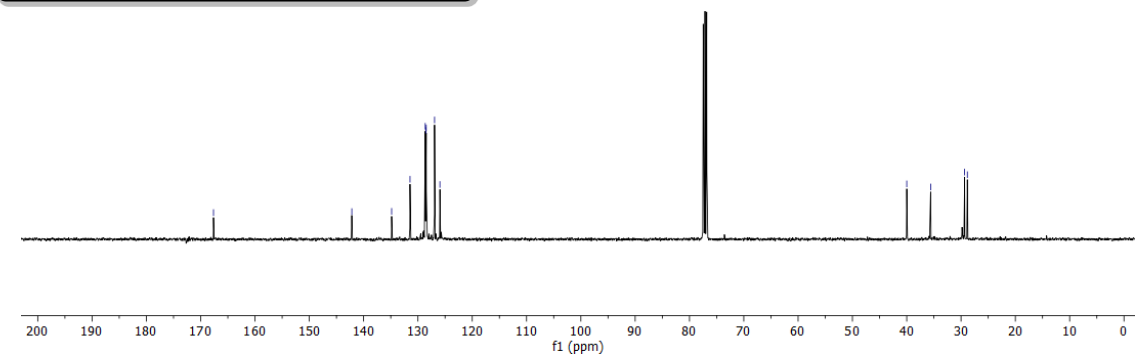
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of 2p

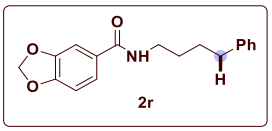


^{1}H NMR (400 MHz, $CDCl_3$) of 2q

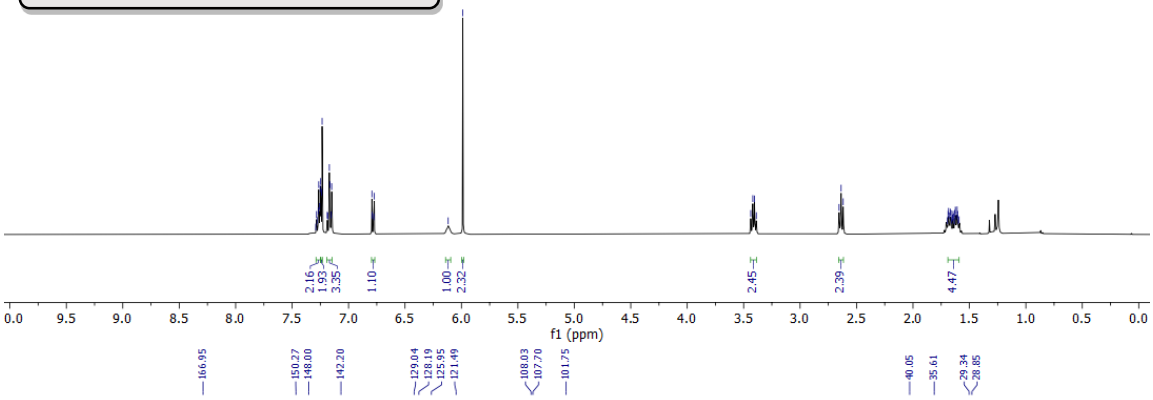


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2q

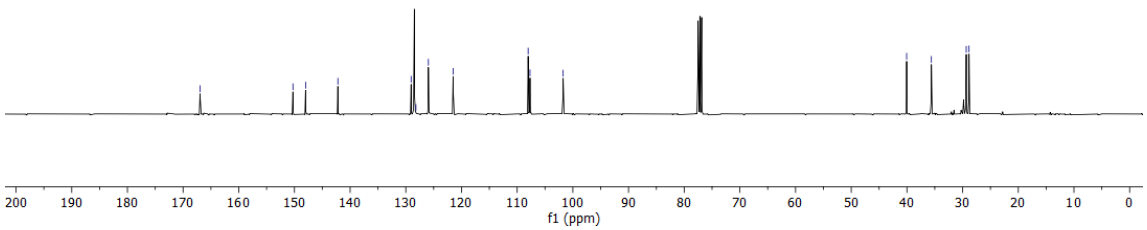


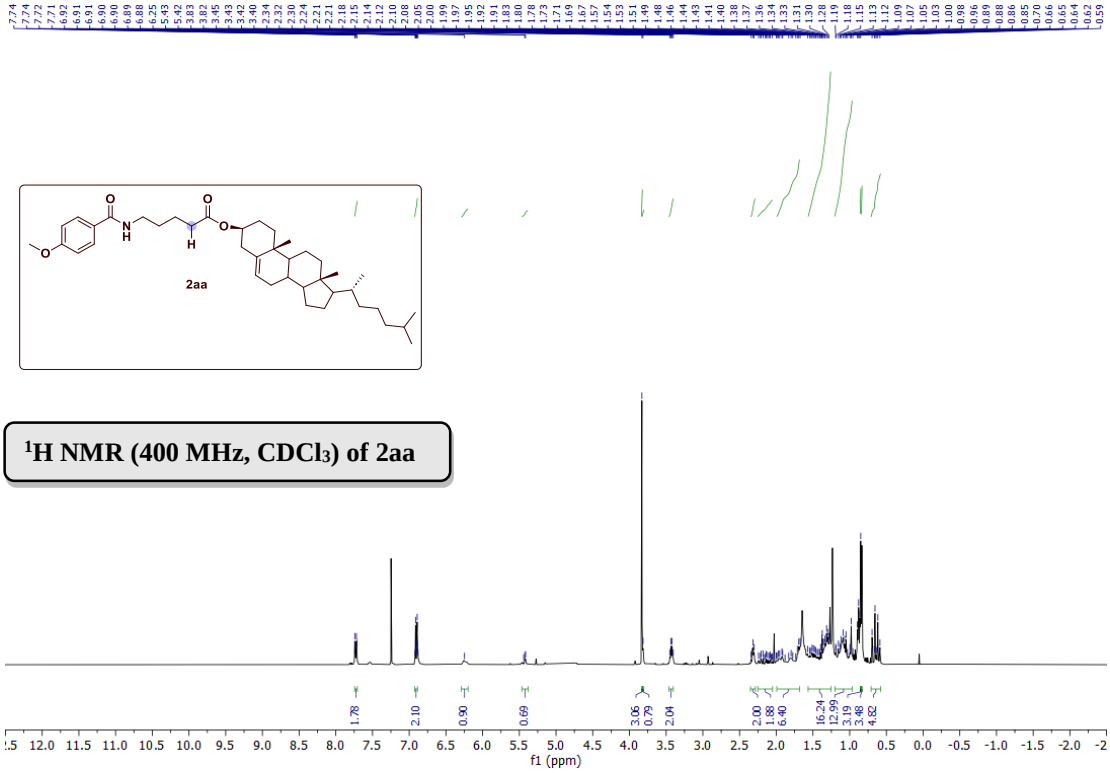


^{1}H NMR (400 MHz, $CDCl_3$) of 2r

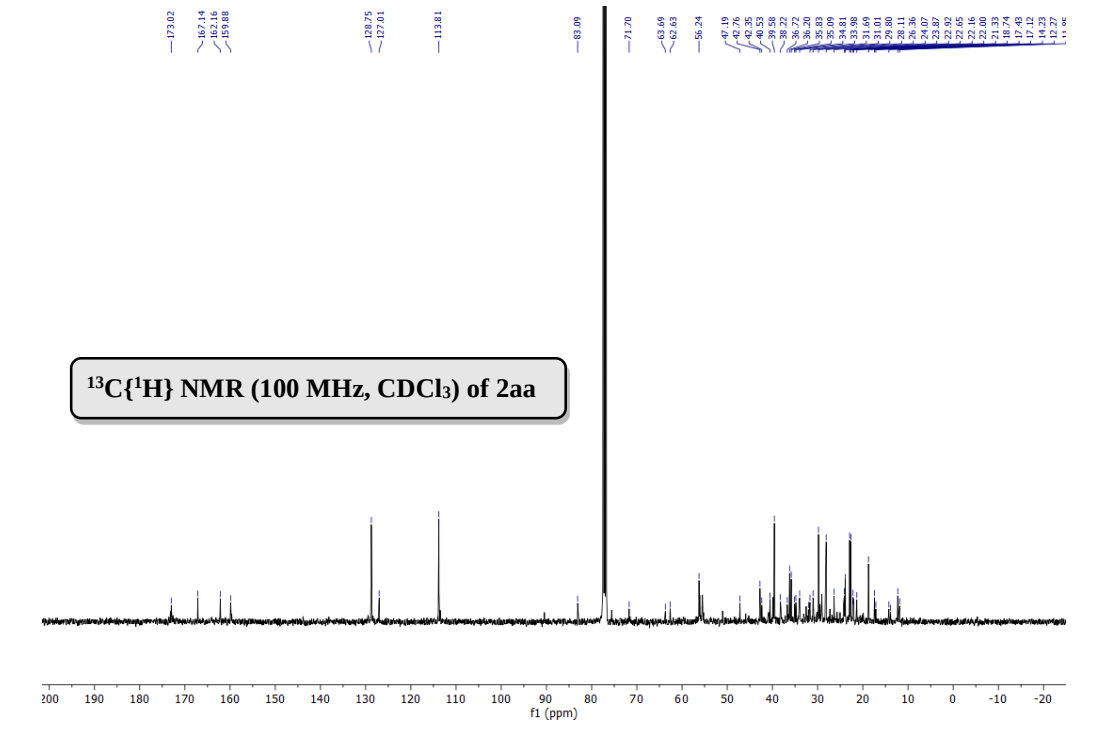


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2r

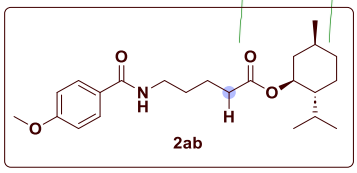




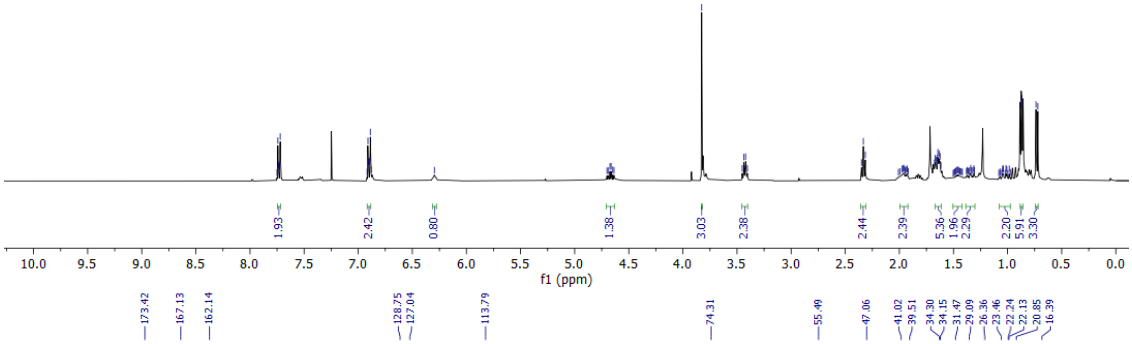
^{1}H NMR (400 MHz, $CDCl_3$) of 2aa



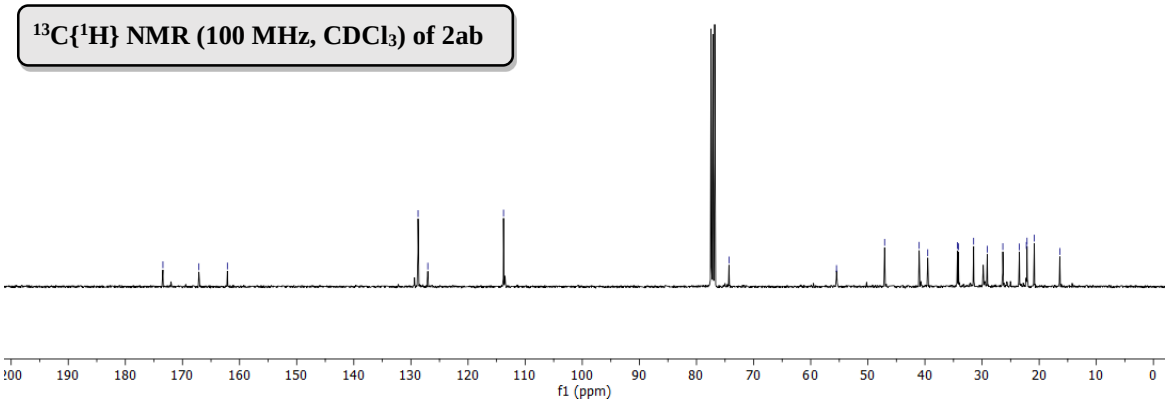
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2aa



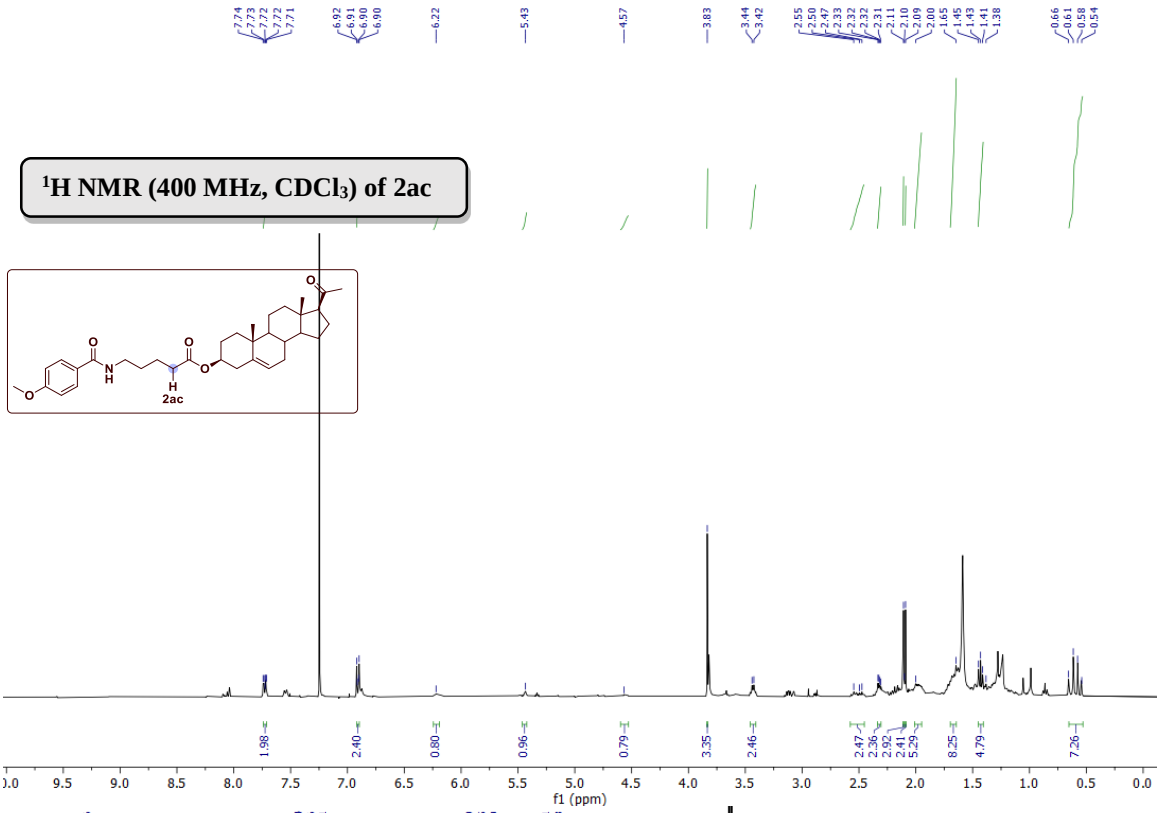
^{1}H NMR (400 MHz, $CDCl_3$) of 2ab



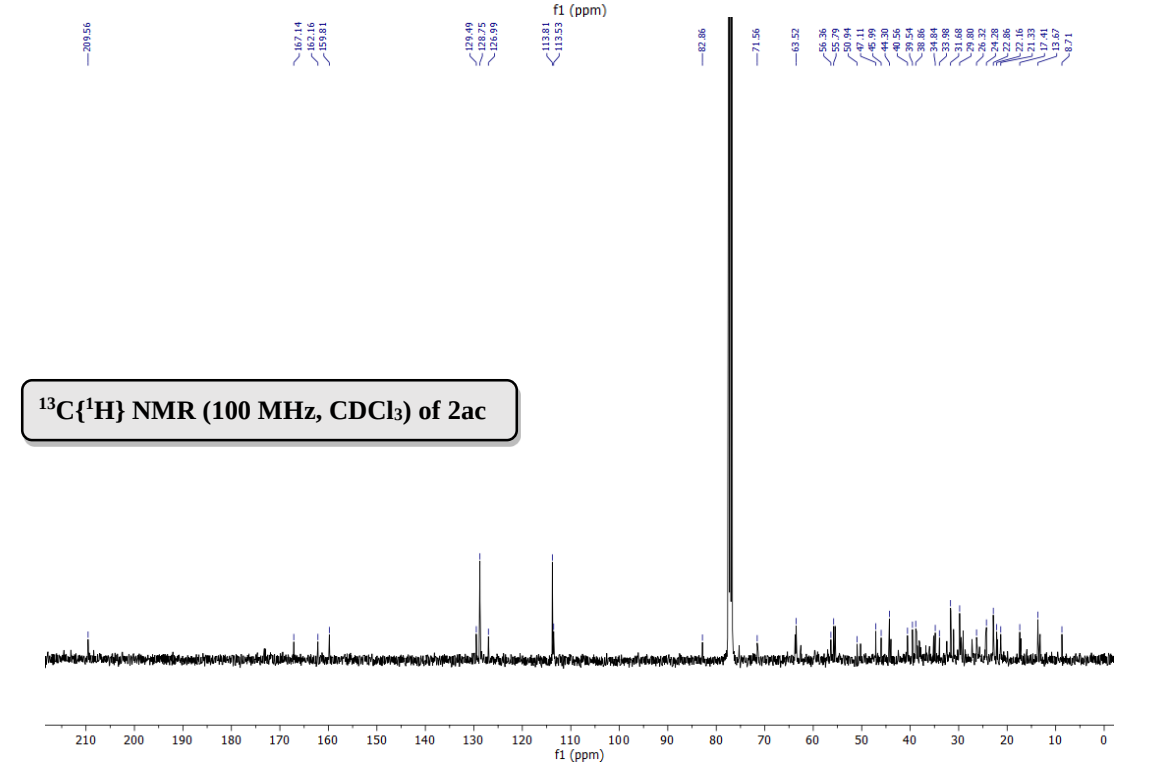
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2ab

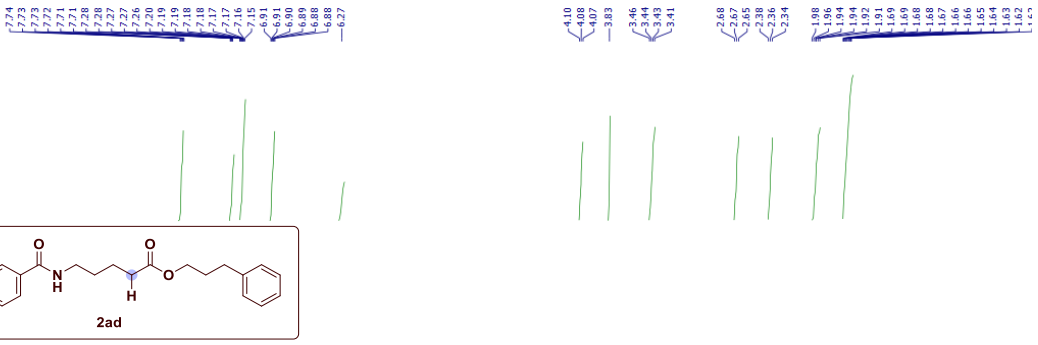


^{1}H NMR (400 MHz, $CDCl_3$) of 2ac

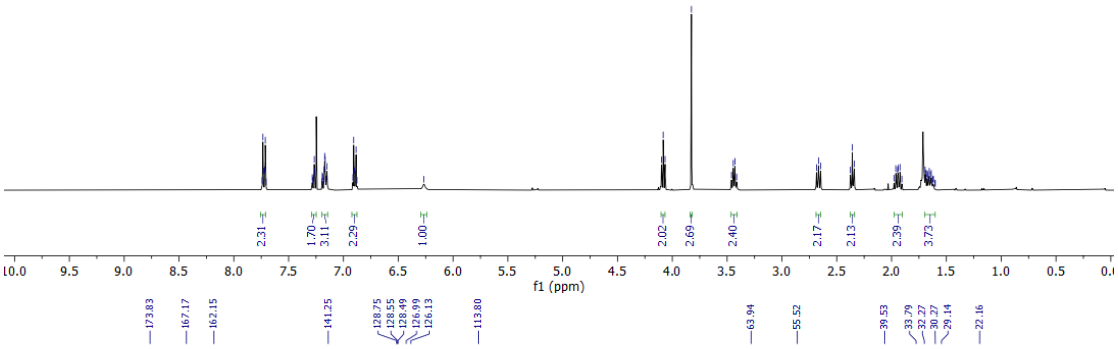


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2ac

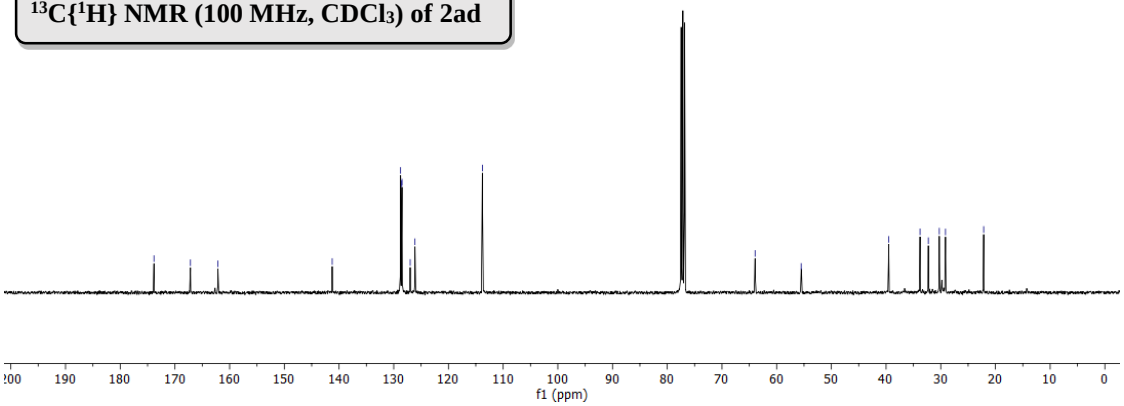


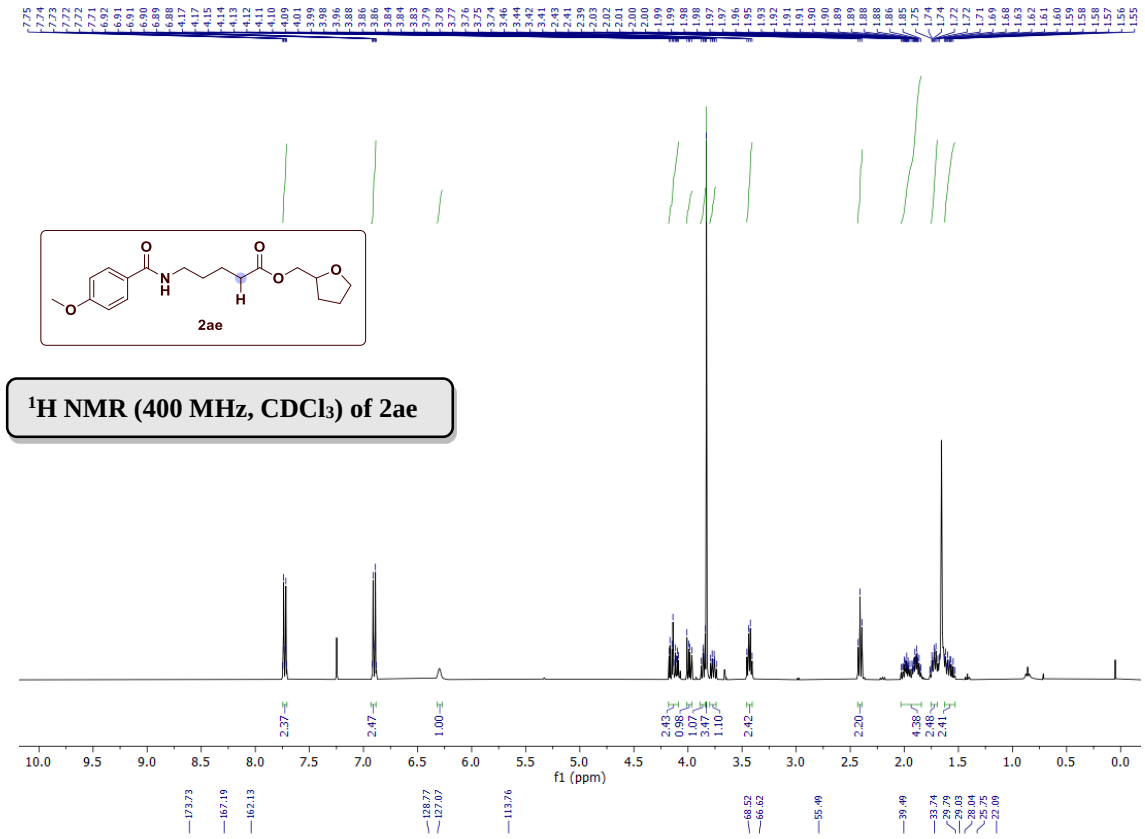


^{1}H NMR (400 MHz, $CDCl_3$) of 2ad

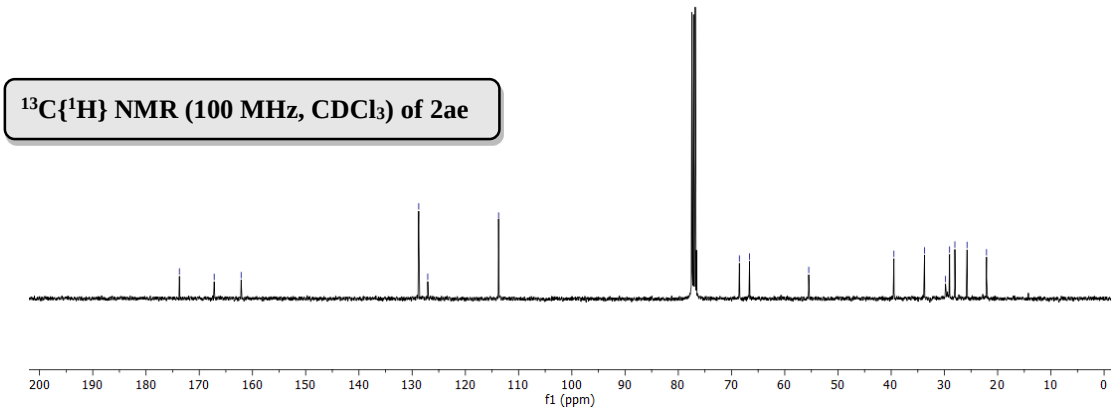


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2ad

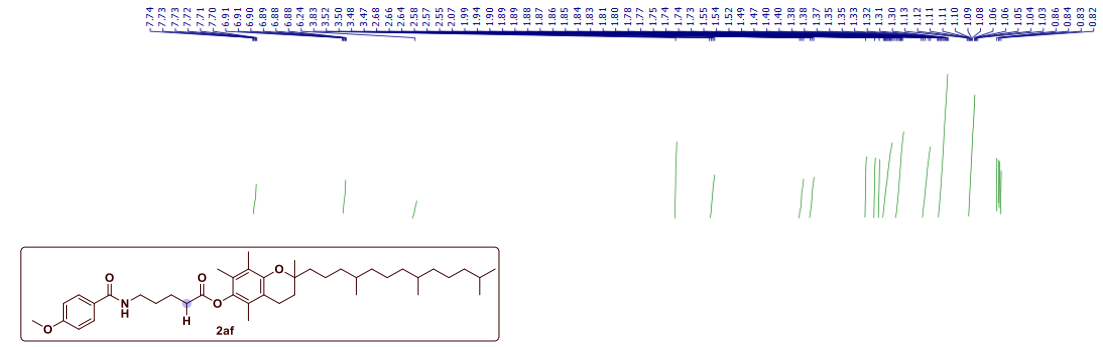




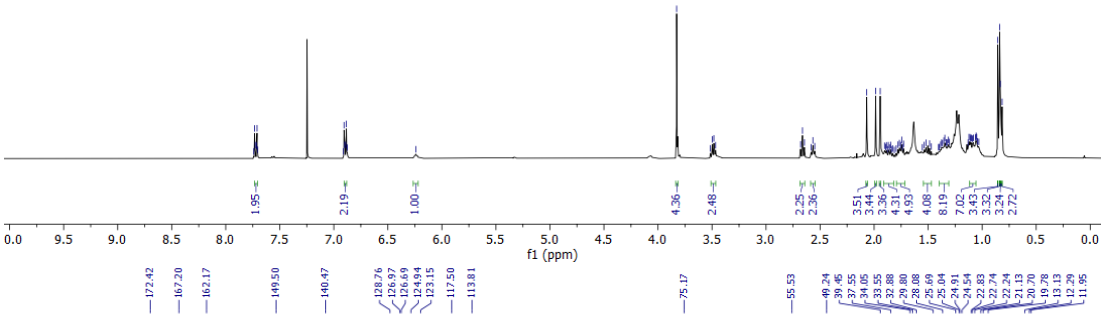
^{1}H NMR (400 MHz, $CDCl_3$) of 2ae



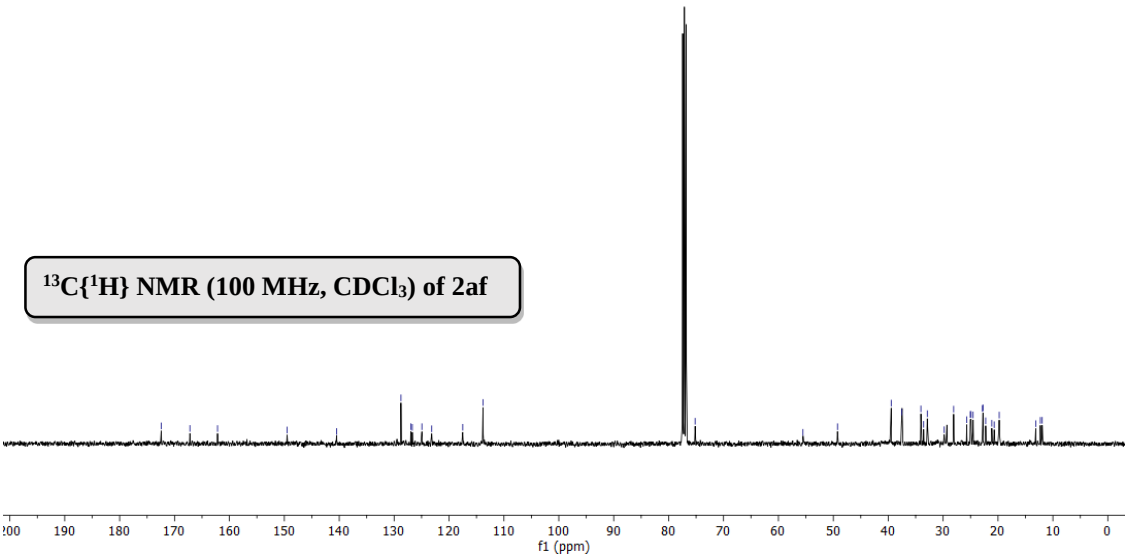
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2ae

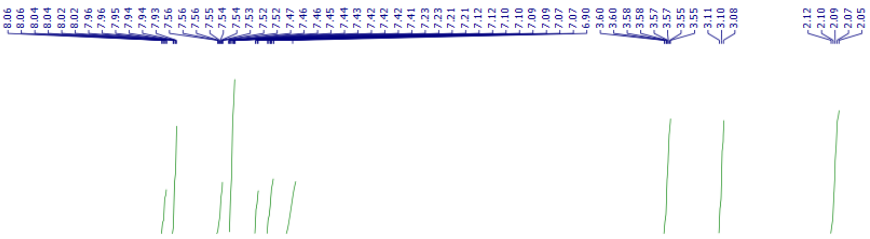


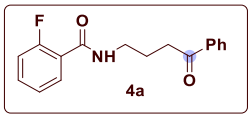
^{1}H NMR (400 MHz, $CDCl_3$) of 2af



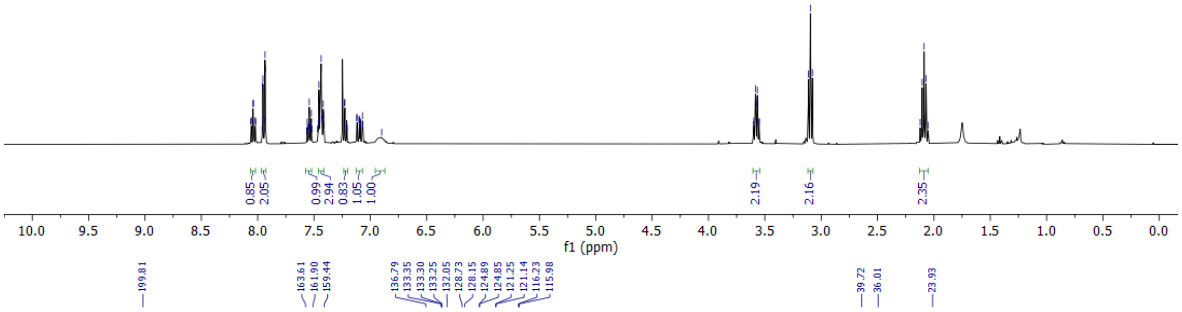
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2af



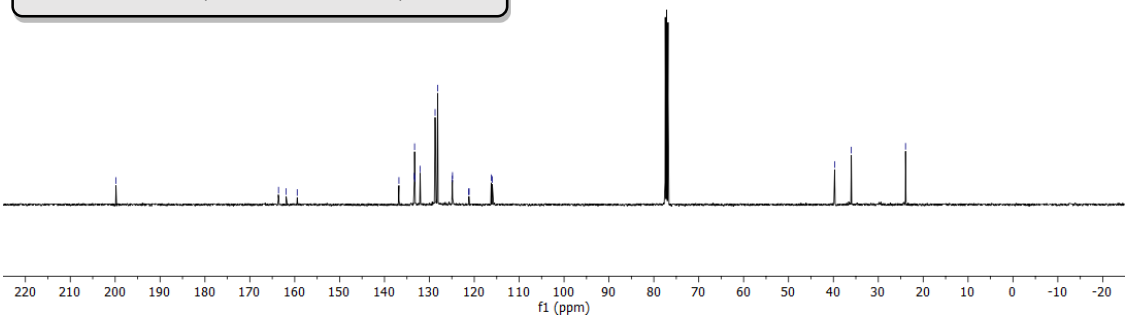




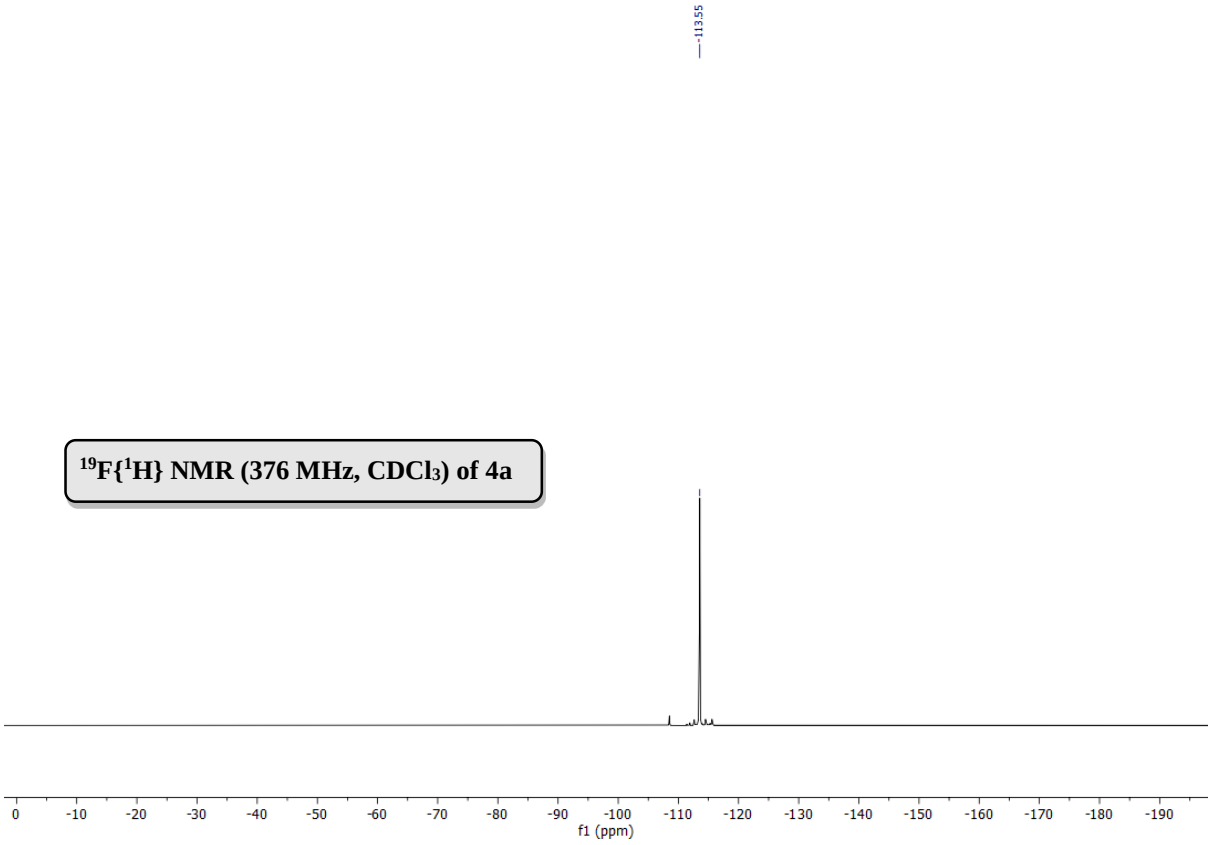
^{1}H NMR (400 MHz, $CDCl_3$) of 4a

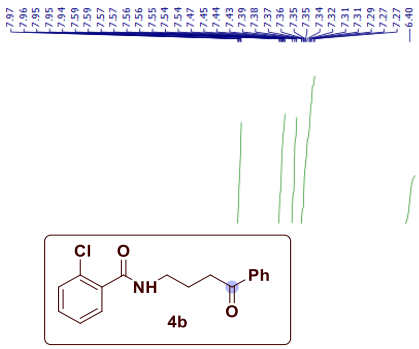


$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of 4a

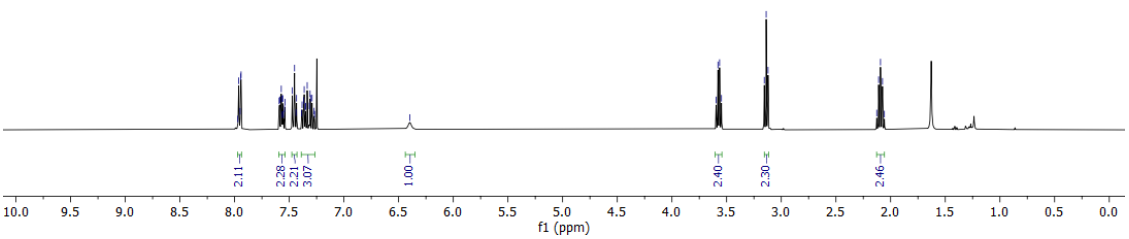


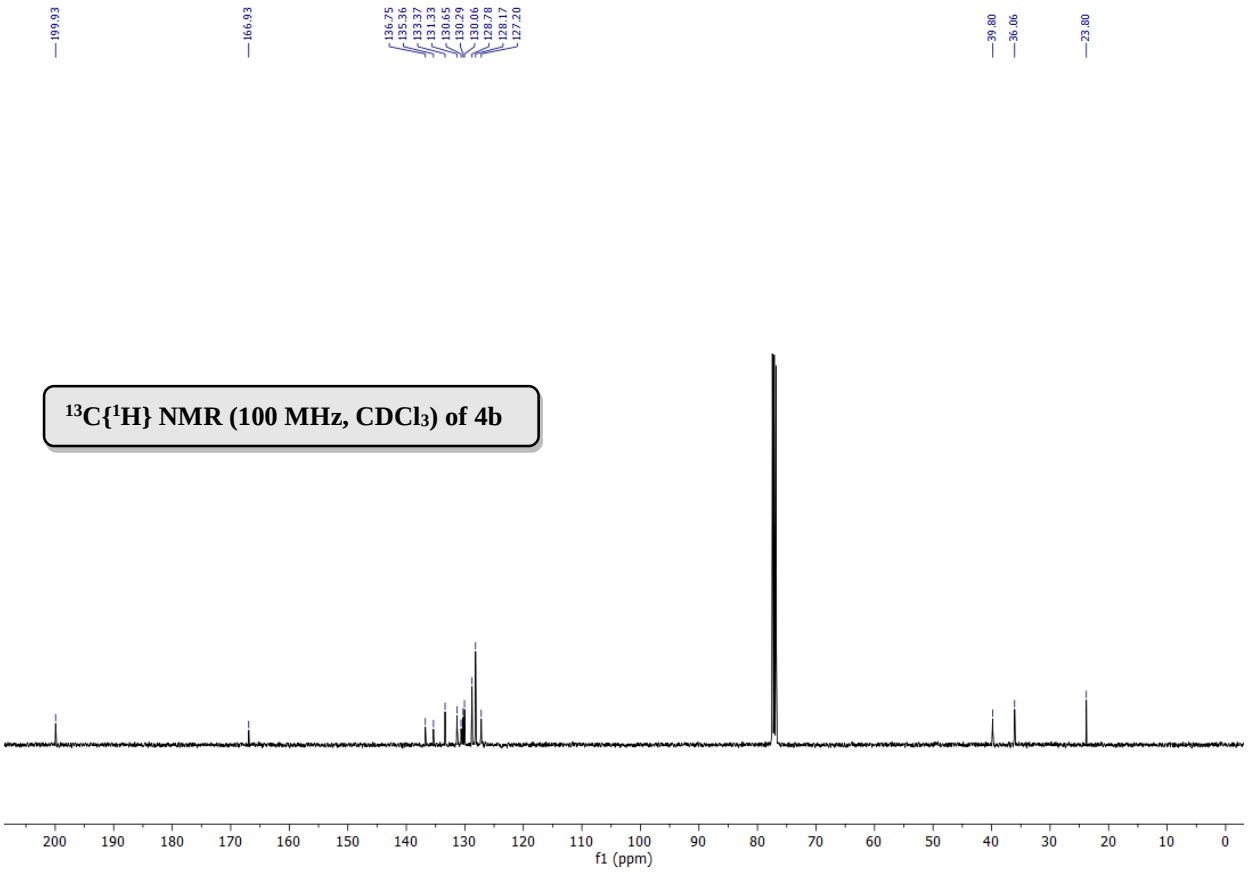
$^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) of 4a



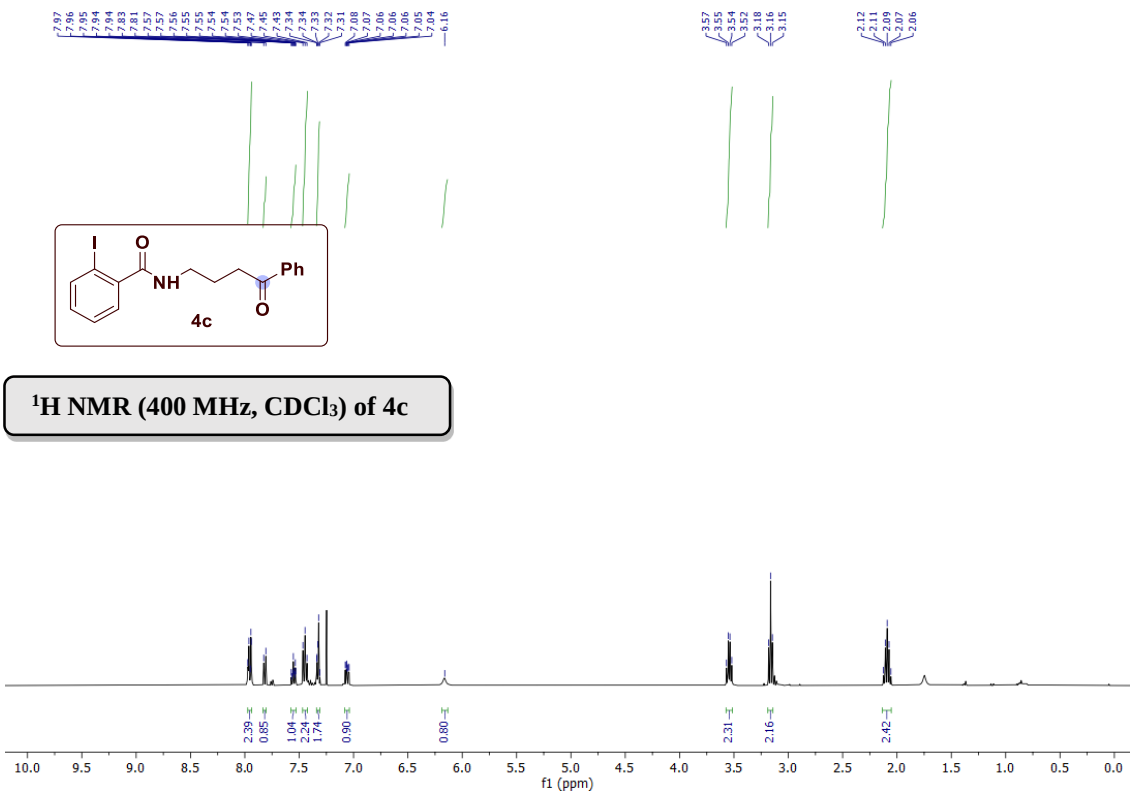


^{1}H NMR (400 MHz, $CDCl_3$) of 4b



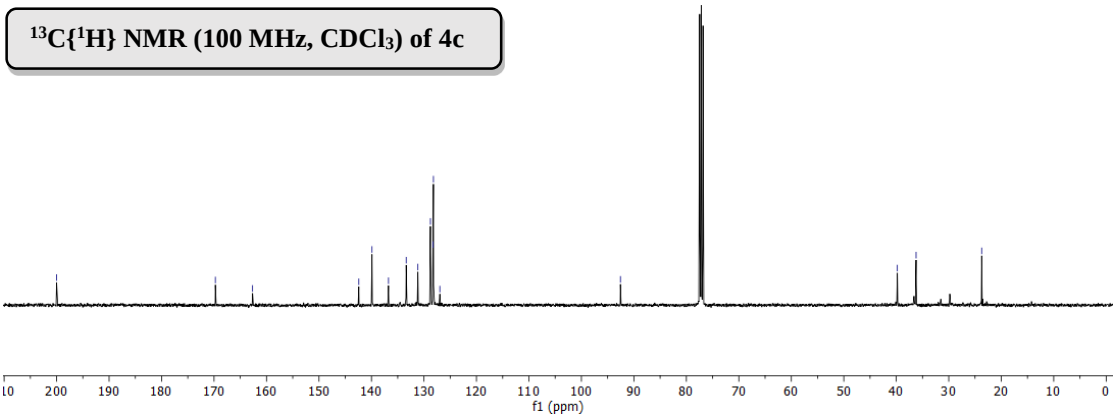


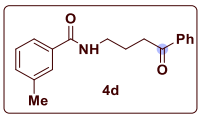
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of 4b



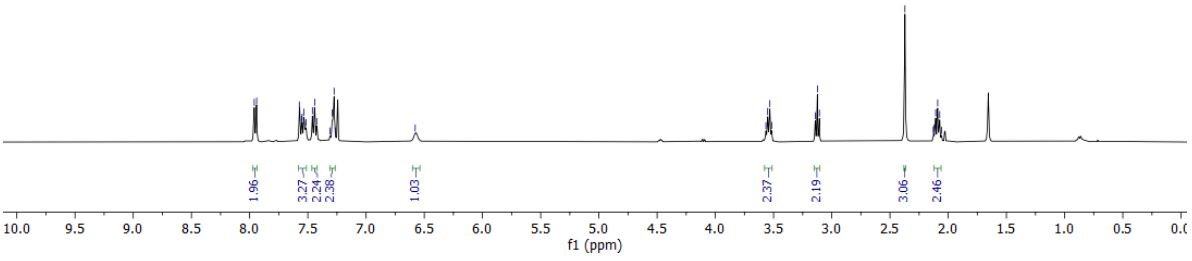
^{1}H NMR (400 MHz, $CDCl_3$) of 4c

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of 4c

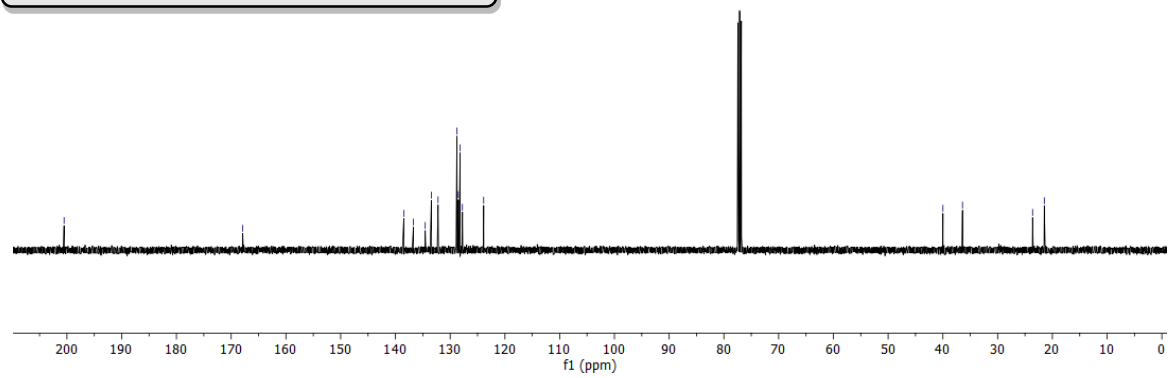


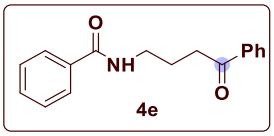


^{1}H NMR (400 MHz, $CDCl_3$) of 4d

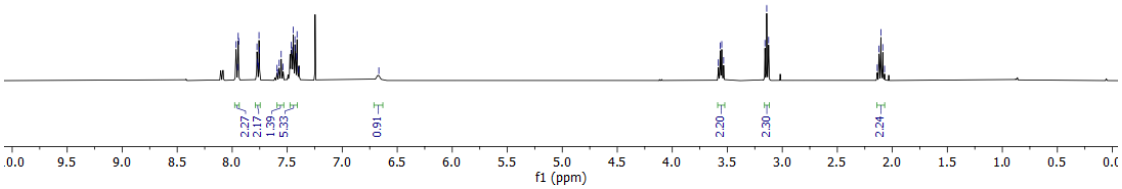


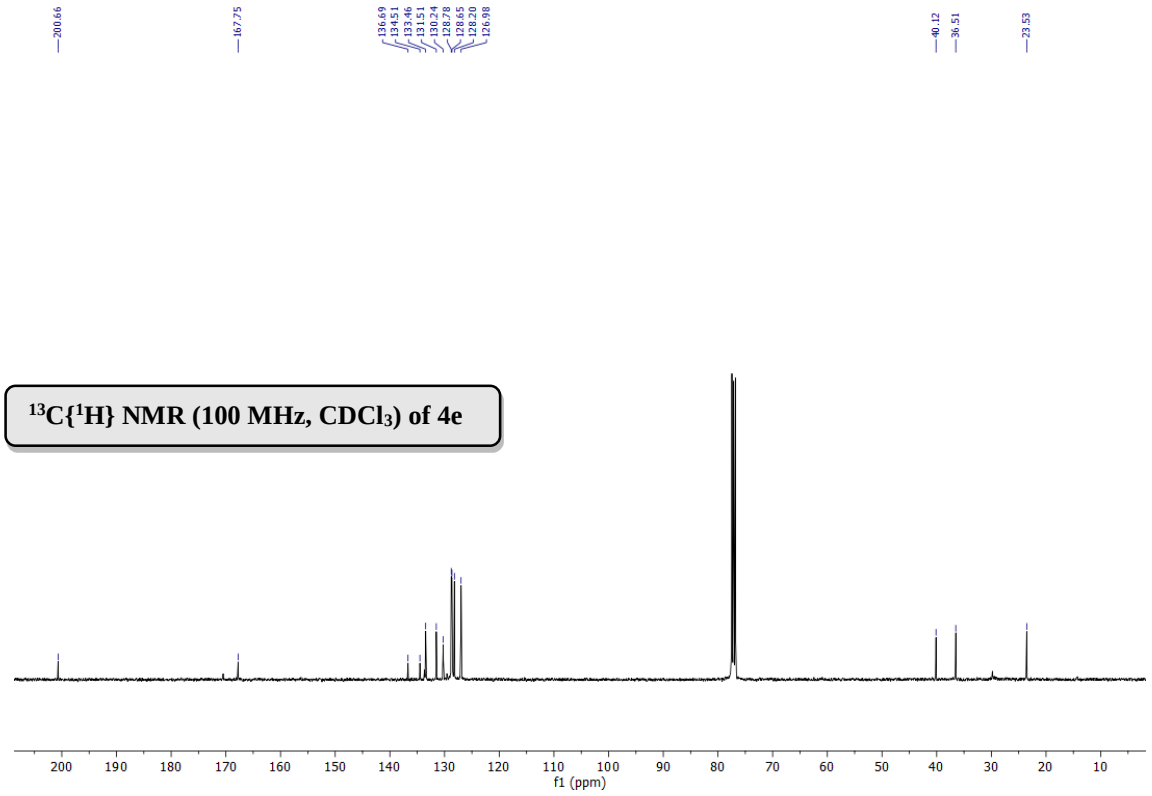
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of 4d



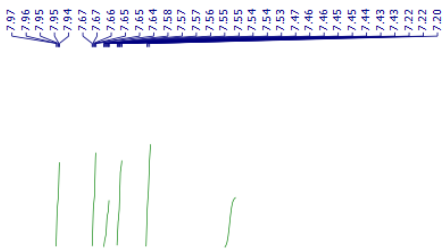


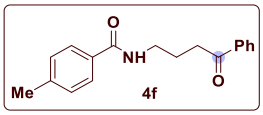
^{1}H NMR (400 MHz, $CDCl_3$) of 4e



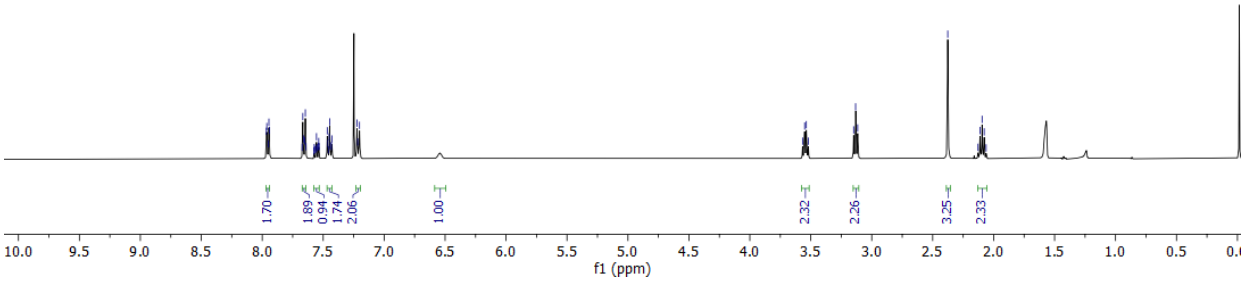


$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of 4e

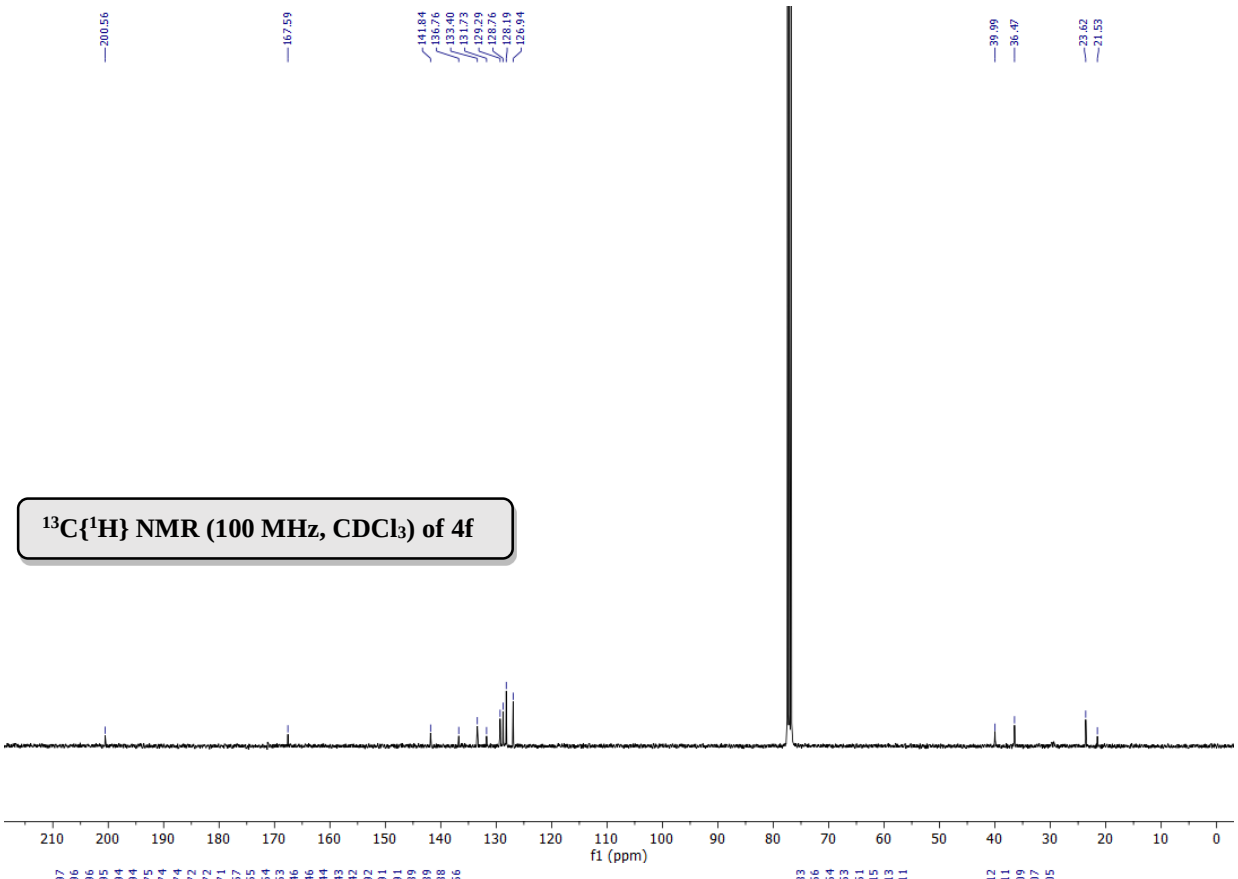


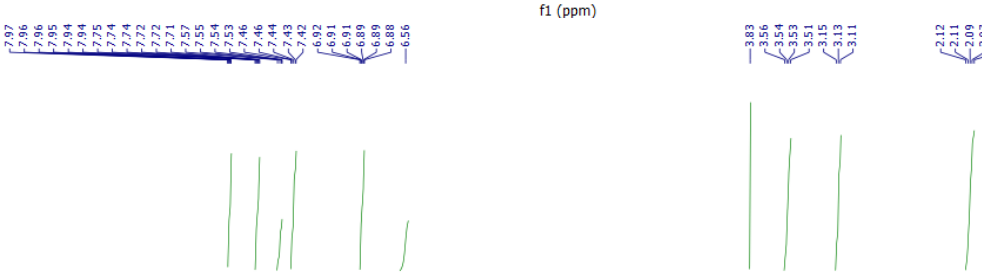


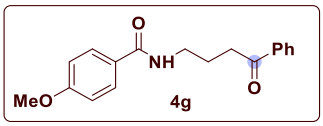
^{1}H NMR (400 MHz, $CDCl_3$) of 4f



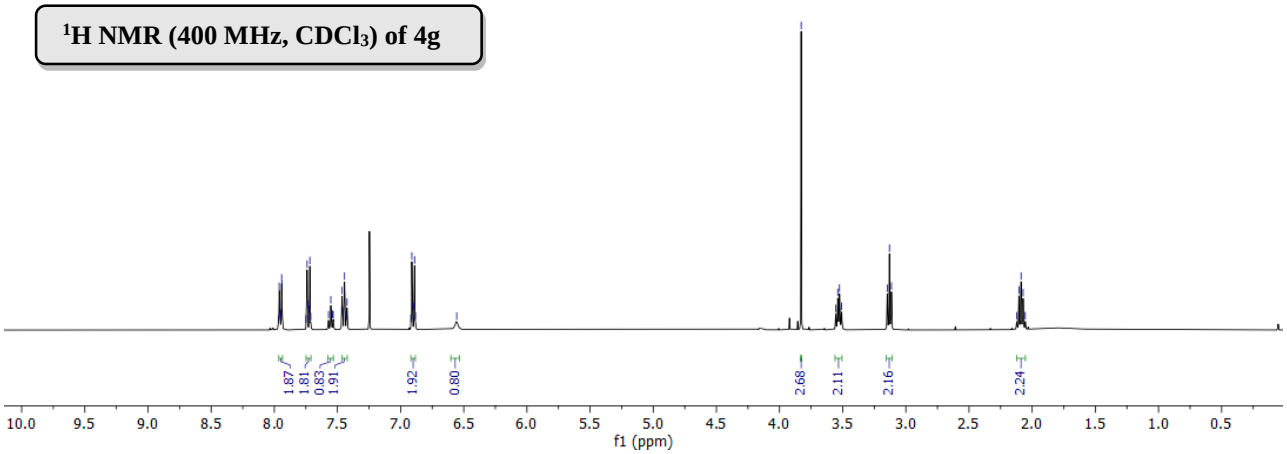
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of 4f

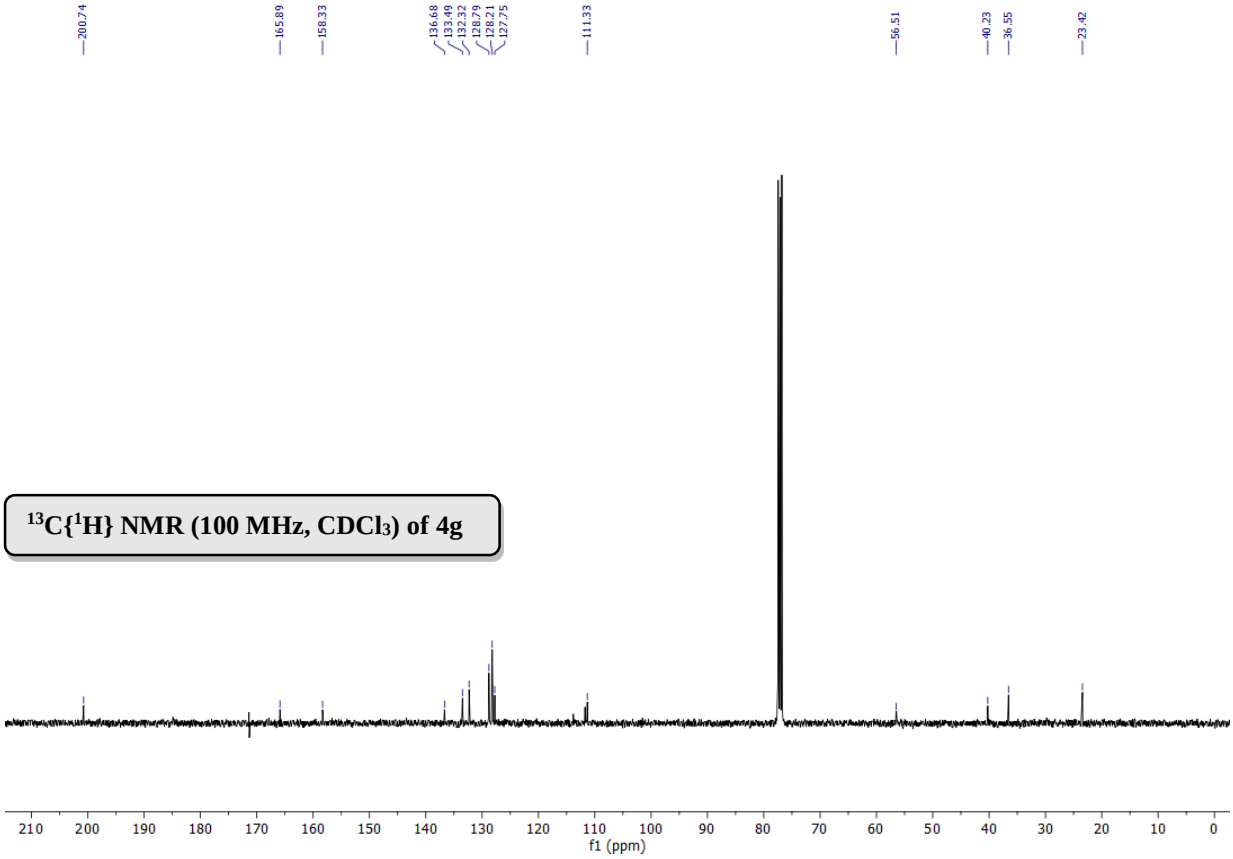




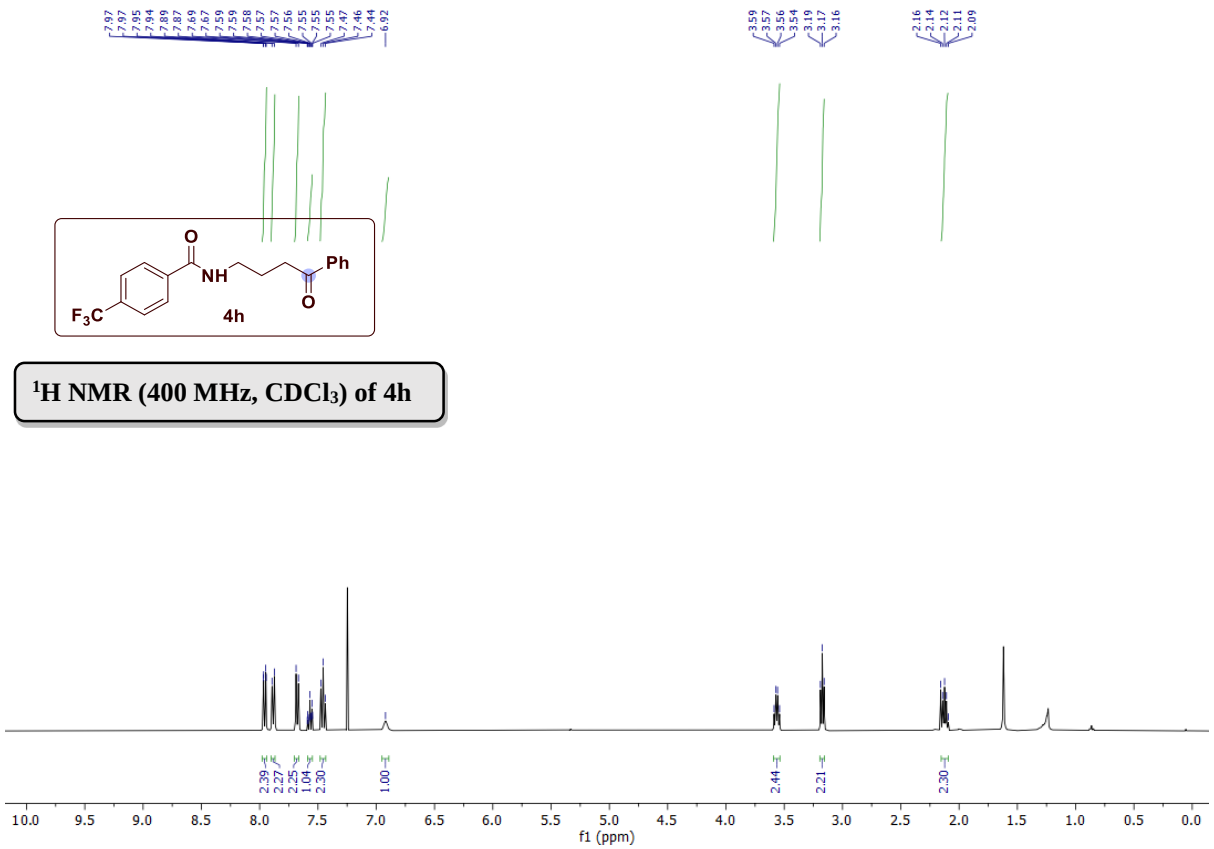


^{1}H NMR (400 MHz, $CDCl_3$) of 4g



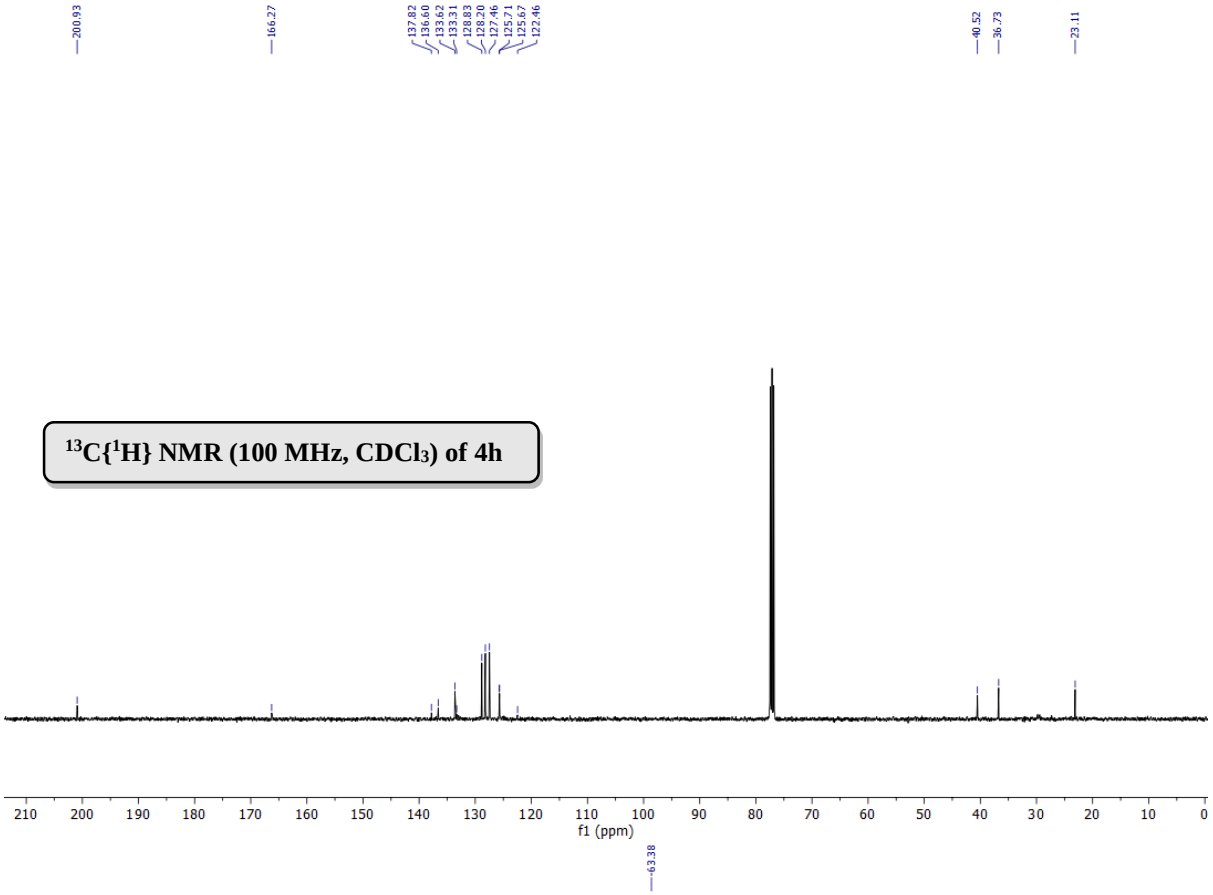


$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of 4g

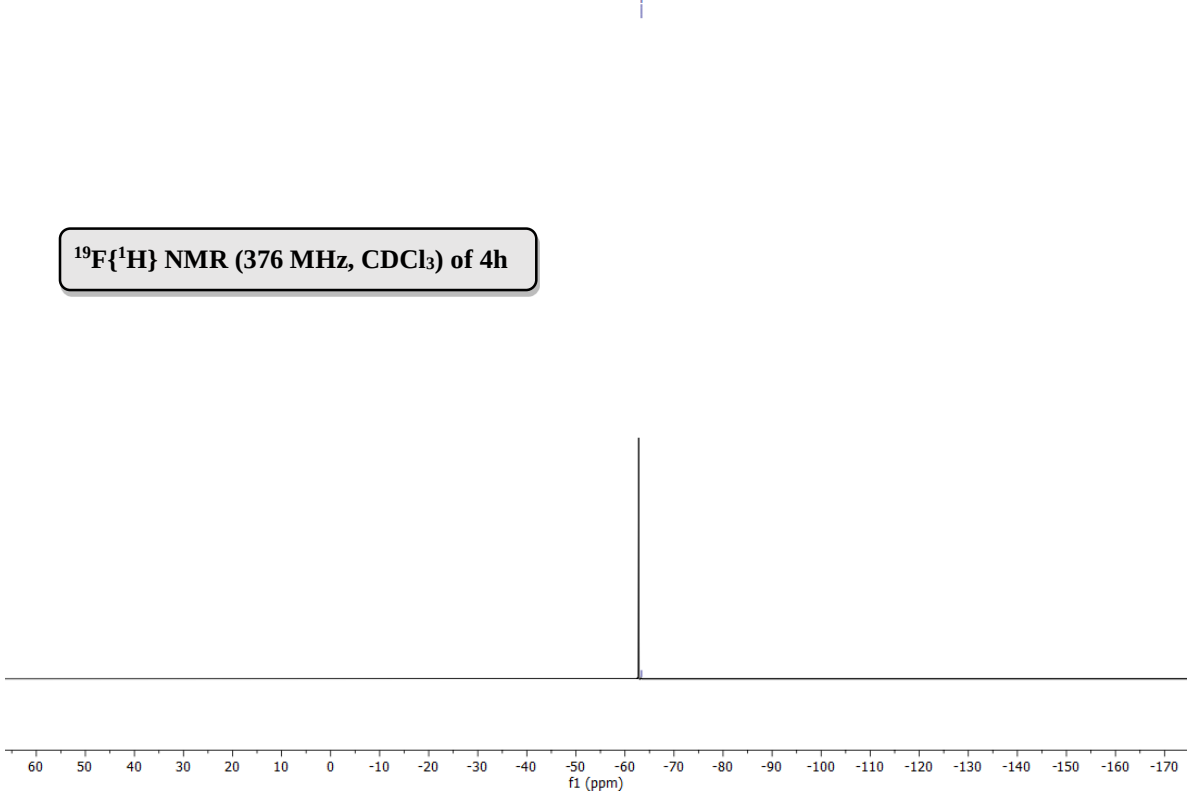


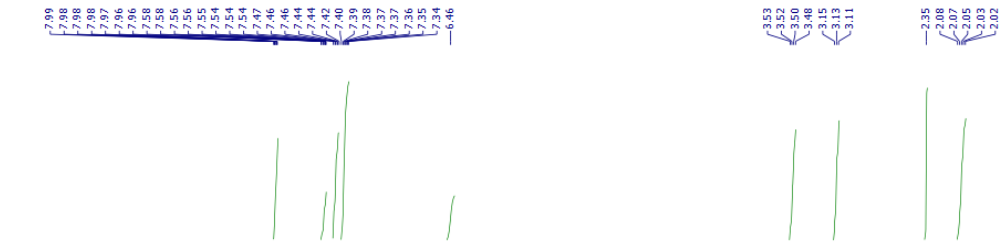
^{1}H NMR (400 MHz, $CDCl_3$) of 4h

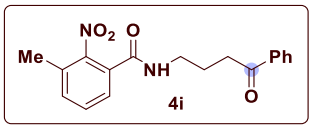
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of 4h



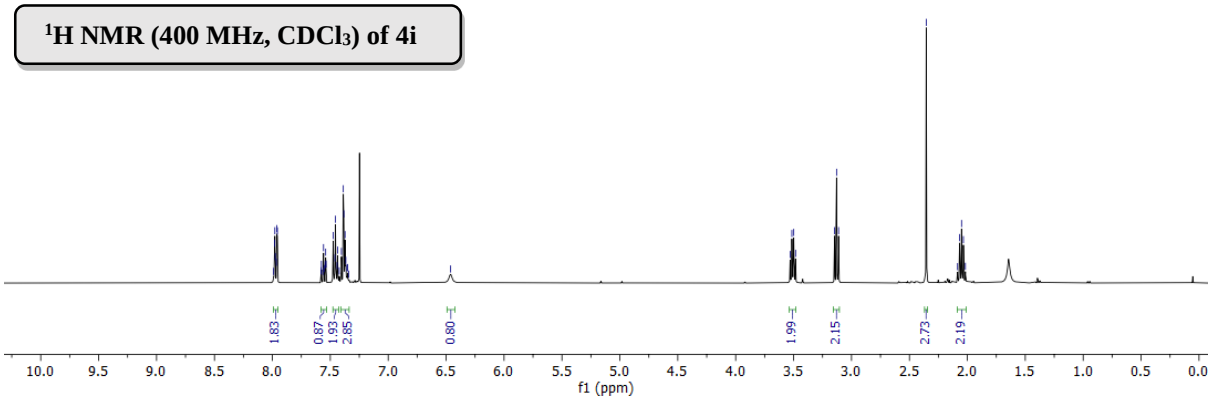
$^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) of 4h

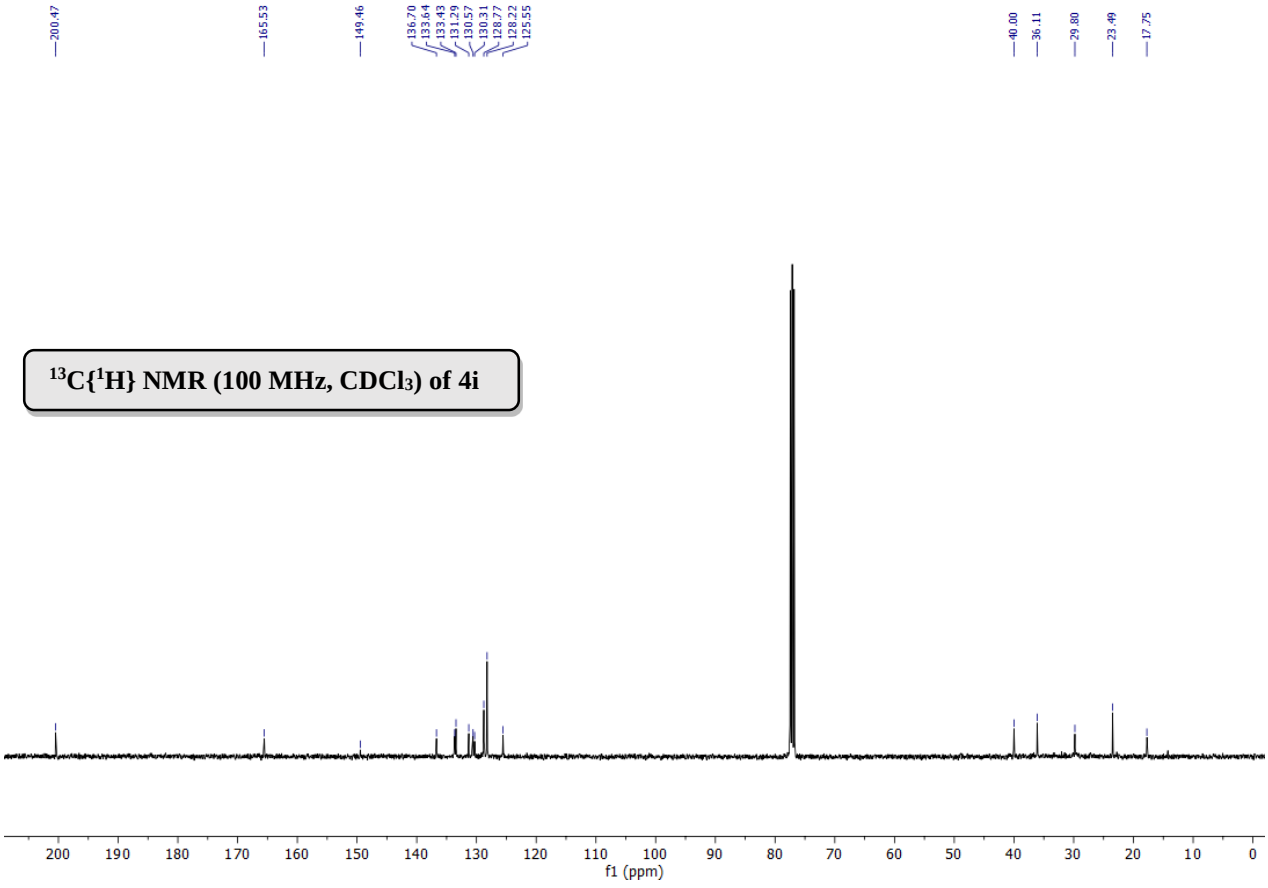




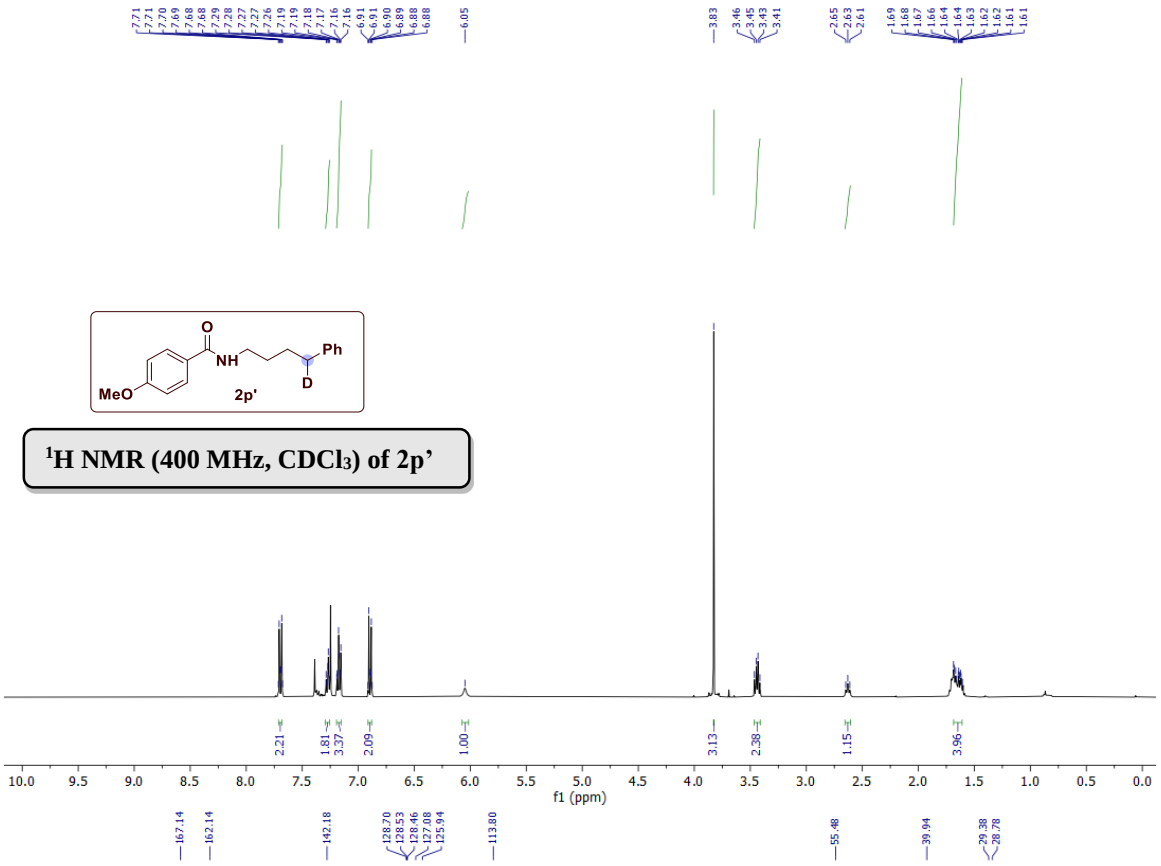


^{1}H NMR (400 MHz, $CDCl_3$) of 4i

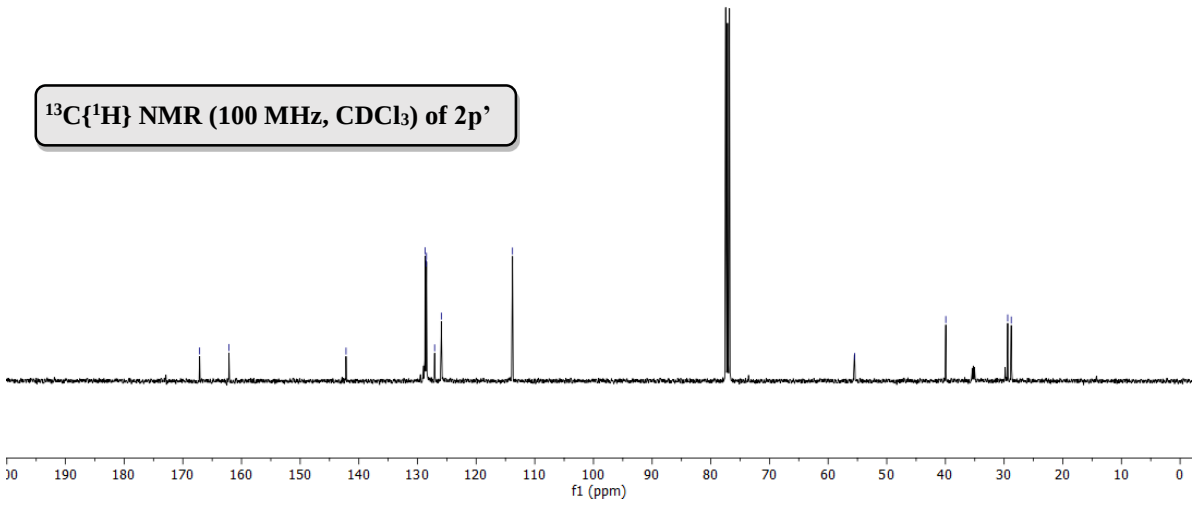




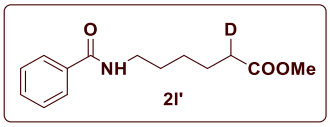
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 4i



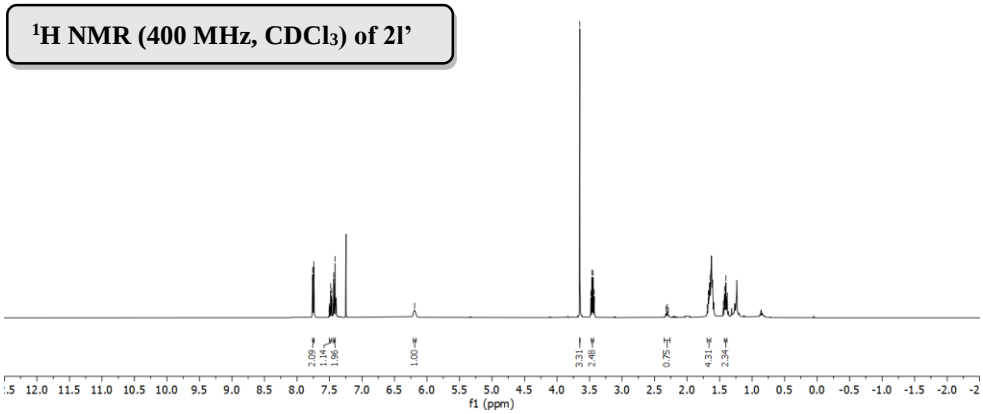
^{1}H NMR (400 MHz, $CDCl_3$) of 2p'

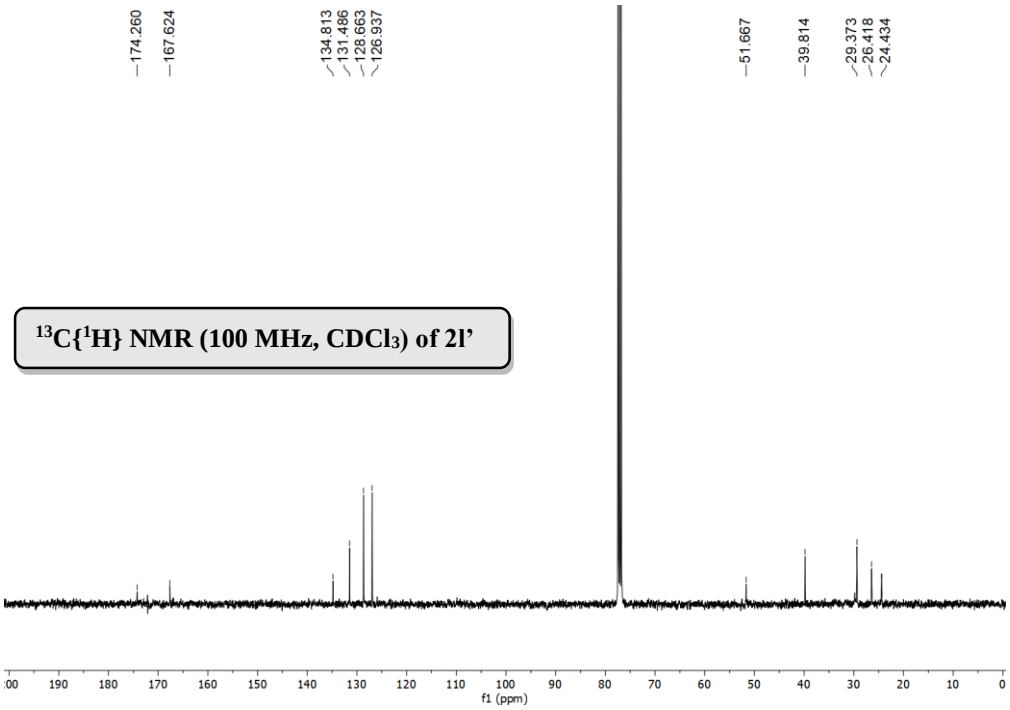


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2p'

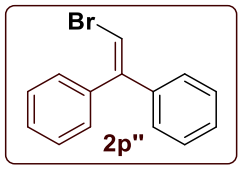


^{1}H NMR (400 MHz, $CDCl_3$) of 2l'

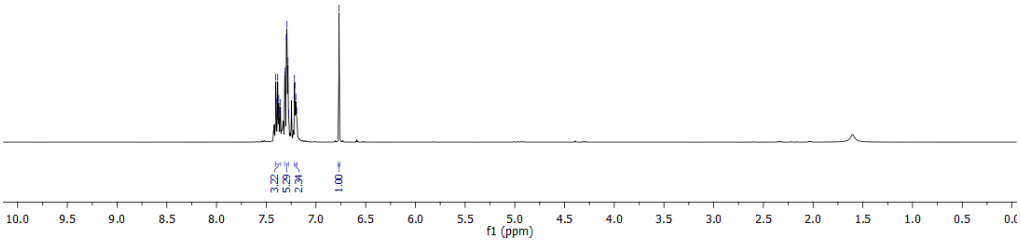




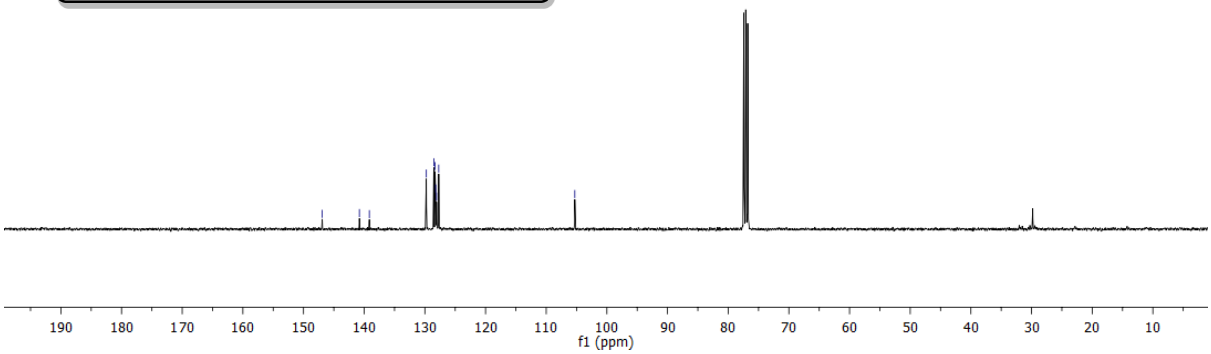
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2l'

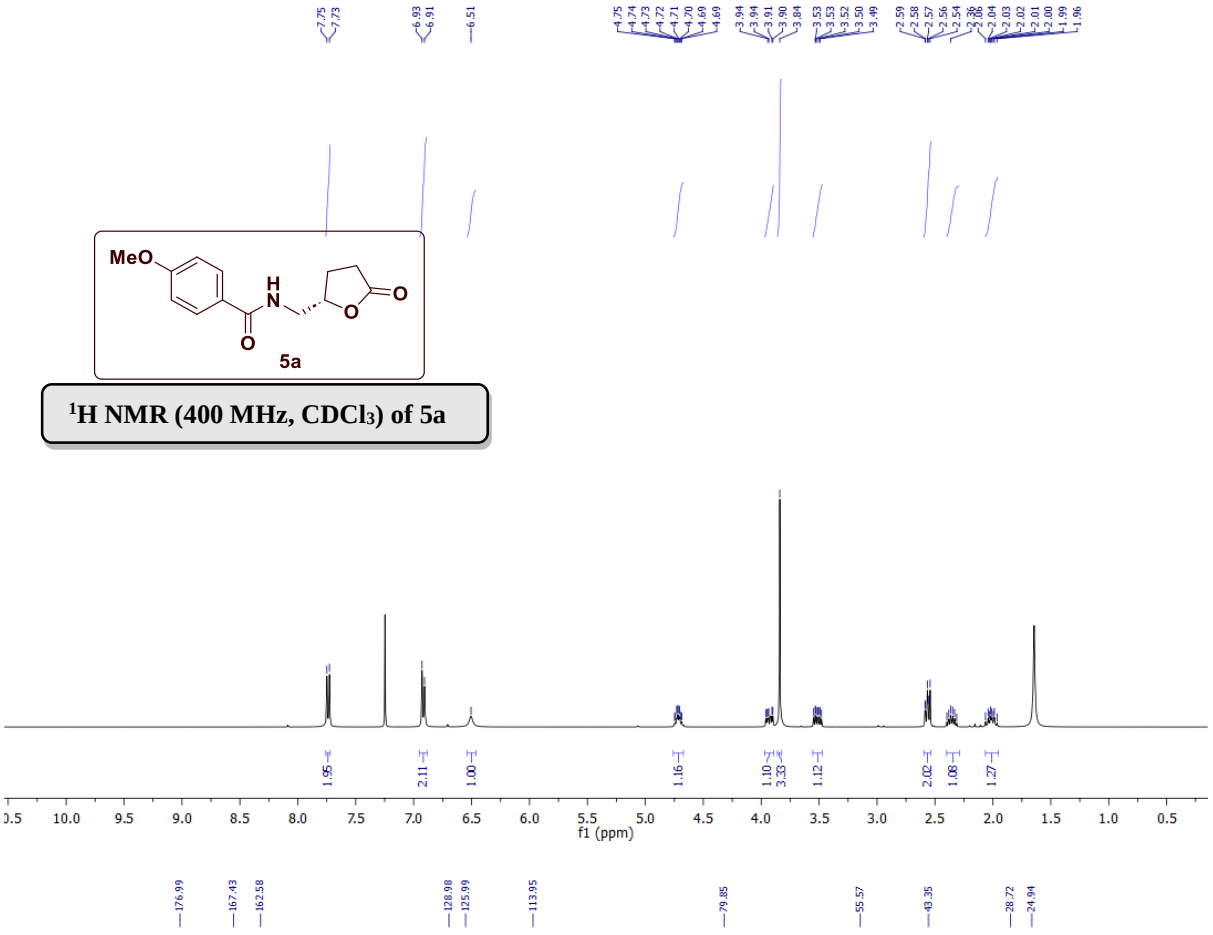


^{1}H NMR (400 MHz, $CDCl_3$) of 2p''

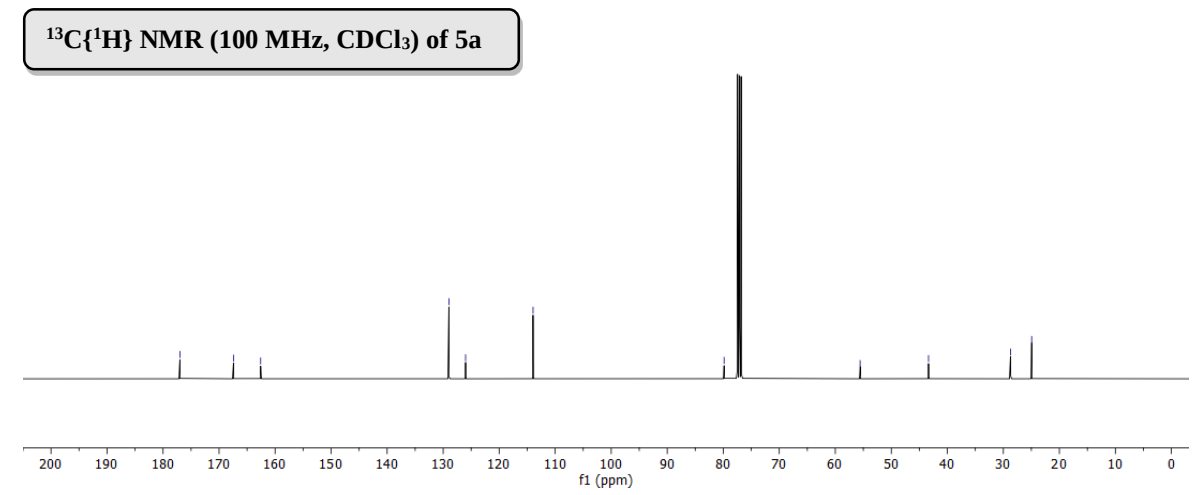


^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2p''

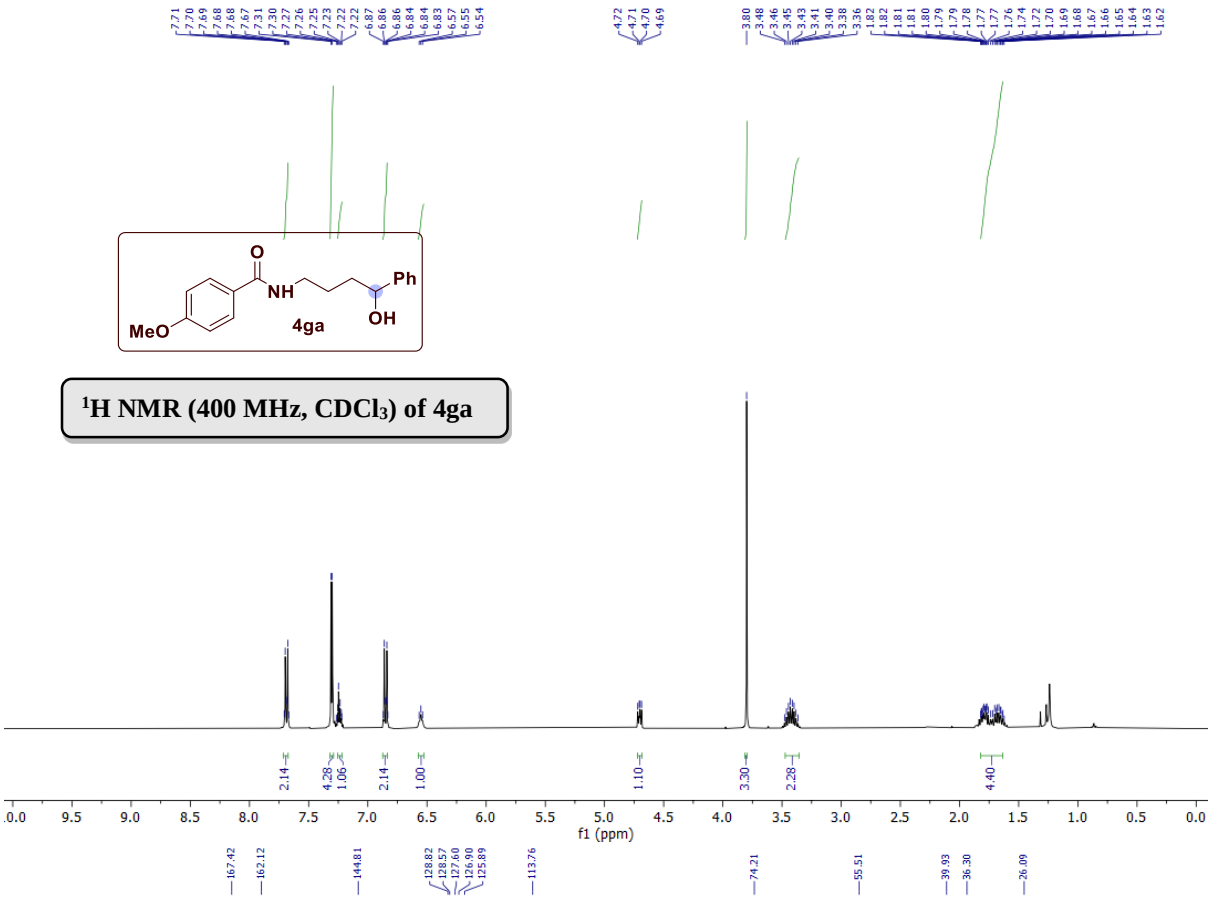




^{1}H NMR (400 MHz, $CDCl_3$) of 5a

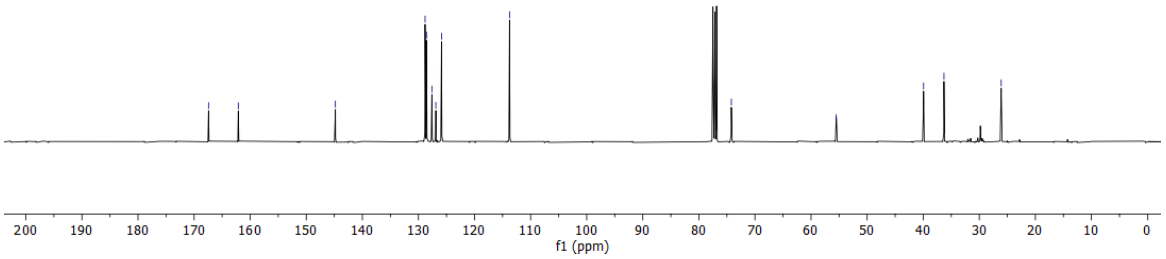


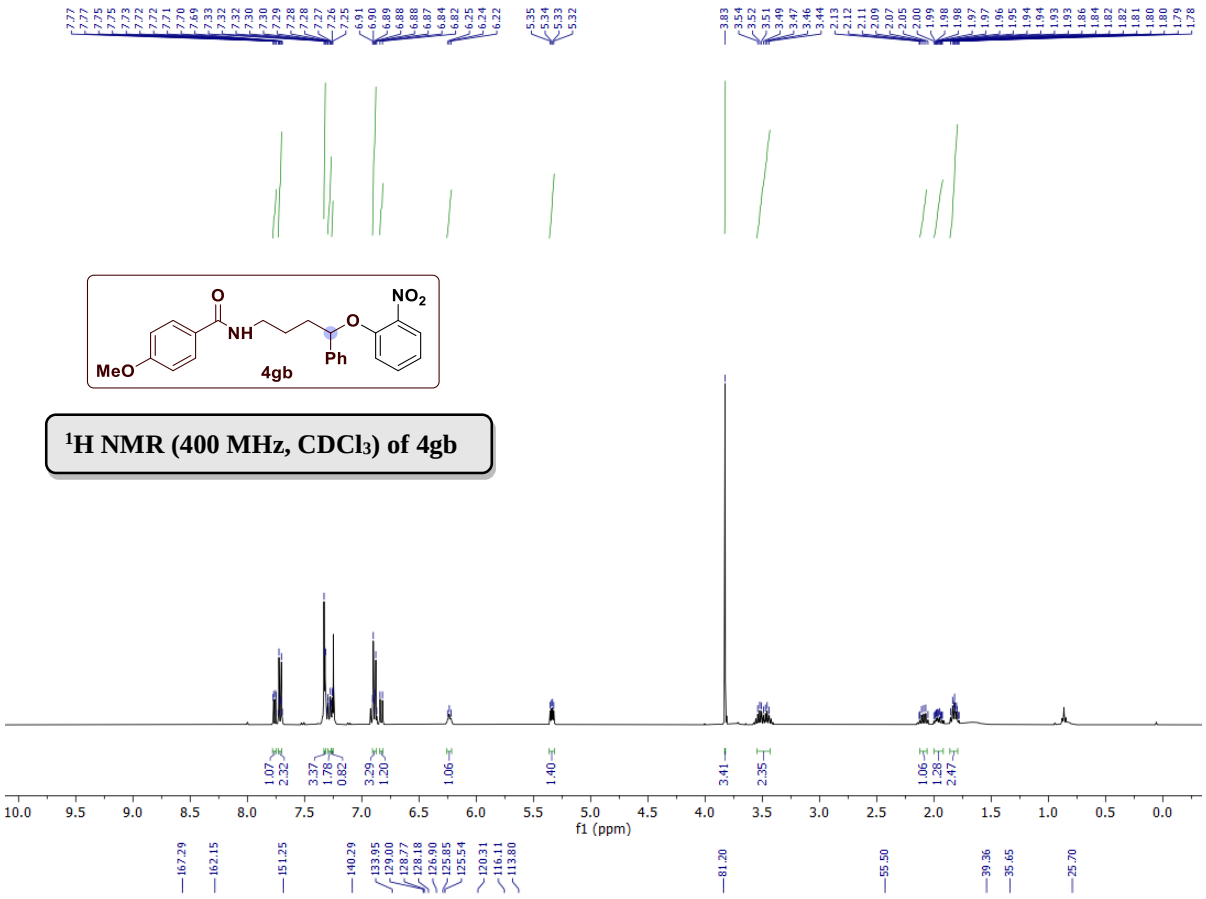
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of 5a



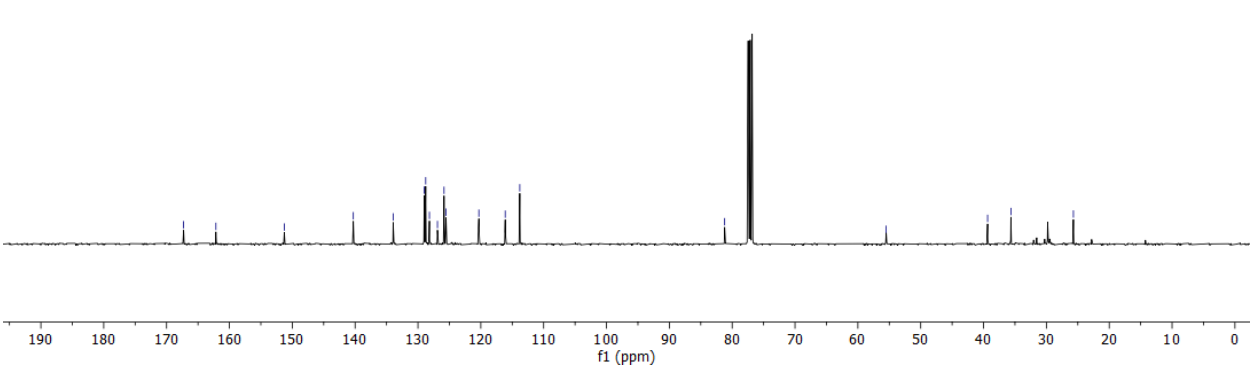
^{1}H NMR (400 MHz, $CDCl_3$) of 4ga

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 4ga

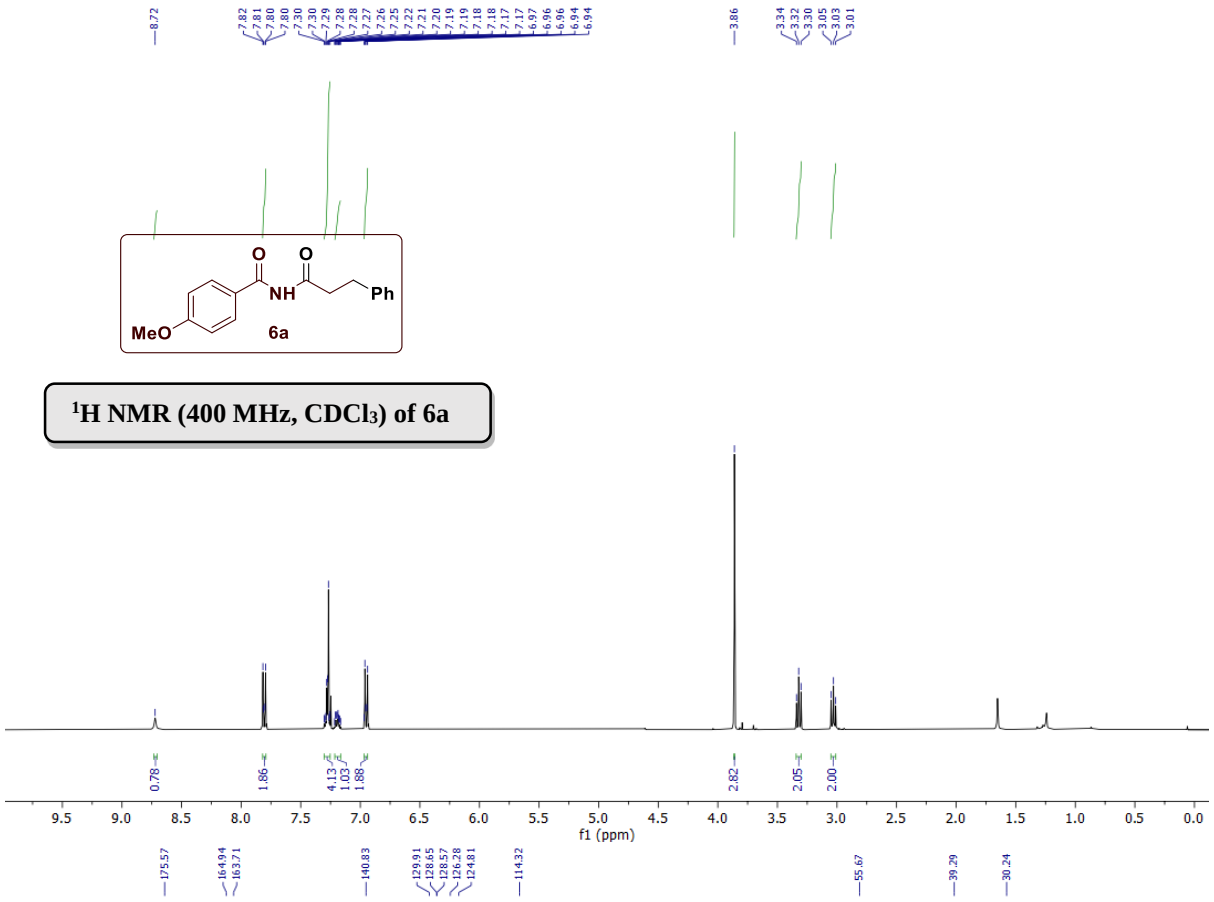




^{1}H NMR (400 MHz, $CDCl_3$) of 4gb

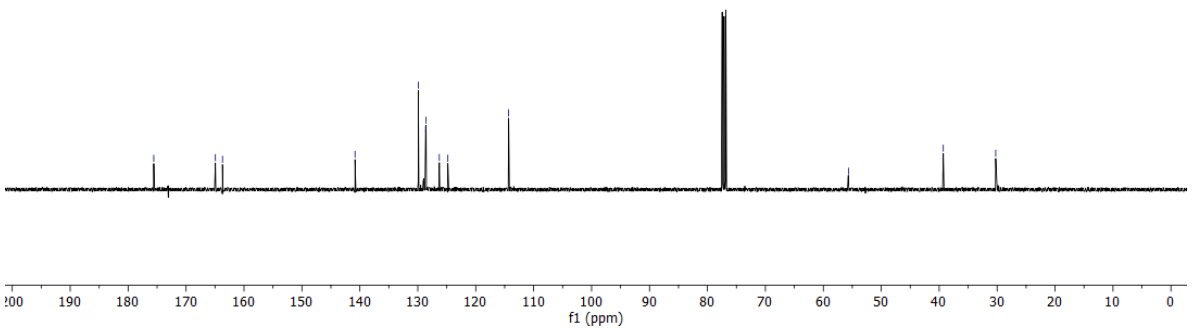


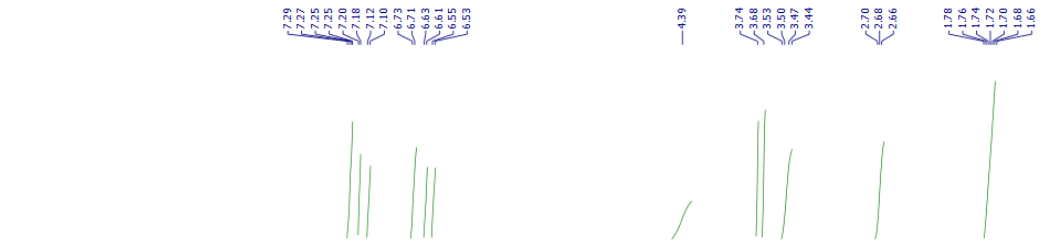
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of 4gb

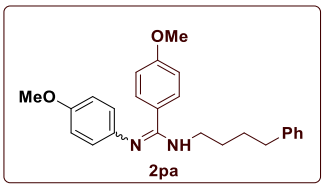


^{1}H NMR (400 MHz, $CDCl_3$) of 6a

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 6a

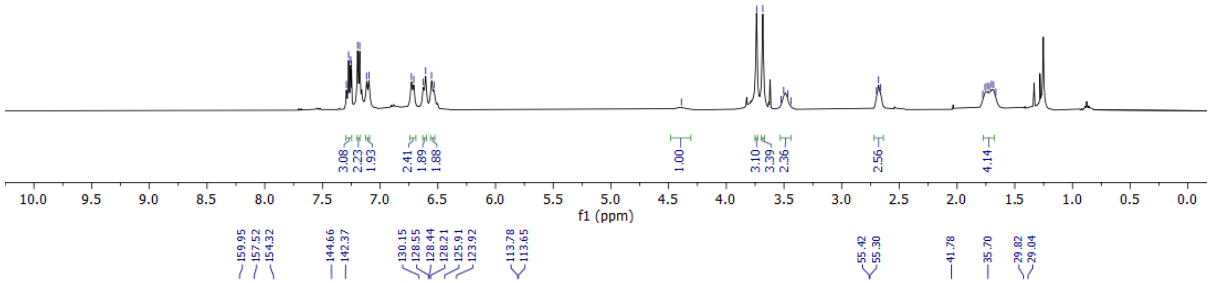




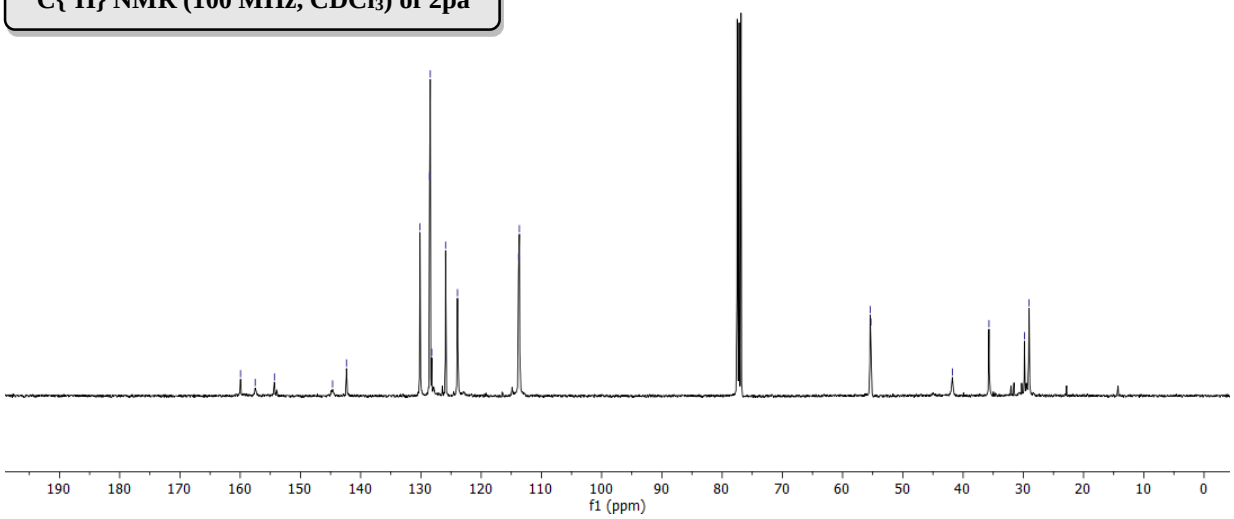


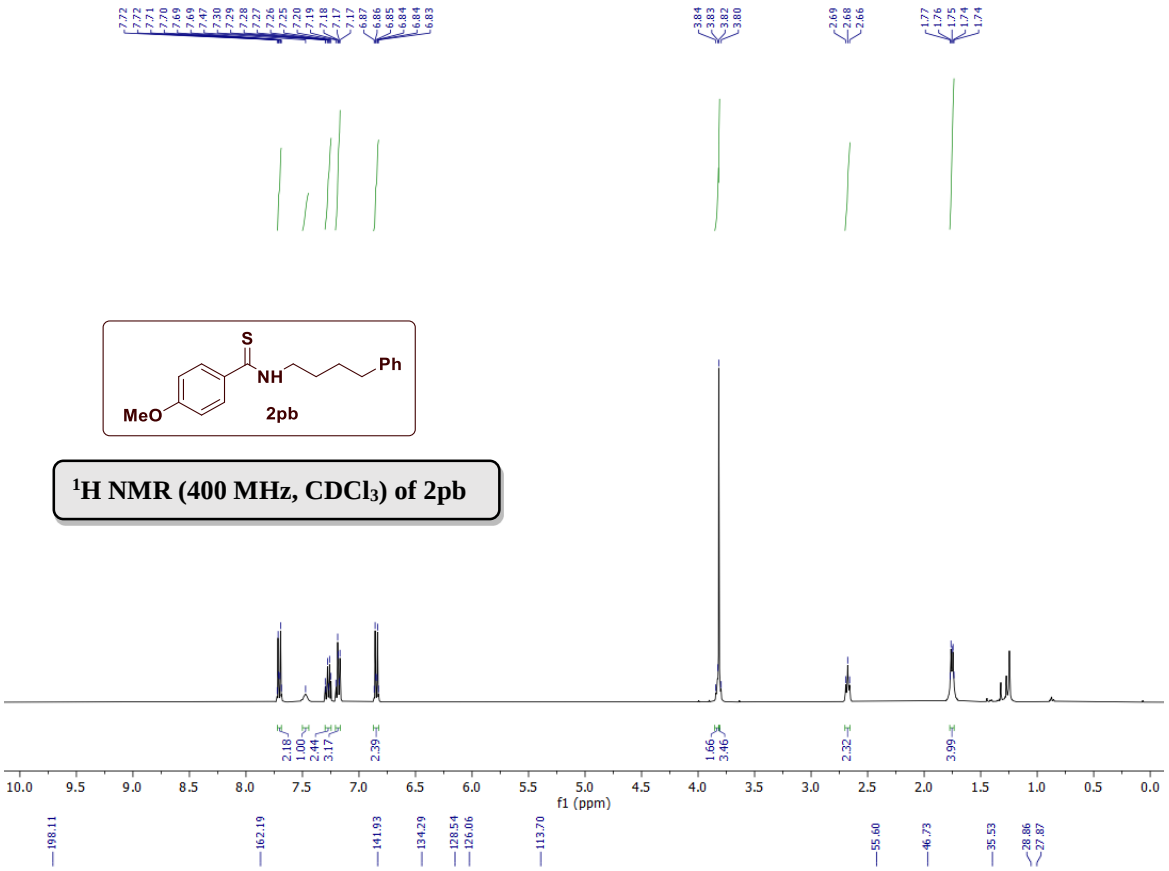
2pa

^{1}H NMR (400 MHz, $CDCl_3$) of 2pa



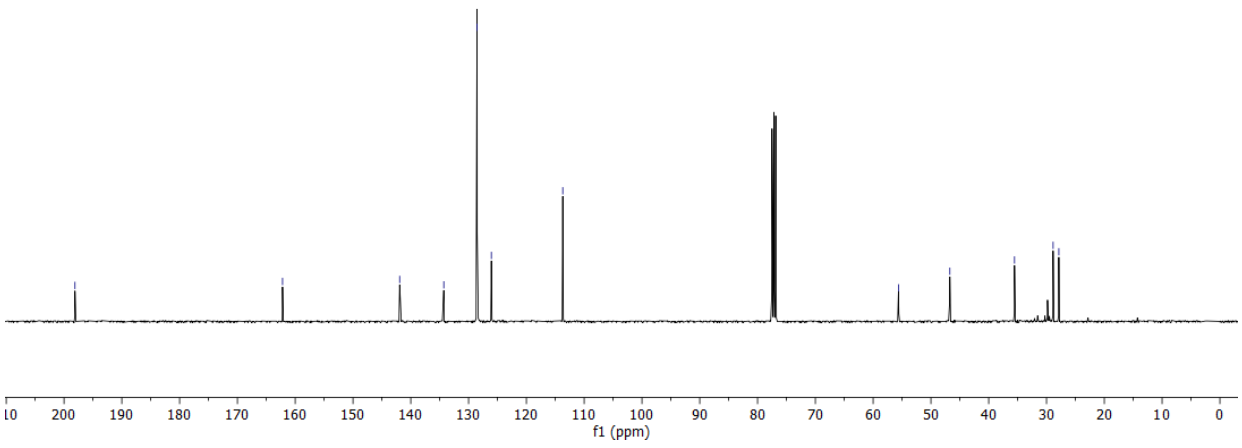
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2pa

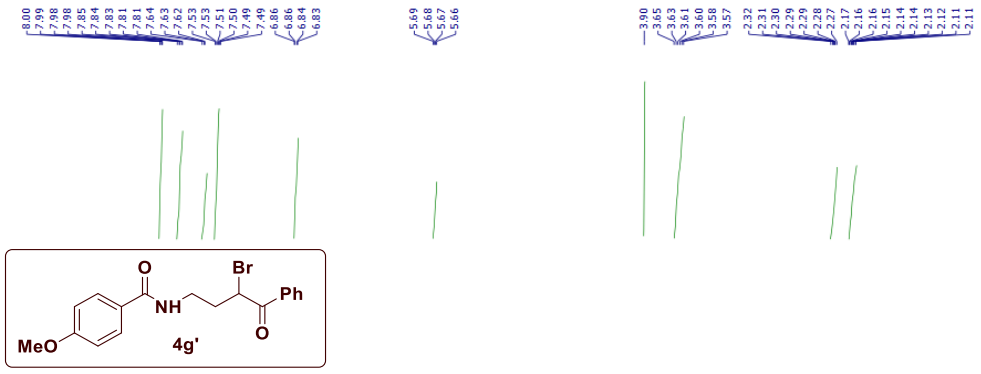




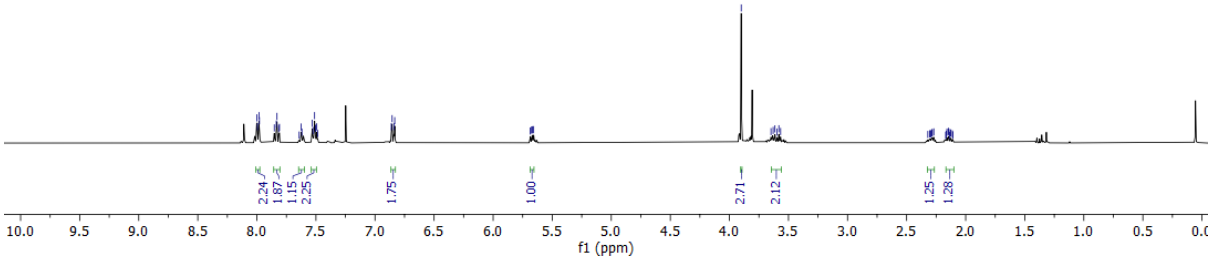
^{1}H NMR (400 MHz, $CDCl_3$) of 2pb

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 2pb

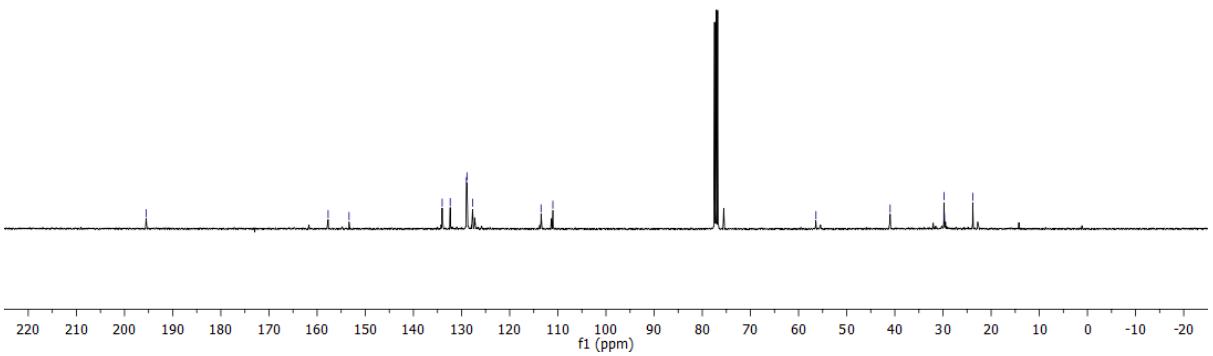




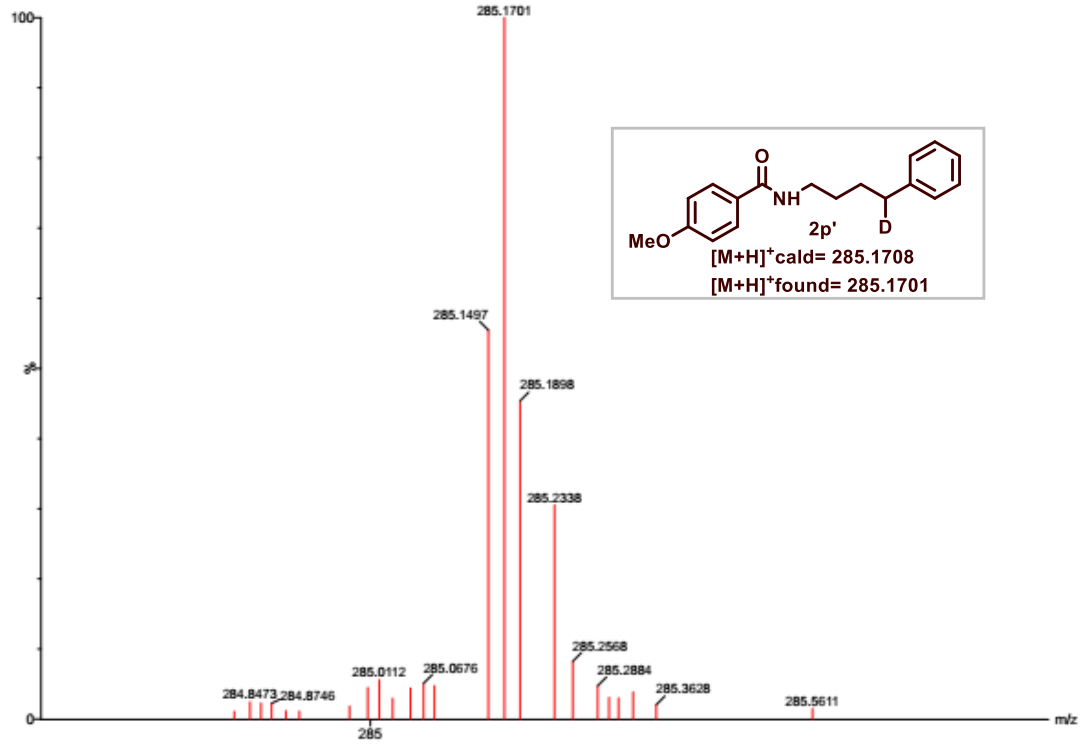
^{1}H NMR (400 MHz, $CDCl_3$) of 4g'



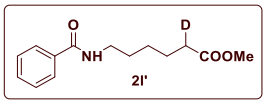
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of 4g'



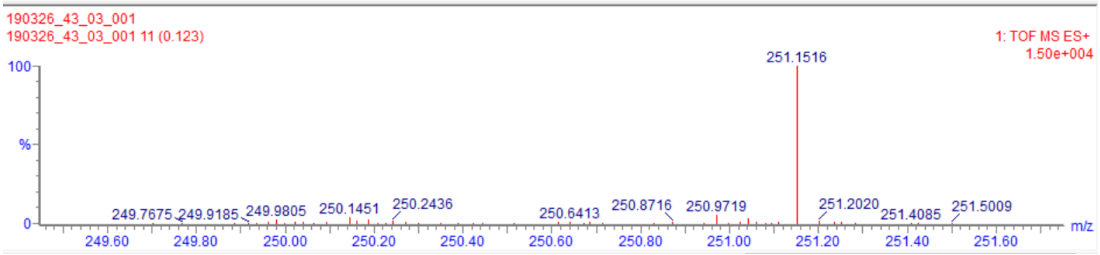
➢ **HRMS** of intermediates **2p', 2l', 2a' and 2p''**

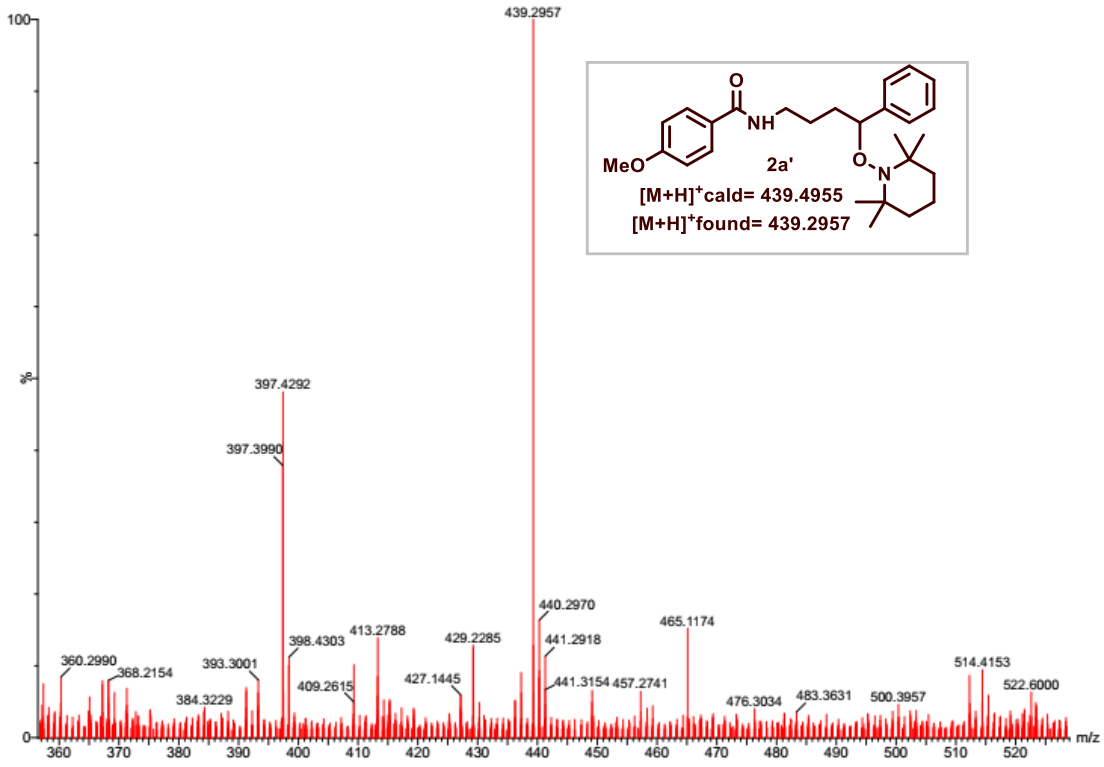


Single Mass Analysis
Tolerance = 100.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
7 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:



Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	N	O	2H	1H
251.1516	251.1506	1.0	4.0	5.5	C14 N O3 2H 1H19	83.8	n/a	n/a	14	1	3	1	19





Single Mass Analysis

Tolerance = 100.0 PPM / DBE: min = -1.5, max = 50.0

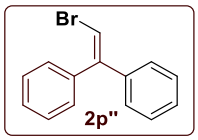
Element prediction: Off

Number of isotope peaks used for i-FIT = 3

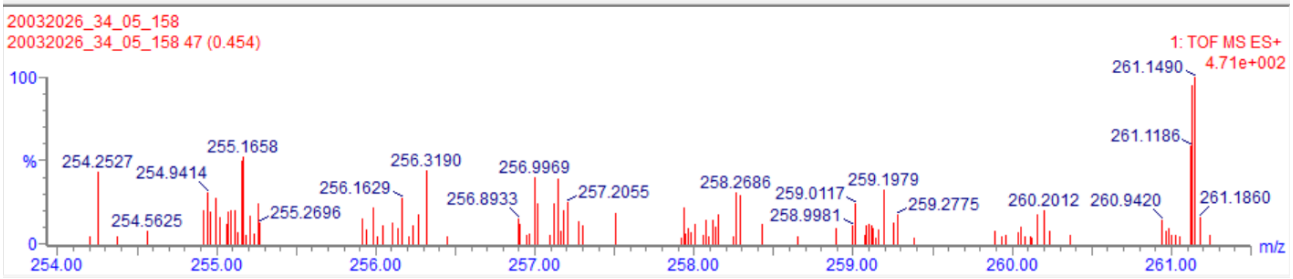
Monoisotopic Mass, Even Electron Ions

2 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:



Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	Br
259.0117	259.0122	-0.5	-1.9	8.5	C14 H12 Br	264.7	n/a	n/a	14	12	1



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