

Manganese catalyzed oxidative deamination of benzyl amines with water

6.1. History, Background and Objective

Amines play a crucial role as structural motifs in a wide array of biomolecules and pharmaceuticals.³³⁹ In recent decades, considerable focus has been placed on the synthesis of amines through the amination of alcohols or ketones.^{84,340–349} Nevertheless, the reverse process – the deamination of primary amines – has long been acknowledged as a critical but synthetically demanding transformation. Despite its importance, developing efficient and selective methods for deaminating primary amines has remained a persistent challenge in synthetic chemistry.^{350–352}

The deamination reaction is a highly valuable transformation for generating a range of important intermediates, such as carbonyl compounds, acids, imines, and amides, which are critical in synthetic chemistry and the production of bioactive molecules.³³⁹ However, despite its significant potential, deamination remains an underexplored area of chemistry, often regarded as synthetically challenging due to the inherent difficulty in selectively removing amine groups under mild conditions.^{350–352}

Traditional methods for amine oxidation typically rely on stoichiometric amounts of strong and often hazardous oxidants, such as potassium permanganate or chromium-based reagents like dichromate.^{353–356} While effective, these approaches have several limitations, including poor chemoselectivity, the generation of unwanted side products, and a narrow tolerance for functional groups. Additionally, the use of such oxidants often requires harsh reaction conditions, which can be detrimental to the overall selectivity and efficiency of the process. These challenges have made the development of milder and more selective deamination methods a key area of interest in synthetic chemistry.^{357,358}

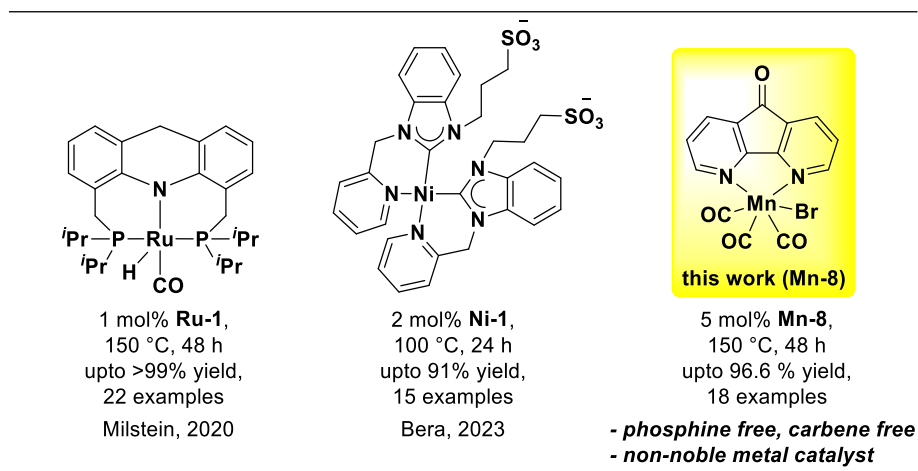


Figure 6.1. Selected examples of complexes for amine deamination to acid.

One notable example of overcoming these challenges is Corey's development of a transamination strategy, which enabled the deaminative synthesis of prostaglandin E1.^{359,360} This approach represented a significant advancement in the field, though it still involved some of the limitations inherent in traditional methods. In parallel, enzymatic oxidative deamination has emerged as an attractive alternative. Enzymes such as amine dehydrogenases (ADHs) and copper amine oxidases (CuAOs) can catalyze the oxidation of primary amines, converting them into aldehydes with high selectivity. These biocatalysts operate under mild conditions, offering a more

In recent years, biomimetic catalysis has garnered significant attention as a promising strategy for amine oxidation. This approach, which mimics the natural enzymatic processes, involves the use of synthetic catalysts that promote the aerobic oxidation of amines.³⁶⁹⁻³⁷³ These catalysts typically function under more controlled conditions, with improved selectivity and fewer side reactions, making them an attractive alternative to conventional oxidative methods. Aerobic oxidation, in particular, offers several advantages, including the use of molecular oxygen as a green oxidant, which reduces the need for hazardous reagents and makes the process more environmentally friendly.

Ortho-naphthoquinone-catalyzed (O-NQ) deamination under aerobic circumstances has been demonstrated by the Oh group.³⁷⁴ On the other hand, Milstein has used water and an acridine-based PNP-Ru catalyst to accomplish oxidative deamination.³⁷⁵ Furthermore, recently, Bera's group have demonstrated a water-soluble Ni-based carbene for amine deamination under water.³⁷⁶

In recent years, significant attempts have been made to develop metal-catalyzed oxidation techniques utilizing water as a potential oxidant.³⁷⁷ Milstein,³⁷⁸ Grützmacher,^{379,380} Prechtel,³⁸¹ and others³⁸²⁻³⁸⁶ have demonstrated the oxidation of alcohol to its analogous acid salt by the "aldehyde-water shift" (AWS) procedure using a basic media.³⁸⁷⁻³⁹¹ Additionally, Milstein have demonstrated an extended version of water oxidation for amine to lactam³⁹² and olefin to carbonyl.³⁹³ Alongside, Beller³⁹⁴⁻³⁹⁶ and Grützmacher³⁹⁷ independently demonstrated methanol and water solution for H₂ production. Furthermore, Nicewicz also designed photoredox catalytic system for water utilization as oxygen source in ketones synthesis via homobenzylic oxygenation reaction.³⁹⁸

In the catalytic synthesis of organic molecules with water as oxidant are exceptionally rare. Nevertheless, they offer some of the most atom-efficient and environmentally benign protocols for chemo-selective oxidation of organic compounds.^{378,388,389,392,393,397,399-401} Milstein in 2016, demonstrated Ru catalyst for selective oxidation of alcohol moiety in amino alcohols.³⁹⁹

6.2. Results and Discussion

Table 6.1. Catalyst screening for catalytic oxidative deamination of amines to carboxylates.^a

Mn-1	Mn-2	Mn-4	Mn-5	Mn-8	Mn-9
trace	trace	trace	6%	97%	trace
Mn-10	Mn-11	Mn-12	Mn(CO) ₅ Br	MnBr ₂	
trace	10%	trace	trace	trace	

^aReaction conditions unless otherwise specified: 0.5 mmol of primary amine, 5 mol% of catalyst **Mn** catalyst, H₂O (1mL) and 1,4-dioxane (1 mL) were heated at 150 °C for 48 h. Isolated yield.

We were inspired from our recent publication on Cr catalysed acceptorless dehydrogenation of primary amine to imines.⁴⁰² As this catalyst wasn't active for oxidative deamination we intended

to explore a related manganese complex bearing dizafluorenone ligand. Herein we report a first example on non-pincer, phosphine free Manganese complex **Mn-8** (Figure 6.1), which was found to be active in the oxidative deamination of primary amine derivative to acid. A plausible mechanism for the amines to acid conversion is proposed based on mechanistic investigations.

Table 6.2. Optimization of the reaction parameter for catalytic oxidative deamination of amines to carboxylates.^a

c1ccccc1CN (1a) $\xrightarrow[\text{base (1.1 equiv.), solvent (2 mL), temp., time, -H}_2, \text{-NH}_3]{\text{catalyst (5 mol \%)}}$ c1ccccc1C(=O)O (2a)

Entry	Catalyst	Solvent (1:1)	Base	T (°C)	Time (h)	Yield (%)
1	Mn-8	1,4-dioxane:water	NaOH	150	48	27
2	Mn-8	1,4-dioxane:water	NaOH (2 eq)	150	48	31
3	Mn-8	1,4-dioxane:water	K ₂ CO ₃	150	48	40
4	Mn-8	1,4-dioxane:water	Na₂CO₃	150	48	97
5	Mn-8	1,4-dioxane:water	Et ₃ N	150	48	9
6	Mn-8	1,4-dioxane:water	KOH	150	48	33
7	Mn-8	1,4-dioxane:water	KO ^t Bu	150	48	44
8	Mn-8	THF:water	Na ₂ CO ₃	150	48	33
9	Mn-8	MeOH:water	Na ₂ CO ₃	150	48	74
10	Mn-8	ACN:water	Na ₂ CO ₃	150	48	20
11	Mn-8	water (2 mL)	Na ₂ CO ₃	150	48	16
12	Mn-8	1,4-dioxane (2 mL)	Na ₂ CO ₃	150	48	trace
13	Mn-8	DMF (2 mL)	Na ₂ CO ₃	150	48	trace
14	Mn-8	DMSO (2 mL)	Na ₂ CO ₃	150	48	trace
15	Mn-8	1,4-dioxane:water	Na ₂ CO ₃	110	48	18
16	Mn-8	1,4-dioxane:water	Na ₂ CO ₃	130	48	32
17	Mn-8	1,4-dioxane:water	Na ₂ CO ₃	160	48	92
18	Mn-8	1,4-dioxane:water	Na ₂ CO ₃	150	24	10
19	Mn-8	1,4-dioxane:water	Na ₂ CO ₃	150	36	26
20	Mn-8	1,4-dioxane:water	Na ₂ CO ₃	150	60	85

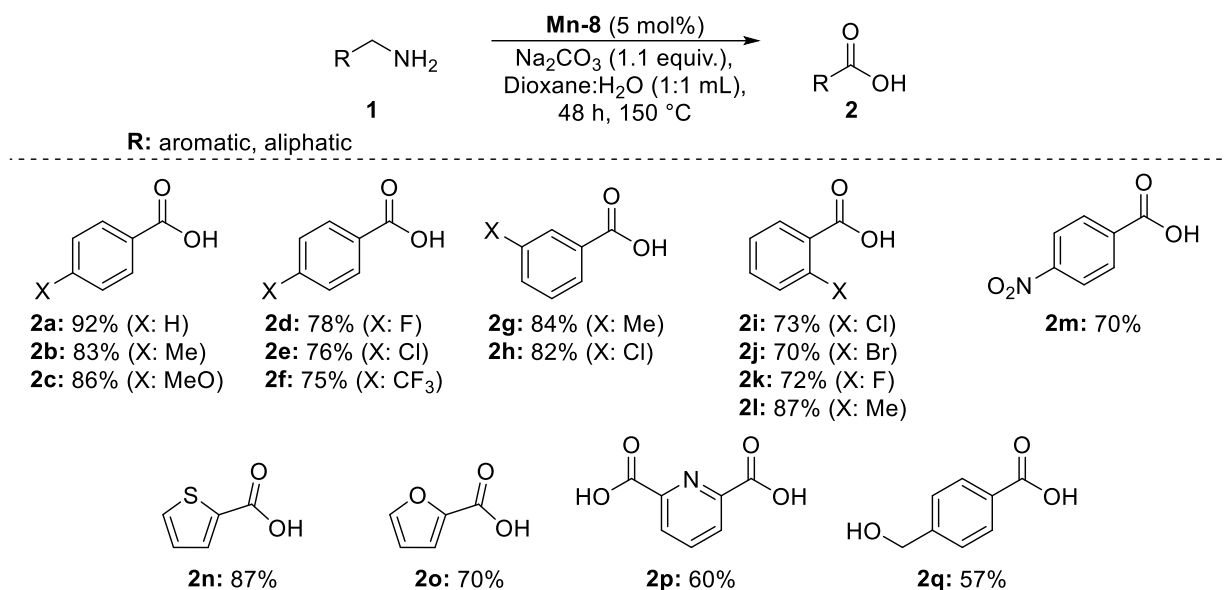
^aReaction conditions unless otherwise specified: 0.5 mmol of primary amine, 5 mol% of catalyst [**Mn-8**], 1.1 equiv. of Na₂CO₃, 1,4-dioxane (1 mL) and H₂O (1.0 mL) were heated at 150 °C for 48 h. Isolated yield.

Mn-1, Mn-2, Mn-4, Mn-5, Mn-8, Mn-9 and Mn-10 were synthesized according to literature procedure.^{191,198,273,329,403–405} All the complexes were characterized by various spectroscopic studies.

Initially, **Mn-8** (5 mol%) was used as a catalyst in the oxidative deamination of primary amine with water/1,4-dioxane (1:1 volumetric ratio) and NaOH (1.1 equiv.) was heated at 150 °C for 48 h, affording a 27% yield of corresponding carboxylate (table 6.2, entry 1). When the base loading was doubled the yield of carboxylate increased to 30.8% (table 6.2, entry 2). The impact of various bases (K₂CO₃, Et₃N, KOH, KO^tBu) was evaluated under comparable conditions, resulting in yields of the carboxylate was ranging from unsatisfactory to insignificant (table 6.2, entries 3, 5–7). A drastic increase in the yield (96.6%) was observed when Na₂CO₃ was used (table 6.2, entry 4). The reaction was significantly slowed down by solvents such as THF, methanol and acetonitrile were used with equivalent amount of water, resulting in only decreased amounts of the desired product (table 6.2, entries 8–10). Furthermore, when only one solvent was used (water, 1,4-dioxane, DMF, DMSO), a drastic decrease in the product yield was observed (Table 6.2, entries

11-14). While screening the temperature a significant decrease in the yield was observed and at 160 °C a small decrease in the yield was observed (as shown in table 6.2, entries 15-17). A yield of approx. 10% and 26% was observed when reaction was carried out for 24 h and 36 h (Table 6.2, entries 18-19), furthermore, when the reaction was carried out for 60 h, 85% yield of carboxylate was observed (table 6.2, entry 20).

Table 6.3. Substrate scope of catalytic oxidative deamination of amines to carboxylates.^{a, b}



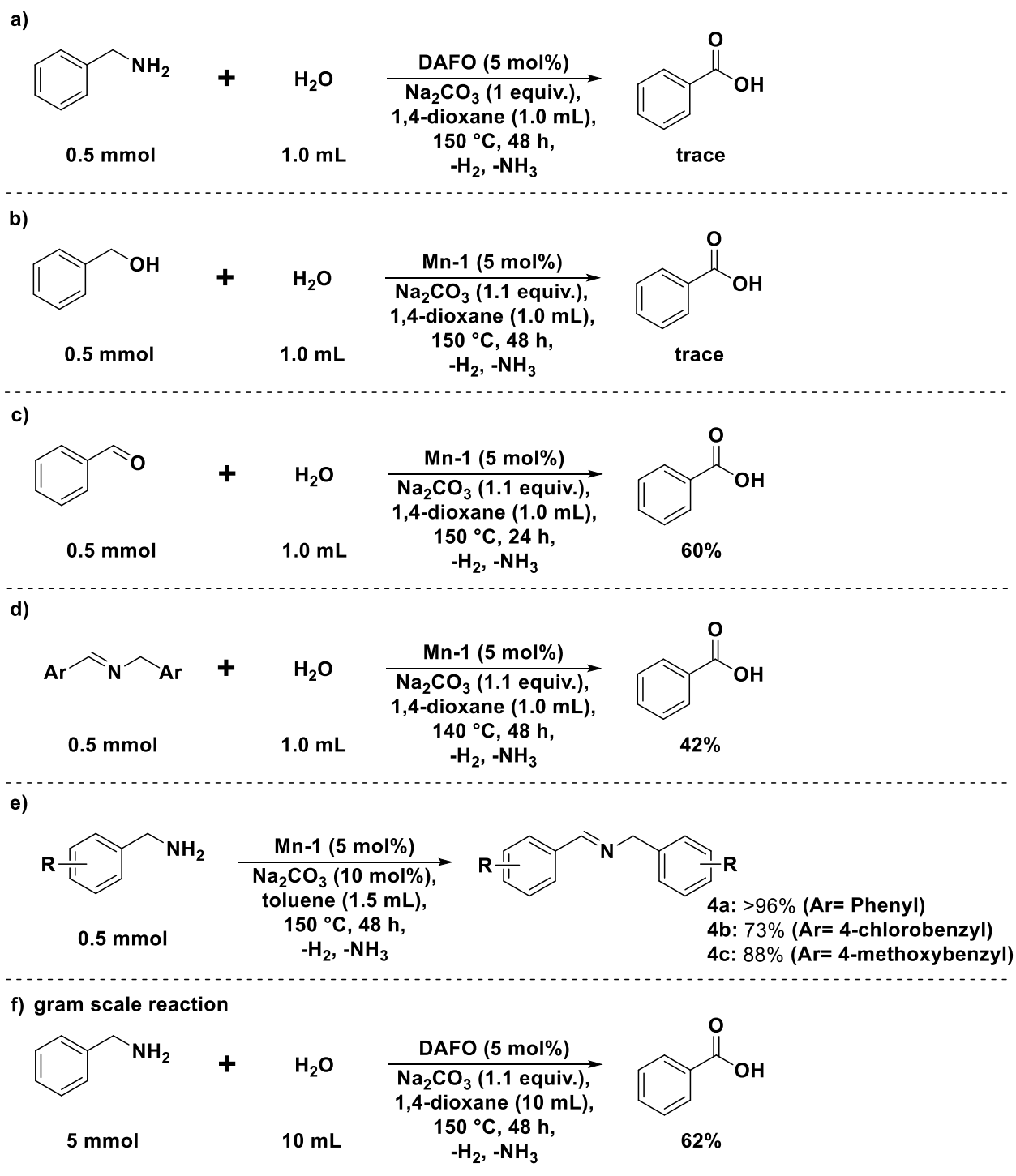
^aReaction conditions unless otherwise specified: 0.5 mmol of primary amine, 5 mol% of catalyst [**Mn-8**], 1.1 equiv. of Na₂CO₃, 1,4-dioxane (1 mL) and H₂O (1.0 mL) were heated at 150 °C for 48 h. ^bYields were determined by ¹H NMR analysis using 1,2,2,2-tetrachloroethane as the internal standard.

In recent years, a variety of manganese pincer complexes have been proven to be efficient catalysts for the dehydrogenation reactions.^{34,107,109,324,406} Therefore, the choice of different manganese pincer complexes was tested for their activities towards the target reaction. A variety of potential catalysts (**Mn-1** (trace), **Mn-2** (trace), **Mn-4** (trace), **Mn-5** (6%), **Mn-8** (97%), **Mn-9** (trace), **Mn-10** (trace), **Mn-11** (10%), **Mn-12** (trace), **Mn(CO)₅Br** (trace), **MnBr₂** (trace)) (table 6.1) which can undergo dehydrogenation, were screened for this transformation. As a result of our tests, we found that **Mn-8**, showed good activity towards catalytic oxidative deamination of amines to carboxylates at 150 °C for 48 h (table 6.1). Other manganese catalysts had much lower activity towards this transformation. The reaction with DAFO as catalyst did not lead to any conversion under the given reaction conditions, showcasing the role of **Mn-8** as the active catalyst (Scheme 6.1).

Excitingly, examination of the gaseous state of the reaction mixture through gas chromatography (GC) with a thermal conductivity detector demonstrated the production of dihydrogen. Nessler's reagent test was also conducted confirming the formation of ammonia in oxidative deamination of amines to carboxylates.

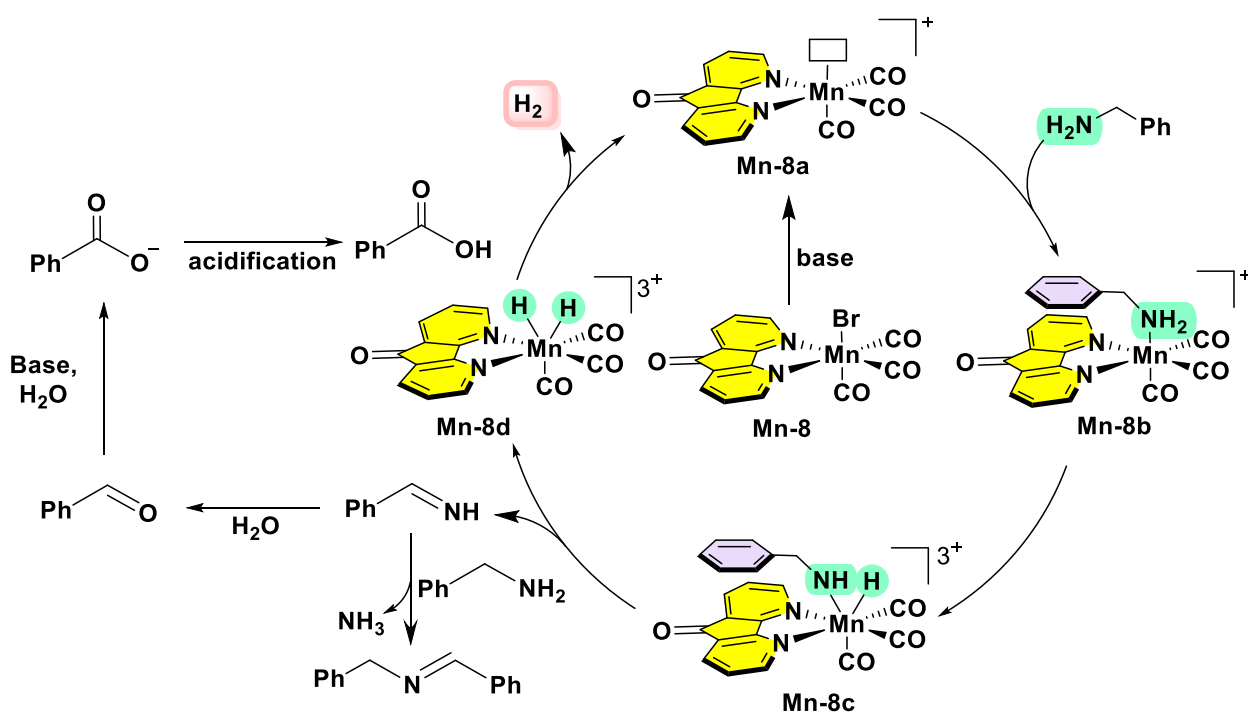
Under optimized conditions, the substrates scope for catalytic oxidative deamination of amines to carboxylates was investigated under optimized conditions, including the use of 1,4-dioxane/water as the solvent mixture and crucial role of base selection (Na₂CO₃ (1.1 equiv.)), a temperature of 150 °C, and a catalyst loading of 5 mol% for 48 h. Notably, electron donating groups at *para*, *meta* and *ortho* positions of benzylamine (Me, OMe) afforded good to excellent yields (83-87%) of the corresponding carboxylates (Table 6.3, **2b-c**, **2g**, **2i**). The deamination Reaction with 2-methylbenzylamine under optimised condition 87% of product (Table 3, **2l**). But in case of 4-methylbenzylamine slightly decrease yield (83%) was observed (table 6.3, **2b**). The electron withdrawing *para*, *meta* and *ortho* substituted benzylamines (F, Cl, CF₃, Br) gave

comparatively lower yields of the carboxylate products (70-82%; table 6.3, **2d-f**, **2h-k**, **2m**). The reaction of 2-F benzylamine resulted in 72% of the desired product under identical conditions (table 6.3, **2k**). However, in case of 4-chlorobenzylamine, slightly increased yield (76%) of the deamination product was noticed (table 6.3, **2e**). Thus, electronics on the substituted benzylamines play a prominent role in determining the yields of the homo-coupled products. The reaction was also found to be tolerant towards heteroaromatic amines like thiophene-2-methylamine (87%, table 6.3, **2i**), Furan-2-ylmethylamine (70%, **2o**) and Pyridine-2,6-diylldimethanamine (60%, **2p**) providing good yields. Interestingly, **Mn-8** converted amino group chemo-selectively to acid derivative (**2q**) when treated with (4-(aminomethyl)phenyl)methanol.



Scheme 6.1. Controlled experiments: a) Reaction of benzyl amine with DAFO as catalyst. b) Reaction of benzyl alcohol with **Mn-1**. c) Reaction of benzaldehyde with **Mn-1**. d) Reaction of *N*-benzylidenebenzylamine with **Mn-1**. e) catalytic dehydrogenation of benzylamine derivatives. f) Gram scale synthesis of benzoic acid.

To understand the importance of Mn-DAFO in this transformation, reaction of benzylamine were carried out with DAFO as a catalyst, which results trace amount of product (scheme 6.1a). Moreover, the reaction was found to be selective for primary amine functionalities over alcohols. When a reaction was carried out in the presence of benzyl alcohol instead of benzylamine, the trace amount of carboxylate product was observed. Thus, benzyl alcohol remained unreacted indicating the chemo-selective nature of **Mn-8** (scheme 6.1b). The oxidation of benzaldehyde also investigated which gives 60% yield of benzoic acid, since aldehyde are also generated from imine intermediates in the reaction (scheme 6.1c). To confirm imine formation in the reaction mixture as intermediate, controlled experiment were carried out with *N*-benzylidenebenzylamine under optimised condition gave 42% yields of the carboxylate product (scheme 6.1d). In order to realize the practical applicability of the dehydrogenative coupling reaction, a largescale reaction was conducted using 5 mmol benzylamine and 5 mol% **Mn-8** under the optimized reaction conditions, and the yield obtained was 62% as revealed by ^1H NMR (Scheme 6.1f). Furthermore, the substrates scope for homocoupling of benzylamine derivatives to imines was investigated under optimized conditions, including the use of toluene as the solvent and base (Na_2CO_3 (10 mol%), at a temperature of 140 $^\circ\text{C}$, and a catalyst loading of 5 mol% for 24 h.



Scheme 6.2. Plausible mechanistic cycle for amine dehydrogenation.

The proposed mechanism involves the coordination of primary amine to form **Mn-8b** via use of base to form **Mn-8a** as intermediate. Next, oxidative addition of the N-H bond of benzylamine on the Mn(I) species **Mn-8b** gives a heptacoordinated 18e⁻ Mn(III) intermediate **Mn-8c**. Then, β hydrogen elimination and removal of benzaldimine from **Mn-8c** affords **Mn-8d**. The expulsion of reactive benzaldimine relieves steric hindrance and subsequently couples with benzylamine to form a secondary imine with the concomitant release of ammonia. Furthermore, the primary imine in the presence of water converts into aldehyde which in presence of base gives acid salt. Whereas **Mn-8a** is regenerated by H_2 elimination from **Mn-8d** and closes the catalytic cycle. Thus, the Mn complex shuttles between (I/III) oxidation states by activating the primary amine substrate.

6.3. Summary

In the conclusion, we are demonstrating the first example of manganese-based non-pincer complexes for oxidative deamination of amines to carboxylic acids. The reaction is catalyzed by **Mn-8** complex [DAFO-Mn(CO)₃Br] encumbered with DAFO (4,5-diazafluoren-9-one) tridentate ligand. The reaction in presence of 1.1 equiv. base generating NH_3 and H_2 as sole by-products.

Dehydrogenative homo-coupling of primary amines to symmetrical secondary imines was also tested furnishing good yields of the corresponding homo-coupled products.

6.4. Experimental procedures and supporting data

All experiments were conducted under inert atmosphere by using standard Schlenk techniques or a nitrogen glove box, unless stated otherwise. Tetrahydrofuran (THF), toluene, dichloromethane (CH_2Cl_2), chloroform, hexane, 1,4-dioxane and methanol (MeOH) were heated under reflux over suitable drying agent (sodium/benzophenone for THF, hexane and toluene; calcium hydride for CH_2Cl_2 , 3 Å molecular sieves for MeOH), distilled and stored under nitrogen atmosphere. Deuterated (toluene, chloroform, benzene) solvents were stored in 3 Å molecular sieves under nitrogen atmosphere. Unless otherwise stated, commercial reagents were used without purification, only 3-Methylbut-2-en-1-ol (prenol) and acetophenone were purified via vacuum distillation. 4,5-diazafluoren-9-one (DAFO),⁴⁰² 4,5-diazafluorene (DAF)⁴⁰² and *N*-(pyridin-2-ylmethyl)quinolin-8-amine¹⁹⁸ were prepared according to literature procedure, Pentacarbonyl manganese bromide ($\text{Mn}(\text{CO})_5\text{Br}$), Cyclopentadienylmanganese (I) tricarbonyl, Manganese (II) bromide and 4,4'-dimethoxy-2,2'-bipyridine were purchased from Sigma-Aldrich, 1, 10 phenanthroline, 1,2-bis(diphenylphosphino)ethane, 1,3-bis(diphenylphosphino)propane and bis(2-(diphenylphosphanyl)ethyl)amine hydrochloride BLD pharma, calcium hydride (CaH_2) and all other materials were purchased from Avra, BLDpharma, TCI and Sigma- Aldrich, stored under nitrogen and used as received. All the reaction for substrate scope was monitored by TLC and isolated by column chromatography or flash chromatography (silica gel 60-120). Then product was condensated with the help of rotta vapour. Then, isolated product was characterized by using ^1H NMR, ^{13}C NMR from Bruker 500 MHz and 400 MHz spectrometer. All spectra were recorded at room temperature, unless otherwise noted. FT-IR spectra were recorded by Perkin-Elmer FT-IR spectrometer. Mass spectra were recorded on Agilent spectrometer.

$\text{Mn}(\text{CO})_3(\text{NN}^{\text{H}}\text{N})\text{Br}$ catalyst synthesis (Mn-1):

Catalyst was synthesised as reported in literature,¹⁹⁸ In the glovebox, A 100ml Schlenk tube is charged with $\text{Mn}(\text{CO})_5\text{Br}$ (0.5mmol) in 5 ml THF and stirred for 5 minutes. To the stirring solution, *N*-(pyridin-2-ylmethyl)quinolin-8-amine (0.5 mmol.) in 5 ml THF added dropwise with vigorous stirring. After addition of ligand, Schenk was closed and kept for stirring at 90 °C for stirring overnight. A yellow-coloured precipitates appeared at the bottom of the Schlenk. Then, the solvent was decanted and solid washed with *n*-hexane (3*5ml) and bright yellow to reddish coloured precipitates collected and dried under vacuo (85% yield). The product was confirmed by analysing the complex by ATR-IR and Single XRD, which matched with the literature reported data.

$\text{PN}^{\text{H}}\text{P}-\text{Mn}(\text{CO})_2\text{Br}$ catalyst synthesis (Mn-2):

Catalyst was synthesised as reported in literature,¹⁹¹ a flame dried Schlenk tube was charged with ligand bis(2-(diphenylphosphanyl)ethyl)amine hydrochloride (478 mg, 1.0 mmol, 1.0 equiv.), toluene (8 mL), water (2 mL) and NaOH (120 mg, 3.0 mmol, 3.0 equiv.). The reaction mixture was stirred at room temperature for 30 min. The two phases were separated, and the organic layer was washed with water (3 × 5 mL). The organic layer was concentrated under reduced pressure. Subsequently, toluene (12 mL) and $\text{Mn}(\text{CO})_5\text{Br}$ precursor were added to the Schlenk tube. The reaction mixture was heated up to 110 °C and the atmosphere was exchanged three times by evacuating and backfilled with nitrogen. After the mixture was stirred for 20 h at reflux temperature, it was cooled to room temperature and concentrated in vacuo. The crude precipitate was washed with pentane and extracted with dichloromethane/diethylether to remove insoluble inorganic side products. The solution was concentrated under reduced pressure and dried to afford the complex **Mn-2** as a yellow powder in 84%. The product was confirmed by analysing the complex by ^{31}P NMR, which matched with the literature reported data.

$\text{Mn}(\text{CO})_3(\text{DPPE})\text{Br}$ catalyst synthesis (Mn-4):

Catalyst was synthesised as reported in literature with slight modifications,²⁷³ In the glovebox, A flame dried Schlenk tube was charged with ligand 1,2-bis(diphenylphosphino)ethane (398 mg, 1.0 mmol, 1.0 equiv.), in toluene (12 mL). Then, Mn(CO)₅Br precursor (275 mg, 1 mmol, 1 equiv.) was added and reaction mixture was stirred at 90 °C for overnight. After the completion of reaction, the reaction mixture was cooled to room temperature and concentrated in vacuo. The crude precipitate was washed with pentane. The solid was dried under reduced pressure to afford the complex **Mn-4** as a yellow powder in 86%. The product was confirmed by analysing the complex by ATR-IR and Single XRD, which matched with the literature reported data.

Mn(CO)₃(DPPP)Br catalyst synthesis (Mn-5):

Catalyst was synthesised as reported in literature with slight modifications,³²⁹ In the glovebox, A flame dried Schlenk tube was charged with ligand 1,3-bis(diphenylphosphino)propane (412 mg, 1.0 mmol, 1.0 equiv.), in toluene (12 mL). Then, Mn(CO)₅Br precursor (275 mg, 1 mmol, 1 equiv.) was added and reaction mixture was stirred at 90 °C for overnight. After the completion of reaction, the reaction mixture was cooled to room temperature and concentrated in vacuo. The crude precipitate was washed with pentane. The solid was dried under reduced pressure to afford the complex **Mn-5** as a yellow powder in 82%. The product was confirmed by analysing the complex by ATR-IR and Single XRD, which matched with the literature reported data.

Mn(CO)₃(DAFO)Br catalyst synthesis (Mn-8):

Catalyst was synthesised as reported in literature with slight modifications,⁴⁰⁴ In the glovebox, A flame dried Schlenk tube was charged with ligand 4,5-diazafluoren-9-one (182 mg, 1.0 mmol, 1.0 equiv.), in toluene (12 mL). Then, Mn(CO)₅Br precursor (275 mg, 1 mmol, 1 equiv.) was added and reaction mixture was stirred at 90 °C for overnight. After the completion of reaction, the reaction mixture was cooled to room temperature and concentrated in vacuo. The crude precipitate was washed with pentane. The solid was dried under reduced pressure to afford the complex **Mn-8** as a yellow powder in 83%. The product was confirmed by analysing the complex by ATR-IR and Single XRD, which matched with the literature reported data.

Mn(CO)₃(DAF)Br catalyst synthesis (Mn-9):

Catalyst was synthesised as reported in literature with slight modifications,⁴⁰³ In the glovebox, A flame dried Schlenk tube was charged with ligand 4,5-diazafluorene (170 mg, 1.0 mmol, 1.0 equiv.), in toluene (12 mL). Then, Mn(CO)₅Br precursor (275 mg, 1 mmol, 1 equiv.) was added and reaction mixture was stirred at 90 °C for overnight. After the completion of reaction, the reaction mixture was cooled to room temperature and concentrated in vacuo. The crude precipitate was washed with pentane. The solid was dried under reduced pressure to afford the complex **Mn-9** as a yellow powder in 85%. The product was confirmed by analysing the complex by ATR-IR and Single XRD, which matched with the literature reported data.

Mn(CO)₃(N[^]N)Br catalyst synthesis (Mn-10):

Catalyst was synthesised as reported in literature with slight modifications,⁴⁰⁵ In the glovebox, A flame dried Schlenk tube was charged with ligand 4,4'-dimethoxy-2,2'-bipyridine (216 mg, 1.0 mmol, 1.0 equiv.), in toluene (12 mL). Then, Mn(CO)₅Br precursor (275 mg, 1 mmol, 1 equiv.) was added and reaction mixture was stirred at 90 °C for overnight. After the completion of reaction, the reaction mixture was cooled to room temperature and concentrated in vacuo. The crude precipitate was washed with pentane. The solid was dried under reduced pressure to afford the complex **Mn-10** as a yellow powder in 88%. The product was confirmed by analysing the complex by ATR-IR and Single XRD, which matched with the literature reported data.

General procedure for Catalyst screening of catalytic oxidative deamination of amines to carboxylates (Table 6.1)

A flame-dried Schlenk tube (25 mL) under a nitrogen atmosphere was added with Mn catalyst (5 mol %) and Na₂CO₃ (58.3 mg, 1.1 equiv. with respect to reactant loading) dissolved in 1 mL of 1,4-dioxane and 1 mL of distilled water (Table 6.1). Next, 0.5 mmol (54.6 μL) of benzylamine were added to the solution, and the mixture was stirred for 5 min. Then, the Schlenk flask was closed

tightly and kept at 150 °C and 48 h. Finally, the Schlenk flask was cooled to room temperature and a saturated brine (5.0 mL) was then added to the reaction mixture and the mixture was extracted with ethyl acetate (3 × 5.0 mL). The aqueous phase was then acidified with 4 M HCl (3.0 mL) and extracted with ethyl acetate (3 × 5.0 mL). The combined organic extracts from the acidified aqueous phase were dried over Na₂SO₄ and all volatiles were removed under vacuum. The isolated product, benzoic acid, was obtained as a pale-yellow solid with yield reported in table 6.1.

General procedure for Optimization of the reaction parameter for catalytic oxidative deamination of amines to carboxylates (Table 6.2)

A flame-dried Schlenk tube (25 mL) under a nitrogen atmosphere was added with **Mn-8** (10 mg, 5 mol %) and a base (58.3 mg, 1.1 equiv. with respect to reactant loading) dissolved in 2 mL of the solvent reported in Table 6.2. Next, 0.5 mmol (54.6 µL) of benzylamine were added to the solution, and the mixture was stirred for 5 min. Then, the Schlenk flask was closed tightly and kept at the reported temperature and time. Finally, the Schlenk flask was cooled to room temperature and a saturated brine (5.0 mL) was then added to the reaction mixture and the mixture was extracted with ethyl acetate (3 × 5.0 mL). The aqueous phase was then acidified with 4 M HCl (3.0 mL) and extracted with ethyl acetate (3 × 5.0 mL). The combined organic extracts from the acidified aqueous phase were dried over Na₂SO₄ and all volatiles were removed under vacuum. The isolated product, benzoic acid, was obtained as a pale-yellow solid with yield reported in table 6.2.

General procedure for Substrate scope of catalytic oxidative deamination of amines to carboxylates (Table 6.3)

A flame-dried Schlenk tube (25 mL) under a nitrogen atmosphere was added with **Mn-8** catalyst (10 mg, 5 mol%) and Na₂CO₃ (58.3 mg, 1.1 equiv. with respect to reactant loading) dissolved in 1 mL of 1,4-dioxane and 1 mL of distilled water. Next, 0.5 mmol (54.6 µL) of benzylamine were added to the solution, and the mixture was stirred for 5 min. Then the Schlenk flask was closed tightly and kept at 150 °C and 48 h. Finally, the Schlenk flask was cooled to room temperature and a saturated brine (5.0 mL) was then added to the reaction mixture and the mixture was extracted with ethyl acetate (3 × 5.0 mL). The aqueous phase was then acidified with 4 M HCl (3.0 mL) and extracted with ethyl acetate (3 × 5.0 mL). The combined organic extracts from the acidified aqueous phase were dried over Na₂SO₄ and all volatiles were removed under vacuum and isolated product was collected.

Procedure for the reaction of DAFO as catalyst with benzylamine (Scheme 6.1a)

A flame-dried Schlenk tube (25 mL) under a nitrogen atmosphere was added with **DAFO** (9.1 mg, 5 mol%) and Na₂CO₃ (58.3 mg, 1.1 equiv. with respect to reactant loading) dissolved in 1 mL of 1,4-dioxane and 1 mL of distilled water. Next, 0.5 mmol (54.6 µL) of benzylamine were added to the solution, and the mixture was stirred for 5 min. Then the Schlenk flask was closed tightly and kept at 150 °C and 48 h. Finally, the Schlenk flask was cooled to room temperature and a saturated brine (5.0 mL) was then added to the reaction mixture and the mixture was extracted with ethyl acetate (3 × 5.0 mL). The aqueous phase was then acidified with 4 M HCl (3.0 mL) and extracted with ethyl acetate (3 × 5.0 mL). The combined organic extracts from the acidified aqueous phase were dried over Na₂SO₄ and all volatiles were removed under vacuum. The product, benzoic acid, was obtained in trace amount.

Procedure for the reaction of Mn-8 with benzyl alcohol (Scheme 6.1b)

A flame-dried Schlenk tube (25 mL) under a nitrogen atmosphere was added with **Mn-8** (10 mg, 5 mol%) and Na₂CO₃ (58.3 mg, 1.1 equiv. with respect to reactant loading) dissolved in 1 mL of 1,4-dioxane and 1 mL of distilled water. Next, 0.5 mmol (54.6 µL) of benzyl alcohol were added to the solution, and the mixture was stirred for 5 min. Then, the Schlenk flask was closed tightly and kept at 150 °C and 48 h. Finally, the Schlenk flask was cooled to room temperature and a saturated brine (5.0 mL) was then added to the reaction mixture and the mixture was extracted with ethyl acetate (3 × 5.0 mL). The aqueous phase was then acidified with 4 M HCl (3.0 mL) and

extracted with ethyl acetate (3 × 5.0 mL). The combined organic extracts from the acidified aqueous phase were dried over Na₂SO₄ and all volatiles were removed under vacuum. The product, benzoic acid, was obtained in trace amount.

Procedure for the reaction of Mn-8 with benzaldehyde (Scheme 6.1c)

A flame-dried Schlenk tube (25 mL) under a nitrogen atmosphere was added with **Mn-8** (10 mg, 5 mol%) and Na₂CO₃ (58.3 mg, 1.1 equiv. with respect to reactant loading) dissolved in 1 mL of 1,4-dioxane and 1 mL of distilled water. Next, 0.5 mmol (54.6 µL) of benzaldehyde were added to the solution, and the mixture was stirred for 5 min. Then the Schlenk flask was closed tightly and kept at 150 °C and 48 h. Finally, the Schlenk flask was cooled to room temperature and a saturated brine (5.0 mL) was then added to the reaction mixture and the mixture was extracted with ethyl acetate (3 × 5.0 mL). The aqueous phase was then acidified with 4 M HCl (3.0 mL) and extracted with ethyl acetate (3 × 5.0 mL). The combined organic extracts from the acidified aqueous phase were dried over Na₂SO₄ and all volatiles were removed under vacuum. The product, benzoic acid, was obtained as a pale-yellow solid in 60%.

Procedure for the reaction of Mn-8 with *N*-benzylidenebenzylamine (Scheme 6.1d)

A flame-dried Schlenk tube (25 mL) under a nitrogen atmosphere was added with **Mn-8** (10 mg, 5 mol%) and Na₂CO₃ (58.3 mg, 1.1 equiv. with respect to reactant loading) dissolved in 1 mL of 1,4-dioxane and 1 mL of distilled water. Next, 0.5 mmol (54.6 µL) of *N*-benzylidenebenzylamine were added to the solution, and the mixture was stirred for 5 min. Then the Schlenk flask was closed tightly and kept at 150 °C and 48 h. Finally, the Schlenk flask was cooled to room temperature and a saturated brine (5.0 mL) was then added to the reaction mixture and the mixture was extracted with ethyl acetate (3 × 5.0 mL). The aqueous phase was then acidified with 4 M HCl (3.0 mL) and extracted with ethyl acetate (3 × 5.0 mL). The combined organic extracts from the acidified aqueous phase were dried over Na₂SO₄ and all volatiles were removed under vacuum. The product, benzoic acid, was obtained as a pale-yellow solid in 42%.

General procedure for the reaction of Mn-8 with benzylamine to form imine (Scheme 6.1e)

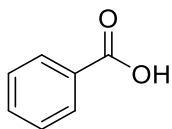
A flame-dried Schlenk tube (25 mL) under a nitrogen atmosphere was added with **Mn-8** (10 mg, 5 mol%) dissolved in 2 mL of toluene. Next, 0.5 mmol (54.6 µL) of benzylamine were added to the solution, and the mixture was stirred for 5 min. Then, the Schlenk flask was closed tightly and kept at 140 °C and 24 h. Finally, the Schlenk flask was cooled to room temperature. After the completion of the reaction, it was allowed to cool down to room temperature and opened carefully under a fume hood, releasing the gases H₂ and NH₃ formed during the reaction. The products were isolated by column chromatography using neutral alumina (Al₂O₃) as the stationary phase and *n*-hexane as the eluent and the isolated products were characterized by the NMR technique.

Experimental Procedure for the Gram-Scale Reaction (scheme 6.1f)

A flame-dried Schlenk tube (100 mL) under a nitrogen atmosphere was added with **Mn-8** (100 mg, 5 mol%) and Na₂CO₃ (58.3 mg, 1.1 equiv. with respect to reactant loading) dissolved in 10 mL of 1,4-dioxane and 10 mL of distilled water. Next, 5 mmol (546.12 µL) of benzylamine were added to the solution, and the mixture was stirred for 5 min. Then the Schlenk flask was closed tightly and kept at 150 °C and 48 h. Finally, the Schlenk flask was cooled to room temperature and a saturated brine (50 mL) was then added to the reaction mixture and the mixture was extracted with ethyl acetate (30 × 50 mL). The aqueous phase was then acidified with 4 M HCl (30 mL) and extracted with ethyl acetate (30 × 50 mL). The combined organic extracts from the acidified aqueous phase were dried over Na₂SO₄ and all volatiles were removed under vacuum. The product, benzoic acid, was obtained as a pale-yellow solid in 62%.

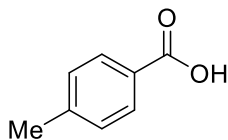
¹H and ¹³C NMR data of isolated products³⁷⁶

benzoic acid (2a)



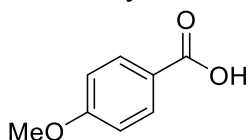
^1H NMR (500 MHz, CDCl_3) δ 12.33 (s, 1H), 8.20 – 8.13 (m, 2H), 7.68 – 7.62 (m, 1H), 7.51 (t, J = 7.6 Hz, 2H). **^{13}C NMR** (126 MHz, CDCl_3) δ 172.64, 133.98, 130.38, 129.48, 128.64.

4-methylbenzoic acid (2b)



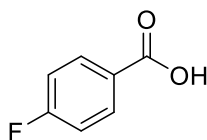
^1H NMR (500 MHz, CDCl_3) δ 8.04 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 2.46 (s, 3H). **^{13}C NMR** (126 MHz, CDCl_3) δ 172.47, 144.80, 130.41, 129.36, 126.74, 21.91.

4-methoxybenzoic acid (2c)



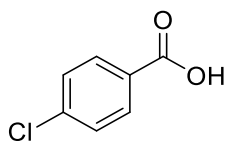
^1H NMR (500 MHz, CDCl_3) δ 11.97 (s, 1H), 8.07 (d, J = 8.8 Hz, 2H), 6.99 – 6.92 (m, 2H), 3.88 (s, 3H). **^{13}C NMR** (126 MHz, CDCl_3) δ 164.21, 132.52, 113.91, 55.64.

4-fluorobenzoic acid (2d)



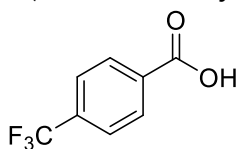
^1H NMR (500 MHz, DMSO) δ 8.04 – 7.97 (m, 2H), 7.31 (t, J = 8.8 Hz, 2H). **^{13}C NMR** (126 MHz, DMSO) δ 166.60, 166.09, 164.10, 132.29 (d, J = 9.4 Hz), 127.48 (d, J = 2.8 Hz), 115.79 (d, J = 22.1 Hz).

4-chlorobenzoic acid (2e)



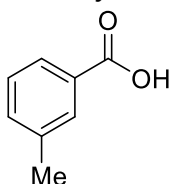
^1H NMR (500 MHz, DMSO) δ 7.97 – 7.91 (m, 2H), 7.58 – 7.53 (m, 2H). **^{13}C NMR** (126 MHz, DMSO) δ 166.68, 138.00, 131.32, 129.76, 128.91.

4-(trifluoromethyl)benzoic acid (2f)



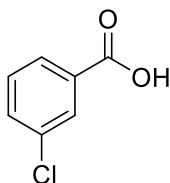
^1H NMR (500 MHz, DMSO) δ 8.13 (d, J = 8.0 Hz, 2H), 7.86 (d, J = 8.1 Hz, 2H). **^{13}C NMR** (126 MHz, DMSO) δ 166.45, 134.76, 132.69 (d, J = 32.1 Hz), 130.30, 125.79 (d, J = 3.9 Hz), 125.07, 122.90.

3-methylbenzoic acid (2g)



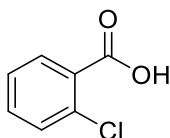
¹H NMR (500 MHz, CDCl₃) δ 12.80 (s, 1H), 7.97 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 2.45 (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 172.86, 138.33, 134.65, 130.75, 129.30, 128.41, 127.42, 21.28.

3-chlorobenzoic acid (2h)



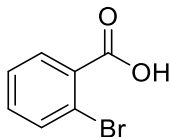
¹H NMR (500 MHz, CDCl₃) δ 11.74 (s, 1H), 8.10 (t, *J* = 1.9 Hz, 1H), 8.01 (d, *J* = 7.8 Hz, 1H), 7.62 – 7.57 (m, 1H), 7.43 (t, *J* = 7.9 Hz, 1H). **¹³C NMR** (126 MHz, CDCl₃) δ 171.20, 134.88, 134.08, 131.10, 130.43, 130.01, 128.48.

2-iodobenzoic acid (2i)



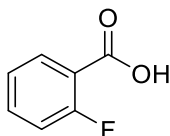
¹H NMR (500 MHz, CDCl₃) δ 11.48 (s, 1H), 8.09 (dd, *J* = 7.9, 1.2 Hz, 1H), 8.05 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.48 (td, *J* = 7.6, 1.2 Hz, 1H), 7.23 (td, *J* = 7.6, 1.7 Hz, 1H). **¹³C NMR** (126 MHz, CDCl₃) δ 171.34, 142.15, 133.74, 133.25, 132.27, 128.19.

2-bromobenzoic acid (2j)



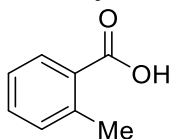
¹H NMR (500 MHz, CDCl₃) δ 11.49 (s, 1H), 8.02 (dd, *J* = 7.2, 2.4 Hz, 1H), 7.72 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.41 (qt, *J* = 7.5, 3.4 Hz, 2H). **¹³C NMR** (126 MHz, CDCl₃) δ 134.93, 133.62, 132.54, 127.32, 122.66.

2-fluorobenzoic acid (2k)



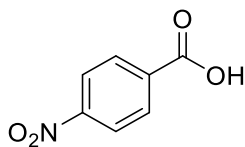
¹H NMR (500 MHz, CDCl₃) δ 11.91 (s, 1H), 8.07 (td, *J* = 7.6, 1.9 Hz, 1H), 7.68 – 7.57 (m, 1H), 7.31 – 7.25 (m, 1H), 7.20 (ddd, *J* = 11.0, 8.4, 1.1 Hz, 1H). **¹³C NMR** (126 MHz, CDCl₃) δ 163.84, 161.76, 135.82, 135.74, 132.93, 124.27 (d, *J* = 4.0 Hz), 117.42, 117.24.

2-methylbenzoic acid (2l)



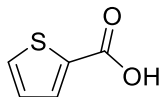
¹H NMR (500 MHz, CDCl₃) δ 12.48 (s, 1H), 8.13 – 8.07 (m, 1H), 7.48 (td, *J* = 7.5, 1.5 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 2H), 2.70 (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 173.44, 141.54, 133.12, 132.08, 131.75, 128.46, 126.02, 22.27.

4-nitrobenzoic acid (2m)



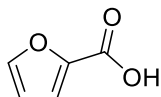
$^1\text{H NMR}$ (500 MHz, DMSO) δ 8.30 – 8.22 (m, 2H), 8.14 – 8.09 (m, 2H). $^{13}\text{C NMR}$ (126 MHz, DMSO) δ 166.06, 150.19, 136.56, 130.89, 123.87.

thiophene-2-carboxylic acid (2n)



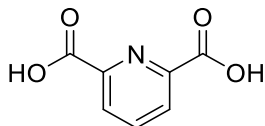
$^1\text{H NMR}$ (500 MHz, DMSO) δ 13.07 (s, 1H), 7.86 (dd, J = 5.0, 1.3 Hz, 1H), 7.73 (dd, J = 3.6, 1.3 Hz, 1H), 7.17 (dd, J = 5.0, 3.7 Hz, 1H). $^{13}\text{C NMR}$ (126 MHz, DMSO) δ 163.41, 135.13, 133.68, 128.67.

furan-2-carboxylic acid (2o)



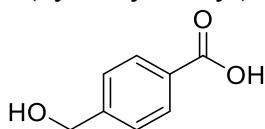
$^1\text{H NMR}$ (500 MHz, DMSO) δ 13.04 (s, 1H), 7.89 (d, J = 1.8 Hz, 1H), 7.21 (d, J = 3.5 Hz, 1H), 6.63 (dd, J = 3.5, 1.7 Hz, 1H). $^{13}\text{C NMR}$ (126 MHz, DMSO) δ 159.80, 147.45, 145.38, 118.16, 112.53.

pyridine-2,6-dicarboxylic acid (2p)



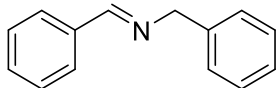
$^1\text{H NMR}$ (500 MHz, DMSO) δ 13.36 (s, 2H), 8.29 – 8.12 (m, 3H). $^{13}\text{C NMR}$ (126 MHz, DMSO) δ 165.91, 148.53, 139.70, 127.97.

4-(hydroxymethyl)benzoic acid (2q)



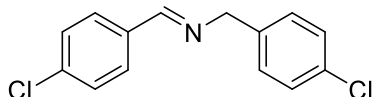
$^1\text{H NMR}$ (500 MHz, DMSO) δ 12.88 (s, 1H), 7.91 (d, J = 7.7 Hz, 2H), 7.43 (d, J = 7.8 Hz, 2H), 5.36 (t, J = 5.7 Hz, 1H), 4.57 (d, J = 3.4 Hz, 2H). $^{13}\text{C NMR}$ (126 MHz, DMSO) δ 167.76, 148.24, 129.66, 126.64, 62.90.

N-benzyl-1-phenylmethanimine (4a)



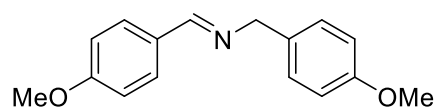
$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 8.47 (s, 1H), 7.89 (dd, J = 6.7, 3.0 Hz, 2H), 7.64 – 7.39 (m, 6H), 7.44 – 7.30 (m, 1H), 4.91 (s, 2H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 161.96, 139.33, 136.18, 130.76, 128.61, 128.50, 128.29, 127.99, 126.99, 65.03.

N-(4-chlorobenzyl)-1-(4-chlorophenyl)methanimine (4b)



$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 8.33 (s, 1H), 7.71 (d, J = 8.2 Hz, 2H), 7.47 – 7.11 (m, 6H), 4.77 (s, 2H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 160.87, 137.69, 136.90, 134.51, 132.85, 129.51, 129.31, 128.68, 64.19.

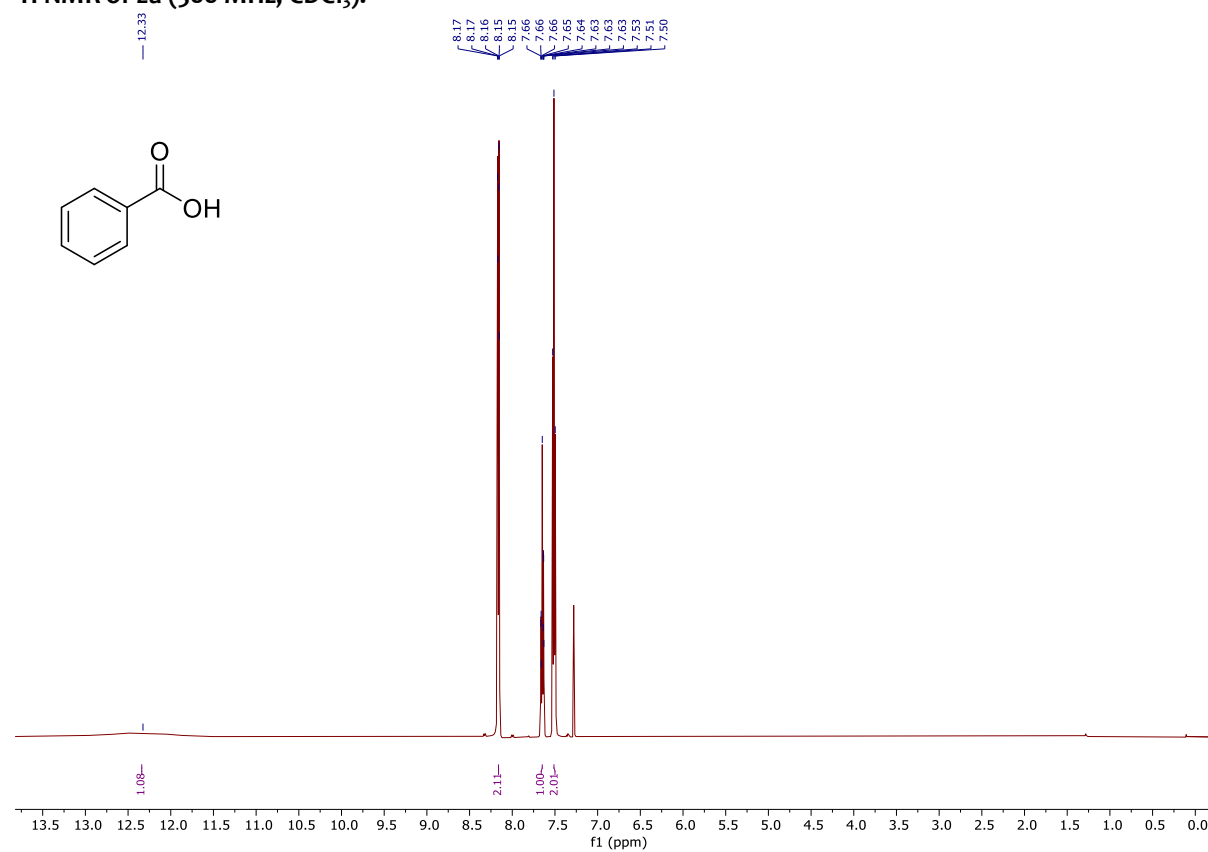
N-(4-methoxybenzyl)-1-(4-methoxyphenyl)methanimine (4c)



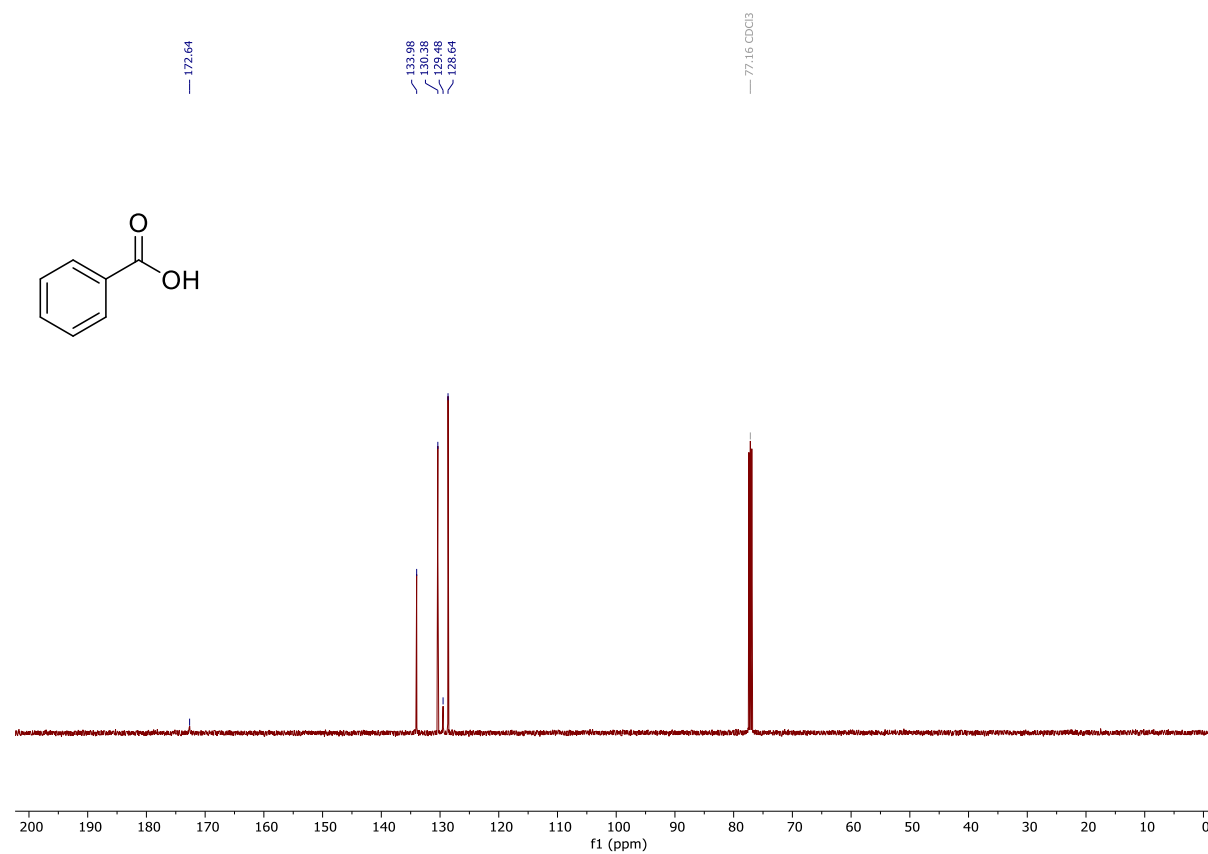
¹H NMR (500 MHz, CDCl₃) δ 8.36 (s, 1H), 7.44 – 7.38 (m, 1H), 7.31 (ddd, *J* = 20.0, 15.5, 7.7 Hz, 3H), 7.00 (d, *J* = 7.9 Hz, 1H), 6.97 – 6.89 (m, 2H), 6.83 (dd, *J* = 8.1, 2.6 Hz, 1H), 4.81 (s, 2H), 3.83 (d, *J* = 17.3 Hz, 6H). **¹³C NMR** (126 MHz, CDCl₃) δ 162.05, 159.88 (d, *J* = 15.5 Hz), 140.87, 137.62, 129.56 (d, *J* = 9.5 Hz), 121.68, 117.60, 113.68, 112.47, 111.70, 64.92, 55.32 (d, *J* = 21.4 Hz).

^1H and ^{13}C NMR data of isolated products

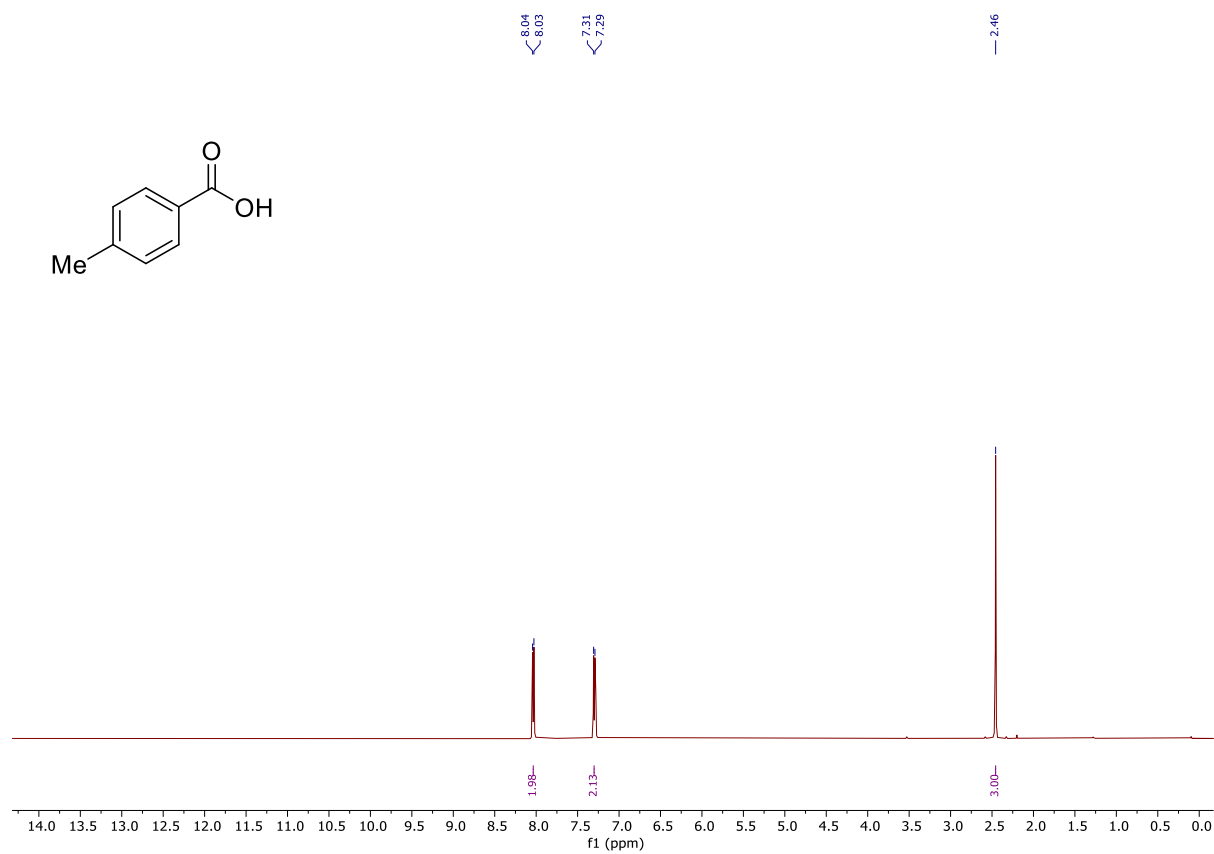
^1H NMR of 2a (500 MHz, CDCl_3):



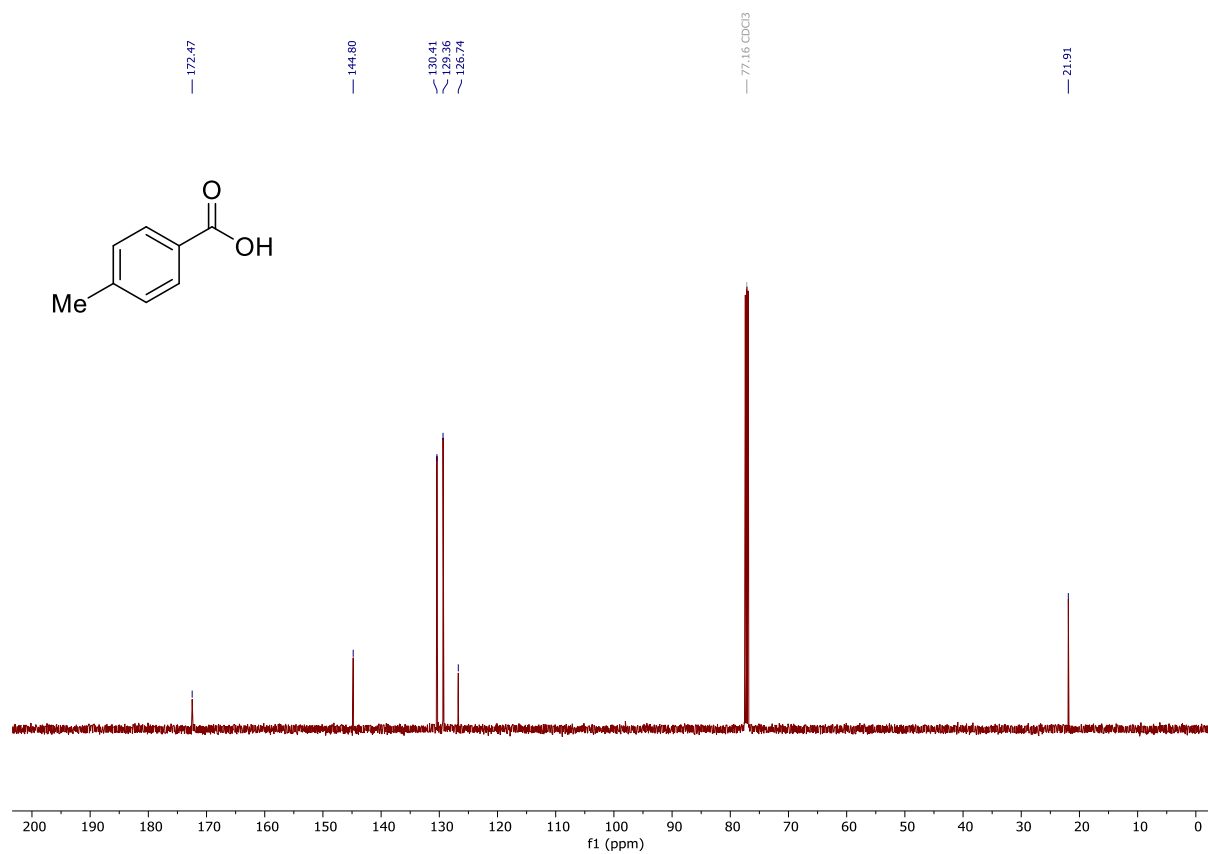
^{13}C NMR of 2a (126 MHz, CDCl_3):



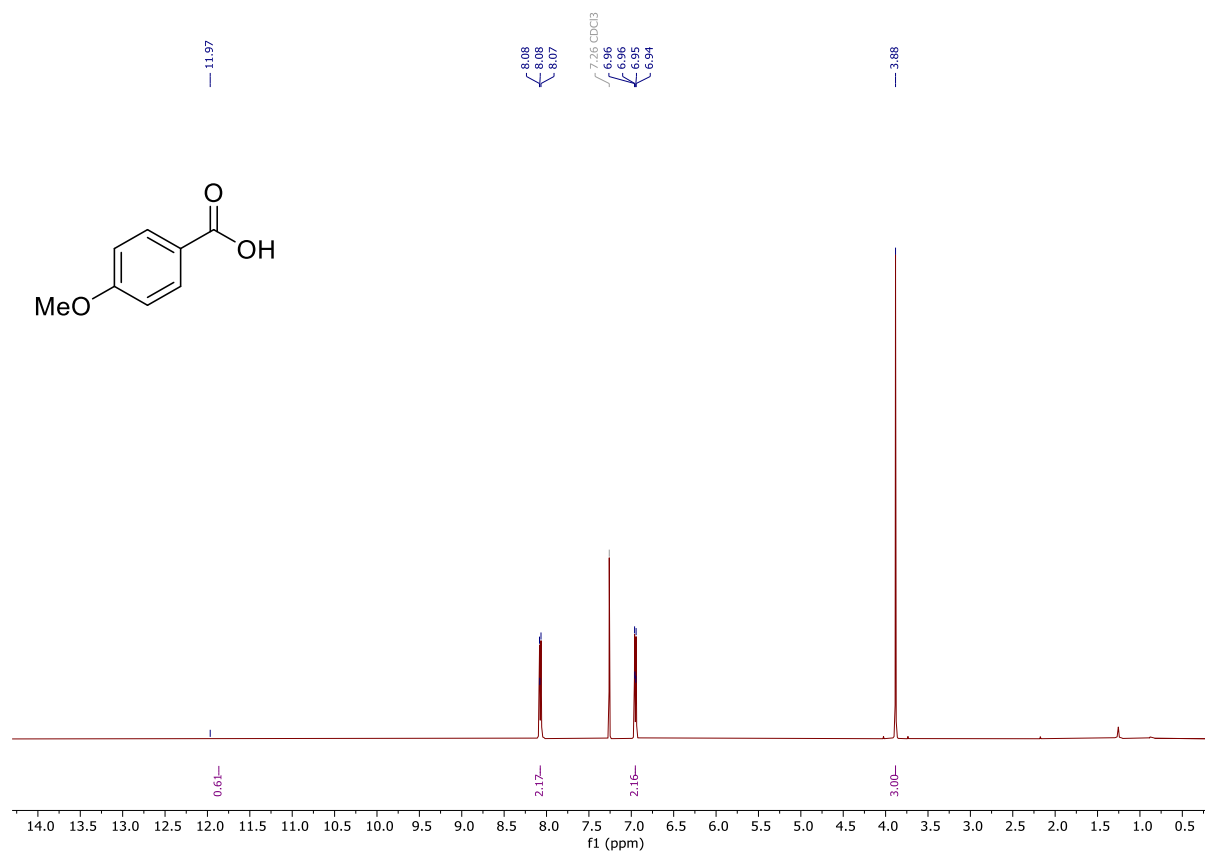
¹H NMR of 2b (500 MHz, CDCl₃):



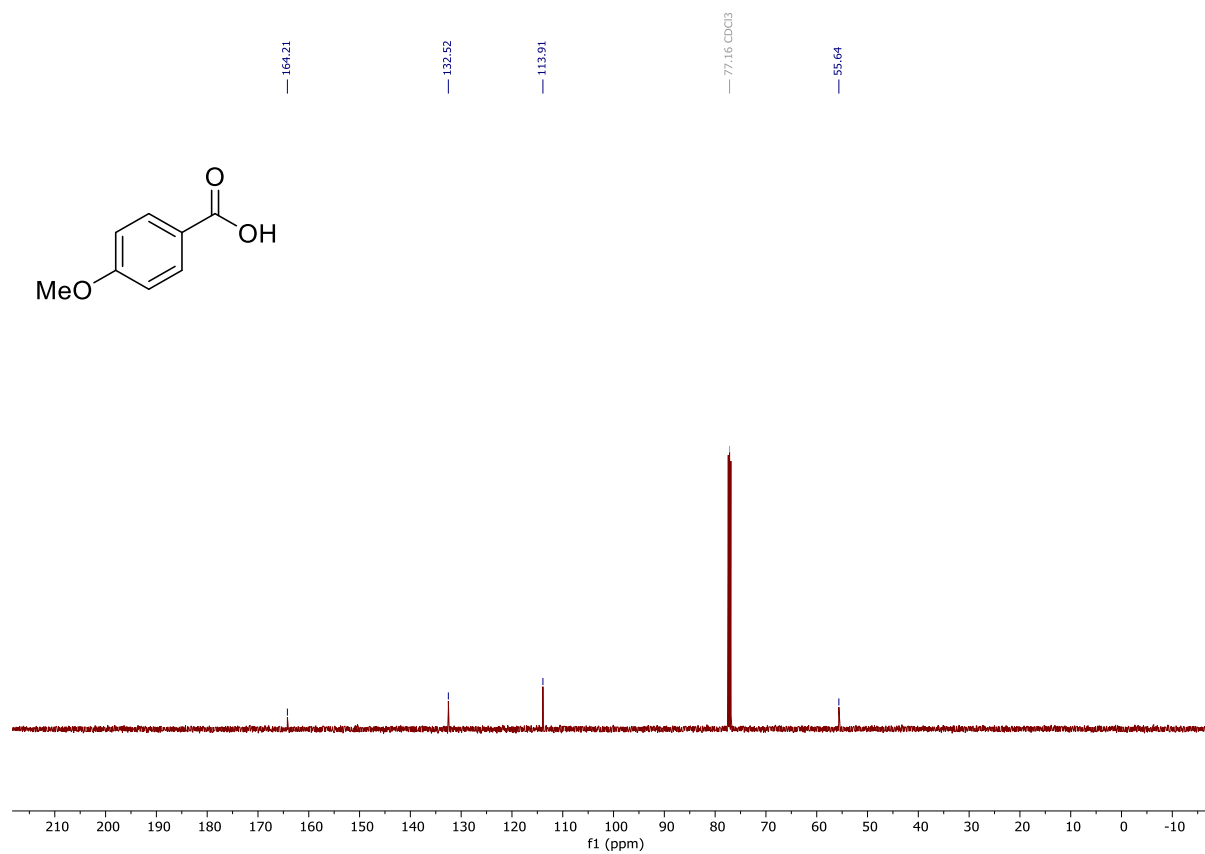
¹³C NMR of 2b (126 MHz, CDCl₃):



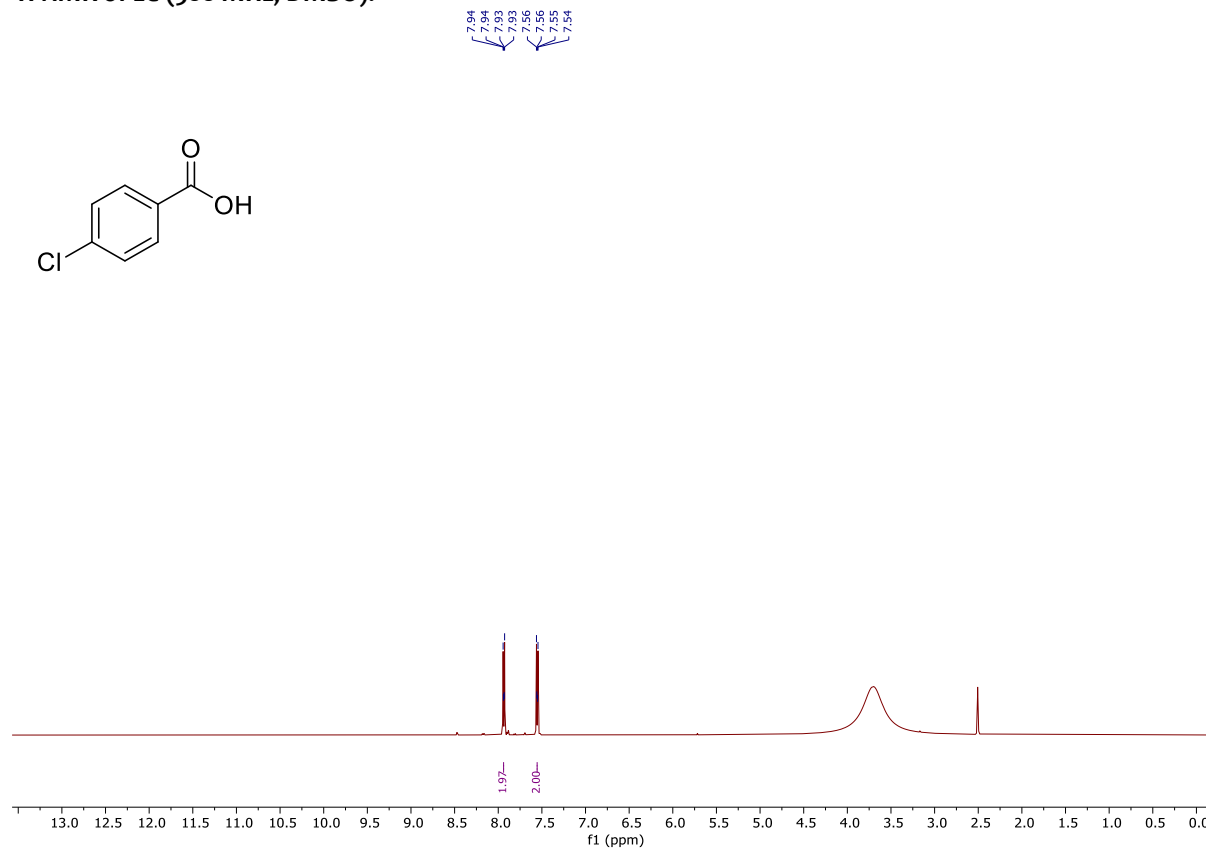
¹H NMR of 2c (500 MHz, CDCl₃):



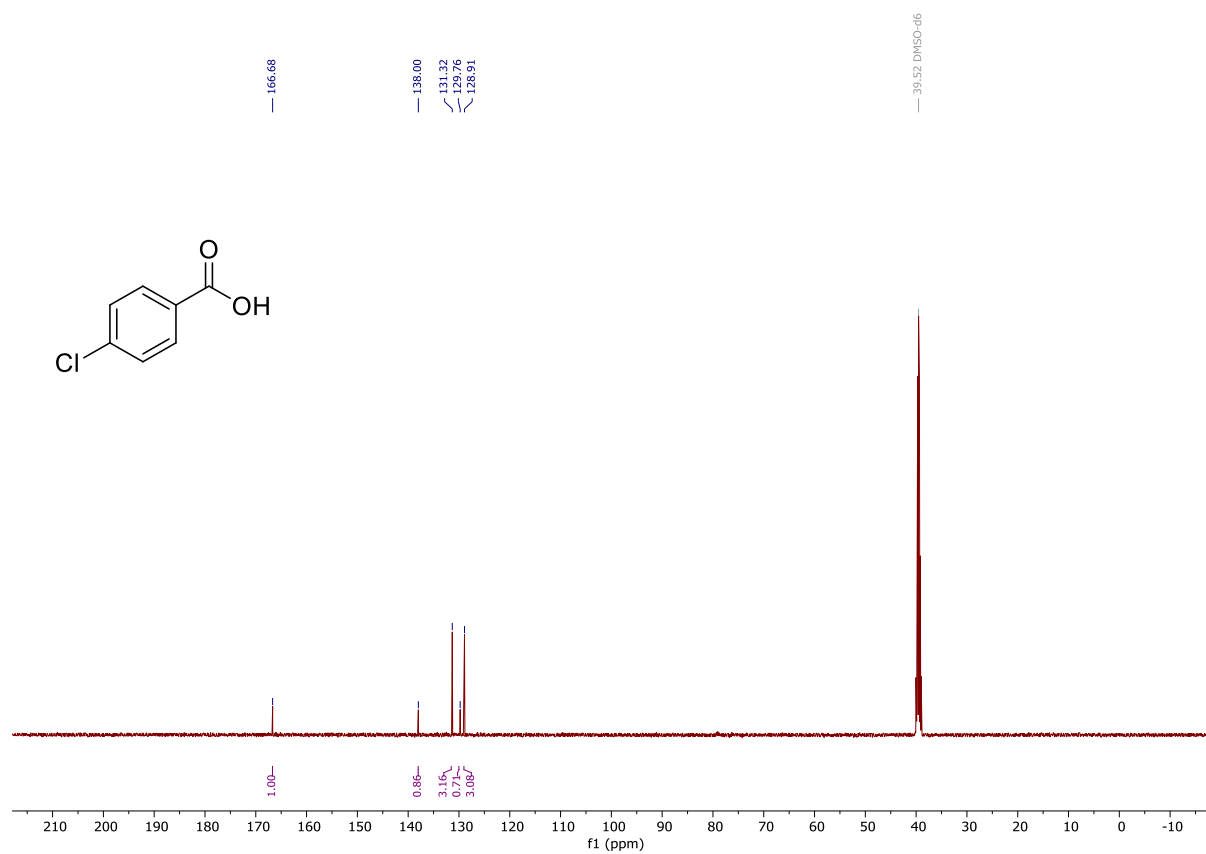
¹³C NMR of 2c (126 MHz, CDCl₃):



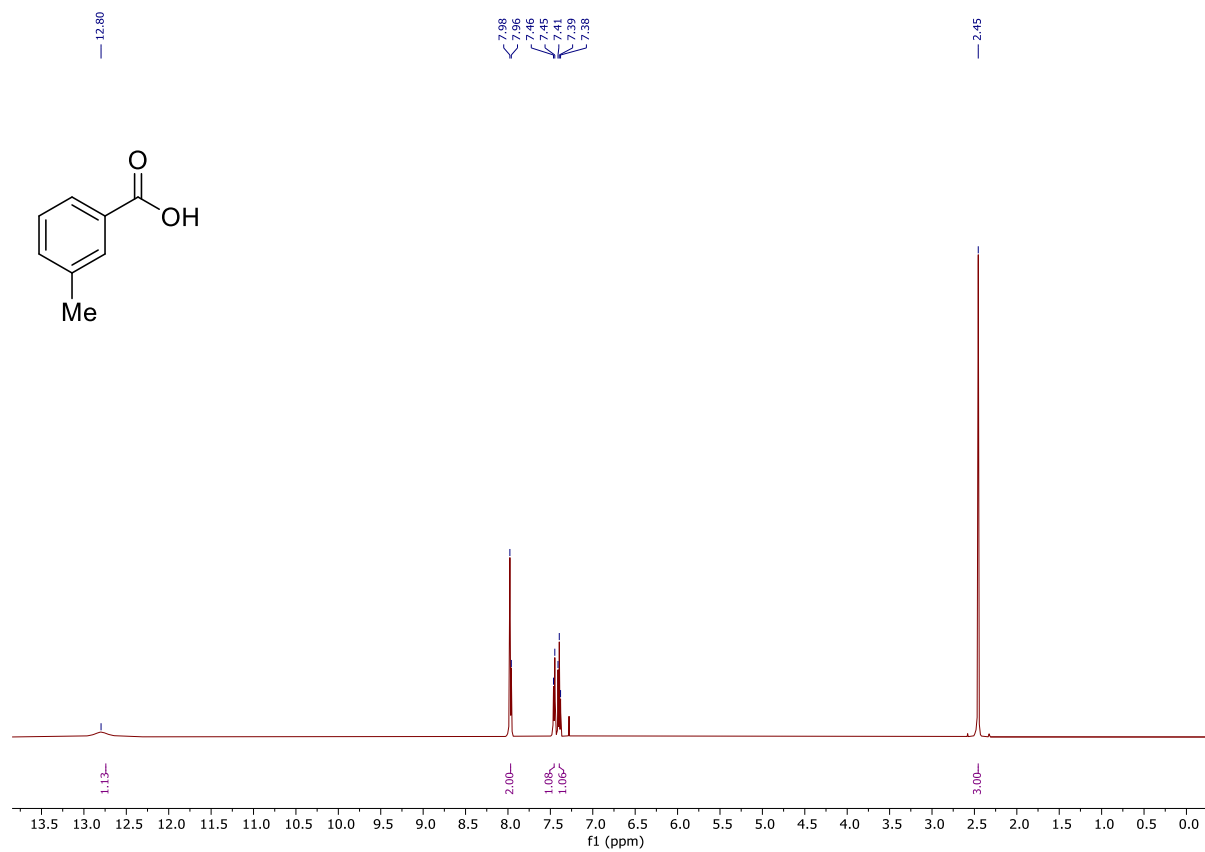
¹H NMR of 2e (500 MHz, DMSO):



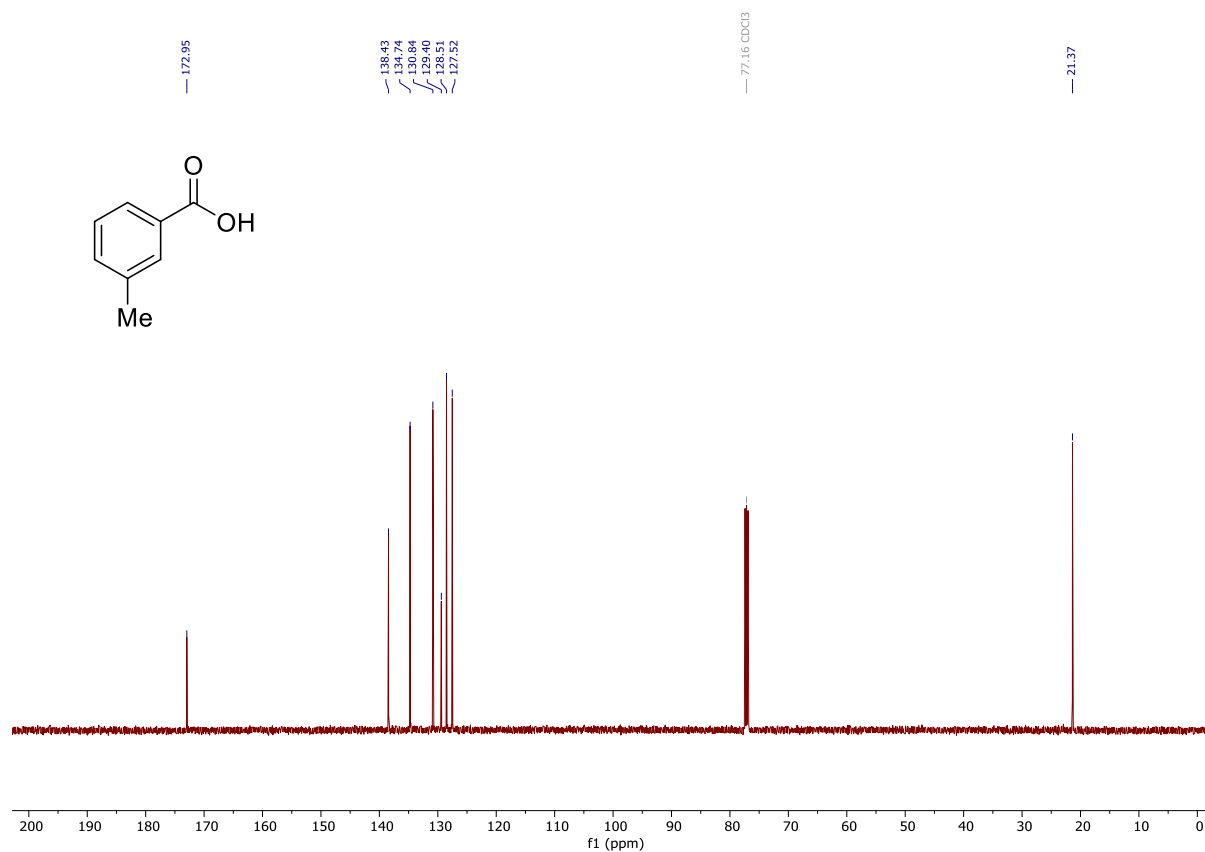
¹³C NMR of 2e (126 MHz, DMSO):



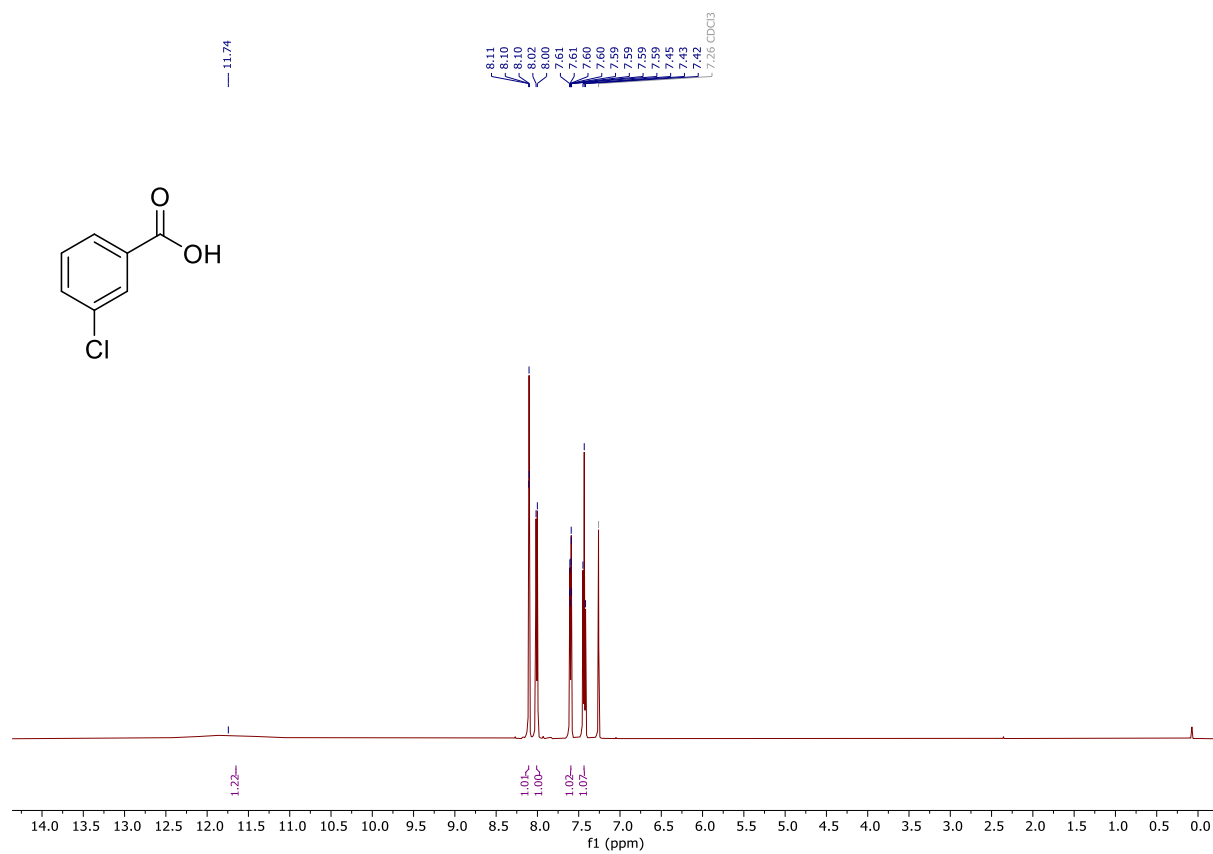
¹H NMR of 2g (500 MHz, CDCl₃):



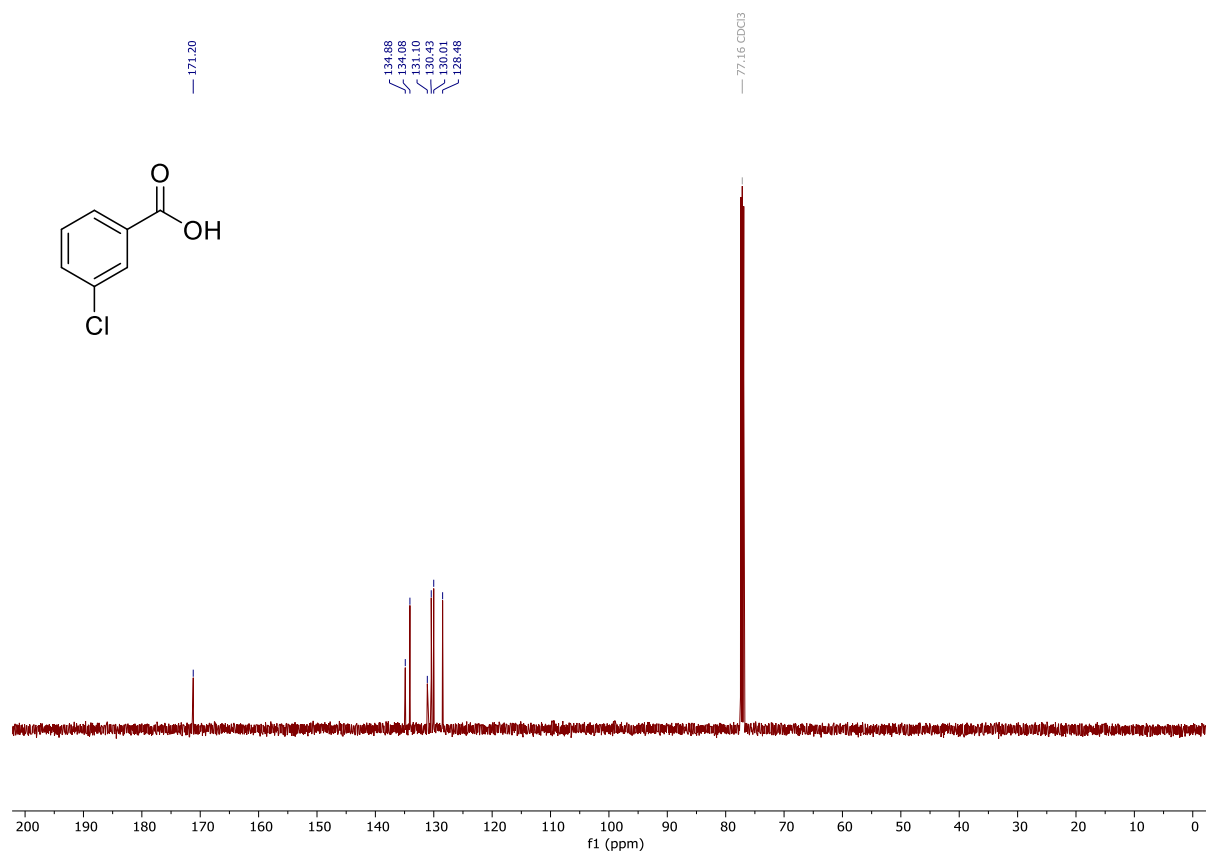
¹³C NMR of 2g (126 MHz, CDCl₃):



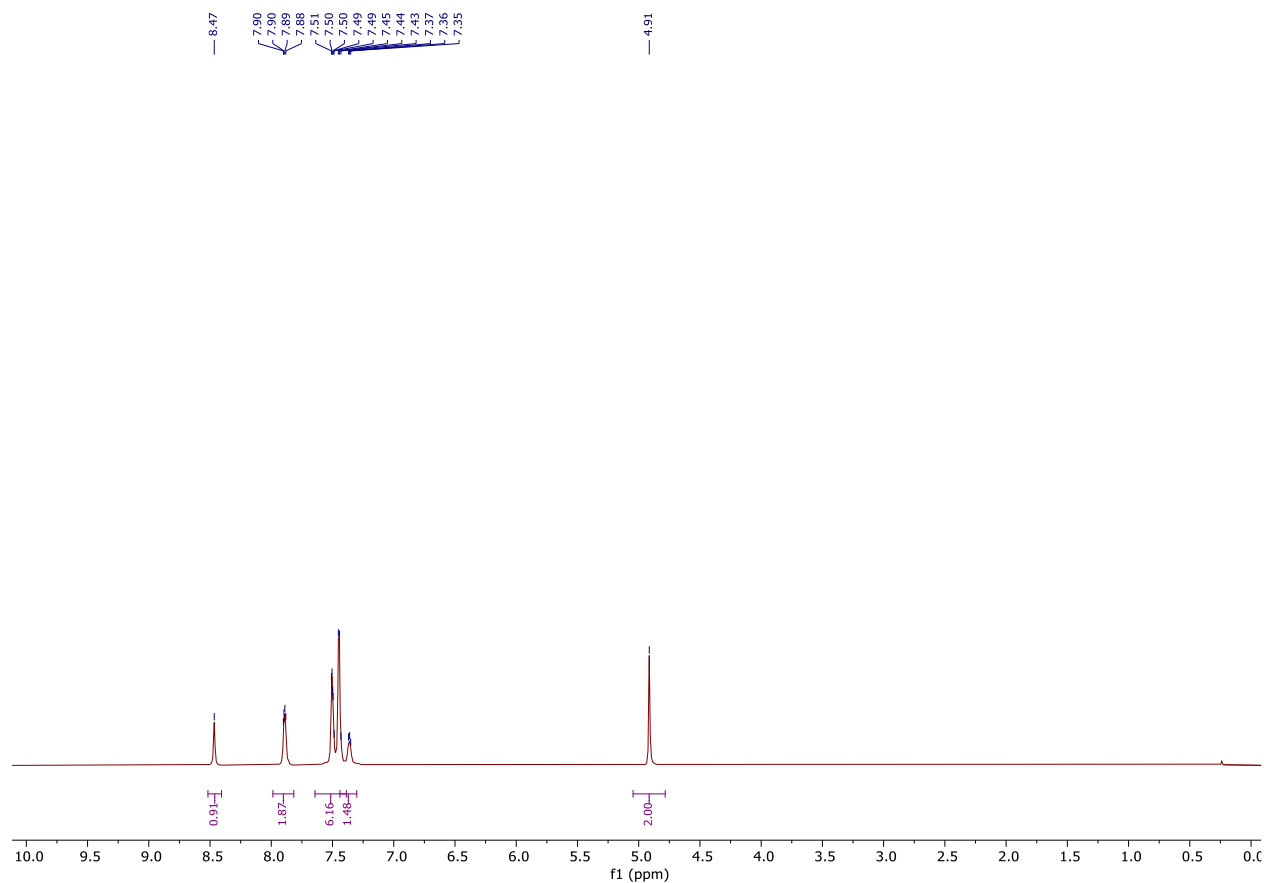
¹H NMR of 2h (500 MHz, CDCl₃):



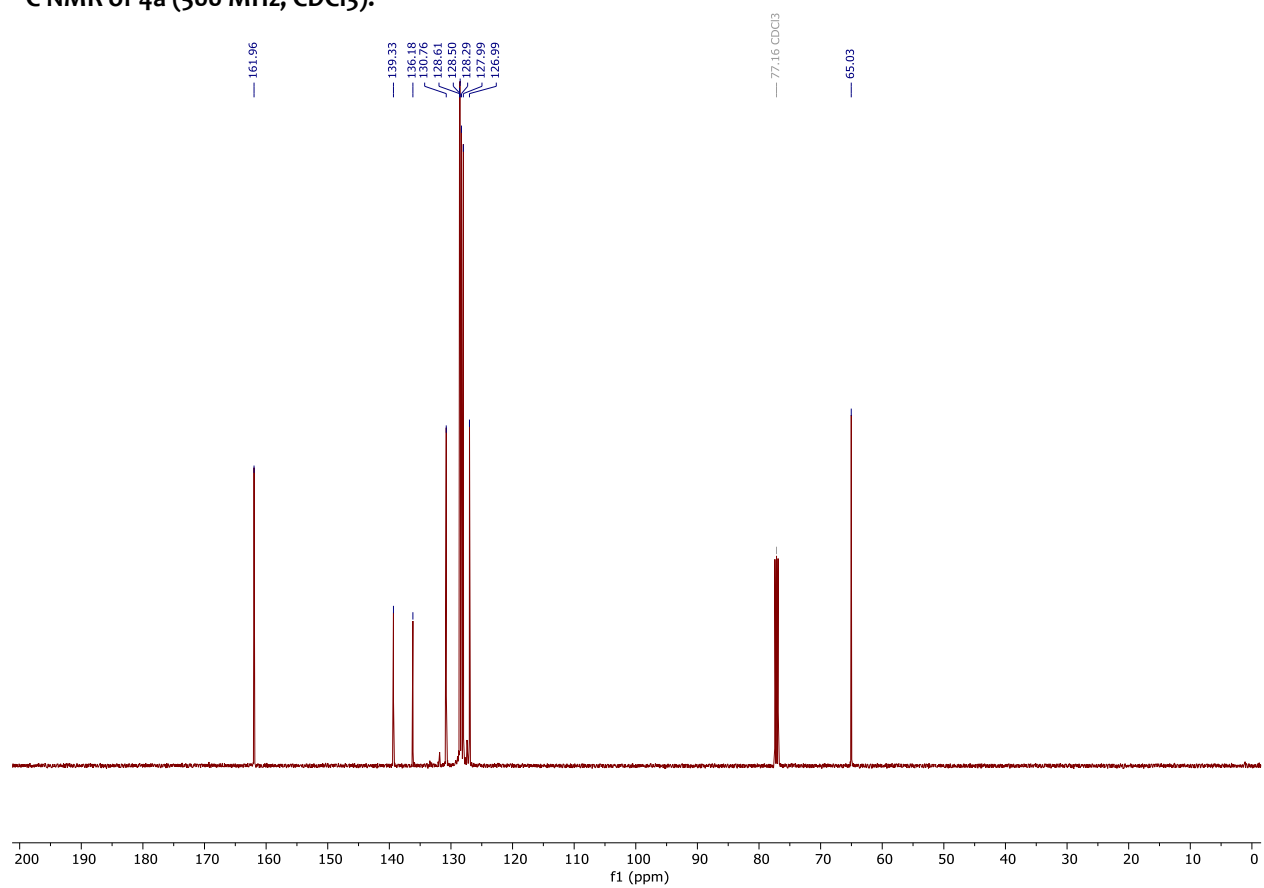
¹³C NMR of 2h (126 MHz, CDCl₃):



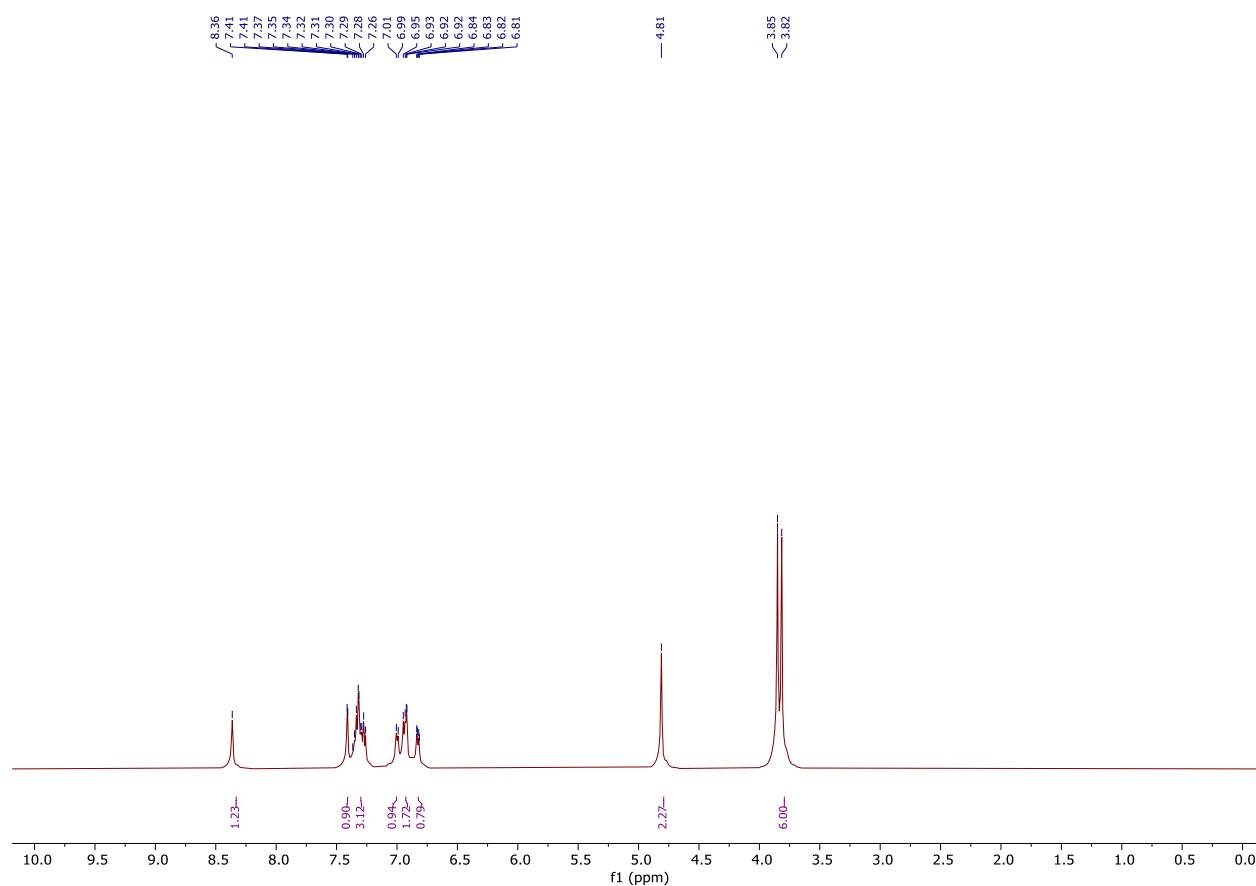
¹H NMR of 4a (500 MHz, CDCl₃):



¹³C NMR of 4a (500 MHz, CDCl₃):



¹H NMR of 4b (500 MHz, CDCl₃):



¹³C NMR of 4b (500 MHz, CDCl₃):

