CHAPTER 5

Lactic acid/ KI Catalyzed One-Pot Tandem Beckmann Rearrangement of Carbonyls in Metal-Free Condition

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5.1 Introduction

Amides are considered as an essential privileged structure in natural products and pharmaceutical compounds and also play a vital role in the elaborating protein and peptide synthesis. The organic compounds containing amide groups have broadly investigated due to industrial purpose for synthesizing color pigments, detergent, lubricants, cosmetics, treatment of drinking and sewage water and used in polymer chemistry for the lactam synthesis (Naik et al. 2015, Asif 2016, Carey et al. 2006, García et al. 2010, Pattabiraman et al. 2011, Hu et al. 2019). Some valuable commercial drugs which contain amide group are shown in **Figure 5.1.**

Traditionally amides are synthesized by coupling of ammonia with acid derivatives e.g., acid chloride, acid anhydride and esters etc. Hydrolysis of cyanide and transamidation are also important methods for the synthesis of amides derivatives (Dunetz et al. 2016, Gawande et al. 2013, Mylavarapu et al. 2007, Mishra et al. 2018). Different name reactions are also reported as the alternative methods for amide synthesis. Beckmann reaction is one of the most intriguing method due to its peculiar properties (Valizadeh et al. 2014, Eshghiet al. 2006, Reinares-Fisac et al. 2019, Tamaddon et al. 2007).

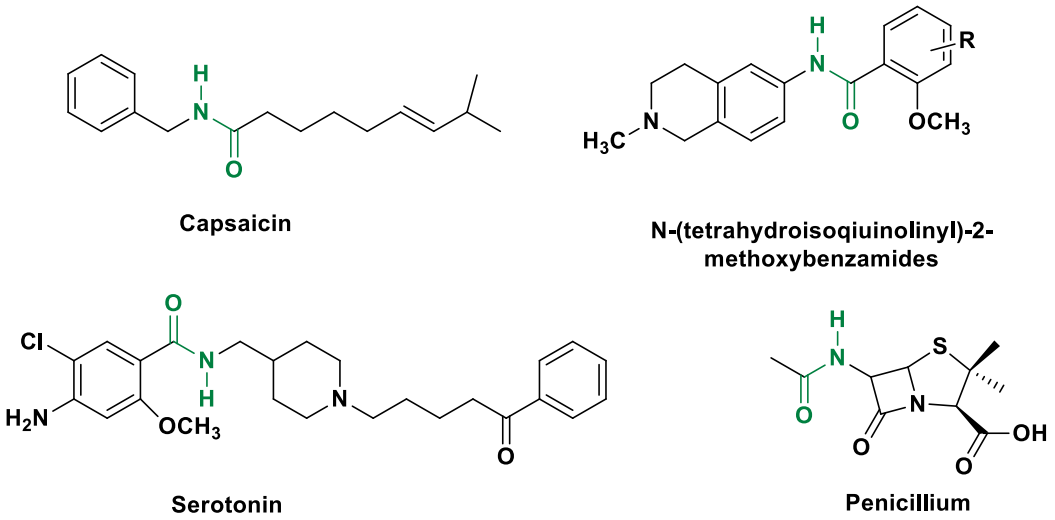


Figure 5.1 Some examples of bioactive substituted amides.

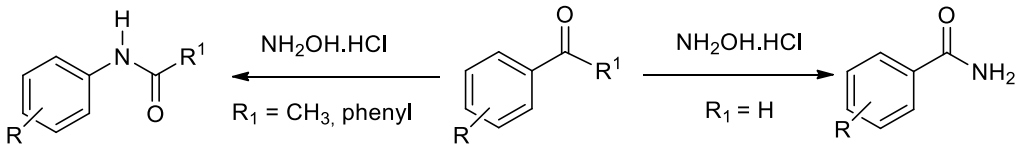
Beckmann reaction is generally catalyzed by strong lewis and bronsted acids at high temperature. A large variety of catalysts have been used for the synthesis of amides such as Al_2O_3/CH_3SO_3H (Sharghi et al. 2001), $(NH_4)_2S_2O_8$ (Mahajan et al. 2016), $SiO_2@H_2SO_4$ (Eshghi et al. 2007), SiO_2@HCOOH (Kuksenok et al. 2016), TsOH (Hyodo et al. 2018), Cs_2CO_3 (Wang et al. 2014), $FeCl_3$ (Gowda et al. 2011), $Sc(OTf)_3$ (Allam et al. 2011), Zn (Kumari et al. 2017), Cu(II) (Rezaei et al. 2017), Ru(II) (Kanchanadevi et al. 2015), Rh (Raja et al. 2014), Pd(II) (Rostamnia et al. 2016, Ali et al. 2010), nano-sulfated titania (Hosseini-Sarvari et al. 2011), Fe_3O_4 (KarimKoshteh et al. 2017), ionic liquid (Rani et al. 2016, Khalafi-Nezhad et al. 2014) etc. Some non-conventional microwave irradiation (Eshghi et al. 2003), ultrasound-assisted, electrochemical (Ke et al. 2019) and photocatalytic (Chen et al. 2019) methods have also been reported. Although, most of these

methods have their own benefits and drawbacks like harsh reaction conditions, expensive metallic catalysts, harmful non-volatile organic solvents, non-recyclability of catalyst, long reaction time, tedious reaction workup and low yield of the products. Considering the above facts, the development of an environmentally efficient and greener protocol for the synthesis of the amides is still in demand and we have directed our studies towards finding a suitable green catalystic system for the synthesis of primary and secondary amides.

Recently, green solvents (e.g. polyethylene glycol, fluorous compounds, ionic liquids, water) and bio-based solvents (fatty acid, ethyl lactate, glycerol, *p*-cymene) got much more attention due to eco-compatibility and sustainability of the reactions. In continuation of this, lactic acid is also used as solvent which is widely used in the agricultural, food, pharmaceutical, textile and cosmetic industries. Commercial lactic acid is produced naturally by fermentation of carbohydrates such as glucose, sucrose or lactose it is white, odorless, non-toxic bio-based weak acid pKa is 3.7, in solution lactic acid can lose a proton from the acidic group, producing the lactate ion $CH_3CH(OH)COO^-$. Recently, Bodireddy *et al.* has developed green and efficient multicomponent reactions (MCR) catalysed by lactic acid (Bodireddy et al. 2016, Gupta et al. 2015, Yu et al. 2016). Due to its unique properties, it is continuously used in organic synthesis as a catalyst as well as solvent.

Iodine containing molecules (such as molecular iodine, potassium iodide and sodium iodine) plays a vital role in organic synthesis due to its various benefits. Various

type of organic reaction e.g. Michael addition, Aldol reaction, esterification, one-pot multicomponent reactions and oxidation reactions etc. are catalyzed by iodine, KI or hypervalent iodine containing molecules (Chen et al. 2017, Song et al. 2015, Zhang et al. 2018, Yoshimura et al. 2013). Potassium iodide is less toxic, cheaper and environmental friendly as compare to molecular iodine. In view of the above, herein, we disclose the use of lactic acid/ KI as an efficient catalytic system for the synthesis of amides by one-pot tandem Beckmann rearrangement under metal and solvent free condition (**Scheme 5.1**).



Scheme 5.1 Conversion of aldehydes/ ketones to amides via Beckmann rearrangement

5.2 Results and discussion

5.2.1 Optimsation of reaction conditions

At the outset, Beckmann reaction of benzaldehyde (**1a**) was investigated with hydroxylamine hydrochloride (**2**) (molar ratio 1: 1.2) in the presence of KI/ lactic acid catalytic system in order to optimize reaction conditions. The consequences of different parameters including solvents, type of catalyst, catalyst loading, reaction temperature and reaction time were studied.

Several solvents were tested in the presence of KI/ lactic acid (0.5/1 equiv.) for the synthesis of benzamide. Reactions were performed in both polar protic (ethanol, methanol and water), polar aprotic (acetonitrile, dichloroethane) and also in non-polar solvents (xylene, toluene) at 80 ^{o}C. In case of polar solvents it gave (30-60%) yield of the product (**Table 5.1, entries 1-5**) while in case of non-polar solvents very poor yield only 10% was obtained (**Table 5.1, entries 6-7**). The results were not satisfactory and show that these solvents were not efficient for the conversion of carbonyl to amide in excellent yield. To our great delight, a significant improvement was observed when the reaction was proceeded without additional solvent at 80 ^{o}C reaction was completed in 2h with 90% yield of the product (3a) it indicates that the extent of conversion was independent of solvent (**Table 5.1, entry 8**). After optimizing solvents, different iodine containing compouds (molecular iodine, sodium iodide, lithium iodide and 2-iodoxybenzoic acid) in the presence of lactic acid were also applied for the amide synthesis and we got (10-60%) yield of the product in 5 h (**Table 5.1, entries 12-15**). The results indicate that KI/ lactic acid found the best catalytic system (**Table 5.1, entry 9)**.

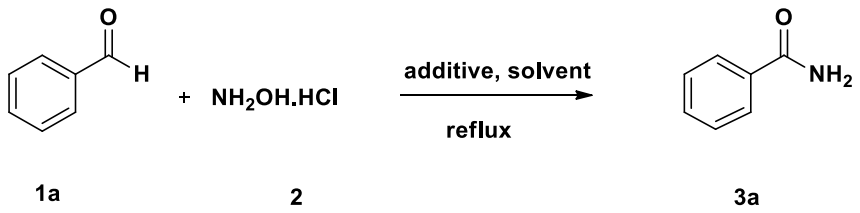
In order to optimize the amount of the catalyst we started optimization of catalyst KI with 1 equiv. of lactic acid, the first experiment was carried out in the absence of KI and the reaction did not afford the final product (3a) and stopped after intermediate formation (oxime) (**Table 5.1, entry 11**). Next we increased the amount of KI (0.2-0.7 equiv.) and got 45-91% yield of the product in 2h. These results show that increasing the amount of KI from 0 to 0.5 equiv affects the yield of amide, but further any increment in

the amount of KI from 0.5 to 0.7 did not make any significant difference in the yield of the product (**Table 5.1, entries 16-18**). Next the amount of the lactic acid was also optimized (0.5-2 equiv.) with 0.5 equiv. of KI, in the absence of lactic acid no product was obtained (**Table 5.1, entry 10**) and the best result was obtained when the reaction was performed with 1 equiv. of lactic acid (**Table 5.1, entry 8**). This also shows that tuning of the equivalent of KI and lactic acid had an effect on the yield of 3a and it is essential for this reaction (**Table 5.1, entry 19, 20**).

To find out the effect of temperature, the model reaction was carried out at different temperatures by using KI/ lactic acid (0.5/1 equiv.). At room temperature, no desired product was obtained but the yield of the product (3a) was improved as the temperature was increased (40-80^{0}C) and observed maximum yield 90% at 80^{0}C. Further increase in temperature did not improve the yield of the product (**Table 5.1, entries 21-24**).

The results show a combination of lactic acid and KI was found efficient to catalyze Beckmann reaction in a high yield. So the optimized conditions for Beckmann reaction is benzaldehyde (1.0 mmol), hydroxylamine hydrochloride (1.2 mmol) in the presence of KI/ lactic acid (0.5/1equiv.) catalytic system at 80 ^{0}C was the optimum condition for the synthesis of benzamide.

Table 5.1 Optimization of different reaction conditions on the yield of 3a[a]



1a 2 3a

Entry	Solvent	Catalyst (equiv.)	Time (h)	Temp.	Yield[%][b]
1	Acetonitrile	KI /Lactic acid (0.5/1)	5	80	30
2	Dichloro-Methane	KI /Lactic acid (0.5/1)	5	80	30
3	Ethanol	KI /Lactic acid (0.5/1)	3	80	40
4	Methanol	KI /Lactic acid (0.5/1)	3	80	32
5	Water	KI /Lactic acid (0.5/1)	3	80	60
6	Xylene	KI /Lactic acid (0.5/1)	5	80	10
7	Toluene	KI /Lactic acid (0.5/1)	5	80	10
8	-	KI /Lactic acid (0.5/1)	2	80	90
9	-	-	2	80	NR
10	-	KI (0.5)	2	80	NR
11	-	Lactic acid (1)	2	80	NR
12	-	I_2/Lactic acid (0.5/1)	5	80	30
13	-	LiI/Lactic acid (0.5/1)	5	80	10

14	-	NaI/ Lactic acid (0.5/1)	5	80	10
15	-	IBX /Lactic acid (0.5/1)	5	80	60
16	-	KI/ Lactic acid (0.2/1)	5	80	45
17	-	KI/ Lactic acid (0.4/1)	5	80	80
18	-	KI /Lactic acid (0.7/1)	2	80	91
19	-	KI /Lactic acid (0.5/0.5)	2	80	40
20	-	KI /Lactic acid (0.5/2)	2	80	90
21	-	KI/ Lactic acid (0.5/1)	2	RT	NA
22	-	KI /Lactic acid (0.5/1)	2	40	30
23	-	KI/ Lactic acid (0.5/1)	2	60	67
24	-	KI/ Lactic acid (0.5/1)	2	100	90

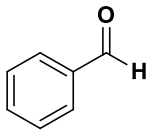
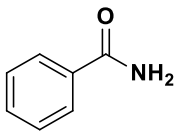
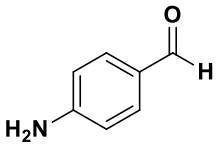
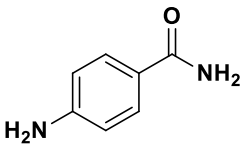
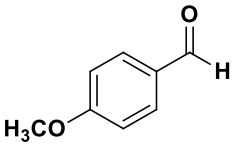
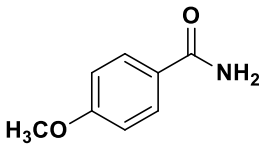
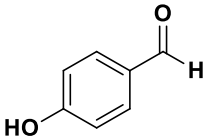
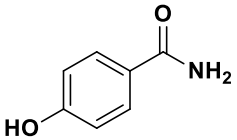
[a] **Reaction condition:**Benzaldehyde **1a** (1.0 mmol), hydroxylamine hydrochloride **2** (1.2 mmol) in 0.2 mL solvents and with different catalytic system. [b] Isolated yield.

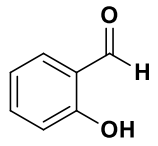
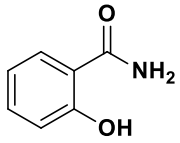
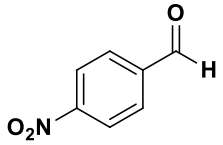
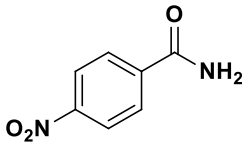
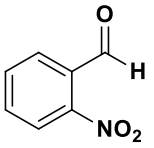
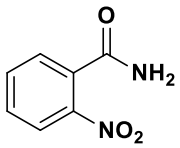
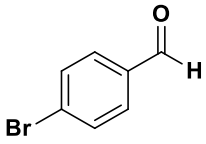
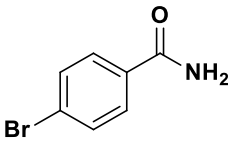
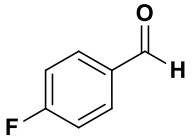
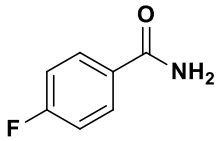
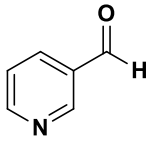
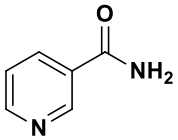
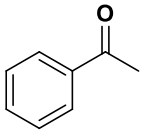
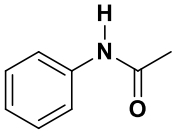
5.2.2. Substrate Scope

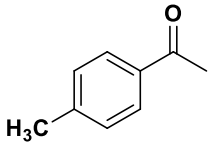
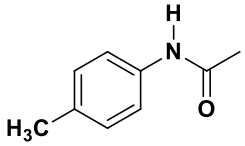
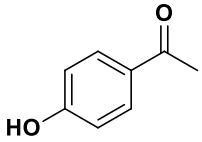
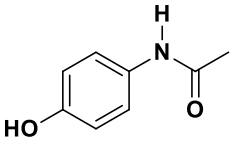
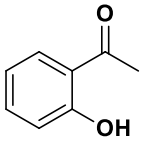
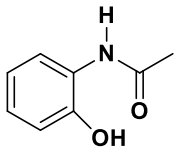
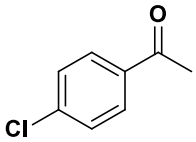
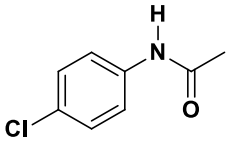
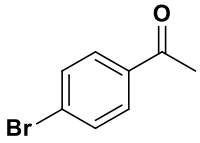
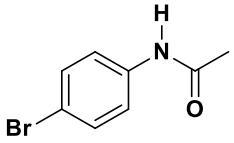
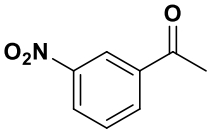
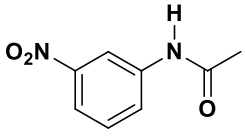
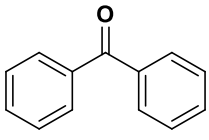
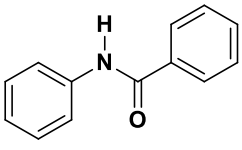
With the established optimized reaction conditions in hand, we examined the scope and compatibility of the aromatic aldehydes such as benzaldehyde (**1a**), 4-aminobenzaldehyde (**1b**), 4-methoxybenzaldehyde (**1c**), 4-hydroxybenzaldehyde (**1d**), 2-hydroxybenzaldehyde (**1e**), 4-nitrobenzaldehyde (**1f**), 2-nitrobenzaldehyde (**1g**), 4-bromobenzaldehyde (**1h**), 4-fluorobenzaldehyde (**1i**) and nicotinaldehyde (**1j**) gave corresponding primary amide benzamide (**3a**), 4-aminobenzamide (**3b**),

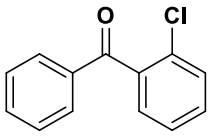
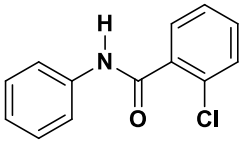
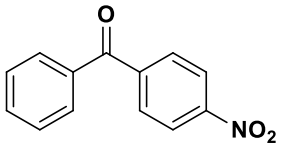
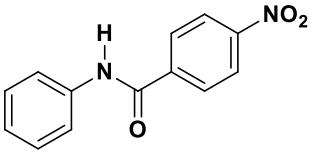
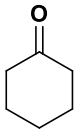
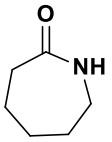
4-methoxybenzamide (**3c**), 4-hydroxybenzamide (**3d**), 2-hydroxybenzamide (**3e**), 4-nitrobenzamide (**3f**), 2-nitrobenzamide (**3g**), 4-bromobenzamide (**3h**), 4-fluorobenzamide (**3i**) and nicotinamide (**3j**) in good to excellent yield. Aromatic aldehyde containing electron-withdrawing group gave the desired product in excellent yield in shorter reaction time than the electrondonating groups (**Table 5.2**).

Table 5.2 Synthesis of substituted primary and secondary amides[a]

Entry	Reactant	Product	Time (h)	Yield [%][b]
1	 1a	 3a	2	90
2	 1b	 3b	2.5	86
3	 1c	 3c	2.5	85
4	 1d	 3d	2.5	88

5	 1e	 3e	2.5	87
6	 1f	 3f	2	90
7	 1g	 3g	2	91
8	 1h	 3h	2	89
9	 1i	 3i	2	87
10	 1j	 3j	2.5	84
11	 1k	 3k	2.5	92

12	 1l	 3l	2.5	90
13	 1m	 3m	2.5	88
14	 1n	 3n	2.5	87
15	 1o	 3o	2	85
16	 1p	 3p	2	87
17	 1q	 3q	2	89
18	 1r	 3r	2	87

19	 1s	 3s	2	88
20	 1t	 3t	2	89
21	 1u	 3u	2.5	85

[a]**Reaction conditions**: Aromatic aldehydes/ ketones **1** (1.0 mmol), hydroxylamine hydrochloride **2** (1.2 mmol) and KI /Lactic acid (0.5/1equiv.) were heated at 80 ^{0}C. [b] Isolated yield.

Due to the achievement of the above methodology in primary amide synthesis, this methodology was also applied for the synthesis of a secondary amides from ketones. Various aromatic ketone such as acetophenone (**1k**) *p*-methylacetopheone (**1l**), *p*-hydroxyacetophenone (**1m**), *o*-hydroxyacetophenone (**1n**), *p*-chloroacetophenone (**1o**), *p*-bromoacetophenone (**1p**), *m*-nitroacetophenone (**1q**), benzophenone (**1r**), 2-chlorobenzophenone (**1s**), 4-nitrobenzophenone (**1t**) and aliphatic cyclic ketone cyclohexanone gave secondary amides *N*-phenylacetamide (**3k**), *N*-(p-tolyl)acetamide (**3l**), *N*-(4-hydroxyphenyl)acetamide (**3m**), *N*-(2-hydroxyphenyl)acetamide (**3n**), *N*-(4-chlorophenyl)acetamide (**3o**), *N*-(4-bromophenyl)acetamide (**3p**), *N*-(3-nitrophenyl)acetamide (**3q**), *N*-phenylbenzamide (**3r**), (2-chlorophenyl)(phenyl)methanone

(**3s**), (4-nitrophenyl)(phenyl)methanone (**3t**), azepan-2-one (**3u)** respectively in excellent yield. Acetophenone derivatives with electron-donating and electron-withdrawing substituents could be accommodated to afford amides in excellent yields (85–92%) (**Table 5.2 entries 11-21**).

5.2.3 Appilcation of this methodology (Synthesis of Paracetamol and caprolactum)

To demonstrate the utility of this mild method, we accomplish the synthesis of Paracetamol, a commercial analgesics and antipyretics is used for the treatment of pain and fever directly from aldehyde. Excitingly 4-hydroxy acetophenone gave 88% of the Paracetamol (**3m**) under the optimized conditions in 2h. This methodology is also useful for the synthesis of caprolactum (**3u**), yield 85 % in 2.5h from cyclohexanone which is used for the synthesis of polymer Nylon 6 and several medicinally active drugs such as pentylenetetrazol, meptazinol and laurocapram etc. These examples illustrate the potential synthetic utility of this method.

5.2.4 Plausible reaction Mechanism

A plausible reaction pathway for the conversion of carbonyl derivatives into the corresponding amides is outlined in (**Figure 5.2**). Firstly, combination of lactic acid and KI gives hydrogen iodide, which polarizes the carbonyl group that facilitates the reaction with hydroxylamine hydrochloride and gave oxime (**I**), which upon dehydration produces cyanide (**II**) and then the hydrolysis of cyanide gives amide derivatives **(3**).

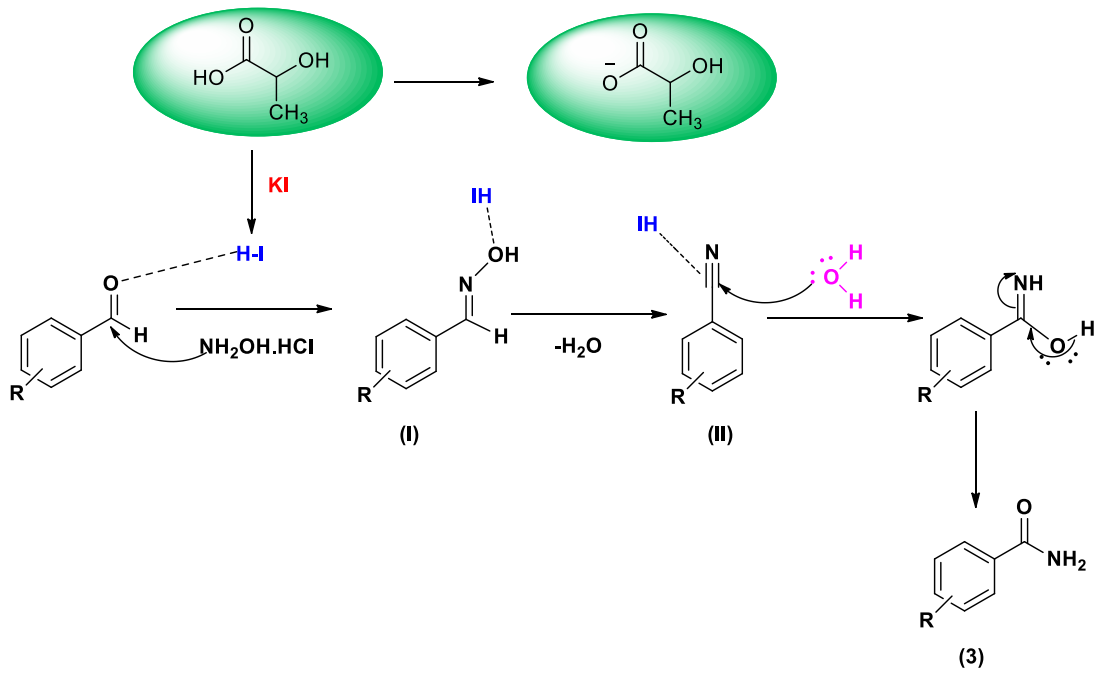


Figure 5.2 A plausible reaction pathway for the conversion of aldehyde derivatives to amides.

5.3 Experimental section

5.3.1 General procedure for the synthesis of amides

A mixture of aldehyde/ketone (1.0 mmol), hydroxylamine hydrochloride (1.2 mmol) and KI/ lactic acid (0.5/1equiv) was stirred at 80 ^{0}C for the appropriate time. The progress of reaction was monitored by thin-layer chromatography (n hexane: ethyl acetate). After completion, the reaction mixture was allowed to cool to room temperature and diluted with ethylactate and washed with water, organic layer was dried over sodium sulfate, concentrated and purified through column chromatography (Hexane: ethyl acetate).

5.4 Analytical data

5.4.1 Analytical data of primay and secondary amide

Benzamide (3a) Yield 90 %; White solid; m.p. 128-129 ^{0}C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 7.80 -7.79 (d, 2H) 7.50-7.49 (t, 1H), 7.44-7.41 (t, 2H), 6.20 (s, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ (ppm): 169.59, 133.35, 131.96, 128.59, 127.31.

4-Aminobenzamide (3b) Yield 86 %; White solid; m.p.180- 181 ^{0}C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ (ppm): 7.62-7.61 (d, 2H), 6.90 (s, 2H), 6.55-6.54 (d, 2H), 5.60 (s, 1H, NH_2); **^{13}C NMR** (125 MHz, DMSO-d_6) δ (ppm): 168.30, 151.74, 129.23, 121.00, 112.60.

4-Methoxybenzamide (3c) Yield 85 %; White solid; m.p. 166-167 ^{0}C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ (ppm): 7.77-7.75 (d, 2H), 6.92-6.90 (d, 2H), 3.83 (s, 3H), 1.64 (s, 2H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ (ppm): 169.59, 163.30, 129.97, 126.27, 114.50, 56.12.

4-Hydroxybenzamide (3d) Yield 88 %; White solid; m.p. 161-162 ^{0}C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ (ppm): 9.94 (s, 1H, OH), 7.74-7.74 (d, 2H), 7.07 (s, 2H), 6.78-6.77 (d, 2H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ (ppm): 167.27, 159.73, 129.05, 124.56, 114.26.

2-Hydroxybenzamide (3e) Yield 87 %; White solid; m.p. 140-141 ^{0}C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ (ppm): 12.91 (s, 1H, OH), 8.37 (s, 2H, NH_2) 7.82-7.80(t, 1H), 7.40-7.37 (m, 1H), 6.88- 6.85 (t, 2H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ (ppm): 171.8, 160.63, 134.02, 128.00, 118.40, 117.24, 114.28.

4-Nitrobenzamide (3f) Yield 90 %; White solid; m.p. 199-201 ^{0}C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ (ppm): 8.30-8.29 (d, 2H), 8.10-8.08 (d, 2H), 7.72 (s, 2H**)**; **^{13}C NMR** (125 MHz, DMSO-d_6) δ (ppm): 165.67, 148.54, 139.47, 128.38, 122.92.

2-Nitrobenzamide (3g) Yield 91 %; White solid; m.p. 176-177 ^{0}C; **^{1}H NMR** (125 MHz, DMSO-d_6) δ (ppm): 8.15 (s, 2H), 8.00-7.99 (d, 1H), 7.78-7.75(t, 1H), 7.69-7.63(m, 2H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ (ppm): 166.66, 146.73, 132.83, 132.07, 130.12, 128.33, 123.44.

4-Bromobenzamide (3h) Yield 89 %; White solid; m.p. 190-191 ^{0}C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 7.81-7.80 (d, 2H), 7.67-7.65 (d, 2H), 7.45 (s, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ (ppm): 166.42, 132.89,130.73, 129.09, 124.50.

4-Fluorobenzamide (3i) Yield 87 %; White solid; m.p. 155-156 ^{0}C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.18 (s, 2H), 7.60-7.57 (d, 2H), 7.09-7.07 (d, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ (ppm): 164.57, 149.66, 128.92, 127.97, 115.58.

Picolinamide (3j) Yield 84 %; White solid; m.p. 110-112 ^{0}C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 9.04 (s, 2H), 8.70-8.69 (d, 1H), 8.21-8.17 (m, 1H), 7.61 (s, 4H), 7.50-7.47(d, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ (ppm): 166.00, 151.39, 148.19, 134.65, 129.18, 122.89.

N-Phenylacetamide (3k) Yield 92 %; White solid; m.p. 114-115 ^{0}C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 7.62 (s, 1H), 7.43-7.42 (d, 2H), 7.24-7.21 (t, 2H), 7.04-7.02(t, 1H), 2.08

(s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ (ppm): 168.82, 137.96, 128.76, 124.26, 120.25, 24.29.

N-(p-Tolyl)acetamide (3l) Yield 90 %; White solid; m.p. 152-153 ^{0}C; **^{1}H NMR** (500 MHz $CDCl_3$) δ (ppm): 7.45 (s, 1H), 7.35-7.34 (d, 2H), 7.09-7.07 (d, 2H), 2.28 (s, 3H), 2.12(s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ (ppm): 168.82, 137.89, 128.76, 124.26, 120.25, 24.29.

N-(4-Hydroxyphenyl)acetamide (3m) Yield 88 %; White solid; m.p. 169-170 ^{0}C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ (ppm): 9.71 (s, 1H), 9.38 (s, 1H), 7.29-7.27 (d, 2H), 6.67-6.65 (d, 2H), 1.96 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ (ppm): 168.32, 153.12, 130.68, 121.18, 115.04, 23.49.

N-(2-Hydroxyphenyl)acetamide (3n) Yield 87 %; White solid; m.p. 207-208 ^{0}C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 7.50-7.47 (d, 1H), 7.45-7.44 (d, 1H), 7.12-7.08 (d, 1H) 7.08- 6.98 (d, 1H), 2.60 (s, 3H), 2.02 (s, 1H), 1.22 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ (ppm): 171.16, 155.52, 154.10, 134.88, 127.26, 120.60, 119.68, 115.49, 21.02.

N-(4-Chlorophenyl)acetamide (3o) Yield 85 %; White solid; m.p. 178-179 ^{0}C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 7.39-7.37 (d, 2H), 7.21-7.20 (d, 2H), 2.11(s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ (ppm): 168.25, 151.02, 136.40, 129.00, 121.04, 24.56.

N-(4-Bromophenyl)acetamide (3p) Yield 87 %; White solid; m.p. 168-169 ^{0}C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ (ppm): 10.07 (s, 1H), 7.57-7.45 (d, 4H), 2.03 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ (ppm): 168.04, 138.19, 131.00, 120.39, 114.03, 23.54.

N-(3-Nitrophenyl)acetamide (3q) Yield 94 %; White solid; m.p. 155-156 ^{0}C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.34 (s, 1H), 7.94-7.92 (s, 1H), 7.69 (s, 1H), 7.46 (t, 1H), 2.22 (s, 3H), 1.64 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ (ppm): 168.77, 148.61, 138.65, 129.49, 125.49, 125.03, 118.72, 118.72, 114.31, 24.25.

N-Phenylbenzamide (3r) Yield 89 %; White solid; m.p. 162-163 ^{0}C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 7.86-7.84 (d, 3H), 7.63-7.62 (d, 2H), 7.55-7.52 (t, 1H), 7.48-7.45(t, 2H), 7.37-7.34 (t, 2H), 7.15-7.12 (t, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ (ppm): 165.74, 137.90, 135.00, 131.83, 129.09, 128.78, 127.00, 124.57, 120.19.

N-(2-Chlorophenyl)benzamide (3s) Yield 87%; White solid; m.p. 97-98 ^{0}C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ (ppm): 8.58-8.59 (d, 1H), 8.45 (s, 1H), 7.93-7.91(t, 2H), 7.59-7.57(m, 1H), 7.53-7.50 (t, 2H), 7.42-7.41 (d, 1H), 7.35-7.32 (t, 1H), 7.10-6.99 (t, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ (ppm): 165.26, 134.73, 134.61, 132.17, 129.01, 128.93, 127.87, 127.07, 124.73, 121.49.

N-(4-Nitrophenyl)benzamide (3t) Yield 89 %; White solid; m.p. 97-98 ^{0}C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ (ppm): 8.27-8.26 (d, 2H), 8.07-8.05 (d, 2H), 7.98-7.96 (m, 1H), 7.56-7.55 (d, 1H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ (ppm): 165.25, 159.37, 157.31, 135.23, 127.58, 121.99, 115.54.

azepan-2-one (3u) Yield 85 %; White solid; m.p. 54-56 ^{0}C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ (ppm): 7.52 (s, 1H), 3.19-3.16 (m, 2H), 2.21 (t, 2H), 1.72-1.60 (m, 4H). **^{13}C NMR** (125 MHz, DMSO-d_6) δ (ppm): 172.9, 42.0, 31.4, 22.1, 20.8

5.5 Spectral data of few products

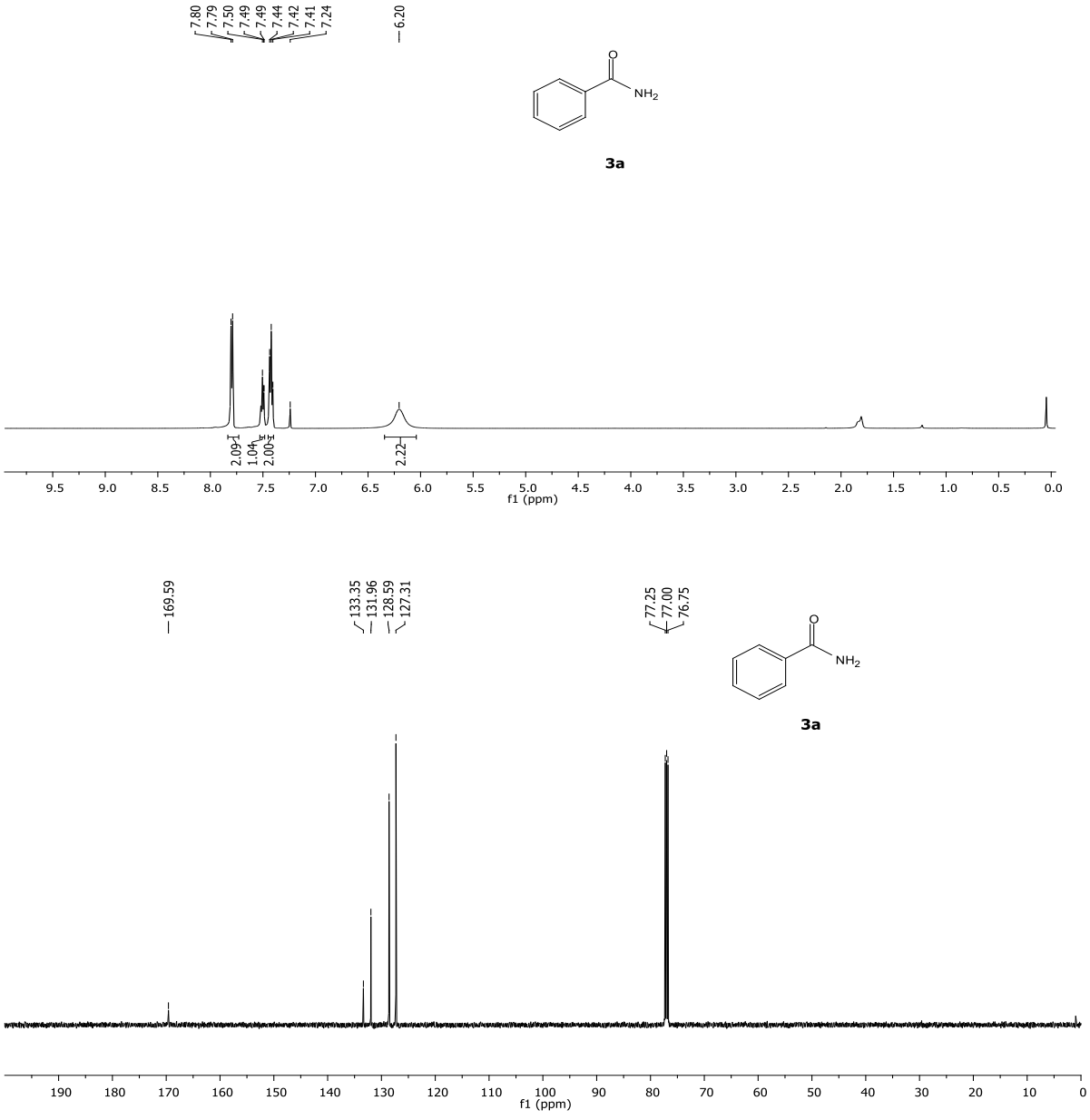


Figure 5.3 ^{1}H and ^{13}C NMR of benzamide (3a)

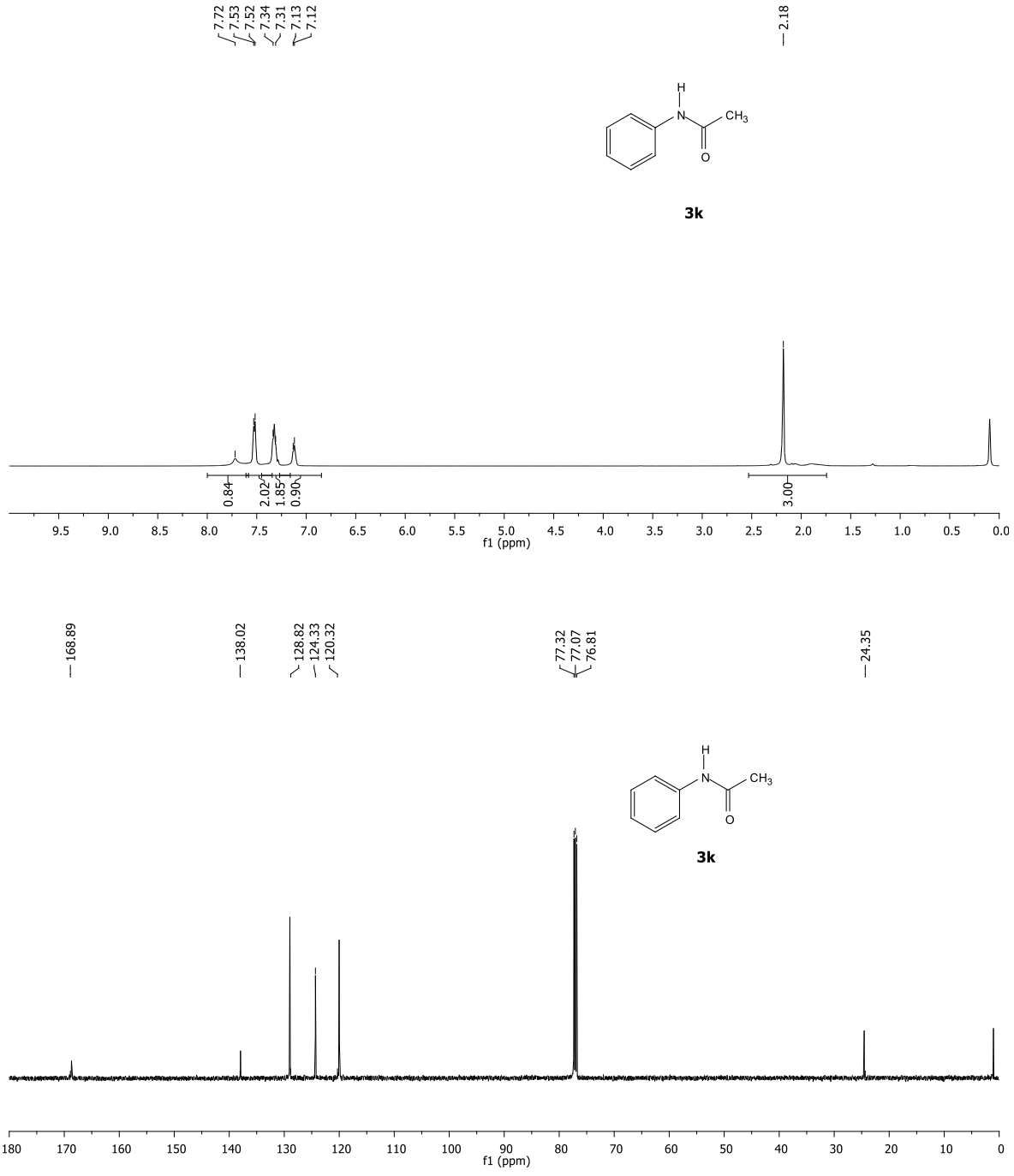


Figure 5.4 ^{1}H and ^{13}C NMR of *N*-Phenylacetamide (3k)

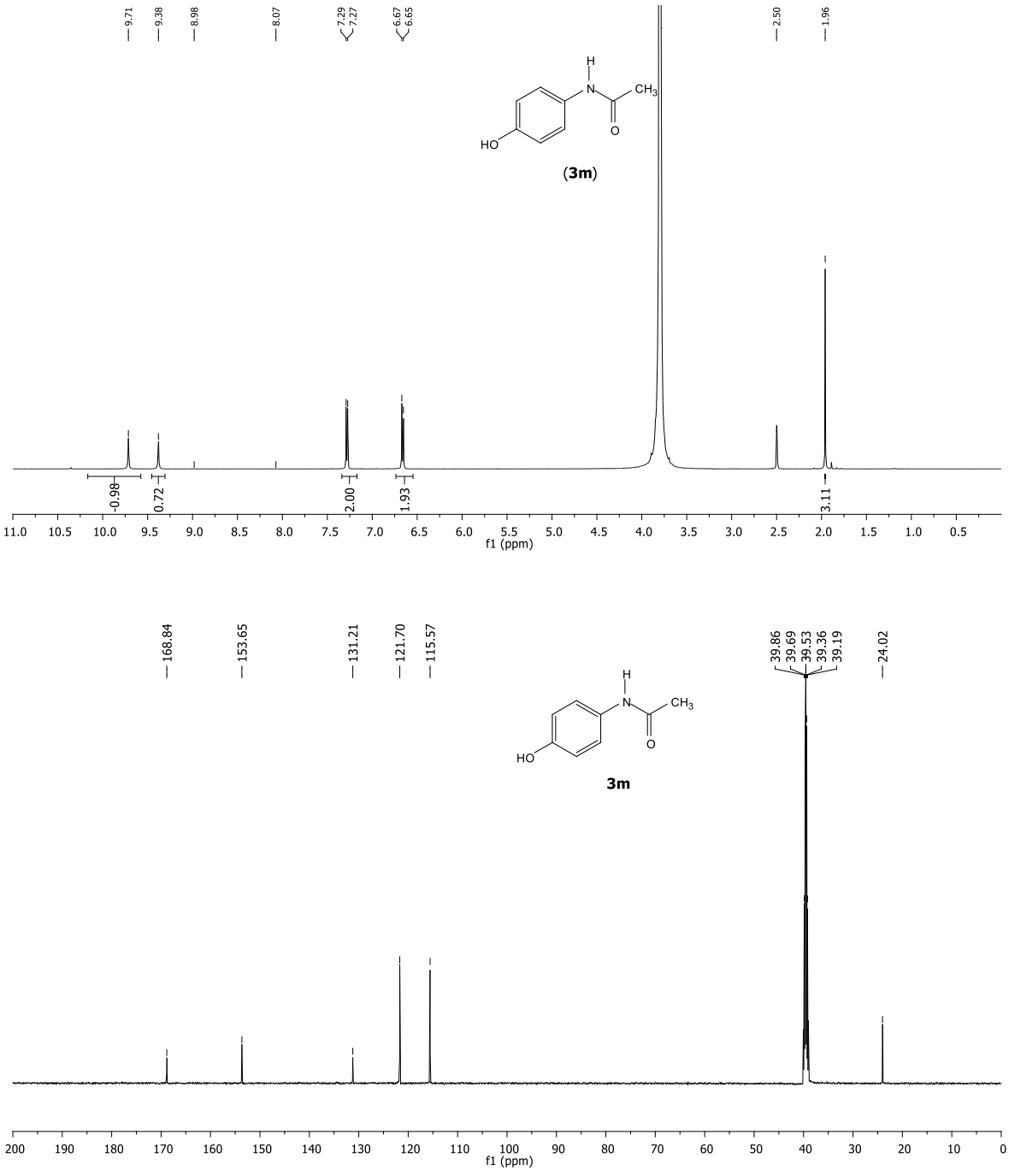


Figure 5.5 ^{1}H and ^{13}C NMR of *N-(*4-Hydroxyphenyl)acetamide (3m)

5.6 References

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