A mild and convenient approach for the synthesis of $N$-aryl amides
The present chapter is divided into three sections

1. **Section A** contains a brief introduction to N-Aryl amides
2. Section B contains Copper (I) iodide - catalyzed Amidation of Phenylboronic acids/Aryl Bromides using 4-Dimethyl aminopyridine as Ligand.
3. Section C contains experimental part for the compounds synthesized in section B

**SECTION A**

**Brief introduction to N-Aryl amides**

Amide bond formation is one of the most important reactions in organic chemistry and amides are pharmaceutically and biologically more active compounds. But existing methods are reaching their inherent limits, and concerns about their waste and expense. Despite the amide formation reaction being a key reaction in organic chemistry, the direct amide formation reaction is little explored. Acceptance of the feasibility and general applicability of this reaction depends upon the development of both an understanding of the mechanism of the reaction, and the design of catalysts, which can promote the reaction on a wide range of substrates and under ambient conditions **Scheme 2.1.**

![Scheme 2.1](image)

**Scheme 2.1** Direct amide formation reaction.

D. G. Hall *et al* (Gernigon, 2012) reported, catalytic amount of substituted phenylboronic acids (MIBA) to give direct amidation from carboxylic acids and amines providing good yields of amide products **Scheme 2.2.**

![Scheme 2.2](image)

**Scheme 2.2** MIBA catalyzed N-aryl amides.
Y.-J. Yoon et al (Kim, 2012) was tert-butoxide catalyzed synthesis of aromatic/aliphatic amides from esters under mild conditions. 

![Scheme 2.3](image)

**Scheme 2.3** Transition metal free amidation by Yoon.

A. Chen et al (Ghosh, 2012) was reported one pot synthetic method for the amidation of aldehydes with amine HCl salts by using copper sulfate as a catalyst and aqueous t-BuOOH as an oxidant. 

![Scheme 2.4](image)

**Scheme 2.4** Copper sulfate catalyzed amidation by Chen.

V. K. Tiwari et al (Prasad, 2012) said that, synthesis of a series of amides from aldehydes and amines at ambient temperature by using PhI(OAc)₂ and ionic liquid.

![Scheme 2.5](image)

**Scheme 2.5** One-pot synthesis of amides from aldehydes.

Zhang et al (Zhang, 2012) was described a direct amidation from α-carbonyl aldehydes and amines in the presence of copper bromide as a catalyst. Many types of amines are tolerant in this conversion. 

![Scheme 2.6](image)

**Scheme 2.6**
Chapter II  Section A

Scheme 2.6 Aerobic oxidative cross-dehydrogenative coupling of amines by Zhang.

Hosseini-Sarvari et al (Hosseini-Sarvari, 2011) reported that direct amidation of fatty acids by using a sol-gel hydrothermal process under solvent-free conditions. **Scheme 2.7**

**Scheme 2.7** Sol-gel hydrothermal process by Hosseini

J. R. Dunetz et al (Dunetz, 2011) reported T3P (n-propanephosphonic acid anhydride) and pyridine catalyzed synthesis of amid bond formation from various racemization-prone acid substrates and amines. **Scheme 2.8.**

**Scheme 2.8** T3P catalyzed amidation by Dunetz.

J. Chen et al (Chung, 2011) has reported aluminium derivative catalyzed synthesis of corresponding amides from free carboxylic acids and amines in toluene at 90°C after 1 hour **Scheme 2.9.**

**Scheme 2.9** Carboxylic acids are converted into amides by Chen.
Talukdar et al (Talukdar, 2011) described for the synthesis of N-methylamides derivatives in the presence of reusable catalyst ZrOCl$_2$.8H$_2$O under microwave irradiation conditions Scheme 2.10.

![Scheme 2.10](image)

**Scheme 2.10** ZrOCl$_2$ catalyzed direct condensation of carboxylic acids by Talukdar.

Mao et al (Mao, 2011) reported, preparation of Cbz-protected arylamides from N-Cbz-protected amino acids in the presence of methanesulfonyl chloride and N-methylimidazole under mild conditions Scheme 2.11.

![Scheme 2.11](image)

**Scheme 2.11**. Preparation of N-substituted amides from N-Cbz-protected amino acids.

D. Crich et al (Sasaki, 2011) was described DIPEA catalyzed for the synthesis amides from aliphatic, aromatic, and heteroaromatic carboxylic acids with aryl isocyanates at room temperature Scheme 2.12.

![Scheme 2.12](image)

**Scheme 2.12** Synthesis of N-aryl amides from isocyanates.

Larrive-Aboussafy et al (Larrive-Aboussafy, 2010) reported DBUcatalyzes the amidation of acyl imidazoles. DBU offers safety and cost advantages Scheme 2.13.
Studer et al (De Sarkar, 2010) reported preparation of N-amide derivatives by using transition metal-free organo catalytic system. **Scheme 2.14.**

**Scheme 2.14** Transition metal-free organocatalytic system by Studer.

Xian-Ying Shi et.al (Xian-Ying, 2015) reported the rhodium-catalyzed amidation of substituted benzoic acids with isocyanates by directed C-H functionalization followed by decarboxylation to afford the corresponding N-aryl benzamide. In which the carboxylate serves as a unique. **Scheme 2.15.**

**Scheme 2.15** Rhodium-catalyzed amidation by Xian
SECTION B

Section B contains Copper (I) iodide–catalyzed Amidation of Phenylboronic acids/Aryl Bromides using 4-Dimethyl aminopyridine as Ligand.

N-Aryl amides are important structural motifs widely employed in the fields of pharmaceutical chemistry and materials science (Evano, 2004; Masse, 1998; Satyanarayana, 2007; Evano, 2008 and Allen, 2011). As a more efficient and facile method, the transition metal-catalyzed coupling reaction of aryloboronic acid / aryl halides and amides has been attractive for many years (Steven, 2013). The Cu-promoted amide arylation synthesis was pioneered by Ullmann type reactions (Goldberg reaction) and Chan-Lam-type reactions more than hundred years ago (Goldberg, 1906; Florian, 2009 and Jennifer, 2011). Until many reports are available for the construction of N-aryl amides. Since Shakespeare’s first reported on Pd-catalyzed amide arylation (Shakespeare, 1999), many Pd-based catalytic systems have been developed for the coupling reaction between aryl amide and aryl bromides (Fangfang, 2012; Dallas, 2005; McLaughlin, 2006; Yin, 2002 and Yin, 2000) aryl sulfonates (Klapars, 2005; Wallace, 2003; Dooleweerdt, 2010 and Hicks, 2009) and more recently aryl chlorides (Ikawa, 2007; Shen, 2005 and Ghosh, 2003), which proved to be useful to synthetic chemists. However, traditional Goldberg reactions are usually carried out under harsh conditions, which limit its broad application in organic synthesis. In recent decades, the ligand-assisted copper-catalyzed amidation of aryl halides has aroused great interest among organic chemists as a practical and efficient method for the construction of C-N and bonds (Spivey, 2004; Zhang, 2012; Xin, 2007 and Debasish, 2013). The use of this strategy in the Goldberg reaction greatly simplifies the synthesis of N-aryl amides (Figure 2.3).
However, these protocols suffered from the limitation of harsh conditions, tedious synthetic procedures, and unsatisfactory yields. Therefore, there is a need to develop more economical, eco-friendly, and potential alternative methods for the synthesis of \(N\)-aryl amides. Catalytic activity of DMAP has been well explored in organic synthesis (Navale, 2013 and Subhasish, 2015) However, there are a very few reports on the use of DMAP as a ligand for metal catalyzed cross-coupling reaction. It has been observed that Cu-based catalytic systems are found to be very attractive because of their low cost and low toxicity. Herein, we report novel and direct synthesis of \(N\)-arylamides from phenylboronic acid / arylbromide using DMAP as a Ligand and employing CuI as the catalyst.

![Figure 2.1. Preparation of substituted \(N\)-Arylbenzamide.](image)

In an initial trial, we examined the reaction of benzamide (1a) with phenylboronic acid (2a) in the presence of a catalytic amount of catalyst. By surveying different reaction conditions the results are summarized in Table-1. The reaction was first tested with various terminal catalysts such as CuI, CuBr and CuCl\(_2\). Among them, CuI was efficient.
for the reaction, giving 3a in 81% yield (Table 1, entry 4). The remaining copper halides CuBr and CuCl₂ were totally ineffective for the reaction (Table 1, entries 10 & 11). Next, the reaction was tested with various bases such as K₂CO₃, K₃PO₄, Na₂CO₃ and Cs₂CO₃. Among the bases tested, Cs₂CO₃ was most effective. The remaining bases K₂CO₃, K₃PO₄ & Na₂CO₃ were less effective giving 3a in 45%, 56% and 40% yields, respectively (Table 1, entries 1, 2 & 3). After screening, the reaction was examined by using different ligands and L1 was found to be most effective affording the desired product in 81% yield (Table 1, entry 4). Other ligands did not make the reaction more effective, such as L2, L3 and L4 (Table 1, entries 5,6 & 7). Next, the reaction was tested with various B(OH)₂, Br and Cl Phenyl substrates. Among them B(OH)₂ and Br give good yields (Table 1, entries 4 and 9).

**Table 1:** Effect of various catalysts in the synthesis of 3a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst(mol%)</th>
<th>Ligand</th>
<th>X</th>
<th>Base</th>
<th>Yield (%)b</th>
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<tr>
<td>1</td>
<td>CuI</td>
<td>L₁</td>
<td>B(OH)₂</td>
<td>K₂CO₃</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>CuI</td>
<td>L₁</td>
<td>B(OH)₂</td>
<td>K₃PO₄</td>
<td>56</td>
</tr>
<tr>
<td>3</td>
<td>CuI</td>
<td>L₁</td>
<td>B(OH)₂</td>
<td>Na₂CO₃</td>
<td>40</td>
</tr>
<tr>
<td>4</td>
<td>CuI</td>
<td>L₁</td>
<td>B(OH)₂</td>
<td>Cs₂CO₃</td>
<td>81(80,68)c</td>
</tr>
<tr>
<td>5</td>
<td>CuI</td>
<td>L₂</td>
<td>B(OH)₂</td>
<td>Cs₂CO₃</td>
<td>15</td>
</tr>
<tr>
<td>6</td>
<td>CuI</td>
<td>L₃</td>
<td>B(OH)₂</td>
<td>Cs₂CO₃</td>
<td>12</td>
</tr>
</tbody>
</table>

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X: Organic halides, B(OH)², Br and Cl Phenyl substrates.

Table 1: Effect of various catalysts in the synthesis of 3a (mol%)

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For X: Organic halides, B(OH)², Br and Cl Phenyl substrates.
Then we optimized the reaction conditions to increase the yield of the product and to reduce the reaction time. Thus, we investigated the effect of various solvents such as DMF, DMA, DMSO, Toluene and THF. Among them, DMF was more effective for the reaction, giving 3a in 81% yield (Table 2, entry 5). Other solvents such as DMA and DMSO were less effective, providing 3a in 51% and 70% yields, respectively (Table 2, entry 2 and 3). The remaining solvents such as toluene, THF and DCM were totally ineffective (Table 2, entry 1, 4 and 6).

**Table 2:** Effect of various solvents in the synthesis of 3a:
With identification of the optimized reaction conditions, the substrate scope was studied. As examined in Table 3, it was found that various substrates were converted into the corresponding products with excellent yields under the conditions. Benzamides having electron-withdrawing groups gave slightly lower yields (Table 3, entry 7) when compared to benzamides having electron-donating groups. Next, different phenylboronic acids and aryl halogens were investigated as the reaction substrates (Table 2). In general, the reactions of benzamide with various phenylboronic acid derivatives with an electron-withdrawing (such as NO$_2$) substituent gave higher yields of C-N arylated products than those with an electron-donating groups (such as CH$_3$, OCH$_3$) on the aromatic ring gave moderate to good yields. The Cu Catalyzed reaction of aryl bromide gave slightly lower yields. For example, arylation of benzamide with phenylboronic acid and bromobenzene furnished N-phenylbenzamide in 81% and 78% yield respectively (Table 3, entry 1 & 15).

Table 3: Synthesis of various substituted N-arylbenzamide from the corresponding phenylboronic acids/arylbromides and benzamides.
\[
\begin{align*}
\text{Chapter II} & \quad \text{Section B} \\
\begin{array}{cccc}
\text{Entry} & R_1 & R_2 & \text{Product} \\
1 & \begin{array}{c}
\text{CONH}_2
\end{array} & \begin{array}{c}
\text{B(OH)}_2
\end{array} & 3a & 81 \\
2 & \begin{array}{c}
\text{CONH}_2
\end{array} & \begin{array}{c}
\text{B(OH)}_2
\end{array} & 3b & 84 \\
3 & \begin{array}{c}
\text{CONH}_2
\end{array} & \begin{array}{c}
\text{B(OH)}_2
\end{array} & 3c & 86 \\
4 & \begin{array}{c}
\text{CONH}_2
\end{array} & \begin{array}{c}
\text{B(OH)}_2
\end{array} & 3d & 89 \\
5 & \begin{array}{c}
\text{CONH}_2
\end{array} & \begin{array}{c}
\text{Cl}
\end{array} & 3e & 80 \\
6 & \begin{array}{c}
\text{CONH}_2
\end{array} & \begin{array}{c}
\text{Cl}
\end{array} & 3f & 86 \\
7 & \begin{array}{c}
\text{CONH}_2
\end{array} & \begin{array}{c}
\text{Cl}
\end{array} & 3g & 86
\end{array}
\end{align*}
\]
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<th>Section B</th>
</tr>
</thead>
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</tr>
<tr>
<td>16</td>
<td><img src="image9" alt="Chemical Structure" /></td>
</tr>
</tbody>
</table>
Scheme 2.16 Proposed catalytic mechanism for this transformation.
The probable catalytic mechanism for this transformation is illustrated in Scheme 2.23. Initially, the amides 1 under basic condition produced the amide salt B, which is exposed to the copper catalyst A to generate the metallic intermediates C. Aryl halides 1 undergo an oxidative addition to intermediates C to form the metallic intermediates D (Lefevre, 2012), which produce the final products 3 through a reductive elimination reaction and release the catalyst A to complete the catalytic cycle.

In conclusion, we have developed a simple, efficient and eco-friendly convenient general method for the synthesis of N-arylbenzamide from phenylboronic acid / arylbromide and benzamide, using DMF as a solvent and employing CuI as the catalyst and under mild conditions. This method provided structurally diverse N-arylbenzamides in excellent yields. N-arylbenzamides derivatives are biologically and pharmaceutically active molecules, and therefore, the present protocol could be of wide application in medicinal chemistry and organic chemistry.
**SECTION C**

**Materials & Methods:**

Melting points were recorded on a Mel-Temp melting point apparatus, in open capillaries and are uncorrected. $^1$H NMR (300 MHz), $^{13}$C NMR (75 MHz) spectra were recorded on a Bruker AMX 300 MHz NMR spectrometer using TMS as internal standard and the values for chemical shifts (δ) being given in ppm and coupling constants (J) in Hertz (Hz). Mass spectra were recorded on an Agilent 1100 ESI. Acme silica gel G and silica gel (100–200 mesh) were used for analytical TLC and column chromatography, respectively. Other chemicals were purchased from Sigma Aldrich and used without further purification.

**General experimental procedure for the synthesis of $N$-arylbenzamide 3a – 3o:**

A mixture of benzamide (1.8 mmol), phenylboronic acid (1.7 mmol) or aryl bromide (1.7 mmol), DMF (5 ml), CuI (5 mol %) DMAP (20 mol %) and Cs$_2$CO$_3$ (1 mmol) was heated to 80 °C for 30 minutes. After completion of the reaction as monitored by TLC, reaction mixture was cooled to room temperature, aqueous Na$_2$CO$_3$ solution (10 ml) was added and extracted with ethyl acetate (2 × 15 ml). The combined organic layers were dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure to get crude. The crude was purified by silica gel column chromatography using EtOAc : hexane (7:3) as eluents to afford pure 3a – 3o.
Characterization data:

**Synthesis of N-phenylbenzamide (3a):**

M.p: 164–166 °C  
**IR (KBr)** $\nu_{\text{max}}$ in cm$^{-1}$: 3344, 3177, 2922, 2852, 1748, 1655, 1599, 1532, 1491, 1438, 1322. *(Figure 2.5)*

**$^1$H NMR** (300 MHz, DMSO $d_6$): 12.23 (s, 1H), 7.93 – 7.95 (m, 2H), 7.85 – 7.87 (m, 1H), 7.77 (d, $J$=7.8 Hz, 2H), 7.44 – 7.58 (m, 3H), 7.34 (t, $J$=7.8 Hz, 2H), 7.06 – 7.11 (m, 1H). *(Figure 2.6)*

**$^{13}$C NMR** (75 MHz, DMSO $d_6$): 168.2, 165.9, 139.5, 135.3, 131.8, 128.9, 128.7, 128.5, 127.9, 127.8, 124.0, 120.7. *(Figure 2.7)*

**ESI-MS:** $m/z$ 197 [M]$^+$  
Anal. Calcd for C$_{13}$H$_{11}$NO: C, 79.16; H, 5.62; N, 7.10.  
Found: C, 79.12; H, 5.64; N, 7.12.

**Synthesis of N-p-tolylbenzamide (3b):**

M.p: 156–158 °C  
**IR (KBr)** $\nu_{\text{max}}$ in cm$^{-1}$: 3368, 3102, 2922, 2855, 1712, 1596, 1523, 1493, 1426, 1324.

**$^1$H NMR** (300 MHz, DMSO $d_6$): 10.15 (s, 1H, NH), 7.92 – 7.95 (m, 2H, Ar-H), 7.65 (d, $J$=8.4 Hz, 2H, Ar-H), 7.49 – 7.58 (m, 3H, Ar-H), 7.15 (d, $J$=8.4 Hz, 2H, Ar-H), 2.28 (s, 1H, CH$_3$). *(Figure 2.8)*

**$^{13}$C NMR** (75 MHz, DMSO $d_6$): 165.6, 137.0, 135.4, 132.9, 131.7, 129.3, 128.6,
127.9, 120.7, 20.8. (Figure 2.9)

**ESI-MS:** \( m/z \) 211 \([M]^+ \) (Figure 2.10);

Anal. Calcd for \( \text{C}_{14}\text{H}_{13}\text{NO} \): C, 79.59; H, 6.20; N, 6.63. Found: C, 79.69; H, 6.11; N, 6.76.

**Synthesis of \( \text{N-}(\text{4-methoxyphenyl})\text{benzamide (3c):} \)**

\[ \text{M.p: 174–176 °C} \]

**IR (KBr)** \( \nu_{\text{max}} \) in cm\(^{-1} \): 3342, 3102, 2931, 2856, 1740, 1599, 1486, 1412, 1336.

\( ^1\text{H NMR} \) (300 MHz, DMSO \( d_6 \)): 10.11 (s, 1H, NH), 7.92 – 7.95 (m, 2H, Ar-H), 7.65 – 7.68 (m, 2H, Ar-H), 7.49 – 7.57 (m, 3H, Ar-H), 6.91 – 6.94 (q, 2H, Ar-H), 3.74 (s, 3H, OCH\(_3\)). (Figure 2.11)

\( ^{13}\text{C NMR} \) (75MHz, DMSO \( d_6 \)): 165.4, 155.9, 135.4, 132.5, 131.7, 128.6, 127.8, 122.3, 114.1, 55.5. (Figure 2.12)

**ESI-MS:** \( m/z \) 228 \([M]^+ \) Anal. Calcd for \( \text{C}_{14}\text{H}_{13}\text{NO}_2 \): C, 73.99; H, 5.77; N, 6.16. Found: C, 74.12; H, 5.67; N, 6.27.

**Synthesis of \( \text{N-}(\text{4-nitrophenyl})\text{benzamide (3d):} \)**

\[ \text{M.p: 198–200 °C} \]

**IR (KBr)** \( \nu_{\text{max}} \) in cm\(^{-1} \): 3359, 3150, 2965, 2801, 1712, 1624, 1523, 1450, 1362;

\( ^1\text{H NMR} \) (300 MHz, DMSO \( d_6 \)): 11.08 (br s, 1H), 8.52 (d, \( J= 9.3 \) Hz, 2H), 8.39 (d, \( J= 9.3 \) Hz, 2H), 8.27 (dd, \( J= 8.4, 1.2 \) Hz, 2H), 7.89 (ddd, \( J= 8.4, 8.4, 1.2 \) Hz, 1H), 7.83-7.73 (m, 2H);
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\[ \text{\(^{13}\text{C NMR (75 MHz, } \delta)\text{}} 166.7, 146.2, 143.2, \]
\[ 134.8, 132.4, 128.8, 128.2, 125.0, 120.1 \]

**ESI-MS:** \( m/z \ 242 \ [M]^+ \)  
Anal. Calcd for  
\[ \text{C}_{13}\text{H}_{10}\text{N}_{2}\text{O}_3: \text{ C, 64.46; H, 4.16; N, 11.56.} \]
Found: C, 64.40; H, 4.20; N, 11.58.

**Synthesis of \( \text{N-(2-chlorophenyl)benzamide (3c):} \)**

\[ \text{M.p} \: 204–206 \ ^\circ \text{C} \]
\[ \text{IR (KBr) } \nu_{\text{max}} \text{ in cm}^{-1} : 3460, 3109, 2901, 1723, 1651, 1593, 1518, 1493, 1444, 1322, 672; \]
\[ \text{\(^{1}\text{H NMR (300 MHz, DMSO } d_6\text{)}: 10.36 \ (s, 1H, NH), 7.93 – 7.95 \ (m, 3H, Ar-H), 7.69 – 7.72 \ (m, 1H, Ar-H), 7.55 – 7.60 \ (m, 3H, Ar-H), 7.40 \ (t, J=8.3 \ Hz, 1H, Ar-H), 7.15 – 7.13 \ (m, 1H, Ar-H);} \]
\[ \text{\(^{13}\text{C NMR (75MHz, DMSO } d_6\text{)}: 166.6, 141.2, 134.5, 133.3, 132.1, 130.8, 128.7, 128.2, 123.6, 120.4, 118.6;} \]
\[ \text{ESI-MS: } m/z \ 231 \ [M]^+ \text{ Anal. Calcd for} \]
\[ \text{C}_{13}\text{H}_{10}\text{ClNO: C, 67.39; H, 4.35; N, 6.05.} \]
Found: C, 67.33; H, 4.37; N, 6.13.

**Synthesis of \( \text{N-(2-chlorophenyl)benzamide (3f):} \)**

\[ \text{M.p: 179–181 } \circ \text{C} \]
\[ \text{IR (KBr) } \nu_{\text{max}} \text{ in cm}^{-1} : 3464, 3110, 2920, 1734, 1651, 1592, 1524, 1493, 1446, 1322, 672. (Figure 2.13) \]
\[ \text{\(^{1}\text{H NMR (300 MHz, DMSO } d_6\text{)}: 10.40 \ (s, 1H, NH), 7.93 – 7.98 \ (m, 3H, Ar-H), 7.70 – 7.73 \ (m, 1H, Ar-H), 7.51 – 7.61 \ (m, 3H, Ar-} \]
H), 7.38 (t, J=8.1 Hz, 1H, Ar-H), 7.14 –
7.17 (m, 1H, Ar-H) (Figure 2.14).

$^{13}$C NMR (75MHz, DMSO $d_6$): 166.1,
141.0, 134.9, 133.3, 132.1, 130.6, 128.7,
128.0, 123.6, 120.0, 118.9 (Figure 2.15)

ESI-MS: $m/z$ 231 [M]$^+$ (Figure 2.16);
Anal. Calcd for C$_{13}$H$_{10}$ClNO: C, 67.39; H,
4.35; N, 6.05. Found: C, 67.30; H, 4.39; N,

**Synthesis of N-(2-chlorophenyl)benzamide (3g):**

M.p: 199–201 °C

IR (KBr) $\nu_{\text{max}}$ in cm$^{-1}$: 3449, 3105, 2920,
2851, 1731, 1655, 1595, 1519, 1493, 1446,
1331, 690. (Figure 2.17)

$^1$H NMR (300MHz, DMSO $d_6$): 10.36 (s,
1H, NH), 7.93 – 7.96 (m, 2H, Ar-H), 7.82
(d, J=9 Hz, 2H, Ar-H), 7.53 – 7.58 (m, 3H,
Ar-H), 7.41 (d, J=9 Hz, 2H, Ar-H). (Figure
2.18)

$^{13}$C NMR (75 MHz, DMSO $d_6$): 166.0,
138.5, 135.0, 132.0, 128.8, 128.7, 128.0,
127.6, 122.21. (Figure 2.19)

ESI-MS: $m/z$ 231 [M]$^+$ (Figure 2.20) Anal.
Calcd for C$_{13}$H$_{10}$ClNO: C, 67.39; H, 4.35;
N, 6.05. Found: C, 67.35; H, 4.37; N, 6.09.

**Synthesis of 4-nitro-N-phenylenzamide (3h):**

M.p: 214–216 °C

IR (KBr) $\nu_{\text{max}}$ in cm$^{-1}$: 3452, 3132, 2923,
2856, 1744, 1661, 1523, 1493, 1448, 1332.
\( ^1H \text{NMR} \) (300MHz, DMSO \( d_6 \)): 10.56 (s, 1H, NH), 8.73 (s, 1H), 8.36 – 8.48 (m, 2H, Ar-H), 7.83 (t, \( J=8.0 \) Hz, 1H, Ar-H), 7.76 (d, \( J=8.3 \) Hz, 2H, Ar-H), 7.14 – 7.36 (m, 4H, Ar-H).

\( ^{13}C \text{NMR} \) (75 MHz, DMSO \( d_6 \)): 163.6, 146.2, 138.3, 135.2, 134.1, 130.2, 128.7, 126.4, 124.3, 120.8.

ESI-MS: \( m/z \) 242 [M]+

Anal. Calcd for \( \text{C}_{13}\text{H}_{10}\text{N}_{2}\text{O}_3 \): C, 64.46; H, 4.16; N, 11.56. Found: C, 64.44; H, 4.18; N, 11.56.

**Synthesis of 4-methyl-N-phenylbenzamide (3i):**

M.p: 145–147 °C

IR (KBr) \( \nu_{\text{max}} \) in cm\(^{-1} \): 3350, 3058, 2917, 2852, 1743, 1650, 1596, 1524, 1508, 1439, 1320. (Figure 2.21)

\( ^1H \text{NMR} \) (300 MHz, DMSO \( d_6 \)): 10.14 (s, 1H, NH), 7.87 (d, \( J=8.4 \) Hz, 2H, Ar-H), 7.75 – 7.78 (m, 2H, Ar-H), 7.31 – 7.36 (m, 4H, Ar-H), 7.10 (d, \( J=7.2 \) Hz, 1H, Ar-H), 2.38 (s, 3H, CH\(_3\)). (Figure 2.22)

\( ^{13}C \text{NMR} \) (75 MHz, DMSO \( d_6 \)): 165.6, 141.8, 139.6, 132.4, 129.2, 128.9, 128.0, 123.8, 120.7, 21.3. (Figure 2.23)

ESI-MS: \( m/z \) 210 [M]+ (Figure 2.24); Anal. Calcd for \( \text{C}_{14}\text{H}_{13}\text{NO} \): C, 79.59; H, 6.20; N, 6.63. Found: C, 79.66; H, 6.18; N, 6.54.
Synthesis of 4-methyl-N-p-tolylbenzamide (3j):

\[
\text{M.p: } 158–160 ^\circ C
\]

\[
\text{IR (KBr) } \nu_{\text{max}} \text{ in cm}^{-1}: 3358, 3071, 2929, 2853, 1722, 1654, 1592, 1531, 1515, 1448, 1326. \text{ (Figure 2.25)}
\]

\[
\text{\textsuperscript{1}H NMR (300 MHz, DMSO } d_6\text{): } 10.06 \text{ (s, 1H, NH), 7.87 – 7.84 (m, 2H, Ar-H), 7.66 – 7.63 (m, 2H, Ar-H), 7.32 (d, } J=8.1, 2H, \text{ Ar-H), 7.14 (d, } J=8.1, 2H, \text{ Ar-H), 2.38 (s, 3H, CH}_3\text{), 2.27 (s, 3H, CH}_3\text{). (Figure 2.26)}
\]

\[
\text{\textsuperscript{13}C NMR (75 MHz, DMSO } d_6\text{): } 165.4, 141.7, 137.0, 132.8, 132.5, 129.3, 129.2, 127.9, 120.7, 21.3, 20.8. \text{ (Figure 2.27)}
\]

\[
\text{ESI-MS: } m/z 226 [M+1]^+ \text{ (Figure 2.28)}
\]

\[
\text{Anal. Calcd for C}_{15}\text{H}_{15}\text{NO: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.89; H, 6.23; N, 6.57.}
\]

Synthesis of N-(4-methoxyphenyl)-4-methylbenzamide (3k):

\[
\text{M.p: } 176–178 ^\circ C
\]

\[
\text{IR (KBr) } \nu_{\text{max}} \text{ in cm}^{-1}: 3321, 3132, 2923, 2852, 1722, 1655, 1599, 1536, 1521, 1446, 1326, 1234.
\]

\[
\text{\textsuperscript{1}H NMR (300 MHz, DMSO } d_6\text{): } 10.16 \text{ (s, 1H, NH), 7.89 – 7.93 (m, 2H, Ar-H), 7.63 – 7.68 (m, 2H, Ar-H), 7.52 – 7.57 (m, 3H, Ar-H), 6.92 – 6.96 (q, 2H, Ar-H), 3.72 (s, 3H, OCH}_3\text{), 2.36 (s, 1H, CH}_3\text{).}
\]

\[
\text{\textsuperscript{13}C NMR (75 MHz, DMSO } d_6\text{): } 166.1, 155.7, 134.6, 133.1, 131.5, 128.6, 128.1, 123.1, 114.1, 55.7, 21.6.
\]
ESI-MS: \( m/z \ 241 \ [M]^+ \) Anal. Calcd for C\(_{15}\)H\(_{15}\)NO\(_2\): C, 74.67; H, 6.27; N, 5.81. Found: C, 74.64; H, 6.28; N, 5.79.

Synthesis of 4-methyl-N-(4-nitrophenyl)benzamide (3l):

\[
\text{M.p:} \ 168–170 \ ^\circ \text{C} \\
\text{IR (KBr)} \ \nu_{\text{max}} \text{ in cm}^{-1}: 3368, 3091, 2921, 2440, 1925, 1596, 1537, 1513, 1471, 1374.
\]

\[
^1\text{H NMR} \ (300 \text{ MHz, DMSO } d_6): 10.71 \text{ (s, 1H, NH)}, 8.26 \text{ (d, } J=9.2 \text{ Hz, 2H, Ar-H)}, 8.06 \text{ (d, } J=9.6 \text{ Hz, 2H, Ar-H)}, 7.98 – 7.89 \text{ (m, 2H, Ar-H)}, 7.37 \text{ (d, } J=6.0 \text{ Hz, 2H, Ar-H}), 2.40 \text{ (s, 3H, CH}_3\text{).}
\]

\[
^{13}\text{C NMR} \ (75 \text{ MHz, DMSO } d_6): 166.4, 147.7, 145.9, 142.75, 142.72, 139.0, 131.6, 129.3, 128.3, 125.2, 125.1, 120.1, 104.6, 21.4.
\]

ESI-MS: \( m/z \ 256 \ [M]^+ \) Anal. Calcd for C\(_{14}\)H\(_{12}\)N\(_2\)O\(_3\): C, 65.62; H, 4.72; N, 10.93. Found: C, 65.55; H, 4.76; N, 10.96.

Synthesis of N-(3-chlorophenyl)-4-methylbenzamide (3m):

\[
\text{M.p:} \ 148–150 \ ^\circ \text{C} \\
\text{IR (KBr)} \ \nu_{\text{max}} \text{ in cm}^{-1}: 3265, 3084, 2921, 2853, 1934, 1752, 1647, 1595, 1537, 1508, 1478, 1377, 635. \text{(Figure 2.9)}
\]

\[
^1\text{H NMR} \ (300 \text{ MHz, DMSO } d_6): 10.29 \text{ (s, 1H, NH)}, 7.95 \text{ (t, } J=1.8 \text{ Hz, 1H, Ar-H)}, 7.85 \text{ (d, } J=8.1 \text{ Hz, 2H, Ar-H)}, 7.68 - 7.71 \text{ (m, 1H, Ar-H)}, 7.39 - 7.32 \text{ (m, 3H, Ar-H)}, 7.15
\]

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− 7.12 (m, 1H, Ar-H), 2.37 (s, 3H, CH₃).
(Figure 2.30)

¹³C NMR (75 MHz, DMSO d₆): 165.9, 142.2, 141.1, 133.2, 132.0, 130.6, 129.3, 128.0, 123.5, 120.0, 118.9, 21.3. (Figure 2.31)

ESI-MS: m/z 245 [M]+ (Figure 2.32);
Anal. Calcd for C₁₄H₁₂ClNO: C, 68.44; H, 4.92; N, 5.70. Found: C, 68.40; H, 4.94; N, 5.72.

Synthesis of N-(4-chlorophenyl)-4-methylbenzamide (3n):

M.p: 170–172 °C
IR (KBr) νmax in cm⁻¹: 3349, 3112, 3032, 2919, 2851, 1928, 1655, 1610, 1596, 1524, 1507, 1399, 631. (Figure 2.33)

¹H NMR (300 MHz, DMSO d₆): 10.29 (s, 1H, NH), 7.88 – 7.80 (m, 4H, Ar-H), 7.41 – 7.32 (m, 4H, Ar-H), 2.38 (s, 3H, CH₃). (Figure 2.34)

¹³C NMR (75 MHz, DMSO d₆): 165.7, 142.1, 138.1, 132.1, 129.2, 128.8, 128.0, 127.4, 122.1, 21.3. (Figure 2.35)

ESI-MS: m/z 245 [M]+ (Figure 2.36);
Anal. Calcd for C₁₄H₁₂ClNO: C, 68.44; H, 4.92; N, 5.70. Found: C, 68.42; H, 4.93; N, 5.71.

Synthesis of N-(4-fluorophenyl)benzamide (3o):

M.p: 191–193 °C
IR (KBr) νmax in cm⁻¹: 3339, 3102, 2919,
2851, 1922, 1658, 1612, 1596, 1527, 1507, 1398, 646.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 10.23 (s, 1H, NH), 7.87–7.91 (m, 2H), 7.62 (d, $J = 8.0$ Hz, 2H), 7.36 (t, $J = 8.8$ Hz, 2H), 7.18 (t, $J = 8.8$ Hz, 3H).

$^{13}$C NMR (75 MHz, DMSO) $\delta$ 165.5, 164.3, 162.7, 139.1, 131.4, 130.6, 128.6, 123.8, 120.4, 115.5, 115.2.

ESI-MS: $m/z$ 215 [M]$^+$ Anal. Calcd for C$_{13}$H$_{10}$FNO: C, 72.55; H, 4.68; N, 6.51. Found: C, 72.50; H, 4.71; N, 6.53


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Figure 2.5: IR spectrum of compound 3e
Figure 2.6. $^1$H NMR spectrum of 3a
Figure 2.7. $^{13}$C NMR spectrum of 3a
Figure 2.8. $^1$H NMR spectrum of $3b$
Figure 2.9. $^{13}$C NMR spectrum of 3b
Figure 2.10: ESI-MS spectrum of compound 3b
Figure 2.11. $^1$H NMR spectrum of compound 3c
Figure 2.12. $^{13}$C NMR spectrum of compound 3c
Figure 2.13. IR spectrum of compound 3f
Figure 2.14. $^1$H NMR spectrum of compound 3f
Figure 2.15. $^1$C NMR spectrum of compound 3f
Figure 2.16. ESI-MS spectrum of compound 3f
Figure 2.17. IR spectrum of 3g
Figure 2.18. $^1$H NMR spectrum of 3g
13C NMR of G3-14 in DMSO-d6
Date 15/02/15
(D:/Laurin/External-2015/002/1)

Figure 2.19. $^{13}$C NMR spectrum of 3g
Figure 2.20. ESI-MS spectrum compound 3g
Figure 2.21. IR spectrum of compound 3i
Figure 2.22. $^1$H NMR spectrum of 3i
Figure 2.23. $^{13}$C NMR spectrum of 3i
Figure 2.24. ESI-MS spectrum of compound 3i
Figure 2.25. IR spectrum of compound 3j
Figure 2.26. $^1$H NMR spectrum of compound 3j
$^{13}$C NMR of CS-7 in DMSO-$d_6$
Date 15/02/15

Figure 2.27. $^{13}$C NMR spectrum of 3j
Figure 2.28. ESI-MS spectrum of compound 3j
Figure 2.29. IR spectrum of 3m
Figure 2.30. $^1$H NMR spectrum of compound 3m
Figure 2.31. $^1$C NMR spectrum of 3m
Figure 2.32. ESI-MS spectrum of compound 3m
Figure 2.33. IR spectrum of compound 3n
Figure 2.34. $^1$H NMR spectrum of 3n
Figure 2.35. $^{13}$C NMR spectrum of compound 3n
Figure 2.36. ESI-MS spectrum of compound 3n