Transition metal-free hydration of nitriles to amides mediated by NaOH

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Abstract
A transition metal-free NaOH mediated hydration of organo nitriles to amides under mild reaction conditions has been described. Both aliphatic and aromatic/hetero nitriles were smoothly converted into corresponding amides in moderate to good yields.

Introduction
Amides are an important key intermediate in many organic transformations, as well as they are basic building blocks in biological molecules, agrochemicals, polymers etc.[1,2] The amide linkage is one of the most important functional group in nature, because they are key connector in peptides and proteins in living organisms.[2,3] The synthesis of amides were also significant importance in the field of pharmaceutical, medicinal chemistry. Amides are present in around 25% of top-selling in pharmaceuticals industry. Compared to secondary and tertiary amides, the primary amides are important intermediates in organic synthesis and these are raw materials for the synthesis of plastics, detergents and lubricants.[4] Due to the numerous applications of amides, a number of elegant methods have been developed in recent years. Generally, the amide bonds are formed by the condensation of carboxylic acid and esters with amines,[5] or coupling reactions between alcohol/aldehydes with amines,[6] and hydroamination of unsaturated hydrocarbons.[6] Apart from these methods, hydration of nitriles is one of the classic transformation as well as simple and straightforward method for the synthesis of variety of amides, in green chemistry point of view. The nitrile hydration methods were also promote as atom efficiency and avoids the generation of environmental waste. Based on these advantages, the hydration of nitriles to amides is a well-established method in the pharmaceutical industry for the synthesis of various amides in large scale production. Recently various groups were reported the hydration of the nitriles to amides using different catalysts such as acids, bases, ionic liquids, and transition metals.[7,8] Of the available transition metal-free methods, a number of elegant methods have been developed in recent years. Generally, the amide bonds are formed by the condensation of carboxylic acid and esters with amines, or coupling reactions between alcohol/aldehydes with amines and hydroamination of unsaturated hydrocarbons. Apart from these methods, hydration of nitriles is one of the classic transformation as well as simple and straightforward method for the synthesis of variety of amides, in green chemistry point of view. The nitrile hydration methods were also promote as atom efficiency and avoids the generation of environmental waste. Based on these advantages, the hydration of nitriles to amides is a well-established method in the pharmaceutical industry for the synthesis of various amides in large scale production. Recently various groups were reported the hydration of the nitriles to amides using different catalysts such as acids, bases, ionic liquids, and transition metals.[7,8]

Results and Discussion
In continuation of our interest in the development of green and sustainable methods for amides,[9,10] we describe herein hydration of nitriles to the corresponding amides using inexpensive and commercially available NaOH as promoter under metal-free mild conditions. We initiated our studies with benzonitrile (1a) as a model substrate, using NaOH as a promoter at room temperature with isopropyl alcohol (IPA) as solvent, under these conditions the desired product (2a) was obtained in 21% isolated yield after 24 h (Table 1, entry 1).

Based on the initial observation, we raised the reaction temperature (from room temperature) to 55 and 60 °C under the same reaction conditions; the yield of the desired product was significantly increased to 86% and 93% respectively (Table 1, entries 2 & 3). When the amount of base was reduced to 0.5 equivalents, the yield was dropped to 65% (Table 1, entry 4). Under the same conditions, we tested the reaction with other inorganic bases like, K2CO3 and Na2CO3 no product formation was observed (Table 1, entries 5 & 6). However, lower yield of the product was obtained with LiOH.H2O and CsOH as base (Table 1, entries 7 & 8). With KOH as a promoter, 85% yield of 2a was obtained.

Scheme 1. Selective hydration of nitriles to amides

Key words: nitriles, base, hydration, amides

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under the same conditions (Table 1, entry 9). Further, keeping with NaOH as promoter, different solvents (EtOH, H2O, CH3CN, toluene, DMSO and tBuOH) were screened to examine the yield of the product, lower yield to no reaction was observed with these solvents (Table 1, entries 10–15). After screening for various parameters, the optimum conditions identified for the present transformation are as follows: 1.0 equiv. of NaOH as base, and 1.0 mL of IPA at 60 °C, 24h reaction time (Table 1, entry 3).

With the optimized conditions in hand, the substrate scope of the reaction for the hydration of various nitriles were investigated (Table 2). The reactions were found to be very facile with both electron rich and electron deficient groups. In electron donating groups such as -Me, -OMe, -Ph at para position of benzonitriles gave the corresponding amides in excellent yields (51–89%) under the present conditions. To our delight the optimized conditions were also applicable to aliphatic nitriles and afford the corresponding aliphatic amides 3h–i in good yields (59–63%).

Based on experimental observations and literature reports[8d, 9d] an ionic mechanism has been proposed for the present transformation (Scheme 2). Initially, IPA in presence of NaOH forms iso-propoxy anion intermediate, it reacts with nitrile and produces the intermediate I which exist as keto - enol form and easily hydrolyzes to form corresponding desired amide.

### Table 1. Optimization of reaction conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base (equiv.)</th>
<th>Solvent</th>
<th>Tem (°C)</th>
<th>Yield (%)</th>
</tr>
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<tr>
<td>1</td>
<td>NaOH (1.0)</td>
<td>IPA</td>
<td>RT</td>
<td>21</td>
</tr>
<tr>
<td>2</td>
<td>NaOH (1.0)</td>
<td>IPA</td>
<td>50</td>
<td>86</td>
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<tr>
<td>3</td>
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<td>IPA</td>
<td>60</td>
<td>93</td>
</tr>
<tr>
<td>4</td>
<td>K2CO3 (1.0)</td>
<td>IPA</td>
<td>60</td>
<td>65</td>
</tr>
<tr>
<td>5</td>
<td>Na2CO3 (1.0)</td>
<td>IPA</td>
<td>60</td>
<td>60 N.R.</td>
</tr>
<tr>
<td>6</td>
<td>NaOH (1.0)</td>
<td>IPA</td>
<td>60</td>
<td>60 Trace</td>
</tr>
<tr>
<td>7</td>
<td>LiOH H2O</td>
<td>IPA</td>
<td>60</td>
<td>20</td>
</tr>
<tr>
<td>8</td>
<td>KOH (1.0)</td>
<td>IPA</td>
<td>60</td>
<td>20 Trace</td>
</tr>
<tr>
<td>9</td>
<td>NaOH (0.5)</td>
<td>IPA</td>
<td>60</td>
<td>59</td>
</tr>
<tr>
<td>10</td>
<td>NaOH (1.0)</td>
<td>EtOH</td>
<td>60</td>
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</tr>
<tr>
<td>11</td>
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<td>H2O</td>
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</tr>
<tr>
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<td>CH3CN</td>
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<td>NaOH (1.0)</td>
<td>Toluene</td>
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<td>NaOH (1.0)</td>
<td>DMSO</td>
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<td>67</td>
</tr>
<tr>
<td>15</td>
<td>NaOH (1.0)</td>
<td>BuOH</td>
<td>60</td>
<td>59</td>
</tr>
</tbody>
</table>

*aReaction Conditions: amide (2 mmol), base (2 mmol) and solvent (1.0 mL), isolated yields.

### Table 2. Substrates scope of the benzonitriles

*Reaction Conditions: Nitrile (2 mmol), NaOH (2 mmol) and IPA (1.0 mL), 60 °C, 24h, isolated yields.

### Table 3. Substrates scope of the hetero and aliphatic nitriles

*Reaction Conditions: Nitrile (2 mmol), NaOH (2 mmol) and IPA (1.0 mL), 60 °C, 24h, isolated yields.
In conclusion, we have developed an efficient protocol for the hydration of various benzonitriles to corresponding benzamides using inexpensive and commercially available base (NaOH) under very mild conditions (60°C). The conditions also applicable to heteroaromatic nitriles and aliphatic nitriles and afford the good to excellent yields. The present method represents a significant development for the hydration of nitriles under transition metal-free conditions.

**Experimental Section**

**General information**

All commercially available chemicals and reagents were used without any further purification unless otherwise indicated. 1H and 13C NMR spectra were recorded at 500, 600 and 125, 150 MHz, respectively. The spectra were recorded in CDCl3 and DMSO-d6 as a solvent. Multiplicity was indicated as follows: s (singlet); d (doublet); t (triplet); m (multiplet); dd (doublet of doublets), etc. Coupling constants (J) were given in Hz. Chemical shifts are reported in δ relative to TMS as an internal standard. The peaks around δ values of 7.26 (1H NMR), 77.0 (13C NMR) correspond to CDCl3. The peaks around δ values of 2.50 (1H NMR), 39.9 (13C NMR) are corresponding to DMSO. The peak around δ values of 3.35 (1H NMR) is corresponding to the H2O present in DMSO solvent. Progress of the reactions was monitored by thin layer chromatography (TLC). Silica gel 100-200 mesh size was used for column chromatography using a hexane/ethyl acetate eluent unless otherwise indicated.

**General experimental procedure for the synthesis of benzamide from benzonitrile (3a)**

A 20 mL round bottomed flask was charged with benzonitrile (2 mmol), sodium hydroxide (2 mmol) dissolved in isopropyl alcohol (1.0 mL). Then the reaction mixture was placed at indicated temperature and time, and the progress of the reaction was monitored by TLC. After completion of the reaction, the crude mixture was dissolved with dichloromethane and filtered the mixture and evaporated to dryness. The residue was then purified by column chromatography (hexane/EtOAc) to get the pure product. All amide products were characterized by NMR.

**Characterization data**

**Benzamide (2a)**

(Eluent: 40% EtOAc/hexane); 93% yield (225.1 mg); white solid; 1H NMR (500 MHz, CDCl3): δ 7.82 (s, 1H), 7.81 (d, J = 2.0 Hz, 1H), 7.53 (t, J = 6.5 Hz, 1H), 7.44 (t, J = 7.0 Hz, 2H), 6.17 (br, NH, 2H). 13C NMR (125 MHz, CDCl3) δ 169.5, 133.3, 131.9, 128.5, 127.3.

**4-Methylbenzamide (2b)**

(Eluent: 40% EtOAc/hexane); 93% yield (225.1 mg); white solid; 1H NMR (500 MHz, CDCl3): δ 7.82 (s, 1H), 7.81 (d, J = 2.0 Hz, 1H), 7.53 (t, J = 6.5 Hz, 1H), 7.44 (t, J = 7.0 Hz, 2H), 6.17 (br, NH, 2H). 13C NMR (125 MHz, CDCl3) δ 169.5, 133.3, 131.9, 128.5, 127.3.

**3-methoxybenzamide (2d)**

(Eluent: 35% EtOAc/hexane); 89% yield (270.1 mg); white solid; 1H NMR (600 MHz, CDCl3): δ 7.40 (s, 1H), 7.35 (m, 2H), 7.08 (d, J = 7.5 Hz, 1H), 6.10 (br, NH, 2H). 13C NMR (150 MHz, CDCl3) δ 169.2, 159.9, 134.8, 129.7, 119.2, 118.3, 112.6, 55.5.

**3-Methylbenzamide (2e)**

(Eluent: 40% EtOAc/hexane); 82% yield (221.5 mg); white solid; 1H NMR (600 MHz, CDCl3): δ 7.65 (s, 1H), 7.59 (d, J = 5.5 Hz, 1H), 7.30 (t, J = 6.0 Hz, 2H), 6.49 (br, NH, 2H), 2.37 (s, 3H). 13C NMR (150 MHz, CDCl3) δ 170.1, 138.4, 133.4, 132.6, 128.4, 128.1, 124.3, 21.3.

**2-methoxybenzamide (2f)**

(Eluent: 40% EtOAc/hexane); 86% yield (232.2 mg); white solid; 1H NMR (500 MHz, CDCl3): δ 7.72 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 6.10 (br, NH, 2H). 13C NMR (125 MHz, CDCl3) δ 169.5, 142.5, 130.5, 129.2, 127.3, 21.4.

**4-Methoxybenzamide (2c)**

(Eluent: 30% EtOAc/hexane); 92% yield (278 mg); white solid; 1H NMR (600 MHz, CDCl3): δ 7.79 (d, J = 7.0 Hz, 2H), 6.94 (d, J = 7.5 Hz, 2H), 5.99 (br, NH, 2H), 3.86 (s, 3H). 13C NMR (150 MHz, DMSO-d6) δ 167.9, 162.0, 129.8, 127.0, 113.8, 55.8.
(Eluent: 30% EtOAc/hexane); 84% yield (255.1 mg); white solid; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.22 (dd, $J$ = 5.0 Hz, 1H), 7.49 (m, 1H), 7.08 (t, $J$ = 6.0 Hz, 1H), 7.00 (d, $J$ = 6.5 Hz, 1H), 6.06 (br, NH, 2H), 3.97 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 167.1, 157.8, 133.4, 132.6, 121.3, 120.8, 111.4, 56.0.

4'-Methyl-[1, 1'-biphenyl]-4-carboxamide (2g) (Eluent: 40% EtOAc/hexane); 71% yield (301.6 mg); white solid; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.86 (d, $J$ = 7.0 Hz, 2H), 7.64 (d, $J$ = 7.0 Hz, 2H), 7.50 (d, $J$ = 6.5 Hz, 2H), 6.08 (br, NH, 2H), 2.39 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 168.0, 143.1, 137.9, 136.8, 133.3, 130.1, 128.6, 127.2, 126.6, 21.2.

4-Fluorobenzamide (2h) (Eluent: 40% EtOAc/hexane); 69% yield (193.1 mg); white solid; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.83 (m, 2H), 7.12 (t, $J$ = 9.0 Hz, 2H), 6.06 (br, NH, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 168.3, 166.0, 129.8 (d, $J$ = 8.75 Hz), 129.7, 115.8 (d, $J$ = 0.17 Hz), 115.6.

3-Fluorobenzamide (2i) (Eluent: 40% EtOAc/hexane); 61% yield (170.7 mg); white solid; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.56 (t, $J$ = 6.5 Hz, 1H), 7.43 (q, $J$ = 6.5 Hz, 1H), 6.12 (br, NH, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 168.1, 163.6 (d, $J$ = 246 Hz), 162.0, 135.7, 130.4 (d, $J$ = 7.5 Hz), 130.3, 122.89 (d, $J$ = 3.0 Hz), 122.87, 119.2, 119.0, 114.9, 114.7.

4-Bromobenzamide (2j) (Eluent: 35% EtOAc/hexane); 68% yield (271.3 mg); white solid; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.97 (s, 1H), 7.72 (d, $J$ = 6.5 Hz, 1H), 7.67 (d, $J$ = 7.0 Hz, 1H), 7.33 (t, $J$ = 6.0 Hz, 1H), 6.11 (br, NH, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 167.8, 135.2, 135.0, 130.6, 130.2, 125.8, 122.8.

3-Bromobenzamide (2k) (Eluent: 35% EtOAc/hexane); 68% yield (271.3 mg); white solid; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.97 (s, 1H), 7.72 (d, $J$ = 6.5 Hz, 1H), 7.67 (d, $J$ = 7.0 Hz, 1H), 7.33 (t, $J$ = 6.0 Hz, 1H), 6.11 (br, NH, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 167.8, 135.2, 135.0, 130.6, 130.2, 125.8, 122.8.

2-Bromobenzamide (2l) (Eluent: 30% EtOAc/hexane); 70% yield (278.3 mg); white solid; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.64 (d, $J$ = 6.5 Hz, 1H), 7.38 (t, $J$ = 6.0 Hz, 1H), 7.30 (m, 1H), 6.11 (br, NH, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 169.1, 136.5, 131.7, 129.9, 127.6, 119.2.

4-Chlorobenzamide (2m) (Eluent: 40% EtOAc/hexane); 97% yield (300.2 mg); white solid; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.75 (d, $J$ = 7.0 Hz, 2H), 7.41 (t, $J$ = 6.5 Hz, 2H), 5.82 (br, NH, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 168.2, 138.4, 131.6, 129.0, 128.8.

2-Chlorobenzamide (2n) (Eluent: 40% EtOAc/hexane); 73% yield (225.8 mg); white solid; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.79 (d, $J$ = 7.0 Hz, 1H), 7.42 (d, $J$ = 6.5 Hz, 1H), 7.39 (d, $J$ = 5.5 Hz, 1H), 7.35 (t, $J$ = 7.0 Hz, 1H), 6.37 (br, NH, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 168.0, 133.7, 131.9, 130.88, 130.81, 130.4, 127.2.

3-Chlorobenzamide (2o) (Eluent: 35% EtOAc/hexane); 90% yield (358.0 mg); white solid; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.68 (d, $J$ = 7.0 Hz, 2H), 7.60 (d, $J$ = 7.5 Hz, 2H), 6.05 (br, NH, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 168.2, 132.1, 131.9, 128.9, 126.8.

3-Bromobenzamide (2p) (Eluent: 30% EtOAc/hexane); 70% yield (218.2 mg); white solid; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.80 (q, $J$ = 6.5 Hz, 1H), 7.50 (d, $J$ = 7.0 Hz, 1H), 7.38 (t, $J$ = 6.0 Hz, 1H), 6.09 (br, NH, 2H). $^{13}$C NMR (125 MHz,CDCl$_3$) $\delta$ 167.9, 135.0, 134.8, 132.0, 129.9, 127.7, 125.3.

4-Iodobenzamide (2p) (Eluent: 40% EtOAc/hexane); 84% yield (255.1 mg); white solid; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.22 (dd, $J$ = 5.0 Hz, 1H), 7.49 (m, 1H), 7.08 (t, $J$ = 6.0 Hz, 1H), 7.00 (d, $J$ = 6.5 Hz, 1H), 6.06 (br, NH, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 167.1, 157.8, 133.4, 132.6, 121.3, 120.8, 111.4, 56.0.
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(Eluent: 40% EtOAc/hexane); 95% yield (469.6 mg); white solid; 1H NMR (600 MHz, CDCl3): δ 7.82 (d, J = 7.5 Hz, 2H), 7.54 (d, J = 7.5 Hz, 2H), 6.02 (br, NH, 2H). 13C NMR (150 MHz, DMSO-d6) δ 167.7, 137.6, 132.0, 129.9, 118.5, 99.4.

[1, 1’-Biphenyl]-4-carboxamide (2q)

(Eluent: 40% EtOAc/hexane); 77% yield (304.9 mg); white solid; 1H NMR (600 MHz, CDCl3): δ 7.90 (d, J = 7.0 Hz, 2H), 7.67 (d, J = 7.0 Hz, 2H), 7.61 (d, J = 6.5 Hz, 2H), 7.47 (t, J = 6.5 Hz, 2H), 7.40 (t, J = 6.0 Hz, 1H), 6.11 (br, NH, 2H). 13C NMR (150 MHz, DMSO-d6) δ 168.0, 143.2, 139.7, 133.6, 129.5, 128.6, 128.5, 127.4, 126.9.

1-Naphthamide (2r)

(Eluent: 40% EtOAc/hexane); 69% yield (235.9 mg); white solid; 1H NMR (500 MHz, CDCl3): δ 8.44 (d, J = 7.0 Hz, 1H), 7.95 (d, J = 6.5 Hz, 1H), 7.72 (d, J = 5.0 Hz, 2H), 7.47 (t, J = 5.0 Hz, 2H), 7.40 (t, J = 6.5 Hz, 2H), 5.80 (br, NH, 2H). 13C NMR (150 MHz, CDCl3) δ 171.5, 133.7, 133.0, 131.2, 130.0, 128.3, 127.3, 126.5, 125.4, 124.6.

Thiophene-2-carboxamide (3a)

(Eluent: 30% EtOAc/hexane); 89% yield (226.8 mg); white solid; 1H NMR (600 MHz, CDCl3): δ 7.54 (t, J = 5.0 Hz, 2H), 7.10 (t, J = 3.5 Hz, 1H), 5.80 (br, NH, 2H). 13C NMR (150 MHz, CDCl3) δ 163.3, 137.6, 131.0, 129.3, 127.8.

Thiophene-3-carboxamide (3b)

(Eluent: 30% EtOAc/hexane); 87% yield (221.0 mg); white solid; 1H NMR (600 MHz, CDCl3): δ 7.91 (s, 1H), 7.40 (d, J = 4.0 Hz, 1H), 7.36 (t, J = 4.0 Hz, 1H), 5.84 (br, NH, 2H). 13C NMR (150 MHz, CDCl3) δ 164.5, 136.4, 129.3, 126.7, 126.3.

Picolinamide (3c)

(Eluent: 40% EtOAc/hexane); 60% yield (146.3 mg); white solid; 1H NMR (500 MHz, CDCl3): δ 8.58 (d, J = 4.5 Hz, 1H), 8.20 (d, J = 7.5 Hz, 1H), 7.86 (m, 1H), 7.45 (m, 1H), 6.10 (br, NH, 2H). 13C NMR (150 MHz, CDCl3) δ 166.9, 149.5, 148.3, 137.2, 126.4, 122.4.

Nicotinamide (3d)

(Eluent: 45% EtOAc/hexane); 77% yield (124.2 mg); white solid; 1H NMR (600 MHz, CDCl3): δ 9.03 (s, 1H), 8.76 (d, J = 3.5 Hz, 1H), 8.17 (d, J = 6.5 Hz, 1H), 7.42 (t, J = 4.5 Hz, 1H), 6.28 (br, NH, 2H). 13C NMR (150 MHz, CDCl3) δ 167.3, 152.7, 148.2, 135.5, 129.1, 123.6.

Isonicotinamide (3e)

(Eluent: 45% EtOAc/hexane); 65% yield (158.4 mg); white solid; 1H NMR (600 MHz, CDCl3): δ 8.78 (d, J = 4.5 Hz, 1H), 7.65 (q, J = 2.5 Hz, 2H), 6.18 (br, NH, 2H). 13C NMR (150 MHz, CDCl3) δ 167.1, 150.7, 141.0.

Pyrazine-2-carboxamide (3f)

(Eluent: 50% EtOAc/hexane); 68% yield (167.3 mg); white solid; 1H NMR (600 MHz, CDCl3): δ 9.43 (s, 1H), 8.78 (d, J = 2.5 Hz, 1H), 8.56 (d, J = 1.5 Hz, 1H), 5.98 (br, NH, 2H). 13C NMR (125 MHz, CDCl3) δ 165.3, 147.5, 144.6, 144.1, 142.7.

4-((Imidazo [1, 2-a] pyridin-2-yl) benzamide (3g)

(Eluent: 70% EtOAc/hexane); 75% yield (270.1 mg); white solid; 1H NMR (600 MHz, DMSO-d6): δ 8.56 (d, J = 4.5 Hz, 1H), 8.52 (s, 1H), 8.04 (t, J = 5.5 Hz, 3H), 7.97 (d, J = 5.5 Hz, 2H), 7.63 (d, J = 7.0 Hz, 1H), 7.38 (s, 1H), 7.31 (t, J = 5.0 Hz, 1H), 6.95 (s, 1H). 13C NMR (150 MHz, CDCl3) δ 168.1, 145.2, 143.5, 136.7, 133.8, 128.5, 127.6, 126.2, 125.7, 117.0, 113.2, 110.7.

Acetamide (3h)
(Eluent: 40% EtOAc/hexane); 58% yield (68.9 mg); white solid; 1H NMR (600 MHz, CDCl3): δ 5.82 (br, NH, 2H), 1.98 (s, 3H). 13C NMR (125 MHz, CDCl3) δ 172.9, 22.7.

Pentanamide (3i)

\[
\text{NH}_2
\]

(Eluent: 40% EtOAc/hexane); 59% yield (119.4 mg); white solid; 1H NMR (600 MHz, DMSO- d 6): δ 7.23 (br, NH, 2H) 2.02 (t, J = 6.0 Hz, 2H), 1.26 (q, J = 5.5 Hz, 3H).

13C NMR (150 MHz, DMSO- d 6): δ 174.9, 27.7, 22.3, 14.2.

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