4a.1. INTRODUCTION

The wedding of two emergent area of twenty first century, nanocatalysis and green chemistry holds the answer of sustainability. Catalyst builds the main strategy for organic reactions via modulation of energy. Nano-catalysis (N-CAT) is one of them as growing research area due to their unique properties. The efficiency of Metal-based heterogeneous nanoparticles catalysis in organic synthesis can be improved by employing nano-sized catalysts because of their extremely small and large surface to volume ratio. Recently, Nanoparticles (NPs) as catalyst have been attracting much attention because they can be easily recovered from the reaction mixture and ZnO-NPs is one of them. According to the recent literature survey ZnO-NPs is inexpensive, non-toxic catalyst and also has environmental advantages i.e., disposal of the catalyst and utilize for waste water treatment by removing chemical and biological contaminants after reused. Many researchers have been reported the potential utility of ZnO-NPs in biological field such as anti-cancer, and anti-bacterial.

More recently, numerous functionalized NPs have been employed in a variety of organic transformations, showing excellent catalytic properties in C-C bond formation, hydrogenation, oxidation amination, and Ritter reactions. However, it is an innovative stratagems, if multi-component reactions could be carried out via green
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protocol with nanoparticle, it would be most proficient synthetic method
for organic synthesis.

4a.2. BASIS OF WORK

Nitrogen-containing heterocyclic molecules constitute the largest
portion of chemical entities, which are part of many natural products, fine
chemicals, and biologically active pharmaceuticals vital for enhancing the
quality of life. Phenylacetimidamide, phenylacetamide and α-amino acid scaffold display a wide range of biological activities (Figure 4a.1).

Figure. 4a.1. Biologically active compounds containing amidine, amide
and amino acid skeleton.
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4a.3 CHEMISTRY

The most widely studied MCR is Ugi-4CR\textsuperscript{19} (Figure 4a.2, path a) have generated much interest because of their wide synthetic and medicinal application.\textsuperscript{20} Recently, List and Pan interestingly modified Ugi-4CR into Ugi-3CR (ABC type) for the synthesis of 2-amino-2-phenylacetamide b from aldehyde, amine and isocyanide catalyzed by phenyl phosphinic acid.\textsuperscript{21} (Figure 4a.2, path b).

Figure 4a.2. (a) Ugi-4CR (b) a newly reported three-component reaction by List and Pan.

Inspired from Ugi-3CR, we focused our efforts towards the search of new efficient methodology using ZnO-NPs as a catalyst for reaction and we surprised to obtain 2-arylamino-2-phenylacetimidamide 5 (AB2C) type product (scheme 4a.1) instead of expected 2-amino-2-phenylacetamide b. In order to establish the utility of 5, we hydrolyzed it under green conditions which yielded 2-arylamino-2-phenylacetamides 6 and N-substituted amino acids 7 respectively.
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Scheme 4a.1. ZnO-NPs catalyzed Ugi three-component reaction for the synthesis of 2-arylamino-2-phenylacetimidamide 5.

Previously, researcher\(^2\) reported the synthesis of 2-arylamino-2-phenylacetimidamide derivative using bromodimethylsulphonium bromide (BDMS) with acetonitrile. This methodology suffer from severe drawback such as longer reaction time, harsh reaction conditions, use of non-biodegradable solvent and expensive, harmful, unstable catalyst. In continuation of our quest for developing green protocols\(^3\) herein, we wish to report a first (\(AB^2C\)) Ugi type 3-CR for the synthesis of 2-arylamino-2-phenylacetimidamide derivatives 5 from aldehyde 1, aniline 2 and isocyanide 3 by employing the catalytic amount of ZnO-nanoparticle as an efficient, heterogeneous and reusable catalyst (Scheme 4a.1). To the best of our knowledge, none methodology has been reported till now of the use of ZnO-NPs as a reusable catalyst for the synthesis of 2-arylamino-2-phenylacetimidamide derivatives.
Table 4a.1. Optimization of reaction conditions for the synthesis of 2-arylamino-2-phenylacetimidamide 5a.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time (h)</th>
<th>Yield (%)(^e)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>4</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
<td>-</td>
<td>5</td>
<td>28</td>
</tr>
<tr>
<td>4</td>
<td>BF(_3)</td>
<td>8</td>
<td>32</td>
</tr>
<tr>
<td>5</td>
<td>TiCl(_4)</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>6</td>
<td>CuI</td>
<td>6</td>
<td>42</td>
</tr>
<tr>
<td>7</td>
<td>TiO(_2)</td>
<td>7</td>
<td>43</td>
</tr>
<tr>
<td>8</td>
<td>ZnO(^b)</td>
<td>8</td>
<td>48</td>
</tr>
<tr>
<td>9</td>
<td>ZnO(^b)</td>
<td>6</td>
<td>50</td>
</tr>
<tr>
<td>10</td>
<td>ZnO(^b)</td>
<td>15 min</td>
<td>60</td>
</tr>
<tr>
<td>11</td>
<td>ZnO(^c)</td>
<td>5 min</td>
<td>90</td>
</tr>
<tr>
<td>12</td>
<td>ZnO(^d)</td>
<td>6 min</td>
<td>90</td>
</tr>
</tbody>
</table>

\(^a\)Reaction Conditions: Benzaldehyde (1 mmol), Aniline (2 mmol), tert-butyl isocyanide, (1 mmol), and ZnO-NPs (15 mol %) in water (3 ml) at rt.  
\(^b\)10 mol% of ZnO(NPs).  
\(^c\)15 mol% ZnO(NPs).  
\(^d\)20 mol% ZnO(NPs).  
\(^e\)Isolated yield.

Our initial efforts were focused on the actual effectiveness of catalysts for the modified Ugi three-component reaction. The model
reaction of benzaldehyde 1, aniline 2 and tert-butyl isocyanide 3 was performed without use of any catalyst in different solvents at room temperature. Only a trace amount of the product was formed (Table 4a.1, entries 1-3). The obtained results prompted us to catalyze the reaction with different catalysts. First we choose BF$_3$ (non-metal Lewis acid) to catalyzed the reaction mixture, resulted to the formation of desired product in 32% yield (Table 4a.1, entry 4). We did not found satisfactory results when we used metal Lewis acids such as TiCl$_4$ and CuI (Table 4a.1, entries 5 and 6). After screening of Lewis acid catalysts we turned our attention towards the use of nano-particles like TiO$_2$-NPs as a heterogeneous catalyst but no improvement was observed in the yield of desired product 5a (Table 4a.1 entry7). Fortunately, we acquired pleasant result when we carried out the reaction with ZnO-NPs (Table 4a.1, entry 11). Among the catalysts evaluated, ZnO-NPs was superior to others and provided the best yield of the compound 2-arylamino-2-phenylacetimidamide 5a.

It was found that catalyst loading also played important role in this reaction and 15 mol % ZnO-NPs was found to be sufficient to obtained the desired product 5 with excellent yield. (Table 4a.1, entry 11). The yield remained unaffected when the catalyst loading was increased 15 to 20 mol % (Table 4a.1, entry 12).

The reaction was also screened in different solvents as well. We used a variety of polar and nonpolar solvents like DMSO, ethanol, methanol toluene, THF and CH$_3$CN (Table 4a.2). We observed that polar
protic solvent afforded moderate yield than other solvents. By keeping the vital aspect of water in mind we tried the same reaction in aqueous medium and found the best results (Table 4a.2 entry 7).

**Table 4a.2.** Effect of solvents for the synthesis of 2-arylamino-2-phenylacetimidamide catalysed by ZnO-NPs.\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DMSO</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>Toluene</td>
<td>34</td>
</tr>
<tr>
<td>3</td>
<td>THF</td>
<td>40</td>
</tr>
<tr>
<td>4</td>
<td>CH(_3)CN</td>
<td>45</td>
</tr>
<tr>
<td>5</td>
<td>ethanol</td>
<td>48</td>
</tr>
<tr>
<td>6</td>
<td>Methanol</td>
<td>50</td>
</tr>
<tr>
<td>7</td>
<td>H(_2)O</td>
<td>90</td>
</tr>
</tbody>
</table>

\(^a\)**Reaction conditions**: aniline (1 mmol), benzaldehyde (1 mmol), and tert-butyl-isocyanide (1 mmol) with 15 mol % ZnO-NPs at r.t. for a given time. \(^b\)**Isolated yield.**

Therefore, the survey of solvents with ZnO-NPs revealed that water was the best choice (Table 4a.2, entry 7) whereas other organic solvents diminished the reactivity (Table 4a.2, entries 1-6).
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The obtained results demonstrated the viability of ZnO-NPs catalyzed strategy, therefore we explored the scope and generality of the reaction. The desired product 5 obtained in good to high yields by using a wide range of aldehydes including aromatic/hetero-aromatic, substituted aniline, and different isocyanides. In contrast to the aniline with electron-withdrawing substituents, the formation of desired product took slightly longer reaction time than aniline with electron-donating groups (Table 4a.3, entries 1-15).

**Table 4a.3.** Synthesis of 2-arylamino-2-phenylacetimidamide 5 via modified Ugi three-component reaction.a

<table>
<thead>
<tr>
<th>Entry</th>
<th>R1</th>
<th>R2</th>
<th>R3</th>
<th>Prod.</th>
<th>Time(h)</th>
<th>Yieldb(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>H</td>
<td>tBuNC</td>
<td>5a</td>
<td>5</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>4-Cl</td>
<td>4-OMe</td>
<td>cHexNC</td>
<td>5b</td>
<td>8</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>4-OMe</td>
<td>4-Cl</td>
<td>cHexNC</td>
<td>5c</td>
<td>5</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>3-OMe</td>
<td>3-Cl</td>
<td>tBuNC</td>
<td>5d</td>
<td>6</td>
<td>82</td>
</tr>
<tr>
<td>5</td>
<td>H</td>
<td>3-OMe</td>
<td>tBuNC</td>
<td>5e</td>
<td>7</td>
<td>88</td>
</tr>
<tr>
<td>6</td>
<td>4-Cl</td>
<td>4-F</td>
<td>pTsCH2</td>
<td>5f</td>
<td>5</td>
<td>84</td>
</tr>
<tr>
<td>7</td>
<td>4-Cl</td>
<td>3-OMe</td>
<td>tBuNC</td>
<td>5g</td>
<td>5</td>
<td>79</td>
</tr>
<tr>
<td>8</td>
<td>4-Br</td>
<td>3-OMe</td>
<td>tBuNC</td>
<td>5h</td>
<td>5</td>
<td>80</td>
</tr>
<tr>
<td>9</td>
<td>4-Cl</td>
<td>4-OMe</td>
<td>tBuNC</td>
<td>5i</td>
<td>5</td>
<td>83</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Reaction Conditions: bezaldehyde (1 mmol), aniline (2 mmol), isocyanide (1 mmol), and 15 mol% ZnO-NPs in water (3 mL) at rt. Isolated Yield.</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 4-F 4-OMe cHexNC 5j 5 80</td>
</tr>
<tr>
<td>11 H 2,4diMe cHexNC 5k 6 82</td>
</tr>
<tr>
<td>12 4-py 4-Cl cHexNC 5l 5 75</td>
</tr>
<tr>
<td>13 4-py H tBuNC 5m 5 80</td>
</tr>
<tr>
<td>14 4-Cl 4-Cl 2-morp ethyl 5n 5 73</td>
</tr>
<tr>
<td>15 H 4-NO2 tBuNC 5o 15 70</td>
</tr>
</tbody>
</table>

Figure 4a.3. Structures of Synthesized 2-arylamino-2-phenylacetimidamide
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![Chemical Structures](image)
The Green Chemistry movement has developed a series of metrics to support and reinforce behaviour change on both industry and academia in the move towards green and more sustainable chemistry. Two most common green metrics, Atom economy and Atom efficiency are calculated below.

Atom Economy = \( \frac{357.22}{(106.04+186.12+83.07) \times 100} \) = 95.2%

Atom Efficiency = 90% × 95.2% = 85.6%

From the green chemistry point of view, efficient recovery and reuse of the catalyst are highly desirable, thus the recovery and reusability of ZnO-NPs were investigated. After completed the reaction, ethylacetate was added until the solid crude product was dissolved. Then, ZnO-NPs as the catalysts were isolated from the mixture of reaction by simple filtration and reused again after washing with ethylacetate.

**Figure 4a.4.** Recovery and Reuse of ZnO-Nanoparticle for the Synthesis of 5a.
The structural data of compound 5a, highlighted the possibility of tautomeric structures 5A and 5B. In order to address this issue it was anticipated that the hydrolysis of 5a could offer either 6a when 5A form is predominant or 8 when 5B is predominant (Figure 4a.4).

**Figure 4a.5.** Representation of possible tautomeric structure.

Neutral hydrolysis of 5a, 5b, 5h, 5i, and 5k in the presence of I₂/SDS(sodium dodecyl sulfate)/water afforded corresponding 2-amino-2-phenylacetamide derivatives 24 6 (Table 4a.4), which suggested that compound 5A was the actual isomer instead of 5B.
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Table 4a.4. Synthesis of 2-arylamino-2-phenylacetamide 6 via hydrolysis of 2-arylamino-2-phenylacetimidamide 5.a

<table>
<thead>
<tr>
<th>Entry</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
<th>R&lt;sup&gt;3&lt;/sup&gt;</th>
<th>Prod.</th>
<th>Time(h)</th>
<th>Yield&lt;sup&gt;b&lt;/sup&gt;(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>H</td>
<td>tBuNC</td>
<td>6a</td>
<td>5</td>
<td>70</td>
</tr>
<tr>
<td>2</td>
<td>4-Cl</td>
<td>4-OMe</td>
<td>cHexNC</td>
<td>6b</td>
<td>7</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>4-Br</td>
<td>3-OMe</td>
<td>tBuNC</td>
<td>6h</td>
<td>6</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>4-Cl</td>
<td>4-OMe</td>
<td>tBuNC</td>
<td>6i</td>
<td>5</td>
<td>75</td>
</tr>
<tr>
<td>5</td>
<td>H</td>
<td>2,4-diMe</td>
<td>cHexNC</td>
<td>6k</td>
<td>10</td>
<td>74</td>
</tr>
</tbody>
</table>

*aReaction conditions**: 2-Arylamino-2-phenylacetimidamide 5 (1 mmol) with I<sub>2</sub> (20 mol %), and SDS (10 mol %), in water (3 mL) at 80°C. *b* Isolated Yield.

Searching for the utility of 5 we further converted it into N-substituted α-amino acid 7 via alkaline hydrolysis. To demonstrate the feasibility of this reaction, initially experiments were performed using 5a and found the expected product 7a. To generalize this scope various derivatives of 5 were successfully hydrolyzed and results have been shown
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in Table 4.

Table 4a.5. Synthesis of α-amino acid via alkaline hydrolysis of 2-arylamino-2-phenylacetimidamide 5.

<table>
<thead>
<tr>
<th>Entry</th>
<th>R₁</th>
<th>R₂</th>
<th>R₃</th>
<th>Prod.</th>
<th>Time (h)</th>
<th>Yieldb (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>H</td>
<td>tBuNC</td>
<td>7a</td>
<td>9</td>
<td>70</td>
</tr>
<tr>
<td>2</td>
<td>4-Cl</td>
<td>4OMe</td>
<td>cHexNC</td>
<td>7b</td>
<td>8</td>
<td>72</td>
</tr>
<tr>
<td>3</td>
<td>4-Cl</td>
<td>OMe</td>
<td>tBuNC</td>
<td>7b</td>
<td>10</td>
<td>65</td>
</tr>
<tr>
<td>4</td>
<td>H</td>
<td>2,4-diMe</td>
<td>cHexNC</td>
<td>7k</td>
<td>10</td>
<td>69</td>
</tr>
</tbody>
</table>

aReaction conditions: 2-Arylamino-2-phenylacetimidamide 5 (1 mmol), NaOH (20 mol%) in H₂O:EtOH (1:3, 4 mL) at 70°C. bIsolated Yield.

On the basis of the above observations and the literature survey, we hypothesised the plausible mechanism for the synthesis of 2-arylamino-2-phenylacetimidamide 5a as shown in Scheme 2. The reaction commences with the formation of shiff-base (1a) from aldehyde and aniline catalyzed by ZnO-NPs. Now 1a was further activated by ZnO-NPs via protonation favouring the nucleophilic attack of isocyanide to provide
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the intermediate 1b. Subsequently, another molecule of aniline react with 1b, leads to the formation of α-amino amidines 4 which undergoes [1,3] hydrogen shift to yield the desired product 5.

**Figure 4a.6.** Plausible mechanistic pathway for the synthesis of 2-arylamino-2-phenylacetimidamide 5.

4a.4. CONCLUSION

In conclusion, we have demonstrated Nano-particle Catalyzed Reaction (NPCR) Ugi type three-component reaction in water. A highly efficient and environmentally green methodology for the synthesis of 2-arylamino-2-phenylacetimidamide derivatives from amine, aldehyde and isocyanide has been developed. 2-Arylamino-2-phenylacetamide have
been synthesized by using green hydrolysis system I$_2$/SDS(sodium dodecyl sulfate)/water from 2-arylamino-2-phenylacetimidamide. N-substituted α-amino acids via alkaline hydrolysis. These ecofriendly procedures can be regarded as new methods for the preparation of pharmaceutically relevant phenylacetimidamide, phenylacetamide and α-amino acid derivatives.

4a.5. EXPERIMENTAL DETAILS WITH SPECTRAL AND ANALYTICAL DATA

1. All reactions were monitored by TLC over silica gel plate. The spots on TLC plates were visualized under UV lamp or by iodine vapors.
2. Temperature mentioned through room temperature (throughout the year).
4. IR spectra were recorded using Perkin-Elmer’s Spectrum RX I FTIR spectrophotometer as KBr disc.
5. $^1$H-NMR, and $^{13}$C-NMR spectra were recorded on Bruker Avance DPX-300 MHz or Avance DPX-200 MHz FT Bruker spectrometers, using deuteriated solvents and TMS as an internal standard. Data expresses the chemical shift values in δ ppm from downfield to upfield in both $^1$H-NMR
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and $^{13}$C-NMR spectra. For all compounds, $^1$H-NMR data is reported in the following order: Chemical shift (multiplicity, $J$ value, number of protons).

6. ES mass spectra were recorded in Merck M-8000 LCMS system or Micromass Quadro LCMS system and HR/EI mass were done on JEOL-600H at 70eV.

7. Elemental analyses were carried out on Carlo-Erba-1108 instrument or Elementar’s Vario EL III micro-analysers.

4a.6. GENERAL EXPERIMENT PROCEDURE FOR THE SYNTHESIS OF COMPOUND (5)

Aldehyde (1.0 mmol), aniline (2.0 mmol), isocyanide (1.0 mmol) and catalyst CellSA (50 mg) were placed into a flask. Water (5 mL) was added to the mixture and stirred for 30 min at room temperature. Progress of reaction was monitored by TLC, after completion of the reaction, the reaction mixture was diluted with water and extracted with ethyl acetate, dried over sodium sulphate and evaporated under vacuum to give crude product, which was purified by silica gel (100-200 mesh) column chromatography to afford the corresponding product.

4a.6.1. CHARACTERIZATION DATA FOR SYNTHESIZED COMPOUND (5a-o).

N-Tert-butyl-N',2-diphenyl-2-(phenylamino)acetimidamide (5a)

White solid, ESI MS ($m/z$) = 358 (M+H), IR (KBr) $\nu_{\text{max}}$ : 3289, 3027, 2966, 2906, 1634, 1601, 1591, 1485, 1310, 1253, 1185, 1166, 1070, 745 cm$^{-1}$. $^1$H
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NMR (300 MHz; CDCl₃) δ_H: 1.48 (s, 9H), 4.22 (s, 1H, NH), 4.92 (s, 1H, CH), 6.26 (s, 1H, NH), 6.54 (d, J = 5.7 Hz, 2H), 6.66 (t, J = 1.0 Hz, 1H), 6.96 (d, J = 5.0 Hz, 2H), 7.08-7.13 (m, 5H), 7.29 (t, J = 4.2 Hz, 1H), 7.40 (q, J = 1.3 Hz, 4H). ¹³C NMR (50 MHz; CDCl₃) δ_C : 29.6, 52.0, 56.5, 112.1, 119.0, 120.0, 123.4, 127.4, 128.8, 128.9, 139.7, 146.0, 148.3, 158.6. Analysis calculated for : C₂₄H₂₇N₃, C 80.63, H 7.61, N 11.75, Found : C 80.58, H 7.53, N 11.82.

2-(4-Chlorophenyl)-N-cyclohexyl-N'-(4-methoxyphenyl)-2-4ethoxyphenylamino)acetimidamide (5b)

White solid, ESI MS (m/z) = 478 (M+H), IR (KBr) ν_max : 3319, 3030, 2860, 2730, 2140, 1650, 747 cm⁻¹. ¹H NMR (300 MHz; CDCl₃) δ_H : 1.27-1.59 (m, 8H), 1.60 (br, s, 2H), 1.91 (br, s, 1H), 3.80 (s, 3H, OCH₃), 3.95 (s, 3H, OCH₃), 4.67 (s, 1H, NH), 5.32 (s, 1H, CH), 6.11 (s, 1H, NH), 6.44 (d, J = 8.5 Hz, 2H), 6.94 (d, J = 8.6 Hz, 2H), 7.04 (d, J = 6.4 Hz, 4H), 7.28-7.37(m, 4H). ¹³C NMR (50 MHz; CDCl₃) δ_C : 25.4, 26.5, 32.8, 53.9, 55.3, 56.6, 113.9, 114.1, 114.7, 122.9, 128.2, 128.5, 132.6, 136.4, 141.3, 141.5, 141.7, 154.3, 154.7, 158.2. Analysis calculated for : C₂₈H₃₂ClN₃O₂, C 70.35, H 6.75, N 8.79 Found : C 70.23, H 6.87, N 8.66.
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N’-(4-Chlorophenyl)-2-(4-chlorophenylamino)-N-cyclohexyl-2-(4-methoxyphenyl)acetimidamide (5c)

White solid, ESI MS (m/z) = 482 (M+H), IR (KBr) 
ν\text{max} : 3384, 2967, 2901, 1641, 1491, 1482, 1284, 746 cm\(^{-1}\). \(^1\)H NMR (300 MHz; CDCl\(_3\)) \(\delta\)H : 1.10-1.37 (m, 4H), 1.49 (t, \(J = 4.7 \text{ Hz}, 2\)H), 1.67 (t, \(J = 14.5 \text{ Hz}, 4\)H), 2.01 (t, \(J = 13.5 \text{ Hz}, 1\)H), 3.74 (s, 3H, OCH\(_3\)), 4.33 (s, 1H, NH), 4.61 (s, 1H, CH), 5.85 (s, 1H, NH), 6.11 (s, 1H), 6.75 (d, \(J = 8.4 \text{ Hz}, 4\)H), 7.08 (s, 1H), 7.18 (d, \(J = 8.6 \text{ Hz}, 4\)H), 7.28 (d, \(J = 3.5 \text{ Hz}, 2\)H). \(^{13}\)C NMR (75 MHz; CDCl\(_3\)) \(\delta\)C : 24.6, 24.7, 25.3, 29.6, 32.7, 32.9, 48.4, 55.3, 58.8, 113.1, 114.7, 120.4, 122.9, 127.7, 128.3, 128.8, 130.1, 141.4, 159.8. Analysis calculated for : C\(_{27}\)H\(_{29}\)Cl\(_2\)N\(_3\)O, C 67.22, H 6.06, N 8.71 Found : C 67.13, H 5.96, N 8.83.

N-Tert-butyl-N’-(3-chlorophenyl)-2-(3-chlorophenylamino)-2-(3 methoxyphenyl)acetimidamide (5d)

White solid, ESI MS (m/z) = 456 (M+H), IR (KBr) 
ν\text{max} : 3373, 2966, 1719, 1669, 1633, 1588, 1492, 1373, 1212, 1127, 1033, 749 cm\(^{-1}\). \(^1\)H NMR (300 MHz; CDCl\(_3\)) \(\delta\)H :1.46 (s, 9H), 3.74 (s, 3H, OCH\(_3\)), 4.76 (s, 1H, NH), 5.31( s, 1H, CH), 5.89 (s, 1H, NH), 6.40 (d, \(J = 8.3 \text{ Hz}, 2\)H), 6.58 (d, \(J = 7.3 \text{ Hz}, 2\)H), 6.84 (d, \(J = 5.7 \text{ Hz}, 2\)H), 7.12-7.18 (m, 4H), 7.19 (d, \(J = 8.4 \text{ Hz}, 2\)H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\)C : 29.6, 51.9, 55.2, 58.0, 111.1, 112.5, 114.6, 115.3, 118.8,
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119.4, 119.6, 121.4, 123.9, 129.1, 130.2, 130.9, 133.4, 134.2, 141.1, 148.1, 149.2, 157.2, 159.8. Analysis calculated for : C_{25}H_{27}Cl_{2}N_{3}O, C 65.79, H 5.96, N 9.21 Found : C 65.88, H 6.08, N 9.12.

N-Tert-butyl-N'-(3-methoxyphenyl)-2-(3-methoxyphenylamino)-2-phenylacetimidamide (5e)

White solid, ESI MS (m/z) = 418 (M+H), IR (KBr) ν_{max} : 3375, 2976, 1720, 1668, 1589, 1482, 1383, 1128, 1071, 746 cm^{-1}. ^{1}H NMR (300 MHz; CDCl_{3}) δ_{H} : 1.51 (s, 9H), 3.75 (s, 3H, OCH_{3}), 3.79 (s, 3H, OCH_{3}), 4.34 (s, 1H, NH), 4.70 (s, 1H, CH), 6.03 (s, 1H, NH), 6.20 (d, J = 1.2 Hz, 1H), 6.55 (t, J = 1.3 Hz, 1H), 6.74-6.87 (m, 4H), 6.95 (t, J = 4.9 Hz, 1H), 7.10 (d, J = 5.9 Hz, 3H), 7.13 (d, J = 2.6 Hz, 3H)^{13}C NMR (50 MHz; CDCl_{3}) δ_{C} : 29.6, 51.9, 55.1, 55.4, 57.9, 100.7, 104.9, 105.8, 106.0, 106.0, 106.3, 106.9, 116.3, 127.4, 127.5, 128.9, 129.6, 130.0, 140.0, 147.9, 149.6, 157.3, 158.9, 158.9. Analysis calculated for : C_{26}H_{31}N_{3}O_{2}, C 74.79, H 7.48, N 10.06, Found : C 74.68, H 7.57, N 9.93.

2-(4-Chlorophenyl)-N'-(4-fluorophenyl)-2-(4-fluorophenylamino)-N-(tosylmethyl)acetimidamide (5f)

Pale yellow solid, ESI MS (m/z) = 540 (M+H), IR (KBr) ν_{max} : 3469, 2989, 1730, 1678, 1589, 1482, 1383, 1128, 1089, 751 cm^{-1}. ^{1}H NMR (300 MHz; CDCl_{3}) δ_{H} : 2.42 (s, 3H, CH_{3}), 4.36 (s, 1H, NH),
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4.46 (s, 2H), 4.93 (s, 1H, CH), 6.35 (s, 1H, NH), 6.50 (t, J = 6.0 Hz, 2H), 6.75 (d, J = 6.1 Hz, 2H), 7.01-7.09 (m, 4H), 7.17-7.20 (m, 6H), 7.80 (d, J = 6.4 Hz, 2H), \(^1^3\)C NMR (75 MHz; CDCl\(_3\)) \(\delta_C\): 21.0, 46.2, 57.7, 114.8, 114.8, 115.6, 115.8, 116.0, 116.2, 123.6, 123.6, 128.2, 128.3, 128.4, 130.1, 132.6, 133.1, 136.5, 143.1, 143.3, 143.4, 143.5, 143.7, 156.9, 159.5. Analysis calculated for: C\(_{28}\)H\(_{24}\)ClF\(_2\)N\(_3\)O\(_2\)S, C 62.27, H 4.48, N 7.78, Found: C 62.18, H 4.32, N 7.89.

**N-Tert-butyl-2-(4-chlorophenyl)-N’-(3-methoxyphenyl)-2-(3-methoxyphenylamino)acetimidamide (5g)**

White solid, ESI MS (m/z) = 452 (M+H), IR (KBr) \(\nu_{\text{max}}\): 3359, 2965, 2828, 1616, 1590, 1495, 1291, 1214, 1170, 1099, 748 cm\(^{-1}\). \(^1^H\) NMR (300 MHz: CDCl\(_3\)) \(\delta_H\): 1.51 (s, 9H), 3.67 (s, 3H, OCH\(_3\)), 3.80 (s, 3H, OCH\(_3\)), 4.41 (s, 1H, NH), 4.48 (s, 1H, CH), 6.00 (s, 1H, NH), 6.29 (d, J = 8.6 Hz, 1H), 6.47 (d, J = 7.9 Hz, 2H), 6.64 (s, 1H), 6.74 (d, J = 7.6 Hz, 1H), 6.82-6.88 (m, 2H), 7.20 (dd, J = 7.2, 16.0, Hz, 4H), 7.31 (t, J = 5.3 Hz, 2H), \(^1^3\)C NMR (50 MHz: CDCl\(_3\)) \(\delta_C\): 29.6, 51.9, 55.1, 55.4, 58.0, 100.7, 104.9, 105.8, 106.0, 106.0, 106.3, 106.9, 116.3, 127.8, 128.1, 128.2, 128.4, 129.6, 130.0, 132.6, 137.4, 147.3, 149.3, 157.3, 158.9. Analysis calculated for: C\(_{26}\)H\(_{30}\)ClN\(_3\)O\(_2\), C 69.09, H 6.69, N 9.30, Found: C 69.18, H 6.78, N 9.18.
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2-(4-Bromophenyl)-N-tert-butyl-N'(3-methoxyphenyl)-2-(3-methoxyphenylamino)acetimidamide (5h)

White solid, ESI MS (m/z) = 496 (M+H), IR (KBr) ν\text{max} : 3380, 3362, 2958, 1637, 1595, 1508, 1481, 1329, 749 cm\(^{-1}\).\(^1\)H NMR (300 MHz; CDCl\(_3\)) δ\text{H} : 1.49 (s, 9H), 3.67 (s, 3H, OCH\(_3\)), 3.84 (s, 3H, OCH\(_3\)), 4.35 (s, 1H, NH), 4.48 (s, 1H, CH), 6.04 (s, 1H, NH), 6.27 (d, \(J = 5.0\) Hz, 1H), 6.47 (d, \(J = 6.9\) Hz, 1H), 6.64 (s, 1H), 6.74 (d, \(J = 6.0\) Hz, 1H), 6.81-6.88 (m, 2H), 7.21 (d, \(J = 6.5\) Hz, 2H), 7.33 (t, \(J = 6.5\) Hz, 2H), 7.51 (d, \(J = 6.7\) Hz, 2H), \(^1\)C NMR (50 MHz; CDCl\(_3\)) δ\text{C} : 29.6, 51.9, 55.2, 55.5, 57.7, 101.7, 105.9, 105.8, 106.0, 106.0, 106.3, 106.9, 116.3, 121.7, 128.4, 129.6, 130.0, 131.5, 138.2, 147.3, 149.6, 158.9. Analysis calculated for : C\(_{26}\)H\(_{30}\)BrN\(_3\)O\(_2\), C 62.90, H 6.09, N 8.46. Found: C 62.98, H 5.99, N 8.34.

N-Tert-butyl-2-(4-chlorophenyl)-N'(4-methoxyphenyl)-2-(4-methoxyphenylamino)acetimidamide (5i)

White solid, ESI MS (m/z) = 452 (M+H), IR (KBr) ν\text{max} : 3319, 3050, 2870, 2760, 2150, 1630, 752 cm\(^{-1}\).\(^1\)H NMR (300 MHz; CDCl\(_3\)) δ\text{H} : 1.51 (s, 9H), 3.75 (s, 3H, OCH\(_3\)), 3.80 (s, 3H, OCH\(_3\)), 4.38 (s, 1H, NH), 4.70 (s, 1H, CH), 6.03 (s, 1H, NH), 6.20 (d, \(J = 3.2\) Hz, 1H), 6.71 (t, \(J = 1.3\) Hz, 1H), 6.74-6.87 (m, 4H), 6.98-7.23 (m, 4H), 7.26 (t, \(J = 2.6\) Hz, 2H).\(^1\)C NMR (75 MHz; CDCl\(_3\)) δ\text{C} : 29.6, 52.0, 55.3, 56.1, 113.6, 113.9, 114.1, 121.7, 127.7, 128.1, 128.1, 128.4, 132.6, 137.4, 139.1, 141.9,
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154.7, 155.1, 158.2. Analysis calculated for : C_{26}H_{30}ClN_{3}O_{2}, C 69.09, H 6.69, N 9.30; Found : C 68.97, H 6.76, N 9.21.

**N-Cyclohexyl-2-(4-fluorophenyl)-N’-(4-methoxyphenyl)-2-(4-methoxyphenylamino)acetimidamide (5j)**

![Chemical Structure of 5j](image)

White solid, ESI MS (m/z) = 462 (M+H), IR (KBr) ν_{max} : 3356, 2935, 2852, 1640, 1428, 1255, 1095, 1012, 747 cm\(^{-1}\). \(^1\)H NMR (300 MHz; CDCl\(_3\)) δ\(_H\) : 1.12-1.14 (m, 5H), 1.15 (t, J = 5.6 Hz, 2H), 1.17(t, J = 11.9 Hz, 3H), 2.12 (t, J = 5.4 Hz, 1H), 3.72 (s, 3H, OCH\(_3\)), 3.79 (s, 3H, OCH\(_3\)), 4.25 (s, 1H, NH), 4.71 (s, 1H, CH), 6.10 (br, s, 1H, NH), 6.34 (br, s, 1H), 6.74 (t, J = 6.3 Hz, 1H), 6.72-6.94 (m, 4H), 6.97 (d, J = 6.8 Hz, 4H), 7.29 (d, J = 5.4 Hz, 2H). \(^{13}\)C NMR (75 MHz; CDCl\(_3\)) δ\(_C\) : 25.4, 26.5, 32.8, 53.9, 55.3, 56.8, 113.9, 114.1, 114.7, 114.9, 122.9, 128.2, 128.3, 134.1, 134.1, 141.3, 141.5, 141.7, 154.7, 158.2. Analysis calculated for : C\(_{28}\)H\(_{32}\)FN\(_3\)O\(_2\), C 72.86, H 6.99, N 9.10, Found : C 72.76, H 7.09, N 9.21.

**N-Cyclohexyl-N’-(2,4-dimethylphenyl)-2-(2,4-dimethylphenylamino)-2-phenylacetimidamide (5k)**

![Chemical Structure of 5k](image)

Yellow solid, ESI MS (m/z) = 440 (M+H), IR (KBr) ν_{max} : 3355, 2934, 2855, 2870, 1640, 1600, 14292, 1256, 1091, 1013, 754 cm\(^{-1}\).\(^1\)H NMR (300 MHz; CDCl\(_3\)) δ\(_H\) : 1.28-1.60 (m, 6H), 1.68 (t, J = 6.3 Hz, 5H), 2.16 (s, 6H, CH\(_3\)), 2.30 (s, 6H, CH\(_3\)), 4.08 (br, s, 1H, NH), 4.33 (br, s,
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1H, CH), 5.32 (br, s, 1H, NH), 6.25 (d, J = 7.5 Hz, 1H), 6.51 (d, J = 7.2 Hz, 1H), 6.68 (s, 1H), 6.74 (d, J = 7.7 Hz, 1H), 6.84 (d, J = 9.2 Hz, 2H), 7.01 (s, 1H), 7.45 (d, J = 8.5 Hz, 2H), 8.01 (d, J = 8.4 Hz, 2H). $^{13}$C NMR (50 MHz; CDCl$_3$) δ$_{C}$: 17.7, 18.1, 20.5, 20.9, 25.4, 26.5, 32.9, 53.7, 56.3, 112.6, 119.6, 122.6, 125.3, 127.1, 127.4, 127.6, 127.7, 128.9, 130.3, 131.8, 132.1, 133.2, 140.6, 142.2, 154.5, 158.6. Analysis calculated for : C$_{30}$H$_{37}$N$_{3}$, C 81.96, H 8.48, N 9.56, Found : C 82.04, H 8.41, N 9.49.

N’-(4-Chlorophenyl)-2-(4-chlorophenylamino)-N-cyclohexyl-2-(pyridin-4-yl)acetimidamid (5l)

Pale yellow solid, ESI MS (m/z) = 453 (M+H), IR (KBr) $\nu_{\text{max}}$: 3356, 2939, 2850, 2875, 1645, 1430, 1255, 1093, 1013, 756 cm$^{-1}$. $^1$H NMR (300 MHz; CDCl$_3$) δ$_{H}$ 1.25-1.55 (m, 5H), 1.67 (d, J = 13.9 Hz, 3H), 1.72 (br, s, 2H), 2.12 (t, J = 5.4 Hz, 1H), 4.36 (s, 1H, NH), 4.55 (s, 1H, CH), 6.24 (s, 1H, NH), 6.48 (d, J = 6.1 Hz, 2H), 6.79 (d, J = 6.1 Hz, 2H), 7.08 (d, J = 6.1 Hz, 2H), 7.23-7.28 (m, 4H), 8.50 (d, J = 4.5 Hz, 2H). $^{13}$C NMR (75 MHz; CDCl$_3$) δ$_{C}$: 25.4, 26.4, 32.8, 53.9, 55.9, 114.0, 122.6, 123.6, 125.0, 129.3, 129.4, 130.4, 144.8, 146.5, 146.6, 149.6, 159.9. Analysis calculated for : C$_{25}$H$_{26}$Cl$_{2}$N$_{4}$, C 66.22, H 5.78, N 12.36, Found : C 66.31, H 5.67, N 12.45.
N-Tert-butyl-N'-phenyl-2-(phenylamino)-2-(pyridin-4-yl)acetimidamide (5m)

White solid, ESI MS ($m/z$) = 359 (M+H), IR (KBr) $\nu_{\text{max}}$ : 3360, 2940, 2853, 2870, 1648, 1435, 1260, 1093, 1019, 752 cm$^{-1}$. $^1$H NMR (300 MHz; CDCl$_3$) $\delta_H$: 1.51 (s, 9H), 4.28 (s, 1H, NH), 4.69 (s, 1H, CH), 6.10 (s, 1H, NH), 6.51 (d, $J = 5.7$ Hz, 2H), 6.68 (t, $J = 5.6$ Hz, 1H), 6.94 (d, $J = 1.0$ Hz, 2H), 7.08-7.12 (m, 3H), 7.28 (d, $J = 4.4$ Hz, 2H), 7.41 (t, $J = 5.6$ Hz, 2H), 8.50 (d, $J = 4.5$ Hz, 2H). $^{13}$C NMR (75 MHz; CDCl$_3$) $\delta_C$: 29.6, 52.0, 56.3, 112.1, 118.9, 120.0, 123.4, 128.8, 128.9, 146.0, 146.8, 148.3, 149.8, 158.8. Analysis calculated for: C$_{23}$H$_{26}$N$_4$, C 77.06, H 7.31, N 15.63, Found: C 76.98, H 7.38, N 15.58.

N,2-Bis(4-chlorophenyl)-2-(4-chlorophenylamino)-N-(2-morpholinoethyl)acetimidamide (5n)

Light brown solid, ESI MS ($m/z$) = 517 (M+H), IR (KBr) $\nu_{\text{max}}$ : 3359, 2947, 2855, 2868, 1640, 1433, 1261, 1019, 754 cm$^{-1}$. $^1$H NMR (300 MHz; DMSO-d$_6$) $\delta_H$: 2.19 (t, $J = 5.1$ Hz, 2H), 2.29 (s, 4H), 3.51 (t, $J = 4.3$ Hz, 2H), 3.70 (s, 4H), 4.45 (s, 1H, NH), 5.10 (s, 1H, CH), 5.94 (s, 1H, NH), 6.54 (d, $J = 5.7$ Hz, 2H), 6.66 (t, $J = 4.6$ Hz, 2H), 6.91 (d, $J = 5.0$ Hz, 2H), 7.08 (d, $J = 5.2$ Hz, 2H), 7.29 (t, $J = 3.9$ Hz, 1H), 7.40 (t, $J = 1.3$ Hz, 3H). $^{13}$C NMR (75 MHz; DMSO d$_6$) $\delta_C$: 58.6, 62.0, 62.5, 69.3, 114.2, 122.6, 125.0, 128.3, 128.6, 129.0, 129.3, 130.4, 132.6, 137.0, 144.8, 146.2, 157.9. Analysis calculated
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for: C_{26}H_{27}Cl_{3}N_{4}O, C 60.30, H 5.25, N 10.82, Found: C 60.42, H 5.14, N 10.76.

4a.6.1. GENERAL PROCEDURE FOR SYNTHESIS OF 2-ARYLAMINO-2-PHENYLACETAMIDE (6)

In a 50-mL round-bottom flask, iodine (0.2 mmol), 2-arylamino-2-phenylacetimidamide (1 mmol), and surfactant (sodium dodecyl sulfate, 10 mol %) were added in H_{2}O (3 mL) and stirred for 6 h at 80°C and reaction was monitored by TLC. The aqueous part was diluted and extracted with ethyl acetate, the organic layer was washed with brine and dried over anhydrous Na_{2}SO_{4}. Evaporation of solvent gave a crude product which was purified by column chromatography (silica gel, ethyl acetate:hexane)

4a.6.2. CHARACTERIZATION DATA FOR SYNTHESIZED COMPOUND (5a-o).

N-Tert-butyl-2-phenyl-2-(phenylamino)acetamide (6a)

Oily, ESI MS (m/z) = 283 (M+H), IR (KBr) ν_{max}: 3382, 1641, 1531, 1473, 749, cm^{-1}.^{1}H NMR (300 MHz; CDCl_{3}) δ_{H}: 1.49 (s, 9H), 4.49 (s, 1H, NH) 4.95 (s, 1H, CH), 6.06 (s, 1H, NH), 6.57 (d, J = 5.7 Hz, 2H), 6.66 (t, J = 5.5 Hz, 1H), 6.98 (d, J = 3.7 Hz, 2H), 7.14 (t, J = 5.8 Hz, 2H), 7.28 (m, 3H).^{13}C NMR (75 MHz; CDCl_{3}) δ_{C}: 29.0, 49.6, 63.3, 113.7, 119.4, 127.4, 127.8, 127.8, 128.0, 128.8, 128.9, 139.2, 146.8, 169.7.
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Analysis calculated for: C\textsubscript{18}H\textsubscript{22}N\textsubscript{2}O: C 76.56, H 7.85, N 9.92, Found : C 76.42, H 7.97, N 9.81.

**N-Cyclohexyl-2-(2,4-dimethylphenylamino)-2-phenylacetamide (6k)**

Solid, ESI MS \((m/z) = 337\) (M+H), IR (KBr) \(\nu_{\text{max}} \): 3374, 1633, 1531, 1475, 749 cm\(^{-1}\). \(^1\)H NMR (300 MHz; CDCl\textsubscript{3}) \(\delta_H\) : 1.18-1.49 (m, 6H), 1.58 (d, \(J = 16.8\) Hz, 4H), 2.28 (s, 6H, CH\textsubscript{3}), 3.59-3.79 (m, 1H), 4.07 (s, 1H, NH), 4.53 (s, 1H, CH), 6.03 (s, 1H, NH), 6.35 (d, \(J = 3.4\) Hz, 1H), 6.76 (s, 1H), 6.84 (d, \(J = 6.09\) Hz, 1H), 7.01 (d, \(J = 4.71\) Hz, 2H), 7.32 (t, \(J = 5.52\) Hz, 3H). \(^{13}\)C NMR (75 MHz; CDCl\textsubscript{3}) \(\delta_C\) : 18.3, 20.5, 25.2, 26.3, 32.8, 49.8, 62.4, 113.2, 122.4, 127.7, 127.8, 128.0, 128.9, 130.8, 132.0, 139.1, 143.6, 170.1. Analysis calculated for: C\textsubscript{22}H\textsubscript{28}N\textsubscript{2}O, C 78.53, H 8.39, N 8.33, Found : C 78.68, H 8.47, N 8.21.

**N-Tert-butyl-2-(4-chlorophenyl)-2-(4-methoxyphenylamino)acetamide (6i)**

Solid, ESI MS \((m/z) = 347\) (M+H), IR (KBr) \(\nu_{\text{max}} \): 3383, 1639, 1535, 1478, 751cm\(^{-1}\). \(^1\)H NMR (300 MH; CDCl\textsubscript{3}) \(\delta_H\) : \(1.49\) (s, 9H), 3.69 (s, 3H, OCH\textsubscript{3}), 4.45 (s, 1H, NH), 4.91 (s, 1H, CH), 6.03 (s, 1H, NH), 6.74 (dd, \(J = 6.6, 6.6\) Hz, 4H), 7.06 (dd, \(J = 6.4, 6.3\) Hz, 4H). \(^{13}\)C NMR (75MHZ; CDCl\textsubscript{3}) \(\delta_C\) : 29.9, 49.8, 55.3, 63.1, 114.1, 114.5, 128.3, 128.5, 133.1, 137.0, 140.6, 153.8, 168.8. Analysis calculated for: C\textsubscript{19}H\textsubscript{23}ClN\textsubscript{2}O\textsubscript{2}, C 65.79, H 6.68, N 8.08, Found : C 65.86, H 6.78, N 7.98.
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2-(4-Chlorophenyl)-N-cyclohexyl-2-(4-methoxyphenylamino)acetamide (6b)

![Chemical Structure of 6b](image)

Solid, ESI MS \((m/z) = 373\) (M+H), IR (KBr) \(\nu_{\text{max}}\): 3381, 1635, 1528, 1469, 756 cm\(^{-1}\). \(^1\)H NMR (300 MHz; CDCl\(_3\)) \(\delta_H\): 1.13-1.28 (m, 5H), 1.45 (t, \(J = 4.31\) Hz, 3H), 1.65 (t, \(J = 10.6\) Hz, 2H), 3.39-3.61 (m, 1H), 3.67 (s, 3H, OCH\(_3\)), 4.14 (s, 1H, NH), 4.43 (s, 1H, CH), 6.03 (s, 1H, NH), 6.76 (q, \(J = 6.6\) Hz, 4H), 7.06 (d, \(J = 6.2\) Hz, 2H), 7.16 (d, \(J = 6.3\) Hz, 2H). \(^{13}\)C NMR (75 MHz; CDCl\(_3\)) \(\delta_C\): 25.2, 26.3, 32.8, 49.6, 55.3, 61.6, 114.1, 115.1, 128.6, 129.0, 133.1, 135.8, 140.9, 153.8, 169.5.


2-(4-Bromophenyl)-N-tert-butyl-2-(3-methoxyphenylamino)acetamide (6h)

![Chemical Structure of 6h](image)

Solid, ESI MS \((m/z) = 391\) (M+H), IR (KBr) \(\nu_{\text{max}}\): 3389, 1638, 1533, 1479, 747, cm\(^{-1}\). \(^1\)H NMR (300 MHz; CDCl\(_3\)) \(\delta_H\): 1.49 (s, 9H), 3.67 (s, 3H, OCH\(_3\)), 4.39 (s, 1H, NH), 4.93 (s, 1H, CH), 6.01 (s, 1H, NH), 6.11 (s, 1H), 6.28 (d, \(J = 5.1\) Hz, 1H), 6.45 (d, \(J = 4.6\) Hz, 1H), 6.87 (d, \(J = 5.8\) Hz, 3H), 7.44 (d, \(J = 6.3\) Hz, 2H). \(^{13}\)C NMR (75 MHz; CDCl\(_3\)) \(\delta_C\): 28.9, 49.4, 55.3, 63.1, 111.1, 114.3, 116.3, 122.4, 128.6, 129.6, 132.1, 138.2, 147.7, 141.8, 159.8, 169.5. Analysis calculated for: C\(_{19}\)H\(_{23}\)BrN\(_2\)O\(_2\), C 58.32, H 5.92, N 7.16, Found: C 58.42, H 5.81, N 7.27.
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4a.6.2. GENERAL PROCEDURE FOR THE SYNTHESIS OF α-AMINO ACID (7)

In a 50-mL round-bottom flask, 2-arylamino-2-phenylacetimidamide (1 mmol) was added in 1:3 ratio of H₂O: EtOH with 20 mol% NaOH and stirred for 3 h at 70°C. After completion of reaction as evidenced by TLC, solvent was removed in vacuum. The aqueous part was diluted and extracted with ethyl acetate, the organic layer was washed with brine and dried over anhydrous Na₂SO₄. Evaporation of solvent gave a crude product which was purified by column chromatography (silica gel, ethyl acetate:hexane).

2-Phenyl-2-(phenylamino)acetic acid (7a)

Solid, ESI MS (m/z) = 228 (M+H). IR (KBr) ν_max : 3400, 3331, 1671, 749 cm⁻¹. ¹H NMR (300 MHz, DMSO-d₆) δ_H : 4.33 (s, 1H, NH), 4.92 (s, 1H, CH), 6.29 (d, J = 5.7 Hz, 2H), 6.69 (t, J = 1.0 Hz, 1H), 7.14 (t, J = 5.7 Hz, 2H), 7.30-7.35 (m, 5H), 8.31 (s, 1H). ¹³C NMR (75 MHz, DMSO-d₆) δ_C : 60.3, 114.2, 119.4, 127.19, 127.7, 128.1, 128.3, 128.9, 129.3, 137.5, 145.8, 169.4. Analysis calculated for : C₁₄H₁₃NO₂, C 73.99, H 5.77, N 6.16, Found : C 74.09, H 5.62, N 6.25.

2-(4-Chlorophenylamino)-2-(4-methoxyphenyl)acetic acid (7b)

Solid, ESI MS (m/z) = 292 (M+H), IR (KBr) ν_max : 3419, 3292, 1678, 748 cm⁻¹. ¹H NMR (300 MHz, DMSO-d₆) δ_H : 3.67 (s, 3H, OCH₃), 4.48 (s, 1H, NH),
4.83 (s, 1H, CH), 6.51 (d, $J = 6.5$ Hz, 2H), 6.80 (d, $J = 6.5$ Hz, 2H), 7.26 (d, $J = 6.4$ Hz, 2H), 7.42 (d, $J = 6.4$ Hz, 2H), 8.30 (s, 1H). $^{13}$C NMR (50 MHz, DMSO-$d_6$) δC: 55.3, 59.6, 115.3, 116.1, 128.5, 128.8, 129.2, 130.3, 133.6, 135.7, 141.4, 154.8, 170.3. Analysis calculated for: C$_{15}$H$_{14}$ClNO$_3$, C 61.76, H 4.84, N 4.80, Found: C 61.85, H 4.73, N 4.93.

2-(2,4-Dimethylphenylamino)-2-phenylacetic acid (7k)

Solid, ESI MS ($m/z$) = 256 (M+H), $^1$H NMR (300 MHz, DMSO-$d_6$) δH: 2.25 (s, 6H, CH$_3$), 4.30 (s, 1H, NH), 4.90 (s, 1H, CH), 6.04 (d, $J = 6.0$ Hz, 1H), 6.76 (s, 1H), 6.84 (d, $J = 6.0$ Hz, 1H), 7.30-7.35 (m, 5H), 8.29 (s, 1H). $^{13}$C NMR (50 MHz, DMSO-$d_6$) δC: 18.2, 20.5, 60.7, 113.8, 121.7, 127.9, 128.1, 128.8, 129.0, 130.8, 132.7, 137.94, 143.8, 169.7. Analysis calculated for: C$_{16}$H$_{17}$NO$_2$, C 75.27, H 6.71, N 5.49, Found: C 75.37, H 6.62, N 5.58.
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REFERENCES
5. (a) Rao, G.B. D.; Kaushik M.P.; Halve, A.K. An efficient synthesis of naphtha[1,2-e]oxazinone and 14-substituted-14H-dibenzo[a,j]xanthen derivatives promoted by zinc oxide nanoparticle under thermal and
A Novel and efficient Multi-Component synthesis of 2-arylamino-2-phenylacetamide catalyzed via ZnO-NPs in aqueous media."

2014


8. (a) Shantikumar, N.; Abhilash, S.; Rani, V V. D.; Deepthy, M.; Seema, N.; Manzoor K.; Satish, R. "Role of size scale of ZnO nanoparticles and microparticles on toxicity toward bacteria and osteoblast cancer cells." J. Mater Sci: Mater Med., 2009, 20, 235; (b) Premanathan, M.; Karthikeyan,
Chapter 4a
A Novel and efficient Multi-Component synthesis of 2-arylamino-2-phenylacetamide catalyzed via ZnO-NPs in aqueous media


10.(a) Xuan, S. H.; Jiang, W. Q. X. L.; Gong,. "Immobilization of Pd nanocatalysts on magnetic rattles and their catalytic property." Dalton. Trans., 2011, 40, 7827; (b) Liu, M.; Peng, J. X. G.; Sun, W.; Zhao, Y. W.; Xia, C. G. "Magnetically separable Pd catalyst for carbonylative Sonogashira coupling reactions for the synthesis of α, β-alkynyl ketones." Org. Lett., 2008, 10, 3933; (c) Baruwati, B.; Guin D.; Manorama, S. V. "Pd on surface-modified NiFe2O4 nanoparticles: a
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A Novel and efficient Multi-Component synthesis of 2-arylamino-2-phenylacetamide catalyzed via ZnO-NPs in aqueous media


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3-alken-2-ones: preparation and applications in heterocyclic synthesis."


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Figure 4a.6 $^1$H and $^{13}$C spectra of 5a.
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Figure 4a.7. $^1$H and $^{13}$C spectra of 6a.
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Figure 4a.8. $^1$H and $^{13}$C spectra of