2.1 INTRODUCTION

Diaryl ketones have received increasing attention because of their occurrence in natural products, several biological and pharmacological active molecules (Chiang et al., 2003). It is used as photo initiators in UV-curing applications like inks, imaging, and clear coatings in the printing industry (Budavari, 1989). For instance, Macurin and Vismiaphenone E are the benzophenone derivatives which have been isolated from the stems of Garcinia multiflora and Vismia cayennensis respectively, are known to exhibit cytotoxic, antioxidative and antiviral activities (Ito et al., 2003; Fuller et al., 1999). Oxybenzone and Cotoin have been reported as active ingredients in sunscreens. Whereas, Suprofen and Ketoprofen are used as nonsteroidal, anti-inflammatory agent (Calafat et al., 2008) (Figure 2.1).

Figure 2.1 Important diaryl ketone derivatives.

A common route for the synthesis of diaryl ketones involves Friedel-Crafts acylation of substituted aromatic ring compounds with acyl halides (Olah, 1973). The crucial disadvantage of Friedel-Crafts acylation is the use of more than a stoichiometric amount of aluminium trichloride, which is incompatible with many functional groups and generates large amount of waste. Furthermore, the regioselectivity is limited to the para-position. Other synthetic strategies for the synthesis of diaryl ketones involves, acylation of aryl metal species with carboxylic acid derivatives (Silbestri, 2006), palladium-catalyzed coupling of boronic acids with carboxylic anhydride (Goosen, 2001) or nickel-catalyzed coupling reactions of aryl iodides with aromatic aldehydes (Huang, 2002).
However, the promising method for the synthesis of unsymmetrical diaryl ketones is the transition metal catalyzed three component cross-coupling of aryl-halides, carbon monoxide (CO) and aryl metal reagents. But the coupling reaction of aryl metal reagents like organomagnesium (Brunet and Chauvin, 1995), organoaluminium (Bumagin, 1985), organosilane (Hatanaka, 1992) or organozinc and organoindium compounds (Echavarren, 1988) with aryl halides having electron withdrawing substituent were severely limited due to the formation of biaryl side product formed due to without CO insertion. Here, electron-withdrawing groups on the aryl ring accelerate the rate of transmetallation to form the Ar-Pd-Ar intermediate and hinder the insertion of carbon monoxide into the Ar-Pd-Ar species.

In 1993, Suzuki and co-workers reported a facile protocol for the synthesis of diaryl ketones from carbon monoxide, aryl halide and arylboronic acid using palladium catalyst which is popularly known as carbonylative Suzuki coupling reaction (Scheme 2.1). In principle, this reaction provided a versatile tool for organic synthesis, as boronic acids are generally non-toxic and stable to air and moisture. They used PdCl$_2$(PPh$_3$)$_2$ as a catalyst for this transformation and investigated the effect of various reaction parameters to obtain good yields of carbonylated products.

\[
\text{Ar-}B(OH)_2 + \text{CO} + \text{I-Ar}' \xrightarrow{\text{PdCl}_2(\text{PPh}_3)_2, \text{K}_2\text{CO}_3, \text{Anisole}} \text{Ar-CO-Ar}'
\]

**Scheme 2.1** PdCl$_2$(PPh$_3$)$_2$ catalyzed carbonylative Suzuki coupling reaction.

After this first report, same group extended the protocol for the carbonylative Suzuki coupling reaction of aryl bromides and triflates (Scheme 2.2) (Ishiyama et al., 1998). PdCl$_2$(PPh$_3$)$_2$ as a catalyst was used for aryl iodides whereas PdCl$_2$(dppf) was used for the bromides or the triflates. The carbonylation of arylboronic acids with benzyl halides was also studied which provided arylbenzyl ketones as a product.

\[
\text{Ar-B(OH)$_2$ + CO + X} \xrightarrow{\text{Pd-cat, Base}} \text{Ar-CO-} \text{Ar}'
\]

**Scheme 2.2** Pd catalyzed carbonylative Suzuki coupling reaction.
Maerten et al. (2003) reported a simple and efficient method for the synthesis of heterocyclic ketone derivative like α-pyridyl ketone from chloropyridines using N-heterocyclic carbene (NHC) type ligands with palladium acetate as a catalyst (Scheme 2.3). Various pyridine-chlorides were carbonylated with phenylboronic acid to yield desired heteroaryl ketones in moderate to good yields (51-86%).

![Scheme 2.3 Pd(OAc)₂/NHC catalyzed carbonylative Suzuki coupling reaction.](image)

Further, application of carbonylative Suzuki coupling reaction for the synthesis of heteroaryl ketones was explored by Castanet and group (2001) (Scheme 2.4). They developed a high yielding protocol for the synthesis of α-pyridyl ketone using PdCl₂(PCy₃)₂ as a catalyst. The protocol was applied for various halopyridines which provided moderate to excellent yield of the respective heteroaryl ketone.

![Scheme 2.4 PdCl₂/(PCy₃)₂ catalyzed carbonylative Suzuki reaction of halopyridines.](image)

Palladium(II) acetate and N,N-bis-(2,6-diisopropylphenyl)dihydroimidazolium chloride (2 mol%) was used to catalyze the carbonylative coupling of aryl diazonium tetrafluoroborate salts and arylboronic acids to form aryl ketones by Song et al. (2002) (Scheme 2.5). The catalytic system was applicable for coupling reaction of variety of aryl diazonium tetrafluoroborate salts and arylboronic acid derivatives.

![Scheme 2.5 Carbonylative Suzuki coupling of aryl diazonium tetrafluoroborate salts.](image)
Kollar and group (2006) developed the carbonylative Suzuki coupling reaction of 1-iodocyclohexene with phenylboronic acid and 3-trifluoromethoxyphenylboronic acid using Pd(PPh₃)₄ complex (Scheme 2.6). The active catalyst Pd(0) was generated in-situ by the reaction of Pd(OAc)₂ and PPh₃. The catalyst showed excellent activity and provided good to excellent yield of the desired carbonylated product however; a substantial amount of by product was also formed.

![Scheme 2.6 Carbonylative Suzuki coupling reaction of 1-iodocyclohexene.](image)

A protocol for the carbonylative cross-coupling of sterically hindered, ortho-disubstituted aryl ketones was reported by O’Keefe et al. (2011) (Scheme 2.7). The PEPPSI-IPr catalyst efficiently promoted the carbonylative cross-coupling reaction of hindered ortho-disubstituted aryl iodides to give diaryl ketones. The developed catalytic system was further explored for Negishi cross-coupling reaction.

![Scheme 2.7 PEPPSI-IPr catalyzed carbonylative Suzuki coupling.](image)

Carbonylative Suzuki coupling of aryl iodonium salts with arylboronic acid was developed by Kang and co-workers (1998) (Scheme 2.8). The protocol worked at room temperature and provided unsymmetrical aromatic ketones in moderate yields.

![Scheme 2.8 Carbonylative coupling of aryliodonium salts with arylboronic acid.](image)
A new and efficient approach for the synthesis of α-ketosulfoxides by carbonylative Suzuki coupling reaction between α-bromo sulfoxide, carbon monoxide and aromatic boronic acids using Pd(PPh$_3$)$_4$ has been developed by Asensio et al. (2005) (Scheme 2.9). The carbonylative cross-coupling reaction was strongly favoured over competing direct cross-coupling and homo-coupling processes, except with boronic acids carrying strong electron-withdrawing substituents. The reaction took place under very mild conditions and with high selectivity for a wide range of boronic acids. This method does not require an overpressure of carbon monoxide.

Scheme 2.9 Carbonylative Suzuki coupling reaction of α-bromo sulfoxide.

Beller and co-workers (2008) reported Pd(OAc)$_2$/di-1-adamantyl-n-butylphosphine (cata. CXium A) as a highly active homogeneous catalyst for the three-component Suzuki carbonylation reaction (Scheme 2.10). The catalytic system was applicable for a broad range of aryl/heteroaryl bromides and arylboronic acids at low catalyst loading. This reaction offered efficient access to various biologically active compounds like Suprofen and Ketoprofen.

Scheme 2.10 Pd/cataCXiumA catalyzed carbonylative Suzuki coupling reaction.

Thiourea ligand was applied in the Pd-catalyzed carbonylative Suzuki coupling reactions by Mingji et al. (2004) (Scheme 2.11). According to this report, the metal-sulphur bond in the thiourea complexes is stronger than the metal-phosphorus bond of typical phosphine complexes, thiourea ligands generally do not easily
dissociate from the metal centre under catalytic conditions, thus establishes the thiourea ligand-based palladium complexes as effective catalysts for the palladium-catalyzed carbonylative Suzuki coupling reactions. The synthesized ligand complex was tested for the carbonylative Suzuki coupling reaction of different aryl iodides and aryl diazonium salt with arylboronic acid derivatives.

**Scheme 2.11** Pd/Thiourea ligand catalyzed carbonylative Suzuki coupling reaction.

For the first time, CO free approach for the carbonylative Suzuki coupling was developed by Kashani and co-workers (Scheme 2.12) (2011). The reaction was carried out by using molybdenum hexacarbonyl [Mo(CO)₆] which act as a source of carbon monoxide, Pd(OAc)₂ as a catalyst within 12 h at 140 °C. Varieties of substituted diaryl ketones without direct use of carbon monoxide were synthesized.

**Scheme 2.12** CO free carbonylative Suzuki coupling reaction using Mo(CO)₆.

However, despite of their potential utility all the above catalytic protocols employed so far for the carbonylative Suzuki coupling reactions were homogeneous and palladium-phosphine based complexes without consideration of recyclability aspect. In the above reported protocols it is very difficult to separate precious metal catalyst form the reaction mixture, which possibly creates contamination of the desired product. Furthermore, use of an expensive, toxic and air/moisture sensitive phosphine ligands, limits their applications. Moreover, from the literature data it is clear that there is no any heterogeneous, recyclable Pd catalyst applied for the carbonylative Suzuki coupling reaction. Thus, there is a need to develop an efficient heterogeneous, reusable protocol, which can efficiently catalyze carbonylative Suzuki coupling reaction of both aryl and heteroaryl iodides with variety of arylboronic acids.
Chapter 2

2.2 Results and Discussion

The present work reports an efficient protocol for the carbonylative Suzuki cross-coupling reaction of arylboronic acid with various aryl and heteroaryl iodides using Pd/C as a heterogeneous, recyclable catalyst (Scheme 2.13). The developed catalytic system was found to be effective for the carbonylative coupling reaction of aryl, heteroaryl and bicyclic heteroaryl iodides (5-iodoindole and 3-iodoquinoline) with various arylboronic acid derivatives providing good to excellent yields of the desired products. The protocol is advantageous due to the ease in handling of the catalyst and simple work-up procedure, with effective catalyst recyclability.

![Scheme 2.13 Pd/C catalyzed carbonylative Suzuki coupling reaction.](image)

To optimize the reaction conditions, the carbonylative cross coupling reaction of iodobenzene with phenylboronic acid was chosen as a model system in the presence of (10%) Pd/C as a catalyst. The influence of various reaction parameters such as solvent, base, temperature, CO pressure and time were examined on the model reaction (Table 2.1). Initially the influence of solvents on the carbonylative Suzuki coupling reaction was investigated (Table 2.1, entries 1-6). Polar solvents like N,N-dimethylforamide (10%), acetonitrile (18%) and water (25%) provided lower yield of the product, it was due to the fact that the polar solvent form a complex with metal ion which affects the reaction progress. The non polar solvent like toluene (76%), diospropyl (74%) and anisole (90%) provided excellent yield of the desired product. However, as the maximum yield of benzopheneone was obtained with anisole, it was used for further studies (Table 2.1, entry 6).
Table 2.1 Effect of reaction parameters on carbonylative Suzuki coupling reaction

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Base</th>
<th>Temp.  (°C)</th>
<th>Yield (%)^b</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>DMF</td>
<td>K₂CO₃</td>
<td>100</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>Acetonitrile</td>
<td>K₂CO₃</td>
<td>100</td>
<td>18</td>
</tr>
<tr>
<td>1</td>
<td>Water</td>
<td>K₂CO₃</td>
<td>100</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>Toluene</td>
<td>K₂CO₃</td>
<td>100</td>
<td>76</td>
</tr>
<tr>
<td>2</td>
<td>Di-ispropyl ether</td>
<td>K₂CO₃</td>
<td>100</td>
<td>74</td>
</tr>
<tr>
<td>6</td>
<td>Anisole</td>
<td>K₂CO₃</td>
<td>100</td>
<td>90</td>
</tr>
</tbody>
</table>

**Effect of solvent**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Base</th>
<th>Temp.  (°C)</th>
<th>Yield (%)^b</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Anisole</td>
<td>Et₃N</td>
<td>100</td>
<td>25</td>
</tr>
<tr>
<td>8</td>
<td>Anisole</td>
<td>Cs₂CO₃</td>
<td>100</td>
<td>70</td>
</tr>
<tr>
<td>9</td>
<td>Anisole</td>
<td>K₃PO₄</td>
<td>100</td>
<td>40</td>
</tr>
<tr>
<td>10</td>
<td>Anisole</td>
<td>Morpholine</td>
<td>100</td>
<td>--</td>
</tr>
<tr>
<td>11</td>
<td>Anisole</td>
<td>Piperidine</td>
<td>100</td>
<td>--</td>
</tr>
<tr>
<td>12</td>
<td>Anisole</td>
<td>DBU</td>
<td>100</td>
<td>--</td>
</tr>
</tbody>
</table>

**Effect of base**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Base</th>
<th>Temp.  (°C)</th>
<th>Yield (%)^b</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>Anisole</td>
<td>K₂CO₃</td>
<td>80</td>
<td>70</td>
</tr>
<tr>
<td>14</td>
<td>Anisole</td>
<td>K₂CO₃</td>
<td>120</td>
<td>89</td>
</tr>
<tr>
<td>15^c</td>
<td>Anisole</td>
<td>K₂CO₃</td>
<td>100</td>
<td>75</td>
</tr>
<tr>
<td>16^d</td>
<td>Anisole</td>
<td>K₂CO₃</td>
<td>100</td>
<td>87</td>
</tr>
</tbody>
</table>

^a Reaction conditions: Iodobenzene (1 mmol), Phenylboronic acid (1.2 mmol), 10% Pd/C (2 mol %), K₂CO₃ (3 mmol), solvent (10 mL), 8 h, CO pressure = 200 psi.

^b Yield based on GC analysis.

^c CO pressure = 100 psi.

^d Reaction time = 6 h.

It is well known that base plays a crucial role in carbonylative coupling reactions; hence different organic and inorganic bases were screened for the reaction (Table 2.1, entries 6-12). Among the various bases screened inorganic carbonates such as K₂CO₃ and Cs₂CO₃ provided the desired product in good to excellent yield as compared to other organic and inorganic bases. The reaction using morpholine and
piperidine yielded unexpected aminocarbonylated products instead of diaryl ketones (Table 2.1, entries 10-12). Thus, further reactions were carried out using K$_2$CO$_3$ as a base. In order to examine the effect of temperature, the reaction was carried out at different temperatures ranging from 80-120 °C (Table 2.1, entries 6 and 13-14). It was observed that at 80 °C yield of the desired product was low whereas, by increasing the reaction temperature up to 100 °C, 90% yield of benzophenone was obtained within 8 h. With further increase in reaction temperature, there was no profound increase in yield of benzophenone was observed. The influences of CO pressure and time were also studied, and the optimum pressure and time were used for further studies.

The optimized reaction conditions were; iodobenzene (1 mmol), phenylboronic acid (1.2 mmol), CO pressure (200 psi), 10% Pd/C (2 mol%), K$_2$CO$_3$ (3 mmol) in anisole (10 mL) at 100 °C for 8 h. These optimized reaction conditions were applied for the coupling of variety of phenylboronic acids with a range of aryl and heteroaryl halides. Various electron donating and withdrawing groups like -CH$_3$, -OCH$_3$, -NO$_2$, -Br, -COCH$_3$, -NH$_2$ on both aryl iodide and arylboronic acid smoothly undergoes carbonylative Suzuki coupling reaction providing good to excellent yield of the desired diaryl ketones (Table 2.2, entries 1-15).

Iodobenzene reacts efficiently with phenylboronic acid within 8 h and provided 90% isolated yield of benzophenone (Table 2.2, entry 1). The carbonylative cross coupling reaction of electron donating substituents such as -CH$_3$, and -OCH$_3$ at para and ortho position with phenylboronic acid underwent smoothly providing good to excellent yield of corresponding product (Table 2.2, entries 2-5). The reaction of 2-iodoaniline with phenylboronic acid yielded 2-aminobenzophenone in moderate amount (83%, Table 2.2, entry 6). The reaction of aryl iodide bearing electron withdrawing groups such as -NO$_2$, -Br and -COCH$_3$ also permitted the carbonylative coupling reaction with phenylboronic acid giving desired products in moderate to good yield under optimized reaction conditions (Table 2.2, entries 7-8). The carbonylation of bulky 1-iodonaphthalene with phenylboronic acid provided 92% yield of naphthalen-1-yl(phenyl)methanone (Table 2.2, entry 9). 1,2-diiodobenzene provided moderate yield (2-iodophenyl)(phenyl)methanone (Table 2.2, entry 10).

Thereafter, effect of substituents on the phenylboronic acid was investigated. Phenylboronic acids substituted with electron-donating groups like -CH$_3$, -OCH$_3$ at
the *para* or even *ortho* position provided desired products in moderate to high yields (Table 2.2, entries 11-14). Whereas, the reaction of iodo benzene with *p*-bromo phenylboronic acid provided 70% yield of (4-bromophenyl)(phenyl)methanone under the optimized reaction conditions (Table 2.2, entry 15).

**Table 2.2** Carbonylative Suzuki coupling reaction of aryl iodides with various arylboronic acids$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aryl iodide</th>
<th>Arylboronic acid</th>
<th>Product</th>
<th>Yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Iodide" /></td>
<td><img src="image2" alt="B(OH)2" /></td>
<td><img src="image3" alt="Product" /></td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td><img src="image4" alt="Iodide" /></td>
<td><img src="image5" alt="B(OH)2" /></td>
<td><img src="image6" alt="Product" /></td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td><img src="image7" alt="Iodide" /></td>
<td><img src="image8" alt="B(OH)2" /></td>
<td><img src="image9" alt="Product" /></td>
<td>89</td>
</tr>
<tr>
<td>4</td>
<td><img src="image10" alt="Iodide" /></td>
<td><img src="image11" alt="B(OH)2" /></td>
<td><img src="image12" alt="Product" /></td>
<td>93</td>
</tr>
<tr>
<td>5</td>
<td><img src="image13" alt="Iodide" /></td>
<td><img src="image14" alt="B(OH)2" /></td>
<td><img src="image15" alt="Product" /></td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td><img src="image16" alt="Iodide" /></td>
<td><img src="image17" alt="B(OH)2" /></td>
<td><img src="image18" alt="Product" /></td>
<td>83</td>
</tr>
<tr>
<td>7</td>
<td><img src="image19" alt="Iodide" /></td>
<td><img src="image20" alt="B(OH)2" /></td>
<td><img src="image21" alt="Product" /></td>
<td>85</td>
</tr>
<tr>
<td>8</td>
<td><img src="image22" alt="Iodide" /></td>
<td><img src="image23" alt="B(OH)2" /></td>
<td><img src="image24" alt="Product" /></td>
<td>70</td>
</tr>
<tr>
<td>9</td>
<td><img src="image25" alt="Iodide" /></td>
<td><img src="image26" alt="B(OH)2" /></td>
<td><img src="image27" alt="Product" /></td>
<td>92</td>
</tr>
<tr>
<td>10</td>
<td><img src="image28" alt="Iodide" /></td>
<td><img src="image29" alt="B(OH)2" /></td>
<td><img src="image30" alt="Product" /></td>
<td>51</td>
</tr>
<tr>
<td>11</td>
<td><img src="image31" alt="Iodide" /></td>
<td><img src="image32" alt="B(OH)2" /></td>
<td><img src="image33" alt="Product" /></td>
<td>80</td>
</tr>
</tbody>
</table>

© Mayur Vinodrao Khedkar, Institute of Chemical Technology (ICT), Mumbai, India
Chapter 2

© Mayur Vinodrao Khedkar, Institute of Chemical Technology (ICT), Mumbai, India

78

<table>
<thead>
<tr>
<th>12</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\[ a \text{ Reaction conditions: aryl iodide (1 mmol), arylboronic acid (1.2 mmol), CO (200 psi), 10\% Pd/C (2 mol\%), K}_2\text{CO}_3 (3 mmol), anisole (10 mL), 100 °C, 8 h.} \]

\[ b \text{ Isolated yield.} \]

In order to generalize the protocol, catalytic system was extended for the carbonylative Suzuki coupling reaction of heteroaryl iodides such as 2-iodopyridine, 3-iodopyridine, 2-iodothiophene, 5-iodoindole and 3-iodoquinolene with a variety of arylboronic acids (Scheme 2.14, Table 2.3, entries 1-14).

**Scheme 2.14** Carbonylative Suzuki coupling reaction of heteroaryl iodides.

Initially, the reaction of 3-iodopyridine with phenylboronic acid was optimized with respect to different parameters, the optimized reaction parameters were; catalyst (10\%) Pd/C (2.5 mol\%), solvent (toluene), base (K}_2\text{CO}_3), reaction temperature (100 °C), CO pressure (200 psi) and reaction time (10 h). The coupling reaction of 3-iodopyridine and 2-iodopyridine with phenylboronic acid in the presence of carbon monoxide afford 89% and 86% isolated yield of phenyl(pyridin-3-yl)methanone and phenyl(pyridin-2-yl)methanone respectively (Table 2.3, entry 1-2).
The effect of substituents on arylboronic acid partner with heteroaryl iodides was also explored. Electron donating group such as \(-\text{CH}_3\) and \(-\text{OCH}_3\) on arylboronic acids provided 90\% & 86\% yield of expected heteroaryl ketones respectively (Table 2.3, entry 3-4). The reaction of 3-iodopyridine with 4-bromo phenylboronic acid provided moderate yield of (4-bromophenyl)(pyridin-3-yl)methanone (Table 2.3, entry 5). In case of reaction of 2-iodothiophene with phenylboronic acid, 90\% yield of phenyl(thiophen-2-yl)methanone was obtained (Table 2.3, entry 6). Further, the effect of various substituents on arylboronic acid partner demonstrated that electron donating group (-\text{CH}_3 and -\text{OCH}_3) and withdrawing group (-\text{Br}) furnishes good to excellent yields (75-88\%) of desired product under optimized reaction parameters (Table 2.3, entries 7-9).

**Table 2.3** Carbonylative Suzuki coupling reaction of heteroaryl iodides with various arylboronic acids

<table>
<thead>
<tr>
<th>Entry</th>
<th>Heteroaryl iodide</th>
<th>Arylboronic acid</th>
<th>Product</th>
<th>Yield (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1.png" alt="Iodopyridine" /></td>
<td><img src="image2.png" alt="Phenylboronic acid" /></td>
<td><img src="image3.png" alt="Heteroarylmethanone" /></td>
<td>89</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td><img src="image1.png" alt="Iodopyridine" /></td>
<td><img src="image2.png" alt="Phenylboronic acid" /></td>
<td><img src="image3.png" alt="Heteroarylmethanone" /></td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td><img src="image1.png" alt="Iodopyridine" /></td>
<td><img src="image2.png" alt="Phenylboronic acid" /></td>
<td><img src="image3.png" alt="Heteroarylmethanone" /></td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td><img src="image1.png" alt="Iodopyridine" /></td>
<td><img src="image2.png" alt="Phenylboronic acid" /></td>
<td><img src="image3.png" alt="Heteroarylmethanone" /></td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td><img src="image1.png" alt="Iodopyridine" /></td>
<td><img src="image2.png" alt="Phenylboronic acid" /></td>
<td><img src="image3.png" alt="Heteroarylmethanone" /></td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td><img src="image4.png" alt="Iodothiophene" /></td>
<td><img src="image2.png" alt="Phenylboronic acid" /></td>
<td><img src="image3.png" alt="Heteroarylmethanone" /></td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td><img src="image4.png" alt="Iodothiophene" /></td>
<td><img src="image2.png" alt="Phenylboronic acid" /></td>
<td><img src="image3.png" alt="Heteroarylmethanone" /></td>
<td>88</td>
<td></td>
</tr>
</tbody>
</table>
Encouraged from these results, carbonylative Suzuki coupling reactions of 5-iodoindole and 3-iodoquinoline with various arylboronic acids was studied. To the best of our knowledge, there was no general method reported for the synthesis of sterically hindered heteroaryl ketones from iodoindole and iodoquinoline through carbonylative Suzuki cross coupling reaction. It was noticed that, 5-iodoindole smoothly undergoes carbonylative coupling reaction with phenylboronic acid, providing 85% yield of (1H-indol-5-yl)(phenyl)methanone (Table 2.3, entry 10). Electron donating and electron withdrawing groups such as -OCH$_3$ and -Br on phenylboronic acid were well tolerated and provided desired heteroaryl ketone in good to excellent yields (Table 2.3, entries 11-12). The reaction of 3-iodoquinoline with phenylboronic acid, provided 85% yield of phenyl(quinolin-3-yl)methanone (Table 2.3, entry 13). Reaction of 3-methyl phenylboronic acid with 3-iodoquinoline...
underwent smoothly with excellent yield of quinolin-3-yl-\textit{m}-tolylmethanone (Table 2.3, entry 14).

It is believed that, at higher temperature supported metal detaches from the solid support, thereby goes into the solvent and the reaction is catalyzed mainly by this dissolved metal species which is referred as leaching of metal. Thus, to confirm whether there was leaching of palladium during reaction, ICP-AES (Inductively coupled plasma atomic emission spectroscopy) analysis of the reaction the mixture was carried out, it showed only 0.24 ppm of palladium in solution, which reveal no significant leaching of palladium in the solution.

Reusability of the catalyst was also examined for the standard reaction of iodobenzene with phenylboronic acid. The Pd/C was found to be recycled for four consecutive cycles maintaining high activity and selectivity (Figure 2.2). There was no significant decrease in yield during the three recycle, however, yield decreased up to 80\% for the fourth cycle. This decrease in yield was mainly due to work-up loss or handling loss of the catalyst during the successive recycles. When the catalyst that was lost during the first four recycles was compensated, 88\% yield of the product was observed (see Figure 1, IV*). It should be noted that the compensated catalyst was taken from parallel sets of recycling experiments after the third recycle. Thus, the catalyst was successfully recycled up to four times with consistent results.

![Figure 2.2 Reusability study of Pd/C catalyst.](image)
As a result the developed protocol proved to be general for the carbonylative Suzuki coupling reaction of various structurally and electronically different aryl and heteroaryl iodides with different arylboronic acids, providing good to excellent yield of the desired diaryl ketones.

2.3 Conclusion

❖ In conclusion, a simple, efficient and heterogeneous catalytic system for the carbonylative Suzuki coupling reaction of aryl and heteroaryl iodides with various arylboronic acids has been developed.

❖ The present system circumvents the use of phosphine containing ligands.

❖ The developed catalytic system is simple, efficient and offers practical advantages such as; easy handling, separation from product and reuse.

❖ The present protocol is applicable to a wide variety of aryl/heteroaryl iodides and phenylboronic acids providing good to excellent yields of the desired products.

❖ For the first time bicyclic heteroaryl iodides derivatives are used for carbonylative Suzuki coupling reaction.

❖ Leaching of palladium metal was examined by ICP-AES analysis, which showed 0.24 ppm Pd content in the solution, this result indicates no significant leaching of palladium metal in the solution during the reaction.

❖ Pd/C was found to be recycled for consecutive four cycles without any significant loss in catalytic activity.
2.4 EXPERIMENTAL

2.4.1. General: All chemicals were purchased from Lancaster (Alfa-Aesar), Sigma Aldrich, S. D. fine chemical and commercial suppliers. Gas chromatography (GC) analysis was carried out on Perkin-Elmer Clarus 400 GC equipped flame ionization detector with a capillary column (Elite-1, 30 m × 0.32 mm × 0.25 μm) using the external standard method. A GC/MS-QP 2010 instrument (Rtx-17, 30 m × 25 mm i.d., film thickness 0.25 μm df) (column flow 2 mL min⁻¹, 80-240 °C at 10 °C/min rise). The ¹H NMR spectra were recorded on Varian-300 MHz FT-NMR spectrometer in CDCl₃ using TMS as the internal standard. The ¹³C NMR spectra were recorded with a JEOL FT-NMR, model-AL300 (75 MHz) spectrometer in CDCl₃. Chemical shifts were reported in parts per million (δ) relative to tetramethylsilane as the internal standard. J (coupling constant) values were reported in hertz (Hz). Proton splitting patterns are described as s (singlet), d (doublet), t (triplet), and m (multiplet).

2.4.2. Experimental setup: All carbonylation reactions were performed in a 100 mL high pressure stainless-steel (SS-316) autoclave (Amar equipment) with teflon coated sealing (Figure 2.3).

Figure 2.3 High pressure reactor (autoclave).
For safety reasons, the entire reactor system was placed in a high pressure chamber. The reactor was equipped with a magnetically coupled stirrer, whose speed could be adjusted manually. The autoclave was heated by an electrical ceramic band heating mental with ceramic wool insulation and cladding and cooled by circulation of water through an inner cooling coil. The reactor withstands a temperature up to 250 °C and a pressure up to 100 bar. The temperature and the pressure of the reactor was controlled by compact SS control panel with microprocessor based accurate PID temperature/pressure and RPM controller cum indicator. The pressure was measured by a piezoelectric pressure gauge and in addition by a membrane based pressure gauge. Further, a pressure relief valve was connected to an expansion vessel, and the autoclave could be vented with an outlet valve, purging the gas to the exhaust gas system of the high-pressure chamber.

A schematic diagram of the experimental setup is shown in Figure 2.4 which shows the gas inlet, gas release valve, cooling water feed line, pressure gauge and rupture disk were situated on the top of vessel.

![Schematic diagram of the experimental setup](image)

**Figure 2.4** Schematic representation of high pressure reactor (1) reactor (2) stirrer shaft (3) impeller (4) cooling water (5) sampling valve (6) magnetic stirrer (7) vent valve (8) thermo well; T1: thermocouple, P1: Pressure transducer, RPM: Rotation per min. indicator; PR1: Reactor pressure indicator; TR1: Reactor temperature indicator; PR: Pressure regulator with non-returnable valve; CPR: Constant pressure regulator.
Safety note: The experiments described in this work involve the use of high pressure and require equipment with an appropriate pressure rating. Due to the use of carbon monoxide (CO) sufficient ventilation and the use of carbon monoxide detector (Figure 2.5) which can detect the presence of CO in ppm level is required.

Figure 2.5 Carbon monoxide detector.

2.4.3 General experimental procedure for carbonylative Suzuki coupling reaction of aryl iodide with arylboronic acid: To a 100 ml autoclave aryl iodide (1.0 mmol), arylboronic acid (1.2 mmol), 10% Pd/C (2 mol %), anisole (10 mL) and K$_2$CO$_3$ (3 mmol) was added. The mixture was first stirred for 10 min. and flushed with CO, then 200 psi of CO was taken and the reaction mixture was heated at 100 °C for 8 h. After completion of reaction, the reaction mixture was cooled to room temperature and the remaining CO gas was carefully vented and the reactor was opened. The reactor vessel was thoroughly washed with ethyl acetate (2 x 10 mL) to remove any traces of product and catalyst if present. The catalyst was filtered and the reaction mixture was evaporated under vacuum. The residue obtained was purified by column chromatography (silica gel, 60-120 mesh; petroleum ether/ethyl acetate, 95:05) to afford the desired product. The products were characterized by GC-MS, $^1$H NMR, $^{13}$C NMR and IR spectroscopic techniques.
2.4.4 Procedure for catalyst recycling:
The catalyst obtained after filtration was washed with distilled water (10 mL × 3) and then with methanol (5 mL × 3) to remove any organic material present. The resulting catalyst was dried in oven at 200 °C for 12 h and used for the next cycle.

2.4.5 General experimental procedure for carbonylative Suzuki reaction of heteroaryl iodide with arylboronic acid:
To a 100 ml autoclave heteroaryl iodide (1.0 mmol), arylboronic acid (1.2 mmol), 10% Pd/C (2.5 mol %), toluene (10 mL) and K$_2$CO$_3$ (3 mmol) was added. The mixture was first stirred for 10 min. and flushed with CO, then 200 psi of CO was taken and the reaction mixture was heated at 100 °C for 10-12 h. After completion of reaction, the reaction mixture was cooled to room temperature. The catalyst was filtered and residue obtained was purified by column chromatography (silica gel, 60-120 mesh; petroleum ether/ethyl acetate) to afford the desired carbonylated product. The products were confirmed by GC-MS, $^1$H NMR, $^{13}$C NMR and IR spectroscopic techniques.
2.5 Spectral Data

2-Aminobenzphenone

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 6.1 (br, 2 H), 6.61-6.55 (t, $J$ = 7.9 Hz, 1 H), 6.73-6.7 (d, $J$ = 8 Hz, 1 H), 7.3-7.24 (m, 2 H), 7.46-7.42 (t, $J$ = 5.9 Hz, 1 H), 7.51-7.49 (d, $J$ = 7.3 Hz, 2 H), 7.64-7.61 (d, $J$ = 8 Hz, 2 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 199.09 (CO), 150.99 (C), 140.16 (C), 134.59 (CH), 134.24 (CH), 131.04 (CH), 129.13 (2CH), 128.1 (2CH), 118 (CH), 117.04 (CH), 115.53 (CH); GC-MS (EI, 70 eV): $m/z$ (%) = 197 (100), 120 (41), 105 (16), 92 (31), 77 (44), 65 (36), 51 (19); IR (KBr) $\nu$ = 3436, 3318, 3054, 2934, 1626, 1589, 1553, 1479, 1449, 1328, 1303, 1250, 1151, 1025, 938, 912, 745, 703, 645 cm$^{-1}$.

4-Acetyl benzophenone

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 2.66 (s, 3 H), 7.52-7.47 (t, $J$ = 7.5 Hz, 2 H), 7.65-7.59 (t, $J$ = 8.8 Hz, 1 H), 7.82-7.79 (d, $J$ = 8.4 Hz, 2 H), 7.88-7.87 (d, $J$ = 8.4 Hz, 2 H), 8.07-8.04 (d, $J$ = 8.8 Hz, 2 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 197.47 (CO), 195.89 (CO), 141.36 (C), 139.62 (C), 136.97 (C), 132.99 (CH), 130.11 (2CH), 130.05 (2CH), 128.49 (2CH), 128.18 (2CH), 22.71 (CH$_3$); GC-MS (EI, 70 eV): $m/z$ (%) = 224 (53), 209 (100), 181 (10), 147 (35), 105 (80), 77 (78), 43 (35); IR (KBr) $\nu$ = 2920, 2852, 1689, 1657, 1593, 1445, 1402, 1358, 1277, 1072, 963, 931, 845! 795, 698 cm$^{-1}$.

2-Iodobenzophenone

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 7.31-7.17 (m, 1 H), 7.5-7.41 (m, 3 H), 7.62-7.55 (m, 2 H), 7.81-7.78 (d, $J$ = 8.4 Hz, 1 H), 7.93-7.9 (d, $J$ = 8.1 Hz, 2 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 197.21 (CO), 144.68 (C), 139.76 (C), 135.69 (CH), 133.74 (CH), 132.43 (CH), 131.15 (CH), 130.51 (2CH), 128.69 (2CH), 127.83 (CH), 92.25 (C); GC-MS (EI, 70 eV): $m/z$ (%) = 308 (10), 231 (28), 203 (10), 181 (18), 152 (23), 105 (100), 77 (76), 45 (71); IR (KBr) $\nu$ = 3059, 2922, 2852, 1743, 1669, 1595, 1580, 1448, 1314, 1285, 1251, 1194, 1157, 1078, 1015, 927, 799, 762, 703, 954 cm$^{-1}$.

Pyridin-3-yl-o-tolylmethanone

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 2.38 (s, 3 H), 7.46-7.26 (m, 5 H), 8.16-8.14 (d, $J$ = 8.1 Hz, 1 H), 8.81-8.79 (d, $J$ = 6.2 Hz, 1 H), 8.93 (s, 1 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 196.81 (CO), 153.12 (CH), 151.31 (CH), 147.11 (C), 137.28 (CH), 133.4 (C), 131.48 (C), 131.13 (CH), 129.01 (CH), 125.47 (CH), 123.59 (CH), 119 (CH),
14.14 (CH₃); GC-MS (EI, 70 eV): m/z (%) = 196 (100), 197 (45), 182 (5), 168 (34), 141 (5), 119 (51), 106 (11), 91 (75), 89 (22), 78 (30), 65 (41), 51 (31), 45 (34); IR (KBr) ν = 2925, 2851, 1729, 1670, 1584, 1463, 1292, 1270, 1190, 1081, 1025, 966, 925, 796, 737, 650 cm⁻¹.

(2-Methoxy-phenyl)-pyridin-3-yl-methanone

¹H NMR (300 MHz, CDCl₃): δ = 3.69 (s, 3 H), 7.02-6.99 (d, J = 8.4 Hz, 1 H), 7.1-7.05 (dd, J = 7.3, 7.69 Hz, 1 H), 7.54-7.38 (m, 3 H), 8.14-8.11 (d, J = 8.1 Hz, 1 H), 8.75-8.73 (d, J = 6.6 Hz, 1 H), 8.91 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃): δ = 194.88 (CO), 157.48 (C), 152.78 (CH), 151.06 (CH), 136.56 (CH), 133.43 (C), 133.01 (CH), 130.09 (CH), 127.49 (CH), 123.28 (CH), 120.85 (C), 111.44 (CH), 55.43 (CH₃); GC-MS (EI, 70 eV): m/z (%) = 196 (100), 197 (45), 182 (5), 168 (34), 141 (5), 119 (51), 106 (11), 91 (75), 89 (22), 78 (30), 65 (41), 51 (31), 45 (34); IR (KBr) ν = 2925, 2851, 1729, 1670, 1584, 1463, 1292, 1270, 1190, 1081, 1025, 966, 925, 796, 737, 650 cm⁻¹.

Thiophen-2-yl-o-tolylmethanone

¹H NMR (300 MHz, CDCl₃): δ = 2.38 (s, 3 H), 7.12-7.11 (dd, J = 3.66, 4.0 Hz, 1 H), 7.3-7.25 (m, 2 H), 7.45-7.36 (m, 2 H), 7.71-7.62 (m, 1 H); ¹³C NMR (75 MHz, CDCl₃): δ = 190.46 (CO), 145 (C), 138.54 (C), 136.52 (C), 135.49 (CH), 134.9 (CH), 131.12 (CH), 130.37 (CH), 128.08 (2CH), 125.19 (CH), 14.17 (CH₃); GC-MS (EI, 70 eV): m/z (%) = 202 (100), 187 (5), 169 (28), 141 (24), 128 (10), 119 (15), 111 (59), 91 (47), 83 (13), 65 (34), 45 (14); IR (KBr) ν = 3449, 2962, 1641, 1513, 1411, 1354, 1297, 1262, 1097, 1047, 848, 795, 7338 cm⁻¹.

(2-Methoxy-phenyl)-thiophen-2-yl-methanone

¹H NMR (300 MHz, CDCl₃): δ = 3.78 (s, 3 H), 6.95-6.92 (d, J = 8.4 Hz, 1 H), 7.1-6.98 (m, 2 H), 7.46-7.38 (dd, J = 4.4, 7.3 Hz, 1 H), 7.66 (d, J = 1.1 Hz, 1 H), 7.85 (d, J = 1.83 Hz, 1 H), 7.87 (d, J = 1.46 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃): δ = 188.22 (CO), 164.52 (C), 144.91 (C), 135.18 (CH), 134.56 (CH), 132.87 (CH), 131.9 (CH), 129.2 (CH), 121.23 (CH), 120.23 (C), 116.1 (CH), 55.71 (CH₃); GC-MS (EI, 70 eV): m/z (%) = 213 (30), 182 (4), 135 (100), 107 (11), 92 (25), 77 (51), 64 (11), 51 (32), 45 (29); IR (KBr) ν = 3359, 2962, 1641, 1513, 1411, 1354, 1297, 1262, 1097, 1047, 848, 795, 7338 cm⁻¹.
### Thiophen-2-yl-m-tolymethanone

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 2.41$ (s, 3 H), 7.15-7.14 (dd, $J = 4.03$, 3.66 Hz, 1 H), 7.37-7.32 (m, 2 H), 7.66-7.62 (m, 3 H), 7.7-7.68 (d, $J = 4.8$ Hz, 1 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 188.43$ (CO), 156.4 (CH), 143.46 (C), 138.16 (CH), 137.91 (CH), 134.88 (C), 134.16 (CH), 132.99 (CH), 129.49 (CH), 128.12 (CH), 126.27 (CH), 21.21 (CH$_3$); GC-MS (EI, 70 eV): $m/z$ (%) = 202 (68), 187 (25), 174 (4), 141 (3), 119 (48), 111 (100), 91 (40), 83 (10), 65 (26), 45 (15); IR (KBr) $\nu$ = 3391, 3100, 2921, 1633, 1513, 1412, 1353, 1289, 1209, 1123, 1052, 931, 861, 776, 735, 652 cm$^{-1}$.

### (1H-Indol-5-yl)-phenylmethanone

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 6.62$ (d, $J = 2.2$ Hz, 1 H), 7.27-7.26 (dd, $J = 2.56$, 2.93 Hz, 1 H), 7.45-7.44 (m, 3 H), 7.5-7.47 (d, $J = 8.06$ Hz, 1 H), 7.57-7.55 (d, $J = 7.3$ Hz, 1 H), 7.83-7.77 (dd, $J = 6.96$, 8.8 Hz, 2 H), 8.13 (s, 1 H), 8.93 (br, 1 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 197$ (CO), 139.01 (C), 138.45 (C), 131.76 (CH), 129.98 (2CH), 129.57 (C), 128.17 (2CH), 127.19 (C), 125.99 (CH), 125.41 (CH), 124.15 (CH), 111.21 (CH), 104.14 (CH); IR (KBr) $\nu$ = 3292, 2923, 2851, 1621, 1607, 1572, 1431, 1322, 1116, 1092, 957, 880, 734 cm$^{-1}$.

### (1H-Indol-5-yl)-(4-methoxyphenyl)methanone

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 3.88$ (s, 3 H), 6.6 (d, $J = 2.2$ Hz, 1 H), 6.98-6.95 (d, $J = 8.8$ Hz, 2 H), 7.26-7.25 (d, $J = 2.6$ Hz, 1 H), 7.42-7.4 (d, $J = 8.4$ Hz, 1 H), 7.73-7.7 (d, $J = 7$ Hz, 1 H), 7.86-7.83 (d, $J = 8.8$ Hz, 2 H), 8.1 (s, 1 H), 8.9 (br, 1 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 196.67$ (CO), 162.77 (C), 138.2 (C), 132.56 (2CH), 131.44 (C), 130.19 (C), 127.16 (C), 125.94 (CH), 124.86 (CH), 124.07 (CH), 113.59 (CH), 113.35 (CH), 111.07 (CH), 104.15 (CH), 55.5 (CH$_3$); IR (KBr) $\nu$ = 3262, 2929, 2840, 1624, 1508, 1420, 1308, 1252, 1175, 1116, 1093, 1029, 964, 885, 849, 823, 760, 731, 614, 576 cm$^{-1}$.

### (4-Bromo-phenyl)-(1H-indol-5-yl)methanone

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 6.65$ (d, $J = 2.2$ Hz, 1 H), 7.3-7.26 (d, $J = 12.46$ Hz, 1 H), 7.47-7.44 (d, $J = 8.8$ Hz, 2 H), 7.7-7.67 (d, $J = 8.4$ Hz, 2 H), 7.77-7.73 (d, $J = 9.9$ Hz, 2 H), 8.09 (s, 1 H), 8.6 (br, 1 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 196.29$ (CO), 138.46 (C), 137.82 (C), 131.55 (2CH), 131.47 (2CH), 129.46 (C), 127.3

© Mayur Vinodrao Khedkar, Institute of Chemical Technology (ICT), Mumbai, India 89
(C), 126.61 (C), 125.95 (CH), 125.22 (CH), 124.18 (CH), 111.21 (CH), 104.4 (CH); IR (KBr) ν = 3269, 1644, 1595, 1429, 1329, 1284, 1303, 1284, 1203, 1100, 1067, 1011, 977, 878, 841, 773, 754, 729 cm⁻¹.

Phenyl-quinolin-3-yl-methanone

1H NMR (300 MHz, CDCl₃): δ = 7.55 (m, 3 H), 7.67-7.5 (dd, J = 7.7, 8.1 Hz, 1 H), 7.87-7.8 (m, 2 H), 7.92-7.89 (d, J = 8.1 Hz, 2 H), 8.2-8.18 (d, J = 8.43 Hz, 1 H), 8.53 (s, 1 H), 9.33 (s, 1 H); 13C NMR (75 MHz, CDCl₃): δ = 194.81 (CO), 150.29 (CH), 149.37 (C), 138.83 (CH), 136.95 (C), 133.06 (CH), 131.85 (CH), 130.01 (2CH), 129.4 (C), 129.15 (C), 128.63 (3CH), 127.57 (CH), 126.55 (CH); GC-MS (EI, 70 eV): m/z (%) = 233 (100), 204 (12), 176 (3), 156 (29), 128 (50), 105 (66), 77 (78), 45 (89); IR (KBr) ν = 3052, 2924, 2853, 1649, 1598, 1572, 1493, 1445, 1367, 1290, 1245, 1178, 1122, 935, 911, 860, 759, 726, 698, 595 cm⁻¹.

Quinolin-3-yl-m-tolylmethanone

1H NMR (300 MHz, CDCl₃): δ = 2.42 (s, 3 H), 7.45-7.38 (m, 2 H), 7.67-7.6 (dd, J = 7.3, 7.0 Hz, 1 H), 7.95-7.81 (m, 4 H), 8.23-8.2 (d, J = 8.8 Hz, 1 H), 8.56 (s, 1 H), 9.31 (s, 1 H); 13C NMR (75 MHz, CDCl₃): δ = 194.82 (CO), 149.94 (CH), 148.85 (C), 138.88 (C), 138.72 (CH), 138.43 (CH), 134.61 (C), 133.76 (CH), 131.8 (CH), 130.93 (C), 130.18 (CH), 130.01 (C), 129.05 (CH), 128.3 (CH), 127.5 (CH), 126.45 (CH), 21.14 (CH₃); GC-MS (EI, 70 eV): m/z (%) = 247 (100), 232 (81), 218 (7), 204 (6), 156 (30), 128 (57), 119 (78), 101 (40), 91 (75), 75 (19), 65 (34), 51 (14), 45 (27); IR (KBr) ν = 3057, 2917, 1656, 1617, 1596, 1495, 1415, 1368, 1292, 1189, 1039, 788, 758, 588 cm⁻¹.
2.5.1 Spectras

Figure 2.6 $^1$H NMR (300 MHz) spectrum of 2-Aminobenzphenone.

Figure 2.7 $^{13}$C NMR (75 MHz) spectrum of 2-Aminobenzphenone.
Figure 2.8 GC-MS Spectrum of 2-Aminobenzphenone.

Figure 2.9 IR Spectrum of 2-Aminobenzphenone.
Figure 2.10 $^1$H NMR (300 MHz) spectrum of 4-Acetyl benzophenone.

Figure 2.11 $^{13}$C NMR (75 MHz) spectrum of 4-Acetyl benzopheneone.
Figure 2.12 GC-MS spectrum of 4-Acetyl benzophenone.

Figure 2.13 IR spectrum of 4-Acetyl benzophenone.
Figure 2.14 $^1$H NMR (300 MHz) spectrum of 2-Iodobenzophenone.

Figure 2.15 $^{13}$C NMR (75 MHz) spectrum of 2-Iodobenzophenone.
Figure 2.16 GC-MS spectrum of 2-Iodobenzophenone.

Figure 2.17 IR spectrum of 2-Iodobenzophenone.
Figure 2.18 $^1$H NMR (300 MHz) spectrum of Pyridin-3-yl-o-tolyl-methanone.

Figure 2.19 $^{13}$C NMR (75 MHz) spectrum of Pyridin-3-yl-o-tolyl-methanone.
Chapter 2

Figure 2.20 GC-MS spectrum of *Pyridin-3-yl-o-tolyl-methanone*.

Figure 2.21 IR spectrum of *Pyridin-3-yl-o-tolyl-methanone*. 

© Mayur Vinodrao Khedkar, Institute of Chemical Technology (ICT), Mumbai, India
Figure 2.22 $^1$H NMR (300 MHz) spectrum of (2-Methoxy-phenyl)-pyridin-3-yl-methanone.

Figure 2.23 $^{13}$C NMR (75 MHz) spectrum of (2-Methoxy-phenyl)-pyridin-3-yl-methanone.
Figure 2.24 GC-MS spectrum of (2-Methoxy-phenyl)-pyridin-3-yl-methanone.

Figure 2.25 IR spectrum of (2-Methoxy-phenyl)-pyridin-3-yl-methanone.
Figure 2.26 $^1$H NMR (300 MHz) spectrum of Thiophen-2-yl-o-tolyl-methanone.

Figure 2.27 $^{13}$C NMR (75 MHz) spectrum of Thiophen-2-yl-o-tolyl-methanone.
Figure 2.28 GC-MS spectrum of Thiophen-2-yl-o-tolyl-methanone.

Figure 2.29 IR spectrum of Thiophen-2-yl-o-tolyl-methanone.
Figure 2.30 $^1$H NMR (300 MHz) spectrum of (2-Methoxy-phenyl)-thiophen-2-yl-methanone.

Figure 2.31 $^{13}$C NMR (75 MHz) spectrum of (2-Methoxy-phenyl)-thiophen-2-yl-methanone.
Figure 2.32 GC-MS spectrum of (2-Methoxy-phenyl)-thiophen-2-yl-methanone.

Figure 2.33 IR spectrum of (2-Methoxy-phenyl)-thiophen-2-yl-methanone.
Figure 2.34 $^1$H NMR (300 MHz) spectrum of Thiophen-2-yl-m-tolyl-methanone.

Figure 2.35 $^{13}$C NMR (75 MHz) spectrum of Thiophen-2-yl-m-tolyl-methanone.
Figure 2.36 GC-MS spectrum of Thiophen-2-yl-m-tolyl-methanone.

Figure 2.37 IR spectrum of Thiophen-2-yl-m-tolyl-methanone.
Figure 2.38 $^1$H NMR (300 MHz) spectrum of (1H-Indol-5-yl)-phenyl-methanone.

Figure 2.39 $^{13}$C NMR (75 MHz) spectrum of (1H-Indol-5-yl)-phenyl-methanone.
Figure 2.40 IR spectrum of (1H-Indol-5-yl)-phenyl-methanone.

Figure 2.41 $^1$H NMR (300 MHz) spectrum of (1H-Indol-5-yl)-(4-methoxy-phenyl)-methanone.
Figure 2.42 ¹³C NMR (75 MHz) spectrum of (1H-Indol-5-yl)-(4-methoxy-phenyl)\-methanone.

Figure 2.43 IR spectrum of (1H-Indol-5-yl)-(4-methoxy-phenyl)\-methanone.
Figure 2.44 $^1$H NMR (300 MHz) spectrum of (4-Bromo-phenyl)-(1H-indol-5-yl) methanone.

Figure 2.45 $^{13}$C NMR (75 MHz) spectrum of (4-Bromo-phenyl)-(1H-indol-5-yl) methanone.
Figure 2.46 IR spectrum of (4-Bromo-phenyl)-(1H-indol-5-yl)-methanone.

Figure 2.47 $^1$H NMR (300 MHz) spectrum of Phenyl-quinolin-3-yl-methanone.
Figure 2.48 $^{13}$C NMR (75 MHz) spectrum of Phenyl-quinolin-3-yl-methanone.

Figure 2.49 GC-MS spectrum of Phenyl-quinolin-3-yl-methanone.
Figure 2.50 IR spectrum of Phenyl-quinolin-3-yl-methanone.

Figure 2.51 $^1$H NMR (300 MHz) spectrum of Quinolin-3-yl-m-tolyl-methanone.
Figure 2.52 $^{13}$C NMR (75 MHz) spectrum of Quinolin-3-yl-m-tolyl-methanone.

Figure 2.53 GC-MS spectrum of Quinolin-3-yl-m-tolyl-methanone.
Figure 2.54 IR spectrum of Quinolin-3-yl-m-tolyl-methanone.