Gallic acid derived palladium(0) nanoparticles as \textit{in situ}-formed catalyst for Suzuki-Miyaura cross-coupling reaction in water

\textbf{Abstract:} In this chapter, we present a simple method for the Suzuki-Miyaura coupling in water. The method uses gallic acid reduced \textit{in situ} palladium(0) nanoparticles (PdNPs). With low loading, short reaction time, wide functional group tolerance and four time recyclability the methodology is highly versatile and scalable.
4.1. Background

Traditional Suzuki-Miyaura cross-coupling reactions are carried out in the presence of expensive ligands at high temperature. For example, phosphine,

$1$ amines,$^2$ NHC,$^3$ Schiff base,$^4$ palladacyle.$^5$ However, after the development of ligandfree methods,$^6$ simple palladium precursors like PdCl$_2$ or Pd(OAc)$_2$ are highly used.$^7$ So far, chemists have reported numerous efficient ligandless methods for Suzuki-Miyaura reaction.

Recently, de Vries and Reetz have experimentally proved that the palladium salts during the Suzuki-Miyaura reaction get transform into palladium nanoparticles (PdNPs) at high temperature.$^8$ This has lead to the development of novel methods for the synthesis of PdNPs. Conventionally, PdNPs are prepared by the chemical reduction or thermal decomposition of palladium salt solutions. However, reaction medium (solvent), reducing agent and temperature often determine the reaction process and nanoparticle yield. These include reducing agents like NaBH$_4$, hydrazine, formaldehyde, potassium bitartrate, hydroxylamine hydrochloride and hazardous organic solvents.$^9$ Conversely, for the economic and environmental benifits, the use of non-toxic chemicals, optimal reaction conditions and renewable materials are highly encouraged in chemical industries.$^{9,10}$ Moreover, the shape and size of the formed nanoparticles and their extent of aggregation signifies the catalytic efficiency of the reaction. Thus, with simple and economical methodologies, a procedure that utilizes natural ingredients as reducing agent in the absence of any additional ligand has become the need of current manufacturing process to establish sustainable strategy. Nowadays, researchers are highly interested in using simple and non-toxic natural reagents, which act as both reducing and/or stabilizing agents during nanoparticle
formation.\textsuperscript{11} But, there are only a few methods which use these PdNPs as catalyst in Suzuki-Miyaura reactions (Table 4.1).\textsuperscript{12} Therefore, novel methods for PdNPs synthesis, using biochemical medium, for catalysis in coupling reaction is highly essential for the improvement of this field.

<table>
<thead>
<tr>
<th>Reactants</th>
<th>Conditions</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{Ar}^1\text{B(OH)}_2 + \text{Ar}^2\text{-Br}, \text{Cl}$</td>
<td>Pd(OAc)$_2$ (3 mol%), TBAOH, glucose (0.25 mol%), H$_2$O, 6 h, 40-90 °C</td>
<td>$\text{Ar}^1$-$\text{Ar}^2$ (73-95%)$^{12a}$</td>
</tr>
<tr>
<td>$\text{Ar}^1\text{B(OH)}_2 + \text{Ar}^2$-I</td>
<td>Pd(OAc)$_2$ (1 mol%), glucose, (5 mol%), K$_2$CO$_3$, iPrOH, 100 °C, 20 h or 120 °C (MW), 2 h</td>
<td>$\text{Ar}^1$-$\text{Ar}^2$ (54-94%)$^{12b}$</td>
</tr>
<tr>
<td>$\text{Ar}^1\text{B(OH)}_2 + \text{Ar}^2$-Br</td>
<td>Pd(OAc)$_2$ (3 mol%), mannose, (3 equiv), K$_2$CO$_3$, DMF-H$_2$O (3:1), 130 °C (MW), 1 h</td>
<td>$\text{Ar}^1$-$\text{Ar}^2$ (74-93%)$^{12c}$</td>
</tr>
<tr>
<td>$\text{Ar}^1\text{B(OH)}_2 + \text{Ar}^2$-I</td>
<td>Pd(OAc)$_2$ (2 mol%), glucose, (4 mol%), K$_2$CO$_3$, H$_2$O-MeCN (3:1), 100 °C, 16 h</td>
<td>$\text{Ar}^1$-$\text{Ar}^2$ (65-98%)$^{12d}$</td>
</tr>
</tbody>
</table>

Thus, with the aim to reduce chemical waste using renewable sources, we have chosen to study the role of gallic acid in Suzuki-Miyaura reaction. Gallic acid is a naturally occurring trihydroxyphenolic acid and is found in bio-waste like grape pomace, tea leaves or oak bark.\textsuperscript{13} Herein, we present a novel single-pot method for the \textit{in situ} synthesis of mono-dispersed nanosized palladium nanoparticles. The method uses gallic acid as reducing agent and is a simple, efficient and highly cost-effective protocol for the Suzuki-Miyaura reactions in water at room temperature.

\subsection*{4.2. Results and Discussion}

\subsubsection*{4.2.1. Catalyst evaluation and optimization of the reaction conditions}

To identify the role of gallic acid in the palladium catalyzed Suzuki-Miyaura cross-coupling reaction, we have chosen phenylboronic acid and 4-bromoanisole as the
model substrates. The cross-coupling reaction proceeds very effectively (99%) in the presence of gallic acid (2 mol%), PdCl₂ (1 mol%), K₂CO₃ in water at room temperature (Table 4.2, entry 2). Thereafter, the reaction was studied with different catalyst loading to optimize the reaction conditions. Finally, the best result was achieved by using gallic acid (1 mol%), PdCl₂ (0.5 mol%) and K₂CO₃ in water at room temperature (Table 4.2, entries 1-3).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Time</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>K₂CO₃</td>
<td>10 min</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>K₂CO₃</td>
<td>5 min</td>
<td>99 ‡</td>
</tr>
<tr>
<td>3</td>
<td>K₂CO₃</td>
<td>1 h</td>
<td>42 ‡</td>
</tr>
<tr>
<td>4</td>
<td>Na₂CO₃</td>
<td>15 min</td>
<td>89</td>
</tr>
<tr>
<td>5</td>
<td>Cs₂CO₃</td>
<td>30 min</td>
<td>83</td>
</tr>
<tr>
<td>6</td>
<td>K₃PO₄</td>
<td>2 h</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>Na₃PO₄</td>
<td>2.5 h</td>
<td>86</td>
</tr>
<tr>
<td>8</td>
<td>KOH</td>
<td>6 h</td>
<td>56</td>
</tr>
<tr>
<td>9</td>
<td>NaOH</td>
<td>12 h</td>
<td>43</td>
</tr>
<tr>
<td>10</td>
<td>NaHCO₃</td>
<td>12 h</td>
<td>40</td>
</tr>
<tr>
<td>11</td>
<td>NEt₃</td>
<td>12 h</td>
<td>29</td>
</tr>
<tr>
<td>12</td>
<td>-</td>
<td>12 h</td>
<td>No reaction</td>
</tr>
<tr>
<td>13</td>
<td>K₂CO₃</td>
<td>12 h</td>
<td>29 ‡</td>
</tr>
<tr>
<td>14</td>
<td>K₂CO₃</td>
<td>3 h</td>
<td>No reaction</td>
</tr>
</tbody>
</table>

*Reaction conditions: 4-bromoanisole (1 mmol), phenylboronic acid (1.1 mmol), PdCl₂ (0.5 mol%), gallic acid (1 mol%), base (2 mmol) in water (4 mL) at room temperature (ca. 28 °C). ‡Isolated yield. ‡PdCl₂ (1 mol%), gallic acid (2 mol%), ‡PdCl₂ (0.25 mol%), ‡Without gallic acid. ‡Without PdCl₂.

Based on the literature survey we have identified that the Suzuki-Miyaura coupling reaction is highly dependent on the presence and strength of a base which generates the catalytically active species involve in the transmetalation step. Thus, the use of a weak base is unable to activate the arylboronic acid, whereas, a strong base interacts with the substituted functional groups. Therefore, further investigations were carried
out to investigate the influence of different bases in the coupling reaction using PdCl₂ and gallic acid in water at room temperature (Table 4.2, entries 3-11). The use of metal carbonates such as K₂CO₃, Na₂CO₃, Cs₂CO₃, and phosphates like K₃PO₄ or Na₃PO₄, delivered the coupling products in good to excellent yields (Table 4.2, entries 3-7). However, in the presence of alkali bases like KOH, NaOH or NaHCO₃ lower amount of the coupling product was isolated (Table 4.2, entries 8-10). Organic base such as Et₃N was also examined and found to be completely ineffective in the present catalytic system (Table 4.2, entry 11). Moreover, the reaction failed to proceed in absence of base (Table 4.2, entry 12), which confirmed the role of base during the reaction. Thus, K₂CO₃ was found to be the most efficient base.

4.2.2 Catalyst Identification and Characterization

To demonstrate the role of gallic acid in this reaction, various control experiments were also performed. Reaction under above-derived conditions but without gallic acid did not work well (Table 4.2, entry 13), whereas, no cross-coupling was observed in the absence of PdCl₂ (Table 4.2, entry 14). Thus, the presence of gallic acid is very essential for the high efficiency of this system.

The general mechanism for ligand-free Suzuki-Miyaura cross-coupling reaction proceeds by an oxidative addition-transmetallation-reductive elimination cycle involving an Pd(0)-Pd(II) step.¹⁴ Thus, we assume that the presence of gallic acid, an reducing agent, may assist in the reduction of Pd(II) salts to Pd(0) nanospecies. To identify this active catalytic species, we monitor the reaction using Hg-poisoning test.¹⁵ Firstly, a sample was prepared by mixing PdCl₂ (0.5 mol%) and gallic acid (1 mol%) in water (4 mL), which was then stirred for 10 minutes at room
temperature. Followed by the addition of excess mercury (molar ratio to [Pd] ~400) the reaction mixture was stirred at room temperature for another 20 minutes. This mixture was then subjected to cross-coupling by adding the desired amount of substrates and base. However, after stirring for 30 minutes no coupling product was observed. This suggested the presence of palladium as heterogeneous catalyst.

The reduction of Pd(II) to Pd(0) could be monitored visually. Upon addition of gallic acid to the PdCl₂ solution, there occurs a gradual change in the color of the mixture from brown to dark brown within 10 minutes at room temperature. The observed color is due to the surface plasmon resonance (SPR) feature of Pd(0) NPs. The reduction of Pd(II) ions was studied using UV-Vis spectroscopy, which is a simple technique for the preliminary investigation of the reduction process. **Figure 4.1** shows the absorption spectrum of Pd(0) suspension after 10 minutes of addition of gallic acid. The absorption spectrum of PdCl₂ solution is also shown for better comparison. In the PdCl₂ solution a distinct peak at around 424 nm indicates the presence of Pd(II) ion in the mixture. However, this absorption peak disappeared after 10 minutes, which confirms the reduction of Pd(II) to Pd(0) particles.¹⁶

---

**Figure 4.1.** The UV-Visible absorption spectra of PdCl₂ and PdNPs.
The *in situ* formation of PdNPs during Suzuki-Miyaura cross-coupling reaction was also investigated by using Transmission Electron Microscopy (TEM). The TEM image of the reaction mixture after its completion shows the presence of nanosized palladium particles (PdNPs) with spherical aggregate structures having average dimensions of 15 nm (*Figure 4.2*(a) and (d)). In the high resolution-TEM image the interplanar spacing for the lattice fringes was found to be 0.23 nm (*Figure 4.2*b*), which corresponds to the (111) lattice plane. The selected-area electron diffraction (SAED) pattern (*Figure 4.2*c*) with five bright circular rings corresponds to the (111), (200), (220) (311) and (222) planes of Pd with face-centered cubic (fcc) structure.

---

**Figure 4.2.** (a) TEM and (b) High resolution-TEM image of *in situ* formed PdNPs; (c) Selected-area electron diffraction (SAED) pattern of the PdNPs, (d) particle size distribution derived from TEM images, based on 100 randomly selected particles
In the SEM images the aggregates of palladium particles were found to be in dispersed phase over the layers of gallic acid (Figure 4.3). This may be due to the coating of individual palladium nanoparticles by the hydrophilic shell of gallic acid which keep them closely attached to each other.

**Figure 4.3.** SEM images showing the gallic acid coated PdNPs

The PdNPs were further examined using energy dispersive X-ray spectroscopy (EDS) analysis (Figure 4.4). The EDS spectrum shows the characteristic peak of palladium, which indicates the formation of pure PdNPs by gallic acid.

**Figure 4.4.** EDS spectrum of the PdNPs

Powder X-ray diffraction (XRD) patterns of the Pd(0) (Figure 4.5) shows the presence of five peaks, which corresponds to different crystal planes of PdNPs in fcc. This result is in consistent with the SAED results (Figure 4.2c). This also suggests that the PdNPs have the features of polycrystalline structure. The diffraction peaks at
37.9°, 47.2°, 68.0°, 81.9° and 83.6° belong to the diffraction of (111), (200), (220), (311) and (222) planes of PdNPs. Overall, these results suggest the complete reduction of Pd(II) to Pd(0)NPs having cubic fcc structure.

![Powder X-ray diffraction patterns of PdNPs](image)

**Figure 4.5.** Powder X-ray diffraction patterns of PdNPs

### 4.2.3. Possible mechanism of catalyst formation

Based on literature reports,¹⁸ we believed that multiple factors are responsible for the reduction of Pd(II) species by gallic acid. In gallic acid, the π-electrons of the aromatic ring, carboxylic double bond and the lone pairs of hydroxyl group form a conjugated system. This conjugation assist in the reduction of Pd(II) to Pd(0) species. The loss of electrons during this process produces dehydrogallic acid which retains the electron conjugation of the moiety (Scheme 4.1).¹⁹

![Mechanism of reduction process](image)

**Scheme 4.1.** Mechanism of the reduction process for the formation of PdNPs.
Gallic acid is an efficient (electron + proton) donor which represents a redox system via the oxidation of gallic acid to dehydrogallic acid. This low energy redox system (reduction potential of gallic acid is \( \sim 0.863 \) V vs. SCE)\(^{20}\) is sufficient for the conversion of Pd(II) to Pd(0) particles (reduction potential 0.915 V vs. SCE).\(^{21}\)

4.2.4. Scope and Limitations of Substrates

To evaluate the scope and limitations of the present catalytic system, we examined the Suzuki-Miyaura coupling reaction of various aryl bromide substrates (Table 4.3). A wide range of electronically diverse aryl bromides have been studied to give excellent isolated yields (Table 4.3, entries 1-18). It is observed that the presence of strong electron-donating substituent in arylboronic acid increases the catalytic activity (Table 4.3, entries 3, 6 and 9). It is believed that electron-donating group in arylboronic acid accelerates the transmetalation step and enhances the reaction rate. However, lower yield with electron-deficient arylboronic acids, which transmetalate slowly, could be due to homo-coupling\(^{21b,22}\) and protodeboronation.\(^{23}\) We have also studied the coupling reaction using heteroaryl substrates under the present reaction condition, and found excellent results (Table 4.3, entries 15-18). We next tried to examine the reactivity of aryl chloride under present catalyst loading, but no conversion was noticed probably due to higher bond energy of C-Cl compared to C-Br (Table 4.3, entries 19 and 20). These results are very important as the reactions are carried out in water and at room temperature (ca. 28 °C) within short reaction time, as summarized in the Table 4.3.
Table 4.3.
Suzuki-Miyaura reaction of aryl halides with a variety of arylboronic acids at room temperature$^a$

$$
\begin{array}{cccc}
\text{Entry} & X & R^1 & R^2 & \text{Time (minute)} & \text{Yield [%]} \\
1 & \text{Br} & \text{MeO-} & \text{H-} & 10 & 99 \\
2 & \text{Br} & \text{MeO-} & \text{F-} & 25 & 95 \\
3 & \text{Br} & \text{MeO-} & \text{MeO-} & 15 & 96 \\
4 & \text{Br} & \text{MeCO-} & \text{H-} & 15 & 94 \\
5 & \text{Br} & \text{MeCO-} & \text{Cl-} & 45 & 93 \\
6 & \text{Br} & \text{MeCO-} & \text{MeO-} & 20 & 99 \\
7 & \text{Br} & \text{CHO-} & \text{H-} & 20 & 97 \\
8 & \text{Br} & \text{CHO-} & \text{Cl-} & 60 & 98 \\
9 & \text{Br} & \text{CHO-} & \text{MeO} & 20 & 99 \\
10 & \text{Br} & \text{NO}_2- & \text{H-} & 20 & 96 \\
11 & \text{Br} & \text{NO}_2- & \text{Cl-} & 35 & 94 \\
12 & \text{Br} & \text{H-} & \text{H-} & 10 & 100 \\
13 & \text{Br} & \text{H-} & \text{MeO-} & 15 & 99 \\
14 & \text{Br} & \text{H-} & \text{F-} & 30 & 95 \\
15 & \text{Br} & 5\text{-bromopyrimidine} & \text{H-} & 50 & 89 \\
16 & \text{Br} & 5\text{-bromopyrimidine} & \text{MeO-} & 40 & 93 \\
17 & \text{Br} & 5\text{-bromopyrimidine} & \text{F-} & 55 & 91 \\
18 & \text{Br} & 5\text{-bromopyrimidine} & (6\text{-methoxy}3\text{-yl}) \text{boronic acid} & 70 & 90 \\
19 & \text{Cl} & \text{Me-} & \text{H-} & 120 & \text{trace} \\
20 & \text{Cl} & \text{NO}_2- & \text{H-} & 120 & \text{trace} \\
\end{array}
$$

$^a$Reaction conditions: Aryl halides (1.0 mmol), arylboronic acid (1.1 mmol), PdCl$_2$ (0.5 mol%), gallic acid (1 mol%), K$_2$CO$_3$ (2 mmol) in water (4 mL) at room temperature (ca. 28 °C). $^b$Isolated yield.

4.3 Catalyst Recycling

The catalyst recycling without significant loss in activity and efficiency is a major concern from the perspective of green chemistry. Considering this, the recyclability of the in situ derived PdNPs catalyst was further investigated by consecutive Suzuki-Miyaura cross-coupling reactions of 4-bromoanisole with phenylboronic acid. In the
present method, the extraction of coupling products using diethyl ether from the reaction mixture was found to be efficient procedure for all reactions and led to the highest yields.

Notably, we did not detect any noticeable leaching of palladium particle in the isolated product (using ICP-AES). Moreover, we could easily isolate the biaryl products and recover the catalytic solution, allowing repetitive catalytic runs. After the completion of first cycle, the recovered catalytic solution can be reused with no further modification for the next cycles following the addition of fresh reactants (Table 4.4). However, after the first recycle a slight loss in activity is also observed. The average yield over four recycles was 94% (Table 4.4, entries 1-4). The catalyst was collected after 4th run and was analyzed by TEM (Figure 4.6).

Table 4.4.
Catalyst recycle of the Suzuki-Miyaura cross-coupling reaction

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalytic run</th>
<th>Time (min)</th>
<th>Yield [%]a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1st cycle</td>
<td>10</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>2nd cycle</td>
<td>20</td>
<td>95</td>
</tr>
<tr>
<td>3</td>
<td>3rd cycle</td>
<td>25</td>
<td>92</td>
</tr>
<tr>
<td>4</td>
<td>4th cycle</td>
<td>30</td>
<td>91</td>
</tr>
</tbody>
</table>

aReaction conditions: Aryl halides (1.0 mmol), arylboronic acid (1.10 mmol), PdCl2 (0.5 mol%), gallic acid (1 mol%), K2CO3 (2 mmol) in water (4 mL) at room temperature (ca. 28 °C). b Isolated yield.

The TEM image shows that the size of nanoparticles gets reduced under the prolong treatment of gallic acid, but the spherical shape and aggregation are conserved (Figure 4.6). However, with successive cycles the reaction time gets slightly increases. This is probably due to the release of salt by-products during the coupling reaction which retards the progress of the coupling reaction.24
4.4 Conclusion

In summary, we have developed a simple and green method to synthesize palladium nanoparticle for the Suzuki-Miyaura coupling reaction in water at room temperature. The reaction is highly compatible with a wide and diverse range of functional groups. Moreover, the use of gallic acid influenced both rate of the reaction and size distribution of the PdNPs.

4.5 Experimental Section

4.5.1 Materials and Instrumentation

Materials and Instruments used are identical with Chapter 3, Section 2, unless otherwise mention. The following abbreviations are used for the description of $^1$H NMR signals: s (singlet), d (doublet), t (triplet), m (multiplet). Coupling constants ($J$) were measured in Hz.

4.5.2 Catalytic Studies

A 25 mL round-bottom flask was charged with aryl bromide (1 mmol), arylboronic acid (1.1 mmol), $K_2CO_3$ (2 mmol), PdCl$_2$ (0.5 mol%) gallic acid (1 mol%) and water (4 mL) and the mixture was stirred at room temperature for the required time. After
completion of the reaction, monitored by TLC, the mixture was diluted with water (10 mL) and extracted with diethyl ether (3×10 mL). The combined organic extract washed with brine (2×10 mL), dried over anhydrous Na₂SO₄. After evaporation of the solvent in a rotavapor, the residue was subjected to column chromatography (silica gel, eluent: ethyl acetate-hexane; 0.5:9.5) to isolate the desired products.

4.5.3. Characterization data of the isolated

4-Methoxybiphenyl: (Table 4.1, entry 1):²⁵ White solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ: 7.55-7.51 (m, 4H), 7.42-7.40 (m, 2H), 7.32-7.29 (m, 1H), 6.98-6.96 (m, 2H), 3.84 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm) δ: 159.2, 140.9, 133.8, 128.8, 128.2, 126.8, 126.7, 114.2, 55.4; GC-MS m/z: 184.1 (M⁺, 100).

4-Flouro-4'-methoxybiphenyl: (Table 4.1, entry 2):²⁵ White solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ: 7.47-7.45 (m, 4H), 7.10-7.08 (m, 2H), 6.97-6.95 (m, 2H), 3.84 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm) δ: 163.4, 160.9, 159.1, 137.0, 132.9, 128.3 (d, J=7.6 Hz, 1C), 115.7 (d, J=20.9 Hz, 1C), 114.3, 55.4; GC-MS m/z: 202.4 (M⁺, 100).

4, 4'-Dimethoxybiphenyl: (Table 4.1, entry 3):²⁵ Colourless solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ: 7.48-7.46 (m, 4H), 6.96-6.94 (m, 4H), 3.84 (s, 6H); ¹³C NMR (CDCl₃, 100 MHz, ppm) δ: 158.7, 133.5, 127.8, 114.2, 55.43; GC-MS m/z: 214.10 (M⁺, 100).
4-Acetyl biphenyl (Table 4.1, entry 4):\textsuperscript{25} White solid, \textsuperscript{25}1H NMR (CDCl\textsubscript{3}, 400 MHz, ppm, TMS) δ: 8.04-8.03 (m, 2H), 7.70-7.68 (m, 2H), 7.64-7.62 (m, 2H), 7.50-7.48 (m, 2H), 7.45-7.44 (m, 1H), 2.64 (s, 3H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 100 MHz, ppm) δ: 197.8, 145.8, 139.9, 135.9, 129.1, 129.0, 128.3, 127.4, 127.3, 26.7; GC-MS m/z: 196.10 (M\textsuperscript{+}, 100).

1-(4'-Chloro-[1,1'-biphenyl]-4-yl)ethanone (Table 4.1, entry 5):\textsuperscript{25} White solid, \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 400 MHz, ppm) δ: 8.04-8.02 (m, 2H), 7.66-7.63 (m, 2H), 7.56-7.54 (m, 2H), 7.47-7.45 (m, 2H), 2.64 (s, 3H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 100 MHz, ppm) δ: 197.7, 144.5, 138.3, 136.1, 134.5, 129.2, 129.0, 128.5, 127.1, 26.7; GC-MS m/z: 230.10 (M\textsuperscript{+}, 100).

4-Acetyl-4'-methoxy biphenyl (Table 4.1, entry 6):\textsuperscript{25} White solid, \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 400 MHz, ppm) δ: 8.01-7.99 (m, 2H), 7.65-7.64 (m, 2H), 7.59-7.57 (m, 2H), 7.01-6.99 (m, 2H), 3.86 (s, 3H), 2.63 (s, 3H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 100 MHz, ppm) δ: 197.7, 159.9, 145.4, 135.3, 132.3, 129.0, 128.4, 126.7, 114.4, 55.4, 26.7; GC-MS m/z: 226.10 (M\textsuperscript{+}, 100).
[1,1'-Biphenyl]-4-carbaldehyde (Table 4.1, entry 7): White solid, $^1$H NMR (CDCl$_3$, 400 MHz, ppm) δ: 10.05 (s, 1H), 7.96 (d, J= 8.28 Hz, 2H), 7.75 (d, J= 8.28 Hz, 2H), 7.63 (d, J= 7.36 Hz, 2H) 7.47 (d, J= 7.36 Hz, 2H), 7.42-7.40 (m, 1H); $^{13}$C NMR (CDCl$_3$, 100 MHz, ppm) δ: 192.0, 147.3, 139.7, 135.2, 130.3, 129.1, 128.5, 127.7, 127.4.; GC-MS m/z: 182.1 (M$^+$, 100).

4-Formyl-4'-chloro biphenyl (Table 4.1, entry 8): White solid, $^1$H NMR (CDCl$_3$, 400 MHz, ppm) δ: 10.0 (s, 1H), 7.94 (d, J= 8.16 Hz, 2H), 7.71 (d, J= 8.16 Hz, 2H), 7.62-7.58 (m, 2H), 7.20-7.14 (m, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz, ppm) δ: 191.8, 145.9, 138.2, 135.4, 134.8, 130.4, 129.3, 128.6, 127.6; GC-MS m/z: 216.10 (M$^+$, 100).

4'-Methoxy-[1,1'-biphenyl]-4-carbaldehyde (Table 4.1, entry 9): White solid, $^1$H NMR (CDCl$_3$, 400 MHz, ppm) δ: 10.03 (s, 1H), 7.93-7.91 (m, 2H), 7.72-7.71 (m, 2H), 7.60-7.58 (m, 2H), 7.02-7.00 (m, 2H), 3.87 (s, 3H); $^{13}$C NMR (CDCl$_3$, 100 MHz, ppm) δ: 192.0, 160.1, 146.8, 134.7, 132.1, 130.4, 128.5, 127.1, 114.5, 55.4; GC-MS m/z: 212.1 (M$^+$, 100).

4-Nitrobiphenyl (Table 4.1, entry 10): Yellow solid, $^1$H NMR (CDCl$_3$, 400 MHz, ppm) δ: 8.31-8.29 (m, 2H), 7.75-7.73 (m, 2H), 7.64-7.60 (m, 2H), 7.51-7.48 (m, 3H); $^{13}$C NMR (CDCl$_3$, 100 MHz, ppm) δ: 147.7, 147.1, 138.8, 129.2, 129.0, 127.8, 127.4, 124.1; GC-MS m/z: 199.1 (M$^+$, 100).
4-Chloro-4'-nitro-biphenyl (Table 4.1, entry 11):$^{25}$ White solid, $^1$H NMR (CDCl$_3$, 400 MHz, ppm) $\delta$: 8.31-8.28 (m, 2H), 7.70-7.68 (m, 2H), 7.60-7.59 (m, 2H), 7.20-7.19 (m, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz, ppm) $\delta$: 147.1, 146.6, 137.2, 135.0, 129.2, 129.1, 127.7, 124.2; GC-MS $m/z$: 233.10 (M$^+$, 100).

1,1'-Biphenyl (Table 4.1, entry 12):$^{25}$ White solid, $^1$H NMR (CDCl$_3$, 400 MHz, ppm) $\delta$: 7.64-7.62 (m, 4H), 7.49-7.46 (m, 4H), 7.39-7.36 (m, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz, ppm) $\delta$: 141.1, 128.9, 127.3, 126.9; GC-MS $m/z$: 154.10 (M$^+$, 100).

4-Methoxybiphenyl: (Table 4.1, entry 13):$^{25}$ White solid, $^1$H NMR (CDCl$_3$, 400 MHz, ppm) $\delta$: 7.55-7.51 (m, 4H), 7.42-7.39 (m, 2H), 7.32-7.28 (m, 1H), 6.98-6.96 (m, 2H), 3.84 (s, 3H); $^{13}$C NMR (CDCl$_3$, 100 MHz, ppm) $\delta$: 159.2, 140.9, 133.8, 128.8, 128.2, 126.8, 126.7, 114.2, 55.4; GC-MS $m/z$: 184.1 (M$^+$, 100).

4-Flouro biphenyl (Table 4.1, entry 14):$^{32}$ White solid, $^1$H NMR (CDCl$_3$, 400 MHz, ppm) $\delta$: 7.55-7.53 (m, 4H), 7.44-7.42 (m, 2H), 7.36-7.35 (m, 1H), 7.14-7.12 (m, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz, ppm) $\delta$: 163.3, 161.3, 140.1, 137.2, 128.7, 127.1, 126.9, 115.6; GC-MS $m/z$: 173.10 (M$^+$, 100).
5-Phenylpyrimidine (Table 4.1, entry 15):\textsuperscript{33} White solid, \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 400 MHz, ppm) δ: 9.22 (s, 1H), 8.97 (m, 2H), 7.59-7.50 (m, 5H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 100 MHz, ppm) δ: 157.3, 154.9, 134.5, 134.2, 129.5, 129.1, 127.0; GC-MS \textit{m/z}: 156.1 (M\textsuperscript{+}, 100).

5-(4'-Methoxyphenyl)pyrimidine (Table 4.1, entry 16):\textsuperscript{34} Yellow solid, \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 400 MHz, ppm) δ: 9.14 (s, 1H), 8.91 (s, 2H), 7.52-7.49 (m, 2H), 7.04-7.01 (m, 2H), 3.17 (s, 3H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 100 MHz, ppm) δ: 160.3, 156.7, 154.3, 133.8, 128.0, 126.4, 114.8, 55.3; GC-MS \textit{m/z}: 186.1 (M\textsuperscript{+}, 100).

5-(4-Fluorophenyl)pyrimidine (Table 4.1, entry 17):\textsuperscript{34} White solid, \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 400 MHz, ppm) δ: 9.21 (s, 1H), 8.92 (s, 2H), 7.57-7.55 (m, 2H), 7.25-7.22 (m, 2H), \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 100 MHz, ppm) δ: 162.2, 157.5, 154.8, 128.9, 128.8, 116.7, 116.5; GC-MS \textit{m/z}: 174.1 (M\textsuperscript{+}, 100).

5-(6-Methoxypyridin-3-yl)pyrimidine (Table 4.1, entry 18):\textsuperscript{33} Yellow solid, \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 400 MHz, ppm) δ: 9.21 (s, 1H), 8.92 (s, 2H), 8.40 (d, J= 2.32 Hz, 1H), 7.80-7.78 (m, 1H), 6.91-6.89 (m, 1H), 4.01 (s, 3H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 100 MHz, ppm) δ: 156.7, 128.8, 116.7, 116.4, 56.1.
ppm) δ: 164.7, 157.4, 154.4, 145.1, 137.1, 131.6, 123.3, 111.8, 53.9; GC-MS m/z: 187.1 (M⁺, 100).

¹H and ¹³C NMR spectra of 4, 4′-Dimethoxybiphenyl (Table 4.1, entry 3)
4.6. Reference


H. Sarker, S. N. Barnaby, A. P. Dowdell, N. Nakatsuka and I. A. Banerjee, 


