Abstract

In this chapter microwave assisted Fluoride-Free, sodium hydroxide activated, Hiyama cross-coupling reaction between aryl halides and phenyltrimethoxysilane catalyzed by resin supported palladium and gold nanoparticles is discussed. The effect of various parameters such as catalyst concentration, time, temperature on the reaction and the recyclability of the PdNPs and AuNPs was investigated. The progress of the reaction was studied by GC-MS and products after isolation were characterized by $^1$H NMR. The activity of catalyst in terms of TON and TOF was excellent recyclability in the coupling of aryl halides with phenyltrimethoxysilane, under microwave heating.
4.1. Introduction

Palladium catalyzed cross-coupling reactions have emerged as the most efficient methodologies for the production of unsymmetrical biaryls and are extensively utilized in the synthesis of polymers, agrochemicals, pharmaceutical intermediates, etc. [1]. Among the coupling reactions, three most frequently employed are Stille [2], Suzuki-Miyaura [3], and Hiyama [4,5] reactions. In spite of the excellent yields, high stereoselectivity and superior functional group tolerance, the use of toxic tin reagents in Stille couplings, and the difficulties in the preparation and purification of boron reagents required for the Suzuki reactions, are major disadvantages. Therefore, the Hiyama coupling reaction that uses environmentally benign, cheaper and easy to prepare organosilicon reagents has many advantages in comparison to others. Hiyama et al. [6–8] have developed several methods for this transformation, using various Pd catalysts in the presence of phosphine ligands. Earlier, corrosive fluoride anions were used for the activation of C–Si bond of alkylsilanes but later on, the activity of C–Si bond was enhanced by using alkenylfluorosilanes [9], alkenylalkoxysilanes [10–12], and organosilanols [13–15]. Subsequently, with the development of sodium hydroxide as an effective promoter [16,17] for alkoxysilanes in aqueous media, the potential of Hiyama reaction as a viable synthetic process was demonstrated. Though, the aqueous Hiyama reaction made significant progress, either toxic phosphine ligands or expensive palladocycles were still required. Of late, nanoparticles have emerged as efficient catalysts for coupling reactions in the absence of ligands.

In the last decade, the use of metal nanoparticles as efficient catalysts in organic reactions have attracted considerable interest. The high surface-to-volume ratio of nanoparticles provide larger number of active sites per unit area compared to their heterogeneous counterparts. Recently, two procedures involving preformed palladium-coated nickel nanoclusters [18] and palladium nanoparticles [19] have been reported for Hiyama reaction. Rothenberg et al. [18], first reported the usage of bimetallic core–shell Ni–Pd
nanoclusters to catalyze Hiyama cross-coupling reaction between various halo arenes and phenyltrimethoxysilane. High product yields were obtained with a variety of iodo and bromo aryls in tetrahydrofuran using tetra-butylammonium fluoride (TBAF) as the activator. Sarkar et al. [20] reported efficient catalysis of NaOH activated ligand less Hiyama cross-coupling reaction using polyethylene glycol (PEG) capped palladium nanoparticles, in aqueous media. Ranu et al. [21] demonstrated that in situ generated Pd (0) nanoparticles can catalyze Hiyama cross-coupling reaction in a very short time. Sodium dodecyl sulphate (SDS) was used as surfactant in this reaction. These methods, which used colloidal nanoparticles, lacked recyclability. Hence, there is a growing need to develop stable and recyclable catalyst systems. There are only a few reports of AuNPs catalyzed C-C coupling reaction [22-23]. We have for the first time reported Hiyama reaction catalyzed by resin-AuNPs. In this chapter, we investigated the behavior of PdNPs and AuNPs, supported on an inert non-functional macroporous polymer resin for the Flouride-Free Hiyama cross-coupling reaction.

4.2. Experimental

4.3.1 Materials

All chemicals used were of analytical grade or of the highest purity available. All glassware was thoroughly cleaned with freshly prepared 3:1 HCl/HNO₃ (aqua regia) and rinsed thoroughly with Millipore-Q water. Phenyltrimethoxysilane was purchased from Aldrich. Aryl halides were obtained from BDH and Merck. All aryl halide standards were of 98–99% purity. Dichloromethane (DCM), diethyl ether (Et₂O), and NaOH were purchased from Finar chemicals. Water was purified by Millipore system and used in all experiments.

4.3.2 Instrumentation

Melting points were taken on Veego (VMP-DS) using a Melt-Temp Instrument. GC-MS measurements were carried on Perkin Elmer USA Auto system XL. The GC/MS programs applied throughout the analysis was
as follows: the column temperature was 40 ºC at the beginning of the program and it was heated with a rate of 5 ºC/min up to 250 ºC. ¹H NMR spectra were recorded on Bruker Advance II 400 MHz NMR spectrometer. Reactions were carried out in CEM Microwave synthesizer (benchmate), in closed vessels with external cooling under aerobic conditions.

4.3.3 Protocol for Hiyama cross-coupling reaction using resin encapsulated PdNPs

Into a 10 mL vial phenyltrimethoxysilane (1.5 mmol), resin-PdNPs (150 mg) and ethanol (1.5 mL) were taken. The reaction mixture was stirred vigorously and 3M NaOH (1 mL, 3 mmol) was added drop wise. Then aryl halide (1 mmol) was added and vial heated in CEM microwave (50 w, 110 ºC) for different intervals of time (Scheme 4.1). The reaction was quenched by filtering the hot solution into 10 mL cold water. The resulting solution was extracted with Et₂O/DCM (2×5 mL). The combined organic extract dried over anhydrous MgSO₄ and the solvent was removed using a rotary evaporator. The crude product, thus isolated, was recrystallized from appropriate solvent.

![Scheme 4.1: Hiyama reaction catalyzed by resin-PdNPs](image)

4.3.4 Protocol for Hiyama cross-coupling reaction using resin encapsulated AuNPs

Into a 10 mL vial phenyltrimethoxysilane (1.5 mmol), resin-AuNPs (200 mg) and ethanol (2.0 mL) were taken. The reaction mixture was stirred vigorously and 4M NaOH (1 mL, 4 mmol) was added drop wise. Then aryl halide (1 mmol) was added and vial heated in CEM microwave (100 w, 110 ºC) for different intervals of time (Scheme 4.2). The reaction was quenched by filtering the hot solution in 10 mL cold water. The resulting solution was extracted with Et₂O/DCM (2×5 mL). The combined organic extract dried over
anhydrous MgSO$_4$ and the solvent was removed using a rotary evaporator. The crude product, thus isolated, was recrystallized from appropriate solvent.

\[
\begin{align*}
\text{Resin-AuNPs, NaOH} \\
\text{MW, 110 °C}
\end{align*}
\]

**SCHEME 4.2:** Hiyama reaction catalyzed by resin-AuNPs

### 4.3. Result and discussion

#### 4.3.1 Resin-PdNPs catalyst Hiyama cross-coupling reaction.

The effect of various parameters such as base, solvent, temperature, catalyst concentration, time and recyclability were studied taking coupling of 4-bromoacetophenone and phenyltrimethoxysilane as the standard reaction (Scheme 4.3).

**SCHEME 4.3:** The Hiyama cross-coupling reaction of 4-bromoacetophenone with phenyltrimethoxysilane catalyzed by resin-PdNPs

\[
\begin{align*}
\text{Resin-PdNPs} \\
\text{Base, MW}
\end{align*}
\]

**Condition:** 4-bromoacetophenone (1.0 mmol), phenyltrimethoxysilane (1.5 mmol), NaOH (3.0 mmol, 3M 1 mL), EtOH (1.5 mL), and resin-PdNPs catalyst

#### 4.3.1.1 Effect of base

Organosilane reagent are more environmentally friendly compared to boronic acid. However the organosilicon bond is weak and requires activation. In Hiyama reaction base helps in transmetalation by activating organosilicon compound. Literature showed different in-organic bases [19,21] can be used as activator in Hiyama cross-coupling reaction. Here, two common inorganic bases viz. sodium hydroxide and sodium carbonate in different molar ratio were tried. It was observed that conversion to biphenyl was not complete using sodium carbonate. However, in the case NaOH, % yield was high and we achieved maximum conversion by using 3 mmol NaOH.
The results are shown in Fig. 4.1. A general catalytic cycle [21] for this reaction is represented in Fig. 4.2.

![Figure 4.1. Effect of base on the yield of standard Hiyama reaction](image)

**Figure 4.1.** Effect of base on the yield of standard Hiyama reaction

![Figure 4.2. The proposed catalytic cycle with NaOH as activator](image)

**Figure 4.2.** The proposed catalytic cycle with NaOH as activator

4.3.1.2 **Effect of catalyst concentration**

The efficiency of catalyst is measured by Its TON and TOF. The catalytic activity of the nanoparticle system was investigated by varying the amount of catalyst while keeping the other parameters constant. The results are shown in Fig. 4.3. It was observed that 150 mg of resin (≈ 0.00035 mmol of Pd, 0.035 mol% with respect to aryl halide) was sufficient for completing the reaction. Using the obtained result, we calculated the, TON and TOF (h⁻¹) values which were found to be 2,912 and 29,120 respectively.
4.3.1.3 Effect of solvent

This study was carried out to optimize appropriate solvent system that strongly favors the Hiyama coupling of 4-bromoacetophenone with phenyltrimethoxysilane by resin-PdNPs. On the bases of our earlier studies with Suzuki reaction and in our endeavor to utilize low boiling benign organic solvents, only alcohols and alcohol/water mixtures were tried as solvents. The results are presented in table 4.1. It was once again observed that water alone is not sufficient due to poor solubility of reactants. Even pure methanol and ethanol as solvent resulted in low product yield. Best yield were obtained when EtOH:H₂O in 2:1 ratio was used. It was concluded that presence of water is essential for the reaction.

Table 4.1: The effect of solvent on the Hiyama cross-coupling reactions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H₂O</td>
<td>Trace</td>
</tr>
<tr>
<td>2</td>
<td>MeOH</td>
<td>48.0</td>
</tr>
<tr>
<td>3</td>
<td>MeOH:H₂O (1:1)</td>
<td>75.0</td>
</tr>
<tr>
<td>4</td>
<td>MeOH:H₂O (2:1)</td>
<td>90.0</td>
</tr>
<tr>
<td>5</td>
<td>EtOH</td>
<td>55.0</td>
</tr>
<tr>
<td>6</td>
<td>EtOH:H₂O (1:1)</td>
<td>85.0</td>
</tr>
<tr>
<td>7</td>
<td>EtOH:H₂O (2:1)</td>
<td>99.0</td>
</tr>
</tbody>
</table>

Figure 4.3. Effect of resin-PdNPs catalyst concentration on the yield (GC determined) of 4-bromoacetophenone in Hiyama reactions
4.3.1.4  **Effect of time**

The kinetics of the reaction was studied by taking TLC of the reaction mixture at different interval of time and confirmed by the GC-MS at the end of reaction (Fig. 4.4). Total conversion of 4-bromoacetophenone could be obtained in 6 min. The GC-MS analysis of the ether extract showed that 4-acetylbiphenyl is the sole product (retention time = 19.07 min). The mass spectrum of the peak at retention time = 19.07 min was identified as 4-acetylbiphenyl from its molecular peak in the highest mass region at m/z 196. The other prominent peaks were found at m/z 181, 152, 127, 91 and 76 (See appendix).

![Figure 4.4](image.png)

**Figure 4.4.** Time course of Hiyama reaction between 4-bromoacetophenone and phenyltrimethoxysilane

4.3.1.5  **Leaching test or hot filtration test**

Leaching of the metal from the catalyst was probed by hot filtration test. The reaction between 4-bromoacetophenone and phenyltrimethoxysilane was stopped after 2 min and the resin filtered off while the solution was still hot. The filtrate was further heated and the reaction mixture analyzed by GC-MS after 3, 4, 5, and 6 min. The results shown in Fig. 4.5 indicate that the reaction stops after the resin is filtered off. Additionally, the reaction mixture was extracted with ether and aqueous layer was analyzed for palladium by ICP-AES. Total palladium concentration was found to be 35±10 ppb. The negative results of the hot filtration test indicate that the leaching of palladium is negligible and most probably, the reaction is heterogeneous in nature.
4.3.1.6 Recyclability of the catalyst

Recovery and catalyst reuse are important issues in the cross-coupling reactions. Easy catalyst separation and recycling in successive batch operations can greatly increase the efficiency of the reaction. At the completion of the reaction, the catalyst was recovered by simple filtration. The resin beads were collected and washed with hot water/alcohol/DCM to remove the product sorbed by the resin and reused. The recovered catalyst was employed in the next run with further addition of substrates, in appropriate amount using optimum reaction conditions. The catalyst showed unchanged catalytic activity up to four reaction cycles and the decrease was about 5% in the 5th cycle. The results are shown in Fig. 4.6.

Figure 4.6. Recycling of the catalyst for the standard Hiyama coupling reaction

4.3.1.7 Reaction with aryl halides

The excellent results obtained in the cross-coupling of 4-bromoacetophenone with phenyltrimethoxysilane prompted us to carry out the reaction with other aryl bromides. A series of aryl bromides with both
electron withdrawing and donating groups were used and the results are summarized in Table 4.2. The reaction was uniform irrespective of the nature of the substituents (electron withdrawing or electron donating) on the aromatic ring. A wide range of substituents, which included -CH₃, -CHO, -OCH₃, -NO₂, and -COCH₃, were compatible with this procedure. In case of aldehyde, chemo selectivity was totally in favor of Hiyama cross-coupled product. We also carried out the reaction with 2-bromo thiophene (entry 8) and isolated coupled product in good yield. In case of -NHCOCH₃ group (entry 5), 4-aminobiphenyl was also isolated. -COOH and -CN groups were found to be incompatible. No reaction occurred with 4-bromobenzoic acid and in case of 4-bromobenzonitrile, only hydrolysed product was isolated. We also tried reaction with aryl chlorides (entry 10-12) and found that under the present set of conditions reaction with chlorobenzene (entry 10), did not proceed to completion. However, on increasing the reaction time from 6 to 12 min, we could isolate the products in high yields. We also carried out the reaction with 4-bromo iodobenzene using same amount of phenyltrimethoxysilane and found the isolated coupled product was 4-bromobiphenyl. When 2 mmol of phenyltrimethoxysilane was used terphenyl was isolated product (Fig. 4.7). So, this is indicated that the reactivity order of haloarenes in Hiyama reaction was I>Br>Cl. All the products were of high purity and were characterized by matching their ¹H NMR spectra with the reported data.

![Figure 4.7. Selectivity in Hiyama cross-coupling reaction](image-url)
Table 4.2: Resin-PdNPs catalyst Hiyama cross-coupling reaction with various aryl halides with phenyltrimethoxysilane

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aryl halide</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bromobenzene</td>
<td>![image]</td>
<td>6</td>
<td>94</td>
</tr>
<tr>
<td>2</td>
<td>4-bromobenzaldehyde</td>
<td>![image]</td>
<td>6</td>
<td>95</td>
</tr>
<tr>
<td>3</td>
<td>4-bromoacetophenone</td>
<td>![image]</td>
<td>6</td>
<td>96</td>
</tr>
<tr>
<td>4</td>
<td>4-bromoanisole</td>
<td>![image]</td>
<td>6</td>
<td>96</td>
</tr>
<tr>
<td>5</td>
<td>4-bromoacetanilide</td>
<td>![image]</td>
<td>6</td>
<td>76</td>
</tr>
<tr>
<td>6</td>
<td>2-bromoacetophenone</td>
<td>![image]</td>
<td>6</td>
<td>92</td>
</tr>
<tr>
<td>7</td>
<td>3-bromotoulene</td>
<td>![image]</td>
<td>6</td>
<td>90</td>
</tr>
<tr>
<td>8</td>
<td>2-bromothiophene</td>
<td>![image]</td>
<td>8</td>
<td>90</td>
</tr>
<tr>
<td>10</td>
<td>Chlorobenzene</td>
<td>![image]</td>
<td>12</td>
<td>89</td>
</tr>
<tr>
<td>11</td>
<td>4-chloronitrobenzene</td>
<td>![image]</td>
<td>12</td>
<td>92</td>
</tr>
<tr>
<td>12</td>
<td>2-chlorobenzaldehyde</td>
<td>![image]</td>
<td>12</td>
<td>85</td>
</tr>
<tr>
<td>13</td>
<td>1-bromo-4-chlorobenzene</td>
<td>![image]</td>
<td>10**</td>
<td>95</td>
</tr>
<tr>
<td>14</td>
<td>1-bromo-4-iodobenzene</td>
<td>![image]</td>
<td>6</td>
<td>92</td>
</tr>
</tbody>
</table>

**Conditions:** Aryl halide (1.0 mmol); phenyltrimethoxysilane (1.5 mmol); resin-PdNPs (150 mg); NaOH (3.0 mmol, 3 M 1 mL); EtOH (1.5 mL); (Microwave conditions, 110 °C, 50 w).

*Isolated yields. ** use 2.0 mmol phenyltrimethoxysilane
4.3.1.8  Comparison with other reported methods

Table 4.3 provides a comparison of the results obtained from the present catalytic system with those reported in the literature. From Table 3, it can be seen that present catalyst exhibited equally high conversions and yields without using any activator. Reactions were completed in short time compared to others. Moreover the resin-PdNPs were easily separated and recycled many times.

**Table 4.3:** A comparison of the present method with the other reported methods

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Reaction Condition</th>
<th>Yield %</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Resin-PdNPs</td>
<td>1 mL 3M NaOH, EtOH (2 mL), 50 w, 110 ºC, 6 min.</td>
<td>99</td>
<td>Present</td>
</tr>
<tr>
<td>2</td>
<td>Core-shall Ni-Pd clusters</td>
<td>1.5 mmol TBAF, 5.0 mL THF, N₂, 65 ºC, 24 h.</td>
<td>62</td>
<td>18</td>
</tr>
<tr>
<td>3</td>
<td>Pd-PEG NPs</td>
<td>5 M NaOH, 90 ºC, 2 h.</td>
<td>98</td>
<td>19</td>
</tr>
<tr>
<td>4</td>
<td>PdNPs in situ formation</td>
<td>NaOH, SDS, 100 ºC, 5 min.</td>
<td>96</td>
<td>20</td>
</tr>
<tr>
<td>5</td>
<td>ortho-palladated complexes</td>
<td>TBAF 3H₂O (1.2 mL), DMF (2 mL), 600 w, 100 ºC, 7 min.</td>
<td>90</td>
<td>21</td>
</tr>
</tbody>
</table>
4.3.2 Resin-AuNPs catalyst Hiyama cross-coupling reaction

The effect of various parameters such as base, solvent, temperature, catalyst concentration, time and recyclability was studied taking coupling of 4-Iodoacetophenone and phenyltrimethoxysilane as the standard reaction. Once again it was observed that with gold nanoparticles show good catalytic activity when more reactive 4-iodoarenes were used. The reaction of 4-iodoacetophenone and phenyltrimethoxysilane was chosen as the standard reaction and the effect of various parameters on this reaction was studied (Scheme 4.4).

SCHEME 4.4: The Hiyama cross-coupling reaction of 4-iodoacetophenone with phenyltrimethoxysilane catalyzed by resin-AuNPs

\[
\begin{align*}
\text{Condition:} & \quad 4\text{-iodoacetophenone (1.0 mmol), phenyltrimethoxysilane (1.5 mmol), NaOH (4.0 mmol, 4M 1 mL), EtOH (3 mL), and resin-AuNPs catalyst} \\
\end{align*}
\]

4.3.2.1 Effect of base

Nature of the base and its quantity has a great effect on the yield of the biphenyl. On the basis of earlier studies only NaOH was tried as base and it gave satisfactory results at a conc. of four mmol. The results are shown in Fig. 4.8.

Figure 4.8. Effect of Conc. of NaOH on the yield of standard Hiyama reaction
4.3.2.2 Effect of catalyst concentration

The catalytic activity of both the nanoparticle systems was investigated by varying the amount of catalyst while keeping the other parameters constant. The results are shown in Fig. 4.9. It was observed that 200 mg resin (≈ 0.0006 mmol of Au, 0.06 mol% with respect to aryl halide) was sufficient for completing the reaction. Using the obtained result, we calculated the, TON and TOF (h⁻¹) values which were found to be 1,666 and 10,036 respectively.

![Graph showing the effect of catalyst concentration on yield.](image)

**Figure 4.9.** Effect of resin-AuNPs catalyst concentration on the yield (GC determined) of 4-iodoacetophenone in Hiyama reactions

4.3.2.3 Effect of solvent

A mixture of ethanol water was in the ratio of 2:1 gave, quantitative yields.

4.3.2.4 Effect of time

The kinetics of reaction was studied by taking TLC of the reaction mixture of different interval of time and confirmed by the GC-MS at the end of reaction. It was observed that after 10 min (Fig. 4.10) the peak for 4-iodoacetophenone disappeared completely and 4-acetyl biphenyl was identified as the sole coupling product by its mass spectrum (See appendix).
4.3.2.5 Leaching test or hot filtration test

To probe the leaching of the catalyst, hot filtration test was performed. The reaction between 4-iodoacetophenone and phenyltrimethoxysilane was stopped after 2 min and the resin was removed from the hot reaction mixture by filtration and the filtrate was monitored for continued activity. The results indicate (Fig. 4.11) that the reaction did not proceed after the removal of the catalyst. Additionally in the standard reaction mixture, the solvent was evaporated and the residue was analyzed for the presence of gold by ICP-AES. Au could not be estimated in the solution. The absence of leaching as indicated by the hot filtration test points toward the heterogeneous nature of catalysis.

4.3.2.6 Recyclability of the catalyst

Resin-AuNPs catalyst was found to have good recyclability in Hiyama cross-coupling reaction. At the completion of the reaction, the catalyst

Figure 4.10. Time course of Hiyama reaction between 4-Iodoacetophenone and phenyltrimethoxysilane

Figure 4.11. Time course of the Hiyama reaction between 4-iodoacetophenone and phenyltrimethoxysilane (standard run) and after hot filtration of the resin
was recovered by simple filtration. The resin beads were treated as usual and reused. The recovered catalyst was employed in the next run with further addition of substrates in appropriate amount under optimum reaction conditions. The catalytic activity of various circles is shown in Fig. 4.12.

![Figure 4.12](image.png)

**Figure 4.12.** Recycling efficiency of resin-AuNPs in Hiyama coupling reaction

### 4.3.2.7 Reaction with aryl halides

Hiyama reaction of aryl halides with phenyltrimethoxysilane, which is predominately catalyzed by palladium (Pd) catalysts, is a powerful and convenient synthetic method for the generation of biaryl in organic chemistry. We have for the first time reported AuNPs catalyzed Hiyama reaction. We carried out Hiyama cross-coupling with other substituted iodobenzenes containing both electron withdrawing and electron releasing groups. The results are summarized in Table 4.4. A wide range of substituents, which include -CH₃, -CHO, -OCH₃, -NO₂, and -COCH₃, were compatible with this procedure. In all the cases very high conversion of iodobenzenes was observed in short reaction times. Bromobenzene and chlorobenzene were also used for coupling with phenyltrimethoxysilane (entries 9 and 10). Their reactivities were however, found to be lower than that of iodobenzene. This decrease may be attributed to the differences in the strengths of C-I bond, C-Br bond and C-Cl bond. This reaction confirms that order of reactivity for alkyl halides is I > Br > Cl. All the products were of high purity and were characterized by matching their ¹H NMR spectra with the reported data.
### Table 4.4: Resin-AuNPs catalyst Hiyama cross-coupling reaction of various aryl halides with phenyltrimethoxysilane

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aryl halide</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Iodobenzene</td>
<td><img src="image" alt="Iodobenzene" /></td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>4-iodobenzaldehyde</td>
<td><img src="image" alt="4-Iodoaldehyde" /></td>
<td>10</td>
<td>92</td>
</tr>
<tr>
<td>3</td>
<td>4-iodonitrobenzene</td>
<td><img src="image" alt="4-Iodonitrobenzene" /></td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>4-iodoacetophenone</td>
<td><img src="image" alt="4-Iodoacetophenone" /></td>
<td>10</td>
<td>92</td>
</tr>
<tr>
<td>5</td>
<td>4-bromoanisole</td>
<td><img src="image" alt="4-Bromoanisole" /></td>
<td>10</td>
<td>92</td>
</tr>
<tr>
<td>6</td>
<td>2-iodoacetophenone</td>
<td><img src="image" alt="2-Iodoacetophenone" /></td>
<td>10</td>
<td>85</td>
</tr>
<tr>
<td>7</td>
<td>3-iodotoluene</td>
<td><img src="image" alt="3-Iodotoluene" /></td>
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<td>85</td>
</tr>
<tr>
<td>8</td>
<td>1-bromo-4-iodobenzene</td>
<td><img src="image" alt="1-Bromo-4-Iodobenzene" /></td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>9</td>
<td>Bromobenzene</td>
<td><img src="image" alt="Bromobenzene" /></td>
<td>14</td>
<td>60</td>
</tr>
<tr>
<td>10</td>
<td>Chlorobenzene</td>
<td><img src="image" alt="Chlorobenzene" /></td>
<td>14</td>
<td>35</td>
</tr>
</tbody>
</table>

**Conditions:** Aryl halide (1.0 mmol); phenyltrimethoxysilane (1.5 mmol); resin-AuNPs (200 mg); NaOH (4.0 mmol, 4 M 1 mL); EtOH (2.0 mL); (Microwave conditions, 110 °C, 100 w). *Isolated yields.*
4.4. Characterization of products

1. Biphenyl, Colorless solid; Reported mp 68.5-71 °C; Observed mp 69 °C; 
   \(^1\text{H NMR}\) \((\text{CDCl}_3 400 \text{ MHz})\) \(\delta 7.59 (d, J = 8.8 \text{ Hz}, 2H), 7.43 (d, J = 8.8 \text{ Hz}, 2H), 7.34 (d, J = 6.8 \text{ Hz}, 1H)\).

   \[
   \begin{array}{c}
   \text{C} \quad \text{C} \\
   \end{array}
   \]

2. 4-Biphenylcarbdehyde, Light yellow solid; Reported mp 57-60 °C; Observed mp 60 °C; \(^1\text{H NMR}\) \((\text{CDCl}_3 400 \text{ MHz})\) \(\delta 7.93 (d, J = 8.6 \text{ Hz}, 2H), 7.73 (d, J = 8.6 \text{ Hz}, 2H), 7.62 (d, J = 6.8 \text{ Hz}, 2H), 7.49-7.40 (m, 3H)\).

   \[
   \begin{array}{c}
   \text{C} \quad \text{CHO} \\
   \end{array}
   \]

3. 4-Nitrobiphenyl, Pale yellow solid; Reported mp 112-114 °C; Observed mp 114 °C; \(^1\text{H NMR}\) \((\text{CDCl}_3 400 \text{ MHz})\) \(\delta 8.26-8.32(m,2H), 7.70-7.75 (m, 2H), 7.61-7.65 (m, 2H), 7.42-7.54 (m, 3H)\).

   \[
   \begin{array}{c}
   \text{C} \quad \text{NO}_2 \\
   \end{array}
   \]

4. 4-Acetylbiphenyl, Colorless solid; Reported mp 118-123 °C; Observed mp 117 °C; \(^1\text{H NMR}\) \((\text{CDCl}_3 400 \text{ MHz})\) \(\delta 8.01-8.04 (d, 2H), 7.68(d, 2H) 7.61-7.63 (d, 2H), 7.44 (t, 2H), 7.38-7.41 (tt, 1H), 2.64 (s, 3H). m/z 181, 152, 127, 91 and 76.

   \[
   \begin{array}{c}
   \text{C} \quad \text{CHO} \\
   \end{array}
   \]

5. 4-Methoxybiphenyl, Colorless solid; Reported mp 86-90 °C; Observed mp 89 °C; \(^1\text{H NMR}\) \((\text{CDCl}_3 400 \text{ MHz})\) \(\delta 7.51-7.56 (m, 4H), 7.39 - 7.43 (m, 2H), 7.28 - 7.3 (t, 1H), 6.96 - 6.99 (m, 2H), 3.84 (s, 3H). m/z 184, 169, 153, 141, 139, and 115.

   \[
   \begin{array}{c}
   \text{C} \quad \text{OCH}_3 \\
   \end{array}
   \]

6. 4-Phenyl acetanilide, Colorless solid; Reported mp 172 °C; Observed mp 170 °C; \(^1\text{H NMR}\) \((\text{CDCl}_3 400 \text{ MHz})\) \(\delta 8.2(s, 1H) 7.49-7.58 (m, 4H), 7.38-7.45 (m, 4H), 7.30-7.34 (t, 1H), 2.15 (s, 3H). m/z 211, 169, 152, 139 and 115.

   \[
   \begin{array}{c}
   \text{C} \quad \text{NHCOCH}_3 \\
   \end{array}
   \]
7. **2-Acetyl biphenyl**, Yellow Liquid; Reported bp 337 °C; Observed bp 335 °C; $^1$H NMR: (CDCl$_3$ 400 MHz) $\delta$ 7.53-7.55 (d, 1H), 7.45-7.51 (m, 1H), 7.36-7.43 (m, 5H), 7.31-7.33 (m, 2H), 1.99 (s, 3H).

8. **3-Methyl biphenyl**, Colorless Liquid; Reported bp 272 °C; Observed bp 270 °C; $^1$H NMR: (CDCl$_3$ 400 MHz) $\delta$ 7.56-7.58 (d, 2H), 7.37-7.43 (m, 4H), 7.33 (m, 2H), 7.11 (d, 1H), 2.41 (s, 3H).

9. **2-phenyl thiophene**, Semi Solid; Reported bp 256 °C; Observed bp 255 °C; $^1$H NMR: (CDCl$_3$ 400 MHz) $\delta$ 7.66-7.68 (d, 2H), 7.29-7.39 (m, 5H), 7.07-7.09 (dd, 1H).

10. **Terphenyl**, Colorless Solid; Reported mp 212-213 °C; Observed mp 213 °C; $^1$H NMR: (CDCl$_3$ 400 MHz) $\delta$ 7.62 (s, 4H), 7.56-7.58 (d, 4H), 7.36-7.42 (t, 4H), 7.28-7.32 (t, 2H).

11. **4-Bromobiphenyl**, Colorless Solid; Reported mp 82-86 °C; Observed mp 84 °C; $^1$H NMR: (CDCl$_3$ 400 MHz) $\delta$ 7.49-7.46 (m, 4H), 7.14-7.19 (m, 5H).
4.5. Conclusion

The role of the microwave synthesis is increasing day by day. To the best of our knowledge, this is the first study of Hiyama cross-coupling reaction under microwave heating using resin supported palladium and gold nanoparticles. The substrates show significant increase in reactivity and reduction in reaction times under the microwave irradiation conditions. The significant improvements offered by the present method are: operational simplicity, general applicability, recyclability and the absence of hazardous organic solvents, fluoride activators, phosphine ligands, surfactants, etc. This can contribute to the development of green strategy for the synthesis of biaryls.
CHAPTER 4

Hiyama Reaction

4.6. References:

Supported Palladium Nanoparticles Catalyzed Ligand-Free Mizoroki-Heck Coupling Reaction