4.1 Introduction

In the past four decades, after the first report in 1965, much attention has been devoted to the Huisgen 1,3-dipolar cycloaddition reaction of organic azides with alkynes and the term “Click chemistry”, first introduced by Sharpless and co-workers in 2001, is now widely used for this reaction.\(^2,3\) Meldal\(^4\) and Sharpless\(^5\) have reported Cu(I)-catalyzed union of terminal alkynes and organic azides to give 1,4-disubstituted triazoles. Cu(I)-catalyzed cycloaddition of water insoluble aliphatic/aryl azides with alkynes at room temperature has been extensively reported.\(^6a-c\) Apart from the Cu complexes, Pd,\(^7\) and Ru\(^8a,b\) complexes have also been found to be efficient catalysts for the synthesis of 1,5-disubstituted triazoles. Cu(I)-zeolites\(^9a-c\) and Cu\(^{II}\)-hydrotalcite\(^10\) serve as efficient heterogeneous catalysts for Huisgen (3+2) cycloaddition reactions. Microwave (MW) irradiation\(^11\) and ultrasound (US) method\(^12\) accelerate the nanocopper catalyzed azide-alkyne cycloaddition reactions. The products of the reaction exhibit remarkably broad scope in the field of metal ion sensors,\(^13a,b\) as chelating agents\(^14\) and medicinal chemistry.\(^15a,b\)

Nanomaterials are of topical interest, because of their intriguing properties different from those of their corresponding bulk materials. Due to their unique properties, nanomaterials are employed in electronic, optical, catalytic, coating, medical and sensor applications.\(^16\) Metal nanoparticles are very attractive catalysts compared to bulk catalysts since they have a high surface to volume ratio and their surface atoms are very active.\(^17\) Numerous review articles highlight the use of many different types of organic and inorganic reactions of noble metal nanoparticles suspended in colloidal solutions as well as those adsorbed onto different supports as catalysts.\(^18a-d\) Copper, in the nanoform, is known for the past one decade to show fascinating catalytic activity for the various organic reactions.\(^19a-d\) Copper nanoparticles are of great interest in a broad technological arena including catalysis and energy conversion.\(^20,21\)

Copper is less expensive compared to Au, Ag, Pd, Pt, Ru and Rh which have been extensively used as catalysts for organic transformations. The size of the
nanocatalyst is of utmost importance in catalysis for providing highly active catalyst surface, which maximizes the reaction rates and minimizes consumption of the catalyst.\textsuperscript{19} The tunability of size and spacing, of metal nanoparticles with the polymer, polyethyleneimine (PEI) opens a new way to synthesize nanomaterials with controlled diameter and leading to the tuning of catalytic activity with the change of size of nanoparticles in the range 20-100 nm.\textsuperscript{22a-c} The capping layer of the CuNPs can be varied or modified, thus providing a unique possibility to control their surface and catalytic properties. We have synthesized the low cost CuNPs with a specific size, well defined surface composition, isolable and redispersable properties. Polyvinylpyrrolidone (PVP) and surfactant stabilized CuNPs\textsuperscript{23a,b} nanostructured CuO materials,\textsuperscript{24} Cu/C,\textsuperscript{25a,b} Cu/CuO,\textsuperscript{26} hetero bimetallic Cu-Ni/C\textsuperscript{27} and Cu/AlO(OH)\textsuperscript{28} have been widely employed as catalysts for “Click” reactions. The heterogeneous Cu/SiO\textsubscript{2} catalyst has been used as the active catalyst in hydroxylation of phenol using hydrogen peroxide\textsuperscript{29} and for the selective conversion of ethanol to acetaldehyde.\textsuperscript{30}

The formation of C-S bond represents a key step in the synthesis of many organic molecules that are of biological, pharmaceutical, and materials science interest.\textsuperscript{31a,b} For example, a large variety of aryl sulfides are in use for diverse clinical applications, particularly for the treatment of cancer\textsuperscript{32} and human immunodeficiency virus diseases\textsuperscript{33} and for photoinduced electron transfer reactions.\textsuperscript{34a-d} In recent years, transition metal nanoparticles catalyzed cross-coupling reaction of aryl halides with thiols has been developed into a versatile and efficient method for a variety of synthetic organic transformations.\textsuperscript{35a-d} In order to obtain high catalytic activity, metal nanoparticles are generally dispersed on support materials, which offer high thermal and chemical stabilities combined with a well-developed porous structure and high surface area, meeting the requirements for most applications.\textsuperscript{36} Nanoparticles can also be easily prepared and further functionalized, adding value to their use as support or catalyst. Depending on the chemical reactivity of the support, metal oxides can be classified as inert (e.g. SiO\textsubscript{2}) and reactive (e.g. CeO\textsubscript{2}) metal oxides. Among the metal oxides, SiO\textsubscript{2},\textsuperscript{37} Al\textsubscript{2}O\textsubscript{3},\textsuperscript{38} TiO\textsubscript{2},\textsuperscript{39} CeO\textsubscript{2}\textsuperscript{40} and ZrO\textsubscript{2}\textsuperscript{41} are the most commonly employed supports.
4.1.1 Copper nanoparticles based synthesis of 1,2,3-triazoles and C-S coupling reactions.

Unsupported CuNPs catalyzed 1,3-dipolar cycloaddition of terminal alkynes with azides are carried out under mild conditions, in short reaction times and in the absence of any stabilizing additive or ligand as shown in Scheme 4.1.\textsuperscript{19c}

\begin{equation}
\begin{array}{c}
  R_1-N_3 + R_2= & \xrightarrow{\text{CuNPs}} & R_1-N=N-N-R_2 \\
& \text{Et}_3N, \text{THF, 65°C} & \\
\end{array}
\end{equation}

\textit{Scheme 4.1 General conditions for the CuNPs catalyzed 1,3-dipolar cycloaddition of azides with terminal alkynes.}

Highly stable poly(N-vinyl-2-pyrrolidone) (PVP) protected CuNPs serve as effective catalyst for 1,3-dipolar cycloaddition reaction between terminal alkynes and azides to get 1,2,3-triazoles in excellent yields under mild reaction conditions (Scheme 4.2).\textsuperscript{23a}

\begin{equation}
\begin{array}{c}
  \text{Ph-N}_3 + \text{Ph-} & \xrightarrow{\text{Cu Nanoparticles in formamide}} & \text{Ph-N=N-N-Ph} \\
& \text{RT} & \\
\end{array}
\end{equation}

\textit{Scheme 4.2 Synthesis of the triazoles prepared using the CuNPs catalyzed cycloaddition reaction.}

The heterogeneous copper/carbon (Cu/C) catalyst has been developed as a one pot procedure for the synthesis of 1,2,3-triazole derivatives via the three-component coupling reaction between terminal alkynes, benzyl or alkyl halides, and sodium azides as shown in Scheme 4.3.\textsuperscript{25b}
Chapter IV

Scheme 4.3 The reaction of benzyl halide with terminal alkyne and sodium azide catalyzed by Cu/C in water at 100 °C.

Copper nanoparticles prepared in ionic liquids has been exploited for 1,3-dipolar cycloaddition between aryl and sugar based azides and terminal alkynes as a recyclable medium (Scheme 4.4).\(^{55}\)

Scheme 4.4 Copper nanoparticles catalyzed 1,3-dipolar cycloaddition in ionic liquid.

Sreedhar and coworkers\(^ {19b} \) have attempted the hetero-Michael addition of \( \alpha,\beta \)-unsaturated esters with thiols (Scheme 4.5). At room temperature, thiophenol is introduced at the \( \beta \)-position of different acrylates with ease to afford the corresponding Michael adducts in good yields.

Scheme 4.5 Hetero-Michael addition of thiols to \( \alpha,\beta \)-unsaturated compounds.

Simple and efficient ligand free CuNPs catalyzed C-S bond formation in excellent yields under microwave irradiation for 5-7 mins is shown in Scheme 4.6.\(^ {35b,e} \)
Scheme 4.6 Condensation of aryl iodides with thiols using nano copper under microwave irradiation in the presence of a base.

An efficient ligand-free C-S cross-coupling of aryl halides with aromatic/alkyl thiols has been developed using a catalytic amount of nanocrystalline indium oxide as a recyclable catalyst with KOH as the base in DMSO at 135 °C as shown in Scheme 4.7. A variety of aryl sulfides can be synthesized in excellent yields utilizing this protocol.\textsuperscript{35c}

Scheme 4.7 Nano In$_2$O$_3$ catalyzed C-S cross coupling of iodobenzene with different sulfur sources.

Alumina supported copper efficiently catalyzes the S-arylation of aromatic, hetero aromatic and aliphatic thiols with aryl as well as hetero aryl halides under aerobic, ligand-free conditions (Scheme 4.8).\textsuperscript{35d}

Scheme 4.8 Cross-coupling of aryl halides and thiols.

CuO\textsuperscript{33a} and CuO on mesoporous silica\textsuperscript{63} catalyzed the C-S cross coupling of aryl and alkyl thiols with iodobenzene in excellent yields as shown in Scheme 4.9.
Scheme 4.9 CuO on mesoporous silica-catalyzed S-arylation of aryl iodides with thiols.

The goal of this work is the development of new, highly efficient catalyst systems for the cycloaddition and C-S coupling reactions using copper nanocatalysts which can be recycled and reused several times with little loss of their catalytic activity. The catalytic activity of nano Cu/SiO$_2$ (Catalyst II) for the 1,3-dipolar cycloaddition and C-S coupling reactions as detailed in Scheme 4.10 is investigated and presented in this chapter.

Scheme 4.10 Synthesis of 1,2,3-triazoles and thioethers using catalyst II.

4.2 Experimental

4.2.1 Synthesis of silica supported PEI/CuNPs

Monodisperse spherical SiNPs are synthesized by following the Stöber method$^{42}$ from tetraethyl orthosilicate using liq.NH$_3$ as catalyst. The synthesis of amino surface-modified SiNPs is carried out using the literature procedure.$^{19b,43a,b}$ The PEI stabilized CuNPs are prepared by the method of Pulkkinen et al.$^{44}$ In a typical synthesis, 2.4 g (2 mmol) of PEI is dissolved in 150 mL of water. A sample of 269 mg (2.0 mmol) of CuCl$_2$ is mixed with 757 mg (20.0 mmol) of NaBH$_4$
carefully and degassed with nitrogen for about 30 min. The reaction mixture is agitated to obtain a homogeneous Cu/PEI solution under deaerated condition. The growth of CuNPs is monitored using UV-vis absorption spectroscopy. Amine modified SiO$_2$ (100 mg) is added to CuNPs by stirring for 30 min and sonicated for 45 min. Dark brown colored PEI/CuNPs are bound on the surface of SiNPs with elapsing of reaction time, and the reaction proceeded for 2.5 h. The Cu/SiO$_2$ nanocatalyst is referred to as catalyst II. Finally, the particles are washed with ethanol, centrifuged and dried under vacuum. The entire synthetic procedure is given in Scheme 4.11. In the absence of a suitable support, metal particles aggregate, have reduced surface area and restricted control over particle size.

Scheme 4.11 Schematic representation of four-step process for the synthesis of catalyst II.
4.2.2 Synthesis of 1,2,3-triazoles

In our initial exploration, for the synthesis of 1,2,3-triazoles the reaction of benzyl bromide with sodium azide and phenylacetylene is chosen as a model reaction. Alkyl azides are synthesized at room temperature from the corresponding bromides by nucleophilic substitution with sodium azide in DMSO. First the alkyl halide and sodium azide with 1:1.2 molar ratio are suspended on dry DMSO with vigorous stirring for 10-15 min at room temperature, 1.2 mole ratio of phenylacetylene and 0.05 mol % of catalyst II are added and stirring continued to get the corresponding 1,2,3-triazoles in good yield. The product formed is then extracted with ether and dried under reduced pressure to obtain the desired triazole as a white crystalline solid. The results are collected in Table 4.1.

Table 4.1 Yields of the 1,2,3-triazoles prepared using the catalyst II[a]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Azides</th>
<th>Alkynes</th>
<th>Products</th>
<th>Time (min)</th>
<th>Yield (%)^[b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td><img src="image1.png" alt="image" /></td>
<td><img src="image2.png" alt="image" /></td>
<td>15</td>
<td>98^[e]</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3.png" alt="image" /></td>
<td><img src="image4.png" alt="image" /></td>
<td><img src="image5.png" alt="image" /></td>
<td>10</td>
<td>98,92^[d], 89^[e], 0^[f]</td>
</tr>
<tr>
<td>3</td>
<td><img src="image6.png" alt="image" /></td>
<td><img src="image7.png" alt="image" /></td>
<td><img src="image8.png" alt="image" /></td>
<td>25</td>
<td>97</td>
</tr>
<tr>
<td>4</td>
<td>CH₃-N₃</td>
<td><img src="image9.png" alt="image" /></td>
<td><img src="image10.png" alt="image" /></td>
<td>20</td>
<td>92</td>
</tr>
<tr>
<td>5</td>
<td>C₃H₇-N₃</td>
<td><img src="image11.png" alt="image" /></td>
<td><img src="image12.png" alt="image" /></td>
<td>35</td>
<td>83</td>
</tr>
<tr>
<td>6</td>
<td>C₆H₁₁-N₃</td>
<td><img src="image13.png" alt="image" /></td>
<td><img src="image14.png" alt="image" /></td>
<td>30</td>
<td>95</td>
</tr>
<tr>
<td>No.</td>
<td>Formula</td>
<td>Structure</td>
<td>Yield 1</td>
<td>Yield 2</td>
<td></td>
</tr>
<tr>
<td>-----</td>
<td>-----------</td>
<td>-----------</td>
<td>---------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>C$<em>{10}$H$</em>{21}$N$_3$</td>
<td><img src="image1.png" alt="Structure" /></td>
<td>35</td>
<td>95</td>
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</tr>
<tr>
<td>8</td>
<td>C$<em>{12}$H$</em>{25}$N$_3$</td>
<td><img src="image2.png" alt="Structure" /></td>
<td>30</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>C$<em>{16}$H$</em>{33}$N$_3$</td>
<td><img src="image3.png" alt="Structure" /></td>
<td>35</td>
<td>62</td>
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</tr>
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<td>10</td>
<td>N$<em>5$C$</em>{10}$H$_{20}$N$_3$</td>
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<td></td>
<td><img src="image7.png" alt="Structure" /></td>
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<td>95</td>
<td></td>
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<tr>
<td>14</td>
<td>C$_3$H$_7$N$_3$</td>
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<td>90</td>
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<tr>
<td>15</td>
<td>C$<em>6$H$</em>{13}$N$_3$</td>
<td><img src="image9.png" alt="Structure" /></td>
<td>50</td>
<td>94</td>
<td></td>
</tr>
</tbody>
</table>

[a] Reaction conditions: Azide (1.2 mmol), aryl or alkyl halide (1.0 mmol) and alkyne (1.2 mmol), catalyst II (0.05 mol%) and DMSO (5.0 mL) at RT.

[b] Yield refer to column chromatography yield.

c] Alkyne 2.4 mmol used in DMSO at 15 min.

d],[e] Yield after 2$^{nd}$ and 3$^{nd}$ cycle.

g] Silica, 3h;

[h] 1,10-Dibromodecane (1.0 mmol), azide (2.2 mmol) and alkyne (2.4 mmol) were used.
In addition, the great difficulty in purification of the product when the reaction is incomplete is that some alkyl azides decompose rapidly with danger of explosion or distilling. Furthermore, alkyl azides, generally, have boiling temperature adjacent to the corresponding alkyl bromides. Thus, we decided to initiate a systematic study of the versatility of the nucleophilic substitution of bromide utilizing NaN\textsubscript{3} in DMSO at ambient temperature. Herein, we discuss the successful preparation, in high yield of various alkyl azides in excellent purity.

4.2.3 C-S coupling reaction

A stirred solution of aryl or alkyl thiol (1.0 mmol) is mixed with aryl halide (1.1 mmol), catalyst II (1.5 mol%), and KOH (1.5 mmol) in DMSO (3.0 mL). The solution is heated at 110 °C in N\textsubscript{2} atmosphere. The progress of the reaction is monitored by TLC. The reaction mixture is then cooled to room temperature and treated with diethyl ether (10 mL). The aqueous layer is separated, extracted with diethyl ether (2×5 mL), and dried over anhydrous Na\textsubscript{2}SO\textsubscript{4}. The combined organic extracts are concentrated in vacuum, and the resulting product is purified by column chromatography on silica gel with a mixture of ethyl acetate and n-hexane (2:8) as eluent to afford analytically pure C-S cross-coupling products. Aryl and alkyl sulfides are isolated in good yields reported in Table 4.2. Products are characterized using \textsuperscript{1}H-NMR and \textsuperscript{13}C-NMR spectra and the spectra are given in Section 4.6.

Table 4.2 Cross-coupling reactions of aryl/alkyl thiols with aryl halides

<table>
<thead>
<tr>
<th>Entry</th>
<th>Halides</th>
<th>Thiols</th>
<th>Products</th>
<th>Time (h)</th>
<th>Yield (%)\textsuperscript{[b]}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="image" /></td>
<td><img src="image2" alt="image" /></td>
<td><img src="image3" alt="image" /></td>
<td>9</td>
<td>96, 96\textsuperscript{[a]}, 82\textsuperscript{[b]}</td>
</tr>
<tr>
<td>2</td>
<td><img src="image4" alt="image" /></td>
<td><img src="image5" alt="image" /></td>
<td><img src="image6" alt="image" /></td>
<td>12</td>
<td>91</td>
</tr>
<tr>
<td>3</td>
<td><img src="image7" alt="image" /></td>
<td><img src="image8" alt="image" /></td>
<td><img src="image9" alt="image" /></td>
<td>12</td>
<td>89</td>
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</tbody>
</table>
Chapter IV

<table>
<thead>
<tr>
<th>No.</th>
<th>Thiol</th>
<th>Aryl Halide</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>HCHO</td>
<td>HCHO</td>
<td></td>
<td>10 92</td>
</tr>
<tr>
<td>5</td>
<td>HCHO</td>
<td>HCHO</td>
<td></td>
<td>11 90 (83)&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td>NO₂</td>
<td>HCHO</td>
<td></td>
<td>10 87 (75)&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>7</td>
<td>H₂O₂</td>
<td>HCHO</td>
<td></td>
<td>12 70 (65)&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>8</td>
<td>HCHO</td>
<td>HCHO</td>
<td></td>
<td>11 85</td>
</tr>
<tr>
<td>9</td>
<td>HCHO</td>
<td>HCHO</td>
<td></td>
<td>11 88 (80)&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>10</td>
<td>C₂H₅-SH</td>
<td></td>
<td></td>
<td>11 91</td>
</tr>
<tr>
<td>11</td>
<td>C₁₂H₂₅-SH</td>
<td></td>
<td></td>
<td>12 92</td>
</tr>
<tr>
<td>12</td>
<td>C₁₂H₂₅-SH</td>
<td></td>
<td></td>
<td>11 90 (85)&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

[a] Reaction conditions: Thiol (1.2 mmol), aryl halide (1.0 mmol) catalyst II (1.5 mol%) KOH (1.5 mmol) and DMSO (3.0 mL) at 110°C, under N₂ atmosphere.

[b] Yields of isolated products.

[c], [d] Isolated yields after 2<sup>nd</sup> and 3<sup>rd</sup> cycle.

[e] 4-Bromo acetophenone is used.
4.3 Results and discussion

Unsupported or in the absence of surface capping agents and stabilizers, the surface atoms of metallic nanoparticles with their typically high surface energy become susceptible to aggregation into bulk material. To overcome this problem, catalytic nanoparticles are immobilized on solid supports. Surface coverage by a polymer is advantageous because in addition to stabilizing and protecting the nanoparticles, polymers offer unique possibilities for modifying both the environment around catalytic sites and access to these sites. Hence the protective polymer not only influences particle size and morphology but can also have a tremendous influence on catalytic activity and selectivity. According to Scheme 4.11 we have used the four step process to synthesize the PEI/Cu NPs supported onto the SiO$_2$ surface: (1) synthesis of the SiNPs, (2) amine functionalization of the SiO$_2$ surface, (3) synthesis of the PEI/CuNPs, and (4) attachment of the PEI/CuNPs onto the amine functionalized SiO$_2$ surface. In the presence of the reducing agent the Cu$^{2+}$ is reduced to Cu$^{0}$ on the polymer (Scheme 4.11), preventing the agglomeration of the metallic nanoparticles. PEI/CuNPs are covalently attached to the functionalized SiO$_2$ colloids via the Cu-N bond. The silica colloids are functionalized with APTES which is confirmed by FT-IR spectroscopy. In this section, we examine the silica nanosphere surface properties and demonstrate the presence of surface silanol groups (-SiOH) which can be used to sequester active Cu sites for the selective formation of 1,2,3-triazoles and thioethers.

4.3.1 XRD studies

X-Ray powder diffraction (XRD) data (Figure 4.1) are used for the identification and quantification of the crystalline phases, along with the measurement of the crystallite size. XRD peaks for SiO$_2$ are not observed and thus, could be attributed to the amorphous nature. XRD analysis of the catalyst II reveals its metallic nature (Figure 4.1). All the samples exhibit face centered cubic (fcc) structure.
Chapter IV

Figure 4.1 XRD pattern of catalyst II.

XRD patterns are analyzed to determine peak intensity, position and width. Full width at half-maximum (FWHM) data are used with the Scherrer’s formula to determine mean particle size. All Bragg’s reflections at $2\theta = 43.5$, 50.6, and 74.3 can be indexed as the [111], [200] and [220] planes of copper. It obviously indicates that CuNPs are in Cu(0) state not as oxidized species (CuO, Cu$_2$O) and no impurity diffraction peaks are detected. After the reaction is completed, the recovered catalyst II is checked with its XRD analysis and the XRD patterns are given in Figure 4.2.

Figure 4.2 XRD patterns of catalyst II before (a) and after (b) the reaction.

This is to be expected for small CuNPs and more so for those embedded within silica shell. Nevertheless, the diffraction patterns clearly indicated the presence of Cu and no significant copper oxide phase.
4.3.2 HRTEM analysis

HRTEM images of monodisperse spheres of bare SiNPs with a smooth surface and a homogeneous size are shown in Figure 4.3. All the particles are spherical and the diameter of the particles depends on the preparation conditions (TEOS concentration and reaction time).

Figure 4.3 HRTEM images (a) SiNPs and (b) amino functionalized SiNPs.

The measured average size of the bare SiO$_2$ spheres obtained without addition of CuNPs is 180 ± 30 nm. Figure 4.4 shows the HRTEM image of catalyst II nanospheres prepared by using modified Stöber method and the size of CuNPs is about 5 ± 2 nm. The HRTEM measurements show that SiNPs are homogeneously attached with CuNPs (Figure 4.4a). The inset in Figure 4.4d shows a typical selected-area electron diffraction pattern of the CuNPs which reveals the characteristic [111], [200] and [220] diffraction peaks of metallic copper, indicating the formation of crystallized state in the face centered cubic (fcc) structure$^{50}$ in accordance with the JCPDS file no 04-836.
Figure 4.4 HRTEM photographs of catalyst II. Here a, b and d correspond to the different images of the representative catalyst II; Figure 4.4c shows EDX analysis of catalyst II and inset 4.4d show SEAD spectrum of catalyst II.

After the reaction is completed, the recovered catalyst is checked with its HRTEM image given in Figure 4.5. Interestingly it is observed that the shape and size of the particles remain unchanged and support the proposal that the morphology of the catalyst remains the same even in the used condition.
Figure 4.5 HRTEM images (a) before and (b) after the third cycle.

Analysis through energy dispersive X-ray (EDX) spectrometers confirmed the presence of elemental copper and silicon signals from the catalyst II (Figure 4.4c). The vertical axis displays the number of X-ray counts whilst the horizontal axis displays energy in keV. Identification lines for the major emission energies of Si metal from the catalyst II are displayed and these correspond with peaks in the spectrum, thus giving confidence that copper has been correctly identified. These results support our conclusion that SiO$_2$ particles construct the surface layer of the CuNPs.

4.3.3 BET surface area studies

$N_2$ adsorption-desorption isotherms of the samples at 77 K are obtained on a Micromeritics ASAP 2020 instrument. Before $N_2$ adsorption, catalyst samples are evacuated for 4 h at 350 °C. The Brunauer-Emmett-Teller (BET) equation is used to calculate the surface areas, pore volumes and pore sizes estimated at a relative pressure of 0.99. The Barrett-Joyner-Halenda (BJH) method applied to the desorption isotherm is used to determine the pore diameter distribution.$^{50b,c}$ The surface area of the synthesized silica is found to be 115.9 m$^2$/g, when the CuNPs are loaded on the surface of pure SiO$_2$, the BET surface area and the pore volume decreased from 115.9 to 104.41 m$^2$/g and 0.60 to 0.22 cm$^3$/g respectively. The $N_2$ sorption isotherms
of the calcined pure SiO$_2$ and Cu/SiO$_2$ catalysts are presented in Figures 4.6a and 4.6b. It could be seen that pure SiO$_2$ and Cu/SiO$_2$ exhibit Langmuir type IV isotherms. A sharp inflection of the adsorption and desorption isotherms, in particular around P/Po = 0.9728 (for N$_2$ at 77 K), indicates a forced closure of the hysteresis loop. In Figure 4.6a the inset figure shows a sharp inflection of the adsorption and desorption isotherm in the P/Po range 0.8-1.0 (dotted square) emphasizing the TSE (tensile strength effect) at P/Po = 0.97.

Figure 4.6 N$_2$ adsorption-desorption isotherms (a) amine functionalized SiO$_2$ and (b) catalyst II (Cu/SiO$_2$).

The (4V/A) term used in the estimation of pore average sizes corresponds to the assumed cylindrical model of pores. However, this assumption of cylindrical model of pores is also cited in BJH estimates of pore volume and surface area distributions. Figure 4.6b shows the adsorption and desorption isotherm value of catalyst II at P/Po = 0.9730. According to these measurements, the BET surface area, Langmuir surface area, pore volume and pore diameter are calculated and the data are given in Table.4.3.
### Table 4.3 Physicochemical properties of the SiO₂ and catalyst II.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Cu content (wt%)</th>
<th>BET surface area (m²/g)</th>
<th>Langmuir surface area (m²/g)</th>
<th>t-Plot external surface area (m²/g)</th>
<th>Average pore diameter (nm)</th>
<th>Pore volume (cm³/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SiO₂</td>
<td>-</td>
<td>110.8</td>
<td>186.9</td>
<td>126.9</td>
<td>33.0</td>
<td>0.60</td>
</tr>
<tr>
<td>Catalyst II</td>
<td>1.5</td>
<td>104.1</td>
<td>168.6</td>
<td>115.5</td>
<td>27.6</td>
<td>0.21</td>
</tr>
</tbody>
</table>

#### 4.3.4 SEM analysis

The scanning electron microscopy (SEM) images of SiNPs synthesized by Stöber method are shown in Figure 4.7. The silica particles show very uniform spherical morphology and monodisperse distribution. The mean diameter of these particles is ∼180 nm with very little distribution in particle size as given in the Figure 4.7.

![Figure 4.7 SEM images of the pure SiNPs in different magnifications (a) × 2500 and (b) × 40000.](image)

#### 4.3.5 AFM analysis

AFM method is used to provide an independent and quantitative measurement of catalyst II particle size in the sol. The objective is to image the
individual particles of catalyst II on a flat substrate using tapping mode (contact mode) AFM technique. The size and morphology of the catalyst II are clearly seen from the two-dimensional (2-D) and three-dimensional (3-D) AFM images given in Figure 4.8.

![AFM images of catalyst II](image)

**Figure 4.8 AFM images of catalyst II (a) in two-dimension (2-D) and (b) three-dimension (3-D).**

By achieving a good dispersion of the nanoparticles it is possible to image them individually using AFM. This technique enables measuring the size of the particle, considering the particle height rather than its width because the particle may be distorted by the AFM tip geometry. Individual Cu/SiO$_2$ particles are clearly visible in this image. The diameter of each particle is estimated by examining the height profile or bearing ratio mapped by the AFM tip. Spherical particles are assumed, and the height measured by AFM is taken as the particle diameter. The average size of the copper nanostructures is estimated to be 5-6 nm according to the voltage profile of AFM images.

### 4.3.6 UV-vis absorption spectral analysis

**Figure 4.9** shows the slow reduction of copper ions leading to the formation of CuNPs, (a) Cu$^{2+}$ solution (b) mixture of Cu$^{2+}$ and PEI solution and (c) after the addition of NaBH$_4$. The SPR (Surface Plasma Resonance) peak appeared at 583 nm.$^{51}$ The Cu(0) nanoparticles supported on SiNPs are extremely stable for
several months in N₂ atmosphere. There is a substantial colour change during the reduction of copper salt and the details are shown in Figure 4.9.

![Absorption Spectra](image)

**Figure 4.9** UV-visible absorption spectral changes during the formation of CuNPs and inset figure shows the SPR band (583 nm) of CuNPs.

### 4.3.7 FT-IR spectral analysis

FT-IR spectra of pure SiO₂, amino modified SiO₂ and catalyst II are recorded in the regions 2700-3500 and 1300-2000 cm⁻¹. The FT-IR spectral assignments of dried and calcined samples of pure SiO₂, amino modified SiO₂ (NH₂-SiO₂) and copper coated SiO₂ (catalyst II) are shown in **Figure 4.10** and the relevant data collected in **Table 4.4**.
Table 4.4 FT-IR Peak assignments and wavenumbers for SiO$_2$, NH$_2$-SiO$_2$ and catalyst II.

<table>
<thead>
<tr>
<th></th>
<th><strong>SiO$_2$</strong></th>
<th><strong>NH$_2$-SiO$_2$</strong></th>
<th><strong>Catalyst II</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Assignment</td>
<td>cm$^{-1}$</td>
<td>Assignment</td>
<td>Assignment</td>
</tr>
<tr>
<td>$\nu$(O-H)</td>
<td>3441</td>
<td>$\nu$(O-H)</td>
<td>$\nu$(O-H)</td>
</tr>
<tr>
<td>$\nu$as(Si-O-Si)</td>
<td>1103</td>
<td>$\nu$as(Si-O-Si)</td>
<td>$\nu$as(Si-O-Si)</td>
</tr>
<tr>
<td>$\nu$as(Si-O-Si)</td>
<td>800</td>
<td>$\nu$as(Si-O-Si)</td>
<td>$\nu$as(Si-O-Si)</td>
</tr>
<tr>
<td>$\delta$(Si-O-Si)</td>
<td>427</td>
<td>$\delta$(Si-O-Si)</td>
<td>$\delta$(Si-O-Si)</td>
</tr>
<tr>
<td>$\nu$(Si-O-(H))</td>
<td>954</td>
<td>$\nu$(Si-O-(H))</td>
<td>$\nu$(Si-O-(H))</td>
</tr>
<tr>
<td>$\nu$(C-H) of-CH$_2$-</td>
<td>-</td>
<td>$\nu$(C-H) of-CH$_2$-</td>
<td>2856</td>
</tr>
<tr>
<td>$\delta$(NH) of the NH$_2$</td>
<td>-</td>
<td>$\delta$(NH) of the NH$_2$</td>
<td>1544</td>
</tr>
</tbody>
</table>

The 2929 and 2856 cm$^{-1}$ bands are assigned to $\nu_{CH}$ of the -CH$_2$ groups, and the bands at 1544 cm$^{-1}$ and 1542 cm$^{-1}$ to $\delta_{NH}$ of the -NH$_2$ groups, both of which are associated with amino modified SiO$_2$ and catalyst II skeleton respectively.

Figure 4.10 FT-IR spectra of (a) pure SiO$_2$, (b) pure NH$_2$-SiO$_2$ and (c) catalyst II.
The strong peaks at 1076 and 790 cm\(^{-1}\) are due respectively to \(\nu_{\text{asym}}(\text{Si-O})\) and \(\nu_{\text{sym}}(\text{Si-O})\) of the Cu/SiO\(_2\) skeleton.\(^{52a-c}\) Moreover, the presence of the amino groups confirms the formation of the amine-modified particles. The broad peak centered at 3400 cm\(^{-1}\) is an envelope of \(\nu_{\text{O-H}}\) for the adsorbed water, silanol groups, and \(\nu_{\text{N-H}}\) of the amino groups. It should be pointed out here that the band corresponding to the Si-OH group appears at 960 cm\(^{-1}\) as a shoulder (arrow) of the 1076 cm\(^{-1}\) Si-O-Si skeleton peak, and is little weaker than that found ever in the conventional SiO\(_2\) particles that exhibit a clear and well-defined peak of the Si-OH groups.

4.3.8 TGA analysis

The synthesized catalyst II is initially examined by thermogravimetric analysis (TGA) under nitrogen atmosphere. Identification of the evolved gas fragments or decomposition components, confirms the presence of the spacer 3-aminopropylsilane (APTES) on the synthesized catalyst.\(^{25b}\) The thermogravimetric profile of the catalyst II shows removal of small amount of water and APTES as two-step degradation process given in Figure 4.11.

![Figure 4.11 TGA curve of catalyst A under N\(_2\) atmosphere at heating rate of 20 °C min\(^{-1}\)](image-url)
Pulkkinen *et al.* \(^{44}\) reported the TGA data which also show that the CuNPs carrying a trace amount of protecting agent (PEI) is decomposed at lower temperature than the free PEI. The products contain 12-15 wt % of volatile components, regardless of the reaction time. This indicates that longer synthesis times will not increase the amount of protecting agent left on the particle.

### 4.3.9 Optimization of Click reaction condition

To optimize the reaction conditions, benzyl bromide, phenyl acetylene and NaN\(_3\) are selected as the test reagents for the synthesis of 1-benzyl-4-phenyl-1,2,3-triazole to examine the effect of catalyst II (0.05 mol%), at room temperature. The results are evaluated qualitatively using TLC (*Table 4.1*). To get the maximum yield the best condition is that the reagents, catalyst A, phenyl acetylene, benzyl bromide and NaN\(_3\), have to be taken in the ratio 0.05:1.2:1.0:1.2 mmol at room temperature. The reaction is allowed to continue for 10 min using DMSO as solvent. Synthetic procedure for the synthesis of azides and their NMR spectra are given in the *Section 4.6*. An increase in the amount of catalyst II from 0.05 to 2.0 mol % has negligible effect on the efficiency of the reaction. Using these optimized conditions, the reaction of various terminal acetylenes (phenyl acetylene, 2-methylbut-3-yn-2-ol), benzyl/alkyl halides and NaN\(_3\) is investigated (*Scheme 4.1a*). It is found that all the reactions proceed smoothly to give the corresponding 1,4-disubstituted-1,2,3-triazoles in high yield 98% (*Table 4.1, entry 2*), which clearly indicate the generality and scope of the reaction with respect to terminal alkynes and halides. When phenyl acetylene (2.4 mmol) alone is added to catalyst II (0.05 mol %) it affords 1,4-diphenylbuta-1,3-diyne and 2,7-dimethylocta-3,5-diyne-2,7-diol as homocoupling products (*Table 4.1 entry 1 and 11*). Thus, this procedure can also be utilized for homocoupling reactions. The \(^1\)H and \(^{13}\)C-NMR spectra of homocoupling products are collected and given in the *Section 4.6*.
Chapter IV

4.3.10 Influence of different solvents on catalyst II catalyzed Click reaction

After stabilizing the optimum conditions for the reaction we turn our attention to investigate the effect of changing the solvent on the efficiency of the coupling reaction and the results are shown in Table 4.5.

Table 4.5 Influence of different solvents on catalyst II catalyzed Click reaction\(^{[a]}\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (min)</th>
<th>Yield (%)(^{[b]})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Toluene</td>
<td>60</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>EtOH</td>
<td>25</td>
<td>90</td>
</tr>
<tr>
<td>3</td>
<td>CH(_3)CN</td>
<td>50</td>
<td>60</td>
</tr>
<tr>
<td>4</td>
<td>CH(_2)Cl(_2)</td>
<td>90</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>H(_2)O</td>
<td>75</td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td>DMSO</td>
<td>10</td>
<td>98</td>
</tr>
<tr>
<td>7</td>
<td>Dioxane</td>
<td>85</td>
<td>38</td>
</tr>
</tbody>
</table>

\(^{[a]}\)The reaction condition: Phenyl acetylene (1.2 mmol), benzyl bromide (1.2 mmol), NaN\(_3\) (1.2 mmol), catalyst II (0.05 mol %) and DMSO (5.0 mL) at RT.

\(^{[b]}\)Yield refer to after column chromatography yield.

When the reaction is conducted in water, ethanol and dimethyl sulfoxide the yield of the products is good to excellent (85, 90 and 98%, respectively; Table 4.5, entries 2, 5 and 6). The use of toluene, acetonitrile, dichloromethane and dioxane as solvents leads to the lower yields of the products (Table 4.5, entries 1, 3, 4 and 7). During our optimization studies, various solvents are examined and it is found that the solvent plays a significant role in terms of reaction rate, isolated yield, and selectivity. The reaction of benzyl bromide with phenylacetylene and sodium azide in the presence of 0.05 mol% of catalyst II in DMSO, furnished the 1,4-disubstituted triazole product in 98% yield after stirring for 10 min at ambient temperature Table 4.1).
Chapter IV

The use of DMSO as the suitable solvent in this study deserves comments. Generally, benzyl bromide and phenylacetylene have poor solubility in water; it required more than 75 mins for the completion of the reaction in water at ambient temperature. However, our interest is to develop more efficient system having the high reactivity within a short reaction time to give good yields. The use of DMSO in Click coupling reactions results in an increase in the activity of catalyst II and the yield is 98%. In terms of the sufficient solubility of azide, alkyl/ aryl halides and alkynes also DMSO is a suitable medium. In order to show the efficiency of DMSO solvent system, the same reactions were also performed in EtOH (Table 4.5, entries 2 and 6) but it afforded 90% yield after 25 mins. Generally DMSO is a relatively inexpensive, stable and environmentally compatible solvent in organic and inorganic synthesis due to its specific chemical and physical properties. The advantage of DMSO as the solvent is attributed to: (i) it exerts sufficient interaction with the surface of the metal nanoparticles to effectively passivate and stabilize the nanoparticle dispersion as created within this solvent medium. (ii) DMSO acts as a stabilizer during the reaction, no precipitation/agglomeration occurs. (iii) Cu does not suffer from aerobic oxidation during the reaction at ambient temperature (DMSO is acting as an additional capping agent in this case). The points (i)-(iii) suggest that DMSO is a sound reaction medium/solvent for the synthesis of 1,2,3-triazoles, that meets contemporary demands for more benign condition. The other solvents do not possess this type of vital properties.

4.3.11 Comparison with other catalyst systems

In order to evaluate the efficiency of the different supporting material carrying copper nanocatalyst, we have compiled the data on the synthesis of 1,2,3-triazoles using copper catalysts and the data collected in Table 4.6.
Table 4.6 Comparison with other catalyst systems.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst[a]</th>
<th>Size (nm)</th>
<th>Mol (%)</th>
<th>Time (h)</th>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PVP-Cu²³⁷</td>
<td>10-35</td>
<td>5.0</td>
<td>20 min</td>
<td>Formamide</td>
<td>91</td>
</tr>
<tr>
<td>2</td>
<td>Cu nanoclusters²³ᵇ</td>
<td>1.6 - 2.1</td>
<td>0.01mmol</td>
<td>18</td>
<td>H₂O/t-BuOH</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>CuO²⁴</td>
<td>&gt; 20</td>
<td>5</td>
<td>3</td>
<td>H₂O/t-BuOH</td>
<td>98</td>
</tr>
<tr>
<td>4</td>
<td>Cu/C²⁵ᵇ</td>
<td>80-300</td>
<td>1</td>
<td>0.6</td>
<td>H2O²⁶</td>
<td>91</td>
</tr>
<tr>
<td>5</td>
<td>Cu/CuO²⁶</td>
<td>14</td>
<td>13-20</td>
<td>3-4</td>
<td>Toluene</td>
<td>95</td>
</tr>
<tr>
<td>6</td>
<td>Cu/AlO(OH)²⁸</td>
<td>5-8</td>
<td>6</td>
<td>6</td>
<td>n-hexane</td>
<td>94</td>
</tr>
<tr>
<td>7</td>
<td>Cu/Al₂O₃⁴⁵</td>
<td>&gt;100</td>
<td>10</td>
<td>3-8</td>
<td>H₂O</td>
<td>92</td>
</tr>
<tr>
<td>8</td>
<td>Cu nanopowder⁵⁴</td>
<td>50-60</td>
<td>10</td>
<td>2</td>
<td>H₂O/t-BuOH</td>
<td>90</td>
</tr>
<tr>
<td>9</td>
<td>CuNPs/IL⁵⁵</td>
<td>80-130</td>
<td>5.0</td>
<td>18 min</td>
<td>-</td>
<td>89</td>
</tr>
<tr>
<td>10</td>
<td>CuNPs/L⁵⁶</td>
<td>3.0 ± 1.5</td>
<td>10</td>
<td>10</td>
<td>THFᵇ</td>
<td>98</td>
</tr>
<tr>
<td>11</td>
<td>Pure SiO₂</td>
<td>&gt;100</td>
<td>0.05</td>
<td>3</td>
<td>DMSO</td>
<td>Traceᵈᵉ</td>
</tr>
<tr>
<td>12</td>
<td>NH₂-SiO₂</td>
<td>&gt;100</td>
<td>0.05</td>
<td>3</td>
<td>DMSO</td>
<td>25ᵉ</td>
</tr>
<tr>
<td>13</td>
<td>Catalyst II</td>
<td>5 ± 2</td>
<td>0.05</td>
<td>10</td>
<td>DMSO</td>
<td>98ᶠ</td>
</tr>
<tr>
<td>14</td>
<td>CuCl₂</td>
<td>-</td>
<td>0.05</td>
<td>3</td>
<td>DMSO</td>
<td>0ᶠ</td>
</tr>
<tr>
<td>15</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>10</td>
<td>DMSO</td>
<td>0ᵇ</td>
</tr>
</tbody>
</table>

[a]References.
[b],[c] Kept at 65 and 100⁰C.
[d-h] Reaction conditions as exemplified in the experimental procedure.

Where L= Ligand, IL= Ionic liquid

The data in Table 4.6 show that although the yields are comparable for many catalyst systems, and mol% and the size of CuNPs used in the present study are smallest and the selectivity is better than the other systems i.e., metal nanoparticles are very attractive catalysts compared to bulk catalytic materials due to their high surface-to-volume ratio. The data in Table 4.6 evidently indicate that the catalyst II is smaller in size compared to alumina supported CuNPs,⁴⁵ PVP capped CuNPs,²³ᵃ Cu(0) nanosized activated powder,⁵⁴ CuNPs in ionic liquids⁵⁵ and Cu/C²⁵ᵇ catalyst system. The novelty of this catalyst system is that a lesser quantity of catalyst (0.05 mol %) is needed compared to other catalyst systems reported.
Chapter IV

The additional advantage with the present system is that the reaction is conducted at room temperature but in the unsupported CuNPs\textsuperscript{25c, 56} and Cu/C\textsuperscript{24} the reaction conditions 65 and 100\textdegree{}C were maintained. In order to find the role of Cu/SiO\textsubscript{2} for the Huisgen 1,3-dipolar cycloaddition reaction, we have carried out the reaction in the presence of silica (SiO\textsubscript{2}), amino modified silica (SiO\textsubscript{2}-NH\textsubscript{2}), and CuCl\textsubscript{2} under the similar experimental conditions but we get lower yields and the results are summarized in Table 4.6. Thus, it is concluded that the heterogeneous catalyst II catalyzes the reaction efficiently and the corresponding triazole is obtained in high yield with low amount of catalyst.

4.3.12 The role of PEI as a stabilizer

PEI is a hydrophilic polymer with primary (25\%), secondary (50\%) and tertiary (25\%) amino groups and carries an overall positive charge in the neutral aqueous solution. Because of its abundant positive charge, it is widely used as the stabilizer for the CuNPs to achieve surface functionalization.\textsuperscript{57} It also stabilizes Ag, Au, and Pd metal nanoparticles\textsuperscript{58a-d} and semiconductor quantum dots (QDs).\textsuperscript{59} When NaBH\textsubscript{4} is added to CuCl\textsubscript{2} and PEI mixture, colloidal nucleation is achieved and the nanoparticles begin to grow. Under vigorous stirring, PEI diffused quickly to the colloids and is adsorbed on the surface of colloids because of the electrostatic interaction between positively charged PEI and small negatively charged CuNPs which results in the positively charged colloids. The high cationic charge density and the “steric” effect of PEI kept each nanoparticle apart which results in the formation of nanoparticles stable up to three months without any aggregation.

4.3.13 Proposed mechanism for Click reaction

A reaction mechanism proposed for the CuNPs catalyzed 1,3-dipolar cycloaddition of terminal alkynes with azides is outlined in Scheme 4.12 on the basis of the previous reports.\textsuperscript{25b,19c}
The proposed mechanism (Scheme 4.12) for the reaction is similar to the one established in earlier report. During the reaction, it is proposed that CuNPs are attracted towards the phenylacetylene to form Cu(I)-acetylidine complex in step I (Scheme 4.12). Formation of Cu(I)-acetylidine complex by initial coordination between CuNPs and alkyne is followed by the addition to azide group to give 1,2,3-triazole. The proposed mechanism involves the following steps: (1) conversion of the alkyne to the Cu-acetylidine, (2) addition of synthesized aryl or alkyl azides for attachment to the Cu-acetylidine, (3) formation of π-complex as intermediate product, (4) attack of the distal nitrogen of the azide to the C-2 carbon of the Cu-acetylidine to give a six-membered metallacycle, (5) ring contraction to afford a Cu(I) triazolide complex and (6) formation of triazole as a product. The copper in nanoparticle state exhibits both zero as well as one oxidation state during the reaction because of its unsatisfied surface valences.\textsuperscript{19}a Orgueira \textit{et al.}\textsuperscript{54} have reported the use of Cu(0) nanosize activated powder as catalyst for cycloaddition between terminal alkynes and azides. During the course of the reaction, zero-valent copper gets oxidized to the Cu(II) state via the Cu(I) state, which preclude the use of catalyst for further use. For the completion of the reaction 10-15 mins are required to get the product in excellent yields.
4.3.14 C-S coupling reaction using catalyst II

The catalyst II is also applied to C-S bond formation via coupling of thiols with aryl halides. The results show that this heterogeneous catalyst also could successfully promote the C-S coupling reactions, and the desired products are obtained in good to excellent yields when the 1.5 % mole of catalyst II is used as shown in Table 4.7.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst II (Mol %)</th>
<th>Yield (%) [b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>Trace</td>
</tr>
<tr>
<td>2</td>
<td>0.5</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td>1.0</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>1.5</td>
<td>96</td>
</tr>
<tr>
<td>5</td>
<td>2.0</td>
<td>96</td>
</tr>
</tbody>
</table>

[a] Reaction conditions: Catalyst II (1.5 mol%), benzenethiol (1.0 mmol), aryl halide (1.2 mmol), KOH (1.5 mmol), and DMSO (3.0 mL) were stirred at 110 °C for 9 h under a N₂ atmosphere.

[b] Isolated yields.

On the other hand, a slight to large decrease in yield is noticed when the amount of catalyst II is lowered from 1.5 mol % to 1.0 mol% and 0.5 mol % respectively. As a summary of the above results, the optimized system presented here involves the reaction between iodobenzene and thiophenol in DMSO neat solvent conditions at 110 °C, in the presence of 1.5 mmol of KOH and 1.5-2.0 mol % catalyst II.

To check the scope of the procedure, the reaction of different thiols with three aryl halides is then studied (Table 4.2). On comparing the reactivity and yields
of products, the iodobenzene is more reactive than bromo-and chlorobenzenes with aryl thiols (Table 4.2). To determine the scope of the catalytic system, the present protocol is applied to reactions of a range of commercially available aryl iodides and thiophenols. As shown in Table 4.2, the coupling of thiophenol with different aryl halide moieties is successful, leading to the desired products in good yields. These reaction conditions are also suitable for the coupling of different aryl/alkyl thiols with iodobenzenes (Table 4.2); ethane-, dodecane, and cyclohexanethiol afforded the desired cross-coupled products in 91-97% yield (Table 4.2, entries 8-12). The reaction of substrates with a longer alkyl chain (dodecanethiol) and of benzenethiol required slightly longer time to reach completion (Table 4.2, entries 1 and 11) respectively. The yields are low compared to bromo acetophenone (Table 4.2 entries 5, 9 and 12) and similar for the nitro and hydroxyl derivatives (Table 4.2 entries 6 and 7). Bromobenzene is less reactive than iodo derivatives (Table 4.2). The coupling also proceeded well with substituted thiophenols and alkanethiols. This reaction is also very chemoselective and high yielding. In the absence of catalyst II the coupling reaction is not initiated at all. It is found that 1.5 mol% of catalyst II provides the best results in terms of reaction time and yield. DMSO is found to be the solvent of choice furnishing best results among other solvents such as EtOH and DMF.

4.3.15 Effect of solvents and bases on C-S coupling reaction

For this C-S coupling reaction between iodobenzene and benzenethiol different parameters were optimized to develop the scope of this reaction further. First we tried the significant dependence of the S-arylation on the nature of the different solvents and bases (Tables 4.8 and 4.9).
Table 4.8 Screening of solvents for the catalyst II catalyzed C-S coupling reaction\textsuperscript{[a]}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Yield (%)\textsuperscript{[b]}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H\textsubscript{2}O</td>
<td>Trace</td>
</tr>
<tr>
<td>2</td>
<td>EtOH</td>
<td>Trace</td>
</tr>
<tr>
<td>3</td>
<td>DMF</td>
<td>70</td>
</tr>
<tr>
<td>4</td>
<td>Toluene</td>
<td>28</td>
</tr>
<tr>
<td>5</td>
<td>MeOH</td>
<td>Trace</td>
</tr>
<tr>
<td>6</td>
<td>DMSO</td>
<td>96</td>
</tr>
<tr>
<td>7</td>
<td>THF</td>
<td>Trace</td>
</tr>
<tr>
<td>8</td>
<td>Benzene</td>
<td>Trace</td>
</tr>
<tr>
<td>9</td>
<td>TEA</td>
<td>75\textsuperscript{[c]}</td>
</tr>
</tbody>
</table>

\textsuperscript{[a]}Reaction conditions: Catalyst II (1.5 mol\%), benzenethiol (1.0 mmol), aryl halide (1.2 mmol), KOH (1.5 mmol), and solvent (3.0 mL) were stirred at 110\textdegree C for 9 h, under N\textsubscript{2} atmosphere.

\textsuperscript{[b]}Isolated yields

\textsuperscript{[c]}Triethyl amine acting as a base as well as a solvent.

The solvents EtOH and DMF are less effective than DMSO. A variety of bases were tested in which NaOH, pyridine and K\textsubscript{2}CO\textsubscript{3} provided the arylated products in moderate to excellent yields (Table 4.9 entries 2, 5 and 6).
Table 4.9 Screening of bases for the catalyst II catalyzed C-S coupling reaction[^a]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Yield (%)[^b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NaOAc</td>
<td>Trace</td>
</tr>
<tr>
<td>2</td>
<td>NaOH</td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>Na₂CO₃</td>
<td>Trace</td>
</tr>
<tr>
<td>4</td>
<td>KOH</td>
<td>96</td>
</tr>
<tr>
<td>5</td>
<td>Pyridine</td>
<td>50</td>
</tr>
<tr>
<td>6</td>
<td>K₂CO₃</td>
<td>65</td>
</tr>
</tbody>
</table>

[^a]Reaction conditions: Catalyst II (1.5 mol%), benzenethiol (1.0 mmol), aryl halide (1.2 mmol), base (1.5 mmol), and DMSO (3.0 mL) were stirred at 110°C for under N₂ atmosphere.

[^b]Isolated yields.

Other bases such as NaOAc, and Na₂CO₃ gave trace or small amounts of diaryl sulfide (Table 4.9, entries 1 and 3). But in presence of KOH the DMF provides 60 % yield compared to DMSO (Table 4.8).

4.3.16 C-S coupling of thiophenol with different aryl halides

First, we studied the cross coupling of iodobenzene with thiophenol as the model substrate (Table 4.10). The reaction afforded the desired C-S cross coupling product to form diphenyl sulfide in 96% yield when the substrate is stirred in DMSO at 110 °C for 9 h in the presence of 1.5 mol % of Cu/SiO₂ nanocatalyst. Finally, the influence of the amount of catalyst II is evaluated. Increasing the amount of catalyst A to 2.0 mol % did not affect the efficiency of the coupling reaction as shown in Table 10.
Table 4.10 C-S coupling of thiophenol with different aryl halides\[a\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Halides</th>
<th>Thiol</th>
<th>Time (h)</th>
<th>Yield (%)[b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Image" /></td>
<td><img src="image2" alt="Image" /></td>
<td>9</td>
<td>96</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3" alt="Image" /></td>
<td><img src="image4" alt="Image" /></td>
<td>9</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5" alt="Image" /></td>
<td><img src="image6" alt="Image" /></td>
<td>9</td>
<td>30</td>
</tr>
</tbody>
</table>

\[a\]Reaction conditions: Catalyst II (1.5 mol %), benzenethiol (1.0 mmol), aryl halide (1.2 mmol), KOH (1.5 mmol), and DMSO (3.0 mL) were stirred at 110°C under N\textsubscript{2} atmosphere.

\[b\]Isolated yields.

### 4.3.17 Mechanism for C-S cross coupling reaction

Generally thiols(-SH) interact strongly with the transition metal nanoparticles. The experimental details clearly suggest that the reaction involves a heterogeneous process and the catalysis may occur on the surface of the CuNPs. Both, the aryl halides and thiols adsorbed on the surface of the CuNPs couple efficiently to form the thioethers. The details of the mechanism of the reaction are shown in Scheme 4.13.

![Scheme 4.13 Proposed mechanism for catalyst II catalyzed C-S coupling reaction.](image7)
4.3.18 Evaluation of the efficiency of different catalysts on C-S coupling reaction

The results from the study on the effect of various supported nanocatalysts on the aryl sulfide formation with different conditions are shown in Table 4.11. Among these metal nanoparticles catalyst A is found to be a very effective catalyst for C-S coupling reaction. However, In$_2$O$_3$, CuO, and CuO/SiO$_2$, nanoparticles have been reported to promote the C-S arylation without the assistance of any additional ligand. But the drawback of these systems is that more time is required for the reaction. The size and mol % of the other catalyst systems collected in Table 4.11 (entry 3, 4 and 7) show that large size and high mol% are used in other systems.

For hexagonal microporous silica (HMS) and Cu/Al$_2$O$_3$ systems CH$_3$CN and DMF are used as the solvent. We compare the activities of SiO$_2$, NH$_2$-SiO$_2$, and commercially available CuCl$_2$ catalysts for the C-S arylation at 110°C. All these catalysts are inactive (Table 4.11, entry 8, 9 and 11). The coupling reaction does not occur in the absence of the catalyst (Table 4.11, entry 12).
Table 4.11 Evaluation of different catalysts for the C-S coupling reaction.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalysts[a]</th>
<th>Size (nm)</th>
<th>Mol (%)</th>
<th>Time (h)</th>
<th>Temp (°C)</th>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>In$_2$O$_3$NPs$^{61}$</td>
<td>15-25</td>
<td>3.0</td>
<td>24</td>
<td>135</td>
<td>DMSO</td>
<td>97</td>
</tr>
<tr>
<td>2</td>
<td>CuONPs$^{62a}$</td>
<td>33</td>
<td>1.26</td>
<td>10</td>
<td>80</td>
<td>DMSO</td>
<td>95</td>
</tr>
<tr>
<td>3</td>
<td>CuONPs$^{62b}$</td>
<td>&gt;20</td>
<td>2.5</td>
<td>20</td>
<td>80</td>
<td>DMSO</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>CuO/SiO$_2$$^{63}$</td>
<td>&gt;50</td>
<td>5.0</td>
<td>21</td>
<td>110</td>
<td>DMSO</td>
<td>80-85</td>
</tr>
<tr>
<td>5</td>
<td>Cu-MW-HMS$^{64}$</td>
<td>2-3</td>
<td>0.05</td>
<td>10</td>
<td>&lt;100</td>
<td>CH$_3$CN</td>
<td>&gt;99</td>
</tr>
<tr>
<td>6</td>
<td>CuNPs$^{35b}$</td>
<td>4-6</td>
<td>20.0</td>
<td>5</td>
<td>120</td>
<td>DMF</td>
<td>98</td>
</tr>
<tr>
<td>7</td>
<td>Cu/Al$_2$O$_3$$^{65}$</td>
<td>&gt;100</td>
<td>5.0</td>
<td>7</td>
<td>110</td>
<td>DMF</td>
<td>70-98</td>
</tr>
<tr>
<td>8</td>
<td>Pure SiO$_2$</td>
<td>&gt;100</td>
<td>1.5</td>
<td>9</td>
<td>110</td>
<td>DMSO</td>
<td>0[b]</td>
</tr>
<tr>
<td>9</td>
<td>NH$_2$-SiO$_2$</td>
<td>&gt;100</td>
<td>1.5</td>
<td>9</td>
<td>110</td>
<td>DMSO</td>
<td>0[e]</td>
</tr>
<tr>
<td>10</td>
<td>Catalyst II</td>
<td>5 ± 2</td>
<td>1.5</td>
<td>9</td>
<td>110</td>
<td>DMSO</td>
<td>96[f]</td>
</tr>
<tr>
<td>11</td>
<td>CuCl$_2$</td>
<td>-</td>
<td>1.5</td>
<td>9</td>
<td>110</td>
<td>DMSO</td>
<td>0[e]</td>
</tr>
<tr>
<td>12</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>9</td>
<td>110</td>
<td>DMSO</td>
<td>0[f]</td>
</tr>
</tbody>
</table>

[a]References
[b-f] Reaction conditions as exemplified in the experimental procedure.
MW- HMS = Microwave assisted-hexagonal microporous silica.

4.4 Conclusions

In conclusion, we have developed a simple and reproducible synthetic method using a precipitating sol-gel technique for the preparation of highly dispersed SiO$_2$ supported CuNPs as a recyclable heterogeneous copper nanocatalyst (catalyst II). The catalyst is employed for the synthesis of 1,4-disubstituted-1,2,3-triazoles via Huisgen 1,3-dipolar cycloaddition and C-S coupling reactions using DMSO as the solvent. The surface morphology, particle size and optical properties of catalyst II are determined by using XRD, HRTEM, EDX, SEM, AFM, UV-vis, FT-IR and TGA spectral techniques. Furthermore, the catalyst can be recovered by centrifugation, washed with ethanol three or four times, then dried in vacuum and reused as the catalyst in the subsequent runs. The characterization of final products is done by $^1$H and $^{13}$C-NMR analysis. Such a wide scope demonstrated by a single
catalyst has not been reported earlier and this procedure provides a convenient route to a variety of substituted 1,2,3-triazoles and organic sulfides. Further investigations on other useful applications of this catalyst are in process.

Moreover, these heterogeneous nanocatalysts are stable showing negligible Cu leaching and aggregation, and can be recycled multiple times without loss of catalytic activity.
4.5 Spectral analysis

4.5.1 NMR data of azides

Benzyl azide: Yellow oil, \(^{1}H\)-NMR (300 MHz, CDCl\(_3\)): \(\delta\) 4.3 (s, 2H), 7.27-7.39 (m, 5H); \(^{13}C\)-NMR (75 MHz, CDCl\(_3\)): \(\delta\) 54.8, 128.2, 128.3, 128.8, 135.4.

\(\text{C}_6\text{H}_{13}\text{-N}_3\) 1-Azido hexane: Colorless oil, \(^{1}H\)-NMR (300 MHz, CDCl\(_3\)): \(\delta\) 3.25 (t, 2H, \(J = 7.0\) Hz), 1.55-1.64 (m, 2H), 1.25-1.41 (m, 6H), 0.89 (t, 3H, \(J = 6.8\) Hz); \(^{13}C\)-NMR (75 MHz, CDCl\(_3\)): \(\delta\) 51.4 (-CH\(_2\)N\(_3\)).

\(\text{C}_{10}\text{H}_{21}\text{-N}_3\) 1-Azido decane: Colorless oil, \(^{1}H\)-NMR (300 MHz, CDCl\(_3\)): \(\delta\) 0.88 (m, 5H), 1.54-1.62 (m, 14H), 3.25 (t, \(J = 7.2\) Hz, 2H). \(^{13}C\)-NMR (75 MHz, CDCl\(_3\)): \(\delta\) 51.5 (-CH\(_2\)N\(_3\)).

\(\text{N}_3\text{-C}_{10}\text{H}_{20}\text{-N}_3\) 1,10-diazidodecane: Yellow oil, \(^{1}H\)-NMR (300 MHz, CDCl\(_3\)): \(\delta\) 1.38-1.54 (m, 18H); 3.40 (t, \(J = 6.9\) Hz, 2H). \(^{13}C\)-NMR (75 MHz, CDCl\(_3\)): \(\delta\) 51.4 (-CH\(_2\)N\(_3\)).

\(\text{C}_{12}\text{H}_{25}\text{-N}_3\) 1-Azido dodecane: Yellow oil, \(^{20e}\) \(^{1}H\)-NMR (300 MHz, CDCl\(_3\)): \(\delta\) 0.88-1.12 (m, 8H), 1.62-1.27 (m, 15H), 3.40 (t, \(J = 6.3\) Hz, 2H). \(^{13}C\)-NMR (75 MHz, CDCl\(_3\)): \(\delta\) 51.4 (-CH\(_2\)N\(_3\)).

\(\text{C}_{16}\text{H}_{33}\text{-N}_3\) 1-Azido hexadecane: Colorless oil, \(^{1}H\)-NMR (300 MHz, CDCl\(_3\)): \(\delta\) 0.88-0.96 (m, 3H), 1.54-1.62 (m, 28H), 3.40 (t, \(J = 6.9\) Hz, 2H). \(^{13}C\)-NMR (75 MHz, CDCl\(_3\)): \(\delta\) 51.5 (-CH\(_2\)N\(_3\)).
Chapter IV

4.5.2 NMR spectra of azides

Figure 4.5.1 $^1$H-NMR spectrum of benzyl azide.

Figure 4.5.2 $^{13}$C-NMR spectrum of benzyl azide.
Figure 4.5.3 $^1$H-NMR spectrum of 1-azido hexane.

Figure 4.5.4 $^{13}$C-NMR spectrum of 1-azido hexane.
Figure 4.5.5 $^1$H-NMR spectrum of 1-azido decane.

Figure 4.5.6 $^{13}$C-NMR spectrum of 1-azido decane.
Figure 4.5.7 $^1H$-NMR spectrum of 1-azido dodecane.

Figure 4.5.8 $^{13}C$-NMR spectrum of 1-azido dodecane.
Figure 4.5.9 $^1$H-NMR spectrum of 1-azido hexadecane.

Figure 4.5.10 $^{13}$C-NMR spectrum of 1-azido hexadecane.
Figure 4.5.11 $^1\text{H}$-NMR spectrum of 1,10-diazidodecane.

Figure 4.5.12 $^{13}\text{C}$-NMR spectrum of 1,10-diazidodecane.
4.5.3 NMR data of 1,2,3-triazole products

1,4-diphenylbuta-1,3-diyne: colorless solid (Table 4.1, Entry 1) $^1$H-NMR (CDCl$_3$, 300 MHz) $\delta$ 7.38-7.28 (m, 6H), 7.53-7.47 (m, 4H); $^{13}$C-NMR (CDCl$_3$, 75 MHz) $\delta$ 73.9, 81.5, 121.7, 128.4, 129.1, 132.4.

1-benzyl-4-phenyl-$IH$-$1,2,3$-triazole: colorless solid (Table 4.1, Entry 2) $^1$H-NMR (CDCl$_3$, 300 MHz) $\delta$ 5.58 (s, 2H), 7.43-7.26 (m, 8H), 7.66 (s, 1H), 7.81 (d, 2H); $^{13}$C-NMR (CDCl$_3$, 75 MHz) $\delta$ 54.2, 119.4, 125.6, 128.0, 128.1, 128.7, 129.5, 130.5, 134.6, 137.5, 147.6.

1-phenyl-4-phenyl-$IH$-$1,2,3$-triazole: colourless (Table 4.1, Entry 3) $^1$H-NMR (CDCl$_3$, 300 MHz) $\delta$ 7.13-7.49 (m, 7H), 7.70-7.86 (m, 3H), 8.14 (s, 1H); $^{13}$C-NMR (CDCl$_3$, 75 MHz) $\delta$ 117.8, 126.4, 128.6, 128.9, 129.3, 129.6, 129.9, 130.4, 137.2, 148.5.

1-methyl-4-phenyl-$IH$-$1,2,3$-triazole: colourless (Table 4.1, Entry 4) $^1$H-NMR (CDCl$_3$, 300 MHz) $\delta$ 4.13 (s, 3H), 7.33-7.45 (m, 5H), 7.83 (s, 1H); $^{13}$C-NMR (CDCl$_3$, 75 MHz) $\delta$ 46.8, 128.6, 128.3, 128.2, 125.8, 120.7, 137.6.

1-propyl-4-phenyl-$IH$-$1,2,3$-triazole: colourless (Table 4.1, Entry 5) $^1$H-NMR (CDCl$_3$, 300 MHz) $\delta$ 0.99-1.12 (m, 3H), 1.88-1.99 (m, 2H), 4.34 (t, 2H),
7.36-7.63 (m, 5H), 7.74 (s, 1H); $^1$C-NMR (CDCl$_3$, 75 MHz) δ 11.0, 23.7, 51.9, 119.5, 125.6, 128.0, 128.8, 130.7, 147.6.

1-hexyl-4-phenyl-1H-1,2,3-triazole: $^{67,74}$ colourless (Table 4.1, Entry 6) $^1$H-NMR (CDCl$_3$, 300 MHz) δ 0.88 (t, 3H), 1.25-1.32 (m, 2H), 1.89-1.96 (m, 2H), 4.39 (t, 2H), 7.26-7.38 (m, 1H), 7.39-7.47 (m, 2H), 7.74 (s, 1H), 7.85 (d, 2H); $^1$C-NMR (CDCl$_3$, 75 MHz) δ 13.9, 22.3, 26.1, 30.2, 31.1, 50.4, 119.3, 125.6, 128.0, 128.7, 130.6, 147.6.

1-docyl-4-phenyl-1H-1,2,3-triazole: $^{74}$ colourless (Table 4.1, Entry 7) $^1$H-NMR (CDCl$_3$, 300 MHz) δ 0.87 (t, 3H), 1.25-1.35 (m, 14H), 1.69-1.96 (m, 2H), 4.39 (t, 2H), 7.26-7.35 (m, 1H), 7.40-7.45 (m, 2H), 7.74 (s, 1H), 7.82-7.85 (m, 2H); $^1$C-NMR (CDCl$_3$, 75 MHz) δ 14.4, 22.7, 26.6, 29.8, 30.5, 31.7, 50.8, 119.7, 126.1, 128.0, 128.4, 131.6, 148.1.

1-dodecyl-4-phenyl-1H-1,2,3-triazole: $^{20c}$ colourless (Table 4.1, Entry 8) $^1$H-NMR (CDCl$_3$, 300 MHz) δ 0.87 (t, 3H), 1.24-1.33 (m, 18H), 1.93-2.01 (m, 2H), 4.38 (t, 2H), 7.32-7.34 (m, 1H), 7.39-7.44 (m, 2H), 7.74 (s, 1H), 7.84-7.82 (m, 2H); $^1$C-NMR (CDCl$_3$, 75 MHz) δ 14.0, 22.5, 22.6, 26.4, 28.9, 29.2, 29.3, 29.4, 29.5, 30.3, 31.8, 50.3, 119.3, 125.0, 128.0, 128.7, 130.6, 147.6.

1-hexadecyl-4-phenyl-1H-1,2,3-triazole: colourless (Table 4.1, Entry 9) $^1$H-NMR (CDCl$_3$,
300 MHz) $\delta$ 0.87 (t, 3H), 1.24-1.31 (m, 26H), 1.92 (m, 2H), 4.36 (t, 2H), 7.33-7.31 (m, 1H), 7.43-7.38 (m, 2H), 7.73 (s, 1H), 7.83-7.81 (m, 2H), $^{13}$C-NMR (CDCl$_3$, 75 MHz) $\delta$ 14.0, 22.6, 26.4, 28.1, 28.7, 28.9, 29.3, 29.4, 29.6, 30.3, 30.8, 31.8, 32.7, 34.0, 50.3, 119.3, 128.0, 128.7, 129.1, 130.6, 147.6.

**1,10-bis(4-phenyl-1H-1,2,3-triazol-1-yl)decane:**
colourless (Table 4.1, Entry 10) $^1$H-NMR (CDCl$_3$, 300 MHz) $\delta$ 1.68-1.25 (m, 14H), 1.97-1.94 (m, 2H), 4.39 (t, 4H), 7.36-7.31 (m, 1H), 7.45-7.40 (m, 2H), 7.74 (s, 1H), 7.85-7.82 (m, 2H); $^{13}$C-NMR (CDCl$_3$, 75 MHz) $\delta$ 26.3, 28.6, 28.8, 29.1, 51.3, 119.2, 125.5, 128.0, 128.7, 130.5, 147.5.

**2,7-dimethylocta-3,5-diyne-2,7-diol:**
colourless (Table 4.1, Entry 11) $^1$H-NMR (300 MHz, CDCl$_3$): $\delta$ 2.04 (s, 2H), 1.54 (s, 12H). $^{13}$C-NMR (67.8 MHz, CDCl$_3$) $\delta$ 31.0, 66.5, 66.3, 83.9.

**2-(1-Benzyl-1H-1,2,3-triazol-4-yl)-2-propanol**
colourless $^1$H-NMR (300 MHz, CDCl$_3$): $\delta$ 1.57 (s, 6 H), 3.20 (s, 1H), 5.49 (s, 2H), 7.25-7.39 (m, 5H), 7.42 (s, 1H); $^{13}$C-NMR (75 MHz, CDCl$_3$): $\delta$ 30.6, 54.6, 68.8, 119.9, 128.6, 128.8, 129.5, 134.5, 152.9.
4.5.4 NMR spectra 1,2,3-triazoles

Figure 4.5.13 $^1$H-NMR spectrum of 1,4-diphenylbuta-1,3-diyne (Table 4.1 Entry 1).

Figure 4.5.14 $^{13}$C-NMR spectrum for 1,4-diphenylbuta-1,3-diyne (Table 4.1 Entry 1).
Figure 4.5.15 $^1$H-NMR spectrum of 1-benzyl-4-phenyl-1H-1,2,3-triazole (Table 4.1 Entry 2).

Figure 4.5.16 $^{13}$C-NMR spectrum of 1-benzyl-4-phenyl-1H-1,2,3-triazole (Table 4.1 Entry 2).
Figure 4.5.17 $^1$H-NMR spectrum of 1-methyl-4-phenyl-1H-1,2,3-triazole (Table 4.1 Entry 4).

Figure 4.5.18 $^{13}$C-NMR spectrum of 1-methyl-4-phenyl-1H-1,2,3-triazole (Table 4.1 Entry 4).
Figure 4.5.19 $^1$H-NMR spectrum of 1-propyl-4-phenyl-1H-1,2,3-triazole (Table 4.1 Entry 5).

Figure 4.5.20 $^{13}$C-NMR spectrum of 1-propyl-4-phenyl-1H-1,2,3-triazole (Table 4.1 Entry 5).
Chapter IV

Figure 4.5.21 $^1$H-NMR spectrum of 1-hexyl-4-phenyl-1H-1,2,3-triazole (Table 4.1 Entry 6).

Figure 4.5.22 $^{13}$C-NMR spectrum of 1-hexyl-4-phenyl-1H-1,2,3-triazole (Table 4.1 Entry 6).
Chapter IV

Figure 4.5.23 $^1$H-NMR spectrum of 1-decyl-4-phenyl-1H-1,2,3-triazole (Table 4.1 Entry 7).

Figure 4.5.24 $^{13}$C-NMR spectrum of 1-decyl-4-phenyl-1H-1,2,3-triazole (Table 4.1 Entry 7).
Figure 4.5.25 \(^1\)H-NMR spectrum of 1-dodecyl-4-phenyl-1H-1,2,3-triazole (Table 4.1 Entry 8).

Figure 4.5.26 \(^1\)H-NMR spectrum of 1-dodecyl-4-phenyl-1H-1,2,3-triazole (Table 4.1 Entry 8).
Figure 4.2.27 $^1$H-NMR spectrum of 1-hexadecyl-4-phenyl-1H-1,2,3-triazole (Table 4.11 Entry 9).

Figure 4.2.28 $^{13}$C-NMR spectrum of 1-hexadecyl-4-phenyl-1H-1,2,3-triazole (Table 4.1 Entry 9).
Figure 4.5.29 $^1$H-NMR spectrum of 1, 10-bis(4-phenyl-1H-1, 2, 3-triazol-1-yl)decane (Table 4.1 Entry 10).

Figure 4.5.30 $^{13}$C-NMR spectrum of 1, 10-bis(4-phenyl-1H-1, 2, 3-triazol-1-yl)decane (Table 4.1 Entry 10).
Figure 4.5.31 $^1$H-NMR spectrum of 2,7-Dimethyl octa-3,5-diyne-2,7-diol (Table 4.1 Entry 11).

Figure 4.5.32 $^{13}$C-NMR spectrum of 2,7-Dimethyl octa-3,5-diyne-2,7-diol (Table 4.1 Entry 11).
4.5.5 NMR data of C-S coupling products

Diphenyl sulfide: superscript 35c colorless liquid (Table 4.2, Entry 1) $^1$H-NMR (300 MHz, CDCl$_3$) $\delta$ 7.49-7.71 (10H, m); $^{13}$C-NMR (75 MHz, CDCl$_3$) $\delta$ 126.7, 128.9, 130.7, 135.5.

4-Iodo diphenyl sulfide: superscript 35c colorless liquid (Table 4.2, Entry 2) $^1$H-NMR (CDCl$_3$, 300 MHz) $\delta$ 7.20 - 7.44 (m, 5H), 7.46 (d, $J = 6.8$Hz, 2H), 7.12 (d, $J = 6.8$Hz, 2H); $^{13}$C-NMR (CDCl$_3$, 75 MHz) $\delta$ 117.3, 120.8, 122.3, 128.7, 129.0, 130.0, 136.2, 136.5,

4-Tolylphenyl sulfide: superscript 35a colorless liquid (Table 4.2, Entry 3) $^1$H-NMR (CDCl$_3$, 300 MHz) $\delta$ 2.32 (s, 3H), 7.10-7.26 (m, 5H), 7.32 (d, $J = 7.2$Hz, 2H), 7.46 (d, $J = 7.2$Hz, 2H); $^{13}$C-NMR (CDCl$_3$, 75 MHz) $\delta$ 21.1, 126.4, 129.2, 129.7, 130.0, 131.2, 132.3, 137.1, 137.6

4-Acetyl-diphenyl phenyl sulfide: superscript 75 colorless liquid (Table 4.2, Entry 4) $^1$H-NMR (300 MHz, CDCl$_3$) $\delta$ 2.54 (s, 3H), 7.21 (d, $J = 7.2$Hz, 2H), 7.38-7.39 (m, 3H), 7.90-7.47 (m, 2H), 8.09 (d, $J = 7.2$Hz, 2H); $^{13}$C-NMR (75 MHz, CDCl$_3$) $\delta$ 26.45, 127.37, 128.77, 128.25, 129.64, 131.99, 133.85, 134.39, 144.90, 196.13.

4-Nitrophenyl phenyl sulfide: superscript 75 light yellow color liquid (Table 4.2, Entry 6) $^1$H-NMR (300 MHz, CDCl$_3$) $\delta$ 7.18 (d, $J = 9.0$ Hz, 2H), 7.47-7.55 (m, 5H), 8.07 (d, $J = 9.0$ Hz, 2H); $^{13}$C-NMR (75 MHz, CDCl$_3$)
Chapter IV

δ 124.0, 126.7, 129.6, 130.0, 130.5, 134.7, 145.4, 148.4.

**Cyclohexyl phenyl sulfide:** (Table 4.2, Entry 8) \(^1\)H-NMR (300 MHz, CDCl\(_3\)) δ 1.25-1.42 (m, 5H), 1.61-1.59 (m, 1H), 1.77-1.75 (m, 2H), 1.97-1.99 (m, 2H), 3.05-3.13 (m, 1H), 7.19-7.24 (m, 1H), 7.26-7.29 (m, 2H), 7.31-7.40 (m, 2H); \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)) δ 126.7, 128.9, 130.7, 135.5.

**Ethyl phenyl sulfide:** (Table 4.2, Entry 10) \(^1\)H-NMR (CDCl\(_3\), 300 MHz) δ 1.31 (t, 3H), 2.94 (q, 2H), 7.19-7.10 (m, 1H), 7.30-7.21 (m, 4H); \(^{13}\)C-NMR (CDCl\(_3\), 75 MHz) δ 14.3, 27.5, 125.9, 128.4, 129.23, 136.79.

**Dodecyl phenyl sulfide:** (Table 4.2, Entry 11) \(^1\)H-NMR (300 MHz, CDCl\(_3\)) δ 0.88 (t, 3H), 1.26-1.32 (m, 16H), 1.58-1.60 (m, 2H), 1.61-1.69 (m, 2H), 2.91 (t, 2H), 7.08-7.13 (m, 1H), 7.26-7.35 (m, 4H); \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)) δ 14.0, 22.6, 28.5, 29.1, 29.2, 29.3, 29.5, 29.6, 30.8, 31.8, 33.6, 39.1, 127.3, 128.7, 130.1, 137.4.

**1-(4-(dodecylthio)phenyl)ethanone:** (Table 4.2, Entry 12) \(^1\)H-NMR (300 MHz, CDCl\(_3\)) δ 0.88 (t, 3H) 1.26-1.59 (m, 16H), 1.60-1.69 (m, 2H), 2.65(t, 2H), 7.27 (d, 2H), 7.84 (d, 2H); \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)) δ 13.7, 22.2, 26.1, 28.8, 28.8, 29.1, 29.2, 29.2, 31.5, 38.7, 127.8, 129.4, 131.4, 135.3, 196.5.
4.5.6 NMR Spectra of C-S coupling products.

Figure 4.5.33 $^1$H-NMR spectrum of diphenyl sulfide (Table 4.2 Entry1).

Figure 4.5.34 $^{13}$C-NMR spectrum of diphenyl sulfide (Table 4.2, Entry1).
Figure 4.5.35 $^1$H-NMR spectrum of 4-iodo diphenyl sulfide (Table 4.2, Entry 2).

Figure 4.5.36 $^{13}$C-NMR spectrum of 4-iodo diphenyl sulfide (Table 4.2, Entry 2).
Figure 4.5.37 $^1$H-NMR spectrum of 4-tolylphenyl sulfide (Table 4.2, Entry 3).

Figure 4.5.38 $^1$H-NMR spectrum of 4-tolylphenyl sulfide (Table 4.2, Entry 3).
Figure 4.5.39 $^1$H-NMR spectrum of 4-acetyl diphenyl sulfide (Table 4.2 Entry 4)

Figure 4.5.40 $^{13}$C-NMR spectrum of 4-acetyl diphenyl sulfide (Table 4.2, Entry 4).
Figure 4.5.41 $^1$H-NMR spectrum of cyclohexyl phenyl sulfide (Table 4.2 Entry 8).

Figure 4.5.42 $^{13}$C-NMR spectrum of cyclohexyl phenyl sulfide (Table 4.2 Entry 8).
Figure 4.5.43 $^1$H-NMR spectrum of n-ethyl thiobenzene (Table 4.2, Entry 10).

Figure 4.5.44 $^{13}$C-NMR spectrum of n-ethyl thiobenzene (Table 4.2, Entry 10).
Figure 4.5.45 $^1$H-NMR spectrum of dodecyl phenyl sulfide (Table 4.2, Entry 11).

Figure 4.5.46 $^{13}$C-NMR spectrum of dodecyl phenyl sulfide (Table 4.2, Entry 11).
Figure 4.5.47 $^1$H-NMR spectrum of 1-(4-(dodecylthio)phenyl)ethanone (Table 4.2, Entry 12).

Figure 4.5.48 $^{13}$C-NMR spectrum of 1-(4-(dodecylthio)phenyl)ethanone (Table 4.2, Entry 12).
4.6 References

Chapter IV

V.V. Fokin, K. B. Sharpless, M. Galleni, C. Bebrone, P. Lassaux, P. Hodder, 


203
5.1 Introduction

The application of metal nanoparticles in catalysis has become a frontier area of research in recent years and numerous review articles appeared during the last decade on both heterogeneous and homogeneous catalysis. Heterogeneous catalysis is attractive for both laboratory and large scale synthesis. In fact, one of the challenging areas of research is heterogeneous catalysis with nanocatalysts supported on a solid surface. Among the different metal nanocatalysts, palladium nanoparticles (PdNPs) have gained much reputation, because palladium is a versatile catalyst in modern organic synthesis and is widely used for a significant number of synthetic transformations such as Heck, Suzuki, Stille, and Sonogashira cross coupling reactions.

Some types of traditional nanocatalysts include transition metal nanoparticles in colloidal suspension, and those adsorbed onto bulk supports. Transition metal nanoparticles in colloidal suspension have been synthesized by using a wide variety of reducing agents such as hydrogen, sodium borohydride, and ethanol. Different types of stabilizers such as surfactants, polymers, dendrimers, as well as different types of ligands have been used as capping agents to stabilize the nanoparticles. In the case of metal nanoparticles adsorbed onto bulk supports, a wide variety of support materials such as carbon, mesoporous silica, titania, alumina, zeolites, and resins have been used. Among many NPs, silica-based NPs have been well studied because of the following reasons: (i) SiNPs are easy to synthesise at room temperature, (ii) NP size can be easily tuned, (iii) easy adjustment of synthesis parameters leads to NPs with narrow size distribution (‘monodispersed NPs’), (iv) SiNPs are stable in organic solvents, and (v) they are environmentally friendly materials. Due to these attractive features, SiNPs find wide-spread applications in the synthesis of nanomaterial for catalysis of organic reactions.
5.1.1. Palladium as a versatile catalyst for Suzuki, Heck and Sonogashira coupling reactions

Palladium nanoparticles, highly dispersed on various supports, have been widely studied over the last few years due to their interesting properties with applications in catalysis. The properties and catalytic activities of the systems are highly dependent on the supports, particle size, type and method of preparation of the noble metal. The type of support employed is indeed a critical factor in the performance of the resulting supported material. Two key features should be considered when employing a material as a support. Firstly, the material needs to be both thermally and chemically stable during the reaction process. Secondly, the structure of the support has to be such that the active sites are well dispersed on its surface and that these sites are easily accessible.

Palladium is among the most popular transition metals in modern organic synthesis and widely used for a significant number of synthetic transformations. However, its use is often complicated by issues surrounding the separation of the palladium and ligands from the desired product while reuse, ideally without loss of catalytic activity, becomes a major practical and economic issue with respect to large-scale applications.

5.1.2. Suzuki coupling reactions

Carbon-carbon coupling reaction such as Heck, Sonogashira, Suzuki, Stille, Negishi, Hiyama, Corriu-Kumada, Tsuji-Trost, and Ullmann reactions have profound importance for application in the industries as shown in Scheme 5.1. These reactions have been studied extensively in homogeneous condition using a variety of palladium-containing complexes as catalyst. The Suzuki-Miyaura coupling reaction is one of the most useful methods for selective C-C bond formation for the construction of biaryl skeletons, which are often included as partial structures in pharmaceuticals, natural products and functional materials.
Scheme 5.1 Pd catalyzed C-C bond formation with aryl halides and triflates.

El-Sayed and coworkers\textsuperscript{56} have used PdNPs stabilized by PVP as efficient catalyst for the Suzuki reactions in aqueous medium. The effect of Pd particle size on the Suzuki reaction between phenylboronic acid and iodobenzene is investigated by the use of four Pd catalysts with mean particle sizes of 3.0, 3.9, 5.2, and 6.6 nm, respectively (Scheme 5.2).

Scheme 5.2 Suzuki coupling reactions catalyzed by PVP-PdNPs.
Scheme 5.3 shows hollow palladium spheres have been used as recyclable heterogeneous catalysts for Suzuki coupling reactions between iodothiophene and arylboronic acids.\textsuperscript{40a}

\begin{center}
\includegraphics{scheme5_3}
\end{center}

\textit{Scheme 5.3 Suzuki coupling of iodothiophene and arylboronic acids.}

Diaconescu and coworkers\textsuperscript{55a} have reported the use of polyaniline (PANI) as a support as well as a reducing agent and stabilizer. These advantages translate into easy and reproducible systems that make PdNPs supported by PANI as a promising catalyst for C-C coupling reactions as shown in Scheme 5.4.

\begin{center}
\includegraphics{scheme5_4}
\end{center}

\textit{Scheme 5.4 Suzuki coupling of aryl chlorides and PhB(OH)\textsubscript{2}.}

The ligand-free heterogeneous layered double hydroxide supported nanopalladium (LDH-Pd\textsuperscript{0}) catalyst has been extended to the Suzuki-, Sonogashira-, and Stille-type coupling reactions of chloroarenes in an effort to understand the scope and utility of the reaction Scheme 5.5.\textsuperscript{51b}

\begin{center}
\includegraphics{scheme5_5}
\end{center}

\textit{Scheme 5.5 Suzuki coupling reactions of chloroarenes with arylboronic acids using LDH-Pd\textsuperscript{0} catalyst.}
Gude and Narayanan have reported the synthesis of amine or thiol functionalized silica colloids attached PdNPs to utilize for coupling reactions as shown in Scheme 5.6.\textsuperscript{30a}

![Scheme 5.6 Suzuki coupling reactions catalyzed by Pd/SiO$_2$ nanocatalysts.](image)

After the full course of the Suzuki reaction, it is observed that there are structural changes in the silica colloids after which it becomes porous and the PdNPs are still bound to the silica colloids. Magnetically recoverable and stable recyclable Pd@Fe$_3$O$_4$ catalyst for hydrogenation and Suzuki-Miyaura reactions as shown in Scheme 5.8.\textsuperscript{45c}

![Scheme 5.7 Schematic illustration of Suzuki–Miyaura coupling reactions.](image)

Chitosan-AgNP composite\textsuperscript{57a} has been used as an efficient catalyst in selective C-C coupling of phenolic compounds in the presence of molecular iodine as shown in Scheme 5.8

![Scheme 5.8 Chitosan-AgNPs catalyzed o-p phenolic coupling reaction.](image)
Diamine-modified glycidyl methacrylate polymer (GMA-CHDA)\textsuperscript{48b} and linear polystyrene stabilized PdONPs serve as efficient catalysts for C-C coupling reactions in water Scheme 5.9.\textsuperscript{57b,58}

![Scheme 5.9 Suzuki coupling reaction in water.](image)

### 5.1.3. Heck coupling reactions

Heck reaction is one of the most powerful methods to form a new carbon-carbon (C\textsubscript{sp}\textsuperscript{2}-C\textsubscript{sp}\textsuperscript{2}) bond in modern synthetic chemistry. Of several commonly used C-C coupling reactions such as the Heck, Suzuki, Stille, and Sonogashira reactions, the most attractive is perhaps the Heck reaction because of a high selectivity for producing fine chemicals including pharmaceuticals in a single operation.\textsuperscript{41, 47b, 58b, 59-63}

All forms of Pd can be used as precatalysts to carry out simpler Heck reactions (e.g., activation of aryl iodides and bromides). The catalysis by ligand-free supported Pd metal has been attracting great interest in the area of C-C coupling.\textsuperscript{64-66} Much work has been reported on the application and performance of supported Pd metal catalysts such as Pd\textsuperscript{0}/C, Pd\textsuperscript{0}/oxide, Pd\textsuperscript{0}/zeolite, Pd\textsuperscript{0}/MCM-41, Pd/NiFe\textsubscript{2}O\textsubscript{4} and Pd\textsuperscript{0}/SBA-15 in a variety of Heck reactions.\textsuperscript{39b,66-71}

Wang and co-workers\textsuperscript{72} have reported the Heck reaction using Ni(0) nanoparticles (NiNPs) as catalysts in hydrothermal method. The coupling reactions of a variety of aryl halides with different alkenes were investigated under optimum reaction conditions as shown in Scheme 5.10.

![Scheme 5.10 Heck-type cross-coupling using nickel nanoparticles.](image)
Huang et al.\textsuperscript{40b} have reported Heck coupling between bromobenzene and styrene over conventionally prepared Pd/SiO\textsubscript{2} at 135 °C under argon atmosphere with Na\textsubscript{2}CO\textsubscript{3} as the base as shown in Scheme 5.11.

\begin{center}
\includegraphics[width=0.7\textwidth]{scheme511.png}
\end{center}

\textit{Scheme 5.11 Heck coupling of bromobenzene and styrene over Pd\textsuperscript{0}/SiO\textsubscript{2}.}

Palladium nanoparticles have been immobilized on the silica-based mesoporous material to develop catalyst Pd(0)-MCM-41, which is found to be highly active in carbon-carbon coupling reactions as shown in Scheme 5.12. It has shown high catalytic activity and turn-over numbers.\textsuperscript{39a}

\begin{center}
\includegraphics[width=0.7\textwidth]{scheme512.png}
\end{center}

\textit{Scheme 5.12 Heck olefination of aryl halides over Pd(0)-MCM-41 catalyst.}

Wang and coworkers\textsuperscript{45a} reported a new type of diatomite supported PdNPs used for Heck and Suzuki coupling reactions as shown in Scheme 5.13.

\begin{center}
\includegraphics[width=0.7\textwidth]{scheme513.png}
\end{center}

\textit{Scheme 5.13 Heck reaction of aryl halides with olefins.}
Han and coworkers\textsuperscript{49a} have reported the Heck arylation of olefins with aryl halides in solvent-free conditions with a Pd catalyst supported on 1,1,3,3-tetramethylguanidinium(TMG)-modified molecular sieve SBA-15 (designated as SBA-TMG-Pd) (Scheme 5.14).

![Scheme 5.14 Heck reaction between iodobenzene and methylacrylate.](image1)

**Scheme 5.14 Heck reaction between iodobenzene and methylacrylate.**

Proch \textit{et al.}\textsuperscript{73a} report on a systematic study of the use of PdNPs immobilized on spherical polyelectrolyte brushes Pd@SPB for Heck- and Suzuki type coupling reactions (Scheme 5.15).

![Scheme 5.15 Heck-type cross-coupling using palladium nanoparticles stabilized on SPB.](image2)

**Scheme 5.15 Heck-type cross-coupling using palladium nanoparticles stabilized on SPB.**

Blum and coworkers\textsuperscript{73b} describe two different pathways for palladium-catalyzed Heck and Suzuki coupling reactions. Here, the sol-gel entrapped palladium acetate is used as a catalyst as shown in Scheme 5.16.

![Scheme 5.16 Palladium nanoparticles in the Heck reactions.](image3)

**Scheme 5.16 Palladium nanoparticles in the Heck reactions.**

Nickel nanoparticles stabilized by PANI catalyzed the Heck coupling reaction as shown in Scheme 5.17.\textsuperscript{73c}
Scheme 5.17 Heck couplings catalyzed by Ni(0)/PANI composites.

5.1.4 Sonogashira coupling reactions

Palladium-catalyzed cross-coupling reactions are one of the most frequently used synthetic tools for the construction of new carbon-carbon bonds in organic synthesis.\(^{74a}\) Aryliodides, bromides and triflates are excellent coupling partners in these transformations, but the application of chlorides is more beneficial. Though, the technique for the Heck, Suzuki, Stille coupling on aryl-chlorides is successfully developed, the formation of Csp\(^2\)-Csp bond in Sonogashira reaction is still challenging.\(^{74b}\)

The Sonogashira cross-coupling reaction of terminal acetylenes with aryl or vinyl halides has proved to be a powerful method for the creation of substituted alkynes,\(^{75,76}\) and this method has been widely applied in the synthesis of natural products,\(^{77,78}\) biologically active molecules\(^{79,80}\) and materials science.\(^{81}\) The other transition metals Au,\(^{82}\) Ru,\(^{83}\) Rh,\(^{84}\) and Cu\(^{85}\) are also employed for Sonogashira coupling reactions.

Choudary et al.\(^{51b}\) employed the active LDH-Pd\(^0\) in Sonogashira coupling reactions as shown in Scheme 5.18.

![Scheme 5.18 LDH-Pd\(^0\) catalyzed Sonogashira coupling of chloroarenes with phenylacetylene.](image)

Li et al.\(^{86}\) have reported, a recoverable PdNPs catalyzed Sonogashira reaction of aryl iodides and bromides with terminal alkynes in the absence of ligand,
copper and amine. The protocol involved the use of an environmental friendly reaction system with ethanol as the solvent, potassium carbonate as a base, and PVP supported nanosized palladium metal colloids as the catalyst as shown in Scheme 5.19.

![Scheme 5.19 Ligand and copper free Sonogashira coupling reactions.](image)

A highly active heterogeneous catalyst (Pd/MOF-5) has been successfully applied (Scheme 5.20) in the ligand and copper free Sonogashira coupling reactions.

![Scheme 5.20 Sonogashitra C-C coupling reaction using Pd/MOF-5 catalyst.](image)

The bimetallic (Ni/Pd), Pd/Co and trimetallic (Au/Ag/Pd) catalysts were also atom-economically applied for various Sonogashira coupling reactions as shown in Scheme 5.21.

![Scheme 5.21 Sonogashira C-C coupling reaction using Au/Ag/Pd nanoparticles.](image)

A magnetically separable palladium (Pd/Fe₃O₄) is an efficient catalyst for the carbonylative Sonogashira coupling reaction of aryl iodides with terminal alkynes under phosphine-free conditions as shown in Scheme 5.22. This catalyst is
completely magnetically recoverable due to the super paramagnetic behavior of Fe₃O₄ and can be reused with sustained selectivity and activity.⁸⁹

\[
\text{Scheme 5.22 Sonogashira carbonylative coupling of alkynes and aryl iodides.}
\]

Sonogashira reaction has been achieved in short reaction times, excellent chemoselectivity, and high isolated yields at ambient temperature under ultrasonic irradiation in a molecular solvent as well as a room-temperature ionic liquid even in the absence of a phosphine ligand and copper cocatalysts (Scheme 5.23).⁹⁰

\[
\text{Scheme 5.23 Sonogashira coupling of alkynes and aryl iodides by microwave method.}
\]

Scheme 5.24 shows the embedded PdNPs on the surface of gelatin. It is a safe, edible, naturally occurring and cheap support. No extra reducing agents are used for the generation of Pd(0) nanoparticles from the Pd(II) salt.

\[
\text{Scheme 5.24 Sonogashira coupling between alkynes and aryl iodides.}
\]

The reactions were carried out at 100°C in molten tetrabutylammonium bromide (TBAB) or polyethylene glycol (PEG 400) in the presence of potassium acetate as a base in argon atmosphere.⁹¹
Nano palladium catalyzed oxidative cross-coupling reaction of arylboronic acids with terminal alkynes is shown in Scheme 5.25.}

\[
\text{Scheme 5.25 Nanopalladium catalyzed oxidative cross-coupling reaction of terminal alkynes with arylboronic acids.}
\]

The Sonogashira reaction of iodobenzene with phenylacetylene was carried out in water using Pd/C as catalyst and surfactants as additives. The effect of various cationic and anionic surfactants on the activity of Pd/C for the above reaction was studied as shown in Scheme 5.26.

\[
\text{Scheme 5.26 Pd/C catalyzed Sonogashira reaction between iodobenzene and phenylacetylene.}
\]

Paramagnetic magnetite (Fe₃O₄) have been used as an efficient catalyst for carbon-carbon bond formation via the Sonogashira reaction under heterogeneous ligand-free conditions in ethylene glycol (EG) as described in Scheme 5.27.

\[
\text{Scheme 5.27 Fe₃O₄NPs catalyzed Sonogashira coupling reaction in ethylene glycol.}
\]
In the present work, we have carried out the reduction of Pd\(^{2+}\) salt in aqueous polymer solutions (polyethylenimine, PEI) at room temperature with ascorbic acid as the reducing agent without the assistance of any surfactant and ligands.\(^{91d}\) The synthesized PEI capped PdNPs are immobilized on the surface of amine functionalized SiNPs, which is used as a heterogeneous catalyst (Pd/SiO\(_2\)). It is utilized for the C-C, C=C and C≡C coupling reactions which can be recycled and reused several times without any loss of their catalytic activity. The catalyst Pd/SiO\(_2\) is employed as an efficient catalyst in coupling reactions and its catalytic role is schematically represented in Scheme 5.28.

Scheme 5.28 Pd/SiO\(_2\) catalyzed Suzuki, Heck and Sonogashira coupling reactions.

5.2 Experimental section

5.2.1 Synthesis of silica supported PEI/PdNPs

The silica colloids were synthesized by using the Stöber synthesis method as shown in detail in Chapter II.\(^{92}\) The palladium nanoparticles (PdNPs) were synthesized by using palladium precursor (Pd(OAc)\(_2\)) and ascorbic acid reduction method similar to that described previously.\(^{93}\) The PEI stabilized metal nanoparticles are prepared by the method described below.\(^{94}\) The palladium precursor solution is prepared by mixing Pd(OAc)\(_2\) (0.064 g) with 5.0 mL of PEI (1.0 wt%) and then
diluting to 25 mL with doubly distilled water. 1.0 mL of 100 mM aqueous solution of ascorbic acid is injected into the reaction mixture via syringe within few seconds. After additional stirring for 10-15 min, the reaction solution is stored under dark. Synthesis of functionalized silica colloids is discussed in the previous chapter (Chapter IV).

Amine modified SiO$_2$ (100 mg) is added to PdNPs by stirring for 30 min and sonicated for 45 min. Dark black colored PEI/PdNPs are bound on the surface of SiNPs with elapsing of reaction time, and the reaction proceeded for 2.5 h. The synthesized palladium nanocatalyst (Pd/SiO$_2$) is referred as Catalyst III. Finally, the particles are washed with ethanol, centrifuged and dried under vacuum. The entire synthetic procedure is given in Scheme 5.29.

Scheme 5.29 Schematic representation of four-step process for the synthesis of Pd/SiO$_2$. 

![Scheme 5.29](image-url)
In the absence of a suitable support, metal particle aggregates have reduced surface area and restricted control over particle size.

5.2.2 Suzuki coupling reaction

To halobenzene (1.0 mmol), phenylboronic acid (1.2 mmol), K₂CO₃ (276 mg, 2.0 mmol), TBAB (161 mg, 0.5 mmol) and Pd/SiO₂ nanocatalyst (0.5 mol%) are added to a 25 mL round bottom flask equipped with a magnetic stirrer bar. 2.0 mL of H₂O is added and the reaction mixture is stirred at 60-70°C for 2-3 h. After the reaction, the Pd nanocatalyst is separated by centrifuging and washed with diethyl ether (20 mL) followed by deionized water (20 mL). The collected Pd nanocatalyst is dried and reused for the next run. The aqueous phase is extracted with diethyl ether (20 mL) and the combined organic phases are concentrated and purified with thin layer chromatography (TLC, SiO₂). The results are collected in Table 5.1.

Table 5.1 Suzuki coupling of aryl halides with phenylboronic acid

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reactants</th>
<th>Products</th>
<th>Time (h)</th>
<th>Yield (%)^[b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1.png" alt="Reactant 1" /></td>
<td><img src="image2.png" alt="Product 1" /></td>
<td>1</td>
<td>96(90)[c][f]</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3.png" alt="Reactant 2" /></td>
<td><img src="image4.png" alt="Product 2" /></td>
<td>3(5)</td>
<td>82(70)[c]</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5.png" alt="Reactant 3" /></td>
<td><img src="image6.png" alt="Product 3" /></td>
<td>3(5)</td>
<td>90(87)[d]</td>
</tr>
<tr>
<td>4</td>
<td><img src="image7.png" alt="Reactant 4" /></td>
<td><img src="image8.png" alt="Product 4" /></td>
<td>45 min (5)</td>
<td>93(82)[c]</td>
</tr>
<tr>
<td>5</td>
<td><img src="image9.png" alt="Reactant 5" /></td>
<td><img src="image10.png" alt="Product 5" /></td>
<td>4(6)</td>
<td>92(85)[c]</td>
</tr>
<tr>
<td>6^[e]</td>
<td><img src="image11.png" alt="Reactant 6" /></td>
<td><img src="image12.png" alt="Product 6" /></td>
<td>6</td>
<td>85^[e]</td>
</tr>
</tbody>
</table>

^[a] Reaction conditions: Aryl halide (1.0 mmol), arylboronic acid (1.2 mmol), catalyst III (0.5 mol%), TBAB (0.5 mmol), H₂O (2.0 mL).

^[b] Yield were determined from the mass of biaryl products after column purification.
chromatography.

[a] Reaction temperature: 60-70°C; [b] 100°C.

[c] Pyridineboronic acid is used.

d] Reusability of the catalyst III for 1st, 2nd and 3rd runs of yields is 96, 87 and 70 respectively.

Where X = Br, I.

5.2.3 Heck coupling reaction

To a suspension of halobenzenes (1.0 mmol), styrene (1.2 mmol), K₂CO₃ (2.0 mmol) and Pd nanocatalyst (0.5 mol%) are added to a 25 mL round-bottom flask equipped with a magnetic stirrer. 5.0 mL of distilled dry DMF is added and the reaction mixture is stirred at 110 °C with heating on an oil bath for 4-6 h. The reaction is monitored by TLC (or GC if necessary). On completion of the reaction, the mixture is filtered and the filtrate poured into water (50 mL) and extracted with CH₂Cl₂ (3 × 15 mL). The combined organic phases are dried over Na₂SO₄ or Mg₂SO₄, filtered and evaporated in vacuum. The mixture is then purified by column chromatography over silica-gel or recrystallization to afford a product with high purity. Characterization of the products is performed by comparison of their ¹H-NMR, ¹³C-NMR and physical data with those of the authentic samples.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reactants</th>
<th>Products</th>
<th>Time (h)[c]</th>
<th>Yield (%)[b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td>2</td>
<td>95(91)[e]</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
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<td>89</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
<td>4</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
<td>5</td>
<td>85</td>
</tr>
<tr>
<td>5</td>
<td><img src="image9.png" alt="Image" /></td>
<td><img src="image10.png" alt="Image" /></td>
<td>3</td>
<td>90</td>
</tr>
</tbody>
</table>
[a] Reaction conditions: Aryl halide (1.0 mmol), styrene (1.2 mmol), Pd/SiO$_2$ (0.5 mol%), base (2.0 mmol) and DMF (3.0 mL).

[b] Yield was determined from the mass of biaryl products after column chromatography.

[c] Reaction temperature: 110°C.

[d] Styrene 2.4 mmol used.

[e] Reusability of the catalyst III for 1$^{st}$, 2$^{nd}$ and 3$^{rd}$ runs 95, 88 and 70 respectively. Where X = Br, I.

According to the above procedure after the completion of the reaction, the suspension is cooled down to room temperature and filtered off. The Pd/SiO$_2$ is washed with DMF, water and acetone. It is dried under vacuum and then used in the next reaction cycle with a new portion of reagents without any pretreatment.

5.2.4 Sonogashira coupling reaction

To a 50 mL round bottom flask equipped with a magnetic stirrer under N$_2$ atmosphere, ethylene glycol (3.0 mL) is added to the nanoparticles of Pd/SiO$_2$ (0.5 mol%), K$_2$CO$_3$ (2.0 mmol, 276 mg), aryl halide (1.0 mmol) and phenylacetylene (2.0 mmol) and the mixture is heated at 120-130°C for the appropriate reaction time. The progress of the reaction is monitored by TLC. After completion of the reaction, the reaction mixture is extracted with ethyl acetate or diethyl ether (25 mL) and the upper organic phase is separated and evaporated. Further purification is performed by column chromatography (EtOAc/n-hexane) to obtain the desired coupling product. For the recycling test, the recovered catalyst is further washed sufficiently with ethanol followed by water.
Table 5.3 Results of Sonogashira coupling reactions catalyzed by catalyst III\([a]\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reactants</th>
<th>Products</th>
<th>Time (h)([e])</th>
<th>Yield (%)([b])</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[image]</td>
<td>[image]</td>
<td>2</td>
<td>98(93)([e])</td>
</tr>
<tr>
<td>2</td>
<td>[image]</td>
<td>[image]</td>
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<tr>
<td>3</td>
<td>[image]</td>
<td>[image]</td>
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<td>85</td>
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<tr>
<td>4</td>
<td>[image]</td>
<td>[image]</td>
<td>5</td>
<td>92</td>
</tr>
</tbody>
</table>

\[a\] Reaction conditions: Aryl halide (1.0 mmol), phenylacetylene (1.5 mmol), catalyst III (0.5 mol %), base (2.0 mmol) and ethylene glycol (3.0 mL).

\[b\] Yield was determined from the mass of biaryl products after column chromatography.

\[c\] Reaction temperature: 120-130°C.

\[d\] Reusability of the catalyst III for 1\(^{st}\), 2\(^{nd}\) and 3\(^{rd}\) runs 98, 90 and 80 respectively.

Where X = Br, I.

5.3 Results and discussion

5.3.1 XRD Results

Powder XRD diffraction patterns (Figure 5.1) obtained for the mesoporous materials exhibit a broad reflection corresponding to the amorphous silica support. Four additional reflections are found in the XRD pattern that could be attributed to elemental palladium, in good agreement with the JCPDS 46-1043 file.\[95a\] All materials prepared exhibit a similar XRD pattern. Of note is the absence of any other reflections in the diffractogram, indicating the absence of significant quantities of the Pd precursor on the support. The PdNPs size is estimated from the XRD pattern using the Scherrer equation.\[95b\]
Figure 5.1 The XRD patterns of the catalyst III.

The peaks are observed in XRD pattern 2θ values at 40°, 45°, 68.3° and 81.5° these peaks correspond to the [111], [200], [220] and [311] planes of a fcc lattice, respectively, indicating that the PEI-Pd nanoparticles synthesized in the present study have the fcc structure.⁹⁵

5.3.2 HRTEM analysis

Synthesis of SiNPs and modified or functionalized with amine group on the surface of SiNPs are discussed in previous Chapter IV. Extremely small PdNPs have been successfully obtained from reduction of Pd(OAc)₂ precursor with highly branched polymer PEI. The morphology of these supported metal nanocomposites is characterized by high-resolution transmission electron microscopy (HRTEM). Specimens for HRTEM examination are prepared by dispersing a fraction of products in alcohol in the ultrasonic bath and then placing a drop of suspension on a copper grid coated with carbon film. Figure 5.2 shows the HRTEM images of as-prepared PEI capped PdNPs and it is found that spherical morphologies with size in the range of 5-10 nm are formed.
Figure 5.2 HRTEM images of PEI capped PdNPs. Scale bars (a) 50 nm, (b) 20 nm, (c) 10 nm and (d) 5 nm.
Palladium nanoparticles are adsorbed or covalently attached to the surface of the silica colloids. The PdNPs are verified to contain a great deal of palladium according to EDX analysis in Figure 5.3d.

5.3.3 BET surface area studies

Nitrogen adsorption and desorption isotherms on all the carbon samples at 77 K are measured to characterize their pore textural properties including BET surface area, pore volume, and pore size distribution. To verify the changes of the surface area and porous characteristics of the pure silica and PdNPs immobilized silica samples are evaluated by N₂ sorption analysis as shown in Figures 5.4a and 5.4b respectively.

Table 5.4 summarizes some physicochemical properties of the SiO₂ and Pd/SiO₂ catalysts. The BET surface area of the SiO₂ is 110.8 m²/g whereas those of the Pd/SiO₂ catalyst in the 87.8 m²/g respectively.
Figure 5.4 N\textsubscript{2} adsorption-desorption isotherms (a) amine functionalized SiO\textsubscript{2} and (b) corresponding Pd/SiO\textsubscript{2}.

Figure 5.4b, shows the corresponding isothermal curves of 1.0 wt\% Pd, which belongs to type IV sorption isotherms with hysteresis loop of type H1 according to the IUPAC classification.\textsuperscript{96a} The specific surface areas of the samples are estimated by the BET method (Brunauer-Emmet-Teller) in the relative pressure range of 0.05-0.20 from nitrogen desorption isotherms,\textsuperscript{96b} and the pore size distribution is determined by the BJH method (Barrett-Joyner-Halenda). The specific surface area of the silica decreases from 110.08 m\textsuperscript{2}/g to 87.08 m\textsuperscript{2}/g for catalyst III (Pd/SiO\textsubscript{2}) due to the immobilization of PdNPs, which may result from the deposition of PdNPs on the surface of silica. The small hysteresis of the composite indicates less mesoporosity present in the silica. From the N\textsubscript{2} sorption analysis, it is known that the total pore volume is reduced from 0.60 cm\textsuperscript{3}/g for silica to 0.17 cm\textsuperscript{3}/g for Pd/SiO\textsubscript{2}. This is due to pore blockages of metal particles during impregnation and/or calcination step. The same type of effects are observed for Pd/Al\textsubscript{2}O\textsubscript{3} and Pt/TiO\textsubscript{2} nanocatalysts.\textsuperscript{96c,d} Since the Pd catalysts tested, their nitrogen adsorption-desorption isotherms did not vary with respect to bare carriers and the BET area only decreased slightly upon palladium incorporation.\textsuperscript{96ef}

Finally, all the adsorption/desorption isotherms are of type IV as per IUPAC classification, and the hysteresis loops in the isotherms suggest the presence of mesopores in SiO\textsubscript{2}. 

\textsuperscript{96a}
### Table 5.4 Physicochemical properties of the SiO$_2$ and catalyst III

<table>
<thead>
<tr>
<th>Sample</th>
<th>Pd content (wt%)</th>
<th>BET surface area (m$^2$/g)</th>
<th>Langmuir surface area (m$^2$/g)</th>
<th>t-Plot external surface area (m$^2$/g)</th>
<th>Average pore diameter (nm)</th>
<th>Pore volume (cm$^3$/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SiO$_2$</td>
<td>-</td>
<td>110.8</td>
<td>186.9</td>
<td>126.9</td>
<td>33.0</td>
<td>0.60</td>
</tr>
<tr>
<td>Catalyst III</td>
<td>1.0</td>
<td>87.8</td>
<td>142.4</td>
<td>96.5</td>
<td>25.2</td>
<td>0.17</td>
</tr>
</tbody>
</table>

#### 5.3.4 SEM analysis

The scanning electron microscopy (SEM) images of SiNPs synthesized by Stöber method$^{92}$ are shown in Figure 5.5. The silica particles show very uniform spherical morphology and monodispersed distribution. The mean diameter of these particles is $\sim$180 nm, with very little distribution in particle size as shown in Figure 5.5.

![Figure 5.5](image)

**Figure 5.5** SEM images of the pure SiNPs in different magnifications (a) x 2500 and (b) x 9,500.
5.3.5 AFM analysis

Atomic force microscopy (AFM) is the one of the most widely used visualization techniques for micro and nanosized objects, and it suits the characterization of Pd/SiO$_2$ nanoparticles because it can give 3D information about the object under study in contrast to electron microscopy that usually represents only 2D images. The AFM images in two- and three dimension are shown in Figures 5.6a and 5.6b.

![AFM images of Pd/SiO$_2$](image)

Figure 5.6 AFM images of Pd/SiO$_2$ (a) in two-dimension (2-D) and (b) three dimension (3-D), (c) and (d) are high magnification of Pd/SiO$_2$ in 2-D and corresponding 3-D.
A magnified view highlights the presence of smaller PEI capped PdNPs “little bright spots” on the SiO$_2$ surface as shown in Figures 5.6c and 5.6d. The SiO$_2$ nanoparticle sizes are 100-150 nm but the size of PdNPs are not measured exactly from the AFM images.

5.3.6 UV-visible absorption spectroscopy

Heating played a critical role in the synthesis of the PEI capped Pd nanoparticles, from the reduction of Pd$^{2+}$ to Pd$^0$ with ascorbic acid. At 95 °C, the PEI-Pd$^{2+}$ solution turned to transparent light brown as soon as ascorbic acid is added, indicating rapid reduction of Pd$^{2+}$ and formation of fine PdNPs. UV-vis absorption spectroscopy is used to monitor the complete reduction of Pd$^{2+}$ to Pd$^0$ state.$^{97}$

The Pd$^{2+}$ is mixed with 1.0 wt % of PEI and stirred for 15-20 mins to form dark colored solution of PdNPs. Pd$^{2+}$ (yellow) is reduced, step-by-step, to Pd(0) (dark black) during the reaction: (a) Pd$^{2+}$ salt only, (b) mixture of Pd$^{2+}$ and PEI, (c) at approximately 15 min (d and e). After about 15 min, the absorption peak disappeared completely, which indicated that Pd$^{2+}$ is entirely reduced to Pd(0) Figures 5.7e and 5.7f. The increasing scattering absorbance at wavelengths between 300 and 800 nm with time reveal full conversion of Pd$^{2+}$ to Pd(0).

Figure 5.7 UV-vis absorption spectra of PEI stabilized PdNPs.
Spectra collected in Figures 5.7f and 5.7g show representative UV-vis absorption spectra of the prepared PEI-stabilized PdNPs in 30 days and 3 months after preparation. Both spectra feature a continual increase of absorbance at shorter wavelengths characteristic of nanosized palladium, which can account for the overall dark black colour appearance of the dispersion. Although both spectra show virtually identical profiles, it is observed that there is a slight decrease in the overall absorbance recorded after 3 month in comparison to that of the after 30 days.

5.3.7 FT-IR Spectroscopy

FT-IR spectra of pure SiO$_2$, amino modified SiO$_2$ and Pd/SiO$_2$ are recorded in the regions 4004-400 cm$^{-1}$. The FT-IR spectral assignments of dried and calcined samples of pure SiO$_2$, amino modified SiO$_2$ (NH$_2$-SiO$_2$) and palladium coated SiO$_2$ (Pd/SiO$_2$) are shown in Figure 5.8. The 2929 and 2856 cm$^{-1}$ bands are assigned to $\nu_{\text{CH}}$ of the -CH$_2$ groups, and the bands at 1544 cm$^{-1}$ and 1542 cm$^{-1}$ to $\delta_{\text{NH}}$ of the -NH$_2$ groups, both of which are associated with amino modified SiO$_2$ and Pd/SiO$_2$ catalyst skeleton respectively.
The strong peaks at 1076 and 790 cm\(^{-1}\) are due respectively to \(\nu_{\text{asym}}(\text{Si-O})\) and \(\nu_{\text{sym}}(\text{Si-O})\) of the Pd/SiO\(_2\) skeleton.\(^9\) Moreover, the presence of the amino groups confirms the formation of the amine-modified particles. The broad peak centered at 3400 cm\(^{-1}\) is an envelope of \(\nu_{\text{O-H}}\) for the adsorbed water, silanol groups, and \(\nu_{\text{N-H}}\) of the amino groups. It should be pointed out here that the band corresponding to the Si-OH group appears at 960 cm\(^{-1}\) as a shoulder (arrow) of the 1076 cm\(^{-1}\) Si-O-Si skeleton peak, and is little weaker than that found ever in the conventional SiO\(_2\) particles that exhibit a clear and well-defined peak of the Si-OH groups.

5.3.8 Suzuki coupling reaction of different aryl halides

Generally, the palladium-catalyzed Suzuki coupling reaction is performed under an inert atmosphere because the catalytic species are sensitive to oxygen or moisture. In this study, we investigated the effect of the atmosphere on the Suzuki reaction catalyzed by the Pd/SiO\(_2\) system. The results are shown in Table 5.1.

Nowadays, the Suzuki reaction is probably one of the most popular Pd-catalyzed coupling reactions.\(^\text{101}\) This reaction involving heterocycles is of interest to the pharmaceutical industry because of the special biological activities displayed by the hetero biaryl compounds.\(^\text{102}\) We first tested Pd/SiO\(_2\) in the Suzuki reaction of aryl iodides with phenylboronic acid in water (Table 5.1). We used water as the reaction medium for environmental benefit, even though the activity is accelerated in organic solvents. Tetrabutylammonium bromide (TBAB), a phase transfer agent is added to enhance the reactivity in water. Various substituted (-CH\(_3\), -OCH\(_3\), -COCH\(_3\) and -NO\(_2\)) iodo- and bromobenzenes were coupled with arylboronic acid in the presence of 0.5 mol% of catalyst III at 60-70\(^\circ\)C to afford the corresponding products in excellent yields (entries 1-6).

Suzuki cross coupling reactions of various aryl halides are carried out using the Pd/SiO\(_2\) catalyst. Aryl iodides produced the coupling products close to 90% yield, except for 4-iodotoluene (82%, Table 5.1, entries 1-6). The aryl bromides give executable product yields (66-92%, Table 5.1, entries 1-6). Overall, the catalyst III shows excellent catalytic activity in the Suzuki cross-coupling reaction with the need of phase transfer reagent (TBAB) in water. 4-Bromopyridine reacts with pyridin-4-
ylboronic acid to give low yield (85%) compared with phenylboronic acid. It is less soluble in water so that the phenylboronic acid reacts faster than the pyridin-4-ylboronic acid.

The feasibility of recycling the Pd/SiO$_2$ catalyst is also examined. After the reaction, the catalyst III is simply recovered by ultracentrifugation followed by washing with ethanol and drying in vacuum for 2-3 days. However, we observe that for the catalytic activity of vacuum dried catalyst III, is decreased only little amount in the third cycle.

5.3.9 Effect of solvents and bases on Suzuki coupling reaction

The chemical conditions for performing Suzuki-Miyaura coupling reactions generally employ the use of phosphine ligands along with Pd. However, Pd-catalyzed Suzuki coupling under phosphine-free conditions is a topic of considerable interest because of both economic and environmental reasons. Another limitation of Suzuki-Miyaura coupling is that more economical aryl bromides are less reactive than aryl iodides.
Table 5.5 Suzuki coupling reaction between iodobenzene and phenylboronic acid in the presence of different bases

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NaOAc</td>
<td>H₂O</td>
<td>81</td>
</tr>
<tr>
<td>2</td>
<td>NaOH</td>
<td>H₂O</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>K₂CO₃</td>
<td>H₂O</td>
<td>96</td>
</tr>
<tr>
<td>4</td>
<td>KOH</td>
<td>H₂O</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>Triethylamine</td>
<td>H₂O</td>
<td>89</td>
</tr>
<tr>
<td>6</td>
<td>Pyridine</td>
<td>H₂O:EtOH</td>
<td>82 [c]</td>
</tr>
<tr>
<td>7</td>
<td>Na₂CO₃</td>
<td>H₂O</td>
<td>60</td>
</tr>
</tbody>
</table>

[a] Reaction conditions: Iodobenzene (1.0 mmol), arylboronic acid (1.2 mmol), catalyst III (0.5 mol%), TBAB (0.5 mmol), H₂O (2.0 mL) and 60-70°C.

[b] The yields were determined from the mass of biaryl products after column chromatography.

[c] EtOH:H₂O (1:1) was used.

In order to determine the optimal reaction conditions, various types of bases were screened in Table 5.5. Among the bases examined in the reaction of 4-iodobenzene and phenylboronic acid, K₂CO₃ was found to be most suitable because it gave the highest product yield (Table 5.5, entry 3). The Suzuki cross-coupling reactions with our supported catalyst (Pd/SiO₂) were carried out in water at 60-70 °C using aryl bromides and iodides as substrates and phenyl boronic acids as nucleophiles. Also in this case, reaction conditions were chosen after a series of initial experiments carried out at different solvents and with different bases. Among the latter, TBAB (phase transfer catalyst) was confirmed as the most efficient. In addition, the aqueous medium proved to have a positive effect on the reaction rate probably because of its ability to dissolve boron side products coating the catalyst surface.
5.3.10 Proposed mechanism for Suzuki reaction

The proposed mechanism for the Suzuki coupling reaction as shown in Scheme 5.30.

Scheme 5.30 Possible mechanism of Suzuki coupling reaction.

In step I, the formation of PdNPs is shown from the source of Pd(OAc)$_2$ using ascorbic acid as reducing agent. It is believed that Pd(0) is the catalytic species and that the reaction proceeds through the usual interaction of aryl halide and silica supported on Pd(0) to form the aryl-palladium halide complex [Ar-(Pd$^{2+}$)-X] as shown in Step II.$^{33b,103}$ The aryl palladium halide complex then couples with arylboronic acid, (Ph-B(OH)$_2$) in the presence of a base to produce the aryl-Pd(II) intermediate [Ar-(Pd$^{2+}$)-Ph] in Step III, and finally providing the biaryl product (Ar-Ph) via the reductive elimination of Pd$^{2+}$ to Pd(0) as in Step IV and also outlined in Scheme 5.30. The coupling reaction does not proceed at all in the absence of PdNPs.$^{103}$
5.3.11 Comparison of other catalyst systems on Suzuki reaction

A number of articles describing the use of supported palladium nanoparticles or composites as catalysts have been published.\textsuperscript{104-107} Most of them employed phenylboronic acid with bromo- and iodoarenes in C-C coupling reactions with yields altered from 21\% to 99\% as shown in Table 5.6.

The iron oxide (Fe\textsubscript{2}O\textsubscript{3}) supported PdNPs show good catalytic activity in the Suzuki reaction of iodobenzene with phenylboronic acid to form C-C of biaryls (Table 5.6 entry 2-8, and 12-15). The Pd/NiFe\textsubscript{3}O\textsubscript{4} nanocatalyst shows very large size (100-300 nm) compared to other catalysts systems. Toluene is one of the environmental toxic solvents (Table 5.6 entry 2, and 17); it causes environmental pollution and health troubles in living animals. In this study, we investigate the reaction carried out with Pd/SiO\textsubscript{2} catalyst with water as the solvent, to develop a green and low-cost strategy.

Comparison of our results with those of some of the recently published procedures using different nanocatalysts for Suzuki coupling.\textsuperscript{104-107} We find that this procedure provides significant advantages in terms of reaction time, simplicity of operation, and yields of products compared to other catalytic systems. In addition, this procedure provides the products without assistance of any copper salts and ligands.
Table 5.6 Comparison of other catalyst systems on Suzuki reaction of halobenzenes with phenylboronic acid.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalysts[^a]</th>
<th>Size (nm)</th>
<th>Mol (%)</th>
<th>Time (h)</th>
<th>Temp (°C)</th>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Au-G[^104a]</td>
<td>2-3</td>
<td>1.0</td>
<td>4</td>
<td>100</td>
<td>H₂O</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td>Fe₂O₃-Bpy-Pd(OAc)₂[^104b]</td>
<td>6-20</td>
<td>15 mg</td>
<td>6</td>
<td>80</td>
<td>Toluene</td>
<td>&gt;99</td>
</tr>
<tr>
<td>3</td>
<td>Pd/NiFe₂O₄[^104c]</td>
<td>100-300</td>
<td>0.1</td>
<td>5</td>
<td>90</td>
<td>DMF: H₂O (1:1)</td>
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</tr>
<tr>
<td>4</td>
<td>Pd/NiFe₂O₄[^104d]</td>
<td>10-12</td>
<td>50 mg</td>
<td>30</td>
<td>110</td>
<td>DMF</td>
<td>97</td>
</tr>
<tr>
<td>5</td>
<td>Pd/NiFe₂O₄[^106a]</td>
<td>&gt;50</td>
<td>0.08</td>
<td>4</td>
<td>80</td>
<td>NMP: H₂O (5:2)</td>
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</tr>
<tr>
<td>6</td>
<td>Pd-Fe₃O₄ nanocrystals[^104d]</td>
<td>36</td>
<td>1.0</td>
<td>24</td>
<td>&gt;80</td>
<td>DME: H₂O (3:1)</td>
<td>99</td>
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<tr>
<td>7</td>
<td>Pd/G[^105a]</td>
<td>7-9</td>
<td>0.3</td>
<td>10</td>
<td>~80</td>
<td>H₂O: EtOH (1:1)</td>
<td>&gt;99</td>
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<td>8</td>
<td>Pd/GO[^105a]</td>
<td>12-18</td>
<td>0.3</td>
<td>10</td>
<td>~80</td>
<td>H₂O: EtOH (1:1)</td>
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<tr>
<td>9</td>
<td>Pd-SBA-15[^105b]</td>
<td>1.5</td>
<td>0.5</td>
<td>30 min</td>
<td>100</td>
<td>H₂O: EtOH (3:2)</td>
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<tr>
<td>10</td>
<td>Pd-SBA-16[^47b]</td>
<td>10-25</td>
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<td>5</td>
<td>50</td>
<td>EtOH</td>
<td>99</td>
</tr>
<tr>
<td>11</td>
<td>Fe₂O₃-Pd(0)[^105c]</td>
<td>8-10</td>
<td>5.0</td>
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<td>50</td>
<td>DMF</td>
<td>54</td>
</tr>
<tr>
<td>12</td>
<td>Ru/Al₂O₃[^106b]</td>
<td>2-3</td>
<td>5.0</td>
<td>12</td>
<td>60</td>
<td>DME: H₂O (1:1)</td>
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</tr>
<tr>
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<td>LDH-Pd(0)[^51b]</td>
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<td>1.0</td>
<td>10</td>
<td>100</td>
<td>1,4-Dioxane: H₂O (5:1)</td>
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<td>14</td>
<td>Diatomite-Pd(0)[^66a]</td>
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<td>20 min</td>
<td>110</td>
<td>DME: H₂O (1:1)</td>
<td>95</td>
</tr>
<tr>
<td>15</td>
<td>Polyoxometallate-Pd(0)[^106c]</td>
<td>15-20</td>
<td>0.01</td>
<td>12</td>
<td>80-85</td>
<td>H₂O: EtOH (1:4)</td>
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</tr>
<tr>
<td>16</td>
<td>MES-Mes(20%)-Pd[^107a]</td>
<td>&gt;20</td>
<td>0.5</td>
<td>24</td>
<td>80</td>
<td>Isopropyl alcohol</td>
<td>78</td>
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<tr>
<td>17</td>
<td>Organostannoxane-Pd(0)[^107b]</td>
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<td>5.0 mg</td>
<td>4</td>
<td>110</td>
<td>Toluene</td>
<td>95</td>
</tr>
<tr>
<td>18</td>
<td>Pd/SiO₂[^107c]</td>
<td>&gt;100</td>
<td>100 mg</td>
<td>12</td>
<td>100</td>
<td>CH₃CN: H₂O (3:1)</td>
<td>&gt;90</td>
</tr>
<tr>
<td>19</td>
<td>SiO₂</td>
<td>&gt;100</td>
<td>0.5</td>
<td>12</td>
<td>60-70</td>
<td>H₂O</td>
<td>Trace[^b]</td>
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<tr>
<td>20</td>
<td>NH₂-SiO₂</td>
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<td>0.5</td>
<td>12</td>
<td>60-70</td>
<td>H₂O</td>
<td>Trace[^c]</td>
</tr>
<tr>
<td>21</td>
<td>Catalyst III</td>
<td>5-6</td>
<td>0.5</td>
<td>1</td>
<td>60-70</td>
<td>H₂O</td>
<td>96[^d]</td>
</tr>
</tbody>
</table>
5.3.12 The role of the Pd/SiO$_2$ on Heck coupling reactions

The Heck coupling, often referred to as the Mizoroki-Heck reaction is, first reported by Heck in 1968, is the alkenylation of aromatic compounds through the reaction of substituted aromatics (halides, triflates, or diazonium derivatives called the Matsuda-Heck reaction, etc.) and alkenes.$^{108}$

The Pd/SiO$_2$ catalyst is also examined for a series of Heck coupling reactions in DMF solvents by using derivatives of bromo, iodoarenes with styrene. The results are listed in Table 5.2. As shown in Table 5.2, all of the obtained products are trans-isomers, which are identified by $^1$H-NMR analysis. When activated aryl bromides are used as starting materials, good conversion is also obtained with K$_2$CO$_3$ as the base (Table 5.2, entries 5-7). We introduced dibromo arenes (Table 5.2, entries 6 and 7), 2.4 mmol of styrene are required to complete the reaction to afford good yields 92 and 90 % respectively.

5.3.13 Effect of solvents and bases on Heck coupling reactions

The activity of the silica supported Pd nanocatalyst is first examined in the Heck coupling reaction of different aryl halides with styrene in Table 5.2. In a model reaction, the coupling of iodobenzene with styrene is initially studied. In the process of coupling reaction the choice of solvent and base is crucial, so these parameters are optimized and the results are summarized in Table 5.7. It is found that the best system is DMF as the solvent and K$_2$CO$_3$ as the base using 0.5 mol% of Pd/SiO$_2$ catalyst at 120$^\circ$C.
Table 5.7 Effect of different solvents and bases on the reaction of iodobenzene with styrene\textsuperscript{[a]}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Solvent\textsuperscript{[c]}</th>
<th>Yield (%)\textsuperscript{[b]}</th>
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</thead>
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<tr>
<td>1</td>
<td>NaOAc</td>
<td>H\textsubscript{2}O</td>
<td>70</td>
</tr>
<tr>
<td>2</td>
<td>NaOH</td>
<td>EtOH</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>K\textsubscript{2}CO\textsubscript{3}</td>
<td>EtOH</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>KOH</td>
<td>EtOH</td>
<td>89</td>
</tr>
<tr>
<td>5</td>
<td>Triethylamine</td>
<td>H\textsubscript{2}O</td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td>Pyridine</td>
<td>DMSO</td>
<td>78</td>
</tr>
<tr>
<td>7</td>
<td>K\textsubscript{2}CO\textsubscript{3}</td>
<td>DMF</td>
<td>95</td>
</tr>
<tr>
<td>8</td>
<td>NaOH</td>
<td>DMF</td>
<td>90</td>
</tr>
<tr>
<td>9</td>
<td>Cs\textsubscript{2}CO\textsubscript{3}</td>
<td>DMF</td>
<td>93</td>
</tr>
<tr>
<td>10</td>
<td>Na\textsubscript{2}CO\textsubscript{3}</td>
<td>DMF</td>
<td>60</td>
</tr>
</tbody>
</table>

\textsuperscript{[a]}Reaction conditions: Iodobenzene (1.0 mmol), styrene (1.2 mmol), catalyst III (0.5 mol%), base (2.0 mmol) and solvent (3.0 mL).

\textsuperscript{[b]}The yields were determined from the mass of biaryl products after column chromatography.

\textsuperscript{[c]}Reaction temperature: 110\degree C.

5.3.14 Proposed mechanism for Heck reaction

The possible mechanism for the silica supported PdNPs catalyzed Heck reaction is shown in Scheme 5.31.\textsuperscript{33b,62} The process starts from reduction of Pd(OAc)\textsubscript{2} and formation of Pd(0) nanoparticles (Step I). The oxidative addition of aryl halide to a silica supported nano Pd(0) to form a complex is a key step in Heck reaction. Activation of aryl halide [Ar-X] via oxidative addition produces a Pd(II) complex [Ar-Pd\textsuperscript{2+}-X] with aryl and halide ligands coordinated to the palladium metal as shown in Step II.
Scheme 5.31 Possible mechanism of Heck coupling reaction.

The formed complex next reacts with olefin forming an \( \pi \)-olefin complex (Step III). The olefin bonded to palladium undergoes a migratory insertion forming a new C-C bond, followed by \( \beta \)-hydride elimination (Steps IV and V) and removal of the final product (Step VI), arylated olefin from the coordination sphere of palladium. Palladium remains after this stage in the form of a hydrido complex and is converted back to the initial form by reaction with a base acting as H-X acceptor (Scheme 5.31).\(^{1c}\).

5.3.15. Comparison with other catalyst systems on Heck reaction

The Heck reaction is one of the most versatile tools in modern synthetic chemistry and has great potential for future industrial applications. However, heterogeneous palladium catalysts suffer from reusability, due to either aggregation of the particles or leaching of the particles from the supports during the reactions.
Therefore, we are interested in evaluating the performance of our nanocatalyst (Pd/SiO$_2$) for arylation of styrene with iodobenzene (Scheme 5.28).

Comparison of the activity of various heterogeneous nanocatalysts on the Heck reaction of bromobenzene with styrene is listed in Table 5.8. Different kinds of support have large impact on the dispersion of PdNPs. Also, the interaction between PdNPs and support is different, which has great influence on the stability of Pd. It seems that most of the reactions are conducted in DMF medium (Table 5.8, entries 3, 5, 12 and 16-18). Due to its wide liquid temperature range, good chemical and thermal stability (even at its boiling point, 153 °C), high polarity and wide solubility range for both organic and inorganic compounds. This unique versatile and powerful chemical has been used as a solvent in a wide variety of synthetic procedures, including preparation of colloids,$^5$ and many types of organic chemical reactions. Our catalyst system performed in very short time to complete the reaction (2 h) to afford moderate yield (95 %).
Table 5.8 Comparison of other catalyst systems in Heck reaction of halobenzenes with styrene.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalysts $^a$</th>
<th>Size (nm)</th>
<th>Mol (%)</th>
<th>Time (h)</th>
<th>Temp ($^\circ$C)</th>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NHC-Pd/SBA-16-IL $^{47b}$</td>
<td>10-20</td>
<td>0.01</td>
<td>40</td>
<td>140</td>
<td>NMP</td>
<td>94</td>
</tr>
<tr>
<td>2</td>
<td>Ni(0)NPs</td>
<td>&gt;100</td>
<td>0.02</td>
<td>16</td>
<td>140</td>
<td>H$_2$O</td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>Polyaniline/Ni(0)</td>
<td>1.52</td>
<td>5.0</td>
<td>15-20</td>
<td>130</td>
<td>DMF</td>
<td>95</td>
</tr>
<tr>
<td>4</td>
<td>[Pd]-APTS-Y $^{109a}$</td>
<td>4.5-5</td>
<td>0.075g</td>
<td>2</td>
<td>120</td>
<td>DMAC</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>Pd/(C@ (Au@Fe)) $^{109b}$</td>
<td>250-300</td>
<td>0.25</td>
<td>4</td>
<td>100</td>
<td>DMF</td>
<td>98</td>
</tr>
<tr>
<td>6</td>
<td>Hollow Pd-Fe $^{109c}$</td>
<td>200</td>
<td>0.02</td>
<td>24</td>
<td>90</td>
<td>H$_2$O</td>
<td>95</td>
</tr>
<tr>
<td>7</td>
<td>Pd/C $^{109d}$</td>
<td>2.4-23</td>
<td>0.01</td>
<td>2-3</td>
<td>80-140</td>
<td>NMP</td>
<td>88</td>
</tr>
<tr>
<td>8</td>
<td>Pd/(SiO$_2$/Fe$_3$O$_4$) $^{110a}$</td>
<td>100</td>
<td>15 mg</td>
<td>12</td>
<td>80-90</td>
<td>CH$_3$CN:H$_2$O (1:3)</td>
<td>71</td>
</tr>
<tr>
<td>9</td>
<td>Fe$_3$O$_4$-NH$_2$-Pd $^{110b}$</td>
<td>35</td>
<td>5.0</td>
<td>10</td>
<td>130</td>
<td>NMP</td>
<td>&gt;99</td>
</tr>
<tr>
<td>10</td>
<td>PIC-PdNPs $^{110c}$</td>
<td>2.6-2.7</td>
<td>1.0</td>
<td>20</td>
<td>80</td>
<td>H$_2$O</td>
<td>99</td>
</tr>
<tr>
<td>11</td>
<td>Pd/PS-IL[Cl] $^{110d}$</td>
<td>4-6</td>
<td>0.2</td>
<td>6</td>
<td>100</td>
<td>H$_2$O</td>
<td>42</td>
</tr>
<tr>
<td>12</td>
<td>Ru/Al$_2$O$_3$ $^{106h}$</td>
<td>2-3</td>
<td>5.0</td>
<td>12</td>
<td>135</td>
<td>DMF</td>
<td>91$^f$</td>
</tr>
<tr>
<td>13</td>
<td>LDH-Pd(0)$^{51h}$</td>
<td>4-6</td>
<td>3.0</td>
<td>0.5</td>
<td>130</td>
<td>NMP</td>
<td>95</td>
</tr>
<tr>
<td>14</td>
<td>Diatomite-Pd(0)$^{45a}$</td>
<td>20-100</td>
<td>0.1</td>
<td>2</td>
<td>120</td>
<td>DME:H$_2$O (1:1)</td>
<td>92</td>
</tr>
<tr>
<td>15</td>
<td>Pd/C Nanofiber $^{111a}$</td>
<td>40-150</td>
<td>0.01</td>
<td>10</td>
<td>120</td>
<td>NMP</td>
<td>95</td>
</tr>
<tr>
<td>16</td>
<td>Pd(0)MCM-41$^{59a}$</td>
<td>3-4</td>
<td>0.05g</td>
<td>24</td>
<td>100</td>
<td>DMF</td>
<td>90</td>
</tr>
<tr>
<td>17</td>
<td>PVP-Pd/SiO$_2$ $^{111b}$</td>
<td>20-25</td>
<td>0.5</td>
<td>1.0</td>
<td>120</td>
<td>DMF</td>
<td>93</td>
</tr>
<tr>
<td>18</td>
<td>Polyoxometalate -Pd(0)$^{111c}$</td>
<td>20</td>
<td>63mg</td>
<td>2.0</td>
<td>100</td>
<td>DMF</td>
<td>93</td>
</tr>
<tr>
<td>19</td>
<td>SiO$_2$</td>
<td>&gt;100</td>
<td>0.5</td>
<td>12</td>
<td>110</td>
<td>DMF</td>
<td>trace</td>
</tr>
<tr>
<td>20</td>
<td>NH$_2$-SiO$_2$</td>
<td>&gt;100</td>
<td>0.5</td>
<td>12</td>
<td>110</td>
<td>DMF</td>
<td>trace</td>
</tr>
<tr>
<td>21</td>
<td>Catalyst III</td>
<td>5-6</td>
<td>0.5</td>
<td>2</td>
<td>110</td>
<td>DMF</td>
<td>95</td>
</tr>
</tbody>
</table>
References.

Reactions conditions as exemplified in the experimental procedure.

Where, PIC = Polyion complex; DMF = Dimethylformamide; DME = Dimethyl ether; NMP = N-Methyl-2-pyrrolidone; DMAC = N,N'-dimethyl acetamide; CH$_3$CN = Acetonitrile respectively.

5.3.16. Effect of solvents and bases in Sonogashira coupling reactions

The effect of different solvents upon the reaction of iodobenzene (1.0 mmol) with phenylacetylene (2.0 mmol) as a model reaction in the presence of K$_2$CO$_3$ (2.0 mmol) and 0.5 mol% of the nanocatalyst (catalyst III) at 125°C is studied (Table 5.9). The results show that ethylene glycol (EG) is a suitable solvent for the reaction. EG possesses negligible vapour pressure, is thermally stable, is not so expensive with a low toxicity.$^{112}$ Ethylene glycol is highly soluble in water, and can be easily separated from the organic phase by addition of water to the reaction mixture.
Table 5.9 Effect of different solvents and bases on the reaction of iodobenzene and phenylacetylene[^a]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Solvent[^c]</th>
<th>Yield (%)[^b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NaOAc</td>
<td>H₂O</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>NaOH</td>
<td>DMF</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>K₂CO₃</td>
<td>EG</td>
<td>98</td>
</tr>
<tr>
<td>4</td>
<td>KOH</td>
<td>EG</td>
<td>70</td>
</tr>
<tr>
<td>5</td>
<td>Triethylamine</td>
<td>EG</td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td>Pyridine</td>
<td>DMSO</td>
<td>75</td>
</tr>
<tr>
<td>7</td>
<td>K₂CO₃</td>
<td>Toluene</td>
<td>Trace</td>
</tr>
<tr>
<td>8</td>
<td>NaOH</td>
<td>EG</td>
<td>65</td>
</tr>
<tr>
<td>9</td>
<td>Na₂CO₃</td>
<td>EG</td>
<td>83</td>
</tr>
</tbody>
</table>

[^a]: Reaction conditions: Aryl halide (1.0 mmol), phenylacetylene (1.2 mmol), catalyst III (0.5 mol%), base (2.0 mmol) and solvent (3.0 mL).

[^b]: Yields were determined from the mass of products after column chromatography.

[^c]: Reaction temperature: 120°C.

5.3.17 Proposed mechanism for Sonogashira reaction

This proposed mechanism of Sonogashira reaction is similar to the Heck coupling reaction as shown in Scheme 5.32.
Scheme 5.32 Possible mechanism of Sonogashira coupling reaction.

The active nano Pd(0) catalyst, reduced from a Pd(II) precursor, enters a catalytic cycle where subsequent oxidative addition of an aryl halide occurs. This process is followed by adduct alkylation to give the aryl alkynyl derivative of palladium which regenerates Pd(0) by the reductive elimination of substitution product (Steps I-VI). Various metal nanoparticles (e.g., Pd, Ti, and Ru) were also prepared by virtue of the formation of metals carbon (M-C≡) single bonds. It is evident for the interaction of alkyne group with metal nanoparticles.

5.3.18 Comparison with other catalyst systems in Sonogashira reaction

Comparison of the activity of various heterogeneous nanocatalysts in the Sonogashira reaction of iodo- and bromobenzene with phenylacetylene published in the literature is listed in Table 5.10.
Hyeon and co-workers synthesized Pd/Ni bimetallic nanoparticles with a cheap metal core (Ni) and a noble metal shell (Pd), which can be used in Sonogashira coupling reactions. The toxic organic solvent diisopropylamine (DIA) or toluene, however, should be used for this reaction. At high temperature was maintained $>120 \, ^\circ\text{C}$ to complete the reaction (Table 5.10, entries 2, 8 and 10).

Lanthana ($\text{La}_2\text{O}_3$) supported AuNPs$^{82a}$ applying Sonogashira coupling reactions of iodobenzene and phenylacetylene to yield both the desired Sonogashira cross-coupling product (diphenylacetylene) and the two homocoupling side products (diphenyldiacetylene and biphenyl) are identified. But our case no byproducts are observed. Cu$_2$O$^{85}$ and Pd-containing bimetallic hollow nanospheres$^{114b}$ successfully used to catalyze the Sonogashira reaction, but one of the drawbacks is the reaction proceeded with assistance of co-catalysts and ligand (CuI and PPh$_3$). But our system without assistance of any copper and other ligands required in the reaction.

The temperature range from 30 to 140 $^\circ\text{C}$ has been the most commonly used to Sonogashira transformations using different types of palladium catalysts as shown in Table 5.10. Indeed, it was previously reported that the Sonogashira reaction using phosphine-based catalysts could also occur at 80 $^\circ\text{C}$. The effect of temperature on the reaction conversion was therefore addressed. Experimental results showed that pure (-SiO$_2$) and amine modified silica (-NH$_2$-SiO$_2$) afforded traces amount are observed. (Table 5.10 entries 16 and 17). The Sonogashira reaction was carried out in EG using 0.5 mol% palladium catalyst (Catalyst III) to gives 98 % of yield was achieved after 1 h at the reaction temperature of 120$^\circ$C. The most effective temperature range for the Sonogashira reaction using the immobilized palladium catalyst in this research was in good agreement with the literatures shown in Table 5.10.

The effect of catalyst concentration on the reaction conversion was then studied, using EG as the solvent and K$_2$CO$_3$ as the base at 120$^\circ$C. As with previous reports, the higher the catalyst concentration (Table 5.10, entries 3, 8, 11-13 and 18) was used, the higher the reaction rate was observed. It was observed that 98% conversion was achieved after 1 h at the palladium concentration of 0.5 mol%. The catalyst concentrations used in this study were comparable to those of several
previous reports covering different aspects of the Sonogashira reaction, where the palladium concentrations varied from less than 0.5 mol% to more than 5 mol%, depending on the nature of the catalysts as well as the substrates as shown Table 5.10. We could be rationalized based on the fact that the homo-coupling of phenylacetylene increased significantly at 1.0 mol% catalyst, leaving no phenylacetylene for the cross-coupling reaction. It was therefore decided to use 0.5 mol% catalyst for further experiments.
Table 5.10 Comparison of other catalyst systems on Sonogashira reaction of halobenzenes with phenylacetylene.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalysts$^{[a]}$</th>
<th>Size (nm)</th>
<th>Mol (%)</th>
<th>Time (h)</th>
<th>Temp ($^\circ$C)</th>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pd-Ni$^{88a}$</td>
<td>2-3</td>
<td>2.0</td>
<td>2</td>
<td>80</td>
<td>Toluene</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>Au/Ag/Pd$^{88c}$</td>
<td>4.2-4.4</td>
<td>0.5</td>
<td>2</td>
<td>140</td>
<td>DMF:H$_2$O (3:1)</td>
<td>99</td>
</tr>
<tr>
<td>3</td>
<td>Gelatin-Pd$^{114a}$</td>
<td>4-7</td>
<td>0.05</td>
<td>45min</td>
<td>100</td>
<td>PEG</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>PdCo bimetallic hollow nanospheres$^{114b}$</td>
<td>60-90</td>
<td>0.05</td>
<td>6</td>
<td>80</td>
<td>H$_2$O</td>
<td>92</td>
</tr>
<tr>
<td>5</td>
<td>CoFe$_2$O$_4$-NH$_2$-Pd-complex$^{114c}$</td>
<td>30-40</td>
<td>1.0</td>
<td>2</td>
<td>80</td>
<td>DMF</td>
<td>93</td>
</tr>
<tr>
<td>6</td>
<td>Rh/Al$_2$O$_3$ $^{114d}$</td>
<td>2.0</td>
<td>100 mg</td>
<td>24</td>
<td>120</td>
<td>DMF</td>
<td>57</td>
</tr>
<tr>
<td>7</td>
<td>PS-PdO$^{97}$</td>
<td>2.3</td>
<td>1.5</td>
<td>6</td>
<td>80</td>
<td>H$_2$O</td>
<td>99</td>
</tr>
<tr>
<td>8</td>
<td>Cu$_2$O$^{85}$</td>
<td>10</td>
<td>10</td>
<td>24</td>
<td>135-140</td>
<td>DMF</td>
<td>96</td>
</tr>
<tr>
<td>9</td>
<td>Pd(0)/[bbim]BF$_4$ $^{90}$</td>
<td>3-8</td>
<td>0.02</td>
<td>15 min</td>
<td>30</td>
<td>Acetone</td>
<td>85</td>
</tr>
<tr>
<td>10</td>
<td>La$_2$O$_3$-Au(0)$^{82a}$</td>
<td>20</td>
<td>30 mg</td>
<td>160</td>
<td>145</td>
<td>DMF</td>
<td>0.41</td>
</tr>
<tr>
<td>11</td>
<td>LDH-Pd(0)$^{51b}$</td>
<td>4-6</td>
<td>1.0</td>
<td>30-48</td>
<td>80</td>
<td>THF:H$_2$O (1:1)</td>
<td>95</td>
</tr>
<tr>
<td>12</td>
<td>PVP-Pd(0)$^{96}$</td>
<td>7.0</td>
<td>1.06 mg</td>
<td>6</td>
<td>80</td>
<td>EtOH</td>
<td>95</td>
</tr>
<tr>
<td>13</td>
<td>Pd/MOF-5$^{87}$</td>
<td>3-6</td>
<td>3.0 wt%</td>
<td>3</td>
<td>80</td>
<td>MeOH</td>
<td>86</td>
</tr>
<tr>
<td>14</td>
<td>Ru/Al$_2$O$_3$ $^{83}$</td>
<td>2-3</td>
<td>5.0</td>
<td>24</td>
<td>90</td>
<td>CH$_3$CN</td>
<td>85</td>
</tr>
<tr>
<td>15</td>
<td>Fe$_3$O$_4$ $^{91d}$</td>
<td>&lt;30</td>
<td>11 mg</td>
<td>35</td>
<td>125</td>
<td>EG</td>
<td>92</td>
</tr>
<tr>
<td>16</td>
<td>SiO$_2$</td>
<td>&gt;100</td>
<td>0.5</td>
<td>12</td>
<td>120</td>
<td>EG</td>
<td>Trace$^{[b]}$</td>
</tr>
<tr>
<td>17</td>
<td>NH$_2$-SiO$_2$</td>
<td>&gt;100</td>
<td>0.5</td>
<td>12</td>
<td>120</td>
<td>EG</td>
<td>Trace$^{[b]}$</td>
</tr>
<tr>
<td>18</td>
<td>Catalyst III</td>
<td>5-6</td>
<td>0.5</td>
<td>1</td>
<td>120</td>
<td>EG</td>
<td>98$^{[d]}$</td>
</tr>
</tbody>
</table>

$^{[a]}$ Size, mol, time, solvent and yield refer to the original data, and the catalyst systems used in the experiments.
5.3.19 The role of ascorbic acid as reducing agent

Aqueous solution of ascorbic acid (vitamin C) has been widely used as a reducing agent.\textsuperscript{115} To prevent oxidation, the reaction solutions are carefully deoxygenated and the entire process is were performed under rigorous protection of inert gas in many reported studies.\textsuperscript{116} Synthesis of the PEI stabilized PdNPs in aqueous solution using ascorbic acid as the reducing agent at room temperature is investigated. While ascorbic acid (standard electrode potential, $E^0 = 0.058$ V for dehydroascorbic acid/ascorbic acid redox system) is capable of reducing Pd$^{2+}$ into Pd(0) ground-state at room temperature ($E^0 = 0.915$ V for Pd$^{2+}$/Pd redox system).\textsuperscript{117}

During the synthesis process, ascorbic acid plays a role as reducing agent, and in the storage, excessive ascorbic acid is essential to avoid oxidation of PdNPs. The antioxidant properties of ascorbic acid come from its ability to scavenge free radicals and reactive oxygen molecule, accompanying the donation of electrons to give the semi-dehydroascorbate radical and dehydroascorbic acid (Scheme 5.33).

Scheme 5.33 Reduction reaction of Pd$^{2+}$ with ascorbic acid.

Therefore, ascorbic acid plays dual roles of reducing agent and antioxidant of PdNPs. The reaction can complete without protective gas. The brief 10 min heating
played a critical role in the synthesis of the Pd nanoparticles, \(i.e.,\) reduction of \(\text{Pd}^{2+}\) to \(\text{Pd}^0\) with ascorbic acid. At 95 \(^\circ\text{C}\), the PEI-Pd\(^{2+}\) solution is turned to transparent dark black as soon as ascorbic acid is added indicating rapid reduction of \(\text{Pd}^{2+}\) and formation of fine PdNPs as given in **Figure 5.7**.

### 5.4 Conclusions

In summary, we have demonstrated that synthesized silica supported PdNPs is successfully employed in the Suzuki, Heck and Sonogashira coupling reactions. The PdNPs are synthesized using highly branched PEI as a capping agent and ascorbic acid as a reducing agent in aqueous solution at 95\(^\circ\text{C}\). Though the Suzuki cross-coupling reaction occurs in aqueous media, Heck and Sonogashira coupling reactions are conducted in DMF and ethylene glycol respectively. The catalysts are characterized by XRD, HRTEM, BET, SEM-EDX, AFM, FT-IR, and UV-vis spectral techniques.
5.5 Spectral analysis

5.5.1 NMR data of Suzuki reaction products

**Biphenyl**: Colorless solid.\(^{118}\) (Table 5.1, Entry 1) \(^1\)H-NMR (300 MHz, CDCl\(_3\)): \(\delta = 7.48-7.52\) (m, 6H), 7.75 (d, \(J = 7.5\) Hz, 4H), \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)): \(\delta\) 127.2, 127.3, 128.8, 141.3.

![](image)

**4-Methylbiphenyl** Colorless solid.\(^{118}\) (Table 5.1, Entry 2) \(^1\)H-NMR (300 MHz, CDCl\(_3\)): \(\delta\) 2.38 (s, 3H), 7.29 (d, \(J = 8.1\) Hz, 2H), 7.33-7.39 (m, 1H), 7.36-7.39 (m, 2H), 7.45 (d, \(J = 7.2\) Hz, 2H), 7.59 (d, \(J = 8.1\) Hz, 2H); \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)): \(\delta\) 21.2, 126.8, 126.9, 128.5, 129.3, 136.88, 138.2, 141.8.

![](image)

**4-Methoxybiphenyl**: Colorless solid.\(^{118}\) (Table 5.1, Entry 3) \(^1\)H-NMR (300 MHz, CDCl\(_3\)): \(\delta\) 3.78 (s, 3H), 6.68 (d, \(J = 7.2\) Hz, 2H), 7.41-7.48 (m, 5H), 7.59 (d, \(J = 7.2\) Hz, 2H); \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)): \(\delta\) 55.3, 116.3, 126.3, 126.6, 128.0, 128.7, 133.5, 140.5, 159.4.

![](image)

**4-Acetyl biphenyl**: Colorless solid.\(^{118}\) (Table 5.1, Entry 4) \(^1\)H-NMR (300 MHz, CDCl\(_3\)): \(\delta\) 2.61 (s, 3H), 7.51-7.57 (m, 3H), 7.59 (d, \(J = 7.5\) Hz, 2H), 7.61 (d, \(J = 8.1\) Hz, 2H), 8.09 (d, \(J = 7.5\) Hz, 2H); \(^{13}\)CNMR (75 MHz, CDCl\(_3\)): \(\delta\) 26.2, 126.9, 127.0, 128.1, 128.4, 128.6, 135.2, 139.6, 145.4, 197.3.

![](image)

**4-Nitrobiphenyl** Light yellow solid.\(^{118}\) (Table 5.1, Entry 5) \(^1\)H-NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.53-7.42 (m,
3H), 7.64-7.61 (m, 2H), 7.72 (d, \( J = 7.2 \) Hz, 2H), 8.31 (d, \( J = 7.2 \) Hz, 2H); \(^{13}\text{C-NMR} (75 \text{ MHz, CDCl}_3): \delta 124.5, 127.7, 128.2, 129.3, 129.5, 139.1, 147.5, 148.0.

**4,4’-Bipyridine: Colorless solid.**\(^{11}\) (Table 5.1, Entry 6) \(^1\text{H-NMR} (300 \text{ MHz, CDCl}_3): \delta 7.55 (d, \( J = 7.8 \) Hz, 4H), 8.75 (d, \( J = 7.8 \) Hz, 4H); \(^{13}\text{C-NMR} (75 \text{ MHz, CDCl}_3): \delta 120.7, 144.6, 150.0.\)
5.5.2. NMR spectra of Suzuki reaction products

**Figure 5.5.1** $^1$H-NMR spectrum of biphenyl (Table 5.1, Entry 1).

**Figure 5.5.2** $^{13}$C-NMR spectrum of biphenyl (Table 5.1, Entry 1).
Figure 5.5.3 \(^1\)H-NMR spectrum of 4-methoxy biphenyl (Table 5.1, Entry 3).

Figure 5.5.4 \(^{13}\)C-NMR spectrum of 4-methoxy biphenyl (Table 1, Entry 3).
Figure 5.5.5 $^1$H-NMR spectrum of 4-nitro biphenyl (Table 5.1, Entry 5).

Figure 5.5.6 $^{13}$C-NMR spectrum of 4-nitro biphenyl (Table 5.1, Entry 5).
Figure 5.5.7 $^1H$-NMR spectrum of 4,4'-bipyridine (Table 5.1, Entry 6).

Figure 5.5.8 $^{13}$C-NMR spectrum of 4,4'-bipyridine (Table 5.1, Entry 6).
5.5.3 NMR data of Heck reactions

**Stilbene:** Colorless solid.\(^{119}\) (Table 5.2, Entry 1) \(^1\)H-NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.25 (d, \(J = 15.3\) Hz, 1H); 7.39 (d, \(J = 15.3\) Hz, 1H), 7.49-7.53 (m, 6H), 7.63 (d, \(J = 7.5\) Hz, 4H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 126.3, 127.6, 128.5, 128.9, 130.2, 137.6.

**4-Methyl stilbene:** White plates.\(^{119}\) (Table 5.2, Entry 2) \(^1\)H-NMR (300 MHz, CDCl\(_3\)) \(\delta\) 2.30 (s, 3H), 6.98 (d, \(J = 16.3\) Hz, 1H), 6.99 (d, \(J = 7.2\) Hz, 2H), 7.10 (d, \(J = 7.5\) Hz, 2H), 7.19 (d, \(J = 16.3\) Hz, 1H), 7.26 (t, \(J = 7.5\) Hz, 3H), 7.42 (d, \(J = 7.2\) Hz, 2H); \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)) \(\delta\) 21.9, 126.3, 126.5, 127.6, 127.1, 128.2, 128.6, 129.8, 134.9, 137.6, 137.9.

**4-Methoxy stilbene:** pale yellow plates.\(^{119}\) (Table 5.2, Entry 3); \(^1\)H-NMR (300 MHz, CDCl\(_3\)) \(\delta\) 3.73 (s, 3H), 6.78 (d, \(J = 8.4\) Hz, 2H), 6.85 (d, \(J = 16.4\) Hz, 1H), 6.95 (d, \(J = 16.4\) Hz, 1H), 7.12 (t, \(J = 7.2\) Hz, 1H), 7.23 (t, \(J = 7.2\) Hz, 2H), 7.33 (d, \(J = 8.4\) Hz, 2H), 7.37 (d, \(J = 7.2\) Hz, 2H); \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)) \(\delta\) 55.2, 114.2, 126.4, 126.8, 127.2, 127.8, 128.4, 128.7, 130.3, 137.8, 159.4.

**4-Acetyl stilbene:** Colorless crystals.\(^{119}\) (Table 5.2, Entry 4); \(^1\)H-NMR (300 MHz, CDCl\(_3\)) \(\delta\) 2.30 (s, 3H), 7.09 (d, \(J = 16.4\) Hz, 1H), 7.19 (d, \(J = 16.4\) Hz, 1H), 7.26-7.39 (m, 3H), 7.56 (d, \(J = 8.0\) Hz, 2H), 7.59 (d, \(J = 8.0\) Hz, 2H), 7.95 (d, \(J = 8.0\) Hz, 2H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 26.3, 126.6, 127.4, 127.6, 128.9, 129.4, 129.5, 131.6, 136.5, 136.9, 142.5, 196.9.
4-Styryl-stilbene: light yellow solid.\textsuperscript{119c} (Table 5.2, Entry 7) \textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}) δ 6.57 (d, $J = 12.0$ Hz 1H), 6.61 (d, $J = 7.2$ Hz, 2H), 7.05 (d, $J = 12.0$ Hz, 1H), 7.09 (d, $J = 7.2$ Hz, 1H), 7.20-7.30 (m, 8H), 7.33-7.38 (m, 4H), 7.51 (d, $J = 7.2$ Hz, 2H).

9,10-Distyrylnaphthalene: Yellow solid.\textsuperscript{119c} (Table 5.2, Entry 6) \textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}) δ 7.25 (d, $J = 7.5$ Hz, 2H), 7.36 (d, $J = 16.5$ Hz, 2H), 7.42-7.51 (m, 8H) 7.70 (d, $J = 7.5$ Hz, 4H), 7.94 (d, $J = 16.5$ Hz, 2H) 8.37 (d, $J = 6.3$ Hz, 2H); \textsuperscript{13}C-NMR (75 MHz, CDCl\textsubscript{3}) δ 123.4, 124.2, 125.6, 125.9, 126.6, 127.7, 128.6, 131.5, 134.7, 137.5.

9,10-Distyrylanthracene: Yellow solid.\textsuperscript{119c} (Table 5.2, Entry 7) \textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}) δ 6.95 (d, $J = 7.5$ Hz, 2H), 7.37 (d, $J = 16.5$ Hz, 2H), 7.46-7.49 (m, 8H) 7.70 (d, $J = 7.5$ Hz, 4H), 7.94 (d, $J = 16.5$ Hz, 2H), 8.39-8.41 (m, 4H); \textsuperscript{13}C-NMR (75 MHz, CDCl\textsubscript{3}) δ 125.1, 125.2, 126.6, 126.4, 128.0, 128.8, 129.5, 132.6, 137.2, 137.4.
5.5.4 NMR Spectra of Heck coupling reactions

Figure 5.5.11 $^1$H-NMR spectrum of 9,10-distyrylnaphthlene (Table 5.2, Entry 6).

Figure 5.5.11 $^{13}$C-NMR spectrum of 9,10-distyrylnaphthlene (Table 5.2, Entry 6).
Figure 5.5.13 $^1H$-NMR spectrum of 9,10-distyrylanthracene (Table 5.2, Entry 7).

Figure 5.5.14 $^{13}C$-NMR spectrum of 9,10-distyrylanthracene (Table 5.1, Entry 6).
5.5.5 NMR data of Sonogashira coupling reactions

1,2-diphenylethyne: white solid\(^{120}\) (Table 5.3, entry 1):
\(^1\)H-NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.37-7.31 (m, 6H), 7.55-7.50 (m, 4H); \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)): \(\delta\) 89.4, 123.3, 128.2, 128.3, 131.6. FT-IR (KBr, cm\(^{-1}\)) \(\nu\) 3060, 2961, 1559, 1493, 1443, 1254, 1071, 756, 686.

4-(phenylethynyl)toluene: colorless solid\(^{120}\) (Table 5.3, entry 2) \(^1\)H-NMR (300 MHz, CDCl\(_3\)) 2.38 (s, 3H), 7.18 (d, \(J = 7.8\) Hz, 2H) 7.35-7.39 (m, 3H), 7.46 (d, \(J = 7.8\) Hz, 2H), 7.51 (dd, \(J = 7.8\)Hz, 1.6Hz, 2H); \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)) 21.8, 88.7, 90.1, 120.6, 123.5, 127.9, 128.5, 129.3, 131.9, 131.4, 138.5; (FT-IR, cm\(^{-1}\)) 3070, 2219, 1601, 1518, 1446, 828, 759, 696.

4-(phenylethynyl)anisole: colorless solid\(^{120}\) (Table 5.3, entry 3) \(^1\)H-NMR (300 MHz, CDCl\(_3\)) 3.79 (s, 3H), 6.85 (d, \(J = 8.7\) Hz, 2H), 7.22-7.36 (m, 3H), 7.42 (d, \(J = 7.2\) Hz, 2H), 7.48 (d, \(J = 8.7\)Hz, 2H); \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)) 55.8, 88.1, 89.4, 113.9, 115.2, 123.6, 127.9, 128.3, 131.5, 133.0, 159.8; FT-IR (KBr, cm\(^{-1}\)) 2218, 1599, 1249, 1179, 1142, 839, 758, 696.

4-Acetyldiphenylethyne: colorless solid\(^{120}\) (Table 5.3, entry 4) \(^1\)H-NMR (300 MHz, CDCl\(_3\)): 2.31 (s, 3H), 7.26-7.39 (m, 3H), 7.56-7.59 (m, 2H), 7.60 (d, \(J = 8.6\) Hz, 2H), 7.98 (d, \(J = 8.6\) Hz, 2H); \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)) \(\delta\) 26.9, 88.5, 92.8, 122.9, 128.1, 128.8, 129.5, 131.5, 131.2, 136.1, 197.8.
5.5.6 NMR Spectra of Sonogashira coupling reactions

Figure 5.5.8 $^1$H-NMR spectrum of 1,2-diphenylethyne (Table 5.3, entry 1).

Figure 5.5.8 $^{13}$C-NMR spectrum of 1,2-diphenylethyne (Table 5.3, entry 1).
5.6 References


Chapter V


270

112. Science lab.com, Ethylene glycol MSDS.


