Asymmetric Diels-Alder Reactions on Supported Bis(oxazoline) Catalysts

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Abstract: Periodic mesoporous ethane-silicas functionalized with sulfonic acid, cesium salts of 12-tungstophosphoric acid, activated silica, and SBA-15 have been used as solid supports for the immobilization of the bis(oxazoline) copper (II) catalyst via non-covalent interactions. These heterogeneous catalysts have been evaluated for the Diels-Alder reaction between 3-((E)-2-butenoyl)-1,3-oxazolin-2-one and cyclopentadiene. The performance of the catalyst relies on the nature of both the support and the anion on the surface of the support. The small number of the silanol groups on the support leads to poor enantioselectivity when SBA-15 is used.

Key Words: supported catalyst; bis(oxazoline) complex; Diels-Alder reaction; activated silica; SBA-15

Asymmetric catalysis is a powerful method for the preparation of pharmaceuticals and fine chemicals. Chiral bis(oxazoline) (BOX) catalysts have found applications in a variety of enantioselective reactions [1]. The Diels-Alder (DA) reaction is one of the most important C–C bond forming reactions in organic synthesis. However, relatively large amounts of the BOX catalysts are required in the DA reaction, which makes the recovery and the reuse of the catalysts necessary. Many strategies have been applied to immobilize the catalysts for recycling [2–4]. The immobilization of the catalysts through non-covalent binding can avoid chemical modification of the chiral ligands, which often decreases the enantioselectivity (ee). Recently, we successfully immobilized BOX catalysts on silica via the hydrogen bonding interaction between the silanols and CF\textsubscript{3}SO\textsubscript{3}– (triflate), and the resulting heterogeneous catalysts were recycled without the significant loss of enantioselectivity [5]. We also found that a higher ee can be obtained using the heterogeneous catalyst compared with the homogeneous analogue. Apparently, the nature of the support influences the performance of the heterogeneous catalyst.

In this work, a periodic mesoporous ethane-silica functionalized with sulfonic acid (PMO-SO\textsubscript{3}H), a cesium salt of 12-tungstophosphoric acid (Cs\textsubscript{3}PW\textsubscript{12}O\textsubscript{40}), an activated silica, and SBA-15 were used as the solid supports for the immobilization of the phenyl-substituted bis(oxazoline) copper(II) catalyst (PhBOX-Cu(II)) via non-covalent interactions, resulting in heterogeneous catalysts S1, S2, S3 and S4, respectively. The DA reaction between 3-((E)-2-butenoyl)-1,3-oxazolin-2-one and cyclopentadiene was carried out at room temperature using these heterogeneous catalysts (Scheme 1).

The preparation of PMO-SO\textsubscript{3}H was similar to the previous study but with modification [6]. The BET surface area of PMO-SO\textsubscript{3}H was 542 m\textsuperscript{2}/g with a pore diameter of 7.4 nm.
Cs₃PW₁₂O₄₀ was synthesized according to the literature [7]. The activated silica (pore diameter = 9.7 nm, $A_{\text{BET}} = 390 \text{ m}^2/\text{g}$) and SBA-15 (pore diameter = 6 nm, $A_{\text{BET}} = 696 \text{ m}^2/\text{g}$) were commercially purchased.

Recently, a series of sulfonic acid-functionalized mesoporous silicas have been synthesized and used in some catalytic reactions [6, 8]. In order to explore more applications with these materials, the ion-exchange method was used to immobilize the homogeneous catalyst PhBOX-Cu(II) on PMO-SO₃H in this study. In addition, heteropoly acids as the tethering agents to support homogeneous catalysts have been reported [9–11]. Because of the relatively large BET surface area of Cs₃PW₁₂O₄₀ (~150 m²/g), PhBOX-Cu(II) was directly immobilized on Cs₃PW₁₂O₄₀.

These experiments demonstrated that the acidic sites of PMO-SO₃H had a negative influence on the catalyst performance in the present case. Hence, PMO-SO₃H was firstly exchanged with an aqueous solution of 1 mol/L NaCl to form PMO-SO₃Na, and PhBOX-Cu(II) was then immobilized on PMO-SO₃Na in methanol. The concentration of the prepared homogeneous catalyst PhBOX-Cu(II) was 0.03 mol/L and the amount of the support PMO-SO₃Na used was ~1 kg per mole of PhBOX-Cu(II). The immobilization using Cs₃PW₁₂O₄₀ as the support was also carried out in methanol and the amount of Cs₃PW₁₂O₄₀ used was ~1.6 kg per mole of PhBOX-Cu(II). After stirring at room temperature for 24 h, the solids were isolated by centrifugation and washed with methanol and dichloromethane. The solids were dried at 60°C in vacuum. The procedures of the immobilization of PhBOX-Cu(II) on activated silica and SBA-15 were similar to our previous work [5].

All the solvents used in this study were purified and dried using standard procedures. The DA reaction was conducted under an argon atmosphere. Elemental analysis was performed with an inductively coupled plasma atomic emission spectrometer (ICP-AES). Fourier transform infrared spectra (FTIR) of the catalysts were recorded on a Thermo Nicolet Impact 470 FTIR spectrometer in the range of 4000–400 cm⁻¹.

As shown in Fig. 1, a relatively intense band at ~1630 cm⁻¹ was observed in the FTIR spectra of S1, S2, S3, and S4, which corresponded to the stretching vibration of the C=N bond and was similar to that of the homogeneous catalyst PhBOX-Cu(II) (~1633 cm⁻¹). In addition, the stretching vibration of the C=C bond of benzyl was also observed at 1600–1450 cm⁻¹. The results indicated that the BOX ligand was successfully immobilized on these supports. According to the analysis of ICP-AES, the loadings of the copper in the resulting heterogeneous catalysts were ca. 0.5%, 0.3%, 1.1%, and 1.4% for S1, S2, S3, and S4, respectively.

Dichloromethane has been found to be a desirable solvent in homogeneous reactions catalyzed by BOX complexes. However, to avoid general leaching of the catalysts immobilized via non-covalent interactions, toluene was used as the solvent for the heterogeneous reactions because of its low polarity and low solubility for catalyst PhBOX-Cu(II). The catalytic results obtained are listed in Table 1. As can be seen in the table, the DA reaction catalyzed by S2 had a lower conversion (77%) compared with the other heterogeneous catalysts (100%). It is also seen that in comparison with the 15% enantiomeric excess (ee) obtained in the homogeneous reaction, three heterogeneous catalysts (S1, S2, and S3) yielded products with higher ee values (39%, 37%, and 42%, respectively). However, a lower ee value (9%) was obtained using SBA-15 as the support.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Conversion (%)</th>
<th>Endo/exo</th>
<th>ee of endo (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PhBOX-Cu(II)</td>
<td>100</td>
<td>89:11</td>
<td>15</td>
</tr>
<tr>
<td>S1</td>
<td>100</td>
<td>82:18</td>
<td>39</td>
</tr>
<tr>
<td>S2</td>
<td>77</td>
<td>79:21</td>
<td>37</td>
</tr>
<tr>
<td>S3</td>
<td>100</td>
<td>83:17</td>
<td>42</td>
</tr>
<tr>
<td>S4</td>
<td>100</td>
<td>80:20</td>
<td>9</td>
</tr>
</tbody>
</table>

Reactions were performed in toluene at room temperature for 22 h with a catalyst/substrate molar ratio of 1/10. The conversion was determined by $^1$H NMR (400 MHz). The endo/exo ratio was analyzed by chiral HPLC (Chiralcel OD-H column with hexane/ethanol (98/2) as the eluant) and was confirmed by $^1$H NMR. The ee value of the endo isomer was analyzed by chiral HPLC.

Table 1 Asymmetric Diels-Alder (DA) reaction over homogeneous and supported PhBOX-Cu(II) catalysts

It has been shown that a considerable amount of micropores exists together with the mesopores in Cs₃PW₁₂O₄₀ [12]. Thus, the lower conversion can be ascribed to the inaccessible catalytic sites and diffusion limitation in the micropores. This can also be attributed to the nature of the anion PW₁₂O₄₀⁻, as for...
It has been well documented that in the homogeneous DA reactions, it has been demonstrated that the counterrions of the BOX catalysts play crucial roles on the activity and enantioselectivity [13].

It has been described in the literature that the anion support with a weak interaction with the complex leads to better enantioselectivity in the cyclopropanation reaction with BOX complexes [14]. When PMO-SO\textsubscript{3}Na and Cs\textsubscript{3}PW\textsubscript{12}O\textsubscript{40} were used as the supports, catalyst PhBOX-Cu(II) was primarily immobilized via the electrostatic interactions between the copper(II) center and the anion (PMO-SO\textsubscript{3}\textsuperscript{−} and PW\textsubscript{12}O\textsubscript{40}\textsuperscript{−}) supports. When activated silica was used, hydrogen-bonding interactions took place between the silanols and the triflate anions [5]. However, the copper(II) center was still immobilized mainly via an ionic interaction with the support surface (modified with triflates). Whether the anion was sulfonate immobilized mainly via an ionic interaction with the support surface [19]. The above analysis implied that although both the SBA-15 and the activated silica are silica-based materials, the small number of the silanol groups on SBA-15 resulted in the lower enantioselectivity.

In summary, the homogeneous catalyst PhBOX-Cu(II) was immobilized on PMO-SO\textsubscript{3}H, Cs\textsubscript{3}PW\textsubscript{12}O\textsubscript{40}, activated silica, and SBA-15 via non-covalent methods. The resulting heterogeneous catalysts can be applied to the DA reaction between 3-((E)-2-butenoyl)-1,3-oxazolin-2-one and cyclopentadiene. Experimental data indicated that the performance of the catalysts depends on the nature of both the support and the anion on the surface of the support. The best activity and enantioselectivity were obtained with an activated silica calcined at 300°C as the support. However, the small number of the silanol groups on SBA-15 resulted in the poor enantioselectivity when SBA-15 was used as the support.

References


