Polymer-Supported Terpyridine–Palladium Complex for the Allylic Alkylation with Arylboronic Acid in Water

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A novel homogeneous transition-metal catalyst, a polymer-supported terpyridine–palladium(II) complex, was found to promote the allylic alkylation with phenylboronic acid under phosphine-free conditions in water with good yield. The catalyst was recovered and reused several times without loss of catalytic activity. To our knowledge, this is the first example of the allylic alkylation with phenylboronic acid in water using a polymer-supported terpyridine–palladium(II) complex under aerobic conditions. The stereochemistry of the allylic alkylation with phenylboronic acid was demonstrated to be not net retention.

Key words: allylic alkylation, palladium, terpyridine, water, phosphine-free

1. INTRODUCTION

Palladium-catalyzed allylic alkylation of allyl esters is recognized to be one of the most useful reactions catalyzed by transition metal complexes [1]. These allylic alkylation reactions are generally catalyzed with soluble palladium-phosphine ligand complexes in an organic solvent or in a mixture of water and an organic solvent. However, there has been a continuing challenge with such catalyst systems regarding their efficient separation and recycling, which are important considerations for economic and ecological reasons. In addition, compared with phosphine ligands of palladium complexes, other types of ligands (N, O, S, etc.) for allylic alkylation chemistry have not received much attention.

On the other hand, we recently developed an amphiphilic polystyrene–poly(ethylene glycol) (PS–PEG) resin-supported terpyridine–palladium complex as a phosphine-free catalyst and found it to be effective for metal-catalyzed reactions in water under heterogeneous and aerobic conditions with high recyclability [2]. As an extension of that study, we investigated the catalytic utility of the PS–PEG–terpyridine–palladium(II) complex for the allylic alkylation with phenylboronic acids using our polymeric catalyst to produce the corresponding allylic substitution products in water [3].

We herein report the results of this investigation and demonstrate that the complex effectively catalyzes the allylic alkylation of various arylboronic acids in water under phosphine-free conditions (Scheme 1). In addition we described for the stereochemistry of the presented allylic alkylation with phenylboronic acid in water. This catalyst system presents three benefits: (1) It is the low-cost method for synthesis of triarylpropene to use the reusable catalyst (2) It is not necessary to use valuable inert gas for the reaction (3) It enables the allylic alkylation reaction to meet green chemical requirements.

\[
\text{ArB(OH)}_2 + \text{Na}_2\text{CO}_3 \rightarrow \text{ArCHR} + \text{NaB(OH)}_2
\]

\[
\text{ArCHR} \text{OAc} + \text{ArB(OH)}_2 + \text{Na}_2\text{CO}_3 \rightarrow \text{ArCHR} + \text{NaB(OH)}_2
\]

\[
\text{ArCHR} \text{OAc} + \text{ArB(OH)}_2 + \text{Na}_2\text{CO}_3 \rightarrow \text{ArCHR} + \text{NaB(OH)}_2
\]

Scheme 1. Allylic Alkylation Reaction in Water Using the PS–PEG–Terpyridine–Pd Complex

2. EXPERIMENTAL SECTION

2.1 General Methods

All manipulations were conducted under aerobic conditions. Water was deionized with a Millipore Milli-Q Gradient A10 system. NMR spectra were recorded on a Bruker AVANCE spectrometer (400 MHz for \(^1\)H and 100 MHz for \(^13\)C). NMR spectra were recorded in CDCl\(_3\) and dimethyl sulfoxide-\(d_6\) (DMSO-\(d_6\)) at 25 °C. Chemical shifts of \(^13\)C are given relative to CDCl\(_3\) and DMSO-\(d_6\) as an internal standard (\(\delta 39.7\) ppm). Mass spectra were measured on a JEOL JMS-T100GcV MS detector (GC–MS) and a JEOL JMS-T100LP MS detector (LC–MS); the base peak is denoted as “bp.” GC and IR analyses were performed on a Shimadzu GC-2014 and a Jasco FTIR-410 detector, respectively. ICP–AES spectra were measured on a Shimadzu ICPE-9000.

2.2 Materials

PS–PEG-supported terpyridine–palladium complex (PS–PEG–terpyridine–Pd; 1) was prepared from a PS–PEG amino-resin (Tenta Gel S NH\(_2\), average diameter is 90 mm, 1% divinylbenzene cross-linked, loading value of amino residue 0.31 mmol/g; purchased...
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2.3 Allylic Alkylation

The general procedure to obtain allylic alkylation products 4a–i is as described here. 1,3-diphenyl-2-propenyl acetate (2a, 100 mg, 0.40 mmol) was added to a mixture of polymeric catalyst (1:77 mg, 0.02 mmol), base Na2CO3 (169 mg, 1.60 mmol), and phenylboronic acid (3a; 97 mg, 0.80 mmol) in H2O (3.0 mL). The reaction mixture was stirred at 40 °C for 24 h under aerobic conditions and then filtered. The recovered resin beads were rinsed with H2O and extracted thrice with EtOAc (6 mL). The EtOAc layer was separated and the aqueous layer was extracted with EtOAc (3 mL). The combined EtOAc extracts were washed with brine (2 mL) and dried over MgSO4. The reaction mixture was evaporated and the filtrate was chromatographed on silica gel PTLC (hexane) to give 68.0 mg (63% yield) of (E)-prop-2-en-1,1,3-triyltribenzene (4a).

4a: 1H-NMR (CDCl3-d): 0.87, 7.17, 7.71 (m, 15H), 6.67 (d, J = 15.8, 7.5 Hz, 1H), 6.37 (d, J = 16.5 Hz, 1H), 4.89 (d, J = 7.5 Hz, 1H); 13C-NMR (CDCl3-d): 184.3, 137.2, 132.5, 131.4, 128.6 (4C), 128.5 (3C), 128.4 (4C), 127.3, 126.4 (2C), 126.3 (2C), 126.2 (2C), 126.0, 53.3; IR (ATR) (cm⁻¹): v 3080, 3024, 1597, 1491, 969; HR-EL-MS: calculated for C25H20 (M⁺) 320.1565, found 320.1657.

4b: 1H-NMR (CDCl3-d): 7.37-7.16 (m, 14H), 6.66 (d, J = 15.8, 6.9 Hz, 1H), 6.21 (d, J = 15.8 Hz, 1H), 5.07 (d, J = 6.9 Hz, 1H), 2.28 (s, 3H); 13C-NMR (CDCl3-d): 161.2, 144.6, 137.3, 136.4, 123.2, 131.3, 130.5, 128.9 (2C), 128.5, 128.5 (2C), 128.3 (2C), 127.2, 126.5, 126.3, 126.2 (2C), 126.0, 50.4, 19.7; IR (ATR) (cm⁻¹): v 3078, 3030, 1598, 1459, 982; HR-EL-MS: calculated for C25H20O (M⁺) 270.1409, found 270.1446.

4c: 1H-NMR (CDCl3-d): 7.4-7.1 (m, 1H), 7.78-7.76 (m, 1H), 7.46-7.09 (m, 14H), 6.65 (dd, J = 15.9, 6.8 Hz, 1H), 6.26 (d, J = 15.9 Hz, 1H), 5.65 (d, J = 6.8 Hz, 1H); 13C-NMR (CDCl3-d): 162.7, 160.3, 143.3, 139.1 (d, J = 4.5 Hz), 131.7, 132.4, 130.6, 131.8, 131.7, 128.8 (2C), 128.7, 128.4 (4C), 127.4, 127.3, 126.4 (2C), 126.3 (2C), 126.0, 125.4, 125.3, 124.6, 50.1; IR (ATR) (cm⁻¹): v 3078, 3020, 1595, 1489, 982; HR-EL-MS: calculated for C25H20F (M⁺) 220.1565, found 220.1579.

4d: 1H-NMR (CDCl3-d): 8.4-8.01 (m, 1H), 7.88-7.78 (m, 1H), 7.78-7.76 (m, 1H), 7.46-7.17 (m, 1H), 6.80 (dd, J = 15.9, 6.8 Hz, 1H), 6.26 (d, J = 15.9 Hz, 1H), 5.65 (d, J = 6.8 Hz, 1H); 13C-NMR (CDCl3-d): 162.4, 160.3, 143.3, 139.1 (d, J = 4.5 Hz), 131.7, 132.4, 130.6, 131.8, 131.7, 128.8 (2C), 128.7, 128.4 (4C), 127.4, 127.3, 126.4 (2C), 126.3 (2C), 126.0, 125.4, 125.3, 124.6, 50.1; IR (ATR) (cm⁻¹): v 3078, 3020, 1595, 1489, 982; HR-EL-MS: calculated for C25H20 (M⁺) 320.1565, found 220.1579.

The results for various arylboronic acids are as follows. The bases potassium hydroxide and cesium hydroxide (KOH) and (CsOH) showed that the allylic alkylation of water and extracted with EtOAc to afford the corresponding products.

3. RESULTS AND DISCUSSION

The amphiphilic PS-PEG resin-bound terpyridine–palladium complex 1 was readily prepared from 4-methoxycarbonylbenezaldehyde, 2-acetylpyrindine, PS–PEG–NH2 resin, and (C6H5CN)2PdCl2 in accordance with the reported procedures [2, 4]. Polymeric catalyst 1 exhibited catalytic activity for the allylic alkylation using phenylboronic acid in water.

Allylic alkylation of 1,3-diphenyl-2-propenyl acetate (2) was performed in water with phenylboronic acid (3a) and catalyst 1 (5 mol% Pd) in the presence of four equivalents of the base at 40 °C for 24 h under aerobic conditions. The reaction mixture was filtered and the recovered resin beads were rinsed with a small portion of water and extracted with EtOAc to afford the corresponding product 4a.

Initially, we screened various bases using allyl ester and phenylboronic acid as the model substrate for the
purpose of the optimization of the reaction conditions.

The scope of suitable bases for the allylic alkylation in water using catalyst 1 was examined (Table I). The reaction efficiency greatly varied according to the base used. The bases lithium carbonate, sodium carbonate, potassium carbonate, and cesium carbonate afforded 4a in 43%, 46%, 46%, and 32% yields, respectively (runs 1–4). The bases potassium hydroxide and cesium hydroxide afforded 4a in 11% and 30% yields, respectively (runs 5–6). Organic base (DBU) furnished 4a in 2.0% yield (run 7). Yield lowered due to hydrolysis of allyl ester 2a at 50 °C (run 8). The most effective base proved to be sodium carbonate, which afforded 61% yield of 4a with prolonged reaction time (run 10).

Table I. Effect of Base on the Allylic Alkylation of 1,3-Diphenyl-2-Propenyl Acetate with Phenylboronic Acid Using Polymeric Catalyst 1 in Water

<table>
<thead>
<tr>
<th>Run</th>
<th>3a (eq.)</th>
<th>Base</th>
<th>Temp. (°C)</th>
<th>Time (h)</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>Li2CO3</td>
<td>40</td>
<td>6</td>
<td>43</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>Na2CO3</td>
<td>40</td>
<td>6</td>
<td>46</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>K2CO3</td>
<td>40</td>
<td>6</td>
<td>36</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>Cs2CO3</td>
<td>40</td>
<td>6</td>
<td>32</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>KOH</td>
<td>40</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>CsOH</td>
<td>40</td>
<td>6</td>
<td>30</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>DBU</td>
<td>40</td>
<td>6</td>
<td>2.0</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>Na2CO3</td>
<td>50</td>
<td>6</td>
<td>23</td>
</tr>
<tr>
<td>9</td>
<td>4</td>
<td>Na2CO3</td>
<td>40</td>
<td>6</td>
<td>43</td>
</tr>
<tr>
<td>10</td>
<td>2</td>
<td>Na2CO3</td>
<td>40</td>
<td>24</td>
<td>63</td>
</tr>
<tr>
<td>11</td>
<td>2</td>
<td>Na2CO3</td>
<td>40</td>
<td>48</td>
<td>63</td>
</tr>
</tbody>
</table>

All reactions were performed with 1,3-diphenyl-2-propenyl acetate (2, 0.2 mmol), phenylboronic acid (3a; 0.4 mmol), and base (0.8 mmol) in the presence of the polymeric catalyst 1 in 1.5 mL of H2O at 40 °C for 24 h under aerobic conditions.

The scope of suitable arylboronic acids for the allylic alkylation reaction in water using catalyst 1 was also examined (Table II). The general process involved conducting the reaction of the allyl acetate with phenylboronic acid (2 equiv.) and Na2CO3 (4 equiv.) in the presence of catalyst 1 (5 mol% Pd) under aerobic conditions in water to afford the corresponding products. The results for various arylboronic acids are as follows.

The aryloboronic acid derivatives 3b–g bearing electron-donating (EDG) substituents at their ortho, meta, and para-positions afforded the corresponding products 4b, 4c, 4d, 4e, 4f, and 4g in 53%, 32%, 52%, 13%, 36%, and 37% yields, respectively (runs 2–7). The para-fluorophenylboronic acid 3i was reacted with 2 to afford the coupling product derivatives bearing fluoro-substituents 4i in 10% yield (run 9).

Next, we studied the stereochemistry of the palladium-catalyzed allylic alkylation with the phenylboronic acid as a nucleophile. In our studies using the cis-cyclohexenyl acetate 5 (6), it was demonstrated that the phenylboronic acid behaves as a hard carbon nucleophile attacking the π-allyl moiety from the same side to palladium via transmetallation and reductive elimination. Thus, the reaction of cis-5-methoxy carbonyl-2-cyclohexenyl acetate (5) with phenylboronic acid in the presence of polymeric catalyst 1 in water gave a coupling product 6 in 21% yield (Scheme 2).

4. SUMMARY

We developed a novel polymer-supported terpyridine–palladium complex that efficiently catalyzes the allylic alkylation of allyl esters with aryloboronic acids in water under phosphine-free conditions to afford the corresponding allylic substitution products in good yield. The catalyst can be recovered and reused several times without any loss of catalytic activity. We also demonstrated that the presented allylic alkylation with phenylboronic acids proceeded in stereo inversion. We are still investigating the scope of the allylic alkylation with the other soft and hard carbon nucleophiles and possible applications of the catalyst to other organic transformations.
Table II. Allylic Alkylation with Various Arylboronic Acids Using Polymeric Catalyst 1 in Water

<table>
<thead>
<tr>
<th>Run</th>
<th>ArB(OH)₂</th>
<th>Products 4</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhB(OH)₂</td>
<td>4a</td>
<td>63</td>
</tr>
<tr>
<td>2</td>
<td>2-tolylB(OH)₂</td>
<td>4b</td>
<td>53</td>
</tr>
<tr>
<td>3</td>
<td>3-tolylB(OH)₂</td>
<td>4c</td>
<td>32</td>
</tr>
<tr>
<td>4</td>
<td>4-tolylB(OH)₂</td>
<td>4d</td>
<td>52</td>
</tr>
<tr>
<td>5</td>
<td>2-anisylB(OH)₂</td>
<td>4e</td>
<td>13</td>
</tr>
<tr>
<td>6</td>
<td>3-anisylB(OH)₂</td>
<td>4f</td>
<td>36</td>
</tr>
<tr>
<td>7</td>
<td>4-anisylB(OH)₂</td>
<td>4g</td>
<td>37</td>
</tr>
<tr>
<td>8</td>
<td>naphthylB(OH)₂</td>
<td>4h</td>
<td>20</td>
</tr>
<tr>
<td>9</td>
<td>4-FC₆H₄B(OH)₂</td>
<td>4i</td>
<td>10</td>
</tr>
</tbody>
</table>

All reactions were performed with allyl acetate (2; 0.4 mmol), ArB(OH)₂ (3; 0.8 mmol), and Na₂CO₃ (1.6 mmol) with the catalyst 1 in 3.0 mL of H₂O at 40 °C for 24 h under aerobic conditions.

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REFERENCES


[5] After recycling experiments, ICP–AES analysis showed that leaching of Pd to the aqueous solution occurred at <1 ppm.


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