**Gold-catalyzed Cycloisomerization of Propargylic Ureas**

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**Introduction**

Gold catalysis has often shown its potential in C-C and C-X (X=N, S, O) bond formation and its application in natural product synthesis.[1] By using gold catalysis in cycloisomerization reactions a wide range of products such as pyrans, furans, pyrroles or thiophenes are available.[2] Another highly interesting group of heterocycles are 2-imidazolones which show pharmacological activity as dopamine receptor antagonists,[3] potential antitumor agents[4] and antioxidants.[5]

Van der Eycken et al.[2] reported an access to tetrasubstituted 2-imidazolones with moderate yield by cycloisomerization of propargylic ureas with stoichiometric amounts of Ag(I) at elevated temperatures. It appears reasonable to assume that gold catalysis can be used to improve the synthesis of tetrasubstituted 2-imidazolones.[7]

In this study we investigate the gold-catalyzed cycloisomerization of propargylic ureas in combination with different additives.

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**Results**

**Synthesis of Propargylic Ureas**

Propargylic amine 4 was easily prepared starting from alkyne 1, aldehyde 2, and amine 3. With microwave heating a yield of 75% was obtained (Scheme 2).[6]

Phenyl isocyanate was used to convert propargylic amine 4 into the corresponding urea 5 (Scheme 3).

**Gold-catalyzed cycloisomerization of propargylic urea 5**

Table 1 shows the cycloisomerization study of propargylic amine 5 by different gold catalysts including gold(I)- and gold(III)-salts.

Table 3. Optimization of the cycloisomerization reaction.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Additive</th>
<th>Solvent</th>
<th>Temp</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph$_2$PAuNTf$_2$</td>
<td>-</td>
<td>toluene</td>
<td>100 °C</td>
<td>94%</td>
</tr>
<tr>
<td>2</td>
<td>I</td>
<td>-</td>
<td>toluene</td>
<td>100 °C</td>
<td>94%</td>
</tr>
<tr>
<td>3</td>
<td>AgOTf</td>
<td></td>
<td>toluene</td>
<td>100 °C</td>
<td>94%</td>
</tr>
<tr>
<td>5</td>
<td>Ph$_2$PAuCl</td>
<td>AgOTf</td>
<td>toluene</td>
<td>100 °C</td>
<td>94%</td>
</tr>
<tr>
<td>6</td>
<td>Ph$_2$PAuCl</td>
<td>AgOTf</td>
<td>toluene</td>
<td>80 °C</td>
<td>94%</td>
</tr>
<tr>
<td>7</td>
<td>Ph$_2$PAuCl</td>
<td>AgOTf</td>
<td>toluene</td>
<td>70 °C</td>
<td>94%</td>
</tr>
<tr>
<td>8</td>
<td>Ph$_2$PAuCl</td>
<td>AgOTf</td>
<td>toluene</td>
<td>60 °C</td>
<td>68%</td>
</tr>
<tr>
<td>9</td>
<td>Ph$_2$PAuCl</td>
<td>AgOTf / NEt$_3$</td>
<td>toluene</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Ph$_2$PAuCl</td>
<td>AgOTf / TfOH</td>
<td>toluene</td>
<td>100 °C</td>
<td></td>
</tr>
</tbody>
</table>

**Optimization of the reaction** included the use of more reactive phosphine- and NHCl-gold complexes and other additives such as acids or bases (Table 3).


In conclusion, we investigated the catalysis of cycloisomerization of propargylic urea with PaAuCl and AgOTf. At moderate temperature we observed full conversion to the corresponding highly substituted product. The scope of the reaction will be studied for more derivatives and the reaction pathway for endo- and exo-product will be investigated.

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**References**


[8] Gold catalysis has often shown its potential in C-C and C-X (X=N, S, O) bond formation and its application in natural product synthesis.[1] By using gold catalysis in cycloisomerization reactions a wide range of products such as pyrans, furans, pyrroles or thiophenes are available.[2] Another highly interesting group of heterocycles are 2-imidazolones which show pharmacological activity as dopamine receptor antagonists,[3] potential antitumor agents[4] and antioxidants.[5] Van der Eycken et al.[2] reported an access to tetrasubstituted 2-imidazolones with moderate yield by cycloisomerization of propargylic ureas with stoichiometric amounts of Ag(I) at elevated temperatures. It appears reasonable to assume that gold catalysis can be used to improve the synthesis of tetrasubstituted 2-imidazolones.[7]