Oxidative Mannich reactions using Cu(II) 2-quinoxalinol salen catalyst and tert-butyl hydroperoxide
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INTRODUCTION

• The Mannich reaction is a useful tool to form carbon-carbon bonds.
• Many historical syntheses require key Mannich couplings.
• Several challenges arise when forming the iminium ion intermediate.
• Harsh conditions, long reaction times, expensive transition metals, or high catalyst loading.
• C-H oxidation could provide a direct route to forming the iminium ion.
• Previous examples require expensive catalyst such as Rh₂(cap)₄ or low yielding Cu(II)₁,²
• Herein, we report the use of Cu(II) 2-quinoxalinol salen (Salqu) catalyst for oxidative Mannich reactions.³

CATALYST PREPARATION

Table 1. Optimization of Reaction Conditions.

<table>
<thead>
<tr>
<th>entry</th>
<th>conditions</th>
<th>time (h)</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 (1 mol%), MeOH, 60 °C</td>
<td>1</td>
<td>64</td>
</tr>
<tr>
<td>2</td>
<td>1 (1 mol%), MeOH, 60 °C</td>
<td>2</td>
<td>81</td>
</tr>
<tr>
<td>3</td>
<td>1 (1 mol%), MeOH, 60 °C</td>
<td>3</td>
<td>92</td>
</tr>
<tr>
<td>4</td>
<td>1 (1 mol%), MeOH, 60 °C</td>
<td>4</td>
<td>98</td>
</tr>
<tr>
<td>5</td>
<td>1 (1 mol%), [O₂] (2 equiv)</td>
<td>4</td>
<td>82</td>
</tr>
<tr>
<td>6</td>
<td>1 (1 mol%), K₂CO₃, MeOH, 60 °C</td>
<td>4</td>
<td>trace</td>
</tr>
<tr>
<td>7</td>
<td>1 (1 mol%), MeCN, 60 °C</td>
<td>4</td>
<td>52</td>
</tr>
<tr>
<td>8</td>
<td>CuOAC₃ (5 mol%), MeOH, 60 °C</td>
<td>4</td>
<td>62</td>
</tr>
<tr>
<td>9*</td>
<td>1 (1 mol%), MeOH, 60 °C</td>
<td>4</td>
<td>51</td>
</tr>
</tbody>
</table>

*Reaction conditions: CuOAC₃ (5 mol%), MeOH, 60 °C, 4 h. *Conditions were done using 2.5 mmol, 8.0 mL MeCN, 1 H₂O⁻2 mol H₂O, NaOAc (1 equiv), MeCN (1.2 mL), T = 60 °C, 4 h. Yields of isolated products.

RESULTS AND DISCUSSION

PREVIOUS OXIDATIONS

Figure 2. Formation of iminium ion using different methods

CONCLUSIONS

• We report the use of an earth abundant transition metal copper for oxidative Mannich reactions.
• A range of different 3° amine substrates were tested producing yields up to 98% in 3-4 h.
• A simple catalytic cycle has been proposed which we believe is generating Cu(III); however, more studies will be done to better understand this reaction.

REFERENCES

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