Heterogeneous Cu-catalysts for the reductive deoxygenation of aromatic ketones without additives

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Abstract—Carbonyl groups conjugated with aromatic systems can be selectively converted into methylene ones under extremely mild conditions and without the need of any acidic additive over a heterogeneous Cu/SiO 2 catalyst.

In fine chemicals synthesis, the elimination of functional groups may be as useful as their introduction. In particular, the carbonyl to methylene conversion is especially useful to convert polyfunctional natural products into useful building blocks or into bioactive molecules or to convert Friedel Crafts acylation products into less easily accessible alkylation ones.

Traditional Clemmensen and Wolff–Kishner reductions require very drastic reaction conditions and also catalytic hydrogenolysis over Pd takes place in the presence of HCl. A number of milder direct and indirect methods have been proposed involving the use of sodium(cyano)borohydride, borane, LAH, trialkylsilanes and hydrosiloxane–borane combinations. Most of these methods require acidic conditions including the use of protic acids, mainly CF 3 COOH, and a variety of Lewis acids. Metallic selenium with CO and water can also be used. Recently, the use of supercritical 2-propanol has been proposed.

When tested in the deoxygenation of fluorenone, the first one exhibited a poor selectivity while Cu/SiO 2 –ZrO 2 was found to be an effective catalyst (Table 1).

However, the use of an acidic support was found not to be essential and Cu/SiO 2 turned out to be the best catalyst for this transformation.

Selected results are reported in Table 2.

These data suggest that the reaction proceeds through a carbocationic intermediate. The richer the incipient carbocation, the lower the conversion. As the reaction is also strongly dependent on the activation temperature, we can easily switch the selectivity towards methylene formation.

First, we tried to combine the hydrogenation activity of the metal with a support showing acidic activity such as SiO 2 modified with small amounts of Al 2 O 3 or ZrO 2. These two materials have proved to be effective Lewis acid catalysts for the isomerization of α-pinene epoxide. Moreover, Cu deposited on SiO 2–Al 2 O 3 was found to be a bifunctional catalyst for the direct conversion of limonene oxide into carvenone and Cu on SiO 2–ZrO 2 for the direct transformation of α,β-unsaturated ketones into bicyclic ethers.

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Table 1. Reductive deoxygenation over different copper catalysts

<table>
<thead>
<tr>
<th>Entry</th>
<th>t (h)</th>
<th>Catalyst</th>
<th>Conv (%)</th>
<th>Sel (%)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5</td>
<td>Cu/SiO 2–Al 2 O 3</td>
<td>100</td>
<td>48</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>Cu/SiO 2–ZrO 2</td>
<td>100</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>Cu/SiO 2</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

* Substrate: fluorenone, toluene, 90 °C, 1 atm H 2.
carbenium ion in the electrons the fastest will the reaction be, although steric effects also play a role. The hypothesis of a reduction–dehydration–reduction mechanism can be ruled out from the comparison between α- and β-tetralone (entry 8 vs 9). Thus, when the carbonyl group is alpha to the aromatic ring it can be converted into methylene whereas when it is beta, that is, no more in benzylic position, it can only be reduced to alcohol. Moreover, although formation of the carbinol intermediate is sometimes evident during reaction, the corresponding olefin has never been detected.

On the other hand, diphenylcarbinol under the same reaction conditions gives diphenylmethane in 90% yield (entry 4).

Selectivity is also very high for polycyclic substrates, while acetophenones, particularly when containing elec-

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Table 2. Reductive deoxygenation of different substrates with Cu/SiO$_2$ (toluene, 90 °C, 1 atm H$_2$)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrates</th>
<th>Product</th>
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</thead>
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<tr>
<td></td>
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<tr>
<td>10</td>
<td><img src="k" alt="Substrate" /></td>
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</tr>
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</table>

* Reaction carried out with cat/substrate = 1/5 wt/wt.
tron donor substituents, give also some condensation compounds (entry 5). The specific reduction of 9,10-anthraquinone to 9,10-dihydro-anthracene is worth highlighting as this reaction usually gives mixture of products.\textsuperscript{11,12}

Entry 1b shows that the catalyst/substrate ratio can be conveniently reduced to 1/5 without loss in productivity expressed as mmol$_{\text{prod}}$/g$_{\text{cat}}$ h. However, a further decrease in the ratio results in much slower reactions.

This work shows that the use of Cu/Al$_2$O$_3$ or Cu/SiO$_2$ represents a powerful catalytic switch in the reduction of aromatic ketones. Thus, preparation of the material using Al$_2$O$_3$ as the support and pre-reduction at 180 °C result in a very mild catalyst showing excellent selectivity towards formation of the corresponding alcohols without the need of any basic additive.\textsuperscript{13} On the other hand, by only changing the support and rising the activation temperature to 270 °C it is possible to obtain a catalyst that selectively converts aromatic carbonyl groups into methylene ones under very mild conditions and without the use of any acidic additive.

Both catalysts can be prepared in a simple way and are not pyrophoric nor pyrogenic even in their reduced form. Their heterogeneous nature and very high selectivity avoid formation of inorganic and organic wastes.

Catalyst preparation: 20 g of SiO$_2$ (Grace Davison, BET $= 320 \text{ m}^2/\text{g}$, PV = 1.79 mL/g) was added to a [Cu(NH$_3$)$_4$]$^{2+}$ solution prepared by adding NH$_4$OH to a Cu(NO$_3$)$_2$·3H$_2$O solution (8 g in 50 ml) until pH = 9. After 20 min under stirring, the slurry held in ice bath was slowly diluted to allow hydrolysis of the copper complex and deposition of the finely dispersed product to occur. The solid was separated by filtration, washed with water, dried overnight at 120 °C and calcined in air at 350 °C for 4 h. Before reaction, the catalyst obtained (Cu = 8% by weight) was reduced at 270 °C with H$_2$ (1 atm) before use, removing water formed under reduced pressure.

Experimental conditions: A solution of the substrate (100 mg) in toluene (8 mL) was transferred under N$_2$ in the reaction vessel containing the catalyst previously reduced (100 mg). Catalytic tests were carried out at 90 °C at atmospheric pressure of hydrogen under magnetic stirring. Reaction mixtures were analyzed by GC (5% phenyl–95% methylpolysiloxane capillary column, 30 m), GC–MS and by $^1$H NMR.

References and notes