A Sustainable Heterogeneous Catalytic Reductive Amination of Lignin Models to Produce Aromatic Tertiary Amines

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Supporting Information

1. Experimental

1.1 Reagents

The following analytical grade chemicals were purchased from commercial vendors: ZrOCl\textsubscript{2}, NH\textsubscript{3}·H\textsubscript{2}O, Mg(OH)\textsubscript{2}, MgO, Zn(OH)\textsubscript{2}, ZnO, ZrCl\textsubscript{4}, NaOH, HZSM-5, Al\textsubscript{2}O\textsubscript{3}, Al(OH)\textsubscript{3}, 3,4,5-trimethoxybenzaldehyde, anhydrous N,N-dimethylformamide, benzaldehyde, Anhydrous, 15 tetrahydrofuran, n-propanol, zirconium n-propoxide, vanillin, furfural, formic acid, dimethylamine. Nitrogen supplied in a high-pressure cylinder was used through a reducing valve without further treatment.

1.2 The preparation of catalyst

The preparation of ZrO(OH)\textsubscript{2} and ZrO\textsubscript{2}

The catalyst was prepared by 4.04 g of zirconium oxychloride (Alfa, hydrated) in 400 mL of deionized water. The solution was stirred at room temperature, and then ammonia solution was added until the pH was equal to 10. The gel was aged for 72 h, filtered and washed with deionized water until pH =7, then the obtained solid was dried at 80°C for 12 h. After grinding, the ZrO(OH)\textsubscript{2} catalyst was obtained.

The ZrO\textsubscript{2} catalyst was obtained after the ZrO(OH)\textsubscript{2} catalyst was calcined at 600°C for 4 hours.

The synthesis of the Zr(OH)\textsubscript{4} catalyst

Typically, 40 mL ZrCl\textsubscript{4} aqueous solution (0.16 mol/L) was taken into a beaker, and its pH value was adjusted to 10 by dropwise addition of aqueous solution of 0.1 mol/L NaOH under vigorous stirring and monitored with a pH meter. After a staying time of 72 h, the suspension was filtered and
washed with deionized water until pH = 7, then the obtained solid was dried at 80°C for 12 h. After grinding, the Zr(OH)$_4$ catalyst was obtained.

**The synthesis of the t-ZrO$_2$ catalyst**

First, the gel was obtained through continuous stirring and reflux of 60.0 g n-propanol, 5.6g 5 zirconium n-propoxide, 5.28g acetic acid, and 12.8g deionized water for 12 h at 70°C. The gels were then kept at room temperature (25°C) for 24h. Then the gels were filtered and washed with ethanol for three times. And the white solid was dried at 80°C for 12 h, and then calcined at 600°C for 4 hours. Finally, the t-ZrO$_2$ catalyst was obtained.

1.3 General procedure for the reductive amination of aromatic aldehydes

All catalytic experiments are performed in a 120 mL autoclave equipped with the magnetic stirring and automatic temperature control. A typical procedure of reductive amination is as follows: 0.2 g of compound 1, 15 mL DMF solution and 0.05 g catalyst were charged into the reactor, and the atmosphere inside is replaced with the pure nitrogen after the reactor is sealed. Then the autoclave is heated to 160 °C, and then kept for 4 h with continuous stirring. After reaction, the autoclave was cooled and the obtained mixture is analysed by GC and GC-MS.

1.4 The separation of products

After the reductive amination of aldehyde, a purification procedure was carried out to obtain the pure product. Typically, the reaction solution was dried on a rotary evaporator under reduced pressure to obtain a deposition, then the obtained concentrate was dissolved in 15 mL ethyl acetate, and washed with a saturated brine for several times to completely remove DMF of the organic phase, and the organic phase was collected and dried again by a rotary evaporator to obtain a pure compound. Then the pure compound was characterized by $^1$H NMR.

2. The characterization of the catalyst
XRD characterization of the zirconia after being recycled was shown in Figure S1. It can be seen that both the diffraction peak width of zirconia and the peak intensity are elevated as the number of recycle being increased. According to the calculation of the Jade 6.5 software by Scherrer’s formula, the average size of catalyst is 13.4, 13.7, 14.0, 13.3 and 14.5 nm after 1~5 times of reuse, respectively. Thus, it is concluded that the crystal size does not change significantly. On the other hand, the change of the diffraction peak intensity indicates that only the crystallinity of zirconium oxide crystals continuously increases during the cycles.

Figure S2 Thermogravimetric analysis of zirconium hydroxide before and after reaction
The zirconium hydroxide that was used as catalyst after reaction at 160°C for 4 h in the anhydrous DMF is marked as U-Zr, and the fresh zirconium hydroxide is marked as the F-Zr. The U-Zr was used as catalyst in non-aqueous DMF with a conversion of 37%, much lower than the 92% conversion of the F-Zr under similar conditions, compared with a high conversion up to 99% in the aqueous DMF solvent.

Thermogravimetric analysis (Figure S2) and infrared detection (Figure S3) were employed to characterize the changes of zirconium hydroxide before and after reaction. On the thermogravimetric curve, the U-Zr showed a lower mass loss rate (Figure S2), especially in the low temperature range (150°C-240°C), indicating that it experienced a dehydration process during the reaction. But, a stronger hydroxyl absorption peak occurs that provide a high catalytic activity if the U-Zr was used in the aqueous DMF solvent. Based on above results, it could be considered that the combination of zirconium hydroxide and a certain amount of water show a high catalytic activity, and the presence of water can effectively improve the catalytic activity of ZrO$_2$ and ZrO(OH)$_2$. 
In the pyridine-IR detection, the pyridine was used as a probe molecule to characterize the Brøsted acid (B acid) and Lewis acid (L acid) on the surface of catalyst. In the Figure S4, the adsorption at 1440 cm\(^{-1}\) corresponds to the center of L acid, the absorption band at 1540 cm\(^{-1}\) indicates that pyridine is adsorbed at the center of B acid, and the hydrogen formed at the surface of catalyst is hydrogen bond to pyridine at 1585 cm\(^{-1}\). It can be seen that the absorption peak of pyridine on the HZSM-5 is at 1530 cm\(^{-1}\), which shows that it has a B acid center. For the zirconium oxide, zirconium hydroxide and aluminium oxide, the adsorption peak at surface is only 1440 cm\(^{-1}\). These show that the surfaces only contain Lewis acid sites. Therefore, it can infer that the activities of heterogeneous catalysts are not only related to the surface acid but also are strongly influenced by the metallic components.

Figure S5 SEM images of the ZrO(OH)\(_2\) and ZrO\(_2\) catalyst
Figure S5 shows the SEM images of the ZrO(OH)$_2$ and ZrO$_2$ catalyst, it can be seen that the catalyst keeps almost unchanged after being used in the reductive amination reaction of aromatic aldehydes.

Table S1. The BET surface area, pore diameter and pore volume of different catalytic materials

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>BET Surface Area (m$^2$/g)</th>
<th>BJH Adsorption average pore diameter (Å)</th>
<th>BJH Adsorption cumulative volume of pore (cm$^3$/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZrO$_2$</td>
<td>26.48</td>
<td>64.87</td>
<td>0.04087</td>
</tr>
<tr>
<td>ZrO(OH)$_2$</td>
<td>241.39</td>
<td>23.96</td>
<td>0.1299</td>
</tr>
<tr>
<td>MgO</td>
<td>11.29</td>
<td>57.24</td>
<td>0.0138</td>
</tr>
<tr>
<td>Al$_2$O$_3$</td>
<td>139.79</td>
<td>60.90</td>
<td>0.2081</td>
</tr>
<tr>
<td>HZSM-5</td>
<td>260.14</td>
<td>37.95</td>
<td>0.11621</td>
</tr>
<tr>
<td>ZnO</td>
<td>3.41</td>
<td>48.67</td>
<td>0.0032</td>
</tr>
</tbody>
</table>

The BET data of different catalyst were presented in the Table S1. It is found that the specific surface area of the synthesized ZrO(OH)$_2$ was 241.39 m$^2$/g, and the surface area of obtained zirconia after calcination was reduced to 26.48 m$^2$/g, and the high surface area of zirconium hydroxide probably facilitates the happening of catalytic reaction. The specific surface area of zinc oxide and magnesium oxide is relatively small, which were only 3.41 m$^2$/g and 11.29 m$^2$/g, respectively. In addition, the specific surface area of alumina is 139.79 m$^2$/g, and the specific surface area of HZSM-5 is as high as 260.14 m$^2$/g. So, the existence of zirconium element is also crucial to the catalytic activity on the reductive amination of aromatic aldehyde with DMF.

3. The characterization of the products

Figure S6 The GC-MS analysis for the reductive amination of compound 1 with ZrO(OH)$_2$ catalyst
Figure S7 The $^1$H NMR of the reductive amination production with the 3,4,5-trimethoxybenzaldehyde as the substrate

$^1$H NMR spectrum of 3,4,5-Trimethoxy-N, N-dimethylbenzylamine (400 MHz, Chloroform-$d$) $\delta$ 6.54 (s, 2H), 3.80 (s, 6H), 3.76 (s, 3H), 3.40 (s, 2H), 2.26 (s, 6H).

Figure S8 The $^1$H NMR spectrum of the reductive amination production with the 4-ethoxybenzaldehyde as the substrate

$^1$H NMR spectrum of 4-Ethoxy-N, N-dimethylbenzylamine (400 MHz, Chloroform-$d$) $\delta$ 7.19 (d, $J$ = 8.4 Hz, 2H), 6.86 (d, $J$ = 8.4 Hz, 2H), 5.37 (d, $J$ = 14.0 Hz, 1H), 5.31 (s, 2H), 2.26 (s, 6H), 1.39 (s, 3H), $^2$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.19 (d, $J$ = 8.4 Hz, 2H), 6.86 (d, $J$ = 8.4 Hz, 2H), 5.37 (d, $J$ = 14.0 Hz, 1H), 5.31 (s, 2H), 2.26 (s, 6H), 1.39 (s, 3H)
$^1$H NMR spectrum of N, N-dimethyl-4-ethoxybenzylamine (400 MHz, Chloroform-$d$) $\delta$ 7.18 (d, $J = 8.6$ Hz, 2H), 6.83 (d, $J = 8.6$ Hz, 2H), 3.97 (d, $J = 14.0$ Hz, 2H), 3.33 (s, 2H), 2.20 (s, 6H), 1.38 (t, $J = 7.0$ Hz, 3H).

Figure S9 The $^1$H NMR spectrum of the reductive amination production with the 4-methoxybenzaldehyde as the substrate

$^1$H NMR spectrum of N, N-dimethyl-4-methoxylbenzylamine (400 MHz, Chloroform-$d$) $\delta$ 7.21 (d, $J = 8.6$ Hz, 2H), 6.90 – 6.81 (m, 2H), 3.78 (s, 3H), 3.36 (s, 2H), 2.21 (s, 6H).
Figure S10 The $^1$H NMR spectrum of the reductive amination production with the $m$-nitrobenzaldehyde as the substrate

$^1$H NMR spectrum of N, N-Dimethyl(4- nitrophenyl)methanamine (400 MHz, Chloroform-$d$) δ 8.16 (d, $J = 8.7$ Hz, 2H), 7.50 (d, $J = 8.7$ Hz, 2H), 3.52 (s, 2H), 2.26 (s, 6H).

Figure S11 The $^1$H NMR spectrum of the reductive amination production with the $o$-nitrobenzaldehyde as the substrate
$^1$H NMR spectrum of N, N-Dimethyl(2-nitrophenyl)methanamine (400 MHz, Chloroform-$d$) $\delta$ 7.84 (dd, $J = 8.1$, 1.3 Hz, 1H), 7.62 (d, $J = 1.6$ Hz, 1H), 7.55 (d, $J = 1.4$ Hz, 1H), 7.39 (td, $J = 7.7$, 1.5 Hz, 1H), 3.75 (s, 2H), 2.25 (s, 6H).

Figure S12 The $^1$H NMR spectrum of the reductive amination production with the 2,4-dinitrobenzaldehyde as the substrate

$^1$H NMR spectrum of 2,4-Dinitrobenzyldimethylamin (400 MHz, Chloroform-$d$) $\delta$ 8.76 (d, $J = 2.4$ Hz, 1H), 8.29 (dd, $J = 8.4$, 2.4 Hz, 1H), 7.51 (d, $J = 8.5$ Hz, 2H), 3.74 (s, 1H), 2.67 (d, $J = 2.6$ Hz, 6H)
Figure S13 The $^1$H NMR spectrum of the reductive amination production with the furfural as the substrate

$^1$H NMR spectrum of N, N-dimethyl-furfurylamine (400 MHz, Chloroform-$d$) $\delta$ 7.47 (s, 1H), 6.42 (s, 2H), 3.99 (s, 2H), 2.55 (s, 6H).

Figure S14 The $^1$H NMR spectrum of the reductive amination production with the syringaldehyde as the substrate

$^1$H NMR spectrum of N, N-dimethyl-(3,5-dimethoxy-4-hydroxybenzyl)methanamine (400 MHz, Chloroform-$d$) $\delta$ 6.56 (s, 2H), 3.85 (s, 6H), 3.36 (s, 2H), 2.24 (s, 6H).
Figure S15 The $^1$H NMR spectrum of the reductive amination production with the vanillin as the substrate

$^1$H NMR spectrum of N, N-dimethyl-(3-methoxyl-4-hydroxybenzyl) methanamine (400 MHz, Chloroform-$d$) $\delta$ 6.98 (d, $J = 1.9$ Hz, 1H), 6.84 – 6.64 (m, 2H), 3.82 (s, 3H), 3.62 (s, 2H), 2.39 (s, 6H).

Figure S16 The $^1$H NMR spectrum of the reductive amination production with the benzaldehyde as the substrate

$^1$H NMR spectrum of N, N-Dimethylbenzylamine (400 MHz, Chloroform-$d$) $\delta$ 7.19 (d, $J = 4.4$ Hz, 4H), 7.12 (ddd, $J = 8.8, 5.0, 3.8$ Hz, 1H), 3.29 (s, 2H), 2.11 (s, 6H).
Figure S17 GC-MS spectrum analysis for the production of 5-hydroxymethylfurfural

Figure S18 GC-MS spectra of 1-dimethylamino-3-phenylpropane

4. The study of reaction mechanism
Table S2. The results of control experiments to study the mechanism \(^{[a]}\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Reaction system</th>
<th>Conv. (%)</th>
<th>Yield (%) (^{[b]})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ZrO(OH)(_2)</td>
<td>Compound 1 + anhydrous DMF</td>
<td>92.5</td>
<td>92.5</td>
</tr>
<tr>
<td>2</td>
<td>ZrO(_2) + H(_2)O</td>
<td>Compound 1 + anhydrous DMF</td>
<td>95.8</td>
<td>95.8</td>
</tr>
<tr>
<td>3</td>
<td>none</td>
<td>Compound 1 + anhydrous DMF</td>
<td>&lt; 1</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>H(_2)O</td>
<td>Compound 1 + anhydrous DMF</td>
<td>17.8</td>
<td>17.8</td>
</tr>
<tr>
<td>5(^{[c]})</td>
<td>ZrO(_2)</td>
<td>Compound 1 + Dimethylamine+ Formic acid</td>
<td>74.1</td>
<td>74.1</td>
</tr>
<tr>
<td>6(^{[c]})</td>
<td>ZrO(OH)(_2)</td>
<td>Compound 1 + Dimethylamine+ Formic acid</td>
<td>62.6</td>
<td>61.8</td>
</tr>
<tr>
<td>7(^{[c]})</td>
<td>none</td>
<td>Compound 1 + Dimethylamine+ Formic acid</td>
<td>73.9</td>
<td>73.9</td>
</tr>
<tr>
<td>8(^{[d]})</td>
<td>ZrO(_2)</td>
<td>Compound 1 + Dimethylamine</td>
<td>28.1</td>
<td>0</td>
</tr>
<tr>
<td>9(^{[d]})</td>
<td>ZrO(OH)(_2)</td>
<td>Compound 1 + Dimethylamine</td>
<td>14.5</td>
<td>0.3</td>
</tr>
<tr>
<td>10(^{[d]})</td>
<td>none</td>
<td>Compound 1 + Dimethylamine</td>
<td>4.5</td>
<td>0</td>
</tr>
</tbody>
</table>

\(^{[a]}\) Reaction conditions: 0.2 g of 1, 0.05 g catalyst, in 15 mL of anhydrous DMF, under 0.3 MPa of N\(_2\), reaction time 4 h, temperature 160 °C. \(^{[b]}\) The data are obtained by GC with the internal standard technique. \(^{[c]}\) The molar ratio of 1: dimethylamine: formic acid is 1: 5: 5 (33 wt% dimethylamine and 88 wt% formic acid aqueous solution), in a 15 mL of tetrahydrofuran solvent. \(^{[d]}\) Reaction was carried out in a 15 mL of tetrahydrofuran solvent

In the DMF solvent, the reaction showed extremely low activity without the participation of Zr(IV). When tetrahydrofuran was used as the solvent, the reduction reaction could not proceed without the presence of formic acid, and the presence of Zr(IV) did not significantly promote the reduction reaction.

In the isotope experiment, a GC-MS analysis and \(^{1}\)H NMR spectroscopy confirmed that, after a reaction with heavy water participation. a tertiary amine product did not contain any deuterium in the structure, confirming that all the added H in the final product was derived from DMF.

![Figure S19. The MS spectra of the reductive amination of compound 1 with ZrO\(_2\) + H\(_2\)O system (a) or ZrO\(_2\) + D\(_2\)O system (b) in DMF solvent](image-url)
Figure S20. The $^1$H NMR spectra of the reductive amination of compound 1 with ZrO$_2$ + H$_2$O system (a) or ZrO$_2$ + D$_2$O system (b) in DMF solvent.

[With ZrO$_2$ + H$_2$O system: $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 6.54 (s, 2H), 3.80 (s, 6H), 3.76 (s, 3H), 3.40 (s, 2H), 2.26 (s, 6H). With ZrO$_2$ + D$_2$O system: $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 6.55 5 (s, 2H), 3.86 (s, 6H), 3.84 (s, 3H), 3.35 (s, 2H), 2.24 (s, 6H).]