Note

Cu–exchanged Y–zeolite: A heterogeneous catalyst for the synthesis of \( \alpha \)-aminoketones

Prodeep Phukan* & A Sudalai

Process Development Division, National Chemical Laboratory, Pune 411008

Received 16 November 1999; accepted (revised) 14 June 2000

Cu-zeolite catalyzes the amination of silyl enol ethers using Phl=NTs producing \( \alpha \)-amino ketones in good yields.

The amination of carbonyl compounds is an important reaction because of its potential as a synthetic method for a variety of biologically active compounds and unnatural amino acids. The resulting \( \alpha \)-amino ketones are important reagents because they possess both nucleophilic and electrophilic centers, which are useful in the construction of nitrogen containing heterocycles. Among the many methods available for the synthesis of \( \alpha \)-amino ketones, the use of N-[(p-toluenesulfonyl)iminophenyl]iododianane, Phl=NTs, is found to be a good aminating reagent. The aziridination of enol silanes reported by Evans could afford the \( \alpha \)-N-tosylamino ketones in the presence of various copper salts as catalysts. This method uses the homogeneous condition, which is always associated with many disadvantages including tedious workup procedures. Transition metal exchanged zeolites can be used as catalysts for a variety of chemical transformations. Noble metals highly dispersed in zeolites are commercially available catalysts. As part of our investigation on metal exchanged catalysts for various organic transformations, we wish to report a new heterogeneous catalytic method for the direct preparation of \( \alpha \)-N-tosylamino ketones from silyl enol ethers using Phl=NTs over Cu-Y zeolite (Scheme I).

Results and Discussion

Preparation of silyl enol ethers was carried out following a very convenient procedure reported recently by Lin. Cu-exchanged Y-zeolite (Cu-Y) was prepared by an ion exchange method in an aqueous solution of copper acetate. The Cu exchanged Y-

\[ \begin{align*}
\text{OTMS} & \quad \text{Phl=NTs} \\
(1) & \quad \text{Cu-Y, MeCN} \\
& \quad 25^\circ\text{C} \\
R_1, R_2 & = \text{aryl and cycloalkyl}
\end{align*} \]

zeolite was filtered out, washed with distilled water and dried at 100°C for 12 hr and further calcined for 3hr at 400°C. The metal content of the clay was determined by electron dispersive X-ray microprobe (EDX) (Kevex, US) connected to a JEOL, scanning electron microscope. Copper loading was 2.1 wt%. The amination reactions were carried out by adding the Cu-Y catalyst to a mixture of the silyl enol ether and Phl=NTs in dry acetonitrile at room temperature under inert atmosphere. Table I shows the result of amination of various silyl enol ethers.

The Cu-Y zeolite catalyzes efficiently the amination of silyl enol ethers to furnish the \( \alpha \)-amino ketones at room temperature. Yields are lower in case of cyclic substrates than that of acyclic one. But the rate of reaction is faster in case of cyclic system due to strain in the ring. The catalyst filtered was successfully recycled two times in case of 1-styryloxy- trimethylsilane without affecting the reactivity of the process. However, the yield of the product was observed to reduce by 2% when the catalyst was recycled for the second time, which is not significant. The recycled catalyst was activated at 120 °C for four hours before use.

In conclusion new heterogeneous catalytic method has been developed for the synthesis of amino ketones from silyl enol ethers using Phl=NTs in the presence of copper exchanged Y-zeolite as catalyst. The methodology is attractive due to the ease of separation of the catalyst from the reaction mixture and the scope of reusability of the catalyst.

Experimental Section

All solvents were distilled before use. Compounds were purified by flash chromatography over silica gel. IR spectra were recorded on a Perkin–Elmer 137 E spectrometer; \(^1\)H and \(^{13}\)C NMR spectra on 200 MHz...
Table 1.— Amination of various silyl enol ethers with Phl=NTs in presence of Cu-Y

<table>
<thead>
<tr>
<th>Expt. No.</th>
<th>Silyl enol ether</th>
<th>α-Amino ketone</th>
<th>Reaction period (hr)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OTMS</td>
<td>O</td>
<td>3</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>OTMS</td>
<td>O</td>
<td>3</td>
<td>63</td>
</tr>
<tr>
<td>3</td>
<td>OTMS</td>
<td>O</td>
<td>2</td>
<td>54</td>
</tr>
<tr>
<td>4</td>
<td>OTMS</td>
<td>O</td>
<td>2</td>
<td>52</td>
</tr>
<tr>
<td>5</td>
<td>OTMS</td>
<td>O</td>
<td>2</td>
<td>48</td>
</tr>
</tbody>
</table>

* a: Isolated yield after chromatographic purification

**General procedure for α-amination of silyl enol ethers.** To a stirred mixture of Phl=NTs (0.25g, 0.67 mmole) and 1-styrenylxy-trimethylsilane (0.19 g, 1mmole) in dry acetonitrile (10 mL) in a two necked round bottom flask, Cu-Y catalyst (25 mg) was added under nitrogen atmosphere (a slow stream of nitrogen was allowed to flow out while adding the catalyst). The reaction was stirred for 3hr. Turbidity went down to minimal during reaction. Solution was filtered through celite and evaporated. The crude material was chromatographed using 10% ethyl acetate—petroleum ether (boiling range 60—80°C) to get the pure product.

**N-(p-Toluenesulfonyl) aminooacetophenone:** Yield 121 mg (60 %); m.p 113—14 °C (lit° m.p.113—14 °C); IR (CHCl₃): 3250, 1700, 1345, 1290, 1215, 1160, 1095, 780, 750, 680cm⁻¹; ¹H NMR (200 MHz, CDCl₃): δ 2.35 (s, 3H), 4.45 (d, J=4.1 Hz, 2H), 5.7 (bs, 1H), 7.3 (d, J=8.1Hz, 1H), 7.45 (t, J=8.1Hz, 1H), 7.65 (t, J=8.1Hz, 1H), 7.8 (d, J=8.1Hz), 7.85 (d, J=8.1Hz, 1H); ¹³CNMR (50 MHz, CDCl₃): δ 21.27, 48.64, 127.04(×2), 127.74(×2), 128.78, 129.64, 133.87, 134.12, 143.52, 192.69.

**2-[N-(p-Tolylsulfonyl)amino] propiophenone:** Yield 63 %; m.p 112—13 °C (lit° mp 115—16 °C); IR (CHCl₃): 3285, 1670, 1585, 1400, 1340, 1220, 1160, 1090, 960, 860, 750, 700, 660cm⁻¹; ¹H NMR (200MHz, CDCl₃): δ 1.4 (d, J = 8.1 Hz, 3H), 2.3 (s, 3H), 4.95 (m, 1H, CHN), 5.8 (d, J = 8.1 Hz, 1H, NH), 7.20 (d, J = 8.1 Hz, 2H), 7.45 (t, J = 8.1 Hz, 2H), 7.60 (t, J = 8.1 Hz, 1H), 7.7 (d, J = 8.1 Hz, 2H), 7.8 (d, J = 8.1 Hz); MS (m/z, rel. intensity): 303 (M⁺, 1), 199 (10); 198 (100), 155 (70), 105 (36), 91 (26), 90 (16), 77 (11).
2-[(N-(p-Tolylsulfonyl)amino)cyclohexanone: Yield 54%; mp 132–34°C (lit. 165°C); IR (CHCl3): 3290, 1695, 1585, 1350, 1310, 1265, 1160, 1090, 815, 740, 670 cm⁻¹; ¹H NMR (300 MHz, CDCl3): δ 1.55 (m, 3H), 1.8 (m, 1H), 2.05 (m, 1H), 2.2 (dt, 1H) 2.35 (s, 3H), 2.5 (m, 2H), 3.7 (m, 1H, CHN), 5.75 (d, J=6.2 Hz, 1H, NH), 7.20 (d, J= 9.4 Hz, 2H) 7.7 (d, J= 9.4 Hz, 2H); MS (m/z, % rel. intensity): 239 (68), 211 (20), 155 (83), 154 (41), 139 (23), 133 (12), 111 (17), 97 (12), 91 (100), 84 (42), 83 (33), 73 (7).

2-[(N-(p-Tolylsulfonyl)amino)-4-methylcyclohexanone: Yield 52%; mp 99–100 °C; IR (CHCl3): 3280, 1695, 1590, 1400, 1220, 1160, 1090, 920, 810, 740, 660 cm⁻¹; ¹H NMR (200MHz, CDCl3): 0.9 (d, J= 8.1 Hz, 3H), 1.15-1.35 (m, 2H), 1.6-1.7 (m, 1H), 1.9-2.0 (m, 1H), 2.25-2.35 (m, 1H), 2.4 (s, 3H), 2.4-2.5 (m, 2H), 3.75 (m, 1H, CHN ), 5.75 (d, J= 5.4 Hz, 1H, NH), 7.3 (d, J= 9.2 Hz, 2H), 7.7 (d, J= 9.2 Hz, 2H); MS (m/z, % rel. intensity): 281 (M+, 6), 237 (8), 224 (51), 216 (51), 155 (88), 133 (9), 126 (26), 98 (81), 91 (100), 81 (29), 70 (14), 65 (37), 55 (15).

2-[(N-(p-Tolylsulfonyl)amino)-4-tert-butylcyclohexanone: Yield 48%; mp 120–21 °C; IR (CHCl3): 3290, 1700, 1600, 1340,1290, 1160, 1090, 980, 920, 810, 760, 670 cm⁻¹; ¹H NMR (200MHz, CDCl3): 0.9 (s, 9H), 1.25 – 1.5 (m, 2H), 1.55-1.7 (m, 1H), 2.05 – 2.15 (m, 1H) 2.2 – 2.35 (m, 1H), 2.4 (s, 3H), 2.45 – 2.6 (m, 2H), 3.75 (m, 1H, CHN), 5.75 (bd, J= 5.4 Hz, 1H, NH), 7.25 (d, J= 9.2 Hz, 2H); ¹3C NMR (CDCl3, 50.3 MHz): δ 21.7, 27.8, 28.6, 32.6, 38.3, 39.9, 46.0, 60.4, 127.3, 129.9, 143.8, 206.4; MS (m/z, % rel. intensity): 323 (M⁺, 3), 266 (54), 238 (22), 210 (25), 172 (9), 155 (49), 140 (17), 123 (24), 110 (17), 91 (100), 82 (20), 77 (7), 65 (36), 57 (70), 55 (49).

Acknowledgement

P P thanks the CSIR, New Delhi for the grant of research fellowship.

References