Rapid Communication

Metallic bismuth and aluminium: New and efficient catalysts for the preparation of various amides

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A new and efficient method for the preparation of various amides has been achieved by a simple reaction of an acid chloride with primary and secondary amines in the presence of bismuth or aluminium powder in anhydrous toluene.

The amide function occupies a unique position in organic chemistry because of its interesting chemistry and commercial importance. They are used as protecting groups in synthetic organic chemistry, because they offer the advantage of very good stability to a wide range of conditions. More recently, they have been found to give high selectivities in carbonyl directed catalyses. Several methods are available for the activation of carboxyl function in order to make it react with amine and most of the time it is achieved by converting the carboxyl function to the more reactive intermediate acid chloride. These methods have their own limitations for aliphatic or benzylic amino acid amides. Some of the methods use dimethylformamide as solvent, which is inconvenient to remove from the reaction mixture. Moreover, the use of triethylamine can lead to the problems with epimerisation during amino acid amide formation. Milder catalysts such as 2-pyridone and boron tribromide have been reported but the generality of these reagents has not been tested. We have been exploring the use of metals like cadmium, bismuth and aluminium. In continuation of this project in hand we wished to exploit the utility of metallic bismuth and aluminium in amide synthesis which is the subject of this communication.

When an acid chloride 2 was reacted with an amine 1 in anhydrous toluene in the presence of bismuth or aluminium powder, the corresponding amide 3 (cf. Scheme I) was obtained in an excellent yield (cf. Table I).

In a typical case, a mixture of benzoyl chloride (1.40g, 10 mmol) and bismuth powder (1.04 mg, 5 mmol) was stirred in dry toluene (25 mL) for 10 min. at room temperature. An anhydrous toluene solution of aniline (0.93g, 10 mmol in 15 mL) was then added slowly, and the reaction mixture stirred for 10 min. at the same temperature. The progress of the reaction was monitored by TLC. After the reaction was over, the reaction mixture was filtered and the solid washed with ether (100 mL). The combined filtrate was washed with 10% NaHCO₃ solution, water and dried over anhydrous Na₂SO₄. Removal of solvent followed by purification by passing through a short column of silica gel using chloroform as eluent, afforded the corresponding benzamidine in 95% yield (entry 1, Table I), mp 162 °C (lit. mp 162 °C) without the formation of any side products. Similar treatment of other substrates gave the corresponding amides 3 in 80-95% yields (Table I). Several examples illustrating this novel and rapid procedure are given in Table I. Furthermore, in order to show the preparative utility of this method it was applied to the synthesis of alkenamides. Thus, the reaction of crotonoyl chloride with aniline was carried out in the
Table I: Bi and Al mediated amide formation

<table>
<thead>
<tr>
<th>Entry</th>
<th>Acid chloride</th>
<th>Amine</th>
<th>Reaction period</th>
<th>YIELD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bi (min)</td>
<td>Al (min)</td>
</tr>
<tr>
<td>1</td>
<td>C_6H_5COCl</td>
<td>PhNH_2</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>4-NO_2C_6H_5COCl</td>
<td>PhNH_2</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>PhCH=CHCOCl</td>
<td>EtNH</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>C_6H_5CH=CHCOCl</td>
<td>EtNH</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>Ph--COCl</td>
<td>H_N</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>Ph--Cl</td>
<td>PhNH_2</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>7</td>
<td>4-CIC_6H_5COCl</td>
<td>N NH_2</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>8</td>
<td>Ph--COCl</td>
<td>N NH_2</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>9</td>
<td>4-CIC_6H_5COCl</td>
<td>S NH_2</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>4-CIC_6H_5COCl</td>
<td>NH_2</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>11</td>
<td>Ph--COCl</td>
<td>N</td>
<td>12</td>
<td>15</td>
</tr>
</tbody>
</table>

*The purity of the products were determined by elemental analyses and ^1_H NMR.

In conclusion, this new method of amide formation using metals (Bi and Al) offers a significant improvement over the existing procedures and thus helps facile entry into a host of products of potentially high synthetic utility. Also, this simple and easily reproducible technique affords various amides in excellent yields without involvement of an expensive material and without the formation of undesirable side products in comparison to the classical methods.

References
RAPID COMMUNICATIONS


5 For catalytic amidation between carboxylic acids and amines see:


10 Bismuth and aluminium used were of commercial grade and procured from Central Drug House (Pvt) Ltd, New Delhi 110002. Acid Chlorides either were obtained commercially or prepared according to known procedure and distilled before use.
