A conversion of aldoximes to nitriles using dabco/thionyl chloride complex

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Aldoximes undergo rapid dehydration with 1,4-diazabicyclo[2.2.2]octane, dabco, thionyl chloride complex, under mild reaction condition to afford nitriles in high yields.

Since nitriles serve as useful precursors for the synthesis of amines, carboxylic acids, amides and ketones, their synthesis is a topic of current interest to organic chemists, particularly in the light of recent developments in enzymatic processes. Dehydration of aldoximes represents an important route for the synthesis of nitriles. A great variety of reagents have emerged as a result of sustained efforts by chemists to discover new and mild methods to effect this conversion. However, many of these methods are deficient in some respect such as low yields, expensive or not readily accessible reagents, harsh reaction conditions, tedious work-up, or, perhaps, most importantly, a lack of generality for both the aliphatic and aromatic aldoximes. Reagents like triethylamine-sulfur dioxide and sulfuryl chloride fluoride allow the rapid and mild dehydration of aldoximes. However, the preparation of the reagents is inconvenient (-70°C). Effective conversion of aldoximes to nitriles with zeolites (CsX) requires high temperature (350°C) whereas montmorillonite KSF and Envirocet EPZG require very long reaction time (12-24 hr). The reagent like phosgene, diphosgene and triphosgene are hazardous to use. Recently, application of polyvinylpyrrolidone-thionyl chloride as an effective polymeric reagent was reported. Consequently, it seems that there is a still great demand for a new and efficient catalyst. We report herein the conversion of various types of aldoximes to the corresponding nitriles under mild reaction conditions by dabco/thionyl chloride complex in CH₂Cl₂ in high isolated yields.

The reagent was easily prepared in essentially quantitative yield as a white solid by the reaction of thionyl chloride with stoichiometric amount of dabco in dichloromethane at 0°C. At first, dabco/thionyl chloride complex (I) is probably formed, this kind of mechanism has been proposed in the reaction of thionyl chloride and polyvinylpyrrolidone, N-methylpyrrolidone, or N,N-dimethylformamide. Since this white complex was sensitive to moisture, it was used directly in its crude form suspended in dichloromethane. Representative aldoximes were treated with this complex in CH₂Cl₂ at 0°C. The reaction proceeded, probably via O-substituted aldoxime (II), which then underwent fragmentation to afford the corresponding nitriles in high yield (Scheme 1).

![Scheme 1](image-url)
Table I - Conversion of aldoximes to their corresponding nitriles using dabco/thionyl chloride complex. a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>@-CH=NOH</td>
<td>@-CN</td>
<td>40</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>Cl-@-CH=NOH</td>
<td>Cl-@-CN</td>
<td>55</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>MeO-@-CH=NOH</td>
<td>MeO-@-CN</td>
<td>50</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>Me-@-CH=NOH</td>
<td>Me-@-CN</td>
<td>45</td>
<td>85</td>
</tr>
<tr>
<td>5</td>
<td>Br-@-CH=NOH</td>
<td>Br-@-CN</td>
<td>50</td>
<td>82</td>
</tr>
<tr>
<td>6</td>
<td>O2N-@-CH=NOH</td>
<td>O2N-@-CN</td>
<td>45</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>O2N-@-CH=NOH</td>
<td>O2N-@-CN</td>
<td>50</td>
<td>85</td>
</tr>
<tr>
<td>8</td>
<td>O2N-@-CH=NOH</td>
<td>O2N-@-CN</td>
<td>70</td>
<td>85</td>
</tr>
<tr>
<td>9</td>
<td>Cl-@-CH=CH:CH=NOH</td>
<td>Cl-@-CH=CH:CN</td>
<td>40</td>
<td>88</td>
</tr>
<tr>
<td>10</td>
<td>CH3(CH2)3CH(CH2=CH)=NOH</td>
<td>CH3(CH2)3CH(CH2=CH)CN</td>
<td>50</td>
<td>85</td>
</tr>
<tr>
<td>11</td>
<td>CH3(CH2)3CH(CH2=CH)=NOH</td>
<td>CH3(CH2)3CH(CH2=CH)CN</td>
<td>45</td>
<td>90</td>
</tr>
</tbody>
</table>

a) Molar ratio of substrate to reagent was 1:3. b) Yields refer to isolated yields. c) Products were characterized by comparison of their physical data, IR, NMR spectra with known samples.

The procedure turned out to be general for a range of structurally diverse aldoximes. Aromatic aldoximes with electron-withdrawing or electron-donating groups, were cleanly, easily and efficiently dehydrated and afforded the corresponding nitriles as the exclusive products in short reaction time periods and in excellent yields. They were of high purity as determined by TLC and 'H NMR spectroscopy. Table I includes representative examples.

The advantage of using dabco/SOC12 as reagent for the dehydration of aldoximes is shown by comparing our results with those previously reported in the literature (Table II).

Compared to some previously reported reagents with major or minor drawbacks, several noteworthy features of this reagent are apparent. These are: the easy work-up procedure, availability of the reagent, operational simplicities, and use of inexpensive reagent. It is also worthy to note that attempts to perform the dehydration with thionyl chloride alone were not successful due to its very high reactivity and mixture of unidentified products were obtained.

In conclusion, the present one pot procedure for dehydration of aldoximes provides an easy, mild, efficient, versatile and general methodology for the preparation of nitriles from different classes of
40-70 dabeo. To the reaction mixture, aldoxime was slowly added and stirred at room temperature for 5 min. Thionyl chloride (3.85 ml, 0.092 mole) was added slowly. The mixture was stirred for about 5 min to effect the complete reaction of thionyl chloride and dabeo. To the reaction mixture, aldoxime (1 mmole) was slowly added and stirred at room temperature for 40-70 min. Progress of the reaction was monitored by TLC. On completion of reaction, the reaction mixture was poured into water (15 mL) and extracted with CH$_2$Cl$_2$ (15 mL). The organic layer was dried over anhydrous sodium sulfate and solvent evaporated under reduced pressure to afford the TLC and $^1$H NMR pure products in 80-92\% isolated yields.

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## References