Rapid Communication

Iodine mediated novel and facile dehydration of aldoximes to nitriles

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Aldoximes can be induced to loose water to yield nitriles at room temperature by treatment with iodine in acetonitrile in excellent yields.

The synthetic properties of the nitriles have been widely recognised as a useful intermediate and their utility in organic transformations. In recent years, it was demonstrated that nitriles could be converted to thiazole derivatives as inhibitors of superoxide, condensed with β-amino alcohol in the presence of iodine to give new chiral 2-oxazolines as FLC dopants or used as a starting material for synthesizing triazolo[1,5-a]pyrimidines with potential antiasthma activity. A variety of synthetic methods for the introduction of the cyano group to organic substrates have been well documented. A general procedure for the preparation of nitriles involves the nucleophilic substitution of a leaving group with a metal cyanide. Organic halogen compounds, arylsulfonates, alcohols, esters, ethers, nitro or amino compounds and diazonium salts could be used as substrates suitable for this type of reaction. Reagents like triethylamine/sulfur dioxide and sulfuryl chloride allow the rapid and mild dehydration of aldoximes. But, the preparation of the reagent is inconvenient (at -78 °C), and dehydration with zeolite (CsX) requires high temperature (350 °C). Also currently, peroxy-monosulfate on alumina, carbomethoxy, N,N-dimethylhydrazonium salts and phthalic anhydride have been employed. There are several other methods for the dehydration of aldoximes but the practical application of these methods may suffer from disadvantages such as the use of expensive or less easily available reagents, vigorous reaction conditions, prolonged standing or heating at moderately high temperatures, tedious manipulations in the isolation of the pure products, and limited adaptability both to aryl and alkyl substitution of aldoximes. Consequently there is a need for the development of protocol using rapidly available and safer reagents which lead to high yields of nitrite compounds. A very recent report13 prompted us to disclose our results for the novel conversion of aldoximes to nitriles using iodine in acetonitrile (Scheme 1). The reaction is complete within 1.5 - 2.5 hr, work-up is simple, the reagents are readily available, the yields are high and the method is applicable to aliphatic, aromatic, heterocyclic aldoximes and is free from any explosion.

Scheme 1

In a typical case, iodine crystals (0.25 g, 1 mmole) were taken in anhydrous acetonitrile (15 mL) and the solution was stirred magnetically for 5 min. To this solution benzaldoxime (0.12 g, 1 mmole) was added and the resulting mixture was further stirred for 1.5 hr. After completion of the reaction (monitored by TLC), the solvent was removed and the residue was treated with dichloromethane, washed with sodium thiosulfate (15 mL of 5% solution) and the organic layer was dried over anhydrous sodium sulfate. Removal of solvent under reduced pressure gave the corresponding benzonitrile in 95% yield. Similarly, other substituted aryl aldoximes and aliphatic aldoximes were reacted and the corresponding nitriles were isolated in high yields (Table 1). All the compounds thus obtained were characterised by infrared and 1H NMR spectroscopic data and finally by comparison with authentic samples. It is remarkable to note that when benzophenone or acetophenone oxime was treated with iodine, under same conditions, it did not yield any Beckmann rearranged product rather the parent carbonyl compound was regenerated. It is worth noting here that aldehydes can be converted directly to nitriles using ammonia gas saturated in methanol containing iodine or electrooxidation in methanolic ammonia solution containing potassium iodide or bubbling ammonia gas in dry benzene followed by addition of Pb(OAc)4. But the main drawback with these methods is that ammonia gas is to be bubbled in dry
Table 1—Iodine mediated a facile dehydration of aldoximes

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Products</th>
<th>Time (hr)</th>
<th>Yield (%)</th>
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<tr>
<td>1</td>
<td>PhCH=NOH</td>
<td>PhCN</td>
<td>1.5</td>
<td>95</td>
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<td>2</td>
<td>4Cl-C_6H_5CH=NOH</td>
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<td>2.0</td>
<td>80</td>
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<tr>
<td>6</td>
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<td>PhCH=CH-CN</td>
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<tr>
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<td>2.5</td>
<td>50</td>
</tr>
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</table>

*Yields refer to pure isolated products, fully characterized by ^1H NMR and IR spectroscopy*

benzene and under certain conditions iodine reacts with ammonia to give nitrogen triiodide monoamine which is an explosive\(^1\). In contrast, we have developed iodine a mild Lewis acid in character, for the dehydration of aldoximes, to provide excellent yields of the corresponding nitriles.

In conclusion, this simple and easily reproducible technique using iodine offer significant improvements over the existing procedure and affords various nitriles in excellent yields without the involvement of toxic and expensive material and without the formation of any undesirable side products.

References


   (b) Desai D G, Swami S S & Mahale G D, Synthetic Commun, 30, 2000, 1623