Indium-Mediated Facile Dehydration and Beckmann Rearrangement of Oximes

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Indium chloride has been developed as an efficient reagent for the conversion of aldoximes to nitriles and the Beckmann rearrangement of ketoximes to anilides.

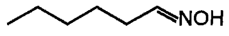
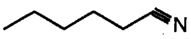
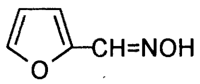
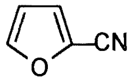
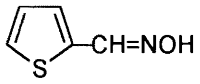
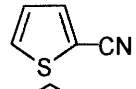
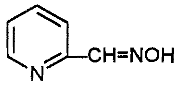
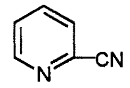
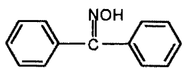
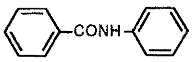
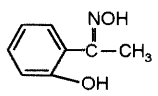
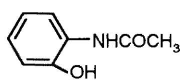
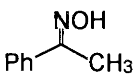
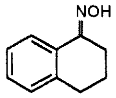
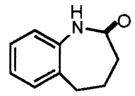
The synthesis of nitriles from aldoximes is an important functional group transformation in organic synthesis.[1] In recent reports, it was demonstrated that nitriles could be converted to thiazole derivatives as inhibitors of superoxide,[2] condensed with β-amino alcohol in the presence of catalyst to give new chiral 2-oxazolines as FLC dopants[3] or used as a starting material for synthesizing triazolo[1,5-*c*]pyrimidines with potential antiasthma activity.[4] Numerous methods have been developed for the conversion of aldoximes into nitriles such as 4,6-diphenyl-2-methylthiopyrylium tetrafluoroborate, phenyl chlorosulfite, sulfuryl chloride fluoride, chlorosulfonyl isocyanate, trifluoroacetic anhydride, triflic anhydride, iodotriethoxy phosphoranes, cyanuric chloride, trichloroacetyl chloride,[5] 2,4-dinitrophenylhydroxylamine[6] (expensive), hydroxylamine *o*-sulfonic acid,[7] aluminum iodide,[8] selenium dioxide[9] (hazardous) or formic acid[10] (corrosive) reagents. Also very recently peroxymonosulfate on alumina,[11] carbomethoxy *N*,*N*-dimethylhydrazonium salts[12] and phthalic anhydride[13] have been reported. Some of these methods require the use of strong bases, acids, or oxidizing agents and may thus lead to the formation of side products. Further, the practical application of these methods in organic synthesis 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 readily available and safer reagents which lead to high yields of nitrile compounds. The difficulties associated with these reagents can be overcome by the use of indium chloride as a dehydrating agent. In continuation to our studies on indium metals[14] we report herein the novel utility of indium[15] chloride as an efficient reagent for the conversion of aldoximes to nitriles and the Beckmann rearrangement of ketoximes to anilides. The method is applicable to aliphatic, aromatic, and heterocyclic aldoximes.

$$\underset{\mathbf{1}}{\text{R–CH = N-OH}} \xrightarrow{\text{InCl}_3} \underset{\mathbf{2}}{\text{R-C}\equiv\text{N}}$$

Scheme 1.

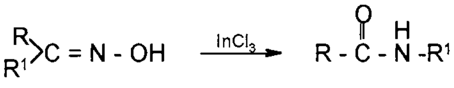
In a typical case, benzaldoxime (0.12 g, 1 mmol, R=Ph) was taken in dry acetonitrile (10 mL) and stirred for 2 min to dissolve the aldoxime. Then catalytic amount of anhydrous indium chloride (0.13 mmol 0.03 g) was added to it and the resulting mixture was refluxed for 1.5 h. After completion (monitored vide tlc) the solvent was removed and the residue was treated with dichloromethane, washed with water (15 mL) and the organic layer was dried over anhydrous sodium sulfate. Removal of solvent under reduced pressure gave the corresponding benzonitrile in 98% yield. Similarly substituted arylaldoximes and aliphatic oximes afforded corresponding nitriles (entries 2–11) in high yields (Table 1). When benzophenone oxime reacted with indium chloride under the same reaction conditions in dry acetonitrile, interestingly the Beckmann rearrangement occurred within 15 min to give the corresponding benzanilide (entry 12) in 95% yield (Scheme 2). Acetophenone oxime (entry 14) also reacted with $InCl_3$ to

Table 1 : Dehydration and Beckmann rearrangement of oximes

Entry	Substrate	Products	Time h	Yield[a] %
1	PhCH=NOH	PhCN	1.5	98
2	$4Cl\text{-}C_6H_4CH{=}NOH$	$4Cl\text{-}C_6H_4CN$	1.5	95
3	$4NO_2\text{-}C_6H_4CH{=}NOH$	$4NO_2\text{-}C_6H_4CN$	1.0	96
4	$4MeO\text{-}C_6H_4CH{=}NOH$	$4MeO\text{-}C_6H_4CN$	0.5	98
5	$4Me_2NC_6H_4CH{=}NOH$	$4Me_2NC_6H_4CN$	1.5	90
6	PhCH=CH-CH=NOH	PhCH=CH-CN	1.0	85
7	$PhCH_2\text{-}CH_2\text{-}CH{=}NOH$	$PhCH_2\text{-}CH_2CN$	1.5	80
8			1.5	75
9			1.5	75
10			1.5	85
11			1.5	80
12			.25	95
13			0.5	80
14		PhNHCOCH$_3$	0.5	50
15			0.5	72

[a] Yields refer to pure isolated products, fully characterised by ^1H NMR and IR spectroscopy.

afford acetanilide in moderate yield. It is remarkable to note that in the case of *o*-hydroxyacetophenone oxime (entry 13) the reaction occurred selectively to yield the corresponding anilide without the formation of benzoxazole as reported[16] by earlier workers as a result of an intramolecular ring closure. All the compounds obtained were characterised by infrared and ^{1}H NMR spectroscopies and finally by comparison with authentic samples.



3 **4**

Scheme 2.

In conclusion this simple and easily reproducible technique using indium chloride affords various nitriles and anilides in excellent yields without involvement of toxic and expensive material and without the formation of any undesirable side products.

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