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Gallium (III) triflate catalyzed dehydration of aldoximes

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Gallium triflate catalyzed dehydration of aldoximes to nitriles is described in good to excellent yields. Good catalytic and dehydrating capabilities of gallium triflate are demonstrated through this dehydration reaction.

KEY WORDS: gallium triflate; catalysis; dehydration; aldoxime; nitriles.

1. Introduction

Dehydration of aldoximes is a useful method for the synthesis of nitriles, which are important synthetic intermediates for pharmaceuticals, agricultural chemicals, dyes, and materials [1]. Nitriles are also versatile precursors for the synthesis of various carbonyl compounds and carboxylic acids. Although numerous reagents have been developed for the dehydration of aldoximes, a mild, general, highly efficient and catalytic process is still in great demand. Even recently, new reagents [2] are being pursued for this reaction, such as a rhenium(VII) oxo complex, Wilkinson's catalyst, alumina, indium triflate, etc. Due to the environmentally benign and yet powerful nature [3] of gallium (III) triflate ($Ga(OTf)_3$), we studied its use as a practical catalyst for the dehydration of aldoximes. The results are reported below.

2. Experimental

Benzaldoxime (98%) and cinnamaldehyde oxime (98%, mixture of *syn* and *anti*-isomers) were purchased from Lancaster. 9-Anthraldehyde oxime (99%, predominantly *syn*), 2-nitrobenzaldoxime (99%), 4-nitrobenzaldoxime (99%), *syn*-2-pyridinealdoxime (99%+), 4-pyridinealdoxime (98%), salicylaldoxime (98%) and 5-hydroxy-1-pentaloxime were obtained from Aldrich. Acetonitrile (DriSolv®) was from EM Science. Anhydrous gallium triflate was prepared as reported before [3].

A typical reaction was carried out in a capped 20 ml Carius glass tube. The oxime (1 mmol) was weighed into the glass tube and dissolved in 2 ml of CH_3CN, and then 26 mg (0.05 mmol) of gallium triflate was added to give a homogeneous reaction mixture under a dry stream of nitrogen. In the cases of less reactive substrates, increased amounts of $Ga(OTf)_3$ were used (Table 1). The tube was heated to the desired temperature. The reaction mixture was periodically monitored by TLC for completion. At the end of reaction, the mixture was cooled down. In cases, wherein the products precipitated they were easily separated by filtration followed by washing with a small amount of acetonitrile. Otherwise, 10 ml of water was added to the reaction mixture and the mixture was extracted 3 to 5 times (20 ml at a time) using diethyl ether. The combined organics were dried over anhydrous magnesium sulfate and then the solvents were removed at reduced pressure to give the product. In most cases, the product was almost pure and directly characterized by GC–MS and NMR. Otherwise the product was purified by column chromatography before analysis. The catalyst, $Ga(OTf)_3$ can be easily recovered from the aqueous phase by evaporation of water and drying around 200 °C and recycled. The activity of the catalyst hardly diminished even after three cycles.

3. Results and discussion

In order to determine the scope and efficacy of the dehydration reaction, we treated a wide variety of aldoximes with $Ga(OTf)_3$. For best miscibility, the highly polar solvent acetonitrile is used as reaction medium to dissolve both the aldoxime starting material and the catalyst. In most cases, 5 mol% of catalyst at 85 °C is sufficient to give satisfactory yields. As shown in Table 1, both aryl aldoxime and aliphatic aldoxime can be dehydrated readily. Also the double bond and hydroxyl functions are tolerant of the reaction conditions. Conjugated cinnamaldehyde oxime (entry 2) and 5-hydroxy-1-pentaldoxime (entry 9) are dehydrated to give cinnamonitrile and 5-hydroxy-pentanitrile, respectively, without side reactions. However, for salicylaldehyde oxime (entry 8), the dehydration hap-

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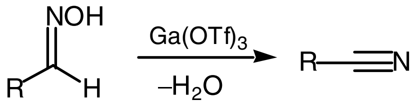
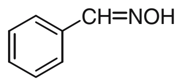
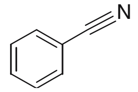
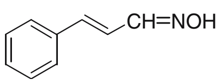
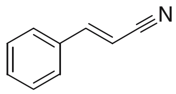
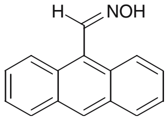
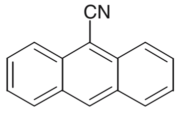
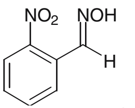
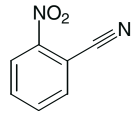
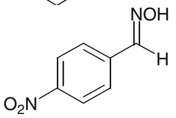
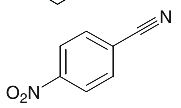
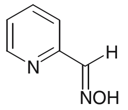
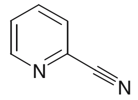
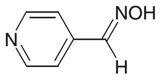
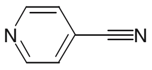
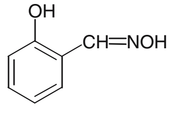
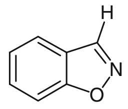
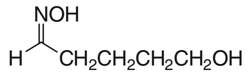
Table 1

Dehydration of aldoxime to nitiles[a] catalysed by $Ga(OTf)_3$



	Aldoxime	Product	Temp (°C)	Time (h)	Catalyst (mol%)	Yield (%)
1			85	5	5	85
2			85	2	5	90
3			85	10	5	87
4			85	16	5	100
5			120	16	5	82
6			120	16	5	81
7			120	16	5	87
8			85	4	10	80
9	 $\mathrm{H{-}CH({=}NOH)\,CH_2CH_2CH_2CH_2OH}$	$HOCH_2CH_2CH_2CH_2{-}C{\equiv}N$	85	20	5	85

[a] All products were thoroughly characterized by spectroscopic means and were compared with literature data.

pened between the *ortho*-hydroxy group and the oxime to give 1, 2-benzisoxazole, which gradually decomposes during silica gel separation to give the 2-hydroxybenzonitrile eventually. Most aldoximes were obtained as a mixture of *syn* and *anti*-isomers and the *anti*-isomer is more active than *syn* due to the favorable orientation of the two leaving groups in the elimination process. This explains why in some substrates (entry 5, 6, 7), the highest achievable yield at 85 °C is only 50% in spite of prolonged reaction time. Increasing the amount of the catalyst was not helpful. But after raising the temperature to 120 °C, higher product yields were obtained, since the *syn* isomer is also activated for dehydration by virtue of its fast isomerization to *anti*-isomer at this temperature.

4. Conclusion

Gallium trifluoromethanesulfonate is found to be a good and recoverable catalyst for the dehydration of aldoximes to nitriles. This methodology is currently being extended to other kinds of dehydration reactions due to the mild reaction conditions, high activity of the catalyst and potential recycling ability.

Acknowledgment

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