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Bismuth compounds in organic synthesis. Deprotection of ketoximes using bismuth bromide-bismuth triflate

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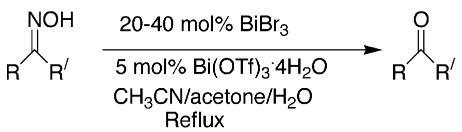
Abstract—Ketoximes undergo deprotection in CH_3CN/acetone/H_2O (3:6:1) in the presence of 20–40 mol% $BiBr_3$/5 mol% $Bi(OTf)_3$. Bismuth(III) salts are relatively non-toxic, insensitive to air and inexpensive. These features coupled with the use of a relatively non-toxic solvent system make this method an attractive alternative to existing routes for deprotection of ketoximes.

Oximes are frequently used to protect carbonyl compounds and hence considerable attention has been given to develop methods for their deprotection.[1] Oximes can also be synthesized from non-carbonyl compounds and thus their conversion to carbonyl compounds constitutes a useful synthesis of the latter.[2] The classical method for deprotection of oximes viz. hydrolytic cleavage requires the use of strong mineral acids and often results in low yields due to the formation of polymeric by-products. Hence a number of oxidative methods have been developed for the cleavage of oximes. Some examples include Dess–Martin periodinane,[3] PCC,[4] TBHP,[5] I_2/CH_3CN,[6] manganese acetate/benzene,[7] and potassium peroxymonopersulfate.[8] However, many of these reagents or the solvents used are toxic, corrosive or difficult to handle, especially on a large scale. With increasing environmental concerns, it is imperative that new 'environment friendly' reagents be developed.[9] One example of a mild method for deprotection of oximes uses DOWEX-50 resin.[10] Recently, bismuth compounds have become attractive candidates for use as reagents in organic synthesis because most bismuth compounds are relatively non-toxic, readily available at low cost and are fairly insensitive to small amounts of water.[11] Bismuth has an electron configuration of $[Xe]4f^{14}5d^{10}6s^{2}6p^{3}$. Due to the weak shielding of the 4*f* electrons (Lanthanide contraction), bismuth(III) compounds exhibit Lewis acidity. $BiCl_3$/microwave,[12] $BiCl_3$ in the presence of benzyltriphenylphosphonium peroxymonosulfate[13] and $Bi(NO_3)_3{\cdot}5H_2O$[14] have been used for the deprotection of oximes. We now report the use of a new bismuth-based catalyst system (bismuth bromide/bismuth triflate) for the deprotection of ketoximes.



Scheme 1.

Our continued work with bismuth(III) reagents has led to the development of bismuth bromide/bismuth triflate as an efficient reagent for the conversion of ketoximes to ketones (Scheme 1, Table 1).

The reaction is carried out using 20–40 mol% $BiBr_3$ and 5 mol% $Bi(OTf)_3{\cdot}4H_2O$ as a co-catalyst. The use of an inert atmosphere is not required for these reactions. Several solvents were investigated during the course of this study. The best results were achieved using CH_3CN/acetone/H_2O (3:6:1, v/v/v). The results of this study are summarized in Table 1.

While detailed mechanistic studies were not carried out, a few points merit comment. While $BiBr_3$ alone was effective in catalyzing the deprotection, the addition of $Bi(OTf)_3$ accelerated the reaction considerably. The use of 5 mol% $Bi(OTf)_3$ alone (no $BiBr_3$) was almost ineffective in catalyzing the deprotection. However, when 40 mol% $Bi(OTf)_3$ was used alone, the deprotection did

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Keywords: bismuth and compounds; oximes; deprotection; environment-friendly chemistry.

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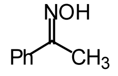
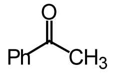
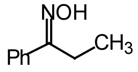
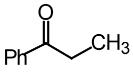
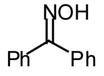
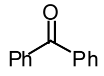
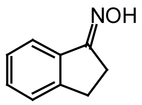
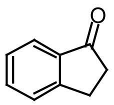
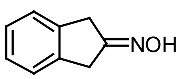
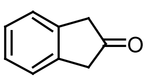
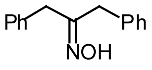
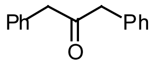
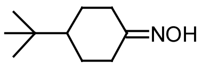
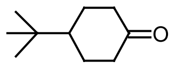
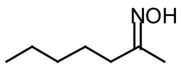
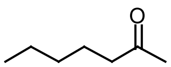
Table 1. Deprotection of ketoximes using $BiBr_3$-$Bi(OTf)_3 \cdot 4H_2O$ in CH_3CN/acetone/H_2O

Entry	Oxime	Time, h	Product	Yield (%) [a,b]
1		2.5		68 (94)
2		2		77 (98)
3		22		76 (98)[c]
4		3		79 (96)
5		0.7 h		65 (95)
6		4		85 (96)[c]
7		1		79 (93)
8		1		64 (92)

[a] Yields are not optimized. Refers to yield of isolated product. .

[b] Numbers in parentheses refer to percent purity of crude product as estimated by ^1H & ^{13}C NMR spectroscopy and GC analysis. The remainder was oxime in all cases.

[c] Product was purified by recrystallization from hexane.

proceed smoothly. Since $BiBr_3$ is commercially available, we found it more practical to use $BiBr_3$ with $Bi(OTf)_3$ as a co-catalyst.[15] A suspension of the catalyst system in water is acidic (pH 2). Hence it is possible that the true catalyst is HBr and/or TfOH, released from hydrolysis of $BiBr_3$ and $Bi(OTf)_3$. Indeed, the deprotection of 1-indanone oxime using 1.2 equivalents of HBr and 15 mol% TfOH proceeded smoothly, but the highly corrosive nature of HBr and TfOH detract from their use. The attempted deprotection of 1-indanone oxime using $BiBr_3$ and $Bi(OTf)_3$ in the presence of proton-sponge®(*N*,*N*,*N*′,*N*′-tetramethyl-1,8-naphthalenediamine)[16] was unsuccessful suggesting that the main role of the catalysts is to provide an acidic reaction medium.

The choice of solvents also merits comments. Acetone/H_2O was found to be effective but the rate of deprotection was considerably slower in this solvent system. For example, the deprotection of 1-indanone oxime in acetone/H_2O took over 12 h, while the addition of the polar coordinating solvent CH_3CN accelerated the reaction considerably (reaction time = 3 h). Acetone oxime was found to be a product of the reaction. This is not surprising in light of the fact that oximes have been synthesized from aldehydes and ketones by acid catalyzed transoximations using acetone oxime.[17] This suggests that the role of acetone is to drive the equilibrium towards product formation. The deprotection of 1-indanone oxime in acetonitrile/water (6:4) was only 78% complete after 5 h, suggesting that acetone plays a crucial role in driving the reaction. Water is also necessary for the deprotection since the reaction was significantly slower in CH_3CN/acetone as the solvent.

The deprotection works well with a variety of ketoximes. Aldoximes on the other hand proved much more resistant to the deprotection conditions. With benzaldehyde oxime, the reaction reached a 1:1 equilibrium mixture of benzaldehyde and the starting oxime within an hour. When the reaction was carried out with 40 mol% $BiBr_3$/20 mol% $Bi(OTf)_3$, the reaction reached a 3.5:1 equilibrium mixture of benzaldehyde and the starting oxime in 1 h.

A representative procedure is given here: A solution 1-indanone oxime (0.500 g, 3.40 mmol) in CH_3CN/acetone/H_2O (3:6:1, v/v/v) (5.00 mL) was stirred as $BiBr_3$ (0.609 g, 1.36 mmol), and $Bi(OTf)_3 \cdot 4H_2O$ (0.111 g, 0.170 mmol) were added. The mixture was stirred and heated at reflux. Reaction progress was followed by GC analysis. After 3 h, 10% aqueous acetic acid was added and the mixture was suction filtered and the solids were rinsed with ether (20 mL). The combined filtrates were concentrated on a rotary evaporator to remove the organic solvents. The residue was extracted with ether (2×40 mL). The organic layer was washed successively with 2 M NaOH (15 mL), H_2O (3×15 mL), saturated aqueous NaCl (20 mL), dried (Na_2SO_4) and concentrated on a rotary evaporator to yield 0.356 g (79%) of 1-indanone that was determined to be at least 96% pure by ^1H and ^{13}C NMR spectroscopy and GC analysis.

In summary, this work demonstrates a new and useful method for deprotection of ketoximes. The advantages of this method include (1) the use of relatively non-toxic reagents that are insensitive to air and small amounts of moisture and (2) the use of a relatively non-toxic solvent system.

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