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A facile deprotection of oximes using glyoxylic acid in an aqueous medium

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Abstract—Oximes of ketones and aldehydes are efficiently deprotected with glyoxylic acid in an aqueous medium at room temperature. Oximes can be cleaved selectively in the presence of a TBDMS group. This method is high yielding, fast, clean, safe, cost effective, and therefore very suitable for practical organic synthesis.

Oximes are frequently used to protect carbonyl compounds in the course of total syntheses and hence a plethora of reagents and methods[1] have been devised for the deprotection of oximes. Methods so far developed to regenerate carbonyl compounds from oximes consist of oxidative[2–6] or acid catalyzed[7] or reductive reactions.[8] Most of the methods involve reagents that are often hazardous or very toxic, expensive or not readily available.[9–18] These reagents often need to be freshly prepared or the reaction requires drastic conditions, long reaction times, and tedious work up. With increasing environmental concerns, it is imperative that new environmentally friendly reagents be developed.

The identification of aqueous glyoxylic acid as a mild and chemoselective reagent for the deprotection of oximes under solvent-free conditions formed the basis of this investigation. Organic reactions in water, without the use of any harmful organic solvents, are of great current interest, because water is an easily available, economical, safe, and environmentally benign solvent. Levulinic acid[19] and pyruvic acid[20] have been reported for *trans*-oximation, but the former procedure uses 1 N HCl, and the latter method acetic acid at reflux. This is not a very desirable situation when other acid-sensitive groups are present in the molecule.

Intrigued by the presence of two functional groups, viz acid as well as reactive aldehyde in glyoxylic acid, it was anticipated that both functionalities could be utilized and exploited for functional group transformations of carbonyl compounds. Encouraged by the ability of glyoxylic acid to effect deprotection of oxathiolanes[21] we wanted to explore the potential of the activated aldehyde in glyoxylic acid as an acceptor of oxime. We postulated that the activated aldehyde would serve as an excellent acceptor, in the presence of the internal acid, and would be able to transform oximes into the corresponding carbonyl compounds. We now report that glyoxylic acid is an efficient reagent for the selective deprotection of oximes derived from ketones and aldehydes (Scheme 1). The experimental procedure is very simple and involves stirring the oxime with 50% aq glyoxylic acid at room temperature. The reaction is fast and the product can be isolated by simple aqueous work up. The reaction is monitored by TLC. After completion of the reaction, reaction mixture is extracted with ether. The ether layer is separated, washed with 10 mL aq $NaHCO_3$, (10%) dried over anhydrous Na_2SO_4, filtered, and solvent is removed under reduced pressure to furnish carbonyl compound in pure form. Glyoxylic acid is commercially available as a 50% aqueous solution and requires no special handling. The reactions are performed in aqueous medium without any additional organic solvent. The carbonyl compounds thus obtained were sufficiently pure

R, R' = alkyl, aryl, H

Scheme 1.

Keywords: Ketone; Aldehyde; Oxime.
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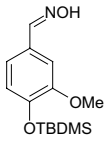
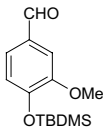
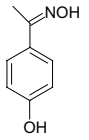
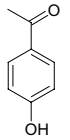
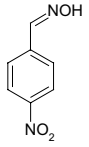
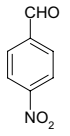
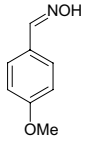
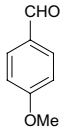
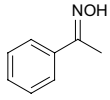
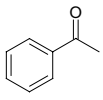
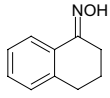
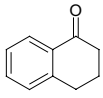
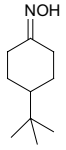
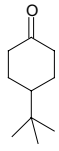
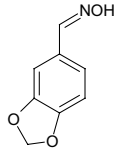
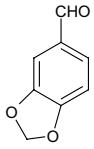
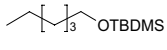
Table 1. Deprotection of oximes

Entry	Substrate	Product	Time (h)	Yield (%)
1			1	96
2			1	94
3			1.2	94
4			1	95
5			1	94
6			1	94
7			1.5	93
8			1.5	92
9			1.5	90
10			1	92
11		No reaction	1.5	

All compounds are characterized by IR and NMR spectroscopy.

and required no additional purification. The results of this study are summarized in Table 1.

Oximes derived from aromatic as well as simple ketones were smoothly deprotected at room temperature. Lack of reactivity was observed with phenolic *t*-butyl dimethyl silyl ether. To demonstrate the chemoselectivity of this reagent we prepared the TBDMS ether (entry 1). We were able to selectively deprotect the oxime group without affecting the TBDMS group in an excellent yield.

Thus this method could be used to selectively deprotect oximes in the presence of a TBDMS ether in a multifunctional compound.

In conclusion, this paper describes the use of glyoxylic acid for the chemoselective deprotection of oximes in an aqueous medium. The advantages of this method are the ease of work up, the observed selectivity and the use of environmentally benign reagent that is easy to handle and is inexpensive.

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