A Facile, Catalytic Deoximation Method Using Potassium Bromide and Ammonium Heptamolybdate in the Presence of Hydrogen Peroxide in an Aqueous Medium

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Abstract: A simple, mild and efficient procedure for the cleavage of a wide range of ketoximes and aldoximes to the corresponding carbonyl compounds in an aqueous medium using catalytic amounts of potassium bromide and ammonium heptamolybdate tetrahydrate in combination with 30% hydrogen peroxide is described.

Key words: oximes, potassium bromide, ammonium heptamolybdate tetrahydrate, hydrogen peroxide

Oximes are extensively used for protection, characterization and purification of carbonyl compounds.¹ Apart from their usefulness as latent protected forms of aldehydes and ketones, oximes occupy a key position in the chemical space that correlates carbonyl compounds with nitroalkanes, amines and carboxamides.^{2,3} Thus, the synthesis of oximes from non-carbonyl sources and subsequent cleavage to carbonyl compounds constitutes a number of useful entries to carbonyl compounds. Development of a plethora of deoximation methods by way of oxidative, hydrolytic and reductive cleavage of the C=N bond over the years^{4,5} attests to its synthetic importance. Currently, a fervent search for newer protocols addressing green chemistry issues, such as utilization of nontoxic reagents and photosensitizers, use of water as the reaction medium avoiding volatile organic solvents and replacement of stoichiometric by catalytic methods, is continuing. Thus, platinum(II) terpyridyl acetylide complex,⁶ chloranil/hv,⁷ a catalytic amount of iodine/surfactant/water,8 silicon bromide on wet silica gel,9 iodic acid for 'nonaqueous' hydrolysis,¹⁰ 2,2'-dipyridyl diselenide with triphenylphosphine,¹¹ 2-iodylbenzoic acid in the presence of β -cyclodextrin catalyst,¹² glyoxylic acid,¹³ functional ionic liquids physically confined in silica gel,¹⁴ and chloramine T^{15} have been employed for this purpose.

Our interest in developing deprotection protocols utilizing hydrogen peroxide and related compounds¹⁶ prompted us to explore a catalytic deoximation method in an aqueous medium¹⁷ based on hydrogen peroxide as the terminal oxidant. The low cost, high active oxygen content and formation of water as the only byproduct are the key advantageous features¹⁸ of this environment-friendly oxidant. However, although a thermodynamically powerful oxidant, oxidations of organic compounds with hydrogen peroxide are usually kinetically slow and require catalytic activation. A wide array of catalysts involving early transition metals (Ti, V, Mo, W) that form peroxo complexes are well documented.¹⁹ We identified ammonium heptamolybdate tetrahydrate for electrophilic activation of hydrogen peroxide in view of its ready availability and low cost, and particularly because oxidations employing molybdenum(VI) and hydrogen peroxide such as epoxidation, oxybromination and the Hunsdiecker reaction have been previously effectively carried out at higher pH (5-7) compared to similar vanadium(V)-catalyzed reactions in aqueous media.^{20,21} Herein, we delineate a mild, simple and convenient method of regeneration of aldehydes and ketones from their oximes employing catalytic amounts of potassium bromide and ammonium heptamolybdate tetrahydrate in combination with 30% hydrogen peroxide and a trace of perchloric acid in aqueous solution (Scheme 1).

$$\begin{array}{c} R^{1} \\ \searrow \\ R^{2} \\ R^{2} \\ R^{2} \\ R^{2} \\ HClO_{4} (trace), r.t. \\ R^{2} \\ R^$$

R¹, R² = alkyl, aryl, H

To this end, we initially set out to investigate the efficacy of a catalytic combination of ammonium heptamolybdate tetrahydrate and 30% hydrogen peroxide.²² Oximes of aromatic aldehydes and ketones were found to be resistant to cleavage with a reagent system comprising 30% hydrogen peroxide (1 mL/mmol substrate) and 20 mol% ammonium heptamolybdate tetrahydrate in aqueous solution. Addition of anionic surfactant (SDS) to the reaction mixture was also of no avail. However, benzaldehyde oxime and acetophenone oxime were cleaved to the parent carbonyl compounds in 70% and 75% yield in tetrahydrofuran/water (4:1 v/v) in 24 and 18 hours, respectively. The disappointingly slow reaction rates and, very importantly, failure to regenerate carbonyl compounds in aqueous solution without an organic solvent compelled us to explore an alternative oxidant system.

At this stage, we observed a dramatic increase in cleavage rate and yield upon addition of a catalytic amount of po-

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tassium bromide to the above reaction mixture in aqueous solution. Optimization experiments with benzaldehyde oxime as the model substrate revealed that 30% hydrogen peroxide (1 mL/mmol substrate) in the presence of 20 mol% each of ammonium heptamolybdate tetrahydrate and potassium bromide, and a trace of perchloric acid, yielded benzaldehyde, unaccompanied by any byproduct arising out of its further oxidation, in reasonable time (3 h) and excellent yield (95%) (Table 1, entry 3).

Table 1Cleavage of Benzaldehyde Oxime to Benzaldehyde with30% Hydrogen Peroxide, Catalyzed by Potassium Bromide andAmmonium Heptamolybdate Tetrahydrate, in Aqueous Solution

Entry	H ₂ O (mL)	KBr (mol%)	$\begin{array}{l}(NH_{4})_{6}Mo_{7}O_{24}\cdot\\ 4H_{2}O\ (mol\%)\end{array}$	HClO ₄ (mL)	Time ^a (h)	Yield ^b (%)
1	1	20	10	_	10	60
2	1	20	20	-	7	75
3	1	20	20	0.1	3	95
4	1	30	20	0.1	3	92
5	2	20	20	0.1	3	94
6	2	10	10	0.1	8	68
7	1	20	-	0.1	6	85

^a Reactions were conducted on 1 mmol of substrate at r.t.

^b Isolated yield upon column chromatography.

The fact that deoximation takes place with the potassium bromide/hydrogen peroxide combination, albeit slowly, even without ammonium heptamolybdate tetrahydrate is compatible with a cleavage process that is mediated by Br₂ or a Br⁺ equivalent. Ammonium heptamolybdate tetrahydrate catalyzes the oxybromination process, particularly in the presence of traces of perchloric acid. It has been demonstrated²³ that a proton source is required for oxyhalogenation and perchloric acid in trace amounts precisely fulfills this requirement thereby facilitating deoximation. The optimized reaction conditions²⁴ worked well for a wide range of substrates²⁵ including oximes of aromatic aldehydes and ketones, cyclic ketones with different levels of steric congestion, and α , β -unsaturated aldehydes and ketones, as shown in Table 2. It was gratifying to observe that oxidation-prone aryl aldoximes as well as cinnamaldehyde oxime (entry 16) underwent cleavage without further oxidation to the corresponding carboxylic acids. Remarkably, citral oxime (entry 20), which is often susceptible to acid-catalyzed rearrangement,²⁶ yielded citral cleanly. Sterically hindered oximes, such as camphor oxime (entry 18) and a 1-tetralone oxime derivative (entry 17), were cleaved with ease. No fragmentation product, such as a nitrile, was formed from camphor oxime, which often characterizes such highly branched ketoximes with a quaternary α -carbon atom facilitating formation of tertiary carbenic ion-mediated fragmentations.11 The absence of byproducts with bromine substitution in the side chain of acetophenone or the aromatic ring of activated carbonyl compounds containing hydroxy/methoxy groups is another remarkable feature of this method. This methodology is compatible with common functional groups such as hydroxy, methoxy, benzyloxy, ester, nitro, amino and methylenedioxy, and with conjugated as well as isolated double bonds.

Table 2Deoximation with 30% Hydrogen Peroxide and CatalyticAmounts of Potassium Bromide and Ammonium HeptamolybdateTetrahydrate in Water

Entry	Substrate	Time ^a (h)	Yield ^b (%)
1	NOH	3	95
2	но	4	92
3	HO	5	90
4	NOH	3	95
5	NOH	5	98
6	NO ₂ NOH	5	85
7	NOH	1.5	95
8	H ₂ N NOH	2	80
9	NOH NO2	3	85
10	NOH	3	90
11	NOH NO ₂ NO ₂	7	78
12	NOH	2.5	88

O (Z-isomer)

Table 2Deoximation with 30% Hydrogen Peroxide and CatalyticAmounts of Potassium Bromide and Ammonium HeptamolybdateTetrahydrate in Water (continued)



^a Reaction conditions: KBr (20 mol%), (NH₄)₆Mo₇O₂₄·4H₂O (20 mol%), 30% H₂O₂ (1 mL), HClO₄ (0.1 mL), r.t.

^b Refers to chromatographically pure products; all products were identified by IR and ¹H NMR spectra, and comparison with authentic samples.

In conclusion, a simple, mild and clean catalytic method of deoximation in aqueous solution utilizing inexpensive, commercially available potassium bromide and ammonium heptamolybdate tetrahydrate as catalysts and 30% hydrogen peroxide has been developed. The absence of overoxidation and other byproducts of released carbonyl compounds, operational simplicity, good balance of yield and reaction time, and avoidance of organic solvents as the reaction medium are the key advantageous features of this protocol.

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- (24) **Typical Deoximation Procedure:** To a thoroughly stirred soln of $(NH_4)_6Mo_7O_{24}$.4H₂O (296 mg, 0.24 mmol) in H₂O (0.5 mL) was added 30% H₂O₂ soln (1.2 mL). After stirring for 10 min, a soln of KBr (29 mg, 0.24 mmol) in H₂O (0.5 mL) was added followed by a drop of HClO₄ (0.1 mL)

whereupon the reaction mixture assumed a yellow coloration. Benzaldehyde oxime (145 mg, 1.2 mmol) was slowly added and the resulting mixture was stirred for 3 h (monitored by TLC); the mixture turned almost colorless. The reaction mixture was washed successively with 5% NaHSO₃ soln (2 × 2 mL) and H₂O (2 mL), and was then extracted with EtOAc (2 × 10 mL) and dried (Na₂SO₄). The concentrated extract was subjected to column chromatography (silica gel, 60–120 mesh; light petroleum) to yield benzaldehyde (120 mg, 95%). Its identity was confirmed by co-TLC (and superimposable IR spectrum) with an authentic sample.

- (25) The oximes were prepared using standard methods, see: Vogel, A. I. A Textbook of Practical Organic Chemistry, 3rd ed.; ELBS and Longman Group: London, 1973, The E- and Z-isomers of the oximes were not separated, unless otherwise stated (entry 12).
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