Simple, Economical and Environmentally Benign Selective Regeneration of Carbonyl Compounds from Oximes and *N*,*N*-Dimethyl Hydrazones

D. Subhas Bose,* A. V. Narsimha Reddy, A. P. Rudra Das

Organic Chemistry Division III, Fine Chemical Laboratory, Indian Institute of Chemical Technology, Hyderabad, 500 007, India
Fax +91(40)27160387; E-mail: dsb@iict.ap.nic.in

Received 23 April 2003

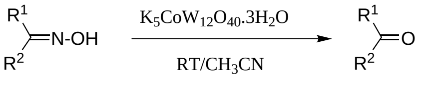
Abstract: A mild, efficient, selective method for the regeneration of carbonyl compounds from oximes and *N*,*N*-dimethylhydrazones in MeCN at ambient temperature or aqueous media has been carried out in excellent yields under $K_5CoW_{12}O_{40}\cdot 3\ H_2O$ (0.01 equiv) catalysis.

Key words: hydrazones, catalysis, oximes, aldehydes, ketones, protecting groups

Developing mild and efficient methods for the selective cleavage of nitrogen-containing derivatives to afford carbonyl compounds continues to be a significant aspect of organic chemical transformation. Oximes are highly stable and readily prepared compounds, which are used, extensively for the protection of carbonyl groups,[1] for the purification and characterization of carbonyl compounds,[2] and also in the preparation of amides via Beckmann rearrangement.[3] Oximes represent a series of derivatives for the classical identification of carbonyl compounds, as exemplified in the synthesis of erythromycin derivatives.[4] Since oximes could be prepared from non-carbonyl starting materials, such as the Barton reaction,[5] their conversion to carbonyl functionality is important from a synthetic point of view. Although several methods are available for converting oximes to carbonyl compounds consisting of oxidative or reductive procedures, the discovery of newer efficient methods is of practical importance. Some of the methods reported earlier for deoximation of carbonyl compounds involve PCC,[6] PCC–H_2O_2,[7] triethylammonium chlorochromate,[8] Raney nickel,[9] CrO_3–TMCS,[10] Dowex-50,[11] dimethyldioxirane,[12] *t*-BuO_2H,[13] titanium silicalite-1,[14] $Mn(OAc)_3$,[15] *N*-haloamides,[16] $NaIO_4$–silica,[17] *o*-iodoxybenzoic acid (IBX),[18] Dess–Martin periodinane,[19] $NaBiO_3$–silica,[20] quinolium fluorochromate (QFC),[21] $Mg(HSO_4)_2$–wet SiO_2,[22] and microwave-assisted[23] deoximation reactions.

However, many of the conventional procedures for the preparation of carbonyl compounds from their nitrogen derivatives have several limitations; i.e. the reagents used are often hazardous and expensive transition metals etc, along with reactions requiring long reaction times or reflux temperatures. In addition, some of the methods cited in the literature do not describe the deoximation of aldoximes, or they give low yields of aldehydes, or the liberated aldehydes are overoxidised. Moreover, Dess–Martin periodinane causes an explosion under excessive heating during preparation. Consequently, there is scope for further development of milder reaction conditions and better yields.

Recently, polyoxometalates have proved to be good catalysts in various oxidations.[24] They are applied in bulk or supported forms, and both homogeneous and heterogeneous catalysis is possible. Due to their acidic and redox properties, heteropoly compounds (heteropoly acids and salts) are useful and versatile catalysts in a number of transformations.[25] The versatility of potassium dodecatangestocobaltate trihydrate encouraged us to carry out the deoximation under mild reaction conditions. In the course of our studies on the use of heterogeneous catalysis in fine organic chemistry, we developed a method which allows the practical route for the selective regeneration of carbonyl compounds by using inexpensive and reusable $K_5CoW_{12}O_{40}\cdot 3\ H_2O$[26] (0.01 molar equiv) catalyst in MeCN at ambient temperature (Scheme 1). To our knowledge, however, the generality and applicability of $K_5CoW_{12}O_{40}\cdot 3\ H_2O$ in the regeneration of carbonyl compounds from the corresponding oximes and *N*,*N*-dimethylhydrazones is not known. The salient features of our method are: that the reaction proceeds efficiently in high yields (78–95%) at room temperature within a few minutes, the mild nature of $K_5CoW_{12}O_{40}\cdot 3\ H_2O$, and easy work-up procedure. Moreover, the catalyst could be quantitatively recovered from the reaction mixture by using simple filtration of the contents and washing with solvent, and could be reused after thermal activation. For example, the catalyst was reused for the deoximation of 2,4-dimethoxybenzaldehyde more than two times with no loss of catalytic activity.



R^1,R^2 = alkyl,aryl, or H

Scheme 1

To explore the generality and scope of this process, diverse aliphatic and aromatic aldoximes were studied to illustrate this novel and general method for the selective regeneration of carbonyl compounds (Scheme 1) and the results are summarized in Table 1. It is noteworthy that,

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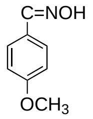
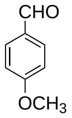
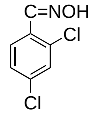
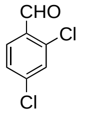
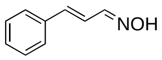
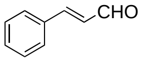
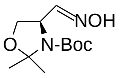
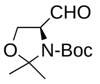
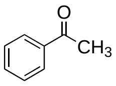
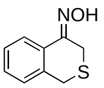
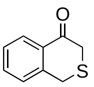
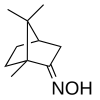
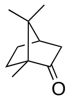
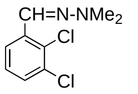
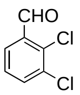
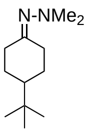
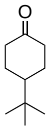
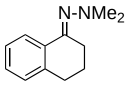
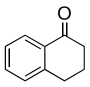
Synthesis 2003, No. 12, Print: 02 09 2003. Web: 07 08 2003.
Art Id.1437-210X,E;2003,0,12,1883,1885,ftx,en;Z05403SS.pdf.
DOI: 10.1055/s-2003-40998

unlike other oxidative hydrolytic methods, the major drawback of over-oxidation of the resulting aldehydes, was not observed under the reaction conditions. Even the sterically hindered camphor oxime has been successfully converted to camphor in good yields. Interestingly, the α,β-unsaturated oximes underwent deoximation very efficiently without affecting the C=C bond and the reaction is essentially chemoselective. In addition to that, stereochemical integrity at the aldehyde-bearing carbon was retained (entry 4).[27]

Table 1 Oxidative Deprotection of Oximes and *N*,*N*-Dimethylhydrazones Using $K_5CoW_{12}O_{40}\cdot 3\ H_2O$

Entry	Substrate	Time (min)	Product[a]	Yield (%)[b]
1[c]		60		95 (1st run) 90 (2nd run) 88 (3rd run)
2		45		90 88[d]
3		30		93
4		45		86
5		90		92
6		90		89
7		60		85
8	Me(CH$_2$)$_5$CH=NOH	90	Me(CH$_2$)$_5$CHO	78
9		45		84
10		90		88
11		120		91

[a] All the products were identified by comparing mp, IR, ^{1}H NMR and TLC with those of authentic samples.[28]

[b] Yield refers to isolated products.

[c] Catalyst was reused at least three times.

[d] The reaction was carried out in H_2O.

Another noteworthy advantage of the reagent is the exclusive oxidation of oximes and *N*,*N*-dimethylhydrazones irrespective of the presence of tosylhydrazones, phenylhydrazones or semicarbazones (Scheme 2). When mixtures of equimolar amounts of 2,4-dimethoxybenzaldehyde oxime, *N*,*N*-dimethylhydrazone and 2,4-dimethoxybenzaldehyde semicarbazone or 2,4-dimethoxybenzaldehyde phenylhydrazone were reacted with potassium dodecatangestocobaltate trihydrate, only the oxime and *N*,*N*-dimethylhydrazone was selectively oxidized to their corresponding carbonyl compound and the semicarbazone or phenylhydrazone remained unchanged. However, oxidation of semicarbazones or phenylhydrazones with potassium dodecatangestocobaltate requires a higher molar ratio of catalyst, much longer reaction times, reflux temperature in acetonitrile, and gives low yields.

In conclusion, we have reported herein several noteworthy features of a new catalyst for the regeneration of carbonyl compounds. The reaction proceeds under essentially neutral conditions, and the catalyst is recoverable and reusable. This protocol can be readily applied to large-scale processes with high efficiency and selectivity, making it an economical and environmentally friendly process for the regeneration of carbonyl compounds.

Deprotection of Oximes and Hydrazones; General Procedure

Method A

To a stirred solution of oxime or *N*,*N*-dimethylhydrazone (2.0 mmol) in MeCN (5 mL) was added solid catalyst $K_5CoW_{12}O_{40}\cdot 3\ H_2O$ (0.01 mmol, 32 mg) in portions over 2–3 min. The suspension was vigorously stirred at r.t. for the specified time (Table 1). The progress of the reaction was monitored by TLC. The reaction mixture was filtered to separate the catalyst, the solid material was washed with MeCN (20 mL), and the solvent was removed in vacuo to afford the crude product which was purified by column chromatography (silica gel, E-Merck 60–120 mesh) in 78–95% yields.

Method B

2,4-Dichlorobenzaldoxime (2.0 mmol) was suspended in H_2O (5 mL) along with potassium dodecatangestocobaltate trihydrate (0.01 mmol, 32 mg), and the heterogeneous mixture was stirred rapidly and refluxed for 2 h (monitored by TLC). The reaction mixture after being cooled to r.t. was extracted with CH_2Cl_2 (15 mL) and the solvent was removed in vacuo to afford the corresponding pure carbonyl compound in 88% yield.

l-Oxazolidine Oxime

$[\alpha]_D^{20}$ –25.3 (*c*, 2.5, $CHCl_3$).

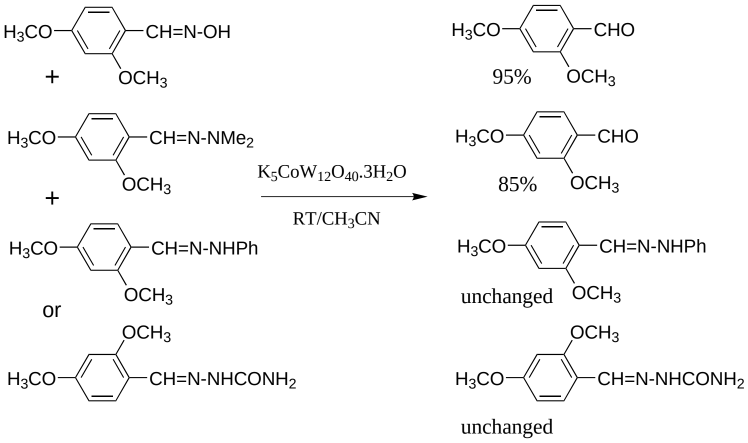
^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.32 (s, 9 H), 1.38 (br s, 3 H), 1.55 (br s, 3 H), 3.72 (dd, 1 H, *J* = 8.7, 8.3 Hz), 3.85 (dd, 1 H, *J* = 8.7, 2.9 Hz), 4.05–4.12 (m, 1 H), 6.71–6.83 (br s, 1 H), 7.29–7.42 (m, 1 H).

l-Oxazolidine Aldehyde

Mp 132–135 °C (Lit. 134–135); $[\alpha]_D^{20}$–88.5 (*c* 0.5; $CHCl_3$) [Lit[26] –91.7 (*c* 1.34, $CHCl_3$).

IR (neat): 1735, 1700 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.35 (s, 9 H), 1.41 (br s, 3 H), 1.54 (br s, 3 H), 3.75 (dd, 1 H, *J* = 8.7, 8.3 Hz), 3.92 (dd, 1 H, *J* = 8.7, 2.9 Hz), 3.97–4.01 (m, 1 H), 9.54 (br s, 1 H).



Scheme 2

Oxime (Entry 6)

^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.65 (s, 2 H), 3.78 (s, 2 H), 7.03–7.35 (m, 3 H), 7.81 (m, 1 H).

Potassium Dodecatangestocobaltate Trihydrate ($K_5CoW_{12}O_{40}\cdot3$ H_2O) Catalyst

Cobaltous acetate (5.0g, 0.01 mol) and sodium tangestate (39.6g, 0.06 mol) were initially treated with acetic acid (5 mL) and H_2O at pH 6.5 to 7.5 to give sodium tangestodicobalt(II)ate. The sodium salt was then converted into the potassium salt by treatment with potassium chloride (26.0 g). Finally, the cobalt(II) complex was oxidized to the cobalt(III) complex by potassium persulfate (21.0 g) in H_2SO_4 (2 M; 80 mL). The crystals of $K_5CoW_{12}O_{40}\cdot3$ H_2O were dried at 200 ºC. After recrystallization with MeOH, potassium dodecatangestocobaltate trihydrate ($K_5CoW_{12}O_{40}.3$ H_2O) was obtained.

Yield: 17.5g (55%); light blue solid.

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