Highly Efficient Regeneration of Carbonyl Compounds from Oximes, Tosylhydrazones, 1,3-Dithiolanes, and 1,3-Dithianes Using Cupric Nitrate Supported on Silica Gel

Jong Gun Lee* and Je Pil Hwang
Department of Chemistry, College of Natural Sciences, Pusan National University, Pusan 609-735, Korea

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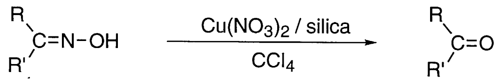
Cupric nitrate supported on silica gel is exceptionally efficient in regenerating aldehydes and ketones from oximes, tosylhydrazones, 1,3-dithiolanes, and 1,3-dithianes.

Several nitrosonium and nitronium ion donors were reported to be effective for the regeneration of carbonyl compounds from protected derivatives.[1,2] Nitronium or nitrosonium tetrafluoroborate,[3] sodium nitrate or nitrite coupled with chlorotrimethylsilane,[4] clay supported ferric and cupric nitrate[5] are such reagents used for deprotecting oximes and hydrazones.

Recently copper and some other metallic nitrates supported on silica gel[6] were reported to be effective for the oxidation of alcohols. We wish to report that cupric nitrate supported on silica gel is an exceptionally efficient reagent for regenerating aldehydes and ketones quantitatively from their corresponding oximes, tosylhydrazones, 1,3-dithiolanes and 1,3-dithianes.

Silica gel supported cupric nitrate was prepared according to the known procedure.[7] Most aromatic aldoximes and ketoximes were easily cleaved by this supported reagent and produced the corresponding carbonyl compounds in high yields within an hour at room temperature.[8] The reactions of some aliphatic oximes were slower and had to be refluxed for the complete conversion to carbonyl compounds in a reasonably short period of time. The results for some representative oximes using silica gel supported cupric nitrate are summarized in Table 1.

Table 1. Regeneration of Aldehydes and Ketones from Oximes[a] Using $Cu(NO_3)_2$ Supported on Silica Gel



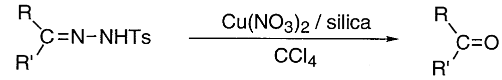
Run	Carbonyl Compounds	Temp./°C	Time/min.	Yield/%[b]
1	Benzaldehyde	25	30	95
2	*p*-Chlorobenzaldehyde	25	10	93
3	Octanal	80	100	97
4	Cinnamaldehyde	25	50	94
5	Acetophenone	25	60	95
6	Benzophenone	25	30	97
7	Benzoin	25	60	97
8	Cyclohexanone	80	50	95
9	1,2-Cyclohexanedione[c]	80	50	72
10	1,2-Cyclohexanedione[d]	25	50	85
11	Cyclopentanone	80	60	93
12	4-*t*-Butylcyclohexanone	80	60	98
13	3,3-Dimethyl-2-butanone	80	60	97
14	2-Cyclohexen-1-one	25	50	94

[a] Commercially unavailable oximes were prepared according to the known procedures.[9] [b] Isolated yield. Not optimized. [c] From its monooxime. [d] From its dioxime.

The present deoximation procedure was equally effective or better than any reagents[2-4] reported so far in the literature. The simple isolation procedure was an additional advantage. The reaction probably involves an attack of nitronium ion to the nitrogen of oximes. The subsequent decomposition leading to carbonyl regeneration are not clear yet.

Hydrazones in general are less readily hydrolyzed and the deprotection of them requires more reactive reagents or harsher reaction conditions compared with oximes. A number of methods and reagents have been developed for regenerating carbonyl compounds from their hydrazone derivatives.[10-12] Cupric nitrate supported on silica gel turned out to be more or equally efficient than these reported reagents. Tosylhydrazones were dissolved or suspended in carbon tetrachloride and stirred with slightly more than one equivalent of cupric nitrate supported on silica. Simple filtration of the reaction mixture through a pad of silica gel gave carbonyl compounds in excellent yields.

Table 2. Aldehydes and Ketones from Tosylhydrazones Using $Cu(NO_3)_2$ Supported on Silica Gel[a]



Run	Carbonyl Compounds	Temp./°C	Time/min.	Yield/%[b]
1	Benzaldehyde	25	120	92
2	*o*-Chlorobenzaldehyde	80	10	93
3	*p*-Methoxybenzaldehyde	80	15	97
4	Cyclohexanecarboxaldehyde	80	90	92
5	Octanal	80	120	97
6	Cinnamaldehyde	80	180	92
7	Acetophenone	80	60	85
8	2-Acetylnaphthalene	80	60	92
9	Benzophenone	80	60	88
10	3-Methyl-2-butanone	80	60	97
11	Cyclohexanone	25	180	95
12	4-*t*-Butylcyclohexanone	80	90	97
13	3-Methyl-2-butanone	80	60	97

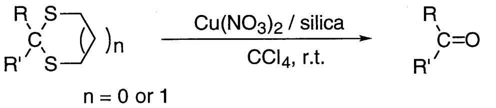
[a] Commercially unavailable tosylhydrazones were prepared according to the known procedures.[13] [b] Isolated yield. Not optimized.

Most tosylhydrazones of ketones or aldehydes tested were easily deprotected to the corresponding ketones and aldehydes. Some aromatic ketones such as acetophenone, propiophenone were obtained in somewhat lower yields (< 90 %). The overoxidation of the regenerated aldehydes to the acid derivatives was not observed for any aldehydes. The carbonyl compounds regenerated from *p*-tosylhydrazones are listed in Table 2.

The chemistry of 1,3-dithianes and dithiolanes in synthetic organic chemistry is well established.[14] At certain point along the synthetic sequence, the cyclic thioketal moiety has to be converted to the carbonyl group. Numerous procedures and reagents have been developed over a period of decades.[1] More recently nitrogen containing reagents such as nitrosonium and nitronium tetrafluoroborate, Clay-cop or Clay-fen[5] were reported to be satisfactory for the deprotection of dithioacetals.

Silica gel supported cupric nitrate was also proved to be remarkably efficient for the deprotection of cyclic thioketals.[15] 1,3-Dithiolanes and dithianes were deprotected much more readily than the corresponding oximes and tosylhydrazones. Thus, when an 1,3-dithiolane was treated with an equivalent of supported cupric nitrate at room temperature, the corresponding carbonyl compound was rapidly and quantitatively regenerated.[16]

Table 3. Dethioacetalization of 1,3-Dithiolanes and 1,3-Dithianes by $Cu(NO_3)_2$ Supported on Silica Gel[a]



Run	Carbonyl Compounds	Yield[b] (%) from	
		1,3-Dithiolane	1,3-Dithiane
1	Benzaldehyde	98	98
2	*o*-Chlorobenzaldehyde	98	98[c]
3	*p*-Methoxybenzaldehyde	98	98
3	*p*-Nitrobenzaldehyde	98[c]	97
4	3-Methylbutanal	96	93
5	Octanal	98	98
6	Cyclohexanecarboxaldehyde	97	97
7	Cyclohexene-4-carboxaldehyde	96[c]	97
8	Cinnamaldehyde	98	98
9	Acetophenone	98	98
10	Propiophenone	99	99[c]
11	Benzophenone	99	98[c]
12	2-Acetylnaphthalene	98	98[c]
13	Cyclohexanone	97	98
14	4-*t*-Butylcyclohexanone	98	98
15	3,3-Dimethyl-2-butanone	93	94

[a] Reactions at room temperature took less than 15 minutes for 1,3-dithiolanes and 25 minutes for 1,3-dithianes unless otherwise mentioned. [b] Not optimized isolated yield. [c] Reaction took slightly longer but less than 1 hour.

Most of 2,2-dialkyl-1,3-dithiolanes were completely cleaved to their parent ketones within 10 minutes. 2-Alkyl-1,3-dithiolanes were dethioketalized usually within 15 minutes, although *p*-nitrobenzaldehyde and 1,2,5,6-tetrahydrobenzaldehyde took slightly longer time (1 hr) for completion.

Most of ketones and aldehydes were also recovered quantitatively from the corresponding 1,3-dithianes in similar reactions. For most dithiolanes, the reactions in general were slightly slower compared with 1,3-dithiolanes. The results of dethioketalization of 1,3-dithiolanes and 1,3-dithianes are summarized together in Table 3.

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References and Notes

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7 The supported reagent was prepared from $Cu(NO_3)_2 1.5H_2O$ (18.76 g) and Merck Kieselgel 60 (70-230 mesh ASTM, 60 g) according to the known procedure (see Ref. 6).
8 $Cu(NO_3)_2$/silica (0.69 g) and benzaldoxime (122 mg, 1.0 mmol) were stirred in 5 mL of CCl_4 at room temperature for 30 minutes. The color of the solid turned dark blue. The mixture was filtered through a pad of magnesium sulfate, and the filtrate was concentrated to obtain essentially pure benzaldehyde in 95 % yield.
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15 1,3-Dithianes and 1,3-dithiolanes used in this report were prepared by treating carbonyl compounds with either 1,3-propanedithiol or 1,2-ethanedithiol in the presence of silica gel pretreated with tetrachlorosilane. J. G. Lee, H. T. Cha, and J. P. Hwang, *Org. Prep. Proc. Int.*, submitted.
16 The reaction of 2-phenyl-1,3-dithiolane is representative. Powdered $Cu(NO_3)_2$/silica (0.69 g) and 2-phenyl-1,3-dithiorane (1.0 mmol) were stirred in 5 mL of CCl_4 at room temperature for 20 minutes. The mixture was filtered through anhydrous $MgSO_4$, and the filtrate was concentrated to obtain essentially pure benzaldehyde in 98 % yield.