# The MTO-catalyzed oxidative conversion of *N,N*-dimethylhydrazones to nitriles

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Methyltrioxorhenium catalyzes the fast and efficient oxidation of aldehyde *N,N*-dimethylhydrazones to the corresponding nitriles in high yield.

N,N-Dimethylhydrazones derived from aldehydes (**1**) can be oxidatively transformed into nitriles (**2**) using hydrogen peroxide as the oxidizing agent and methyltrioxorhenium (CH₃ReO₃, abbreviated as MTO) as the catalyst, usually at the 1% level, as shown in eqn. (1). Ten specific examples are
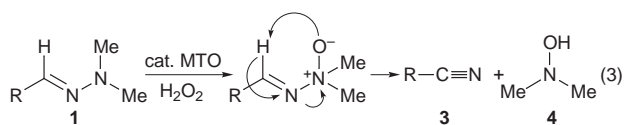
(1)
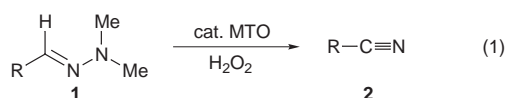
presented in Table 1.

MTO is a well established catalyst for oxidations utilizing hydrogen peroxide,[1,2] including oxidations of various nitrogen-containing compounds.[3–7] The reactions were best carried out in acetonitrile–acetic acid–pyridine solvent, 94.5 : 5 : 0.5. The use of acetic acid was mandatory since the hydrazones are sufficiently basic to deactivate MTO to the inactive perrhenate.[8] Without pyridine, however, the reaction was accompanied by 5–10% hydrolysis to the parent aldehyde. Hydrolysis can effectively be suppressed by a small amount of pyridine, to reduce the Lewis acidity of MTO and its peroxo adducts. This procedure prevents the hydrolysis of epoxides formed by the oxidation of alkenes by MTO–hydrogen peroxide.[9] Pyridine also accelerates the formation of the catalytically active peroxorhenium complexes as in eqn. (2).

(2)
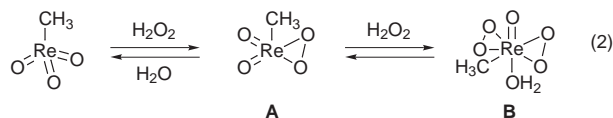
Under the described conditions the hydrazones **1** were completely transformed into the corresponding nitriles after several minutes as indicated by GC–MS analysis. The reaction is quite general: *N,N*-dimethylhydrazones of aliphatic, unsaturated, aromatic and heterocyclic aldehydes were successfully oxidized to the corresponding nitriles. Other present oxidizable functionalities did not interfere (see Table 1, entry 8 where the hydrazone was oxidized without the pyridine *N*-oxide being formed). In this particular example pyridine was not used, since the starting hydrazone itself functions in this regard. Also in entry 10, as expected, the double bond was not epoxidized during the reaction, indicating far greater reactivity of the hydrazone moiety compared to the double bond.

The oxidation of **1** presumably goes through the oxide **2**, which undergoes a Cope-type elimination[10] to yield the nitrile **3** and dimethylhydroxylamine **4**, eqn. (3). *N,N*-Dialkylhydrox-

ylamines are known to undergo oxidation to nitrones with H₂O₂–MTO.[7] No attempts were made to detect either dimethylhydroxylamine or its oxidation product.

N,N-Dialkylhydrazones are versatile and useful intermediates in organic synthesis, especially in carbon–carbon bond forming[11] reactions, which has led to considerable interest in the development of mild methods for their transformation into nitriles. Non-oxidative procedures *via N,N,N*-trimethylhydrazonium salts or directly, in hyperbasic media,[12,13] have been used, but they require high temperatures and strong bases. Several mild oxidative procedures for the use of hydrogen peroxide, using 3-chloroperbenzoic acid and magnesium monoperoxyphthalate, have been reported.[10,14,15] These reactions, however, are rather slow; for example, the 3-chloroperbenzoic acid reactions require several hours.

Hydrogen peroxide is a desirable reagent on several counts. Selenium dioxide and 2-nitrobenzeneselenic acid catalyze its reactions, giving good yields of nitriles from aromatic and

Table 1 Preparation of nitriles from aldehyde *N,N*-dimethylhydrazones[a]

Entry	Hydrazone	Product	Yield[b] (%)
1			88
2			90
3			92
4			95
5			93
6			94
7			93
8			92[c]
9			94
10			91

[a] With 10 mM substrate, 300 mM H₂O₂, 25 mM pyridine and 1 mM MTO in acetonitrile, acetic acid, pyridine (94.5:5:0.5) for 15 min. [b] Isolated yield. [c] Without pyridine.

(3)

unsaturated *N,N*-dimethylhydrazones, but hours, even days, are required. Moreover, these catalysts give poor results with aliphatic *N,N*-dimethylhydrazones which are largely hydrolyzed. Phosphomolybdic acid, $H_3PO_4 \cdot 12MoO_3 \cdot 12H_2O$, performs better with aliphatic hydrazones but it gives by-products such as the corresponding acids. Compared to these catalysts, MTO is clearly superior. MTO also catalyzes the oxidative cleavage of ketone hydrazones to the parent carbonyl compounds; these reactions are now being investigated.

A typical experimental procedure is as follows: **1** (100 mmol) was added to a rapidly stirred solution of MTO (1 mM), hydrogen peroxide (0.3 M, added as 30% solution in water), pyridine (25 mM) in 100 ml of acetonitrile containing 5 vol% HOAc. After 15 min, most of the acetonitrile was removed by rotary evaporation, and the residue poured into 300 ml of diethyl ether, washed successively with 0.1 M HCl and saturated sodium hydrogen carbonate. (In the case of 4-cyanopyridine, entry 8, the ether solution was washed only once with saturated sodium hydrogen carbonate.) The ethereal solution was then dried over anhydrous sodium sulfate, and the product obtained after evaporation. The crude nitriles were purified by column chromatography (*n*-hexane–acetone).

Notes and References

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