# MTO catalyzed oxidation of aldehyde *N*,*N*-dimethylhydrazones with hydrogen peroxide: high yield formation of nitriles and *N*-methylene-*N*-methyl *N*-oxide

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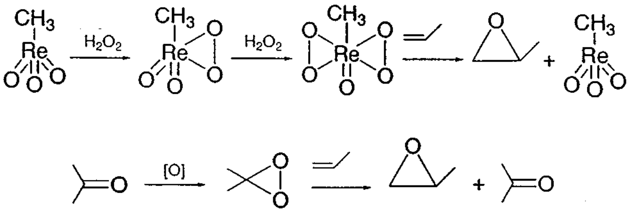
***N*,*N*-Dimethylhydrazones of aldehydes react with hydrogen peroxide at −50 °C in the presence of catalytic amounts of methyltrioxorhenium (MTO) to give in high yield the corresponding nitriles and *N*-methylene-*N*-methyl *N*-oxide.**

The transformation of aldehydes into nitriles is an important process in organic synthesis.[1,2] Several procedures are available for that purpose and very recently the oxidative conversion of *N*,*N*-dimethylhydrazones of aldehydes using dimethyldioxirane has been described.[3] Such a transformation has also been achieved by the use of peracids.[4] Both methods suffer from serious drawbacks: they both use stoichiometric amounts of oxidants which are either expensive (low yield formation of dimethyldioxirane from potassium peroxysulfate) and/or are waste-forming processes (acids from peracids). The use of hydrogen peroxide alone[2] or associated with a catalyst (either phosphomolybdic acid or sodium tungstate)[5] has also drawbacks: in the first case satisfactory yields were observed only in the case of hydrazones derived from aromatic aldehydes, whereas in the second case side reactions took place.

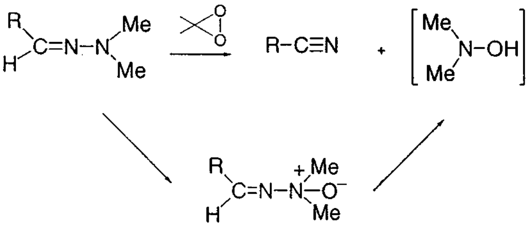
During our search for new applications of MTO[6] in organic synthesis, mainly based on the analogy which exists between dimethyldioxirane and the peroxo derivatives obtained upon oxidation of MTO with hydrogen peroxide (*e.g.* the epoxidation of olefins, Scheme 1),[7–11] we surmised that this system might be a good and efficient candidate for the catalytic transformation of *N*,*N*-dimethylhydrazones of aldehydes into nitriles.



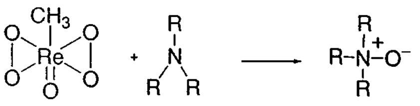
Scheme 1

Indeed, the mechanism which was suggested for the oxidative cleavage of dimethylhydrazones involved an electrophilic oxygen transfer from dioxirane to the terminal nitrogen atom leading to an *N*-oxide.[3] An intramolecular elimination of dimethylhydroxylamine was then supposed to lead to the nitrile (Scheme 2).

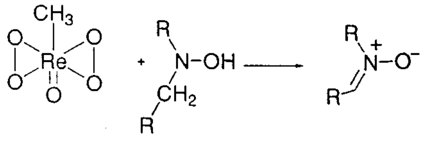
It is known that MTO catalyzes the oxidation of tertiary amines to *N*-oxides (Scheme 3).[12] Moreover, hydroxylamines are also catalytically converted into nitrones by the same system (Scheme 4).[13,14] Taken together, these two reactions would imply the formation of nitriles and *N*-methylene-*N*-methyl *N*-oxide from *N*,*N*-dimethylhydrazones of aldehydes. This indeed turned out to be the case (Scheme 5).



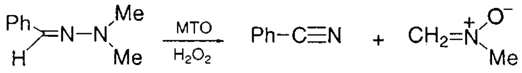
Scheme 2



Scheme 3



Scheme 4



1 2 3

Scheme 5

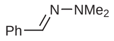
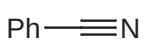
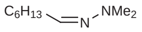
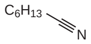
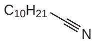
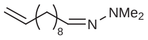
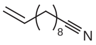
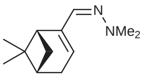
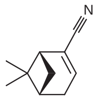
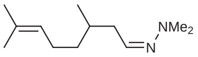
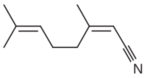
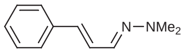
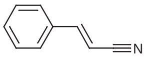
Thus, an ethanolic solution of the *N*,*N*-dimethylhydrazone of heptanal[15] (0.45 g, 2 ml of EtOH) was added dropwise to a yellow solution of MTO and $H_2O_2$ (1.5%, 2 equiv. of 35% $H_2O_2$) in EtOH at −50 °C. The solution was then allowed to warm to room temperature over 1 h. Evaporation of most of the solvent followed by the addition of water and extraction with $Et_2O$ gave, after evaporation of the organic solvent, the expected nitrile (0.29 g, 90%). The aqueous layer was also evaporated *in vacuo* to give an oily yellow liquid, which was also soluble in $CH_2Cl_2$. The mass spectrum of this product confirmed the molecular formula $C_2H_5NO$ (*m/z* 59). The $^1H$ NMR spectrum disclosed two signals: a singlet at $\delta$ 3.60 for the NMe group and an AB system for two hydrogens at $\delta$ 6.67. The $^{13}C$ NMR spectrum confirmed the presence of a methyl and a methylene group (DEPT experiment), respectively, at $\delta$ 132.5 and 50.85.[11]

An NMR experiment with stoichiometric amounts of preformed MTO diperoxide[9] and the *N*,*N*-dimethylhydrazone of benzaldehyde clearly demonstrated the formation of the expected nitrone. It appears therefore that the transformation of the hydrazones into a mixture of nitriles and nitrone **3**‡ *via* dimethylhydroxylamine requires indeed 2 equiv. of $H_2O_2$.

Similar results, shown in Table 1, were observed under the same experimental conditions, starting from a series of hydrazones, and giving high yields of the expected nitriles.

Interestingly, epoxidation of the carbon–carbon double bonds of the hydrazones **4**–**7** was not observed under these precise reaction conditions. However, addition of an excess of $H_2O_2$ (3–4 equiv.) led, in the case of **6**, to the expected epoxy-nitrile

**Table 1** Synthesis of nitriles *via* oxidation of *N*,*N*-dimethylhydrazones with MTO and $H_2O_2$ yield (%)[a]

| Entry | Hydrazone | Nitrile | Yield (%)[a] |
|---|---|---|---|
| 1 |  |  | 93 |
| 2 |  |  | 90 |
| 3 |  |  | 98 |
| 4 |  |  | 83 |
| 5 |  |  | 83 |
| 6 |  |  | 96 |
| 7 |  |  | 99 |

[a] Isolated yield.

arising from the oxidation of the non-conjugated double bond. Thus, the low temperature formation of the nitriles in the presence of stoichiometric amounts of $H_2O_2$ is compatible with the presence of less reactive functional groups.

Under the same conditions, *N*,*N*-dimethylhydrazones of ketones (*e.g.* phenyl ethyl ketone) led to the corresponding ketones, whereas imines derived from aldehydes (*e.g.* *N*-benzylidenemethylamine) gave essentially the corresponding amides (55%) and those derived from ketones (*e.g.* *N*-cyclohexylidenepropylamine), mixtures of oxaziridines and nitrones. Work is in progress to assess the scope of these latter transformations.

## Notes and References

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‡ All new compounds exhibited appropriate $^1$H and $^{13}$C NMR spectra and elemental analyses. *Selected data* for **3**: $\delta_H$ (200 MHz, $D_2O$, $SiMe_4$) 6.71 (d, $J_{HH}$ 6, N=C*H*), 6.63 (d, $J_{HH}$ 6, N=C*H*), 3.60 (s, NC$H_3$); $\delta_c$ (50 MHz, $D_2O$) 132.50 (N=*C*), 50.85 (N*C*$H_3$).

1 D. Barton and W. D. Ollis, in *Comprehensive Organic Chemistry*, Pergamon, Oxford, UK, 1979, vol. 2, ch. 8, pp. 534–535.
2 R. F. Smith, J. A. Albright and A. M. Waring, *J. Org. Chem.*, 1966, **31**, 4100.
3 A. Altamura, L. D'Accolti, A. Detomaso, A. Dinoi, M. Fiorentino, C. Fusco and R. Curci, *Tetrahedron Lett.*, 1998, **39**, 2009.
4 R. Fernandez, C. Gasch, J. M. Lassaletta, J. M. Llera and J. Vazquez, *Tetrahedron Lett.*, 1993, **34**, 141.
5 S. I. Murahashi, T. Shiota and Y. Imada, in *Organic Synthesis*, Wiley, New York, 1991, vol. 70, pp. 265–271.
6 W. A. Herrmann and F. Kühn, *Acc. Chem. Res.*, 1997, **30**, 169.
7 H. Rudler, J. Ribeiro Gregorio, B. Denise and J. Vaissermann, *J. Organomet. Chem.*, 1997, **548**, 295.
8 H. Rudler, J. Ribeiro Gregorio, Bernard Denise, J. M. Brégeault and A. Deloffre, *J. Mol. Catal. A, Chem.*, 1998, in the press.
9 W. A. Herrmann, R. W. Fischer, W. Scherer and M. U. Rauch, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 1157.
10 A. M. Al-Ajlouni and J. H. Espenson, *J. Org. Chem.*, 1996, **61**, 3969.
11 T. H. Zauche and J. H. Espenson, *Inorg. Chem.*, 1997, **36**, 5257.
12 Z. Zhu and J. H. Espenson, *J. Org. Chem.*, 1995, **60**, 1326.
13 R. W. Murray, K. Iyanar, J. Chen and J. T. Wearing, *Tetrahedron Lett.*, 1996, **37**, 805.
14 A. Goti and L. Nannelli, *Tetrahedron Lett.*, 1996, **37**, 6025.
15 M. Yamashita, K. Matsumiya and K. Nakano, *Bull. Chem. Soc. Jpn.*, 1993, **66**, 4100.

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