

Catalyzed oxidation of alcohols by *cis*-dioxomolybdenum(VI) complexes via oxygen atom transfer from sulfoxides[†]

Christian Y Lorber, Irene Pauls, John A Osborn^{†*}

Laboratoire de chimie des métaux de transition et de catalyse, URA au CNRS 424,
Université Louis-Pasteur, Institut Le Bel, 4, rue Blaise-Pascal, 67000 Strasbourg, France

(Received 29 February 1996; accepted 14 June 1996)

Summary — Catalytic amounts of *cis*-dioxomolybdenum(VI) complexes in association with sulfoxides can be used to oxidize alcohols into carbonyl compounds. For primary alcohols, the oxidation into aldehyde is selective, no further oxidation into carboxylic acid is observed. The oxidation is most effective for benzylic and allylic alcohols. The mechanism is shown not to be of a Swern-type Me₂SO oxidation but probably involves a hydride transfer from a coordinated alkoxide to an oxo ligand on the Mo(VI) thereby forming aldehyde and an Mo(IV) species, the latter being reoxidized to Mo(VI) by the sulfoxide in an oxygen atom transfer step.

catalytic oxidation / alcohol / sulfoxide / oxo-complex / molybdenum

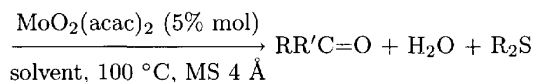
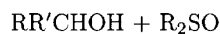
Résumé — Oxydation d'alcools catalysée par les complexes du *cis*-dioxomolybdène(VI) via un transfert d'oxygène provenant du sulfoxyde. Les complexes de *cis*-dioxomolybdène (VI) en quantités catalytiques associés à des sulfoxydes peuvent être utilisés pour l'oxydation des alcools en composés carbonyles. Pour les alcools primaires, l'oxydation en aldéhyde est sélective et ne conduit pas à l'acide carboxylique. Les meilleurs résultats sont observés pour les alcools allyliques et benzyliques. Le mécanisme réactionnel n'est pas du type Swern mais implique probablement un transfert d'hydruure de l'alcoolate coordonné au ligand oxo du molybdène (VI). Le molybdène (IV), formé dans le milieu, peut être réoxydé par le sulfoxyde via un transfert d'oxygène.

oxydation catalytique / alcool / sulfoxyde / complexe oxo / molybdène

Introduction

Oxidation of alcohols is one of the fundamental transformations in organic synthesis, and various stoichiometric reactions using transition-metal-oxo complexes are well known. The most frequently used reagents are a series of modified chromate species, MnO₄[−], V₂O₅ and, more recently, high oxidation state Ru complexes [1]. For several reasons (eg, economic, environmental), the development of catalytic processes for alcohol oxidation is an important goal, and would be particularly useful if O₂ could be used as the oxidant. During the course of our studies [2] on the catalyzed rearrangement of allylic and propargylic alcohols with molybdenum(VI) catalysts, we found that dioxomolybdenum(VI) complexes such as MoO₂(OBu^{*t*})₂ could also oxidize primary and secondary alcohol functions and that the reaction could be made catalytic in presence of excess Me₂SO. Subsequently, we found that the inexpensive and easily accessible MoO₂(acac)₂ could be used as the catalyst precursor (acac = acetylacetonate). We report here our preliminary results on the catalytic oxidation of var-

ious alcohols using sulfoxides as the oxidizing source (scheme 1) and compare the efficiency of these molybdenum catalysts when amine oxides are used as the oxidants.



Scheme 1

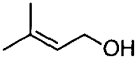
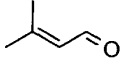
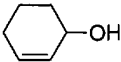
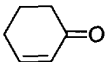
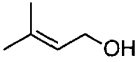
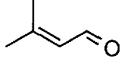
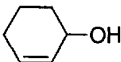
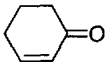
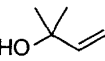
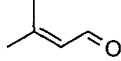
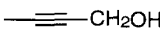
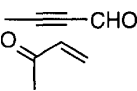

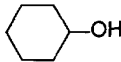
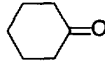
Results and discussion

The catalytic oxidation of various alcohols (20 equiv) was generally carried out using the MoO₂(acac)₂ catalyst (1 equiv) [3] in presence of the sulfoxide (40 equiv) in toluene or 1,2-dichlorobenzene solution except in the studies involving Me₂SO, where Me₂SO was used both as oxidant and solvent. The results are presented [4] in table I and figure 1. We initially anticipated that the

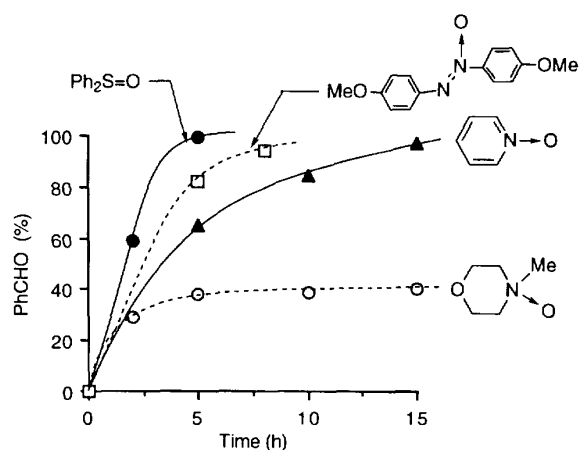
[†] This article is dedicated to my good colleague and friend, the ageless Raymond Weiss.

* Correspondence and reprints. E-mail: osborn@chimie.u-strasbg.fr

Table I. Catalytic oxidation of various alcohols using $\text{MoO}_2(\text{acac})_2/\text{R}_2\text{S}=\text{O}$ system^a.

Entry	Substrate	Oxidant ^b	Time (h)	Product ^c	Yield	Unreacted substrate
1		Me_2SO	7		99	0
2		Me_2SO	8		98	0
3	PhCH_2OH	Me_2SO	10	PhCHO	38	61
4	$t\text{-BuCH}_2\text{OH}$	Me_2SO	5 ^d	$t\text{-BuCHO}$	42	58
5		$\text{Me}_2\text{SO} + 1 \text{ equiv } \text{H}^+$	3		82	12
6		$\text{Me}_2\text{SO} + 1 \text{ equiv } \text{H}^+$	1		51	12 ^e
7	PhCH_2OH	$\text{Me}_2\text{SO} + 1 \text{ equiv } \text{H}^+$	10	PhCHO	98	1
8	PhCH_2OH	Ph_2SO	15	PhCHO	97	1
9	PhCH_2OH	$\text{Ph}_2\text{SO} + 1 \text{ equiv } \text{H}^+$	5 ^f	PhCHO	99	0
10	$\text{PhCH}(\text{OH})\text{Me}$	Ph_2SO	10 ^f	$\text{PhC}(\text{O})\text{Me}$	50	50
11		Me_2SO	10		25 ^g	75
12		Ph_2SO	5	 	9 18 ^h	45
13		$\text{Ph}_2\text{SO} + 1 \text{ equiv } \text{H}^+$	10 ^{d,i}		20	20 ^j

^a Conditions: $\text{MoO}_2(\text{acac})_2$ (1 equiv), substrate (20 equiv), 100 °C. ^b Me_2SO used as solvent and cooxidant; Ph_2SO used as 40 equiv in toluene; H^+ is $p\text{-TsOH}$ (1 equiv). ^c Yield in carbonyl product, in % (GC-determination). ^d 140 °C. ^e Formation of cyclohexene by GC-MS analysis. ^f MS 4 Å added. ^g Via oxidation after prior isomerization of the tertiary into the primary allylic alcohol. ^h Isomerization of propargylic alcohol. ⁱ $o\text{-Dichlorobenzene}$ used as solvent. ^j Formation of cyclohexene and dicyclohexyl ether (GC-MS analysis).



Conditions: $\text{MoO}_2(\text{acac})_2$ (1 equiv), PhCH_2OH (20 equiv), oxidant (40 equiv), $p\text{-TsOH}$ (1 equiv), MS 4 Å, toluene, 100 °C, GC analysis.

Fig 1. Oxidation of benzyl alcohol (20 equiv) at 100 °C catalyzed by $\text{MoO}_2(\text{acac})_2$ comparing diphenyl sulfoxide with various amine oxide oxidants.

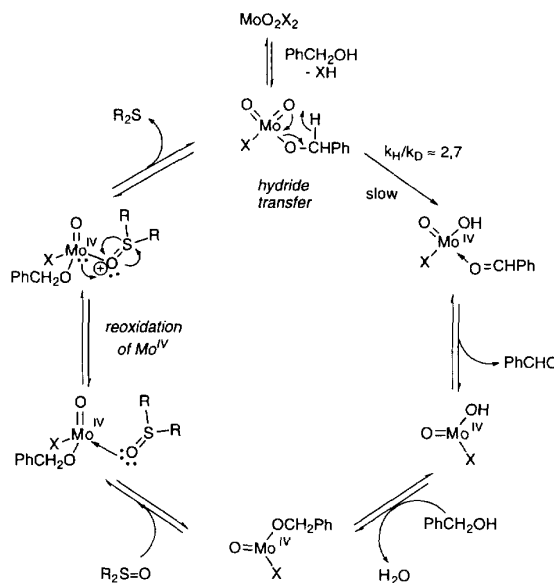
water formed in the reaction would cause degradation of the molybdenum catalyst and thus molecular sieves (MS, 4 Å) were added in many of our earlier experiments. Later, however, we found that this was unnecessary in most cases. We found that allyl and benzyl alcohols were oxidized by Me_2SO at 100 °C with nearly total selectivity to aldehydes (entries 1–3, table I) with, importantly, no further oxidation to acids. Aliphatic alcohols such as neopentanol were only sluggishly oxidized even at higher temperatures (140 °C) but nevertheless gave only the aldehyde product (entry 4). We found that certain of these oxidations could be accelerated by the addition of 1 equiv acid ($p\text{-TsOH}$) (eg, entries 5–7) but often at the price of increased competitive dehydration processes (entries 6, 13). Certain other sulfoxides were found to be more effective than Me_2SO , eg, Ph_2SO in toluene (entries 8, 9). The reaction rate appears to be sensitive to the steric factors near the alcohol functional group (entry 9). Further, we observe that concomitant rearrangement [2c] of allyl and propargylic alcohols may also take place during the oxidation process (entries 11, 12). The chemoselectivity of the $\text{MoO}_2(\text{acac})_2/\text{R}_2\text{S}=\text{O}$ catalyst appears similar to the Griffith oxidation [5] system $\text{RuO}_4^-/$

N-methylmorpholine-*N*-oxide where, for example, organic functions such as alkene, alkyne or aldehyde groups are not oxidized. However we found that catalytic oxidation of PPh_3 and PhSH can be carried out with the Mo system yielding the phosphine oxide and disulfide [6], respectively. Similar oxidations have been also catalyzed by certain molybdenum-dioxo complexes which were designed as synthetic models of molybdoenzymes [7].

Other single oxygen donor oxidants have been tried in place of the sulfoxide, in particular *N*-oxides such as tertiary amine-*N*-oxides, pyridine-*N*-oxides or azoxy compounds. However, although these are thermodynamically stronger oxidants [8] (by ca 10–15 kcal/mol) than the sulfoxides, the *N*-oxides are less efficient than the sulfoxides in this catalytic oxidation process (fig 1). We see that in all cases that the initial rates of oxidation using the *N*-oxides are lower than that using the sulfoxide and that, in the case of *N*-methylmorpholine-*N*-oxide, the catalyst also becomes readily deactivated. Although we have not yet investigated these results in detail, at least a part of this deactivation process seems to involve inhibition by the product amine.

When the oxidation of PhCH_2OH was carried out using $\text{Me}_2\text{SO}-d^6$, only $\text{Me}_2\text{S}-d^6$ was formed, the absence of $\text{Me}_2\text{S}-d^5$ indicating that a Swern-type mechanism [9] can probably be excluded. This is, of course, also consistent with the fact that other oxidants such as Ph_2SO or amine oxides are effective in these systems but not for the Swern oxidation. Studies on the oxidation of a series of *para*-substituted benzyl alcohols ($\text{R} = \text{CH}_3, \text{H}, \text{Cl}, \text{F}, \text{CF}_3$) show no correlation with Hammett σ parameters and little variation in rate on the substituent R. Hence benzyl radicals would appear not to be involved in the oxidation process, a conclusion which is further supported by the observation that radical traps such as 2,4,6-tri-*tert*-butylphenol or duroquinone have no effect on the rate of oxidation. Stoichiometric decomposition of $\text{MoO}_2(\text{OCHDC}_6\text{H}_5)_2$ at 95 °C as well as the catalytic oxidation of $\text{C}_6\text{H}_5\text{CHDOH}$ by $\text{MoO}_2(\text{acac})_2/\text{Ph}_2\text{SO}$ at 100 °C both yield the product ratio of $\text{C}_6\text{H}_5\text{CHO}/\text{C}_6\text{H}_5\text{CDO} = 2.7$. The overall rate of the catalytic oxidation of $\text{C}_6\text{H}_5\text{CH}_2\text{OH}$ and $\text{C}_6\text{H}_5\text{CD}_2\text{OH}$ in parallel experiments yield the values of $k_{\text{H}}/k_{\text{D}} = 1.8$ with Ph_2SO as oxidant and $k_{\text{H}}/k_{\text{D}} = 2.6$ using the system $\text{Ph}_2\text{SO}/p\text{-TsOH}$. Overall these results indicate that benzylic C-H cleavage is involved in the rate-determining step.

We propose the following catalytic cycle (scheme 2) for the oxidation of benzyl alcohol based on the above observations. The first step involves the formation of an alkoxide complex by displacement of the X (eg, acac) ligand. Previous experiments carried out in our laboratory show that such exchange processes occur readily at such electrophilic Mo(VI) centers [2]. A concerted, two-electron hydride transfer from the C-H bond of the alkoxo ligand to one of the oxo ligands on molybdenum follows in a rate-determining step with formation of benzaldehyde and a Mo(IV) species. This transfer would result in the observed isotope effects. After liberation of benzaldehyde, the Mo(IV) species can be reoxidized by oxygen atom transfer from a coordinated sulfoxide to reform the dioxo-Mo(VI) active species and R_2S . This last step has been studied in detail for the



Scheme 2. Proposed catalytic cycle for PhCH_2OH oxidation using $\text{MoO}_2(\text{acac})_2/\text{Ph}_2\text{S=O}$ system ($\text{X} = \text{anion}$). Certain apparently low coordinate species represented in this scheme will have additional ligands such as solvent, sulfoxide, or alcohol which have been omitted for simplicity.

Mo(VI)/Mo(IV) chemistry involved in the model systems used to mimic oxotransferase activity of molybdenum enzymes [10].

In conclusion this dioxomolybdenum(VI)/sulfoxide catalytic system is capable of oxidizing alcohols selectively to aldehydes and ketones apparently tolerating a range of other functionalities. Although the activity of this catalyst is lower than that of $\text{RuO}_4^-/\text{NMO}$ system, the relative oxidation rates found for alcohols using this Mo system (ie, allyl > benzyl >> primary) may well find synthetic use, particularly since the price of the catalyst is low. Furthermore, preliminary results indicate that the rate of oxidation of alcohols can be greatly enhanced by appropriate ligand substitution about the dioxomolybdenum moiety. Surprisingly, the use of sulfoxide as an oxygen atom transfer agent in catalytic oxidation processes has not been fully exploited despite the availability and low cost of Me_2SO . Moreover, the product sulfide is a weakly coordinating ligand (particularly when compared with the amine resulting from amine oxide oxidation reactions) and will not inhibit the catalyst as the reaction proceeds. Thus if Me_2SO is used as oxidant, Me_2S can be readily evacuated from the reaction medium. In a future publication we will show that sulfoxides can indeed also be used for efficient catalytic oxidation in conjunction with other metal-oxo complexes.

Acknowledgments

We gratefully acknowledge the support of this research by the Centre National de la Recherche Scientifique (Unité de Recherche Associée No 424). Fellowships from Rhône Poulenc (for CL) and the Deutsche Forschungsgemeinschaft (for IP) are greatly appreciated.

References

- 1 a) Wiberg KB, in *Oxidation in Organic Chemistry*, Academic, New York, 1965
 b) Sheldon RA, Kochi JK, in *Metal-Catalyzed Oxidations of Organic Compounds*, Academic, New York, 1981
 c) Nugent WA, Mayer JM, in *Metal-Ligand Multiple Bonds*, Wiley, New York, 1988
- 2 a) Belgacem J, Kress J, Osborn JA, *J Am Chem Soc* (1992) 114, 1501-1502
 b) Belgacem J, Kress J, Osborn JA, *J Mol Catal* (1993) 86, 267-285
 c) Lorber CY, Osborn JA, *Tetrahedron Lett* (1996) 37, 853-856
- 3 $\text{MoO}_2(\text{alkoxide})_2$ complexes were used initially as catalysts, but we found that $\text{MoO}_2(\text{acac})_2$ is a more convenient catalyst precursor and has similar activity. MoO_2X_2 complexes (X = halide) are also effective but the liberation of HX in the reactions leads to less clean behavior.
- 4 *Typical Experimental Procedure for Catalytic Oxidation of PhCH₂OH*. In a screw cap vial under an inert atmosphere of argon, PhCH₂OH (257 mg, 2.38 mmol) was oxidized using a system composed of $\text{MoO}_2(\text{acac})_2$ (39 mg, 0.119 mmol), Ph₂SO (962 mg, 4.75 mmol), *p*-TsOH (20 mg, 0.119 mmol) and molecular sieves (4 Å) (400 mg) in dry toluene (2 g). The reaction mixture was heated to 100 °C under stirring. After 5 h, the mixture was analyzed by gas chromatography; yield of benzaldehyde 99%.
- 5 a) Griffith WP, Ley SV, Whitcomb GP, White AD, *J Chem Soc, Chem Commun* (1987) 1625-1627
 b) Ley SV, Norman J, Griffith WP, Marsden SP, *Synthesis* (1994) 639-666
- 6 a) Formation of 100% of Ph₃P=O after 4 h (80 °C) by oxidation of 20 equiv PPh₃ using $\text{MoO}_2(\text{acac})_2$ (1 equiv) and Ph₂SO (40 equiv) in toluene
 b) Formation of 97% of PhSSPh after 1 h (100 °C) by oxidation of 20 equiv PhSH using $\text{MoO}_2(\text{acac})_2$ (1 equiv) and Ph₂SO (40 equiv) in toluene
- 7 a) Durant R, Garner CD, Hyde MR, Mabbs FE, Parsons JR, Richens D, *J Less-Common Metals* (1977) 54, 459-464
 b) Harlan EW, Berg JM, Holm RH, *J Am Chem Soc* (1986) 108, 6992-7000
- 8 For example, the energy of dissociation of X-O bond, eg, Py → O: 72 kcal mol⁻¹; Me₂S=O: 87 kcal mol⁻¹
- 9 See for example:
 a) Mancuso AJ, Swern D, *Synthesis* (1981) 165-185
 b) Tidwell TT, *Synthesis* (1990) 857-870
 c) Epstein WW, Sweat FW, *Chem Rev* (1967) 67, 165-260
- 10 See for example:
 a) Holm RH, *Coord Chem Rev* (1990) 100, 183-221 and references therein
 b) Ueyama N, Oku H, Kondo M, Okamura T, Yoshinaga N, Nakamura A, *Inorg Chem* (1996) 35, 643-650