Silane/MoO$_2$Cl$_2$ as an efficient system for the reduction of esters

Ana C. Fernandes *, Carlos C. Romão

Instituto de Tecnologia Química e Biológica da Universidade Nova de Lisboa, Quinta do Marquês, EAN, Apt 127, 2781-901 Oeiras, Portugal

Abstract

The first method for the reduction of esters using a high oxidation state oxo complex as a catalyst is reported. The system silane/MoO$_2$Cl$_2$ (5 mol%) proved to be very efficient for the reduction of aliphatic and aromatic esters to the corresponding alcohols in good yields.
© 2006 Elsevier B.V. All rights reserved.

Keywords: Reduction; Esters; Dioxomolybdenum dichloride; Silanes

1. Introduction

The conversion of esters to the corresponding alcohols, a fundamental process in organic synthesis, has gained renewed interest due to the need of converting fatty acid esters and other natural carboxylic acid derivatives into fuels or chemical feedstocks [1]. Heterogeneous catalytic hydrogenation of esters still presents selectivity and kinetic problems [2].

Besides the traditional hydride reducing agents, specially those of boron and aluminum [3], silanes have been used in search of controlled reduction selectivity. Silane activation with B(C$_6$F$_5$)$_3$ can reduce carboxylic functions to alkanes [4]. The hydrosilylation of esters in the presence of a transition metal such as Ti [5], Rh [6], and Ru [7] has been investigated in the last years and it is an alternative to the traditional methods.

We have recently developed a new method for hydrosilylation reactions using a silane in the presence of a catalytic amount of dioxomolybdenum (MoO$_2$Cl$_2$). This new system proved to be very efficient for the hydrosilylation of aldehyde and ketones, yielding the corresponding silyl ethers in good yields [8].

This first example of the use of a high valent Mo(VI)O$_2$ complex as catalyst for organic reductions was also applied in the chemeoselective reduction of imines in excellent to moderate yields [9]. This reaction was carried out with several silanes including phenylsilane, dimethylphenylsilane, triethylsilane, triphenylsilane and with a hydrosiloxane, polymethylhydrosiloxane (PMHS).

In order to extend the scope of the use of the MoO$_2$Cl$_2$ as a catalyst for organic reductions, in this work we investigated the reduction of esters with the system silane/MoO$_2$Cl$_2$.

2. Result and discussion

The reduction of methyl (4-trifluoromethyl)benzoate **1** catalyzed by MoO$_2$Cl$_2$ was studied with several silanes and solvents, as summarized in Table 1. The best results were obtained with phenylsilane in toluene or benzene at reflux temperature (entries 1 and 2). When the reduction was carried out in THF or CH$_2$Cl$_2$, the alcohol **2** was obtained in only 17% and 12% conversion, respectively (entries 3 and 4), and in acetonitrile the reduction did not proceed.

The ester **1** was also reduced to the corresponding alcohol **2** with the silanes, polymethylhydrosiloxane (PMHS), triethylsilane (Et$_3$SiH) and dimethylphenylsilane (DMPSH) in 97%, 39% and 40% conversion, respectively. No catalysis was observed with triphenylsilane (entry 9).

The system PhSiH$_3$/MoO$_2$Cl$_2$ (5 mol%) was investigated in the reduction of a variety of esters in refluxing toluene (Table 2). As shown in the Table 2, this catalytic system is suitable for the reduction of a wide scope of aromatic and aliphatic esters in good yields. One exception was observed in the reduction of methyl 4-nitrobenzoate, which afforded the methyl 4-aminobenzoate in 50% yield (entry 4). The reaction of methyl(phenylsulfinyl)acetate with this system yielded the 2-

---
* Corresponding author. Tel.: +351 214469758; fax: +351 214411277.
E-mail address: anacris@itqb.unl.pt (A.C. Fernandes).

Table 1
Reduction of methyl (4-trifluoromethyl)benzoate catalyzed by MoO_2Cl_2
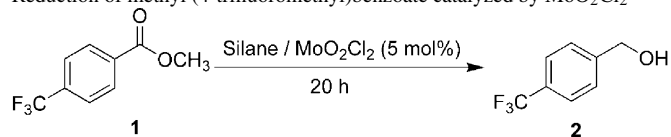
Entry	Silane	Silane (mol%)	Solvent[a]	Conversion[b] (%)
1	$PhSiH_3$	200	Toluene	100
2	$PhSiH_3$	200	Benzene	100
3	$PhSiH_3$	200	THF	17
4	$PhSiH_3$	200	CH_2Cl_2	12
5	$PhSiH_3$	200	CH_3CN	No reaction
6	PMHS	10	Toluene	97
7	Et_3SiH	300	Toluene	39
8	DMPSH	300	Toluene	40
9	Ph_3SiH	300	Toluene	No reaction

[a] Reflux temperature.
[b] Conversion was determined by ^1H NMR.

Table 2
Reduction of esters with the system $PhSiH_3/MoO_2Cl_2$[a]

Entry	Ester	Product	Yield[b]
1			79
2			75
3			72
4			50
5			81
6			75
7			73
8			82
9			80
10			75

[a] The reactions were carried out with 1.0 mmol of esters, 2.0 mmol of $PhSiH_3$ and 5 mol% of MoO_2Cl_2 in refluxing toluene during 20 h.
[b] Isolated yields.
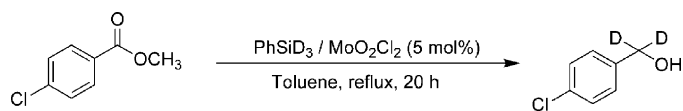
Scheme 1. Reduction of methyl 4-chlorobenzoate with the system $PhSiD_3/MoO_2Cl_2$.

(phenylthio)ethanol in 75% yield (entry 10), with reduction of both sulfinyl and carboxyl groups.

To the best of our knowledge, this is the first example of the use of a high oxidation state oxo complex as a catalyst in reduction of esters. These results confirm the new role of oxo complexes in catalytic reductions [8–10], which unexpectadly adds to their well established abilities to catalyze oxygen-transfer reactions to olefins, phosphines and sulfites [11].

Several experiments were carried out in order to ascertain some fundamental mechanistic aspects of this reduction. As no reaction was observed when the ester **1** was treated with 5 mol% MoO_2Cl_2 without phenylsilane or when the ester **1** was treated with excess of phenylsilane without catalyst in refluxing toluene, these results suggest that MoO_2Cl_2 catalyzes the reaction by activation of the silane, producing a hydride species (Mo–H).

The reaction of the ester **1** with phenylsilane-d_3, under the same experimental conditions, results in the incorporation of two deuterium atoms in the carbonyl carbon, as confirmed by ^1H NMR (Scheme 1). This result is consistent with the formation of an alkyl silyl acetal, resulting from the reaction between the ester and the hydride species (Mo–H), which is easily converted into the corresponding aldehyde. The aldehyde reacts with a second equivalent of hydride species (Mo–H) producing a silyl ether, followed by a rapid hydrolysis to the alcohol. The intimate mechanism of formation of these intermediates and their subsequent reactivity is not entirely clear and is under experimental and computational modelling. The solvents clearly play a major role in the reaction (Table 1). Surprisingly in this respect is the fact that the best solvents (benzene and toluene) are precisely those where MoO_2Cl_2 is completely insoluble and the reaction is, most likely, heterogeneous. This observation contrasts with findings on the reduction of aldehydes where solvent dependence is not so strong and favors CH_3CN over CH_2Cl_2 and benzene or toluene.

Not unexpectedly, $PhSiH_3$ is the most active silane studied. Remarkable is, however, the high reactivity of the cheaper and user friendlier polymeric silane, PMHS.

3. Experimental

All manipulations were carried out using standard Schlenk-line techniques under a nitrogen atmosphere. Solvents were purified by conventional methods and distilled under nitrogen, prior to use. The silanes were obtained from Aldrich. Phenylsilane-d_3 was prepared by the reduction of phenyltrichlorosilane with $LiAlD_4$ according to literature procedures [12]. Flash chromatography was performed on MN Kieselgel 60 M 230–400 mesh.

3.1. General procedure for the reduction of esters with the system PhSiH₃/MoO₂Cl₂

To a solution of MoO_2Cl_2 (5% mol) in dry toluene (5 ml) was added the ester (1.0 mmol) and $PhSiH_3$ (2.0 mmol) under nitrogen atmosphere. The reaction mixture was stirred at reflux temperature during 20 h. After evaporation, the reaction mixture was purified by silica gel column chromatography with the appropiate mixture of *n*-hexane and ethyl acetate.

4. Conclusion

In conclusion, we have developed a new reliable catalytic system for the reduction of aliphatic and aromatic esters to the corresponding alcohols in good yields. It is the first example of the use of a high valent oxo complex as a catalyst for the reduction of esters. These results extend the scope of the use of MoO_2Cl_2 as an effective catalyst for reduction reactions.

The reduction of the nitro and sulfoxide groups observed in the reaction of methyl 4-nitrobenzoate and methyl(phenyl-sulfinyl)acetate suggests two future applications for this system in the synthesis of amines and sulfides.

Other organic reductions with this system as well as mechanistic studies are now under investigation in our group.

References

[1] U. Biermann, W. Friedt, S. Lang, W. Lühs, G. Machmüller, J.O. Metzger, M. Rüsch, H.J. Schafer, J.P. Schneiderr, Angew. Chem. Int. Ed. 39 (2000) 2206.
[2] (a) R.A. Grey, G.P. Pez, A. Wallo, J. Corsi, J. Chem. Soc., Chem. Commun. 16 (1980) 783;
(b) R.A. Grey, G.P. Pez, A. Wallo, J. Am. Chem. Soc. 103 (1981) 7536;
(c) S.M. Santos, A.M. Silva, E. Jordão, M.A. Fraga, Catal. Commun. 5 (2004) 377;
(d) F.C.A. Figueiredo, E. Jordão, W.A. Carvalho, Catal. Today 107–108 (2005) 223;
(e) S. Van den Hark, M. Hanod, Ind. Res. Chem. 40 (2001) 5052.
[3] J. March, Advanced Organic Chemistry, 4th ed., Wiley, New York, 1992, 1213.
[4] V. Gevorgyan, M. Rubin, J.-X. Liu, Y. Yamamoto, J. Org. Chem. 66 (2001) 1672.
[5] (a) S.C. Beck, K.A. Kreutzer, S.L. Buchwald, J. Am. Chem. Soc. 113 (1991) 5093;
(b) S.C. Beck, S.L. Buchwald, J. Org. Chem. 57 (1992) 3751;
(c) K.J. Barr, S.C. Beck, S.L. Buchwald, J. Org. Chem. 59 (1994) 4323;
(d) M.T. Reding, S.L. Buchwald, J. Org. Chem. 60 (1995) 7884.
[6] (a) I. Ojima, T. Kogure, M. Kumagai, J. Org. Chem. 42 (1977) 1671;
(b) T. Ohta, M. Kamiya, K. Kusui, T. Michibata, M. Nobutomo, I. Furukawa, Tetrahedron Lett. 40 (1999) 6963.
[7] K. Matsubara, T. Iura, T. Maki, H. Nagashima, J. Org. Chem. 67 (2002) 4985.
[8] A.C. Fernandes, R. Fernandes, C.C. Romão, B. Royo, Chem. Commun. (2005) 213.
[9] A.C. Fernandes, C.C. Romão, Tetrahedron Lett. 46 (2005) 8881.
[10] (a) J.J. Kennedy-Smith, K.A. Nolin, H.P. Gunterman, F.D. Toste, J. Am. Chem. Soc. 125 (2003) 4056;
(b) B. Royo, C.C. Romão, J. Mol. Catal. A: Chem. 236 (2005) 107;
(c) K.A. Nolin, R.W. Aln, F.D. Toste, J. Am. Chem. Soc. 127 (2005) 12462;
(d) E.A. Ison, E.R. Trivedi, R.A. Corbin, M.M. Abu-Omar, J. Am. Chem. Soc. 127 (2005) 15374.
[11] (a) Z. Petrovski, M. Pillinger, A.A. Valente, I.S. Gonçalves, A. Hazell, C.C.C. Romão, J. Mol. Catal. A: Chem. 227 (2005) 67;
(b) S. Gago, J.E. Rodriguez- Borges, A. Teixeira, M. Santos, J. Zhao, M. Pillinger, C.D. Nunes, Z. Petrovski, T.M. Santos, F.E. Kuhn, C.C. Romão, I.S. Gonçalves, J. Mol. Catal. A: Chem. 236 (2005) 1;
(c) B.S. Hammes, B.S. Chohan, J.T. Hoffman, S. Einwächter, C. Carrano, J. Inorg. Chem. 43 (2004) 7800;
(d) K. Most, J. Hoßbach, D. Vidović, J. Magull, N. Mösch-Zanetti, Adv. Synth. Catal. 347 (2005) 463;
(e) R.H. Holm, Chem. Rev. 87 (1987) 1401.
[12] W.H. Nebergall, J. Am. Chem. Soc. 72 (1950) 4702.