Available online at www.sciencedirect.com

SCIENCE DIRECT

Tetrahedron Letters 46 (2005) 8881–8883

Tetrahedron Letters

A novel method for the reduction of imines using the system silane/MoO_2Cl_2

Ana C. Fernandes* and Carlos C. Romão

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

Received 8 August 2005; revised 14 October 2005; accepted 18 October 2005
Available online 4 November 2005

Abstract—A novel catalytic system, silane/MoO_2Cl_2 (10 mol %), for the reduction of imines in excellent to moderate yields and chemoselectivity was designed. These results extend the scope of the use of MoO_2Cl_2 as an effective catalyst for reduction reactions.

The synthesis of amines is an important area of research and sometimes is a key step in the industrial synthesis of medicinal supplies and agricultural chemicals. Primary and secondary amines are usually obtained by reduction of the corresponding imines using metal hydrides such as $LiAlH_4$,[1] $NaBH_4$,[1] Bu_2SnClH,[2] $(\eta\text{-}C_5H_5)_2MoH_2$,[3] $RuHCl(PPh_3)_3$,[4] CaH_2[5] or hydrogenation catalysts like Pd–C and Pt.[6]

The hydrosilylation of imines, in which the Si–H bond is added across the C=N bond, is an attractive alternative approach to hydrogenation of imines as it is experimentally simple, does not require high pressure or temperature, and makes use of readily available silanes. Many transition metal complexes with metals including Ru,[7,8] Rh,[9] Ti,[10,11] Ir,[12] Cu,[13] Sn and Zn[14] have been used as catalysts for imine hydrosilylation.

Recently, we have developed a new system for the hydrosilylation of aldehydes and ketones using dimethylphenylsilane in the presence of a catalytic amount of dioxomolybdenum dichloride (MoO_2Cl_2).[15] It was the first example of the use of this high valent molybdenum-dioxo complex as a catalyst for organic reductions. This result represents a complete reversal of the traditional role of MoO_2Cl_2, which is known for its ability to catalyze oxygen-transfer reactions to sulfides, phosphines and olefins.[16]

We became interested in the possibility of applying the system silane/MoO_2Cl_2 to other organic reductions. In this work, we investigated the use of this system for the reduction of imines.

Initially, we studied the reaction conditions for the reduction of imine **1** with several silanes, solvents and catalytic amounts of dioxomolybdenum dichloride, as summarized in Table 1. The best result was obtained with phenylsilane in the presence of 10 mol % of MoO_2Cl_2 in tetrahydrofuran at reflux temperature (entry 1). In these reaction conditions imine **1** was quantitatively converted into amine **2**. When the reaction of **1** was carried out using 5 mol % of MoO_2Cl_2, amine **2** was obtained in 75% yield (entry 2). At room temperature, the reaction required significantly longer reaction times (20 h).

Among the solvents tested, tetrahydrofuran proved to be the best. In dichloromethane, the reaction required longer times and in toluene, amine **2** was obtained in moderate yield (50%).

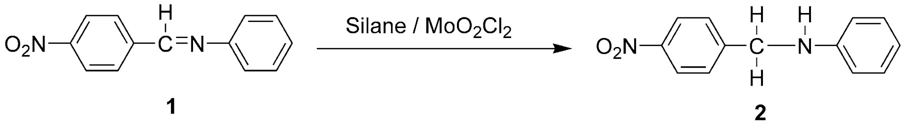
This reaction was also studied with several silanes, including dimethylphenylsilane (DMPSH), triethylsilane, triphenylsilane and with an hydrosiloxane, polymethylhydrosiloxane (PMHS). With PMHS, a stable, inexpensive and non-toxic hydrosiloxane, imine **1** was completely converted into amine **2** after 10 h (entry 7). The reaction with DMPSH yielded the desired amine in 91% conversion (entry 8), and with the more sterically encumbered silanes, Et_3SiH and Ph_3SiH, amine **2** was obtained in only 65% and 45% conversion, respectively.

Keywords: Reduction; Imines; Dioxomolybdenum dichloride.

* Corresponding author. Tel.: +351 214469758; fax: +351 214411277; e-mail: anacris@itqb.unl.pt

0040-4039/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2005.10.076

Table 1. Reduction of *N*-(4-nitrobenzylidene)aniline **1** catalyzed by MoO_2Cl_2



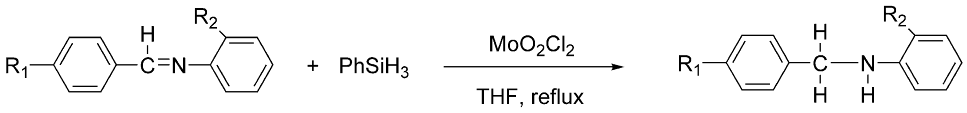
Entry	Silane	Silane (mol %)	MoO_2Cl_2 (mol %)	Solvent[a]	Temperature (°C)	Time (h)	Conversion[b] (%)
1	$PhSiH_3$	100	10	THF	67	2	100
2	$PhSiH_3$	100	5	THF	67	2	75
3	$PhSiH_3$	100	10	THF	rt	20	75
4	$PhSiH_3$	100	10	CH_2Cl_2	rt	30	90
5	$PhSiH_3$	100	10	CH_2Cl_2	40	20	90
6	$PhSiH_3$	100	10	Toluene	110	3	50
7	PMHS	10	10	THF	67	10	100
8	DMPSH	200	10	THF	67	3	91
9	Et_3SiH	200	10	THF	67	3	65
10	Ph_3SiH	200	10	THF	67	3	45

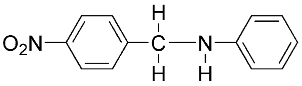
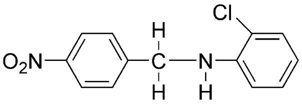
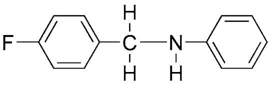
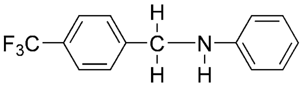
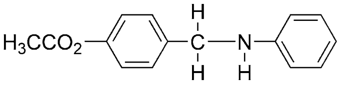
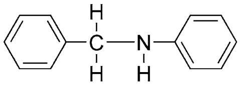
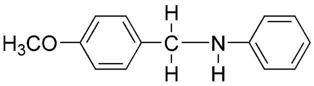
[a] Volume of solvent (5 ml).

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

To explore the scope of this catalytic reaction, the reduction of a variety of imines with the system $PhSiH_3$/MoO_2Cl_2 was investigated (Table 2). Imines were reduced in excellent to moderate yields as indicated in Table 2. The best results were obtained with imines having electron-withdrawing groups. Imines bearing a

Table 2. Synthesis of amines using the system $PhSiH_3$/MoO_2Cl_2[a]



Entry	Amine	Time (h)	Yield (%)[b]
1		2	97
2		2	97
3		24	96
4		24	86
5		24	78
6		24	65
7		24	50

[a] All reactions were carried out in THF with 1.0 mmol of imine, 1.0 mmol of $PhSiH_3$, using 10 mol % of MoO_2Cl_2.

[b] Isolated yield.

fluoro, chloro, ester or a nitro group were chemoselectively reduced to the corresponding amines.

In a typical procedure, to a solution of MoO_2Cl_2 (10 mol %) in dry THF (5 ml) were added the imine (1.0 mmol) and $PhSiH_3$ (1.0 mmol) under nitrogen atmosphere. The reaction mixture was stirred at reflux temperature (the reaction times are indicated in Table 2) and monitored periodically by TLC. Upon completion, the reaction mixture was diluted with hexane, loaded directly on to a silica-gel column and chromatographed with the appropriate mixture of *n*-hexane and ethyl acetate. All the compounds were characterized by spectroscopy (IR, NMR) in many instances against the literature data.

Several experiments were carried out in order to ascertain some fundamental mechanistic aspects of this reduction. No reaction was observed when imine **1** was treated with 10 mol % of MoO_2Cl_2 without phenylsilane or when imine **1** was treated with excess of phenylsilane without catalyst in refluxing THF after 24 h. These results show that MoO_2Cl_2 catalyzes the reaction by activation of the silane and this rapid reaction is still under investigation. At this point it is not clear how this activation takes place. A similar activation of silanes by $(PPh_3)_2Re(O)_2I$ produces a Re–H that was observed by NMR.[17] Unfortunately, all our experiments to detect a Mo–H species in situ were unsuccessful at various concentrations, and temperatures and with different silanes. However, it is inescapable that a functional equivalent of a hydride (Mo–H) is produced since the reaction of imine **1** with dimethylphenylsilane-*d*, under the same experimental conditions, resulted in the incorporation of the deuterium only in the carbon of the double bond, as confirmed by ^1H NMR. This result is consistent with the hydrosilylation of the imine to give an intermediate *N*-silylamine, followed by a rapid hydrolysis, probably, due to the presence of a trace of water in the imine or, more likely, due to hydrolysis of the N–Si bond on the silica-gel during work-up and purification. This mechanism is analogous to that proposed for hydrosilylation of aldehydes and ketones where a silyl ether is formed that can be later hydrolyzed to the alcohol. However, nothing can yet be said as to the nature of the intermediates that are involved in these hydrogen transfers and the following elimination of the silylimine from the catalyst.

In summary, we have developed a novel method for the reduction of imines to the corresponding amines in excellent to moderate yields. This result confirms the ability of MoO_2Cl_2 as an effective catalyst for hydrosilylation reactions. This novel catalytic system is suitable for chemoselective reduction of imines bearing fluoro, chloro, ester and nitro groups. Other organic reductions with this system as well as mechanistic studies are now under investigation in our group.

References and notes

1. Hutchins, R. O.; Hutchins, M. K. *Comprehensive Organic Synthesis*; Pergamon Press: Oxford, 1991; Vol. 8, pp 25–78.
2. Shibata, I.; Moriuchi-Kawakami, T.; Tanizawa, D.; Suwa, T.; Sugiyama, E.; Matsuda, H.; Baba, A. *J. Org. Chem.* **1998**, *63*, 383–385.
3. Minato, M.; Fujiwara, Y.; Ito, T. *Chem. Lett.* **1995**, 647–648.
4. Mizushima, E.; Yamaguchi, M.; Yamagishi, T. *Chem. Lett.* **1997**, 237–238.
5. Aida, T.; Kuboki, N.; Kato, K.; Uchikawa, W.; Matsuno, C.; Okamoto, S. *Tetrahedron Lett.* **2005**, *46*, 1667–1669.
6. Freifelder, M. *Catalytic Hydrogenation in Organic Synthesis Procedures and Commentary*; John Wiley and Sons: New York, 1978; pp 65–77.
7. Nishibayashi, Y.; Takei, I.; Uemura, S.; Hidai, M. *Organometallics* **1998**, *17*, 3420–3422.
8. Hashimoto, H.; Aratani, I.; Kabuto, C.; Kira, M. *Organometallics* **2003**, *22*, 2199–2201.
9. Nishibayashi, Y.; Segawa, K.; Singh, J. D.; Fukuzawa, S.-I.; Ohe, K.; Uemura, S. *Organometallics* **1996**, *15*, 370–379.
10. Verdaguer, X.; Lange, U. E. W.; Reding, M. T.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 6784–6785.
11. Hansen, M. C.; Buchwald, S. L. *Org. Lett.* **2000**, *2*, 713–715.
12. Field, L. D.; Messerle, B. A.; Rumble, S. L. *Eur. J. Org. Chem.* **2005**, 2881–2883.
13. Lipshutz, B. H.; Shimizu, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 2228–2230.
14. Ireland, T.; Fontanet, F.; Tchao, G.-G. *Tetrahedron Lett.* **2004**, *45*, 4383–4387.
15. Fernandes, A. C.; Fernandes, R.; Romão, C. C.; Royo, B. *Chem. Commun.* **2005**, 213–214.
16. Holm, R. H. *Chem Rev.* **1987**, *87*, 1401–1449.
17. Kennedy-Smith, J. J.; Nolin, K. A.; Gunterman, H. P.; Toste, F. D. *J. Am. Chem. Soc.* **2003**, *125*, 4056–4057.