



Short Communication

Efficient and selective oxidation of alcohols catalyzed by oxo-rhenium complexes



Sara C.A. Sousa, Joana R. Bernardo, Pedro R. Florindo, Ana C. Fernandes*

Centro de Química Estrutural, Instituto Superior Técnico, Universidade Técnica de Lisboa, Av. Rovisco Pais, 1049-001 Lisboa, Portugal

ARTICLE INFO

Article history:

Received 28 February 2013

Received in revised form 12 June 2013

Accepted 13 June 2013

Available online 19 June 2013

Keywords:

Oxidation

Alcohols

Oxo-rhenium complexes

Sulfoxides

ABSTRACT

This work reports the catalytic activity of several oxo-rhenium complexes in the oxidation of alcohols, using a sulfoxide as oxidant agent. The catalytic system bis(4-chlorophenyl) sulfoxide/ $\text{ReOCl}_3(\text{PPh}_3)_2$ (10 mol%) proved to be efficient for the oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones. The primary alcohols are selectively oxidized to the corresponding aldehydes with no further oxidation to acids. The bis(4-chlorophenyl) sulfide, isolated as by-product in high yields, can be used as a substrate in other reactions or can be oxidized and reused in this procedure.

© 2013 Elsevier B.V. All rights reserved.

1. Introduction

The oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones is a fundamental process in organic chemistry. In particular, the oxidation of primary alcohols to aldehydes is very important since they find wide applications as intermediates in chemical and pharmaceutical industries. Traditionally, the oxidation of alcohols is carried out using stoichiometric inorganic oxidants such as Cr(VI) based reagents, which generates large amount of heavy metal waste [1].

The Swern oxidation (using DMSO coupled with the electrophile oxalyl chloride) is also an efficient and widely used method for the oxidation of primary and secondary alcohols [2,3]. However, these reagents bring some disadvantages: the by-product dimethyl sulfide is volatile (bp 37 °C) and has an unpleasant smell; the electrophile oxalyl chloride is moisture sensitive, toxic and its vapors are powerful irritants, particularly to the respiratory system; the activation of DMSO can be violent and exothermic, and it must occur at low temperatures (−60 °C). Several modifications on the Swern methodology have been accomplished in order to overcome some of these disadvantages [4–8].

Among several metal transition complexes that have been used for the oxidation of alcohols, oxo-vanadium [9,10], oxo-molybdenum [11–13] and oxo-rhenium [14] complexes proved to be efficient catalysts in the presence of molecular oxygen or using a hydroperoxide compound as oxidant agent. Only few studies have also been reported for the oxidation of alcohols with DMSO catalyzed by oxo-molybdenum or -rhenium complexes [15–18].

Recently, we reported a novel method for the oxidation of benzyl alcohol to the corresponding aldehydes catalyzed by the oxo-complexes MoO_2Cl_2 , $\text{MoO}_2(\text{acac})_2$, $\text{VO}(\text{acac})_2$, WO_2Cl_2 and HReO_4 via oxygen transfer from sulfoxide [19]. The results obtained demonstrate that HReO_4 is a very efficient catalyst for the selective oxidation of benzyl alcohols to the corresponding aldehydes, with no further oxidation to acids. However, this catalyst is not very effective for the oxidation of secondary alcohols.

In this work we decide to explore the catalytic activity of other oxo-rhenium complexes in the oxidation of primary and secondary alcohols, using a sulfoxide as oxidant agent.

2. Experimental

2.1. General

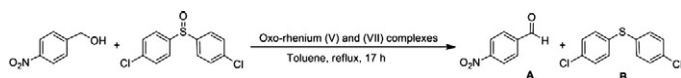
All of the reactions were carried out in air and without any dry solvents. Alcohols, sulfoxides and catalysts were obtained from commercial suppliers and were used without further purification. $\text{ReO}_2(\text{PPh}_3)_2$ [20] and $\text{ReOBr}_3(\text{PPh}_3)_2$ [21] were prepared using the method reported in the literature. Flash chromatography was performed on MN Kieselgel 60 M of 230–400 mesh. ^1H NMR and ^{13}C NMR spectra were measured on a Bruker Avance II 400 MHz and 300 MHz spectrometers. Chemical shifts are reported in parts per million (ppm) downfield from an internal standard.

2.2. General procedure for the oxidation of alcohols catalyzed by $\text{ReOCl}_3(\text{PPh}_3)_2$ using bis(4-chlorophenyl) sulfoxide as oxidant agent

To a solution of $\text{ReOCl}_3(\text{PPh}_3)_2$ (0.083 g, 0.1 mmol) in toluene (3 mL) was added the bis(4-chlorophenyl) sulfoxide (0.271 g, 1 mmol) and the

* Corresponding author. Tel.: +351 218419264; fax: +351 218464457.
E-mail address: anacristinafernandes@ist.utl.pt (A.C. Fernandes).

Table 1
Oxidation of alcohols catalyzed by oxo-rhenium (V) and (VII) complexes using bis(4-chlorophenyl) sulfoxide as oxidant agent^a.



Entry	Catalyst	Catalyst (mol%)	Yield A/B (%) ^b
1	ReOCl ₃ (PPh ₃) ₂	10	93/94
2	ReOCl ₃ (PPh ₃) ₂	5	55/63
3	ReOCl ₃ (PPh ₃) ₂	2	41/62
4	Re ₂ O ₇	10	88/80 (10) ^c
5	ReOBr ₃ (PPh ₃) ₂	10	82/90
6	ReIO ₂ (PPh ₃) ₂	10	70/85 (25) ^d
7	ReOCl ₃ (dppm)	10	55/69 (45) ^d
8	MTO	10	No reaction
9	–	–	No reaction

^a All reactions were carried out with 1.0 mmol of sulfoxide and 1.0 mmol of alcohol.

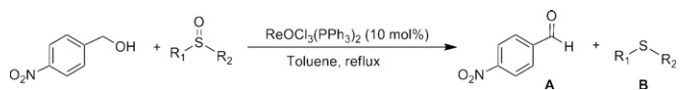
^b Isolated yield.

^c Sulfoxide recovered.

^d Alcohol recovered.

alcohol (1.0 mmol). The reaction mixture was heated at reflux temperature in air (the reaction times are indicated in Tables 1–4) and the progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was evaporated and purified by silica gel column chromatography with *n*-hexane to afford carbonyl compounds and bis(4-chlorophenyl) sulfide, which are all known compounds and their ¹H NMR and ¹³C NMR data are consistent with those of the commercial products.

Table 2
Oxidation of 4-nitrobenzyl alcohol catalyzed by ReOCl₃(PPh₃)₂ using different sulfoxides as oxidant agents^a.



Entry	Sulfoxide	Time (h)	Yield (%) ^b (A/B)
1		17	93/94
2		17	91/94
3		17	85/87
4		17	81/91 (8) ^c
5		24	70/– (26) ^c
6		17	No oxidation
7	–	24	No oxidation

^a All reactions were carried out with 1.0 mmol of sulfoxide and 1.0 mmol of alcohol.

^b Isolated yield.

^c Alcohol recovered.

3. Results and discussion

In order to find the best catalytic conditions for the oxidation of alcohols, initially we carried out several preliminary studies using different oxo-rhenium complexes, sulfoxides, solvents and temperatures (Tables 1–3).

3.1. Effect of the catalyst

The oxidation of alcohols was explored with the test substrate 4-nitrobenzyl alcohol in the presence of the oxo-rhenium complexes ReOCl₃(PPh₃)₂, ReOBr₃(PPh₃)₂, ReIO₂(PPh₃)₂, ReOCl₃(dppm), Re₂O₇, and CH₃ReO₃ (MTO) using bis(4-chlorophenyl) sulfoxide as an oxidant agent. The reactions were carried out in refluxing toluene (Table 1), and the progress of the oxidations was monitored by thin layer chromatography. The best results were obtained with ReOCl₃(PPh₃)₂ (10 mol%), affording 4-nitrobenzaldehyde in 93% yield after 17 h (Table 1, entry 1). Using only 5 mol% or 2 mol% of ReOCl₃(PPh₃)₂ the reactions gave moderate yields of aldehyde (Table 1, entries 2 and 3). The oxo-rhenium complexes Re₂O₇, ReOBr₃(PPh₃)₂, and ReIO₂(PPh₃)₂ produced good yields of the aldehyde (88–70%) (Table 1, entries 4–6) and ReOCl₃(dppm) only afforded moderate yield of the product (55%) (Table 1, entry 7). Finally, no oxidation was observed with MTO (Table 1, entry 8) and in the absence of catalyst (Table 1, entry 9).

3.2. Effect of the oxidant agent

Several sulfoxides were also tested as oxidant agents in the reaction of 4-nitrobenzyl alcohol catalyzed by 10 mol% of ReOCl₃(PPh₃)₂ in reflux of toluene. Among all of the sulfoxides, the reaction with bis(4-chlorophenyl) sulfoxide produced the best yield (93%) of 4-nitrobenzaldehyde (Table 2, entry 1). Using the sulfoxides di-*p*-tolyl sulfoxide, diphenyl sulfoxide and 4-nitrophenyl phenyl sulfoxide as oxidant agents, good yields of 4-nitrobenzaldehyde were also obtained (91–81%) (Table 2, entries 2–4). In the presence of DMSO, 4-nitrobenzyl alcohol was oxidized in 70% yield (Table 2, entry 5), and using dibenzyl sulfoxide or in absence of sulfoxide, no oxidation of the alcohol was observed (Table 2, entries 6 and 7). Good yields of the sulfides were also isolated (Table 2, entries 1–4).

3.3. Effect of solvent and temperature

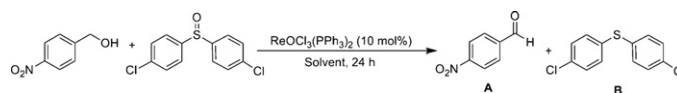
The reaction between the test substrate 4-nitrobenzyl alcohol and the oxidant agent bis(4-chlorophenyl) sulfoxide catalyzed by ReOCl₃(PPh₃)₂ (10 mol%) was studied in different solvents. Toluene proved to be the best solvent at reflux temperature, affording 4-nitrobenzaldehyde in 93% yield and 94% of sulfide (Table 3, entry 1). At room temperature, this oxidation only gave moderate yield of the aldehyde (Table 3, entry 2). In benzene, dichloromethane and chloroform the aldehyde was obtained in 56–79% yields and the sulfide was obtained in 77–82% yields (Table 3, entries 3–5). In contrast, low yields of aldehydes (5–27%) were obtained in acetonitrile and THF (Table 3, entries 6 and 7). However, the sulfide was obtained in good yields from these solvents (75–94%).

3.4. Scope and limitations

In order to assess the scope and limitations of this methodology, we decided to study the oxidation of several primary and secondary alcohols using bis(4-chlorophenyl) sulfoxide as oxidant agent catalyzed by 10 mol% of ReOCl₃(PPh₃)₂ in reflux of toluene (Table 4).

The oxidation of primary alcohols gave selectively the corresponding aldehydes in good to excellent yields with no further oxidation to acids. 4-Nitrobenzaldehyde, methyl 4-formylbenzoate, 4-fluorobenzaldehyde, 4-iodobenzaldehyde, 4-bromobenzaldehyde,

Table 3
Oxidation of alcohols catalyzed by $\text{ReOCl}_3(\text{PPh}_3)_2$ in different solvents^a.



Entry	Solvent	Temperature	Yield A/B (%) ^b
1	Toluene	Reflux	93/94 (5) ^c
2	Toluene	r.t.	59/93 (36) ^c
3	Benzene	Reflux	79/82 (9) ^c
4	Dichloromethane	Reflux	65/82 (30) ^c (8) ^d
5	Chloroform	Reflux	56/77 (42) ^c (15) ^d
6	Acetonitrile	Reflux	27/75 (68) ^c
7	THF	Reflux	5/80 (83) ^c

^a All reactions were carried out with 1.0 mmol of sulfoxide and 1.0 mmol of alcohol.

^b Isolated yield.

^c Alcohol recovered.

^d Sulfone formed.

4-chlorobenzaldehyde, and 4-cyanobenzaldehyde were obtained in 76–93% yields (Table 4, entries 1–7). Another interesting result was the selective oxidation of cinnamyl alcohol in 79% yield without affecting the double bond (Table 4, entry 8). In contrast, the oxidation of 2-phenylethanol only produced the phenylacetaldehyde in low yield (44%) (Table 4, entry 9).

The catalytic activity of the system bis(4-chlorophenyl) sulfoxide/ $\text{ReOCl}_3(\text{PPh}_3)_2$ was also investigated in the oxidation of several secondary alcohols. Excellent yields of ketones were also obtained in the oxidation of the alcohols 1-(4-nitrophenyl)ethanol and 1-(4-bromophenyl)ethanol (93% and 92%) (Table 4, entries 10 and 11). The oxidation of 1-(4-cyanophenyl)ethanol and 1-(4-iodophenyl)ethanol produced the corresponding ketones in 76% and 62% yields, respectively (Table 4, entries 12 and 13). The reactions of 1-(4-bromophenyl)ethanol and 1-(4-cyanophenyl)ethanol (Table 4, entries 11 and 12) were carried out at a lower temperature (80 °C), since the boiling points of 1-(4-bromophenyl)ethanol and 4-acetylbenzoxonitrile are very similar to the reflux temperature of toluene.

Finally, the oxidation of the secondary diaromatic alcohols (4-nitrophenyl)(phenyl)methanol and bis(4-chlorophenyl)methanol afforded the corresponding ketones in 85% and 40% yields, respectively (Table 4, entries 14 and 15). For all of the reactions, the sulfide was isolated in high yields (82–96%).

The results obtained demonstrate that the catalytic system bis(4-chlorophenyl) sulfoxide/ $\text{ReOCl}_3(\text{PPh}_3)_2$ is efficient for the oxidation of primary and secondary alcohols, and highly selective for the oxidation of primary alcohols to the corresponding aldehydes with no further oxidation to acids, which is of extreme importance for the industry. Comparison between the catalytic systems bis(4-chlorophenyl) sulfoxide/ $\text{ReOCl}_3(\text{PPh}_3)_2$ and di-*p*-tolyl sulfoxide/ HReO_4 , used in our previous work [19], shows that both systems give similar yields of aldehydes, but the oxidations with HReO_4 require less amount of catalyst. Nevertheless, the system bis(4-chlorophenyl) sulfoxide/ $\text{ReOCl}_3(\text{PPh}_3)_2$ proved to be also efficient for the oxidation of secondary alcohols to the corresponding ketones, in contrast to low activity of the system di-*p*-tolyl sulfoxide/ HReO_4 [19] in the oxidation of secondary alcohols.

This methodology is also an excellent alternative to the Swern oxidation since it does not use DMSO as oxidant agent, avoiding the production of the volatile and unpleasant dimethyl sulfide. Another advantage of this method is that the bis(4-chlorophenyl) sulfide, obtained as by-product in high isolated yields, can be used as substrate in other reactions or can be oxidized and reused in this procedure. This novel method does not require the addition of any other

compound such as oxalyl chloride, which is toxic, a powerful irritant, and an expensive substance.

The mechanism for the oxidation of alcohols using the system of bis(4-chlorophenyl) sulfoxide/ $\text{ReOCl}_3(\text{PPh}_3)_2$ (10 mol%), should involve the coordination of the sulfoxide to the rhenium with the formation of the complex $\text{ReOCl}_3(\text{SR}_2)(\text{OPPh}_3)$ as reported by other authors [22–24]. The addition of the alcohol to this species should result in the oxidation of the alcohol to the corresponding carbonyl compound with the liberation of a molecule of water and sulfide.

Further mechanistic studies and new applications of this methodology to the oxidation of other substrates are now under investigation in our group.

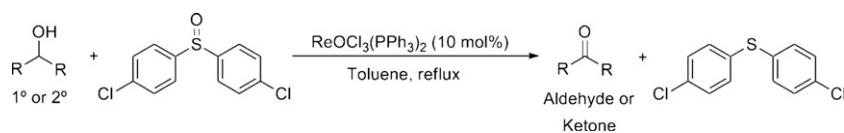
4. Conclusion

In conclusion, we have demonstrated that the oxo-rhenium complex $\text{ReOCl}_3(\text{PPh}_3)_2$ is a good catalyst for the oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones, using a sulfoxide as oxidant agent. The catalytic system bis(4-chlorophenyl) sulfoxide/ $\text{ReOCl}_3(\text{PPh}_3)_2$ is also selective for the oxidation of primary alcohols to the corresponding aldehydes with no further oxidation to acids.

This practical method shows some advantages compared to other methods for the oxidation of alcohols: 1) use of a sulfoxide (other than DMSO) as oxidant agent; 2) does not require the addition of any other reagents; 3) applicability to a variety of alcohols; 4) use of commercial and easy-to-handle catalysts; 5) high isolated yields of carbonyl compounds; 6) selective oxidation of primary alcohols to aldehydes; 7) high isolated yields of the sulfide that can be used in other reactions or oxidized and reused in this method; and 8) simple experimental operation. All of these features make this method an attractive and useful alternative for the oxidation of primary and secondary alcohols.

Acknowledgment

This research was supported by FCT through project PTDC/QUI-QUI/110080/2009. S.C.A. Sousa (SFRH/BD/63471/2009), J.R. Bernardo (SFRH/BD/90659/2012) and P.R. Florindo thank FCT for the grants. The authors thank the project Pest-OE/QUI/UI0100/2013 and the Portuguese NMR Network (IST-UTL Center) for providing access to the NMR facilities.

Table 4Oxidation of primary and secondary alcohols catalyzed by $\text{ReOCl}_3(\text{PPh}_3)_2$ using bis(4-chlorophenyl) sulfoxide as oxidant agent^a.

Entry	Alcohol	Carbonyl compound	Time (h)	Yield (%) ^b A/B
1			17	93/94
2			24	91/95
3			24	91/94
4			17	86/93
5			17	83/93
6			17	77/92
7			17	76/85
8			17	79/82
9			19	44/86 (52) ^c
10			19	93/95
11			17	92/90 ^d
12			17	76/95 ^d
13			24	62/85 (27) ^c (8) ^e
14			24	85/90 (9) ^c
15			24	40/96 (40) ^c

^a All reactions were carried out with 1.0 mmol of sulfoxide and 1.0 mmol of alcohol.^b Isolated yield.^c Alcohol recovered.^d The reaction was carried out at 80 °C.^e Iodostyrene formed.

References

- [1] G. Cainelli, G. Cardillo, *Chromium Oxidations in Organic Chemistry*, Springer, 1984.
- [2] A.J. Mancuso, D. Swern, *Synthesis* (1981) 165–185.
- [3] T.T. Tidwell, *Synthesis* (1990) 857–870.
- [4] L. De Luca, G. Giacomelli, A. Porcheddu, *J. Org. Chem.* 66 (2001) 7907–7909.
- [5] D.C. Cole, J.R. Stock, J.A. Kappel, *Bioorg. Med. Chem. Lett.* 12 (2002) 1791–1793.
- [6] A. Dubey, S.R.V. Kandula, P. Kumar, *Synth. Commun.* 38 (2008) 746–753.
- [7] J.M. Harris, Y. Liu, S. Chai, M.D. Andrews, J.C. Vederas, *J. Org. Chem.* 63 (1998) 2407–2409.
- [8] A. Bisai, M. Chamdrasekhar, V. Singh, *Tetrahedron Lett.* 43 (2002) 8355–8357.
- [9] K. Alagiri, K.R. Prabhu, *Tetrahedron* 67 (2011) 8544–8551.
- [10] J.A.L. Silva, Fraústo da Silva, A.J.L. Pombeiro, *Coord. Chem. Rev.* 255 (2011) 2232–2248.
- [11] A.V. Biradar, M.K. Dongare, S.B. Umbarkar, *Tetrahedron Lett.* 50 (2009) 2885–2888.
- [12] S. Velusamy, M. Ahamed, T. Punniyamurthy, *Org. Lett.* 6 (2004) 4821–4824.
- [13] K. Jeyakumar, D.K. Chand, *Appl. Organomet. Chem.* 20 (2006) 840–844.
- [14] C.A. Lippert, K. Riener, J.D. Soper, *Eur. J. Inorg. Chem.* (2012) 554–561.
- [15] B. Monteiro, S. Gago, P. Neves, A.A. Valente, I.S. Gonçalves, C.C.L. Pereira, C.M. Silva, M. Pillinger, *Catal. Lett.* 129 (2009) 350–357.
- [16] Y.-L. Wong, A.R. Cowley, J.R. Dilworth, *Inorg. Chim. Acta* 357 (2004) 4358–4372.
- [17] C.Y. Lorber, I. Pauls, J.A. Osborn, *Bull. Soc. Chim. Fr.* 133 (1996) 755–758.
- [18] J.B. Arterburn, M.C. Perry, *Org. Lett.* 1 (1999) 769–771.
- [19] S.C.A. Sousa, J.R. Bernardo, A.C. Fernandes, *Tetrahedron Lett.* 53 (2012) 6205–6208.
- [20] J.J. Kennedy-Smith, K.A. Nolin, H.P. Gunterman, F.D. Toste, *J. Am. Chem. Soc.* 125 (2003) 4056–4057.
- [21] J. Chatt, G.A. Rowe, *J. Chem. Soc.* (1962) 4019.
- [22] M.M. Abu-Omar, S.I. Khan, *Inorg. Chem.* 37 (1998) 4979–4985.
- [23] J.C. Bryan, R.E. Stenkamp, T.H. Tulip, J.M. Mayer, *Inorg. Chem.* 26 (1987) 2283–2288.
- [24] J.B. Arterburn, M.C. Perry, S.L. Nelson, B.R. Dible, M.S. Holguin, *J. Am. Chem. Soc.* 119 (1997) 9309–9310.