

Asymmetric oxidation of sulfides by LDH supported OsO₄ catalyst

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Abstract

The asymmetric oxidation of sulfides to sulfoxides is realised with layered double hydroxides (LDH)-supported OsO₄ catalyst using *N*-methyl morpholine *N*-oxide as co-oxidant and (DHQD)₂PHAL (hydroquinidine 1,4-phthalazinediyl diether) as a chiral ligand in good yields albeit moderate enantiomeric excess (e.e.'s).

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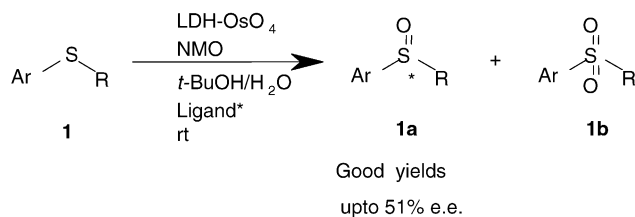
Keywords: Osmium; Layered double hydroxides; Sulfides; Chiral sulfoxides; Cinchona alkaloids

1. Introduction

Chiral sulfoxides have emerged as versatile building blocks in the synthesis of pharmaceutical products and chiral ligands in asymmetric catalysis [1–3]. Kagan [4,5] and Furia and Modena [6] independently reported high enantioselectivities using modified versions of Sharpless epoxidation system: alkyl hydroperoxide/titanium tetrakisopropoxide/diethyl tartrate. Later, catalytic versions of this titanium-mediated reaction and other catalytic systems using salen complexes were also developed [7–10]. Bolm and Bienewald [11a] reported vanadium-chiral Schiff base complex-catalyzed asymmetric sulfur oxidation using hydrogen peroxide as the oxidant with good enantioselectivity. Later, Anson and co-workers [11b] and Katsuki and co-workers [11c] further improved the enantioselectivity using more complex Schiff bases. In the recent years, efforts are devoted to the development of processes using a highly robust and recyclable catalyst that provides higher atom utilization and minimized pollution levels using greener ingredients [12].

Layered double hydroxides (LDHs) or hydrotalcite-like compounds (HTLCs) [13] have recently received much attention in view of their potential usefulness as adsorbents, anion exchangers and most importantly as catalysts [14]. The hydrophilicity of the LDH material makes the hosted oxidation catalyst water compatible to conduct the reactions using water as a solvent. Recently, we have designed and developed a recoverable and reusable osmium catalyst immobilized on layered double hydroxides (LDHs) by the ion-exchange of OsO₄²⁻ for asymmetric dihydroxylation of olefins employing NMO as the co-oxidant [15] and effective oxidation of sulfides directly to sulfones using molecular oxygen as the stoichiometric oxidant [16]. Considering that one could expect that a good asymmetric dihydroxylation catalyst can also work for the oxidation of sulfides, and also based on the earlier report of OsO₄-catalyzed oxidation of sulfides to sulfones in the presence of NMO under homogeneous conditions [17] by Kaldor and Hammond, we opted for the asymmetric oxidation of sulfides by LDH OsO₄. We report in this paper heterogeneous osmate-exchanged Mg-Al-LDH catalyst for the asymmetric oxidation of sulfides to sulfoxides using NMO (*N*-methyl morpholine *N*-oxide) as co-oxidant and (DHQD)₂PHAL (hydroquinidine 1,4-phthalazinediyl diether) as a chiral ligand, with good yields albeit moderate e.e.'s (Scheme 1).

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Scheme 1.

2. Experimental

$K_2OsO_4 \cdot 2H_2O$, $MgCl_2 \cdot 6H_2O$, $AlCl_3 \cdot 6H_2O$, $(DHQD)_2PHAL$, NMO, *t*BuOH, NaOH, and thioanisole were purchased from Aldrich and used as such without further purification. $(DHQD)_2PHAL$ was purchased from Fluka and used as such without further purification. High-performance liquid chromatography (HPLC) was performed using the following apparatus: SHIMADZU LC-10AT (liquid chromatograph), SHIMADZU SPD-10A (UV detector), and SHIMADZU C-R6A Chromatopac. ACME silica gel (100–200 mesh) was used for column chromatography and thin-layer chromatography was performed on Merck-precoated silica gel 60-F₂₅₄ plates. Optical rotations were obtained on a Jasco P-1020 polarimeter. Slow addition of the sulfide was carried out using a syringe pump. All the other solvents and chemicals were obtained from commercial sources and purified using standard methods.

2.1. Preparation of the catalysts

2.1.1. The preparation of LDH (Mg–Al–Cl)

A mixture of $MgCl_2 \cdot 6H_2O$ (30.49 g, 0.15 mmol) and $AlCl_3 \cdot 6H_2O$ (12.07 g, 0.05 mmol) was dissolved in 200 ml of deionized water [15]. To this, aqueous solution was then slowly added at 25 °C, 100 ml of NaOH (2 M) solution at pH 10 under a nitrogen flow. The pH of the reaction mixture was maintained at this value by the continuous addition of 2 M NaOH. The resulting suspension was stirred overnight under a nitrogen flow at 70 °C. The solid product was isolated by filtration, washed thoroughly with deionized water, and dried overnight at 80 °C. All synthetic steps were carried out using decarbonated water.

Table 1

Asymmetric oxidation of methyl phenyl sulfide catalyzed by LDH OsO_4 using NMO with different ligands^a

Ligand	Conversion (%)	Selectivity (1a/1b) ^b	Isolated yield ^c (e.e., %) ^d	Configuration ^e
$(DHQD)_2PHAL$	100	80/20	74 (28)	(R)
$(DHQ)_2PHAL$	100	75/25	71 (23)	(S)
(+) Diisopropyl L-tartrate	100	78/22	69 (24)	(R)
(+)-DET	100	78/22	69 (26)	(R)

^a Sulfide (3 mmol), NMO (3.9 mmol), LDH OsO_4 (0.03 mmol) and $(DHQD)_2PHAL$ (0.03 mmol) in *tert*-butanol- H_2O (1:1, 10 ml) for 3 h.

^b Sulfoxide/sulfone based on ¹H NMR spectroscopic integration of crude product.

^c Isolated yield of sulfoxide after column chromatography.

^d Determined by HPLC analysis using Chiralcel OD column (conditions: hexane:2-propanol (9:1), 0.5 ml/min).

^e The configurations were assigned by comparing optical rotations and HPLC elution orders with known literature data [5,6,9,18,19].

Table 2

Effect of Osmium/ligand on the LDH OsO_4 -catalyzed oxidation of methyl phenyl sulfide^a

Entry	Osmium/ligand	Conversion (%)	Selectivity (1a/1b) ^b	Isolated yield ^c (e.e., %) ^d
1	1:1	100	80/20	74 (28)
2	1:3	100	82/18	71 (36)
3	1:5	92	81/11	67 (51)
4	1:10	100	77/23	65 (30)

^a Methyl phenyl sulfide (3 mmol), NMO (3.9 mmol), $(DHQD)_2PHAL$ (0.03 mmol), and LDH OsO_4 (0.03 mmol) in a given solvent (10 ml) were stirred at room temperature for 3 h.

^b Values in parenthesis (sulfoxide/sulfone) are based on ¹H NMR spectroscopic integration of crude product.

^c Isolated yields of sulfoxides after column chromatography.

^d Determined by HPLC analysis using Chiralcel OD column (conditions: hexane:2-propanol (9:1), 0.5 ml/min).

2.1.2. The preparation of LDH OsO_4

One gram of Mg–Al–Cl LDH was suspended in 100 ml of 0.689 g (1.87 mmol) aqueous potassium osmate solution and stirred at 25 °C for 12 h under nitrogen atmosphere. The solid catalyst was filtered, washed thoroughly with 300 ml of water, and vacuum-dried to obtain 1.416 g of LDH OsO_4 (1.34 mmol of Os per gram).

2.1.3. Typical procedure asymmetric oxidation of methyl phenyl sulfide

LDH OsO_4 (0.03 mmol), $(DHQD)_2PHAL$ (0.03 mmol), and *N*-methylmorpholine *N*-oxide (3.9 mmol) were taken in a round-bottomed flask containing *t*BuOH-water (1:1, 10 ml) and stirred at room temperature. Then sulfide (3 mmol) was added slowly for 1 h and the reaction mixture was stirred. After completion of the reaction as indicated by TLC, the catalyst was filtered and washed with methanol. After removing the solvent by rotavapor, the crude material was chromatographed on silica gel to afford the corresponding oxidation product.

3. Results and discussion

We first examined the asymmetric oxidation of methyl phenyl sulfide by LDH OsO_4 with NMO using different

Table 3
Effect of solvent on the LDH OsO₄-catalyzed oxidation of methyl phenyl sulfide^a

Entry	Solvent	Conversion (%)	Selectivity (1a/1b) ^b	Isolated yield ^c (e.e. %) ^d
1	H ₂ O-acetone (1:3)	100	82/18	71 (23)
2	Acetone-DCE (1:1)	100	78/22	67 (18)
3	H ₂ O-CH ₃ CN (1:3)	100	77/23	65 (23)
4	H ₂ O- ^t BuOH (1:3)	100	80/20	70 (28)

^a Methyl phenyl sulfide (3 mmol), NMO (3.9 mmol), (DHQD)₂PHAL (0.03 mmol), and LDH OsO₄ (0.03 mmol) in a given solvent (10 ml) were stirred at room temperature for 3 h.

^b Values in parenthesis(sulfoxide/sulfone) are based on ¹H NMR spectroscopic integration of crude product.

^c Isolated yields of sulfoxides after column chromatography.

^d Determined by HPLC analysis using Chiralcel OD column (conditions: hexane:2-propanol (9:1), 0.5 ml/min).

Table 4
Reusability of LDH OsO₄ catalyst in the oxidation of methyl phenyl sulfide^a

Cycle	Conversion (%)	Selectivity (1a/1b) ^b	Isolated yield ^c (e.e. %) ^d
1	100	80/20	74 (28)
2	100	78/22	67 (15)
3	100	77/23	65 (9)
4	85	66/19	60 (4)

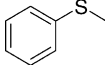
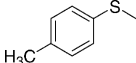
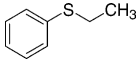
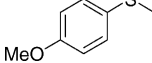
^a Methyl phenyl sulfide (3 mmol), NMO (3.9 mmol), (DHQD)₂PHAL (0.03 mmol), and LDH OsO₄ (0.03 mmol) in a given solvent (10 ml) were stirred at room temperature for 3 h.

^b Values in parenthesis(sulfoxide/sulfone) are based on ¹H NMR spectroscopic integration of crude product.

^c Isolated yields of sulfoxides after column chromatography.

^d Determined by HPLC analysis using Chiralcel OD column (conditions: hexane:2-propanol (9:1), 0.5 ml/min).

Table 5
Asymmetric oxidation of sulfides catalyzed by LDH OsO₄ using NMO at room temperature^a

S.No	Sulfide	Ligand	Conversion (%)	Selectivity (1a/1b) ^b	Isolated yield ^c (e.e. %) ^d	Configuration ^e
1		(DHQD) ₂ PHAL	100	80/20	74 (28)	(R)
2		(DHQD) ₂ PHAL	100	82/18	76 (27)	(R)
3		(DHQD) ₂ PHAL,	100	80/20	71 (28)	(R)
4		(DHQD) ₂ PHAL,	100	82/18	73 (26)	(R)

^a Sulfide (3 mmol), NMO (3.9 mmol), LDH OsO₄ (0.03 mmol) and (DHQD)₂PHAL (0.03 mmol) in *tert*-butanol-H₂O (1:1, 10 ml) for 3 h.

^b Sulfoxide/sulfone based on ¹H NMR spectroscopic integration of crude product.

^c Isolated yield of sulfoxide after column chromatography.

^d Determined by HPLC analysis using Chiralcel OD column (conditions: hexane:2-propanol (9:1), 0.5 ml/min).

^e The configurations were assigned by comparing optical rotations and HPLC elution orders with known literature data [5,6,9,18,19].

ligands (Table 1). The e.e. is slightly lower with hydroquinine 1,4-phthalazinediyl diether (DHQ)₂PHAL when compared to (DHQD)₂PHAL. With K₂OsO₄, under similar conditions, only sulfone was obtained. The reaction at 25 °C gave sulfoxide and sulfone in 80/20 ratio and the enantiomeric excess (e.e) is 28% with (DHQD)₂PHAL ligand. The reaction proceeded at 0 °C with 80% conversion (60/20), and no e.e. We have examined the effect of L/Os (ligand: osmium) on e.e's (Table 2) and the higher e.e. is obtained using L/Os ratio 5. *tert*-Butanol/water gave the best results among the solvents examined in the oxidation of sulfides (Table 3). The catalyst was reused for three cycles successfully, whereas in the fourth cycle the catalyst shows slightly reduced activity.

However, the e.e.'s of the sulfoxides were reduced in the recycle experiments (Table 4). There was no leaching of Os even after the fourth cycle as determined by SEM-EDAX. The asymmetric oxidation of other sulfides is summarized in Table 5.

4. Conclusions

In conclusion, asymmetric oxidation of sulfides has been developed using osmate-exchanged LDHs in the presence of cinchona alkaloids for the first time. The reactions proceeded with good yields, albeit moderate e.e.'s.

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References

- [1] (a) M.C. Carreno, *Chem. Rev.* 95 (1995) 1717;
(b) I. Fernandez, N. Khiar, *Chem. Rev.* 103 (2003) 3651.
- [2] (a) F. Pezet, H. Ait-Haddou, J.-C. Daran, I. Sasaki, G.G.A. Balavoine, *Chem. Commun.* (2002) 510;
(b) K. Hiroi, Y. Suzuki, I. Abe, R. Kawagishi, *Tetrahedron* 56 (2000) 4701;
(c) R. Tokunoh, M. Sodeoka, K. Aoe, M. Shibasaki, *Tetrahedron Lett.* 36 (1995) 8035.
- [3] (a) P. Pitchen, *Chem. Ind. (London)* 16 (1994) 636;
(b) M. Tanaka, H. Yamazaki, H. Hakusui, N. Nakamichi, H. Sekino, *Chirality* 9 (1997) 17;
(c) S. von Unge, V. Langer, L. Sjolín, *Tetrahedron: Asymmetry* 8 (1997) 1967;
(d) H. Cotton, T. Elebring, M. Larsson, L. Li, H. Sorensen, S. von Unge, *Tetrahedron: Asymmetry* 11 (2000) 3819.
- [4] (a) H.B. Kagan, *Catalytic Asymmetric Synthesis*, Wiley-VCH, New York, 2000;
(b) H.B. Kagan, *Asymmetric Oxidation Reactions: Practical Approach in Chemistry*, Oxford University Press, Oxford, 2001, Chapter 4.1.
- [5] P. Pitchen, E. Dunach, M.N. Deshmukh, H.B. Kagan, *J. Am. Chem. Soc.* 106 (1984) 8188.
- [6] F. Di Furia, G. Modena, R. Seraglia, *Synthesis* (1984) 325.
- [7] (a) J.M. Brunel, H.B. Kagan, *Synlett* (1996) 404;
(b) J.M. Brunel, H.B. Kagan, *Bull. Chim. Soc. Fr.* 133 (1996) 1109.
- [8] (a) K. Nakajima, K. Kojima, J. Fujita, *Chem. Lett.* (1986) 1483;
(b) K. Nakajima, K. Kojima, M. Kojima, T. Aoyama, J. Fujita, *Bull. Chem. Soc. Jpn.* 63 (1990) 2620.
- [9] A.H. Vetter, A. Berkessel, *Tetrahedron Lett.* 39 (1998) 1741.
- [10] M. Palucki, P. Hanson, E.N. Jacobsen, *Tetrahedron Lett.* 33 (1992) 7111.
- [11] (a) C. Bolm, F. Bienewald, *Angew. Chem. Int. Ed. Engl.* 34 (1995) 2640;
(b) B. Pelotier, M.S. Anson, I.B. Campbell, S.J.F. Macdonald, G. Priem, R.F.W. Jackson, *Synlett* (2002) 1055;
(c) C. Ohta, H. Shimizu, A. Kondo, T. Katsuki, *Synlett* 1 (2002) 161.
- [12] D.E. Vos, I.F.K. Vankelecom, P.A. Jacobs (Eds.), *Chiral Catalyst Immobilization and Recycling*, Wiley, Weinheim, 2000.
- [13] F. Cavani, F. Trifiro, A. Vaccari, *Catal. Today* 11 (1991) 173.
- [14] (a) M. Lakshmi Kantam, B.M. Choudary, Ch.V. Reddy, K.K. Rao, F. Figueras, *Chem. Commun.* (1998) 1033;
(b) B.M. Choudary, M. Lakshmi Kantam, B. Kavita, Ch.V. Reddy, K.K. Rao, F. Figueras, *Tetrahedron Lett.* 39 (1998) 3555;
(c) B.M. Choudary, M. Lakshmi Kantam, B. Bharathi, Ch.V. Reddy, *Synlett* (1998) 1203;
(d) P.S. Kumbhar, J.S. Valente, J. Lopez, F. Figueras, *Chem. Commun.* (1998) 535;
(e) B.F. Sels, D.E. De Vos, M. Buntinx, F. Pierard, A.K. Mesmaeker, P.A. Jacobs, *Nature* 400 (1999) 855;
(f) B.M. Choudary, M. Lakshmi Kantam, A. Rahman, Ch.V. Reddy, K.K. Rao, *Angew. Chem., Int. Ed.* 40 (2001) 763.
- [15] (a) B.M. Choudary, N.S. Chowdari, M. Lakshmi Kantam, K.V. Raghavan, *J. Am. Chem. Soc.* 123 (2001) 9220;
(b) B.M. Choudary, N.S. Chowdari, K. Jyothi, M. Lakshmi Kantam, *J. Am. Chem. Soc.* 124 (2002) 5341.
- [16] B.M. Choudary, Ch. Venkat Reddy, B.V. Prakash, M. Lakshmi Kantam, B. Sreedhar, *Chem. Comm.* (2003) 754.
- [17] S.W. Kaldor, M. Hammond, *Tetrahedron Lett.* 32 (1991) 5043.
- [18] (a) K. Mislow, M.M. Green, P. Laur, J.T. Melillo, T. Simmons, A.L. Ternay Jr., *J. Am. Chem. Soc.* 87 (1965) 1958;
(b) J. Legros, C. Bolm, *Angew. Chem., Int. Ed.* 42 (2003) 5487.
- [19] J.M. Brunel, P. Diter, M. Duetsch, H.B. Kagan, *J. Org. Chem.* 60 (1995) 8086.