Available online at www.sciencedirect.com
ScienceDirect
Journal of Molecular Catalysis A: Chemical 260 (2006) 295–298
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
www.elsevier.com/locate/molcata

Catalytic epoxidation of olefins using MoO_3 and TBHP: Effect of the addition of chiral 2-substituted pyridines on the catalytic rate and asymmetric induction

Elisabete da Palma Carreiro [a], Carlos Monteiro [a], Guo Yong-en [a], Anthony J. Burke [a,*], Ana Isabel Rodrigues [b]

[a] *Departamento de Química and Centro de Química de Évora, Universidade de Évora, Rua Romão Romalho 59, 7000 Évora, Portugal*
[b] *Departamento de Tecnologia de Indústrias Químicas, Instituto Nacional de Engenharia, Tecnologia e Inovação, Estrada do Paço do Lumiar, Edifício F, 1649-038 Lisboa, Portugal*

Received 17 March 2006; received in revised form 18 July 2006; accepted 18 July 2006
Available online 1 September 2006

Abstract

Attempts were made at epoxidising enantioselectively some simple olefins using MoO_3 (0.17 mol%), TBHP and five different chiral non-racemic 2-substituted pyridine ligands. A maximum conversion of 88% using 4-methylstyrene, and a maximum selectivity of ≥98% using 1-methylcyclohexene and 1-phenylcyclohexene were obtained. All ligands screened showed the ability to accelerate the reaction. However, it was ligand **4**, that was the quickest to do so and showed the greatest acceleration. The observation of a reaction rate acceleration in the presence of such ligands appeared to indicate the formation of a Mo(VI)oxoperoxy-ligand complex. In no case was asymmetric induction observed.

Keywords: Molybdenum(VI) trioxide; Catalysis; Epoxidation; Chiral ligands

1. Introduction

The catalytic enantioselective epoxidation of olefins giving chiral non-racemic epoxides is an important reaction as it is an extremely elegant and efficient method for the instalment of stereochemically defined oxirane ring units [1].

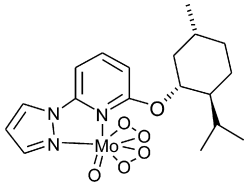
Over the last 25 years or so, chiral Mo(VI) catalysts have been explored for the catalytic asymmetric epoxidation of olefins in an effort to find a general highly selective catalytic epoxidation method [2] that can compete with the highly popular titanium [3] and manganese [4] catalytic systems of Sharpless–Katsuki and Jacobsen. Chiral oxo-organomolybdenum(VI) complexes have been extensively studied for the enantioselective catalytic epoxidation of olefins by a number of groups over the last 5 years [5–9]. Shi and co-workers reported the highest enantioselectivity (80% ee) for these complexes [9]. Kagan et al. [10] reported the first synthesis of a chiral oxo-diperoxo molybdenum(VI) complex, which was used subsequently for the stoichiometric epoxidation of olefins and for which a maximum enantioselectivitiy of 35% ee was achievied. Other chiral oxo-diperoxo molybdenum(VI) complexes have been prepared and used for the stoichiometric enantioselective epoxidation of unfunctionalized olefins [11,12]. The first report of a catalytic version of this reaction, as far as we know, is that of Park et al. [13] who synthesised oxo-diperoxo molybdenum(VI) complexes derived from (*R*)-piperidinylmandelamide and (*R*)-piperidinylphenylacetamide and which furnished ees of 26–81% for the epoxidation of *cis*- and *trans*-β-methylstyrene. Brito et al. [14] reported the preparation of the first chiral molybdenum(VI) oxo-diperoxo oxazoline–pyridine complex, which was used for the catalytic epoxidation of cyclooctene and (*R*)-limonene. The ees were not measured. We recently, introduced a new chiral oxodiperoxo-[2-(1-pyrazolyl)-6-menthylpyridine]molybdenum(VI) complex **1** [15], which was tested in a number of catalytic epoxidations, unfortunately a maximum ee of only 6% was obtained.

Although our preliminary investigations using the oxodiperoxo-[2-(1-pyrazolyl)-6-menthylpyridine]molybdenum(VI) **1** in catalytic asymmetric olefin epoxidations were disap-

* Corresponding author. Tel.: +351 266745310; fax: +351 266745303.
E-mail address: ajb@dquim.uevora.pt (A.J. Burke).

1381-1169/$ – see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.molcata.2006.07.047

pointing [15], and this we attribute to the distance of the stereogenic centre from the reaction centre or possible fast on/off exchange of the ligands from the coordination sphere of a Mo(VI) complex, we considered employing a series of Mo(VI) catalysts with a superior design which should allow improved enantioselectivities.



1

We recently reported a new method for the epoxidation of olefins using MoO_3 and *tert*-butylhydroperoxide and showed that heterocyclic aromatic amines, like pyridine and pyrazole accelerated the reaction [16]. Some of our preliminary experiments indicated that the key catalytic species was the coordinated alkyl hydroperoxide species [16] which on the basis of literature precedent [17] might be expected to have the second peroxide oxygen coordinated to the metal with a concomitant triangular arrangement (Fig. 1). We were interested to see if chiral bi-dentate ligands would coordinate with this putative active complex and if the resulting chiral complex could impart some asymmetric induction during the epoxidation reaction.

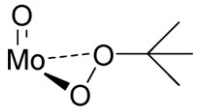


Fig. 1. Postulated mode of coordination for the putative Mo(VI) alkyl hydroperoxide species.

To achieve this objective we choose the following *N*,*N*-chiral ligands **2**–**5** (Scheme 1). These ligands were chosen because they are stable to oxidation and quite easily synthesised.

Ligands **2** and **3** were previously used by us in an approach to develop an asymmetric version of the MTO catalysed epoxidation of olefins [18] and were selected for this study on account of: (1) the relatively close proximity of the stereogenic centre to the reaction site and (2) putative dinuclear complex formation. We selected ligand **4** [19] because chiral non-racemic bis-amide ligands have in the past shown promise for metal catalysed asymmetric epoxidations [20]. It was also established that ligand **4** forms stable complexes with Mo [21,22] when it was shown by ^{15}N NMR that the pyridine nitrogen and the amide carbonyl oxygen chelated with the metal [22]. The pyrazole–pyridine **5** was selected as it contains a bulkier chiral group than that encountered in Mo complex **1**, thus potentially increasing the chances of obtaining greater asymmetric induction in the reaction. Given that the preparation of chiral oxo-diperoxo molybdenum(VI) complexes is both a tedious and a time consuming undertaking, we decided to explore the possibility of forming some chiral Mo(VI) peroxy-oxo complexes in situ by substituting the achiral ligands previously used [16] with these chiral ligands.

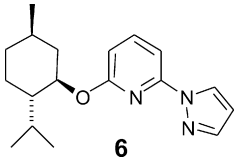
2. Results and discussion

2.1. Chiral ligand synthesis

The ligands **2**–**5** were prepared as outlined previously [18].

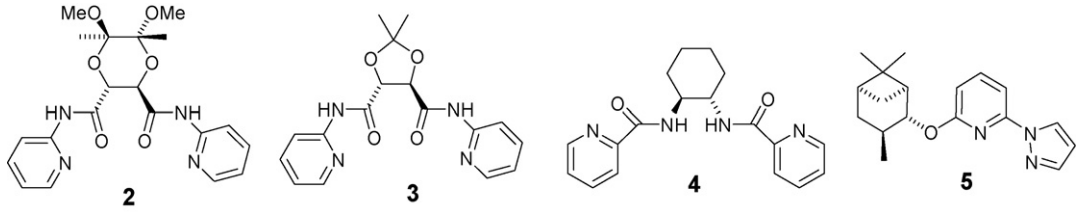
2.2. Catalytic studies

Using our established procedure [16], we set about screening ligands **2**–**5** including the pyrazole–pyridine ligand **6** [15] which forms part of complex **1** in a number of olefin epoxidation reactions. The results are shown in Table 1.



6

The epoxide selectivities were in general very good with the best selectivities obtained for the less acid sensitive epoxides, namely, 1-methylcyclohexene oxide and 1-phenylcyclohexene oxide, respectively (≥98%). In the case of styrene and 4-methylstyrene, the highest selectivity obtained was for the epoxidation of 4-methylstyrene with ligand **6** (94%, entry 10). The lowest was obtained for the epoxidation of styrene with ligand **2** (84%, entry 1). When the reaction was carried out at a temperature of 55 °C, surprisingly, only a selectivity of 48% was obtained (entry 8). We attribute this result to the presence of lewis acidic species in solution out competing the epoxidation catalyst. The best conversion was obtained for 4-methylstyrene (88%, entry 9) with ligand **5**. In the case of styrene the ligands **3**, **4** and **6** showed the best conversions, 61, 60% (68 with 0.5 mol% of **4**, entry 5, Table 1) and 58% (entries 3, 4 and 7). Ligand **5** was the worst (45%, entry 6) perhaps on account of the bulky nature of the chiral terpene appendage? Although in the case of styrene it was impossible to obtain a conversion as high as that using complex **1** (61% opposed to 86% [15]), when 4-methylstyrene was used, it was indeed possible to obtain a much better conversion with the in situ method (88% as opposed to 49% [15]). The



2 **3** **4** **5**

Scheme 1. Chiral bis-pyridinamides and pyridine–pyrazole ligands for Mo(VI) catalysed olefin epoxidations.

Table 1
Mo(VI) catalysed epoxidation of simple olefins with chiral ligands **2–6**

Entry	Olefin	Ligand	Reaction time (h)	Conversion[a] (%)	Epoxide selectivity (%)
1	Styrene	**2**	15	52	84
2	Styrene[b]	**2**	15	56	73
3	Styrene	**3**	15	61	90
4	Styrene	**4**	15	60	92
5	Styrene	**4**[c]	15	68	89
6	Styrene	**5**	15	45	92
7	Styrene	**6**	14	58	91
8	Styrene[d]	**6**	14	13	48
9	4-Methylstyrene	**5**	12	88	86
10	4-Methylstyrene	**6**	12	80	94
11	1-Methylcyclohexene	**4**	5	32	≥98
12	1-Methylcyclohexene	**5**	5	28	≥98
13	1-Methylcyclohexene	**6**	5	71	≥98
14	1-Phenylcyclohexene	**5**	13	45	≥98
15	1-Phenylcyclohexene	**6**	13	47	≥98

MoO_3 (0.17 mol%), chiral ligand (0.17 mol%), THBP (1.1 equiv.), olefin, toluene, 100 °C.

[a] Conversion refers to the transformation of olefin to epoxide and the corresponding aldehyde in some cases (entries 1–10).

[b] MoO_3 was added to TBHP and heated to 100 °C in toluene for 2 h, the ligand was added at this temperature and after 1 h (the reaction solution became slightly yellow) the olefin was added.

[c] 0.5 mol% ligand.

[d] 55 °C.

Table 2
Ligand acceleration study

Entry	Olefin	Ligand	Reaction time (h)	Conversion[a] (%)	Epoxide selectivity (%)
1	Styrene	None	1	17	83
2	Styrene	**2**	1	19	87
3	Styrene	**3**	1	16	90
4	Styrene	**4**	1	27	88
5	Styrene	**5**	1	12	85
6	Styrene	**6**	1	18	84
7	Styrene	None	2	25	82
8	Styrene	**2**	2	33	91
9	Styrene	**3**	2	33	92
10	Styrene	**5**	2	33	88
11	Styrene	**6**	2	30	90

MoO_3 (0.17 mol%), chiral ligand (0.17 mol%), THBP (1.1 equiv.), olefin, toluene, 100 °C.

[a] Conversion refers to the transformation of olefin to epoxide and benzaldehyde.

reaction conducted at 55 °C (entry 8) showed that a temperature of 100 °C is vital for high conversions. The principle side products for styrene and 4-methylstyrene were; benzaldehyde and 4-methylbenzaldehyde. When we pre-mixed ligand **2** with the putative Mo(VI) peroxy complex for 1 h prior to the addition of styrene (Table 1, entry 2), there was only a 4% increase in the conversion and an 11% drop in epoxide selectivity.

Unfortunately, no enantioselectivities were observed. This might be due to one of the following reasons: (1) perhaps there were other chiral or achiral Mo(VI) peroxy or peroxo species in solution competing with the principal oxo-peroxy complex (in our previous paper we obtained support for the presence of oxo-peroxo complexes [16]), (2) the labile nature of the peroxy appendage, particularly at the high temperature applied during the reaction, leading to the generation of a number of competing diasteromeric transition states, (3) fast on/off exchange of the ligands or part of the ligands from the coordination sphere of the Mo(VI) peroxy complex or (4) there was no complex formation in situ (vide infra). The observation of an increase in the conversion of 8% (Table 1, entry 5) when the quantity of ligand was increased to 0.5 mol%, seemed to eliminate the last hypothesis.

We also carried out a series of additional experiments to determine if the ligands were complexing with the Mo(VI) peroxy complex. These are shown in Table 2.

We discovered that over the first hour it was only ligand **4** that had any effect on the rate of the catalytic reaction, as a difference of 10% in the reaction conversion was obtained (entry 4) over the control experiment (entry 1). As a catalytic induction period might have been at work in the case of the other ligand containing reactions, we decided to determine the conversions after a 2 h period (entries 7–11). We found that indeed these ligands (**2**, **3**, **5** and **6**) imparted some rate acceleration to the reaction, but to a lesser extent than that shown by ligand **4**. Using the conditions used previously [15], we have recently found that ligand **4** complexes readily with Mo(VI) to form a Mo(VI) peroxo complex whose overall structure at present remains elusive even though spectroscopic analysis would seem to indicate that it is an oxo-peroxo complex [23].

We carried out a series of NMR experiments to establish what was happening to the ligand during the putative complexation process. For this task, we carried out number of ^{1}H NMR experiments between room temperature (300 K) and 100 °C (373 K) on a mixture of MoO_3, TBHP and ligand **4** dissolved in DMSO-d_6 in an NMR tube. We discovered that there was no change in the chemical shifts of the key proton resonances (e.g., the pyridine hydrogens and NHC*H* peaks) as the temperature varied between 300 and 373 K. The NH signals did vary somewhat, but the same variation was also observed for the free ligand when the spectrum was recorded at 373 K in DMSO-d_6. However, it is extremely likely based on literature precedence, that both the ligand and the complex Mo(VI) peroxy-ligand **4** complex share almost exactly the same ^{1}H NMR patterns. For instance, we found that Mo(VI) complex **1** has a ^{1}H NMR spectrum very similar to ligand **6** [15]. We also observed no ligand decomposition when the temperature was increased to 373 K. We also tried to detect the presence of Mo-OO-*t*Bu species in solution between 300 and 373 K, by mixing MoO_3 with TBHP in an NMR tube with DMSO-d_6, but unfortunately, we did not detect signals, which might indicate the presence of such species.

3. Conclusions

A range of chiral bi-dentate pyridine ligands (**2–6**) was screened in the Mo(VI) catalysed epoxidation of some non-functionalised olefins. Our preliminary study indicated the

occurrence of ligand-induced acceleration which would imply the formation of Mo(VI)-ligand complexes during the course of the reaction, this acceleration was most pronounced in the case of ligand **4**. No enantioselectivities were observed and this is most likely due to: (1) the labile nature of the peroxy appendage or (2) fast on/off exchange of the ligands from the coordination sphere of a Mo(VI) species which could not be confirmed from our NMR experiments. On the other hand, some highly satisfactory olefin conversions (94% using 4-methylstyrene) and epoxide selectivities (≥98% with 1-methyl- and 1-phenylcyclohexene) were observed. Work is in progress at further elucidating the reaction mechanism for the epoxidation of the olefins using this methodology and at optimising the reaction conditions so that significantly better conversions and enantioselectivities may be obtained in the future.

4. Experimental

4.1. General remarks

All reagents were obtained from Aldrich, Lancaster Synthesis or Acros; ca. 5.5 M TBHP in nonane (Fluka) stored over molecular sieves was used. The toluene used was dried using the standard procedure [24].

Gas chromatographic (GC) analyses of the products obtained from the epoxidation reactions were performed on a Hewlett Packard (HP) 6890 series instrument equipped with a flame ionization detector (FID). The chromatograph was fitted with a cyclodex-B capillary column (30 m, 250 μm, 0.25 μm) (Agilent 112–2532).

In all cases, the olefin conversions were calculated by simply determining the ratio of the peak areas for the olefin substrate, the epoxide product and known decomposition products in some cases.

*4.2. Catalytic epoxidation of olefins using in situ formed putative oxo-peroxy Mo(VI) complexes in the presence and absence of ligands **2–6***

To a suspension of MoO_3 (2.4 mg, 0.017 mmol) and chiral ligand (0.017 mmol), in dry toluene (1 mL) was added TBHP (2 mL, 11 mmol in nonane) and a solution of olefin (10 mmol) in toluene (3 mL). The mixture was heated to 100 °C over a 5–15 h period. An aliquot of reaction mixture was removed and analysed in triplicate by chiral GC (see Table 1).

(*Note:* In the case of entry 10, Table 1, 5 mmol of olefin were used and the quantities of the other reagents were halved accordingly.)

Acknowledgements

We wish to thank the Fundação para a Ciência e a Tecnologia and the Programma Opercional para Ciência Tecnologia e Inovação (POCTI/QUI/35358/2000) for funding, including a postdoctoral grant (GY-E), which was partly funded by the European Community fund FEDER.

References

[1] R.A. Sheldon, J.K. Kochi, Metal-Catalysed Oxidations of Organic Compounds, Academic Press, New York, 1981.
[2] For reviews see:
(a) V. Schurig, F. Betschinger, Chem. Rev. 92 (1992) 873;
(b) F.E. Kühn, J. Zhao, W.A. Herrmann, Tetrahedron: Asymm. 16 (2005) 3469.
[3] R.A. Johnson, K.B. Sharpless, in: I. Ojima (Ed.), Catalytic Asymmetric Synthesis, second ed., Wiley-VCH, New York, 2000, p. 231 (Chapter 6A).
[4] T. Katsuki, in: I. Ojima (Ed.), Catalytic Asymmetric Synthesis, second ed., Wiley-VCH, New York, 2000, p. 287 (Chapter 6B).
[5] W.A. Herrmann, J.J. Haider, J. Fridgen, G.M. Lobmaier, M. Spiegler, J. Organomet. Chem. 603 (2000) 69.
[6] F.E. Kühn, A.M. Santos, A.D. Lopes, I.S. Gonçalves, J.E. Rodríguez-Borges, M. Pillinger, C.C. Romão, J. Organomet. Chem. 621 (2001) 207.
[7] I.S. Gonçalves, A.M. Santos, C.C. Romão, A.D. Lopes, J.E. Rodríguez-Borges, M. Pillinger, P. Ferreira, J. Rocha, F.E. Kühn, J. Organomet. Chem. 626 (2001) 1.
[8] S. Gago, J.E. Rodríguez-Borges, C. Teixeira, A.M. Santos, J. Zhao, M. Pillinger, C.D. Nunes, Ž. Petrovski, T.M. Santos, F.E. Kühn, C.C. Romão, I.S. Gonçalves, J. Mol. Catal. A: Chem. 236 (2005) 1.
[9] X.-Y. Wang, H.-C. Shi, C. Sun, Z.-G. Zhang, Tetrahedron 60 (2004) 10993.
[10] H.B. Kagan, H. Mimoun, C. Mark, V. Schurig, Angew. Chem. Int. Ed. Engl. 18 (1979) 485.
[11] V. Schurig, K. Hintzer, U. Leyrer, M. Pitchen, H.B. Kagan, J. Organomet. Chem. 370 (1989) 81.
[12] O. Bartolini, F. Di Furia, G. Modena, A. Schionato, J. Mol. Catal. 35 (1986) 47.
[13] S.-W. Park, K.-J. Kim, S.S. Yoon, Bull. Korean Chem. Soc. 21 (2000) 446.
[14] J.A. Brito, M. Gómez, G. Muller, H. Teruel, J.-C. Clinet, E. Duñach, M.A. Maestro, Eur. J. Inorg. Chem. (2004) 4278.
[15] E.P. Carreiro, Y.-E. Guo, A.J. Burke, Inorg. Chim. Acta. 359 (2006) 1519.
[16] E.P. Carreiro, A.J. Burke, J. Mol. Catal. A: Chem. 247 (2006) 123.
[17] A.O. Chong, K.B. Sharpless, J. Org. Chem. 42 (1977) 1587.
[18] E.P. Carreiro, Y.-E. Guo, A.J. Burke, J. Mol. Catal. A: Chem. 235 (2005) 285.
[19] B.M. Trost, I.J. Hachiya, J. Am. Chem. Soc. 120 (1998) 1104.
[20] N. End, L. Macko, M. Zehnder, A. Pfaltz, Chem. Eur. J. 4 (1998) 818.
[21] S.W. Krska, D.L. Hughes, R.A. Reamer, D.J. Mathre, Y. Sun, B.M. Trost, J. Am. Chem. Soc. 124 (2002) 12656.
[22] B.M. Trost, K. Dogra, I. Hachiya, T. Emura, D.L. Hughes, S. Krska, R.A. Reamer, M. Palucki, N. Yasuda, P.J. Reider, Angew. Chem. Int. Ed. 41 (2002) 1929.
[23] A.J. Burke, C. Monteiro, unpublished results.
[24] W.L.F. Armarego, D.D. Perrin, Purification of Laboratory Chemicals, fourth ed., Butterworth Heinmann, Oxford, 1996.