

An Efficient Recyclable Catalytic System for Asymmetric Dihydroxylation of Olefins

Ru Jiang, Yongqing Kuang, Xiaoli Sun, and Shengyong Zhang*

Department of Chemistry, Fourth Military Medical University, 710032 Xi'an, China.

E-mail: syzhang@fmmu.edu.cn

Received 18-07-2005

Abstract

A recoverable and reusable catalytic system for asymmetric dihydroxylation of olefins was developed by using TentaGel-OsO₄ **1** and mono-quaternized bis-cinchona alkaloid chiral ligand **2** combined with ionic liquid [bmim]PF₆. Both the osmium and ligand could be recovered efficiently. It could be recycled ten times with only 0.5 mol% of **1** and 2.0 mol% of **2**. The system is effective in the AD reactions of a range of olefins.

Key words: chiral ligand, TentaGel-OsO₄, ionic liquid, asymmetric dihydroxylation

Introduction

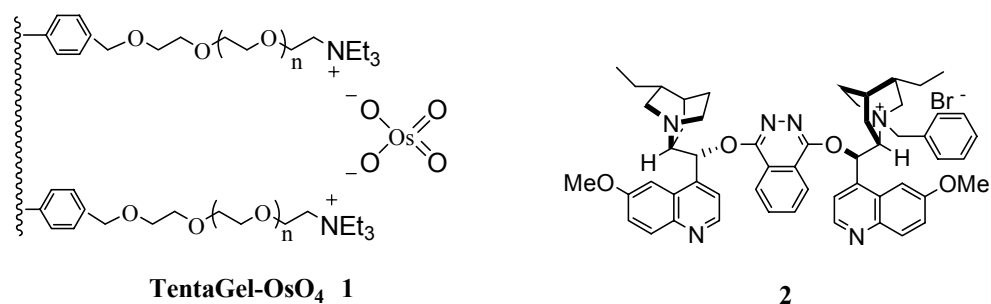
The catalytic asymmetric dihydroxylation (AD) of olefins provides one of the most efficient methods for the preparation of chiral vicinal diols, which act as intermediaries in the synthesis of many biologically active substances.¹ The obstacles to its large-scale application in the pharmaceutical and fine chemicals industries remain the high cost of osmium tetroxide and cinchona alkaloid ligands as well as the high toxicity and volatility of the osmium component. There is a growing interest for exploring the repetitive use of both the catalytic components (OsO₄ and chiral ligand) in the past few years. Attachment of the ligand to a soluble or insoluble support covalently² or immobilization of osmium tetroxide based on microencapsulation,³ ion-exchange techniques,⁴ osmylation of resins^{5,6}, and adopting PEG[poly(ethylene glycol)] as a recyclable medium⁷ has made it possible to recover and reuse the ligand or osmium, but has failed to recycle the two catalytic components at the same time. Recently, room-temperature ionic liquids (RTILs), especially those based on 1,3-dialkylimidazolium cations have been adopted as a recyclable medium in the AD reaction.^{8–10} In these solvents, catalysts having polar or ionic character can be immobilized and thus the ionic solutions containing the catalyst can be easily separated from reagents and products. When the reaction was finished, the product diol could be extracted by ether, while most of the alkaloid ligand and osmium tetroxide were remained in the ionic liquid phase. However, leaching of both catalytic components was inevitable during extraction of the product with ether, because the

ligand can dissolve in ether to some extent and bring out some osmium by complexation. Very recently, Branco *et al* adopted *sc*CO₂ in the separation process to minimize osmium catalyst loss and make its reuse possible.¹¹

We reported a recyclable catalytic system for AD reaction in the ionic liquid with a mono-quaternized bis-cinchona alkaloid ligand in 2004.¹² Both the ligand and OsO₄ could be recovered. But the amount of OsO₄ required is higher (1.5 mol%) than that needed for homogeneous AD reaction (0.2–0.5 mol%).¹³ Quantitative analysis of OsO₄ by iodometry showed that about 2 mol% of the total amount of OsO₄ was transferred into the ether layer during the extraction of diol with ether. To address this problem, we immobilized OsO₄ on the TentaGel resin. Herein we report the successful application of TentaGel-OsO₄ **1** and mono-quaternized bis-cinchona alkaloid ligand **2** in the AD reaction with [bmim] PF₆ as the recovery medium and *N*-methylmorpholine oxide (NMO) as co-oxidants (scheme 1).

Results and discussion

TentaGel resin is a special macromolecular material in which a polyethylene glycol (PEG) spacer is placed between the polystyrene backbone and the reactive site. Being soluble in many solvents such as dichloromethane, *tert*-butanol and water *etc.*, the PEG spacer places the reactive site in a more “solution-like” environment. Therefore, TentaGel-OsO₄ has the advantage of one-phase catalysis and two-phase separation. **1** was prepared as scheme 2. The FT-IR spectra of **1** showed that the sharp band which was

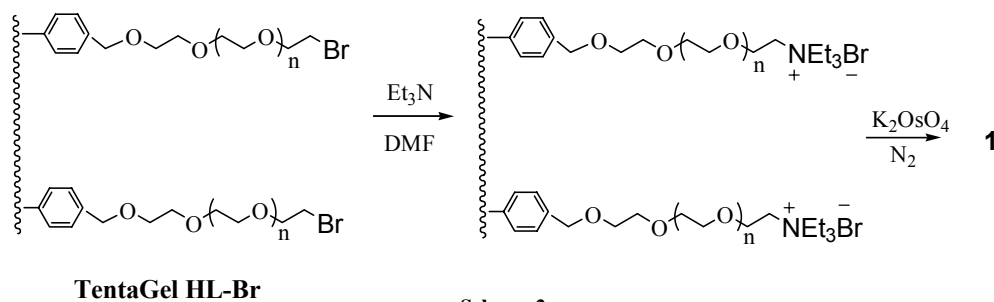


Scheme 1

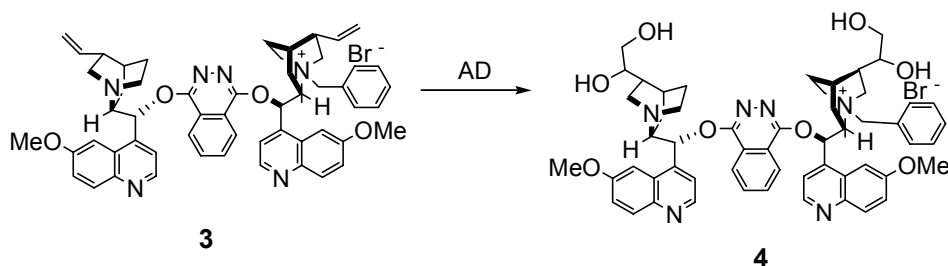
assigned to the vibrational asymmetric O=Os=O stretching (819 cm^{-1} in the spectrum of free potassium osmate) disappeared. The scanning electron microscopy-energy-dispersive X-ray analysis (SEM-EDX) of **1** substantiated the presence of osmium in the surface of the resin, and this result was reevaluated by titration of the potassium bromide formed in the ion-exchange process (loading = 0.075 mmol of Os per g).

We had reported the mono-quaternized bis-cinchona alkaloid ligand **3** (Scheme 3).¹² In the AD

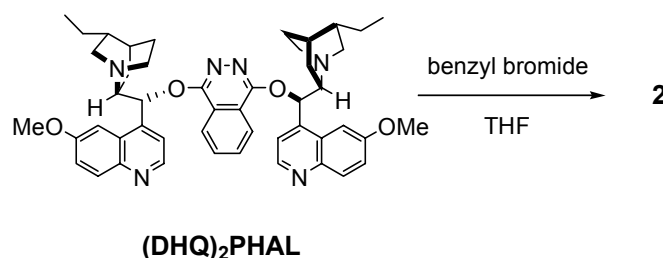
reaction, the double bonds present in **3** underwent dihydroxylation to produce the tetrahydroxylated analogues **4**. Being higher polar, **4** could be strongly immobilized in the ionic liquid much more⁸. In order to study the recoverability of bis-cinchona alkaloid ligand with only quaternized nitrogen group, we designed ligand **2** which couldn't be dihydroxylated in the AD reaction. **2** was prepared conveniently by quaternization of 1,4-bis(9-*O*-dihydroquininyl)phthalazine [(DHQ)₂PHAL] (Scheme 4).



Scheme 2



Scheme 3



Scheme 4

Table 1. Reusability of TentaGel-OsO₄ **1** and ligand **2** in the AD reaction of *trans*-stilbene in [bmim][PF₆].^a

| Run | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|------------------------|----|----|----|----|----|----|----|----|----|----|
| Yield (%) | 84 | 82 | 85 | 79 | 80 | 81 | 78 | 74 | 69 | 70 |
| Ee (%) ^b | 95 | 93 | 90 | 91 | 90 | 88 | 89 | 87 | 88 | 89 |
| Yield (%) ^c | 86 | 65 | 31 | | | | | | | |
| Ee (%) ^c | 95 | 88 | 23 | | | | | | | |

^a Recycle experiments were carried out on a 2 mmol reaction scale of olefin using **1** (0.01 mmol), **2** (0.04 mmol), NMO (2.6 mmol) and [bmim][PF₆] (2 mL) in acetone-H₂O (v/v, 10:1, 20 mL). Olefins were added by a syringe pump for 10 h; ^b The ee values were determined by chiral HPLC analysis; ^c Recycle experiments were carried out on a 2 mmol reaction scale of olefin by using OsO₄ instead of **1**.

As the model reaction, we studied the AD reaction of *trans*-stilbene using TentaGel-OsO₄ (0.5 mol%) **1** and chiral ligand **2** (2.0 mol%) in the acetone-H₂O-[bmim][PF₆] with NMO as co-oxidant. After completion of the reaction, all the volatiles were removed under reduced pressure and the chiral diol extracted with *tert*-butyl methyl ether. The remaining ionic liquid layer containing **1** and **2** was then subjected to the next run with a new batch of NMO and the olefin. High catalytic activity and enantioselectivity were obtained even in the tenth cycle, whereas the catalytic system could be only recycled 3 times by using 0.5 mol% of OsO₄ instead of 0.5 mol% of TentaGel-OsO₄ **1** (Table 1).

Encouraged by these promising results, we further performed the AD reactions of 9 olefins under the same conditions. The results are summarized in Table 2. In most case, the desired diols were formed in high yields and ees. A low concentration of the substrate in the reaction is necessary for high enantioselectivity. So the substrates should be added slowly during a period of 10 h (Table 2, entry 3, 7 and 9). This is in agreement with the earlier observation.⁸ The results of Table 2 showed that this catalytic system delivered much higher enantioselectivity for *trans*-disubstituted olefins than that for terminal olefins (Table 2, entry 8, 10 and 11). Additionally, higher ees were obtained for aromatic olefins than that for aliphatic olefins (Table 2, entry 12).

The ligand **2** couldn't be dihydroxylated in the catalytic reaction. Although possessing fewer polar groups, **2** delivered the same catalytic activity and recoverability with ligand **3**. It indicated that mono-quaternized bis-cinchona alkaloid ligand without other polar groups exhibited good recoverability in this catalytic system.

Conclusion

we have developed a highly effective recoverable and reusable system for AD reaction which provides

Table 2. AD reaction of olefins using **1** and **2** in [bmim]PF₆.^a

| Entry | Olefin | yield (%) | ee (%) ^b | config. ^c |
|----------------|---------------------------------------|-----------|---------------------|----------------------|
| 1 | <i>trans</i> -Stilbene | 84 | 95 | <i>S,S</i> |
| 2 | Ethyl <i>trans</i> -cinnamate | 73 | 95 | <i>2R,3S</i> |
| 3 ^d | Ethyl <i>trans</i> -cinnamate | 70 | 77 | <i>2R,3S</i> |
| 4 | Methyl <i>trans</i> -cinnamate | 71 | 95 | <i>2R,3S</i> |
| 5 | Propyl <i>trans</i> -cinnamate | 77 | 95 | <i>2R,3S</i> |
| 6 | <i>trans</i> - β -Methylstyrene | 83 | 96 | <i>S,S</i> |
| 7 ^d | <i>trans</i> - β -Methylstyrene | 87 | 74 | <i>S,S</i> |
| 8 | α -Methylstyrene | 86 | 70 | <i>S</i> |
| 9 ^d | α -Methylstyrene | 80 | 62 | <i>S</i> |
| 10 | Styrene | 88 | 80 | <i>S</i> |
| 11 | <i>p</i> -Chlorostyrene | 90 | 83 | <i>S</i> |
| 12 | <i>trans</i> -5-Decene | 85 | 54 | <i>S,S</i> |

^a All reactions were carried out on 2 mmol reaction scale of olefin **1** (0.01 mmol), **2** (0.04 mmol), NMO (2.6 mmol) and [bmim][PF₆] (2 mL) in acetone-H₂O (v/v, 10:1, 20 mL). Olefins were added by a syringe pump for 10 h; ^b The ee values were determined by chiral HPLC analysis; ^c The absolute configurations of the diols were determined by comparison of their optical rotations with literature values; ^d Olefins were added in one portion.

a simple and practical approach to immobilization of both catalytic components (osmium and ligand). With 0.5 mol% of TentaGel-OsO₄ and 2.0 mol% ligand, the catalytic system could be recycled 10 times. The system is effective in the AD reactions of a range of olefins.

Experimental

General

TentaGel HL-Br and [bmim][PF₆] were purchased from Acros; (DHQ)₂PHAL, K₂OsO₄·2H₂O, OsO₄ and NMO were purchased from Aldrich; *trans*-stilbene, α -methylstyrene and *trans*- β -methylstyrene were purchased from Fluka.

IR spectra for samples as KBr pellets were recorded on a AVATAR 360 FTIR spectrometer. ¹H-NMR (400 MHz) and ¹³C-NMR (100 MHz) spectra were recorded on a Bruker AV-400 spectrometer (CDCl₃ or CD₃OD and TMS as internal standard). High performance liquid chromatography (HPLC) was performed by Agilent 1100 interfaced to a HP 71 series computer workstation with Daicel Chiralcel OJ-H, OD-H, OB-H chiral column. Optical rotations were obtained on a Perkin-Elmer 343 polarimeter.

Preparation and titration of **1**

TentaGel HL-Br (1g, 0.48 mmol) was added to a 25 mL round-bottom flask charged with 5 mL dry DMF and swelled for 2 h at room temperature. Then dry Et₃N (1.7 mL, 12 mmol) was added, and the mixture was stirred in 80 °C for 24 h. The resulted mixture was cooled to room temperature and filtered. The quaternized resin was washed with DMF and ethanol, then vacuum-

dried. The quaternized resin was stirred in saturated K_2OsO_4 aqueous solution (0.37 g, 1.0 mmol) for 24 h under nitrogen at room temperature. The mixture was filtered, then the solid was extracted with deionized water in Soxhlet apparatus and vacuum-dried to give TentaGel- OsO_4 .

The filtrate combined with extracted liquid was titrated by addition of saturated $NH_4Fe(SO_4)_2$ indicator (2 drops), $0.1\text{ mol}\cdot\text{L}^{-1}$ $AgNO_3$ (5 mL), followed by back-titration with $0.1\text{ mol}\cdot\text{L}^{-1}$ KSCN until the solution turned red. The load of osmium on the surface of TentaGel- OsO_4 is $0.075\text{ mmol}\cdot\text{g}^{-1}$ according to the consumed volume of KSCN (3.5 mL).

Preparation of ligand 2

Benzyl bromide (0.30 g, 1.8 mmol) in dry THF (12 mL) was added dropwise into a solution of $(DHQ)_2PHAL$ (2.0 g, 2.6 mmol) in dry THF (28 mL) under reflux. The mixture was further refluxed for 1.5 h, and the solvent was removed in vacuo, with the resulting residue purified by flash column chromatography ($CHCl_3/MeOH$ 20:1) to give 1.06 g of **2** as a light yellow solid (43% yield). 1H NMR (400 MHz, $CDCl_3$): δ 7.19–8.66 (m, 21H), 5.03–5.06 (m, 2H), 4.18 (s, 3H), 4.10 (s, 3H), 3.85 (m, 3H), 3.61 (m, 3H), 3.39 (m, 3H), 2.54–2.57 (m, 6H), 1.2–2.2 (m, 12H), 0.8 (m, 3H), 0.69 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 157.9, 157.5, 155.6, 147.3, 146.8, 144.6, 144.1, 139.0, 133.8, 131.7, 131.6, 130.6, 129.2, 127.1, 126.5, 126.1, 123.4, 122.9, 122.8, 122.4, 122.0, 119.6, 102.1, 101.5, 69.3, 66.7, 63.4, 61.7, 59.9, 58.4, 56.5, 55.8, 51.6, 42.9, 37.3, 36.0, 28.4, 27.7, 26.0, 25.5, 25.3, 24.3, 23.5, 22.2, 12.1, 11.3. HRMS (ESI): calcd for $[M-Br^{-1}]$: 869.4754, found 869.4749. $[\alpha]_D = +279.9$ (c 1, EtOH).

Asymmetric dihydroxylation of olefins

A 50 mL flask was charged with acetone- H_2O (10:1, v/v, 16 mL), $[bmim][PF_6]$ (2 mL), ligand **2** (38 mg, 0.04 mmol), TentaGel- OsO_4 **1** (133 mg, 0.01 mmol). After stirring for 10 min, NMO (352 mg, 2.6 mmol) was added. The olefin (2 mmol) dissolved in acetone- H_2O (10:1, v/v, 4 mL) was added by a syringe pump for 10 h at room temperature. After completion of the reaction, all the volatiles were removed under reduced pressure and *tert*-butyl methyl ether was added into the flask and the mixture was stirred for 5 min. The ether layer was separated and the procedure repeated (3×10 mL). The combined ether layer was washed with

water and brine, dried over anhydrous Na_2SO_4 . After removing the solvent, the crude product was purified by flash column chromatography on silica to give the diol. The ionic liquid layer containing TentaGel- OsO_4 **1** and ligand **2** was reused for the next reaction.

Recycling and re-use of

TentaGel- OsO_4 -ligand-ionic liquid

To the ionic liquid layer recovered from the above experiment was added acetone- H_2O (10:1, v/v, 16 mL) and NMO (352 mg, 2.6 mmol). The olefin (2 mmol) dissolved in acetone- H_2O (10:1, v/v, 4 mL) was added by a syringe pump for 10 h at room temperature. After completion of the reaction, the procedure for workup is the same as above.

Acknowledgments

We thank National Natural Science Foundation of China (NSFC) for financial support. Nos. 20372083 20302014.

References

- H. C. Kolb, M. S. Vannieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483–2547.
- C. E. Song, S.-g. Lee, *Chem. Rev.* **2002**, *102*, 3495–3524.
- S. Kobayashi, T. Ishida, R. Akiyama, *Org. Lett.* **2001**, *3*, 2649–2652.
- B. M. Choudary, N. S. Chowdari, K. Jyothi, M. L. Kantam, *J. Am. Chem. Soc.* **2002**, *124*, 5341–5349.
- J. W. Yang, H. Han, E. J. Roh, S.-g. Lee, C. E. Song, *Org. Lett.* **2002**, *4*, 4685–4688.
- C. H. Jo, S.-H. Han, J. W. Yang, E. J. Roh, U.-S. Shin, C. E. Song, *Chem. Commun.* **2003**, *11*, 1312–1314.
- S. Chandrasekhar, Ch. Narsihmulu, S. Shameem Sultana, N. Ramakrishna Reddy, *Chem. Commun.* **2003**, *14*, 1716.
- C. E. Song, D.-u. Jung, E. J. Roh, S.-g. Lee, D. Y. Chi, *Chem. Commun.* **2002**, *24*, 3038–3040.
- Q. B. Liu, Z. H. Zhang, F. V. Rantwijk, R. A. Sheldon, *Journal of Molecular Catalysis A: Chemical* **2004**, *224*, 213–216.
- L. C. Branco, C. A. M. Afonso, *J. Org. Chem.* **2004**, *69*, 4381–4389.
- L. C. Branco, A. Serbanovic, M. N. Ponte, C. A. M. Afonso, *Chem. Commun.* **2005**, *1*, 107–110.
- R. Jiang, Y. Q. Kuang, X. L. Sun, S. Y. Zhang, *Tetrahedron: Asymmetry* **2004**, *15*, 743–746.
- K. B. Sharpless, W. Amberg, Y. L. Bennani, G. A. Crispino, J. Hartung, K. S. Jeong, *J. Org. Chem.* **1992**, *57*, 2768–2771.

Povzetek

Na osnovi TentaGel- OsO_4 **1**, monokvaterniziranega bis-cinkona alkaloida **2** kot kiralnega liganda in ionske tekočine $[bmim]PF_6$ smo razvili sistem za katalitsko asimetrično dihidrosilacijo olefinov. Tako osmij, kot tudi kiralni ligand je možno učinkovito reciklirati do desetkrat. Sistem je učinkovit tudi pri ostalih reakcijah adicije na alkene.