Catalytic Asymmetric Dihydroxylation of Olefins Using a Recoverable and Reusable Polymer-Supported Osmium Catalyst

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Received August 26, 1999

Osmium-catalyzed asymmetric dihydroxylation of olefins provides one of the most efficient methods for the preparation of chiral diols.[1] Although the reactions could be applied to the synthesis of pharmaceuticals, fine chemicals, etc., the high cost of osmium and ligands as well as the high toxicity of osmium catalysts, which may contaminate the obtained products, obstruct their use in industry. To address this issue, soluble and insoluble polymer-supported ligands have been developed by several groups,[2,3] but complete recovery and reuse of the osmium have not yet been accomplished.[4,5] In 1998, we reported microencapsulated osmium tetroxide on the basis of polystyrene (PS-MC OsO_4) as a polymer-supported osmium catalyst, which first achieved complete recovery and reuse of the osmium component in achiral oxidations.[6] In this paper, we report recoverable and reusable osmium-catalyzed asymmetric dihydroxylation of olefins based on the microencapsulation technique.

In our initial studies, we intended to apply PS-MC OsO_4 to the asymmetric oxidation. After many trials, however, the yields and selectivities as well as recovery of the catalyst were not satisfactory, and we decided to change the polymer support. Several polymer supports and preparative conditions were examined, and finally the desired osmium catalyst for the catalytic asymmetric dihydroxylation of olefins was prepared using an acryronitrile−butadiene−polystyrene (ABS) polymer as follows:[7] ABS polymer[8] (1.000 g) was dissolved in tetrahydrofuran (20 mL) at 70−80 °C, and to this solution was added OsO_4 (0.200 g) as a core. The mixture was stirred for 1 h at this temperature and then slowly cooled to 0 °C. Coacervates (phase separation) were found to envelop the core dispersed in the medium, and methanol (30 mL) was added to harden the capsule walls. After 8 h, the capsules were washed with methanol several times and dried at room temperature for 24 h. Unencapsulated OsO_4 was recovered from the washings.[9]

ABS-based OsO_4 (ABS-MC OsO_4) thus prepared was first tested in achiral dihydroxylation of olefins. In the presence of ABS-MC OsO_4 (5 mol %), styrene was treated with *N*-methylmorpholine *N*-oxide (NMO) in H_2O−acetone−acetonitrile (1:1:1). Styrene was not a good substrate in the dihydroxylation using PS-MC OsO_4 because styrene dissolved PS-MC OsO_4. After 12 h at room temperature, methanol was added and the mixture was stirred for 10 min. After filtration, the corresponding diol was obtained in 93% yield and ABS-MC OsO_4 was recovered quantitatively. The recovered catalyst was used in the second, third, and fourth runs, and no loss of activity was observed (93, 90, 87, and 89% yields, respectively, and ABS-MC OsO_4 was recovered quantitatively in all cases). Several other olefins were then examined, and the results are summarized in Table 1. Various olefins including cyclic and acyclic, terminal, mono-, di-, tri-, and tetra-substituted olefins worked well to give the corresponding diols in high yields.

Encouraged by these promising results, we then performed asymmetric dihydroxylation of olefins according to the Sharpless procedure.[10] We chose *trans*-methylstyrene as a model, and several reaction conditions were examined. When 1,4-bis(9-*O*-dihydroquinidinyl)phthalazine ($(DHQD)_2PHAL$) was used as a chiral source and *trans*-methylstyrene was slowly added over 24 h to a mixture of ABS-MC OsO_4, ($(DHQD)_2PHAL$ (5 mol % each), and NMO, the desired diol was obtained in 88% yield with 84% ee.[11] The osmium catalyst was recovered quantitatively by simple filtration, and the chiral ligand was also recovered by simple acid/base extraction (>95% recovery).[12] The recovered catalyst and the chiral source were reused several times, and no loss of activity was observed even after the fifth use (Table 2).[13] This system was applied to other olefins and the results are

(1) (a) Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: Weinheim, 1993. (b) Kolb, H. C.; Van Nieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483. (c) Poli, G.; Scolastico, C. In *Stereoselective Synthesis*; Helmchen, G.; Hoffmann, R. W.; Mulzer, J.; Schaumann, E., Eds.; Thieme: Stuttgart, 1996; p 4547.

(2) Review: (a) Bolm, C.; Gerlach, A. *Eur. J. Org. Chem.* **1998**, *21*, 1. (b) Salvadori, P.; Pini, D.; Petri, A. *Synlett* **1999**, 1181. (c) Gravert, D. J.; Janda, K. D. *Chem. Rev.* **1997**, *97*, 489.

(3) (a) Kim, B. M.; Sharpless, K. B. *Tetrahedron Lett.* **1990**, *31*, 3003. (b) Pini, D.; Petri, A.; Nardi, A.; Rosini, C.; Salvadori, P. *Tetrahedron Lett.* **1991**, *32*, 5175. (c) Lohray, B. B.; Thomas, A.; Chittari, P.; Ahuja, J. R.; Dhal, P. K. *Tetrahedron Lett.* **1992**, *33*, 5453. (d) Pini, D.; Petri, A.; Salvadori, P. *Tetrahedron*: *Asym.* **1993**, *4*, 2351. (e) Lohray, B. B.; Nandanan, E.; Bhushan, V. *Tetrahedron Lett.* **1994**, *35*, 6559. (f) Pini, D.; Petri, A.; Salvadori, P. *Tetrahedron* **1994**, *50*, 11321. (g) Song, C. E.; Roh, E. J.; Lee, S. G.; Kim, I. O. *Tetrahedron*: *Asym.* **1995**, *6*, 2687. (h) Petri, A.; Pini, D.; Rapaccini, S.; Salvadori, P. *Chirality* **1995**, *7*, 580. (i) Pini, D.; Petri, A.; Salvadori, P. *Tetrahedron Lett.* **1995**, *36*, 1549. (j) Han, H.; Janda, K. D. *J. Am. Chem. Soc.* **1996**, *118*, 7632. (k) Song, C. E.; Yang, J. W.; Ha, H. J.; Lee, S. G. *Tetrahedron*: *Asym.* **1996**, *7*, 645. (l) Lohray, B. B.; Nandanan, E.; Bhushan, V. *Tetrahedron*: *Asym.* **1996**, *7*, 2805. (m) Salvadori, P.; Pini, D.; Petri, A. *J. Am. Chem. Soc.* **1997**, *119*, 6929. (n) Han, H.; Janda, K. D. *Tetrahedron Lett.* **1997**, *38*, 1527. (o) Nandanan, E.; Sudalai, A.; Ravindranathan, T. *Tetrahedron Lett.* **1997**, *38*, 2577. (p) Song, C. E.; Yang, J. W.; Ha, H. J.; Lee, *Tetrahedron*: *Asym.* **1997**, *8*, 841. (q) Bolm, C.; Maischak, A.; Gerlach, A. *J. Chem. Soc., Chem. Commun.* **1997**, 2353. (r) Han, H.; Janda, K. D. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1731. (s) Bolm, C.; Gerlach, A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 741.

(4) Since amine ligands coordinate to osmium under equilibrium conditions, recovery of the osmium using polymer-supported ligands is generally difficult.

(5) For achiral polymer-supported osmium tetroxide see: (a) Cainelli, G.; Contento, M.; Manescalahi, F.; Plessi, L. *Synthesis* **1989**, 45. (b) Herrmann, W. A.; Kratzer, R. M.; Blumel, J.; Friedrich, H. B.; Fischer, R. W.; Apperley, D. C.; Mink, J.; Berkesi, O. *J. Mol. Catal., A* **1997**, *120*, 197.

(6) Nagayama, S.; Endo, M.; Kobayashi, S. *J. Org. Chem.* **1998**, *63*, 6094.

(7) This is a standard procedure for the preparation of microcapsules. (a) Donbrow, M. *Microcapsules and Nanoparticles in Medicine and Pharmacy*; CRC Press: Boca Raton, 1992. Microcapsules have been used for coating and isolating substances until such time as their activity is needed, and their application to medicine and pharmacy has been extensively studied. We first applied this technique for immobilizing a catalyst onto a polymer. (b) Kobayashi, S.; Nagayama, S. *J. Am. Chem. Soc.* **1998**, *120*, 2985.

(8) Stylac 200 (Asahi Chemical).

(9) Ca. 10% of OsO_4 was washed out at this stage. Details are shown in Supporting Information.

(10) Wai, J. S. M.; Markó, I.; Svendsen, J. S.; Finn, M. G.; Jacobsen, E. N.; Sharpless, K. B. *J. Am. Chem. Soc.* **1989**, *111*, 1123.

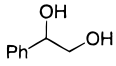
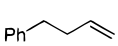
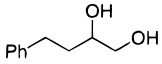
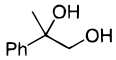
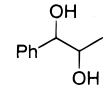
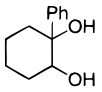
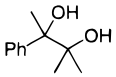
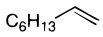
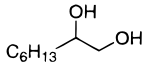
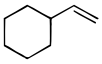
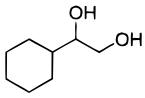
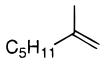
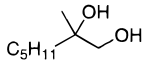
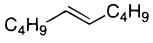
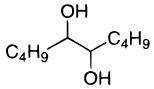
(11) A typical experimental procedure is as follows: ABS-MC OsO_4 (76.7 mg, 5 mol %), ($(DHQD)_2PHAL$ (21.5 mg, 5 mol %), and *N*-methylmorpholine *N*-oxide (NMO, 0.72 mmol) were combined in H_2O−acetone−acetonitrile (1:1:1, 3.5 mL) at room temperature. To this mixture was added an olefin (0.55 mmol) slowly for 24 h. Methanol (10 mL) was added, and the mixture was stirred for 10 min. ABS-MC OsO_4 was separated by filtration. After washing the solution with methanol, combined filtrates were concentrated under reduced pressure. After a usual workup, the crude material was chromatographed on silica gel to afford the corresponding cis-diol.

(12) Details are described in Supporting Information.

(13) Higher enantioselectivities were obtained in the 2nd, 3rd, 4th, and 5th runs compared to the 1st run. We do not have a clear explanation for these results, but the following control experiment and the standard Sharpless conditions that require an excess of a chiral ligand to osmium may suggest a solution. The control experiment we performed was oxidation of *trans*-methylstyrene. *trans*-Methylstyrene was slowly added over 24 h to a mixture of fresh ABS-MC OsO_4 (5 mol %), ($(DHQD)_2PHAL$ (10 mol %), and NMO, and the desired diol was obtained in 91% ee.

10.1021/ja993099m CCC: $18.00
Published on Web 11/18/1999

Table 1. Achiral Dihydroxylation of Olefins Using ABS-MC OsO_4[a]

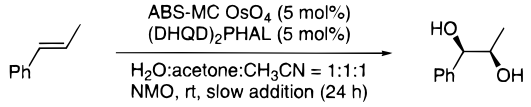
Olefin	Product	Yield (%)
		94
		82
		quant
		95
		87
		83[b]
		73
		74
		82
		77

[a] All reactions were carried out using MC OsO_4 (5 mol %) and NMO in H_2O−acetone−CH_3CN (1/1/1) at room temperature for 12 h. [b] Carried out at 60 °C.

summarized in Table 3. In most cases, the desired diols were obtained in high yields with high enantiomeric excesses.[14,15]

Finally, a 100 mmol-scale experiment was demonstrated. To a mixture of ABS-MC OsO_4 (1.0 mmol, 1.0 mol %), $(DHQD)_2$-PHAL (2.0 mmol, 2.0 mol %), and NMO (130 mmol)[15] was slowly added *trans*-methylstyrene (100 mmol) over 24 h. The desired diol was obtained in 91% yield with 89% ee, and >95% of ABS-MC OsO_4 and the chiral ligand was recovered.

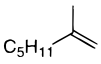
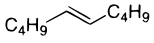
Table 2. Reuse of ABS-MC OsO_4



run	yield (%)	ee (%)	recovery[a,b]
1	88	84	quant
2	75	95	quant
3	97	94	quant
4	81	96	quant
5	88	95	quant

[a] Recovery of ABS-MC OsO_4. [b] Recovery of $(DHQD)_2PHAL$ = >95%.

Table 3. Asymmetric Dihydroxylation Using ABS-MC OsO_4

Olefin	ABS-MC OsO_4 /mol%	Chiral Ligand /mol%	Yield /%	ee /%
	5	10	75	91
	2.5	5	90	92
	1	2	97	86[a]
	5	5	98	78
	5	5	64	86
	5	5	90	60
	2.5	5	85	63
	5	5	36	85

[a] 20 mmol-scale experiment was performed.

In summary, we have developed a recoverable and reusable polymer-supported osmium catalyst for asymmetric dihydroxylation of olefins. The catalyst was readily prepared from OsO_4 and an ABS polymer based on a microencapsulation technique. It is noted that complete recovery of the toxic osmium catalyst has been accomplished.

Acknowledgment. This work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, Japan. S.N. thanks the JSPS fellowship for Japanese Junior Scientists.

Supporting Information Available: Experimental details and ^1H and ^{13}C NMR data of the products (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA993099M

(14) The yields and selectivities obtained are comparable to those obtained using OsO_4. For example, 73% yield and 95% ee were obtained in the oxidation of *trans*-methylstyrene using 5 mol % of OsO_4, 10 mol % of $(DHQD)_2PHAL$, and NMO (slow addition, 24 h).

(15) Our preliminary experiments revealed that the use of ABS-MC OsO_4, $(DHQD)_2PHAL$, and potassium ferricyanide[17] without slow addition also worked well to afford the desired diols in high yields with high selectivities. Details will be reported in due course.

(16) Quite recently, Bäckvall et al. has developed osmium-catalyzed dihydrozylation of olefins using a catalytic amount of NMO. Bergstad, K.; Piet, J. J. N.; Bäckvall, J.-E. *J. Org. Chem.* **1999**, *64*, 2545.

(17) Sharpless, K. B.; Amberg, W.; Beller, M.; Chen, H.; Hartung, J.; Kawanami, Y.; Lübben, D.; Manoury, E.; Ogino, Y.; Shibata, T.; Ukita, T. *J. Org. Chem.* **1991**, *56*, 4585.