Microencapsulated Osmium Tetroxide-Catalyzed Asymmetric Dihydroxylation of Olefins in Water without Using Organic Cosolvents

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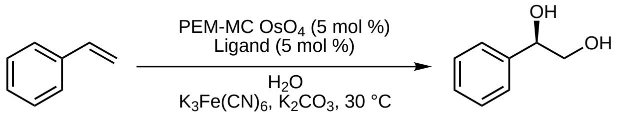
Abstract: The asymmetric dihydroxylation of olefin using phenoxyethoxymethyl-polystyrene (PEM)-based microencapsulated osmium tetroxide (PEM-MC OsO_4) proceeded smoothly in water as the sole solvent. The catalyst was recovered quantitatively by simple filtration and reused several times without loss of activity.

Keywords: asymmetric dihydroxylation; microencapsulation; osmium tetroxide; polymer-supported

Organic reactions in water without the use of any harmful organic solvents are now of great interest in organic synthesis, because water is a safe, economical, and environmentally benign solvent.[1] We have recently reported that surfactant-type Lewis or Brønsted acids effectively catalyze carbon-carbon bond-forming reactions such as Mukaiyama aldol reactions,[2] Mannich-type reactions,[3] etc.,[4] in water. In these reactions, hydrophobic emulsion particles or droplets, which are essential for efficient catalysis, are formed from small amounts of these catalysts and hydrophobic substrates.

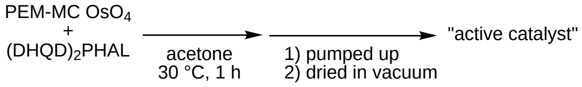
On the other hand, the catalytic asymmetric dihydroxylation of olefins using a catalytic amount of osmium tetroxide in the presence of a chiral ligand allows access to a wide variety of enantiomerically pure vicinal diols.[5] In 1992, Sharpless et al. reported a catalytic system based on a biscinchona alkaloid such as 1,4-bis(9-*O*-dihydroquinidinyl)phthalazine [$(DHQD)_2$-PHAL].[6] While the system has received a great deal of interest due to a broad scope of substances available and high enantioselectivities attained, the toxicity of OsO_4 has tended to suppress industrial application of this useful reaction. In 1998, to address this issue, we developed polystyrene-based microencapsulated OsO_4 to attain complete recovery and reuse of OsO_4 without leaching.[7] We have also developed a new type of microencapsulated osmium tetroxide based on poly(phenoxyethoxymethylstyrene-*co*-styrene) (PEM-MC OsO_4), and have achieved asymmetric dihydroxylation of olefins in H_2O-acetone (1:1) with $K_3Fe(CN)_6$ as a cooxidant.[8,9] In this reaction, it was assumed that the reaction proceeded on the surface-area of PEM-MC OsO_4 and that the hydrophilic part of the PEM polymer acted as a surfactant. We then decided to examine the PEM-MC OsO_4-catalyzed asymmetric dihydroxylation of olefins in water without using any organic cosolvents.

Table 1. Dihydroxylation of olefins in water.



Entry	Ligand	Time [h]	Yield (%)	ee [%]	Recovery [%][a]
1	NMM	6	45	–	quant
2	NMM	24	65	–	quant
3	$(DHQD)_2$PHAL	24	43	18	quant
4[b]	$(DHQD)_2$PHAL	24	65	38	quant

[a] Recovery of the catalyst.



Scheme 1. Preparation of "active catalyst".

First, we carried out dihydroxylation of styrene (0.55 mmol) in water (5 mL) using PEM-MC OsO_4 (5 mol %), *N*-methylmorphorine (NMM, 5 mol %), $K_3Fe(CN)_6$, and K_2CO_3 (3.0 equivs.). The reaction proceeded in water to afford the corresponding diol in low yield, which could be improved by prolonging the reaction time from 6 to 24 hours (Table 1, entries 1and 2). We next applied the reaction to asymmetric dihydroxylation using $(DHQD)_2$PHAL as a ligand. However, the desired product was obtained in low yield with low enantiomeric excess, presumably because the ligand scarcely dissolved in H_2O (entry 3). To address this solubility issue, we prepared an active catalyst by combining PEM-MC OsO_4 and $(DHQD)_2$PHAL in

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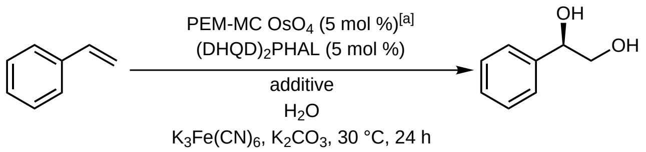
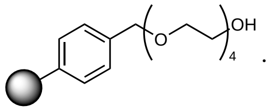
Table 2. Effect of additives.



Entry	Additive	Yield [%]	ee [%]
1	none	65	38
2	polystyrene-resin	trace	–
3	PEG-resin[b]	33	55
4	MS 4 Å	42	53
5	$CH_3(CH_2)_{11}SO_3Na$ (10 mol %)	67	41
6	$CH_3(CH_2)_{11}N(CH_3)_3Br$ (10 mol %)	12	40
7	$CH_3(CH_2)_{11}N(CH_3)_2[(CH_2)_2SO_3]$ **1** (10 mol %)	80	74

[a] PEM-MC OsO_4 and the ligand were combined before the dihydroxylation (see Scheme 1).

[b] PEG-resin =  .

acetone first, followed by removal of the solvent. The use of this active catalyst slightly increased the yield and selectivity (entry 4).

To further improve the chemical yields and enantiomeric excesses, several kinds of additives were tested (Table 2). It was observed during the reaction that the catalyst changed from a powder to lumps, and that the active surface area of the catalyst decreased gradually. Therefore, several types of powders were added to disperse the osmium catalyst; however, no improvement was observed (entries 2–4). Next, we added cationic, anionic, or zwitter-type surfactants to activate the surface of the catalyst (entries 5–7). As a result, it was exciting to find that the chemical yield and ee were improved significantly when a zwitter-type surfactant was added (entry 7).

We further examined several surfactants, and the results are summarized in Table 3. When the zwitter-type surfactant **1** was used, significant leaching of the osmium component was observed,[10] presumably because the ammonium part of the surfactant strongly coordinated to the osmium atom (Table 3, entry 1). Based on this consideration, we examined non-ionic surfactants. It was found that surfactants containing polyethylene glycol parts were more effective, and that Triton® X-405 suppressed the leaching of the osmium component effectively (entry 7). At this stage, it was also observed that the pre-preparation step of the osmium-ligand complex was not required to improve the chemical yield and enantiomeric excess. The ligand was then directly added to the reaction mixture. The desired product was obtained in better yield and no deactivation of the catalyst was observed even after the third use (entry 8). To suppress the leaching completely, the reaction mixture was neutralized by aqueous H_2SO_4 to convert the osmium species from osmate(VIII) to osmium(VIII) entirely. As a result, no osmium leaching occurred, and high yields and selectivity were retained during the three reuses of the catalyst (entry 9). It was also found that the reaction proceeded smoothly even using only 3 mol % of Triton® X-405 (entry 10).

This system was applied to other olefins (see Experimental Section), and the results are summarized in Table 4. In most cases, the desired products were obtained in good yields using water as the sole solvent. When *trans*-β-methylstyrene was used, the desired *cis*-diol was obtained in high enantiomeric excess. It should be noted that the reaction system did not require the addition of excess amounts of the cooxidant and the base separately,[8] and that the catalyst was separated from the reaction mixture easily by simple filtration without leaching of the osmium component.

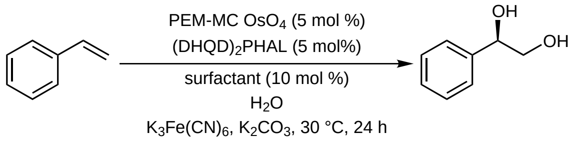
In summary, we have found that asymmetric dihydroxylation of olefins proceeds smoothly in water with catalytic amounts of PEM-MC OsO_4, a chiral ligand, and Triton® X-405. It is noteworthy that the reaction proceeds smoothly to afford the desired diols in high yields and selectivity using water as the sole solvent. PEM-MC OsO_4 can be easily separated from the reaction mixture by simple filtration, recovered quantitatively, and reused without loss of activity.

Experimental Section

Typical Procedure for the Catalytic Asymmetric Dihydroxylation of Olefins

Olefin (0.55 mmol), PEM-MC OsO_4 (46.3 mg, 5 mol %), $(DHQD)_2PHAL$ (21.5 mg, 5 mol %), $K_3Fe(CN)_6$ (543.3 mg,

Table 3. Effect of several types of surfactants.



Entry	Surfactant	Yield [%]	ee [%]	Leaching of Os [%]
1	**1**	82	68	26.4
2	Span® #20	77	54	8.0
3	Tween® #20	quant	77	3.5
4	Triton® WR-1339[a]	91	76	2.7
5	Triton® CF-10[a]	84	76	7.4
6	Triton® X-100	84	75	5.3
7	Triton® X-405	68	75	1.6
8[b]	Triton® X-405	80, 86,[e] 83[f]	74, 73[e], 73[f]	1.8, 1.6,[e] 1.5[f]
9[b, c]	Triton® X-405	86, 82,[e] 83[f]	74, 76[e], 75[f]	n.d, n.d,[e] n.d[f]
10[b, c]	Triton® X-405[d]	76, 74,[e] 76[f]	74, 74[e], 70[f]	n.d, n.d,[e] n.d[f]

n.d. = not detected

[a] 2 mg/mL surfactant was used.

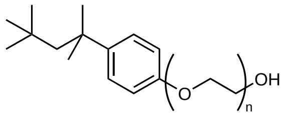
[b] The ligand was directly added.

[c] The reaction mixture was neutralized by aqueous H_2SO_4 (2 N) to quench the reaction.

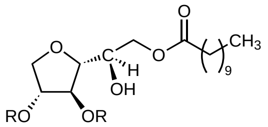
[d] 3 mol % of Triton® X-405 was used.

[e] 2nd run.

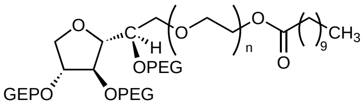
[f] 3rd run.



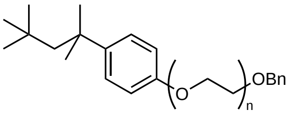
Triton® X-100 (n = ca. 8)
Triton® X-405 (n = ca. 39)



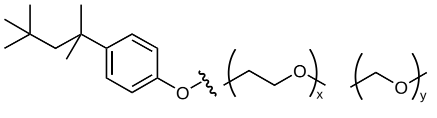
Span® #20



Tween® #20



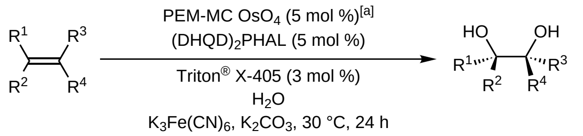
Triton® CF-10

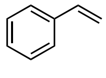
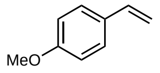
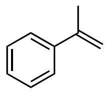
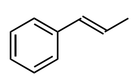
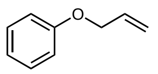
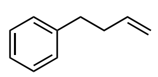


Triton® WR-1339

3.0 equivs.), K_2CO_3 (228.0 mg, 3.0 equivs.), and Triton® X-405 (108.3 mg, 3 mol %) were combined in H_2O at 30 °C, and the heterogeneous slurry was stirred at 30 °C for 24 h. Aqueous H_2SO_4 (2 N, 1.1 mL) was added slowly, and the mixture was further stirred for 10 min. Ethanol (10 mL) was added, and the mixture was stirred for 1 min. PEM-MC OsO_4 was separated by filtration and reused. The crude product was purified by chromatography on silica gel to afford the desired *cis*-diol. The optical purity of the product was determined by HPLC analysis (Table 4, entries 1–5) or ^{1}H NMR analysis of the di-MTPA ester of the corresponding 1,2-diol (Table 4, entry 6).

Table 4. Asymmetric dihydroxylation of olefins using water as a solvent.



Entry	Substrate	Yield [%]	ee [%][b]
1		76	74
2		68	89
3[c]		85	80
4		76	92
5		79	55
6		76	66[d]

[a] Leaching of the osmium component was not observed in each reaction.

[b] ees were determined by chiral HPLC analysis.

[c] Triton® X-405 (5 mol %) was used.

[d] ee value obtained from ^1H NMR analysis of the di-MTPA ester of the corresponding 1,2-diol.

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[10] Confirmed by fluorescent X-ray analysis.