A Novel Microencapsulated Osmium Catalyst Using Cross-Linked Polystyrene as an Efficient Catalyst for Asymmetric Dihydroxylation of Olefins in Water

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Abstract: A novel microencapsulated osmium catalyst (PSresin-MC Os) was developed using cross-linked polystyrene. The concept of this method may go beyond that of microencapsulation. The catalyst was successfully used in asymmetric dihydroxylation in water, and it was recovered quantitatively by simple filtration and reused several times without loss of activity. The shape of the catalyst was maintained even after several uses. Moreover, no leaching of the Os component was detected.

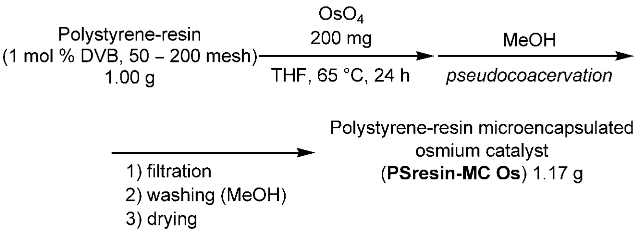
Keywords: asymmetric dihydroxylation; microencapsulation; osmium tetroxide; polymer-supported

Osmium tetroxide (OsO_4) is among the most effective catalysts for the dihydroxylation of olefins.[1] In particular, catalytic asymmetric dihydroxylation of olefins using a catalytic amount of OsO_4 with a chiral ligand is often used for the synthesis of biologically important natural products and others in the laboratory.[2] However, since OsO_4 is expensive, highly toxic, and is easily sublimed, its use for the synthesis of medicines and fine chemicals on an industrial scale has been limited. In 1998, we reported on a linear, polystyrene-based microencapsulated osmium (PS-MC Os), with which complete recovery and reuse of the osmium catalyst without leaching of the osmium component were attained.[3,4] After that, we also developed a new type of microencapsulated osmium catalyst based on poly(phenoxyethoxymethylstyrene-*co*-styrene) (PEM-MC Os), and achieved a more practical asymmetric dihydroxylation of olefins in H_2O-acetone (1/1) with $K_3Fe(CN)_6$ as a co-oxidant.[5–7] While these catalysts have several advantages over OsO_4, they were found to be soluble in some solvents because they were prepared based on liner polymers. When the catalysts dissolved even partially, leaching of the osmium component occurred. Moreover, the shapes of the catalysts were sometimes changed to lumps, which decreased their surface area, thus lowering the catalytic activity. To address these issues, we decided to prepare microencapsulated catalysts using *cross-linked* polystyrene. In this paper, we describe the use of cross-linked polymers for the preparation of a microencapsulated osmium catalyst.[8] The concept of this method may go beyond that of microencapsulation.[9]

The use of cross-linked polymers is quite unusual because microcapsules are generally formed from linear polymers, and indeed, only few successful examples to prepare microcapsules using cross-linked polymers were reported before this work.[8] Contrary to this, we thought that microcapsules might be formed even from cross-linked polymers if the polymers were flexible and swollen well. A polystrene-1% divinylbenzene (DVB) cross-linked polymer (polystyrene-resin) was prepared using suspension polymerization. Polystyrene-resin (1.00 g) thus prepared was combined with OsO_4 (200 mg) in THF, and the mixture was stirred for 24 h at 65 °C. After cooling, MeOH was added, and the resulting resin was filtered, washed with MeOH, and dried. Interestingly, OsO_4 (170 mg) was immobilized in the polystyrene-resin according to this method (Scheme 1).

The polystyrene-resin based, microencapsulated osmium catalyst (PSresin-MC Os) thus prepared was then observed using the scanning electron microscope (SEM) and transmission electron microscope (TEM) (Figure 1). It was exciting to find that very small capsules (10–20 nm) were formed on the particles of the PSresin beads.

We assumed that these small capsules included Os, and indeed, the Os energy-dispersive X-ray (EDX)



Scheme 1. Preparation of the polystyrene-resin microencapsulated osmium catalyst.

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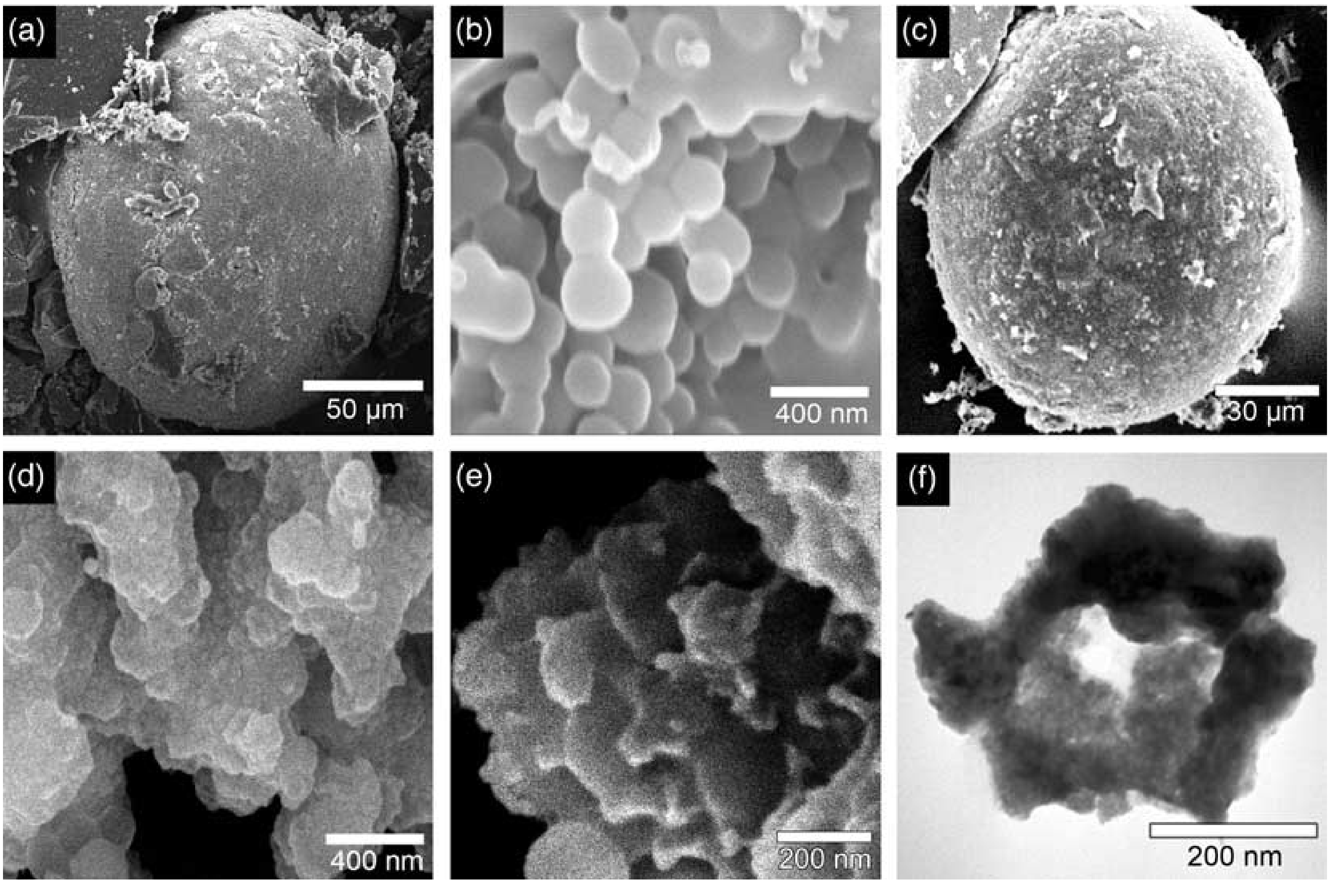


Figure 1. SEM and TEM images of the polystyrene-resin and PSresin-MC Os; (**a**) the polystyrene-resin beads, (**b**) the polystyrene-resin particles inside the beads, (**c**) the PSresin-MC Os beads, (**d**) and (**e**) the PSresin-MC Os particles inside the beads, (**f**) TEM image of PSresin-MC Os.

map showed that the capsules were filled with Os (Figure 2). Thus, the Os component was formed on the particles of the PSresin beads.

We then examined the catalytic activity of PSresin-MC Os in the asymmetric dihydroxylation of styrene. It was found that the asymmetric oxidation proceeded smoothly in water using PSresin-MC Os, whose activity was comparable to that of PEM-MC Os.[5b] Moreover, it was noted that leaching of the Os component was not detected by fluorescent X-ray analysis even using cross-linked polystyrene. The effect of the ratios of DVB in polystyrene-resins on reactivity and selectivity was also examined (Table 1). When a polystrene-0.5% DVB cross-linked polymer was used as polymer backbone, a slightly higher activity of the catalyst was noted, but a small amount of the leaching of the Os component was observed (entry 1). We assume that the polymer was physically weaker and was partially destroyed, which led to the Os leaching. On the other hand, when the amount of DVB was increased to 2% and 5%, the catalytic activity was decreased, especially in the reused catalysts. It was observed that these catalysts did not swell well with the substrate, and this might lead to lower activity of the catalyst.

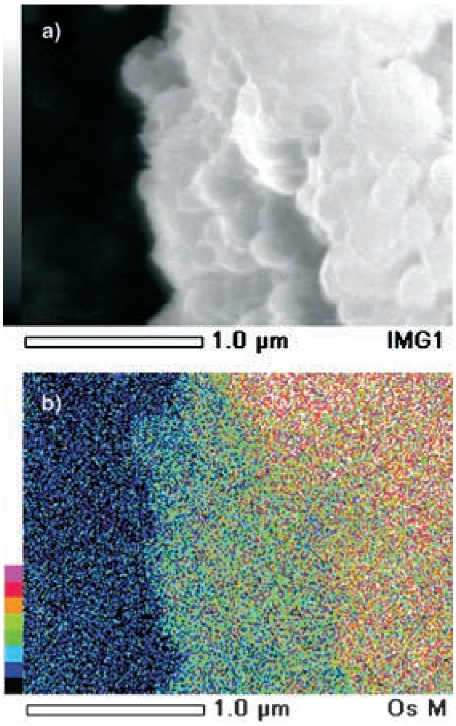
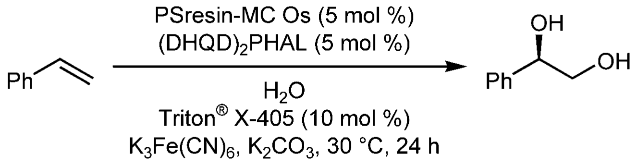


Figure 2. Os EDX mapping image of PSresin-MC Os (the upper panel is an SEM image about the same point of the mapping).

Table 1. Effect of the ratio of divinylbenzene.



Entry	DVB [mol %][a]	Yield [%] (ee [%]) {Os leaching [%]}[b]				
		1st run	2nd run	3rd run	4th run	5th run
1	0.5	92 (79) {1.2}	83 (77) {n.d.}	95 (76) {n.d.}	87 (76) {n.d.}	96 (73) {0.9}
2	1.0	81 (78) {n.d.}	84 (76) {n.d.}	78 (77) {n.d.}	86 (74) {n.d.}	85 (72) {n.d.}
3	2.0	78 (77) {n.d.}	72 (74) {n.d.}	73 (74) {n.d.}	79 (69) {n.d.}	67 (69) {n.d.}
4	5.0	84 (76) {n.d.}	41 (68) {1.1}	48 (72) {n.d.}	–	–

[a] The ratio of DVB in the polystyrene-resin.

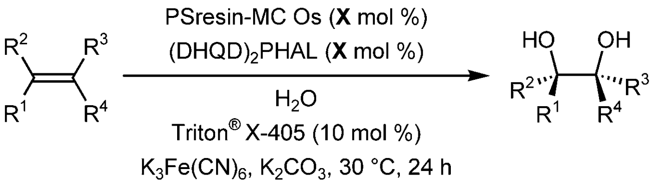
[b] The leaching of the osmium component was determined by fluorescent X-ray analysis (a percentage of the original osmium content of the catalyst).
n.d. = not detected (<0.8%).

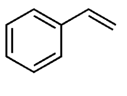
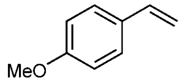
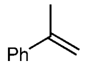
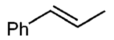
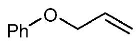
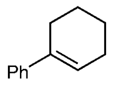
By using PSresin-MC Os containing a polystyrene-1% DVB cross-linked polymer, we tested other substrates, and the results are summarized in Table 2. When the amount of the catalyst was decreased to 0.2 mol %, the reaction also proceeded smoothly to afford the desired adduct in high yield with high enantioselectivity (entry 4). Terminal, *trans*, and trisubstituted olefins worked well to provide the corresponding dihydroxylated products in high yields with good to excellent enantioselectivities. In the reaction of 1-phenyl-1-cyclohexene, the yield and enantiomeric excess were much improved using PSresin-MC Os compared with those obtained using PEM-MC Os (entry 11).[5] In all cases, the catalysts were recovered quantitatively, and reused several times without loss of activity. It is noteworthy that the shape of the catalyst was retained without forming lumps even after several uses. In addition, no leaching of the Os component was detected by fluorescence X-ray analysis in all cases.

In summary, we have developed a novel microencapsulated Os catalyst using cross-linked polystyrene. The concept of this method may go beyond that of microencapsulation. The salient features of this new catalyst are as follows.

(1) A microencapsulated catalyst is prepared using a cross-linked polymer. The catalyst is not soluble in many solvents.
(2) The catalyst is successfully used in asymmetric dihydroxylation.
(3) The catalyst is recovered quantitatively by simple filtration and reused several times without loss of activity.
(4) The shape of the catalyst is maintained even after several uses.
(5) No leaching of the Os component is detected.
(6) Water is used as the sole solvent.

Table 2. Asymmetric dihydroxylation of olefins using PSresin-MC Os.[a]



Entry	X	Substrate	Yield [%]	ee [%][b]
1	5		81	78
2	1		92	75
3	0.5		82	76
4	0.2		84	73
5	0.05		36	68
6	5		85	89
7	5		90	79
8	5		84	94
9	5		99	55
10[c]	5		91	61
11	5		82 (26)[d]	94 (86)[d]

[a] The leaching of the osmium component was not observed by fluorescent X-ray analysis in all cases.

[b] The enantiomeric excess was determined by HPLC analysis.

[c] $(DHQD)_2AQN$ was used as a ligand.

[d] PEM-MC Os was used instead of PSresin-MC Os.

In addition to these characteristics, since it is expected that several other metal catalysts could be immobilized using the same method, this work should expand the possibility of providing microencapsulated catalysts with wide uses in organic synthesis.

Experimental Section

Preparation of Polystyrene-Resin (PS-resin)

Styrene (50.00 g, 480 mmol), divinylbenzene (washed with 1 N NaOH, 80 wt %; 781.0 mg, 4.8 mmol), polyvinyl alcohol (n= *ca.* 2000; 500.0 mg), and 2,2′-azobis(isobutyronitrile) (500.0 mg, 3.04 mmol) were combined in H_2O-toluene (3/1; 120 mL), and the two-phase mixture was stirred vigorously using a mechanical stirrer at 90 °C for 12 h. After cooling to room temperature, an excess amount of tetrahydrofuran (THF, 200 mL) was added and the mixture was further stirred for 1 h at the same temperature. The heterogeneous mixture was filtered and the residue was washed with THF. The obtained polymer was swollen with THF and dropped into a large excess amount of methanol, and this procedure was repeated twice. The washed polymer was dried under reduced pressure and divided into 50–200 mesh sieves to afford the desired polystyrene-resin; yield: 2.96 g (29%).

Preparation of PS-resin Microencapsulated Osmium Catalyst

The prepared polystyrene-resin (1.00 g) was stirred in THF (20 mL) at 65 °C for 1 h, and then OsO_4 (0.20 g) was added. The suspension was stirred for 24 h at 65 °C, and then methanol was added slowly at 0 °C. The mixture was allowed to stand at room temperature for 12 h, and the catalyst was then washed with methanol (100 mL). PSresin-MC Os (1.17 g, Os loading: 0.6 mmol/g) was obtained after drying at room temperature for 48 h. The loading of the osmium component was determined by X-ray fluorescence analysis of the filtrate.

Typical Experimental Procedure for the Catalytic Asymmetric Dihydroxylation of Olefins

Olefin (0.55 mmol), PSresin-MC Os (46.0 mg, 5 mol %), $(DHQD)_2PHAL$ (21.5 mg, 5 mol %), $K_3Fe(CN)_6$ (543.3 mg, 3.0 equivs.), K_2CO_3 (228.0 mg, 3.0 equivs.), and Triton® X-405 (108.3 mg, 10 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. PSresin-MC Os was separated by filtration and washed with water and ethanol, and then reused. The filtrate was analyzed by fluorescent X-ray analysis to determine the leaching of the osmium component. 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 using chiral stationary columns.

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