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Microencapsulated Osmium Tetraoxide. A New Recoverable and Reusable Polymer-Supported Osmium Catalyst for Dihydroxylation of Olefins

Satoshi Nagayama, Masahiro Endo, and
Shū Kobayashi*[†,§]

Graduate School of Pharmaceutical Sciences, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan, and Department of Applied Chemistry, Faculty of Science, Science University of Tokyo (SUT), Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan

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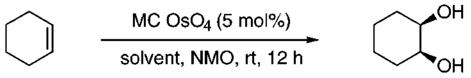
Osmium tetraoxide (OsO_4) is the most reliable reagent for the dihydroxylation of olefins to give the corresponding diols.[1] The reaction proceeds in the presence of a catalytic amount of OsO_4 using a cooxidant such as metal chlorates, hydrogen peroxide, *tert*-butyl hydroperoxide, potassium ferricyanide, or most commonly, *N*-methylmorpholine *N*-oxide (NMO). Although a number of processes have gained wide acceptance in this dihydroxylation, few fruitful industrial applications have been accomplished, probably because OsO_4 is highly toxic, expensive, volatile, and cannot be recovered.

Immobilized osmium catalysts are expected to solve these problems, and such efforts have been made, but recovery and reuse of polymer catalysts has not been satisfactory.[2,3] Recently, we have developed an unprecedented polymer-supported Lewis acid, a microencapsulated scandium trifluoromethanesulfonate (triflate) (MC $Sc(OTf)_3$).[4] This demonstrates a new method for immobilizing a catalyst onto a polymer on the basis of physical envelopment by the polymer and on electron interactions between the π electrons of the benzene rings of the polystyrene-based polymer and a vacant orbital of the Lewis acid. We intended to apply this new technology for immobilizing osmium tetraoxide. In this paper, we describe microencapsulated osmium tetraoxide that can be recovered and reused and that is effective in dihydroxylation of olefins.

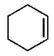
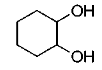
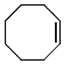
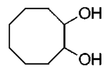
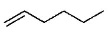
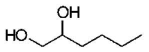
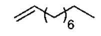
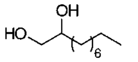
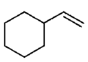
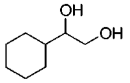
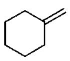
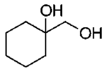
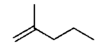
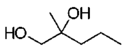
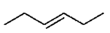
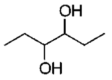
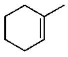
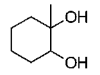
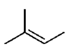
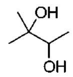
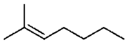
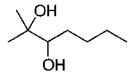
Preparation of microencapsulated osmium tetraoxide (MC OsO_4) was performed as follows: polystyrene[5] (1.000 g) was dissolved in cyclohexane (20 mL) at 40 °C, and to this solution was added OsO_4[6] (0.20 g) as a core (OsO_4 was dissolved). The mixture was stirred for 1 h at this temperature and then 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. The mixture was stirred at room temperature (rt) for 1 h, and the capsules were then washed with methanol several times and dried at room temperature for 24 h. Unencapsulated OsO_4 was recovered from the washings.

Table 1. Effect of Solvents and Cooxidants



solvent	cooxidant	yield (%)
H_2O−acetone (2/1)	NMO	15
H_2O−^tBuOH (1/1)	NMO	20
H_2O−acetone−CH_3CN (1/1/1)	NMO	84
H_2O−acetone−CH_3CN (1/1/1)	Me_3NO	57
H_2O−acetone−CH_3CN (1/1/1)	H_2O_2	30
H_2O−acetone−CH_3CN (1/1/1)	^tBuOOH	18
H_2O−acetone−CH_3CN (1/1/1)	$K_3Fe(CN)_6$	0

Table 2. Dihydroxylation of Olefins Using MC OsO_4[a]

Olefin	Product	Yield (%)
		84
		81
		89
		68
		83
		84
		78
		74
		76
		63
		83[b]

[a] All reactions were carried out using MC OsO_4 (5 mol %) and NMO in H_2O−acetone−CN_3CN (1/1/1) at rt for 6−48 h. [b] Carried out at 60 °C.

MC OsO_4 thus prepared[7,8] was first used in the dihydroxylation of cyclohexene, and several solvents and co-

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[†] Present address: Graduate School of Pharmaceutical Sciences, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan.

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(3) Polymer-supported chiral ligands were reported. (a) Kim, B. M.; Sharpless, K. B. *Tetrahedron Lett.* **1990**, *31*, 3003. (b) Lohray, B. B.; Thomas, A.; Chittari, P.; Ahuja, J. R.; Dhal, P. K. *Tetrahedron Lett.* **1992**, *33*, 5453. (c) Han, H.; Janda, K. D. *J. Am. Chem. Soc.* **1996**, *118*, 7632. (d) Bolm, C.; Gerlach, A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 741. A problem of these approaches is that recover and recycle of osmium are difficult. Cf. (e) Bolm, C.; Gerlach, A. *Eur. J. Org. Chem.* **1998**, 21.

(4) Kobayashi, S.; Nagayama, S. *J. Am. Chem. Soc.* **1998**, *120*, 2985.

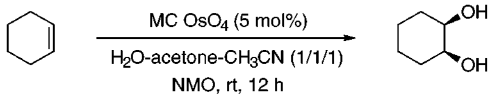
(5) Average M_w ca. 280 000. Purchased from Aldrich, Co. Ltd.

(6) Purchased from Soekawa Rika, Co. Ltd.

(7) 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. Donbrow, M. *Microcapsules and Nanoparticles in Medicine and Pharmacy*; CRC Press: Boca Raton, 1992. We first applied this technique for immobilizing a catalyst onto a polymer.[4]

S0022-3263(98)01127-X CCC: $15.00

Table 3. Recovery and Reuse of MC OsO_4

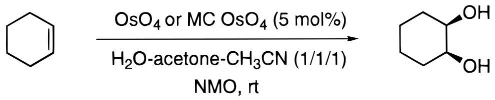


run	1	2	3	4	5
yield of product (%)	84	84	83	84	83
recovery of catalyst (%)	quant	quant	quant	quant	quant

oxidants were examined (Table 1). All the reactions were carried out on a 10 mmol scale using MC OsO_4 containing ca. 0.12 g of OsO_4 (5 mol %) in a batch system. When a solvent such as H_2O−acetone or H_2O−^{t}BuOH (which is used in typical OsO_4-catalyzed dihydroxylations)[1] was used, lower yields were obtained. The yield was, however, dramatically improved when acetonitrile was added to the H_2O−acetone solution. We also examined several cooxidants. While the reaction was successfully carried out using NMO, moderate yields were obtained using trimethylamine *N*-oxide, and much lower yields were observed using hydrogen peroxide or potassium ferricyanide.

Several examples of the MC OsO_4-catalyzed dihydroxylation of olefins in the presence of NMO in H_2O−acetone−acetonitrile are summarized in Table 2. Cyclic and acyclic exo as well as internal olefins worked well under these conditions. Moreover, bulky olefins such as 1-methylcyclohexene and 2-methyl-2-butene also reacted smoothly in the presence of MC OsO_4 to afford the corresponding diols. The polymer catalyst was recovered quantitatively by simple filtration and could be reused. The activity of the recovered catalyst did not decrease even after the fifth use (Table 3). The experimental procedure was very simple: mix an olefin, MC OsO_4, and NMO.[9] After the reaction, simple filtration separated the product and the catalyst. In addition, it was assumed that no OsO_4 was released from MC OsO_4 during or after the reaction, since MC OsO_4 was recovered quantitatively (by weight) in all cases. This was confirmed by the qualitative analysis of OsO_4 using the iodometry.[10] Since the titration is very sensitive, these results indicate that no OsO_4 contamination of the products occurs. Finally, a preliminary study on the rate of conversion of the starting olefin was performed by using OsO_4 and MC OsO_4 in a model dihydroxylation of cyclohexene using NMO as a cooxidant (Table 4). It was found that the reaction proceeded faster using OsO_4 than using MC OsO_4.[11] While an 81% yield of the diol was obtained using OsO_4 for 3 h, a 75% yield was obtained using MC OsO_4 under the same reaction conditions.

Table 4. Preliminary Study on the Rate of Conversion of the Starting Olefin



time (min)	1	10	30	60	180
yield (OsO_4) (%)	11	79	78	78	81
yield (MC OsO_4) (%)		7	37	55	75

In summary, we have successfully immobilized OsO_4 onto a polymer using a microencapsulating technique. The polymer-supported catalyst (MC OsO_4) was very effective in the dihydroxylation of olefins. MC OsO_4 was readily prepared could be recovered quantitatively by simple filtration, and could be reused. It should be noted that the volatile property of OsO_4 is very much depressed by this immobilization and that no contamination of OsO_4 in the products occurs. Further investigations to apply MC OsO_4 to large-scale syntheses as well as asymmetric syntheses are now in progress.

Acknowledgment. S.N. thanks the JSPS fellowship for Japanese Junior Scientists.

Supporting Information Available: Experimental procedures and physical data of the products (3 pages).

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[8] Although the preparative method was similar to conventional protocols for the preparation of microcapsules, it was assumed that small capsules of MC OsO_4 adhered to each other probably due to the small size of the core and that OsO_4 was located all over the polymer surface. Similar phenomena were observed in MC $Sc(OTf)_3$.[4]

[9] Details are shown in the Supporting Information.

[10] OsO_4 is treated with potassium iodide and HCl, and the produced iodine is titrated with sodium thiosulfate in the presence of starch. See the Supporting Information.

[11] It was found that some reactions proceeded faster using microencapsulated scandium triflate (MC $Sc(OTf)_3$) than using $Sc(OTf)_3$ due to the polymer effect.[4,12] This would be the case in the initial step of the dihydroxylation using MC OsO_4 or OsO_4 (interaction between an olefin and MC OsO_4 or OsO_4); however, the observed slower reaction using MC OsO_4 instead of OsO_4 would be ascribed to the slower oxidation step of a microencapsulated osmium ester with NMO (the rate-determining step).

[12] Kobayashi, S.; Nagayama, S. *Synlett* **1997**, 653.