ORGANIC
LETTERS

2003
Vol. 5, No. 2
185−187

Microencapsulation of Osmium Tetroxide in Polyurea

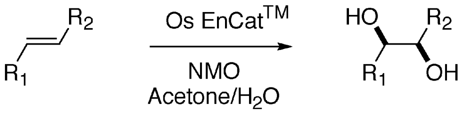
Steven V. Ley,*,[†] Chandrashekar Ramarao,[†] Ai-Lan Lee,[†] Niels Østergaard,[†] Stephen C. Smith,[‡] and Ian M. Shirley[‡]

*University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, UK, and
Syngenta, Jealott's Hill International Research Center, Bracknell,
Berkshire, RG42 6EY, UK*

svl1000@cam.ac.uk

Received November 4, 2002

ABSTRACT



Osmium tetroxide has been microencapsulated in a polyurea matrix using an in situ interfacial polymerization approach. These microcapsules have been effectively used as recoverable and reusable catalysts in the dihydroxylation of olefins

Transition-metal-based catalytic processes are of vital importance to pharmaceutical, agrochemical, and fine chemical industries. A vast proportion of such catalytic metal species are often expensive and toxic, thereby making operational handling potentially hazardous. The current trend toward "clean and rapid" synthesis has driven the generation of a number of new strategies for reagent immobilization to enable easy recovery, reuse, and disposal at an acceptable economic cost.[1] Microencapsulation, the process of entrapping material in a polymeric coating, has recently been demonstrated to be a useful alternative strategy for reagent immobilization.[2,3] Microcapsules that efficiently entrap active material can be manufactured in sizes ranging from a few microns to 4000 μm using a plethora of techniques.[4] Polyurea microcapsules[5] are prepared by an in situ interfacial polymerization approach, which involves the dispersion of a solution of isocyanates and the reagent to be encapsulated in a suitable organic solvent into an aqueous mixture containing surfactants. The resultant oil-in-water microemulsion is allowed to cure, during which time polymerization occurs at the oil−water interface. The resultant polyurea microcapsules are completely insoluble in aqueous and organic solvents and have been proven to be extremely robust without any degradation under normal reaction conditions. It has been demonstrated that metal species such as palladium(II) acetate can be microencapsulated in polyurea (Pd EnCat) and used as recoverable and reusable catalysts without significant leaching or loss of activity.[2,6] It is thought that the urea functionality, which forms the backbone of the polymer, ligates and retains the metal species within the polymeric matrix. The ease with which these polyurea microcapsules could be recovered and reused prompted investigations to encapsulate other catalytic species such as osmium tetroxide.[7]

Osmium tetroxide is the most efficient catalyst for the synthesis of *syn*-diols from olefins.[8] The high toxicity[7] and

---

[†] University Chemical Laboratory.

[‡] Syngenta.

(1) For example, see: (a) Ley, S. V.; Baxendale, I. R.; Bream, R. N.; Jackson, P. S.; Leach, A. G.; Longbottom, D. A.; Nesi, M.; Scott, J. S.; Storer, R. I.; Taylor, S. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3815. (b) Kirschning, A.; Monenschein, H.; Wittenberg, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 650. (c) Clapham, B.; Reger, T. S.; Janda, K. D. *Tetrahedron* **2001**, *57*, 4637.

(2) Ramarao, C.; Ley, S. V.; Smith, S. C.; Shirley, I. M.; DeAlmeida, N. *Chem. Commun.* **2002**, 1132.

(3) Akiyama, R.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 2602.

(4) Mars, G. J.; Scher, H. B. In *Controlled Delivery of Crop Protecting Agents*; Wilkens, R. M., Ed.; Taylor and Francis: London, 1990; p 65. (b) Jain, R. A. *Biomaterials* **2000**, *21*, 2475. (c) Shimofure, S.; Koizumi, S.; Ichikawa, K.; Ichikawa, H.; Dobashi, T. *J. Microencapsulation* **2001**, *18*, 13. (d) Uludag, H.; De Vos, P.; Tresco, P. A. *Adv. Drug Delivery Rev.* **2000**, *42*, 29. (e) Tsuji, K. *J. Microencapsulation* **2000**, *18*, 137.

(5) Scher, H. B. US Patent 4,285,720, 1980.

(6) (a) Ley, S. V.; Ramarao, C.; Gordon, R. S.; Holmes, A. B.; Morrison, A. J.; McConvey, I. F.; Shirley, I. M.; Smith, S. C.; Smith, M. D. *Chem. Commun.* **2002**, 1134. (b) Brenmeyer, N.; Ley, S. V.; Ramarao, C.; Shirley, I. M.; Smith, S. C. *Synlett* **2002**, 1843.

(7) Hammond, C. R. In *CRC Handbook of Chemistry and Physics*, 81st ed.; Lide, D. R., Ed.; CRC Press: Boca Raton, FL; pp 4−21.

10.1021/ol020225+ CCC: $25.00

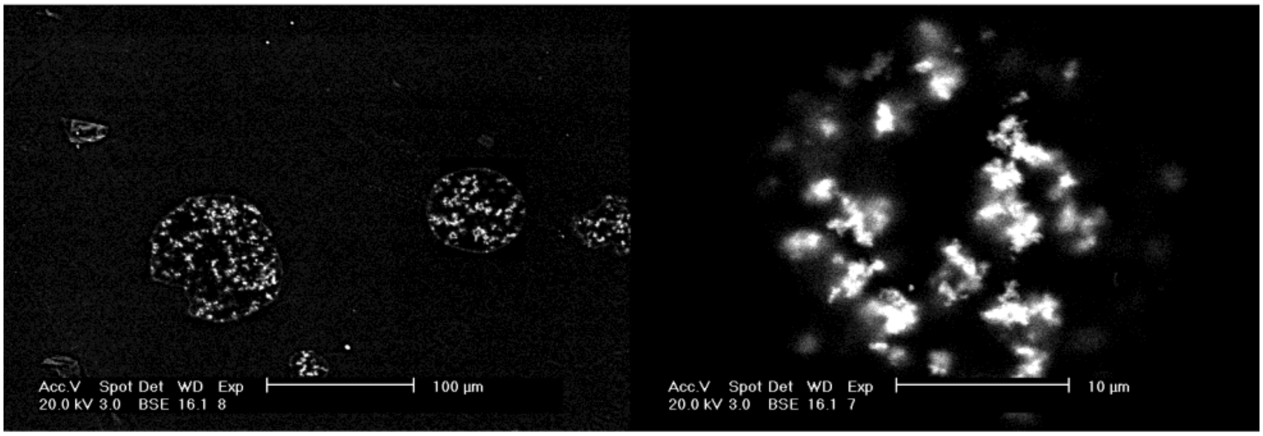


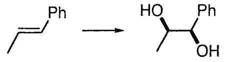
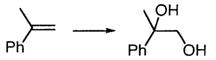
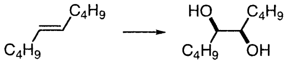
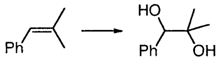
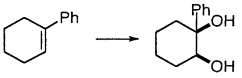
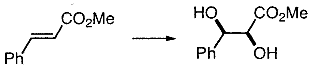
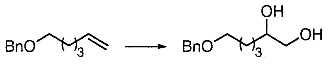
Figure 1. Scanning electron micrograph (SEM) of the polyurea microcapsule sections showing the OsO_4 distribution (bright spots) within the polyurea matrix.

expense of this volatile reagent is a deterrent for use in large-scale operations. To overcome these issues, several groups have adopted different strategies to immobilize this reagent on soluble and insoluble supports, achieving varying levels of success.[9]

The preparation of polyurea microcapsules containing osmium tetroxide (Os EnCat) is straightforward. A mixture of osmium tetroxide (0.396 g) and polymethylene polyphenylene diisocyanate (SUPRASEC 5025, average functionality of 2.7, 7 g) in Solvesso 200[10] (10 g) was dispersed (at 800 rpm using a Heidolph 33 mm rotary flow impeller) into an aqueous solution containing sodium lignosulfonate (Reax 100 M, 1.8 g),[11] poly(vinyl alcohol) (Goshenol GL03, 0.6 g),[11] and the polyoxypropylene polyoxyethylene ether of butyl alcohol (Tergitol XD, 0.3 g)[11] in deionized water (45 mL). This operation resulted in an oil-in-water microemulsion with a particle size range of 20−250 μm that was gently paddle-stirred for 36 h to yield the insoluble polyurea microcapsules. The microcapsules were filtered and washed with deionized water and a range of organic solvents and dried.[12]

The use of scanning electron microscopy (SEM) helped ascertain the metal distribution within the polymeric matrix. The electron micrograph (backscattered mode) shows the distribution of the metal within the flocculent polyurea matrix (Figure 1, bright spots).[12] These microcapsules proved to be effective in the dihydroxylation of a range of olefins (Table 1). The reactions were carried out at room temperature using 5 mol % (loading = ca. 0.2 mmol/g, based on the metal content and the assumption that there is no loss of OsO_4 during the encapsulation process) of the polyurea catalyst in a 10:1 acetone−water solvent system with *N*-methyl morpholine *N*-oxide as the co-oxidant.[13] The microcapsules were recovered by a simple filtration and reused five times, showing no significant loss in activity. (Table 2).

Table 1. Dihydroxylations of Olefins Using Os EnCat[a]

entry	transformation	yield[b] %
1		80
2		84
3		90
4		84
5		83
6		82
7		85
8		73

[a] Reagents and conditions: Os EnCat 5 mol %, NMO, 10:1 acetone/H_2O, rt, 12−24 h. [a] Based on isolated yields.

---

(8) (a) Schroder, M. *Chem. Rev.* **1980**, *80*, 187. (b) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.

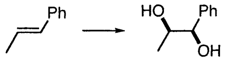
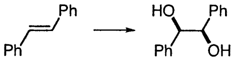
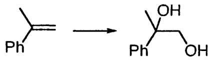
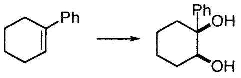
(9) (a) Cainelli, G.; Contento, M.; Manescalchi, F.; Plessi, L. *Synthesis* **1989**, 45. (b) Nagayama, S.; Endo, M.; Kobayashi, S. *J. Org. Chem.* **1998**, *63*, 6094. (c) Salvadori, P.; Pini, D.; Petri, A. *Synlett* **1999**, 1181. (d) Kobayashi, S.; Endo, M.; Nagayama, S. *J. Am. Chem. Soc.* **1999**, *121*, 11229. (e) Kobayashi, S.; Ishida, T.; Akiyama, R. *Org. Lett.* **2001**, *3*, 2649. (f) Severeyns, A.; De Vos, D. E.; Fiermans, L.; Verpoort, F.; Grobet, P. J.; Jacobs, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 586. (g) Choudary, B. M.; Chowdari, N. S.; Jyothi, K.; Kantam, M. L. *J. Am. Chem. Soc.* **2001**, *123*, 9220. (h) Yao, Q. *Org. Lett.* **2002**, *4*, 2197.

(10) Solvesso 200 is a high-boiling (230−257 °C) mixture of aromatics (predominantly naphthalenes) and a product of the Exxon Mobil Corporation.

(11) Polymethylene polyphenylene diisocyanate (SUPRASEC 5025) was purchased from Huntsman ICI Polyurethanes; Reax 100M, Goshenol GL03, and Tergitol XD were bought from Westvaco, British Traders and Shippers, Ltd., and Union Carbide, respectively.

(12) see Supporting Information.

Table 2. Recycling Experiments with Os EnCat[a]

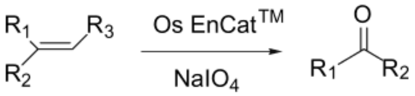
run	transformation	yield[b] %
1		74
2		86
3		88
4		83
5		77
6		88

[a] Reagents and conditions: Os EnCat 5 mol %, NMO, 10:1 acetone/H_2O, rt, 12−24 h. [b] Based on isolated yields.

No sign of cross-contamination was evident when the microcapsules were used in recycling experiments with different substrates. This suggests that the reagents and products are not imbibed and retained in the polymer matrix after the workup procedure (washings). When used after storage for 10 months without any special precautions (such as an inert atmosphere), the microcapsules were just as effective in these oxidations. Qualitative leach test experiments were carried out by stirring the microcapsules in solution for 24 h. The microcapsules were filtered, and the solution was used in catalytic osmylation experiments. No reaction occurred, suggesting that significant leaching of an active osmium species had not taken place.[14]

Osmium tetroxide is used as a catalyst for the generation of carbonyl compounds from olefins by oxidative cleavage of the formed glycols using sodium periodate ($NaIO_4$).[15] This transformation can also be carried out using Os EnCat. Treatment of a range of olefins with Os EnCat (2 mol %) and $NaIO_4$ (3 equiv) in 2:1 THF−H_2O gave the required carbonyl compounds in good yields (Table 3).[12] Os EnCat was easily recovered by a simple filtration and reused several times.

Table 3. Oxidative Cleavage of Olefins Using Os EnCat[a]



entry	R_1	R_2	R_3	yield%
1	n-C_6H_{13}	H	H	66^d (100)^c
2	Ph	H	H	92^b
3	Ph	H	Me	79
4	H	Ph	Ph	99
5	Ph	H	Ph	98^b
6	Ph	H	CO_2Me	95^b
7	n-C_6H_{13}	H	n-C_6H_{13}	55^d (100)^c
8	Ph	Ph	H	99^b

[a] Reagents and conditions: Os EnCat 2 mol %, $NaIO_4$ (3 equiv), 2:1 THF/H_2O, rt, 1−8 h. [b] Isolated and identified as the phenyl hydrazone. [c] GC yield. [d] Isolated yield of the alcohol formed upon treatment of crude product with PhMgBr.

In summary, another polyurea microcapsule-based catalytic system has been developed that has proved to be effective and easy to handle. The manufacture of these microcapsules is cost-effective and can be easily translated to meet large-scale requirements for industrial applications. Current work involves the extension of this system to asymmetric dihydroxylation reactions. The incorporation of other chelating and ligating functional groups within the polyurea framework will help ascertain if any rate enhancement in these reactions can be achieved.

Acknowledgment. The authors thank J. Skepper (Multi Imaging Center, Cambridge University) for microscopy. This work was funded by Syngenta Limited.

Supporting Information Available: Experimental procedures and NMR data of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

OL020225+

---

(13) **General Procedure for Dihydroxylations using Os EnCat:** Os Encat (5 mol %) was added to a solution of olefin (1 mmol) and *N*-methyl morpholine *N*-oxide (NMO) (1.5 mmol) in 10:1 acetone−H_2O (10 mL), and the reaction mixture was stirred at room temperature for 12−24 h (monitored by thin-layer chromatography (TLC)). The reaction mixture was filtered, and the recovered microcapsules were washed with H_2O and acetone. The filtrate was treated with saturated aqueous sodium metabisulfite (20 mL), extracted with ethyl acetate, and dried ($MgSO_4$). Evaporation under reduced pressure and purification by column chromatography gave the products.

(14) (a) The authors refrain from referring to this catalyst system as a heterogeneous system because the possibility of these microcapsules functioning as a reservoir and an efficient scavenger of homogeneous catalytic species exists. (b) Davies, I. W.; Matty, L.; Hughes, D. L.; Reider, P. J. *J. Am. Chem. Soc.* **2001**, *123*, 10139.

(15) (a) Pappo, R.; Allen, D. S.; Lemieux, R. U.; Johnson, W. S. *J. Org. Chem.* **1956**, *21*, 478. (b) Cainelli, G.; Contento, M.; Manescalchi, F.; Plessi, L. *Synthesis* **1989**, 47.