

Osmium tetroxide in poly(ethylene glycol) (PEG): a recyclable reaction medium for rapid asymmetric dihydroxylation under Sharpless conditions^{†‡}

S. Chandrasekhar,* Ch. Narsihmulu, S. Shameem Sultana and N. Ramakrishna Reddy

Indian Institute of Chemical Technology, Hyderabad 500 007, India. E-mail: srivaric@iict.ap.nic.in;

Fax: (+91)-40-27160512

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PEG (400) has been used as a recyclable and rapid reaction medium for the asymmetric dihydroxylation of olefins; Sharpless ligand is efficiently recovered and recycled with good enantioselectivity.


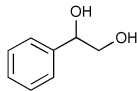

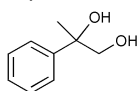
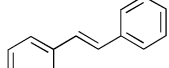
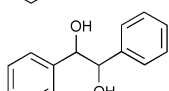

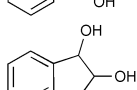
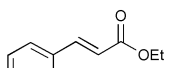
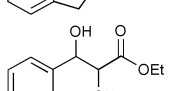
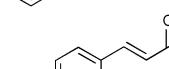
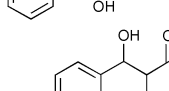

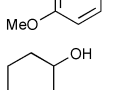

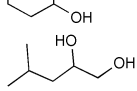
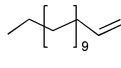
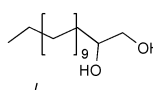
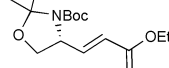
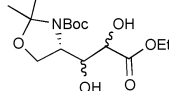
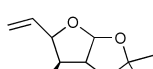
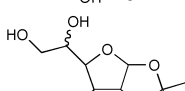
Undoubtedly, the dihydroxylation of olefins using catalytic amounts of OsO₄ is the most sought after method for the preparation of vicinal diols.¹ The importance of this reaction has been enhanced substantially through the use of cinchona alkaloids which result in chiral vicinal diols as reported by Sharpless *et al.*² Even though the products of dihydroxylation have a prominent role in pharmaceuticals and fine chemicals,³ the cost, toxicity⁴ and contamination of products with osmium restrict its use in industry.

Efforts are thus directed at heterogenizing the OsO₄ on a polymer or silica gel, or even *via* encapsulation,⁵ to avoid contamination in the final product and also as a means of recycling the osmium species. Kobayashi *et al.* have used microencapsulation⁶ of OsO₄ in polymer to achieve recyclability of the catalyst. Choudary *et al.* have heterogenized the catalyst by an ion exchange technique⁷ and ionic liquids⁸ have been used by Yao to recycle OsO₄. Even though all these methodologies are steps forward in avoiding the problems, none of these are yet to reach "the ultimate solution". Also, there are additional steps involved in the microencapsulation or heterogenization. Similarly the use of ionic liquids⁹ as ecofriendly solvents is yet to be authenticated. Recently, we have observed¹⁰ that PEG (MW 2000) can be used as a recyclable solvent system for the Heck reaction and also found that Pd species used as catalyst remain in PEG and can be recycled. We intended to apply this procedure to Os catalysis and found very interesting observations. In this communication, we describe for the first time OsO₄ in PEG not only as a recoverable and reusable system for dihydroxylation but also as a medium where reaction is rapid (2 h) and high yielding at very low concentrations of osmium tetroxide, 0.5 mol%, (Schemes 1 and 2). All the reported protocols require 1–5 mol% catalyst and

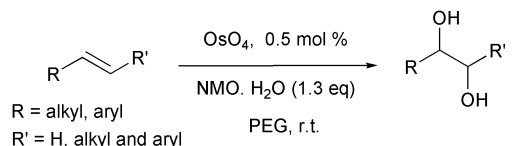
12–24 hours time for completion for a similar result. We also describe efficient asymmetric dihydroxylation using Sharpless reagent wherein the chiral ligand is efficiently recycled.

In the initial studies, readily available styrene (entry 1, Table 1) and α -methyl styrene (entry 2) were subject to dihydroxylation using OsO₄ (0.5 mol%) in PEG (400 MW) using NMO (1.3 eq.) as the reoxidant and to our utmost satisfaction dihydroxylation was completed within 2 h and 94% and 97% yields respectively were obtained after a standardized workup protocol.[§]

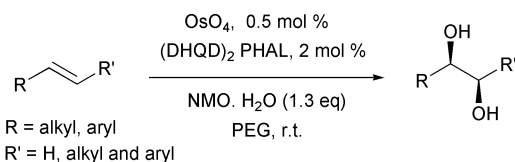
Table 1 OsO₄ Catalyzed dihydroxylation of olefins in PEG

| Entry | Olefin | Product | Time/h | Yield (%) ^a |
|-------|--|---|--------|------------------------|
| 1 |  |  | 2 | 94 |
| 2 |  |  | 2 | 97 |
| 3 |  |  | 2 | 95 |
| 4 |  |  | 3 | 90 |
| 5 |  |  | 2 | 93 |
| 6 |  |  | 2 | 95 |
| 7 |  |  | 3 | 92 |
| 8 |  |  | 3 | 89 |
| 9 |  |  | 2 | 95 |
| 10 |  |  | 3 | 92 ^b |
| 11 |  |  | 3 | 88 ^c |

^a Yields based on isolation of chromatographically homogeneous products. ^b de 55% (by NMR). ^c de 91% (by NMR).



Scheme 1



Scheme 2

[†] Dedicated to Prof. Goverdhan Mehta on his 60th birthday.

[‡] Electronic supplementary information (ESI) available: experimental details. See <http://www.rsc.org/suppdata/cc/b3/b305154b/>

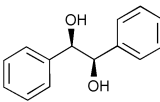
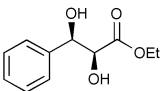
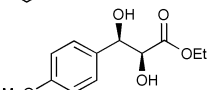
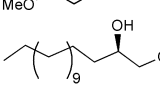
To substantiate our results and check versatility, other olefins were subjected to dihydroxylation. For instance, *trans*-stilbene (entry 3) produced 1,2-diphenyl-1,2-ethanediol in 95% yield. Electron deficient olefins *viz.*, *trans*-ethyl cinnamate (entry 5), ethyl-4-methoxy cinnamate (entry 6) and the conjugated ester obtained on Wittig olefination between Garner aldehyde and (carboethoxymethylene)triphenylphosphorane (entry 10) produced diols in 93, 95 and 92% yield with ease. Furanose derivative (entry 11) yielded the hexose sugar in 88% yield and greater than 90% de. To check the reusability of OsO₄, styrene was subjected to dihydroxylation after each extraction with ether and we found that even after the fifth run we could isolate diol in 90% yield (Table 2)! This experiment proved to us beyond doubt that OsO₄ is never extracted into ether and successfully recycled for dihydroxylation. Attempts to identify osmium tetroxide in the ether layer by atomic absorption spectroscopy (AAS) showed the presence of osmium to an extent of less than 2 ppm.

Table 2 Dihydroxylation of styrene using OsO₄ in PEG (recycling studies)

| Run | 1 | 2 | 3 | 4 | 5 |
|--------------------|----|----|----|----|----|
| Isolated yield (%) | 94 | 94 | 92 | 93 | 90 |

Encouraged by these promising results, we then attempted the asymmetric dihydroxylation of olefins according to the Sharpless procedure. We chose *trans*-stilbene as an initial substrate (entry 1, Table 3) and subjected it to dihydroxylation as follows. To (DHQD)₂PHAL (2 mol%) and OsO₄ (0.5 mol%) *trans*-stilbene (2 mmol) in PEG (2 g) was added and stirred for 2 h. The reaction mixture was extracted with ether. The ether layer was washed with 10% HCl and then with water and brine. The ether layer yielded 1,2-diphenyl-1,2-ethanediol in 94% ee and 95% chemical yield. Conventionally, the reaction required longer reaction hours (up to 24 h) and addition of 1 eq. of methane sulfonamide for dihydroxylation of internal double bonds. Interestingly the present protocol is very rapid and no additional reagents like methane sulfonamide were required. Similarly three more experiments were carried out on olefins, namely ethyl cinnamate (entry 2, Table 3), ethyl-4-methoxy cinnamate (entry 3, Table 3) and 1-tetradecene (entry 4, Table 3). With the exception of 1-tetradecene, the chemical and optical purities were all very high. Again to check the recyclability of OsO₄ and possibly ligand as well *trans*-stilbene was subjected to asymmetric dihydroxylation (Table 4). After 2

Table 3 Asymmetric dihydroxylation using (DHQD)₂PHAL, OsO₄ and NMO·H₂O in PEG

| Entry | Product | Time/h | Yield (%) | ee (%) ^a |
|-------|---|--------|-----------|---------------------|
| 1 |  | 2 | 95 | 94 |
| 2 |  | 2 | 92 | 91 |
| 3 |  | 2 | 94 | 96 |
| 4 |  | 2 | 96 | 44 |

^a The products ee was determined by chiral GC analysis (Cyclosil-B).

Table 4 Reusability of OsO₄ and (DHQD)₂PHAL in PEG

| Run | Time/h | Yield (%) | ee (%) |
|-----|--------|-----------|----------------------|
| 1 | 2 | 95 | 94 |
| 2 | 2 | 91 | 92 (81) ^a |
| 3 | 2 | 92 | 95 (83) ^a |
| 4 | 2 | 92 | 92 (80) ^a |
| 5 | 2 | 91 | 90 (65) ^a |

^a The ee in parentheses is for the run without additional ligand added.

h, the product was separated by ether extraction and fresh *trans*-stilbene was added. To our great surprise, in the second run diol was obtained with more than 80% ee, which indicates that ligand loss during the extraction was minimal. Further addition of 0.5 mol% ligand helped us to obtain diol with more than 95% ee. Fourth and fifth runs with additional ligand (0.25 mol%) and no addition of OsO₄ consistently furnished products in over 90% yield and ee.

In summary, we have developed for the first time, PEG as a natural encapsulation medium for OsO₄ and also for ligand to some extent. Application of other metal catalyzed reactions is currently pursued.

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Notes and references

§ *Typical experimental procedure:* To styrene (208 mg, 2 mmol) in poly(ethylene glycol) (400 MW, 2 g) was added OsO₄ (2.5 mg, 0.5 mol%) and NMO·H₂O (351 mg, 2.6 mmol) under an inert atmosphere and stirred at ambient temperature (25 °C). The reaction mixture was diluted with ether (5 mL) and stirred for five minutes. The ether layer was decanted and the procedure repeated (4 × 5 mL). The combined ether layer was washed with water and brine then dried over Na₂SO₄. Volatiles were removed on a rotary evaporator and subsequent column chromatography (30% EtOAc in hexane) gave styrene diol (260 mg) in 94% yield. The PEG layer was reused for dihydroxylation.

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