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Ionic liquid-immobilized catalytic system for biomimetic dihydroxylation of olefins†

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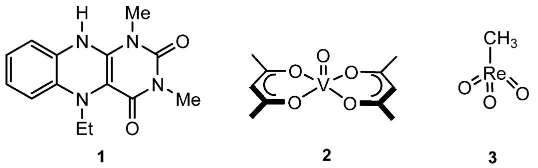
A biomimetic catalytic system for dihydroxylation of olefins consisting of OsO_4, *N*-methylmorpholine, and a flavin has been immobilized in an ionic liquid. This immobilized catalytic system is highly efficient for dihydroxylation with 30% aqueous H_2O_2 and it can be reused (at least 5 times) without loss of activity.

The osmium-catalyzed dihydroxylation of olefins is one of the most useful and easily performed oxidation reactions in organic synthesis.[1] In this process, osmium(VIII) is reduced to osmium(VI) by reaction with an olefin to yield a vicinal diol. A range of oxidants for recyling Os(VI) to Os(VIII) have been reported.[1–4]

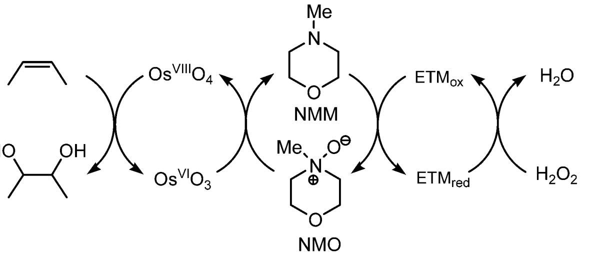
We have recently developed biomimetic catalytic systems for the dihydroxylation of olefins with hydrogen peroxide.[4–6] A stepwise low-energy electron transfer[7] *via* electron transfer mediators (ETMs), in analogy with biological systems, leads to a mild and selective dihydroxylation by hydrogen peroxide. The latter is an inexpensive and environmentally friendly oxidant.[8,9] In Scheme 1, *N*-methyl morpholine (NMM) and an additional ETM was used to carry electrons from Os(VI) to H_2O_2. Examples of H_2O_2-activating ETMs in Scheme 1 that we have used are **1**,[4] **2**,[5] and **3**[6] (Fig. 1).

One of the mildest oxidation systems according to Scheme 1 was obtained with flavin **1** as the H_2O_2-activating ETM. Flavin **1** is an efficient ETM but fragile and attempting to isolate it after the reaction is difficult. Also, the other catalysts of the triple catalytic system (Scheme 1) are difficult to recover and reuse. One way to circumvent this problem would be to immobilize one or more components of the catalytic system. We now report on a successful and novel[10] ionic-liquid immobilization of the whole biomimetic system of Scheme 1, where the three-component system can be recovered and reused.



1 **2** **3**

Fig. 1 Electron Transfer Mediators (ETMs) successfully used in a triple catalytic system.



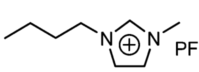
Scheme 1 Biomimetic system for dihydroxylation of olefins.

Various methods for immobilization of OsO_4 have been reported in the literature.[11–13] Recent developments have concerned polymer encapsulation of osmium tetroxide,[12a–c] chemically anchoring of osmium to a solid support,[12d–f] and dissolving osmium tetroxide in ionic liquids.[13] Ionic liquids have recently attracted much attention.[14,15] Changing one or both of the counterions can result in a change in solubility properties, which has given them the name "designer solvents".[16] For example, [bmim]PF_6 is hydrophobic.[17]

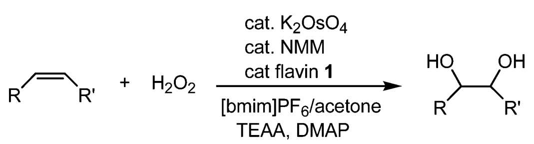
We realized that use of ionic liquids presented an especially convenient method of immobilizing not only one, but multiple components. Accordingly, we began investigations using [bmim]PF_6 and the components of our triple catalytic system with flavin **1** as ETM (Scheme 1). The components of the biomimetic triple catalytic system were immobilized in the ionic liquid ([bmim]PF_6) and TEAA and DMAP were added. Acetone was added as co-solvent and reaction of styrene with aqueous 30% H_2O_2 in this medium for 3h at room temperature afforded the diol product in 85% isolated yield after workup (Scheme 2, Table 1, entry 1).

A number of representative olefins were dihydroxylated using these reaction conditions. In this series of reactions, 1.5 equiv. of hydrogen peroxide (30% aqueous solution) was added over a 1.5 h period *via* syringe pump, followed by a further 1.5 h of stirring. After this time, the acetone was removed under reduced pressure and the reaction mixture was extracted with diethyl ether. The crude product obtained was chromatographed on silica gel to give the diol in good yield. The results are summarized in Table 1. The isolated yields of diol from these simple olefins ranged from 75–88%.

After obtaining these promising results, we moved on to testing the reusability of the system. The remaining ionic liquid residues from the reaction of α-methyl styrene and allyl phenyl ether were therefore recharged with 1 equiv. of olefin. Co-solvents and hydrogen peroxide were added as above with the same reaction times. Reaction workup was carried out again by removing volatile solvents under reduced pressure followed by extractions with diethyl ether and silica gel chromatography of the crude extracts. The ionic liquid was recovered and again submitted to further reactions with fresh starting material, co-solvents, and hydrogen peroxide until five cycles were reached. The yields for each of the five cycles were good, although with some minor variations. We were pleased to find that the flavin as well as the osmium and NMM (NMO) were retained within the ionic liquid for multiple runs, allowing for continued H_2O_2-based dihydroxylation to occur without loss of activity.‡ The results are given in Table 2. Control reactions run without flavin under otherwise identical conditions



[bmim]PF_6



Scheme 2 Biomimetic dihydroxylation in ionic liquid.

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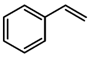
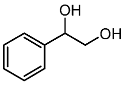
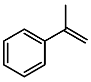
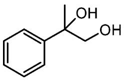
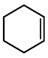
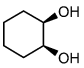
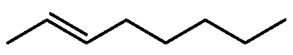
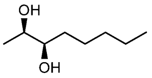
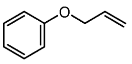
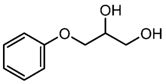
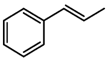
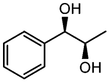
† Electronic supplementary information (ESI) available: experimental details. See http://www.rsc.org/suppdata/cc/b4/b403333g/

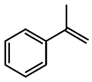
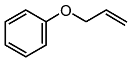
DOI: 10.1039/b403333g

Table 1 Biomimetic dihydroxylation in ionic liquid[a]

Entry	Olefin	Product	Yield[b]
1			85%
2			84%
3			75%
4			84%
5			88%
6			79%

[a] Unless otherwise noted 7.2 mg of K_2OsO_4 (1 mol%), 16 mg of flavin **1** (3 mol%), 28 μL of *N*-methyl morpholine (NMM) (12 mol%), 2.6 mg of DMAP and $Et_4N^+OAc^-$ (TEAA) (0.5 equiv.) were stirred in 0.5 mL of [bmim]PF_6. 1 mL of acetone and 0.25 mL of H_2O were added as co-solvents together with the olefin (2 mmol). 30% H_2O_2 (3 mmol) was added over 1.5 h followed by 1.5 h of reaction. [b] Isolated yields.

Table 2 Yields of diol in dihydroxylation after catalyst recycling

		Yield[a]				
Entry	Olefin	Run 1	Run 2	Run 3	Run 4	Run 5
1		84%	84%	90%	71%	89%
2		88%	76%	90%	73%	84%

[a] Isolated yields.

resulted in 66% yield of diol from α-methyl styrene and 35% yield of diol from *trans*-2-octene on the first runs, indicating that direct H_2O_2 oxidation is possible, but not as efficient as with the flavin-based system. We also performed some experiments using VO(acac)$_2$ (**2**) as ETM, which gave essentially the same results as with flavin **1** for the styrenes. However, the results were not as consistent for the other olefins as with the flavin system.

The yields are consistently good over the five reaction cycles, demonstrating the effective immobilization of the complete biomimetic system of Scheme 1, where the ETM is flavin **1**. The successful recycling of the triple catalytic system components allows for a more economic and environmentally friendly process. It becomes operationally very simple: after extraction of the product, new olefin and hydrogen peroxide are added to the immobilized biomimetic system for an additional dihydroxylation.

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Notes and references

‡ At the end of the reaction the NMM is in the form of polar NMO and the flavin is in a cationic form. Therefore they are not extracted.

1 Review: H. C. Kolb, M. S. Van Nieuwenhze and K. B. Sharpless, *Chem. Rev.*, 1994, **94**, 2483–2547.

2 (*a*) V. VanRheenen, R. C. Kelly and D. F. Cha, *Tetrahedron Lett.*, 1976, **17**, 1973–1976; (*b*) M. Minato, K. Yamamato and J. Tsuji, *J. Org. Chem.*, 1990, **55**, 766–768.

3 (*a*) C. Döbler, G. M. Mehltretter and M. Beller, *Angew. Chem. Int. Ed.*, 1999, **38**, 3026–3028; (*b*) C. Döbler, G. M. Mehltretter, U. Sundermeier and M. Beller, *J. Am. Chem. Soc.*, 2000, **122**, 10289–10297.

4 (*a*) K. Bergstad, S. Y. Jonsson and J.-E. Bäckvall, *J. Am. Chem. Soc.*, 1999, **121**, 10424–10425; (*b*) S. Y. Jonsson, K. Färnegårdh and J. E. Bäckvall, *J. Am. Chem. Soc.*, 2001, **123**, 1365–1371; (*c*) S. Y. Jonsson, H. Adolfsson and J. E. Bäckvall, *Org. Lett.*, 2001, **3**, 3463–3466.

5 A. H. Éll, S. Y. Jonsson, A. Börje, H. Adolfsson and J. E. Bäckvall, *Tetrahedron Lett.*, 2001, **42**, 2569–2571.

6 (*a*) S. Y. Jonsson, H. Adolfsson and J. E. Bäckvall, *Chem. Eur. J.*, 2003, **9**, 2783–2788; (*b*) A. H. Éll, A. Closson, H. Adolfsson and J. E. Bäckvall, *Adv. Synth. Catal.*, 2003, **345**, 1012–1016.

7 D. V. Deubel, *J. Am. Chem. Soc.*, 2004, **126**, 996–997.

8 G. Strukul, *Catalytic Oxidations with Hydrogen Peroxide as Oxidant*, Kluwer, Dordrecht, The Netherlands, 1992.

9 Direct reoxidation of Os(VI) in dihydroxylation reactions without ETMs lead to nonselective reactions and over-oxidation: (*a*) N. A. Milas and S. Sussman, *J. Am. Chem. Soc.*, 1936, **58**, 1302–1304; (*b*) N. A. Milas, J. H. Trepagnier, J. T. Nolan and M. I. Iliopulos, *J. Am. Chem. Soc.*, 1959, **81**, 4730–4733.

10 The only immobilization previously done with a H_2O_2 driven Os-catalyzed dihydroxylation was on solid support with layered double-hydroxides (LDHs).[10a] Jacobs and DeVos have also reported on a related immobilized system on solid support, but there the Os-catalyzed dihydroxylation and the NMM recycling by H_2O_2 had to be run in separate compartments.[10b] (*a*) B. M. Choudary, N. S. Showdari, S. Madhi. and M. L. Kantam, *Angew. Chem. Int. Ed.*, 2001, **40**, 4619–4623; (*b*) A. Severeyns, D. E. De Vos and P. A. Jacobs, *Green Chem.*, 2002, **4**, 380–384.

11 (*a*) C. Bolm and A. Gerlach, *Eur. J. Org. Chem.*, 1998, 21–27; (*b*) G. Cainelli, M. Contento, F. Manescalchi and L. Plessi, *Synthesis*, 1989, 45–47; (*c*) W. A. Herrmann, R. M. Kratzer, J. Blümel, H. B. Friedrich, R. W. Fischer, D. C. Apperley, J. Mink and O. Berkesi, *J. Mol. Catal. A*, 1997, **120**, 197–205.

12 (*a*) S. Nagayama, M. Endo and S. Kobayashi, *J. Org. Chem.*, 1998, **63**, 6094–6095; (*b*) S. Kobayashi, M. Endo and S. Nagayama, *J. Am. Chem. Soc.*, 1999, **121**, 11229–11230; (*c*) S. Kobayashi, T. Ishida and A. Akiyama, *Org. Lett.*, 2001, **3**, 2649–2652; (*d*) A. Severyns, D. E. De Vos, L. Fiermans, F. Verpoort, P. J. Grobert and P. A. Jacobs, *Angew. Chem. Int. Ed.*, 2001, **40**, 586–589; (*e*) B. M. Choudary, N. S. Chowdari, K. Jyothi, N. S. Kumar and M. L. Kantam, *Chem. Commun.*, 2002, 586–587; (*f*) B. M. Choudary, N. S. Chowdari, K. Jyothi and M. L. Kantam, *J. Am. Chem. Soc.*, 2002, **124**, 5341–5349.

13 (*a*) Q. Yao, *Org. Lett.*, 2002, **4**, 2197–2199; (*b*) L. C. Branco and C. A. M. Afonso, *Chem Commun.*, 2002, 3036–3037; (*c*) R. Yanada and Y. Takemoto, *Tetrahedron Lett.*, 2002, **43**, 6849–6851; (*d*) C. E. Song, D. Jung, E. J. Roh, S. Lee and D. Y. Chi, *Chem. Commun.*, 2002, 3038–3039.

14 (*a*) S. T. Handy, *Chem. Eur. J.*, 2003, **9**, 2938–2944; (*b*) J. H. Davis Jr. and P. A. Fox, *Chem. Commun.*, 2003, 1209–1212; (*c*) C. E. Song, *Chem. Commun.*, 2004, 1033–1043; (*d*) C. Baudequin, J. Baudoux, J. Levillain, D. Cahard, A. C. Gaumont and J. C. Plaquevent, *Tetrahedron: Asymmetry*, 2003, **14**, 3081–3093.

15 Review: (*a*) T. Welton, *Chem. Rev.*, 1999, **99**, 2071–2083; (*b*) P. Wasserscheid and W. Keim, *Angew. Chem. Int. Ed.*, 2000, **39**, 3772–3789.

16 Review: J. Dupont, R. F. de Souza and P. A. Z. Suarez, *Chem. Rev.*, 2002, **102**, 3667–3692.

17 J. S. Yadav, B. V. S. Reddy and G. Baishy, *J. Org. Chem.*, 2003, **68**, 7098–7100.