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Phase selectively soluble dendrimer-bound osmium complex: a highly effective and easily recyclable catalyst for olefin dihydroxylation†

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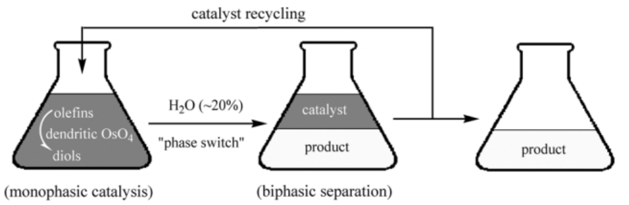
A new switched biphasic catalysis system for highly effective olefin dihydroxylation has been described, in which the dendritic osmium catalyst preferred to dissolve in the non-polar organic layer and could be easily separated from the polar diol products through phase separation induced by addition of water at the end of the reaction.

Osmium tetroxide (OsO_4) is by far the most versatile catalyst for the dihydroxylation of olefins to give the corresponding diols.[1] Although the reactions have had widespread applications in organic synthesis, few fruitful industrial applications have been accomplished due to toxicity, high cost performance, and volatility of this reagent. Possible solutions to these drawbacks have focused on the engineering of immobilized catalysts. Heterogenization of OsO_4 by immobilisation in various organic and inorganic supports has been successful, but lower activity, leaching and stability of the complex still remain severe problems.[2,3] Another approach is the use of two-phase systems, in which the phase of preference of the complex differs from that of the substrate or product, but only limited success has been achieved. Recently, Yao's group[4] and Takemoto's group[5] independently reported that ionic liquids could be used as vehicles for the immobilisation of osmium catalyst for non-asymmetric dihydroxylation. Song and co-workers[6] developed a highly efficient and recyclable catalyst system by combining the ionic liquid and OsO_4–$(QN)_2$PHAL for asymmetric dihydroxylation. Chandrasekhar and co-workers[7] described a rapid asymmetric dihydroxylation under Sharpless condition in poly(ethylene glycol) (PEG). However, the separation and re-use of the osmium catalyst was not straightforward, needing the use of large amounts of flammable organic solvent (*e.g.* ether) to isolate the reaction products, as well as to recover the ionic liquid or PEG themselves. Therefore, it is still highly desirable to develop a more practical and efficient approach to the immobilisation of the osmium catalyst.

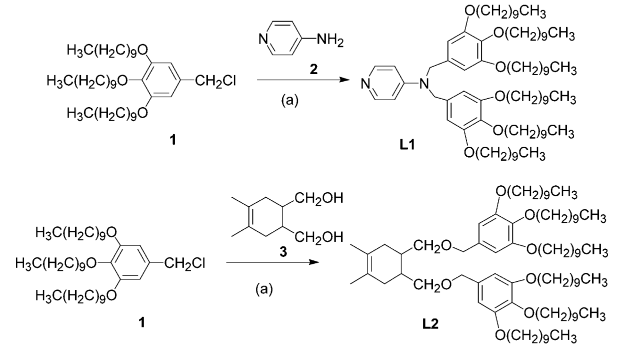
Herein, we report a novel switched biphasic catalysis system[8–11] for highly effective dihydroxylation and superior recyclability of the catalyst. Our strategy employed the dendritic osmium catalyst together with a quaternary solvent system (^{t}BuOH–MeCN–hexane–H_2O, 2 : 1 : 1 : 0.2, v/v) that could be switched to biphase by addition of about another 20% water. In contrast to the ionic liquid and PEG systems, the dendritic osmium catalyst preferred to dissolve in the non-polar organic layer, while the polar product remained in the polar layer upon phase separation at the end of the reaction (Scheme 1). Our system thus provided the following two key advantages: (a) Unlike the organic or inorganic solid supported osmium catalysts, the dendritic catalyst could be employed for homogenous dihydroxylation and consequently resulted in high efficiency. In addition, the structure of the dendritic catalyst is well defined and could be analyzed by using common spectral techniques, such as NMR, TOF mass spectroscopy. (b) As compared to the ionic liquid or PEG systems, this strategy avoided the use of large amounts of other organic solvents such as ether for product extraction. Therefore, this system has the potential to combine the advantages of homogeneous and heterogeneous catalysis.



Scheme 1 Illustration of the switched biphasic catalysis.

To test the efficacy of our new system for the separation of osmium catalyst, we chose two different types of ligand for this study. One is a derivative of 4-(dimethylamino)pyridine (DMAP), which can coordinate with OsO_4 to form a reversible complex.[4] Another one is a tetrasubstituted olefin, which reacts with OsO_4 to form hydrolytically stable Os monoglycolate.[3c] The synthesis of these two types of dendritic ligands is outlined in Scheme 2. The coupling of 3,4,5-tri(n-decan-1-yloxy)benzyl chloride (**1**)[12] with 4-aminopyridine (**2**) or 4,5-dimethyl-*cis*-Δ^4-tetrahydrophthalyl alcohol (**3**)[13] was successfully carried out using NaH as the deprotonation reagent to afford the dendritic ligands **L1** and **L2** in moderate yields, respectively. Both ligands were purified by flash column chromatography and characterized by ^1H, ^{13}C NMR and high-resolution mass spectroscopy. All results are consistent with the compounds synthesized.

We then explored various solvent compositions for the switched biphasic system. Since the ^{t}BuOH–H_2O solvent pair has been found to be best for most dihydroxylation reactions, the ternary system ^{t}BuOH–H_2O–hexane was studied initially. It was found that the miscibility of the mixture containing all three of these solvents depended on the proportions of solvents used. For example, a 2 : 1 : 0.2 (v/v) mixture of ^{t}BuOH, hexane and H_2O is monophasic at room temperature, but with the addition of more H_2O is biphasic. In order to achieve the best phase separation, however, large amounts of H_2O (more than 150% v/v) were required. Fortunately, it was found that the addition of MeCN could significantly enhance the phase separation of the above solvent system. Among numerous compositions of these solvents, an appropriate mixture of ^{t}BuOH–MeCN–hexane–H_2O (2 : 1 : 1 : 0.2, v/v), which is monophasic, albeit biphasic by addition of about 20% water, was finally found to best meet the requirement of this strategy.



Scheme 2 Synthesis of the dendritic ligands. *Reagents and conditions*: (a) NaH, THF, refluxing for 5–10 h.

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† Electronic supplementary information (ESI) available: synthesis details, characterization of the osmium complexes, dihydroxylation and recycling procedure. See http://www.rsc.org/suppdata/cc/b4/b401994f/

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To avoid handing the poisonous OsO_4, hexavalent $K_2OsO_2(OH)_4$ was used as an Os source for the preparation of the dendritic catalysts. $K_2OsO_2(OH)_4$ was firstly oxidized *in situ* to OsO_4 with *N*-methylmorpholine *N*-oxide (NMO) in ^{t}BuOH–hexane (2 : 1). **L1** (1.2 equiv.) was directly added into the pre-formed OsO_4 solution, giving the catalyst **C1**. **L2** (1.0 equiv.) reacted with OsO_4 followed by oxidation with NMO to give the catalyst **C2**, which could further react with **L2** to give the inactive catalyst Os(**L2**)$_2$.‡ It was found that these dendritic ligands and their osmium catalysts preferred to dissolved in the non-polar solvent system. In the case of ligand **L2** and catalyst **C2**, for example, more than 99% of the ligand or catalyst could be extracted to the non-polar hexane phase in a ^{t}BuOH–MeCN–H_2O–hexane (2 : 1 : 1 : 1, v/v) biphasic system.

The dendritic osmium catalysts thus prepared were first evaluated for their reusability by choosing cyclohexene as the model substrate. In the presence of the dendritic catalysts (2 mol% of **C1**), cyclohexene was treated with NMO in ^{t}BuOH–MeCN–H_2O–hexane (2 : 1 : 0.2 : 1). After 24 h at room temperature, water (about 20%) was added to the reaction mixture, resulting in two phases. The corresponding diol was obtained in 83% yield, and the recovered catalyst was then used in the next run with a new batch of the olefin under otherwise identical conditions. It is noteworthy that the diol was isolated in 88% yield (Table 1) indicating that the catalyst was recyclable and reusable. However, further recycling and reuse of the catalyst system resulted in a dramatic decrease in the yield of the product (only 22% yield in the fourth run). We attributed this to the competing coordination to Os by the reduced product of NMO where a polar osmium species could be formed. These results showed that a more stable immobilized OsO_4, which could prevent complex dissociation during the reaction, was very important to this strategy. To our delight, dendritic catalyst **C2** could be recycled and reused at least 10 times without deterioration in yield (Table 1). Importantly, the recycling of the catalyst could be simply carried out by addition of small amounts of water followed by liquid–liquid phase separation. To investigate leaching of the catalyst, we determined the content of Os in the product by using ICP analysis and found the presence of Os to an extent less than 5 ppm.

Having established the superior recyclability and reusability of the dendritic catalyst **C2**, we next examined a variety of other substrates including mono- and disubstituted aliphatic as well as aromatic olefins (Table 2). In all the cases tested, the dihydroxylation reaction proceeded smoothly at room temperature with only 1 mol% catalyst, giving almost quantitative reaction yields (entries 1–6 in Table 2). It is noteworthy that use of a reduced amount (0.5 and 0.25 mol%) of the catalyst also led to high reaction yield (entries 7–9, Table 2).

In summary, this work demonstrates that the combination of the dendritic osmium catalyst and a switched biphasic solvent system provides a simple and practical approach to the immobilisation of OsO_4 for dihydroxylation reactions. The present strategy combines the advantages of homogeneous catalysis and the traditional biphasic catalysis. Thus, we hope that the method described here might open up new perspectives for immobilisation of catalyst for dihydroxylation and other catalytic reactions.

Table 1 Dihydroxylation of cyclohexene using the dendritic osmium catalyst with NMO as co-oxidant^a

Catalyst (%)	Isolated yield (%)				
	1st run	2nd run	3rd run	4th run	5th run
C1 (2%)	83	88	76	22	
C2 (1%)	93	88	91	83	94
	6th run	7th run	8th run	9th run	10th run
C2 (1%)	83	91	90	86	87

^{a} The cyclohexene (2 mmol) and dendritic OsO_4 in ^{t}BuOH–MeCN–hexane–H_2O (2 : 1 : 1 : 0.2, v/v) was stirred with NMO at rt for 24–36 h.

Table 2 Dihydroxylation of various olefins using the dendritic osmium catalyst **C2** with NMO as co-oxidant^a

Entry	Olefins	Os (%)	Time (h)	Yield (%)
1	1-octene	1	36	98
2	1-decene	1	36	97
3	1-dodecene	1	36	97
4	styrene	1	36	99
5	1,1-diphenylethylene	1	48	98
6	*trans*-stilbene	1	36	98
7	*trans*-stilbene	0.5	36	90
8	*trans*-stilbene	0.25	36	86
9	*trans*-stilbene	0.25	72	96

^{a} The olefins (2 mmol) and dendritic OsO_4 in ^{t}BuOH–MeCN–hexane–H_2O (2 : 1 : 1 : 0.2, v/v) was stirred with NMO at rt.

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Notes and references

‡ The formation of **C2** or Os(**L2**)$_2$ depended on the ratio of Os/NMO/**L2** used. Both complexes could be prepared and were characterized by TOF MS (See: Electronic Supplementary Information†).

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