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Asymmetric dihydroxylation catalyzed by ionic polymer-supported osmium tetroxide

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Abstract—Osmium tetroxide was immobilized onto a short-length PEGylated ionic polymer, which exhibited excellent catalytic performance in OsO4-catalyzed asymmetric dihydroxylation. The resulting polymer was recycled five times without any loss of yield or enantioselectivity. In addition to the immobilization of osmium, the polymer also exhibited an ability to immobilize a significant amount of chiral ligand.

Economic and environmental considerations continue to provide impetus for the recycling of homogeneous metal catalysts via immobilization.[1] As polymer-supported metal catalysts can be recovered from reaction mixtures by simple filtration and recycled, product contamination by the catalyst is far less of a concern than when homogeneous catalysts are used. The osmium-catalyzed asymmetric dihydroxylation (AD) of olefins is one of the most widely used methods for the synthesis of chiral vicinal diols.[2] Although the AD reaction offers an elegant approach that can be applied to the synthesis of chiral drugs, natural products, and fine chemicals, the high cost of osmium and chiral ligands, as well as the high toxicity and possible contamination of osmium catalysts restricts its use in the industry.

Immobilization of osmium-chiral ligand complexes has been attempted by several groups using both soluble and insoluble polymers and silica gel.[3] However, complete recovery and re-use of osmium metal was not achieved because of weak affinity of the immobilized ligands for osmium metal. To circumvent this problem, Kobayashi et al. applied a microencapsulation technique using soluble polystyrene affording recyclable OsO_4.[4] Other techniques include OsO_4 directly immobilized in the form of an osmium bisdiolate complex through reaction with olefin-containing solid supports,[5,6] and immobilized osmium in the form of $K_2OsO_4{\cdot}2H_2O$ using an ion exchange resin.[7] Clearly, while important strides have been made in this area, additional research efforts are warranted.

Recently, we reported the immobilization of ytterbium triflate ($Yb(OTf)_3$) on a series of ionic polymers. The optimal polymer-catalyst combination found was successfully recycled 10 times without any loss of activity or catalyst leaching when it was examined in the context of β-amino ketone synthesis.[8] Within this letter, we provided evidence that unlike other immobilization mechanisms (vide supra), our technique was dependent on ion-(induced) dipole interactions between the ionic polymer and the metal–ligand complex. Herein, we extend the application of our ionic polymers to the immobilization of OsO_4 and its use in the AD reaction.

Ionic polymers **3a**–**d** containing a mesylate anion were prepared by quarternization of poly(4-vinylpyridine/styrene) (^{x}P/S), where superscript x denotes pyridine content, $x = 10$ (**1a**), 20 (**1b**), 30 (**1c**), 50 (**1d**) with tri(ethylene glycol) monomesylate monomethyl ether (MsO-PEG$_3$-OMe) at 80 °C (Scheme 1). Our previous work had shown that short-length PEG (specifically PEG$_2$) attached to the ^{x}P/S polymer provides distinct advantages in immobilizing metal species, preventing catalyst leaching and improving resin swelling.[8] However, since the hydroxylation reaction requires the use

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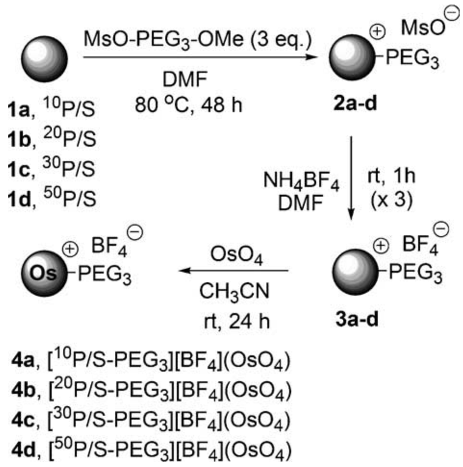


Scheme 1. Preparation of ionic polymers.

of polar solvents, we investigated polymers with higher PEG content. Polymers containing six PEG units were sticky to handle and therefore we settled on polymers containing three PEG units, since these provided ease of handling and sufficient swelling in polar solvents. The mesylate ionic polymers were treated with ammonium tetrafluoroborate (NH_4BF_4) for quantitative anion exchange of mesylate with BF_4^-, which was confirmed by IR spectroscopy (OMs^-; 1174, 1039 cm^{-1} and BF_4^-; 1031 cm^{-1}). Immobilization of OsO_4 was achieved by shaking a suspension of OsO_4 and the BF_4 ionic polymer in acetonitrile/water. After 24 h, the now black resins were filtered and washed with acetonitrile and THF. Both weight increase of the resins and UV analysis (250 nm) of the filtrate revealed that all the osmium was immobilized onto the ionic polymer. The final loading of OsO_4 was therefore calculated to be 0.19 mmol/g.

Resin (**4b**) [^{20}P/S-PEG$_3$][BF$_4$](OsO$_4$) (2 mol % as OsO_4) was used in the dihydroxylation of *trans*-stilbene-4-carboxaldehyde (**5**) in several solvent systems to determine optimal conditions using 1.5 equiv of *N*-methylmorpholine oxide as a co-oxidant (Table 1). Water in combination with acetonitrile solvent (1:9) was selected as the solvent of choice as this ionic polymer showed better swelling in acetonitrile than acetone, which resulted in high olefin conversion. Investigations were also conducted with $K_3Fe(CN)_6$ as a co-oxidant and K_2CO_3; surprisingly, no hydroxylation reaction took place, probably due to the low solubility of $K_3Fe(CN)_6$ and K_2CO_3. As the four OsO_4-immobilized ionic polymers **4a–d** had been prepared, we also undertook experimentation to determine the optimal polymer for the hydroxylation reaction by assessing these resins using H_2O–acetonitrile (1:9) as the solvent system (Table 1). After 12 h, % conversion was determined by HPLC, resin (**4c**) [^{30}P/S-PEG$_3$][BF$_4$](OsO$_4$) proved to have the best activity. Gratifyingly, this finding concurs with our previous study of ionic polymer-supported $Yb(OTf)_3$.

The resin (**4c**) [^{30}P/S-PEG$_3$][BF$_4$](OsO$_4$) was engaged for the AD reaction of **5** using $(DHQH)_2PHAL$ ligand for chiral induction (Table 2). Importantly, we observed that the reaction time was reduced by a factor of three in the presence of the chiral ligand; presumably, this was due to the fact that OsO_4-catalyzed dihydroxylation is known to be accelerated by ligand interaction.[9] High enantioselectivity (96–97% ee) was also observed in this reaction. With regards to recycling, the resin was used four times by recovering the catalyst via simple filtration at the conclusion of the reaction. Although the activity of the catalyst was slightly decreased after reuse of the resin (note extended reaction times), the desired diol was

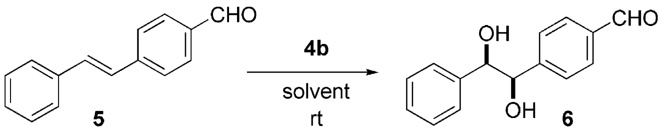
Table 2. Asymmetric dihydroxylation with recycled **4c** resin[a]

Run	Time (h)	Conversion (%)	ee (%)[b]
1	3	99	96
2	4	99	96
3	6	99	97
4	10	99	97
5	12	99	96

[a] Asymmetric dihydroxylation of **5** was carried out using $(DHQD)_2$ PHAL ligand.

[b] Determined by chiral HPLC analysis.

Table 1. Dihydroxylation of **5** with resins (**4a–d**) in various solvents[a]



Entry	Resin	Time (h)	Solvent	Conversion (%)
1	**4b**	24	H_2O–acetone–CH_3CN (1:1:1)	13
2	**4b**	24	H_2O–CH_3CN (1:1)	1
3	**4b**	24	H_2O–CH_3CN (1:2)	4
4	**4b**	24	H_2O–CH_3CN (1:4)	14
5	**4b**	24	H_2O–CH_3CN (1:9)	70
6	**4a**	12	H_2O–CH_3CN (1:9)	27
7	**4b**	12	H_2O–CH_3CN (1:9)	33
8	**4c**	12	H_2O–CH_3CN (1:9)	99
9	**4d**	12	H_2O–CH_3CN (1:9)	76

[a] All reactions were carried out with **5** (0.1 mmol), **4a–d** (2 mol %) and NMO (0.15 mmol) in solvent (1.5 mL); all data within Table 1 are % conversion of **5** as determined by HPLC.

Table 3. Asymmetric dihydroxylation of several olefins with recycled **4c** resin[a]

Entry	Olefins	Yield (%)[b]	ee (%)[c]
1	Styrene	97	88
2	4-Methoxystyrene	88	99
3	*trans*-Stilbene	96	98
4	*trans*-4-Stilbene carboxaldehyde	99	97
5	Methyl-*trans*-cinnamate	89	99

[a] All reactions were carried out with the olefins (1.0 mmol), **4c** (2 mol %), $(DHQD)_2$ PHAL (3 mol % for first use, 1.4 mol % for cycles 2–5), and NMO (1.5 mmol) for 6–24 h at room temperature.

[b] Isolated yield.

[c] Determined by chiral HPLC analysis.

consistently obtained in excellent conversion/yield (99%) and enantioselectivity (96–97% ee). Notably, when the reaction was performed without additional chiral ligand after the first use, 88% ee was obtained. This result implies that a significant amount of $(DHQH)_2$PHAL ligand might also be immobilized onto the ionic polymer in the form of an osmium–ligand complex. These promising findings allowed us to reduce the amount of the $(DHQH)_2$PHAL ligand to 0.7 equiv relative to OsO_4 without any reduction of enantioselectivity. The filtrates from recycled reactions were analyzed for osmium metal by ICP-AES analysis to quantitate catalyst retention and leaching. A small amount of osmium metal was found in the filtrates (4%, 5%, 4%, 3%, and 3%).

To demonstrate the utility of resin **4c**, the AD reaction was performed using other olefins, and the results are summarized in Table 3.[10] The results as shown in Table 3 were obtained using a single catalyst that was recovered after each use (between different olefins), thus demonstrating recyclability of the immobilized catalyst without cross-contamination. All corresponding diols were obtained in good yield and enantioselectivity.

In summary, we have applied short-length PEGylated ionic polymers to immobilize osmium tetroxide by the interaction between ions and induced dipole of OsO_4 in the same manner as ionic liquids. The resulting OsO_4-immobilized ionic polymers are air-stable, nonvolatile, and much easier to handle and recycle than soluble OsO_4. [^{30}P/S-PEG$_3$][BF$_4$](OsO$_4$) (**4c**) resin showed excellent catalytic performance in the AD reaction of various olefins and could be recycled several times without any loss of yield or enantioselectivity. Significant immobilization of the chiral ligand was observed, which allowed reduction of the ligand, hence reduction in costs of subsequent reactions using the same immobilized catalyst. Investigations into improved ionic polymers where metal leaching is reduced will be reported in due course.

Acknowledgments

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Supplementary data

The supplementary data describing the experimental procedures for the preparation of resins and their applications in the AD reaction are available online with the paper in ScienceDirect at doi:10.1016/j.tetlet.2005.04.113.

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10. Typical procedure for asymmetric dihydroxylation of various olefins: To a suspension of [^{30}P/S-PEG$_3$]-[BF$_4$](OsO$_4$) (**4c**) (110 mg, 2 mol %) and NMO (176 mg, 1.50 mmol) in H_2O–acetonitrile (1:9) (12 mL), 300 μL (3 mol %) of 0.1 M solution of $(DHQD)_2$ PHAL in acetonitrile was added. After shaking for 30 min, olefin (1.00 mmol) was added. The mixture was shaken until the reactant olefin was entirely consumed (monitored by TLC). The reaction mixture was filtered with a plastic syringe equipped with a polyethylene frit. The crude mixture was purified by flash column chromatography. The filtered resin was washed with acetonitrile three times and dried under reduced pressure. This recovered resin was reused in the same procedure with 140 μL (1.4 mol %) of 0.1 M solution of $(DHQD)_2$PHAL in acetonitrile.