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Catalytic Asymmetric Dihydroxylation of Olefins with New Catalysts: The First Example of Heterogenization of OsO_4^{2-} by Ion-Exchange Technique

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Osmium-catalyzed asymmetric dihydroxylation of olefins provides one of the most elegant methods for the preparation of chiral vicinal diols.[1] Although the reactions could be applied to the synthesis of pharmaceuticals, fine chemicals, and so forth, the high cost, toxicity, and possible contamination of osmium catalysts in the products restrict its use in industry. Heterogenization of the ligands on polymer or silica gel support and eventual complexation with osmium, a possible solution to address this issue attempted by several groups, failed to recover and reuse the osmium, since the coordination of anchored ligands and osmium tetroxide is in equilibrium.[2−4] The microencapsulation technique adopted by Kobayashi to envelop osmium tetroxide in the polymer capsule afforded a recoverable and reusable osmium catalyst for asymmetric dihydroxylation.[5] Recently Jacobs et al. immobilized OsO_4 on silica through a tetrasubstituted olefin and used for achiral dihydroxylations only.[6]

In this communication, we report the design of an ion-exchange technique for the development of recoverable and reusable osmium catalysts immobilized on layered double hydroxides (LDH), modified silica and resin for asymmetric dihydroxylation of olefins for the first time. The catalysts thus developed through ion-exchange technique show higher performance over Kobayashi catalyst in terms of activity and ee.

To understand the scope and generality of ion-exchange technique for immobilization of osmate catalyst, various ion exchangers sourced from inorganic and organic materials[7,8] were prepared and examined in dihydroxylation reactions. Layered double hydroxides (LDH) consist of alternating cationic $M(II)_{1-x}$-$M(III)_x\ (OH)_2^{x+}$ and anionic $A^{n-}\cdot zH_2O$ layers. The positively charged layers in layered double hydroxides (LDH) contain edge-shared metal M(II) and M(III) hydroxide octahedra, with charges neutralized by A^{n-} anions located in the interlayer spacing or at the edges of the lamellae. LDHs have recently received much attention in view of their potential usefulness as anion exchangers[7a−c] and catalysts.[9] Small hexagonal LDH crystals with $Mg_{1-x}Al_x(OH)_2(Cl)_x\cdot zH_2O$ composition are synthesized following existing procedures (here $x = 0.25$).[7c] OsO_4^{2-} is exchanged onto the chloride-saturated LDH to obtain LDH−OsO_4. X-ray powder diffraction patterns of the initial LDH and the LDH−OsO_4 hardly differ in the range $2\theta = 3{-}65°$. The observed d_{003} basal spacing of the support that appeared at ~7.8 Å remained unchanged after the anion exchange, which indicates that OsO_4^{2-} is mainly located in edge positions.

Similarly, the OsO_4^{2-} is also exchanged onto quaternary ammonium groups of silica and organic resin to obtain SiO_2−OsO_4 and resin−OsO_4. All of these catalysts are well characterized[10] by IR and UV-DRS, which indicate that the majority of the osmate is unaffected during the exchange process except for experiencing very weak interaction with the support. The osmium content in the catalysts LDH−OsO_4 (0.975 mmol g^{-1}), resin−OsO_4 (0.641 mmol g^{-1}), and SiO_2−OsO_4 (0.317 mmol g^{-1}) is determined by SEM-EDX and counterchecked with the quantitative analysis of potassium halide formed in the exchange process.

The exchanger−OsO_4 catalysts thus prepared are first screened for achiral dihydroxylation of *trans*-stilbene. In a general experimental procedure, a mixture composed of *trans*-stilbene, *N*-methylmorpholine *N*-oxide (NMO), and 1 mol % of catalyst in H_2O−CH_3CN−acetone (1:1:1) was stirred at room temperature. After completion of the reaction (2−5 h), the catalyst was filtered and washed with methanol to obtain the corresponding diol.[10] An activity profile of the dihydroxylation of *trans*-stilbene with various exchanger−OsO_4 catalysts conducted under similar conditions described in Figure 1 reveals that LDH−OsO_4 displays the highest activity and the heterogenized catalysts in general have distinctly faster reactivity than $K_2OsO_4\cdot 2H_2O$. The large positive electric potential and spatial organization of the exchanger−OsO_4 may be responsible for the superior performance. This result is in consonance with LDH−WO_4-catalyzed oxidative bromination[7a] and ionic polymer-supported osmium tetroxide in achiral dihydroxylation.[4a] All of these catalysts are reused for five cycles with consistent activity.

Encouraged by these promising results, we then performed asymmetric dihydroxylation of olefins according to the Sharpless procedure[11] using the exchanger−OsO_4 catalysts (Scheme 1). We chose *trans*-stilbene as a model, and varying conditions are examined. When *trans*-stilbene was added to a mixture of LDH−OsO_4, 1,4-bis(9-O-dihydroquinidinyl)phthalazine $(DHQD)_2PHAL)$, a chiral ligand (1 mol % each) and NMO, the desired diol is obtained in 96% yield with 99% enantiomeric excess (ee).[12] Similarly, excellent ees are obtained with resin−OsO_4 and SiO_2−OsO_4 in the dihydroxylation of *trans*-stilbene.[10] The LDH−OsO_4 is further subjected to the dihydroxylation of other olefins, and

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[12] Experimental procedure is as follows: Exchanger−OsO_4 (0.01 mmol), $(DHQD)_2PHAL$ (7.8 mg, 0.01 mmol), and *N*-methylmorpholine *N*-oxide (NMO, 1.3 mmol) were taken in a round-bottomed flask containing ^{t}BuOH-water (1:1, 6 mL) and stirred at room temperature. To this mixture was added an olefin (1 mmol) slowly for 12 h. After completion of the reaction, the catalyst was filtered and washed with methanol. Ethyl acetate and 1 N HCl were added to the combined filtrates. The chiral ligand was recovered from the aqueous layer. After removing the solvent, the crude material was chromatographed on silica gel to afford the corresponding *cis*-diol.

[13] Our preliminary experiments revealed that the use of exchanger-OsO_4, $(DHQD)_2PHAL$ and potassium ferricynide also worked well to afford the desired diols in high yields and ees without resorting to slow addition. Details will be reported in due course.

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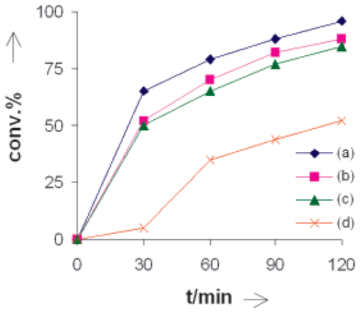


Figure 1. An activity profile of the dihydroxylation of *trans*-stilbene with NMO as oxidant in H_2O–CH_3CN–acetone (1:1:1) solvent by (a) LDH–OsO_4, (b) resin–OsO_4, (c) SiO_2–OsO_4, (d) K_2OsO_4•$2H_2O$.

Scheme 1. Dihydroxylation of *trans*-Stilbene

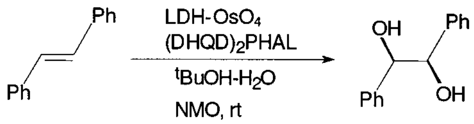
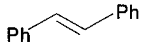
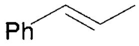
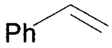
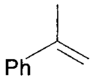
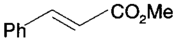
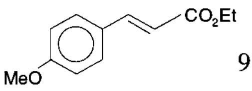
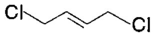
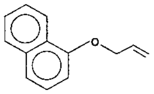
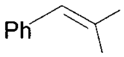


Table 1. Asymmetric Dihydroxylation of Olefins with LDH–OsO_4

Entry	Olefin	Isolated yield(%)	ee(%)[a]	Abs. config.[b]
1		96	99	RR
2		97	97	RR
3		94	95	R
4		89	90	R
5		96	99	2S,3R
6		93	99	2S,3R
7		90	82[c,d]	SS
8		94	77[c,d]	S
9		92	91[d]	R

[a] Determined by HPLC analysis. [b] The absolute configuration was determined by comparison of the specific rotation with literature value. [c] Determined by comparison of specific rotation with literature value. [d] Two equivalents of TEAA is used.

the results are summarized in Table 1. Slow addition of olefin to the reaction mixture is warranted except in case of *trans*-stilbene (as indicated above) to keep the availability of the olefin at a bare minimum level to achieve higher ee.[10,14] Various olefins ranging from mono- to trisubstituted, activated to simple, are subjected to dihydroxylations. In most cases, the desired diols are formed in higher yields, albeit with almost similar ees as reported in the homogeneous system. The trisubstituted olefin is also dihydroxylated to the corresponding diol with higher ee in the presence of tetraethylammonium acetate (TEAA) additive (Table 1, entry 9). This phenomenon substantiates that the hydrolysis of osmate ester, a pronounced slow process in case of trisubstituted olefin, is accelerated with the addition of the additive to afford higher yield and ee.[11,12]

The present LDH–OsO_4 is superior in terms of activity, enantioselectivity, and scope of the reaction on comparison with that of Kobayashi catalyst. For example, the present LDH–OsO_4 catalyst is 30-fold more active than the Kobayashi catalyst in achiral dihydroxylation of *trans*-β-methylstyrene.[5b,10] Second, the scope of the LDH–OsO_4 is extended successfully to encompass stilbene (entry 1), cinnamates (entries 5,6), and aryl allyl ether (entry 8) in the present studies over the Kobayashi methodology,[5b] because these chiral diol derivatives are important intermediates to several chiral ligands and drugs such as taxol, diltiazem, propranolol, and so forth. As to the enantioselectivities in asymmetric dihydroxylation, the present system offers distinctly higher ees 90 and 91% as against the 78 and 85% with Kobayashi catalyst for entries 4 and 9, respectively.

The osmate in all the exchangers is localized on the surface. This assumes significance in particular in LDH, wherein the other possible option of intercalation of osmate is ruled out. The complexation of the large chiral ligand, $(DHQD)_2PHAL$ is only possible with the OsO_4^{2-} located at the edge (surface), as accessibility of the chiral ligand to OsO_4^{2-} present in very small interlamellar space, 3 Å of LDH is very remote. These results reconfirm the presence of OsO_4^{2-} at the surface of the LDH as is evident from XRD.

The LDH–OsO_4 was recovered quantitatively by simple filtration, and the chiral ligand was also recovered by simple acid/base extraction (>95% recovery). The recovered catalyst along with the replenished chiral ligand (to make up 1 mol %) was reused, and consistent activity was noticed even after the fifth cycle.[10] When the reaction was conducted with the filtrate obtained by treatment of the catalyst in a solvent system for prolonged time, no product formation was observed. The absence of osmium in the filtrate is further reconfirmed using the iodometry test.[5b] All the catalysts exhibited similar trend, when subjected to the above protocol. It is thus unambiguously demonstrated that osmium was bound to the support, while undergoing redox cycle Os(VI)/Os(VIII) during the reaction. The neutral Os(VIII) complex formed during reaction is physisorbed on the support.[10]

In summary, the active osmium catalysts are readily prepared from nonvolatile, K_2OsO_4•$2H_2O$ by a simple ion-exchange technique on various supports such as LDH, organic resin, and silica. These catalysts afford chiral diols with high yields and ee's having consistency over a number of cycles, which contributes to the development of benign chemical processes and products.

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Supporting Information Available: Experimental details, preparation and characterization of catalysts as well as products of the reaction (PDF). This material is avilable free of charge via the Internet at http://pubs.acs.org.

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