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Heterogeneous catalytic asymmetric aminohydroxylation of olefins using LDH-supported OsO_4

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Abstract

Recently prepared layered double hydroxides (LDH)-supported OsO_4, developed by the ion-exchange technique, was employed for catalytic asymmetric aminohydroxylation (AA) of olefins of varied nucleophilicity using Chloramine-T and $(DHQ)_2PHAL$ to afford chiral vicinal N-protected amino alcohols, important building blocks for many biologically active compounds and precursors for chiral ligands with moderate yields and ee's for the first time. Strong electron deficient olefins undergo AA reaction offering better yields than the less electron deficient and electron rich olefins due to the greater polarization of Os=NTs group in the former. The catalyst could be reused without any loss of enantioselectivity albeit a reduced activity.

Keywords: Amino alcohols; Asymmetric catalysis; Aminohydroxylation; Chloramine-T; LDH-OsO_4

1. Introduction

The asymmetric aminohydroxylation (AA) of olefins using catalytic amounts of potassium osmate $K_2OsO_4{\cdot}2H_2O$ in the presence of cinchona alkaloid derivatives has become the most powerful method for the preparation of a wide variety of enantiomerically pure amino alcohols [1–4]. The resulting chiral amino alcohols are the most abundant structural units present in the biologically active compounds as well as the precursors for many chiral ligands [5–7]. Further, the products obtained by the AA process can be easily transformed into aziridines or into precursors for α,β-diaminoacids [8].

Heterogenization of enantioselective catalysis is particularly attractive because it allows production and ready separation of large quantities of chiral products while using a small amount of catalyst. Although the AA reaction offers a number of processes that could be employed in the synthesis of pharmaceuticals, fine chemicals, etc., the high cost, toxicity, and a possible contamination of the osmium catalyst in the products restrict its use in industry. The AA reaction by the use of heterogenized quinine ligands have been reported in the literature. Heterogenization of the ligands on polymers [9,10] or silica gel support [11] and eventual complexation with osmium does not allow one to recover and reuse osmium from the AA reactions as the affinity of anchored ligands for osmium tetroxide is weak.

With the divergent conceptual approach, we designed and developed an ion-exchange technique for the preparation of recoverable and recyclable osmium

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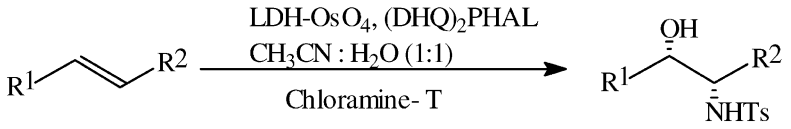


Scheme 1.

catalyst immobilized on layered double hydroxides (LDH) by the ion-exchange of OsO_4^{2-} and performed the asymmetric dihydroxylation of olefins successfully [12,13]. In this article, we report the use of LDH-OsO_4 in AA of various olefins to chiral vicinal N-protected amino alcohols for the first time with modest yields and enantioselectivities (Scheme 1).

In an effort to understand the scope and usefulness of the ion-exchange technique, AA of olefins was carried out employing Chloramine-T as a nitrogen source and oxidant, 1,4-bis (9-*O*-dihydroquininyl) phthalazine ($(DHQ)_2$PHAL) as a chiral ligand and layered double hydroxides-supported OsO_4 (LDH-OsO_4) as a catalyst prepared by the ion-exchange technique. LDHs have recently received much attention in view of their potential usefulness as anion exchangers and catalysts [14–17]. LDH is a class of layered material consisting of alternating cationic $M(II)_{1-x}M(III)_x(OH)_2^{X+}$ and anionic $A^{n-}\cdot zH_2O$ layers. The cationic layers are separated from each other by anions and water molecules. The positively charged layers in LDH contain edge shared metal(II) and metal(III) hydroxide octahedra, with charges neutralized by A^{n-} anions located in the interlayer spacing or at the edges of the lamellae. Small hexagonal LDH crystals with $Mg_{1-x}Al_x(OH)_2(Cl)_x\cdot zH_2O$ were synthesized following existing procedure. OsO_4^{2-} was exchanged onto chloride saturated LDH to obtain LDH-OsO_4 and was well characterized [12].

2. Experimental

$K_2OsO_4\cdot 2H_2O$, $MgCl_2\cdot 6H_2O$, $AlCl_3$, $(DHQ)_2$PHAL, Chloramine-T trihydrate and all olefins were purchased from Aldrich and used as such without further purification except Chloramine-T trihydrate, which was re-crystallized before use. All the other solvents and chemicals were obtained from commercial sources and purified using standard methods.

2.1. Preparation of LDH-OsO_4

The preparation of LDH (Mg–Al–Cl) was based on literature procedure [16]. A mixture of $MgCl_2\cdot 6H_2O$ and $AlCl_3\cdot 6H_2O$ was dissolved in deionized water. To this aqueous solution was slowly added 2 M NaOH solution at 25 °C and a further amount of 2 M NaOH solution was added to maintain a pH of 10 under nitrogen flow. The resulting suspension was stirred at 70 °C. The solid product was isolated by filtration, washed thoroughly with deionized water, and dried overnight at 80 °C. All of the synthetic steps were carried out using decarbonated water.

2.1.1. LDH-OsO_4

An amount of 1.5 g of LDH (Mg–Al–Cl) was suspended in 150 ml of 0.689 g (1.87 mmol) aqueous potassium osmate solution and stirred at 25 °C for 12 h under nitrogen atmosphere. The solid catalyst was filtered, washed thoroughly with 500 ml of water and vacuum dried to obtain 1.916 g of LDH-OsO_4 (0.975 mmol of Os/g).

2.2. General procedure

In a typical reaction, an olefin (1 mmol), LDH-OsO_4 (4 mol%), $(DHQ)_2$PHAL ligand (5 mol%), Chloramine-T (3 eq.) were taken in a round-bottomed flask containing acetonitrile–water (1:1, 15 ml) and stirred for 24 h at room temperature. After completion of the reaction (by TLC analysis), the reaction mixture was quenched by addition of aqueous sodium sulfite; this caused phase separation. The catalyst was filtered and washed with ethyl acetate. The aqueous phase was separated and extracted with ethyl acetate. The combined organic phases were dried over $MgSO_4$ and concentrated to afford the crude product (impurities were mainly *p*-toluene sulfonamide and diol). The crude material was chromatographed on silica gel to afford the corresponding chiral vicinal N-protected amino alcohol.

2.2.1. Methyl (2R,3S)-N-(p-toluenesulfonyl)-3-amino-3-phenyl-2-hydroxypropanoate

^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.6$–7.1 (m, 9H), 5.75 (m, 1H), 4.8 (m, 1H), 4.3 (brs, 1H), 3.7 (s, 3H), 3.3 (s, 1H), 2.3 (s, 3H). HPLC (Daicel Chiralcel OG, 30% *i*-PrOH/hexane, flow rate $= 1\,ml\,min^{-1}$) 21.8 min (2S,3R), 28.3 min (2R,3S).

2.2.2. Ethyl (2R,3S)-N-(p-toluenesulfonyl)-3-amino-2-hydroxybutanoate

^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.8$–7.3 (m, 9H), 3.94 (m, 1H), 3.81 (qdd, $J = 9.4$, 6.9, 2.7 Hz, 1H) 3.4 (brs, 1H), 2.5 (brs, 1H), 2.3 (s, 3H), 1.25 (d, $J = 6.9$ Hz, 3H). HPLC (Daicel Chiralcel OD-H, 15% *i*-PrOH/hexane, flow rate $= 1\,ml\,min^{-1}$) 7.5 min (2S,3R), 13.4 min (2R,3S).

2.2.3. (1S,2S)-N-(p-toluenesulfonyl)-2-amino-1,2-diphenylethanol

^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.4$–7.2 (m, 9H), 5.42 (d, $J = 7$ Hz, 1H), 4.84 (m, 1H), 4.4 (m, 1H), 2.3 (s, 3H), 1.45 (brs, 1H). HPLC (Daicel Chiralcel OD-H, 15% *i*-PrOH/hexane, flow rate $= 1\,ml\,min^{-1}$) 16.2 min (1S,2S), 26.0 min (1R,2R).

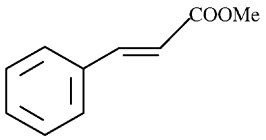
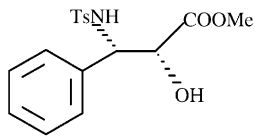
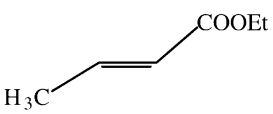
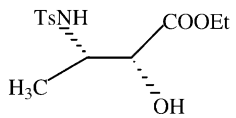
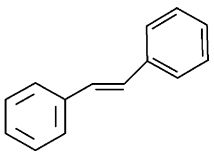
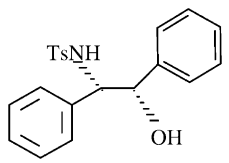
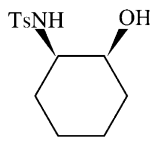
2.2.4. (1S,2R)-N-(p-toluenesulfonyl)-2-amino-1-hydroxycyclohexane

^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.8$ (d, $J = 7$ Hz, 2H), 7.4 (d, $J = 7$ Hz, 2H), 5.12 (d, $J = 5.5$ Hz, 1H), 3.8 (brs, 1H), 3.25 (m, 1H), 2.5 (s, 3H), 2.1 (brs, 1H), 1.85–1.1 (m, 8H). HPLC (Daicel Chiralcel OG, 15% *i*-PrOH/hexane, flow rate $= 0.5\,ml\,min^{-1}$) 28.5 min (1S,2R), 34.4 min (1R,2S).

3. Results and discussion

LDH-OsO_4 (4 mol%) catalyzed AA of olefins of different nucleophilicty using 3 eq. of Chloramine-T as an oxidant and nitrogen source and $(DHQ)_2$PHAL ligand (5 mol%) in acetonitrile and water (1:1) solvent system at room temperature affording chiral vicinal N-protected amino alcohols in moderate yields and enantioselectivity. Decreasing the amount of

Table 1
Asymmetric aminohydroxylation of olefins with LDH-OsO_4[a]

Entry	Substrate	Product	Isolated yield	ee (%)[b] $(DHQ)_2$PHAL
1			55	78
2			50	72
3			45	60
4			50	40

[a] Olefin (1 mmol), Chloramine-T (3 eq.), $(DHQ)_2$PHAL (5 mol%), and LDH-OsO_4 (4 mol%) in H_2O–acetonitrile (1:1, 15 ml) were stirred at room temperature for 24 h.

[b] The absolute configuration was determined by comparison of the specific rotation with literature value.

Chloramine-T reduces the yields of the AA reaction. The results are summarized in Table 1. The data show that all reactions examined using LDH-OsO_4 exhibited moderate yields and enantioselectivities in AA of olefins. Diols are formed in significant amounts in AA reactions. The product distribution in the AA of methyl cinnamate in terms of regioselectivity of C_3/C_2 is 5:1. Strong electron deficient methyl cinnamate (entry 1) and ethyl crotonate (entry 2) undergo AA reaction offering better yields than the less electron deficient stilbene (entry 3), and electron rich cyclohexene (entry 4), which is in consonance to the results obtained by homogeneous osmate reaction due to the greater polarization of Os=NTs group in the former [4]. The AA of methyl cinnamate provides (2R,3S)-*N*-(*p*-toluenesulfonyl)-2-hydroxy-3-amino-3-phenyl propanoate, a precursor of taxol side chain, in good yields and enantioselectivites. The ee's and yields obtained by the LDH-OsO_4 are little lower (2–5%) to the results reported by Sharpless and co-workers [1].

LDH-OsO_4 was recycled for three cycles in AA of stilbene, in which consistent enantioselectivity is noticed, although the catalyst is deactivated in each cycle (Fig. 1). The deactivation is ascribed to the leaching of the osmium species. Slow addition of oxidant has not improved recyclability. The XPS of the osmium (Fig. 2) in the fresh and used catalysts show $4f_{7/2}$ and $4f_{5/2}$ lines corresponding to the Os(VI) oxidation state. The osmium content of the used catalyst is estimated as 40% of the fresh catalyst at the end of the third recycle as determined by AAS. It is thus observed that

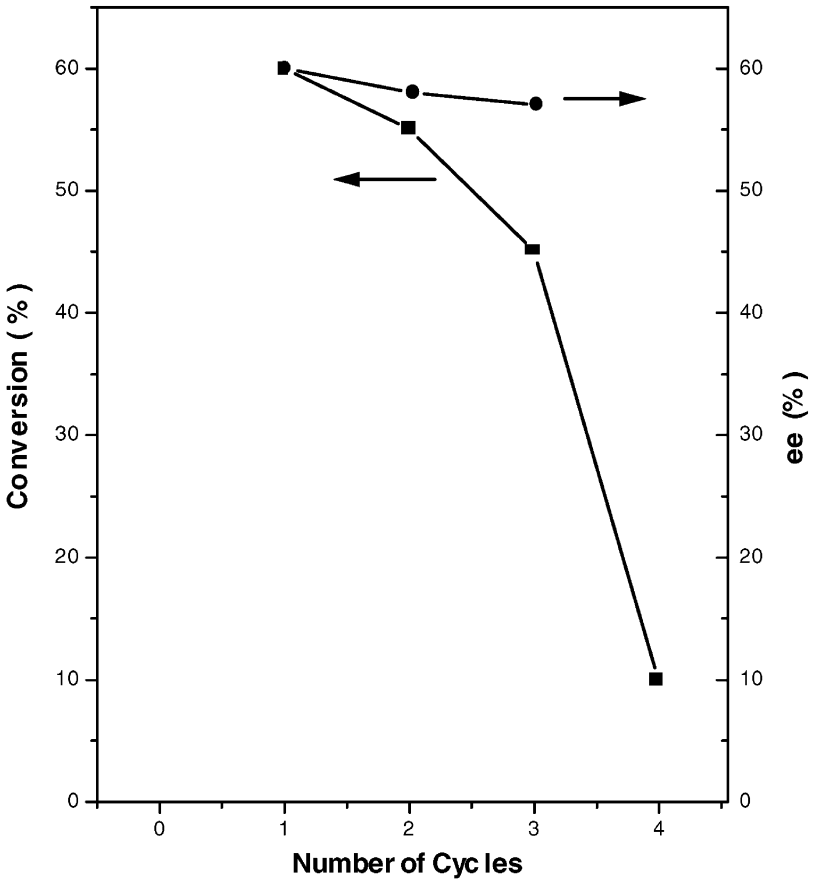


Fig. 1. Recycle profile: conversion (left-hand side scale) and enantioselectivity (right-hand side scale) of the LDH-OsO_4 in AA of *trans*-stilbene.

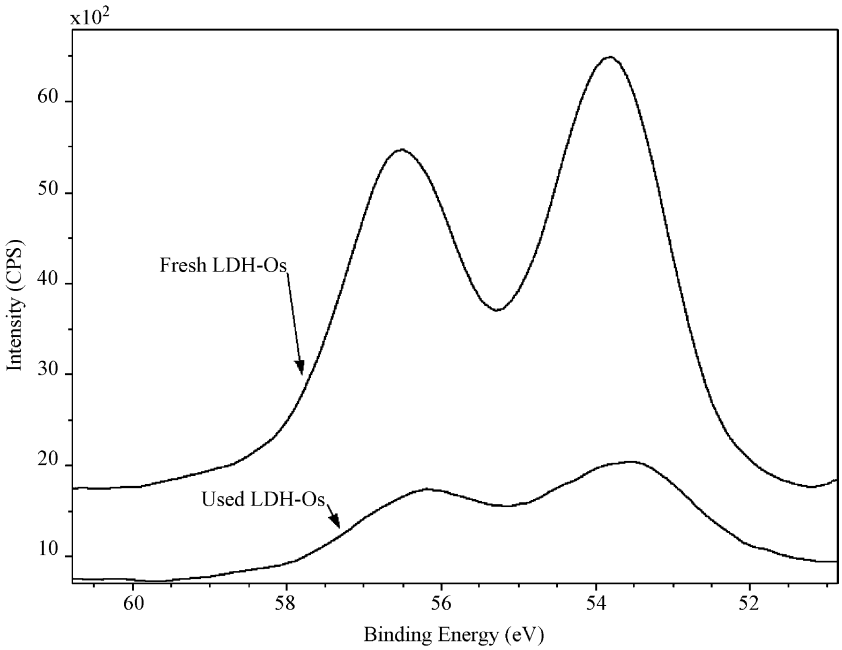


Fig. 2. XPS data of fresh and used LDH-OsO_4.

the 10% conversion is not directly proportional to the osmium content in the catalyst. Some of the catalyst is likely poisoned during the reaction. In order to understand the heterogeneity of the reaction, we conducted two experiments, which are described as follows.

3.1. Experiment 1

A mixture of the LDH-OsO_4, Chlormine-T, stilbene was stirred for 24 h in CH_3CN:H_2O. After completion of the reaction, the catalyst was removed by filtration. To the filtrate, methyl cinnamate and Chloramine-T were added and stirred at room temperature for 24 h. The amino alcohol was obtained in 15% yield.

3.2. Experiment 2

LDH-OsO_4 was treated with Chloramine-T under stirring for 24 h in CH_3CN:H_2O. *trans*-Stilbene was then added and after the completion of the reaction, the catalyst was recovered. Two separate experiments were conducted both with recovered catalyst and filtrate as described. Recovered catalyst, methyl cinnamate and Chloramine-T in CH_3CN:H_2O were stirred for 24 h. The amino alcohol was obtained in 10% yield. To the filtrate, methyl cinnamate and Chloramine-T were added and stirred at room temperature for 24 h. The amino alcohol was obtained in 70% yield.

In the experiment 1 wherein the reaction was conducted in the presence of the olefin, the leaching is somewhat averted and the reaction proceeds predominantly on the heterogeneous phase. Result of the experiment 2 strongly suggests that the leached Os species on treatment with Chloramine-T in the absence of olefin could not be re-exchanged on the support during the reaction. Therefore, the LDH-OsO_4 is not acting as a reservoir.

Earlier studies indicated that the OsO_4 leaches from LDH-OsO_4 in presence of oxidant and without olefin [12,13]. However, the catalyst is robust during the AD reaction, which was recyclable for several times with consistent activity and selectivity. In the present AA reaction, the strong oxidant Chloramine-T had a deleterious effect causing slow leaching of OsO_4 from the catalyst. As the reactivity pattern is almost identical to that of homogeneous reaction, a similar redox cycle of osmium holds good.

4. Conclusion

In summary, the active LDH-OsO_4 is readily prepared from the non-volatile $K_2OsO_4 \cdot 2H_2O$ by a simple ion-exchange technique. The catalyst affords chiral vicinal N-protected amino alcohols with modest yields and enantioselectivites in AA of olefins.

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