Bifunctional Catalysts Stabilized on Nanocrystalline Magnesium Oxide for One-Pot Synthesis of Chiral Diols

Boyapati M. Choudary,* Karangula Jyothi, Moumita Roy, Mannepalli L. Kantam, Bojja Sreedhar

Indian Institute of Chemical Technology, Hyderabad 500 007, India
Fax: (+91)-40-2716-0921,e-mail: choudary@iict.res.in

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Abstract: New bifunctional catalysts composed of $PdCl_4^{2-}$, OsO_4^{2-} and OsO_4^{2-}, WO_4^{2-} designed and prepared by a counterionic stabilization technique involving the reactions of Na_2PdCl_4-K_2OsO_4 and K_2OsO_4-Na_2WO_4 with nanocrystalline MgO are well characterized. These bifunctional catalysts, NAP-Mg-PdOs and NAP-Mg-OsW perform tandem Heck asymmetric dihydroxylation and asymmetric dihydroxylation-*N*-oxidation reactions, respectively, in the presence of the chiral ligand 1,4-bis(9-*o*-dihydroquinidinyl)phthalazine [$(DHQD)_2PHAL$] in a single pot. It is quite impressive to note that H_2O_2 is used as a terminal oxidant to provide *N*-methylmorpholine *N*-oxide (NMO) *in situ* by the oxidation of *N*-methylmorpholine (NMM) in the asymmetric dihydroxylation-*N*-oxidation catalyzed by NAP-Mg-OsW.

Keywords: asymmetric synthesis; bifunctional catalysis; chiral diols; counterionic stabilization; nanocrystalline magnesium oxide

Introduction

The performance of multistep syntheses in one pot, prevalent in biosystems, is an attractive strategy to improve the efficiency of organic processes in terms of conservation of energy, lowering the process time and inventory of equipment and minimizing the use of chemicals and the production of waste.[1] Significant progress using a combination of two catalysts for effecting tandem reactions has been achieved.[2] The recent design of a single matrix bifunctional catalyst comprising a BINOL-BINOP copolymer for the tandem asymmetric diethylzinc addition and hydrogenation of acetylbenzaldehydes marks a new era in bifunctional catalysis.[3]

The Sharpless catalytic asymmetric dihydroxylation (AD) of olefins, an inspiring invention, provides the most elegant method for the preparation of chiral vicinal diols.[4a–d] Chiral vicinal diol units are often observed as key structures of natural products and are also used in the synthesis of chloramphenical (broad-spectrum antibiotic), diltiazem hydrochloride (calcium channel blocker), the taxol side chain, macrocyclic antitumor drugs and β-lactams. Although the AD reaction offers a number of processes that could be applied to the synthesis of pharmaceuticals, fine chemicals, etc., the high cost, toxicity and possible contamination of osmium catalysts in the products restrict its use in industry. Heterogenization of OsO_4 *via* microencapsulation,[4e–h] an ion-exchange technique,[5] and covalent anchoring[6] is employed to address the issue of complete recovery of osmium from the reaction medium.

An interesting development was made by Bäckvall et al. in realizing the higher economical process by using H_2O_2, the stoichiometric oxidant, and *N*-methylmorpholine (NMM) in catalytic amounts to continuously generate *N*-methylmorpholine *N*-oxide (NMO) *in situ via* oxidation using biomimetic flavin[7a, b] or vanadyl acetylacetonate[7c] as the electron transfer mediator in a multicomponent catalytic system for the AD reaction of olefins. We demonstrated the reoxidation of NMM to facilitate continuous *in situ* production of NMO to sustain the Os(VI)/Os(VIII) catalytic cycle induced by a bifunctional heterogeneous catalyst composed of osmium and tungsten oxides on the single matrix using H_2O_2 as the terminal oxidant.[5c] Recently, we immobilized osmium tetroxide on nanocrystalline MgO by the counterionic stabilization technique for achiral dihydroxylation.[8] We now report the design and development of new bifunctional heterogeneous catalysts composed of palladium/osmium and osmium/tungsten systems on the nanocrystalline MgO matrix and the performance of Heck-AD and *N*-oxidation-AD reactions using H_2O_2 as the terminal oxidant.

The nanocrystalline metal oxides, MgO, CaO, Al_2O_3 and ZnO are porous inorganic solids in the 4–7 nm particle size range, which make up a new realm of matter in which physical and chemical properties change as size changes. Furthermore, these solids can exist with numerous surface sites with enhanced surface reactivity such as crystal corners, edges or ion vacancies.[9] Nanocrystalline

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metal oxides have attracted great attention due to their unusual magnetic, optical, physical and surface chemical and catalytic properties.[10–16] These nanoporous materials are mainly used as efficient destructive chemisorbents for toxic gases, NO_2, SO_2, SO_3 and HCl, as well as chlorinated and phosphorus-containing compounds.[11] Nanocrystalline MgO is found to be very active in the dehydrohalogenation of chlorohydrocarbons at high temperatures.[12] Due to the high surface area, these nanostructured solid materials exhibit high activity. The reactivity of these materials is further enhanced by depositing very thin layers of transition metal oxides on the crystallites of MgO.[17] The presence of edge-corner and other defect sites allow the nanostructured MgO materials to possess a high concentration of reactive surface ions. The reactive sites on the surface of MgO are as follows:[18] 1) Mg^{2+} site, which is of the Lewis acid type, 2) O^{2-} site which is of the Lewis base type, 3) lattice bound and isolated hydroxyl groups, and 4) anionic and cationic vacancies. The presence of corner and edge sites on the surface of NAP-MgO (aerogel prepared) could approach 20% while on NA-MgO (conventionally prepared) it is less than 0.5% and on CM-MgO (commercially prepared) essentially 0%.[19] For example, an edge, or even more so, a corner O^{2-} anion is coordinatively unsaturated and is seeking Lewis acids (electron-deficient species) to help stabilize and delocalize its negative charge. Conversely, an Mg^{2+} ion on an edge or corner is seeking Lewis bases (electron-rich species) to stabilize and delocalize its positive charge. Therefore, these coordinatively unsaturated O^{2-} and Mg^{2+} ions readily accept incoming reagents with Lewis acid or Lewis base character. The excess positive charge will always be satisfied with an anion deficiency and therefore the structure will not loose its anion exchange capacity during the reaction. The best example is that nano-MgO can absorb up to 13% by weight of Cl_2 in the reaction with chlorine gas at room temperature and atmospheric pressure.[20]

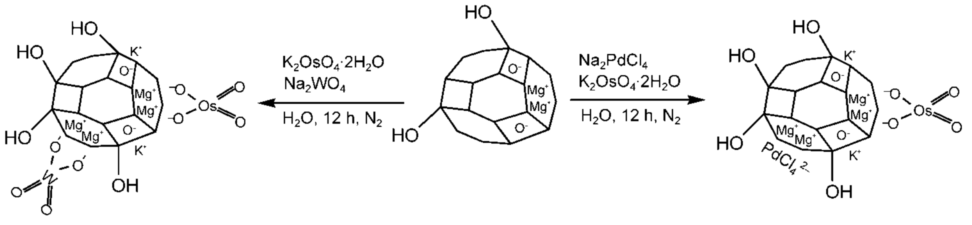
Results and Discussion

Preparation of Crystalline MgO-Supported Catalysts

This situation presents an opportunity to prepare new and unusual materials, wherein the highly reactive ions could be stabilized by forming adducts with the reactive-accepting surface sites on the MgO. In an effort to obtain counterionic stabilization of $PdCl_4^{2-}$, OsO_4^{2-} and WO_4^{2-} with Mg^{2+} of the MgO, commercially available CM-MgO [surface area (SA) 30 m^2/g], conventionally prepared NA-MgO (SA 250 m^2/g) and aerogel prepared NAP-MgO (SA 600 m^2/g) were treated with Na_2PdCl_4, K_2OsO_4 and Na_2WO_4 to afford the samples of Mg-OsO_4, Mg-$PdCl_4$-OsO_4 (Mg-PdOs), and Mg-OsO_4-WO_4 (Mg-OsW). The preparation and characterization of NAP-Mg-OsO_4 catalyst was reported in our earlier communication.[8] In the reaction with NAP-MgO, (SA 600 m^2/g) the entire amounts of Na_2PdCl_4, K_2OsO_4 and Na_2WO_4 used were consumed. On the other hand, a small amount each ($<0.3\%$) of palladate, osmate and tungstate was detected in the treated samples of CM-MgO and NA-MgO. During the preparation of the catalyst, which involves the reaction with Na_2PdCl_4, K_2OsO_4 and Na_2WO_4, the Na^+, K^+ ions will interact with the O^{x-} sites/anionic vacancies. The $PdCl_4^{2-}$, OsO_4^{2-} and WO_4^{2-} will interact with the Mg^{2+} sites/cationic vacancies present on corner or edge of nanocrystalline NAP-MgO to form bifunctional catalysts as described (Scheme 1) for the synthesis of chiral diols successfully in a single pot.

Characterization of Nanocrystalline MgO-Supported Catalysts

All the catalysts developed were well characterized by FTIR, SEM-EDAX and XPS. In the FTIR spectra of these counterionic stabilized catalysts, broad absorption bands appear near 815–860 cm^{-1}, which are assigned to the vibrational asymmetric O=M=O (M = Os and/or W) stretching unlike the sharp bands observed at 819 cm^{-1} in the case of potassium osmate and at 831, 857 cm^{-1} in the case of sodium tungstate spectra. The observation of broad bands in the same region for the catalysts indicates that the osmate and tungstate are unaffected upon counterion stabilization onto the support, while experiencing very weak interactions with the support (Figure 1a). During the preparation of these catalysts, the surface of NAP-MgO was hydroxylated as indicated by non-H-bonded OH groups at 3715 cm^{-1} in the IR (Figure 1b). This is consistent with the reactive profile



NAP-MgOsW NAP-MgO NAP-Mg-PdOs

Scheme 1. Preparation of NAP-MgO supported bifunctional catalysts.

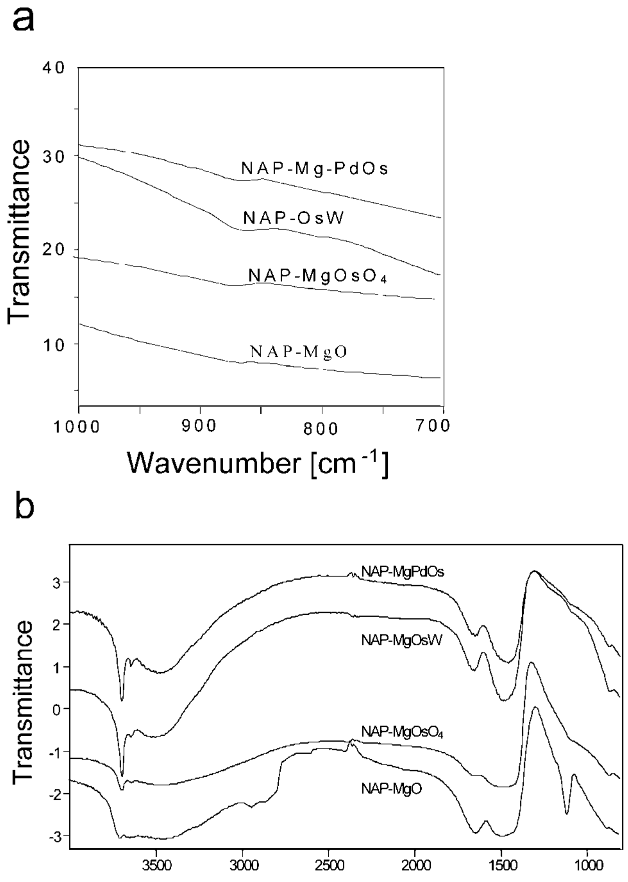


Figure 1. **a** FTIR spectra of NAP-MgO-supported catalysts. **b** During the preparation of NAP-MgO-supported catalysts, the surface of NAP-MgO was hydroxylated as indicated by non-H bonded OH groups at 3715 cm^{-1} in the IR.

Table 1. XPS binding energies for NAP-MgO supported catalysts.

Catalyst	Pd		Os		W	
	$3d_{5/2}$	$3d_{3/2}$	$4f_{7/2}$	$4f_{5/2}$	$4f_{7/2}$	$4f_{5/2}$
NAP-Mg-OsO_4			54.0	56.5		
NAP-Mg-PdOs[a]	336.9	342.3	54.6	57.0		
NAP-Mg-PdOs[b]	337.0	341.9	54.2	56.8		
NAP-Mg-OsW[a]	–	–	54.5	57.0	35.5	37.5
NAP-Mg-OsW[b]	–	–	54.4	57.0	35.0	37.2

[a] Fresh catalyst.
[b] Used catalyst.

of NAP-MgO with water.[21] The surface of the nano-MgO is only hydroxylated to $Mg(OH)_n$, and it takes a longer time and heating to transform the bulk nano-MgO. The XRD of the NAP-Mg-OsO_4, NAP-Mg-PdOs, NAP-Mg-OsW samples also indicate the formation of $Mg(OH)_n$ during the preparative protocol (Figure 2).[22] The SEM-EDX (scanning electron microscopy-energy dispersive X-ray analysis) of NAP-Mg-OsO_4, NAP-Mg-PdOs and NAP-Mg-OsW shows the presence of metals – 8.96% (Os), 3.98% (Pd), 7.15% (Os) and 7.04% (Os), 6.81% (W) in the respective samples. The X-ray photoelectron spectroscopic (XPS) results of the fresh and used bifunctional NAP-Mg-PdOs and NAP-Mg-OsW catalysts show almost identical binding energies for Pd,[23] Os,[24] and W [25] (Table 1). This confirms that the oxidation states of the respective metals remain static during the counterionic stabilization process and at the end of the reaction.

All these results ruled out the formation of bimetallic species. All these studies indicate the retention of the coordination geometries of the specific divalent anions

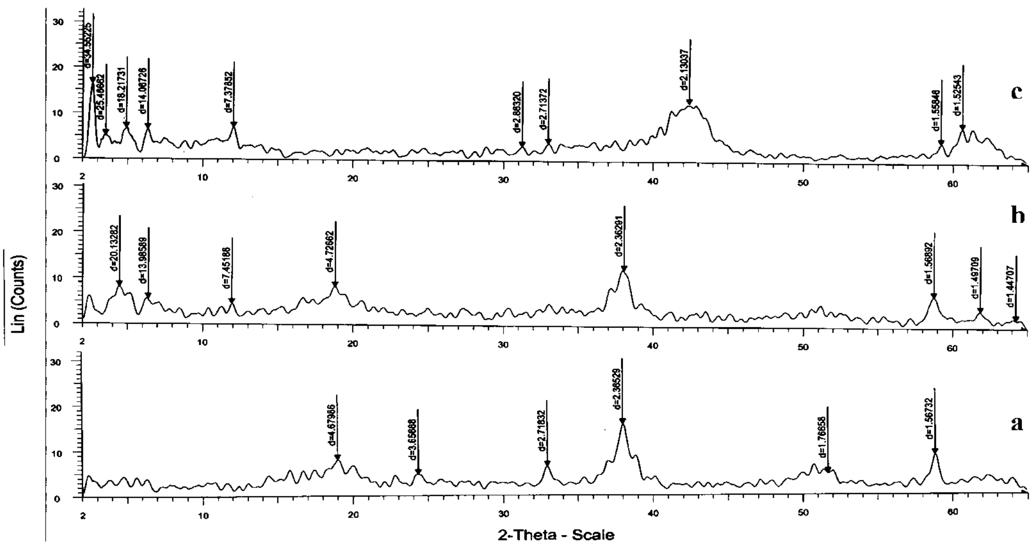
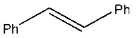
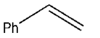
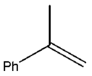
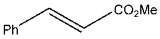
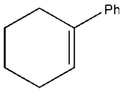


Figure 2. The XRD of the a NAP-$MgOsO_4$, b NAP-Mg-PdOs, and c NAP-Mg-OsW catalysts.

Table 2. Asymmetric dihydroxylation of olefins with NAP-Mg-OsO_4.

Entry	Olefin	Isolated yield [%]	ee [%][a]	Abs. config.[b]
1		85	99	*RR*
2		91	77	*R*
3		90	80	*R*
4		96	94	2*S*,3*R*
5		87	58[c]	1*R*,2*R*

[a] Determined by HPLC analysis.
[b] The absolute configuration was determined by comparison of the specific rotation with the literature value.
[c] 2 equivalents of TEAA were added.

anchored to nano-MgO in their monomeric form upon counterionic stabilization and use.

Asymmetric Dihydroxylation of Olefins

Earlier, NAP-Mg-OsO_4 was found to be an excellent catalyst in the achiral dihydroxylation of olefins. In the present studies, we performed AD of *trans*-stilbene by using NAP-Mg-OsO_4. A mixture of NAP-Mg-OsO_4, NMO, 1 mol % of 1,4-bis(9-*o*-dihydroquinidinyl)phthalazine [$(DHQD)_2PHAL$] ligand was charged into a round-bottomed flask containing *t*-BuOH-H_2O (5:1, 6 mL). *trans*-Stilbene was added to the reaction mixture slowly over a period of 12 h and continued stirring for another 3 h at room temperature afforded the corresponding chiral diol in 85% yield with 99% ee.

NAP-Mg-OsO_4 was further subjected to AD of various olefins and the results are summarized in Table 2. Slow addition of olefin to the reaction mixture is warranted to keep the availability of the olefin at a bare minimum level in order to achieve higher ees. Olefins ranging from mono- to trisubstituted, activated to simple, were subjected to the dihydroxylation. In most cases, the desired diols were formed in higher yields, albeit with reduced ees, when compared with results obtained in the homogeneous system.

The scope of the NAP-Mg-OsO_4 catalyst was extended successfully to the hydroxylation of relatively larger substrates such as stilbene (Table 2, entry 1) and methyl cinnamate (Table 2, entry 4). It is interesting to note that 1) the microencapsulated catalyst developed by Kobayashi was never reported for the AD of the above substrates with NMO cooxidant and 2) these chiral diol derivatives are important intermediates to several chiral ligands and drugs such as taxol, diltiazem, propranolol, etc.

Table 3. Influence of additive and slow addition of olefin on the ee in the AD reaction of methyl cinnamate.

Entry	Catalyst	Additive	Slow addition [h]	ee [%]
1	$K_2OsO_4 \cdot 2\,H_2O$	–	–	88
2	NAP-Mg-OsO_4	–	–	45
3	NAP-Mg-OsO_4	–	12	94
4	NAP-Mg-OsO_4	$Et_3N \cdot HI$	12	95

It is well documented in the literature that bases or, less often, acids are used in the dihydroxylation reactions for the hydrolysis of osmate esters. Additives such as Et_4NOH, Et_4NOAc, Et_4NF, $C_6H_5PO_3(Et_4N)_2$, $(Et_4N)_2CO_3$, HCl, HI and tetraethylammonium salts of chelating diacids such as *o*-phthalic, camphoric and *cis*-1,2-cyclohexanedicarboxylic acids were effectively used to accelerate the hydrolysis of osmium monoglycolate ester and thus prevent the formation of the bisglycolate ester (second cycle) to achieve higher ee.[26] Introduction of additives and/or slow addition of olefin to the reaction mixture to allow the hydrolysis of the formed osmium monoglycolate were also resorted to to obtain higher ee. We conducted experiments to study the influence of the heterogeneous catalyst and $Et_3N \cdot HI$ additive on the ee (Table 3).

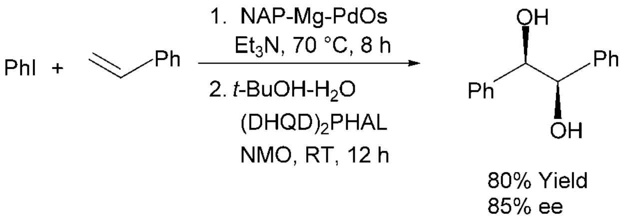
In the AD of methyl cinnamate under homogeneous conditions using the NMO as oxidant in H_2O-*t*-BuOH, 88% ee was obtained without slow addition of olefin. In the AD of methyl cinnamate catalyzed by NAP-Mg-OsO_4 using NMO as the oxidant with slow addition, we obtained 94% ee and in the presence of $Et_3N \cdot HI$ as an additive in *t*-BuOH-H_2O, 95% ee was obtained. The $Et_3N \cdot HI$ salt can accelerate the hydrolysis of the osmium monoglycolate complex to subdue the second cycle as was done by tetraethylammonium acetate, which is known for faster rates and higher ee.[27] The higher ee achieved in this case is attributed to $Et_3N \cdot HI$, which is responsible for the acceleration of the hydrolysis of the osmium monoglycolate ester.

Thus, these results unambiguously demonstrate that in the present system composed of a new variant, $Et_3N \cdot HX$ facilitates the hydrolysis of osmium monoglycolate ester to subdue the formation of bisglycolate ester to achieve higher ee.

One-Pot Synthesis of Chiral Diols

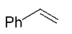
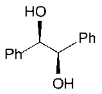
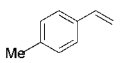
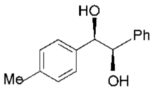
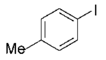
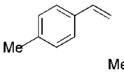
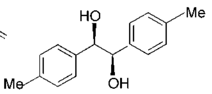
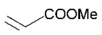
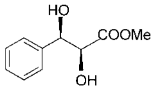
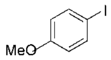
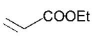
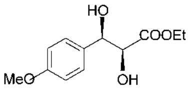
Palladium-Osmium Catalytic System

In order to generate the prochiral olefins *in situ* for the AD reaction, NAP-Mg-PdOs was first tested in a tandem Heck-AD reaction, which involved stirring of iodobenzene, styrene and Et_3N at 70 °C in acetonitrile as solvent for 12 h in the presence of 3 mol % of catalyst to



Scheme 2. Tandem Heck-asymmetric dihydroxylation catalyzed by the NAP-Mg-PdOs bifunctional catalyst.

Table 4. Tandem Heck-AD of olefins catalyzed by heterogeneous bifunctional NAP-Mg-PdOs catalyst.[a]

Entry	Aryl halide	Olefin	Product	Yield [%]	ee [%][b]
1	PhI			80	85
2	PhI			75	67
3				70	82
4	PhI			85	73
5				82	78

[a] Mg-PdOs (3 mol %), aryl halide (1 mmol), olefin (1 mmol) and Et_3N (1.3 mmol) in CH_3CN (2 mL) were stirred at 70 °C for 12–16 h. After completion of the Heck coupling, the heating was stopped and NMO (1.3 mmol) and $(DHQD)_2$ PHAL (7.8 mg, 0.01 mmo) in t-BuOH-H_2O (5:1, 6 mL) were added under stirring.

[b] ee was determined by HPLC analysis.

give *trans*-stilbene. After completion of the reaction, as monitored by TLC, the heating was stopped and a mixture of $(DHQD)_2PHAL$ (1 mol %) and NMO in t-BuOH-H_2O (5:1, 6 mL) was introduced and stirred at room temperature for 12 h to obtain the desired diol in 80% yield with 85% ee (Scheme 2). The methodology described here uses bulk chemicals such as styrene and acrylates as starting materials to prepare the prochiral substrates, stilbenes and cinnamates, *in situ* and upon dihydroxylation gives chiral diols in a single-pot process. The results are outlined in Table 4. This catalyst exhibits good performance for a number of cycles with NMO as cooxidant. After completion of the reaction the catalyst was recovered by simple filtration.

We examined the effect of the solvent on the activity and enantioselectivity in the NAP-Mg-PdOs-catalyzed AD of *trans*-stilbene using NMO as the cooxidant (Table 5). H_2O-acetone and H_2O-CH_3CN-acetone proved to be good solvents for obtaining high yields. However, H_2O-*t*-BuOH was found to be the best solvent to obtain high enantioselectivities similar to that obtained in the case of homogenous catalysis[27] and the order was found to be: H_2O-CH_3CN < H_2O-CH_3CN-acetone < H_2O-acetone < H_2O-*t*-BuOH.

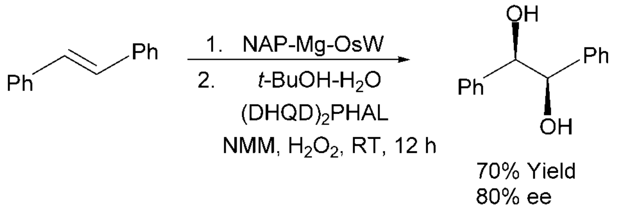
Table 5. Solvent effects in the AD of *trans*-stilbene using heterogeneous bifunctional NAP-Mg-PdOs catalyst.[a]

Entry	Solvent	Yield [%]	ee [%]
1	H_2O-acetone	90	81
2	H_2O-CH_3CN-acetone	85	80
3	H_2O-CH_3CN	64	58
4	H_2O-*t*-BuOH	80	85

[a] To the formed *trans*-stilbene product in the Heck reaction, $(DHQD)_2PHAL$ (1 mol %) and NMO (1.3 equivs.) were added in the solvent (6 mL).

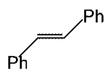
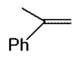
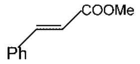
Osmium-Tungsten Catalytic System

Encouraged with the results obtained in the AD by using monofunctional NAP-Mg-OsO_4, we employed the heterogeneous bifunctional catalyst, NAP-Mg-OsW for



Scheme 3. Asymmetric dihydroxylation of *trans*-stilbene using NAP-Mg-OsW.

Table 6. Synthesis of chiral diols by heterogeneous bifunctional NAP-Mg-OsW catalyst using H_2O_2 as the terminal oxidant.[a]

Entry	Olefin	Yield [%]	ee [%]
1		70	80
2		75	70
3		80	75

[a] The olefin (1 mmol), NAP-Mg-OsW (3 mol %), $(DHQD)_2PHAL$ (1 mol %) and NMM (50 mol %) were taken in the solvent (6 mL) and H_2O_2 was slowly added over 12 h under stirring.

Table 7. Solvent effects in the AD-*N*-oxidation of *trans*-stilbene catalyzed by NAP-Mg-OsW catalyst.[a]

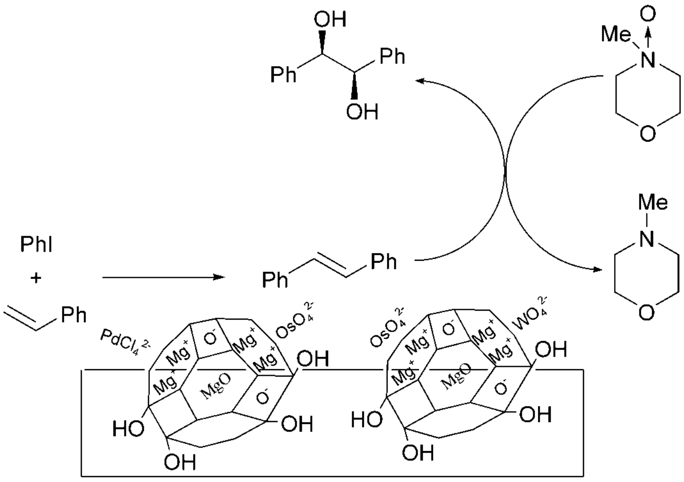
Entry	Solvent	Yield [%]	ee [%]
1	H_2O-acetone	82	75
2	H_2O-CH_3CN-acetone	80	70
3	H_2O-CH_3CN	60	55
4	H_2O-*t*-BuOH	70	80

[a] The olefin (1 mmol), NAP-Mg-OsW (3 mol %), $(DHQD)_2PHAL$ (1 mol %) and NMM (50 mol %) were taken in the solvent (6 mL) and H_2O_2 was slowly added over 12 h under stirring.

the simultaneous AD of *trans*-stilbene and *N*-oxidation of NMM in the presence of H_2O_2, used as terminal oxidant, and $(DHQD)_2PHAL$ as ligand. To a mixture of 3 mol % of NAP-Mg-OsW, 3 mol % of $(DHQD)_2$ PHAL ligand, *trans*-stilbene and NMM in *t*-BuOH-H_2 O (5:1, 6 mL), H_2O_2 was slowly added over a period of 12 h to afford the desired diol (Scheme 3). Various olefins, mono- and disubstituted, activated and simple, were subjected to AD and the results are presented in Table 6.

We also examined the effect of the solvent on the activity and enantioselectivity in the NAP-Mg-OsW-catalyzed AD of *trans*-stilbene using H_2O_2 as the terminal oxidant (Table 7). The H_2O-acetone system proved to be a good solvent for obtaining high yields. However, *t*-BuOH-H_2O was found to be the best solvent to obtain high enantioselectivities similar to that obtained in the case of homogenous catalysis[27] and the order was found to be: H_2O-CH_3CN < H_2O-CH_3CN-acetone < H_2O-acetone < H_2O-*t*-BuOH.

The novel protocol used here afforded diols using NMM in catalytic amounts and a cheaper oxidant, H_2 O_2, by a heterogeneous catalyst instead of NMO in stoichiometric amounts currently used in dihydroxylations. This methodology offers the diols with higher yields and moderate ees. This process rivals that employed by Bäckvall et al. using flavin, a biomolecule, induced catalytic oxidation of NMM to NMO in the dihydroxylation.[28] The flavin-based process suffers from the serious problem of catalyst recovery, while the basic advantage of our process is the recyclability of the catalysts which will be established in a later section.



Scheme 5. A schematic representation of NAP-Mg-PdOs- and NAP-Mg-OsW-catalyzed synthesis of chiral diols.

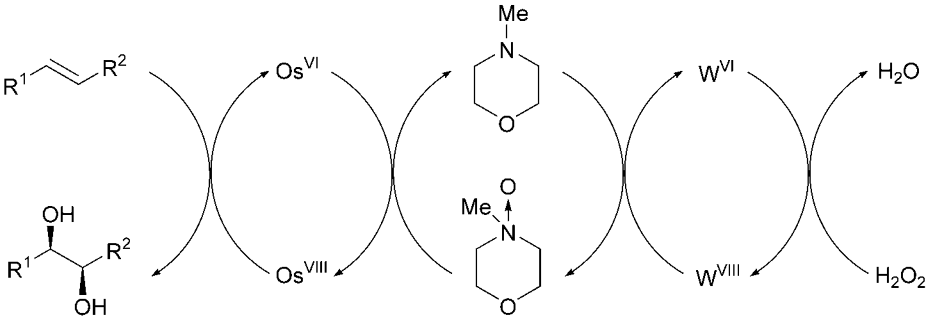
We have obtained higher ees with the monofunctional osmium catalyst than with the bifunctional catalysts. The slow addition of olefins is an effective factor with the monofunctional catalysis.

A plausible mechanism for the triple catalytic H_2O_2 oxidation with osmium-tungsten oxides is depicted in Scheme 4. The peroxo species generated from tungstate and H_2O_2 rapidly recycles the NMM to NMO, which in turn reoxidizes Os^{VI} to Os^{VIII}.

In summary, the bifunctional catalysts, NAP-Mg-PdOs and NAP-Mg-OsW, were subjected to tandem Heck-AD and AD-*N*-oxidation reactions in a single-pot separately as described in Scheme 5 to obtain chiral diols.

Reusability and Heterogeneity

These catalysts were recovered quantitatively by simple filtration. The recovered catalysts were reused



Scheme 4. Os- and W-catalyzed synthesis of diols using H_2O_2 as the terminal oxidant.

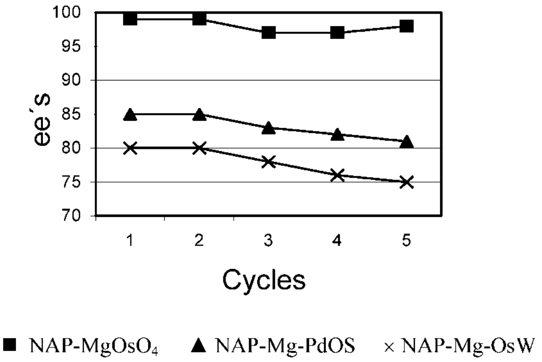


Figure 3. Enantioselectivities obtained in multiple uses of NAP-MgOsO$_4$, NAP-Mg-PdOs, NAP-Mg OsW in the AD of *trans*-stilbene.

and consistent activity and enantioselectivity were noticed even after the fifth cycle (Figure 3). When the fresh reaction was conducted with the filtrate obtained at the end of the dihydroxylation reaction, no product formation was observed. Moreover, the absence of osmium as determined by iodometry, SEM-EDAX and no progress of the dihydroxylation reaction with the filtrate samples withdrawn periodically during reaction and filtered rule out the leaching of osmium and unambiguously provide evidence for heterogeneity throughout the reaction (see Experimental Section for further details).

It is interesting to note that the NAP-AP-MgO holds both the OsO_4^{2-} and the Os(VIII) species possibly through electrostatic interactions. The other possibility could be that the reduction of Os(VIII) to Os(VI) is too fast to detach neutral OsO_4 from the support. However, when NAP-Mg-OsO_4 is treated with the oxidant in the absence of olefin, osmium is found to leach from the support, which indicates that the NAP-Mg-OsO_4 catalyst is not stable in the oxidative environment.

The bifunctional catalysts comprising of Pd, Os, W performed Heck coupling, *N*-oxidation and AD reactions, exhibiting their characteristic features in the diversified bifunctional activities without loosing their identity. These results substantiate the retention of coordination geometries of metal complexes in their monomeric form as supported by IR spectral data and rule out the formation of biheterometallic species during the stabilization process and the dihydroxylation reaction. The large positive electric potential of the exchanged catalyst surface induces an enrichment of cooxidant close to the surface. Similarly, the olefin and the aryl halide also build up their concentrations close to the surface as it has a high adsorption coefficient on the support surface. Apart from this, spatial organization and electrical shielding[29] are responsible for the excellent performance of the exchanged catalysts.

Conclusion

In summary, a single-pot biomimic synthesis of chiral diols mediated by bifunctional solid catalysts consisting of active palladium, osmium and tungsten species embedded on a matrix of the nano-MgO, representing a low-cost process, is described. Here the desired prochiral olefins and *N*-methylmorpholine *N*-oxide, key intermediates for AD, are generated *in situ* in the most economical way by Heck coupling and *N*-oxidation of *N*-methylmorpholine, respectively. Dispensing with the usual protocol of isolation and purification of the intermediates, the bifunctional catalysts trigger the reaction, to obtain the chiral diols with minimum waste and maximum conservation of energy. The oxidant, H_2O_2, employed here in place of NMO is environmentally acceptable, as the only byproduct is water. More interestingly, even the water produced from H_2O_2 during the *N*-oxidation is consumed in the AD reaction to mark the highest atom economy in the production of chiral diols. This protocol provides the desired prochiral olefins *in situ* en route to chiral diols from cheaper precursors and NMO *via in situ* oxidation to minimize the unit operations. The possible large-scale synthesis of diols employing this catalytic system using H_2O_2 as the oxidant directed to minimize the solid waste effluent is addressed. In contrast to the homogeneous catalysts, the heterogeneous bifunctional catalysts were easily recovered from the reaction by simple filtration and reused successfully in the AD. The recyclable catalysts and the use of cheaper oxidant, H_2O_2, employed here make the process more economical than the earlier processes. The simple procedure, easy recovery and reusable catalytic systems are expected to contribute to the development of benign chemical processes and products.

Experimental Section

General Remarks

IR spectra for samples as KBr pellets were recorded on a BIO-RAD 175C FTIR spectrometer. ^{1}H NMR spectra were recorded on a Varian Gemini 200 MHz spectrometer. Chemical shifts (δ) are reported in ppm, using TMS as internal standard. X-ray powder diffraction (XRD) data were collected on a Siemens/D-5000 diffractometer using Cu-Kα radiation ($\lambda = 1.5405$ Å). SEM-EDAX (scanning electron microscopy-energy dispersive X-ray analysis) was performed on a Hitachi SEM S-520, EDX-Oxford Link ISIS-300 instrument. High performance liquid chromatography (HPLC) was performed using the following apparatus: Shimadzu LC-10AT (liquid chromatograph), Shimadzu SPD-10A (UV detector) and Shimadzu C-R6A Chromatopac. ACME silica gel (100–200 mesh) was used for column chromatography and thin layer chromatography was performed on Merck precoated silica gel 60-F$_{254}$ plates. X-ray photoemission spectra were recorded on a Kratos AXIS 165 with a dual anode (Mg and Al) apparatus using the MgKα anode. The pressure in the spectrometer was about 10^{-9} Torr. For energy calibration, we have used the carbon 1 s photoelectron line. The carbon 1 s binding energy was taken to be 285.0 eV. Spectra were deconvoluted using Sun Solaris based Vision 2 curve resolver. The location and the full width at half maximum (FWHM) for a species were first determined using the spectrum of a pure sample. The location and FWHM of products, which were not obtained as pure species, were adjusted until the best fit was obtained. Symmetrical Gaussian shapes were used in all cases. Binding energies for identical samples were, in general, reproducible to within ±0.1 eV.

$K_2OsO_4 \cdot 2\,H_2O$, TEAA, $(DHQD)_2PHAL$ and NMO were purchased from Aldrich. Haloarenes and olefins were purchased from Aldrich. All the other solvents and chemicals were obtained from commercial sources and used as such without further purification.

Preparation of the NAP-MgO-Supported Catalysts

NAP-Mg-OsO$_4$: NAP-MgO (SA 600 m^2/g, 1 g) was treated with K_2OsO_4 (0.184 g, 0.5 mmol) dissolved in decarbonated water with stirring for 12 h under a nitrogen atmosphere to afford NAP-Mg-OsO_4. Then the catalyst was filtered off and washed with deionized water, acetone, and dried.

NAP-Mg-PdOs: Na_2PdCl_4 and K_2OsO_4 (0.147 g and 0.184 g, each 0.5 mmol) were dissolved in decarbonated water. NAP-MgO (SA 600 m^2/g, 1 g) was added to the mixture and stirred for 12 h under a nitrogen atmosphere to afford NAP-Mg-PdOs. Then the catalyst was filtered and washed with deionized water, acetone, and dried to obtain 1.235 g of Mg-PdOs (0.375 mmol g^{-1} each of Pd and Os).

NAP-Mg-OsW: K_2OsO_4 and Na_2WO_4 (0.184 g and 0.165 g each 0.5 mmol) were dissolved in decarbonated water and then NAP-MgO (SA 600 m^2/g, 1 g) was added to the mixture and stirred for 12 h under a nitrogen atmosphere to afford NAP-Mg-OsW. Then the catalyst was filtered and washed with deionized water, acetone, and dried to obtain 1.345 g of Mg-OsW (0.370 mmol g^{-1} each of Os and W).

Synthesis of Chiral Diols with NAP-Mg-OsO$_4$ using NMO as the Cooxidant

NAP-Mg-OsO_4 (71 mg, 3 mol %), NMO (175 mg, 1.3 mmol), $(DHQD)_2PHAL$ (7.8 mg, 1 mol %) were taken in a round-bottomed flask containing H_2O-*t*-BuOH (1:5, 6 mL). To the reaction mixture, 1 mmol of olefin was added slowly over a period of 12 h and the reaction was continued for 3 h at room temperature. After completion of the reaction (TLC analysis), Na_2SO_3 (0.8 g) and ethyl acetate were added to the reaction mixture, which was stirred for 10 minutes, then the catalyst was filtered off and washed with ethyl acetate (10 mL). The combined filtrates were extracted with 1 N HCl (2 × 5 mL) to recover the chiral ligand from the aqueous layer. The resulting organic phase was further washed with brine solution (5 mL) and the solvent was removed. After removing the solvent, the crude material was chromatographed on silica gel using hexane/ethyl acetate (2:1) as an eluent to afford the corresponding *cis*-diol.

General Procedure for Synthesis of Chiral Diols *via* Tandem Heck-Asymmetric Dihydroxylation using NAP-Mg-PdOs Bifunctional Catalyst

The heterogeneous bifunctional catalyst NAP-Mg-PdOs (80 mg, 3 mol %), aryl halide (1 mmol), olefin (1 mmol) and Et_3N (111 mg 1.1 mmol) were taken in acetonitrile solvent and stirred at 70 °C for 12–16 h. At this stage, the heating was stopped and a mixture of $(DHQD)_2PHAL$ (7.8 mg, 1 mol %), NMO (175 mg, 1.3 mmol) and H_2O-*t*-BuOH (1:5, 6 mL) was added to the above reaction mixture and stirred at room temperature. After completing the reaction (TLC analysis), Na_2SO_3 (0.8 g) and ethyl acetate were added to the reaction mixture and the catalyst was filtered off and washed with ethyl acetate (10 mL). The combined filtrates were extracted with 1 N HCl (2 × 5 mL) to recover the chiral ligand from the aqueous layer. The resulting organic phase was further washed with brine solution (5 mL) and the solvent was removed. The thus obtained crude material was chromatographed on silica gel using hexane/ethyl acetate (2:1) as an eluent to afford the corresponding *cis*-diol.

Asymmetric Dihydroxylation of Olefins using NAP-Mg-OsW and H_2O_2 as the Terminal Oxidant

The heterogeneous bifunctional NAP-Mg-OsW (81 mg, 3 mol %), an olefin (1 mmol), $(DHQD)_2PHAL$ (7.8 mg, 1 mol %) and NMM (50.5 mg, 0.5 mmol) were taken in a round-bottomed flask containing H_2O-*t*-BuOH (1:5, 6 mL). To this mixture was added H_2O_2 (169 μL, 30% aqueous, 1.5 mmol) over a period of 12 h. After completion of the reaction as indicated by TLC analysis, Na_2SO_3 (0.8 g) and ethyl acetate were added to the reaction mixture, and stirred for 10 minutes. The catalyst was then filtered off and washed with ethyl acetate (10 mL). The combined filtrates were extracted with 1 N HCl (2 × 5 mL) to recover the chiral ligand from the aqueous layer. The resulting organic phase was further washed with brine solution (5 mL) and the solvent was removed. The thus obtained crude material was chromatographed on silica gel using hexane/ethyl acetate (2:1) as an eluent to afford the corresponding *cis*-diol.

Heterogeneity Tests

We evaluated the heterogeneity of the catalysts in all respects. To understand the stability and heterogeneity of the mono- and bifunctional catalysts, we conducted a series of experiments to obtain clear evidence for the heterogeneity of the reaction.

Experiment 1: A mixture of the Mg-OsO_4, α-methylstyrene and NMO in H_2O-CH_3CN-acetone was stirred for 8 h. After completion of the reaction, the catalyst was separated by filtration. To one part of the filtrate were added fresh α-methylstyrene, NMO and the mixture was stirred for 24 h. There was no enhancement of the product in the reaction using the fresh α-methylstyrene. To the second part of the solution were added a different olefin, *trans*-stilbene, NMO and the mixture was stirred for 24 h. No stilbene diol was formed.

Experiment 2: A mixture of the Mg-OsO_4, α-methylstyrene and NMO in H_2O-CH_3CN-acetone and was stirred. At different intervals (for every 2 h) the samples were withdrawn and filtered (four times). To these filtrates were added a different olefin, *trans*-stilbene, NMO and the mixture was stirred for 24 h. No stilbene diol was formed. Furthermore, no osmium was detected in those filtrates by the SEM-EDX. These results strongly suggest that the OsO_4 is bound to the support during the reaction when all the constituents are present. It appears that during oxidation with NMO the anionic form of OsO_4 transforms into an Os(VIII) species, but is bound on MgO through some other electrostatic interaction that includes hydrogen bonding interaction with the Bronsted hydroxyl groups of MgO. From the above results we have observed that no Os was leached during the reaction.

Experiment 3: A mixture of Mg-OsO_4 and NMO in H_2O-CH_3CN-acetone was stirred for 24 h at room temperature and filtered. To the filtrate was added α-methylstyrene and the mixture was stirred for 8 h. The diol was formed in good yields. The result clearly shows that the catalyst suffers from leaching of osmium upon treatment with cooxidant in the absence of olefin.

Experiment 4: Mg-OsO_4 was stirred with NMO for 24 h in *t*-BuOH-H_2O. *trans*-Stilbene was then added and the mixture was stirred for 10 h. After completion of the reaction, the catalyst was removed by filtration. Two separate experiments were conducted both with the recovered catalyst and the filtrate as described. A mixture of the recovered catalyst, α-methylstyrene and NMO in *t*-BuOH-H_2O was stirred for 8 h. The diol was obtained in 10% yield. To the filtrate, α-methylstyrene and NMO were added and stirred at room temperature for 8 h. The diol was obtained in good yield.

These results strongly suggest that the leached Os species on treatment with NMO in the absence of olefin could not be re-exchanged on the support during the reaction after the addition of olefin.

Experiment 5: When the reaction was conducted with the filtrate obtained by the treatment of the catalyst, Mg-PdOs and Mg-OsW, in a solvent system used as described above, for a prolonged time, no product formation was observed and reconfirmed by SEM-EDAX.

These results as presented here indicate that the palladium, osmium and tungsten metals remained bound on the MgO matrix throughout the reaction

Iodometry Test

The absence of osmium in the filtrate is further confirmed using the iodometry test. The iodometry test was performed the treatment of the catalyst in H_2O-CH_3CN-acetone (1:1:1) solvent system. The catalyst was filtered and the filtrate was treated with potassium iodide and HCl. The solution was titrated with sodium thiosulfate in the presence of starch, and no formation of iodine was observed.

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