Origin of α-Hydroxy Ketones in the Osmium Tetroxide-Catalyzed Asymmetric Dihydroxylation of Alkenes†

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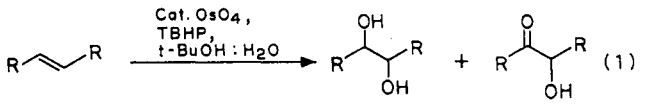
The origin and the mechanism of formation of α-hydroxy ketones in the osmium tetroxide-catalyzed asymmetric *cis*-dihydroxylation (ADH) of alkenes in the presence of *tert*-butyl hydroperoxide is described. The formation of α-hydroxy ketones has been established to proceed through either the hydration of monooxobisglycolate ester **2** followed by oxidation with *tert*-butyl hydroperoxide (TBHP) or by acid-catalyzed addition of TBHP on the intermediate bisglycolate ester **2**. On the basis of the mechanistic insight, it has been possible to shut down the formation of α-hydroxy ketones and other side products in the ADH reaction, even when TBHP is used as an oxygen source. It is possible to prepare α-hydroxy ketones in good yields but the optical purity of ketols has been found to be very low, which not only shed significant light on the mechanism of their formation, but also delineated the improbability of synthesizing them in optically active forms by ADH reaction of alkenes.

Stereoselective embodiment of two hydroxyl groups in the unfunctionalized alkenes framework by osmium tetroxide-catalyzed asymmetric dihydroxylation (ADH) is the essential reason for its recent popularity in synthetic organic chemistry.[1] During the course of our studies on the ADH reaction of olefins,[2] we have observed in a few cases, the formation of a small amount of α-hydroxy carbonyl compounds[3] and other oxidation products, even when *N*-methylmorpholine *N*-oxide (NMO) is used as a stoichiometric oxygen transferring reagent. The yield of these overoxidation products increases significantly when *tert*-butyl hydroperoxide or hydrogen peroxide is used instead of NMO.[4] Under carefully controlled conditions, it has been even possible to increase the formation of α-hydroxy ketone (overoxidation product) in the ADH reaction of olefins at the expense of diol.

On the other hand, use of NMO in the ADH reaction leads to much lower yield of overoxidation products. However, it is desirable to completely eliminate the formation of such side products in order to make this reaction synthetically useful. In addition, the use of NMO on a preparative scale is not very lucrative and the enantiomeric excess of the diols are also not satisfactory.



(1)

In contrast, use of potassium ferricyanide–potassium carbonate as cooxidant in *t*-butyl alcohol–water furnish exclusively *cis*-diols in high enantiomeric excess,[5] albeit the reaction seems to be impractical for large-scale preparative purposes. Thus, this cheap cooxidant is limited synthetically to laboratory-scale preparation only. Therefore, there is still a need for the development of an alternative cheaper cooxidant such as *tert*-butyl hydroperoxide (TBHP) or even hydrogen peroxide for the ADH reaction, however, without the formation of side products. Also, since the yield of α-hydroxy ketones can be amplified at will by controlling the reaction conditions, it should be possible to synthesize optically active α-hydroxy carbonyl compounds,[6] which are important fragments of several natural products[7] by the osmium tetroxide oxidation of alkenes.

Results

Several olefins were dihydroxylated using TBHP as cooxidant and osmium tetroxide as catalyst. The results are summarized in Table 1. Large amount of α-hydroxy ketone is formed in each case. Thus, when *trans*-stilbene was oxidized with osmium tetroxide in the presence of aqueous TBHP in acetonitrile–water (4:1) at *ca* 0 °C, a mixture of benzoin (28%), hydrobenzoin (35%), and benzaldehyde (30%) were isolated (Table 1, entry 1). Similar results were obtained in the oxidation of *trans*-3-hexene (Table 1, entry 2) and *trans*-5-decene (Table 1, entry 3), which gave α-hydroxy ketones (50–66% yield) along with diols (40–25% yield). The oxidation of *trans*-2-octene lead to a mixture of 2-hydroxy-3-octanone and 3-hydroxy-2-octanone (3:2) (35%) along with 2,3-octanediol (Table 1, entry 4, 55%).

As a control experiment, diol was subjected to otherwise identical experimental conditions (dihydroxylation method). However, no significant oxidation of diol to ketol was observed. We also examined the effect of tetraethylammonium acetate (TEAA) on the dihydroxylation of *trans*-3-hexene (Table 1, entry 5), which afforded not only

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Table 1. Oxidation of Alkenes Catalyzed by Osmium Tetroxide Using *t*-Butyl Hydroperoxide as Cooxidant

			products				
			diols		α-hydroxy ketone		
entry	substrate	conditions[a]	%yield	%ee (config)[c]	%yield	%ee (config)[c]	diol/ketol[b]
1	*trans*-stilbene	TBHP (4 equiv)	35	–	28	–	55:45
2	*trans*-3-hexene	TBHP (4 equiv)	40	–	50	–	44:56
3	*trans*-5-decene	TBHP (4 equiv)	25	–	66	–	27:73
4	*trans*-2-octene	TBHP (4 equiv)	55	–	35	–	62:38
5	*trans*-3-hexene	TBHP (4 equiv) + TEAA (2 equiv)	69	–	–	–	17:1
6	*trans*-3-hexene	slow addition of olefin (18 h) + TBHP + TEAA (2 equiv)	75	–	–	–	22:1
7	*trans*-3-hexene	slow addition of olefin + TBHP (18 h) + TEAA (2 equiv)	78	–	–	–	35:1
8	*trans*-3-hexene	slow addition of olefin + TBHP (18 h) + TEAA (2 equiv) + C_2-DHQD	73	68 (*R,R*)[d]	–	–	15:1
9	*trans*-2-octene	–do (16 h)–	75	62 (*R,R*)[e]	–	–	14:1
10	*trans*-5-decene	–do (16 h)	77	70 (*R,R*)[f]	–	–	12:1
11	*trans*-stilbene	–do (12 h)	50	79 (*R,R*)[g]	–	–	
12	*trans*-stilbene	C_2-DHQD + TBHP (4 equiv)	37	66 (*R,R*)	29	6(*R*)	56:44
13	*trans*-stilbene	C_2-DHQ + TBHP (4 equiv)	34	62 (*S,S*)	30	4(*S*)	53:47
14	*trans*-stilbene	DHQD-CLB + TBHP (4 equiv)	38	64 (*R,R*)	20	7(*R*)	65:35
15	*trans*-3-hexene	DHQD-CLB + TBHP (4 equiv)	30	28 (*R,R*)	52	2(*R*)	36:64
16	*trans*-5-decene	DHQD-CLB + TBHP (4 equiv)	29	30 (*R,R*)	61	–	32:68
17	*trans*-2-octene	DHQD-CLB + TBHP (4 equiv)	51	27 (*R,R*)	30	–	63:37

[a] All the reactions were carried out in acetonitrile:water (4:1) at ca. 0 °C. [b] The ratios of diol/ketol were determined by gas chromatography. [c] The %ee and the absolute configuration of the diols and ketols were determined by ^{1}H NMR using shift reagents Eu(hfc)$_3$ on the corresponding acetate derivatives and/or comparison of optical rotation with the known samples. [d] $[\alpha]^{22}_D$ = +10.8° (*c*, 0.41, $CHCl_3$). [f] $[\alpha]^{22}_D$ = +23.8° (*c*, 1.0, EtOH). [g] $[\alpha]^{22}_D$ = +73.5° (*c*, 1.98, EtOH).

the improved yield of diol but also significantly altered the ratio of diol *versus* ketol from 44:56 (Table 1, entry 2) to 17:1 (Table 1, entry 5). Addition of olefin slowly to the reaction mixture containing osmium tetroxide and TBHP (4 equiv) in CH_3CN/H_2O (4:1) further improved both the yield and the diol/ketol ratio (22:1) (Table 1, entry 6). Since TBHP undergoes slow decomposition in the presence of osmium tetroxide, the addition of TBHP as well as the olefin were carried out slowly *via* separate syringes. This led to a dramatic improvement in the ratio of diol *versus* ketol (Table 1, entry 7; 35:1).

Under the above optimized conditions, asymmetric dihydroxylation of *trans*-3-hexene was performed in 18 h using bisdihydroquinidine terephthalate ester (C_2-DHQD) as the chiral auxiliary.[2a] Although the yield of the diol remained unaffected, a small amount of 3-hydroxy-4-hexanone was observed (Table 1, entry 8, diol/ketol 15:1). The enantiomeric excess of the 3,4-hexanediol was found to be 68% (*R,R*). Similar results were observed when *trans*-2-octene (Table 1, entry 9, 16 h, diol/ketol 14:1; 62% ee of (*R,R*)-2,3-octanediol) and *trans*-5-decene (Table 1, entry 10, 16 h, diol/ketol 12:1; 70% ee of (*R,R*)-5,6-decanediol) were subjected to ADH reaction using C_2-DHQD as chiral controller. In contrast, ADH reaction of *trans*-stilbene always furnished overoxidation products (benzoin and benzaldehyde) along with hydrobenzoin (Table 1, entry 11, 12 h, 79% ee of (*R,R*)-hydrobenzoin).

We further investigated the possibility of the formation of optically active α-hydroxy carbonyl compound directly in the ADH reaction of alkenes. Thus, *trans*-stilbene was subjected to ADH reaction using C_2-DHQD, C_2-DHQ (C_2-bisdihydroquinine terephthalate), and DHQD-CLB (dihydroquinidine 4-chlorobenzoate) as chiral auxiliaries under identical experimental conditions as in the case of entry 1. The yield and the ratio of the diol *versus* ketol remained virtually unchanged as in the case of racemic reaction (Table 1, entries 12–14 *versus* entry 1). The enantiomeric excess of hydrobenzoin was slightly lower (62–66% ee). In contrast to the optical purity of hydrobenzoin, the benzoin isolated from this reaction was nearly racemic (Table 1, entry 12–14, 4–7% ee). Similar observations were made for *trans*-3-hexene (Table 1, entry 15), *trans*-5-decene (Table 1, entry 16), and *trans*-2-octene (Table 1, entry 17).

In order to ascertain the origin of poor enantioselectivity of α-hydroxy ketones, dioxomono(glycolato)osmium(VI) **4** (L = –, DGQD-CLB, $DHQD_2$) and monooxobis(glycolato)osmium(VI) **2** were prepared by the known methods.[8] The intermediate trioxomonoglycolate **3** (Scheme 1) could not be prepared. However, the oxidation of the dioxomonoglycolate **4** (L = –) in $CHCl_3$ using dry TBHP gave an intermediate species having IR bands at 965, 910, and 855 cm^{-1}. The addition of olefin to this reaction mixture led to the disappearance of bands at 910 and 855 cm^{-1}.

The treatment of bisglycolate **2** with aqueous TBHP led to the formation of α-hydroxy ketone (50%) along with the diol (40%). Though the hydrated bisglycolate **6** could not be synthesized, its corresponding dipotassium salt was prepared by treating osmium tetroxide with methanolic KOH, and the resulting dipotassium tetramethoxyosmium(VI) was dissolved in water in the presence of hexane-3,4-diol to furnish a rose-pink-colored dipotassium bis(hexane-3,4-diolato)osmium(VI). This complex on treatment with dry TBHP led to the formation of 4-hydroxy-3-hexanone along with 3,4-hexanediol in 14:86 ratio. Oxidation of **2** with dry TBHP gave only a small amount of α-hydroxy ketone (15%). On the other hand, the reaction of **2** in CH_2Cl_2 with dry TBHP in the presence of a catalytic amount of glacial acetic acid led to the formation of α-hydroxy ketone along with 3,4-hexanediol in nearly 1:1 ratio (80% yield). Attempts to prepare dioxobisglycolate **5** from bisglycolate **2** was unsuccessful.

Discussion

The detailed catalytic cycle (Scheme 1) of the dihydroxylation of alkenes catalyzed by osmium tetroxide–cinchona alkaloid complex is well established,[9] which

(8) Criegee, R. *Annalen* **1936**, *522*, 75. (b) Criegee, R.; Manchard, B.; Wannowinus, H. *Annalen* **1942**, *550*, 99.

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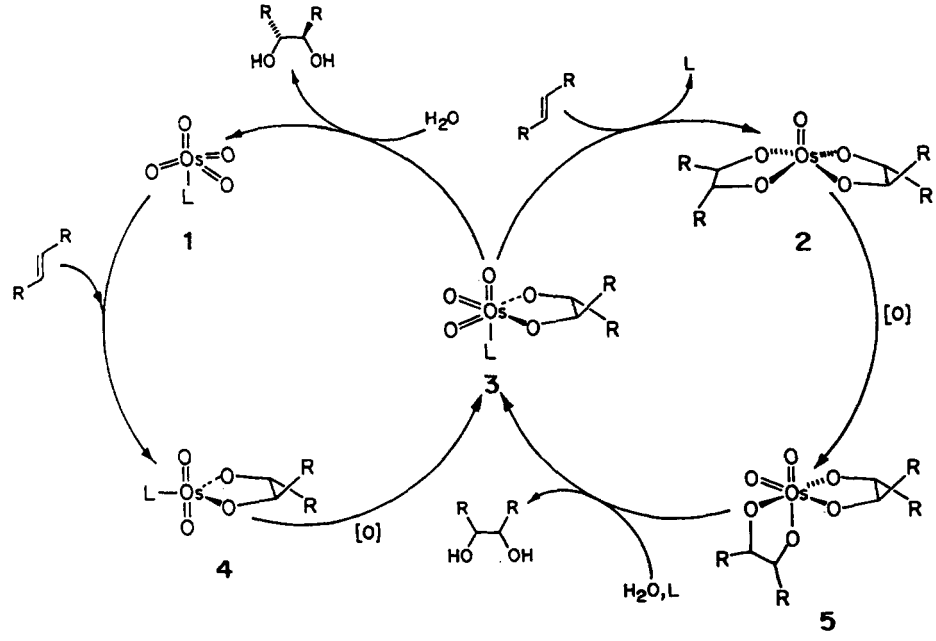
Scheme 1. Sharpless Cycle for Asymmetric Dihydroxylation of Alkenes



involves dioxomono(glycolato)osmium(VI) 4, trioxomono-(glycolato)osmium(VIII) 3, and monooxobis(glycolato)-osmium(VI) 2 as the intermediate species. Sharpless and co-workers[9] have fully established the origin of diols of high enantiomeric purity as well as the reason for poor enantioselectivity observed in the catalytic ADH reaction. The hydrolysis of trioxomono(glycolato)osmium(VIII) 3 led to the formation of diol of high enantiomeric purity. On the other hand, the reaction of 3 with another equivalent of olefin led to bisglycolate 2 which is believed to be the prime reason for poor enantioselectivity in the ADH reaction. In order to determine if any of these species are functioning either as catalyst or as precursor to the formation of ketol, we attempted an oxidation of 3,4-hexanediol using dry TBHP and 4 as catalyst in acetonitrile. Interestingly, no 3-hydroxy-4-hexanone was detected, instead the unchanged 3,4-hexanediol was isolated. This suggests that the intermediate 4 is not a catalyst for the ketol formation.

The intermediate 3 could be anticipated as the catalyst for the formation of α-hydroxy ketone. Thus it was generated *in situ* by the oxidation of dioxomonoglycolate 4 (L = –) in $CHCl_3$ using dry TBHP and was detected by IR spectroscopy. The IR spectrum showed bands at 965, 910, and 855 cm^{-1} perhaps due to Os=O bond.[10] The bands at 910 and 855 cm^{-1} quickly disappeared on addition of *trans*-3-hexene presumably due to the formation of monooxobis(glycolato)osmium(VI) 2, the structure of which has been assigned by comparison of IR spectra. From the absence of ketol formation in these experiments, it is certain that the intermediates 3 or 4 in the presence of dry TBHP would not be the oxidizing agents of alkenes or diols to α-hydroxy ketones. Instead they act as precursors to the formation of monooxobisglycolate 2. Thus, the formation of the α-hydroxy ketone in the ADH reaction by aqueous TBHP ascertains the pivotal role of water in the reaction. The presence of water is inevitable for the formation of diol as well as α-hydroxy ketone, however, they arise from different intermediates.

Since the formation of diol of poor enantiomeric excess arises from bisglycolate 2 (Scheme 1), it was reasoned that α-hydroxy ketones which are essentially obtained in racemic form, might be originating through the intermediacy of 2 (*vide supra*). Thus the bisglycolate 2 was prepared by a known method[8,11] and was treated with aqueous TBHP which furnished 50% yield of α-hydroxy ketone along with diol (40%). Hence it is reasonable to assume that the intermediate 2 forms a hydrated osmium-(VI) bisglycolate 6 (Scheme 2). This assumption is based on the fact that there exits an equilibrium between bisglycolate 2 and monoglycolate 4 *via* the intermediate formation of 6. Support for this assumption comes from the ^{18}O-labeling studies of Griffith.[12] This indicates that the initial step is the hydration of bisglycolate 2 to give 6 which serves as the precursor to the formation of α-hydroxy ketones. The intermediacy of 6 is supported by the fact that the oxidation of dipotassium salt of 6[11] with anhydrous TBHP led to the formation of 4-hydroxy-3-hexanone, along with 3,4-hexanediol. Thus, the hydrated species 6 might undergo hydrolysis to furnish nearly racemic diol or could undergo ligand exchange with TBHP to give the osmate ester 7 depending on the relative rates of the reaction (Scheme 2).

The possibility that water might catalyze the addition of TBHP on bisglycolate 2 by protonating the oxo ligand was further examined. Since the oxidation of 2 by dry TBHP furnished only 15% yield (determined by GC) of 4-hydroxy-3-hexanone, and oxidation of 2 in the presence of glacial acetic acid gave a mixture of diol and ketol (1:1) in ca. 80% yield, it clearly suggests that (a) even though TBHP might add directly on the intermediate 2 to furnish 7, which finally produces α-hydroxy ketone, it may not be a very favorable pathway (Scheme 3); (b) Improved yield of both diol and α-hydroxy ketone (1:1; 80%) in the oxidation of 2 with dry TBHP in the presence of glacial acetic acid supports the hypothesis of the initial protonation of oxo ligand of 2 which makes this intermediate more susceptible to nucleophilic attack by TBHP to give 7 (Scheme 3).[13]

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(11) Griffith, W. P. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Ed.; Pergamon Press, New York, 1987; Vol 4, p 519.

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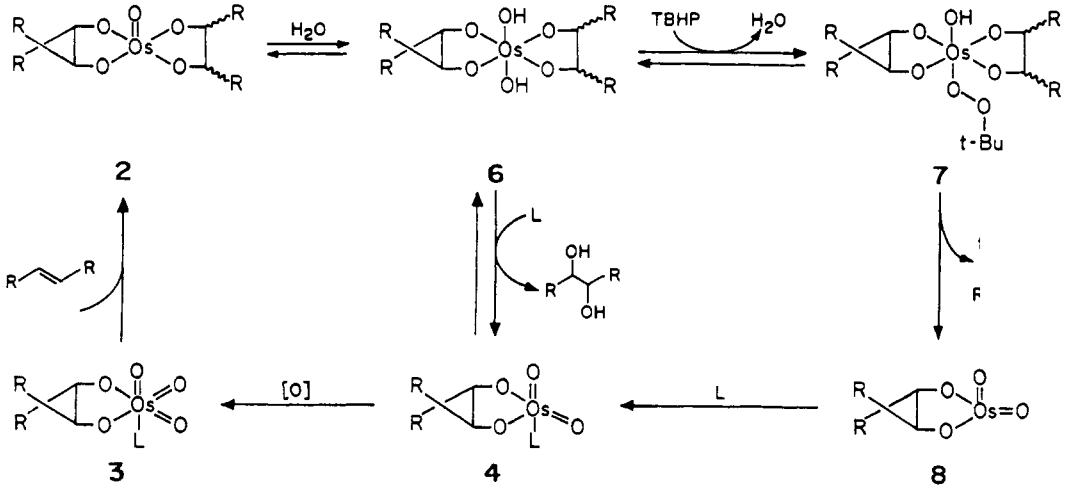
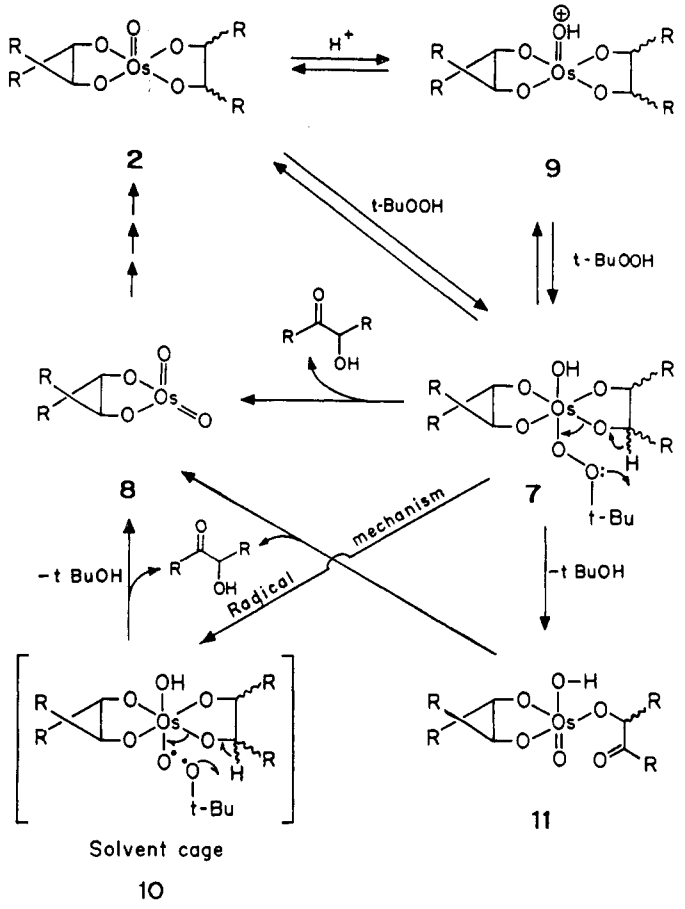
(13) We are thankful to the referee for this suggestion.

Scheme 2. Mechanism of Formation of α-Hydroxy Ketones in the Osmium Tetroxide-Catalyzed Oxidation of Akenes



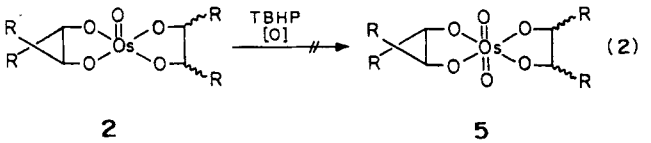
Scheme 3. Acid-Catalyzed Oxidation of Osmium(VI) Bisglycolate Ester 2 by TBHP to α-Hydroxy Ketone



The formation of increased yield of α-hydroxy ketone in the oxidation of bisglycolate **2** in the presence of glacial acetic acid and dry TBHP suggests that the initial step in the oxidation of **2** might be the protonation of the oxo ligand of **2** and therefore enhances the electrophilicity of the osmium center, which in turn might be attacked by TBHP to furnish **7**.

The intermediate **7**, formed by either of the pathways can in turn get oxidized to furnish α-hydroxy ketone. The bisglycolate **7** (which is a mixture of diastereomers) may undergo hydrogen atom abstraction by the oxygen lone pair attached to the *tert*-butyl group from the glycolate moiety to furnish racemic α-hydroxy ketone. An alternative route might be the possibility of oxidation of either of the intermediates **6** or **7** by hydrogen atom abstraction initiated by *tert*-butoxy radical (obtained by the decomposition of TBHP by OsO_4) which might furnish the α-hydroxy ketone. Since the dipotassium salt of **6** led to the formation of α-hydroxy ketone in the presence of TBHP (where no free OsO_4 is present which could generate *tert*-butoxy radical), it is likely that *t*-BuO· is not externally involved in such a process. However, intermediate **7** might undergo O–O bond scission to generate *t*-BuO· (Scheme 3; **10**) which can abstract an H atom within the solvent cage from the neighboring glycolate moiety to furnish dioxomono(glycolato)osmium(VI) and *t*-BuOH.[13] Thus, even though intramolecular H atom abstraction may not be a facile route, intramolecular *t*-BuO· generation following H atom abstraction is a viable pathway for α-hydroxy ketone formation.[13]

Another possible route to the formation of diol or ketol may be visualized *via* the oxidation of bisglycolate **2** to dioxobisglycolate **5** followed by hydrolysis. However, it is ruled out based on control experiments (eq 2). Thus, the oxidation of **2** with anhydrous TBHP in the presence of *trans*-3-hexene did not furnish any trisglycolate ester.[14] This excludes the possibility of intermediacy of dioxobisglycolate ester **5**.



(2)

Therefore, in light of the detailed mechanistic route of ketol generation, it is clear that the synthesis of α-hydroxy ketones is not possible in high enantiomeric excess by the asymmetric oxidation of alkenes catalyzed by osmium tetroxide–cinchona alkaloid complex as is also evident from the results in the Table 1 (entries 12–17).

Establishing the origin of α-hydroxy ketones, it is now possible to stop the formation of ketol in the ADH reaction by impeding the formation of bisglycolate **2** and by

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accelerating the hydrolysis of trioxomonoglycolate 3 (using the method similar to the one reported by Sharpless). Addition of base such as tetraethylammonium acetate (TEAA) is known to accelerate the hydrolysis of the intermediate ester 3.[15] The addition of TEAA to the osmium-catalyzed ADH reaction employing TBHP as a cooxidant not only improved the rate and the enantiomeric excess of the diols but also increased the ratio of diol *vs* ketol significantly (Table 1, entry 6 *vs* 2). It has been noted that the formation of α-hydroxy ketones is in poor yield when NMO is used as a cooxidant. This is attested by the fact that *N*-methylmorpholine formed during the course of the reaction makes the reaction medium basic and speeds up the hydrolysis of osmate ester 3. Also, NMO is sterically more bulky and less nucleophilic than TBHP or H_2O_2 in addition to its poor solubility in aqueous acetone. This makes the availability of the oxidant in the reaction medium limited and hence diminishes the overoxidation product. In contrast, TBHP or H_2O_2 is completely miscible in the reaction mixture and functions as a better nucleophile.

On the basis of the aforementioned mechanistic perception, the catalytic asymmetric dihydroxylation of *trans*-3-hexene was carried out using excess of aqueous TBHP in the presence of TEAA (Table 1, entry 5) which led to the improved yield and the diol *vs* ketol ratio. It may be argued that if the intermediate 3 plays a key role in the asymmetric dihydroxylation of alkenes,[9] then slow addition of the olefin as well as TBHP should not only improve the yield of the diol but also the ratio of diol *versus* ketol which has been found to be the case. Thus employing the slow addition of olefin and TBHP to the ADH reaction in the presence of TEAA, 3,4-hexanediol was isolated in improved yield (73%) and enantioselectivity (68%) (Table 1, entry 8). Similarly, improved selectivity and yield of diols in several cases (Table 1, entries 9[16]–11, 62–70% ee; 75–77% yield) were observed.

To summarize, we have been able to identify the origin of formation of α-hydroxy ketones and based on the probable mechanism, experimental conditions have been devised to attenuate their formation. This allows one to use much cheaper cooxidant such as TBHP without any significant yield of over oxidation products in the enantioselective production of diols from alkenes. However, it is noteworthy to point out that further modifications in experimental conditions are required to attain even higher enantiomeric purity of the diols.

Experimental Section

Commercially available reagents were used without further purification. Solvents were purified by standard methods. Compounds were purified by flash chromatography over silica gel. Solvents were evaporated on a rotary evaporator at reduced pressure using water bath, and drying of the reaction mixture after aqueous workup was carried out over anhydrous sodium sulfate. The petroleum ether used was of bp 60–80 °C. The reaction at room temperature means 20–25 °C.

^{1}H NMR spectra were recorded on a Brucker WP-200 or WP-90 spectrometer. Chromatograms were run on Hewlett-Packard 5890 using a 17 HP phenyl methyl silicone capillary column. An aqueous solution of TBHP (70%) was used as cooxidant. *N*-methylmorpholine *N*-oxide was prepared by known procedure.[3] Dry TBHP in methylene chloride was prepared by extraction of 70% aqueous TBHP solution with CH_2Cl_2 and drying over molecular sieves (4 Å), and the concentration was determined by ^{1}H NMR. Osmium tetroxide was dissolved in toluene to make a 0.5 M stock solution. IR spectra were recorded on a Perkin-Elmer 599B infrared spectrophotometer. Specific rotations were measured on a JASCO polarimeter.

General Procedure for the Oxidation of *trans*-Alkenes by OsO_4 in the Presence of TBHP. In a 25-mL round-bottom flask equipped with a magnetic stir bar was placed osmium tetroxide (20 μL, 0.01 mmol, 0.5 M in toluene) in acetonitrile:water (4:1). *trans*-Alkene (1 mmol) was added at room temperature with stirring followed by the addition of aqueous TBHP (70%, 0.55 mL, 4 mmol). The reaction mixture was stirred until all the starting material disappeared (TLC controlled). The excess of TBHP and osmium tetroxide were reduced by the addition of sodium metabisulfite (2 g, 10.5 mmol) to the reaction mixture, and the stirring was continued for an additional 1 h. The reaction mixture was diluted with ethyl acetate (25 mL) and filtered through a pad of Celite, and the Celite bed was washed with ethyl acetate (3 × 25 mL). The combined organic filtrate was washed with water (20 mL), brine (25 mL), and dried. The solvent was removed to give a residue which was chromatographed over silica gel or analyzed by gas chromatography to determine the ratio of diol and ketol.

Oxidation of *trans*-3-Hexene with Aqueous TBHP in the Presence of Tetraethylammonium Acetate (TEAA). In a 5-mL screw-capped vial was placed *trans*-3-hexene (25 μL, 0.2 mmol), aqueous TBHP (70%, 0.11 mL, 0.8 mmol), and TEAA (75 mg, 0.4 mmol) in acetonitrile:water (4:1; 0.5 mL), and the reaction mixture was stirred at room temperature. Osmium tetroxide (5 μL, 2.5 × 10^{-3} mmol) was added and the reaction mixture was stirred further for 18 h. The reaction was quenched with sodium metabisulfite (0.2 g, 1.05 mmol), and the product was analyzed by gas chromatography indicating a 17:1 ratio of diol *vs* α-hydroxy ketone.

Oxidation of *trans*-3-Hexene with Aqueous TBHP under Slow Addition of Olefin in the Presence of TEAA. In a 10-mL septum-capped vial was placed aqueous TBHP (70%, 0.55 mL, 4.0 mmol) and TEAA (375 mg, 2 mmol) in acetonitrile:water (4:1; 5 mL). Osmium tetroxide (20 μL, 0.01 mmol) was added and the reaction mixture was stirred at ca 20 °C with the slow addition of *trans*-3-hexene (125 μL, 1 mmol) during 18 h. The reaction was quenched with sodium metabisulfite (1.0 g, 5.25 mmol) and the product was analyzed by gas chromatography indicating a 22:1 ratio of diol *vs* α-hydroxy ketone. The diol (89 mg; 75%) was isolated by flash chromatography over silica gel using a mixture of ethyl acetate and petroleum ether (1:1).

Oxidation of *trans*-3-Hexene with Aqueous TBHP under Slow Addition of Olefin and TBHP in the Presence of TEAA. In a 10-mL septum-capped vial was placed TEAA (375 mg, 2 mmol) in acetonitrile:water (4:1; 5 mL). Osmium tetroxide (20 μL, 0.01 mmol) was added and the reaction mixture was stirred at ca. 20 °C with the slow addition of *trans*-3-hexene (125 μL, 1 mmol) and aqueous TBHP (0.55 mL, 4 mmol) during 18 h. The reaction was quenched with sodium metabisulfite (1.0 g, 5.25 mmol) and the product was analyzed by gas chromatography indicating a 35:1 ratio of diol *vs* α-hydroxy ketone. The diol (92 mg; 78%) was isolated by flash chromatography over silica gel using a mixture of ethyl acetate and petroleum ether (1:1).

General Procedure for Asymmetric Dihydroxylation of *trans*-Alkenes with Aqueous TBHP under Slow Addition of Olefin and TBHP in the Presence of TEAA. In a 10-mL septum-capped vial was placed TEAA (375 mg, 2 mmol) and dihydroquinidine 4-chlorobenzoate (20 mg, 0.025 mmol) in acetonitrile:water (4:1; 5 mL). Osmium tetroxide (20 μL, 0.01 mmol) was added and the reaction mixture was stirred at ca. 20 °C with the slow addition of both the olefin (1.0 mmol) and aqueous TBHP (0.55 mL, 4 mmol) during 18 h using separate syringe pumps. The reaction was quenched with sodium metabisulfite (1.0 g, 5.25 mmol) and the product was analyzed by gas chromatography to determine the ratio of the diol *versus* ketol. The diol was isolated by flash chromatography over silica gel using a mixture of ethyl acetate and petroleum ether (1:1).

General Procedure of Asymmetric Dihydroxylation of *trans*-Alkenes with Aqueous TBHP. In a 25-mL round-bottom flask equipped with a magnetic bar was placed bisdihydroquinidine terephthalate ester (32 mg, 0.04 mmol) in acetonitrile:water (4:1; 5 mL); and osmium tetroxide (20 μL, 0.01

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mmol) was added with stirring. The reaction mixture turned to orange red. *trans*-Alkene (1 mmol) was added at room temperature (20 °C) followed by addition of aqueous TBHP (70%, 0.55 mL, 4 mmol). The reaction mixture was stirred until all the starting material disappeared (TLC monitored). The reaction was quenched with sodium metabisulfite (2.0 g, 10.5 mmol) and the stirring was continued for an additional 1 h. The reaction was diluted with ethyl acetate (25 mL) and filtered through a pad of Celite, and the Celite bed was washed with ethyl acetate (3 × 25 mL). The combined organic filtrate was washed with water (20 mL) and brine (20 mL) and dried. The solvent was removed to give a residue which was chromatographed over silica gel to furnish the products.

Oxidation of *trans*-Stilbene. The oxidation of *trans*-stilbene (180 mg, 1 mmol) by the above procedure afforded benzoin [(59 mg, 28%) mp 134–136 °C, $[\alpha]^{22}_D$ = –6.5° (*c*, 1.3, acetone)], hydrobenzoin[2a] [(75 mg, 35% mp 148 °C; $[\alpha]^{22}_D$ = +66.2° (*c*, 2.0, EtOH)], and benzaldehyde (32 mg, 30%).

Oxidation of *trans*-3-Hexene. *trans*-3-Hexene (125 μL, 1 mmol) was oxidized using the above experimental procedure to afford 58 mg (50%) of 3-hydroxy-4-hexanone $[\alpha]^{22}_D$ = –2.2° (*c*, 2.0, $CHCl_3$)[6b] and 3,4-hexanediol[2a] (47 mg, 40%), $[\alpha]^{22}_D$ = + 6.2° (*c*, 1.5, H_2O).

Oxidation of *trans*-5-Decene. *trans*-5-Decene (190 μL, 1 mmol) was oxidized under the above experimental condition to furnish 5-hydroxy-6-decanone (114 mg, 66%) and 5,6-dihydroxydecane [5] (43 mg, 25%); $[\alpha]^{22}_D$ = +9.1° (*c*, 1, EtOH).

Oxidation of *trans*-2-Octene. *trans*-2-Octene (156 μL, 1 mmol) was oxidized under the above experimental condition to furnish a mixture of 2-hydroxy-3-octanone and 3-hydroxy-2-octanone (3:2; 50 mg, 35%) and 2,3-octane diol[16] (80 mg, 55%): $[\alpha]^{22}_D$ = +5.1° (*c*, 0.4, $CHCl_3$).

Attempted Oxidation of 3,4-Hexanediol with Osmium Tetroxide–TBHP. In a 10-mL round bottom flask was placed 3,4-hexanediol (30 mg; 0.25 mmol) in acetonitrile–water (4:1, 0.5 mL), and osmium tetroxide (5 μL; 2.5×10^{-3} mmol) and aqueous TBHP (70%, 138 μL, 1 mmol) were added. The reaction mixture was stirred for 1 h and quenched with sodium metabisulfite (ca. 0.5 g). The reaction mixture was extracted with CH_2Cl_2 and analyzed by gas chromatography which indicated the presence of only unreacted 3,4-hexanediol.

Preparation of Dipotassium Bis(hexane-3,4-diolato)-osmium(VI) (6).[8] This complex was prepared by Criegee's method.[8]

Preparation of Oxobis(hexane-3,4-diolato)osmium(VI) (2). The complex **2** was prepared by a modified Criegee's procedure.[8] In a 10-mL screw-capped vial was placed osmium tetroxide (13 mg, 0.05 mmol) in CH_2Cl_2 (2 mL), and *trans*-3-hexene (8.4 mg, 0.1 mmol) was added. After stirring for 5 min at ca. 0 °C, *N*-methylmorpholine *N*-oxide (NMO, 23 mg, 0.2 mmol) was added and the dark-black reaction mixture was stirred for an additional 1 h at room temperature. The reaction mixture was diluted with petroleum ether (5 mL) and filtered. The filtrate was evaporated and the residual dark-black liquid was chromatographed over silica gel using a mixture of ethyl acetate and petroleum ether (1:4) to furnish nearly quantitative yield of complex **2**. IR (Neat) ν_{max} 2995, 2950, 2900, 1475, 1395, 1325, 1125, 1080, 1005, 960, 905, 885, 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.55 (m, 4 H), 1.85 (m, 8 H), 1.0 (m,12 H); ^{13}C NMR ($CDCl_3$) δ 9.31, 9.46, 9.61, 9.75, 27.58, 27.75, 27.86, 95.60, 95.85, 97.27, 97.45. Anal. Calcd for $C_{12}H_{24}O_5Os$: C, 32.87; H, 5.48; Os, 43.37. Found: C, 33.01; H, 5.50; Os, not analyzed.

Preparation of Dioxomono(glycolato)osmium (VI) Complex 4. In a 10-mL round bottom flask was placed bisdihydroquinidine terephthalate ester (40 mg, 0.05 mmol) in dry CH_2Cl_2 (0.5 mL), and osmium tetroxide (25.5 mg, 0.1 mmol) was added to give a deep orange solution. After 10 min at room temperature, *trans*-3-hexene (12.5 μL, 0.1 mmol) was added to furnish a deep green colored solution. The reaction mixture was allowed to stand at room temperature for 2 h, followed by dilution with petroleum ether to precipitate the green colored solid product: IR (Nujol) ν_{max} 1730, 1630, 1520, 1470, 1385, 1275, 1110, 1025 cm^{-1}; ^1H NMR ($CDCl_3$) : 8.75 (d, *J* = 5 Hz, 2 H), 8.25 (S, 4 H), 8.05 (d, *J* = 10 Hz, 2 H), 7.6 (bs, 2 H), 7.4 (m, 4 H), 6.9 (bs, 2 H), 4.6 (bm, 2 H), 4.0 (S, 6 H), 3.45 (bm, 4 H), 3.0 (bm, 8 H), 1.9 (bm, 6 H), 1.55 (bm, 12 H), 1.0 (m, 12 H); ^{13}C NMR ($CDCl_3$) δ 164.37, 158.14, 147.19, 144.68, 133.88, 131.77, 129.72, 126.76, 122.1, 118.26, 101.27, 74.30, 59.23, 55.75, 52.31, 49.74, 41.42, 37.03, 36.29, 29.60, 27.82, 26.63, 26.02, 25.29, 22.94, 21.54, 11.73, 9.88. Anal. Calcd for $C_{54}H_{86}N_4Os_2O_{14}$ (1374): C, 47.16; H, 4.80; N, 4.07; Os, 27.65. Found: C, 50.02; H, 4.89; N, 4.00; Os, not analyzed.

Oxidation of Osmium(VI) Complex 4 (L = –) by Dry TBHP to Trioxomonoglycolate Intermediate 3. Detection by IR Spectroscopy and Reaction with *trans*-3-Hexene. In a screw-capped vial containing osmium(VI) complex **4** (L = –) (14 mg, 0.04 mmol) was dissolved in $CHCl_3$ (1 mL) to form a 0.1 mM solution. The IR spectrum was recorded and then the reaction mixture was treated with anhydrous TBHP (4.0 M in $CHCl_3$) (20 μL, 0.08 mmol). The dark green solution instantaneously turned colorless. The IR spectrum was recorded which showed bands at 965, 910 and 855 cm^{-1} characteristic of Os=O bond. These bands at 910 and 855 cm^{-1} disappeared after addition of *trans*-3-hexene (12.5 μL, 0.1 mmol). This is expected due to the formation of monooxobis(glycolato)osmium(VI) species in the reactiion.

Oxidation of Hexane-3,4-diol by Osmium(VI) Complex 4. In a-10 mL screw-capped vial was placed **4** (28 mg, 0.02 mmol) in 0.2 mL of dry CH_2Cl_2, and hexane-3,4-diol (3 μL, 0.025 mmol) was added with stirring. After stirring for 6 h at *ca* 20 °C, the reaction mixture was quenched with moist sodium metabisulfite (0.1 g), extracted with CH_2Cl_2 (2 × 2 mL), and analyzed by gas chromatography, which indicated only 3,4-hexanediol.

Oxidation of *trans*-3-Hexene by Osmium(VI) Complex 2. Oxidation of *trans*-3-hexene (7 μL, 0.056 mmol) was carried out using complex **2** (25 mg, 0.056 mmol) in CH_2Cl_2 (0.2 mL) for 6 h at room temperature, and the reaction mixture after usual workup was analyzed by gas chromatography which indicated the presence of the starting material and no 4-hydroxy-3-hexanone.

Oxidation of Hexane-3,4-diol by Osmium(VI) Complex 2. Oxidation of hexane-3,4-diol (8 mg, 0.067 mmol) was carried out with **2** (24 mg, 0.05 mmol) under the above experimental conditions and the reaction mixture was analyzed by gas chromatography which indicated only 3,4-hexanediol and the absence of 4-hydroxy-3-hexanone.

Oxidation of Osmium(VI) Complex 2 with Anhydrous TBHP. In a 5- mL screw-capped vial was placed **2** (48 mg, 0.1 mmol) in acetonitrile (0.5 mL) to which dry TBHP (100 μL, 0.4 mmol, 4 M in CH_2Cl_2) was added, and the reaction mixture was stirred for 6 h at *ca.* 20 °C. The reaction mixture after usual workup was analyzed by gas chromatography which indicated only 4-hydroxy-3-hexanol (3 mg, 15%).

Oxidation of Osmium(VI) Complex 2 with Anhydrous TBHP in the Presence of Catalytic Amount of Glacial Acetic Acid. In a 5-mL screw-capped vial was placed **2** (48 mg, 0.1 mmol) in CH_2Cl_2 (0.5 mL) to which glacial acetic acid (5 μL) and dry TBHP (100 μL, 0.4 mmol, 4 M in CH_2Cl_2) were added, and the reaction mixture was stirred for 6 h at ca. 20 °C. The reaction mixture after usual workup was analyzed by gas chromatography which indicated the presence of 4-hydroxy-3-hexanol and 3,4-hexanediol in 1:1 ratio (combined yield, 16 mg, *ca.* 80%).

Oxidation of Osmium(VI) Complex 2 with Aqueous TBHP. In a 5-mL screw-capped vial was placed complex **2** (48 mg, 0.1 mmol) in 0.5 mL of acetonitrile, aqueous TBHP (55 μL, 0.4 mmol, 70%) was added, and the reaction mixture was stirred for 6 h at *ca* 20 °C. The reaction mixture after the usual workup was analyzed by gas chromatography, which indicated 4-hydroxy-3-hexanone and hexane-3,4-diol in 39:61 ratio.

Oxidation of Dipotassium Osmium(VI) Complex 6 with Anhydrous TBHP. Oxidation of complex **6** (53 mg, 0.1 mmol) was carried out using dry TBHP (100 μL, 0.4 mmol, 4 M in CH_2Cl_2) for 6 h at 20 °C. The reaction mixture was analyzed by GC which indicated the presence of 4-hydroxy-3-hexanone and 3,4-hexanediol in 14:86 ratio.

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