exist between zeolites synthesized in hydroxide and fluoride media in this respect. Further study is necessary to determine the underlying mechanisms of this intriguing behavior. However, the overall NMR results presented here strongly suggest that the substitution of Al atoms into the ZSM-5 framework during the crystallization process may be kinetically, rather than energetically, controlled. This led us to believe that the substitution patterns of other heteroatoms (e.g., B, Ga, Ti, etc.) in the ZSM-5 framework would also be nonrandom, although they may differ in manner from Al substitution. In fact, recent neutron powder diffraction studies on TS-1, the titanosilicate analogue of ZSM-5, showed that Ti atoms are not uniformly distributed over the 12 ZSM-5 T-sites.[13] Finally, it is of interest whether our concept can be applied to other important high-silica materials with multiple T-sites such as zeolites β and MCM-22.[1]

Experimental Section

Six ZSM-5 zeolites with different Si/Al ratios were synthesized by using NH_4F (+98%, Aldrich) and TPABr (98%, Aldrich) in fluoride media to minimize the possible influence of connectivity defects on the distribution of Al in the ZSM-5 framework, according to procedures described elsewhere.[14] The Si/Al ratio in the final product was varied by adjusting the amount of $Al(NO_3)_3 \cdot 9H_2O$ (99%, Wako) that was added to the synthesis mixture as Al source. Amorphous silica (Aerosil 200, Degussa) was used as Si source. All ZSM-5 zeolites prepared here were phase-pure and highly crystalline (powder XRD, Rigaku Miniflex, $Cu_{K\alpha}$ radiation). The Si/Al ratios of these six as-made samples were analyzed in the Analytical Laboratory of KIST. The absence of any detectable line at $\delta \sim 0$ in the ^{27}Al MAS NMR spectra (Figure 1) indicates that all the Al atoms in these samples are isomorphously incorporated into the T-sites of the ZSM-5 framework. Also, thermogravimetric and differential thermal analyses (TA Instruments SDT 2960) reveals that they contain 3.8–4.3 TPA cations per unit cell.

The ^{27}Al MAS NMR spectra were recorded on a Bruker DSX 400 NMR spectrometer that operates at a ^{27}Al frequency of 104.27 MHz and a spinning rate of 13 kHz. The spectra were obtained by acquisition of 300–400 pulse transients, which was repeated with a $\pi/12$ rad pulse length of 0.8 μs and a recycle delay of 1 s. The ^{27}Al chemical shifts are referenced to a 1N $[Al(H_2O)_6]^{3+}$ solution. The 2D ^{27}Al 3Q MAS NMR spectra were recorded on a Varian INOVA 400 NMR spectrometer by the two-pulse *z*-filtered procedure with rotor synchronization[15] at a spinning rate of 10 kHz, with an excitation pulse of 6 μs and a conversion pulse of 1.8 μs for an rf field strength of 84 kHz. For each t_1 384 or 768 scans were accumulated, and t_1 was incremented 64 times.

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A New Approach to Osmium-Catalyzed Asymmetric Dihydroxylation and Aminohydroxylation of Olefins**

Malin A. Andersson, Robert Epple, Valery V. Fokin,* and K. Barry Sharpless*

Osmium-catalyzed asymmetric dihydroxylation (AD) of olefins using cinchona alkaloid derived ligands is known for its exceptional scope and reliability across nearly the entire

[*] Prof. V. V. Fokin, Prof. K. B. Sharpless, Dr. M. A. Andersson, Dr. R. Epple
Department of Chemistry
and The Skaggs Institute for Chemical Biology, BCC-315
The Scripps Research Institute
10550 N. Torrey Pines Rd.
La Jolla, CA 92037 (USA)
Fax: (+1) 858-784-7562
E-mail: fokin@scripps.edu, sharples@scripps.edu

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range of olefin types and substitution patterns on both laboratory and industrial scales.[1] Its sister reaction, the asymmetric aminohydroxylation (AA), is the aza-analogue of the parent transformation and represents a powerful, direct route to vicinal amino alcohols.[2] After its discovery in 1996, a great deal of effort has been devoted to make it as reliable, versatile, and convenient to use as its dihydroxylation counterpart. Although the AA process has already found substantial use in organic synthesis, it still lacks the generality and reliability of the AD process. In many cases, problems arise that appear to be related to some combination of the following issues: 1) selectivities (chemo-, regio-, and enantio-), 2) substrate scope, and 3) catalyst activity. Of these, chemoselectivity is the most serious, with up to 70% of corresponding vicinal diol being produced in unfavorable cases.

A uniquely helpful mechanistic insight about these osmium(VIII)-catalyzed systems arose during our process improvement endeavors on the AD—namely, there are two catalytic cycles producing the diol (Scheme 1).[3] Under homogeneous conditions, where the reoxidant has constant access to all the catalytic intermediates, the turnover is locked into the second cycle, simply because hydrolysis steps (h^1 and h^2) are *much slower* than the redox steps (r^1, r^2, and r^3). As a consequence, the osmium(VI) bis(glycolate) (**II**) is the resting form of the catalyst.

In the last few years, we have discovered that certain classes of olefins give extraordinary results when subjected to the standard reaction conditions for either the osmium-catalyzed dihydroxylation or aminohydroxylation process.[4, 6] In the absence of the alkaloid ligand, and even with very low catalyst loadings, these special olefins undergo rapid and nearly quantitative conversion to the expected products, vicinal diols or amino alcohols. This is in sharp contrast to other olefins, whose turnover is crucially dependent on the ligand-acceleration effect.[5] Having recently found that unsaturated carboxylic acid[6] substrates constitute an extreme example, even within this "special" reactivity zone, we redoubled efforts to get at the mechanistic underpinnings which account for such phenomenally vigorous catalysis.

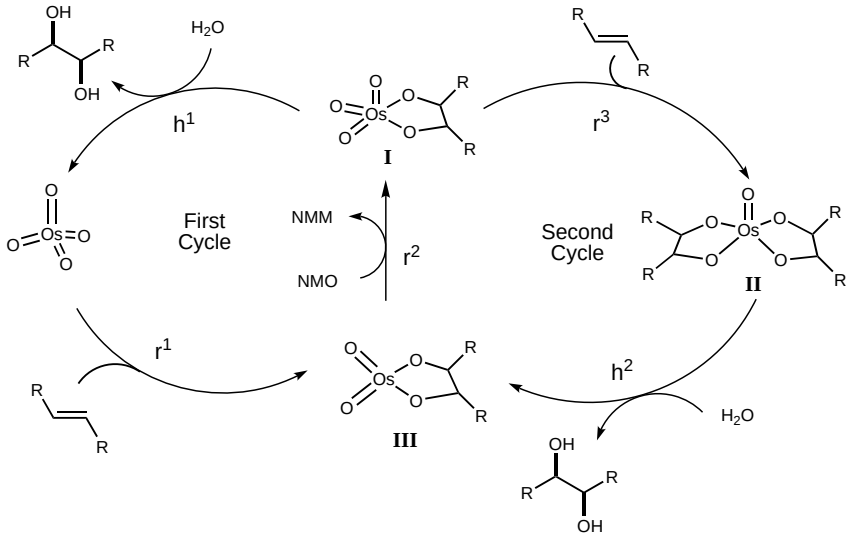
With all the "special" substrates only racemic products are formed, even when an enormous excess of the chiral ligand is added. This and other available evidence[7] strongly suggest that these olefins turnover almost exclusively in the second catalytic cycle, in which osmium(VI) bis(glycolate) (**II**) (or the bis(azaglycolate) in the case of aminohydroxylation) is the most stable intermediate—it is so stable that it is the only detectable osmium complex present under steady-state conditions. According to our current mechanistic hypothesis, the resident carboxylate groups ($-COO^-$) in this complex facilitate the rate-determining step, hydrolysis, thereby accounting for the dramatically increased reactivity of these substrates.

Although we had traditionally sought to avoid the second cycle at all costs, deleterious as it is to enantioselectivity, the enticing possibilities it offers for a new way to control osmium(VIII) catalysis have been clear since the time of its discovery in 1982. Although early attempts to obtain enantioselectivity with second-cycle ligands failed, the recent enormous jump in effectiveness of the second-cycle systems[6] convinced us that their inherent advantages *must* be exploited to develop new catalytic processes. To tame the second cycle, one needs to design a ligand that a) is chiral and capable of controlling stereochemistry in the olefin oxidation step r^3; b) aids in the hydrolytic release (h^2) of the diol from the initial Os^{VI}–product complex (**II**); and c) is not itself hydrolytically removed from the osmium coordination sphere.[8]

Herein, we describe the first ligands found to induce asymmetry in the osmium-catalyzed dihydroxylation and aminohydroxylation proceeding in the second catalytic cycle. As a simple model for screening the ligand candidates shown in Table 1, we have chosen the dihydroxylation of styrene under the Upjohn conditions.[9] Incidentally, overoxidation of the product diol, a fairly common side reaction in the Upjohn dihydroxylation, was not observed.

Even tartaric acid, although needed in quantity of 25 mol%, showed asymmetric induction. Finding ligands with a higher affinity for osmium was an obvious requirement to reduce the amount of ligand. Since *N*-sulfonyl-1,2-hydroxyamines (vicinal hydroxysulfonamides) have much higher binding constants for osmium than analogous 1,2-diols, a number of *N*-toluenesulfonyl derivatives of α,β-hydroxyamino acids were screened resulting in the improvement of the enantiomeric excess (*ee*) to 42%. The *ee* values remained constant throughout the course of reactions and, more importantly, as little as 1.5–2 mol% ligand was sufficient to attain the ceiling enantioselectivity (Figure 1).[10]

Simple structure–activity studies have revealed that a free carboxylate group appears to be an essential component of a successful ligand. Thus, only racemic diol was obtained when the methyl ester of **1** was used as a ligand. Location of the HO and TsNH groups was found to play an



Scheme 1. The two catalytic cycles in the osmium-catalyzed dihydroxylation of olefins using 4-methylmorpholine-*N*-oxide (NMO) as reoxidant.

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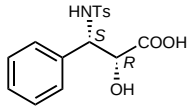
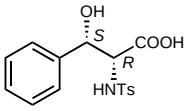
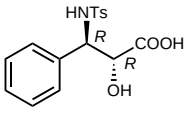
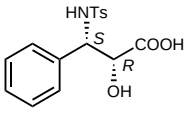
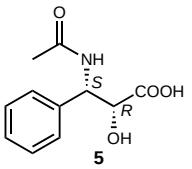
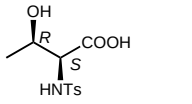
Tabelle 1. Dihydroxylation of styrene with novel ligands.[a]

Entry	Ligand	Ligand [mol%]	Conversion [%]	*ee* [%] (abs. conf.)[b]
1	 **1**	5	>99	25 (*R*)
2		2	>99	25 (*R*)
3	 **2**	5	>99	7 (*R*)
4	 **3**	5	>99	29 (*R*)
5	 **4**	5	>99	42 (*R*)
6		2	>99	42 (*R*)
7	 **5**	5	>99	5 (*R*)
8	 **6**	5	>99	25 (*S*)

[a] All reactions were performed on 1 mmol scale at 0.5 M concentration in *t*BuOH/H_2O (1:1) with 1.1 equiv NMO and 0.2 mol% of OsO_4. The progress was monitored by GC, and *ee* values were determined by HPLC (Chiralcel OB, 10% *i*PrOH/Hexane). [b] The absolute configuration of styrene diol was assigned by comparison with authentic samples.

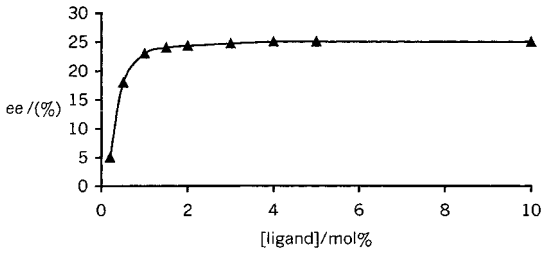
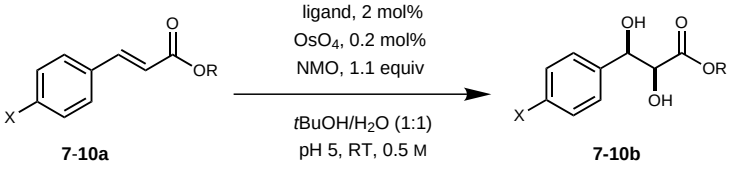


Figure 1. Dependence of enantioselectivity on ligand concentration in dihydroxylation of styrene with **1** as a ligand.

important role as well. For example, the phenylisoserine-based ligand **1** afforded a higher *ee* value than its regioisomer **2**. The absolute configuration of the diol product appears to be determined by the stereochemistry of the α-carbon atom of the ligand (see Table 1, entries 1, 4, and 8). Additional investigations have shown that modification of the substituents on the sulfonamide group (R-SO_2NH-) has only a minor effect on the stereochemical outcome of the reaction. However, the ligand should preferentially contain an *N*-sulfonyl moiety, as its replacement with an amide (as in **5**, see Table 1, entry 7) or a carbamate resulted in very low to no enantioselectivity.

Most of the ligands discussed above can be readily prepared in enantiomerically enriched form by using previously developed catalytic olefin transformations.[2] Furthermore, some hydroxyamino acids are commercially available compounds, and can be easily converted to their corresponding *N*-sulfonyl derivatives.[11] For example, *N*-(*p*-toluenesulfonyl)threonine, (2*S*,3*R*)-**6** (see Table 1, entry 8) has been found to be particularly effective for dihydroxylation of cinnamate esters, with 70% *ee* realized in one case (Table 2).[12]

Tabelle 2. Asymmetric dihydroxylation of cinnamates using new ligands.



7-10a **7-10b**

Olefin	X	R	*ee* [%] (ligand **4**)	*ee* [%] (ligand **6**)
7	H	Me	48	51
8	H	Et	50	48
9	H	*i*Pr	53	44
10	NO_2	Me	40	70

In initial studies on the effects of these new second-cycle ligands on the related osmium-catalyzed aminohydroxylation process, we found that both styrene and methyl cinnamate were converted to the corresponding hydroxysulfonamides in high yields with *ee* values ranging from 25 to 55% (Table 3). Very importantly (and in stark contrast to the traditional AA with the cinchona alkaloid derived ligands), no diol formation was detected, and the products were free of osmium contamination.

In summary, a new way of controlling osmium-catalyzed oxidations is offered by a powerful class of ligands, which enforce second-cycle turnover by never leaving the catalytic center. Such processes offer many variables for optimization (in fact, considerably more than the AD offered when it was at the same stage of development) and present an opportunity for a quantum jump in the utility of the osmium-catalyzed oxidation processes. If these second-cycle processes can be optimized, and there are many obvious variables to explore, they should surpass, and thence replace, the existing AD and AA, which as first-cycle processes are dependent on external chiral ligands.

Experimental Section

Typical dihydroxylation procedure as exemplified for methyl 4-nitrocinnamate: Methyl 4-nitrocinnamate (207 mg, 1 mmol) and *N*-(4-toluenesulfonyl)-(L)-threonine (13.6 mg, 5 mol%)[11] were dissolved in a *t*BuOH/H_2O mixture (1:1, 6 mL). NMO (50 wt% in water, 228 μL, 1.1 mmol) and OsO_4 (0.1 M in acetonitrile, 20 μL, 0.002 mmol) were added successively. The pH was adjusted to 5 by addition of 2 N H_2SO_4 (150 μL), and the reaction mixture was stirred vigorously for 24 h, at which time the pH was adjusted

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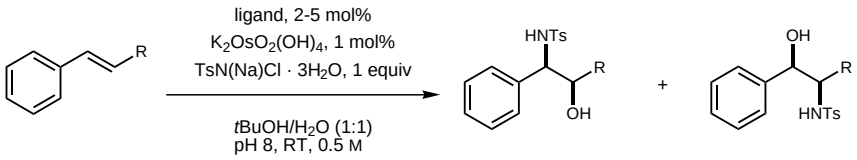
Tabelle 3. Asymmetric aminohydroxylation of olefins using ligands **4** and **6**.[a]



11 **12** **13**

R	Ligand (mol%)	Conversion [%]	ratio **12**:**13**	*ee* of **12** [%] (absolute conf.)[b]	*ee* of **13** [%] (absolute conf.)[b]
H	**4** (2)	89	1:2	45 (*S*)	55 (*R*)
	4 (5)	86	1:2	48 (*S*)	55 (*R*)
	6 (2)	80	1:2	30 (*S*)	25 (*R*)
	6 (5)	75	1:2	47 (*S*)	38 (*R*)
$COOCH_3$	**4** (2)	85	1:2	52 (*2S*,*3R*)	24 (*2R*,*3S*)
	4 (5)	93	1:2	59 (*2S*,*3R*)	25 (*2R*,*3S*)

[a] The reactions were typically run for 20 h and were monitored by HPLC at 228 nm. The regioisomers were separated by reversed-phase preparative liquid chromatography and the *ee* values were determined for each regioisomer separately (R = H, **12**: Chiralcel OG (30% *i*PrOH in hexane), **13**: Chiralpak AS (15% *i*PrOH in hexane); R = $COOCH_3$, **12**: Chiralcel OG (30% *i*PrOH in hexane), **13**: Chiralpak AD (20% *i*PrOH in hexane)). [b] The absolute configuration of the products was assigned by comparison with authentic samples.

to 5 again. After an additional 24 h (= 98% conversion by liquid chromatography), methyl (2*R*,3*S*)-(+)-2,3-dihydroxy-3-(*p*-nitrophenyl)-propionate[13] was obtained in 70% *ee* (HPLC: Chiralcel OG, 20% *i*PrOH/hexane). The reaction time can be reduced to about 24 h by maintaining constant pH using a pH-stat. A 10 mmol scale reaction, performed under these conditions, afforded product as white solid in 75% yield (1.8 g) and 70% *ee*. Recrystallization from ethanol produced needle-shaped crystals in 57% yield and 81% *ee*.

Typical aminohydroxylation procedure as exemplified for styrene: (2*R*,3*S*)-*N*-(4-Toluenesulfonyl)-4-nitroisophenylserine (190 mg, 0.5 mmol) and sodium bicarbonate (8.4 mg, 1 mmol) were dissolved in *t*BuOH/H_2O (1:1, 20 mL). Styrene (1.040 mg, 10 mmol), Chloramine-T trihydrate (2.870 mg, 10 mmol), and $K_2OsO_2(OH)_4$ (36 mg, 0.1 mmol) were then added successively. The reaction mixture was stirred at room temperature for 20 h, at which point HPLC analysis indicated 90% conversion. Sodium sulfite (100 mg) was added, and the mixture was stirred for an additional hour. It was then extracted (ethyl acetate, 3 × 25 mL), dried, and concentrated to yield amorphous solid. Flash chromatography purification afforded a mixture of regioisomers **12**:**13** (29:71, determined by NMR) as a white crystalline product (2.5 g, 86%). Regioisomers were separated by preparative HPLC (CH_3CN/H_2O, 30:70, 0.1% trifluoroacetic acid (TFA), YMC C18 column, 100 mg scale). Enantiomeric excess was determined by chiral HPLC and the absolute configuration was established by comparing optical rotation with authentic samples. (*S*)-**12**, 51%, (Chiralcel-OG, *i*PrOH/hexane, 30:70, 1.5 mL min^{-1}) and (*R*)-**13** , 54% (Chiralcel-AS, *i*PrOH/hexane, 30:70, 1.5 mL min^{-1}).

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[8] This restriction is not really so severe—it only has to *dominate* the catalysis. This can be achieved with a mobile ligand too (e.g., ligand-accelerated catalysis or simply the equilibrium favoring the desired osmium complex in the olefin oxidation step).

[9] V. Van Rheenen, R. C. Kelly, P. Y. Cha, *Tetrahedron Lett.* **1976**, 1973.

[10] To ensure that the maximum possible *ee* value was afforded by each ligand, 5 mol% of ligand was routinely used. We now know from different examples that 1.5 – 2.0 mol% is sufficient. The finding that the dependence of the enantioselectivity on the amount of the ligand shows saturation behavior points to the fact that the process in its present form operates at the maximum *ee* afforded by the ligand.

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