Enantioselective Vicinal Hydroxylation of Terminal and *E*-1,2-Disubstituted Olefins by a Chiral Complex of Osmium Tetraoxide. An Effective Controller System and a Rational Mechanistic Model†

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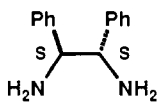
The suprafacial hydroxylation of olefins by osmium tetraoxide, though a much used synthetic method,[1] would become even more important if three conditions could be met: (1) modification to achieve high and predictable enantioselectivity and acyclic diastereoselectivity, (2) clarification of reaction mechanism, and (3) facilitated recovery and recycling of osmium. This paper reports progress on all three fronts. Several other laboratories have been actively involved in the development of chiral ligands for enantioselective dioxyosmylation of olefins, most notably those of Sharpless,[2] Tomioka,[3] Narasaka,[4] Snyder,[5] Hirama,[6] and Cinquini,[7] with a gratifying measure of success. On the mechanistic side, the picture has been very unclear,[1] not only in terms of stereochemical detail but also with regard to the matter of [3 + 2] cycloaddition (O=Os=O + C=C)[8] and [2 + 2] cycloaddition (Os=O + C=C)[9,2a,3b] pathways.

Our approach involves the use of the chiral ligand **2** derived from chiral 1,2-diphenyl-1,2-diaminoethane (**1**), a controller group that has recently been shown to provide highly enantioselective versions of several powerful synthetic constructions, for example, Diels–Alder, aldol, and carbonyl allylation processes.[10-12] The



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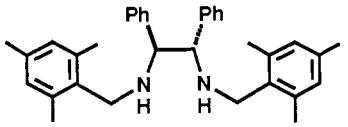

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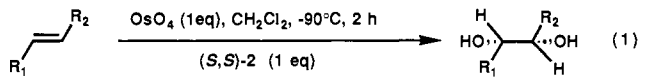
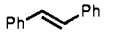
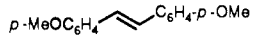
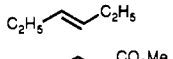
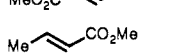
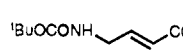
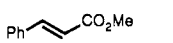
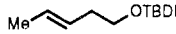
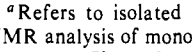
synthesis of (*S*,*S*)-**2** was accomplished by the sequence (1) heating of (*S*,*S*)-**1** with 2.5 equiv of mesitaldehyde in toluene solution at 60 °C with removal of water and (2) reduction of the resulting *N*,*N*′-bis(2,4,6-trimethylbenzylidene) derivative of **1** with sodium borohydride in 1:1 toluene–methanol, to give diamine **2** (96%), mp 131–132 °C, $[\alpha]^{23}_D$ +24.6° (*c* = 1.1, $CHCl_3$).[13] An equimolar mixture of **2** and osmium tetraoxide in toluene or CH_2Cl_2 solution at −78 °C leads to enormously accelerated olefin dioxyosmylation at −78 to −90 °C in toluene or CH_2Cl_2 solution, conditions under which there is no reaction between olefin and osmium tetraoxide.

Table I. Enantioselective Hydroxylation of Olefins by OsO_4·**2**



(1)

olefin	yield,[a] %	ee,[b] %	config[c]
	81	92	*S*
	95	93	*S*,*S*
	95	92	*S*,*S*
	90	82	(*S*,*S*)[d]
	90	98	*S*,*S*
	75	92	2*R*,3*R*
	82	97	2*R*,3*S*[e]
	91	97	2*R*,3*S*[f]
	83	92	2*R*,3*S*
	87	95	(2*S*,3*S*)[d]

[a] Refers to isolated yield after chromatography. [b] Determined by NMR analysis of mono and bis MTPA esters: Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512. [c] Unless otherwise stated, the absolute configuration was determined by comparison of the optical rotation of previously reported diols: Tomioka, K.; Nakajima, M.; Koga, K. *J. Am. Chem. Soc.* **1987**, *109*, 6213. [d] Absolute configuration was assigned by analogy. [e] Absolute configuration was determined by comparison with the bis MTPA ester of authentic diol synthesized from L-threonine: Myer, E.; Rose, W. C. *J. Biol. Chem.* **1936**, *115*, 721. [f] Absolute configuration determined by comparison with the bis MTPA ester of authentic diol synthesized from (*R*,*R*)-(+)-dimethyl L-tartrate: Musich, J. A.; Rapoport, H. *J. Am. Chem. Soc.* **1978**, *100*, 4865.

A variety of olefins were oxidized by using the 1:1 mixture of ligand **2** and osmium tetraoxide in CH_2Cl_2 at −90 °C for a period of 2.3 h, to provide vicinal diol by (1) removal of solvent, (2) reduction of the dark complex of Os(IV), diol, and diamine **2** by heating at reflux for 2 h with 1:1 saturated aqueous sodium bisulfite–tetrahydrofuran (THF), (3) separation of the aqueous and THF layers, (4) basification of the aqueous layer with sodium bicarbonate and extraction with ethyl acetate, (5) concentration of the combined THF and ethyl acetate solutions in vacuo, and (6) column chromatography on silica gel, to give pure diol (80–95%) and recovered diamine **2** (ca. 80% of theory). A black osmium-containing material was deposited at the top of the silica gel column. Removal of that top layer of darkened silica and reaction with 1.3:1 CH_2Cl_2–30% aqueous hydrogen peroxide at 23 °C for 2 h produced, after separation of the CH_2Cl_2 layer and drying ($MgSO_4$), a concentrated CH_2Cl_2 solution of OsO_4 containing >80% of the originally used osmium; the resulting solution of OsO_4 could be used directly for olefin hydroxylation with ligand **2** as described above, with identical results. Thus, this method of product isolation allows the recovery of pure diol and catalytic diamine **2** and the recycling of OsO_4, all with good efficiency.

The enantioselective hydroxylation of a variety of olefins by **2** and OsO_4 as summarized in Table I occurred in the sense expressed by eq 1 and with excellent enantioselectivity, in several cases 95% ee or better.

The stereochemical results summarized in Table I can be understood in terms of a rational model involving a bidentate, octahedrally coordinated complex of **2** with OsO_4 as the reactive species. It is likely that the transition state for the dioxyosmylation is of the [3 + 2] cycloaddition type, since the [2 + 2] cycloaddition pathway.[9,2a,3b] would involve prohibitive steric repulsions about hexacoordinate octahedral osmium. Recent theoretical work[8]

† Dedicated to the memory of Professor Roger Adams in this the centennial year of his birth.

(1) For a review, see: Schröder, M. *Chem. Rev.* **1980**, *80*, 187.
(2) (a) Hentges, S. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 4263. (b) Jacobsen, E. N.; Markó, I.; Mungall, W. S.; Schröder, G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 1968. (c) Wai, J. S. M.; Markó, I.; Svendsen, J. S.; Finn, M. G.; Jacobsen, E. N.; Sharpless, K. B. *J. Am. Chem. Soc.* **1989**, *111*, 1123. (d) Svendsen, J. S.; Markó, I.; Jacobsen, E. N.; Pulla Rao, Ch.; Bott, S.; Sharpless, K. B. *J. Org. Chem.* **1989**, *54*, 2264.
(3) (a) Tomioka, K.; Nakajima, M.; Koga, K. *J. Am. Chem. Soc.* **1987**, *109*, 6213. (b) Tomioka, K.; Nakajima, M.; Iitaka, Y.; Koga, K. *Tetrahedron Lett.* **1988**, *29*, 573.
(4) Yamada, T.; Narasaka, K. *Chem. Lett.* **1986**, 131.
(5) Tokles, M.; Snyder, J. K. *Tetrahedron Lett.* **1986**, *27*, 3951.
(6) Hirama, M.; Oishi, T.; Itô, S. *J. Chem. Soc., Chem. Commun.* **1989**, 665.
(7) Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L.; Stefenelli, S. *Tetrahedron Lett.* **1987**, *28*, 3139.
(8) Jorgensen, K. A.; Hoffman, R. *J. Am. Chem. Soc.* **1986**, *108*, 1867.
(9) Sharpless, K. B.; Teranishi, A. Y.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1977**, *99*, 3120.
(10) Corey, E. J.; Imwinkelried, R.; Pikul, S.; Xiang, Y. B. *J. Am. Chem. Soc.* **1989**, *111*, 5493.
(11) Corey, E. J.; Yu, C.-M.; Kim, S. S. *J. Am. Chem. Soc.* **1989**, *111*, 5495.
(12) Corey, E. J. *31st National Organic Chemistry Symposium Booklet*; American Chemical Society: Washington, DC, 1989; p 1.
(13) Trace impurities were removed from **2** either by recrystallization from ether at −20 °C or by passage through a column of silica gel with 20:1 hexane–ethyl acetate.

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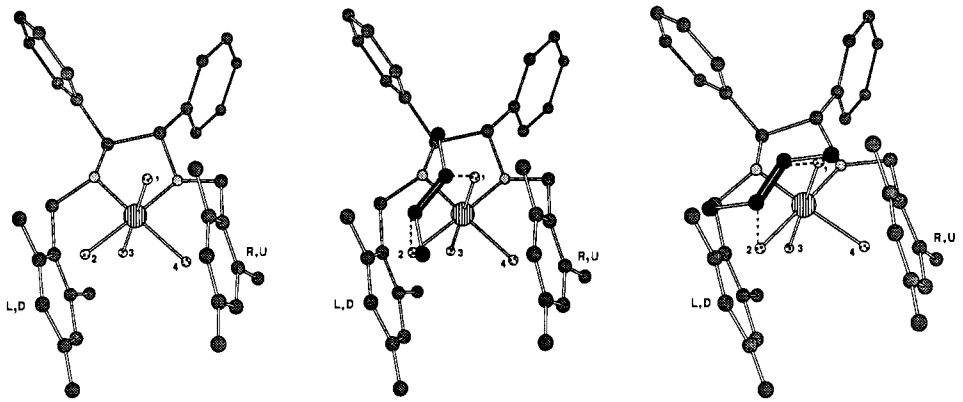

Figure 1. Left panel: complex of OsO_4 and diamine **2**; mesityl group at left projects downward, LD, and mesityl group at right projects upward, RU. Center panel: *si,si* face of (*E*)-2-butene approaching O(1) and O(2) of OsO_4·**2** complex. Right panel: *re,re* face of (*E*)-2-butene approaching O(1) and O(2) of OsO_4·**2** complex.

indicates no obstacles to the [3 + 2] pathway. Further, it is assumed that, in the transition state for cycloaddition, the geometry of the ligand approaches a C_2 symmetric structure in which there is staggering of the substituents about the N–CH_2Ar bond and placement of the mesityl groups so as to minimize steric repulsion with the nearby phenyl and Os=O substituents on the chelate ring, as shown in the left panel of Figure 1, which depicts one view of the C_2 complex. We also propose that, in the [3 + 2] cycloaddition to C=C, one of the oxygens attaching to carbon is axial and the other is equatorial to the chelate ring. This condition, which seems chemically logical since the equatorial oxygens (O(2) and O(4)) should be electron rich (electron donation from N to σ^* of trans Os–O) relative to the axial oxygens (O(1) and O(3)), provides the distinction between the four oxygens that is essential to the phenomenon of high enantioselectivity. It also provides a basis for understanding the acceleration of olefin dioxyosmylation resulting from complexation of OsO_4 with **2**, since the complex allows concerted, synergistic attack on the olefin by one relatively *electrophilic* and one relatively *nucleophilic* oxygen, in a process in which osmium is throughout six-coordinated and octahedral. The mechanistic model leads to an unambiguous prediction of absolute enantioselectivity, which is in full accord with the data in Table I.

Attack by an olefin at O(2) and O(3) is totally blocked by one mesityl group (LD; left, down in Figure 1), as is attack at O(1) and O(4) by the other mesityl (RU; right, up in Figure 1). Therefore, O(1) and O(2) and the equivalent pair O(3) and O(4) represent a unique reactivity site for attack by the olefin. Shown in Figure 1 are assemblies in which the complex is becoming attached at O(1) and O(2) to the *si,si* face (center panel) or the *re,re* face (right panel) of (*E*)-2-butene (black atoms). Attack by O(1) and O(2) on the *si,si* face of the olefin is sterically favorable since the olefin fits nicely into a groove between the mesityl groups without serious repulsion; this geometry leads to the observed major enantiomeric diol from the olefins listed in Table I. Dioxyosmylation at the *re,re* face of the olefin, in contrast, involves severe steric repulsion between the olefin and the mesityl groups, as is clear from Figure 1, right panel. Thus, the mechanistic model leads to an unambiguous prediction of the absolute configuration of the 1,2-diol products that accords with the experimental results. It should be noted that the intermediate osmium(VI) diol complex that is postulated as the primary [3 + 2] cycloadduct may undergo isomerization to a structure with two axial Os=O linkages and diol and diamine chelate rings roughly coplanar, a geometry that has been observed in known crystalline Os(VI) glycol esters.[3b,14] A mechanistic model in which olefin is attacked by the in-plane oxygens O(2) and O(4) (Figure 1, left panel) leads to an incorrect prediction of reaction stereochemistry.

The mechanistic model proposed above also provides a clear and simple explanation of the results obtained with the other effective bidentate chiral ligands that have been studied by Tomioka[3] and Hirama.[6] In addition, our model predicts lower enantioselectivity in the hydroxylation of *Z*-1,2-disubstituted and trisubstituted olefins, which is also in accord with our experimental data. For example, the following olefins were hydroxylated by the complex of **2** with OsO_4 with the indicated enantioselectivity: 1-phenylcyclohexene (60% ee); methyl (*R*)-cyclohex-3-ene-1-carboxylate (50% de); methyl 6-methyl-5-heptenoate (67% ee); (*S*)-citronellol benzoate (76% de). However, on the basis of the mechanistic model, it should be possible to devise a catalytic ligand that will be more effective for substrates such as these.

In summary, we have described a system for the enantioselective hydroxylation of *E* olefins that is unsurpassed in terms of enantioselectivity, ready availability and recoverability of the chiral controller ligand,[15] and recoverability of osmium, and we have presented the first clear mechanistic model for understanding enantioselective dioxyosmylation of olefins.[16]

(14) Schröder, M.; Nielson, A. J.; Griffith, W. P. *J. Chem. Soc., Dalton Trans.* **1979**, 1607 and references cited therein.

(15) In either enantiomeric form; the antipode of **2** provides products opposite in absolute configuration to those listed in Table I. The *N,N'*-bis-(benzyl) analogue of **2** was not an effective controller due to greater rotational flexibility.

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Generation and Reactivity of the 1-Nitrocyclopropyl Anion

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Cyclopropyl anions have been a popular subject of study for physical organic chemists for many decades.[1] While cyclopropane is more acidic than propane,[2] nitrocyclopropane, cyclopropyl phenyl ketone, and cyclopropyl phenyl sulfone are less acidic than their acyclic counterparts.[3] These anions also exhibit novel reactivity. Particularly striking is the report by Seebach and co-workers that deprotonation of nitrocyclopropane (pK_a = 26.9 in DMSO)[4] followed by addition of an electrophile does not result in capture of the nitrocyclopropyl anion. Instead, only coupled products result.[5] Herein we report our results on the successful

(1) For a review, see: Boche, G.; Walborsky, H. M. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; Wiley: New York, 1987.

(2) Cram, D. J. In *Fundamentals of Carbanion Chemistry*; Academic Press: New York, 1965.

(3) Bordwell, F. G.; Vanier, N. R.; Matthews, W. S.; Hendrickson, J. B.; Skipper, P. L. *J. Am. Chem. Soc.* **1975**, *97*, 7160.

(4) Bordwell, F. G.; Bartmess, J. E.; Hautala, J. A. *J. Org. Chem.* **1978**, *43*, 3113.

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