CHAPTER 1

HYDROGEN-BONDING-MEDIATED DIRECTED OSMIUM DIHYDROXYLATION

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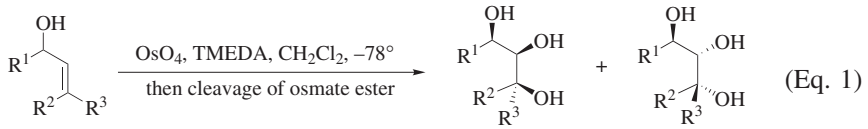
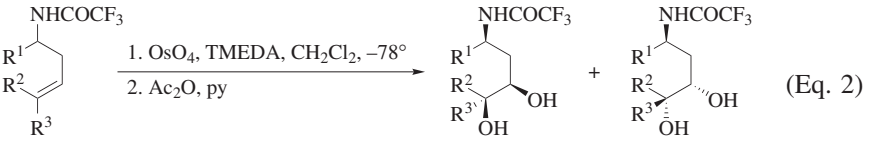
INTRODUCTION

This review focuses on the dihydroxylation of alkenes using osmium tetroxide (OsO_4) that is directed by alcohols and amine derivatives through hydrogen bonding between the substrate and the oxidant.

Discussion focuses on the different types of directing groups that are viable. The outcome from directed dihydroxylation of all the major classes of alkenes, including cyclic and acyclic substrates and varied alkene substitution patterns, is also addressed (Eqs. 1 and 2).[1]



(Eq. 1)



(Eq. 2)

The mechanism section outlines the different reactivity patterns that various ligands can impart onto the osmium oxidant, together with the importance of choosing a solvent that encourages hydrogen bonding. The influence that the directing group has on *syn* selectivity is also discussed, in both the context of its position in space with respect to the alkene, and the relationship between the pKa of the acidic proton and *syn* selectivity.

Criegee first reported the controlled oxidation of alkenes using stoichiometric amounts of OsO_4,[2] and later expanded upon those original observations by noting that pyridine acts as a ligand for osmium and accelerates the dihydroxylation process.[3] Osmium tetroxide has since established itself as the reagent of choice for the *syn*-dihydroxylation of olefins, primarily because of its inertness toward other functional groups and lack of over-oxidation products.[4]

Researchers from the UpJohn company reported a convenient and reliable procedure for dihydroxylation that involved substoichiometric amounts of OsO_4 (typically 5 mol %) and *N*-methymorpholine-*N*-oxide (NMO) as a stoichiometric co-oxidant. This landmark paper defined a procedure that has since enjoyed widespread use.[5]

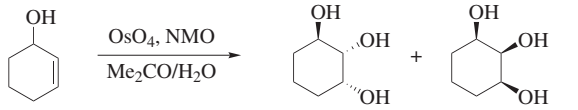
Observations as to the outcome from the dihydroxylation of chiral substrates were given a basis by Kishi, who reported that *anti* selectivity is generally attained during the oxidation of a wide range of allylic alcohols and protected derivatives thereof.[6,7,8,9] This mode of reactivity, whereby the heteroatom compels oxidation to occur on the opposite face of the alkene (most easily envisaged in cyclic systems) has proven to be very reliable with few exceptions reported. In fact, the high level of *anti* selectivity that is observed in such dihydroxylations has led to a problem: how to overturn this bias and obtain dihydroxylation on the same face as the directing group? Because the facial bias of the substrate (particularly allylic alcohols) is so strong, and often cyclic *cis*-alkenes are involved, it is frequently not possible to use the impressive asymmetric dihydroxylation system developed by Sharpless to control the diastereoselective dihydroxylation of a chiral substrate.[10,11] Therefore, the notion of a heteroatom-directed dihydroxylation becomes an interesting and useful proposition; and as such, the method discussed here forms an excellent counterpart to that described by Kishi.

Remarkably, only a few other synthetic methods are known that accomplish the direct addition of a diol unit or a protected diol unit across an alkene while

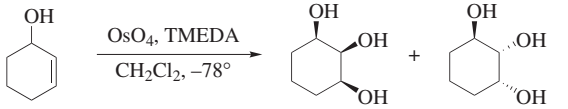
controlling the stereochemical course of the process. In fact, in addition to oxidation with high-valent metal oxo species, only iodine/silver acetate, the Woodward modification of the Prevost reaction,[12] will add two oxygen atoms in a *syn* fashion across an alkene. While this reaction has not enjoyed widespread use in the chemistry community it is discussed in some detail in the "Comparison with Other Methods" section.

MECHANISM AND STEREOCHEMISTRY

The hydrogen bond accepting ability of OsO_4 is enhanced upon complexation by amines. This behavior can be explained simply by the coordination of a Lewis base to the metal center, which leads to increased electron density on the oxo-ligands. Equations 3 and 4 compare the differences of reactivity between the OsO_4–NMO and the OsO_4•TMEDA complexes.



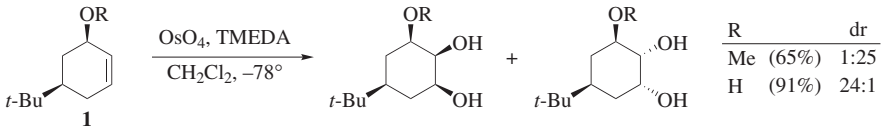
(Eq. 3)



(Eq. 4)

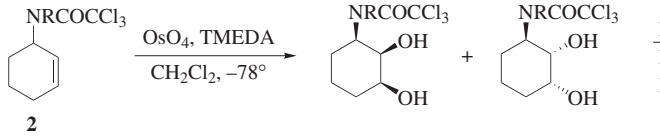
Corey showed, through low-temperature X-ray crystallographic analysis, that chiral 1,2-diamines form unique bidentate complexes with OsO_4.[13,14] These findings suggest that an OsO_4•diamine system should benefit from the bidentate nature of the ligand, which would exert an enhanced donor effect on the metal and also on the oxo-ligands. Spectroscopic analysis of the complex, formed at low temperature between OsO_4 and TMEDA (N,N,N',N'-tetramethyl-1,2-ethanediamine), has been carried out. ^{1}H NMR spectra of a 1:1 mixture of OsO_4 and TMEDA reveal the presence of a single, symmetrical compound. Low temperature IR spectroscopy studies indicate a reduction in the Os=O bond order as one traverses the series OsO_4, OsO_4•monodentate amine, OsO_4•chelating-diamine. These findings support the hypothesis that the increase in *syn* selectivity in directed dihydroxylation, following the order OsO_4 < OsO_4•monodentate amine < OsO_4•chelating-diamine, arises from an augmentation in hydrogen bond forming ability.[15]

The importance of hydrogen-bonding is further substantiated by the dihydroxylation of methyl ether **1** (R = Me) (Eq. 5) and *N*-methyl trichloroacetamide **2** (R = Me) (Eq. 6).[15] The absence of a hydrogen bond donor in these substrates has a pivotal influence on the stereochemical outcome of the reaction: the *anti* isomer is obtained as the major product in both cases. Also, it is noteworthy that these dihydroxylation reactions are significantly slower than the oxidation of the parent alcohol or trichloroacetamide.



R		dr
Me	(65%)	1:25
H	(91%)	24:1

(Eq. 5)



R		dr
Me	(78%)	1:10
H	(99%)	>25:1

(Eq. 6)

Further studies established that the OsO_4•TMEDA complex reacts through a hydrogen bond between the substrate and an oxo ligand (see **A**, Fig. 1), rather than a non-ligated amino group of TMEDA (see **B**, Fig. 1).

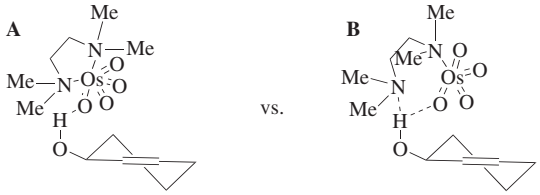
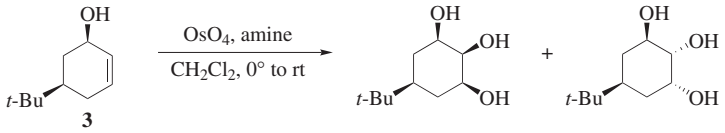


Figure 1. Possible hydrogen-bonding between the substrate and the OsO_4•TMEDA complex.

The results for the dihydroxylation of alcohol **3** in the presence of several bifunctional analogues of TMEDA are shown in Eq. 7. It is noteworthy that all of the amines fail to match the *syn* selectivity observed with TMEDA.[15]



Amine	dr
none	1:1.7
Me_3N	1.2:1
$Me_2N(CH_2)_2OMe$	1.1:1
$Me_2N(CH_2)_2OH$	1.1:1
$Me_2NCH_2NMe_2$	1.6:1
$Me_2N(CH_2)_2NMe_2$	4.6:1
$Me_2N(CH_2)_3NMe_2$	2.8:1

(Eq. 7)

High levels of *syn* stereoselectivity are achieved for chelating amines only;[15] if the hypothetical model **B** were correct, it is expected that amines with pendant

oxygen functionality should be able to form a hydrogen bond to the substrate and hence direct the dihydroxylation to some degree. Clearly this is not the case, as the level of selectivity in these reactions is comparable to those found using a simple monodentate amine such as Me_3N. These studies provide further evidence for the existence and reaction of a chelated OsO_4•TMEDA complex. Model **A** is, therefore, to be considered the reacting species.[15]

More information on the OsO_4•TMEDA system can be gathered by a closer analysis of the osmate esters produced, which are quite stable and can be easily purified. The X-ray crystal structure of *syn*-osmate ester **4**, obtained from the corresponding alkene and OsO_4•TMEDA, clearly shows the chelating nature of the diamine ligand (Fig. 2).[15]

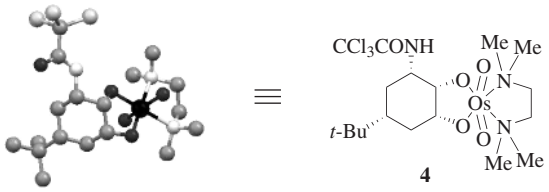


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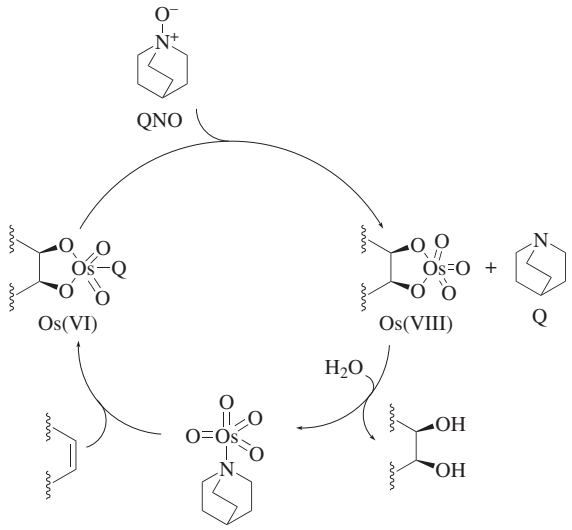
Figure 2. X-ray crystal structure of *syn*-osmate ester **4**. Hydrogen atoms have been omitted for clarity.

Another feature of the dihydroxylation reaction using OsO_4 in the presence of amines is the increased reactivity of the reagents towards alkenes. On the basis of literature data, approximate relative rate values for olefin oxidation with OsO_4, OsO_4•quinuclidine, and OsO_4•TMEDA are 1, 100, and 10,000 respectively.[13,16] The use of TMEDA as an additive generates an extraordinarily powerful dihydroxylating system, which is able to react with alkenes even at -78°. Under the same conditions, both OsO_4 and OsO_4•quinuclidine are essentially inert. This unique feature of the complex has enabled wide use in different dihydroxylation reactions where standard protocols are found to be ineffective.[17,18]

A disadvantage of the OsO_4•TMEDA system is the requirement for stoichiometric amounts of transition metal due to the inability of the resulting osmate(VI) ester to undergo either direct hydrolysis or in situ oxidation to a more easily hydrolyzed Os(VIII) species. By switching to monodentate amines such as quinuclidine, introduced as its *N*-oxide (QNO), the reactivity and hydrogen-bonding ability of the osmium complex decrease but the dihydroxylation reaction can be carried out with a substoichiometric amount of metal.[19] As the reaction progresses and QNO is reduced, OsO_4 can bind to the released quinuclidine and oxidize the alkene preferentially in a *syn* fashion. The resulting osmate ester is then able to undergo fast oxidation with more QNO, and subsequent hydrolysis (there is no need for the addition of water, as QNO is normally used as a monohydrate) releases the product and regenerates the catalytic species, as shown in Scheme 1.



Scheme 1

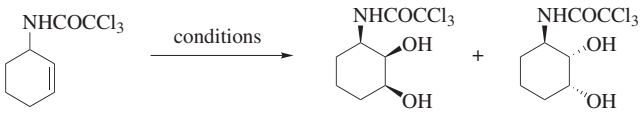
SCOPE AND LIMITATIONS

Although the osmium(VIII) dihydroxylation reaction can be influenced by a number of factors (electronic effects, steric effects, etc.), this chapter focuses on reactions wherein hydrogen-bonding effects are important. The presence of a directing group (usually an amide or alcohol) in either the allylic or homoallylic position combined with a complex of osmium tetroxide with an amine (generally OsO_4•TMEDA) can allow *syn* stereoselectivity and site selectively in the oxidation of a double bond.

Success of the hydrogen-bonding-mediated directed dihydroxylation depends upon a few essential elements. The level of stereoselectivity attained can be widely variable depending upon the geometry, substitution pattern, and position of the alkene relative to the directing group, and other steric or stereoelectronic factors.

Nature of the Amine

The weaker directing effect of the OsO_4•quinuclidine complex results in moderate levels of diastereoselectivity with allylic alcohols. Better results are obtained when trichloroacetamides are used as the directing element. Good levels of *syn* selectivity can be attained with trichloroacetamides due to the enhanced hydrogen bond forming ability of these acidic species, which allows a stronger interaction between the osmium complex and the substrate (Eq. 8).[15,19,20] Protocols that are catalytic in OsO_4[19] are less selective than the stoichiometric method[15,20] but do provide significant levels of *syn* selectivity, with the QNO system being slightly superior to the Me_3NO (TMO) system.



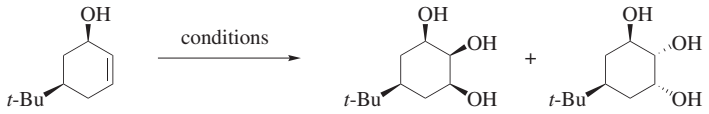
Conditions		dr
OsO_4, TMEDA, CH_2Cl_2, –78° to rt	(99%)	>25:1
OsO_4 (5 mol %), QNO•H_2O (1.3 equiv), CH_2Cl_2, rt	(86%)	4.3:1
OsO_4 (cat), Me_3NO, CH_2Cl_2	(93%)	3:1
OsO_4 (cat), NMO, Me_2CO/H_2O, rt	(98%)	1:3.2

(Eq. 8)

The use of a monodentate amine also represents a distinct advantage when the dihydroxylation of hindered allylic trichloroacetamides is required. Because of the smaller size of the OsO_4•quinuclidine complex compared to the OsO_4•TMEDA system, increased levels of selectivity are obtained in the directed oxidation of sterically demanding substrates.[19] Replacing QNO•H_2O, which needs to be prepared beforehand, with commercially available Me_3NO•$2H_2O$ makes the dihydroxylation process easier to perform while maintaining good levels of *syn* selectivity.[19]

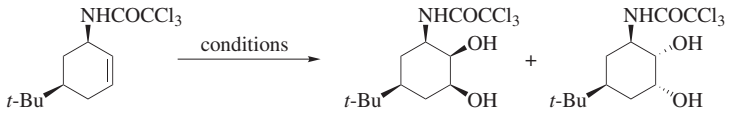
Nature of the Directing Group

The dihydroxylation can be directed if an alcohol or secondary amide group is present within reasonable proximity of the alkene. In general, suitably activated amide derivatives are prone to higher *syn* selectivity than their alcohol counterparts (Eqs. 9 and 10). The enhanced acidity of the trichloroacetamide and trifluoroacetamide relative to that of the corresponding alcohol (pKa values are approximately 11.2, 10.7, and 15 respectively) means that hydrogen-bonding to the OsO_4•TMEDA reagent is more effective, resulting in a higher *syn* selectivity. Oxidation of amide derivatives bearing less acidic proton donors (Me_3CONHR, *t*-BuOCONHR) afford only moderate *syn* selectivities.[15] The more acidic sulfonamides are not as selective, a result that is probably due to their greater steric bulk. Good levels of *syn* selectivity can be attained with substrates bearing amide directing groups using the hydrogen-bonding conditions catalytic in OsO_4 (QNO•H_2O, CH_2Cl_2).[19,21]



Conditions		dr
OsO_4, TMEDA, CH_2Cl_2, –78° to rt	(91%)	25:1
OsO_4 (5 mol %), QNO•H_2O (1.3 equiv), CH_2Cl_2, rt	(—)	1.2:1
OsO_4 (cat), NMO, Me_2CO/H_2O, rt	(91%)	1:4

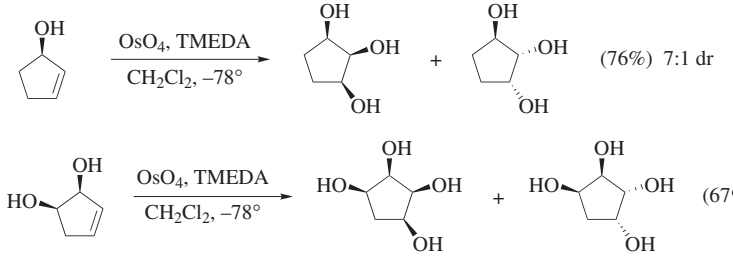
(Eq. 9)



(Eq. 10)

Conditions		dr
OsO_4, TMEDA, CH_2Cl_2, –78° to rt	(96%)	24:1
OsO_4 (cat), Me_3NO, CH_2Cl_2	(81%)	6:1
OsO_4 (5 mol %), QNO•H_2O (1.3 equiv), CH_2Cl_2, rt	(77%)	13:1
OsO_4 (cat), NMO, Me_2CO/H_2O, rt	(86%)	1:1.6

An additional hydroxy group in the vicinity of the allylic hydroxy group can reduce the selectivity of the hydroxylation. Equations 11 and 12 illustrate this effect.[15,21]

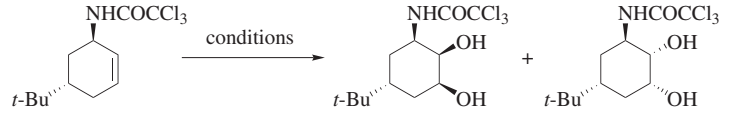


(Eq. 11)

(Eq. 12)

Steric Effects

Adverse steric effects can, of course, affect the *syn* selectivity dramatically. The bulk of the OsO_4•TMEDA complex hampers its ability to oxidize the hindered faces of alkenes. 1-Amino-2-cyclohexene derivatives and 2-cyclohexenols give the best *syn* selectivity when the donor group is in an equatorial position. When a conformationally locked substrate contains a pseudoaxially disposed directing group, the *syn* selectivity is poor (Eq. 13),[15,20] because hydrogen-bonding of the large oxometal species is discouraged by sterics (Fig. 3). As was mentioned previously, the *syn* selectivity of dihydroxylation of hindered allylic trichloroacetamides is increased when TMEDA, a bidentate ligand, is replaced by quinuclidine, a monodentate ligand. Even though the OsO_4•quinuclidine complex displays weaker inherent hydrogen bond accepting ability, the reduced steric bulk provides moderate *syn* selectivity in this system.



(Eq. 13)

Conditions		dr
OsO_4, TMEDA, CH_2Cl_2, –78° to rt	(97%)	1.7:1
OsO_4, quinuclidine, CH_2Cl_2, –78°	(66%)	4.9:1

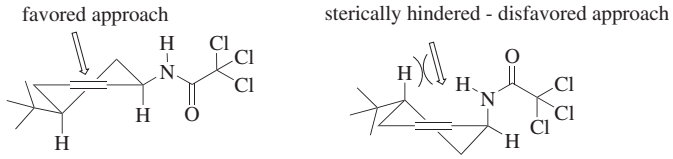
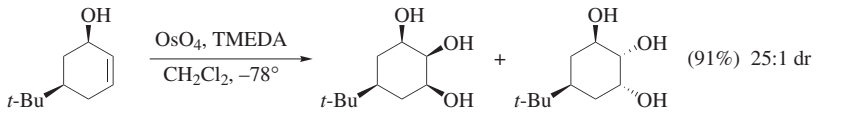
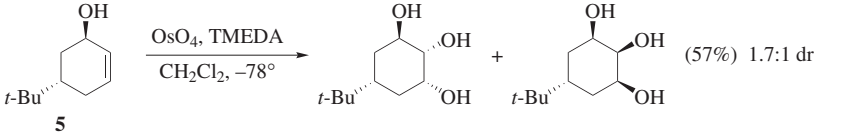


Figure 3. Steric effects in a conformationally locked substrate.

The same lack of *syn* selectivity is also observed with pseudo-axially biased alcohol **5** (Eqs. 14 and 15).[15,21]

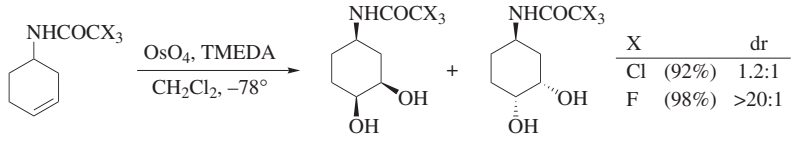


(Eq. 14)



(Eq. 15)

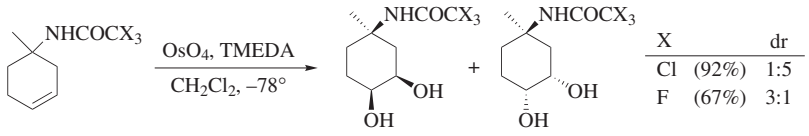
Clearly, the directing functionality must also be placed in a position where it can interact freely with the osmium complex. In contrast to allylic substrates, the directing group in homoallylic substrates needs to be in an axial position to deliver the oxidant intramolecularly. For example, poor selectivity is observed when 4-trichloroacetamido-1-cyclohexene is oxidized, probably because the bulky amide group has to adopt an unfavored axial position in order to deliver the oxidant (Eq. 16).[22] However, when the trichloroacetamide is replaced by the smaller and more acidic trifluoro derivative (approximate pKa of $Cl_3C(O)CNHR = 11.2$ and $F_3C(O)CNHR = 10.7$), the oxidation proceeds with excellent *syn* selectivity (Eq. 16).[22]



(Eq. 16)

It is noteworthy that in both the trichloroacetamide and trifluoroacetamide cases, the *syn* selectivity is greatly affected by the presence of an alkyl group on the carbon bearing the amide functionality (Eq. 17).[22] In this example, the directing group may be able to adopt the preferred axial conformation, but cannot point

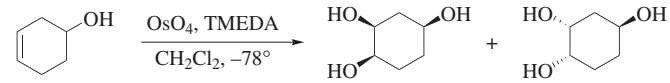
the N–H group towards the alkene without encountering steric hindrance from the geminal alkyl group, which leads to dramatic reduction of *syn* selectivity.[22,23,24]



X		dr
Cl	(92%)	1:5
F	(67%)	3:1

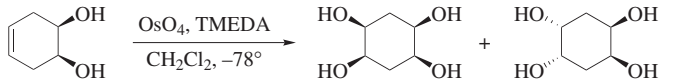
(Eq. 17)

The requirement for an axial directing group would also explain the difference in selectivity between substrate **7** (which must always have one hydroxy group in an axial position) and substrate **6** (Eqs. 18 and 19).[22,25]



6 (92%) 3:1 dr

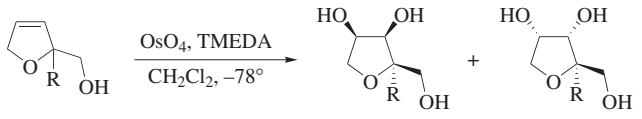
(Eq. 18)



7 (82%) 12.4:1 dr

(Eq. 19)

With the five-membered ring homoallylic alcohol **8**, the dihydroxylation using OsO_4•TMEDA proceeds unselectively (Eq. 20). The exocyclic methylene side-chain may be sufficiently bulky to interfere with effective directed dihydroxylation. This hypothesis is supported by the results of substrate **9**, wherein an alkyl substituent has been introduced to block the face of the alkene opposite to the hydroxymethyl group. As expected, the directed dihydroxylation then proceeds well and with good *syn* selectivity. Furthermore, the directed dihydroxylation of substrate **10** confirms this rationale as the *p*-methoxybenzyl group completely blocks *anti* attack and therefore excellent *syn* selectivity is obtained.[22,25]



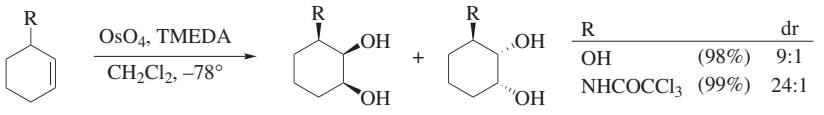
	R		dr
8	H	(55%)	1:1
9	Me	(83%)	6:1
10	*p*-$MeOC_6H_4CH_2$	(82%)	99:1

(Eq. 20)

Nature of the Substrate

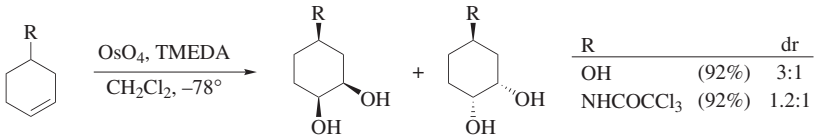
Allylic versus Homoallylic Substrates. As a rule, allylic substrates lead to better stereoselectivity than homoallylic substrates. The main reason for this is

that the directing group in the latter is now positioned further away from the double bond where it cannot influence the approach of the oxidant as easily. In cyclic homoallylic systems, it is more difficult for the hydrogen bond donor group to adopt a position that allows the osmium complex to attack the double bond in a *syn* selective fashion whilst participating in hydrogen-bonding. This issue has been already detailed in the "Steric Effects" section. Eqs. 21 and 22 directly compare examples of allylic and homoallylic alcohols.[22,25]



R		dr
OH	(98%)	9:1
$NHCOCCl_3$	(99%)	24:1

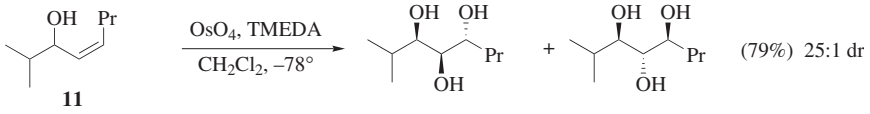
(Eq. 21)



R		dr
OH	(92%)	3:1
$NHCOCCl_3$	(92%)	1.2:1

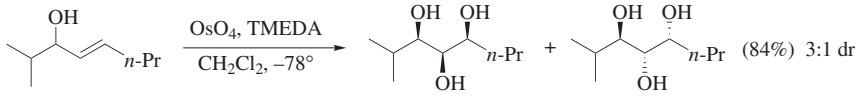
(Eq. 22)

Conformational Factors Determined by the Alkene Substitution Pattern. In cyclic systems, the rigidity of the structure and consequent steric effects lead to high levels of *syn* selectivity. In acyclic systems, the alkene substitution pattern is crucial to obtaining high *syn* stereoselectivity. It is interesting to note that the *syn* selectivity increases dramatically in acyclic systems when the double bond bears a *cis* substituent, as in substrate **11** (Eqs. 23 and 24).[24,26]



(79%) 25:1 dr

(Eq. 23)



(84%) 3:1 dr

(Eq. 24)

Within each type of alkene, the levels of *syn* selectivity reported in the literature for directed epoxidation with peracid (most notably *m*-CPBA) are similar to those observed for directed dihydroxylation. It is suggested that, in the transition structure, the dihedral angle between the C–O and the C=C is most favorable at approximately 120°. The two possible transition structures are distinguished by the difference in $A^{[1,3]}$ strain between the R group and the R_{cis} substituent

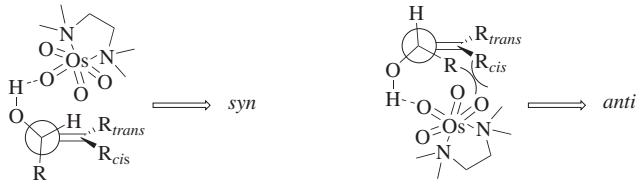
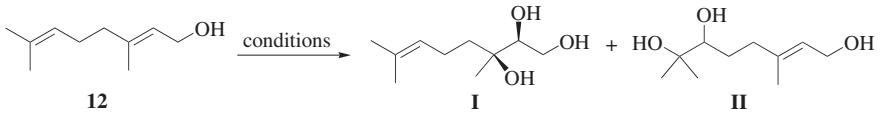


Figure 4. The two possible transition structures for directed dihydroxylation.

and explains why a large group in the R_{cis} position leads to higher levels of stereocontrol than the same group in the R_{trans} position (Fig. 4).[24]

Site Selectivity of the Directed Dihydroxylation Reaction. The directed dihydroxylation also expresses high site selectivity. Treatment of geraniol (**12**) with the OsO_4•TMEDA complex leads to highly selective oxidation of the 2,3-alkene (Eq. 25).[21] When the same substrate is oxidized under Sharpless asymmetric dihydroxylation conditions, the site selectivity is reversed, and oxidation of the most electron-rich double bond is observed.[27]



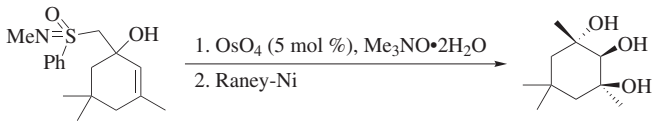
12 **I** **II**

Conditions		**I**:**II**
OsO_4, TMEDA, CH_2Cl_2, –78° to rt	(74%)	>25:1
OsO_4 (1 mol %), $(DHQD)_2$-PHAL (5 mol %), $K_3Fe(CN)_6$, K_2CO_3, $MeSO_2NH_2$, *t*-BuOH/H_2O, 0°	(89%)	1:>49

(Eq. 25)

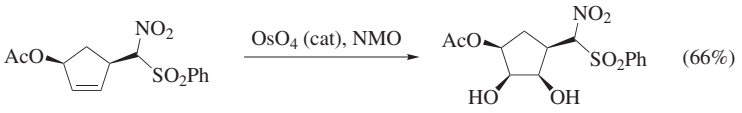
Alternative Directing Groups

Dihydroxylation reactions of allylic alcohols normally give the *anti* product under standard osmium tetroxide oxidation conditions.[6,7] However, scattered reports in the literature suggest that the natural steric bias of certain substrates may be overcome when heteroatomic substituents such as sulfoximines and nitro groups are present within the molecule and a reagent–substrate interaction is postulated to occur. Sulfoximine-directed dihydroxylation of alkene **13**, followed by desulfurization affords triol **14** as a single diastereomer (Eq. 26).[28] Osmium tetroxide oxidation of cyclopentene **15** unexpectedly gives all-*syn* product **16** (Eq. 27).[29] Although association of OsO_4 with the nitrosulfone side-chain is suggested to account for this selectivity,[29] the results from oxidizing a number of simpler analogs do not support a substrate–oxidant association and are interpreted in terms of substrate conformation.[30]



13 **14**

(Eq. 26)

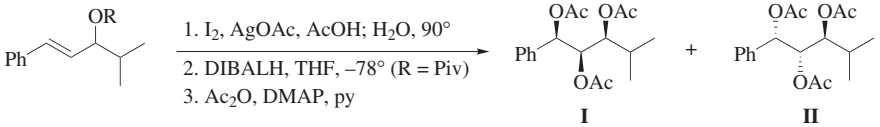


15 **16** (Eq. 27)

Although interesting, these findings are of limited utility because they cannot be easily interpreted, rationalized, and extended; whereas hydrogen-bonding may come into play in some cases, steric effects are sometimes sufficient to account for the configuration of the products. On the contrary, the OsO_4•TMEDA system relies unequivocally on the hydrogen-bonding ability of the metal complex and shows broad applicability over a large number of allylic alcohol and amine derivatives and enhanced reactivity towards alkenes even at very low temperature.

COMPARISON WITH OTHER METHODS

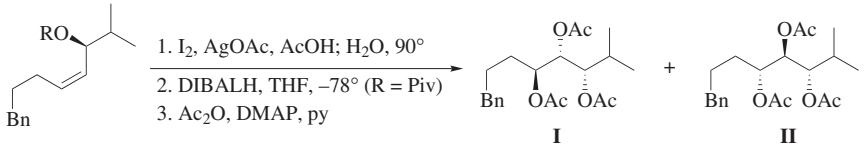
It is noteworthy that the modified Woodward alkene oxidation,[12] which involves the reaction of the alkene with AgOAc and I_2 in HOAc, followed by the addition of H_2O, affords moderate levels of *syn* selectivity in the *cis*-dihydroxylation of some allylic alcohols (Eqs. 28 and 29).[31] Selectivities depend upon the alkene substituents and configuration and the size of the *O*-protecting group, and are generally modest. The *syn* selectivity reflects attack of the iodonium ion on the face of the alkene that is opposite to the –OR group, followed by neighboring group attack within the initially formed β-acetoxy iodocompound. The reversal of stereoselectivity when the same protocol is applied to the free alcohol is attributed to hydrogen-bonding between the –OH and the electrophile.



I **II**

R		**I**:**II**
H	(—)	1:12
Ac	(71%)	2.5:1
Piv	(65%)	4:1

(Eq. 28)

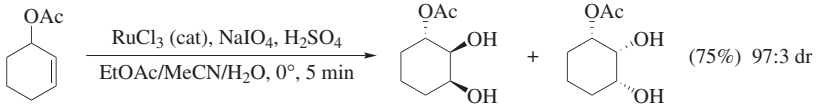


I **II**

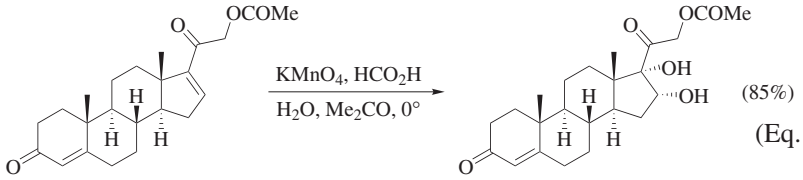
R		**I**:**II**
H	(75%)	1:2.6
Ac	(90%)	14.3:1
Piv	(85%)	12.4:1

(Eq. 29)

Alternative, direct oxidations of an alkene to a *syn*-diol have been reported in the literature; we restricted our search to reactions of prochiral substrates possessing a stereogenic center in the allylic position. Although stereocontrolled reactions involving other high-valent metal oxidants are known, no coordination-induced directing effect has been described. For example, ruthenium(VIII)-promoted dihydroxylation leads to *anti* selectivity with respect to the original stereocenter (Eq. 30),[32] and stereocontrolled permanganate-mediated oxidation of a steroidal enone is presumably sterically directed away from the angular methyl group (Eq. 31).[33]



(Eq. 30)



(Eq. 31)

EXPERIMENTAL CONDITIONS

The osmium-mediated dihydroxylation reaction is carried out under an inert atmosphere such as argon or nitrogen and the solvents (CH_2Cl_2, acetone, THF) must be anhydrous. *Osmium tetroxide is toxic, volatile, and sublimes quite easily; it should therefore be handled in a well-ventilated fume-hood. The aqueous layers from the osmium-mediated reactions and any other waste materials should be disposed of properly.*

EXPERIMENTAL PROCEDURES

General Procedure for Stoichiometric Dihydroxylation

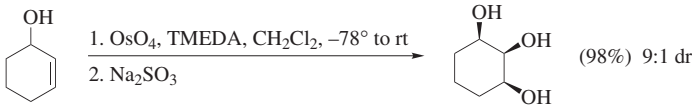
OsO_4·TMEDA.[15] To a solution of substrate (0.50 mmol) and TMEDA (0.55 mmol) in CH_2Cl_2 precooled to -78° was added a solution of OsO_4 (0.53 mmol) in CH_2Cl_2 ($\sim$1 mL). The solution turned deep red and then brown-black. It was stirred until the reaction was complete (TLC analysis, ca. 1 h) before being allowed to warm to rt.

Isolation Procedures for 0.50 mmol of Substrate

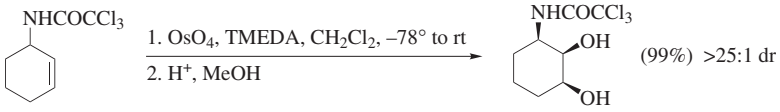
Sodium Sulfite.[15] After completion of the oxidation, the solvent was removed under vacuum and replaced with THF (10 mL) and sodium sulfite (aq saturated solution, 10 mL). This mixture was heated at reflux for 3 h and the work-up completed as indicated.

Acidic Methanol.[15] After completion of the oxidation, the solution was concentrated under vacuum and the resulting residue was dissolved in MeOH (10 mL) before addition of HCl (concentrated, ~5 drops). The solution was stirred for 2 h, concentrated under vacuum, and the product isolated as indicated.

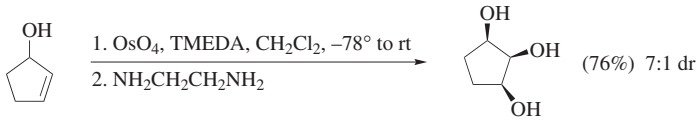
Ethylenediamine.[15] After completion of the oxidation, ethylenediamine (5.0 equiv) was added to the crude reaction mixture at rt and the resulting solution was stirred for 48 h during which time a brown precipitate formed. The solution was then concentrated under vacuum and the product isolated as indicated.



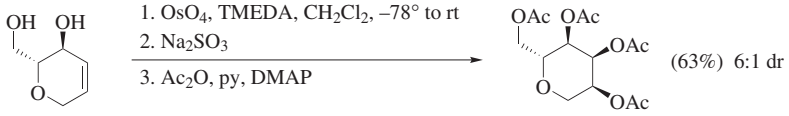
(1*R, 2*S**, 3*S**)-Cyclohexane-1,2,3-triol [Directed Dihydroxylation of an Allylic Cyclic Alcohol Using OsO_4·TMEDA].**[15] 2-Cyclohexene-1-ol (50 mg, 0.51 mmol) was oxidized with OsO_4•TMEDA using the sodium sulfite work-up. The crude reaction mixture was then concentrated under vacuum to afford a grey powder; EtOH (30 mL) was added and the suspension stirred at rt for 1 h. Filtration of the resulting suspension through Celite and concentration of the filtrate under vacuum gave a colorless solid (80 mg). Purification by column chromatography (SiO_2, EtOAc/petroleum ether 7:1) afforded the title compound as an inseparable mixture of isomers (66 mg, 98%, *syn*/*anti* 9:1): IR (film) 3192, 2927 cm^{-1}; ^1H NMR (300 MHz, D_2O) δ 3.81 (t, $J = 2.6$ Hz, 1H), 3.52 (ddd, $J = 10.0, 4.6, 2.6$ Hz, 2H), 1.80–1.00 (m, 6H); ^{13}C NMR (75 MHz, D_2O) δ 72.6, 70.3, 26.3, 18.8; CIMS (m/z): $[M + NH_4]^+$ 150 (100); CI (m/z): $[M + NH_4]^+$ calcd for $C_6H_{16}NO_3$, 150.1130; found, 150.1128.



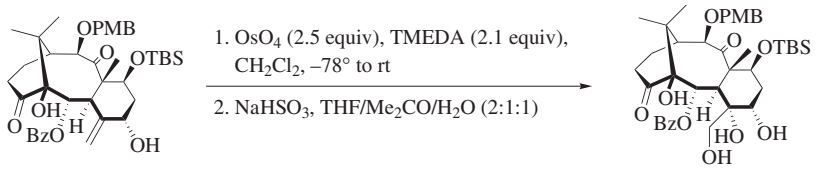
2,2,2-Trichloro-*N*-[(1*R, 2*R**, 3*S**)-2,3-dihydroxycyclohexyl]acetamide [Directed Dihydroxylation of an *N*-Allylic Cyclic Amide Using OsO_4·TMEDA].**[15] 2,2,2-Trichloro-*N*-(cyclohex-2-enyl)acetamide (100 mg, 0.412 mmol) was oxidized with OsO_4•TMEDA using the methanolic work-up; the resulting orange mixture was purified by column chromatography (SiO_2, petroleum ether/EtOAc 1.5:1) to yield the title product (111 mg, 99%) as a colorless oil: IR (film) 3407, 2942, 1698, 1515 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.86 (br s, 1H), 4.06–3.86 (m, 3H), 3.70–3.00 (m, 2H), 1.84–1.58 (m, 5H), 1.46–1.32 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.8, 92.6, 70.8, 70.3, 52.1, 28.4, 26.1, 18.2; CIMS (m/z): 295 (91), $[M + NH_4]^+$ 293 (100); CI (m/z): $[M + H]^+$ calcd for $C_8H_{13}NO_3Cl_3$, 275.9961; found, 275.9966.



(1*R, 2*S**, 3*S**)-Cyclopentane-1,2,3-triol [Directed Dihydroxylation of an Allylic Cyclic Alcohol Using OsO_4·TMEDA].**[15] Cyclopent-2-enol (100 mg, 1.19 mmol) was oxidized with OsO_4•TMEDA using the ethylenediamine work-up. The residue was redissolved by sonication in a mixture of EtOH (7.5 mL) and EtOAc (40 mL); the resulting solution was filtered through Celite and concentrated under vacuum. Column chromatography (SiO_2, EtOAc) afforded the title compound as a clear oil (66 mg, 76%, *syn*/*anti* 7:1, by ^{1}H NMR). (1*R**, 2*S**, 3*S**)-Cyclopentane-1,2,3-triol was obtained by repeated chromatography: IR (neat) 3365, 2962, 2926 cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD) δ 4.09–4.02 (m, 2H), 3.82 (t, $J = 5$ Hz, 1H), 1.95–1.76 (m, 4H); ^{13}C NMR (75 MHz, CD_3OD) δ 71.9, 69.9, 27.1; CIMS (*m*/*z*): $[M + NH_4]^+$ 154 (100), 90(40); CI (*m*/*z*): $[M + NH_4]^+$ calcd for $C_5H_{14}NO_3$, 136.0974; found, 136.0979.

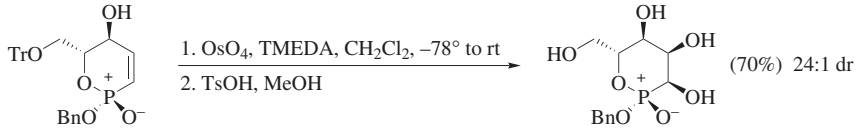


(2*R, 3*R**, 4*S**, 5*S**)-2-(Acetoxymethyl)tetrahydro-2*H*-pyran-3,4,5-triyl Triacetate [Directed Dihydroxylation of an Allylic Cyclic Alcohol Using OsO_4·TMEDA and Subsequent Peracetylation].**[15] (2*R**, 3*S**)-2-(Hydroxymethyl)-3,6-dihydro-2*H*-pyran-3-ol (100 mg, 0.771 mmol) was oxidized with OsO_4•TMEDA using the sodium sulfite work-up. The aqueous mixture was concentrated under vacuum to a grey solid, which was powdered before the sequential addition of pyridine (10 mL), Ac_2O (5 mL) and DMAP (cat). The resulting black suspension was stirred at rt under an atmosphere of nitrogen for 48 h; Et_2O (100 mL) was then added and the mixture filtered through Celite (washing further with Et_2O (200 mL)). The filtrate was washed with HCl (aq solution, 2M, 100 mL), $NaHCO_3$ (aq saturated solution, 100 mL) and brine (100 mL). The organic extracts were dried ($MgSO_4$) and concentrated under vacuum to afford a light-brown oil (201 mg) as a mixture of isomers (*syn*/*anti* 6:1 by ^{1}H NMR). Purification by column chromatography (SiO_2, petroleum ether/EtOAc 6:1) gave the title product (161 mg, 63%) as a colorless oil: $[\alpha]^{27}_D + 7.5$ (*c* 0.2, $CHCl_3$); IR (film) 2996, 1747 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60 (t, $J = 2.6$ Hz, 1H), 4.95 (ddd, $J = 10.0$, 5.5, 2.6 Hz, 1H), 4.84 (ddd, $J = 10.0$, 5.5, 2.6 Hz, 1H), 4.14–4.10 (m, 2H), 3.88–3.78 (m, 2H), 3.60 (t, $J = 10.0$ Hz, 1H), 2.10 (s, 3H), 2.02 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.69, 169.89, 169.30, 169.11, 71.71, 67.77, 66.40, 66.27, 63.45, 62.49, 20.70 (2) and 20.55 (2); CIMS (*m*/*z*): $[M + NH_4]^+$ 350(10), 249(100); CI (*m*/*z*): $[M + NH_4]^+$ calcd for $C_{14}H_{24}NO_9$, 350.1451; found, 350.1454.



17 (72%) 1 diastereomer

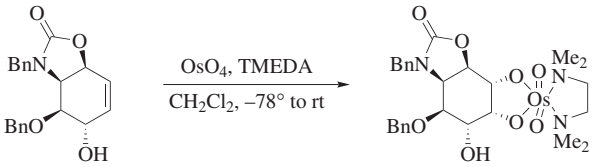
Tricyclic Tetraol [Directed Dihydroxylation of an Exocyclic Allylic Alcohol Using OsO_4·TMEDA].[17] A solution of alkene **17** (590 mg, 0.842 mmol) in CH_2Cl_2 (32.4 mL) was cooled to −78° and treated sequentially with TMEDA (0.32 mL, 2.1 mmol) and OsO_4 (531 mg, 2.09 mmol). The reaction mixture was stirred at this temperature for 2 h, allowed to warm to rt over 15 min, and concentrated under vacuum. The residue was taken up in THF (80 mL), acetone (40 mL), and water (40 mL), treated with sodium bisulfite (7.5 g), and stirred for 3 h. Water (100 mL) and EtOAc (100 mL) were then added, the aqueous layer was extracted with EtOAc (2 × 50 mL), and the combined organic phases were concentrated under vacuum. THF (80 mL), acetone (40 mL), water (40 mL), and sodium bisulfite (4.0 g) were added, and the mixture was stirred at rt for 20 h. The resultant mixture was filtered through a pad of Celite and the residue rinsed with EtOAc (3 × 150 mL). The layers were separated, the aqueous phase was extracted with EtOAc (2 × 50 mL), the combined organic phases were evaporated, and the residue was purified by column chromatography (SiO_2, hexanes/EtOAc 1.2:1) to give the title product as a colorless oil (460 mg, 72%). The spectroscopic properties of the tricyclic tetraol were identical to those previously reported:[34] $[\alpha]^{20}_D$ +5.2 (*c* 0.56, $CHCl_3$); IR (neat) 3470, 1719, 1706, 1514 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, $J = 7.2$ Hz, 2H), 7.54–7.52 (m, 1H), 7.44–7.40 (m, 2H), 7.26 (d, $J = 8.5$ Hz, 2H), 6.81 (d, $J = 8.5$ Hz, 2H), 5.71 (d, $J = 5.8$ Hz, 1H), 4.79 (d, $J = 4.0$ Hz, 1H), 4.55 (dd, $J = 4.3$, 11.6 Hz, 1H), 4.43 (d, $J = 10.5$ Hz, 1H), 4.06 (d, $J = 10.6$ Hz, 1H), 3.99 (s, 1H), 3.87 (br s, 1H), 3.82 (d, $J = 5.8$ Hz, 1H), 3.74 (s, 3H), 3.56 (d, $J = 10.2$ Hz, 1H), 3.43–3.41 (m, 1H), 3.36 (s, 1H), 3.16–3.06 (m, 1H), 2.77 (s, 1H), 2.77–2.72 (m, 1H), 2.36–2.26 (m, 2H), 2.18–2.16 (m, 1H), 1.94–1.93 (m, 1H), 1.88–1.80 (m, 1H), 1.80–1.70 (m, 1H), 1.30 (s, 3H), 1.03 (s, 3H), 0.87 (s, 3H), 0.78 (s, 9H), 0.01 (s, 3H), −0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.3, 208.9, 165.2, 159.4, 152.8, 133.8, 129.8, 129.5, 128.98, 128.9, 113.8, 84.2, 81.6, 75.2, 74.0, 73.5, 71.5, 67.2, 62.9, 58.7, 55.2, 51.3, 42.1, 38.9, 38.0, 32.9, 31.0, 29.6, 25.7, 22.7, 18.2, 10.0, −2.1, −4.2; ES HRMS (*m*/*z*): [M + Na^+] calcd for $C_{40}H_{56}O_{11}SiNa$, 763.3490; found, 763.3432.



18 (70%) 24:1 dr

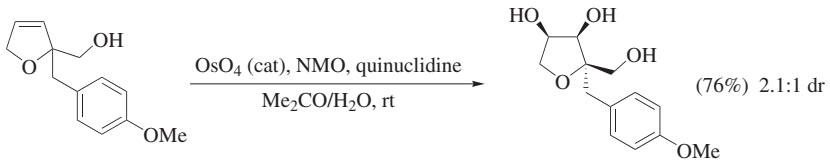
(2S_P^*,3*S,4*R**,5*S**,6*R**)-2-Phenylmethoxy-6-(hydroxymethyl)-3,4,5-trihydroxy-1,2-oxaphosphorinane-2-oxide) [Directed Dihydroxylation of an Allylic Cyclic Alcohol Using OsO_4·TMEDA].**[35] To a solution of OsO_4

(43 mg, 0.17 mmol) in CH_2Cl_2 (0.6 mL) at -78° was added TMEDA (22 mg, 0.19 mmol) followed by the alcohol **18** (68 mg, 0.13 mmol) in CH_2Cl_2 (1.0 mL). The reaction mixture was stirred for 3 h at -78°, warmed to rt, and stirred for 15 min. The solution was concentrated under vacuum to give the crude osmate ester, which was dissolved in MeOH (1 mL) and treated with citric acid (40 mg, 0.21 mmol) for 24 h. The solution was concentrated under vacuum; the residue was dissolved in a small amount of MeOH, and filtered through silica gel (EtOAc/MeOH 9:1). The crude product was dissolved in MeOH (1 mL), treated with a catalytic amount of $TsOH{\bullet}H_2O$, and stirred for 8 h. The solution was then concentrated under vacuum and the crude product was purified by column chromatography (SiO_2, EtOAc/MeOH 9:1) to afford the title compound (28 mg, 70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.31 (m, 5H), 5.21–5.11 (m, 2H), 4.55–4.50 (m, 1H), 4.24 (dt, $J = 33.7$, 2.7 Hz, 1H), 4.01 (dd, $J = 9.8$, 3.4 Hz, 1H), 3.90 (ddd, $J = 12.5$, 4.4, 2.9 Hz, 1H), 3.75 (dd, $J = 9.8$, 2.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7 (d, $J_{CP} = 6.4$ Hz), 129.7, 129.6, 129.2, 78.4 (d, $J_{CP} = 4.4$ Hz), 75.5 (d), 71.4, 69.6 (dt, $J_{CP} = 6.4$ Hz), 69.0 (d), 67.7 (d, $J_{CP} = 144.5$ Hz), 62.8 (dt, $J_{CP} = 8.0$ Hz); ^{31}P NMR δ 24.5; HRMS-FAB (m/z): $[M + H]^+$ calcd for $C_{38}H_{36}O_8P$, 651.2148; found, 651.2131.

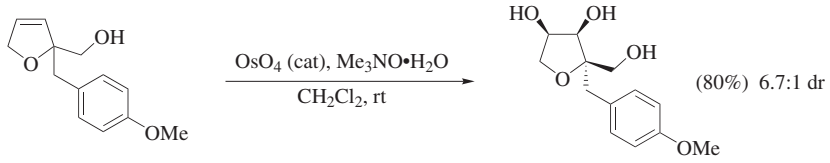


(100%) 1 diastereomer

Osmate ester of (3a*R,4*S**,5*S**,6*R**,7*R**,7a*R**)-3-Benzyl-4-benzyloxy-5,6,7-trihydroxyhexahydrobenzo[*d*]oxazol-2(3*H*)-one [Preparation of an Osmate Ester Using $OsO_4{\cdot}$TMEDA].[36]** A solution of OsO_4 (140 mg, 0.551 mmol) in CH_2Cl_2 (0.7 mL) was added to a solution of (3a*S**, 4*S**, 5*S**,7a*S**)-3-benzyl-4-(benzyloxy)-5-hydroxy-3,3a,4,5-tetrahydrobenzo[*d*]oxazol-2(7a*H*)-one (184 mg, 0.532 mmol) and TMEDA (87.0 μL, 0.580 mmol) in CH_2Cl_2 at -78° and the reaction mixture was stirred for 2 h. The solution was allowed to warm to rt, concentrated onto silica and the crude material was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH 19:1) to afford the title compound as a brown foam (379 mg, 100%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.18 (m, 10H), 4.90 (dd, $J = 8.8$, 4.8 Hz, 1H), 4.84 (d, $J = 15.2$ Hz, 1H), 4.75 (d, $J = 11.6$ Hz, 1H), 4.68 (t, $J = 5.6$ Hz, 1H), 4.56 (dd, $J = 11.2$, 5.6 Hz, 1H), 4.53 (m, 1H), 4.48 (d, $J = 12.0$ Hz, 1H), 4.01 (app quart, 1H), 4.01 (app quart, 1H), 3.93 (d, $J = 15.2$ Hz, 1H), 3.76, (d, $J = 2.8$ Hz, 1H), 3.16–3.08 (m, 4H), 2.93 (s, 3H), 2.90 (s, 3H), 2.89 (s, 3H), 2.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 138.0, 136.4, 128.6, 128.4, 128.1, 128.0, 127.7, 127.6, 87.9, 82.1, 75.2, 74.6, 72.9, 68.0, 64.7, 64.3, 53.6, 52.6, 52.3, 52.0, 51.6, 46.8; ESI^+ (m/z): $[M + MeCN + NH_4]^+$ 724 (100); ESI^+ (m/z): $[M + MeCN + NH_4]^+$ calcd for $C_{27}H_{38}N_3O_8Os$, 724.2274; found, 724.2278.

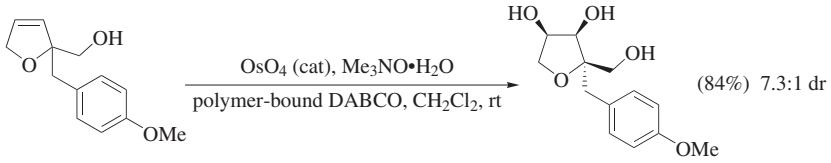


(2*R,3*R**,4*R**)-2-Hydroxymethyl-2-(4-methoxybenzyl)tetrahydrofuran-3,4-diol [Directed Dihydroxylation of a Homoallylic Alcohol Using Catalytic OsO_4·Quinuclidine and NMO].[37]** 4-Methylmorpholine-*N*-oxide (240 mg, 2.01 mmol) was added to a stirred solution of 2-hydroxymethyl-2-(4-methoxybenzyl)-2,5-dihydrofuran (150 mg, 0.681 mmol) in acetone (20 mL) and water (5 mL) at rt, followed by quinuclidine (5 mg, 7 mol %) and OsO_4 (5 mg, 3 mol %). The reaction mixture was stirred overnight. Acetone was removed under vacuum before the addition of EtOAc (20 mL) and brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum to give the crude product as a mixture of diastereomers (*syn*/*anti* 2.1:1, by HPLC). Purification by column chromatography (SiO_2, CH_2Cl_2/*i*-PrOH 19:1) gave (2*R**,3*S**,4*S**)-2-hydroxymethyl-2-(4-methoxybenzyl)tetrahydrofuran-3,4-diol (41 mg, 24%) as a crystalline solid, mp 103–105°, and (2*R**, 3*R**, 4*R**)-2-(hydroxymethyl)-2-(4-methoxybenzyl)tetrahydrofuran-3,4-diol (89 mg, 52%) as a crystalline solid, mp 93–95°. Analytical data for the major isomer: R_f (CH_2Cl_2/*i*-PrOH 95:5) 0.26; IR 3232, 1249 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 7.20–7.16 (m, 2H), 6.85–6.81 (m, 2H), 4.04 (d, $J = 5.3$ Hz, 1H), 3.81 (dd, $J = 8.3$, 4.7 Hz, 1H), 3.76 (s, 3H), 3.71–3.61 (m, 3H), 3.52 (d, $J = 11.4$ Hz, 1H), 2.81 (d, $J = 13.9$ Hz, 1H), 2.71 (d, $J = 13.9$ Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.9, 131.7, 129.1, 113.5, 85.4, 75.2, 71.9, 71.8, 64.3, 54.6, 40.2; ESI^+ (*m*/*z*): $[M + Na^+]$ 277 (100); ESI^+ (*m*/*z*): $[M + Na]^+$ calcd for $C_{13}H_{18}O_5Na$, 277.1046; found, 277.1046; Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.41; H, 7.14. Found: C, 61.37; H, 7.16.

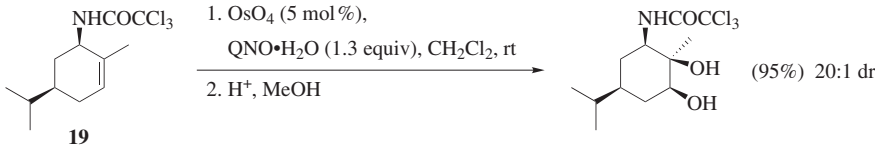


(2*R,3*R**,4*R**)-2-Hydroxymethyl-2-(4-methoxybenzyl)tetrahydrofuran-3,4-diol [Directed Dihydroxylation of a Homoallylic Alcohol Using Catalytic OsO_4 and TMO].[37]** Trimethylamine-*N*-oxide dihydrate (5.7 g, 51 mmol) was added to a stirred solution of 2-hydroxymethyl-2-(4-methoxybenzyl)-2,5-dihydrofuran (3.78 g, 17.2 mmol) in CH_2Cl_2 (200 mL) at rt. OsO_4 (50 mg, 0.20 mmol) was then added and the mixture stirred overnight. Sodium sulfite (aq saturated solution, 20 mL) was added and the mixture stirred for 20 min. The organic layer was dried ($MgSO_4$) and concentrated under vacuum to give the crude product as a mixture of diastereomers (*syn*/*anti* 6.7:1, by HPLC). Purification by column

chromatography (SiO_2, CH_2Cl_2/i-PrOH 19:1) gave the *anti*-triol (0.45 g, 10%) and the *syn*-triol (3.04 g, 70%).



(2*R,3*R**,4*R**)-2-Hydroxymethyl-2-(4-methoxybenzyl)tetrahydrofuran-3,4-diol [Directed Dihydroxylation of a Homoallylic Alcohol Using Catalytic OsO_4, TMO, and Polymer-Bound DABCO].[37]** Polymer-bound 1,4-diazabicyclo[2.2.2]octane chloride (100 mg, 1% DVB, 100-200 mesh) was added to a solution of OsO_4 (26 mg) in cyclohexane (5 mL); the solvent was then evaporated, and the solid so obtained (100 mg, ~10 mol % OsO_4) was added to a solution of 2-hydroxymethyl-2-(4-methoxybenzyl)-2,5-dihydrofuran (100 mg, 0.451 mmol) in CH_2Cl_2 (15 mL) at rt. Trimethylamine-*N*-oxide dihydrate (150 mg, 1.40 mmol) was added and the mixture was shaken overnight; the polymer was then removed by filtration and the filtrate was concentrated under vacuum to give the crude product as a mixture of diastereomers (*syn*/*anti* 7.3:1, by HPLC). Purification by column chromatography (SiO_2, CH_2Cl_2/i-PrOH 19:1) gave the *anti*-triol (12 mg, 10%) and the *syn*-triol (85 mg, 74%).

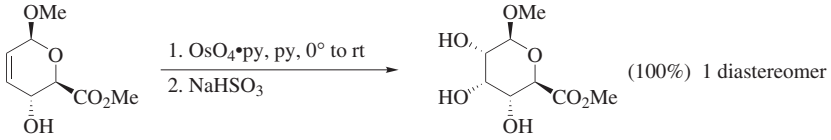


19

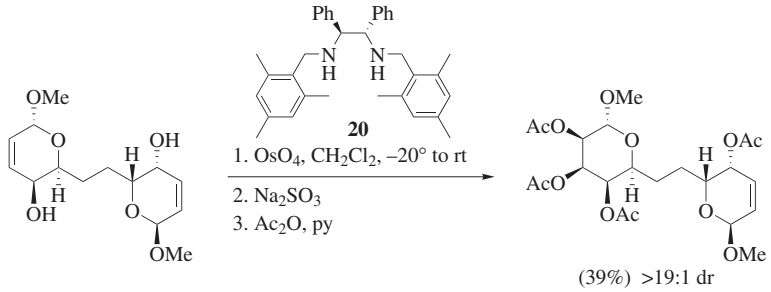
2,2,2-Trichloro-*N*-((1*R,2*R**,3*S**,5*S**)-2,3-dihydroxy-5-isopropyl-2-methylcyclohexyl)acetamide [Directed Dihydroxylation of an Allylic Cyclic Amide Using Catalytic OsO_4 and QNO].[19]** Quinuclidine (1.00 g, 9.01 mmol) was dissolved in CH_2Cl_2 (20 mL) under nitrogen and cooled to -78° before the addition of recrystallised *m*-CPBA (1.94 g, 11.24 mmol) in one portion. The mixture was stirred for 30 min and then allowed to warm to rt. The crude reaction mixture was flushed through a column of silica gel using CH_2Cl_2 as eluent until all of the benzoic acid byproduct was removed, then the solvent gradient was increased (CH_2Cl_2/MeOH 2.3:1) to strip quinuclidine-*N*-oxide from the column. Concentration under vacuum produced a brown oil, which crystallised on standing under high vacuum conditions to produce QNO as an off-white solid (1.25 g, 95%) and this was stored under reduced pressure. KF analysis showed this hygroscopic material contained 11% water by weight (~QNO•H_2O), and on standing open to air this increased to 40% water by weight (~QNO•$5H_2O$).

Quinuclidine-*N*-oxide monohydrate (0.36 g, 2.18 mmol) was added in one portion to a stirred solution of trichloroacetamide **19** (0.50 g, 1.68 mmol) in

CH_2Cl_2 at rt. OsO_4 (0.02 g, 0.08 mmol) was then added and the reaction mixture was stirred until complete consumption of the starting amide was observed by TLC. MeOH (10 mL) and HCl (concd, 4 drops) were added and the resulting solution was stirred for 2 h and then concentrated under vacuum to afford a dark yellow, viscous oil. Purification by column chromatography (SiO_2, petroleum ether/Et_2O 1:4) yielded the title compound (0.53 g, 95%, *syn*/*anti* 20:1, by HPLC) as a colorless crystalline solid. The analytical data for the product was not reported in this reference.



(2*R, 3*R**, 4*S**, 5*S**, 6*S**)-Methyl 3,4,5-Trihydroxy-6-methoxytetrahydro-2*H*-pyran-2-carboxylate [Directed Dihydroxylation of an Allylic Cyclic Alcohol Using OsO_4·Pyridine].**[38] (2*R**, 3*R**, 6*S**)-Methyl 3-Hydroxy-6-methoxy-3,6-dihydro-2*H*-pyran-2-carboxylate (50 mg, 0.25 mmol) in pyridine (4 mL) was added to an OsO_4 (70 mg, 0.28 mmol, 1.1 equiv) solution in pyridine (0.5 mL). After 2 h at rt, the reaction was quenched with $NaHSO_3$ (aq saturated solution, 1 mL) and dry loaded onto SiO_2. Purification by column chromatography (SiO_2, CH_2Cl_2/MeOH 9:1) gave the title compound as a colorless oil (60 mg, 0.25 mmol, 100%): IR (neat) 3418, 2930, 1736, 1084, 734 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.56 (d, $J = 6.8$ Hz, 1H), 4.26–4.16 (m, 3H), 3.86 (dd, $J = 3.0$, 9.0 Hz, 1H), 3.49 (s, 3H), 3.47 (dd, $J = 3.4$, 7.1 Hz, 1H), 2.78 (br s, 3H), 1.26 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 102.4, 73.5, 71.0, 69.7, 69.5, 62.2, 57.8, 14.4; EIMS (*m*/*z*): [M−H_2O] 218 (1), [M + H−MeOH] 205 (2), 71 (100). CIMS (*m*/*z*): $[M + H]^+$ 237 (1), [M + H−MeOH] 205 (18), 187 (100).



(2*R, 3*S**, 4*S**, 5*S**, 6*S**)-2-{2-[(2*S**, 3*S**, 6*R**)-3-Acetoxy-6-methoxy-3,6-dihydro-2*H*-pyran-2-yl]ethyl}-3,4,5-triacetoxy-6-methoxytetrahydropyran [Directed Dihydroxylation Using OsO_4 and a Chiral Amine].**[39] A solution of diamine **20** (33.9 mg, 0.071 mmol) in CH_2Cl_2 (0.5 mL) was added to a stirred

solution of OsO_4 (20 mg, 0.071 mmol) in CH_2Cl_2 (1.5 mL). The yellow solution was cooled to -20°; (2*R**, 3*S**, 6*R**)-2-(2-((2*R**, 3*R**, 6*S**)-3-hydroxy-6-methoxy-3,6-dihydro-2*H*-pyran-2-yl)ethyl)-6-methoxy-3,6-dihydro-2*H*-pyran-3-ol (20 mg, 0.071 mmol) was added in one portion and the reaction mixture was stirred for 5 h, warmed to rt, stirred for 2 d and evaporated under vacuum. The residue was dissolved in THF/sodium sulfite (aq saturated solution, 1:1, 2 mL), refluxed for 2 h and evaporated under vacuum to give a crude product. Crude (2*R**, 3*R**, 4*R**, 5*R**, 6*R**)-2-(2-((2*R**, 3*R**, 6*S**)-3-hydroxy-6-methoxy-3,6-dihydro-2*H*-pyran-2-yl)ethyl)-6-methoxytetrahydro-2*H*-pyran-3,4,5-triol was dissolved in a mixture of Ac_2O (2 mL) and pyridine (1 mL), stirred for 5 h at rt, and evaporated under vacuum to give the crude product. Purification by column chromatography (petroleum ether/EtOAc 2.3:1) afforded the title product (13.2 mg, 39%) as a viscous colorless oil: $[\alpha]_D^{20}$ +90.9 (*c* 0.033, $CHCl_3$); R_f 0.31 (petroleum ether/EtOAc 2.3:1); IR (thin film) 2960, 2924, 2853, 1742, 1678, 1455, 1373, 1259, 1083 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.08 (ddd, $J = 10.0$, 5.5, 1.0 Hz, 1H), 6.00 (ddd, $J = 10.0$, 3.0, 0.4 Hz, 1H), 5.27 (t, $J = 3.8$ Hz, 4H), 5.21 (dd, $J = 3.8$, 1.2 Hz, 1H), 5.10 (dt, $J = 3.8$, 1.2 Hz, 1H), 4.91 (d, $J = 3.0$ Hz, 1H), 4.76 (d, $J = 1.2$ Hz, 1H), 4.02 (td, $J = 9.3$, 2.6 Hz, 1H), 3.97 (ddd, $J = 9.3$, 3.8, 1.0 Hz, 1H), 3.41 (s, 3H), 3.39 (s, 3H), 2.14 (s, 3H), 2.14 (s, 3H), 2.08 (s, 3H), 1.99 (s, 3H) and 1.77–1.68 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 170.4, 170.1, 169.6, 130.4, 125.9, 99.4, 95.2, 68.8, 68.3, 67.5, 66.0, 64.5, 55.7, 55.2, 27.1, 26.4, 21.0, 20.8, 20.7, 20.6; ESI^+ (*m*/*z*): $[M + Na]^+$ 511 (100); ESI^+ (*m*/*z*): $[M + Na]^+$ calcd for $C_{22}H_{32}O_{12}Na$, 511.1791; found, 511.1768.

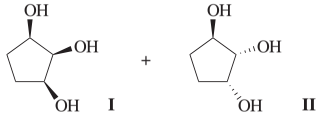
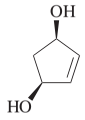
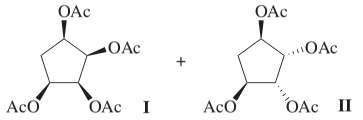
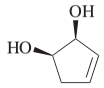
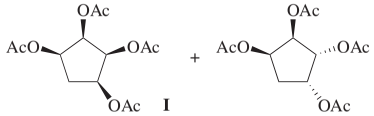
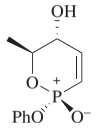
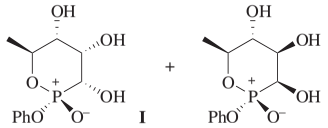
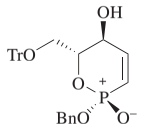
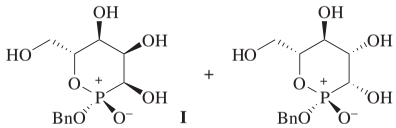
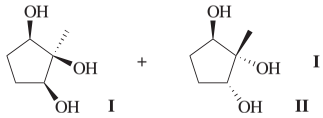
TABULAR SURVEY

The literature has been covered through the end of September 2007. The tables are organized by substrate type. Entries in the tables are in order of increasing number of carbons. Protecting groups and *O*-methyl groups are excluded from the count. The symbol (—) indicates that no yield was reported and the symbol — indicates that no dr (*syn*/*anti*) was reported.

Abbreviations used in the tables are as follows:

ee	enantiomeric excess
eq	equivalents
QNO	quinuclidine *N*-oxide
TBDPS	*tert*-butyldiphenylsilyl

TABLE 1. DIRECTED DIHYDROXYLATION OF ALLYLIC CYCLIC ALCOHOLS

Substrate	Conditions	Product(s), Yield(s) (%), and dr (*syn*:*anti*)	Refs.
C_5 	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then $NH_2(CH_2)_2NH_2$	 **I** + **II** (76), **I**:**II** = 7:1	21, 15
	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then $NH_2(CH_2)_2NH_2$ 2. Ac_2O, py	 **I** + **II** (73), **I**:**II** = 25:1	15
	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then $NH_2(CH_2)_2NH_2$ 2. Ac_2O, py	 **I** + **II** (67), **I**:**II** = 2:1	15
	OsO_4, TMEDA, CH_2Cl_2, –60° to rt; then citric acid, MeOH	 **I** + **II** (70), **I**:**II** = 13.5:1	35
	OsO_4, TMEDA, CH_2Cl_2, –60° to rt; then TsOH, MeOH	 **I** + **II** (70), **I**:**II** = 24:1	35
C_6 	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then $NH_2(CH_2)_2NH_2$	 **I** + **II** (88), **I**:**II** = 25:1	15

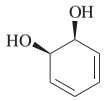
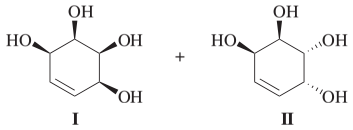
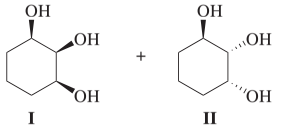
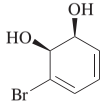
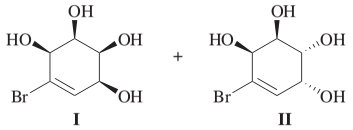
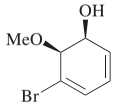
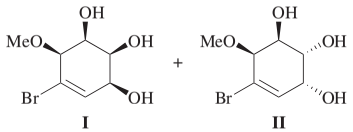
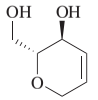
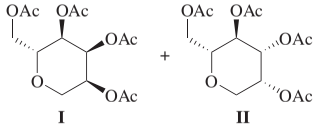
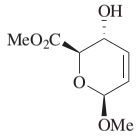
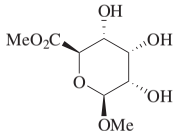
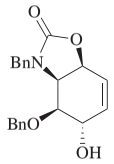
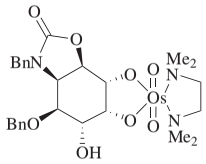
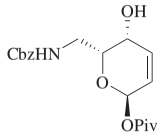
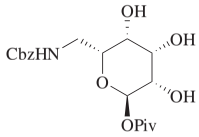
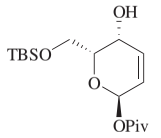
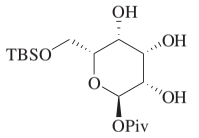
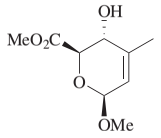
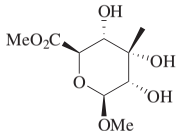
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then Na_2SO_3	 **I** + **II**	**I** + **II** (54), **I**:**II** = 16:1	21, 15
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then Na_2SO_3	 **I** + **II**	**I** + **II** (98), **I**:**II** = 9:1	15
	OsO_4 (cat), $Me_3NO•2H_2O$, CH_2Cl_2	 **I** + **II**	**I** + **II** (79), **I**:**II** = 4.6:1	21
	OsO_4, quinuclidine, CH_2Cl_2, –78°	 **I** + **II**	**I** + **II** (71), **I**:**II** = 2.2:1	40
	OsO_4 (cat), $Me_3NO•2H_2O$, CH_2Cl_2	**I** + **II** (40), **I**:**II** = 2:1		40
	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then Na_2SO_3 2. Ac_2O, py	 **I** + **II**	**I** + **II** (63), **I**:**II** = 6:1	21, 15

TABLE 1. DIRECTED DIHYDROXYLATION OF ALLYLIC CYCLIC ALCOHOLS (*Continued*)

	Substrate	Conditions	Product(s), Yield(s) (%), and dr (*syn*:*anti*)	Refs.
C_6		OsO_4•py, py, 0° to rt; then $NaHSO_3$	 (100), 1 diastereomer	38
		OsO_4, TMEDA, CH_2Cl_2, –78° to rt	 (100), 1 diastereomer	36
		OsO_4, TMEDA, CH_2Cl_2, –78°; then $NH_2(CH_2)_2NH_2$	 (47), 1 diastereomer	41
		OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then Na_2SO_3	 (80), 1 diastereomer	42, 20, 15
C_7		OsO_4•py, py, 0° to rt; then $NaHSO_3$	 (60), 1 diastereomer	38

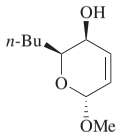
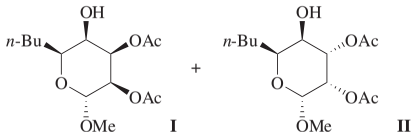
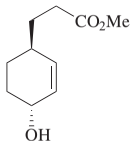
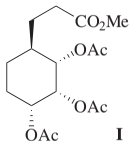
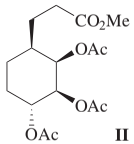
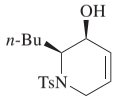
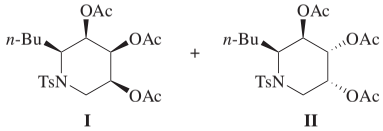
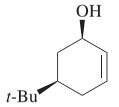
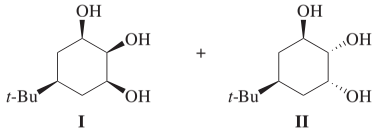
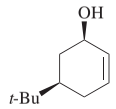
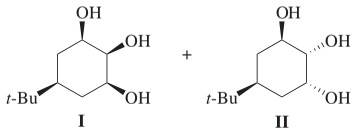
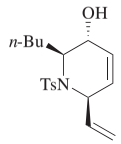
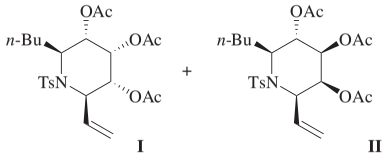
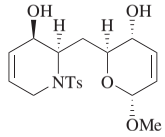
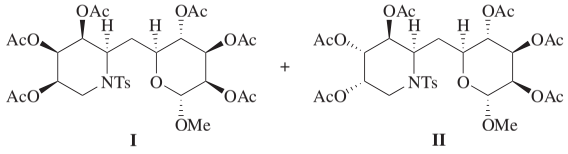
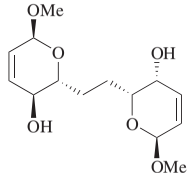
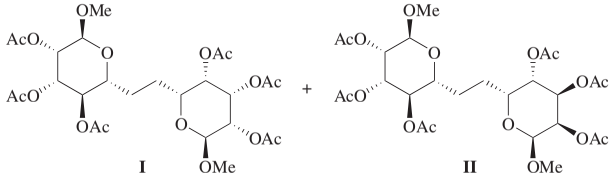
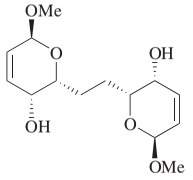
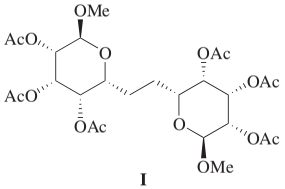
C_9		1. OsO_4, TMEDA, CH_2Cl_2, –78° 2. Ac_2O, py	 **I** + **II**	**I** + **II** (94), **I**:**II** = >19:1	43
		1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then Na_2SO_3 2. Ac_2O, py	 **I**	(—), 1 diastereomer	44
		1. OsO_4•py, py, 0° to rt; then $Na_2S_2O_5$ 2. Ac_2O, DMAP, py	**I** +  **II**	**I** + **II** (32), **I**:**II** = 1:1	44
		1. OsO_4, TMEDA, CH_2Cl_2, –78° 2. Ac_2O, py	 **I** + **II**	**I** + **II** (74), **I**:**II** = 24:1	45, 46
C_{10}		OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then Na_2SO_3	 **I** + **II**	**I** + **II** (95), **I**:**II** = 25:1	21, 15

TABLE 1. DIRECTED DIHYDROXYLATION OF ALLYLIC CYCLIC ALCOHOLS (*Continued*)

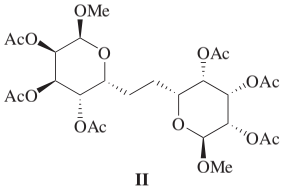
Substrate	Conditions	Product(s), Yield(s) (%), and dr (*syn*:*anti*)	Refs.
C_{10} 	OsO_4, amine, CH_2Cl_2, 0° to rt; then Na_2SO_3	 **I** + **II** (—)	Amine **I**:**II**: TMEDA 4.6:1; Me_3N 1.2:1; $Me_2NCH_2NMe_2$ 1.6:1; $Me_2N(CH_2)_2OH$ 1.1:1; $Me_2N(CH_2)_2OMe$ 1.1:1; $Me_2N(CH_2)_3NMe_2$ 2.8:1	15
C_{12} 	1. OsO_4, TMEDA, CH_2Cl_2, –78° 2. Ac_2O, py	 **I** + **II** (25), **I**:**II** = 3:1		45, 46
	1. OsO_4, TMEDA, CH_2Cl_2, –78° 2. Ac_2O, py	 **I** + **II** (17), **I**:**II** = 24:1		45, 46
	1. OsO_4, TMEDA, CH_2Cl_2, –78° 2. Ac_2O, py	 **I** + **II** (83), **I**:**II** = 19:1		47, 48



1. OsO_4, TMEDA, CH_2Cl_2, –78°
2. Ac_2O, py



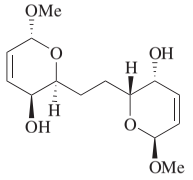
I

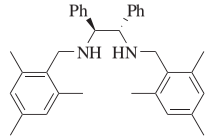


II

47, 48

I + **II** (78), **I**:**II** = 24:1

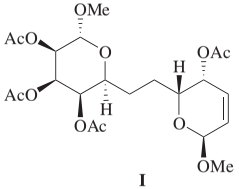


1. 

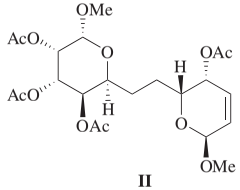
OsO_4, CH_2Cl_2, –20°

2. Ac_2O, py

,



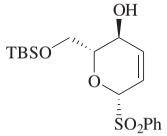
I



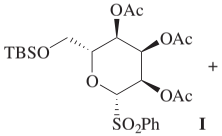
II

39

I + **II** (39), **I**:**II** = 19:1

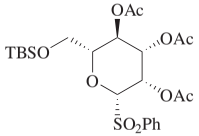


1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH
2. Ac_2O, py



I

+

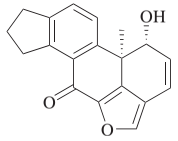


II

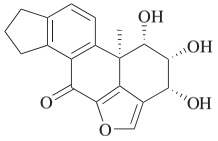
I + **II** (82), **I**:**II** = 25:1

15

C_{19}



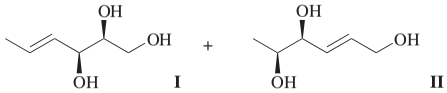
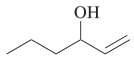
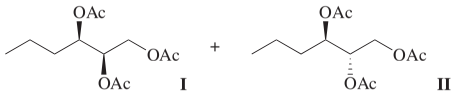
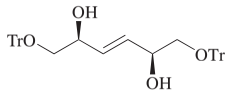
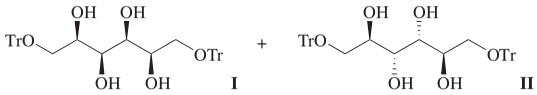
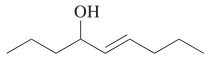
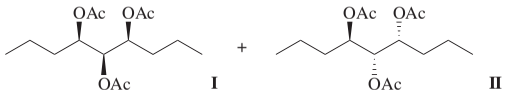
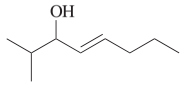
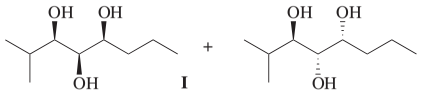
OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then py/H_2O/$NaHSO_3$ (35:30:2)



(76), 1 diastereomer

49

TABLE 2. DIRECTED DIHYDROXYLATION OF ACYCLIC AND EXOCYCLIC ALLYLIC ALCOHOLS

Substrate	Conditions	Product(s), Yield(s) (%), and dr (*syn*:*anti*)	Refs.
C_6			
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** + **II** (70), **I**:**II** = 5:1	21
	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (74), **I**:**II** = 5:1	50
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** + **II** (95), **I**:**II** = 1.1:1	51
C_9			
	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (83), **I**:**II** = 3:1	50
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** + **II** (84), **I**:**II** = 3:1	50

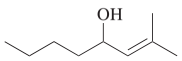
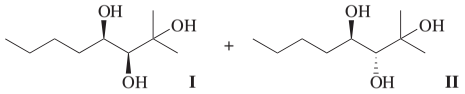
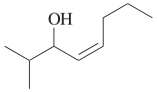
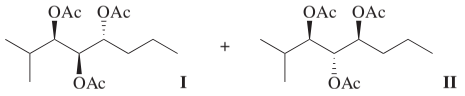
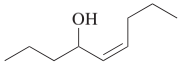
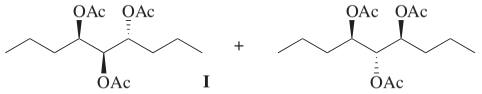
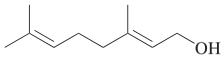
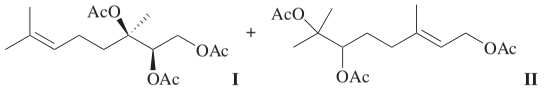
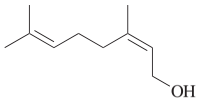
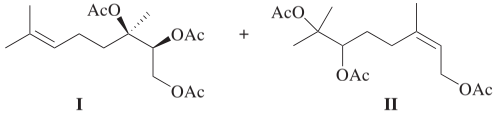
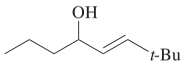
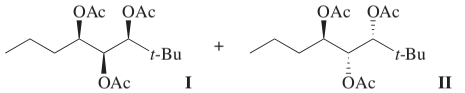
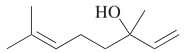
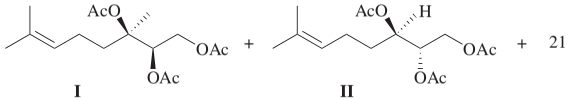
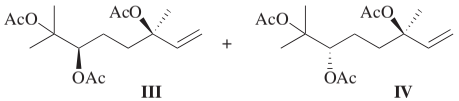
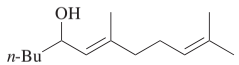
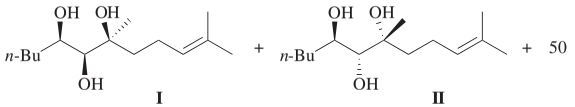
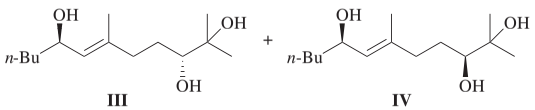
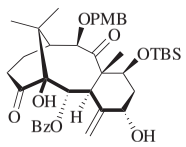
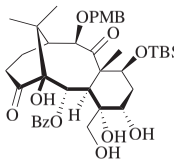
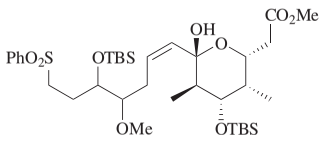
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** + **II** (78), **I**:**II** = 25:1	50
	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (79), **I**:**II** = 25:1	50
	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (74), **I**:**II** = 25:1	50
C_{10} 	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (74), **I**:**II** = >25:1	21
	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (68), **I**:**II** = 4:1	21
	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (75), **I**:**II** = 4:1	50

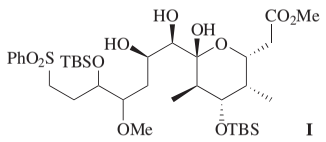
TABLE 2. DIRECTED DIHYDROXYLATION OF ACYCLIC AND EXOCYCLIC ALLYLIC ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s), Yield(s) (%), and dr (*syn*:*anti*)	Refs.
C_{10} 	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** + 21  **III** + **IV** **I + II** (70); **I:II** 2.5:1; **III + IV** (6); **III:IV** —	
C_{14} 	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** + 50  **III** + **IV** **I + II** (70); **I:II** 24:1; **III + IV** (<5); **III:IV** —	
C_{19} 	OsO_4 (2.5 eq), TMEDA (2.1 eq), CH_2Cl_2, –78° to rt; then $NaHSO_3$, THF/acetone/H_2O (2:1:1)	 (72), 1 diastereomer	17

C_{22}



OsO_4 (1.0 eq), TMEDA (1.1 eq),
CH_2Cl_2, –78° to rt; then $NaHSO_3$

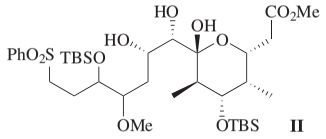


+

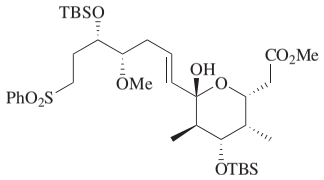
52

I

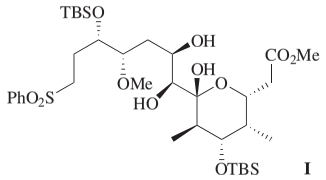
I + **II** (100), **I**:**II** = 9:1



II



OsO_4 (1.0 eq), TMEDA (1.1 eq),
CH_2Cl_2, –78° to rt; then $NaHSO_3$

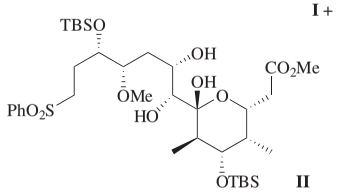


+

52

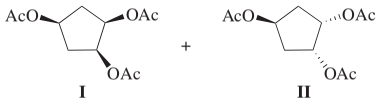
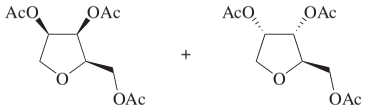
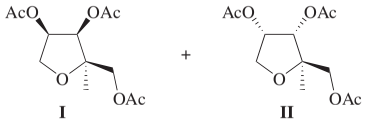
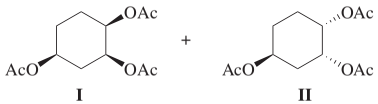
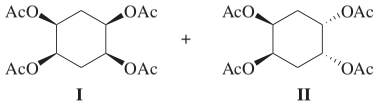
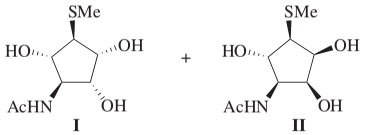
I

I + **II** (100), **I**:**II** = 5:1



II

TABLE 3. DIRECTED DIHYDROXYLATION OF HOMOALLYLIC CYCLIC ALCOHOLS

	Substrate	Conditions	Product(s), Yield(s) (%), and dr (*syn*:*anti*)	Refs.
C_5		1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II**	**I** + **II** (71), **I**:**II** = 25:1	25, 22
		1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II**	**I** + **II** (55), **I**:**II** = 1:1	25, 22
C_6		1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II**	**I** + **II** (83), **I**:**II** = 6:1	25, 22
		1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II**	**I** + **II** (92), **I**:**II** = 3:1	25, 22
		1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II**	**I** + **II** (55), **I**:**II** = 12.4:1	25, 22
		OsO_4, TMEDA, CH_2Cl_2, –78° to rt	 **I** + **II**	**I** + **II** (71), **I**:**II** = 6:1	53

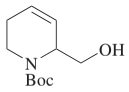
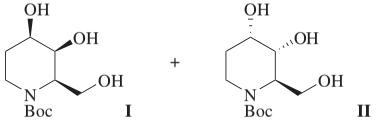
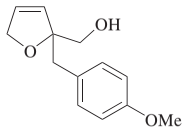
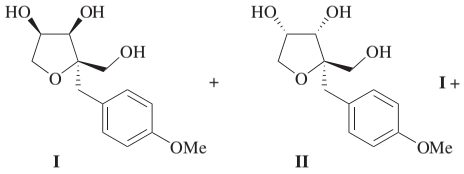
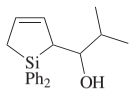
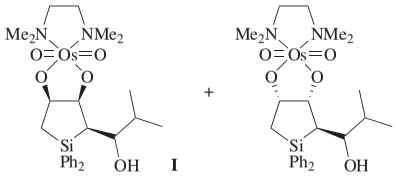
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** + **II**	**I** + **II** (86), **I**:**II** = 2:1	54
C_{12}				
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** + **II**	**I** + **II** (82), **I**:**II** = 99:1	37
	OsO_4 (cat), quinuclidine, acetone/H_2O	**I** + **II** (76), **I**:**II** = 2.1:1		37
	OsO_4 (cat), $Me_3NO•2H_2O$, CH_2Cl_2	**I** + **II** (80), **I**:**II** = 6.7:1		37
	OsO_4 (cat), $Me_3NO•2H_2O$, polymer-bound DABCO, CH_2Cl_2	**I** + **II** (84), **I**:**II** = 7.3:1		37
C_{20}				
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt	 **I** + **II**	**I** + **II** (—), **I**:**II** = 1.2:1	55

TABLE 4. DIRECTED DIHYDROXYLATION OF HOMOALLYLIC EXOCYCLIC ALCOHOLS

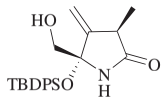
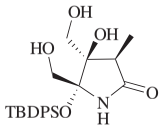
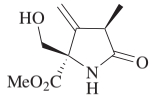
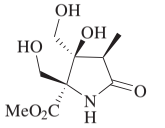
Substrate	Conditions	Product(s), Yield(s) (%), and dr (*syn*:*anti*)	Refs.
C_7 	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH		(99), 1 diastereomer	56
C_8 	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH		(35), 1 diastereomer	56

TABLE 5. DIRECTED DIHYDROXYLATION OF *N*-ALLYLIC AMINE DERIVATIVES

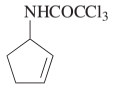
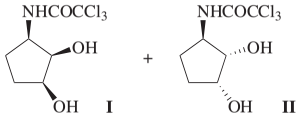
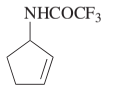
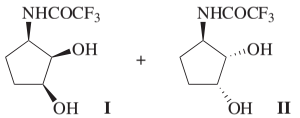
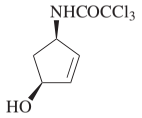
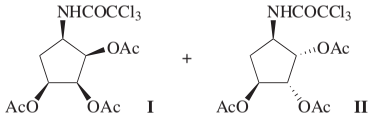
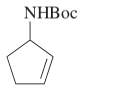
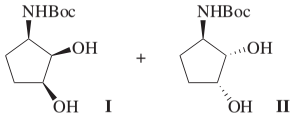
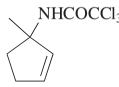
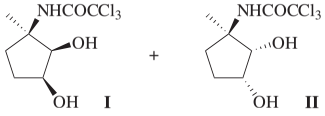
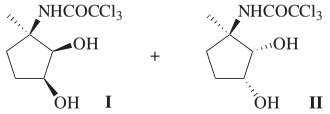
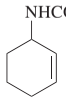
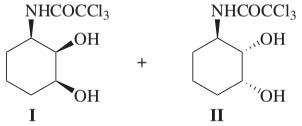
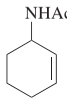
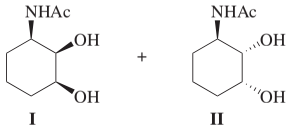
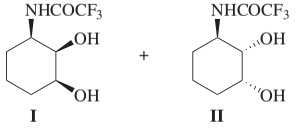
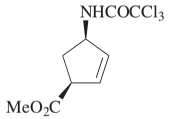
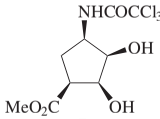
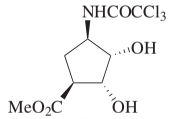
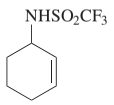
Substrate	Conditions	Product(s), Yield(s) (%), and dr (*syn*:*anti*)	Refs.
C_5 	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** + **II** (80), **I**:**II** = 24:1	20, 15
	OsO_4 (cat), $Me_3NO•2H_2O$ (1.5 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (84), **I**:**II** = 7.8:1	19
	OsO_4 (0.05 eq), $QNO•H_2O$ (1.3 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (69), **I**:**II** = 13:1	19
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then aq Na_2SO_3, reflux	 **I** + **II** (—), **I**:**II** = 25:1	15
	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (83), **I**:**II** = 17:1	15
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then aq Na_2SO_3, reflux	 **I** + **II** (—), **I**:**II** = 9:1	15
C_6 	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** + **II** (81), **I**:**II** = 24:1	15

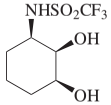
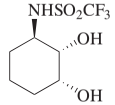
TABLE 5. DIRECTED DIHYDROXYLATION OF *N*-ALLYLIC AMINE DERIVATIVES (*Continued*)

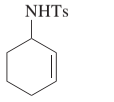
Substrate	Conditions	Product(s), Yield(s) (%), and dr (*syn*:*anti*)	Refs.
C_6 	OsO_4 (cat), $Me_3NO{\bullet}2H_2O$ (1.5 eq), CH_2Cl_2, rt; then HCl, MeOH	 **I** + **II** (81), **I**:**II** = 9:1	19
	OsO_4 (0.05 eq), $QNO{\bullet}H_2O$ (1.3 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (69), **I**:**II** = 13:1	19
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** + **II** (99), **I**:**II** = 24:1	20, 15
	OsO_4 (cat), $Me_3NO{\bullet}2H_2O$ (1.5 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (93), **I**:**II** = 3:1	19
	OsO_4 (0.05 eq), $QNO{\bullet}H_2O$ (1.3 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (86), **I**:**II** = 4.3:1	19
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then aq Na_2SO_3, reflux	 **I** + **II** (—), **I**:**II** = 1.8:1	15
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then aq Na_2SO_3, reflux	 **I** + **II** (—), **I**:**II** = 24:1	15

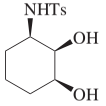
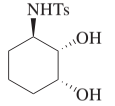


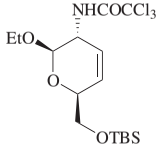
OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** +  **II**	**I** + **II** (93), **I**:**II** = 5:1	20, 15
OsO_4 (cat), $Me_3NO•2H_2O$ (1.5 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (81), **I**:**II** = 1.5:1		19
OsO_4 (0.05 eq), $QNO•H_2O$ (1.3 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (69), **I**:**II** = 1.6:1		19



OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then aq Na_2SO_3, reflux	 **I** +  **II**	**I** + **II** (—), **I**:**II** = 4.2:1	15



OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then aq Na_2SO_3, reflux	 **I** +  **II**	**I** + **II** (—), **I**:**II** = 3.5:1	15



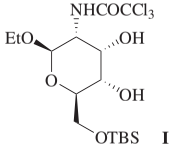
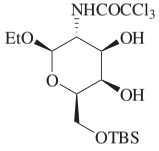
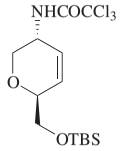
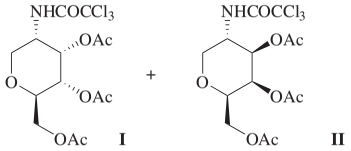
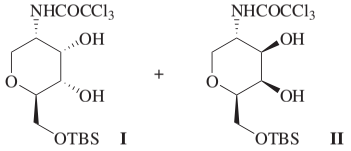
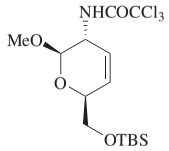
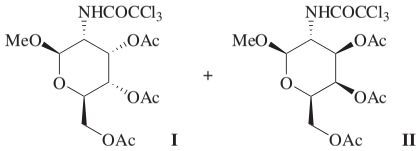
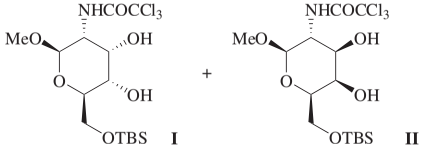
OsO_4 (cat), $Me_3NO•2H_2O$ (1.5 eq), CH_2Cl_2, rt; then HCl, MeOH	 **I** +  **II**	**I** + **II** (80), **I**:**II** = 20:1	19
OsO_4 (0.05 eq), $QNO•H_2O$ (1.3 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (91), **I**:**II** = 20:1		19

TABLE 5. DIRECTED DIHYDROXYLATION OF *N*-ALLYLIC AMINE DERIVATIVES (*Continued*)

	Substrate	Conditions	Product(s), Yield(s) (%), and dr (*syn*:*anti*)	Refs.
C_6		1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O	 **I** + **II** (78), **I**:**II** = 24:1	20
		OsO_4 (cat), $Me_3NO•2H_2O$ (1.5 eq), CH_2Cl_2, rt; then HCl, MeOH	 **I** + **II** (85), **I**:**II** = 20:1	19
		OsO_4 (0.05 eq), QNO•H_2O (1.3 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (89), **I**:**II** = 25:1	19
		1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O	 **I** + **II** (92), **I**:**II** = 4:1	57
		1. OsO_4, quinuclidine (1.1 eq), CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O	**I** + **II** (90), **I**:**II** = 24:1	57
		OsO_4 (cat), QNO•H_2O (1.3 eq), CH_2Cl_2, rt; then HCl, MeOH	 **I** + **II** (80), **I**:**II** = 20:1	57

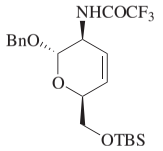
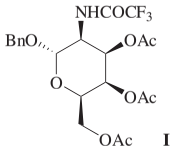
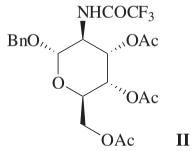
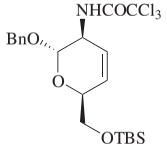
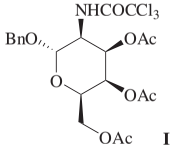
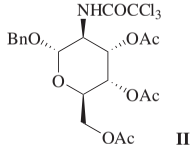
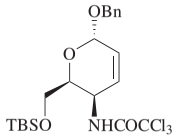
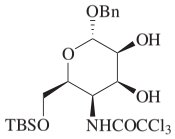
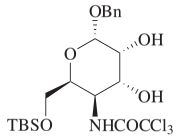
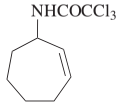
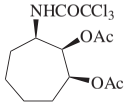
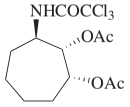
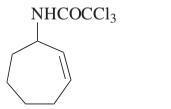
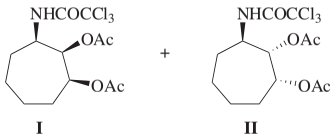
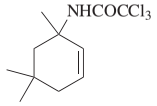
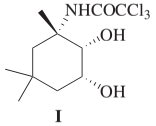
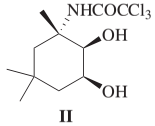
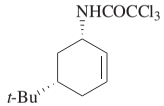
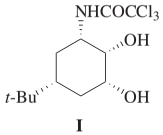
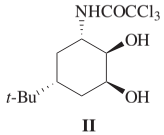
	OsO_4 (cat), $Me_3NO•2H_2O$ (1.5 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (87), **I**:**II** = 14:1		57
	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O	 **I**	+  **II**	**I** + **II** (82), **I**:**II** = 25:1	15
	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O	 **I**	+  **II**	**I** + **II** (89), **I**:**II** = 25:1	57
	OsO_4 (cat), $Me_3NO•2H_2O$ (1.5 eq), CH_2Cl_2, rt; then HCl, MeOH	 **I**	+  **II**	**I** + **II** (90), **I**:**II** = 2:1	19
	OsO_4 (0.05 eq), QNO•H_2O (1.3 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (94), **I**:**II** = 2.4:1			19
C_7 	1. OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I**	+  **II**	**I** + **II** (78), **I**:**II** = 25:1	15

TABLE 5. DIRECTED DIHYDROXYLATION OF *N*-ALLYLIC AMINE DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s), Yield(s) (%), and dr (*syn*:*anti*)	Refs.
C_7 	1. OsO_4 (cat), $Me_3NO•2H_2O$ (1.5 eq), CH_2Cl_2, rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II**	**I** + **II** (87), **I**:**II** = 10:1	19
	1. OsO_4 (0.05 eq), $QNO•H_2O$ (1.3 eq), CH_2Cl_2, rt; then HCl, MeOH 2. Ac_2O, py	**I** + **II** (82), **I**:**II** = 17:1	19
C_9 	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** +  **II**	**I** + **II** (92), **I**:**II** = 24:1	20, 15
	OsO_4 (cat), $Me_3NO•2H_2O$ (1.5 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (81), **I**:**II** = 11:1	19
	OsO_4 (0.05 eq), $QNO•H_2O$ (1.3 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (79), **I**:**II** = 20:1	19
C_{10} 	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** +  **II**	**I** + **II** (96), **I**:**II** = 24:1	20, 15

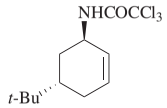
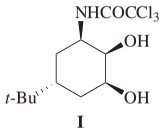
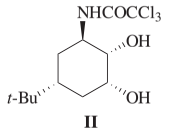
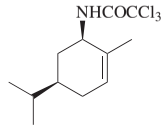
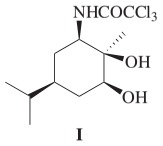
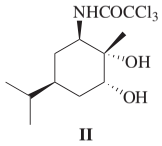
	OsO_4 (cat), $Me_3NO•2H_2O$ (1.5 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (81), **I**:**II** = 6:1		19
	OsO_4 (0.05 eq), QNO•H_2O (1.3 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (77), **I**:**II** = 13:1		19
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** +  **II**	**I** + **II** (97), **I**:**II** = 1.7:1	20, 15
	OsO_4, quinuclidine, CH_2Cl_2, –78°; then HCl, MeOH	**I** + **II** (66), **I**:**II** = 4.9:1		20
	OsO_4 (cat), $Me_3NO•2H_2O$ (1.5 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (91), **I**:**II** = 1.6:1		19
	OsO_4 (0.05 eq), QNO•H_2O (1.3 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (88), **I**:**II** = 2.1:1		19
	OsO_4 (cat), $Me_3NO•2H_2O$ (1.5 eq), CH_2Cl_2, rt; then HCl, MeOH	 **I** +  **II**	**I** + **II** (84), **I**:**II** = 13:1	19
	OsO_4 (0.05 eq), QNO•H_2O (1.3 eq), CH_2Cl_2, rt; then HCl, MeOH	**I** + **II** (95), **I**:**II** = 20:1		19

TABLE 5. DIRECTED DIHYDROXYLATION OF *N*-ALLYLIC AMINE DERIVATIVES (*Continued*)

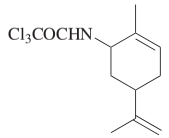
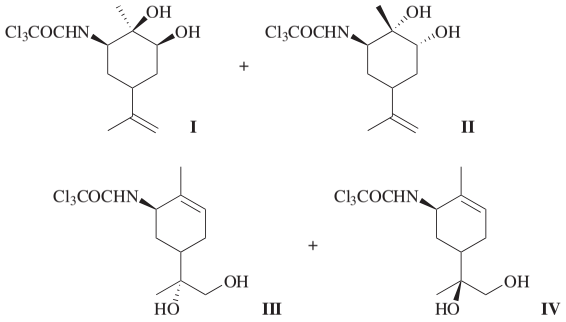
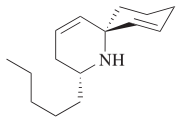
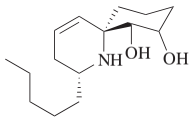
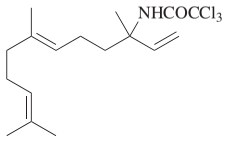
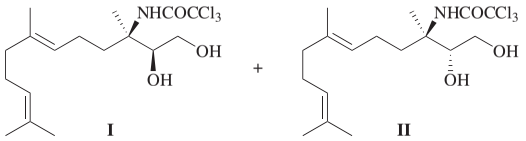
Substrate	Conditions	Product(s), Yield(s) (%), and dr (*syn*:*anti*)	Refs.
C_{10} 	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** + **II**; **III** + **IV**	58
		I + **II** (71), **I**:**II** 25:1, **III** + **IV** (<3), **III**:**IV** —	
C_{15} 	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 (60), 1 diastereomer	59
	OsO_4, TMEDA, CH_2Cl_2, –78° to rt; then HCl, MeOH	 **I** + **II** (68), **I**:**II** = 13:1	58

TABLE 6. DIRECTED DIHYDROXYLATION OF *N*-HOMOALLYLIC CYCLIC AMIDES

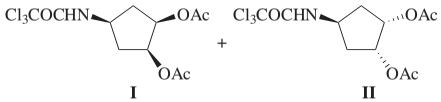
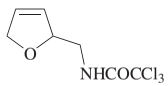
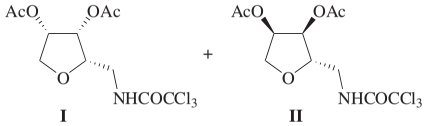
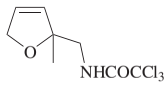
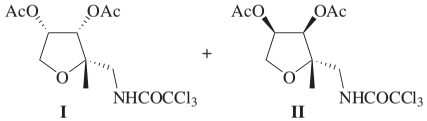
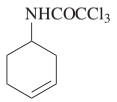
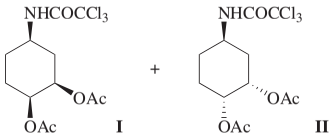
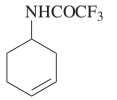
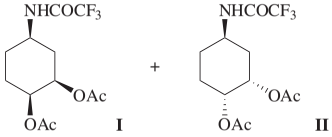
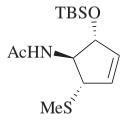
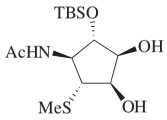
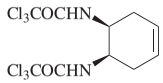
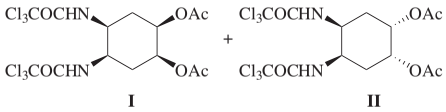
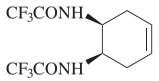
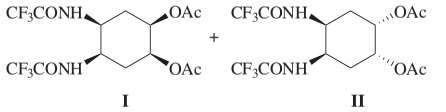
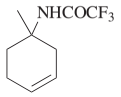
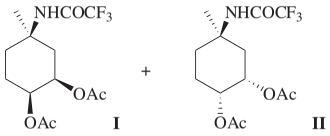
	Substrate	Conditions	Product(s), Yield(s) (%), and dr (*syn*:*anti*)	Refs.
C_5		1. OsO_4, TMEDA, CH_2Cl_2, −78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (94), **I**:**II** = >25:1	22
		1. OsO_4, TMEDA, CH_2Cl_2, −78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (72), **I**:**II** = 2:1	22
C_6		1. OsO_4, TMEDA, CH_2Cl_2, −78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (88), **I**:**II** = >25:1	22
		1. OsO_4, TMEDA, CH_2Cl_2, −78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (92), **I**:**II** = 1.2:1	22
		1. OsO_4, TMEDA, CH_2Cl_2, −78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (90), **I**:**II** = >20:1	22

TABLE 6. DIRECTED DIHYDROXYLATION OF *N*-HOMOALLYLIC CYCLIC AMIDES (*Continued*)

Substrate	Conditions	Product(s), Yield(s) (%), and dr (*syn*:*anti*)	Refs.
C_6 	OsO_4•py, py, rt; then $Na_2S_2O_5$, THF/H_2O, 65°	 (81), 1 diastereomer	53
	1. OsO_4, TMEDA, CH_2Cl_2, −78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (100), **I**:**II** = 3:1	22
	1. OsO_4, TMEDA, CH_2Cl_2, −78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (95), **I**:**II** = >25:1	22
C_7 	1. OsO_4, TMEDA, CH_2Cl_2, −78° to rt; then HCl, MeOH 2. Ac_2O, py	 **I** + **II** (67), **I**:**II** = 5:1	22

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