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ON STEREOCHEMISTRY OF OSMIUM TETRAOXIDE OXIDATION OF ALLYLIC ALCOHOL SYSTEMS

EMPIRICAL RULE

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(*Received in Japan* 23 *August* 1983)

Abstract—An empirical formulation is presented to predict the stereochemistry of major osmylation products of allylic alcohols and their derivatives.

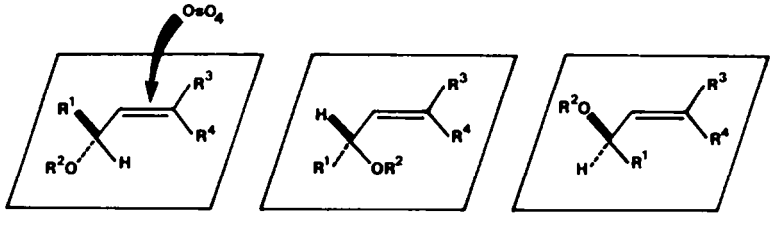
In connection with studies on the marine natural product palytoxin,[1-3] we have been interested in examining the stereochemical outcome of the osmium tetroxide oxidation of olefins, generalized in eqn (1).[4] Judging from our previous experiments on hydroboration[5] and epoxidation[6] of similar systems, we expected this process might be stereoselective.

(1)

Thus, the olefins **1a–p** were subjected to osmium tetroxide oxidation under stoichiometric and catalytic[7] conditions. After the usual work-up, the ratios of the two expected products **2a–p** and **3a–p** were determined by the appropriate methods (Table 1). The stereochemistry of the major products **2a–e** and **2j–n** was established by their transformation to the corresponding pentitol pentaacetates and comparison with authentic samples.[8] The stereochemistry of osymlation products **2f–h** and **3o–p** was determined by independent syntheses of the corresponding tetraacetates.

The results summarized in Table 1 deserve several comments. First, the stoichiometric procedure provided slightly higher stereoselectivity than the catalytic procedure. Second, protecting groups of the hydroxyl at the chiral center, except acyl groups, were found to have only a limited effect in determining the stereochemical course of the oxidation. For the cases of acyl derivatives, however, the stereoselectivity diminished noticeably or completely. Third, the hydroxyl or alkoxyl oxygen seems to play the important role in obtaining a high degree of stereoselectivity. The examples listed in Table 2 support this view. Fourth, the degree of stereoselectivity observed for the *cis*-olefins **1a–g** is higher than that for the corresponding *trans*-olefins **1j–p**, which may be attributed to the different degrees of preference of one eclipsed conformation over the others (*vide infra*). Fifth and most importantly, *the relative stereochemistry between the preexisting hydroxyl or alkoxyl group and the adjacent newly introduced hydroxyl group of the major product in all cases is erythro.* Although conclusions as to the mechanistic rationalization for this formulation must await further experimentation, an explanation, based on the conformational analysis of sp^3–sp^2 single bond systems, seems worth mentioning.

An eclipsed conformation is known to be preferred for such systems.[9] Among the three eclipsed conformations, **A**, **B**, and **C**, of the olefins **1**, the conformation **A** is considered to be most preferred, since it is sterically least compressed. Assuming this conformational preference is reflected in the transition state, the stereochemistry of the major product is formulated as arising from the preferential approach of osmium tetroxide to the face of the olefinic bond opposite to that of the preexisting hydroxyl or alkoxyl group.[10] The stereochemistry of the major product could alternatively be formulated as the approach of osmium tetroxide took place preferentially from the top face of the olefinic bond in either conformation **B** or **C**. However, the fact that the stereoselectivity observed for osmylation of the *cis*-olefins **1a–g** was always higher than that for the corresponding *trans*-olefins **1j–p** seems to suggest the mode **A** of reagent approach to be most probable, since the preference of the conformation **A** over **B** and **C** is expected to be more significant for the *cis*-olefins than for the corresponding *trans*-olefins. Although there is no convincing example known in the literature to compare the relative reactivity of these three modes of reagent approach, the mode **A**



A B C

Table 1.

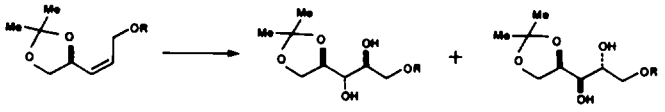
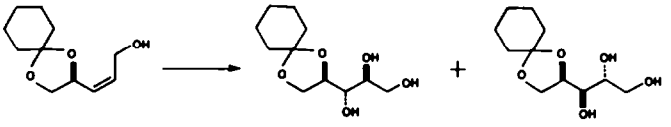
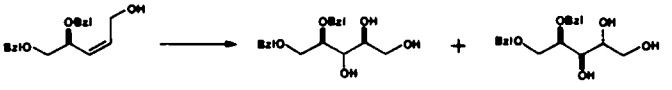
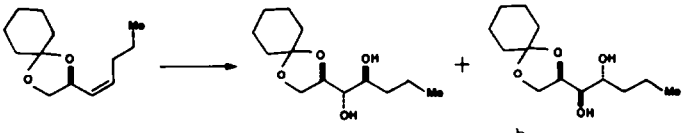
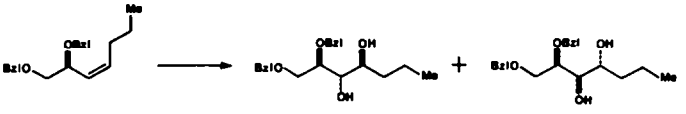
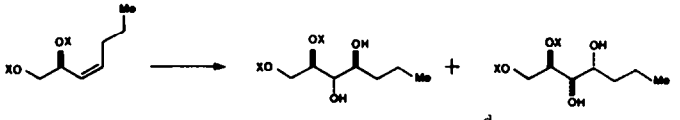
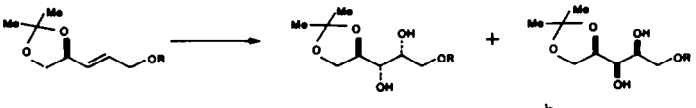
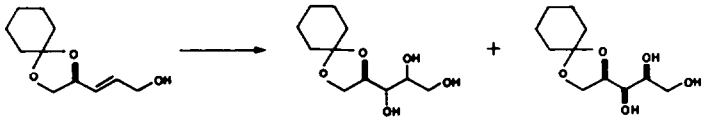
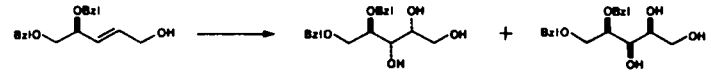
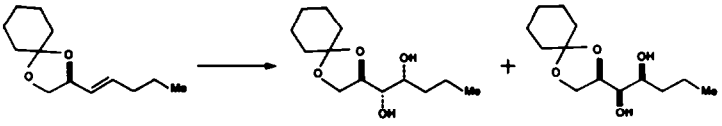
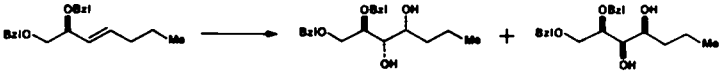
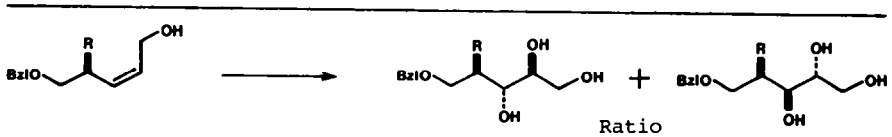
	1	2	3
a :		R = H	stoichiometric 6.3 : 1.0[b] catalytic 6.0 : 1.0[c]
b :		R = $COC(Me)_3$	stoichiometric 6.3 : 1.0[b] catalytic 6.1 : 1.0[c]
c :		R = $Si(Ph)_2(t\text{-}Bu)$	stoichiometric 8.0 : 1.0[b] catalytic 7.2 : 1.0[b]
d :			stoichiometric 6.2 : 1.0[b] catalytic 6.1 : 1.0[b]
e :			stoichiometric 8.0 : 1.0[b] catalytic 7.0 : 1.0[b]
f :			stoichiometric 11.0 : 1.0[b] catalytic 8.1 : 1.0[b]
g :			stoichiometric 8.9 : 1.0[d] catalytic 7.6 : 1.0[d]
			
h :		X = $COCH_3$	catalytic 2 : 1[d]
i :		X = $COC_6H_4NO_2$-p	catalytic 1 : 1[d]
			
j :		R = H	stoichiometric 3.3 : 1.0[b] catalytic 3.0 : 1.0[c]
k :		R = $COC(Me)_3$	stoichiometric 4.2 : 1.0[b] catalytic 4.0 : 1.0[c]

Table 1 (*Contd*)

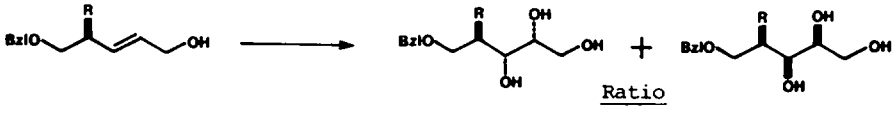
l :	R = $Si(Ph)_2(t\text{-}Bu)$	stoichiometric	3.3 : 1.0[b]
		catalytic	3.1 : 1.0[b]
m :		stoichiometric	3.6 : 1.0[b]
		catalytic	3.1 : 1.0[b]
n :		stoichiometric	4.2 : 1.0[b]
		catalytic	3.1 : 1.0[b]
o :		stoichiometric	4.3 : 1.0[b]
		catalytic	3.7 : 1.0[b]
p :		stoichiometric	7 : 1[b]
		catalytic	6 : 1[b]

a. Stoichiometric represents the results under the conditions of OsO_4 (1.2 eq.), py-THF (1:4), RT, and catalytic represents the results under the conditions of OsO_4 (0.05 eq.), N-methylmorpholine N-oxide (2.0 eq.), water-acetone (1:8), RT.
b. The product ratio was determined by HPLC analysis.
c. The product ratio was determined by isolation of products.
d. The product ratio was determined by PMR analysis.

Table 2.



		Ratio	
1a : R = OBzl	2a	6 : 1	3a
1q : R = Me[19]	2q	1 : 1	3q

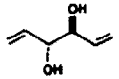


		Ratio	
1n : R = OBzl	2n	4.2 : 1.0	3n
1r : R = Me[19]	2r	1.5 : 1.0	3r

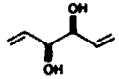
Table 3.

A. Acyclic Systems

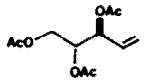
a. Nonconjugated Compounds - 1



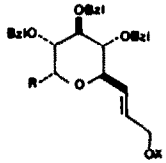
4[20] : Ratio = 1:0[21]



5[20] : Ratio = 1:0[21]



6[20] : Ratio = 1:1[21]



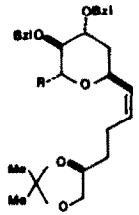
7[22] : Ratio = 6:1
R = X = H

8[22] : Ratio = 8:1
R = OMe, X = $COC(Me)_3$

9[22] : Ratio = 4:1
R = $(CH_2)_2OCH_2OMe$, X = H

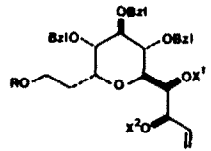
10[22] : Ratio = 4:1
R = $(CH_2)_2OCH_2OMe$,
X = $Si(Ph)_2(t\text{-}Bu)$

11[22] : Ratio = 8:1
R = $(CH_2)_2OCH_2OMe$,
X = $COC(Me)_3$



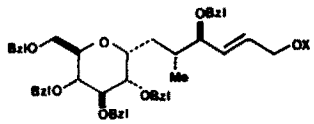
12[23] : Ratio = 11:1
R = $CH_2OSi(Ph)_2(t\text{-}Bu)$

13[24] : Ratio = 7:1
R = $(CH_2)_2OSi(Ph)_2(t\text{-}Bu)$



14[22] : Ratio = 1:0
R = X^2 = H, X^1 = CH_2OMe

15[22] : Ratio = 2:1
R = CH_2OMe, X^1 = X^2 = acetonide



16[25] : Ratio = 1:0
X = $Si(Me)_2(t\text{-}Bu)$

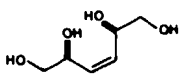
17[25] : Ratio = 1:0
X = $Si(Ph)_2(t\text{-}Bu)$, R = β-OH

18[25] : Ratio = 4:1
X = $Si(Ph)_2(t\text{-}Bu)$, R = β-OBzl

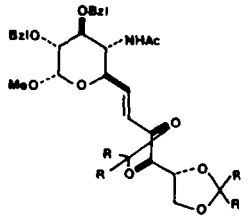
19[25] : Ratio = 10:1
X = $Si(Ph)_2(t\text{-}Bu)$, R = α-OBzl

20[25] : Ratio = 1:1
X = $Si(Ph)_2(t\text{-}Bu)$, R = α-OCOPh

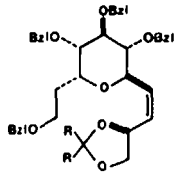
a. Nonconjugated Compounds - 2



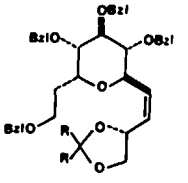
21[20] : Ratio = 1:0[21]



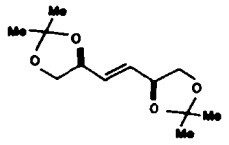
23[26] : Ratio = 1:0
R = $-(CH_2)_5-$



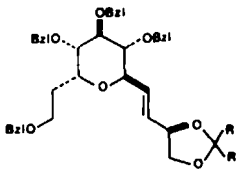
24[22] : Ratio = >10:1
R = $-(CH_2)_5-$



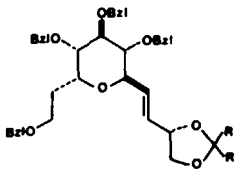
25[22] : Ratio (β:α) = 3:1
R = $-(CH_2)_5-$



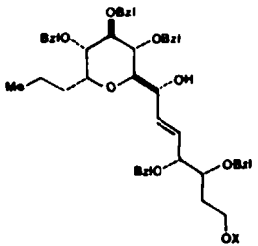
22[22] : Ratio = 10:1



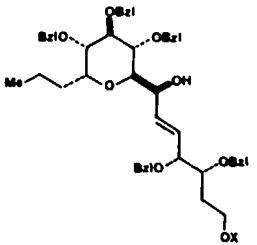
26[22] : Ratio = 1:0
R = $-(CH_2)_5-$



27[22] : Ratio = 1:1
R = $-(CH_2)_5-$



28[22] : Ratio = >10:1
X = $Si(Ph)_2(t\text{-}Bu)$

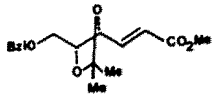


29[22] : Ratio (α:β) = 2:1
X = $Si(Ph)_2(t\text{-}Bu)$

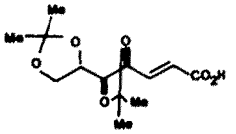
Table 3 (*Contd*)

A. Acyclic Systems

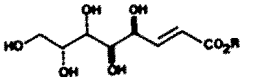
b. Conjugated Carbonyl Compounds



30[27] : Ratio = 8:1



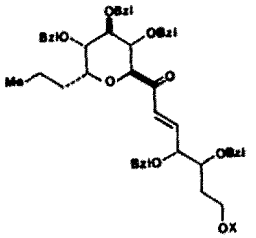
31[28] : Ratio = 1.8:1



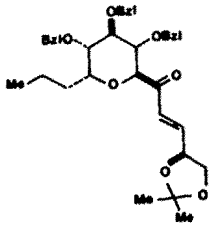
32[28] : Ratio = 2.2:1
R = H

33[28] : Ratio = 1.8:1
R = Et

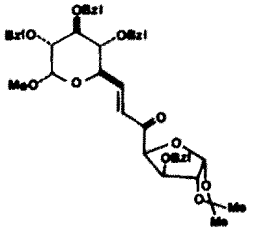
34[29] : Ratio = 16:1



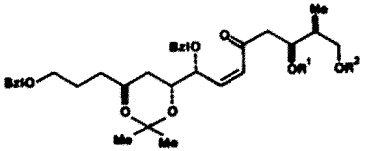
35[22] : Ratio = 10:1
X = Si(Ph)$_2$(t-Bu)



36[22] : Ratio = 4:1



37[22] : Ratio = 2:1



38[13] : Ratio = 1:2
$R^1 = R^2$ = acetonide

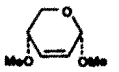
39[30] : Ratio = 1:4
$R^1 = R^2$ = Bzl

B. Cyclic Systems

40[31] : Ratio = 1:0

41[31] : Ratio = 50:1

42[22,32] : Ratio = 4:1



may most be favored on the considerations of stereoelectronic ground.

It is interesting to add that osmylation of 2-cyclohexen-1-ol yielded 1β,2α,3α-cyclohexanetriol as the major product.[11,12] Thus, the stereochemical outcome for both acyclic and cyclic systems can superficially be formulated as osmium tetroxide approaches preferentially to the face of the olefinic bond opposite to that of the preexisting hydroxyl or alkoxyl group.

This empirical formulation seems to agree extremely well with the examples known in the literature. Some selected examples are listed in Table 3 with classification of (A) acyclic and (B) cyclic systems. Acyclic systems are further divided into (a) nonconjugated compounds and (b) conjugated carbonyl compounds. Finally, nonconjugated compounds are classified into (1) the cases where a chiral center due to a hydroxyl or alkoxyl group is present at only one end of the olefinic bond, and (2) the cases where a chiral center due to a hydroxyl or alkoxyl group is present at both ends of the olefinic bond. The ratio indicated for each compound represents the ratio of the major and minor stereoisomers, predicted by this empirical formulation.

Seventeen examples under A-a-1 do not require further explanation except to point out the fact that, as mentioned before, acyl groups are poor in directing stereoselective osmylation (examples **6** and **20**). For the cases where a chiral center due to a hydroxyl or alkoxyl group is present at both ends of the olefinic bond (examples under A-a-2), their effects seem to be additive; that is, the effects of two groups complement one another in compounds **21**, **22**, **23**, **24**, **26** and **28**, while they counteract each other in compounds **25**, **27** and **29**. Slightly different degree of stereoselectivity observed for the olefins **1n** and **1p** (Table 1) may be explained in this term.

This formulation seems to be applicable also for conjugated carbonyl compounds (examples under A-b). However, application to these systems must be made carefully, since at least two exceptions are known (examples **38** and **39**).[13,14] This might be attributed to the difference in the preferred conformation between α,β-unsaturated carbonyl and isolated olefinic systems; unsaturated carbonyl compounds may have the preferred conformation somewhat resembling the one suggested for the dipole model in the Cram's rule.[15]

Related to this empirical formulation of osmylation, it should be interesting to examine the stereochemical course of some other reactions on allylic alcohols and their derivatives. Preliminary experiments on permanganate oxidation of the olefins described in Table 1 have shown that the stereochemistry of the major products corresponds to that of the major products obtained by osmium tetroxide oxidations.[16,17] Bromohydrin formation also seems to follow this empirical formulation.[18]

Application of this chemistry to the synthesis of palytoxin as well as carbohydrates is in progress in our laboratories.

EXPERIMENTAL

Reagents and solvents were commercial grades and were used as supplied with the following exceptions: CH_2Cl_2: distilled; ether and tetrahydrofuran (THF) distilled from sodium benzophenone ketyl; pyridine and Et_3N: dried over KOH. All reactions sensitive to oxygen or moisture were conducted under argon atmosphere.

Analytical TLC was performed on 0.25 mm precoated silica gel plates purchased from E. Merck. Preparative TLC separations were performed on plates (20 × 20 cm) prepared with a 2 mm layer of silica gel PF_{254} from E. Merck. HPLC analyses were performed by using 5μ Spherical Resolve Column from Waters Association.

NMR spectra were recorded on a JEOL 270-FX (270 MHz) instrument in the Fourier transform mode. Chemical shifts are reported in ppm downfield from TMS (δ) as internal standard. Following abbreviations are used for spin multiplicity; *s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet and *m* = multiplet. MS spectra were determined in Kratos MS-50 double focusing instrument in the EI mode (70 eV). IR spectra were recorded on a Perkin–Elmer Model 727 spectrometer.

Synthesis of olefins **1a–e, j–n**

The olefins **1a** and **1j** were prepared from O-isopropylidene glyceraldehyde according to the known procedure.[8] Using the same procedures, the olefins **1d**, **1e**, **1m**, and **1n** were synthesized from O-cyclohexylidene glyceraldehyde and O-dibenzyl glyceraldehyde, respectively. Conversion of **1a** and **1j** to **1b** and **1k**, respectively, were performed under the standard conditions [$(Me)_3CCOCl$, py, RT]. Conversion of **1a** and **1j** to **1c** and **1l**, respectively, were performed under the standard conditions [$(Ph)_2$(t-Bu)SiCl, imidazole, DMF, RT].

NMR of **1b** ($CDCl_3$) 5.64 ppm (1H, ddt, J = 11.2, 7.9, 0.7 Hz), 5.73 (1H, dtd, 11.2, 6.6, 0.8). NMR of **1c** ($CDCl_3$) 5.45 ppm (1H, ddt, J = 11.2, 8.6, 1.3 Hz), 5.81 (1H, dtd, J = 11.2, 7.3, 1.3). NMR of **1d** ($CDCl_3$) 6.08 (1H, ddd, J = 11.5, 6.6, 1.6 Hz), 6.51 (1H, dd, J = 11.5, 7.2). NMR of **1e** ($CDCl_3$) 5.64 ppm (1H, ddt, J = 11.2, 8.9, 0.8), 5.98 (1H, dtd, J = 11.2, 6.9, 1.0). NMR of **1k** ($CDCl_3$) 5.73 ppm (1H, ddt, J = 15.5, 6.9, 1.0 Hz), 5.89 (1H, dt, J = 15.5, 5.3). NMR of **1l** ($CDCl_3$) 5.74 ppm (1H, ddt, J = 15.5, 7.2, 1.0 Hz), 5.87 (1H, dt, J = 15.5, 4.3). NMR of **1m** ($CDCl_3$) 5.70 ppm (1H, ddt, J = 15.5, 7.3, 1.7 Hz), 5.97 (1H, dt, J = 15.5, 4.9). NMR of **1n** ($CDCl_3$) 5.66 ppm (1H, ddt, J = 15.5, 7.3, 1.7 Hz), 5.92 (1H, dtd, J = 15.5, 5.3, 0.7).

Synthesis of olefins **1f** and **1g**

To an ether (10 ml) soln of (n-butyl)triphenylphosphonium bromide (1.1 mmol) at RT was added a 2.5 M n-BuLi soln in hexane (1 mmol). The mixture was stirred at RT for 1 hr. To the resulting red-orange soln was added THF (5 ml). The mixture was cooled at −78°, and the soln of O-cyclohexylidene glyceraldehyde (0.5 mmol in 2 ml of THF) was added dropwise. After the addition was complete the cooling bath was removed. The mixture was stirred at 0° for 20 min and quenched with sat NH_4Claq. The organic layer was separated, washed with water, dried ($MgSO_4$) and concentrated. Preparative TLC (silica gel, 10:1 hexanes–EtOAc) gave the pure *cis* olefin **1f** in 70% yield. NMR ($CDCl_3$) 5.41 ppm (1H, ddt, J = 10.5, 8.2, 1.5 Hz), 5.62 (1H, dtd, J = 10.5, 7.4, 1.0).

Similarly, olefin **1g** was prepared from O-dibenzyl glyceraldehyde. NMR ($CDCl_3$) 5.39 ppm (1H, ddt, J = 11.2, 9.2, 1.0 Hz), 5.69 (1H, dt, J = 11.2, 7.6).

Synthesis of olefins **1o** *and* **1p**

To a soln of (n-butyl)triphenylphosphonium bromide (1.65 mmol) in a mixture of ether (3 ml) and THF (6 ml) at −68° was added dropwise a 2M PhLi soln in cyclohexane–ether (1.65 mmol). The mixture was stirred at −68° for 45 min, and the soln of O-cyclohexylidene glyceraldehyde (1.65 mmol) in THF (5 ml) was added slowly. After 10 min at this temp, an additional PhLi (1.65 mmol) was added. The mixture was stirred at −68° for 5 min and allowed to warm up to −23°. t-BuOK in t-BuOH (3 eq.) was added, and the mixture was left overnight. The mixture

was quenched with sat NH_4Claq. The organic layer was separated, washed with water, dried ($MgSO_4$), and concentrated to give the crude *trans*-olefin **1o** contamination with about 10% of *cis*-olefin **1f**. Pure *trans*-olefin **1o** was isolated by preparative TLC (silica gel, 10:1 hexanes-EtOAc). NMR ($CDCl_3$) 5.50 ppm (1H, ddt, J = 15.9, 8.1, 2.0 Hz), 5.80 (1H, dt, J = 15.9, 6.5).

Similarly, olefin **1p** was prepared from O-dibenzyl glyceraldehyde. NMR ($CDCl_3$) 5.50 ppm (1H, dd, J = 15.5, 7.9 Hz), 5.73 (1H, dt, J = 15.5, 6.6).

Synthesis of olefins **1h** and **1i**

To Li–liq. NH_3 soln (8 mmol of Li in 60 ml of liq. NH_3) **1g** (0.3 mmol of **1g** in 15 ml THF + 3 ml t-BuOH) was added at −78°. The mixture was stirred at −78° for 10 min, warmed to −33°, and stirred for 35 min, then quenched with NH_4Claq. Usual workup gave the crude diol, which was used for acetylation (Ac_2O, py, RT). Olefin **1h** was isolated by preparative TLC (silica gel, 1:1 hexanes–ether) in about 55% overall yield. NMR ($CDCl_3$) 5.32 ppm (1H, ddt, J = 10.9, 9.2, 1.6 Hz), 5.66 (1H, dtd, J = 10.9, 7.6, 1.0).

Olefin **1j** was prepared from the crude diol described above. To a CH_2Cl_2-py soln (2 ml + 1 ml) of the crude diol was added *p*-nitrobenzoyl chloride (0.4 mmol) and dimethylaminopyridine (catalytic amount) at 0°. The mixture was stirred for 10 hr at RT, diluted with CH_2Cl_2, and washed with sat NaCl containing 1N HCl, then with $NaHCO_3$. The organic layer was dried ($MgSO_4$) and evaporated. Pure **1i** was isolated by preparative TLC (silica gel, 1:1 hexanes–EtOAc). NMR ($CDCl_3$) 5.55 ppm (1H, ddt, J = 10.9, 9.2, 1.6 Hz), 5.83 (1H, dtd, J = 10.9, 7.6, 1.0).

General procedure of osmylation

A. Stoichiometric. To a soln of the olefin in a 1:4 mixture of py-THF at RT was added osmium tetroxide (1.2 eq.). The mixture was left at RT overnight, and then diluted with MeOH. H_2S was bubbled through, and the resulting black ppt was filtered off through celite. The clear filtrate was diluted with EtOAc, washed with brine, dried ($MgSO_4$) and concentrated. Preparative TLC gave pure products.

B. Catalytic procedure. To a soln of the olefin in an 1:8 mixture of water–acetone at RT were added N-methylmorpholine N-oxide monohydrate (2.0 eq.), and then a t-BuOH soln of osmium tetroxide (0.05 eq.). The mixture was left at RT overnight and quenched with sat $NaHSO_3$aq. After stirring for 10 min, the products were extracted with EtOAc twice, washed with brine, dried ($MgSO_4$) and concentrated. Preparative TLC gave pure products.

Structure proof of osmylation products

The major product of osmylation of **1a-e** was proved to yield the same pentaacetate [NMR ($CDCl_3$) 2.05 ppm (6H, s), 2.09 (3H, s), 2.10 (6H, s)], which was identical with the authentic sample[8] in every respect (NMR, IR, TLC). Transformation of **2a** and **2d** into the pentaacetate was carried out in 2 steps: 1. 5% conc HCl in MeOH, reflux, and 2. Ac_2O, py, RT. Transformation of **2b** into the pentaacetate was performed in 3 steps: 1. 5% conc HCl in MeOH, reflux, 2. $LiAlH_4$, Et_2O, 0°, and 3. Ac_2O, py, RT. Transformation of **2c** into the pentaacetate was carried out in 3 steps 1.5% conc HCl in MeOH, reflux, 2. $(n\text{-}Bu)_4N^+F^-$, THF, RT, and 3. Ac_2O, py, RT. Transformation of **2e** into the pentaacetate was performed in 2 steps: 1. H_2 (1 atm), 10% Pd on C, 3% AcOH in MeOH, RT, and 2. Ac_2O, py, RT.

The major product of osmylation of **1j–n** was proved to yield the same pentaacetate [NMR ($CDCl_3$) 2.04 ppm (3H, s), 2.030 (3H, s), 2.060 (3H, s) 2.065 (3H, s), 2.08 (3H, s), 2.13 (3H, s)], which was identical with the authentic sample[8] in every respect (NMR, IR, TLC). The same procedures as the ones given to the corresponding *cis*-series were used for preparations of the pentaacetate.

The major product of osmylation of **1f–h** was proved to yield the same tetraacetate [NMR ($CDCl_3$) 0.90 ppm (3H, t, J = 7.6 Hz), 2.04 (3H, s), 2.06 (3H, s), 2.07 (3H, s), 2.08 (3H, s)], which was identical with the authentic sample obtained by the independent synthesis. Preparation of the tetraacetate from **2f** was performed in 2 steps: 1. 5% conc HCl in MeOH, reflux, and 2. Ac_2O, py, RT. Transformation of **2g** into the tetraacetate was carried out in 2 steps: 1. H_2 (1 atm), 3% AcOH in MeOH, RT, and 2. Ac_2O, py, RT. Acetylation (Ac_2O, py, RT) of **2h** gave the tetraacetate. The authentic sample of the tetraacetate was prepared from **2c** in 9 steps: 1. $CH_3C(OCH_3)_2CH_3$, acetone, *p*-TSA, RT, 2. $(n\text{-}Bu)_4N^+F^-$, THF, RT, 3. Swern oxidation,[35] 4. $(i\text{-}PrO)_2P(O)CH_2CO_2Et$, t-BuOK, THF, −78°. 5. DIBAL, CH_2Cl_2, C_6H_6, −23°, 6. NBS, $P(C_6H_5)_3$, CH_2Cl_2, 0°. 7. H_2 (1 atm), 10% Pd on C, EtOH, RT, 8. 5% conc HCl in MeOH, reflux, and 9. Ac_2O, py, RT.

By using the same procedures of transformation, the minor product of osmylation of **1f–h** was proved to yield the same tetraacetate [NMR ($CDCl_3$) 0.90 ppm (3H, t, J = 7.6 Hz), 2.03 (3H, s), 2.05 (3H, s), 2.08 (3H, s), 2.12 (3H, s)].

The minor product of osmylation of **1o** and **1p** was proved to yield the same tetraacetate [NMR ($CDCl_3$) 0.90 ppm (3H, t, J = 7.6 Hz), 2.05 (3H, s), 2.08 (6H, s), 2.10 (3H, s)], which was identical with the authentic sample obtained by the independent synthesis. The same procedures as the ones given to the corresponding *cis*-series were used for preparation of the tetraacetate from **3o** and **3p**. The authentic sample of the tetraacetate was prepared from 2,3:4,5-di-O-isopropylidene-D-xylose diethyl dithioacetal[36] in 7 steps: 1. HgO-$HgCl_2$, aq. acetone, RT, 2. −7. follow the steps 4 through 9 of the synthesis of the above authentic sample of tetraacetate.

By using the same procedures of transformation, the major product of osmylation of **1o** and **1p** was proved to yield the same tetraacetate [NMR ($CDCl_3$) 0.90 ppm (3H, t, J = 7.6 Hz), 2.06 (6H, s), 2.07 (3H, s), 2.13 (3H, s)].

The stereochemistry of **2r** [NMR of the corresponding triacetate ($CDCl_3$) 0.95 ppm (3H, d, J = 6.8 Hz), 2.03 (3H, s), 2.04 (3H, s), 2.07 (3H, s)] was determined by independent synthesis of **2r** from 4-methyl-5-(phenylmethoxy)-2-(Z)-pentene-1-ol[6a] in 4 steps: 1. MCPBA, CH_2Cl_2, 0°, 2. $ClCO_2CH_2C_6H_5$, py, THF, 0°, 3. $AlCl_3$, Et_2O, 0°, and 4. 1N NaOH, RT (see Ref. 8).

HPLC analysis of osmylation products

The product ratio of **c**, **g**, **l**, and **p** series was determined by HPLC analysis (1 ~ 20:1 hexane-EtOAc) of the crude osmylation products. The product ratio of **a**, **d**, **e**, **f**, **j**, **m**, **n**, and **o** series was determined by HPLC analysis (4 ~ 6:1 hexane-EtOAc) of the peracetate mixture obtained from the crude osmylation products under the standard conditions (Ac_2O, py, RT). The product ratio of **b** and **k** series was determined by HPLC (6:1 hexane–EtOAc) of the acetonide mixture obtained from the crude osmylation products under the standard conditions [$CH_3C(OCH_3)_2CH_3$, **p**-TSA, RT].

Osmylation of 2-cyclohexen-1-ol and its acetate

2-Cyclohexen-1-ol and its acetate[37] were, respectively, subjected to osmylation under the catalytic conditions. The crude product was acetylated (Ac_2O, py, RT) to yield a major triacetate. The NMR spectrum of this product [NMR ($CDCl_3$) 2.01 ppm (3H, s), 2.03 (3H, s), 2.07 (3H, s), 4.92 (1H, dd, J = 9.2, 3.0 Hz), 5.10 (1H, ddd, J = 9.2, 9.2, 4.6), 5.34 (1H, not-well resolved ddd with $W_{1/2}$ = 11 Hz)] allowed the assignjment of the stereochemistry described in the text. The stereoselectivity of both cases were estimated to about 5:1 from the ^{1}H-NMR spectra in C_6D_6.

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[11]In the cases of cyclic systems, a high degree of stereoselectivity was observed not only for the substrates having an α-hydroxyl or α-alkoxyl substituent but also for those having other α-substituents. For example, OsO_4 oxidation of 3-methyl-1-cyclohexene yielded 3β-methyl-1α, 2α-cyclohexanediol as the major product. The effect from a Me group seems to be about the same as that from an OH group, as OsO_4 oxidation of 3-methyl-3-hydroxy-1-cyclohexene gave a *ca* 1:1 mixture of two possible products.

[12]Unlike the acyclic systems, acyl groups are effective in directing stereoselective osmylation. For example, 2-cyclohexen-1-ol acetate yielded 1β-acetoxy-2α, 3α-dihydroxycyclohexane as the major product with the comparable stereoselectivity with the 2-cyclohexen-1-ol.

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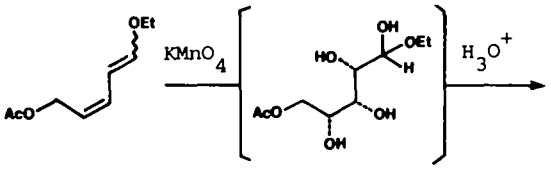
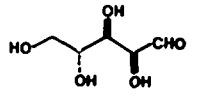


46 47



48 : arabinose

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