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ON STEREOCHEMISTRY OF OSMIUM TETROXIDE OXIDATION OF ALLYLIC ALCOHOL SYSTEMS: EMPIRICAL RULE

J. K. Cha, W. J. Christ, and Y. Kishi*
Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138, USA

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

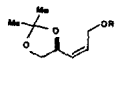
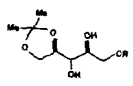
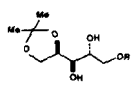
In connection with studies on the marine natural product palytoxin,[1,2] we have been interested in examining the stereochemical outcome of the osmium tetroxide oxidation of olefins, generalized in eq. 1.[3] Judging from our previous experiments based on the conformational analysis of the sp^3-sp^2 single bond systems, we expected this process might be stereoselective.[4,5]

eq. 1

Thus, the olefins 1a-p were subjected to osmium tetroxide oxidation under stoichiometric and catalytic conditions.[6] 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.[7,8] The stereochemistry of osmylation products 2f, 2g, 3o and 3p was determined by independent syntheses of the corresponding tetraacetates.[9]

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).[4] 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

Table 1

		1	2	3
a	R = H			
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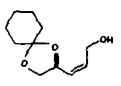
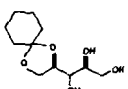
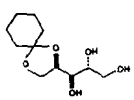
			catalytic	6.0 : 1.0[c]
b	R = $COC(Me)_3$		stoichiometric	6.3 : 1.0[b]
			catalytic	6.1 : 1.0[c]
c	R = $Si(Ph)_2(t\text{-}Bu)$		stoichiometric	8.0 : 1.0[b]
			catalytic	7.2 : 1.0[b]
d				
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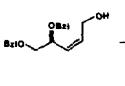
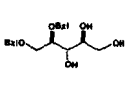
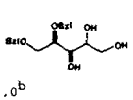
e				
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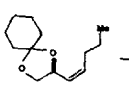
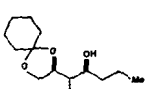
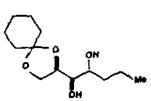
f				
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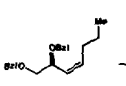
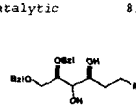
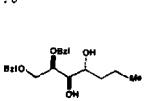
g				
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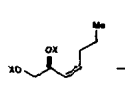
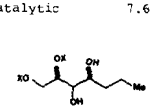
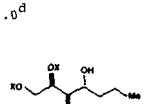
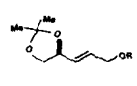
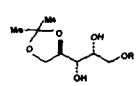
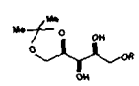
h	X = $COCH_3$			
			catalytic	2 : 1[d]
i	X = $COC_6H_4NO_2$-p		catalytic	1 : 1[d]

		1	2	3
j	R = H			
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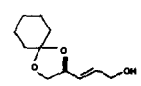
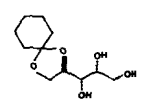
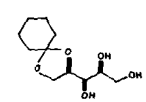
			catalytic	4.0 : 1.0[c]
l	R = $Si(Ph)_2(t\text{-}Bu)$		stoichiometric	3.3 : 1.0[b]
			catalytic	3.1 : 1.0[b]
m				
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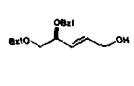
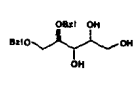
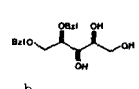
n				
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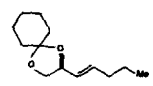
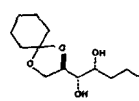
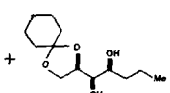
			catalytic	3.1 : 1.0[b]
o				
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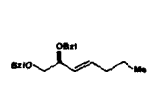
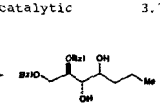
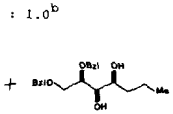
p				
			stoichiometric	7 : 1[b]
			catalytic	6 : 1[b]

Footnotes for Table 1

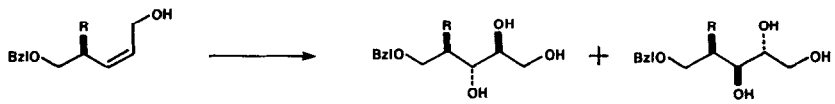
a. Stoichiometric represents the results under the conditions of OsO_4 (1.2 eq.), py-THF (1:4), RT, and catalytic represents the results under the conditions of OsO_4 (0.05 eq.), N-methylmorpholine N-oxide (2.0 eq.), water-acetone (1:8), RT.

b. The product ratio was determined by HPLC analysis.

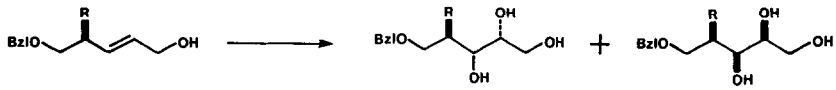
c. The product ratio was determined by isolation of products.

d. The product ratio was determined by PMR analysis.

Table 2



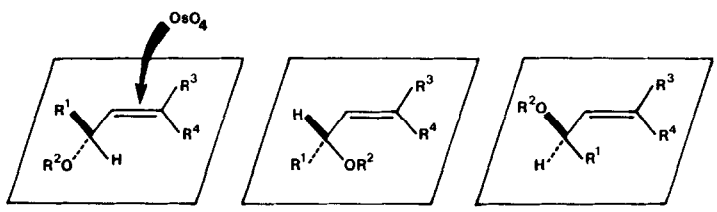
		Ratio	
R = OBzl : 1a	2a	6 : 1	3a
R = Me : 1q	2q	1 : 1	3q



		Ratio	
R = OBzl : 1n	2n	4.2 : 1.0	3n
R = Me : 1r	2r[13]	1.5 : 1.0	3r

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.[10] 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.[4] Assuming this conformational preference is reflected in the transition state, the stereochemistry of the major product is



A B C

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.[5,11] 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 support this explanation, 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.[4]

It is interesting to add that osmylation of 2-cyclohexen-1-ol yielded exclusively 1β,2α,3α-cyclohexanetriol.[12] Thus, the stereochemical outcome for both acyclic and cyclic systems can be formulated empirically 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 be consistent with the examples known in the literature. Some of these examples are listed in the following paper. Applications of this chemistry to the syntheses of palytoxin as well as carbohydrates are in progress in our laboratories.

Acknowledgment Financial assistance from the National Science Foundation (CHE 78-06296) and the National Institutes of Health (NS 12108) is gratefully acknowledged. One of us (WJC) expresses his appreciation for a postdoctoral fellowship from Merck, Sharp and Dohme.

References and Footnotes

1. For the stereochemistry of palytoxin, see J. K. Cha, W. J. Christ, J. M. Finan, H. Fujioka, Y. Kishi, L. L. Klein, S. S. Ko, J. Leder, W. W. McWhorter, Jr., K.-P. Pfaff, M. Yonaga, D. Uemura, and Y. Hirata, J. Am. Chem. Soc., 104, 7369 (1982) and preceding papers. Also, see R. E. Moore, G. Bartolini, J. Barchi, A. A. Bothner-By, J. Dadok, and J. Ford, J. Am. Chem. Soc., 104, 3776 (1982).

2. For the gross structure of palytoxin, see a. D. Uemura, K. Ueda, Y. Hirata, H. Naoki, and T. Iwashita, Tetrahedron Lett., 22, 2781 (1981) and references cited therein. b. R. E. Moore and G. Bartolini, J. Am. Chem. Soc., 103, 2491 (1981) and references cited therein.

3. For a recent review on osmium tetroxide oxidation, see M. Schroder, Chem. Rev., 80, 187 (1980).

4. (a) G. Schmid, T. Fukuyama, K. Akasaka, and Y. Kishi, J. Am. Chem. Soc., 101, 259 (1979). (b) M. R. Johnson, T. Nakata, and Y. Kishi, Tetrahedron Lett., 4343 (1979). (c) Y. Kishi, Aldrichimica Acta, 13, 23 (1980). (d) Y. Kishi, Pure & Appl. Chem., 53, 1163 (1981).

5. Based on ab initio calculations, Houk suggested staggered models for the transition state structures; M. N. Paddon-Row, N. G. Rondan, and K. N. Houk, J. Am. Chem. Soc., 104, 7162 (1982) and K. N. Houk, Pure & Appl. Chem., 55, 277 (1983).

6. V. VanRheenen, R. C. Kelly, and D. Y. Cha. Tetrahedron Lett., 1973 (1976).

7. N. Minami, S. S. Ko, and Y. Kishi, J. Am. Chem. Soc., 104, 1109 (1982).

8. This transformation was performed in 2 steps: 1. deprotection (5% conc. HCl-MeOH, reflux for 2a-d and 2j-m, or H_2, Pd-C, 3% AcOH-MeOH for 2e and 2n) and acetylation (Ac_2O, py, RT). In the cases of 2b, 2c, 2k, and 2l, deprotection [$LiAlH_4$, Et_2O, 0°C or $(n\text{-}Bu)_4N^+F^-$, THF, RT] was carried out prior to the above 2 steps.

9. The authentic sample of the tetraacetate corresponding to 2f-g 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 [A. J. Mancuso, S.-L. Huang, and D. Swern, J. Org. Chem, 43, 2480 (1978)], 4. $(i\text{-}PrO)_2P(O)CH_2CO_2Et$, t-BuOK, THF, -78°C. 5. DIBAL, CH_2Cl_2, C_6H_6, -23°C, 6. NBS, $P(C_6H_5)_3$, CH_2Cl_2, 0°C. 7. H_2, 10% Pd-C, EtOH, RT, 8. 5% conc. HCl-MeOH, reflux, and 9. Ac_2O, py. The authentic sample of the tetraacetate of 3o-p was prepared from 2,3:4,5-di-D-isopropylidene-D-xylose diethyl dithioacetal [M. Y. H. Wong and G. R. Gray, J. Am. Chem. Soc., 100, 3548 (1978)] in 7 steps: 1. HgO-$HgCl_2$, aq. acetone, RT, 2. - 7. follow the steps 4 through 9 of the above synthesis.

10. For a review on conformation of sp^3-sp^2 single bond systems, see G. J. Karabatsos and D. J. Fenglio, "Topics in Stereochemistry", ed. E. L. Eliel and N. L. Allinger, Vol. 5, page 167ff, Wiley-Interscience, New York, 1970.

11. Of course, the stereochemistry of the major product can also be formulated as arising from the preferential approach of OsO_4 to the top face of the olefinic bond of either conformation B or C. However, there is no convincing example known in the literature to compare the relative reactivity of the three conformations toward OsO_4.

12. 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 exclusively 3β-methyl-1α,2α-cyclohexanediol. The effect from a methyl group seems to be about the same as that from a hydroxyl group, as OsO_4 oxidation of 3-methyl-3-hydroxy-1-cyclohexene gave a ca. 1:1 mixture of two possible products.

13. The stereochemistry of 2r was determined by independent synthesis of 2r from 4-methyl-5-(phenylmethoxy)-2-(Z)-pentene-1-ol[4b] in 4 steps: 1. MCPBA, CH_2Cl_2, 0°C, 2. $ClCO_2CH_2C_6H_5$, py, THF, 0°C, 3. $AlCl_3$, Et_2O, 0°C, and 4. 1N NaOH, MeOH, RT (see reference 7).

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