Tetrahedron: Asymmetry Vol. 4, No. 1, pp. 5-8, 1993
Printed in Great Britain

0957-4166/93 $6.00+.00
Pergamon Press Ltd

Vicinal Diol Controller Approach to Highly Diastereoselective Hydroxy-Directed MCPBA Epoxidations of Allylic Alcohols with Oxygen–Bearing Stereocenters

Seiki Saito,* Hiroyuki Itoh, Yukiji Ono, Kagetada Nishioka, and Toshio Moriwake*

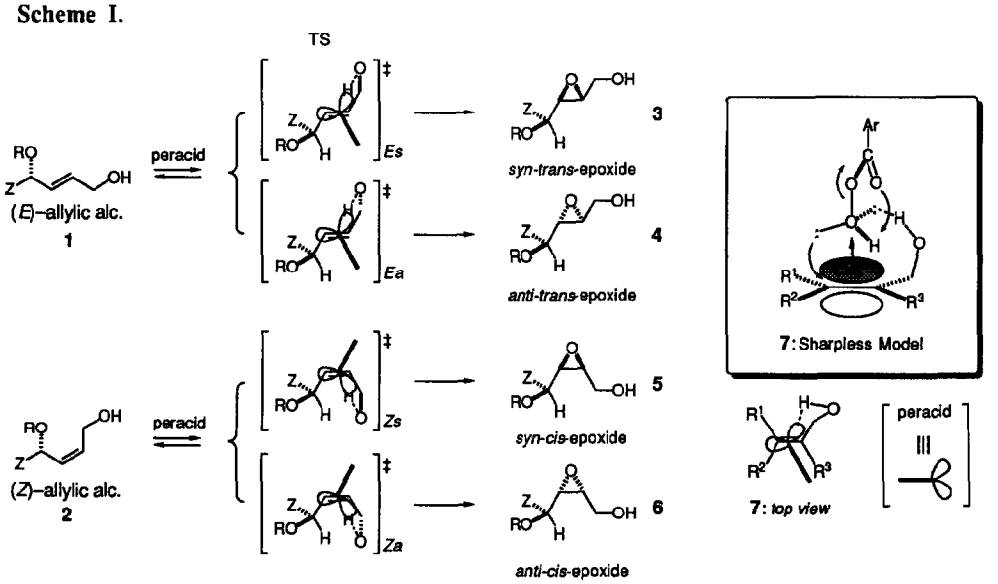
Department of Applied Chemistry, Faculty of Engineering, Okayama University, Tsushima, Okayama 700, Japan

(*Received in UK* 30 *October* 1992)

Abstract: The diastereofaces of primary allylic alcohols bearing (4*S*,5*S*)-bis(*t*-butyldimethylsiloxy)–framework as a controller of acyclic conformation have been differentiated with high %de's in hydroxy-directed MCPBA epoxidations. The stereochemical outcome of this process has been discussed and rationalized by invoking both the "outside–inside bias" concept previously proposed and the possible transition state structure proposed by Sharpless.

Differentiation of the diastereofaces of allylic alcohols having an oxygen-linking stereocenter by oxidizing agents such as *m*-chloroperbenzoic acid (MCPBA) or transition metal-mediated *t*-butylhydroperoxide (TBHP) provides us with diverse opportunities for gaining access to valuable chiral building blocks in target-orienting total syntheses.[1] The *E*-isomer system (**1**) illustrated in Scheme I leads to diastereoisomeric syn- or anti-*trans*-2,3-epoxy alcohols (**3** and **4**) regioselectively in high yields on treatment with MCPBA even in the presence of other carbon-carbon double bond in Z provided they are not accompanied by an allylic hydroxyl group. Similarly, the *Z*-isomer system (**2**) is a desired precursor for syn- or anti-*cis*-2,3-epoxy alcohols (**5** and **6**)

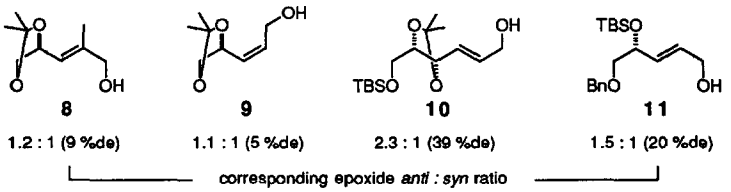
Scheme I.



A possible transition–state structure for this electrophilic addition process of carbon–carbon double bonds has been proposed by Sharpless[1] to involve **7** as shown above. This structure reasonably satisfies a stereoelectronic ensemble among the bonding and anti-bonding π-orbitals of the carbon–carbon double bond, the antibonding σ-orbital (O—O) of the peracid, and the two unshared electron pairs on the oxygen atom of the peracid one of which makes hydrogen bond to the allylic hydroxyl group at the transition state.

To the best our knowledge, no proposal has been recorded so far with regard to the relative disposition between the substituents on the stereocenter and incoming hydrogen-bonded peracid within the systems **1** and **2**. Important consequences of the model **7** should be invoked for this purpose: the *m*-chlorobenzoyl subunit, denoted by thick lines (Scheme I), occupies a space opposite to the hydroxymethylene subunit with regard to an axis around the carbon–carbon double bond. On this basis each transition state for epoxidations of **1** and **2** can be illustrated as $[Ea]^{\ddagger}$ or $[Es]^{\ddagger}$ and $[Za]^{\ddagger}$ or $[Zs]^{\ddagger}$, respectively (Scheme I). This situation, in turn, means that a diastereofacial bias generated by the oxygen-bearing stereocenters would be disappointingly small because no enhanced propinquity of the peracid to the most demanding space seems assured as reasonably and quickly recognized from the spatial occupation of the peracid designated in those structures.

Thus, the diastereomeric excess for epoxidation of this class is, in general, moderate or very low irrespective of the geometry of carbon-carbon double bonds. For instance, the compounds shown below (**8**,[2] **9**,[3] **10**,[4] **11**[2]) have demonstrated that such is the case. After every endeavor to overcome this drawback, we have succeeded in achieving very high diastereomeric excesses in MCPBA epoxidations of the related compounds[5] relying on the protected vicinal diol controller,[6] which is the subject of this communication.

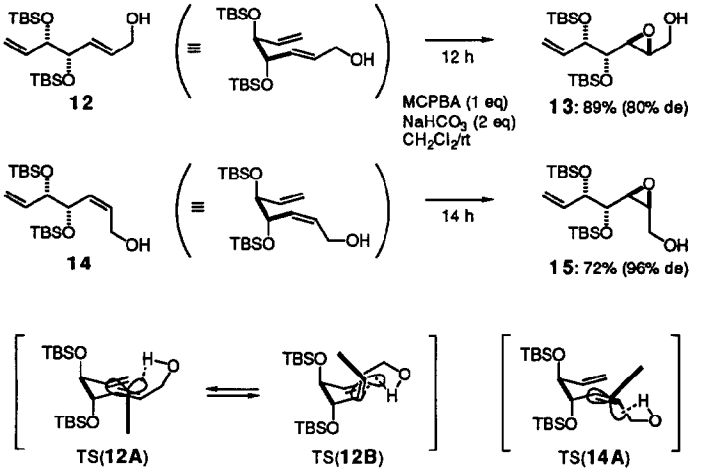


The first representative results are shown in Scheme II.[7] The stereochemical results over 80 %de can be rationalized on the basis of the specific conformations of substrates **12** and **14** as depicted, for which the imbedded vicinal TBSO groups is responsible.[6a] In these conformations an oxidant is allowed to attack only from the outside.[8] In particular, *Z*-allylic substrate (**14**) afforded a mixture of anti- (**15**) and syn-isomers in a ratio 52:1 (96 %de) in sharp contrast to the case of **9** (5 %de), for which a transition state assembly such as TS(**14A**) should be responsible. On the other hand, *E*-allylic substrate (**12**) led to a 9:1 (80 %de) mixture of epoxides in preference to anti-adduct (**13**). Similar interpretation as above brings us to the conclusion that a transition state leading to **13** illustrated as TS(**12A**) would unavoidably suffer from steric congestion between the hydrogen-bonded peracid and the C(4)-TBSO group. The situation would dictate rotation around the C(3)—C(4)-bond to become free from such a steric disadvantage, leading to TS(**12B**) though this, in particular the C(2)–hydrogen, must in turn be pitted against constraint from the C(5)–TBSO group. If so, the oxidant may approach to the opposite π-(C=C)-face that turned inside out. Formation of a minor but still a considerable amount of syn-epoxide (10%) from **12** could be rationalized in this way.

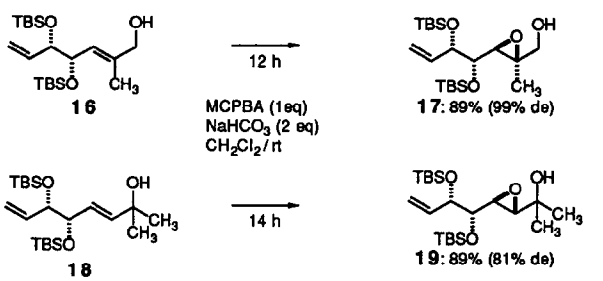
In order to make this point clear and understandable at an interpreting level and to test the feasibility of the present strategy, more substituted derivatives such as **16** and **18** were epoxidized in a similar way. These

second representative results were shown in Scheme III.[7] Introduction of a methyl group to the C(2) of **12** was expected for **TS(12A)**–to–**TS(12B)**–type interconversion to be highly encumbered for steric reason. This idea has proven to be exquisitely powerful to lead to the exclusive formation of anti-epoxide (**17**) (>99 %de). This degree of diastereoselection is highly delightful if we recall the disappointing level of that (9 %de) observed for the related compound **8**. In contrast to this remarkable control, introduction of a methyl group three-carbon away from the C(4)-stereocenter has proven no more effective. Indeed, epoxidation of 1,1-dimethyl version (**18**), which is considered not to result in sizable steric crowding on both C(4) and C(5)–TBSO groups, remained at an essentially identical level of diastereoselection (**19**: 81 %de) as that of **12** (80 %de).

Scheme II.



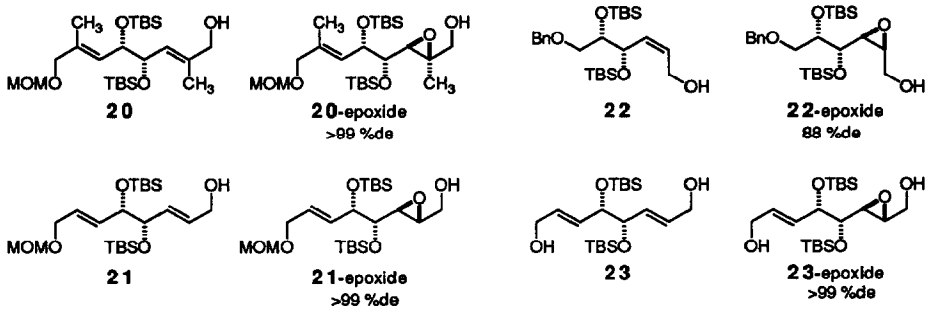
Scheme III.



These satisfactory results observed for **12**, **14**, **16**, and **18** led us to examine further the particular advantage inherent to the protected vicinal diol controller in terms of diastereoselection using various structural types **20**—**23**. As expected these compounds turned out to give satisfactory diasetereomeric excesses as shown.

From the synthetic standpoint, though not an essential breakthrough, the present protected vicinal diol controller approach offers a simple and promising solution to highly diastereoselective hydroxy-directed MCPBA epoxidation of allylic alcohols since such processes using acetonide or single bulky protection (**8**—**11**)

resulted only in 9, 5, 39, and 20 %de's, respectively. Several novel chiral oxirane templates available in this way should be highly useful in the light of their versatility and tolerance for latent functionality elaboration.



Acknowledgment: We thank Mr. Y. Morikawa (Daicel Chem. Co.) for his contribution to the preliminary experiments. We deeply appreciate "The SC–NMR Laboratory of Okayama University" for 500–MHz NMR experiments.

References and Notes

(1) Sharpless, K. B.; Verhoeven, T. R. *Aldrichmica Acta*, **1979**, *12*, 63 and references cited therein.
(2) Saito, S.; Ono, Y.; Nishioka, K.; Moriwake, T. unpublished observations.
(3) Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1387.
(4) Aoyagi, S.; Fujimaki, S.; Yamasaki, N.; Kibayashi, C. *J. Org. Chem.* **1991**, *56*, 815.
(5) All the substrates were prepared from L-tartaric acid esters which will be reported elsewhere.
(6) (a) Saito, S.; Hirohara, Y.; Narahara, O.; Moriwake, T. *J. Am. Chem. Soc.* **1989**, *111*, 4533. (b) Saito, S.; Morikawa, Y.; Moriwake, T. *J. Org. Chem.* **1990**, *55*, 5424. (c) Saito, S.; Morikawa, Y.; Moriwake, T.*Synlett* **1990**, 523. (d) Saito, S.; Hama, H.; Matsuura, Y.; Okada, K.; Moriwake, T. *ibid.* **1991**, 819. (e) Saito, S.; Yamamoto, T.; Matsuoka, M.; Moriwake,T. *ibid.* **1992**, 239. (f) Saito, S.; Hara, T.; Naka, K.; Moriwake, T. *ibid.* **1992**, 241. (g) Saito, S. *J. Syn. Org. Chem. Jpn.* **1992**, *50*, 316. (h) Saito, S.; Harunari, T.; Shimamura, N.; Asahara, M.; Moriwake, T. *Synlett* **1992**, 325.
(7) Epoxidations were carried out with a slight excess of MCPBA in methylene chloride in the presence of suspended $NaHCO_3$ as an acid scavenger at room temperature. The products were purified by column chromatography over silica gel and subjected to NMR diagnosis (500 MHz) for structure or isomer ratio determination. The isomers could usually be separated by a careful chromatography including HPLC and each isomer served for absolute structure confirmation and as an analytical sample as well. *No epoxidation was observed at all for other carbon–carbon double bonds if not accompanied by a free allylic hydroxyl group such as terminal vinyl groups etc. under the above reaction conditions.* A series of routine reactions from epoxides involving primary hydroxy protection (or deprotection of the TBSO-groups), deprotection of the TBSO-groups (or primary hydroxy protection), oxidative diol cleavage [$Pb(OAc)_4$], and final reduction ($NaBH_4$) of a formyl group, led to 1-*O*-protected-2,3-epoxy-1,4-butanediol derivatives, the signs of optical rotations of which were compared with those of authentic samples: for the authentic samples, see ref. (3) and Roush, W. R.; Brown, R. J. *J. Org. Chem.* **1982**, *47*, 1373. For the more substituted series such as **17**, **19**, and **20**, their absolute structures were estimated based on the mechanism and steric course of the epoxidations embodied in the text.
(8) For definition with regard to the term *"outside"* or *"inside"*, see ref. (6). A paper with respect to our recent efforts concerned with chemical, physical, and theoretical corroborations in support of the *"outside–inside bias"* concept will be submitted for publication soon.