Pergamon

Tetrahedron Letters 39 (1998) 4517–4520

TETRAHEDRON LETTERS

Highly Stereoselective Epoxidation of a 4-Methyl-5-(triethylsilyl)oxyallyl Alcohol System with *m*-Chloroperoxybenzoic Acid

Kimiyuki Maruyama, Masato Ueda, Shinobu Sasaki, Yasuhiro Iwata, Masahiro Miyazawa, and Masaaki Miyashita*

Division of Chemistry, Graduate School of Science, Hokkaido University, Sapporo 060, Japan

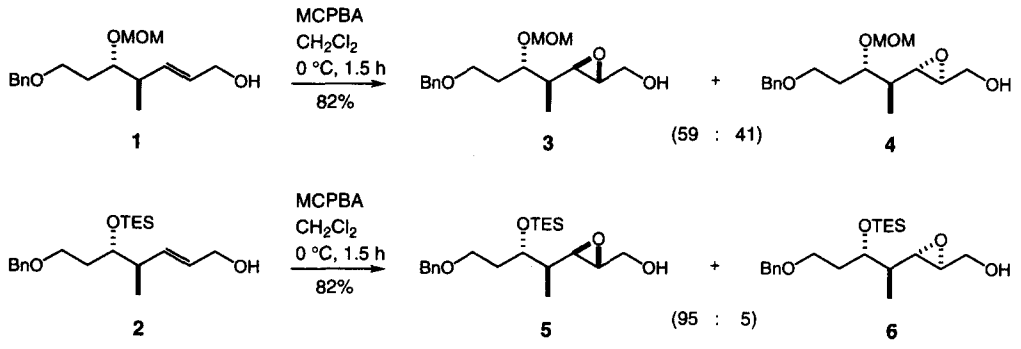
Received 20 March 1998; accepted 13 April 1998

Abstract: Epoxidation of 4-methyl-5-(triethylsilyl)oxyallyl alcohol system with *m*-chloroperoxybenzoic acid (MCPBA) has been found to occur highly stereoselectively and in high yields from the opposite side of the C_5 triethylsilyloxy group regardless of the stereochemistry of an adjacent methyl group.

Stereoselective epoxidation of allylic alcohols is an important reaction in organic synthesis. Particularly, diastereoselective epoxidation of allyl alcohols is of critical importance in natural product synthesis as well as the Katsuki-Sharpless asymmetric epoxidation.[1] So far, the diastereoselective epoxidation of some 5-alkoxy-2,4-dimethylallyl alcohols[2] and 5-(*tert*-butyldimethylsilyl)oxy-4-methylallyl alcohols[2b] with *m*-chloroperoxybenzoic acid (MCPBA) or *tert*-butyl hydroperoxide-Ti(O^iPr)$_4$ has been developed and successfully used in natural product synthesis. However, all the substrates used so far have been limited to only *syn*-compounds, namely, *syn*-5-alkoxy-4-methylallyl alcohols. On the other hand, Nakata has very recently reported the *anti*-selective epoxidation of primary 5-(*tert*-butyldimethylsilyl)oxyallylic alcohols without a 4-methyl group with MCPBA.[3] During the course of our synthetic studies on polypropionate-derived natural products by the use of the stereospecific methylation of γ,δ-epoxy acrylates with trimethylaluminum,[4] we required the diastereoselective epoxidation of various types of *anti*- and *syn*-5-hydroxy-4-methylallyl alcohols. We report here an efficient and highly diastereoselective epoxidation of a 4-methyl-5-(triethylsilyl)oxyallyl alcohol system with MCPBA.

In order to gain preliminary information, we initially examined the epoxidation of the optically active *anti*-7-benzyloxy-5-(methoxymethyl)oxy-4-methyl-2-hepten-1-ol (**1**) and the *anti*-7-benzyloxy-4-methyl-5-(triethylsilyl)oxy-2-hepten-1-ol (**2**). Thus, treatment of **1** with MCPBA in CH_2Cl_2 at 0 °C resulted in non-stereoselective epoxidation giving rise to a 59:41 mixture of β- and α-epoxy alcohols **3** and **4** in 82% yield, while the epoxidation of **2** with MCPBA occurred stereoselectively under the same conditions affording a 95:5 mixture of **5** and **6** in 82% yield (Scheme 1). The stereochemistry of the products was unambigously determined by comparison with those obtained by the Katsuki-Sharpless asymmetric epoxidation of **1** and **2**, respectively. These results imply that the epoxidation of *anti*-4-methyl-5-silyloxyallyl alcohols with MCPBA should occur highly diastereoselectively as well as the previously studied *syn*-analogues. Furthermore, these outcomes demonstrate that a triethylsilyl group serves as an effective directing group for the stereoselective epoxidation of this type of allyl alcohols, although only a sterically more bulky *tert*-butyldimethylsilyl or *tert*-butyldiphenylsilyl group has been used so far as a

0040-4039/98/$19.00
PII: S0040-4039(98)00804-1



Scheme 1

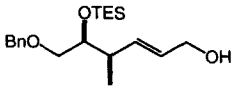
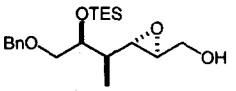
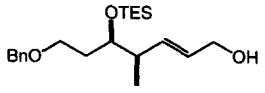
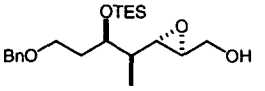
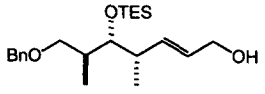
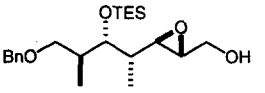
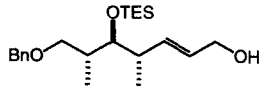
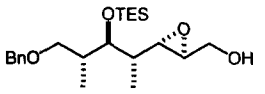
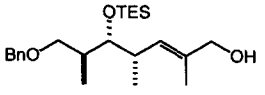
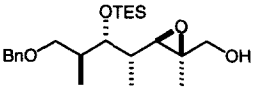
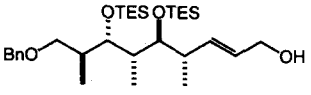
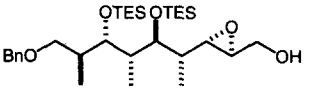
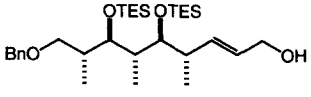
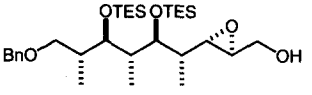
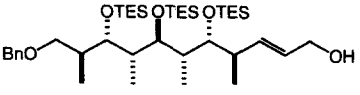
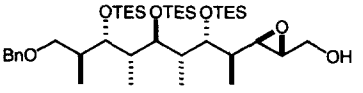
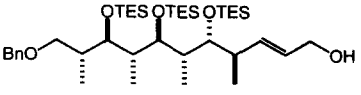
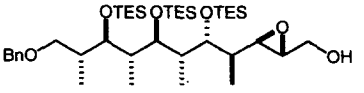
directing group. We therefore investigated the diastereoselectivity in the epoxidation of various types of 4-methyl-5-(triethylsilyl)oxyallyl alcohols with MCPBA in CH_2Cl_2. The results are summarized in Table 1.

The epoxidation of the *syn*-6-benzyloxy- and *syn*-7-benzyloxy-4-methyl-5-(triethylsilyl)oxyallyl alcohols with MCPBA in CH_2Cl_2 occurred with complete stereoselectivity from the opposite side of the C_5 (triethylsilyl)oxy group to give the *anti*-epoxide as a single product in 95% yield, respectively (entries 1 and 2). Similarly, epoxidation of the homologous compound having three contiguous chiral centers with MCPBA proceeded under the same conditions highly stereoselectively to yield the sole 3,4-*anti*-epoxide quantitatively (entry 3). In these substrates, both the C_5 (triethylsilyl)oxy and C_4 methyl groups serve as the cooperative directing group culminating in the extremely high diastereoselective epoxidation. Moreover, we found that the epoxidation of the 4,5-*anti*-5,6-*anti*-4,6-dimethyl-5-(triethylsilyl)oxyallyl alcohol with MCPBA occurred with complete diastereoselectivity again to afford the single 3,4-*syn*-epoxide in 98% yield, wherein MCPBA reacted exclusively from the reverse side of the bulky C_5 (triethylsilyl)oxy group (entry 4). As anticipated, the epoxidation of 4,5-*syn*-5,6-*anti*-5-(triethylsilyl)oxy-2,4,6-trimethylallyl alcohol with MCPBA produced solely the 3,4-*anti*-epoxy alcohol in 95% yield (entry 5).

Previous studies on the epoxidation of 5-hydroxy-4-methylallyl alcohols have been limited to compounds having rather simple structures containing two or three asymmetric centers, and epoxidation of the more complex structures involving several stereogenic centers has scarcely been studied. Therefore, we in turn investigated the epoxidation of substrates having a polypropionate structure. As shown in entries 6, 7, 8, and 9, the epoxidation of such compounds with MCPBA has been found to occur exclusively from the opposite side of the C_5 (triethylsilyl)oxy group regardless of the stereochemistry of the adjacent C_4 methyl group.[5]

The results in Table 1 demonstrate that the triethylsilyl group serves not only as effective protective groups for secondary hydroxyl groups but also as an extremely effective directing group for the diastereoselective epoxidation of 4-methyl-5-(triethylsilyl)oxyallyl alcohol systems including the polypropionate structures.[6] On the other hand, these results strongly support that the epoxidation of 4-methyl-5-silyloxy allyl alcohols dose not proceed via the coordination of MCPBA with both the C_5 silyloxy and allylic hydroxyl groups previously proposed[2a,2c] but occurs stereoselectively from the opposite side of the bulky C_5 silyloxy group as shown in Fig. 1 (based on MM2 force field on a Macro Model), in which MCPBA coordinates only with the allylic hydroxyl group and the main carbon chain takes the most favorable linear *anti*-conformation. Very recently, Nakata has proposed a similar transition state in the

Table 1. Epoxidation of 4-Methyl-5-(triethylsilyl)oxyallyl Alcohols with MCPBA[a)]

Entry	Substrate[b)]	Reaction Time (h)	Product	Yield (%)	Diastereo-selectivity[c)]
1		1		95	>99
2		1		95	>99
3		1		99	>99
4		1		98	>99
5		1		95	>99
6		2		79	>99
7		2.5		91	97 : 3
8		2		85	>99
9		20		88	97 : 3

a) The reaction was carried out at 0 °C.

b) All the substrates are optically acitve.

c) The diastereoselectivity was determined by ^{1}H NMR (300 and 500 MHz).

anti-selective epoxidation of primary 5-(*tert*-butyldimethylsilyl)oxyallylic alcohols having no methyl group at the C_5 position with MCPBA.[3]

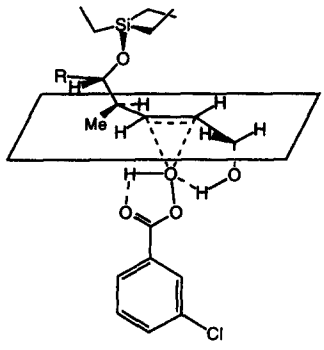


Fig 1.

In conclusion, the epoxidation of various types of 4-methyl-5-(triethylsilyl)oxyallyl alcohols with MCPBA has been demonstrated to occur highly stereoselectively from the opposite side of the C_5 triethylsilyloxy group regardless of the stereochemistry of an adjacent C_4 methyl group. The present work should provide important information for natural product synthesis.

Acknowledgment. We thank Prof. T. Nakata (The Institute of Physical and Chemical Research (RIKEN)) for valuable discussions. We are grateful to the Ciba-Geigy Foundation (Japan) for the Promotion of Science for their financial support. This work was also supported by a Grant-in-Aid for Scientific Research on Priority Areas (No. 08245101) and a Grant-in-Aid for Exploratory Research (No. 09874149) from the Ministry of Education, Science, Sports and Culture of Japan.

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6 We have found that some attempts to protect all the hydroxyl groups in the compounds having a polypropionate structure such as entries 6-9 by *tert*-butyldimethylsilyl groups were unsuccessful owing to steric interference, while their protection by triethylsilyl groups can be performed in excellent yields.