ANTI-SELECTIVE EPOXIDATION OF PRIMARY 5-(*tert*-BUTYLDIMETHYLSILYL)OXYALLYLIC ALCOHOLS WITH *m*-CHLOROPEROXYBENZOIC ACID

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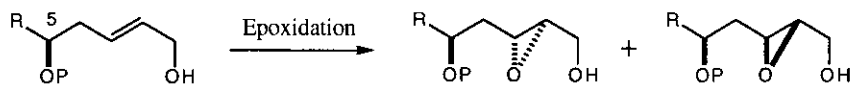
Abstract - Epoxidation of primary 5-(*tert*-butyldimethylsilyl)oxyallylic alcohols with *m*-chloroperoxybenzoic acid produced *anti*-epoxides with high stereoselectivity.

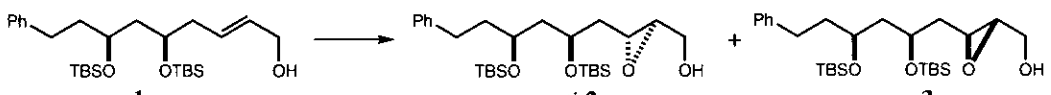
Stereoselective epoxidation of allylic alcohols is an important reaction for the synthesis of natural products. During our synthetic studies on natural products having 1,3-polyol, we investigated epoxidation of primary allylic alcohols (**i**) having a protected hydroxy group at the C5-position to give *anti*- and *syn*-epoxides (**ii**) and (**iii**) stereoselectively. We now report on a highly *anti*-selective epoxidation of primary 5-(*tert*-butyldimethylsilyl)oxyallylic alcohols (**i**: P=TBS) with *m*-chloroperoxybenzoic acid (*m*-CPBA).



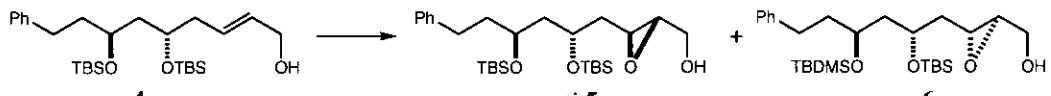
i *anti*-**ii** *syn*-**iii**

The epoxidation of several 5-silyloxyallylic alcohols was investigated as shown in Table 1. Among the many epoxidation reactions, the Sharpless asymmetric epoxidation (AE) of allylic alcohols is one of the most useful and reliable methods with high stereo- and enantioselectivities.[1] First, the Sharpless AE of (5*R*,7*S*)-di(*tert*-butyldimethylsilyl)oxy-9-phenyl-2-nonen-1-ol (**1**) with *tert*-BuOOH (TBHP), (+)-diethyl tartarate (DET), and Ti(O-*iso*-Pr)$_4$ in CH_2Cl_2 was carried out to give the desired *syn*-epoxide (**3**) with high stereoselectivity (entry 1, *anti*-**2**:*syn*-**3**=1:18).[2] However, the same reaction of **1** using (-)-DET produced

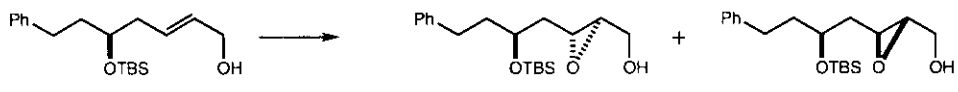
Table 1. Epoxidation of Primary 5-(*tert*-Butyldimethylsilyl)oxyallylic Alcohols



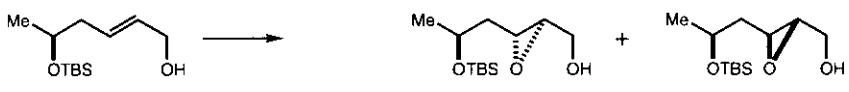
entry	conditions	yield	ratio [a] (*anti*:*syn*)
1	TBHP, (+)-DET [b]	85%	1 : 18
2	TBHP, (-)-DET [c]	90%	4.5 : 1
3	*m*-CPBA [d]	77%	>99 : <1



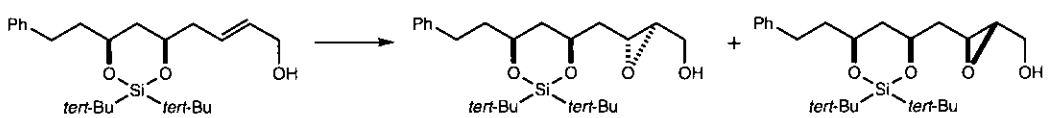
4	TBHP, (+)-DET [b]	95%	10 : 1
5	TBHP, (-)-DET [c]	84%	1 : 7.5
6	*m*-CPBA [d]	91%	13.5 : 1



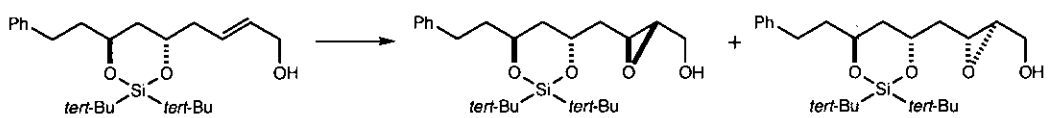
7	TBHP, (+)-DET [b]	83%	1 : 10
8	TBHP, (-)-DET [c]	76%	11 : 1
9	*m*-CPBA [d]	87%	60 : 1



10	TBHP, (+)-DET [b]	80%	1 : 70
11	TBHP, (-)-DET [c]	88%	40 : 1
12	*m*-CPBA [d]	73%	19 : 1



13	TBHP, (+)-DET [b]	100%	1 : 13
14	TBHP, (-)-DET [c]	94%	12 : 1
15	*m*-CPBA [d]	87%	1 : 1.8



16	TBHP, (+)-DET [b]	79%	8 : 1
17	TBHP, (-)-DET [c]	78%	1 : 13
18	*m*-CPBA [d]	85%	1 : 1.1

a) Ratios were determined by ^{1}H NMR data.
b) TBHP (5 equiv), (+)-DET (1.4 equiv), Ti(O-*iso*-Pr)$_4$, molecular sieves (4A), CH_2Cl_2, -21 °C, overnight.
c) TBHP (5 equiv), (-)-DET (1.4 equiv), Ti(O-*iso*-Pr)$_4$, molecular sieves (4A), CH_2Cl_2, -21 °C, overnight.
d) *m*-CPBA (2 equiv), CH_2Cl_2, 0 °C, *ca.* 1~2 h .

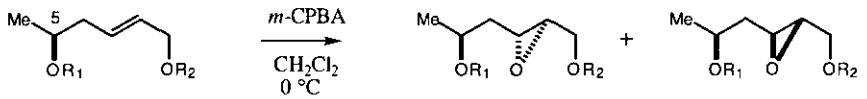
the expected *anti*-epoxide (**2**) with low stereoselectivity (entry 2, *anti*-**2**:*syn*-**3**=4.5:1). We therefore searched for more *anti*-selective epoxidation conditions. After several attempts, we found that epoxidation of **1** with *m*-CPBA in CH_2Cl_2 at 0 °C proceeded with almost complete stereoselectivity to give only *anti*-epoxide (**2**) (entry 3). Isobe[3] and Miyashita[4] independently reported this type of epoxidation, in which 5-silyloxyallylic alcohols *with a 4-methyl group* were treated with *m*-CPBA to give the *anti*-epoxides with high stereoselectivity.[5] Our results which gave high stereoselectivity even in the case of 5-silyloxyallylic alcohol (**1**) *without the 4-methyl group* proved to be extremely interesting and we further investigated the *m*-CPBA epoxidation of this type of compounds. Thus, (5*S*,7*S*)-di(*tert*-butyldimethylsilyl)oxy-9-phenyl-2-nonen-1-ol (**4**) was subjected to epoxidation with *m*-CPBA, which effectively afforded the *anti*-epoxide (**5**) with high stereoselectivity (entry 6, *anti*-**5**:*syn*-**6**=13.5:1). In the case of **4** the Sharpless AE gave moderate stereoselectivity (entries 4 and 5). The epoxidation of (5*S*)-monosilyloxyallylic alcohols (**7**) and (**10**)[6] with *m*-CPBA afforded the *anti*-epoxides (**8**) and (**11**), respectively, with high stereoselectivity (entry 9, *anti*-**8**:*syn*-**9**=60:1; entry 12, *anti*-**11**:*syn*-**12**=19:1). The Sharpless AE using (+)- and (-)-DET also gave high stereoselectivity of *anti*-**8**:*syn*-**9**=1:10, 11:1 and *anti*-**11**:*syn*-**12**=1:70, 40:1 (entries 7, 8, 10 and 11, respectively). Thus in general, epoxidation of primary 5-(*tert*-butyldimethylsilyl)oxyallylic alcohols with *m*-CPBA afforded *anti*-epoxides with high stereoselectivity.

In order to examine the role of the allylic hydroxy group in this stereoselective *m*-CPBA epoxidation, the corresponding benzyl ether (**13**) and methyl ether (**16**) were prepared from the allylic alcohol (**10**). Upon treatment with *m*-CPBA, the epoxidation of **13** and **16** took place very slowly with low stereoselectivity, giving a 1.8:1 mixture of *anti*- and *syn*-epoxides (**14**) and (**15**), and a 1.4:1 mixture of *anti*-**17** and *syn*-**18**, respectively (Table 2, entries 1 and 2). Therefore, in the present epoxidation of primary 5-silyloxyallylic alcohols, coordination of *m*-CPBA with the allylic hydroxy group plays an important role in attaining the high *anti*-stereoselectivity. In addition, epoxidation of 5-benzyloxyallylic alcohol (**19**) with *m*-CPBA gave virtually no selectivity (Table 2, entry 3),[7] which indicated the importance of the silyloxy group for the high *anti*-stereoselectivity. The low stereoselectivity in epoxidation of **19** with *m*-CPBA is noteworthy, since the similar reaction of 5-benzyloxyallylic alcohols with a 4-methyl group was reported to give high stereoselectivity by cooperative effect by allylic hydroxy and benzyloxy groups.[8]

Furthermore, we examined epoxidation of allylic alcohols (**22**) and (**25**) with a 5,7-di-*tert*-butylsilylene as protective group (Table 1). If the present stereoselective epoxidation proceeds *via* coordination of *m*-CPBA with both the silyloxy and allylic hydroxy groups as shown in Figure 1, the high stereoselectivity in the

epoxidation of **22** and **25** should be observed similarly to that of **1** and **4**. However, the epoxidtion of 5,7-*syn*- and 5,7-*anti*-derivatives (**22**) and (**25**) with *m*-CPBA produced a mixture of *anti*- and *syn*-epoxides (**23**) : (**24**), and (**26**) : (**27**), in the ratios of 1:1.8 and 1.1:1, respectively (Table 1, entries 15 and 18). Thus, these results supported that the epoxidation should not proceed *via* coordination of *m*-CPBA with both the silyloxy and allylic hydroxy groups.[9]

Table 2. Epoxidation of 5-Silyloxyallylic Ethers and 5-Benzyloxy-allylic Alcohol with *m*-CPBA



13: R_1=TBS, R_2=Bn
16: R_1=TBS, R_2=Me
19: R_1=Bn, R_2=H

14: R_1=TBS, R_2=Bn
17: R_1=TBS, R_2=Me
20: R_1=Bn, R_2=H

15: R_1=TBS, R_2=Bn
18: R_1=TBS, R_2=Me
21: R_1=Bn, R_2=H

entry	compound	time	yield	ratio (*anti*:*syn*)
1	**13**	47 h	70%	1.8 : 1
2	**16**	27 h	38%	1.4 : 1
3	**19**	2 h	78%	1.4 : 1

An NMR analysis of a reaction mixture of the 5-silyloxyallylic alcohol (**10**) and *m*-CPBA in CD_2Cl_2 at 0 ℃ suggested that **10** would not be fixed as one predominant conformer as exemplified in Figure 1.[10] The epoxidation of primary 5-(*tert*-butyldimethylsilyl)oxyallylic alcohols with *m*-CPBA would proceed stereoselectively *via* the transition state shown in Figure 2, in which the carbon chain would mostly exist in a linear conformation, although the chain might be flexible. In this transition state the *m*-CPBA reagent, coordinated only with the allylic hydroxy group,[11] would attack the olefin from the less hindered side, *i.e.*, from the opposite side of the bulky (*tert*-butyldimethylsilyl)oxy group.[4,5] The low stereoselectivity in *m*-CPBA epoxidation of **22** and **25** could well be explained by the decreased hindrance due to the formation of cyclic di-*tert*-butylsilylene moving the bulky silyl group away from the olefin.

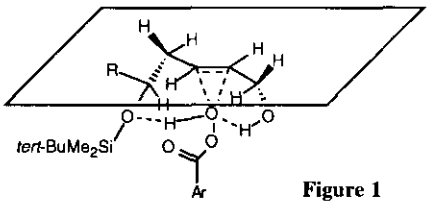


Figure 1

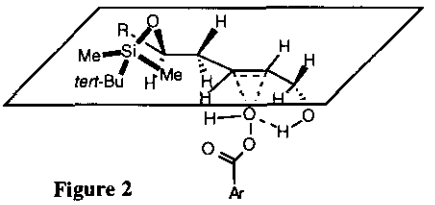


Figure 2

In conclusion, the epoxidation of 5-(*tert*-butyldimethylsilyl)oxyallylic alcohols with *m*-CPBA produced *anti*-epoxides with high stereoselectivity and will be very useful for the synthesis of natural products.

ACKNOWLEDGMENTS

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