Stereoselective Epoxidation of Acyclic Allylic Ethers Using Ketone-Oxone® System

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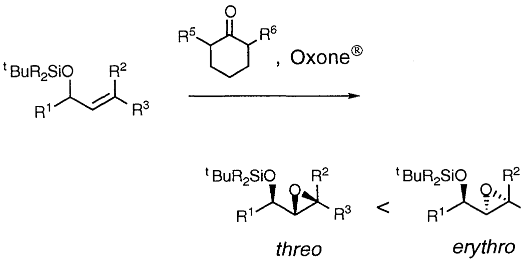
The stereoselective oxidation of acyclic allylic silyl ethers with dioxiranes generated *in situ* from Oxone® and ketones provided *erythro* epoxides.

Dioxiranes are powerful and versatile reagents as oxidants in organic synthesis.[1] We have shown that dioxiranes generated *in situ* from cyclohexanone derivatives in a homogeneous solvent system play a major role as bulky oxidants and stereoselectively oxidize cyclic olefins yielding *trans* epoxides.[2]

Stereoselective epoxidation of acyclic allylic alcohols with peracid or metal/alkyl peroxide was reported by several workers[3] and they revealed the relation between selectivity and structure in epoxidation process of allylic alcohols. Adam *et al.* investigated the epoxidation of acyclic allylic alcohols with dimethyldioxirane and found *threo* selectivity and the formation of enones.[4]

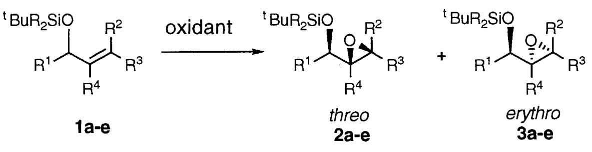
In this paper, we describe the epoxidation of acyclic allylic silyl ethers, protected allylic alcohols, using the ketone-Oxone® (active constituent $KHSO_5$) system in order to obtain *erythro* epoxides (Scheme 1).[5]



Scheme 1.

The epoxidation of substrates with dioxiranes generated *in situ* were carried out in a homogeneous solvent system (CH_2Cl_2-MeOH-buffer) under basic condition (pH 11) as reported earlier.[2]

Different types of five acyclic allylic ethers were epoxidized (Figure 1) and the results are summarized in Table1.

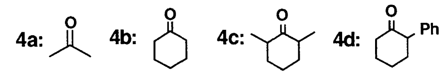


a: R=Me	b: R=Me	c: R=Me	d: R=Me	e: R=Ph
$R^1=C_5H_{11}$	R^1=Me	R^1=Me	R^1=Me	R^1=Me
R^2=H	R^2=H	R^2=H	R^2=Me	R^2=Me
R^3=H	R^3=Me	R^3=Me	R^3=Me	R^3=Me
R^4=H	R^4=H	R^4=Me	R^4=H	R^4=H

Figure 1.

Table 1. Stereoselective epoxidation of acyclic allylic ethers

entry	olefin	oxidant	method[a]	yield/%[b]	*threo* : *erythro*[c]
1	1a	*m*-CPBA	A	74	51 : 49
2	1a	4c, Oxone	B	21	26 : 74
3	1a	4d, Oxone	B	28	25 : 75
4	1b	*m*-CPBA	A	90	66 : 34
5	1b	4a, Oxone	B	54	43 : 57
6	1b	4b, Oxone	B	84	42 : 58
7	1b	4c, Oxone	B	50	29 : 71
8	1b	4d, Oxone	B	84	22 : 78
9	1c	*m*-CPBA	A	91	57 : 43
10	1c	4c, Oxone	B	24	58 : 42
11	1c	4d, Oxone	B	13	61 : 39
12	1d	*m*-CPBA	A	78	57 : 43
13	1d	4b, Oxone	B	81	32 : 68
14	1d	4c, Oxone	B	54	30 : 70
15	1d	4d, Oxone	B	99	11 : 89
16	1e	4c, Oxone	B	28	10 : 90
17	1e	4d, Oxone	B	94	02 : 98



[a] Method A: A mixture of olefin (1 mmol) and *m*-CPBA (3 mmol) in CH_2Cl_2 was stirred at rt for 3 h. *Method B:* A solution of Oxone (4 mmol) in water was added dropwise to a well-stirred mixture of CH_2Cl_2 (5 ml), MeOH (20 ml) and buffered water (10 ml, pH 11.0, 0.5 M phosphate buffer) containing olefin (1mmol) and ketone (10 mmol) at rt over 6 h. During the addition, the pH of the reaction mixture was kept constant using a pH-stat. [b] Isolated yields. [c] Ratios were determined by NMR. In each case, stereochemistry was assigned by correlation with known structures.

Epoxidation with the ketone-Oxone ® system gave *erythro* selectivities (entries 2, 3, 5–8, 13–15, 16 and 17) in contrast to low *threo* selectivities with *m*-CPBA (entries 1, 4, 9 and 12). Allylic ether **1c** with an α-substituent showed different selectivities (entries 10 and 11). The use of 2-phenylcyclohexanone **4d** as a ketone in place of 2, 6-dimethylcyclohexanone **4c**, resulted in better selectivities and yields of the epoxides. High selectivities and yields were obtained when the trisubstituted olefin was used (entries 15 and 17). In the case of large R^1 or α-substituents present in allylic ethers, yields were low (entries 2, 3, 10 and 11). When a trisubstituted olefin protected by *t*-butyldiphenylsilyl **1e** was treated with 2-phenylcyclohexanone **4d** and Oxone the best selectivity (2 : 98) was given.

Mechanistic approaches of electrophilic additions to acyclic allylic ethers have been reported by several workers.[6] We propose that the epoxidation with bulky dioxiranes proceeds via the transition states shown in Figure 2. *Erythro* products arise from the transition state I that has the largest group($OSiR_2{}^tBu$) anti to the attacking dioxiranes and the smallest group(H) inside due to the effect of allylic 1,3-strain.[7] Moreover, we assume that the observed higher selectivities in entries 15 and 17 of Table 1, can be attributed to the repulsion between R^1 and R^2(=Me). In the case of olefin **1c**, *threo* selectivites were observed because interaction between R^1 and R^4(=Me) might make transition state I unstable.[3c]

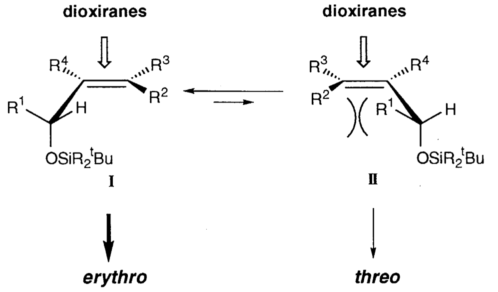


Figure 2.

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