Ring Opening Reactions of Cyclic α,β-Epoxysilanes with BF_3·OEt_2

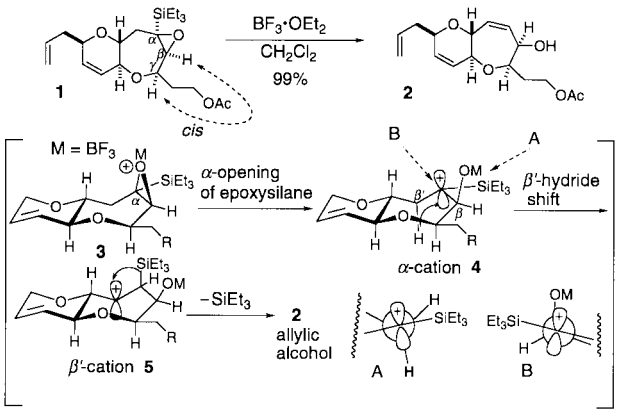
Kazunobu Kira and Minoru Isobe*
Laboratory of Organic Chemistry, School of Bioagricultural Sciences, Nagoya University, Chikusaku, Nagoya 464-8601

(Received March 1, 2001; CL-010174)

Stereospecific ring opening reactions of cyclic α,β-epoxysilanes are described. The reaction pathways are governed by the conformation of the cation intermediates in oxepane.

Many ring opening reactions of α,β-epoxysilanes have been investigated to show that the reactions of α,β-epoxysilanes undergo with strong preference for cleavage of the α C–O bond under various conditions.[1] To the best of our knowledge, there is no example which clearly discusses the stereochemical process in oxepane system. This communication describes the stereospecificity based on the conformation of oxepane ring.

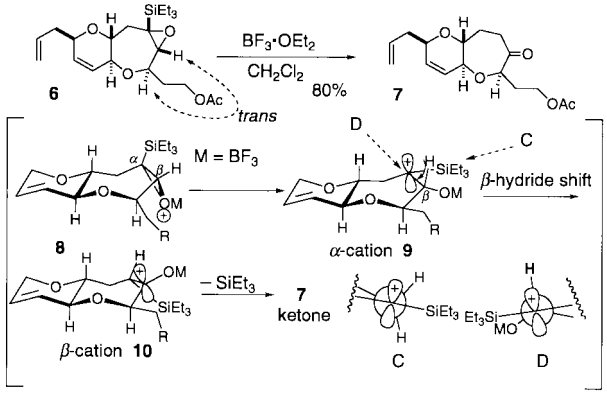
Stereospecific ring opening reaction of α,β-epoxysilanes has been one of the key reactions in the synthetic study on ciguatoxin 1B[2] that is in progress in our laboratory.[3] Treatment of *cis*-epoxysilane **1** (*cis* β-H/γ-H) with BF_3·OEt_2 gave the allylic alcohol **2**. A possible mechanism of the ring opening reaction to form the allylic alcohol **2** is shown in Scheme 1. Treatment of **1** with BF_3·OEt_2 proceeded with ring opening at the α-carbon to give α-cation intermediate **4**. Although it is assumed that the ring opening reactions took place in a concerted manner, but the cation intermediates are expressed with open form in this paper in order to simplify. To this α-cation **4**, a hydride shift of the pseudo axial hydrogen at the β′-carbon (β′-hydride shift) would occur preferentially to give the β′-cation **5**, which might be stabilized by the silyl group. Then the β′-cation **5** undergoes rapid loss of the silyl group, resulting in the allylic alcohol **2**.



Scheme 1.

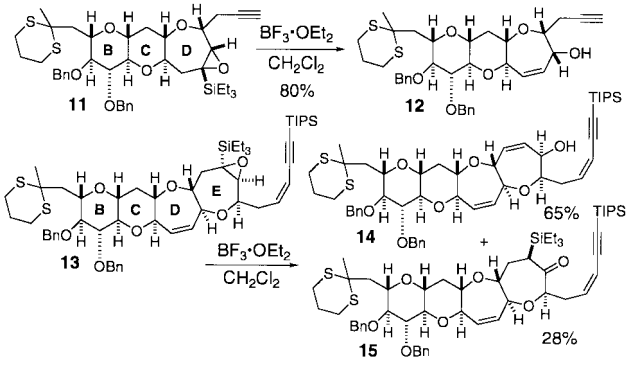
Interestingly, *trans*-epoxysilane **6** (*trans* β-H/γ-H), stereoisomer of **1**, predominantly gave oxepanone **7**. The possible mechanism of this conversion is shown in Scheme 2. In this case, β-hydride shift occurred to the α-cation **9** with an assistance of the lone pair electron on the oxygen atom. Then the β-cation **10** undergoes rapid loss of the silyl group, resulting in the ketone **7**.

These different products **2** and **7** were yielded due to the different conformation of the α-cation intermediates (**4**, **9**). Hydride shift to the α-cation should occur from pseudo axial hydrogen at the β or β′-carbon that was oriented in antiperiplanar to the generating empty p-orbital. So the β′-hydride shift (Newman projection A) occurred predominantly in **1**, while the β-hydride shift (Newman projection D) took place in **6**.



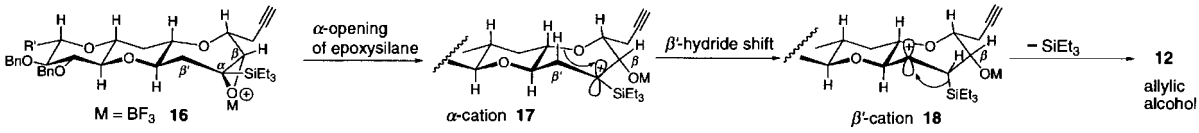
Scheme 2.

We employed this conversion method of the *cis*-α,β-epoxysilane (**1** to **2**) for the synthesis of the BCDE rings of ciguatoxin 1B.[4] Treatment of the *cis*-α,β-epoxysilanes (**11**, **13**) with BF_3·OEt_2 gave allylic alcohols (**12**, **14**) as major products, respectively (Scheme 3).

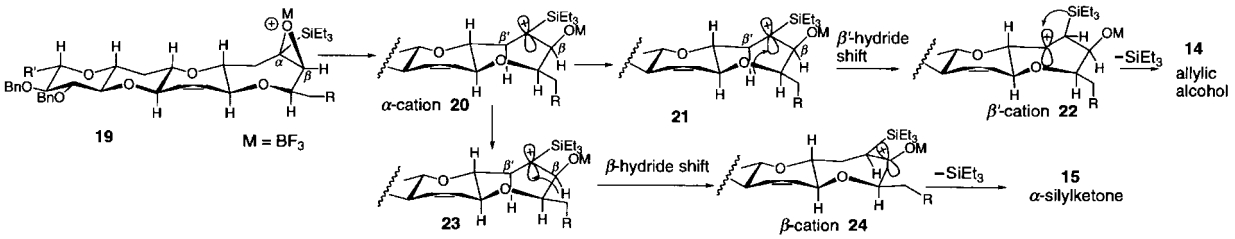


Scheme 3.

But in the case of tetracyclic precursor **13**, the yield of allylic alcohol product **14** was moderate because of the formation of α-silylketone **15** as a sideproduct. The β′-hydride shift occurred predominantly in **11** which was linking to a rigid 6-membered ether ring (Scheme 4), but β and β′-hydride shift competed in **13** which linked to a flexible 7-membered ether ring (Scheme 5). It was assumed that a subtle difference of conformation influences the reaction pathway. The possible mechanism of this competitive ring opening reaction of **13** is summarized in Scheme 5. The β′-hydride shift to the α-cation **20**



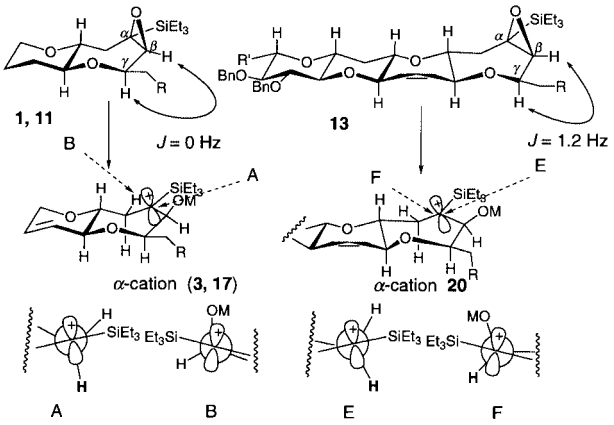
Scheme 4.



Scheme 5.

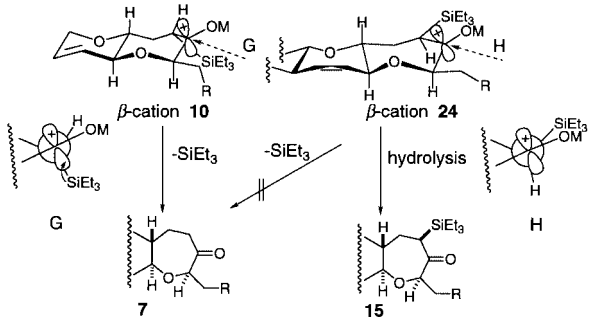
resulted in an allylic alcohol **14**, while the β-hydride shift to the α-cation **20** with an assistance of the lone pair electron on the oxygen atom gave an α-silylketone **15**.

Evidence for the different conformation between these *cis*-α,β-epoxysilanes was suggested from coupling constants. The values between β and γ-proton were 0 Hz with **1** and **11** but 1.2 Hz with **13** (Scheme 6). This fact implied that the conformation of the α-cation **20** might be different from **3** and **17**. This conformational difference should affect the selectivity of hydride shifts (β or β'). The pseudo axial hydrogen at β'-carbon was oriented in antiperiplanar to the generating empty p-orbital (Newman projection A) in the α-cation (**3**, **17**), while any hydrogen at the β and β'-carbon was not oriented in antiperiplanar completely to the generating empty p-orbital (Newman projections E and F) in the α-cation (**20**), resulting in competition of the β or β'-hydride shift.



Scheme 6.

As shown in Scheme 2, the β-cation **10** underwent rapid loss of the silyl group, resulting in a ketone **7**, while the β-cation **24** did not lose the silyl group, providing an α-silylketone **15** in Scheme 5. It was not difficult to understand this gap between the two experiments. In the case of β-cation **10**, the silyl group was oriented in coplanarity to the empty p-orbital (Newman projection G); on the other hand, the silyl group was oriented perpendicular to the p-orbital (Newman projection H) of the β-cation **24** (Scheme 7).



Scheme 7.

The stereospecific ring opening reaction of cyclic α,β-epoxysilanes with $BF_3{\cdot}OEt_2$ was concluded to be conducted by conformational factors of the cation intermediates in oxepane. These factors determine the fate of the cation intermediates to result in the different hydride shift (β or β'), thus three products.

This work was supported by JSPS-RFTF, Grant-In-Aid for Scientific Research, and JSPS-DC fellowship.

References

1 a) P. Cuadrado and A. M. Gonzalez-Nogal, *Tetrahedron Lett.*, **41**, 1111 (2000). b) P. F. Hudrlik, L. Tafesse, and A. M. Hudrlik, *J. Am. Chem. Soc.*, **119**, 11689 (1997). c) Y. Kobayashi, K. Shimizu, and F. Sato, *Chem. Commun.*, **1997**, 493. d) P. Raubo and J. Wicha, *Tetrahedron Asym.*, **7**, 763 (1996). e) A. R. Bassindale, P. G. Taylor, and Y. Xu, *Tetrahedron Lett.*, **37**, 555 (1996). f) J. A. Soderquist and B. Santiago, *Tetrahedron Lett.*, **30**, 5693 (1989). g) M. Shimizu and H. Yoshioka, *Tetrahedron Lett.*, **30**, 967 (1989). h) Y. Zhang, J. A. Miller, and E. Negishi, *J. Org. Chem.*, **54**, 2043 (1989). i) K. Tamao, E. Nakajo, and Y. Ito, *J. Org. Chem.*, **53**, 414 (1988).

2 M. Satake, A. Morohashi, H. Oguri, T. Oishi, M. Hirama, N. Harada, and T. Yasumoto, *J. Am. Chem. Soc.*, **119**, 11325 (1997).

3 K. Kira and M. Isobe, *Tetrahedron Lett.*, **41**, 5951 (2000).

4 K. Kira and M. Isobe, *Tetrahedron Lett.*, **2001**. in press.