

Torque control by metal-orbital interactions*

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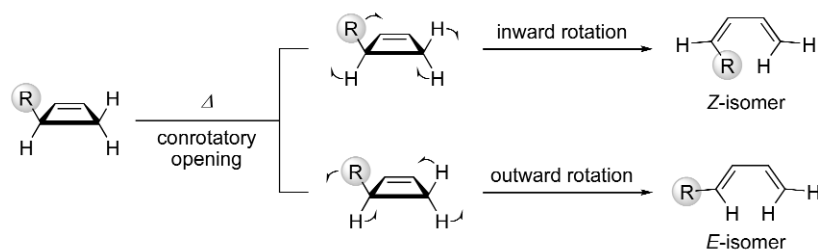
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Abstract: The silyl substituent of 3-silylcyclobutene prefers inward rotation rather than outward rotation during a thermal ring-opening reaction, giving the *Z*-isomer predominantly. This intriguing behavior was explained by assuming electron-accepting interactions between the low-lying σ^* -orbital of the silicon–carbon linkage and the highest occupied molecular orbital (HOMO) of the opening cyclobutene system, which are possible only in the inward transition state. On the basis of this finding, a novel method for the stereoselective synthesis of functionalized 1,3-butadiene derivatives from cyclobutenones was developed. Boryl substituents exhibit even stronger preference for inward rotation than silyl substituents as a result of electron delocalization from the cyclobutene HOMO into the vacant *p*-orbital of boron at the inward transition state.

Keywords: torquoselectivity; cyclobutenes; hyperconjugation; Woodward–Hoffmann rules; thermal ring-opening.

INTRODUCTION

The electrocyclic ring-opening of cyclobutenes is a classical textbook example of concerted pericyclic reactions that proceed under the control of the Woodward–Hoffmann rules [1]. Substituents located at the 3- and 4-positions can move either toward the breaking bond (inward) or away from it (outward) during the thermal ring-opening reaction, provided that their movements are conrotatory (Scheme 1).



Scheme 1 Torquoselectivity in the thermal ring-opening of cyclobutenes.

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For example, *E*-penta-1,3-diene and the corresponding *Z*-isomer can both arise from 3-methylcyclobutene without violating the Woodward–Hoffmann rules. Simple steric arguments would predict that outward rotation is preferred over inward rotation, because significant steric congestion develops when the methyl substituent rotates inward during the ring-opening reaction. In fact, the *E*-isomer is formed exclusively from 3-methylcyclobutene, being consistent with this prediction on steric grounds [2]. The inward transition state of 3-methylcyclobutene was calculated to be energetically higher than the outward transition state by 5.3 kcal/mol [MP2/6-31G(d)//3-21G] [3]. Rondan and Houk, however, proved that the selectivity of the rotational direction, termed “torquoselectivity”, is subject to electronic control as well [4]. Their theory states that an electron-accepting substituent at the 3-position prefers inward rotation. Delocalization of electron density of the HOMO of the opening cyclobutene skeleton to the electron-accepting substituent stabilizes the inward transition state. The electronic stabilization can outweigh or counterbalance the steric congestion developing during inward rotation [5]. For example, a formyl group can accept electron density into its antibonding π^* -orbital, and thus rotates with high inward selectivity [5a]. We recently discovered the interesting preference for inward rotation of silyl and boryl substituents. Although those metallic elements are less electronegative than carbon, they have energetically low-lying unoccupied orbitals that are able to accept electron density from the HOMO of the opening cyclobutene skeleton, stabilizing the inward transition state. We herein describe the results of our recent studies on this subject.

COMPUTATIONAL STUDIES ON THE SUBSTITUENT EFFECT OF SILICON

We carried out computational studies taking 3-silylcyclobutene as a model of proto-structure, to compare with the results of 3-methylcyclobutene [6]. The transition states for outward and inward reactions were computationally located [DFT, B3LYP/6-31G(d)]. The potential energy diagram for 3-silylcyclobutene shown in Fig. 1 (the produced 1,3-butadienes are depicted in *s-cis* conformation for convenience in this manuscript) suggests that the calculated preference is just the opposite to that of 3-methylcyclobutene. The activation energy for inward rotation is 1.7 kcal/mol lower than that for outward rotation. It is predicted that 3-silylcyclobutene would prefer inward rotation despite the developing steric congestion. In addition, rate acceleration might be expected.

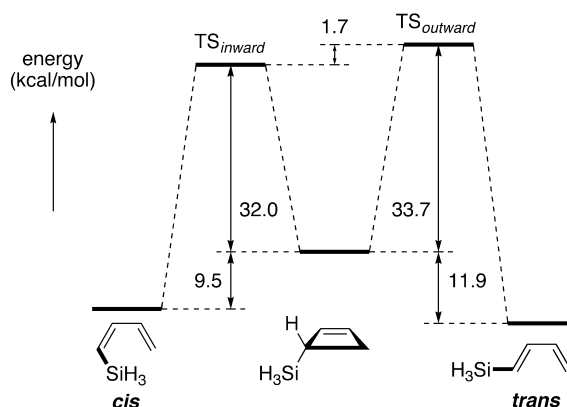
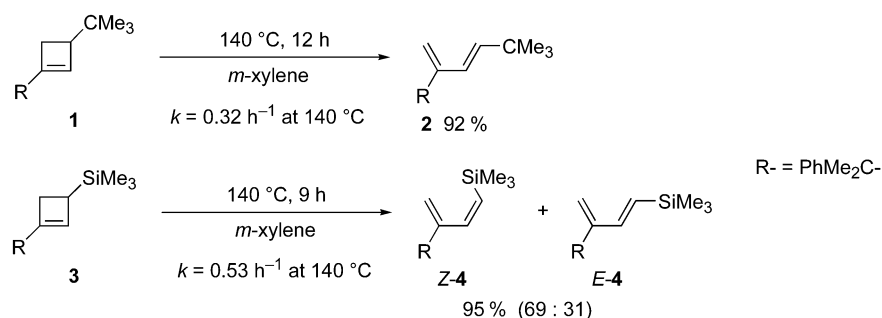


Fig. 1 Calculated energy diagram of the ring-opening reaction of 3-silylcyclobutene.

EXPERIMENTAL STUDIES ON THE SUBSTITUENT EFFECT OF SILICON

In order to verify the theoretical predictions, the cyclobutenes **1** and **3** were prepared and their reactivities were compared. The structures of these cyclobutenes are exactly identical except for the tertiary elements. Cyclobutene **1** has a carbon atom of a tertiary butyl group, whereas cyclobutene **3** has a silicon atom of a trimethylsilyl group. When heated at 140 °C, cyclobutene **1** underwent ring-opening with outward rotation to give the *E*-isomer **2** exclusively. On the other hand, cyclobutene **3** furnished a mixture of *Z*- and *E*-isomers with the *Z*-isomer predominating by a ratio of *Z*-**4**:*E*-**4** = 69:31. The ratio was constant through the reaction and even after heating for a longer period of time, suggesting that it was kinetically determined. Inward rotation is favored over outward rotation, which is opposite to what would be predicted as a result of simple steric arguments. In addition, the reaction of **3** ($k = 0.53 \text{ h}^{-1}$ at 140 °C) was faster than that of the carbon counterpart **1** ($k = 0.32 \text{ h}^{-1}$ at 140 °C). These results with **1** and **3** confirm the computational prediction that a silyl substituent at the 3-position of cyclobutene accelerates the ring-opening reaction, and prefers inward rotation rather than outward rotation [7]. It is remarkable that even though silicon is immediately below carbon in the periodic table, it possesses an opposite rotational preference.



EXPLANATIONS OF THE SUBSTITUENT EFFECT OF SILICON

We interpreted the remarkable contrastive behavior that the silyl substituent exhibited by assuming a negative hyperconjugative stabilization; silicon can accommodate electron density from a neighboring p-orbital into its σ^* -orbital, which is energetically rather low-lying. This effect has been used to explain various phenomena of silicon compounds, like the relatively low basicity of the oxygen atom of a silyl ether, the short Si–O distance, and the higher acidity of silanols (Fig. 2).

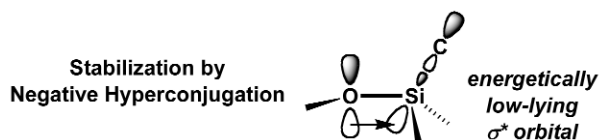


Fig. 2 Negative hyperconjugation in a Si–O linkage.

The highest occupied molecular orbital (HOMO) of the transition state of ring-opening reaction of cyclobutene is primarily concentrated on the breaking C₃–C₄ σ-orbital (Fig. 3). This HOMO can be a good electron donor. Upon inward rotation, the silyl substituent approaches closer to the HOMO (left figure). The low-lying σ*-orbital would possibly accept the HOMO electron. This electron delocalization results in its stabilization. On the other hand, the silyl substituent goes away from the HOMO upon outward rotation (right figure). Therefore, analogous stabilizing interaction is expected to be much smaller than on inward rotation. Thus, the inward preference and accelerating effect of a silyl substituent can be explained by assuming electron-accepting interactions of the rather low-lying σ*-orbital of the silicon atom with the HOMO. There are two other groups studying the preference of inward rotation of silyl substituents from the theoretical point of view. Whereas Inagaki and his coworkers explain it by assuming geminal σ-bond participation [8], the study by Houk's group supports our interpretation [9].

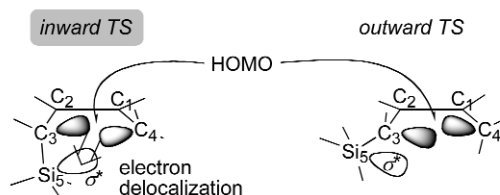
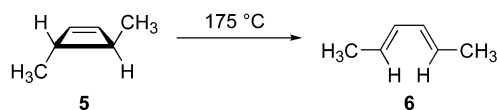


Fig. 3 Inward and outward transition states for the ring-opening of 3-(trimethylsilyl)cyclobutene.

RING-OPENING OF *TRANS*-3,4-BIS(TRIMETHYLSILYL)CYCLOBUTENE

In the case of *trans*-3,4-disubstituted cyclobutenes, the disadvantage of the inward transition state in which both substituents rotate in the sterically unfavorable direction would be enormous. For example, *E,E*-hexa-2,4-diene **6** is exclusively formed during the ring-opening of *trans*-3,4-dimethylcyclobutene **5** [10]. The calculated energy difference of the inward and outward transition states amounts to 13.0 kcal/mol (RHF/3-21G) [4b]. Organic chemistry textbooks present this reaction as a typical instance of conrotatory ring-opening.



We next examined the ring-opening reaction of *trans*-3,4-bis(trimethylsilyl)cyclobutene **7**, in which the two methyl substituents of **5** are replaced with two significantly bulkier trimethylsilyl substituents [11]. The steric congestion arising from inward rotation of the two bulkier substituents may become insurmountable. Thus, we consider this a true test of the power of electronic stabilization. The cyclobutene **7** was synthesized and heated at 110 °C in *n*-decane. It underwent ring-opening in a conrotatory fashion ($t_{1/2} = 1.7$ h) to afford a mixture of *Z,Z*-1,3-diene **8** and the corresponding *E,E*-isomer **9**. Remarkably, the *Z,Z*-isomer **8** predominated over **9** by a ratio of 78:22. The two trimethylsilyl substituents preferred inward rotation despite the significantly greater steric constraints on this reaction pathway.

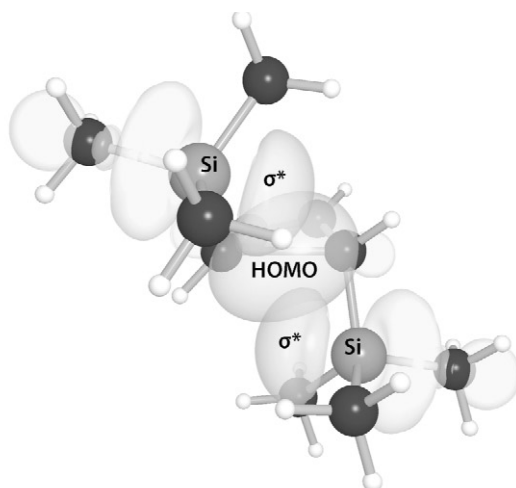
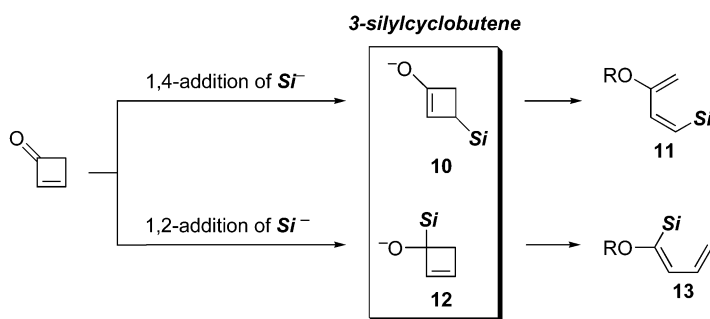


Fig. 4 Orbital overlap image of the inward transition state of 7.

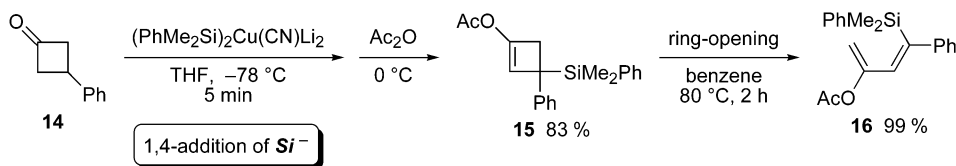
SYNTHETIC APPLICATION OF THE SUBSTITUENT EFFECT OF SILICON

We next applied the interesting effect of the silyl substituent to the synthetic reactions [13]. The key substrate required for this strategy is cyclobutene having a silyl substituent at the 3-position. Such cyclobutenes can be conveniently prepared by nucleophilic addition of a silyl anion to cyclobutenones. The 1,4-addition provides 3-silylcyclobutene **10**, which opens up to functionalized 1,3-diene **11**. On the other hand, 1,2-addition provides 3-silylcyclobutene **12** of different structure, which opens up to isomeric functionalized 1,3-diene **13**.

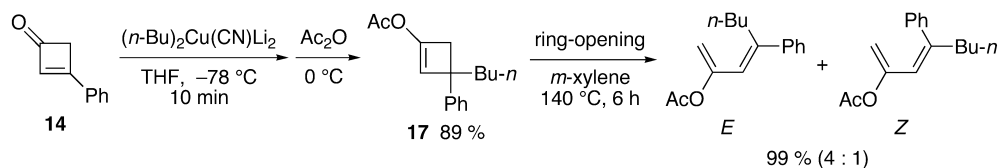


1,4-Addition

To effect the 1,4-addition, cyclobutenone **14** was treated with a higher-order silylcuprate at $-78\text{ }^{\circ}\text{C}$ for 5 min. The resultant 1,4-adduct was trapped with acetic anhydride to afford 3-silyl-1-cyclobutene **15**. The isolated product was heated in refluxing benzene for 2 h. A ring-opening reaction occurred with unidirectional rotation of the substituents. The silyl group rotated inward and the phenyl group outward to furnish the 1-silyl-1,3-diene having *Z*-geometry **16** in quantitative yield.

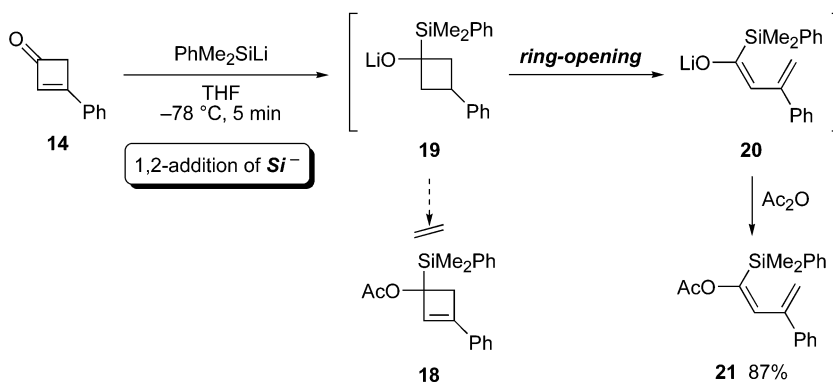


To examine the effect of silicon, substrate **17** having a butyl substituent in place of a silyl substituent was prepared by the 1,4-addition of butylcuprate followed by treatment with acetic anhydride. Unlike the silyl counterpart **15**, the resulting cyclobutene **17** was unreactive even in refluxing toluene. Ring-opening required heating at 140°C to form a mixture of *E*- and *Z*-isomers. In this case, the butyl and phenyl groups competed for outward rotation. These contrasting results clearly demonstrate that the silyl group plays the dual role of accelerating the ring-opening reaction and controlling the torquoselectivity.

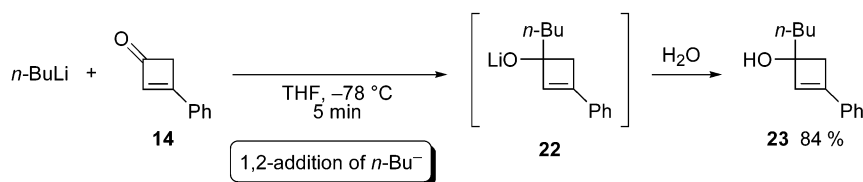


1,2-Addition

We initially expected that a 1,2-addition reaction using silyllithium instead of silylcuprate, followed by acetylation, would afford 3-silylcyclobutene **18**. In fact, however, the reaction of cyclobutenone with silyllithium at -78°C directly produced the 1-silyl-1,3-diene having *Z*-geometry **21** instead. Stereoselective formation of **21** was explained by assuming that initial 1,2-addition of silyllithium to the carbonyl group was immediately followed by torquoselective ring-opening of the 1,2-adduct **19**. The resulting lithium enolate **20** was trapped with acetic anhydride to give the product **21**.

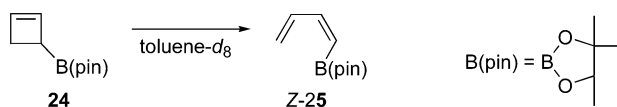


As a comparison, butyllithium was reacted with cyclobutenone **14**. Unlike the silyllithium case, the intermediate 1,2-adduct **22** failed to undergo a ring-opening reaction at -78°C , and after aqueous work-up, cyclobutenol **23** was obtained. These contrasting results again demonstrate that a silyl substituent accelerates the ring-opening reaction.



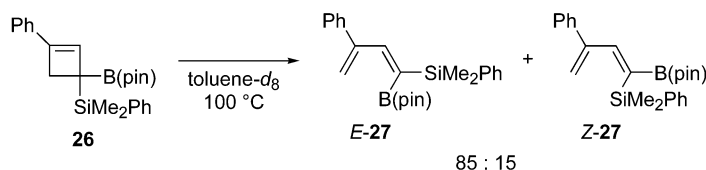
SUBSTITUENT EFFECT OF BORON

A tri-substituted organoborane has an energetically low-lying vacant p-orbital, and the vacant orbital can accept electron density from another molecule (Lewis acid–base complexation), or inside the molecule (delocalization or conjugation). Rondan and Houk predicted in 1985 that a boryl substituent would have a strong preference for inward rotation [4b]. The inward transition state of 3-(dimethylboryl)cyclobutene was calculated to be lower than the outward transition state by as much as 10.5 kcal/mol [13], although there has been no experimental validation of this basic issue. We synthesized 3-(pinacolatoboryl)cyclobutene **24** and examined its rotational behavior [14]. The cyclobutene **24** was heated in toluene- d_8 in the presence of a small amount of galvinoxyl in the dark in order to suppress radical pathways for olefin isomerization of 1,3-dienes produced. The ring-opening reaction of **24** proceeded at temperatures as low as 70 °C and completed after 4 h at 92 °C. More importantly, (*Z*)-1-borylbuta-1,3-diene **25** was exclusively formed.



Thus, appending a boryl group at the 3-position of cyclobutene had a huge effect on the reactivity of the parent cyclobutene skeleton [15]. These results can be understood by invoking the electronic participation of the boryl substituent. In the inward transition state, the vacant p-orbital accepts electron density from the breaking distorted σ -orbital of the parent cyclobutene skeleton. This electron delocalization provides significant stabilization to the inward transition state.

We have demonstrated that both boryl and silyl groups prefer to rotate inward in the cyclobutene ring-opening reaction due to electronic reasons despite the steric congestion. It is of much interest to compare the magnitude of the inward preferences of boryl and silyl groups. Thus, we prepared cyclobutene **26** having both boryl and silyl groups at the 3-position according to the procedure developed by Shimizu and Hiyama [16]. The ring-opening reaction of the cyclobutene **26** proceeded at 100 °C affording a mixture of (*E*)- and (*Z*)-1-boryl-1-silylbuta-1,3-diene **27**. The diene (*E*)-**27**, in which the boryl substituent had rotated inward, predominated over (*Z*)-**27** in a ratio of 85:15. The stereochemical outcome demonstrates that the boryl group has a stronger preference for inward rotation than the silyl group. The boron vacant p-orbital accepts electron density more efficiently than the antibonding σ^* -orbital of silicon in the transition state.



CONCLUSION

Although steric arguments are commonly employed to understand the stereochemical outcomes of organic reactions, electronic effects may have a greater impact than generally supposed. In the system described herein, the effects are so dramatic that the more sterically hindered substrate prefers to react via a more crowded reaction pathway. These results will hopefully provide organic chemistry textbooks with a prime example of systems in which electronic effects are dominant over steric effects in determining the stereochemical outcome of a reaction.

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