

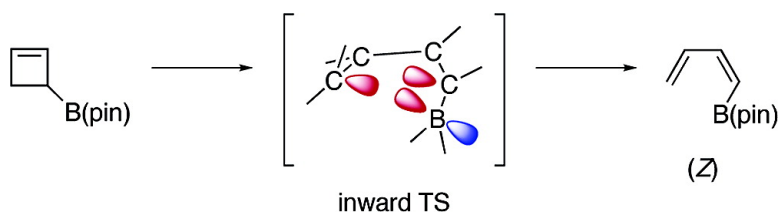
Communication

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 Ring-Opening Reaction by a Vacant Boron p Orbital**

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## Contrastric Stereochemical Dictation of the Cyclobutene Ring-Opening Reaction by a Vacant Boron p Orbital

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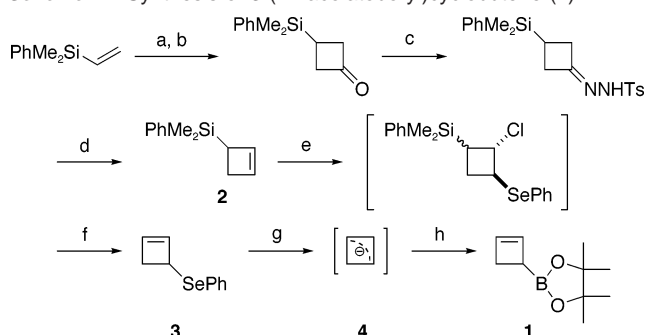
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The torquoselectivity of the thermal ring-opening reaction of cyclobutene has been a subject of fundamental importance in organic and theoretical chemistry.<sup>1</sup> Houk's theory states that an electron-accepting substituent at the 3-position prefers inward rotation.<sup>2</sup> 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.<sup>3</sup> For example, a formyl group can accept electron density into its antibonding  $\pi^*$  orbital and thus rotates with high inward selectivity.<sup>3a</sup> We recently discovered the interesting preference of silyl groups to rotate inward.<sup>4,5</sup> Although silicon is less electronegative than carbon, the antibonding  $\sigma^*$  orbital of a silicon-carbon linkage is energetically low-lying and able to accept electron density, favoring the inward transition state.<sup>4a,6,7</sup>

A trisubstituted 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). In 1985, Rondan and Houk predicted that a boryl substituent would have a strong preference for inward rotation.<sup>2</sup> The inward transition state of 3-(BMe<sub>2</sub>)cyclobutene was calculated to be lower than the outward transition state by as much as 10.5 kcal/mol.<sup>8</sup> Remarkably, there has been no experimental validation of this basic issue, possibly due to the difficulty in the preparation of 3-borylcyclobutenes. We now report the synthesis of 3-(pinacolatoboryl)cyclobutene (**1**) and its rotational behavior.<sup>9</sup>

At first, we envisaged that the nucleophilic substitution reaction of a boronic acid derivative with a cyclobutenyl anion would provide a straightforward synthetic access to 3-borylcyclobutene. However, attempts to generate cyclobutenyllithium by reductive lithiation of 3-halocyclobutene were unsuccessful. Thus, we developed an alternative route to 3-borylcyclobutene **1** via 3-selenylcyclobutene. The synthesis was achieved in eight steps starting from dimethylphenylvinylsilane (Scheme 1). [2 + 2] Cycloaddition with dichloroketene, followed by dechlorination with zinc-copper couple furnished 3-(dimethylphenylsilyl)cyclobutanone. The cyclobutanone was transformed to the corresponding tosylhydrazone, which was then subjected to the Shapiro olefination reaction<sup>10</sup> affording 3-(dimethylphenylsilyl)cyclobutene (**2**). Treatment of the cyclobutene **2** with phenylselenenyl chloride gave 2-chloro-1-silyl-3-selenylcyclobutane as a diastereomeric mixture, which upon treatment with tetrabutylammonium fluoride (TBAF) underwent elimination of the chloro and silyl groups to afford 3-(phenylselenyl)cyclobutene (**3**).<sup>11</sup> Reductive removal of the selenyl group with lithium naphthalenide produced the cyclobutenyl anion **4**.<sup>12,13</sup> Addition of trimethyl borate to the anion **4** followed by treatment with pinacol furnished the 3-(pinacolatoboryl)cyclobutene (**1**). Thus, a method for the generation of cyclobutenyllithium has been developed via reductive cleavage of a selenium-carbon bond. This

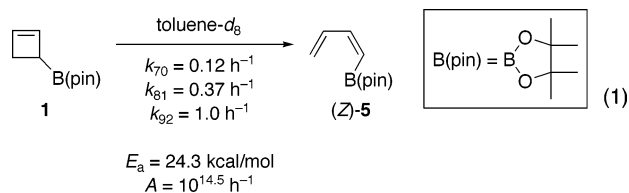
**Scheme 1.** Synthesis of 3-(Pinacolatoboryl)cyclobutene (**1**)<sup>a</sup>



<sup>a</sup> Reagents and conditions: (a) Cl<sub>3</sub>CCOCl, Zn-Cu, 1,2-dimethoxyethane, Et<sub>2</sub>O, room temperature. (b) Zn-Cu, THF, H<sub>2</sub>O (54%, two steps). (c) TsNHNH<sub>2</sub>, EtOH, room temperature (91%). (d) *n*-BuLi, hexane-*N,N,N',N'*-tetramethylethylenediamine (10:1), -78 °C to room temperature, then H<sub>2</sub>O, -78 °C (61%). (e) PhSeCl, CH<sub>2</sub>Cl<sub>2</sub>, -78 °C to room temperature. (f) TBAF, THF, -78 °C to room temperature (45% from **2**). (g) lithium naphthalenide, THF, -78 °C. (h) i) B(OMe)<sub>3</sub>, -78 °C, ii) H<sub>3</sub>O<sup>+</sup>, -78 °C, iii) pinacol (32% from **3**).

procedure also provides a facile route for the nucleophilic incorporation of cyclobuten-3-yl groups into various organic skeletons.

The cyclobutene **1** thus obtained was heated in toluene-*d*<sub>6</sub> in the presence of a small amount of galvinoxyl to suppress olefin isomerization by radical pathways.<sup>14</sup> The ring-opening reaction of **1** in the dark proceeded at 92 °C with a rate of  $k = 1.0 \text{ h}^{-1}$  and was almost complete after 4 h (eq 1). Exclusive formation of (*Z*)-1-borylbuta-1,3-diene **5** was observed by <sup>1</sup>H NMR up to 80% conversion, beyond which the (*E*)-isomer gradually appeared by isomerization of (*Z*)-**5** initially formed. The kinetics of the ring opening were investigated at varying temperatures, and activation parameters  $k = 10^{14.5} \exp(-24.3/RT) \text{ h}^{-1}$  were obtained from the Arrhenius plot.

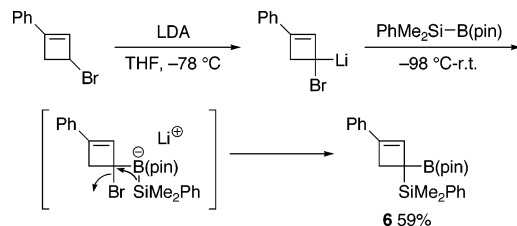


Thus, appending a boryl group at the 3-position of cyclobutene had a huge effect on the reactivity of the parent cyclobutene skeleton, permitting the electrocyclic ring-opening reaction at temperatures as low as 70 °C. Furthermore, the more sterically demanding inward rotation occurred exclusively. These results can be understood by invoking the electronic participation of the boryl substituent, as theoretically predicted.<sup>2</sup> In the inward transition state, the vacant p orbital accepts electron density from the breaking distorted  $\sigma$  orbital, that is the HOMO of the parent cyclobutene skeleton (Figure 1). This electron delocalization provides significant stabilization to the inward transition state.



**Figure 1.** Electron-accepting interaction of the vacant boron p orbital with the HOMO in the inward transition state.

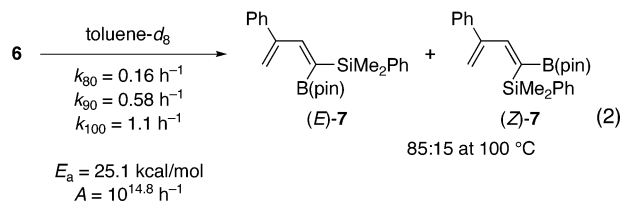
**Scheme 2.** Synthesis of 3-Boryl-3-silylcyclobutene **6**



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 that is generated. It is of much interest to compare the magnitude of the inward preferences of boryl and silyl groups by experiment. Thus, we prepared cyclobutene **6** having both boryl and silyl groups at the 3-position according to the procedure developed by Shimizu and Hiyama.<sup>15</sup>  $\alpha$ -Bromoallyllithium, generated in situ from 3-bromo-1-phenylcyclobutene and lithium diisopropylamide (LDA), was reacted with (dimethylphenylsilyl)pinacolborane in THF, and the desired 3-boryl-3-silylcyclobutene **6** was obtained in 59% yield (Scheme 2).

The ring-opening reaction of the cyclobutene **6** proceeded at 100 °C with a rate of  $k = 1.1 \text{ h}^{-1}$  affording a mixture of *E*- and *Z*-1-boryl-1-silylbuta-1,3-diene **7** (eq 2). The diene (*E*)-**7**, in which the boryl substituent had rotated inward, predominated over (*Z*)-**7** in a ratio of 85:15.<sup>16</sup> An Arrhenius plot provided activation parameters  $k = 10^{14.8} \exp(-25.1/RT) \text{ h}^{-1}$ . The stereochemical outcome demonstrates that the boryl group has a stronger preference for inward rotation than the silyl group and that the boron vacant p orbital accepts electron density more efficiently than the antibonding  $\sigma^*$  orbital of silicon in the transition state.

In summary, we have developed a valuable preparative method for the generation of cyclobutenyl anion **4** and verified the exclusive inward rotation of a boryl substituent in the cyclobutene ring-opening reaction. It was also experimentally demonstrated that boron is more powerful than silicon in terms of directing inward rotation.



**Acknowledgment.** This paper is dedicated to Professor Iwao Ojima on the occasion of his 60th birthday.

**Supporting Information Available:** Experimental details and selected spectral data for new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (16) The *E* stereochemistry of the major product was unambiguously confirmed by <sup>1</sup>H NMR NOE experiments.

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