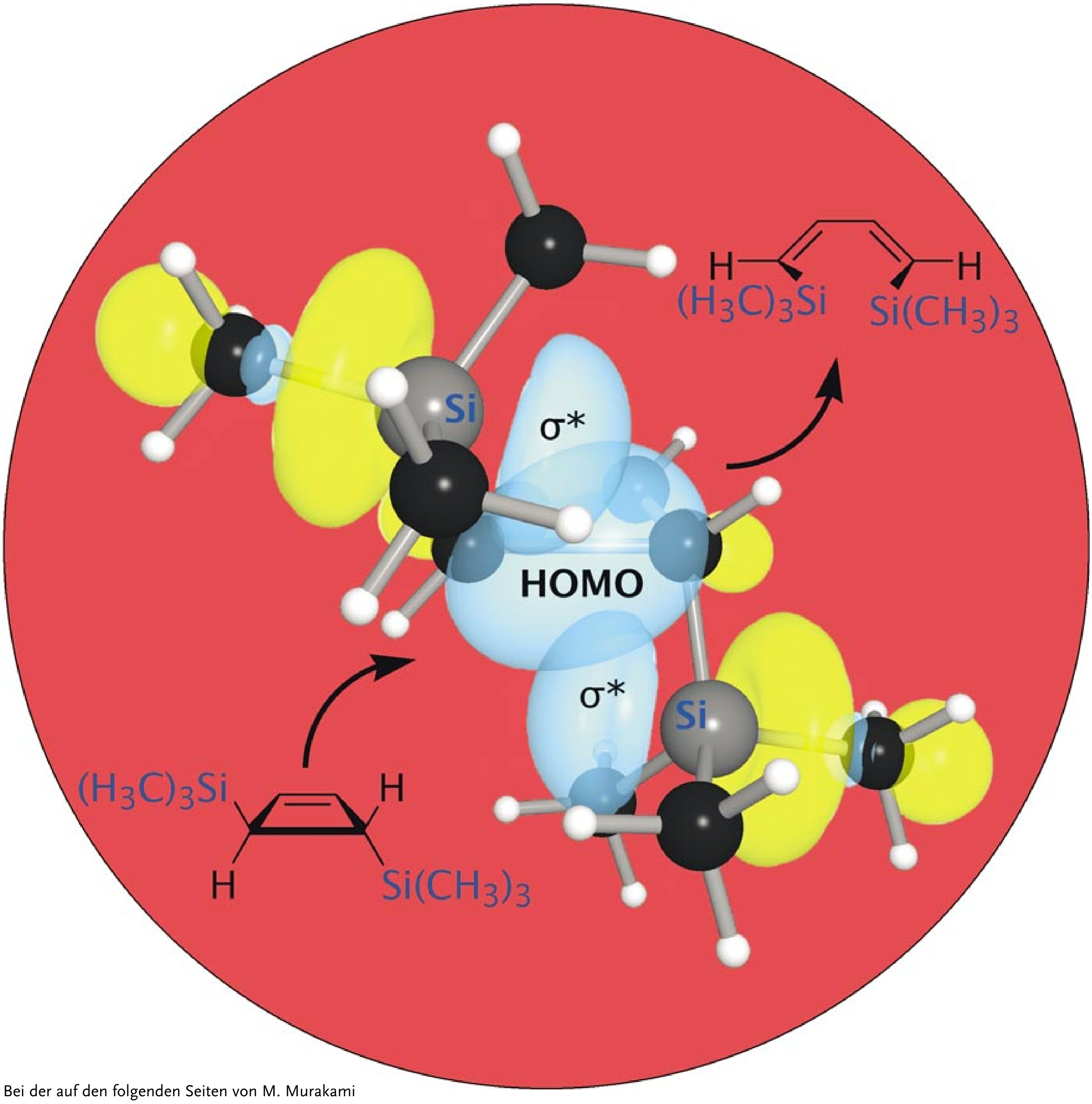
# Zuschriften



Bei der auf den folgenden Seiten von M. Murakami und M. Hasegawa beschriebenen Reaktion sind die elektronischen Effekte so drastisch, dass das Substrat bevorzugt über den sterisch ungünstigeren Weg reagiert. Diese Reaktion sollte ein Lehrbuchbeispiel für Systeme werden, in denen bei der Festlegung des stereochemischen Reaktionsverlaufs elektronische Effekte über sterische Effekte dominieren.

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Electronic Effects

# Synthesis and Thermal Ring Opening of *trans*-3,4-Disilylcyclobutene

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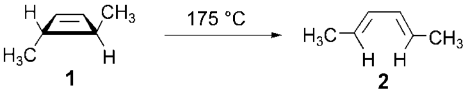
The electrocyclic ring opening of substituted cyclobutenes is a classical textbook example of concerted pericyclic reactions that obey the Woodward–Hoffmann rules.[1] Substituents located at the 3- and 4-positions can move either toward the breaking bond (inward) or away from it (outward) during the thermal ring-opening reaction, provided that their movements are conrotatory. For example, (*E*)-penta-1,3-diene and the corresponding *Z* isomer can both arise from 3-methylcyclobutene without violating the Woodward–Hoffmann rules. However, experimentally, the *E* isomer is formed exclusively.[2] The outward preference is intuitively reasonable, because significant steric congestion develops when the methyl substituent rotates inward during the ring-opening reaction. The inward transition state was calculated to be energetically higher than the outward transition state by 5.3 kcal mol$^{-1}$ (MP2/6-31G(d)//3-21G) in the case of 3-methylcyclobutene.[3] On the other hand, theoretical studies predicted that an electron-accepting substituent would prefer to rotate inward.[4] The delocalization of electron density from the highest occupied molecular orbital (HOMO) of the opening cyclobutene skeleton to the electron-accepting substituent stabilizes the inward transition state. This prediction has been verified experimentally with carbonyl-substituted cyclobutenes.[5] We recently discovered the remarkable effects of a silyl substituent located at the 3-position.[6,7] Although silicon is more electropositive than carbon, silyl substituents accelerate the reaction and promote inward rather than outward rotation, in spite of steric considerations. Stabilization of the inward transition state was explained by assuming that the energetically low-lying antibonding σ* orbital of the silicon–carbon bond accepts electron density from the HOMO.[6a,8,9]

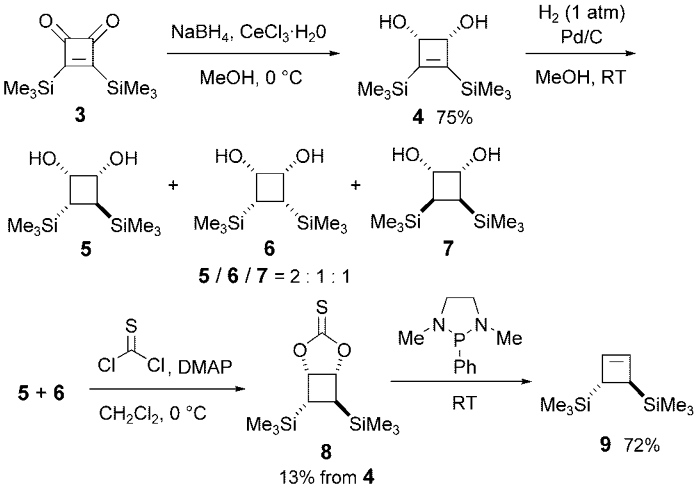
In the case of *trans*-3,4-disubstituted cyclobutenes, the disadvantage of the inward transition state in which both substituents rotate in the sterically unfavorable direction would be enormous. For example, (2*E*,4*E*)-hexadiene (**2**) is exclusively formed during the ring-opening of *trans*-3,4-dimethylcyclobutene (**1**) (Scheme 1).[10] The calculated energy difference of the inward and outward transition states amounts to 13.0 kcal mol$^{-1}$ (RHF/3-21G).[4b] Organic chemistry textbooks present this reaction as a typical example of conrotatory ring opening.[11]



***Scheme 1.*** Ring-opening reaction of *trans*-3,4-dimethylcyclobutene **1**.

Previous studies on the effects of silyl substituents prompted us to examine the ring-opening reaction of *trans*-3,4-bis(trimethylsilyl)cyclobutene (**9**; Scheme 2), in which the two methyl substituents of **1** are replaced with two significantly bulkier trimethylsilyl substituents. The steric congestion arising from the inward rotation of two bulkier substituents may become insurmountable. Thus, we consider this a true test of the power of electronic stabilization.

The synthesis of *trans*-3,4-bis(trimethylsilyl)cyclobutene (**9**) is shown in Scheme 2. Cyclobutenedione **3**, prepared according to a literature procedure,[12] was reduced to the *cis* diol **4** with NaBH$_4$/CeCl$_3$.[13] Hydrogenation over Pd/C in methanol afforded a diastereomeric mixture of diols **5**, **6**, and **7**.[14] The diols **5** and **6** were separated from **7** by chromatography. The *cis* 1,2-diol unit was converted into a carbon–carbon double bond by using the Corey–Hopkins method.[15] When a mixture of **5** and **6** was treated with thiophosgene, the diol **5** reacted much faster than **6**, probably as a result of steric reasons, permitting the isolation of the cyclic thiocarbonate **8**. The desired cyclobutene **9** was obtained by the reaction of **8** with 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine.



***Scheme 2.*** Synthesis of *trans*-3,4-bis(trimethylsilyl)cyclobutene (**9**). DMAP = 4-dimethylaminopyridine.

The cyclobutene **9** thus obtained was heated in *n*-decane at 110 °C and underwent ring opening in a conrotatory fashion ($t_{1/2} = 1.7$ h) to afford a mixture of diene (1*Z*,3*Z*)-**10** and the corresponding *E*,*E* isomer **11** (both depicted in the s-*cis* conformation for convenience in Scheme 3). Remarkably, the *Z*,*Z* isomer **10** predominated over **11**, with a ratio of 78:22.[16] The two trimethylsilyl substituents preferred inward rotation despite the significantly greater steric constraints on this reaction pathway.

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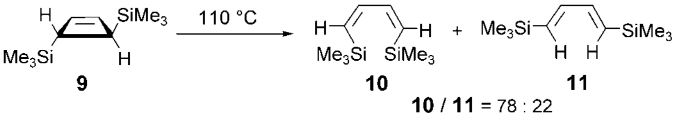

*Scheme 3.* Ring-opening reaction of **9**.

Computational studies were carried out on the reaction of **9**. The energy diagram obtained by density functional calculations [B3LYP/6-31G(d)][17,18] is shown in Figure 1. The inward transition state is lower in energy than the outward transition state by 0.51 kcal mol$^{-1}$, whereas the product ratio experimentally obtained at 110 °C (78:22) corresponds to an energy difference of 0.96 kcal mol$^{-1}$. Interestingly, the reaction through the inward pathway leads directly to **10** in the s-*trans* conformation, without the intervention of an energy minimum that corresponds to the s-*cis* (or gauche) conformation.[19] In contrast, in the outward pathway the initial product **11** in the gauche conformation (the dihedral angle $C_1$-$C_2$-$C_3$-$C_4$ = 21°) exists as a local minimum before the final product s-*trans*-**11** is formed. The contrasting reaction profiles are another indication of the magnitude of steric congestion of the inward ring opening.

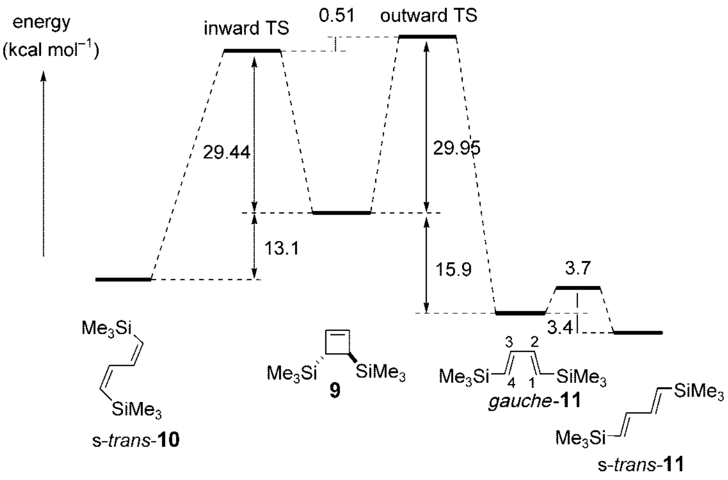

*Figure 1.* Potential energy diagram for the ring opening of **9** (383 K).

We attribute the counterintuitive rotational behavior of **9** to the electron-accepting nature of the two antibonding orbitals on the silicon atoms based on Houk's theory.[4] The inward transition state is shown in Figure 2, in addition to the natural bond orbital (NBO) overlap image[20] for the two antibonding orbitals of the Si5–C6 and Si9–C10 links, and the breaking C1–C4 σ bond, that is, the HOMO of the opening cyclobutene skeleton. This clearly shows the overlap of the antibonding orbitals with the HOMO. Electronic stabilization arising from the dual delocalization of the electron density of the HOMO into the two antibonding orbitals overcomes the steric congestion at the inward transition state, leading to the predominance of **10**.

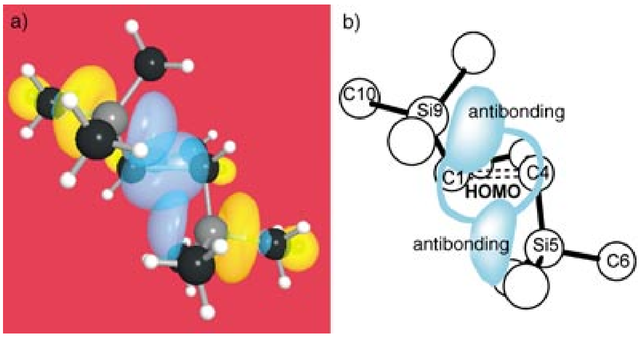

*Figure 2.* Overlap of the two antibonding orbitals on the silicon atoms with the HOMO in the inward transition state.

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 through a more crowded reaction pathway. This Communication 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. It is also remarkable that even though silicon is immediately below carbon in the periodic table, it exhibits a totally opposite rotational preference.

## Experimental Section

Ring opening of **9**: A solution of **9** (19.8 mg, 0.10 mmol) and galvinoxyl (2.0 mg, 4.7 μmol; added to prevent isomerization of the olefin geometries of the products)[21] in *n*-decane (50 μL) was placed in a screw-capped vial under a nitrogen atmosphere. The mixture was then stirred at 110 °C in an oil bath. The ring-opening reaction to form **10** and **11** was monitored by $^1$H NMR spectroscopy. **10**: $^1$H NMR (300 MHz): $\delta = 6.98$–$7.06$ (m, 2H), 5.74–5.82 (m, 2H), 0.17 ppm (s, 18H); $^{13}$C NMR (75 MHz): $\delta = 145.0, 135.1, 0.3$ ppm. **11**: $^1$H NMR (300 MHz): $\delta = 6.51$–$6.58$ (m, 2H), 5.89–5.96 (m, 2H), 0.10 ppm (s, 18H); $^{13}$C NMR (75 MHz): $\delta = 146.6, 134.8, -1.3$ ppm.[22]

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