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Theoretical and Experimental Studies on the Thermal Ring-Opening Reaction of Cyclobutene Having a Stannyl Substituent at the 3-Position

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Abstract: The ring-opening reaction of 3-(trimethylstannyl)cyclobutene gave a mixture of the (*Z*)- and (*E*)-1,3-dienes, whereas that of 3-*tert*-butylcyclobutene exclusively afforded the (*E*)-1,3-diene due to the steric influences. The contrasting rotational behaviors suggest that there is some effect operating with the 3-stannylcyclobutene to stabilize the inward transition state, counteracting the steric influences. This contrasteric effect is ascribed to negative hyperconjugation. The stannyl group in the inward transition state accommodates electron density from the breaking σ orbital of the cyclobutene into its low-lying tin−carbon σ^* orbital. Theoretical studies supported this interpretation.

The thermal conrotatory ring-opening reaction of cyclobutene to produce 1,3-butadiene is one of the most fundamental concerted electrocyclic reactions. During this reaction, substituents located at the 3-position rotate in either an outward or an inward direction. The selectivity of the rotational direction of the substituent is termed *torquoselectivity*. Theoretical studies by Rondan and Houk revealed that torquoselectivity is subject to electronic control as well as steric control.[1] While an electron-donating substituent prefers outward rotation, an electron-accepting substituent favors inward rotation despite the resulting steric congestion. Yet the experimental verifications for the inward preference of an electron-accepting substituent have been limited.[2] Recently, we have discovered the interesting effects that a silyl substituent has on the thermal conrotatory ring opening reaction of 3-silylcyclobutene.[3] Although it is σ-donative and stereodemanding, the silyl substituent accelerates the reaction and prefers inward rotation to furnish (*Z*)-1-silyl-1,3-
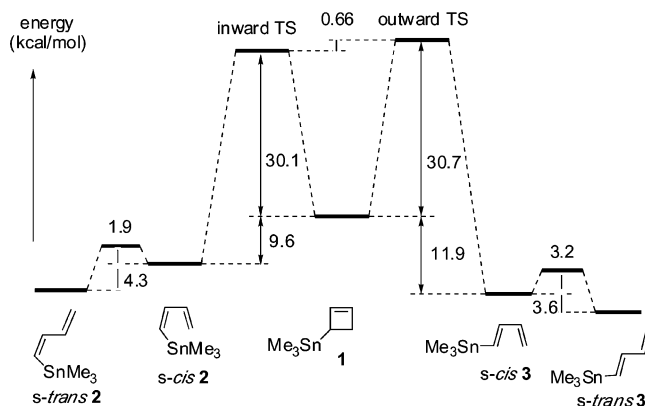
FIGURE 1. Potential energy diagram of ring opening of 3-(trimethylstannyl)cyclobutene **1**.

butadiene rather than the (*E*)-isomer.[4] These effects are primarily explained by assuming that the inward transition state is stabilized by electron delocalization from the breaking C−C σ orbital of cyclobutene to the low-lying Si−C σ^* orbital.[5] This previous study on 3-silylcyclobutene prompted us to expect analogous effects with a stannyl substituent, since a tin−carbon bond also has a low-lying σ^* orbital.[6] Herein we report the results of the theoretical and experimental studies on the thermal ring-opening reaction of 3-stannylcyclobutene.

At first, we carried out theoretical calculations employing 3-(trimethylstannyl)cyclobutene **1** as a model. The ground states of the reactant (**1**) and the products (**2** and **3**), as well as the transition states of the outward and inward rotations, were determined by density functional calculations. The energy diagram is shown in Figure 1. The activation energy of the inward rotation is 0.66 kcal/mol *lower* than that of the outward rotation. These results predict that inward rotation would be favored over outward rotation, despite the obvious steric congestion that arises. The initial products, (*Z*)- and (*E*)-1-stannyl-1,3-butadienes (**2** and **3**, respectively), in s-cis conformations ultimately rotate to s-trans conformations. (*E*)-1-Stannyl-1,3-butadiene **3** in an s-trans conformation is thermodynamically more stable than the corresponding (*Z*)-1-stannyl-1,3-butadiene **2** by 1.6 kcal/mol.

For the corresponding silicon analogue, it has been reported that the activation energy of the inward rotation is 1.0−1.3 kcal/mol lower than that of the outward rotation.[5]

For comparison, we also carried out calculations on 3-*tert*-butylcyclobutene **4** (Figure 2). The structure of the model cyclobutene **4** is identical to that of **1** except for the tertiary element; the tin atom of **1** is replaced by a carbon atom in **4**. The activation energy for outward

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(1) (a) Kirmse, W.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1984**, *106*, 7989. (b) Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 2099.

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(4) An analogous effect has been reported in the ring opening of oxetene: Shindo, M.; Matsumoto, K.; Mori, S.; Shishido, K. *J. Am. Chem. Soc.* **2002**, *124*, 6840.

(5) A recent theoretical paper by Houk et al. supports our interpretation: Lee, P. S.; Zhang, X.; Houk, K. N. *J. Am. Chem. Soc.* **2003**, *125*, 5072. For a different explanation assuming geminal σ bond participation, see: Ikeda, H.; Kato, T.; Inagaki, S. *Chem. Lett.* **2001**, 270.

(6) Giordan, J. C.; Moore, J. H. *J. Am. Chem. Soc.* **1983**, *105*, 6541.
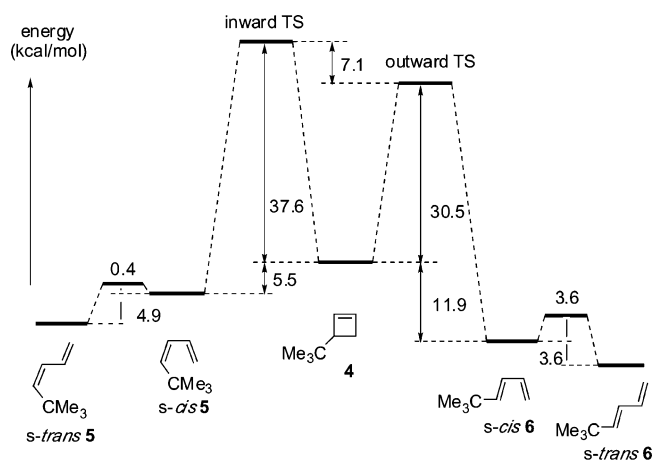
FIGURE 2. Potential energy diagram of ring opening of 3-*tert*-butylcyclobutene **4**.

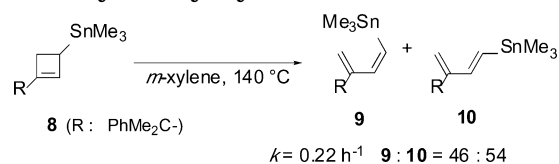**SCHEME 1. Synthesis of 1-Substituted 3-(Trimethylstannyl)cyclobutene 8**
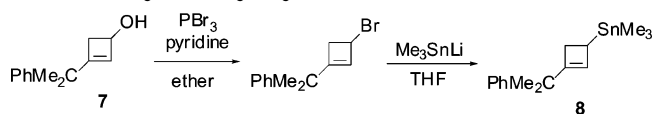
rotation (30.5 kcal/mol) is similar to that of the tin analogue **1** (30.7 kcal/mol). Unlike the case of **1**, however, the inward transition state of **4** is higher than the outward one by as much as 7.1 kcal/mol. This remarkable difference between the inward and outward transition states, which is even larger than that for 3-methyl-cyclobutene [5.3 kcal/mol (MP2/6-31G*//3-21G)],[7] is primarily ascribed to steric repulsions that arise on inward rotation of the bulkier *tert*-butyl group.[8] As for the ring-opened products, (*E*)-1-*tert*-butyl-1,3-butadiene **6** in the s-trans conformation is thermodynamically more stable than the corresponding (*Z*)-isomer (**5**) by 5.1 kcal/mol.

The contrasting stereochemical trends were theoretically predicted for 3-stannylcyclobutene **1** and the carbon analogue **4**. This suggests that there is a contrasteric effect operating with **1** to stabilize the inward transition state, which otherwise simple steric influences would intrinsically disfavor. We next tested and verified the theoretical results by experiments. 3-(Trimethylstannyl)-cyclobutene **8** was synthesized as shown in Scheme 1. The hydroxyl group of 1-substituted cyclobuten-3-ol **7** was substituted first by a bromide ion and then by a trim-ethylstannyl anion. As a result, the stannyl group was introduced at the less substituted allylic positions.

The ring-opening reaction of **8** was conducted in the dark in the presence of a small amount of 2,6-di-*tert*-butyl-4-methylphenol (BHT) in order to suppress any radical pathways. It proceeded with a rate of $k = 0.22$ h^{-1} at 140 °C and was almost complete after 15 h. A mixture of (*Z*)- and (*E*)-1-stannyl-1,3-butadienes **9** and **10**, respectively, was formed in a ratio of 46:54.[9] The ratio

(7) Niwayama, S.; Kallel, E. A.; Spellmeyer, D. C.; Chimin, C.; Houk, K. N. *J. Org. Chem.* **1996**, *61*, 2813.

(8) Kallel, E. A.; Wang, Y.; Spellmeyer, D. C.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 6759.

(9) Stereochemical assignments were based on the vicinal coupling constants of the olefinic protons: $J = 13.2$ Hz for (*Z*)-butadiene **9**, and $J = 19.2$ Hz for (*E*)-butadiene **10**.

SCHEME 2. Ring Opening of 1-Substituted 3-(Trimethylstannyl)cyclobutene 8

SCHEME 3. Ring Opening of 1-Substituted 3-(*tert*-Butyl)cyclobutene 11
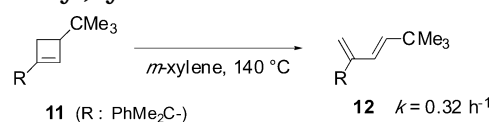
was constant throughout the reaction, and even after a longer period of time.

The two isomeric butadienes were separated by chromatography and independently heated at 140 °C. Neither **9** or **10** isomerized to the other isomer in the presence of BHT. On the contrary, when heated in the *absence* of BHT, (*Z*)-1,3-butadiene **9** gradually isomerized to the (*E*)-butadiene **10**, probably via a radical pathway, while (*E*)-butadiene **10** remained unchanged. These experimental results suggest that (*E*)-butadiene **10** is thermodynamically more stable than (*Z*)-isomer **9**, consistent with the theoretical results.

These experiments established that the isomeric ratio **9**:**10** = 46:54 observed in the ring-opening reaction of **8** at 140 °C in the presence of BHT was *kinetically* determined. Thus, it was experimentally proved that the inward and outward transition states are of approximately the same energy, although the calculations predicted the inward preference for the stannyl group by 0.66 kcal/mol.[10] In the case of **8**, the bulky 1-methyl-1-phenylethyl substituent located at the 1-position may extend the steric influences to cancel the advantage of the inward transition state.

As reported previously,[3a] 3-*tert*-butylcyclobutene **11**, which is the exact carbon analogue of **8**, undergoes unidirectional outward ring opening to form the (*E*)-isomer **12** exclusively (Scheme 3). This torquoselectivity agrees with the theoretical result on the model compound (**4**) mentioned above.

Both calculations and experiments have shown that, in contrast to a tertiary butyl substituent, which exerts steric influences to hamper inward rotation, the trim-ethylstannyl group has an extraordinary electronic effect that counterbalances the steric effect. We interpreted this contrasteric effect observed with 3-stannylcyclobutene in terms of negative hyperconjugation, as with the case of 3-silylcyclobutene.[3a] Because of the electronegativity difference between Sn and C, the Sn−C antibonding orbital is polarized toward the tin atom. Energetically, this antibonding orbital lies even lower than the antibonding σ^* orbital of an Si−C linkage.[6] Hence, the σ^* orbital of an Sn−C linkage can accommodate electron density from an appropriate donor orbital, provided that they are geometrically as well as energetically located close enough.
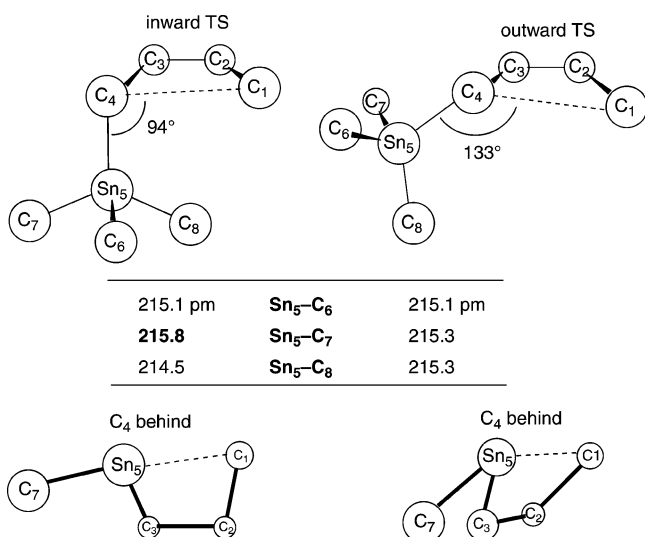
The calculated structures of the inward and outward transition states of **1** are shown in Figure 3 with some

(10) Corresponds to a 69:31 ratio at 140 °C.

FIGURE 3. Transition state structures of the ring opening of **1** (at the bottom are projections from the Sn_5-C_4(behind) axes, wherein the C6 and C8 atoms have been omitted).

TABLE 1. Populations in the Natural Bond Orbitals

inward TS			outward TS	
σ-orbital	σ^*-orbital		σ-orbital	σ^*-orbital
1.9642	0.0480	Sn_5-C_6	1.9676	0.0364
1.9594	0.0557	Sn_5-C_7	1.9639	0.0371
1.9641	0.0388	Sn_5-C_8	1.9661	0.0397

geometrical values being noted. In the inward transition state, the angle $C_1C_4Sn_5$ is 94° and the dihedral angle $C_1C_4Sn_5C_7$ is 171°. Thus, the Sn_5-C_7 σ^* orbital is located right at the position to accommodate the HOMO electron that is concentrated around the breaking C_1-C_4 σ bond. On the other hand, the angle $C_1C_4Sn_5$ in the outward transition state is as much as 133°. This larger angle of $C_1C_4Sn_5$ keeps the Sn−C σ^* orbitals away from the HOMO electron around the breaking C_1-C_4 bond, diminishing an analogous hyperconjugative stabilizing interaction.

Other calculated structural features also support the stabilization of the inward transition state by negative hyperconjugation. Among the three $Sn-CH_3$ bonds of the inward transition states, the Sn_5-C_7 bond is longer than the other two by 0.7 and 1.3 pm, respectively. The hyperconjugative delocalization increases the electron density in the Sn_5-C_7 σ^* orbital, weakens the σ bond and, consequently, elongates it. In the outward transition state, all three $Sn-CH_3$ distances fall into a narrow range of 215.1−215.3 pm, suggesting a lack of hyperconjugative delocalization with a σ^* orbital.

Finally, the hyperconjugative delocalization is manifested in the natural bond orbital (NBO) analysis[11] (Table 1). A consistent trend is observed in the NBO occupancies of the $Sn-CH_3$ bonds in the inward transition states. The Sn_5-C_7 bond of the inward transition state has a substantially lower occupancy of the bonding σ orbital and a higher occupancy of the antibonding σ^* orbital relative to the other $Sn-CH_3$ bonds. The stabilization
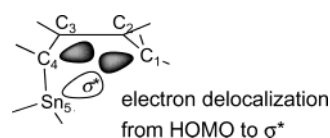

FIGURE 4. Hyperconjugation of the σ^*Sn-C orbital with the HOMO in the inward transition state.

energy associated with delocalization from the bonding C_1-C_4 orbital to the antibonding Sn_5-C_7 orbital is estimated to be 3.5 kcal/mol in the inward transition state and 1.2 kcal/mol in the outward transition state.

Thus, we interpret the contrasteric rotational behavior of 3-stannylcyclobutene by assuming that the inward transition state gains the negative hyperconjugative stabilization, which counteracts the unfavorable steric influences (Figure 4).

Interestingly, the effects of the stannyl group on the rate and the inward preference in the ring opening of **8** were not larger than those observed with the silicone analogue **13** [$k = 0.53$ h^{-1} at 140 °C, (Z):(E) = 69:31].[3a] This can be ascribed to a longer Sn−C bond length (ca. 215 pm) relative to an Si−C bond length (ca. 187 pm). Actually, the Sn_5-C_1 distance in the inward transition state of **1** (316 pm) is larger than the corresponding Si_5-C_1 distance for the silicon case (302 pm). The geometrical remoteness would decrease the overlap between the σ^* orbital and the breaking HOMO orbital.[6]

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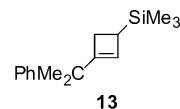
The ring opening of 3-(trimethylstannyl)cyclobutene was shown to give a mixture of the (Z)- and (E)-1,3-dienes, whereas that of 3-tert-butylcyclobutene exclusively afforded the (E)-1,3-diene. The contrasteric effect that the stannyl group exerts to lower the activation barrier for inward rotation is ascribed to the negative hyperconjugative stabilization. This interpretation is in line with the hypothesis by Rondan and Houk that a preference for inward rotation originates from the electron-accepting interaction of a substituent with the breaking HOMO orbital.[1]

A tin atom can exercise ambivalent electronic effects on reactions of an organotin compound; with an Sn−C σ bond, the tin atom donates electron density toward the carbon. In contrast, the unoccupied antibonding orbital of an Sn−C linkage is energetically low-lying and may accept electron density if there is an appropriate electron donor nearby. The latter electron-accepting feature was clearly exemplified by the present study. In addition, this work provides the first example in which a stannyl substituent extends electronic influences over the stereochemical course of a purely thermal concerted electrocyclic reaction.[12]

Methods

Theoretical Calculations. The density functional calculations using the Lee−Yang−Parr form of the correlation functional and the Becke exchange (B3LYP) were conducted with

(11) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.

(12) For the rhodium-catalyzed cyclopropanation, see: Lin, Y.-L.; Turos, E. *J. Organomet. Chem.* **2001**, *630*, 57.

the Gaussian 98 program (Gaussian 98, Revision A.6; Gaussian, Inc.: Pittsburgh, PA, 1998). Geometries and energies of ground states of organotin compounds (**1**−**3**) and the transition states of the ring-opening reactions were obtained by using LANL2DZ basis sets augmented by one polarization function on H and C. The effective core potential with triple-ζ basis set plus p- and d-type polarizations functions was used for Sn. Calculations on the carbon analogue (**4**) were carried out using 6-31G(d) basis sets. All geometries obtained here were fully optimized by the gradient methods, and all energies include zero-point energies. Frequency calculations verified that all the stable points are true local minima and all transition states have only one imaginary frequency.

THF Solution of (Trimethylstannyl)lithium. Under an argon atmosphere, lithium granules (278 mg, 40 mmol) and dry THF (8 mL) were placed in a flask equipped with a dropping funnel. A THF solution of chlorotrimethyltin (8.0 mL, 1.0 M) was added at 0 °C, and the mixture was stirred vigorously for 3 h. The resulting green solution of (trimethylstannyl)lithium (approximately 0.5 M) was used without storing.

1-(1-Methyl-1-phenylethyl)-3-(trimethylstannyl)cyclobutene (8). To a solution of the cyclobutenol **7** (1.25 g, 6.6 mmol) and pyridine (0.63 mL, 6.6 mmol) in Et$_2$O (15 mL) at 0 °C was added dropwise tribromophosphine (0.54 mL, 6.6 mmol). Ice−water was added after the mixture was stirred for 1 h. The mixture was extracted with ether three times. The combined organic layer was washed with brine, dried over MgSO$_4$, and evaporated in vacuo. The residue was quickly passed through a short column of florisil with hexane/ether (20:1) to afford the 3-bromocyclobutene, which was immediately used in the next step.

To a THF solution (10 mL) of the 3-bromocyclobutene (500 mg, 2.0 mmol) at −78 °C was added dropwise a THF solution of (trimethylstannyl)lithium (4.0 mL, 0.5 M). The reaction was monitored by GC. After the starting material was consumed, water was carefully added. The mixture was extracted with ether three times. The combined organic layer was washed with brine, dried over MgSO$_4$, and evaporated in vacuo. The residue was quickly passed through a short column of florisil with hexane to afford **8** (210 mg, 10% in two steps). ^{1}H NMR: δ 0.04 (t, $J = 25.2$ Hz, 9H), 1.41 (d, $J = 4.0$ Hz, 6H), 2.43 (d, $J = 13.6$ Hz, 1H), 2.42 (d, $J = 4.4$ Hz, 1H), 2.69 (dd, $J = 13.6, 4.4$ Hz, 1H), 4.07 (s, 1H), 7.15−7.19 (m, 1H), 7.25−7.36 (m, 4H). ^{13}C NMR: δ 11.1, 25.2, 27.2, 27.6, 32.7, 40.5, 125.6, 126.2, 128.0, 130.2, 147.7, 153.0. HRMS: calcd for C$_{16}$H$_{24}$Sn, 336.0900; found, 336.0902.

Thermal Ring-Opening Reaction of 8. A degassed *m*-xylene solution (10 mL) of **8** (80 mg, 0.24 mmol) and BHT (5.2 mg, 10 mol %) was heated at 140 °C in the dark. A portion of the solution was taken out of the flask by a syringe at intervals, evaporated, and monitored by ^{1}H NMR. (*Z*)-butadiene **9**: δ 0.17 (s, 9H), 1.42 (s, 6H), 5.02 (s, 1H), 5.13 (s, 1H), 5.77 (d, $J = 13.2$ Hz, 1H), 6.57 (d, $J = 13.2$ Hz, 1H), 7.14−7.37 (m, 5H). (*E*)-butadiene **10**: δ 0.02 (s, 9H), 1.45 (s, 6H), 5.08 (s, 1H), 5.33 (s, 1H), 6.07 (d, $J = 19.2$ Hz, 1H), 6.31 (d, $J = 19.2$ Hz, 1H), 7.14−7.37 (m, 5H).

Supporting Information Available: Experimental procedures, optimized geometries of stationary points as Cartesian coordinates, and copies of ^{1}H (**9** and **10**) and ^{13}C (**8**) NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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