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Accelerated Electrocyclic Ring-Opening of Benzocyclobutenes under the Influence of a β-Silicon Atom

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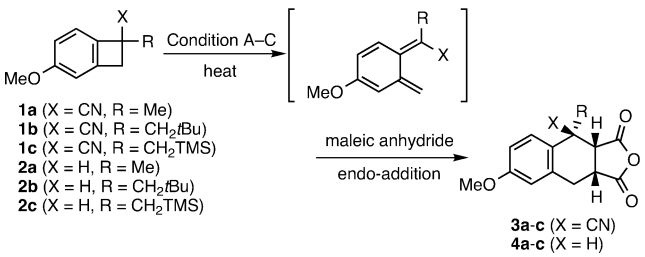
Interconversion between cyclobutenes and 1,3-dienes is one of the most familiar and fundamental electrocyclic reactions. Thermal conrotatory process of this reaction has been proven by both theoretical and experimental studies,[1] and the direction of the conrotation, either inward or outward in the case of 3-substituted cyclobutenes (i.e., "torquoselectivity"), has been increasingly predictable owing to the extensive research in this field.[2] In particular, recent topical reports on this subject have dealt with a remarkable effect of 3-silyl substituents, which prefer inward rotation despite the steric congestion and significantly accelerate the electrocyclic ring-opening reaction.[3] Similar cleavage rate enhancement of cyclobutenes has also been documented for the 3-hydroxy (and its anion)[4] and 3-dithioketal derivatives[5] as well as the cyclobutenes bearing an adjoining carbanion stabilized by a sulfur or a phosphorus atom at the 3-position.[6] It is expected that these substituent effects affecting the rate of the electrocyclic reaction will be exhibited in the conversion of benzocyclobutenes to *o*-quinodimethanes. In fact, remarkable acceleration of the *o*-quinodimethane formation through the thermal electrocyclic ring opening has been reported under influence of α-oxy anionic centers on the cyclobutene ring.[7] However, qualitative and quantitative studies on the acceleration of the electrocyclic ring opening of benzocyclobutenes are surprisingly limited,[8] although this transformation has been widely applied to the stereoselective construction of a variety of complex molecules such as steroids and alkaloids.[9] Herein, we wish to report the first observation on the acceleration of *o*-quinodimethane formation caused by a β-silicon atom on the cyclobutene ring.

Unlike the case of the electrocyclic reaction of monocyclic cyclobutenes, an immediate evaluation of the reaction efficiency seems to be difficult with regard to benzocyclobutenes, because of the instability of the *o*-quinodimethanes produced and easy cycloreversion due to the stable 6π system of the benzene ring. These drawbacks, however, can be overcome by a rapid Diels−Alder capture of the *o*-quinodimethanes utilizing a highly reactive dienophile such as maleic anhydride, as demonstrated in the study on torquoselectivity of benzocyclobutenes.[10] In the course of our continuous research on *o*-quinodimethane chemistry,[9,11] we focused our interest on the substituent effect for the thermal cleavage of benzocyclobutenes, especially on the silyl substituents in conjunction with recent reports on their rate enhancement effects for that of monocyclic cyclobutenes.[3] Therefore, we prepared several silylated benzocyclobutenes as well as the corresponding alkylated compounds for comparison (**1a**−**c** and **2a**−**c**)[12] from readily available 4-methoxybenzocyclobutene-1-carbonitrile.[13]

The compounds **1a**−**c** and **2a**−**c** were conducted to the thermal electrocyclic reaction involving a concurrent [4 + 2] cycloaddition with maleic anhydride. Three different conditions were applied to each compound to estimate and compare the reaction efficiencies in the presence of an excess amount of the dienophile (Scheme 1). As shown in Figure 1a, when compound **1a** was subjected to

Scheme 1



condition A (toluene, reflux, 24 h), only a small amount of an adduct **3a** was formed (9% yield). Likewise, compound **1b** afforded **3b** in only 30% yield. On the other hand, a notable acceleration of the reaction was observed for the β-silylated benzocyclobutene **1c**, which gave an adduct **3c** in 68% yield under the same condition. A similar effect of the silyl group was also noticed under condition B (xylene, reflux, 3 h), in which compound **1c** gave a nearly quantitative yield of **3c** as compared with **1a** and **1b** resulting in low to moderate yields. Under the more drastic condition C (*o*-dichlorobenzene, reflux, 2 h), all three substrates were almost transformed into adduct **3**, although a slight difference was observed among the yields. Products **3a**−**c** were formed as a purely single stereoisomer, depicted in Scheme 1.[14] This fact showed that the reaction proceeded through the formation of the *o*-quinodimethane having indicated geometry followed by the endo cycloaddition with the dienophile (Scheme 1), in consideration of a strong preference of maleic anhydride for endo addition[10,15] and reported torquoselectivity of benzocyclobutenes.[10] The same experiments were repeated using compounds **2a**−**c** as a substrate, and a similar acceleration effect of the β-silyl group was confirmed as shown in Figure 1b. A stereochemical outcome of adducts **4a**−**c** was again dictated by the outward torquoselectivity of the substituent R, affording the same stereoisomer as **3a**−**c** as a major product, concomitant with a small amount of the diastereomer (R = β-configuration, ratio 1/10 to 1/15).[16]

In every case, no side reactions were involved and the starting benzocyclobutenes remained unchanged when the reactions were

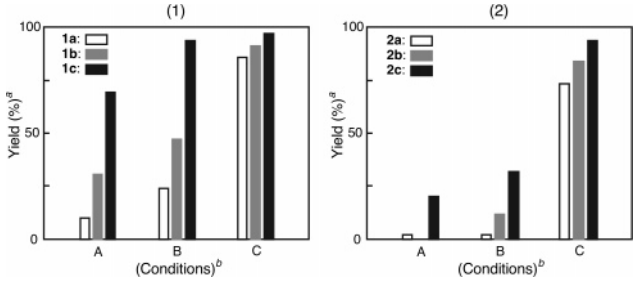


Figure 1. Comparison of the *o*-quinodimethane formation efficiency among compounds **1a**−**c** (a) and **2a**−**c** (b). Yield was estimated by ^{1}H NMR spectroscopy using an internal standard. Conditions were as follow. A: Reflux in toluene (110 °C), 24 h. B: Reflux in xylenes (140 °C), 3 h. C: Reflux in *o*-dichlorobenzene (180 °C), 2 h.

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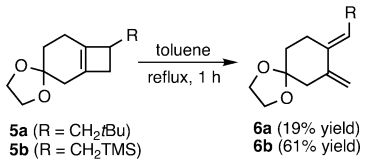
Scheme 2



5a (R = CH_2tBu)
5b (R = CH_2TMS)

6a (19% yield)
6b (61% yield)

incomplete. In addition, 1,5-sigmatropic rearrangement of the *o*-quinodimethane to give a toluene derivative,[17] which often competes with the Diels−Alder reaction, could not be observed at all. These facts indicate that the Diels−Alder trap was so sufficiently rapid that the yields shown in Figure 1 could reflect the efficiency of the electrocyclic ring opening of the benzocyclobutene derivatives. It is an important note that the structural difference between **1b** (**2b**) and **1c** (**2c**) is only the kind of β-element, carbon or silicon, minimizing a steric factor on the reaction. Thus, we can consider that the β-silyl substituent on the benzocyclobutene ring causes a significant acceleration effect on the electrocyclic reaction.

A rationale for the observed acceleration effect still remains unclear, but apparently it should differ from that of the α-silyl effect reported for monocyclic cyclobutenes,[18] where it has been reasonably explained by the electronic interaction between the low-lying σ^* orbital of a silicon atom and the HOMO concentrated on the cleaving C−C σ-bond, in the inward transition state.[3] The β-silicon atom, however, cannot participate in such interactions because of a longer distance from the cleaving bond, and moreover because the silyl-containing substituent showed a high degree of outward torquoselectivity in the present experiments. We are assuming that the present acceleration effect can be attributed to the σ-donating ability of the C(α)−Si(β) bond, which is associated with so-called β-effect of a silicon atom. This assumption closely relates to electrocyclic reactions accelerated by α-anion, mainly including α-oxy anion, which is a good electron donor and can weaken an adjacent σ-bond (cloven during the electrocyclic process).[19] In fact, the degree of the σ-donating ability of the C(α)−X(β) bond in the test compounds used here seems to be parallel with the results shown in Figure 1, which reflect the efficiency of the electrocyclic reaction; namely, σ_{C-H} (**1a**, **2a**) < $\sigma_{C-C(4°)}$ (**1b**, **2b**) < σ_{C-Si} (**1c**, **2c**). This relationship suggests that the σ-donating nature of the C−Si bond can facilitate the *o*-quinodimethane formation of the benzocyclobutenes through the electrocyclic bond cleavage.

Finally, we performed an analogous examination utilizing simple, non-benzo-type cyclobutene derivatives **5a** and **5b**, which were easily prepared from **1b** and **1c**, respectively, by means of Birch reduction followed by ketalization.[12] As shown in Scheme 2, substrate **5a** gave a ring-opened diene product **6a** only in 19% yield after 1 h in refluxing toluene, whereas the corresponding β-silyl substrate **5b** afforded a diene **6b** in 61% yield under the same condition.[14,20] These results clearly indicate that the accelerating effect of a β-silyl element can have a wide generality for the electrocyclic ring cleavage reaction of various cyclobutene derivatives.

In this communication, we first disclosed a significant acceleration of the electrocyclic ring opening of benzocyclobutene derivatives under the influence of a β-silicon atom. These effects are associated with the adjacent anion driven electrocyclic reactions such as oxy-Cope rearrangement, in light of a strong σ-donating effect of a C−Si bond. Further mechanistic considerations including theoretical studies will be performed and reported in due course.

Supporting Information Available: Details of experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) These thermal reactions proceeded cleanly without any side reactions, and NMR analyses of the reaction mixture indicated the presence of only dienes and cyclobutenes. The torquoselectivity of the reaction was exclusively outward, which was confirmed by NOE observation of the product dienes.

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