Stereoselective Synthesis of Isomeric Functionalized 1,3-Dienes from Cyclobutenones

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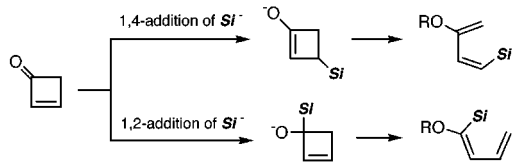
The synthesis of organic compounds with control over stereochemistry is a subject of continuing interest. As olefins are often key starting materials for the construction of a wide variety of complex molecules, methods for synthesizing them as pure geometric isomers are especially important. In this report, we describe a novel method for the stereoselective synthesis of functionalized 1,3-butadiene derivatives from cyclobutenones via a torquoselective electrocyclic ring-opening reaction of cyclobutene intermediates.[1]

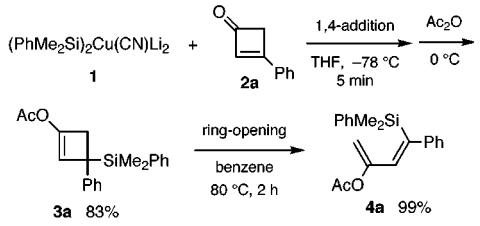
This strategy emanates from our recent discovery of the remarkable effect that silyl substituents have on the ring-opening reaction of cyclobutenes.[2] A silyl substituent at the 3-position accelerates the electrocyclic reaction, and inter alia promotes inward rotation despite the resulting steric congestion experienced in the product. These intriguing effects were explained by the electron-accepting interactions between the low-lying σ^* orbital of the silicon atom and the HOMO orbital of the opening cyclobutene system, possible only in the inward transition state.[3] As shown in eq 1, the starting silyl-substituted cyclobutenes



(1)

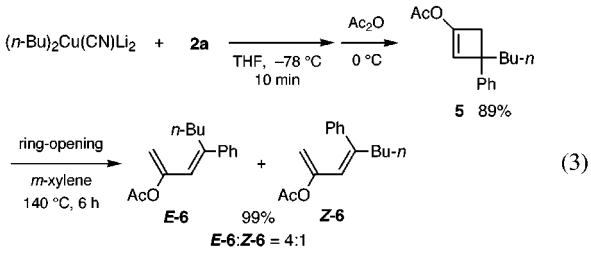
required for this strategy can be conveniently prepared from cyclobutenones.[4,5] Addition of a silyl nucleophile, either in a 1,4- or 1,2-fashion, provides an efficient route to 3-silyl-1-cyclobutene, which opens up to isomeric functionalized 1,3-diene.

To effect the 1,4-addition, cyclobutenone **2a** was treated with silylcuprate **1**[6] at −78 °C for 5 min. The resultant 1,4-adduct was trapped with acetic anhydride to afford 3-silyl-1-cyclobutene **3a** in 83% yield (eq 2).[7] When heated in refluxing benzene for 2 h, **3a** underwent a ring-opening reaction with unidirectional rotation of the substituents. The silyl group rotated inward and the phenyl group outward[8] to furnish the 1-silyl-1,3-diene having *Z*-geometry **4a** in 99% yield.[7] The other stereoisomer was not detected.



(2)

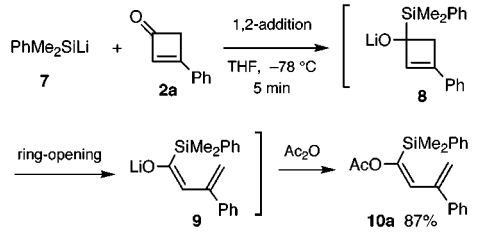
To examine the effect of silicon on this rearrangement, substrate **5**[7] was prepared by reaction of $(n\text{-Bu})_2\text{Cu(CN)Li}_2$ with **2a** followed by treatment with acetic anhydride (eq 3). Unlike **3a**,



(3)

cyclobutene **5** was unreactive even in refluxing toluene (110 °C). Ring-opening was observed at 140 °C to afford a mixture of *E*-**6** and *Z*-**6**.[7] In this case, the butyl and phenyl groups competed for outward rotation.[9] These results clearly demonstrate that the silyl group of **3a** plays the dual role of accelerating the ring-opening reaction and controlling the torquoselectivity.

We surmised that isomeric 3-silyl-1-cyclobutenes such as **8** could be obtained by the 1,2-addition of silyllithium reagents to cyclobutenones. Reaction of cyclobutenone **2a** with silyllithium **7** in THF at −78 °C followed by treatment with acetic anhydride did not, in fact, provide the expected cyclobutene derivative. Instead, **2a** was directly converted to a 1-silyl-1,3-diene having *Z*-geometry (**10a**) in 87% yield (eq 4).[7] The other stereoisomer



(4)

was not detected. Stereoselective formation of **10a** was explained by assuming that the 1,2-addition of **7** to the carbonyl group was followed by immediate and torquoselective ring-opening of the 1,2-adduct **8**. The resulting lithium enolate **9** was trapped with acetic anhydride to give **10a**, a constitutional isomer of **4a**.

As previously noted, the thermal ring-opening of cyclobutenes **3a** is accelerated by the silyl substituent, but still requires heating at 80 °C. Therefore, the direct ring-opening reaction of intermediate **8** at −78 °C was quite remarkable. As a comparison, butyllithium was reacted with **2a**. Unlike **8**, the intermediate 1,2-adduct **11** failed to undergo a ring-opening reaction at −78 °C, and after aqueous workup, cyclobutenol **12** was obtained in 84% yield (eq 5).[7] However, when the reaction with butyllithium was carried out at 0 °C, the intermediate 1,2-adduct **11** did undergo spontaneous ring-opening to give 1,3-diene **13** (64% yield) after treatment with acetic anhydride.[7] On the other hand, ring-opening

(1) For an excellent review on torquoselective ring-opening reactions of cyclobutenes, see: Dolbier, W. R., Jr.; Koroniak, H.; Houk, K. N.; Sheu, C. *Acc. Chem. Res.* **1996**, *29*, 471.

(2) Murakami, M.; Miyamoto, Y.; Ito, Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 189.

(3) A different explanation assuming geminal σ bond participation recently appeared: Ikeda, H.; Kato, T.; Inagaki, S. *Chem. Lett.* **2001**, 270.

(4) For the preparation of cyclobutenones, see: (a) Danheiser, R. L.; Savariar, S. *Tetrahedron Lett.* **1987**, *28*, 3299. (b) Ammann, A. A.; Rey, M.; Dreiding, A. S. *Helv. Chim. Acta* **1987**, *70*, 321.

(5) A cyclobutenone itself undergoes an electrocyclic ring-opening reaction: (a) Danheiser, R. L.; Gee, S. K. *J. Org. Chem.* **1984**, *49*, 1672. (b) Danheiser, R. L.; Nishida, A.; Savariar, S.; Trova, M. P. *Tetrahedron Lett.* **1988**, *29*, 4917 and references therein.

(6) Crump, R. A. N. C.; Fleming, I.; Hill, J. H. M.; Parker, D.; Reddy, N. L.; Waterson, D. *J. Chem. Soc., Perkin Trans. 1* **1991**, 3277.

(7) The products were satisfactorily characterized by ^{1}H and ^{13}C NMR and elemental composition established by combustion analysis or HRMS. See Supporting Information.

(8) Pomerantz, M.; Hartman, P. H. *Tetrahedron Lett.* **1968**, 991.

(9) Curry, M. J.; Stevens, I. D. R. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1391.

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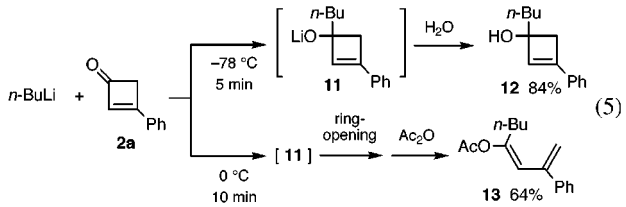
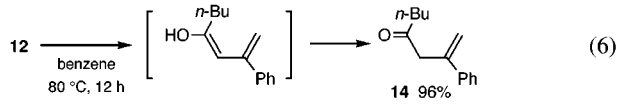
of the isolated cyclobutenol **12** occurred only after heating in refluxing benzene. Nonconjugated β,γ-unsaturated ketone **14** was obtained in 96% yield,[7] suggesting outward rotation of the hydroxyl group (eq 6).[10] Note this temperature with **12** is still considerably milder than that required for ring-opening of **5**.



(5)



(6)

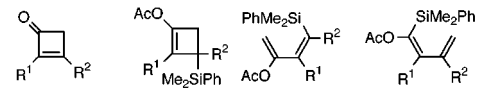
These results demonstrated that an oxy substituent at the 3-position facilitates the ring-opening reaction and favors outward rotation.[11] Both an anionic oxy substituent and a neutral hydroxyl group are accelerating, but the former has a larger effect.[12] Therefore, the remarkably fast ring-opening reaction of intermediate **8** can be explained by the combined effects of the silyl substituent and the anionic oxy substituent, both placed at the 3-position. Moreover, as the rotational preferences of both substituents are matched, the *Z*-isomer **9** is formed exclusively.

(10) Inward rotation would have caused facile 1,5-hydrogen shift to afford an α,β-unsaturated ketone: Jefford, C. W.; Boschung, A. F.; Rimbault, C. G. *Tetrahedron Lett.* **1974**, 3387.

(11) Kirmse, W.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1984**, *106*, 7989.

(12) For examples for α-anion driven pericyclic reactions, see: (a) Choy, W.; Yang, H. *J. Org. Chem.* **1988**, *53*, 5796. (b) Kametani, T.; Tsubuki, M.; Nemoto, H.; Suzuki, K. *J. Am. Chem. Soc.* **1981**, *103*, 1256. (c) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765. (d) Hill, R. K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 785−826. (e) Bronson, J. J.; Danheiser, R. L. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 999−1035.

Table 1. Synthesis of 1-Silyl-1,3-dienes **4** and **10**



2 / R^1, R^2	**3** / % [a]	**4** / % [b]	**10** / % [c]
2b / H, *n*-Bu	**3b** / 83	**4b** / 98	**10b** / 81
2c / H, *t*-Bu	**3c** / 85	**4c** / 96	**10c** / 83
2d / *n*-Pr, *n*-Pr	**3d** / 85	**4d** / 99 [d]	**10d** / 78

[a] $(PhMe_2Si)_2Cu(CN)Li_2$ (1.1 equiv), THF, −78 °C, 5 min, then Ac_2O (1.2 equiv), 0 °C, 10 min. [b] Benzene, 80 °C, 2 h. [c] $PhMe_2SiLi$ (1.1 equiv), THF, −78 °C, 5 min, then Ac_2O (1.2 equiv), −78 °C, 10 min. [d] Toluene, 110 °C, 3 h.

When the lithium enolate **9** was trapped with chlorosilane, a 1-siloxy-1-silyl-1,3-diene having *Z*-geometry (**15**) was obtained in 88% yield (eq 7).[7] Similar 1,3-dienes having *E*-geometry can

(7)

be prepared by the allylsilane carbonylation described by Murai and co-workers.[13] The stereochemistry observed in our reaction is complementary to the carbonylative method.

Other examples of the stereoselective synthesis of 1-silyl-1,3-dienes **4** and **10** from cyclobutenones **2** are listed in Table 1.[7]

In conclusion, the highly functionalized 1,3-dienes are synthesized as single isomers via the ring-opening of cyclobutenes, which are conveniently prepared from cyclobutenones. The success of the synthetic scheme arises from the substituents located at the 3-position, which accelerate the ring-opening reaction and provide complete control over the torquoselectivity.

Supporting Information Available: Experimatal details (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA010639I

(13) Ryu, I.; Yamamoto, H.; Sonoda, N.; Murai, S. *Organometallics* **1996**, *15*, 5459.