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Electron Transfer Promoted Regioselective Ring-Opening Reaction of Cyclopropyl Silyl Ethers†

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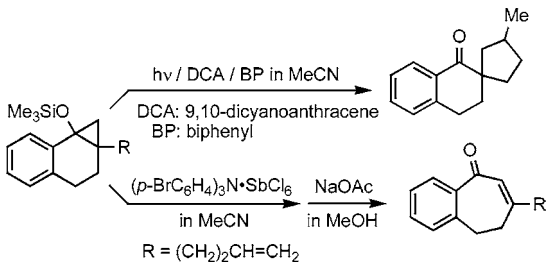
ABSTRACT



Oxidative ring-opening reactions of cyclopropyl silyl ethers incorporated into bicyclo[*m*.1.0]alkane framework were investigated. The results show that the regioselectivities for ring-opening of intermediate radical cations, formed by single electron transfer, are governed by the nature of the nucleophile as well as oxidizing species.

Radical ions that are generated by single electron transfer (SET) reduction and oxidation (redox) of neutral organic molecules have been extensively investigated due to the frequent role they play as intermediates in chemical and biological redox processes.[1,2] Photoinduced electron transfer (PET) is a repeatedly employed method used to generate radical ions.[1,3] Owing to the characteristic reactivity of their radical cations, cyclopropanol derivatives are both mechanistically and synthetically attractive substrates.[4] Many examples of electron transfer reactions of cyclopropanol derivatives with various metal-based oxidizing agents have been reported.[5] Surprisingly, only a few examples of PET-induced cyclopropane ring-opening reactions of cyclopropanol derivatives have been described[6] in spite of the fact

† Dedicated to Professor Patrick S. Mariano (University of New Mexico), who is a pioneer of mechanistic as well as synthetic photoinduced electron transfer chemistry, on the occasion of his 65th birthday.

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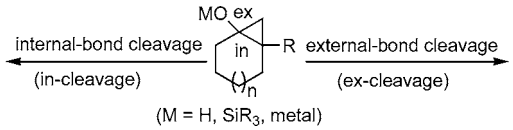
that cyclopropanes are among the most thoroughly investigated target molecules in PET chemistry.[3,7,8]

The regioselectivity of bicyclo[*m*.1.0]alkane containing cyclopropanol radical cation ring-opening, viz., internal-bond cleavage vs external-bond cleavage (Scheme 1), is an

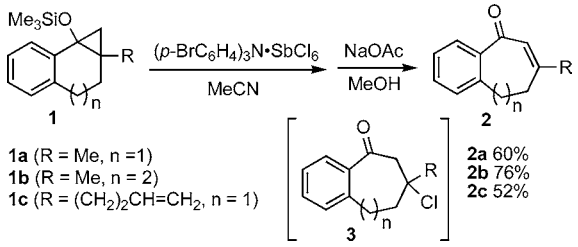
Scheme 1



interesting mechanistic and synthetic issue.[9] In this Letter, we report the preliminary results of a study probing the factors that govern the reaction pathways followed in PET reactions of cyclopropyl silyl ethers embedded in bicyclo[*m*.1.0]alkane frameworks.

Initially, we probed reactions of cyclopropyl silyl ethers **1** with tris-*p*-bromophenylaminium hexachloroantimonate (TBPA), a well-known hole catalyst,[10] to determine if and how these compounds react with a nonmetal-based oxidizing agent. Treatment of **1a** with TBPA (2 equiv) in MeCN at room temperature for 2 h resulted in the generation of ring-expanded product **3a**[5g] (Scheme 2). Subjecting the crude reaction mixture to refluxing methanolic NaOAc (5 equiv) for 2 h produced enone **2a** (60%). In a similar manner, enones **2b** and **2c** were obtained in 76% and 52% yields, starting with **1b** and **1c**, respectively. The results clearly show

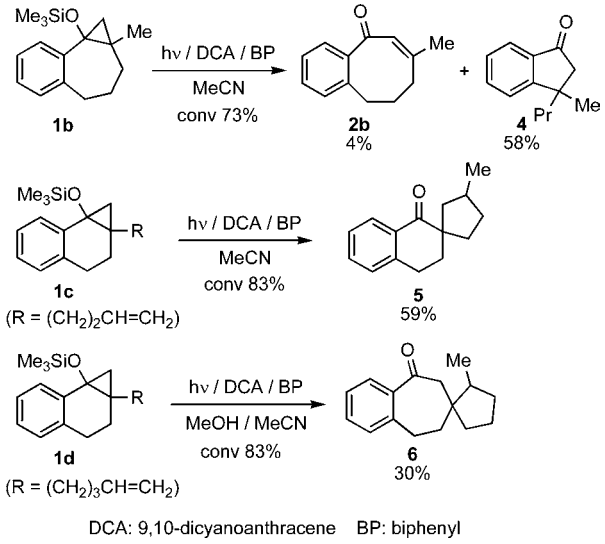
Scheme 2



that radical cations, formed as intermediates in these SET oxidation reactions, undergo regioselective cleavage of the internal-bond of the cyclopropane ring.

Next, the redox sensitization method was chosen to explore the PET reactivity of these substrates. This method employs 9,10-dicyanoanthracene (DCA) and biphenyl (BP) to generate the biphenyl radical cation, which acts as the hole catalyst.[11,12] By using DCA (0.1 equiv) and BP (1.2 equiv) in MeCN with irradiation (λ > 340 nm) for 8 h, **1a** was quantitatively recoverd. In contrast, these conditions promoted PET reaction of **1b** to form the unexpected product **4** (58%) and a small amount of **2b** (4%) at 73% conversion (Scheme 3). Surpris-

Scheme 3



ingly, PET reaction of **1c** again generated the spirocyclic ketone **5** (59% based on 83% conversion), a product that is different from that formed by using TBPA as the oxidant. In the cases of **1b** and **1c**, no reaction took place in the

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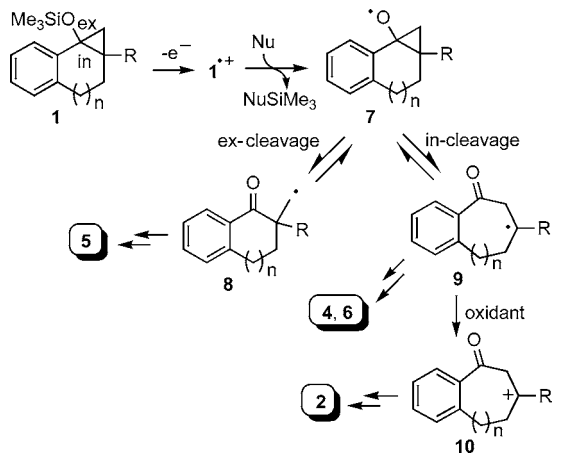
(12) On the basis of the redox potentials of the compounds, both the singlet excited state of DCA (^{1}DCA*) and the radical cation of BP (BP$^{\bullet+}$) could accept a single electron from **1**. However, the former electron transfer generates a radical ion pair that often undergoes energy wasting back electron transfer.[6] Detailed redox data and discussion are described in the Supporting Information.

absence of BP. Noteworthy is the observation that **1d**, a side chain homolog of **1c**, was inert under the redox senstitization conditions. However, when the solvent mixture contained MeOH (MeCN−MeOH = 3:1), reaction of **1d** took place to form the spirocyclic product **6** although its yield was not high, ca. 30% yield at 83% conversion. Also, the presence of MeOH enabled the conversion of **1c** to **5** to occur (57% yield at 37% conversion) in the absence of BP. The silophilic nature of MeOH, which promotes desilylation of the silyl ether radical cations, is the apparent source of these differences.[13]

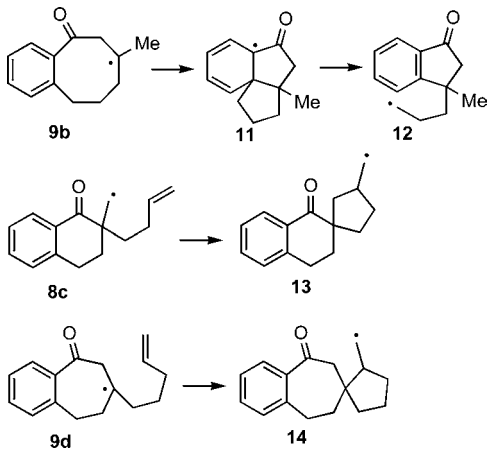
The observations summarized above show that reactions of **1** promoted by the tris-*p*-bromophenylamine radical cation and the PET generated biphenyl radical cation follow different cyclopropane ring-opening pathways. In addition, the presence of nucleophiles, such as chloride ion and MeOH, alter the SET reactions by enhancing desilylation of the radical cation derived from **1**. A plausible explanation for these findings is found in the reaction mechanism presented in Scheme 4. Single electron transfer of **1** and subsequent

Scheme 4



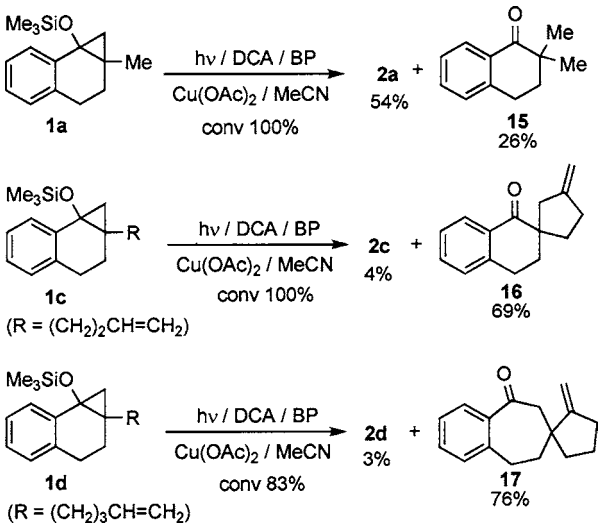
nucleophile assisted desilylation of $\mathbf{1}^{\bullet+}$ gives the cyclopropoxy radical **7**, which undergoes either external- or internal-bond cleavage to generate the respective primary alkyl radical **8** or tertiary alkyl radical **9**.[14] In the reaction promoted by TBPA, **9** is oxidized by another equivalent of TBPA to form the tertiary carbocation **10**, from which **3** and finally **2** is formed. On the contrary, when formed under PET conditions, **8c**, **9b**, and **9d** undergo radical rearrangements to give the products **5**, **4**, and **6**, respectively (Scheme 5).[15] In these cases, the oxidizing species such as ^{1}DCA* and $BP^{\bullet+}$ have short lifetimes and, as a result, their steady-state concentrations are too low to oxidize **9**.

Scheme 5



The proposal made above leads to the suggestion that addition of external oxidants to the PET system should alter the course of the reactions, favoring pathways via cationic intermediates. Indeed, PET reaction of **1a** in the presence of $Cu(OAc)_2$ (1.2 equiv) (Scheme 6)[16,17] led to production

Scheme 6



of **2a** (54%), the same product that is generated in the TBPA-promoted reaction, along with **15** (26%). A control experiment, involving direct irradiation of **1a** in the presence and

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(15) (a) While 5-exo hexenyl radical cyclization corresponding to the rearrangements **8c** → **13** and **9d** → **14** is a well-known process,[15b] same type of rearrangement as the transformation of **9b** → **11** → **12** was previously reported.[6c] (b) Griller, D.; Ingold, K. U. *Acc. Chem. Soc.* **1980**, *13*, 317−323.

(16) Cu(II) ion is known to act as an effective oxidant toward alkyl radicals. Snider, B. B. *Chem. Rev.* **1996**, *96*, 339−363.

(17) Use of Cu(II) salts for PET reactions. (a) Mizuno, K.; Yoshioka, K.; Otsuji, Y. *Chem. Lett.* **1983**, 941−944. (b) Takahashi, Y.; Nishioka, N.; Endoh, F.; Ikeda, H.; Miyashi, T. *Tetrahedron Lett.* **1996**, *37*, 1841−1844. (c) Lee, J.; Jong, S. U.; Blackstock, S. C.; Cha, J. K. *J. Am. Chem. Soc.* **1997**, *119*, 10241−10242. (d) Lee, H. B.; Sung, M. J.; Blackstock, S. C.; Cha, J. K. *J. Am. Chem. Soc.* **2001**, *123*, 11322−11324.

absence of $Cu(OAc)_2$, resulted in the complete recovery of **1a**. Unexpectedly, PET reactions of **1c** and **1d** with $Cu(OAc)_2$ present produced the respective spirocyclic products **16** (69%) and **17** (76%) along with small amounts of **2c** (4%) and **2d** (3%).[18]

As discussed above, nucleophiles such as chloride ion, MeOH, and acetate anion would promote the desilylation of $\mathbf{1}^{\bullet+}$ to produce **7** (see Scheme 4). However, information about the reactivity of such radical cations in the absence of nucleophiles is limited. According to the literature,[6e] cyclopropyl silyl ether radical cations that possess long-bond character rearrange to ring-opened distonic radical cations, which behave as alkyl radicals. If this description is applicable to $\mathbf{1}^{\bullet+}$ (Figure 1), it would be difficult to

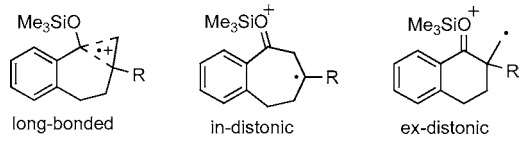
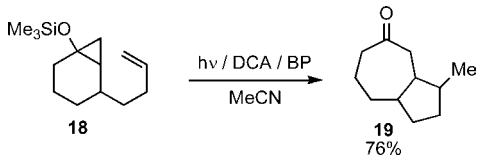


Figure 1. Structures of cyclopropyl silyl ether radical cations.

understand why **1c** undergoes PET reaction and **1d** does not in the absence of MeOH. In both cases, in-distonic and ex-distonic radical cations can be formed even though some differences should exist in the rate constants for their ensuing 5-exo-radical cyclizations.[19] Also, PET reaction of **1a** does not take place in MeCN in the presence of 1,4-cyclohexadiene (CHD), a hydrogen atom donor expected[20] to trap the ex-distonic radical efficiently and form **15**. In contrast, PET reaction of **1a** with CHD in 3:1 MeCN−MeOH produces **15** in 43% yield (30% conversion). These results suggest that $\mathbf{1}^{\bullet+}$ has long-bond character in a manner similar to cyclopropane radical cations,[21] and that it reacts intramolecularly with the pendant alkene group prior to cyclopropane ring-opening.

To further evaluate the redox sensitization method, we explored the reactivity of the aliphatic substrate **18** (Scheme 7). DCA photosensitized PET reaction of **18** was already

Scheme 7



reported[6d] to produce an extremely low yield (10%) of **19**, likely formed through an internal-bond cleavage and 5-exo cyclization sequence. In contrast, we observed that PET reaction of **18**, using the DCA-BP system, afforded **19** in a much higher yield (76%). We also observed that **18** did not react to form **19** when BP was absent and a complicated product mixture was formed when **18** was treated with TBPA.

Our studies of electron transfer promoted oxidative ring-opening reactions of aryl-substituted cyclopropyl silyl ethers have shown that the regioselectivity for cyclopropane ring-opening can be controlled by the choice of electron transfer conditions. The above results and discussion allow us to conclude that reaction pathways of the radical cations of these compounds are strongly influenced by the control of the following steps. In other words, the initial cyclopropane bond cleavage, which would be reversible, is not a product-determing step if a rapid follow-up step is not available. Another notable finding is the cooperative effect seen in PET processes promoted by DCA, BP, and Cu(II). Observations have been made which suggest that cyclopropyl silyl ether radical cations have long-bond structures and are reactive with intramolecularly existing carbon−carbon double bonds. Finally, although not optimized, a redox sensitization reaction of an aliphatic cyclopropyl silyl ether has been observed.

Acknowledgment. We thank Professors Ilhyong Ryu and Hiroshi Ikeda of Osaka Prefecture University for their valuable comments. We also thank Mr. Junichi Sakai of Niigata University for his assistance in measuring HRMS.

Supporting Information Available: General and reaction procedures, spectral data of cyclopropyl silyl ethers and products, and additional discussion. This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) Compounds **16** and **17** could be formed through the sequence described as follows. Electron transfer between Cu(II) and $DCA^{\bullet-}$ produces Cu(I) ion.[17a] Then, the Cu(I) ion reacts with the alkyl radicals **13** and **14** to give the organo copper compounds, which undergo β-hydride elimination[9e] to produce **16** and **17**, respectively.

(19) (a) The rate constants for 5-exo hexenyl radical cyclizations for primary and tertiary alkyl radicals are reported to be 2.3×10^5 to 3.6×10^6 s^{-1} and 3.5×10^5 s^{-1}, respectively.[19b] (b) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925−3941.

(20) (a) It is reported that the rate constant of hydrogen atom abstraction from CHD by a primary alkyl radical is 5×10^5 s^{-1} M^{-1}.[20b] Under this condition, the estimated rate is 1.1×10^6 s^{-1} at 2.1 M of CHD. (b) Newcomb, M. *Tetrahedron* **1993**, *49*, 1151−1176.

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