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Tetrahedron 62 (2006) 6589–6593
Tetrahedron

Facile ring opening of siloxy cyclopropanes by photoinduced electron transfer. A new way to *β-keto* radicals

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Received 6 December 2005; accepted 12 February 2006
Available online 17 April 2006

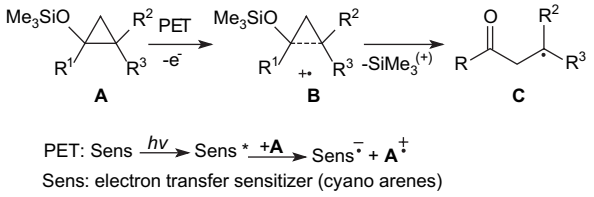
Abstract—Siloxy cyclopropanes undergo ring opening and fragmentation of formal silyl cations under formation of *β-keto* radicals. These reactive intermediates can be used in inter- and intramolecular addition reactions leading to complex ring systems if more than one unsaturated side chain is present in the starting material. Beside some synthetic examples mainly the mechanism will be discussed focusing on the structure of the primarily formed radical cations, the regioselectivity of cyclopropane cleavage (*endo* vs *exo* ring opening), leaving of the silyl group, and termination by H-transfer.

1. Introduction

Single Electron Transfer (SET)[1] and especially Photoinduced Electron Transfer (PET)[2] has become a powerful tool in organic synthesis[3] after fundamental research, which started already in 1960s, e.g., by Marcus,[4] Weller,[5] and others.[6] Early highlights of synthetic applications are related to the work of Arnold,[7] Mariano,[8] Schuster,[9a] Steckhan,[9b] and many other groups[10] including ourselves.[11]

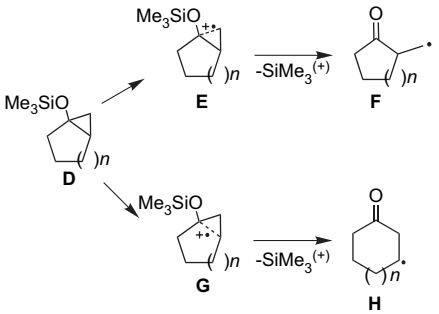
The very simple but even most powerful concept behind this methodology is based on the weakening of bonds by oxidation/reduction under formation of radical cations/radical anions leading to an increased reactivity of the molecules.[12] Examples of synthetic applications cover addition,[13] cycloaddition,[14] fragmentation,[15] substitutions,[16] and other reactions.[17] Often the details of the mechanisms involved in these reactions are not yet completely known although the primary and initiating step is always PET. Especially in fragmentation and addition reactions radical species may also be involved.[18]

In this report we will focus on a new method of generating *β-keto* radicals from siloxy cyclopropanes by oxidative PET (Scheme 1). The primary step is oxidation of the starting material under cleavage of the cyclopropane **A** leading to a distonic radical cation **B**, which finally forms the *β-keto* radical **C**.



Scheme 1. Cleavage and fragmentation of siloxy cyclopropanes **A** to radical cations **B** and *β-keto* radicals **C**.

Both the radical cation **B** and the *β-keto* radical **C** are very useful intermediates especially in intramolecular addition reactions to π-systems leading to new cyclized products. We have made use of this method for synthesizing polycyclic compounds.[19] Beside some exemplary reactions we will discuss in more detail the mechanism involved especially regarding bicyclic siloxy cyclopropanes (Scheme 2).



Scheme 2. *exo*- and *endo*-cleavage of bicyclic siloxy cyclopropanes.

Keywords: Siloxy cyclopropanes; Photoinduced electron transfer; Radical cations; Radicals; Radical cascade reactions; Reaction mechanism.
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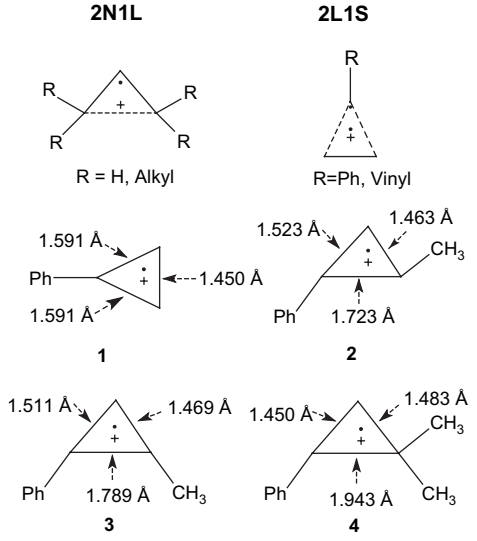
0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.03.060

Important questions concern the structure of siloxy cyclopropane radical cations in comparison with unsubstituted or alkyl-substituted cyclopropane radical cations, the regioselectivity of *endo*- versus *exo*-cleavage of bicyclic cyclopropanes **D** yielding **E** and **G**, and the factors controlling the fragmentation of **D** to the *β-keto* radicals **F** and **H**.

2. Structure of siloxy cyclopropane radical cations

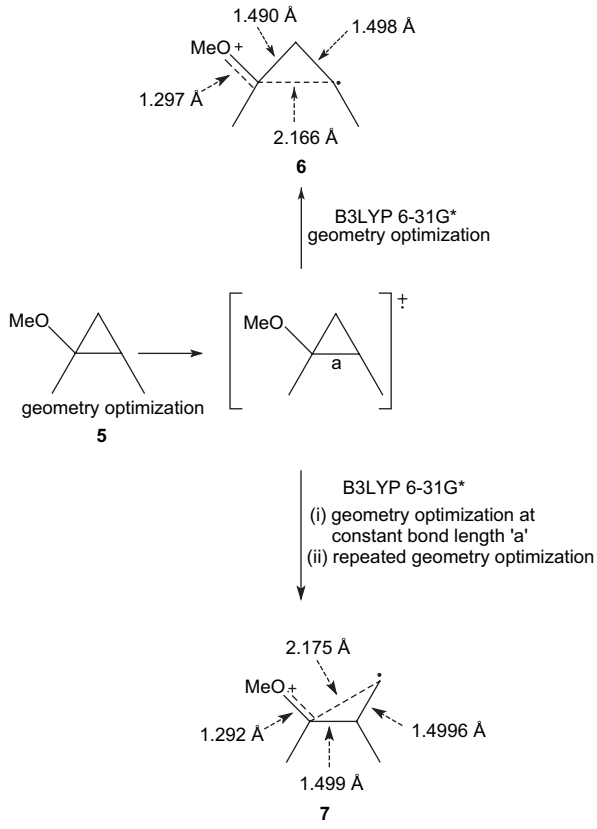
Upon ionization, cyclopropane derivatives can form two types of radical cations depending on the substitution pattern (Scheme 3, top).[20,21] The **2N1L** type (2 normal, 1 long) shows a long one electron-two center bond in the range of 1.85–1.95 Å. The calculated bond lengths of the radical cations **2**–**4** indeed confirm this classification (Scheme 3, bottom). On the contrary, aryl- and vinyl-substituted cyclopropanes prefer the **2L1S** type (2 long, 1 short) as shown for 1-phenylcyclopropane **1** (Scheme 3).



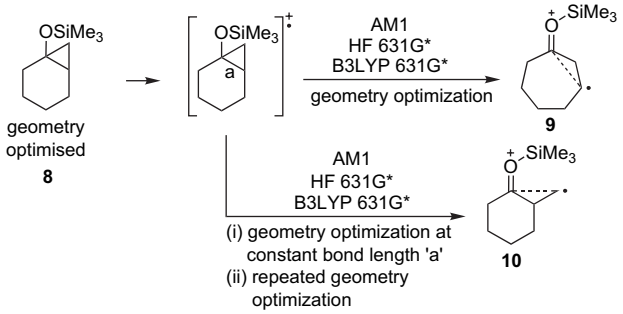
Scheme 3. Types of cyclopropane radical cations according to *Hudson* and structural details of selected examples (for Refs. 20 and 21 see text).

Following this classification for siloxy cyclopropanes of the type **D** should give radical cations of the type **2N1L** after oxidation. Scheme 4 shows the results of an ab initio calculation of the model compound 1-methoxy-1,2-dimethylcyclopropane **5**. Note, that the elongated C–C bonds of **6** and **7** are even longer (ca. 2.17 Å) compared to **2**–**4** (ca. 1.72–1.94 Å). However, the results considering only the energetics show that it is not possible to differentiate between the two ways of cleavage leading to **6** and **7**, respectively.

Even similar calculations on the radical cations **9** and **10** generated from the bicyclic siloxy cyclopropane **8** upon oxidation (cf. Scheme 2, **D**, n=2) do not allow a differentiation between *endo*- versus *exo*-cleavage (Scheme 5). Both semiempirical and ab initio methods lead to extremely elongated *endo*- and *exo*-bonds (ca. 2.4–2.5 Å).[22] Only a calculation of the transition states and the complete potential hypersurface clearly verify the preferred cleavage of the *endocyclic* bond under formation of **9**. Details of this theoretical analysis including matrix isolation studies on the reactive intermediates will be published separately.[23]



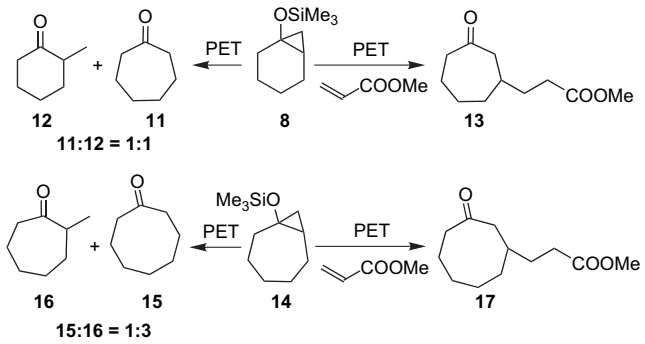
Scheme 4. Structural details of radical cations of 1-methoxy-1,2-dimethylcyclopropane.



Scheme 5. Quantum chemical calculations on the structure of radical cations **9** and **10**.

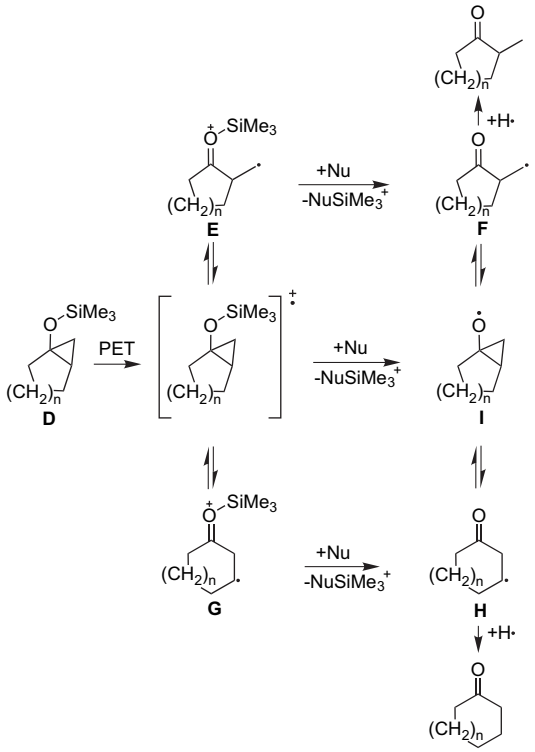
3. Experimental studies on *endo*- versus *exo*-cleavage of bicyclic siloxy cyclopropanes of structure D

Irradiation of bicyclic siloxy cyclopropanes **D** leads to the ring opening of the three-membered ring under ring enlargement (*endo*-cleavage) or under preservation of the ring (*exo*-cleavage) depending on the ring size (Scheme 6). However, in presence of methyl acrylate as scavenger only the ring enlarged addition products are formed (e.g., **8**→**13** and **14**→**17**). This observation strongly indicates that the primary step after oxidation is ring opening of the *endocyclic* bond of **8** and **14**.



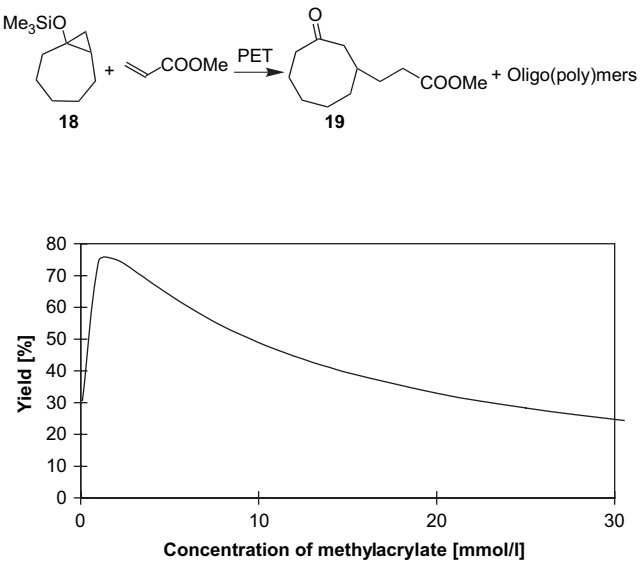
Scheme 6. PET reactions of bicyclic siloxy cyclopropanes in the absence and presence of methyl acrylate as scavenger.

The ring opening may already occur at the level of the radical cation of the **D** (leading to **G**) or at the level of the oxy radical **I** generated after fragmentation of the trimethylsilyl cation (leading to **H**). These results also show that the possible equilibrium between ring-preserved and ring-opened intermediates (**E** ↔ **G** and **F** ↔ **H**) is slow compared to the fast scavenging reactions in the presence of the methyl acrylate (Scheme 7).



Scheme 7. Equilibrium between ring-opened and ring-preserved intermediates (radical cations **E** and **G** structures are presented with already broken C–C bond, cf. Scheme 2).

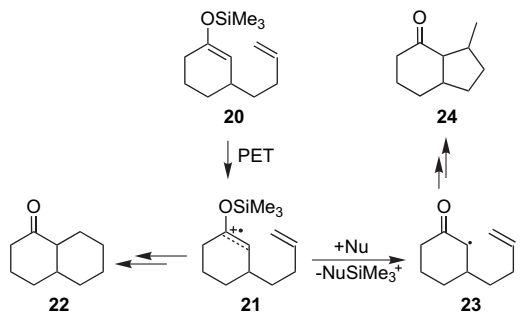
Further studies on the kinetics of **18** as model compound in the presence of methyl acrylate confirm these findings and furthermore, show that the termination step (H-abstraction) is relatively slow (Scheme 8). A detailed analysis is reported elsewhere.[22,24]



Scheme 8. Yield of the trapping product **19** in dependence on the methyl acrylate concentration.

4. Fragmentation of the trimethylsilyl group

One important question concerns the timing of loss of the silyl group. Recent studies on the PET reactions of silyl enol ethers have shown that this cleavage is strongly influenced by nucleophiles such as alcohols or even the solvents (most often acetonitrile whose nucleophilicity can be increased by high pressure).[18,24] Silyl enol ethers give nondistonic radical cations on PET-oxidation, whereas siloxy cyclopropane radical cations undergo C–C bond cleavage activationless according to quantum chemical calculations.[22,25] Therefore, we assume that the loss of the silyl group takes place only at the stage of the distonic radical cations **E** and **G**. Using silyl enol ethers the course of the reaction, i.e., radical cation versus radical reaction pathway, can be controlled by timing the cleavage of the silyl group. For example, in solvent mixtures of high nucleophilicity loss of the silyl group leads to the corresponding *α-keto* radical **23**, which preferentially undergoes 5-*exo* cyclization to **24** if a suitable unsaturated side chain is present.[18,24] However, in the absence of nucleophiles 6-*endo* is the preferred cyclization mode leading to **22** (Scheme 9).



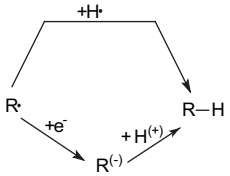
Scheme 9. Radical cations versus radical cyclization pathways in PET reactions of the silyl enol ethers.

In the case of siloxy cyclopropanes this dependency on the reaction medium is not as pronounced as for silyl enol

ethers.[19a,22] This might be taken as an indication for the higher reactivity of the distonic radical cations compared to nondistonic ones.

5. Termination by H-transfer

An often discussed question is related to the mechanism of the final step of PET-induced cyclizations of unsaturated silyl enol ethers and siloxy cyclopropanes. In all examples studied by us this termination is based on H-transfer to the final radical intermediate of the cascade fragmentation addition process (cf. Schemes 6–9). Two mechanisms can be discussed, i.e., a formal H-atom transfer (e.g., from the solvent) and a two-step process via electron and proton transfer (Scheme 10). The reduction of the radical $\mathbf{R}^{\bullet}$ may occur by electron transfer from the radical anion of the sensitizer (cf. Scheme 1).



Scheme 10. Possible H-saturation pathways.

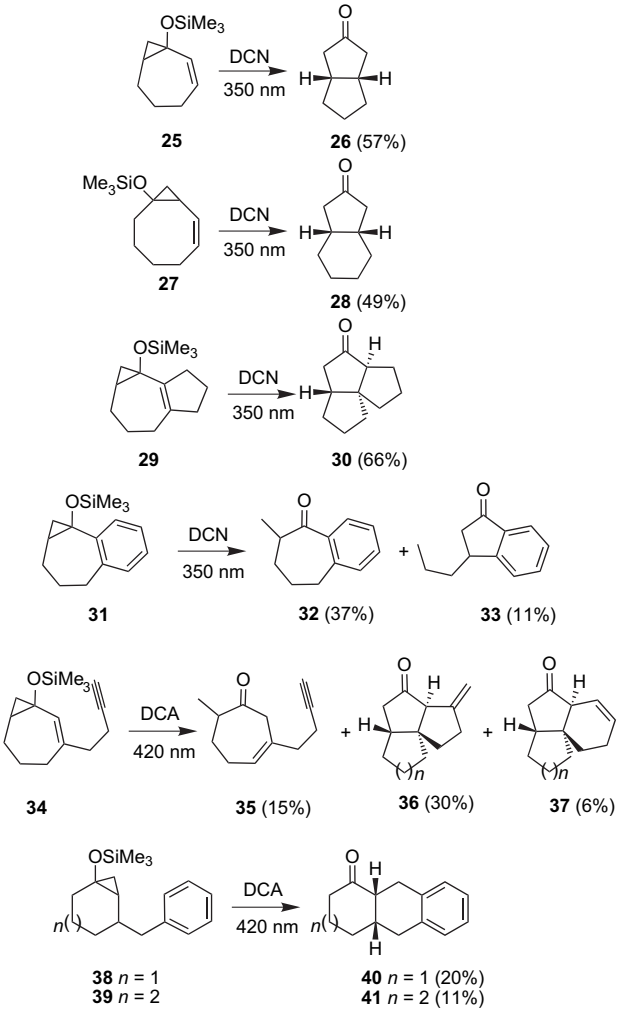
We have shown by a comprehensive study using deuterated solvents that both acetonitrile and water are sources for this saturation. In addition, kinetic isotope effects of H-transfer from acetonitrile influence the ratio of direct and two-step H-transfer as well. These effects are even stronger for secondary radicals.

In summary, both H-atom transfer from the solvent and return electron transfer followed by protonation from water are responsible for the final saturation process.

6. Synthetic examples of radical cationic/radical cascade cyclizations

As shown above siloxy cyclopropanes are useful starting materials for generation of *β-keto* radicals. These radicals can be used in further cyclization reactions leading to new rearranged products or even in radical cascade reactions involving two cyclization steps. Examples are shown in Scheme 11 and were taken from recent reports.[19] The primary step after PET-oxidation is cleavage of the *endocyclic* C–C-bond of the cyclopropane followed by transannular cyclization (e.g., **25**→**26**, **27**→**28**, and **29**→**30**).

The PET reaction of **31** is somewhat more complicated. Compound **32** is probably formed via a cyclopropyloxy radical rearrangement, whereas the formation of **33** requires first transannular addition of the *β-keto* radical to the benzene ring followed by second C–C bond cleavage.[19a] This latter example already indicates some limitations of the method regarding aryl substituents. However, examples **38**→**40** and **39**→**41** show that this protocol is still applicable to arene systems in moderate yields.[19b] Example **34**→**36**



Scheme 11. Examples of radical cationic/radical cascade cyclization reactions (DCA=9,10-dicyanoanthracene; DCN=1,4-dicyanonaphthalene).

and **37** demonstrate that even more complicated condensed ring systems are accessible by this method.[19b]

Acknowledgements

Our studies on PET reactions have been supported by Deutsche Forschunggemeinschaft DFG (Bonn) and the Volkswagenstiftung (Hannover). We are very grateful to these funding agencies. In particular we are very grateful to Thomas Bally (Fribourg) for fruitful discussions and critical reading of the manuscript.

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