Regioselectivity in Nucleophilic Addition of Siloxyalkenes to an Alkylideneallyl Cation

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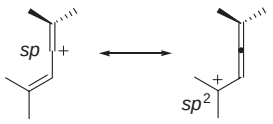
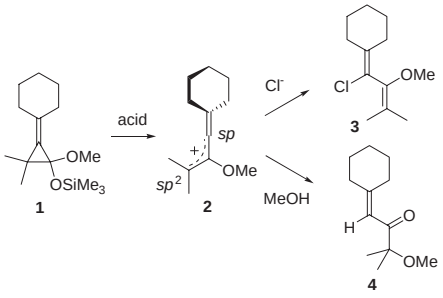
Alkylideneallyl cation generated from Lewis acid-mediated ring-opening reaction of alkylidenecyclopropanone acetal was employed for the reaction with siloxyalkenes to give [3 + 2] cycloaddition and acyclic addition products. All the products are the result of nucleophilic addition to the sp^2 center of the alkylideneallyl cation, and there is no sign of the nucleophilic addition to the sp center. The regioselectivity is independent of the electronic and steric effects of siloxyalkene nucleophiles, and is compatible with charge distribution of the allylic cation.

Alkylideneallyl cations can be described as a hybrid of resonance structures of 1-vinyl-substituted vinyl cation and allenylmethyl cation, and thus contains two reaction sites, sp and sp^2 carbons, for nucleophilic attack (Scheme 1).[1,2] Relative electrophilicity of this ambident electrophile has been evaluated from the charge distribution calculated[1] as well as the ^{13}C chemical shift[2] measured at low temperature under superacidic conditions. The charge distributions are affected by substituents of the cation: The sp^2 carbon is more positive than the sp one when two methyl groups are introduced at the sp^2 carbon.

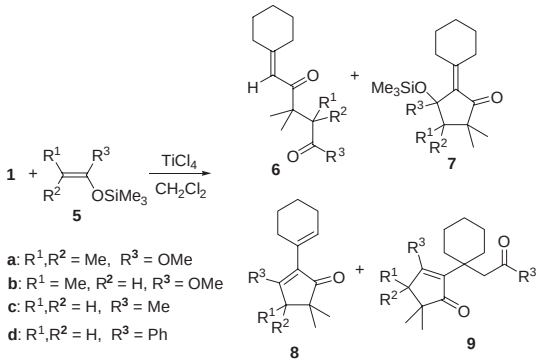


Scheme 1.

We have recently developed a novel method for generation of alkylideneallyl cation **2** from alkylidenecyclopropanone acetal **1** (Scheme 2).[3] This method provides a nice opportunity to examine regioselectivity of nucleophilic addition to the ambident cation. The previous report showed different regioselectivity observed between the methanol and chloride additions to the cation intermediate: Methanol selectively attacks at the sp^2 carbon to give **4** while chloride gives the sp-addition product **3**. To further examine the regioselectivity, siloxyalkenes are employed for nucleophiles. The nucleophilic addition selectively proceeds at the sp^2 carbon to give the [3 + 2] cycloadduct as well as an acyclic adduct depending on the reaction conditions. These results are summarized in this communication.



Scheme 2.



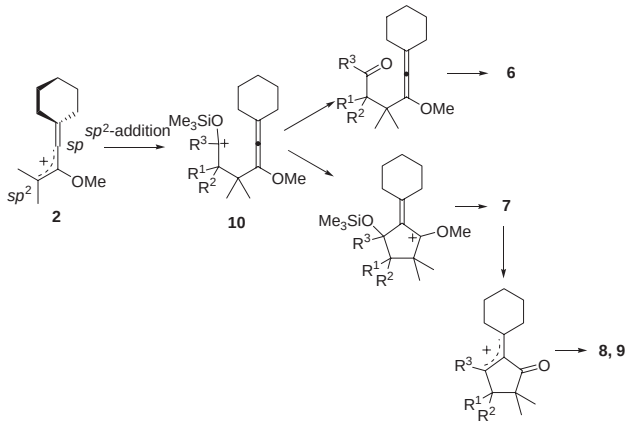
Scheme 3.

Reaction of **1** with $TiCl_4$ was carried out in the presence of siloxyalkene **5** (Scheme 3) and the results are summarized in Table 1. In the reaction with ketene silyl acetals **5a** and **5b** at −78 °C, γ-ketoesters **6a** and **6b** were obtained instead of chloride product **3** which is a major product in the absence of **5**. The product **6** is rationalized by a result of trapping of alkylideneallyl cation **2** with **5** at the sp^2 carbon, followed by hydrolysis under acidic conditions. In contrast, the reactions with silyl enol ethers **5c** and **5d** gave no acyclic product **6**, but gave cyclopentanone derivatives **7**–**9**. The GC analysis of the reaction mixture from **5c** showed siloxycyclopentanone **7c** was a major product (Entry 3), but the attempted isolation of the product resulted in a mixture of mainly three cyclopentanone derivatives, cylopentenone **8c** and double addition product **9c** in addition to **7c** (Entry 4). Use of excess amounts of **5c** and $TiCl_4$ increased the yield of the double addition product **9c** (Entry 5). Reaction with **5d** also gave cyclopentenone **8d**, which were isolated in a good yield

Table 1. Reaction of **1** with siloxyalkene **5**[a]

Entry	**5**[b]	10^3[$TiCl_4$]/ mol dm^{-3}	Yield/%			
			6	**7**	**8**	**9**
1	**5a**(0.07)	14	90		<1	
2	**5b**(0.10)	41	81			
3	**5c**(0.02)	15		72	<1	<1
4	**5c**(0.03)	14		37[c]	37[c]	12[c]
5	**5c**(0.25)	120		<1	38	24
6	**5d**(0.04)	20			73[c,d]	
7[e]	**5a**(0.05)	70	0		41[c]	

[a]Reaction of **1** (0.01 mol dm^{-3}) was carried out in CH_2Cl_2 at −78 °C for 10 min, and yields were determined by GC. [b]The values in parentheses are the concentration of **5** (mol dm^{-3}). [c]Yield of isolated products. [d]The crude mixture obtained was further treated with $TiCl_4$, and then purified to give the product. [e]Reaction was carried out at 0 °C.



Scheme 4.

after further treatments of the reaction mixture with $TiCl_4$ to convert to a stable form **8d** (Entry 6). Structures of these cycloadducts were determined by two-dimensional NMR including HMBC and HMQC measurements after isolation,[4] and any other regioisomers were not detected by GC or ^{1}H NMR measurements of the reaction mixtures. Judging from these structures, **8** and **9** must be secondary products derived from **7**. To determine the pathways for formation of **8** and **9**, some transformations of **7** were carried out by using the isolated **7c**. Reaction of **7c** with $TiCl_4$ gave **8c** in 98% yield, and the $TiCl_4$-mediated reaction in the presence of **5c** gave **9c** in 91% yield. Thus, **8** and **9** should be the secondary products.

A plausible mechanism for the reactions of alkylideneallyl cation **2** with siloxyalkenes **5** is illustrated in Scheme 4. The cation **2**[5] generated from **1** is trapped by siloxyalkene at the sp^2 position to give the cationic intermediate **10** stabilized by the oxy group(s). Desilylation from **10** results in formation of acyclic adduct **6**, and intramolecular cyclization of **10** gives the cycloadduct with such regioisomeric orientation.[6] If the stepwise [3 + 2] cycloaddition were initiated by the addition at the sp carbon of **2**, the different orientation of the cycloadduct should have been obtained. Thus, all the products **6**–**9** are the result of nucleophilic attack at the sp^2 carbon of **2**. The regioselective addition at the sp^2 carbon of **2** is rationalized by the charge distribution estimated from calculations and ^{13}C NMR: the sp^2 carbon is more positive than the sp carbon of 2,5-dimethylhexa-3,4-dien-2-yl cation (2,5-dimethylhexa-2,4-dien-3-yl cation).[1a,2a,7] The regioselectivity is not affected by the steric effect of the siloxyalkenes employed, and the reaction with dimethylketene silyl acetal **5a** allows the smooth connection of the two contiguous quaternary carbon centers.

The reaction with silyl enol ether **5c** and **5d** gave only the [3 + 2] cycloadducts in comparison with effective formation of acyclic adduct **6** in the reaction with ketene silyl acetal **5a** and **5b** at lower reaction temperature. This can be explained by the reactivity of cationic intermediates **10**: The intermediate from **5c** and **5d** is more reactive owing to lower stabilization by oxy group than that from **5a**, **5b**, and reacts with the internal allene more efficiently to give the cycloadduct(s). Cyclic product **8a** could be obtained at higher temperature from the reaction of **5a**.[8]

In summary, the alkylideneallyl cation **2** generated from alkylidenecyclopropanone acetal **1** was employed for the reaction with siloxyalkenes.[9] The [3 + 2] cycloaddition product and acyclic addition product were obtained depending on the reaction conditions, and all the products are the result of nucleophilic attack at the sp^2 center of alkylideneallyl cation **2**. The regioselectivity is compatible with charge distribution of the allylic cation despite of varying the electronic nature and steric bulkiness of the nucleophile from the simple alcoholic nucleophile.[3,10]

References and Notes

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4 The orientation of the five-membered ring of **7**–**9** is also confirmed by the conversion reaction from **7** to **8** and **9**. The diene structure of **8** indicates that the siloxy of **7** is at allylic position.

5 A siloxy derivative of **2** could be generated from **1**, but the reaction of **1** with $TiCl_4$ in the absence of **5** gives **3** selectively. This suggests the allylic cation contains methoxy group.

6 a) [3 + 2] cycloadditions via trimethylenemethane intermediate have been reported in the reaction of 1,1-dialkoxy-2-methylenecyclopropane with electron-deficient olefins. The ring-opening reaction of the cyclopropane substrate takes place between the C1 and C3, and is different from the reaction of **1**.[6b] b) E. Nakamura, S. Yamago, *Acc. Chem. Res.* **2002**, *35*, 867, and references cited therein.

7 The vacant orbital at the sp carbon of **2** may be shielded by the cyclohexane ring, but some nucleophiles including chloride and furans prefer the sp attack. So, the present selectivity may be controlled mainly by the charge distribution.

8 For the reaction with **5a**, alternative pathways for the cyclic product **8a** are also possible owing to the symmetric nature of the five-membered ring. However, the common pathways in the cycloadditions of **5a**–**5d** are limited, and one of the simple pathways to cycloadducts is shown in Scheme 4. Mukaiyama–Michael addition of **5** to **7** can be an alternative pathway to the double addition product **9**. Although some details during the formation of **8** and **9** are uncertain, the electrophilic reaction site of **2** is the sp^2 center.

9 Lewis acid-mediated reactions of cyclopropanes with siloxyalkenes, see: a) M. Ohno, S. Matsuoka, S. Eguchi, *J. Org. Chem.* **1986**, *51*, 4553. b) K. Saigo, S. Shimada, T. Shibasaki, M. Hasegawa, *Chem. Lett.* **1990**, 1093.

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