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Cyclopropanation of Tin-Substituted Acetals with Olefinic Alcohols *via In Situ* Transacetalization

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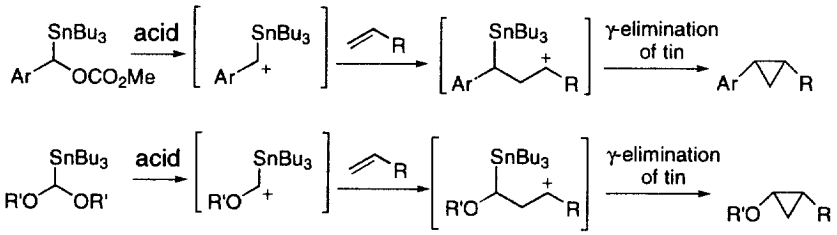
Abstract

Reactions of a tin-substituted acetal with olefinic alcohols in the presence of an acid resulted in facile transacetalization followed by intramolecular cyclopropanation to give the cyclized products in high yields and stereoselectivity.

Keywords: Carbonium ions; Cyclopropanes; Cyclopropanation; Stereospecificity

An intramolecular reaction is generally more favorable than the intermolecular counterpart owing to lesser demand in the decrease of entropy. Therefore, intramolecularization [1] of chemical reactions has been developed from view points of both efficiency and selectivity. For the approach to intramolecularization, *in situ* approach [2] seems to be quite useful because two reaction sites are pre-connected by *in situ* intermolecular reaction, and therefore, there is no need for the isolation of the pre-connected intermediate. Recently we have developed a new "tin carbenoid" [3] (Scheme 1) using remarkable γ effect of tin [4,5]. In this paper we report the intramolecularization of the cyclopropanation of "tin carbenoid" *via in situ* transacetalization [6].

Scheme 1.



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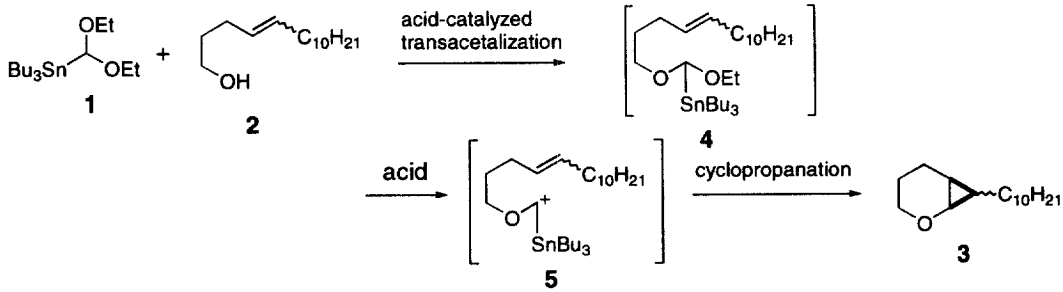
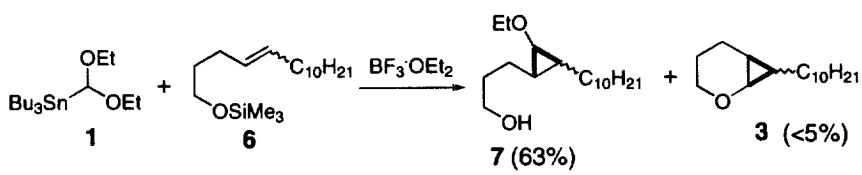
We found that stannyl substituted acetal **1** [7] is quite effective for the intramolecularization of cyclopropanation *via in situ* transacetalization (Scheme 2). For example, the treatment of **1** with Lewis acids such as TMSOTf and BF_3•OEt_2 in the presence of olefinic alcohol **2** gave rise to facile formation of bicyclic cyclopropane **3** in 95%, and 82% yields, respectively. The reaction seems to proceed by the initial transacetalization of **1** with **2** to give mixed acetal **4** which then undergoes acid promoted elimination of the ethoxy group to generate tin substituted carbocation **5** (Scheme 2). The carbcation adds to the carbon-carbon double bond and the subsequent γ-elimination of tin [8] to achieve the intramolecular cyclopropanation.

Scheme 2



It is noteworthy that the reaction of **1** with trimethylsilyl protected olefinic alcohol **6** mainly gave rise to the formation of the monocyclic compound **7** (Scheme 3). Probably the transacetalization did not take place with the protected alcohol and the cyclopropanation of **1** took place directly at the olefinic part of **6**. The desilylation occurred probably at the work-up to give **7**. The treatment of **7** with BF_3•OEt_2 (2 eq) did not give the bicyclic compound **3** at all. This result indicates that **3** was formed by the initial transacetalization followed by the intramolecular cyclopropanation as shown in Scheme 2.

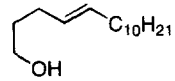
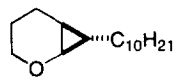
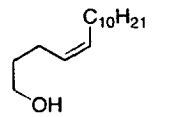
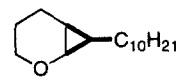
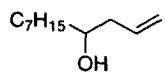
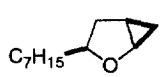
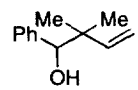
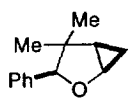
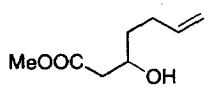
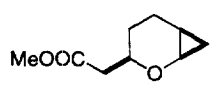
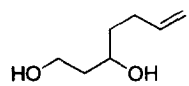
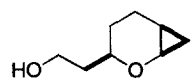
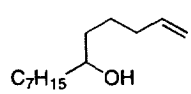
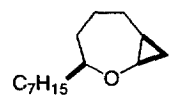
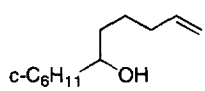
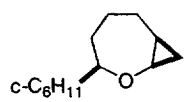
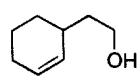
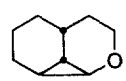
Scheme 3



The stereospecificity of the present reaction is remarkable. *Exo*-**3** was obtained exclusively from *E*-**2** and *endo*-**3** was obtained exclusively from *Z*-**2** (Table 1, entries 1 and 2). Complete stereospecificity suggests that the addition of the carbocation to the double bond and

the elimination of tin takes place in a synchronous fashion.

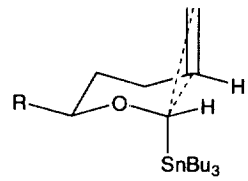
Table 1. Transacetalization-Intramolecular Cyclopropanation Reaction of **1**[a] with Olefinic Alcohols

entry	olefinic alcohol	product	yield(%)[b]
1			85
2			97
3			63 (>99/1)[c]
4			93 (87/13)[c]
5			82 (91/9)[c]
6			80 (84/16)[c]
7			91 (91/9)[c]
8			87 (94/6)[c]
9			43 (>99/1)[c]

[a]Reactions were carried out with 0.22 mmol of **1**, 0.20 mmol of an olefinic alcohol, and 0.22 mmol of TMSOTf in CH_2Cl_2 (0.60 ml) at room temperature for 30 min. [b]Isolated yields *via* flash column chromatography. [c] The ratio was determined by ^1H NMR.

The reactions of **1** with various olefinic alcohols took place smoothly to give the corresponding bicyclic compounds in good yields (Table 1). The present reaction is generally applicable to the formation of bicyclic compounds having five, six, and seven-membered rings.

The construction of a highly strained tricyclic compound can also be accomplished by the present reaction (entry 9). It is also noteworthy that cis products were formed preferentially from secondary olefinic alcohols. In the case of the formation of six-membered rings, this stereoselectivity can be explained in terms of the diaxial orientation of the C-C double bond and the C-Sn bond which attains the maximum overlap of the π^* orbital and the C-Sn σ orbital [9], although more data should be accumulated for the elucidation of the detailed mechanism.



In summary, we have developed an *in situ* sequential transacetalization-intramolecular cyclopropanation reaction of a stannyl acetal with an olefinic alcohol. The present reaction provides an efficient method for the construction of oxygen-containing bicyclic and tricyclic compounds involving a cyclopropane ring with high stereoselectivity.

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