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Synthesis of 1-hydrocarbon substituted cyclopropyl silyl ketones

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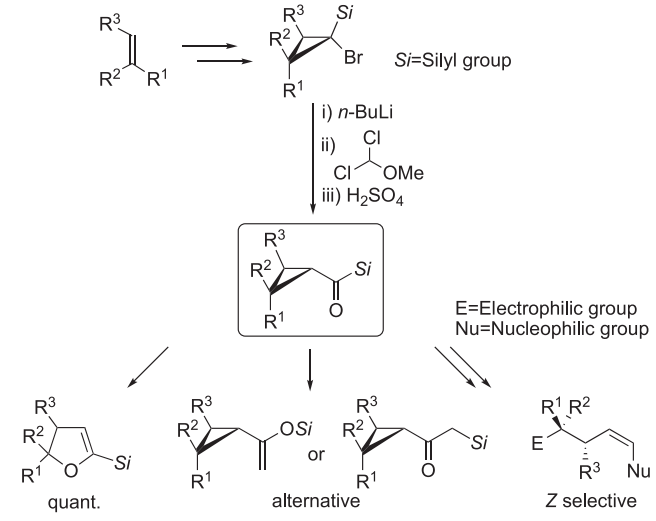
ABSTRACT

The synthesis of cyclopropyl silyl ketones possessing a hydrocarbon group at 1-position of three-membered ring was investigated. The reaction of sulfoxonium ylide with α,β-unsaturated acylsilanes derived from α,β-unsaturated aldehydes did not afford the desired acylsilane derivatives. Instead, the corresponding silyl enol ethers were yielded exclusively. On the other hand, the Corey-Chaykovsky cyclopropanation of α-substituted α,β-unsaturated aldehydes proceeded well to give 1-substituted cyclopropyl aldehydes. The silyl substitution of formyl proton in the obtained aldehydes via umpolung of carbonyl group afforded the target acylsilanes.

Introduction

Acylsilanes will become useful synthetic intermediates due to specific properties of sterically congested and electrically positive silyl group and carbonyl group that is one of the most reactive organic functional groups [1]. We have currently investigated the newly synthetic methods for functionalized acylsilanes [2] and their synthetic utilities [3]. Especially, cyclopropyl silyl ketones have attracted attention as useful synthetic intermediates, because three specific reaction sites, cyclopropyl group, silyl group, and carbonyl group are present in one molecule [4]. Therefore we have become interested in exploring the chemistry of cyclopropyl silyl ketones. For example, we have previously described a route to cyclopropyl silyl ketones via three steps beginning with simple alkenes [5], and then reported that the efficient synthesis of silyl-substituted dihydrofurans [6], silyl enol ethers or β-ketosilanes [7] and the stereoselective synthesis of *Z*-homoallyl derivatives [8] using specific reaction sites of cyclopropyl silyl ketones (Scheme 1). Our synthetic method is convenient and gives many kinds of cyclopropyl silyl ketones having various hydrocarbon substituents on 2- and/or 3-positions of three-membered ring. However, this procedure is valuable to make cyclopropyl silyl ketones possessing an electrophilic group such as halogen, phenylthio group, phenylseleno group on 1-position, but cannot afford 1-hydrocarbon substituted cyclopropyl silyl ketones that would be useful building brocks in organic synthesis for multiply substituted hydrocarbon compounds [5a]. Hitherto, only one example of



Scheme 1. Synthesis and reactions of cyclopropyl silyl ketones.

synthesis of cyclopropyl silyl ketones having a methyl group on 1-position of cyclopropane ring has been reported by Danhaizer about 30 years ago [4a,4e,9]. In this letter, we wish to describe the investigation into the silylation and cyclopropanation of α,β-unsaturated aldehydes as starting materials in two routes to prepare 1-hydrocarbon substituted cyclopropyl silyl ketones in which no one has ever synthesized (Scheme 2). Herein we would also like to state about the reaction behavior of α,β-unsaturated acylsilanes in Corey-Chaykovsky reaction [10].

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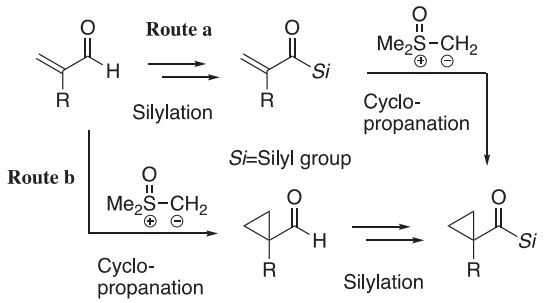


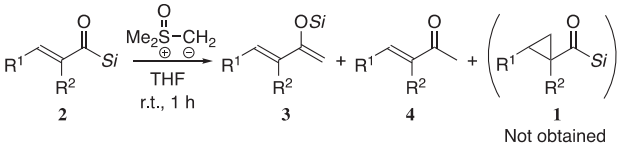
Scheme 2. Two synthetic routes to cyclopropyl silyl ketones from α,β-unsaturated aldehydes.

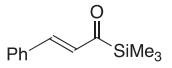
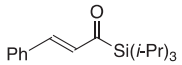
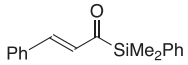
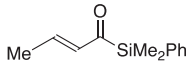
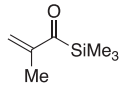
Results and discussion

Initially the cyclopropanation of α,β-unsaturated acylsilanes by Corey-Chaykovsky reaction to obtain cyclopropyl silyl ketones **1** was carried out (Route a in Scheme 2). The results were summarized in Table 1. First of all, to optimize the conditions of Corey-Chaykovsky reaction using α,β-unsaturated acylsilanes, the reaction of readily accessible β-substituted α,β-unsaturated acylsilanes **2** with dimethylsulfoxonium methylide was explored (Entries 1–4). The β-substituted α,β-unsaturated acylsilanes **2** were prepared according to the literature methods [2c]. The 3-phenyl substituted ethenyl silyl ketones reacted with sulfoxonium ylide [11] that was generated by the reaction of trimethylsulfoxonium iodide with *n*-butyllithium. However, in these reactions, the Corey-Chaykovsky cyclopropanation did not proceed at all, and the corresponding silyl enol ethers **3** and hydrolyzed ketones **4** were exclusively afforded (Entry 1). The reaction under low temperature showed lower yield (Entry 2). The ylide derived from sulfoxonium chloride reacted with acylsilane to give nearly the same result (Entry 3). The reaction using ylide generated from sulfoxonium iodide with sodium hydride instead of *n*-butyllithium preferentially provided **4** with low yield (Entry 4). In other reactions using different acylsilanes, **3** and **4** were also yielded independent of the kind of substituents on silicon atom or alkene moiety (Entries 5–7). Then the cyclopropanation of 2-methylethenyl silyl ketone, which should afford the desired 1-methyl substituted cyclopropyl silyl ketone, also proceeded to give the corresponding silyl enol ether exclusively (Entry 8). The results mentioned above suggest the following mechanism for the reaction (Scheme 3). Generally, Corey-Chaykovsky cyclopropanation proceeds via 1,4-addition of sulfoxonium ylide to α,β-unsaturated ketone **2** to afford cyclopropyl ketone through an intermediate **A**. However, in the reaction using α,β-unsaturated silyl ketone and sulfur ylide, 1,2-addition took precedence due to the resonance stabilization of allyl anions **C** and **D** derived via Brook rearrangement [12] of silyl group through the 1,2-adduct intermediate **B**. Resultingly, the elimination of dimethyl sulfoxide from allyl anion **C** gave the silyl enol ether **3** [7]. In other words, the presence of easy rearrangeable silyl group prevents the Corey-Chaykovsky cyclopropanation of α,β-unsaturated carbonyl compounds. These results strongly suggest that the target compounds, 1-hydrocarbon substituted cyclopropyl silyl ketones cannot be synthesized via route a in Scheme 2.

As mentioned above, it became clear that the presence of silyl group interfered with the 1,4-addition of the ylide to the acylsilanes that would lead to the formation of desired cyclopropyl ketones, then the order of silylation and cyclopropanation using α,β-unsaturated aldehydes were reversed (Route b in Scheme 2). According to the literature, α,β-unsaturated aldehydes having a *n*-hexyl, benzyl, isopropyl, or phenyl group were prepared from simple and accessible aldehydes, as starting materials for cyclopropanation [13,14]. Firstly Corey-Chaykovsky reaction of enone

Table 1
Reaction of α,β-unsaturated acylsilanes **2** with dimetylsulfoxonium methylide.



Entry	Substrate	Temp. (°C)	Total yield (%)[a]	Relative ratio **3**/**4**
1		r.t.	83	98/2
2		−50	50[b]	92/8
3		r.t.	83[b,c]	>99/1
4		r.t.	22[d]	8/92
5		r.t.	98[b]	>99/1
6		r.t.	61[b]	84/16
7		r.t.	75[b]	90/10
8		r.t.	70	>99/1

Molar ratio; acylsilane (**2**)/ylide = 1:1.2.
Ylide was generated by reaction of trimethylsulfoxonium iodide with *n*-BuLi.
[a] Isolated yield.
[b] Determined by ^{1}H NMR.
[c] Ylide was prepared from sulfoxonium chloride with *n*-BuLi.
[d] Ylide was prepared from sulfoxonium iodide with NaH.

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