

Reactions of homoallylstannanes with carbon electrophiles: stereoselective cyclopropylmethylation based on the γ -effect of tin

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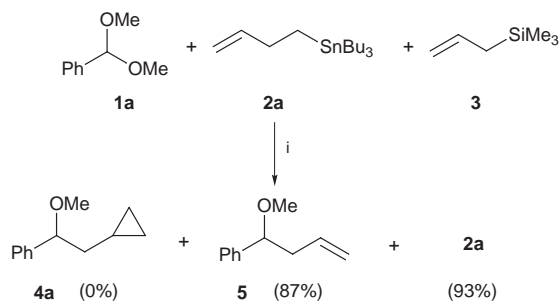
Received (in Cambridge, UK) 7th January 1999, Accepted 29th January 1999

Homoallylstannanes reacted with carbon electrophiles such as acetals, acid chlorides and aldehydes in the presence of Lewis acids to give the cyclopropylmethylated products with high stereoselectivities.

Enormous advances have been made in the study of the β -effect of silicon, and a number of reactions have been developed based on this effect and utilized for a variety of synthetic applications.¹ The γ -effect of silicon, however, seems to be less effective and has not been embraced as a viable principle in organic synthesis.² On the other hand, studies on the γ -effect of tin revealed the effectiveness of this effect³ and have uncovered a rich variety of synthetic applications in recent years.⁴ Previously, we have reported that the γ -effect of tin is stronger than the β -effect of silicon in intramolecular competition and that cationic cyclopropanation of 'tin carbenoids' with alkenes can be achieved based on the γ -effect of tin.⁵ We have also been interested in the intermolecular competition between the γ -effect of tin and the β -effect of silicon. During the course of this study we found a cyclopropylmethylation reaction using homoallylstannanes that would be useful in organic synthesis.⁶ We report here the preliminary results of these studies.

The intermolecular competition between the γ -effect of tin and the β -effect of silicon was examined using an electrophilic reaction of a homoallylstannane and an allylsilane. Thus, a 1 : 1 mixture of homoallyltributylstannane **2a** and allyltrimethylsilane **3** in CH_2Cl_2 was treated with 1 equiv. of benzaldehyde dimethyl acetal **1a** in the presence of TMSOTf (Scheme 1). Most of **2a** was recovered unchanged and only allylated product **5** was obtained in 87% yield. The cyclopropylmethylated product **4a** was not detected.

This result indicates that **3** is much more reactive than **2a** toward the oxonium ion ($\text{PhCH}=\text{OMe}^+$) generated from **1a** and suggests that the β -effect of silicon is stronger than the γ -effect of tin in intermolecular competition. In other words, the β -silyl group activates the carbon-carbon double bond more effectively toward the electrophilic reaction than the γ -stannyl group. This difference can be explained in terms of molecular orbital considerations. In the case of allylsilane **3**, the energy level of the π orbital of the carbon-carbon double bond is increased by interaction with the neighboring carbon-silicon σ orbital (σ - π interaction).⁷ Therefore, the reactivity toward electrophiles is



Scheme 1 Reagents and conditions: i, TMSOTf (1.05 equiv.), CH_2Cl_2 , -78°C , 3 h.

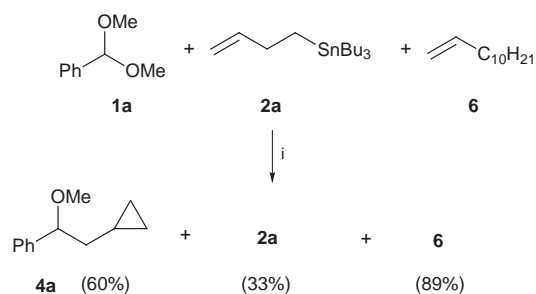
increased. In the case of homoallylstannane **2a**, however, the energy level of the π orbital should be similar to that for normal carbon-carbon double bonds, because the interaction between the π orbital of the carbon-carbon double bond and the carbon-tin σ orbital seems to be very weak, due to the flexibility of the conformation.⁸

The next question which naturally emerged in our mind is whether the reactivity of the carbon-carbon double bond of the homoallylstannane is the same as those of simple terminal alkenes. Thus, we examined the intermolecular competition between the homoallylstannane and normal terminal alkenes. A 1 : 1 mixture of homoallylstannane **2a** and dodec-1-ene **6** was allowed to react with **1a** in the presence of TMSOTf. Although it required a slightly higher temperature, the reaction of **1a** and **2a** took place to give the cyclopropylmethylated product **4a** in 60% yield. Most of **6** was recovered unchanged (Scheme 2).

This result indicates that the homoallylstannane is definitely more reactive toward electrophiles than terminal alkenes. Therefore, there seems to exist some interaction between the carbon-tin σ orbital and the π orbital of the carbon-carbon double bond (**B** in Fig. 1) even if it is not particularly strong. This led us to a new aspect of the γ -effect of tin.

The following mechanism seems to be plausible. The oxonium ion is generated by the reaction of acetal **1a** with TMSOTf and then adds to the carbon-carbon double bond of homoallylstannane **2a** to give the γ -carbocation to tin. The facile γ -elimination of tin to form a cyclopropane ring takes place to give the final product **4a**.

The successful reaction of homoallylstannane **2a** and acetal **1a** prompted us to develop new reactions of homoallylstannanes with carbon electrophiles. As shown in Table 1, acetals, acid



Scheme 2 Reagents and conditions: i, TMSOTf (1.05 equiv.), CH_2Cl_2 , -50°C , 3 h.

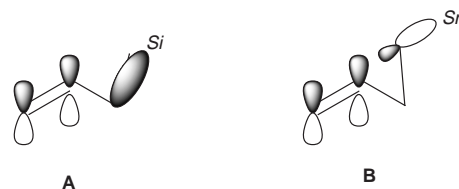

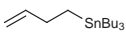
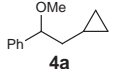
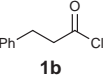
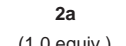
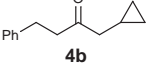
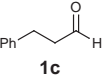
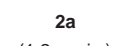
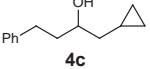

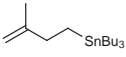
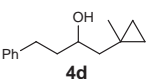

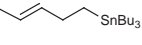
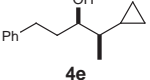


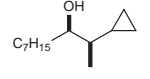
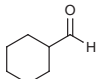
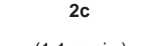
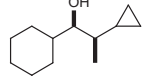

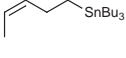



Fig. 1 σ - π Interactions in the allylsilane (A) and the homoallylstannane (B).

Table 1 Reactions of homoallylstannanes with carbon electrophiles in the presence of Lewis acids^a

$E^+ + \text{Homoallylstannane} \xrightarrow[\text{-Bu}_3\text{Sn}^+]{\text{Lewis acid}} E\text{-Cyclopropyl} + E\text{-Allyl} \text{ (minor)}$			
1	2	4	7 (minor)
Yield (%)			
Electrophile	Homoallylstannane	4	4 (erythro:threo) ^c 7
 1a^b	 2a (1.3 equiv.)	 4a	87 ^{1d}
 1b	 2a (1.0 equiv.)	 4b	87 12
 1c	 2a (1.2 equiv.)	 4c	76 7
 1c	 2b (1.3 equiv.)	 4d	86 10
 1c	 2c (<i>E:Z</i> = 88:12) (1.1 equiv.)	 4e	87 (97:3) 7
 1d	 2c (1.1 equiv.)	 4f	83 (>99:1) 3 ^d
 1e	 2c (1.1 equiv.)	 4g	87 (97:3) 5 ^d
 1e	 2d (<i>E:Z</i> = 1:>99) (1.2 equiv.)	 4g	78 (68:32) ^{1d}

^a Reaction conditions; 0.50 mmol of **1**, 1.0–1.3 equiv. of **2** and 1.1 equiv. of TiCl_4 in CH_2Cl_2 (1.8 ml) at -78°C for 3 h. ^b TMSOTf (1.05 equiv.) was used instead of TiCl_4 , at -40°C , 3 h. ^c Determined by GLC. ^d The homoallylated product **7** was not fully characterized.

halides and aldehydes were found to be effective as carbon electrophiles. In the case of acid halides and aldehydes, TiCl_4

was more effective than TMSOTf. The corresponding cyclopropylmethylated products **4** were obtained in good yields together with small amounts of homoallylated by-products **7**.²

The diastereoselectivity of the present reaction is remarkable. For example, the *erythro* product was obtained selectively (97:3) starting from **1e** and (*E*)-pent-3-enyltributylstannane (*E:Z* = 88:12).⁹ Presumably, the addition to the carbonyl group took place in an antiperiplanar fashion.¹⁰ The reaction of **1e** and (*Z*)-pent-3-enyltributylstannane (*E:Z* = 1:99), however, resulted in a decrease of the selectivity (68:32). The low selectivity of the *cis* isomer might be explained in terms of the competition between the antiperiplanar transition state and the synclinal transition state.¹¹

In summary, intermolecular competition revealed that a β -silyl group activates carbon–carbon double bonds toward electrophilic reactions more effectively than a γ -stannyl group. It was also found that the γ -stannyl group activates the carbon–carbon double bond slightly more effectively than alkyl groups. We also found that the reactions of homoallylstannanes with carbon electrophiles such as acetals, acid halides and aldehydes took place smoothly in the presence of Lewis acids. These reactions serve as a stereoselective method for cyclopropylmethylation of carbonyl compounds. Further mechanistic studies on the evaluation of the γ -effect of tin and its synthetic applications are under investigation.

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Communication 9/00228F