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Z-Selective Synthesis of Homoallylic Alcohols *via* 2-Alkenylation of Aldehydes by 1-(Tributylstannyl)-2-alkene

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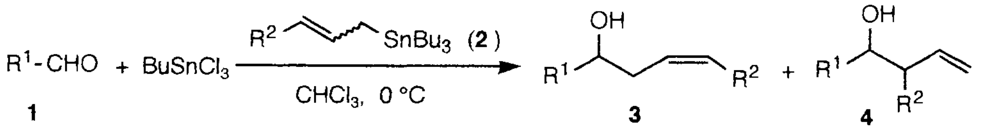
1-(Tributylstannyl)-2-alkene reacts with a solution of an aldehyde and $BuSnCl_3$ to give (*Z*)-homoallylic alcohol. *Z*-Selective 2-methyl-2-butenylation can be accomplished by using (Z)-2-methyl-1-(tributylstannyl)-2-butene instead of 1-(tributylstannyl)-2-alkene. This reaction is useful as a new method to make (Z)-double bond. An application of the present method for a synthesis of pheromones is also described.

Stereoselective introduction of a (*Z*)-double bond is a very important process in organic synthesis. Wittig reaction1) and hydrogenation of triple bond2) are useful conventional methods for this purpose. The transition metal-catalyzed cross-coupling between organometalics and alkyl or alkenyl halides or esters is also useful.3) However, stereo-selective synthesis of the alkenyl organometalics and/or alkenyl halides is necessary for it.

In this paper, we wish to report a new method to introduce the (Z)-double bond by *Z*-selective 2-alkenylation of an aldehyde. Although an addition of the allylic tin compound to aldehyde proceed *Z*-selectively in the presence of Lewis acids4) such as $SnCl_4$,4a) $MgBr_2$,4b) or $BF_3•OEt_2$,4c) an alkoxy substituent such as benzyloxy group on allylic tin compound is necessary for it. Thermal reaction of the allylic tin compound with aldehyde4d) also proceeds *Z*-selectively. However, a migration of the double bond occurs in this method.

Although Bu_2SnCl_2 mediated *Z*-selective 2-butenylation of aldehydes by 1-(tributylstannyl)-2-butene proceed with excellent yield and excellent stereoselectivity,5) *Z*-selective 2-alkenylation other than 2-butenylation is not successful probably because of poor reactivity of Bu_2SnCl_2 for transmetallation with 1-(tributylstannyl)-2-alkene. We have been studying the transmetalation of 1-(tributylstannyl)-2-alkene with $BuSnCl_3$, which is more reactive than Bu_2SnCl_2, and the following addition to aldehydes,6) and in this paper, we wish to report the $BuSnCl_3$ mediated *Z*-selective 2-alkenylation of an aldehyde by an *E*,*Z* mixture of 1-(tributylstannyl)-2-butene.



(1)

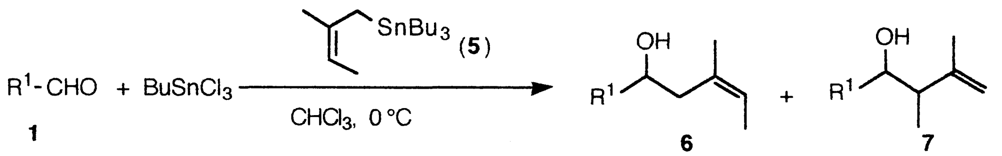
When a $CHCl_3$ solution of an aldehyde (**1**) and $BuSnCl_3$ was treated with an *E*,*Z* mixture7) of 1-(tributylstannyl)-2-alkene (**2**), the *Z*-selective 2-alkenylation of **1** proceed smoothly to give *Z* homoallylalcohol (**3**). Results were summarized in Table 1. In all cases shown in Table 1, (*E*)-isomers were not detected in NMR analysis. However, small amount of the regioisomers (**4**) were obtained. The 2-alkenylation of **1f**, **1g**, and **1h** proceeded with poor diastereoselectivity to give **3f**, **3g**, and **3h**, respectively, as a mixture of diastereomers. The configurations of the diastereomers were not determined.

Table 1. *Z*-Selective 2-alkenylation of **1**

	R^1		R^2	Main product	Yield/% [a]	**3** : **4**
1a	Ph	**2a**	Pn	**3a**	94	95 : 5 [b]
1b	Et	**2a**	Pn	**3b**	81	97 : 3 [b]
1c	Hex	**2b**	Pr	**3c**	86	98 : 2 [b]
1d	AcO(CH$_2$)$_5$	**2b**	Pr	**3d**	92	98 : 2 [b]
1e	AcO(CH$_2$)$_9$	**2b**	Pr	**3e**	87	98 : 2 [b]
1f	MeCH(SPh)CH$_2$	**2c**	Pn	**3f**	76	97[d] : 3 [c]
1g	MeCHSPh	**2a**	Pn	**3g**	79	96[e] : 4 [c]
1h	PhCH(SPh)CH$_2$	**2a**	Pn	**3h**	79	97[d] : 3 [c]
1i	CH$_2$=CH	**2a**	Pn	**3i**	75	93 : 7 [b]

a) Total isolated yield of **3** and **4**. b) Determined by GLC. c) Determined by NMR.
d) About 5:4 mixture of diastereomers. e) About 3:2 mixture of diastereomers.

2-Methyl-2-butenylation also proceeded successfully under similar conditions by using (*Z*)-2-methyl-1-(tributylstannyl)-2-butene (**5**), which can be prepared easily by Pd(0) catalyzed hydrostannation of isoprene.[8] Results were summarized in Table 2. In the case of **1a**, using 2 eq of **1a**, based on BuSnCl$_3$, is effective to improve the regioselectivity. However, the yield of **6a** decreased to some extent.



(2)

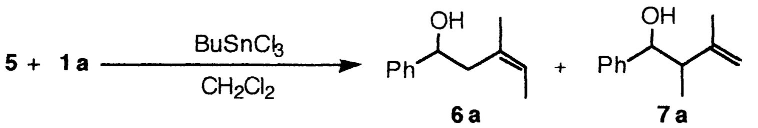
Table 2. *Z*-Selective 2-methyl-2-butenylation of **1**

	R^1	Main product	Yield/%[a]	**6** : **7**[b]
1a	Ph	**6a**	79	90 : 10
1a	Ph	**6a**	64	93 : 7 [c]
1c	*n*-Hex	**6b**	84	99 : 1
1j	*i*-Pr	**6c**	77	99 : 1
1k	*i*-Bu	**6d**	77	99 : 1
1l	*c*-Hex	**6e**	52	99 : 1

a) Total isolated yield of **6** and **7**. b) Determined by GLC.
c) Molar ratio of **1a**:BuSnCl$_3$:**5** is 2.4:1.2:1.

It must be noted that 1-(tributylstannyl)-2-alkenes (**2** or **5**) must be added last. If **1** or BuSnCl$_3$ was added last, the regio selectivity of 2-alkenylation decreased considerably. For example, when BuSnCl$_3$ was added to a

CH_2Cl_2 solution of **5** and **1a** at 0 °C, **7a** was obtained in 86% yield, and **6a** was not obtained (Eq. 3). And even when $BuSnCl_3$ was added at -78 °C, **6a** was obtained in 62% yield, and the regioisomer **7a** was obtained in 28% yield. Similarly, when **1a** was added last at 0 °C, **6a** was not obtained (Eq. 4).

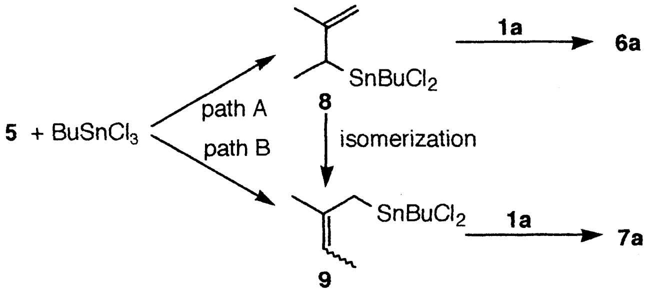


6a **7a** (3)

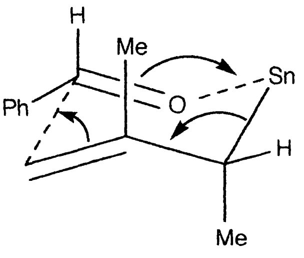
	6a	7a
0 °C	0%	86% (6:1 mixture of diastereomers)
- 78 °C → 0 °C	62%	28% (4:1 mixture of diastereomers)

$$5 + BuSnCl_3 \xrightarrow[CH_2Cl_2,\ 0\ °C,\ 10\ min]{} \xrightarrow[0\ °C,\ 10\ min]{1a} \underset{0\%}{6a} + \underset{86\%\ (1:1\ mixture\ of\ diastereomers)}{7a} \quad (4)$$

The mechanism of this reaction can be explained as follows. The transmetalation of allylic tin compound with $BuSnCl_3$ or Bu_2SnCl_2 is well-established reaction.[5,6,9] As we have reported recently, the regioselectivity of the transmetalation depends on the stereo-chemistry of the double bond.[6] When **5** is not added last, considerable amount of **5** reacts with $BuSnCl_3$ by path B in Scheme 1 to give **9**, and the alternative product **8** readily isomerize at 0°C to more stable **9**. The transmetalation product **8** and **9** react with **1a** to give **6a** and **7a**, respectively. The well-established cyclic chair-like transition state (Scheme 2) can explain it.[5,6] The reaction of **5** and **1a** at -78 °C, the isomerization of **8** to **9** is slow enough to give considerable amount of **6a**. On the other hand, the corresponding reaction at 0 °C, the isomerization is too fast to give **6a**. When **5** is added last, the oxygen atom of **1a** coordinates to $BuSnCl_3$.[10] The coordination of **1a** reduces the electrophilicity of $BuSnCl_3$, and it is effective to improve the regio-selectivity of the transmetalation. Further study on the transmetalation is now in progress.

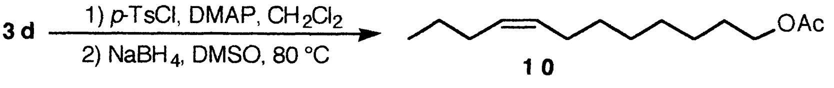


Scheme 1.



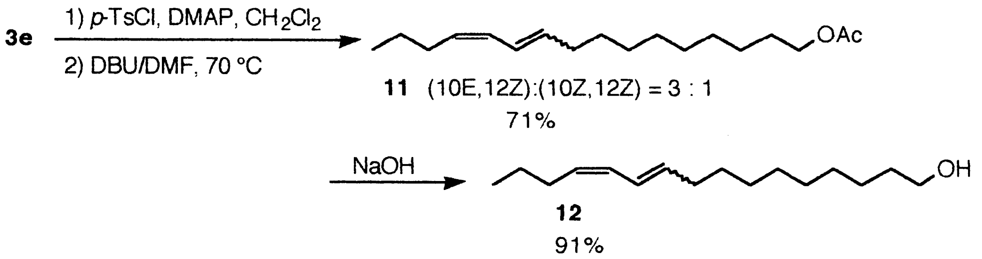
Scheme 2. Chair-like transition state (**1a** +**8**).

The present method can be applied to a stereoselective synthesis of pheromones which have (*Z*)-double bonds. Tosylation of **3d** and the subsequent reduction by $NaBH_4$ in DMSO gave (*Z*)-8-dodecenyl acetate (**10**), sex pheromone of *Grapholitha molesta*, in 58% yield. Bombykol (**12**), sex pheromone of *Bombyx mori*, can also be synthesized from **3e**. Results are summarized as follows.



1 0

58% (5)



11 (10E,12Z):(10Z,12Z) = 3 : 1
71%

12
91%

(6)

This method provides a new method for an introduction of (*Z*)-double bond from *E*,*Z*-mixture of 1-(tributylstannyl)-2-alkenes which can be prepared by various methods.

A typical procedure for the *Z*-selective 2-alkenylation is as follows. To a $CHCl_3$ (2 ml) solution of **1a** (0.21 g, 2.0 mmol), was added $BuSnCl_3$ (0.42 g, 1.5 mmol) in $CHCl_3$ (0.5 ml) at 0 °C. After stirring at this temperature for 2 min, **2a** (0.40 g, 1.0 mmol) in $CHCl_3$ (1 ml) was added slowly. The mixture was stirred at 0 °C for 30 min. Then it was poured into water and extracted with ether. The organic layer was separated and dried over $MgSO_4$, and evaporated. The crude product was purified with flash chromatography on silica gel to give a mixture of **3a** and **4a** (95:5, total 0.205 g, 0.94 mmol) in 94% yield.

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