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 BuSnCl₃ 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 reaction $^{(1)}$ and hydrogenation of triple bond $^{(2)}$ 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. 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 SnCl₄,^{4a)} MgBr₂,^{4b)} or BF₃•OEt₂,^{4c)} an alkoxy substituent such as benzyloxy group on allylic tin compound is necessary for it. Thermal reaction of the allylic tin compound with aldehyde^{4d)} also proceeds Z-selectively. However, a migration of the double bond occurs in this method.

Although Bu₂SnCl₂ 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 Bu₂SnCl₂ for transmetallation with 1-(tributylstannyl)-2-alkene. We have been studying the transmetalation of 1-(tributylstannyl)-2-alkene with Bu₂SnCl₃, which is more reactive than Bu₂SnCl₂, and the following addition to aldehydes,⁶⁾ and in this paper, we wish to report the Bu₂SnCl₃ mediated Z-selective 2-alkenylation of an aldehyde by an E,Z mixture of 1-(tributylstannyl)-2-butene.

$$R^{1}\text{-CHO} + \text{BuSnCl}_{3} \xrightarrow{R^{2}} \text{SnBu}_{3} \text{ (2)}$$

$$CHCl_{3}, \text{ 0 °C}$$

$$R^{1} \xrightarrow{\text{CHCl}_{3}} \text{ R}^{2} + R^{1} \xrightarrow{\text{R}^{2}} \text{ (1)}$$

When a CHCl3 solution of an aldehyde (1) and BuSnCl3 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.

	R^1		R^2	Main product	Yield/% a)	3 : 4
1a	Ph	2a	Pn	3a	94	95 : 5 ^b
1 b	Et	2a	Pn	3 b	81	97 : 3 b)
1 c	Hex	2 b	Pr	3 c	86	98 : 2 ^b
1 d	AcO(CH ₂) ₅	2 b	Pr	3 d	92	98 : 2 b)
1 e	AcO(CH ₂) ₉	2 b	Pr	3 e	87	98 : 2 b)
1 f	MeCH(SPh)CH ₂	2 c	Pn	3 f	76	97 ^d): 3 ^c)
1 g	MeCHSPh	2a	Pn	3 g	79	96 ^{e)} : 4 ^{c)}
1 h	PhCH(SPh)CH ₂	2a	Pn	3 h	79	97 ^d): 3 ^c)
1 i	CH2=CH	2a	Pn	3 i	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 BuSnCl₃, is effective to improve the regionselectivity. However, the yield of 6a decreased to some extent.

$$R^{1}$$
-CHO + BuSnCl₃ CHCl₃, 0 °C R^{1} C

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)}
1 c	n-Hex	6 b	84	99 : 1
1j	i-Pr	6 c	77	99 : 1
1 k	<i>i</i> -Bu	6 d	77	99 : 1
11	c-Hex	6 e	52	99 : 1

- a) Total isolated yield of 6 and 7. b) Determined by GLC.
- c) Molar ratio of 1a:BuSnCl3:5 is 2.4:1.2:1.

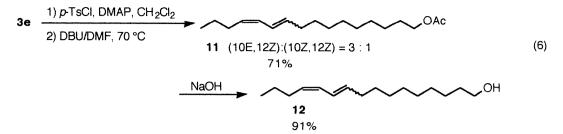
It must be noted that 1-(tributylstannyl)-2-alkenes (2 or 5) must be added last. If 1 or BuSnCl3 was added last, the regio selectivity of 2-alkenylation decreased considerably. For example, when BuSnCl3 was added to a

CH₂Cl₂ solution of **5** and **1a** at 0 °C, **7a** was obtained in 86% yield, and **6a** was not obtained (Eq. 3). And even when BuSnCl₃ 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).

5 + 1a
$$\xrightarrow{\text{BuSnCl}_3}$$
 $\xrightarrow{\text{CH}_2\text{Cl}_2}$ $\xrightarrow{\text{Ph}}$ $\xrightarrow{\text{C}}$ $\xrightarrow{\text{C}}$

The mechanism of this reaction can be explained as follows. The transmetalation of allylic tin compound with BuSnCl₃ or Bu₂SnCl₂ 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 BuSnCl₃ 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 BuSnCl₃.¹⁰⁾ The coordination of 1a reduces the electrophilicity of BuSnCl₃, and it is effective to improve the regio-selectivity of the transmetalation. Further study on the transmetalation is now in progress.

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 NaBH4 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.



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 CHCl₃ (2 ml) solution of **1a** (0.21 g, 2.0 mmol), was added BuSnCl₃ (0.42 g, 1.5 mmol) in CHCl₃ (0.5 ml) at 0 °C. After stirring at this temperature for 2 min, **2a** (0.40 g, 1.0 mmol) in CHCl₃ (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 MgSO₄, 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.

References

- 1) I. Gosney and A. G. Rowley, "Organophosphorus Reagents in Organic Synthesis," ed by J. I. G. Cadogan, Academic Press, New York (1979); M. Schlosser, *Top. Stereochem.*, 5, 1 (1970).
- 2) H. Lindlar, Helv. Chim. Acta, 35, 446 (1952); E. N. Marvell and T. Li, Synthesis, 1973, 457.
- 3) F. J. McQuillin, D. G. Parker, and G. R. Stephenson, "Transition Metal Organometallics for Organic Synthesis," Cambridge University Press, Cambridge (1991), Chap. 10.
- Reviews: Y. Yamamoto and N. Asao, Chem. Rew., 93, 2207 (1993); Y. Nishigaichi, A. Takuwa, Y. Naruta, and K. Maruyama, Tetrahedron, 34, 7395 (1993); a) A. H. McNeill and E. J. Thomas, Tetrahedron Lett., 31, 6239 (1990); 33, 1369 (1992); 34, 1669, 3933 (1993); b) J. A. Marshall and G. P. Luke, J. Org. Chem., 56, 483 (1991), c) B. W. Gung, D. T. Smith, M. A. Wolf, Tetrahedron Lett., 32, 13 (1991); B. W. Gung, A. J. Peat, B. M.Snook, and D. T. Smith, ibid, 32, 457 (1991), d) C. Hull, S. Mortlock, and E. J. Thomas, Tetrahedron, 45, 1007 (1989); A. J. Pratt and E. J. Thomas, J. Chem. Soc. Perkin Trans. 1, 1989, 1521.
- 5) A. Gambaro, P. Ganis, D. Marton, V. Peruzzo, and G. Tagliavini, *J. Organomet. Chem.*, 231, 307 (1982); A. Gambaro, V. Peruzzo, G. Plazzogna, and G. Tagliavini, *ibid.*, 197, 45 (1980).
- 6) H. Miyake and K. Yamamura, Chem. Lett., 1992, 1369, 2221; 1993, 1473.
- 7) E/Z ratios of 2 are in the range of 2/1 to 3/1.
- 8) H. Miyake and K. Yamamura, Chem. Lett., 1992, 507, 1099.
- 9) R. L. Marshall and D. Young, Tetrahedron Lett., 33, 2369 (1992).
- M. Ochiai, S. Iwaki, Y. Nagao, S. Kitagawa, and M. Munakata, Tetrahedron Lett., 32, 4945 (1991); M. Ochiai, S. Iwaki, T. Ukita, Y. Matsuura, M. Shiro, and Y. Nagao, J. Am. Chem. Soc., 110, 4606 (1988); E. Vedejes, D. E. Erdman, and D. R. Powell, J. Org. Chem., 58, 2840 (1993).

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