Novel Method of Three-Carbon Elongation Using Bis(tributylstannyl)propanol

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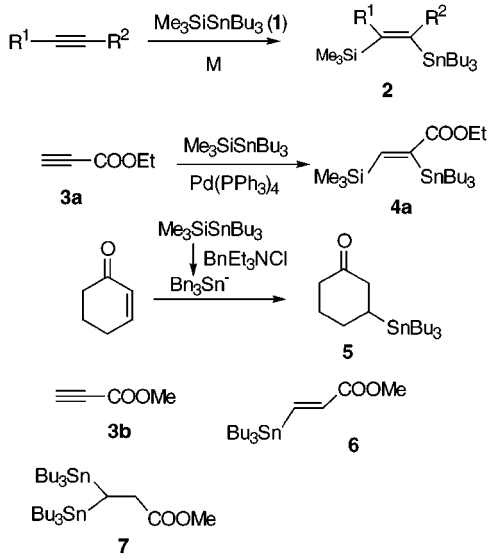
The reaction of $Me_3SiSnBu_3$ (**1**) with methyl propiolate in DMF in the presence of $BnEt_3NCl$ gave methyl 3,3-bis(tributylstannyl)propionate (**7**) in high yield. Reduction of **7** with $LiAlH_4$ followed by treatment with MOMCl gave 3,3-bis(tributylstannyl)propanol derivative **17d** in a quantitative yield, which was a useful reagent for C-3 unit elongation. Treatment of **17d** with BuLi in THF in the presence of HMPA gave α-stannylated carbanion **II**, which reacted with various electrophiles, such as aldehydes, ketones, esters, and alkyl halides, to give C-3 elongation products **III**.

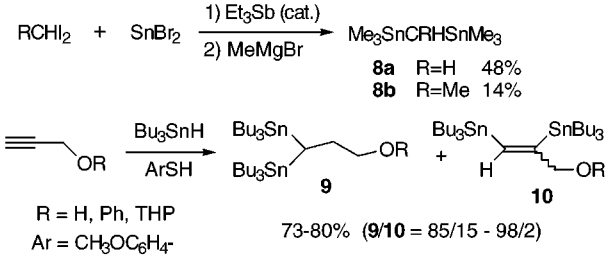
$Me_3SiSnBu_3$[1] (**1**) is useful for synthetic organic chemistry.[1c,2] The addition of $Me_3SiSnBu_3$ to alkynes in a transition metal complex catalyzed reaction is an elegant method for simultaneously adding a silyl group and a stannyl group to two alkyne carbon atoms.[1c,2c−j] The reaction of $Me_3SiSnBu_3$ with ethyl propiolate (**3a**) using a palladium catalyst was reported by Mitchell,[2d] and methyl α-stannyl-β-silylacrylate **4a** was obtained in 75% yield (Scheme 1).

We found that the reaction of $Me_3SiSnBu_3$ (**1**) with $BnEt_3NCl$ produced the stannyl anion,[3] which was effective for a halogen−metal exchange reaction,[3a] and for Michael addition into an α,β-unsaturated compound to give the stannylated compound **5**.[2d,3a,f] We expected that the reaction of $Me_3SiSnBu_3$ with methyl propiolate (**3b**) in the presence of R_4NX would give methyl β-(tributylstannyl)acrylate **6**, which would be a useful transmetalation reagent with palladium complex. When methyl propiolate was reacted with $Me_3SiSnBu_3$ in the presence of $BnEt_3NCl$, methyl bis(tributylstannyl)propionate (**7**) was formed in high yield. We tried to use this compound as a three-carbon elongation reagent.[3j,k] There have been a few reports on methods for the synthesis of bis-stannylated compounds **8**.[4] Reaction of diiodoalkane with $SnBr_2$ in the presence of Et_3Sb followed by treatment with MeMgBr gave bis-stannylated alkane **8** (Scheme 2). A recent report of a radical reaction indicated that propargyl alcohol derivatives reacted with Bu_3SnH and

Scheme 1



Scheme 2



(1) (a) Tamborski, C.; Soloski, E. J. *J. Org. Chem.* **1963**, *28*, 237. (b) Schumann, H.; Ronecker, S. *Z. Naturforsch. B* **1967**, *B22*, 452. (c) Chenard, B. L.; Van Zyl, C. M. *J. Org. Chem.* **1986**, *51*, 3561.

(2) (a) Azizian, H.; Eaborn, C.; Pidcock, A. *J. Organomet. Chem.* **1981**, *215*, 49. (b) Kosugi, M.; Ohya, T.; Migita, T. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 3539. (c) Mitchell, T. N.; Killing, H.; Dicke, R.; Wickenkamp, R. *J. Chem. Soc., Chem. Commun.* **1985**, 354. (d) Mitchell, T. N.; Wickenkamp, R.; Amamria, A.; Dicke, R.; Schneider, U. *J. Org. Chem.* **1987**, *52*, 4868. (e) Murakami, M.; Morita, Y.; Ito, Y. *J. Chem. Soc., Chem. Commun.* **1990**, 428. (f) Murakami, M.; Amii, H.; Takizawa, N.; Ito, Y. *Organometallics* **1993**, *12*, 4223. (g) Hada, M.; Tanaka, Y.; Ito, M.; Murakami, M.; Amii, H.; Ito, Y.; Nakatsuji, H. *J. Am. Chem. Soc.* **1994**, *116*, 8754. (h) Casson, S.; Kocienski, P.; Reid, G.; Smith, N.; Street, J. M.; Webster, M. *Synthesis* **1994**, 1301. (i) Murakami, M.; Yoshida, T.; Kawanami, S.; Ito, Y. *J. Am. Chem. Soc.* **1995**, *117*, 6408. (j) Ito, Y.; Bando, T.; Matsuura, T.; Ishikawa, M. *J. Chem. Soc., Chem. Commun.* **1986**, 980. (k) Tsuji, Y.; Obora, Y. *J. Am. Chem. Soc.* **1991**, *113*, 9368. (l) Lipshutz, B. H.; Reuter, D. C.; Ellsworth, E. L. *J. Org. Chem.* **1989**, *54*, 4975. (m) Chenard, B. L.; Laganis, E. D.; Davidson, F.; RajanBabu, T. V. *J. Org. Chem.* **1985**, *50*, 3666. (n) Obora, Y.; Tsuji, Y.; Asayama, M.; Kawamura, T. *Organometallics* **1993**, *12*, 4697.

(3) (a) Mori, M.; Kaneta, N.; Isono, N.; Shibasaki, M. *Tetrahedron Lett.* **1991**, *32*, 6139. (b) Mori, M.; Kaneta, N.; Isono, N.; Shibasaki, M. *J. Organomet. Chem.* **1993**, *455*, 255. (c) Mori, M.; Kaneta, N.; Shibasaki, M. *Ibid.* **1994**, *464*, 35. (d) Mori, M.; Isono, N.; Kaneta, N.; Shibasaki, M. *J. Org. Chem.* **1993**, *58*, 2972. (e) Mori, M.; Hashimoto, A.; Shibasaki, M. *J. Org. Chem.* **1993**, *58*, 6503. (f) Honda, T.; Mori, M. *Chem. Lett.* **1994**, 1013. (g) Sato, H.; Isono, N.; Okamura, K.; Date, T.; Mori, M. *Tetrahedron Lett.* **1994**, *35*, 2035. (h) Kinoshita, A.; Mori, M. *Chem. Lett.* **1994**, 1475. (i) Isono, N.; Mori, M. *J. Org. Chem.* **1995**, *60*, 115. (j) Isono, N.; Mori, M. *Tetrahedron Lett.* **1995**, *36*, 9345. (k) Isono, N.; Mori, M. *Main Group Metal Chem.* **1996**, *19*, 277. (l) Sato, H.; Isono, N.; Irie, M.; Mori, M. *Tetrahedron* **1996**, *52*, 8143. (m) Isono, N.; Mori, M. *J. Org. Chem.* **1996**, *61*, 7867.

(4) (a) Bulten, E. J.; Gruter, H. F.; Martens, H. F. *J. Organomet. Chem.* **1976**, *117*, 329. (b) Sato, T.; Kawase, A.; Hirose, T. *Synlett* **1992**, 891.

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Scheme 3. Plan for the Carbon-3 Elongation

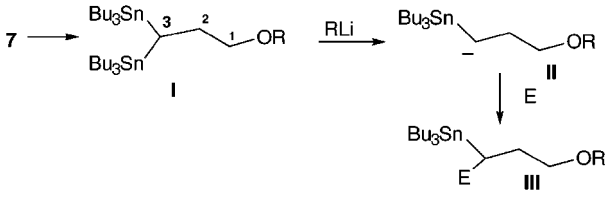
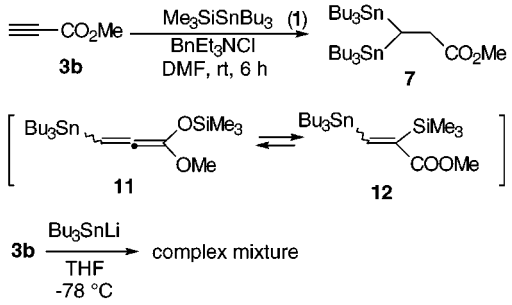


Table 1. Reaction of 3b with $Me_3SiSnBu_3$ (1)[a]

MX	$Me_3SiSnBu_3$ (equiv)	yield of 7 (%) based on **3b**	yield of 7 (%) based on **1**
$BnEt_3NCl$	1	46	93
$BnEt_3NCl$	2	91	92
CsF	2	80	

[a] Reaction was carried out at room temperature.

Scheme 4



ArSH to give bis-stannylated product **9** along with vinylstannane **10**, but the reaction mechanism was not reported.[5]

Since the α-anion of the stannyl group is stabilized by dπ-pπ interaction, anion **II** is expected to be generated by treatment of **I**, which was derived from **7** and RLi (Scheme 3). This generated anion **II** could be useful as a C-3 elongation reagent; i.e., anion **II** should react with various electrophiles, such as aldehyde, ketone, ester, and alkyl halide, to give **III**, which has a stannyl group at the α-position of the electrophiles. Thus, subsequent conversion using this stannyl group would be expected.

Formation of Methyl Bis(tributylstannyl)propionate from Methyl Propiolate and $Me_3SiSnBu_3$ in the Presence of $BnEt_3NCl$. When a DMF solution of methyl propiolate (1 equiv), $Me_3SiSnBu_3$ (1 equiv), and $BnEt_3NCl$ (1 equiv) was stirred at room temperature for 6 h, 3,3-bis(tributylstannyl)propionate (**7**) was obtained in 46% yield. The yield based on $Me_3SiSnBu_3$ (**1**) was 93%, and monostannylated compound **6** was not obtained. When 2 equiv of **1** was used for this reaction, the yield of **7** increased to 91%. The use of CsF instead of $BnEt_3NCl$ gave a similar result, and **7** was obtained in 80% yield (Table 1). Although it is not clear why bis-stannylated product **7** was obtained, the intermediate would be **11**, which is in a state of equilibrium with **12** (Scheme 4). The reaction of methyl propiolate **3b** with Bu_3SnLi, generated from Bu_3SnH and LDA, gave a complex mixture, although GC/MS data indicated that only a trace amount of **7** was produced.

A THF−DMF solution of $Me_3SiSnBu_3$ (2 equiv), methyl propiolate (1 equiv), and $BnEt_3NCl$ (2 equiv) was monitored by ^{119}Sn NMR spectroscopy. The results are shown in Figure 1. First, the signal at δ −121 due to $Me_3SiSnBu_3$ appeared. After 30 min, a new signal at 10.1 ppm, which represents methyl bis(tributylstannyl)propiolate (**7**), appeared, and no other signals were observed. After 4 h, the signals of $Me_3SiSnBu_3$ disappeared and only the signal at δ10.1 ppm was seen. These results indicate that only the signals of the starting material and the product are shown during this reaction.

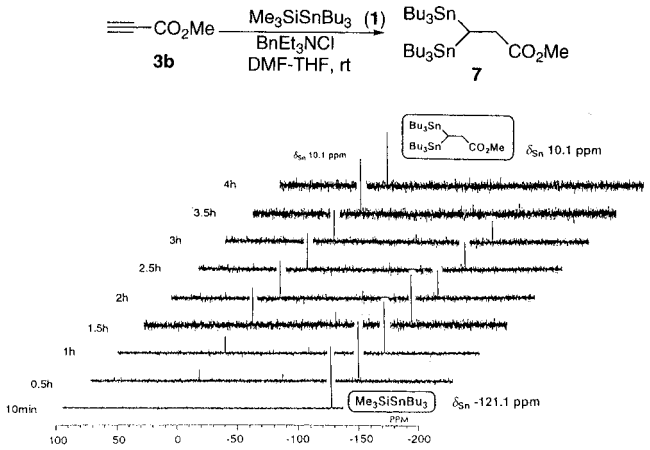


Figure 1. Reaction of **1** with methyl propiolate in the presence of $BnEt_3NCl$ was carried out in DMF−THF and was monitored by ^{119}Sn NMR.

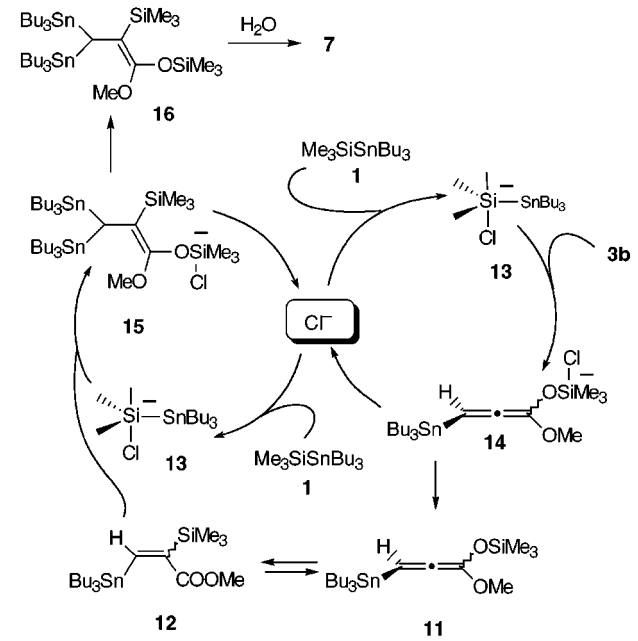
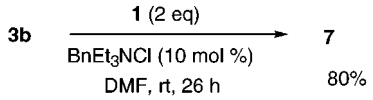


Figure 2.

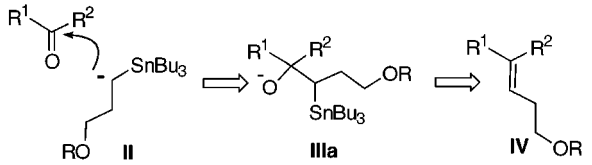
Although it is not clear from the reaction mechanism, it may be possible to consider that this reaction proceeds as shown in Figure 2. The chloride ion of $BnEt_3NCl$ coordinates to the silicon of $Me_3SiSnBu_3$ (**1**) to give hypervalent silicate **13**, which reacts with methyl propiolate (**3b**) to give **14**. This converts into ketene silyl acetal **11**, which should be in a state of equilibrium with α,β-unsaturated ester **12**. This then reacts with **1** in the presence of Cl^- to give **15**, which converts into **16** and Cl^-. Hydrolysis of **16** gave **7**. The fact that the chloride ion is regenerated means that a catalytic cycle is established with regard to the chloride ion. Thus, when a catalytic amount of $BnEt_3NCl$ (10 mol %) was used for

(5) Meurice, J.-C.; Vallier, M.; André, S.; Ratier, M.; Duboudin, J.-G. *J. Organomet. Chem.* **1995**, *491*, C-5.

Scheme 5



Scheme 6. Plan for the Three-Carbon Elongation of a Ketone



this reaction, methyl bis(tributylstannyl)propionate (**7**) was obtained in 80% yield after 26 h (Scheme 5).

Three-Carbon Elongation of Aldehydes and Ketones. Our plan for C-3 unit elongation is shown in Scheme 6. The generated anion **II** reacts with the carbonyl group to produce β-hydroxystannane **IIIa**. If an aldehyde or ketone is used for this reaction, β-hydroxystannane would be formed and a Peterson-type olefination reaction[6] would then occur to give olefin **IV**.

The conversion of a ketone to methylene compounds with an α-stannylated anion has been reported by two groups. In one case, reaction with [(trialkylstannyl)methyl]lithium gave a β-hydroxy stannane, which was converted into the methylene compounds.[7] The other group treated the hydroxy stannane with KH to give the alkene.[8]

Initially, methyl bis(tributylstannyl)propionate (**7**) was converted into bis(tributylstannyl)propanol (**17a**) by treatment of **7** with $LiAlH_4$. The reaction of **17a** with benzaldehyde was attempted for the C-3 elongation reaction. To a THF solution of **17a** was added BuLi (2 equiv) at −78 °C, and the solution was stirred at 0 °C for 1 h. To this solution was added benzaldehyde at −78 °C, and the solution was stirred at 0 °C for 3 h. After the usual workup, the desired product was not obtained, but monostannylated product **18a** was obtained in 46% yield along with **17a** (47% yield). Although the coupling product was not obtained, the results indicated that the anion **20a** was generated (Scheme 7).

Thus, the reactions of the ethers **17b**−**d** with benzaldehyde were examined. In the reaction of **17b** (R = ^{t}BuMe$_2$Si) with benzaldehyde, only 3-(*tert*-butyldimethylsilyl)-3-(tributylstannyl)propanol (**19**) was obtained in 65% yield. In the reaction of **17c** (R = Bn) with benzaldehyde, a complex mixture was obtained. When compound **17d** (R=MOM) was treated in a similar manner and then subjected to silica gel column chromatography,[7a] the desired alkene **21a** was obtained in 4% yield.[9] The yield was improved when HMPA was added to the THF solution. The results are shown in Table 2. The addition of 2 equiv of HMPA gave the best result, and the ratio of

Scheme 7

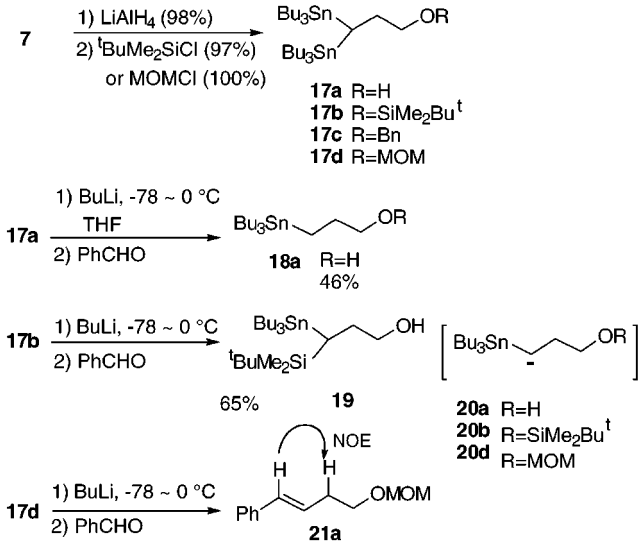
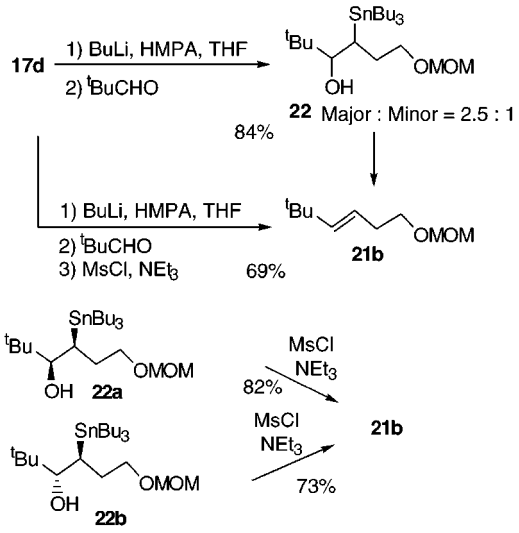


Table 2. Reaction of 9d with Benzaldehyde

run	BuLi (equiv)	Additive	yields (%) **26a** (*E*:*Z*)[a]	**9d**
1	3.0		4	86
2	3.0	HMPA	64 (21:1)	
3	2.0	HMPA	80 (35:1)	
4	1.5	HMPA	72 (21:1)	9
5	1.1	HMPA	51 (17:1)	31

[a] The isomer ratio was determined by ^{1}H-NMR.

Scheme 8



E/*Z* for the product was 35:1. The stereochemistry of **21a** was determined by NOE experiments, which demonstrated that the *E*-olefin was formed. Next, pivalaldehyde was chosen for the reaction. In this case, β-hydroxy stannyl compound **22** was obtained as an inseparable mixture in 84% yield after silica gel column chromatography (Scheme 8).

(6) (a) Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780. (b) Hudrlik, P. F.; Peterson, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 1464. (c) Hudrlik, P. F.; Peterson, D. J.; Rona, R. J. *J. Org. Chem.* **1975**, *40*, 2264. (d) Kauffmann, T. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 410. (e) Kauffmann, T.; Kriegesmann, R.; Hamsen, A. *Chem. Ber.* **1982**, *115*, 1818.

(7) (a) Murayama, E.; Kikuchi, T.; Sasaki, K.; Sootome, N.; Sato, T. *Chem. Lett.* **1984**, 1897. (b) Kauffmann, T.; Kriegesmann, R.; Woltermann, A. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 862.

(8) Kawashima, T.; Iwama, N.; Okazaki, R. *J. Am. Chem. Soc.* **1993**, *115*, 2507.

(9) The crude product was considered to be β-hydroxystannane because of the following observations. The reaction mixture was spotted on a TLC plate and the plate was allowed to stand for several minutes. When it was developed with the reaction mixture, the spot that was allowed to stand on the TLC plate was different from that of the reaction mixture.

Table 3. Peterson-Type Olefination Reaction Using 17d

Entry	Electrophile	Product	Yield of **21**
1[a]	**23c**	**21c**	79%
2[a]	**23d**	**21d**	48%[c]
3[b]	**23e**	**21e**	85% (*Z*:*E*=2:1)
4[b]	**23f**	**21f**	56%[d] (*Z*:*E*=3:1)
5[a]	**23g**	**21g**	80% (*E*:*Z*=2:1)

[a] The crude product was treated with MsCl and Et_3N. [b] Elimination products were obtained without treatment with MsCl and Et_3N. [c] **23d** was obtained in 35% yield. [d] **23f** was obtained in 43% yield.

Scheme 9

II **IIIb**

Various attempts were made to convert **22** into alkene **21b**. We found that treatment of **22** with MsCl in the presence of Et_3N[6] at 0 °C gave *E*-olefin **21b** in good yield. We were able to separate these β-hydroxy stannanes, **22a** and **22b**, and each isomer was treated in a similar manner to give the same *E*-olefin **21b**, respectively. Although it is reported that Peterson elimination occurs by an E2-elimination[6a,b,c] or *syn*-elimination[6d,e] these results indicate that the elimination would occur via an E1-mechanism. To obtain alkene **21b** directly from **17d**, the crude reaction product was treated with MsCl in the presence of NEt_3 to give **21b** in 69% yield.

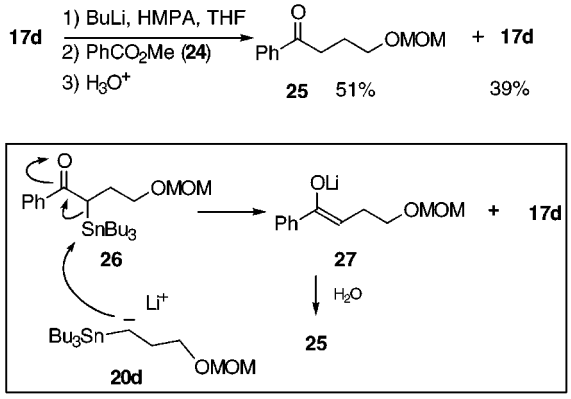
In a similar manner, various ketones were treated with **17d**, and the results are shown in Table 3.

The saturated and unsaturated ketones gave the corresponding olefins and dienes in good to moderate yields. Even in the case of the five-membered ketones **23d** and **23f**, the desired olefination products, **21d** and **21f**, were both obtained in moderate yields (Table 3, entries 2 and 4). A fair amount of destannylated compound **18d** (R = MOM) was obtained with the more enolizable ketones.

Reaction of Bis(tributylstannyl)propanol Derivative with Esters. If anion **II** were to react with an ester, α-stannylated ketone **IIIb** would be produced, as shown in Scheme 9.

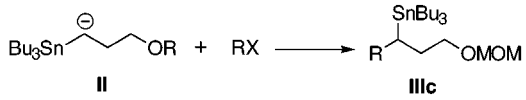
For this part of the study, methyl benzoate was treated with anion **20d** in a similar manner. In this reaction, destannylated ketone **25** was obtained in 51% yield along with the starting bis(tributylstannyl) compound **17d** in 39% yield. This means that the stannyl group of the desired α-stannylated ketone **26** was attacked by anion **17d** to form the lithium enolate **27** and bis(tributylstannyl)propanol derivative **17d** (Scheme 10).[10]

Scheme 10



Scheme 11

Scheme 12



II **IIIc**

It is expected that the enolate **27** would react further with an electrophile. Thus, the reaction of methyl benzoate with 2 equiv of **17d** was carried out, and MeI was then added to the reaction mixture. After the usual workup, the desired α-methylated ketone **28** was obtained in 84% yield. The results indicate that compound **17** is equivalent to dianion **29**, and two different electrophiles could be introduced to the bisstannylated carbon of **17** (Scheme 11).

The Reaction of Bis(tributylstannyl)propanol with Alkyl Halides. To develop a further carbon−carbon bond-forming reaction using this procedure, the reaction of anion **II** with allyl or alkyl halides was examined. In this case, the γ-stannylated alcohol derivative **IIIc** would be obtained (Scheme 12).

To a THF solution of the anion, generated from **17d** and BuLi at −78 °C, was added allyl bromide **30a**, and the solution was stirred at 0 °C for 2 h. After the usual workup, the desired allylation product **31a** was obtained in 56% yield. Various alkyl halides were used for this reaction, and the γ-stannylated alcohol derivatives **31** were obtained in good yields (Table 4).

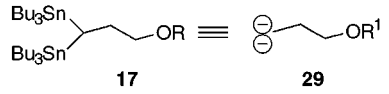
Next, we wanted to convert the stannyl group of product **31** into a hydroxy group. Conversion of the trimethylstannyl group into a hydroxy group was reported by Ochiai[11] along the lines of Tamao (Scheme 13).[12]

The stannylated product **31b** was treated with ICl to give stannyl chloride **32b**. The fact that the chemical shift in the ^{119}Sn NMR of compound **32b** (δ_{Sn} 63.7 ppm) appeared at a lower field than that of the starting

(10) (a) Sato, T.; Matsuoka, H.; Igarashi, T.; Murayama, E. *Tetrahedron Lett.* **1986**, *27*, 4339. (b) Sato, T.; Ariura, S. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 163.

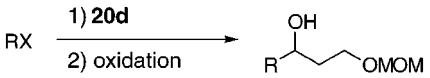
(11) Ochiai, M.; Iwaki, S.; Ukita, T.; Matsuura, Y.; Shiro, M.; Nagao, Y. *J. Am. Chem. Soc.* **1988**, *110*, 4606.

(12) Tamao, K.; Ishida, N.; Ito, Y.; Kumada, M. *Organic Syntheses*; Wiley: New York, 1993; Collect. Vol. VIII, p 315.



17 **29**

Figure 3.



30 **33**

Figure 4.

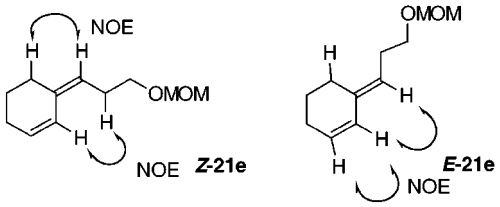
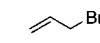
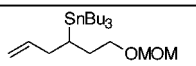
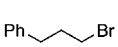
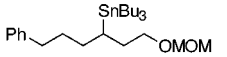
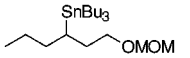
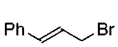
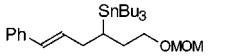
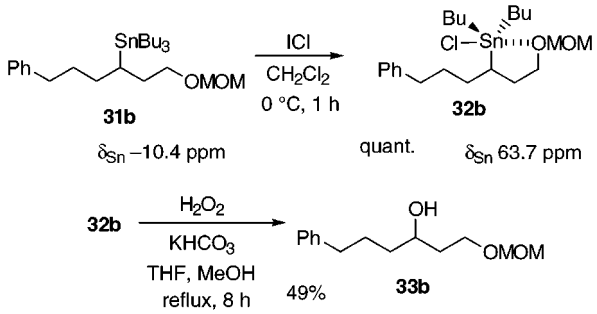


Figure 5.

Table 4. Three-Carbon Unit Elongation of Alkyl Halides

Entry	Electrophile	Product	Yield
1	 **30a**	 **31a**	56%
2	 **30b**	 **31b**	75%
3	 **30c**	 **31c**	78%
4	 **30d**	 **31d** $\alpha:\gamma = 5.7:1$	61%

Scheme 13



material **31b** (δ_{Sn} −10.4 ppm) and at a higher field than that of Bu_3SnCl (δ_{Sn} 156.70 ppm) indicates that the stannyl group is coordinated by oxygen of the methoxymethyl ether. Treatment of **32b** with H_2O_2 in the presence of $KHCO_3$[12] gave alcohol **33b** in 49% yield, which shows that one stannyl group is converted into an alkyl group and the other one is converted into a hydroxy group (Figure 4).

In conclusion, the three-carbon elongation reagent, 3,3-bistributylstannyl propanol derivative **17d**, is readily obtainable in high yield by the reaction of methyl propiolate with $Me_3SiSnBu_3$ in the presence of $BnEt_3NCl$ or CsF in DMF followed by treatment with $LiAlH_4$ and protection with MOMCl (Scheme 14). The three-carbon unit, bearing a hydroxy group, can be introduced to the

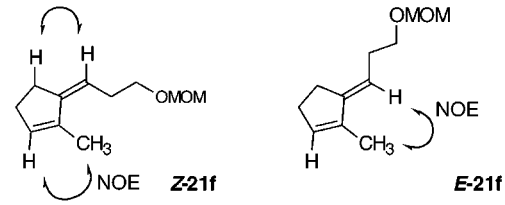


Figure 6.

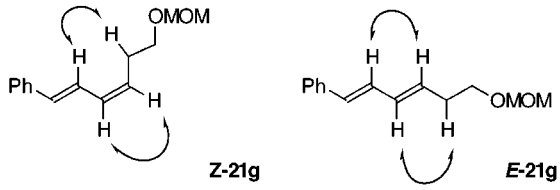
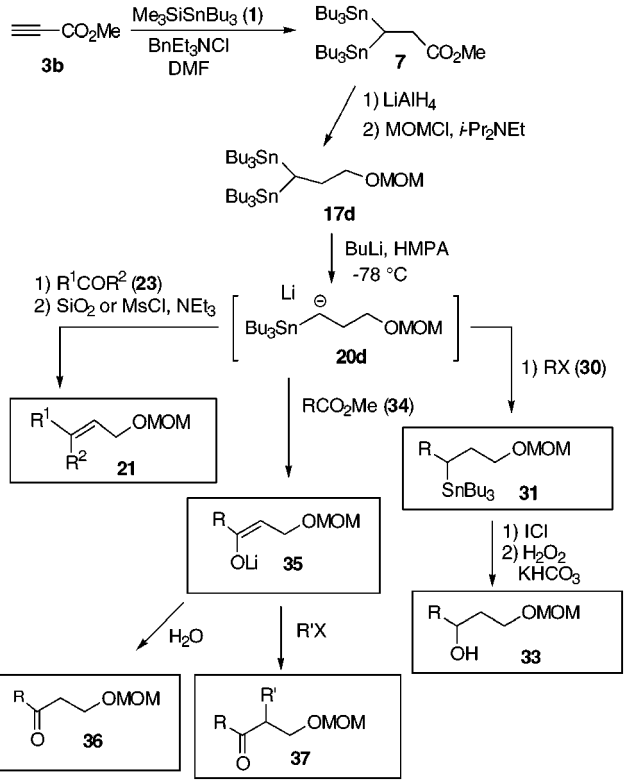


Figure 7.

Scheme 14



carbon of an aldehyde, ketone, ester, or alkyl halide to give alkene **21**, ketones **36**, **37**, and 1,3-diol derivative **31**.

Experimental Section

Solvents were distilled under an argon atmosphere from sodium benzophenone ketyl (THF) or CaH_2 (DMF and CH_2Cl_2). All other reagents and solvents were purified when necessary using standard procedures. Column chromatography was performed on silica gel 60 (70−230 mesh, 60 Å), and flash chromatography was performed on silica gel 60 (230−400 mesh, 60 Å) using the indicated solvent.

Methyl 3,3-Bis(tributylstannyl)propionate (7). To a solution of benzyltriethylammonium chloride (138 mg, 0.607 mmol) and methyl propiolate (27 μL, 0.303 mmol) in DMF (2.0 mL) was added $Me_3SiSnBu_3$ (210 μL, 0.601 mmol) at 0 °C, and the solution was stirred at room temperature for 6 h. To this solution was added an aqueous 10% NH_4Cl solution, and the aqueous layer was extracted with ethyl acetate. The organic

layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 100:1−20:1) to give a colorless oil of **7** (184 mg, 91%): IR (neat) 1736, 1196 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.76−0.95 (m, 31 H), 1.22−1.57 (m, 24 H), 2.78 (d, J = 7.4 Hz, 2 H, $^3J(^{119}Sn-^1H)$ = 30.5, 30.5 Hz), 3.65 (s, 3 H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −2.0, 10.1, 13.6, 27.6, 29.3, 35.3, 51.6, 176.1; ^{119}Sn NMR (100.55 MHz, $CDCl_3$) δ 11.4; MS m/z 665 (M^+ − 1), 609, 552, 319; EI-HRMS m/z calcd for $C_{24}H_{51}O_2{}^{120}Sn_2$ (M^+ − Bu) 611.1934, found 611.1923. Anal. Calcd for $C_{28}H_{60}O_2Sn_2$: C, 50.48; H, 9.08. Found: C, 50.50; H, 9.08.

3,3-Bis(tributylstannyl)propanol (17a). To a solution of **7** (368 mg, 0.552 mmol) in THF (5 mL) was added $LiAlH_4$ (21 mg, 0.559 mmol) at −78 °C and the mixture was stirred at 0 °C for 2 h. To this mixture was added $Na_2SO_4{\cdot}10H_2O$, and the mixture was stirred for 1 h. Undissolved material was filtered off, and the filtrate was concentrated. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 20:1−5:1) to give a colorless oil of **17a** (344 mg, 98%): IR (neat) 3326 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.68 (t, J = 7.6 Hz, 1 H, $^2J(^{119}Sn-^1H)$ = 30.4, 30.4 Hz), 0.77−0.93 (m, 30 H), 1.21−1.56 (m, 25 H), 2.06 (dt, J = 7.6, 7.3 Hz, 2 H, $^3J(^{119}Sn-^1H)$ = 30.7, 30.7 Hz), 3.53 (dt, J = 7.3, 5.6 Hz, 2 H); ^{119}Sn NMR (100.55 MHz, $CDCl_3$) δ 10.4; MS m/z 581 (M^+ − Bu), 523, 353, 289. EI-HRMS m/z calcd for $C_{23}H_{51}O^{120}Sn_2$ (M^+ − Bu) 583.1984, found 583.1944. Anal. Calcd for $C_{27}H_{60}OSn_2$: C, 50.81; H, 9.48. Found: C, 50.69; H, 9.65.

1,1-Bis(tributylstannyl)-3-[(methoxymethyl)oxy]propane (17d). To a solution of **17a** (1.31 g, 2.04 mmol) in CH_2Cl_2 (10 mL) were added diisopropylethylamine (1.4 mL, 8.04 mmol) and chloromethyl methyl ether (0.31 mL, 4.08 mmol) at 0 °C, and the solution was stirred at room temperature for 24 h. To this solution was added an aqueous saturated $NaHCO_3$, solution and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by chromatography on silica gel (hexane/ethyl acetate 50:1) to give a colorless oil of **17d** (1.39 g, 100%): IR (neat) 1148, 1110, 1038 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.67 (t, J = 7.5 Hz, 1 H, $^2J(^{119}Sn-^1H)$ = 30.7, 30.7 Hz), 0.72−0.94 (m, 30 H), 1.21−1.55 (m, 24 H), 2.10 (dt, J = 7.5, 7.4 Hz, 2 H, $^3J(^{119}Sn-^1H)$ = 31.6, 31.6 Hz), 3.36 (s, 3 H), 3.42 (t, J = 7.4 Hz, 2 H), 4.61 (s, 2 H); ^{119}Sn NMR (100.55 MHz, $CDCl_3$) δ 10.6; MS m/z 625 (M^+ − Bu), 567, 289, 235, 179, 45; EI-HRMS m/z calcd for $C_{25}H_{55}O_2{}^{120}Sn_2$ (M^+ − Bu) 627.2246, found 627.2244. Anal. Calcd for $C_{29}H_{64}O_2Sn_2$: C, 51.05; H, 9.46. Found; C, 51.14; H, 9.30.

General Procedure for the C-3 Elongation Procedure. Method A. To a solution of **17d** (0.15 mmol) in THF (1.5 mL) were added BuLi (0.30 mmol) and HMPA (0.30 mmol) at −78 °C, and the solution was stirred at the same temperature for 30 min. To this solution was added an electrophile (0.45 mmol) at −78 °C, and the solution was stirred at 0 °C for 2 h. To this solution was added aqueous NH_4Cl solution and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was dissolved in an appropriate solvent, and silica gel was added. The solution was concentrated, and the residual silica gel was placed on a column of silica gel and eluted with the appropriate solvent. **Method B.** After the procedure of method A, the residue was dissolved in CH_2Cl_2 (1.5 mL). To this solution were added NEt_3 (1.5 mmol) and methanesulfonyl chloride (0.75 mmol) at 0 °C, and the solution was stirred at 0 °C for 2 h. An aqueous saturated $NaHCO_3$ solution was added, and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by chromatography on silica gel. **Method C.** After the procedure of method A, the residue was purified by chromatography on silica gel.

***(E)*-1-[(Methoxymethyl)oxy]-4-phenyl-3-butene (21a).** The crude product, which was prepared from **17d** (105 mg, 0.15 mmol) and benzaldehyde (80 μL, 0.79 mmol) using method A, was purified by column chromatography on silica gel (hexane/ethyl acetate, 10:1) to give a colorless oil of **21a** (24 mg, 80%, E/Z = 35:1): IR (neat) 1494, 1448, 1148, 1110, 1036 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.52 (ddt, J = 6.9, 6.7, 1.0 Hz, 2 H), 3.37 (s, 3 H), 3.66 (t, J = 6.7 Hz, 2 H), 4.65 (s, 2 H), 6.24 (dt, J = 15.9, 6.9, Hz, 1 H), 6.47 (dt, J = 15.9, 1.0 Hz, 1 H), 7.18−7.35 (m, 5 H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 33.4, 55.1, 67.2, 96.4, 126.0, 126.8, 127.0, 128.4, 131.7, 137.5; MS m/z 192 (M^+), 161, 131, 117, 104, 91, 45; EI-HRMS m/z calcd for $C_{12}H_{16}O_2$ (M^+) 192.1150, found 192.1158. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.92; H, 8.44.

5,5-Dimethyl-4-hydroxy-1-[(methoxymethyl)oxy]-5-(tributylstannyl)hexane (22). The crude product, which was prepared from **17d** (138 mg, 0.20 mmol) and pivalaldehyde (110 μL, 1.01 mmol) using method C, was purified by preparative chromatography on silica gel (hexane/Et_2O, 10:1) to give a colorless oil of **22** (80 mg, 83%, **22a:22b** = 2.5:1). **22a**: IR (neat) 3854, 1152, 1110, 1044 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.77−0.90 (m, 15 H), 0.89 (s, 9 H), 1.27−1.34 (m, 6 H), 1.40−1.54 (m, 6 H), 1.74 (dt, J = 4.1, 3.6 Hz, 1 H), 1.84−2.01 (m, 3 H), 3.36 (s, 3 H), 3.40 (dd, J = 3.6, 3.6 Hz, 1 H), 3.49 (ddd, J = 9.2, 8.4, 1.9 Hz, 1 H), 3.54 (ddd, J = 9.2, 8.7, 5.8 Hz, 1 H), 4.60 (d, J = 6.5 Hz, 1 H), 4.62 (d, J = 6.5 Hz, 1 H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 11.0, 13.7, 26.2, 27.7, 29.4, 29.4, 33.9, 36.1, 55.2, 68.3, 83.5, 96.5; ^{119}Sn NMR (100.55 MHz, $CDCl_3$) δ −21.8; MS m/z 423 (M^+ − Bu + 1), 361, 331, 251, 45. **22b**: ^1H NMR (500 MHz, $CDCl_3$) δ 0.83−0.90 (m, 15 H), 0.96 (s, 9 H), 1.27−1.35 (m, 6 H), 1.40−1.52 (m, 6 H), 1.88 (ddd, J = 8.1, 5.4, 2.3 Hz, 1 H), 1.98−2.12 (m, 2 H), 2.24 (d, J = 6.9 Hz, 1 H), 3.36 (s, 3 H), 3.46 (dd, J = 6.9, 2.3 Hz, 1 H), 3.49 (ddd, J = 9.6, 9.2, 6.6 Hz, 1 H), 3.51 (ddd, J = 9.6, 9.3, 6.7 Hz, 1 H), 4.61 (s, 2 H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 9.8, 13.7, 27.5, 27.7, 28.0, 29.3, 37.6, 55.4, 69.1, 81.1, 96.4; ^{119}Sn NMR (100.55 MHz, $CDCl_3$) δ −6.1.

***(E)*-5,5-Dimethyl-1-[(methoxymethyl)oxy]-3-hexene (21b).** The crude product which was prepared from **17d** (105 mg, 0.15 mmol) and pivalaldehyde (85 μL, 0.78 mmol) using method B, was purified by preparative chromatography on silica gel (hexane/Et_2O, 10:1) to give a colorless oil of **21b** (18 mg, 69%): IR (neat) 1150, 1112, 1040 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.99 (s, 9 H), 2.28 (ddt, J = 7.1, 6.7, 1.2 Hz, 2 H), 3.36 (s, 3 H), 3.54 (t, J = 7.1 Hz, 1 H), 4.62 (s, 2 H), 5.33 (dt, J = 15.4, 6.7 Hz, 1 H), 5.54 (dt, J = 15.4, 1.2 Hz, 1 H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 29.7, 32.9, 33.1, 55.1, 67.8, 96.3, 120.7, 143.7; MS m/z 141 (M^+ − OMe), 127, 110, 97, 45; EI-HRMS m/z calcd for $C_9H_{17}O$ (M^+ − OMe) 141.1279, found 141.1280.

1-[(Methoxymethyl)oxy]-4-phenyl-4-butanone (25). The crude product, which was prepared from **17d** (104 mg, 0.15 mmol) and methyl benzoate (60 μL, 0.48 mmol) using method C, was purified by column chromatography on silica gel (hexane/ethyl acetate, 100:1−10:1) to give a colorless oil of **25** (16 mg, 51%): IR (neat) 1686, 1598, 1448, 1148, 1112, 1040 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 2.05 (tt, J = 7.1, 6.3 Hz, 2 H), 3.10 (t, J = 7.1 Hz, 2 H), 3.36 (s, 3 H), 3.63 (t, J = 6.3 Hz, 2 H), 4.62 (s, 2 H), 7.43−7.60 (m, 3 H), 7.95−7.99 (m, 2 H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 24.3, 35.1, 55.2, 66.9, 96.4, 128.0, 128.6, 133.0, 137.0, 199.8; MS m/z 208 (M^+), 177, 163, 146, 105, 45; EI-HRMS m/z calcd for $C_{12}H_{16}O_3$ (M^+) 208.1100, found 208.1115.

1-[(Methoxymethyl)oxy]-3-methyl-4-phenyl-4-butanone (28). To a solution of **17d** (110 mg, 0.16 mmol) in THF (1.6 mL) were added BuLi (1.62 *N* hexane solution, 200 μL, 0.32 mmol) and HMPA (60 μL, 0.35 mmol) at −78 °C, and the solution was stirred at the same temperature for 30 min. To this solution was added methyl benzoate (10 μL, 0.080 mmol) at −78 °C, and the solution was stirred at the same temperature for 1 h. Then MeI (10 μL, 0.080 mmol) was added at −78 °C, and the solution was stirred at 0 °C for 2 h. An aqueous saturated NH_4Cl solution was added, and the organic layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 100:1−10:1) to give a colorless oil of **28** (15 mg, 84%): IR (neat) 1682, 1448, 1154, 1110, 1048 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.23 (d, J = 7.0 Hz, 3 H), 1.71 (dddd, J = 13.8, 6.9, 6.1, 5.7 Hz, 1 H), 2.17 (dddd, J = 13.8, 6.9, 6.9, 6.0

Hz, 1 H), 3.29 (s, 3 H), 3.52 (ddd, J = 9.9, 6.1, 6.0 Hz, 1 H), 3.60 (ddd, J = 9.9, 6.9, 5.7 Hz, 1 H), 3.71 (ddq, J = 7.0, 6.9, 6.9 Hz, 1 H), 4.55 (d, J = 6.6 Hz, 1 H), 4.57 (d, J = 6.6 Hz, 1 H), 7.46 (dd, J = 7.6, 7.4 Hz, 2 H), 7.55 (t, J = 7.4 Hz, 1 H), 7.98 (d, J = 7.6 Hz, 2 H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 17.5, 33.4, 37.3, 55.2, 65.4, 96.4, 128.3, 128.6, 132.9, 136.6, 204.0; MS m/z 223 (M^+ + 1), 191, 177, 161, 134, 105, 77, 45; EI−HRMS m/z calcd for $C_{13}H_{18}O_3$ (M^+) 222.1256, found 222.1255. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 69.94; H, 8.23.

1-[(Methoxymethyl)oxy]-3-(tributylstannyl)-5-hexene (31a). A crude product, which was prepared from **17d** (103 mg, 0.15 mmol) and allyl bromide (40 μL, 0.46 mmol) using method C, was purified by column chromatography on silica gel (hexane/ethyl acetate, 100:1−10:1) to give a colorless oil of **31a** (36 mg, 56%): IR (neat) 1150, 1110, 1044 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.78−0.93 (m, 15 H), 1.23−1.56 (m, 13 H), 1.87 (dt, J = 7.1, 6.7 Hz, 2 H), 2.34 (t, J = 7.1 Hz, 2 H), 3.36 (s, 3 H), 3.52 (t, J = 7.1 Hz, 2 H), 4.61 (s, 2 H), 4.94−5.06 (m, 2 H), 5.74 (ddt, J = 17.0, 9.9, 7.1 Hz, 1 H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 9.1, 13.7, 22.1, 27.6, 29.3, 32.6, 37.4, 55.1, 67.6, 96.4, 115.2, 139.1; MS m/z 433 (M^+), 377, 331, 235, 177, 45; EI-HRMS m/z calcd for $C_{16}H_{33}O_2{}^{120}Sn$ (M^+ − Bu) 377.1503, found 377.1530.

1-[(Methoxymethyl)oxy]-6-phenyl-3-(dibutylchlorostannyl)hexane (32b). To a solution of **31b** (97 mg, 0.19 mmol) in CH_2Cl_2 (2.0 mL) was added ICl (37 mg, 0.23 mmol) in CH_2Cl_2 (0.36 mL) at 0 °C, and the solution was stirred at the same temperature for 1.25 h. An aqueous 10% sodium thiosulfate solution and the aqueous layer were extracted with Et_2O. The ethereal layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH, 100:1−30:1) to give a colorless oil of **32b** (93 mg, 100%): IR (neat) 1446, 1152, 1030 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89−0.93 (m, 6 H), 1.07−1.40 (m, 8 H), 1.56−1.81 (m, 8 H), 1.91 (dddd, J = 14.5, 6.7, 3.6, 3.4 Hz, 1 H), 1.95−2.00 (m, 1 H), 2.06 (dddd, J = 14.5, 8.9, 4.3, 4.1 Hz, 1 H), 2.65 (t, J = 7.0 Hz, 2 H), 3.34 (s, 3 H), 3.52 (ddd, J = 8.9, 6.7, 4.1 Hz, 1 H), 3.60 (ddd, J = 8.9, 8.9, 3.4 Hz, 1 H), 4.56 (s, 2 H), 7.14−7.29 (m, 5 H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 13.6, 13.6, 17.6, 18.8, 26.9, 27.0, 28.0, 30.7, 30.9, 31.3, 31.3, 35.9, 55.9, 65.8, 96.2, 125.6, 128.2, 128.4, 142.5; ^{119}Sn NMR (100.55 MHz, $CDCl_3$) δ 63.7; MS m/z 455 (M^+ − Cl + 1), 433, 353, 91, 45; EI-HRMS m/z calcd for $C_{18}H_{30}O_2Cl^{120}$-Sn (M^+ − Bu) 433.0957, found 433.0932. Anal. Calcd for $C_{22}H_{39}O_2ClSn$: C, 53.96; H, 8.03; Cl, 7.24. Found: C, 54.02; H, 8.10; Cl, 7.12.

1-[(Methoxymethyl)oxy]-3-hydroxy-6-phenylhexane (33b). To a solution of **33b** (22 mg, 0.046 mmol) and $KHCO_3$ (27 mg, 0.27 mmol) in THF (0.75 mL) and MeOH (0.75 mL) was added H_2O_2 (30 μL, 0.25 mmol) every 2 h, and the solution was refluxed for 2 h. Then H_2O_2 was added (30 μL, 0.25 mmol), and the solution was refluxed for 8 h. An aqueous 10% $NaHSO_3$ solution was added, and the aqueous layer was extracted with Et_2O. The ether layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate, 5:1−1:1) to give a colorless oil of **33b** (5.3 mg, 49%): IR (neat) 3420, 1496, 1452, 1150, 1108, 1042 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.46−1.57 (m, 2 H), 1.65−1.85 (m, 4 H), 2.54 (brs, 1 H), 2.65 (t, J = 7.6 Hz, 2 H), 3.36 (s, 3 H), 3.68 (ddd, J = 9.7, 7.7, 4.7 Hz, 1 H), 3.75 (ddd, J = 9.7, 6.1, 5.1 Hz, 1 H), 3.78−3.85 (m, 1 H), 4.62 (s, 2 H), 7.15−7.29 (m, 5 H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 27.4, 35.9, 36.4), 37.0, 55.4, 66.3, 70.9, 96.5, 125.7, 128.3, 128.4, 142.4; MS m/z 238 (M^+), 221, 206, 160, 104, 91, 45; EI-HRMS m/z calcd for $C_{14}H_{22}O_3$ (M^+) 238.1569, found 238.1563.

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Supporting Information Available: The experimental procedures of compounds **17b**,**c**, **19**, **21c**−**g**, and **31b**−**d** (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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