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Combined Lewis acid catalysts in shotgun process: a convenient synthesis of the female sex pheromone of the red-bollworm moth

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Abstract—The combined use of Lewis acid and distannoxane catalysts gives rise to a new variant of the shotgun process. The unwanted acetylation of a secondary homoallyl alcohol by the former catalyst is suppressed through hybridization with the latter resulting in one-pot aldehyde allylation and primary alcohol acetylation of ω-hydroxy alkanal without protection/deprotection procedures.

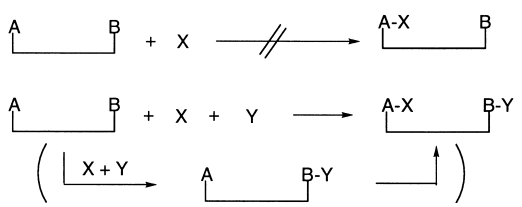
1. Introduction

Previously, we advanced a new concept for one-pot reaction, 'shotgun process'.[1] This treatment allows multiple reaction sites in a substrate to undergo separate transformations in one pot and thus the tedious protection/deprotection procedure is no longer necessary resulting in straightforward access to a target molecule. Another advantage is the unique chemoselectivities that are not feasible in simple elementary reactions. Scheme 1 presents the simplest case where treatment of the substrate bearing two reaction sites, A and B, with X alone leads to an unsatisfactory outcome because the desired reaction between A and X is interfered by the coexisting function B. However, the situation is changed if another reagent Y coexists that does not react with A but reacts with B much faster than the reaction between A and X. Rapid consumption of B enables the latter reaction to occur without interference from B.[2] It is further important to note in such process that the respective reactions are strongly influenced by the functionalities of the coexisting other substrates and reagents. In this paper, we disclose that the combination of Lewis acid catalysts also leads to alteration in catalytic activity, thus giving rise to a useful variant of shotgun process.

The effectiveness of this new protocol will be exemplified by a convenient synthesis of 9,11-dodecadien-1-yl acetate (**1**), a female sex pheromone of the red-bollworm moth *Oiparopsis castanea*, for which a number of synthetic achievements were reported so far.[3] Among them, a synthetic route employing 9-hydroxynonanal (**2**) as a starting material seems to be extremely practical because of facile availability of this compound through ozonolysis of 9-decen-1-ol. In a preceding report,[3i] the hydroxyl of **2** was protected as a THP ether and the three carbon elongation was achieved by treating the aldehyde function with vinyl lithium followed by Wittig methylenation of the resulting enal to give a terminal 1,3-diene moiety in a stepwise manner. Finally, the tetrahydopyranyloxy group was converted to the acetate. Our much simpler synthetic plan is shown in Scheme 2. The key step is one-pot conversions of both aldehyde and primary alcohol functions into the homoallyl alcohol and the primary acetate, respectively, leaving the resulting homoallylic alcohol function intact to afford an intermediate **3**. Then, dehydration completes a compact synthetic route to **1**.

2. Results and discussion

First, an intermolecular process was screened by use of nonanal and octanol substrates (Table 1). Since both allylation of aldehyde[4] and acetylation of hydroxyl[5] are catalyzed by $Sc(OTf)_3$, the equimolar substrates were exposed to a mixture of tetrallyltin (**4**) and Ac_2O (**5**) in the presence of 2 mol% of $Sc(OTf)_3$ (entry 1). The allylation of aldehyde and acetylation of the primary alcohol



Scheme 1.

Keywords: shotgun process; Lewis acid catalyst; allylation; acetylation.

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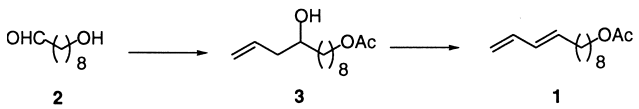
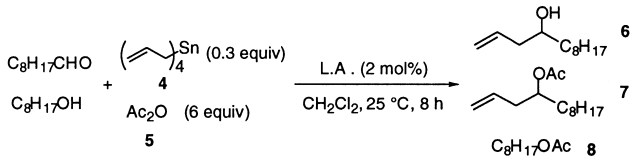


Scheme 2.

Table 1. Intermolecular shotgun process by various Lewis acid

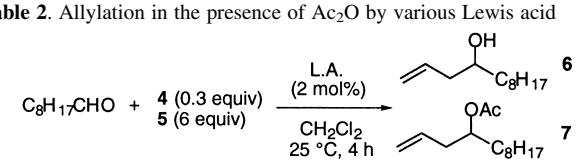


Entry	L.A.	Yield (%)[a]					
		6	**7**	**6**+**7**	**8**	$C_8H_{17}OH$	**8**+$C_8H_{17}OH$
1	$Sc(OTf)_3$	78	20	98	98	0	98
2	$Bi(OTf)_3$	95	2	97	86	12	98
3	$Cu(OTf)_2$	92	1	93	62	22	84
4	TMSOTf	93	2	95	57	21	78
5	$BF_3{\cdot}OEt_2$	96	1	97	81	8	89

[a] Determined by GLC.

proceeded quantitatively. Unfortunately, however, the homoallyl alcohol also underwent acetylation beyond the limit allowed for synthetic purpose. This is reasonable because $Sc(OTf)_3$ is a highly powerful catalyst for acetylation of even secondary and tertiary alcohols. Notwithstanding, it should be pointed out that the acetylation of the homoallyl alcohol was greatly retarded in the shotgun process. As shown in entry 1, Table 2, exposure of nonanal in the absence of octanol to **4** and **5** resulted in acetylation of most of the in situ produced homoallyl alcohol. Apparently, the coexisting octanol works for suppressing the homoallyl alcohol acetylation. Then, we employed less active Lewis acids (Table 1, entries 2–5). Although these catalysts had not been known to effect the reaction between aldehyde and **4** except $Cu(OTf)_2$,[6] the allylation took place quantitatively. Remarkably, the acetylation of the homoallyl alcohol was almost suppressed.[7] This also exemplifies the unique feature of the shotgun process because the reaction in the absence of octanol predominantly or exclusively furnished the homoallyl acetate (Table 2, entries 2–5) under similar conditions. Despite such advantage, the less active catalyst process suffered from insufficient yields of the primary acetate.

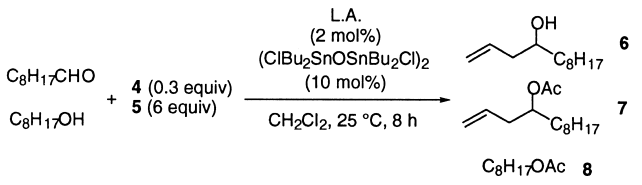
Table 2. Allylation in the presence of Ac_2O by various Lewis acid



Entry	L.A.	Yield (%)[a]	
		6	**7**
1[b]	$Sc(OTf)_3$	9	85
2	$Bi(OTf)_3$	31	63
3	$Cu(OTf)_2$	21	68
4	TMSOTf	0	95
5	$BF_3{\cdot}OEt_2$	28	60

[a] Determined by GLC.
[b] Reaction time: 1 h.

Table 3. Shotgun process by catalysts combined with 1,3-dicholoro-tetrabutyldistannoxane

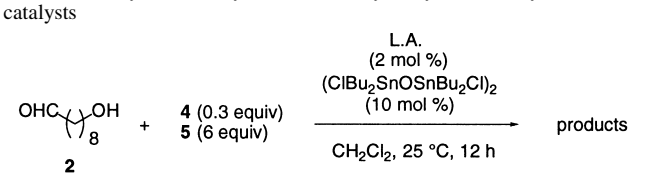


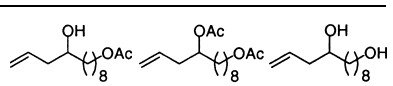
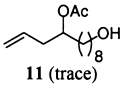
Entry	L.A.	Yield (%)[a]					
		6	**7**	**6**+**7**	**8**	$C_8H_{17}OH$	**8**+$C_8H_{17}OH$
1	$Sc(OTf)_3$	92	5	97	99	0	99
2	$Bi(OTf)_3$	94	4	98	99	0	99
3	$Cu(OTf)_2$	96	3	99	97	0	97
4	TMSOTf	92	3	95	93	0	93
5	$BF_3{\cdot}OEt_2$	92	3	95	96	0	96

[a] Determined by GLC.

As such, we were confronted with the problems to decrease the amount of homoallyl acetate without decreasing the yield of the primary acetate in the $Sc(OTf)_3$ system or to increase the yield of the primary acetate without increasing the amount of the homoallyl acetate with less active catalysts. Mindful of our earlier success in effective discrimination of primary alcohol from secondary or tertiary alcohol with 1,3-dichlorotetraalkyldistannoxane catalyst,[8] we were intrigued by making use of this catalyst to overcome the above problems. Gratifyingly, the hybridization of a Lewis acid (2 mol%) and the distannoxane (10 mol%) led to an almost perfect shotgun process (Table 3). In the $Sc(OTf)_3$-based reaction, the yield of **7** was decreased to 5% concomitant with increase in the yield of **6**, whereas the primary alcohol acetylation was not deteriorated at all (entry 1). On the other hand, octanol was completely acetylated with the other catalysts although the

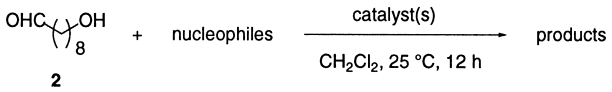
Table 4. Allylation/acetylation of ω-hydroxynonanal by combined catalysts

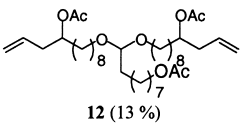
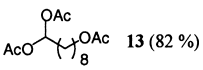


Entry	L.A.	Products[a]
1	$Sc(OTf)_3$	 **3** (88 %) **9** (8 %) **10** (1 %)
2	$Bi(OTf)_3$	**3** (87%); **9** (5%); **10** (2%);  **11** (trace)
3[b]	$Cu(OTf)_2$	**3** (84%); **9** (8%); **10** (5%); **11** (trace)
4	TMSOTf	**3** (90%); **9** (4%); **10** (2%); **11** (1%)
5	$BF_3{\cdot}OEt_2$	**3** (89%); **9** (6%); **10** (trace)

[a] Isolated yield based on **2** after column chromatography.
[b] Reaction time: 15 h.

Table 5. Allylation/acetylation of ω-hydroxynonanal by single or combined catalysts



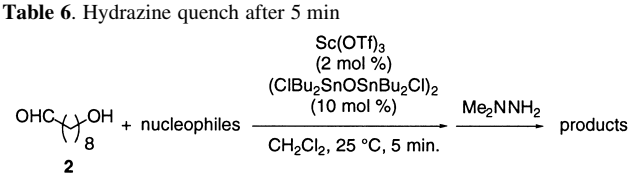
Entry	Nucleophiles	Catalyst(s)	Products[a]
1	**4** (0.3 equiv.) **5** (6 equiv.)	$Sc(OTf)_3$ (2 mol%)	**3** (40%); **9** (21%) **10** (19%); **11** (12%)
2[b]	**4** (0.3 equiv.)	$Sc(OTf)_3$ (2 mol%)	**9** (51 %);  **12** (13 %)
3[b]	**4** (0.3 equiv.)	$Sc(OTf)_3$ (2 mol%), $(ClBu_2SnOSnBu_2Cl)_2$ (10 mol%)	**9** (77%); **12** (7%)
4[c]	**5** (6 equiv.)	$Sc(OTf)_3$ (2 mol%), $(ClBu_2SnOSnBu_2Cl)_2$ (10 mol%)	 **13** (82 %)

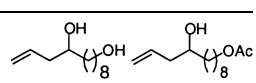
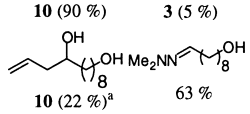
[a] Isolated yield based on **2** after column chromatography.
[b] The crude products mixture was acetylated.
[c] Reaction time: 8 h.

amount of **7** was increased slightly but within the limit for synthetic use.

Armed with the above results, we addressed ourselves to explore the shotgun process with the substrate **2**. As shown in Table 4, all the combined catalysts furnished the desired product **3** in high yields through allylation of aldehyde and acetylation of primary alcohol although small amounts of diacetate **9** and diol **10** were formed. Achievement of such high preference for **3** is specific to the shotgun process with combined catalysts, the characteristic features of which were scrutinized with $Sc(OTf)_3$ catalyst (Table 5). When the shotgun process was conducted with $Sc(OTf)_3$ alone, no selectivity was attained with acetylation resulting in all three possible modes of acetylation products, **3**, **9**, and **11**, together with naked diol **10** (entry 1). A simple allylation in the absence of **5** (entry 2) enabled the allylation to proceed only moderately (60%=51%+13×2/3%), and what is worse, a portion of the allylation product **10** was caught by unreacted aldehyde to give acetal **12** (after acetylation). When the reaction with the combined catalysts was quenched with Me_2NNH_2 in 5 min,[9] it turned out that the allylation was complete while the acetylation proceeded only in 5% yield (Table 6, entry 1), a typical feature of the shotgun process. The merits of this process are further apparent from comparison with reactions given in the last two entries in Table 5. Reaction with **4** alone provided **9** in 77% yield together with **12** (7% yield after acetylation) (entry 3). Obviously, a part of the initial allylation product was consumed by the remaining aldehyde function. Thus, rapid disappearance of this function in the shotgun process (Table 4, entry 1) avoided the acetal formation. When Ac_2O was exposed to **2** in the absence of **4**, the products were constituted by acylal triacetate **13** and unidentifiable byproducts (Table 5, entry 4). Again, it is evident that exclusive acetylation of the primary hydroxyl in the shotgun process was achieved by rapid consumption of the aldehyde which otherwise would furnish the acylal. Notably, the combined catalyst system holds the same characteristic features as previously observed for the single $Sc(OTf)_3$ catalyst: acceleration of allylation by Ac_2O and retardation of acetylation by aldehyde.[1] The former feature is apparent from the comparison between entry 1 in Table 4 and entry 3 in Table 5: the allylation yield was lowered from 97 to 83% (=77%+7×2/3%) when Ac_2O was absent. The acceleration of allylation rate by Ac_2O was further substantiated by comparison between entries 1 and 2 in Table 6: reaction of **2** with **4** alone resulted in only 37% conversion (i.e. 63% recovery of the hydrazone of **2**) with a 22% yield of **8** after 5 min.

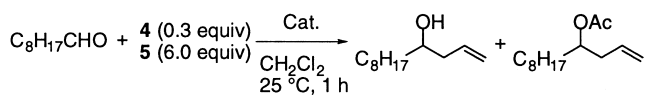
Table 6. Hydrazine quench after 5 min



Entry	Nucleophiles	Products
1	**4** (0.3 equiv.) **5** (6 equiv.)	 **10** (90 %) **3** (5 %)
2	**4** (0.3 equiv.)	 **10** (22 %)[a] 63 %

[a]Determined as diacetate **8**.

Most importantly, the success of shotgun process with the combined catalysts lies in the modification of $Sc(OTf)_3$. Normally, this catalyst effects acetylation with a 1 mol% concentration or less even for secondary and tertiary



Cat.		
$Sc(OTf)_3$ (2 mol %)	9 %	85 %
$Sc(OTf)_3$ (2 mol %) $(ClBu_2SnOSnBu_2Cl)_2$ (10 mol %)	28 %	69 %

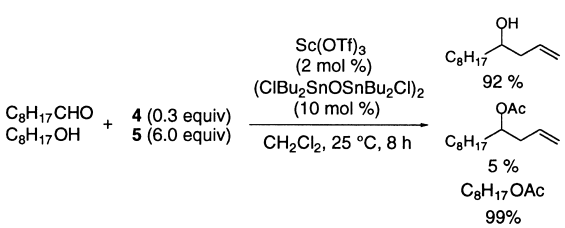
Scheme 3.

Table 7. Interaction between $(ClBu_2SnOSnBu_2Cl)_2$ and $Sc(OTf)_3$ studied by ^{119}Sn NMR spectra

Ratio of $(ClBu_2SnOSnBu_2Cl)_2$ and $Sc(OTf)_3$	δ (ppm)
100:0	−90.0, −140.2
1:2	−62.4, −108.7
5:1	−65.3, −90.9, −141.2, −151.6

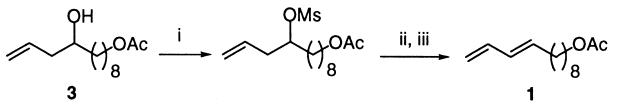
In 1.0 mmol containing $C_8H_{17}OH$.

alcohols. Thus, it is rather surprising that the high selectivity for primary alcohol was attained in the present shotgun protocol. This is probably ascribed to generation of a new scandium species upon mixing with the distannoxane so that the activity for acetylation has been killed while the efficacy for allylation is retained. It should be noted, however, that retardation of the acetylation activity of $Sc(OTf)_3$ is not solely responsible for the high selectivity. The effect of addition of the distannoxane to $Sc(OTf)_3$ for suppressing acetylation of a secondary homoallyl alcohol after the aldehyde allylation is shown in Scheme 3. Actually, with $Sc(OTf)_3$ alone, most of the homoallyl alcohol was acetylated, yet even in the presence of the distannoxane catalyst, the acetylation occurred on a major portion of the alcohol. In striking contrast, upon addition of a primary alcohol to this reaction system, the acetylation of the secondary homoallyl alcohol was almost suppressed concomitant with quantitative formation of the primary acetate (Eq. (1)). It follows that the coexistence of both ditannoxane and primary alcohol is crucial for killing the acetylation activity of $Sc(OTf)_3$. Although no information about the newly generated active species is available at the moment, the interaction between $Sc(OTf)_3$ and the distannoxane was apparent from ^{119}Sn NMR spectra (Table 7): addition of an equimolar amount of $Sc(OTf)_3$ to the distannoxane resulted in complete diappearance of signals at −90.0 and 140.2 ppm diagnostic of the free distannoxane with alternative emergence of a new set of signals at −62.4 and −108.7 ppm. For the same composition as the standard shotgun conditions (5:1 distannoxane/$Sc(OTf)_3$), a new set of signals at −65.3 and 151.6 ppm was observed in addition to the original one (at −90.9 and −141.2 ppm). Apparently, $Sc(OTf)_3$ was modified to a new species while a major part of the distannoxane remained as its innate form under these conditions. Probably, the former is active only for the aldehyde allylation and the latter plays a crucial role in the selective acetylation. This was supported by the fact that the selectivity as well as the yield of **3** was slightly decreased when the concentration of the distannoxane was reduced to 5 mol% in the standard shotgun reaction as entry 1 in Table 4. Conceivably, the shotgun process with other Lewis acids possesses similar features although the interaction of these species with the distannoxane is somewhat different.



(1)

With **3** in high yield as mentioned above in hand, we



Scheme 4. *Reaction conditions*: (i) Et_3N (1.2 equiv.), MsCl (1.1 equiv.), CH_2Cl_2, 0°C, 2 h: 95%; (ii) DBU (3.0 equiv.), toluene, reflux, 12 h: 75% (*E*/*Z*=80:20); (iii) I_2, benzene, room temperature, 12 h: 91% (*E*/*Z*=89:11).

completed the synthesis of **1** (Scheme 4). Mesylation of **3** followed by elimination afforded the target molecule. The *E*,*Z* ratio of **1** thus obtained was found to be 80:20, the same value produced by red-bollworm moth. It is known that the attractiveness of **3** is highest for the *E* content of 88–93%.[3b] The diene with an 89%-*E* content was obtained by treating the above reaction product with I_2 in benzene.

In summary, hybridization of the distannoxane with Lewis acids enables aldehyde allylation and selective acetylation of primary alcohol in one pot, giving rise to a new variant of shotgun process. In this protocol, no protection–deprotection procedure is needed and multi-step synthetic processes can enjoy compaction. Since similar preferable modification may be available with other combination of catalysts, the new version disclosed herein will find a broad range of applications. Finally, it is worthy to note that combination of different reactions does not lead to the simple superimposition of elementary reactions. The interactions between functional groups in substrates and reagents as well as catalysts alter the reaction modes. Of course, both positive and negative effects may arise from these interactions. If such effects are taken in positively, the shotgun process will be able to develop a new horizon in synthetic chemistry.

3. Experimental

3.1. General

All reactions were carried out under an atmosphere of nitrogen with freshly distilled solvents, unless otherwise noted. CH_2Cl_2 was distilled from CaH_2. Silica gel (Daiso gel IR-60) was used for Column chromatography. NMR spectra were recorded at 20°C on JEOL Lambda 300 and 500 instruments and calibrated with tetramethylsilane (TMS) as an internal reference. The following abbreviations are used to indicate multiplicities: s singlet; d doublet; t triplet; q quartet; m multiplet. Mass spectra were recorded on a Jeol MStation JMS-700 spectrometer.

3.1.1. The preparation of 9-hydroxynonanal 2. A stream of ozone was bubbled through a solution of 9-decen-1-ol (1.56 g, 10.0 mmol) in CH_2Cl_2 (40 mL) at −78°C until the solution turned to pale blue, and then a stream of N_2 was bubbled through the solution until the solution turned to colorless. Triethylamine (2.79 mL, 20.0 mmol) was added and the mixture was stirred at room temperature for 5 h. After addition of $NaHCO_3$ aq. (20 mL) and usual workup (AcOEt/water), the combined organic layer was washed with brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. The crude mixture was subjected to column chromatography on Frorisil® (3:2 hexane/AcOEt) and subsequent Kugelrohr

distillation (150°C/1.0 mm Hg) to afford **2** (853 mg, 54%). **2**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33–1.66 (m, 12H), 2.43 (dt, J=1.8, 7.3 Hz, 2H), 3.64 (t, J=6.6 Hz, 2H), 9.77 (t, J=1.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.0, 25.6, 29.0, 29.1, 29.2, 32.7, 43.8, 62.9, 203.0. HRMS (EI) calcd for $C_9H_{18}O_2$: 158.1307. Found: 158.1320.

3.1.2. Table 1 (entry 1 as representative procedure). To a suspension of $Sc(OTf)_3$ (10.0 mg, 0.02 mmol) in CH_2Cl_2 (8 mL) were added a mixture of nonanal (142 mg, 1.00 mmol) and octanol (130 mg, 1.00 mmol) in CH_2Cl_2 (1 mL) and then a mixture of tetraallyltin **4** (0.07 mL, 0.30 mmol) and Ac_2O **5** (0.57 mL, 6.00 mmol) in CH_2Cl_2 (1 mL) at 25°C. After the mixture had been stirred for 8 h, $NaHCO_3$ aq. (10 mL) and NH_4F (800 mg) were added, and insoluble solids were removed by filtration. After usual workup (AcOEt/water), the organic layer was washed with $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. GC analysis of the crude mixture showed the formation of **6** (78% yield), **7** (20% yield) and **8** (98% yield). **6**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, J=6.6 Hz, 3H), 1.28–1.46 (m, 14H), 2.09–2.35 (m, 2H), 3.60–3.68 (m, 1H), 5.11–5.17 (m, 2H), 5.77–5.09 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.6, 25.6, 29.2, 29.55, 29.64, 31.9, 36.8, 41.9, 70.7, 117.0, 134.9. HRMS (EI) calcd for $C_{12}H_{24}O$: 184.1827. Found: 184.1827. **7**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, J=6.7 Hz, 3H), 1.26–1.55 (m, 14H), 2.03 (s, 3H), 2.25–2.35 (m, 2H), 4.91 (qui, J=6.3 Hz, 1H), 5.04–5.09 (m, 2H), 5.71–5.79 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 21.2, 22.6, 25.2, 29.2, 29.41, 29.43, 31.8, 33.5, 38.6, 73.3, 117.5, 133.8, 170.7. HRMS (EI) calcd for $C_{14}H_{26}O_2$: 226.1933. Found: 226.1934.

3.1.3. Table 2 (entry 1 as representative procedure) and Scheme 3 ($Sc(OTf)_3$-catalyzed allylation in the presence of Ac_2O). To a suspension of $Sc(OTf)_3$ (10.0 mg, 0.02 mmol) in CH_2Cl_2 (8 mL) were added nonanal (142 mg, 1.00 mmol) in CH_2Cl_2 (1 mL), and then a mixture of tetraallyltin (0.07 mL, 0.30 mmol) and Ac_2O (0.57 mL, 6.00 mmol) in CH_2Cl_2 (1 mL) at 25°C. After the mixture had been stirred for 1 h, $NaHCO_3$ aq. (10 mL) and NH_4F (800 mg) were added, and insoluble solids were removed by filtration. After usual workup (AcOEt/water), the organic layer was washed with $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. GC analysis of the crude mixture showed the formation of **6** (9% yield) and **7** (85% yield).

3.1.4. Table 3 (entry 1 as representative procedure) and Eq. (1). To a suspension of $Sc(OTf)_3$ (10.0 mg, 0.02 mmol) and $(ClBu_2SnOSnBu_2Cl)_2$ (110 mg, 0.10 mmol) in CH_2Cl_2 (8 mL) were added a mixture of nonanal (142 mg, 1.00 mmol) and octanol (130 mg, 1.00 mmol) in CH_2Cl_2 (1 mL), and then a mixture of tetraallyltin (0.07 mL, 0.30 mmol) and Ac_2O (0.57 mL, 6.00 mmol) in CH_2Cl_2 (1 mL) at 25°C. After the mixture had been stirred for 8 h, $NaHCO_3$ aq. (10 mL) and NH_4F (800 mg) were added, and insoluble solids were removed by filtration. After usual workup (AcOEt/water), the organic layer was washed with $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. GC analysis of the crude mixture showed the formation of **6** (92% yield), **7** (5% yield) and **8** (99% yield).

3.1.5. Table 4 (entry 1 as representative procedure). To a suspension of $Sc(OTf)_3$ (10.0 mg, 0.02 mmol), $(ClBu_2SnOSnBu_2Cl)_2$ (110 mg, 0.10 mmol) and **2** (158 mg, 1.00 mmol) in CH_2Cl_2 (9 mL) were added a mixture of tetraallyltin (0.07 mL, 0.30 mmol) and Ac_2O (0.57 mL, 6.00 mmol) in CH_2Cl_2 (1 mL) at 25°C. After the mixture had been stirred for 12 h, $NaHCO_3$ aq. (10 mL) and NH_4F (800 mg) were added, and insoluble solids were removed by filtration. After usual workup (AcOEt/water), the organic layer was washed with $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. The crude mixture was subjected to column chromatography on silica gel to afford **9** (19:1 hexane/AcOEt, 23 mg, 8% yield), **3** (17:3 hexane/AcOEt, 213 mg, 88% yield) and **10** (3:2 hexane/AcOEt, 2 mg, 1% yield). **10**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32–1.61 (m, 14H), 2.05–2.35 (m, 2H), 3.64 (t, J=6.6 Hz, 3H), 5.10–5.18 (m, 2H), 5.76–5.90 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.6, 25.7, 29.3, 29.49, 29.51, 32.7, 36.7, 41.9, 63.0, 70.6, 118.1, 134.9. HRMS (EI) calcd for $C_{12}H_{24}O_2$: 200.1776. Found: 200.1778. **9**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29–1.66 (m, 14H), 2.04 (s, 3H), 2.05 (s, 3H), 2.22–2.37 (m, 2H), 4.05 (t, J=6.8 Hz, 2H), 4.91 (qui, J=6.2 Hz, 1H), 5.04–5.11 (m, 2H), 5.68–5.82 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 21.2, 25.2, 25.8, 28.5, 29.1, 29.31, 29.33, 33.5, 38.6, 64.6, 73.3, 117.5, 133.8, 170.8, 171.2. HRMS (EI) calcd for $C_{16}H_{28}O_4$: 284.1988. Found: 284.1986. **3**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31–1.66 (m, 14H), 1.75 (br, 1H), 2.05 (s, 3H), 2.09–2.35 (m, 2H), 3.60–3.68 (m, 1H), 4.05 (t, J=6.7 Hz, 2H), 5.11–5.17 (m, 2H), 5.77–5.90 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 25.6, 25.8, 28.5, 29.1, 29.4, 29.5, 36.7, 41.9, 64.6, 70.6, 118.0, 134.9, 171.2. HRMS (EI) calcd for $C_{14}H_{26}O_3$: 242.1882. Found: 242.1855.

3.1.6. Table 5 (entry 1). To a suspension of $Sc(OTf)_3$ (10.0 mg, 0.02 mmol) and **2** (158 mg, 1.00 mmol) in CH_2Cl_2 (9 mL) were added a mixture of tetraallyltin (0.07 mL, 0.30 mmol) and Ac_2O (0.57 mL, 6.00 mmol) in CH_2Cl_2 (1 mL) at 25°C. After the mixture had been stirred for 12 h, $NaHCO_3$ aq. (10 mL) and NH_4F (800 mg) were added, and insoluble solids were removed by filtration. After usual workup (AcOEt/water), the organic layer was washed with $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. The crude mixture was subjected to column chromatography on silica gel to afford **9** (19:1 hexane/AcOEt, 60 mg, 21% yield), **3** (17:3 hexane/AcOEt, 97 mg, 40% yield), **11** (17:3 hexane/AcOEt, 29 mg, 12% yield) and **10** (3:2 hexane/AcOEt, 38 mg, 19% yield). **11**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29–1.60 (m, 14H), 2.03 (s, 3H), 2.22–2.37 (m, 2H), 3.63 (t, J=6.6 Hz, 2H), 4.91 (qui, J=6.2 Hz, 1H), 5.04–5.10 (m, 2H), 5.68–5.82 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.2, 25.2, 25.6, 29.2, 29.3, 29.4, 32.7, 33.5, 38.6, 62.9, 73.3, 117.5, 133.8, 170.8. HRMS (EI) calcd for $C_{14}H_{26}O_3$: 242.1882. Found: 242.1875.

3.1.7. Table 5 (entry 2). To a suspension of $Sc(OTf)_3$ (10.0 mg, 0.02 mmol) and **2** (158 mg, 1.00 mmol) in

CH_2Cl_2 (10 mL) were added tetraallyltin (0.07 mL, 0.30 mmol) at 25°C. After the mixture had been stirred for 12 h, $NaHCO_3$ aq. (10 mL) and NH_4F (800 mg) were added, and insoluble solids were removed by filtration. After usual workup (AcOEt/water), the organic layer was washed with $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. The crude mixture was subjected to column chromatography on silica gel (3:2 hexane/AcOEt) to afford a mixture of **10** and triol form of **12**. To these crude products were added pyridine (2 mL) and Ac_2O (0.75 mL, 8.00 mmol) at 0°C, and the mixture was stirred at room temperature for 12 h. After addition of 1N HCl at 0°C and usual workup (AcOEt/water), the combined organic layer was washed with H_2O, $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. The crude mixture was subjected to column chromatography on silica gel to afford **9** (19:1 hexane/AcOEt, 145 mg, 51% yield) and **12** (19:1 hexane/AcOEt, 29 mg, 13% yield). **12**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25–1.64 (m, 42H), 2.03 (s, 6H), 2.05 (s, 3H), 2.25–2.35 (m, 4H), 3.39 (dt, J=6.7, 9.2 Hz, 2H), 3.55 (dt, J=6.7, 9.2 Hz, 2H), 4.05 (t, J=6.9 Hz, 2H), 4.45 (t, J=5.6 Hz, 1H), 4.91 (qui, J=6.3 Hz, 2H), 5.04–5.09 (m, 4H), 5.71–5.79 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 21.2, 24.8, 25.3, 25.9, 26.2, 28.6, 29.2, 29.39, 29.40, 29.42, 29.5, 29.9, 33.4, 33.5, 38.6, 64.6, 65.5, 73.3, 103.1, 117.5, 133.8, 170.8, 171.3. HRMS (EI) calcd for $C_{39}H_{70}O_8$: 666.5071. Found: 666.5062.

3.1.8. Table 5 (entry 3). To a suspension of $Sc(OTf)_3$ (10.0 mg, 0.02 mmol), $(ClBu_2SnOSnBu_2Cl)_2$ (110 mg, 0.10 mmol) and **2** (158 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) was added tetraallyltin (0.07 mL, 0.30 mmol) at 25°C. After the mixture had been stirred for 12 h, $NaHCO_3$ aq. (10 mL) and NH_4F (800 mg) were added, and insoluble solids were removed by filtration. After usual workup (AcOEt/water), the organic layer was washed with $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. The crude mixture was subjected to column chromatography on silica gel (3:2 hexane/AcOEt) to afford a mixture of **10** and triol form of **12**. To these crude products were added pyridine (2 mL) and Ac_2O (0.75 mL, 8.00 mmol) at 0°C, and the mixture was stirred at room temperature for 12 h. After addition of 1N HCl at 0°C and usual workup (AcOEt/water), the combined organic layer was washed with H_2O, $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. The crude mixture was subjected to column chromatography on silica gel to afford **9** (19:1 hexane/AcOEt, 219 mg, 77% yield) and **12** (19:1 hexane/AcOEt, 15 mg, 7% yield).

3.1.9. Table 5 (entry 4). To a suspension of $Sc(OTf)_3$ (10.0 mg, 0.02 mmol), $(ClBu_2SnOSnBu_2Cl)_2$ (110 mg, 0.10 mmol) and **2** (158 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) was added Ac_2O (0.57 mL, 6.00 mmol) at 25°C. After the mixture had been stirred for 8 h, $NaHCO_3$ aq. (10 mL) and NH_4F (800 mg) were added, and insoluble solids were removed by filtration. After usual workup (AcOEt/water), the organic layer was washed with $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. The crude mixture was subjected to column chromatography on silica gel to afford **13** (17:3 hexane/AcOEt, 248 mg, 82% yield). **13**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (m, 10H), 1.59–1.77 (m, 4H), 2.05 (s, 3H), 2.08 (s, 6H), 4.05 (t, J=6.7 Hz, 2H), 6.77 (t, J=5.6 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.7, 20.9, 23.2, 25.7, 28.4, 28.91, 28.93, 29.1, 33.0, 64.4, 90.4, 168.9, 171.1. HRMS (EI) calcd for $C_{15}H_{26}O_6$: 302.1729. Found: 302.1749.

3.1.10. Table 6 (entry 1). To a suspension of $Sc(OTf)_3$ (10.0 mg, 0.02 mmol), $(ClBu_2SnOSnBu_2Cl)_2$ (110 mg, 0.10 mmol) and **2** (158 mg, 1.00 mmol) in CH_2Cl_2 (9 mL) was added a mixture of tetraallyltin (0.07 mL, 0.30 mmol) and Ac_2O (0.57 mL, 6.00 mmol) in CH_2Cl_2 (1 mL) at 25°C, and the mixture was stirred for 5 min. After addition of Me_2NNH_2 (1 mL), the mixture was stirred for 10 min, and $NaHCO_3$ aq. (10 mL) and NH_4F (800 mg) were added. The insoluble solids were removed by filtration. After usual workup (AcOEt/water), the organic layer was washed with $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. The crude mixture was subjected to column chromatography on silica gel to afford **3** (17:3 hexane/AcOEt, 12 mg, 5% yield) and **10** (3:2 hexane/AcOEt, 180 mg, 90% yield).

3.1.11. Table 6 (entry 2). To a suspension of $Sc(OTf)_3$ (10.0 mg, 0.02 mmol), $(ClBu_2SnOSnBu_2Cl)_2$ (110 mg, 0.10 mmol) and **2** (158 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) was added tetraallyltin (0.07 mL, 0.30 mmol) at 25°C, and the mixture was stirred for 5 min. After addition of Me_2NNH_2 (1 mL), the mixture was stirred for 10 min, and $NaHCO_3$ aq. (10 mL) and NH_4F (800 mg) were added. The insoluble solids were removed by filtration. After usual workup (AcOEt/water), the organic layer was washed with $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. The crude mixture was subjected to column chromatography on silica gel to afford hydrazone of **2** (1:1 hexane/AcOEt, 126 mg, 63% yield) and a mixture of **10** and triol form of **12** (3:2 hexane/AcOEt). To the mixture of **10** and triol form of **12** were added pyridine (2 mL) and Ac_2O (0.75 mL, 8.00 mmol) at 0°C, and the mixture was stirred at room temperature for 12 h. After addition of 1N HCl at 0°C and usual workup (AcOEt/water), the combined organic layer was washed with H_2O, $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. The crude mixture was subjected to column chromatography on silica gel to afford **9** (19:1 hexane/AcOEt, 63 mg, 22% yield) and **12** (19:1 hexane/AcOEt, trace). hydrazone of **2**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32–1.57 (m, 12H), 2.19–2.26 (m, 3H), 2.72 (s, 3H), 3.61 (t, J=6.6 Hz, 2H), 6.67 (t, J=5.6 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.6, 27.6, 29.0, 29.2, 29.3, 32.6, 32.9, 43.4, 62.7, 140.2. HRMS (EI) calcd for $C_{11}H_{24}N_2O$: 200.1889. Found: 200.1879.

3.1.12. Table 7 ($(ClBu_2SnOSnBu_2Cl)_2$/$Sc(OTf)_3$=1:2 as representative procedure). To a suspension of $Sc(OTf)_3$ (246 mg, 0.50 mmol) and $(ClBu_2SnOSnBu_2Cl)_2$ (276 mg, 0.25 mmol) in CH_2Cl_2 (0.7 mL) was added octanol (157 μL, 1.00 mmol) at room temperature and the mixture

was stirred for 1 h. The mixture was transferred to an NMR sample tube, and ^{119}Sn NMR was measured with reference to Me_4Sn as an external standard and by use of d_8-toluene as an external lock. Signals at −62.4 and −108.7 ppm were observed.

3.1.13. Scheme 3 (allylation by use of $Sc(OTf)_3$ and $(ClBu_2SnOSnBu_2Cl)_2$ in the presence of Ac_2O). To a suspension of $Sc(OTf)_3$ (10.0 mg, 0.02 mmol) and $(ClBu_2SnOSnBu_2Cl)_2$ (110 mg, 0.10 mmol) in CH_2Cl_2 (8 mL) was added nonanal (142 mg, 1.00 mmol) in CH_2Cl_2 (1 mL) and then a mixture of tetraallyltin (0.07 mL, 0.30 mmol) and Ac_2O (0.57 mL, 6.00 mmol) in CH_2Cl_2 (1 mL) at 25°C. After the mixture had been stirred for 1 h, $NaHCO_3$ aq. (10 mL) and NH_4F (800 mg) were added, and insoluble solids were removed by filtration. After usual workup (AcOEt/water), the organic layer was washed with $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. GC analysis of the crude mixture showed the formation of **6** (28% yield) and **7** (69% yield).

3.1.14. Scheme 4 (step i: mesylation). To a solution of **3** (242 mg, 1.00 mmol) in CH_2Cl_2 (5 mL) was added triethylamine (0.17 mL, 1.20 mmol) and methanesulfonyl chloride (0.09 mL, 1.10 mmol) at 0°C. After the mixture had been stirred for 2 h, $NaHCO_3$ aq. (10 mL) was added. After usual workup (AcOEt/water), the combined organic layer was washed with brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. The crude mixture was subjected to column chromatography on silica gel to afford mesylate of **3** (17:3 hexane/AcOEt, 305 mg, 95% yield). Mesylate of **3**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31–1.73 (m, 14H), 2.05 (s, 3H), 2.45–2.50 (m, 2H), 3.00 (s, 3H), 4.05 (t, J=6.7 Hz, 2H), 4.73 (qui, J=6.1 Hz, 1H), 5.14–5.19 (m, 2H), 5.73–5.87 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 24.9, 25.8, 28.5, 29.05, 29.13, 29.2, 34.1, 38.7, 39.0, 64.5, 82.8, 118.9, 132.5, 171.2. HRMS (EI) calcd for $C_{15}H_{28}O_5S$: 320.1657. Found: 320.1683.

3.1.15. Scheme 4 (step ii: preparation of 9,11-dodecadien-1-yl acetate 1). To a solution of mesylate of **3** (305 mg, 0.95 mmol) in toluene (10 mL) was added DBU (0.43 mL, 2.85 mmol) at room temperature, and then the mixture was heated to reflux for 12 h. After addition of water (10 mL) at room temperature and usual workup (AcOEt/water), the combined organic layer was washed with 1N HCl, $NaHCO_3$ aq. and brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. The crude mixture was subjected to column chromatography on silica gel to afford **1** (19:1 hexane/Et_2O, 160 mg, 75% yield, E/Z=80:20).

3.1.16. Scheme 4 (iodine-catalyzed isomerization of 1). A solution of **1** (160 mg, 0.71 mmol), I_2 (1 mg) in benzene (10 mL) was stirred for 12 h at room temperature under atmosphere of Ar. After addition of $Na_2S_2O_3$ aq. and usual workup (AcOEt/water), the combined organic layer was washed with brine. After drying over Na_2SO_4 and filtration, the organic layer was concentrated under reduced pressure. The crude mixture was subjected to column chromatography on silica gel to afford **1** (19:1 hexane/Et_2O, 146 mg, 91% yield, E/Z=89:11).

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9. Aqueous quenching is not employable because the reaction of **4** with aldehydes proceeds in the presence of water.[4] We have found that addition of Me_2NNH_2 can quench the reaction instantaneously to allow the quantitative analysis.