Allylstannylation of Carbon−Carbon and Carbon−Oxygen Unsaturated Bonds via a Radical Chain Process[1]

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In the presence of a radical initiator, allyltributylstannanes bearing an electron-withdrawing group at the β-position smoothly reacted with electron-deficient terminal alkenes to give allylstannylated products in good yields. The stannyl group was introduced into the terminal carbon with high regioselectivity. The allylstannylation of homochiral 8-phenylmenthyl acrylate proceeded with moderate to good diastereoselectivity. Terminal and electron-deficient internal alkynes as well efficiently underwent the radical-initiated allylstannylation in an anti addition mode. The reaction of terminal alkynes showed the same regioselectivity as that of terminal alkenes. The present radical reaction was applicable to allylation of aromatic aldehydes and ketones.

Introduction

The carbometalation of alkenes and alkynes is one of the most useful reactions for the stereocontrolled construction of organic molecules because it usually proceeds with high regio- and stereoselectivity, and the resultant organometallics react with various electrophiles with retention of the stereochemical integrity.[2] A variety of organometallics are known to add to the carbon−carbon unsaturated bond spontaneously or by the aid of a catalyst. In particular, carbometalation with allylmetals, that is allylmetalation, has been extensively studied in view of their unique reactivities, the ease of preparation, and the synthetically useful products.[2−5] The known allylmetalation reactions can be classified into the following three types: uncatalyzed concerted reactions using reactive allylmetals, transition metal-catalyzed reactions, and Lewis acid-catalyzed reactions through ionic intermediates. In contrast, we reported a novel type of allylmetalation, which proceeds via a radical chain mechanism.[6−8]

Allylstannanes are valuable reagents for allylation of various carbon radical precursors such as alkyl halides, dithiocarbonates, sulfides, and selenides.[9−11] Acyclic stereocontrol of the homolytic allylation has been the focus of intensive investigation in recent years.[12] In the radical chain process, an allylstannane plays two important roles as a radical transfer agent. One is to generate a stannyl radical, which abstracts an atom or group from a substrate to provide an alkyl radical, and the other is to allylate the alkyl radical with regeneration of the stannyl radical. It is also well-established that a stannyl radical easily adds to an alkene to form a β-stannylalkyl radical.[11a] From this knowledge, it occurred to us that a radical-initiated reaction of an alkene with an allylstannane could realize homolytic allylstannylation by the stannyl radical addition to the alkene and the subsequent allylation with the allylstannane.[13] Under this premise, we initially found that electron-deficient alkenes actually underwent the allylstannylation, and further investi-

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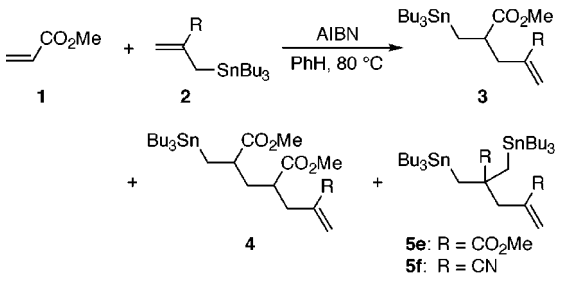
Table 1. Allylstannylation of Methyl Acrylate[a]



	allylstannane			isolated yield/%	
entry	R		time/h	**3**	**4**
1	H	**2a**	4	13	40[b]
2	Me	**2b**	2	21	47[b]
3	$SiMe_3$	**2c**	4	48	33[b]
4	Ph	**2d**	2	69	<3[c]
5	CO_2Me	**2e**	1	88[d,e]	
6	CN	**2f**	2	81[d]	

[a] All reactions were performed with a substrate (0.50 or 1.00 mmol), **2** (4.0 equiv), and AIBN (5 mol %) in benzene (5 mL per 1 mmol of the substrate) at 80 °C. [b] Diesters **4a**−**c** were obtained as a ca. 3:2 mixture of diastereomers. [c] Including unidentified impurities. One diastereomer could be characterized by ^{1}H NMR analysis. [d] Allylstannane **2e** or **2f** was recovered in 72% or 73% yield based on the initial amount, respectively. In addition, the formation of a trace amount of **5e** or **5f**, dimer of the allylstannane, was observed. [e] The reaction with 2.0 equiv of **2e** gave **3e** in 77% yield.

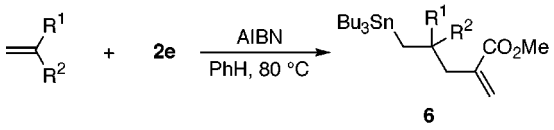
gated its applicability to other unsaturated bonds. Herein we wish to disclose the scope and limitations of the homolytic allylstannylation of alkenes, alkynes, and carbonyl compounds.[6]

Results and Discussion

Allylstannylation of Alkenes. First, methyl acrylate (**1**), a good radical acceptor, was selected as a substrate to evaluate the reactivities of some allylstannanes (Table 1). Treatment of **1** with 4 equiv of allyltributylstannane (**2a**) in the presence of AIBN at 80 °C gave α-allyl-*β*-stannylester **3a** in only 13% yield (Table 1, entry 1). A diastereomeric mixture of diester **4a** consisting of two molecules of **1** and one molecule of **2a** was obtained as a major product. The reactivity of methallylstannane **2b** to **1** was similar to that of **2a** (Table 1, entry 2), while the radical-initiated reaction with **2c** formed **3c** in preference to **4c** (Table 1, entry 3). Introduction of a phenyl group as R effectively suppressed the formation of 2:1 adduct **4d** to improve the efficiency of allylstannylation (Table 1, entry 4). Allylstannanes **2e**,**f** bearing an electron-withdrawing group as R smoothly reacted with **1** to afford allylstannylated products **3e**,**f** in high yields without 2:1 adducts **4e**,**f** (Table 1, entries 5 and 6). In these reactions, dimerization of **2e**,**f** to **5e**,**f** was observed; however, **2e**,**f** were recovered in high yields. The decreased amount (2.0 equiv) of **2e** lowered the yield of **3e** to 77%.

The allylstannylation of several mono- and 1,1-disubstituted alkenes with **2e** was next attempted to examine its applicability to alkenes. As shown in Table 2, monosubstituted alkenes were more reactive than the corresponding 1,1-disubstituted ones. Electron-deficient alkenes readily underwent the allylstannylation to give adducts **6** in good yields (Table 2, entries 1, 4, and 5), while styrene and α-methylstyrene exhibited much lower reactivity (Table 2, entries 2 and 6). The use of 1-decene resulted in no adduct even after prolonged reaction time (Table 2, entry 3).

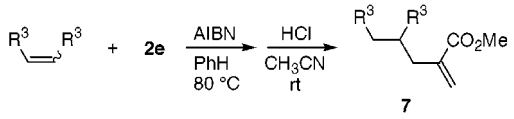
Table 2. Allylstannylation of Mono- and 1,1-Disubstituted Alkenes with 2e[a]



	alkene				
entry	R^1	R^2	time/h	product	isolated yield/%[b]
1	CN	H	4	**6a**	83
2	Ph	H	2	**6b**	40
3	C_8H_{17}	H	24	**6c**	no reaction
4	CO_2Me	Me	2	**6d**	63
5	CN	Me	4	**6e**	62
6	Ph	Me	2	**6f**	7

[a] See footnote a in Table 1. [b] In all entries, the formation of **5e** was observed.

Table 3. Allylation of Internal Alkenes with 2e[a]



alkene R^3	geometry	time[b]/h	product	isolated yield[c]/%
CO_2Me	*Z*	2	**7a**	67
CO_2Me	*E*	2	**7a**	40
CN	*Z*	4	**7b**	76

[a] After the reaction of an alkene (1.00 mmol) with **2e** was performed under the conditions described in Table 1, the resultant mixture was evaporated and treated with concentrated HCl (0.5 mL) in CH_3CN (3.5 mL) for 20 min. [b] The reaction time of the allylstannylation. [c] See footnote b in Table 2.

In marked contrast with methyl acrylate, methyl crotonate did not react with **2e** under the same conditions. However, highly electron-deficient internal alkenes such as dimethyl maleate, dimethyl fumarate, and fumaronitrile were reactive to **2e** although the allylstannylated products could not be isolated because of their partial destannylation in purification by silica gel column chromatography. After the crude products were treated with hydrochloric acid for complete destannylation, allylated products **7a**,**b** were obtained in moderate to good yields (Table 3).

A plausible mechanism for the formation of allylstannylated products **3** or **6** and 2:1 adducts **4** is shown in Scheme 1. In the initiation step, the radical generated from AIBN, that is $Me_2(NC)C^\bullet$, reacts with an allylstannane **2** to generate tributylstannyl radical. Reversible addition of the stannyl radical to an alkene gives a *β*-stannylalkyl radical **8**,[14] which leads to **3** or **6** by homolytic allylation with **2**. Further addition of **8** to the alkene and the subsequent allylation gives **4**. The origin of the regioselective allylstannylation is that terminal addition of the stannyl radical is favored over internal

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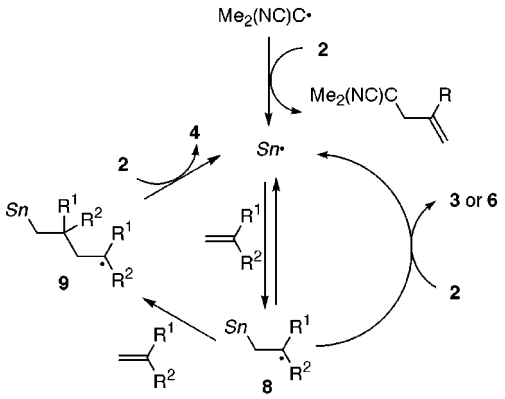
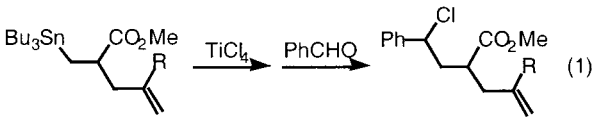
Scheme 1



addition in view of the low steric hindrance and the high stability of the resultant radical **8**.

For successful allylstannylation, the allylation of **8** must be faster than the reversion (β-elimination) and the further addition to the alkene. The high efficiency of the allylstannylation with **2e**,**f** in Table 1 is probably because the electron-withdrawing β-substituent R (CO_2Me or CN) accelerates the allylation of **8a** ($R^1 = CO_2Me$, $R^2 = H$). The selective formation of **4a**,**b** with **2a**,**b** indicates that the reaction of **8a** with methyl acrylate (**1**) is faster than that with **2a**,**b**. The high reactivity of **8a** to **1** and **2e**,**f** supports the assumption that **8a** has a nucleophilic character although the substituent on the radical center is an electron-withdrawing group. However, the comparison between the results with **2a**,**b** implies that **8a** has slightly higher reactivity to more electron-donating allylstannane **2b** than to **2a**.[15] Accordingly, in a strict sense, **8a** seemed to be an ambiphilic radical rather than a nucleophilic radical.[11b,16] The reason for the diminished reactivity of 1,1-disubstituted alkenes is unclear (Table 2), but it may be due to deceleration of the allylation of **8** by the increased steric bulkiness around the radical center. The insensitivity of 1-decene to **2e** is attributable to the instability of the corresponding β-stannylalkyl radical intermediate **8** ($R^1 = C_8H_{17}$, $R^2 = H$), which would induce the reversion to prevent the subsequent allylation.[14,17]

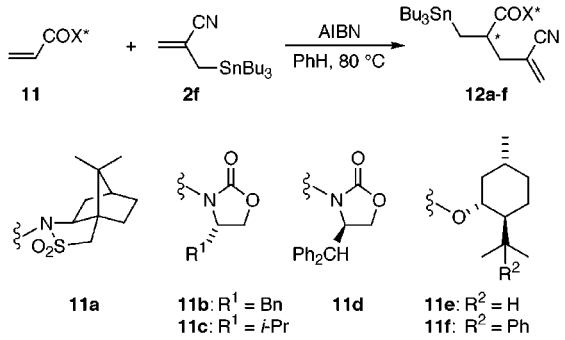
It is known that β-stannyl esters can be converted into titanium homoenolates by treatment with $TiCl_4$ and the homoenolates smoothly add to carbonyl compounds.[18] Therefore, we attempted the $TiCl_4$-mediated reactions of **3e**,**f** with benzaldehyde to show the synthetic utility of the allylstannylated products. As expected, the reactions afforded adducts **10** in moderate yields (eq 1). These results disclosed that the present products served as homoenolate equivalents.[19]



Asymmetric Homolytic Allylstannylation. Asymmetric induction by chiral auxiliary control is now known to be a reliable method for the enantioselective carbon−carbon bond formation in radical processes as well as ionic processes.[12,20] In particular, allylation of α-carbonyl carbon radicals bearing a chiral auxiliary with allylstannanes promises high levels of diastereoselectivity.[21] This fact induced us to investigate asymmetric homolytic allylstannylation using acrylic acid derivatives with a chiral auxiliary.

Initially, we prepared six homochiral acrylic acid derivatives **11** according to the reported procedure.[22] Then, they were subjected to the AIBN-initiated reaction with **2f** in benzene at 80 °C (Table 4). *N*-Acryloylcamphor sultam **11a** was insensitive to **2f**, contrary to our expectation (Table 4, entry 1),[21a] while *N*-acryloyloxazolidinones **11b**−**d** and menthyl acrylates **11e**,**f** smoothly reacted with **2f** to give the corresponding allylstannylated products **12** in good yields (Table 4, entries 2−6). 8-Phenylmenthyl acrylate **11f** showed the best diastereoselectivity of the five.[23]

Table 4. Diastereoselective Allylstannylation with 2f[a]



				isolated yield/%		
entry	substrate	time/h	product	major	minor	dr
1	**11a**	24	**12a**	0	0	
2	**11b**	1	**12b**	49	22	69:31
3	**11c**	1	**12c**	56	22	72:28
4	**11d**	1	**12d**	38	23	62:38
5	**11e**	4	**12e**	79[b]		63:37[b]
6	**11f**	4	**12f**	67	15[c]	82:18

[a] All reactions were performed with **11** (0.40 mmol), **2f** (1.60 mmol), and AIBN (0.02 mmol) in benzene (2.5 mL) at 80 °C. [b] The product was obtained as a diastereomeric mixture. The diastereomeric ratio was determined by ^{1}H NMR analysis. [c] The product was contaminated by **11f**. The yield was determined by ^{1}H NMR analysis.

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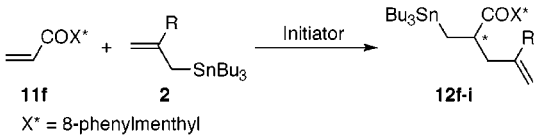
Table 5. Allylstannylation of Acrylate 11f[a]



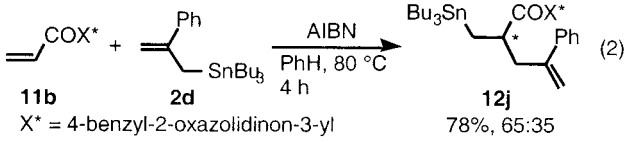
11f **2** **12f-i**

X* = 8-phenylmenthyl

entry	allylstannane R		solvent	*T*/°C	time/h	product	yield[b]/%	dr[b]
1	Me	**2b**	PhH	80	4	**12g**	39 (50)	63:37
2	Ph	**2d**	PhH	80	4	**12h**	81 (0)	84:16
3	CO_2Me	**2e**	PhH	80	4	**12i**	68 (20)	70:30
4	CN	**2f**	AcOEt	77	4	**12f**	82 (12)	83:17
5	CN	**2f**	THF	67	4	**12f**	47 (49)	83:17
6	CN	**2f**	hexane	69	4	**12f**	69 (23)	86:14
7	CN	**2f**	hexane	25	24	**12f**	72 (6)	90:10
8	CN	**2f**	hexane	−78	10	**12f**	38 (51)	91:9
9	Ph	**2d**	hexane	25	24	**12h**	39 (43)	87:13
10	CO_2Me	**2e**	hexane	25	24	**12i**	68 (16)	87:13

[a] All reactions were performed with **11f** (0.40 mmol), **2** (1.60 mmol), and AIBN (0.02 mmol, entries 1−6) or Et_3B (0.40 mmol, entries 7−10) in solvent (2.5 mL). [b] The yield and diastereomeric ratio were determined by ^1H NMR analysis of a mixture of **11f** and **12** obtained after purification by column chromatography. The recovery (%) of **11f** is shown in parentheses.

The AIBN-initiated allylstannylation of **11f** with **2b**,**e** in benzene resulted in lower diastereoselectivity, while the reaction with **2d** proceeded with good selectivity (entries 1−3 in Table 5). The use of **2d** in the allylstannylation of **11b** was not effective in improving the selectivity (eq 2). To achieve higher diastereoselectivity, the reaction of **11f** with **2f** was carried out under several reaction conditions (Table 5, entries 4−8). As a result, the Et_3B-initiated reaction in hexane at 25 °C improved the selectivity to 90% (Table 5, entry 7).[24] The allylstannylation with **2d**,**e** showed good selectivity under these conditions (Table 5, entries 9 and 10).



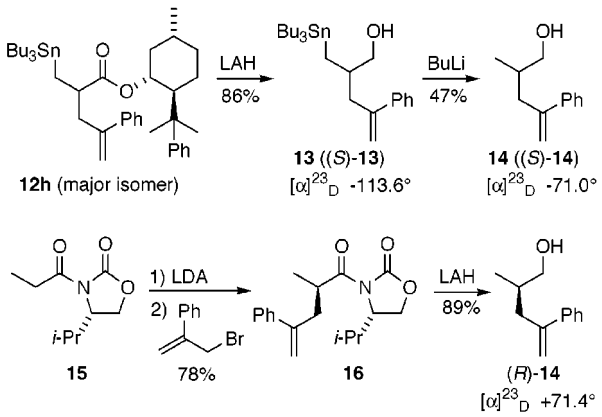
11b **2d** **12j**

X* = 4-benzyl-2-oxazolidinon-3-yl 78%, 65:35

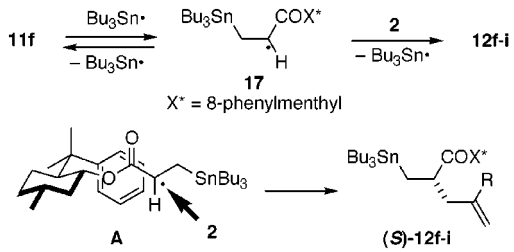
Lewis acids are now routinely used for stereoselectivity control of radical reactions as well as ionic and concerted reactions.[12] However, our efforts to attain high levels of diastereoselectivity in the Lewis acid-controlled homolytic allylstannylation of **11b**,**d**,**f** resulted in failure.

To determine the absolute configuration of **12f**−**i**, the major isomer of adduct **12h** (X* = 8-phenylmenthyl, R = Ph) was converted into alcohol **14** by reduction with LAH followed by destannylation with BuLi (Scheme 2).[25] In addition, the authentic sample of (*R*)-**14** was prepared from (*S*)-propanoyloxazolidinone **15** by the stereodefined method reported by Evans et al.[26] The sign of **14** in optical

Scheme 2



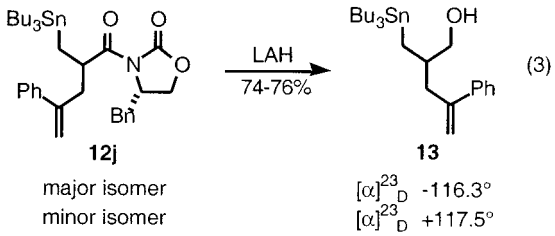
Scheme 3



rotation was opposite to that of (*R*)-**14**.[27] Accordingly, the major isomers of **12h** and other adducts derived from **11f** were determined to possess *S*-configuration at the carbon α to the carbonyl group.

The allylstannylation of **11f** with **2** would proceed through radical intermediate **17** having a planar structure by conjugation with the carbonyl group (Scheme 3).[20b] Judging from the previous studies on the reactions of α-carbonyl carbon radicals bearing an 8-phenylmenthyl group,[23] **17** presumably takes conformation **A**, in which the stannylmethyl group is anti to the alkoxy group and the phenyl group shields one face of the prostereogenic radical center.[28] Attack of **2** to **A** on the opposite side to the phenyl group well agrees with the present stereochemical outcome.

The LAH-reduction of the major isomer of **12j** was found to give the same enantiomer of **13** ((*S*)-**13**) as derived from the major isomer of **12h** by measurement of optical rotation (eq 3). Thus, the major isomers of **12b**,**j**



12j **13**

major isomer [α]23D -116.3°

minor isomer [α]23D +117.5°

were determined to have (4*S*,2′*S*)-configuration. This

(23) For diastereoselective reactions of α-carbonyl radicals generated from 8-phenylmenthyl esters, see: (a) Crich, D.; Davies, J. W. *Tetrahedron Lett.* **1987**, *28*, 4205. (b) Hamon, D. P. G.; Razzino, P.; Massy-Westropp, R. A. *J. Chem. Soc., Chem. Commun.* **1991**, 332. (c) Hamon, D. P. G.; Massy-Westropp, R. A.; Razzino, P. *Tetrahedron* **1993**, *49*, 6419. (d) Chen, M.-Y.; Fang, J.-M.; Tsai, Y.-M.; Yeh R.-L. *J. Chem. Soc., Chem. Commun.* **1991**, 1603.

(24) Nozaki, K.; Oshima, K.; Utimoto, K. *J. Am. Chem. Soc.* **1987**, *109*, 2547.

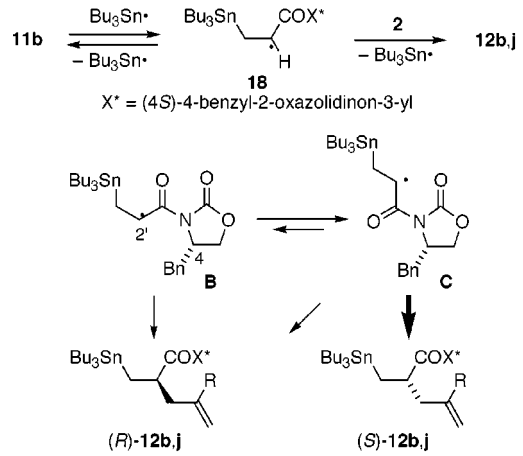
(25) (a) Meyer, N.; Seebach, D. *Chem. Ber.* **1980**, *113*, 1290. (b) Brieden, W.; Ostwald, R.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 582.

(26) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737.

(27) Alcohol **14** and the authentic sample of (*R*)-**14** were proved to be enatiomerically pure by their conversion into the diastereomeric MTPA esters with (+)-MTPA-Cl. See the Supporting Information and: Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.

(28) The intramolecular π-stacking interaction between the phenyl group and the α-carbonyl radical is likely to effect the conformation. 8-Phenylmenthyl crotonate is known to have such an interaction between the phenyl group and the carbon−carbon double bond. Mezrhab, B.; Dumas, F.; d'Angelo, J.; Riche, C. *J. Org. Chem.* **1994**, *59*, 500.

Scheme 4



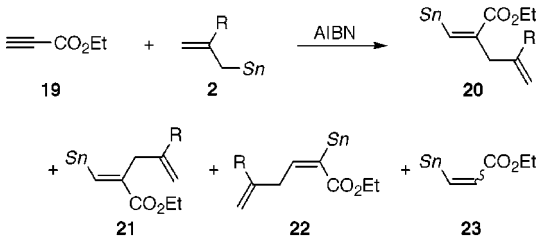
diastereoselectivity in the allylstannylation of **11b** is opposite to that in the Lewis acid-controlled allylation of α-carbonyl carbon radicals bearing a chiral oxazolidinone auxiliary.[29] Under the present conditions, the radical intermediate **18** generated from **11b** would favor conformation **C** over **B** because **B** has a dipole−dipole repulsion between the two carbonyl groups (Scheme 4). The observed selectivity may be due to the reaction of conformer **C** with **2** although the origin of the diastereoface-selectivity is not clear.

Allylstannylation of Alkynes. We next directed our efforts to homolytic allylstannylation of alkynes to develop a new stereoselective route to functionalized vinylstannanes. Ethyl propynoate (**19**) was first elected as a substrate for the reaction with allylstannanes **2**. The AIBN-initiated reaction of **19** with the parent allylstannane **2a** gave a mixture of α-allyl-*β*-stannyl-substituted acrylate **20a** (12%) and (*Z*)-*β*-stannylacrylate **23** (1.4%) after purification by silica gel column chromatography (Table 6). A mixture of **21a**, **22a** (stereo- and regioisomers of **20a**), and (*E*)-**23** was also obtained although each yield was fairly low (<0.5%). On the other hand, *β*-substituted allylstannanes exhibited higher reactivity than **2a** as shown in the allylstannylation of methyl acrylate. In particular, **2e**,**f** efficiently reacted with **19** to give trans adducts **20e**,**f** selectively.

To investigate the scope and limitations of the allylstannylation, a variety of alkynes were subjected to the reaction with **2e** (Table 7). In these cases, the formation of cis-adducts **26** was not observed except for entry 8. Phenylacetylene (**24a**) showed high reactivity to **2e**, leading to vinylstannane **25a** in a high yield without regioisomer **27a** (Table 7, entry 1). Although the reaction of 1-dodecyne (**24b**) also gave only **25b**, isolation of **25b** from the reaction mixture including **2e** and its dimer **5e** was a laborious process (Table 7, entry 2). The yield of **25b** was estimated to be 63% by the ^{1}H NMR analysis of the crude product, but it was isolated in only 44% yield (>98% pure) by distillation. Protonolysis of the crude product with HCl−CH_3CN provided 1,4-diene **28** in 70% isolated yield. The reactivity of **24b** is in sharp contrast to that of 1-decene, which was insensitive to **2e** under the same reaction conditions. 3-Butyn-1-ol (**24c**) as well as **24a**,**b** smoothly underwent the allylstannylation to form only **25c** (Table 7, entry 3). Thus, the present reaction is tolerable to a hydroxy group unlike most of the known allylmetalation reactions. The use of 3-butyn-2-ol (**24d**) as a substrate resulted in three adducts, both regioisomers **25d**, **27d**, and *δ*-lactone **29** (Table 7, entry 4). Protection of the hydroxy group of **24d** was fairly effective to suppress the formation of **27e** as well as lactonization (Table 7, entry 5).

(29) Sibi et al. have reported that the addition of multipoint binding Lewis acids (e.g., $Yb(OTf)_3$, $MgBr_2$) changes the diastereoselectivity in the allylation of such carbon radicals. See ref 21d and: Sibi, M. P.; Rheault, T. R. *J. Am. Chem. Soc.* **2000**, *122*, 8873.

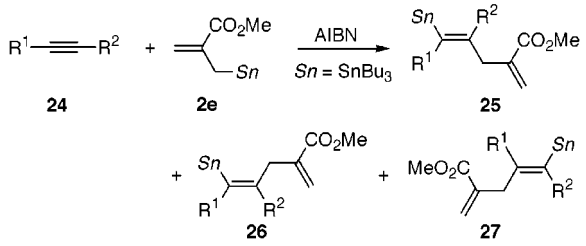
Table 6. Allylstannylation of Ethyl Propynoate[a]



entry	allylstannane R		time/h	yield/% 20[b,c]	21 + 22[c,d]	21:22[e]
1	H	**2a**[f]	4	12[g]	<1[h]	66:34
2	Me	**2b**	2	27[g]	<2[h]	75:25
3	$SiMe_3$	**2c**[f]	2	38	<2	50:50
4	Ph	**2d**	1	61	<5	34:66
5	CO_2Me	**2e**[f]	1	70	<15	73:27
6	CN	**2f**[f]	1	66	11[i]	100:0[i]

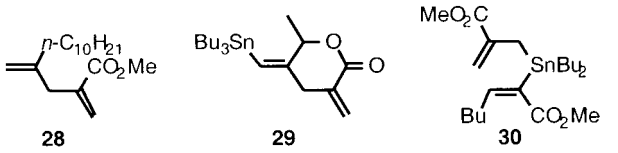
[a] See footnote a in Table 1. [b] Isolated yield of a pure product except for entries 1 and 2. [c] The configurations of **20**−**22** were assigned by NOE experiments, chemical shifts of the olefinic protons, and coupling constants between the olefinic proton and ^{119}Sn or ^{117}Sn. See the Supporting Information. [d] The mixture of vinylstannanes **21** and **22** was contaminated by unidentified impurities except for entry 6. [e] Determined by ^{1}H NMR analysis. [f] The allylstannane was recovered in 62−74% yield based on the initial amount. [g] Including (*Z*)-**23**. The yield was estimated by ^{1}H NMR analysis. [h] Including (*E*)-**23**. [i] Only **21f** was obtained.

Table 7. Allylstannylation of Alkynes 24[a]



entry	alkyne R^1	R^2		time/h	isolated yield/%[b] 25	27
1	H	Ph	**24a**	1	94	
2	H	n-$C_{10}H_{21}$	**24b**	6	44[c]	
3	H	$(CH_2)_2OH$	**24c**	2	69	
4	H	CH(OH)Me	**24d**	2	34[d,e]	5[d]
5	H	CH(OAc)Me	**24e**	2	62	
6	Bu	CO_2Me	**24f**	2	15[f]	38
7	Ph	CO_2Me	**24g**	1	2	84
8	MeO_2C	CO_2Me	**24h**	1	85[g]	
9	Bu	Ph	**24i**	6	19	
10	n-C_5H_{11}	n-C_5H_{11}	**24j**	24	no reaction	

[a] See footnote a in Table 1. [b] The configuration of product was assigned mainly by NOE experiments and/or the coupling constant between ^{1}H and ^{119}Sn or ^{117}Sn. See the Supporting Information. [c] Treatment of the crude product with HCl−CH_3CN gave **28** in 70% yield. [d] A mixture of **25d** and **27d** was obtained. The yields were determined by ^{1}H NMR analysis. [e] Lactone **29** was also obtained (<4%). [f] Allylvinylstannane **30** was also obtained (7%). [g] The formation of cis adduct **26h** was observed (<1%).



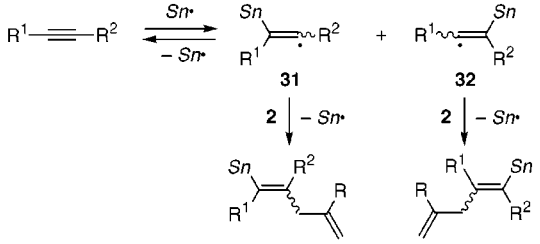
Internal alkynes conjugated with an ester group were also available for the allylstannylation. The reaction of methyl 2-heptynoate (**24f**) gave trans-adducts **25f** and **27f** with a 1:2 regioselectivity along with allylvinylstannane **30** (Table 7, entry 6). When methyl 3-phenyl-2-propynoate (**24g**) was employed, the regioselectivity increased to more than 40:1 (Table 7, entry 7). Dimethyl acetylenedicarboxylate (**24h**), a highly electron-deficient alkyne, also underwent the trans-allylstannylation in high efficiency (Table 7, entry 8). In contrast, internal alkynes with no electron-withdrawing group were much less reactive to **2e** than electron-deficient alkynes (Table 7, entries 9 and 10).

A plausible mechanism for the homolytic allylstannylation of alkynes is illustrated in Scheme 5. First, tributylstannyl radical generated from an allylstannane **2** by the action of AIBN adds to an alkyne reversibly. Then, the resulting vinyl radical **31** or **32** reacts with **2** to afford the corresponding allylstannylated product and regenerate the stannyl radical. The formation of **23** in the reaction of **19** with **2a**,**b** is probably due to low radical-allylating ability of **2a**,**b**, which allows hydrogen abstraction of the radical intermediate **31** ($R^1 = H$, $R^2 = CO_2Et$). As mentioned above, the high reactivity of **2e**,**f** toward the homolytic allylstannylation would be imparted by the β-substituent, thus accelerating the allylation step.

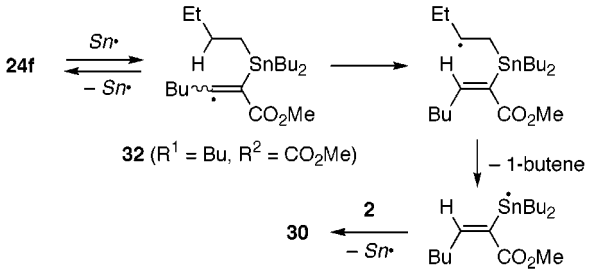
In the case of terminal alkynes ($R^1 = H$), the regioselective introduction of the stannyl group can be rationalized by avoidance of steric repulsion from the substituent R^2 and the formation of more stabilized radical intermediate **31**. The formation of **22** and **27d** from terminal alkynes **19** and **24d** indicates that the ester and hydroxy groups facilitate addition of the stannyl radical to the internal acetylenic carbon close to them. This directing effect was distinctly observed in the reaction of internal alkyne **24f**. It is known that homolytic hydrostannylations of 2-alkynoates and propargyl alcohols with Bu_3SnH show a similar trend in regioselectivity.[30,31] However, the origin of the directing effect remains obscure at present. The results with phenyl-substituted alkynes **24g**,**i** disclose that the phenyl group effectively controls the regioselectivity. The regiocontrol would be caused by strong stabilization of the corresponding radical intermediates by the phenyl group.

The reason for the preferred formation of trans-adducts in the present allylstannylation is that **2** approaches the radical center of **31** or **32** from the opposite side to the stannyl group to avoid its steric hindrance.[32,33] In the reaction of **19**, the stannyl radical-mediated isomerization

Scheme 5



Scheme 6



of products would also affect the stereoselectivity.[14,34] Indeed, (*E*)-vinylstannanes **20** were partly isomerized to the *Z*-isomers **21** in the presence of Bu_3SnH and Et_3B.[35]

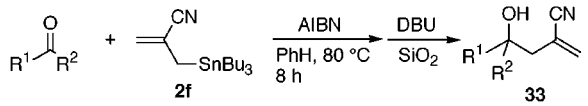
The difference between 1-decene and 1-dodecyne in reactivity to **2e** is attributable to the lifetimes of the β-stannyl carbon radical intermediates arising from these substrates. β-Stannylalkyl radicals are believed to revert to stannyl radicals faster than β-stannylvinyl radicals.[36] The high reactivity of 1-dodecyne is probably because the corresponding β-stannylvinyl radical intermediate has enough lifetime to react with **2e** unlike the β-stannylalkyl one from 1-decene.

The formation of **30** can be explained by the stepwise mechanism shown in Scheme 6, which consists of (1) addition of tributylstannyl radical to the α-carbon of ester **24f**, (2) 1,5-hydrogen transfer from sp^3-carbon to sp^2-carbon, (3) elimination of a dibutylvinylstannyl radical from the rearranged radical, and (4) allylation of the stannyl radical by S_H2' process. There are two factors that assist the 1,5-hydrogen transfer. One is that the vinyl radical intermediate **32** ($R^1 = Bu$, $R^2 = CO_2Me$), which is not stabilized by conjugation, has enough reactivity to cause the 1,5-hydrogen transfer.[37] The other is that the steric bulkiness around the radical center decelerates the intermolecular allylation with **2e**.

Allylation of Carbonyl Compounds. The allylation of carbonyl compounds with allylstannanes is significantly valuable for regio- and stereoselective carbon−carbon bond formation.[3,11a,c] Allylstannanes react with aldehydes and ketones spontaneously or in the presence of a Lewis acid to give homoallyl alcohols. The allylation reactions are generally believed to proceed via a concerted or ionic process. There is no example of the radical-initiated allylation of carbonyl carbons except for our previous work.[38,39] In contrast, hydrostannanes are known to reduce aldehydes and ketones to alcohols by a radical

(30) (a) Konoike, T.; Araki, Y. *Tetrahedron Lett.* **1992**, *33*, 5093. (b) Ensley, H. E.; Buescher, R. R.; Lee, K. *J. Org. Chem.* **1982**, *47*, 404.
(31) (a) Leusink, A. J.; Budding, H. A. *J. Organomet. Chem.* **1968**, *11*, 533. (b) Leusink, A. J.; Budding, H. A.; Marsman, J. W. *J. Organomet. Chem.* **1967**, *9*, 285.
(32) (a) Giese, B.; González-Gómez, J. A.; Lachhein, S.; Metzger, J. O. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 479. (b) Journet, M.; Malacria, M. *J. Org. Chem.* **1992**, *57*, 3085.
(33) (a) Miura, K.; Itoh, D.; Hondo, T.; Hosomi, A. *Tetrahedron Lett.* **1994**, *35*, 9605. (b) Miura, K.; Saito, H.; Itoh, D.; Hosomi, A. *Tetrahedron Lett.* **1999**, *40*, 8841.
(34) Leusink, A. J.; Budding, H. A.; Drenth, W. *J. Organomet. Chem.* **1968**, *11*, 541.
(35) Taniguchi, M.; Nozaki, K.; Miura, K.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 349.
(36) Stork, G.; Mook, R., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 2829.
(37) (a) Curran, D. P.; Shen, W. *J. Am. Chem. Soc.* **1993**, *115*, 6051. (b) Bogen, S.; Malacria, M. *J. Am. Chem. Soc.* **1996**, *118*, 3992.
(38) We have recently reported the radical-initiated allylsilylation of aldehydes and ketones. See ref 7.

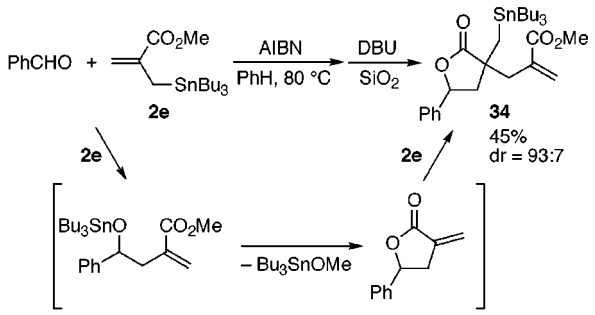
Table 8. Allylation of Aldehydes and Ketones[a]



	carbonyl compound			
entry	R^1	R^2	product	isolated yield/%
1	Ph	H	**33a**	59
2	4-$MeOC_6H_4$	H	**33b**	35
3	2-furyl	H	**33c**	53
4	$Ph(CH_2)_2$	H	**33d**	0
5	Ph	Me	**33e**	29

[a] See footnote a in Table 1. The resulting reaction mixture was treated with DBU and passed through a short silica gel column.

Scheme 7



chain mechanism as well as a concerted or ionic process.[11c,17] The homolytic reduction involves addition of a stannyl radical to the carbon−oxygen bond as a propagation step. Therefore, our attention was next focused on the homolytic allylation of carbonyl compounds.

Treatment of benzaldehyde with **2f** in the presence of AIBN and the subsequent destannylative workup gave homoallyl alcohol **33a** in a moderate yield (entry 1 in Table 8). The reaction without AIBN resulted in no adduct. This observation supports our assumption that the present allylation proceeds via a radical process. As expected from the above results, **2a** hardly reacted with benzaldehyde even in the presence of AIBN. The use of **2e** gave lactone **34** exclusively, which would be formed by the allylstannylation−lactonization−allylstannylation process shown in Scheme 7. While other aromatic aldehydes and acetophenone also underwent the AIBN-initiated allylation with **2f** (Table 8, entries 2, 3, and 5), 3-phenylpropanal was quite insensitive to **2f** (Table 8, entry 4).

Conclusion

We have found that, in the presence of a radical initiator, allyltributylstannanes react with alkenes and alkynes to give the corresponding allylstannylated products. This homolytic allylstannylation involves two propagation steps: reversible addition of tributylstannyl radical to the unsaturated bonds and allylation of the resultant β-stannyl carbon radicals with allylstannanes. Introduction of an electron-withdrawing group into the β-position of allylstannanes accelerates the latter allylation step to attain high efficiency. Electron-deficient alkenes and various alkynes smoothly undergo the homolytic allylstannylation. The high reactivity of these substrates can be rationalized by the stability of radical intermediates arising from them. Namely, β-stannylalkyl radicals stabilized by an electron-withdrawing group or β-stannylvinyl radicals have enough lifetimes to react with allylstannanes before their reversion to the substrates and tributylstannyl radical. The present allylstannylation provides a new method for the synthesis of functionalized β-stannylesters and vinylstannanes, which are used as potent carbon nucleophiles for carbon−carbon bond formation.[11a,c,18] The use of acrylates bearing a chiral auxiliary enables asymmetric allylstannylation reaction. In addition, the radical-initiated reaction with allylstannanes can be utilized for the allylation of aromatic carbonyl compounds. In conclusion, we have developed a novel type of carbometalation reaction with wide applicability, which proceeds via a radical chain mechanism unlike the known carbometalation reactions.

Experimental Section

General Methods. Unless otherwise noted, all reactions and distillation of solvents were carried out under N_2. Solvents were dried by distillation from sodium metal/benzophenone ketyl (THF, Et_2O) and CaH_2 (benzene, hexane, CH_2Cl_2). Bu_3SnCl was simply distilled in vacuo. All other commercial reagents were used as received.

Synthesis of Substrates. Homochiral acrylic acid derivatives **11** were prepared by the reported procedure.[22] 1-Methyl-2-propynyl acetate (**24e**) was obtained from 3-butyn-2-ol by acetylation with AcCl−Et_3N in Et_2O.[40] The reaction of methyl chloroformate with lithium acetylide derived from 1-hexyne was carried out for the synthesis of methyl 2-heptynoate (**24f**).[41] Other substrates were purchased.

Synthesis of Allylstannanes. Allylstannanes **2a**−**e** were prepared by reductive coupling between the corresponding allyl bromides and Bu_3SnCl using Mg and a catalytic amount of $PbBr_2$.[42] 2-Trimethylsilyl-3-bromo-1-propene,[43] 3-bromo-2-phenyl-1-propene,[44] and methyl 2-(bromomethyl)acrylate[45] were prepared by the reported procedures. Allylstannane **2f** was synthesized from the corresponding allyl sulfonates by homolytic substitution with Bu_3SnH.[46]

AIBN-Initiated Allylstannylation (General Procedure). Allylstannane **2** (4.0 equiv) was added to a solution of a substrate (1.0 equiv, 0.50 or 1.00 mmol) and AIBN (5 mol %) in benzene (5.0 mL per 1.00 mmol of the substrate). The mixture was stirred at reflux. After completion of the reaction, the resultant mixture was evaporated and purified by silica gel column chromatography. In the reaction of **11**, 0.40 mmol of **11** and 2.5 mL of benzene or other solvent were used.

Allylation of Internal Alkenes and 1-Dodecyne. The AIBN-initiated reaction of an electron-deficient internal alkene (0.5 mmol) with **2e** was performed under the same conditions as the above general procedure. After concentration of the reaction mixture, it was diluted with CH_3CN (3.5 mL) and treated with concentrated HCl (0.5 mL) for 10 min. The resultant mixture was neutralized with saturated aqueous

(39) Enholm et al. have reported that the AIBN-initiated reactions of cyclopropyl and α,β-unsaturated ketones with allylstannanes give γ- and β-allylated ketones, respectively. (a) Enholm, E. J.; Jia, Z. J. *J. Org. Chem.* **1997**, *62*, 9159. (b) Enholm, E. J.; Moran, K. M.; Whitley, P. E. *Tetrahedron Lett.* **1998**, *39*, 971.

(40) Nakamura, K.; Takenaka, K.; Ohno, A. *Tetrahedron*: *Asymmetry* **1998**, *9*, 4429.
(41) Zhou, Z.; Larouche, D.; Bennett, S. M. *Tetrahedron* **1995**, *51*, 11623.
(42) Tanaka, H.; Abdul Hai, A. K. M.; Ogawa, H.; Torii, S. *Synlett* **1993**, 835.
(43) Lee, E.; Yu, S.-G.; Hur, C.-U.; Yang, S.-M. *Tetrahedron Lett.* **1988**, *29*, 6969.
(44) Hatch, L. F.; Patton, T. L. *J. Am. Chem. Soc.* **1954**, *76*, 2705.
(45) Byun, H.-S.; Reddy, K. C.; Bittman, R. *Tetrahedron Lett.* **1994**, *35*, 1371.
(46) Baldwin, J. E.; Adlington, R. M.; Lowe, C.; O'Neil, I. A.; Sanders, G. L.; Schofield, C. J.; Sweeney, J. B. *J. Chem. Soc., Chem. Commun.* **1988**, 1030.

$NaHCO_3$ (20 mL) and extracted with Et_2O (2 × 15 mL). The extract was treated with DBU (0.5 mL) for 5 min and passed through a short silica gel column.[47] The filtrate was evaporated and purified by silica gel column chromatography. This method was also used for allylstannylation of 1-dodecyne (**24b**) with **2e** followed by protonolysis (footnote c in Table 7).

$TiCl_4$-Mediated Reaction of β-Stannylester 3e with Benzaldehyde.[18] To a solution of **3e** (475 mg, 1.00 mmol) in CH_2Cl_2 (3.5 mL) at room temperature was added $TiCl_4$ (1.0 M in CH_2Cl_2, 0.80 mL, 0.80 mmol). After 30 min, benzaldehyde (74 mg, 0.70 mmol) was added to the mixture. After 7 h, the resultant mixture was poured into saturated aqueous $NaHCO_3$ (20 mL) and extracted with Et_2O (2 × 15 mL). A halostannane byproduct was removed from the extract by the above DBU−silica gel method.[47] Purification of the crude product by silica gel column chromatography gave **10a** (144 mg, 0.46 mmol) in 66% yield.

Et_3B-Initiated Allylstannylation of Acrylate 11f. Et_3B (1.0 M in hexane, 0.40 mL, 0.40 mmol) was added to a solution of **11f** (0.40 mmol) and **2** (1.6 mmol) in hexane (2.5 mL) at 25 or −78 °C. Then, dry air (5 mL) was introduced into the mixture. After completion of the reaction, the resultant mixture was evaporated and purified by silica gel column chromatography.

Stannyl Radical-Induced Isomerization of 20 (Typical Procedure). To a solution of **20a** (86 mg, 0.20 mmol) in benzene (0.4 mL) at room temperature were added Bu_3SnH (22 μL, 0.08 mmol) and Et_3B (1.0 M in hexane, 0.08 mL, 0.08 mmol). The mixture was stirred for 12 h and concentrated in vacuo. Purification of the residual oil by silica gel column chromatography (hexane−CH_2Cl_2 2:1) gave **21a** (4.3 mg, 0.010 mmol) in 5% yield with 62% recovery of **20a**. Other (*Z*)-vinylstannanes **20** as well were partially isomerized to **21** under these conditions.

Allylation of Carbonyl Compounds. The AIBN-initiated reaction of a carbonyl compound (0.5 mmol) with **2f** was performed under the same conditions as the above general procedure. After concentration of the reaction mixture, it was diluted with Et_2O (10 mL), treated with DBU (0.3 mL) for 5 min, and passed through a short silica gel column.[47] The filtrate was evaporated and purified by silica gel column chromatography.

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Supporting Information Available: Experimental procedure for the synthesis of allylstannanes **2** and alcohol **14**, characterization data for allylstannanes and products, and discussion on configurational assignment of vinylstannane products. This material is available free of charge via the Internet at http://pubs.acs.org.

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