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Communications

Diastereoselective 1,4-Addition of Stannyl Radical in the Presence of Lewis Acid: A Novel Synthetic Route to Optically Active *β*-Stannyl Esters

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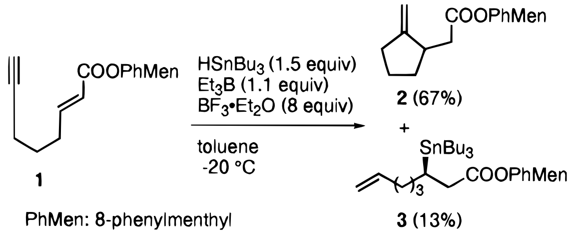
Organostannyl compounds, which have a C−Sn bond at a stereocenter, are useful reagents for stereoselective syntheses.[1,2] In particular, the addition of allylstannane to a carbonyl group has been widely investigated[3,4] and extended to asymmetric allylation using enantioenriched allylstannanes. Several methods have been developed to prepare optically active alkyl- and allylstannanes.[5] However, none of these approaches are widely applicable.

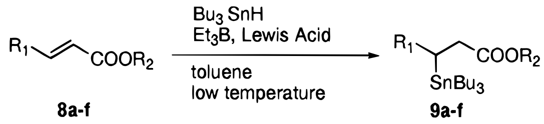
Recently, we reported a Lewis acid-promoted *β*-diastereoselective radical cyclization using α,*β*-unsaturated 8-phenylmenthyl ester as a chiral radical acceptor (Scheme 1).[6] We have subsequently expanded our investigation in this area to consider the reaction of a stannyl radical to α,*β*-unsaturated 8-phenylmenthyl esters to give optically active *β*-stannyl esters. We report here an auxiliary-controlled asymmetric synthesis of *β*-tributylstannyl esters, which have proven to be useful building blocks for the synthesis of optically active cyclopropanes.

In our previous studies on *β*-diastereoselective radical cyclizations, a low reaction temperature was important to achieve high diastereoselectivities. The addition of stannyl radicals to α,*β*-unsaturated esters generally occurs under thermal conditions (such as at 80 °C) and does not occur at 0 °C or below (*vide infra*). However, in the reaction of **1**, we found that a small amount of **3** (13%) was produced even at −20 °C in the presence of $BF_3 \cdot OEt_2$, along with the cyclized product.[6a]

Scheme 1



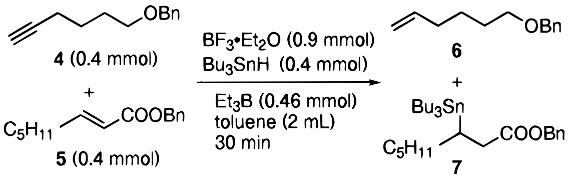
Scheme 2



a: $R_1 = CH_2{=}CHCH_2CH_2$, $R_2 = Me$
b: $R_1 = PhCH_2CH_2$, $R_2 = Me$
c: $R_1 = Me$, $R_2 = Et$
d: $R_1 = C_{11}H_{23}$, $R_2 = PhMen$
e: $R_1 = PhCH_2CH_2$, $R_2 = PhMen$
f: $R_1 = Me$, $R_2 = PhMen$

PhMen : 8-phenylmenthyl

To determine the relative reactivities of alkyne **4** and α,*β*-unsaturated ester **5** in the reaction with a stannyl radical, a mixture of **4** (0.4 mmol) and **5** (0.4 mmol) was treated with Bu_3SnH (0.4 mmol) in the presence of $BF_3 \cdot OEt_2$ and a radical initiator (Et_3B) for 30 min (eq 1). At 0 °C, the hydrostannylation of **4** proceeded faster (45% yield of **6**, which was produced by hydrostannylation followed by destannylation) than the 1,4-addition of the stannyl radical to **5** (5% yield of **7**). On the other hand, hydrostannylation dramatically slowed at −40 °C (5% yield of **6**), while **5** maintained its reactivity (18% yield of **7**). Therefore, the relative reactivity varied with the reaction temperature.



(1)

These data suggest that the 1,4-addition of stannyl radical could occur with a reasonable reaction rate in the presence of a Lewis acid even at 0 °C or below. Thus, the reactions of achiral and chiral unsaturated esters were investigated (Scheme 2).[7] The results in Table 1 clearly show that the presence of a Lewis acid is essential for this reaction to proceed at less than 0 °C (runs 1 and 2).[8] The reaction of **8a** proceeded smoothly to give *β*-stannyl ester **9a** at a yield of 64% (run 2, Table 1). While this reaction also proceeded with Me_2AlCl or bis(2,6-di-*tert*-butyl-4-methylphenoxy)aluminum chloride (runs 5 and 6, Table 1), trialkylaluminum reagents, such as *i*-Bu_3Al, were ineffective.

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(7) Representative procedure: (Run 3) to a solution of **8b** (38 mg, 0.2 mmol) in toluene (2.0 mL) were added $BF_3 \cdot OEt_2$ (0.8 mmol), Et_3B (1 M in hexane, 0.23 mmol), and Bu_3SnH (0.33 mmol) at −25 °C under Ar, and the mixture was stirred for 3.5 h. (Run 11) to a solution of **8f** (60 mg, 0.2 mmol) in toluene (1.6 mL) were added Bu_3SnH (0.33 mmol), Et_2AlCl (1 M in hexane, 0.4 mmol), and Et_3B (1 M in hexane, 0.23 mmol) at −25 °C under Ar, and the mixture was stirred for 1.5 h.

(8) Related Lewis acid-enhanced reactivity in a radical reaction has been reported recently: Urabe, H.; Yamashita, K.; Suzuki, K.; Kobayashi, K.; Sato F. *J. Org. Chem.* **1995** *60*, 3576.

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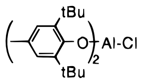
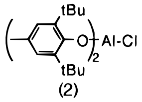
Table 1. 1, 4-Addition of Stannyl Radical

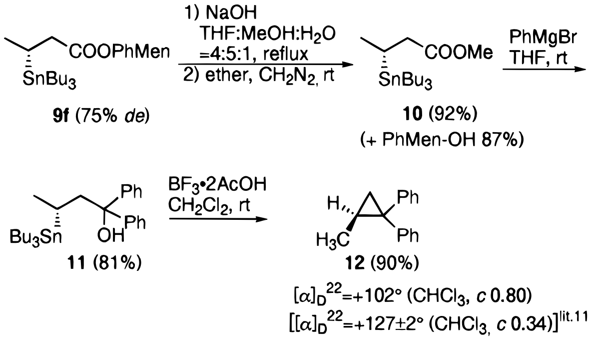
run	substrate	Lewis acid (equiv)	temp (°C)	time (h)	yield of **9** (%)	selectivity
1	**8a**	none	0	1.5	0	
2	**8a**	$BF_3 \cdot OEt_2$ (4)	0	0.5	64	
3	**8b**	$BF_3 \cdot OEt_2$ (4)	-25	3.5	67	
4	**8c**	$BF_3 \cdot OEt_2$ (5)	0	0.7	68	
5	**8c**	Me_2AlCl (2)	-25	1.5	86	
6	**8c**	 (2)	-25	2.0	80	
7	**8d**	$BF_3 \cdot OEt_2$(4)	-25	2.0	78	19:1
8	**8e**	$BF_3 \cdot OEt_2$ (4)	-25	2.0	78	19:1
9	**8f**	$BF_3 \cdot OEt_2$ (4)	-25	1.5	80	6:1
10	**8f**	Me_2AlCl (2)	-25	1.5	80	6:1
11	**8f**	Et_2AlCl (2)	-25	1.5	82	7:1
12	**8f**	 (2)	-25	1.8	70	7:1

Since stannyl ester **3** was obtained as a single diastereomer,[6a,9] high diastereoselectivity was expected in reactions using **8d-f** (runs 7–12, Table 1). All of these reactions proceeded at −25 °C and provided *β*-stannyl esters in good yields. Higher diastereoselectivity was observed in reactions using α,*β*-unsaturated esters with a bulky substituent at the *β*-position, such as **8d** and **8e**. In our intramolecular version of this reaction, bulky aluminum reagents were effective in achieving higher diastereoselectivities. However, in reactions with **8f**, a significant enhancement of diastereoselectivity was not observed in the reaction using bis(2,6-di-*tert*-butyl-4-methylphenoxy)aluminum chloride (run 12, Table 1).

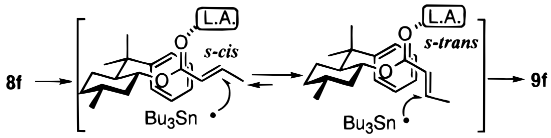
The diastereoselectivities of **9d**–**f** were determined as follows. The *β*-stannyl esters **9d**–**f** were first transformed into *γ*-hydroxystannanes (LAH, ether, 70–80%), and then converted to their respective Mosher esters [DCC, (−)-MTPA, 85–100%]. Their diastereoselectivities were then determined by ^{1}H-NMR (600 MHz).

The *β*-stannyl ester **9f** (a 7:1 mixture of diastereomers, 75% *de*) was converted to the optically active cyclopropane **12** (Scheme 3).[1,10] Since the reaction of **9f** with a large excess of PhMgBr at room temperature did not give

Scheme 3



Scheme 4



11, the chiral auxiliary of **9f** was removed by standard hydrolysis. The methyl ester **10** was then converted to **11**. Cyclopropane formation proceeded efficiently, and the optical rotation of the resulting cyclopropane **12** was $[\alpha]_D$ +102°. The absolute configuration of **12** was determined to be *S* by comparison with the reported $[\alpha]_D$ value.[11] According to a previously reported mechanism for cyclopropane formation,[10c] the absolute configuration of the asymmetric carbon with the stannyl group in **9f** was *R*. This result is consistent with the transition state that we propose for Lewis acid-promoted *β*-diastereoselective cyclization (Scheme 4).[6]

In conclusion, the diastereoselective 1,4-addition of stannyl radical to α,*β*-unsaturated (−)-8-phenylmenthyl ester in the presence of a Lewis acid is a convenient method for preparing optically active *β*-stannyl esters, which are building blocks for chiral cyclopropane synthesis.

Supporting Information Available: Experimental procedures for the 1,4-addition of stannyl radical (Table 1), including the determination of diastereoselectivity, conversion of **9f** to **12** (Scheme 3), and preparation of chiral substrates **8d**,**e**,**f** (32 pages).

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[9] Diastereoselectivity was determined by ^{1}H-NMR. The stereochemistry of **3** could not be determined and was tentatively assigned as shown on the basis of the transition-state model.

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[11] The optical rotation of (*S*)-methyl-2,2-diphenylcyclopropane was reported to be $[\alpha]^{22}_D$ = +127 ± 2° ($CHCl_3$, *c* 0.34). (a) Walborsky, H. M.; Pitt, C. G. *J. Am. Chem. Soc.* **1962**, *84*, 4831. (b) Impastato, F. J.; Walborsky, H. M. *J. Am. Chem. Soc.* **1962**, *84*, 4838.