Selective α-Stannylated Addition of Di-*n*-butyliodotin Hydride Ate Complex to Simple Aliphatic Alkynes

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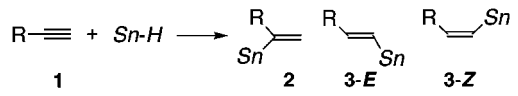
Received October 16, 2000

Hydrostannation of alkynes with tri-*n*-butyltin hydride is one of the simplest and direct routes to vinylstannanes, which have great versatility as building blocks in synthesis.[1] However, in the case of terminal alkynes **1**, it is possible to form three types of vinylstannanes, **2** (α-adduct) and **3**-***E*** and **3**-***Z*** (*β*-adduct) (Scheme 1). For the application to the synthesis of complex molecules via subsequent cross coupling with the vinylstannanes,[2] the control of regioselectivity in the hydrostannation is an extraordinarily important issue.

Three types of activators in the hydrostannation with tri-*n*-butyltin hydride have been developed as follows: (1) radical initiators such as azobisisobutyronitrile,[3a] Et_3B,[3b] and ultrasound,[3c] furnishing a mixture of *β*-adducts, **3**-***E*** and **3**-***Z***, (2) Lewis acid catalysts[4] to give **3**-***Z***, and (3) transition metal catalysts such as Pd, Rh, and Mo complexes[5] to predominantly furnish **3**-***E***. Namely, a selective formation of α-adduct (α-stannylation) is very difficult in these typical methods. Recently, regio- and stereoselective α-stannylation has been achieved for alkynes bearing carbonyl,[5d] oxygen-containing,[5e] and aromatic substituents.[5f] The α-stannylation of simple aliphatic alkynes, however, is particularly difficult because of having no such anchor substituents. Scheme 2 shows the general hydrostannations of aliphatic alkynes, in which α-adduct can be obtained only as a minor adduct in the Pd-catalyzed reaction (eq 3). From these backgrounds, no effort has been reported so far for the selective α-stannylation of aliphatic alkynes and it is apparent that a novel hydrostannation reagent is required for the formation of α-adduct.

Recently, we have reported a pentacoordinated tin hydride ate complex. $Li^+[n\text{-}Bu_2SnI_2H]^-$, which is formed in situ from *n*-Bu_2-SnIH and LiI and induces selective 1,4-hydrostannation of enals where unusual superior attack of Sn−I bond to Sn−H bond is assumed to determine the regioselectivity.[6] In the context of our studies on tin ate complexes, we have found a novel tin hydride complex, $[MgBr]^+[n\text{-}Bu_2SnBrIH]^-$ (**A**), to give α-adducts **2** selectively in the hydrostannation of simple aliphatic alkynes.

Scheme 1



Scheme 2

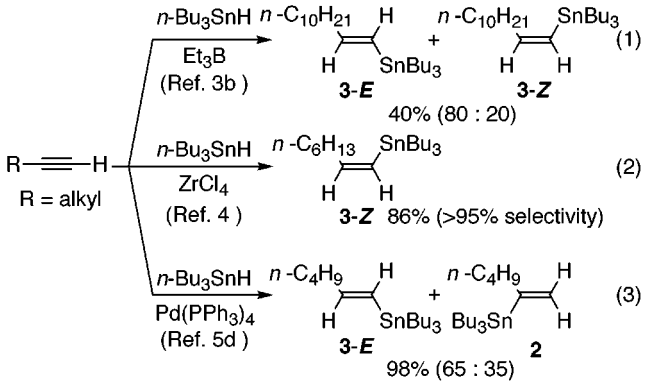
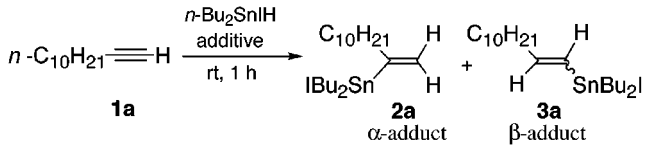


Table 1. Additive Effect in Hydrostannation of 1-Dodecyne[a]



			yield/%		
entry	additive	solvent	**2a**	**3a-*E***	**3a-*Z***
1[b]	none	THF	0	0	0
2	none	THF	0	27	26
3	LiI	THF	trace	trace	trace
4[c]	$Mg(ClO_4)_2$	THF	0	43	7
5	$MgCl_2$	THF	0	24	21
6	MgI_2	THF	8	9	0
7	$MgBr_2{\cdot}OEt_2$	THF	44	16	0
8[d]	$MgBr_2{\cdot}OEt_2$	THF	33	23	0
9[e]	$MgBr_2{\cdot}OEt_2$	THF	53	7	0
10	$MgBr_2{\cdot}OEt_2$	DMSO	0	6	0
11	$MgBr_2{\cdot}OEt_2$	MeOH	0	24	0
12	$MgBr_2{\cdot}OEt_2$	toluene	27	37	0
13	$MgBr_2{\cdot}OEt_2$	Et_2O	26	0	0
14	$MgBr_2{\cdot}OEt_2$	EtOAc	59	0	0
15[e]	$MgBr_2{\cdot}OEt_2$	EtOAc	86	6	0

[a] 1-Dodecyne/*n*-Bu_2SnIH/additive = 1/1/1 mmol, solvent 1 mL. [b] *n*-Bu_3SnH was used instead of *n*-Bu_2SnIH. [c] 24 h. [d] *n*-Bu_2SnClH was used instead of *n*-Bu_2SnIH. [e] 1-Dodecyne/*n*-Bu_2SnIH/$MgBr_2{\cdot}OEt_2$ = 0.5/1/2 mmol.

Table 1 shows the investigations on the hydrostannation of 1-*n*-dodecyne (**1a**) with various tin hydride systems. In contrast to no activity of *n*-Bu_3SnH (entry 1), the sole use of iodotin hydride, *n*-Bu_2SnIH, gave a mixture of **3a**-***E*** and **3a**-***Z*** (entry 2). The reported tin hydride ate complex, $Li^+[n\text{-}Bu_2SnI_2H]^-$, was ineffective (entry 3). We then investigated the effect of magnesium salts instead of LiI as an additive to *n*-Bu_2SnIH. Among the magnesium salts examined, $MgBr_2{\cdot}OEt_2$ showed the highest effect where α-di-*n*-butyliodostannylated alkene **2a** was predominantly obtained as a Mg salt-free form in 44% yield along with 16% of **3a**-***E*** (entry 7). The use of *n*-Bu_2SnClH instead of *n*-Bu_2SnIH gave a comparable formation of **2a** (entry 8). These results

(1) Recent reviews: (a) Smith, N. D.; Mancuso, J.; Lautens, M. *Chem. Rev.* **2000**, *100*, 3257−3282. (b) Davis. A. G. *Organotin Chemistry*; VCH: New York, 1997; pp 37−42. (c) Pereyre, M.; Quintard, J. P.; Rahm, A. *Tin in Organic Synthesis*; Butterworth: London, 1987. (d) Omae, I. *Organotin Chemistry*; Elsevier: Amsterdam, 1989; pp 167−188.

(2) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic: New York, 1985. Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508−524.

(3) With radical initiators. (a) Use of AIBN: Leusink, A. J.; Budding, H. A. *J. Organomet. Chem.* **1968**, *11*, 533−539. (b) Use of Et_3B: Nozaki, K.; Oshima, K.; Utimoto, K. *J. Am. Chem. Soc.* **1987**, *109*, 2547−2549. Nozaki, K.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3465−3467. (c) Use of ultrasound: Nakamura, E.; Imanishi, Y.; Machii, D. *J. Org. Chem.* **1994**, *59*, 8178. Nakamura, E.; Machii, D.; Inubishi, T. *J. Am. Chem. Soc.* **1989**, *111*, 6849−6850.

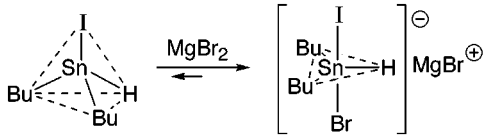
(4) With Lewis acid catalysts. (a) Asao, N.; Liu, J.-X.; Sudoh, T.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1995**, 2405−2406. (b) Asao, N.; Liu, J.-X.; Sudoh, T.; Yamamoto, Y. *J. Org. Chem.* **1996**, *61*, 4568−4571. (c) Gevorgyan, V.; Liu, J.-X.; Yamamoto, Y. *Chem. Commun.* **1998**, 37−38.

(5) With Mo, Pd, or catalysts. (a) Ichinose, Y.; Oda, H.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3468−3470. (b) Zhang, H. X.; Guibe, F.; Balavoine, G. *Tetrahedron Lett.* **1988**, *29*, 619−622. (c) Miyake, H.; Yamamura, K. *Chem. Lett.* **1989**, 981−984. (d) Zhang, H. X.; Guibe, F.; Balavoine, G. *J. Org. Chem.* **1990**, *55*, 1857−1867. (e) Kazmaier, U.; Schauss, D.; Pohlman, M. *Org. Lett.* **1999**, 1017−1019. (f) Kikukawa, K.; Umekawa, H.; Wada, F.; Matsuda, T. *Chem. Lett.* **1988**, 881−884. (g) Mitchell, T. N.; Moschref, S.-N. *Synlett* **1999**, 1259−1260.

(6) Suwa, T.; Shibata, I.; Baba, A. *Organometallics* **1999**, *18*, 3965−3967.

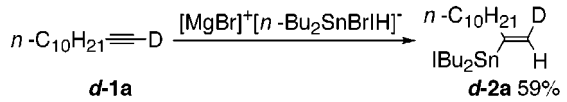
10.1021/ja0056973 CCC: $20.00
Published on Web 04/07/2001

Scheme 3



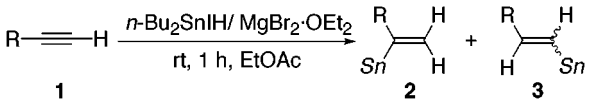
Tin Hydride Ate Complex (**A**)

Scheme 4



***d*-1a** ***d*-2a** 59%

Table 2. Hydrostannation with Tin Hydride Ate Complex[a]



1 **2** **3**

			yield/%[b]		
entry	R		**2**	**3-*E***	**3-*Z***
1	*n*-$C_{10}H_{21}$	a	86	6	0
2[c]	*n*-C_6H_{13}	b	77	tr.	0
3[c]	*n*-Bu	c	67	tr.	0
4	$PhCH_2$	d	60	0	0
5[c]	*i*-Bu	e	61	tr.	0
6	*n*-$C_8H_{17}CH$(*n*-Pr)	f	16	0	0
7	*n*-Bu	g	0	0	0

[a] Alkyne/*n*-$Bu_2SnIH/MgBr_2{\cdot}OEt_2$ = 0.5/1/2 mmol, EtOAc 1 mL. [b] The yield of products was based on **1**. [c] 3 h.

strongly indicate the importance of the formation of ate complex as aforementioned. The use of 2 equiv of $MgBr_2{\cdot}OEt_2$ and 0.5 equiv of **1a** somewhat improved the yield to 53% (entry 9). Moreover, the employment of EtOAc as a solvent sharply increased the yield of **2a** up to 86% (entry 15). The use of other solvents such as dimethyl sulfoxide, methanol, toluene, and ether resulted in poor yields (entries 10−13). Consequently, the conditions noted in entry 15 are optimized ones.

The structure of the ate complex was determined by ^{119}Sn NMR in a similar manner already reported for the tin hydride ate complex, $Li^+[n\text{-}Bu_2SnI_2H]^-$. The peak corresponding to *n*-Bu_2-SnIH (−70.7 ppm) gradually shifted to −146.7 ppm until an equimoler amount of $MgBr_2{\cdot}OEt_2$ was added, and further addition still caused no more shift. Similar gradual increases in the coupling constant, $^1J(^{119}Sn\text{-}^1H)$ and $^1J(^{119}Sn\text{-}^{13}C)$, were observed, from 2022 to 2304 Hz and from 382 to 500 Hz, respectively. These phenomena strongly indicate the formation of the TBP type of 1:1 complex **A** in equilibrium between $MgBr_2{\cdot}OEt_2$ and *n*-Bu_2-SnIH as shown in Scheme 3.[7] Neither $MgCl_2$ nor MgI_2 was confirmed to form ate complexes because of observing no change of the coupling constants and chemical shift of *n*-Bu_2SnIH. On the other hand, *n*-Bu_2SnClH and $MgBr_2$ facilely formed an ate complex, which could achieve the α-stannylation in a moderate yield (Table 1, entry 8). These results again support the idea that an ate complex directly promotes the α-stannylation.[8]

To determine the reaction mechanism, the hydrostannation of the 1-deuterio-1-dodecyne (***d*-1a**) and the addition of a radical inhibitor were carried out. The selective formation of the *E*-isomer strongly suggests the cis addition of the ate tin hydride (Scheme 4). Moreover, the complete depression by a radical inhibitor, galvinoxyl, indicated that the radical mode step is included in the formation of vinylstannanes.

These results and the characteristic α-stannylation are unexplainable by any reported mechanism, and an alternate reaction manner would be expected for this α-stannylation, because, for example, the usual radical addition has given a mixture of *E*- and *Z*-isomer.[9]

Table 2 shows the results of hydrostannation to some aliphatic terminal alkynes by using the tin hydride ate complex **A**. Besides 1-*n*-dodecyne (**1a**) (entry 1), alkynes bearing primary alkyl substituents such as *n*-hexyl, *n*-butyl, and benzyl were also applicable to give α-adducts **2b**−**d** without any *β*-adducts (entries 2−4). Although isobutylethyne (**1e**) was still reactive to give **2e** in 61% yield (entry 5), secondary and tertiary substituents strongly disturbed the α-stannylation because of a large steric hindrance with the stannyl moiety (entries 6 and 7).

In conclusion, we have accomplished the first α-stannylation of simple aliphatic alkynes using a tin hydride ate complex, $[MgBr]^+[n\text{-}Bu_2SnBrIH]^-$.

Acknowledgment. This work was financially supported by JSPS Research Fellowships for Young Scientists and the Grant-in-aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, Japan.

Supporting Information Available: Experimental procedures and IR, ^{1}H, ^{13}C NMR, and HRMS data for **2a**−**f**, and ^{1}H, ^{13}C, and ^{119}Sn NMR data for the tin hydride ate complex **A** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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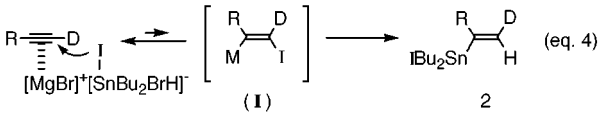
(7) For example: (a) Davis. A. G. *Organotin Chemistry*; VCH: New York, 1997; pp 18−24. (b) Harrison, P. G. *Chemistry of Tin*; Blackie: London, 1989; pp 71−89. (c) Holecek, J.; Nádvorník, M.; Handlír, K.; Lycka, A. *J. Organomet. Chem.* **1983**, *241*, 177−184. (d) Nádvorník, M.; Holecek, J.; Handlír, K.; Lycka, A. *J. Organomet. Chem.* **1984**, *275*, 43−51.

(8) In THF solvent, although until the addition of 0.5 equiv of $MgBr_2{\cdot}OEt_2$ to *n*-Bu_2SnIH the values of chemical shift and coupling constants were increased, further addition did not change the values. This fact indicates that EtOAc is superior to THF for the clear formation of pentacoordinated tin complex, which is consistent with the result of the α-selectivity in hydrostannation (Table 1, entries 2, 7, and 14).

(9) As a tentative mechanism: The initial iodide attack at the less hindered site of **1** activated by magnesium bromide cation affords 2-iodovinylmetal **I**. The resulting vinyl iodide is reduced immediately in a radical manner to give α-adduct **2** stereospecifically (eq 4). Unfortunately, it was unsuccessful in confirming the vinyl iodide. Selective nucleophilic attack at a less hindered site by a larger and stronger group like iodine would be more appropriate than chlorine. In fact, chlorotin hydride complex resulted in poor selectivity of **2a** (Table 1, entry 8). The acidity of $[MgBr]^+$ may play an important role in the activation of alkynes because hydrostannation with a similar ate complex, $Li^+[n\text{-}Bu_2SnI_2H]^-$, did not proceed.



As an alternative mechanism, a single electron transfer from a tin ate complex to an alkyne is of course not excluded at this stage.