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Homolytic Carbostannylation of Alkenes and Alkynes with Tributylstannyl Enolates

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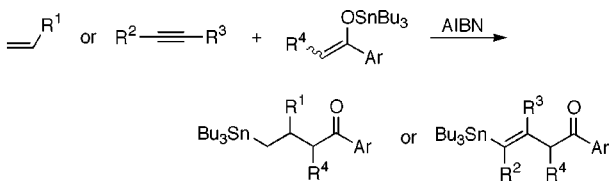
ABSTRACT

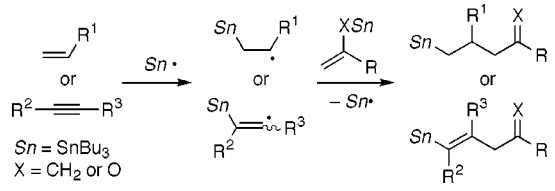


In the presence of AIBN, tributylstannyl enolates derived from aromatic ketones reacted with electron-deficient alkenes and a variety of alkynes to give the corresponding carbostannylated adducts. The reactions with methyl acrylate gave α-tributylstannylmethyl-γ-ketoesters, unlike the known Michael-type reaction of stannyl enolates forming δ-ketoesters. The carbostannylation of alkynes proceeded in an anti addition mode to afford β,γ-unsaturated ketones. The reactivity of stannyl enolates as radical transfer agents could be utilized for radical cyclization of 1,6-enynes.

Carbometalation of alkenes and alkynes with metal enolates has been intensively studied in recent years because it provides a straightforward and stereoselective method for carbon chain elongation and functionalization of carbonyl compounds.[1−3] However, the intermolecular version has remained comparatively unexplored. The known approaches to this challenging subject include the use of metalated unsaturated bonds or zinc enolates of hydrazones and esters.[2,3] The carbometalation of common (unmetalated) alkenes and alkynes with ketone enolates has not yet been established.

Previously, we have reported homolytic allylstannylation of alkenes and alkynes via a radical chain process,[4] in which allyltributylstannanes work as radical transfer agents to perform allylation of carbon radical intermediates accompanied by generation of a tributylstannyl radical (Scheme 1, X = CH_2).[5] Although stannyl enolates, oxygen analogues

Scheme 1



of allylstannanes, also have been proposed to undergo the S_H2' reaction with carbon radicals,[6] no reliable evidence supporting the evolution of stannyl radicals has been reported yet, and the synthetic utility of stannyl enolates as radical

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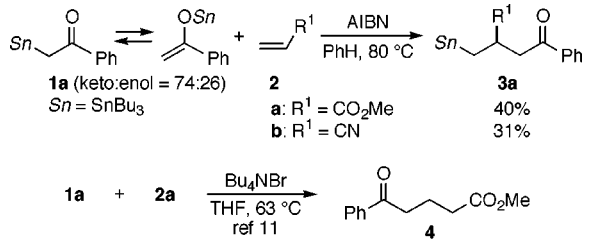
transfer agents is rather limited.[7] Therefore, our interest was focused on homolytic carbostannylation utilizing the reactivity of stannyl enolates. We describe herein the AIBN-initiated carbostannylation of alkenes and alkynes with ketone stannyl enolates (Scheme 1, X = O) and its application to the cyclization of 1,6-enynes.

Trialkylstannyl enolates are in metalotropic equilibrium between O- and C-stannylated forms (enol and keto forms).[8] The keto form would not be available for the homolytic substitution.[6] Our study commenced with cyclohexanone tributylstannyl enolate,[9] which exists only as the enol form.[8] Contrary to our expectation, the AIBN-initiated reaction of methyl acrylate (**2a**), a good stannyl radical acceptor, with the enolate resulted in no desired adduct. As the result of experiments with several stannyl enolates, aromatic ketone enolates were found to be generally reactive toward carbometalation of electron-deficient alkenes.

Acetophenone tributylstannyl enolate (**1a**) forms a 74:26 tautomeric mixture of keto and enol forms in C_6D_6 at room temperature.[10] In the presence of AIBN (0.2 equiv), treatment of **2a** with **1a** (4 equiv) in benzene at 80 °C gave the carbostannylated product **3aa** in 40% yield (Scheme 2). The

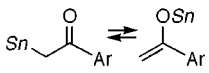
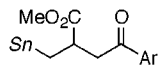
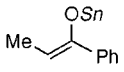
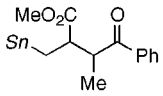
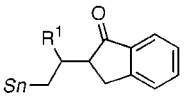
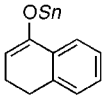
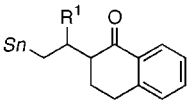
Scheme 2



reactivity of acrylonitrile (**2b**) to **1a** was similar to that of **2a**. Without AIBN, the carbometalation was completely suppressed. Baba et al. have reported that the bromide anion promoted reaction of **2a** with **1a** affords the Michael adduct **4**.[11] This observation is consistent with the well-established reactivity of stannyl enolates as carbon nucleophiles.[12] In contrast, the present reaction did not form **4** at all. Thus, the radical-initiated system dramatically changed the reaction course of **1a**.

Introduction of a fluorine atom at the para position of **1a** (**1b**, keto:enol = 74:26) did not affect the reactivity toward carbostannylation (entry 1 in Table 1). Interestingly, *p*-

Table 1. Carbostannylation of Alkenes **2** with Stannyl Enolates **1**[a]

entry	stannyl enolate[b]	alkene	time / h	product, yield / % (dr)[c]
				
1	**1b**: Ar = C_6H_4-*p*-F	**2 a**	2	**3ba**, 39
2	**1c**: Ar = C_6H_4-*p*-OMe	**2 a**	3	No reaction.
				
3	**1 d**	**2 a**	2	**3da**, 33 (66:34)
				
4	**1 e**	**2 a**	3	**3ea**, 48 (64:36)
5		**2 b**	5	**3eb**, 62 (52:48)
				
6	**1 f**	**2 a**	3	**3fa**, 72 (65:35)
7		**2 b**	5	**3fb**, 62 (51:49)
8		**2 c**[d]	3	**3fc**, 76 (66:34)

[a] All reactions were performed with **1** (2.00 mmol), **2** (0.50 mmol), and AIBN (0.10 mmol) in benzene (2.5 mL) at 80 °C. [b] Sn = $SnBu_3$. The ratios of keto to enol in C_6D_6 at room temperature are as follows: **1b**, 74:26; **1c**, 99:<1; **1d**−**f**, <1:99. The value "<1" means that the minor tautomer was not detected by 270 MHz ^{1}H NMR. [c] The relative configuration was not determined. [d] **2c**: cyclohexyl acrylate (R^1 = CO_2-*c*-Hex).

methoxy derivative **1c** takes only the keto form. As predicted from the structure, **1c** was insensitive to **2a** (entry 2). Stannyl enolate **1d** derived from propiophenone consists of only the enol form feasible for the S_H2' reaction; however, the use of **1d** was not effective in improving the efficiency of carbostannylation (entry 3). On the other hand, indanone and tetralone stannyl enolates, **1e** and **1f**, showed higher reactivity to electron-deficient alkenes, although they also are substituted at the reaction site (entries 4−8). Unfortunately, the carbostannylation of styrene and 1-octene did not proceed even with **1f**.

As shown in Table 2, the carbostannylation of alkynes with stannyl enolates **1a** and **1f** proceeded in an anti addition mode to afford β,γ-unsaturated ketones.[13] A similar trend in stereoselectivity was observed in our previous study on the radical-based allylstannylation.[4] The stereochemical

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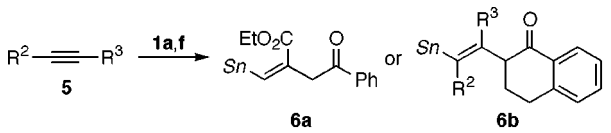
(12) Davies, A. G. *Organotin Chemistry*; VCH: Weinheim, 1997.

Table 2. Carbostannylation of Alkynes **5** with Stannyl Enolates **1**[a]



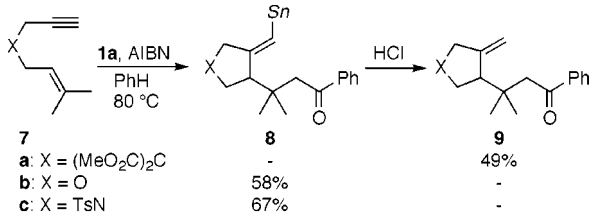
entry	enolate	alkyne	R^2	R^3	time, (h)	product, yield (%)
1	**1a**	**5a**	H	CO_2Et	5	**6a**, 26
2	**1f**	**5a**	H	CO_2Et	4	**6ba**,[b] 66
3	**1f**	**5b**	H	Ph	4	**6bb**, 70
4	**1f**	**5c**	H	C_6H_4-*p*-Me	5	**6bc**, 69
5	**1f**	**5d**	H	cyclohexen-1-yl	5	**6bd**, 50
6	**1f**	**5e**	H	$C_{10}H_{21}$	5	**6be**, 15
7	**1f**	**5f**	H	SPh	4	**6bf**, 16
8	**1f**	**5g**	CO_2Me	CO_2Me	4	**6bg**, 41

[a] See footnote a in Table 1. Except for entry 2, only anti adducts were obtained. [b] *Z*:*E* = 82:18. See ref 13.

outcome is probably a result of the approach of the stannyl enolates to vinyl radical intermediates from the opposite side of the stannyl group to avoid its steric hindrance (Scheme 1).[14] Stannyl enolate **1f** exhibited higher reactivity than **1a** as in the reaction with alkenes (entries 1 and 2). Not only electron-deficient alkynes but also other conjugated alkynes were available for the carbostannylation with **1f** in moderate to good yields (entries 3−5). In addition, electron-rich alkynes such as 1-dodecyne and ethynyl phenyl sulfide could be carbostannylated, although the yields were rather low (entries 6 and 7).

The reactivity of stannyl enolates as radical transfer agents is applicable to radical cyclization of 1,6-enynes (Scheme 3).[15] The AIBN-initiated reaction of **7a** with **1a** gave a

Scheme 3



mixture of the cyclized product **8a** and unidentified impurities. After protonolysis of the mixture with HCl−CH_3CN, methylenecyclopentane **9a** was isolated in 49% yield. Allyl propargyl ether **7b** and amine **7c** were smoothly converted to the stannylated heterocycles **8b** and **8c** in reasonable isolated yields. Unlike the above results, **1f** was not effective in the cyclization of **7**.

In conclusion, we have developed a novel type of carbometalation reaction via a radical chain process. To the best of our knowledge, the present reaction is the first example of intermolecular carbometalation of unmetalated C−C multiple bonds with ketone metal enolates. The formation of carbostannylated products **3**, **6**, and **8** provides reliable evidence that trialkylstannyl enolates actually undergo the S_H2' reaction to generate a trialkylstannyl radical. In addition, we have disclosed the synthetic utility of stannyl enolates as radical transfer agents.

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Supporting Information Available: Experimental details and spectroscopy data of stannyl enolates and the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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