

# Mild Procedure for the Catalytic Bis(stannylation) of Alkynes with Hexaalkylditins

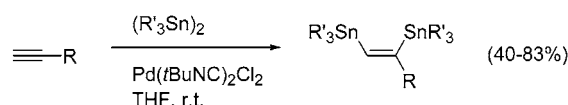
John Mancuso and Mark Lautens\*

Davenport Chemical Laboratories, Department of Chemistry, University of Toronto,  
80 St. George Street, Toronto, Ontario, M5S 3H6, Canada

mlautens@chem.utoronto.ca

Received February 18, 2003

## ABSTRACT



Bis(stannylation) of terminal alkynes is achieved through the use of a palladium–isonitrile catalyst complex using a hexaalkylditin as a stannyl group transfer reagent in an atom-efficient and mild catalytic process. Functional group tolerance is good, allowing the presence of amine, carbamate, silyl, ester, and ether moieties. An activated internal alkyne also underwent bis(stannylation) in moderate yield, allowing access to symmetrical bis(alkenyl)stannanes.

The selective reactions of bis(metalated)alkenyl species with various electrophiles allows for the synthesis of complex products in a sequential fashion (“one-pot process”).<sup>1</sup> These bis(anion) equivalents are used often for the construction of multiple carbon–carbon or carbon–heteroatom bonds. Indeed, they may also act as precursors to more reactive nucleophilic species through the action of a transition metal catalyst and serve as organic group transfer reagents. Often, the metallic groups in a nonsymmetric bis(metalated)species will exhibit significant changes in reactivity as a result of their proximity to other functional groups, allowing discrimination and selective modification.

As part of a long-term project investigating various methods for the preparation of functionalized organostannanes, we recently focused on transition-metal-catalyzed hydrostannylation<sup>2</sup> and silylstannylation<sup>3</sup> of substrates bearing acetylenic groups.

During the course of our silylstannylation study, we discovered that an isonitrile-ligated palladium dichloride catalyst

could be used to bis(stannylate) alkynes with hexabutylditin. We appended this as a footnote in our communication and Kazmaier has recently shown that a tungsten-based isonitrile complex can achieve the same transformation using tri-*n*-butyltin hydride.<sup>4</sup>

Palladium-catalyzed bis(stannylation) of alkynes has been demonstrated previously,<sup>5</sup> whereby hexamethylditin was used in conjunction with Pd(PPh<sub>3</sub>)<sub>4</sub> as a catalyst. However, there are only a few examples using hexabutylditin as a stannylating reagent in the literature. Mitchell reported incomplete reaction conversions when using (Bu<sub>3</sub>Sn)<sub>2</sub> and difficulty with product purification, resulting in low yields (~30%). Distillation led to partial decomposition of the products, and protodestannylation occurred with silica gel column chromatography.<sup>5a</sup>

Quintard reported one successful example using hexabutylditin in the bis(stannylation) of 3,3-diethoxypropyne whereby the bis(stannylated) product was obtained in 52%

(1) For a review on element–element addition to alkynes, see: Beletskaya, I.; Moberg, C. *Chem. Rev.* **1999**, *99*, 3435.

(2) (a) For a review, see: Smith, N. D.; Mancuso, J.; Lautens, M. *Chem. Rev.* **2000**, *100*, 3257. (b) Lautens, M.; Mancuso, J. *Org. Lett.* **2000**, *2*, 671. (c) Lautens, M.; Smith, N. D.; Ostrovsky, D. *J. Org. Chem.* **1997**, *62*, 8970.

(3) Lautens, M.; Mancuso, J. *Synlett* **2002**, 394.

(4) Braune, S.; Kazmaier, U. *Angew. Chem., Int. Ed.* **2003**, *42*, 306.

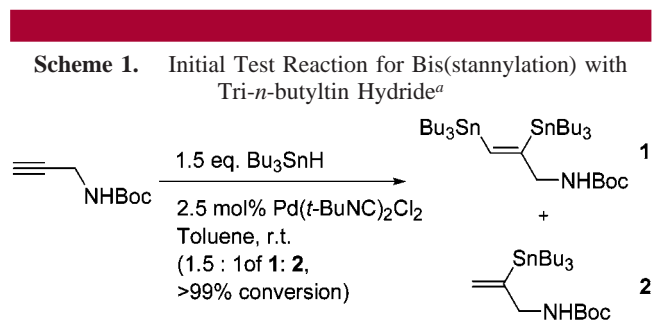
(5) (a) Mitchell, T. N.; Amamria, A.; Killing, H.; Rutchow, D. *J. Organomet. Chem.* **1986**, *304*, 257. (b) Piers, E.; Skerlj, R. T. *J. Chem. Soc., Chem. Commun.* **1986**, 626. (c) Piers, E.; Skerlj, R. T. *Can. J. Chem.* **1994**, *72*, 2468. (d) Mabon, R.; Richcoeur, A. M. E.; Sweeney, J. B. *J. Org. Chem.* **1999**, *64*, 328. (e) Casson, S.; Kocienski, P.; Reid, G.; Smith, N.; Street, J. M.; Webster, M. *Synthesis* **1994**, 1301. (f) Beaudet, I.; Parrain, J.-L.; Quintard, J.-P. *Tetrahedron Lett.* **1991**, *32*, 6333.

yield.<sup>5f</sup> Bis(stannylation) of internal alkynes is generally a difficult process and can be facilitated by conjugation to an electron-withdrawing group, as Sweeny demonstrated in the bis(stannylation) of two nonterminal alkynoate substrates with  $(\text{Bu}_3\text{Sn})_2$  in high yield.<sup>5d</sup>

In this communication, we wish to disclose a more in-depth study on our palladium-based bis(stannylation) system as well as demonstrate the good functional group tolerance of the method.

Our foray into bis(stannylation) began through screening of various palladium catalysts for more selective and efficient alkyne hydrostannylation methodologies to favor internal ( $\alpha$ -) or terminal ( $\beta$ -) vinylstannanes. Studies by Kazmaier had appeared describing a Mo-based *tert*-butylisocyanide catalyst that gave highly regioselective hydrostannylation of terminal alkynes with tri-*n*-butyltin hydride to favor the  $\alpha$ -vinyl stannane.<sup>6</sup> We had also noted Guibé's hydrostannylation study<sup>7</sup> with Mo- and Pd-based catalysts and wanted to determine if isocyanide ligands could be beneficial for a palladium-based catalyst as well.

The complex  $\text{Pd}(t\text{-BuNC})_2\text{Cl}_2$  was readily synthesized<sup>8</sup> and tested with a simple terminal alkyne such as *N*-Boc propargylamine with slow addition of 1.3 equiv of tin hydride. Unexpectedly, we obtained a 1.5:1 ratio of bis(stannylated)-alkene<sup>9</sup> (**1**) to  $\alpha$ -vinylstannane (**2**) as determined from an NMR study of the crude reaction mixture (Scheme 1).



<sup>a</sup>Ratio determined by  $^1\text{H}$  NMR.

Repeating the reaction with a full 2 equiv of tri-*n*-butyltin hydride led to the formation of the bis(stannyl)alkene as the sole product in 67% isolated yield. Interestingly, the addition of 0.2 equiv of *t*-BuNC suppressed bis(stannylation) of the alkyne but did allow for dimerization of the tin hydride.

Replacement of tri-*n*-butyltin hydride with hexabutyliditin was equally successful in promoting the bis(stannylation).

A series of alkynes was subjected to  $(\text{R}_3\text{Sn})_2$  to determine the scope of this reaction (Table 1). No  $\alpha$ - or  $\beta$ -vinyl

**Table 1.** Bis(stannylation) of Terminal Alkynes Using  $\text{Pd}(t\text{-BuNC})_2\text{Cl}_2$  as a Catalyst

entry <sup>a</sup>	alkyne	$(\text{R}'_3\text{Sn})_2$	product	Yield (%)
1		$(\text{Bu}_3\text{Sn})_2$	<b>1</b>	83
2		$(\text{Bu}_3\text{Sn})_2$	<b>3</b>	79
3		$(\text{Bu}_3\text{Sn})_2$	<b>4</b>	72
4		$(\text{Bu}_3\text{Sn})_2$	<b>5</b>	76
5		$(\text{Bu}_3\text{Sn})_2$	<b>6</b>	67
6		$(\text{Bu}_3\text{Sn})_2$	<b>7</b>	75
7		$(\text{Me}_3\text{Sn})_2$	<b>8</b>	70
8		$(\text{Bu}_3\text{Sn})_2$	<b>9</b>	40 <sup>b</sup>
9		$(\text{Bu}_3\text{Sn})_2$	<b>10</b>	57

<sup>a</sup> Conditions: 1.1 equiv of ditin, 1 mmol of alkyne, 2.5 mol %  $\text{Pd}(t\text{-BuNC})_2\text{Cl}_2$ , 0.2 M THF,  $\text{N}_2$  atmosphere, rt, 12–16 h. All products isolated by column chromatography. <sup>b</sup> Stirred at rt for 48 h.

stannane products could be observed from  $^1\text{H}$  NMR analysis of the crude reaction mixture. Yields were generally good and required the use of deactivated silica gel or basic alumina for column chromatography to prevent extensive proto-destannylation.<sup>10</sup>

Various functional groups were tolerated, including carbamates (entry 1), amines (entry 2), sulfonamides (entry 3), ethers (entries 4–5, 8), esters (entries 6–7), and alcohols (entry 9). No competitive alkene bis(stannylation) or carbocyclization of the cinnamyl ether (entry 5) was observed. Hexamethylditin (entry 7) could also be used as the stannylating agent and showed no difference in activity versus hexabutyliditin. A silyl homopropargylic ether (entry 8) showed lower reactivity versus propargylic substrates, giving a modest yield of the desired product. A sterically bulky tertiary alcohol (entry 9) surprisingly underwent smooth conversion, indicating that the catalyst may be fairly tolerant of substrate steric properties.

(10) If the silica is not properly deactivated, small amounts of monostannylated products are generated and are difficult to separate from the bis(stannylated) product.

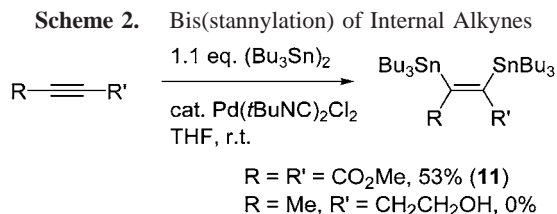
(6) (a) Kazmaier, U.; Schauss, D.; Pohlman, M. *Org. Lett.* **1999**, *1* (7), 1017. (b) Kazmaier, U.; Pohlman, M.; Schauss, D. *Eur. J. Org. Chem.* **2000**, 2761. (c) Kazmaier, U.; Schauss, D.; Raddat, S.; Pohlman, M. *Chem. Eur. J.* **2001**, *7*, 456. (d) Braune, S.; Kazmaier, U. *J. Organomet. Chem.* **2002**, *641*, 26.

(7) Zhang, H. X.; Guibé, F.; Balavoine, G. *J. Org. Chem.* **1990**, *55*, 1857.

(8) (a) Otsuka, S.; Tatsuno, Y.; Ataka, K. *J. Am. Chem. Soc.* **1971**, *93*, 6705. (b) Otsuka, S.; Nakamura, A.; Tatsuno, Y. *J. Am. Chem. Soc.* **1969**, *91*, 6994.

(9)  $^{119}\text{Sn}$  NMR analysis indicated formation of only the (*Z*)-bis(stannyl)-alkene.

Bis(stannylation) of a disubstituted alkyne was attempted; however, this was found to be feasible only with an activated alkyne such as dimethylacetylene dicarboxylate (Scheme 2). Reaction with 3-pentyn-1-ol was unsuccessful.



The terminal stannane moiety is known to be more reactive than the internal one in unsymmetrical bis(stannyl)alkenes.<sup>11</sup> This difference could be exploited to generate bifunctionalized alkenes, and various electrophilic reactions on bis(stannylated)alkenes were demonstrated in an extensive study by Mitchell.<sup>12</sup>

Isonitrile-based palladium complexes have been previously reported for the bis(silylation)<sup>13</sup> and silylstannylation<sup>14</sup> of alkenes and alkynes. However, in those cases, the complex was prepared in situ using palladium acetate and an excess of the isonitrile ligand. In our case, the use of excess isonitrile was detrimental to the reaction, making the use of preformed catalyst essential.

A proposed catalytic cycle<sup>15</sup> is shown in (Scheme 3). To initiate the cycle, it is possible that the Pd(II) catalyst (**I**) is transformed to the required (Bu<sub>3</sub>Sn)<sub>2</sub>Pd(II) species (**II**) through a  $\sigma$ -bond metathesis (transmetallative) process with 2 equiv of ditin to eliminate an equivalent amount of tributyltin chloride.<sup>16</sup> The active Pd(II) catalyst can stannylpalladate the alkyne, with regioselective preference for the palladium to add internally to give **III**.<sup>17</sup> Reductive elimination then occurs to generate the bis(stannyl)alkene **IV** and Pd(0).<sup>18</sup>

(11) Proto- and iodo-destannylation occurs preferentially at the terminal stannyl group; see refs 5a and 5f, respectively.

(12) Niestroj, M.; Neumann, W. P.; Mitchell, T. N. *J. Organomet. Chem.* **1996**, *519*, 45.

(13) (a) Ito, Y.; Sugimoto, M.; Murakami, M. *J. Org. Chem.* **1991**, *56*, 1948. (b) Murakami, M.; Andersson, P. G.; Sugimoto, M.; Ito, Y. *J. Am. Chem. Soc.* **1991**, *113*, 3987. (c) Murakami, M.; Oike, H.; Sugawara, M.; Sugimoto, M.; Ito, Y. *Tetrahedron* **1993**, *49*, 3933.

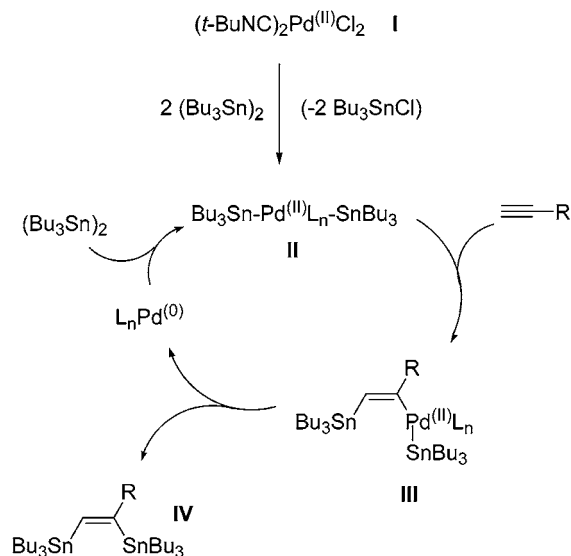
(14) Murakami, M.; Amii, H.; Takizawa, N.; Ito, Y. *Organometallics* **1993**, *12*, 4223.

(15) Our proposed catalytic cycle is similar to that of Piers and Skerlj; see ref 5c.

(16) Alternatively, passage through a palladium(IV) intermediate via an oxidative process cannot be ruled out.

(17) We have observed that terminal 1-ene-6-yne will, in addition to generating the expected bis(stannylated) product, cyclize in a 5-*exo-trig* fashion to yield minor amounts (<30%) of bis(stannylated) *exo*-methylene-cyclopentane products. This provides further evidence concerning the regioselectivity of the stannylpalladative step.

**Scheme 3.** Proposed Catalytic Cycle for Bis(stannylation) with Hexaalkylditins



In the case of tri-*n*-butyltin hydride, the reduction of Pd(II) salts to Pd(0) with elimination of H<sub>2</sub> and bis(stannane) is a known process.<sup>5</sup> The use of less than the full 2 equiv of tin hydride allows for isolation of the  $\alpha$ -vinyl stannane as a side-product, which indicates that the hydrostannylation process is competing with the dimerization of Bu<sub>3</sub>SnH.

In summary, we have described a system that generates improved yields of bis(stannylated) products from terminal and internal alkynes. The protocol requires neither heating nor the addition of a radical inhibitor. The palladium–isonitrile catalyst complex is easily prepared from commercially available materials and is an air-stable solid. Hexabutyltin, which is easier to handle than tri-*n*-butyltin hydride, can be used in only a slight excess. As stannylated synthons are increasingly used in complex syntheses, we anticipate that easier access to this particular class of compound will be of interest.

**Acknowledgment.** We thank NSERC (Canada) and the University of Toronto for financial support of this work. J.M. thanks the Walter C. Sumner Foundation and the University of Toronto for financial support in the form of doctoral fellowships.

**Supporting Information Available:** Characterization data, including proton, carbon, and tin NMR spectral data for all stannylated products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL034284E

(18) Catalyst system involving Pd(OAc)<sub>2</sub> and 2 equiv of (*t*-Bu)<sub>3</sub>P, which generates an underligated, electron-rich palladium complex, failed for this reaction, giving only trace amounts of product.