

## One-Pot, Yet Two-Step, Hydrotitanation of 1-Silyl- or 1-Stannyl-1-alkynes, Showing the Opposite Regioselectivity to the Routine Hydrometalations

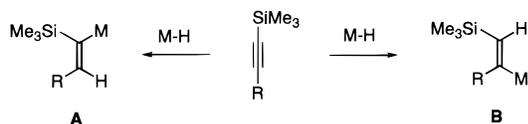
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Hydrometalation of 1-silyl-1-alkynes with metal hydrides MH (M = metal) is a dependable and versatile method to generate regio- and stereo-defined (silylalkenyl)metal species,<sup>1</sup> which are, in turn, essential for the selective construction of ubiquitous di- or trisubstituted double bonds of organic compounds.<sup>2</sup> Hydrometalation of acetylenes of this class usually takes place in a *cis*-fashion, and the majority of the known hydrometalation reactions involving hydroboration,<sup>3</sup> hydromagnesiation,<sup>4</sup> hydroaluminum,<sup>5</sup> hydrotitanation,<sup>6</sup> hydrozincation,<sup>7</sup> and hydrozirconation<sup>8</sup> uniformly yield the alkenylmetal species **A** as shown in Scheme 1. The utility

**Scheme 1.** Hydrometalation of 1-Silyl-1-alkynes



of the resultant organometallic species has been amply demonstrated in the syntheses of naturally occurring products.<sup>9</sup> Hydrometalation giving another regioisomer **B** is conceptually possible and, considering the flexible synthetic design, it should be an important process as well.<sup>10</sup> Nonetheless, a method for the generation of **B** is so far notably lacking except one case that is a Pt-catalyzed hydrosilylation of 1-silylalkynes.<sup>11</sup> However, in this transformation, discrimination between two silyl groups in subsequent reactions does not appear to be guaranteed. Herein we would like to show a method to generate **B** via a novel route,

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(8) Wipf, P.; Jahn, H. *Tetrahedron* **1996**, 52, 12853. Labinger, J. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 8, p 667.

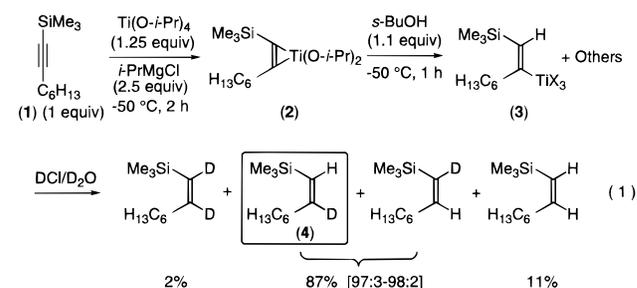
(9) Langkopf, E.; Schinzer, D. *Chem. Rev.* **1995**, 95, 1375.

(10) Another stereoisomer of **A** may be prepared by the hydroaluminum under different conditions (see ref 5). Alternatively, in general, the preparation of stereoisomers of both **A** and **B** has been achieved via carbo- or silylcupration of silylacetylene ( $R_3SiC\equiv CH$ ) or terminal alkynes (see ref 1; Knochel, P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 4, pp 900–901).

(11) Hudrlik, P. F.; Schwartz, R. H.; Hogan, J. C. *J. Org. Chem.* **1979**, 44, 155. See also: Bock, H.; Seidl, H. *J. Organomet. Chem.* **1968**, 13, 87.

which consists of the formation of the acetylene–metal complex followed by regioselective monoprotection.

We recently reported that an alkyne–titanium complex, ( $\eta^2$ -alkyne)Ti(O-*i*-Pr)<sub>2</sub>, is readily prepared by the treatment of an alkyne with Ti(O-*i*-Pr)<sub>4</sub> and *i*-PrMgCl in ether at a low temperature.<sup>12,13</sup> When a proton source (*s*-BuOH) was introduced to a solution of ( $\eta^2$ -1-silyl-1-alkyne)Ti(O-*i*-Pr)<sub>2</sub> (**2**) thus formed from silylalkyne **1** as shown in eq 1, we found that the protonation<sup>14</sup> took place exclusively at the  $\alpha$ -silylcarbon–titanium bond of **2** to give the ( $\beta$ -silylalkenyl)titanium species **3**, which does belong to the aforementioned species **B**, as evidenced by the selective formation of the corresponding mono- $\beta$ -deuterated alkenylsilane **4** after DCl/D<sub>2</sub>O workup.<sup>15</sup> (Olefinic regioselectivities are shown in square brackets throughout the text and the stereoisomer could not be detected within the limits of detection.) The byproducts, bis- or nondeuterated vinylsilanes, apparently arose from the unchanged **2** or exhaustive protonation of **2**.<sup>13</sup>



To establish this one-pot, yet two-step, hydrotitanation of 1-silyl-1-alkynes as a useful protocol, we then turned our attention to its validity in organic synthesis. The resulting titanium species **3** (via eq 1) could be directly utilized in a few representative transformations for functionalization and carbon–carbon bond formation, which are exemplified in Scheme 2.<sup>16</sup> Iodinolysis of **3** afforded the alkenyl iodide **5**, a versatile surrogate for reactions that are difficult to achieve by the alkenyltitanium reagent **3** itself. Allylation of **3** could be performed in the presence of a stoichiometric amount of a copper species. An ester group in the substrate survived the reaction conditions to give **6**. The alkenyltitanium underwent the addition to an aldehyde.<sup>17</sup> In addition, conjugate addition of **3** to  $\alpha,\beta$ -unsaturated carbonyl compounds could be carried out under copper catalysis to give the adducts **8** or **9** in good yields. As the synthetic application of titanium/copper transmetalation is quite rare and is so far limited to *alkyl*/titanium

(12) Sato, F.; Urabe, H.; Okamoto, S. *J. Synth. Org. Chem., Jpn.* **1998**, 56, 424.

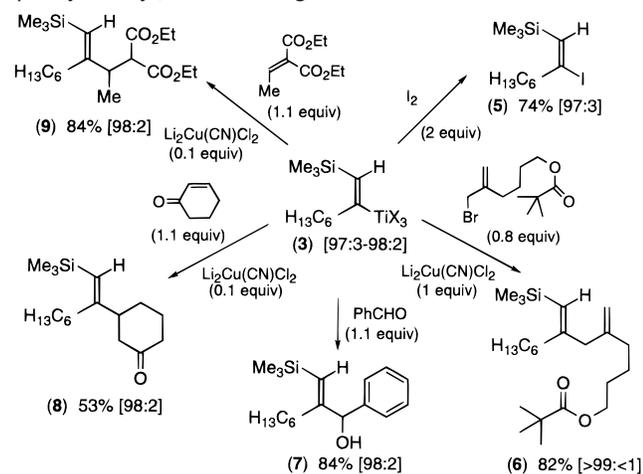
(13) Harada, K.; Urabe, H.; Sato, F. *Tetrahedron Lett.* **1995**, 36, 3203.

(14) Monoprotection of olefin or benzyne complexes of group 4 metals having cyclopentadienyl ligands has been mentioned. Cohen, S. A.; Bercaw J. E. *Organometallics* **1985**, 4, 1006. Buchwald, S. L.; Kreuzer, K. A.; Fisher, R. A. *J. Am. Chem. Soc.* **1990**, 112, 4600. Buchwald, S. L.; Watson, B. T.; Huffman, J. C. *J. Am. Chem. Soc.* **1986**, 108, 7411. Monoprotection of other acetylene–metal complexes derived from niobium or tantalum has not been reported. Cf. Kataoka, Y.; Miyai, J.; Oshima, K.; Takai, K.; Utimoto, K. *J. Org. Chem.* **1992**, 57, 1973. Hartung, J. B.; Pedersen, S. F. *J. Am. Chem. Soc.* **1989**, 111, 5468.

(15) In place of *s*-BuOH (1.1 equiv), the addition of *s*-BuOH (1.0 or 1.4 equiv), *n*- or *t*-BuOH (1.1 equiv), H<sub>2</sub>O (1.1 equiv), or CH<sub>2</sub>(CO<sub>2</sub>Et)<sub>2</sub> (1.1 equiv) as the proton source afforded less satisfactory results.

(16) For survey of transformations based on organotitanium reagents, see: (a) Reetz, M. T. *Organotitanium Reagents in Organic Synthesis*; Springer-Verlag: Berlin, 1986. (b) Ferreri, C.; Palumbo, G.; Caputo, R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 1, p 139. (c) Reetz, M. T. In *Organometallics in Synthesis*; Schlosser, M., Ed.; Wiley: Chichester, 1994; p 195.

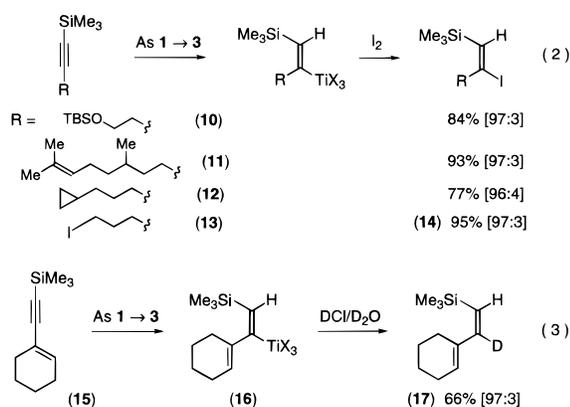
(17) Boeckman, R. K., Jr.; O'Connor, K. J. *Tetrahedron Lett.* **1989**, 30, 3271. Schick, H.; Spanig, J.; Mahrwald, R.; Bohle, M.; Reiher, T.; Pivnitsky, K. T. *Tetrahedron* **1992**, 48, 5579. Urabe, H.; Sato, F. *J. Org. Chem.* **1996**, 61, 6756.

**Scheme 2.** Synthetic Applications of the ( $\beta$ -Silylalkenyl)titanium Reagent<sup>a</sup>

<sup>a</sup> Equivalents and yields are based on **1**. Yield of **6** is based on the allyl bromide.

reagents,<sup>18</sup> the copper-mediated or -catalyzed reactions shown in Scheme 2 are the first demonstration of the feasibility of such a process starting from alkenyltitanium reagents. The regioselectivity indicated for each product (97:3 to >99:<1) is comparable to or, in one case, better than that of the starting ( $\beta$ -silylalkenyl)-titanium reagent **3** (97:3–98:2). The latter phenomenon may be attributable to the difference in reactivity between the  $\alpha$ - and  $\beta$ -silylalkenyl reagents under the reaction conditions.

The same treatment of several silylalkynes **10–13** and **15** having a functional group revealed the generality of this method as shown in eqs 2 and 3. The resulting alkenyltitanium species

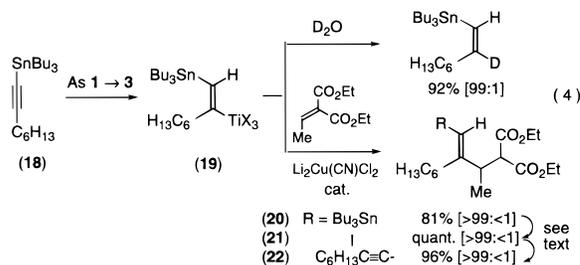


were conveniently confirmed by iodinolysis or deuteriolysis. The double bond in the citronellylacetylene **11** as well as a cyclopropane ring in **12** survived the reaction conditions. Moreover, an alkyl iodide moiety in **13** was not affected (i.e., neither reduced nor alkylated) to furnish the expected diiodide **14** in good yield and with high regioselectivity. It should be also noted that extension of this method to a conjugated enyne system seems to

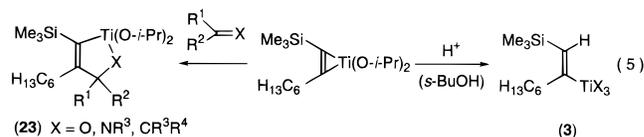
(18) Arai, M.; Lipshutz, B. H.; Nakamura, E. *Tetrahedron* **1992**, *48*, 5709. An unsuccessful copper-mediated reaction of an allyltitanium reagent has been described in ref 16a, p 89.

be viable as exemplified by the conversion of **15**  $\rightarrow$  **16**  $\rightarrow$  **17** (eq 3, the moderate yield of **17** may reflect its volatility).

To our best knowledge, hydrometalation of 1-stannyl-1-alkynes that gives a bimetallic reagent of the type **B** (Scheme 1) has not been executed.<sup>19</sup> Gratifyingly, the stannylalkyne **18** again proved to be a good substrate in this reaction to give the  $\beta$ -titanated alkenylstannane **19**,<sup>20</sup> which was identified by deuteration and underwent copper-catalyzed 1,4-addition, in both a highly regio- and stereoselective manner (eq 4). Utility of the alkenyltin compound such as **20** in selective organic synthesis was demonstrated by its stereospecific conversion to the iodoalkene **21** (slight excess of iodine, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C  $\rightarrow$  rt)<sup>20</sup> followed by the Sonogashira coupling reaction (1-octyne, PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>-CuI cat., HNEt<sub>2</sub>, rt),<sup>21</sup> which furnished a stereodefined trisubstituted olefin **22** virtually as a single isomer with the malonate portion remaining intact.



The above regioselection observed for the (silylalkyne)-titanium complex toward proton (ROH) would be quite anomalous, because we have experienced that the same complex reacted with various compounds such as aldehydes,<sup>13</sup> ketones,<sup>13</sup> imines,<sup>22</sup> and olefins<sup>23,24</sup> always at the  $\beta$  position to the silyl group to afford ( $\alpha$ -silylalkenyl)titanium intermediates **23** as shown in eq 5. The



origin of the inherent preference in regioselection dependent upon the reacting partners will be reported in due course.

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**Supporting Information Available:** Typical experimental procedures and characterization data of products (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(20) For review on synthetic applications of alkenylstannanes, see: Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworth: London, 1987. Mitchell, T. N. *Synthesis* **1992**, 803.

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(22) Gao, Y.; Harada, K.; Sato, F. *Tetrahedron Lett.* **1995**, *33*, 5913.

(23) Takayama, Y.; Gao, Y.; Sato, F. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 851.

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