Direct Formation of Propargyltin Compounds via C−H Activation

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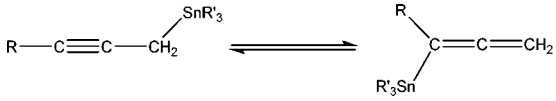
Received February 13, 2008

Summary: The mixed reagent $Sn[C(SiMe_3)_2CH_2CH_2C(SiMe_3)_2]$*/ArI reacts with alkynes to give primary and secondary propargylic C−H activation. Alkynes tested include 1-phenylpropyne, 1-phenylbutyne, 1-trimethylsily1hexyne, and 2-hexyne. Aryl halides tested include iodobenzene and 2,4,6-triisopropyliodobenzene. An X-ray crystal structure is reported for the product of the secondary propargylic activation of 2-hexyne.*

A variety of synthetic methods have been developed for the synthesis of propargylmetal compounds.[1] Such compounds are useful as coupling reagents for the formation of C−C bonds.[2–4] Propargyltin compounds are especially useful due to their functional group tolerance and air stability.[5,6] One of the main challenges in their synthesis is avoiding the formation of allenyl isomers. This difficulty arises because both electron donor solvents and Lewis acids catalyze the interconversion of propargyl- and allenyltin isomers (eq 1).[7]



(1)

Propargyl chlorides react with hexamethylditin in the presence of a Pd(II) catalyst that contains a pincer ligand. In optimal cases, 7:1 to 10:1 ratios of propargyl-/allenyltin isomers are obtained. However, many propargylic chlorides react to give less than 50% of the propargyl isomer, and others give only the allenyl isomer.[8,9] Propargyl acetates, carbonates, and phosphates can be stoichiometrically converted to propargyltin complexes upon reaction with tributyltin chloride after activation with a $Ti(O^iPr)_4/2\ ^iPrMgCl$ reagent. This method frequently gives excellent propargyl/allenyl ratios of >40:1 with both primary and secondary propargyl carbonates.[6] In addition, this method has been extended to the formation of chiral propargyltin compounds by starting with chiral, secondary propargyl phosphates.[5]

All of these methods for the synthesis of propargyl tin compounds require the propargyl acetate, carbonate, halide, or phosphate species. Many of these species are not commercially available, and examination of alternative routes to propargyl compounds that do not involve such starting materials was of interest. Direct C−H activation at the carbon atom alpha to the triple bond, concomitant with tin−carbon bond formation, could, in principle, provide a direct route to propargyltin compounds. However, C−H activations involving alkynes are rare and have not been used to yield a tin−carbon bond. Previously, we have demonstrated that the mixed reagent $Sn[N(SiMe_3)_3]_2$/PhI can directly activate C−H bonds and form a tin−carbon bond in substrates such as THF, pentane, cyclohexane, cyclopentane, and 2-methoxy-2-methylpropane.[10] Recently, we have also shown that we can perform allylic C−H activation using the $Sn[C(SiMe_3)_2CH_2CH_2C(SiMe_3)_2]$ (**1**)/PhI combination.[11] These reactions were carried out at ambient temperature. On the basis of these previous results, we explored the reactivity of $Sn[N(SiMe_3)_2]_2$/PhI with alkynes, but no propargylic C−H activation was observed. However, we discovered that **1** did not react with any of the alkynes used in this study and that the **1**/ArI combination was effective in activating both primary and secondary propargyl C−H bonds. These reactions could be carried out at ambient temperature and did not require electron donor solvents or Lewis acid additives. Thus, no problems with isomerization to allenyl isomers were encountered.

Activation of the propargylic C−H bond was achieved when 1 equiv of **1** dissolved in 10 mL of benzene and 15 mL of alkyne was added to 1.1 equiv of aryl iodide dissolved in 5 mL of 1-phenylpropyne, 1-phenylbutyne, or 2-hexyne.[12] When employing phenyl iodide, simple mixing of the reagents also gave oxidative-addition product $PhISn[C(SiMe_3)_2CH_2CH_2C(SiMe_3)_2]$ (**2**).[11] The amount of **2** formed could be minimized and/or eliminated by employing syringe pump addition of PhI and/or the use of bulkier aryl iodides such as 2,4,6-trimethyliodobenzene or 2,4,6-triisopropyliodobenzene. Addition rates were chosen such that a substantial degree of red color did not build up during the addition of the intensely red stannylene solution to the aryl iodide solution. For the cases of 1-phenylpropyne, 1-phenylbutyne, and 2-hexyne, employing the syringe pump techniques and using 2,4,6-triisopropyliodobenzene resulted in quantitative formation of propargylic C−H activation products **3**, **4**, and **6**, respectively. For the case

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(12) A one-necked 100 mL flask fitted with a rubber septum was charged with 315 mg of 2,4,6-triisopropyliodobenzene (0.95 mmol, 1 equiv) and 5 mL of 1-phenylpropyne. A solution containing 400 mg of **1** (0.86 mmol, 0.9 equiv), 15 mL of 1-phenylpropyne, and 10 mL of benzene was placed in a gastight syringe equipped with a 20-gauge needle. Then 25 mL of the red stannylene solution was added to the 2,4,6-triisopropyliodbenzene/alkyne solution at a rate of 8 mL/h using a syringe pump. The last 5 mL was added at 2 mL/h. The solution was stirred for 8 h yielding a cloudy, white solution containing only the C−H activation product as indicated by ^1H NMR spectroscopy. The volatiles were removed in vacuo, and the resulting solid was recrystallized from pentane at −78 °C to give a white powder (402 mg, 67.4% yield). Full spectroscopic details are provided in the Supporting Information.

10.1021/om800132h CCC: $40.75
Publication on Web 06/05/2008

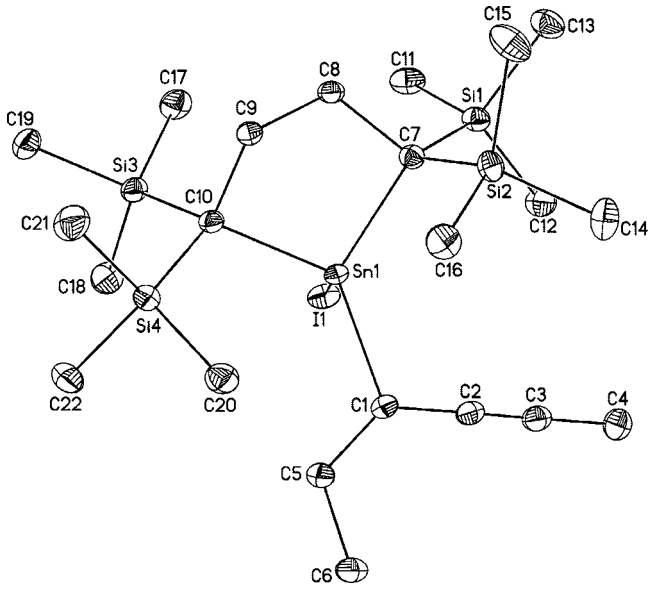


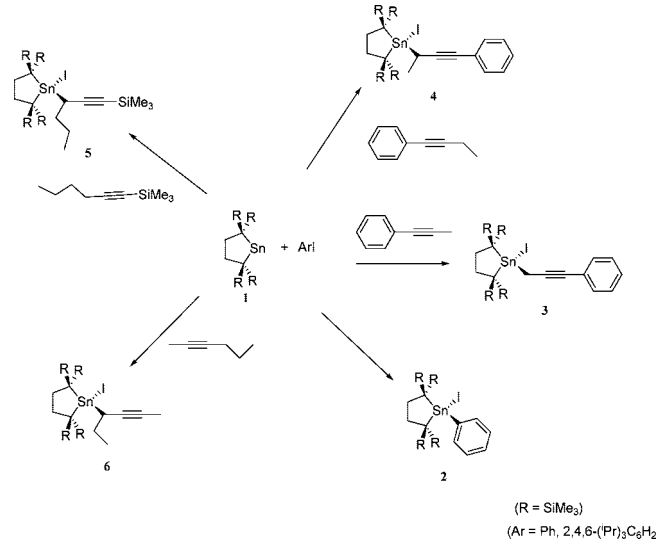
Figure 1. ORTEP diagram of $(C_6H_9)ISnC(SiMe_3)_2CH_2CH_2C(SiMe_3)_2$ (**6**) (50% thermal ellipsoids). Selected bond lengths (Å) and angles (deg): Sn−C1, 2.1841(14); Sn−I, 2.73712(19); C1−C2, 1.455(2); C2−C3, 1.193(2); C3−C4, 1.460(2); C1−C5, 1.533(2); C5−C6, 1.525(2); Sn−C10, 2.1841(14); Sn−C7, 2.1832(14); Sn−C1−C2, 107.86(10); Sn−C1−C5, 111.73(9); C2−C1−C5, 112.97(12);C1−C2−C3, 178.89(17); C2−C3−C4, 178.18(18); C7−Sn−C1, 121.32(5); C10−Sn−C1,122.18(5); C7−Sn−I, 113.24(4); C10−Sn−I, 111.63(4); I−Sn−C1, 96.61(4).

of 1-trimethylsily1hexyne, 1 equiv of **1** dissolved in 15 mL of alkyne was added to 1.1 equiv of iodobenzene dissolved in 5 mL of alkyne. ^{1}H NMR spectroscopy of the reaction mixture indicated a 95% conversion to propargylic C−H activation product **5** along with 5% conversion to oxidative-addition product **2**. The use of alkyne as solvent dramatically reduces the amount of **2** formed. When stoichiometric amounts of alkyne are employed, **2** is the predominant product. Even when employing alkyne as solvent, it is necessary to employ high-dilution techniques to minimize formation of **2** and give high yields of the desired C−H activation product.

All compounds were characterized by a combination of ^{1}H, ^{13}C, and ^{119}Sn NMR spectroscopy, infrared spectroscopy, mass spectrometry, and elemental analysis. Compound **3**, the result of the C−H activation of a primary C−H bond, exhibits two $-SiMe_3$ resonances in the ^{1}H NMR spectrum. Compounds **4**, **5**, and **6**, the result of the C−H activation of a secondary C−H bond, all exhibit four $-SiMe_3$ resonances. In the case of compound **5**, an additional $-SiMe_3$ resonance is present from the 1-trimethylsily1hexyne substrate. The ^{119}Sn NMR spectrum also provided a means of differentiating the primary versus secondary C−H activation products, as the resonance of **3** occurred at 96.59 ppm, whereas the resonances of **4**, **5**, and **6** were observed at 142.76, 130.55, and 132.72 ppm, respectively. The assignment of a $^5J_{Sn-H}$ coupling constant of 36.49 Hz for compound **6** was surprising. To confirm this spectroscopic assignment, an X-ray crystallographic study of **6** was undertaken using a colorless crystal grown from pentane at 25 °C (Figure 1). The bond connectivity assigned spectroscopically was confirmed including the propargylic C−H activation and the presence of the triple bond.

Comparing this approach to the previously published methods of Szabó et al.[8,9] the use of hexamethylditin/Pd(II) pincer catalyst/(3-chloroprop-1-ynl)benzene resulted in an 87% isolated yield of trimethyl(3-phenylprop-2-ynyl)tin with an 8:1 propargylic/allenyl product ratio. The reaction of **1**/2,4,6-triisopropyliodobenzene with 1-phenylpropyne proceeded quantitatively

Scheme 1. Reactions of $SnC(SiMe_3)_2CH_2CH_2C(SiMe_3)_2$/ArI with Alkynes



(67% isolated yield) with no formation of the allenyl isomers. Attempts to use hexamethylditin and the Pd(II) pincer catalyst to give secondary propargylic products resulted in purely allenyl products. No propargylic isomer could be detected by ^{1}H NMR spectroscopy for other substrates such as (1-chloroprop-2-ynyl)benzene, (2-chlorobut-3-ynyl)benzene, and (3-chloroprop-1-yne-1,3-diyl)dibenzene. In contrast, secondary C−H activations proceeded quantitatively employing the **1**/2,4,6-triisopropyliodobenzene combination to give compounds **4** and **6**. Using the **1**/PhI reagent, **5** was obtained with 95% conversion, as indicated by ^{1}H NMR spectroscopy (45% isolated yield). Sato et al. previously have reported effective methods for the synthesis of secondary propargylic tin compounds. For example, ethyl non-2-yn-4-ylcarbonate was converted to tributyl(non-2-yn-4-yl)tin in 72% yield with a 31:1 propargylic/allenyl product ratio using the mixed $Ti(O^iPr)_4/2^iPrMgCl$ reagent.[6]

All three of the synthetic methods published to date have their advantages and drawbacks. Our approach requires the synthesis and use of air-sensitive stannylene **1**, the use of a syringe pump and/or a bulky aryl iodide, and the use of alkyne as solvent. The primary advantages are that it does not require the preparation of alkynes with leaving groups and leads to no detectable amount of isomerization to allenyl products. The method of Szabó et al. requires the synthesis of the palladium pincer catalysts, the use of hexamethylditin, and the use of alkynes with a leaving group (typically Cl) at the appropriate position but can be employed with functional groups (COOEt, OH, NAc) not tolerated by the stannylene. The method of Sato et al. requires preparation of carbonate-functionalized alkynes but can be employed to make stereospecific propargyltin compounds.

Acknowledgment. This work was supported by National Science Foundation grant CHE-0453849.

Supporting Information Available: Text giving complete experimental preparation details is available for compounds **3**, **4**, **5**, and **6**. A CIF file giving crystallographic data for compound **6** is available. This material is available free of charge via the Internet at http://pubs.acs.org.

OM800132H