Ni, Co, and Mo-catalyzed alkyne hydrostannations using Bu₃SnCl/PMHS/KF/18-crown-6 as an in situ Bu₃SnH source

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A B S T R A C T
A number of terminal alkynes were subjected to nickel, cobalt, and molybdenum catalyzed hydrostannations in presence of tributyltin chloride, polymethylhydrosiloxane, potassium fluoride and 18-crown-6 as an in situ organotin hydride source to produce vinylstannanes.

Vinylstannanes are useful and versatile building blocks for organic synthesis.[1] Among the many ways to generate these reactants,[2] transition-metal-catalyzed hydrostannations of alkynes[3] (or alkenes[4]) with tributyltin hydride are widespread. Just as common though are the problems associated with the direct use of this reagent.[5] For example, adventitious exposure to air can efficiently convert Bu₃SnH to (Bu₃Sn)O, rendering the reagent useless. Similarly, in the presence of transition metals Bu₃SnH can immediately form Bu₃SnBu₃Sn, often complicating the desired reaction and product purification.[6] Similarly, overcoming any loss of Bu₃SnH to either the oxide or dimer often requires excess use of the relatively expensive and toxic Bu₃SnH.

To ameliorate the negatives associated with the direct use of Bu₃SnH, processes have been developed that use in situ generated organotin hydrides in hydrostannation reactions.[7] Our own contributions to these efforts include the establishment of Bu₃SnCl/polymethylhydrosiloxane (PMHS)/aqueous KF as an in situ source of Bu₃SnH for radical or palladium catalyzed alkyne hydrostannations.[8] This PMHS mediated hydrostannation protocol was integral to the invention of a one-pot hydrostannation/Stille coupling sequence that was catalytic in tin.[9] In conjunction with efforts aimed at developing the next generation of Stille couplings that are catalytic in tin, we became interested in mixed catalyst systems where the hydrostannation and cross-coupling steps were catalyzed by different metals. With this goal in mind we set out to learn if other previously disclosed hydrostannation catalysts were compatible with our Bu₃SnCl/PMHS/KF(aq) protocol and how such conditions would impact the distal/proximal and E/Z ratios of the product vinyltins.

We began our study by employing NiCl₂(PPh₃)₂, 9 CoCl₂(PPh₃)₂, 9 and Mo(CO)₆(NC-Bu)₃ (MoBu₃) 10 under our Bu₃SnCl/PMHS/KF(aq) conditions. With the Ni-catalyst, heating at 65 °C in THF for 1–2 days, afforded the expected vinylstannanes, but yields were very inconsistent and even in the best cases moderate. The Co- and Mo-catalysts behaved even worse in that no vinylstannanes were ever observed. We subsequently realized that water used to dissolve the KF was the offending element and that an anhydrous method would be required.

We had previously shown that the Bu₃SnF, PMHS, and catalytic quantities of tetrabutylammonium fluoride (TBAF) allowed for the in situ generation and reaction of Bu₃SnH under anhydrous conditions. 7d However, given the demands of our own Stille process and the relative availability and expense of triorganotin fluorides versus triorganotin chlorides, 11 our search for an anhydrous method was conducted with the criterion that Bu₃SnCl be employable.

We tried to run heterogeneous reactions with KF being added as a solid, but not surprisingly such attempts failed to produce vinyltins. We quickly then moved to explore adding 18-crown-6 to the reactions, owing to this crown ether’s ability to homogenize potassium salts and organic solvents. 12

Starting with the marginally successful NiCl₂(PPh₃)₂ catalyzed 9 reactions that we had run with aqueous KF, we ran reactions on alkynes with 1.5 equiv of Bu₃SnCl, 1.5 equiv of PMHS, 3 equiv of KF, and 3 equiv of 18-crown-6 (Table 1). Following our previous leads, 7d we also included 1 mol % TBAF as an additive. Likewise, we also added 9 mol % hydroquinone to inhibit unwanted free radical generation. 10 Under these conditions the reactions...
regioselectivities and yields trended lower relative to those observed in other reported protocols, cols. On the other hand, while the regiochemical preferences were reproducibly observed, they generally gave moderate to good yields and required much less reaction time (4–5 h) to complete as compared to the aqueous KF protocol. Successful reactions did exhibit some reliability problems. Successful reactions displayed a blue color when progressing as desired. This characteristic blue color was present, reaction yields were consistent from run to run. On occasions when the mixture did not go to blue, no reaction was always the result.

We also explored the hydrostannation of 2 in the presence of catalytic amounts of [RhCl(COD)]2, RuCl3(η5-C5Me5), or RuCl3(η5-C5H5). Unfortunately, all three of these catalysts proved incompatible with not only water, but with the Bu3SnCl/PMHS/KF/18-crown-6 combination in general. Additional studies are aimed at identifying the exact offender as well as conditions that could be amenable to the use of these catalysts.

Perhaps our most interesting results came about during the application of Bu3SnCl/PMHS/KF/18-crown-6 conditions to Mo-catalyzed hydrostannations. Kazmaier has shown that Mo(CO)3(η5-C5H5)Bu3 (aka MoB3) catalyzed hydrostannations typically favor formation of the proximal vinylstannanes.10 As illustrated in Scheme 1, this regiochemical preference has been explained by the addition of an intermediate Mo–Sn species across the triple bond whereby the sterically demanding molybdenum fragment ends up on the less hindered side of the alkyne (distal to R). This of course, places the triorganotin moiety on the more hindered side of the alkyne and forms the proximal stannane as the major isomer.3c To the best of our knowledge though, all of the reported MoB3 hydrostannations were carried out on hetero atom substituted and/or highly polarized alkynes. As such, we used our own study herein to address the more global question of how alkynes that are incapable of heteroatom direction would perform under MoB3 catalysis.

To begin our examination, THP-protected propargyl alcohol (1) was subjected to Bu3SnCl/PMHS/KF/18-crown-6 and 5 mol % MoB3 in different solvents and at different temperatures (Table 3). After 18 h, reaction of 1 in THF at 65 °C afforded a 4:1 ratio of the proximal to distal vinylstannanes (1a and 1b) in 57% yield (based on 13C recovered 1). Reaction in toluene at 110 °C resulted in disappearance of the alkyne after 24 h. However, the combined yields of 1a and 1b was lower (47%), although the ratio of 1a/1b (8:1) was higher (8:1). In contrast, running the reaction in benzene at 80 °C for 24 h gave the highest yield (66%) of the proximal isomer albeit with a return to the 4:1 ratio of 1a/1b (82% combined yield).

Using the highest yielding solvent, benzene, several alkynes were subjected to MoB3 catalyzed hydrostannations. Most alkynes behaved well giving good to excellent yields of the vinylstannane products (Table 4). The ratio of proximal to distal isomer also

### Table 1
CoCl2(PPh3)2 catalyzed hydrostannations

<table>
<thead>
<tr>
<th>Entry</th>
<th>R Products</th>
<th>Yielda (ratio of a:b)b</th>
<th>Bu2SnCl/KF/PMHS</th>
<th>Bu3SnH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH3OH</td>
<td>9a/b</td>
<td>42% (1.5/1)</td>
<td>60% (4/1)</td>
</tr>
<tr>
<td>2</td>
<td>CH3OTHP</td>
<td>10a/10b</td>
<td>45% (1/1.7)</td>
<td>49% (7/1)</td>
</tr>
<tr>
<td>3</td>
<td>CH3OH/pH</td>
<td>11a/11b</td>
<td>42% (1/4.1)</td>
<td>69% (13/1)</td>
</tr>
<tr>
<td>4</td>
<td>OCH3(H2)</td>
<td>12a/12b</td>
<td>54% (1/1.7)</td>
<td>46% (1/3.4)</td>
</tr>
<tr>
<td>5</td>
<td>CH3Cl(5)</td>
<td>13a/13b</td>
<td>57% (1/1.99)</td>
<td>100% (1/1.43)</td>
</tr>
<tr>
<td>6</td>
<td>CH3OTBS(6)</td>
<td>14a/14b</td>
<td>36% (1/4.1)</td>
<td>52% (4/1)</td>
</tr>
</tbody>
</table>

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### Table 2
CoCl2(PPh3)2 catalyzed hydrostannations

<table>
<thead>
<tr>
<th>Entry</th>
<th>R Products</th>
<th>Yielda (ratio of a:b)b</th>
<th>Bu2SnCl/KF/PMHS</th>
<th>Bu3SnH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH3CH2CH2OH</td>
<td>15a/15b</td>
<td>45% (1/1.91)</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>CH3OTHP</td>
<td>10a/10b</td>
<td>51% (1/1.51)</td>
<td>65% (1.5/1)</td>
</tr>
<tr>
<td>3</td>
<td>CH3Cl(5)</td>
<td>13a/13b</td>
<td>39% (1/1.99)</td>
<td>96% (1/3)</td>
</tr>
<tr>
<td>4</td>
<td>CH3OTBS(6)</td>
<td>14a/14b</td>
<td>31% (1/4.1)</td>
<td>—</td>
</tr>
</tbody>
</table>

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*Yields refer to spectroscopically pure products unless otherwise noted.

Isomeric ratios were determined by 1H NMR analysis of the crude reaction mixture.

Reaction was run in THF.

Yield determined by 1H NMR using HDMS as an internal standard.
increased when the alkylate had a more bulky substituent (entry 1 vs 2 and 3 vs 4), as should be expected from Kazmaier’s model.

Comparing entries 3 and 6 of Table 4 is also interesting. Under our Bu₃SnCl/KF/18-crown-6/PMHS conditions the proximal to distal isomer ratio of the products are the same for both substates, suggesting that heteroatom direction is not a regiochemical driver. Yet, the isomeric ratios of the products are the same for both substates, suggesting that Kazmaier’s model.

Table 4
Optimization of MoB₃I₂-catalyzed hydrostannations

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Temperature (°C)</th>
<th>Time (h)</th>
<th>Yield (a) (ratio of 10a/10b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>THF</td>
<td>65</td>
<td>18</td>
<td>57%° (4/1)</td>
</tr>
<tr>
<td>2</td>
<td>Toluene</td>
<td>110</td>
<td>24</td>
<td>47% (8/2.1)</td>
</tr>
<tr>
<td>3</td>
<td>Benzene</td>
<td>80</td>
<td>24</td>
<td>82% (4/1)</td>
</tr>
</tbody>
</table>

* Yield refers to spectroscopically pure products unless otherwise noted.

Conclusions

We have demonstrated that Bu₃SnCl/PMHS/KF can serve as an in situ tin hydride source for hydrostannation reactions under several non-Pd transition metal catalysts. Key to the success of these moisture sensitive reactions is the use of 18-crown-6 and dry (rather than aqueous) KF. Our results show for the first time that MoB₃I₂ catalyzed hydrostannations of nonheteroatom containing alkynes can afford proximal vinyltin作为 the major product, although further studies are clearly required to have a thorough understanding of the mechanistic origins of the observed regiochemical outcomes.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.08.005.

References and notes


14. Based on 13% recovered.

15. Conformation and Astellas for funding.

16. We thank undergraduate researcher Wenzheng Chong and Project SEED student Anna Foster for their contributions in this work. We also thank National Institute of Health, National Science Foundation and Astellas for funding.

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18. Chemical outcomes.

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20. We also thank National Institute of Health, National Science Foundation and Astellas for funding.