A New Approach for the Generation and Reaction of Organotin Hydrides: The Development of Reactions Catalytic in Tin

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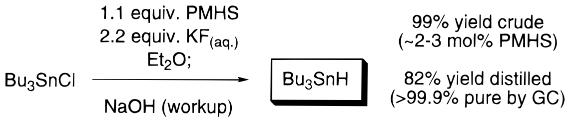
Organotin compounds are versatile reagents in organic chemistry.[1] Among the most commonly used tin reagents is tributyltin hydride.[2] One of tributyltin hydride's major applications is in free-radical reactions[3] such as dehalogenations of alkyl, vinyl, or aryl halides, often followed by intra- or intermolecular C−C coupling. These chain reactions allow the formation of quite complex ring systems and the installation of multiple new stereocenters in one pot. Since these reactions proceed under very mild conditions, a large variety of functional groups is tolerated, avoiding laborious protection and deprotection sequences. Tributyltin hydride has also been used in the reduction of halides, tosylates (via the iodide), thiols, isonitriles, nitrates, and α,β-unsaturated aldehydes (1,4-reduction).[4,5] The reagent is also employed in the generation of vinyl stannanes, which are important and useful building blocks in organic synthesis.[6,7]

Despite the broad applications of organotin hydrides, their utilization is not unproblematic. Tributyltin hydride is relatively expensive, unstable, and toxic. Furthermore, the tin byproducts of its reactions are not always easy to separate and represent an ever increasing disposal problem.[8] The invention and development of new methods allowing for the catalytic employment of organostannanes in such reactions would significantly reduce the amount of tin waste and thereby be of great value with respect to both environmental and practical concerns. As such, a specific aim of this research program is the development of reaction procedures that will allow for the in situ generation of organotin hydrides and their subsequent use in organic reactions.

Several research groups have investigated reaction methodologies that allow the in situ formation of tin hydride from cheaper starting materials or the employment of catalytic amounts of tin. An early method developed for the in situ generation of tin hydride involved the reduction of tributyltin halides by $NaBH_4$.[9] In fact, in one of the first examples of a reaction catalytic in tin, Corey et al.[10] used sodium borane to successfully recycle the tin halide byproduct of a dehalogenation reaction. More recently, Fu et al.[11] have developed several elegant methodologies to perform "classical" reactions of tin hydride with only catalytic amounts of tin by using silanes such as polymethylhydrosiloxane (PMHS) to regenerate the tin. However, both of these methods have drawbacks. For example, the use of $NaBH_4$ is not compatible with functional groups susceptible to borohydride or borane reductions. As for the silanes, they do not reduce tin halides, and therefore, their utilization has been limited to the recycling of tin alkoxides. Given such limitations, we believed a mild method that allowed the recycling of tin halides back to tin hydrides would be highly desirable.

Scheme 1



As fluoride had already been shown to heighten the reducing properties of PMHS,[12] we wondered whether polymethylhydrosiloxane (PMHS) made hypervalent by the action of KF[13] could efficiently convert tin halides to tin hydrides (Scheme 1). In fact, we found that simply stirring an ethereal solution of Bu_3SnCl with 1.1 equiv of PMHS and 2.2 equiv of an aqueous KF solution for 3.5 h, followed by NaOH workup, extraction, and removal of the ether provides Bu_3SnH in nearly quantitative yield, albeit with approximately 2−3 mol % of residual PMHS. Distillation of this "crude" material affords analytically pure Bu_3SnH in 82% yield.

We assume the active species in this reaction to be a hypervalent silane species,[13] as neither Bu_3SnCl or Bu_3SnF reacts with PMHS in the absence of KF.[14] However, we have not ruled out the involvement of highly coordinated organotin species in the process.[15] In either event, we were interested in determining whether the tin hydride generated under theses conditions could be employed in subsequent in situ chemical transformations.

We were pleased to find that our combination of Bu_3SnCl, aqueous KF, and PMHS performs well in "classical" tin hydride reactions, such as free-radical dehalogenations. Since tin halides are the byproducts of these reactions, we hoped to be able to recycle them, allowing us to perform these reactions with catalytic amounts of tin. Our results summarized in Scheme 2 demonstrate that we are indeed able to perform these reactions with catalytic amounts of tin. Importantly, we could show in control experiments that the halides are not reduced by the reagent combination PMHS/potassium fluoride, which is known to act as a reducing agent.[12,13] Apparently the hypervalent silane alone requires more polar solvents or anhydrous conditions in order to serve as an effective reducing agent.

Given our success at free-radical hydrodehalogenations with catalytic amounts of tin hydride, we decided to investigate the reaction of more complex substrates and the possible formation of carbon−carbon bonds. All such reac-

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(14) The employment of less than 1 equiv of KF significantly diminishes the production of tributyltin hydride. This fact along with preliminary ^{119}Sn NMR data suggests a rapid conversion of Bu_3SnCl into Bu_3SnF (ref 8) prior to reduction. However, the mechanism of this reaction needs further study.

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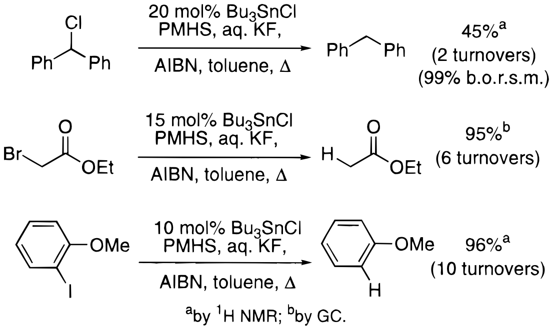
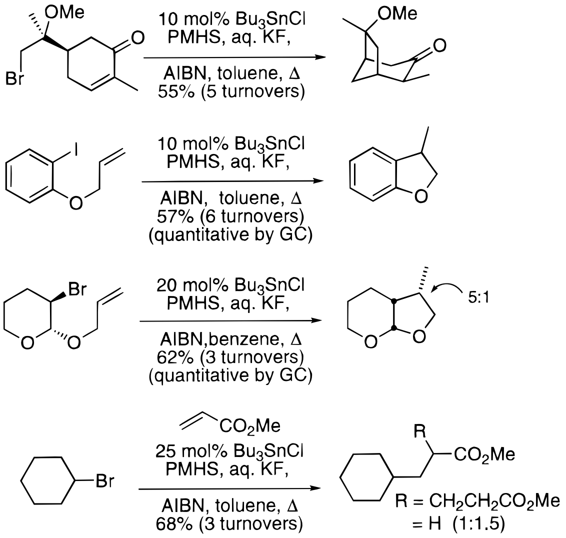
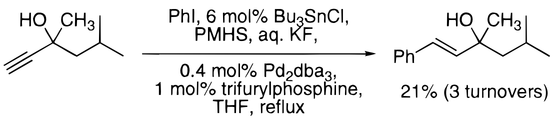
Scheme 2



Scheme 3



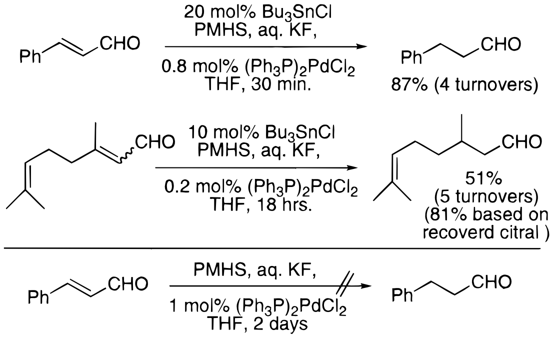
Scheme 4



tions studied to date (Scheme 3) proceeded well with the successful recycling of tributyltin hydride and no observable reduction of starting material.

We have also secured evidence that it is possible to carry out multiple transformations in the reaction pot. Namely, we have employed this method to our recently described protocol for a one-pot palladium-mediated hydrostannylation/Stille cross-coupling with catalytic amounts of tin.[16] Stirring a THF solution of 3,5-dimethyl-1-hexyn-3-ol and iodobenzene, in the presence of PMHS, aqueous KF, and catalytic amounts of Pd_2dba_3, trifurylphosphine, and tributyl tin chloride, for 48 h produced the anticipated 1,3-diene (Scheme 4). While the overall yield and turnovers for this sequence were low,[17] the results of this experiment clearly showed that the tin is indeed recycled.

Scheme 5



Finally, the catalytic Bu_3SnCl/PMHS/KF combination is not limited to reactions that produce tin halide byproducts. We have applied our tin hydride recycling methodology to the reduction of α,β-unsaturated carbonyls.[18] Keinan et al.[5] have shown that the tin hydride reduction of the π-allyl palladium species is a very mild way for the exclusive 1,4-reduction of such compounds. However, their method required 1.5- to 3-fold excess of the hydride. By recycling the tin with aqueous KF and PMHS, we were able to generate the desired saturated aldehydes in good yields, using only 20 or 10 mol % of tin, respectively. The reduction of cinnamyl aldehyde proceeds within 30 min at room temperature, while citral required several hours to generate citronellal in 51% yield, which corresponds to a tin turnover of 5 (Scheme 5). Control experiments showed that no reduction of the α,β-carbonyl compound occurs in absence of the tin halide.[19] Furthermore, no reduction of the carbonyl functionality was observed, although Kobayashi et al.[20] have shown that PMHS/TBAF reduces cinnamyl aldehyde to the corresponding alcohol in high yields.

In summary, we have developed a methodology that allows the in situ generation of tin hydride from inexpensive starting materials that can be applied to the recycling of tributyltin hydride in reactions catalytic in tin. Furthermore, since carbonyl compounds are not reduced under these reaction conditions it would appear this methodology is inherently more chemoselective than the borohydride method of recycling tin halides back to tin hydride. Current studies are aimed at increasing our mechanistic understanding of tin hydride formation, as well as broadening the scope and efficiency of the reactions discussed herein. The results of these studies will be reported in due course.

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Supporting Information Available: Spectroscopic data for all new compounds pictured as well as selected experimental procedures.

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(17) The overall stepwise yield for this reaction is 59%.

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(19) Stirring cinnamaldehyde in the presence of 20 mol % Bu_3SnH, PMHS, Pd (cat.), H_2O, and THF (*no KF*) for 2 days did give a 50% yield of hydrocinnamaldehyde, 10% cinnamyl alcohol, and 40% starting material.

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