Organotin hydrides are the most frequently employed hydrogen-atom donors in radical reactions of carbohydrates. Clearly, the compound of choice is tri-\textit{n}-butyltin hydride (Section II.A). Phenyl-substituted compounds, such as triphenyltin hydride, can serve in the same role, but they offer no advantage and are rarely used. Polymer-supported (Section II.B) and fluorous (Section II.C) tin hydrides have been used as replacements that avoid some of the difficulties inherent in the use of tri-\textit{n}-butyltin hydride.

A. Tri-\textit{n}-butyltin Hydride

1. Advantages of Tri-\textit{n}-butyltin Hydride

In some ways \textit{Bu}_3\text{Sn}H is an ideal hydrogen-atom transfer. It reacts rapidly with a carbon-centered radical to produce a carbon–hydrogen bond and, at the same time, generates the chain-transfer agent (\textit{Bu}_3\text{Sn}·) required for successful reaction. An important characteristic of \textit{Bu}_3\text{Sn}· is that it does not cause side reactions by abstracting hydrogen atoms from carbon–hydrogen bonds.

2. Problems Associated With the Use of Tri-\textit{n}-butyltin Hydride

Even with its extensive, successful applications and significant advantages, tri-\textit{n}-butyltin hydride suffers from several substantial drawbacks. One of these is that complete separation of tin-containing compounds from deoxygenated products is often difficult.\textsuperscript{1–11} Another problem is that the toxicity of \textit{Bu}_3\text{Sn}H\textsuperscript{12,13} and the tin-containing substances it produces are a danger to those handling these materials and a complication for waste disposal.\textsuperscript{1–11} This combination of problems places a severe limitation on the use of \textit{Bu}_3\text{Sn}H in the synthesis of therapeutic agents and other compounds destined for biological applications.\textsuperscript{14} Another concern about tri-\textit{n}-butyltin hydride is that although it is not too costly for small-scale laboratory use, large-scale reactions with this compound are expensive.\textsuperscript{1,2,11}

3. Reducing the Negative Impact of Tri-\textit{n}-butyltin Hydride

The modifications to the use of tri-\textit{n}-butyltin hydride that are described in the next three sections reduce its negative impact. One approach is to use \textit{Bu}_3\text{Sn}H in catalytic amounts and to regenerate this tin hydride during reaction. Sodium borohydride and polymethylhydrosiloxane are two reagents that can regenerate \textit{Bu}_3\text{Sn}H in a reaction mixture quickly after it is consumed. Recycling using these reagents allows complete reaction to take place when only a small amount of tin-containing material is present. Product purification is easier for reactions run under these conditions. A different approach to product purification calls for potassium fluoride to be added to a reaction mixture after reaction is complete. This addition precipitates insoluble tin fluorides and permits them to be removed by filtration.

a. Reagents That Regenerate Tri-\textit{n}-butyltin Hydride During a Reaction
(1). Sodium Borohydride

The tin-containing product from reaction of a halogenated carbohydrate with tri-\(n\)-butyltin hydride is a tri-\(n\)-butyltin halide. Sodium borohydride regenerates hydride from halide (eq 1) rapidly enough that \(Bu_3SnH\) can be used in far less than stoichiometric amounts.\(^{15}\) Using sodium borohydride naturally is limited to situations in which undesired side reactions with this reagent [or the diborane it produces (eq 1)] do not take place. Equation 2 describes a reaction in which tin-containing compounds are used in only catalytic amounts due to the presence of sodium borohydride.\(^{16}\)

\[
2Bu_3SnX + 2NaBH_4 \rightarrow 2Bu_3SnH + 2NaX + B_2H_6 \quad (1)
\]

\(X = I, Br, Cl\)

(2). Polymethylhydrosiloxane

Polymethylhydrosiloxane [PMHS, (MeSiHO)\(_n\)] in the presence of potassium fluoride reacts with tri-\(n\)-butyltin halides to produce \(Bu_3SnH\) (eq 3).\(^{17}\) Since this reaction can generate \(Bu_3SnH\) \textit{in situ}, only 10 mol\% of a tri-\(n\)-butyltin iodide, bromide, or chloride in the presence of excess KF and PMHS is sufficient for complete hydrogen-for-halogen substitution. Tri-\(n\)-butyltin hydride formation depends on fluoride ion converting PMHS into a powerful reducing agent,\(^{18}\) one which is thought to contain hypervalent silicon atoms.\(^{17,19}\)

\[
Bu_3SnX + (MeSiHO)\_n \quad \text{PMHS} \xrightarrow{KF \quad Et_2O} \quad Bu_3SnH \quad (3)
\]

Another way in which the inexpensive, nontoxic PMHS generates tri-\(n\)-butyltin hydride is when it reacts with bis(tri-\(n\)-butyltin) oxide (Scheme 1).\(^{20-24}\) Not only is the Barton-McCombie reaction shown in eq 4 successful when \(Bu_3SnH\) is generated in this way, but recycling is rapid enough that only a catalytic amount (7.5 mol\%) of \((Bu_3Sn)\_2O\) is necessary for complete reaction.\(^{20}\) The reactions that describe the cycle for using and continuously refreshing the \(Bu_3SnH\) supply are given in equations 5 and 6. (For the reaction shown in eq 5 including \(BuOH\) as a cosolvent substantially increases the yield of \(Bu_3SnH\).\(^{20}\))
b. Reagents That Assist in Removing Tin-Containing Residues
(1). Potassium Fluoride

The difficulty in purification of a reaction mixture after organotin hydride reduction stems from the release of organotin compounds by slow hydrolysis of tin-containing byproducts during the chromatography that typically is part of product isolation.\textsuperscript{25} These tin-containing byproducts can be precipitated by addition of potassium fluoride to the reaction mixture after reaction is complete. The insoluble "polymeric" tin fluorides that form can be removed by filtration (eq 7).\textsuperscript{26-28}

\[
\text{Bu}_3\text{SnX} + \text{F}^- \rightarrow \text{Bu}_3\text{SnF} + X^- \quad (7)
\]

(2). Sodium Borohydride

Tin-containing residues also can be removed by treating a crude reaction mixture with sodium borohydride prior to chromatography. This treatment converts organotin compounds into tri-n-butyltin hydride and, thereby, eliminates their slow release from the chromatography column. Deoxygenated products then can be isolated in much purer form, and the regenerated $\text{Bu}_3\text{SnH}$ can be recovered in high yield.\textsuperscript{25}

B. Polymer-Supported Tin Hydrides

A different approach to solving problems created by tin-containing byproducts in radical reactions is to replace the tri-$n$-butyltin hydride with a polymer-supported, organotin hydride.\textsuperscript{29,30} Polymer-based reagents, such as 1, make purification of reaction mixtures much simpler because tin-containing materials can be removed by filtration; as a result, risks associated with exposure to organotin compounds are greatly reduced. Also, polymer-supported reagents such as 1 can be regenerated and used again.

Using polymer-supported reagents in catalytic amounts further reduces exposure to and contamination from tin-containing materials.\textsuperscript{31,32} In such reactions trimethoxysilane can serve as a source of hydrogen atoms to regenerate the spent polymer. When the level of tin residue in these reactions is compared to that in typical, organotin hydride reductions, the difference is striking. Dehalogenation of 1-bromoadamantane by the catalytic, polymer-based procedure yields a tin residue in the product of less than 26 ppm (the detection level), while reduction of the same compound with tri-$n$-butyltin hydride gives a product which, after chromatography, has a tin-residue level of 152,000 ppm. The product yields with the polymer-supported reagent are comparable to those from tri-$n$-butyltin hydride reactions.

Although the insolubility of polymer-supported reagents allows their simple removal from a reaction mixture, this insolubility creates other problems. The two-phase nature of reactions involving insoluble reagents can require long reaction times and large excesses of reagents and initiators.\textsuperscript{33} One way to overcome these problems is by using an
organotin hydride that is part of a noncross-linked, polystyrene polymer. This polymer is soluble in many organic solvents, does not require long reaction times, or need to be used in excess. Flash chromatography removes the polymer from the reaction mixture and reduces the tin-containing materials in the products to "minute" levels.33

C. Fluorous Tin Hydrides

Highly fluorinated organotin hydrides, such as compound 2, provide a different approach to solving the problems created by the use of tri-<i>n</i>-butyltin hydride.34 This new approach depends upon the solubility characteristics of highly fluorinated compounds in relation to typical organic and inorganic ones. Fluorocarbon liquids are extremely poor solvents for most organic and inorganic compounds but are excellent solvents for highly fluorinated compounds such as the tin hydride 2.35

Compound 2 is comparable in reactivity to tri-<i>n</i>-butyltin hydride, and its reaction products can be separated completely from nonfluorous compounds by partitioning the components of the reaction mixture between a fluorocarbon solvent (e.g., perfluoromethylcyclohexane) and a nonfluorocarbon solvent such as dichloromethane. (If water soluble compounds are present, the reaction mixture can be partitioned among three phases: water, dichloromethane, and perfluoromethylcyclohexane.) Following such partitioning, fluorous compounds (and only fluorous compounds) are dissolved in the fluorous phase and nonfluorous, organic compounds in the organic phase. Partitioning thus provides a simple procedure for separating various reaction products; in particular, it places 2 and tin-containing byproducts in the fluorous phase.

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