

(Bu₃Sn)₂-TBAF: a new combination reagent for the reduction and deuteration of aryl bromides and iodides†

David C. Harrowven,* Ian L. Guy and Michael I. T. Nunn

Department of Chemistry, University of Southampton, Southampton SO17 1BJ, UK.

E-mail: dch2@soton.ac.uk

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The combination of (Bu₃Sn)₂ and TBAF has been shown to reduce aromatic bromides and iodides in excellent yields under mild conditions. When the residual water in TBAF is exchanged for D₂O, the halogen is replaced by a deuterium atom.

The use of halides as both directing and protecting groups in aromatic chemistry is well established. They may be introduced, for example, to prevent the addition of an electrophile to a given carbon centre during aromatic substitution reactions or to control the

regiochemical course of directed *ortho*-metallation and photocyclisation reactions.^{1–3} Having served its function as a protecting/directing group, the halide may be further functionalised or removed by reduction. The latter is commonly achieved by metallation and protonation, though there are many alternatives.⁴ These include catalytic hydrogenolysis, reductive homolysis with a radical mediator such as tributyltin hydride, and reductions with various metal hydride reagents.⁴ In each case compatibility issues arise with polyfunctional substrates and these can be difficult to resolve.

Herein we report a new method for effecting the reduction of aromatic bromides and iodides using a combination of hexabutylditin and TBAF (or Bu₃SnH and TBAF). The method is mild and effective over a broad range of substrates (Table 1), is trivial to effect and generally proceeds in excellent yield. It also provides a convenient way of introducing deuterium at aromatic carbon centres.

The reaction was discovered during an attempt to effect the reduction of aldehyde **1** to alcohol **2** with the Shibata and Baba reagent combination of Bu₃SnH and TBAF.⁵ Unexpectedly, piperonyl alcohol **3** was observed as the major product of the reaction, showing that aryl iodides were also susceptible to reduction under the reaction conditions (Scheme 1). On further study it became apparent that tributyltin hydride served only as a precursor of hexabutylditin,⁶ and that that reagent, when used in conjunction with TBAF, was equally effective for the reduction of aryl iodides and bromides. The examples indicated in Table 1 are testament to the effectiveness of the new procedure. In each case products were attained in near quantitative yield and in a high state of purity following column chromatography using 10% KF/silica as the stationary phase.⁷

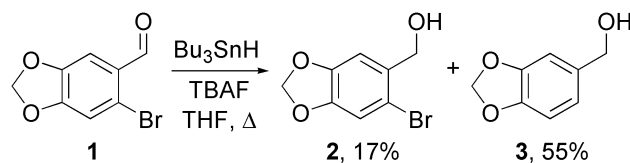
At this juncture we decided to probe the mechanistic course of the reaction. To test if free radical intermediates were involved we exposed *cis*-bromostilbene **20** to both the Bu₃SnH–TBAF and

Table 1 Reductions effected with (Bu₃Sn)₂-TBAF and Bu₃SnH-TBAF

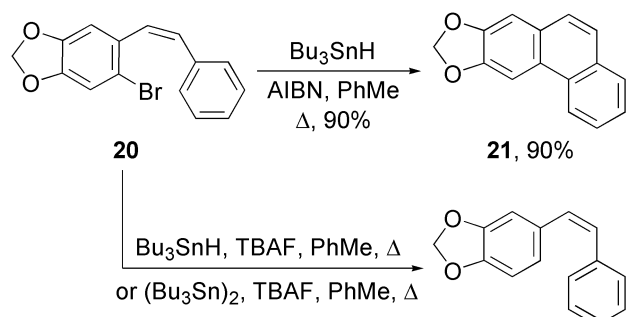
Entry	Halide	Product and yield
1		 5, 97% ^a [99%] ^b
2		 7, 90% ^a [98%] ^b
3		 9, 91% ^{a,b}
4		 11, 96% ^{a,b}
5		 13, 96% ^a [93%] ^b
6		 15, 96% ^a
7–9		 17, 98% ^{a,b} 18, 0% + 18, 95% 19, 0% + 19, 95%

^a Isolated yield using (Bu₃Sn)₂-TBAF. ^b Isolated yield using Bu₃SnH-TBAF.

† Electronic supplementary information (ESI) available: sample procedures for (Bu₃Sn)₂-TBAF; Bu₃SnH-TBAF and Bu₃SnH-TBAF, D₂O. See http://www.rsc.org/suppdata/cc/b4/b406103a/



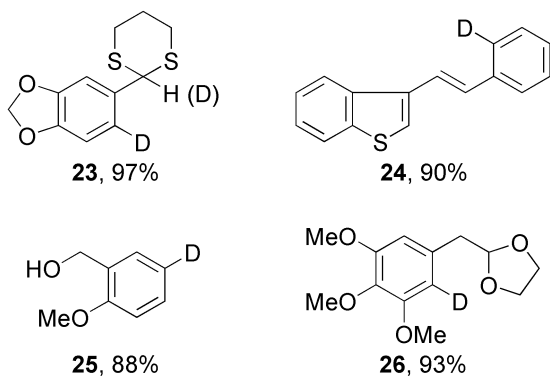
Scheme 1



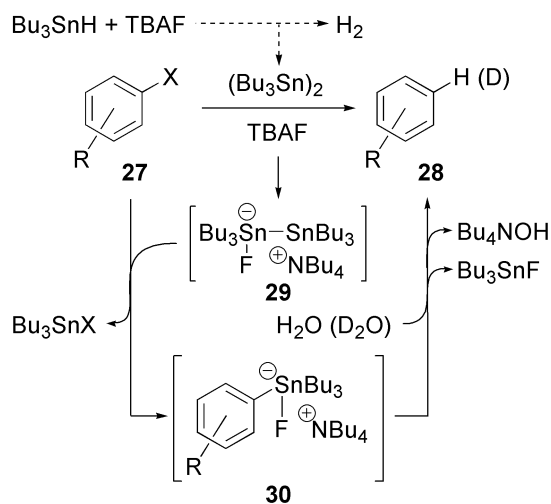
Scheme 2

hexabutyliditin–TBAF reagent combinations. In each case *cis*-stilbene **22** was formed rather than phenanthrene **21**, the product given under standard radical cyclisation conditions (Scheme 2).⁸

With a free radical mechanism negated, we concluded that the likely course of the reduction was halogen to metal exchange followed by protonation. To test that hypothesis, and in the hope of extending the method to deuteration, we exchanged the residual water in TBAF for D₂O and used that solution in reductions of **4**, **6**, **10** and **14**. Pleasingly, in each case the deuterated products, **23–26** respectively, were given in excellent yield. Analysis of **23** showed that deuteration had also occurred, to some extent, at C2 of the dithiane, implicating the formation of tetrabutylammonium hydroxide as a by-product.



Thus we postulate that hexabutyliditin and TBAF first interact to form **29**. Halogen to metal exchange follows producing tributyltin halide and the ate complex **30**. Protonation with water (or deuteration with D₂O) then gives **28** (Scheme 3). Our observation



Scheme 3

that aromatic chlorides and fluorides are inert to these reagent combinations (Table 1, entries 8 and 9) provides additional support in favour of this mechanism.

In summary, the reagent combination of hexabutyliditin and TBAF (or Bu₃SnH–TBAF) is effective for the reduction of aromatic bromides and iodides under mild conditions. The reaction is believed to proceed *via* halogen to metal exchange followed by protonation. It also provides a convenient method for deuteration of arenes—an extension that requires nothing more than to exchange the residual water in TBAF for D₂O. Notably, the reaction overcomes some of the limitations associated with classical methods of reducing aromatic halides, as exemplified by the conversion of **20** to **22**. No reduction of the *cis*-alkene was observed when using hexabutyliditin–TBAF (or Bu₃SnH–TBAF), a complication that arises with catalytic hydrogenolysis. Similarly, no products derived from radical cyclisation to the pendent arene were observed, offering an advantage with respect to homolytic reduction procedures.

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