

CONVENIENT PREPARATION AND MANIPULATION OF  $\text{Me}_3\text{SnH}$  FROM  $\text{Me}_3\text{SnCl}$ .  
FORMATION AND USE OF MIXED TRIMETHYLSTANNYL CUPRATES  
VIA TRANSMETALATION REACTIONS

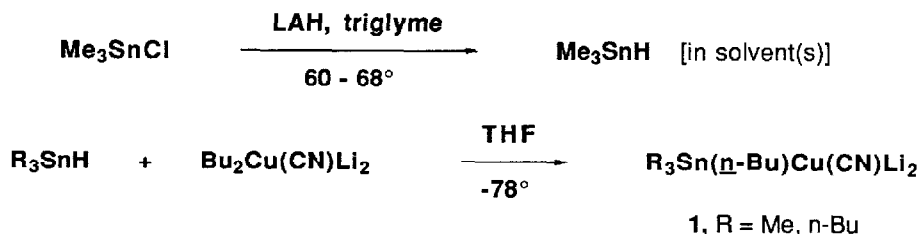
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**Abstract:** Details for the straightforward generation of  $\text{Me}_3\text{SnH}$  in either the neat state or in solution are presented. Treatment of  $\text{Me}_3\text{SnH}$  with a higher order cyanocuprate affords a mixed trimethylstannylcuprate which selectively delivers the  $\text{Me}_3\text{Sn}$  moiety to organic substrates. The process bypasses prior formation of  $\text{Me}_3\text{SnLi}$  from  $\text{Me}_3\text{SnCl}$ ,  $\text{Me}_3\text{SnH}$ , or  $(\text{Me}_3\text{Sn})_2$ .

In the course of developing new organometallic lynchpins for polyene construction via cuprate-mediated transmetalation reactions,<sup>[1]</sup> we required a mild method for specifically introducing the trimethylstannyl group ( $\text{Me}_3\text{Sn}-$ ) into a variety of substrates. Procedures which rely on formation of  $\text{Me}_3\text{SnLi}$  from  $\text{Me}_3\text{SnCl}$ ,<sup>[2]</sup> in our hands, were not as straightforward as implied, and for purposes of inclusion into cuprates requires titration prior to use. Hexamethylditin averts this shortcoming but is quite expensive and necessitates sacrificing half of this educt if an organolithium ( $\text{RLi}$ ) is used for cleavage to  $\text{Me}_3\text{SnLi} + \text{Me}_3\text{SnR}$ .<sup>[3,4]</sup> Reduction of  $(\text{Me}_3\text{Sn})_2$  with lithium metal is the alternative, more cost effective route to  $2\text{Me}_3\text{SnLi}$  from this distannane,<sup>[2,3]</sup> but such an option is rarely chosen based on a lack of convenience. In a recent report we demonstrated that tributyltin cuprates (assumed to be  $\text{R}_3\text{Sn}(\underline{n}\text{-Bu})\text{Cu}(\text{CN})\text{Li}_2$ , **1**,  $\text{R} = \underline{n}\text{-Bu}$ ) can be prepared in a trivial way by mixing  $\underline{n}\text{-Bu}_3\text{SnH}$  with  $\text{Bu}_2\text{Cu}(\text{CN})\text{Li}_2$  in THF at  $-78^\circ$  for 10 minutes.<sup>[5]</sup> Initially, the prospect of substituting  $\text{Me}_3\text{SnH}$  for  $\underline{n}\text{-Bu}_3\text{SnH}$  in this context was rather unappealing, especially in light of the known toxicity of this volatile material.<sup>[6]</sup> We felt, however, that if a simple, safe procedure could be developed for generating  $\text{Me}_3\text{SnH}$  such that a minimum number of operations would be involved and the hydride formed could be conveniently handled neat or in a solvent(s) of one's choosing, then the benefits associated with the cuprate transmetalation<sup>[5]</sup> to form **1**,  $\text{R} = \text{Me}$ , could be applied to our goal. We now describe a streamlined protocol for generating  $\text{Me}_3\text{SnH}$  from  $\text{Me}_3\text{SnCl}$ , along with the formation and subsequent reactions of this novel mixed stannylcuprate  $\text{Me}_3\text{Sn}(\underline{n}\text{-Bu})\text{Cu}(\text{CN})\text{Li}_2$ .



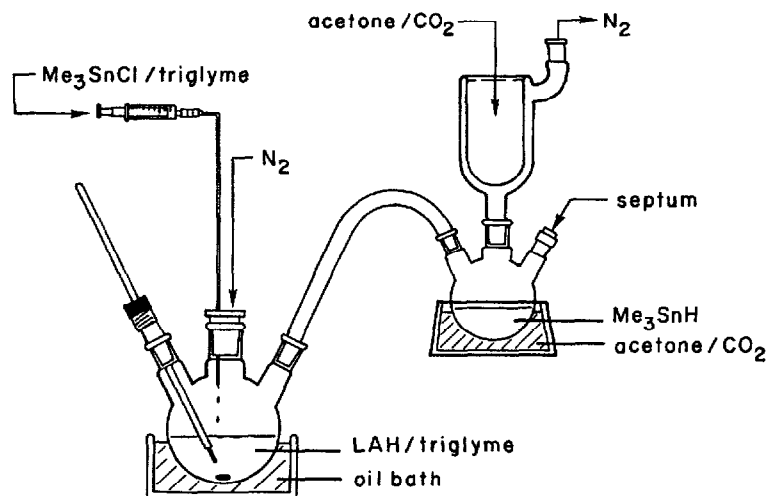


Figure 1. Experimental design for generation and collection of  $\text{Me}_3\text{SnH}$ .

Table I. Reactions of  $\text{Me}_3\text{Sn}(\underline{n}\text{-Bu})\text{Cu}(\text{CN})\text{Li}_2$  in THF with representative substrates.

Entry	Educt	Conditions	Product(s)	Yield(%) <sup>a</sup>
1		1.2 eq -78°, 30 min		83
2		1.3 eq -78°, 30 min		81
3		1.7 eq -78° to rt, 30 min		94
4		2.5 eq -78°, 30 min		89 <sup>b</sup>
5		1.7 eq -78°, 30 min		66

<sup>a</sup>All yields refer to isolated, chromatographically pure materials. <sup>b</sup>Ratio determined by capillary GC.

Conversion of  $\text{Me}_3\text{SnCl}$ <sup>[7]</sup> to  $\text{Me}_3\text{SnH}$  can be *routinely* carried out on a 5 to 25g scale using the experimental set-up illustrated in Figure 1.<sup>[8]</sup> A slurry of LAH in warm triglyme under  $\text{N}_2$  is prepared to which is added slowly, preferably by syringe pump, a concentrated solution of  $\text{Me}_3\text{SnCl}$  in triglyme. The  $\text{Me}_3\text{SnH}$  is collected in a connected adjacent flask cooled to  $-78^\circ$  to which is affixed a cold finger condenser also maintained at  $-78^\circ$ . Although operationally simple, especially critical for success are the following points of information: (1) the internal temperature of the LAH/triglyme solution should not exceed  $68^\circ$ ;<sup>[9]</sup> (2) triglyme is ideal for this process since (in addition to being relatively inexpensive versus diglyme or tetraglyme<sup>[10a]</sup>) only trace amounts co-distill; hence, a second distillation/fractionation is not required;<sup>[10b]</sup> (3) efficient trapping of  $\text{Me}_3\text{SnH}$  occurs at  $-78^\circ$ , but not at other higher temperatures (e.g., those obtained with a water-cooled condenser).

Once the  $\text{Me}_3\text{SnH}$  is accumulated, it can be transferred to a flask or ampoule for storage as a neat liquid,<sup>[10]</sup> or alternatively dissolved in one or more solvents and used immediately. Since for our purposes the presence of trace quantities of an etherial "impurity" (i.e., triglyme) is of no consequence for the ensuing transmetalation, (all or part of) the  $\text{Me}_3\text{SnH}$  (2 equiv) so formed is then added *via* syringe directly to a  $-78^\circ$  solution of  $\underline{n}\text{-Bu}_2\text{Cu}(\text{CN})\text{Li}_2$  (1 equiv) in THF.<sup>[11]</sup> After 30 minutes at this temperature, substrate is introduced and the reaction is quenched upon completion (with 10%  $\text{NH}_4\text{OH}$  / sat. aqueous  $\text{NH}_4\text{Cl}$ ). Representative examples are listed in Table I and reflect the selective transfer of the trimethylstannyl group over the  $\underline{n}$ -butyl ligand from  $\underline{1}$ ,  $\text{R} = \text{Me}$ .<sup>[12]</sup>

In summary, an expedient means of arriving at  $\text{Me}_3\text{SnH}$  which minimizes handling yet maximizes flexibility for subsequent usage is described. Direct incorporation of the  $\text{Me}_3\text{Sn}$  residue into a higher order mixed cuprate then follows by way of transmetalation schemes. This valued moiety can then be selectively and efficiently delivered into organic substrates using substitution, stannylcupration, and conjugate addition coupling reactions.

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## References and Notes

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6. Pereyre, M., Quintard, J.-P., Rahm, A., in "Tin in Organic Synthesis", Butterworths, London, 1987. For a number of other uses of this group, see "Organotin Compounds in Organic Synthesis", Tetrahedron Symposia-in-Print Number 36, Yamamoto, Y., Ed., 1989.
7.  $\text{Me}_3\text{SnCl}$  was prepared from  $\text{Me}_2\text{SnCl}_2$  according to the following procedure based on a modification of a US patent (no. 4,282,165; August 4, 1981). A 300 mL flask was charged with 79.3 g (361 mmol) of  $\text{Me}_2\text{SnCl}_2$ , 20.03 g (359 mmol) of Fe filings (Fisher Scientific, ca. 40 mesh) and 10 mL (555.5 mmol) of  $\text{H}_2\text{O}$ . A catalyst consisting of 3.14 g (12.02 mmol) of  $\text{Ph}_3\text{P}$  dissolved in 15 mL THF and 1.4 mL (11.85 mmol) of  $\text{SnCl}_4$  was poured into the flask and the mixture vigorously refluxed for 1.5 h. Distillation at 60-84° gave THF, followed by a fraction collected between 90-140°. When distillation slowed, the pot was cooled and 55 mL of  $\text{H}_2\text{O}$  were added. Resumption of distillation gave an additional fraction boiling between 90-105° containing  $\text{Me}_3\text{SnCl}$  and water. The two distillates were combined to which was added ether (60 mL) and excess saturated aqueous NaCl solution. The ethereal layer was separated and dried over  $\text{Na}_2\text{SO}_4$ . Distillation of the more volatile solvents at atmospheric pressure left behind 46.21 g of  $\text{Me}_3\text{SnCl}$  which was used as obtained. Both  $\text{Me}_2\text{SnCl}_2$  (in bulk) and the patent were provided by Dr. M. Fisch and Mr. O. Loeffler of the Argus Chemical Company.
8. The procedure involves the following: Two dry 3-necked flasks were arranged as shown in Figure 1. To the 250 mL flask was added 4.74 g (124.8 mmol) of LAH and 70 mL of dry triethylene glycol dimethyl ether (triglyme). The suspension was heated to 60-62° and 24.68 g (111.6 mmol) of trimethyltin chloride in 10 mL triglyme were added *via* syringe pump over 3h (10 mL/h) such that the pot temperature was maintained between 62-68°. Upon completion of addition, the mixture was stirred for an additional 30 minutes. Collected in the 100 mL flask were 14.92 g (81%)  $\text{Me}_3\text{SnH}$  consisting of trace amounts of triglyme as determined by  $^1\text{H}$  NMR. Although not necessary for our purposes, a second distillation removes residual triglyme. The  $\text{Me}_3\text{SnH}$  was transferred *via* cannula to a dry flask under argon for storage;  $^1\text{H}$  NMR (benzene- $d_6$ )  $\delta$  4.75 (m, 1H), 0.05 (s, 9H,  $^2J_{\text{SnH}} = 58$  Hz).
9. Yields of  $\text{Me}_3\text{SnH}$  dropped considerably if the pot temperature was allowed to drift continuously above ca. 75°.
10. (a) Kuivila, H.G., Dixon, J.E., Maxfield, P.L., Scarpa, N.M., Topka, T.M., Tsai, K.-H., Wursthorn, K.R., *J. Organomet. Chem.*, **1975**, 86, 89; (b) Fish, R.H., Kuivila, H.G., Tyminski, I.J., *J. Am. Chem. Soc.*, **1967**, 89, 5861.
11. Lipshutz, B.H., *Synthesis*, **1987**, 325; Lipshutz, B.H., Wilhelm, R.S., Kozlowski, J.A., *Tetrahedron*, **1984**, 40, 5005. The ratio of  $\text{Me}_3\text{SnH}$  to  $n\text{-Bu}_2\text{Cu}(\text{CN})\text{Li}_2$  used in all cases was 2:1.
12. All new compounds were fully characterized by IR, NMR, MS, and HRMS analyses.

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