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A Practical One-Pot Synthesis of Vinylstannanes from Ketones

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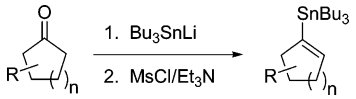

Treatment of ketones with Bu_3SnLi followed by addition of $MsCl/Et_3N$ to the resulting alkoxide provides vinylstannanes. Cyclic vinylstannanes are particularly amenable to this procedure and isolated yields of 81−83% could be consistently attained. Traces of Bu_3SnH in crude reaction products could be removed by stirring in $CHCl_3$ with a catalytic amount of AIBN followed by filtration through silica gel.

Vinylstannanes have enjoyed widespread popularity as synthetic intermediates.[1] They are useful in palladium-catalyzed (Stille) couplings,[2,3] as precursors to vinylanions,[4] and in other processes.[5] Vinylstannanes have been prepared most commonly by hydrostannation,[6,7] by stannylmetalation[8] or hydrometalation/stannylation[9] of alkynes, or from carbonyl compounds. Methods of preparation from carbonyl compounds include enol triflate formation followed by substitution with a stannyl copper reagent[10] or Pd-catalyzed coupling with R_3SnSnR_3,[11] hydrazone formation followed by base-induced (Shapiro) fragmentation and trapping with R_3SnCl,[12] and addition of Bu_3SnLi followed by conversion of the stannyl alcohol to an iodide and E_2 elimination (Scheme 1).[13] A one-pot conversion of carbonyl compounds to vinylstannanes involving addition of $Bu_3SnMgCl$, conversion to sulfamates, and subsequent thermolysis has been reported, but yields are typically modest and this method has not been widely adopted.[14] Other preparative methods have also been developed.[15] While each of the routes from carbonyl compounds provides vinylstannanes in relatively few steps, each involves the isolation of an intermediate or a step that may be low-yielding. In pondering a simplified route to vinylstannanes, we wondered if it might be possible to just add Bu_3SnLi to a carbonyl compound, then convert the alkoxide to a good leaving group and perform an E_2 elimination in situ. We now report that this approach is an excellent method to prepare vinylstannanes from ketones, particularly cyclic ones.

Initial experiments involved addition of Bu_3SnLi[16] (Bu_3SnH/LDA, THF, −78 °C) to cyclohexanone to afford the expected hydroxystannane in high (93%) yield after aqueous workup (eq 1). It is known that such compounds are not particularly stable, so the crude hydroxystannane was treated immediately with MsCl and Et_3N (THF, −78 °C to room temperature). We were delighted to find that elimination occurred cleanly to afford the desired vinylstannane **2a** in 97% yield.

We then developed a one-pot procedure wherein the intermediate alkoxide was not quenched with water but was treated directly with $MsCl/Et_3N$. When 1−2 equiv of MsCl was employed, incomplete reactions were observed; however, the

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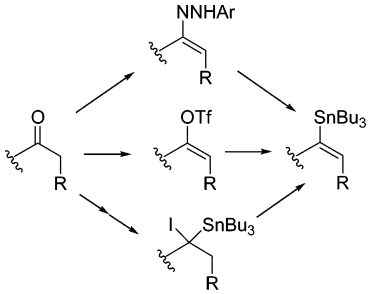
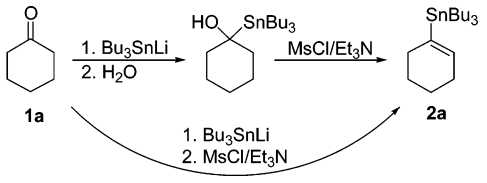
SCHEME 1



use of excess (4 equiv) MsCl allowed for complete consumption of the intermediate alkoxide and stannane **2a** could be isolated in 85% yield. The requirement for excess MsCl is likely due to competitive reactions with diisopropylamine (from LDA used to generate Bu_3SnLi) and Et_3N,[17] but since MsCl is relatively inexpensive and the polar byproducts were easily removed by partitioning between hexane (nonpolar stannanes) and acetonitrile (polar materials), this was not considered to be a significant drawback.

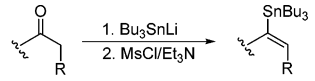


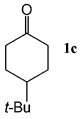
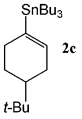
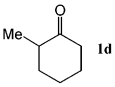
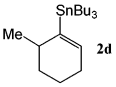
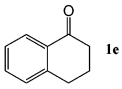
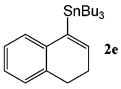
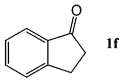
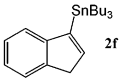
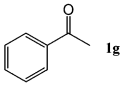
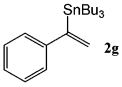
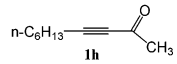
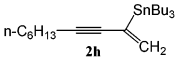
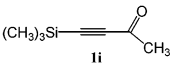
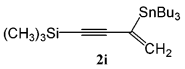
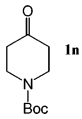
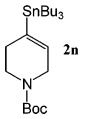
(1)

Other ketones were subjected to this one-pot protocol (Table 1). In general, the corresponding vinylstannane could be isolated in good to excellent yields. The reactions were quite clean, and the only tin-containing materials in the crude reaction mixture (after a hexane/acetonitrile partition) were the desired vinylstannane and traces of Bu_3SnH. For vinylstannanes containing functionalities other than hydrocarbon residues (e.g., entries 12−14), this very nonpolar impurity was easily removed by silica gel chromatography. Other vinylstannanes, having R_f values close to 1.0 on silica gel even with hexane as eluant, presented much more of a challenge for purification. A number of methods have been developed for the removal of organotin residues, but these are intended primarily for the removal of tributyltin halides[18] and were not applicable here. Fortunately, we found that crude reaction mixtures could be stirred in warm chloroform containing a catalytic amount of azobis(isobutyronitrile), AIBN, to convert the nonpolar impurities into polar materials while leaving the vinylstannanes unaffected.[19] Pure vinylstannanes could then be isolated by simple filtration through silica gel. Alternatively, C18 silica, as recommended by Farina,[20,21]could be used without pretreatment of the sample.

For the cyclic ketones examined, yields were consistently ~80−83% regardless of ring size (5 or 6), conjugation with an aromatic ring, whether the ring is carbocyclic or heterocyclic, and the scale of the reaction (1 to 15 mmol). In most cases, only one vinylstannane is possible. In the case of 2-methylcyclohexanone (**1d**), only the less substituted isomer **2d** is

TABLE 1. Synthesis of Vinylstannanes from Ketones



Entry	Ketone	Stannane	Yield of **2** (%)[a]
1	 **1a**	 **2a**	82
2	 **1b**	 **2b**	83
3	 **1c**	 **2c**	81
4	 **1d**	 **2d**	81
5	 **1e**	 **2e**	80
6	 **1f**	 **2f**	81
7	 **1g**	 **2g**	88
8	 **1h**	 **2h**	91
9	 **1i**	 **2i**	72
10	 **1j**	 **2j**	78
11	 **1k**	 **2k**	61
12	 **1l**	 **2l**	75
13	 **1m**	 **2m**	79
14	 **1n**	 **2n**	80

[a] Isolated yields of purified products.

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(19) This procedure was inspired by the serendipitous observation that attempts to record NMR spectra of Bu_3SnH in $CDCl_3$ invariably showed Bu_3SnCl and $CHDCl_2$. We now use C_6D_6: Darwish, A.; Chong, J. M. *Synth. Commun.* **2004**, *34*, 1885−1890.

(20) Farina, V. *J. Org. Chem.* **1991**, *56*, 4985−4987.

(21) C18 (reverse phase) silica is readily available but expensive. It can be made by a simple procedure (Evans, M.B. *Chromatographia*, **1980**, *13*, 5−10.), and columns may be used multiple times.

observed.[22] This regiochemistry may arise from predominantly axial attack of Bu_3SnLi on **1d**, which would situate the mesyloxy group and methine proton *cis* to each other;[23] E_2 (anti) elimination could then occur only with one of the methylene protons and regioisomer **2d** would be produced.

Aryl methyl ketones such as acetophenone also worked well (entry 7), as did alkynyl methyl ketones (entries 8 and 9). However, propiophenone gave low yields of a mixture of stereoisomers (Z:E = ~5:1) and was not further investigated. 2-Tetralone did not give any vinylstannane, likely due to competing enolization. Similarly, camphor proved to be highly resistant to addition of Bu_3SnLi. Bu_3SnLi added well to aliphatic aldehydes but treatment of the alkoxides or alcohols with MsCl/Et_3N did not provide vinylstannanes but rather unidentified materials, possibly α-chlorostannanes arising from displacement rather than elimination of the intermediate mesylates.[24]

Dialkyl ketones were also examined, but satisfactory results were obtained only for acetone (entry 10) and methyl isopropyl ketone (**1j**, entry 11). As in the case of 2-methylcyclohexanone (**1d**), only the less substituted vinylstannane from ketone **1j** was observed. With 2-hexanone, where there is less steric differentiation between the alkyl groups, mixtures of regioisomers (~2:1 in favor of the less substituted isomer) that were deemed to be not synthetically useful were formed.

Interestingly, it was found that acyclic dialkyl ketones required the use of relatively fresh bottles of *n*-BuLi (used to prepare LDA for Bu_3SnLi generation) to obtain good yields. This sensitivity was not observed for any of the cyclic ketones, alkyl aryl ketones, or alkyl alkynyl ketones examined. We surmise that traces of alkoxides in older bottles of *n*-BuLi may be responsible for inducing side reactions that some classes of ketones are more susceptible to.

Overall, we have developed a simple one-pot procedure for the preparation of vinylstannanes from ketones. Classes of ketones that are good substrates for this procedure as well as those that are not amenable to this chemistry are delineated. Yields compare very favorably with overall yields obtained using other routes, reagents are inexpensive and readily available, and the procedure is operationally straightforward. We have also developed a simple purification procedure for "hydrocarbon only" vinylstannanes that is applicable on multigram scales. This route to vinylstannanes should be very useful for preparing these versatile building blocks.

Experimental Section

Representative Procedure for Preparation of Vinylstannane 2a. To a cold (0 °C) stirred solution of diisopropylamine (2.29 mL, 1.65 g, 16.3 mmol) in THF (80 mL) was added *n*-BuLi (1.6 M in hexanes, 10.1 mL, 16.2 mmol). The solution was stirred at 0 °C for 10 min, then Bu_3SnH (4.00 mL, 4.33 g, 14.9 mmol) was added, and the resulting yellow solution was stirred at 0 °C for an additional 10 min. The solution was then cooled to −78 °C, and cyclohexanone (**1a**, 1.43 g, 14.6 mmol) dissolved in THF (3 mL) was added dropwise. After 10 min, Et_3N (15.4 mL, 11.2 g, 110 mmol) and MsCl (4.6 mL, 6.8 g, 59 mmol) were added. The reaction mixture was then allowed to warm to room temperature. After 30 min at room temperature, hexanes (300 mL) was added, and the organic layer was washed with CH_3CN (3 × 100 mL). Concentration of the hexanes layer provided crude vinylstannane, which was dissolved in 80 mL of $CHCl_3$ containing AIBN (0.1 g). The solution was stirred at 40 °C, and the disappearance of Bu_3SnH was monitored by ^{13}C NMR spectroscopy. After 4 h, no Bu_3SnH remained. Volatiles were removed, and the residue was chromatographed on silica gel (50 g, hexanes/ether, 7:1) to provide vinylstannane **2a** (4.43 g, 82%). Spectral data was consistent with that previously reported:[10,12,14,15a,b] ^1H NMR δ 5.78 (1H, s, J_{Sn-H} = 68.9 Hz), 2.70 − 2.50 (4H, m), 2.14 − 2.04 (4H, m), 1.54−0.82 (27H, m).

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Supporting Information Available: General experimental procedures and spectral data for stannanes **2a**−**2n**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(22) Exclusive formation of **2d** was also reported for the pyrolysis of the corresponding stannyl acetate (ref 15b).

(23) It has previously been shown that addition of Bu_3SnLi to 4-*tert*-butylcyclohexanone under the same conditions (THF, −78 °C) proceeds with an axial:equatorial selectivity of 93:7: Sawyer, J. S.; Kucerovy, A.; Macdonald, T.; McGarvey, G. J. *J. Am. Chem. Soc.* **1988**, *110*, 842−853. Structural assignments were based on ^{13}C NMR data of MOM ethers with the major (axial) isomer showing a lower field quaternary carbon (87.8 vs 80.9 ppm) and smaller $^3J_{Sn-C}$ (<3 vs 40 Hz) compared to the equatorial isomer. With ketone **1d**, we observed a 95:5 mixture of diastereomers when the intermediate hydroxystannanes were isolated as their MOM ethers. Here the quaternary carbon of the major (axial) isomer appears at 93.9 vs 85.8 ppm for the equatorial isomer and the axial isomer also exhibits significantly smaller $^3J_{Sn-C}$ (~0 vs 35−40 Hz).

(24) Seitz, D. E.; Carroll, J. J.; Cartaya, M.; Claudia, P.; Lee, S. H.; Zapata, A. *Synth. Commun.* **1983**, *13*, 129−134.