A New Tin Mediated Pummerer Synthesis of Vinyl Stannanes

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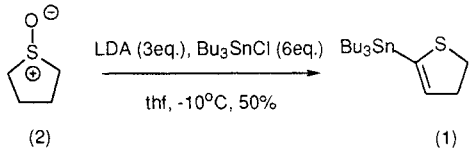
Dedicated to Professor Dieter Seebach on the occasion of his 60th birthday

Abstract: Treatment of a range of sulfoxides with 3 equivalents of LDA and 6 equivalents of tri-n-butyltin chloride yields the corresponding α-tributylstannyl vinyl sulfides in good yield. When a *tert*-butyl sulfoxide is used the α-tributylstannyl vinyl sulfide is isolated as a single geometric isomer.

Vinyl stannanes have emerged as highly useful building blocks in organic chemistry[1]. In particular, palladium catalysed coupling reactions[2] of vinyl stannanes have led to their use as key intermediates in a number of complex natural products synthesis[3]. As part of a project directed towards the total synthesis of 4'-thionucleosides we have previously prepared 4,5-dihydro-2-tributylstannylthiophene (1) from γ-thiobutyrolactone[4]. The vinyl stannane (1) was shown to undergo smooth tin-lithium exchange to give the corresponding vinyllithium, which could be quenched with a range of aldehydes and ketones.

In this letter, we wish to report a one pot synthesis of the key vinyl stannane (1) from tetramethylene sulfoxide (2) *via* novel tin mediated Pummerer chemistry, and the extension of this method to a general synthesis of α-tri-*n*-butylstannyl vinyl sulfides. In 1984, Miller and Hassig reported an interesting silicon mediated Pummerer type conversion of tetramethylene sulfoxide (2) to 4,5-dihydro-2-trimethylsilylthiophene. Thus, treatment of the sulfoxide (2) with 3 equivalents of LDA and 6 equivalents of trimethylsilyl chloride at -10 °C gave the α-trimethylsilyl vinyl sulfide in good yield[5].

We have found that replacement of trimethylsilyl chloride with tri-*n*-butyl tin chloride gives the corresponding α-tributylstannyl vinyl sulfide in good yield. The reaction is experimentally very simple; it can be carried out in one pot and on a large scale (Scheme 1). The product was purified by chromatography on neutral alumina (grade 2).

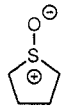
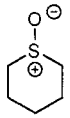
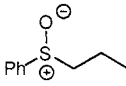
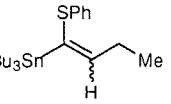
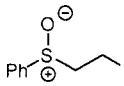
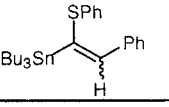
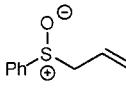
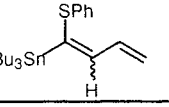
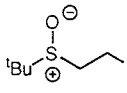
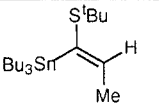
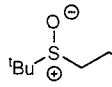
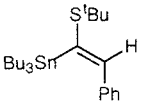
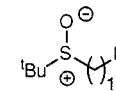
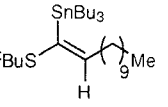


Scheme 1

To the best of our knowledge this is the first example of the use of tri-*n*-butyltin chloride as an activator in a Pummerer type reaction and the first use of the Pummerer reaction[6] in the synthesis of functionalized vinyl stannanes[7]. Quayle and coworkers have reported a "tin-Pummerer" reaction; however, in this case the substrate contained a vinyl tri-*n*-butyl group which was lost during the reaction[8]. The synthesis of α-trimethylstannyl vinyl sulfides has been previously reported by Seebach and coworkers[9]. They were prepared *via* a Peterson olefination between the lithio anion of (methylthio)(trimethylsilyl)(trimethylstannyl)methane and the appropriate carbonyl compound, yielding the product as mixtures of the *E* and *Z* isomers.

We have explored the scope of this reaction by investigating the use of other sulfoxide substrates to generate the corresponding α-tributylstannyl vinyl sulfides. The results are summarized in the Table below.

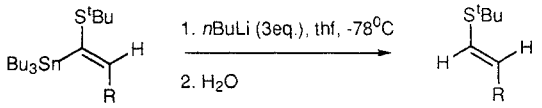
Table. Preparation of vinyl stannanes from sulfoxides

Entry	Sulfoxide	Product	*E*/*Z*	% Yield
1			–	50
2			–	43
3			–	85
4			1:1	75
5			1:1	60
6			1:1	67
7			>20:1	70
8			>20:1	30
9			>20:1	65

The first two sulfoxides (entries 1 and 2) yielded the corresponding the vinyl stannanes in modest yield when 3eqs of LDA and 6eqs of Bu_3SnCl were used. In addition, unstable by-products were isolated which were tenatively identified as bis-(stannylated) materials by NMR; however, these were unstable and decomposed rapidly. When the 2eqs of LDA and 3eqs of Bu_3SnCl were used, the reaction was much cleaner giving the vinyl stannane as the sole product in a lower yield of 35%.

Entries 3-6 used a thiophenol derived sulfoxide, and gave the corresponding α-tributylstannyl vinyl sulfides as a mixture of the two geometric isomers. However, when *tert*-butyl derived sulfoxides were the substrates (entries 7-9), the α-tributylstannyl vinyl sulfides were

formed as **single geometric isomers** as indicated by ^{1}H-NMR (> 20:1). The configuration of the products was established by conversion of vinyl stannanes (entries 8,9) to the corresponding vinyllithium by tin-lithium exchange, using an excess of *n*BuLi. The corresponding vinyllithiums were quenched with water to give the vinyl sulfides in quantitative yield (Scheme 2).



Scheme 2

Measurement of the coupling constant for the product vinyl sulfide when R = Ph and $(CH_2)_9CH_3$ (entries 8 and 9) gave J = 15.7 and 15.1 Hz respectively, indicating that in each case the *E* product had been isolated. Therefore, the starting vinyl stannane also possessesd the *E* configuration. We have previously shown that vinyl stannane (1) undergoes tin-lithium exchange and the resulting vinyl anion can be trapped with aldehydes and ketones to give the corresponding cyclic trisubstituted vinyl sulfides[4]. The high degree of selectivity in the formation of α-tributylstannyl *tert*-butyl vinyl sulfides should allow for the preparation of trisubstituted vinyl sulfides (and hence trisubstituted vinyl sulfoxides and sulfones) as single geometric isomers.

We attempted to optimise the reaction when using thiophenol and *tert*-butyl derived sulfoxides by reducing the amounts of LDA and Bu_3SnCl used, but found a drop in yield when the quantities of either of these reagents was changed.

We are currently investigating the mechanism of this reaction and applications of these novel and versatile building blocks in the synthesis of natural products.

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   DeLucchi, O.; Miotti, U.; Modena, G. *Org. React.*, **1991**, *40*, 157.
7. General Procedure: Preparation of 1-phenylthio-1-(tributylstannyl)ethene.
   To a stirred solution of phenyl ethyl sulfoxide (0.200g, 1.30 mmol) in dry thf (10 ml) cooled to -10 °C under nitrogen, was added LDA (3.90 mmol, 2.0M in heptane/thf/ethylbenzene, purchased from Aldrich). The solution was stirred for 10 minutes before neat Bu_3SnCl (2.30 ml, 7.8 mmol) was added. The reaction mixture was stirred for 1 hour whilst it was allowed to warm to 0 °C. The mixture was partitioned between water (10 ml) and CH_2Cl_2 (10 ml). The aqueous layer was extracted with CH_2Cl_2 (2 x 10 ml) and the combined organic extracts were dried over $MgSO_4$. The solvent was removed *in vacuo* to give a yellow oil. The crude product was purified by column chromatography (neutral alumina, eluting with petroleum ether) to give the vinyl stannane (0.47g, 85%) as a colourless oil. υ_{max} (film, cm^{-1}) 3060, 2960, 2930, 2880, 2860, 1580, 1560, 1460, 1440, 1380, 1070, 1020, 870.
   δ_H($CDCl_3$ 200MHz) 0.95 (9H, m), 1.15-1.65 (18H, m), 5.20 (1H, s, H *cis* to tin), 5.50 (1H, s, H *trans* to tin), 7.20-7.55, (5H, m, aromatic).
   (m/z, CI, NH_3) 427 (M+ H)$^+$. $C_{20}H_{35}S^{116}Sn$ requires [M+H]$^+$ 423.14769, found 423.14838.
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