

A ROUTE TO THE PREPARATION OF γ -HYDROXYVINYLSTANNANES

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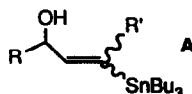
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Abstract: A series of propargyl alcohols bearing alkyl, aryl, silyl and stannyl groups on the acetylene were hydrometalated using Cp_2TiCl_2 and isobutylmagnesium bromide and the resulting Grignard reagents trapped with Bu_3SnCl .

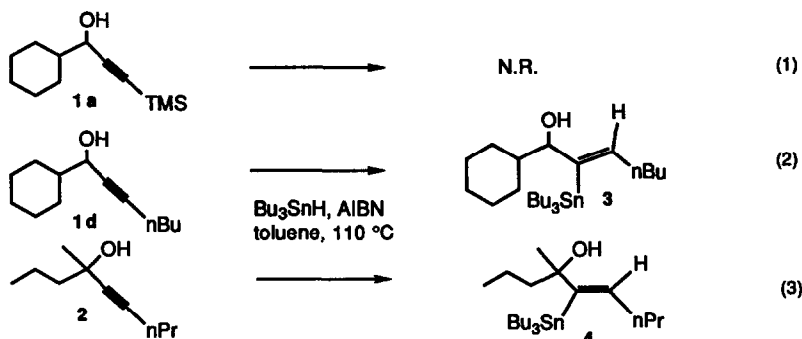
Vinylstannanes have become extremely versatile intermediates in organic synthesis.² For example, Stille has elegantly demonstrated the generality of palladium catalyzed coupling reactions between a vinyltin compound and a variety of electrophiles such as, aryl halides, acid chlorides, vinyl halides and vinyl triflates.³

There are several methods commonly employed for the preparation of vinylstannanes including: the stannylcupration of an acetylene and subsequent trapping with an electrophile, or the trapping of a vinyl lithium species (generated from a Shapiro reaction) with a tin halide.² (E)- γ -Hydroxy vinylstannanes are prepared by stereoselective addition of tributyltin hydride to a terminal propargyl alcohol.⁴ Fujita has also published a route to these compounds which involves the Michael addition of tributylstannyl lithium to a β -stannyl or β -silyl substituted vinyl sulfone and subsequent reaction of the carbanion with an aldehyde.⁵ The Z-isomer is also readily available through the trapping of an aluminum species with tributylstannyl triflate.⁶

Most of the existing methods have not been applied to the synthesis of highly substituted vinyltin derivatives and thus, a need exists for synthetic methods which permit the preparation of γ -hydroxyvinylstannanes of general structure A bearing a variety of R and R' groups. As a consequence of several ongoing synthetic projects in our laboratory, we had need for the synthesis of these derivatives and thus a study was undertaken to find a convenient and general method for their synthesis. In this paper we describe a simple entry into these compounds.

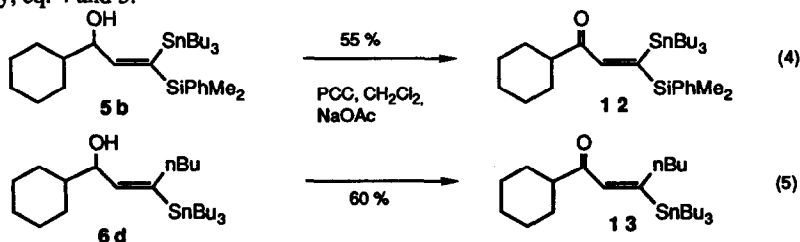


Our initial experiments focused on the reaction of substituted acetylenes **1a,d** and **2** with tributyltin hydride in the presence of AIBN, eq. 1-3. The regioselectivity of addition in hindered secondary and tertiary alcohols of this type was not known.⁷ In spite of several different reaction conditions, no reaction was observed with **1a** even when it was heated in neat tributyltin hydride at temperatures up to 180 °C. However, **1d** and **2** reacted with tributyltin hydride at 80-90 °C in toluene providing **3** and **4** in 77% and 46% yields respectively. The stereochemistry of the addition was readily apparent from the ¹H NMR spectra which showed a (³J_{Sn117-H}) coupling constant of 125-140 Hz, fully in accord with a Z geometry and overall trans addition of tin hydride.⁸



In light of these results and our interest in preparing the regioisomeric stannanes, we turned our attention to attempting to modify a reaction first reported by Sato⁹ who showed that: 1) titanium complexes catalyze the regio- and stereoselective hydromagnesiation of a propargyl alcohol and 2) the resulting vinylmagnesium reagent can be trapped with reactive alkyl halides or a proton.¹⁰ We found that tributyltin chloride is also an extremely good electrophile toward the intermediate Grignard species and very good yields of the vinylstannanes arise through the use of this sequence. Several examples are shown in Table 1.¹¹ The results indicate that 1°, 2°, and 3° alcohols are reactive and exhibit high regioselectivity toward the position distal from the alcohol. The initial hydrometallation reaction is best performed in ether while the stannylation is much more facile in THF.¹² The stereochemistry of the β -stannyl olefins was also determined by examination of the ¹¹⁷Sn-H coupling constant; when the proton and tin were cis $J= 50\text{-}80$ Hz and $J= 95\text{-}155$ Hz when they were trans.

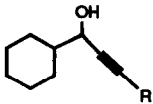
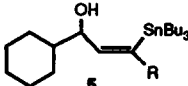
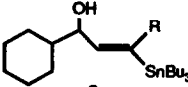
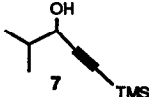
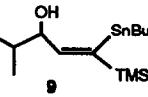

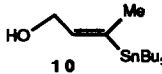
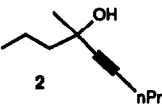
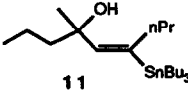
Several of the results are noteworthy. An acetylenic C-Sn bond is stable under the reaction conditions and subsequent stannylation gives a 1,1-distannyl olefin. Following the initial hydrometallation, the intermediate appears to undergo an isomerization from the *Z* to the more stable *E* Grignard species before being trapped with the tin halide. This result was easily demonstrated by trapping the initial magnesium species with a proton instead of a tin halide.¹³ Novel stannyl-silyl and distannyl¹⁴ compounds are readily available using this methodology (entries 1a-c, 2). Alkyl and aryl substituted acetylenes do not isomerize and give the *E* isomer with very high selectivity (>95 %) regardless of the steric hindrance of the group attached to the acetylene.¹⁵ Adducts 5, 6, 9, and 10 are closely related to the *Z*- β -stannyl enones recently reported to arise from a palladium catalyzed addition of hexamethylditin to an ynone or ynal.¹⁶ When we subjected the products from the titanium catalyzed reaction 5b and 6d to oxidation with PCC, we obtained the *Z*- or *E*- β -stannyl enones depending on their initial stereochemistry, eq. 4 and 5.



For the case when R = alkyl, oxidation gave β -stannyl enones of opposite configuration to those obtained

using Piers' methodology and thus an entry into these compounds is in hand. The $^3\text{J}_{117\text{Sn-H}}$ was 139.6 Hz for 12 and 65.5 Hz for 13 confirming that no isomerization had occurred during oxidation.

Table 1 Titanium Catalyzed Hydrostannylation of Propargyl Alcohols

Entry	Propargyl Alcohol ¹	Time(T ₁ , T ₂) ²	Product ²	Yield ^{3,4}
1				
	a R = TMS	3.5h, 4h	5	67%
	b R = SiPhMe ₂	3h, 2h		73%
	c R = SnBu ₃	2h, 1h		75%
	d R = n-Bu	6h, 2h		75%
e R = Ph	1h, 1h		72%	
2				
	7	4.5h, 4h	9	72%
3		3h, 2h ⁵		50% ⁶
8			10	
4		2h, 1h		79%
2			11	

1. Propargyl alcohols prepared by addition of an acetylide (n-BuLi, THF, -78° to 0°C) to the corresponding aldehyde or ketone. 2. T₁ = time at reflux in ether, T₂ = time at reflux in THF after removal of ether and addition of Bu₃SnCl. 3. Yield after purification by flash chromatography. 4. Approximately 5-10% of the protonated material (net hydrogenation) was also isolated. 5. Reactions carried out at room temperature. 6. Unoptimized yield.

In conclusion, we have shown that the Sato reaction can be used for the rapid preparation of vinylstannanes with a variety of substituents on the carbon bearing the tin. Applications of these compounds in natural product synthesis is currently underway.

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References and Notes

1. NSERC(Canada) University Research Fellow 1987-1992. Bio-Mega Young Investigator Awardee, 1990-1992.
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3. Stille, J.K. *Angew. Chem. Int. Ed. Engl.* **1986**, 25, 508 and references therein.
4. Jung, M.E.; Light, L.A. *Tetrahedron Letters*, **1982**, 23, 3851.
5. Ochiai, M.; Ukita, T.; Fujita, E. *Tetrahedron Letters*, **1983**, 24, 4025.
6. Corey, E.J.; Eckrich, T.M. *Tetrahedron Letters*, **1984**, 25, 2415, 2419.
7. Substitution of the terminal hydrogen by an alkyl group as in 2-butyne-1-ol has previously been shown to cause a reversal in regiochemistry in Sn-H addition such that the Z- β -hydroxy vinyltin compound is isolated, see: Ensley, H.E.; Buescher, R.R.; Lee, K. *J. Org. Chem.*, **1982**, 47, 404.
8. Leusink, A.J.; Budding, H.A.; Marsman, J.W. *J. Organomet. Chem.*, **1967**, 9, 285.
9. Sato, F. *J. Organomet. Chem.*, **1985**, 285, 53 and references therein.
10. Silyl chlorides have also been shown to act as suitable electrophiles but require the addition of HMPA, see: Kang, J.; Cho, W.; Lee, W.K. *J. Org. Chem.*, **1984**, 49, 1838.
11. Satisfactory NMR, IR, and mass spectra and/or combustion analyses were obtained for all new compounds.
12. A typical experimental follows: A Schlenk flask was charged with isobutylmagnesium chloride (2.1 mmol of a solution in ether) and ether (2 mL). The solution was cooled in an ice-bath and dicyclopentadienyltitanium dichloride (10-15 mol%) was added in one portion causing a metallic green precipitate to form. The alcohol (1 mmol) was added dropwise and the resulting mixture was heated to reflux until tlc indicated the hydromagnesiation was complete. The solvent was removed under vacuum and the resulting solid dissolved in THF. Tributyltin chloride was added dropwise and the reaction mixture was again heated to reflux. Standard work-up techniques and flash chromatography gave the vinylstannanes. Typically the vinylstannanes were contaminated with 5-10% of the protonated product which was substantially more polar and thus easily separated by flash chromatography.
13. Sato has observed a similar isomerization with trimethylsilyl acetylenes, see: Sato, F.; Watanabe, H.; Tanaka, Y.; Sato, M. *J. Chem. Soc. Chem. Commun.* **1982**, 1126.
14. For some elegant chemistry of 1,1-distannyl olefins see: Mitchell, T.N.; Reiman, W. *J. Organomet. Chem.*, **1987**, 322, 141.
15. Hydromagnesiation and trapping of the isopropyl and tertbutyl acetylenes also occurs without isomerization, unpublished results of C. Crudden of these laboratories.
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