The Journal of Organic Chemistry

VOLUME 59, NUMBER 13 JULY 1, 1994

Communications

Synthesis of *Syn* and *Anti* Homopropargylic and Allenic Alcohols through Diastereoselective S_E2' Addition of a Common Chiral Allenylstannane Precursor to Aldehydes

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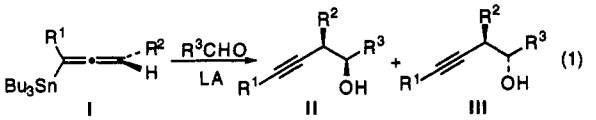
Received April 25, 1994[⊗]

Summary: The (tri-*n*-butylallenyl)stannanes **3** and **17** afford the allenyl adducts **8** and **19** upon brief treatment with stannic chloride and then addition of isobutyraldehyde, whereas preequilibration with $SnCl_4$ and subsequent aldehyde addition leads to the *anti* homopropargylic adducts **5** and **19**.

We recently described a route to chiral nonracemic allenylstannanes (**I**) through S_N2' displacement of enantioenriched secondary propargylic mesylates with a cuprate reagent derived from Bu_3SnLi and $CuBr{\cdot}SMe_2$.[1] These allenylstannanes undergo highly selective S_E2' additions to aldehydes in the presence of $BF_3{\cdot}OEt_2$, yielding *syn* homopropargylic alcohols **II** as the major products (eq 1). In further explorations of that methodology we

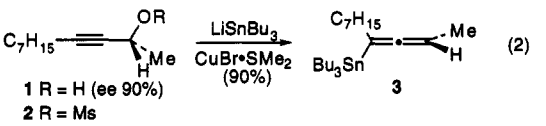


I II III (1)

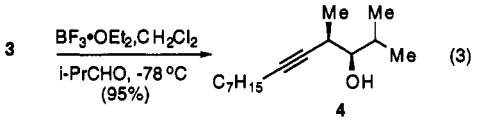
have discovered conditions for reversing both the diastereoselectivity and the regioselectivity of the additions through choice of Lewis acid and reaction conditions.

As previously reported, the (*S*)-allenylstannane **3**, prepared as described in eq 2, affords the *syn*-homopropargylic alcohol **4** in high yield upon treatment with isobutyraldehyde and $BF_3{\cdot}OEt_2$ in CH_2Cl_2 at −78 °C (eq 3).[1]

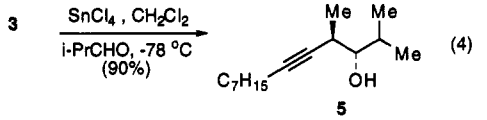
We now find that when $SnCl_4$ is employed as the Lewis acid, the isomeric *anti* adduct **5** is obtained as the sole product (eq 4).



1 R = H (ee 90%)
2 R = Ms
3 (2)

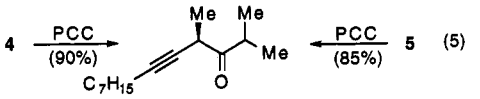


4 (3)



5 (4)

Surprisingly, adducts **4** and **5** are epimeric at the carbinyl rather than the propargylic center. Each affords the sameketone **6** upon oxidation with PCC on neutral alumina (eq 5).[2]



(5)

6 $[\alpha]_D$ -68.3 from **4**
6 $[\alpha]_D$ -64.6 from **5**

The formation of the *anti* product **5** is suggestive of a *syn* S_E2' pathway *via* a cyclic six-center transition state.[3]

[⊗] Abstract published in *Advance ACS Abstracts,* June 1, 1994.

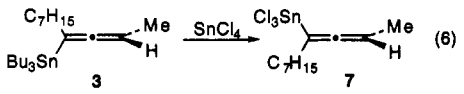
(1) Marshall, J. A.; Wang, X.-J. *J. Org. Chem.* **1992**, *57*, 1242.

(2) Cheng, Y.-S.; Liu, W.-L.; Chen, S.-H. *Synthesis* **1980**, 223.

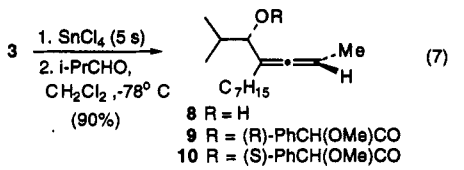
(3) For an overview of S_E2' additions of propargyl and allenyl organometallics, see: Yamamoto, H. In *Comprehensive Organic Synthesis*; Trost, B. M., Pergamon Press: Oxford, 1991; Vol. 2, Chapter 1.3.

0022-3263/94/1959-3509$04.50/0

Presumably, exchange of Cl_3Sn for Bu_3Sn occurs prior to such an addition.[4] Since adducts **4** and **5** have the same absolute configuration at the propargylic center, this exchange must occur with *inversion* leading to the (*R*)-allenylstannane **7** (eq 6).

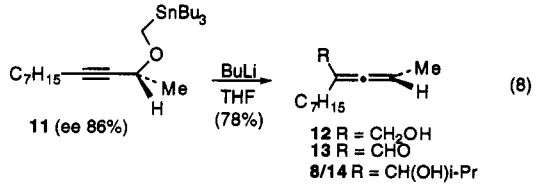


A priori, the conversion of allenylstannane **3** to **7** could occur by an unprecedented addition of $SnCl_4$ to the allenyl double bond, leading to a vinyl cation which then undergoes stereospecific loss of Bu_3Sn. A more likely pathway would involve successive S_E2' substitutions, one of which proceeds with inversion and the other with retention of configuration. Evidence for this pathway was secured by premixing the allenylstannane **3** and $SnCl_4$ at −78 °C, followed by the immediate addition of isobutyraldehyde, whereupon the allenylcarbinol **8** was obtained to the near exclusion of homopropargylic alcohol **5** (eq 7).



Further support for this pathway came from a ^1H NMR experiment. Upon addition of $SnCl_4$ to a sample of allenylstannane **3** in CD_2Cl_2 at 25 °C, the characteristic allenyl proton signal at 4.5 ppm gave way to new signals at 5.6 and 3.5 ppm, indicative of the allenic proton in the rearranged Cl_3Sn allene **7** and the propargylic proton of its precursor **16** (see Figure 1). This latter signal disappeared in favor of the former on standing.

The absolute configuration of the carbinyl center in alcohol **8** was ascertained through ^1H NMR analysis of the (*R*)- and (*S*)-*O*-methyl mandelates **9** and **10**.[5] The allene stereochemistry was established by independent synthesis. Accordingly, Still–Wittig rearrangement[6] of the stannyl ether **11** derived from alcohol **1** and subsequent Swern oxidation[7] afforded the allenyl aldehyde **13** (eq 8). Addition of isopropylmagnesium bromide led to a mixture of alcohol diastereoisomers **8/14**.



(4) Exchanges of this type have been well studied in allyl and crotyl systems. *Cf*: (a) Denmark, S. E.; Weber, E. J.; Wilson, T. M.; Willson, T. M. *Tetrahedron* **1989**, *45*, 1053. (b) Keck, G. E.; Andrus, M. B.; Castellino, S. *J. Am. Chem. Soc.* **1989**, *111*, 8136. (c) Naruta, Y.; Nishigaichi, Y.; Maruyama, K. *Tetrahedron* **1989**, *45*, 1067. (d) Nishigaichi, Y.; Takawa, A.; Naruta, Y.; Maruyama, K. *Tetrahedron* **1993**, *49*, 7395. (e) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207. (f) Boaretto, A.; Marton, D.; Tagliavini, G. *J. Organomet. Chem.* **1985**, *297*, 149.

(5) *Cf*: Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. D. *J. Org. Chem.* **1986**, *51*, 2370.

(6) *Cf*: Still, W. C.; Mitra, A. *J. Am. Chem. Soc.* **1978**, *100*, 1927.

(7) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651.

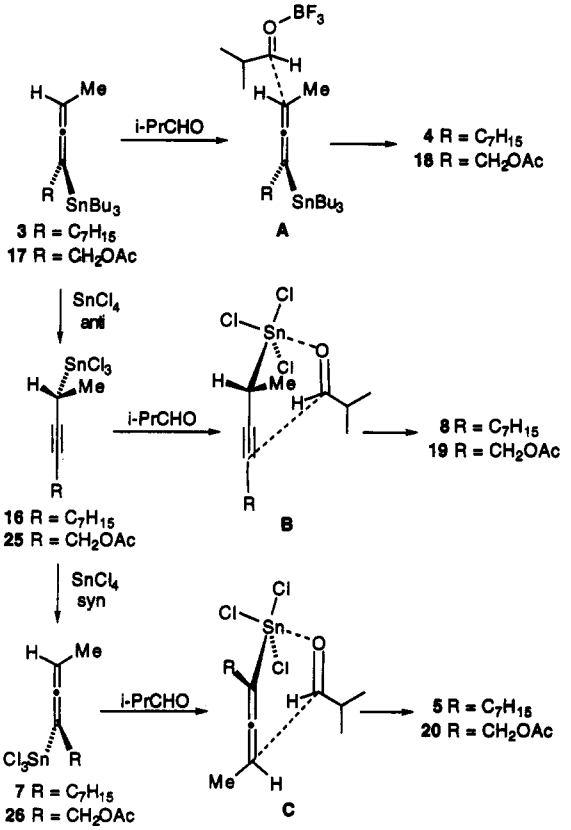
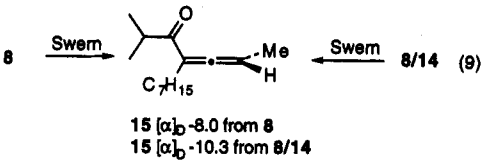


Figure 1. Transition states for additions of stannanes to i-PrCHO.

Upon Swern oxidation, both alcohol **8** and the epimeric alcohol mixture **8/14** gave rise to the same allenone **15** (eq 9).



The foregoing observations are consistent with a rapid *anti* S_E2' addition of $SnCl_4$ to stannane **3**, followed by a slower *syn* 1,3-isomerization of the intermediate propargylic stannane **16** to allenylstannane **7** (Figure 1). We have previously demonstrated that BF_3-promoted additions of the Bu_3Sn reagent **3** occur through an *anti* pathway as depicted in **A**.[1] Additions of the Cl_3Sn reagents **16** and **7** most likely occur by a cyclic *syn* pathway as depicted in **B** and **C**.[3] We assume that the carbonyl occupies an apical coordination site[8] on the electron-deficient Sn grouping in these cyclic transition states to enable the π system of the allene or alkyne to attack the coordinated aldehyde at the optimum Dunitz–Bergi angle.[9]

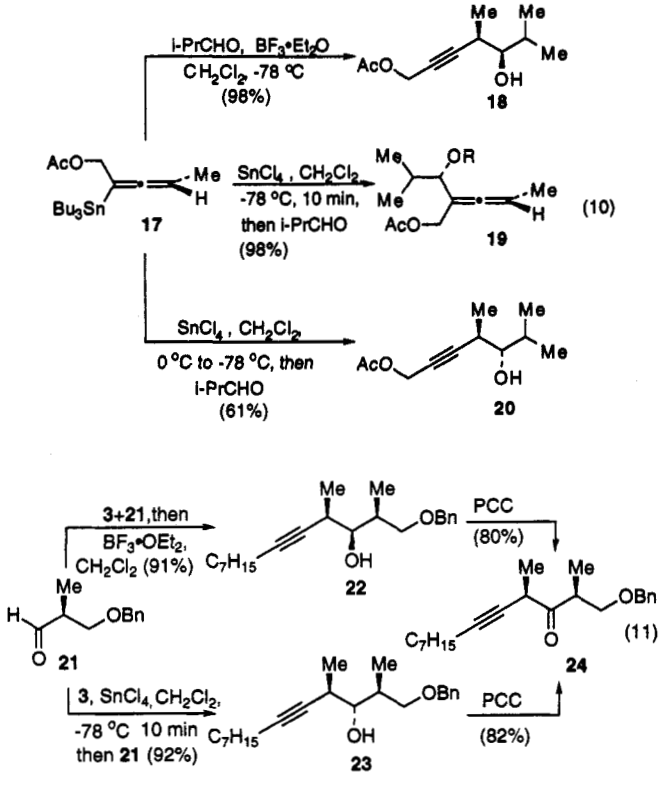
The stereochemical preference shown in **B** for the propargylstannane is at first sight surprising because of the *syn* orientation of the isopropyl and methyl substituents. Indeed, considering the separation of these two substituents, little or no diastereoselectivity might be expected. However, in transition state **B** the methyl substituent is staggered with respect to the equatorial Cl and apical carbonyl ligands, whereas the propargyl H

(8) *Cf*: Harrison, P. G.; King, T. J.; Healy, M. A. *J. Organomet. Chem.* **1979**, *182*, 17.

(9) Bergi, H. B.; Dunitz, J. D.; Lehn, J. M.; Wipff, G. *Tetrahedron* **1974**, *30*, 1563.

nearly eclipses the apical Cl ligand. The reverse arrangement would be sterically disfavored.

Additional applications of the methodology are summarized in eqs 10 and 11. We have previously shown that allenylstannane **17** affords the *syn* homopropargylic alcohol **18** upon addition to isobutyraldehyde in the presence of $BF_3{\cdot}OEt_2$.[1] When $SnCl_4$ was employed as the Lewis acid, the allenylcarbinol **19** was secured as the sole



product at −78 °C, even if addition of the aldehyde was delayed for 30 min. Evidently, the acetoxy substituent retards the propargyl−allenyl stannane isomerization (see Figure 1). However, when stannane **17** and $SnCl_4$ were stirred at 0 °C for 1 h, the isomerization proceeded to completion. Subsequent recooling to −78 °C and then addition of isobutryaldehyde led to the *anti* homopropargyl alcohol **20** in high yield.

The structure of alcohol **20** was ascertained through oxidation to the ketone likewise secured from the known *syn* alcohol **18**[1] as described for the analogues **4** and **5**. The structure of allenylcarbinol **19** was surmised from the ^1H NMR spectra of the *O*-methyl mandelates and by analogy with **8**. The *anti,anti* adduct **23** was similarly oxidized to the corresponding ketone, **24**, which was identical to the ketone secured through oxidation of the *syn,syn* alcohol **22**.[1]

The foregoing results provide important mechanistic insight into 1,3-isomerizations of allylic and propargylic organometallic compounds and considerably extend the utility of chiral allenylstannanes as synthetic reagents.

Acknowledgment. This work was supported by a research grant from the National Science Foundation (CHE-9220166), for which we are grateful.

Supplementary Material Available: Experimental procedures for compounds **5**, **6**, **8**, **14**, **15**, **18**–**20**, and **22**–**24**, ^1H NMR spectra of all new compounds, and ^{13}C spectra of selected compounds (40 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.