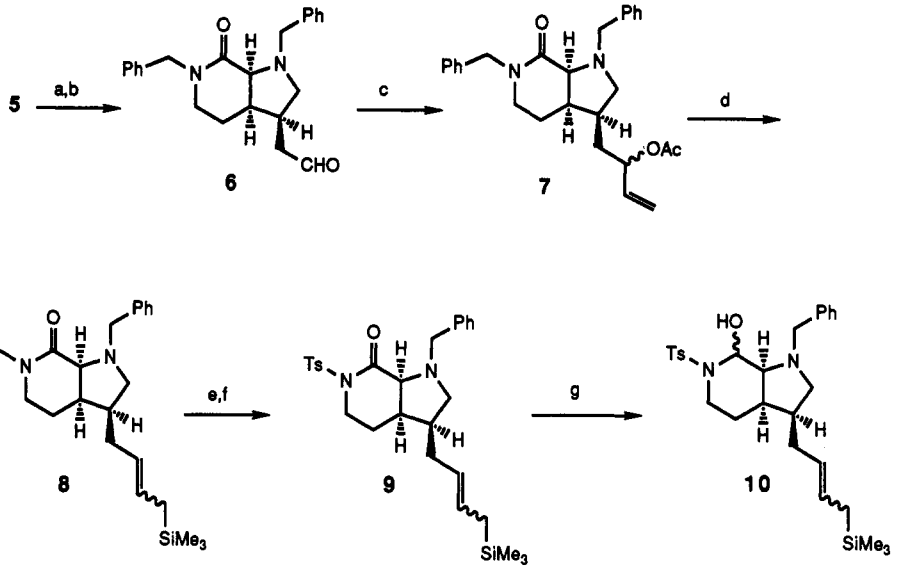
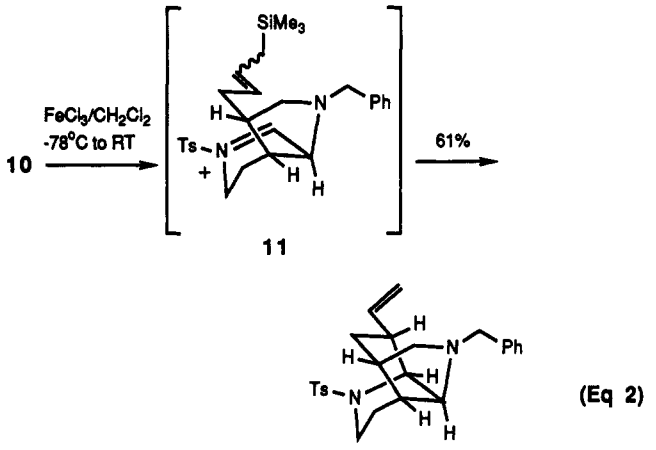
Scheme I[a]



[a] (a) $BBr_3/CH_2Cl_2/0$ °C; (b) Swern oxidation; (c) CH_2=CHMgBr/THF/0 °C to rt; $Ac_2O/NEt_3/DMAP/CH_2Cl_2$ 35% from 5; (d) $(TMS)_2(CN)Li_2Cu$/THF:HMPA (2:1)/-25 °C/50%; (e) Na/NH_3/tBuOH/THF/-78 °C/95%; (f) TsCl/LiHMDS, THF/DMAP/71%; (g) DIBALH/CH_2Cl_2/-78 °C to rt/93%.

The crucial cyclization of 10 could be effected in 61% yield by using anhydrous ferric chloride to afford tricyclic compound 12 as a single stereoisomer (eq 2). For reasons



(Eq 2)

we cannot explain, other Lewis acids (e.g., $TiCl_4$, $BF_3{\cdot}Et_2O$) gave complex product mixtures containing little, if any, 12. This cyclization probably occurs via *N*-sulfonyliminium intermediate 11, which has the allylsilane group in a quasi-equatorial position.[12] It should be noted that although allylsilane cyclizations onto *N*-acyliminium species are now well documented,[13] examples of analogous *N*-sulfonyliminium ion cyclizations are apparently unknown.[14] We are currently investigating the utilization of the approach outlined here in a total synthesis of sarain A (1).

Acknowledgment. This work was supported by the National Institutes of Health (GM-32299).

Supplementary Material Available: Experimental and spectral data for all new compounds and ^1H and ^{13}C NMR spectra and NOE data for cyclization product 12 (9 pages). Ordering information is given on any current masthead page.

(12) The stereochemistry of cyclization product 12 was established by NOE experiments, for which we thank Drs. A. Freyer and A. Benesi. (See supplementary material.)

(13) For reviews, see: Speckamp, W. N.; Hiemstra, H. *Tetrahedron* **1985**, *41*, 4367. Hiemstra, H.; Speckamp, W. N. In *The Alkaloids*; Brossi, A., Ed.; Academic Press: San Diego, 1988; Vol. 32, p 271. See also: Gramain, J.-C.; Remuson, R.; *Heterocycles* **1989**, *29*, 1263.

(14) For intermolecular additions of allylsilanes to *N*-tosyliminium species, see: Shono, T.; Matsumura, Y.; Uchida, K.; Nakatani, F. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3029. Ralbovsky, J. L.; Kinsella, M. A.; Sisko, J.; Weinreb, S. M. *Synth. Commun.* **1990**, *20*, 573. Shono, T.; Matsumura, Y.; Katoh, S.; Takeuchi, K.; Sasaki, K.; Kamada, T.; Shimizu, R. *J. Am. Chem. Soc.* **1990**, *112*, 2368.

Highly Diastereoselective S_E' Additions of Enantioenriched Allenylstannanes to (*S*)-2-(Benzyloxy)propanal

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Summary: The BF_3-promoted addition of (*S*)-allenylstannane (*S*)-6 to aldehyde 16 afforded a 68:32 mixture of diastereomeric homopropargylic alcohols 17 and 18 whereas $MgBr_2$-promoted addition gave adduct 17 as the exclusive product. The (*R*)-allenylstannane (*R*)-6, on the other hand, yielded a 30:1 mixture of syn and anti alcohol adducts 19 and 20 with $BF_3{\cdot}OEt_2$ and a 1:92 mixture favoring the anti adduct 20 under $MgBr_2$ catalysis.

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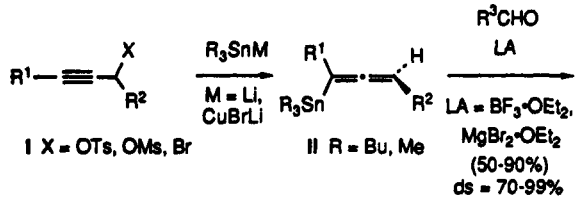
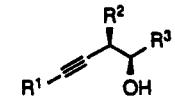
We recently reported preliminary findings on the synthesis of racemic allenylstannanes II from propargylic derivatives I and their stereoselective additions to aldehydes to yield homopropargylic alcohols III (eq 1).[1] With



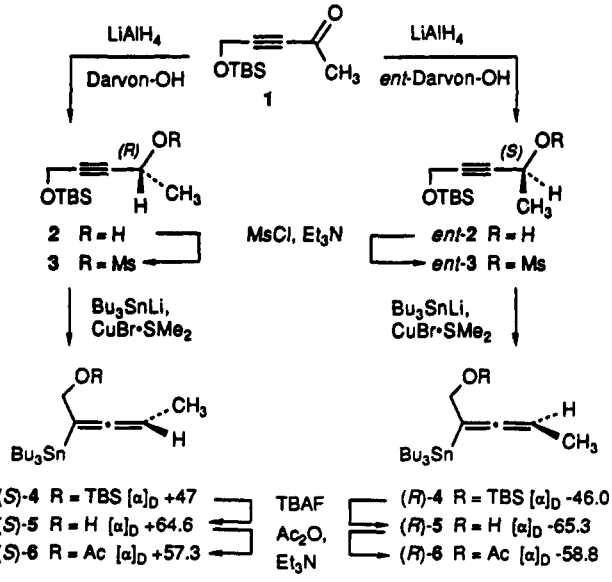


(1)

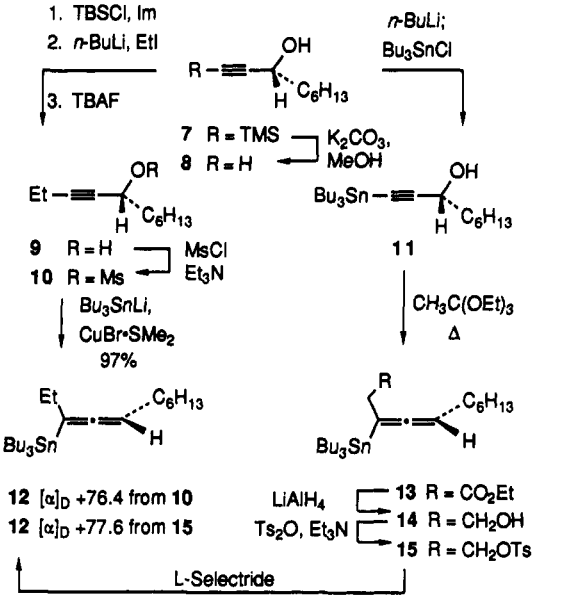
III $R^1 = C_7H_{15}$, R^2 = Me
$R^3 = C_6H_{13}$, i-Pr, t-Bu,
CH(Me)CH(OMOM)CHMe$_2$

α-branched aldehydes formation of the syn diastereomers was highly favored. We now describe additional studies with previously unreported nonracemic allenylstannanes that considerably extend the applicability of the additions to the synthesis of both syn and anti homopropargylic alcohols of high ee.

The enantioenriched allenylstannanes (*S*)-6 and (*R*)-6 employed in these studies were prepared by reduction of alkynone 1 with the complex of $LiAlH_4$ and Darvon alcohol[2] (2, 90% ee) or *ent*-Darvon alcohol[3] (*ent*-2, 90% ee) followed by S_N2' displacement of the derived mesylates 3 or *ent*-3 with the cuprate prepared from Bu_3SnLi and $CuBr{\cdot}SMe_2$.[4] No isomeric propargylic stannanes arising from S_N2 displacement were observed. The allenylstannanes 4 were not isomerized or racemized by prolonged exposure to the cuprate or by chromatography on silica gel.[5]

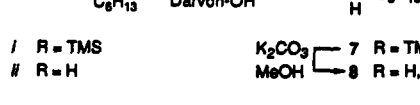


It has previously been shown that S_N2' displacements of propargylic mesylates with cuprates proceed by an anti pathway.[6] To verify that stannylcuprates behave analogously, we carried out the following correlation in which allenylstannane 12 was prepared by cuprate displacement on mesylate 10[7] and by Claisen ortho ester rearrangement[8] starting from propargylic alcohol 11.[7] The close agreement in optical rotation of the two samples of allenylstannane supports a predominantly anti S_N2' pathway for the cuprate reaction.



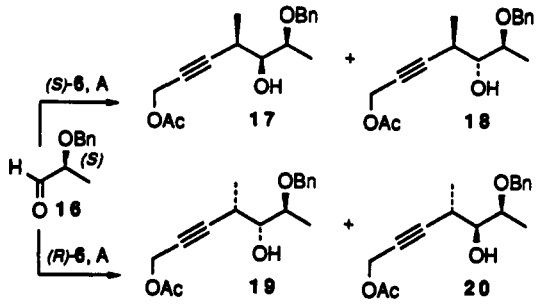
Looking for possible double asymmetric induction effects[9] we examined additions of the (*S*)- and (*R*)-allenylstannanes to (*S*)-2-(benzyloxy)propanal (16).[10] Our findings, summarized in Table I, clearly show that diastereoselectivity depends upon chirality matching between the two reacting partners. In the BF_3-promoted reactions the *S*/*R* pairing is matched (entry 3) and the *S*/*S* pairing is mismatched (entry 1), but both favor syn adducts (19 and 17, respectively).[11] Interestingly, the diastereoselective sense of the $MgBr_2$-promoted additions is completely reversed by changing the configuration of the allenylstannane (entries 2 and 4). *S*/*S* pairing yields the syn adduct 17 exclusively whereas *R*/*S* pairing gives a 92:1 preference for the anti adduct 20.[12] It is of further interest

(1) Marshall, J. A.; Wang, X.-J. *J. Org. Chem.* **1990**, *55*, 6246.
(2) Yamaguchi, S.; Mosher, H. S. *J. Org. Chem.* **1973**, *38*, 1870. Alcohols of ~90% ee are generally obtained from acetylenic ketones.
(3) Marshall, J. A.; Salovich, J. M.; Shearer, B. G. *J. Org. Chem.* **1990**, *55*, 2398.
(4) House, H. O.; Chu, C.-Y.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, *40*, 1460.
(5) Cf.: LeQuan, M.; Cadiot, P. *Bull. Soc. Chim. Fr.* **1965**, 45. LeQuan, M.; Guillern, G. *J. Organomet. Chem.* **1973**, *54*, 153. Claesson, A.; Olsson, L.-I. *J. Chem. Soc., Chem. Commun.* **1979**, 524.
(6) Elsevier, C. J.; Vermeer, P. *J. Org. Chem.* **1989**, *54*, 3726.
(7) The starting alcohol for these studies was prepared by reduction of alkynone i with the $LiAlH_4$–Chirald (Darvon alcohol) reagent.[2] Alcohol 7 of 82% ee was thereby obtained. Analogous reduction of alkynone ii afforded alcohol 8 of only 40% ee. Accordingly, 8 was prepared by desilylation of 7.



(8) Cf.: Johnson, W. S.; Werthmann, L.; Bartlett, W. R.; Brocksom, T. J.; Li, T.; Faulkner, T. J.; Peterson, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741.
(9) Cf.: Masamune, S., Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1.
(10) Ireland, R. E.; Thaisrivongs, S.; Dussault, P. H. *J. Am. Chem. Soc.* **1988**, *110*, 5768.
(11) Analogous reactions of crotylstannanes with such aldehydes typically give ~90:10 mixtures of syn and anti homoallylic alcohols. Yamamoto, Y.; Yatagi, H.; Ishikara, Y.; Maeda, M.; Maruyama, K. *Tetrahedron* **1984**, *40*, 2239. Keck, G. E.; Boden, E. P. *Tetrahedron Lett.* **1984**, *25*, 1879.

Table I. Double Diastereodifferentiation Effects in S_E' Additions of Allenylstannane 6 to 2-(Benzyloxy)propanal (16)



entry	stannane	A	yield, %	% yield 17	18	19	20
1	(S)-6	BF_3	95	62	29	4[a]	0
2	(S)-6	$MgBr_2$	97	94	0	0	3[a]
3	(R)-6	BF_3	97	2[b]	1[b]	91	3
4	(R)-6	$MgBr_2$	97	4[b]	0	1	92

[a] From 5% of (R)-6 present in starting stannane. [b] From 5% of (S)-6 present in starting stannane.

that the allenyl stereochemistry is faithfully reproduced at the propargylic sp^3 center of the adducts in accord with a stereospecific anti S_E' process.[13,14] These findings support the transition state arrangements depicted in Figure 1. In both A and B attack occurs anti to the CH_3 substituent of the chelated aldehyde. The γ-H of the allenylstannane is oriented over the face of this chelate in preference to the more bulky CH_3 or allenyl groupings. In A the aldehyde carbonyl and the allenyl double bond assume an anti arrangement, whereas in B the orientation is gauche.[15] Thus, the torsional alignment of these two moieties plays a secondary role to stereoelectronic (anti $SnBu_3$) and steric effects.[12,15]

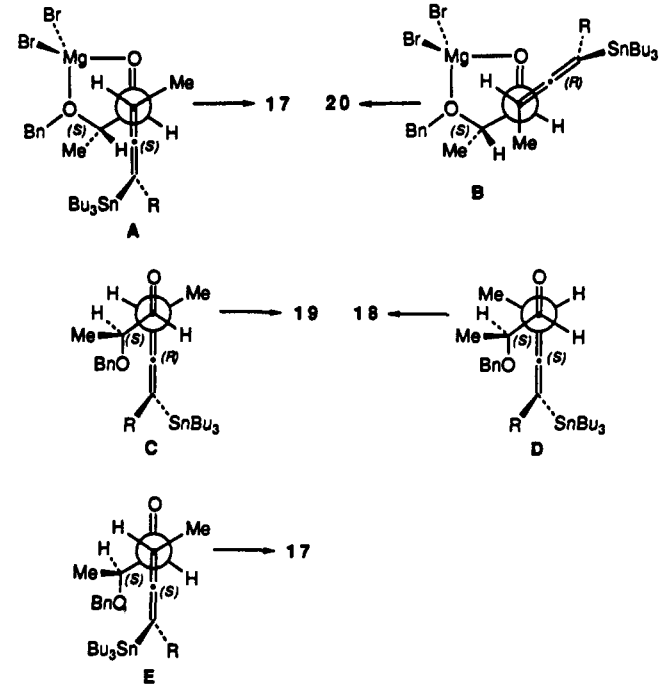


Figure 1. Transition-state arrangements for S_E' additions of allenylstannanes.

The BF_3·OEt_2-promoted additions can be accommodated by transition states C–E in which the Cornforth conformation is depicted for the aldehyde partner.[16] The matched *S/R* alignment, as in C, is favored by steric as well as stereoelectronic factors. For the mismatched *S/S* case the analogous arrangement, as in D, suffers from steric interactions of the allenyl CH_3. These interactions are alleviated in E, but addition must now occur by anti-Cram attack on the aldehyde.[17]

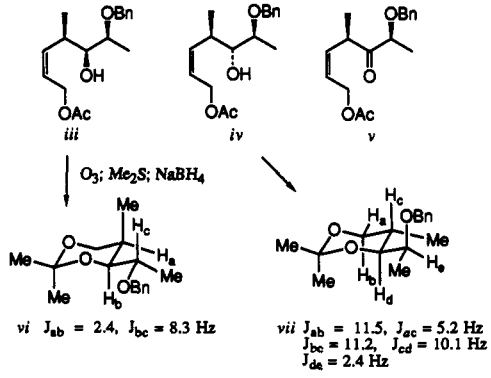
These findings, coupled with our earlier studies on racemic stannanes,[1] provide a good foundation for the development of allenylstannanes as reagents for the stereorational synthesis of acyclic, heterocyclic, and macrocyclic ionophore and polypropionate natural products.

Acknowledgment. This work was supported by a research grant (CHE 8912745) from the National Science Foundation for which we are grateful. We thank James E. Audia and the Eli Lilly Company for a gift of *ent*-Darvon alcohol.

(12) Reactions of (α-methylcrotyl)stannanes with racemic aldehyde 16 have been shown to yield a predominance of the anti S_E' adduct under chelation controlled conditions. Mikami, K.; Kawamoto, K.; Loh, T.-P.; Nakai, T. *J. Chem. Soc., Chem. Commun.* **1990**, 1161.

(13) This is also true for α- and γ-alkoxyallylic stannanes: Marshall, J. A.; Gung, W. Y. *Tetrahedron* **1989**, *45*, 1043. Marshall, J. A.; Welmaker, G. S.; Gung, B. W. Y. *J. Am. Chem. Soc.* **1991**, *113*, 647.

(14) The absolute configuration of each alcohol was established from the ^1H NMR spectra of the *O*-methyl mandelates.[13] Alcohols 17 and 18 were shown to be epimeric by Lindlar hydrogenation to iii and iv followed by oxidation to ketone v. The relative stereochemistry of alcohols iii and iv was established by analysis of the ^1H NMR coupling constants of the derived acetonides vi and vii. The stereochemistry of alcohols 19 and 20 can be deduced from the absolute configuration of the carbinol center and a knowledge of the configuration of 17 and 18.



(15) The anti (antiperiplanar) orientation was first suggested by Yamamoto et al.[11] Certain intramolecular additions of allylstannanes to aldehydes require gauche (synclinal) arrangements. Demark, S. E.; Weber, E. J. *J. Am. Chem. Soc.* **1984**, *106*, 7970. For a discussion, see ref 12 and Gung, B. W.; Smith, D. T.; Wolf, M. A. *Tetrahedron Lett.* **1991**, *32*, 13.

(16) Cf.: Cornforth, J. W.; Cornforth, R. H.; Mathew, K. K. *J. Chem. Soc.* **1959**, 112.

(17) This would also be true for the Felken–Ahn conformation of 16. Chêrest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199.