Interconversion of Nonracemic α-OTBS Crotyl and γ-OTBS Methallyl Tri-*n*-butylstannanes. Additions of the (*E*)-Methallyl Isomer to Representative Aldehydes

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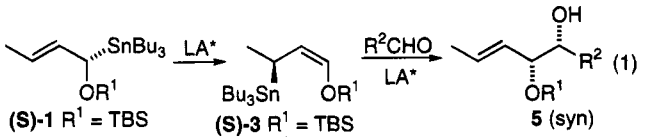
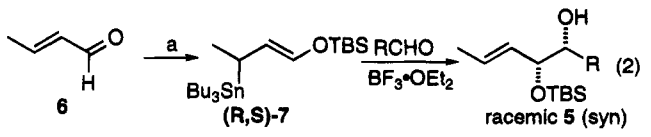
In our evolving studies on the chemistry of nonracemic α- and γ-oxygenated allylic stannanes as reagents for S_E2' additions to aldehydes, we found improved *syn:anti* diastereoselectivity for OTBS *vs* OMOM methallyl derivatives **3** and **4** (eq 1).[1]



R^1	R^2	syn:anti	series
MOM	c-C_6H_{11}	95:5	a
TBS	c-C_6H_{11}	97:3	a
MOM	(E)-BuCH=CH	94:6	b
TBS	(E)-BuCH=CH	>99:1	b
MOM	Bu—≡	90:10	c
TBS	Bu—≡	93:7	c

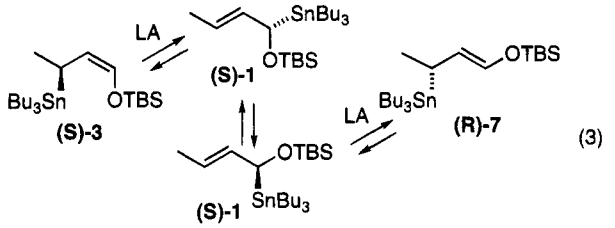
The γ-oxygenated reagents **3** and **4** were readily prepared by a stereospecific *anti* 1,3-isomerization of the α-isomers **1** and **2** in the presence of catalysts such as BF_3•OEt_2, TBSOTf, Bu_3SnOTf, or even $LiClO_4$ in Et_2O.[2] In all cases examined, no more than traces of the (*E*)-isomers of **3** or **4** were ever detected. It should be noted that prolonged exposure of these stannanes to Lewis acid catalysts led to complete decomposition without producing the (*E*)-isomer.

We subsequently prepared the (*E*)-γ-OTBS methallylstannane (*R,S*)-**7**, in racemic form, through conjugate addition of the Lipshutz higher order cyanocuprate Bu(Bu$_3$Sn)Cu(CN)Li$_2$[3] to crotonaldehyde and *in situ* trapping of the intermediate enolate with TBSCl.[1] This stannane exhibited remarkably high *syn* diastereoselectivity in BF_3-promoted additions to aldehydes. Particularly noteworthy is the nearly exclusive formation of *syn* adduct **5c** with 2-heptynal (eq 2).



R	syn:anti	series
c-C_6H_{11}	>99:1	a
(E)-BuCH=CH	>99:1	b
Bu—≡	97:3	c

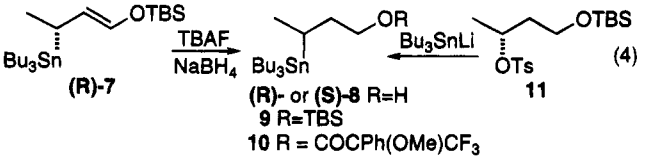
In a study aimed at finding other promoters or catalysts for these additions, we examined a number of lanthanide triflates.[4] Although these were not effective for the additions, we found that they catalyzed isomerization of the double bond in the γ-OTBS stannane (*S*)-**3**. They also catalyzed the conversion of α-OTBS stannane (*S*)-**1** to a separable mixture of (*Z*)- and (*E*)-γ-OTBS isomers (*S*)-**3** and (*R*)-**7**. Best results were obtained with Yb(OTf)$_3$, as summarized in eq 3.[5]



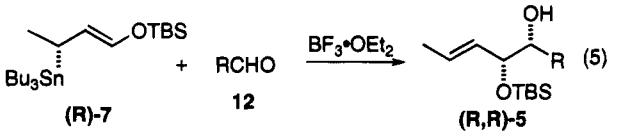
stannane	LA	(S)-3:(R)-7	yield,%
(S)-1	BF_3•OEt_2	100:0	80
(S)-3	BF_3•OEt_2	a	-
(S)-1	Yb(OTf)$_3$	76:24	82
(S)-3	Yb(OTf)$_3$	76:24	71
(R,S)-7	Yb(OTf)$_3$	77:23[b]	56

a) decomposition
b) racemic

The stereochemistry of the isomerizations was elucidated by conversion of the previously unknown (*E*)-isomer (*R*)-**7** to the dihydro derivative (*R*)-**9**, $[\alpha]_D$ −12.5, as shown in eq 4. The enantiomer (*S*)-**9**, $[\alpha]_D$ 12.9, was prepared from tosylate **11**.[6] The ee of material obtained by both routes was found to be >90% by ^{19}F NMR analysis of the Mosher ester derivative **10**.



We next examined the addition of stannane (*R*)-**7** to representative aldehydes as summarized in eq 5. The *syn:anti* ratios of products were determined by GC analysis. Not surprisingly, these were identical to those previously found (eq 2) for the racemic stannane.



R	syn:anti	ee,%	yield,%	series
c-C_6H_{11}	>99:1	>95	79	a
(E)-BuCH=CH	>99:1	>95	83	b
Bu—≡	97:3	20	87	c

The ee of the *syn* adducts was obtained through ^1H NMR analysis of the Mosher esters. The ee of the cyclohexanecarboxaldehyde and 2-heptenal adducts (*R,R*)-**5a** and (*R,R*)-**5b** was comparable to that of the starting stannane (*R*)-**7**, as expected for a stereospecific reaction.

(1) Marshall, J. A.; Welmaker, G. S. *J. Org. Chem.* **1992**, *57*, 7158.
(2) Henry, K. J., Jr.; Grieco, P. A.; Jagoe, C. T. *Tetrahedron Lett.* **1992**, *33*, 1817.
(3) Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Reuter, D. C. *Tetrahedron Lett.* **1989**, *30*, 2065.
(4) For relevant examples, see: (a) Aspinall, H. C.; Browning, A. F.; Greeves, N.; Ravenscroft, P. *Tetrahedron Lett.* **1994**, *35*, 4639. (b) Hachiya, I.; Kobayashi, S. *J. Org. Chem.* **1993**, *58*, 6958.
(5) The isomerization could also be effected with Sc(OTf)$_3$, La(OTf)$_3$, and Bu_3SnOTf, but the reactions were slower and recoveries were lower.
(6) Tosylate **11** was prepared by reduction of (*R*)-ethyl-3-hydroxybutanoate (Aldrich Chemical Co.) with $LiAlH_4$ followed by monoprotection with TBSCl, imidazole, and tosylation with *p*-TsCl in pyridine.

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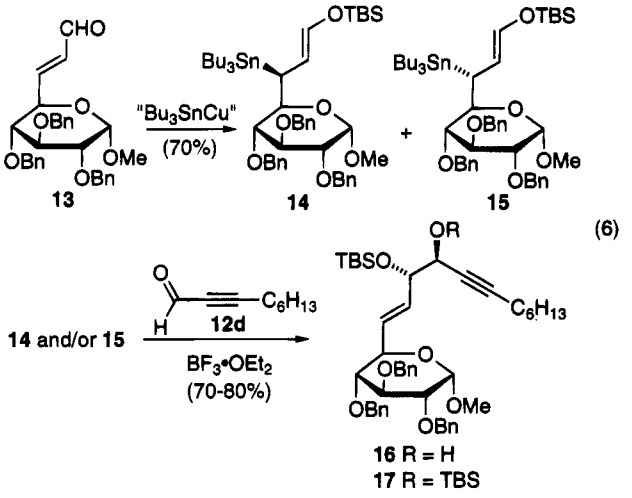
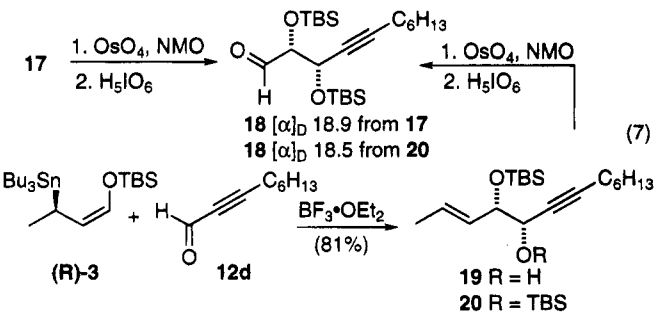
The 2-heptynal adduct (*R*,*R*)-**5c**, however, was nearly racemic. This experiment was repeated several times with the same outcome. A control experiment in which excess stannane (*R*)-**7** was employed showed that negligible racemization of the stannane occurred under the reaction conditions. The recovered (*R*)-**7** afforded alcohol **8** of the same ee as that of the starting sample according to analysis of the Mosher ester **10** by ^{19}F NMR (see eq 4). We are thus led to the inescapable conclusion that addition of stannane (*R*)-**7** to 2-heptynal occurs with nearly equal facility by a *syn* and *anti* S_E2' pathway. Furthermore, the *syn* pathway does not involve a concerted cyclic transition state, as such a process would afford the *anti* adduct—which comprised only 3% of the total product.

In an application of this chemistry with potential for carbohydrate homologations, we prepared a *ca.* 1:1 mixture of the chromatographically separable diastereomeric stannanes **14** and **15** (stannane configuration as yet unknown) through addition of the Lipschutz cuprate[3] to the glucopyranose-derived enal **13**.[7] Addition of each diastereomer to 2-nonynal led to the identical major adduct **16** (eq 6).[8]



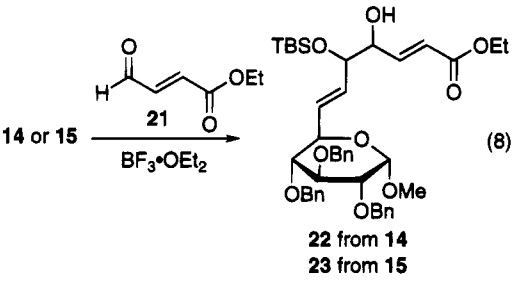
(6)

The stereochemistry of the TBS derivative **17** of adduct **16** was ascertained by the sequence depicted in eq 7 and comparison of the degradation product **18** with an authentic sample prepared from 2-nonynal (**12d**) and stannane (*R*)-**3**.[1]



(7)

Stannanes **14** and **15**, unlike (*R*)-**7**, are stereochemically biased. Evidently this bias helps to override the intrinsic preference for anti S_E2' addition normally exhibited by trialkylated allylic stannanes.[9] In contrast to their reaction with 2-nonynal, stannanes **14** and **15** afford diastereomeric products, of as yet undetermined stereochemistry, with enal **21**.[10] Each of the two products shows similar but clearly different spectral properties.



(8)

To our knowledge, these are the first examples of Lewis acid promoted additions of Bu_3Sn allylic stannanes to aldehydes that proceed by an acyclic *syn* reaction pathway. As the analogous process is not observed with aldehydes **12a**, **12b**, and **21**, it seems likely that the triple bond is somehow responsible for this unprecedented reaction outcome.

Acknowledgment. This work was supported by a grant from NIH, the National Institute of Allergy and Infectious Diseases (2R01-AI31422).

Supplementary Material Available: Experimental procedures and NMR spectra for new compounds (51 pages).

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(7) Jarosz, S.; Fraser-Reid, B. *J. Org. Chem.* **1989**, *54*, 4011.
(8) One of the diastereomeric stannanes **14**/**15** afforded only adduct **16** whereas the other gave adduct **16** as the major product along with lesser amounts of inseparable stereoisomers of **16**.
(9) *Cf.* Yamamoto, Y.; Shida, N. *Advances in Detailed Reaction Mechanisms*; JAI Press, Inc.: Greenwich, CT, 1994; Vol. 3, pp 1–44.
(10) Veysoglu, T.; Mitscher, L. A.; Swayze, J. K. *Synthesis* **1980**, 807.