Diastereoselective Additions of Allenylstannanes to Aldehydes

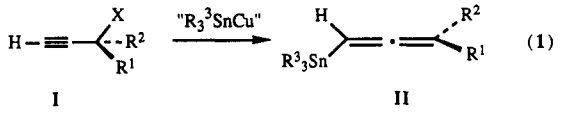
James A. Marshall* and Xiao-jun Wang

Department of Chemistry, The University of South Carolina, Columbia, South Carolina 29208

Received October 2, 1990

Summary: The allenylstannane **4** undergoes highly syn selective additions to α-branched aldehydes **8b** and **8c** in the presence of $BF_3{\cdot}OEt_2$. With the β-alkoxy aldehyde **21**, Cram–Felkin addition results with $BF_3{\cdot}OEt_2$ as the Lewis acid, whereas $MgBr_2$ leads to chelation-controlled addition.

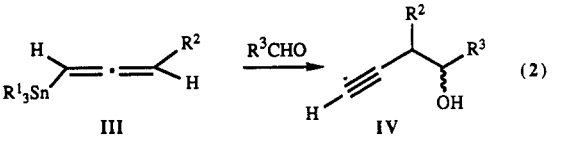
Studies on the synthesis of allenylstannanes by S_N2' displacements on propargylic derivatives (eq 1)[1] and additions of allenylstannanes to aldehydes (eq 2)[2] have been reported by several groups working independently. However, no systematic investigation on the stereochemistry of such additions has been carried out. As part of an



(1)

I II

X = Br, $MeSO_3$, $MeSO_2$
R^1, R^2 = H, Me; H, Ph; Me, Me; $(CH_2)_4$; $(CH_2)_5$; H, *t*-Bu
R^3 = Ph, Me

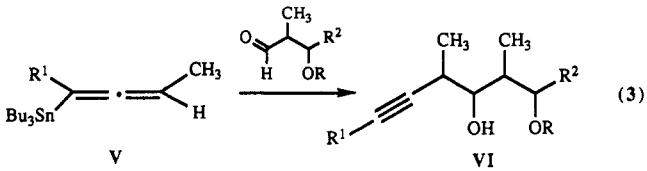


(2)

III IV

R^1 = Bu, Cl
R^2 = H, R^3 = alkyl; R^2 = Me, R^3 = Cl_3C

ongoing program directed toward polypropionate natural products, we were interested in the possible use of allenylstannanes for stereocontrolled assemblage of acyclic chains with alternating CH_3 and OH substituents (eq 3).[3]



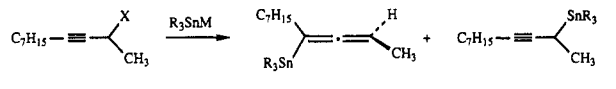
(3)

V VI

Preliminary to these applications we wished to examine reaction conditions and stereochemical characteristics of the S_E' addition with simple aldehydes. Our findings, detailed below, show that readily available allenylstannanes add to aldehydes in the presence of Lewis acids to give homopropargylic alcohols in excellent yields. With α-branched aldehydes the addition is highly stereoselective, leading to syn isomers as major or exclusive products.

The prototype allenylstannanes **4** and **5** were prepared from the propargylic alcohol **1** (Scheme I). Reaction of the derived tosylate **3** with Bu_3SnLi in THF–HMPA at −78 °C gave a 90:10 separable mixture of allenyl- and propargylstannanes **4** and **6** in 78% yield (Table I, entry 3).

Table I. Synthesis of Allenic and Propargylic Stannanes



2 X = Br
3 X = OTs

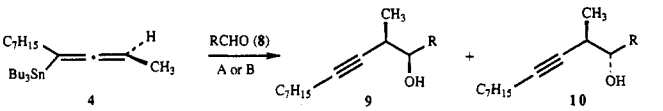
4 R = Bu
5 R = Me

6 R = Bu
7 R = Me

entry	X	R	conditions[a]	yield (%)	allenyl: propargyl
1	Br	Bu	A	67	50:50
2	Br	Bu	B	69	40:60
3	OTs	Bu	C	78	90:10
4	OTs	Me	D	75	100:0

[a] (A) Bu_3SnLi, THF, −78 °C, normal addition; (B) Bu_3SnLi, THF, −78 °C, inverse addition; (C) Bu_3SnLi, THF–HMPA (5:1), −78 °C; (D) $Me_3SnCuBrLi$, THF.

Table II. Additions of Allenylstannanne 4 to Aldehydes 8a–c



4 9 10

entry	RCHO (8)	series	conditions	yield (%)	syn/anti (9:10)
1	*n*-$C_6H_{13}CHO$ (**8a**)	**a**	A	83	37:63
2	*n*-$C_6H_{13}CHO$ (**8a**)	**a**	B	56	69:31
3	*i*-PrCHO (**8b**)	**b**	A	80	99:1
4	*i*-PrCHO (**8b**)	**b**	B	48	88:12
5	*t*-BuCHO (**8c**)	**c**	A	92	99:1

[a] (A) $BF_3{\cdot}OEt_2$, CH_2Cl_2, −78 °C, 30 min; (B) $MgBr_2{\cdot}OEt_2$, CH_2Cl_2, 5 °C, 24 h.

Appreciable S_N2 displacement was observed with the propargylic bromide **2** (Table I, entries 1 and 2), albeit under different reaction conditions. The cuprate derived from halide-free $(CH_3)_3SnLi$ and CuBr effected complete S_N2' displacement of tosylate **3** (Table I, entry 4).[1,4]

Additions of allenylstannane **4** to three representative aldehydes, heptanal (**8a**), isobutyraldehyde (**8b**), and pivaldehyde (**8c**), were carried out at −78 °C in the presence of $BF_3{\cdot}OEt_2$ (Table II). Reactions were generally complete within 30 min. With heptanal, a 40:60 mixture of syn and anti alcohols **9a** and **10a** was obtained in 83% yield whereas isobutyraldehyde and pivaldehyde gave the syn adducts **9b** and **9c** as the only detectable products (entries 1, 3, 5).[5] Additions could also be effected with $MgBr_2{\cdot}OEt_2$ in CH_2Cl_2 (entries 2, 4). However, these reactions were slower and less selective than those employing $BF_3{\cdot}OEt_2$.[6]

The stereochemistry of the isobutyraldehyde adduct **9b** was ascertained through Lindlar hydrogenation of the MOM ether **11** to the *Z* olefin **12** followed by ozonolysis

(1) Ruitenberg, K.; Westmijze, H.; Meijer, J.; Elsevier, C. J.; Vermeer, P. *J. Organomet. Chem.* **1983**, *241*, 417. Ruitenberg, K.; Westmijze, H.; Kleijn, H.; Vermeer, P. *J. Organomet. Chem.* **1984**, *277*, 227.

(2) Boaretta, A.; Marton, D.; Tagliavani, G.; Gambaro, A. *J. Organomet. Chem.* **1985**, *286*, 9. Nokami, J.; Tamaoka, T.; Koguchi, T.; Okawara, R. *Chem. Lett.* **1984**, 1939. Mukaiyama, T.; Harada, T. *Chem. Lett.* **1981**, 621. Lequan, M.; Guillern, G. *J. Organomet. Chem.* **1973**, *54*, 153.

(3) Cf. Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 489.

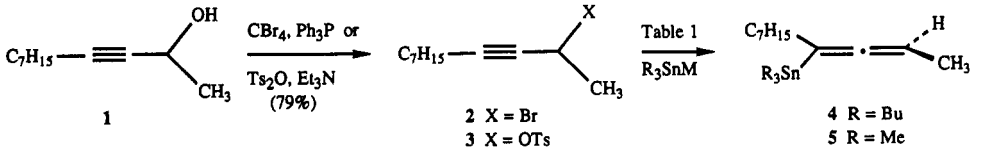
(4) Prepared from $Me_3SnSnMe_3$ and halide-free MeLi.

(5) $BF_3{\cdot}OEt_2$-promoted additions of crotylstannanes to aliphatic saturated aldehydes typically give ca. 90:10 mixtures of syn and anti products. Yamamoto, Y.; Yatagai, H.; Ishikara, Y.; Maeda, N.; Maruyama, K. *Tetrahedron* **1984**, *40*, 2239. Marshall, J. A.; DeHoff, B. S. *J. Org. Chem.* **1986**, *51*, 863.

(6) $MgBr_2$-promoted additions of crotylstannanes to β-alkoxy aldehydes under chelation-controlled conditions proceed with ca. 90:10 syn:anti selectivity. Keck, G. E.; Abbott, D. E. *Tetrahedron Lett.* **1984**, *25*, 1883.

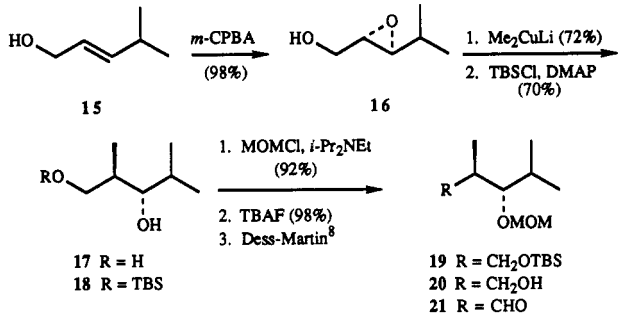
0022-3263/90/1955-6246$02.50/0

Scheme I[a]

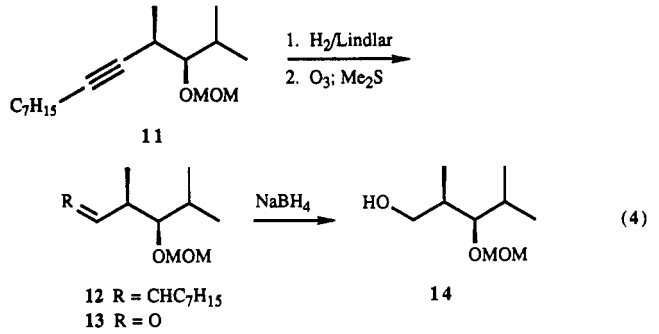


[a] All compounds are racemic.

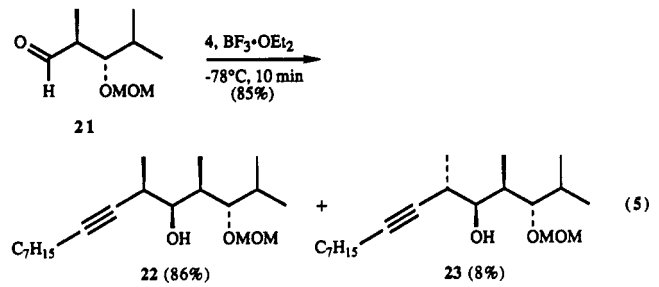
Scheme II



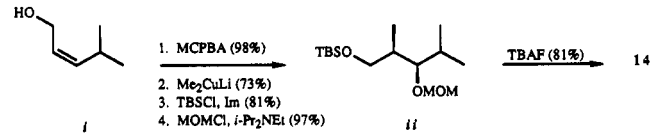
and reduction to alcohol **14** (eq 4). Alcohol **14** and the corresponding anti diastereomer were synthesized independently.[7]



Encouraged by these preliminary findings, we turned our attention to a prototype α-methyl-β-alkoxy aldehyde **21**, prepared as outlined in Scheme II. With allenylstannane **4** the BF_3·OEt_2-promoted reaction was complete within 10 min at −78 °C and afforded a separable 86:8 mixture of Cram products, **22** and **23**, along with 6% of an inseparable mixture containing two isomeric products (eq 5). The



(7) The epoxy alcohol–cuprate sequence of Kishi was employed as follows:



The anti isomer was similarly prepared starting from the *E* allylic alcohol **15** (see Scheme II). Cf.: Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873.

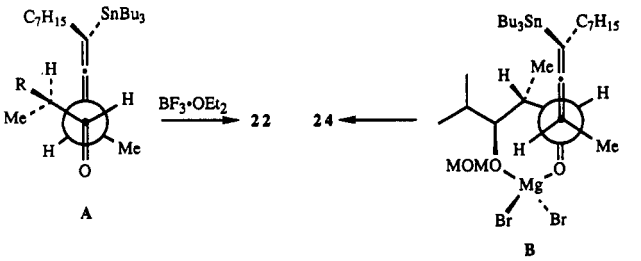
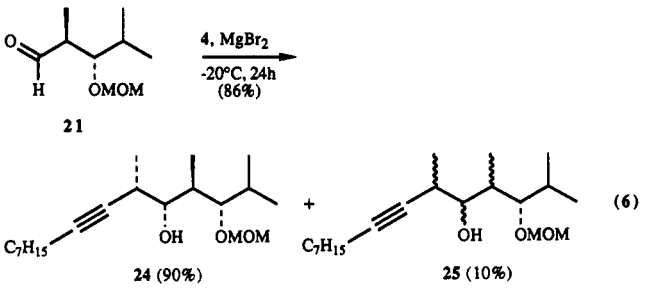
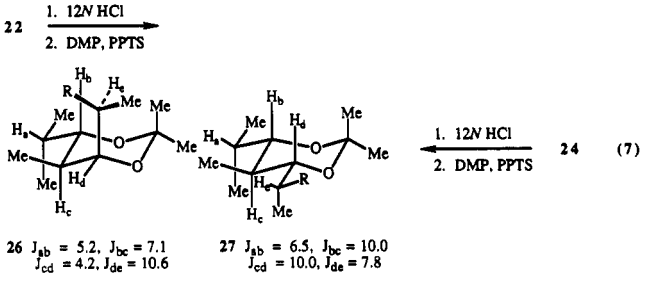


Figure 1. Favored transition-state arrangements for additions of allenylstannane **4** to aldehyde **21**.

corresponding $MgBr_2$-promoted reaction required 24 h at −20 °C and produced a mixture of alcohols containing 90% of the syn isomer **24** (eq 6). Alcohol **24** could be separated from the mixture of other diastereoisomers, which, in view of the prolonged reaction time, may contain products derived from epimerized aldehyde **21**.



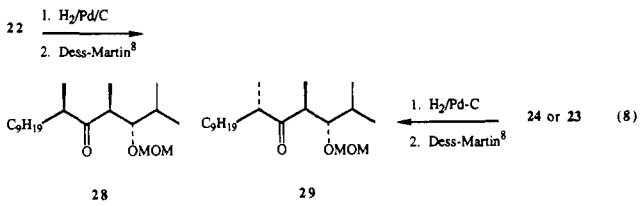
Support for the stereochemistry of the carbinol stereocenter of each major alcohol was secured through hydrolysis of the respective OMOM ethers and conversion of the diols to acetonide derivatives **26** and **27** (eq 7).



Coupling constants and ^{13}C chemical shifts were in accord with the assigned structures.[9] Assuming that the BF_3·OEt_2 and $MgBr_2$·OEt_2 reactions both yield principally syn products, the structures can be assigned as shown. Additional evidence was secured through hydrogenation of each major adduct and Dess–Martin oxidation[8] whereupon two different ketones **28** and **29** were secured (eq 8). Furthermore, the minor product of the BF_3·OEt_2 reaction (**23**) was different from the major product of the $MgBr_2$

(8) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4156.

(9) Rychnovsky, S. D.; Skalitzky, D. J. *Tetrahedron Lett.* **1990**, *31*, 945. The chair conformation of acetonide **26** is shown but the NMR data support a twist-boat conformation.



reaction (**24**). However, upon hydrogenation and oxidation both were converted to ketone **29**.

Likely transition states for the BF_3- and $MgBr_2$-promoted additions are depicted in Figure 1. In each case an anti C=O/C=C arrangement satisfactorily accounts for the observed diastereoselectivity assuming an anti disposition for the $SnBu_3$ moiety.[10] A Cram-Felkin mode of addition is preferred in the BF_3-mediated reaction whereas $MgBr_2$ induces chelation control.[6] Extensions of these findings and further scrutiny of the proposed transition state through the use of enantioenriched aldehydes and stannanes is in progress.

Typical Experimental Procedure. 2,4-Dimethyl-5-tridecyn-3-ol (9b). To a solution of 0.20 mL (1.68 mmol) of $BF_3{\cdot}Et_2O$ in 8 mL of CH_2Cl_2 was added dropwise a mixture of 180 mg (0.40 mmol) of allenic stannane **4** and 0.10 mL (1.12 mmol) of isobutyraldehyde (**8b**) in 3 mL of CH_2Cl_2 at -78 °C. The mixture was stirred at -78 °C for 30 min, quenched with saturated $NaHCO_3$, and extracted with ether. The ether layer was dried over $MgSO_4$ and concentrated. The residue was chromatographed on silica gel (hexane-ether, 4:1) to yield 72 mg (80%) of alcohol **9b** as a single isomer: IR (film) ν 3442, 2929, 2856, 1467, 1378, 1133, 990 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.25 (m, J = 4.3 Hz, 1 H, HOC*H*), 2.56 (m, 1 H, propargylic CH), 2.13 (dt, J = 2.3, 7.1 Hz, 2 H, propargylic CH_2), 1.95 (m, 1 H, C*H*$(CH_3)_2$), 1.68 (d, J = 4.1 Hz, 1 H, OH), 1.46-1.26 (m, 10 H, $(CH_2)_5$), 1.13 (d, J = 6.9 Hz, 3 H, C≡CCHC*H*$_3$), 0.94 (d, J = 6.7 Hz, 3 H, CH(C*H*$_3)_2$), 0.89 (d, J = 6.7 Hz, 3 H, CH(C*H*$_3)_2$), 0.87 (t, J = 7.0 Hz, 3 H, CH_2C*H*$_3$); MS calcd for $C_{15}H_{28}O$ (M - CH$(CH_3)_2$) 181, found 181. Anal. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.20; H, 12.54.

Acknowledgment. Support from the National Institutes of Health (Research Grant 2 RO1 GM29475) and the National Science Foundation (Research Grant CHEM 8912745) is gratefully acknowledged.

Supplementary Material Available: Experimental procedures and ^1H NMR spectra for compounds **4**, **9a-c**, **14**, **20**, **22**, **24**, and **26-29** (23 pages). Ordering information is given on any current masthead page.

(10) The anti orientation was first suggested by Yamamoto.[5] Certain intramolecular additions have been shown to proceed through a *synclinal* arrangement. Denmark, S. E.; Weber, E. J. *J. Am. Chem. Soc.* **1984**, *106*, 7970. Marshall, J. A.; Gung, W. Y. *Tetrahedron* **1989**, *45*, 1043.

Tris(trimethylsilyl)silane (TTMSS): Formation of Carbon-Centered Radicals from 1,3-Dithiolanes and 1,3-Dithianes[1]

Prabhat Arya,* Connie Samson,[2] Maurice Lesage, and David Griller[3]

Steacie Institute for Molecular Sciences, National Research Council of Canada, Ottawa, Ontario, Canada K1A 0R6

Received August 13, 1990

Summary: Tris(trimethylsilyl)silane (TTMSS), a nontoxic reagent, can be used to generate carbon-centered radicals from 1,3-dithiolanes and 1,3-dithianes.

The formation of carbon-carbon bonds through free-radical reactions is an important strategy in synthetic chemistry.[4] Tributyltin hydride, a free-radical mediator, has been the reagent of choice for the formation of radicals for many years because organotin radicals generate carbon-centered radicals from a variety of functional groups. However, the high toxicity of this reagent and the difficulty of removing it from the reaction products makes it less than optimal.

$$RX + Bu_3Sn^{\bullet} \rightarrow R^{\bullet} + Bu_3SnX$$

$$R^{\bullet} + Bu_3SnH \rightarrow RH + Bu_3Sn^{\bullet}$$

X = I, Br, Cl, SPh, SePh

Recently, we have shown that tris(trimethylsilyl)silane (TTMSS) can be used as a free-radical mediator due to its low Si-H bond energy.[5] Many trialkylsilicon hydrides are not suitable because of the high silicon-hydrogen bond strengths. TTMSS has a Si-H bond strength of 79 kcal mol^{-1}, which is very close to Sn-H bond strength 74 kcal mol^{-1} in Bu_3SnH. The weaker bond strength of tris(trimethylsilyl)silane is probably due to the bonding interaction between β-silicon d orbitals and the semioccupied p orbital on the central atom in the corresponding silyl radical.[6] The nontoxic TTMSS is ecologically superior to tributyltin hydride, and the ready purification of the products from the reaction mixtures makes it an attractive reagent.

$$RX + (Me_3Si)_3Si^{\bullet} \rightarrow R^{\bullet} + (Me_3Si)_3SiX$$

$$R^{\bullet} + (Me_3Si)_3SiH \rightarrow RH + (Me_3Si)_3Si^{\bullet}$$

X = I, Br, SePh

The role of Bu_3SnH for the desulfurization of dithiolanes and the corresponding cyclizations from thioxalanes have been studied by Gutierrez[7a] and Fallis.[7b] In this paper, we

(1) Issued as NRCC publication number 32311.
(2) NRC summer student, 1990.
(3) Present address: Peat Marwick Stevenson & Kellogg, Management Consultants, Ottawa, Canada.
(4) (a) Hart, D. J. *Science* **1984**, *223*, 883. (b) Giese, B. In *Radicals in Organic Synthesis Formation of Carbon-Carbon Bonds*; Pergamon: New York, 1986. (c) Neuman, W. P. *Synthesis* **1987**, 665. (d) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (e) Curren, D. P. *Synthesis* **1988**, 417 and 489.
(5) (a) Chatgilialoglu, C.; Griller D.; Lesage, M. *J. Org. Chem.* **1988**, *53*, 3641. (b) Chatgiliagloglu, C.; Griller D.; Lesage, M. *J. Org. Chem.* **1989**, *54*, 364. (c) Lesage, M.; Chatgilialoglu, C.; Griller, D. *Tetrahedron Lett.* **1989**, *30*, 2733. (d) Giese, B.; Kopping, B.; Chatgilialoglu, C. *Tetrahedron Lett.* **1989**, *30*, 681. (e) Alberti, A.; Chatgilialoglu, C. *Tetrahedron* **1990**, *46*, 3963. (f) Jurgen, K.; Giese, B. *Synlett* **1990**, 91.
(6) Kanabus-Kaminska, J. M.; Hawari, J. A.; Griller, D.; Chatgilialoglu, C. *J. Am. Chem. Soc.* **1987**, *109*, 5267.

0022-3263/90/1955-6248$02.50/0 Published 1990 by the American Chemical Society