JOC Article

Syntheses and Reactions of Optically Active α-Aminoallenylstannanes

Peter B. D. Ranslow, Louis S. Hegedus,* and Cristobal de los Rios

Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523

hegedus@lamar.colostate.edu

Received September 8, 2003

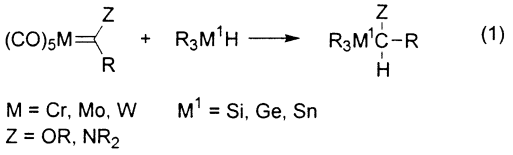
Lithiation/stannylation of optically active *N*-propargyloxazolidinones produced optically active α-oxazolidinonylallenylstannanes. Reaction of these with aldehydes in the presence of $BF_3{\cdot}OEt_2$ produced *β*-hydroxypropargylamines with high syn diastereoselectivity and ee. These were converted to *γ*-hydroxy-*β*-amino acids by oxidative cleavage of the alkyne.

Introduction

Chiral allenylstannanes have been extensively developed, primarily by Marshall,[1] for stereoselective aldol reactions wherein both the relative (syn/anti) and absolute (*R*/*S*) stereochemistries can be controlled. They undergo reactions with aldehydes in the presence of Lewis acids ($BF_3{\cdot}OEt_2$, $MgBr_2{\cdot}OEt_2$) via a S_E2' process to produce homopropargylic alcohols. The absolute stereochemical outcome of this reaction is dependent on both the substrate and Lewis acid used but has been shown to proceed with high absolute stereoselectivity in a number of cases.[1] The relative (syn/anti) stereochemistry is also dependent on the substrate and Lewis acid used; however, in simple cases, selectivity for the formation of *syn*-homopropargylic alcohols has been observed. With chiral α-alkoxyaldehydes, double diastereoselection is operable, and the syn/anti ratios depend both on the absolute configuration of the allene and on the Lewis acid.

In contrast, chiral propargylstannanes are rarely studied, primarily because of their propensity to rearrange to the corresponding allenylstannane.[2] Those that are known undergo reactions with aldehydes in the presence of tetra- or trichlorotin or boron promoters to give homopropargylic alcohols, via the allenylmetal intermediate.[3] In contrast, terminal propargylstannanes underwent reactions with aldehydes in the presence of Ti(IV)−(S)BINOL to give optically active allenyl alcohols.[4] Optically active propargylstannanes could be isolated from the reaction of optically active allenyltitanium species with trialkyltin chlorides via a syn S_E2' mechanism.[5] They also rearrange to the allenylstannane under mild conditions.

Group 6 heteroatom-stabilized metal (Cr, Mo, W) carbene complexes undergo M−H insertion reactions with group 4 metal (Si, Ge, Sn) hydrides to give the corresponding α-heteroatom group 4 metal species (eq 1).[6] Carbene complexes having α-chiral centers on the alkyl side chain undergo this reaction with good to excellent



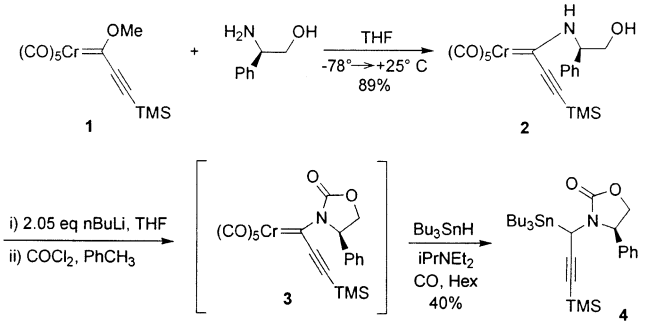
diastereoselectivity,[7] as do carbene complexes having chiral oxazolidinones[8] or imidazolidinones[9] as the heteroatom substituent. Alkenyl- and alkynylcarbene complexes produce allyl- and propargylstannanes,[10] respectively, although allenylstannanes result when the alkyne substituents are relatively unhindered.

α-Heteroatom propargylstannanes are rare, although an α-methoxypropargylstannane has been made and was shown to react with aldehydes in the presence of butyltin trichloride to give *anti*-1,2-diols.[3a] α-Aminopropargylcopper species alkylated aldehydes with high anti selectivity, producing α-aminopropargylic alcohols.[11] Propargylstannanes having a chiral oxazolidinone α to tin (potentially accessible from the carbenechromium complex chemistry

(1) For a review, see: Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31−47.
(2) Marshall, J. A.; Perkins, J. *J. Org. Chem.* **1994**, *59*, 3509−3511.
(3) (a) Savall, B. M.; Powell, N. A.; Roush, W. R. *Org. Lett.* **2001**, *3*, 3057−3060. (b) Carter, R. G.; Weldon, D. J. *Org. Lett.* **2000**, *2*, 3913−3916. (c) Kadota, I.; Hatakeyama, D.; Seki, K.; Yamamoto, Y. *Tetrahedron Lett.* **1996**, *37*, 3059−3062.
(4) Yu, C.-M.; Yoon, S.-K.; Lee, S.-J.; Lee, J.-Y.; Kim, S.-S. *Chem. Commun.* **1998**, 2749−2750.
(5) Okamoto, S.; Matsuda, S.-i.; An, D. K.; Sato, F. *Tetrahedron Lett.* **2001**, *42*, 6323−6326.
(6) (a) Fischer, E. O.; Dötz, K. H. *J. Organomet. Chem.* **1972**, *36*, C4. (b) Connor, J. A.; Day, J. P.; Turner, R. M. *J. Chem. Soc., Dalton Trans.* **1976**, 108. (c) Connor, J. A.; Day, J. P.; Turner, R. N. *J. Chem. Soc., Dalton Trans.* **1976**, 283.
(7) Nakamura, E.; Tanaka, K.; Aoki, S. *J. Am. Chem. Soc.* **1992**, *114*, 9715.
(8) (a) Masters, J. J. Ph.D. Dissertation, Colorado State University, Fort Collins, CO, 1993. (b) Dubuisson, C. Ph.D. Dissertation, Colorado State University, Fort Collins, CO, 1996.
(9) (a) Parisi, M.; Solo, A.; Wulff, W. D.; Guzei, I. A.; Rheingold, A. L. *Organometallics* **1998**, *17*, 3696. (b) Powers, T. S.; Wulff, W. D.; Quinn, J.; Shi, Y.; Jiang, W.; Shung, R.; Parisi, M.; Rahm, A.; Jiang, X. W.; Yap, G. P. A.; Rheingold, A. L. *J. Organomet. Chem.* **1998**, *617*−*618*, 182−208.
(10) (a) Merlic, C. A.; Albaneze, J. *Tetrahedron Lett.* **1995**, *36*, 1007. (b) Merlic, C. A.; Albaneze, J. *Tetrahedron Lett.* **1995**, *36*, 1011.
(11) Bernaud, F.; Vrancken, E.; Mangeney, P. *Org. Lett.* **2003**, *5*, 2567.

10.1021/jo0302861 CCC: $27.50
Published on Web 12/12/2003

SCHEME 1



described above) could provide routes to the optically active 1,2-amino alcohols by similar reaction chemistry. Studies addressing this issue are detailed below.

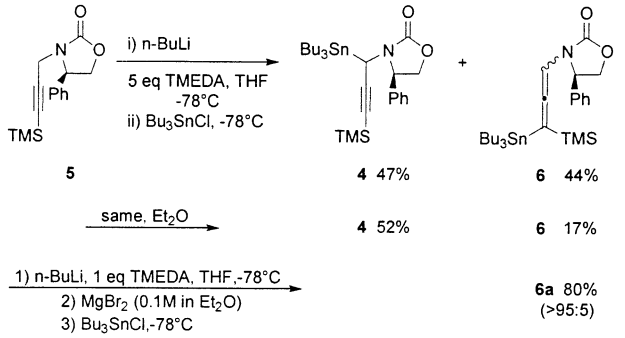
Results and Discussion

Synthesis of Propargylstannanes and Allenylstannanes. The initial approach to optically active α-aminoalkynylstannanes involved the tin hydride cleavage of chiral (oxazolidinone)(alkynyl)carbenechromium complexes discussed above.[9] The requisite carbene complex **2** was synthesized by the reaction of (methoxy)-(trimethysilylethynyl)carbenechromium complex **1** with (*R*)-2-amino-2-phenylethanol to give aminocarbene complex **2**.[9b] Deprotonation of the amino alcohol with 2 equiv of *n*-butyllithium followed by treatment with phosgene produced the desired oxazolidinone carbene complex **3** (Scheme 1). Although formed in good yield, the complex was rather unstable and decomposed on purification, handling, and storage. To minimize this, the THF solution of freshly prepared **3** was concentrated under reduced pressure, taken up in hexane, and directly treated with tributyltin hydride to produce the desired α-oxazolidinonylpropargylstannane **4** in 40% yield. The material was a single diastereoisomer according to the ^{1}H NMR spectrum of the crude reaction mixture, but its configuration was unknown (Scheme 1). Because this approach proved to be inefficient, an alternate route was sought.

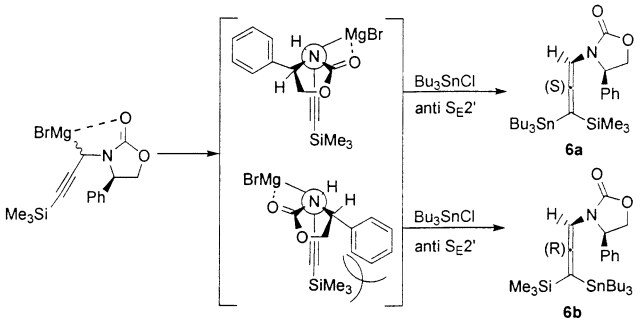
α-Alkoxypropargylstannanes have been prepared by α metalation of propargyl ethers followed by the reaction with tributyltin chloride.[3a] Propargyloxazolidinone **5** could be prepared by literature methods either from propargyl bromide and the anion of the oxazolidinone, followed by the silylation of the terminal alkyne, or by the reaction of the anion of the oxazolidinone with (trimethylsilyl)propargyl bromide. The attempted propargylic stannylation under the reported[3a] conditions (*t*-BuLi, $ZnCl_2$, Bu_3SnCl) gave a complex mixture of products. Omission of the zinc chloride and addition of TMEDA produced a mixture of a single propargylstannane, identical to that obtained from tin hydride cleavage of carbenechromium complex **3**, along with two diastereoisomeric allenylstannanes (Scheme 2). When the solvent was changed to ether, a slightly higher yield of **4** was obtained along with smaller amounts of allenylstannanes.

In an attempt to increase the yield of **4**, magnesium bromide etherate was added prior to the addition of tributyltin chloride. A single allenylstannane, corresponding to the major allenylstannane obtained in Scheme

SCHEME 2



SCHEME 3



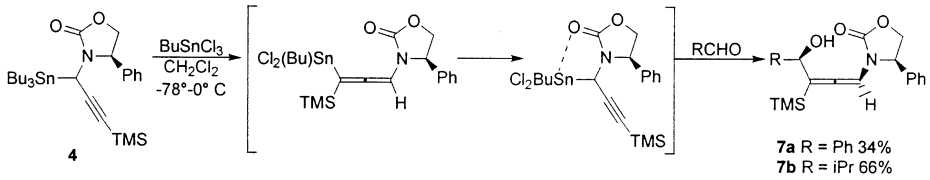
2, was obtained in excellent yield. The configuration of the allenylstannane was tentatively assigned as *S* based on the assumption that transmetalation from magnesium to tin occurred by an anti-S_E2' process[1] from the less sterically congested chelated organomagnesium complex (Scheme 3). With both propargylstannane **4** and allenylstannane **6a** in hand, Lewis acid catalyzed reactions with aldehydes were examined.

Reaction of propargylstannane **4** with aldehydes under conditions reported for the corresponding α-alkoxypropargylstannane[3a] ($BuSnCl_3$, CH_2Cl_2, −78 °C) did *not* lead to the expected homopropargylic alcohol but rather to the allenylcarbinol as a single diastereoisomer (Scheme 4). The relative and absolute stereochemistries of **7b** were determined by single-crystal X-ray diffraction. Tin(IV)-catalyzed reactions of propargylstannanes are thought to proceed by transmetalation by an anti-S_E2' process to produce the more stable allenylstannane,[2] which then reacts with aldehydes by once again an anti-S_E2' mechanism to give homopropargyl alcohols. In the case of **4**, either the reaction proceeds by a different mechanism or the initially formed allenylstannane rearranges to the propargylstannane which can by stabilized by chelation to the oxazolidinone carbonyl group. This then reacts by an anti-S_E2' process to give the observed allenylcarbinol (Scheme 4).

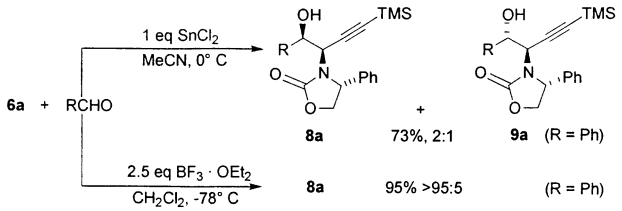
Because of both the relatively low yields of propargylstannane **4** and the unexpected production of allenylcarbinols rather than homopropargyl alcohols, the reaction of allenylstannane **6a** with aldehydes was next examined. Reaction of **6a** with benzaldehyde under the conditions of Scheme 4 resulted in extensive decomposition of the allenylstannane. Using stannous chloride[12] in place of trichlorobutylstannane resulted in 71% yield of

(12) Wei, L.-L.; Hsung, R. P.; Xiong, H.; Mulder, J. A.; Nkansah, N. T. *Org. Lett.* **1999**, *1*, 2145.

SCHEME 4



SCHEME 5[a]



[a] Reported yields are for pure, isolated material; diastereoselectivity estimated from ^{1}H NMR spectra of the crude reaction mixtures.

a 2:1 mixture of diastereoisomeric homopropargyl alcohols **8a** and **9a** (Scheme 5). The relative and absolute stereochemistry was determined by single-crystal X-ray diffraction. The use of conditions developed specifically for the condensation of allenylstannanes with aldehydes (2.5 equiv of BF_3·OEt_2, CH_2Cl_2, −78 °C)[13] produced the desired homopropargyl alcohol in high yield with greater than 95:5 diastereoselectivity based on the ^{1}H NMR spectrum of the crude material.

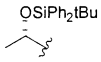
The reaction proved to be general for a range of aldehydes (Table 1). Aromatic, straight- and branched-chain aliphatic, and α,*β*-unsaturated aldehydes all underwent the reaction in high yield and diastereoselectivity. In contrast, the electron-rich formylimidazole was unreactive.

The reaction was relatively insensitive to α chirality in the aldehyde partner with both *S* and *R* enantiomeric aldehydes, R = $CH_3CH(OBn)$, giving almost exclusively the same syn disposition of the newly formed homopropargyl alcohol center and oxazolidinone in products **8f** and **8g**. Neither acetophenone nor the *N*-tosylimine of benzaldehyde underwent BF_3·OEt-catalyzed condensation with **6a**. Only decomposition of the tin reagent was observed, suggesting that this process will be restricted to aldehydes.

The stereochemical outcome of the condensation of **6a** with aldehydes is consistent with the Felkin−Ahn transition-state model developed by Marshall et al.[1,14] for BF_3·OEt_2-catalyzed reactions of aldehydes with allenylstannanes (Scheme 6). This requires the aldehyde to approach from the face opposite the tributyltin group with the large oxazolidinone anti to the large R group of the aldehyde.

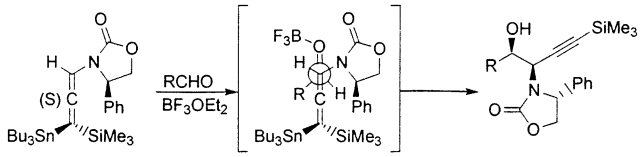
Conversion of Homopropargyl Alcohols to *γ*-Hydroxy-*β*-amino Acids. The ability to generate *syn*-amino alcohols with high diastereo- and enantioselectivity, coupled with the absence of double diastereoselectivity with α-chiral aldehydes as substrates, makes this methodology applicable to the synthesis of a variety of biologically active compounds having adjacent contiguous chiral

TABLE 1. Reactions of 6a with RCHO (Scheme 5)

R	Product (syn)	Yield, %[a]	dr[b](syn/anti)
Ph	**8a**	95	>95:5[c]
iPr	**8b**	95	>95:5
nPr	**8c**	93	>95:5
	**8d**	80	>90:10
	**8e**	68	85:15
	**8f**	87	92:8[c]
	**8g**	87	–[c]
		N.R.	

[a] Reported yields are for isolated, purified single diastereoisomers. [b] Estimated from the ^{1}H NMR spectrum of the crude reaction mixture. [c] Stereochemistry determined by single-crystal X-ray diffraction.

SCHEME 6

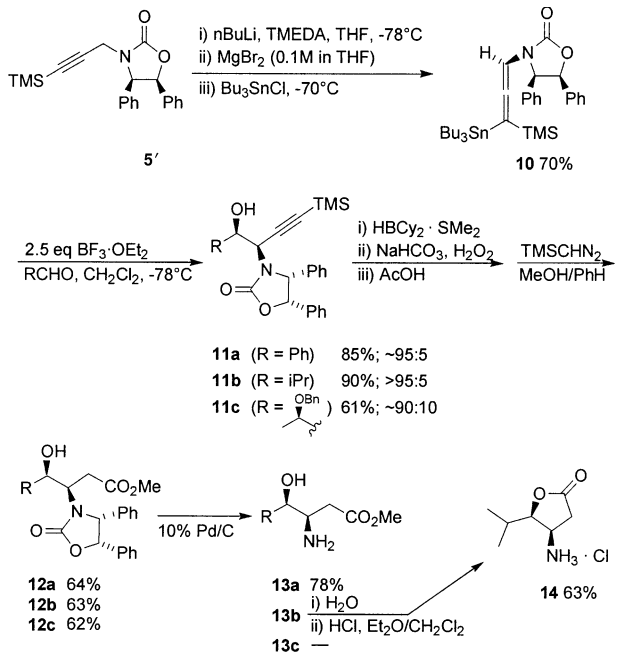


centers. Terminal alkynes are readily converted to terminal carboxylic acids by a hydroboration/oxidation sequence,[16] making these homopropargyl alcohols sources of the *γ*-hydroxy-*β*-amino acid functional group array.

Although the monophenyloxazolidinone used above was an effective chiral auxiliary, conversion to the free amino group would require harsh hydrolysis or reduction conditions incompatible with sensitive functionality, limiting its use in the synthesis. In contrast, the diphenyloxazolidinone[12] is easily cleaved by mild hydrogenolysis.[17] Conversion of propargyldiphenyloxazolidinone **5′** to protected amino ester **12** proceeded in good yield and with high stereoselectivity (Scheme 7). Reductive cleavage of oxazolidinone proceeded in good yield with **12a** (R = Ph).

(13) Yasuda, M.; Sugawa, Y.; Yamamoto, A.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **1996**, *37*, 5951.
(14) Marshall, J. A.; Yanik, M. M. *J. Org. Chem.* **2001**, *66*, 1373.
(15) Marshall, J. A.; Wang, X.-J. *J. Org. Chem.* **1991**, *56*, 3211.
(16) Alemany, C.; Bach, J.; Farràs, J.; Garcia, J. *Org. Lett.* **1999**, *1*, 1831.
(17) Masters, J. J.; Hegedus, L. S. *J. Org. Chem.* **1993**, *58*, 4547.

SCHEME 7[a]



[a] Reported yields are for isolated, purified single diastereoisomers. Diastereoisomeric ratios were determined by ^{1}H NMR spectroscopy of the crude reaction mixture.

In contrast, **12c** (R = CH_3CHCOB_n) produced an inseparable mixture of products arising from the competitive cleavage of the *O*-benzyl group followed by cyclization of a mixture (by infrared spectroscopy) of lactones. Compound **12b** (R = ^{i}Pr) cleaved without complication, but the product amino ester was volatile and difficult to isolate. Conversion to the more tractable lactone amine hydrochloride led to a fair yield of **14**.

In summary, an efficient, highly stereoselective synthesis of α-aminoallenylstannanes has been developed. These underwent reactions with aldehydes that had high syn diastereoselectivity and high enantioselectivity.

Experimental Section

Synthesis of [(Trimethylsilyl)propargyl]aminocarbene Complex 2. To a stirred solution of [(trimethylsilyl)propargyl]-methoxycarbene complex **1**[9b] (1.0 g, 3.0 mmol) in THF (10 mL) at −78 °C was added (*R*)-2-amino-2-phenylethanol (0.46 g, 3.3 mmol) in one portion. The reaction was stirred at −78 °C for 1 h, then warmed to room temperature, and stirred an additional 2.5 h. The reaction mixture was then filtered through a plug of 1:1 silica/Celite, rinsed thoroughly with THF (20 mL), and concentrated under reduced pressure to give the crude reaction product as a deep orange oil. Purification via flash column chromatography with silica gel, eluting with 3:1 hexanes/ethyl acetate, gave [(trimethylsilyl)propargyl]aminocarbene complex **2** (1.17 g, 89%) as a deep orange, viscous oil contaminated with a small amount of ethyl acetate. This compound was used without further purification.

^{1}H NMR δ: 9.50 (m, 1H), 7.38 (m, 3H), 7.29 (m, 2H), 5.36 (p, *J* = 4.2 Hz, 1H), 4.13 (m, 1H), 4.05 (m, 1H), 1.72 (t, *J* = 5.7 Hz, 1H), 0.20 (s, 9H).

Synthesis of Propargylstannane 4 from [(Trimethylsilyl)propargyl]aminocarbene Complex 2. To a stirred solution of carbene complex **2** (0.20 g, 0.46 mmol) in THF (3 mL) at −78 °C was slowly added *n*-butyllithium (1.6 M in hexane, 0.94 mmol). The reaction was stirred at −78 °C for 45 min followed by the addition of a phosgene solution (1.9 M in toluene, 0.5 mmol). The reaction was stirred for an additional 20 min at −78 °C, then warmed to room temperature, and stirred a final 15 min. The solvent was removed under reduced pressure at 0 °C with stirring. To ensure that no phosgene remained in the removed solvent, it was trapped through a tube of potassium hydroxide. Once the reaction had been sufficiently concentrated, hexane (3 mL) was added. The reaction was placed under a carbon monoxide atmosphere, cooled to 0 °C, and Hunig's base (2 drops) and tributyltin hydride (123 μL, 0.46 mmol) were added. After stirring for 30 min, the reaction was again concentrated and purified by flash column chromatography on silica gel, eluting with 5% diethyl ether in hexane, to give propargylstannane **4** (0.10 g, 40%) as a pale yellow oil.

^{1}H NMR δ: 7.42 (m, 3H), 7.30 (m, 2H), 5.05 (t, *J* = 8.4 Hz, 1H), 4.63 (t, *J* = 8.7 Hz, 1H), 4.09 (t, *J* = 8.4 Hz, 1H), 3.15 (s, 1H), 1.52 (m, 6H), 1.30 (m, 6H), 1.04 (m, 6H), 0.89 (t, *J* = 7.2 Hz, 9H), 0.15 (s, 9H). ^{13}C NMR (75 MHz) δ: 159.1, 137.9, 129.4, 129.2, 127.6, 105.0, 69.6, 60.7, 31.2, 29.2, 27.6, 14.0, 12.9, 0.4.

General Procedure for the Synthesis of (Trimethylsilyl)propargyloxazoldinones 5 and 5′. (Trimethylsilyl)-propargyloxazolidinone 5. To a stirred solution of propargyloxazolidinone (1.24 g, 6.20 mmol) in THF (30 mL, 0.2 M) cooled to −78 °C was added lithium hexamethyldisilazane (1.0 M in THF, 6.8 mmol). After stirring for 5 min at −78 °C, trimethylsilyl chloride (875 μL, 6.9 mmol) was added. After stirring an additional 10 min, the reaction was quenched by the addition of a saturated ammonium chloride solution (15 mL) at −78 °C and allowed to warm to room temperature. Once the mixture had warmed to room temperature, water (5 mL) and diethyl ether (60 mL) were added, and the organic layer was separated. The aqueous layer was again extracted with diethyl ether (60 mL), and the combined organic layer was dried over magnesium sulfate, filtered, and concentrated under reduced pressure to afford the crude reaction product. Purification via flash column chromatography with silica gel, eluting with 5:1 hexane/ethyl acetate, gave (trimethylsilyl)-propargyloxazolidinone **5** (1.41 g, 83%) as a white solid.

Mp: 64−66 °C. [α] $^{22}_D$ −166 (*c* 1.1, $CHCl_3$). IR ν (thin film): 1761 cm^{-1} (CO). ^{1}H NMR δ: 7.42 (m, 3 H), 7.31 (m, 2H), 4.96 (t, *J* = 8.4 Hz, 1 H), 4.67 (t, *J* = 8.7 Hz, 1H), 4.42 (d, *J* = 17.4 Hz, 1H), 4.17 (t, *J* = 7.5 Hz, 1H), 3.44 (d, *J* = 17.7 Hz, 1H), 0.17 (s, 9H). ^{13}C NMR (75 MHz) δ: 157.9, 137.1, 129.5, 129.4, 127.5, 98.2, 90.7, 70.1, 59.3, 33.3, 0.0. Elem anal. Calcd for $C_{15}H_{19}NO_2Si$: C, 65.90; H, 7.00; N, 5.12. Found: C, 65.08; H, 6.96; N, 5.03.

(Trimethylsilyl)propargyloxazolidinone 5′. Following the above procedure, using propargyloxazolidinone (350 mg, 1.26 mmol), lithium hexamethyldisilazane (1.0 M, 1.39 mmol), and trimethylsilyl chloride (192 μL, 1.51 mmol) in THF (6.3 mL, 0.2 M) led to the isolation of (trimethylsilyl)propargyl-oxazolidinone **5′** (388.6 mg, 88%) as a white solid.

Mp: 122−123 °C. IR ν (thin film): 1760 cm^{-1} (CO). ^{1}H NMR δ: 7.18 (m, 6 H), 6.98 (m, 2H), 6.86 (m, 2H), 5.91 (d, *J* = 8.4 Hz, 1H), 5.25 (d, *J* = 8.4 Hz, 1H), 4.56 (d, *J* = 17.7 Hz, 1H), 3.53 (d, *J* = 17.7 Hz, 1H), 0.17 (s, 9H). ^{13}C NMR (75 MHz) δ: 157.9, 134.8, 133.6, 128.7, 128.6, 128.2, 128.1, 128.0, 126.2, 98.5, 90.6, 79.8, 64.2, 33.9, 0.0. Elem anal. Calcd for $C_{21}H_{23}NO_2Si$: C, 72.17; H, 6.63; N, 4.01. Found: C, 71.83; H, 6.58; N, 3.95.

Preparation of Propargylstannane 4 from Propargyloxazolidinone 5. To a stirred mixture of (trimethylsilyl)-propargyloxazolidinone **5** (100 mg, 0.37 mmol) and TMEDA (275 μL, 1.83 mmol) in diethyl ether (3.6 mL) at −78 °C was added *n*-butyllithium (1.54 M, 0.40 mmol). The reaction mixture was stirred for 1 h at −78 °C, during which an orange color developed. At this time, tributyltin chloride (99 μL, 0.37 mmol) was added, and the reaction was stirred a final 30 min at −78 °C. The reaction was quenched by the addition of a 10% aq ammonium chloride solution (5 mL) and allowed to warm to room temperature. Diethyl ether (40 mL) was added, and the aqueous layer was separated. The organic layer was

washed with brine (5 mL), dried with magnesium sulfate, filtered, and concentrated under reduced pressure to give the crude reaction product. Purification via flash column chromatography with silica gel, eluting with 9:1 hexane/diethyl ether, gave compound **4** (106.9 mg, 52%) as a clear oil. Spectroscopic data matched that reported above. The later fractions contain a mixture of diastereomeric allenylstannanes **6**, which constitute the bulk of the remaining material.

Synthesis of Allenylstannanes 6a and 10 from (Trimethylsilyl)propargyloxazolidinone 5 and 5′. Allenylstannane 6a. To a stirred solution of (trimethylsilyl)-propargyloxazolidinone **5** (1.0 g, 3.66 mmol) and TMEDA (550 μL, 3.66 mmol) in THF (36 mL) cooled to −78 °C was added *n*-butyllithium (1.48 M in hexane, 4.03 mmol). The mixture was stirred for 45 min at −78 °C, during which an orange color developed, then magnesium(II) bromide (0.12 M in THF, 4.03 mmol) was added, and the reaction was stirred an additional 15 min. Tributyltin chloride (990 μL, 3.66 mmol) was added, and the reaction was stirred a final 30 min at −78 °C. The reaction was quenched by the addition of a saturated aq sodium bicarbonate solution (25 mL) at −78 °C, allowed to warm to room temperature, and extracted with diethyl ether (200 mL). The organic layer was dried with magnesium sulfate, filtered, and concentrated under pressure to give the crude reaction product. Purification via silica flash chromatography with silica gel, eluting with 4:1 hexane/diethyl ether, gave allenylstannane **6a** (1.60 g, 80%) as a white wax of >95% de (determined by comparison of the tin satelites of the major diastereomer to the minor peak of the allenyl proton in the ^{1}H NMR spectrum).

^{1}H NMR (400 MHz) δ: 7.36 (m, 3H), 7.23 (m, 2H), 6.23 (s, 1H), 4.66 (m, 2H), 4.04 (dd, $J_1 = 4.5$ Hz, $J_2 = 7.8$ Hz, 1H), 1.28 (m, 12H), 0.89 (t, $J = 7.2$ Hz, 9H), 0.66 (m, 6H), 0.09 (s, 9H). ^{13}C NMR (75 MHz) δ: 202.2, 155.8, 140.0, 129.4, 128.8, 126.5, 102.9, 84.9, 70.8, 60.3, 29.1, 28.1, 27.8, 27.5, 13.9, 10.8, 0.0.

Allenylstannane 10. This compound was made by the procedure described above, using (trimethylsilyl)propargyloxazolidinone **5′**, which gave allenylstannane **10** (2.55 g, 70%) as an off-white oil of >95% de (determined by comparison of the tin satelites of the major diastereomer to the minor peak of the allenyl proton in the ^{1}H NMR spectrum).

^{1}H NMR (400 MHz) δ: 7.05 (m, 6H), 6.94 (m, 2H), 6.79 (m, 2H), 6.32 (s, 1H), 5.86 (d, $J = 8.1$ Hz, 1H), 4.87 (d, $J = 8.1$ Hz, 1H), 1.20 (m, 12 H), 0.84 (t, $J = 6.6$ Hz, 9H), 0.57 (m, 6H), 0.10 (s, 9H). ^{13}C NMR (75 MHz) δ: 202.5, 155.3, 135.1, 134.4, 128.4, 128.2, 128.1, 128.0, 127.4, 126.5, 102.9, 85.0, 80.5, 65.1, 29.1, 27.7, 27.4, 13.9, 10.7, 0.0.

General Method for the Butyltin Trichloride Promoted Condensation of Propargylstannane 4 with Aldehydes. Synthesis of Allenylcarbinol 7a. To a stirred solution of (trimethylsilyl)propargylstannane **4** (50 mg, 0.09 mmol) and benzaldehyde (7.5 μL, 0.074 mmol) cooled to −78 °C was added butyltin trichloride (1 M in methylene chloride, 0.09 mmol) dropwise. The resulting solution was stirred, gradually, over approximately 1 h, allowed to warm to 0 °C, and stirred at that temperature for a further 30 min. The reaction was quenched by the addition of dilute aq hydrochloric acid (0.1 N, 500 μL) and extracted with diethyl ether (4 mL). The resulting solution was stirred with potassium fluoride/Celite (100 mg) for 1.5 h, then filtered through a plug of Celite, and concentrated under reduced pressure to give the crude reaction product. Purification via flash column chromatography with silica, eluting with 5:1 hexane/ethyl acetate, gave allenylcarbinol **7a** (9.5 mg, 34%) as a white crystalline solid.

Mp: 112−116 °C. $[\alpha]^{22}_D$ −86 (*c* 1.4, $CHCl_3$). IR ν (thin film): 3554 (OH), 1754 cm^{-1} (CO). ^{1}H NMR δ: 7.46 (m, 3H), 7.34 (m, 2H), 7.21 (m, 3H), 6.96 (m, 2H), 6.79 (d, $J = 2.1$ Hz, 1H), 4.92 (dd, $J_1 = 6.6$ Hz, $J_2 = 9.3$ Hz, 1H), 4.76 (t, $J = 9.3$ Hz, 1H), 4.62 (dd, $J_1 = 2.7$ Hz, $J_2 = 4.5$ Hz, 1H), 4.11 (dd, $J_1 = 6.6$ Hz, $J_2 = 8.4$ Hz, 1H), 1.29 (d, $J = 4.8$ Hz, 1H), −0.10 (s, 9H). ^{13}C NMR (75 MHz) δ: 199.3, 155.7, 142.1, 138.3, 129.6, 129.4, 129.3, 128.7, 128.6, 128.3, 127.6, 127.4, 126.6, 126.4, 117.0, 93.9, 75.7, 74.3, 70.6, 70.5, 60.6, 59.9, 0.0, −0.4. Elem anal. Calcd for $C_{22}H_{25}NO_3Si$: C, 69.62; H, 6.64; N, 3.69. Found: C, 69.57; H, 6.68; N, 3.58.

Allenylcarbinol 7b. This compound was prepared by the general method described above, using isobutyraldehyde, which gave allenylcarbinol **7b** (27.1 mg, 66%) as a white crystalline solid.

Mp: 116−117 °C. $[\alpha]^{22}_D$ −184 (*c* 1.4, $CHCl_3$). IR ν (thin film): 3487 (OH), 1748 cm^{-1} (CO). ^{1}H NMR δ: 7.41 (m, 3H), 7.25 (m, 2H), 6.65 (d, $J = 1.8$ Hz, 1H), 4.83 (dd, $J_1 = 6.6$ Hz, $J_2 = 9.0$ Hz, 1H), 4.72 (t, $J = 8.7$ Hz, 1H), 4.09 (dd, $J_1 = 6.3$ Hz, $J_2 = 8.4$ Hz, 1H), 3.08 (bs, 1H), 1.64 (m, 1H), 0.66 (d, $J = 6.6$ Hz, 6H), 0.12 (s, 9H). ^{13}C NMR (75 MHz) δ: 199.2, 155.6, 138.4, 129.4, 129.0, 126.6, 116.4, 92.9, 79.6, 70.6, 59.8, 32.8, 28.1, 27.1, 19.8, 17.7, 17.2, 13.8, 0.0. The absolute configuration of this product was determined by single-crystal X-ray analysis (see the Supporting Information).

Tin(II) Chloride Promoted Condensation of Allenylstannane 6a with Benzaldehyde. Synthesis of Diastereomeric Homopropargylic Alcohols 8a and 9a. To a stirred solution of allenylstannane **6a** (500 mg, 0.89 mmol) and benzaldehyde (91 μL, 0.89 mmol) cooled to 0 °C was added tin(II) chloride (169 mg, 0.89 mmol) in one portion. The reaction was stirred at 0 °C for 4 h and then allowed to slowly warm to room temperature overnight. The reaction was quenched by pouring in 10% aq ammonium chloride (25 mL) and diluted with diethyl ether (100 mL). The organic layer was separated, washed with brine, dried with magnesium sulfate, filtered, and concentrated under reduced pressure to give the crude reaction product. NMR spectroscopy of the crude reaction mixture showed an approximate 2:1 mixture of the diastereomeric products. Purification via flash column chromatography with silica gel, eluting with 3:1 hexane/ethyl acetate, gave homopropargylic alcohol **8a** (156.7 mg, 46%) and homopropargylic alcohol **9a** (89.9 mg, 27%) both as white solids.

8a. Mp: 171−173 °C. $[\alpha]^{22}_D$ −145 (*c* 1.1, $CHCl_3$). IR (thin film): 3438 (OH), 1731 cm^{-1} (CO). ^{1}H NMR (400 MHz) δ: 7.32 (m, 8H), 7.14 (m, 2H), 5.11 (t, $J = 5.6$ Hz, 1H), 4.88 (t, $J = 8.4$ Hz, 1H), 4.54 (t, $J = 8.4$ Hz, 1H), 4.39 (d, $J = 6.8$ Hz, 1H), 4.05 (dd, $J_1 = 7.6$ Hz, $J_2 = 8.4$ Hz, 1H), 3.85 (d, $J = 5.6$ Hz, 1H), 0.00 (s, 9H). ^{13}C NMR (75 MHz) δ: 159.2, 140.1, 137.5, 129.2, 128.4, 128.3, 127.6, 126.8, 98.8, 92.9, 74.6, 71.2, 60.4, 53.6, −0.2. The absolute configuration of this product was determined by single-crystal X-ray analysis.

Minor Diastereomer 9a. $[\alpha]^{22}_D$ −86 (*c* 1.4, $CHCl_3$). ^{1}H NMR (400 MHz) δ: 7.35 (m, 3H), 7.30 (s, 5H), 7.14 (m, 2H), 5.22 (t, $J = 3.9$ Hz, 1H), 4.88 (t, $J = 8.4$ Hz, 1H), 4.60 (t, $J = 8.7$ Hz, 1H), 4.16 (d, $J = 4.5$ Hz, 1H), 4.09 (t, $J = 7.8$ Hz, 1H), 3.92 (d, $J = 3.6$ Hz, 1H), 0.09 (s, 9H). Some minor impurities are visible in this spectrum. The absolute configuration of this product was determined by single-crystal X-ray analysis (see the Supporting Information).

General Procedure for the Condensation of Allenylstannanes 6a and 10 with Aldehydes. Synthesis of Homopropargylic Alcohol 7a. To a stirred solution of allenylstannane **6a** (100 mg, 0.18 mmol) and benzaldehyde (24 μL, 0.23 mmol) in methylene chloride (900 μL) at −78 °C was added boron trifluoride diethyl etherate (55 μL, 0.45 mmol). The reaction was stirred at −78 °C for 2.5−3 h, until no allenylstannane remained by TLC, then quenched at −78 °C with saturated sodium bicarbonate (5 mL), and stirred an additional 15−20 min while warming to room temperature. The reaction mixture was diluted with diethyl ether (40 mL), and the organic phase was separated, dried with magnesium sulfate, filtered, and concentrated under reduced pressure to give the crude reaction product. The diastereoselectivity of the reaction was determined to be >95:5. Purification through silica gel, eluting with 3:1 hexane/ethyl acetate, gave homopropargylic alcohol **7a** (64.2 mg, 95%) as a white solid. Also a small, unweighed portion of the minor diastereomer **8a** could

be isolated in this way. The spectral data matched that reported previously.

Homopropargyl Alcohol 8b. This compound was made according to the general procedure, using isobutyraldehyde, which gave homopropargylic alcohol **8b** (58.6 mg, 95%) as a white crystalline solid. The diastereoselectivity of the reaction was determined to be >95:5.

Mp: 167−168 °C. $[\alpha]^{22}_D$ −104 (*c* 1.7, $CHCl_3$). IR ν (thin film): 3342 (OH), 1714 cm^{-1} (CO). ^1H NMR δ: 7.38 (m, 5H), 5.04 (dd, $J_1 = 6.9$ Hz, $J_2 = 8.7$ Hz, 1H), 4.65 (t, $J = 8.7$ Hz, 1H), 4.43 (d, $J = 7.8$ Hz, 1H), 4.16 (dd, $J_1 = 6.9$ Hz, $J_2 = 7.5$ Hz, 1H), 3.77 (ddd, $J_1 = 5.1$ Hz, $J_2 = 7.2$ Hz, $J_3 = 12.0$ Hz, 1H), 2.36 (d, $J = 6.9$ Hz, 1H), 1.96 (m, 1H), 0.94 (dd, $J_1 = 7.2$ Hz, $J_2 = 12.6$ Hz, 6H), −0.01 (s, 9H). ^{13}C NMR (75 MHz) δ: 159.1, 138.4, 129.1, 129.0, 127.8, 99.9, 92.0, 76.6, 71.1, 59.6, 50.3, 30.0, 20.1, 15.9, −0.1. Elem anal. Calcd for $C_{19}H_{27}NO_3Si$: C, 66.05; H, 7.88; N, 4.05. Found: C, 65.94; H, 7.85; N, 4.05.

Homopropargyl Alcohol 8c. This compound was made according to the general procedure, using *n*-butyraldehyde, which gave homopropargylic alcohol **8c** (56.9 mg, 93%) as a white crystalline solid. The diastereoselectivity of the reaction was determined to be >95:5.

Mp: 123−126 °C. $[\alpha]^{22}_D$ −97 (*c* 1.2, $CHCl_3$). IR ν (thin film): 3494 (OH), 1716 cm^{-1} (CO). ^1H NMR δ: 7.38 (s, 5H), 5.04 (dd, $J_1 = 5.1$ Hz, $J_2 = 6.3$ Hz, 1H), 4.66 (t, $J = 6.6$ Hz, 1H), 4.23 (d, $J = 5.4$ Hz, 1H), 4.15 (dd, $J_1 = 5.4$ Hz, $J_2 = 6.6$ Hz, 1H), 3.99 (dq, $J_1 = 2.4$ Hz, $J_2 = 6.6$ Hz, 1H), 2.69 (d, $J = 4.8$ Hz, 1H), 1.62 (m, 2 H), 1.42 (m, 2H), 0.93 (t, $J = 5.4$ Hz, 3H), 0.0 (s, 9H). ^{13}C NMR (75 MHz) δ: 159.0, 138.2, 129.2, 127.8, 99.8, 92.2, 72.3, 71.1, 59.9, 52.5, 36.3, 19.0, 14.2, −0.1. Elem anal. Calcd for $C_{19}H_{27}NO_3Si$: C, 66.05; H, 7.88; N, 4.05. Found: C, 66.26; H, 8.05; N, 4.20.

Homopropargyl Alcohol 8d. This compound was made according to the general procedure, using crotonaldehyde, which gave homopropargylic alcohol **8d** (49.4 mg, 80%) as a white crystalline solid. The diastereoselectivity of the reaction was determined to be >90:10.

Mp: 179−183 °C. $[\alpha]^{22}_D$ −97 (*c* 2.2, $CHCl_3$). IR ν (thin film): 3398 (OH), 1747 cm^{-1} (CO). ^1H NMR δ: 7.38 (s, 5H), 5.82 (ddq, $J_1 = 1.2$ Hz, $J_2 = 6.6$ Hz, $J_3 = 15.3$ Hz, 1H), 5.47 (ddd, $J_1 = 1.5$ Hz, $J_2 = 6.0$ Hz, $J_3 = 15.0$ Hz, 1H), 5.02 (dd, $J_1 = 7.2$ Hz, $J_2 = 8.7$ Hz, 1H), 4.63 (t, $J = 8.4$ Hz, 1H), 4.44 (q, $J = 6.6$ Hz, 1H), 4.30 (d, $J = 6.9$ Hz, 1H), 4.14 (dd, $J_1 = 6.9$ Hz, $J_2 = 8.4$ Hz, 1H), 2.88 (d, $J = 6.3$ Hz, 1H), 1.73 (d, $J = 6.6$ Hz, 3H), 0.0 (s, 9H). ^{13}C NMR (75 MHz) δ: 159.0, 138.2, 129.6, 129.3, 129.2, 129.1, 127.8, 99.2, 92.6, 73.1, 71.1, 59.9, 52.4, 18.0, −0.1. Elem anal. Calcd for $C_{19}H_{25}NO_3Si$: C, 66.44; H, 7.34; N, 4.08. Found: C, 66.28; H, 7.13; N, 4.06.

Homopropargyl Alcohol 8e. This compound was made according to the general procedure, using (*S*)-2-(*tert*-butyldiphenylsilyloxy)propanal, which gave homopropargylic alcohol **8e** (70.8 mg, 68%) as a white crystalline solid. The diastereoselectivity of the reaction was determined to be 85:15.

Mp: 197−198 °C. $[\alpha]^{22}_D$ −60 (*c* 1.3, $CHCl_3$). IR ν (thin film): 3381 (OH), 1705 cm^{-1} (CO). ^1H NMR (400 MHz) δ: 7.68 (m, 4H), 7.42 (m, 5H), 7.36 (m, 6H), 4.94 (t, $J = 8.8$ Hz, 1H), 4,90 (d, $J = 10.0$ Hz, 1H), 4.63 (t, $J = 8.8$ Hz, 1H), 4.26 (q, $J = 10.4$ Hz, 1H), 4.12 (t, $J = 10$ Hz, 1H), 3.65 (t, $J = 10.0$ Hz, 1H), 2.50 (d, $J = 10.8$ Hz, 1H), 1.04 (d, $J = 7.2$ Hz, 3H), 1.03 (s, 9H), −0.01 (s, 9H). ^{13}C NMR (75 MHz) δ: 159.5, 138.5, 136.1, 136.0, 134.3, 133.0, 130.1, 129.9, 129.6, 129.0, 128.0, 127.7, 127.5, 99.7, 92.1, 75.2, 71.0, 68.7, 59.0, 49.8, 27.1, 26.9, 21.1, 19.7, 0.1, −0.2. Elem anal. Calcd for $C_{34}H_{43}NO_4Si$: C, 69.70; H, 7.40; N, 2.47. Found: C, 69.80; H, 7.47; N, 2.47.

Homopropargyl Alcohol 8f. This compound was made according to the general procedure, using (*S*)-2-benzyloxypropanal, which gave homopropargylic alcohol **8f** (67.7 mg, 87%) as a white crystalline solid. The diastereoselectivity of the reaction was determined to be 92:8.

Mp: 110−112 °C. $[\alpha]^{22}_D$ −28 (*c* 1.4, $CHCl_3$). IR ν (thin film): 3382 (OH), 1713 cm^{-1} (CO). ^1H NMR (400 MHz) δ: 7.37 (m, 7H), 7.29 (m, 3H), 4.95 (t, $J = 8.7$ Hz, 1H), 4.80 (d, $J = 9.9$ Hz, 1H), 4.64 (d, $J = 12.9$ Hz, 1H), 4.62 (t, $J = 8.4$ Hz, 1H), 4.44 (d, $J = 11.7$ Hz, 1H), 4.11 (t, $J = 8.4$ Hz, 1H), 3.87 (q, $J = 6.3$ Hz, 1H), 3.73 (t, $J = 10.2$ Hz, 1H), 2.36 (d, $J = 10.5$ Hz, 1H), 1.31 (d, $J = 6.3$ Hz, 3H), −0.07 (s, 9H). ^{13}C NMR (75 MHz) δ: 159.3, 138.4, 138.0, 129.1, 129.0, 128.6, 128.0, 127.9, 99.8, 92.0, 74.8, 72.7, 71.4, 71.0, 59.0, 49.6, 16.7, −0.2. The absolute configuration of this product was determined by single-crystal X-ray analysis (see the Supporting Information).

Homopropargyl Alcohol 8g. This compound was made according to the general procedure, using (*R*)-2-benzyloxypropanal, which gave homopropargylic alcohol **8g** (67.5 mg, 87%) as a white crystalline solid. The diastereoselectivity of the reaction was not able to be determined.

Mp: 220−221 °C. $[\alpha]^{22}_D$ −90 (*c* 1.0, $CHCl_3$). IR ν (thin film): 3347 (OH), 1719 cm^{-1} (CO). ^1H NMR (400 MHz) δ: 7.32 (M, 10 H), 5.00 (dd, $J_1 = 6.9$ Hz, $J_2 = 8.7$ Hz, 1H), 4.57 (m, 3H), 4.44 (d, $J = 11.7$ Hz, 1H), 4.10 (m, 2H), 3.75 (dq, $J_1 = 4.2$ Hz, $J_2 = 6.3$ Hz, 1H), 2.85 (d, $J = 4.5$ Hz, 1H), 1.24 (d, $J = 6.3$ Hz, 3H), −0.04 (s, 9H). ^{13}C NMR (75 MHz) δ: 159.0, 138.4, 129.1, 129.0, 128.6, 128.0, 127.9, 99.4, 92.1, 74.9, 73.1, 71.0, 70.8, 59.4, 48.5, 13.9, −0.2. The absolute configuration of this product was determined by single-crystal X-ray analysis (see the Supporting Information).

Homopropargyl Alcohol 11a. This compound was made according to the general procedure, using benzaldehyde and allenylstannane **10**, which gave homopropargylic alcohol **11a** (308.5 mg, 85%) as a white crystalline solid. The diastereoselectivity of the reaction was determined to be ∼95:5.

Mp: 252−254 °C. $[\alpha]^{22}_D$ −111 (*c* 0.9, $CHCl_3$). IR ν (thin film): 3434 (OH), 1721 cm^{-1} (CO). ^1H NMR (300 MHz) δ: 7.41 (m, 5H), 7.03 (m, 6H), 6.85 (m, 2H), 6.70 (d, $J = 6.9$ Hz, 2H), 5.64 (d, $J = 7.8$ Hz, 1H), 5.15 (t, $J = 6.0$ Hz, 1H), 5.05 (d, $J = 7.8$ Hz, 1H), 4.71 (d, $J = 6.9$ Hz, 1H), 3.61 (d, $J = 5.7$ Hz, 1H), −0.07 (s, 9H). ^{13}C NMR (75 MHz) δ: 158.9, 139.8, 134.4, 134.2, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 126.9, 126.4, 98.5, 93.9, 81.2, 75.0, 64.7, 53.5, −0.3. Elem anal. Calcd for $C_{28}H_{29}NO_3Si$: C, 73.81; H, 6.42; N, 3.07. Found: C, 74.00; H, 6.47; N, 3.18.

Homopropargyl Alcohol 11b. This compound was made according to the general procedure, using isobutyraldehyde and allenylstannane **10**, which gave homopropargylic alcohol **11b** (295.9 mg, 90%) as a white crystalline solid. The diastereoselectivity of the reaction was determined to be >95:5.

Mp: 96−106 °C. $[\alpha]^{22}_D$ −23 (*c* 0.3, $CHCl_3$). IR ν (thin film): 3531 (OH), 1725 cm^{-1} (CO). ^1H NMR (300 MHz) δ: 7.06 (m, 6H), 6.93 (m, 4H), 5.85 (d, $J = 7.5$ Hz, 1H), 5.29 (d, $J = 8.1$ Hz, 1H), 4.71 (d, $J = 6.9$ Hz, 1H), 3.75 (q, $J = 6.0$ Hz, 1H), 2.37 (d, $J = 5.7$ Hz, 1H), 2.03 (septet, $J = 6.0$ Hz, 1H), 1.04 (d, $J = 6.9$ Hz, 3H), 0.99 (d, $J = 6.6$ Hz, 3H), −0.1 (s, 9H). ^{13}C NMR (75 MHz) δ: 158.7, 134.9, 134.3, 128.3, 128.2, 128.1, 128.0, 126.4, 99.7, 92.9, 81.1, 78.1, 64.3, 50.2, 30.1, 20.0, 16.6, −0.3. Elem anal. Calcd for $C_{25}H_{31}NO_3Si$: C, 71.22; H, 7.41; N, 3.32. Found: C, 71.41; H, 7.24; N, 3.40.

Homopropargyl Alcohol 11c. This compound was made according to the general procedure, using (*R*)-2-benzyloxypropanal and allenylstannane **10**, which gave homopropargylic alcohol **11c** (245.9 mg, 61%) as a white crystalline solid. The diastereoselectivity of the reaction was determined to be ∼90:10.

Mp: 150−152 °C. $[\alpha]^{22}_D$ −38 (*c* 1.1, $CHCl_3$). IR ν (thin film): 3459 (OH), 1733 cm^{-1} (CO). ^1H NMR (300 MHz) δ: 7.37 (m, 5H), 7.07 (m, 6H), 6.89 (m, 4H), 5.71 (d, $J = 7.5$ Hz, 1H), 5.21 (d, $J = 7.8$ Hz, 1H), 4.83 (d, $J = 7.2$ Hz, 1H), 4.65 (d, $J = 11.4$ Hz, 1H), 4.50 (d, $J = 11.4$ Hz, 1H), 4.05 (m, 1H), 3.81 (quintet, $J = 5.7$ Hz, 1H), 2.73 (d, $J = 4.5$ Hz, 1H), 1.32 (d, $J = 6.3$ Hz, 3H), −0.12 (s, 9H). ^{13}C NMR (75 MHz) δ: 158.6, 138.3, 135.0, 134.5, 128.7, 128.3, 128.2, 128.1, 128.0, 127.9, 126.4, 99.2, 92.9, 81.0, 74.9, 74.3, 71.0, 64.0, 48.7, 14.3, −0.3. Elem anal. Calcd for $C_{31}H_{35}NO_4Si$: C, 72.48; H, 6.87; N, 2.73. Found: C, 72.43; H, 6.78; N, 2.59.

Hydroboration/Oxidation of (Trimethylsilyl)alkynes. Synthesis of β-Amino Ester 12a. To a stirred solution of cyclohexene (115 μL, 1.1 mmol) in THF (1.1 mL) cooled to 0 °C was added the borane methyl sulfide complex (55 μL, 0.55 mmol). The reaction was warmed to room temperature, stirred for 1 h, and then recooled to 0 °C. Homopropargylic alcohol **11a** (50 mg, 0.11 mmol) in THF (1.1 mL) was added dropwise, and reaction was again allowed to warm to room temperature and stirred for 1.5 h (until no **11a** was visible by TLC). The reaction was then quenched by the addition of a saturated ammonium bicarbonate solution (1.1 mL) followed by the addition of 30% aq hydrogen peroxide (400 μL). The reaction was stirred a final 3 h and recooled to 0 °C, and acetic acid (220 μL) was added. The reaction was stirred overnight and then extracted with methylene chloride (4 × 5 mL). The combined organic extracts were dried with magnesium sulfate, filtered, and concentrated under reduced pressure. The white residue, thus generated, was redissolved in 4:1 benzene/methanol (2.2 mL). (Trimethylsilyl)diazomethane (2.0 M in hexane, 0.22 mmol) was added, and the reaction was allowed to stir for 30 min and then was concentrated under reduced pressure to give the crude reaction product. Purification by flash column chromatography with silica gel, eluting with 95:5 methylene chloride/ethyl acetate, gave β-amino ester **12a** (30.6 mg, 64%) as a white solid with some (<1 equiv) dimethyl sulfone contaminant. The dimethyl sulfone was removed by sublimation under reduced pressure by heating to approximately 40 °C, and this compound was used without further purification.

IR ν (thin film): 3467 (OH), 1735 cm^{-1} (CO). ^1H NMR (300 MHz) δ: 7.30 (m, 5H), 7.05 (m, 4H), 6.91 (m, 2H), 6.80 (m, 2H), 6.41 (bs, 2H), 5.71 (d, J = 8.4 Hz, 1H), 5.21 (d, J = 8.4 Hz, 1H), 4.99 (t, J = 7.5 Hz, 1H), 4.64 (d, J = 8.4 Hz, 1H), 3.99 (q, J = 6.0 Hz, 1H), 3.67 (s, 3H), 2.86 (dd, J_1 = 7.5 Hz, J_2 = 16.8 Hz, 1H), 2.77 (dd, J_1 = 5.7 Hz, J_2 = 16.8 Hz, 1H). ^{13}C NMR (75 MHz) δ: 172.0, 159.9, 141.3, 134.6, 133.7, 128.7, 128.6, 128.5, 128.2, 128.1, 128.0, 127.9, 126.6, 126.1, 81.0, 75.2, 66.2, 57.4, 52.2, 34.4. HRMS (FAB$^+$) (M + H) m/z: calcd for $C_{26}H_{27}NO_5$, 432.1811; found, 432.1804.

Synthesis of γ-Hydroxy Ester 12b. This compound was made according to the general procedure, using **11c**, which gave γ-hydroxy ester **12c** (35.5 mg, 63%) as a white solid.

[a] $^{22}_D$ +31 (c 0.4, $CHCl_3$). IR (thin film): 3468 (OH), 1747 (CO), 1719 cm^{-1} (CO). ^1H NMR (300 MHz) δ: 7.09 (m, 6H), 7.00 (m, 4H), 5.90 (d, J = 8.4 Hz, 1H), 5.32 (d, J = 8.1 Hz, 1H), 4.19 (dt, J_1 = 4.5 Hz, J_2 = 7.2 Hz, 1H), 3.64 (s, 3H), 3.36 (dt, J_1 = 3.3 Hz, J_2 = 4.5 Hz, 1H), 3.17 (d, J = 7.2 Hz, 1H), 2.68 (dd, J_1 = 7.8 Hz, J_2 = 16.2 Hz, 1H), 2.49 (dd, J_1 = 6.3 Hz, J_2 = 16.5 Hz, 1H), 1.72 (sextet, J = 6.6 Hz, 1H), 0.97 (d, J = 6.6 Hz, 3H), 0.69 (d, J = 6.6 Hz, 3H). ^{13}C NMR (75 MHz) δ: 172.2, 158.9, 135.8, 134.6, 128.7, 128.4, 128.1, 127.9, 126.0, 80.9, 78.4, 65.9, 53.6, 52.1, 35.9, 31.1, 19.6, 18.4. HRMS (FAB$^+$) (M + H) m/z: calcd for $C_{23}H_{28}NO_5$, 398.1967; found, 398.1959.

Synthesis of β-Amino Ester 12c. This compound was made by the procedure described above, using **11c**, which gave β-amino ester **12c** (88.4 mg, 62%) as a white solid.

IR ν (thin film): 3416 (OH), 1740 cm^{-1} (CO). ^1H NMR (300 MHz) δ: 7.25 (m, 5H), 7.06 (m, 6H), 6.93 (m, 4H), 5.74 (d, J = 8.1 Hz, 1H), 5.28 (d, J = 7.8 Hz, 1H), 4.44 (d, J = 11.4 Hz, 1H), 4.39 (m, 1H), 3.94 (d, J = 10.8 Hz, 1H), 3.80 (d, J = 6.6 Hz, 1H), 3.71 (q, J = 3.6 Hz, 1H), 3.61 (s, 3H), 3.53 (t, J = 6.3 Hz, 1H), 2.79 (dd, J_1 = 7.5 Hz, J_2 = 16.8 Hz, 1H), 2.51 (dd, J_1 = 6.0 Hz, J_2 = 17.1 Hz, 1H), 1.31 (d, J = 5.7 Hz, 3H).

Synthesis of γ-Hydroxy-β-amino Ester 13a. A stirred solution of β-amino ester **12a** (29.8 mg, 0.069 mmol) in ethanol (7.0 mL) under argon was added to 10% palladium on carbon (15 mg, 0.014 mmol). The reaction mixture was flushed with hydrogen gas for 15 s and then stirred under a balloon of hydrogen for 17 h. The reaction was filtered through a pad of Celite, rinsing with ethanol (5 mL), and concentrated under reduced pressure to give the crude reaction mixture. The crude residue was dissolved in diethyl ether, filtered again through a pad of Celite to remove any insoluble impurities, and concentrated again under reduced pressure. The dibenzyl byproduct was removed by trituration with hexane (4 × 1 mL) to give γ-hydroxy-β-amino ester **13a** (11.2 mg, 78%) as a white crystalline solid.

Mp: 97−98 °C. [α] $^{22}_D$ −20 (c 0.2, $CHCl_3$). IR ν (thin film): 3123 (OH), 1729 cm^{-1} (CO). ^1H NMR (300 MHz) δ: 7.36 (s, 5H), 4.44 (d, J = 6.0 Hz, 1H), 3.68 (s, 3H), 3.35 (m, 1H), 2.50 (dd, J_1 = 4.2 Hz, J_2 = 15.9 Hz, 1H), 2.34 (dd, J_1 = 9.3 Hz, J_2 = 16.2 Hz, 1H), 2.13 (bs, 2H). ^{13}C NMR (75 MHz) δ: 172.8, 141.8, 128.7, 128.1, 126.8, 76.6, 54.6, 51.9, 39.0. Elem anal. Calcd for $C_{11}H_{15}NO_3 \cdot 0.5H_2O$: C, 60.54; H, 7.39; N, 6.42. Found: C, 60.27; H, 6.94; N, 6.17.

Synthesis of β-Amino-γ-butyrolactone Hydrochloride Salt 14. A stirred solution of γ-hydroxy-β-amino ester **12b** (50 mg, 0.126 mmol) in THF (6.3 mL) under argon was added to 10% palladium on carbon (53.2 mg, 0.05 mmol). The reaction mixture was flushed with hydrogen gas for 15 s and then stirred under a balloon of hydrogen for 24 h. The reaction was filtered through a pad of Celite, rinsing with THF (10 mL), and concentrated under reduced pressure to give the crude reaction mixture, in which γ-hydroxy-β-amino ester **13b** was clearly visible in the ^1H NMR spectrum. This crude residue was dissolved in diethyl ether, filtered again through a pad of Celite to remove any insoluble impurities into a small round-bottomed flask, and concentrated again under reduced pressure. Water (2 mL) was then added, and the suspension was gently heated and swirled for approximately 2−3 min. The suspension was filtered through a plug of cotton, and the filtrate was extracted with methylene chloride (5 × 5 mL) and dried with sodium sulfate. The residue on the cotton filter and in the round-bottomed flask were dissolved in methylene chloride, dried with sodium sulfate, combined with the dried methylene chloride layer from the extraction, and concentrated under reduced pressure to approximately a 5 mL volume. Excess hydrochloric acid (saturated in diethyl ether, 250 μL) was added, and the solution was allowed to stand for 1−2 min and then was concentrated to dryness under reduced pressure. The dibenzyl byproduct was removed by trituration with hexane (4 × 1 mL), and the remaining solid was recrystallized from ethanol/hexane (3 crops total) to give β-amino-γ-butyrolactone hydrochloride salt **14** (14.2 mg, 63%) as a white, cottony solid.

Mp: 228−230 °C. IR ν (thin film): 2918 (NH_3^+), 1770 cm^{-1} (CO). ^1H NMR (300 MHz, methanol-d_4) δ: 4.26 (m, 2H), 3.25 (dd, J_1 = 6.1 Hz, J_2 = 18.3 Hz, 1H), 2.62 (d, J = 18.3 Hz, 1H), 1.92 (d septets, J_1 = 6.0 Hz, J_2 = 4.2 Hz, 1H), 1.19 (d, J = 6.0 Hz, 3H), 1.03 (d, J = 6.6 Hz, 3H). ^{13}C NMR (75 MHz) δ: 174.8, 87.4, 51.4, 36.8, 28.7, 20.4, 18.1. Elem anal. Calcd for $C_7H_{14}ClNO_3$: C, 46.80; H, 7.86; N, 7.80. Found: C, 47.03; H, 7.65; N, 7.73.

Acknowledgment. Support for this research under Grant GM26178 from the National Institutes of Health is gratefully acknowledged. Mass spectra were obtained on instruments supported by the National Institutes of Health shared instrumentation Grant GM 49631.

Supporting Information Available: ^1H NMR spectrum of **3**; ^1H and ^{13}C NMR spectra of **6a**, **7b**, **8a**, **8f**, **8g**, **10**, **9a**, **12a**, **12b**, and **13a**; X-ray structural data for **7b**, **8a**, **8f**, **8g**, and **9a**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0302861