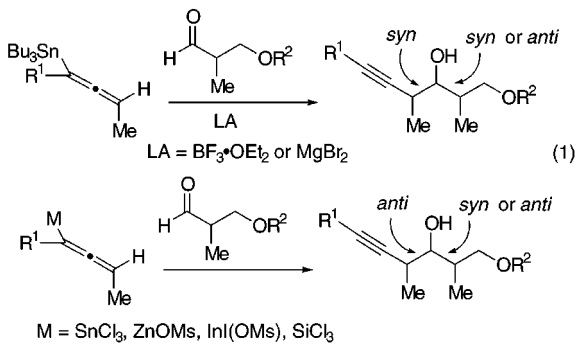
Stereoselective Synthesis of Stereotriad Subunits of Polyketides through Additions of Nonracemic Allenylsilanes to *(R)*- and *(S)*-2-Methyl-3-oxygenated Propanals

James A. Marshall* and Karin Maxson

Department of Chemistry, University of Virginia Charlottesville, Virginia 22904

Received October 5, 1999

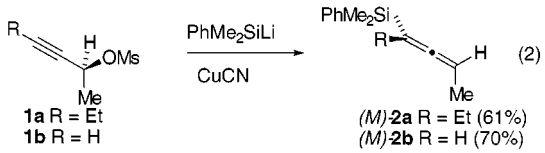
In 1992, we reported a method for the synthesis of the diastereomeric stereotriad subunits of polyketide natural products.[1] The approach utilized enantioenriched allenyl tributyltin reagents and α-methyl, *β*-oxygenated aldehydes as the two reacting partners (eq 1). Lewis acid promoted additions led to the syn,syn or syn,anti diastereomers through acyclic Felkin−Anh or acyclic chelation-controlled transition states. The anti,syn and anti,anti diastereomers were secured through transmetalation of the tributylstannanes with $SnCl_4$ and subsequent in situ addition of the derived allenyl trichlorotin reagents to the aforementioned aldehydes. These latter additions proceed via cyclic transition states under Felkin−Anh or chelation control.



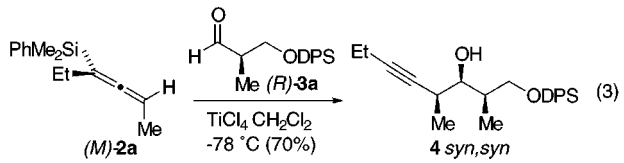
Subsequent studies led to the development of methods for the in situ formation of nonracemic allenylzinc,[2] indium,[3] and chlorosilane[4] reagents and their addition to aldehydes to yield anti adducts. We were thus able to circumvent the use of environmentally objectionable tributyl tin compounds for the preparation of these diastereomers. However, alternative allenylmetal reagents for the synthesis of syn adducts were not available. These reactions proceed by an acyclic transition state and require the metal to be relatively non-Lewis acidic. The Bu_3Sn moiety nicely fits this requirement. In addition, the hyperconjugative electron donation by the Bu_3Sn moiety enhances double bond reactivity and contributes to the rigidity of the transition state resulting in highly diastereoselective additions.

An obvious replacement for Bu_3Sn in these additions would be an R_3Si grouping. Though somewhat less reactive than the corresponding stannanes, allenylsilanes have been prepared, and their additions to aldehydes have been examined.[5] Such additions afford, as expected, mainly syn adducts. However, studies on additions of enantioenriched allenylsilanes to enantioenriched α-methyl-substituted aldehydes appropriate for polyketide synthesis have not been reported.[6] A possible problem with this approach is the relative unreactivity of allenylsilanes compared to allenylstannanes. Whereas the latter react with aldehydes in the presence of fairly mild Lewis acids (BF_3•OEt_2, $MgBr_2$), the latter additions typically require $TiCl_4$, a much stronger Lewis acid. Thus, concerns about protecting group compatibility and aldehyde racemization come to mind.

The enantioenriched allenylsilanes (*M*)-**2a** and (*M*)-**2b** were prepared by the silylcuprate S_N2' displacement method of Fleming (eq 2).[7] Propargylic mesylates **1a** and **1b** of >95% ee were employed in this work. It has been shown that such displacements proceed with nearly 100% inversion with stannyl cuprates and propargylic mesylates,[1] and with silyl cuprates and allylic esters.[7] In the present case, the ee of the allenylsilanes was shown to be >95% by GC analysis on an α-DEX column.



Preliminary screening was conducted with allenylsilane **2a** and cyclohexanecarboxaldehyde. Use of BF_3•OEt, $BiBr_3$,[8] or $Sc(OTfl)_3$[9] as Lewis acid promoters gave no adducts at −78 °C and led to multiple decomposition products at temperatures ranging from 0 to 25 °C. A systematic examination of temperature was not carried out as the reaction proceeded readily when $TiCl_4$ was employed at −78 °C. Under these conditions, allenylsilane (*M*)-**2a** underwent addition to the ODPS aldehyde (*R*)-**3a**[10] to afford the syn,syn adduct **4** in 70% yield, as the sole detectable stereoisomer (eq 3). The stereochemistry is assigned in consideration of the likely transition state and by analogy to the related allenylstannane addition.[1]

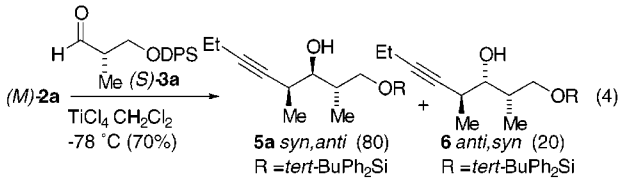


* To whom correspondence should be addressed. E-mail: jam5x@virginia.edu.

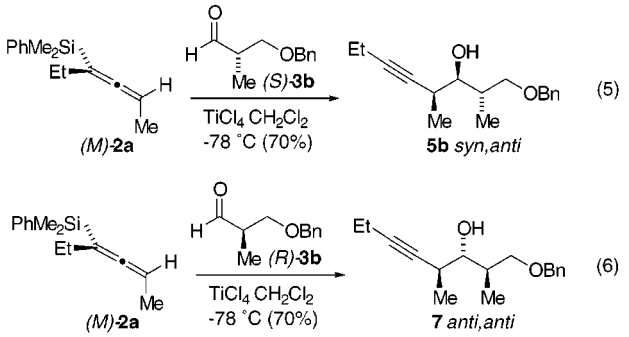
(1) Marshall, J. A.; Wang, X.-j. *J. Org. Chem.* **1992**, *57*, 1242.
(2) Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1998**, *63*, 3812. Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1999**, *64*, 5201.
(3) Marshall, J. A.; Grant, C. M. *J. Org. Chem.* **1999**, *64*, 696.
(4) Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1997**, *62*, 8976.
(5) Danheiser, R. L.; Carini, D. J.; Kwasigroch, C. A. *J. Org. Chem.* **1986**, *51*, 3870.
(6) Fleming and Buckle have shown that (*P*)-1-trimethylsilyl-1,2-butadiene adds to isobutyraldehyde to afford the syn homopropargylic alcohol adduct by an anti S_E2' pathway. Buckle, M. J. C.; Fleming, I. *Tetrahedron Lett.* **1993**, *34*, 2383.
(7) Fleming, I.; Terrett, N. K. *J. Organomet. Chem.* **1984**, *264*, 99. Fleming, I.; Waterson, D. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1809.
(8) Komatsu, N.; Uda, M.; Suzuki, H.; Takahashi, T.; Domae, T.; Wada, M. *Tetrahedron Lett.* **1997**, *38*, 7215.
(9) Aggarwal, V. K.; Vennall, G. P. *Tetrahedron Lett.* **1996**, *37*, 3745.
(10) Roush, W. R.; Palkowitz, A. D.; Palmer, M. A. J. *J. Org. Chem.* **1987**, *52*, 316.

10.1021/jo991543y CCC: $19.00
Published on Web 12/23/1999

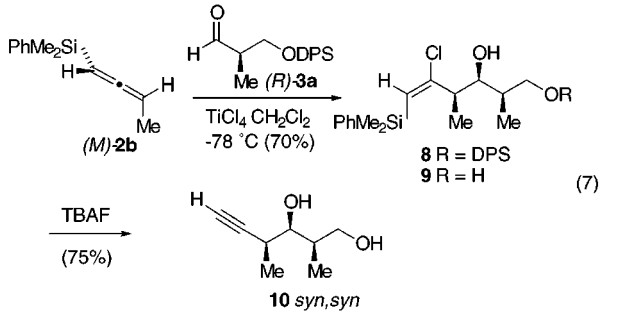
Addition of allenylsilane (*M*)-**2a** to the enantiomeric aldehyde (*S*)-**3a** led to an 80:20 mixture of syn,anti and anti,syn adducts **5a** and **6** (eq 4). These results closely parallel the mismatched BF_3-promoted allenylstannane reaction with aldehyde (*S*)-**3b** which gives the analogous (R = Bn) diastereomeric adducts as an 84:16 mixture.[1]



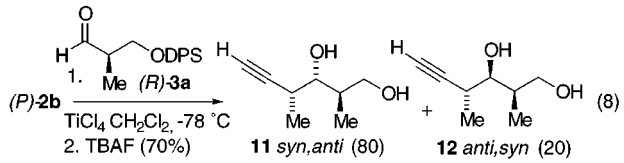
The α-Me, *β*-OBn aldehydes (*S*)- and (*R*)-**3b** gave remarkably different results from their ODPS counterparts. Addition of allenylsilane (*M*)-**2a** to (*S*)-**3b**, a presumably mismatched pairing, yielded the syn,anti product as the sole adduct (eq 5). Moreover, the matched pairing of silane (*M*)-**2a** and aldehyde (*R*)-**3b** afforded the anti,anti adduct **7** (eq 6)! The stereochemistry of these adducts was assigned by comparison with authentic samples prepared by allenylstannane additions to aldehyde (*R*)-**3b**.[1]



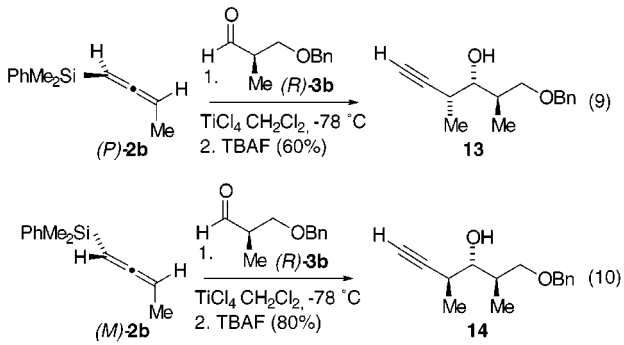
An analogous series of experiments was carried out with allenylsilane **2b**. Addition of (*M*)-**2b** to aldehyde (*R*)-**3a**, a matched pairing, afforded the syn,syn vinyl chloride **8** (eq 7). This product results from attack on an incipient vinyl cation by chloride, a process previously noted by Danheiser for additions of trimethylsilylallene to aldehydes promoted by $TiCl_4$.[5] Cleavage of the DPS ether with aqueous HCl afforded the crystalline alcohol **9** whose structure was confirmed through X-ray analysis.[11] Treatment of this alcohol, or the DPS ether **8** with TBAF in THF effected dechlorosilation to the *syn*,*syn*-diol **10**, also a crystalline solid amenable to X-ray structure analysis.[11] Cleavage of the aforementioned TMS-substituted vinylic chloride was effected with KF in DMSO, by Danheiser.[5]



The mismatched addition of allenylsilane (*P*)-**2b** to aldehyde (*R*)-**3a** yielded an 80:20 mixture of the syn,anti and anti,syn adducts **11** and **12** after treatment of the crude vinyl chloride adducts with TBAF in THF (eq 8). The latter isomer afforded crystals suitable for X-ray structure analysis.[11]



The "mismatched" pairing of allenylsilane (*P*)-**2b** with the benzyloxy aldehyde (*R*)-**3b** and subsequent dechlorosilation of the adduct with TBAF afforded the syn,anti adduct **13** as the sole product (eq 9). The analogous addition of (*M*)-**2b** to aldehyde (*R*)-**3b** led to the anti,anti adduct **14** (eq 10). The structure of this product was confirmed by spectral comparison with an authentic sample.[12]

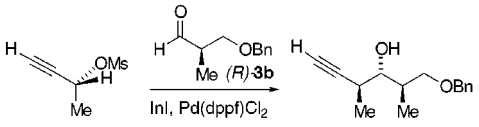


Whereas additions of the allenylsilanes **2a** and **2b** to the ODPS aldehydes (*R*)- and (*S*)-**3a** closely parallel BF_3-promoted additions of the analogous allenylstannanes, the results with the OBn aldehydes (*R*)- and (*S*)-**3b** are strikingly different. Allenylsilane (*M*)-**2a** affords the syn,anti adduct **5b** with (*S*)-**3b** and the anti,anti adduct **7** with (*R*)-**3b** as the exclusive products. Silanes (*P*)- and (*M*)-**2b** show analogous behavior with aldehyde (*R*)-**3b**. By comparison, the (*P*)-stannane counterpart of allenylsilane **2a** affords an 84:16 mixture of syn,anti and anti,syn adducts (mismatched) and the (*M*)-stannane gives the syn,syn isomer (matched) as the sole adduct with aldehyde (*R*)-**3b**.[1]

A possible explanation for these results is depicted in Figure 1. The matched pairings of the *β*-ODPS aldehyde (*R*)-**3a** with allenylsilanes (*M*)-**2a** and **2b** proceed through the acyclic antiperiplanar Felkin−Anh transition state **A.** The mismatched addition to aldehyde (*S*)-**3a** favors either the anti-Felkin−Anh antiperiplanar arrangement **B** or, quite possibly, a chelation arrangement comparable to **D**.[13] The minor mismatched anti,syn adducts would be formed via the synclinal Felkin−Anh arrangement **C**. The reactions that proceed by way of acyclic transition

(11) This analysis was performed by Dr. Michael Sabat of this department.

(12) The authentic sample was prepared by Dr. Brian Johns according to the following sequence.[3]



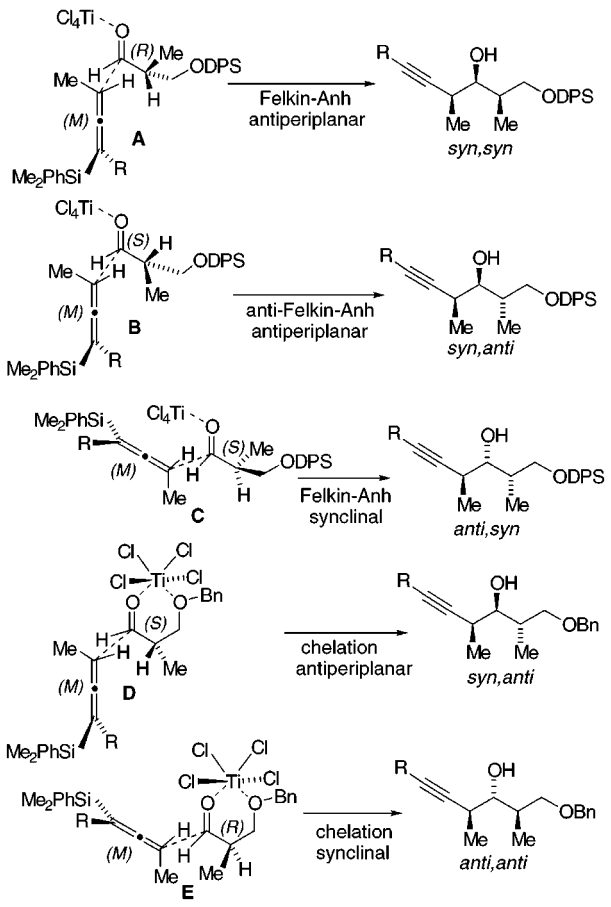


Figure 1. Proposed transition states for $TiCl_4$-promoted additions of allenylsilanes to α-methyl *β*-oxygenated aldehydes.

states are reagent controlled. Additions to the *β*-OBn aldehydes (*S*)- and (*R*)-**3b**, on the other hand, proceed via the chelated transition states **D** and **E**. In these additions the chelated aldehyde strongly directs the approach of the allenylsilane reagent (substrate control). In contrast, the analogous $MgBr_2$-promoted addition of the allenylstannane corresponding to (*M*)-**2a** affords a 1:1 mixture of the syn,syn and anti,anti adducts with aldehyde (*R*)-**3b**.[1] Evidently, $TiCl_4$ is a more effective chelating Lewis acid than $MgBr_2$.

The present studies show that the $TiCl_4$-promoted reaction of allenylsilanes with α-methyl-*β*-oxygenated aldehydes can be utilized to synthesis syn,syn and syn,anti adducts of possible use for polyketide synthesis. The additions proceed without epimerization of α-chiral aldehydes. However, some care must be exercised in the choice of a *β*-oxygen substituent. We have found that OTBS groups are desilylated to a large extent under these reaction conditions. *p*-Methoxybenzyl ethers are also extensively cleaved.

Experimental Section

(*S*)-1-(Dimethyl)phenylsilyl-1,2-butadiene [(*M*)-2b]. The procedure is a modification of methodology published by Fleming.[7] (Dimethyl)phenylchlorosilane (1.15 g, 6.70 mmol) was dissolved in THF (6 mL), and 4 Å molecular sieves and Li wire (250 mg, 33.7 mg atom) were added. The mixture was stirred for 12 h at room temperature. The resulting red/brown solution was transferred by cannula into a slurry of CuCN (305 mg, 3.4 mmol) in THF (12 mL) at 0 °C. The mixture was stirred for 30 min then cooled to −78 °C. To mesylate **1b** (500 mg, 3.37 mmol) in THF (25 mL) at −78 °C was added the silyl cuprate via cannula. The reaction mixture was stirred at −78 °C for 3 h and then poured into a mixture of 9:1 NH_4Cl/NH_4OH and stirred until the black emulsion disappeared to leave a bright blue aqueous layer. The product was extracted with pentane and dried, and the solvent was removed under aspirator vacuum to yield a colorless liquid that was distilled under reduced pressure (100 °C at 20 Torr) to afford 430 mg (70%) of allene (*M*)-**2b**: IR (neat) 1938 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.54 (m, 2H), 7.35 (m, 3H), 5.01 (m, 1H), 4.80 (p, J = 6.9 Hz, 1H), 1.63 (m, 3H), 0.34 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) 191.0 133.8, 129.0, 128.4, 127.7, 80.4, 78.4, 13.1, −2.3; $[\alpha]^{20}_D$ = +53.0 (c = 2.6, CH_2Cl_2). Anal. Calcd for $C_{12}H_{16}Si$: C, 76.53; H, 8.56. Found: C, 76.47; H, 8.70.

(*R*)-4-(Dimethyl)phenylsilyl-2,3-hexadiene [(*M*)-2a]. The procedure for the synthesis of allene (*M*)-**2b** was followed with (dimethyl)phenylchlorosilane (775 mg, 4.50 mmol) in THF (4 mL) containing 4 Å molecular sieves and Li wire (160 mg, 22.7 mg atom), CuCN (203 mg, 2.30 mmol), and mesylate **1a** (400 mg, 2.30 mmol). The product was extracted with pentane and dried, and the solvent was removed under aspirator vacuum to yield a colorless liquid that was purified on silica gel (1:20 EtOAc/hexanes) affording 300 mg (61%) of allenylsilane (*M*)-**2a**: IR 2968, 2916, 1938 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.52 (m, 2H), 7.35 (m, 3H), 4.86 (m, 1H), 1.92 (dq, J = 3.3, 7.5 Hz, 2H), 1.63 (d, J = 6.6 Hz, 3H), 0.98 (t, J = 7.5 Hz, 3H), 0.35 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) 207.3, 139.0, 133.8, 129, 127.6, 96.3, 81.1, 22.5, 13.9 13.6, −2.87; $[\alpha]^{20}_D$ = −23 (c = 1.0, CH_2Cl_2). Anal. Calcd for $C_{14}H_{20}Si$: C, 77.71; H, 9.32. Found: C, 77.47; H, 9.48.

Addition of Allenylsilanes (*M*)-2 to Aldehyde (*R*)-3b. Procedure A: (2*R*,3*S*,4*S*)-1-Benzyloxy-2,4-dimethyl-5-octyn-3-ol (7). Aldehyde (*R*)-**3b** (32 mg, 0.18 mmol) and allene (*M*)-**2a** (50 mg, 0.27 mmol) were dissolved in CH_2Cl_2 (1.0 mL) and cooled to −78 °C. $TiCl_4$ (0.20 mL of 1 M in hexanes, 0.20 mmol) was added to the mixture with stirring until TLC analysis showed complete consumption of the aldehyde (∼30 min). NH_4Cl (aq) was added, and the reaction mixture was allowed to warm to room temperature. The mixture was poured into CH_2Cl_2, the layers were separated, and the organic portion was washed with $NaHCO_3$ (aq). The organic phase was then dried ($MgSO_4$) and the solvent removed under aspirator vacuum. The product was purified on silica gel (1:9 EtOAc/hexanes) to yield 32 mg (70%) of the anti,anti alcohol **7**:[1] ^1H NMR (300 MHz, $CDCl_3$) 7.33 (m, 5H), 4.52 (s, 2H), 3.68−3.57 (m, 4H), 3.28 (m, 1H), 3.06 (bs, 1H), 2.67 (m, 1H), 2.19 (dq, J = 6.0, 2.1 Hz, 2H), 2.11 (m, 1H), 1.24 (d, J = 6.9 Hz, 3H), 1.13 (t, J = 6.0 Hz, 3H), 0.93 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 128.4, 127.6, 78.14, 74.62, 73.38, 37.60; 30.31, 18.42, 14.09; $[\alpha]^{20}_D$ +3.55 (c = 0.60, CH_2Cl_2).

Procedure B: (2*R*,3*S*,4*S*)-1-Benzyloxy-2,4-dimethyl-5-hexyn-3-ol (14). Aldehyde (*R*)-**3b** (570 mg, 3.03 mmol) and allene (*M*)-**2b** (340 mg, 4.55 mmol) were dissolved in CH_2Cl_2 (8.0 mL) and cooled to −78 °C. $TiCl_4$ (2.25 mL of 1 M in hexanes, 2.25 mmol) was added dropwise to the mixture with stirring until TLC analysis showed complete consumption of the aldehyde (∼30 min). NH_4Cl (aq) was added, and the reaction mixture was allowed to warm to room temperature. The mixture was poured into CH_2Cl_2, the layers were separated, and the organic portion was washed with $NaHCO_3$ (aq). The organic phase was then dried ($MgSO_4$) and the solvent removed under aspirator vacuum. The resulting oil was dissolved in THF, and TBAF (5 mL of 1 M in THF) was added at room temperature. The reaction was allowed to stir for 15 min. It was then poured into water, and the product was extracted with ether. The organic extracts were combined and dried ($MgSO_4$), and the solvent was removed under aspirator vacuum to yield a colorless oil. The product was chromatographed on silica gel (1:9 EtOAc/hexanes) to remove the unreacted allene and the silicon byproducts affording 381 mg (86%) of the anti,anti alcohol **14**: ^1H NMR (300 MHz, $CDCl_3$) 7.4−7.26 (m, 5H), 4.53 (s, 2H), 3.63 (A of ABX, J_{AX} = 4.50 Hz, J_{AB} = 9.0 Hz, 1H), 3.55 (B of ABX, J_{BX} = 8.1 Hz, J_{AB} = 9.0 Hz, 1H), 3.46 (bs, 1H), 3.36 (dd, J = 3.0, 8.4 Hz, 1H), 2.70 (m, 1H),

(13) Recent work with methylaluminum halide Lewis acids has shown that additions to *β*-OTBS aldehydes can proceed by chelation-controlled transition states. Evans, D. A.; Allison, B. D.; Yang, M. G. *Tetrahedron Lett*. **1999**, *40*, 4457. Evans, D. A.; Halstead, D. P.; Allison, B. D. *Tetrahedron Lett*. **1999**, *40*, 4461.

2.14 (m, 1H), 2.1 (d, J = 2.4 Hz, 1H), 1.3 (d, J = 7.2 Hz, 3H), 0.93 (d, J = 6.9 Hz, 3H);. ^{13}C NMR (75 MHz, $CDCl_3$) 133, 128, 127.8, 127.6, 78.1, 74.9, 73.4, 70.3, 37.3, 30.1, 17.9, 13.8; $[\alpha]^{20}_D$ = −13.24 (c = 1.32, CH_2Cl_2).

(2*R*,3*R*,4*S*)-1-(*tert*-Butyldiphenylsilyl)oxy-2,4-dimethyl-5-octyn-3-ol (4). Procedure A described above was employed. Aldehyde (*R*)-**2b** (100 mg, 0.31 mmol) and allene (*M*)-**2a** (100 mg, 0.365 mmol) were dissolved in CH_2Cl_2 (1.0 mL), and $TiCl_4$ (340 μL of 1 M in hexanes) was added at −78 °C. The mixture was stirred until TLC analysis showed complete consumption of the aldehyde (∼30 min). The product was purified on silica gel (1:9 EtOAc/hexanes) to remove the unreacted allene and the silicon byproducts affording 110 mg (70%) of the syn,syn alcohol **4**: IR 3510, 2963, 2931, 1728 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.70−7.66 (m, 6H), 7.42−7.33 (m, 4H), 3.84 (A of ABX, J_{AX} = 3.3 Hz, J_{AB} = 9.9 Hz, 1H), 3.70 (m, 2H), 3.11 (m, 1H), 2.51 (m, 1H), 2.18 (m, 1H), 2.13 (dq, J = 2.1, 7.8 Hz, 2H) 1.26 (d, 3H, J = 6.9 Hz), 1.08 (t, J = 7.5 Hz, 3H), 1.07 (m, 12H), 1.01 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 135.7, 135.5, 129.8, 127.74, 83.53, 81.18, 78.08, 69.6, 36.7, 30.34, 26.8, 19.16, 18.05, 14.26, 12.36, 9.56; $[\alpha]^{20}_D$ = −4.0 (c = 1.0, CH_2Cl_2).

(2*S*,3*R*,4*S*)-1-Benzyloxy-2,4-dimethyl-5-octyn-3-ol (5b). Procedure A described above was employed. Aldehyde (*S*)-**3b** (32 mg, 0.31 mmol) and allene (*M*)-**2a** (50 mg, 0.365 mmol) were dissolved in CH_2Cl_2 (1.0 mL), and $TiCl_4$ (195 μL of 1 M in hexanes) was added at −78 °C. The mixture was stirred until TLC analysis showed complete consumption of the aldehyde (∼30 min). The product was purified on silica gel (1:9 EtOAc/hexanes) to remove unreacted allene and silicon byproducts to yield 32 mg (70%) of the syn,anti alcohol **5b**: IR 3493, 2960, 1737 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.32 (m, 5H), 4.51 (s, 2H), 3.75 (A of ABX, J_{AX} = 4.2 Hz, J_{AB} = 9.3 Hz, 1H), 3.54 (B of ABX, J_{BX} = 4.5 Hz, J_{AB} = 9.3 Hz, 1H), 3.42 (dd, J = 6.0, 12.0 Hz, 1H), 3.06 (d, J = 5.7 Hz, 1H), 2.54 (m, 1H), 2.15 (dq, J = 2.1, 7.8 Hz, 2H), 2.14 (m, 1H), 1.20 (d, J = 6.9 Hz, 3H), 1.1 (t, J = 7.5 Hz, 3H), 1.07 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 137.9, 128.4, 127.7, 127.5, 83.4, 81.6, 78.6, 73.5, 35.3, 30.9, 29.7, 16.4,15.0, 14.2, 12.4; $[\alpha]^{20}_D$ = −20.1 (c =1.2, CH_2Cl_2). Reported for *ent*-**5b** $[\alpha]_D$ = +20.8 (c = 0.53, $CHCl_3$).[1]

(*E*,2*R*,3*R*,4*R*)-5-Chloro-2,4-dimethyl-6-(dimethyl)phenylsilyl-1-(*tert*-butyldiphenylsilyl)oxy-5-hexen-3-ol (8). A solution of aldehyde (*R*)-**3a** (100 mg, 0.303 mmol) and allene (*M*)-**2b** (90 mg, 0.455 mmol) in CH_2Cl_2 (1.0 mL) was cooled to −78 °C, and then $TiCl_4$ (280 μL of 1 M in hexanes) was added dropwise. The mixture was stirred until TLC analysis showed complete consumption of the aldehyde (∼30 min). NH_4Cl (aq) was added, and the reaction was allowed to warm to room temperature. The mixture was poured into CH_2Cl_2, the layers were separated, and the organic portion was washed with $NaHCO_3$ (aq). The organic phase was then dried ($MgSO_4$), and the solvent was removed under aspirator vacuum. The product was purified on silica gel (1:20 EtOAc/hexanes) to afford unreacted allene and 125 mg (80%) of the vinyl chloride **8**: IR(neat) 3467, 2960, 2934 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.64−7.34 (m, 15H), 5.78 (s, 1H), 3.97 (d, J = 8.4 Hz, 1H), 3.74 (dd, J = 9.9, 3.6 Hz, 1H), 3.56 (dd, J = 9.75, 5.1 Hz, 1H), 2.6 (m, 2H), 1.75 (m, 1H), 1.16 (d, J = 6.3 Hz, 3H), 1.05 (s, 9H), 0.70 (d, J = 6.6 Hz, 3H), 0.43 (d, J = 4.2 Hz, 6H).

(*E*,2*R*,3*R*,4*R*)-5-Chloro-2,4-dimethyl-6-(dimethyl)phenylsilyl-5-hexene-1,3-diol (9). The vinyl chloride **8** (125 mg, 0.24 mmol) was dissolved in methanol (15 mL) and 5% HCl was added at 0 °C. The reaction mixture was stirred at room temperature overnight and poured into $NaHCO_3$ (aq), and the product was extracted into ether. The organic extract was dried ($MgSO_4$), and the solvent was removed under aspirator vacuum to yield diol **9**, which was purified on silica gel (1:9 EtOAc/hexanes) to remove the silyl byproducts affording 53 mg (70%) of a white solid. Crystallization from hexane afforded an X-ray quality crystal: ^{1}H NMR (300 MHz, $CDCl_3$) 7.54−7.26 (m, 5H), 5.81 (s, 1H), 3.91 (d, J = 8.7 Hz, 1H), 3.69 (A of ABX, J_{AX} = 3.9 Hz, J_{AB} = 10.8 Hz, 1H), 3.58 (B of ABX, J_{BX} = 5.1 Hz, J_{AB} = 10.2 Hz, 1H), 2.6 (m, 2H), 1.75 (m, 1H), 1.13 (d, J = 6.3 Hz, 3H), 0.72 (d, J = 6.6 Hz, 3H), 0.43 (d, J = 4.2, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) 133.7, 129.5, 128.0, 126.5, 15.9, 68.0, 45.1, 36.5, 29.3, 28.9, 16.3, 8.9, −1.15; MS m/z 313, 277, 235, 223, 107.

(2*R*,3*R*,4*S*)-5-Hexyne-1,3-diol (10). ProcedureB described above was employed. Aldehyde (*R*)-**3a** (72 mg, 0.303 mmol) and allene (*M*)-**2b** (100 mg, 0.255 mmol) were combined in CH_2Cl_2 (1.0 mL), and $TiCl_4$ (300 μL of 1 M in hexanes) was added at −78 °C. The mixture was stirred until TLC analysis showed complete consumption of the aldehyde (∼30 min). The resulting oil was dissolved in THF and TBAF (765 μL of 1 M in THF) was added. The product was purified on silica gel (1:5 EtOAc/hexanes) to remove the unreacted allene and the silicon byproducts affording 25 mg (70%) of the syn,syn diol **10**: ^{1}H NMR (300 MHz, $CDCl_3$) 3.82−3.65 (m, 3H), 2.55 (m, 1H), 2.45 (bs, 2H), 2.2 (m, 1H), 2.08 (d, J = 2.7 Hz, 1H), 1.29 (d, J = 6.9 Hz, 3H), 0.984 (d, J = 6.9 Hz, 3H); $[\alpha]^{20}_D$ = −13.5 (c = 2.5, CH_2Cl_2). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.46; H, 9.95.

(2*R*,3*S*,4*R*)-1-Benzyloxy-2,4-dimethyl-5-hexyn-3-ol (13). Procedure B described above was employed. Aldehyde (*R*)-**3b** (100 mg, 0.56 mmol) and allene (*P*)-**2b** (158 mg, 0.84 mmol) were dissolved in CH_2Cl_2 (2.0 mL), and $TiCl_4$ (620 μL of 1 M in hexanes) was added. The mixture was stirred until TLC analysis showed complete consumption of the aldehyde (∼30 min). The resulting oil was dissolved in THF and TBAF (765 μL of 1 M in THF). The product was purified on silica gel (1:9 EtOAc/hexanes) to remove unreacted allene and silicon byproducts affording 75 mg (60%) of the syn,anti alcohol **13**: IR 3370, 3301, 2968, 2357, 2113 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.33 (m, 5H), 4.51 (s, 2H), 3.77 (dd, J = 3.6, 9.0 Hz, 1H), 3.50 (m, 2H), 3.26 (d, 1H), 2.57 (ddq, J = 2.4, 6.6, 6.6 Hz, 1H), 2.16 (m, 1H), 2.08 (d, J = 3.0 Hz, 1H), 1.26 (d, J = 6.9 Hz, 3H), 1.07 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 137.65, 128.41, 127.75, 127.61, 86.83, 78.39, 73.57, 69.68, 35.12, 30.61, 15.92, 14.97; $[\alpha]^{20}_D$ = +18.78 (c = 1.65, CH_2Cl_2).

Acknowledgment. This work was supported by Research Grant CHE9525974 from the National Science Foundation. We are grateful to Dr. Michal Sabat for helpful assistance in the selection of crystals and for performing the X-ray structure analyses.

Supporting Information Available: Experimental procedures for adducts **5a/6** and **11/12**, ^{1}H NMR spectra for all products, and ORTEP diagrams for **9**, **10**, and **12**.This material is available free of charge via the Internet at http://pubs.acs.org.

JO991543Y