Sequential Homoaldolization–Cuprate Rearrangement in a Stereoselective Synthesis of Stannyl Dienes: Application to the Synthesis of the Western C10–C15 Subunit of (±)-Tylosin Aglycon

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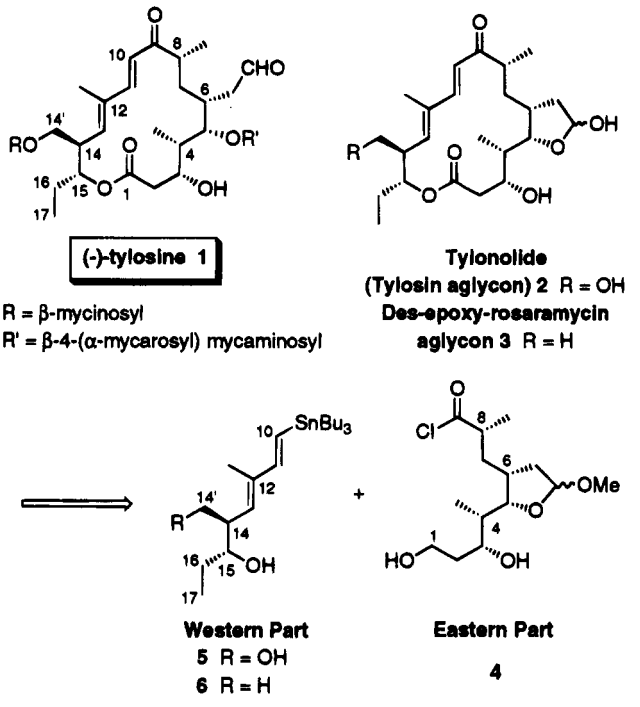
Received January 20, 1995[⊗]

A stereospecific synthesis of stannyl diene **5**, corresponding to the C10–C15 fragment of (±)-tylosin aglycon **2**, was reported. Silyl carbamate **16**, submitted to the Hoppe homoaldolization conditions with propanal, gave the *anti* aldol product **17** in 89% yield. Further treatment including oxidation of the silyl group led to lactone **21**. The corresponding dihydrofuran **23** was then transformed into vinylstannane **25**, *via* an efficient Kocienski rearrangement. An iodine exchange was performed on **25** and followed by a Stille coupling reaction with tributylstannyl acetylide. Stannyl cupration of the resulting silylated enyne **27** led in 44% yield to a 1:1 mixture of the desired (*E,E*)-stannyl diene **5b** and the unexpected (*E,Z*) isomer **29**. The same reaction performed on desilylated enyne **28** delivered in 85% yield the pure (*E,E*)-stannyl diene **5**.

As part of a program directed toward our studies in the field of natural products, we were interested in developing new methods for the synthesis of macrocyclic antibiotics. The retrosynthetic approach of tylonolide **2** (aglycon of tylosine **1**),[1] which was selected for its typical 16-membered macrolactone structure (Scheme 1), involved the preparation of the eastern portion **4** and the western stannylated diene **5**. In this paper we describe the construction of the racemic C10–C15 moiety **5**, corresponding to the western part of (±)-tylonolide **2**.

In a preceding work[2] about the synthesis of the C10–C15 moiety of desepoxyrosaramycin aglycon **3** (Scheme 1), we combined a Hoppe homoaldolization reaction[3] and a metallate rearrangement[4] to build stannyl diene **6** in good yield. During this synthesis, a homoaldolization reaction was performed on carbamate **7** and propanal, leading to racemic **8** in 90% yield. The Hoppe reaction was also conducted with (−)-spartein, to give **8** in 75% yield and 92% enantiomeric excess.[2b] In order to prepare the stannyl diene **6** (Scheme 2), the second key step was initially envisaged through a Kocienski metallate rearrangement by reaction between the trimethylstannyl

Scheme 1



derivative **8a** and the bis((*E*)-2-(tributylstannyl)ethylidene)dilithiocyanocuprate **A**.[5] Unfortunately the expected vinyl stannyl transfer did not occur, and stannyl diene **6** was not obtained.[6] We were therefore constrained to transform vinyl carbamate **8** into the corre-

[⊗] Abstract published in *Advance ACS Abstracts,* June 1, 1995.

(1) Tatsuta, K.; Amemiya, Y.; Kanemura, Y.; Takahashi, H.; Kinoshita, M. *Tetrahedron Lett.* **1982**, *23*, 3375. Nicolaou, K. C.; Seitz, S. P.; Pavia, M. R. *J. Am Chem. Soc.* **1982**, *104*, 2030. Masamune, S.; Lu, L. D-L.; Jackson, W. P.; Kaiho, T.; Toyoda, T. *J. Am. Chem. Soc.* **1982**, *104*, 5523. Grieco, P. A.; Inanaga, J.; Lin, N-H.; Yanami, T. *J. Am. Chem. Soc.* **1982** *104*, 5781. Tanaka, T.; Oikawa, Y.; Hamada, T.; Yonemitsu, O. *Chem. Pharm. Bull.* **1987**, *35*, 2219. Omura, S., Ed. *Macrolides Antibiotics*; Academic Press: 1984. Kirst, H. A. *J. Antimicrob. Chemother.* **1991**, *28*, 787. Kirst, H. A. In *Recent progress in the Chemical Synthesis of Antibiotics*; Lukacs, G., Ohno, M., Ed.; Springer Verlag: Berlin, 1990, p 39.

(2) (a) Le Ménez, P.; Firmo, N.; Fargeas, V.; Ardisson, J.; Pancrazi, A. *Synlett* **1994**, 995. (b) Le Ménez, P.; Berque, I.; Fargeas, V.; Ardisson, J.; Pancrazi, A. *Synlett* **1994**, 998.

(3) (a) Hoppe, D. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 932. (b) Zschage, O.; Hoppe, D. *Tetrahedron* **1992**, *48*, 5657.

(4) Kocienski, P.; Barber, C. *Pure Appl. Chem.* **1990**, *62*, 1933. Kocienski, P.; Wadman, S. *J. Am. Chem. Soc.* **1989**, *111*, 2363. Kocienski, P.; Dixon, N. J. *Synlett* **1989**, 52. Pimm, A.; Kocienski, P.; Street, S. D. A. *Synlett* **1992**, 886. Kocienski, P. In *Organic Synthesis via Organometallics, OMS 4,* Proceedings of the Fourth Symposium in Aachen, July 15–18, 1992.

(5) (a) (*E*)-1,2-Lithio(tributylstannyl)ethylidene: Corey, E. J.; Wollenberg, R. H. *J. Am. Chem. Soc.* **1974**, *96*, 5581. Renaldo, A. F.; Labadie, J. W.; Stille, J. K. *Org. Synth.* **1988**, *67*, 86. Seyferth, D.; Vick, S. C. *J. Organomet. Chem.* **1978**, *144*, 1. (b) Cuprate formation *via* exchange reaction: Behling, J. R.; Babiak, K. A.; Ng, J. S.; Campbell, A. L.; Moretti, R.; Koerner, M.; Lipshutz, B. H. *J. Am. Chem. Soc.* **1988**, *110*, 2641.

(6) Le Ménez, P.; Fargeas, V.; Poisson, J.; Ardisson, J.; Lallemand, J.-Y.; Pancrazi, A. *Tetrahedron Lett.* **1994**, *35*, 7767.

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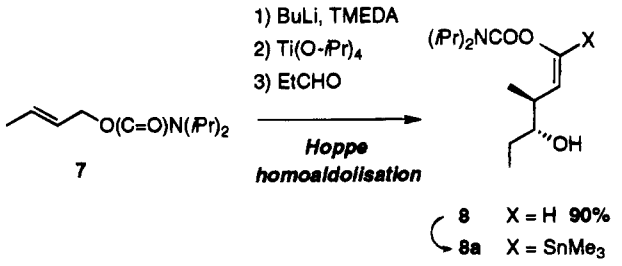
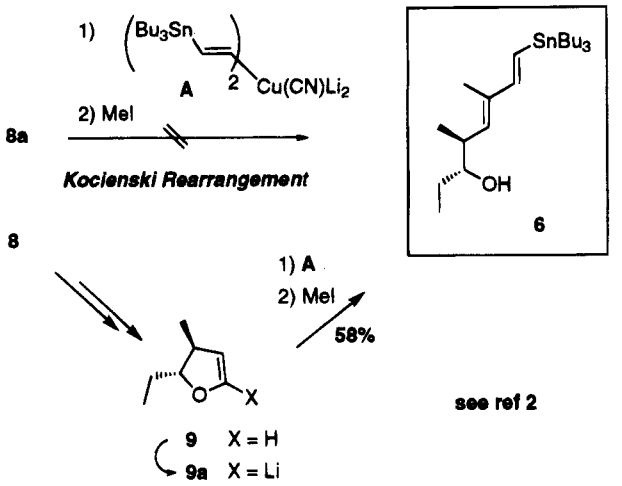
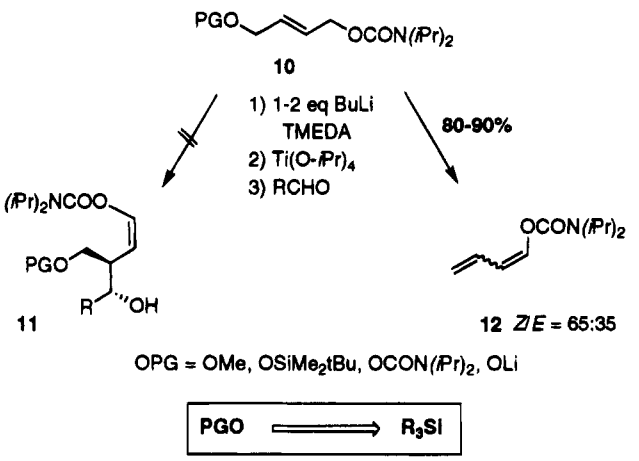
Scheme 2





Scheme 3



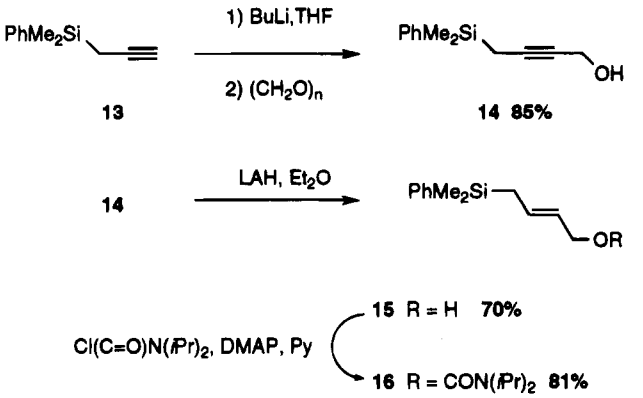
sponding dihydrofuran **9**. This compound led to stannyl diene **6** in 58% yield after treatment of its lithio derivative **9a** with the high-order cyanocuprate **A** and subsequent methylation.

For an application of this reaction sequence to the preparation of the western part **5** of tylonolide bearing a primary hydroxy group at C-14′, we tried to perform a homoaldolization reaction on the bis-allylic derivatives **10** (Scheme 3). The expected vinyl carbamate **11** was not isolated, and as reported in analogous cases,[7] an elimination reaction took place leading to a 65:35 mixture of *Z*/*E* dienes **12**,[8] even when using a different protecting group of the allylic alcohol (OMe, OTBS, OCON(*i*-Pr)$_2$, OLi).

(7) Corey, E. J.; Mehrotra, M. M. *Tetrahedron Lett.* **1986**, *27*, 5173. Adams, J.; Fitzsimmons, B. J.; Rokach, J. *Tetrahedron Lett.* **1984**, *25*, 4713. Le Merrer, Y.; Bonnet, A.; Depezay, J. C. *Tetrahedron Lett.* **1988**, *29*, 2647. See also: Gravier-Pelletier, C.; Dumas, J.; Le Merrer, Y.; Depezay, J. *Prog. Lipid. Res.* **1990**, *29*, 229.

(8) Unpublished results.

Scheme 4



We therefore decided to mask the allylic hydroxyl function as an allylic silyl group which would not undergo the undesired elimination reaction and which could be oxidized to a hydroxyl function in a latter step.[9]

The corresponding (dimethylphenylsilyl)prop-2-yne **13** (Scheme 4) was therefore prepared from propargyl bromide.[10] After a classical homologation reaction,[10] the resulting 1-hydroxy-4-silyl-2-butyne derivative **14** was reduced with $LiAlH_4$[11] to furnish the pure *E*-allylic alcohol **15** which was in turn transformed into diisopropyl carbamate **16**.

At this stage the homoaldolization reaction was performed by treatment of **16** with butyllithium in the presence of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine, followed by transmetalation with titanium tetraisopropoxide, and final reaction with propanal. The expected *anti* aldol product **17** was obtained in 89% yield (Scheme 5). Structural confirmation was obtained by ^{1}H NMR analysis and NOE experiments carried out on lactone **21** and **22**[12] (*vide infra*).

After the first key step was resolved, we focused on transformation of **17** into the dihydrofuran intermediate previously envisaged. Hydrolysis of the carbamate function of **17** followed by an MCPBA oxidation[13] gave the silyl lactone **18** in 68% yield. The crucial subsequent oxidation of the dimethylphenylsilyl function[9b] furnished the major acetate derivative **19** (60% yield) together with the hydroxy lactone **20** (15% yield). Deprotection of the acetoxy group of lactone **19** using guanidine[14] smoothly delivered the hydroxylactone **20** in 80% yield. For an adequate protection of the hydroxyl group, the TIPS derivative **21** was prepared together with the corresponding TBS compound **22**.

The two lactone derivatives **21** and **22** were first reduced into the corresponding lactols (Scheme 6) which

(9) (a) Tamao, K.; Nakajo, E.; Ito, Y. *J. Org. Chem.* **1987**, *52*, 957. Tamao, K.; Kawachi, A.; Ito, Y. *J. Am. Chem. Soc.* **1992**, *114*, 3989. (b) Fleming, I.; Henning, R.; Plaut, H. *J. Chem. Soc., Chem. Commun.* **1984**, 29. Fleming, I.; Sanderson, P. E. J. *Tetrahedron Lett.* **1987**, *28*, 4229.

(10) (a) Nativi, C.; Taddei, M.; Mann, M. *Tetrahedron* **1989**, *45*, 1131. (b) Majetich, G.; Hull, K.; Casares, A. M.; Khetani, V. *J. Org. Chem.* **1991**, *56*, 3958.

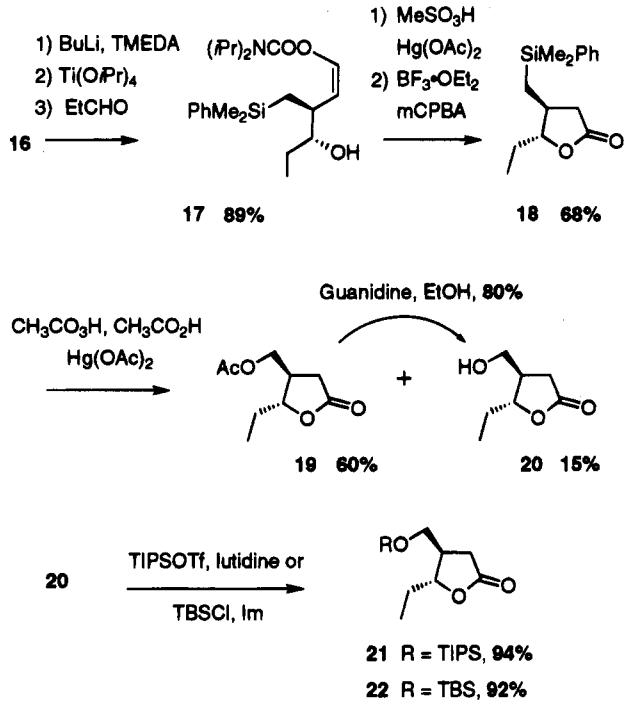
(11) Mastalerz, H. *J. Org. Chem.* **1984**, *49*, 4092. Hiemstra, H.; Sno, M. H. A. M.; Vijn, R. J.; Speckamp, W. N. *J. Org. Chem.* **1985**, *50*, 4014.

(12) In order to prepare optically active compounds **17**, the Hoppe homoaldolization reaction using (−)-spartein was investigated on the silylallyl carbamate **16**.

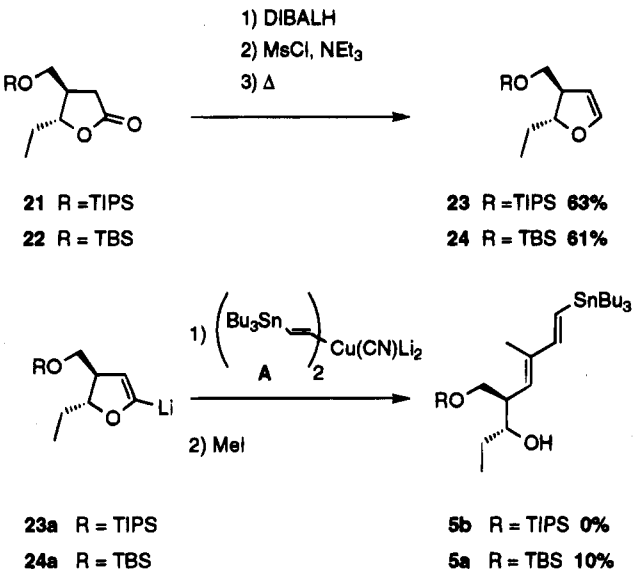
(13) Hoppe, D.; Brönneke, A. *Tetrahedron Lett.* **1983**, *24*, 1687. Grieco, P. A.; Oguri, T.; Yokoyama, Y. *Tetrahedron Lett.* **1978**, 419, see also ref 3b.

(14) Kunesch, N.; Miet, C.; Poisson, J. *Tetrahedron Lett.* **1987**, *28*, 3569.

Scheme 5



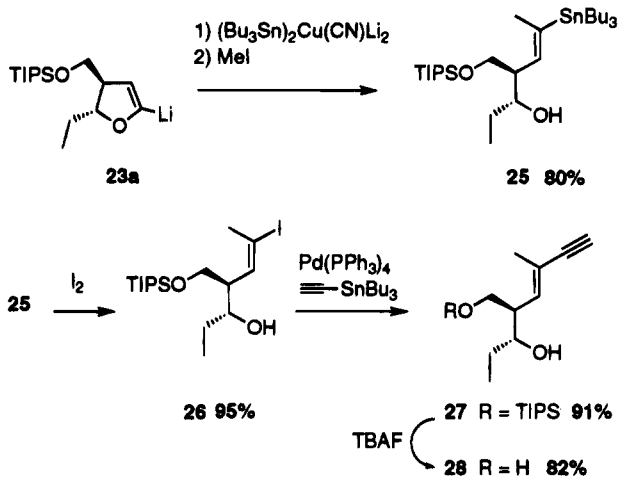
Scheme 6



were esterified with methanesulfonyl chloride before basic treatment[15] to afford the expected dihydrofurans **23** and **24** in 63 and 61% yields respectively, for the two steps.

Preparation of **23** and **24** was designed for the following reason. In a preliminary experiment, the TIPS derivative **23** was preferred to the TBS analog **24** to avoid some problems during metalation of the dihydrofuran function.[16] The lithio derivative **23a**, obtained quantitatively from **23** using *t*-BuLi was submitted to a cuprate rearrangement reaction by treatment with the cyanocuprate **A**, using the same conditions employed in our preceding work.[2a] Vinyl stannyl transfer did not occur in this case,

Scheme 7



and this disappointing result was interpreted in terms of steric hindrance of the TIPS protecting group. This reaction was then tested with the TBS derivative **24**, and its lithiodihydrofuran **24a** reacted with the (stannyl)-vinylcuprate **A** to give the expected vinyl stannyl transfer leading to the stannyl diene **5a** in only 10% yield in spite of the numerous conditions we tried.

The latter difficulties led us to use a slightly modified strategy, and taking advantage of preliminary results we obtained in the metallate rearrangement,[2,6] we decided to perform a stannyl transfer rather than a vinyl stannyl one. Reaction of the lithiated dihydrofuran **23a** with the stannyl homocuprate $(Bu_3Sn)_2Cu(CN)Li_2$,[17] followed by MeI alkylation, afforded the pure *E*-vinyl stannane **25** in 80% yield (Scheme 7). An iodine exchange led in quantitative yield to the vinyl iodide **26** which was coupled with (tributylstannyl)acetylene[5d] with a catalytic amount of $Pd(PPh_3)_4$ to furnish enyne **27** in 91% yield.

This new strategy involved at the final stage a regio- and stereospecific addition of a stannyl group. The results obtained earlier[2b] by us in this area, by Oehlschlager[18] in the stannyl cupration study of an enyne, and by Hamada and Shioiri[19] led us to realize a stannyl cupration of enyne **27** using the mixed stannyl cyanocuprate $(Bu_3Sn)(Bu)Cu(CN)Li_2$.[20] This reaction was conducted at −30 °C and quenched with methanol before pouring the reaction mixture in a 4:1 mixture of saturated aqueous NH_4Cl/concentrated ammonia. These conditions led in 44% yield to a 1:1 mixture of the desired (*E*,*E*)-stannyl diene **5b** and the unexpected (*E*,*Z*) isomer **29** (Scheme 8). Formation of the (*E*,*Z*)-stannyl diene **29** cannot be explained at this moment, and it is therefore interesting to note that the first similar example of a *trans* stannyl cupration was recently reported[21] in the literature.

(15) Takle, A.; Kocienski, P. *Tetrahedron* **1990**, *46*, 4503.

(16) Imanieh, H.; Quale, P.; Voaden, M.; Conway, J.; Street, S. D. A. *Tetrahedron Lett.* **1992**, *33*, 543. Barber, C.; Jarowicki, K.; Kocieński, P. *Synlett* **1991**, 197. Shimano, M.; Meyers, A. I. *Tetrahedron Lett.* **1994**, *35*, 7727.

(17) This cuprate was obtained from Bu_3SnLi and CuCN as described by Gilbertson, S. R.; Challener, C. A.; Bos, M. E.; Wulff, W. D. *Tetrahedron Lett.* **1988**, *29*, 4795. In our case Bu_3SnLi was prepared using $(Bu_3Sn)_2$ and BuLi as reported by Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836.

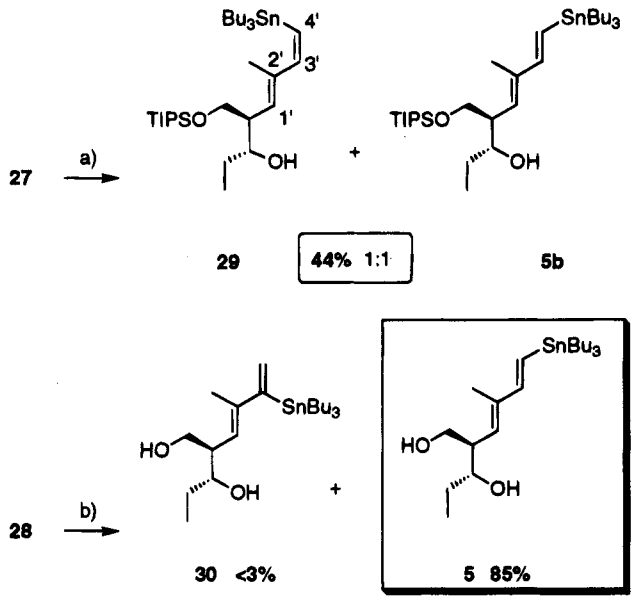
(18) (a) Aksela, R.; Oehlschlager, A. C. *Tetrahedron* **1991**, *47*, 1163. (b) Cabezas, J. A.; Oehlschlager, A. C. *Synthesis* **1994**, 432. For stannyl cupration of acetylenic derivatives, see also: Barbero, A.; Cuadrado, P.; Fleming, I.; Gonzalez, A. M; Pulido, F. J. *J. Chem. Soc., Chem. Commun.* **1992**, 351. Barbero, A.; Cuadrado, P.; Fleming, I.; Gonzales, A. M.; Pulido, F. J.; Rubio, R. *J. Chem. Soc., Perkin Trans. I* **1993**, 1657.

(19) Yokokawa, F.; Hamada, Y.; Shioiri, T. *Tetrahedron Lett.* **1993**, *34*, 6559.

(20) Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Reuter, D. C. *Tetrahedron Lett.* **1989**, *30*, 2065.

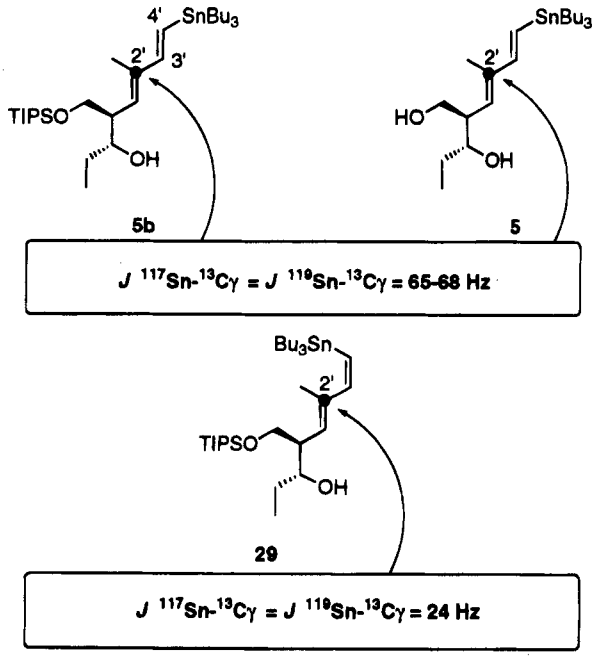
(21) Cummins, C. H.; Gordon, E. J. *Tetrahedron Lett.* **1994**, 35, 8133.

Scheme 8



a) 2.2eq $(Bu_3Sn)(Bu)Cu(CN)Li_2$
b) 3.3eq $(Bu_3Sn)(Bu)Cu(CN)Li_2$

Scheme 9



Assuming that the bulky TIPS protecting group generated some deleterious influence, the enyne **27** was deprotected to enyne diol **28**. Stannyl cupration of **28** was realized in the same manner as above and led after purification to the pure distal (*E,E*)-stannyl diene **5** in 85% yield; the regioisomer **30** was detected by ^1H NMR spectral analysis of the crude residue (less than 3% formed).

Structural identifications of the stannyl dienes obtained in this study were obtained by ^1H and ^{13}C NMR spectral analysis and also HCOR experiments ($^1H-^{13}C$ correlations). These studies led us to observe in ^{13}C NMR analysis that the γ olefinic carbon presents $J(^{119}Sn-^{13}C)$ and $J(^{117}Sn-^{13}C)$ coupling constants depending of the geometry of the stannyl diene. As shown in Scheme 9 the (*E,E*)-stannyl dienes present $J(^{119}Sn-^{13}C) = J(^{117}Sn-^{13}C) = 65-68$ Hz, whereas the (*E, Z*) isomers have a lower coupling constant, $J(^{119}Sn-^{13}C) = J(^{117}Sn-^{13}C) = 24$ Hz. This observation could be a useful tool for structural elucidation of some stannyl dienes whose ^1H NMR spectra cannot be easily interpreted. It also was in agreement with the results we reported earlier in the vinyl stannyl series.[22]

In conclusion, a new route is presented for the preparation of the western part (C10–C15) **5** of tylosine **1** with the following main strategic points:

1. A variation of the Hoppe homoaldolization reaction was developed using silylcrotyl carbamate **16** as a convenient precursor for the intermediate dihydrofuran **23** required for tylosine synthesis. The chemical and *anti* stereoselectivities of this reaction leading to **17** are good, and it will probably find other synthetic applications. Current studies are underway to develop an enantioselective form of this reaction using sparteine as homochiral auxiliary.

2. The dihydrofuran **23a** was found to be a convenient substrate for an efficient cuprate rearrangement leading to the stereocontrolled substituted vinylstannane **25**.

3. Unexpectedly the last stannyl cupration step required preliminary removal of the TIPS protecting group of enyne **27** which led to a 1:1 (*E/Z*) mixture of diene isomers **29** and **5b**. The required (*E,E*)-stannyl diene **5** was obtained in 85% yield when the enyne diol **28** was used for this reaction.

This unexpected stereochemical course of the stannyl cupration reaction, along with further progress toward the complexion of the synthesis of tylosine **1**, are currently under study.

Experimental Section

For large $Sn-^1H$ or $Sn-^{13}C$ coupling constants (250–350 Hz), the central signal was associated with two close pairs of satellites corresponding to both ^{117}Sn and ^{119}Sn isotopes; in this case two different coupling constants were reported. For small $Sn-^1H$ and $Sn-^{13}C$ (<100 Hz), the two pairs of satellites collapse and only one coupling constant was observed. When necessary, assignments were obtained using *J*-mod experiments. Microanalyses were performed on a CHN 240 Perkin-Elmer instrument. Tetrahydrofuran and diethyl ether were distilled from sodium–benzophenone, dichloromethane from Al_2O_3, triethylamine and pyridine from KOH, pentane and hexane from phosphoric anhydride, and benzene and toluene from sodium. HPLC chromatography was performed on a Microbondapak C18 Waters (10 mμ) column.

1-(Dimethylphenylsilyl)-prop-2-yne (13). Under nitrogen pressure, magnesium turnings (99.8%, 5 g, 0.2 mol, 1.25 equiv) and $HgCl_2$ (50 mg, 0.11 mmol, 0.7 equiv) were successively added in dry diethyl ether (Et_2O, 30 mL) at ambient temperature. A solution of propargyl bromide (80% weight in toluene, 23.8 g, 0.16 mol) in Et_2O (130 mL) was then slowly added until the reaction started. A dropwise addition of the ethereal solution of propargyl bromide was realized to keep the temperature at 20 °C. After the addition was complete, the solution was stirred for 30 min at 20 °C. After the solution was cooled down to 0 °C, chlorodimethylphenylsilane (25 g, 0.15 mol, 0.9 equiv) was added. The resulting solution was allowed to rise to ambient temperature and stirred at this temperature for 12 h. At 0 °C the mixture was diluted with brine and extracted with Et_2O. The combined organic phases were then washed with brine, dried over sodium sulfate, and filtered, and the solvent was removed under reduced pressure, leading to an oil which was purified by flash chromatography (hexane) on silica gel and distillation to give the title compound

(22) Ardisson, J.; Férézou, J. P.; Li, Y.; Liu, L.W.; Pancrazi, A. *Bull. Soc. Chim. Fr.* **1992**, *129*, 401.

13 (21 g, 82%): bp 64–66 °C/2 mm Hg; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.39 (s, 6H), 1.73 (d, J = 2.7 Hz, 2H), 1.91 (t, J = 2.7 Hz, 1H), 7.45 (m, 3H), 7.67 (m, 2H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −3.6 ($2CH_3$), 6.2 (CH_2), 67.5 (CH), 82.0 (C), 127.8 (2CH), 129.4 (CH), 133.5 (2CH), 137.3 (C); IR ($CDCl_3$) 3300, 3060, 2950, 2110, 2095, 1420, 1250, 1140, 1110 cm^{-1}; EIMS m/e (relative intensity) 174 (M^+, 27), 159 (60), 135 (100); CIMS (NH_3) m/e (relative intensity) 174 (M^+, 25), 159 (55), 135 (100), 105 (12).

Anal. Calcd for $C_{11}H_{14}Si$, 174.28: C, 75.80; H, 8.10. Found: C, 75.67; H, 8.01.

4-(Dimethylphenylsilyl)but-2-yn-1-ol (14). To a solution of propynyl silane **13** (21.3 g, 0.122 mol) in tetrahydrofuran (THF, 150 mL) at −60 °C was added a 1.6 M hexane solution of *n*-butyllithium (*n*-BuLi, 84 mL, 0.134 mol, 1.1 equiv) slowly under nitrogen, and then the temperature was allowed to rise to −10 °C. After dilution with THF (50 mL), a stream of formaldehyde, obtained by depolymerization of dried paraformaldehyde (17 g, 0.57 mol, 4.6 equiv) at 180 °C, was blown on the surface of the anion solution. After being stirred for 4 h at 20 °C, the solution was poured into a cold (0 °C) saturated aqueous ammonium chloride (NH_4Cl) solution. After extraction with diethyl ether, the crude oil was purified by flash chromatography on silica gel (hexane/ethyl acetate 90:10) to furnish the propargylic alcohol **14** (21.2 g, 85% yield): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.42 (s, 6H), 1.79 (t, J = 2.5 Hz, 2H), 1.90 (s wide, 1H), 4.27 (t, J = 2.5 Hz, 2H), 7.48 (m, 3H), 7.64 (m, 2H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −3.6 ($2CH_3$), 6.4 (CH_2), 51.3 (CH_2), 77.8 (C), 83.6 (C), 127.8 (2CH), 129.3 (CH), 133.4 (2CH), 137.3 (C); IR ($CDCl_3$) 3610, 3060, 2945, 2200, 1420, 1370, 1300, 1050, 995 cm^{-1}; CIMS (NH_3) m/e (relative intensity) 222 (MH^+ + 17, 25), 205 (MH^+, 12), 187 (65), 165 (35), 152 (95), 137 (25), 135 (100), 124 (45), 75 (60).

Anal. Calcd for $C_{12}H_{16}OSi$, 204.31: C, 70.54; H, 7.89. Found: C, 70.43; H, 7.85.

(2*E*)-4-(Dimethylphenylsilyl)but-2-en-1-ol (15). To a solution of **14** (9.9 g, 48.5 mmol) in anhydrous Et_2O (55 mL) under nitrogen was slowly added a 1 M solution of lithium aluminum hydride in diethyl ether ($LiAlH_4$, 57 mL, 57 mmol, 1.2 equiv). The reaction mixture was then heated to reflux for 2 h. After being cooled to 0 °C, the mixture was carefully and successively treated with water (18 mL), sodium hydroxide (35%, 5 mL), and water (5 mL), and the organic phase was filtered. The insoluble residue was washed with Et_2O, and the combined ethereal phases were dried and evaporated under reduced pressure. Purification by chromatography on a silica gel column (hexane/ethyl acetate, 80:20) led to the expected derivative **15** (6.98 g, 70% yield): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.33 (s, 6H), 1.39 (s wide, 1H), 1.79 (d, J = 7.4 Hz, 2H), 4.09 (d, J = 5.9 Hz, 2H), 5.58 (dt, J = 15.0, 5.9 Hz, 1H), 5.72 (dt, J = 15.0, 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −3.4 ($2CH_3$), 21.8 (CH_2), 63.9 (CH_2), 127.7 (2CH), 128.2 (CH), 129.1 (CH), 129.7 (CH), 133.6 (2CH), 138.4 (C); IR ($CHCl_3$) 3610, 3500–3400, 1650, 1425, 1400, 1375, 1250, 1150, 1110, 980, 960, 850 cm^{-1}; CIMS (NH_3) m/e (relative intensity) 206 (M^+, 7), 189 (27), 152 (100), 135 (5).

Anal. Calcd for $C_{12}H_{18}OSi$, 206.32: C, 69.95; H, 8.79. Found: C, 69.81; H, 8.89.

(2*E*)-1-[(*N*,*N*-Diisopropylcarbamoyl)oxy]-4-(dimethylphenylsilyl)but-2-ene (16). To a solution of **15** (10.5 g, 51 mmol) and 4-(dimethylamino)pyridine (DMAP, 0.8 g, 6.5 mmol, 13 mol %) in anhydrous pyridine (50 mL) and under a nitrogen atmosphere was added a solution of diisopropylcarbamoyl chloride (10.5 g, 64 mmol, 1.25 equiv) in THF (15 mL), and the reaction mixture was heated for 12 h at 110 °C. The cooled solution (0 °C) was diluted with diethyl ether, treated with an aqueous 2 N HCl solution, and extracted with diethyl ether (×3). After the combined organic phases were washed with water and dried on $MgSO_4$, the diethyl ether was removed under reduced pressure. The crude oily residue was purified by flash chromatography on silica gel (hexane/ethyl acetate 90:10) to give the allylic carbamate **16** (13.8 g, 81%): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.27 (s, 6H), 1.18 (d, J = 7.0 Hz, 12H), 1.76 (d, J = 7.5 Hz, 2H), 3.92 (m wide, 2H), 4.52 (d, J = 6.0 Hz, 2H), 5.52 (dt, J = 15.0, 6.0 Hz, 1H), 5.8 (dt, J = 15.0, 7.5 Hz, 1H), 7.39 (m, 3H), 7.58 (m, 2H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −3.5 ($2CH_3$), 20.9 ($4CH_3$), 21.9 (CH_2), 45.6 (2CH), 65.4 (CH_2), 124.0 (CH), 127.2 (2CH), 128.9 (CH), 131.6 (CH), 133.5 (2CH), 138.4 (C), 155.6 (C); IR (CCl_4) 2960, 1690, 1470, 1440, 1310, 1280, 1215, 1150, 1130, 1050, 970, 930 cm^{-1}; CIMS (NH_3) m/e (relative intensity) 334 (MH^+, 1), 318 (3), 280 (20), 264 (5), 202 (100), 189 (10), 152 (35).

Anal. Calcd for $C_{19}H_{31}NO_2Si$, 333.51: C, 68.42; H, 9.37; N, 4.20. Found: C, 68.33; H, 9.40; N, 4.05.

(3*R,4*S**,5*Z*)-6-[(*N*,*N*-diisopropylcarbamoyl)oxy]-4-[(dimethylphenylsilyl)methyl]hex-5-en-3-ol (17).** To a solution of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA, 8.3 mL, 55 mmol, 1.25 equiv) in Et_2O (34 mL) at −78 °C under argon was added *via* syringe *n*-BuLi (1.6 M in hexane, 36 mL, 58 mmol, 1.3 equiv). After being stirred for 30 min, an ethereal solution (30 mL) of the carbamate **16** (14.8 g, 44.4 mmol) was slowly added. The reaction mixture was stirred for 45 min at −78 °C before addition of titanium tetraisopropoxide (50 mL, 0.19 mol, 4.4 equiv); the mixture turned red-orange and was stirred for another 35 min. Freshly redistillated propanal (7 mL, 98 mmol, 1.8 equiv) was then added to the preceding solution, which was stirred for 2 h at −78 °C. The temperature was then allowed to rise to 0 °C. The mixture was diluted with diethyl ether, treated with aqueous 2 N HCl, and extracted with diethyl ether (×3). After the combined organic phases were washed with water, dried over $MgSO_4$, and evaporated under reduced pressure, the oily residue was purified by flash chromatography on silica gel to furnish the title product **17** (15.46 g, 89% yield): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.27, 0.30 (2s, 6H), 0.78 (m, 1H), 0.91 (t, J = 7.2 Hz, 3H), 1.03 (m, 1H), 1.21, 1.26 (2s wide, 12H), 1.45 (m, 2H), 1.54 (d, J = 4.0 Hz, 1H), 2.8 (tt, J = 10.5, 4.5 Hz, 1H), 3.35 (ddt, J = 10.5, 4.0, 6.5 Hz, 1H), 3.95 (m, 2H), 4.59 (dd, J = 10.4, 6.0 Hz, 1H), 7.12 (d, J = 6.0 Hz, 1H), 7.41 (m, 3H), 7.58 (m, 2H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −2.7, −1.9 ($2CH_3$), 9.9 (CH_3), 18.5 (CH_2), 20.4 ($2CH_3$), 21.3 ($2CH_3$), 26.9 (CH_2), 36.9 (CH), 46.0 (CH), 46.1 (CH), 77.3 (CH), 112.6 (CH), 127.6 (2CH), 128.7 (CH), 128.9 (CH), 133.5 (2CH), 139.4 (C), 152.4 (C); IR (CCl_4) 3580, 1710, 1660, 1460, 1430, 1370, 1310, 1280, 1245 1210, 1130, 1110, 1070, 960, 940 cm^{-1}; CIMS (NH_3) m/e (relative intensity) 392 (MH^+, 3), 374 (2), 314 (5), 270 (3), 247 (5), 205 (5), 152 (5), 128 (100), 102 (15), 86 (3).

Anal. Calcd for $C_{22}H_{37}O_3NSi$, 391.59: C, 67.47; H, 9.52; N, 3.57. Found: C, 66.68; H, 9.62; N, 3.31.

(4*S,5*R**)-4-[(Dimethylphenylsilyl)methyl]-5-ethyldihydrofuran-2-one (18).** To a solution of vinyl carbamate **17** (6.6 g, 16.9 mmol) in anhydrous MeOH (60 mL) at 0 °C and under nitrogen was added methanesulfonic acid ($MeSO_3H$, 1.1 mL, 16.9 mmol, 1 equiv) followed by mercuric acetate ($Hg(OAc)_2$, 67 mg, 0.21 mmol, 1 mol %). After being stirred for 3 h at 20 °C, the mixture was concentrated under reduced pressure. The oily residue was dissolved in dried dichloromethane (120 mL) at 0 °C and treated with boron trifluoride–diethyl ether complex (BF_3·OEt_2, 0.5 mL, 4 mmol, 24 mol %) and with *m*-chloroperbenzoic acid (MCPBA 55%, 7 g, 22 mmol, 1.3 equiv). Stirring was maintained for 12 h at 20 °C, and the reaction mixture was cooled at 0 °C. Excess MCPBA was destroyed by addition of dimethyl sulfide. The mixture was washed with an aqueous saturated sodium bicarbonate solution ($NaHCO_3$) and with brine. Removal of the solvent under vacuo gave an oily residue which was purified by chromatography on silica gel (hexane/ethyl acetate 80:20) to give silyl lactone **18** (3 g, 68% yield): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.30 (s, 6H), 0.78 (dd, J = 15.0, 10.5 Hz, 1H), 1.0 (t, J = 7.5 Hz, 3H), 1.09 (dd, J = 15.0, 3.5 Hz, 1H), 1.51 (sext, J = 7.5 Hz, 1H), 1.75 (m, 1H), 2.06 (m, 1H), 2.15 (quint d, J = 7.5, 3.5 Hz, 1H), 2.51 (m, 1H), 3.98 (ddd, J = 8.5, 7.5, 3.5 Hz, 1H), 7.47 (m, 3H), 7.58 (m, 2H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −2.7 ($2CH_3$), 9.9 (CH_3), 19.8 (CH_2), 26.2 (CH_2), 37.3 (CH), 37.5 (CH_2), 89.9 (CH), 128.1 (2CH), 129.4 (CH), 133.3 (2CH), 137.7 (C), 176.7 (C); IR ($CDCl_3$) 1700, 1550, 1425, 1330, 1250, 1220, 1170, 1110, 960 cm^{-1}; CIMS (NH_3) m/e (relative intensity) 280 (MH^+ + 17, 50), 263 (MH^+, 25), 247 (40), 185 (80), 156(55),135 (100), 116 (45).

Anal. Calcd for $C_{15}H_{22}O_2Si$, 262.39: C, 68.66; H, 8.45. Found: C, 68.47; H, 8.64.

(4R*,5R*)-4-(Acetoxymethyl)-5-ethyldihydrofuran-2-one (19). A solution of silyl lactone **18** (4.44 g, 16.9 mmol) in acetic acid (8 mL) and peracetic acid (32% solution in acetic acid, 16 mL, 68 mmol, 4 equiv) at 0 °C was treated with $Hg(OAc)_2$ (10 g, 31 mmol, 1.8 equiv) and $MeSO_3H$ (0.5 mL, 7.7 mmol, 0.45 equiv). The reaction mixture was then stirred for 12 h at 45 °C. After the mixture was cooled to 0 °C, excess peracetic acid was destroyed by addition of dimethyl sulfide. The mixture was then neutralized with saturated aqueous $NaHCO_3$ at 0 °C and extracted (×3) with ethyl acetate. The combined organic phases were washed with water and dried on magnesium sulfate, and the solvent was removed under vacuo leading to an oil which was purified by flash chromatography on silica gel column (hexane/ethyl acetate, 50:50) to give the acetoxy lactone **19** (1.86 g, 60% yield) and the corresponding deacetylated derivative **20** (0.35 g, 15% yield, see below). **19**: ^1H NMR ($CDCl_3$, 200 MHz) δ 1.03 (t, J = 7.5 Hz, 3H), 1.72 (m, 2H), 2.08 (s, 3H), 2.39 (dd, J = 15.5, 6.5 Hz, 1H), 2.55 (m, 1H), 2.73 (dd, J = 15.5, 8.0 Hz, 1H), 4.15 (d, J = 5.5 Hz, 2H), 4.27 (dt, J = 7.5, 5.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 9.2 (CH_3), 20.3 (CH_3), 27.5 (CH_2), 31.4 (CH_2), 38.9 (CH), 63.9 (CH_2), 83.5 (CH), 170.2 (C), 175.3 (C); IR ($CHCl_3$) 1775, 1745, 1455, 1440, 1365, 1230, 1180, 1030, 970 cm^{-1}.

Anal. Calcd for $C_9H_{14}O_4$, 186.20: C, 58.05; H, 7.58. Found: C, 58.21; H, 7.67.

(4R*,5R*)-5-Ethyl-4-(hydroxymethyl)dihydrofuran-2-one (20). To a solution of the above acetoxy lactone **19** (1.86 g, 10 mmol) in absolute EtOH (40 mL) was added guanidine (0.6 g, 10 mmol, 1 equiv) at ambient temperature. After being stirred for 1.5 h, the reaction mixture was concentrated under reduced pressure and the crude residue was purified by chromatography on silica gel to furnish the title product **20** (1.15 g, 80% yield): ^1H NMR ($CDCl_3$, 200 MHz) δ 0.97 (t, J = 6.5 Hz, 3H), 1.60 (quint, J = 7.5 Hz, 1H), 1.71 (sext d, J = 7.5, 2.7 Hz, 1H), 2.36 (m, 1H), 2.50 (dd, J = 17.5, 7.0 Hz, 1H), 2.64 (dd, J = 7.5, 9.5 Hz, 1H), 3.64 (d, J = 5.5 Hz, 2H), 4.30 (dt, J = 7.5, 5.5 Hz, 1H), 4.76 (m, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 9.6 (CH_3), 27.9 (CH_2), 31.4 (CH_2), 41.9 (CH), 62.7 (CH_2), 84.3 (CH), 176.1 (C); IR ($CHCl_3$) 3500–3400, 1780, 1500, 1450, 1330, 1170, 1150, 970 cm^{-1}; CIMS (NH_3) m/e (relative intensity) 162 (MH^+ + 17, 70), 145 (MH^+, 100), 127 (40), 109 (10), 81 (10).

Anal. Calcd for $C_7H_{12}O_3$, 144.17: C, 58.31; H, 8.39. Found: C, 58.49; H, 8.25.

(4R*,5R*)-5-Ethyl-4-{[(triisopropylsilyl)oxy]methyl}-dihydrofuran-2-one (21). The above hydroxy lactone **20** (1.5 g, 10.4 mmol) in CH_2Cl_2 (14 mL) was treated with 2,6-lutidine (2 mL, 17 mmol, 1.6 equiv) and triisopropylsilyl triflate (TIPSOTf, 3.1 mL, 11.5 mmol, 1.1 equiv) at 20 °C for 1.5 h. Extraction with CH_2Cl_2 and chromatography on silica gel (hexane/ethyl acetate 90:10) led to lactone **21** (2.9 g, 94% yield): ^1H NMR ($CDCl_3$, 200 MHz) δ 1.06 (t, J = 7.5 Hz, 3H), 1.09 (m, 21H), 1.75 (m, 2H), 2.39 (m, 1H), 2.55 (dd, J = 17.0, 9.0 Hz, 1H), 2.67 (dd, J = 17.0, 9.0 Hz, 1H), 3.79 (d, J = 5.5 Hz, 2H), 4.42 (dt, J = 7.0, 5.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 9.7 (CH_3), 11.8 (3CH), 17.9 ($6CH_3$), 28.1 (CH_2), 31.2 (CH_2), 42.4 (CH), 63.4 (CH_2), 84.1 (CH), 176.6 (C); IR (CCl_4) 1780, 1460, 1190, 1170, 1110, 970 cm^{-1}; CIMS (NH_3) m/e (relative intensity) 318 (MH^+ + 17, 100), 301 (MH^+, 60).

Anal. Calcd for $C_{16}H_{32}O_3Si$, 300.47: C, 63.95; H, 10.73. Found: C, 63.86; H, 10.68.

(4R*,5R*)-5-Ethyl-4-{[(*tert*-butyldimethylsilyl)oxy]-methyl}dihydrofuran-2-one (22). To a solution of hydroxy lactone **20** (1.75 g, 12 mmol) in CH_2Cl_2 (12 mL) under nitrogen was added imidazole (Im,1.2 g, 17 mmol) followed by a solution of *tert*-butyldimethylsilyl chloride (TBSCl, 2.0 g, 13.3 mmol) in CH_2Cl_2 (10 mL) at 0 °C. After 12 h of stirring at ambient temperature, extraction with CH_2Cl_2 and chromatography on silica gel (hexane/ethyl acetate 9:1) led to the lactone **22** (2.8 g, 90% yield): ^1H NMR ($CDCl_3$, 200 MHz) δ 0.06 (s, 6H), 0.89 (s, 9H), 1.02 (t, J = 7.3 Hz, 3H), 1.70 (m, 2H), 2.35 (m, 1H), 2.45 (m, 1H), 2.57 (m, 1H), 3.63 (d, J = 5.1 Hz, 2H), 4.28 (ddd, J = 7.0, 5.4, 5.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.4 ($2CH_3$), 9.6 (CH_3), 18.4 (C), 26.0 ($3CH_3$), 28.3 (CH_2), 31.5 (CH_2), 42.5 (CH), 63.6 (CH_2), 84.2 (CH), 176.3 (C); IR (CCl_4) 1780, 1455, 1190, 1160, 1110, 960 cm^{-1}; CIMS (NH_3) m/e (relative intensity) 276 (MH^+ + 17, 55), 259 (MH^+, 100), 241 (10), 201 (10), 155 (10), 127 (20).

Anal. Calcd for $C_{13}H_{26}O_3Si$, 258.39: C, 60.42; H, 10.14. Found: C, 60.53; H, 10.08.

(2R*,3R*)-2-Ethyl-3-{[(triisopropylsilyl)oxy]methyl}-2,3-dihydrofuran (23). To a solution of lactone **21** (2.93 g, 9.7 mmol) in anhydrous CH_2Cl_2 (10 mL) at −78 °C was slowly added a 1 M solution of diisobutylaluminum hydride in toluene (DIBALH, 12 mL, 12 mmol, 1.2 equiv). After being stirred for 1 h at −78 °C, the reaction mixture was poured into an aqueous 2 N HCl solution and extracted with CH_2Cl_2. The combined organic phases were filtered on Celite, washed with a saturated aqueous $NaHCO_3$ solution, and dried over magnesium sulfate, and the solvent was removed in vacuo. The crude residue was dissolved in THF (14 mL) at −15 °C and treated with triethylamine (NEt_3, 5 mL, 36 mmol, 3.7 equiv) and methanesulfonyl chloride (MsCl, 1.25 mL, 16 mmol, 1.6 equiv), and the resulting white suspension was stirred for 1 h between −15 and −5 °C and then warmed for 3 h at reflux. The mixture was diluted with water and extracted with diethyl ether to give, after removal of the solvent under reduced pressure, the title product **23** which was purified by flash chromatography on silica gel (hexane) and distillation (1.73 g, 63%): bp 105 °C/ 2 mmHg; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.00 (t, J = 7.2 Hz, 3H), 1.09 (m, 21H), 1.64 (m, 2H), 2.90 (m, 1H), 3.55 (t, J = 9.0 Hz, 1H), 3.97 (dd, J = 9.0, 5.5 Hz, 1H), 4.3 (q, J = 6.0 Hz, 1H), 4.78 (t, J = 2.5 Hz, 1H), 6.33 (dd, J = 2.5, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 9.4 (CH_3), 12.0 (3CH), 18.0 ($6CH_3$), 28.7 (CH_2), 50.6 (CH), 66.9 (CH_2), 86.2 (CH), 100.2 (CH), 146.0 (CH); IR (CCl_4) 1615, 1460, 1380, 1240, 1140, 1110, 1060, 1050, 870 cm^{-1}; CIMS (NH_3) m/e (relative intensity) 302 (MH^+ + 17, 13), 285 (MH^+, 100), 272 (15), 248 (12), 241 (15), 178 (10), 111 (35).

Anal. Calcd for $C_{16}H_{32}O_2Si$, 284.48: C, 67.55; H, 11.34. Found: C, 67.41; H, 11.26.

(2R*,3R*)-2-Ethyl-3-{[(*tert*-butyldimethylsilyl)oxy]-methyl}-2,3-dihydrofuran (24). To a solution of the above TBS lactone **22** (1.58 g, 6 mmol) in anhydrous CH_2Cl_2 (7 mL) at −78 °C and under nitrogen, was slowly added a solution of diisobutylaluminum hydride (DIBALH 1.5 M solution in toluene, 5 mL, 7.5 mmol, 1.25 equiv). After being stirred at −78 °C for 1 h, the reaction mixture was poured into an aqueous 2 N HCL solution at 0 °C and extracted with CH_2Cl_2. The combined organic phases were filtered on a pad of Celite, washed with a saturated aqueous $NaHCO_3$ solution, and dried over magnesium sulfate, and the solvent was removed in vacuo. The crude residue was taken up in THF (12 mL) at −15 °C and treated with triethylamine (NEt_3, 3.5 mL, 2.5 mmol, 4.2 equiv) and methanesulfonyl chloride (MsCl, 1 mL, 13 mmol, 2.2 equiv), and the resulting white suspension was stirred for 1 h at −15 °C and then warmed for 3 h at reflux. The mixture was diluted with water and extracted with diethyl ether to give, after removal of the solvent under reduced pressure, the title product **24** which was purified by chromatography on silica gel (hexane) and distillation (0.88 g, 61%): bp 105 °C/2 mmHg; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.14 (s, 6H), 0.95 (s, 9H), 1.00 (t, J = 7.4 Hz, 3H), 1.65 (m, 2H), 2.79 (m, 1H), 3.44 (dd, J = 9.5, 8.0 Hz, 1H), 3.63 (dd, J = 9.5, 5.5 Hz, 1H), 4.22 (q, J = 6.2 Hz, 1H), 4.78 (t, J = 2.5 Hz, 1H), 6.29 (t, J = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.4 ($2CH_3$), 9.3 (CH_3), 18.3 (C), 25.9 ($3CH_3$), 28.7 (CH_2), 50.5 (CH), 66.6 (CH_2), 86.2 (CH), 100.1 (CH), 146.0 (CH); IR (CCl_4) 1610, 1460, 1375, 1230, 1130, 1060, 980, 880 cm^{-1}; CIMS (NH_3) m/e (relative intensity) 260 (MH^+ + 17, 20), 243 (MH^+, 100), 230 (15), 228 (10), 115 (20), 111 (10).

Anal. Calcd for $C_{13}H_{26}O_2Si$, 242.34: C, 64.41; H, 10.81. Found: C, 64.34; H, 10.66.

[2R*(1E,3E),3R*]-2-(2-Methyl-4-(tributylstannyl)buta-1,3-dienyl)-1-[(*tert*-butyldimethylsilyl)oxy]pentan-3-ol (5a). To a solution of (*E*)-bis(tributylstannyl)ethylidene (1.7 g, 2.8 mmol, 2.5 equiv) in THF (4 mL) at −78 °C, and under an argon atmosphere, was added a 1.6 M pentane solution of *n*-BuLi (2.5 mL, 4 mmol, 3.6 equiv). The reaction temperature was allowed to rise to −10 °C over 30 min. This lithiostannyl solution was slowly added *via* cannula to a suspension of dried CuCN (0.1 g, 1.1 mmol, 1 equiv) in diethyl ether (5 mL) at

−60 °C. The temperature was then allowed to rise to −15 °C over 1 h. In a second flask, *t*-BuLi (1.7 M in pentane, 0.8 mL, 1.36 mmol, 1.2 equiv) was slowly added to a solution of dihydrofuran **24** (0.27 g, 1.1 mmol) in Et_2O (4 mL) at −60 °C. Stirring was maintained for 10 min at −60 °C, and the flask was rapidly put in an ice bath for 50 min. This lithiodihydrofuran solution was then rapidly added to the preceding cuprate solution at −15 °C. After being stirred for 2.5 h at 0 °C, the reaction mixture was cooled to −50 °C, and freshly distilled methyl iodide (MeI, 0.5 mL, 7 mmol, 6.6 equiv) was added. The temperature was allowed to rise to 20 °C over 4 h. The mixture was then poured into a vigorously stirred mixture of a saturated aqueous NH_4Cl/concentrated ammonia (4:1 vol/vol) at 0 °C. Extraction with diethyl ether and chromatography on neutral alumina (ethyl acetate 0−5% in hexane containing 2% of NEt_3) gave the expected stannyl diene **5a** (60 mg, 10%): ^1H NMR ($CDCl_3$, 200 MHz) δ 0.1 (s, 6H), 0.96 (m, 27H), 1.37 (m, 6H), 1.52 (m, 8H), 1.85 (d, J = 0.5 Hz, 3H), 2.7 (m, 1H), 3.10 (m, 1H), 3.83 (m, 2H), 3.90 (m, 1H), 5.61 (dq, J = 10.5, 0.5 Hz, 1H), 6.17 (d, J = 19.5 Hz, 1H, $J(^{117}Sn-H) = J(^{119}Sn-H)$ = 67 Hz), 6.63 (d, J = 19.5 Hz, 1H, $J(^{117}Sn-H) = J(^{119}Sn-H)$ = 64.0 Hz); ^{13}C NMR ($CDCl_3$, 50.3 MHz), HCOR experiment δ −5.6 ($2CH_3$), 9.5 ($3CH_2$, $J(^{117}Sn-C)$ = 345.0 Hz, $J(^{119}Sn-C)$ = 330.0 Hz), 10.5 (CH_3), 12.3 (CH_3), 13.7 ($3CH_3$), 18.1 (C), 25.8 ($3CH_3$), 27.3 ($3CH_2$, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 55.0 Hz), 27.7 (CH_2), 29.1 ($3CH_2$, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 20.0 Hz), 44.4 (CH), 66.4 (CH_2), 75.6 (CH), 125.9 (CH, $J(^{117}Sn-C)$ = 390.0 Hz, $J(^{119}Sn-C)$ = 380.0 Hz), 128.2 (CH), 137.9 (C, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 65.0 Hz), 150.9 (CH); IR ($CHCl_3$) 3500, 1670, 1560, 1460, 1370, 1250, 1090, 970, 950, 910 cm^{-1}; CIMS (NH_3), calcd for ^{120}Sn major isotope, m/e (relative intensity) 575 (1), 308 (20), 291 (17), 250 (15) 153 (30), 135 (100), 106 (10), 95 (5).

Anal. Calcd for $C_{31}H_{64}O_2SiSn$, 615.58: C, 60.48; H,10.48. Found: C,60.57; H,10.61.

[2*R(1*E*),3*R**]-2-[2-(Tributylstannyl)prop-1-enyl]-1-[(triisopropylsilyl)oxy]pentan-3-ol (25).** To a solution of hexabutylditin (7 mL, 13.9 mmol, 3 equiv) in THF (7 mL), at −30 °C, under argon, was added a 2 M pentane solution of *n*-BuLi (6.8 mL, 13.6 mmol, 3 equiv). After being stirred for 30 min, during which time the temperature was allowed to rise to −10 °C, this lithiostannyl solution was added *via* cannula to a suspension of dried CuCN (0.4 g, 4.5 mmol, 1 equiv) in diethyl ether (15 mL) at −60 °C. The temperature was then allowed to rise to −10 °C over 1 h. In a second flask, *t*-BuLi (1.6 M in pentane, 3.4 mL, 5.5 mmol, 1.2 equiv) was slowly added to a solution of dihydrofuran **22** (1.29 g, 4.5 mmol) in Et_2O (5 mL) at −65 °C. Stirring was maintained for 15 min at −60 °C and for 45 min at −5 °C. This lithiodihydrofuran solution was then added to the preceding cuprate solution at 0 °C. After being stirred for 1 h at 0 °C, the reaction mixture was cooled to −60 °C and methyl iodide (MeI, 1.4 mL, 22.5 mmol, 5 equiv) was added. The temperature was allowed to rise to 20 °C over 4 h. The mixture was then poured into a vigorously stirred mixture of a saturated aqueous NH_4Cl/concentrated ammonia (4:1 vol/vol) at 0 °C. Extraction with diethyl ether and chromatography on neutral alumina (ethyl acetate 0−5% in hexane containing 2% of NEt_3) gave vinylstannane **25** (2.14 g, 80%): ^1H NMR ($CDCl_3$, 200 MHz) δ 0.90 (m, 15H), 0.92 (t, J = 7.5 Hz, 3H), 1.09 (m, 21H), 1.36 (m, 6H), 1.51 (m, 8H), 1.88 (d, J = 1.8 Hz, 3H, $J(^{117}Sn-H) = J(^{119}Sn-H)$ = 45.0 Hz), 2.78 (m, 1H), 3.30 (d, J = 3.0 Hz, 1H), 3.85 (m, 1H), 3.90 (m, 2H), 5.77 (dq, J = 9.5, 1.8 Hz, 1H, $J(^{117}Sn-H) = J(^{119}Sn-H)$ = 70.0 Hz); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 9.1 ($3CH_2$, $J(^{117}Sn-C)$ = 328.0 Hz, $J(^{119}Sn-C)$ = 314.0 Hz), 10.4 (CH_3), 11.8 (3CH), 13.7 ($3CH_3$), 17.9 ($6CH_3$), 19.6 (CH_3), 27.3 ($3CH_2$, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 54.0 Hz), 27.5 (CH_2), 29.2 ($3CH_2$, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 20.0 Hz), 43.6 (CH, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 52.0 Hz), 67.2 (CH_2), 75.8 (CH), 136.6 (CH, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 30.0 Hz), 141.5 (C); IR (CCl_4) 3500, 1550, 1460, 1370, 1280, 1080, 1050, 880 cm^{-1}; CIMS (NH_3) calcd for ^{120}Sn major isotope, m/e (relative intensity) 591 (MH^+, 70), 550 (12), 533 (12), 308 (100), 299 (55), 291 (50), 109 (55).

Anal. Calcd for $C_{29}H_{62}O_2SiSn$, 589.55: C, 58.95; H, 10.60. Found: C, 59.02; H, 10.52.

(2*R,3*R**)-2-(2-Iodoprop-1-enyl)-1-[(triisopropylsilyl)oxy]pentan-3-ol (26).** To a solution of vinyl stannane **25** (2.1 g, 3.6 mmol) in CH_2Cl_2 (5 mL) under argon was added drop by drop a solution of iodine (0.95 g, 3.8 mmol, 1.1 equiv) in CH_2Cl_2 (50 mL) at 0 °C. Addition was stopped when the red color became persistent (after 20 min). The solvent was removed under reduced pressure, and the residue was dissolved in Et_2O (3 mL) and treated with aqueous potassium fluoride (KF, 2 g in 10 mL). After being stirred for 3 h at 20 °C, the mixture was filtered on a pad of Celite and the ethereal layer was evaporated in vacuo. The crude residue was purified by chromatography on silica gel (hexane/ethyl acetate 93:7) to give the title product **26** (1.45 g, 95% yield) which was distilled: bp 170 °C/0.02 mmHg; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.94 (t, J = 7.5 Hz, 3 H), 1.06 (m, 21H), 1.48 (m, 2H), 2.39 (d, J = 1.6 Hz, 3H), 2.51 (m, 1H), 3.06 (d, J = 3.0 Hz, 1H), 3.8 (m, 1H), 3.88 (d, J = 5.0 Hz, 2H), 6.42 (dq, J = 10.2, 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 10.6 (CH_3), 11.4 (3CH), 18.1 ($6CH_3$), 27.9 (CH_2), 28.4 (CH_3), 47.3 (CH), 66.4 (CH_2), 75.1 (CH), 96.2 (C), 138.2 (CH); IR ($CHCl_3$) 3350, 2950, 2910, 2860, 2840, 1550, 1460, 1370, 1100, 1050 cm^{-1}; CIMS (NH_3) m/e (relative intensity) 444 (MH^+ + 17, 10), 427 (MH^+, 100), 148 (7).

Anal. Calcd for $C_{17}H_{35}O_2SiI$, 426.43: C, 47.88; H, 8.27. Found: C, 47.99; H, 8.30.

(2*R,3*R**)-2-(2-Methylbut-1-en-3-ynyl)-1-[(triisopropylsilyl)oxy]pentan-3-ol (27).** To a solution of tetrakis(triphenylphosphine)palladium ($Pd(PPh_3)_4$, 51 mg, 5 mol %) in THF (3 mL) under argon were successively added a solution of vinyl iodide **26** (376 mg, 0.88 mmol) in THF (3 mL) and a solution of (tributylstannyl)acetylene ($Bu_3SnC{\equiv}CH$, 360 mg, 1.14 mmol, 1.3 equiv) in THF (3 mL). The reaction mixture was stirred for 1 h at 50 °C, poured into a saturated aqueous NH_4Cl solution at −5 °C, and extracted with diethyl ether.The crude residue was taken up in Et_2O (3 mL), treated with aqueous KF (2 g in 10 mL water), and stirred for 3 h at 20 °C. After filtration on a pad of Celite, the ethereal phase was evaporated and the residue purified by chromatography on silica gel (hexane/ethyl acetate 97:3) and then by preparative HPLC (reverse phase, CH_3CN) to furnish the enyne **27** (260 mg, 91% yield): bp 140 °C/0.02 mmHg; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.88 (t, J = 7.5 Hz, 3H), 1.0 (m, 21H), 1.39 (m, 2H), 1.76 (d, J = 1.5 Hz, 3H), 2.51 (m, 1H), 2.69 (s, 1H), 2.93 (d, J = 4.0 Hz, 1H), 3.72 (m, 1H), 3.78 (d, J = 5.0 Hz, 2H), 6.01 (dq, J = 10.0, 1.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 10.5 (CH_3), 11.9 (3CH), 17.7 (CH_3), 18.0 ($6CH_3$), 27.8 (CH_2), 45.1 (CH), 66.2 (CH_2), 74.2 (CH), 75.2 (CH), 86.6 (C), 119.6 (C), 135.9 (CH); IR ($CHCl_3$) 3500, 2940, 2860, 1630, 1460, 1370, 1120, 1040, 950 cm^{-1}; CIMS (NH_3) m/e (relative intensity) 342 (MH^+ + 17, 2), 325 (MH^+, 100), 307 (20), 151 (20).

Anal. Calcd for $C_{19}H_{36}O_2Si$, 324.54: C, 70.31; H, 11.18. Found: C,70.11; H, 11.09.

(2*R,3*R**)-2-(2-Methylbut-1-en-3-ynyl)pentane-1,3-diol (28).** To a solution of the silylated enyne **27** (230 mg, 0.7 mmol) in THF (3 mL) under argon was added a 1.1 M solution of tetrabutylammonium fluoride in THF (0.95 mL, 1.05 mmol, 1.5 equiv) at 20 °C. After 1.5 h, the mixture was poured into a saturated aqueous NH_4Cl solution and extracted with diethyl ether. The crude residue was purified by chromatography on silica gel (hexane/ethyl acetate 25:75) and then by preparative HPLC (reverse phase, CH_3CN) to furnish the expected diol **28** (98 mg, 82% yield): ^1H NMR ($CDCl_3$, 200 MHz) δ 1.01 (t, J = 7.5 Hz, 3H), 1.52 (m, 3H), 1.91 (d, J = 1.6 Hz, 3H), 2.68 (m, 1H), 2.86 (s, 1H), 2.98 (m, 1H), 3.76 (m, 2H), 3.85 (m, 1H), 6.0 (dq, J = 10.6, 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 10.5 (CH_3), 17.8 (CH_3), 28.1 (CH_2), 45.4 (CH), 64.5 (CH_2), 74.5 (CH), 74.7 (CH), 86.5 (C), 120.6 (C), 135.3 (CH); IR ($CHCl_3$) 3600−3500, 2950, 2850, 2100, 1460, 1380, 1240−1220, 1100, 1050, 980, 880 cm^{-1}; CIMS (NH_3) m/e (relative intensity) 186 (MH^+ + 17, 100), 168 (60), 151 (45), 139 (10), 133 (10), 121 (15), 110 (20).

Anal. Calcd for $C_{10}H_{16}O_2$, 168.23: C, 71.39; H, 9.59. Found: C, 71.48; H, 9.69.

[2*R(1*E*,3*E*),3*R**]-2-(2-Methyl-4-(tributylstannyl)buta-1,3-dienyl)-1-[(triisopropylsilyl)oxy]pentan-3-ol (5b). [2*R**-(1*E*,3*Z*),3*R**]-2-(2-Methyl-4-(tributylstannyl)buta-1,3-di-**

enyl)-1-[(triisopropylsilyl)oxy]pentan-3-ol (29). Entry 1. To a suspension of CuCN (67 mg, 0.7 mmol, 2.2 equiv) in THF (4 mL) at −30 °C under argon was added *n*-BuLi (1.6 M in hexane, 0.94 mL, 1.5 mmol, 4.4 equiv). After 5 min at −30 °C, the cold bath was removed for 15 min and replaced so that the temperature reached −30 °C; then tributylstannyl hydride (0.4 mL, 1.5 mmol, 4.4 equiv) was added. After being stirred for another 30 min at −30 °C, a solution of the silylated enyne **27** (110 mg, 0.34 mmol) in THF (2 mL) was slowly added. Stirring was maintained for 30 min at −30 °C, and the reaction was quenched by addition of MeOH (2 mL). After being stirred for 30 min, the mixture was poured into a 4:1 mixture of a saturated aqueous NH_4Cl/concentrated ammonia at −10 °C. Extraction with diethyl ether gave an oil which was purified by chromatography on alumina (hexane with 2% NEt_3) to give starting material (28 mg, 25%) and a 1:1 mixture of stannyl dienes **5b** and **29** (52 mg, 44%). For **5b:** ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.8−1.0 (m, 18H), 1.12 (m, 21H), 1.36 (m, 6H), 1.54 (m, 8H), 1.84 (d, J = 0.5 Hz, 3H), 2.75 (m, 1H), 3.30 (d, J = 3.5 Hz, 1H), 3.85 (m, 1H), 3.96 (m, 2H), 5.69 (dq, J = 10.5, 0.5 Hz, 1H), 6.21 (d, J = 21.0 Hz, 1H, $J(^{117}Sn-H) = J(^{119}Sn-H)$ = 73.0 Hz), 6.66 (d, J = 21.0 Hz, 1H, $J(^{117}Sn-H) = J(^{119}Sn-H)$ = 68.0 Hz); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 9.6 ($3CH_2$, $J(^{117}Sn-C)$ = 345.0 Hz, $J(^{119}Sn-C)$ = 330.0 Hz), 10.6 (CH_3), 11.9 (3CH), 12.4 (CH_3), 13.8 ($3CH_3$), 18.0 ($6CH_3$), 27.2 ($3CH_2$, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 55.0 Hz), 27.6 (CH_2), 29.1 ($3CH_2$, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 20.0 Hz), 44.5 (CH), 67.0 (CH_2), 75.6 (CH), 125.7 (CH, $J(^{117}Sn-C)$ = 390.0 Hz, $J(^{119}Sn-C)$ = 380.0 Hz), 128.2 (CH), 137.8 (C, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 68.0 Hz), 151.0 (CH). For **29:** ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.80−1.20 (m, 39H), 1.36 (m, 6H), 1.54 (m, 8H), 1.84 (d, J = 0.5 Hz, 3H), 2.75 (m, 1H), 3.15 (d, J = 5.0 Hz, 1H), 3.85 (m, 1H), 3.96 (m, 2H), 5.60 (dq, J = 10.5, 0.5 Hz, 1H), 5.82 (d, J = 15.0 Hz, 1H, $J(^{117}Sn-H) = J(^{119}Sn-H)$ = 50 Hz), 7.18 (d, J = 15.0 Hz, 1H, $J(^{117}Sn-H) = J(^{119}Sn-H)$ = 150 Hz); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 9.6 ($3CH_2$, $J(^{117}Sn-C)$ = 345.0 Hz, $J(^{119}Sn-C)$ = 330.0 Hz), 11.7 (CH_3), 11.8 (3CH), 14.5 (CH_3), 13.8 ($3CH_3$), 17.9 ($6CH_3$), 27.2 ($3CH_2$, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 55.0 Hz), 27.7 (CH_2), 29.1 ($3CH_2$, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 20.0 Hz), 44.8 (CH), 66.8 (CH_2), 75.2 (CH), 126.9 (CH, $J(^{117}Sn-C)$ = 370.0 Hz, $J(^{119}Sn-C)$ = 340.0 Hz), 128.0 (CH), 138.2 (C, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 24.0 Hz), 151.5 (CH). For **5b** and **29**: IR ($CHCl_3$) 2950, 2915, 2860, 2830, 1650, 1560, 1520, 1380, 1120, 1070, 980, 890 cm^{-1}; CIMS (NH_3) m/e (relative intensity) calcd for ^{120}Sn major isotope 617 (MH^+, 35), 559 (10), 443 (10), 327 (20), 308 (100), 291 (60), 268 (15), 251 (20), 193 (5), 153 (20), 135 (65).

Anal. Calcd for $C_{31}H_{64}O_2SiSn$, 615.58: C, 60.48; H,10.48. Found: C, 60.57; H,10.61.

(2*R(1*E*,3*E*),3*R**)-2-(2-Methyl-4-(tributylstannyl)buta-1,3-dienyl)pentane-1,3-diol (5). [2*R**(1*E*),3*R**]-2-(2-Methyl-3-(tributylstannyl)buta-1,3-dienyl)pentane-1,3-diol (30). Entry 2.** To a suspension of CuCN (156 mg, 1.7 mmol, 3.3 equiv) in THF (5 mL) at −30 °C under argon was added *n*-BuLi (1.6 M in hexane, 2.2 mL, 3.5 mmol, 6.6 equiv). After 5 min at −30 °C, the cold bath was removed for 15 min and replaced so that the temperature reached −30 °C, and tributylstannyl hydride (0.94 mL, 3.5 mmol, 6.6 equiv) was added. After being stirred for another 30 min at −30 °C, a solution of the enyne **28** (88 mg, 0.5 mmol) in THF (2 mL) was slowly added. Stirring was maintained for 30 min at −30 °C, and the reaction was quenched by addition of MeOH (2 mL). After being stirred for 30 min, the mixture was poured into a 4:1 mixture of saturated aqueous NH_4Cl/concentrated ammonia at −10 °C. Extraction with diethyl ether gave an oil which was purified by chromatography on alumina (2.5% NEt_3 in hexane/ethyl acetate 1:1) to give the pure diene **5** (204 mg, 85%). The corresponding regioisomer **30** was only detected by ^{1}H NMR of the crude residue (**5**/**30** > 97:3)

Entry 3. The above procedure was used except that MeOH was not added before treatment with NH_4Cl/ NH_4OH at −10 °C. Purification led to the to stannyl dienes **5** and **30** in an 80:20 ratio (149 mg, 63%). For **5**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.80−1.00 (m, 18H), 1.33 (m, 6H), 1.51 (m, 8H), 1.85 (d, J = 1.5 Hz, 3H), 2.06 (t, J = 5.0 Hz, 1H), 2.20 (d, J = 5.0 Hz, 1H), 2.83 (m, 1H), 3.88 (m, 3H), 5.58 (d, J = 10.0 Hz, 1H), 6.18 (d, J = 19.0 Hz, 1H, $J(^{117}Sn-H) = J(^{119}Sn-H)$ = 68.0 Hz), 6.63 (d, J = 19.0 Hz, 1H, $J(^{117}Sn-H) = J(^{119}Sn-H)$ = 64.0 Hz); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 9.4 ($3CH_2$, $J(^{117}Sn-C)$ = 350.0 Hz, $J(^{119}Sn-C)$ = 330.0 Hz), 10.2 (CH_3), 12.3 (CH_3), 13.5 ($3CH_3$), 27.2 ($3CH_2$, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 54.0 Hz), 27.7 (CH_2), 28.9 ($3CH_2$, $J(^{117}Sn-C) = J(^{119}Sn-C)$ = 20.0 Hz), 45.1 (CH), 64.8 (CH_2), 74.7 (CH), 126.5 (CH, $J(^{119}Sn-C)$ = 385.0 Hz, $J(^{117}Sn-C)$ = 380.0 Hz), 127.3 (CH), 139.1 (C, $J(^{119}Sn-C) = J(^{117}Sn-C)$ = 65.0 Hz), 150.5 (CH); IR ($CHCl_3$) 3350, 2950, 2920, 2860, 2840, 1650, 1550, 1500, 1370, 1100, 1050, 980, 890 cm^{-1}; CIMS (NH_3) calcd for ^{120}Sn major isotope, m/e (relative intensity) 461 (MH^+, 75), 420 (10), 403 (10), 369 (10), 308 (100), 291 (30), 188 (15), 153 (40).

Anal. Calcd for $C_{22}H_{44}O_2SiSn$, 459.27: C, 57.53; H, 9.65. Found: C, 57.48; H, 9.79.

For **30:** ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.90−1.00 (m, 18H), 1.33 (m, 6H), 1.51 (m, 8H), 1.87 (d, J = 1.5 Hz, 3H), 2.73 (m, 1H), 3.80 (m, 3H), 5.28 (d, J = 1.0 Hz, 1H, $J(^{117}Sn-H) = J(^{119}Sn-H)$ = 64.0 Hz), 5.37 (d, J = 9.0 Hz, 1H), 5.84 (d, J = 1.0 Hz, 1H, $J(^{117}Sn-H) = J(^{119}Sn-H)$ = 133.0 Hz).

Acknowledgment. Thanks are due to Dr. J. Prunet and J. P. Férézou for helpful discussions and to Professor A. Cavé for continual support.

JO950126S