of 1,10-phenanthroline in 3 mL of THF was slowly added 670 μL of 1.78 M *n*-butyllithium in hexane resulting in a red-brown solution. This mixture was treated with 435 μL (2.5 mmol) of HMPA followed by 155 μL (1.3 mmol) of benzyl bromide, the bath was removed, and the mixture was allowed to warm to room temperature whereupon the deep red solution faded to pale yellow. This solution was stirred for 1 h and subsequently treated with 3.5 mL of 1.0 M tetra-*n*-butylammonium fluoride in THF. This mixture was stirred for 2 h and partitioned between ether and water. The organic layer was washed with water, dried ($MgSO_4$), filtered, and concentrated under reduced pressure, and purified by column chromatography on silica gel affording 657 mg (89%) of alcohol B12 as a viscous clear oil: ^1H NMR (400 MHz) δ 1.56, 1.63 (s, vinyl CH_3s), 1.67 (s, isopropenyl CH_3), 2.01 (t, J = 9.0 Hz, allylic H's), 2.11 (br s, allylic H's), 2.85 (q, J = 9.8 Hz, C-13 H), 3.40 (AB of ABX, $\Delta\nu$ = 116.4 Hz, J_{AB} = 16.3 Hz, J_{AX} = 6.3 Hz, J_{BX} = 9.0 Hz, C-14 H's), 3.95 (s, C-1 H), 4.32 (dd, J = 6.2, 11.2 Hz, C-12 H), 4.34 (ABq, $\Delta\nu$ = 118.7 Hz, J_{AB} = 11.8 Hz, C-12 $PhCH_2O$–), 4.44 (s, $-CH_2OCH_2Ph$), 4.74, 4.83 (s, isopropenyl vinyl H's), 5.11 (m, vinyl H), 5.31 (d, J = 10.1 Hz, C-11 H), 5.36 (t, J = 6.2 Hz, vinyl H); 7.21–7.37 (br m, $PhCH_2O$–), 7.48 (t, J = 6.2 Hz, $PhSO_2$–), 7.59 (m, $PhSO_2$–), 7.86 (d, J = 6.8 Hz, $PhSO_2$–). Anal. Calcd for $C_{40}H_{50}O_5S$: C, 74.73; H, 7.84; S, 4.99. Found: C, 74.54; H, 7.86; S, 4.91.

***rel*-(1*R*,2*S*)-(3*E*,7*E*,11*E*)-1-Isopropenyl-2-(benzyloxy)-4-[(benzyloxy)methyl]-8,12-dimethyl-14-(phenylsulfonyl)-3,7,11-cyclotetradecatriene (B15).** To a stirred, cooled (0 °C) solution of 152 mg (0.23 mmol) of alcohol B12, 120 mg (0.45 mmol) of freshly recrystallized triphenylphosphine and 35 mg (0.51 mol) of freshly recrystallized imidazole in 0.4 mL of acetonitrile and 0.6 mL of ether was added in a portionwise fashion 140 mg (0.55 mol) of iodine resulting in a brown-black slurry. This mixture was stirred for 30 min, diluted with ether, and sequentially washed with saturated aqueous $Na_2S_2O_3$, saturated aqueous $CuSO_4$, and water. The organic layer was briefly dried over $MgSO_4$, filtered, and carefully concentrated under reduced pressure affording a mixture of crystalline triphenylphosphine oxide and iodide B14 as a pale yellow oil. The entire crude mixture was taken up in 6.8 mL of THF and added over 9.3 h via syringe pump to a stirred, cooled (0 °C) solution of 60 mg (0.23 mol) of 18-crown-6, and 0.78 mL of 0.65 M potassium hexamethyldisilyazide in toluene diluted to 12 mL with THF. The solution was stirred for 10 h following this addition and partitioned between ether and water. The organic layer was dried ($MgSO_4$), filtered, concentrated, and purified via column chromatography on silica gel (1:9 ether–hexane) affording 78 mg (53%) of cyclotetradecatriene B15 as a viscous pale yellow oil: ^1H NMR (400 MHz) δ 1.49, 1.60 (s, vinyl CH_3's), 1.81 (s, isopropenyl CH_3), 2.04–2.12, 2.51–2.64 (m, allylic H's), 4.84, 5.06 (s, isopropenyl vinyl H's), 7.20–7.61 (br m, aromatic H's), 7.83 (m, $PhSO_2$–).

***rel*-(1*R*,2*S*)-(3*R*,7*E*,11*E*)-1-Isopropenyl-4-(hydroxymethyl)-8,12-dimethyl-3,7,11-cyclotetradecatrien-2-ol (7-(8)-Desoxyasperdiol) (B16).** To a stirred solution of 68 mg (0.10 mmol) of sulfone B15 in ca. 8 mL of refluxing ammonia and 300 μL of THF was added 13 mg (0.6 mg-atom) of sodium. The solution immediately became dark blue and was subsequently stirred for 1 h. The reaction was quenched via the addition of solid NH_4Cl, and the ammonia was allowed to evaporate giving a slurry which was diluted with ether and partitioned between ether and water. The organic layer was dried briefly over $MgSO_4$, filtered, concentrated under reduced pressure and purified via column chromatography on silica gel (1:1 ether–hexane) to afford 22 mg (71%) of diol B16 as a viscous clear oil which crystallized on standing, mp 97–98.5 °C: ^1H NMR (400 MHz) δ 1.55 (s, C-8 CH_3), 1.62 (s, C-12 CH_3), 1.65 (m, C-14 H), 1.78 (s, isopropenyl CH_3), 1.84–2.39 (br m, allylic Hs), 4.10 (ABq, $\Delta\nu$ = 29.2 Hz, J_{AB} = 13.0 Hz, CH_2OH), 4.36 (dd, J = 3.8, 8.7 Hz, C-3 H), 4.75, 4.96 (br s, isopropenyl vinyl H's), 5.03 (br m, C-7 and C-11 vinyl H's), 5.54 (d, J = 8.7 Hz, C-3 H). Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 78.79; H, 10.66.

A mixture of the above sample and an authentic sample, mp 96.5–98 °C, provided by Professor Kato exhibited mp 96.5–97.5 °C.

***rel*-(1*R*,2*S*)-(3*E*,7*E*,11*E*)-1-Isopropenyl-4-[(benzoyloxy)methyl]-8,12-dimethyl-3,7,11-cyclotetradecatrien-2-ol (B17).** To a stirred solution of 10 mg (0.033 mmol) of diol B16, 5 mg of 4-(*N*,*N*-dimethylamino)pyridine, and 5 μL (0.04 mmol) of triethylamine in 300 μL of CH_2Cl_2 was added 4 μL (0.033 mmol) of benzoyl chloride. The resulting solution was stirred for 6 h, and the crude product was purified by column chromatography on silica gel (1:5 ether–hexane) to afford 9 mg (67%) of benzoate B17 as a clear oil: ^1H NMR (200 MHz) δ 1.56 (s, C-8 CH_3), 1.62 (s, C-12 CH_3), 1.67 (m, C-14 H), 1.79 (s, isopropenyl CH_3), 1.86–2.41 (br m, allylic H's), 4.40 (m, C-2 H), 4.76 (br s, isopropenyl vinyl H), 4.79 (ABq, $\Delta\nu$ = 35.30 Hz, J_{AB} = 14.28 Hz, $-CH_2OCOPh$), 4.95 (br s, isopropenyl vinyl H), 5.06 (m, C-7 and C-11 vinyl H's), 5.66 (d, J = 9.4 Hz, C-2 H), 7.4 (t, J = 6.7 Hz, $PhCO_2$–), 7.54 (m, $PhCO_2$–), 8.02 (d, J = 9.6 Hz, $PhCO_2$–).

Acknowledgment. We thank Dr. Alan Hochstetler and Givaudan Corporation (Clifton) for a generous donation of geraniol and Professor Tadahiro Kato for providing the ^1H NMR spectrum and a sample of diol B16. The cooperation of the National Science Foundation Regional Nuclear Magnetic Resonance Center is gratefully acknowledged. We are indebted to the National Institutes of Health for support of this work through a research grant (National Institute of General Medical Sciences Grant GM 29475).

The Synthesis of Cembranolide Precursors via Addition of Allylstannanes to Conjugated Aldehydes

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The Lewis acid promoted addition of functionalized allylstannanes **A9**, **C10**, and **C11** to a variety of conjugated aldehydes was examined as a possible route to acyclic precursors of macrocyclic diterpenoids. Additions to crotonaldehyde proceeded as expected, giving the erythro adduct **1** with BF_3 catalysis and the threo adduct **2** with a premixed $TiCl_4$–stannane complex at −78 °C. Attempted additions of allylstannanes to the β-substituted crotonaldehydes **B5** and geranial (**B6**), on the other hand, failed completely, giving either recovered starting material at low temperature (−78 to −30 °C) or extensive decomposition at higher temperatures. The acetylenic aldehyde **A3** and the β-iodo-substituted crotonaldehyde **A7**, however, showed normal reactivity with allylstannanes affording adducts **3**–**14**. The steric course of these reactions was confirmed through conversion of the adducts **D3** and **D4** to the δ-lactones **D9** and **D10** via rhodium-catalyzed carbonylation and oxidation. These lactones showed ^1H NMR coupling patterns consistent with the assigned stereochemistry.

The coupling of allylstannanes with aldehydes has received considerable attention recently, much of which has focused on stereochemical and mechanistic aspects of the reaction.[1] Yamamoto's pioneering work showed that the

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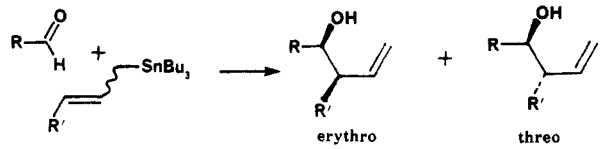
Table I. Additions of Allylstannanes to Conjugated Aldehydes



entry	RCHO	stannane	conditions[a]	product	yield, %[b]	erythro/threo
1	$CH_3CH{=}CHCHO$	**A9**	A	**1/2**	73	90:10[c,d]
2	$CH_3CH{=}CHCHO$	**A9**	B	**1/2**	47	5:95[c,d]
3	**B5**	**A9**	C		0	
4	**B6**	**A9**	C		0	
5	**A3**	**A9**	A	**3/4**	81	90:10[c,d]
6	**A3**	**A9**	B	**3/4**	60	5:95[c,d]
7	**A7**	**A9**	A	**5/6**	57	75:25[d]
8	**A3**	**C10**	D	**7/10**	81	75:25[d]
9	**A3**	**C11**	D	**8/11**	70	80:20[d]
10	**A3**	**C11**	A	**8/11**	78	85:15[d]
11	**A3a**[e]	**C10**	A	**9/12**	74	90:10[d]
12	**A7**	**C10**	A	**13/14**	74	70:30[d]
13	**B5**	**C10**	C		0	
14	**B6**	**C10**	C		0	
15	**D1**	**D2**	A	**D3/D4**	62	90:10[d]
16	**D1**	**D2**	B	**D3/D4**	50	5:95[d]
17	$CH_3C{\equiv}CCHO$	**A9**	A	**24/26**	82	88:12[c]
18	$CH_3CH{=}CHCHO$	**A9**	A	**1/2**	73	90:10[c]
19	$CH_3CH_2CH_2CHO$	**A9**	A	**25/27**	64	95:5[c]

[a] (A) 1.1 equiv of $BF_3{\cdot}OEt_2$ at −78 °C; (B) 1.1 equiv of $TiCl_4$ premixed with 1.0 equiv of stannane at −78 °C to which 1.0 equiv of aldehyde was added at −78 °C; (C) 2–10 equiv of $BF_3{\cdot}OEt_2$ at −78 to 0 °C; (D) 2.0 equiv of $BF_3{\cdot}OEt_2$ at −78 °C. [b] Isolated yield after purification via column chromatography on silica gel. [c] Analysis via glass capillary gas chromatography. [d] Analysis via integration of the 400-MHz ^1H NMR spectrum. [e] *tert*-Butyldiphenylsilyl analogue of **A3**.

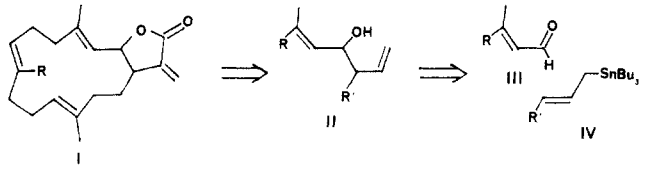
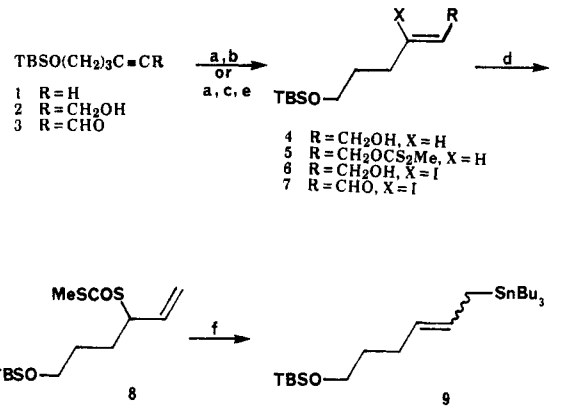


Figure 1. Retrosynthetic analysis of a cembranoid.

BF_3-catalyzed coupling affords mainly erythro[2] adducts independent of allyl double bond geometry.[3] Under thermal or hyperbaric conditions (*E*)-allylstannanes give mainly threo adducts while the *Z* isomers favor erythro. The difference has been ascribed to a chelated cyclic transition state in the latter case and an extended acyclic transition state in the former.[3] Keck found that $TiCl_4$-promoted reactions can be made to favor threo or erythro products by adjustments in stoichiometry and the order of mixing the three reaction partners.[4] An allyltitanium is postulated as the reactive species when a premixed excess of allylstannane and $TiCl_4$ is employed. In such cases, the product stereochemistry is consistent with a chelated cyclic transition state.

We were attracted to the possible coupling of allylstannanes such as IV with β-substituted crotonaldehydes III as a potential route to stereochemically defined homoallylic alcohols II envisioned as possible acyclic precursors of certain natural cembranolides I (Figure 1).[5] Owing to the small sampling of conjugated aldehydes and structurally complex allylstannanes employed by previous workers, we thought it wise to conduct preliminary studies with prototypes of our chosen synthons in order to optimize reaction conditions and stereochemistry. In the course of these studies we encountered some unexpected reactivity patterns which necessitated a modification of our synthetic plan.

Scheme I. Series A Compounds[a,b]



[a] (a) *n*-BuLi, $(CH_2O)_n$, THF (86%); (b) $NaAlH_2(OCH_2CH_2OEt)_2$, THF, 0 °C (77%); (c) $NaAlH_2(OCH_2CH_2OEt)_2$, THF, 0 °C; I_2, THF (72%); (d) NaH, CS_2, MeI, C_6H_6 (73%); (e) MnO_2, CH_2Cl_2 (92%); (f) Bu_3SnH, $Me_2C(CN)N{=}NC(CN)Me_2$, C_6H_6 (89%). [b] TBS = *tert*-$BuSiMe_2$.

Our first studies were conducted with allylstannane **A9**, a mixture of *E* and *Z* isomers, prepared as shown in Scheme I.[6,7] The BF_3-promoted coupling of this allyl-

(1) Cf.: Denmark, S. E.; Weber, E. J. *J. Am. Chem. Soc.* **1984**, *106*, 7970. Jephcote, V. J.; Pratt, A. J.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1984**, 800. Otera, J.; Kawasaki, Y.; Mizuno, H.; Shimizu, Y. *Chem. Lett.* **1983**, 1529. Keck, G. E.; Abbott, D. E. *Tetrahedron Lett.* **1984**, *25*, 1883. Keck, G. E.; Boden, E. P. *Tetrahedron Lett.* **1984**, *25*, 1879, 265.

(2) The convention of Heathcock is employed whereby that isomer with adjacent syn substituents in the conformer having the "backbone" of the condensation in the extended zig-zag arrangement is designated erythro. Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066.

(3) Cf.: Yamamoto, Y.; Yatagai, H.; Ishihara, Y.; Maeda, N.; Maruyama, K. *Tetrahedron* **1984**, *40*, 2239.

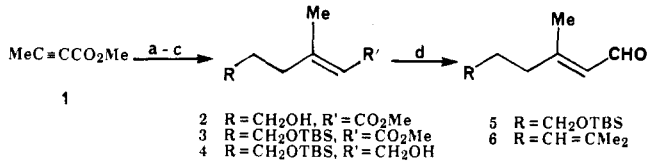
(4) Keck, G. E.; Abbott, D. E.; Boden, E. P.; Enholm, E. J. *Tetrahedron Lett.* **1984**, *25*, 3927.

(5) Both cis- and trans-fused γ-lactones have been isolated from natural sources. Cf.: Weinheimer, A. J.; Chang, C. W. J.; Matson, J. A. *Fortschr. Chem. Org. Naturst.* **1979**, *36*, 286.

(6) 4-Pentyn-1-ol is available from Farchan Laboratories, Inc., Gainesville, FL.

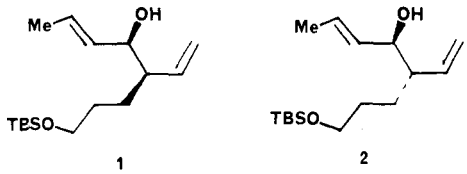
(7) Ueno, Y.; Sano, H.; Okawara, M. *Tetrahedron Lett.* **1980**, *21*, 1767.

Scheme II. Series B Compounds[a,b]



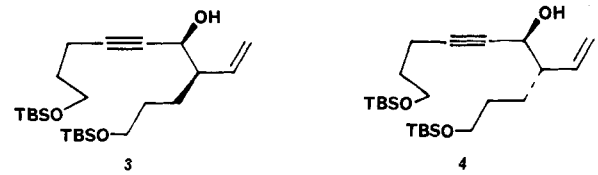
[a] (a) $ClMg(CH_2)_3OMgCl$, CuI, Me_2S, THF, −78 °C; (b) TBSCl, Et_3N, 4-$(Me_2N)C_5H_4N$, CH_2Cl_2; (c) $(i\text{-Bu})_2AlH$, CH_2Cl_2; (d) MnO_2, CH_2Cl_2. [b]TBS = *tert*-$BuSiMe_2$.

stannane mixture with crotonaldehyde at −78 °C along the lines of Yamamoto[3] led to a 90:10 mixture of (presumed) erythro and threo[2] allylic alcohols **1** and **2** in 73% yield. This same coupling could also be effected by ethylaluminum dichloride with comparable stereoselectivity but in somewhat lower yield. With $TiCl_4$ as the catalyst, in a modified Keck procedure,[4] a 5:95 mixture of **1** and **2** was obtained in 47% yield (Table I, entries 1 and 2).



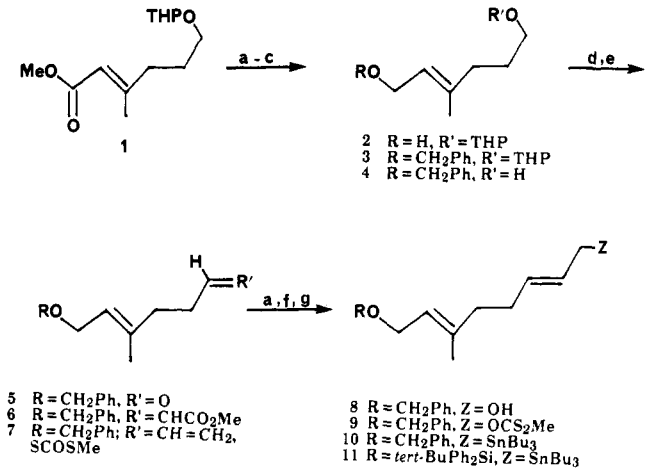
We next examined the coupling of stannane **A9** with aldehyde **B5**, prepared via addition of a Normant-type 3-(hydroxypropyl)copper reagent[8] to methyl tetrolate (**B1**) followed by alcohol protection, ester reduction, and MnO_2 or Swern oxidation[9] (Scheme II). To our surprise and dismay, we were unable to effect this coupling despite numerous and varied attempts. TLC monitoring from −78 to 0 °C indicated that no reaction occurred below −30 °C whereas between −30 and 0 °C extensive decomposition took place. Suspecting interference by the OTBS grouping of aldehyde **B5**, we substituted geranial (**B6**)[10] in its place, but to no avail. The same reactivity pattern was observed (Table I, entries 3 and 4).

Considering the contrasting behavior of crotonaldehyde vs. the geranyl systems **B5** and **B6**, we speculated that the additional β-substituent of the latter two aldehydes was somehow responsible for their diminished reactivity. This line of reasoning led us to examine the propargylic aldehyde **A3** (secured via MnO_2 oxidation of alcohol **A2**) as a coupling partner for **A9**. The results were highly encouraging. A 90:10 mixture of (presumed) erythro and threo[2] alcohols **3** and **4** was obtained in 81% yield with 1.1 equiv of $BF_3{\cdot}OEt_2$ at −78 °C. With 1.1 equiv of premixed $TiCl_4$ and allylstannane **A9**, a 5:95 mixture of **3** and **4** was isolated in 60% yield (Table I, entries 5 and 6).

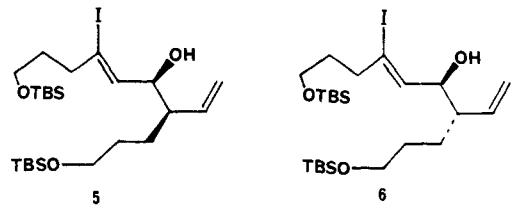


The β-iodo unsaturated aldehyde **A7** (prepared by reducing propargylic alcohol **A2** with Red-Al, quenching with iodine, and subsequent MnO_2 oxidation) also proved suitable as a coupling partner for allylstannane **A9**. Under BF_3 catalysis a 75:25 mixture of (presumed) erythro and threo[2] adducts **5** and **6** was obtained in 57% yield (Table I, entry 7).

Scheme III. Series C Compounds[a,b]

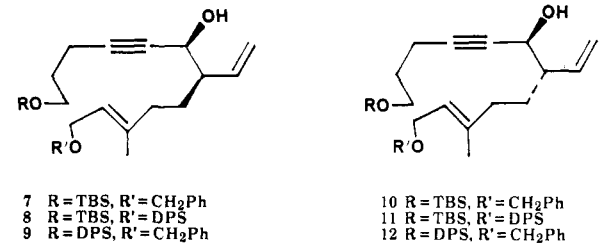


[a] (a) $(i\text{-Bu})_2AlH$, CH_2Cl_2, −78 °C (100%); (b) $PhCH_2Br$, NaH, THF (88%) or *t*-$BuPh_2SiCl$, Et_3N, 4-$(Me_2N)C_5H_4N$, CH_2Cl_2 (90%); (c) AG 50W-X8 H^+ resin, MeOH (100%); (d) $(COCl)_2$, Me_2SO, Et_3N, CH_2Cl_2 (100%); (e) $Ph_3P{=}CHCO_2Me$, CH_2Cl_2 (71%); (f) NaH, CS_2, MeI, C_6H_6 (70%); (g) Bu_3SnH, $Me_2C(CN)$-N=NC(CN)Me_2, C_6H_6 (98%). [b]THP = 2-tetrahydropyranyl.



With these promising results we turned to allylstannanes more closely related to our intended application. To that end, an *E*/*Z* mixture of stannane **C10** was prepared as shown in Scheme III from the THP derivative (**C1**) of hydroxy ester **B2**. The analogous sequence of steps was used to convert alcohol **C2** to the *tert*-butyldiphenylsilyl-protected stannane **C11**, as a similar *E* and *Z* mixture.

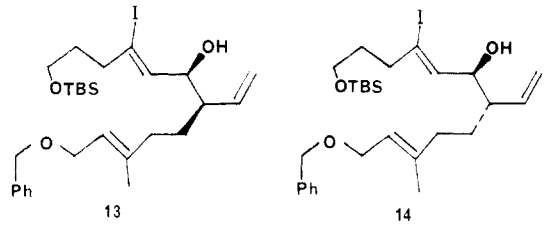
Addition of the benzyloxy allylstannane **C10** to acetylenic aldehyde **A3** afforded a 75:25 mixture of (presumed) erythro and threo[2] alcohols **7** and **10** with 2.0 equiv of $BF_3{\cdot}OEt_2$ at −78 °C. The silyloxystannane **C11** gave an 80:20 mixture of the analogous alcohols **8** and **11** when 2.0 equiv of catalyst was used and an 85:15 mixture with 1.1 equivs (Table I, entries 8–10). Our best result in this series was obtained with the *tert*-butyldiphenylsilyl analogue of acetylenic aldehyde **A3** which gave a 90:10 mixture of (presumed) erythro and threo[2] products **9** and **12** in 71% yield with stannane **C10** (Table I, entry 11).



The β-iodo unsaturated aldehyde **A7** also condensed with allylstannane **C10** under BF_3 catalysis giving a 70:30 mixture of (presumed) erythro and threo[2] alcohols **13** and **14** in 74% yield (Table I, entry 12). Neither **C10** nor **C11** gave any identifiable product with the β-methyl substi-

(8) Cahiez, G.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1978**, 3013.
(9) Omura, K.; Swern, D. *Tetrahedron* **1978**, 1651.
(10) Cf.: Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.

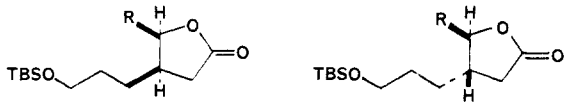
tuted enals **B5** or **B6** under a variety of conditions as previously described for **A9**.



13 14

Throughout these studies we have assumed that BF_3-catalyzed reactions afford mainly erythro products while premixed $TiCl_4$–stannane couplings give predominantly threo products. These assumptions follow from the prior work of Yamamoto[3] and Keck.[4] However, virtually all previous examples involve simple crotylstannanes whereas ours employ ω-functionalized, alkyl-substituted crotylstannanes. While the extrapolation is mechanistically defensible on simple steric grounds,[3] we were unable to discount possible interactive forces, such as internal chelation, that might invalidate the analogy. Hence we sought independent proof of stereochemistry.

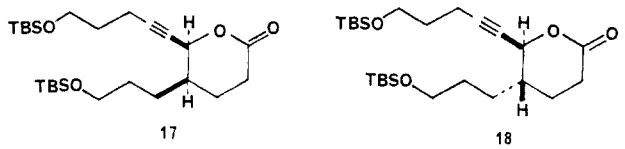
Our first efforts in this direction involved oxidation of alcohols **1** and **2** to the γ-lactones **15** and **16**.[11] Unfortunately, the two isomers showed no differences in their carbinyl coupling patterns, even at 400 MHz.[12]



15 16

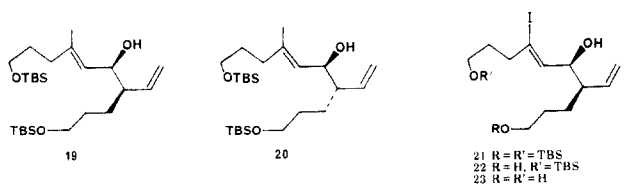
R = *trans*-$CH_3CH=CH$

We next considered preparing the δ-lactones **17** and **18** via carbonylation–oxidation according to the recent procedure of Wuts.[13] Experience has shown such lactones to give distinctive and structurally characteristic ^1H NMR spectra.[14] However, alkynol **3**, when subjected to the Wuts



17 18

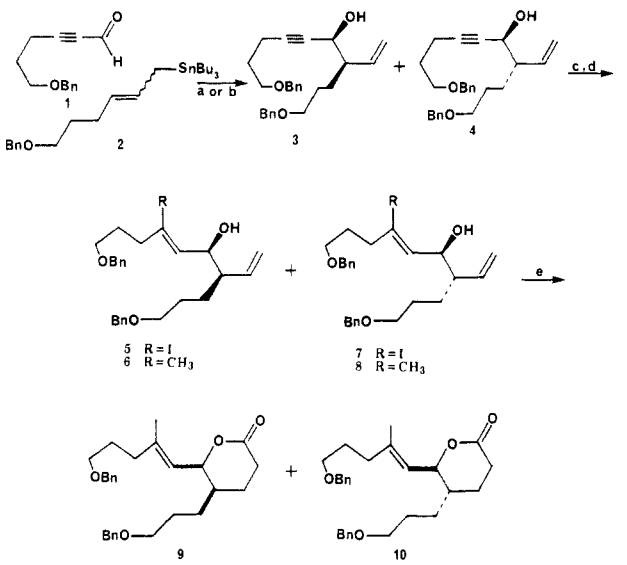
carbonylation conditions,[13] afforded a complex mixture of products. Suspecting involvement of the alkyne moiety, we decided to prepare allylic alcohols **19** and **20** through the reduction–iodination–methylation sequence devised by Corey.[15] It was hoped that the trisubstituted double bond of these alcohols would not interfere with the carbonylation reaction.



19 20

21 R = R' = TBS
22 R = H, R' = TBS
23 R = R' = H

Scheme IV. Series D Compounds[a,b]



[a] (a) $BF_3 \cdot OEt_2$, CH_2Cl_2, −78 °C (59%); (b) $TiCl_4$, CH_2Cl_2, −78 °C (50%); (c) $Na(MeOCH_2CH_2O)_2AlH_2$, 0 to 25 °C; I_2, −78 to 0 °C, THF; **5** (80%), **7** (64%); (d) $LiMe_2Cu$, Et_2O, 0 °C, MeI; **6** (91%), **8** (98%); (e) $[Rh(OAc)_2]_2$, Ph_3P, EtOAc, 1:1 CO/H_2 350 psi, 100 °C; $C_5H_5NHCrO_3Cl$, CH_2Cl_2; **9** (68%), **10** (73%). [b] Bn = CH_2Ph.

Treatment of alkynol **3** with Red-Al in ether–toluene followed by addition of iodine gave the desired vinyl iodide **21**, but the reaction was sluggish and the TBS-cleaved diol **22** was formed as a major byproduct.[16] Under forcing conditions, the reaction was complete, but then the major product was the highly polar and difficult to manage triol **23**. An in situ resilylation procedure was developed but the overall efficiency was low (40–50%). Similar results were obtained when lithium aluminum hydride was employed as the reducing agent.[16]

To alleviate the unwanted and detrimental TBS cleavage, we turned to the benzyl group as protection for our terminal hydroxyl functions. Accordingly, aldehyde **D1** was prepared from benzyl 4-pentynyl ether[6] via formylation and subsequent oxidation (Scheme IV). Allylstannane **D2** was secured from the same formylation product along the lines of Chart A.[7]

The coupling of aldehyde **D1** with allylstannane **D2** closely paralleled the silylated analogues; $BF_3 \cdot OEt_2$ afforded a 90:10 mixture and the premixed $TiCl_4$–stannane complex gave a 5:95 mixture of the (presumed) erythro and threo[2] products **D3** and **D4**. The unstable vinyl iodides **D5** and **D7** were prepared without incident via treatment of alkynols **D3** and **D4** with Red-Al followed by I_2 trapping. Coupling of these iodides with lithium dimethylcuprate[15] proceeded cleanly and efficiently to yield the desired methylated olefins **D6** and **D8**. These olefins were smoothly carbonylated via the Wuts procedure[13] to the corresponding lactols which were oxidized with buffered PCC to lactones **D9** and **D10**. The carbinyl proton of the former showed coupling of 9 Hz with its vinyl proton neighbor and 3 Hz with its ring proton neighbor, consistent with cis stereochemistry, whereas the carbinyl proton of **D10** showed 9 Hz coupling to both neighboring protons in keeping with the assigned trans stereochemistry. Thus

(11) A multistep sequence was employed involving (i) acetylation; (ii) selective hydroboration–oxidation (H_2O_2, NaOH); (iii) Swern oxidation; and (iv) Ag_2O oxidation. DeHoff, B., unpublished results.

(12) The carbinyl protons of **15** and **16** appeared at 4.90 and 4.40 ppm both as triplets with J = 6 Hz.

(13) Wuts, P. G. M.; Obrzut, M. L.; Thompson, P. A. *Tetrahedron Lett.* **1984**, *25*, 4051.

(14) Cf.: Marshall, J. A.; Coghlan, M. J.; Watanabe, M. *J. Org. Chem.* **1984**, *49*, 747. Pirkle, W. H.; Adams, P. E. *J. Org. Chem.* **1980**, *45*, 4117.

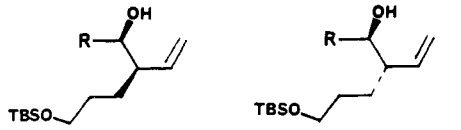
(15) Corey, E. J.; Katzenellenbogen, J. A.; Posner, G. H. *J. Am. Chem. Soc.* **1967**, *89*, 4245. Corey, E. J.; Posner, G. H. *J. Am. Chem. Soc.* **1968**, *90*, 5615.

(16) Metal hydride cleavages of silyl ethers with γ-alcohol substituents have been previously reported. Ziegler, F. E.; Klein, S. I.; Pati, U. K.; Wang, T.-F. *J. Am. Chem. Soc.* **1985**, *107*, 2730. Martinez, G.; Grieco, P. A.; Williams, E.; Kanai, K.; Srinivasan, C. V. *J. Am. Chem. Soc.* **1982**, *104*, 1436. It seems unlikely that intramolecular processes, as postulated for these cleavages, can account for the present observations.

allylstannane **D2** and alkynal **D1** react in the same stereochemical sense as their crotyl analogues. We assume that allylstannanes **A9**, **C10**, and **C11** follow suit.

The failure of β-substituted crotonaldehydes such as **B5** and **B6** to give coupling products is noteworthy. The diminished reactivity of such aldehydes may reflect added hyperconjugative electron release to the carbonyl grouping from the additional β-alkyl substituent. This effect would be absent in the β-iodo aldehyde **A7**. In any case, the Corey sequence[15] allows propargylic aldehydes to be used as synthetic equivalents of unreactive β-alkyl crotonaldehydes such as **B5**, thereby permitting the stereocontrolled synthesis of acyclic isoprenoid precursors of macrocyclic terpenoids, as desired.

Throughout these studies we observed erythro–threo selectivities in the range of 85:15 to 90:10 with propargylic aldehydes using $BF_3{\cdot}OEt_2$ as the catalyst. Most previous studies have employed saturated aliphatic aldehydes or benzaldehyde,[1,3,4] so as a matter of interest, we wished to examine the effect of changing hybridization of the aldehyde substituent on the stereoselectivity of the coupling reaction. Accordingly, the addition of allylstannane **A9** to 2-butynal, *trans*-2-butenal, and butanal was effected under the standard BF_3 conditions, and the products were analyzed by glass capillary gas chromatography (Table I, entries 17–19). It can be seen that the saturated aldehyde,



24 R = $CH_3C{\equiv}C$ **26** R = $CH_3C{\equiv}C$
1 R = $CH_3CH{=}CH$ **2** R = $CH_3CH{=}CH$
25 R = $CH_3CH_2CH_2$ **27** R = $CH_3CH_2CH_2$

butanal, shows a slightly greater erythro selectivity (~20:1 vs. 9:1) over its olefinic and acetylenic counterparts but at some sacrifice in yield. The differences in stereoselectivity may result from simple steric considerations[3,4] whereas the diminished yields possibly reflect the greater tendency of butanal and butenal to participate in side reactions such as aldol condensation and Michael addition.

Experimental Section

The apparatus and methods described by G. W. Kramer, M. M. Midland, and A. B. Levy[17] were used to maintain an argon or nitrogen atmosphere in the reaction flask. Anhydrous solvents were obtained by distillation from sodium benzophenone ketyl (diethyl ether, tetrahydrofuran), calcium hydride (dichloromethane), or sodium (benzene). Carbon disulfide was distilled from calcium chloride, and iodomethane was distilled from copper wire. Infrared absorption maxima are reported in wavenumbers (cm^{-1}). Proton magnetic resonance samples were prepared as dilute solutions in deuteriochloroform ($CDCl_3$). Chemical shifts (δ) are reported downfield from tetramethylsilane (Me_4Si), in parts per million (ppm) of the applied field. Peak multiplicities are abbreviated: singlet, s; doublet, d; triplet, t; quartet, q; pentuplet, p; envelope, e; multiplet, m. Coupling constants (*J*) are reported in hertz (Hz). Glass capillary gas chromatography was performed on a Superox 4 25M column. Combustion microanalyses were performed by Atlantic Laboratories, Atlanta, GA. Analytical thin-layer chromatography (TLC) was routinely used to monitor reactions. Plates precoated with E. Merck silica gel 60 F254 of 0.25-mm thickness, supplied by Brinkmann Instruments, were used. E. Merck silica gel 60 (230–400 ASTM mesh) was employed for column chromatography according to the procedure of Still.[18]

4-Pentynyl *tert*-Butyldimethylsilyl Ether (A1). To a solution of 3.45 g (41 mmol) of 4-pentyn-1-ol[6] in 50 mL of CH_2Cl_2 were added 12.8 mL (92 mmol) of triethylamine, 6.9 g (46 mmol) of *tert*-butyldimethylsilyl chloride, and a catalytic amount of 4-(dimethylamino)pyridine. The resulting mixture was stirred for 6 h at room temperature and then poured into 50 mL of 2% HCl and 50 mL of CH_2Cl_2. The organic layer was washed with water, and the combined aqueous layers were extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to 7.5 g (92%) of a yellow oil, which was used without further purification: IR (film) ν 3290, 2940, 2920, 2875, 2840, 2110, 1470, 1255, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.01 (s, CH_3Si), 0.85 (s, *tert*-butyl), 1.7 (m, CH_2CH_2O), 1.87 (t, J = 2 Hz, acetylenic H), 2.23 (d of t, J = 7.2 Hz, propargylic CH_2), 3.65 (t, J = 6 Hz, CH_2O).

6-[(*tert*-Butyldimethylsilyl)oxy]-2-hexyn-1-ol (A2). To a solution of 7.5 g (37.8 mmol) of the acetylene **A1** in 50 mL of dry THF at −78 °C under argon was added 16.7 mL of 2.4 M *n*-BuLi in hexane. The resulting yellow solution was stirred for 1 h at −78 °C and then 1.8 g (60.5 mmol) of paraformaldehyde was added. The resulting mixture was allowed to warm slowly to room temperature with stirring overnight. The reaction was quenched with saturated NH_4Cl and extracted twice with ether. The ether extracts were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to a yellow oil. Purification by chromatography on silica gel (20% ether–hexanes) afforded 7.4 g (86%) of a pale yellow oil: IR (film) ν 3340, 2940, 2880, 2850, 1480, 1270, 1115 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.04 (s, CH_3Si), 0.89 (s, *tert*-butyl), 1.63 (p, J = 6 Hz, $CH_2CH_2CH_2$), 1.97 (t, J = 6 Hz, OH), 2.17–2.3 (m, propargylic CH_2), 3.66 (t, J = 6 Hz, CH_2OSi), 4.13–4.2 (m, CH_2OH). Anal. Calcd for $C_{12}H_{24}O_2Si$: C, 63.10; H, 10.59. Found: C, 63.13; H, 10.61.

6-[(*tert*-Butyldimethylsilyl)oxy]-2-hexynal (A3). A slurry of 1.16 g (5.08 mmol) of propargylic alcohol **A2** and 3.5 g (40.2 mmol) of freshly prepared MnO_2 in 15 mL of CH_2Cl_2 was stirred overnight at room temperature. The mixture was filtered through a pad of Celite with the aid of ether. The filtrate was concentrated under reduced pressure affording 1.05 g (91%) of a pale yellow oil, which was used without further purification: IR (film) ν 2950, 2925, 2880, 2850, 2285, 2210, 1675, 1480, 1495, 1265, 1145, 1110, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.03 (s, CH_3Si), 0.88 (s, *tert*-butyl), 1.73 (p, J = 6 Hz, $CH_2CH_2CH_2$), 2.49 (t, J = 6 Hz, propargylic CH_2), 3.65 (t, J = 6 Hz, CH_2O), 9.12 (s, aldehyde H).

(*E*)-6-[(*tert*-Butyldimethylsilyl)oxy]-2-penten-1-ol (A4). To a solution of 16.4 g (71.7 mmol) of acetylenic alcohol **A2** in 100 mL of dry THF at −10 °C under argon was added 33.7 mL of 3.4 M Red-Al in toluene dropwise. The resulting solution was stirred overnight at 0 °C, and then 250 mL of saturated sodium potassium tartrate (Rochelle's salt) was added. The clear organic layer was washed with saturated Rochelle's salt, and the combined aqueous layers were extracted with ether. The ether layers were dried over anhydrous $MgSO_4$ and concentrated to a yellow oil. Purification by chromatography on silica gel (20% ether–hexanes), yielded 12.7 g (77%) of allylic alcohol **A4**: IR (film) ν 3325, 2950, 2925, 2875, 2850, 1670, 1475, 1460, 1260, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.05 (s, CH_3Si), 0.80 (s, *tert*-butyl), 1.5–1.8 (m, H-5, OH), 2.02–2.26 (m, propargylic CH_2), 3.59 (t, J = 6 Hz, CH_2OSi), 4.08 (d, J = 4 Hz, CH_2OH), 5.60–5.75 (m, vinyl H's). Anal. Calcd for $C_{12}H_{26}O_2Si$: C, 62.55; H, 11.37. Found: C, 62.67; H, 11.38.

(*Z*)-3-Iodo-6-[(*tert*-butyldimethylsilyl)oxy]-2-hexen-1-ol (A6). To a solution of 910 mg (3.98 mmol) of propargylic alcohol **A2** in 10 mL of dry THF at 0 °C was added 1.9 mL of 3.4 M Red-Al in toluene dropwise. The resulting solution was stirred overnight at 0 °C and then cooled to −78 °C, and 1.9 g (7.56 mmol) of iodine in 5 mL of THF was added. The resulting dark mixture was warmed to 0 °C and quenched with 50 mL of saturated Rochelle's salt. The aqueous layer was extracted with ether, and the combined ether layers were successively washed with saturated Rochelle's salt, saturated $Na_2S_2O_3$ and water. The organic layer was dried over anhydrous $MgSO_4$ and concentrated to an oil. The oil was purified by chromatography on silica gel (15% ether–hexanes), giving 1.1 g (78%) of pale yellow iodide **A6**: IR (film) ν 3325, 2950, 2925, 2885, 2855, 1645, 1480, 1265, 1115, 845, 785 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.01 (s, CH_3Si), 0.85 (s, *tert*-butyl), 1.53–1.87 (m, $CH_2CH_2CH_2$, OH), 2.56 (br t, J = 7 Hz, allylic CH_2), 3.57 (t, J = 6 Hz, CH_2OSi), 4.16 (br d, J = 6 Hz, CH_2OH), 5.84 (t, t, J = 6, 1 Hz, vinyl H); MS, calcd for $C_{12}H_{25}O_2ISi$ m/e 356.3. Found m/e (M^+ − $C(CH_3)_3$ 299. Anal. Calcd for

(17) Brown, H. C. "Organic Syntheses via Boranes"; Wiley: New York, 1975; pp 191–202.
(18) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

$C_{12}H_{25}O_2ISi$: C, 40.45; H, 7.07. Found: C, 40.54; H, 7.12.

(*Z*)-3-Iodo-6-[(*tert*-butyldimethylsilyl)oxy]-2-hexenal (A7). A mixture of 1.0 g (2.8 mmol) of allylic alcohol **A6** and 3.0 g (34.5 mmol) of freshly prepared MnO_2 in 10 mL of CH_2Cl_2 was stirred overnight. The mixture was filtered through a pad of Celite with the aid of ether. The filtrate was concentrated under reduced pressure to afford 810 mg (81%) of the aldehyde as a yellow oil: IR (film) ν 2945, 2925, 2880, 2850, 1685, 1605, 1260, 1110, 840, 780 cm^{-1}; ^1H NMR ($CDCl_3$) 0.04 (s, CH_3Si), 0.89 (s, *tert*-butyl), 1.79 (p, J = 6 Hz, $CH_2CH_2CH_2$), 2.85 (br t, J = 7 Hz, allylic CH_2), 3.61 (t, J = 6 Hz, CH_2OSi), 6.19 (br d, J = 6 Hz, vinyl H), 9.55 (d, J = 6 Hz, aldehyde H). This material was used without further purification.

Methyl 4-[(*tert*-Butyldimethylsilyl)oxy]-1-vinylbutyl Dithiocarbonate (A8). A slurry of 96 mg (4.0 mmol) of NaH in 15 mL of benzene was stirred at room temperature while 715 mg (3.16 mmol) of allylic alcohol **A4** in 3 mL of benzene was added. The resulting mixture was heated in reflux for 1 h and then cooled to 0 °C, and 0.24 mL (4.0 mmol) of CS_2 was added. The reaction was stirred for 12 h at room temperature, and then 0.28 mL (4.5 mmol) of CH_3I was added. The mixture was stirred for 2 h at room temperature then heated to reflux for 2 h. The reaction mixture was poured into water and extracted twice with ether. The organic layer was dried over anhydrous $MgSO_4$ and the solvent was removed by rotary evaporation. The orange oil was purified by chromatography on silica gel (5% ether–hexanes), providing 714 mg (73%) of dithiocarbonate **A8**: IR (film) ν 2950, 2925, 2880, 2855, 1650, 1480, 1265, 1110, 870, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.06 (s, CH_3Si), 0.90 (s, *tert*-butyl), 1.56–1.76 (m, CH_2CH_2), 2.41 (s, CH_3S), 3.62 (t, J = 6 Hz, CH_2OSi), 4.07–4.33 (m, H-1), 5.01–5.36 (m, $CH{=}CH_2$), 5.60–5.97 (m, $CH{=}CH_2$). Anal. Calcd for $C_{14}H_{28}O_2S_2Si$: C, 52.45; H, 8.80. Found: C, 52.55; H, 8.89.

(*E*,*Z*)-6-(Tri-*n*-butylstannyl)-4-hexenyl *tert*-Butyldimethylsilyl Ether (A9). A solution of 778 mg (2.4 mmol) of dithiocarbonate **A8**, 0.75 mL (2.8 mmol) of tri-*n*-butyltin hydride, and a catalytic amount of AIBN in 10 mL of benzene was heated to reflux for 3 h whereupon the solution faded from yellow to clear. The benzene was removed, and the oil was purified by chromatography on deactivated silica gel (4% triethylamine–hexane) with hexane as the eluant, affording 1.07 g (89%) of allylstannane **A9**: IR (film) ν 3000, 2950, 2920, 2850, 1650, 1470, 1260, 1110, 845, 780 cm^{-1}; ^1H NMR δ 0.08 (s, CH_3Si), 0.75–1.05 (m, CH_3CH_2), 0.92 (s, *tert*-butyl), 1.05–1.82 (m, CH_2's), 1.82–2.20 (m, allylic CH_2), 3.62, 3.65 (t, J = 6 Hz, CH_2OSi of *E* and *Z* isomers), 4.82–5.81 (m, vinyl H). Anal. Calcd for $C_{24}H_{52}OSiSn$: C, 57.26; H, 10.41. Found: C, 57.45; H, 10.37.

Methyl (*E*)-3-Methyl-6-hydroxy-2-hexenoate (B2). To a solution of 11.04 g (57.9 mmol) of CuI in 200 mL of dry THF and 10 mL of Me_2S at −78 °C under an argon atmosphere was added 290 mL of 0.2 M Grignard reagent in tetrahydrofuran. The Grignard reagent was prepared by deprotonating 3-chloro-1-propanol with isopropylmagnesium chloride (1.0 mol equival of a 2.0 M solution in THF) and treating the resultant alkoxide with 1.5 mol equiv of Mg powder in THF.[8] The resulting yellow mixture was stirred 30 min at −78 °C then 5.6 g (58 mmol) of methyl tetrolate (**B1**) in 10 mL of dry THF was added dropwise. The resulting slurry was stirred at −78 °C for 3 h and then quenched with 100 mL of saturated NH_4Cl and 50 mL of 3% aqueous NH_4OH. After warming to room temperature, the mixture was extracted with ether. The combined organic layers were washed with 3% NH_4OH until the washings were clear. The blue aqueous layers were combined and extracted two times with ether. The combined ether layers were washed with water, dried over anhydrous $MgSO_4$, and concentrated in vacuo to an oil, which was purified by bulb-to-bulb distillation (oven temperature, 95–105 °C (0.5 mm)), affording 6.5 g (90%) of clear oil: IR (film) ν 3410, 2945, 1725, 1650, 1445, 1235, 1160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.5–1.9 (m, CH_2CH_2O), 2.13 (d, J = 1 Hz, vinyl CH_3), 2.24 (t, J = 7 Hz, allylic CH_2), 3.5–3.75 (m, CH_2CH_2OH), 3.68 (s, OCH_3), 5.69 (t, J = 1 Hz, vinyl H). Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.78; H, 8.93.

Methyl (*E*)-3-Methyl-6-[(*tert*-butyldimethylsilyl)oxy]-2-hexenoate (B3). A solution of 160 mg (1.01 mmol) of alcohol **B2**, 182 mg (1.2 mmol) of *tert*-butyldimethylsilyl chloride, 0.33 mL (2.4 mmol) of triethylamine, and a catalytic amount of 4-(dimethylamino)pyridine in 4 mL of CH_2Cl_2 was stirred at room temperature for 4 h. The reaction was filtered through a short plug of silica gel and concentrated to 221 mg (80%) of silyl ether **B3**: IR (film) ν 2935, 2910, 2875, 2840, 1720, 1645, 1435, 1260, 1225, 1155 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.07 (s, CH_3Si), 0.91 (s, *tert*-butyl), 1.58–1.89 (m, CH_2), 2.17–2.38 (m, allylic CH_2), 2.29 (s, vinyl CH_3), 3.60 (t, J = 6 Hz, CH_2OSi), 3.65 (s, OCH_3), 5.63–5.72 (m, vinyl H).

(*E*)-3-Methyl-6-[(*tert*-butyldimethylsilyl)oxy]-2-hexen-1-ol (B4). A solution of 12.5 g (45.9 mmol) of ester **B3** in 60 mL of CH_2Cl_2 at −78 °C under argon was treated with 100 mL of 1 M DIBAH in hexane. The mixture was stirred for 30 min at −78 °C and then quenched with 10% aqueous NaOH. After warming to room temperature the layers were separated and the organic layer was washed with 10% aqueous NaOH. The combined aqueous layers were extracted with ether, and the ether layers were dried over anhydrous $MgSO_4$. Removal of solvent left an oil, which was purified by silica gel chromatography (20% ether–hexanes), affording 9.5 g (85%) of alcohol **B4** as a clear oil: IR (film) ν 3350, 2935, 2905, 2865, 2840, 1660, 1470, 1260, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.03 (s, CH_3Si), 0.90 (s, *tert*-butyl), 1.50–1.83 (m, CH_2, OH), 1.67 (s, vinyl CH_3), 1.98–2.20 (m, allylic CH_2), 3.56 (t, J = 6 Hz, CH_2OSi), 4.12 (d, J = 6 Hz, CH_2OH), 5.39 (br t, J = 8 Hz, vinyl H). Anal. Calcd for $C_{13}H_{28}O_2Si$: C, 63.87; H, 11.55. Found: C, 63.75; H, 11.50.

(*E*)-3-Methyl-6-[(*tert*-butyldimethylsilyl)oxy]-2-hexenal (B5). The procedure described for **A3** was followed using 2.4 g (9.8 mmol) of allylic alcohol **B4** and 10 g (115 mmol) of MnO_2 in 30 mL of CH_2Cl_2. After 16 h at ambient temperature the product was isolated as described, providing 2.1 g (88%) of a pale yellow oil, which was used without further purification: IR (film) ν 2940, 2910, 2870, 2840, 1675, 1260, 1105 cm^{-1}; ^1H NMR ($CHCl_3$) δ 0.04 (s, CH_3Si), 0.89 (s, *tert*-butyl), 1.50–1.85 (m, CH_2), 2.15 (s, vinyl CH_3), 2.14–2.37 (m, allylic CH_2), 3.59 (t, J = 6 Hz, CH_2OSi), 5.85 (br d, J = 8 Hz, vinyl H), 9.96 (d, J = 8 Hz, aldehyde H).

Methyl (*E*)-3-Methyl-6-(tetrahydropyranyloxy)-2-hexenoate (C1). A solution of 11.06 g (69.9 mmol) of alcohol **B2** and 12.8 mL of dihydropyran in 70 mL of CH_2Cl_2 containing a catalytic amount of pyridinium *p*-toluenesulfonate was stirred at room temperature overnight. The mixture was poured into 125 mL of ether and washed three times with 50% aqueous NaCl solution. The organic layer was dried and concentrated to 17.8 g (>100%) of a pale yellow oil: IR (film) ν 2925, 2845, 1718, 1655, 1438 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.4–2.0 (m, tetrahydropyranyl CH_2's), 2.19 (d, J = 1 Hz, vinyl CH_3), 2.27 (t, J = 7 Hz, allylic CH_2), 3.27–4.3 (carbinyl CH_2's), 4.57 (m, acetal H), 5.7 (t, J = 1 Hz, vinyl H). This material was used without further purification. The analytical sample was purified via flash chromatography on silica gel using 10% ether–hexanes as the eluant. Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.40; H, 9.15.

(*E*)-3-Methyl-6-(tetrahydropyranyloxy)-2-hexen-1-ol (C2). To a stirred solution of 17.77 g (73.3 mmol) of crude ester **C1** in 75 mL of hexane at −78 °C under argon was added 150 mL of 1 M DIBAH in CH_2Cl_2. The resulting solution was stirred 15 min at −78 °C and then quenched with 200 mL of 10% aqueous NaOH. The mixture was warmed to room temperature, and the layers were separated. The organic layer was washed with 10% aqueous NaOH and the combined aqueous layers were extracted with ether. The organic layers were combined, washed with saturated aqueous NaCl and dried over anhydrous $MgSO_4$. Removal of solvent left 15.6 g (100%) of a cloudy oil: IR (film) ν 3375, 2925, 2850, 1665, 1455, 1440, 1140, 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27–1.8 (m, tetrahydropyranyl CH_2's), 1.67 (d, J = 1 Hz, vinyl CH_3), 2.10 (t, J = 7 Hz, allylic CH_2), 3.2–4.0 (m, carbinyl CH_2's), 4.11 (t, J = 6 Hz, CH_2OH), 4.53 (m, acetal H), 5.40 (t of t, J = 7, 1 Hz, vinyl H). This material was used without further purification. The analytical sample was prepared by flash chromatography on silica gel using 25% ether–hexanes as the eluant. Anal. Calcd for $C_{12}H_{21}O_3$: C, 67.26; H, 10.35. Found: C, 67.33; H, 10.37.

(*E*)-3-Methyl-6-(tetrahydropyranyloxy)-2-hexenyl Benzyl Ether (C3). A slurry of 120 mg (5.0 mmol) of NaH in 5 mL of THF was stirred at room temperature, while 839 mg (3.9 mmol) of alcohol **C2** in 2 mL of THF was added. The resulting mixture was stirred at room temperature for 2 h, and then 0.54 mL (4.5 mmol) of benzyl bromide was added neat. The resulting slurry was stirred overnight. The mixture was poured into 25 mL of

water and 30 mL of ether. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were washed with water and dried over anhydrous $MgSO_4$. Removal of solvent left an oil, which was purified by flash chromatography on silica gel (10% ether–hexanes), affording 1.05 g (88%) of a clear oil: IR (film) ν 3060, 3025, 2930, 2850, 1665, 1500, 1460, 1445, 1210, 1145, 1130, 1080, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.37–1.8 (m, tetrahydropyranyl CH_2's), 2.11 (t, J = 7 Hz, allylic CH_2), 3.2–3.87 (m, carbinyl CH_2's), 4.01 (d, J = 6 Hz, CH_2OBz), 4.47 (s, benzylic CH_2), 4.54 (m, acetal H), 5.41 (t, J = 7 Hz, vinyl H), 7.32 (s, Ar). Anal. Calcd for $C_{19}H_{28}O_3$: C, 74.97; H, 9.27. Found: C, 74.89; H, 9.31.

(*E*)-4-Methyl-6-(benzyloxy)-4-hexen-1-ol (C4). A mixture of 2.56 g (8.4 mmol) of tetrahydropyranyl ether **C3** in 20 mL of methanol containing a catalytic amount of Bio Rad AG 50W-X8 acidic ion-exchange resin was stirred overnight. The resin was removed by filtration, and the filtrate was concentrated under reduced pressure to afford 1.85 g (100%) of a pale yellow oil: IR (film) ν 3400, 3060, 3040, 2940, 2860, 1675, 1465, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.64 (s, vinyl CH_3), 1.57–1.74 (m, CH_2CH_2OH), 2.14 (t, J = 7 Hz, allylic CH_2), 3.60 (t, J = 6 Hz, CH_2OH), 4.0 (d, J = 7 Hz, CH_2OBz), 4.50 (s, benzylic CH_2), 5.43 (t, J = 6 Hz, vinyl H), 7.33 (s, Ar). This material was used without further purification.

(*E*)-4-Methyl-6-(benzyloxy)-4-hexenal (C5). To a solution of 1.03 mL (11.7 mmol) of oxalyl chloride in 20 mL of CH_2Cl_2 at −78 °C under argon was added 1.7 mL (23.4 mmol) of dry Me_2SO. The resulting slurry was stirred for 5 min, and then 1.85 g (8.4 mmol) of alcohol **C4** was added in 3 mL of CH_2Cl_2. This mixture was stirred for 20 min at −78 °C, and then 5.8 mL (42.0 mmol) of triethylamine was added. The thick white mixture was warmed to 0 °C and poured into water and CH_2Cl_2. The organic layer was washed with 2% aqueous HCl, the aqueous layers were extracted with CH_2Cl_2, and the combined organic layers were washed with water and dried over anhydrous $MgSO_4$. Removal of solvent left 1.84 g (100%) of a pale yellow oil: IR (film) ν 3100, 3090, 2960, 2890, 2755, 1760, 1530, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.63 (s, vinyl CH_3), 2.2–2.66 (m, CH_2CH_2CHO), 4.01 (d, J = 7 Hz, CH_2OBz), 4.47 (s, benzylic CH_2), 5.40 (t, J = 7 Hz, vinyl H), 7.29 (s, Ar), 9.75 (t, J = 1 Hz, aldehyde H). This material was used without further purification.

Methyl (*E*,*E*)-6-Methyl-8-(benzyloxy)-2,6-octadienoate (C6). A solution of 1.8 g (8.4 mmol) of crude aldehyde **C5** and 4.0 g (11.9 mmol) of methyl (triphenylphosphorylidene)acetate in 15 mL of CH_2Cl_2 was stirred overnight at room temperature. The mixture was concentrated, and the oil was triturated with two 50-mL portions of hexane. The precipitated triphenylphosphine oxide was removed by filtration, and the filtrate was concentrated to an oil, which was purified by column chromatography on silica gel (5% ethyl acetate–hexane), yielding 1.66 g (71%) of a clear oil: IR (film) ν 3060, 3025, 2945, 2850, 1725, 1660, 1460, 1440, 1280, 1215, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.64 (s, vinyl CH_3), 2.0–2.45 (m, allylic CH_2's), 3.69 (s, OCH_3), 4.02 (d, J = 7 Hz, CH_2OBz), 4.48 (s, benzylic CH_2), 5.40 (t, J = 7 Hz, H-7), 5.79 (d, J = 16 Hz, H-2), 6.93 (dt, J = 16, 6 Hz, H-3), 7.33 (s, Ar). Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.42; H, 8.14.

Methyl (*E*)-4-Methyl-6-(benzyloxy)-1-vinyl-4-hexenyl Dithiocarbonate (C7). The procedure described for **A8** was employed with 177 mg (7.3 mmol) of NaH and 1.49 g (6.0 mmol) of alcohol **C8** in 15 mL of benzene followed by 0.42 mL (7.0 mmol) of CS_2 and 0.45 mL (7.0 mmol) of CH_3I. Column chromatography (silica gel, 5% ether–hexanes) afforded 1.42 g (70%) of a light yellow oil: IR (film) ν 3025, 2925, 2850, 1645, 1460, 1220, 1075, 870 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.5–1.9 (m, $CHCH_2CH_2$), 1.9–2.2 (m, allylic CH_2), 2.35 (s, CH_3S), 3.97 (d, J = 7 Hz, CH_2OBz), 4.17 (t, J = 8 Hz, H-1), 4.46 (s, benzylic CH_2), 5.0–5.32 (m, CH_2=CH), 5.37 (t, J = 7 Hz, H-5), 5.53–5.93 (m, CH_2=CH), 7.31 (s, Ar). Anal. Calcd for $C_{18}H_{24}O_2S_2$: C, 64.25; H, 7.19; S, 19.05. Found: C, 64.34; H, 7.22; S, 19.12.

(*E*,*E*)-6-Methyl-8-(benzyloxy)-2,6-octadien-1-ol (C8). To a solution of 1.66 g (6.0 mmol) of ester **C7** in 10 mL of hexane at −78 °C was added 15 mL of 1 M DIBAH in CH_2Cl_2. The resulting solution was stirred 15 min at −78 °C, and then 30 mL of 10% aqueous NaOH was added dropwise. The mixture was warmed to room temperature, and the layers were separated. The organic layer was washed with 10% aqueous NaOH, the combined aqueous layers were extracted with ether, and the combined ether layers were washed with water and then dried over anhydrous $MgSO_4$. Removal of solvent left 1.49 g (100%) of a pale yellow oil, which was used without further purification: IR (film) ν 3360, 3350, 3310, 2900, 2840, 1665, 1495, 1455, 1480, 1470, 1210 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.61 (s, vinyl CH_3), 2.0 (s, OH), 2.22 (s, allylic CH_2's), 3.80–4.20 (m, CH_2OBz, CH_2OH), 4.49 (s, benzylic CH_2), 5.37 (t, J = 7 Hz, H-7), 5.5–5.8 (m, H-2, H-3), 7.33 (s Ar).

[(6*E*)-6-Methyl-8-(benzyloxy)-2,6-octadienyl]tri-*n*-butylstannane (C10). A solution of 1.25 g (3.7 mmol) of dithiocarbonate **C7** and 1.1 mL (4 mmol) of tri-*n*-butyltin hydride in 10 mL of benzene containing a catalytic amount of AIBN was heated at reflux for 3 h. During this time the reaction solution faded from yellow to water white. Removal of solvent left an oil, which was purified by chromatography on deactivated silica gel (2% triethylamine–hexane) with hexane as the eluant yielding 1.9 g (98%) of a clear oil: IR (film) ν 2950, 2920, 1500, 1475, 1460, 1385, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.65–1.9 (m, CH_3CH_2), 1.0–1.8 (m, CH_2s), 1.54 (s, vinyl CH_3), 2.0–2.15 (m, allylic CH_2's), 4.05 (d, J = 7 Hz, CH_2OBz), 4.47 (s, benzylic CH_2), 4.9–5.2 (m, H-2, H-3), 5.40 (t, J = 7 Hz, H-7), 7.33 (s, Ar). Anal. Calcd for $C_{28}H_{48}OSn$: C, 64.75; H, 9.32. Found: C, 64.84; H, 9.33.

6-(Benzyloxy)-2-hexynal (D1). To a slurry of 1.68 g (70 mmol) of NaH in 50 mL of dry THF at room temperature was added 5.4 g (64 mmol) of 4-pentyn-1-ol.[6] The mixture was stirred for 4 h and then 7.9 mL (66 mmol) of benzyl bromide was added. The reaction was stirred overnight and quenched by pouring into saturated NH_4Cl. The layers were separated, and the aqueous layer was extracted with ether. The organic layers were dried over anhydrous $MgSO_4$ and concentrated to 11.15 g (100%) of a yellow oil, which was used without further purification: IR (film) ν 3265, 3055, 3035, 3005, 2930, 2840, 2100, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.68 (m, HC≡C, C≡CCH_2CH_2), 2.20–2.44 (m, propargylic CH_2), 3.57 (t, J = 7 Hz, CH_2OBn), 4.51 (s, benzylic CH_2), 7.35 (s, Ar).

The procedure described for **A2** was followed with 11.15 g (64 mmol) of the foregoing alkyne in 75 mL of dry THF at −78 °C to which 30 mL of 2.5 M *n*-BuLi in hexane and 3.07 g (102.4 mmol) of paraformaldehyde was added. Following workup and flash chromatography 9.8 g (75%) of propargylic alcohol was obtained as a clear oil: IR (film) ν 3380, 3050, 3020, 2915, 2850, 2220, 1460, 1370, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.68–1.97 (m, $CH_2CH_2CH_2$, OH), 2.20–2.47 (m, propargylic CH_2), 3.54 (t, J = 7 Hz, CH_2OBn), 4.11–4.30 (m, CH_2OH), 4.50 (s, benzylic CH_2), 7.34 (s, Ar). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.44; H, 7.94.

The procedure described for **A3** was followed with 1.6 g (7.79 mmol) of the foregoing propargylic alcohol and 7.0 g (80.5 mmol) of MnO_2 in 20 mL of CH_2Cl_2. Following workup, 1.4 g (90%) of aldehyde **D1** was obtained as a yellow oil. This material was used without further purification: IR (film) ν 3070, 3050, 3020, 2915, 2850, 2275, 2200, 1665, 1455, 1370, 1145, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.77–2.04 (p, J = 6 Hz, $CH_2CH_2CH_2$), 2.53 (t, J = 6 Hz, propargylic CH_2), 3.53 (t, J = 6 Hz, CH_2OBn), 4.50 (s, benzylic CH_2), 7.33 (s, Ar), 9.12 (s, aldehyde H).

(*E*,*Z*)-6-(Tri-*n*-butylstannyl)-4-hexenyl Benzyl Ether (D2). The procedure described for **A4** was followed. Addition of 3.0 g (14.6 mmol) of crude 6-(benzyloxy)-2-hexyn-1-ol in 15 mL of dry THF to 6.9 mL (23.5 mmol) of Red-Al in toluene at 0 °C followed by overnight stirring at room temperature and flash chromatography afforded 2.3 g (76%) of (*E*)-6-(benzyloxy)-2-hexen-1-ol: IR (film) ν 3360, 3020, 2925, 2850, 1455, 1370, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40–1.87 (m, $CH_2CH_2CH_2O$, OH), 2.00–2.27 (m, allylic CH_2), 3.43 (t, J = 6 Hz, CH_2OBn), 3.97–4.12 (m, CH_2OH), 4.47 (s, benzylic CH_2), 5.55–5.70 (m, vinyl Hs), 7.30 (s, Ar); MS, calcd for $C_{13}H_{18}O_2$ m/e 206.3; Found m/e (M^+) 206, ($M^+ - H_2O$) 188.

The procedure described above for **A8** was followed. A slurry of 189 mg (7.9 mmol) of NaH in 10 mL of benzene was treated at appropriate intervals with 0.45 mL (7.5 mmol) of CS_2 and 0.46 mL (7.5 mmol) of CH_3I. After 1 h at reflux the reaction was worked up as described earlier to give 1.69 g (100%) of crude dithiocarbonate as a light orange oil: IR (film) ν 3070, 3020, 2920, 2840, 1640, 1220, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.52–1.86 (m, $CH_2CH_2CH_2O$), 2.37 (s, SCH_3), 3.46 (t, J = 6 Hz, CH_2OBn), 4.01–4.32 (m, $CHSCOSCH_3$), 4.48 (s, benzylic CH_2), 4.99–5.33 (m,

vinyl H's), 5.50–5.99 (m, vinyl H), 7.32 (s, Ar). This material was used without further purification.

The procedure described for **A9** was employed. A solution of 1.69 g (5.67 mmol) of the foregoing crude dithiocarbonate, 1.5 mL (5.67 mmol) of tri-*n*-butyltin hydride, and a catalytic amount of AIBN in 25 mL of benzene was heated at reflux for 3 h. Following workup, flash chromatography on deactivated silica gel (2% triethylamine–hexane) with hexane eluant gave 2.05 g (75%) of allylstannane **D2** as a clear oil: IR (film) ν 3020, 2945, 2920, 2840, 1460, 1110 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.74–1.03, 1.10–1.85 (m, aliphatic CH_2's), 1.9–2.25 (m, allylic CH_2), 3.48 (t, J = 7 Hz, CH_2OBn), 4.52 (s, benzylic CH_2), 4.80–5.70 (m, vinyl Hs), 7.38 (s, Ar).

***erythro*-4-Vinyl-1,10-bis(benzyloxy)-6-decyn-5-ol (D3).** The coupling procedure described below for **1** was followed by using 224 mg (1.11 mmol) of aldehyde **D1** in 4 mL of CH_2Cl_2 at −78 °C to which 150 μL (1.22 mmol) of BF_3·OEt_2 and 534 mg (1.11 mmol) of allylstannane **D2** in 3 mL of CH_2Cl_2 was added. Following workup and silica gel chromatography (30% ether–hexanes), 272 mg (62%) of alcohol **D3** was isolated as an 85:15 mixture of erythro and threo isomers: IR (film) ν 3405, 3050, 3020, 2925, 2845, 1650, 1455, 1370, 1105 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40–1.49, 1.52–1.73, 1.77–1.84 (m, CH_2's), 1.89 (d, J = 8 Hz, OH), 2.24 (sept, J = 5 Hz, allylic CH), 2.34 (dt, J = 7 Hz, $J_{1,4}$ = 2 Hz, propargylic CH_2), 3.46 (t, J = 7 Hz, threo CH_2OBn), 3.54 (t, J = 7 Hz, erythro CH_2OBn), 4.18–4.23 (m, threo carbinyl CH), 4.25–4.30 (m, erythro carbinyl CH), 4.49, 5.01 (s, benzylic CH_2), 5.13 (dd, J_{trans} = 17 Hz, $J_{1,3}$ = 2 Hz, vinyl H), 5.21 (dd, J_{cis} = 10 Hz, $J_{1,3}$ = 2 Hz, vinyl H), 5.69 (ddd, J_{trans} = 17 Hz, J_{cis} = 10 Hz, J_{vic} = 9 Hz, vinyl H), 7.24–7.37 (m, Ar). Anal. Calcd for $C_{26}H_{32}O_3$: C, 79.56; H, 8.22. Found: C, 79.42; H, 8.30.

***threo*-4-Vinyl-1,10-bis(benzyloxy)-6-decyn-5-ol (D4).** The coupling procedure described below for **2** was followed by adding 358 mg (1.77 mmol) of aldehyde **D1** in 2 mL of CH_2Cl_2 to a premixed black solution of 850 mg (1.77 mmol) of allylic stannane **D2** and 210 μL (1.95 mmol) of $TiCl_4$ in 7 mL of CH_2Cl_2. Following workup and silica gel chromatography (25% ether–hexanes) 348 mg (50%) of alcohol **D4** was isolated as a ~95:5 mixture of threo and erythro isomers: IR (film) ν 3405, 3050, 3020, 2925, 2850, 2200, 1665, 1460, 1375, 1110 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35–1.44, 1.48–1.58, 1.61–1.89 (m, CH_2's), 1.85 (d, J = 5 Hz, OH), 2.17–2.24 (m, allylic CH), 2.34 (dt, J = 7 Hz, $J_{1,4}$ = 2 Hz, propargylic CH_2), 3.46 (dt, J = 7 Hz, J_w = 2 Hz, CH_2OBn), 3.53 (t, J = 7 Hz, CH_2OBn), 4.18–4.23 (m, carbinyl CH), 4.48, 4.49 (s, benzylic CH_2), 5.13 (dd, J_{trans} = 18 Hz, J_{cis} = 2 Hz, vinyl H), 5.18 (dd, J_{cis} = 10 Hz, $J_{1,3}$ = 2.4 Hz, vinyl H), 5.62 (ddd, J_{trans} = 18 Hz, J_{cis} = 10 Hz, J_{vic} = 9 Hz, vinyl H), 7.24–7.37 (m, Ar).

***erythro*-(*Z*)-4-Vinyl-7-iodo-1,10-bis(benzyloxy)-6-decen-5-ol (D5).** To a solution of 0.65 mL (2.18 mmol) of 3.4 M Red-Al in toluene in 6 mL of dry THF at 0 °C was added 505 mg (1.29 mmol) of propargylic alcohol **D3** in 3 mL of dry THF. The resulting solution was stirred overnight at room temperature and then was cooled to −10 °C, and 0.5 mL of ethyl acetate was added. After being stirred for 15 min at −10 °C, the mixture was cooled to −78 °C, and 655 mg (2.58 mmol) of iodine in 3 mL of dry THF was added. The mixture was stirred at −78 °C for 30 min. The cooling bath was removed, and after warming to 0 °C, the mixture was poured into saturated sodium–potassium tartrate and saturated $Na_2S_2O_3$ covered with ether. The layers were separated, and the aqueous layer was extracted twice with ether. The combined ether layers were dried over anhydrous $MgSO_4$ and concentrated to an oil. Purification by silica gel chromatography (30% ether–hexanes) afforded 558 mg (83%) of vinyl iodide **D5** as a pale yellow oil: IR (film) ν 3400, 3045, 3010, 2925, 2840, 1635, 1455, 1370, 1100, 920 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28–1.40, 1.48–1.59, 1.63–1.73, 1.79–1.88 (m, CH_2's), 1.87 (d, J = 5 Hz, OH), 2.22–2.31 (m, allylic CH_2), 2.54–2.67 (m, allylic CH), 3.42–3.48 (m, CH_2OBn), 4.22 (dt, J_d = 9 Hz, J_t = 7 Hz), 4.48, 4.50 (s, benzylic CH_2), 5.07 (dd, J_{trans} = 18 Hz, $J_{1,3}$ = 2 Hz, vinyl H), 5.11 (dd, J_{cis} = 10 Hz, $J_{1,3}$ = 2 Hz, vinyl H), 5.53 (d, J = 8 Hz, vinyl H), 5.58 (ddd, J_{trans} = 18 Hz, J_{cis} = 10 Hz, J_{vic} = 9 Hz, vinyl H), 7.24–7.37 (m, Ar).

***erythro*-(*E*)-7-Methyl-4-vinyl-1,10-bis(benzyloxy)-6-decen-5-ol (D6).** To a slurry of 871 mg (4.57 mmol) of CuI in 6 mL of dry THF at 0 °C was added 6.6 mL of 1.4 M CH_3Li in diethyl ether dropwise. The resulting champagne-colored solution was treated with 476 mg (0.91 mmol) of vinyl iodide **D5** in 2 mL of dry THF. The mixture was stirred overnight at 0 °C and then was quenched with 0.57 mL (9.1 mmol) of CH_3I. After being stirred for 6 h at 0 °C the mixture was poured into saturated NH_4Cl covered with ether. The layers were separated, and the organic layer was washed with 3% NH_4OH until the washings were clear. The combined aqueous layers were extracted twice with ether, and then the ether extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo to an oil. Purification by silica gel chromatography (30% ether–hexanes) provided 338 mg (91%) of alcohol **D6** as a clear oil: IR (film) ν 3415, 3050, 3010, 2910, 2835, 1455, 1365, 1105 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22–1.33, 1.48–1.77 (m, CH_2's, OH), 1.67 (d, $J_{1,3}$ = 1 Hz, vinyl CH_3), 2.08 (t, J = 7 Hz, allylic CH_2), 2.14–2.23 (m, allylic CH), 3.44 (t, J = 7 Hz, CH_2OBn), 4.26 (dt, J_d = 9 Hz, J_t = 7 Hz, carbinyl CH), 4.49 (s, benzylic CH_2's), 5.03–5.17 (m, vinyl H), 5.56 (dt, J_d = 17 Hz, J_t = 10 Hz, vinyl H), 7.24–7.36 (m, Ar). Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.10; H, 8.90.

***threo*-(*Z*)-4-Vinyl-7-iodo-1,10-bis(benzyloxy)-6-decen-5-ol (D7).** The procedure described above for **D5** was followed using 0.4 mL of 3.4 M Red-Al in toluene in 3 mL of dry THF at 0 °C to which 333 mg (0.85 mmol) of propargylic alcohol **D4** in 2 mL of THF and 432 mg (1.7 mmol) of iodine in 2 mL of THF were added at appropriate intervals. After workup and silica gel chromatography (30% ether–hexanes) 282 mg (62%) of vinyl iodide **D7** was isolated as a pale yellow oil: IR (film) ν 3410, 3050, 3020, 2940, 2850, 1640, 1460, 1110 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33–1.44, 1.49–1.73, 1.79–1.88 (m, CH_2's), 1.07–2.17 (m, allylic CH), 2.56–2.66 (m, allylic CH_2), 3.45, 2.46 (t, J = 7 Hz, CH_2OBn), 4.15 (br t, J = 7 Hz, carbinyl CH), 4.48, 4.49 (s, benzylic CH_2), 5.10 (dd, J_{trans} = 17 Hz, $J_{1,3}$ = 2 Hz, vinyl H), 5.19 (dd, J_{cis} = 10 Hz, $J_{1,3}$ = 2 Hz, vinyl H), 5.55 (dt, J = 8 Hz, $J_{1,3}$ = 1 Hz, vinyl H), 5.65 (ddd, J_{trans} = 17 Hz, J_{cis} = 10, J_{vic} = 9 Hz, vinyl H), 7.24–7.37 (m, Ar).

***threo*-(*E*)-7-Methyl-4-vinyl-1,10-bis(benzyloxy)-6-decen-5-ol (D8).** The procedure described above for **D6** was followed by using 461 mg (2.42 mmol) of CuI in 5 mL of dry THF to which 5.0 mL of 1 M CH_3Li in diethyl ether and 252 mg (0.48 mmol) of vinyl iodide **D7** in 2 mL of dry THF was added at appropriate intervals. Following quench with 0.3 mL of CH_3I and isolation, 189 mg (96%) of alcohol **D8** was obtained as a clear oil: IR (film) ν 3400, 3040, 3000, 2900, 2835, 1450, 1365, 1105 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16–1.27, 1.45–1.57, 1.61–1.80 (m, CH_2's), 1.68 (d, J = 1 Hz, vinyl CH_3), 1.95–2.04 (m, allylic CH), 2.11 (br t, J = 8 Hz, allylic CH_2), 3.39–3.48 (m, CH_2OBn), 4.13 (t, J = 7 Hz, carbinyl CH), 4.48, 4.49 (s, benzylic CH_2's), 5.12 (dd, J_{trans} = 17 Hz, $J_{1,3}$ = 2 Hz, vinyl H), 5.17 (br d, J = 7 Hz, vinyl H), 5.20 (dd, J_{cis} = 10 Hz, $J_{1,3}$ = 2 Hz, vinyl H), 5.59 (ddd, J_{trans} = 17 Hz, J_{cis} = 10 Hz, J_{vic} = 9 Hz, vinyl H), 7.24–7.37 (m, Ar).

***cis*-(*E*)-7-Methyl-4-[3-(benzyloxy)propyl]-10-(benzyloxy)-5-hydroxy-6-decenoic Acid δ-Lactone (D9).** The procedure of Wuts was followed.[13] A steel bomb was charged with 114 mg (0.28 mmol) of alcohol **D6**, 44 mg (0.17 mmol) of triphenylphosphine, 30 mg of rhodium acetate dimer, and 6 mL of ethyl acetate. The bomb was pressurized to 350 psi with a 1:1 mixture of CO and H_2 and heated at 100 °C for 5 h. After cooling, the contents of the bomb were concentrated, and the crude lactol was oxidized with 121 mg (0.56 mmol) of pyridinium chlorochromate buffered with 46 mg (0.56 mmol) of sodium acetate in 5 mL of CH_2Cl_2. The mixture was stirred at room temperature for 2 h, then diluted with ether, and filtered through silica gel. Chromatography on silica gel afforded 83 mg (68%) of lactone **D9** as a cloudy oil: IR (film) ν 3010, 2910, 2840, 1720, 1450, 1360, 1105 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18–1.29, 1.33–1.43, 1.38–1.77, 1.80–1.89 (m, CH_2's), 1.73 (d, J = 1 Hz, vinyl CH_3), 1.92–2.00 (m, CH), 2.13 (t, J = 8 Hz, CH_2CO), 2.45–2.62 (m, allylic CH_2), 3.44, 3.46 (t, J = 6 Hz, CH_2OBn), 4.48 (s, benzylic CH_2), 5.11 (dd, J = 9, 4 Hz, carbinyl CH), 5.29 (br d, J = 9 Hz, vinyl H), 7.24–7.37 (m, Ar).

***trans*-(*E*)-7-Methyl-4-[3-(benzyloxy)propyl]-10-(benzyloxy)-5-hydroxy-6-decenoic Acid δ-Lactone (D10).** The procedure described above for **D9** was followed by using 112 mg (0.27 mmol) of alcohol **D8**, 43 mg (0.16 mmol) of triphenylphosphine, 30 mg of rhodium acetate dimer, and 6 mL of ethyl acetate at 375 psi of 1:1 CO/H_2. After 4 h, the contents of the bomb were treated with 175 mg (0.81 mmol) of pyridinium chlorochromate

and 22 mg (0.27 mmol) of sodium acetate in 6 mL of CH_2Cl_2. Following workup and chromatography on silica gel, 86 mg (73%) of lactone **D10** was isolated as a cloudy oil: IR (film) ν 3040, 3015, 2925, 2845, 1725, 1455, 1210, 1110 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.08–1.20, 1.45–1.78 (m, CH_2's), 1.70 (d, J = 1 Hz, vinyl CH_3), 1.96–2.05 (m, CH), 2.13 (t, J = 8 Hz, allylic CH_2), 2.38–2.48, 2.58–2.67 (m, CH_2CO), 3.38–3.47 (m, CH_2OBn), 4.48 (s, benzylic CH_2), 4.69 (t, J = 9 Hz, carbinyl CH), 5.16 (br d, J = 9 Hz, vinyl H), 7.24–7.35 (m, Ar). Anal. Calcd for $C_{28}H_{36}O_4$: C, 77.03; H, 8.31. Found: C, 76.93; H, 8.36.

Coupling Studies. The following procedure is representative of BF_3-mediated couplings: ***erythro*-(*E*)-5-Vinyl-8-[(*tert*-butyldimethylsilyl)oxy]-2-octen-4-ol (1).** To a solution of 0.10 mL (1.21 mmol) of crotonaldehyde in 5 mL of CH_2Cl_2 at −78 °C was added 0.15 mL (1.25 mmol) of $BF_3{\cdot}OEt_2$. The resulting white slurry was stirred at −78 °C for 2 min, and then 573 mg (1.14 mmol) of allylstannane **A9** in 3 mL of CH_2Cl_2 was added. The solution was stirred at −78 °C for 2 h and then poured into saturated $NaHCO_3$. The aqueous layer was extracted with ether, and the combined ether layers were dried over anhydrous $MgSO_4$. Removal of solvent at reduced pressure left an oil, which was purified by chromatography on silica gel (15% ether–hexanes) affording 236 mg (73%) of a 9:1 mixture of **1** and **2**: IR (film) ν 3400, 2920, 2845, 1470, 1260, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.06 (s, CH_3Si), 0.91 (s, *tert*-butyl), 1.21–1.31, 1.40–1.60 (m, CH_2's), 1.65 (m, OH), 1.70 (dd, J_{vic} = 6 Hz, $J_{1,3}$ = 2 Hz, vinyl CH_2), 2.16–2.28 (m, allylic CH), 3.59 (t, J = 6 Hz, CH_2OSi), 3.96–4.02 (m, carbinyl CH), 5.09 (dd, J_{trans} = 18 Hz, $J_{1,3}$ = 2 Hz, terminal vinyl H), 5.14 (dd, J_{cis} = 11 Hz, $J_{1,3}$ = 2 Hz, terminal vinyl H), 5.45 (ddd, J_{trans} = 16 Hz, J_{vic} = 8 Hz, $J_{1,3}$ = 2 Hz, crotyl vinyl H), 5.54–5.70 (m, terminal vinyl H, crotyl vinyl H). Anal. Calcd for $C_{16}H_{32}O_2Si$: C, 67.54; H, 11.34. Found: C, 67.66; H, 11.36.

The following procedure is representative of $TiCl_4$-mediated couplings:

***threo*-(*E*)-5-Vinyl-8-[(*tert*-butyldimethylsilyl)oxy]-2-octen-4-ol (2).** To a solution of 0.14 mL (1.28 mmol) of $TiCl_4$ in 4 mL of CH_2Cl_2 at −78 °C under argon was added 322 mg (0.64 mmol) of allylstannane **A9** in 2 mL of CH_2Cl_2 dropwise. The resulting dark mixture was stirred at −78 °C for 10 min, and then 83 μL (1.0 mmol) of crotonaldehyde was added. The dark reaction was stirred at −78 °C for 2 h and then poured into saturated $NaHCO_3$. The aqueous layer was extracted with ether, and the organic layers were washed with 2% HCl and dried over anhydrous $MgSO_4$. Solvent removal under reduced pressure afforded a pale yellow oil, which was purified by chromatography on silica gel (20% ether–hexanes) to provide 129 mg (71%) of a 95:5 mixture of **2** and **1**: IR (film) ν 3420, 2940, 2920, 2850, 1390, 1265, 1115 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, CH_3Si), 0.91 (s, *tert*-butyl), 1.13–1.28, 1.37–1.48, 1.50–1.60 (m, CH_2's), 1.72 (dd, J_{vic} = 7 Hz, $J_{1,3}$ = 2 Hz, vinyl CH_3), 1.74 (d, J = 3 Hz, OH), 1.98–2.07 (m, allylic CH), 3.58 t, J = 7 Hz, CH_2OSi), 3.81 (br t, J = 7 Hz, carbinyl CH), 5.15 (dd, J_{trans} = 18 Hz, $J_{1,3}$ = 2 Hz, terminal vinyl H), 5.22 (dd, J_{cis} = 10 Hz, $J_{1,3}$ = 2 Hz, terminal vinyl H), 5.44 (ddd, J_{trans} = 15 Hz, J_{vic} = 7 Hz, $J_{1,3}$ = 2 Hz, H-3), 5.56–5.75 (m, H-2, terminal vinyl H).

***erythro*-4-Vinyl-1,10-bis[(*tert*-butyldimethylsilyl)oxy]-6-decyn-5-ol (3).** The procedure described above for alcohol **1** was followed. To a solution of 770 mg (3.4 mmol) of aldehyde **A3** and 0.46 mL (3.74 mmol) of $BF_3{\cdot}OEt_2$ in 8 mL of CH_2Cl_2 at −78 °C was added 1.73 g (3.4 mmol) of allylstannane **A9** in 2 mL of CH_2Cl_2. After 1 h at −78 °C the reaction was quenched and worked up as stated earlier. Purification on silica gel (15% ether–hexanes) provided 1.22 g (81%) of alcohol **5** as a 90:10 mixture of erythro and threo isomers: IR (film) ν 3400, 2940, 2915, 2875, 2845, 1265, 1115 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, CH_3Si), 0.91 (s, *tert*-butyl), 1.40–1.60 (m, CH_2's), 1.71 (p, J = 5 Hz, $CH_2CH_2CH_2$), 1.90 (d, J = 9 Hz, OH), 2.29 (dt, J_t = 7 Hz, J_d = 2 Hz, allylic CH), 3.61 (t, J = 6 Hz, CH_2OSi), 3.68 (t, J = 6 Hz, CH_2OSi), 4.27–4.33 (m, carbinyl CH), 5.17 (dd, J_{trans} = 18 Hz, J_{gem} = 2 Hz, vinyl H), 5.23 (dd, J_{cis} = 10 Hz, J_{gem} = 2 Hz, vinyl H), 5.73 (ddd, J_{trans} = 18 Hz, J_{cis} = 10 Hz, J_{vic} = 9 Hz, vinyl H). Anal. Calcd for $C_{24}H_{48}O_3Si_2$: C, 65.39; H, 10.98. Found: C, 65.46; H, 11.02.

***threo*-4-Vinyl-1,10-bis[(*tert*-butyldimethylsilyl)oxy]-6-decyn-5-ol (4).** The procedure described above for alcohol **2** was followed. To a premixed black solution of 0.39 mL (3.5 mmol) of $TiCl_4$ and 1.62 g (3.2 mmol) of allylstannane **A9** in 10 mL of CH_2Cl_2 at −78 °C was added 727 mg (3.2 mmol) of aldehyde **A3** in 3 mL of CH_2Cl_2. The resulting black solution was stirred for 0.5 h at −78 °C. Following quench, workup and chromatography on silica gel, 673 mg (48%) of alcohol **4**, a 91:9 mixture of threo and erythro isomers, was isolated: IR (film) ν 3400, 2940, 2915, 2875, 2845, 1265, 1115 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.05 (s, CH_3Si), 0.89 (s, *tert*-butyl), 1.22–1.50, 1.52–1.77 (m, CH_2's), 1.69 (p, J = 6 Hz, $CH_2CH_2CH_2$), 1.83 (d, J = 6 Hz, OH), 2.18–2.25 (m, allylic CH), 2.28 (dt, J_{vic} = 8 Hz, $J_{1,4}$ = 2 Hz, propargylic CH_2), 3.59 (dt, J = 6 Hz, J_w = 2 Hz, CH_2OSi), 3.66 (t, J = 6 Hz, CH_2OSi), 4.18–4.23 (m, carbinyl CH), 5.13 (dd, J_{trans} = 17 Hz, $J_{1,3}$ = 2 Hz, vinyl H), 5.19 (dd, J_{cis} = 10 Hz, $J_{1,3}$ = 2 Hz, vinyl H), 5.63 (ddd, J_{trans} = 17 Hz, J_{cis} = 10 Hz, J_{vic} = 10 Hz, vinyl H).

***erythro*-(*E*)-3-Methyl-6-vinyl-1-(benzyloxy)-12-[(*tert*-butyldimethylsilyl)oxy]-2-dodecen-8-yn-7-ol (7).** The procedure described for **1** was followed by using 135 mg (0.6 mmol) of aldehyde **A3** in 2 mL of CH_2Cl_2 at −78 °C to which 81 μL (0.66 mmol) of $BF_3{\cdot}OEt_2$ and 311 mg (0.6 mmol) of allylstannane **C10** in 2 mL of CH_2Cl_2 were added. Following workup and chromatography on silica gel (20% ether–hexanes) 207 mg (72%) of product was obtained as an 85:15 mixture of alcohols **7** and **10**: IR (film) ν 3420, 3025, 2945, 2920, 2880, 2850, 1640, 1260, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.06 (s, CH_3Si), 0.91 (s, *tert*-butyl), 1.65 (s, vinyl CH_3), 1.65–1.87 (m, CH_2's), 1.87 (d, J = 8 Hz, OH), 1.94–2.13, 2.20–2.29 (m, allylic CH_2's), 2.30 (dt, J_t = 6 Hz, J_d = 2 Hz, propargylic CH_2), 3.68 (t, J = 6 Hz, CH_2OSi), 4.03 (d, J = 8 Hz, CH_2OBn), 4.28–4.34 (m, carbinyl H), 4.41 (s, benzylic CH_2), 5.17 (dd, J_{trans} = 18 Hz, $J_{1,3}$ = 2 Hz, vinyl H), 5.25 (dd, J_{cis} = 10 Hz, $J_{1,3}$ = 2 Hz, vinyl H), 5.42 (br t, J = 7 Hz, vinyl H), 5.74 (ddd, J_{trans} = 18 Hz, J_{cis} = 10 Hz, J_{vic} = 10 Hz, vinyl H), 7.35 (d, J = 4 Hz, Ar). Anal. Calcd for $C_{28}H_{44}O_3Si$: C, 73.63; H, 9.71. Found: C, 73.53; H, 9.74.

***erythro*-(*E*)-3-Methyl-6-vinyl-1-(benzyloxy)-12-[(*tert*-butyldiphenylsilyl)oxy]-2-dodecen-8-yn-7-ol (9).** The procedure for **1** was followed by using 386 mg (1.1 mmol) of the *tert*-butyldiphenylsilyl analogue of aldehyde **A3** in 3 mL of CH_2Cl_2 at −78 °C to which 0.15 mL (1.2 mmol) of $BF_3{\cdot}OEt_2$ and 425 mg (1.1 mmol) of allylstannane **C10** in 2 mL of CH_2Cl_2 were added. Workup and chromatography on silica gel (15% ethyl acetate–hexanes) afforded 480 mg (71%) of alcohol as a 90:10 mixture of erythro and threo isomers **9** and **12**: IR (film) ν 3420, 3065, 2930, 2855, 1670, 1435, 1120 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.08 (s, CH_3Si), 1.43–1.55, 1.60–1.70 (m, CH_2's), 1.78 (p, J = 6 Hz, $CH_2CH_2CH_2$), 1.95 (d, J = 9 Hz, OH), 1.95–2.03, 2.05–2.14 (m, allylic CH_2's), 2.20–2.28 (m, allylic CH), 2.39 (dt, J = 7, 2 Hz, propargylic CH_2), 3.76 (t, J = 6 Hz, CH_2OSi), 4.04 (d, J = 7 Hz, CH_2OBn), 4.26–4.32 (m, carbinyl CH), 4.52 (s, benzylic CH_2), 5.17 (dd, J_{trans} = 18 Hz, $J_{1,3}$ = 2 Hz, vinyl H), 5.22 (dd, J_{cis} = 11 Hz, $J_{1,3}$ = 2 Hz, vinyl H), 5.42 (br t, J = 7 Hz, vinyl H), 5.71 (ddd, J_{trans} = 18 Hz, J_{cis} = 11 Hz, J_{vic} = 10 Hz, vinyl H), 7.31–7.47 (m, Ar), 7.64–7.72 (m, Ar). Anal. Calcd for $C_{38}H_{48}O_3Si$: C, 78.57; H, 8.33. Found: C, 78.66; H, 8.36.

***erythro*-(*Z*,*E*)-3-Methyl-1-(benzyloxy)-6-vinyl-9-iodo-12-[(*tert*-butyldimethylsilyl)oxy]-2,8-dodecadien-7-ol (13).** The procedure for **1** was followed by using 380 mg (1.07 mmol) of aldehyde **A7** in 3 mL of CH_2Cl_2 at −78 °C to which 150 μL (1.2 mmol) of $BF_3{\cdot}OEt_2$ and 571 mg (1.1 mmol) of allylstannane **C10** in 3 mL of CH_2Cl_2 was added. After workup and chromatography on silica gel (20% ether–hexanes), 461 mg (79%) of alcohol was isolated as a 70:30 mixture of erythro and threo isomers **13** and **14**: IR (film) ν 3405, 3015, 2940, 2845, 1640, 1260, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, CH_3Si), 0.92 (s, *tert*-butyl), 1.65 (s, vinyl CH_3), 1.70–1.81 (m, CH_2's, OH), 1.92–2.03, 2.06–2.18, 2.26–2.33 (m, allylic CH_2's), 2.52–2.64 (m, allylic CH), 3.57–3.64 (m, CH_2OSi), 4.03 (d, J = 8 Hz, CH_2OBn), 4.13–4.20 (m, threo carbinyl CH), 4.21–4.29 (m, erythro carbinyl CH), 4.52 (s, benzylic CH_2), 5.08–5.26 (m, vinyl Hs), 5.42 (br t, J = 8 Hz, vinyl H), 5.53–5.73 (m, vinyl H), 7.35 (d, J = 6 Hz, Ar). Anal. Calcd for $C_{28}H_{45}O_3SiI$: C, 57.52; H, 7.76. Found: C, 57.39; H, 7.80.

***erythro*-(*Z*)-4-Vinyl-7-iodo-1,10-bis[(*tert*-butyldimethylsilyl)oxy]-6-decen-5-ol (21).** The procedure for **1** was followed by using 267 mg (0.75 mmol) of aldehyde **A7** in 2 mL of CH_2Cl_2 at −78 °C to which 101 μL (0.82 mmol) of $BF_3{\cdot}OEt_2$ and 379 mg (0.75 mmol) of allylstannane **A9** in 3 mL of CH_2Cl_2 was added.

After workup and chromatography on silica gel (20% ether–hexanes), 241 mg (57%) of alcohol **21** was obtained as a 75:25 mixture of erythro and threo isomers: IR film ν 3400, 2940, 2865, 2840, 1640, 1470, 1260, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, CH_3Si), 0.91 (s, *tert*-butyl), 1.23–1.38, 1.41–1.50, 1.51–1.67 (m, CH_2's), 1.73 (p, J = 6 Hz, $CH_2CH_2CH_2$), 1.83 (d, J = 6 Hz, OH), 2.10–2.18 (m, threo allylic CH), 2.26–2.34 (m, erythro allylic CH), 2.53–2.64 (m, allylic CH_2's), 2.56–2.66 (m, CH_2OSi), 4.12–4.8 (m, threo carbinyl CH), 4.22–4.28 (m, erythro carbinyl CH), 5.08–5.25 (m, vinyl H's), 5.53–5.72 (m, vinyl H's); MS, calcd for $C_{24}H_{49}O_3Si_2I$ m/e 568.7, found m/e ($M^+ - C(CH_3)_3$) 511. Anal. Calcd for $C_{24}H_{49}O_3Si_2I$: C, 50.69; H, 8.68. Found: C, 50.79; H, 8.70.

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An Asymmetric Synthesis of (+)-Morphinans in High Enantiomeric Purity

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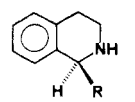
The synthesis of the narcotic analgesic dextrorphan (**4**) and its desoxy derivative has been accomplished via an asymmetric alkylation of octahydroisoquinoline **10**. The latter, converted to its chiral formamidine **13**, underwent highly selective alkylation to give the 1-benzyl derivative **16** in >98% ee. Grewe cyclization then produced the title compounds.

In the continuing study on chiral formamidines, as precursors to α-lithio anions, which have thus far led to asymmetric synthetic methods for tetrahydroisoquinolines **1**,[1] β-carbolines **2**,[2] piperidines and pyrrolidines **3**, and



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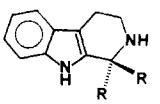

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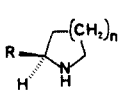

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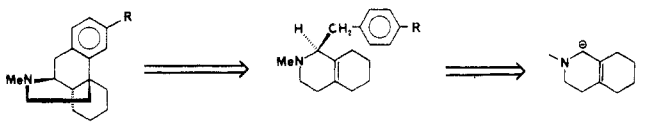
benzomorphans,[3,4] we describe an efficient synthesis of morphinans which includes the preparation of dextrorphan (**4**) and its unsubstituted derivative. These substances

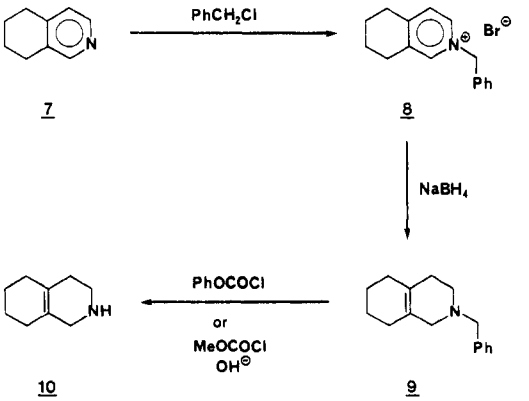


4, R = H, OH **5** **6**

have been the subject of considerable effort over the past 35 years due to their analgesic and antitussive properties. Synthetic approaches to the morphine-based system have also enjoyed considerable success[5] and continue even in recent years.[6] However, there are no reported asymmetric syntheses to these systems and it is the purpose of this paper to disclose a successful entry into enantiomercially enriched (>98%) morphinans.

Our approach is to generate a chiral carbanion from the octahydroisoquinoline **6** via formamidines and to alkylate, in a stereoselective manner, to the benzyl derivative **5**. The final construction to the morphinan **4** makes use of the well-known Grewe cyclization[7] under acidic condtions.

The synthetic scheme begins with the acquisition of the octahydroisoquinoline (**10**), which was prepared in 30–40% overall yield from isoquinoline. The latter was reduced[8] with hydrogen–palladium–trifuloroacetic acid to the tetrahydroisoquinoline **7** followed by quaternization with benzyl bromide to furnish the *N*-benzyl salt **8**. Reduction



7 **8** **9** **10**

with sodium borohydride gave the *N*-benzyloctahydroisoquinoline **9**, which was debenzylated to 1,2,3,4,5,6,7,8-octahydroisoquinoline (**10**). Transformation into the chiral

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