Synthesis of a C22–34 Subunit of the Immunosuppressant FK-506

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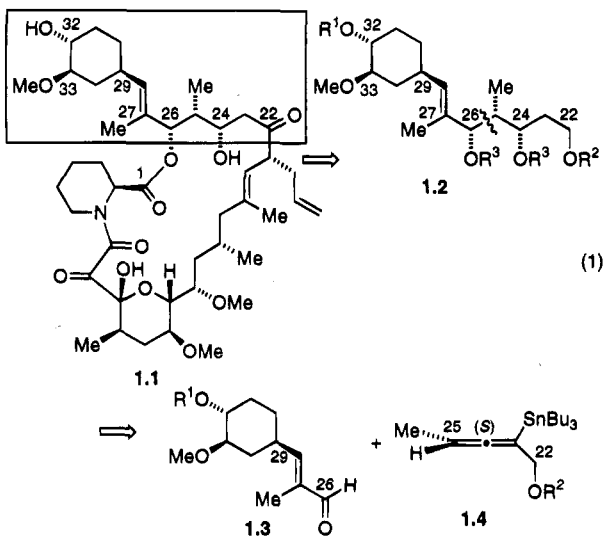
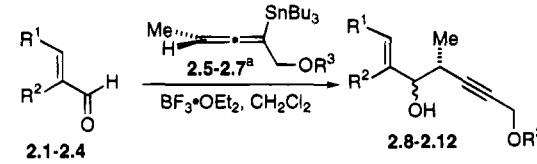
A new route to the C22–34 subunit of FK-506 was developed. A highly diastereoselective Diels–Alder reaction of 1,3-butadiene with the bis-acrylate of (*R,R*)-hydrobenzoin and subsequent saponification provided the cyclohexenecarboxylic acid **6.4** of 95% ee. Elaboration to the enal **9.2** was effected by known transformations. Enal **9.2** underwent diastereoselective and enantiospecific S_E2' addition of allenyl stannane (*S*)-**3.9** affording the homopropargylic alcohol **9.3** as an 85:15 *syn/anti* mixture. The PMB ether **9.5** was converted to the known benzylidene derivative **10.4** by sequential treatment with Red-Al, epoxidation, a second reduction with Red-Al, and oxidative benzylidene formation with DDQ.

Over the past several years we have been developing methodology for the synthesis of *syn* or *anti* β-methyl homopropargylic alcohols through Lewis acid-promoted additions of enantioenriched allenic stannanes such as **1.4** to aldehydes.[1] With nonracemic α-methyl aldehydes these additions give rise to intermediates related to polypropionate natural products. In a continuation of those studies we were interested in a potential application of the methodology to conjugated aldehydes such as **1.3** which, if successful, could provide an efficient convergent route to intermediates (*e.g.* **1.2**) related to the immunosuppressant FK-506 (**1.1**).[2]



(1)

As these previous studies involved only saturated aldehydes,[1] we decided to conduct a brief survey of additions to conjugated aldehydes. The reaction of stannane **2.5** with (*E*)-2-heptenal (**2.1**) occurred readily at −78 °C affording a 65:35 mixture of diastereomeric alcohols, presumed to favor the *syn* isomer **2.8**. As is the case with saturated aldehydes, branching at the α-position improved the *syn/anti* ratio.[1] The α-methyl enal **2.2** was converted to a 78:22 mixture of diastereomers.[5] However, the reaction was considerably slower with this aldehyde. The cyclohexyl analogue **2.3** likewise showed diminished reactivity. Somewhat improved *syn/anti* diastereoselectivity was realized with the pivaloyl-protected allenic stannane **2.6**. The α-bromo enal **2.4** was more reactive but the diastereoselectivity was only *ca.* 70:30.



(2)

R¹	R²	R³	T, °C	yield, %	syn:anti
n-C_4H_9	H(**2.1**)	Bn(**2.5**)	-78	90	65:35(**2.8**)
n-C_4H_9	Me(**2.2**)	Bn(**2.5**)	-40	57	78:22(**2.9**)
c-C_6H_{11}	Me(**2.3**)	Bn(**2.5**)	-50	91	79:21(**2.10**)
c-C_6H_{11}	Me(**2.3**)	Piv(**2.6**)	-50	81	81:19(**2.11**)
c-C_6H_{11}	Br(**2.4**)	Ac(**2.7**)	-78	73	71:29(**2.12**)

ª racemic

The enantioenriched allenic stannane (*S*)-**3.9** was prepared by an improved route starting from (*R*)-methyl lactate as outlined in eq 3.[6] As in our previous work, the Bu_3Sn grouping was introduced by stereospecific S_N2' displacement of a chiral mesylate (in this case **3.8**) with the cuprate derived from Bu_3SnLi and $CuBr{\cdot}SMe_2$.[1] The present synthesis of **3.8** allows for greater choice of primary alcohol protecting groups and affords material of consistently higher ee than our former route in which the precursor propargyl alcohol (*e.g.* **3.7**) was secured through reduction of an alkynone with Noyori's BINAL-H or with the $LiAlH_4$–Chirald complex hydride.[1]

Enal **1.3** and its precursor **4.5** have served as key intermediates in several previous synthetic approaches

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(1) Marshall, J. A.; Perkins, J. F.; Wolf, M. A. *J Org. Chem.* **1995**, *60*, 5556. Marshall, J. A.; Perkins, J. F. *J .Org. Chem.* **1994**, *59*, 3509. Marshall, J. A.; Wang, X-j. *J. Org. Chem.* **1992**, *57*, 1242.

(2) For previous work on the sythesis of FK-506 along these lines, see: White, J. D.; Toske, S. G.; Yakura, T. *Synlett* **1994**, 591 and references cited therein.

(3) White and co-workers[2] obtained a *ca.* 70:30 mixture of diastereomeric *syn* adducts upon addition of Roush's (*R,R*)-diisopropyl tartrate-derived (*Z*)-crotylboronate[4] to a SEM protected derivative of enal **1.3**.

(4) Roush, W. R.; Ando, K.; Powers, D. B.; Palkowitz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 6339.

(5) Enals **2.2** and **2.3** were prepared by application of the Corey–Peterson sequence to pentanal and cyclohexanecarboxaldehyde: (a) Corey, E. J.; Enders, D.; Bock, M. G. *Tetrahedron Lett.* **1976**, 7. (b) Schlessinger, R. H.; Poss, M. A.; Richardson, S.; Lin, P. *Tetrahedron Lett.* **1985**, *26*, 2391.

(6) An analogous sequence has recently appeared for the preparation of (*S*)-3-butyn-2-ol derivatives: Ku, Y.-Y.; Patel, R. R.; Elisseou, E. M.; Savick, D. P. *Tetrahedron Lett.* **1995**, *36*, 2733.

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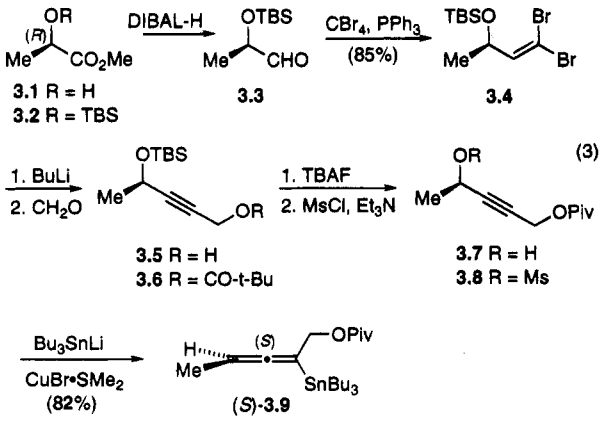
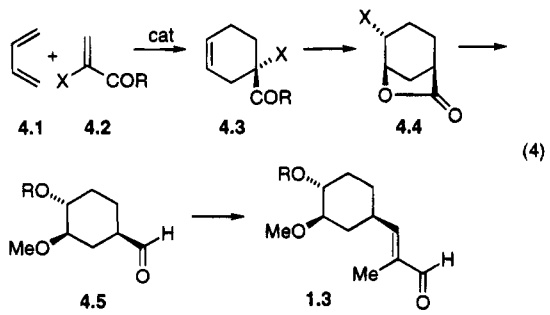
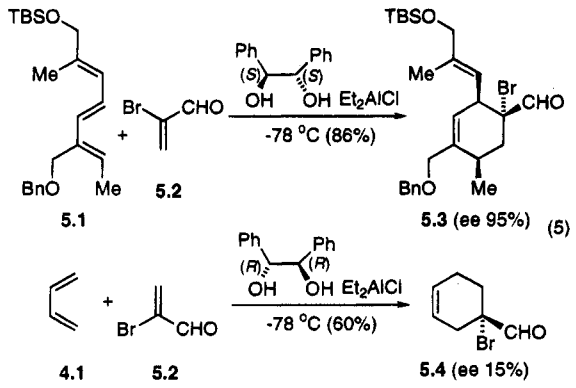


to FK-506.[3] We planned to access an enantioenriched ester progenitor **4.3** of enal **1.3** through Diels–Alder addition of 1,3-butadiene (**4.1**) to an acrolein or acrylate derivative **4.2** (R = H or OR, X = H or Br). Subsequent conversion of the cycloadduct **4.3** to enal **1.3** is closely precedented.[7]

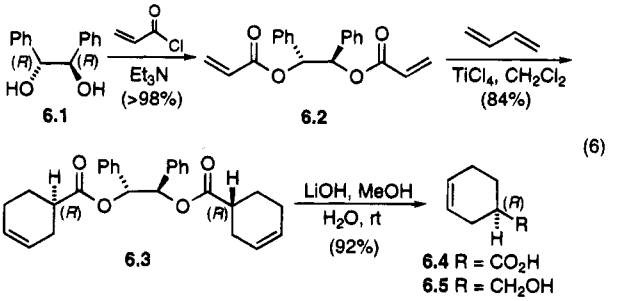


In studies directed toward the macrocyclic antibiotic kijanolide, we found that α-bromoacrolein (**5.2**) undergoes efficient Diels–Alder reaction with diene **5.1** in the presence of chiral Lewis acid catalysts.[8,9] One of the most effective catalysts for this cycloaddition was the 1:1 complex of hydrobenzoin and Et_2AlCl. However, in the present case, this catalyst system afforded the cycloadduct **5.4** of 1,3-butadiene (**4.1**) and α-bromoacrolein (**5.2**) in modest yield and low ee.



In a search for alternative routes to a nonracemic cyclohexenecarboxylate **4.3**, we decided to examine hydrobenzoin as a chiral auxiliary rather than a chiral ligand.[10] Our thinking along these lines was influenced by the observations of Saito and co-workers who noted profound conformational preferences for certain acyclic 1,5-dienes bearing bulky vicinal allylic OTBS groupings.[11]

The requisite bis-acrylate **6.2** was prepared in near quantitative yield by esterification of (*R,R*)-hydrobenzoin (**6.1**) with acryloyl chloride. Addition of 1,3-butadiene to the crude acrylate **6.2**, in the presence of $TiCl_4$, proceeded in high yield to afford the bis-adduct **6.3**. Saponification with LiOH in aqueous methanol gave acid **6.4** of 90–92% ee as determined by reduction of the adduct **6.3** to the known alcohol **6.5**.[12] When the sequence was performed on recrystallized adduct **6.3**, acid **6.4** of 95% ee was secured in 92% yield and recovered hydrobenzoin in 93% yield.



Assuming the phenyl substituents of bis-acrylate **6.2** prefer an *anti* conformation, for steric reasons, and taking into account the calculations of Houk and co-workers on preferred conformations of acrylate–Lewis acid complexes,[13] we envisioned a transition state resembling **7.1** to account for the observed facial selectivity of the cycloaddition.[14] Isoprene and 1,3-cyclopentadiene also undergo highly selective [4 + 2] cycloadditions with acrylate **6.2** affording adducts **7.2** and **7.4** which were converted to alcohols **7.3**[15] and **7.5**[16] of high ee. However reactions of the related bis-methacrylic or crotonic esters of (*R,R*)-hydrobenzoin (**6.1**) with butadiene under the foregoing conditions were slow and led to adducts of low ee in poor yield. Presumably, the additional Me substituents adversely influence the conformational preference for transition states analogous to **7.1** in these derivatives.

The conversion of unsaturated acid **6.4** to ester **8.6** is well precedented.[7] The route depicted in eq 8 proved most practical in our hands. Enantiomeric enrichment to nearly 100% could be achieved through recrystallization of iodolactone **8.1**.

The sequence of Corey and co-workers[5] was followed for the conversion of ester **8.6** to enal **9.2**. This enal, upon treatment with the allenic stannane (*S*)-**3.9** and BF_3·OEt_2 at −45 °C in CH_2Cl_2, afforded an 85:15 mixture of the

(7) (a) Linde, R. G.; Egbertson, M.; Coleman, R. S.; Jones A. B.; Danishefsky, S. J. *J. Org. Chem.* **1990**, *55*, 2771. (b) Corey, E. J.; Huang, H.-C. *Tetrahedron Lett.* **1989**, *30*, 5235.

(8) Marshall, J. A.; Xie, S. *J. Org. Chem.* **1992**, *57*, 2987. Xie, S. MS. Thesis, Univeristy of South Carolina, 1992.

(9) For a recent review of chiral catalysts employed in [4 + 2] cycloadditions, see: Oh, T.; Reilly, M. *Org. Prep. Proced. Int.* **1994**, *26*, 129.

(10) Wang, Z-M.; Sharpless, K. B. *J. Org. Chem.* **1994**, *59*, 8302.

(11) Saito, S.; Morikawa, Y.; Moriwake, T. *J. Org.Chem.* **1990**, *55*, 5424. Gung, B. W.; Melnick, J. P.; Wolf, M. A.; Marshall, J. A. *J .Org. Chem.* **1994**, *59*, 5609.

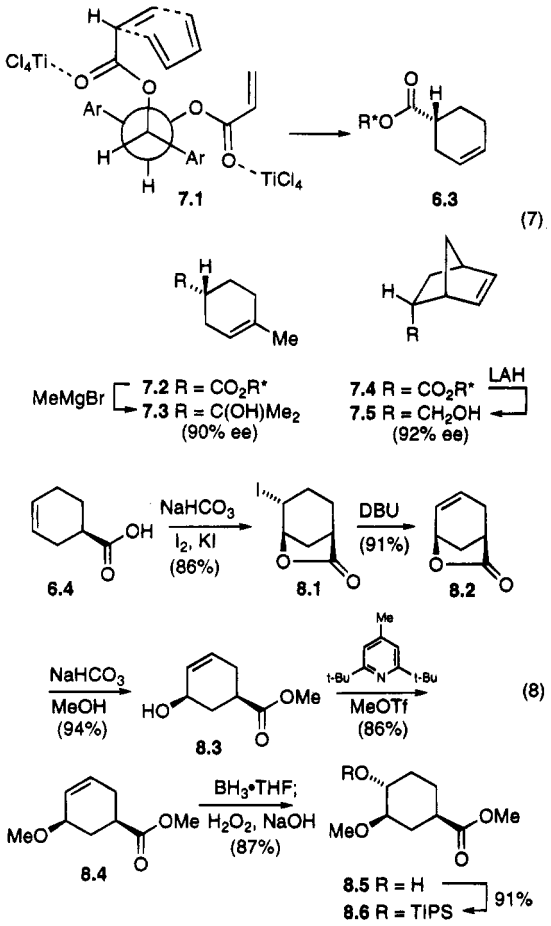
(12) Ceder, O.; Hansson, B. *Acta Chem. Scand.* **1970**, *24*, 2693.

(13) Loncharick, R. J.; Schwartz, T. R.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 14.

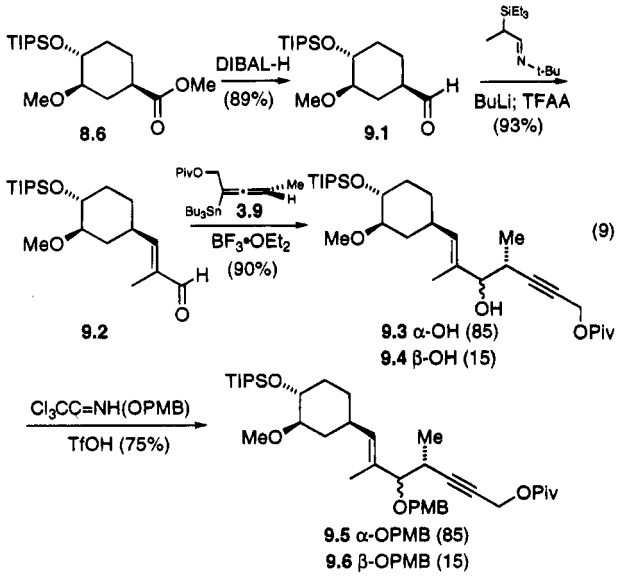
(14) For a related use of C_2-symmetric dispiroketal chiral auxiliaries, see: Bezuidenhoudt, B. C. B.; Castle, G. H.; Geden, J. V.; Ley, S. V. *Tetrahedron Lett.* **1994**, *35*, 7451. For additional considerations on the question of acrylate conformation, see: Shida, N.; Kabuto, C.; Niwa, T.; Ebata, T.; Yamamoto, Y. *J. Org. Chem.* **1994**, *59*, 4068.

(15) (a) Colonge, J.; Crabalona, J. *Bull. Chim. Soc. Fr.* **1960**, 102. (b) *The Merck Index*, 11th ed.; Budavari, S., Ed.; Merck & Co., Inc.: Rahway, NJ, 1989; p 9105 and references therein.

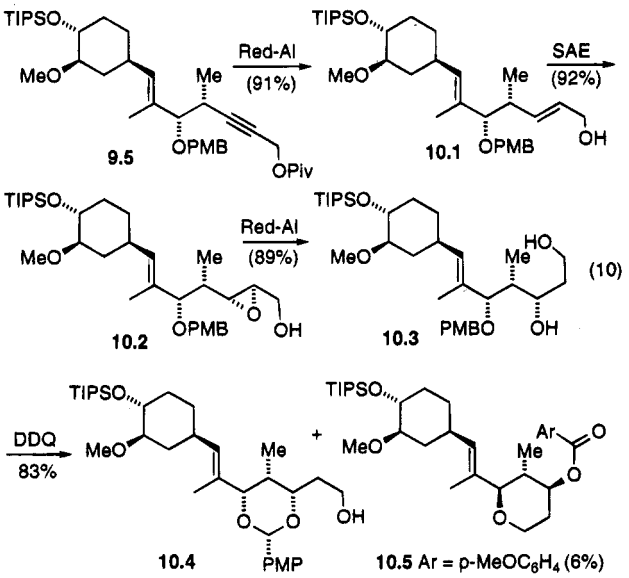
(16) Farmer, R. F.; Hamer, J. *J. Org. Chem.* **1966**, *31*, 2418.



syn adduct **9.3** and the alcohol epimer **9.4** in 90% yield. The stereochemistry of the *syn* adduct was ascertained through its conversion to the known acetal **10.4**.[17] To that end, we prepared the *p*-methoxybenzyl (PMB) ethers **9.5** and **9.6**. These proved to be readily separable by column chromatography.



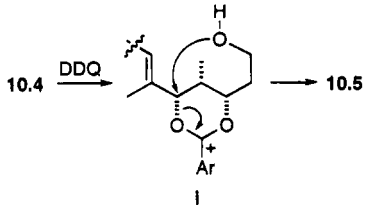
Removal of the pivalate and concomitant reduction of the triple bond was achieved through treatment of propargylic ester **9.5** with Red-Al. The (*E*)-allylic alcohol **10.1** was thereby secured in high yield. Sharpless asymmetric epoxidation, with D-(−)-diethyl tartrate as the chiral ligand, afforded epoxy alcohol **10.2** with excellent diastereoselectivity.[18] This epoxy alcohol underwent regioselective cleavage with Red-Al affording the *syn,syn* product **10.3**. Upon treatment with DDQ, the PMB ether diol **10.3** was converted to the *p*-methoxybenzylidene derivative **10.4** and a small amount of a byproduct whose ^{1}H NMR and mass spectra are suggestive of structure **10.5**.[19] The spectral properties and optical rotation of alcohol **10.4** were in complete agreement with those reported by Danishefsky.[17]



Although the diastereoselectivity of the key allenylstannane addition to enal **9.2** is lower than that for related saturated aldehydes,[1] the present route is still one of the most efficient yet devised for the C22−34 segment of FK-506. The high diastereoselectivity of the Diels−Alder reaction of bis-acrylate **6.2** is especially noteworthy.

Experimental Section[20]

(±)-2-(Tributylstannyl)-1-(benzyloxy)-2,3-pentadiene (2.5). To a solution of 1.20 g (6.31 mmol) of 5-(benzyloxy)-3-pentyn-2-ol[21] in 32 mL of CH_2Cl_2 was successively added 1.76 mL (12.6 mmol) of Et_3N and 0.73 mL (9.5 mmol) of MsCl (dropwise over 3 min) at −78 °C. The resulting white slurry was stirred at −78 °C for 1 h and then quenched with



(17) Jones, A. B.; Villalobos, A.; Linde, R. G., II; Danishefsky, S. J. *J. Org. Chem.* **1990**, *55*, 2786.

(18) The stoichiometric procedure gave the best results: Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.

(19) A possible genesis of this interesting byproduct could entail hydride abstraction from the benzylidene acetal **10.4** and internal displacement of the resultant oxo cation i.

(20) Unless otherwise stated, ^{1}H and ^{13}C NMR spectra were determined at 300 and 100.6 MHz, respectively, on dilute solutions of sample in $CDCl_3$. Solvent removal was achieved on a rotary evaporator under aspirator vacuum. For typical experimental protocols, see: Marshall, J. A.; Wang, X-j. *J. Org. Chem.* **1991**, *56*, 960.

(21) Prepared by addition of lithio-3-(benzyloxy)-1-propyne to acetaldehyde.

saturated $NaHCO_3$. After being warmed to rt and stirred for 15 min, the mixture was extracted three times with Et_2O. The combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure to afford 1.72 g of mesylate as a colorless liquid. This material was used for the cuprate addition without further purification.

To a solution of 1.41 mL (10.1 mmol) of *i*-Pr_2NH and 2 mg of 2,6-di-*tert*-butyl-4-methylphenol (BHT) in 30 mL of THF was added 3.8 mL (9.5 mmol) of 2.5 M *n*-BuLi in hexanes under argon at 0 °C. The yellow solution was stirred for 20 min, followed by dropwise addition of 2.5 mL (9.5 mmol) of Bu_3SnH. After being stirred at 0 °C for 10 min, the solution was cooled to −78 °C, and 1.95 g (9.47 mmol) of $CuBr{\cdot}SMe_2$ was added in one portion. The initial yellow solution gradually turned dark while being stirred for 30 min at −78 °C. Then 1.72 g (*ca.* 6.31 mmol) of unpurified mesylate in 2 mL of THF was added dropwise over 5 min. Stirring was continued at −78 °C for 10 min. The reaction was quenched with saturated $NaHCO_3$, warmed to rt, diluted with ether, and filtered through a Celite pad to remove the solid generated in the workup. The aqueous layer of the filtrate was extracted three times with Et_2O. The combined organic extracts were successively washed with 1:9 NH_4OH/saturated NH_4Cl and brine, dried over anhydrous $MgSO_4$, concentrated under reduced pressure, and chromatographed on silica gel. Elution with hexanes removed the hexabutylditin byproduct. Further elution with 5% Et_2O–hexanes afforded 2.30 g (79% for two steps) of allenyl stannane **2.5** as a colorless liquid: IR (film) 1931 cm^{-1}; ^1H NMR δ 0.83–1.50 (m, 27 H), 1.62 (d, J = 6.9 Hz, 3 H), 4.11 (m, 2 H), 4.48 (s, 2 H), 4.69 (m, 1 H), 7.26–7.32 (m, 5 H).

(±)-(*E*,4*R*,5*S*)-4,6-Dimethyl-5-hydroxy-7-cyclohexyl-6-hepten-2-ynyl 1,1,1-Trimethylacetate (2.11 *syn*) and (±)-(*E*,4*R*,5*R*)-4,6-Dimethyl-5-hydroxy-7-cyclohexyl-6-hepten-2-ynyl 1,1,1-Trimethylacetate (2.11 *anti*). Typical Procedure for Addition of an Allenyl Stannane to an α,β-Unsaturated Aldehyde. A mixture of 1.50 g (9.85 mmol) of aldehyde **2.3** and 8.10 g (17.7 mmol) of allenylstannane **2.6** (prepared as described for (***S***)-**3.9**) in 10 mL of CH_2Cl_2 was cooled to −78 °C, and 4.24 mL (34.5 mmol) of $BF_3{\cdot}OEt_2$ was added dropwise. The resulting brown solution was warmed to −50 °C and stirred for 36 h. The mixture was recooled to −78 °C, diluted with 20 mL of CH_2Cl_2, and quenched with saturated $NaHCO_3$. Upon being warmed to rt, the mixture was extracted three times with CH_2Cl_2. The combined organic extracts were filtered through a short pad of Celite 545 to remove particulates, and the filtrate was washed with saturated brine and dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure to yield a yellow residue. The ^1H NMR (400 MHz) spectrum showed well-separated signals of the *syn* and *anti* carbinyl protons (3.90 vs 3.73 ppm). Integration of these signals indicated an 81:19 ratio of isomers favoring the *syn* adduct. This material was chromatographed on silica gel. Elution with 5–20% Et_2O–hexanes afforded 2.55 g (81%) of oily product **2.11** as an 82:18 *syn*/*anti* mixture. A careful second chromatography on silica gel (15–20% Et_2O–hexanes) provided a small amount of pure *syn* product.

2.11 *syn*: ^1H NMR δ 0.95–1.30 (m, 6 H), 1.13 (d, J = 6.9 Hz, 3 H), 1.19 (s, 9 H), 1.55–1.70 (m, 4 H), 1.62 (d, J = 1.3 Hz, 3 H), 1.72 (d, J = 3.8 Hz, 1 H), 2.19 (m, 1 H), 2.69 (m, 1 H), 3.90 (dd, J = 6.7, 3.8 Hz, 1 H), 4.61 (d, J = 2.1 Hz, 2 H), 5.27 (d, J = 9.2 Hz, 1 H).

2.11 *anti*: ^1H NMR δ 0.95–1.31 (m, 6 H), 1.03 (d, J = 7.0 Hz, 3 H), 1.19 (s, 9 H), 1.57 (d, J = 1.3 Hz, 3 H), 1.58–1.72 (m, 4 H), 1.73 (br s, 1 H), 2.18 (m, 1 H), 2.67 (m, 1 H), 3.73 (dd, J = 8.2, 3.1 Hz, 1 H), 4.64 (d, J = 2.0 Hz, 2 H), 5.23 (d, J = 9.1 Hz, 1 H).

Methyl (*R*)-2-[(*tert*-Butyldimethylsilyl)oxy]propionate (3.2). To a solution of 10.0 g (96.1 mmol) of methyl (*R*)-(+)-lactate in 240 mL of DMF was added 14.5 g (96.1 mmol) of TBSCl in one portion at 0 °C, followed by addition of 9.81 g (144 mmol) of imidazole in three portions over 10 min. The reaction mixture was warmed to rt and stirred for 4.5 h. After being cooled to 0 °C, the mixture was poured into 0.5 N HCl and extracted three times with Et_2O. The combined organic extracts were successively washed with saturated $NaHCO_3$ and brine and dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure to give 21.0 g (quantitative) of crude silyl ether **3.2** as a colorless liquid. The material was used for the next step without further purification. An analytical sample was obtained by passing a small amount of the crude material through a short pad of silica gel (80% Et_2O–hexanes): $[\alpha]^{24}_D$ 28.8 (*c* 2.35, $CHCl_3$); IR (film) 1760 cm^{-1}; ^1H NMR δ 0.047 (s, 3 H, $SiCH_3$), 0.074 (s, 3 H), 0.88 (s, 9 H), 1.38 (d, J = 6.7 Hz, 3 H), 3.70 (s, 3 H), 4.31 (q, J = 6.7 Hz, 1 H). Anal. Calcd for $C_{10}H_{22}O_3Si$: C, 55.00; H, 10.15. Found: C, 55.11; H, 10.10.

(*R*)-2-[(*tert*-Butyldimethylsilyl)oxy]propanal (3.3). To a solution of 20.0 g (91.6 mmol) of methyl ester **3.2** in 305 mL of Et_2O was added 110 mL (110 mmol) of 1.0 M DIBAL-H (in hexanes) at −78 °C over 10 min. The reaction mixture was gradually warmed to −40 °C over 1.5 h. TLC indicated complete reaction with formation of only a trace amount of a more polar alcohol byproduct. The reaction was quenched with a saturated solution of Rochelle's salt. After being warmed to rt, the mixture was stirred vigorously for 2 h and extracted three times with Et_2O. The combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure to give 17.8 g (quantitative) of aldehyde **3.3** as a light yellow liquid. This volatile liquid containing a small amount of solvent was used for the next step without further purification. A purified sample was obtained by passing a small amount through a short pad of silica gel (50% Et_2O–hexanes): $[\alpha]^{24}_D$ 12.8 (*c* 1.59, $CHCl_3$); IR (film) 1741 cm^{-1}; ^1H NMR δ 0.071 (s, 3 H), 0.083 (s, 3 H), 0.90 (s, 9 H), 1.26 (d, J = 6.9 Hz, 3 H), 4.07 (dq, J = 6.9, 1.3 Hz, 1 H), 9.59 (d, J = 1.3 Hz, 1 H); ^{13}C NMR δ 204.2, 73.8, 25.6, 18.5, −3.7, −4.8.

(*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-1,1-dibromo-1-butene (3.4). To a solution of 94.7 g (361 mmol) of Ph_3P in 451 mL of CH_2Cl_2 was added 59.9 g (181 mmol) of CBr_4 in five portions at 0 °C over 20 min. After being warmed to rt and stirred for 30 min, the mixture was recooled to 0 °C, followed by addition of 17.0 g (*ca.* 90.3 mmol) of aldehyde **3.3** in 26 mL of CH_2Cl_2 over 10 min. The reaction mixture was warmed to rt and stirred for 3 h. The solvent was mostly removed under reduced pressure, and ~300 mL of hexanes was added. After being stirred at room temperature for 1.5 h, the granular suspension was filtered through No. 2 Whatman filter paper and washed with three portions of hexanes. The combined filtrate and washings were concentrated under reduced pressure to yield a residue that contained solid particles. This material was chromatographed on silica gel. Elution with 5% Et_2O–hexanes afforded 26.5 g (85% based on methyl lactate) of dibromide **3.4**: $[\alpha]^{24}_D$ −6.1 (*c* 4.8, $CHCl_3$); ^1H NMR δ 0.052 (s, 3 H), 0.065 (s, 3 H), 0.87 (s, 9 H), 1.21 (d, J = 6.3 Hz, 3 H), 4.43 (dq, J = 7.8, 6.3 Hz, 1 H), 6.40 (d, J = 7.8 Hz, 1 H).

(*R*)-4-[(*tert*-Butyldimethylsilyl)oxy]-2-pentyn-1-ol (3.5). To a solution of 18.0 g (52.3 mmol) of dibromide **3.4** in 262 mL of THF was added 43.9 mL (110 mmol) of 2.5 M *n*-BuLi (in hexanes) at −78 °C over 10 min. The solution was stirred at −78 °C for 1 h. After the cooling bath was removed, the mixture was allowed to warm to near rt over 35 min and then recooled to −78 °C. To the solution was added 3.13 g (105 mmol) of dry paraformaldehyde in two portions over 5 min. After being gradually warmed to rt over 1 h, the mixture was stirred for an additional 2 h. The reaction was quenched with saturated NH_4Cl and extracted three times with Et_2O. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to afford 11.0 g (98%) of alcohol **3.5** as a light yellow liquid. This material was used in the next step without further purification. An analytical sample was obtained by passing a small amount through a short pad of silica gel (60% Et_2O–hexanes): $[\alpha]^{24}_D$ 53.0 (*c* 1.42, $CHCl_3$); ^1H NMR δ 0.094 (s, 3 H), 0.11 (s, 3 H), 0.89 (s, 9 H), 1.39 (d, J = 6.5 Hz, 3 H), 1.44 (t, J = 6.2 Hz, 1 H), 4.27 (dd, J = 6.2, 1.7 Hz, 2 H), 4.54 (tq, J = 6.5, 1.7 Hz, 1 H). Anal. Calcd for $C_{11}H_{22}O_2Si$: C, 61.63; H, 10.34. Found: C, 61.39; H, 10.25.

(*R*)-4-[(*tert*-Butyldimethylsilyl)oxy]-2-pentynyl 1,1,1-Trimethylacetate (3.6). To a solution of 5.71 g (*ca.* 26.6

mmol) of unpurified propargyl alcohol **3.5** in 133 mL of CH_2Cl_2 at 0 °C was successively added 4.92 mL (40.0 mmol) of trimethylacetyl chloride, 5 mg of DMAP, and 11.1 mL (79.9 mmol) of Et_3N (dropwise over 10 min). The cooling bath was removed, and the mixture was stirred for 3 h. The mixture was poured into saturated $NaHCO_3$, stirred for 30 min, and extracted three times with Et_2O. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to afford 7.80 g (98%) of pivalate **3.6** as a light yellow liquid. This material was used in the next step without further purification: ^1H NMR (400 MHz) δ 0.089 (s, 3 H), 0.10 (s, 3 H), 0.88 (s, 9 H), 1.19 (s, 9 H), 1.38 (d, J = 6.5 Hz, 3 H), 4.52 (tq, J = 6.5, 1.8 Hz, 1 H), 4.65 (d, J = 1.8 Hz, 2 H).

(*R*)-4-Hydroxy-2-pentynyl 1,1,1-Trimethylacetate (3.7). To a solution of 7.50 g (*ca.* 25 mmol) of unpurified silyl ether **3.6** in 25 mL of THF was added 55.3 mL (55.3 mmol) of 1 M TBAF (in THF) at 0 °C over 5 min. The cooling bath was removed, and the mixture was stirred for 1.5 h. After being recooled to 0 °C, the mixture was poured into ice–water and extracted three times with Et_2O. The combined extracts were washed with brine, dried over anhydrous $MgSO_4$, concentrated under reduced pressure, and chromatographed on silica gel. Elution with 45% Et_2O–hexanes afforded 4.20 g (90%) of propargyl alcohol **3.7** as a colorless oil (87% from dibromide **3.4**): $[\alpha]^{24}_D$ 17.6 (*c* 1.73, $CHCl_3$); ^1H NMR δ 1.20 (s, 9 H), 1.43 (d, J = 6.6 Hz, 3 H), 4.53 (tq, J = 6.6, 1.7 Hz, 1 H), 4.66 (d, J = 1.7 Hz, 2 H). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.18; H, 8.76. Found: C, 65.17; H, 8.78.

(*R*)-1-Methyl-4-(1,1,1-trimethylacetoxy)-2-butynyl Methanesulfonate (3.8). The procedure for the mesylate precursor of **2.5** was applied to 3.50 g (19.0 mmol) of alcohol **3.7**, 5.29 mL (38.0 mmol) of Et_3N and 2.21 mL (28.5 mmol) of MsCl in 76 mL of CH_2Cl_2 at −78 °C to afford 5.00 g (quantitative) of mesylate **3.8** as a colorless liquid. This material was used for the next step without further purification: ^1H NMR δ 1.19 (s, 9 H), 1.62 (d, J = 6.7 Hz, 3 H), 3.94 (s, 3 H), 4.68 (d, J = 1.6 Hz, 2 H), 5.30 (tq, J = 6.7, 1.6 Hz, 1 H).

(S)-2-(Tributylstannyl)-2,3-pentadienyl 1,1,1-Trimethylacetate (3.9). The procedure for stannane **2.5** was applied to 3.86 mL (27.5 mmol) of *i*-Pr_2NH, 2 mg of BHT, 10.6 mL (26.6 mmol) of 2.5 M *n*-BuLi, 7.15 mL (26.6 mmol) of Bu_3SnH, 5.00 g (*ca.* 19 mmol) of mesylate **3.8**, and 5.49 g (26.6 mmol) of $CuBr{\cdot}SMe_2$ to afford 7.10 g (82% for two steps) of allenyl stannane **3.9** as a colorless liquid: $[\alpha]^{24}_D$ 49.6 (*c* 1.97, $CHCl_3$); IR (film) 1936, 1732 cm^{-1}; ^1H NMR δ 0.85–1.49 (m, 27 H), 1.19 (s, 9 H), 1.58 (d, J = 6.9 Hz, 3 H), 4.53–4.59 (d, m, 2 H), 4.63–4.75 (m, 1 H). Anal. Calcd for $C_{22}H_{42}O_2Sn$: C, 57.79; H, 9.26. Found: C, 57.55; H, 9.14.

Bis-Acrylate of (*R,R*)-Hydrobenzoin (6.2). To a suspension of 5.00 g (23.4 mmol) of (*R, R*)-hydrobenzoin[10] in 116 mL of CH_2Cl_2 was added 13.7 mL (98.0 mmol) of Et_3N at rt. The resultant solution was cooled to 0 °C, and 5.92 mL (70.0 mmol) of acryloyl chloride was added dropwise over 10 min. After being stirred at 0 °C for 20 min, the mixture was poured into 58 mL of water. After brief shaking, the organic layer was separated and the aqueous layer was extracted twice with CH_2Cl_2. The combined extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give 8.20 g (quantitative) of bis-acrylate **6.2** as a yellow solid which was slightly contaminated with $Et_3N{\cdot}HCl$. This material was used for the next step without further purification. An analytical sample was obtained by filtration through a short pad of silica gel (Et_2O) and recrystallization from 1:4 CH_2Cl_2–hexanes: mp 113 °C; $[\alpha]^{24}_D$ 10.2 (*c* 1.30, $CHCl_3$); ^1H NMR (400 MHz) δ 5.83 (dd, J = 10.4, 1.4 Hz, 2 H), 6.12 (dd, J = 17.3, 10.4 Hz, 2 H), 6.15 (s, 2 H), 6.41 (dd, J = 17.3, 1.4 Hz, 2 H), 7.13–7.20 (m, 10 H); ^{13}C NMR δ 164.9, 135.9, 131.4, 128.5, 128.22, 128.16, 127.6, 76.7. Anal. Calcd for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63. Found: C, 74.71; H, 5.68.

Bis-(*R*)-3-Cyclohexenecarboxylate of (*R,R*)-Hydrobenzoin (6.3). To a solution of 1.49 g (*ca.* 4.24 mmol) of bis-acrylate **6.2** in 21 mL of CH_2Cl_2 was added 4.20 mL (4.20 mmol) of 1 M $TiCl_4$ (in CH_2Cl_2) at −50 °C. The brown solution was stirred for 15 min, and 2.1 mL (26 mmol) of 1,3-butadiene (condensed into a calibrated test tube through a column of anhydrous $CaSO_4$ at −78 °C) was added by cannula. A small amount of precipitate formed but then dissolved as the reaction mixture was warmed to −25 °C with stirring. After 3 days, a suspension again formed. The mixture was poured into 21 mL of water, and after warming to rt, the organic layer was separated and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give 1.99 g of diester **6.3** as a yellow solid. This material in Et_2O was filtered through a short pad of silica gel and recrystallized from 4:1 Et_2O–hexanes to yield 1.53 g (84%) of diester **6.3** as white cubic crystals: mp 99 °C; $[\alpha]^{24}_D$ 41.1 (*c* 1.34, $CHCl_3$); IR (CH_2Cl_2) 1732 cm^{-1}; ^1H NMR (400 MHz) δ 1.56–1.66, 1.93–1.98 (m, 4 H), 2.04–2.06 (m, 4 H), 2.19–2.21 (m, 4 H), 2.53–2.61 (m, 2 H), 5.62–5.68 (m, 4 H), 6.07 (s, 2 H), 7.10–7.19 (m, 10 H); ^{13}C NMR δ 174.4, 136.3, 128.3, 128.2, 127.4, 126.7, 125.0, 77.0, 39.4, 27.3, 24.8, 24.3. Anal. Calcd for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02. Found: C, 78.06; H, 7.07.

The ^1H and ^{13}C NMR spectra and the GC indicated only one diastereomer. Reduction of the recrystallized cycloadduct with $LiAlH_4$ (see below) gave alcohol **6.5** of 97% ee based on optical rotation.[12] Reduction of the crude cycloadduct gave alcohol **6.5** of 90–92% ee.

(*R*)-3-Cyclohexenecarboxylic Acid (6.4). To a suspension of 1.43 g (3.32 mmol) of recrystallized diester **6.3** in 8 mL of MeOH was added 318 mg (13.3 mmol) of LiOH at rt. After being stirred for 12 h at rt, the suspension became homogeneous. The mixture was then treated with 4.0 mL of water and stirred for an additional 12 h. About half of the solvent was removed under reduced pressure with slight heating. The resulting slurry was diluted with half-saturated $NaHCO_3$ solution and extracted twice with Et_2O. From the extracts, 662 mg (93%) of (*R,R*)-hydrobenzoin was recovered after crystallization from Et_2O–hexanes. The aqueous layer was slowly acidified with 3 N HCl with ice cooling and the acidic mixture was extracted three times with Et_2O, washed with brine, dried over anhydrous $MgSO_4$, concentrated under reduced pressure, and chromatographed on silica gel. Elution with 80% Et_2O–hexanes afforded 771 mg (92%) of carboxylic acid **6.4** as a colorless liquid: $[\alpha]^{24}_D$ 89.6 (*c* 6.45, MeOH) (lit.[12] $[\alpha]^{22}_D$ 94.5 (*c* 7.00, MeOH)) corresponding to an ee of 95%; IR (film) 3023 (br), 1700 cm^{-1}; ^1H NMR (400 MHz) δ 1.64–1.74, 1.99–2.09 (m, 2 H), 2.10–2.20 (m, 2 H), 2.24–2.28 (m, 2 H), 2.55–2.62 (m, 1 H), 5.64–5.70 (m, 2 H). Anal. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.49; H, 7.98.

In a separate experiment 5.66 g (71%) of carboxylic acid was obtained from 13.7 g (31.8 mmol) of cycloadduct after short path distillation (85–90 °C, 0.9 Torr).

(*R*)-1-(3-Cyclohexenyl)methanol (6.5). To a solution of 100 mg (0.232 mmol) of recrystallized diester **6.3** in 4.5 mL of THF was added 0.46 mL (0.46 mmol) of 1 M $LiAlH_4$ (in THF) at 0 °C. The mixture was stirred at 0 °C for 3 h and then quenched by careful addition of a saturated solution of Rochelle's salt. After being stirred for an additional 30 min, the mixture was extracted three times with ether. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and chromatographed on silica gel. Elution with 45% Et_2O–hexanes afforded 48.5 mg (93%) of alcohol **6.5** as a colorless liquid: $[\alpha]^{24}_D$ 92.7 (*c* 2.51, MeOH) (lit.[12] $[\alpha]_D$ 96 (*c* 3.0, MeOH)) corresponding to an ee of 97%; IR (film) 3333, 1656 (very w) cm^{-1}; ^1H NMR (400 MHz) δ 1.20–1.33 (m, 1 H), 1.59 (br. s, 1 H), 1.67–1.80 (m, 3 H), 2.02–2.11 (m, 3 H), 3.46–3.54 (m, 2 H), 5.62–5.67 (m, 2 H); ^{13}C NMR δ 127.1. 125.9, 67.8, 36.3, 28.1, 25.2, 24.6.

This compound was volatile and prolonged solvent removal with a vacuum pump led to significant material loss.

Reduction of the crude diester (200 mg) from the Diels–Alder reaction by the above procedure gave alcohol (92.9 mg, 89% yield) of $[\alpha]^{24}_D$ 88.3 (*c* 2.42, MeOH) corresponding to ~90–92% ee.

(1*R*,2*R*,5*R*)-2-Iodo-7-oxabicyclo[3.2.1]octan-6-one (8.1). A solution of 1.52 g (18.1 mmol) of $NaHCO_3$ in 25 mL of water was added to 760 mg (6.02 mmol) of carboxylic acid **6.4** with ice cooling. After the suspension dissolved, a solution of 6.0 g

(36.1 mmol) of KI and 1.61 g (6.33 mmol) of iodine in 15 mL of water was added. The mixture was warmed to rt and stirred for 24 h. The resulting suspension was treated with $CHCl_3$, and the aqueous layer was extracted 4 times with $CHCl_3$. The combined extracts were washed with half-saturated $Na_2S_2O_3$, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The resulting yellow solid (1.50 g) was dissolved in ~4 mL of EtOH with slight heating. After standing at rt for 3 days, the colorless crystalline solid was collected by filtration and dried under reduced pressure to provide 1.30 g (86%) of iodo lactone **8.1**: mp 132 °C (lit.[22] mp 135–136 °C); $[\alpha]^{24}_D$ 40.9 (*c* 2.49, $CHCl_3$) (lit.[22] $[\alpha]^{24}_D$ 37.6 (*c* 2.03, $CHCl_3$)); ^1H NMR (400 MHz) δ 1.82–1.86 (m, 1 H), 1.86–1.92 (m, 1 H), 2.10 (dd, J = 16.5, 5.3 Hz, 1H), 2.35–2.47 (m, 2 H), 2.65 (br s, 1 H), 2.78 (dd, J = 12.3 Hz, 1H), 4.49 (br t, J = 5.3 Hz, 1 H), 4.80 (br t, J = 5.0 Hz, 1 H).

(1*R*,5*R*)-7-Oxabicyclo[3.2.1]oct-2-en-6-one (8.2). To a solution of 1.01 g (4.01 mmol) of iodo lactone **8.1** in 28 mL of THF was added 0.90 mL (6.0 mmol) of DBU, and the mixture was stirred at reflux for 8 h. Upon being cooled to rt, the mixture was poured into 0.5 N HCl and extracted three times with Et_2O. The combined extracts were washed with brine, dried over anhydrous $MgSO_4$, concentrated under reduced pressure, and chromatographed on silica gel. Elution with 80% Et_2O–hexanes afforded 453 mg (91%) of olefin **8.2** as a colorless liquid: $[\alpha]^{24}_D$ 191 (*c* 3.18, $CHCl_3$) (lit.[22] $[\alpha]^{23}_D$ 179.2 (*c* 9.76, $CHCl_3$)); IR (film) 1770, 1634 cm^{-1}; ^1H NMR δ 2.03 (d, J =11.2 Hz, 1 H), 2.32–2.52 (m, 2 H), 2.44 (d, J = 11.2 Hz, 1H), 2.84 (m, 1 H), 4.70 (t, J = 5.4 Hz, 1H), 5.75–5.80 (m, 1 H), 6.14–6.19 (m, 1 H). Anal. Calcd for $C_7H_8O_2$: C, 67.73; H, 6.50. Found: C, 67.66; H, 6.51.

In general, a near-quantitative yield of crude product was obtained and this could be used in the next step without further purification.

Methyl (1*R*,3*R*)-3-Hydroxy-4-cyclohexenecarboxylate (8.3). To a solution of 389 mg (3.13 mmol) of lactone **8.2** in 16 mL of anhydrous MeOH was added 263 mg (3.13 mmol) of $NaHCO_3$. The mixture was stirred at rt for 10 h and the solvent was removed under reduced pressure with slight heating (~35 °C). The residue was diluted with water and extracted three times with Et_2O. The combined extracts were washed with brine, dried over anhydrous $MgSO_4$, concentrated under reduced pressure, and chromatographed on silica gel. Elution with 90% Et_2O–hexanes afforded 460 mg (94%) of alcohol **8.3** as a colorless liquid: $[\alpha]^{24}_D$ −4.6 (*c* 2.25, $CHCl_3$); ^1H NMR δ 1.66 (ddd, J =12.9, 11.0, 8.3 Hz, 1 H), 2.07–2.27 (m, 3 H), 2.61–2.70 (m, 2 H), 3.64 (s, 3 H), 4.23 (br s, 1H), 5.65–5.73 (m, 2 H); ^{13}C NMR δ 175.7, 130.9, 126.8, 66.0, 51.9, 37.8, 34.1, 27.4. Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.42; H, 7.72.

In general, a near-quantitative yield of crude product was obtained, and this material was used in the next step without further purification.

The (*S*)- and (*R*)-*O*-methylmandelates[23] of alcohol **8.3** were found to be diastereomerically pure according to the ^1H NMR spectra. (*S*)-Mandelate: ^1H NMR δ 1.60 (ddd, J = 12.6, 12.4, 9.6 Hz, 1 H), 2.18–2.27 (m, 3 H), 2.63 (m, 1 H), 3.38 (s, 3 H), 3.62 (s, 3H), 4.73 (s, 1 H), 5.43 (m, H), 5.63 (m, 1H), 5.86 (m, 1 H), 7.28–7.43 (m, 5 H). (*R*)-Mandelate: ^1H NMR δ 1.75 (ddd, J = 12.4, 12.1, 9.3 Hz, 1 H), 2.24–2.28 (m, 2 H), 2.34–2.42 (m, 1 H), 2.68 (m, 1 H), 3.39 (s, 3 H), 3.67 (s, 3 H), 4.72 (s, 1 H), 5.40–5.44 (m, 2 H), 5.75–5.82 (m, 1 H), 7.28–7.43 (m, 5 H).

Methyl (1*R*,3*R*)-3-Methoxy-4-cyclohexenecarboxylate (8.4). To a solution of 410 mg (2.63 mmol) of alcohol **8.3** in 13 mL of CH_2Cl_2 was added 1.62 g (7.88 mmol) of 2,6-di-*tert*-butyl-4-methylpyridine in one portion. The solution was cooled to 0 °C, followed by addition of 0.89 mL (7.9 mmol) of methyl triflate over 3 min. After being stirred at rt for 20 h, the mixture was poured into a saturated $NaHCO_3$ solution and extracted three times with CH_2Cl_2. The combined extracts were washed with brine, dried over anhydrous $MgSO_4$, concentrated under reduced pressure, and chromatographed on silica gel. Elution with 5% Et_2O–hexanes afforded 1.60 g (99%) of recovered pyridine base. Further elution with 20% Et_2O–hexanes provided 385 mg (86%) of methyl ether **8.4** as a colorless liquid: $[\alpha]^{24}_D$ −32.9 (*c* 1.54, $CHCl_3$) (lit.[24] $[\alpha]^{23}_D$ −28.3 (*c* 0.46, $CHCl_3$)); IR (film) 1736 cm^{-1}; ^1H NMR (400 MHz) δ 1.61 (dt, J =12.4, 9.5 Hz, 1 H), 2.23–2.26 (m, 2 H), 2.33–2.37 (m, 1 H), 2.57–2.65 (m, 1 H), 3.35 (s, 3 H), 3.68 (s, 3 H), 3.85–3.92 (m, 1H), 5.70–5.79 (m, 2 H).

(1*R*,2*R*,4*R*)-4-Carbomethoxy-2-methoxycyclohexanol (8.5). To a solution of 1.70 g (9.99 mmol) of olefin **8.4** in 100 mL of THF was added 15.0 mL (15.0 mmol) of 1.0 M BH_3·THF complex dropwise at −78 °C over 10 min. After being stirred at −78 °C for 40 min and then at 0 °C for 1 h, the reaction was quenched by careful addition of 5.7 mL (17 mmol) of 3 N NaOH solution and 1.9 mL (17 mmol) of 30% H_2O_2. The mixture was warmed to room temperature and stirred for 3 h. Upon being cooled back to 0 °C, the mixture was treated with 8 mL of saturated $Na_2S_2O_3$ and stirred for 5 min. The mixture was diluted with 15 mL of water and extracted six times with EtOAc, and the combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to yield 1.80 g of crude alcohol **8.5**. The ^1H NMR spectrum indicated the presence of three isomers in the ratio of about 81:11:3 (based on integration of the methyl signals). Chromatography on silica gel (70–85% EtOAc–hexanes) afforded 1.64 g (87%) of alcohol **8.5** as a colorless oil. This product was contaminated with less than 9% of one of the two unidentified isomers. An analytical sample was obtained by a second chromatography on silica gel (80% EtOAc-hexanes): $[\alpha]^{24}_D$ −82.5 (*c* 1.50, $CHCl_3$) (lit.[24] $[\alpha]^{23}_D$ −72.4 (*c* 1.25, $CHCl_3$)); IR (film) 3444, 1732 cm^{-1}; ^1H NMR (400 MHz) δ 1.23–1.37 (m, 2H), 1.46 (dq, J =13.1, 3.2 Hz, 1 H), 1.93–2.00 (m, 1 H), 2.05 (ddd, J = 12.7, 4.5, 3.3 Hz, 1H), 2.28–2.39 (m, 2 H), 2.73 (br s, 1 H), 2.93–2.99 (m, 1H), 3.39 (s, 3 H), 3.40–3.43 (m, 1H), 3.66 (s, 3 H). Anal. Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.53; H, 8.53.

Methyl (1*R*,3*R*,4*R*)-3-Methoxy-4-[(triisopropylsilyl)oxy]cyclohexanecarboxylate (8.6). To a solution of 310 mg (1.65 mmol) of alcohol **8.5** in 16 mL of CH_2Cl_2 was successively added 0.39 mL (2.8 mmol) of Et_3N and 0.58 mL (2.1 mmol) of triisopropylsilyl triflate at 0 °C. After being stirred at 0 °C for 1 h, the mixture was poured into saturated $NaHCO_3$ and extracted three times with CH_2Cl_2. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, concentrated under reduced pressure, and chromatographed on silica gel. Elution with 15% Et_2O–hexanes afforded 516 mg (91%) of silyl ether **8.6** as a colorless liquid: $[\alpha]^{24}_D$ −42.8 (*c* 1.82, $CHCl_3$) (lit.[24] $[\alpha]^{23}_D$ −43.0 (*c* 1.62, $CHCl_3$)); IR(film) 1739 cm^{-1}; ^1H NMR δ 1.04–1.05 (m, 21 H), 1.30–1.51 (m, 3 H), 1.85–1.92 (m, 1 H), 1.98–2.00 (m, 1 H), 2.23–2.36 (m, 2 H), 2.97 (ddd, J =10.0, 7.7, 4.2 Hz, 1 H), 3.35 (s, 3 H), 3.60 (ddd, J = 9.6, 8.0, 4.4 Hz, 1H), 3.65 (s, 3 H); ^{13}C NMR δ 175.2, 83.2, 73.4, 57.2, 51.6, 40.4, 32.2, 31.0, 25.7, 18.0, 12.5. Anal. Calcd for $C_{18}H_{36}O_4Si$: C, 62.74; H, 10.53. Found: C, 62.69; H, 10.47.

(1*R*,3*R*,4*R*)-3-Methoxy-4-[(triisopropylsilyl)oxy]cyclohexanecarboxaldehyde (9.1). To a solution of 501 mg (1.45 mmol) of ester **8.6** in 10 mL of anhydrous hexanes was added 1.74 mL (1.74 mmol) of 1 M DIBAL-H solution (in hexanes) dropwise at −78 °C. The mixture was warmed to −20 °C and stirred for 2.5 h. Upon being quenched with saturated Rochelle salt solution, the mixture was stirred at rt for 1 h and extracted three times with Et_2O. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The ^1H NMR spectrum revealed the presence of a small amount of alcohol reduction product. Chromatography on silica gel (15% Et_2O–hexanes) yielded 407 mg (89%) of aldehyde **9.1** as a yellow liquid: $[\alpha]^{24}_D$ −49.8 (*c* 1.67, $CHCl_3$) (lit.[24] $[\alpha]^{23}_D$ −49.7 (*c* 1.25, $CHCl_3$)); IR (film) 1728 cm^{-1}; ^1H NMR δ 1.04–1.06 (m, 21 H), 1.38–1.47 (m, 1 H), 1.58–1.69 (m, 2 H), 1.58–1.69 (m, 2 H),

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1.86–1.94 (m, 2 H), 2.18–2.27 (m, 2 H), 3.13 (ddd, J =10.3, 7.5, 4.2 Hz, 1 H), 3.32 (s, 3 H), 3.75 (ddd, J = 10.3, 7.9, 4.5 Hz, 1H), 9.64 (s, 1 H); ^{13}C NMR δ 203.8, 81.3, 70.8, 57.0, 46.2, 29.0, 26.9, 20.8, 18.1, 12.4.

(*E*)-2-Methyl-3-[(1*R*,3*R*,4*R*)-3-methoxy-4-[(triisopropylsilyl)oxy]cyclohexyl]-2-propenal (9.2). To a solution of 1.91 g (8.39 mmol) of the *N-tert*-butylimine of 2-(triethylsilyl)-propanal[5] in 28 mL of THF was added 3.36 mL (8.39 mmol) of 2.5 M *n*-BuLi (in hexanes) dropwise at −78 °C. The reaction mixture was gradually warmed to −30 °C over 1.5 h and then recooled to −78 °C. To the yellow solution was added 1.76 g (5.60 mmol) of aldehyde **9.1** as a solution in 2 mL of THF. After being gradually warmed to −23 °C over 1.5 h, the mixture was treated with 1.5 mL of TFA and then warmed to 0 °C and stirred for 3 h, followed by addition of 3.1 mL of water. After being stirred at 0 °C for an additional 12 h (overnight), the mixture was diluted with water and extracted three times with Et_2O. The combined organic extracts were successively washed with saturated $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The resulting brown residue was chromatographed on silica gel. Elution with 20% Et_2O–hexanes yielded 1.85 g (93%) of aldehyde **9.2** as a yellow liquid: $[\alpha]^{24}_D$ −28.5 (*c* 1.36, $CHCl_3$); IR (film) 1694, 1641 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.06–1.12 (m, 21 H), 1.12–1.26 (m, 2 H), 1.39–1.50 (m, 1 H), 1.67–1.70 (m, 1 H), 1.74 (d, J = 1.3 Hz, 3 H), 1.97–2.06 (m, 2 H), 2.57 (m, 1 H), 3.04 (ddd, J =10.3, 7.5, 4.3 Hz, 1 H), 3.36 (s, 3 H), 3.62 (ddd, J = 10.3, 7.9, 4.5 Hz, 1H), 6.29 (d, J = 9.5 Hz, 1 H), 9.36 (s, 1 H); ^{13}C NMR δ 195.4, 157.4, 138.0, 83.7, 74.1, 57.5, 35.8, 34.3, 33.1, 29.2, 18.1, 12.6, 9.3. Anal. Calcd for $C_{20}H_{38}O_3Si$: C, 67.74; H, 10.80. Found: C, 67.73; H, 10.76.

(*E*,4*R*,5*S*)-4,6-Dimethyl-5-hydroxy-7-[(1*R*,3*R*,4*R*)-3-methoxy-4-[(triisopropylsilyl)oxy]cyclohexyl]-6-hepten-2-ynyl 1,1,1-Trimethylacetate (9.3) and (*E*,4*R*,5*R*)-4,6-Dimethyl-5-hydroxy-7-[(1*R*,3*R*,4*R*)-3-methoxy-4-[(triisopropylsilyl)oxy]cyclohexyl]-6-hepten-2-ynyl 1,1,1-Trimethylacetate (9.4). The procedure for alcohol **2.11** was applied to 1.51 g (4.26 mmol) of aldehyde **9.2**, 4.28 g (9.37 mmol) of (*S*)-allenylstannane **3.9**, and 1.57 mL (12.8 mmol) of $BF_3{\cdot}OEt_2$ in 7 mL of CH_2Cl_2 at −45 °C for 60 h. The ^{1}H NMR (400 MHz) spectrum of the crude material showed signals for the *syn* and *anti* carbinyl protons at 3.90 and 3.73 ppm. Integration of these signals indicated an ~85:15 ratio of isomers favoring the *syn* adduct. This material was chromatographed on silica gel. Elution with 10% Et_2O–hexanes yielded 1.46 g (34%) of recovered stannane **3.9**. Further elution with 50% Et_2O–hexanes provided 2.00 g (90%) of an inseparable 85:15 *syn/anti* mixture of alcohols **9.3** and **9.4**.

9.3: ^{1}H NMR (400 MHz) δ 0.93–1.19 (m, 2 H, broad), 1.06–1.20 (m, 21 H), 1.12 (d, J = 6.9 Hz, 3 H), 1.19 (s, 9 H), 1.34–1.43 (m, 1 H), 1.50–1.60 (m, 1 H), 1.62 (d, J = 1.3 Hz, 3 H), 1.77 (d, J = 3.6 Hz, 1 H), 1.90 (m, 2 H), 2.26 (m, 1 H), 2.68 (m, 1 H), 2.96 (ddd, J =10.3, 7.6, 4.0 Hz, 1 H), 3.37 (s, 3 H), 3.53 (ddd, J = 10.3, 8.1, 4.4 Hz, 1 H), 3.90 (dd, J = 6.4, 3.6 Hz, 1 H), 4.60 (d, J = 2.1 Hz, 2 H), 5.25 (d, J = 9.1 Hz, 1H); MS (EI$^+$) *m/e* (relative intensity) 523 ([M + H]$^+$, 20), 505 (40), 473 (100), 447 (25); HRMS (EI$^+$) calcd for $C_{27}H_{47}O_5Si$ ([M − *i*-Pr]$^+$) 479.3193, found 479.3193.

9.4: ^{1}H NMR (400 MHz) δ 0.93–1.19 (m, 2 H, broad), 1.12 (d, 3 H, broad), 1.18 (m, 21 H), 1.19 (s, 9 H), 1.34–1.43 (m, 1 H), 1.50–1.60 (m, 1 H), 1.59 (d, J = 1.3 Hz, 3 H), 1.90 (m, 2 H), 2.17 (d, J = 3.5 Hz, 1 H), 2.26 (m, 1 H), 2.68 (m, 1 H), 2.96 (ddd, J = 10.3, 7.6, 4.0 Hz, 1 H), 3.36 (s, 3 H), 3.53 (ddd, J = 10.3, 8.1, 4.4 Hz, 1 H), 3.73 (dd, J = 8.1, 3.1 Hz, 1 H), 4.64 (d, J = 2.0 Hz, 2 H), 5.21 (d, J = 9.1 Hz, 1 H). Anal. Calcd for $C_{30}H_{54}O_5Si$: C, 68.92; H, 10.41. Found: C, 68.79; H, 10.60.

(*E*,4*R*,5*S*)-4,6-Dimethyl-5-[(*p*-methoxybenzyl)oxy]-7-[(1*R*,3*R*,4*R*)-3-methoxy-4-[(triisopropylsilyl)oxy]cyclohexyl]-6-hepten-2-ynyl 1,1,1-Trimethylacetate (9.5) and (*E*,4*R*,5*R*)-4,6-Dimethyl-5-[(*p*-methoxybenzyl)oxy]7-[(1*R*,3*R*,4*R*)-3-methoxy-4-[(triisopropylsilyl)oxy]cyclohexyl]-6-hepten-2-ynyl 1,1,1-Trimethylacetate (9.6). To a solution of 1.65 g (3.16 mmol) of alcohols **9.3** and **9.4** (85:15) and 1.78 g (6.31 mmol) of *p*-methoxybenzyl trichloroacetimidate[25] in 32 mL of anhydrous Et_2O was added *ca.* 20 μL of triflic acid at 0 °C. The reaction mixture was gradually warmed to rt over 50 min. The mixture was poured into water and extracted three times with Et_2O, and the combined organic extracts were successively washed with saturated $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on silica gel. Elution with 10% Et_2O–hexanes afforded 1.52 g (75%) of *syn* PMB ether **9.5** as a yellow liquid. The more polar *anti* product **9.6** (310 mg) was eluted along with some unknown impurities.

9.5: $[\alpha]^{24}_D$ −58.5 (*c* 1.41, $CHCl_3$); IR (film) 1737, 1613 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.01–1.12 (m, 2 H, broad), 1.06–1.16 (m, 21 H), 1.17 (s, 9 H), 1.19 (d, J = 6.9 Hz, 3 H), 1.33–1.43 (m, 1 H), 1.53–1.67 (m, 1 H), 1.60 (d, J = 1.2 Hz, 3 H), 1.90–1.94 (m, 1 H), 2.04 (d, J = 12.6 Hz, 1 H), 2.32–2.34 (m, 1 H), 2.64–2.68 (m, 1 H), 3.00 (ddd, J =10.9, 7.5, 3.6 Hz, 1 H), 3.35 (d, J = 8.9 Hz, 1 H), 3.41 (s, 3 H), 3.56 (ddd, J = 10.6, 8.0, 4.7 Hz, 1H), 3.76 (s, 3 H), 4.26 (AB q, J_{AB} = 11.5 Hz, $\Delta\nu$ = 108 Hz, 2 H), 4.55 (d, J = 2.1 Hz, 2 H), 5.16 (d, J = 9.0 Hz, 1 H), 6.84 (d, J = 8.7 Hz, 2 H), 7.18 (d, J = 8.7 Hz, 2 H); ^{13}C NMR δ 177.8, 159.1, 135.3, 131.4, 130.5, 129.5, 113.7, 88.6, 87.3, 84.5, 75.8, 75.0, 69.5, 57.7, 55.2, 52.7, 38.7, 36.5, 35.0, 34.1, 30.7, 29.9, 27.1, 18.1, 17.8, 12.6, 11.0; MS (EI$^+$) *m/e* (relative intensity) 642 (M$^+$, 1), 599 ([M − *i*-Pr]$^+$, 100), 597 (25), 475 (38); HRMS (EI$^+$) calcd for $C_{35}H_{55}O_6Si$ ([M − *i*-Pr]$^+$) 599.3768, found 599.3769.

9.6: ^{1}H NMR (400 MHz) δ 0.95 (d, J = 7.0 Hz, 3 H), 1.01–1.14 (m, 2 H, broad), 1.06–1.16 (m, 21 H), 1.20 (s, 9 H), 1.35–1.44 (m, 1 H), 1.55 (d, s, 3 H), 1.56–1.65 (m, 1 H), 1.93–1.97 (m, 2 H), 2.30–2.32 (m, 1 H), 2.62–2.66 (m, 1 H), 2.97 (ddd, J =10.9, 7.5, 3.6 Hz, 1 H), 3.37 (s, 3 H), 3.55 (ddd, J = 10.6, 8.0, 4.5 Hz, 1H), 3.78 (s, 3 H), 4.27 (AB q, J_{AB} = 11.9 Hz, $\Delta\nu$ = 108 Hz), 4.66 (d, J = 1.8 Hz, 2 H), 5.13 (d, J = 8.5 Hz, 1 H), 6.84 (d, J = 8.4 Hz, 2 H), 7.24 (d, J = 8.4 Hz, 2 H).

(2*E*,4*R*,5*S*,6*E*)-4,6-Dimethyl-5-[(*p*-methoxybenzyl)oxy]-7-[(1*R*,3*R*,4*R*)-3-methoxy-4-[(triisopropylsilyl)oxy]cyclohexyl]-2,6-heptadien-1-ol (10.1). To a solution of 1.33 g (2.07 mmol) of ester **9.5** in 41 mL of THF was added 3.73 mL (12.4 mmol) of 65+ wt % sodium bis(2-methoxyethoxy)-aluminum hydride (Red-Al) solution in toluene dropwise at 0 °C. After being stirred at 0 °C overnight (15 h), the reaction was carefully quenched with saturated Rochelle salt solution. The mixture was stirred for an additional 2 h and extracted three times with Et_2O. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, concentrated under reduced pressure, and chromatographed on silica gel. Elution with 50% Et_2O–hexanes yielded 1.05 g (91%) of allylic alcohol **10.1** as a colorless thick liquid: $[\alpha]^{24}_D$ −55.4 (*c* 1.51, $CHCl_3$); IR (film) 3445, 1613, 1608 cm^{-1}; ^{1}H NMR δ 0.97–1.02 (m, 1 H), 1.03 (d, broad), 1.06 (m, 21 H), 1.09–1.15 (m, 1 H), 1.30–1.50 (m, 2 H), 1.54 (d, J = 1.2 Hz, 3 H), 1.88–1.94 (m, 1 H), 2.03 (d, J = 6.7 Hz, 1 H), 2.23–2.39 (m, 2 H), 2.98 (ddd, J =11.2, 8.4, 4.1 Hz, 1 H), 3.22 (d, J = 9.0 Hz, 1 H), 3.41 (s, 3 H), 3.55 (ddd, J = 11.0, 8.4, 4.7 Hz, 1 H), 3.76 (s, 3 H), 3.98 (t, J = 5.5 Hz, 2 H), 4.25 (AB q, J_{AB} = 11.6 Hz, $\Delta\nu$ = 86.4 Hz, 2 H), 5.05 (d, J = 8.1 Hz, 1 H), 5.38 (dd, J = 15.5, 7.9 Hz, 1 H), 5.53 (dt, J = 15.5, 5.5 Hz, 1 H), 6.84 (d, J = 8.6 Hz, 2 H), 7.20 (d, J = 8.6 Hz, 2 H); ^{13}C NMR δ 159.0, 135.1, 134.5, 132.3, 130.8, 129.4, 128.0, 113.7, 88.3, 84.4, 75.0, 69.3, 63.8, 57.7, 55.2, 39.2, 36.5, 34.9, 34.1, 30.8, 18.1, 17.2, 12.6, 11.3; MS (EI$^+$) *m/e* (relative intensity) 578 ([M + NH$_4$]$^+$, 17), 423 (35), 355 (15), 137 (70), 121 (100); HRMS (EI$^+$) calcd for $C_{30}H_{49}O_5Si$ ([M − *i*-Pr]$^+$) 517.3349, found 517.3336.

(*E*,2*R*,3*R*,4*S*,5*S*)-4,6-Dimethyl-2,3-Epoxy-5-[(*p*-methoxybenzyl)oxy]-7-[(1*R*,3*R*,4*R*)-3-methoxy-4-[(triisopropylsilyl)oxy]cyclohexyl]-6-hepten-1-ol (10.2). To a suspension of 238 mg of powdered molecular sieves (activated) in 15 mL of CH_2Cl_2 at −22 °C was successively added 0.27 mL (1.6 mmol) of D-(−)-diethyl tartrate, 0.35 mL (1.2 mmol) of Ti(O*i*-Pr)$_4$ and 0.63 mL (3.2 mmol) of TBHP (dried over granular 4 A molecular sieves before use). The mixture was stirred at

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−22 °C for 50 min, and then 890 mg (1.59 mmol) of allylic alcohol **10.1** in 3 mL of CH_2Cl_2 was added dropwise over 5 min. The reaction mixture was stirred at −22 °C for 15 h, warmed to 0 °C, and quenched with 6 mL of water. After 30 min without external cooling, the mixture was treated with 3 mL of 30% NaOH (saturated with NaCl), stirred for 40 min, and diluted with CH_2Cl_2. The aqueous layer was extracted four times with CH_2Cl_2. The combined organic extracts were filtered through a short pad of Celite 545 to remove particulates, and the filtrate was washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to afford a yellow residue. The ^1H NMR spectrum indicated two compounds in a ratio of 97.5:2.5. The residue was chromatographed on silica gel. Elution with 65% Et_2O–hexanes afforded 832 mg (91%) of epoxide **10.2** as a colorless liquid: $[\alpha]^{24}_D$ −60.6 (*c* 1.37, $CHCl_3$); IR (film) 3444, 1612 cm^{-1}; ^1H NMR δ 1.02 (br d, 3 H), 1.06 (m, 21 H), 1.19 (t, 1 H, J = 7.0 Hz), 1.34–1.41 (m, 1 H), 1.51–1.55 (m, 1H), 1.58 (s, 3 H), 1.59–1.65 (m, 2 H), 1.91–1.96 (m, 1 H), 2.01–2.05 (m, 1 H), 2.30–2.35 (m, 1 H), 2.61 (dd, J = 7.7, 2.2 Hz, 1H), 2.99 (ddd, J =11.9, 8.5, 4.3 Hz, 1 H), 3.36–3.47 (m, 3 H), 3.41 (s, 3 H), 3.55 (ddd, J = 11.0, 8.5, 4.6 Hz, 1H), 3.76-3.81 (m, 1 H), 3.79 (s, 3 H), 4.25 (AB q, J_{AB} = 11.6 Hz, $\Delta\nu$ = 121 Hz, 2 H), 5.18 (d, J = 9.0 Hz, 1 H), 6.85 (d, J = 8.6 Hz, 2 H), 7.19 (d, J = 8.6 Hz, 2 H); ^{13}C NMR δ 159.1, 134.7, 131.9, 130.5, 129.4, 113.7, 85.5, 84.4, 74.9, 69.1, 61.6, 58.4, 58.0, 57.8, 55.2, 38.3, 36.5, 35.0, 34.0, 30.8, 18.1, 13.7, 12.6, 11.7; MS (EI^+) *m/e* (relative intensity) 533 ([M − *i*-Pr]$^+$, 4), 475 (1), 323 (5), 121 (100); HRMS (EI^+) calcd for $C_{30}H_{49}O_6Si$ ([M − *i*-Pr]$^+$) 533.3298, found 533.3290. Anal. Calcd for $C_{33}H_{56}O_6Si$: C, 68.71; H, 9.78. Found: C, 68.65; H, 9.77.

(*E*,3*S*,4*R*,5*S*)-4,6-Dimethyl-5-[(*p*-methoxybenzyl)oxy]-7-[(1*R*,3*R*,4*R*)-3-methoxy-4-[(triisopropylsilyl)oxy]cyclohexyl]-6-hepten-1,3-diol (10.3). The procedure for **10.1** was applied to 700 mg (1.21 mmol) of epoxide **10.2** and 1.46 mL (4.85 mmol) of 65+% Red-Al (in toluene) in 15 mL of THF at −5 °C for 20 h. The ^1H NMR spectrum of the crude material indicated two compounds in a ratio greater than 98:2. The crude product was chromatographed on silica gel. Elution with 60% Et_2O–hexanes afforded 625 mg (89%) of diol **10.3** as a viscous colorless liquid: $[\alpha]^{24}_D$ −68.9 (*c* 1.48, $CHCl_3$); IR (film) 3412, 1740, 1614 cm^{-1}; ^1H NMR δ 0.88 (d, J = 7.0 Hz, 3 H), 0.98–1.16 (m, 2 H), 1.06 (m, 21 H), 1.38–1.57 (m, 1 H), 1.57 (d, J = 1.1 Hz, 3 H), 1.57–1.62 (m, 1 H), 1.75–1.88 (m, 1 H), 1.91–2.02 (m, 1 H), 2.30–2.35 (m, 1 H), 2.69 (bt, J = 4.1 Hz, 1 H), 3.01 (ddd, J =11.2, 8.3, 4.3 Hz, 1 H), 3.06 (br s, 1 H), 3.39 (s, 3 H), 3.56 (ddd, J = 10.9, 8.4, 4.4 Hz, 1 H), 3.71–3.76 (m, 3 H), 3.78 (s, 3 H), 4.29 (AB q, J_{AB} = 11.2 Hz, $\Delta\nu$ = 87.8 Hz, 2 H), 5.25 (d, J = 9.1 Hz, 1 H), 6.85 (d, J = 8.7 Hz, 2 H), 7.21 (d, J = 8.7 Hz, 2 H); ^{13}C NMR: δ 159.2, 132.4, 131.0, 130.1, 129.6, 113.9, 87.4, 84.4, 75.0, 74.6, 70.1, 62.0, 57.6, 55.2, 40.6, 36.7, 36.3, 34.9, 34.1, 30.9, 18.1, 13.2, 12.6, 7.1; MS (EI^+) *m/e* (relative intensity) 578 (M^+, 1), 538([M − *i*-Pr]$^+$, 100), 517 (18), 475 (70); HRMS (EI^+) calcd for $C_{30}H_{51}O_6Si$ ([M − *i*-Pr]$^+$) 535.3455, found 535.3439.

3,5-(*p*-Methoxybenzylidene) Derivative of (*E*,3*S*,4*R*,5*S*)-4,6-Dimethyl-7-[(1*R*,3*R*,4*R*)-3-methoxy-4-[(triisopropylsilyl)oxy]cyclohexyl]-6-hepten-1,3,5-triol (10.4). A solution of 325 mg (0.561 mmol) of diol **10.3** in 7 mL of CH_2Cl_2 containing 163 mg of powdered molecular sieves (activated) was cooled to 0 °C, followed by addition of 153 mg (0.674 mmol) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in three portions over 5 min. The resulting green mixture turned brown within 15 min at which time the reaction was essentially complete. After an additional 15 min at 0 °C, the mixture was poured into water and extracted four times with CH_2Cl_2. The combined extracts were filtered through a pad of Celite 545 to remove particulates, and the filtrate was washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The resulting residue was chromatographed on silica gel. Elution with 10% Et_2O–hexanes afforded 19 mg (6%) of benzoate byproduct **10.5**. Further elution with 75% Et_2O–hexanes provided 269 mg (83%) of benzylidene acetal **10.4** as a yellow liquid: $[\alpha]^{24}_D$ −48.8 (*c* 1.46, $CHCl_3$) (lit.[17] $[\alpha]^{25}_D$ −49.0 (*c* 1.25 $CHCl_3$)); IR (film) 3426, 2938, 2852, 1616, 1518, 1464 cm^{-1}; ^1H NMR (400 MHz) δ 0.83 (d, J = 6.9 Hz, 3 H), 0.94–1.20 (m, 2 H), 1.06 (m, 21 H), 1.32–1.41 (m, 1 H), 1.57–1.64 (m, 2 H), 1.58 (s, 3 H), 1.90–1.98 (m, 4 H), 2.28–2.32 (m, 2 H), 2.97 (ddd, J = 11.2, 8.4, 4.4 Hz, 1 H), 3.39 (s, 3 H), 3.54 (ddd, J = 11.0, 8.4, 4.6 Hz, 1 H), 3.75–3.89 (m, 5 H), 4.12 (dt, J = 9.3, 2.4 Hz, 1 H), 4.20 (br s, 1 H), 5.35 (d, J = 9.2 Hz, 1 H), 5.55 (s, 1 H), 6.87 (d, J = 8.7 Hz, 2 H), 7.41 (d, J = 8.7 Hz, 2 H); ^{13}C NMR: δ 159.9, 131.3, 130.7, 129.0, 127.5, 113.5, 101.2, 84.5, 82.9, 79.9, 75.1, 61.0, 57.6, 55.3, 36.5, 35.5, 34.9, 34.2, 34.0, 30.9, 18.1, 13.5, 12.6, 6.1; MS (EI^+) *m/e* (relative intensity) 577 ([M^+ + 1], 25), 441 (55), 355 (25), 137 (100); HRMS (EI^+) calcd for $C_{30}H_{49}O_6Si$ ([M − *i*-Pr]$^+$) 533.3298, found 533.3286. Anal. Calcd for $C_{33}H_{56}O_6Si$: C, 68.71; H, 9.78. Found: C, 68.65; H, 9.78.

Benzoate 10.5: ^1H NMR (400 MHz) δ 0.75 (d, J = 6.7 Hz, 3 H), 1.05 (s, 21 H), 1.15–1.95 (m, 8 H), 1.66 (s, 3 H), 2.09 (dd, J = 12.5, 4.0 Hz, 1H), 2.29 (m, 1 H), 2.95 (ddd, J =11.2, 8.4, 4.4 Hz, 1 H), 3.37 (s, 3 H), 3.56 (m, 3 H), 3.85 (s, 3 H), 4.03 (dd, J = 10.5, 3.0 Hz, 1 H), 4.82 (dt, J = 10.5, 4.6 Hz, 1 H), 5.22 (d, J = 9.0 Hz, 1 H), 6.91 (d, J = 8.8 Hz, 2 H), 8.00 (d, J = 8.8 Hz, 2 H); MS (EI^+) *m/e* (relative intensity) 575 (60), 531 (12), 423 (61), 379 (100), 217 (58), 137 (62); HRMS (EI^+) calcd for $C_{30}H_{47}O_6Si$ ([M − *i*-Pr]$^+$) 531.3142, found 531.3145.

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Supporting Information Available: Experimental procedures for compounds **2.8–2.10**, **2.12** and **7.2–7.5** and copies of ^1H NMR spectra of key intermediates (39 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the Journal and can be ordered from the ACS; see any current masthead page for ordering information.

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