Studies Directed toward the Total Synthesis of Cerorubenic Acid-III. 3. A Convergent Enantioselective Approach Involving New Arrangements for the Actuation of Ring D Cyclization[1]

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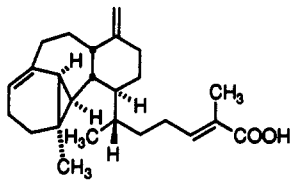
Received March 22, 1993

A possible enantiocontrolled route to cerorubenic acid-III (1) is described herein. The central elements of the approach take advantage of the ready availability of both optical antipodes of citronellol and of the tricyclic ketone 8. Although the absolute configuration of 1 is not known, its relative stereochemistry has been established by X-ray crystallography. On this basis, it is possible to match the reaction partners with the long-range view of establishing experimentally the actual configuration of 1. Assembly of the two structural halves was accomplished via a vinylstannane intermediate whose construction required utilization of an intramolecular S_N2 displacement in order to overcome the weakly nucleophilic nature of a stannyl-substituted ester enolate. The coupling reaction leading to 38 and 39 proved highly stereoselective as before, thereby setting the stage for conversion to D-seco derivatives of 1 via anionic oxy-Cope rearrangement. Although this phase of the strategy had previously been worked out on simpler systems, 38, 39, and analogs thereof isomerized with concomitant α-hydroxylation of the intermediate enolates. These conversions proceeded smoothly and efficiently. Although conditions were found that curtailed this adventitious oxygenation, the conversions proceeded so slowly that degradation was now competitive with the formation of 41 and 43.

In the exploratory phases of our quest for cerorubenic acid-III (1), an ovipositional stimulant of the encyrtid parasitoid *Anicetus beneficus*,[4] we have been directed away from the adaptation of Diels–Alder and extraannular Robinson annulation tactics as means for elaborating the D ring and its pendant side chain. The lessons learned in



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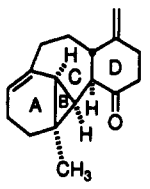

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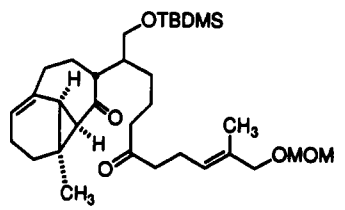

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the [4 + 2] cycloaddition approach are that ketone 2 with its trans C/D ring fusion is the thermodynamically preferred diastereomer and epimerization of the cis isomer to 2 is very facile.[5] The tactic of elaborating 3 in highly convergent fashion proceeded expediently as planned. However, the structural features of both diastereomers of this diketone proved unsuited to ring closure under basic conditions.[1,6]

The facts known to us suggested that the more conventional intrannular version of the Robinson annulation scheme for ring D construction was worthy of exploration. If retrosynthetic thinking is consequently focused on 4–7 (Scheme I), several noteworthy advantages are made clearly apparent. On first account, the stereocenter located on the side chain can now be unambiguously defined in 7 and not be an item of later concern. A successful assault on 1 in this manner would require complete knowledge of the absolute configurations of vinylstannane 7 and ketone 8. The two asterisked atoms in 7 are of no stereochemical consequence since they are ultimately destined to become trigonal centers in later steps. Strategic matching in this fashion offers the added benefit that the absolute configuration of cerorubenic acid-III (1) would thereby be unequivocally defined. Presently, only the relative stereochemistry of its seven stereogenic centers has been established.[7] In order to gain broader and more quantitative appreciation of insect receptor recognition selectivities, both enantiomers of 1 were targeted for eventual synthesis.

Results and Discussion

Resolution of Tricyclic Ketone 8. The subgoal of acquiring 1 in both of its antipodal forms required that racemic 8[5,8] be resolved by a method that would allow definition of the absolute configuration of its two enantiomers. Two approaches to this issue were taken, both based on the chiral sulfoximine methodology originally

(1) Part 2. Preceding paper in this issue.
(2) Postdoctoral Fellow of the American Cancer Society, 1989–1991.
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(4) (a) Noda, T.; Kitamura, C.; Takahashi, S.; Takagi, K.; Kashio, T.; Tanaka, M. *Appl. Ent. Zool.* **1982**, *17*, 350. (b) Takahashi, S.; Takabayashi, J. *Appl. Ent. Zool.* **1984**, *19*, 117; **1985**, *20*, 173.
(5) Paquette, L. A.; Poupart, M.-A. First of three papers in this issue.
(6) The use of acidic reagents was precluded because of the sensitivity of the bridgehead vinylcyclopropane double bond to protonation and ensuing self-destruction.
(7) Tempesta, M. S.; Iwashita, T.; Miyamoto, F.; Yoshihara, K.; Naya, Y. *J. Chem. Soc., Chem. Commun.* **1983**, 1182.
(8) Poupart, M.-A.; Paquette, L. A. *Tetrahedron Lett.* **1988**, *29*, 269.

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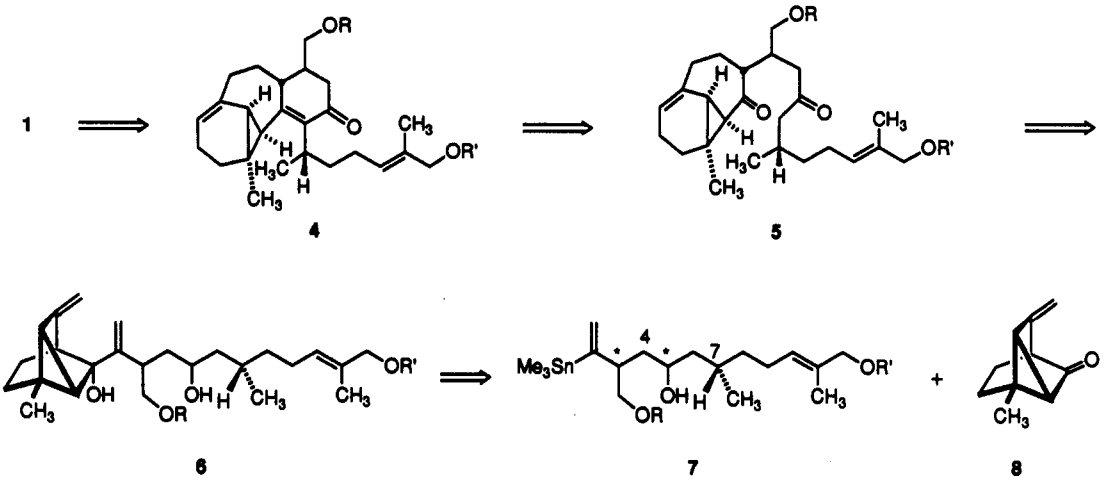
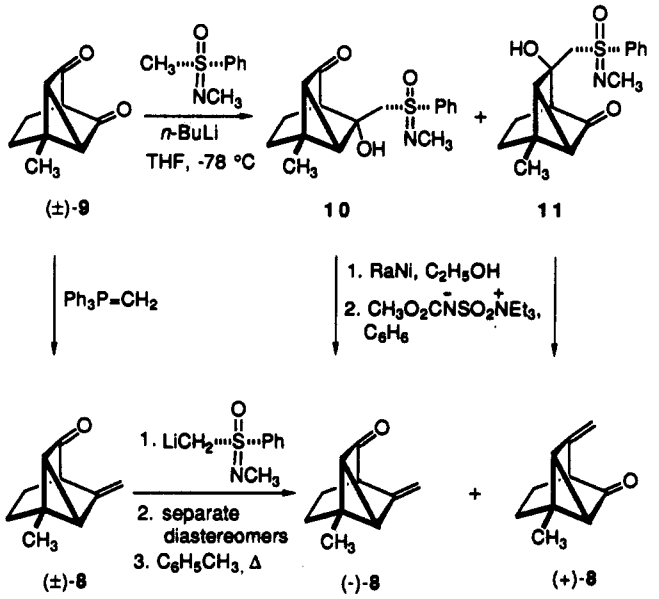
Scheme I



Scheme II



developed by Johnson.[9] Initially, advantage was taken of the C_s symmetry of diketone **9**[10] and the recognized kinetic preference for nucleophilic addition to either of its carbonyl groups from the direction syn to the non-methyl-substituted cyclopropane bond. In the present circumstances, condensation of **9** with the lithium salt of (+)-(*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximine afforded **10** and **11** (Scheme II). These diastereomers proved to be especially amenable to chromatographic separation. Once purified, each was reduced with Raney nickel[11] and dehydrated with the Burgess reagent[12] to give (−)-**8**, $[\alpha]_D$ −105.4° (*c* 2.55, $CHCl_3$) and (+)-**8**, $[\alpha]_D$ +110.9° (*c* 2.10, $CHCl_3$), respectively. Assignment of absolute configuration to these ketones was made possible by an X-ray crystallographic analysis of **10** (Figure 1).[32]

At the preparative level, it proved more expedient and efficient to effect ketone methylenation prior to optical resolution. Thus, the preferred route involved indepen-

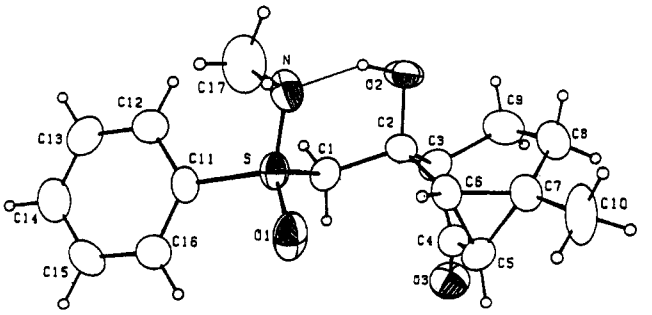


Figure 1. Computer-generated perspective drawing of **10** as determined by X-ray crystallography. The atom numbering is arbitrary.

dent pyrolysis[13] of the sulfoximine adducts produced directly from racemic **8**.

Construction of the Vinylstannane. In light of the fact that the two C-7 enantiomers of the alicyclic precursor **7** were of comparable importance, several methods for their dual preparation were considered. Of these, that involving a C4–C5 disconnection held particular attraction since the larger segment could in principle be derived directly from citronellol, both antipodes of which are commercially available. With but one chiral center of direct concern, the pathway to **7** would appear superficially to be straightforward. However, as will be seen, the structural features of the units to be conjoined do not lend themselves particularly well to reaction efficiency.

(*R*)-(+)-Citronellol (**12**) was converted to its acetate **13** in 93% yield.[14] The stereoselective allylic oxidation of the terminal methyl group of O-protected citronellols has been reported on several occasions.[15] In the earliest example, the tetrahydropyranyl ether was treated with a stoichiometric amount of selenium dioxide in pyridine.[15a] More recently, the use of *tert*-butyl hydroperoxide as cooxidant in the presence of a catalytic quantity of SeO_2 was recommended.[15b] In our hands, however, this method produced **14a** in only 28% yield (Scheme III). Matters improved somewhat (to 37%) when the SeO_2 was sup-

(9) (a) Johnson, C. R.; Schroeck, C. W.; Shanklin, J. R. *J. Am. Chem. Soc.* **1973**, *95*, 7424. (b) Johnson, C. R. *Aldrichimica Acta* **1985**, *18*, 3.

(10) Poupart, M.-A.; Lassalle, G.; Paquette, L. A. *Org. Synth.* **1990**, *69*, 173.

(11) Johnson, C. R.; Stark, C. J., Jr. *J. Org. Chem.* **1982**, *47*, 1196.

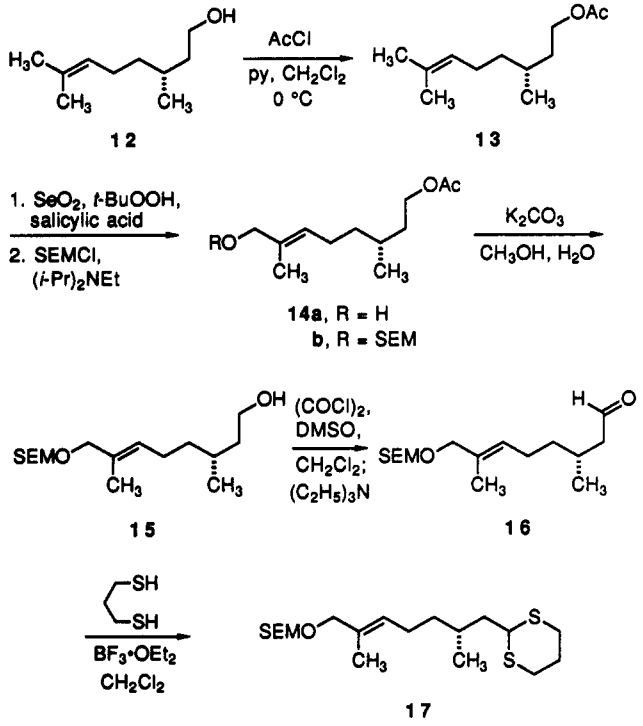
(12) Burgess, E. M.; Penton, H. R., Jr.; Taylor, E. A. *J. Org. Chem.* **1973**, *38*, 26.

(13) Johnson, C. R.; Zeller, J. R. *J. Am. Chem. Soc.* **1982**, *104*, 4021.

(14) A parallel series of experiments was also carried out on the (*S*)-(−)-enantiomer. These structures will not be illustrated, but the distinctive optical rotations are, of course, essentially identical though opposite in sign.

(15) (a) Camps, F.; Coll, J.; Parente, A. *Synthesis* **1978**, 215. (b) Tanis, S. P.; Chuang, Y. H.; Head, D. B. *J. Org. Chem.* **1988**, *53*, 4929. (c) Chhabra, B. R.; Hayno, K.; Ohtsuka, T.; Shirahama, H.; Matsumoto, T. *Chem. Lett.* **1981**, 1703.

Scheme III



12 13 15 16 17

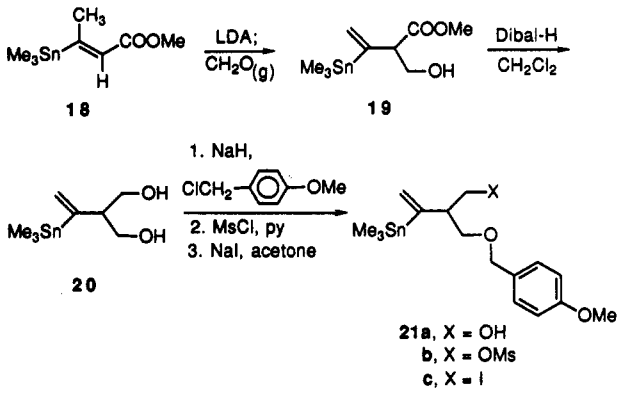
ported (5% w/w) on silica gel[15c] prior to introduction of the hydroperoxide. These inert additives proved not to be necessary, the coaddition of salicyclic acid as a buffer[16] serving ultimately to provide **14a** in preparatively useful amounts (66%) once the aldehyde produced by overoxidation was reduced with sodium borohydride.

To complete the transformation of (+)-citronellol into a suitably nucleophilic reagent, **14a** was protected as the [β-(trimethylsilyl)ethoxy]methyl ether (SEM derivative) according to the Lipshutz procedure[17] in advance of acetate hydrolysis and Swern oxidation[18] to furnish aldehyde **16**. Although this intermediate proved to be somewhat sensitive to acid, conversion to dithiane **17** could be accomplished with 2 equiv of 1,3-propanedithiol in the presence of 2% boron trifluoride etherate.

We were rather apprehensive from the start about the possibility of using the homoallylic iodide **21c** in an intermolecular S_N2 displacement. The fear of kinetically more rapid E_2 elimination ultimately proved to be well founded. When the anion of stannyl crotonate **18**[19] failed to undergo clean S_N2 displacement on 4-methoxybenzyl chloromethyl (PMB) ether,[20] the less direct pathway outlined in Scheme IV was followed. Condensation of the same anion with the more electrophilic gaseous formaldehyde proceeded regioselectively to afford **19**, which was reduced to symmetrical diol **20** with Dibal-H. Advantage was then taken of this symmetry during subsequent monoprotection as the ether **21a**. Mesylation followed by a Finkelstein reaction of **21b** proceeded smoothly to generate **21c**.

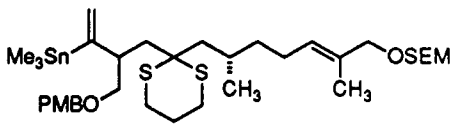
The condensation of **17** with **21c** initially followed lines strictly analogous to those utilized in many successful

Scheme IV



18 19 20

dithianyl anion condensations.[21] Following treatment of **17** with 1 equiv of *n*-butyllithium in THF at −40 to −20 °C, the iodide was introduced along with 1,3-dimethylpropylene urea (DMPU).[22] These mild conditions afforded **22** in a maximum yield of 8%! All attempts to force the alkylation only succeeded in enhancing elimination still more. Clearly, an alternative access route to intermediates of this type required development. Simple polarity reversal was not a viable option in this instance since the Grignard reagent formed from **21c** was found to experience rapid self-destruction.



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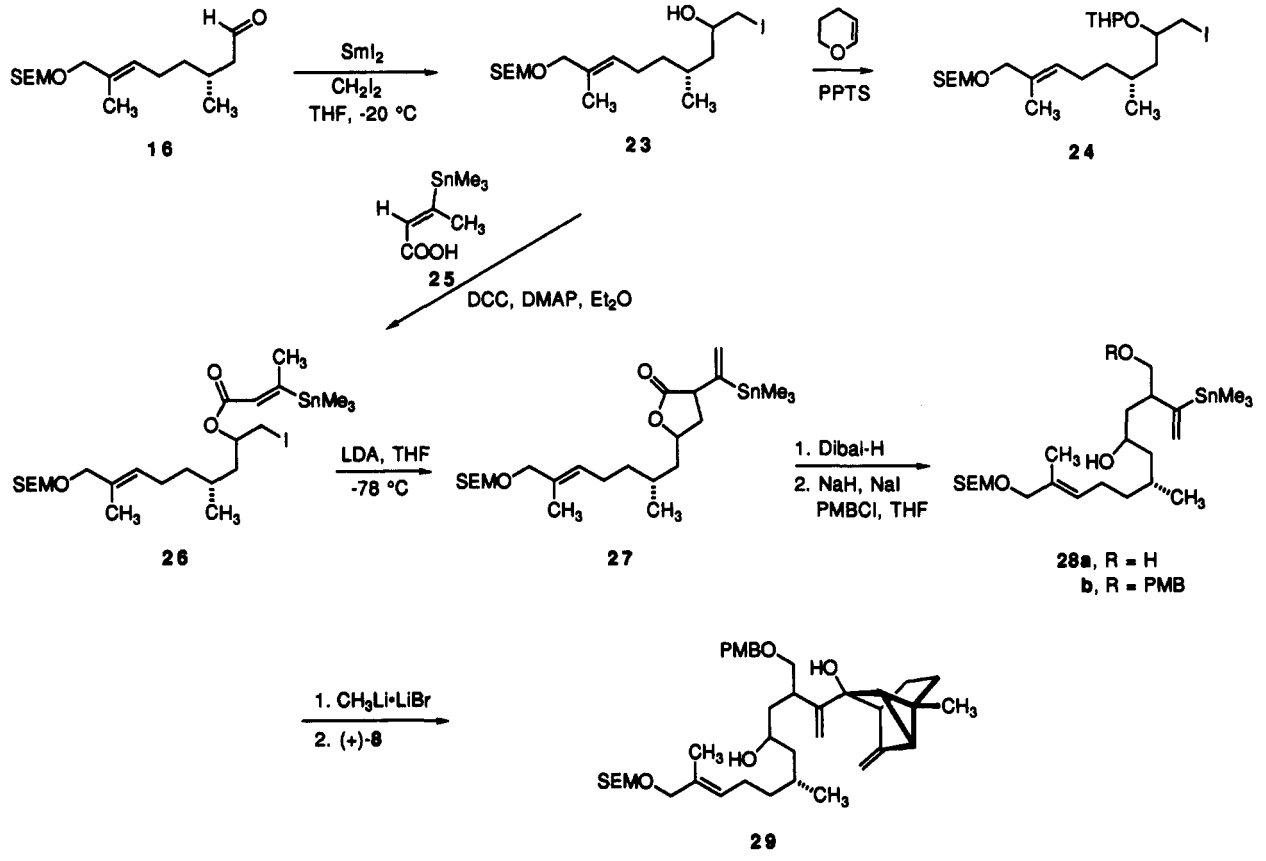
We next undertook a study of the homologation of **16** hoping to allow for direct coupling to the enolate of **18**. The need for a suitably functionalized one-carbon nucleophile led us to consider iodomethylation of the aldehyde with samarium(II) iodide.[23] This reaction proved to be highly serviceable and made iodo alcohol **23** available as an approximate 1:1 mixture of inseparable diastereomers (Scheme V). Following protection of the hydroxyl group as the THP ether, all attempts to effect the alkylation of **24** with **18** only returned unchanged starting materials. Similar observations in other related contexts served to alert us to the fundamentally weak nucleophilic character of this tin-substituted anion.

A satisfactory solution to this problem was realized by capitalizing on an intramolecular variant. If the difficulty truly resides in a slow rate of bimolecular displacement, then kinetic acceleration should be achieved by resorting to an intramolecular alternative, provided that the ring being formed is five- or six-membered. Thus, carbodiimide-promoted[24] esterification of the *E*-carboxylic acid **25**[25] with **23** yielded the ester iodides **26**. To our delight,

(16) (a) Umbreit, M. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 5526. (b) Tanis, S. P.; Chuang, Y.-H.; Head, D. B. *J. Org. Chem.* **1988**, *53*, 4929.
(17) Lipshutz, B. H.; Pegram, J. J. *Tetrahedron Lett.* **1980**, *21*, 3343.
(18) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651.
(19) Piers, E.; Morton, H. E. *J. Org. Chem.* **1980**, *45*, 4263.
(20) Benneche, T.; Straude, P.; Undheim, K. *Synthesis* **1983**, 762.
(21) Seebach, D.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 231.
(22) Mukhopadhyay, T.; Seebach, D. *Helv. Chim. Acta* **1982**, *65*, 385. Seebach, D.; Henning, R.; Mukhopadhyay, T. *Chem. Ber.* **1982**, *115*, 1705.
(23) (a) Imamoto, T.; Takeyama, T.; Koto, H. *Tetrahedron Lett.* **1986**, *27*, 3243. (b) Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 3891.
(24) Smith, M.; Moffatt, J. G.; Khorana, H. G. *J. Am. Chem. Soc.* **1958**, *80*, 6204.
(25) Saponification of ester **18** with 2 M KOH in methanol at reflux gave a mixture of *E* and *Z* acids that were chromatographically separated and used individually. However, since a later reaction equilibrates the stereoisomers, this separation was superfluous and not routinely performed.

Scheme V



exposure of **26** to LDA in THF eventuated in lactone formation (40%).[26] After chromatographic separation, reduction with Dibal-H afforded two sets of diols which were carried forward separately.

In the major series, the primary hydroxyl functionality was protected as the PMB ether (**28b**). The oxy-Cope precursor **29** was readily obtained by addition of the vinyl anion derived by transmetalation of **28b** to the dextrorotatory enone (+)-8. Unfortunately, the anionically promoted [3,3] sigmatropic rearrangement of **29** could be accomplished only alongside competing degradation. Extensive screening of this reaction revealed that the conditions necessary to promote a reasonable rate of isomerization required that the alkoxide be generated in "naked" condition. These strongly nucleophilic circumstances disrupted the integrity of the SEM protecting group and gave rise in large part to tricyclic ketones in which the SEM unit was desilylatively truncated or removed altogether. In addition, α-hydroxylation of the intermediate enolate[27] was noted. As a consequence of these developments, the decision was made to change the blocking group while masking the allylic hydroxyl as the PMB ether.

Aldehyde **30** was therefore prepared and transformed into the *E*-iodo ester **31** as before (Scheme VI). In parallel with earlier observations, coupling to the *Z*-isomer of **25** was equally efficient, and both sets of diastereomeric esters underwent intramolecular alkylation to give closely comparable mixtures of the α,β- and β,γ-unsaturated lactones. The **32**:**33** ratio varied from 1:3.1 to 1:6.6 depending on the run. The two classes of lactones were amenable to chromatographic separation, but the diastereomers of each subtype eluted together. Conveniently, **32** could be transformed into **33** by deprotonation with LDA and quenching of the enolate with NH_4Cl under kinetically controlled conditions.[28]

Dibal-H reduction of lactones **33** gave rise to two pairs of diols, with the **34a**/**35a** subset predominating over **36a**/**37a** by 9–13:1. The desired vinylstannanes **34b**/**35b** were obtained in turn by selective protection with *p*-methoxybenzyl chloride.[29]

Arrival at the oxy-Cope precursors **38** and **39** was accomplished by addition of the anions generated from **34b** and **35b** to (+)-8 (Scheme VII). In the light of preliminary studies that showed the subsequent [3,3] sigmatropic rearrangement to proceed faster if the secondary hydroxyl groups in diols **38** and **39** were first protected, the *tert*-butyldimethylsilyl ethers were prepared[29] and subjected to the action of potassium hexamethyldisilazide and 18-crown-6 in THF.[30] Although the intended chemical transformation did materialize in both examples, DEPT experiments performed on the individual products showed them to be **40** and **42**, respectively. Accordingly, in situ oxygenation of the enolates formed as a result of the oxy-Cope process were being transformed with notable rapidly and efficiency into the α-hydroxy ketones.[27]

(26) For other examples of lactone formation from esters, see: (a) Stork, G.; Nakamura, E. *J. Org. Chem.* **1979**, *44*, 4010. (b) Porter, N. A.; Chang, V. H.-T. *J. Am. Chem. Soc.* **1987**, *109*, 4976.

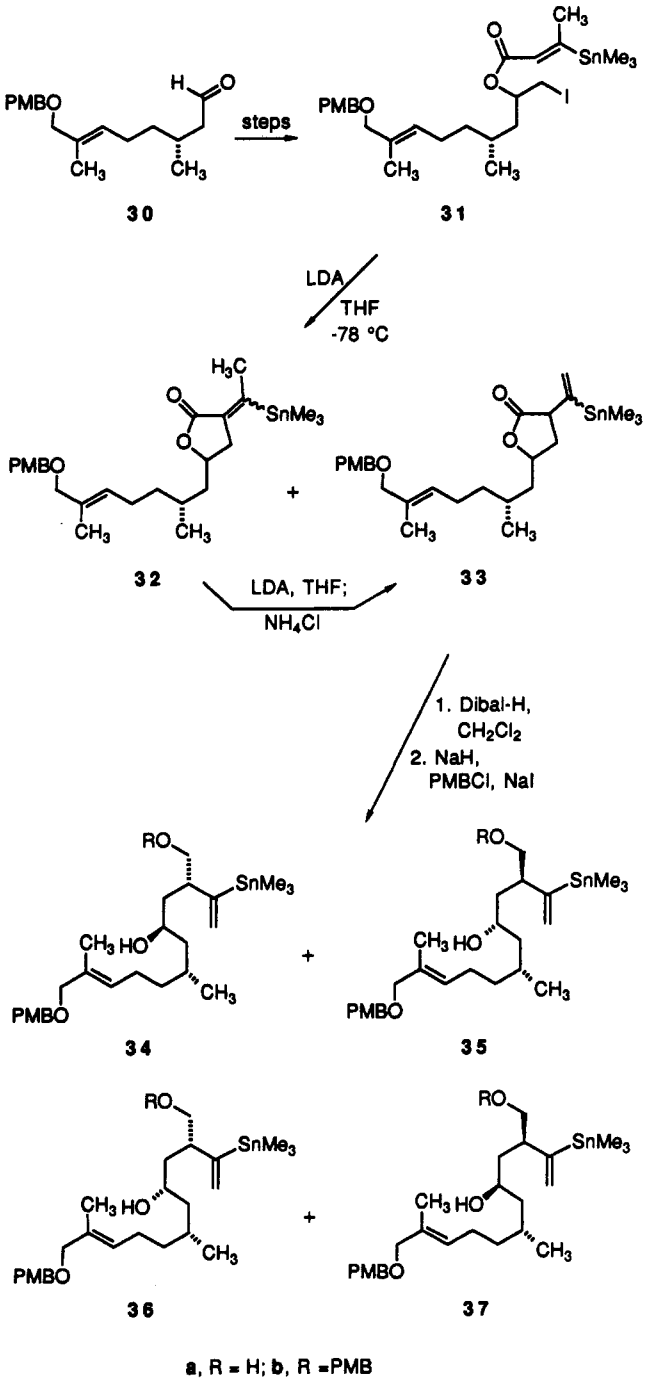
(27) Paquette, L. A.; DeRussy, D. T.; Pegg, N. A.; Taylor, R. T.; Zydowsky, T. M. *J. Org. Chem.* **1989**, *54*, 4576.

(28) (a) Piers, E.; Jean, M.; Marrs, P. S. *Tetrahedron Lett.* **1987**, *28*, 5075. (b) Danishefsky, S. J.; Armistead, D. M.; Wincott, F. E.; Selnick, H. G.; Hungate, R. *J. Am. Chem. Soc.* **1987**, *109*, 8117.

(29) Corey, E. J.; Cho, H.; Rucker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.

(30) These conditions led to substantial deprotection of the TBS ether prior to isolation, but advance protection was nevertheless beneficial.

Scheme VI



a, R = H; b, R = PMB

These results led to a detailed reexamination of the anionically-induced isomerization (see Experimental Section for added examples). Strict purification of the 18-crown-6 promoter was undertaken via its acetonitrile complex. Argon was bubbled through each reaction mixture prior to introduction of the base. Notwithstanding, enolate oxygenation persisted. It was subsequently discovered that only by *not* employing 18-crown-6 and by performing the reaction under argon could **41** and **43** be obtained. However, longer reaction times were now required, during which time decomposition proved to be competitive with rearrangement. In contrast to the high yields associated with formation of the α-hydroxy ketones, the maximum yields realized for the conversions to **41** and **43** were generally low and disappointing. Consequently, despite earlier precedent that indicated conversions related to those in Scheme VI to proceed without undue complication,[1,5] the structurally more ornate analogues reported herein are not as readily manipulated and demonstrate an ease for adventitious oxygenation and decomposition not heretofore encountered.

These untoward properties proved to be an insurmountable roadblock, and quantities of **41** and **43** adequate to advance to **1** were never produced. As an interesting sidenote, Jones oxidation of **40** and **42** provided diastereomerically related diketones that failed to cyclize on attempted Robinson annulation.[31] It remains unclear whether this rate retardation stems from adverse inductive contributions arising from the angular hydroxyl substituent, the structural features surrounding the α-cyclopropyl carbonyl group, or steric effects imposed by the stereoelectronic requirements of the intramolecular cyclization.

Experimental Section

See ref 5 for a listing of generic experimental details.

(*S*)-*S*-[[(1*R*,2*S*,5*R*,6*R*,7*S*)-6-Hydroxy-2-methyl-8-oxotricyclo[3.2.1.0^{2,7}]oct-6-yl]methyl]-*N*-methyl-*S*-phenylsulfoximine (10) and (*S*)-*S*-[[(1*S*,2*R*,5*S*,6*S*,7*R*)-6-Hydroxy-2-methyl-8-oxotricyclo[3.2.1.0^{2,7}]oct-6-yl]methyl]-*N*-methyl-*S*-phenylsulfoximine (11). A solution of (+)-(*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximine[9] (221 mg, 1.30 mmol) in dry THF (10 mL) was cooled to 0 °C and treated with *n*-butyllithium in hexanes (0.752 mL of 1.6 M, 1.20 mmol), stirred for 10 min, cooled further to −78 °C, and treated dropwise with a solution of racemic **9** (151 mg, 1.00 mmol) in 1 mL of THF during 5 min. After 30 min, the reaction mixture was quenched with saturated NH_4Cl solution (5 mL), diluted with water (30 mL), and extracted with ether (4 × 10 mL). The combined organic phases were dried and evaporated to leave a residue that was chromatographed on silica gel (elution with 50% ethyl acetate in petroleum ether). There was isolated 38 mg (25%) of unreacted **9**, 81 mg (25%) of **10**, and 62 mg (19%) of **11**.

For **10**:[32] colorless crystals; mp 133.5–135.0 °C; IR (CH_2Cl_2, cm^{-1}) 3500–3100, 1715; ^1H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, J = 7.1 Hz, 2 H), 7.68–7.56 (m, 3 H), 7.50–7.22 (br s, 1 H), 3.12 (d, J = 5.3 Hz, 1 H), 3.05 (d, J = 13.7 Hz, 1 H), 2.68 (s, 3 H), 2.38–2.29 (m, 1 H), 2.10 (dt, J = 4.3, 13.7 Hz, 1 H), 1.93 (d, J = 5.3 Hz, 1 H), 1.89–1.68 (m, 2 H), 1.31–1.13 (m, 1 H), 1.20 (s, 3 H), 0.87 (m, 1 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 209.8, 138.6, 133.5, 129.7, 129.0, 73.8, 62.8, 52.1, 41.6, 37.8, 28.8, 24.1, 23.4, 22.8 (1 C not observed); MS m/z (M^+) calcd 319.1242, obsd 319.1258.

Anal. Calcd for $C_{17}H_{21}NO_3S$: C, 63.92; H, 6.63. Found: C, 63.91; H, 6.81.

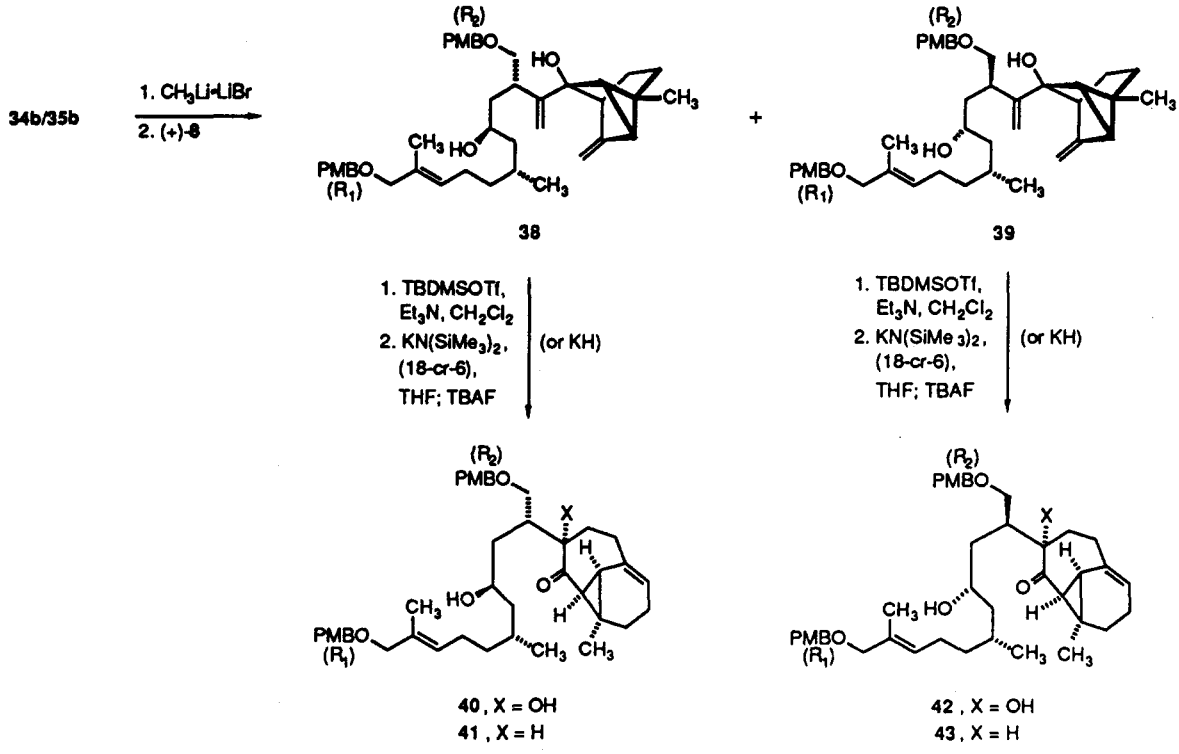
For **11**: colorless crystals: mp 140–143 °C; IR (CH_2Cl_2, cm^{-1}) 3400–3100, 1720; ^1H NMR (300 MHz, $CDCl_3$) δ 7.88 (m, 2 H), 7.64–7.55 (m, 4 H), 3.53 (d, J = 13.8 Hz, 1 H), 3.03 (d, J = 14.0 Hz, 1 H), 2.88 (br s, 1 H), 2.62 (s, 3 H), 2.37 (dt, J = 3.1, 9.7 Hz, 1 H), 2.03 (m, 2 H), 1.78 (m, 3 H), 1.25 (t, J = 7.1 Hz, 1 H), 1.11 (s, 3 H), 0.80 (m, 1 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 209.9, 138.8, 133.4, 129.7, 129.0, 74.2, 62.5, 48.7, 42.5, 40.6, 37.0, 28.9, 24.1, 22.7; MS m/z (M^+) calcd 319.1242, obsd 319.1252.

(+)-(1*R*,2*S*,5*R*,7*R*)-2-Methyl-8-methylenetricyclo[3.2.1.0^{2,7}]-octan-6-one ((+)-8). A solution of **11** (62 mg, 0.195 mmol) in absolute ethanol (10 mL) was treated with W-2 Raney nickel (200 mg). After 30 min of vigorous stirring, the reducing agent was removed by filtration through Celite, and the filtrate was concentrated. The remaining oil was dissolved in benzene (10 mL), and the Burgess inner salt (93 mg, 0.391 mmol) was introduced. The reaction mixture was stirred at rt for 3 h,

(31) Deaton, D. N. Unpublished work.

(32) The authors have deposited atomic coordinates for **10** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Scheme VII



concentrated, and chromatographed on silica gel. There was isolated 8 mg (28%) of (+)-8 along with 4 mg (11%) of tertiary alcohol.

For (+)-8: $[\alpha]^{22}_D$ +89.9° (*c* 0.81, CH_2Cl_2).

(−)-(1*R*,2*S*,5*R*,7*R*)-2-Methyl-8-methylenetricyclo[3.2.1.0^{2,7}]-octan-6-one ((−)-8). Analogous treatment of **10** furnished (−)-8, $[\alpha]^{22}_D$ −90.9° (*c* 0.57, CH_2Cl_2).

Independent Preparation of (−)-8 and (+)-8. To a solution of 16.20 g (95.70 mmol) of (+)-(*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximine[9] in 320 mL of dry THF at 0 °C was added 61.35 mL (92.02 mmol) of a 1.5 M solution of *n*-butyllithium in hexanes, and the mixture was stirred for 15 min and then cooled to −78 °C, at which point 10.91 g (73.62 mmol) of racemic 8[5] in 48 mL of THF was added. The resulting mixture was stirred for 2 h while being allowed to warm to −20 °C, quenched with 45 mL of saturated NH_4Cl solution and brine (150 mL), and extracted with ether. The combined organic layers were washed with brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 1:6 ethyl acetate/petroleum ether) to afford 11.64 g (49%) of adduct **A** and 11.59 g (49%) of adduct **B**.

For **A**: colorless crystals; mp 72–73 °C; IR (neat, cm^{-1}) 3220, 1660; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84–7.81 (m, 2 H), 7.69–7.48 (m, 3 H), 6.58 (br s, 1 H), 4.66 (s, 2 H), 3.21 (ABq, J_{AB} = 3.8 Hz, $\Delta\nu_{AB}$ = 60.6 Hz, 2 H), 2.87 (s, 1 H), 2.55 (s, 3 H), 2.13 (tt, *J* = 11.9, 3.2 Hz, 1 H), 1.86 (dt, *J* = 11.2, 4.4 Hz, 1 H), 1.70 (dt, *J* = 11.5, 4.6 Hz, 1 H), 1.57 (d, *J* = 5.5 Hz, 1 H), 1.41 (tt, *J* = 11.9, 3.7 Hz, 1 H), 1.33 (d, *J* = 5.6 Hz, 1 H), 0.91 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 152.2, 139.0, 133.0, 129.4, 128.9, 102.4, 77.8, 61.6, 44.6, 38.1, 33.6, 28.9, 26.8, 24.0, 23.2; MS *m*/*z* (M$^+$) calcd 317.1449, obsd 317.1467; $[\alpha]^{25}_D$ −11.0° (*c* 0.95, $CHCl_3$).

For **B**: colorless crystals; mp 104–106 °C; IR (neat, cm^{-1}) 3255, 1660; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83–7.81 (m, 2 H), 7.60–7.50 (m, 3 H), 7.06 (br s, 1 H), 4.62 (s, 1 H), 4.42 (s, 1 H), 3.16 (ABq, J_{AB} = 3.7 Hz, $\Delta\nu_{AB}$ = 39.2 Hz, 2 H), 2.62 (s, 3 H), 2.34 (d, *J* = 5.6 Hz, 1 H), 2.11 (tt, *J* = 12.2, 3.5 Hz, 1 H), 1.90 (dt, *J* = 14.6, 4.3 Hz, 1 H); 1.83 (s, 1 H), 1.73 (s, 1 H), 1.72 (dt, *J* = 12.5, 4.5 Hz, 1 H), 1.36 (tt, *J* = 12.0, 3.6 Hz, 1 H), 1.00 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 152.1, 138.9, 133.1, 129.5, 128.9, 101.9, 77.3, 62.6, 48.3, 36.6, 34.5, 28.9, 27.5, 24.1, 23.5, 23.4; MS *m*/*z* (M$^+$) calcd 317.1449, obsd 316.1459; $[\alpha]^{25}_D$ +29.8° (*c* 1.11, $CHCl_3$).

Anal. Calcd for $C_{18}H_{23}NO_2S$: C, 68.11; H, 7.30. Found: C, 67.94; H, 7.43.

A solution of **A** (11.64 g, 36.67 mmol) in toluene (36.7 mL) was refluxed overnight, then purified by flash chromatography on silica gel (elution with 1:9 ethyl acetate/petroleum ether) to afford 5.00 g (92%) of (−)-8, $[\alpha]^{25}_D$ −105.0° (*c* 2.56, $CHCl_3$).

A solution of **B** (11.59 g, 36.51 mmol) in toluene (36.5 mL) was refluxed overnight and purified as above to give 5.16 (95%) of (+)-8, $[\alpha]^{25}_D$ +107.7° (*c* 1.58, $CHCl_3$).

(*R*)-(+)-β-Citronellol Acetate (13). To 5.00 g (32.00 mmol) of (*R*)-(+)-β-citronellol (**12**) in 64 mL of CH_2Cl_2 at 0 °C under an argon atmosphere were added 9.70 mL (119.98 mmol) of pyridine and 3.41 mL (48.00 mmol) of acetyl chloride. The mixture was stirred overnight at rt, quenched with ice–water, and extracted with ether. The combined organic layers were washed with saturated $CuSO_4$ solution and 5% HCl, dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 1:24 ethyl acetate/petroleum ether) to afford 5.90 g (93%) of **13** as a colorless oil: IR (film, cm^{-1}) 1745; ^{1}H NMR (300 MHz, $CDCl_3$) 5.09 (tt, *J* = 7.1, 1.7 Hz, 1 H), 4.16–4.03 (m, 2 H), 2.25–1.82 (m, 2 H), 2.04 (s, 3 H), 1.73–1.12 (m, 5 H), 1.68 (s, 3 H), 1.60 (s, 3 H), 0.92 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 170.9, 131.1, 124.5, 62.9, 36.9, 35.4, 29.4, 25.6, 25.3, 20.9, 19.2, 17.5; MS *m*/*z* (M$^+$-HOAC) calcd 138.1409, obsd 138.1424; $[\alpha]^{25}_D$ +3.7° (*c* 3.29, $CHCl_3$).

(6*R*)-8-Acetoxy-2,6-dimethyl-2-octen-1-ol (14a). To 1.01 g (9.08 mmol) of selenium dioxide and 4.39 g (31.77 mmol) of salicyclic acid in 100 mL of CH_2Cl_2 at 0 °C was added 100.8 mL (907.72 mmol) of 90% *tert*-butyl hydroxperoxide. Then 60.00 g (302.57 mmol) of **13** in 100 mL of CH_2Cl_2 was added dropwise and the mixture stirred for 42 h at rt. After dilution with 150 mL of benzene, the reaction mixture was concentrated and the residue was taken up in ether and washed four times with $NaHCO_3$ solution, dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 1:4 ethyl acetate/petroleum ether) to afford 27.35 g (42%) of **14a** and 16.54 g (26%) of the aldehyde. The aldehyde was dissolved in 52 mL of ethanol and treated slowly with 2.06 g (54.48 mmol) of sodium borohydride at 0 °C. After 2 h of stirring, the reaction mixture was quenched with $NaHCO_3$ solution, poured into water, and extracted with ether (3 × 40 mL). The combined organic layers were washed with brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 1:4 ethyl acetate/petroleum ether) to afford an additional 14.14 g (22%) of **14a**: colorless oil; IR (film, cm^{-1}) 3430, 1735; ^{1}H NMR (300

MHz, $CDCl_3$) δ 5.27 (t, J = 7.1 Hz, 1 H), 4.02–3.94 (m, 2 H), 3.85 (s, 2 H), 2.66 (s, 1 H), 1.98–1.88 (m, 2 H), 1.93 (s, 3 H), 1.59–1.24 (m, 4 H), 1.54 (s, 3 H), 1.17–1.10 (m, 1 H), 0.81 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 170.9, 134.5, 125.4, 68.2, 62.7, 36.4, 35.1, 29.2, 24.7, 20.7, 19.1, 13.3; MS m/z (M^+) calcd 214.1569, obsd 214.1582; $[\alpha]^{25}_D$ +4.1° (c 3.65, $CHCl_3$).

Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 67.21; H, 10.41.

(3*R*,6*E*)-3,7-Dimethyl-8-[[2-(trimethylsilyl)ethoxy]methoxy]-6-octen-1-ol Acetate (14b). To a solution of 20.00 g (93.33 mmol) of **14a** in 300 mL of CH_2Cl_2 was added 81.3 mL (466.64 mmol) of diisopropylethylamine and 46.68 g (279.93 mmol) of SEMCl in 10 mL of CH_2Cl_2. The reaction mixture was stirred for 4 h at rt and quenched with 500 mL of saturated $NaHCO_3$ solution. The separated aqueous layer was extracted with ether (2 × 250 mL), and the combined organic layers were washed with brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 1:19 ethyl acetate/petroleum ether) to afford 31.64 g (98%) of **14b** as a colorless oil: IR (film, cm^{-1}) 1740; ^1H NMR (300 MHz, $CDCl_3$) δ 5.37 (t, J = 7.0 Hz, 1 H), 4.61 (s, 2 H), 4.08–4.01 (m, 2 H), 3.89 (s, 2 H), 3.59 (dd, J = 8.5, 7.1 Hz, 2 H), 2.06–1.97 (m, 2 H), 1.99 (s, 3 H), 1.67–1.17 (m, 5 H), 1.62 (s, 3 H), 0.91 (dd, J = 8.4, 7.2 Hz, 2 H), 0.8 (d, J = 6.4 Hz, 3 H), –0.01 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 170.8, 131.6, 128.2, 93.5, 73.2, 64.8, 62.7, 36.4, 35.3, 29.4, 24.9, 20.8, 19.2, 18.0, 13.8, –1.55; MS m/z ($M^+ - Me_3Si$) calcd 271.1909, obsd 271.1855; $[\alpha]^{25}_D$ +3.2° (c 3.4, $CHCl_3$).

Anal. Calcd for $C_{18}H_{36}O_4Si$: C, 62.74; H, 10.53. Found: C, 62.78; H, 10.53.

(3*R*,6*E*)-3,7-Dimethyl-8-[[2-(trimethylsilyl)ethoxy]methoxy]-6-octenol (15). To a solution of 31.64 g (91.82 mmol) of **14b** in 460 mL of methanol at 0 °C was added 183.7 mL (91.82 mmol) of 0.5 M K_2CO_3 solution, and the mixture was stirred overnight at rt, concentrated, and extracted with ether (3 × 150 mL). The combined organic layers were washed with brine, dried, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 1:4 ethyl acetate/petroleum ether) to afford 27.45 g (99%) of **15** as a colorless oil: IR (film, cm^{-1}) 3240; ^1H NMR (300 MHz, $CDCl_3$) δ 5.36 (dt J = 7.1, 1.1 Hz, 1 H), 4.59 (s, 2 H), 3.87 (s, 2 H), 3.61–3.53 (m, 2 H), 3.57 (dd, J = 9.9, 8.5 Hz, 2 H), 2.27 (s, 1 H), 2.02–1.94 (m, 2 H), 1.59 (s, 3 H), 1.56–1.49 (m, 1 H), 1.38–1.25 (m, 2 H), 1.21–1.11 (m, 2 H), 0.92–0.87 (m, 2 H), 0.85 (d, J = 6.6 Hz, 3 H), –0.04 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 131.3, 128.7, 93.4, 73.3, 64.9, 60.6, 39.7, 36.6, 29.1, 25.0, 19.4, 18.0, 13.9, –1.5; MS m/z ($M^+ - Me_3Si(CH_2)_2OCH_2OH$) calcd 154.1357, obsd 154.1387; $[\alpha]^{25}_D$ +3.7° (c 3.3, $CHCl_3$).

Anal. Calcd for $C_{16}H_{34}O_3Si$: C, 63.52; H, 11.33. Found: C, 63.55; H, 11.40.

(3*R*,6*E*)-3,7-Dimethyl-8-[[2-(trimethylsilyl)ethoxy]methoxy]-6-octenal (16). To a solution of 1.21 mL (13.88 mmol) of oxalyl chloride in 16 mL of CH_2Cl_2 at –60 °C under an argon atmosphere was added 1.97 mL (27.77 mmol) of dimethyl sulfoxide in 7 mL of CH_2Cl_2. The mixture was stirred for 20 min, treated with 2.00 g (6.61 mmol) of **15** in 10 mL of CH_2Cl_2, and allowed to stir for 40 min. Finally, 7.65 mL (54.87 mmol) of triethylamine was introduced, and the solution was allowed to warm to rt, stirred for 30 min, quenched with water, and extracted with ether. The combined organic layers were washed with 1.0 N HCl and brine, dried, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 1:19 ethyl acetate/petroleum ether) to afford 1.98 g (100%) of **16** as a colorless oil: IR (film, cm^{-1}) 1725; ^1H NMR (300 MHz, $CDCl_3$) δ 9.70 (s, 1 H), 5.36 (t, J = 7.1 Hz, 1 H), 4.60 (s, 2 H), 3.88 (s, 2 H), 3.58 (t, J = 7.8 Hz, 2 H), 2.39 (dd, J = 16.3, 5.8 Hz, 1 H), 2.19 (ddd, J = 16.4, 8.1, 2.7 Hz, 1 H), 2.11–1.92 (m, 3 H), 1.61 (s, 3 H), 1.42–1.08 (m, 2 H), 0.92 (d, J = 6.5 Hz, 3 H), 0.90 (t, J = 8.3 Hz, 2 H), –0.03 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 202.4, 132.0, 127.7, 93.6, 73.2, 64.9, 50.8, 36.4, 27.7, 25.0, 19.7, 18.0, 13.9, –1.5; MS m/z ($M^+ - Me_3SiCH_2$) calcd 213.1490, obsd 213.1482; $[\alpha]^{25}_D$ +10.6° (c 3.90, $CHCl_3$).

[2-[[[(2*E*,6*R*)-7-*m*-Dithian-2-yl-2,6-dimethyl-2-heptenyl]oxy]methoxy]ethyl]trimethylsilane (17). A solution of 3.0 g (10 mmol) of **16** and 2.16 g (20 mmol) of 1,3-propanedithiol in 60 mL of dry CH_2Cl_2 was cooled to 0 °C, treated with 28 mg (0.02 equiv) of boron trifluoride etherate, and stirred for 2 h at rt. After the addition of 10% NaOH solution (150 mL), the product was extracted into ether (3 × 200 mL), and the combined organic layers were washed with water and brine and then dried and concentrated. The residue was purified by silica gel chromatography (elution with 1:19 ethyl acetate/petroleum ether) gave 2.44 g (63%) of **17** as a colorless oil: IR ($CHCl_3$, cm^{-1}) 1460, 1420, 1380, 1250; ^1H NMR (300 MHz, $CDCl_3$) δ 5.40 (t, J = 7.0 Hz, 1 H), 4.65 (s, 2 H), 4.08 (dd, J = 6.5, 8.2 Hz, 1 H), 3.92 (s, 2 H), 3.62 (dd, J = 7.5, 8.2 Hz, 2 H), 2.90–2.75 (m, 4H), 2.20–2.00 (m, 2 H), 1.64 (s, 3 H), 2.0–1.5 (m, 5 H), 1.40–1.30 (m, 1 H), 1.25–1.10 (m, 1 H), 0.90 (d, J = 6.4 Hz, 3 H), 1.0–0.8 (m, 2 H), 0.01 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 131.7, 128.4, 93.7, 73.4, 65.0, 45.5, 42.5, 36.4, 30.6, 30.4, 29.5, 26.1, 25.0, 19.3, 18.1, 14.0, –1.4; MS m/z (M^+) calcd 390.2034, obsd 390.2058; $[\alpha]^{25}_D$ –3.5° (c 2.2, $CHCl_3$).

Methyl 2-(Hydroxymethyl)-3-(trimethylstannyl)-3-butenoate (19). A cold (–20 °C) solution of freshly distilled diisopropylamine (1.5 mL, 10.7 mmol) in 30 mL of anhydrous THF was treated with *n*-butyllithium (7.5 mL of 1.4 M in hexanes, 1.05 equiv), stirred for 15 min at 0 °C, cooled to –78 °C, and treated with 18[19] (2.63 g, 10 mmol) dissolved in dry THF (15 mL). After 30 min at –78 °C and 1 h at 0 °C, the enolate anion solution was returned to –78 °C, treated with formaldehyde (prepared by distilling 2.1 g (7 equiv) of paraformaldehyde into 50 mL of THF), stirred for 30 min, and quenched with saturated NH_4Cl solution (10 mL) and brine (50 mL). The separated aqueous layer was extracted with ether (2 × 50 mL), and the combined organic solutions were washed with water and brine, dried, and concentrated. The residue was chromatographed on silica gel (elution with 1:4 ethyl acetate/petroleum ether) to provide 915 mg (31%) of **19** as a colorless oil: IR ($CHCl_3$, cm^{-1}) 3580, 1715; ^1H NMR (300 MHz, $CDCl_3$) δ 5.84 (tq, J = 0.8, 67.5 Hz, 1 H), 5.44 (dt, J = 1.95, 31.4 Hz, 1 H), 3.95–3.80 (m, 1 H), 3.72 (s, 3 H), 3.75–3.60 (m, 1 H), 3.50–3.45 (m, 1 H), 2.12 (br t, 1 H), 0.17 (t, J = 26.9 Hz, 9 H); MS m/z ($M^+ - CH_3$) calcd 279.0042, obsd 279.0091.

2-[1-(Trimethylstannyl)vinyl]-1,3-propanediol (20). A cold (–50 °C), magnetically stirred solution of **19** (22.43 g, 76.6 mmol) in dry CH_2Cl_2 (400 mL) was treated with diisobutylaluminum hydride (338 mL of 1 M in hexanes, 4.4 equiv). The mixture was stirred for 4 h at –40 °C, warmed to –10 °C during 1.5 h, and quenched with methanol (50 mL) and sodium potassium tartrate solution (800 mL of 0.7 M). Stirring was maintained at rt for 18 h before the separated aqueous layer was extracted with ether (3 × 300 mL). The combined organic solutions were washed with brine, dried, and concentrated. The residue was purified by chromatography on silica gel (elution with 1:1 ethyl acetate/petroleum ether) to give 13.02 g (64%) of **20** as a colorless oil: IR ($CHCl_3$, cm^{-1}) 3610; ^1H NMR (300 MHz, $CDCl_3$) δ 5.85 (tt, J = 1.4, 66.7 Hz, 1 H), 5.41 (dt, J = 2.4, 30.5 Hz, 1 H), 3.80–3.65 (m, 4 H), 2.74 (m, 1 H), 1.92 (t, J = 5.5 Hz, 2 H), 0.18 (t, J = 26.5 Hz, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 153.0, 128.5, 64.7, 54.5, –8.4; MS m/z ($M^+ - CH_3$) calcd 251.0099, obsd 251.0110.

Anal. Calcd for $C_8H_{18}O_2Sn$: C, 36.27; H, 6.85. Found: C, 36.27; H, 6.85.

2-[[(*p*-Methoxybenzyl)oxy]methyl]-3-(trimethylstannyl)-3-buten-1-ol (21a). A cold (0 °C) solution of **20** (9.3 g, 35.1 mmol) in dry THF (60 mL) was treated with sodium hydride (1.685 g, 42.1 mmol), stirred at rt for 1 h, and treated sequentially with 4-methoxybenzyl chloride (6.05 g, 38.6 mmol) and sodium iodide (5.26 g, 35.1 mmol). After 6 h, an additional 2.75 g of the chloride was introduced. Reaction was judged complete (TLC analysis) after another 12 h. Saturated NH_4Cl solution (100 mL) was added, the separated aqueous phase was extracted with ether (2 × 150 mL), and the combined organic solutions were washed with water and brine, dried, and concentrated. Chromatography of the residue on silica gel (elution with 1:7 ethyl acetate/petroleum ether) delivered 8.50 g (63%) of **21a** as a colorless, viscous oil: IR ($CHCl_3$, cm^{-1}) 3600, 1605; ^1H NMR (300 MHz, $CDCl_3$) δ 7.17 (d, J = 8.5 Hz, 2 H), 6.82 (d, J = 8.5 Hz, 2 H), 5.73 (tt, J = 1.1, 62.0 Hz, 1 H), 5.28 (dt, J = 2.3, 34.2 Hz, 1 H), 4.38 (s, 2 H), 3.75 (s, 3 H), 3.7–3.5 (m, 2 H), 3.48 (m, 2 H), 2.75 (m, 1 H), 2.10 (br s, 1 H), 0.15 (dt, J = 1.1, 12.2, 9.0 Hz, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.3, 153.1, 129.9, 129.4, 127.9, 113.8, 73.0, 72.4, 65.1, 55.3, 52.4, –8.3; MS m/z ($M^+ - CH_2C_6H_4OCH_3$) calcd 251.0090, obsd 251.0090.

Anal. Calcd for $C_{16}H_{26}O_3Sn$: C, 49.91; H, 6.81. Found: C, 50.20; H, 6.85.

[2-[[[(2*E*,6*S*)-7-[2-[(2*RS*)-2-[[(*p*-Methoxybenzyl)oxy]methyl]-3-(trimethylstannyl)-3-butenyl]-*m*-dithian-2-yl]-2,6-dimethyl-2-heptenyl]oxy]methoxy]ethyl]trimethylsilane (22). To a solution of **21a** (2.45 g, 6.39 mmol) in dry CH_2Cl_2 (50 mL) cooled to −30 °C was added triethylamine (1.79 mL, 12.7 mmol) followed by methanesulfonyl chloride (2.19 g, 19.1 mmol). After 1.5 h of stirring, the reaction temperature was increased to −10 °C, ice–water (150 mL) was introduced followed by ether (200 mL), and the separated aqueous layer was extracted with ether (2 × 100 mL). The combined organic solutions were washed with brine, dried, and concentrated. The residue was chromatographed on silica gel (gradient elution from 4:1 CH_2Cl_2/petroleum ether to CH_2Cl_2) to give 2.52 g (85%) of **21b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.7 Hz, 2 H), 6.86 (d, *J* = 8.7 Hz, 2 H), 5.82 (tt, *J* = 1.0, 61.5 Hz, 1 H), 5.36 (dt, *J* = 2.0, 26.0 Hz, 1H), 4.43 (d, *J* = 11.4 Hz, 1 H), 4.35 (d, *J* = 11.4 Hz, 1 H), 4.30 (dd, *J* = 6.7, 9.5 Hz, 1 H), 4.19 (dd, *J* = 6.5, 9.5 Hz, 1 H), 3.79 (s, 3 H), 3.53 (dd, *J* = 4.6, 9.2 Hz, 1 H), 3.43 (dd, *J* = 3.7, 9.2 Hz, 1 H), 2.91 (s, 3 H), 3.00–2.70 (m, 1 H), 0.11 (dt, *J* = 1.1, 26 Hz, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.3, 151.8, 129.8, 129.6, 129.1, 113.8, 73.1, 70.1, 69.5, 55.3, 50.0, 37.2, −7.8.

A solution of **21b** (2.52 g, 5.44 mmol) and sodium iodide (8.44 g, 56.3 mmol) in acetone (90 mL) was refluxed for 15 h, diluted with pentane (300 mL), and placed atop a silica gel column. Elution with 1:19 ethyl acetate/petroleum ether furnished 2.60 g (97%) of **21c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.5 Hz, 2 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 5.76 (dt, *J* = 1.9, 61.3 Hz, 1 H), 5.34 (dt, *J* = 1.9, 27 Hz, 1 H), 4.43 (q, *J* = 11.3 Hz, 2 H), 3.81 (s, 3 H), 3.60 (dd, *J* = 4.5, 9.3 Hz, 1 H), 3.55–3.40 (m, 2 H), 3.14 (dd, *J* = 6.9, 9.5 Hz, 1 H), 3.0–2.6 (m, 1 H), 0.12 (t, *J* = 27.0 Hz, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.3, 154.9, 130.0, 129.6, 127.9, 113.8, 73.1, 72.5, 55.3, 52.9, 9.7, −7.9.

A solution of **17** (120 mg, 0.307 mmol) in dry THF (0.7 mL) was cooled to −40 °C, treated with *n*-butyllithium (0.23 mL of 1.58 M, 1.2 equiv), stirred at −20 °C for 2 h, cooled to −78 °C, and treated with a solution of **21c** (183 mg, 1.2 equiv) in THF (0.3 mL) and DMPU (0.3 mL). After 4 h at −78 °C, the reaction mixture was quenched with saturated NH_4Cl solution (1 mL) and brine (5 mL) prior to ether extraction (3 × 10 mL). The combined organic solutions were washed with brine, dried, and concentrated. Chromatography of the residue on silica gel (elution with 1:19 ethyl acetate/petroleum ether) resulted in the isolation of **22** (18 mg, 8%) as a 5:1 mixture of two diastereomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, *J* = 6.9 Hz, 2 H), 6.85 (d, *J* = 6.9 Hz, 2 H), 5.78 (s, 1 H), 5.42 (t, *J* = 7.0 Hz, 1 H), 5.24 (d, *J* = 2.1 Hz, 1 H), 4.66 (s, 2 H), 4.42 (s, 2 H), 3.93 (s, 2 H), 3.80 (s, 3 H), 3.63 (dd, *J* = 8.5, 8.0 Hz, 2 H), 3.40–3.25 (m, 2 H), 3.0–2.5 (m, 6 H), 2.35 (ddd, *J* = 4.0, 7.5, 15.0 Hz, 1 H), 1.65 (s, 3 H), 2.10–1.00 (series of m, 12 H), 1.00 (m, 2 H), 0.13 (t, *J* = 26.9 Hz, 9 H), 0.02 (s, 9 H); MS *m/z* ($M^+ - CH_3$) calcd 593.2652, obsd 593.2668.

(2*RS*,4*R*,7*E*)-1-Iodo-4,8-dimethyl-9-[[2-(trimethylsilyl)ethoxy]methoxy]-7-nonen-2-ol (23). To 336.8 mL (33.68 mmol) of a 0.1 M blue-green solution of samarium(II) iodide in THF at 0 °C was added a solution of 5.06 g (16.84 mmol) of **16** and 2.7 mL (33.68 mmol) of diiodomethane in 34 mL of THF. The mixture was stirred for 10 min (solution turned yellow), quenched with 1.0 M HCl, extracted with ether, and washed with sodium thiosulfate solution and brine. The combined organic layers were dried, filtered, and concentrated to leave a residue which was purified by flash chromatography on silica gel (elution with 1:9 ethyl acetate/petroleum ether) to afford 6.05 g (81%) of **23**: IR (neat, cm^{-1}) 3440; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.37 (t, *J* = 7.2 Hz, 1 H), 4.61 (s, 2 H), 3.89 (s, 2 H), 3.62–3.52 (m, 1 H), 3.59 (dd, *J* = 8.8, 8.2 Hz, 2 H), 3.34–3.27 (m, 1 H), 3.19–3.13 (m, 1 H), 2.23 (br s, 1 H), 2.16–1.96 (m, 2 H), 1.67–1.12 (m, 5 H), 1.61 (s, 3 H), 0.93–0.87 (m, 2 H), 0.89 (d, *J* = 6.6 Hz, 3 H), −0.02 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 131.7, 128.6, 93.6, 73.3, 68.8, 65.0, 43.9, 36.2, 29.4, 24.9, 20.0, 18.1, 17.0, 14.0, −1.5; MS *m/z* ($M^+ - Me_3SiCH_2CH_2OCH_2O$) calcd 295.0518, obsd 295.0496.

Anal. Calcd for $C_{17}H_{35}IO_3Si$: C, 46.15; H, 7.97. Found: C, 46.43; H, 8.01.

(*E*)- and (*Z*)-(Trimethylstannyl)-2-butanoic Acid (25). To 17.69 g (67.29 mmol) of **18** in 224 mL of methanol was added 100.9 mL (201.9 mmol) of 2 M KOH solution, and the mixture was heated at reflux for 15 min, concentrated, diluted with water, extracted with ether, acidified with 1.0 M HCl, and extracted with ether (3×). The combined organic layers were dried, filtered, and concentrated to leave a residue that was purified by flash chromatography on silica gel (elution with 1:19 ethyl acetate/petroleum ether). There was isolated 12.73 g (76%) of the acids, which were separated by MPLC on silica gel.

For the major (*E*)-acid **25**: colorless solid, mp 52–54 °C; IR (film, cm^{-1}) 2725, 2620, 2550, 1685; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.50 (br s, 1 H), 6.02 (q, *J* = 1.9 Hz, 1 H), 2.41 (d, *J* = 1.9 Hz, 3 H), 0.20 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 172.6, 169.9, 127.3, 21.7, −10.0; MS *m/z* ($M^+ - CH_3$) calcd 234.9780, obsd 234.9777.

Anal. Calcd for $C_7H_{14}O_2Sn$: C, 33.78; H, 5.67. Found: C, 34.07; H, 5.84.

For the minor (*Z*)-acid: colorless solid; mp 128–130 °C; IR ($CHCl_3$, cm^{-1}) 2720, 2615, 2530, 1730, 1680; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.87 (br s, 1 H), 6.44 (q, *J* = 1.7 Hz, 1 H), 2.19 (d, *J* = 1.7 Hz, 3 H), 0.18 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 176.7, 172.9, 128.4, 27.3, −7.7; MS *m/z* ($M^+ - CH_3$) calcd 234.9780, obsd 234.9791.

(3*RS*,5*RS*)-5-[(2*R*,5*E*)-2,6-Dimethyl-7-[[2-(trimethylsilyl)ethoxy]methoxy]-5-heptenyl]dihydro-3-[1-(trimethylstannyl)vinyl]-2(3*H*)-furanone (27). To a solution of the isomeric acids **25** (21.56 g, 86.7 mmol) and **23** (28.5 g, 64.4 mmol) in anhydrous ether (250 mL) was added dicyclohexylcarbodiimide (17.9 g, 86.8 mmol) dissolved in ether (50 mL) at 0 °C. Following the addition of 4-(dimethylamino)pyridine (1.18 g, 9.7 mmol) at 0 °C, the reaction mixture was stirred at rt for 10 h, filtered, and concentrated. The residue was chromatographed on silica gel (elution with 3.5% ethyl acetate in petroleum ether) to give an *E*/*Z* isomeric mixture of **26** (35.48 g, 82%). Comparable reactions with the isomerically pure acids gave the isomerically pure esters. However, since isomerization about this double bond occurs at a later step, this separation was superfluous.

A solution of freshly distilled diisopropylamine (9.78 mL, 69.9 mmol) in dry THF (350 mL) was treated with *n*-butyllithium (46.6 mL of 1.5 M in hexanes, 69.9 mmol) at −20 °C. After 20 min, the reaction mixture was cooled to −78 °C, and **26** (31.37 g, 46.6 mmol) dissolved in THF (200 mL) was added during 30 min. Stirring was continued for 3 h as the temperature was allowed to warm to 30 °C. Quenching was accomplished with saturated NH_4Cl solution (100 mL) and brine (100 mL), and the product was extracted into ether (3 × 500 mL). The combined organic layers were washed with brine, dried, and concentrated to give **27** and α,β-unsaturated isomers thereof. Chromatography on silica gel (gradient elution with 6–7.5% ethyl acetate in petroleum ether) gave the desired **27** (4.52 g, 18%) and its α,β-unsaturated isomer (7.70 g, 30%). The latter was isomerized by treatment with 2 equiv of LDA in dry THF (100 mL) at −78 → 0 °C for 2 h and inverse addition to saturated NH_4Cl solution (150 mL) at 0 °C. Comparable workup and chromatography gave 5.56 g (22%) of additional **27** and 1.24 g (5%) of the α,β-unsaturated isomer. Reprocessing of the latter material provided an additional 730 mg (3%) of **27**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.75 (d, *J* = 1.5 Hz, 1 H), 5.45 (m, 1 H), 5.41 (d, *J* = 1.7 Hz, 1 H), 4.66 (s, 2 H), 4.51 (m, 1 H), 3.93 (s, 2 H), 3.63 (t, *J* = 8.7 Hz, 2 H), 3.48 (m, 1 H), 2.47 (m, 1 H), 2.15–2.0 (m, 2 H), 1.66 (s, 3 H), 1.9–1.2 (series of m, 6 H), 0.95 (m, 5H), 0.25 (s, 9 H), 0.20 (t, *J* = 26.5, Hz, 9 H); MS *m/z* ($M^+ - CH_3$) calcd 531.1951, obsd 531.1951.

Anal. Calcd for $C_{24}H_{46}O_4SiSn$: C, 52.85; H, 8.50. Found: C, 52.76; H, 8.45.

(3*RS*,5*RS*,7*R*,10*E*)-7,11-Dimethyl-12-[[2-(trimethylsilyl)ethoxy]methoxy]-2-(trimethylstannyl)-1,10-dodecadiene-3,5-diol (28a). A solution of **27** (7.87 g, 144.3 mmol) in dry CH_2Cl_2 (100 mL) was cooled to −40 °C and treated with diisobutylaluminum hydride (46.7 mL of 1 M in hexanes, 3.3 equiv), stirred for 2 h at −40 → 0 °C and for 3 h at rt, and then quenched with methanol (5 mL) and potassium sodium tartrate solution (200 mL of 0.7 M). After 2 h of stirring at rt, the aqueous layer was separated and extracted with ether (2 × 200 mL). The combined organic solutions were washed with brine, dried, and evaporated to leave a residue that was chromatographed on silica gel (elution with 27.5% ethyl acetate in petroleum ether). This enabled separation of the two isomers.

For the major, more polar isomer: 6.74 g (85%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82 (tt, J = 2.4, 74.5 Hz, 1 H), 5.41 (t, J = 7.0 Hz, 1 H), 5.35 (t, J = 35.5 Hz, 1 H), 4.66 (s, 2 H), 3.93 (s, 2 H), 3.70 (m, 1 H), 3.63 (dd, J = 8.6, 8.6 Hz, 2 H), 3.50 (m, 2 H), 2.70 (m, 1 H with coupling to Sn, J = 45 Hz), 2.2–1.9 (m, 4 H), 1.65 (s, 3 H), 1.7–1.1 (series of m, 7 H), 0.92 (m, 5 H), 0.18 (t, J = 26.2 Hz, 9 H), 0.025 (s, 9 H).

Anal. Calcd for $C_{24}H_{50}O_4SiSn$: C, 52.47; H, 9.17. Found: C, 52.51; H, 9.14.

For the minor, less polar isomer: 0.57 g (7%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82 (dt, J = 1.9, 71.8 Hz, 1 H), 5.42 (t, J = 6.0 Hz, 1H), 5.35 (dt, J = 1.8, 39.9 Hz, 1 H), 4.66 (s, 2 H), 3.93 (s, 2 H), 3.77 (m, 1 H), 3.63 (dd, J = 8.5, 8.5 Hz, 2 H), 3.50 (m, 2 H), 2.66 (m, 1 H with coupling to Sn, J = 48 Hz), 2.2–1.9 (m, 4 H), 1.66 (s, 3 H), 1.7–1.1 (series of m, 7 H), 0.93 (m, 5 H), 0.20 (t, J = 26.5 Hz, 9 H), 0.024 (s, 9 H); MS m/z ($M^+ - CH_3$) calcd 535.2265, obsd 535.2278.

(3*RS*,5*RS*,7*R*,10*E*)-3-[[(*p*-Methoxybenzyl)oxy]methyl]-7,11-dimethyl-12-[[2-(trimethylsilyl)ethoxy]methoxy]-2-(trimethylstannyl)-1,10-dodecadien-5-ol (28b). A suspension of sodium hydride (857 mg, 21.4 mmol) in THF (150 mL) was treated with major diol **28a** (8.72 g, 15.87 mmol) dissolved in THF (70 m) and stirred at rt for 1 h. To this mixture was added 4-methoxybenzyl chloride (3.73 g, 23.8 mmol) followed by sodium iodide (3.57 g, 23.8 mmol). After 3 h of stirring at rt, an additional 2.49 g of the chloride was introduced and stirring was maintained for 18 h prior to quenching with saturated NH_4Cl solution (10 mL) and brine (200 mL). The separated aqueous phase was extracted with ether (3 × 200 mL), and the combined organic solutions were washed with brine, dried, and evaporated to leave a residue that was chromatographed on silica gel (elution with 13.5% ethyl acetate in petroleum ether) to give **28b** (9.82 g, 92%) as a viscous, colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, J = 8.6 Hz, 2 H), 6.92 (d, J = 8.6 Hz, 2 H), 5.80 (t, J = 74.7 Hz, 1 H), 5.42 (t, J = 6.8 Hz, 1 H), 5.28 (dt, J = 2.2, 34.4 Hz, 1 H), 4.67 (s, 2 H), 4.45 (d, J = 3.3 Hz, 2 H), 3.93 (s, 2 H), 3.79 (s, 3 H), 3.70 (m, 1 H), 3.63 (t, J = 8.5 Hz, 2 H), 3.31 (m, 2 H), 2.74 (m, 1 H with coupling to Sn: J = 45 Hz), 2.4–2.3 (m, 1 H), 2.0 (m, 2 H), 1.66 (s, 3 H), 1.6–1.0 (series of m, 7 H), 0.95–0.80 (m, 5H), 0.19 (t, J = 26.8 Hz, 9 H), 0.10 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.2, 157.2, 131.43, 131.39, 129.94, 129.90, 129.5, 129.0, 187.6, 126.3, 113.9, 113.7, 93.6, 93.4, 74.4, 74.2, 73.4, 73.79, 72.77, 65.0, 60.4, 55.2, 48.9, 48.8, 45.6, 45.5, 41.6, 41.1, 37.5, 36.3, 29.4, 29.0, 25.2, 25.1, 21.0, 20.3, 19.2, 18.1, 14.0, −1.4, −8.1; MS m/z ($M^+ - CH_3$) calcd 653.2821, obsd 653.2828.

Anal. Calcd for $C_{32}H_{58}O_5SiSn$: C, 57.40; H, 8.73. Found: C, 57.21; H, 8.70.

(α*RS*,γ*RS*,1*S*,2*R*,5*S*,6*S*,7*S*)-α-[(2*R*,5*E*)-2,6-Dimethyl-7-[[2-(trimethylsilyl)ethoxy]methoxy]-5-heptenyl]-6-hydroxy-γ-[[(*p*-methoxybenzyl)oxy]methyl]-2-methyl-δ,8-dimethylenetricyclo[3.2.1.0^{2,7}]octane-6-butanol (29). To a solution of **28b** (5.37 g, 8.0 mmol) in dry THF (50 mL) cooled to −78 °C was added 1.5 M methyllithium–lithium bromide complex in ether (13.4 mL, 20.1 mmol), and the mixture was stirred at this temperature for 30 min and at −35 °C for 1 h prior to introduction of (+)-8 (2.37 g, 16.0 mmol) in dry THF (25 mL) at −78 °C. After 3 h of stirring at −78 → −20 °C, brine (150 mL) was added and the separated aqueous phase was extracted with ether (3 × 100 mL). The combined organic solutions were washed with brine, dried, and concentrated to leave a residue that was twice chromatographed on silica gel (gradient elution with 20–25% ethyl acetate in petroleum ether) to give the less polar isomer **C** (2.05 g, 39%) and the more polar isomer **D** (2.39 g, 46%).

For **C**: IR (neat, cm^{-1}) 3395, 1655, 1610; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, J = 8.6 Hz, 2 H), 6.83 (d, J = 8.6 Hz, 2 H), 5.38 (t, J = 6.6 Hz, 1 H), 5.13 (s, 1 H), 4.84 (s, 1 H), 4.62 (s, 2 H), 4.55 (s, 1 H), 4.38 (s, 2 H), 4.31 (s, 1 H), 4.89 (s, 2 H), 3.75 (s, 3 H), 3.75–3.70 (m, 1 H), 3.60 (t, J = 8.4 Hz, 2 H), 3.33–3.20 (m, 2 H), 2.76–2.72 (m, 1 H), 2.13 (br s, 1 H), 2.09–1.05 (series of m, 17 H), 1.61 (s, 3 H), 1.00 (s, 3 H), 0.91 (t, J = 8.5 Hz, 2 H), 0.85 (d, J = 6.5 Hz, 3 H), −0.01 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.1, 152.7, 151.5, 131.2, 130.2, 129.1, 128.9, 113.6, 110.6, 101.2, 93.5, 81.1, 75.6, 73.4, 72.4, 66.2, 64.9, 55.1, 45.3, 44.8, 42.3, 37.0, 36.1, 34.9, 29.0, 27.3, 25.1, 24.4, 24.3, 23.4, 19.4, 18.0, 13.9, −1.5; MS m/z (M^+) calcd 654.4270, obsd 654.4293; $[\alpha]^{25}_D$ +4.9° (c 0.29, $CHCl_3$).

For **D**: IR (neat, cm^{-1}) 3435, 1655, 1610; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, J = 8.6 Hz, 2 H), 6.82 (d, J = 8.6 Hz, 2 H), 5.36 (t, J = 6.7 Hz, 1 H), 5.17 (s, 1 H), 4.82 (s, 1 H), 4.61 (s, 2 H), 4.58 (s, 1 H), 4.46 (s, 1 H), 4.43 (s, 2 H), 3.88 (s, 2 H), 3.75 (s, 3 H), 3.63–3.56 (m, 1 H), 3.59 (t, J = 8.4 Hz, 2 H), 3.45–3.40 (m, 1 H), 3.20 (t, J = 8.7 Hz, 1 H), 2.92–2.86 (m, 1 H), 2.28 (br s, 1 H), 2.13–1.05 (series of m, 17 H), 1.60 (s, 3 H), 1.01 (s, 3 H), 0.91 (t, J = 8.3 Hz, 2 H), 0.81 (d, J = 6.5 Hz, 3 H), −0.01 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.2, 153.7, 153.2, 131.4, 129.5, 129.3, 128.7, 113.7, 110.2, 100.6, 93.5, 79.8, 76.7, 73.3, 72.8, 66.8, 64.0, 55.1, 45.9, 45.3, 40.8, 37.4, 36.4, 36.2, 35.0, 29.3, 27.7, 25.0, 24.7, 24.4, 23.5, 20.0, 18.0, 13.9, −1.5; MS m/z ($M^+ - H_2O$) calcd 636.4210, obsd 636.4245; $[\alpha]^{25}_D$ −7.0° (c 0.36, $CHCl_3$).

Anal. Calcd for $C_{39}H_{62}O_6Si$: C, 71.52; H, 9.54. Found: C, 71.79; H, 9.80.

(3*R*,6*E*)-8-[(*p*-Methoxybenzyl)oxy]-3,7-dimethyl-6-octenal (30). To a solution of 20.00 g (93.33 mmol) of **14a** in 52 mL of ether was added 18.98 mL (139.99 mmol) of 4-methoxybenzyl chloride followed by 23.79 g (102.66 mmol) of silver(I) oxide slowly so as to maintain a gentle reflux. After completion of the addition, the reaction mixture was heated at reflux for 4 h, filtered, washed with ether, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 1:13 ethyl acetate/petroleum ether) to afford 15.13 g (49%) of the ether acetate and 9.25 g of the recovered alcohol.

For the ether acetate: IR (neat, cm^{-1}) 1735, 1615; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (m, 2 H), 7.23 (m, 2 H), 5.39 (dt, J = 7.1, 0.8 Hz, 1 H), 4.36 (s, 2 H), 4.10 (m, 2 H), 3.85 (s, 2 H), 3.77 (s, 3 H), 2.10–2.00 (m, 2 H), 2.01 (s, 3 H), 1.72–1.64 (m, 1 H), 1.66 (s, 3 H), 1.64–1.50 (m, 1 H), 1.49–1.33 (m, 2 H), 1.28–1.18 (m, 1 H), 0.92 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 170.9, 159.0, 132.1, 130.6, 129.1, 128.1, 113.6, 75.8, 70.9, 62.7, 55.1, 36.4, 35.3, 29.4, 24.9, 20.8, 19.2, 13.8; MS m/z (M^+) calcd 334.2144, obsd 334.2158; $[\alpha]^{25}_D$ +3.6° (c 3.05, $CHCl_3$).

Anal. Calcd for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Found: C, 71.70; H, 8.89.

To a solution of 21.51 g (64.31 mmol) of the above material in 320 mL of a 1:1 mixture of methanol and water was added 5.15 g (128.63 mmol) of NaOh. The mixture was stirred overnight at rt, concentrated, and extracted with ether (3 × 150 mL). The combined organic layers were dried, filtered, and concentrated to leave a residue that was purified by flash chromatography on silica gel (elution with 1:4 ethyl acetate/petroleum ether). There was obtained 17.68 g (94%) of the ether alcohol: IR (neat, cm^{-1}) 3410; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27–7.21 (m, 2 H), 6.89–6.82 (m, 2 H), 5.40 (dt, J = 7.1, 1.1 Hz, 1 H), 4.37 (s, 2 H), 3.86 (s, 2 H), 3.78 (s, 3 H), 3.67–3.54 (m, 2 H), 2.13–1.96 (m, 3 H), 1.66 (s, 3 H), 1.63–1.52 (m, 2 H), 1.44–1.30 (m, 2 H), 1.27–1.17 (m, 1 H), 0.90 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.0, 131.8, 130.4, 129.2, 128.5, 113.6, 75.9, 70.9, 60.7, 55.1, 39.7, 36.7, 29.1, 25.0, 19.4, 13.8; MS m/z (M^+) calcd 292.2038, obsd 292.2019; $[\alpha]^{25}_D$ +3.8° (c 2.84, $CHCl_3$).

Anal. Calcd for $C_{18}H_{28}O_3$: C, 73.93; H, 9.65. Found: C, 73.64; H, 9.64.

To a solution of 1.70 mL (19.53 mmol) of oxalyl chloride in 30 mL of CH_2Cl_2 at −60 °C under an argon atmosphere was added 2.77 mL (39.07 mmol) of dimethyl sulfoxide in 7 mL of CH_2Cl_2, and the mixture was stirred for 20 min. Then 2.72 g (9.30 mmol) of the above ether alcohol in 9 mL of CH_2Cl_2 was added, and stirring was maintained for 40 min. Finally, 10.76 mL (77.20 mmol) of triethylamine was introduced, and the mixture was allowed to warm to rt, stirred for 30 min, and quenched with water. The separated organic layer was washed with 1.0 N HCl solution and brine, dried, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 1:19 ethyl acetate/petroleum ether) to provide 2.62 g (97%) of **30**: IR (neat, cm^{-1}) 1725; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.71 (t, J = 2.2 Hz, 1 H), 7.25–7.21 (m, 2 H), 6.87–6.82 (m, 2 H), 5.38 (dt, J = 7.9, 1.1 Hz, 1 H), 4.35 (s, 2 H), 3.84 (s, 2 H), 3.75 (s, 3 H), 2.41–2.16 (ABXm, 2 H), 2.10–2.00 (m, 3 H), 1.65 (s, 3 H), 1.45–1.24 (m, 2 H), 0.95 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 202.3, 158.9, 132.3, 130.4, 129.0, 127.4, 113.5, 75.6, 70.9, 54.9, 50.7, 36.3, 27.5, 24.8, 19.6, 13.7; MS m/z ($M^+ - MeOC_6H_4CH_2CHO$) calcd 140.1201, obsd 140.1212; $[\alpha]^{25}_D$ +11.1° (c 2.16, $CHCl_3$).

(1*RS*,3*R*,6*E*)-1-(Iodomethyl)-8-[(*p*-methoxybenzyl)oxy]-3,7-dimethyl-6-octenyl (*E*)-3-(Trimethylstannyl)crotonate (31). To 166.67 mL (16.67 mmol) of a 0.1 M blue-green solution of samarium(II) iodide in THF at 0 °C was added a solution of 2.42 g (8.33 mmol) of **30** and 1.34 mL (16.67 mmol) of diiodomethane in 17 mL of THF. The mixture was stirred for 15 min (solution turned yellow), quenched with 1.0 M HCl, and extracted with ether. The combined organic phases were washed with sodium thiosulfate solution and brine, dried, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 1:9 ethyl acetate/petroleum ether) to afford 2.22 g (62%) of two diastereomeric hydroxy iodides: IR (neat, cm^{-1}) 3425; ^1H NMR (300 MHz, $CDCl_3$) δ 7.27–7.24 (m, 2 H), 6.89–6.85 (m, 2 H), 5.46–5.38 (m, 1 H), 4.37 (s, 2 H), 3.86 (s, 2 H), 3.78 (s, 3 H), 3.66–3.51 (m, 1 H), 3.35–3.14 (ABxm, 2 H), 2.29 (m, 1 H), 2.18–2.01 (m, 2 H), 1.67 (s, 3 H), 1.66–1.16 (m, 5 H), 0.93 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.0, 132.0, 130.5, 129.2, 113.6, 75.8, 71.0, 68.8, 55.1, 43.8, 36.1, 29.1, 24.9, 19.9, 17.0, 13.9; MS m/z (M^+ – MeOH) calcd 401.0937, obsd. 401.0943.

Anal. Calcd for $C_{19}H_{29}IO_3$: C, 52.78; H, 6.76. Found: C, 53.07; H, 6.86.

To 1.30 g (3.01 mmol) of the above iodo alcohols and 1.12 g (4.51 mmol) of the *E*-carboxylic acid in 15 mL of ether at 0 °C under an argon atmosphere was added 0.93 g (4.51 mmol) of dicyclohexylcarbodiimide in 15 mL of ether, followed by 0.04 g (0.30 mmol) of 4-(dimethylamino)pyridine. The reaction mixture was allowed to warm to rt, stirred overnight, and filtered. The filtrate was washed with ether, and the combined organic solutions were concentrated. The residue was purified by flash chromatography on silica gel (elution with 1:32 ethyl acetate/petroleum ether) to afford 1.72 g (86%) of two diastereomers of **31**.

For one *E*-isomer: IR (neat, cm^{-1}) 1705, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.26–7.21 (m, 2 H), 6.88–6.83 (m, 2 H), 5.96 (q, J = 1.9 Hz, 1 H), 5.37 (dt, J = 7.2, 1.2 Hz, 1 H), 4.89–4.81 (m, 1 H), 4.35 (s, 2 H), 3.84 (s, 2 H), 3.78 (s, 3 H), 3.36–3.25 (m, 2 H), 2.39 (d, J = 1.9 Hz, 3 H), 2.09–2.00 (m, 2 H), 1.78–1.71 (m, 1 H), 1.65 (s, 3 H), 1.57–1.16 (series of m, 4 H), 0.92 (d, J = 6.2 Hz, 3 H), 0.18 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 170.0, 163.5, 159.1, 132.2, 130.7, 129.3, 128.2, 127.3, 113.7, 76.0, 71.1, 69.7, 55.2, 41.5, 37.0, 29.0, 25.1, 21.7, 19.4, 13.9, 9.4, –10.0; MS m/z (M^+ – CH_3) calcd 649.0839; obsd 649.0838; $[\alpha]^{25}_D$ –4.7° (*c* 1.50, $CHCl_3$).

For the other *E*-isomer: IR (neat, cm^{-1}) 1705, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, J = 8.5 Hz, 2 H), 6.85 (g, J = 8.6 Hz, 2 H), 5.96 (q, J = 1.8 Hz, 1 H), 5.37 (t, J = 7.0 Hz, 1 H), 4.83–4.75 (m, 1 H), 4.35 (s, 2 H), 3.84 (s, 2 H), 3.78 (s, 3 H), 3.39–3.24 (m, 2 H), 2.39 (d, J = 1.8 Hz, 3 H), 2.09–1.99 (m, 2 H), 1.69–1.13 (series of m, 5 H), 1.64 (s, 3H), 0.93 (d, J = 6.0 Hz, 3 H), 0.18 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 170.0, 163.4, 158.1, 132.3, 130.7, 129.3, 128.3, 127.3, 113.7, 76.0, 71.1, 69.9, 55.3, 41.4, 36.3, 29.2, 24.9, 21.7, 19.8, 13.9, 9.3, –10.0; MS m/z (M^+ – CH_3) calcd 649.0839, obsd 649.0828; $[\alpha]^{25}_D$ +13.4° (*c* 0.83, $CHCl_3$).

Comparable processing of the *Z*-carboxylic acid (154 mg, 0.62 μmol) afforded the mixture of *Z*-esters (232 mg) in 85% yield. For the major isomer: IR (neat, cm^{-1}) 1700, 1615, 1605; ^1H NMR (300 MHz, $CDCl_3$) δ 7.25–7.21 (m, 2 H), 6.88–6.83 (m, 2 H), 6.39 (q, J = 1.6 Hz, 1 H), 5.37 (t, J = 7.1 Hz, 1 H), 4.90–4.79 (m, 1 H), 4.35 (s, 2 H), 3.84 (s, 2 H), 3.78 (s, 3 H), 3.37–3.21 (m, 2 H), 2.12 (d, J = 1.6 Hz, 3 H), 2.09–1.98 (m, 2 H), 1.78–1.13 (series of m, 5 H), 1.65 (s, 3 H), 0.90 (d, J = 6.0 Hz, 3 H), 0.16 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 173.3, 167.2, 159.1, 132.2, 129.3 (2 C), 128.6, 128.2, 113.7 (2 C), 76.0, 71.1, 70.3, 55.2, 41.4, 36.1, 28.9, 26.8, 25.0, 19.8, 13.9, 9.0, –7.8 (3 C); MS m/z (M^+ – CH_3) calcd 647.0801, obsd 647.0816.

Anal. Calcd for $C_{26}H_{41}IO_4Sn$: C, 47.09; H, 6.23. Found: C, 47.44; H, 6.28.

(3*RS*,5*RS*)-Dihydro-5-[(2*R*,5*E*)-7-[(*p*-methoxybenzyl)oxy]-2,6-dimethyl-5-heptenyl]-3-[1-(trimethylstannyl)vinyl]-2(3*H*)-furanone (33). To 13.32 mmol of lithium diisopropylamide in 60 mL of THF (prepared from 8.33 mL (13.22 mmol) of 1.5 M *n*-butyllithium and 1.87 mL (13.32 mmol) of diisopropylamine) at –78 °C was added 5.89 g (8.88 mmol) of the ester iodides in 29 mL of THF, and the solution was stirred for 3 h while being allowed to warm to –30 °C. The reaction mixture was poured into saturated NH_4Cl solution and extracted with ether. The combined organic layers were washed with brine, dried, filtered, and concentrated to leave a residue that was purified by flash chromatography on silica gel (elution with 1:13 ethyl acetate/petroleum ether) to afford 0.30 g (6%) of **32** and 1.61 g (34%) of **33**.

For **32**: IR (neat, cm^{-1}) 1730, 1625, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.27–7.24 (m, 2 H), 6.88–6.84 (m, 2 H), 5.40 (t, J = 7.0 Hz, 1 H), 4.65–4.59 (m, 1 H), 4.38 (s, 2 H), 3.86 (s, 2 H), 3.79 (s, 3 H), 3.07–2.97 (m, 1 H), 2.48–2.39 (m, 1 H), 2.13–1.98 (m, 2 H), 2.05 (d, J = 1.4 Hz, 3 H), 1.82–1.22 (series of m, 5 H), 1.66 (s, 3 H), 0.97 (d, J = 6.4 Hz, 3 H), 0.18 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 171.6, 161.5, 159.1, 132.7, 132.2, 130.7, 129.2, 128.0, 113.7, 76.1, 75.9, 71.1, 55.2, 44.3, 36.3, 33.5, 29.3, 24.9, 23.2, 19.1, 13.9, –7.8; MS m/z (M^+ – CH_3) calcd 519.1710, obsd 519.1676.

Anal. Calcd for $C_{26}H_{40}O_4Sn$: C, 58.34; H, 7.53. Found: C, 58.58; H, 7.55.

For **33**: IR (neat, cm^{-1}) 1755, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.25–7.21 (m, 2 H), 6.87–6.82 (m, 2 H), 5.74–5.72 (m, 1 H), 5.39–5.36 (m, 2 H), 4.50–4.42 (m, 1 H), 4.36 (s, 2 H), 3.87 (s, 2 H), 3.77 (s, 3 H), 3.48–3.40 (m, 1 H), 2.49–2.40 (m, 1 H), 2.10–2.01 (m, 2 H), 1.81–1.53 (series of m, 4 H), 1.65 (s, 3 H), 1.46–1.35 (m, 1 H), 1.28–1.21 (m, 1 H), 0.95 (d, J = 6.2 Hz, 3 H), 0.17 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 177.4, 159.0, 150.7, 132.3, 130.6, 129.2, 127.9, 127.2, 113.7, 75.9, 71.1, 55.2, 50.0, 42.7, 36.9, 36.4, 35.5, 29.4, 24.9, 19.1, 13.8, –8.2; MS m/z (M^+ – CH_3) calcd 519.1710, obsd 519.1730.

Equilibration of 32. To 2.93 mmol of lithium diisopropylamide in 10 mL of THF (prepared from 1.96 mL (2.93 mmol) of 1.5 M *n*-butyllithium and 411 μL (2.93 mmol) of diisopropylamine) at –78 °C was added 0.80 g (1.47 mmol) of the lactones **32** in 5 mL of THF, and the solution was stirred for 20 min at –78 °C. The reaction mixture was poured into saturated NH_4Cl solution and extracted with ether. The combined organic phases were washed with brine, dried, filtered, and concentrated to leave a residue that was purified by flash chromatography on silica gel (elution with 1:19 ethyl acetate/petroleum ether) to afford 0.36 g (45%) of **32** and 0.34 g (43%) of **33**.

Dibal-H Reduction of 33. To a solution of 288.4 mg (538.8 μL) of –33 in 5.4 mL of CH_2Cl_2 at –40 °C under an argon atmosphere was added 2.16 mL (2.16 mmol) of a 1.0 M solution of diisobutylaluminum hydride in hexanes. The reaction mixture was allowed to warm to rt, stirred for 3 h, quenched with methanol at 0 °C followed by a saturated solution of potassium sodium tartrate, stirred for 4 h, and extracted with ether. The combined organic phases were dried and concentrated, and the residue was purified by flash chromatography on silica gel (elution with 1:2 ethyl acetate/petroleum ether) to afford 266 mg (91%) of the diols **34a** and **35a** and 22 mg (8%) of the diols **36a** and **37a**.

For **34a/35a**: IR (neat, cm^{-1}) 3480, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.27–7.23 (m, 2 H), 6.90–6.85 (m, 2 H), 5.81–5.79 (m, 1 H), 5.43–5.38 (m, 1 H), 5.33 (t, J = 2.2 Hz, 1 H), 4.38 (s, 2 H), 3.86 (s, 2 H), 3.80 (s, 3 H), 3.72–3.66 (m, 1 H), 3.53–3.49 (m, 2 H), 2.72–2.67 (m, 1 H), 2.34 (br s, 2 H), 2.11–2.02 (m, 2 H), 1.67 (s, 3 H), 1.63–1.12 (series of m, 7 H), 0.92 (d, J = 6.6 Hz, 3 H), 0.17 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.1, 157.1, 132.0, 130.7, 129.3, 128.5, 127.4, 113.7, 76.0, 71.1, 67.7, 66.4, 55.2, 51.5, 45.9, 40.4, 37.5, 29.3, 25.0, 20.3, 13.9, –8.2; MS m/z (M^+ – CH_3) calcd 523.2022, obsd 523.1973.

For **36a/37a**: IR (neat, cm^{-1}) 3390, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.5 Hz, 2 H), 6.86 (d, J = 8.5 Hz, 2 H), 5.80 (d, J = 1.9 Hz, 1 H), 5.40 (t, J = 7.2 Hz, 1 H), 5.33 (t, J = 2.8 Hz, 1 H), 4.37 (s, 2 H), 3.86 (s, 2 H), 3.79 (s, 3 H), 3.84–3.77 (m, 1 H), 3.58–3.44 (m, 2 H), 2.67–2.65 (m, 1 H), 2.27 (br s, 2 H), 2.11–2.02 (m, 2 H), 1.67 (s, 3 H), 1.63–1.14 (series of m, 7 H), 0.92 (d, J = 6.8 Hz, 3 H), 0.19 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.1, 158.0, 132.0, 130.6, 129.3, 128.6, 127.3, 113.7, 76.0, 71.1, 68.3, 65.7, 55.2, 50.6, 44.7, 40.4, 37.5, 29.2, 25.0, 19.2, 13.9, –8.2; MS m/z (M^+ – CH_3) calcd 523.2023, obsd 523.2021.

Anal. Calcd for $C_{26}H_{44}O_4Sn$: C, 57.90; H, 8.22. Found: C, 58.14; H, 8.21.

(3*R*,5*R*,7*R*,10*E*)- and (3*S*,5*S*,7*R*,10*E*)-12-[(*p*-Methoxybenzyl)oxy]-3-[[(*p*-methoxybenzyl)oxy]methyl]-7,11-dimethyl-2-(trimethylstannyl)-1,10-dodecadien-5-ol (34b and 35b). To a suspension of 70.3 mg (1.76 mmol) of a 60% dispersion of sodium hydride in mineral oil in 9.6 mL of THF was added 0.79 g (1.46 mmol) of the diols **34a/35a** in 5 mL of THF, and the mixture was stirred for 45 min. 4-Methoxybenzyl chloride (279 μL, 2.20 mmol)

was introduced at 0 °C, followed by 329.3 mg (2.20 mmol) of sodium iodide, and the mixture was stirred for 18 h at rt, quenched with saturated NH_4Cl solution and brine, and extracted with ether. The combined organic solutions were dried and concentrated, and the residue was purified by flash chromatography on silica gel (elution with 1:4 ethyl acetate/petroleum ether) to afford 712 mg (74%) of **34b/35b** as a colorless oil: IR (neat, cm^{-1}) 3440, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.27–7.20 (m, 4 H), 6.88–6.83 (m, 4 H), 5.74 (t, J = 1.7 Hz, 1 H), 5.39 (dt, J = 7.2, 1.1 Hz, 1 H), 5.24 (d, J = 1.4 Hz, 1 H), 4.46–4.37 (ABq, J_{AB} = 11.9 HZ, $\Delta\nu_{AB}$ = 9.8 Hz, 2 H), 4.36 (s, 2 H), 3.84 (s, 2 H), 3.78 (s, 6 H), 3.68–3.61 (m, 1 H), 3.37–3.34 (m, 2 H), 2.79–2.58 (m, 1 H), 2.37–2.15 (m, 1 H), 2.09–1.98 (m, 2 H), 1.68–1.04 (series of m, 7 H), 1.65 (s, 3 H), 0.89 (d, J = 6.6 Hz, 3 H), 0.10 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.2, 159.1, 157.3, 132.0, 130.8, 130.0, 129.3, 128.7, 126.3, 113.7, 76.1, 74.5, 72.8, 71.0, 67.9, 55.2, 48.9, 45.7, 41.6, 36.4, 29.0, 25.2, 19.2, 13.9, -8.1; MS m/z ($M^+ - CH_3$) calcd 643.2614, obsd 643.2605.

($\alpha R,\gamma S,1S,2R,5S,6S,7S$)-6-Hydroxy-$\alpha$-[(2R,5E)-7-[(p-methoxybenzyl)oxy]-2,6-dimethyl-5-heptenyl]-γ-[[(p-methoxybenzyl)oxy]methyl]-2-methyl-δ,8-dimethylenetricyclo-[3.2.1.$0^{2,7}$]octane-6-butanol (38) and ($\alpha S,\gamma R,1S,2R,5S,6S,7S$)-6-Hydroxy-$\alpha$-[(2R,5E)-7-[(p-methoxybenzyl)oxy]-2,6-dimethyl-5-heptenyl]-γ-[[(p-methoxybenzyl)oxy]methyl]-2-methyl-δ,8-dimethylenetricyclo[3.2.1.$0^{2,7}$]octane-6-butanol (39). To a solution of 1.33 g (2.02 mmol) of the **34b/35b** mixture in 30 mL of THF at -78 °C was added 3.23 mL (4.84 mmol) of a 1.5 M solution of methyllithium–lithium bromide complex. The mixture was stirred for 30 min, warmed to -35 °C, stirred for 90 min, cooled to -78 °C, treated with 598 mg (4.03 mmol) of (+)-8 in 10 mL of THF, and allowed to warm to 0 °C during 150 min. After quenching with brine and extraction with ether, the combined organic layers were dried and concentrated to leave a residue which was purified by flash chromatography on silica gel (elution with 3:10 ethyl acetate/petroleum ether). There was isolated 445 mg (34%) of **38** and 467 mg (36%) of **39**.

For **38**: IR (neat, cm^{-1}) 3380, 1655, 1615; ^1H NMR (300 MHz, $CDCl_3$) δ 7.26–7.19 (m, 4 H), 6.87–6.82 (m, 4 H), 5.38 (dt, J = 7.0, 1.2 Hz, 1 H), 5.15 (s, 1 H), 4.86 (s, 1 H), 4.58 (d, J = 1.2 Hz, 1 H), 4.40 (s, 2 H), 4.35 (s, 2 H), 4.34 (s, 1 H), 3.84 (s, 2 H), 3.82–3.72 (m, 1 H), 3.78 (s, 3 H), 3.77 (s, 3 H), 3.33–3.23 (m, 2H), 3.12 (br s, 2 H), 2.82–2.75 (m, 1 H), 2.16 (br s, 1 H), 2.12–0.84 (series of m, 15 H), 1.65 (s, 3 H), 1.02 (s, 3 H), 0.87 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.14, 159.06, 152.7, 151.6, 131.9, 130.7, 130.3, 129.3, 129.2, 128.7, 113.7, 110.8, 101.3, 81.2, 76.0, 75.7, 72.5, 71.0, 66.4, 55.2, 45.3, 44.9, 42.4, 37.2, 36.2, 35.9, 35.0, 29.1, 27.4, 25.1, 24.5, 24.3, 23.4, 19.4, 13.9; MS m/z (M^+ - OH) calcd 627.4049, obsd 627.4015.

For **39**: IR (neat, cm^{-1}) 3420, 1650, 1630, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.26–7.17 (m, 4 H), 6.87–6.81 (m, 4 H), 5.37 (dt, J = 7.1, 1.2 Hz, 1 H), 5.18 (s, 1 H), 4.84 (s, 1 H), 4.60 (d, J = 1.3 Hz, 1 H), 4.49 (d, J = 0.9 Hz, 1 H), 4.44 (s, 2 H), 4.35 (s, 2 H), 3.84 (s, 2 H), 3.76 (2s, 3 H each), 3.67–3.60 (m, 1 H), 3.46–3.41 (m, 1 H), 3.22 (t, J = 8.6 Hz, 1 H), 2.96–2.87 (m, 1 H), 2.30 (br s, 2 H), 2.22–0.83 (series of m, 16 H), 1.64 (s, 3 H), 1.03 (s, 3 H), 0.85 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.2, 159.0, 153.7, 153.2, 131.9, 130.6, 129.5, 129.23, 129.20, 128.5, 113.69, 113.65, 110.1, 100.6, 79.8, 76.7, 75.9, 72.8, 70.9, 66.8, 55.1, 45.9, 45.4, 40.9, 37.4, 36.5, 36.2, 35.0, 29.4, 27.7, 25.0, 24.7, 24.4, 23.5, 19.9, 13.8; MS m/z (M^+ - OH) calcd 627.4049, obsd 627.4023.

(1S,2S,4R,11R)-4-[(1S,3R,5R,8E)-3-Hydroxy-10-[[p-(methoxybenzyl)oxy]-1-[[(p-methoxybenzyl)oxy]methyl]-5,9-dimethyl-8-decenyl]-11-methyltricyclo[5.4.0.$0^{2,11}$]undec-7-en-3-one (41). To a solution of 445 mg (690 μmol) of **38** in 6.9 mL of CH_2Cl_2 at 0 °C under an argon atmosphere was added 144.3 μL (1.035 mmol) of triethylamine and 190 μL (828 μmol) of *tert*-butyldimethylsilyl triflate. The reaction mixture was stirred at rt for 18 h, quenched with brine, and extracted with ether. The combined organic phases were dried and concentrated to leave a residue that was purified by flash chromatography on silica gel (elution with 1:15 ethyl acetate/petroleum ether) to give 421 mg (80%) of the monosilyl ether: IR (neat, cm^{-1}) 1655, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.25–7.18 (m, 4 H), 6.87–6.82 (m, 4 H), 5.37 (t, J = 7.2 Hz, 1 H), 5.10 (s, 1 H), 4.80 (s, 1 H), 4.56 (d, J = 1.0 Hz, 1 H), 4.40 (ABq, J_{AB} = 11.8 Hz, $\Delta\nu_{AB}$ = 9.3 Hz, 2 H), 4.38 (s, 1 H), 4.35 (s, 2 H), 3.96–3.91, (m, 1H), 3.84 (s, 2 H), 3.78 (s, 3 H), 3.77 (s, 3 H), 3.31–3.17 (m, 2 H), 2.86–2.77 (m, 1 H), 2.20–0.83 (series of m, 17 H), 1.64 (s, 3 H), 1.00 (s, 3 H), 0.87 (s, 9 H), 0.86 (d, J = 6.0 Hz, 3 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.2, 159.1, 154.4, 154.1, 132.0, 130.8, 130.3, 129.3, 129.1, 128.7, 113.74, 113.72, 110.1, 100.3, 80.0, 76.1, 75.4, 72.5, 71.1, 70.7, 55.3, 45.9, 43.5, 41.1, 36.9, 36.6, 34.89, 34.87, 29.0, 27.7, 26.1, 25.1, 25.0, 24.5, 23.6, 19.9, 18.3, 13.9, -3.8, -4.3; MS m/z (M^+ - OH) calcd 741.4914, obsd 741.4884.

A solution of 49 mg (64 μmol) of the above material in 1.6 mL of THF at rt under an argon atmosphere was added to 154 μL (77 μmol) of a 0.5 M solution of potassium bis(trimethylsilyl)-amide in toluene, and the reaction mixture was refluxed for 2 h, cooled to 25 °C, and quenched with argon-purged methanol. Saturated NH_4Cl solution was added, and the product was extracted into ether, dried, concentrated, and purified by flash chromatography (elution with 1:2 ethyl acetate/petroleum ether) to afford 5 mg (13%) of **41**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.25–7.18 (m, 4 H), 6.87–6.83 (m, 4 H), 5.68 (d, J = 5.6 Hz, 1 H), 5.38 (t, J = 6.1 Hz, 1 H), 4.38 (ABq, J_{AB} = 6.0 Hz, $\Delta\nu_{AB}$ = 11.8 Hz, 2 H), 4.35 (s, 2 H), 3.83 (s, 2 H), 3.77 (s, 3 H), 3.77 (s, 3 H), 3.65–3.55 (m, 1 H), 3.54–3.33 (m, 2 H), 2.82–2.70 (m, 1 H), 2.34–2.20 (m, 1 H), 2.10–0.89 (series of m, 20 H), 1.64 (s, 3 H), 1.14 (s, 3 H), 0.85 (d, J = 6.6 Hz, 3 H); MS m/z (M^+ - OH) calcd 627.4049, obsd 627.4036.

(1S,2S,4R,11R)-4-[(1R,3S,5R,8E)-3-Hydroxy-10-[(p-methoxybenzyl)oxy]-1-[[(p-methoxybenzyl)oxy]methyl]-5,9-dimethyl-8-decenyl]-11-methyltricyclo[5.4.0.$0^{2,11}$]undec-7-en-3-one (43). To a solution of 467 mg (724 μmol) of **39** in 7.2 mL of CH_2Cl_2 at 0 °C under an argon atmosphere was added 151.3 μL (1.086 mmol) of triethylamine and 200 μL (869 μmol of *tert*-butyldimethylsilyl triflate. The reaction mixture was allowed to warm to rt, stirred for 23 h, quenched with brine, and extracted with ether. The combined organic layers were dried and concentrated to leave a residue which was purified by flash chromatography on silica gel (elution with 1:13 ethyl acetate/petroleum ether) to afford 434 mg (79%) of the monosilyl ether: IR (neat, cm^{-1}) 3435, 1655, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.26–7.17 (m, 4 H), 6.88–6.82 (m, 4 H), 5.38 (dt, J = 7.1, 1.0 Hz, 1 H), 5.13 (s, 1 H), 4.84 (s, 1 H), 4.60 (d, J = 1.2 Hz, 1H), 4.48 (s, 1 H), 4.44 (s, 2 H), 4.36 (s, 2 H), 4.28 (s, 1 H), 3.85 (s, 2 H), 3.78 (s, 3 H), 3.77 (s, 3 H), 3.82–3.72 (m, 1 H), 3.53–3.45 (m, 1 H), 3.16 (t, J = 8.2 Hz, 1 H), 2.87–2.81 (m, 1 H), 2.22–0.82 (series of m, 16 H), 1.65 (s, 3 H), 1.04 (s, 3 H), 0.86 (s, 9 H), 0.83 (d, J = 6.2 Hz, 3 H), 0.04 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.2, 159.0, 155.1, 153.9, 131.9, 130.7, 129.7, 129.2, 129.1, 128.5, 113.70, 113.67, 109.8, 100.4, 79.6, 76.5, 76.0, 72.7, 71.0, 70.0, 55.1, 45.7, 45.1, 40.3, 37.4, 37.3, 35.9, 34.9, 29.4, 27.5, 25.9, 25.1, 24.7, 24.5, 23.6, 19.5, 18.1, 13.8, -3.5, -3.8; MS m/z (M^+) calcd 758.4941, obsd 758.4910.

To 54 mg (71 μmol) of the above material was added 23 mg (85 μmol) of 18-crown-6 followed by 1.8 mL of argon-purged THF at rt in the drybox. Then 327 μL (163.6 μmol) of a 0.5 M solution of potassium bis(trimethylsilyl)amide in toluene was added, and the reaction mixture was stirred for 18 h and then quenched with argon-purged methanol and saturated NH_4Cl solution prior to extraction with ether. The combined organic layers were dried and concentrated to leave a residue that was purified by flash chromatography on silica gel (elution with 1:2 ethyl acetate/petroleum ether) to provide 10 mg (22%) of **43** and 15 mg (27%) of the TBS derivative of **43**.

For **43**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.25–7.19 (m, 4 H), 6.89–6.82 (m, 4 H), 5.65 (d, J = 7.0 Hz, 1 H), 5.38 (t, J = 7.1 Hz, 1 H), 4.36 (s, 2 H), 4.33 (ABq, J_{AB} = 11.2, $\Delta\nu_{AB}$ = 21.9 Hz, 2 H), 3.84 (s, 2 H), 3.78 (s, 3 H), 3.76 (s, 3 H), 3.71–3.64 (m, 1 H), 3.34–3.32 (m, 2H), 2.60–2.48 (m, 2 H), 2.29–2.13 (m, 1 H), 2.10–0.79 (series of m, 19 H), 1.64 (s, 3 H), 1.07 (s, 3 H), 0.89 (d, J = 6.6 Hz, 3 H); MS m/z (M^+ - OH) calcd 627.4049, obsd 627.4032.

Exemplary Rearrangements Leading to α-Hydroxy Ketones Related to 40 and 42. A. 40 (R_1 = PMB, R_2 = CH_2SCH_3). After conversion of **38** (R_1 = PMB, R_2 = MTM)[31] to its *tert*-butyldimethylsilyl derivative, an 82-mg (117 μmol) sample and 155 mg (585 μmol) of 18-crown-6 in 3 mL of THF at rt under an argon atmosphere were treated wth 67 mg (585 μmol) of petroleum ether-washed iodine-treated 35 wt % mineral oil dispersion of potassium hydride in 3 mL of THF. The reaction mixture was stirred for 3 h, cooled to -78 °C, quenched with

ethanol, and allowed to warm to rt. Saturated NH_4Cl solution was introduced, and the product was extracted into ether, dried, concentrated, treated with 5 mL of 0.2 M tetra-*n*-butylammonium fluoride in THF, and stirred for 10 h. After dilution with water and ether extraction, the combined organic solutions were concentrated and flash chromatographed on silica gel (elution with 1:3 ethyl acetate/petroleum ether) to afford 43 mg (63%) of **40** (R_1 = PMB; R_2 = MTM); IR (neat, cm^{-1}) 3490, 1700, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, J = 8.4 Hz, 2 H), 6.85 (d, J = 8.6 Hz, 2 H), 5.69 (d, J = 5.9 Hz, 1 H), 5.37 (t, J = 6.8 Hz, 1 H), 4.58 (ABq, J = 11.6 Hz, $\Delta\nu_{AB}$ = 25.6 Hz, 2 H), 4.34 (s, 2 H), 3.91 (dd, J = 9.6, 4.4 Hz, 1 H), 3.83 (s, 2 H), 3.77 (s, 3 H), 3.74–3.64 (m, 2 H), 2.29–0.86 (series of m, 22 H), 2.13 (s, 3 H), 1.63 (s, 3 H), 1.15 (s, 3 H), 0.87 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 210.5, 159.1, 137.8, 131.9, 130.7, 129.3, 128.6, 127.9, 113.7, 86.2, 76.1, 76.0, 71.0, 69.3, 68.0, 55.2, 45.1, 41.0, 39.4, 37.7, 37.4, 37.0, 29.8, 28.9, 27.4, 26.8, 26.4, 25.6, 25.1, 23.1, 19.1, 14.5, 13.9; MS m/z (M – H_2O) calcd 582.3379, obsd 582.3364.

B. 42 (R = PMB, R_2 = CH_2SCH_3). Comparable treatment of the OTBS derivative of **39** (R_1 = PMB, R_2 = MTM)[31] (41 mg, 58.5 μmol) gave **42** (R_1 = PMB, R_2 = MTM) (16 mg, 48%); IR (neat, cm^{-1}) 1700, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, J = 8.7 Hz, 2 H), 6.85 (d, J = 8.6 Hz, 2 H), 5.70 (d, J = 5.7 Hz, 1 H), 5.38 (t, J = 6.2 Hz, 1 H), 4.55 (ABq, J = 11.6 Hz, $\Delta\nu_{AB}$ = 8.4 Hz, 2 H), 4.36 (s, 2 H), 3.84 (s, 2 H), 3.81–3.78 (m, 1 H), 3.78 (s, 3 H), 3.76–3.60 (m, 2 H), 2.33–0.89 (series of m, 22 H), 2.12 (s, 3 H), 1.64 (s, 3 H), 1.17 (s, 3 H), 0.91 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 211.1, 159.1, 137.8, 132.2, 130.7, 129.3, 128.4, 128.2, 113.7, 85.6, 76.0, 75.9, 71.2, 70.1, 68.7, 55.3, 45.7, 41.7, 38.9, 37.9, 36.3, 35.0, 29.4, 29.3, 27.4, 26.9, 26.5, 25.4, 25.1, 23.1, 20.2, 14.7, 14.0; MS m/z (M^+ – H_2O) calcd 582.3379, obsd 582.3380.

C. 40 (R_1 = SEM, R_2 = PMB). A 118-mg sample (179 μmol) of **38** (R_1 = SEM, R_2 = PMB)[31] was silylated in the manner described above in 48% yield: IR (neat, cm^{-1}) 3410, 1655, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.19 (d, J = 8.6 Hz, 2 H), 6.83 (d, J = 8.6 Hz, 2 H), 5.38 (t, J = 6.4 Hz, 1 H), 5.09 (s, 1 H), 4.80 (s, 1 H), 4.63 (s, 2 H), 4.55 (d, J = 1.1 Hz, 1 H), 4.39 (ABq, J_{AB} = 11.9 Hz, $\Delta\nu_{AB}$ = 9.3 Hz, 2 H), 4.37 (s, 1 H), 3.98 (s, 1 H), 3.96–3.87 (m, 1 H), 3.90 (s, 2 H), 3.76 (s, 3 H), 3.61 (t, J = 8.3 Hz, 2 H), 3.31–3.16 (series of m, 2 H), 2.80–2.77 (m, 1 H), 2.16–1.07 (series of m, 15 H), 2.12 (br s, 1 H), 1.62 (s, 3 H), 0.99 (s, 3 H), 0.93 (t, J = 8.5 Hz, 2 H), 0.86 (s, 9 H), 0.85 (d, J = 6.6 Hz, 3 H), 0.04 (s, 3 H), 0.03 (s, 3 H), 0.00 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.1, 154.3, 154.0, 131.5, 130.2, 129.0, 128.8, 113.7, 110.0, 100.2, 93.7, 80.0, 75.3, 73.4, 72.5, 70.6, 65.0, 55.2, 45.8, 43.3, 41.0, 36.8, 36.4, 34.8, 29.0, 27.7, 26.1, 25.1, 25.0, 24.5, 23.5, 19.9, 18.3, 18.1, 14.0, –1.4, –3.9, –4.4; MS m/z (M^+) calcd 768.5180, obsd 768.5182; $[\alpha]^{25}_D$ –7.3° (c 0.19, $CHCl_3$).

Anal. Calcd for $C_{45}H_{76}O_6Si_2$: C, 70.26; H, 9.96. Found: C, 70.26; H, 9.88.

To a solution of 91 mg (118 μmol) of the above material and 37 mg (142 μmol) of 18-crown-6 in 3 mL of THF at rt under an argon atmosphere was added 283 μL (142 μmol) of a 0.5 M solution of potassium bis(trimethylsilyl)amide in toluene. The reaction mixture was stirred for 18 h, cooled to –78 °C, quenched with ethanol, and allowed to warm to rt prior to quenching with NH_4Cl solution and extraction with ether. The usual workup including treatment with TBAF afforded 55 mg (72%) of **40** (R_1 = SEM, R_2 = PMB): IR (neat, cm^{-1}) 3470, 1695, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, J = 8.4 Hz, 2 H), 6.86 (d, J = 8.6 Hz, 2 H), 5.68 (d, J = 5.6 Hz, 1 H), 5.39 (t, J = 6.9 Hz, 1 H), 4.63 (s, 2 H), 4.39 (ABq, J_{AB} = 11.4 Hz, $\Delta\nu_{AB}$ = 15.6 Hz, 2 H), 3.90 (s, 2 H), 3.82–3.78 (m, 1 H), 3.78 (s, 3 H), 3.65–3.57 (m, 2 H), 3.60 (t, J = 8.7 Hz, 2 H), 2.27–0.90 (series of m, 22 H), 1.63 (s, 3 H), 1.15 (s, 3 H), 0.92 (t, J = 8.8 Hz, 2 H), 0.84 (d, J = 6.4 Hz, 3 H), 0.00 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 210.7, 159.5, 137.9, 131.5, 129.51, 129.46, 129.0, 127.8, 113.9, 93.7, 86.3, 73.5, 73.3, 71.0, 68.1, 65.0, 55.3, 45.0, 41.4, 39.4, 37.8, 37.4, 29.7, 28.9, 27.4, 26.8, 26.4, 25.6, 25.2, 23.1, 19.0, 18.1, 14.0, –1.4; MS m/z (M^+ – H_2O) 652.4159, obsd 652.4110; $[\alpha]^{25}_D$ +32.2° (c 0.61, $CHCl_3$).

D. 42 (R_1 = SEM, R_2 = PMB). Silylation of **39** (R_1 = SEM, R_2 = PMB)[31] as above gave a a colorless oil in 87% yield: IR (neat, cm^{-1}) 3440, 1655, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, J = 8.6 Hz, 2 H), 6.83 (d, J = 8.6 Hz, 2 H), 5.37 (t, J = 6.2 Hz, 1 H), 5.11 (s, 1 H), 4.82 (s, 1 H), 4.62 (s, 2 H), 4.57 (d, J = 1.1 Hz, 1H), 4.46 (s, 1 H), 4.43 (s, 2 H), 4.29 (s, 1 H), 3.89 (s, 2 H), 3.76 (s, 3H), 3.76–3.68 (m, 1 H), 3.60 (t, J = 8.3 Hz, 2 H), 3.61–3.46 (m, 1 H), 3.14 (t, J = 8.3 Hz, 1 H), 2.86–2.75 (m, 1 H), 2.02–1.09 (series of m, 15 H), 2.00 (br s, 1 H), 1.62 (s, 3 H), 1.02 (s, 3 H), 0.92 (t, J = 8.4 Hz, 2 H), 0.83 (s, 9 H), 0.79 (d, J = 6.2 Hz, 3 H), 0.01 (s, 6 H), 0.00 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.2, 155.1, 153.9, 131.5, 129.7, 129.2, 128.7, 113.7, 109.8, 100.4, 93.6, 79.6, 76.5, 73.4, 72.8, 70.0, 67.0, 55.2, 45.7, 45.1, 40.3, 37.4, 37.3, 35.9, 34.9, 29.4, 27.5, 25.9, 25.2, 24.7, 24.5, 23.6, 19.5, 18.1, 14.0, –1.4, –3.5, –3.8; MS m/z (M^+) calcd 768.5180, obsd 768.5135; $[\alpha]^{25}_D$ –2.3° (c 0.53, $CHCl_3$).

Rearrangement of 171 mg (222 μmol) of the above material in part C furnished 118 mg (81%) of **42** (R_1 = SEM, R_2 = PMB): IR (neat, cm^{-1}) 3450, 1700, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 7.17 (d, J = 8.5 Hz, 2 H), 6.83 (d, J = 8.5 Hz, 2 H), 5.66 (d, J = 5.8 Hz, 1 H), 5.38 (t, J = 6.8 Hz, 1 H), 4.62 (s, 2 H), 4.32 (ABq, J_{AB} = 11.3 Hz, $\Delta\nu_{AB}$ = 19.6 Hz, 2 H), 3.89 (s, 2 H), 3.75 (s, 3 H), 3.73–3.69 (m, 2 H), 3.59 (t, J = 8.4 Hz, 2 H), 3.56–3.52 (m, 1 H), 2.50 (br s, 1 H), 2.44–0.81 (series of m, 21 H), 1.62 (s, 3 H), 1.12 (s, 3 H), 0.91 (t, J = 8.7 Hz, 2 H), 0.87 (d, J = 8.3 Hz, 3 H), –0.01 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 211.6, 159.4, 137.9, 131.6, 129.6, 129.4, 128.8, 128.0, 113.9, 93.6, 85.9, 73.4, 73.2, 71.9, 68.9, 65.0, 55.1, 45.6, 41.5, 38.6, 37.9, 36.2, 35.2, 29.4, 27.3, 26.8, 26.4, 25.3, 25.0, 23.1, 20.2, 18.1, 14.0, –1.5; MS m/z (M^+ – H_2O) calcd 652.4159, obsd 652.4172; $[\alpha]^{25}_D$ +7.9° (c 0.37, $CHCl_3$).

Acknowledgment. This work was supported financially by the National Institutes of Health (Grant GM-30827) and the Eli Lilly Company. We also thank Prof. Robin Rogers for the X-ray crystallographic analysis, Dr. Dirk Friedrich for NMR measurements, and Dr. Kurt Loening for assistance with nomenclature. A special note of appreciation goes to Dr. Susumu Akutagawa of the Takasago Research Institute, Tokyo, Japan, for graciously providing us with generous samples of (*R*)- and (*S*)-citronellol.

Supplementary Material Available: 300-MHz ^1H and 75-MHz ^{13}C NMR spectra of those compounds lacking combustion data (38 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.