An Approach toward the Ophiobolane Sesterterpenes: Synthesis of the Ceroplastin Nucleus

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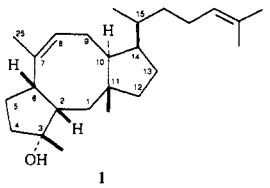
A stereocontrolled route to the 5-8-5 fused-ring nucleus of the ophiobolane sesterterpenes is presented. A McMurry coupling of an appropriately configured dicyclopentane system afforded the ceroplastin nucleus. Stereoselective hydrogenation reactions were used to set the requisite stereochemistry of the A/B and B/C ring junctures.

Introduction

Since their initial structural characterization in 1965,[1] the ophiobolane class of sesterterpenes has attracted considerable attention from synthetic organic chemists. These substances have provided the ultimate target for the development of synthetic methodologies, mainly focused on the construction of the 5-8-5 ring system.[2] Only recently, the total synthesis of naturally occurring members of this class of sesterterpenes[3] have been reported.

The interest in these sesterterpenes stems from their novel structures and significant biological activities.[4] The ophiobolanes comprise the largest class of polycyclic sesterterpenes. Ophiobolin F (1) and ceroplastol I (2)



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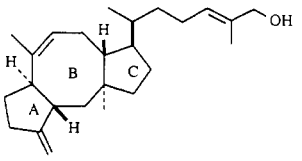
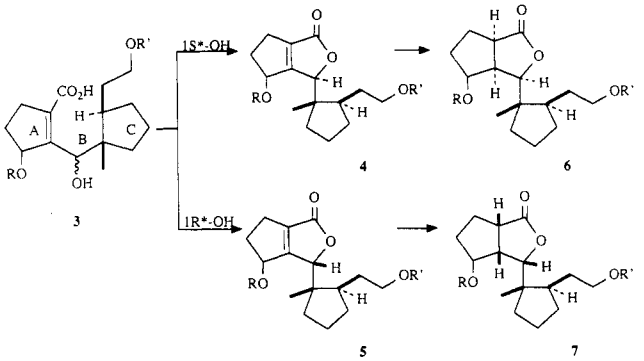


2

represent the two major subclasses of ophiobolanes, the ophiobolins and the ceroplastins, respectively.[5] The ophiobolins have been isolated from a number of phytopathogenic fungi; the ceroplastins have been obtained from the protective wax secreted by a species of scale insects. Characterized by the novel 5-8-5 fused-ring framework, the ophiobolins maintain a cis-syn-trans ring stereochemistry, the ceroplastins a trans-anti-trans arrangement. Though the chirality at C-14 and C-15 is the same in both series, the side chain is cis to the C-10 hydrogen in the ophiobolins and trans to the C-10 hydrogen in the ceroplastins.

To address the various stereochemical challenges by these target nuclei, it is to be noted that while both B/C ring junctures are trans, they are enantiomeric. Although the A/B ring juncture is cis in one series and trans in the other, the important feature is the opposite relationship between the C-2 hydrogen and C-11 methyl group. The synthetic plan was to have a convergent synthesis of **3** to yield both C-1 epimeric alcohols (ophiobolane numbering) and, then, an emergent synthesis to form the two isomeric unsaturated lactones **4** and **5**. The A/B ring juncture stereochemistry will be established by the stereocontrolled addition of hydrogen, due to the spacial arrangement of the bulky cyclopentane moiety, to yield intermediate **6** for the ceroplastins and **7** for the ophiobolins.



Synthesis of the Requisite Convergent Units

The synthesis of the C ring, which started with the condensation of the anion of *tert*-butyl diethylphosphonoacetate[6] with keto ester **8**,[7] proceeded in 90% yield to afford diesters (*E*)-**9a**, (*Z*)-**9a**, and **9b** in a 91:4:5 ratio.[8] The major isomer was obtained pure on a preparative scale by flash chromatography. Though all three diesters were potentially useful in this sequence, the use of a single isomer simplified the subsequent manipulations and analyses. Quantitative deprotection of *tert*-butyl ester (*E*)-**9a** by treatment with trifluoroacetic acid gave carboxylic acid **10**. The carboxylic acid group was reduced selectively in the presence of the methyl ester using diborane in yields ranging from 57 to 69%.[9] The allylic alcohol was protected as the *tert*-butyldimethylsilyl ether, and the methyl ester was reduced with lithium aluminum hydride to afford olefin **13** in 84% overall yield.

The key step in this sequence involved the hydroxyl group directed hydrogenation of olefin **13**. The ability of a hydroxyl group to control the stereochemistry of hydrogen delivery has been established with both heterogeneous and homogeneous catalysis.[10] In such cases the

(1) Nozoe, S.; Morisaki, M.; Tsuda, K.; Iitaka, Y.; Takahashi, N.; Tamura, S.; Ishibashi, M. *J. Am. Chem. Soc.* **1965**, *87*, 4968.

(2) For references referring to such studies, see: Coates, R. M.; Muskopf, J. W.; Senter, P. A. *J. Org. Chem.* **1985**, *50*, 3541. Rigby, J. H.; Senanayake, C. *J. Org. Chem.* **1987**, *52*, 4634.

(3) (a) Kato, N.; Takeshita, H.; Kataoka, H.; Ohbuchi, S.; Tanaka, S. *J. Chem. Soc., Perkin Trans. 1* **1989**, 165 and earlier references. (b) Rowley, M.; Tsukamoto, M.; Kishi, Y. *J. Am. Chem. Soc.* **1989**, *111*, 2735. (c) Boeckman, R. K., Jr.; Arvanitis, A.; Voss, M. E. *J. Am. Chem. Soc.* **1989**, *111*, 2737.

(4) Hanson, J. R. *Nat. Prod. Rep.* **1986**, *3*, 123. Sugawara, F.; Strobel, G.; Strange, R. N.; Siedow, J. N.; Van Duyne, G. D.; Clardy, J. *Proc. Natl. Acad. Sci. U.S.A.* **1987**, *84*, 3081.

(5) The ophiobolane positional numbering and ring letters shown in **1** and **2** are used throughout the discussion section of this paper.

(6) Griffiths, G. F.; Kenner, G. W.; McCombie, S. W.; Smith, K. M. *Tetrahedron* **1976**, 275.

(7) Barco, A.; Beretti, S.; Pollini, G. P. *Synthesis* **1973**, 316.

(8) (a) The stereochemical assignments are consistent with the ^{1}H NMR data. A 0.12 ppm upfield shift for the quaternary methyl group in (*E*)-**9a** versus (*Z*)-**9a** was noted (see Wicha, J.; Bal, K.; Piekut, S. *Synth. Commun.* **1977**, 215). (*E*)-**9a** was converted to **9b** by kinetic quench of the corresponding dienolate anion. (b) In a related study, the condensation of ethyl diethyl phosphonoacetate with keto ester **8** was examined. This reaction was much less efficient and less stereoselective than that yielding the *tert*-butyl ester. The ethyl esters were obtained in 65% yield with the *E,Z* and deconjugated esters in a 10:1:8 ratio.

(9) Kende, A. S.; Fludzinski, P. *Org. Synth.* **1985**, *64*, 104.

(10) (a) Bartok, M. In *Stereochemistry of Heterogeneous Metal Catalysis*; John Wiley and Sons: New York, 1985; pp 53–210. (b) Brown, J. M. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 190.

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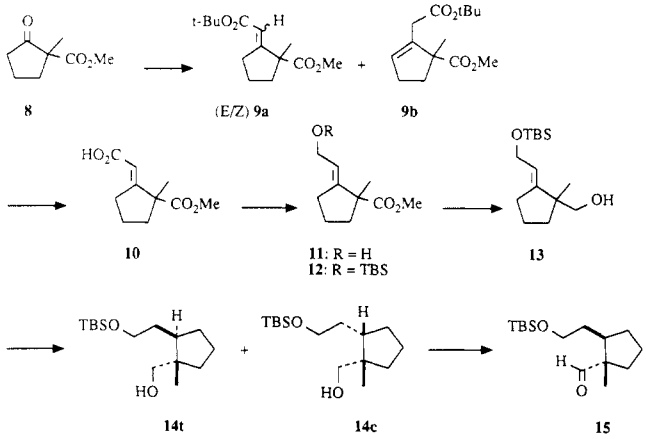


hydroxyl group is believed to coordinate to the catalyst; hydrogen is introduced at the face of the double bond cis to this group. In 1976, Thompson reported a correlation between diastereoselectivity and solvent in the saturation of a hydroxy-substituted hexahydrophenanthrene derivative with palladium on carbon.[11] The directing effect of the hydroxyl group increased by lowering the dielectric constant of the solvent. A similar solvent dependency was observed with platinum on carbon, though the cis-directing effect was greater in all cases.

Results of the hydrogenation of **13** are summarized in Table I. When possible, the ratios were determined using ^{1}H NMR spectroscopy by integration of the quaternary methyl resonances in alcohols **14t** and **14c**. Although these alcohols possessed identical retention times on capillary GC, the corresponding aldehydes were separable. In the case of very high selectivity, analysis of the oxidation product afforded the ratio.

As anticipated, a high degree of stereocontrol was observed using 5% palladium on carbon in a nonpolar solvent. The desired product, **14t**, leading to the ophiobolin–ceroplastin B/C trans ring juncture was favored by a 12:1 ratio over its epimer, **14c**. The ratio decreased in a more polar solvent, absolute ethanol, as expected. However, hydrogenation using the corresponding platinum catalyst in a nonpolar solvent was substantially less selective, contrasting the observations by Thompson. The reason for this discrepancy remained unclear, yet this difference illustrated a foible in heterogeneous catalysis. In general, homogeneous catalysts can be prepared repeatedly with identical and predictable reactivities; poisoning is seldom a problem.[10] This is not true for heterogeneous catalysts. Finally, hydrogenation using the homogeneous Crabtree catalyst[12] afforded the desired epimer **14t** with excellent selectivity.[13]

The structures of these epimers could be assigned initially based upon the hydrogenation results, particularly those with the homogeneous catalyst. These assignments were corroborated by the ^{13}C NMR data. In accordance

Table 1. Hydrogenation of Silyl Ether 13

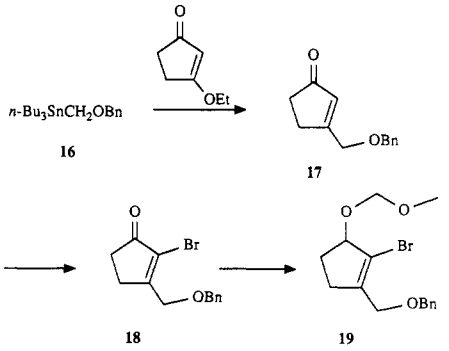
catalyst/conditions	14t: 14c	catalyst/conditions	14t: 14c
5% Pd/C in hexanes	12:1	5% Pt/C in hexanes	2:1
5% Pd/C in ethanol	3:1	$[Ir(cod)(PCy_3)(py)]PF_6$	262:1[a]

[a] This ratio was obtained from aldehydes 15t:15c.

with the concept of steric compression, a substantial upfield shift of 3.89 ppm was observed for the quaternary methyl group of the major epimer, **14t**, relative to that of **14c**.[14] Similarly, the 3.51 ppm downfield shift for the hydroxymethyl carbon in **14t** was consistent with its cis relationship to the ring juncture hydrogen.

The Swern oxidation of **14t** afforded aldehyde **15** in 90% yield. While quaternary aldehydes have been reported to be susceptible to rapid oxidation at room temperature,[15] a solution of **15** in hexanes was stable for at least a year when stored at −78 °C under an argon atmosphere.

The synthesis of the A ring, which started with the addition of the organolithium reagent derived from stannane **16**[16] to 3-ethoxy-2-cyclopenten-1-one,[17] furnished enone **17** in 67% yield following a mild acidic workup.[18]



Attempted formation of the α-bromo enone by the sequential addition of bromine and triethylamine led to a complex mixture of products from which no desired material could be recovered. Smith and others have used this methodology in the preparation of a number of unfunctionalized α-bromo-α,β-cycloalkenones.[19] Using pyridinium bromide perbromide in the presence of excess pyridine, α-bromo enone **18** was isolated in 86% yield.[20] The vinyl bromide **19** was prepared from **18** in 94% overall yield by the sequential sodium borohydride reduction and protection with chloromethyl methyl ether.

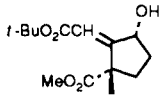
The Convergent Steps

The stage was set for the convergent synthesis. Generation of the vinyllithium reagent derived from vinyl

(11) Thompson, H. W.; McPherson, E.; Lences, B. L. *J. Org. Chem.* **1976**, *41*, 2903.

(12) (a) Crabtree, R. H.; Davis, M. W. *J. Org. Chem.* **1986**, *51*, 2655. (b) Evans, D. A.; Morrissey, M. M. *Tetrahedron Lett.* **1984**, 4637. (c) Stork, G.; Kahne, D. E. *J. Am. Chem. Soc.* **1983**, *105*, 1072.

(13) Treatment of **9a** with LDA, followed by kinetic protonation yielded deconjugated ester **9b**. Epoxidation of this material gave a 3:1 mixture of epoxides. Base-initiated ring opening of the major epoxide gave, in high yield, the following compound which can be utilized for the introduction of a side chain.



(14) Abraham, R. J.; Loftus, P. In *Proton and C-13 NMR Spectroscopy—An Integrated Approach*; Heydon and Sons, Inc.: Philadelphia, 1981; pp 24–33.

(15) Kornblum, N.; Erickson, A. S.; Kelly, W. J.; Henggeler, B. *J. Org. Chem.* **1982**, *47*, 4534.

(16) (a) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481. (b) It has recently been noted that the effectiveness of the α-alkoxyorganolithium reagent can be a function of the time between the trans metallanation and its subsequent use. Therefore, the yield reported for the present reaction may be improved, see: Johnson, C. R.; Medich, J. R. *J. Org. Chem.* **1988**, *53*, 4131.

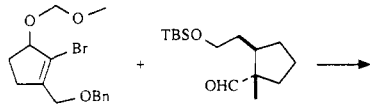
(17) Ruangsiyanand, C.; Rimek, H. J.; Zymalkowski, F. *Chem. Ber.* **1970**, *103*, 2403.

(18) Burke, S. D.; Shearhouse, S. A.; Burch, D. J.; Sutton, R. W. *Tetrahedron Lett.* **1980**, 1285.

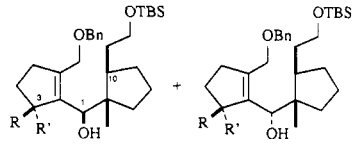
(19) (a) Smith, A. B., III; Branca, S. J.; Guaciaro, M. A.; Wovkulich, P. M.; Korn, A. *Org. Synth.* **1983**, *61*, 65. (b) Guaciaro, M. A.; Wovkulich, P. M.; Smith, A. B., III *Tetrahedron Lett.* **1978**, 4661.

(20) Dauben, W. G.; Warshawsky, A. M. *Synth. Commun.* **1988**, *18*, 1323.

bromide **19** and subsequent condensation with aldehyde **15** afforded a mixture of allylic alcohols in 72% yield. From this material the diastereomer mixture of **20a/21a** with the C-1 and C-3 substituents anti was easily separated, as a single eluate, by flash chromatography from the corresponding mixture of syn isomers **20s/21s**, again as a single eluate. The yield for the anti isomers was 31% and for the syn isomers 41%. In both mixtures, the ratio of diastereomers was 4:1. It was established in later studies that **21** was the predominant one in each mixture.



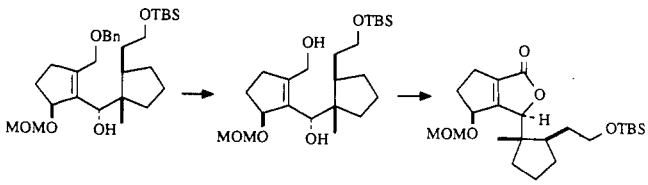
19 **15**



20s : R = OMOM, R' = H : **21a**
20a : R = H, R' = OMOM : **21s**

The stereochemical relationships among these alcohols were narrowed down, initially, by the following experiment. Swern oxidation of the higher R_f mixture of alcohols afforded the corresponding enone(s). Subsequent sodium borohydride reduction of the enone(s) yielded both the higher and lower R_f alcohol mixture. Therefore, the alcohols with a given R_f necessarily differed, at least, in their configurations at C-3. In the ensuing deprotection of the benzyl ethers (Li, NH_3, THF) it was also possible to remove the oxygen function at C-3. It was found that the material of a given R_f yielded two C-1 alcohols. Thus, each component in a single R_f fraction had both C-1 and C-3 oxygen functions in different configurations. Finally, later in the synthesis of a further intermediate, a single-crystal X-ray analysis elucidated the relative configurations shown in **20** and **21**.

The syn and anti mixtures, **20s/21s** and **20a/21a**, were carried separately through the remainder of the synthesis. The inability to separate the 1*S** and 1*R** isomers was unfortunate as the C-1 configuration would later serve to guide the A/B ring juncture stereochemistry. Nonetheless, since in the 4:1 syn/anti mixture the predominant alcohol has the same configuration, the use of the C-1 mixture would permit a reasonable test of the proposed methodology. For simplicity because of this predominance of one C-1 alcohol configuration with the stereochemistry shown in **21**, the **20a/21a** mixture will be designated **21a** and the **20s/21s** will be **21s**.



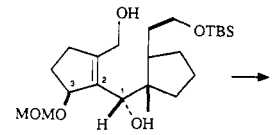
21a **22a** **23a**

The reactions directed toward the preparation of the unsaturated lactones related to structure **23a** first required the removal of the benzyl group. An attempted hydrogenolysis of the benzyl ether **21a** using palladium carbon yielded a complex mixture of products. Using lithium in ammonia with diethyl ether as a cosolvent, the reaction mixture often formed a sticky gum on the bottom of the flask from which product and starting material were recovered. The diols **22a** and **22s** were obtained in 66% and 81% yield, respectively.[21]

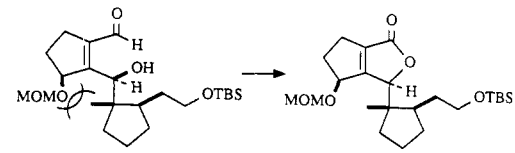
The successful oxidation of each diol **22** to unsaturated lactones of type **23** was achieved using silver carbonate supported on Celite. Chandrasekaran described the efficient conversion of (*Z*)-2-butene-1,4-diols to the corresponding α,β-butenolides using this reagent in refluxing benzene.[22] Earlier, Fétizon reported that for solvents with similar boiling points, the oxidation proceeded faster in those solvents with lower dielectric constants.[23a] It was also observed that in a compound containing both saturated primary and secondary alcohols, selective oxidation of the primary alcohol was achieved using chloroform (bp 61 °C, ϵ 4.8) as the solvent.[23b] In benzene (bp 80 °C, ϵ 2.3), the reaction proceeded much faster and little selectivity was noted.

The oxidation of unsaturated diols **22s** in chloroform afforded the lactone **23s** in 88% yield. The oxidation of **22a** in benzene gave **23a** in 75% yield while in chloroform the yield was only 31%.

In these oxidations, the rapid formation of a UV-active compound was detected by TLC. This compound, presumably the intermediate hydroxy aldehyde, was slowly converted to the lactone. In the oxidation of anti diol **22a**, this latter conversion was extremely slow as seen by TLC. Extended heating led to considerable decomposition. The anti relationship between the C-1 and C-3 substituents may account for these results. The conformation required for intermediate lactol formation from hydroxy aldehyde **24a** would introduce considerable steric interactions between the cyclopentyl and MOM groups. Fortunately, this barrier to further reaction was overcome using benzene as the solvent. The unsaturated lactone **23a** was obtained in 75% yield.



22a



24a **23a**

The hydrogenation of these unsaturated lactones will set the stereochemical relationship between the future A/B and B/C ring junctures in the ophiobolane system. As discussed earlier, the steric influence of the cyclopentane group was expected to guide the stereochemistry of the hydrogenation. Since in both the syn and anti series, the predominant isomer has the 1*S** configuration, the bulky cyclopentane ring will be above the plane of the butenolide in both cases.

This prediction was realized using 5% rhodium on carbon as the hydrogenation catalyst. The rhodium cat-

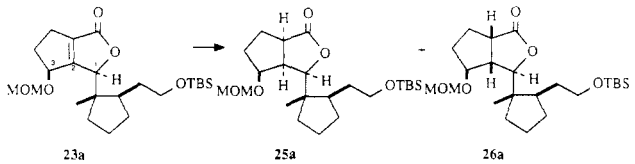
(21) When tetrahydrofuran was used as a cosolvent, considerable reductive cleavage of the allylic methoxymethyl ether (MOM) substituent was noted. With this loss of chirality at C-3 it became clear that the alcohol mixture of a given *Rf* was also inhomogeneous at C-1.

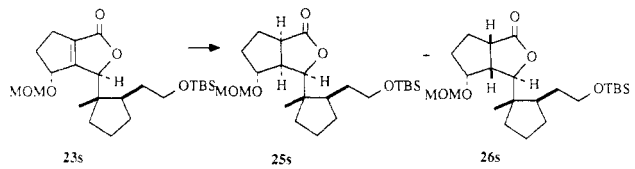
(22) Chakraborty, T. K.; Chandrasekaran, S. *Tetrahedron Lett.* **1984**, 2891.

(23) (a) Kakis, F. J.; Fétizon, M.; Douchkine, N.; Golfier, M.; Mourgues, P.; Prange, T. *J. Org. Chem.* **1974**, *39*, 523. (b) Fétizon, M.; Golfier, M.; Louis, J.-M. *Tetrahedron* **1975**, *31*, 171.

alyst had the advantage of causing a minimum amount of hydrogenolysis of the allyl ether. This result could be explained by the low degree of desorption of the olefin from the metal surface.[24] Additionally, an increased susceptibility to steric factors has been noted with this catalyst.[10a]

A high degree of selectivity would be expected in the hydrogenation of unsaturated lactone **23a** with both the C-1 and C-3 substituent on the same face of the molecule. Hydrogenation of **23a** afforded saturated products in nearly quantitative yield and with a favorable diastereomeric excess.[25] Saturated lactone **25a** was favored over **26a** by ratios in the range 10–15:1. These two products were easily separated by flash chromatography.

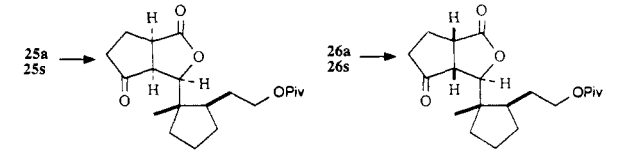


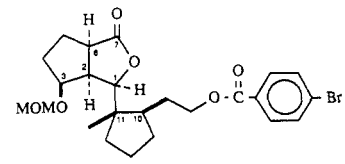


Similarly, in the hydrogenation of the unsaturated lactone **23s** over rhodium on carbon, saturated products were obtained in excellent yields. The lactone **25s** was favored over **26s** by ratios in the range 10–15:1. The C-2 hydrogen/C-1-cyclopentyl trans stereochemistry predominated in each hydrogenation. These results suggest a powerful directing effect of the cyclopentane moiety. The hydrogen was introduced to the face of the double bond opposite that of this bulky group, regardless of the configuration at C-3 bearing the MOM substituent. In both hydrogenations, the major product has a C-2 hydrogen/C-11 methyl group trans stereochemistry found in the ceroplastins.

The hydrogenation of unsaturated lactone **23a** using 5% palladium on carbon also was examined. Saturated lactones **25a** and **26a** were obtained in quantitative yield; however, lactone **26a** was favored over **25a** by a 60:40 ratio. Moreover, no hydrogenolysis of the allylic ether was detected. This slight preference for **26a** was consistent with the general observation that the palladium catalyst generally favors the thermodynamically more stable isomer.[10a] In this case, the predominant product has a C-2 hydrogen/C-11 methyl cis stereochemistry found in the ophiobolins.

Unsaturated lactones **23a** and **23s** differ only in their configuration at C-3. Therefore, the structures of the hydrogenation products could be correlated by elimination of the chirality at this carbon. Thus, MOM ethers **25a**, **25s**, **26a**, and **26s** were converted separately to the corresponding ketones by an efficient four-step sequence. This sequence involved fluoride-induced deprotection of the silyl ether and reprotection of the alcohol as the pivalic ester with trimethylacetyl chloride. Acid-catalyzed deprotection[26] of the MOM ether and subsequent oxidation with pyridinium chlorochromate on alumina[27] afforded the ketones **27** and **28** in good overall yields. The major hydrogenation products **25a** and **25s** were linked through ketone **27**, while the minor products, **26a** and **26s**, were correlated through ketone **28**. Finally, single-crystal X-ray analysis of a *p*-bromobenzoate derivative of the major product in **25a** revealed the C-1, C-2, and C-3 configuration shown below, the configurations which have been used in all the above discussions of **20** and **21**.





Deoxygenation

The next step in the sequence toward the ophiobolane nucleus required removal of the C-1 oxygen in lactone **25**. A few methods exist in the literature for the deoxygenation of an alcohol through its simple alkyl ester.[28] A lactone being merely a cyclic ester, the direct deoxygenation of **25** was undertaken. Literature examples for the deoxygenation of a lactone, however, were scarce.[28a,29] This deoxygenation was attempted using three methods: photochemical electron transfer,[28a] dissolving metal reduction,[28b] and triphenylsilane radical induced cleavage.[28c] Unfortunately, complex product mixtures were obtained in each case from which no trace of the desired product could be recovered.

In response to these findings, a more circuitous though viable sequence of reactions was devised for the deoxygenation at C-1. This strategy involved the potentially facile deoxygenation of a C-1 hydroxyl group. It was appreciated that the cis relationship between the C-2 and C-6 substituents in a simple cyclopentane was thermodynamically disfavored. Thus, reduction of C-7 to the alcohol oxidation state avoided the probable isomerization of this substituent during manipulations at C-1. Lactones **25a** and **25s** were taken separately through this route.

Lactone **25s** was reduced with LAH at −5 °C to diol **29s** in excellent yield. The selective protection of the primary hydroxyl group over the hindered secondary neopentyl group was achieved easily. Monobenzyl ether **30s** was afforded in at least 90% yield via the sodium alkoxide with or without a phase-transfer catalyst. The reaction rate increased dramatically with the catalyst present.[30]

The radical deoxygenation of alcohols offers several advantages over other methods.[31] These radical reactions are less susceptible to steric retardation, take place under neutral conditions, and generally proceed in high yield. A radical deoxygenation seemed well suited for removing the hindered hydroxyl group of **30**. To this end, the methyl

(24) Augustine, R. L.; VanPeppen, J. *Ann. N.Y. Acad. Sci.* **1969**, *158*, 482.

(25) Initially, yields of about 80% were obtained for this reaction. These lower yields were traced to loss of silyl ether. Adding anhydrous potassium carbonate to the reaction mixture improved the yield of the desired product and did not interfere with the reaction rate or selectivity.

(26) Monti, H.; Léandri, G.; Klos-Ringuet, M.; Corriol, C. *Synth. Commun.* **1983**, *13*, 1021.

(27) Cheng, Y.-S.; Liu, W.-L.; Chen, S.-H. *Synthesis* **1980**, 223.

(28) (a) Portella, C.; Deshayes, H.; Pete, J. P.; Scholler, D. *Tetrahedron* **1984**, *40*, 3635. (b) Barrett, A. G. M.; Godfrey, C. R. A.; Hollinshead, D. M.; Prokopiou, P. A.; Barton, D. H. R.; Boar, R. B.; Joukhadar, L.; McGhie, J. F.; Misra, S. C. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1501. (c) Sano, H.; Ogata, M.; Migita, T. *Chem. Lett.* **1986**, 77.

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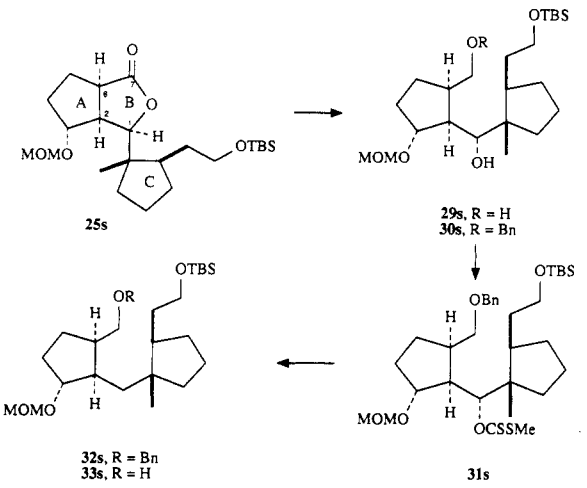
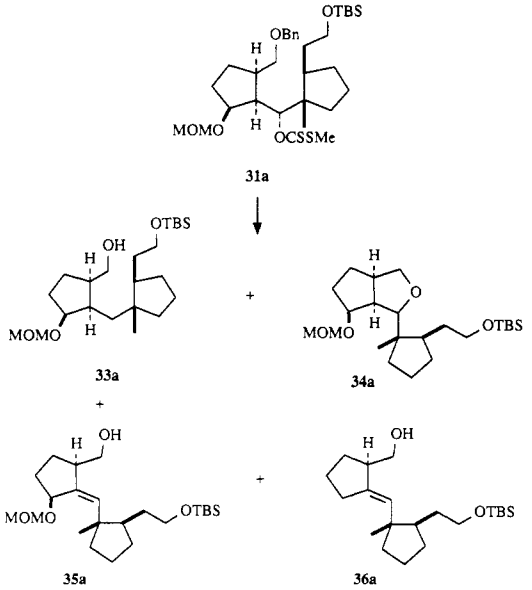
(30) Czernecki, S.; Georgoulis, C.; Provelenghiou, C. *Tetrahedron Lett.* **1976**, 3535.

(31) Hartwig, W. *Tetrahedron* **1983**, *39*, 2609.



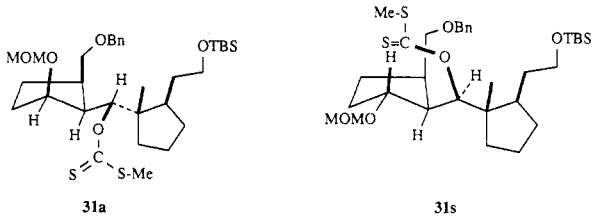
xanthate of **31s** was prepared in high yield under standard conditions. Treatment of xanthate **31s** in refluxing toluene with tri-*n*-butyltin hydride effected deoxygenation to give benzyl ether **32s** in up to 80% yield from alcohol **30s**. The reaction was quite sluggish, taking from 2 to 5 days to reach completion. Alcohol **33s**, resulting from cleavage of the benzyl ether, was also recovered from this reaction in up to 11% yield. Deprotection of benzyl ether **32s** using lithium in ammonia provided **33s** in 82% yield. Thus, deoxygenation of lactone **25s** was accomplished in a reasonable 55% overall yield.

On the other hand, the methyl xanthate **31a** of the alcohol derived from lactone **25a** with the C-3 MOM-ether in the β-configuration failed to deoxygenate under the same reaction conditions. After 12 h, xanthate **31a** was converted cleanly to a product homogeneous by TLC. The ^{1}H NMR spectrum indicated the presence of more than one compound. These compounds could not be separated by HPLC and were treated directly with lithium in ammonia. The four products from this reaction were separable by flash chromatography. Presented in order of



increasing mass recovery, the desired alcohol **33a** comprised only 13% of the product mixture. Compound **36a**[32] resulted from the reductive cleavage of the allylic ether in **35a**. Olefin **35a**[33] was the product expected from the Chugaev reaction[34] of xanthate **31a**. Elimination products **35a** and **36a** comprised 49% of the product mixture. Finally, cyclic ether **34a** was isolated as the major product. The ratio of cyclic ether formation versus elimination varied with the temperature of the deoxygenation reaction. Higher temperatures favored elimination. The ratio changed from roughly 1:1 in toluene to 1:1.5 in xylenes.

The differences in the deoxygenations of xanthates **31a** and **31s** necessarily stem from the differences in their configurations at C-3. The various puckered conformations of the A ring were expected to be relatively close in energy.[35] The conformations shown have proven useful in understanding the experimental results. For the xanthate **31a**, this envelope conformation of the A ring would place the C-3 and C-6 substituents in pseudoaxial orientations and the bulky C-2 substituent in a pseudoequatorial position. The conformation about the C-1,C-2 bond would



place the bulky xanthate and cyclopentyl groups away from the A-ring substituents and nearly parallel to the C-3 and C-6 hydrogen atoms. This orientation is consistent with the products formed in the attempted deoxygenation. The Chugaev reaction involves the syn elimination, and the carbon–sulfur bond near the C-3 hydrogen is required for this reaction. Furthermore, this conformation would permit a facile intramolecular displacement of the xanthate ester by the benzyl ether oxygen.

In the favored conformation of xanthate **31s**, the xanthate group would be replaced on the more sterically favorable position near the C-3 hydrogen but away from the C-2 hydrogen. Such an orientation places the xanthate ester in an unfavorable steric position to participate in a facile elimination or displacement reaction.

Alternate methods for deoxygenation of alcohol **30a** were investigated, and the attempted use of acetate, mesylate, tosylate, and phosphate esters did not meet with success. However, the successful preparation of **33s** permitted continuation of the synthesis.

The Formation of Ring B

The most efficient method for the final ring closure directly to the desired tricyclic nucleus of the ophiobolanes was the intramolecular titanium-induced coupling of the dicarbonyl compound (the McMurry reaction). This coupling reaction is regiospecific, and in the present case would be stereospecific due to ring strain.[36] Of concern, however, was the fate of the mixed acetal (MOM) on ring A since McMurry has found certain ketals are cleaved under the reaction conditions.[36]

Dicarbonyl **40s** was readily available in five manipulations from alcohol **33s**. Swern oxidation of alcohol **33s** afforded aldehyde **37s** in 94% yield. This aldehyde was

(32) This structure was elucidated from ^{1}H NMR data.
(33) This structure was elucidated by a combination of ^{1}H and ^{13}C NMR data.
(34) Nace, H. R. *Org. React.* **1962**, *12*, 57.
(35) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. In *Conformational Analysis*; American Chemical Society: Washington, DC, 1981; pp 200–206.
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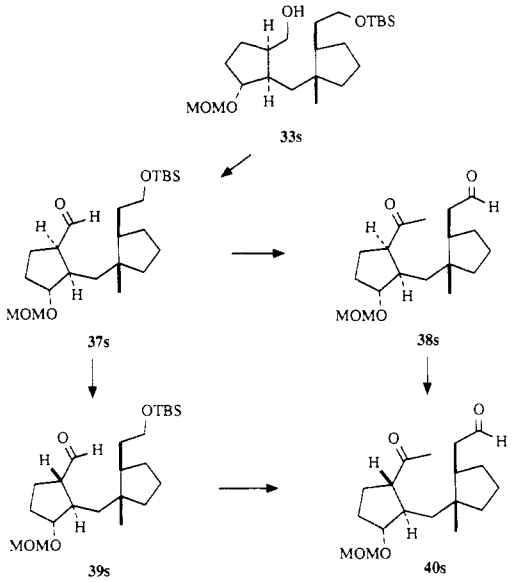
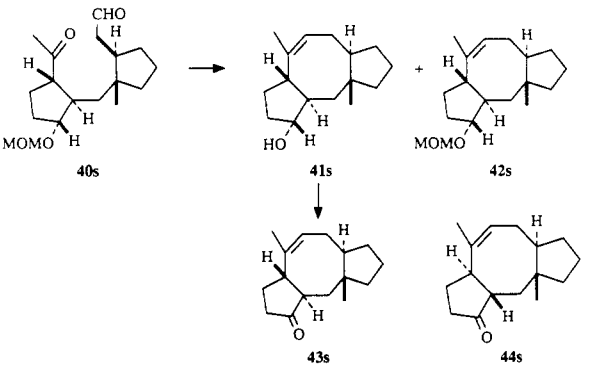
stable to chromatography, yet it could be isomerized readily to the 2,6-trans isomer **39s** by treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).[37] The rate of isomerization was a function of the amount of DBU present as shown by simple ^{1}H NMR experiments. With 0.1 equiv of DBU, the ratio of **37s** and **39s** was only 1:3 after 1 day at ambient temperature. With 1.0 equiv of base, the ratio was 1:13 after 7.5 h. These ratios were determined from integrations of the distinctive aldehyde proton resonances for each isomer. On a preparative scale, aldehydes **37s** and **39s** were isolated in a 1:18 ratio in 95% yield.

Keto aldehydes **38s** and **40s** were easily prepared from these aldehydes in 70% and 62% overall yields, respectively. The first step in this series of reactions involved the addition of methyllithium to the aldehydes affording the corresponding secondary alcohols.[38] Deprotection of the silyl ethers with fluoride and subsequent Swern oxidation of the resulting diols yielded the desired materials.



The thermodynamically less stable 2,6-cis configuration in **37s** survived this series of reactions. The actual isomerization of the C-6 methyl ketone in **38s** proved much more difficult than observed for the corresponding C-6 aldehyde in **37s**. Little isomerization of **38s** was noted with DBU as the base. An 8:1 mixture of **40s** and **38s** resulted upon treatment with sodium methoxide in methanol at ambient temperature; however, several minor byproducts were formed. When the reaction temperature was increased to achieve a more favorable ratio, extensive decomposition resulted.

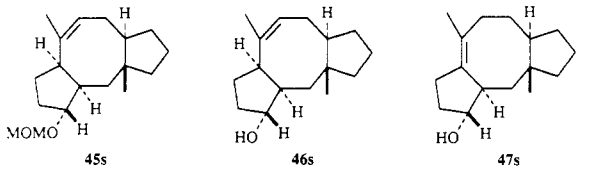
The titanium(0)-mediated coupling of dicarbonyl substrate **40s** afforded cyclized products in 49% yield after flash chromatography. Alcohol **41s** was favored over MOM ether **42s** by a 1.7:1 ratio; both products were at least 87% pure by GC analysis. At this point, it must be recalled that a 4:1 mixture of C-1 isomers emerging from the convergent step of the synthesis was used through the remainder of the sequence. In the final Swern oxidation of alcohol **41s**, a mixture of ketones **43s** and **44s** was isolated in 55% yield and in a ratio of 4:1 after a successful HPLC separation. The ^{1}H NMR spectra of these final products were identical with those of these known substances previously prepared by Coates.[2,39] The isolation of these two isomeric ketones



shows that the stereochemistry of the C-1 alcohol does control the stereochemistry introduced at C-2 during the hydrogenation and the use of pure C-1 alcohols would permit a stereoselective synthesis of ophiobolane nuclei.

The McMurry reaction with the *cis*-2,6 isomer **38s** gave the desired cyclization products in 45% yield; the cis-2,6 configuration remained intact. In this case, the MOM ether **45s** predominated over alcohol **46s**, presumably due to the shorter reaction time employed.

Some interesting chemistry of these tricyclic systems surfaced in bringing about the deprotection of MOM ethers **42s** and **45s**. Under standard aqueous acid conditions, migration of the B-ring double bond was observed. MOM ether **45s** was cleaved in 78% yield to a 3:4 mixture of **46s** and the rearranged alcohol **47s**. Similarly, dou-



ble-bond migration occurred in the deprotection of MOM ether **42s**. Fortunately, none of the 6,7-olefinic alcohols were detected in the McMurry reaction products. Such a propensity for double bond migration can be found in studies dealing with the structure determinations of ophiobolins. Ophiobolin C and F were correlated via a common 6,7-olefinic intermediate resulting from palladium-induced migration of the double bond.[40]

Summary

The primary goal of this work was to develop an effective strategy for controlling the relative ring juncture stereochemistries in a synthesis of the ophiobolane sesterterpenes. The stereocontrolled approach delineated above has met this challenge with considerable success. Both the A/B and B/C ring juncture stereochemistries were set by catalytic hydrogenation reactions. Using a homogeneous iridium catalyst, the hydroxyl group directed hydrogenation of olefin **13** established the B/C ring stereochemistry with excellent stereoselectivity (>99% de). Using 5% rhodium on carbon, the steric-controlled hydrogenation of bicyclic butenolide **23** established the A/B ring stereochemistry. Cis bicyclic lactones were obtained with a favorable diastereomer ratio of 10–15:1. Thus, the chirality of the B/C ring juncture was translated sufficiently to the A/B ring juncture via the transient C-1 chirality generated in the convergent step of this synthesis. Finally, the titanium(0)-mediated cyclization of dicarbonyl substrate **40s** provided the ceroplastin nucleus in moderate yield, but

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(38) Buhler, J. D. *J. Org. Chem.* **1973**, *38*, 904.
(39) We thank Professor Robert M. Coates for kindly providing spectra for comparison.
(40) Nozoe, S.; Morisaki, M. *J. Chem. Soc., Chem. Commun.* **1969**, 1319.

with regiospecific olefin formation. Subsequent reactions revealed the potential for double-bond migration in these 5-8-5 ring-fused systems.

Experimental Section

General. Solvents were purified under a N_2 atmosphere when this was deemed necessary: from sodium benzophenone ketyl–diethyl ether, tetrahydrofuran (THF), 1,2-dimethoxyethane (DME); from CaH_2–benzene, chloroform, dichloromethane, diisopropylamine, dimethyl sulfoxide (DMSO), hexanes, toluene, triethylamine, pyridine, tetramethylenediamine (TMEDA); from $LiAlH_4$–dimethyl sulfide (DMS); with 3-Å molecular sieves–dimethylformamide (DMF). When appropriate, commercial reagents were purified by standard procedures.[41]

Most reactions were monitored by analytical thin-layer chromatography (TLC) using precoated Analtech Uniplates (0.25-mm thick). Compounds were visualized by UV light and ethanolic anisaldehyde spray. Flash chromatography was performed using 230–400-mesh silica gel.[42] High-performance liquid chromatography (HPLC) was performed using a RI detector and a Whatman M9 10/50 partisil column. Analytical gas liquid chromatography (GC) was performed on a DB1 (polymethyl siloxane) fused silica capillary column, 30 m × 0.25 mm (injector and detector temperatures: 200 °C).

Reactions requiring an inert atmosphere were conducted under dry N_2 or dry argon. Temperatures are reported as bath temperatures. Reaction mixtures were stirred using Teflon-coated magnetic stir bars unless otherwise noted. Organic layers were dried using $MgSO_4$; the solvent was removed with a rotary evaporator using a water aspirator, followed by static evaporation with an oil pump (<0.5 Torr). Melting points are uncorrected, as are boiling points. Yields refer to the yields of isolated products which are chromatographically homogeneous, unless otherwise noted.

Since each syn and anti series is an unseparated 4:1 mixture of the two isomers, all spectra were taken with the mixture. In the ^1H NMR spectra, where chemical shifts are different for the same proton in each isomer, the number of protons reported reflect this 4:1 mixture. In the ^{13}C NMR spectra, only the absorptions of the major isomer are reported. High-resolution mass spectral data were collected on a Kratos MS-50 high-resolution mass spectrometer.

Elemental analyses were performed by the Microanalytical Laboratory operated by the College of Chemistry, University of California, Berkeley, CA. The X-ray crystallographic analysis was performed by Dr. F. J. Hollander, staff crystallographer at the UC Berkeley X-Ray Crystallographic Facility.

***tert*-Butyl (*E*)- and (*Z*)-(2-Carbomethoxy-2-methylcyclopentylidene)acetate ((*E*)- and (*Z*)-9a) and *tert*-Butyl (5-Carbomethoxy-5-methyl-1-cyclopentenyl)acetate (9b).** Sodium hydride (0.85 g, 21.2 mmol, 60% oil dispersion) was washed with hexanes, and THF (40 mL) was added. The suspension was cooled to 0 °C, and *tert*-butyl diethylphosphonoacetate (5.90 g, 23.4 mmol) was added, dropwise. The pale green reaction mixture was stirred for 1 h at ambient temperature and was cooled back to 0 °C. Keto ester 8[7] (3.00 g, 19.2 mmol) in THF (10 mL) was added, dropwise, and the cooling bath was removed. After 15 h, the reaction mixture was partitioned between ice–water (125 mL) and ether (125 mL). The organic layer was washed with brine 75 mL), dried, and concentrated to a very pale yellow oil (5.69 g). By GC analysis (column temperature = 165 °C), the oil consisted of (*E*)-**9a** (3.95 min), (*Z*)-**9a** (3.63 min), and **9b** (3.23 min) in a 90.6:4.1:4.8 ratio, respectively. The crude oil was purified by flash chromatography using hexanes:ethyl acetate (10:1) to afford pure (*E*)-**9a** as a colorless oil (3.96 g, 81%). The remaining diesters were obtained as a mixture with the major product (0.42 g, 9%). A pure sample of each was obtained by HPLC using hexanes–ethyl acetate (10:1).

(*Z*)-**9a** (third fraction): mp 54.5–55.5 °C; IR (thin film/CH_2Cl_2) 2960, 2870, 1750, 1710, 1650, 1155 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.40 (s, 12), 1.60–1.86 (m, 3), 1.95–2.06 (m, 1), 2.54–2.60 (m, 2), 3.60 (s, 3), 5.73 (t, 1, *J* = 1.8 Hz); ^{13}C NMR (50.8 MHz, $CDCl_3$) δ 21.69, 22.95, 28.04, 36.57, 41.91, 51.74, 52.28, 79.74, 114.63, 165.08, 166.65, 175.92.

(*E*)-**9a** (first fraction): IR (thin film) 2980, 2900, 1730, 1710, 1650 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.34 (s, 3), 1.46 (s, 9), 1.58 (dt, 1, *J* = 6.4, 12 Hz), 1.64–1.94 (m, 2), 2.30 (dt, 1, *J* = 6.2, 12.4 Hz), 2.74–3.01 (m, 2), 3.67 (s, 3), 5.71 (t, 1, *J* = 2.6 Hz); ^{13}C NMR (50.8 MHz, $CDCl_3$), δ 23.68, 24.41, 28.11, 32.58, 37.79, 52.20, 54.56, 79.67, 115.26, 166.07, 167.92, 175.34. Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.12; H, 8.72. Found: C, 65.99; H, 8.62.

9b (second fraction): ^1H NMR (250 MHz, $CDCl_3$) δ 1.28 (s, 3), 1.43 (s, 9), 1.74–1.82 (m, 1), 2.27–2.52 (m, 3), 2.93 (dd, 1, *J* = 1.5, 16 Hz), 2.99 (dd, 1, *J* = 1.5, 16 Hz), 3.64 (s, 3), 5.72 (br s, 1); ^{13}C NMR (50.8 MHz, $CDCl_3$) δ 22.36, 27.90, 30.20, 34.82, 36.94, 51.73, 56.61, 80.32, 130.29, 139.00, 170.49, 176.35. Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.12; H, 8.72. Found: C, 65.99; H, 8.58.

Preparation of 9b from (*E*)-9a.[13] A solution of diisopropylamine (0.72 mL, 5.1 mmol) in THF (5.0 mL) was cooled in an ice/ethanol bath and treated, dropwise, with *n*-butyllithium (4.10 mL, 5.08 mmol, 1.24 M in hexanes). The solution was stirred for 15 min, and a solution of diester (*E*)-**9a** (1.17 g, 4.62 mmol) in THF (5.0 mL) was added, dropwise, using a cannula. The cooling bath was removed. After 30 min, the pale green solution was poured into water (25 mL) and extracted with ether (2 × 25 mL). The organic layers were dried and concentrated to a yellow oil (1.11 g). A portion of the crude product (551 mg) was purified by flash chromatography using hexanes–ethyl acetate (12:1) to afford **9b** as a colorless oil (388 mg, 67%).

(*E*)-(2-Carbomethoxy-2-methylcyclopentylidene)acetic Acid (10). A dry 1-L, round-bottomed flask equipped with a drying tube containing calcium sulfate was charged with *tert*-butyl ester (*E*)-**9a** (44.9 g, 0.177 mol), dichloromethane (200 mL), and trifluoroacetic acid (51 mL, 0.66 mol). The yellow solution was stirred for 24 h at ambient temperature and concentrated to a yellow oil. Toluene (100 mL) was added, and the mixture was concentrated using a rotary evaporator (3×). The residue was subjected to high vacuum (<0.5 Torr); white crystals were recovered (35.0 g, 100%). An analytical sample was prepared by recrystallization from ether: mp 84–85 °C; IR (thin film/CH_2Cl_2) 3850–2300, 2960, 1730, 1690, 1640 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.38 (s, 3), 1.63 (dt, 1, *J* = 6.5, 12 Hz), 1.70–1.97 (m, 2), 2.33 (dt, 1, *J* = 6.5, 12 Hz), 2.90 (ddt, 1, *J* = 2.1, 7.4, 20 Hz), 2.97 (ddt, 1, *J* = 2.0, 7.3, 20 Hz), 3.69 (s, 3), 5.85, (t, 1, *J* = 2.4 Hz), 10.36 (br s, 1); ^{13}C NMR (50.8 MHz, $CDCl_3$) δ 23.49, 24.14, 33.08, 37.68, 52.27, 54.96, 113.09, 172.12, 172.57, 174.92. Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.81; H, 7.21.

Methyl (*E*)-2-(2-Hydroxyethylidene)-1-methylcyclopentanecarboxylate (11). A 1-L, three-necked flask equipped with a thermometer and pressure-equalizing addition funnel was charged with acid **10** (35.0 g, 0.177 mol) and THF (177 mL) and immersed in an ice–salt–methanol bath. A solution of borane in THF (177 mL, 0.177 mol, 1 M) was added over 1.5 h, maintaining the internal temperature below −10 °C. The system was covered with foil and allowed to warm gradually to ambient temperature. After 20 h, the reaction mixture was quenched by the slow addition of a 1:1 mixture of acetic acid and water (3 mL). The mixture was concentrated using a rotary evaporator to a cloudy residue. This residue was poured slowly into an ice-cold, stirring saturated $NaHCO_3$ solution (250 mL) and was extracted with ether (300 mL). Water was added until the resulting emulsion was eliminated. The aqueous layer was extracted further with ether (2 × 200 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution (2 × 200 mL), dried, and concentrated. The crude product was purified by flash chromatography using hexanes–ethyl acetate (2.5:1) to afford a colorless oil (18.4 g, 57%): IR (thin film) 3720–3090, 1735, 1675, 1270, 1150 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.23 (s, 3), 1.46 (dt, 1, *J* = 7.0, 12 Hz), 1.52–1.81 (m, 2), 2.20 (dt, 1, *J* = 6.6, 12 Hz), 2.28–2.34 (m, 2), 2.73 (br s, 1), 3.56 (s, 3), 4.03 (d, 2, *J* = 6.3 Hz), 5.44 (tt, 1, *J* = 2.6, 6.7 Hz); ^{13}C NMR (50.8 MHz, $CDCl_3$) δ 23.48, 24.53, 29.18, 38.39, 51.95, 52.47, 60.35, 121.59, 149.04, 176.80. Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.20; H, 8.75. Found: C, 64.93; H, 8.77.

Methyl (*E*)-2-[2-(*tert*-Butyldimethylsiloxy)-ethylidene]-1-methylcyclopentanecarboxylate (12). A solution of allylic alcohol 11 (15.77 g, 85.57 mmol) in DMF (200 mL) was treated sequentially with imidazole (18.93 g, 0.287 mol) and

(41) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*; Pergammon Press: New York, 1980.
(42) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

tert-butyldimethylsilyl chloride (21.39, 0.142 mol). The solution was stirred at ambient temperature for 1.5 h. The reaction mixture was poured into ice–water (400 mL) and extracted with petroleum ether (3 × 300 mL). The combined organic layers were dried and concentrated to a pale yellow oil (32.33 g). The crude product was purified by flash chromatography using hexanes–ethyl acetate (12:1) to afford a colorless oil (22.13 g, 87%): IR (thin film) 2970, 2940, 2890, 2870, 1740, 1645, 1260, 1155, 1085 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.00 (s, 6), 0.84 (s, 9), 1.27 (s, 3), 1.48 (dt, 1, J = 7.0, 12 Hz), 1.56–1.86 (m, 2), 2.20–2.32 (m, 3), 3.60 (s, 3), 4.13 (d, 1, J = 6.2 Hz), 5.42 (tt, 1, J = 2.5, 6.1 Hz); ^{13}C NMR (50.8 MHz, $CDCl_3$) δ –5.10, 18.24, 23.72, 24.70, 25.86, 29.45, 38.37, 51.87, 52.42, 61.61, 172.60, 147.00, 176.59. Anal. Calcd for $C_{16}H_{30}O_3Si$: C, 64.38; H, 10.13. Found: C, 64.36; H, 10.20.

[(*E*)-2-[2-(*tert*-Butyldimethylsiloxy)ethylidene]-1-methylcyclopentyl]methanol (13). A rapidly stirred solution of ester **12** (22.31 g, 77.14 mmol) in ether (350 mL) at 0 °C was treated with $LiAlH_4$ (2.60 g, 68.5 mmol). The suspension was stirred at 0 °C for 1 h, and saturated aqueous sodium sulfate solution (10 mL) was added with caution. Sodium sulfate (~20 g) was added, and the cooling bath was removed. The reaction mixture was allowed to warm to ambient temperature. The aluminum salts were filtered and washed with ether (300 mL). The filtrate was dried and concentrated to a colorless oil (19.85 g). The crude product was purified by flash chromatography using hexanes–ethyl acetate (6:1) to afford **13** (19.30 g, 96%): IR (thin film) 3620–3120, 2960, 2940, 2870, 1675, 1270, 1075, 1010 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.04 (s, 6), 0.87 (s, 9), 1.02 (s, 3), 1.38–1.46 (m, 1), 1.63 (quintet, 2, J = 7.0 Hz), 1.73–1.86 (m, 2), 2.18–2.42 (m, 2), 3.28 (d, 1, J = 11 Hz), 3.37 (d, 1, J = 11 Hz), 4.16 (d, 2, J = 6.2 Hz), 5.26 (tt, 1, J = 2.6, 6.2 Hz); ^{13}C NMR (50.8 MHz, $CDCl_3$) δ 5.11, –5.07, 18.33, 22.56, 23.75, 25.93, 29.83, 36.45, 47.56, 61.59, 69.02, 120.97, 148.92. Anal. Calcd for $C_{15}H_{30}O_2Si$: C, 66.61; H, 11.18. Found: C, 66.75; H, 11.31.

[(1*S,2*R**)-2-[2-(*tert*-Butyldimethylsiloxy)ethyl]-1-methylcyclopentyl]methanol (14t). (a) Heterogeneous Catalytic Hydrogenation.** A 250-mL round-bottomed flask was charged with 5% palladium on carbon (800 mg) and dry hexanes (25 mL). The system was evacuated using a water aspirator and purged with hydrogen at atmospheric pressure (3×). To the presaturated catalyst was added olefin **13** (1.91 g, 7.06 mmol) in dry hexanes (25 mL). The system was evacuated and purged with hydrogen (3×). The reaction mixture was stirred for 1.5 h, and hydrogen was removed under aspirator pressure. The suspension was filtered through a small plug of Celite. The filtrate was concentrated to a viscous colorless oil (1.88 g, 98%) homogeneous by TLC using hexanes–ethyl acetate (4:1). From the ^1H NMR spectrum, integration of the quarternary methyl resonances proved this oil to be a 12:1 mixture of C-2 epimers. The methyl resonance at 1.03 ppm for the minor epimer, (1*S**,2*S**)-**14c**, is 0.24 ppm downfield from that of the major epimer, (1*S**,2*R**)-**14t**. Pure samples of each epimer were obtained by HPLC using hexanes:ethyl acetate (7:1).

14t (first fraction): IR (thin film) 3640–3100, 2970, 2940, 2870, 1260, 1100 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.046 (s, 6), 0.79 (s, 3), 0.88 (s, 9), 1.22–1.40 (m, 3), 1.47–1.71 (m, 5), 1.81–1.90 (m, 2), 3.43 (br s, 2), 3.56 (dt, 1, J = 6.8, 9.6 Hz), 3.69 (dt, 1, J = 6.3, 10 Hz); ^{13}C NMR (50.8 MHz, $CDCl_3$) δ –5.34, 18.04, 18.32, 21.71, 25.94, 31.28, 33.53, 36.64, 40.59, 45.44, 62.95, 70.57. Anal. Calcd for $C_{15}H_{32}O_2Si$: C, 66.11; H, 11.84. Found: C, 65.92; H, 11.98.

14c (second fraction): ^{13}C NMR (50.8 MHz, $CDCl_3$) δ –5.32, 21.93, 23.46, 25.97, 31.36, 32.90, 35.93, 45.49, 46.00, 63.14, 67.06.

(b) Homogeneous Catalytic Hydrogenation. A 1-L, round-bottomed flask was charged with olefin **13** (18.76 g, 69.35 mmol) and dry dichloromethane (140 mL). The solution was degassed by cooling to –78 °C, evacuating the system using a water aspirator, and purging with argon (3×). $[Ir(cod)PCy_3(py)]PF_6$[12] (1.3 g, 1.62 mmol) was added at ambient temperature. The system was cooled rapidly to –78 °C, evacuated with a water aspirator, and purged with hydrogen. The cooling bath was removed, and the solution was stirred at ambient temperature for 3 h. The solution was orange initially, changed to a pale yellow color within 10 min, and was orange again when TLC indicated complete hydrogenation. Hydrogen was removed using a water aspirator, and the reaction mixture was concentrated. Ether (200 mL) was added, and the suspension was filtered through Celite. The filtrate was concentrated to an orange oil. The crude product was purified by flash chromatography using hexanes–ethyl acetate (9:1 to 4:1) to afford **14t** as a pale yellow (17.56, 93%). The minor epimer was absent in the ^1H NMR spectrum of the product.

(1*S,2*R**)-2-[2-(*tert*-Butyldimethylsiloxy)ethyl]-1-methylcyclopentanecarboxaldehyde (15t).** Under an argon atmosphere, a solution of oxalyl chloride (6.60 mL, 75.7 mmol) in dichloromethane (150 mL) at –78 °C was treated dropwise with DMSO (11.3 mL, 0.159 mol) in dichloromethane (50 mL). The mixture was stirred for 10 min. A solution of alcohol **14t** (16.62 g, 60.99 mmol, from the homogeneous hydrogenation) in dichloromethane (60 mL) was added dropwise. The suspension was stirred for 10 min, and triethylamine (43 mL, 0.31 mol) was added. After 5 min, the cooling bath was removed, and the thick white suspension was allowed to reach ambient temperature. The reaction mixture was partitioned between dichloromethane (100 mL) and water (100 mL). The organic layer was washed with aqueous 1% hydrochloric acid solution and saturated $NaHCO_3$ solution (100 mL each). The organic layer was dried and concentrated to a yellow oil. The crude product was purified by flash chromatography using hexanes–ethyl acetate (10:1) to afford a colorless oil (15.09 g, 91%). Analysis by GC (column temperature = 170 °C) showed that the product consisted of a 262:1 mixture of C-2 epimers **15t** (4.19 min) and **15c** (3.87 min). A 12:1 mixture of **14t**:**14c** afforded a 12:1 mixture of **15t**:**15c** by this procedure. In the ^1H NMR spectrum of **15c**, the quaternary methyl and aldehyde protons appeared as singlets at 1.15 and 9.61 ppm, respectively.

15t: IR (thin film) 2970, 2920, 2860, 2720, 1730, 1260, 1100 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.00 (s, 6), 0.85 (s, 9), 0.93 (s, 3), 1.29–1.56 (m, 4), 1.58–1.81 (m, 2), 1.85–2.03 (m, 2), 2.06–2.22 (m, 1), 3.53 (dt, 2, J = 1.6, 6.6 Hz), 9.35 (s, 1); ^{13}C NMR (50.8 MHz, $CDCl_3$) δ –5.31, –5.35, 14.00, 18.27, 22.72, 25.91, 30.57, 33.25, 35.29, 41.26, 55.90, 61.90, 205.80; high-resolution mass spectrum calcd for $C_{14}H_{27}O_2Si$ (M – CH_3) 255.1780, found 255.1783.

3-[(Benzyloxy)methyl]-2-cyclopenten-1-one (17). A solution of stannane **16**[16] (54.8 g, 0.133 mol) in THF (300 mL) was cooled to –78 °C and treated dropwise with *n*-butyllithium (78 mL, 0.12 mol, 1.55 M in hexanes). The resulting bright yellow solution was stirred for 15 min, and a solution of 3-ethoxy-2-cyclopenten-1-one[17] (11.39 g, 90.25 mmol) in THF (100 mL) was added using a cannula. After 45 min, the cooling bath was removed and aqueous 5% hydrochloric acid solution 200 mL) was added. The reaction mixture was stirred for 20 min, and the layers were separated. The aqueous layer was extracted with ether (2 × 150 mL), dried, and concentrated to a colorless oil. The crude product was purified by flash chromatography. After eluting with 2 column volumes of hexanes to remove the stannanes, hexanes–ethyl acetate (1:1) was used as the eluent. Enone **17** was obtained as a white crystalline solid (12.2 g, 67%): mp 52.5–53.5 °C; IR (thin film/CH_2Cl_2) 3050, 2980, 2920, 2850, 1705, 1670, 1625, 1435, 1265, 1175, 1130, 1075, 1020 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.40–2.45 (m, 2), 2.56–2.60 (m, 2), 4.31 (s, 2), 4.59 (s, 2), 6.20 (t, 1, J = 1.6 Hz), 7.34 (br s, 5); ^{13}C NMR (50.8 MHz, $CDCl_3$) δ 28.27, 34.64, 69.20, 72.93, 127.49, 127.78, 128.36, 129.04, 137.28, 177.82, 209.02. Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.29; H, 6.79.

2-Bromo-3-[(benzyloxy)methyl]-2-cyclopenten-1-one (18). A solution of enone **17** (15.00 g, 74.15 mmol) in dichloromethane (465 mL) was cooled to 0 °C and treated sequentially with pyridine (12.2 mL, 0.151 mol) and pyridinium bromide perbromide (63 g, 0.18 mol, 90% tech). The orange suspension was stirred at 3 °C for 14 h, diluted with dichloromethane (250 mL), and washed with aqueous 10% sodium thiosulfate solution (2 × 250 mL). The organic layer was dried and concentrated to a light brown oil. The crude material was purified immediately by flash chromatography using hexanes–ethyl acetate (3:1 to 2:1) to afford a pale yellow solid (17.83 g, 86%): mp 41.5–42.5 °C; IR (thin film/CH_2Cl_2) 2920, 2850, 1715, 1620, 1495, 1450, 1430, 1400, 1345, 1265, 1150, 1080, 1025 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.51–2.55 (m, 2), 2.76–2.82 (m, 2), 4.47 (m, 2), 4.58 (s, 2), 7.35 (br s, 5); ^{13}C NMR (50.8 MHz, $CDCl_3$) δ 28.63, 32.69, 68.56, 73.44, 121.83, 127.76, 128.09, 128.55, 137.19, 172.73, 201.25. Anal. Calcd for $C_{13}H_{13}BrO_2$: C, 55.54; H, 4.66; Br, 28.42. Found: C, 55.47; H, 4.68; Br, 28.28.

1-[(Benzyloxy)methyl]-2-bromo-3-(methoxymethoxy)-1-cyclopentene (19). A solution of bromo enone **18** (17.83 g, 63.41

mmol) and cerium(III) chloride heptahydrate (23.63 g, 63.41 mmol) in methanol (170 mL) was cooled in an ice/2-propanol bath. Sodium borohydride (2.40 g, 63.41 mmol) was added in small portions. The suspension was stirred for 20 min, and saturated aqueous NH_4Cl solution (250 mL) was added. Water (30 mL) was added, and the reaction mixture was extracted with ether (2 × 250 mL). The organic layers were concentrated, and the residue was partitioned between dichloromethane (150 mL) and brine (30 mL). The organic layer was dried and concentrated to a pale yellow oil (19.00 g). A solution of the alcohol in dichloromethane (175 mL) was cooled to 0 °C and treated sequentially with diisopropylethylamine (48 mL, 219 mmol) and chloromethyl methyl ether (15.4 mL, 196 mmol). The cooling bath was removed, and the solution was stirred at ambient temperature for 20 h. Aqueous 2.5% hydrochloric acid solution (100 mL) was added, and stirring was continued for 30 min. The reaction mixture was extracted with ether (250 mL). The organic layer was washed with saturated $NaHCO_3$ solution (75 mL), dried, and concentrated to an orange oil (20.7 g). The crude product was purified by flash chromatography using hexanes–ethyl acetate (5.5:1) to afford a colorless oil (19.55 g, 94%): IR (thin film) 2940, 2890, 2850, 1455, 1355, 1215, 1150, 1095, 1030 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.87–1.96 (m, 1), 2.22–2.66 (m, 3), 3.40 (s, 3), 4.15 (d, 1, J = 13 Hz), 4.20 (d, 1, J = 13 Hz), 4.46 (s, 2), 4.62–4.66 (m, 1), 4.71 (d, 1, J = 6.9 Hz), 4.73 (d, 1, J = 6.9 Hz), 7.3 (br s, 5); ^{13}C NMR (50.8 MHz, $CDCl_3$) δ 29.25, 30.92, 55.33, 67.18, 72.23, 84.47, 95.50, 119.72, 127.47, 128.15, 137.80, 142.72. Anal. Calcd for $C_{15}H_{19}BrO_3$: C, 55.06; H, 5.85; Br, 24.42. Found: C, 54.91; H, 5.87; Br, 24.35.

Preparation of Allylic Alcohols 20a/s and 21a/s. A solution of vinyl bromide **19** (2.35 g, 7.18 mmol) in ether (60 mL) at −78 °C was treated dropwise with *tert*-butyllithium (8.45 mL, 14.4 mmol). The pale yellow solution was stirred for 1.5 h. A solution of aldehyde **15** (1.94 g, 7.17 mmol) in ether (20 mL) was added using a cannula. The cooling bath was packed with dry ice and covered with foil. After 5 h, saturated aqueous NH_4Cl solution (10 mL) was added. The reaction mixture was partitioned between water (30 mL) and ether (50 mL). The organic layer was dried and concentrated to a yellow oil (4.0 g). The crude product was purified by flash chromatography using hexanes:ethyl acetate (6:1 to 2.5:1) to afford **20a:21a** (1.16 g, 31.3%) and **20s:21s** (1.50 g, 40.3%) as pale yellow oils. The higher R_f alcohol, **20a:21a**, consisted of an inseparable 4:1 mixture of the 1*S**,3*S**,10*R**,11*S** isomer (**21a**) and the 1*R**,3*R**,10*R**,11*S** isomer (**20a**). The lower R_f alcohol, **20s:21s**, consisted of an inseparable 4:1 mixture of the 1*S**,3*R**,10*R**,11*S** isomer (**21s**) and the 1*R**,3*S**,10*R**,11*S** isomer (**20s**). These allylic alcohols were unstable to $CDCl_3$. Within 30 min, the colorless solution darkened, and a complex mixture of products was evident by TLC. This problem was avoided by using C_6D_6 as the solvent for NMR spectra.

20a:21a: IR (thin film) 3030 (br), 2950, 2870, 1255, 1090, 1025 cm^{-1}; ^1H NMR (250 MHz, C_6D_6) δ 0.00/0.01 (2 s, 6), 0.45 (s, 0.6), 0.82 (s, 2.4), 0.89/0.90 (2 s, 9), 1.03–1.92 (m, 10), 2.02–2.19 (m, 2), 2.49–2.62 (m, 1), 2.98 (s, 0.6), 3.01 (s, 2.4), 3.53–3.68 (m, 2), 3.79 (d, 0.8, J = 4.1 Hz), 3.79–4.0 (m, 0.6), 3.82 (d, 0.8, J = 12 Hz), 3.95 (d, 0.8, J = 12 Hz), 4.18–4.34 (m, 2.4), 4.15 (d, 0.8, J = 7.9 Hz), 4.25 (d, 0.8, J = 8.0 Hz), 4.44 (d, 0.8, J = 4.1 Hz), 4.49 (d, 0.2, J = 5.5 Hz), 4.67–4.75 (m, 0.2), 4.82–4.89 (m, 0.8), 6.96–7.22 (m, 5); major isomer, ^{13}C NMR (50.8 MHz, C_6D_6) δ −4.61, −4.57, 18.98, 19.10, 23.65, 26.75, 30.12, 32.55, 32.90, 36.19, 38.72, 44.17, 50.03, 56.42, 64.15, 67.16, 72.97, 77.51, 87.14, 96.07, 138.84, 139.41, 143.56. Anal. Calcd for $C_{30}H_{50}O_5Si$: C, 69.45; H, 9.71. Found: C, 69.27; H, 9.77.

20s:21s: IR (thin film) 3550 (br), 3060, 2940, 2870, 1260, 1090, 1030 cm^{-1}; ^1H NMR (250 MHz, C_6D_6) δ −0.02 (s, 6), 0.69 (s, 0.6), 0.87 (s, 11.4), 1.10–1.80 (m, 10), 2.00–2.19 (m, 1), 2.21–2.38 (m, 1), 2.46–2.65 (m, 2), 3.12 (s, 3), 3.40–3.61 (m, 2), 4.12 (d, 0.2, J = 12 Hz), 4.24 (d, 0.8, J = 12 Hz), 4.26–4.37 (m, 3.2), 4.39 (d, 0.8, J = 12 Hz), 4.44 (s, 0.4), 4.48 (s, 1.6), 4.52–4.60 (m, 1), 6.96–7.20 (m, 5); major isomer, ^{13}C NMR (50.8 MHz, C_6D_6) δ −4.73, −4.65, 17.13, 19.08, 22.40, 26.73, 30.51, 31.46, 33.87, 35.50, 37.25, 44.44, 50.36, 55.88, 63.82, 68.81, 73.41, 77.81, 87.48, 96.15, 139.67, 141.55, 143.24. Anal. Calcd for $C_{30}H_{50}O_5Si$: C, 69.45; H, 9.71. Found: C, 69.37; H, 9.87.

Preparation of Diol 22a. A solution of allylic benzyl ether **21a**[43] (6.58 g, 12.7 mmol) in ether (25 mL) was diluted with liquid ammonia (250 mL, distilled from lithium). Lithium wire (580 mg, 83.6 mmol) was added, and the blue solution was stirred at reflux for 1.5 h. Saturated aqueous NH_4Cl solution (20 mL) was added with caution to decolorize the reaction mixture, and the ammonia was allowed to evaporate at ambient temperature. The residue was partitioned between water (30 mL) and ether (175 mL). The organic layer was dried and concentrated. The crude product was purified by flash chromatography using hexanes–ethyl acetate (3:2 to 1:1) to afford a 4:1 mixture of **22a** as a viscous colorless oil (3.60 g, 66%). In some trials, the product mixture formed a sticky gum at the bottom of the flask. Magnetic stirring proved ineffective and substantial amounts of starting material were recovered. Mechanical stirring proved more effective: IR (thin film) 3650–3080, 2940, 2860, 1650, 1255, 1150, 1090, 1020 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.04/0.05 (2 s, 6), 0.64 (s, 0.6), 0.88 (s, 7.2), 0.89 (s, 1.8), 0.96 (s, 2.4), 1.20–2.20 (m, 11), 2.51 (t, 2, J = 6.7 Hz), 2.71 (dd, 1, J = 4.0, 8.7 Hz), 3.41 (s, 0.6), 3.42 (s, 2.4), 3.54 (dt, 1, J = 4.5, 10 Hz), 3.67, (d, 1, J = 5.8 Hz), 3.80–3.82 (m, 1), 4.08 (dd, 1, J = 8.2, 13 Hz), 4.24–4.28 (m, 0.2), 4.37 (dd, 1, J = 4.3, 13 Hz), 4.49 (d, 0.8, J = 5.8 Hz), 4.67 (d, 1, J = 7.0 Hz), 4.73 (d, 1, J = 7.0 Hz), 4.90–4.98 (m, 0.2), 4.98–5.05 (m, 0.8); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ −5.37, 18.53, 19.82, 22.23, 26.00, 29.73, 30.69, 31.48, 33.84, 35.88, 41.47, 48.75, 56.34, 58.76, 62.79, 75.82, 86.59, 95.60, 135.80, 145.70. Anal. Calcd for $C_{23}H_{44}O_5Si$: C, 64.44; H, 10.35. Found: C, 64.75; H, 10.43.

Preparation of Diol 22s. A solution of allylic benzyl ether **21s** (1.43 g, 2.76 mmol) in ether (5 mL) was diluted with liquid ammonia (50 mL, distilled from lithium). Lithium wire (125 mg, 18.0 mmol) was added, and the blue solution was stirred at reflux for 1.5 h. Saturated aqueous NH_4Cl solution was added with caution to decolorize the reaction mixture, and the ammonia was allowed to evaporate at ambient temperature. The residue was partitioned between water (10 mL) and ether (75 mL). The organic layer was dried and concentrated. The crude product was purified by flash chromatography using hexanes–ethyl acetate (1:3 to 1.5) to afford an inseparable 4:1 mixture of **22s** (603 mg, 51%) as a colorless oil. Starting material **21s** (755 mg) was recovered and subjected again to lithium in refluxing ammonia. An additional 358 mg (30%) of **22s** was obtained: ^1H NMR (250 MHz, $CDCl_3$) δ 0.071/0.066 (2 s, 6), 0.83 (s, 0.6), 0.87 (s, 2.4), 0.89 (s, 9), 1.20–1.40 (m, 3), 1.50–2.05 (m, 8), 1.68 (br s, 1), 2.24 (ddd, 1, J = 3.3, 8.3, 16 Hz), 2.50–2.66 (m, 1), 3.387 (s, 2.4), 3.394 (s, 0.6), 3.56 (dt, 1, J = 3.8, 10 Hz), 3.66–3.80 (m, 1), 4.15–4.30 (br s, 1), 4.19 (d, 0.2, J = 15 Hz), 4.21 (d, 0.8, J = 15 Hz), 4.28 (s, 1), 4.37 (d, 0.8, J = 15 Hz), 4.44 (d, 0.2, J = 15 Hz), 4.55–4.65 (m, 1), 4.61 (d, 1, J = 6.9 Hz), 4.70 (d, 1, J = 6.9 Hz); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ −5.44, 17.08, 18.47, 21.46, 25.99, 29.10, 31.44, 33.57, 34.05, 37.70, 41.74, 49.48, 55.62, 60.78, 63.26, 76.76, 87.20, 95.45, 138.43, 144.59. Anal. Calcd for $C_{23}H_{44}O_5Si$: C, 64.44; H, 10.35. Found: C, 64.26; H, 10.22.

Preparation of Unsaturated Lactone 23a. A light green suspension containing diol **22a** (3.60 g, 8.40 mmol), silver carbonate on Celite[23a] (39.2 g, 68.6 mmol), and benzene (250 mL) was protected from light and heated at reflux for 14 h. The black reaction mixture was cooled and filtered through Celite. The filter cake was washed with ether (250 mL). The filtrate was concentrated, and the crude product was purified by flash chromatography using hexanes–ethyl acetate (4:1). Lactone **23a** was obtained as a pale yellow oil (2.67 g, 75%): IR (thin film) 2960, 2880, 1775, 1665, 1265, 1160, 1100, 1060 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.038 (s, 6), 0.85 (s, 2.5), 0.88 (s, 9), 0.97 (s, 0.5), 1.14–2.06 (m, 9), 2.28–2.45 (m, 2), 2.56–2.75 (m, 2), 3.39 (s, 3), 3.53–3.74 (m, 2), 4.68 (s, 3), 4.76–4.84 (m, 1.83), 4.87 (m, 0.17); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ −5.43, 16.64, 18.19, 22.61, 22.92, 25.85, 31.48, 34.06, 36.54, 36.86, 43.51, 46.56, 56.07, 62.90, 78.51, 89.83, 96.44, 142.63, 168.90, 170.97. Anal. Calcd for $C_{23}H_{40}O_5Si$: C, 65.05; H, 9.49. Found: C, 64.97; H, 9.30.

Preparation of Unsaturated Lactone 23s. A light green suspension containing diol **22s** (3.86 g, 9.00 mmol), silver carbonate on Celite[23] (42 g, 74 mmol), and chloroform (250 mL, freshly distilled) was protected from light and heated at reflux for 8 h. The black reaction mixture was cooled and filtered through Celite.

(43) From this point on, **20a:21a** will be labeled **21a** and **20s:21s** will be labeled **21s**.

The filter cake was washed with ether (250 mL). The filtrate was concentrated, and the crude product was purified by flash chromatography using hexanes–ethyl acetate (4:1). Lactone **23s** was obtained as a pale yellow oil (3.37 g, 88%): IR (thin film) 2940, 2860, 1755, 1660, 1245, 1140, 1090, 1040 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.033 (s, 6), 0.77 (s, 2.53), 0.88 (s, 9), 0.95 (s, 0.47), 1.20–2.02 (m, 9), 2.32–2.54 (m, 2), 2.56–2.80 (m, 2), 3.38 (s, 3), 3.52–3.69 (m, 2), 4.65 (d, 1, J = 7.0 Hz), 4.70 (d, 1, J = 7.1 Hz), 4.87–4.92 (m, 1.84), 4.99 (m, 0.16); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ –5.35, 16.36, 18.29, 22.46, 23.49, 25.93, 31.15, 34.14, 36.82, 37.03, 43.50, 48.86, 56.00, 62.75, 79.01, 87.60, 96.01, 141.85, 169.04, 172.13. Anal. Calcd for $C_{23}H_{40}O_5Si$: C, 65.05; H, 9.49. Found: C, 64.97; H, 9.52.

Preparation of Saturated Lactones 25a and 26a. A 2-L, round-bottomed flask was charged with unsaturated lactone **23a** (2.67 g, 6.29 mmol), 5% rhodium on carbon (890 mg, standard/dry/reduced), anhydrous potassium carbonate (445 mg), and ethyl acetate (267 mL). The system was evacuted using a water aspirator and purged with hydrogen (3×). The suspension was stirred for 14 h, and the hydrogen was removed at reduced pressure. The reaction mixture was filtered through Celite and washed with ethyl acetate (300 mL). The filtrate was concentrated to a colorless oil (2.70 g). The crude product consisted of two components which were separated by flash chromatography using hexanes–ethyl acetate (3.5:1 to 1:1) to afford white solids (2.64 g, 99%). The lower R_f component (2.40 g, 90%) was **25a**: mp 78.5–79.5 °C (recrystallized from $MeOH/H_2O$); IR (thin film) 2960, 2880, 1775, 1160, 1095, 1045 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.011 (s, 4.8), 0.022 (s, 1.2), 0.84 (s, 0.6), 0.856 (s, 7.2), 0.864 (s, 1.8), 0.94 (s, 2.4), 1.20–2.15 (m, 12), 2.26 (dd, 1, J = 6.9, 13 Hz), 2.54 (ddd, 1, J = 3.7, 4.7, 8.4 Hz), 3.02 (dt, 0.8, J = 4.5, 9.2 Hz), 3.05–3.15 (m, 0.2), 3.31 (s, 0.6), 3.32 (s, 2.4), 3.48–3.68 (m, 2), 4.08–4.15 (m, 1), 4.30 (d, 0.8, J = 4.9 Hz), 4.40 (d, 0.2, J = 4.9 Hz), 4.55 (d, 1, J = 7.0 Hz), 4.58 (d, 1, J = 7.1 Hz); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ –5.35, 17.64, 18.26, 21.68, 22.42, 25.93, 30.00, 33.52, 33.74, 36.38, 45.64, 45.80, 46.79, 51.14, 56.40, 62.41, 80.00, 88.39, 96.03, 180.34. Anal. Calcd for $C_{23}H_{42}O_5Si$: C, 64.75; H, 9.92. Found: C, 64.66; H, 10.02.

The higher R_f product (0.24 g, 9.0%) was **26a**: ^1H NMR (250 MHz, $CDCl_3$) δ 0.025 (s, 6), 0.86 (s, 3), 0.87 (s, 9), 1.20–2.25 (m, 13), 3.04–3.12 (m, 1), 3.08 (dt, 1, J = 2.1, 9.5 Hz), 3.33 (s, 3), 3.50–3.69 (m, 2), 3.90 (d, 1, J = 4.2 Hz), 3.96–4.00 (m, 1), 4.59 (d, ~0.8, J = 7.0 Hz), 4.60 (d, ~0.2, J = 7.0 Hz), 4.62 (d, ~0.8, J = 7.0 Hz), 4.63 (d, ~0.2, J = 7.0 Hz); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ –5.33, 16.44, 18.32, 22.19, 25.96, 28.70, 31.05, 31.43, 34.23, 35.95, 43.67, 44.16, 47.74, 48.41, 55.30, 62.82, 84.44, 91.38, 94.95, 180.11.

Preparation of Saturated Lactones 25s. A 2-L, round-bottomed flask was charged with unsaturated lactone **23s** (3.62 g, 8.52 mmol), 5% rhodium on carbon (1.20 g, standard/dry/reduced), anhydrous potassium carbonate (600 mg), and ethyl acetate (360 mL). The system was evacuted using a water aspirator and purged with hydrogen (3×). The suspension was stirred for 14 h, and the hydrogen was removed at reduced pressure. The reaction mixture was filtered through Celite and washed with ethyl acetate (300 mL). The filtrate was concentrated. The crude product consisted of two components which were separated by flash chromatography using hexanes–ethyl acetate (4:1) to afford colorless oils (3.51 g, 96%). The higher R_f component (3.29 g, 90%) was **25s**: IR (thin film) 2940, 2860, 1765, 1245, 1145, 1085, 1035 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.009 (s, 6), 0.85 (s, 9), 0.91 (s, 3), 1.20–1.40 (m, 2), 1.44–2.18 (m, 11), 2.73–2.83 (m, 0.2), 2.82 (ddd, 0.8, J = 2.7, 6.6, 8.8 Hz), 3.10 (dt, 0.8, J = 2.0, 8.3 Hz), 3.12–3.20 (m, 0.2), 3.47–3.67 (m, 2), 4.28–4.35 (m, 0.2), 4.36 (d, 0.8, J = 6.7 Hz), 4.37–4.42 (m, 0.8), 4.46 (d, 0.2, J = 6.5 Hz), 4.57 (d, 1, J = 7.0 Hz), 4.62 (d, 1, J = 7.0 Hz); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ –5.35, 17.20, 18.30, 22.01, 25.93, 26.53, 30.69, 32.32, 33.68, 35.56, 45.53, 46.25, 46.82, 51.40, 55.62, 62.70, 77.28, 88.80, 94.73, 180.31. Anal. Calcd for $C_{23}H_{42}O_5Si$: C, 64.75; H, 9.92. Found: C, 64.58; H, 9.80.

By flash chromatography the lower R_f component was recovered as a mixture with the higher R_f component (0.22 g, 6.0%). A pure sample of the minor component was obtained by HPLC using hexanes–ethyl acetate (4:1). This material was **26s**: ^1H NMR (250 MHz, $CDCl_3$) δ 0.002 (s, 6), 0.79 (s, 0.6), 0.83 (s, 2.4), 0.84 (s, 9), 1.15–2.10 (m, 13), 2.70 (ddd, 1, J = 2.7, 7.1, 9.8 Hz), 2.96 (dt, 1, J = 2.8, 9.2 Hz), 3.31 (s, 3), 3.46–3.67 (m, 2), 4.04 (dt, 1, J = 4.7, 6.9 Hz), 4.53–4.55 (m, 1), 4.58 (d, 1, J = 6.8 Hz), 4.63 (d, 1, J = 6.8 Hz); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ –5.37, 16.76, 18.26, 22.08, 25.91, 26.66, 31.27, 34.12, 35.84, 43.27, 43.78, 43.98, 47.41, 55.48, 62.80, 79.44, 86.38, 95.48, 180.30.

Preparation of the *p*-Bromobenzoate of Saturated Lactone 25a. A solution of saturated lactone **25a** (200 mg, 0.469 mmol) in THF (5 mL) was cooled to 0 °C and treated with tetrabutylammonium fluoride (0.93 mL, 0.93 mmol, 1.0 M in THF). The cooling bath was removed after 30 min, and stirring was continued at ambient temperature for 2 h. The solution was concentrated, and the residue was purified by flash chromatography using hexanes–ethyl acetate (1:6) to afford a colorless oil (141 mg, 96%). The alcohol (74 mg, 0.24 mmol) was dissolved in dichloromethane (3 mL) and treated sequentially with triethylamine (0.08 mL, 0.5 mmol), 4-bromobenzoyl chloride (100 mg, 0.47 mmol), and 4-(dimethylamino)pyridine (10 mg). The reaction mixture was stirred for 3 h and diluted with ether (25 mL). The suspension was washed with aqueous 2.5% hydrochloric acid solution and saturated $NaHCO_3$ solution (10 mL each). The organic layer was dried and concentrated to a white solid (137 mg, 117%). A 5:1 mixture of isomers was evident from the integrations for the quarternary methyl singlets in the ^1H NMR spectrum; minor isomer, 0.86 ppm; major isomer, 0.97 ppm. The crude material was recrystallized from ethyl acetate to afford a pure sample of the major isomer suitable for X-ray crystallography: mp 188–191 °C; ^1H NMR (250 MHz, $CDCl_3$) δ 0.97 (s, 3), 1.80–1.34 (m, 7), 1.92–2.19 (m, 3), 2.24–2.32 (m, 2), 2.49–2.56 (m, 1), 3.03 (dt, 1, J = 4.5, 9.1 Hz), 3.33 (s, 3), 4.11 (br s, 1), 4.20–4.39 (m, 3), 4.56 (d, 1, J = 7.0 Hz), 4.59 (d, 1, J = 7.0 Hz), 7.55 (d, 2, J = 8.5 Hz), 7.87 (d, 2, J = 8.5 Hz). Anal. Calcd for $C_{24}H_{31}BrO_6$: C, 58.19; H, 6.31. Found: C, 58.11; H, 6.23.

In the X-ray crystallography results the final residuals for 560 variables refined against the 2955 data for which $F^2 > 3\sigma(F^2)$ were R = 4.38%, R_w = 5.44%, and GOF = 1.91. The R value for all 6104 data was 27.6%. (This large value of R_{ALL} is due in part to the relatively large number of unobserved reflections in the data set. It is also due to the fact that a significant number of the "unobserved" data had values of F_o flagged negative to indicate negative measured net intensity, but F_c which were positive. This has the doubled effect of artificially increasing the numerator and decreasing the denominator of the R value.) See the supplementary material for complete details of this study.

Determination of the Relationships between Hydrogenation Products 25a/25s/26a/26s. Preparation of Keto Lactones 27 and 28. General Procedure. (a) A solution of the saturated lactone (0.27 mmol) in THF (3 mL) was treated at 0 °C with tetrabutylammonium fluoride (0.54 mmol, 1.0 M in THF). The solution was stirred for 2 h at ambient temperature and concentrated. The residue was purified by flash chromatography using hexanes–ethyl acetate (1:6).

(b) A solution of the alcohol (0.24 mmol) in dichloromethane (3 mL) was treated sequentially with triethylamine (0.73 mmol), 4-(methylamino)pyridine (cat.), and trimethylacetyl chloride (0.61 mmol). After 3 h, the reaction mixture was poured into ether (20 mL) and was washed with aqueous 2.5% hydrochloric acid solution and saturated $NaHCO_3$ solution (10 mL each). The organic layer was dried and concentrated. The product was purified by flash chromatography using hexanes–ethyl acetate (1:1).

(c) A mixture of pivalate (0.21 mmol), pyridinium *p*-toluenesulfonate (2.1 mmol), and *tert*-butyl alcohol (2.5 mL) was heated at reflux for 12–24 h and cooled to ambient temperature. The reaction mixture was concentrated, and the residue was partitioned between ether (25 mL) and water (5 mL). The organic layer was washed with saturated $NaHCO_3$ solution (10 mL), dried, and concentrated. The crude product was purified by flash chromatography using hexanes–ethyl acetate (1:1 to 1:2).

(d) To a solution of the alcohol (0.18 mmol) in toluene (3 mL) was added pyridinium chlorochromate on alumina[27] (0.55 mmol). The suspension was stirred at ambient temperature for 24–48 h and filtered. The filtrate was condensed, and the product was purified by flash chromatography using hexanes–ethyl acetate (2:1).

By this protocol, lactones **25a** (0.44 mmol, 55% overall) and **25s** (0.27 mmol, 64% overall) were converted, separately, to **27**, a white solid: mp 114–120 °C; IR (thin film/CH_2Cl_2) 2960, 2870,

1775, 1740, 1725, 1480, 1460, 1385, 1180, 1155, 1025, 1005, 980, 945, 935 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.78 (s, 2.5), 1.04 (s, 0.5), 1.15 (s, 9), 1.21–2.54 (m, 13), 2.89 (t, 1, J = 8.1 Hz), 3.39 (t, 1, J = 8.2 Hz), 3.90–4.10 (m, 2), 4.36 (d, 0.17, J = 7.3 Hz), 4.44 (d, 0.83, J = 7.0 Hz); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ 15.18, 21.71, 23.70, 27.16, 29.48, 30.46, 35.18, 38.61, 39.60, 43.96, 46.31, 47.34, 49.50, 64.10, 89.86, 178.28, 178.53, 214.79. Anal. Calcd for $C_{20}H_{30}O_5$: C, 68.55; H, 8.63. Found: C, 68.53; H, 8.65.

By this protocol, lactones **26a** (0.37 mmol, 78% overall) and **26s** (0.39 mmol, 72% overall) were converted, separately, to **28**, a colorless oil: IR (thin film) 2960, 2870, 1770, 1745, 1725, 1480, 1460, 1380, 1150, 1020, 975, 935 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.81 (s, 2.4), 0.84 (s, 0.6), 1.14 (s, 9), 1.2–2.5 (m, 13), 2.75–2.79 (m, 1), 3.31–3.36 (m, 1), 3.91–4.10 (m, 2), 4.23 (d, 1, J = 1.8 Hz); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ 15.79, 21.81, 23.98, 27.12, 29.70, 31.23, 36.30, 36.52, 38.60, 42.16, 44.70, 47.65, 50.09, 63.89, 89.76, 178.26, 178.48, 217.20. Anal. Calcd for $C_{20}H_{30}O_5$: C, 68.55; H, 8.63. Found: C, 68.41; H, 8.71.

Preparation of Diol 29a. A solution of lactone **25a** (553 mg, 1.30 mmol) in ether (25 mL) was cooled in an ice/2-propanol bath and treated with LAH (120 mg, 3.16 mmol). The suspension was stirred for 1 h, and saturated aqueous sodium sulfate solution was added dropwise with caution until the vigorous quenching reaction subsided. Sodium sulfate (~5 g) was added, and the cooling bath was removed. The reaction mixture was allowed to warm to ambient temperature. The white aluminum salts were filtered and washed with ether (50 mL). The filtrate was dried and concentrated to a colorless oil (0.56 g). The crude material was purified by flash chromatography using hexanes–ethyl acetate (2:1) to afford pure diol **29a** (504 mg, 90%): IR (thin film) 3690–3000, 2960–2840, 1250, 1155, 1080, 1065 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ −0.017 (s, 6), 0.71 (s, 0.6), 0.83 (s, 9), 0.89 (s, 2.4), 1.18–2.04 (m, 14), 2.18–2.32 (m, 1), 3.34 (s, 3), 3.46–3.64 (m, 3), 3.72–3.80 (m, 1), 3.85 (dd, 1, J = 2.5, 8.0 Hz), 4.31 (dd, 1, J = 5.5, 7.2 Hz), 4.39–4.48 (m, 2), 4.57 (d, 1, J = 6.7 Hz), 4.64 (d, 1, J = 6.8 Hz); major isomer, ^{13}c NMR (50.8 MHz, $CDCl_3$) δ −5.38, 17.03, 18.25, 21.98, 25.61, 25.88, 31.03, 31.42, 34.79, 37.68, 44.73, 44.83, 47.41, 48.78, 56.45, 63.01, 64.83, 79.72, 83.03, 95.73. Anal. Calcd for $C_{23}H_{46}O_5Si$: C, 64.14; H, 10.77. Found: C, 63.96; H, 10.94.

Preparation of Diol 29s. According to the above procedure, lactone **25s** (3.32 g, 7.78 mmol) was converted to **29s**, a colorless oil (3.09 g, 92%): IR (thin film) 3640–3100, 2940, 2860, 1250, 1140, 1085, 1030 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.025/0.033 (2 s, 6), 0.74 (s, 0.5), 0.86 (s, 9), 0.92 (s, 2.5), 1.20–2.10 (m, 13), 2.18–2.28 (m, 2), 2.85 (br s, 1), 3.33 (s, 3), 3.48–3.63 (m, 2), 3.64–3.78 (m, 4), 4.25–4.35 (m, 1), 4.60 (br s, 2); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ −5.47, 16.08, 18.37, 22.09, 25.92, 27.50, 32.18, 32.97, 33.98, 38.08, 44.05, 45.39, 48.69, 49.68, 55.80, 63.53, 63.76, 78.91, 80.43, 96.11. Anal. Calcd for $C_{23}H_{46}O_5Si$: C, 64.14; H, 10.77. Found: C, 63.99; H, 10.95.

Preparation of Monobenzyl Ether 30a. A solution of diol **29a** (269 mg, 0.625 mmol) in THF (3 mL) was treated with sodium hydride (70 mg, 0.88 mmol, 50% oil dispersion) at ambient temperature. The suspension was stirred for 1.5 h, and benzyl bromide (0.09 mL, 0.7 mmol) was added. After 15 h, saturated aqueous NH_4Cl solution (1.5 mL) was added. The mixture was partitioned between water (5 mL) and ether (25 mL). The organic layer was dried and concentrated to an oil (350 mg). The crude product was purified by flash chromatography using hexanes–ethyl acetate (7:1) to afford **30a** as a colorless oil (295 mg, 91%): ^1H NMR (250 MHz, $CDCl_3$) δ 0.032 (s, 6), 0.76 (s, 0.6), 0.88 (s, 9), 0.89 (s, 2.4), 1.20–2.10 (m, 14), 2.24–2.42 (m, 1), 3.29 (s, 0.6), 3.31 (s, 2.4), 3.50–3.66 (m, 3), 3.73 (t, 1, J = 4.9 Hz), 3.82 (dd, 0.8, J = 4.1, 9.3 Hz), 3.85–3.91 (m, 0.2), 4.02 (d, 0.8, J = 5.5 Hz), 4.08 (d, 0.2, J = 6 Hz), 4.38 (d, 1, J = 4.5 Hz), 4.47 (d, 1, J = 12 Hz), 4.55 (d, 1, J = 6.6 Hz), 4.56 (d, 1, J = 12 Hz), 4.62 (d, 1, J = 6.6 Hz), 7.2–7.4 (m, 5); ^{13}C NMR (50.8 MHz, $CDCl_3$) δ −5.29, 17.08, 18.34, 22.59, 25.99, 27.29, 30.74, 31.70, 35.23, 37.99, 42.19, 44.38, 47.80, 48.73, 56.16, 63.37, 72.78, 72.95, 78.68, 82.72, 95.57, 127.30, 127.61, 128.21, 138.91. Anal. Calcd for $C_{30}H_{52}O_5Si$: C, 69.18; H, 10.06. Found: C, 69.50; H, 10.21.

Preparation of Monobenzyl Ether 30s. A solution of diol **29s** (5.78 g, 13.42 mmol) in THF (40 mL) was cooled to 0 °C and treated with sodium hydride (0.90 g, 19 mmol, 50% oil dispersion). The suspension was stirred at ambient temperature for 1 h, and tetrabutylammonium iodide (49 mg, 0.13 mmol) was added. The mixture was cooled in an ice bath, and benzyl bromide (1.84 mL, 15.4 mmol) was added. The bath was removed, and stirring was continued for 2 h. Saturated aqueous NH_4Cl solution (40 mL) was added, and the mixture was partitioned between water (10 mL) and ether (120 mL). The aqueous layer was extracted further with ether (50 mL). The organic layers were dried and concentrated to a colorless oil (8.29 g). The crude product was purified by flash chromatography using hexanes–ethyl acetate (8:1 to 6:1) to afford **30s** as a colorless oil: IR (thin film) 3670–3270, 2950, 2870, 1255, 1150, 1085, 1040 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.044 (s, 6), 0.76 (s, 0.6), 0.89 (s, 9), 0.92 (s, 2.4), 1.20–2.14 (m, 13), 2.18–2.28 (m, 1), 2.35–2.50 (m, 1), 3.19 (d, 0.2, J = 4 Hz), 3.21 (d, 0.8, J = 4 Hz), 3.36 (s, 3), 3.46–3.60 (m, 4), 3.63–3.74 (m, 1), 4.29–4.44 (m, 1), 4.48 (br s, 1.6), 4.50 (br s, 0.4), 4.62 (br s, 2), 7.31 (br s, 5); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ −5.39, 16.04, 18.32, 22.07, 25.96, 27.47, 31.75, 33.40, 34.30, 37.78, 41.68, 45.46, 48.70, 49.34, 55.72, 63.44, 70.96, 73.18, 78.17, 80.55, 95.80, 127.50, 127.61, 128.28, 138.19. Anal. Calcd for $C_{30}H_{52}O_5Si$: C, 69.18; H, 10.06. Found: C, 68.99; H, 10.11.

Preparation of Xanthate 31a. Following the procedure used to prepare xanthate **31s**, alcohol **30a** (275 mg, 0.528 mmol) afforded **31a** as a yellow oil (280 mg, 87%): IR (thin film) 2960, 2870, 1240, 1150, 1100, 1050 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.016 (s, 6), 0.87 (s, 9), 0.94 (s, 3), 1.18–2.08 (m, 13), 2.42–2.31 (m, 1), 2.33–2.47 (m, 1), 2.51 (s, 3), 3.19 (s, 3), 3.46–3.60 (m, 3), 3.80–3.89 (m, 2), 4.40 (d, 1, J = 8 Hz), 4.46 (d, 1, J = 11 Hz), 4.48 (d, 1, J = 8 Hz), 4.60 (d, 1, J = 11 Hz), 6.22 (d, 1, J = 10 Hz), 7.24–7.40 (m, 5); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ −5.36, 17.55, 18.30, 18.80, 22.91, 25.95, 28.20, 30.79, 31.57, 35.43, 37.82, 40.86, 42.52, 49.38, 55.42, 63.30, 72.62, 73.01, 83.59, 87.75, 97.98, 127.32, 127.79, 128.14, 138.64, 215.03. Anal. Calcd for $C_{32}H_{54}O_5S_2Si$: C, 62.91; H, 8.91. Found: C, 62.90; H, 8.94.

Preparation of Xanthate 31s. A solution of alcohol **30s** (3.50 g, 6.72 mmol) in ether (80 mL) was cooled to 0 °C and treated dropwise with n-butyllithium (7.00 mL, 7.49 mmol, 1.07 M in hexanes). The cooling bath was removed, and the yellow solution was stirred for 1 h. Carbon disulfide (0.81 mL, 13 mmol) was added. The orange solution was heated at reflux for 1.5 h and cooled. Iodomethane (0.84 mL, 13 mmol) was added, and the solution was heated at reflux for 5 h. The mixture was cooled, saturated aqueous NH_4Cl solution (3 mL) was added, and the solvent was removed using a water aspirator. The residue was partitioned between brine (50 mL) and ether (200 mL). The organic layer was dried and concentrated. The crude product was purified by flash chromatography using hexanes–ethyl acetate (8:1) to afford **31s** as a yellow oil (3.71 g, 90): IR (thin film) 2960, 2870, 1235, 1155, 1100, 1045 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.008 (s, 4.9), 0.034 (s, 1.1), 0.86 (s, 7.4), 0.88 (s, 1.6), 0.99 (s, 3), 1.20–2.02 (m, 13), 2.46–2.64 (m, 2), 2.53 (s, 3), 3.37 (s, 3), 3.42–3.58 (m, 3), 3.81 (t, 1, J = 8.8 Hz), 4.34–4.37 (m, 1), 4.47 (d, 1, J = 12 Hz), 4.54 (d, 1, J = 12 Hz), 4.63 (d, 1, J = 6.8 Hz), 4.65 (d, 1, J = 7.0 Hz), 5.91 (br s, 0.18), 6.00 (br s, 0.82), 7.27–7.33 (m, 5); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ −5.36, 17.23, 18.30, 19.12, 22.32, 25.96, 27.15, 31.52, 34.76, 37.38, 41.78, 43.44, 49.37, 50.14, 55.57, 63.32, 70.68, 73.06, 80.60, 87.84, 95.28, 127.35, 127.69, 128.17, 138.46, 215.71. Anal. Calcd for $C_{32}H_{54}O_5S_2Si$: C, 62.91; H, 8.91. Found: C, 63.00; H, 8.85.

Deoxygenation of 31s. Preparation of Benzyl Ether 32s. A solution of tributyltin hydride (4.5 mL, 17 mmol) in dry toluene (50 mL) was heated at reflux, and a solution of xanthate **31s** (3.43 g, 5.61 mmol) in dry toluene (55 mL) was added over 2 h. After 36 h, tin hydride (2.2 mL, 8.5 mmol) in toluene (10 mL) was added over 30 min. An additional 8.5 mmol of tin hydride was added 12 h later. The solution was heated at reflux for 12 h, cooled, and concentrated to a pungent oil. The crude product was purified by flash chromatography using hexanes–ethyl acetate (19:1 to 12:1) to afford **32s** as a colorless oil (2.55 g, 90%). Alcohol **33s** was recovered also as a colorless oil (213 mg, 6%).

32s: IR (thin film) 3040, 2960, 2880, 1265, 1155, 1100, 1045 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.041 (s, 6), 0.73 (s, 0.5), 0.76 (s, 2.5), 0.89 (s, 9), 1.10–1.69 (m, 12), 1.75–2.10 (m, 4), 2.41 (q, 1, J = 6.6 Hz), 3.29–3.39 (m, 1), 3.35 (s, 3), 3.46–3.69 (m, 3), 3.80–3.86 (m, 1), 4.46 (d, 1, J = 12 Hz), 4.49 (d, 1, J = 12 Hz), 4.60 (d, 1, J = 6.8 Hz), 4.64 (d, 1, J = 6.7 Hz), 7.20–7.40 (m, 5); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ −5.28, −5.24, 18.33, 19.68, 21.45, 25.97, 26.11, 29.15, 29.85, 33.79, 36.74, 38.96, 40.35, 44.07, 44.17,

45.93, 55.23, 63.12, 70.88, 72.97, 83.51, 95.31, 127.33, 127.48, 128.19, 138.58. Anal. Calcd for $C_{30}H_{52}O_4Si$: C, 71.38; H, 10.38. Found: C, 71.53; H, 10.47.

Preparation of Alcohol 33s. A solution of benzyl ether **32s** (2.55 g, 5.05 mmol) in ether (8 mL) and ammonium (80 mL, distilled from sodium) was stirred with a mechanical stirrer as lithium wire (350 mg, 50 mmol) was added. The blue reacton mixture was stirred at reflux for 1.5 h and quenched with saturated aqueous NH_4Cl solution (15 mL). The aqueous mixture was saturated with sodium chloride and extracted with ether (1 × 100 mL, 2 × 50 mL). The ether layers were dried and concentrated. The crude product was purified by flash chromatography using hexanes–ethyl acetate (2.5:1) to afford **33s** as a colorless oil (1.71 g, 82%): IR (thin film) 3720–3020, 2960, 2880, 1260, 1155, 1100, 1045 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.014 (s, 6), 0.73 (s, 3), 0.86 (s, 9), 1.12–2.07 (m, 17), 2.27 (dq, 1, J = 6.8, 14 Hz), 3.32 (s, 3), 3.42–3.70 (m, 4), 3.76–3.82 (m, 1), 4.57 (d, 1, J = 6.8 Hz), 4.61 (d, 1, J = 6.8 Hz); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ −5.30, −5.27, 18.41, 20.24, 21.46, 25.45, 25.99, 29.06, 29.79, 33.66, 35.97, 38.69, 43.13, 43.49, 44.03, 44.84, 55.25, 63.04, 63.10, 83.64, 95.25. Anal. Calcd for $C_{23}H_{46}O_4Si$: C, 66.61; H, 11.18. Found: C, 66.43; H, 11.31.

Preparation of Cis Aldehyde 37s. A solution of oxalyl chloride (1.16 mL, 13.3 mmol) in dichloromethane (30 mL) was cooled to −78 °C and treated dropwise with DMSO (2.00 mL, 28.0 mmol). The reaction mixture was stirred for 10 min, and a solution of alcohol **33s** (1.84 g, 4.45 mmol) in dichloromethane (40 mL) was added over 15 min using a cannula. The mixture was stirred for 10 min, and triethylamine (9.0 mL, 65 mmol) was added. After 5 min, the cooling bath was removed. The suspension was allowed to warm to ambient temperature. Dichloromethane (30 mL) was added, and the solution was washed with water, aqueous 1% hydrochloric acid solution, and saturated $NaHCO_3$ solution (25 mL each). The organic layer was dried and concentrated. The crude product was purified by flash chromatography using hexanes–ethyl acetate (4:1) to afford **37s** as a pale yellow oil (1.718 g, 94%): ^1H NMR (250 MHz, $CDCl_3$) δ −0.004 (s, 6), 0.72 (s, 3), 0.84 (s, 9), 1.12–2.10 (m, 15), 2.28 (quintet, 1, J = 6.0 Hz), 3.02 (dq, 1, J = 1.9, 6.8 Hz), 3.33 (s, 3), 3.43–3.64 (m, 2), 3.87 (dt, 1, J = 3.7, 6.0 Hz), 4.58 (d, 1, J = 6.8 Hz), 4.62 (d, 1, J = 6.8 Hz), 9.76 (d, 1, J = 2.1 Hz); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ −5.36, −5.32, 18.30, 19.47, 21.32, 22.09, 25.93, 29.04, 29.61, 33.55, 38.17, 39.08, 44.09, 44.34, 45.30, 53.64, 55.32, 62.85, 82.98, 95.43, 204.17. Anal. Calcd for $C_{23}H_{44}O_4Si$: C, 66.94; H, 10.75. Found: C, 66.79; H, 10.64.

Preparation of Cis Keto Aldehyde 38s. (a) Methyllithium (8.9 mL, 1.4 M in ether) in THF (8 mL) was cooled to −78 °C and treated dropwise with a solution of aldehyde **37s** (1.72 g, 4.16 mmol) in THF (12 mL). The reaction mixture was stirred for 1.5 h and quenched with saturated aqueous NH_4Cl solution (3 mL). The reaction mixture was allowed to warm to ambient temperature and was partitioned between brine (5 mL) and ether (25 mL). The aqueous layer was extracted further with ether (15 mL). The ether layers were dried and concentrated to a yellow oil (1.89 g). The crude product was purified by flash chromatography using hexanes–ethyl acetate (5:1 to 1:1) to afford a pale yellow oil (1.74 g).

(b) The alcohol (4.06 mmol) was dissolved in THF (16 mL), cooled to 0 °C, and treated with tetrabutylammonium fluoride (8.1 mL, 8.1 mmol, 1.0 M in THF). The solution was stirred at ambient temperature for 2 h and concentrated. The residue was purified by flash chromatography using hexanes–ethyl acetate (1:4 to 1:8) to afford a very pale yellow oil (1.29 g).

(c) A solution of oxalyl chloride (1.77 mL, 20.3 mmol) in dichloromethane (55 mL) was cooled to −78 °C and treated dropwise with DMSO (3.02 mL, 42.6 mmol). The reaction mixture was stirred for 10 min, and a solution of the diol (4.06 mmol) in dichloromethane (70 mL) was added over 20 min using a cannula. The mixture was stirred for 10 min, and triethylamine (18 mL, 130 mmol) was added. After 5 min, the cooling bath was removed. The suspension was allowed to warm to ambient temperature and was diluted with dichloromethane (125 mL). The solution was washed with water, aqueous 2.5% hydrochloric acid solution, and saturated $NaHCO_3$ solution (50 mL each). The organic layer was dried and concentrated. The crude product was purified by flash chromatography using hexanes–ethyl acetate (2.5:1 to 1.5:1) to afford **38s** as a pale yellow oil (903 mg, 70% overall): IR (thin film) 2950, 2860, 2820, 2710, 1725, 1705, 1145, 1095, 1035 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.67 (s, 0.6), 0.70 (s, 2.4), 0.88 (dd, 0.2, J = 7.6, 15 Hz), 1.02 (dd, 0.8, J = 4.6, 15 Hz), 1.10–2.21 (m, 14), 2.07 (s, 2.4), 2.08 (s, 0.6), 2.35 (br d, 1, J = 16 Hz), 3.16 (q, 1, J = 7.4 Hz), 3.30 (s, 3), 3.94–3.99 (m, 1), 4.55 (d, 1, J = 6.8 Hz), 4.58 (d, 1, J = 6.9 Hz), 9.70 (dd, 1, J = 1.5, 2.6 Hz); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ 19.69, 21.16, 24.08, 28.95, 29.59, 30.24, 37.36, 38.33, 42.78, 43.75, 45.01, 45.31, 54.46, 55.22, 83.42, 95.18, 202.47, 210.10. Anal. Calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.48; H, 9.82.

Preparation of Trans Aldehyde 39s. A solution of aldehyde **37s** (518 mg, 1.26 mmol) in dichloromethane (14 mL) was treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (0.19 mL, 1.3 mmol, DBU) and allowed to stand at ambient temperature for 19 h. The solution was poured into ether (25 mL) and was washed with aqueous 1% hydrochloric acid solution and saturated $NaHCO_3$ solution (8 mL each). The organic layer was dried and concentrated to a pale yellow oil (494 mg, 95%). This product was pure by spectroscopic analysis and was determined to be a 18:1 mixture of trans:cis aldehydes from the ^1H NMR spectrum. The properties of aldehyde **39s** are: IR (thin film) 2950, 2840, 2710, 1730, 1260, 1150, 1095, 1035 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.009 (s, 6), 0.74 (s, 3), 0.86 (s, 9), 1.0–2.1 (m, 15), 2.3–2.5 (m, 2), 3.30 (s, 0.6), 3.31 (s, 2.4), 3.45–3.66 (m, 2), 3.73–3.79 (m, 0.8), 3.79–3.85 (m, 0.2), 4.55 (br s, 0.4), 4.57 (br s, 1.6), 9.59 (d, 1, J = 2.1 Hz); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ −5.30, 18.32, 19.32, 21.43, 23.49, 25.96, 29.43, 30.74, 33.59, 39.06, 43.18, 44.18, 45.19, 45.81, 55.38, 57.37, 62.94, 85.18, 95.08, 203.47.

Preparation of Trans Keto Aldehyde 40s. According to the protocol delineated for the preparation of keto aldehyde **38s**, aldehyde **39s** (494 mg, 1.20 mmol) was converted to keto aldehyde **40s** as a pale yellow oil (62% overall yield): IR (thin film) 2960, 2870, 2730, 1720, 1155, 1105, 1040 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.73 (s, 0.6), 0.76 (s, 2.4), 0.80–0.94 (m, 0.2), 1.08 (dd, 1, J = 6.6, 14 Hz), 1.2–2.0 (m, 12), 2.17 (s, 3), 2.4–2.6 (m, 3), 3.34 (s, 0.6), 3.35 (s, 2.4), 3.63–3.72 (m, 0.8), 3.72–3.78 (m, 0.2), 4.60 (d, 1, J = 6.9 Hz), 4.63 (d, 1, J = 6.9 Hz), 9.75 (dd, 1, J = 1.8, 2.3 Hz); high-resolution mass spectrum calcd for $C_{18}H_{30}O_4$ 310.2144, found 310.2156.

Preparation of Ophiobolane Nuclei 45s and 46s. Cyclization of 38s. In a glovebox under a N_2 atmosphere, titanium(III) chloride (0.70 g, 4.4 mmol) and zinc–copper couple[36c] (1.14 g, 17.6 mmol) were transfered to a 250-mL round-bottomed flask. The system was removed from the glovebox, and 1,2-dimethoxyethane (30 mL, DME) was added under an argon atmosphere. The suspension was heated at reflux for 3 h. A solution of **38s** (123 mg, 0.396 mmol) in DME (10 mL) was added over 21 h with the aid of a motor-driven syringe pump. The suspension was heated at reflux for an additional 12 h, cooled, and filtered through a column (2 × 17 cm) containing Florisil. The filtrate was condensed to a colorless oil (65 mg). The crude product was purified by flash chromatography using hexanes–ethyl acetate (8:1 to 1:1) to afford MOM ether **45s** (32 mg, 29%) and alcohol **46s** (15 mg, 16%) as colorless oils.

MOM ether **45s**: IR (thin film) 2960, 2880, 1445, 1375, 1150, 1105, 1045, 915 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.75 (s, 2.4), 0.83 (s, 0.6), 1.00–2.40 (m, 16), 1.57 (br s, 3), 3.13 (t, 0.2, J = 7.9 Hz), 3.3–3.5 (m, 1.6), 3.34 (s, 3), 3.63 (dt, 0.2, J = 5.9, 9.9 Hz), 4.59 (d, 1, J = 6.6 Hz), 4.67 (d, 1, J = 6.7 Hz), 5.48 (br d, 1, J = 8.2 Hz).

Alcohol **46s**: ^1H NMR (250 MHz, $CDCl_3$) δ 0.77 (s, 2.4), 0.83 (s, 0.6), 1.0–2.4 (m, 17), 1.57 (br s, 3), 3.16 (t, 0.2, J = 7.9 Hz), 3.46 (dt, 0.8, J = 4.0, 9.9 Hz), 3.58 (dt, 0.8, J = 6.9, 9.9 Hz), 3.78 (dt, 0.2, J = 5.5, 9.9 Hz), 5.48 (br d, 1, J = 8.0 Hz); major isomer, ^{13}C NMR (50.8 MHz, $CDCl_3$) δ 20.60, 22.92, 23.97, 24.47, 30.98, 33.03, 34.89, 39.39, 40.52, 42.13, 44.12, 44.94, 50.23, 78.69, 125.44, 137.52.

Deprotection of MOM Ether 45s. MOM ether (32 mg, 0.12 mmol) in THF, methanol, and aqueous 6 N hydrochloric acid solution (1.5 mL each) was stirred at ambient temperature for 15 h. The organic solvents were removed using a rotary evaporator. The aqueous mixture was saturated with sodium chloride and extracted with ether (20 mL) and ethyl acetate (20 mL). The organic layers were dried and concentrated. The residue was purified by flash chromatography using hexanes–ethyl acetate (4:1) to afford a colorless oil (21 mg, 78%). This oil was separated

by HPLC using hexanes–ethyl acetate (5.25:1) to yield $\Delta^{7,8}$-alcohol **46s** (~9 mg, first peak) and $\Delta^{6,7}$-alcohol **47s** (12 mg, second peak). Alcohol **47s** has the following properties: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.75 (s, 3), 1.20–1.80 (m, 13), 1.63 (br s, 3), 2.00–2.18 (m, 4), 2.33–2.50 (m, 1), 2.62–2.77 (m, 1), 3.79–3.86 (m, 0.92), 3.91–3.95 (m, 0.08); ^{13}C NMR (50.8 MHz, $CDCl_3$) δ 21.16, 22.33, 23.06, 26.36, 30.22, 31.97, 34.77, 35.30, 42.48, 44.82, 46.59, 47.90, 50.10, 78.54, 129.38, 136.68.

Oxidation of Alcohol 46s. Oxalyl chloride (0.04 mL, 0.5 mmol) in dichloromethane (3 mL) was cooled to −78 °C and treated dropwise with DMSO (0.07 mL, 1.0 mmol). The reaction mixture was stirred for 10 min, and a solution of alcohol **46s** (30 mg, 0.13 mmol) in dichloromethane (3 mL) was added dropwise using a cannula. The mixture was stirred for 15 min, and triethylamine (0.32 mL, 2.3 mmol) was added. After 5 min, the cooling bath was removed, and the suspension was allowed to stir to ambient temperature. Dichloromethane (25 mL) was added, and the solution was washed with water, aqueous 2.5% hydrochloric acid solution, and saturated $NaHCO_3$ solution (5 mL each). The organic layer was dried and concentrated. The crude product was purified by flash chromatography using hexanes–ethyl acetate (10:1) to afford a white solid with some colorless oil (28 mg, 94%). By GC analysis (column temperature = 180 °C), the product was 97% pure, consisting of a 7:1 mixture of the (2α,6α)-3-keto and the (2β,6β)-3-keto derivatives of the alcohol with retention times of 9.66 and 9.90 min, respectively. These ophiobolane nuclei were inseparable by HPLC: mp 86–90 °C; IR (thin film/CH_2Cl_2) 2960, 1735 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.76 (s, 2.6), 0.80 (s, 0.4), 1.15–1.28 (m, 3), 1.42–1.59 (m, 3), 1.55 (dd, 3, J = 1.6, 2.3 Hz), 1.69–1.77 (m, 2), 1.94 (dd, 1, J = 2.3, 14 Hz), 2.02–2.25 (m, 4), 2.31–2.37 (m, 3), 3.53–3.58 (m, 0.13), 3.86 (t, 0.87, J = 8.9 Hz); ^{13}C NMR (50.8 MHz, C_6D_6) δ 20.44, 21.79, 22.44, 23.49, 30.70, 32.66, 36.93, 37.22, 39.76, 42.58, 43.52, 45.58, 50.41, 125.90, 136.31, 219.45. Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.48; H, 10.37.

Preparation of Ophiobolane Nuclei 43s and 44s. Cyclization of 40s. In a glovebox under a N_2 atmosphere, titanium(III) chloride (1.85 g, 12.0 mmol) and zinc–copper couple[36c] (1.84 g, 28.1 mmol) were transfered to a 250-mL round-bottomed flask. The system was removed from the glovebox, and DME (80 mL) was added under an argon atmosphere. The suspension was heated at reflux for 6 h. A solution of **40s** (164 mg, 0.528 mmol) in DME (20 mL) was added over 40 h with the aid of a motor-driven syringe pump. The suspension was heated at reflux for an additional 2.5 h, cooled, and filtered through a column (2 × 19 cm) containing Florisil. The filtrate was condensed to a colorless oil (88 mg). The crude product was purified by flash chromatography using hexanes–ethyl acetate (8:1 to 1.5:1) to afford MOM ether **42s** (27 mg, 18%) and alcohol **41s** (38 mg, 31%) as colorless oils. By GC analysis (column temperature = 190 °C), **42s** (9.24 min) and **41s** (6.78, 7.05 min) were 87% and 89% pure, respectively.

MOM ether **42s**: IR (thin film) 3070, 2920, 2890, 1270, 1155, 1105, 1045 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.88 (s, ~0.6), 0.96 (s, ~2.4), 1.1–2.2 (m, 16), 1.62 (s, 3), 2.83–2.95 (m, 1), 3.39 (s, 3), 4.10 (dt, 1, J = 3.9, 8.8 Hz), 4.61 (d, 1, J = 6.9 Hz), 4.70 (d, 1, J = 6.9 Hz), 5.46 (br t, 1, J = 7.8 Hz); high-resolution mass spectrum calcd for $C_{18}H_{30}O_2$ 278.2246, found 278.2240.

Alcohol **41s**: IR (thin film) 3600–3100, 2960, 2880, 1080 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.82 (s, ~0.6), 0.90 (s, ~2.4), 1.1–2.3 (m, 17), 1.57 (s, 3), 2.87 (ddd, 1, J = 6.5, 11, 13 Hz), 4.13 (dt, 1, J = 4.6, 8.8 Hz), 5.43 (br t, 1, J = 7.7 Hz); high-resolution mass spectrum calcd for $C_{16}H_{26}O$ 234.1983, found 234.1978.

Deprotection of MOM Ether 42s. MOM ether (27 mg, 0.097 mmol) in THF, methanol, and aqueous 6 N hydrochloric acid solution (1.5 mL each) was stirred at ambient temperature for 20 h. The reaction mixture was saturated with sodium chloride and extracted with ether (35 mL). The organic layer was washed with saturated $NaHCO_3$ solution (2 mL), dried, and concentrated. The crude product was purified by flash chromatography using hexanes–ethyl acetate (4:1) to afford a mixture of isomeric alcohols as a colorless oil (15 mg, 66%). This mixture was separated by HPLC using hexanes–ethyl acetate (5.25:1). The first peak (5 mg) was identified as the $\Delta^{7(25)}$-alcohol. The fourth peak (7 mg) was identified as a ~3:1 mixture of **41s** and **47s**. The two minor peaks were not isolated in pure form.

The $\Delta^{7(25)}$-alcohol: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.82 (s, 3), 1.22–1.75 (m, 17), 1.76–2.16 (m, 6), 2.28–2.36 (m, 1), 3.70 (dt, 1, J = 6.5, 8.6 Hz), 4.78 (br s, 1), 4.86 (br s, 1).

Oxidation of Alcohol 41s. According to the protocol for the oxidation of alcohol **46s**, alcohol **41s** (38 mg, 0.16 mmol, 89% GC purity) was converted to a colorless oil (22 mg, 58%). The components of this product were separated by HPLC using hexanes–ethyl acetate (19:1) to afford **43s** (17 mg) and **44s** (4 mg) as colorless oils. The ^{1}H NMR spectra of these ophiobolane nuclei showed no significant differences with the spectra of the substances prepared by Coates.[2,39]

Ketone **43s**: IR (thin film) 2960, 2880, 1745, 1460, 1140, 730 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.71 (s, 3), 1.19–2.34 (m, 15), 1.67 (s, 3), 2.42 (dd, 1, J = 8.2, 19 Hz), 3.21 (ddd, 1, J = 5.3, 12, 14 Hz), 5.57 (br t, 1, J = 7.9 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.38, 18.11, 18.83, 24.36, 26.90, 32.17, 34.51, 37.52, 41.67, 44.37, 44.53, 53.74, 54.65, 127.86, 135.16, 218.17.

Ketone **44s**: IR (thin film) 2950, 2870, 1740, 1450, 1135 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.82 (s, 3), 1.08–2.27 (m, 15), 1.72 (s, 3), 2.39 (dd, 1, J = 8.1, 17 Hz), 2.73 (dt, 1, J = 5.5, 11 Hz), 5.54 (br t, 1, J = 7.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 18.75, 21.24, 24.04, 26.32, 28.37, 37.47, 37.72, 41.94, 43.87, 44.02, 46.73, 49.92, 49.97, 126.19, 134.56, 221.04.

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Registry No. **1**, 20098-89-9; **2**, 18674-12-9; (±)-**8**, 126107-08-2; (±)-(*E*)-**9a**, 126019-38-3; (±)-(*Z*)-**9a**, 126019-59-8; (±)-(*E*)-**9a** (1-ethyl ester), 126019-61-2; (±)-(*Z*)-**9a** (1-ethyl ester), 126019-62-3; (±)-**9b**, 126019-67-8; (±)-**9b** epoxide (isomer 1), 126019-64-5; (±)-**9b** epoxide (isomer 2), 126107-16-2; (±)-**9b** (1-ethyl ester), 126019-63-4; (±)-**10**, 126019-39-4; (±)-**11**, 126019-40-7; (±)-**12**, 126035-26-5; (±)-**13**, 126019-41-8; (±)-**14t**, 126019-42-9; (±)-**14c**, 126019-70-3; (±)-**15t**, 126019-71-4; (±)-**15c**, 126019-71-4; **16**, 66222-28-4; **17**, 119090-37-8; **18**, 119090-39-0; (±)-**18** (alcohol), 126019-77-0; (±)-**19**, 126019-44-1; (±)-**20a**, 126107-96-8; (±)-**20s**, 126107-92-4; (±)-**21a**, 126019-72-5; (±)-**21s**, 126107-93-5; (±)-**22a**, 126019-73-6; (±)-**22a** (minor isomer), 126107-38-8; (±)-**22s**, 126107-44-6; (±)-**22s** (minor isomer), 126107-94-6; (±)-**23a**, 126107-19-5; (±)-**23a** (minor isomer), 126107-98-0; (±)-**23s**, 126019-45-2; (±)-**23s** (minor isomer), 126107-45-7; (±)-**25a**, 126107-20-8; (±)-**25a** (minor isomer), 126107-39-9; (±)-**25a** (desilyl derivative), 126019-65-6; (±)-**25a** (desilyl derivative, minor isomer), 126107-17-3; (±)-**25a** (*p*-bromobenzoate), 126019-60-1; (±)-**25a** (*p*-bromobenzoate, minor isomer), 126107-18-4; (±)**25s**, 126019-46-3; (±)-**25s** (minor isomer), 126107-46-8; (±)-**26a** (minor isomer), 126107-40-2; (±)-**26s**, 126107-09-3; (±)-**27**, 126019-47-4; (±)-*epi*-**27**, 126107-22-0; (±)-**28**, 126107-23-1; (±)-*epi*-**28**, 126107-10-6; (±)-**29a**, 126107-41-3; (±)-**29a** (minor isomer), 126107-24-2; (±)-**29s**, 126019-48-5; (±)-**29s** (minor isomer), 126107-48-0; (±)-**30a**, 126107-25-3; (±)-**30a** (minor isomer), 126107-99-1; (±)-**30s**, 126107-49-1; (±)-**30s** (minor isomer), 126019-49-6; (±)-**31a**, 126107-26-4; (±)-**31a** (minor isomer), 126107-42-4; (±)-**31s**, 126019-50-9; (±)-**31s** (minor isomer), 126107-50-4; (±)-**32s**, 126019-51-0; (±)-*epi*-**32s**, 126107-27-5; (±)-**33s**, 126019-52-1; (±)-*epi*-**33s**, 126107-28-6; (±)-**34a**, 126019-74-7; (±)-**34a** (minor isomer), 126107-43-5; (±)-**35a**, 126019-53-2; (±)-*epi*-**35a**, 126107-29-7; (±)-**36a**, 126019-75-8; (±)-**37s**, 126019-54-3; (±)-*epi*-**37s**, 126107-30-0; **37s** (methyllithium addition product), 126019-68-9; (±)-**38s**, 126019-55-4; (±)-*epi*-**38s**, 126107-31-1; **38s** diol, 126019-69-0; (±)-**39s**, 126107-11-7; (±)-*epi*-**39s**, 126107-32-2; (±)-**40s**, 126107-95-7; (±)-*epi*-**40s**, 126107-33-3; (±)-**41s**, 126019-56-5; (±)-*epi*-**41s**, 126107-34-4; (±)-**41s** ($\Delta^{7(25)}$-isomer), 126019-76-9; (±)-*epi*-**41s** ($\Delta^{7(25)}$-isomer), 126107-51-5; (±)-**42s**, 126019-57-6; (±)-*epi*-**42s**, 126107-35-5; (±)-**43s**, 126107-12-8; (±)-**44s**, 126107-13-9; (±)-**45s**, 126107-14-0; (±)-*epi*-**45s**, 126107-97-9; (±)-**46s**, 126107-15-1; (±)-*epi*-**46s**, 126107-36-6; (±)-**46** ketone, 126107-52-6; (±)-(2β,6β)-**46** ketone, 126107-53-7; (±)-**47s**, 126019-58-7; (±)-*epi*-**47s**, 126107-37-7; $(EtO)_2P(O)CH_2CO_2Bu$-*t*, 27784-76-5; *tert*-butyl (±)-*cis*-(2-carbomethoxy-5-hydroxy-2-methylcyclopentylidene)acetate, 126019-66-7; 3-ethoxy-2-cyclopenten-1-one, 22627-70-9.

Supplementary Material Available: Data and information from X-ray crystal analysis of the *p*-bromobenzoate ester of **25a** and ^{1}H and ^{13}C NMR spectra for (*Z*)-**9a** (15 pages). Ordering information is given on any current masthead page.