Total Synthesis of (−)-Coriolin

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Received July 27, 1998

An efficient synthetic method for (−)-coriolin has been developed on the basis of a [3+2] cycloaddition reaction of a 1-(methylthio)-2-siloxyallyl cationic species and vinylsulfides. An enantiomerically pure C-ring unit was prepared through optical resolution of five-membered allyl ester **6b** using a lipase. The first [3+2] cycloaddition reaction of C-ring unit **(*S*)-7** gave bicyclic ketones **8** and **9**, which were easily converted into vinyl sulfide **11**. Stereoselective construction of the A-ring was achieved by the second [3+2] cycloaddition reaction of the BC-ring unit. New methods for introduction of the oxygen functional groups to the triquinane skeleton were also developed for the last stages of the total synthesis. Thus, the C7 hydroxyl group was introduced by epoxidation of dienol silyl ether **17**, and stereocontrolled construction of the spiro epoxide moiety was accomplished on the basis of a Darzens-type reaction.

Introduction

Cyclopentanoid compounds are found in a wide range of natural products,[1] and various kinds of synthetic methods have been explored.[2] While intramolecular ring closure of an acyclic compound is generally applicable to cyclopentane synthesis, a [3+2] cycloaddition approach which produces two C−C bonds in one stage is advantageous from the viewpoint of efficiency.[3] We recently reported a new synthetic method for functionalized cyclopentanones on the basis of a [3+2] cycloaddition reaction of a 1-(methylthio)-2-siloxyallyl cationic species and olefins (eq 1).[4] The wide range of applicability as well as the high selectivities of this transformation led us to develop a straightforward methodology for constructing triquinane skeletons. To this end coriolin,[5] which has attracted much attention due to its highly functionalized, unique carbon framework as well as important biological activities, was chosen as the synthetic target (Figure 1).[6−8]

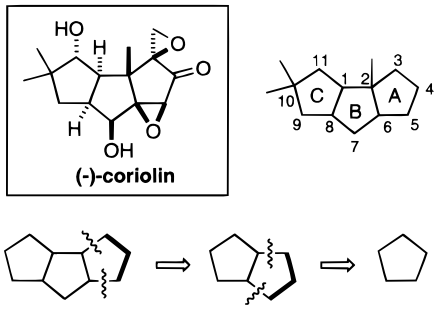
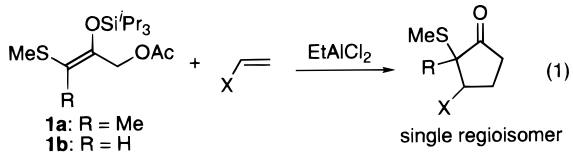


Figure 1. Straightforward methodology for constructing a triquinane skeleton via sequential [3+2] cycloaddition reactions.



The synthetic plan of coriolin was made up of two stages, that is, (I) stereocontrolled synthesis of the known intermediate **E** via sequential [3+2] cycloaddition reactions, and (II) stereoselective introduction of the oxygen functionalities. For stage I, a synthetic route starting

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(1) For reviews, see: (a) *Cyclopentanoid Terpene Derivatives*; Taylor, W. I., Battersby, A. R., Eds.; M. Dekker: New York, 1969. (b) Paquette, L. A. *Top. Curr. Chem.* **1984**, *119*, 1. (c) Paquette, L. A.; Doherty, A. M. *Polyquinane Chemistry: Synthesis and Reactions*; Springer-Verlag: Berlin, 1987. (d) Hudlicky, T.; Rulin, F.; Lovelace, T. C.; Reed, J. W. In *Studies in Natural Products Chemistry*; Atta-ur Rahman, Ed.; Elsevier: Oxford, 1989; Vol. 3, Part B, pp 3−72. (e) Mehta, G.; Srikrishna, A. *Chem. Rev.* **1997**, *97*, 671.

(2) For reviews of cyclopentane synthesis, see: (a) Ramaiah, M. *Synthesis* **1984**, 529. (b) Hudlicky, T.; Price, J. D. *Chem. Rev.* **1989**, *89*, 1467.

(3) For reviews of [3+2] cycloaddition reactions, see: (a) Little, R. D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, Chapter 3.1, pp 239−270. (b) Chan, D. M. T. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, Chapter 3.2, pp 271−314.

(4) (a) Masuya, K.; Domon, K.; Tanino, K.; Kuwajima, I. *Synlett* **1996**, 157. (b) Masuya, K.; Domon, K.; Tanino, K.; Kuwajima, I. *J. Am. Chem. Soc.* **1998**, *120*, 1724. Similar methylenecyclopentane annulation could also be effected by using the substrate having a TMS-methyl group in place of the siloxy group of **1b**. Takahashi, Y.; Tanino, K.; Kuwajima, I. *Tetrahedron Lett.* **1996**, *37*, 5943.

(5) Isolation and characterization of coriolin: (a) Takeuchi, T.; Iinuma, H.; Iwanaga, J.; Takahashi, S.; Takita, T.; Umezawa, H. *J. Antibiot.* **1969**, *22*, 215. (b) Nakamura, H.; Takita, T.; Umezawa, H.; Kunishima, M.; Nakayama, Y. *J. Antibiot.* **1974**, *27*, 301. (c) Nishimura, Y.; Koyama, Y.; Umezawa, S.; Takeuchi, T.; Ishizuka, M.; Umezawa, H. *J. Antibiot.* **1980**, *33*, 404 and references therein.

(6) For a review of total synthesis of coriolin: Mulzer, J. In *Organic Synthesis Highlights*; Mulzer, J., Altenbach, H.-J., Braun, M., Krohn, K., Reissig, H.-U., Eds.; VCH: Weinheim, 1991; pp 323−334.

(7) Fomal total synthesis of (±)-coriolin which were not covered in ref 6: (a) Hijfte, L. V.; Little, R. D. *J. Org. Chem.* **1985**, *50*, 3940. (b) Funk, R. L.; Bolton, G. L.; Daggett, J. U.; Hansen, M. M.; Horcher, L. H. M. *Tetrahedron* **1985**, *41*, 3479. (c) Magnus, P.; Exon, C.; Albaugh-Robertson, P. *Tetrahedron* **1985**, *41*, 5861. (d) Mehta, G.; Murthy, A. N.; Reddy, D. S.; Reddy, A. V. *J. Am. Chem. Soc.* **1986**, *108*, 3443. (e) Wender, P. A.; Correia, C. R. D. *J. Am. Chem. Soc.* **1987**, *109*, 2523. (f) Hijfte, L. V.; Little, R. D.; Petersen, J. L.; Moeller, K. D. *J. Org. Chem.* **1987**, *52*, 4647. (g) Singh, V.; Samanta, B. *Tetrahedron Lett.* **1999**, *40*, 383.

(8) Total synthesis of (−)-coriolin which was not covered in ref 6: Weinges, K.; Braun, R.; Huber-Patz, U.; Irngartinger, H. *Liebigs Ann. Chem.* **1993**, 1133.

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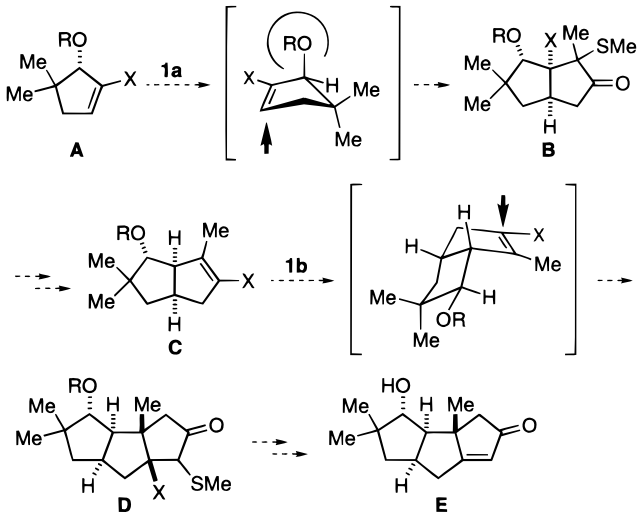
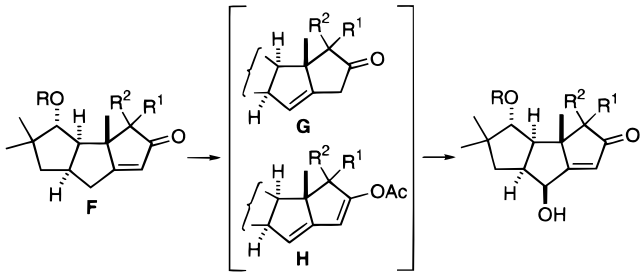
Published on Web 03/26/1999

Scheme 1. Design of a Stereocontrolled Triquinane Synthesis



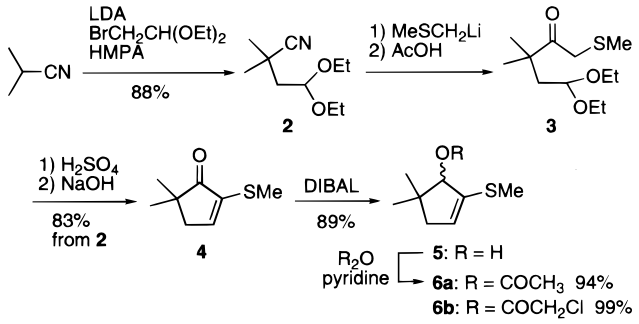
Scheme 2. Conventional Methods for Introducing 7-OH Group

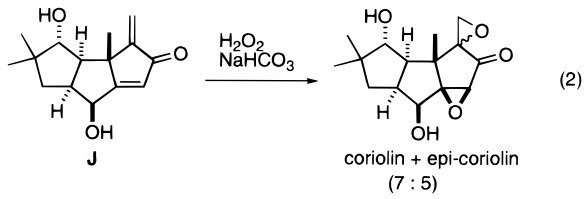


from optically active cyclopentene derivative **A** was designed as shown in Scheme 1. Since the *re*-face of **A** is shielded by the alkoxy group, the [3+2] cycloaddition reaction with **1a** gives bicyclic ketone **B** stereoselectively. In the second [3+2] cycloaddition step, three-carbon unit **1b** is introduced to bicyclic olefin **C** from the convex face to yield **D**, which has the triquinane skeleton with the correct configuration.

For stage II, the following transformations are required: (i) stereoselective introduction of the C7 hydroxyl group, (ii) epoxidation of the C5−C6 double bond, and (iii) stereoselective construction of the spiro epoxide moiety. Although several groups have already finished total synthesis of coriolin through these transformations, there still remain problems from the viewpoint of efficiency. Thus, epoxidation of either β,γ-unsaturated ketone **G**[7c,9] or dienol acetate **H**[10] has always been adopted for step i, despite the fact that preparation of these intermediates suffers from the recovery of significant amounts of the parent α,β-unsaturated ketone **F** (Scheme 2). On the other hand, steps ii and iii have usually been performed in one pot through epoxidation of the corresponding dienone **J** (eq 2).[8,9a,c,11] While complete stereoselection has been achieved for step ii, stereocontrol in step iii has been notoriously difficult.[9c] Therefore, we also explored new methods for introduction of the oxygen functional groups with improved chemical yields as well as high stereoselectivities.[12]

Scheme 3. Preparation of the C-Ring Unit





(2)

Results and Discussion

A. Preparation of the Optically Pure C-Ring Unit. The cyclopentene framework of the C-ring unit was constructed as shown in Scheme 3. The reaction of nitrile **2**, which was prepared by alkylation of isobutyronitrile,[13] with (methylthio)methyllithium followed by acetic acid yielded ketone **3**. Successive treatment of ketone **3** with sulfuric acid and an aqueous NaOH solution gave cyclopentenone **4** via intramolecular aldol condensation of the corresponding keto aldehyde. Since initial attempts for asymmetric reduction of enone **4** by using several chiral borane reagents were fruitless,[14] we explored enzymatic optical resolution[15] of racemic alcohol **5**.

Although the reaction of acetate **6a** with Lipase PS in a buffer solution was found to be extremely sluggish, chloroacetate **6b** underwent smooth hydrolysis to give alcohol **(*S*)-5** (95% ee) in 46% yield along with 51% recovery of **(*R*)-6b**. Finally, **(*S*)-5** was obtained in enantiomerically pure form after repetition of a similar procedure starting from **(*S*)-5** in 95% ee (Scheme 4). The enantiomeric purity of **(*S*)-5** was determined by Mosher's method,[16] and the absolute configuration was confirmed by X-ray crystallographic analysis.[17]

B. Construction of the Triquinane Skeleton via [3+2] Cycloaddition Reactions. Next, the triquinane

(9) (a) Danishefsky, S.; Zamboni, R.; Kahn, M.; Etheredge, S. J. *J. Am. Chem. Soc.* **1980**, *102*, 2097. (b) Shibasaki, M.; Iseki, K.; Ikegami, S. *Tetrahedron Lett.* **1980**, *21*, 3587. (c) Danishefsky, S.; Zamboni, R.; Kahn, M.; Etheredge, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 3460. (d) Trost, B. M.; Curran, D. P. *J. Am. Chem. Soc.* **1981**, *103*, 7380. (e) Iseki, K.; Yamazaki, M.; Shibasaki, M.; Ikegami, S. *Tetrahedron* **1981**, *37*, 4411. (f) Exon, C.; Magnus, P. *J. Am. Chem. Soc.* **1983**, *105*, 2477. (g) Schuda, P. F.; Heimann, P. R. *Tetrahedron* **1984**, *40*, 2365.

(10) (a) Ito, T.; Tomiyoshi, N.; Nakamura, K.; Azuma, S.; Izawa, M.; Maruyama, F.; Yanagiya, M.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1982**, *23*, 1721. (b) Ito, T.; Tomiyoshi, N.; Nakamura, K.; Azuma, S.; Izawa, M.; Maruyama, F.; Yanagiya, M.; Shirahama, H.; Matsumoto, T. *Tetrahedron* **1984**, *40*, 241. (c) Demuth, M.; Ritterskamp, P.; Schaffner, K. *Helv. Chim. Acta* **1984**, *67*, 2023. (d) Demuth, M.; Ritterskamp, P.; Weigt, E.; Schaffner, K. *J. Am. Chem. Soc.* **1986**, *108*, 4149.

(11) (a) Tatsuta, K.; Akimoto, K.; Kinoshita, M. *J. Antibiotics* **1980**, *33*, 100. (b) Tatsuta, K.; Akimoto, K.; Kinoshita, M. *Tetrahedron* **1981**, *37*, 4365.

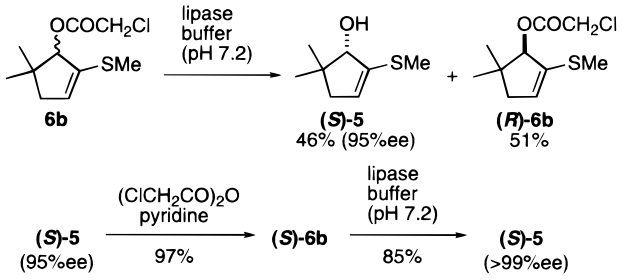
(12) For a preliminary report of a part of this work, see: Domon, K.; Masuya, K.; Tanino, K.; Kuwajima, I. *Tetrahedron Lett.* **1997**, *38*, 465.

(13) Larchevêque, M.; Cuvigny, T. *Tetrahedron Lett.* **1975**, 3851.

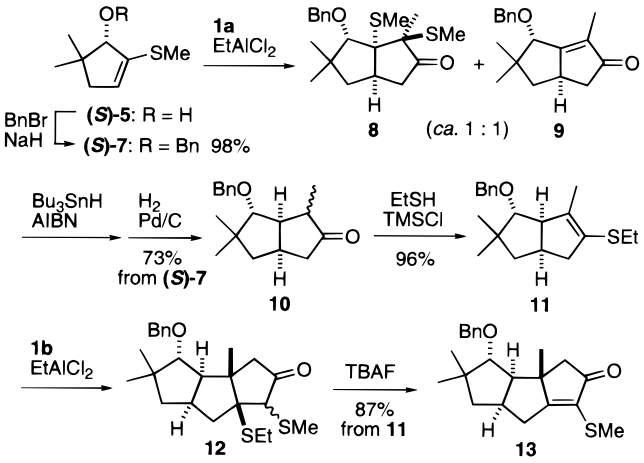
(14) Singh, V. K. *Synthesis* **1992**, 605.

(15) For a recent review, see: Santaniello, E.; Ferraboschi, P. In *Advances in Asymmetric Synthesis*; Hassner, A., Ed.; JAI Press: Greenwich, 1997; Vol. 2, pp 237−283, and references therein.

Scheme 4. Optical Resolution of Ester 6 by Using Lipase

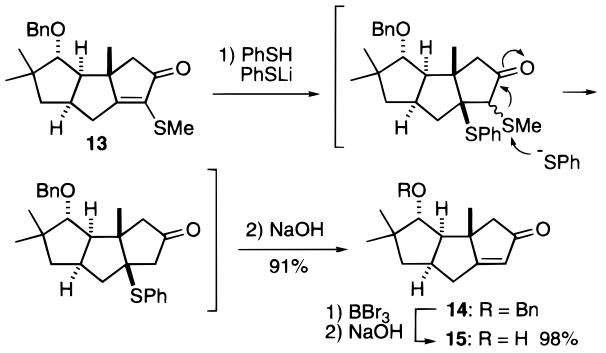


Scheme 5. Construction of the A- and B-Ring by [3+2] Cycloaddition Reactions



carbon framework was constructed via successive [3+2] cycloaddition reactions (Scheme 5). Benzyl ether **(*S*)-7** derived from **(*S*)-5** was subjected to a [3+2] cycloaddition reaction with **1a**, and two annulation products **8** and **9** were obtained in diastereomerically pure form, respectively.[18] It was proved that these products have a common configuration at the benzyloxy group and the angular methyne proton, because ketone **8** was transformed into enone **9** by treating with Raney-Ni. Although direct assignment of the configuration of **8** and **9** was difficult,[19] the cis relationship between the benzyloxy group and the angular methyne proton was confirmed at a later stage (vide infra). This stereochemical feature of the cycloaddition reaction indicates that the *re*-face of **(*S*)-7** was effectively shielded by the benzyloxy group from the attack of the allyl cationic intermediate. The crude mixture of **8** and **9** was eventually transformed into ketone **10** through desulfurization using tributyltin hydride[20] followed by hydrogenation (73% from **(*S*)-7**).

Scheme 6



To set the stage for the second [3+2] annulation reaction, it was required to convert ketone **10** into vinyl sulfide **11** having a fully substituted carbon−carbon double bond. Fortunately, combined use of ethanethiol and chlorotrimethylsilane, which was reported to be useful for dithioacetal synthesis,[21] afforded the desired vinyl sulfide **11** directly. The absence of the corresponding regioisomer of the double bond suggests that the reaction proceeded under thermodynamic control. In the presence of **1b** and $EtAlCl_2$, vinyl sulfide **11** underwent [3+2] annulation reaction to give ketone **12** along with enone **13**. Treatment of the crude mixture with tetrabutylammonium fluoride (TBAF) promoted β-elimination of ethanethiol from **12**, and enone **13** was isolated as a single diastereomer.

Although reductive desulfurization of an α-(alkylthio)-ketone is generally easy, it is not the case for enone **13**, having the C−S bond which is perpendicular to the π-orbital of the carbonyl group. For example, the reaction of **13** with Raney-Ni failed to give the desired enone **14**. On the other hand, it has been reported that a thiolate ion effects desulfurization of an α-(alkylthio)ketone via nucleophilic attack on the alkylthio group.[22] We envisioned that Michael addition of a thiol to enone **13** would give a ketone analogous to **12**, which may undergo one-pot desulfurization promoted by a thiolate ion. Indeed, enone **14** was obtained in good yield by successive treatment of enone **13** with a mixture of thiophenol and the corresponding lithium salt followed by an aqueous NaOH solution (Scheme 6). Removal of the benzyl group by boron tribromide[23] afforded the known alcohol **15**;[24,25] accordingly, the stereochemistry of the tricyclic system

(16) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(17) Treatment of **(*S*)-5** with *N*-*p*-toluenesulfonyl-L-phenylalaninyl chloride and pyridine afforded the corresponding ester, which was then converted into a sulfone derivative. See the Suporting Information.

(18) The reaction mechanism of formation of enone **9** is not clear. We confirmed that the ratio between **8** and **9** is not affected by a prolonged reaction period. Treatment of ketone **8** with $EtAlCl_2$ also failed to give enone **9**, while **8** was slowly converted into **9** by heating at 180 °C.

(19) The stereochemistry of ketone **8** could be determined after conversion into the corresponding enol silyl ether.[4b] See the Suporting information.

(20) (a) Haskell, T. H.; Woo, P. W. K.; Watson, D. R. *J. Org. Chem.* **1977**, *42*, 1302. (b) Gutierrez, C. G.; Stringham, R. A.; Nitasaka, T.; Glasscock, K. G. *J. Org. Chem.* **1980**, *45*, 3393. (c) Gutierrez, C. G.; Summerhays, L. R. *J. Org. Chem.* **1984**, *49*, 5206, and references therein.

(21) Ong, B. S.; Chan, T. H. *Synth. Commun.* **1977**, *7*, 283.

(22) Oki, M.; Funakoshi, W.; Nakamura, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 828−832.

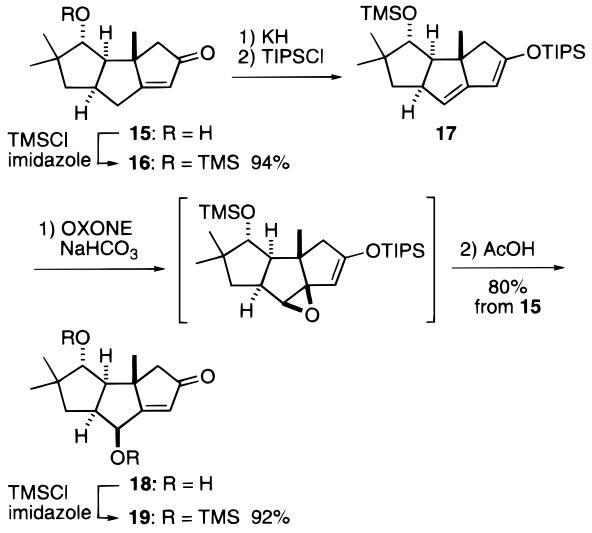
(23) (a) Grieco, P. A.; Nishizawa, M.; Oguri, T.; Burke, S. D.; Marinovic, N. *J. Am. Chem. Soc.* **1977**, *99*, 5773. (b) Demuynck, M.; De Clercq, P.; Vandewalle, M. *J. Org. Chem.* **1979**, *44*, 4863.

(24) Enone **15** in racemic form: Koreeda, M.; Mislankar, S. G. *J. Am. Chem. Soc.* **1983**, *105*, 7203, and refs 7a,b,f, 9d, 10a−c.

(25) Enone **15** in optically active form: Weinges, K.; Dietz, U.; Oeser, T.; Irngartinger, H. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 680, and ref 10d.[26]

(26) The different rotation values for the same compound **15** have been reported by Demuth (−115.4°),[10d] by Weinges (+34°),[25] and now by us (+42.5°). Furthermore, compound **18** was reported to have a rotation of −105.2° by Demuth,[10d] which is quite different from our observation (+90.4°). Weinges determined the stereochemistry of **15** by X-ray crystallographic analysis, and the ^{13}C NMR spectrum of our compound **15** matches that reported by Weinges. In our study, the absolute configuration at the C(11) position was established by X-ray crystallographic analysis[17] in the early stage of the total synthesis, and the rotation of (−)-coriolin was again confirmed at the last stage. We have also confirmed that compound **15** was obtained in optically pure form by our method (Suporting Information). Therefore, it seems that there are some errors in structual assignment made by Demuth, not only for **15** but also for **18**.

Scheme 7



was confirmed at this stage.[26] The (*S*)-configuration at the C2 position (coriolin numbering) indicates that the second [3+2] annulation reaction occurred at the convex face of vinyl sulfide **11**.

C. Introduction of the Oxygen Functional Groups. As was mentioned before, introduction of the C7 hydroxyl group was accomplished by several groups through epoxidation of either a β,γ-unsaturated ketone or a dienol acetate, which were prepared in fairly low yields as a mixture with the parent α,β-unsaturated ketone (Scheme 2). To achieve a complete conversion of the α,β-unsaturated ketone, we chose the corresponding dienol silyl ether as an epoxidation precursor. Successive treatment of enone **16** with potassium hydride and triisopropylsilyl chloride effected selective formation of linear dienol silyl ether **17**. Since **17** was sensitive to silica gel column chromatography, the crude product was directly subjected to oxidation reactions. Although use of *m*-CPBA resulted in rather complex results, OXONE in acetone−water[10d,27] was found to give the desired labile epoxide which was converted into diol **18**[28] by exposure to acetic acid (Scheme 7). It should be noted that no product arising from Baeyer−Billiger reaction or epoxidation at the A ring was detected, probably because the highly strained C6−C7 double bond is much more reactive than the C4−C5 double bond.[29]

While an efficient method for introducing the C7 hydroxyl group has been established, stereocontrolled construction of the spiro epoxide moiety remained as the final problem in coriolin synthesis. To this end, we designed a new approach for epoxide **K** by a Darzens-type[30] reaction of α-haloketone **M** (Figure 2). We envisioned that formaldehyde would react with the enolate of **M** at the convex face of the BC-ring to give halohydrin **L** selectively.

The reaction of the lithium enolate of enone **19** with 5,5-dibromo-2,2-dimethyl-1,3-dioxane-4,6-dione[31] yielded

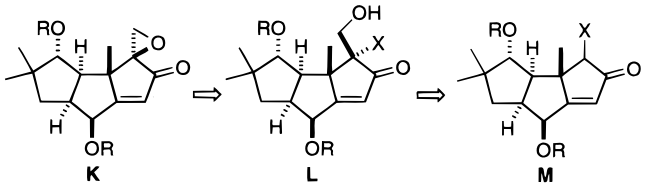
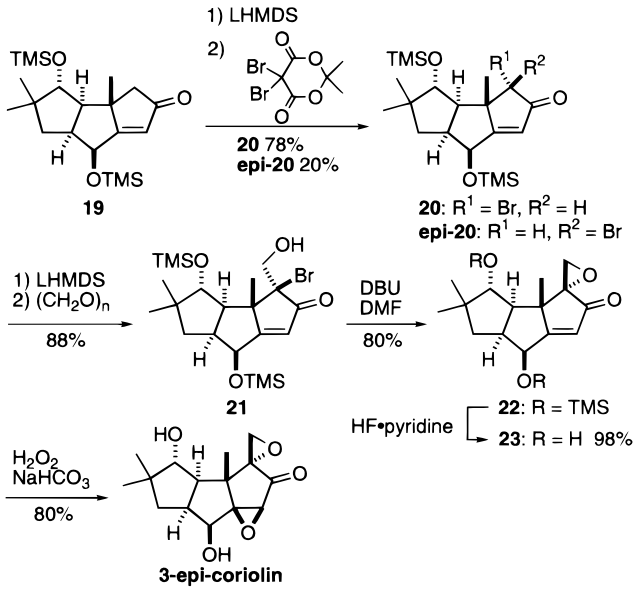


Figure 2. Stereoselective construction of the spiro epoxide moiety.

Scheme 8



bromoketones **20** and **epi-20** as a 4:1 mixture (Scheme 8). The configuration of the major isomer **20** was confirmed by observation of NOE between the angular methyl group and the C3 methyne proton. Successive treatment of the bromoketones with lithium hexamethyldisilazide (LHMDS) and paraformaldehyde afforded bromohydrin **21** as a single diastereomer. While the stereochemistry at the C3 position could not be determined at this stage, **21** was subjected to a cyclization reaction under the influence of several bases. Although use of potassium *tert*-butoxide led to bromoketones **20** and **epi-20** via a retro-aldol reaction, heating with DBU in DMF induced smooth cyclization to give epoxide **22**. Surprisingly, removal of the silyl groups followed by epoxidation of the C5−C6 double bond afforded 3-epi-coriolin, which was reported by Danishefsky[9a,c] as a minor product in the final step of coriolin synthesis. Therefore, the stereochemistry at the C3 position of bromohydrin **21** was assigned as *S*, which indicates that formaldehyde reacted with the enolate of the α-bromoketone at the concave face. It is noteworthy that a similar stereoselectivity was observed in bromination of enone **19**, in which bromoketone **20** was obtained as a major isomer (vide supra). These stereochemical features suggest that the convex face of the enolates exhibits unexpectedly low reactivity, presumably because of the blocking effect of the angular methyl group as shown in Figure 3.

These results allowed us to control the stereochemistry at the C3 position by introducing the substituents in a reversed manner. Indeed, treatment of hydroxyketone **24**, which was prepared from enone **19** and paraformalde-

(27) Curci, R.; Fiorentino, M.; Troisi, L.; Edwards, J. O.; Pater, R. H. *J. Org. Chem.* **1980**, *45*, 4758.
(28) Diol **18** in racemic form: ref 7c, 9d,f, 10a−c. Diol **18** in optically active form: ref 10d.[26]
(29) Suryawanshi, S. N.; Fuchs, P. L. *Tetrahedron Lett.* **1981**, *22*, 4201.
(30) Rosen, T. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 2, Chapter 1.13, pp 409−440.
(31) Bloch, R. *Synthesis* **1978**, 140.

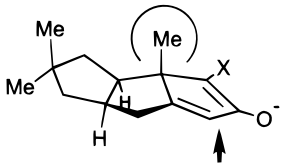
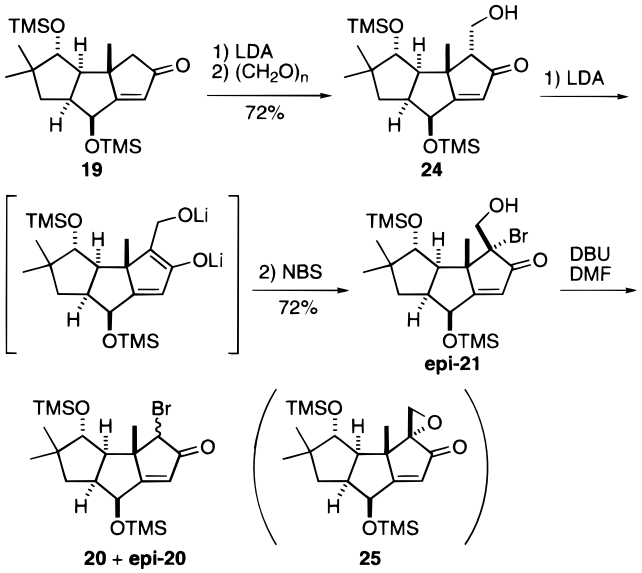
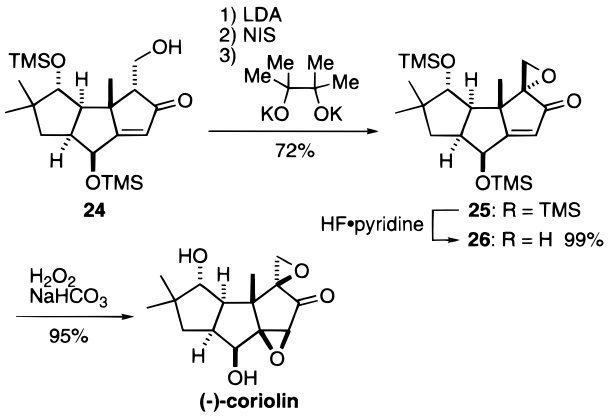


Figure 3.

Scheme 9



Scheme 10



hyde, with an excess amount of LDA followed by NBS afforded the desired bromohydrin **epi-21** as a single diastereomer (Scheme 9). On heating with DBU in DMF, however, **epi-21** underwent a retro-aldol reaction rather than cyclization to epoxide **25**. Since several attempts using other bases were also fruitless, we employed the corresponding iodide in place of the bromide.

Unfortunately, the reactions of the dianion of **24** with NIS, iodine, or iodine monochloride resulted in recovery of **24** or dehydration to give an α-methylene ketone. While addition of HMPA or TMEDA was entirely ineffective, potassium pinacolate was found to enhance the reactivity of the lithium enolate dramatically. Thus, epoxide **25** was directly obtained by successive treatment of the dianion of **24** with NIS and potassium pinacolate[32] (Scheme 10). Although the results suggest that the reactive intermediate is the corresponding potassium enolate, treatment of **24** with KHMDS resulted in rapid decomposition even at −78 °C. Therefore, combined use of the lithium enolate and potassium pinacolate seems to be essential because the labile potassium enolate can be generated in the presence of NIS. Finally, epoxide **25** was converted into (−)-coriolin (mp 175−176 °C; lit.[5a] mp 175−176 °C; $[\alpha]^{26.0}_D = -19.4$ ($c = 0.44$, $CHCl_3$); lit.[5c] $[\alpha]^{20}_D = -21$ ($c = 1.0$, $CHCl_3$)) through removal of the silyl groups followed by epoxidation of the C5−C6 double bond.

Conclusion

In conclusion, an efficient synthetic method for (−)-coriolin has been developed on the basis of a [3+2] cycloaddition reaction of a 1-(methylthio)-2-siloxyallyl cationic species and vinylsulfides. An enantiomerically pure C-ring unit was prepared through optical resolution of a five-membered allyl ester using a lipase. The triquinane skeleton was constructed stereoselectively through successive [3+2] cycloaddition reactions. New methods for introduction of the oxygen functional groups to the triquinane skeleton were also developed for the later stages of the total synthesis. The C7 hydroxyl group was introduced by epoxidation of a dienol silyl ether, and stereocontrolled construction of the spiro epoxide moiety was accomplished on the basis of a Darzens-type reaction. The high overall yield of (−)-coriolin (4.4% from isobutyronitrile) indicates the efficiency of this straightforward methodology based on a [3+2] cycloaddition reaction, and synthetic studies on other natural products are now in progress.

(32) Use of potassium *tert*-butoxide resulted in a much more sluggish transformation.

Experimental Section

General Methods. All reactions were carried out under a positive pressure of dry nitrogen or argon. Diethyl ether and tetrahydrofuran were distilled from sodium and benzophenone immediately before use. CH_2Cl_2 was distilled successively from P_2O_5 and K_2CO_3 under nitrogen and stored over molecular sieves. Hexane was distilled from $LiAlH_4$ under nitrogen and stored over potassium mirror. HMPA and diisopropylamine were distilled from CaH_2 under nitrogen and stored over molecular sieves. Flash chromatography was performed using 40−100 μm mesh KANTO (silica gel 60N, spherical, neutral) or 100 μm mesh Fuji Silysia (FL100DX, spherical, basic) silica gel. Analytical TLC was carried out on 250 μm Merck (Kiesegel 60F-254) silica gel plates. Melting points are corrected. ^1H and ^{13}C NMR spectra were recorded at 270 or 300 MHz (^1H) using $CDCl_3$ with tetramethylsilane as the internal standard.

(*Z*)-1-Acetoxy-3-(methylthio)-2-(triisopropylsiloxy)-2-butene (1a) and (*Z*)-3-Acetoxy-1-(methylthio)-2-(triisopropylsiloxy)-1-propene (1b). These compounds were prepared according to a previously described procedure.[4b]

4,4-Diethoxy-2,2-dimethylbutyronitrile (2). Preparation of this compound was previously described.[13] A solution of lithium diisopropylamide (LDA) was prepared from diisopropylamine (25.4 mL, 180 mmol) and a 1.6 M hexane solution of butyllithium (103 mL, 165 mmol) in THF (300 mL) at 0 °C. The solution was cooled to −78 °C, and isobutyronitrile (13.6 mL, 150 mmol) was added. After being stirred for 2 h, a mixture of HMPA (39 mL, 225 mmol) and THF (20 mL) followed by bromoacetaldehyde diethyl acetal (22.6 mL, 150 mmol) was added. The reaction mixture was allowed to warm to 0 °C over 1 h, and then a saturated aqueous NH_4Cl solution was added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration followed by distillation under reduced pressure (bp 74−77 °C/2.5 mmHg) afforded nitrile **2** (24.3 g, 132 mmol, 88%) as a

colorless oil: ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.23 (t, J = 7.1 Hz, 6 H), 1.41 (s, 6 H), 1.86 (d, J = 5.5 Hz, 2 H), 3.56 (dq, J = 9.4, 7.1 Hz, 2 H), 3.70 (dq, J = 9.4, 7.1 Hz, 2 H), 4.74 (t, J = 5.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 15.13, 27.42, 29.91, 43.77, 61.74, 100.58, 124.63.

5,5-Dimethyl-2-(methylthio)-2-cyclopenten-1-one (4). A mixture of dimethyl sulfide (25.0 mL, 340 mmol), *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (38.5 mL, 255 mmol), and a 1.56 M hexane solution of BuLi (164 mL, 255 mmol) was stirred at 18 °C for 4 h. The solution was cooled to −45 °C, and to this was added a THF (150 mL) solution of nitrile **2** (32.9 mL, 170 mmol). After being stirred at −45 °C for 1 h and at 0 °C for 1 h, 20% aqueous acetic acid (150 mL) was slowly added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with saturated aqueous $NaHCO_3$ solution and concentrated under reduced pressure to afford ketone **3** as a colorless oil: IR (ether) 1700, 1440, 1350 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.12 (t, J = 7.1 Hz, 6 H), 1.17 (s, 6 H), 1.89 (d, J = 5.6 Hz, 2 H), 2.08 (s, 3 H), 3.39 (dq, J = 9.3, 7.1 Hz, 2 H), 3.45 (s, 2 H), 3.59 (dq, J = 9.3, 7.1 Hz, 2 H), 4.44 (t, J = 5.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 15.07, 15.96, 25.34, 39.05, 44.56, 45.36, 62.16, 100.76, 208.71; HRMS (FAB$^+$, glycerol/NaI) calcd for $C_{12}H_{24}O_3SNa$ (M + Na$^+$) 2271.1344, found 271.1358.

The crude product was treated with a mixture of THF (100 mL) and 10% H_2SO_4 (200 mL) at room temperature for 1 h, and then aqueous 15% NaOH solution was slowly added until the solution was pH 13−14 to a pH test paper. After being stirred for 30 min at room temperature, the mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration followed by distillation under reduced pressure (bp 77−81 °C/1.0 mmHg) afforded enone **4** (22.0 g, 141 mmol, 83%) as a pale yellow oil: IR (neat) 1695, 1570 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.16 (s, 6 H), 2.37 (s, 3 H), 2.54 (d, J = 3.1 Hz, 2 H), 6.93 (t, J = 3.1 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.55, 24.94, 43.68, 44.21, 140.64, 147.54, 209.66. Anal. Calcd for $C_8H_{12}OS$: C, 61.50; H, 7.74; S, 20.52. Found: C, 61.65; H, 7.96; S, 20.73.

5,5-Dimethyl-2-(methylthio)-2-cyclopenten-1-ol (5). A solution of enone **4** (6.4 g, 41 mmol) in CH_2Cl_2 (81 mL) was treated with a 0.96 M hexane solution of DIBAL (47 mL, 45 mmol) at −78 °C for 1 h. A saturated aqueous sodium potassium tartarate solution was slowly added, and the mixture was stirred at room temperature. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded alcohol **5** (5.8 g, 36.7 mmol, 89%) as a colorless oil: IR (neat) 3400, 1600, 1060 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.08 (s, 3 H), 1.11 (s, 3 H), 1.57 (d, J = 7.3 Hz, 1 H), 2.23 (ddd, J = 16.0, 2.4, 0.9 Hz, 1 H), 2.26 (ddd, J = 16.0, 2.4, 1.7 Hz, 1 H), 2.31 (s, 3 H), 4.12 (bd, J = 7.3 Hz, 1 H), 5.37 (t, J = 2.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 14.61, 22.30, 27.98, 42.62, 45.59, 85.37, 122.50, 140.63. Anal. Calcd for $C_8H_{14}OS$: C, 60.72; H, 8.92; S, 20.26. Found: C, 61.00; H, 9.22; S, 19.96.

5,5-Dimethyl-2-(methylthio)-2-cyclopenten-1-yl chloroacetate (6b). To a solution of alcohol **5** (5.8 g, 36.7 mmol) and pyridine (5.0 mL, 62 mmol) in CH_2Cl_2 (44 mL) was added a CH_2Cl_2 (27 mL) solution of chloroacetic anhydride (8.0 g, 47 mmol) at 0 °C. After being stirred for 2 h, a saturated aqueous $NaHCO_3$ solution was added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded ester **6b** (8.50 g, 36.2 mmol, 99%) as a colorless oil: IR (neat) 1745, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.06 (s, 3 H), 1.17 (s, 3 H), 2.19 (dd, J = 16.4, 3.0 Hz, 1 H), 2.29 (s, 3 H), 2.39 (ddd, J = 16.4, 3.0, 1.8 Hz, 1 H), 4.51 (s, 2 H), 5.41 (d, J = 1.8 Hz, 1 H), 5.57 (t, J = 3.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 14.75, 22.53, 28.10, 40.76, 42.02, 46.17, 87.59, 126.54, 136.19, 166.97. Anal. Calcd for $C_{10}H_{15}ClO_2S$: C, 51.17; H, 6.44; S, 13.66. Found: C, 50.87; H, 6.56; S, 13.78.

Optical Resolution of Ester 6b Mediated by Lipase. A mixture of ester **6b** (9.78 g, 41.7 mmol), lipase Amano PS (4.9 g), KH_2PO_4 (0.17 g), and Na_2HPO_4 (0.53 g) in water (300 mL) was vigorously stirred for 65 h at room temperature. The pH of the mixture was maintained between 7 and 7.5 by adding an adequate amount of a 5% NaOH solution during the period. The mixture was filtered through a pad of Celite, and the residue was washed with ether. The filtrate was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded **(*S*)-5** (3.00 g, 19.0 mmol, 46%) and **(*R*)-6b** (5.02 g, 21.4 mmol, 51%). The enantiomeric purity of **(*S*)-5** (95% ee) was determined by converting into the corresponding Mosher ester (see the Supporting Information). The resulting **(*S*)-5** (3.0 g, 19.0 mmol) was converted into chloroacetate **(*S*)-6b** (4.30 g, 18.3 mmol, 97%), which was again subjected to optical resolution using lipase Amano PS (2.15 g) to yield **(*S*)-5** (2.46 g, 15.5 mmol, 85%) in enantiomerically pure form. The enantiomeric purity was confirmed by the Mosher method (see the Supporting Information): $[\alpha]^{26}_D = -81.9$ (c = 1.35, EtOH).

(*S*)-3-(Benzyloxy)-4,4-dimethyl-2-(methylthio)-1-cyclopentene ((*S*)-7). To a suspension of NaH (1.36 g, 56.5 mmol) in DMF (50 mL) was successively added a THF (50 mL) solution of alcohol **(*S*)-5** (5.66 g, 35.8 mmol) and benzyl bromide (4.68 mL, 39.4 mmol) at 0 °C. After being stirred for 2 h at room temperature, a saturated aqueous $NaHCO_3$ solution was added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded ether **(*S*)-7** (8.67 g, 35.1 mmol, 98%): $[\alpha]^{26}_D = -96.8$ (c = 1.21, EtOH); IR (neat) 1600, 1455, 735, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.12 (s, 3 H), 1.15 (s, 3 H), 2.10 (dd, J = 15.9, 2.2 Hz, 1 H), 2.21−2.36 (m, involving a singlet at 2.29, 4 H), 3.97 (s, 1 H), 4.68 (s, 2 H), 5.32 (t, J = 2.2 Hz, 1 H), 7.24−7.43 (m, 5 H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 14.06, 23.08, 28.97, 43.15, 46.36, 73.26, 92.56, 121.82, 127.48, 127.87, 128.23, 138.69, 139.73. Anal. Calcd for $C_{15}H_{20}OS$: C, 72.53; H, 8.12; S, 12.91. Found: C, 73.23; H, 8.18; S, 12.96.

Construction of the B-Ring via a [3+2] Cycloaddition Reaction: 6-Benzyloxy-4,7,7-trimethyl-4,5-bis(methylthio)-bicyclo[3.3.0]octan-3-one (8) and (5*R*,8*S*)-8-Benzyloxy-2,7,7-trimethylbicyclo-[3.3.0]oct-1-en-3-one (9). To a mixture of **(*S*)-7** (1.5 g, 6.1 mmol) and **1a** (2.1 g, 6.3 mmol) in CH_2Cl_2 (14 mL) was added a 0.96 M hexane solution of $EtAlCl_2$ (7.2 mL, 6.9 mmol) at −45 °C. After being stirred at −45 °C for 1 h, −23 °C for 1 h, and 0 °C for 1 h, a saturated aqueous $NaHCO_3$ solution was added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded ketone **8** (0.93 g, 2.6 mmol, 42%) and enone **9** (0.68 g, 2.5 mmol, 41%). **8**: $[\alpha]^{22.7}_D = -121.1$ (c = 1.23, CH_2Cl_2); IR (ether) 1730, 1440, 1350, 1170 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.99 (s, 3 H), 1.20 (s, 3 H), 1.64 (s, 3 H), 1.75 (t, J = 12.4 Hz, 1 H), 1.83 (s, 3 H), 1.91 (dd, J = 12.4, 8.0 Hz, 1 H), 1.97 (s, 3 H), 2.43 (dd, J = 19.0, 10.0 Hz, 1 H), 2.74 (dd, J = 19.0, 5.0 Hz, 1 H), 3.00−3.18 (m, 1 H), 4.30 (s, 1 H), 4.41 (d, J = 11.4 Hz, 1 H), 4.84 (d, J = 11.4 Hz, 1 H), 7.30−7.45 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 11.59, 12.56, 17.30, 22.30, 27.10, 39.63, 43.11, 43.96, 47.15, 60.30, 68.22, 73.81, 88.15, 127.47, 127.75, 128.16, 138.42, 208.57. Anal. Calcd for $C_{20}H_{28}O_2S_2$: C, 65.89; H, 7.74; S, 17.59. Found: C, 65.70; H, 7.63; S, 17.30. **9**: $[\alpha]^{25}_D = +68.4$ (c = 1.29, EtOH); IR (neat) 1710, 1675, 1455 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.91 (s, 3 H), 1.08 (dd, J = 12.5, 8.0 Hz, 1 H), 1.25 (s, 3 H), 1.76 (s, 3 H), 2.03 (dd, J = 18.0, 2.6 Hz, 1 H), 2.07 (dd, J = 12.5, 9.9 Hz, 1 H), 2.74 (dd, J = 18.0, 6.4 Hz, 1 H), 3.16−3.31 (m, 1 H), 3.99 (s, 1 H), 4.46 (d, J = 12.0 Hz, 1 H), 4.56 (d, J = 12.0 Hz, 1 H), 7.25−7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 8.70, 23.57, 29.82, 39.50, 43.63, 43.68, 44.33, 71.22, 81.89,

127.16, 127.49, 128.22, 135.22, 138.14, 178.86, 211.07. Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.73; H, 8.50.

(1*R*,2*R*,5*R*,8*R*)- and (1*R*,2*S*,5*R*,8*R*)-8-Benzyloxy-2,7,7-trimethylbicyclo[3.3.0]octan-3-one (10). To a mixture of **(*S*)-7** (6.87 g, 27.8 mmol) and **1a** (10.2 g, 31.6 mmol) in CH_2Cl_2 (75 mL) was added a 0.98 M hexane solution of $EtAlCl_2$ (34 mL, 33 mmol) at −45 °C. After being stirred at −45 °C for 1 h, −23 °C for 1 h, and 0 °C for 1 h, a saturated aqueous $NaHCO_3$ solution was added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure gave the crude product containing ketone **8** and enone **9**, which was used for the next step without purification.

A mixture of the crude product, Bu_3SnH (7.5 mL, 27.8 mmol), and AIBN (0.46 g, 2.8 mmol) in benzene (63 mL) was refluxed for 1.5 h. After cooling, water was added. The organic phase was separated, and the aqueous phase was extracted with ether. The combined organic layer was successively treated with DBU (4.2 mL, 28 mmol) and $MgSO_4$. The insoluble material was removed by filtration through a pad of Celite, and the filtrate was passed through a short column of silica gel to remove polar impurities. Hydrogenation (1 atm) of the crude product catalyzed by 10% Pd−C (0.9 g) in ethanol (80 mL) followed by purification by silica gel column chromatography gave **10** (5.49 g, 20.3 mmol, 73% from **(*S*)-7**) as a 63:37 mixture of C2 epimers; $[\alpha]^{26}_D = +34.2$ ($c = 0.91$, EtOH). Major isomer of **10**: IR (neat) 1740, 1455, 535, 500 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 1.06 (s, 3 H), 1.12 (s, 3 H), 1.17 (d, $J = 7.8$ Hz, 3 H), 1.17−1.36 (m, 1 H), 1.89 (dd, $J = 12.9$, 8.0 Hz, 1 H), 2.06 (dd, $J = 18.2$, 1.9 Hz, 1 H), 2.12 (quintet, $J = 7.8$ Hz, 1 H), 2.30 (ddd, $J = 9.9$, 7.8, 6.0 Hz, 1 H), 2.52 (dd, $J = 18.2$, 9.8 Hz, 1 H), 2.72−2.88 (m, 1 H), 3.38 (d, $J = 6.0$ Hz, 1 H), 4.56 (d, $J = 11.6$ Hz, 1 H), 4.62 (d, $J = 11.6$ Hz, 1 H), 7.25−7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 15.87, 21.64, 28.12, 32.66, 43.35, 43.69, 47.40, 48.66, 53.10, 72.69, 94.97, 127.23, 127.52, 128.33, 138.78, 221.82. Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.24; H, 9.03. Minor isomer of **10**: ^1H NMR ($CDCl_3$, 270 MHz) δ 1.05 (s, 3 H), 1.17 (s, 3 H), 1.17 (d, $J = 9.8$ Hz, 3 H), 1.17−1.36 (m, 1 H), 1.87 (dd, $J = 17.0$, 3.0 Hz, 1 H), 1.96 (dd, $J = 13.4$, 8.2 Hz, 1 H), 2.88 (q, $J = 9.8$ Hz, 1 H), 2.56−2.70 (m, 1 H), 2.61 (dd, $J = 17.9$, 9.8 Hz, 1 H), 2.70−2.78 (m, 1 H), 3.29 (d, $J = 9.0$ Hz, 1 H), 4.46 (d, $J = 10.4$ Hz, 1 H), 4.71 (d, $J = 10.4$ Hz, 1 H), 7.25−7.40 (m, 5 H).

(1*R*,5*R*,8*R*)-8-Benzyloxy-3-(ethylthio)-2,7,7-trimethylbicyclo[3.3.0]oct-2-ene (11). A mixture of ketone **10** (5.73 g, 21.2 mmol), ethanethiol (6.3 mL, 85 mmol), and chlorotrimethylsilane (7.9 mL, 63 mmol) in CH_2Cl_2 (70 mL) was stirred at room temperature for 3 h. The reaction mixture was carefully poured into a saturated aqueous $NaHCO_3$ solution. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded vinyl sulfide **11** (6.40 g, 20.3 mmol, 96%): $[\alpha]^{23}_D = +91.6$ ($c = 0.99$, EtOH); IR (neat) 1500, 1450, 735, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 1.01 (s, 3 H), 1.10 (s, 3 H), 1.13−1.24 (m, 4 H, involving a triplet at 1.20, $J = 7.2$ Hz), 1.72−1.82 (m, 4 H, involving a singlet at 1.80), 2.15 (bd, $J = 14$ Hz, 1 H), 2.58−2.82 (m, 4 H, involving a quartet at 2.64, $J = 7.2$ Hz), 2.98−3.10 (m, 1 H), 3.28 (d, $J = 5.8$ Hz, 1 H), 4.60 (d, $J = 11.6$ Hz, 1 H), 4.63 (d, $J = 11.6$ Hz, 1 H), 7.23−7.46 (m, 5 H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 13.93, 15.55, 21.53, 25.36, 28.05, 35.44, 42.27, 43.25, 47.62, 61.51, 72.98, 92.81, 126.00, 127.39, 127.46, 128.27, 139.03, 139.80. Anal. Calcd for $C_{20}H_{28}OS$: C, 75.90; H, 8.92; S, 10.13. Found: C, 76.09; H, 8.81; S, 9.86.

(3a*S*,3b*R*,4*R*,6a*R*)-4-Benzyloxy-3,3a,3b,4,5,6,6a,7-octahydro-3a,5,5-trimethyl-1-(methylthio)cyclopenta[*a*]pentalen-2-one (13). To a solution of vinyl sulfide **11** (6.40 g, 20.3 mmol) and **1b** (8.3 g, 26.5 mmol) in CH_2Cl_2 (83 mL) was added a 0.96 M hexane solution of $EtAlCl_2$ (30 mL, 29 mmol) at −23 °C. After being stirred for 3 h, a saturated aqueous $NaHCO_3$ solution was added. The mixture was separated, and the aqueous layer was extracted with ether. Concentration of the combined organic layer gave the crude product, which was treated with a 1 M THF solution of tetrabutylammonium fluoride (50 mL, 50 mmol) at room temperature. After being stirred for 1.5 h, a saturated aqueous NH_4Cl was added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded enone **13** (6.26 g, 17.6 mmol, 87%); $[\alpha]^{23}_D = -166.9$ ($c = 0.95$, EtOH); IR (CH_2Cl_2) 1705, 1620 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 1.02 (s, 3 H), 1.03 (s, 3 H), 1.16 (s, 3 H), 1.20−1.35 (m, 1 H), 1.86 (dd, $J = 12.2$, 6.8 Hz, 1 H), 2.10−2.33 (m, 2 H), 2.34 (s, 3 H), 2.38 (d, $J = 17.4$ Hz, 1 H), 2.45 (d, $J = 17.4$ Hz, 1 H), 2.77−2.99 (m, 2 H), 3.64 (d, $J = 6.8$ Hz, 1 H), 4.52 (d, $J = 11.9$ Hz, 1 H), 4.59 (d, $J = 11.9$ Hz, 1 H), 7.20−7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 14.86, 21.19, 25.68, 27.60, 31.97, 41.17, 46.10, 47.50, 47.72, 52.46, 56.36, 71.97, 87.07, 127.12, 127.55, 128.04, 128.37, 138.81, 189.26, 206.15. Anal. Calcd for $C_{22}H_{28}O_2S$: C, 74.11; H, 7.92; S, 8.99. Found: C, 73.92; H, 8.22; S, 9.13.

(3a*S*,3b*R*,4*R*,6a*S*)-4-Benzyloxy-3,3a,3b,4,5,6,6a,7-octahydro-3a,5,5-trimethylcyclopenta[*a*]pentalen-2-one (14). A mixture of enone **13** (164 mg, 0.46 mmol), thiophenol (0.24 mL, 2.3 mmol), and a 1.67 M hexane solution of butyllithium (0.28 mL, 0.46 mmol) in DME (0.5 mL) was heated under reflux for 4 h. After cooling to room temperature, 10% aqueous NaOH solution was added, and the mixture was stirred for 1 h. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded enone **14** (130 mg, 0.42 mmol, 91%): $[\alpha]^{27}_D = -54.5$ ($c = 0.74$, EtOH); IR (CH_2Cl_2) 1700, 1630 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 1.04 (s, 3 H), 1.07 (s, 3 H), 1.18 (s, 3 H), 1.18−1.40 (m, 1 H), 1.86 (dd, $J = 13.3$, 6.6 Hz, 1 H), 2.16−2.32 (m, 2 H), 2.38 (s, 2 H), 2.71−2.94 (m, 2 H), 3.63 (d, $J = 6.8$ Hz, 1 H), 4.52 (d, $J = 12.0$ Hz, 1 H), 4.59 (d, $J = 12.0$ Hz, 1 H), 5.69 (d, $J = 2.0$ Hz, 1 H), 7.22−7.42 (m, 5 H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 21.17, 25.30, 27.53, 32.47, 41.04, 45.97, 47.71, 48.84, 52.83, 56.19, 71.95, 86.97, 122.12, 127.12, 127.49, 128.34, 138.81, 194.72, 210.22. Anal. Calcd for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44. Found: C, 81.43; H, 8.56.

(3a*S*,3b*R*,4*R*,6a*S*)-3,3a,3b,4,5,6,6a,7-Octahydro-4-hydroxy-3a,5,5-trimethylcyclopenta[*a*]pentalen-2-one (15). To a solution of enone **14** (3.92 g, 12.7 mmol) in CH_2Cl_2 (46 mL) was added a 1 M CH_2Cl_2 solution of boron tribromide (25 mL, 25 mmol) at −78 °C. After being stirred for 2 h, 15% aqueous NaOH solution (60 mL) was added. The mixture was stirred at room temperature for 1 h. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded alcohol **15** (2.75 g, 12.5 mmol, 98%): $[\alpha]^{26}_D = +37.1$ ($c = 2.25$, EtOH); $[\alpha]^{25}_D = +42.5$ ($c = 0.20$, $CHCl_3$); IR (CH_2Cl_2) 3600, 1700, 1630 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 0.94 (s, 3 H), 1.07 (s, 3 H), 1.20−1.32 (m, 4 H, involving a singlet at 1.22), 1.67 (bs, 1 H), 1.90 (dd, $J = 11.8$, 7.6 Hz, 1 H), 2.10−2.30 (m, 2 H), 2.34 (d, $J = 16.8$ Hz, 1 H), 2.46 (d, $J = 16.8$ Hz, 1 H), 2.62−2.84 (m, 2 H), 3.80 (d, $J = 8.0$ Hz, 1 H), 5.70 (d, $J = 1.8$ Hz, 1 H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 19.85, 24.88, 26.53, 33.30, 40.15, 45.45, 46.50, 48.12, 53.36, 56.80, 80.91, 122.31, 194.20, 210.70. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.36; H, 9.43.

(3a*S*,3b*R*,4*R*,6a*S*)-3,3a,3b,4,5,6,6a,7-Octahydro-3a,5,5-trimethyl-4-(trimethylsiloxy)cyclopenta[*a*]pentalen-2-one (16). To a solution of alcohol **15** (1.52 g, 6.9 mmol) and imidazole (1.1 g, 16.7 mmol) in DMF (15 mL) was added chlorotrimethylsilane (1.0 mL, 8.4 mmol) at 0 °C. After being stirred for 1 h, a saturated aqueous $NaHCO_3$ solution was added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under

reduced pressure followed by silica gel column chromatography afforded silyl ether **16** (1.89 g, 6.49 mmol, 94%): $[\alpha]^{26.5}_D$ = +12.5 (*c* = 0.87, EtOH); IR (ether) 3050, 2970, 1700, 1630 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 0.11 (s, 9 H), 0.89 (s, 3 H), 0.99 (s, 3 H), 1.16−1.28 (m, 4 H, involving a singlet at 1.21), 1.85 (dd, *J* = 12.5, 7.2 Hz, 1 H), 2.18−2.24 (m, 2 H), 2.35 (s, 2 H), 2.71−2.82 (m, 2 H), 3.81 (d, *J* = 7.5 Hz, 1 H), 5.69 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 0.63, 20.47, 24.85, 26.79, 32.62, 40.40, 45.79, 46.52, 48.16, 52.87, 57.41, 80.85, 122.01, 194.36, 210.30. Anal. Calcd for $C_{17}H_{28}O_2Si$: C, 69.81; H, 9.65. Found: C, 70.10; H, 9.79.

(3a*S*,3b*R*,4*R*,6a*S*,7*S*)-3,3a,3b,4,5,6,6a,7-Octahydro-4,7-dihydroxy-3a,5,5-trimethylcyclopenta[*a*]pentalen-2-one (18). To a suspension of KH (0.19 g, 4.73 mmol) in DME (2.2 mL) was added a solution of enone **16** (461 mg, 1.58 mmol) in DME (3 mL) at 0 °C. After being stirred for 1 h at room temperature, the mixture was cooled to 0 °C, and chlorotriisopropylsilane (0.50 mL, 2.4 mmol) was added. After being stirred for 30 min, the mixture was poured into a saturated aqueous $NaHCO_3$ solution containing a small amount of triethylamine. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure afforded dienol silyl ether **17**, which was used for the next step without purification. **17**: ^1H NMR ($CDCl_3$, 300 MHz) δ 0.08 (s, 9 H), 0.1 (s, 9 H), 0.92 (s, 3 H), 0.98 (s, 3 H), 1.10 (d, *J* = 8.0 Hz, 18 H), 1.15−1.32 (m, 7 H, involving a singlet at 1.2), 1.55 (dd, *J* = 12.1, 6.0 Hz, 1 H), 1.98 (d, *J* = 14.9 Hz, 1 H), 2.36 (d, *J* = 14.9 Hz, 1 H), 2.50 (dd, *J* = 10.1, 5.0 Hz, 1 H), 3.34−3.50 (m, 1 H), 3.96 (d, *J* = 5.0 Hz, 1 H), 4.80 (d, *J* = 4.0 Hz, 1 H), 5.20 (s, 1 H).

To a mixture of crude **17**, $KHCO_3$ (1.6 g, 16 mmol), acetone (11.5 mL), and water (11.5 mL) was added OXONE (0.97 g, 1.6 mmol) at 0 °C. After being stirred for 30 min at room temperature, a saturated aqueous $Na_2S_2O_3$ solution was added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was concentrated under reduced pressure. The crude mixture was dissolved in a mixture of acetic acid (9.5 mL), THF (3.2 mL), and water (3.2 mL). After being stirred for 30 min at room temperature, the mixture was poured into a saturated aqueous $NaHCO_3$ solution. The mixture was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by recrystalization from ethyl acetate/hexane afforded diol **18** (168 mg, 0.71 mmol). The residue was purified by silica gel column chromatography to give additional **18** (131 mg, 0.55 mmol). The yield of **18** based on **16** was 80%: mp 165−169 °C; $[\alpha]^{29}_D$ = +90.4 (*c* = 0.27, CH_2Cl_2); IR (CH_2Cl_2) 3600, 3400, 3060, 2960, 1710, 1640, 1410, 1270, 1260 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.95 (s, 3 H), 1.10 (s, 3 H), 1.45 (s, 3 H), 1.48 (dd, *J* = 13.2, 8.0 Hz, 1 H), 1.84 (dd, *J* = 13.2, 9.5 Hz, 1 H), 2.05 (dd, *J* = 12.4, 9.1 Hz, 1 H), 2.38 (d, *J* = 18.4 Hz, 1 H), 2.52 (d, *J* = 18.4 Hz, 1 H), 2.67−2.78 (m, 1 H), 3.81 (d, *J* = 9.1 Hz, 1 H), 4.65 (d, *J* = 5.4 Hz, 1 H), 5.84 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 20.37, 24.94, 26.57, 35.05, 44.31, 44.93, 47.72, 56.04, 56.50, 68.64, 81.15, 123.83, 190.32, 211.18. Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.12; H, 8.57.

(3a*S*,3b*R*,4*R*,6a*S*,7*S*)-3,3a,3b,4,5,6,6a,7-Octahydro-3a,5,5-trimethyl-4,7-bis(trimethylsiloxy)cyclopenta[*a*]pentalen-2-one (19). To a solution of diol **18** (168 mg, 0.71 mmol) and imidazole (0.34 g, 5.0 mmol) in DMF (3.5 mL) was added chlorotrimethylsilane (0.32 mL, 2.5 mmol) at 0 °C. After being stirred for 10 min, a saturated aqueous $NaHCO_3$ solution was added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded silyl ether **19** (249 mg, 0.65 mmol, 92%): $[\alpha]^{24.5}_D$ = +34.9 (*c* = 0.51, EtOH); IR (ether) 3050, 2980, 1250, 1100 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.08 (s, 9 H), 0.11 (s, 9 H), 0.86 (s, 3 H), 0.99 (s, 3 H), 1.27 (dd, *J* = 12.7, 8.3 Hz, 1 H), 1.34 (s, 3 H), 1.71 (dd, *J* = 12.7, 10.1 Hz, 1 H), 2.14 (dd, *J* = 12.3, 8.3 Hz, 1 H), 2.31 (d, *J* = 18.0 Hz, 1 H), 2.38 (d, *J* = 18.0 Hz, 1 H), 2.61−2.73 (m, 1 H), 3.77 (d, *J* = 8.3 Hz, 1 H), 4.50 (d, *J* = 6.3 Hz, 1 H), 5.72 (s, 1 H); ^{13}C NMR (CDCl3, 75.5 MHz) δ −0.13, 0.86, 21.12, 25.14, 27.08, 35.78, 44.62, 45.70, 47.97, 55.31, 57.15, 68.63, 81.48, 122.71, 191.44, 211.01. Anal. Calcd for $C_{20}H_{36}O_3Si_2$: C, 63.10; H, 9.53. Found: C, 63.07; H, 9.83.

(3*S*,3a*S*,3b*R*,4*R*,6a*S*,7*S*)-3-Bromo-3,3a,3b,4,5,6,6a,7-octahydro-3a,5,5-trimethyl-4,7-bis(trimethylsiloxy)cyclopenta[*a*]pentalen-2-one (20) and (3*R*,3a*S*,3b*R*,4*R*,6a*S*,7*S*)-3-Bromo-3,3a,3b,4,5,6,6a,7-octahydro-3a,5,5-trimethyl-4,7-bis(trimethylsiloxy)cyclopenta[*a*]pentalen-2-one (epi-20). To a solution of enone **19** (54 mg, 0.14 mmol) in THF (0.71 mL) was added a 1 M THF solution of LHMDS (0.17 mL, 0.17 mmol) at −45 °C. After being stirred for 1.5 h, 5,5-dibromo-2,2-dimethyl-1,3-dioxane-4,6-dione (64 mg, 0.21 mmol) was added. After being stirred for 1 h, a saturated aqueous $NaHCO_3$ solution was added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded bromoketone **20** (51 mg, 0.111 mmol, 78%) and **epi-20** (13 mg, 0.028 mmol, 20%). **20**: $[\alpha]^{26.3}_D$ = −47.7 (*c* = 1.37, CH_2Cl_2); IR (ether) 2980, 1960, 1730, 1380, 1120 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.12 (s, 9 H), 0.15 (s, 9 H), 0.95 (s, 3 H), 1.03 (s, 3 H), 1.37 (dd, *J* = 12.9, 9.0 Hz, 1 H), 1.46 (s, 3 H), 1.75 (dd, *J* = 12.9, 9.3 Hz, 1 H), 2.54−2.66 (m, 1 H), 2.97 (dd, *J* = 12.2, 9.0 Hz, 1 H), 3.80 (d, *J* = 8.8 Hz, 1 H), 4.15 (s, 1 H), 4.48 (d, *J* = 5.9 Hz, 1 H), 5.78 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −0.11, 0.99, 21.60, 25.78, 27.31, 35.37, 44.59, 45.35, 51.63, 53.21, 59.89, 69.10, 81.61, 119.09, 188.57, 204.54. Anal. Calcd for $C_{20}H_{35}BrO_3Si_2$: C, 52.27; H, 7.86. Found: C, 52.30; H, 7.93. **epi-20**: ^1H NMR ($CDCl_3$, 300 MHz) δ 0.12 (s, 9 H), 0.19 (s, 9 H), 0.91 (s, 3 H), 1.05 (s, 3 H), 1.37 (dd, *J* = 12.9, 9.3 Hz, 1 H), 1.42 (s, 3 H), 1.77 (dd, *J* = 11.7, 9.0 Hz, 1 H), 2.36 (dd, *J* = 12.2, 9.0 Hz, 1 H), 2.56−2.66 (m, 1 H), 3.79 (d, *J* = 9.0 Hz, 1 H), 4.43 (s, 1 H), 4.48 (d, *J* = 5.6 Hz, 1 H), 5.93 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −0.10, 1.17, 21.43, 24.05, 27.31, 34.98, 44.12, 44.50, 52.19, 57.06, 67.25, 69.16, 81.77, 120.54, 189.48, 201.68.

(3*S*,3a*S*,3b*R*,4*R*,6a*S*,7*S*)-3-Bromo-3,3a,3b,4,5,6,6a,7-octahydro-3-hydroxymethyl-3a,5,5-trimethyl-4,7-bis(trimethylsiloxy)cyclopenta[*a*]pentalen-2-one (21). To a solution of bromoketone **20** (38 mg, 0.083 mmol) in THF (0.41 mL) was added a 1 M THF solution of LHMDS (0.10 mL, 0.10 mmol) at −45 °C. After being stirred for 1.5 h, paraformaldehyde (10 mg, 0.33 mmol) was added. After being stirred for 30 min at 0 °C, a saturated aqueous $NaHCO_3$ solution was added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded bromohydrin **21** (36 mg, 0.073 mmol, 88%): $[\alpha]^{25.7}_D$ = +50.8 (*c* = 0.6, CH_2Cl_2); IR (ether) 3000, 2990, 1720, 1440, 1380, 1350, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.12 (s, 9 H), 0.19 (s, 9 H), 0.93 (s, 3 H), 1.06 (s, 3 H), 1.34−1.42 (m, 1 H), 1.52 (s, 3 H), 1.75−1.82 (m, 1 H), 2.54 (dd, *J* = 9.3, 4.4 Hz, 1 H), 2.60−2.70 (m, 2 H), 3.70 (dd, *J* = 12.1, 9.3 Hz, 1 H), 3.87 (brd, 1 H), 3.92 (dd, *J* = 12.1, 4.4 Hz, 1 H), 4.52 (brd, 1 H), 5.92 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −0.11, 1.09, 21.30, 27.41, 28.49, 35.55, 44.18, 44.54, 50.52, 54.90, 68.32, 68.50, 81.49, 81.94, 120.44, 190.41, 203.75. Anal. Calcd for $C_{21}H_{37}BrO_4Si_2$: C, 51.52; H, 7.62. Found: C, 51.82; H, 7.69.

Epoxide 22. A solution of bromohydrin **21** (34 mg, 0.069 mmol) and DBU (32 μL, 0.21 mmol) in DMF (0.69 mL) was heated at 50 °C for 2.5 h. After cooling to room temperature, a saturated aqueous $NaHCO_3$ solution was added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded epoxide **22** (23 mg, 0.055 mmol, 80%) along with bromoketone **20** (2.5 mg, 0.006 mmol, 16%): $[\alpha]^{25.6}_D$ = −9.88 (*c* = 0.27, CH_2Cl_2); IR (ether) 2980, 2880, 1730, 1440, 1380, 1360, 1110 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.14 (s, 9 H), 0.14 (s, 9 H), 0.90 (s, 3 H), 1.03 (s, 3 H), 1.32−1.41 (m, 4 H, involving a singlet at 1.41), 1.72−1.80 (m, 1 H), 2.51−2.60 (m, 2 H), 2.84 (d, *J* = 5.7 Hz, 1 H), 3.34 (d, *J* = 5.7 Hz, 1 H), 3.73 (d, *J* = 8.3 Hz, 1 H), 4.50 (d, *J* = 4.7 Hz, 1 H) 5.98 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −0.08, 1.13, 21.30, 22.93, 27.40, 35.09, 44.31, 44.86, 47.98,

48.63, 49.30, 68.11, 70.26, 81.49, 122.27, 191.89, 204.58. Anal. Calcd for $C_{21}H_{36}O_4Si_2$: C, 61.72; H, 8.88. Found: C, 61.47; H, 9.09.

Epoxide 23. To a solution of epoxide **22** (19 mg, 0.046 mmol) in THF (0.3 mL) was added a few drops of hydrogen fluoride−pyridine at 0 °C. After being stirred for 5 min, a saturated aqueous $NaHCO_3$ solution was added, and the mixture was extracted with ethyl acetate. Drying over $MgSO_4$ and concentration under reduced pressure followed by silica gel column chromatography afforded epoxide **23** (12 mg, 0.045 mmol, 98%): mp 152−155 °C (dec); $[\alpha]^{25}_D = +27.1$ ($c = 0.14$, CH_2Cl_2); IR (CH_2Cl_2) 3700, 3600, 2930, 1720, 1420 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.94 (s, 3 H), 1.10 (s, 3 H), 1.43−1.53 (m, 4 H, involving a singlet at 1.49), 1.84 (dd, $J = 12.7$, 10.7 Hz, 1 H), 2.43 (dd, $J = 12.0$, 9.5 Hz, 1 H) 2.63−2.75 (m, 1 H), 2.98 (d, $J = 5.5$ Hz, 1 H), 3.37 (d, $J = 5.5$ Hz, 1 H), 3.37 (d, $J = 5.5$ Hz, 1 H), 3.65 (d, $J = 9.5$ Hz, 1 H), 4.73 (d, $J = 5.6$ Hz, 1 H), 6.10 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 20.24, 22.42, 26.61, 35.00, 44.26, 44.51, 47.63, 49.37, 49.97, 67.93, 69.83, 80.34, 123.68, 190.14, 204.24. Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.20; H, 7.93.

3-Epi-coriolin. To a mixture of epoxide **23** (14 mg, 0.053 mmol), $NaHCO_3$ (70 mg, 0.83 mmol), THF (2.1 mL), and water (2.1 mL) was added 35% aqueous H_2O_2 (42 μL, 0.43 mmol) at 0 °C. After being stirred for 45 min, a saturated aqueous NH_4Cl solution was added. The mixture was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded 3-epi-coriolin (12 mg, 0.042 mmol, 80%): mp 206−209 °C (dec); $[\alpha]^{25.5}_D = -95.8$ ($c = 0.16$, acetone); IR (CH_2Cl_2) 3600, 3400, 1760 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.94 (s, 3 H), 1.10 (s, 3 H), 1.37 (s, 3 H), 1.49 (dd, $J = 12.7$, 8.8 Hz, 1 H), 1.81 (dd, $J = 12.7$, 10.7 Hz, 1 H) 2.04 (brs, 1 H), 2.43 (dd, $J = 11.9$, 9.0 Hz, 1 H), 2.76−2.89 (m, 1 H), 2.96 (d, $J = 6.0$ Hz, 1 H), 2.99 (d, $J = 6.0$ Hz, 1 H), 3.51 (s, 1 H), 3.66 (d, $J = 9.0$ Hz, 1 H), 4.06 (d, $J = 6.1$ Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 16.42, 20.16, 26.53, 35.22, 40.88, 41.71, 43.09, 52.31, 53.31, 58.68, 67.71, 71.19, 78.85, 79.85, 204.91.

(3*R*,3a*S*,3b*R*,4*R*,6a*S*,7*S*)-3,3a,3b,4,5,6,6a,7-Octahydro-3-hydroxymethyl-3a,5,5-trimethyl-4,7-bis(trimethylsiloxy)-cyclopenta[*a*]pentalen-2-one (24). To a solution of enone **19** (21 mg, 0.055 mmol) in ether (0.28 mL) was added a 1 M etherial solution of LDA (0.14 mL, 0.14 mmol) at −23 °C. After being stirred for 2 h, paraformaldehyde (5.0 mg, 0.16 mmol) was added. After being stirred for 1 h at 0 °C, a saturated aqueous $NaHCO_3$ solution was added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded hydroxyketone **24** (16 mg, 0.040 mmol, 72%): $[\alpha]^{24.4}_D = +25.36$ ($c = 1.08$, CH_2Cl_2); IR (ether) 2900, 1710, 1440, 1370, 1250, 1180, 1070 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.11 (s, 9 H), 0.19 (s, 9 H), 0.94 (s, 3 H), 1.10, (s, 3 H), 1.35 (dd, $J = 12.7$, 8.7 Hz, 1 H), 1.42 (s, 3 H), 1.80 (dd, $J = 12.8$, 11.0 Hz, 1 H), 2.37 (dd, $J = 12.2$, 8.8 Hz, 1 H), 2.54−2.70 (m, 2 H, involving a doublet−doublet at 2.56, $J = 9.3$, 5.9 Hz), 3.21 (dd, $J = 9.8$, 3.9 Hz, 1 H), 3.56−3.75 (m, 2 H), 3.90 (d, $J = 8.8$ Hz, 1 H), 4.51 (d, $J = 6.3$ Hz, 1 H), 5.73 (s, 1 H), with peaks due to the minor epimer at 1.05 (s), 1.30 (s), 4.45 (d, $J = 5.3$ Hz), 5.79 (s); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −0.12, 1.06, 20.81, 27.23, 27.41, 36.21, 44.51, 44.87, 49.76, 50.21, 61.65, 62.95, 68.57, 82.09, 122.32, 191.03, 210.56. Anal. Calcd for $C_{21}H_{38}O_4Si_2$: C, 61.41; H, 9.33. Found: C, 61.22; H, 9.48.

Epoxide 25. A solution of pinacol (59 mg, 0.5 mmol) in THF (0.5 mL) was slowly added to a suspension of KH (44 mg, 1.1 mmol) in THF (0.5 mL) to afford a 0.5 M suspension of potassium pinacolate. To a solution of hydroxyketone **24** (15 mg, 0.036 mmol) in THF (0.12 mL) was added a 1 M THF solution of LDA (0.12 mL, 0.12 mmol) at −23 °C. After being stirred for 4 h, the mixture was cooled to −78 °C. To this was successively added *N*-iodosuccinimide (40 mg, 0.18 mmol) and a 0.5 M THF suspension of potassium pinacolate (0.24 mL, 0.12 mmol). After being stirred for 1 h, an aqueous Na_2SO_3 solution containing a small amount of triethylamine was added. The mixture was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded epoxide **25** (11 mg, 0.026 mmol, 72%) along with hydroxyketone **24** (1 mg, 0.0024 mmol, 7%): $[\alpha]^{25.1}_D = +25.5$ ($c = 1.1$, CH_2Cl_2); IR (ether) 3057, 2980, 2720, 1280, 1260 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.13 (s, 9 H), 0.14 (s, 9 H), 0.87 (s, 3 H), 1.03 (s, 3 H), 1.28−1.35 (m, 4 H involving a singlet at 1.32), 1.76 (t, $J = 12.7$ Hz, 1 H), 2.24 (dd, $J = 12.4$, 8.6 Hz, 1 H), 2.56−2.69 (m, 1 H), 3.02 (d, $J = 6.8$ Hz, 1 H), 3.11 (d, $J = 6.8$ Hz, 1 H), 3.72 (d, $J = 8.6$ Hz, 1 H) 4.57 (d, $J = 6.1$ Hz, 1 H), 6.05 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −0.08, 0.90, 20.54, 20.92, 27.15, 35.70, 44.55, 44.60, 48.27, 52.78, 54.69, 69.36, 69.43, 81.29, 123.22, 190.15, 204.58. Anal. Calcd for $C_{21}H_{36}O_4Si_2$: C, 61.72; H, 8.88. Found: C, 62.01; H, 9.04.

Epoxide 26. To a solution of epoxide **25** (33 mg, 0.081 mmol) in THF (0.4 mL) was added a few drops of hydrogen fluoride−pyridine at 0 °C. After being stirred for 10 min, a saturated aqueous $NaHCO_3$ solution was added, and the mixture was extracted with ethyl acetate. Drying over $MgSO_4$ and concentration under reduced pressure followed by silica gel column chromatography afforded epoxide **26** (21 mg, 0.080 mmol, 99%): mp 155−156 °C; $[\alpha]^{25.7}_D = +125.7$ ($c = 0.20$, CH_2Cl_2); IR (CH_2Cl_2) 3690, 3600, 3050, 2980, 1720, 1600, 1420 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.94 (s, 3 H), 1.09 (s, 3 H), 1.40 (s, 3 H), 1.49 (dd, $J = 12.7$, 8.5 Hz, 1 H), 1.85 (t, $J = 12.7$ Hz, 1 H), 2.25 (dd, $J = 12.2$, 8.9 Hz, 1 H), 2.68−2.81 (m, 1 H), 3.09 (d, $J = 6.6$ Hz, 1 H), 3.23 (d, $J = 6.6$ Hz, 1 H), 3.74 (d, $J = 8.9$ Hz, 1 H), 4.76 (d, $J = 6.1$ Hz, 1 H), 6.16 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 20.21, 20.34, 26.56, 35.51, 44.23, 44.45, 48.00, 52.89, 53.94, 69.19, 69.37, 80.08, 124.40, 188.97, 204.35. Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 67.90; H, 7.83.

(−)-Coriolin. To a mixture of monoepoxide **26** (20 mg, 0.076 mmol), $NaHCO_3$ (0.10 g, 1.2 mmol), THF (3 mL), and water (3 mL) was added 35% aqueous H_2O_2 (60 μL, 0.57 mmol) at 0 °C. After being stirred for 1.5 h, a saturated aqueous NH_4Cl solution was added. The mixture was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel column chromatography afforded (−)-coriolin (20 mg, 0.072 mmol, 95%): mp 175−176 °C; $[\alpha]^{26.0}_D = -19.4$ ($c = 0.44$, $CHCl_3$); IR (CH_2Cl_2) 3600, 3400, 3000, 1750, 1090 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.92 (s, 3 H), 1.08 (s, 3 H), 1.22 (s, 3 H), 1.49 (dd, $J = 12.9$, 8.8 Hz, 1 H), 2.04 (s, 1 H), 2.32 (dd, $J = 12.2$, 9.3 Hz, 1 H), 2.74−2.86 (m, 1 H), 2.99 (d, $J = 6.8$ Hz, 1 H), 3.13 (d, $J = 6.8$ Hz, 1 H), 3.57 (s, 1 H), 3.76 (d, $J = 9.3$ Hz, 1 H), 4.04 (d, $J = 6.1$ Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.92, 20.22, 26.34, 34.92, 40.12, 42.80, 42.98, 51.54, 54.67, 59.70, 65.74, 70.23, 78.00, 80.33, 204.62.

Acknowledgment. We are grateful to Professor Takeshi Sugai, Department of Chemistry, Keio University, for helpful discussions on optical resolution using enzymes. We express our thanks to Amano Pharmaceutical Co. Ltd. for the kind donation of "Amano Lipase PS". This work was financially supported by the Ministry of Education, Science, Sports, and Culture of the Japanese Government. K.M. thanks JSPS for a predoctral fellowship.

Supporting Information Available: Experimental procedures and characterization data for **6a**, **epi-21**, and MTPA esters of **(*S*)-5** and **15**. Preparation of a *N*-*p*-toluenesulfonyl-L-phenylalaninyl derivative from **(*S*)-5** for X-ray crystallographic analysis. The experimental procedures for determination of the stereochemistry of ketone **8**. The normal and NOE spectra of **20** and **epi-20**. The ^1H and ^{13}C NMR spectra of (−)-coriolin and epi-coriolin. This material is available free of charge via the Internet at http://pubs.acs.org.

JO981478C