Total Syntheses of (−)-Anastrephin, (−)-Epianastrephin, and Their 7a-Epimers: Use of Samarium(II) Iodide-Mediated Intramolecular Reductive Coupling for the Construction of Their Hexahydrobenzofuran-2(3*H*)-one Skeletons

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D-Glucose-derived α,β-unsaturated ester **17**, which includes a geminally and differntially substituted γ-carbon and a terminal aldehyde functionality, was subjected to a SmI_2-mediated intramolecular reductive coupling reaction in a THF solution containing 1/10 volume of HMPA. The reaction proceeded with moderate stereoselectivity to provide a diastereomeric mixture of hexahydrobenzofuran-2(3*H*)-ones, in which *cis*-fused product **25** was obtained as the major isomer in 35% isolated yield. Two *trans*-fused coupling products **26** (17%) and **27** (14%) were also obtained. Starting from major product **25**, the insect sex attractants (−)-anastrephin (**1**) and (−)-epianastrephin (**2**) were synthesized enantiospecifically. Two unnatural stereocongeners, (−)-7a-*epi*-anastrephin (**3**) and (−)-7a-*epi*-epianastrephin (**4**), were also derived from **25**.

Introduction

Lanthanide-mediated organic reactions and their use in organic synthesis have been investigated extensively in this decade.[1] The lanthanide-mediated reductive carbon–carbon bond-forming reaction is one of the most reliable procedures for the construction of the carbon skeletons of structurally complicated synthetic intermediates. Among the known lanthanide reagents, the samarium(II) salts, represented by samarium diiodide (SmI_2), are undoubtedly the eminent reagents, and their use as organic reaction mediators has been actively studied.[2] The use of SmI_2 for the preparation of structurally complicated substrates, especially in the context of natural products synthesis, is of current interest in a number of laboratories.[3] There are also some examples of the application of SmI_2-mediated reactions in the field of synthetic carbohydrate chemistry.[4] As part of our continuing interest in access to enantiomerically pure and versatile carbocyclic building blocks from carbohydrates,[5] we describe herein some SmI_2-mediated reductive coupling reactions of D-glucose-derived γ,γ-differentially substituted α,β-unsaturated esters having a terminal aldehyde or methyl ketone functionality. The possible origin of the stereoselectivity observed in each coupling reaction is discussed. In addition, the major coupling product of the reaction of the aldehyde substrate was efficiently transformed into some insect sex attracting pheromones, (−)-anastrephin (**1**), (−)-epianastrephin (**2**), and their respective 7a-epimers (**3**) and (**4**)[6] (Figure 1).

The insect pheromones (−)-anastrephin (**1**) and (−)-epianastrephin (**2**) were isolated from the male Caribbean fruit fly *Anastrepha suspensa* Loew[7] and also from the Mexican fruit fly *Anastrepha ludens* Loew.[7,8] These

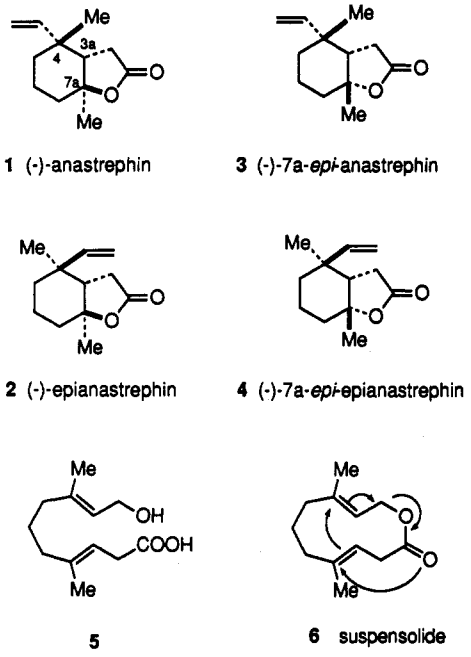

Figure 1.

fruit flies cause production losses in cultivated varieties of citrus crops in Mexico. These pheromones attract females for mating and also act as aggregation substances for both sexes in the field.[9] The natural pheromones are enantiomerically enriched but are not single enantiomers.[7] The constituents and their relative stereochemistries were determined by spectroscopic means (^1H, ^{13}C NMR, IR, and MS)[7,8] and were confirmed by a single-crystal X-ray analysis.[8] The absolute configurations of the major enantiomers of **1** and **2**, which were later established by chemical synthesis, are depicted in Figure 1.

A structural characteristic of these pheromones is a *trans*-fused hexahydrobenzofuran-2(3*H*)-one skeleton with three contiguous stereogenic centers (C-3a, C-4, and C-7a), one of which is an asymmetric quaternary carbon. Some racemic and enantioselective total syntheses of **1** and **2** have been reported so far. In their first communication regarding the isolation and characterization of the anas-

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(2) (a) Inanaga, J. *Yuki Gosei Kagaku Kyoukaishi*, **1989**, *47*, 200; **1990**, *48*, 1024. (b) Kagan, H. B. *New J. Chem.* **1990**, *14*, 453. (c) Soderquist, J. A. *Aldrichim. Acta* **1991**, *24*, 15. (d) Molander, G. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 1, pp 251–282. (e) Curran, D. P.; Fevig, T. L.; Jasperse, C. P.; Totleben, M. J. *Synlett* **1992**, 943.

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trephins,[7] Battiste and co-workers described syntheses of racemic **1**–**4**. Their total syntheses relied on the "spiro-oxirane" approach,[10] which involved sodium benzenethiolate-promoted ring opening of γ,δ-spiroepoxy esters derived from cyclohexanone derivatives. The approach efficiently provided *trans*-fused γ-lactones. Later, they established the absolute stereochemistry of **1** and **2** by chemical resolution of the synthetic recemates using (−)-α-phenylglycinol as the resolving reagent.[11] In 1984, Saito and co-workers reported the BF_3·OEt_2-catalyzed cyclization of 10-hydroxy-4,8-dimethyldeca-(3*E*,8*E*)-3,8-dienoic acid (**5**). This reaction furnished a 1:1 mixture of racemic anastrephin and epianastrephin in a single step.[12] Then, having established an improved route to **5** from geraniol, Mori and Nakazono executed the lactonization of **5** to suspensolide (**6**).[13] They have also achieved the BF_3·OEt_2-catalyzed cyclization of **5**. This approach furnished racemic **1** and **2** in overall yields of 2.2% and 2.7%, respectively, from geraniol. Eventually, resolution of the racemic pheromones using (+)-prolinol as the resolving reagent gave enantiomerically pure **1** and **2**.[13] Quite recently, Battiste and co-workers proposed a biosynthetic pathway from **6** to racemic **1** and **2**.[14] The mechanistic implications of the conformations of **6** were supported by computational calculations. Their assumption that suspensolide (**6**) is the biosynthetic precursor of these pheromones is supported by the fact that the males of the Caribbean fruit fly *Anastrepha suspensa* release **6**.[15]

In order to realize a conceptually novel total synthesis of these pheromones, we preferred an enantiospecific route to the (−)-enantiomers of **1** and **2**, a route that would not necessitate an optical resolution process. Our retrosynthetic analysis is outlined in Scheme I. Target compounds **1** and **2** and their stereoisomers **3** and **4** would be easily derived from highly substituted cyclohexane derivative **A**. Advanced intermediate **A** would be prepared from hexahydrobenzofuran-2(3*H*)-one **B**, possessing a methyl and a vinyl group at C-4. These methyl and vinyl groups could be introduced differentially via functionalization of the geminal substituents (R and R′) in γ-lactone **C**. A key step of our approach is the stereoselective construction of the hexahydrobenzofuran-2(3*H*)-one skeleton in **C**. As a method for the construction of **C**, we envisaged the intramolecular reductive coupling of an α,β-unsaturated ester **D** possessing two different carbon functionalities at the γ-carbon and an aldehyde functionality as the terminal carbon. A one-electron reduction of the aldehyde carbonyl in **D** by SmI_2 would give an intermediary ketyl radical, which would attack the β-carbon of the unsaturated ester.[16] A second one-electron reduction of the resulting six-membered carbocycle(s), protonation of the resulting anionic intermediate(s), followed by lactonization would give **C**. We envisaged enantiomerically pure, highly substituted tetrahydrofuran **17** as the substrate **D** of this reductive coupling reaction. With this synthetic plan in mind, we first investigated the stereoselectivity in the SmI_2-mediated reductive coupling of substrate **17**.

Results and Discussion

Preparation of the Substrates for the SmI_2-Mediated Reductive Coupling Reactions. Compounds **17**, **19**, **22**, and **24** were prepared from our previously reported building block **7**[17,18] as the substrates for the SmI_2-mediated reductive coupling (Scheme II). The ester of **7** was reduced ($LiAlH_4$), and the hydroxyl group in the resulting alcohol **8** was replaced by an iodo group by means of a modified Mitsunobu procedure,[19] affording iodide **9** in 90% yield. Attack of the anion generated from dimethyl malonate (NaH) on the carbon bearing the iodo group in a refluxing THF solution gave diester **10**, which was subjected to demethoxycarbonylation,[20] furnishing ester **11** in 75% yield for two steps.[21] Reduction ($LiAlH_4$) of **11** and protection of the hydroxyl group of the resulting alcohol **12** as a *tert*-butyldimethylsilyl (TBDMS) ether furnished silyl ether **13**. By a series of standard trans-

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(4) (a) Enholm, E. J.; Satici, H.; Trivellas, A. *J. Org. Chem.* **1989**, *54*, 5841. (b) Enholm, E. J.; Trivellas, A. *J. Am. Chem. Soc.* **1989**, *111*, 6463. (c) Kusuda, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1989**, *30*, 2945. (d) Inanaga, J. *Rev. Heteroatom. Chem.* **1989**, *3*, 75. (e) Inanaga, J.; Katsuki, J. Yamaguchi, M. *Chem. Lett.* **1991**, 1025. (f) Chiara, J. L; Cabri, W.; Hanessian, S. *Tetrahedron Lett.* **1991**, *32*, 1125. (g) Enholm, E. J.; Jiang, S. *Ibid.* **1992**, *33*, 313. (h) Hanessain, S.; Girard, C.; Chiara, J. L. *Ibid.* **1992**, *33*, 573. (i) Enholm, E. J.; Jiang, S. *Heterocycles* **1992**, *34*, 2247. (j) Enholm, E. J.; Jiang, S.; *Tetrahedron Lett.* **1992**, *33*, 6069.

(5) See: Tadano, K.; Nagashima, K.; Ueno, Y.; Ogawa, S. *J. Org. Chem.* **1992**, *57*, 4496 and references cited therein for previous work from our laboratories.

(6) The first "chiral" total syntheses of **1** and **3** were reported in a preliminary communication. Tadano, K.; Isshiki, Y.; Minami, M.; Ogawa, S. *Tetrahedron Lett.* **1992**, *33*, 7899.

(7) Battiste, M. A.; Strekowski, L.; Vanderbilt, D. P.; Visnick, M.; King, R. W.; Nation, J. L. *Tetrahedron Lett.* **1983**, *24*, 2611.

(8) Stokes, J. B.; Uebel, E. C.; Warthen, J. D.; Jacobson, M. *J. Agric. Food Chem.* **1983**, *31*, 1162.

(9) Perdomo, A. J.; Nation, J. L.; Barranowski, R. M. *Environ. Entomol.* **1976**, *5*, 1208.

(10) Strekowski, L.; Battiste, M. A. *Tetrahedron Lett.* **1981**, *22*, 279.

(11) Strekowski, L.; Visnick, M.; Battiste, M. A. *J. Org. Chem.* **1986**, *51*, 4836.

(12) Saito, A.; Matsushita, H.; Kaneko, H. *Chem. Lett.* **1984**, 729.

(13) Mori, K.; Nakazono, Y. *Liebigs Ann. Chem.* **1988**, 167.

(14) Battiste, M. A.; Strekowski, L.; Coxon, J. M.; Wydra, R. L.; Harden, D. B. *Tetrahedron Lett.* **1991**, *32*, 5303.

(15) (a) Chuman, T.; Sivinski, J.; Heath, R. R.; Calkins, C. O.; Tumlinson, J. H.; Battiste, M. A.; Wydra, R. L.; Strekowski, L.; Nation, J. L. *Tetrahedron Lett.* **1988**, *29*, 6561. (b) Battiste, M. A.; Rocca, J. R.; Wydra, R. L.; Tumlinson, J. H.; Chuman, T. *Ibid.* **1988**, *29*, 6565.

(16) For some similar intramolecular coupling reactions that gave five-membered carbocycles attached to a γ-lactone ring, see: refs 3c,d,f and 4a,b.

(17) Tadano, K.; Idogaki, Y.; Yamada, H.; Suami, T. *Chem. Lett.* **1985**, 1925; *J. Org. Chem.* **1987**, *52*, 1201.

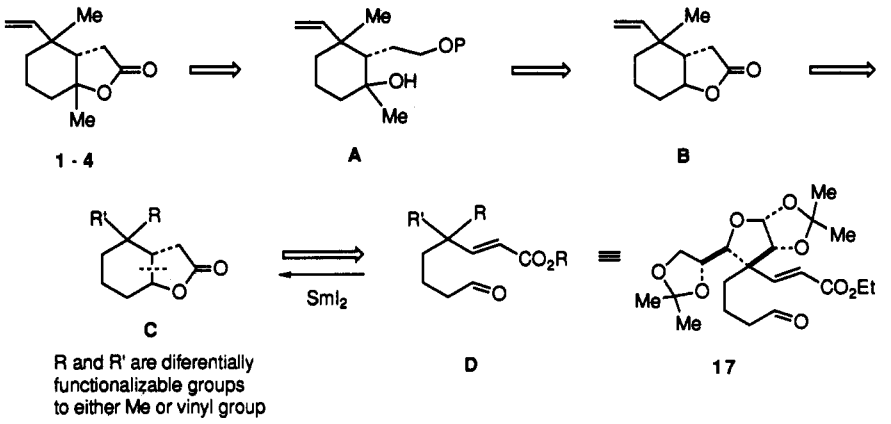
(18) For some examples of the versatility of **7** for natural product synthesis, see: Tadano, K. In *Studies in Natural Products Chemistry*: Atta-ur-Rahman Ed.; Elsevier: Amsterdam, 1992; Vol. 10, pp 405–455.

(19) Loibner, H.; Zbiral, E. *Helv. Chim. Acta* **1976**, 59, 2100.

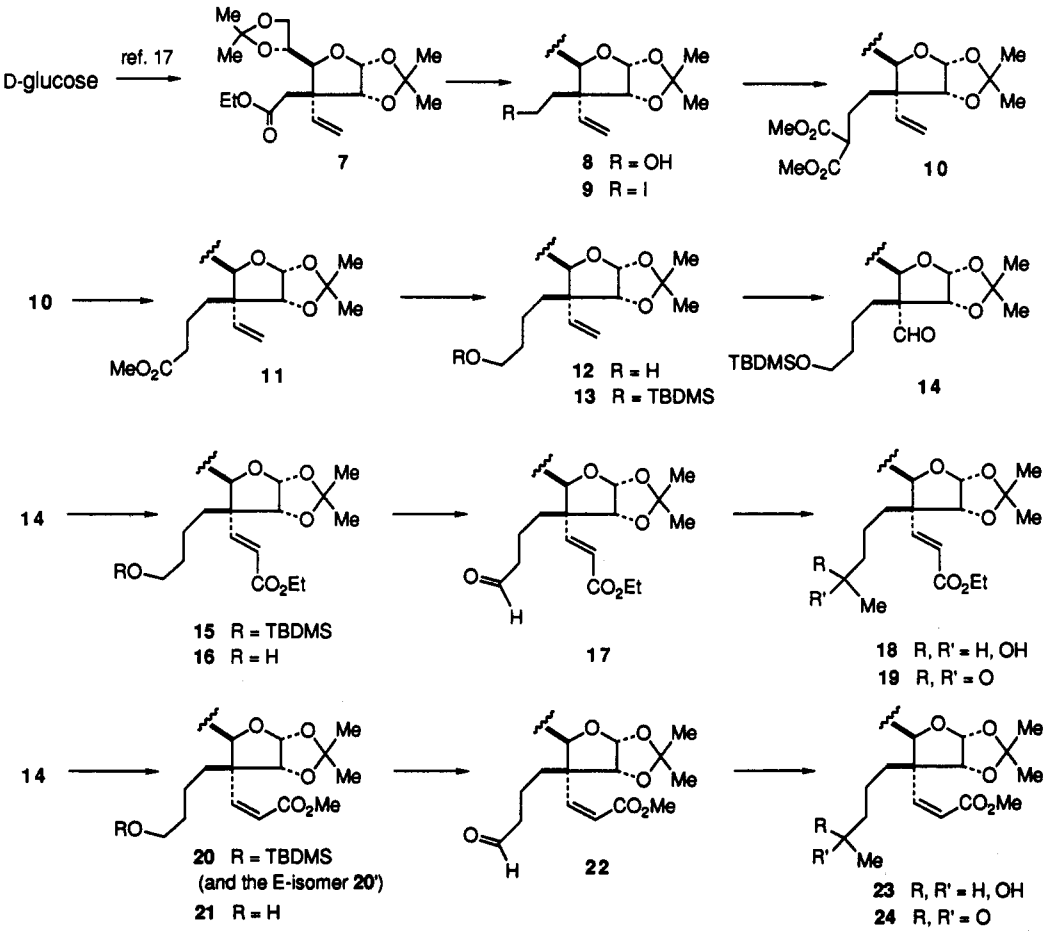
(20) Krapcho, A. P. *Tetrahedron Lett.* **1973**, 957.

(21) We investigated direct conversion of iodide **9** into **11** by means of attack of the anion generated from EtOAc (LDA/THF/−78° to 0 °C); no substitution occurred, and iodide **9** was recovered quantitatively.

Scheme I



Scheme II



formations from **13** (i.e., (1) ozonolysis of the vinyl group followed by reductive workup with triphenylphosphine (**13** to **14**), (2) a Horner–Emmons olefination of the resulting aldehyde **14** with triethyl phosphonoacetate (NaH) (**14** to **15**), and (3) desilylation of **15** with *n*-Bu_4NF), α,β-unsaturated ester **16** was obtained with exclusive *E*-selectivity in an overall yield of 89% from **11**. PCC oxidation[22] of **16** gave substrate **17** in 82% yield. Grignard reaction of **17** with MeMgBr resulted in the formation of an inseparable 1:1 mixture (^{1}H NMR analysis) of diastereomers **18** in 68% yield.[23] The mixture was oxidized (PCC) to afford another substrate, **19**, in 92% yield. The Horner–Emmons reaction of **14** with bis(2,2,2-trifluoroethyl)(methoxycarbonyl)phosphonoacetate[24] in the presence of potassium bis(trimethylsilyl)amide gave *Z*-unsaturated ester **20** in 70% yield along with *E*-isomer **20'** (15%). These geometrical isomers were readily separated by chromatography on silica gel. Desilylation of **20** followed by PCC oxidation of the resulting alcohol **21** gave another substrate, **22**, in 95% yield. In a manner analogous to that described for the conversion of **17** into **19**, *Z*-isomer **22** was transformed into methyl ketone **24**. The ratio of diastereomers **23** was nearly 1:1.

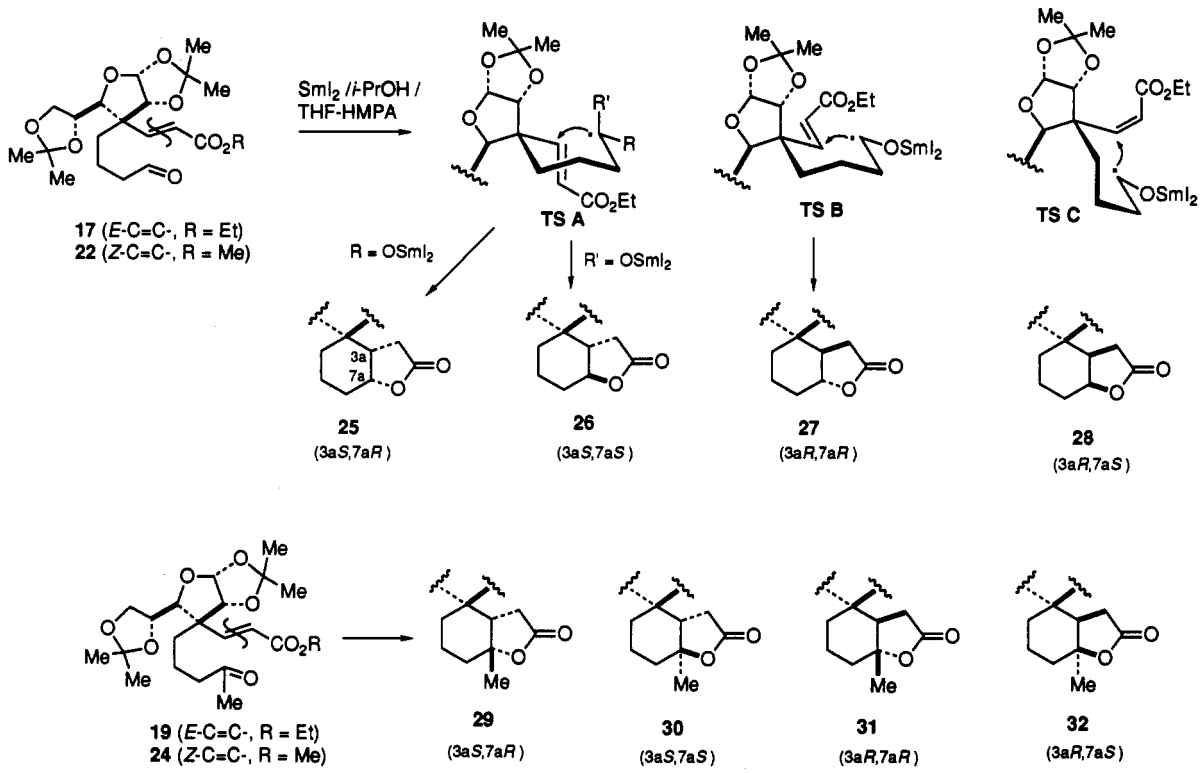
The Reductive Coupling of the Substrates and the Influence of the Transition States on the Stereoselectivity. With four substrates (**17**, **19**, **22**, and **24**) in

(22) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

(23) The Grignard addition to the aldehyde functionality in **17** was accompanied by 1,2- and 1,4-addition of the methyl group to the α,β-unsaturated ester. Thus, the yield of **18** did not exceed 70%.

(24) Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405.

Scheme III



hand, we explored their SmI_2-mediated reductive coupling reactions (Scheme III). Substrate **17** was treated with SmI_2 (2.5 mol equiv) in a mixture of THF and HMPA[25] (10:1 v/v) in the presence of 2-propanol (1.5 mol equiv) at rt. After an aqueous NH_4Cl quench and an extractive workup, the reaction mixture was separated by chromatography on silica gel. Three coupling products **25**, **26**, and **27** were isolated in yields of 35%, 17% , and 14%, respectively. Although unambiguous stereochemical assignment of these products by ^1H NMR analysis was difficult, their stereochemistries were established to be those depicted in Scheme III by stereochemically-defined chemical modifications[26] and eventually by transformation into **1**. The presence of HMPA is essential for smooth coupling. As a precedent reveals,[3b] significant reduction of the aldehyde to a hydroxymethyl group occurred without HMPA. 2-Methyl-2-propanol is also an effective proton source.

We also examined the reductive coupling reactions of substrates **19**, **22**,and **24**. In each case, the ratio of the coupling products was determined on the basis of the integration ratio of characteristic signals in the ^1H NMR (270 MHz) spectrum of the reaction mixture. *Z*-unsaturated ester **22** underwent a smooth coupling reaction under the same conditions used for **17**, affording the possible four products, **25**–**28**, in a ratio of 10:1:1:3 in a combined yield of 80%. In the case of methyl ketone **19**, an inseparable mixture of four coupling products, **29**–**32**, was obtained in a combined yield of 96%. The ratio of **29**–**32** was determined to be 3:18:18:1. 2-Methyl-2-propanol was used as a proton source in this case. The product of reduction of the methyl ketone carbonyl was the sole product when the coupling of **19** was carried out in the absence of HMPA. Determinations of the stereochemistries of the newly introduced stereogenic centers (C-3a and C-7a) in coupling products **29**–**32** was achieved by ^1H NMR comparison with diastereomerically pure **29**–**32**, independently synthesized from **25**.[27] The ratio of coupling products **29**–**32** was determined on the basis of the integration ratio of the ^1H NMR of the mixture. In the case of *Z*-isomer **24**, the ratio of **29**–**32** was almost the same as that obtained from *E*-isomer **19**. Products **29**–**32** were formed quantitatively in a ratio of 4:16:16:1 with either 2-propanol or 2-methyl-2-propanol.

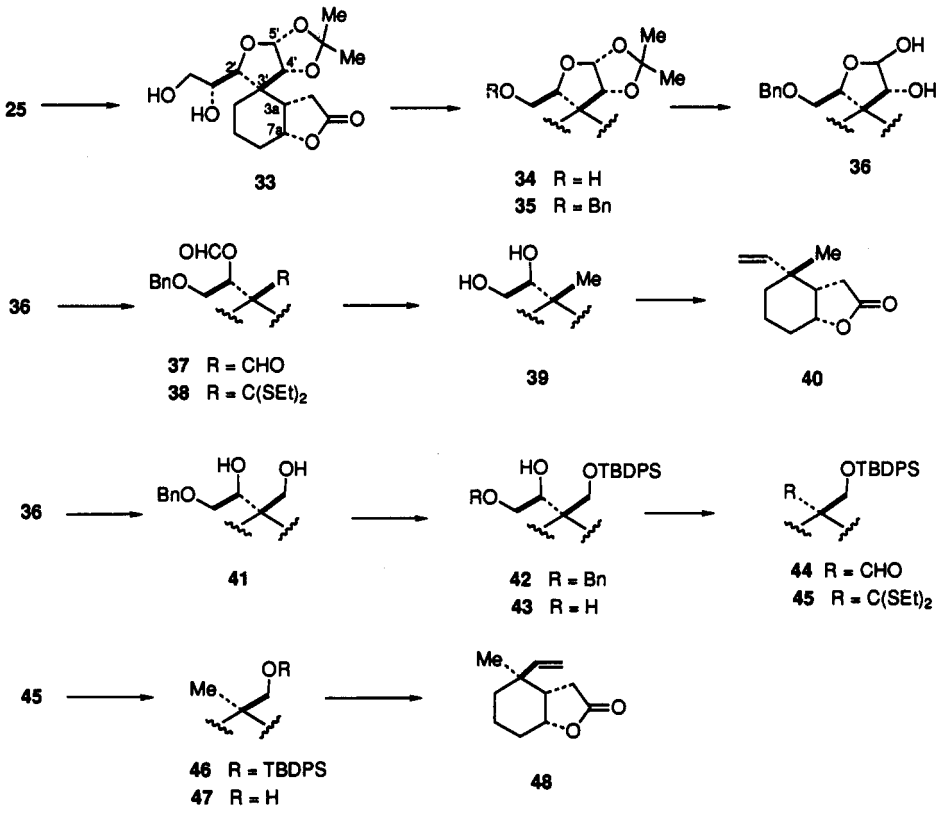
From these results, some conclusions can be drawn. The result obtained from the reaction of substrate **17** reveals that the *E*-configuration of the unsaturated ester is much more effective than the *Z*-isomer **22** for the preferential formation of the *S*-isomers at C-3a (3a*S*/3a*R* = **25** + **26**/**27** = 3.7/1 for **17** vs 3a*S*/3a*R* = **25** + **26**/**27** + **28** = 2.75/1 for **22**). Furthermore, the diastereoselectivity at C-7a is also moderately controlled (7a*R*/7a*S* = **25** + **27**/**26** = 2.9/1) in

(25) In an early report concerning the intermolecular reductive coupling reaction of cyclic ketone and acrylate,[3b] Inanaga and co-workers reported the importance of HMPA for acceleration of the reaction.

(26) Compounds **25** and **26** were converted into mono-*O*-acetylated cyclohexanols by reduction with $LiAlH_4$ and subsequent selective acetylation with Ac_2O/pyr. PCC oxidation of the secondary hydroxyl groups in both products gave the same cyclohexanone derivative. Therefore, **25** and **26** must be diastereomers at C-7a. The configuration at C-3a of **25** was confirmed after the transformation of **25** into an anastrephin C-3a isomer that was different from both anastrephin and epianastrephin. The configurations at C-7a of **25** and **26** were determined by careful examination of the ^1H NMR spectra of their respective di-*O*-acetyl derivatives, which were obtained by $LiAlH_4$ reduction followed by per-*O*-acetylation.

(27) Compounds **29** and **30** were prepared from γ-lactone **25** (or **26**) by the following reaction sequence: (1) $LiAlH_4$/THF, (2) TBDPSCl/imidazole/DMF, (3) PCC/MS4A/CH_2Cl_2, (4) MeLi/Et_2O/−15 °C, (5) separation of two adducts (the ratio of the diastereomers was 3:1, and the major isomer was converted into **29**), (6) *n*-Bu_4NF/THF, and (7) PCC/MS4A/CH_2Cl_2. For the preparation of **31** and **32**, the mono-*O*-acetylated cyclohexanone derivative prepared from **25** as mentioned in ref **26** was treated with $Ph_3P{=}CH_2$ in THF. To our surprise, the Wittig reaction proceeded with complete epimerization at C-3a. From the resulting *exo*-methylene derivative, compounds **31** and **32** were prepared as follows: (1) *m*-CPBA/$NaHCO_3$/CH_2Cl_2 (formation of a 3:1 diastereomeric mixture), (2) $LiAlH_4$/THF/reflux, (3) BzCl/pyridine, (4) separation of the resulting mono-*O*-benzoates, (5) $LiAlH_4$/THF for each mono-*O*-benzoate, and (6) PCC/CH_2Cl_2.

Scheme IV



the case of **17**. Chairlike transition states **A** and **B** may account for the preferential formation of the 3a*S*-isomers. The unsaturated ester group is disposed axially in TS **A** and equatorially in TS **B**. Inspection of Dreiding models of the proposed transition states supports the following explanations. A nonbonded interaction between the ethoxycarbonyl group and the *O*-isopropylidene group attached to the five-membered ring makes TS **B** unfavorable compared to TS **A**. In the intermediary ketyl structures, the samarium(II) alkoxide exists either equatorially (R = $OSmI_2$) or axially (R′ = $OSmI_2$). Apparently, when the samarium(II) alkoxide is axial, TS **A** suffers from a 1,3-diaxial-like interaction. As a result, *cis*-fused **25** is the preferred product. Although other ring-inverted chairlike transition states cannot be ruled out, TS **A** and TS **B** are most likely for **17**. Although somewhat lower stereoselectivity in the formation of the C-3aS isomers was observed in the case of *Z*-unsaturated ester **22**, the same transition-state argument used for **17** seems reasonable. In addition, the ratio of the *R*- and *S*-isomers at C-7a obtained from **22** (7a*R*/7a*S* = **25** + **27**/**26** + **28** = 2.75/1) is comparable to that from **17**. The fact that *cis*-lactone **28** was formed in a moderate ratio in the case of **22** indicates that the contribution of another ring inverted chairlike transition state (TS **C**) may be possible.

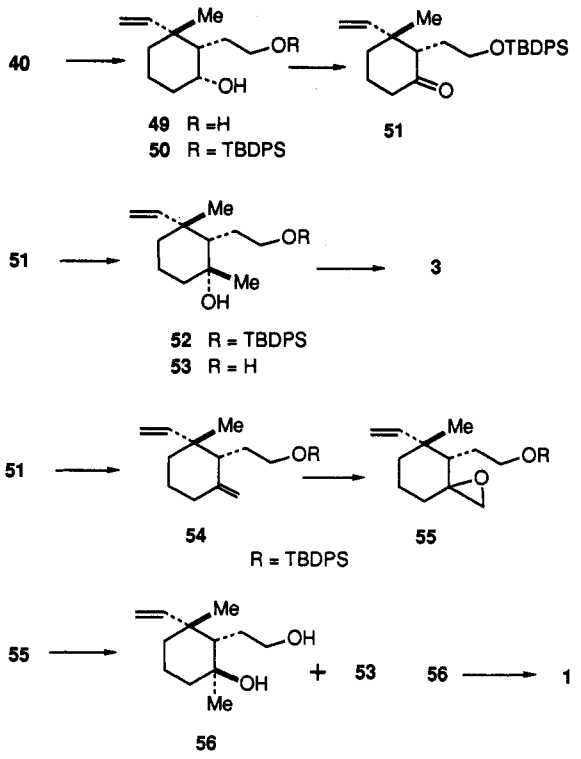
The stereochemical outcome with methyl ketones **19** and **24** was dramatically different than that with aldehydes **17** and **22**. In both cases, two *trans*-lactones, **30** and **31**, were predominant. The ratio of (3a*S*-isomer **30** and (3a*R*)-isomer **31** was almost same for **19** and **24**. These facts indicate that there is no conformation bias with regard to the chairlike transition states for **19** and **24**. It is quite likely that the methyl group in the ketyl (R or R′ = Me or $OSmI_2$) makes the transition states thermodynamically unstable. This conformational ambiguity results in the formation of both C-3a*S*- and *R*-isomers without any stereoselectivity. Although other factors may influence the stereochemistry, we did not investigate further to determine the precise mechanism of this lack of stereoselectivity.

Having established a route to hexahydrobenzofuran-2(3*H*)-one derivatives **25**–**32**, we used major coupling product **25** for the total syntheses of **1** and related pheromones. Although major product **30** already bears the desired C-7a angular methyl group with the correct configuration for synthesizing **1** and **2**, we were unable to remove undesired 3a*R*-isomer **31** from the reaction mixture obtained from **19** or **24**.[28]

Total Syntheses of 1–4. After some derivatizations of the γ-lactone part of **25**, we concluded that functionalization of the tetrahydrofuran part prior to the modification of the γ-lactone part was necessary. Selective removal of the *O*-isopropylidene group attached at C-2′ of **25** gave diol **33** in 80% yield (8% of **25** was recovered) (Scheme IV). The glycol in **33** was cleaved by $NaIO_4$-oxidation, and the resulting aldehyde was reduced with $NaBH_4$ to hydroxymethyl derivative **34** in 90% yield. Temporary protection of the hydroxyl group in **34** as a benzyl ether by means of the standard procedure gave **35**. Removal of the *O*-isopropylidene group in **35** with 60% aqueous TFA gave hemiacetal **36** as an anomeric mixture. The conversion of **34** and **36** was achieved in an overall yield of 68% without accompanying hydrolysis of the γ-lactone ring. $NaIO_4$-mediated glycol cleavage of hemiacetal mixture **36** and subsequent treatment of the resulting aldehyde **37** with EtSH in the presence of

(28) The utility of **30**, prepared independently from compound **25** as described in ref 27, as an attractive precursor was considered. However, selective hydrolysis of the isopropylidene group in the side chain attached at the tetrahydrofuran ring of **30** was found to be difficult after several reaction conditions were examined. The γ-lactone functionality was also easily hydrolyzed under the acidic conditions examined.

Scheme V



concentrated HCl afforded dithioacetal **38** in 79% yield. Desulfurization of dithioacetal **38** with Raney nickel in refluxing EtOH gave **39** in 52% yield as a result of concurrent removal of the benzyl and formyl groups. The glycol in **39** was cleaved, and subsequent Wittig reaction of the resulting aldehyde with methylenetriphenylphosphorane in THF gave vinyl derivatve **40** quantitatively.

Alternatively, $NaBH_4$ reduction of the aldehyde **37** gave diol **41** in 84% yield based on the amount of **36**. Selective protection of the primary hydroxyl group in **41** as a silyl ether afforded *O*-tert-butyldiphenylsilyl (TBDPS) derivative **42** in 83% yield. Hydrogenolytic removal of the benzyl group in **42**, glycol cleavage of the resulting diol **43**, and subsequent treatment of aldehyde **44** with EtSH gave dithioacetal **45** in an overall yield of 67%. Desulfurization of **45** and subsequent removal of the silyl group gave **47** via **46** in 81% yield for two steps. An oxidation–Wittig olefination sequence converted the hydroxyl group in **47** into a vinyl group and afforded **48** in 85% yield. Thus, starting from major coupling product **25**, two key intermediates, **40** and **48**, for the total syntheses of **1** and **2**, respectively, were prepared.

We next investigated the introduction of a methyl group into C-7a of **40** (Scheme V). For this purpose, the γ-lactone ring in **40** was reduced with $LiAlH_4$ to give diol **49**. Then, selective protection of the primary hyroxyl group in **49** as a TBDPS ether afforded **50**. Compound **50** was then converted into cyclohexanone derivative **51** by PCC oxidation. The overall yield of **51** was 79% from **40**. Unfortunately, attack of MeLi on the carbonyl group in **51** occurred exclusively from the undesired *si*-face resulting in the formation of **52** in 82% yield. Deprotection of the silyl group in **52** with *n*-Bu_4NF gave diol **53**. PCC oxidation of **53** gave (−)-7a-*epi*-anastrephin (**3**) in 83% yield. This oxidation was accompanied by γ-lactone formation. Although a preliminary account of the synthesis of racemic **3** has appeared,[7] no details of the procedure and characterization are available so far. As mentioned above, the attack of MeLi on **51** (or **59**) occurred exclusively from the *si*-face regardless of the C-4 configuration. Thus, we expected that epoxidation of an *exo*-methylene derivative such as **54** would also occur from the same direction. If this expectation was confirmed, the β-epoxide thus obtained could be converted into the desired **1**. Methylene derivative **54** was prepared from **51** in 88% yield without concomitant epimerization of the adjacent carbon[29] by means of a modified[30] Takai–Oshima–Nozaki olefination.[31] Epoxidation of **54** with 1.0 mol equiv of *m*-chloroperbenzoic acid (*m*-CPBA) at 0 °C proceeded regioselectively. Monoepoxide **55** was obtained in 57% yield, and 34% of **54** was recovered. The regioisomeric monoepoxide was not formed as a result of epoxidation at the vinyl group attached to the quaternary carbon, nor was diepoxide(s) detected in the reaction mixture. When the epoxidation was executed with excess *m*-CPBA, diepoxides did appear in the reaction mixture. Contrary to our expectation, the epoxidation of **54** proceeded without stereoselectivity and afforded an inseparable mixture of α- and β-epoxides **55**. The oxirane rings in mixture **55** were cleaved with $LiAlH_4$ in refluxing THF. Under these conditions, the hydride attack occurred exclusively at the methylene carbon of the oxirane ring. As a result, tertiary alcohol **56** and its diastereomer **53** were formed. Alcohols **56** and **53** were readily separated by chromatography on silica gel in 57% and 33% yields, respectively. PCC oxidation of **56** gave **1** in 63% yield. The mp and $[\alpha]_D$ of the synthetic **1** agreed with those reported in the literature.[13] Also, the ^1H and ^{13}C NMR of the synthetic **1** were in complete accord with those reported for the antipode and the racemate.[13]

From hexahydrobenzofuran-2-(3*H*)-one derivative **48**, (−)-epianastrephin (**2**) and (−)-7a-*epi*-epianastrephin (**4**) were synthesized by means of virtually the same transformations described for the preparations of **1** and **3** from **40**. Namely, **2** was synthesized by the following reaction sequence (Scheme VI): (1) $LiAlH_4$-reduction of **48**, (2) selective protection of the resulting alcohol **57** as silyl ether **58**, (3) PCC oxidation (**58** to **59**), (4) methylenation of cyclohexanone **59** to afford **62** (overall yield of **62** from **48** was 83%), (5) regioselective epoxidation of *exo*-methylene **62** with *m*-CPBA to afford a mixture of α- and β-epoxides **63** (86% after recycling steps), (6) oxirane ring cleavage and concomitant desilylation of 1:2 diastereomeric mixture **63** with $LiAlH_4$ (96% yield), (7) PCC oxidation of the resulting mixture of diastereomers (**64** and **65**), and finally (8) separation of the mixture of the resulting γ-lactones to afford **2** and **4** in 48% and 32% yields, respectively. The mp, $[\alpha]_D$, and ^1H and ^{13}C NMR of the synthetic **2** were identical with those reported.[13] In the epoxidation, some preference for the formation of the β-epoxide was observed in the case of **62**. Meanwhile, in analogy to **51**, **59** underwent attack by the methyl anion (MeLi) exclusively on the *si*-face and afforded **60** in 74% yield (8% of **59** was recovered). Compound **60** was converted into **4** in the manner described for the conversion of **52** to **3**.

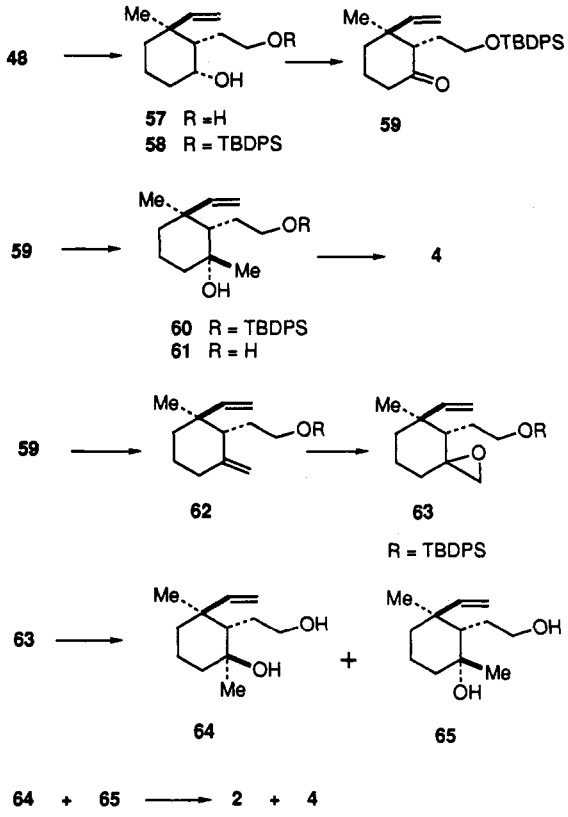
In conclusion, by using carbohydrate-derived structurally congested compound **17** as a substrate, we have shown that SmI_2 works as a mediator for intramolecular reductive

(29) Wittig methylenation of **51** ($Ph_3P{=}CH_2$/THF) also proceeded smoothly; however, partial epimerization of the adjacent carbon occurred (ca. 20%). As a result, a 4:1 (270-MHz NMR) inseparable mixture of the *exo*-methylene derivatives was obtained. This epimerization was also observed in the case of Wittig methylenation of **59**.

(30) Lombardo, L. *Tetrahedron Lett.* **1982**, *23*, 4293.

(31) Takai, K.; Hotta, Y.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1978**, 2417; *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1698.

Scheme VI



coupling reactions. The stereoselectivity of the coupling reaction can be explained in terms of chainlike transition states. Furthermore, the versatility of reductive coupling products such as **25** is evidenced by the transformation of **25** into some natural and unnatural insect pheromones (**1**–**4**).

Experimental Section[32]

(2*R*,3*R*,4*R*,5*S*)-4-(2-Hydroxyethyl)-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (8).[33] To a cold (0 °C), stirred suspension of $LiAlH_4$ (4.37 g, 115 mmol) in THF (100 mL) was added a solution of **7** (20.7 g, 58.2 mmol) in THF (100mL) dropwise. After being stirred at rt for 1 h, the mixture was quenched with H_2O (15 mL) and diluted with 1 M aqueous NaOH (5 mL) and H_2O (15 mL). The resulting white solids were removed by filtration and washed with EtOAc (800 mL). The combined filtrate and washing were washed with H_2O (300 mL). The aqueous layer was extracted with EtOAc (100 mL × 2). The organic layers were combined and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:2)) to give 18.2 g (quantitatively) of **8** as a colorless oil: TLC R_f 0.39 (EtOAc/hexane (1:1)); $[\alpha]^{29}_D$ +41.4° (*c* 1.70, $CHCl_3$); IR (neat) 3460, 2990, 2940, 2890, 1640, 1460, 1380, 1250, 1220, 1160 cm^{-1}; ^1H NMR (90 MHz) δ 1.32, 1.39 (2 s, 9 H, 3 H), 1.66–2.12 (m, 3 H), 3.75–3.89, 3.96–4.16 (2 m, total 6 H), 4.64 (d, *J* = 3.8 Hz, 1 H), 5.27 (dd, *J* = 1.9, 10.4 Hz, 1 H), 5.28 (dd, *J* = 1.9, 18.0 Hz, 1 H), 5.76 (d, *J* = 3.8 Hz, 1 H), 6.01 (dd, *J* = 10.4, 18.0 Hz, 1 H). Anal. Calcd for $C_{16}H_{26}O_6$; C, 61.13; H, 8.34. Found: C, 61.21; H, 8.24.

(2*R*,3*R*,4*R*,5*S*)-4-(2-Iodoethyl)-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (9). The following reaction was carried out under Ar. To a cold (0 °C), stirred solution of **8** (18.2 g, 58.0 mmol) and Ph_3P (30.4 g, 116 mmol) in THF (200 mL) was added diethyl azodicarboxylate (16.5 mL, 107 mmol). After the reaction mixture was stirred for 15 min, MeI (7.25 mL, 116 mmol) was added to the mixture. The mixture was stirred at rt for 8 h and then concentrated. The residue was diluted with EtOAc (600 mL) and washed with H_2O (200 mL × 3). The organic layer was dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:25)) to give 22.2 g (90%) of **9** as white crystals; mp 49.5–51.0 °C; TLC R_f 0.58 (EtOAc/hexane (1:5)); $[\alpha]^{28}_D$ +10.4° (*c* 1.02, $CHCl_3$); IR (neat) 2990, 2940, 2880, 1450, 1380, 1250 cm^{-1}; ^1H NMR (270 MHz) δ 1.32, 1.34, 1.39, 1.52 (4 s, H × 4), 2.02 (ddd, *J* = 5.5, 12.3, 14.1 Hz, 1 H), 2.34 (ddd, 1 H, *J* = 4.9, 12.1, 14.1 Hz, 1 H), 3.18 (ddd, *J* = 5.5, 9.7, 12.1 Hz, 1 H), 3.28 (ddd, *J* = 4.9, 9.7, 12.3 Hz, 1 H), 3.89–4.16 (m, 4 H), 4.46 (d, *J* = 3.3 Hz, 1 H), 5.30 (dd, *J* = 0.9, 17.8 Hz, 1H), 5.34 (dd, *J* = 0.9, 11.4 Hz, 1 H), 5.75 (d, *J* = 3.3 Hz, 1 H), 5.90 (dd, *J* = 11.4, 17.8 Hz, 1 H). Anal. Calcd for $C_{16}H_{25}O_5I$: C, 45.30; H, 5.94. Found: C, 45.65; H, 5.68.

(2*R*,3*R*,4*R*,5*S*)-2,3-(Isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-[3,3-bis(methoxycarbonyl)propyl]-4-vinyltetrahydrofuran (10). The following reaction was carried out under Ar. To a stirred suspension of NaH (6.30 g, 158 mmol) in THF (100 mL) was added $CH_2(COOMe)_2$ (18.0 mL, 158 mmol). After the mixture was stirred for 30 min, a solution of **9** (22.2 g, 52.3 mmol) in THF (100 mL) was added to the mixture dropwise at 0 °C. The resulting solution was refluxed for 24 h. After being cooled to rt, the solution was diluted with saturated aqueous NH_4Cl (30 mL). The diluted solution was concentrated, and the residue was partitioned between EtOAc (600 mL) and H_2O (200 mL). The organic layer was washed with H_2O (200 mL × 2), dried, and concentrated to give TLC-homogeneous **10** (32.5 g), which was used in the next step without further purification. An analytical sample was obtained by chromatography on silica gel (EtOAc/hexane (1:5)). **10**: a pale yellow oil; TLC R_f 0.25 (EtOAc/hexane (1:3)); $[\alpha]^{28}_D$ +17.3° (*c* 0.89, $CHCl_3$); IR (neat) 2990, 2950, 2890, 1750, 1745, 1455, 1435, 1380, 1240, 1210, 1160 cm^{-1}; ^1H NMR (270 MHz) δ 1.33, 1.39, 1.53 (3 s, 6 H, 3 H, 3 H), 1.60–1.68, 1.95–2.05 (2 m, 2 H × 2), 3.34 (t, *J* = 7.3 Hz, 1 H), 3.75, 3.76 (2 s, 3 H × 2), 3.90–3.95, 4.01–4.19 (2 m, 1 H, 3 H), 4.53 (d, *J* = 3.3 Hz, 1 H), 5.28 (dd, *J* = 1.5, 18.3 Hz, 1 H), 5.29 (dd, *J* = 1.5, 11.0 Hz, 1 H), 5.73 (d, *J* = 3.3 Hz, 1 H), 5.93 (dd, *J* = 11.0, 18.3 Hz, 1 H). Anal. Calcd for $C_{21}H_{32}O_9$: C, 58.87; H, 7.53. Found: C, 58.88; H, 7.34.

(2*R*,3*R*,4*R*,5*S*)-2,3-(Isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-[3-(methoxycarbonyl)propyl)]-4-vinyltetrahydrofuran (11). A solution of **10** obtained above (32.5 g) in a mixture of DMSO (210 mL) and H_2O (35 mL) was heated at 160 °C in the presence of NaCl (9.18 g, 157 mmol) for 24 h. After being cooled to rt, the solution was diluted with H_2O (700 mL). The whole was extracted with CH_2Cl_2 (200 mL × 4). The combined extracts were dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:8)) to give 14.5 g (75% from **9**) of **11** as a colorless oil: TLC R_f 0.56 (EtOAc/hexane (1:2)); $[\alpha]^{28}_D$ +24.0° (*c* 1.05, $CHCl_3$); IR (neat) 2990, 2950, 2880, 1740, 1435, 1370, 1250, 1210, 1165 cm^{-1}; ^1H NMR (270 MHz) δ 1.325, 1.330, 1.39, 1.53 (4 s, 3 H × 4), 1.63–1.80, 2.29–2.42 (2 m, 4 H, 2 H), 3.76 (s, 3 H), 3.92–3.99, 4.03–4.15 (2 m, 1 H, 3 H), 4.52 (d, *J* = 3.3 Hz, 1 H), 5.271 (dd, *J* = 1.5, 18.3 Hz, 1 H), 5.273 (dd, *J* = 1.5, 11.0 Hz, 1 H), 5.74 (d, *J* = 3.3 Hz, 1 H), 5.95 (dd, *J* = 11.0, 18.3 Hz, 1 H). Anal. Calcd for $C_{19}H_{30}O_7$: C, 61.60; H, 8.16. Found: C, 61.37; H, 7.98.

(2*R*,3*R*,4*R*,5*S*)-4-(4-Hydroxybutyl)-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (12). To a cold (0 °C), stirred suspension of $LiAlH_4$ (3.00 g, 79.0 mmol) in THF (100 mL) was added a solution of **11** (14.5 g, 39.0 mmol) in THF (100 mL) dropwise. The mixture was stirred at rt for 1 h, and then H_2O (15 mL), 15% aqueous NaOH (5 mL), and H_2O (15 mL) were added successively. The resulting solids were removed by filtration and washed well with EtOAc (400 mL). The combined filtrate and washing were washed

(32) For a general procedure, see ref 5. Commercial NaH (60% emulsion in mineral oil) was used without washing. Commercial methyl iodide (MeI) was washed with diluted aqueous Na_2SO_3 solution and H_2O, dried over $CaCl_2$, and then distilled in the dark. 2-Propanol and 2-methyl-2-propanol were dried over CaO and then distilled. Dimethyl malonate was distilled under reduced pressure. Samarium(II) iodide was purchased from Aldrich Chemical Co. as a 0.1 M solution in THF.

(33) Compounds **8**–**24** were named as derivatives at 2,3,4,4,5-pentasubstituted tetrahydrofuran, compounds **25**–**27** and **33**–**36** as derivatives of 2′,3a,4′,5′,7a-pentasubstituted spiro[hexahydrobenzofuran-4,3′-tetrahydrofuran]-2(3*H*)-one, compounds **38**–**48** and **1**–**4** as derivatives of 4,4-disubstituted hexahydrobenzofuran-2(3*H*)-one, and compounds **49**–**65** as derivatives of substituted cyclohexane.

with H_2O (400 mL). The aqueous layer was extracted with EtOAc (150 mL × 3). The combined organic layers were dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:4)) to give 13.4 g (quantitatively) of **12** as a colorless oil: TLC R_f 0.36 (EtOAc/hexane (1:1)); $[\alpha]^{30}_D$ +37.4° (*c* 1.27, $CHCl_3$); IR (neat) 3450, 2990, 2940, 2880, 1640, 1450, 1380, 1370, 1250, 1215 cm^{-1}; ^1H NMR (270 MHz) δ 1.32, 1.33, 1.40, 1.53 (4 s, 3 H × 4), 1.43–1.70 (2 m, total 7 H), 3.66 (t, *J* = 6.1 Hz, 2 H), 3.91–3.98, 4.03–4.16 (2 m, 1 H, 3 H), 4.49 (d, *J* = 3.3 Hz, 1 H), 5.26 (dd, *J* = 1.5, 18.3 Hz, 1 H), 5.27 (dd, *J* = 1.5, 11.0 Hz, 1 H), 5.73 (d, *J* = 3.3 Hz, 1 H), 5.95 (dd, *J* = 11.0, 18.3 Hz, 1 H). Anal. Calcd for $C_{18}H_{30}O_6$: C, 63.13; H, 8.83. Found: C, 62.96; H, 8.75.

(2*R*,3*R*,4*R*,5*S*)-2,3-(Isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-[4-(*tert*-butyldimethylsilyloxy)-butyl]-4-vinyltetrahydrofuran (13). To a cold (0 °C), stirred solution of **12** (13.0 g, 38.0 mmol) in DMF (150 mL) were added TBDMSCl (8.58 g, 56.9 mmol) and imidazole (7.15 g, 113.8 mmol). After being stirred at rt for 8 h, the mixture was diluted with EtOAc (700 mL). The diluted mixture was washed with H_2O (150 mL × 4). The organic layer was dried and concentrated to give 19.1 g of crude **13**, which was used in the next step without purification. For an analytical sample, crude **13** was purified by column chromatography on silica gel (EtOAc/hexane (1:20)). Compound **13** was obtained as a colorless oil: TLC R_f 0.58 (EtOAc/hexane (1:5)); $[\alpha]^{29}_D$ +24.1° (*c* 0.84, $CHCl_3$); IR (neat) 2990, 2955, 2940, 2860, 1640, 1460, 1380, 1370, 1250, 1220 cm^{-1}; ^1H NMR (270 MHz) δ 0.05 (s, 6 H), 0.89 (s, 9 H), 1.32, 1.33, 1.40, 1.53 (4 s, 3 H × 4), 1.37–1.63 (m, 6 H), 3.62 (t, *J* = 6.1 Hz, 2 H), 3.92–3.98, 4.04–4.15 (2 m, 1 H, 3 H), 4.48 (d, *J* = 3.3 Hz, 1 H), 5.24 (dd, *J* = 1.5, 18.3 Hz, 1 H), 5.25 (dd, *J* = 1.5, 11.0 Hz, 1 H), 5.73 (d, *J* = 3.3 Hz, 1 H), 5.89–6.00 (m, 1 H). Anal. Calcd for $C_{24}H_{44}O_6Si$: C, 63.12; H. 9.71. Found: C, 62.89; H, 9.47.

(2*R*,3*R*,4*R*,5*S*)-4-Formyl-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-[4-*tert*-butyldimethylsilyloxy)butyl]tetrahydrofuran (14). Ozone (ca. 3% in O_2) was bubbled through a cold (−78 °C), stirred solution of **13** obtained above (19.1 g) in CH_2Cl_2 (140 mL) for 5 h. Then Ph_3P (12.9 g, 49.2 mmol) was added to the solution, and the mixture was stirred at −78 °C for 1 h. After being warmed gradually to rt, the mixture was concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:20)) to give 17.6 g of **14**, which used in the next step in spite of contamination by a small amount of $Ph_3P{=}O$. An analytical sample of **14** was obtained by repeated chromatography. Compound **14** was obtained as a colorless oil: TLC R_f 0.44 (EtOAc/hexane (1:5)); $[\alpha]^{30}_D$ +48.3° (*c* 0.71, $CHCl_3$); IR (neat) 3000, 2960, 2940, 2860, 1730, 1460, 1380, 1375, 1255, 1215 cm^{-1}; ^1H NMR (270 MHz) δ 0.05 (s, 6 H), 0.89 (s, 9 H), 1.30, 1.37, 1.57 (3 s, 6 H, 3 H, 3 H), 1.45–1.61, 1.81–1.94 (2 m, 3 H, 1 H), 3.63 (t, *J* = 5.6 Hz, 2 H), 3.95–4.16 (m, 3 H), 4.48 (d, *J* = 8.8 Hz, 1 H), 4.67 (d, *J* = 3.4 Hz, 1 H), 5.79 (d, *J* = 3.4 Hz, 1 H), 9.70 (s, 1 H). Anal. Calcd for $C_{23}H_{42}O_7Si$: C, 60.23; H, 9.23. Found: C, 60.07; H, 9.11.

(2*R*,3*R*,4*R*,5*S*)-4-[(*E*)-2-(Ethoxycarbonyl)etheneyl]-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)-ethyl]-4-[4-(*tert*-butyldimethylsilyloxy)butyl]tetrahydrofuran (15). The following reaction was carried out under Ar. To a cold (0 °C), stirred suspension of NaH (3.80 g, 95.0 mmol) in THF (90 mL) was added $(EtO)_2P(O)CH_2COOEt$ (19.0 mL, 95.0 mmol). After the mixture stirred at rt for 15 min, a solution of **14** (17.6 g) obtained as described above in THF (100 mL) was added to the mixture dropwise. The mixture was stirred at rt for 2 h and then quenched with H_2O (20 mL) at 0 °C and concentrated. The residue was partitioned between EtOAc (700 mL) and H_2O (200 mL). The organic layer was washed with H_2O (200 mL × 2), dried, and concentrated to give 24.1 g of crude **15**, which was used in the next step. An analytical sample of **15** was obtained by column chromatography on silica gel (EtOAc/hexane (1:10)). Compound **15** was obtained as a colorless oil: TLC R_f 0.40 (EtOAc/hexane (1:5)); $[\alpha]^{30}_D$ +34.0° (*c* 1.24, $CHCl_3$); IR (neat) 2990, 2960, 2940, 2860, 1720, 1650, 1460, 1380, 1370, 1310, 1255, 1215 cm^{-1}; ^1H NMR (270 MHz) δ 0.05 (s, 6 H), 0.89 (s, 9 H), 1.30, (t, *J* = 7.3 Hz, 3 H), 1.32, 1.38, 1.52 (3 s, 6 H, 3 H, 3 H), 1.35–1.73 (m, 6 H), 3.61 (t, *J* = 6.1 Hz, 2 H), 3.90–4.15 (m, 4 H), 4.20 (dq, *J* = 1.1, 7.3 Hz, 2 H), 4.53 (d, *J* = 3.3 Hz, 1 H), 5.74 (d, *J* = 3.3 Hz, 1 H), 6.05 (d, *J* = 16.3 Hz, 1 H), 7.06 (d, *J* = 16.3 Hz, 1 H). Anal. Calcd for $C_{27}H_{48}O_8Si$: C, 61.33; H, 9.15. Found: C, 61.30; H, 9.11.

(2*R*,3*R*,4*R*,5*S*)-4-[(*E*)-2-(Ethoxycarbonyl)ethenyl]-4-(4-hydroxybutyl)-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]tetrahydrofuran (16). To a cold (0 °C), stirred solution of **15** (24.1 g), obtained as described above, in THF (150 mL) was added *n*-Bu_4NF (45.5 mL, 45.5 mmol, 1.0 M solution in THF). The mixture was stirred at rt for 7 h and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane, (1:4)) to give 14.0 g (89% overall yield from **12**) of **16** as a colorless oil: TLC R_f 0.35 (EtOAct/hexane (2:3)); $[\alpha]^{30}_D$ +40.2° (*c* 1.35, $CHCl_3$); IR (neat) 3470, 2990, 2940, 2875, 1720, 1665, 1460, 1370, 1310, 1265, 1220 cm^{-1}; ^1H NMR (270 MHz) δ 1.30 (t, *J* = 7.3 Hz, 3 H), 1.31, 1.32, 1.38, 1.56 (4 s, 3 H × 4), 1.40–1.80 (m, 7 H), 3.67 (t, *J* = 6.2 Hz, 2 H), 3.90–4.14 (m, 4 H), 4.21 (dq, *J* = 1.1, 7.3 Hz, 2 H), 4.55 (d, *J* = 3.3 Hz, 1 H), 5.75 (d, *J* = 3.3 Hz, 1 H), 6.08 (d, *J* = 16.3 Hz, 1 H), 7.06 (d, *J* = 16.3 Hz, 1 H). Anal. Calcd for $C_{21}H_{34}O_8$: C, 60.85; H, 8.27. Found: C, 60.51; H, 8.06.

(2*R*,3*R*,4*R*,5*S*)-4-[(*E*)-2-(Ethoxycarbonyl)ethenyl]-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-(oxobutyl)tetrahydrofuran (17). To a cold (0 °C), stirred suspension of PCC (4.26 g, 19.8 mmol) and powdered molecular sieves (4A, 4.00 g) in CH_2Cl_2 (20 mL) was added a solution of **16** (2.05 g, 4.94 mmol) in CH_2Cl_2 (25 mL) dropwise. The mixture was vigorously stirred at rt for 30 min. The solvent was removed by evaporation, and the residue was transferred to a silica gel column (50 g). The column was eluted with an excess of Et_2O to give 1.68 g (82%) of **17** as a colorless oil: TLC R_f 0.49 (EtOAc/hexane (1:1)); IR (neat) 2990, 2940, 2880, 1720, 1650, 1460, 1370, 1310, 1260, 1215 cm^{-1}; ^1H NMR (270 MHz) δ 1.29 (t, *J* = 7.3 Hz, 3 H), 1.31, 1.32, 1.37, 1.52 (4 s, 3 H × 4), 1.42–1.74 (m, 4 H), 2.50–2.54 (m, 2 H), 3.90–4.15 (m, 4 H), 4.20 (dq, *J* = 1.0, 7.3 Hz, 2 H), 4.58 (d, *J* = 3.4 Hz, 1 H), 5.76 (d, *J* = 3.4 Hz, 1 H), 6.08 (d, *J* = 16.3 Hz, 1 H), 7.05 (d, *J* = 16.3 Hz, 1 H), 9.78 (t, *J* = 1.0 Hz, 1 H).

Mixture of (2*R*,3*R*,4*R*,5*S*)-4-[(*E*)-2-(Ethoxycarbonyl)-ethenyl]-4-[(4*R* and -*S*)-4-hydroxypentyl]-2,3-(isopropylidenedioxy)-5-[(1*S*)-1,2-(isopropylidenedioxy)ethyl]-tetrahydrofuran (18). The following reaction was carried out under Ar. To a cold (0 °C), stirred solution of **17** (110 mg, 0.27 mmol) in THF (3 mL) was added MeMgBr (0.34 mL, 0.32 mmol, 0.95 M solution in THF). After being stirred at 0 °C for 30 min, the mixture was quenched with H_2O (0.5 mL) and then diluted with EtOAc (30 mL). The whole was washed with 0.2 M HCl (10 mL × 2), saturated aqueous $NaHCO_3$ (10 mL), and H_2O (10 mL), successively. The organic layer was dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:2)) to give 85.6 mg (68%) of an inseparable mixture **18** as a colorless oil: TLC R_f 0.39 (EtOAc/hexane (1:1)); IR (neat) 3470, 2990, 2940, 2880, 1720, 1650, 1460, 1370, 1310, 1270, 1215, 1170 cm^{-1}; ^1H NMR (270 MHz) δ 1.20 (d, *J* = 6.2 Hz, 3 H), 1.30 (t, *J* = 7.3 Hz, 3 H), 1.32, 1.33, 1.38, 1.52 (4 s, 3 H × 4), 1.41–1.78 (m, 6 H), 3.78–3.86, 3.91–4.03, 3.91–4.14 (3 m, 1 H, 2 H, 2 H), 4.20 (q, *J* = 7.3 Hz, 2 H), 4.54 (d, *J* = 3.3 Hz, 1 H × 1/2), 4.55 (d, *J* = 3.3 Hz, 1 H × 1/2), 5.74 (d, *J* = 3.3 Hz, 1 H × 1/2), 5.75 (d, *J* = 3.3 Hz, 1 H × 1/2), 6.065 (d, *J* = 16.5 Hz, 1 H × 1/2), 6.069 (d, *J* = 16.5 Hz, 1 H × 1/2), 7.06 (d, *J* = 16.5 Hz, 1 H); HRMS calcd for $C_{22}H_{36}O_8$ (M^+) *m/z* 428.2408, found 428.2442.

(2*R*,3*R*,4*R*,5*S*)-4-[(1*E*)-2-(Ethoxycarbonyl)ethenyl]-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)-ethyl]-4-(4-oxopentyl)tetrahydrofuran (19). To a stirred solution of **18** (98 mg, 0.23 mmol) in CH_2Cl_2 (2 mL) were added PCC (230 mg, 1.08 mmol) and powdered molecular sieves (4A, 120 mg). After being stirred for 1 h at rt, the mixture was transferred to a short silica gel column (4 g). The column was eluted with an excess Et_2O to give 90 mg (92%) of **18** as a colorless oil: TLC R_f 0.53 (EtOAc/hexane (1:1)); $[\alpha]^{28}_D$ +31.3° (*c* 0.29, $CHCl_3$); IR (neat) 2990, 2940, 2880, 1720, 1650, 1460, 1370, 1310, 1270, 1215, 1170 cm^{-1}; ^1H NMR (270 MHz) δ 1.30 (t, *J* = 7.3 Hz, 3 H), 1.32, 1.37, 1.52 (3 s, 6 H, 3 H, 3 H), 1.42–1.68 (m, 4 H), 2.17 (s, 3 H), 2.40–2.55 (m, 2 H), 3.91–4.01, 4.06–4.14 (2 m, 2 H × 2), 4.20 (dq, *J* = 1.0, 7.3 Hz, 2 H), 4.61 (d, *J* = 3.3 Hz, 1 H), 5.76 (d,

J = 3.3 Hz, 1 H), 6.08 (d, J = 16.5 Hz, 1 H), 7.05 (d, J = 16.5 Hz, 1 H); HRMS calcd for $C_{22}H_{34}O_8$ (M^+) m/z 426.2251, found 426.2241.

(2*R*,3*R*,4*R*,5*S*)-2,3-(Isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-[(*Z*)-2-(methoxycarbonyl)ethenyl]-4-[4-[(*tert*-butylmethylsilyl)oxy]butyl]tetrahydrofuran (20). The following reaction was carried out under Ar. To a cold (−78 °C), stirred solution of bis(2,2,2-trifluoroethyl)[(methoxycarbonyl)methyl]phosphonate (0.195 mL, 0.92 mmol) and 18-crown-6 (1.23 g, 4.65 mmol) in THF (3 mL) was added $KN(TMS)_2$ (1.84 mL, 0.92 mmol, 0.5 M solution in toluene) dropwise. After the mixture was stirred at −78 °C for 20 min, a solution of **14** (302 mg, 0.66 mmol) in THF (4.5 mL) was added. The mixture was stirred at 5 °C for 14 h, quenched with saturated aqueous NH_4Cl (1 mL), and concentrated. The residue was partitioned between EtOAc (40 mL) and H_2O (15 mL). The organic layer was washed with H_2O (15 mL × 2), dried, and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:20–1:15)) to give 236 mg (70%) of **20** and 51 mg (15%) of the *E*-isomer (**20′**). Compound **20** was obtained as a colorless oil: TLC R_f 0.72 (EtOAc/hexane (1:3)); $[\alpha]^{21}_D$ + 32.0° (*c* 1.59, $CHCl_3$); IR (neat) 2960, 2940, 2860, 1730, 1650, 1440, 1380, 1370, cm^{-1}; ^{1}H NMR (270 MHz) δ 0.03 (s, 6 H), 0.88 (s, 9 H), 1.26, 1.35, 1.42, 1.46 (4 s, 3 H × 4), 1.35–1.75 (m, 6 H), 3.57–3.61, 3.89–3.95, 4.10–4.19 (3 m, 2 H × 3), 3.70 (s, 3 H), 5.00 (d, J = 3.4 Hz, 1 H), 5.66 (d, J = 3.4 Hz, 1 H), 5.90 (d, J = 12.7 Hz, 1 H), 6.26 (d, J = 12.7 Hz, 1 H). Anal. Calcd for $C_{26}H_{46}O_8Si$: C, 60.67; H, 9.01. Found: C, 60.53; H, 8.96. Compound **20′** was obtained as a colorless oil: TLC R_f 0.65 (EtOAc/hexane (1:3)); $[\alpha]^{24}_D$ +33.9° (*c* 1.05, $CHCl_3$); IR (neat) 2960, 2940, 2860, 1730, 1660, 1460, 1440, 1380, 1370 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.04 (s, 6 H), 0.89 (s, 9 H), 1.32, 1.38, 1.52 (3 s, 6 H, 3 H, 3 H), 1.25–1.75 (m, 6 H), 3.60–3.63, 3.93–4.14 (2 m, 2 H, 4 H), 3.74 (s, 3 H), 4.52 (d, J = 3.3 Hz, 1 H), 5.74 (d, J = 3.3 Hz, 1 H), 6.08 (d, J = 16.5 Hz, 1 H), 7.07 (d J = 16.5 Hz, 1 H). Anal. Calcd for $C_{26}H_{46}O_8Si$: C, 60.67; H, 9.01. Found: C, 60.85; H, 9.08.

(2*R*,3*R*,4*R*,5*S*)-4-(4-Hydroxybutyl)-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-[(*Z*)-2-(methoxycarbonyl)ethenyl]tetrahydrofuran (21). To a cold (0 °C), stirred solution of **20** (202 mg, 0.39 mmol) in THF (5 mL) was added *n*-Bu_4NF (0.75 mL, 0.75 mmol, 1.0 M solution in THF). After being stirred at rt for 4 h, the mixture was concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:3)) to give 157 mg (quantitatively) of **21** as a colorless oil: TLC R_f 0.23 (EtOAc/hexane (1:2)); $[\alpha]^{24}_D$ +50.4° (*c* 0.78, $CHCl_3$); IR (neat) 3470, 2990, 2950, 2880, 1730, 1640, 1440, 1380, 1370 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.26, 1.35, 1.43, 1.46 (4 s, 3 H × 4), 1.30–1.77 (m, 7 H), 3.62–3.66, 3.87–4.09, 4.11–4.20 (3 m, 2 H × 3), 3.70 (s, 3 H), 4.99 (d, J = 3.3 Hz, 1 H), 5.68 (d, J = 3.3 Hz, 1 H), 5.92 (d, J = 12.6 Hz, 1 H), 6.26 (d, J = 12.6 Hz, 1 H). Anal. Calcd for $C_{20}H_{32}O_8$: C, 59.98; H, 8.05. Found: C, 59.77; H, 8.26.

(2*R*),3*R*,4*R*,5*S*)-2,3-(Isopropylidenedioxy)-5-[(1*R*)-(1,2-(isopropylidenedioxy)ethyl]-4-[(*Z*)-2-(methoxycarbonyl)ethenyl]-4-(4-oxobutyl)tetrahydrofuran (22). To a stirred solution of **21** (89.4 mg, 0.22 mmol) in CH_2Cl_2 (2 mL) were added PCC (198 mg, 0.92 mmol) and powdered molecular sieves (130 mg). After being stirred at rt for 30 min, the mixture was transferred to a short silica gel column (2 g). The column was eluted with an excess of Et_2O to give 84.0 mg (95%) of **22** as a colorless oil: TLC R_f 0.43 (EtOAc/hexane (1:2)); IR (neat) 2950, 2880, 1720, 1640, 1440, 1380, 1370 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.26, 1.36, 1.43, 1.46 (4 s, 3 H × 4), 1.59–1.79 (m, 4 H), 2.42–2.47 (m, 2 H), 3.71 (s, 3 H), 3.89–3.94, 4.16–4.22 (2 m, 2 H × 2), 5.00 (d, J = 3.4 Hz, 1 H), 5.68 (d, J = 3.4 Hz, 1 H), 5.95 (d, J = 12.7 Hz, 1 H), 6.27 (d, J = 12.7 Hz, 1 H), 9.75 (t, J = 1.5 Hz, 1 H).

Mixture of (2*R*,3*R*,4*R*,5*S*)-4-[(4*R* and -*S*)-4-Hydroxypentyl]-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-[(*Z*)-2-(methoxycarbonyl)ethenyl]tetrahydrofuran (23). The following reaction was carried out under Ar. To a cold (0 °C), stirred solution of **22** (84.0 mg, 0.21 mmol) in THF (2 mL) was added MeMgBr (0.25 mL, 0.24 mmol, 0.95 solution in THF). After being stirred at 0 °C for 45 min, the mixture was quenched with saturated aqueous NH_4Cl (1 mL) and then diluted with EtOAc (20 mL). The whole was washed with H_2O (20 mL × 3). The organic layer was dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:3)) to give 58.3 mg (63%) of an inseparable mixture **23** as a colorless oil: TLC R_f 0.37 (EtOAc/hexane (1:1)); IR (neat) 3450, 2990, 2880, 1720, 1640, 1440, 1370 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.18 (d, J = 6.2 Hz, 3 H), 1.26, 1.35, 1.43, 1.46 (4 s, 3 H × 4), 1.49–1.72 (m, 6 H), 3.70 (s, 3 H), 3.77–3.94, 4.09–4.21 (2 m, 3 H, 2 H), 4.98 (d, J = 3.3 Hz, 1 H × 1/2), 4.99 (d, J = 3.3 Hz, 1 H × 1/2), 5.67 (d, J = 3.3 Hz, 1 H), 5.93 (d, J = 12.8 Hz, 1 H), 6.26 (d, J = 12.8 Hz, 1 H). Anal. Calcd for $C_{21}H_{34}O_8$: C, 60.85; H, 8.27. Found: C, 60.76; H, 8.40.

(2*R*,3*R*,4*R*,5*S*)-2,3-(Isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-[(*Z*)-2-(methoxycarbonyl)ethenyl]-4-(4-oxopentyl)tetrahydrofuran (24). To a stirred solution of mixture **23** (30.7 mg, 0.074 mmol) in CH_2Cl_2 (1 mL) were added PCC (64.0 mg) and powdered molecular sieves (50 mg). After being stirred at rt for 2 h, the mixture was transferred to a short silica gel column (1 g). The column was eluted with an excess of Et_2O to give 28.5 mg (93%) of **24** as a colorless oil: TLC R_f 0.60 (EtOAc/hexane (1:1)); IR (neat) 2990, 2950, 2880, 1720, 1650, 1440, 1380, 1370 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.26, 1.35, 1.42, 1.46 (4 s, 3 H × 4), 1.49–1.77 (m, 4 H), 2.12 (s, 3 H), 2.40–2.45 (m, 2 H), 3.71 (s, 3 H), 3.86–3.96, 4.11–4.27 (2 m, 2 H × 2), 4.99 (d, J = 3.4 Hz, 1 H), 5.68 (d, J = 3.4 Hz, 1 H), 5.93 (d, J = 12.7 Hz, 1 H), 6.27 (d, J = 12.7 Hz, 1 H).

(3a*S*,7a*R*)- (25), (3a*S*,7a*S*)- (26), and (3a*R*,7a*R*)- (27) Isomers of (2′*S*,3′*R*,4′*R*,5′*R*)-4′,5′-(Isopropylidenedioxy)-2′-[(1*R*)-(1,2-isopropylidenedioxy)ethyl]spiro[hexahydrobenzofuran-4,3′-tetrahydrofuran]-2(3*H*)-one. The following reaction was carried out under Ar. To a solution of **17** (1.68 g, 4.07 mmol) in THF (136 mL) were added HMPA (13.6 mL) and 2-propanol (0.48 mL, 6.17 mmol). To this solution at 0 °C was added Sm(II) iodide (0.1 M solution in THF, 100 mL, 10.0 mmol) dropwise over a period of 25 min. The resulting dark blue solution was stirred at rt for 1 h. The mixture was carefully quenched with saturated aqueous NH_4Cl (10 mL) at 0 °C, and the solvents were removed by evaporation. The residue was diluted with EtOAc (300 mL) and washed successively with 0.1 M aqueous HCl (100 mL × 2), saturated $NaHCO_3$ (100 mL), and H_2O (100 mL). The organic layer was dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:5)) to give 526 mg (35%) of **25**, 251 mg (17%) of **26**, and 216 mg (14%) of **27**. Compound **25** was obtained as white crystals: mp 165.5–166.5 °C; TLC R_f 0.50 (EtOAc/hexane (1:1)); $[\alpha]^{29.5}_D$ −6.9° (*c* 1.07, $CHCl_3$); IR (neat) 2980, 2940, 2880, 1780, 1460, 1380 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.33, 1.35, 1.42, 1.53 (4 s, 3 H × 4), 1.20–1.86, 2.10–2.17 (2 m, 5H, 1 H), 2.37 (dd, J = 8.1, 17.6 Hz, 1 H), 2.71 (dd, J = 14.3, 17.6 Hz, 1 H), 3.08 (ddd, J = 6.8, 8.1, 14.3 Hz, 1 H), 3.79 (d, J = 8.4 Hz, 1 H), 3.82 (dd, J = 7.3, 8.1 Hz, 1 H), 3.90–3.98 (m, 1 H), 4.15 (dd, J = 5.9, 8.1 Hz, 1 H), 4.47 (d, J = 4.0 Hz, 1 H), 4.58 (ddd, J = 4.8, 6.8, 11.0 Hz, 1 H), 5.75 (d, J = 4.0 Hz, 1 H). Anal. Calcd for $C_{19}H_{28}O_7$: C, 61.94; H, 7.66. Found: C, 61.95; H, 7.49. Compound **26** was obtained as white crystals: mp 122.5–124.0 °C; TLC R_f 0.58 (EtOAc/hexane (1:1)); $[\alpha]^{28.5}_D$ + 36.7° (*c* 1.40, $CHCl_3$); IR (neat) 2980, 2940, 2880, 1780, 1460, 1380, 1370, 1220, 1200 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.28, 1.36, 1.40, 1.50 (4 s, 3 H × 4), 1.12–1.89 (m, 6 H), 2.22–2.34 (m, 1 H), 2.55 (dd, J = 13.4, 16.5 Hz, 1 H), 2.75 (dd, J = 6.6, 16.5 Hz, 1 H), 3.88 (dd, J = 6.6, 8.4 Hz, 1 H), 3.96 (d, J = 9.5 Hz, 1 H), 4.05 (ddd, J = 5.9, 6.6, 9.5 Hz, 1 H), 4.16 (d, J = 3.7 Hz, 1 H), 4.21 (dd, J = 5.9, 8.4 Hz, 1 H), 4.74 (ddd, J = 4.0, 11.4, 11.4 Hz, 1 H), 5.61 (d, J = 3.7 Hz, 1 H). Anal. Calcd for $C_{19}H_{28}O_7$: C, 61.94; H, 7.66. Found: C, 61.68; H, 7.44. Compound **27** was obtained as white crystals: mp 160.5–161.5 °C; TLC R_f 0.55 (EtOAc/hexane (1:1)); $[\alpha]^{24}_D$ +72.1° (*c* 1.36, $CHCl_3$); IR (neat) 2980, 2940, 2880, 1780, 1460, 1380, 1370, 1220, cm^{-1}; ^{1}H NMR (270 MHz) δ 1.30, 1.35, 1.40, 1.53 (4 s, 3 H × 4), 1.27–2.36, 2.31–2.40 (2 m, total 6 H), 2.43–2.50 (m, 2 H), 3.26 (ddd, J = 4.0, 13.9, 15.0 Hz, 1 H), 3.84 (d, J = 9.2 Hz, 1 H), 3.91 (dd, J = 5.9, 8.4 Hz, 1 H), 4.05 (ddd, J = 5.9, 6.2, 9.2 Hz, 1 H), 4.17 (dd, J = 6.2, 8.4 Hz, 1 H), 4.32 (ddd, J = 4.0, 11.0, 11.0 Hz, 1 H), 4.63 (d, J = 3.7 Hz, 1 H), 5.73 (d, J = 3.7 Hz, 1 H). Anal. Calcd for $C_{19}H_{28}O_7$: C, 61.94; H, 7.66. Found: C, 61.84; H, 7.50.

(2′*S*,3a*S*,3′*R*,4′*R*,5′*R*,7a*R*)-2′-[(1*R*)-Dihydroxyethyl]-4′,5′-(isopropylidenedioxy)spiro[hexahydrobenzofuran-4,3′-tetrahydrofuran)]-2(3*H*)-one (33). A solution of **25** (522 mg, 1.42

mmol) in a mixture of THF and 1 M HCl (1:1, v/v, 20 mL) was stirred at 5 °C for 28 h. The solution was neutralized at 0 °C with saturated aqueous $NaHCO_3$ and then diluted with H_2O (30 mL). The whole was extracted with CH_2Cl_2 (30 mL + 20 mL × 3). The combined extracts were dried and concentrated. The residue was purified by column chromatography on silica gel (acetone/$PhCH_3$ (1:8–1:3)) to give 372 mg (80%) of **33**, and 41 mg (8%) of **25** was recovered. Compound **33** was obtained as a colorless oil: TLC R_f 0.17 (acetone/$PhCH_3$ (1:3)); $[\alpha]^{29}_D$ −25.5° (*c* 1.70, $CHCl_3$); IR (neat) 3420, 2930, 2870, 1760, 1450, 1380, 1370, 1310, 1230, 1210 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.34, 1.53 (2 s, 3 H × 2), 1.23–2.30 (m, 8 H), 2.44 (dd, *J* = 7.9, 17.6 Hz, 1 H), 2.78 (dd, *J* = 14.3, 17.6 Hz, 1 H), 3.09 (ddd, *J* = 7.0, 7.3, 14.3 Hz, 1 H), 3.59–3.87 (m, 4 H), 4.47 (d, *J* = 3.7 Hz, 1 H), 4.59 (ddd, *J* = 6.2, 11.0, 11.0 Hz, 1 H), 5.76 (d, *J* = 3.7 Hz, 1 H); HRMS calcd for $C_{16}H_{25}O_7$ (M + H$^+$) *m/z* 329.1598, found 329.1585.

(2′*S*,3a*S*,3′*R*,4′*R*,5′*R*,7a*R*)-2′-(Hydroxymethyl)-4′,5′-(isopropylidenedioxy)spiro[hexahydrobenzofuran-4,3′-tetrahydrofuran]-2(3*H*)-one (34). To a cold (0 °C), stirred solution of **33** (502.5 mg, 1.53 mmol) in MeOH (10 mL) was added an aqueous solution (2 mL) of $NaIO_4$ (660 mg, 3.09 mmol). The mixture was stirred at rt for 50 min. The resulting solids were removed by filtration and washed with CH_2Cl_2 (50 mL). The combined filtrate and washing were concentrated. The residue was partitioned between CH_2Cl_2 (30 mL) and saturated brine (60 mL). The aqueous layer was extracted with CH_2Cl_2 (30 mL × 2). The combined organic layers were dried and concentrated to give the crude aldehyde (472 mg), which was used in the next step: TLC R_f 0.52 (acetone/$PhCH_3$ (1:3)); IR (neat) 2980, 2940, 2870, 1770, 1460, 1380, 1310 cm^{-1}; ^{1}H NMR (90 MHz) δ 1.37, 1.54 (2 s, 3 H × 2), 1.5–2.3 (m, 6 H), 2.47 (d, *J* = 11.2 Hz, 1 H), 2.48 (d, *J* = 19.2 Hz, 1 H), 3.0–3.5 (m, 1 H), 4.15 (d, *J* = 2.4 Hz, 1 H), 4.54 (d *J* = 3.6 Hz, 1 H), 4.4–4.7 (m, 1 H), 6.02 (d, *J* = 3.6 Hz, 1 H), 9.66 (d, *J* = 2.4 Hz, 1 H).

To a cold (0 °C), stirred solution of the aldehyde obtained (472 mg) in MeOH (10 mL) was added $NaBH_4$ (116 mg, 3.06 mmol). After being stirred at 0 °C for 40 min, the mixture was neutralized with Amberlite IR-120 (H$^+$). The resin was removed by filtration, and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (EtOAc/$PhCH_3$ (1:1)) to give 412 mg of **34** (90%) as white crystals: mp 127.5–128.5 °C; TLC R_f 0.27 (acetone/$PhCH_3$ (1:3)); $[\alpha]^{29.5}_D$ −26.4° (*c* 0.89, $CHCl_3$); IR (neat) 3420, 2980, 2950, 2880, 1770, 1460, 1420, 1370, 1310, 1210 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.35, 1.54 (2 s, 3 H × 2), 1.22–2.20 (m, 7 H), 2.32 (dd, *J* = 8.1, 16.1 Hz, 1 H), 2.49 (dd, *J* = 13.9, 16.1 Hz, 1 H), 3.01–3.12 (m, 1 H), 3.67 (d, *J* = 4.8 Hz, 2 H), 3.97 (t, *J* = 4.8 Hz, 1 H), 4.47 (d, *J* = 3.9 Hz, 1 H), 4.59 (ddd, *J* = 6.2, 11.4, 11.4 Hz, 1 H), 5.85 (d, *J* = 3.9 Hz, 1 H). Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.39; H, 7.43. Found: C, 60.36; H, 7.21.

(2′*S*,3a*S*,3′*R*,4*R*,5′*R*,7a*R*)-2′-[(Benzyloxy)methyl]-4′,5′-(isopropylidenedioxy)spiro[hexahydrobenzofuran-4,3′-tetrahydrofuran]-2(3*H*)-one (35). To a cold (0 °C), stirred suspension of NaH (162 mg, 4.05 mmol) in DMF (5 mL) was added a solution of **34** (401.5 mg, 1.35 mmol) in DMF (5 mL). After being stirred for 15 min, benzyl bromide (0.65 mL, 5.46 mmol) was added dropwise to the mixture. The mixture was stirred at rt for 2 h and quenched with EtOH (1 mL). This mixture was diluted with EtOAc (50 mL), and the whole was washed with H_2O (20 mL × 3). The organic layer was dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:4)) to give 468 mg (89%) of **35** as white crystals: mp 133.5–135.5 °C; TLC R_f 0.64 (acetone/$PhCH_3$ (1:3)); $[\alpha]^{27}_D$ −13.7° (*c* 1.11, $CHCl_3$); IR (neat) 2980, 2940, 2870, 1770, 1450, 1370, 1310, 1250, 1210 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.33, 1.54 (2 s, 3 H × 2), 1.20–2.15 (m, 6 H), 2.21 (dd, *J* = 8.1, 16.9 Hz, 1 H), 2.39 (dd, *J* = 14.3, 16.9 Hz, 1 H), 2.98–3.09 (m, 1 H), 3.48 (d, *J* = 5.1 Hz, 2 H), 4.05 (t, *J* = 5.1 Hz, 1 H), 4.42 (d, *J* = 4.0 Hz, 1 H), 4.49, 4.62 (ABq, *J* = 12.1 Hz, 2 H), 5.83 (d, *J* = 4.0 Hz, 1 H), 7.29–7.37 (m, 5 H). Anal. Calcd for $C_{22}H_{28}O_6$: C, 68.02; H, 7.27. Found: C. 67.82; H, 7.05.

Mixture of (2′*S*,3a*S*,3′*R*,4*R*,5′*R* and -*S*,7a*R*)-2′-[(Benzyloxy)methyl]-4′,5′-dihydroxyspiro[hexahydrobenzofuran-4,3′-tetrahydrofuran]-2(3*H*)-one (36). A solution of **35** (468 mg, 1.20 mmol) in 60% aqueous TFA (10 mL) was stirred at 5 °C for 3 d. The solution was neutralized with 5 M aqueous NaOH (ca. 15 mL) and diluted with H_2O (40 mL). The whole was extracted with CH_2Cl_2 (30 mL × 4). The combined extracts were dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:1)) to give a mixture of **36** (320 mg, 77%) as a colorless oil: TLC R_f 0.23 (acetone/$PhCH_3$ (1:3)); IR (neat) 3420, 2930, 2860, 1760, 1490, 1450, 1420, 1310, 1250 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.1–2.8, 2.05–2.2 (2 m, total 8 H), 2.22–2.46 (m, 2 H), 2.84–3.04 (m, 1 H), 3.46 (d, *J* = 5.5 Hz, 2 H), 3.85 (t, *J* = 2.7 Hz, 1 H × 2/9), 3.97 (br s, 1 H × 7/9), 4.11 (t, *J* = 5.5 Hz, 1 H), 4.50, 4.57 (ABq, *J* = 2.1 Hz, 1 H), 4.82–4.94 (m, 1 H), 5.12 (d, *J* = 2.9 Hz, 1 H × 2/9), 5.43 (br s, 1 H × 7/9), 7.2–7.4 (m, 5 H); HRMS calcd for $C_{19}H_{24}O_6$ (M$^+$) *m/z* 348.1570, found 348.1549.

(3a*S*,4*R*,7a*R*)-4-[(1*S*)-2-(Benzyloxy)-1-(formyloxy)ethyl]-4-[bis(ethylthio)methyl]hexahydrobenzofuran-2(3*H*)-one (38). To a cold (0 °C), stirred solution of **36** (301 mg, 0.86 mmol) in MeOH (6 mL) was added an aqueous solution (2 mL) of $NaIO_4$ (373 mg, 1.74 mmol). After being stirred at rt for 4 h, the mixture was diluted with saturated brine (30 mL). The resulting mixture was extracted with CH_2Cl_2 (20 mL × 4). The combined extracts were dried and concentrated to give crude **37** (300 mg), which was used in the next step without purification: TLC R_f 0.59 (acetone/$PhCH_3$ (1:3)); IR (neat) 2940, 2880, 1770, 1720, 1500, 1460, 1420, 1370, 1320, 1260 cm^{-1}; ^{1}H NMR (90 MHz) δ 0.8–2.0 (m, 2 H), 2.25–2.73 (m, 2 H), 2.94–3.26 (m, 1 H), 3.52 (dd, *J* = 5.6, 10.7 Hz, 1 H), 3.66 (dd, *J* = 4.5, 10.7 Hz, 1 H), 4.49 (s, 2 H), 4.56–4.83 (m, 1 H), 5.25 (dd, *J* = 4.5, 5.6 Hz, 1 H), 8.09 (s, 1 H), 9.58 (s, 1 H).

To a cold (−15 °C), stirred solution of crude **37** (300 mg) in EtSH (6 mL) was added concentrated HCl (10 drops). The mixture was stirred at −15 °C for 3 d and then neutralized with 35% ammonia–water. The resulting mixture was diluted with H_2O (15 mL), and the whole was extracted with CH_2Cl_2 (20 mL × 3). The combined extracts were dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:6)) to give 308 mg of **38** (79% from **36**) as a colorless oil: TLC R_f 0.42 (EtOAc/hexane (1:2)); $[\alpha]^{26}_D$ −40.0° (*c* 0.99, $CHCl_3$); IR (neat) 2960, 2930, 2870, 1760, 1720, 1500, 1460, 1370 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.29, 1.30 (2 t, each *J* = 7.3 Hz, 3 H × 2), 1.35–1.8, 1.95–2.2 (2 m, 4 H, 2 H), 2.5–2.85 (m, 6 H), 3.4–3.5 (m, 1 H), 3.69 (dd, *J* = 6.8,11.2 Hz, 1 H), 3.92 (dd, *J* = 2.9, 11.2 Hz, 1 H), 4.12 (s, 1 H), 4.50 (s, 2 H), 4.52–4.62 (m, 1 H), 5.47 (dd, *J* = 2.9, 6.8 Hz, 1 H), 7.26–7.34 (m, 5 H), 8.14 (s, 1 H); HRMS calcd for $C_{23}H_{32}O_5S_2$ (M$^+$) *m/z* 452.1690, found 452.1711.

(3a*S*,4*R*,7a*R*)-4-[(1*S*)-1,2-Dihydroxyethyl]-4-methylhexahydrobenzofuran-2(3*H*)-one (39). A solution of **38** (308 mg, 0.68 mmol) in EtOH (6 mL) was heated under reflux in the presence of Raney nickel T-4 for 13 h. The catalyst was removed by filtration through a Celite pad and washed well with EtOH. The combined filtrate and washing were concentrated. The residue was purified by column chromatography on silica gel (EtOAc/$PhCH_3$ (1:1)) to give 75.4 mg (52%) of **39** as white crystals: mp 77.5–79.5 °C; TLC R_f 0.14 (acetone/$PhCH_3$ (1:3)); $[\alpha]^{29}_D$ −61.8° (*c* 1.97, $CHCl_3$); IR (neat) 3410, 2940, 2870, 1760, 1460, 1180 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.98 (s, 3 H), 1.20–1.60, 2.05–2.20 (2 m, 5 H, 1 H), 2.45–2.70 (m, 5 H), 3.36 (dd, *J* = 2.6, 9.2 Hz, 1 H), 3.51 (dd, *J* = 9.2, 10.6 Hz, 1 H), 3.73 (dd, *J* = 2.6, 10.6 Hz, 1 H), 4.63 (ddd, *J* = 6.2, 11.0, 11.0 Hz, 1 H). Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.82; H, 8.23.

(3a*S*,4*R*,7a*R*)-4-Methyl-4-vinylhexahydrobenzofuran-2(3*H*)-one (40). To a cold (0 °C), stirred solution of **39** (59.6 mg, 0.28 mmol) in MeOH (1.5 mL) was added an aqueous solution (0.3 mL) of $NaIO_4$ (122 mg, 0.57 mmol). After the reaction mixture was stirred at rt for 1 h, saturated brine (10 mL) was added. The resulting mixture was extracted with CH_2Cl_2 (8 mL × 3). The combined extracts were dried and concentrated to give the aldehyde (55.1 mg), which was used directly in the next step: TLC R_f 0.62 (acetone/$PhCH_3$ (1:3)); IR (neat) 2940, 2860, 1770, 1720, 1460, 1340, 1310, 1160 cm^{-1}; ^{1}H NMR (90 MHz) δ 1.23 (s, 3 H), 1.10–1.85 (m, 6 H), 2.00–2.75 (m, 3 H), 4.52–4.81 (m, 1 H), 9.46 (s, 1 H).

The following reaction was carried out under Ar. To a THF (1.5 mL) solution of the crude aldehyde obtained (55.1 mg) was added $CH_2{=}PPh_3$ (1.0 mL, 0.43 mmol, 0.43 M solution in THF). The mixture was stirred at rt for 10 min and quenched with saturated aqueous NH_4Cl (1 mL). The resulting mixture was diluted with H_2O (8 mL), and the whole was extracted with EtOAc

(10 mL × 3). The combined extracts were dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:20)) to give 50.1 mg (quantitatively) of **40** as a colorless oil: TLC R_f 0.59 (EtOAc/hexane (1:3)); $[\alpha]^{29}_D$ −73.3° (*c* 1.25, $CHCl_3$); IR (neat) 3090, 2940, 2870, 1770, 1640, 1460, 1420, 1340, 1310, 1160 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.11 (s, 3 H), 1.25–1.74, 2.02–2.11 (2 m, 5 H, 1H), 2.25–2.40 (m, 3 H), 4.63 (ddd, *J* = 5.9, 9.5, 9.5 Hz, 1 H), 5.01 (dd, *J* = 1.1, 17.5 Hz, 1 H), 5.02 (dd, *J* = 1.1, 10.5 Hz, 1 H), 5.78 (dd, *J* = 10.5, 17.5 Hz, 1 H); HRMS calcd for $C_{11}H_{16}O_2$ (M^+) *m/z* 180.1148, found 180.1144.

(3a*S*,4*S*,7a*R*)-4-[(1*S*)-2-(Benzyloxy)-1-hydroxyethyl]-4-(hydroxymethyl)hexahydrobenzofuran-2(3*H*)-one (41). Compound **36** (328 mg, 0.94 mmol) was converted into crude **37** (339 mg) as described in the preparation of **38**. To a cold (0 °C), stirred solution of crude **37** (339 mg) in MeOH (8 mL) was added $NaBH_4$ (72 mg, 1.91 mmol). After being stirred at rt for 30 min, the mixture was neutralized by the addition of Amberlite IR-120 (H^+). The resin was removed by filtration and washed with MeOH. The combined filtrate and washing were concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:1)) to give **41** (252 mg, 84% from **36**) as a colorless oil: TLC R_f 0.17 (EtOAc/hexane (1:1)); $[\alpha]^{24.5}_D$ −32.0° (*c* 0.75, $CHCl_3$); IR (neat) 3450, 2940, 2880, 1760, 1550, 1460, 1370, 1320, 1250, 1170 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.02–1.70, 2.01–2.16 (2 m, 7 H, 1 H), 2.45 (dd, *J* = 13.6, 16.9 Hz, 1 H), 2.56 (dd, *J* = 8.0, 16.9 Hz, 1 H), 2.92–3.03 (m, 1 H), 3.47–3.71 (m, 5 H), 4.58 (s, 2 H), 4.57–4.66 (m, 1 H), 7.29–7.41 (m, 5 H); HRMS calcd for $C_{18}H_{24}O_5$ (M^+) *m/z* 320.1621, found 320.1597.

(3a*S*,4*S*,7a*R*)-4-[(1*S*)-2-(Benzyloxy)-1-hydroxyethyl]-4-[[(*tert*-butyldiphenylsilyl)oxy]methyl]hexahydrobenzofuran-2(3*H*)-one (42). To a cold (0 °C), stirred solution of **41** (252 mg, 0.79 mmol) in DMF (8 mL) were added TBDPSCl (0.23 mL, 0.88 mmol) and imidazole (108 mg, 1.58 mmol). After the reaction mixture was stirred at rt for 16 h, additional portions of TBDPSCl (0.23 mL) and imidazole (108 mg) were added. The mixture was stirred at rt for additional 2 h and at 50 °C for 9 h. The mixture was diluted with EtOAc (40 mL) and washed with H_2O (10 mL × 4). The organic layer was dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:10–1:5)) to give 367 mg of **42** (83%) as a colorless oil: TLC R_f 0.52 (EtOAc/hexane (1:2)); $[\alpha]^{26}_D$ −31.1° (*c* 1.14, $CHCl_3$); IR (neat) 3400, 3060, 2950, 2850, 1770, 1580, 1460, 1420, 1360, 1310, 1170 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.06 (s, 9 H), 0.80–1.95 (m, 7 H), 2.38–2.67 (m, 3 H), 3.46, 3.76 (ABq, *J* = 10.4 Hz, 2 H), 3.49–3.70 (m, 3 H), 4.03 (ddd, *J* = 6.2, 6.2, 11.4 Hz, 1 H), 4.51, 4.57 (ABq, *J* = 12.1 Hz, 2 H), 7.29–7.50, 7.60–7.65 (2 m, total 15 H).

(3a*S*,4*S*,7a*R*)-4-[(1*S*)-1,2-Dihydroxyethyl]-4-[[(*tert*-butyldiphenylsilyl)oxy]methyl]hexahydrobenzofuran-2(3*H*)-one (43). A solution of **42** (362 mg, 0.65 mmol) in EtOH (5 mL) was hydrogenolyzed in the presence of palladium on charcoal (182 mg) under atmospheric H_2 for 26 h. The catalyst was removed by filtration through a Celite-pad and washed well with EtOH. The combined filtrate and washing were concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (2:3)) to give 257 mg (85%) of **43** as white crystals: mp 93.0–95.0 °C: TLC R_f 0.23 (EtOAc/hexane (1:1)); $[\alpha]^{25}_D$ −38.9° (*c* 0.95, $CHCl_3$); IR (neat) 3450, 3090, 2950, 2860, 1760, 1590, 1470, 1460, 1420, 1390, 1360, 1320 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.10 (s, 9 H), 0.70–1.50, 1.80–1.90 (2 m, 7 H, 1 H), 2.43 (dd, *J* = 13.9, 16.9 Hz, 1 H), 2.63 (dd, *J* = 7.7, 16.9 Hz, 1 H), 2.79–2.90 (m, 1 H), 3.31 (dd, *J* = 3.5, 7.5 Hz, 1 H), 3.55, 3.71 (ABq, *J* = 10.6 Hz, 2 H), 3.73–3.80 (m, 2 H), 3.87 (ddd, *J* = 6.2, 6.2, 11.4 Hz, 1 H), 7.40–7.56, 7.61–7.66 (2 m, 6 H, 4 H).

(3a*S*,4*S*,7a*R*)-4-Bis(ethylthio)methyl-4-[[(*tert*-butyldiphenylsilyl)oxy]methyl]hexahydrobenzofuran-2(3*H*)-one (45). To a stirred solution of **43** (257 mg, 0.55 mmol) in MeOH (6 mL) was added an aqueous solution (1.5 mL) of $NaIO_4$ (359 mg, 1.68 mmol). After being stirred at rt for 45 min, the mixture was diluted with saturated brine (20 mL). The whole was extracted with CH_2Cl_2 (15 mL × 3). The combined extracts were dried and concentrated to give crude **44** (239 mg), which was used in the next step. Compound **44** was obtained as a colorless oil: TLC R_f 0.43 (EtOAc/hexane (1:3)); IR (neat) 3070, 2940, 2860, 1780, 1730, 1590, 1470, 1460, 1420 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.04 (s, 9 H), 0.82–2.06 (m, 6 H), 2.38 (dd, *J* = 12.0, 17.3 Hz, 1 H), 2.50 (dd, *J* = 8.1, 17.3 Hz, 1 H), 2.71 (ddd, *J* = 6.4, 8.1, 12.0 Hz, 1 H), 3.77 (s, 2 H), 4.28 (ddd, *J* = 6.4, 6.4, 10.3 Hz, 1 H), 7.39–7.50, 7.60–7.65 (2 m, 6 H, 4 H), 9.56 (s, 1 H).

To a cold (−15 °C), stirred solution of crude **44** (239 mg) in EtSH (5 mL) was added concd HCl (0.1 mL). After being stirred at −15 °C for 3 d, the mixture was neutralized with ammonia–water. The resulting mixture was diluted with H_2O (20 mL), and the whole was extracted with CH_2Cl_2 (15 mL × 3). The combined extracts were dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:12)) to give 236 mg (79%) of **45** as a colorless oil: TLC R_f 0.65 (EtOAc/hexane (1:3)); $[\alpha]^{24}_D$ −59.9° (*c* 1.28, $CHCl_3$); IR (neat) 3070, 2950, 2850, 1780, 1580, 1480, 1420 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.09 (s, 9 H), 1.25, 1.29 (2 t, each *J* = 7.3 Hz, 3 H × 2), 1.51–2.00 (m, 6 H), 2.51–2.78 (m, 7 H), 3.61, 3.84 (ABq, *J* = 10.3 Hz, 2 H), 3.96 (s, 1 H), 4.20 (ddd, *J* = 5.9, 5.9, 11.0 Hz, 1 H), 7.36–7.50, 7.62–7.70 (2 m, 6 H, 4 H). Anal. Calcd for $C_{30}H_{42}O_3S_2Si$: C, 66.37; H, 7.80. Found: C, 66.56; H, 7.47.

(3a*S*,4*R*,7a*R*)-4-Methyl-4-[[(*tert*-butyldiphenylsilyl)oxy]methyl]hexahydrobenzofuran-2(3*H*)-one (46). A solution of **45** (236 mg, 0.435 mmol) in EtOH (5 mL) was refluxed in the presence of Raney Ni T-4 for 6.5 h. The catalyst was removed by filtration through a Celite pad and washed well with EtOH. The combined filtrate and washing were concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:12)) to give 174 mg (95%) of **46** as a colorless oil: TLC R_f 0.68 (EtOAc/hexane (1:3)): $[\alpha]^{24}_D$ −27.3° (*c* 1.15, $CHCl_3$); IR (neat) 3070, 2950, 2850, 1770, 1590, 1460, 1420 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.95 (s, 3 H), 1.07 (s, 9 H), 0.83–1.93 (m, 6 H), 2.26–2.58 (m, 3 H), 3.35, 3.39 (ABq, *J* = 10.4 Hz, 2 H), 4.35 (ddd, *J* = 5.9, 5.9, 8.8 Hz, 1 H), 7.38–7.50, 7.60–7.65 (2 m, 6 H, 4 H).

(3a*S*,4*R*,7a*R*)-4-(hydroxymethyl)hexahydrobenzofuran-2(3*H*)-one (47). To a cold (0 °C), stirred solution of **46** (174 mg, 0.41 mmol) in THF (4 mL) was added *n*-Bu_4NF (0.62 mL, 0.62 mmol, 1.0 M solution in THF). After being stirred at rt for 10 h, the mixture was concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (2:3)) to give 64.5 mg (85%) of **47** as a colorless oil: TLC R_f 0.18 (EtOAc/hexane (1:1)); $[\alpha]^{24}_D$ −35.8° (*c* 0.97, $CHCl_3$); IR (neat) 3420, 2930, 2870, 1760, 1460, 1420, 1350, 1180 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.94 (s, 3 H), 1.23–1.80, 1.99–2.06 (2 m, 6 H, 1 H), 2.34–2.60 (m, 3 H), 3.41, 3.47 (ABq, *J* = 10.6 Hz, 2 H), 4.57–4.65 (m, 1 H).

(3a*S*,4*S*,7a*R*)-4-Methyl-4-vinylhexahydrobenzofuran-2(3*H*)-one (48). To a stirred solution of **47** (60.9 mg, 0.33 mmol) in CH_2Cl_2 (2 mL) were added PCC (285 mg, 1.32 mmol) and powdered molecular sieves (200 mg). After being stirred at rt for 50 min, the mixture was transferred to a short silica gel column (3 g). The column was eluted with an excess of Et_2O, and the eluate was concentrated to give the aldehyde (56.4 mg), which was used in the next step, as a colorless oil: TLC R_f 0.26 (EtOAc/hexane (1:2)); IR (neat) 2930, 2860, 1770, 1720, 1460, 1420, 1370, 1310, 1260 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.09 (s, 3 H), 1.06–2.13 (m, 6 H), 2.35 (dd, *J* = 9.3, 16.9 Hz, 1 H), 2.44 (dd, *J* = 12.2, 16.9 Hz, 1 H), 3.02 (ddd, *J* = 6.4, 9.3, 12.2 Hz, 1 H), 4.65 (ddd, *J* = 6.4, 10.3, 10.3 Hz, 1 H), 9.34 (s, 1 H).

The following reaction was carried out under Ar. To a stirred solution of the crude aldehyde (56.4 mg) in THF (1.5 mL) was added $Ph_3P{=}CH_2$ (1.50 mL, 0.68 mmol, 0.45 M solution in THF). After being stirred at rt for 10 min, the mixture was quenched with saturated aqueous NH_4Cl (10 mL). The whole was extracted with EtOAc (8 mL × 3). The combined extracts were dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:15)) to give 50.5 mg (85%) of **48** as a colorless oil: TLC R_f 0.50 (EtOAc/hexane (1:3)); $[\alpha]^{24}_D$ −74.2° (*c* 0.87, $CHCl_3$); IR (neat) 2960, 2930, 2870, 1780, 1640, 1590, 1500, 1460, 1160 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.00 (s, 3 H), 1.30–1.70. 1.99–2.08 (2 m, 5 H, 1 H), 2.36 (dd, *J* = 8.8, 16.9 Hz, 1 H), 2.47 (dd, *J* = 11.4, 16.9 Hz, 1 H), 2.68 (ddd, *J* = 6.6, 8.8, 11.4 Hz, 1 H), 4.61 (ddd, *J* = 6.6, 6.6, 9.5 Hz, 1 H), 5.06 (d, *J* = 17.6 Hz, 1 H), 5.09 (d, *J* = 11.0 Hz, 1 H), 5.72 (dd, *J* = 11.0, 17.6 Hz, 1 H).

(1*R*,2*S*,3*R*)-2-(2-Hydroxyethyl)-3-methyl-3-vinylcyclohexanol (49). To a cold (0 °C), stirred solution of **40** (47.0 mg, 0.26 mmol) in THF (1.5 mL) was added $LiAlH_4$ (20.0 mg, 0.53 mmol). After being stirred at rt for 20 min, the mixture was

quenched with 5 drops of H_2O. The resulting mixture was diluted with 0.1 M HCl (10 mL), and the whole was extracted with EtOAc (10 mL × 3). The combined extracts were dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:2)) to give 48.0 mg (quantitatively) of **49** as a colorless oil: TLC R_f 0.14 (EtOAc/hexane (1:2)); $[\alpha]^{25}_D$ −15.3° (*c* 0.72, $CHCl_3$); IR (neat) 3370, 2940, 2870, 1630, 1460, 1370 cm^{-1}; ^1H NMR (270 MHz) δ 1.04 (s, 3 H), 1.26–1.76 (m, 9 H), 2.46 (br s, 2 H), 3.55 (ddd, *J* = 4.8, 8.1, 10.3 Hz, 1 H), 3.73 (ddd, *J* = 5.1, 10.3, 10.3 Hz, 1 H), 4.05 (ddd, *J* = 4.0, 5.9, 5.9 Hz, 1 H), 4.90 (dd, *J* = 1.5, 17.6 Hz, 1 H), 5.00 (dd, *J* = 1.5, 11.0 Hz, 1 H), 6.04 (dd, *J* = 11.0, 17.6 Hz, 1 H); HRMS calcd for $C_{11}H_{20}O_2$ (M^+) *m/z* 184.1461, found 184.1455.

(2*S*,3*R*)-3-Methyl-2-[2-[(*tert*-butyldiphenylsilyl)oxy]ethyl]-3-vinylcyclohexanone (51). To a stirred solution of **49** (45.1 mg, 0.245 mmol) in DMF (1.5 mL) were added TBDPSCl (0.10 mL, 0.385 mmol) and imidazole (58.8 mg, 0.86 mmol). After being stirred at rt for 1 h, the mixture was diluted with EtOAc (20 mL). The resulting mixture was washed with H_2O (8 mL × 4). The organic layer was dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:40–1:20)) to give **50** (116.6 mg), which was contaminated by the di-*O*-silyl derivative but was used in the next step without further purification: TLC R_f 0.48 (EtOAc/hexane (1:8)). A sample for spectral analysis was obtained by repeated chromatography on silica gel: IR (neat) 3450, 3090, 2940, 2860, 1630, 1590, 1470, 1420, 1110, 1080 cm^{-1}; ^1H NMR (270 MHz) δ 0.99 (s, 3 H), 1.05 (s, 9 H), 1.22–1.79 (m, 9 H), 2.53 (br s, 1 H), 3.59 (ddd, *J* = 5.0, 7.3, 10.1 Hz, 1 H), 3.71 (ddd, *J* = 5.0, 6.2, 10.1 Hz, 1 H), 3.96 (ddd, *J* = 3.3, 3.3, 6.2 Hz, 1 H), 4.92 (dd, *J* = 1.5, 17.2 Hz, 1 H), 4.95 (dd, *J* = 1.5, 10.2 Hz, 1 H), 6.05 (dd, *J* = 10.2, 17.2 Hz, 1 H), 7.35–7.50, 7.60–7.69 (2 m, 6 H, 4 H).

To a stirred solution of **50** obtained above (116.6 mg) in CH_2Cl_2 (1 mL) were added PCC (200 mg, 0.93 mmol) and powdered molecular seives (100 mg). The mixture was stirred at rt for 1 h, and the whole was transferred to a short silica gel column (2 g). The column was eluted with an excess of Et_2O. The combined eluates were concentrated. The residue was further purified by column chromatography on silica gel (EtOAc/hexane (1:50)) to give 81.0 mg (79%) of **51** as a colorless oil: TLC R_f 0.63 (EtOAc/hexane (1:8)); $[\alpha]^{24.5}_D$ +1.4° (*c* 1.29, $CHCl_3$); IR (neat) 3080, 3050, 2970, 2940, 2860, 1710, 1640, 1590, 1430, 1110 cm^{-1}; ^1H NMR (270 MHz) δ 1.03 (s, 9 H), 1.13 (s, 3 H), 1.40–2.38 (m, 9 H), 3.53 (ddd, *J* = 5.3, 8.4, 10.1 Hz, 1 H), 3.69 (ddd, *J* = 4.7, 6.4, 10.1 Hz, 1 H), 4.95 (dd, *J* = 1.1, 17.6 Hz, 1 H), 5.02 (dd, *J* = 1.1, 11.0 Hz, 1 H), 5.62 (dd, *J* = 11.0, 17.6 Hz, 1 H), 7.33–7.48, 7.60–7.72 (2 m, 6 H, 4 H); HRMS calcd for $C_{27}H_{37}O_2Si$ (M + H^+) *m/z* 421.2559, found 421.2560.

(1*R*,2*S*,3*R*)-1,3-Dimethyl-2-[2-[(*tert*-butyldiphenylsilyl)oxy]ethyl]-3-vinylcyclohexanol (52). The following reaction was carried out under Ar. To a cold (−78 °C), stirred solution of **51** (17.4 mg, 0.041 mmol) in Et_2O (1 mL) was added MeLi (0.10 mL, 0.11 mmol, 1.12 M solution in Et_2O) dropwise. After the reaction mixture was stirred at −78 °C for 15 min, an additional portion of MeLi (0.10 mL) was added. The mixture was stirred at −78 °C for 20 min and quenched with saturated aqueous NH_4Cl (5 drops). The resulting mixture was diluted with EtOAc (15 mL) and washed with H_2O (6 mL × 3). The organic layer was dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:30)) to give 15.0 mg (82%) of **52** as a colorless oil: TLC R_f 0.55 (EtOAc/hexane (1:7)); IR (neat) 3470, 3070, 3050, 2950, 2930, 2850, 1630, 1470, 1420, 1380, 1370, 1180 cm^{-1}; ^1H NMR (270 MHz) δ 0.85, 0.96 (2 s, 3 H × 2), 1.05 (s, 9 H), 1.07–1.46, 1.52–1.88 (2 m, 3 H, 7 H), 3.56–3.72 (m, 2 H), 5.03 (dd, *J* = 1.7, 17.8 Hz, 1 H), 5.07 (dd, *J* = 1.7, 11.2 Hz, 1 H), 6.27 (dd, *J* = 11.2, 17.8 Hz, 1 H), 7.34–7.71 (m, 10 H).

(1*R*,2*S*,3*R*)-2-(2-Hydroxyethyl)-1,3-dimethyl-3-vinylcyclohexanol (53). To a stirred solution of **52** (15.0 mg, 0.034 mmol) in THF (1 mL) was added *n*-Bu_4NF (0.070 mL, 0.07 mmol, 1.0 M solution in THF). After being stirred at rt for 5 h, the solution was concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:3)) to give 6.8 mg (quantitatively) of **53** as white crystals: mp 65.0–66.0 °C: TLC R_f 0.19 (EtOAc/hexane (1:2)); $[\alpha]^{22}_D$ −25.1° (*c* 0.52, $CHCl_3$); IR (neat) 3400, 2980, 2920, 2860, 1650 cm^{-1}; ^1H NMR (270 MHz) δ 1.00, 1.16 (2 s, 3 H × 2), 0.88–1.93 (m, 11 H), 3.57–3.75 (m, 2 H), 5.09 (dd, *J* = 1.5, 17.6 Hz, 1 H), 5.10 (dd, *J* = 1.5, 11.4 Hz, 1 H), 6.31 (dd, *J* = 11.4, 17.6 Hz, 1 H); HRMS calcd for $C_{12}H_{22}O_2$ (M^+) *m/z* 198.1618, found 198.1618.

(3a*S*,4*R*,7a*R*)-4,7a-Dimethyl-4-vinyl-2(3*H*)-hexahydrobenzofuranone, (−)-7a-*epi*-Anastrephin (3). To a stirred solution of **53** (6.8 mg, 0.034 mmol) in CH_2Cl_2 (0.8 mL) were added PCC (31.0 mg, 0.14 mmol) and powdered molecular sieves (20 mg). The mixture was stirred at rt for 80 min, and the whole was transferred to a short silica gel column (1 g). The column was eluted with an excess of Et_2O. The eluate was concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:15)) to give 5.5 mg (83%) of **3** as a colorless oil, which gradually crystallized in a freezer: mp 36.5–38.5 °C; TLC R_f 0.56 (EtOAc/hexane (1:3)); $[\alpha]^{25}_D$ = −55.1° (*c* 0.275, hexane); IR (neat) 2920, 2860, 1760, 1630, 1460, 1380, 1250, 1090 cm^{-1}; ^1H NMR (270 MHz) δ 1.15, 1.56 (2 s, 3 H × 2), 1.20–1.92 (m, 6 H), 2.12 (dd, *J* = 9.2, 11.7 Hz, 1 H), 2.39 (d, *J* = 9.2 Hz, 1 H), 2.40 (d, *J* = 11.7 Hz, 1 H), 4.97 (dd, *J* = 0.7, 17.6 Hz, 1 H), 4.98 (dd, *J* = 0.7, 10.6 Hz, 1 H), 5.75 (dd, *J* = 10.6, 17.6 Hz, 1 H); ^{13}C NMR (100 MHz) δ 18.4, 26.0, 27.2, 30.0, 33.8, 34.8, 37.9, 50.7, 85.5, 111.4, 146.2, 175.4; HRMS calcd for $C_{12}H_{18}O_2$ (M^+) *m/z* 194.1305, found 194.1303.

(1*R*,2*R*)-1-Methyl-3-methylene-2-[2-[(*tert*-butyldiphenylsilyl)oxy]ethyl]-1-vinylcyclohexane (54). Zinc powder (extra pure grade) was washed well with 1 M HCl, H_2O, EtOH, and Et_2O, successively, and dried overnight in vacuo. The following reaction was carried out under Ar. To a stirred suspension of the activated zinc (322 mg, 4.93 mmol) in THF (1.5 mL) were added dibromomethane (0.108 mL, 1.54 mmol) and $TiCl_4$ (1.10 mL, 1.10 mmol, 1.0 M solution in CH_2Cl_2) dropwise. The mixture was stirred at rt for 30 min. To the resulting dark brown solution was added a solution of **51** (91.1 mg, 0.22 mmol) in THF (2 mL) dropwise. After being stirred at rt for 3.5 h, the mixture was quenched with H_2O (2 mL). The resulting mixture was diluted with EtOAc (30 mL), and the whole was washed with 0.2 M HCl (10 mL × 2), saturated aqueous $NaHCO_3$ (10 mL × 2), and H_2O (10 mL × 2), successively. The organic layer was dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:100)) to give 79.4 mg (88%) of **54** as a colorless oil: TLC R_f 0.67 (EtOAc/hexane (1:16)); $[\alpha]^{23}_D$ +11.3° (*c* 0.97, $CHCl_3$); IR (neat) 3080, 2940, 2930, 2850, 1640, 1590, 1420, 1380 cm^{-1}; ^1H NMR (270 MHz) δ 0.98 (s, 3 H), 1.03 (s, 9 H), 1.25–1.80, 1.93–2.05 (2 m, 6 H, 3 H), 3.48–3.68 (m, 2 H), 4.51 (d, *J* = 2.2 Hz, 1 H), 4.69–4.70 (m, 1 H), 4.91 (dd, *J* = 1.7, 17.6 Hz, 1 H), 4.96 (dd, *J* = 1.7, 11.0 Hz, 1 H), 5.74 (dd, *J* = 11.0, 17.6 Hz, 1 H), 7.33–7.42, 7.63–7.68 (2 m, 6 H, 4 H); HRMS calcd for $C_{28}H_{38}OSi$ (M^+) *m/z* 418.2690, found 418.2713.

Mixture of (3*R* and -*S*,4*S*,5*R*)-5-Methyl-4-[2-[(*tert*-butyldiphenylsilyl)oxy]ethyl]-5-vinyl-1-oxaspiro[2.5]octane (55). To a cold (0 °C), stirred solution of **54** (77.8 mg, 0.19 mmol) in CH_2Cl_2 (2 mL) were added *m*-CPBA (25.1 mg, 0.145 mmol) and $NaHCO_3$ (15.1 mg, 0.18 mmol). After the reaction mixture was stirred at 0 °C for 17 h, additional portions of *m*-CPBA (6.8 mg) and $NaHCO_3$ (3.4 mg) were added. The mixture was stirred at 0 °C for an additional 4 h and diluted with saturated aqueous $NaHSO_3$ (2 mL) and then with CH_2Cl_2 (30 mL). The whole was washed with saturated aqueous $NaHSO_3$ (8 mL), saturated aqueous $NaHCO_3$ (8 mL), and H_2O (8 mL), successively. The organic layer was dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:50–1:30)) to give 46.1 mg (57%) of mixture **55**, and 26.2 mg (34%) of **54** was recovered. Mixture **55** was obtained as a colorless oil: TLC R_f 0.36 (EtOAc/hexane (1:16)); IR (neat) 3080, 2940, 2850, 1730, 1640, 1590 cm^{-1}; ^1H NMR (270 MHz) δ 1.02 (s, 3 H × 1/2), 1.04 (s, 9 H), 1.12 (s, 3 H × 1/2), 0.80–2.20 (m, 9 H), 2.39, 2.53 (ABq, *J* = 4.6 Hz, 2 H × 1/2), 2.48 (s, 2 H × 1/2), 3.35–3.73 (m, 2 H), 4.85–4.96 (m, 2 H), 5.72 (dd, *J* = 11.0, 17.6 Hz, 1 H × 1/2), 5.83 (dd, *J* = 11.0, 17.6 Hz, 1 H × 1/2), 7.34–7.48, 7.60–7.68 (2 m, 6 H, 4 H); HRMS calcd for $C_{24}H_{29}O_2Si$ [M − $C(CH_3)_3^+$] *m/z* 377.1935, found 377.1938.

(1*S*,2*S*,3*R*)-2-(2-Hydroxyethyl)-1,3-dimethyl-3-vinylcyclohexanol (56) and 1R Isomer 53. The following reaction was carried out under Ar. To a cold (0 °C), stirred suspension of $LiAlH_4$ (30.6 mg, 0.81 mmol) in THF (1 mL) was added a solution of mixture **55** (68.7 mg, 0.16 mmol) in THF (2 mL). The mixture

was heated under reflux for 1 h. After being cooled to rt, the mixture was quenched with H_2O (1 mL) and then diluted with 0.2 M HCl (15 mL). The whole was extracted with EtOAc (10 mL × 3). The combined extracts were dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:3)) to give 17.8 mg (57%) of **56** and 10.3 mg (33%) of **53**. Compound **56** was obtained as a colorless oil: TLC R_f 0.17 (EtOAc/hexane (1:1)); $[\alpha]^{22}_D$ +26.6° (*c* 0.89, $CHCl_3$); IR (neat) 3350, 2930, 2850, 1630, 1460, 1370, cm^{-1}; ^1H NMR (270 MHz) δ 1.01, 1.16 (2 s, 3 H × 2), 0.80–2.25 (m, 10 H), 3.30 (br s, 1 H), 3.49–3.88 (m 2 H), 4.98 (dd, *J* = 1.1, 17.6 Hz, 1 H), 5.01 (dd, *J* = 1.1, 11.0 Hz, 1 H), 5.92 (dd, *J* = 11.0, 17.6 Hz, 1 H); HRMS calcd for $C_{12}H_{22}O_2$ (M^+) *m/z* 198.1619, found 198.1631.

(3a*S*,4*R*,7a*S*)-4,7a-Dimethyl-4-vinylhexahydrobenzofuran-2(3*H*)-one, (−)-Anastrephin (1). To a stirred solution of **56** (16.3 mg, 0.082 mmol) in CH_2Cl_2 (1 mL) were added PCC (71.3 mg, 0.33 mmol) and powdered molecular sieves (50 mg). After being stirred at rt for 1 h, the mixture was transferred to a short silica gel column (1 g). The column was eluted with an excess of Et_2O. The eluate was concentrated, and the residue was further purified by column chromatography on silica gel (EtOAc/hexane (1:15)) to give 10.1 mg (63%) of **1** as white crystals: mp 88.0–89.5 °C; TLC R_f 0.76 (EtOAc/hexane (1:2)); $[\alpha]^{26}_D$ −45.1° (*c* 0.51, *n*-hexane); IR (neat) 2950, 2930, 2870, 1770, 1640, 1465, 1380 cm^{-1}; ^1H NMR (270 MHz) δ 1.03, 1.25 (2 s, 3 H × 2), 1.55–1.85, 1.95–2.03 (2 m, total 6 H), 2.09 (dd, *J* = 6.8, 14.5 Hz, 1 H), 2.37 (dd, *J* = 6.8, 16.1 Hz, 1 H), 2.51 (dd, *J* = 14.5, 16.1 Hz, 1 H), 5.08 (dd, *J* = 1.1, 17.6 Hz, 1 H), 5.10 (dd, *J* = 1.1, 11.4 Hz, 1 H), 5.87 (ddd, *J* = 1.1, 11.4, 17.6 Hz, 1 H); ^{13}C NMR (100 MHz) δ 20.2, 20.4, 29.0, 30.3, 36.2, 37.2, 38.6, 55.6, 86.2, 112.9, 140.0, 176.0; HRMS calcd for $C_{12}H_{18}O_2$ (M^+) *m/z* 194.1305, found 194.1300.

(1*R*,2*S*,3*S*)-2-(2-Hydroxyethyl)-4-methyl-4-vinylcyclohexanol (57). To a cold (0 °C), stirred solution of **48** (48.1 mg, 0.27 mmol) in THF (1.5 mL) was added $LiAlH_4$ (20.3 mg, 0.54 mmol). After being stirred at rt for 20 min, the mixture was quenched with H_2O (2 mL). The resulting mixture was diluted with 0.1 M HCl (10 mL), and the whole was extracted with EtOAc (6 mL × 4). The combined extracts were dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (2:3)) to give 48.7 mg (99%) of **57** as white crystals: mp 116.5–118.0 °C; TLC R_f 0.22 (EtOAc/hexane (1:1)); $[\alpha]^{24}_D$ −8.6° (*c* 0.84, $CHCl_3$); ^1H NMR (270 MHz) δ 1.07 (s, 3 H), 1.26–1.86 (m, 11 H), 3.59–3.68, 3.78–3.81, 4.02–4.07 (3 m, 1 H × 3), 4.97 (dd, *J* = 1.5, 17.4 Hz, 1 H), 4.99 (d, *J* = 1.5, 11.0 Hz, 1 H), 5.70 (dd, *J* = 11.0, 17.4 Hz, 1 H).

(2*S*,3*S*)-3-Methyl-4-[[(*tert*-butyldiphenylsilyl)oxy]-methyl]-3-vinylcyclohexanone (59). To a stirred solution of **57** (46.9 mg, 0.26 mmol) in DMF (2 mL) were added TBDPSCl (73.0 μL, 0.28 mmol) and imidazole (34.7 mg, 0.51 mmol). After the reaction mixture was stirred at rt for 1.5 h, additional portions of TBDPSCl (36.0 μL) and imidazole (17.0 mg) were added. The reaction mixture was heated at 40 °C for 10 h, and then TBDPSCl (70.0 μL) and imidazole (17.0 mg) were added. The mixture was heated at 60 °C for an additional 3 h and then diluted with EtOAc (30 mL). The whole was washed with H_2O (10 mL × 3). The organic layer was dried and concentrated to give crude **58**, which was contaminated by TBDPSCl but was used in the next step without purification.

To a stirred solution of crude **58** in CH_2Cl_2 (3 mL) were added PCC (220 mg, 1.02 mmol) and powdered molecular sieves (150 mg). After being stirred at rt for 75 min, the mixture was transferred to a short silica gel column (7 g). The column was eluted with an excess of Et_2O. The eluates were concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:50)) to give **59** (107 mg, quantitatively) as a colorless oil: TLC R_f 0.72 (EtOAc/hexane (1:8)); $[\alpha]^{27}_D$ +20.0° (*c* 1.05, $CHCl_3$); IR (neat) 2970, 2940, 2860, 1710, 1640, 1510, 1430, 1110 cm^{-1}; ^1H NMR (270 MHz) δ 0.84 (s, 3 H), 1.03 (s, 9 H), 1.40–1.60, 1.75–1.99, 2.15–2.45 (3 m, 3 H, 3 H, 2 H), 2.54 (br d, *J* = 10.3 Hz, 1 H), 3.50 (ddd, *J* = 4.8, 9.9, 9.9 Hz, 1 H), 3.71 (ddd, *J* = 4.8, 6.2, 10.3 Hz, 1 H), 5.00 (dd, *J* = 1.1, 17.2 Hz, 1 H), 5.04 (dd, *J* = 1.1, 10.6 Hz, 1 H), 5.79 (dd, *J* = 10.6, 17.2 Hz, 1 H), 7.31–7.41, 7.60–7.65 (2 m, 6 H, 4 H). Anal. Calcd for $C_{27}H_{36}O_2Si$: C, 77.09; H, 8.63. Found: C, 76.90; H, 8.50.

(1*R*,2*S*,3*S*)-1,3-Dimethyl-2-[[(2-*tert*-butyldiphenylsilyl)-oxy]ethyl]-3-vinylcyclohexanol (60). To a cold (−15 °C), stirred solution of **59** (5.2 mg) in Et_2O (0.6 mL) was added MeLi (0.1 mL, 0.1 mmol, 1.12 M solution in Et_2O). After being stirred at −15 °C for 20 min, the mixture was quenched with saturated aqueous NH_4Cl (0.1 mL). The resulting mixture was diluted with EtOAc (10 mL) and washed with H_2O (5 mL × 3). The organic layer was dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:50)) to give 4.0 mg (74%) of **60**, and 0.4 mg (8%) of **59** was recovered. Compound **60** was obtained as a colorless oil: TLC R_f 0.45 (EtOAc/hexane (1:8)); ^1H NMR (270 MHz) δ 1.02, 1.11 (2 s, 3 H × 2), 1.04 (s, 9 H), 1.18–18.5 (m, 10 H), 3.59 (t, *J* = 7.7 Hz, 2 H), 4.84 (dd, *J* = 1.5, 10.6 Hz, 1 H), 4.89 (dd, *J* = 1.5, 17.6 Hz, 1 H), 5.54 (dd, *J* = 10.6, 17.6 Hz, 1 H), 7.35–7.45, 7.61–7.69 (2 m, 6 H, 4 H).

(1*R*,2*S*,3*S*)-2-(2-Hydroxymethyl)-1,3-dimethyl-3-vinylcyclohexanol (61). To a solution of **60** (4.0 mg, 9.2 μmol) was added *n*-Bu_4NF (20 μL). The mixture was stirred at rt for 6 h and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:2)) to give 1.7 mg (91%) of **61** as a colorless oil: TLC R_f 0.35 (EtOAc/hexane (1:1)); ^1H NMR (270 MHz) δ 1.14, 1.20 (2 s, 3 H × 2), 1.07–1.86 (m, 11 H), 3.54 (ddd, *J* = 7.7, 7.7, 10.3 Hz, 1 H), 3.66 (ddd, *J* = 5.5, 8.8, 10.3 Hz, 1 H), 4.97 (dd, *J* = 1.1, 16.9 Hz, 1 H), 4.96 (dd, *J* = 1.1, 11.4 Hz, 1 H), 5.67 (dd, *J* = 11.4, 16.9 Hz, 1 H).

(3a*S*,4*S*,7a*R*)-4,7a-Dimethyl-4-vinylhexahydrobenzofuran-2(3*H*)-one, (−)-7a-*epi*-Epianastrephin (4). Compound **61** (1.7 mg) as oxidized with PCC (12.7 mg) to afford 1.4 mg of **4** (84%) as a colorless oil: TLC R_f 0.56 (EtOAc/hexane (1:3)); $[\alpha]^{28}_D$ −62.1° (*c* 0.44, *n*-hexane); IR (neat) 2940, 2860, 1760, 1640, 1460, 1380, 1260, 1210 cm^{-1}; ^1H NMR (270 MHz) δ 0.96, 1.44 (2 s, 3 H × 2), 1.14–1.88 (m, 6 H), 2.28 (dd, *J* = 8.3, 13.2 Hz, 1 H), 2.45 (dd, *J* = 8.3, 17.1 Hz, 1 H), 2.55 (dd, *J* = 13.2, 17.1 Hz, 1 H), 5.06 (d, *J* = 17.6 Hz, 1 H), 5.08 (d, *J* = 11.2 Hz, 1 H), 5.81 (ddd, *J* = 1.0, 11.2, 17.6 Hz, 1 H); ^{13}C NMR (100 MHz) δ 18.8, 26.0, 29.0, 30.4, 32.6, 34.4, 38.1, 51.1, 85.9, 112.5, 146.4, 175.3; HRMS calcd for $C_{12}H_{18}O_2$ (M^+) *m/z* 194.1306, found 194.1309.

(1*S*,2*R*)-1-Methyl-3-methylene-2-[[(2-*tert*-butyldiphenylsilyl)oxy]ethyl]-1-vinylcyclohexane (62). The following reaction was carried out under Ar. To a stirred suspension of the activated zinc (350 mg, 5.35 mmol) in THF (1.5 mL) were added dibromomethane (0.12 mL, 1.71 mmol) and $TiCl_4$ (1.20 mL, 1.20 mmol, 1.0 M solution in CH_2Cl_2). After the reaction mixture was stirred at rt for 30 min, a solution of **59** (100 mg, 0.24 mmol) in THF (2 mL) was added. The mixture was stirred at rt for 2.5 h and quenched with H_2O (2 mL). The resulting mixure was diluted with EtOAc (40 mL) and washed successively with 0.2 M HCl (10 mL × 2), saturated aqueous $NaHCO_3$ (10 mL × 2), and H_2O (10 mL × 2). The organic layer was dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:100)) to give 83.5 mg (84%) of **62** as a colorless oil: TLC R_f 0.79 (EtOAc/hexane (1:16)); $[\alpha]^{26}_D$ −10.7° (*c* 1.00, $CHCl_3$); IR (neat) 2940, 2860, 1640, 1470, 1430, 1110 cm^{-1}; ^1H NMR (270 MHz) δ 0.85 (s, 3 H), 1.24 (s, 9 H), 1.25–1.78, 1.86–1.96, 2.07–2.20 (3 m, total 9 H), 3.51–3.71 (m, 2 H), 4.43, 4.73 (2 s, 1 H × 2), 4.95 (dd, *J* = 1.1, 17.2 Hz, 1H), 4.98 (dd, *J* = 1.1, 11.4 Hz, 1 H), 5.79 (dd, *J* = 11.4, 17.2 Hz, 1 H), 7.35–7.43, 7.63–7.69 (2 m, 6 H, 4 H). Anal. Calcd for $C_{28}H_{38}OSi$: C, 80.32; H, 9.15. Found: C, 80.59; H, 9.53.

Mixture of (3*R* and -*S*,4*S*,5*S*)-5-Methyl-4-[2-[(*tert*-butyldiphenylsilyl)oxy]ethyl]-5-vinyl-1-oxaspiro[2.5]octane (63). To a cold (0 °C), stirred solution of **62** (79.7 mg, 0.19 mmol) in CH_2Cl_2 (2 mL) were added *m*-CPBA (28.4 mg, 0.165 mmol) and $NaHCO_3$ (15.6 mg, 0.19 mmol). After the mixture was stirred at 0 °C for 6 h, *m*-CPBA (5.5 mg) was added to the mixture. The mixture was stirred for an additional 1 h and then quenched with saturated aqueous $NaHSO_3$ (2 mL). The resulting mixture was diluted with CH_2Cl_2 (30 mL) and washed with aqeuous $NaHSO_3$ (8 mL), aqueous $NaHCO_3$ (8 mL × 2), and H_2O (8 mL × 2), successively. The organic layer was dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:100–1:60)) to give 39.0 mg (47%) of **63** as a colorless oil, and 42.2 mg (53%) of **62** was recovered. The recovered **62** was resubmitted to the same procedure. After four cycles, 70.7 (86%) of mixture **63** was obtained: TLC R_f 0.36 (EtOAc/hexane (1:16)); IR (neat) 2920, 2850, 1640, 1580, 1470, 1420, 1110 cm^{-1}; ^1H NMR (270 MHz) δ 0.91 (s, 3 H × 2/3), 0.98

(s, 3 H × 1/3), 1.04 (s, 9 H), 1.10–1.80 (m, 8 H), 2.27 (d, J = 4.4 Hz, 1 H × 1/3), 2.43 (d, J = 4.4 Hz, 1 H × 1/3), 2.44 (d, J = 4.4 Hz, 1 H × 2/3), 2.65 (d, J = 4.4 Hz, 1 H × 2/3), 3.52–3.71 (m, 2 H), 4.91–5.00 (m, 2 H), 5.72 (dd, J = 10.6, 17.6 Hz, 1 H × 1/3), 5.78 (dd, J = 10.6, 18.0 Hz, 1 H × 2/3), 7.33–7.44 7.46–7.67 (2 m, 6 H, 4 H).

Mixture of (1*S*,2*S*,3*S*)-2-(2-Hydroxyethyl)-1,3-dimethyl-3-vinylcyclohexanol and 1*R* Isomer 65. The following reaction was carried out under Ar. To a stirred solution of mixture **63** (70.7 mg, 0.16 mmol) in THF (2 mL) was added a suspension of $LiAlH_4$ (24.7 mg, 0.65 mmol) in THF (1 mL). The mixture was refluxed for 1 h and quenched with H_2O (1 mL). The resulting mixture was diluted with 0.5 M HCl (10 mL), and the whole was extracted with EtOAc (8 mL × 4). The combined extracts were dried and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:2)) to give 31.1 mg (96%) of an inseparable mixture of **64** and **65** as a colorless oil: TLC R_f 0.28 (EtOAc/hexane (1:1)); IR (neat) 3320, 2930, 2860, 1640, 1460, 1380 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.94, 1.26 (2 s, each 3 H × 2/3), 1.14, 1.20 (2 s, each 3 H × 1/3), 1.3–1.8 (m, 9 H), 3.40–3.93 (m, 2 H), 4.59–4.99 (m, 2 H), 5.64 (dd, J = 11.0, 17.2 Hz, 1 H × 2/3), 5.65 (dd, J = 10.4, 17.8 Hz, 1 H × 1/3).

(3a*S*,4*S*,7a*S*)-4,7a-Dimethyl-4-vinylhexahydrobenzofuran-2(3*H*)-one, (−)-Epianastrephin (2), and Its 7a*R* Isomer 4. To a stirred solution of the mixture of **64** and **65** (29.6 mg, 0.15 mmol) in CH_2Cl_2 (1 mL) were added PCC (129 mg, 0.60 mmol) and powdered molecular sieves (80 mg). After being stirred at rt for 45 min, the mixture was transferred to a short silica gel column. The column was eluted with an excess of Et_2O. The eluate was concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (1:20)) to give 13.9 mg (48%) of **2** and 9.3 mg (32%) of **4**. Compound **2** was obtained as white crystals: mp 48.0–48.5 °C; TLC R_f 0.76 (EtOAc/hexane (1:2)); $[\alpha]^{28}_D$ −72.5° (c 0.57, n-hexane); IR (neat) 3020, 2950, 2880, 1780, 1640, 1460, 1390, 1300, 1240, 1220, 1200 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.07, 1.39 (2 s, 3 H × 2), 1.41–1.73, 1.80–1.89, 2.00–2.05 (3 m, 4 H, 1 H, 1 H), 2.11 (dd, J = 6.2, 14.7 Hz, 1 H), 2.24 (dd, J = 6.2, 16.3 Hz, 1 H), 2.38 (dd, J = 14.7, 16.3 Hz, 1 H), 4.98 (d, J = 17.6 Hz, 1 H), 4.98 (d, J = 11.4 Hz, 1 H), 5.69 (dd, J = 11.4, 17.6 Hz, 1 H); ^{13}C NMR (100 MHz) δ 16.4, 20.5, 20.9, 29.5, 37.1, 38.0, 38.5, 53.5, 86.0, 111.6, 147.8, 176.0.

Supplementary Material Available: ^{1}H NMR spectra of **17–19, 22, 24, 33, 36, 38, 40–43, 46–57, 60–61, 63, 64 + 65**, and **1–4** and ^{13}C NMR spectra of **1–4** (36 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.