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Nickel-Catalyzed Coupling Producing (2*Z*)-2,4-Alkadien-1-ols, Conversion to (*E*)-3-Alkene-1,2,5-triol Derivatives, and Synthesis of Decarestrictine D

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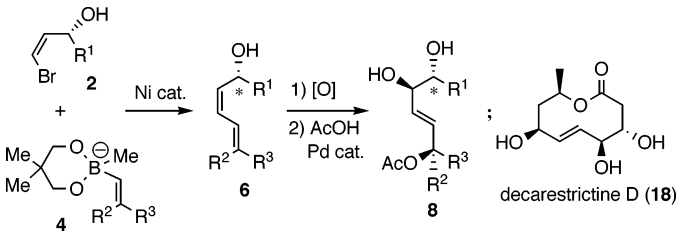

The 3-alkene-1,2,5-triol structure is not only a major framework of biologically important molecules but also a new functional-group-rich unit for synthesis of polyols and sugars. A method furnishing such triol derivatives **8** was developed and successfully applied to synthesis of decarestrictine D (**18**). First, coupling reaction of the unprotected alcohols **2** with borates **4** was investigated to produce the dienyl alcohols **6** with $NiCl_2$(dppf) in Et_2O/THF (5:1) at room temperature. The hydroxyl-group-directed epoxidation of **6** followed by palladium-catalyzed reaction with AcOH (Scheme 1) furnished 3-alkene-1,2,5-triol derivatives **8**. Since each step proceeded with high stereo- and regioselectivities, the stereochemistry of **8** has been correlated with the olefin geometry of **6**. With the above transformation in mind, synthesis of the full carbon skeleton of decarestrictine D (**18**) could be designed easily and was completed successfully. Furthermore, a new seco acid **19b** with the MOM protective group for the three hydroxyl groups was found to afford macrolide **48** in a yield higher than those reported previously.

Introduction

Lithium borates **4** (in *E* and *Z* forms) shown in eq 1 are among the highly reactive organometallics for coupling reactions with organic substrates such as allylic esters,[1] aryl mesylates,[2] and alkenyl halides[3] to produce compounds that had previously been inaccessible because of steric and/or electronic reasons.[4] For example, dienyl alcohol derivatives **5** are synthesized by coupling with *cis* bromides **1**, which are available easily as optically active forms by using several methods.[5] Later, this coupling reaction has been utilized in the synthesis of the dihydroleukotrienes B_4 family[6] and korormicin,[7] in which the dienyl alcohol unit is seen in their core structures.

Through these investigations, we have reconfirmed the advantages mentioned above. We then turned our attention to transformation of **5** or unprotected dienyl alcohols **6** to highly functionalized compounds of specific interest.

We envisioned synthesis of triol derivatives **8** shown in Scheme 1. The first step is a hydroxyl-group-directed epoxidation of dienyl alcohols **6** with *m*-CPBA, and the second step

(1) (a) Kobayashi, Y.; Mizojiri, R.; Ikeda, E. *J. Org. Chem.* **1996**, *61*, 5391−5399. (b) Kobayashi, Y.; Murugesh, M. G.; Nakano, M.; Takahisa, E.; Usmani, S. B.; Ainai, T. *J. Org. Chem.* **2002**, *67*, 7110−7123.

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(7) Kobayashi, Y.; Yoshida, S.; Nakayama, Y. *Eur. J. Org. Chem.* **2001**, 1873−1881.

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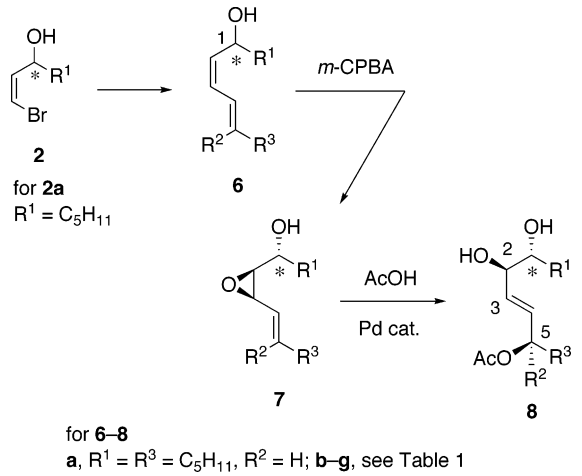
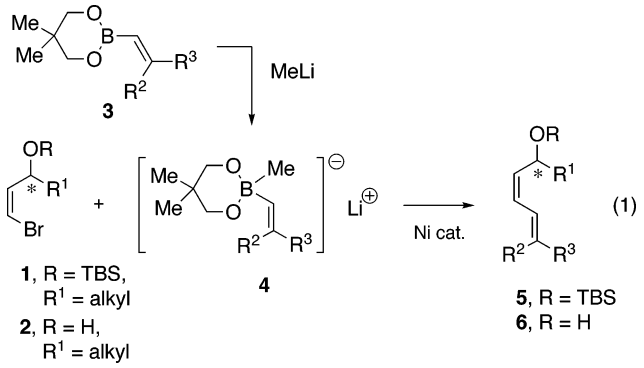
SCHEME 1. An Approach to Triol Derivatives 8



is palladium-assisted reaction of the resulting epoxy alcohols **7** with the acetate anion. The triol structure is seen as such or as a masked form in biologically active molecules such as the lipoxygenase metabolites of fatty acids,[8] decarestrictine D,[9] and acetogenins.[10] To date, several methods have been reported to construct such triol units.[11] In contrast, our approach is quite simple and hence would be an attractive complement to the reported methods. Herein, we present the results of this transformation and a synthesis of decarestrictine D.[12]



Results and Discussion

In the original coupling reaction,[3] silyl ethers **1** derived from alcohols **2** were used as substrates for the coupling reaction with borates **4** to produce dienyl alcohol derivatives **5**. Since unprotected alcohol **6** is required to attain high stereoselectivity in the next epoxidation according to the literature,[13] coupling reaction between alcohols **2** and borates **4** was investigated first. Alcohol **2a** ($R^1 = C_5H_{11}$, R = H) (1 equiv) was added to a mixture of borate (*E*)-**4a** (R^2 = H, $R^3 = C_5H_{11}$) and a Ni(0) species generated from the corresponding boronate ester (*E*)-**3a** (1.5 equiv) and $NiCl_2(PPh_3)_2$ (10 mol %) with MeLi (1.6 equiv) at 0 °C for 15 min, and the reaction was conducted under the original conditions (THF/Et_2O (5:1), rt, overnight) to furnish the *cis*,*trans* dienyl alcohol **6a** ($R^1 = R^3 = C_5H_{11}$, R^2 = R = H) in 49% yield. Although the yield is moderate, the production of **6a** clearly indicates that the borate is compatible with the free hydroxyl group present in **2a**. In order to increase the yield of the coupling, nickel ligands and solvents were examined with the same quantity (1.5 equiv) of (*E*)-**3a**. We found that reaction with $NiCl_2$(dppf) as a catalyst in an Et_2O-rich solvent (Et_2O/THF = 5:1) at room temperature produced **6a** in 72% yield with 95% stereoselectivity (ss) over the *trans*,*trans* isomer (Table 1, entry 1).

The optimized conditions were applied to other combinations of substrates and borates. As summarized in entries 2−7 of Table 1, *cis*,*cis* isomer **6b** ($R^1 = R^2 = C_5H_{11}$, R^3 = H) and other *cis*,*trans* dienyl alcohols **6c**−**g** (R^1 and R^3 = alkyl, R^2 = H) were synthesized in good yields with >90% ss. Among these entries, especially noteworthy is entry 4, where substrate **2** even with the bulky *t*-Bu group as R^1 produced **6d** with similar efficiency to others. On the other hand, **6h** was produced with 86% ss (entry 8). Conjugation of the *cis*,*trans* diene moiety with the phenyl ring in **6h** is probably a reason for the partial isomerization of **6h** to the *trans*,*trans* isomer during routine purification by chromatography on silica gel.[14]

Epoxidation of the *cis*,*trans* dienyl alcohol **6a** of 95% purity with *m*-CPBA under the standard conditions ($NaHCO_3$, CH_2Cl_2, 0 °C) furnished **7a** in 77% isolated yield (Table 1, entry 1). The *cis*,*cis* isomer **6b** was also converted into epoxide **7b** in good yield (entry 2). Epoxides **7a** and **7b** were fairly stable during chromatography on silica gel using hexane/EtOAc with Et_3N (trace). The stereochemistries of **7a** and **7b** were assigned by analogy as drawn in Scheme 1 and confirmed later by derivation to the known compounds.

Palladium-catalyzed reaction of epoxide **7a** with AcOH in the presence of $Pd(PPh_3)_4$ (10 mol %) at 0 °C for 30 min provided acetate **8a** in 71% yield (Table 1, entry 1). The *trans*

(8) (a) Pace-Asciak, C. R.; Martin. J. M.; Corey, E. J.; Su, W.-G. *Biochem. Biophys. Res. Commun.* **1985**, *128*, 942−946. (b) Hamberg, M.; Hamberg, G. *Plant Physiol.* **1996**, *110*, 807−815. (c) Grechkin, A. N.; Mukhtarova, L. S.; Hamberg, M. *Biochem. J.* **2000**, *352*, 501−509.

(9) (a) Grabley, S.; Granzer, E.; Hütter, K.; Ludwig, D.; Mayer, M.; Thiericke, R.; Till, G.; Wink, J.; Philipps, S.; Zeeck, A. *J. Antibiot.* **1992**, *45*, 56−65. (b) Göhrt, A.; Zeeck, A.; Hütter, K.; Kirsch, R.; Kluge, H.; Thiericke, R, *J. Antibiot*. **1992**, *45*, 66−73. (c) Ayer, W. A.; Sun, M.; Browne, L. M.; Brinen, L. S.; Clardy, J. *J. Nat. Prod.* **1992**, *55*, 649−653.

(10) Alali, F. Q.; Liu, X.-X.; McLaughlin, J. L. *J. Nat. Prod.* **1999**, *62*, 504−540.

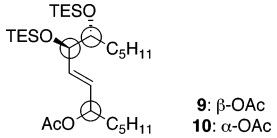
(11) (a) For syntheses of decarestrictine D, see ref 22. (b) Suemune, H.; Harabe, T.; Sakai, K. *Chem. Pharm. Bull*. **1988**, *36*, 3632−3637. (c) Gossé-Kobo, B.; Mosset, P.; Grée, R. *Tetrahedron Lett.* **1989**, *30*, 4235−4236. (d) Yadav, J. S.; Vadapalli, P. *Tetrahedron Lett.* **1994**, *35*, 641−644. (e) Motoyoshi, H.; Ishigami, K.; Kitahara, T. *Tetrahedron* **2001**, *57*, 3899−3908. (f) Pilli, R. A.; Victor, M. M.; de Meijere, A. *J. Org. Chem.* **2000**, *65*, 5910−5916. (g) Sabino, A. A.; Pilli, R. A. *Tetrahedron Lett.* **2002**, *43*, 2819−2821. (h) Taber, D. F.; Pan, Y.; Zhao, X. *J. Org. Chem.* **2004**, *69*, 7234−7240. (i) Taber, D. F.; Zhang, Z. *J. Org. Chem.* **2006**, *71*, 926−933. (j) Conrow, R. E. *Org. Lett.* **2006**, *8*, 2441−2443.

(12) (a) Kobayashi, Y.; Asano, M.; Yoshida, S.; Takeuchi, A. *Org. Lett.* **2005**, *7*, 1533−1536. (b) Yoshida, S.; Asano, M.; Kobayashi, Y. *Tetrahedron Lett.* **2005**, *46*, 7243−7246.

(13) (a) Rossiter, B. E.; Verhoeven, T. R.; Sharpless, K. B. *Tetrahedron Lett.* **1979**, 4733−4736. (b) Narula, A. S. *Tetrahedron Lett.* **1981**, *22*, 2017−2020. (c) Tomioka, H.; Suzuki, T.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1982**, *23*, 3387−3390.

(14) Easy isomerization of the *cis*,*trans*,*trans* conjugated trienyl alcohol during chromatography to the all-*trans* isomer is reported: Kobayashi, Y.; Shimazaki, T.; Taguchi, H.; Sato, F. *J. Org. Chem.* **1990**, *55*, 5324−5335.

(15) In the ^{13}C NMR spectra of **9** and **10**, the carbons circled in the structure appear at 74.6, 74.9, and 75.7 ppm for **9**, and 74.5, 75.2, and 75.7 ppm for **10**.



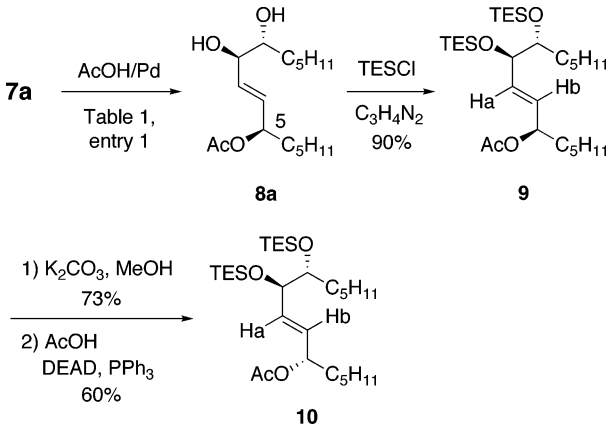
(16) The ^1H NMR spectra of **9** and **10** were superimposed and hence useless for the determination.

TABLE 1. Results of the Transformation to 8

	R^1, R^2, and R^3 for **6**−**8**			compound numbers, yields,[a] and stereoselectivities[b]					
entry	R^1	R^2	R^3	dienyl alcohol **6**		epoxide **7**		acetate **8**	
1	C_5H_{11}	H	C_5H_{11}	**6a**	72%, 95% ss	**7a**	77%	**8a**	71% 93% ds
2	C_5H_{11}	C_5H_{11}	H	**6b**	86%, 92% ss	**7b**	69%	**8b**	88% 93% ds
3	*c*-C_6H_{11}	H	C_5H_{11}	**6c**	73%, 93% ss	**7c**	64%	**8c**	77% 95% ds
4	*t*-Bu	H	C_5H_{11}	**6d**	83%, 90% ss	**7d**	62%[c]	**8d**	49% 91% ds
5	$(CH_2)_2OBn$	H	C_5H_{11}	**6e**	74%, 92% ss	**7e**		**8e**	48%[d] 92% ds
6	C_5H_{11}	H	$(CH_2)_4OTBS$	**6f**	76%, 96% ss	**7f**	76%	**8f**	78% 94% ds
7	C_5H_{11}	H	$CH(n\text{-}Bu)_2$	**6g**	76%, 95% ss	**7g**	83%	**8g**	52%[e] >90% ds
8	C_5H_{11}	H	Ph	**6h**	76%, 86% ss	**7h**		**8h**	

[a] Isolated yields. [b] ss represents stereoselectivities of the cis olefin moiety of **6** over the trans; ds represents diastereoselectivities of **8** and C(5) isomers. [c] Diastereomer of **7d** was produced in 16% yield and was separated by chromatography. [d] Two-step yield from **6e**. [e] Corresponding regioisomer with the AcO group at C(3) position was obtained in 8% yield.

SCHEME 2. Conversion of 8a to Diastereomers 9 and 10 for Calculation of the Diastereoselectivity and for Determination of the Olefin Geometry

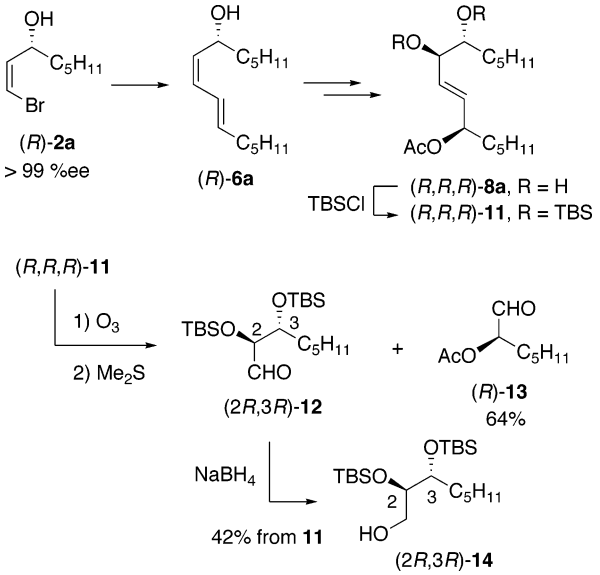


stereochemistry of the olefin moiety was determined by the coupling constant (J_{Ha-Hb} = 16 Hz) of the bis-TES ether **9** derived by silylation (Et_3SiCl, 90%) (Scheme 2), whereas the diastereoselectivity (ds) of the reaction was determined by calculating the height of the ^{13}C NMR signals for **9** and for its diastereomer **10** at 74.9 and 75.2 ppm, respectively.[15,16] The latter isomer was synthesized from **9** through the Mitsunobu reaction.

The relative stereochemistry of **8a** was assigned unambiguously by using the homochiral alcohol (*R*)-**2a** (>99% ee),[5a] which was transformed to (*R*,*R*,*R*)-**8a** through dienyl alcohol (*R*)-**6a** (Scheme 3). Ozonolysis of the derived bis-TBS ether **11** followed by reductive workup with Me_2S afforded a mixture of two aldehydes **12** and **13**. After separation of the two aldehydes by chromatography, the former was reduced to alcohol **14**. The ^1H NMR spectrum of **14** was identical with that of the *syn* isomer,[17] thus allowing assignment of the stereocenter of epoxide **7a** as depicted in the structure. Further evidence for the determination was provided by comparison of the specific rotations: **14** synthesized, $[\alpha]^{26}_D$ +33 (*c* 0.48, $CHCl_3$); (2*S*,3*S*)-**14** in the literature,[17] $[\alpha]^{25}_D$ −33.2 (*c* 1.0, $CHCl_3$). Similarly, the stereochemistry of the acetoxy-carbon of **8a** was determined as depicted: **13** synthesized, $[\alpha]^{26}_D$ +31 (*c* 0.10, $CHCl_3$); (*S*)-**13** in the literature,[18] $[\alpha]^{20}_D$ −37.8 (*c* 0.5, $CHCl_3$).

Next, epoxide **7b** prepared from the *cis*,*cis* dienyl alcohol **6b** was submitted to the palladium-catalyzed reaction with

SCHEME 3. Determination of the Stereochemistry of 8a Derived from (*R*)-2a

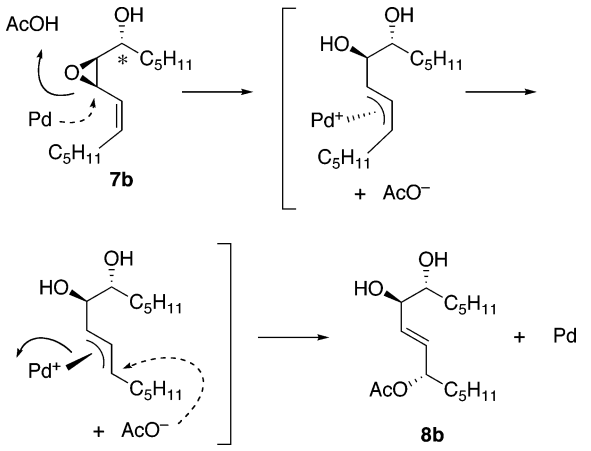


AcOH under similar reaction conditions to produce **8b**, the C(5) diastereomer of **8a**, in 88% yield with 93% ds (Table 1, entry 2). The *trans* olefin geometry of **8b** was determined by ^1H NMR spectroscopy of the derived silyl ether (J_{Ha-Hb} = 16 Hz), which was identical by spectroscopy with **10** prepared through Mitsunobu inversion of **9** (Scheme 2). These facts indicate that the three steps to produce **8b** take place sequentially: (1) oxidative addition to produce the *anti*,*syn* π-allylpalladium complex; (2) conversion to the more stable *syn*,*syn* isomer via σ-allyl complex; and (3) reaction with the acetoxy anion (Scheme 4).

In order to expand the synthetic advantage of the transformation, we explored a variation of the method to produce triol derivatives with the differently protected hydroxyl groups. Epoxy alcohol **7a** was converted to TES ether **15**, which upon palladium-catalyzed reaction with AcOH furnished **16** in 67% yield with 94% ds (Scheme 5). No migration of the TES group to the next C(2)-OH was confirmed by ^1H NMR spectroscopy of **16** and by exclusive production of acetate **17** from **16**. The proton at the C(2) position of **17** appears at 5.17−5.28 ppm. The stereochemistry of **16** was determined by converting it into bis-TES ether **9**, which showed ^1H and ^{13}C NMR spectra and R_f value on TLC identical with those synthesized above from **8a**. It should be noted that differentiation of the hydroxyl groups

(17) Nicolaou, K. C.; Webber, S. E. *Synthesis* **1986**, 453−461.
(18) Noyori, R.; Tomino, I.; Yamada, M.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6717−6725.

SCHEME 4. Three Steps to 8b



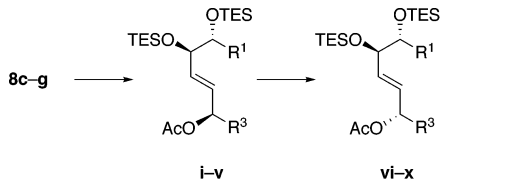
in the vicinal diols is usually difficult to attain without an additional functional group at a proximal position of the diol moiety.[19,20]

The above transformation established for the *cis*,*trans* dienyl alcohol **6a** (Table 1, entry 1) was applied to other *cis*,*trans* analogues **6c**−**h** in order to examine efficiency of the transformation (Scheme 1).[21] Epoxidation of **6c**,**e**−**g** with *m*-CPBA afforded the corresponding epoxides in good yields with exclusive ds. However, **6d** produced **7d** only with 80% ds, and **6h** gave a mixture of products. Epoxides **7c**,**d**,**f**,**g** were fairly stable to allow chromatography on silica gel, whereas **7e** was somewhat unstable and was hence submitted to the next step after short-path chromatography. The stereochemistries of epoxides **7c**−**g** depicted in Scheme 1 are speculated from that of **7a**. Palladium-catalyzed reaction of epoxide **7c** (R^1 = *c*-C_6H_{11}) with AcOH afforded **8c** with similar efficiency (Table 1, entry 3), whereas **7d** with *t*-Bu produced **8d** with somewhat lower efficiency (entry 4), probably because of steric reasons. The steric obstruction by the other side chain (R^3) was also observed in the case of **7g** with CH(*n*-Bu)$_2$, which furnished acetate **8g** as a major product (52%) and the regioisomer (8%) with the AcO group installed at C(3) (structure not shown) (entry 7). However, easy separation by chromatography compensates for the moderate regioselectivity. The alkoxy groups (OBn, OTBS) at the end of the R^1 or R^3 group were compatible with this transformation, thus producing **8e** and **8f** in moderate to good yields (entries 5 and 6).

(19) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483−2547.

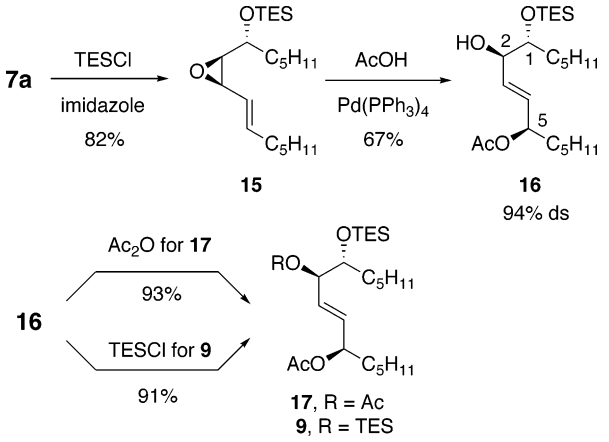
(20) See Tables 53 and 54 of ref 19.

(21) The bis-TES ethers **i**−**v** and their diastereomers **vi**−**x** were prepared from **8c**−**g** as in the cases of **8a** and **8b** in order to establish the *trans* olefin geometry and to calculate diastereomeric ratio of **8c**−**g** by ^{1}H NMR and ^{13}C NMR spectroscopy. See the experimental details in Supporting Information.



for **i** and **vi**: R^1 = *c*-C_6H_{11}, R^3 = C_5H_{11}
ii and **vii**: R^1 = *t*-Bu, R^3 = C_5H_{11}
iii and **viii**: R^1 = $(CH_2)_2OBn$, R^3 = C_5H_{11}
iv and **ix**: R^1 = C_5H_{11}, R^3 = $(CH_2)_4OTBS$
v and **x**: R^1 = C_5H_{11}, R^3 = CH(*n*-Bu)$_2$

SCHEME 5. Synthesis of 1,2,5-Triol Derivative 16 with the Three Hydroxyl Groups Being Differentiated



As mentioned in the Introduction, the structural pattern of **8** (Scheme 1) is seen in decarestrictine D (**18**), isolated from *Penicillium corylophilum* and *Polyporus tuberaster*, which shows inhibitory activity toward HMG-CoA reductase.[9a] Before the publication of our synthesis of **18** as a Letter,[12a] two syntheses were reported by Andrus[22a] and Pilli.[22b,c] Quite recently, another synthesis was reported by Krishna,[22d] who prepared a seco acid similar to our newly designed seco acid. However, some of the chiral centers in the previous syntheses are prepared by chiral induction from the pre-existing chiral center(s) with rather low efficiency, and the lactone ring formation suffers from low yields and/or excess use of the toxic reagent.

Based on the stereochemical correlation summarized in Scheme 1, a synthesis of **18** was deduced as depicted in Scheme 6, in which a precursor is seco acid **19** with properly protected hydroxyl groups at C(3), C(4), and C(7). Preparation of the C(3)−C(7) structure in **19** and its precursor **20** requires the *cis*,*trans* dienyl alcohol **21**, which in turn was disconnected to the borate derived from boronate ester **22** and *cis* bromide **23**.

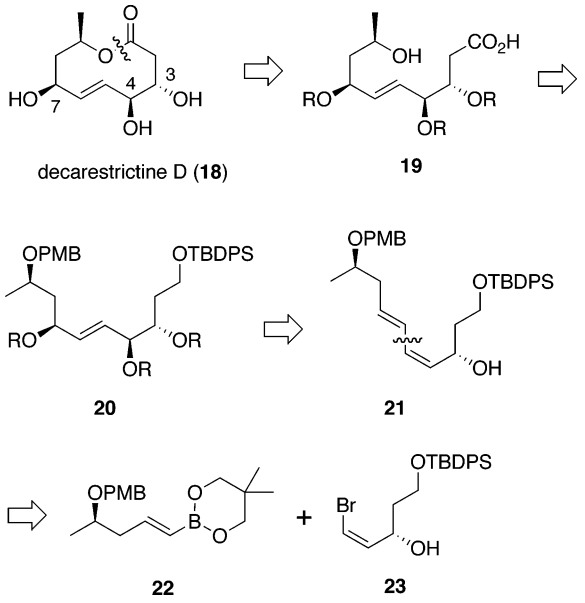
Synthesis of the boronate ester **22** was accomplished by a sequence delineated in Scheme 7 starting with epichlorohydrin **24** of 98.9% ee. The first step was reaction with TMS acetylene, and the resulting chlorohydrin was reduced to **25** in 82% yield from **24**. Protection of **25** with PMBCl (*p*-$MeOC_6H_4CH_2Cl$) under the standard conditions (NaH and NaI in THF)[23] resulted in concomitant removal of the TMS group, though incompletely, to afford a mixture of **26** and PMB ether of **25** in a 1:2 ratio. Without separation, the mixture was treated with K_2CO_3 in MeOH to produce **26** in 81% from **25**. The reverse sequence, i.e., removal of the TMS group from **25** followed by PMB protection, was less productive since most of the volatile alcohol produced in the first step was lost during isolation. Finally, the acetylene part of **26** was converted to the vinyl boronate ester moiety of **22** by hydroboration with $(Ipc)_2BH$, ligand exchange with CH_3CHO,[24] and transesterification with diol **29**.

(22) (a) Andrus, M. B.; Shih, T.-L. *J. Org. Chem.* **1996**, *61*, 8780−8785. (b) Pilli, R. A.; Victor, M. M. *Tetrahedron Lett.* **1998**, *39*, 4421−4424. (c) Pilli, R. A.; Victor, M. M. *J. Braz. Chem. Soc.* **2001**, *12*, 373−385. (d) Krishna, P. R.; Reddy, P. V. N. *Tetrahedron Lett.* **2006**, *47*, 7473−7476.

(23) Paquette, L. A.; Barriault, L.; Pissarnitski, D.; Johnston, J. N. *J. Am. Chem. Soc.* **2000**, *122*, 619−631.

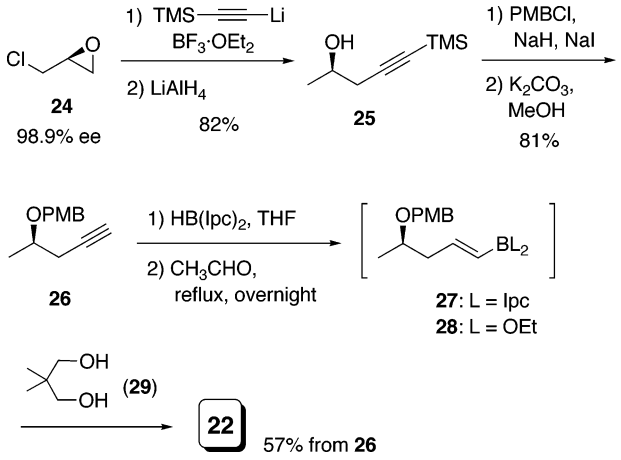
(24) Kamabuchi, A.; Moriya, T.; Miyaura, N.; Suzuki, A. *Synth. Commun.* **1993**, *23*, 2851−2859.

SCHEME 6. Retrosynthesis of Decarestrictine D[a]



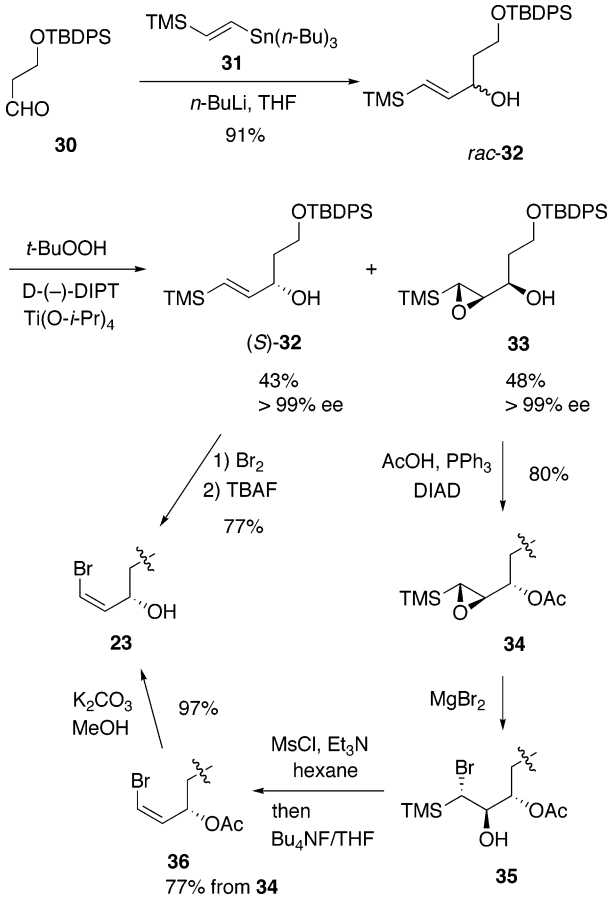
[a] OH groups at C(3), C(4), and C(7) of **19** and **20** should be protected for the transformation. We found that the choice of the protective groups was crucial for the successful macrolactonization.

SCHEME 7. Preparation of the C(6)−C(10) Intermediate 22



Another key intermediate **23** was synthesized by taking advantage of the reactivity of the vinyl silane (Scheme 8). Thus, reaction of aldehyde **30** with the lithium anion derived from **31** and *n*-BuLi afforded racemic alcohol *rac*-**32**. Sharpless asymmetric epoxidation[25] of *rac*-**32** afforded allylic alcohol (*S*)-**32** and epoxy alcohol **33**, which were separated easily by chromatography. As expected from the epoxidation of similar γ-TMS allylic alcohols,[26] both of the products were of high ee (confirmed by the MTPA method) and consequently were transformed to **23**. Bromination of (*S*)-**32** with Br_2 at −78 °C took place without injuring the TBDPS group, and subsequent treatment of the bromine adduct with Bu_4NF at −78 °C afforded **23** in 77% yield. As for **33**, the Mitsunobu inversion with AcOH

SCHEME 8. Preparation of the C(1)−C(5) Fragment 23



afforded **34**, which was free of the diastereomeric acetate derived from **33** (Ac_2O, pyridine) by ^{1}H NMR spectroscopy. Reaction of **34** with $MgBr_2$ proceeded cleanly at the carbon bearing the TMS, and bromohydrin **35** thus formed was subjected to mesylation and reaction with Bu_4NF to produce **36** in 77% yield from **34**. Finally, methanolysis with K_2CO_3 in MeOH produced **23**. The yield from **33** was 60%. The ^{1}H NMR and ^{13}C NMR spectra of each **23** synthesized by the two routes were clean, and the signals corresponding to the *trans* isomer were not detected.

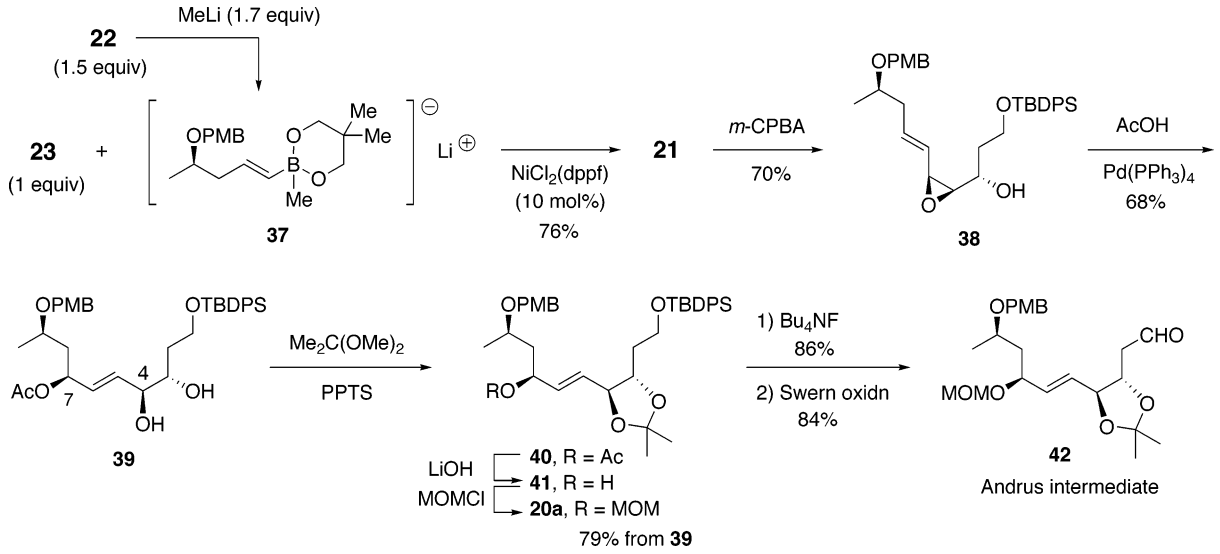
As presented in Scheme 9, nickel-catalyzed coupling reaction of alcohol **23** (1 equiv) and borate **37** derived in situ from boronate **22** (1.5 equiv) proceeded successfully to afford dienyl alcohol **21** in 76% yield as the sole product. Epoxidation with *m*-CPBA followed by palladium-catalyzed reaction of **38** with AcOH furnished **39**, which comprises the full carbon skeleton of **18** and the necessary functional groups. The ^{13}C NMR spectra of **39** and its bis-TES ether showed no signals corresponding to the diastereomer at C(7) (structure not shown). The stereochemistry of **39** tentatively assigned as drawn at this stage was proved by the transformation to the known compounds (see the next paragraph).

The remaining tasks for completion of the synthesis were functional group manipulation and macrocyclization. First, **39** was converted to the Andrus acetonide **42**.[22a] Protection of **39** as the acetonide followed by hydrolysis afforded alcohol **41**, which on reaction with MOMCl furnished the advanced intermediate **20a** of our strategy. Removal of the TBDPS protection from **20a** and Swern oxidation produced **42** in good yield. The ^{1}H NMR and ^{13}C NMR spectra of synthetic **42** were

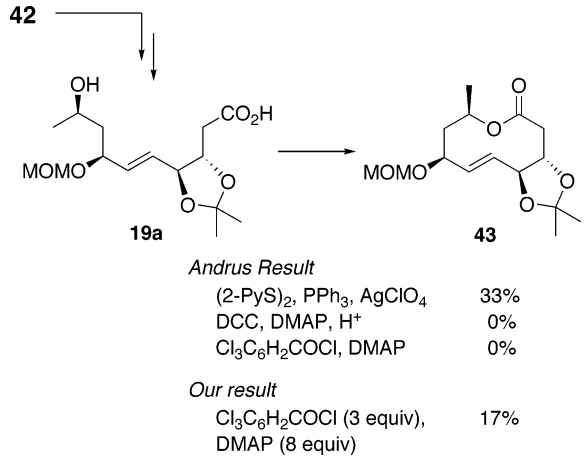
(25) (a) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237−6240. (b) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765−5780.

(26) Kinetic resolution of γ-silylallylic alcohols: Kitano, Y.; Matsumoto, T.; Sato, F. *Tetrahedron* **1988**, *44*, 4073−4086.

SCHEME 9. Synthesis of Triol Derivative 20a and Its Further Conversion to the Known Intermediate 42



SCHEME 10. Macrolactonization of 19a



consistent with the data reported, and thus the chiral centers at C(4) and C(7) of **39** created by the key transformation were established unambiguously.

Previously, macrolactonization of seco acid **19a** derived from **42** was achieved by using the Corey−Nicolaou reagent ((2-PyS)$_2$, PPh$_3$, AgClO$_4$) to produce lactone **43** in 33% yield,[27] whereas the Keck reagent (DCC, DMAP, H$^+$) and Yamaguchi reagent ($Cl_3C_6H_2COCl$, DMAP) did not afford the lactone (Scheme 10).[22a] In order to improve the yield, the same seco acid **19a** was prepared from aldehyde **42** ($NaClO_2$ then DDQ), and the lactonization was studied with the Yamaguchi reagent,[28] since we were especially familiar with this reagent through synthesis of other macrolides.[29] The procedure improved by Yonemitsu[30] did furnish **43** in 17% yield, though it is practically quite low. A reason for the failure by Andrus (0%) and for the low yield observed by us (17%) would probably be the undesired

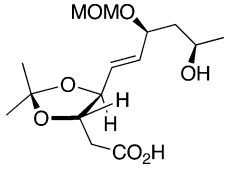


FIGURE 1. Plausible 3D structure of **19a**.

projection of the two reaction sites (CO_2H and OH) into the opposite spaces divided by the acetonide plane, thus increasing the energy barrier for the lactonization (Figure 1). This simple hypothesis led us to examine another seco acid, which is free of such an obstacle.

A new seco acid **19b** was prepared from **39** by a sequence presented in Scheme 11. Toward this end, the acetyl (Ac) group was removed, and the resulting triol **44** was converted to MOM ether **20b**. After removal of the TBDPS protective group, the C(1) carbon of the resulting alcohol **45** was oxidized to the methoxycarbonyl moiety (CO_2Me) by the standard method in 75% yield. The PMB group of **46** thus prepared was removed with DDQ, and the ester group was hydrolyzed to afford **19b**. Yamaguchi lactonization of **19b** furnished **48** in 40% yield.[31,32] The ^{1}H NMR and ^{13}C NMR spectra of lactone **48** are clean and indicate existence of a single conformational isomer.[33]

Deprotection of the MOM group of **48**, the last step, under the standard conditions such as CF_3CO_2H/CH_2Cl_2, Dowex-50/MeOH, and $BF_3{\cdot}OEt_2/(CH_2SH)_2/CH_2Cl_2$ provided a mixture of products. Fortunately, PPTS[34] in refluxing *n*-BuOH was found to proceed well to afford decarestrictine D (**18**) in 81% yield

(27) Professor T.-L. Shih, a co-author of ref 22a, communicated privately that lactonization repeated after their publication produced **43** and two other products, which were probably the corresponding diol- and monool-lactones.

(28) Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989−1993.

(29) (a) Kobayashi, Y.; Nakano, M.; Kumar, G. B.; Kishihara, K. *J. Org. Chem.* **1998**, *63*, 7505−7515. (b) Kobayashi, Y.; Okui, H. *J. Org. Chem.* **2000**, *65*, 612−615. (c) Kobayashi, Y.; Matsuumi, M. *J. Org. Chem.* **2000**, *65*, 7221−7224. (d) Kobayashi, Y.; Kumar, G. B.; Kurachi, T.; Acharya, H. P.; Yamazaki, T.; Kitazume, T. *J. Org. Chem.* **2001**, *66*, 2011−2018. (e) Kobayashi, Y.; Wang, Y.-G. *Tetrahedron Lett.* **2002**, *43*, 4381−4384.

(30) (a) Hikota, M.; Sakurai, Y.; Horita, K.; Yonemitsu, O. *Tetrahedron Lett.* **1990**, *31*, 6367−6370. (b) Makino, K.; Nakajima, N.; Hashimoto, S.; Yonemitsu, O. *Tetrahedron Lett.* **1996**, *37*, 9077−9080.

(31) Perhaps lactonization of **19b** with (2-PyS)$_2$, PPh$_3$, and AgClO$_4$ may furnish a better yield of **48** based on the results summarized in Scheme 10. However, this possibility was not studied partly because of the explosive nature of AgClO$_4$: (a) Brinkley, S. R., Jr. *J. Am. Chem. Soc.* **1940**, *62*, 3524. (b) Hein, F. *Chem. Tech. (Berlin)* **1957**, *9*, 97; *Chem. Abstr.* **1957**, *51*, 54429.

(32) Difficulty in formation of medium ring lactones: Rousseau, G. *Tetrahedron* **1995**, *51*, 2777−2849.

(33) On the other hand, lactone **43** derived from **19a** (Scheme 10) exists as a mixture of the three conformational isomers according to Andrus.[22a]

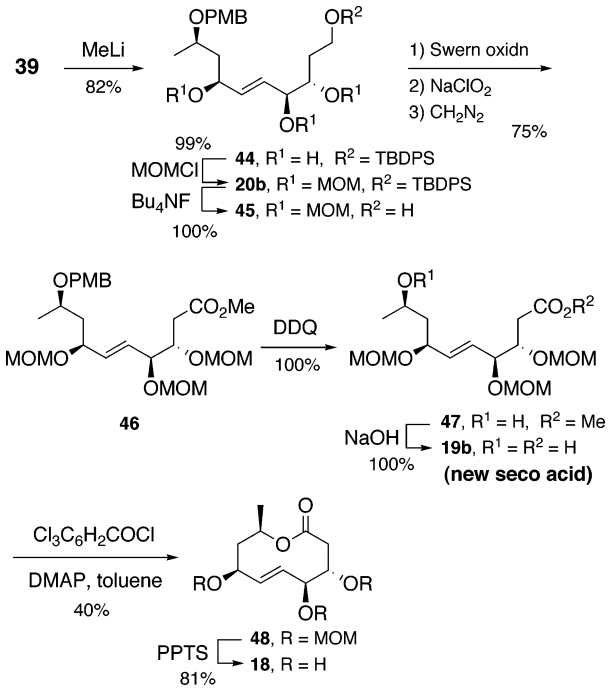
(34) Miyashita, M.; Yoshida, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772−3774.

TABLE 2. Specific Rotations of Synthetic and Natural Decarestrictine D

source of the data	$[\alpha]_D$ in MeOH	$[\alpha]_D$ in $CHCl_3$
our data (synthetic)	$[\alpha]^{24}_D$ −68 (*c* 0.066)[a]	$[\alpha]^{24}_D$ −99 (*c* 0.156)[b]
Andrus (ref 22a) (synthetic)		$[\alpha]_D$ −67 (*c* 0.26)
Krishna (ref 22d) (synthetic)		$[\alpha]^{25}_D$ −60.3 (*c* 0.4)
data cited by Andrus and Krishna for identification		$[\alpha]_D$ −62 (*c* 0.4) (incorrect)[c]
Pilli (ref 22b,c) (synthetic)		$[\alpha]_D$ −70.9 (*c* 1.0 or 0.24)
Wink and Zeeck (ref 9a) (natural)	$[\alpha]^{20}_D$ −62 (*c* 1.0)	
Ayer (ref 9c) (natural)		$[\alpha]^{25}_D$ −31 (*c* 0.4)

[a] After recrystallization from CH_2Cl_2/hexane. [b] The rotation was measured again in $CHCl_3$: $[\alpha]^{24}_D$ −102 (*c* 0.066). [c] This value (−62) was originally measured in MeOH (*c* 1.0) by Wink and Zeeck.[9a]

SCHEME 11. Synthesis of Decarestrictine D (18) through a New Seco Acid 19b



after chromatography. The ^1H NMR and ^{13}C NMR spectra of synthetic **18**[35] measured in $CDCl_3$ and in CD_3OD were identical with those reported.[9c,22a−c]

In addition, we would like to comment on the specific rotation of **18** ($[\alpha]^{24}_D$ −68 (*c* 0.066, MeOH); $[\alpha]^{24}_D$ −99 to −102 (*c* 0.156−0.066, $CHCl_3$)). The value in MeOH was in agreement with that reported for natural **18** by Wink and Zeeck ($[\alpha]^{20}_D$ −62 (*c* 1.0)).[9a] On the contrary, the rotation in $CHCl_3$ was *not* consistent with that reported by Andrus ($[\alpha]_D$ −67 (*c* 0.26, $CHCl_3$)).[22a] Values similar to that of Andrus have been reported later by Pilli[22b,c] and quite recently by Krishna.[22d] Fortunately, the coauthor (T.-L. Shih) of ref 22a informed us (Y.K.) that the data (−67) was actually measured in MeOH and not in $CHCl_3$. The $[\alpha]_D$ values measured by us and others are summarized in Table 2.[36]

(35) Mp (121−123 °C (recrystallized from CH_2Cl_2/hexane)) was also in good agreement with the reported values: 118−120 °C (synthetic);[22a,d] 116 °C (natural);[9b] 114−115 °C (natural).[9c]

(36) Note that the value (−62) in *MeOH* measured by Wink and Zeeck[9a] and that (−68) by us have been used incorrectly as measured in $CHCl_3$ by the authors of ref 22a,d. The lower value reported by Ayer[9c] is probably due to incomplete purification from a natural source.

Conclusion

We have shown a transformation of dienyl alcohols **6** to *trans* 3-alkene-1,2,5-triol derivatives **8** (Scheme 1) and clarified the stereochemical relationship between the olefin moiety of **6** and the chiral centers of **8**. A variation of the method for synthesizing the triol derivatives with the differentiated hydroxyl groups was examined as delineated in Scheme 5, which is an additional synthetic advantage of this method.

With the above relationship in mind, synthesis of decarestrictine D (**18**) was designed easily and executed with minimum effort in differentiating the hydroxyl groups since the hydroxyl group of the *cis* bromo alcohol **23** was compatible with the coupling partner (borate **37**), which is formally a hard anion. Moreover, examination of the negative factor for the lactonization of the seco acid **19a** with the acetonide group led us to design a new seco acid **19b**, which furnished a better yield of lactone **48** using the Yamaguchi reagent. We think that the present synthesis of decarestrictine D would be applicable to that of analogues as well.

Experimental Section

(7*Z*,9*E*)-7,9-Pentadecadien-6-ol (6a). To an ice-cold mixture of boronate ester (*E*)-**3a** (R^2 = H, R^3 = C_5H_{11}) (158 mg, 0.752 mmol) and $NiCl_2$(dppf) (34 mg, 0.050 mmol) in Et_2O (1.0 mL) and THF (0.2 mL) was added MeLi (0.57 mL, 1.41 M in Et_2O, 0.804 mmol) slowly. After 15 min of stirring at 0 °C, bromoalcohol **2a** (R^1 = C_5H_{11}) (104 mg, 0.502 mmol) was added. The resulting mixture was stirred at room temperature overnight and diluted with Et_2O and saturated $NaHCO_3$. The layers were separated, and the aqueous layer was extracted with Et_2O three times. The combined extracts were dried ($MgSO_4$) and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc/Et_3N (trace)) to give **6a** (81 mg) in 72% yield: IR (neat) 3338, 1654 cm^{-1}; ^1H NMR δ 0.88 (t, *J* = 6 Hz, 6 H), 1.16−1.72 (m, 15 H), 2.09 (q, *J* = 7 Hz, 2 H), 4.51−4.63 (m, 1 H), 5.27 (t, *J* = 10 Hz, 1 H), 5.74 (dt, *J* = 15, 7 Hz, 1 H), 6.02 (t, *J* = 11 Hz, 1 H), 6.31 (dd, *J* = 15, 11 Hz, 1 H); ^{13}C NMR δ 137.4, 131.4, 130.5, 125.1, 68.1, 37.6, 33.0, 32.0, 31.6, 29.0, 25.2, 22.8, 22.7, 14.2. Anal. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.18; H, 12.33.

(6*R,7*R**,8*R**,9*E*)-7,8-Epoxy-9-pentadecen-6-ol (7a).** To an ice-cold mixture of **6a** (213 mg, 0.950 mmol) and $NaHCO_3$ (181 mg, 2.13 mmol) in CH_2Cl_2 (4.8 mL) was added *m*-CPBA (246 mg, 80% purity, 1.14 mmol). After 40 min of stirring at 0 °C, Me_2S (0.030 mL, 0.423 mmol) was added to the resulting mixture at the same temperature. The mixture was stirred at 0 °C for 5 min and diluted with Et_2O and saturated $NaHCO_3$. The layers were separated, and the water layer was extracted with Et_2O three times. The combined extracts were dried ($MgSO_4$) and concentrated to give a mixture of an oil and a white precipitate, which was purified by short-path chromatography on silica gel (hexane/EtOAc/Et_3N (trace)) to give **7a** (175 mg) in 77% yield: IR (neat) 3429, 968

cm^{-1}; ^{1}H NMR δ 0.88 (t, J = 6 Hz, 6 H), 1.13−1.71 (m, 14 H), 2.00−2.12 (m, 3 H), 3.02 (dd, J = 8, 4 Hz, 1 H), 3.46−3.56 (m, 2 H), 5.29 (ddt, J = 16, 8, 1 Hz, 1 H), 5.94 (dt, J = 16, 7 Hz, 1 H); ^{13}C NMR δ 138.8, 123.6, 70.1, 62.4, 58.2, 33.8, 32.6, 31.9, 31.4, 28.7, 24.8, 22.71, 22.66, 14.2.

(1*R,2*E*,4*R**,5*R**)-4,5-Dihydroxy-1-pentyl-2-decenyl Acetate (8a).** To an ice-cold mixture of $Pd(PPh_3)_4$ (87 mg, 0.075 mmol) and AcOH (0.062 mL, 1.09 mmol) in THF (2 mL) was added a solution of **7a** (175 mg, 0.728 mmol) in THF (1.0 mL + 0.50 mL × 2) slowly. After 35 min of stirring at 0 °C, H_2O_2 (0.11 mL, 3.6 mmol) was added to the resulting mixture with vigorous stirring. To the mixture were added EtOAc and saturated $NaHCO_3$ with stirring. The layers were separated, and the aqueous layer was extracted with EtOAc three times. The combined extracts were dried ($MgSO_4$) and concentrated to give a yellow oil, which was purified by silica gel chromatography (hexane/EtOAc) to afford **8a** (156 mg) in 71% yield: IR (neat) 3421, 1739, 1241 cm^{-1}; ^{1}H NMR δ 0.87 (t, J = 7 Hz, 3 H), 0.88 (t, J = 7 Hz, 3 H), 1.15−1.74 (m, 16 H), 2.04 (s, 3 H), 2.40 (br s, 1 H), 2.49 (br s, 1 H), 3.39−3.50 (m, 1 H), 3.88−3.96 (m, 1 H), 5.18−5.27 (m, 1 H), 5.63−5.80 (m, 2 H); ^{13}C NMR δ 170.4, 131.8, 131.4, 75.3, 74.6, 74.1, 34.4, 33.0, 32.0, 31.7, 25.4, 24.9, 22.73, 22.68, 21.4, 14.22, 14.17; HRMS-CI m/z ([M + 1]$^+$): calcd for $C_{17}H_{33}O_4$ 301.2379, found 301.2368.

(1*R,2*E*,4*R**,5*R**)-4,5-Bis[(triethylsilyl)oxy]-1-pentyl-2-decenyl Acetate (9).** To an ice-cold solution of **8a** (156 mg, 0.519 mmol) and imidazole (106 mg, 1.56 mmol) in DMF (2 mL) was added triethylsilyl chloride (0.209 mL, 1.25 mmol) slowly, and the resulting solution was stirred at room temperature for 6 h. Hexane and saturated $NaHCO_3$ were added with stirring. The layers were separated, and the aqueous layer was extracted with hexane three times. The combined extracts were dried ($MgSO_4$) and concentrated to give an oil, which was subjected to chromatography on silica gel (hexane/EtOAc) to afford **9** (248 mg) in 90% yield: IR (neat) 1742, 1239, 1016 cm^{-1}; ^{1}H NMR δ 0.57 (q, J = 8 Hz, 6 H), 0.59 (q, J = 8 Hz, 6 H), 0.87 (t, J = 7 Hz, 3 H), 0.88 (t, J = 7 Hz, 3 H), 0.94 (t, J = 8 Hz, 9 H), 0.96 (t, J = 8 Hz, 9 H), 1.14−1.70 (m, 16 H), 2.02 (s, 3 H), 3.52−3.61 (m, 1 H), 4.12 (dt, J = 1.5, 5 Hz, 1 H), 5.26 (q, J = 7 Hz, 1 H), 5.60 (ddd, J = 16, 7, 2 Hz, 1 H), 5.80 (ddd, J = 16, 5, 1 Hz, 1 H); ^{13}C NMR δ 170.2, 132.2, 128.8, 75.7, 74.9, 74.6, 34.7, 32.2, 31.8, 31.5, 25.8, 25.0, 22.8, 22.7, 21.5, 14.3, 14.2, 7.2, 7.0, 5.3, 5.1. Anal. Calcd for $C_{29}H_{60}O_4Si_2$: C, 65.85; H, 11.43. Found: C, 65.89; H, 11.41.

(1*S,2*E*,4*R**,5*R**)-4,5-Bis[(triethylsilyl)oxy]-1-pentyl-2-decenyl Acetate (10) from 9.** A mixture of acetate **9** (15 mg, 0.028 mmol) and K_2CO_3 (20 mg, 0.145 mmol) in MeOH (0.8 mL) was stirred at room temperature for 8 h and diluted with brine and EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc three times. The combined organic layers were dried ($MgSO_4$) and concentrated to afford a residue, which was purified by chromatography on silica gel to furnish the corresponding alcohol (10 mg) in 73% yield: ^{1}H NMR δ 0.58 (q, J = 8 Hz, 6 H), 0.61 (q, J = 8 Hz, 6 H), 0.8−1.1 (m, 21 H), 1.1−1.7 (m, 17 H), 3.54−3.62 (m, 1 H), 4.08−4.19 (m, 2 H), 5.69 (dd, J = 16, 5 Hz, 1 H), 5.76 (dd, J = 16, 4.5 Hz, 1 H).

To an ice-cold solution of the above alcohol (117 mg, 0.240 mmol) and PPh_3 (126 mg, 0.480 mmol) in THF (1.0 mL) was added AcOH (0.027 mL, 0.474 mmol). The resulting solution was allowed to warm to 8 °C over 5 min, and diethyl azodicarboxylate (0.075 mL, 0.476 mmol) was added to it. The resulting solution was stirred at room temperature overnight and diluted with Et_2O and aqueous $NaHCO_3$ with stirring. The layers were separated, and the aqueous layer was extracted with Et_2O twice. The combined extracts were dried ($MgSO_4$) and concentrated to afford an oil, which was purified by silica gel chromatography (hexane/EtOAc) to furnish acetate **10** (76 mg) in 60% yield: IR (neat) 1741, 1239, 1016 cm^{-1}; ^{1}H NMR δ 0.56 (q, J = 8 Hz, 6 H), 0.59 (q, J = 8 Hz, 6 H), 0.86 (t, J = 7 Hz, 6 H), 0.93 (t, J = 8 Hz, 9 H), 0.95 (t, J = 8 Hz, 9 H), 1.11−1.69 (m, 16 H), 2.01 (s, 3 H), 3.51−3.61 (m, 1 H), 4.08 (t, J = 5 Hz, 1 H), 5.26 (q, J = 7 Hz, 1 H), 5.59 (dd, J = 16, 7 Hz, 1 H), 5.77 (dd, J = 16, 5 Hz, 1 H); ^{13}C NMR δ 170.2, 132.3, 128.9, 75.7, 75.2, 74.5, 34.6, 32.2, 31.7, 31.4, 25.8, 25.0, 22.8, 22.7, 21.5, 14.26, 14.19, 7.2, 7.0, 5.3, 5.1.

(1*R*,2*E*,4*R*,5*R*)-4,5-Bis[(*tert*-butyldimethylsilyl)oxy]-1-pentyl-2-decenyl Acetate ((*R*,*R*,*R*)-11). Alcohol (*R*)-**2a** (**2** of R^1 = C_5H_{11}) of >99% ee (by ^{1}H NMR spectroscopy of the MTPA ester) was prepared according to the literature method[5a,26] and transformed into acetate (*R*,*R*,*R*)-**8a** in yields similar to those obtained with the racemic alcohol **2a**.

A solution of (*R*,*R*,*R*)-**8a** (159 mg, 0.529 mmol), TBSCl (191 mg, 1.27 mmol), and imidazole (108 mg, 1.59 mmol) in DMF (1.2 mL) was stirred at room temperature overnight and diluted with Et_2O and saturated $NaHCO_3$ with stirring. The layers were separated, and the aqueous layer was extracted with Et_2O three times. The combined extracts were dried ($MgSO_4$) and concentrated to leave an oil, which was purified by chromatography on silica gel (hexane/EtOAc) to give TBS ether (*R*,*R*,*R*)-**11** (230 mg) in 82% yield: IR (neat) 1742, 1239, 1097 cm^{-1}; ^{1}H NMR δ 0.02 (s, 3 H), 0.03 (s, 3 H), 0.045 (s, 3 H), 0.050 (s, 3 H), 0.89 (br s, 24 H), 1.10−1.70 (m, 16 H), 2.03 (s, 3 H), 3.47−3.62 (m, 1 H), 4.02−4.16 (m, 1 H), 5.26 (q, J = 7 Hz, 1 H), 5.58 (ddd, J = 16, 7, 1.5 Hz, 1 H), 5.78 (dd, J = 16, 5 Hz, 1 H); ^{13}C NMR δ 170.2, 132.0, 128.7, 75.4, 75.0, 74.6, 34.6, 32.1, 31.7, 31.0, 26.03, 26.01, 25.85, 25.0, 22.79, 22.75, 21.5, 18.4, 18.2, 14.25, 14.21, −4.0, −4.36, −4.40, −4.6; $[\alpha]^{25}_D$ +59.4 (*c* 1.19, $CHCl_3$). Anal. Calcd for $C_{29}H_{60}O_4Si_2$: C, 65.85; H, 11.43. Found: C, 65.78; H, 11.17.

Ozonolysis of the Above TBS Ether (*R*,*R*,*R*)-11. Ozone was introduced into a solution of TBS ether (*R*,*R*,*R*)-**11** (78 mg, 0.147 mmol) in CH_2Cl_2 (3 mL) at −78 °C for 30 min. Argon was bubbled gently through the solution for 20 min at −78 °C to purge excess ozone, and then Me_2S (0.156 mL, 2.13 mmol) was added. The solution was allowed to warm to room temperature overnight and concentrated to give an oil, which was subjected to chromatography on silica gel (hexane/Et_2O) to give aldehyde (2*R*,3*R*)-**12** with a small quantity of an unidentified compound(s) (46 mg, ca. 80%) and pure α-acetyloxy aldehyde (*R*)-**13** (16 mg, 64% yield). (2*R*,3*R*)-**12**: IR and ^{1}H NMR spectra were identical with those reported;[17] ^{13}C NMR δ 203.7, 80.1, 74.7, 32.8, 31.9, 25.92, 25.90, 25.7, 22.7, 18.4, 18.2, 14.2, −4.26, −4.30, −4.32, −4.9. (*R*)-**13**: ^{1}H NMR δ 0.89 (t, J = 7 Hz, 3 H), 1.24−1.47 (m, 6 H), 1.65−1.89 (m, 2 H), 2.17 (s, 3 H), 4.98 (dd, J = 8, 5 Hz, 1 H), 9.51 (s, 1 H); $[\alpha]^{26}_D$ +31 (*c* 0.10, $CHCl_3$). Compare (*S*)-**13** of 100% ee, $[\alpha]^{20}_D$ −37.8 (*c* 0.5, $CHCl_3$).[18]

(2*R*,3*R*)-2,3-Bis[(*tert*-butyldimethylsilyl)oxy]-1-octanol ((2*R*,3*R*)-14). To an ice-cold solution of the above aldehyde (2*R*,3*R*)-**12** in MeOH (0.65 mL) and THF (0.01 mL) was added $NaBH_4$ (4.4 mg, 0.12 mmol), and the resulting mixture was stirred for 4 h at 0 °C. The solution was diluted with Et_2O and H_2O. After 10 min of stirring, the layers were separated, and the aqueous layer was extracted with EtOAc four times. The combined extracts were dried ($MgSO_4$) and concentrated to leave a residue, which was purified by short-path chromatography on silica gel (hexane/Et_2O) to afford (2*R*,3*R*)-**14** (24 mg) in 42% yield from (*R*,*R*,*R*)-**11** (2 steps): IR and ^{1}H NMR spectra were identical with those reported;[17] ^{13}C NMR δ 75.5, 73.8, 63.3, 32.0, 30.5, 26.4, 26.0, 25.9, 22.8, 18.2, 18.1, 14.2, −4.0, −4.4, −4.5; $[\alpha]^{26}_D$ +33 (*c* 0.48, $CHCl_3$). Compare (2*S*,3*S*)-**14**: $[\alpha]^{25}_D$ −33.2 (*c* 1.0, $CHCl_3$).[17]

(3*S*,4*Z*,6*E*,9*R*)-1-[(*tert*-Butyldiphenylsilyl)oxy]-9-[(4-methoxybenzyl)oxy]-4,6-decadien-3-ol (21). To an ice-cold suspension of $NiCl_2$(dppf) (34 mg, 0.05 mmol) and boronate ester **22** (239 mg, 0.751 mmol) in Et_2O (1.1 mL) and THF (0.22 mL) was added MeLi (0.56 mL, 1.43 M in Et_2O, 0.801 mmol). After 15 min of stirring at 0 °C, bromoalcohol **23** (210 mg, 0.501 mL) was added to the resulting brown suspension. The mixture was stirred at room temperature overnight and diluted with $NaHCO_3$ and EtOAc with stirring. The layers were separated, and the aqueous layer was extracted with EtOAc three times. The combined extracts were dried ($MgSO_4$) and concentrated to give a brown oil, which was subjected to chromatography on silica gel (hexane/EtOAc/Et_3N (trace)) to afford **21** (208 mg) in 76% yield: IR (neat) 3437, 1513, 1248 cm^{-1};

^{1}H NMR δ 1.06 (s, 9 H), 1.17 (d, J = 6 Hz, 3 H), 1.56−1.73 (m, 1 H), 1.75−1.93 (m, 1 H), 2.19−2.30 (m, 1 H), 2.33−2.44 (m, 1 H), 2.86 (d, J = 3 Hz, 1 H), 3.49−3.59 (m, 1 H), 3.79 (s, 3 H), 3.74−3.91 (m, 2 H), 4.41 (d, J = 11 Hz, 1 H), 4.48 (d, J = 11 Hz, 1 H), 4.85−4.96 (m, 1 H), 5.36 (dd, J = 11, 9 Hz, 1 H), 5.74 (dt, J = 15, 7 Hz, 1 H), 6.01 (t, J = 11 Hz, 1 H), 6.40 (dd, J = 15, 11 Hz, 1 H), 6.86 (dm, J = 9 Hz, 2 H), 7.25 (dm, J = 9 Hz, 2 H), 7.35−7.47 (m, 6 H), 7.64−7.73 (m, 4 H); ^{13}C NMR δ 159.0, 135.53, 135.51, 133.2, 133.1, 132.7, 131.6, 130.9, 129.79, 129.76, 129.71, 129.1, 127.8, 127.7, 127.3, 113.7, 74.3, 70.2, 67.3, 62.4, 55.4, 40.0, 39.3, 27.0, 19.8, 19.3; $[\alpha]^{24}_D$ −8.5 (*c* 0.66, $CHCl_3$). Anal. Calcd for $C_{34}H_{44}O_4Si$: C, 74.96; H, 8.14. Found: C, 74.66; H, 8.31.

(3*S*,4*R*,5*S*,6*E*)-1-[(*tert*-Butyldiphenylsilyl)oxy]-4,5-epoxy-9-(4-methoxybenzyloxy)-6-decen-3-ol (38). To an ice-cold mixture of **21** (259 mg, 0.475 mmol) and $NaHCO_3$ (90 mg, 1.07 mmol) in CH_2Cl_2 (2 mL) was added *m*-CPBA (133 mg, 80% purity, 0.617 mmol). After 50 min of stirring at 0 °C, Me_2S (0.018 mL, 0.25 mmol) was added. The mixture was stirred at 0 °C for 5 min and diluted with Et_2O and saturated $NaHCO_3$ with stirring. The layers were separated, and the aqueous layer was extracted with Et_2O three times. The combined extracts were dried ($MgSO_4$) and concentrated. The residue was purified by short-path chromatography on silica gel (hexane/EtOAc/Et_3N (trace)) to give epoxide **38** (187 mg) in 70% yield: IR (neat) 3421, 1248, 1111 cm^{-1}; ^{1}H NMR δ 1.05 (s, 9 H), 1.15 (d, J = 6 Hz, 3 H), 1.57−1.84 (m, 2 H), 2.17−2.38 (m, 2 H), 2.74−2.80 (m, 1 H), 3.11 (dd, J = 8, 4 Hz, 1 H), 3.44−3.62 (m, 2 H), 3.78 (s, 3 H), 3.71−3.92 (m, 3 H), 4.38 (d, J = 11 Hz, 1 H), 4.47 (d, J = 11 Hz, 1 H), 5.37 (dd, J = 15, 8 Hz, 1 H), 5.99 (dt, J = 15, 7 Hz, 1 H), 6.86 (d, J = 9 Hz, 2 H), 7.25 (d, J = 9 Hz, 2 H), 7.34−7.49 (m, 6 H), 7.62−7.72 (m, 4 H); ^{13}C NMR δ 159.0, 135.49, 135.47, 134.9, 133.2, 133.1, 130.8, 129.79, 129.76, 129.1, 127.75, 127.73, 125.9, 113.8, 74.0, 70.2, 68.9, 62.1, 61.1, 57.3, 55.4, 39.6, 35.7, 27.0, 19.7, 19.3; $[\alpha]^{24}_D$ −7.4 (*c* 1.02, $CHCl_3$).

(1*S*,2*E*,4*S*,5*S*,2′*R*)-7-[(*tert*-Butyldiphenylsilyl)oxy]-4,5-dihydroxy-1-[2′-[(4-methoxyl-benzyl)oxy]propyl]-2-heptenyl Acetate (39). To an ice-cold mixture of $Pd(PPh_3)_4$ (282 mg, 0.244 mmol) and AcOH (0.135 mL, 2.37 mmol) in THF (4 mL) was added a solution of epoxide **38** (664 mg, 1.18 mmol) in THF (2 mL). The reaction was carried out between 8 and 11 °C for 30 min and quenched by addition of H_2O_2 (0.05 mL, 1.64 mmol), EtOAc, and saturated $NaHCO_3$. The layers were separated, and the aqueous layer was extracted with EtOAc three times. The combined extracts were dried ($MgSO_4$) and concentrated to afford a yellow oil, which was purified by chromatography on silica gel (CH_2Cl_2/acetone) to afford **39** (497 mg) in 68% yield: IR (neat) 3448, 1737 cm^{-1}; ^{1}H NMR δ 1.05 (s, 9 H), 1.20 (d, J = 6 Hz, 3 H), 1.59−1.85 (m, 4 H), 1.96 (s, 3 H), 2.72 (d, J = 4 Hz, 1 H), 3.49−3.61 (m, 2 H), 3.79 (s, 3 H), 3.69−3.82 (m, 1 H), 3.86 (t, J = 6 Hz, 2 H), 3.93−4.02 (m, 1 H), 4.29 (d, J = 11 Hz, 1 H), 4.49 (d, J = 11 Hz, 1 H), 5.46−5.58 (m, 1 H), 5.63−5.82 (m, 2 H), 6.86 (d, J = 9 Hz, 2 H), 7.26 (d, J = 9 Hz, 2 H), 7.34−7.50 (m, 6 H), 7.58−7.75 (m, 4 H); ^{13}C NMR δ 170.1, 159.0, 135.48, 135.46, 132.72, 132.66, 131.6, 131.2, 130.5, 129.90, 129.89, 129.6, 127.8, 113.8, 75.0, 74.2, 71.0, 70.3, 70.2, 62.9, 55.4, 42.2, 34.4, 26.9, 21.4, 19.8, 19.2; $[\alpha]^{27}_D$ −38.1 (*c* 0.41, $CHCl_3$). Anal. Calcd for $C_{36}H_{48}O_7Si$: C, 69.64; H, 7.79. Found: C, 69.73; H, 8.11.

(3*S*,4*S*,5*E*,7*S*,9*R*)-1-[(*tert*-Butyldiphenylsilyl)oxy]-9-[(4-methoxybenzyl)oxy]-3,4,7-tri[(methoxymethyl)oxy]-5-decene (20b). To an ice-cold solution of **39** (419 mg, 0.675 mmol) in THF (2 mL) was added MeLi (2.58 mL, 1.65 M in Et_2O, 4.26 mmol). The solution was stirred at room temperature for 2 h and poured into saturated NH_4Cl and EtOAc with stirring. The layers were separated, and the aqueous layer was extracted with EtOAc three times. The combined extracts were dried ($MgSO_4$) and concentrated to leave an oil, which was purified by silica gel chromatography (CH_2Cl_2/acetone) to give triol **44** (319 mg) in 82% yield: IR (neat) 3420, 1249, 1111 cm^{-1}; ^{1}H NMR δ 1.05 (s, 9 H), 1.24 (d, J = 6 Hz, 3 H), 1.55−1.90 (m, 4 H), 2.81 (br d, J = 3 Hz, 1 H), 3.12 (br d, J = 5 Hz, 1 H), 3.44−3.66 (m, 2 H), 3.78 (s, 3 H), 3.64−4.01 (m, 4 H), 4.34 (d, J = 11 Hz, 1 H), 4.38−4.49 (m, 1 H), 4.54 (d, J = 11 Hz, 1 H), 5.72 (dd, J = 16, 6 Hz, 1 H), 5.81 (dd, J = 16, 5 Hz, 1 H), 6.87 (d, J = 9 Hz, 2 H), 7.25 (d, J = 9 Hz, 2 H), 7.36−7.48 (m, 6 H), 7.57−7.76 (m, 4 H).

A solution of **44** (113 mg, 0.195 mmol), MOMCl (0.083 mL, 1.09 mmol), and (*i*-Pr)$_2$NEt (0.27 mL, 1.56 mmol) in CH_2Cl_2 (0.5 mL) was stirred at 40 °C overnight and diluted with EtOAc and saturated $NaHCO_3$ with stirring at 0 °C. The layers were separated, and the aqueous layer was extracted with EtOAc three times. The combined extracts were dried ($MgSO_4$) and concentrated to give an oil, which was purified by silica gel chromatography (hexane/EtOAc) to afford **20b** (137 mg) in 99% yield: IR (neat) 1106, 1035 cm^{-1}; ^{1}H NMR δ 1.04 (s, 9 H), 1.22 (d, J = 6 Hz, 3 H), 1.59−1.97 (m, 4 H), 3.29 (s, 3 H), 3.32 (s, 3 H), 3.35 (s, 3 H), 3.79 (s, 3 H), 3.72−3.88 (m, 4 H), 4.14 (t, J = 5 Hz, 1 H), 4.27−4.37 (m, 1 H), 4.36 (d, J = 11 Hz, 1 H), 4.50 (d, J = 7 Hz, 1 H), 4.54 (d, J = 7 Hz, 1 H), 4.54 (d, J = 11 Hz, 1 H), 4.63 (d, J = 7 Hz, 1 H), 4.65 (d, J = 7 Hz, 1 H), 4.67 (d, J = 7 Hz, 1 H), 4.68 (d, J = 7 Hz, 1 H), 5.53−5.71 (m, 2 H), 6.88 (d, J = 9 Hz, 2 H), 7.23−7.47 (m, 8 H), 7.62−7.71 (m, 4 H); ^{13}C NMR δ 159.0, 135.5, 134.7, 133.79, 133.76, 130.9, 129.6, 129.2, 129.1, 127.6, 113.8, 97.3, 94.3, 94.1, 77.6, 77.0, 73.5, 71.4, 70.4, 60.4, 55.9, 55.8, 55.7, 55.4, 44.0, 34.0, 27.0, 20.1, 19.4; $[\alpha]^{24}_D$ −23.2 (*c* 0.586, $CHCl_3$). Anal. Calcd for $C_{40}H_{58}O_9Si$: C, 67.57; H, 8.22. Found: C, 67.61; H, 8.25.

(3*S*,4*S*,5*E*,7*S*,9*R*)-9-[(4-Methoxybenzyl)oxy]-3,4,7-tri-[(methoxymethyl)oxy]-5-decen-1-ol (45). A solution of **20b** (148 mg, 0.208 mmol) and Bu_4NF (0.25 mL, 1.0 M in THF, 0.25 mmol) in THF (0.25 mL) was stirred at 40 °C for 2 h and diluted with Et_2O and saturated NH_4Cl with stirring. The layers were separated, and the aqueous layer was extracted with EtOAc three times. The combined mixture was dried ($MgSO_4$) and concentrated to leave an oil, which was subjected to chromatography on silica gel (CH_2Cl_2/acetone) to give **45** (98 mg) in 100% yield: IR (neat) 3482, 1514 cm^{-1}; ^{1}H NMR δ 1.22 (d, J = 6 Hz, 3 H), 1.59−1.90 (m, 4 H), 2.64 (t, J = 6 Hz, 1 H), 3.34 (s, 3 H), 3.36 (s, 3 H), 3.42 (s, 3 H), 3.80 (s, 3 H), 3.60−3.87 (m, 4 H), 4.10 (t, J = 6 Hz, 1 H), 4.27−4.36 (m, 1 H), 4.35 (d, J = 11 Hz, 1 H), 4.50 (d, J = 7 Hz, 1 H), 4.53 (d, J = 7 Hz, 1 H), 4.54 (d, J = 11 Hz, 1 H), 4.639 (d, J = 7 Hz, 1 H), 4.644 (d, J = 7 Hz, 1 H), 4.69 (d, J = 7 Hz, 1 H), 4.81 (d, J = 7 Hz, 1 H), 5.55 (dd, J = 16, 7 Hz, 1 H), 5.64 (dd, J = 16, 7 Hz, 1 H), 6.88 (dm, J = 8 Hz, 2 H), 7.28 (dm, J = 8 Hz, 2 H); ^{13}C NMR δ 159.0, 135.6, 130.9, 129.2, 128.3, 113.8, 98.0, 94.5, 93.9, 78.4, 78.2, 73.7, 71.2, 70.3, 59.2, 56.2, 55.7, 55.6, 55.4, 44.0, 33.9, 20.0; $[\alpha]^{30}_D$ −45.6 (*c* 0.838, $CHCl_3$). Anal. Calcd for $C_{24}H_{40}O_9$: C, 61.00; H, 8.53. Found: C, 61.16; H, 8.47.

Methyl (3*S*,4*S*,5*E*,7*S*,9*R*)-9-[(4-Methoxybenzyl)oxy]-3,4,7-tri-[(methoxymethyl)oxy]-5-decenoate (46). According to the synthesis of aldehyde **42**, alcohol **45** (181 mg, 0.383 mmol) in CH_2Cl_2 (2 mL) was converted into the corresponding aldehyde with oxalyl chloride (0.100 mL, 1.15 mmol), CH_2Cl_2 (1.5 mL), DMSO (0.17 mL, 2.4 mmol), and Et_3N (0.48 mL, 3.45 mmol). The product was used for the next reaction without further purification.

To a solution of the above aldehyde and 2-methyl-2-butene (0.40 mL, 3.8 mmol) in H_2O (0.8 mL) and *t*-BuOH (3.2 mL) were added the phosphate buffer (pH = 3.6) (1.2 mL) and $NaClO_2$ (217 mg, purity 80%, 1.92 mmol) at room temperature. The mixture was stirred at room temperature for 2 h and concentrated in vacuo to afford an oily residue, which was diluted with the phosphate buffer (pH = 3.6) and EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined extracts were dried ($MgSO_4$) and concentrated to give the corresponding acid. A sample for characterization was purified by chromatography on silica gel (hexane/EtOAc): IR (neat) 3100 cm^{-1}; ^{1}H NMR δ 1.22 (d, J = 6 Hz, 3 H), 1.61−1.78 (m, 2 H), 2.52 (dd, J = 16, 8 Hz, 1 H), 2.71 (dd, J = 16, 5 Hz, 1 H), 3.35 (s, 3 H), 3.36 (s, 6 H), 3.80 (s, 3 H), 3.70−3.92 (m, 1 H), 4.08 (dt, J = 8, 5 Hz, 1 H), 4.18−4.28 (m, 1 H), 4.28−4.40 (m, 1 H), 4.36 (d, J = 11 Hz, 1 H), 4.51 (d, J = 7 Hz, 1 H), 4.55 (d, J = 11 Hz, 1 H), 4.56 (d, J = 7 Hz, 1 H), 4.64

(d, J = 7 Hz, 1 H), 4.66 (d, J = 7 Hz, 1 H), 4.71 (d, J = 7 Hz, 1 H), 4.73 (d, J = 7 Hz, 1 H), 5.62 (dd, J = 16, 6 Hz, 1 H), 5.68 (dd, J = 16, 6 Hz, 1 H), 6.88 (d, J = 8 Hz, 2 H), 7.29 (d, J = 8 Hz, 2 H).

The above acid was treated with an ethereal solution of CH_2N_2 at 0 °C for 40 min. The solution was concentrated and chromatography of the residue on silica gel (hexane/EtOAc) furnished **46** (144 mg) in 75% yield from alcohol **45** (3 steps): IR (neat) 1739, 1033 cm^{-1}; ^{1}H NMR δ 1.22 (d, J = 6 Hz, 3 H), 1.61−1.78 (m, 2 H), 2.50 (dd, J = 16, 8 Hz, 1 H), 2.66 (dd, J = 16, 4.5 Hz, 1 H), 3.349 (s, 3 H), 3.352 (s, 3 H), 3.357 (s, 3 H), 3.69 (s, 3 H), 3.80 (s, 3 H), 3.70−3.88 (m, 1 H), 4.11 (dt, J = 8, 4.5 Hz, 1 H), 4.18−4.27 (m, 1 H), 4.28−4.40 (m, 1 H), 4.36 (d, J = 11 Hz, 1 H), 4.50 (d, J = 7 Hz, 1 H), 4.54 (d, J = 11 Hz, 1 H), 4.55 (d, J = 7 Hz, 1 H), 4.63 (d, J = 7 Hz, 1 H), 4.66 (d, J = 7 Hz, 1 H), 4.69 (d, J = 7 Hz, 1 H), 4.72 (d, J = 7 Hz, 1 H), 5.61 (dd, J = 16, 2.5 Hz, 1 H), 5.67 (dd, J = 16, 6 Hz, 1 H), 6.88 (d, J = 9 Hz, 2 H), 7.29 (d, J = 9 Hz, 2 H); ^{13}C NMR δ 171.8, 159.0, 135.4, 130.9, 129.3, 128.0, 113.8, 97.3, 94.4, 94.2, 76.9, 76.7, 73.5, 71.3, 70.4, 56.0, 55.8, 55.4, 51.8, 44.0. 36.5, 20.1; $[\alpha]^{25}_D$ −21.8 (*c* 1.724, $CHCl_3$). Anal. Calcd for $C_{25}H_{40}O_{10}$: C, 59.98; H, 8.05. Found: C, 60.15; H, 8.14.

Methyl (3*S*,4*S*,5*E*,7*S*,9*R*)-9-Hydroxyl-3,4,7-tri[(methoxymethyl)-oxy]-5-decenoate (47). To an ice-cold solution of **46** (105 mg, 0.210 mmol) in CH_2Cl_2 (3.7 mL) and H_2O (0.3 mL) was added DDQ (123 mg, 0.542 mmol). The resulting solution was stirred at 0 °C for 2 h and poured into saturated $NaHCO_3$ and CH_2Cl_2 with stirring. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 three times. The combined extracts were dried ($MgSO_4$) and concentrated to afford an oil, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish **47** (79 mg) in 100% yield: IR (neat) 3482, 1735, 1029 cm^{-1}; ^{1}H NMR δ 1.21 (d, J = 6 Hz, 3 H), 1.63−1.76 (m, 2 H), 2.50 (dd, J = 16, 8 Hz, 1 H), 2.59 (d, J = 4 Hz, 1 H), 2.67 (dd, J = 16, 5 Hz, 1 H), 3.355 (s, 3 H), 3.363 (s, 3 H), 3.39 (s, 3 H), 3.69 (s, 3 H), 4.12 (dt, J = 8, 5 Hz, 1 H), 4.00−4.15 (m, 1 H), 4.25 (t, J = 5 Hz, 3 H), 4.32−4.41 (m, 1 H), 4.56 (d, J = 7 Hz, 1 H), 4.58 (d, J = 7 Hz, 1 H), 4.65 (d, J = 7 Hz, 1 H), 4.66 (d, J = 7 Hz, 1 H), 4.69 (d, J = 7 Hz, 1 H), 4.72 (d, J = 7 Hz, 1 H), 5.62−5.78 (m, 2 H); ^{13}C NMR δ 171.8, 134.2, 128.4, 97.3, 94.5, 94.4, 77.0, 74.4, 64.4, 56.0, 55.9, 55.8, 51.8, 44.3, 36.4, 23.6; $[\alpha]^{25}_D$ −53.2 (*c* 0.724, $CHCl_3$). Anal. Calcd for $C_{17}H_{32}O_9$: C, 53.67; H, 8.48. Found: C, 53.62; H, 8.32.

Lactone 48. A mixture of methyl ester **47** (80 mg, 0.21 mmol) and 1 N NaOH (0.32 mL) in THF (1 mL) and H_2O (1 mL) was stirred at room temperature for 40 min and diluted with EtOAc and H_2O. The layers were separated, and EtOAc was added to the aqueous layer. The resulting layers were acidified with 1 N HCl, and the organic layer was separated. The aqueous layer was extracted with EtOAc. The combined extracts were dried ($MgSO_4$) and concentrated to give seco acid **19b** (77 mg) in 100% yield: ^{1}H NMR δ 1.19 (d, J = 6 Hz, 3 H), 1.56−1.77 (m, 2 H), 2.50 (dd, J = 16, 8 Hz, 1 H), 2.69 (dd, J = 16, 5 Hz, 1 H), 3.35 (s, 6 H), 3.38 (s, 3 H), 3.96−4.17 (m, 2 H), 4.25 (t, J = 5 Hz, 1 H), 4.34 (dt, J = 7.5, 5 Hz, 1 H), 4.55 (d, J = 7 Hz, 1 H), 4.58 (d, J = 7 Hz, 1 H), 4.64 (d, J = 7 Hz, 1 H), 4.65 (d, J = 7 Hz, 1 H), 4.68 (d, J = 7 Hz, 1 H), 4.72 (d, J = 7 Hz, 1 H), 5.58−5.78 (m, 2 H); ^{13}C NMR δ 175.8, 134.3, 128.3, 97.2, 94.5, 94.4, 76.9, 76.4, 74.4, 64.5, 56.0, 55.84, 55.80, 44.1, 36.3, 23.5.

To an ice-cold solution of seco acid **19b** (63 mg, 0.172 mmol) and Et_3N (0.029 mL, 0.21 mmol) in THF (2 mL) was added 2,4,6-trichlorobenzoyl chloride (0.040 mL, 0.19 mmol). The mixture was stirred at room temperature for 2 h and diluted with toluene (70 mL). The supernatant was added dropwise over 6 h to a solution of DMAP (70 mg, 0.57 mmol) in toluene (17 mL) under reflux. After the addition, the mixture was refluxed for further 1 h, cooled to room temperature, and diluted with Et_2O. The solution was washed successively with 1 N HCl, saturated $NaHCO_3$, and H_2O, dried ($MgSO_4$), and concentrated. The residue thus obtained was purified by chromatography on silica gel (hexane/EtOAc) to furnish lactone **48** (24 mg) in 40% yield: IR (neat) 1732, 1038 cm^{-1}; ^{1}H NMR δ 1.22 (d, J = 6 Hz, 3 H), 1.79 (dd, J = 14, 11 Hz, 1 H), 1.88 (ddd, J = 14, 3.5, 2.5 Hz, 1 H), 2.44 (dd, J = 14, 7 Hz, 1 H), 2.60 (dd, J = 14, 3 Hz, 1 H), 3.33 (s, 3 H), 3.37 (s, 3 H), 3.44 (s, 3 H), 3.39 (ddd, J = 7, 5, 3 Hz, 1 H), 4.07−4.17 (m, 1 H), 4.25 (dd, J = 6, 1.5 Hz, 1 H), 4.49 (d, J = 7 Hz, 1 H), 4.65 (d, J = 7 Hz, 1 H), 4.66 (d, J = 7 Hz, 1 H), 4.69 (d, J = 7 Hz, 1 H), 4.77 (d, J = 7 Hz, 1 H), 4.82 (d, J = 7 Hz, 1 H), 5.12−5.25 (m, 1 H), 5.69−5.81 (m, 2 H); ^{13}C NMR δ 170.3, 134.1, 128.0, 95.7, 95.2, 93.2, 77.1, 75.9, 75.6, 67.9, 55.9, 55.7, 55.4, 41.0, 34.7, 21.7; $[\alpha]^{26}_D$ −8.6 (*c* 0.266, $CHCl_3$). Anal. Calcd for $C_{16}H_{28}O_8$: C, 55.16; H, 8.10. Found: C, 55.24; H, 8.00.

Decarestrictine D (18). A solution of lactone **48** (20 mg, 0.057 mmol) and PPTS (147 mg, 0.585 mmol) in *n*-BuOH (1 mL) was refluxed for 3.5 h and poured into saturated NH_4Cl and EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined extracts were dried ($MgSO_4$) and concentrated to afford an oil, which was subjected to chromatography on silica gel (hexane/EtOAc) to furnish **18** (10 mg) in 81% yield: IR ($CHCl_3$) 3450, 1696, 1376, 1167 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.25 (d, J = 6.5 Hz, 3 H), 1.76−1.98 (m, 3 H), 2.09 (br s, 1 H), 2.40 (dd, J = 15, 6 Hz, 1 H), 2.62 (dd, J = 15, 2 Hz, 1 H), 4.00−4.11 (m, 1 H), 4.15,−4.26 (m, 1 H), 4.43 (br s), 4.64 (d, J = 8 Hz, 1 H), 5.19−5.31 (m, 1 H), 5.85 (dd, J = 16, 3 Hz, 1 H), 5.90 (dd, J = 16, 8 Hz, 1 H); ^{1}H NMR (MeOH-d_4) δ 1.20 (d, J = 6.5 Hz, 3 H), 1.71 (dt, J = 14, 11 Hz, 1 H), 1.85 (ddd, J = 14, 3.5, 1.5 Hz, 1 H), 2.30 (dd, J = 14, 7 Hz, 1 H), 2.59 (dd, J = 14, 2 Hz, 1 H), 3.88−3.97 (m, 1 H), 4.06 (ddd, J = 11, 9, 4 Hz, 1 H), 4.15−4.24 (m, 1 H), 5.10−5.23 (m, 1 H), 5.73 (dd, J = 16, 3 Hz, 1 H), 5.82 (dd, J = 16, 9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 174.8, 133.7, 129.8, 74.0, 72.6, 72.3, 68.3, 43.2, 33.3, 21.4; ^{13}C NMR (MeOH-d_4) δ 174.4, 135.7, 129.3, 75.3, 73.5, 73.1, 69.3, 44.2, 35.6, 21.7. The IR (in $CHCl_3$),[9c] ^{1}H NMR (in $CDCl_3$[22a] and in CD_3OD)[9c,22b,c] and ^{13}C NMR (in $CDCl_3$[22a−c] and in CD_3OD)[9c] spectra of the product were identical with those reported. The following physical constants of **18** were measured after recrystallization from CH_2Cl_2/hexane: $[\alpha]^{24}_D$ −68 (*c* 0.066, MeOH), lit. $[\alpha]^{20}_D$ −62 (*c* 1.0, MeOH)[9a]; mp 121−123 °C, lit. mp 116 °C[9b], 118−120 °C.[22a]

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Supporting Information Available: Full experimental procedures and spectral data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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