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A Chemoenzymatic Synthesis of Hept-6-ene-2,5-diol Stereomers: Application to Asymmetric Synthesis of Decarestrictine L, Pyrenophorol, and Stagonolide E

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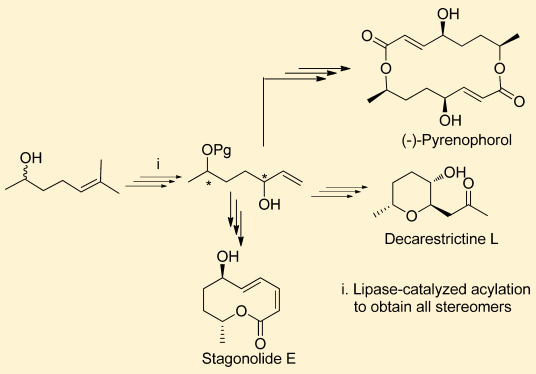
Supporting Information

ABSTRACT: The stereomers of hept-6-ene-2,5-diol derivatives were conceived as useful chiral intermediates and were synthesized starting from sulcatol using two lipase-catalyzed acylation reactions as the key steps. The versatility of the intermediates was demonstrated by converting them to the titled tetrahydropyran, macrolide, and macrodiolide compounds using standard synthetic protocols.



INTRODUCTION

Despite impressive progress, development of simple and efficient strategies for asymmetric syntheses of complex organic molecules remains a challenge.[1] Designing flexible and stereodivergent protocols, leading to several targets from a single starting molecule, has vital significance in organic synthesis. Small chiral intermediates with high functional density and multiple stereogenic centers are especially attractive to synthesize targets of structural and stereochemical diversities. The past two decades have witnessed extensive use of biocatalysts for various enantioselective organic transformations.[2] In particular, the lipases are most frequently used in organic synthesis since they do not require any cofactor, operate on a wide range of substrates, retain good catalytic activity in different media, display good stereoselectivity, and are easy to handle.[3] Our group has extensively employed biocatalytic routes with the aim of developing new chiral intermediates and their subsequent transformations into several natural compounds.[4] In our ongoing research on the development of potential immunomodulatory, anti-inflammatory, and antineoplastic agents,[5] we identified several bioactive compounds **1**−**6** (Figure 1) that contain the hept-6-ene-2,5-diol derivatives **7** (different stereomers and Pgs) as the common structural motif.

This structural feature offered a remarkable opportunity to formulate a divergent strategy for the synthesis of a wide array of complex target molecules starting from the diol derivatives **7** as the ideal small-molecule chiral intermediates. Hence, in the present work, we have formulated a highly efficient biocatalytic route to all the four stereomers of **7** (Pg = TBDPS) as well as two stereomers of another derivative (Pg = PMB), and used

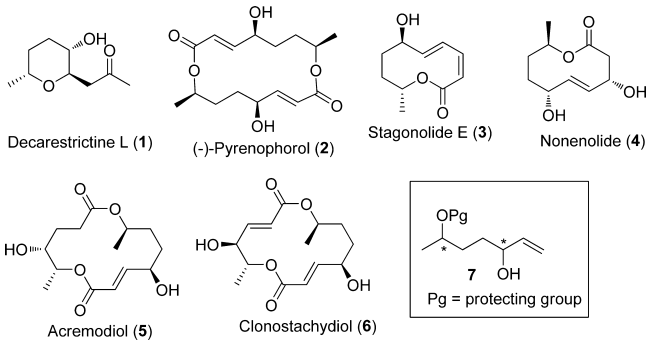


Figure 1. Some representative natural products bearing the hept-6-ene-2,5-diol structural motif.

some of these to devise asymmetric syntheses of (i) decarestrictine L (**1**), isolated from *Penicillium simplicissium*;[6a,b] (ii) pyrenophorol (**2**), isolated from *Byssochlamys nivea*,[6c] *Pyrenophora avenae*,[6d] and *Stemphylium radicinum*[6e] cultures as well as from the imperfect fungus *Alternaria alternata*;[6f] and (iii) stagonolide E (**3**), produced by *Stagonospora cirsii*, a fungal pathogen of *Cirsium arvense*.[6g,h] The decarestrictines including **1** inhibit cholesterol biosynthesis in HEP-G2 liver cancer cells and in vivo.[6a] On the other hand, the diolide **2** is specifically phytotoxic to the host *Avena sterilis* (wild oat), but not to other related plant species.[7a] It also showed antimicrobial activity against *Microbotryum violaceum*, *Chlorella fusca*, *Escherichia coli*, and *Bacillus megaterium*.[7b,c] In addition, it is a promising

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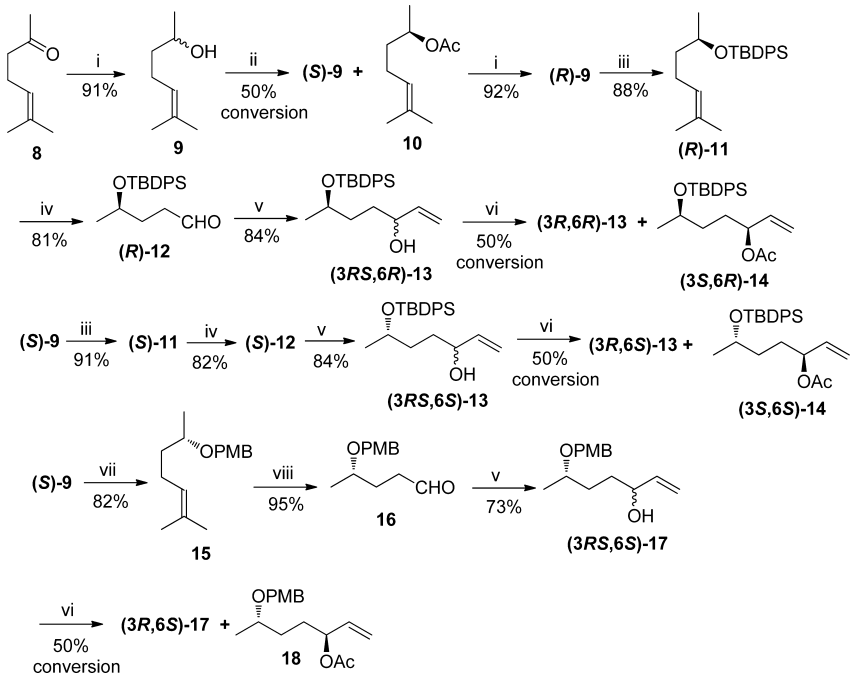
Scheme 1[a]



[a](i) $LiAlH_4/Et_2O$/0 °C/2 h, (ii) Novozyme 435/vinyl acetate/hexane/50 min, (iii) TBDPSCl/imidazole/DMAP/CH_2Cl_2/25 °C/7 h, (iv) O_3/CH_2Cl_2/−78 °C/1.5 h; Ph_3P/−78 to 25 °C/18 h, (v) CH_2=CHMgBr/THF/−78 °C/3 h, (vi) Novozyme 435/vinyl acetate/25 °C/6 h, (vii) NaH/PMBCl/DMF/−5 °C/4 h, (viii) OsO_4/NMO/*t*-BuOH-acetone-H_2O/25 °C/24 h; $NaIO_4/CH_3CN$-H_2O/10 °C/2 h.

nootropic and antidepressant agent.[7d,e] All of these compounds possess interesting structural features such as stereochemically pure carbinol appendages and/or properly placed olefinic moieties of well-defined geometries. These, coupled with their biological activity, make them attractive and challenging synthetic targets. Several enantiomeric syntheses of **1** have been reported, although many of them suffer from long reaction sequences, and low yields.[8] Likewise, a few relatively lengthy (14−21 steps) syntheses of the natural and other stereomers of **2** have been reported.[9] Using a novel asymmetric catalytic alkynylation of acetaldehyde as the key step, a concise synthesis of the tetrahydro analogue of **2** has been recently developed.[10] The previous syntheses of **3** employed well-established asymmetric transformations,[11a,b] or a chiral pool building block.[11c]

RESULTS AND DISCUSSION

To realize our objective of developing a divergent synthetic strategy for the target molecules **1**−**3**, the initial task was the preparation of different stereomers of **7** or its equivalent. We paid particular attention to using commercially available and inexpensive materials to obtain the products in high yields under operationally simple reaction conditions. For this, we relied on the lipase-catalyzed acylation strategy using the inexpensive and robust lipase preparation, Novozym 435 (LC 200207, novozymes), that is an immobilized preparation of lipase from *Candida antarctica* B (CAL-B) on acrylic resin. The choice of the lipase was governed by its ability in resolving methylcarbinols,[12a] and allylic alcohols.[12b,c] Moreover, the enantioselectivity of Novozym 435-catalyzed acylation of linear secondary alcohols can also be tuned by changing the solvent and/or acyl donor.[13a−c] We carried out the transformation using inexpensive vinyl acetate as the acyl donor due to its volatility that would ensure easy isolation of the products. The syntheses of the stereomers of the key intermediate and their conversion to the target molecules are sequentially presented in the following.

Preparation of the Key Intermediates. The synthesis (Scheme 1.) commenced from the commercially available compound, 6-methyl-5-hepten-2-one (**8**) that, on reduction with $LiAlH_4$, furnished the alcohol (±)-**9**. Several protocols for the preparation of (*R*)- or (*S*)-**9** have been reported earlier. These include use of chiral starting materials,[14a] kinetic resolution of (±)-**9** by lipase-catalyzed acylation[14b−e] or microbial oxidation,[14f] asymmetric reduction of **8** with baker's yeast or alcohol dehydrogenases,[14g−i] as well as chemical kinetic resolution.[14j] In the present studies, the alcohol (±)-**9** was efficiently resolved by carrying out its acetylation with vinyl acetate in hexane at room temperature to obtain the (*R*)-acetate **10** and (*S*)-**9** in >98% enantiomeric excesses (ees, $E \geq 195$) after 50% conversion (*cf.* GC, 50 min). We believe that this protocol is significantly better than a similar protocol reported earlier using *C. antarctica B* lipase preparation that required 30 h.[14d] The compounds (*R*)-**10** and (*S*)-**9** were easily separated by column chromatography. Reduction of the acetate (*R*)-**10** with $LiAlH_4$ furnished the alcohol (*R*)-**9**. The % ees of (*R*)-**9** and (*S*)-**9** were determined from the relative intensities of the methoxyl resonances of the corresponding α-methoxytrifluoromethylphenyl acetates (MTPA), prepared using (*R*)-MTPA chloride.[15] The configurations of **9** and **10** were assigned based on their reported optical rotations.[16a] In a recent paper, the same sign of the specific rotations of (*S*)-**9** and (*R*)-**10** have been reported.[16b] Hence, we carried out the reaction at least 10−12 times to report the $[\alpha]_D$ values. Moreover, our results are consistent with those reported by another group.[16c] It is worth mentioning that, despite using CAL-B lipase and similar reaction conditions, the reaction kinetics were found to be significantly different by two groups.[14d,16b] Earlier, Faber and

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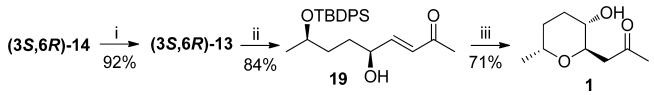
his group have obtained (*R*)-**10** in high yield and ee by combining the lipase-catalyzed acylation with in situ inversion or, alternatively, dynamic kinetic resolution using a Ru catalyst.[14e] However, this protocol is unsuitable for the present work, because we wanted to synthesize all the stereomers of the key intermediate that warranted the availability of both (*R*)-**10** and (*S*)-**10** or the corresponding alcohols **9**.

The enantiomers of the alcohol **9** were individually silylated with *tert*-butyldiphenylsilyl chloride (TBDPSCl) in the presence of imidazole and 4-dimethylaminopyridine (DMAP) to obtain (*R*)-**11** and (*S*)-**11**. Next, the olefin function of (*R*)-**11** and (*S*)-**11** was subjected to reductive ozonolysis (O_3/Ph_3P) in CH_2Cl_2 to get the aldehydes (*R*)-**12** and (*S*)-**12**, respectively. Reaction of (*R*)-**12** with commercially available vinylmagnesium bromide furnished the allylic alcohol (3*RS*,6*R*)-**13** as a 1:1 mixture of C-3 epimers. Its Novozym 435-catalyzed acetylation furnished (3*R*,6*R*)-**13** and (3*S*,6*R*)-**14** in >98% ees at 50% conversion (∼6 h). The reaction was highly stereoselective and did not proceed further even under an extended period (Scheme 1.). A similar sequence of reaction with (*S*)-**12** also proceeded uneventfully and provided the target intermediate diastereomers (3*R*,6*S*)-**13** and (3*S*,6*S*)-**14** in enantiomerically pure forms. The absolute configurations of the alcohol and acetate were empirically assigned based on the fact that the Novozym 435-catalyzed acetylation of allylic alcohols has been found to furnish the (*S*)-acetate.[12,17] This is also consistent with Kazlauskas' empirical rule.[18] These results suggested that chirality at the distant C-6 center did not have any bearing on the diastereoselectivity of the chosen lipase-catalyzed resolution of **13**. Earlier, depending on the choice of hydrophobic supports, different immobilized CAL-B lipase preparations showed different enantioselectivities in the hydrolysis of certain racemic esters.[19] Hence, we also carried out acetylation of (3*RS*,6*R*)-**13** and (3*RS*,6*S*)-**13** using another recombinant CAL-B lipase preparation (Sigma, L4777), expressed in *Aspergillus niger* and adsorbed on a macroporous acrylic resin. However, the reaction was too slow to be of any use in preparative chemistry.

Previously, the synthesis of the analogues of (3*R*,6*S*)-**13** and (3*S*,6*S*)-**14** containing the *tert*-butyldimethylsilyl protection at C-6 has been described, wherein the C-3 stereogenic center was installed using a lipase PS "Amano"-catalyzed acetylation with vinyl acetate in diisopropyl ether. However, the reaction required higher temperature (40 °C) and extended stirring (72 h). Moreover, this protocol is not amenable to the corresponding 6*R*-stereomers as it was derived from (*S*)-ethyl lactate.[20] To exclude any possible involvement of the protecting group at C-6 in the reaction, the alcohol (*S*)-**9** was converted to the *para*-methoxybenzyl (PMB) derivative (*S*)-**15** with *para*-methoxybenzyl chloride (PMBCl) in the presence of NaH. Oxidative cleavage (OsO_4/NMO; $NaIO_4$) of its olefin function, followed by addition of vinylmagnesium bromide to the resultant aldehyde **16**, gave (3*RS*,6*S*)-**17**, another derivative of the key intermediate. As expected, the Novozym 435-catalyzed acetylation of (3*RS*,6*S*)-**17** also furnished (3*R*,6*S*)-**17** and (3*S*,6*S*)-**18** in excellent ees at ∼50% conversion (∼6 h). The enantiomeric ratios (*E*) of the lipase-catalyzed acetylation reactions were >195. Overall, the above simple synthetic strategy provided the target intermediate in its diastereomeric forms, and as differently protected derivatives. With all the stereomers of the intermediate in hand, we proceeded for the synthesis of the target compounds **1**−**3**. This also confirmed the assigned configurations of the intermediates **13**, **14**, **17**, and **18** (all compound 7 equivalents).

Synthesis of Decarestrictine L 1. For the synthesis, the acetate (3*S*,6*R*)-**14** was hydrolyzed to the diol derivative (3*S*,6*R*)-**13**, which was subjected to a cross-metathesis reaction[21] with methyl vinyl ketone (MVK) in the presence of Grubbs' II catalyst by refluxing in dry CH_2Cl_2 to furnish compound **19**. To limit dimerization of **13**, the reaction was carried out using an excess of the less reactive olefin, MVK. Nevertheless, the homodimerized product of **13** was also obtained in ∼7−8% yield. The reaction required use of freshly distilled MVK to get the product in an acceptable yield. The *E*-geometry of the olefin **19** as ascertained from its ^{1}H NMR spectrum was consistent with the proposed model for the cross-metathesis reaction.[22] Desilylation of **19** with Bu_4NF directly afforded the target compound **1** via a concomitant Michael addition of the C-8 alcohol function to the conjugated ketone moiety (Scheme 2.). The physical and spectroscopic data of compound **1** were in accordance with the reported data of natural decarestrictine L.[8a]

Scheme 2[a]



[a](i) K_2CO_3/MeOH/25 °C/6 h, (ii) CH_2=CHCOMe/Grubbs' II catalyst/CH_2Cl_2/reflux/22 h, (iii) Bu_4NF/THF/0 to 25 °C/3 h.

Synthesis of Pyrenophorol 2. For the synthesis, (3*S*,6*R*)-**13** was subjected to a cross-metathesis reaction with ethyl acrylate in the presence of Hoveyda Grubbs' II catalyst to furnish **20**. Its carbinol function was silylated with *tert*-butyldimethylsilyl chloride (TBSCl) in the presence of imidazole and DMAP to obtain **21**. This, on alkaline hydrolysis, furnished the acid **22**. In a parallel sequence, (3*S*,6*S*)-**13** was benzylated with BnBr in the presence of NaH as the base to furnish **23** as a mixture of rotamers, which, on desilylation with Bu_4NF, furnished the alcohol **24**. Esterification of **22** with **24** under the Mitsunobu conditions afforded the ester **25** (mixture of rotamers). Its desilylation with aqueous HF in CH_3CN afforded the diol **26**. The Novozym 435-catalyzed acrylation of **26** with ethyl acrylate furnished the desired acrylate **27** exclusively. The excellent regioselectivity of the reaction is noteworthy, given that Novozym 435 can acylate both 2-alkanols and allylic alcohols.[12] Moreover, the reaction avoided the use of hygroscopic, hazardous, and toxic acryloyl chloride, as well as vinyl acrylate that needs to be synthesized separately.[23] The reaction was slow, but proceeded without any side reaction, and the acrylate was conveniently isolated by filtering the reaction mixture, followed by solvent removal. The *R*-stereochemistry of the methylcarbinol moiety of **26** matched with the inherent enantioselectivity of the chosen lipase. Hence, this strategy may be useful in asymmetric syntheses of compounds possessing a chiral methylcarbinol moiety that is often encountered in various bioactive compounds.[24]

The stage was set for the RCM reaction of **27** that was carried out with Grubbs' II catalyst to obtain **28** in modest yield. Control of the olefin geometry in the RCM-mediated macrocyclization is difficult due to the secondary olefin isomerization. This often leads to *E*/*Z* olefin mixtures with preponderance of the *E*-olefin that is governed by factors such

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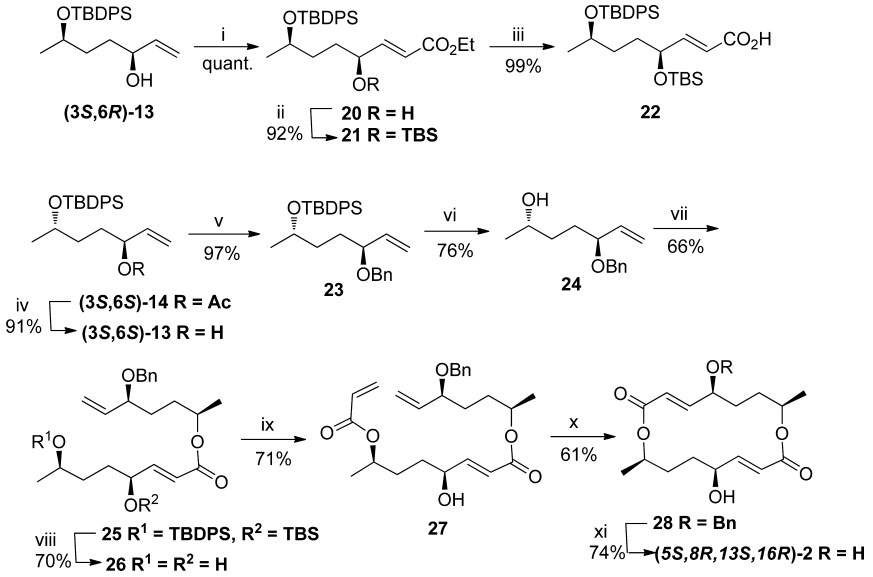
Scheme 3[a]

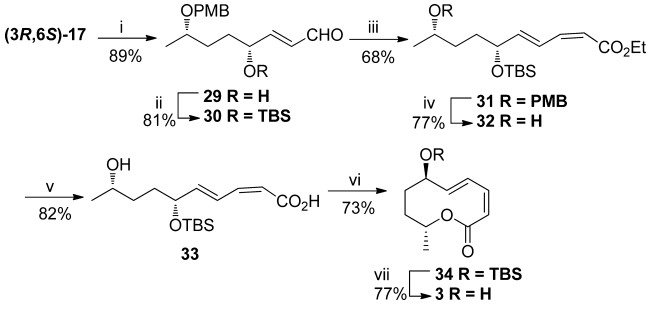


[a](i) CH_2=$CHCO_2Et$/Hoveyda Grubbs' II catalyst/CH_2Cl_2/25 °C/3 h, (ii) TBSCl/imidazole/DMAP/CH_2Cl_2/25 °C/7 h, (iii) aqueous 20% NaOH/MeOH/25 °C/2 h, (iv) K_2CO_3/MeOH/25 °C/6 h, (v) NaH/BnBr/Bu_4NI/THF/reflux/4 h, (vi) Bu_4NF/THF/0 to 25 °C/8 h, (vii) **22**/Ph_3P/DIAD/THF/0 to 25 °C/18 h, (viii) aqueous HF/MeCN/25 °C/16 h, (ix) CH_2=$CHCO_2Et$/Novozyme 435/diisopropyl ether/25 °C/30 h, (x) Grubbs' II catalyst/CH_2Cl_2/reflux/72 h, (xi) $TiCl_4$/CH_2Cl_2/0 to 25 °C/0.5 h.

as solvent, catalyst, temperature, substrate structure, and product ring size. Nevertheless, we did not isolate any *Z*-isomer in the conversion of **27** to **28**, as revealed from the ^{1}H NMR spectrum. A $TiCl_4$-catalyzed debenzylation of **28** completed the synthesis of (5*S*,8*R*,13*S*,16*R*)-**2** (Scheme 3).[25]

Synthesis of Stagonolide E 3. The synthesis of **3** commenced by the Hoveyda Grubbs' II catalyzed cross-metathesis of the intermediate (3*R*,6*S*)-**17** with acrolein to obtain the conjugated aldehyde **29**. After protecting its carbinol function with TBSCl/imidazole/DMAP, the resultant compound **30** was subjected to a *Z*-selective Wittig–Horner reaction with ethyl diphenylphosphonoacetate[26] and NaH in THF to get the ester **31** in a 91/9 *Z*/*E* ratio (based on isolation after column chromatography). Oxidative removal of the PMB group with DDQ to the hydroxy ester **32**, followed by alkaline hydrolysis, furnished the seco acid **33**. This was converted to the target compound **3** by Mitsunobu lactonization to **34** and subsequent desilylation with aqueous HF (Scheme 4).

Scheme 4[a]



[a](i) acrolein/Hoveyda Grubbs' II catalyst/CH_2Cl_2/25 °C/22 h, (ii) TBSCl/imidazole/DMAP/CH_2Cl_2/25 °C/7 h, (iii) NaH/THF/$(PhO)_2P(O)CH_2CO_2Et$/0 °C/1 h; −78 °C/3 h, (iv) DDQ/aqueous CH_2Cl_2/25 °C/3 h, (v) LiOH/THF-H_2O/0 °C/6 h, (vi) Ph_3P/DIAD/toluene/25 °C/16 h, (vii) aqueous HF/MeCN/25 °C/48 h.

CONCLUSION

Overall, in consideration of hept-6-ene-2,5-diol as a common structural motif of several natural products, the stereomers and different derivatives (**13**, **14**, **17**, and **18**) of the diol were synthesized using two highly enantioselective lipase-catalyzed carbinol acetylation as the key steps. The versatility of the intermediates was established by converting some of these derivatives to the natural stereomers of decarestrictine L, pyrenophorol, and stagonolide E. Although these targets have been made before on numerous occasions, we elaborated a new general synthetic strategy, allowing control of both ring size and the configurations of stereogenic carbons into a range of significant materials using the key intermediate. Moreover, since our methodology gives access to all possible stereoisomers of the key intermediate, it would be possible to access all the stereomers of these natural products based on the described methodology. The yields of the target compound via the present stereodivergent strategy were comparable to those of the previously described target-specific syntheses. Given that the carbinol stereochemistry can be easily inverted, the synthetic strategy is also amenable for enantioconvergent routes that would provide the individual targets in much improved yields. Use of inexpensive reagents/materials and application of operationally simple reactions and environmentally benign biocatalysts were the other hallmarks of the flexible, efficient, and scalable syntheses. In addition to its use for traditional kinetic resolution applications, we also demonstrate that the Novozym 435 lipase can be employed to effect regioselective acylation using a nontraditional acyl donor (ethyl acrylate). This transformation is particularly noteworthy and elevates the significance of the work.

EXPERIMENTAL SECTION

(±)-6-Methyl-5-hepten-2-ol 9. To a cooled (0 °C) and stirred suspension of $LiAlH_4$ (2.11 g, 55.56 mmol) in Et_2O (30 mL) was dropwise added **8** (10.00 g, 79.37 mmol) in Et_2O (70 mL). After

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stirring for 2 h, the mixture was treated with aqueous saturated Na_2SO_4 and diluted with Et_2O, and the supernatant was filtered. The filtrate was carefully concentrated, and the residue was distilled to obtain pure **9** (9.2 g, 91%). colorless oil; bp: 90 °C/20 mm; IR: 3373, 1642 cm^{-1}; ^1H NMR: δ 1.14 (d, J = 6.2 Hz, 3H), 1.48−1.59 (m, 2H), 1.65 (s, 3H), 1.71 (s, 3H), 2.00−2.15 (m, 3H), 3.74−3.90 (m, 1H), 5.11−5.19 (m, 1H); ^{13}C NMR: δ 17.5, 23.3, 24.4, 25.6, 39.1, 67.7, 124.0, 131.8.

(*R*)-6-Acetoxy-2-methyl-2-heptene 10. A mixture of (±)-**9** (7.50 g, 58.59 mmol), vinyl acetate (8.1 mL, 87.89 mmol), and Novozym 435 (0.75 g, ∼12 mg/mmol) in hexane (30.0 mL) was agitated on an orbital shaker at 110 rpm for 50 min. The reaction mixture was filtered, and the solution was concentrated in vacuo to get a residue, which, on column chromatography (silica gel, 0−10% EtOAc/hexane), gave pure (*S*)-**9** (3.1 g, 41%) and (*R*)-**10** (4.4 g, 44%). (*S*)-**9**: colorless oil; $[\alpha]_D^{24}$ +10.9 (*c* 1.30, $CHCl_3$) (lit.[16b] $[\alpha]_D^{25}$ +10.5 (*c* 0.4, $CHCl_3$)); IR: 3437 cm^{-1}; ^1H NMR: δ 1.19 (d, J = 6.0 Hz, 3H), 1.41−1.57 (m, 2H), 1.62 (s, 3H), 1.69 (s, 3H), 1.93 (broad s, 1H), 2.00−2.14 (m, 2H), 3.80 (sextet, J = 6.0 Hz, 1H), 5.12−5.22 (m, 1H); ^{13}C NMR: δ 17.7, 23.4, 24.5, 25.7, 39.2, 67.9, 124.1, 132.0. Anal. Calcd for $C_8H_{16}O$: C, 74.94; H, 12.58%; Found: C, 74.77; H, 12.68%.

(*R*)-**10**: colorless oil; $[\alpha]_D^{24}$ −6.5 (*c* 1.01, $CHCl_3$), $[\alpha]_D^{25}$ −6.8 (*c* 1.23, EtOH) (lit.[16c] $[\alpha]_D^{23}$ +7.7 (*c* 0.03, EtOH)); IR: 1736, 1243 cm^{-1}; ^1H NMR: δ 1.21 (d, J = 6.6 Hz, 3H), 1.43−1.57 (m, 2H), 1.59 (s, 3H), 1.68 (s, 3H), 1.97−2.04 (merged m and s at δ 2.03, 5H), 4.83−4.91 (m, 1H), 5.05−5.11 (m, 1H); ^{13}C NMR: δ 17.6, 21.4, 24.0, 25.7, 29.7, 36.0, 70.7, 123.5, 132.1, 170.8. Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66%. Found: C, 70.38; H, 10.36%.

(*R*)-6-Methyl-5-hepten-2-ol (*R*)-9. Reduction of (*R*)-**10** (2.70 g, 15.88 mmol) with $LiAlH_4$ (0.480 g, 12.70 mmol) in Et_2O (60 mL), followed by work up as above, furnished pure (*R*)-**9** (1.9 g, 92%). colorless oil; $[\alpha]_D^{22}$ −11.7 (*c* 1.06, $CHCl_3$); IR: 3050, 1642 cm^{-1}; ^1H NMR: δ 1.16 (d, J = 6.0 Hz, 3H), 1.39−1.55 (m, 2H), 1.59 (s, 3H), 1.68 (s, 3H), 1.83 (broad s, 1H), 2.00−2.09 (m, 2H), 3.72−3.83 (m, 1H), 5.03−5.18 (m, 1H); ^{13}C NMR: δ 17.7, 23.5, 24.5, 25.8, 39.2, 67.9, 124.1, 132.0. Anal. Calcd for $C_8H_{16}O$: C, 74.94; H, 12.58%. Found: C, 74.77; H, 12.68%.

(*R*)-6-*tert*-Butyldiphenylsilyloxy-2-methyl-2-heptene (*R*)-11. To a stirred solution of (*R*)-**9** (2.50 g, 19.53 mmol), imidazole (1.73 g, 25.39 mmol), and DMAP (catalytic) in CH_2Cl_2 (20 mL) was dropwise added TBDPSCl (6.98 g, 25.39 mmol). After stirring the mixture for 7 h at room temperature, it was poured into ice-cold water (20 mL), the organic layer was separated, and the aqueous portion was extracted with $CHCl_3$ (3 × 10 mL). The combined organic extracts were successively washed with H_2O (2 × 10 mL) and brine (1 × 5 mL) and dried. Removal of solvent in vacuo, followed by column chromatography (silica gel, 0−5% EtOAc/hexane) of the residue, afforded pure (*R*)-**11** (6.3 g, 88%). colorless oil; $[\alpha]_D^{24}$ +11.7 (*c* 1.04, $CHCl_3$); IR: 3050, 3013 cm^{-1}; ^1H NMR: δ 1.05 (merged s and d, J = 6.0 Hz, 12H), 1.18−1.26 (m, 2H), 1.53 (s, 3H), 1.63 (s, 3H), 1.88−2.01 (m, 2H), 3.79−3.87 (m, 1H), 4.95−5.00 (m, 1H), 7.32−7.44 (m, 6H), 7.65−7.70 (m, 4H); ^{13}C NMR: δ 17.6, 18.4, 19.3, 23.2, 24.0, 25.7, 26.8, 26.9, 39.6, 69.4, 124.5, 127.4, 127.5, 127.6, 129.4, 129.5, 131.2, 134.3, 134.6, 135.0, 135.6, 135.9. Anal. Calcd for $C_{24}H_{34}OSi$: C, 78.63; H, 9.35%. Found: C, 78.68; H, 9.51%.

(*S*)-6-*tert*-Butyldiphenylsilyloxy-2-methyl-2-heptene (*S*)-11. As above, silylation of (*S*)-**9** (2.20 g, 17.19 mmol) using TBDPSCl (6.12 g, 22.34 mmol), imidazole (1.52 g, 22.34 mmol), and DMAP (catalytic) in CH_2Cl_2 (20 mL) furnished (*S*)-**11** (5.7 g, 91%). colorless oil; $[\alpha]_D^{25}$ −11.8 (*c* 1.03, $CHCl_3$); IR: 3071, 3049, 998 cm^{-1}; ^1H NMR: δ 1.03 (merged s and d, J = 6.2 Hz, 12H), 1.40−1.45 (m, 1H), 1.50−1.55 (m containing a s at δ 1.54, 4H), 1.63 (s, 3H), 1.89−2.01 (m, 2H), 3.84−3.86 (m, 1H), 4.96−4.99 (m, 1H), 7.35−7.42 (m, 6H), 7.67−7.69 (m, 4H); ^{13}C NMR: δ 17.7, 18.5, 19.4, 23.2, 24.1, 25.8, 26.9, 27.1, 39.7, 69.4, 124.5, 127.5, 127.7, 129.5, 129.6, 131.3, 134.7, 135.0, 135.6, 136.0. Anal. Calcd for $C_{24}H_{34}OSi$: C, 78.63; H, 9.35%. Found: C, 78.31; H, 9.23%.

(*R*)-4-*tert*-Butyldiphenylsilyloxypentanal (*R*)-12. Ozone was bubbled through a cooled (−78 °C) solution of (*R*)-**11** (4.84 g, 13.22 mmol) in CH_2Cl_2 (20 mL) for 1 h. After 0.5 h, the excess O_3 was removed by purging with N_2, Ph_3P (5.20 g, 19.84 mmol) was added, and the mixture was stirred for 18 h at room temperature and concentrated in vacuo. The residue was taken in hexane (30 mL), concentrated in vacuo, and purified by column chromatography (silica gel, 0−10% Et_2O/hexane) to obtain pure (*R*)-**12** (3.6 g, 81%). colorless oil; $[\alpha]_D^{22}$ +2.2 (*c* 1.01, $CHCl_3$); IR: 3070, 2717, 1726 cm^{-1}; ^1H NMR: δ 1.06 (merged s and d, J = 6.3 Hz, 12H), 1.70−1.83 (m, 2H), 2.44−2.51 (m, 2H), 3.91−3.95 (m, 1H), 7.37−7.43 (m, 6H), 7.66−7.68 (m, 4H), 9.68 (s, 1H); ^{13}C NMR: δ 19.3, 23.0, 27.0, 27.1, 31.3, 39.6, 68.5, 127.5, 127.7, 129.6, 129.7, 134.1, 134.5, 135.8, 135.9, 202.4. Anal. Calcd for $C_{21}H_{28}O_2Si$: C, 74.07; H, 8.29%. Found: C, 74.18; H, 8.51%.

(*S*)-4-*tert*-Butyldiphenylsilyloxypentanal (*S*)-12. Reductive ozonolysis of (*S*)-**11** (5.01 g, 13.69 mmol) using O_3 and Ph_3P (5.38 g, 20.53 mmol) in CH_2Cl_2 (20 mL), followed by isolation as above, furnished pure (*S*)-**12** (3.8 g, 82%). colorless oil; $[\alpha]_D^{22}$ −1.9 (*c* 1.19, $CHCl_3$); IR: 1727, 2717, 3050 cm^{-1}; ^1H NMR: δ 1.07 (merged s and d, J = 6.1 Hz, 12H), 1.71−1.83 (m, 2H), 2.47−2.49 (m, 2H), 3.92−3.96 (m, 1H), 7.37−7.43 (m, 6H), 7.66−7.68 (m, 4H), 9.68 (s, 1H); ^{13}C NMR: δ 19.3, 23.0, 27.0, 27.1, 31.3, 39.6, 68.5, 127.4, 127.5, 127.6, 127.7, 129.6, 129.7, 134.1, 134.5, 135.8, 135.9, 136.0, 202.4. Anal. Calcd for $C_{21}H_{28}O_2Si$: C, 74.07; H, 8.29%. Found: C, 74.18; H, 8.51%.

(3*RS*,6*R*)-6-*tert*-Butyldiphenylsilyloxyhept-1-en-3-ol (3*RS*,6*R*)-13. To a cooled (−78 °C) and stirred solution of (*R*)-**12** (3.14 g, 9.24 mmol) in THF (30 mL) was added vinylmagnesium bromide (18.5 mL, 18.5 mmol, 1 M in THF). After stirring for 3 h, the mixture was treated with aqueous saturated NH_4Cl (10 mL), the organic was layer separated, and the aqueous portion was extracted with Et_2O (2 × 20 mL). The combined organic extracts were washed with H_2O (2 × 10 mL) and brine (1 × 5 mL), dried, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, 0−10% Et_2O/hexane) to afford pure (3*RS*,6*R*)-**13** (2.8 g, 84%). colorless liquid; $[\alpha]_D^{23}$ +36.1 (*c* 1.22, $CHCl_3$); IR: 3365, 3070, 3050, 1644 cm^{-1}; ^1H NMR: δ 1.04 (merged s and d, J = 6.2 Hz, 12H), 1.45−1.69 (m, 5H), 3.85−3.87 (m, 1H), 3.98−4.00 (m, 1H), 5.01−5.20 (m, 2H), 5.69−5.86 (m, 1H), 7.30−7.40 (m, 6H), 7.63−7.68 (m, 4H); ^{13}C NMR: δ 19.3, 23.1, 27.1, 29.7, 32.3, 32.6, 34.7, 35.1, 69.3, 69.5, 73.0, 73.2, 114.5, 127.5, 127.6, 129.5, 129.6, 134.4, 134.7, 135.0, 136.4, 141.2. Anal. Calcd for $C_{23}H_{32}O_2Si$: C, 74.95; H, 8.75%. Found: C, 74.78; H, 8.84%.

(3*RS*,6*S*)-6-*tert*-Butyldiphenylsilyloxyhept-1-en-3-ol (3*RS*,6*S*)-13. As above, reaction of (*S*)-**12** (2.30 g, 6.76 mmol) with vinylmagnesium bromide (13.6 mL, 13.6 mmol, 1 M in THF) in THF (20 mL) and usual purification afforded pure (3*RS*,6*S*)-**13** (2.1 g, 84%). colorless liquid; $[\alpha]_D^{24}$ −12.1 (*c* 1.16, $CHCl_3$); IR: 3364, 3071, 997 cm^{-1}; ^1H NMR: δ 1.04 (merged s and d, J = 6.2 Hz, 12H), 1.45−1.62 (m containing a s at 1.58, 5H), 3.85−3.87 (m, 1H), 3.96−4.02 (m, 1H), 5.01−5.20 (m, 2H), 5.69−5.86 (m, 1H), 7.33−7.40 (m, 6H), 7.63−7.67 (m, 4H); ^{13}C NMR: δ 19.2, 23.0, 27.0, 32.2, 32.5, 34.6, 35.0, 69.3, 69.4, 73.0, 73.2, 114.5, 127.4, 127.5, 129.4, 129.5, 135.9, 141.1. Anal. Calcd for $C_{23}H_{32}O_2Si$: C, 74.95; H, 8.75%. Found: C, 75.18; H, 8.51%.

(3*S*,6*R*)-3-Acetoxy-6-*tert*-butyldiphenylsilyloxyhept-1-ene (3*S*,6*R*)-14. Acetylation of (3*RS*,6*R*)-**13** (4.16 g, 11.30 mmol) with vinyl acetate (5.0 mL) and Novozym 435 (0.50 g, ∼50 mg/mmol) was carried out as described above to obtain pure (3*R*,6*R*)-**13** (2.0 g, 48%) and (3*S*,6*R*)-**14** (2.1 g, 46%). (3*R*,6*R*)-**13**: colorless oil; $[\alpha]_D^{26}$ +10.4 (*c* 1.14, $CHCl_3$); ^1H NMR: δ 1.06 (merged s and d, J = 6.0 Hz, 12H), 1.47−1.55 (m, 5H), 3.88−3.91 (m, 1H), 3.98−4.00 (m, 1H), 5.01−5.18 (m, 2H), 5.76−5.82 (m, 1H), 7.35−7.43 (m, 6H), 7.67−7.69 (m, 4H); ^{13}C NMR: δ 19.2, 23.0, 27.0, 32.6, 35.1, 69.4, 73.2, 114.5, 127.4, 127.5, 129.5, 129.6, 134.3, 134.6, 135.9, 141.1. Anal. Calcd for $C_{23}H_{32}O_2Si$: C, 74.95; H, 8.75%. Found: C,75.15; H, 8.92%.

(3*S*,6*R*)-**14**: colorless oil; $[\alpha]_D^{26}$ +13.1 (*c* 1.03, $CHCl_3$); IR: 3070, 1739, 1647 cm^{-1}; ^1H NMR: δ 1.04 (merged s and d, J = 7.2 Hz, 12H), 1.35−1.52 (m, 2H), 1.54−1.70 (m, 2H), 2.01 (s, 3H), 3.81−3.90 (m, 1H), 5.09−5.20 (m, 3H), 5.61−5.78 (m, 1H), 7.31−7.42 (m, 6H), 7.63−7.68 (m, 4H); ^{13}C NMR: δ 19.3, 21.2, 23.1, 27.0, 27.1, 29.6, 34.5, 69.0, 74.7, 116.6, 127.5, 129.5, 129.6, 134.4, 134.7, 135.8, 135.9,

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136.0, 136.5, 170.3. Anal. Calcd for $C_{25}H_{34}O_3Si$: C, 73.13; H, 8.35%. Found: C,73.15; H, 8.32%.

(3*S*,6*S*)-3-Acetoxy-6-*tert*-butyldiphenylsilyloxyhept-1-ene (3*S*,6*S*)-14. Following the same procedure (3*RS*,6*S*)-**13** (1.90 g, 5.16 mmol) was acetylated in vinyl acetate (5.0 mL) using Novozym 435 (0.25 g, ~50 mg/mmol) to obtain pure (3*R*,6*S*)-**13** (0.860 g, 45%) and (3*S*,6*S*)-**14** (1.0 g, 47%). (3*R*,6*S*)-**13**: colorless oil; $[\alpha]_D^{25}$ −17.7 (*c* 1.24, $CHCl_3$); IR: 3360, 3065, 998 cm^{-1}; ^1H NMR: δ 1.02 (merged s and d, *J* = 6.0 Hz, 12 H), 1.45−1.59 (m, 5H), 3.84−3.93 (m, 1H), 3.96−4.02 (m, 1H), 5.04−5.21 (m, 2H), 5.71−5.87 (m, 1H), 7.30−7.41 (m, 6H), 7.64−7.68 (m, 4H); ^{13}C NMR: δ 19.2, 23.0, 27.0, 32.3, 34.6, 69.3, 73.0, 114.6, 127.4, 127.5, 129.5, 134.4, 134.7, 135.9, 141.1. Anal. Calcd for $C_{23}H_{32}O_2Si$: C, 74.95; H, 8.75%. Found: C, 75.18; H, 8.51%.

(3*S*,6*S*)-**14**: colorless oil; $[\alpha]_D^{24}$ −13.5 (*c* 1.05, $CHCl_3$); IR: 1736, 1231 cm^{-1}; ^1H NMR: δ 1.04 (merged s and d, *J* = 6.0 Hz, 12H), 1.35−1.50 (m, 2H), 1.52−1.68 (m, 2H), 2.02 (s, 3H), 3.79−3.88 (m, 1H), 5.10−5.20 (m, 3H), 5.60−5.77 (m, 1H), 7.32−7.42 (m, 6H), 7.63−7.69 (m, 4H); ^{13}C NMR: δ 19.2, 21.2, 23.1, 27.0, 29.7, 34.5, 69.1, 74.8, 116.6, 127.4, 127.5, 129.4, 129.5, 134.3, 134.7, 135.8, 136.4, 170.3. Anal. Calcd for $C_{25}H_{34}O_3Si$: C, 73.13; H, 8.35%. Found: C, 73.32; H, 8.04%.

(2*S*)-6-*para*-Methoxybenzyloxy-2-methylhept-2-ene 15. To a cooled (−5 °C) and stirred suspension of hexane-washed NaH (4.52 g, 94.14 mmol, 50% suspension in oil) in DMF (10 mL) was added (*S*)-**9** (4.82 g, 37.66 mmol) in DMF (10 mL). After 1 h, PMBCl (6.13 mL, 45.19 mmol) was dropwise added into the mixture, and stirring continued until completion of the reaction (*cf.* TLC). Water (20 mL) was added to the mixture, which was extracted with Et_2O (3 × 15 mL). The combined organic extracts were washed with H_2O (2 × 10 mL) and brine (1 × 5 mL), dried, and concentrated in vacuo to get a residue, which, on column chromatography (silica gel, 0−5% Et_2O/hexane), afforded pure (*S*)-**15** (7.6 g, 82%). colorless liquid; $[\alpha]_D^{23}$ +29.9 (*c* 1.08, $CHCl_3$); IR: 3090, 1613 cm^{-1}; ^1H NMR: δ 1.18 (d, *J* = 7.0 Hz, 3H), 1.43−1.44 (m, 2H), 1.60 (s, 3H), 1.68 (s, 3H), 2.04−2.06 (m, 2H), 3.47−3.50 (m, 1H), 3.79 (s, 3H), 4.38 (d, *J* = 14.0 Hz, 1H), 4.49 (d, *J* = 14.0 Hz, 1H), 5.09 (t, *J* = 2.4 Hz, 1H), 6.86 (d, *J* = 7.0 Hz, 2H), 7.26 (d, *J* = 7.0 Hz, 2H); ^{13}C NMR: δ 17.6, 19.6, 24.1, 25.7, 36.7, 55.2, 69.9, 74.1, 113.7, 124.3, 129.1, 131.2, 131.5, 159.0. Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74%. Found: C, 77.33; H, 9.61%.

(4*S*)-4-*para*-Methoxybenzyloxypentanal 16. To a stirred solution of (*S*)-**15** (4.46 g, 17.98 mmol) in acetone:water (8:1, 30 mL) was added a mixture of NMO (4.20 g, 35.96 mmol) and OsO_4 (0.230 g, 0.89 mmol) in *t*-BuOH (2 mL). After stirring for 24 h, the mixture was treated with aqueous saturated Na_2SO_3, stirred for 0.5 h, and subsequently extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with H_2O (2 × 10 mL) and brine (1 × 10 mL), dried, and concentrated in vacuo to get a residue, which, on column chromatography (0−30% EtOAc/hexane), furnished pure diol (4.8 g, 95%). colorless oil. $[\alpha]_D^{24}$ +29.2 (*c* 1.03, $CHCl_3$); IR: 3418, 1341, 1138 cm^{-1}; ^1H NMR: δ 1.12−1.26 (merged s and d, *J* = 6.4 Hz, 9H), 1.56−1.81 (m, 4H), 2.56 (broad s, 2H), 3.34 (t, *J* = 7.4 Hz, 1H), 3.45−3.61 (m, 1H), 3.78 (s, 3H), 4.37 (d, *J* = 11.4 Hz, 1H), 4.54 (d, *J* = 11.4 Hz, 1H), 6.87 (d, *J* = 8.7 Hz, 2H), 7.26 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR: 19.4, 19.5, 23.3, 23.4, 26.4, 26.5, 27.5, 27.6, 33.7, 33.8, 55.3, 70.1, 72.9, 73.0, 74.5, 74.7, 78.4, 113.8, 129.4, 129.5, 130.5, 130.7, 159.2. Anal. Calcd for $C_{16}H_{26}O_4$: C, 68.06; H, 9.28%. Found: C, 67.88; H, 9.61%.

To a cooled (10 °C) and stirred solution of the above diol (4.08 g, 14.47 mmol) in aqueous 60% CH_3CN (20 mL) was added $NaIO_4$ (6.19 g, 28.92 mmol) in portions. After stirring for 2 h, the mixture was filtered and the filtrate was treated with aqueous 10% $NaHSO_3$ and extracted with $CHCl_3$ (3 × 15 mL). The organic layer was washed with H_2O (2 × 10 mL) and brine (1 × 5 mL), dried, and concentrated in vacuo to get a residue, which, on column chromatography (silica gel, 0−10% EtOAc/hexane), furnished pure (*S*)-**16** (3.2 g, quant.). colorless liquid; $[\alpha]_D^{24}$ +45.5 (*c* 1.03, $CHCl_3$); IR: 2724, 1723 cm^{-1}; ^1H NMR: δ 1.20 (d, *J* = 6.0 Hz, 3H), 1.79−1.86 (m, 2H), 2.46−2.54 (m, 2H), 3.50−3.56 (m, 1H), 3.80 (s, 3H), 4.36 (d, *J* = 11.4 Hz, 1H), 4.55 (d, *J* = 11.4 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 9.74 (t, *J* = 1.5 Hz, 1H); ^{13}C NMR: δ 19.6, 29.3, 40.3, 55.4, 70.2, 73.5, 113.9, 129.4, 130.7, 159.2, 202.7. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16%. Found: C, 70.05; H, 8.08%.

(3*RS*,6*S*)-6-*para*-Methoxybenzyloxyhept-1-en-3-ol 17. As described earlier, reaction of (*S*)-**16** (2.28 g, 10.27 mmol) with vinylmagnesium bromide (15.40 mL, 15.40 mmol, 1 M in THF) (30 mL), followed by the usual isolation and purification, furnished (3*RS*,6*S*)-**17** (1.9 g, 73%). colorless liquid; $[\alpha]_D^{24}$ +16.3 (*c* 1.02, $CHCl_3$); IR: 3410 cm^{-1}; ^1H NMR: δ 1.15 (d, *J* = 6.3 Hz, 3H), 1.47−1.66 (m, 4H), 2.50 (broad s, 1H), 3.44−3.52 (m, 1H), 3.74 (s, 3H), 3.98−4.05 (m, 1H), 4.33 (d, *J* = 11.4 Hz, 1H), 4.47 (d, *J* = 11.4 Hz, 1H), 5.01−5.18 (m, 2H), 5.74−5.86 (m, 1H), 6.82 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR: δ 19.5, 32.4, 33.0, 55.3, 70.0, 72.9, 74.3, 74.5, 113.8, 114.4, 129.4, 130.8, 141.3, 159.1. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86%. Found: C, 72.21; H, 8.88%.

(3*S*,6*S*)-3-Acetoxy-6-*para*-methoxybenzyloxyhept-1-ene 18. As described earlier, acetylation of (3*RS*,6*S*)-**17** (1.80 g, 7.20 mmol) with vinyl acetate (1.0 mL, 10.8 mmol) in the presence of Novozym 435 (0.540 mg, ~75 mg/mmol) in diisopropyl ether (25 mL), followed by isolation, furnished (3*R*,6*S*)-**17** (0.756 g, 42%) and **18** (0.946 g, 45%). (3*R*,6*S*)-**17**: colorless liquid; $[\alpha]_D^{23}$ +20.7 (*c* 1.00, $CHCl_3$); IR: 3410 cm^{-1}; ^1H NMR: δ 1.19 (d, *J* = 6.3 Hz, 3H), 1.54−1.72 (m, 4H), 2.43 (broad s, 1H), 3.49−3.59 (m, 1H), 3.79 (s, 3H), 4.03−4.11 (m, 1H), 4.38 (d, *J* = 11.4 Hz, 1H), 4.52 (d, *J* = 11.4 Hz, 1H), 5.07−5.26 (m, 2H), 5.80−5.91 (m, 1H), 6.87 (d, *J* = 8.7 Hz, 2H), 7.26 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR: δ 19.5, 32.4, 33.0, 55.3, 70.1, 72.9, 74.5, 113.8, 114.5, 129.4, 130.8, 141.2, 159.1. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86%. Found: C, 72.15; H, 8.75%.

18: colorless liquid; $[\alpha]_D^{24}$ +12.4 (*c* 1.01, $CHCl_3$); IR: 1736, 1646, 990 cm^{-1}; ^1H NMR: δ 1.18 (d, *J* = 6.3 Hz, 3H), 1.39−1.80 (m, 4H), 2.03 (s, 3H), 3.46−3.56 (m, 1H), 3.80 (s, 3H), 4.36 (d, *J* = 11.4 Hz, 1H), 4.49 (d, *J* = 11.4 Hz, 1H), 5.13−5.25 (m, 3H), 5.70−5.81 (m, 1H), 6.87 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR: δ 19.6, 21.3, 30.1, 32.0, 55.3, 70.0, 73.9, 74.7, 113.8, 116.7, 129.2, 131.0, 136.5, 159.1, 170.4. Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27%. Found: C, 69.88; H, 8.33%.

(3*S*,6*R*)-6-*tert*-Butyldiphenylsilyloxyhept-1-en-3-ol (3*S*,6*R*)-13. A mixture of (3*S*,6*R*)-**14** (3.20 g, 7.80 mmol) and K_2CO_3 (1.30 g, 9.36 mmol) in MeOH (20 mL) was magnetically stirred until completion of the reaction (*cf.* TLC, ~6 h). After solvent removal in vacuo, water (25 mL) was added to the residue, followed by extraction with EtOAc (3 × 20 mL). The combined organic extracts were washed with H_2O (2 × 10 mL) and brine (1 × 5 mL), dried, and concentrated in vacuo to get a residue, which, on column chromatography (silica gel, 0−15% EtOAc/hexane), furnished pure (3*S*,6*R*)-**13** (2.7 g, 92%). colorless liquid; $[\alpha]_D^{24}$ +15.0 (*c* 1.12, $CHCl_3$); IR: 3420, 3050, 997 cm^{-1}; ^1H NMR: δ 1.07 (merged s and d, *J* = 6.3 Hz, 12H), 1.42−1.60 (m, 5H), 3.85−3.92 (m, 1H), 3.96−4.02 (m, 1H), 5.07−5.19 (m, 2H), 5.78−5.83 (m, 1H), 7.35−7.43 (m, 6H), 7.67−7.69 (m, 4H); ^{13}C NMR: δ 19.3, 23.1, 27.0, 27.2, 32.3, 34.6, 69.3, 73.0, 114.6, 127.5, 127.6, 129.5, 129.6, 134.4, 134.8, 135.9, 141.2. Anal. Calcd for $C_{23}H_{32}O_2Si$: C, 74.95; H, 8.75%. Found: C, 74.77; H, 8.43%.

(3*E*,5*S*,8*R*)-8-*tert*-Butyldiphenylsilyloxy-5-hydroxynon-3-en-2-one 19. A mixture of (3*S*,6*R*)-**13** (1.0 g, 2.72 mmol), MVK (1.33 g, 19.02 mmol), and Grubbs' II catalyst (5 mol %) in CH_2Cl_2 (5 mL) was refluxed for 22 h. After concentrating the mixture in vacuo, the residue was subjected to column chromatography (silica gel, 0−15% EtOAc/hexane) to give pure **19** (0.936 g, 84%). colorless oil; $[\alpha]_D^{22}$ +15.7 (*c* 0.981, $CHCl_3$); IR: 3414, 1710 cm^{-1}; ^1H NMR: δ 1.07 (merged s and d, *J* = 6.8 Hz, 12H), 1.21−1.35 (m, 4H) 1.61 (broad s, 1H), 2.26 (s, 3H), 3.91−3.97 (m, 1H), 4.18−4.30 (m, 1H), 6.24 (d, *J* = 16.0 Hz, 1H), 6.70 (dd, *J* = 5.0, 16.0 Hz, 1H), 7.34−7.47 (m, 6H), 7.65−7.69 (m, 4H); ^{13}C NMR: δ 19.2, 22.7, 27.0, 27.4, 32.0, 34.9, 69.2, 71.2, 127.5, 127.6, 129.0, 129.6, 129.7, 134.0, 134.2, 135.8, 148.7, 198.5. Anal. Calcd for $C_{25}H_{34}O_3Si$: C, 73.13; H, 8.35%. Found: C, 73.39; H, 8.02%.

Decarestrictine L 1. To a cooled (0 °C) and stirred solution of **19** (0.700 g, 1.71 mmol) in THF (5 mL) was added Bu_4NF (1.7 mL, 1.71 mmol, 1 M in THF). The reaction mixture was brought to room temperature and stirred until the reaction was complete (*cf.* TLC, 3 h).

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The mixture was poured into ice-cold H_2O (15 mL) and extracted with EtOAc (2 × 10 mL). The organic extract was washed with water (2 × 10 mL) and brine (1 × 5 mL) and dried. Removal of solvent, followed by column chromatography of the residue (silica gel, 0−15% EtOAc/hexane), furnished **1** (0.21 g, 71%). colorless oil; $[\alpha]_D^{22}$ + 28.4 (*c* 1.14, $CHCl_3$), lit.[8a] $[\alpha]_D^{25}$ + 28.8 (c 0.49, $CHCl_3$); IR: 3441, 1710 cm^{-1}; ^1H NMR: δ 1.22 (d, *J* = 6.0 Hz, 3H), 1.55−1.58 (m, 1H), 1.69−1.75 (m, 2H), 1.83−1.91 (m, 2H), 2.21 (s, 3H), 2.73 (d, *J* = 6.6 Hz, 2H), 3.40−3.49 (m, 1H), 3.84−3.95 (m, 1H), 4.00 (q, *J* = 6.6 Hz, 1H); ^{13}C NMR: δ 21.2, 29.6, 31.0, 32.8, 47.1, 70.3, 73.6, 78.3, 209.0. Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.59; H, 9.42.

Ethyl (2*E*,4*S*,7*R*)-4-Hydroxy-7-*tert*-butyldiphenylsilyloxyoct-2-enoate 20. Cross-metathesis between (3*S*,6*R*)-**13** (0.730 g, 1.98 mmol) and ethyl acrylate (1.99 g, 19.8 mmol) in the presence of Hoveyda Grubbs' II catalyst (5 mol) in CH_2Cl_2 (15 mL), followed by isolation, furnished **20** (0.870 g, quant.). colorless oil; $[\alpha]_D^{28}$ +28.9 (*c* 1.02, $CHCl_3$); IR: 3453, 1720, 1656, 984 cm^{-1}; ^1H NMR: δ 1.04 (merged s and d, *J* = 6.0 Hz, 12H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.59−1.67 (m, 5H), 3.85−3.94 (m, 1H), 4.14−4.25 (merged m and q at δ 4.20, *J* = 7.2 Hz, 3H), 5.99 (dd, *J* = 1.6, 15.6 Hz, 1H), 6.88 (dd, *J* = 4.6, 15.6 Hz, 1H), 7.35−7.42 (m, 6H), 7.63−7.68 (m, 4H); ^{13}C NMR: δ 14.2, 19.2, 22.9, 27.0, 31.6, 34.2, 60.4, 69.1, 70.8, 120.2, 127.4, 127.6, 129.5, 129.6, 134.0, 134.4, 135.8, 135.9, 150.1, 166.5. Anal. Calcd for $C_{26}H_{36}O_4Si$: C, 70.87; H, 8.23%. Found: C, 70.65; H, 8.36%.

Ethyl (2*E*,4*S*,7*R*)-4-*tert*-Butyldimethylsilyloxy-7-*tert*-butyldiphenylsilyloxyoct-2-enoate 21. As described for **11**, silylation of **20** (0.870 g, 1.98 mmol) with TBSCl (0.445 g, 2.97 mmol), imidazole (0.202 g, 2.97 mmol), and DMAP (catalytic) in CH_2Cl_2 (15 mL) furnished **21** (1.0 g, 92%) after isolation and purification. colorless oil; $[\alpha]_D^{22}$ +25.8 (*c* 1.04, $CHCl_3$); IR: 3071, 3048, 1720, 1656, 997 cm^{-1}; ^1H NMR: δ −0.04 (s, 6H), 0.85 (s, 9H), 1.01 (merged s and d, *J* = 6.0 Hz, 12H), 1.23−1.31 (m containg a t at δ 1.28, *J* = 7.0 Hz, 4H), 1.44−1.50 (m, 3H), 3.77−3.83 (m, 1H), 4.08−4.22 (merged m and q at δ 4.17, *J* = 7.0 Hz, 3H), 5.88 (dd, *J* = 1.8, 15.6 Hz, 1H), 6.82 (dd, *J* = 4.6, 15.6 Hz, 1H), 7.28−7.40 (m, 6H), 7.61−7.65 (m, 4H); ^{13}C NMR: δ 14.3, 18.1, 19.2, 23.2, 25.8, 27.0, 32.8, 34.4, 60.3, 69.2, 71.4, 119.8, 127.4, 127.5, 129.4, 129.5, 134.4, 134.8, 135.8, 135.9, 150.9, 166.7. Anal. Calcd for $C_{32}H_{50}O_4Si_2$: C, 69.26; H, 9.08%. Found: C, 69.47; H, 9.23%.

(2*E*,4*S*,7*R*)-4-*tert*-Butyldimethylsilyloxy-7-*tert*-butyldiphenylsilyloxyoct-2-enoic acid 22. To a stirred solution of **21** (1.01 g, 1.82 mmol) in MeOH (20 mL) was added aqueous 20% NaOH (8 mL). After stirring for 2 h at room temperature, the mixture was concentrated in vacuo. The residue was acidified with aqueous 2 N HCl and extracted with Et_2O (3 × 30 mL). The organic layer was washed with H_2O (2 × 20 mL) and brine (1 × 10 mL). Removal of solvent in vacuo, followed by column chromatography of the residue (silica gel, 0−30% EtOAc/hexane), afforded pure **22** (0.948 g, 99%). colorless oil; $[\alpha]_D^{24}$ +27.1 (*c* 1.17, $CHCl_3$); IR: 3500−2500, 1698 cm^{-1}; ^1H NMR: δ 0.01 (s, 6H), 0.90 (s, 9H), 1.06 (merged s and d, *J* = 6.2 Hz, 12H), 1.27−1.30 (m, 2H), 1.51−1.63 (m, 3H), 3.82−3.88 (m, 1H), 4.11−4.19 (m, 1H), 5.96 (dd, *J* = 1.2, 15.6 Hz, 1H), 6.98 (dd, *J* = 4.4, 15.6 Hz, 1H), 7.34−7.42 (m, 6H), 7.66−7.70 (m, 4H); ^{13}C NMR: δ 18.1, 19.2, 23.2, 25.8, 27.0, 29.7, 32.7, 34.3, 69.1, 71.2, 119.1, 127.4, 127.5, 129.4, 129.6, 134.3, 134.7, 135.8, 135.9, 153.7, 172.2. Anal. Calcd for $C_{30}H_{46}O_4Si_2$: C, 68.39; H, 8.80%. Found: C, 68.04; H, 9.19%.

(3*S*,6*S*)-6-*tert*-Butyldiphenylsilyloxyhept-1-en-3-ol (3*S*,6*S*)-13. Alkaline hydrolysis of (3*S*,6*S*)-**14** (1.20 g, 2.93 mmol) with K_2CO_3 (0.490 g, 3.55 mmol) in MeOH (15 mL), followed by the usual isolation as above, furnished pure (3*S*,6*S*)-**13** (0.981 g, 91%). colorless liquid; $[\alpha]_D^{24}$ −10.1 (*c* 1.06, $CHCl_3$); IR: 3420, 3050, 997 cm^{-1}; ^1H NMR: δ 1.04 (merged s and d, *J* = 5.6 Hz, 12H), 1.50−1.61 (m, 5H), 3.84−3.98 (m, 2H), 5.00−5.19 (m, 2H), 5.69−5.85 (m, 1H), 7.31−7.40 (m, 6H), 7.62−7.68 (m, 4H); ^{13}C NMR: δ 19.0, 22.7, 26.8, 32.3, 34.8, 69.1, 73.0, 114.3, 127.2, 127.3, 129.2, 129.3, 134.4, 135.6, 140.9. Anal. Calcd for $C_{23}H_{32}O_2Si$: C, 74.95; H, 8.75%. Found: C, 74.71; H, 8.83%.

(3*S*,6*S*)-3-Benzyloxy-6-*tert*-butyldiphenylsilyloxyhept-1-ene 23. To a stirred suspension of hexane-washed NaH (0.14 g, 5.64 mmol, 50% suspension in oil) in THF (10 mL) was added (3*S*,6*S*)-**13** (0.690 g, 1.88 mmol) in THF (5 mL). After refluxing the mixture for 1 h, it was brought to room temperature, BnBr (0.48 g, 2.82 mmol) and Bu_4NI (10 mol %) were added, and the mixture was refluxed until completion of the reaction (*cf.* TLC, 4 h). It was brought to room temperature and extracted with Et_2O (2 × 20 mL). The organic extract was washed with H_2O (2 × 10 mL) and brine (1 × 3 mL) and dried. Removal of solvent in vacuo, followed by column chromatography (silica gel, 0−5% EtOAc/hexane) of the residue, afforded pure **23** (0.835 g, 97%). colorless oil; $[\alpha]_D^{23}$ −25.0 (*c* 1.20, $CHCl_3$); IR: 3069, 1643 cm^{-1}; ^1H NMR: δ 1.03 (merged s and d, *J* = 6.0 Hz, 12H), 1.49−1.57 (m, 4H), 3.56−3.66 (m, 1H), 3.78−3.89 (m, 1H), 4.30 (d, *J* = 11.8 Hz, 1H), 4.54 (d, *J* = 11.8 Hz, 1H), 5.06−5.19 (m, 2H), 5.55−5.73 (m, 1H), 7.25−7.29 (m, 5H), 7.32−7.43 (m, 6H), 7.63−7.68 (m, 4H); ^{13}C NMR: δ 19.2, 23.2, 27.0, 31.0, 35.0, 69.5, 69.9, 80.7, 117.1, 127.4, 127.6, 127.7, 128.3, 129.4, 134.4, 134.8, 135.9, 138.8, 138.9. Anal. Calcd for $C_{30}H_{38}O_2Si$: C, 78.55; H, 8.35%. Found: C, 78.37; H, 8.28%.

(2*S*,5*S*)-5-Benzyloxyhept-6-en-2-ol 24. Desilylation of **23** (0.742 g, 1.62 mmol) with Bu_4NF (3.23 mL, 3.23 mmol, 1 M in THF) in THF (10 mL) at 0 °C, followed by isolation, as described earlier, furnished **24** (0.271 g, 76%); colorless oil; $[\alpha]_D^{25}$ −20.6 (*c* 1.06, $CHCl_3$); IR: 3400, 3065, 3030, 1643 cm^{-1}; ^1H NMR: δ 1.17 (d, *J* = 6.0 Hz, 3H), 1.64−1.66 (m, 5H), 3.72−3.83 (m, 2H), 4.34 (d, *J* = 11.8 Hz, 1H), 4.59 (d, *J* = 11.8 Hz, 1H), 5.17−5.26 (m, 2H), 5.67−5.84 (m, 1H), 7.25−7.32 (m, 5H); ^{13}C NMR: δ 23.3, 31.6, 34.9, 67.6, 70.1, 80.5, 117.3, 127.4, 127.7, 128.3, 138.3, 138.6. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15%. Found: C, 76.37; H, 9.51%.

(9*E*,3*S*,6*R*,11*S*,14*R*)-3-Benzyloxy-11-*tert*-butyldimethylsilyloxy-14-*tert*-butyldiphenylsilyloxy-6-methyl-7-oxa-8-oxopenta-1,9-diene 25. To a stirred solution of **24** (0.270 g, 1.23 mmol) in THF (10 mL) were added PPh_3 (0.48 g, 1.85 mmol) and **22** (0.775 g, 1.47 mmol). The reaction mixture was cooled to 0 °C, DIAD (0.36 g, 1.85 mmol) was added, and the mixture was stirred for 18 h. The mixture was extracted with EtOAc (2 × 15 mL), and the organic extract was washed with H_2O (2 × 10 mL) and brine (1 × 5 mL) and dried. After concentrating in vacuo, the residue was subjected to column chromatography (silica gel, 0−20% EtOAc/hexane) to give pure **25** (0.592 g, 66%). colorless oil; $[\alpha]_D^{23}$ +7.7 (*c* 1.06, $CHCl_3$); IR: 1715, 1657, 995 cm^{-1}; ^1H NMR: δ −0.03 (s, 6H), 0.86 (s, 9H), 1.03 (merged s and d, *J* = 6.0 Hz, 12H), 1.22 (d, *J* = 6.2 Hz, 3H), 1.46−1.57 (m, 8H), 3.72−3.85 (m, 2H), 4.12−4.14 (m, 1H), 4.33 (d, *J* = 11.8 Hz, 1H), 4.58 (d, *J* = 11.8 Hz, 1H), 4.93−4.97 (m, 1H), 5.16−5.25 (m, 2H), 5.63−5.77 (m, 1H), 5.86 (dd, *J* = 1.6, 15.6 Hz, 1H), 6.80 (dd, *J* = 4.6, 15.6 Hz, 1H), 7.31−7.37 (m, 11H), 7.63−7.67 (m, 4H); ^{13}C NMR: δ 18.0, 19.1, 19.9, 23.2, 25.8, 27.0, 31.1, 31.5, 32.8, 34.4, 69.1, 70.0, 70.4, 71.3, 79.9, 117.3, 120.1, 127.3, 127.4, 127.6, 128.2, 129.3, 129.4, 134.2, 134.6, 135.7, 138.5, 138.7, 150.5, 166.1. Anal. Calcd for $C_{44}H_{64}O_5Si_2$: C, 72.48; H, 8.85%. Found: C, 72.52; H, 8.70%.

(6*E*,2*R*,5*S*,10*R*,13*S*)-13-Benzyloxy-10-methyl-9-oxa-8-oxopenta-6,14-diene-2,5-diol 26. A mixture of **25** (0.583 g, 0.80 mmol) in CH_3CN (10 mL) and aqueous HF (0.4 mL) in a Teflon vessel was stirred at room temperature for 16 h. The mixture was concentrated in vacuo, and the residue was extracted with EtOAc (3 × 20 mL). The organic layer was washed with H_2O (2 × 10 mL) and brine (1 × 5 mL) and concentrated in vacuo, and the residue was column chromatographed (silica gel, 0−40% EtOAc/hexane) to afford pure **26** (0.210 g, 70%). colorless oil; $[\alpha]_D^{23}$ −24.0 (*c* 1.05, $CHCl_3$); IR: 3417, 3087, 3030, 1714, 990 cm^{-1}; ^1H NMR: δ 1.17 (d, *J* = 6.0 Hz, 3H), 1.20 (d, *J* = 6.0 Hz, 3H), 1.49−1.75 (m, 8H), 3.14 (broad s, 2H), 3.70−3.82 (m, 2H), 4.29−4.35 (merged m and d, *J* = 11.8 Hz, 2H), 4.57 (d, *J* = 11.8 Hz, 1H), 4.92−4.96 (m, 1H), 5.16−5.25 (m, 2H), 5.62−5.79 (m, 1H), 5.99 (dd, *J* = 1.4, 15.6 Hz, 1H), 6.89 (dd, *J* = 4.8, 15.6 Hz, 1H), 7.26−7.33 (m, 5H); ^{13}C NMR: δ 19.9, 23.6, 31.1, 31.6, 33.2, 35.1, 68.1, 70.0, 70.8, 71.0, 80.0, 117.5, 120.4, 127.4, 127.7, 128.3, 138.5, 138.6, 150.0, 166.3. Anal. Calcd for $C_{22}H_{32}O_5$: C, 70.18; H, 8.57%. Found: C, 69.84; H, 8.53%.

(6*E*,2*R*,5*S*,10*R*,13*S*)-2-Acryloxy-13-benzyloxy-10-methyl-9-oxa-8-oxopenta-6,14-dien-5-ol 27. A solution of **26** (0.210 g, 0.56

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mmol), ethyl acrylate (0.450 g, 4.48 mmol), and Novozym 435 (0.50 g, ~890 mg/mmol) in diisopropyl ether (5 mL) was agitated on an orbital shaker at 120 rpm for 30 h. The reaction mixture was filtered, the filtrate was concentrated in vacuo, and the residue was column chromatographed (silica gel, 0−25% EtOAc/hexane) to furnish pure **27** (0.171 g, 71%). colorless oil; $[\alpha]_D^{23}$ −7.1 (*c* 1.13, $CHCl_3$); IR: 3479, 3065, 3030, 1728, 1714, 1657, 985 cm^{-1}; ^1H NMR: δ 1.22 (d, *J* = 6.2 Hz, 3H), 1.25 (d, *J* = 6.4 Hz, 3H), 1.54−1.80 (m, 8H), 3.51 (broad s, 1H), 3.68−3.79 (m, 1H), 4.29−4.35 (merged m and d, *J* = 11.8 Hz, 2H), 4.58 (d, *J* = 11.8 Hz, 1H), 4.88−5.06 (m, 2H), 5.16−5.25 (m, 2H), 5.66−5.83 (m, 2H), 5.95−6.15 (m, 2H), 6.38 (dd, *J* = 1.6, 17.2 Hz, 1H), 6.88 (dd, *J* = 5.0, 15.8 Hz, 1H), 7.29−7.33 (m, 5H); ^{13}C NMR: δ 20.0, 31.1, 31.4, 31.6, 32.0, 70.0, 70.5, 70.7, 70.9, 80.0, 117.5, 120.8, 127.4, 127.7, 128.3, 128.7, 130.6, 138.5, 138.6, 149.5, 165.9, 166.0. Anal. Calcd for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96%. Found: C, 69.44; H, 7.94%.

(*5S,8R,13S,16R*)-Pyrenophorol Monobenzyl Ether 28. A stirred solution of **27** (0.142 g, 0.33 mmol) and Grubbs' II catalyst (20 mol %) in degassed CH_2Cl_2 (10 mL) was refluxed for 72 h. The reaction mixture was concentrated in vacuo, and the residue was subjected to preparative tlc to obtain pure **28** (57 mg, 61% based on conversion) and recovered **27** (40 mg). colorless oil; $[\alpha]_D^{25}$ −39.0 (*c* 1.07, $CHCl_3$); IR: 3470, 1713, 1643 cm^{-1}; ^1H NMR: δ 1.24 (t, *J* = 6.2 Hz, 6H), 1.60−1.86 (m, 9H), 3.78−3.88 (m, 1H), 4.13−4.22 (m, 1H), 4.37 (d, *J* = 12.0 Hz, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 5.03−5.17 (m, 2H), 5.91 (d, *J* = 16.0 Hz, 2H), 6.74 (dd, *J* = 7.8, 16.0 Hz, 1H), 6.82 (dd, *J* = 6.8, 15.6 Hz, 1H), 7.32 (s, 5H); ^{13}C NMR: δ 13.9, 18.4, 29.7, 30.9, 33.4, 43.7, 69.8, 70.7, 77.2, 79.2, 83.4, 124.5, 127.7, 128.6, 146.9, 178.1. Anal. Calcd for $C_{23}H_{30}O_6$: C, 68.64; H, 7.51%. Found: C, 68.56; H, 7.78%.

(*5S,8R,13S,16R*)-Pyrenophorol 2. A mixture of **28** (40 mg, 0.1 mmol) and $TiCl_4$ (11.0 μL, 0.1 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature until the completion of the reaction (*cf.* TLC, 30 min). After concentration in vacuo, the residue was purified by preparative thin layer chromatography to get pure (*5S,8R,13S,16R*)-**2** (23 mg, 74%). sticky solid; $[\alpha]_D^{25}$ −2.9 (*c* 1.00, acetone), (lit.[9f] $[\alpha]_D^{25}$ −3.2 (*c* 0.25, acetone); IR: 3440, 1714, 1651, 985 cm^{-1}; ^1H NMR: δ 1.26 (d, *J* = 6.6 Hz, 6H), 1.64−1.93 (m, 8H), 2.30 (broad s, 2H), 4.26−4.32 (m, 2H), 5.10−5.17 (m, 2H), 5.98 (dd, *J* = 1.6, 15.6 Hz, 2H), 6.90 (dd, *J* = 5.2, 15.6 Hz, 2H); ^{13}C NMR: δ 18.2, 28.9, 30.5, 69.8, 70.4, 122.2, 149.5, 165.0. Anal. Calcd for $C_{16}H_{24}O_6$: C, 61.52; H, 7.74%. Found: C, 61.45; H, 7.92%.

(*2E,4R,7S*)-4-Hydroxy-7-*para*-methoxybenzyloxyoct-2-enal 29. A mixture of (3*R*,6*S*)-**17** (0.690 g, 2.76 mmol), acrolein (0.92 mL, 13.80 mmol), and Hoveyda Grubbs' II catalyst (86 mg, 0.14 mmol) in CH_2Cl_2 (20 mL) was stirred for 22 h at room temperature. After concentrating the mixture in vacuo, the residue was subjected to column chromatography (silica gel, 0−25% EtOAc/hexane) to give pure **29** (0.682 g, 89%). colorless liquid; $[\alpha]_D^{26}$ +16.6 (*c* 1.01, $CHCl_3$); IR: 3426, 2729, 1688 cm^{-1}; ^1H NMR: δ 1.23 (d, *J* = 6.0 Hz, 3H), 1.66−1.83 (m, 5H), 3.44−3.61 (m, 2H), 3.82 (s, 3H), 4.36 (d, *J* = 11.2 Hz, 1H), 4.56 (d, *J* = 11.2 Hz, 1H), 6.25−6.37 (m, 1H), 6.80 (dd, *J* = 4.2, 15.6 Hz, 1H), 6.86−6.93 (m, 2H), 7.25−7.31 (m, 2H), 9.57 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR: δ 19.2, 19.7, 32.4, 55.3, 70.3, 70.7, 74.4, 113.8, 113.9, 129.3, 129.5, 130.1, 130.8, 159.4, 193.7. Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97%. Found: C, 68.93; H, 7.89%.

(*2E,4R,7S*)-4-*tert*-Butyldimethylsilyloxy-7-*para*-methoxybenzyloxyoct-2-enal 30. Silylation of **29** (1.08 g, 3.88 mmol) with TBSCl (0.700 g, 4.66 mmol), imidazole (0.400 g, 5.83 mmol), and DMAP (catalytic) in CH_2Cl_2 (30 mL), followed by the usual isolation, afforded pure **30** (1.23 g, 81%). colorless liquid; $[\alpha]_D^{28}$ −12.7 (*c* 1.00, $CHCl_3$); IR: 2722, 1692 cm^{-1}; ^1H NMR: δ 0.06 (s, 3H), 0.10 (s, 3H), 0.95 (s, 9H), 1.22 (d, *J* = 6.2 Hz, 3H), 1.47−1.78 (m, 4H), 3.49−3.55 (m, 1H), 3.84 (s, 3H), 4.36−4.57 (m, 3H), 6.23−6.35 (m, 1H), 6.81 (dd, *J* = 4.4, 15.4 Hz, 1H), 6.87−6.95 (m, 2H), 7.26−7.31 (m, 2H), 9.60 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR: δ −4.9, −4.7, 18.1, 19.5, 25.7, 32.9, 33.2, 55.2, 69.9, 71.6, 74.2, 113.7, 129.1, 130.7, 130.9, 159.1, 160.0, 193.6. Anal. Calcd for $C_{22}H_{36}O_4Si$: C, 67.30; H, 9.24%. Found: C, 67.26; H, 9.41%.

Ethyl (*2Z,4E,6R,9S*)-6-*tert*-Butyldimethylsilyloxy-9-*para*-methoxybenzyloxydeca-2,4-dienoate 31. To a cooled (0 °C) and stirred suspension of hexane-washed NaH (0.142 mg, 2.95 mmol, 50% suspension in oil) in THF (5 mL) was added ethyl diphenylphosphonoacetate (0.750 g, 2.36 mmol) in THF (5 mL). After 1 h, the solution was cooled to −78 °C, **30** (0.77 g, 1.96 mmol) in THF (5 mL) was injected into it, and stirring continued at −78 °C for 3 h. The mixture was poured into ice−water and extracted with Et_2O (3 × 10 mL). The ether layer was washed with H_2O (2 × 10 mL) and brine (1 × 5 mL), dried, and concentrated in vacuo to get a residue, which, on column chromatography (silica gel, 0−10% EtOAc/hexane), furnished pure **31** (0.620 g, 68%). colorless liquid; $[\alpha]_D^{24}$ −12.9 (*c* 1.00, $CHCl_3$); IR: 1716, 1641 cm^{-1}; ^1H NMR: δ 0.04 and 0.1 (two s, 6H), 0.90 (s, 9H), 1.16 (d, *J* = 6.0 Hz, 3H), 1.27 (t, *J* = 7.6 Hz, 3H), 1.48−1.74 (m, 4H), 3.47−3.53 (m, 1H), 3.80 (s, 3H), 4.15−4.22 (m, 3H), 4.39−4.50 (m, 2H), 5.64 (d, *J* = 11.4 Hz, 1H), 5.96 (dd, *J* = 6.3, 15.3 Hz, 1H), 6.54 (t, *J* = 11.4 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.42 (dd, *J* = 11.4, 15.3 Hz, 1H); ^{13}C NMR: δ −4.8, −4.3, 14.3, 18.2, 19.6, 22.7, 25.9, 29.7, 30.2, 31.7, 32.1, 33.7, 55.2, 59.9, 69.9, 72.7, 73.0, 74.1, 74.5, 113.7, 117.5, 125.6, 129.2, 131.1, 144.2, 146.8, 159.1, 166.3. Anal. Calcd for $C_{26}H_{42}O_5Si$: C, 67.49; H, 9.15%. Found: C, 67.74; H, 9.21%.

Ethyl (*2Z,4E,6R,9S*)-6-*tert*-Butyldimethylsilyloxy-9-hydroxydeca-2,4-dienoate 32. To a solution of **31** (0.620 g, 1.34 mmol) in CH_2Cl_2−H_2O was added DDQ (0.394 g, 1.74 mmol). After stirring for 3 h at room temperature, the reaction mixture was filtered through a pad of Celite. The filtrate was dried and concentrated in vacuo to get a residue, which, on column chromatography (silica gel, 0−10% EtOAc/hexane), furnished pure **32** (0.353 g, 77%). colorless liquid; $[\alpha]_D^{24}$ −7.2 (*c* 0.82, $CHCl_3$); IR: 3415, 1715, 1641 cm^{-1}; ^1H NMR: δ 0.07 (s, 6H), 0.89 (s, 9H), 1.18 (d, *J* = 6.3 Hz, 3H), 1.22 (t, *J* = 6.3 Hz, 3H), 1.31−1.69 (m, 4H), 2.04 (broad s, 1H), 3.78−3.81 (m, 1H), 4.19 (q, *J* = 7.0 Hz, 2H), 4.29−4.35 (m, 1H), 5.65 (d, *J* = 11.9 Hz, 1H), 5.98 (dd, *J* = 15.4, 6.3 Hz, 1H), 6.56 (t, *J* = 11.9 Hz, 1H), 7.39−7.46 (m, 1H); ^{13}C NMR: δ −4.8, −4.3, 14.3, 18.2, 22.7, 23.4, 25.9, 29.7, 31.9, 33.8, 34.4, 59.9, 67.8, 72.8, 114.0, 117.6, 125.8, 139.2, 144.0, 146.3, 166.3. Anal. Calcd for $C_{18}H_{34}O_4Si$: C, 63.11; H, 10.00%. Found: C, 63.18; H, 9.84%.

(*2Z,4E,6R,9S*)-6-*tert*-Butyldimethylsilyloxy-9-hydroxydeca-2,4-dienoic acid 33. A solution of **32** (0.080 g, 0.234 mmol) and aqueous 1 M LiOH (0.351 mL, 0.351 mmol) in THF:H_2O (1:1, 10 mL) was stirred at 0 °C for 6 h. Removal of solvent in vacuo gave a residue, which was purified by preparative thin layer chromatography (silica gel, 40% EtOAc/hexane) to afford **33** (60 mg, 82%). viscous liquid; $[\alpha]_D^{24}$ −6.98 (*c* 1.39, $CHCl_3$); IR: 3500- 2500, 1693, 1639 cm^{-1}; ^1H NMR: δ 0.04 (s, 3H), 0.06 (s, 3H), 0.90 (s, 9H), 1.18 (d, *J* = 6.2 Hz, 3H), 1.48−1.68 (m, 4H), 2.34 (broad s, 1H), 3.75−3.85 (m, 1H), 4.28−4.36 (m, 1H), 5.66 (d, *J* = 11.0 Hz, 1H), 6.04 (dd, *J* = 15.4, 6.0 Hz, 1H), 6.65 (t, *J* = 11.4 Hz, 1H), 7.45 (dd, *J* = 15.4, 11.4 Hz, 1H); ^{13}C NMR: δ −4.7, −4.2, 18.1, 23.1, 25.9, 29.7, 33.5, 33.9, 66.9, 72.5, 126.0, 126.4, 137.9, 142.4, 175.0. Anal. Calcd for $C_{16}H_{30}O_4Si$: C, 61.11; H, 9.61%. Found: C, 61.04; H, 9.76%.

(*3Z,5E,7R,10R*)-7-*tert*-Butyldimethylsilyloxy-10-methyl-7,8,9,10-tetrahydrooxecin-2-one 34. To a cooled (0 °C) and stirred solution of **33** (0.210 g, 0.67 mmol) and PPh_3 (0.352 g, 1.34 mmol) in anhydrous toluene (96 mL) was slowly added DIAD (0.26 mL, 1.34 mmol). The reaction mixture was stirred at room temperature for 16 h and concentrated in vacuo, and the residue was purified by preparative thin layer column chromatography (silica gel, 20% EtOAc/hexane) to furnish **34** (130 mg, 73% based on conversion) along with unreacted **33** (20 mg). colorless liquid; $[\alpha]_D^{24}$ −51.8 (*c* 0.4, $CHCl_3$); IR: 1702, 1643, 1360 cm^{-1}; ^1H NMR: δ 0.04 (s, 3H), 0.08 (s, 3H), 0.89 (s, 9H), 1.32 (d, *J* = 6.2 Hz, 3H), 1.46−1.59 (m, 2H), 1.78−2.01 (m, 2H), 4.02−4.15 (m, 1H), 4.75−4.93 (m, 1H), 5.58 (d, *J* = 11.6 Hz, 1H), 5.90 (dd, *J* = 8.2, 15.4 Hz, 1H), 6.49 (t, *J* = 11.6 Hz, 1H), 7.09 (dd, *J* = 15.4, 11.6 Hz, 1H); ^{13}C NMR: δ −4.8, −4.0, 18.2, 20.9, 25.8, 29.7, 33.7, 35.1, 72.1, 75.3, 119.6, 126.2, 141.9, 146.1, 166.2. Anal. Calcd for $C_{16}H_{28}O_3Si$: C, 64.82; H, 9.52%. Found: C, 64.47; H, 9.22%.

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(3*Z*,5*E*,7*R*,10*R*)-7-Hydroxy-10-methyl-7,8,9,10-tetrahydrooxecin-2-one (Stagonolide E) 3. Desilylation of **34** (40 mg, 0.14 mmol) with aqueous HF (0.4 mL) in CH_3CN (10 mL), followed by isolation, as described above, and purification by preparative thin layer chromatography (silica gel, 15% EtOAc/hexane) furnished pure **3** (19 mg, 77%). colorless oil; $[\alpha]_D^{23}$ −178.0 (*c* 0.342, $CHCl_3$), (lit.[11a] $[\alpha]_D^{25}$ −181 (*c* 0.2, $CHCl_3$); IR: 3478, 1697, 1642 cm^{-1}; ^1H NMR: δ 1.26 (d, *J* = 6.2 Hz, 3H), 1.50−1.76 (m, 4H), 1.90−2.01 (m, 1H), 4.25−4.29 (m, 1H), 4.94−5.12 (m, 1H), 5.68 (d, *J* = 11.4 Hz, 1H), 6.06 (dd, *J* = 15.4, 5.0 Hz, 1H), 6.56 (t, *J* = 11.4 Hz, 1H), 6.77 (dd, *J* = 15.4, 11.2 Hz, 1H); ^{13}C NMR: δ 19.8, 31.8, 32.8, 71.5, 72.6, 118.5, 125.2, 143.0, 145.9, 166.7. Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74%. Found: C, 65.79; H, 7.42%.

■ ASSOCIATED CONTENT

Supporting Information

^1H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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