Asymmetric Total Synthesis of Halicholactone

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Asymmetric Total Synthesis of Halicholactone

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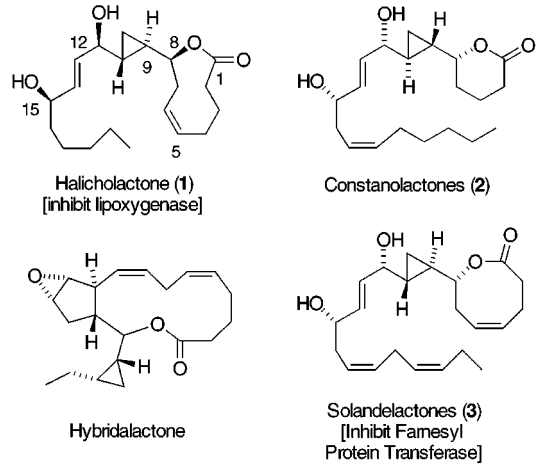
The asymmetric total synthesis of the marine metabolite, halicholactone **1**, is described. The bis-allylic triol **6** with three chiral centers at C8, C12, and C15 was constructed by [2,3]-sigmatropic rearrangement of the sulfoxide **18**, which was prepared stereoselectively using the chirality of (diene)$Fe(CO)_3$ complexes. Introduction of the *trans*-substituted cyclopropane subunit into **21** was successfully achieved using the modified regio- and stereoselective Simmons−Smith reaction. The use of RCM (ring-closing metathesis) methodology (**4** → **35**) was pivotal for the formation of a nine-membered unsaturated lactone fragment of halicholactone **1**. As this approach is flexible and stereoselective, other oxylipins could be synthesized by the protocol described herein.

Introduction

Marine metabolites containing a *trans*-disubstituted cyclopropane subunit and saturated and unsaturated lactones of various ring sizes, which are called oxylipins, are a growing class of natural products. Among these compounds, halicholactone **1**[1] and constanolactones **2**[2] are derived from eicosanoid with a C20 carbon chain, while solandelactones **3**[3] is thought to have originated from docosanoid possessing a C22 carbon chain. These compounds possess important and interesting biological activities such as the inhibition of lipoxygenase and farnesyl protein transferase. From these biological activities and unusual structural features, oxylipins have attracted the wide attention of a number of synthetic organic chemists. Whereas there have already been several reports concerning the total synthesis of related eicosanoids,[4] the stereoselective construction of the stereogenic centers of C9 to C12 still remained to be solved in the synthesis of halicholactone.[5] In planning our approach, we hoped to develop a general and stereocontrolled route that will be sufficiently practical to facilitate the synthesis of these compounds and their analogues from a common intermediate. For this purpose, we employed the modified Simmons−Smith reaction[6] for the regio- and stereoselective cyclopropanation and the RCM (ring-closing metathesis) methodology[7,8] for the formation of an unsaturated or saturated lactone fragment. By this flexible approach, various oxylipins could be synthesized stereoselectively. As an example of this approach, the



present paper[9] describes the asymmetric total synthesis

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[‡] Kyoto University.
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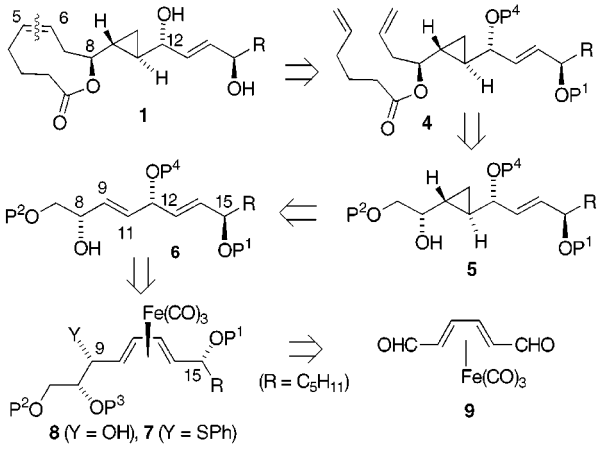
Scheme 1. Retrosynthetic Analysis of Halicholactone 1



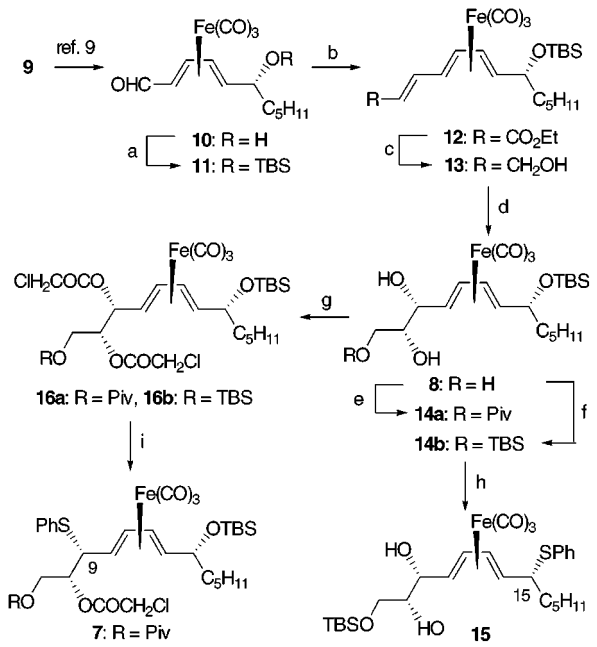
of halicholactone, isolated from the marine sponge *Halichondoria okadai* by the Yamada group as lipoxygenase inhibitors in 1989.[1a]

Results and Discussion

Retrosynthetic Analysis. Recognizing the importance of developing a flexible synthesis of **1**, our synthetic approach to a nine-membered unsaturated lactone involves a *Z*-selective RCM reaction (Scheme 1). Thus, disconnection of the C5−C6 double bond revealed the bisterminal olefin **4** as a potential key intermediate. This compound could be synthesized from the alcohol **5** by epoxidation with inversion of configuration at C8 followed by vinylation and esterification with 5-hexenoic acid. We envisioned the regio- and stereoselective introduction of the desired cyclopropane ring into the C9−C11 olefin of the bis-allylic alcohol **6** via modified Simmons−Smith cyclopropanation to give **5**. The key steps proposed for the conversion of **8** to **6** include a regioselective introduction of the phenylsulfenyl groups and stereoselective [2,3]-sigmatropic rearrangement[10] for the incorporation of the C12 stereocenter via sulfide **7**. We planned to synthesize the triol complex **8** using iron−tricarbonyl chemistry,[11] that is, a catalytic asymmetric alkylation of achiral dialdehyde $Fe(CO)_3$ complex **9**[12] and subsequent stereoselective dihydroxylation with OsO_4.[13]

Synthesis of the Phenyl Sulfide $Fe(CO)_3$ Complex 7. The sequence leading to the required compound **7** is shown in Scheme 2. The known chiral aldehyde $Fe(CO)_3$ complex **10**[12] was initially converted to the *tert*-butyldimethylsilyloxy (TBS) ether **11** (TBSOTf, pyridine, 100%) which was then condensed with triethylphosphonoacetate

Scheme 2[a]



[a] Reagents and conditions: (a) TBSOTf, pyridine, 0 °C, 100%; (b) $(EtO)_2P(O)CH_2CO_2Et$, NaH, THF, 0 °C, 99%; (c) DIBAL-H, CH_2Cl_2, −78 °C, 97%; (d) (i) OsO_4, Py, −20 °C; (ii) saturated aqueous $NaHSO_3$, 94%; (e) PivCL, Py, CH_2Cl_2, 0 °C to room temperature, 97%; (f) TBSOTf, pyridine, 0 °C, 56% (89% based on the consumed 8); (g) $(ClCH_2CO)_2O$, DMAP, CH_2Cl_2, **16a**: 89%, **16b**: 81%; (h) TMSSPh, $Sc(OTf)_3$, CH_2Cl_2, −78 °C to room temperature (62%); (i) Me_2AlSPh, CH_2Cl_2, − 78 °C, 69%.

to give the corresponding α,β-unsaturated ester **12** (99%). DIBAL-mediated reduction of **12**, and sequential dihydroxylation of the resulting allylic alcohol **13** with OsO_4 provided triol complex **8** (91%) as an inseparable diastereoisomeric mixture with good stereoselectivity (α:β ratio ∼9:1, detected from 500 MHz ^{1}H NMR).[13] The protection of the primary hydroxyl group of **8** with PivCl and TBSOTf gave **14a** and **14b**, respectively. Furthermore, the diols **14a** and **14b** were converted into the bischloroacetoxy compounds **16a** and **16b**, respectively. At this stage, the diastereoisomers contaminated in **16a** and **16b** were separated by silica gel column chromatography. Confirmation of the relative stereochemical outcome of the asymmetric alkylation and dihydroxylation was provided by X-ray crystallographic analysis of **16b** (see Figure S1 in Supporting Information). We next examined regio- and stereoselective introduction of a phenylsulfanyl group in at least two synthetic intermediates by substitution with retention of configuration at C3.[14] The diol **14b** was treated with TMSSPh/$Sc(OTf)_3$ or $CH(SPh)_3$/TsOH in CH_2Cl_2 at room temperature, but the undesired product **15** was obtained as the sole product. These results indicate that the C15-hydroxyl group adjacent to the $Fe(CO)_3$ moiety tends to react faster than the C9-hydroxyl group of the 1,2-diol moiety in the Lewis acid-

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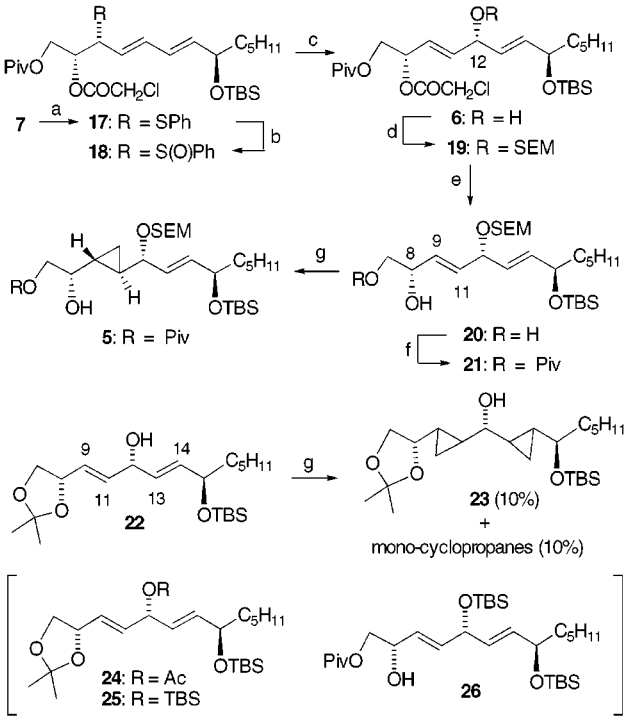
Scheme 3[a]



[a] Reagents and conditions: (a) CAN K_2CO_3, MeCN, −30 °C, 97%; (b) *m*-CPBA, CH_2Cl_2, −78 °C, 95%; (c) $P(OMe)_3$, MeOH, 75 °C, 88%; (d) SEMCl, *i*-Pr_2NEt, *n*-Bu_4NI, CH_2Cl_2, 100%; (e) DIBAL-H, CH_2Cl_2, −78 °C, 91%; (f) PivCl, Py-CH_2Cl_2, 0 °C to room temperature, 64% (85% based on the consumed **20**); (g) Et_2Zn, CH_2I_2, CH_2Cl_2, −20 °C, 69% (77% based on the consumed **21**).

mediated nucleophilic substitution reaction. Then, the reaction of **16a**, bearing a more reactive leaving group, with Me_2AlSPh[15] at −78 °C was conducted to give the desired phenyl sulfide **7** in 69% yield as the single isomer. A key requirement for the success of this reaction is that an equimolar amount of the trimethylaluminum and thiophenol should be premixed prior to the addition of **16a** and the resulting mixture is kept at −78 °C; otherwise, bis-phenyl sulfide was produced as a major product. The relative stereochemistry of C9 and C15 in the sulfides **7** and **15** was elucidated from the reported examples and the well-known reaction mechanism.[11,14] Furthermore, the elucidation was unambiguously confirmed by chemical transformation of **7** into halicholactone **1**.

Synthesis of the Cyclopropane 5. The synthesis of the cyclopropyl alcohol **5** by Simmons−Smith reaction is outlined in Scheme 3. After decomplexation of **7** with ceric(IV) ammonium nitrate (CAN), successive treatment of the resulting sulfide **17** with *m*-CPBA and $P(OMe)_3$ in refluxing MeOH furnished the desired allylic alcohol **6** stereoselectively in 81% overall yield from **7** via sulfoxide **18**. The *S* stereochemistry of the C12 chiral center and the *E* geometry of the C9−C11 double bond were tentatively assigned on the assumption that the [2,3]sigmatropic rearrangement proceeded via the well-precedented chairlike transition state.[10c] This assumption was subsequently confirmed by the total synthesis of halicholactone **1**. At this stage, we presumed that the group-selectivity of the two olefins (C9═C11 vs C13═C14) and

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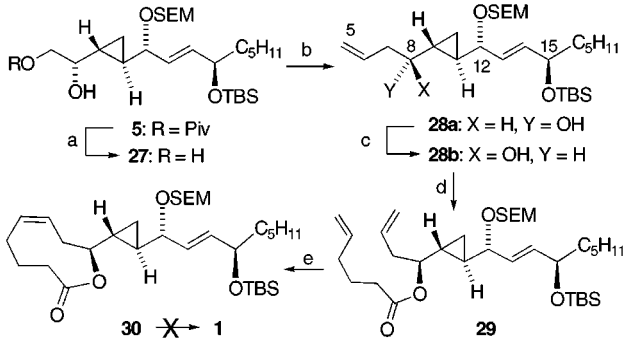
Scheme 4[a]



[a] Reagents and conditions: (a) MeLi, Et_2O, 0 °C, 90%; (b) $Pb(OAc)_4$, Na_2CO_3, CH_2Cl_2, −40 °C; tetraallyltin, $Sc(OTf)_3$, CH_3CN, 68% (**28a**:**298b** = 1:1); (c) DIAD, AcOH, PPh_3, THF; NaH, MeOH, 60% (70% based on the consumed **28a**); (d) $C_5H_9CO_2H$, DCC, DMAP, CH_2Cl_2, 82%; (e) $(Cy_3P)_2RuCl_2$═CHPh, Ti(O*i*-Pr)$_4$, CH_2Cl_2, (6mM) reflux (19%).

diastereomeric face-selectivity of the C9−C11 double bond for the cyclopropanation of **6** could be controlled by the hydroxyl or ether group at C8.[16] To investigate the hypothesis, several alcohols **20** and **26** and acetonides **22**, **24**−**25** were prepared from **6** for the following cyclopropanation. In fact, the modified Simmons−Smith reaction of **22** with Et_2Zn (2.5 equiv) and CH_2I_2 (3 equiv) in CH_2Cl_2 at 0 °C gave rise to the bis-cyclopropanes **23** along with mono-cyclopropane. Furthermore, neither the acetonides **24** and **25** nor alcohol **26** afforded the corresponding cyclopropyl compounds. Fortunately, we found that the same reaction of **21** provided the desired mono-cyclopropanated product **5** in 68% yield as a single product (11% recovery of **21**). These results suggest that the C8-hydroxyl group of **21** plays an important role in promoting the regio- and stereoselective cyclopropanation, while the isopropylidene acetal group of **22**, **24**, and **25** is ineffective for the delivery of a methylene unit to the C9−C11 double bond. In addition, by comparing the results of the SEM ether **5** and the TBS ether **26**, it was revealed that the bulky protecting group (TBS group) of the C12-hydroxyl group impeded the desired cyclopropanation due to steric hindrance.

Synthesis of Halicholactone 1. The final task in the enantioselective synthesis of halicholactone **1** was the formation of a nine-membered lactone possessing a (*Z*)-olefin by the RCM reaction. Two alternative routes to **1** are presented in Schemes 4 and 5. The first elaboration began with the synthesis of allylic alcohol **28b**. The requisite alcohol **28b** was synthesized from **5** by the following sequence: removal of the pivaloyl group with MeLi (90%), cleavage of a 1,2-diol with $Pb(OAc)_4$, and introduction of an allyl group (68%, **28a**/**28b** = 1/1).[17] The stereochemistry of the C8 chiral center of **28a** and **28b** was deduced from the modified MTPA ester method.[18] Thus, esterification of **28b** with both (*R*)- and (*S*)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA)

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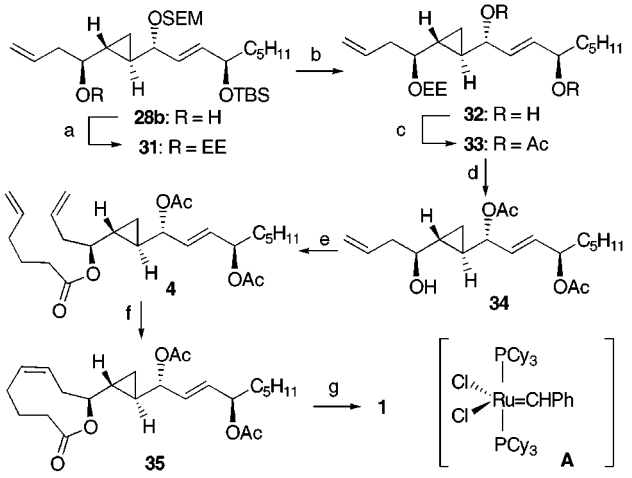
Scheme 5[a]



[a] Reagents and conditions: (a) ethyl vinyl ether, PPTS, CH_2Cl_2, 90%; (b) TBAF, MS 4A, 85 °C, DMPU, 64%; (c) Ac_2O, Et_3N, DMAP, CH_2Cl_2, 88%; (d) PPTS, *t*-BuOH, 69% (71% bsed on the consumed **33**); (e) 5-hexenoic acid, DCC, DMAP, CH_2Cl_2, 82%; (f) catalyst **A**, Ti(O*i*-Pr)$_4$, CH_2Cl_2 (0.1 mM), reflux, 72%; (g) K_2CO_3, MeOH, 61%.

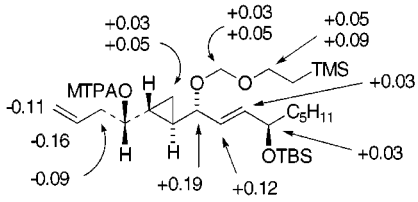


Figure 1. $\Delta\delta = \delta_S - \delta_R$ for (*R*)- and (*S*)-MPTA esters of **28b**.

demonstrated positive chemical shift differences ($\Delta\delta = \delta_S - \delta_R$) for the protons on C9 through C15 (Figure 1), while the protons on C5 through C7 showed negative differences, which is consistent with C8 bearing an *R* configuration. Although this manipulation gave the undesired product **28a** along with **28b**, **28a** was easily converted into **28b** in 70% yield via the standard Mitsunobu protocol.[19] The subsequent assembly of the alcohol **28b** and 5-hexenoic acid was easily performed by the DCC-condensation procedure, giving rise to the ester **29** in 82% yield. The ring-closing metathesis (RCM)[7,8] of the resulting product **29** with Grubbs catalyst **A**[20] afforded the desired lactone **30** only in a disappointingly low yield (19%) together with the recovered starting material (45% yield) and the corresponding dimer (8% yield). We did not optimize this reaction, because we encountered a serious problem in the following reaction. Namely, removal of the protecting groups (TBS and SEM groups) of the obtained product **30** resulted only in decomposed products due to the instability of the cyclopropane and lactone units to the reaction conditions. We expected that the problem could be overcome by replacement of the protecting group of **30** from the TBS and SEM groups to an acetyl group, and we next examined another route as shown in Scheme 5. Treatment of alcohol **28b** with ethyl vinyl ether in the presence of PPTS (90%) was followed by removal of the TBS and SEM groups of **31** with TBAF[21] (64%) and protection of the resulting diol **32**, providing the diacetate **33** (88%). The diacetate **4** was prepared from **33** via **34** by a two-step sequence [i. acid-catalyzed deprotection of the ethoxyethyl group (71%), ii. DCC-mediated esterification (82%)]. After many experiments on the RCM reaction of **4**, it was revealed that the reaction of **4** with the catalyst **A** in the presence of a catalytic amount of Ti(O*i*-Pr)$_4$[8a] under highly diluted conditions (0.1 mM in CH_2Cl_2) gave rise to the desired *Z*-isomer **35** in 72% yield along with the corresponding dimer (11%). When the reaction was performed under more than 1.0 mM concentration of **4**, almost the same amount of the dimer as that of the desired product **35** was produced (20−30% yield). The RCM reaction proceeded with exclusive (*Z*)-selectivity and the (*E*)-isomer of **35** could not be detected under any reaction conditions. Finally, the total synthesis of halicholactone **1** was completed by methanolysis of two acetyl groups (61%). The obtained product **1** was identical (^{1}H NMR, ^{13}C NMR, IR, mass, and $[\alpha]_D$) in all respects to the reported data of the natural halicholactone **1**.[1]

Conclusion

In conclusion, we have achieved the asymmetric total synthesis of halicholactone **1** from the chiral (diene)Fe(CO)$_3$ complex **10**. The Lewis acid-mediated regio- and stereoselective nucleophilic substitution of the ester Fe(CO)$_3$ complex (**16a** → **7**) is the keystone of the strategy for the stereospecific construction of the bis-allylic triol derivative. The salient features of the synthesis are the use of the modified Simmons−Smith reaction for the regio- and stereoselective cyclopropanation (**21** → **5**) as well as the ring-closing metathesis for the formation of a nine-membered lactone (**4** → **35**). The highly stereoselective strategy described herein may be relevant to the synthesis of other oxylipins possessing six- to eight-membered saturated and unsaturated lactone fragments.

Experimental Section

(2*S*,5*R*,6*R*,2*E*,4*E*)-Tricarbonyliron[(η^4-2−5)-6-*tert*-butyldimethylsilyloxyundeca-2,4-dienal] (11). To a stirred solution of **10**[9] (1.36 g, 4.22 mmol) in pyridine (15 mL) was added TBSOTf (2.7 mL, 11.8 mmol) at 0 °C under a nitrogen atmosphere. After 1.5 h, brine was added to the reaction mixture, and the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo, and pyridine was removed azeotropically with toluene. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 6/1) to gave **11** (1.83 g, 100%) as a yellow oil: R_f 0.55 (hexane/AcOEt = 4:1); $[\alpha]^{28}_D$ +120.6 (c = 1.11, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.09 (s, 3H), 0.10 (s, 3H), 0.89 (s, 12H), 1.25−1.34 (m, 6H), 1.36 (dd, 1H, J = 3.7, 7.9 Hz), 1.55−1.67 (m, 3H), 3.53 (m, 1H), 5.40 (dd, 1H, J = 4.9, 8.5 Hz), 5.79 (dd, 1H, J = 4.9, 7.9 Hz), 9.32 (d, 1H, J = 3.7 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ −4.2, −3.8, 14.0, 18.1, 22.6, 24.3, 25.8 (3C), 31.6, 39.2, 55.1, 68.8, 74.3, 81.9, 87.5, 195.9, 208.5; IR (KBr) 2958, 2858, 2060, 1984, 1686 cm^{-1}; MS (EI) *m*/*z* (%) 408 (M^+-CO, 0.2), 352 (M^+ − 3CO, 52), 75 (100). Anal. Calcd for $C_{20}H_{32}FeO_5Si$: C, 55.04; H, 7.39. Found: C, 55.08; H, 7.32.

(4*S*,7*R*,8*R*,2*E*,4*E*,6*E*)-Tricarbonyliron[ethyl (η^4-4−7)-8-*tert*-butyldimethylsilyloxytrideca-2,4,6-trienoate] (12). To a stirred suspension of NaH (washed with hexane, 148 mg, 6.17 mmol) and dry THF (5.5 mL) was added diethoxyphosphonoethyl acetate (1.2 mL, 6.17 mmol) at 0 °C under a

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nitrogen atmosphere. After 10 min, **11** (2.06 g, 4.72 mmol) in dry THF (10 mL) was added to the reaction mixture, and the resulting mixture was stirred for 20 min at 0 °C under a nitrogen atmosphere. The reaction mixture was quenched with ice−water and extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 40/1) to give **12** (2.38 g, 99%) as a yellow oil: R_f 0.48 (hexane/AcOEt = 10/1); $[\alpha]^{28}_D$ +164.6 (c = 1.01, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.08 (s, 3H), 0.10 (s, 3H), 0.89 (s, 12H), 1.28 (t, 3H, J = 7.3 Hz), 1.32−1.54 (m, 7H), 1.60 (m, 2H), 1.75 (m, 1H), 3.44 (m, 1H), 4.17 (q, 2H, J = 7.3 Hz), 5.22 (dd, 1H, J = 4.9, 8.5 Hz), 5.38 (dd, 1H, J = 4.9, 7.3 Hz), 5.89 (d, 1H, J = 15.3 Hz), 6.80 (dd, 1H, J = 10.4, 15.3 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ −4.2, −3.7, 14.0, 14.2, 18.1, 22.6, 24.5, 25.9 (3C), 31.7, 39.2, 56.9, 60.3, 67.3, 74.7, 83.7, 85.1, 119.1, 148.2, 166.5, 210.4; IR (KBr) 2931, 2050, 1986, 1974, 1711, 1630 cm^{-1}; MS (EI) m/z (%) 422 (M^+ − 2CO, 67), 290 (100). Anal. Calcd for $C_{24}H_{38}FeO_6Si$: C, 56.91; H, 7.56. Found: C, 57.11; H, 7.44.

(4*S*,7*R*,8*R*,2*E*,4*E*,6*E*)-Tricarbonyliron[(η⁴-4−7)-8-*tert*-butyldimethylsilyloxytrideca-2,4,6-trienol] (13). To a stirred solution of **12** (2.38 g, 4.70 mmol) in dry CH_2Cl_2 (50 mL) was added DIBAL-H (0.95 M in toluene, 15 mL, 15.3 mmol) at −78 °C under a nitrogen atmosphere. After 15 min, a saturated potassium sodium tartrate solution (18 mL) was added to the reaction mixture at −78 °C, and the resulting mixture was stirred at room temperature. The mixture was extracted with AcOEt, and the extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 5/1) to give **13** (2.12 g, 97%) as a yellow oil: R_f 0.20 (hexane/AcOEt = 5/1); $[\alpha]^{23}_D$ +4.8 (c = 0.96, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.08 (s, 3H), 0.10 (s, 3H), 0.88 (s, 12H), 1.26−1.40 (m, 7H), 1.41−1.50 (m, 3H), 1.88 (t, 1H, J = 9.2 Hz), 3.41 (ddd, 1H, J = 4.9, 5.5, 8.5 Hz), 4.08 (m, 2H), 5.14 (dd, 1H, J = 4.9, 8.5 Hz), 5.19 (dd, 1H, J = 4.9, 7.9 Hz), 5.68 (dd, 1H, J = 10.4, 15.3 Hz), 5.86 (dt, 1H, J = 15.3, 5.5 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ −4.2, −3.7, 14.0, 18.1, 22.6, 24.6, 25.9 (3C), 31.7, 39.3, 61.0, 63.3, 66.3, 75.0, 82.3, 83.5, 130.2, 132.8, 211.6; IR (KBr) 3437, 2044, 1979, 1616 cm^{-1}; MS (EI) m/z (%) 409 (M^+ + 1 − 2CO, 0.5), 381 (M^+ + 1 − 3CO, 1.2), 324 (1.3), 75 (100). Anal. Calcd for $C_{22}H_{36}FeO_5Si$: C, 56.89; H, 7.81. Found: C, 56.80; H, 7.74.

(2*R*,3*S*,4*S*,7*R*,8*R*,4*E*,6*E*)-Tricarbonyliron[(η⁴-4−7)-8-*tert*-butyldimethylsilyloxytrideca-4,6-dienyl-1,2,3-triol] (8). To a stirred solution of **13** (2.12 g, 4.56 mmol) in pyridine (23 mL) was added OsO_4 (1.19 g, 4.68 mmol) in pyridine (4.0 mL) at −20 °C under an argon atmosphere. After 25 min, a saturated $NaHSO_3$ solution (45 mL) was added to the reaction mixture and the resulting mixture was stirred for 12 h at room temperature. The mixture was filtered through a pad of Celite, and the residue was washed thoroughly with AcOEt (200 mL). After the combined filtrates were concentrated to half volume, it was poured into a saturated ammonium chloride, and the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo, and pyridine was removed azeotropically with toluene. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 2/3) to give the triol **8** (2.13 g, 94%) as a yellow oil: R_f 0.23 (hexane/AcOEt = 1/1); $[\alpha]^{30}_D$ +20.4 (c = 1.28, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.07 (s, 3H), 0.10 (s, 3H), 0.88 (s, 12H), 1.26−1.42 (m, 8H), 1.55−1.59 (m, 2H), 2.01 (br s, 1H), 2.49 (br s, 1H), 2.57 (br s, 1H), 3.43 (m, 1H), 3.53 (m, 1H), 3.70 (m, 1H), 3.78 (m, 2H), 5.21(dd, 1H, J = 4.9, 8.5 Hz), 5.33 (dd, 1H, J = 4.9, 7.9 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ −4.2, −3.7, 14.0, 18.1, 22.6, 24.8, 25.9 (3C), 31.7, 39.2, 61.4, 65.2, 67.2, 74.1, 74.7, 74.8, 83.2, 84.7, 211.4; IR (KBr) 3363, 2046, 1977, 1969 cm^{-1}; MS (EI) m/z (%) 499 (M^+ + 1, 0.07), 443 (M^+ + 1 − 2CO, 0.2), 415 (M^+ + 1 − 3CO, 0.5), 75 (100). Anal. Calcd for $C_{22}H_{38}FeO_7Si$: C, 53.01; H, 7.68. Found: C, 53.11; H, 7.57.

(2*R*,3*S*,4*S*,7*R*,8*R*,4*E*,6*E*)-Tricarbonyliron[(η⁴-4−7)-8-*tert*-butyldimethylsilyloxy-2,3-dihydroxytrideca-4,6-dienyl] 2,2-Dimethylpropanoate (14a). To a stirred solution of **8** (1.14 g, 2.68 mmol) in a mixture of pyridine (2.7 mL) and dry CH_2Cl_2 (2.7 mL) was added pivaloyl chloride (PivCl) (0.33 mL, 2.68 mmol) at 0 °C under a nitrogen atmosphere over a period of 30 min. The reaction mixture was stirred for 1 h at 0 °C and at room temperature for 4 h. After brine was added to the reaction mixture, and the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 5/1) to give **14a** (1.35 g, 97%) as a yellow oil: R_f 0.46 (hexane/AcOEt = 2/1); $[\alpha]^{30}_D$ +28.7 (c = 0.87, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.07 (s, 3H), 0.09 (s, 3H), 0.85−0.90 (m, 3H), 0.87 (s, 9H), 1.20 (s, 9H), 1.20−1.46 (m, 8H), 1.57 (ddd, 2H, J = 2.4, 7.3, 14.6 Hz), 2.46 (br s, 1H), 2.51 (br s, 1H), 3.40−3.45 (m, 2H), 3.81 (br s, 1H), 4.14 (dd, 1H, J = 6.1, 11.6 Hz), 4.19 (dd, 1H, J = 6.1, 11.6 Hz), 5.19 (dd, 1H, J = 4.9, 8.5 Hz), 5.34 (dd, 1H, J = 4.9, 8.5 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ −4.2, −3.7, 14.0, 18.1, 22.6, 24.4, 25.8 (3C), 27.8 (3C), 31.6, 38.8, 39.2, 60.8, 65.3, 67.2, 72.8 (2C), 74.7, 84.3, 84.6, 179.3, 210.0; IR (KBr) 3454, 2046, 1979, 1716 cm^{-1}; MS (FAB) m/z 605 ($M + Na$)$^+$. Anal. Calcd for $C_{27}H_{46}FeO_8Si$: C, 55.66; H, 7.95. Found: C, 55.72; H, 7.83.

(2*R*,3*S*,4*S*,7*R*,8*R*,4*E*,6*E*)-Tricarbonyliron[(η⁴-4−7)-8-*tert*-butyldimethylsilyloxy-2,3-bis(chloroacetoxy)trideca-4,6-dienyl] 2,2-Dimethylpropanoate (16a). To a stirred solution of **14a** (1.35 g, 2.32 mmol) in dry CH_2Cl_2 (20 mL) were added 4-(dimethylamino)pyridine (DMAP) (1.42 g, 11.6 mmol) and chloracetic anhydride (1.79 g, 10.4 mmol) at 0 °C under a nitrogen atmosphere. The reaction mixture was stirred for 1 h at 0 °C and at room temperature for 2 h. After brine was added to the reaction mixture, and the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 15/1) to give **16a** (1.52 g, 89%) as a yellow oil: R_f 0.54 (CH_2Cl_2/hexane = 2/1); $[\alpha]^{28}_D$ +12.1 (c = 0.75, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.04 (s, 3H), 0.09 (s, 3H), 0.88 (s, 9H), 0.88−0.90 (m, 3H), 0.98 (t, 1H, J = 8.5 Hz), 1.16 (s, 9H), 1.18−1.42 (m, 7H), 1.54−1.58 (m, 2H), 3.45 (ddd, 1H, J = 4.5, 4.9, 7.9 Hz), 4.07−4.15 (m, 1H), 4.11 (s, 4H), 4.20 (dd, 1H, J = 7.9, 10.9 Hz), 4.95 (dd, 1H, J = 2.4, 9.1 Hz), 5.17−5.22 (m, 2H), 5.48 (dd, 1H, J = 4.8, 8.5 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ −4.2, −3.7, 13.9, 18.1, 22.6, 24.1, 25.8 (3C), 27.1 (3C), 31.7, 38.7, 39.0, 40.5, 40.8, 52.8, 60.0, 68.1, 74.3 (2C), 74.9, 83.6, 85.8, 166.3, 166.8, 179.3, 210.0; IR (KBr) 2051, 1984, 1737 cm^{-1}; MS (FAB) m/z 757 ($M + Na$)$^+$. Anal. Calcd for $C_{31}H_{48}Cl_2FeO_{10}Si$: C, 50.59; H, 6.57. Found: C, 50.54; H, 6.38.

(2*R*,3*S*,4*S*,7*R*,8*R*,4*E*,6*E*)-Tricarbonyliron[(η⁴-4−7)-8-*tert*-butyldimethylsilyloxy-2-chloroacetoxy-3-phenylthiotrideca-4,6-dienyl] 2,2-Dimethylpropanoate (7). To a stirred solution of **16a** (242 mg, 0.330 mmol) in dry CH_2Cl_2 (3.3 mL) was added Me_2AlSPh (0.58 M in CH_2Cl_2−hexane, 2.9 mL, 1.65 mmol) at −78 °C under a nitrogen atmosphere. After 3 h, a saturated $NaHCO_3$ solution was added to the reaction mixture, and the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 30/1) to give **7** (171 mg, 69%) as a yellow oil: R_f 0.51 (hexane/AcOEt = 15/1 × 2); $[\alpha]^{28}_D$ +2.9 (c = 1.06, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.07 (s, 3H), 0.10 (s, 3H), 0.87−0.90 (m, 3H), 0.90 (s, 9H), 1.08 (t, 1H, J = 9.1 Hz), 1.17 (s, 9H), 1.21−1.43 (m, 7H), 1.54 (s br, 2H), 3.08 (dd, 1H, J = 2.4, 10.4 Hz), 3.38−3.42 (m, 1H), 4.08 (s, 2H), 4.37 (dd, 1H, J = 6.7, 11.5 Hz), 4.52 (dd, 1H, J = 5.5, 11.6 Hz), 4.69 (dd, 1H, J = 4.9, 8.5 Hz), 5.05 (dd, 1H, J = 4.9, 8.6 Hz), 5.29 (ddd, 1H, J = 2.4, 7.3, 9.8 Hz), 7.34−7.40 (m, 3H), 7.48−7.50 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.2, −3.6, 14.0, 18.2, 22.6, 24.6, 25.9 (3C), 27.0 (3C), 31.5, 38.7, 39.1, 40.6, 55.1, 59.1, 62.4, 67.6, 74.7, 75.9, 83.0, 84.3, 128.8, 129.3 (2C), 132.7, 134.8 (2C), 166.4, 177.8, 210.3; IR (KBr) 2046, 1980, 1735 cm^{-1}; MS (FAB) m/z 773 ($M + Na$)$^+$. Anal. Calcd for $C_{35}H_{51}ClFeO_8SSi$: C, 55.95; H, 6.84. Found: C, 56.02; H, 6.85.

(2*R*,3*R*,8*R*,4*E*,6*E*)-8-*tert*-Butyldimethylsilyloxy-2-chloroacetoxy-3-phenylthiotrideca-4,6-dienyl 2,2-Dimethylpropanoate (17). To a vigorous stirred suspension of **7** (159 mg, 0.212 mmol), potassium carbonate (146 mg, 1.05 mmol),

and CH_3CN (2.5 mL) was added a solution of ceric(IV) ammonium nitrate (CAN) (285 mg, 0.520 mmol) in dry CH_3CN (4.5 mL) at −30 °C under a nitrogen atmosphere. After 30 mim, a saturated $NaHCO_3$ solution was added to the reaction mixture, and the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 5/1) to give **17** (125 mg, 97%) as a colorless oil: R_f 0.40 (hexane/AcOEt = 20/1 × 2); $[\alpha]^{28}_D$ +18.2 (c = 1.06, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 3H), 0.03 (s, 3H), 0.86−0.92 (m, 3H), 0.88 (s, 9H), 1.14−1.56 (m, 8H), 1.17 (s, 9H), 3.86 (t, 1H, J = 8.8 Hz), 4.01 (d, 2H, J = 2.4 Hz), 4.08 (dt, 1H, J = 6.1, 12.2 Hz), 4.13 (dd, 1H, J = 7.3, 12.2 Hz), 4.44 (dd, 1H, J = 3.0, 12.2 Hz), 5.32 (ddd, 1H, J = 3.0, 7.3, 10.0 Hz), 5.43 (dd, 1H, J = 6.1, 14.6 Hz), 5.58 (dd, 1H, J = 6.1, 14.6 Hz), 5.94 (dd, 1H, J = 10.9, 15.2 Hz), 6.04 (dd, 1H, J = 10.9, 15.2 Hz), 7.27−7.31 (m, 3H), 7.39−7.41 (m, 2H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ −4.8, −3.4, 14.0, 18.2, 22.5, 24.8, 25.8 (3C), 27.1 (3C), 31.7, 38.1, 38.7, 40.6, 52.8, 63.3, 72.7, 74.4, 126.2, 127.4, 128.0, 128.9, 132.6 (2C), 133.8, 133.9 (2C), 138.9, 166.6, 177.9. IR (KBr) 1766 cm^{-1}; MS (FAB)-m/z 633 $(M + Na)^+$. Anal. Calcd for $C_{32}H_{51}ClFeO_5SSi$: C, 62.86; H, 8.40. Found: C, 62.73; H, 8.15.

(2*R*,5*S*,8*R*,3*E*,6*E*)-8-*tert*-Butyldimethylsilyloxy-2-chloroacetoxy-5-hydroxytrideca-3,6-dienyl 2,2-Dimethylpropanoate (6). To a stirred solution of **17** (165 mg, 0.270 mmol) in dry CH_2Cl_2 (2.2 mL) was added m-CPBA (90%, 517 mg, 0.270 mmol) at −78 °C. After 30 mim, a saturated $NaHCO_3$ solution was added to the reaction mixture, and the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 5/1) to give sulfoxide **18** (161 mg, 95%) as a colorless oil. To a stirred solution of **18** (161 mg, 0.257 mmol) in MeOH (2.5 mL) was added trimethyl phosphite (75.7 μL, 0.642 mmol) under a nitrogen atmosphere, and the reaction mixture was stirred at 65 °C for 1.5 h. The reaction mixture was concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 8/1) to give **6** (133 mg, 88%) as a colorless oil: R_f 0.46 (hexane/AcOEt = 2/1); $[\alpha]^{26}_D$ +16.7 (c = 0.92, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.003 (s, 3H), 0.031 (s, 3H), 0.85−0.90 (m, 3H), 0.88 (s, 9H), 1.18 (s, 9H), 1.20−1.47 (m, 8H), 1.66−1.70 (m, 1H), 4.05 (s, 2H), 4.06−4.11 (m, 2H), 4.27 (dd, 1H, J = 3.0, 11.6 Hz), 4.65 (t, 1H, J = 4.8 Hz), 5.57 (dd, 1H, J = 6.7, 15.2 Hz), 5.62 (ddd, 1H, J = 3.0, 7.3, 9.3 Hz), 5.67 (dd, 1H, J = 1.2, 7.9 Hz), 5.70 (dt, 1H, J = 1.2, 7.9 Hz), 5.90 (dd, 1H, J = 5.5, 15.2 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ −4.8, −4.3, 14.0, 18.2, 22.6, 24.8, 25.8 (3C), 27.1 (3C), 31.7, 38.0, 38.8, 40.7, 63.4, 71.9, 72.5, 73.2, 123.5, 129.4, 135.9, 137.0, 166.3, 177.9; IR (KBr) 3523, 1736 cm^{-1}; MS (FAB) m/z 541 $(M + Na)^+$; HRMS (FAB) Calcd for $C_{26}H_{47}ClNaO_6Si$ $(M + Na)^+$: 541.2728. Found: 541.2723.

(2*R*,5*S*,8*R*,3*E*,6*E*)-8-*tert*-Butyldimethylsilyloxy-2-chloroacetoxy-5-(2-trimethylsilyl)ethoxymethoxytrideca-3,6-dienyl 2,2-Dimethylpropanoate (19). To a stirred solution of **6** (809 mg, 1.56 mmol) in dry CH_2Cl_2 (10 mL) were added tetrabutylammonium iodide (28.8 mg, 0.078 mmol), diisopropylethylamine (1.1 mL, 6.24 mmol), and 2-(trimethylsilyl)-ethoxymethyl chloride (0.83 mL, 4.67 mmol) at 0 °C under a nitrogen atmosphere. The reaction mixture was stirred at 0 °C for 1 h and at room temperature for 10 h. After brine was added to the reaction mixture, and the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 20/1) to give **19** (1.01 g, 100%) as a colorless oil: R_f 0.60 (hexane/AcOEt = 2/1); $[\alpha]^{24}_D$ +8.7 (c = 1.14, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.001 (s, 3H), 0.016 (s, 9H), 0.032 (s, 3H), 0.86−0.88 (m, 3H), 0.88 (s, 9H), 0.92 (t, 2H, J = 8.5 Hz), 1.15−1.58 (m, 8H), 1.18 (s, 9H), 3.57−3.66 (m, 2H), 4.04 (s, 2H), 4.04−4.12 (m, 2H), 4.28 (dd, 1H, J = 3.6, 12.2 Hz), 4.58 (t, 1H, J = 6.7 Hz), 4.62 (d, 1H, J = 7.3 Hz), 4.64 (d, 1H, J = 6.7 Hz), 5.44 (dd, 1H, J = 7.3, 15.2 Hz), 5.62 (ddd, 1H, J = 3.6, 7.3, 9.1 Hz), 5.64−5.69 (m, 2H), 5.83 (dd, 1H, J = 6.1, 15.2 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.8, −4.3, −1.4 (3C), 14.0, 18.0, 18.2, 22.6, 24.7, 25.9 (3C), 27.1 (3C), 31.7, 38.1, 38.8, 40.7, 64.4, 65.2, 72.3, 73.2, 74.5, 91.4, 124.6, 127.1, 135.3, 137.6, 166.2, 177.9; IR (KBr) 1737 cm^{-1}; MS (FAB) m/z 671 $(M + Na)^+$. Anal. Calcd for $C_{32}H_{61}ClO_7Si_2$: C, 59.18; H, 9.46. Found: C, 59.07; H, 9.36.

(2*R*,5*R*,8*R*,3*E*,6*E*)-8-*tert*-Butyldimethylsilyloxy-2-hydroxy-5-(2-trimethylsilyl)ethoxymethoxytrideca-3,6-dienyl 2,2-Dimethylpropanoate (21). To a stirred solution of **19** (1.00 g, 1.50 mmol) in dry CH_2Cl_2 (13 mL) was added DIBAL-H (1.0 M in toluene, 9.2 mL, 9.24 mmol) at −78 °C under a nitrogen atmosphere. After 15 min, a saturated potassium sodium tartrate solution (9.5 mL) was added to the reaction mixture at −78 °C, and the resulting mixture was stirred at room temperature. The mixture was extracted with AcOEt, and the extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 2/1) to give diol **20** (684 mg, 84%) as a colorless oil. To a stirred solution of **20** (684 mg, 1.40 mmol) in a mixture of pyridine (1.4 mL) and dry CH_2Cl_2 (1.4 mL) was added PivCl (0.18 mL, 1.47 mmol) at 0 °C. The reaction mixture was stirred for 30 min at 0 °C and at room temperature for 12 h. After brine was added to the reaction mixture, the resulting mixture was extracted with AcOEt. The extracts were washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 5/1 to 4/1 to 1/1) to give **21** (517 mg, 64%) and **20** (138 mg, 20%). **21**: a colorless oil; R_f 0.48 (hexane/AcOEt = 2/1); $[\alpha]^{25}_D$ −11.1 (c = 1.45, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.003 (s, 3H), 0.015 (s, 9H), 0.03 (s, 3H), 0.85−0.90 (m, 3H), 0.87 (s, 9H), 0.92 (t, 2H, J = 8.5 Hz), 1.18−1.50 (m, 8H), 1.21 (s, 9H), 2.12 (d, 1H, J = 4.2 Hz), 3.56−3.67 (m, 2H), 4.01 (dd, 1H, J = 6.7, 11.6 Hz), 4.09 (dt, 1H, J = 14.6, 6.1 Hz), 4.15 (dd, 1H, J = 3.6, 11.6 Hz), 4.37−4.41 (m, 1H), 4.57 (t, 1H, J = 6.1 Hz), 4.64 (d, 1H, J = 6.7 Hz), 4.67 (d, 1H, J = 6.7 Hz), 5.46 (dd, 1H, J = 7.3, 15.2 Hz), 5.66 (dd, 1H, J = 6.1, 15.2 Hz), 5.70 (dd, 1H, J = 5.5, 15.8 Hz), 5.79 (dd, 1H, J = 5.5, 15.2 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.8, −4.2, −1.4 (3C), 14.0, 18.0, 18.2, 22.6, 24.9, 25.9 (3C), 27.2 (3C), 31.7, 38.2, 38.8, 65.1, 67.8, 70.4, 72.8, 75.2, 91.4, 127.6, 130.0, 132.3, 137.2, 178.6; IR (KBr) 3467, 1733 cm^{-1}; MS (FAB) m/z 595 $(M + Na)^+$. Anal. Calcd for $C_{30}H_{60}O_6Si_2$: C, 62.88; H, 10.55. Found: C, 62.57; H, 10.36.

(2*R*)-2-Hydroxy-2-{(1*R*,2*R*)-2-[(1*R*,4*R*,2*E*)-4-*tert*-butyldimethylsilyloxy-1-(2-trimethylsilyl)ethoxymethoxynon-2-enyl]cyclopropyl}ethyl 2,2-Dimethylpropanoate (5). To a stirred solution of **21** (186 mg, 0.324 mmol) in dry CH_2Cl_2 (3.5 mL) was added diethyl zinc (1.0 M in hexane, 0.81 mL, 0.812 mmol) at −20 °C under an argon atmosphere. After 10 min, diiodomethane (78.2 μL, 0.972 mmol) was added dropwise to the mixture. After 10 min, the solution turned to cloudy and stirring was continued for 8 h. After a saturated NH_4Cl solution was added to the mixture, and the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 10/1) to give **21** (21 mg, 11%) and **5** (131 mg, 69%). **5**: a colorless oil; R_f 0.62 (hexane/AcOEt = 4/1× 3); $[\alpha]^{26}_D$ −44.4 (c = 1.11, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.017 (s, 9H), 0.04 (s, 6H), 0.63−0.66 (m, 1H), 0.68−0.76 (m, 1H), 0.85−0.94 (m, 6H), 0.88 (s, 9H), 0.99−1.03 (m, 1H), 1.19−1.34 (m, 6H), 1.21 (s, 9H), 1.40−1.46 (m, 2H), 2.04−2.05 (m, 1H), 3.38 (s br, 1H), 3.49 (ddd, 1H, J = 6.1, 10.4, 14.0 Hz), 3.63 (t, 1H, J = 7.3 Hz), 3.72 (ddd, 1H, J = 6.1, 10.4, 14.0 Hz), 4.05 (dd, 1H, J = 7.3, 11.6 Hz), 4.10 (ddd, 1H, J = 5.6, 6.1, 11.6 Hz), 4.22 (dd, 1H, J = 3.0, 11.6 Hz), 4.63 (s, 2H), 5.44 (dd, 1H, J = 7.3, 15.2 Hz), 5.63 (dd, 1H, J = 6.1, 15.2 Hz);^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.8, −4.3, −1.4 (3C), 7.8, 14.0, 18.1, 18.21, 18.27, 20.2, 22.6, 24.9, 25.9 (3C), 27.2 (3C), 31.7, 38.3, 38.8, 65.0, 68.5, 72.5, 72.6, 77.6, 91.5, 127.5, 137.4, 178.8; IR (KBr) 3491, 1732 cm^{-1}; MS (EI) m/z (%) 529 (M^+ − t-Bu, 23), 439 (M^+ − OSEM, 41), 73 (100); HRMS (EI) Calcd for $C_{27}H_{53}O_6Si_2$ (M^+ − t-Bu): 529.3380. Found: 529.3376.

(2*R*)-2-{(1*R*,2*R*)-2-[(1*R*,4*R*,2*E*)-4-*tert*-Butyldimethylsilyloxy-1-(2-trimethylsilyl)ethoxymethoxynon-2-enyl]cyclopropyl}ethane-1,2-diol (27). To a stirred solution of **5** (107

mg, 0.183 mmol) in dry Et_2O (1.5 mL) was added MeLi (1.0 M in Et_2O, 0.92 mL, 0.915 mmol) at 0 °C under a nitrogen atmosphere. After 1 h, water was added to the reaction mixture, and the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 3/1) to give **27** (83.0 mg, 90%) as a colorless oil: R_f 0.31 (hexane/AcOEt = 2/1); $[\alpha]^{26}_D$ −58.2 (c = 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ −0.005 (s, 3H), 0.016 (s, 9H), 0.04 (s, 3H), 0.61−0.68 (m, 2H), 0.86−0.96 (m, 6H), 0.89 (s, 9H), 0.97−1.03 (m, 1H), 1.26−1.53 (m, 8H), 2.04 (m, 1H), 2.26 (m, 1H), 3.12 (s br, 1H), 3.46−3.51 (m, 1H), 3.53−3.60 (m, 1H), 3.62−3.68 (m, 1H), 3.70−3.75 (m, 2H), 4.10 (dt, 1H, J = 5.4, 5.4 Hz), 4.62 (s, 2H), 5.39 (dd, 1H, J = 7.9, 15.8 Hz), 5.63 (dd, 1H, J = 5.5, 15.2 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.8, −4.4, −1.5 (3C), 8.1, 14.0, 18.08, 18.14, 18.2, 20.6, 22.6, 24.8, 25.8 (3C), 31.7, 38.3, 65.0, 66.6, 72.4, 75.5, 77.5, 91.4, 126.7, 137.9; IR (KBr) 3367 cm^{-1}; MS (FAB) m/z 525 (M + Na)$^+$; HRMS (FAB) Calcd for $C_{26}H_{54}NaO_5Si_2$ (M + Na)$^+$: 525.3408. Found: 525.3398.

(1*R*)-1-{(1*R*,2*R*)-2-[(1*R*,4*R*,2*E*)-4-*tert*-Butyldimethylsilyloxy-1-(2-trimethylsilyl)ethoxymethoxynon-2-enyl]cyclopropyl}but-3-en-1-ol (28a) and (1*S*)-1-{(1*R*,2*R*)-2-[(1*R*,4*R*,2*E*)-4-*tert*-Butyldimethylsilyloxy-1-(2-trimethylsilyl)ethoxymethoxynon-2-enyl]cyclopropyl}but-3-en-1-ol (28b). To a stirred suspension of **27** (377 mg, 0.750 mmol), Na_2CO_3 (95.4 mg, 0.900 mmol), and dry CH_2Cl_2 (5.0 mL) was added lead acetate (90%, 406 mg, 0.825 mmol) at −40 °C. The reaction mixture was stirred from −40 °C to 0 °C for 1.5 h and at room temperature for 30 min and then filtered through a pad of SiO_2. The filtrate was concentrated in vacuo to give aldehyde (288 mg). The crude aldehyde was diluted with dry CH_3CN (5.0 mL), and tetraallyltin (44.2 μL, 0.184 mmol) and $Sc(OTf)_3$ (4.5 mg, 9.20 μmol) were added to the mixture. The resulting mixture was stirred for 1 h at room temperature. After brine was added to the reaction mixture, the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 10/1) to give **28b** (107 mg, 34%) and **28a** (106 mg, 34%). **28b**: a colorless oil; R_f 0.40 (hexane/AcOEt = 5/1); $[\alpha]^{26}_D$ −52.3 (c = 1.08, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.019 (s, 9H), 0.02 (s, 3H), 0.04 (s, 3H), 0.54 (ddd, 1H, J = 4.3, 4.9, 8.5 Hz), 0.60 (ddd, 1H, J = 4.9, 4.9, 8.5 Hz), 0.76−0.90 (m, 5H, C16−H), 0.89 (s, 9H), 0.92−0.97 (m, 1H), 1.02 (m, 1H), 1.26 (m, 6H), 1.42−1.46 (m, 2H), 1.70 (s, 1H), 2.28 (ddd, 1H, J = 6.7, 7.9, 13.4 Hz), 2.37 (m, 1H), 3.07 (dt, 1H, J = 7.9, 12.8 Hz), 3.52 (ddd, 1H, J = 6.7, 10.4, 14.0 Hz), 3.67−3.75 (m, 2H), 4.10 (q, 1H, J = 6.1 Hz), 4.64 (d, 1H, J = 6.7 Hz), 4.67 (d, 1H, J = 7.3 Hz), 5.09−5.14 (m, 2H), 5.47 (dd, 1H, J = 7.3, 15.3 Hz), 5.65 (dd, 1H, J = 5.5, 15.3 Hz), 5.87 (m, 1H);^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.8, −4.3, −1.5 (3C), 8.2, 14.0, 18.1, 18.2, 21.3, 21.8, 22.6, 24.9, 25.9 (3C), 31.7, 38.3, 41.4, 65.0, 72.6, 74.1, 77.9, 91.4, 117.5, 127.2, 134.7, 137.4; IR (KBr) 3439, 1641 cm^{-1}; MS (FAB) m/z 519 (M + Li)$^+$; HRMS (FAB) Calcd for $C_{28}H_{56}LiO_4Si_2$ (M + Li)$^+$: 519.3877. Found: 519.3863; **28a**: a colorless oil; R_f 0.30 (hexane/AcOEt = 5/1); $[\alpha]^{26}_D$ −63.1 (c = 0.67, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 0.019 (s, 9H), 0.02 (s, 3H), 0.04 (s, 3H), 0.61−0.68 (m, 2H), 0.86−0.91 (m, 6H), 0.89 (s, 9H), 0.92 (m, 1H), 1.26 (m, 6H), 1.43 (m, 2H), 1.60 (s, 1H), 2.26 (ddd, 1H, J = 6.7, 7.9, 13.4 Hz), 2.39 (m, 1H), 3.08 (m, 1H), 3.46−3.57 (m, 2H), 3.73 (m, 1H), 4.12 (m, 1H), 4.63 (s, 2H), 5.11−5.15 (m, 2H), 5.48 (dd, 1H, J = 7.9, 15.9 Hz), 5.63 (dd, 1H, J = 5.5, 15.9 Hz), 5.85 (m, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.8, −4.3, −1.4 (3C), 8.7, 14.0, 18.1, 18.2, 21.1, 22.1, 22.6, 24.9, 25.9 (3C), 31.8, 38.4, 41.8, 64.9, 72.5, 74.0, 78.1, 91.3, 118.0, 127.6, 134.7, 137.2; IR (KBr) 3439, 1641 cm^{-1}; MS (FAB) m/z 519 (M + Li)$^+$; HRMS (FAB) Calcd for $C_{28}H_{56}LiO_4Si_2$ (M + Li)$^+$: 519.3877. Found: 519.3892.

Conversion of 28a into 28b by Mitsunobu Protocol. To a solution of **28a** (50.6 mg, 0.0987 mmol) in dry THF (1.0 mL) were added PPh_3 (70.0 mg, 0.266 mmol) and AcOH (15.2 μL, 0.266 mmol) at room temperature. The mixture was cooled to 0 °C, and DIAD (62.2 μL, 0.316 mmol) was added to the reaction mixture. After 10 min, the resulting mixture was warmed to room temperature and then stirred for at room temperature for 16 h. Solvent was removed in vacuo, the residue was diluted with AcOEt, washed with a saturated $NaHCO_3$ solution and brine, dried over $MgSO_4$, and then concentrated in vacuo. After the residue was diluted with MeOH, NaH (60% in oil, 97.5 mg, 2.43 mmol) was added to the mixture. The resulting mixture was stirred for 30 min at room temperature. After water was added to the reaction mixture, MeOH was removed in vacuo, and the residue was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 10/1 to 5/1) to give **28b** (30.2 mg, 60%) and **28a** (7.7 mg, 15%).

(1*S*)-1-{(1*R*,2*R*)-2-[(1*R*,4*R*,2*E*)-4-*tert*-Butyldimethylsilyloxy-1-(2-trimethylsilyl)ethoxymethoxynon-2-enyl]cyclopropyl}but-3-enyl Ethoxyethyl Ether (31). To a stirred solution of **28b** (84.3 mg, 0.164 mmol) in dry CH_2Cl_2 (1.5 mL) were added ethyl vinyl ether (37.3 μL, 0.493 mmol) and PPTS (10.3 mg, 0.0410 mmol) at room temperature. After 15 h, a saturated $NaHCO_3$ solution was added to the reaction mixture, and the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 15/1) to give **31** (86.0 mg, 90%) as a colorless oil: R_f 0.88 (hexane/AcOEt = 7/1); $[\alpha]^{24}_D$ −54.4 (c = 0.92, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.02 (s, 9H), 0.038 (s, 3H), 0.041 (s, 3H), 0.39 (ddd, 1/2H, J = 4.9, 4.9, 8.5 Hz), 0.50−0.58 (m, 1+1/2H), 0.76−0.97 (m, 6H), 0.89 (s, 9H), 1.01−1.08 (m, 1H), 1.17 (q, 3H, J = 7.3 Hz), 1.12−1.31 (m, 6H), 1.25 (d, 3H, J = 5.5 Hz), 1.35−1.45 (m, 2H), 2.29−2.34 (m, 2H), 3.16 (m, 1H), 3.43−3.75 (m, 5H), 4.10 (m, 1H), 4.62−4.64 (m, 2H), 4.77 (q, 1/2H, J = 5.5 Hz), 4.79 (q, 1/2H, J = 5.5 Hz), 5.00−5.09 (m, 2H), 5.47 (dd, 1H, J = 7.3, 15.3 Hz), 5.65 (dd, 1H, J = 6.7, 15.3 Hz), 5.82−5.95 (m, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.8, −4.33, −4.28, −1.4 (3C), 6.6, 7.7, 14.0, 15.1, 18.1, 18.2, 19.3, 19.8, 20.2, 20.4, 21.3, 21.9, 22.6, 24.9, 25.0, 25.9, 31.8, 38.3, 39.4, 40.4, 59.0, 59.2, 64.9, 72.5, 72.7, 77.6, 77.8, 77.9, 91.4, 91.5, 97.8, 116.4, 116.8, 127.5, 127.8, 134.9, 135.4, 136.8, 137.4; IR (KBr) 2931, 1641, 1096, 1030 cm^{-1}; MS (FAB) m/z 607 (M + Na)$^+$; HRMS (FAB) Calcd for $C_{32}H_{64}NaO_5Si_2$ (M + Na)$^+$: 607.4190. Found: 607.4190.

(1*R*,4*R*,2*E*)-1-{(1*R*,2*R*)-2-[(1*S*)-1-Ethoxyethoxybut-3-enyl]cyclopropyl}non-2-ene-1,4-diol (32). To a solution of **31** (83.0 mg, 0.142 mmol) in THF was added TBAF (1.0 M in THF, 1.0 mL, 1.06 mmol), and THF was removed in vacuo. To the residue were added powdered molecular sieves 4A (100 mg) and DMPU (1.0 mL), and the resulting mixture was stirred for 18 h at 85 °C. The reaction mixture was directly purified by column chromatography (SiO_2, hexane/AcOEt = 1/1) to give **32** (30.8 mg, 64%) as a colorless oil: R_f 0.49 (hexane/AcOEt = 1/1); $[\alpha]^{24}_D$ −2.8 (c = 1.48, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.42 (ddd, 1/2H, J = 5.5, 5.5, 8.5 Hz), 0.49 (ddd, 1/2H, J = 4.9, 4.9, 8.5 Hz), 0.55−0.60 (m, 1H), 0.89 (t, 3H, J = 5.5 Hz), 0.94 (m, 1H), 1.07−1.13 (m, 1H), 1.17 (q, 3H, J = 7.3 Hz), 1.26−1.34 (m, 6H), 1.29 (d, 3H, J = 5.5 Hz), 1.34−1.53 (m, 2H), 1.71 (br s, 1H), 2.12 (br s, 1H), 2.32−2.38 (m, 2H), 3.05 (dt, 1/2H, J = 5.5, 13.4 Hz), 3.12 (dt, 1/2H, J = 6.4, 14.0 Hz), 3.46−3.61 (m, 2H), 3.70 (m, 1/2H), 3.84 (m, 1/2H), 4.10 (dt, 1H, J = 6.1, 6.1 Hz), 4.77 (q, 1/2H, J = 5.5 Hz), 4.90 (q, 1/2H, J = 5.5 Hz), 5.03−5.10 (m, 2H), 5.65−5.80 (m, 2H), 5.82−5.93 (m, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 7.0, 7.6, 14.0, 15.2, 15.4, 19.7, 19.8, 20.2, 22.5, 23.9, 24.0, 25.08, 25.13, 31.7, 37.1, 37.2, 39.6, 40.4, 58.9, 59.2, 72.1, 72.3, 73.7, 74.4, 77.9, 79.3, 97.7, 98.3, 116.6, 117.0, 131.4, 131.6, 134.0 134.1, 134.6, 135.1; IR (KBr) 3401, 2931, 1641, 1096, 1032 cm^{-1}; MS (FAB) m/z 363 (M + Na)$^+$; HRMS (FAB) Calcd for $C_{20}H_{36}NaO_4$ (M+Na)$^+$: 363.2511. Found: 363.2515.

(1*R*,4*R*,2*E*)-4-Acetoxy-1-{(1*R*,2*R*)-2-[(1*S*)-1-ethoxyethoxybut-3-enyl]cyclopropyl}non-2-enyl Acetate (33). To a stirred solution of **32** (30.0 mg, 0.0881 mmol) in dry CH_2Cl_2 (1.0 mL) were added Et_3N (49.1 μL, 0.352 mmol) and DMAP (0.5 mg, 4.41 μmol) at room temperature. After the addition of Ac_2O (25.1 μL, 0.264 mmol) to the mixture at 0 °C, the mixture was stirred for 20 min at 0 °C and at room temper-

ature for 2.5 h and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 4/1) to give **33** (31.4 mg, 84%) as a colorless oil: R_f 0.65 (hexane/AcOEt = 2/1); $[\alpha]^{24}_D$ +10.0 (c = 1.53, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.39 (ddd, 1/2H, J = 4.9, 4.9, 8.5 Hz), 0.52−0.62 (m, 1+1/2H), 0.88 (t, 3H, J = 6.7 Hz), 0.93 (m, 1H), 1.12 (m, 1H), 1.17 (q, 3H, J = 7.3 Hz), 1.26−1.30 (m, 9H), 1.52−1.63 (m, 2H), 2.04 (s, 3H), 2.06 (s, 3H), 2.30−2.38 (m, 2H), 3.15 (dt, 1/2H, J = 6.7, 14.0 Hz), 3.15 (dt, 1/2H, J = 6.7, 12.8 Hz), 3.44−3.61 (m, 2H), 4.75 (q, 1/2H, J = 5.5 Hz), 4.85−4.92 (m, 1+1/2H), 5.05 (m, 2H), 5.25 (m, 1H), 5.62−5.70 (m. 2H), 5.71−5.92 (m, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 6.9, 8.1, 13.9, 15.28, 15.33, 20.0, 20.1, 20.7, 21.2 (2C), 22.4, 24.7, 31.42, 31.44, 34.2, 39.4, 40.4, 58.7, 59.3, 73.7, 73.8, 76.0, 76.2, 76.6, 77.4, 97.7, 97.9, 116.7, 117.2, 129.2, 129.6, 131.0, 131.4, 134.4, 135.0, 170.1, 170.2; IR (KBr) 2935, 1740, 1641, 1236 cm^{-1}; MS (FAB)-m/z 447 $(M + Na)^+$; HRMS (FAB) Calcd for $C_{24}H_{40}NaO_6$ $(M + Na)^+$: 447.2723. Found: 447.2738.

(1*R*,4*R*,2*E*)-4-Acetoxy-1-{(1*R*,2*R*)-2-[(1*S*)-1-hydroxybut-3-enyl]cyclopropyl}non-2-enyl Acetate (34). To a stirred solution of **33** (10.3 mg, 0.0532 mmol) in *tert*-BuOH (0.25 mL) was added PPTS (3.1 mg, 0.0122 mmol) at room temperature. After 5 h, a saturated $NaHCO_3$ solution was added to the reaction mixture, and the resulting mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 4/1) to give **33** (0.3 mg, 3%) and **34** (5.9 mg, 69%). **34**: a colorless oil; R_f 0.31 (hexane/AcOEt = 2/1); $[\alpha]^{24}_D$ +20.4 (c = 0.67, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.55 (ddd, 1H, J = 5.5, 5.5, 8.5 Hz), 0.68 (ddd, 1H, J = 4.2, 5.5, 8.5 Hz), 0.85 (m, 1H), 0.88 (t, 3H, J = 6.7 Hz), 1.10 (dddd, 1H, J = 4.2, 4.2, 8.5, 8.5 Hz), 1.25−1.32 (m, 6H), 1.52−1.56 (m, 2H), 1.73 (s, 1H), 2.05 (s, 3H), 2.07 (s, 3H), 2.27 (m, 1H), 2.36 (m, 1H), 3.08 (dt, 1H, J = 7.3, 12.2 Hz), 4.76 (dd, 1H, J = 6.1, 8.5 Hz), 5.11 (m, 1H), 5.16 (m, 2H), 5.66 (dd, 1H, J = 6.1, 15.3 Hz), 5.71 (dd, 1H, J = 5.5, 15.3 Hz), 5.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 8.8, 14.0, 20.5, 21.2 (2C), 22.5, 22.7, 24.7, 31.4, 34.1, 41.6, 73.6, 74.3, 76.6, 117.8, 130.1, 131.1, 134.6, 170.3, 170.6; IR (KBr) 3446, 2953, 1738, 1641, 1240 cm^{-1}; MS (FAB) m/z 375 $(M + Na)^+$; HRMS (FAB) Calcd for $C_{20}H_{32}NaO_5$ $(M + Na)^+$: 375.2148. Found: 375.2141.

(1*S*)-1-{(1*R*,2*R*)-2-[(1*R*,4*R*,2*E*)-1,4-Bis(acetoxy)non-2-enyl]cyclopropyl}but-3-enyl Hex-5-enoate (4). To a stirred solution of **34** (13.2 mg, 0.0374 mmol) in dry CH_2Cl_2 (0.7 mL) was added 5-hexenoic acid (13.3 μL, 0.112 mmol), DMAP (14.6 mg, 0.120 mmol), and DCC (23.1 mg, 0.112 mmol) at room temperature. After being stirred for 15 h, the mixture was filtered through a pad of SiO_2, and the filtrate was concentrated in vacuo. The residue was purified by PTLC (hexane/AcOEt = 2/1) to give **4** (13.8 mg, 82%) as a colorless oil: R_f 0.68 (hexane/AcOEt = 2/1); $[\alpha]^{25}_D$ −4.1 (c = 0.45, $CHCl_3$); ^{1}H NMR (C_6D_6) δ 0.33 (ddd, 1H, J = 4.9, 4.9, 8.5 Hz), 0.61 (ddd, 1H, J = 4.9, 4.9, 8.5 Hz), 0.82 (m, 1H), 0.85 (t, 3H, J = 6.7 Hz), 1.14−1.31 (m, 6H), 1.35 (dddd, 1H, J = 4.9, 4.9, 8.5, 8.5 Hz), 1.50 (m, 1H), 1.60 (m, 1H), 1.70 (s, 3H), 1.71 (s, 3H), 1.74 (m, 2H), 2.00 (q, 2H, J = 7.3 Hz), 2.21−2.33 (m, 4H), 4.51 (dt, 1H, J = 6.7, 6.7 Hz), 4.93−5.06 (m, 5H), 5.42 (dt, 1H, J = 6.1, 6.1 Hz), 5.66−5.76 (m, 2H), 5.76−5.78 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 8.8, 13.9, 20.0, 20.3, 21.2 (2C), 22.5, 24.1, 24.7, 31.5, 33.1, 33.7, 34.3, 39.0, 73.7, 75.2, 75.8, 115.4, 117.8, 129.3, 131.3, 133.4, 137.6, 170.2 (2C), 173.0; IR (KBr) 2929, 1738, 1643 cm^{-1}; MS (FAB) m/z 449 $(M + H)^+$; HRMS (FAB) Calcd for $C_{26}H_{41}O_6$ $(M + H)^+$: 449.2903. Found: 449.2929.

12,15-Bis(acetoxy)halicholactone (35). The solution of **4** (9.3 mg, 0.0207 mmol) and freshly distilled Ti(O*i*-Pr)$_4$ (1.9 μL, 6.22 μmol) in dry CH_2Cl_2 (203 mL) was refluxed for 1.5 h under an argon atmosphere. After a solution of the catalyst **A** (5.1 mg, 6.22 μmol) in dry CH_2Cl_2 (4.0 mL) was added to the mixture, the whole was refluxed for 43 h. The mixture was filtered through a short pad of SiO_2. The solvent of the combined filtrate was removed in vacuo. The residue was purified by column chromatography (SiO_2, hexane/AcOEt = 7/1) to give **35** (6.3 mg, 72%) and dimer (2.0 mg, 11%). **35**: a colorless oil; R_f 0.58 (hexane/AcOEt = 3/1); $[\alpha]^{25}_D$ −56.3 (c = 0.28, $CHCl_3$); ^{1}H NMR (C_6D_6) δ 0.34 (ddd, 1H, J = 4.9, 4.9, 8.5 Hz), 0.65 (ddd, 1H, J = 4.9, 4.9, 8.5 Hz), 0.76 (m, 1H), 0.85 (t, 3H, J = 6.7 Hz), 1.21 (m, 1H), 1.11−1.36 (m, 6H), 1.53 (m, 2H), 1.61 (m, 2H), 1.69 (s, 3H), 1.70 (s, 3H), 1.77 (m, 1H), 1.82 (m, 1H), 2.09 (m, 2H), 2.30 (m, 1H), 2.38 (m, 1H), 4.32 (ddd, 1H, J = 1.2, 7.9, 7.9 Hz), 4.96 (dd, 1H, J = 4.3, 8.5 Hz), 5.41 (dt, 1H, J = 6.1, 6.1 Hz), 5.34−5.39 (m, 2H), 5.79−5.87 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 8.9, 14.0, 20.0, 20.6, 21.3 (2C), 22.4, 24.7, 25.3, 26.5, 31.5, 33.5, 33.8, 34.3, 73.7, 75.73, 75.75, 124.6, 129.7, 131.0, 134.7, 170.2, 170.3, 174.0; IR (KBr) 2927, 1740, 1240 cm^{-1}; MS (EI) m/z (%) 421 ($M^+ + 1$, 0.6), 361 (0.8), 318 (1.4), 300 (1.6), 251 (75), 209 (44), 191 (29), 99 (100); HRMS (FAB) Calcd for $C_{24}H_{37}O_6$ $(M + H)^+$: 421.2590. Found: 421.2567. Dimer of **27**: a colorless oil; R_f 0.30 (hexane/AcOEt = 3/1); ^{1}H NMR (C_6D_6) δ 0.31 (m, 2H), 0.64 (m, 2H), 0.85−0.94 (m, 10H), 1.19−1.28 (m, 12H), 1.53 (m, 4H), 1.63 (m, 4H), 1.72 (m, 12H), 1.77−1.82 (m, 4H), 1.96 (m, 4H), 2.30 (m, 4H), 4.50 (m, 2H), 4.97 (m, 2H), 5.26−5.39 (m, 2H), 5.40−5.45 (m, 4H), 5.75−5.85 (m, 4H); IR (KBr) 2931, 1735, 1240 cm^{-1}; MS (FAB) m/z 841 $(M + H)^+$; HRMS (FAB) Calcd for $C_{48}H_{73}O_{12}$ $(M + H)^+$: 841.5102. Found: 841.5104.

Halicholactone (1). To a stirred solution of **35** (4.8 mg, 0.0114 mmol) in MeOH (0.3 mL) was added K_2CO_3 (6.3 mg, 0.0457 mmol) at room temperature. After being stirred for 30 min, the mixture was filtered, and then the filtrate was concentrated in vacuo. The residue was purified by PTLC (hexane/AcOEt = 1/3) to give **1**[1] (2.3 mg, 62%) as a colorless oil: R_f 0.30 (hexane/AcOEt = 1/3); $[\alpha]^{24}_D$ −79.3 (c = 0.20, $CHCl_3$); ^{1}H NMR (C_6D_6) δ 0.27 (ddd, 1H, J = 4.9, 4.9, 8.5 Hz), 0.45 (ddd, 1H, J = 4.9, 4.9, 8.5 Hz), 0.86 (m, 1H), 0.89 (t, 3H, J = 6.7 Hz), 1.03 (m, 1H), 1.20−1.49 (m, 8H), 1.50 (m, 2H), 1.55 (m, 2H), 1.77 (m, 1H), 1.91 (ddd, 1H, J = 1.2, 7.2, 13.4 Hz), 2.07 (m, 2H), 2.34 (m, 1H), 2.39 (m, 1H), 3.53 (dd, 1H, J = 4.3, 6.7 Hz), 3.92 (m, 1H), 4.33 (ddd, 1H, J = 1.2, 8.5, 12.2 Hz), 5.34−5.44 (m, 2H), 5.63−5.70 (m, 2H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 8.2, 14.0, 19.5, 22.6, 23.4, 25.1, 25.3, 26.5, 31.8, 33.6, 33.9, 37.3, 72.3, 74.1, 76.1, 124.7, 131.7, 134.1, 134.7, 174.0; IR (KBr) 3392, 1734 cm^{-1}; MS (EI) m/z (%) 318 ($M^+ - H_2O$, 0.5), 265 (1.2), 247 (1.7), 238 (4), 209 (31), 82 (100); MS (FAB) m/z: 319 $(M - OH)^+$; HRMS (FAB) Calcd for $C_{20}H_{31}O_3$ $(M - OH)^+$: 319.2273. Found: 319.2269.

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Supporting Information Available: Experimental details for **14b**, **16b**, **15**, **23**, **29**, **30**, MTPA-esters of **28b**, X-ray crystallographic data for **16b**, and proton and carbon NMR data for **1**, **4**, **5**, **6**, **27**, **28a**, **28b**, **31**, **32**, **33**, **34**, **35**. This material is available free of charge via Internet at http://pubs.acs.org.

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