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Convergent synthesis of the ABCDE ring system of ciguatoxin CTX3C

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Abstract—Ciguatoxin CTX3C is a representative congener of the ciguatoxins, which are known to be the principal causative-agents of ciguatera seafood poisoning. The structure of CTX3C spans over three nanometers and is characterized by thirteen ether rings. To attain a practical construction of this molecule, efficient supplies of the structural fragments are crucial. Herein we report the convergent synthesis of the ABCDE ring fragment featuring (i) alkylative coupling of the AB ring and E ring, and (ii) ring-closing olefin metathesis.

1. Introduction

Ciguatera is a major human poisoning that is caused by the consumption of tropical and subtropical fish, and is estimated to affect more than 20,000 persons annually.[1] The symptoms of ciguatera are manifested in a combination of gastrointestinal, neurological, and cardiovascular disturbances, which can persist for months or even years. The causative toxins, such as ciguatoxin (**1**)[2] and CTX3C (**2**),[3] are produced by marine dinoflagellate *Gambierdiscus toxicus* living on macro algae, and are accumulated in fish through the food chain (Scheme 1).[4,5] Since ciguateric fish look, taste, and smell normal, immunochemical methods for detecting ciguatoxins prior to consumption have been highly desirable for a long time.[6] Biological studies have revealed that ciguatoxins exert their toxicity through the activation of voltage-sensitive sodium channels (VSSC).[7] In order to prepare anti-ciguatoxin antibodies and to study the detailed biological profiles of these ciguatoxins, chemical synthesis has been the only plausible solution due to the extremely low concentrations of the toxins in fish,[8,9] and therefore we have undertaken the total synthesis of CTX3C (**2**).[10]

The structures of ciguatoxins are characterized by 12 fused six- to nine-membered cyclic ethers, together with a spirally attached five-membered ketal (Scheme 1). We planned a flexible and convergent synthetic route to construct the highly complex polycyclic structure, in which the final stage of the total synthesis would involve the coupling of ABCDE ring fragment **3** and HIJKLM ring fragment **4**[11] with the simultaneous construction of the central FG ring system.[8f,10] In this full account, we report an efficient and improved synthesis of the left wing **3**, which can be utilized not only for the total synthesis, but also for the preparation of *anti*-ciguatoxin antibodies.[12]

2. Results and discussions

2.1. Synthesis of AB ring and E ring

Retrosynthetically, ABCDE ring fragment **3** was dissected into two parts, AB ring **5** and E ring **6**, which could be assembled by alkylative coupling/ring-closing olefin metathesis strategy (RCM)[13,14] (Scheme 1).[15] We envisioned that the medium-sized ring ethers in structural fragments **5** and **6** could be constructed using RCM from acyclic substrates, in which the stereocenters could originate from those of D-glucose.

As shown in Scheme 2, the synthesis of **5** was started from Kishi's intermediate **7**.[16] The C6-secondary alcohol of **7** was selectively deprotected using Nicotra's two-step protocol (I_2; Zn, AcOH, 70%) to afford **8**,[17] which was then converted to allyl ether **9** in 83% yield. RCM reaction of **9** using Grubbs catalyst[13c] efficiently constructed the bicyclic AB ring system of **10** (97% yield).[12,18] The three benzyl groups of **10** were removed under carefully controlled Birch conditions (Na, NH_3, EtOH), and the resulting 1,3-diol portion was protected as a *p*-methoxybenzylidene

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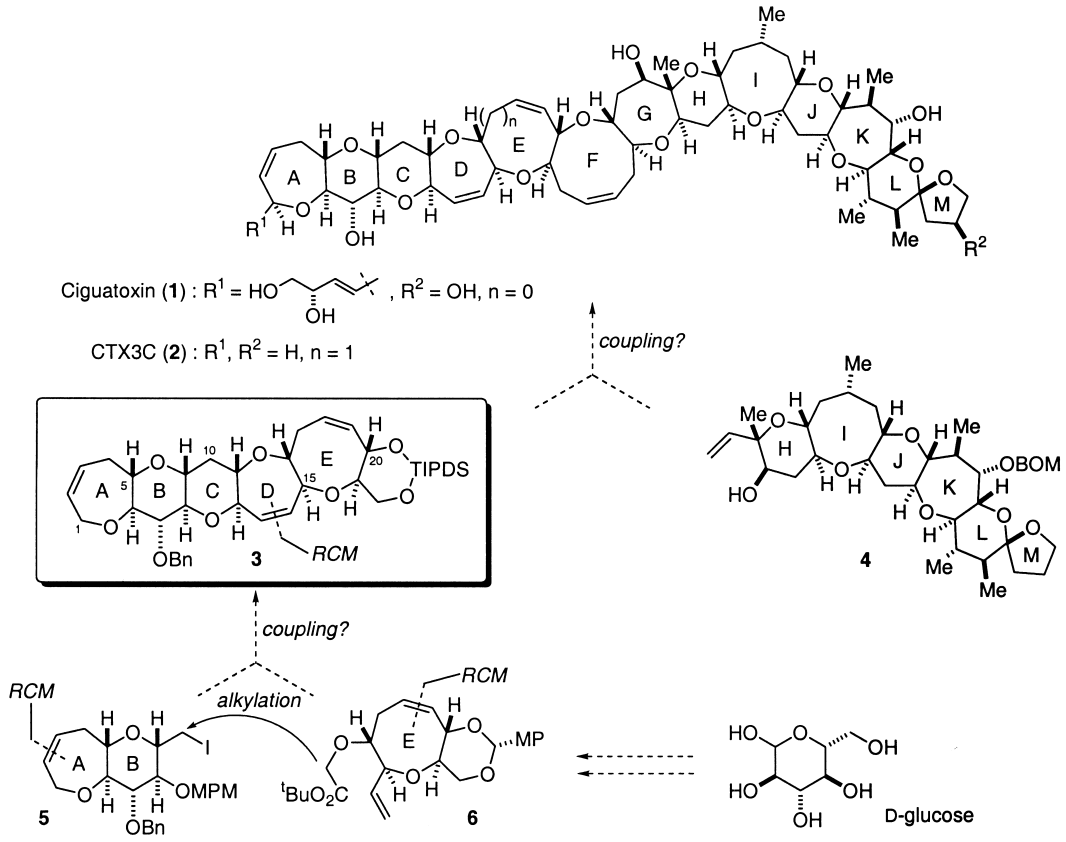
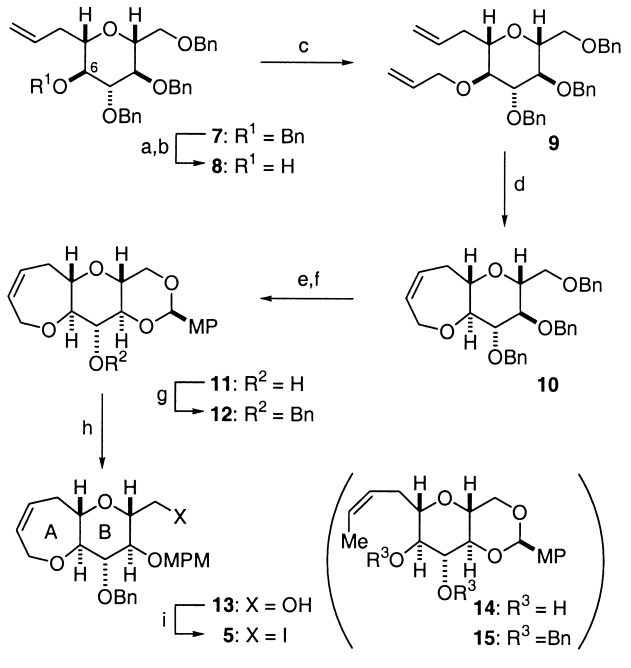


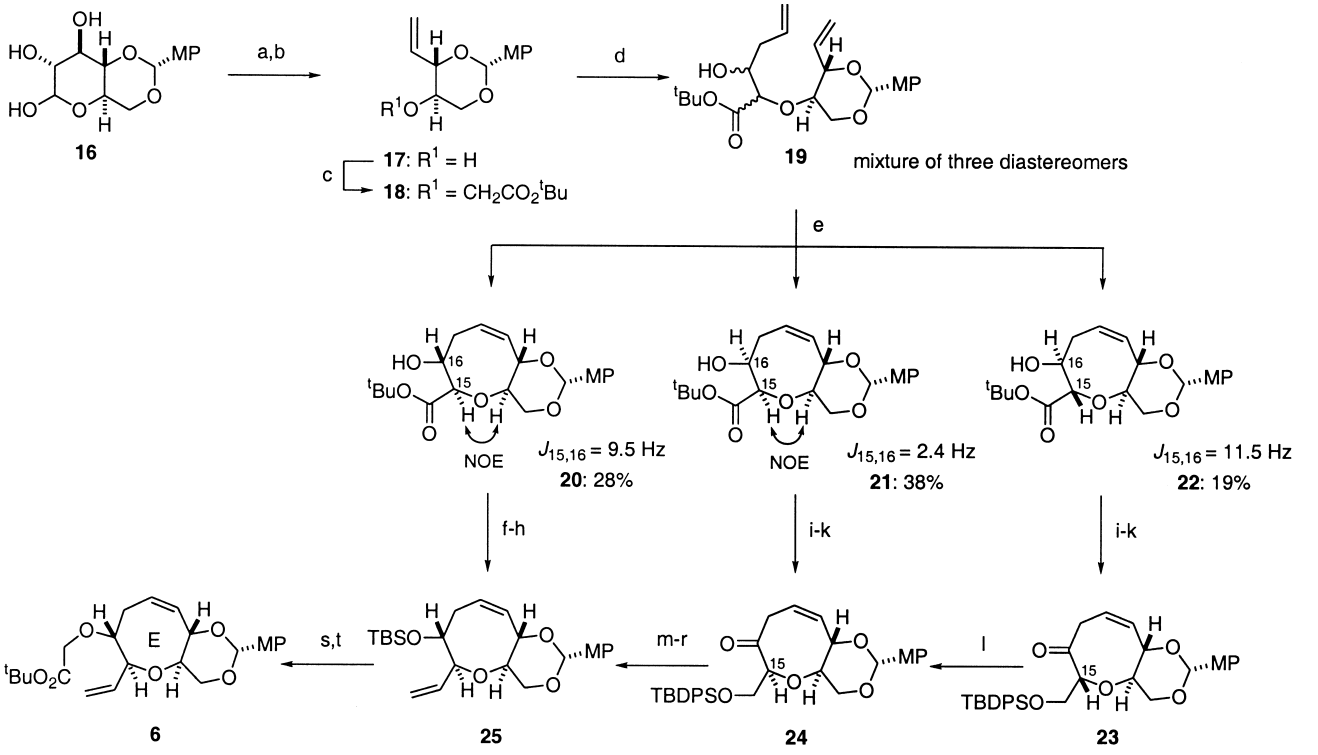
Scheme 1. Structure of ciguatoxins and synthetic strategy for the total synthesis of CTX3C. Bn=benzyl; BOM=benzyloxy methyl; MP=*p*-methoxyphenyl; MPM=*p*-methoxybenzyl; RCM=ring closing olefin metathesis; TIPDS=tetraisopropyl disiloxyl.



Scheme 2. *Reagents and conditions*: (a) I_2, CH_2Cl_2; (b) Zn, AcOH–Et_2O–MeOH, 70% (two steps); (c) allyl bromide, KH, THF, 0°C, 83%; (d) $(PCy_3)_2Cl_2Ru$=CHPh (1 mol%), CH_2Cl_2, rt, 97%; (e) Na, NH_3, THF–EtOH, −78°C; (f) *p*-methoxybenzylaldehyde dimethylacetal, *p*-TsOH, DMF, rt, 59%; (g) BnBr, NaH, THF–DMF, 0°C to rt, 84%; (h) DIBALH, CH_2Cl_2, −78 to −20°C, 82%; (i) I_2, PPh_3, imidazole, toluene, 82%. Cy=cyclohexyl; Bn=benzyl; MP=*p*-methoxyphenyl; MPM=*p*-methoxybenzyl.

acetal to afford **11** in 59% yield (two steps) after a single recrystalization. In the Birch reduction step, partial cleavage of the allylic ether was observed, and the byproduct was purified and characterized after protecting of **14** as the benzyl ether (**15**, 21% yield from **10**). Subsequent benzylation of the secondary alcohol of **11** led to **12** in 84% yield. Finally, the *p*-methoxybenzylidene acetal of **12** was regioselectively cleaved by DIBALH to furnish primary alcohol **13** (82% yield),[19] which was converted to the desired AB ring iodide **5** by a reagent combination of I_2, PPh_3, and imidazole in 82% yield.[20]

As summarized in Scheme 3, construction of the E ring started with the oxidative cleavage of the protected derivative of D-glucose **16**,[21] followed by Wittig reaction to produce olefin **17** in 72% yield (two steps). Treatment of **17** with *t*-butyl bromoacetate under basic conditions gave **18** in 99% yield. Subsequent aldol condensation of ester enolate of **18** with 3-butenal[22] furnished diene **19** as an inseparable mixture of three diastereomers (91%, combined yield).[23] This mixture was subjected to RCM conditions using Grubbs catalyst,[13c] to smoothly yield the eight-membered cyclic ethers **20**–**22** in 28, 38, and, 19% yields, respectively. The stereochemistries of these compounds were assigned from their coupling constants and NOEs, as shown in Scheme 3. The low yield of isomer **20**, which has the correct configuration, was not problematic since all isomers (**20**–**22**) were readily converted to common intermediate **25**, which was used for further synthetic operations. The secondary alcohol of **20** was protected as a TBS ether,

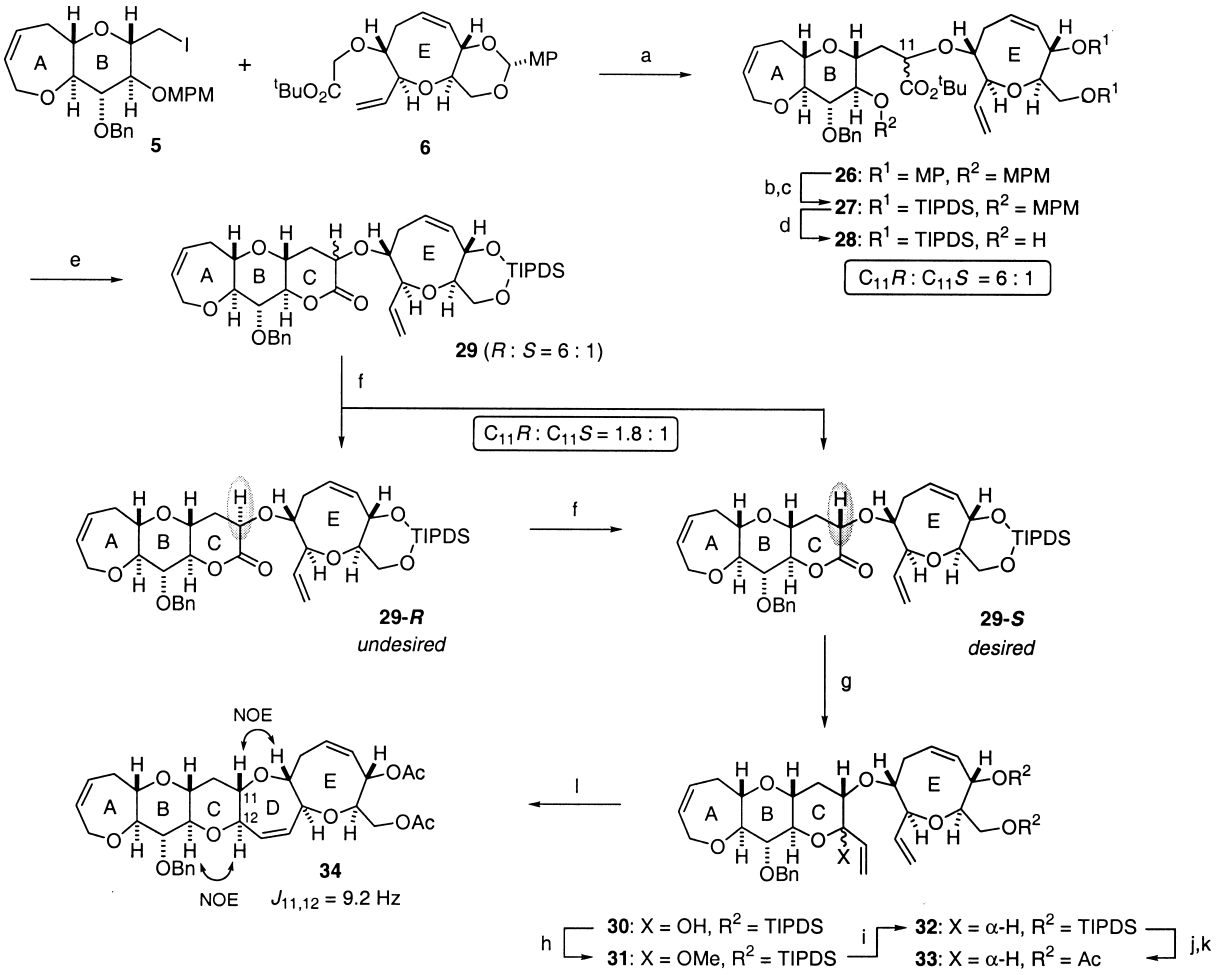


Scheme 3. *Reagents and conditions*: (a) $NaIO_4$, MeOH; (b) Ph_3PMeBr, KO*t*-Bu, THF, 72% (two steps); (c) *t*-butyl bromoacetate, NaH, THF–DMF, 99%; (d) LDA, then CH=CH_2CH_2CHO, THF, −78°C, 91%; (e) $(PCy_3)_2Cl_2Ru$=CHPh (7 mol%), CH_2Cl_2, reflux, 2 days, total yield 85%; (f) TBSCl, imidazole, DMF, 93%; (g) DIBALH, −78 to −50°C; (h) Ph_3PMeBr, KO*t*-Bu, THF, 53% (two steps); (i) $LiAlH_4$, Et_2O, 95% from **21**, 95% from **22**; (j) TBDPSCl, Et_3N, DMAP, CH_2Cl_2, 87% from **21**, 85% from **22**; (k) Dess–Martin periodinane, CH_2Cl_2, 88% (**24**), 83% (**23**); (l) imidazole (5 equiv.), toluene, 70°C, 1 day, 100%; (m) TBAF, AcOH, THF, 64%; (n) $NaBH(OAc)_3$, AcOH, MeCN, 93%; (o) TBSCl, imidazole, DMF, 98%; (p) neutral alumina, H_2O, hexane, 81%; (q) Dess–Martin periodinane, CH_2Cl_2; (r) Ph_3PMeBr, KO*t*-Bu, THF, 85% (two steps); (s) TBAF, THF, 99%; (t) *t*-butyl bromoacetate, NaH, THF–DMF, 75%. Cy=cyclohexyl; DIBALH=diisobutylaluminum hydride; DMAP=4-(dimethylamino)pyridine; DMF=*N*,*N*-dimethylformamide; TBAF=tetrabutylammonium fluoride; TBDPS=*t*-butyldiphenylsilyl; TBS=*t*-butyldimethylsilyl.

and subsequent reduction of the ester to the aldehyde, followed by Wittig olefination, furnished **25**. Ketones **23** and **24** were prepared from **22** and **21**, respectively, via a three step procedure: (i) $LiAlH_4$ reduction, (ii) TBDPS protection, and (iii) Dess–Martin oxidation.[24] Subjecting ketone **23** to heat (110°C) in toluene with imidazole provided **24** in a quantitative yield via C15-epimerization.[25] It is worth noting that isomerization of the β,δ-unsaturated ketones (**23**,**24**) to the α,β-unsaturated ketones were not observed presumably due to the intrinsic ring strain of the transfused eight-membered ring. Following deprotection of the TBDPS group of **24**, stereoselective reduction[26] of the ketone using $NaBH(OAc)_3$ completed the stereochemical adjustment to produce a diol, which was converted to olefin **25** via standard synthetic manipulations. In preparation for the coupling reaction, glycolic acid ester was introduced after the removal of TBS, leading to the appropriately functionalized E ring **6** in 75% yield (two steps).[12]

2.2. Synthesis of ABCDE ring fragment[12]

Following the syntheses of AB ring **5** and E ring **6**, we focused our attention to the coupling of these fragments and the subsequent construction of the CD ring system (Scheme 4). The coupling of the fragments was carried out by the attack of the lithium enolate of **6**, which was generated by treatment with LDA in THF–HMPA, on iodide **5** at −78°C to give alkylated adduct **26** in 51% yield as an inseparable mixture of epimers ($C_{11}R$/$C_{11}S$=6:1) in favor of the undesired stereoisomer. In effort to improve the stereoselectivity of this alkylation, we screened the reaction conditions as well as the substrates. However, satisfactory results were not obtained; for instance, attachment of a chiral auxiliary to the glycolate portion completely retarded the alkylation reaction.[27] Thus, to obtain sufficient amount of the correct stereoisomer, epimerization of C-11 was deemed necessary. Acid-catalyzed removal of the *p*-methoxy benzyl acetal of **26**, followed by TIPDS protection and MPM deprotection, produced secondary alcohol **28**, which was converted to the corresponding lactone **29** by the action of a catalytic amount of CSA (**29**-***R***/**29**-***S***=6:1). After considerable experimentation, this mixture of stereoisomers of **29** (*R*/*S*=6:1) was found to undergo epimerization, upon treatment with imidazole in toluene at 110°C,[25] resulting in an increased amount of **29**-***S*** (*R*/*S*=1.8:1). However, the separation of these isomers was not trivial. At the tens of milligram scale (approx. 50 mg trials), the desired **29**-***S*** was isolated using preparative TLC in 24% yield, whereas the undesired **29**-***R*** was recovered in 48% yield. The instability of the lactones on preparative TLC complicated the problem, especially with large-scale operations. Typically, scale-up of the preparative TLC separation (approx. 300 mg) resulted in a lower yield [**29**-***R*** (14%) and **29**-***S*** (7%)], and the carboxylic acid was obtained due to hydrolysis of **29** on the silica plate. Although this problem was not solved at this stage (vide supra), we decided to proceed with the synthesis of the ABCDE ring fragment. Lactone **29**-***S***

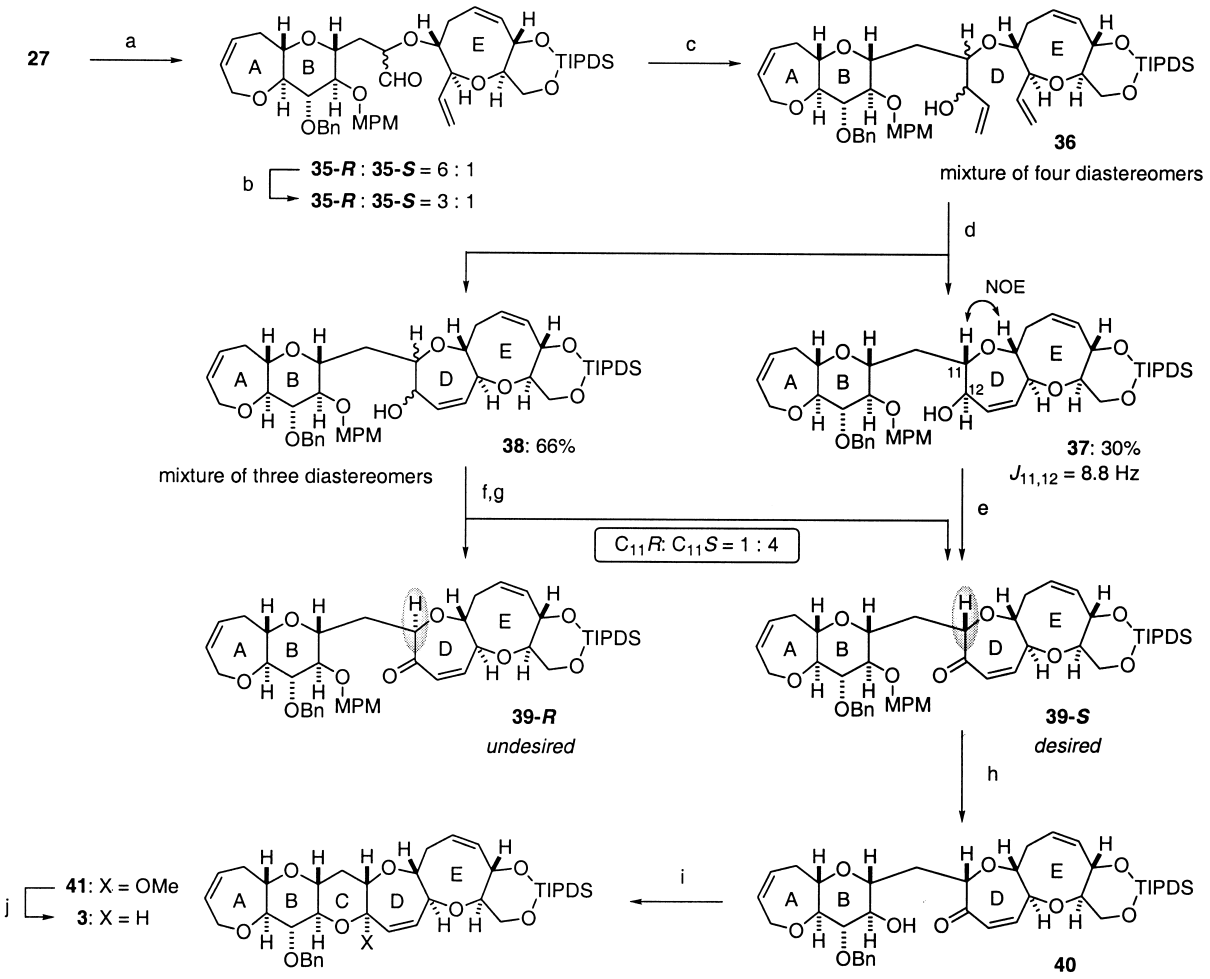


Scheme 4. *Reagents and conditions*: (a) LDA, THF–HMPA, then **5**, −78°C, 51%; (b) PPTS, MeOH, 83%; (c) 1,3-dichlorotetraisopropyldisiloxane, pyridine, 92%; (d) DDQ, CH_2Cl_2, 76%; (e) CSA, toluene, 70°C, 82%; (f) imidazole, toluene, 110°C, 48% (**29-*R***), 24% (**29-*S***); (g) vinylmagnesium bromide, Et_2O, −78°C, 78%; (h) $CH(OMe)_3$, CSA, CH_2Cl_2, 86%; (i) Et_3SiH, $BF_3{\cdot}Et_2O$, −50°C, 87%; (j) TBAF, THF; (k) Ac_2O, py, 82% (two steps); (l) $(PCy_3)_2Cl_2Ru$=CHPh (2.8 mol equiv.), $CDCl_3$, 45°C, 98%. CSA=10-camphorsulfonic acid; Cy=cyclohexyl; DDQ=2,3-dichloro-5,6-dicyano-1,4-benzoquinone; HMPA=hexamethylphosphoric triamide; PPTS=pyridinium *p*-toluenesulfonate; TBAF=tetrabutylammonium fluoride; TIPDS=tetraisopropyldisiloxyl.

was converted to diene **32**, a potential RCM substrate in three steps: (i) addition of vinylmagnesium bromide, (ii) conversion of the resulting hemiacetal **30** to the methyl acetal **31**, and (iii) reduction of the acetal using Et_3SiH in the presence of $BF_3{\cdot}OEt_2$.[8d,16,28] Ring-closure to the seven-membered D ring from diene **32** using Grubbs catalyst[13c] did not proceed, with only the recovery of the starting material. We suspected that the bulky TIPDS group might be attributable to the inertness of **32** toward RCM, and to test this possibility, the TIPDS group of **32** was converted to diacetate **33** in 82% yield (two steps). By treating **33** with Grubbs reagent,[13c] the cyclization proceeded smoothly and selectively, despite the presence of potentially reactive olefins in rings A and E, to produce the ABCDE ring fragment **34** of CTX3C in excellent yield (98%). The structure of the product is supported by the indicated NOEs and the coupling constant ($J_{11,12}$=9.2 Hz). Although this synthetic route demonstrated the effectiveness of our alkylation/RCM sequence[15] within a complex chemical context, the supply of **34** in multi-gram quantities remained to be overcome.

2.3. Modification of the construction of CD ring system

For the practical synthesis of the ABCDE ring fragment, avoiding the chemically unstable lactone intermediate (**29**) seemed reasonable, and therefore we modified our synthetic route with a change in the order of construction of the CD ring system (from C→D to D→C, Scheme 5). The diastereomeric mixture of ester **27** (*R*/*S*=6:1) was reduced to the aldehyde in 89% yield (**35-*R*/35-*S***=6:1). Epimerization of the aldehyde with the use of imidazole in toluene at 110°C gave an inseparable 3:1 mixture of **35-*R*** and **35-*S***,[25] which was reacted with vinyl lithium at −78°C to afford **36** as a mixture of four diastereomers in 94% yield. RCM reaction[13] of **36** gave a mixture of four diastereomeric cyclized products, from which desired diastereomer **37** was chromatographically isolated in 30% yield, along with the remaining three diastereomers (collectively **38**) in 66% yield. The structure of **37** was unambiguously determined by ^1H–^1H coupling constant ($J_{11,12}$=8.8 Hz) and NOEs, as indicated in Scheme 5. Compound **37** was oxidized using Swern conditions to give enone **39-*S***. On the other hand, the diastereomers **38** were subjected to an oxidation/thermodynamic-isomerization sequence to produce a 1:4 mixture of ketones **39-*R*** and **39-*S***, which were chemically stable and chromatographically separable. Formation of the desired **39-*S*** as the major isomer in the basic treatment was particularly favorable for our synthetic operation. Final



Scheme 5. *Reagents and conditions*: (a) DIBALH, CH_2Cl_2, −78 to −60°C, 89%; (b) imidazole, toluene, 100°C, 99%; (c) tetravinyltin, MeLi, Et_2O, −78°C, 94%; (d) $(PCy_3)_2Cl_2Ru$=CHPh (7 mol%), CH_2Cl_2, 35°C, 2.5 h, total yield 96%; (e) $(COCl)_2$, DMSO, Et_3N, −78 to −35°C, 78%; (f) $(COCl)_2$, DMSO, Et_3N, −78 to −35°C, 88%; (g) DBU, toluene, 95°C, 14 h, 95% (**39-*R*/39-*S***=1: 4); (h) DDQ, CH_2Cl_2, 94%; (i) CSA, $CH(OMe)_3$, CH_2Cl_2, 64%; (j) Et_3SiH, $BF_3{\cdot}Et_2O$, CH_2Cl_2, −78 to −30°C, 98%. CSA=camphorsulfonic acid; Cy=cyclohexyl; DBU=1,8-diazabicyclo[5.4.0]undec-7-ene; DDQ=2,3-dichloro-5,6-dicyano-1,4-benzoquinone; DIBALH=diisobutylaluminum hydride; DMSO=dimethyl sulfoxide; TIPDS=tetraisopropyldisiloxyl.

construction of ring C was achieved in three steps: (i) removal of the MPM group in **39-*S*** using DDQ (94% yield), (ii) conversion of **40** to the methyl ketal **41** under acidic conditions in 64% yield, and (iii) Lewis acid-mediated reductive etherification of **41** to afford ABCDE ring fragment **3** in 98% yield.[8d,16] This synthetic route is superior to the initial route in terms of yield, efficiency, and applicability to large-scale operations (typical overall yield from **27**: initial route, 11% vs modified route, 25%).

3. Conclusion

We have achieved an efficient construction of the ABCDE ring system of CTX3C by coupling AB ring **5** and E ring **6**, both of which were prepared from D-glucose. It is particularly noteworthy that all the medium-sized ring ethers of **3** were constructed through a RCM reaction. The results described herein demonstrate the efficiency and applicability of our alkylative coupling/RCM strategy for the synthesis of fused polycyclic ether. Further studies toward the efficient synthesis of CTX3C as well as other ciguatoxin congeners are currently underway in this laboratory.

4. Experimental

All reactions sensitive to air or moisture were carried out under argon or nitrogen atmosphere in dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. Diethyl ether (Et_2O) and THF were distilled from sodium/benzophenone, acetonitrile, benzene, dichloromethane (CH_2Cl_2), diisopropylamine, pyridine, triethylamine, and toluene from calcium hydride, and DMF, DMSO, HMPA and DMPU from calcium hydride under reduced pressure. All other reagents were used as supplied unless otherwise stated.

Analytical thin-layer chromatography (TLC) was performed using E. Merck Silica gel 60 F254 precoated plates. Column chromatography was performed using 100–210 μm Silica Gel 60N (Kanto Chemicals Co., Inc.), and for flash column chromatography 40–50 μm Silica Gel 60N (Kanto Chemicals Co., Inc.) was used.

^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 200 (200 MHz), Varian Mercury 200 (200 MHz), Varian INOVA 500 (500 MHz), JOEL GX-400 (400 MHz), JOEL

α-500 (500 MHz), or Brucker AM-600 (600 MHz) spectrometer and referenced to residual $CHCl_3$ [^{1}H NMR (7.26), ^{13}C NMR (77.00)] as an internal standard unless otherwise noted. IR spectra were recorded on JASCO FT/IR-7000, or Perkin–Elmer Spectrum BX FT-IR spectrometer. Optical rotations were recorded on a JASCO DIP-370 polarmeter. Low- and high-resolution mass spectra (MS, HRMS) were recorded on a JOEL HX-110, JMS-DX 303, JMS-AX 500, or HITACHI M-2500-S instrument. Time of flight mass spectra (MALDI-TOF MS) were recorded on a PerSeptive Biosystem Voyager DE STR SI-3 instrument. Elemental analysis was conducted with a Yanako CHN corder MT-5. Melting points were measured on Yanagimoto micro-melting point apparatus, and uncorrected.

4.1. Synthesis of AB ring and E ring

4.1.1. Allyl ether (9). A solution of **8** (63 g, 132 mmol) and allyl bromide (13.8 mL, 159 mmol) in THF (660 mL) at 0°C was treated with NaH (6.3 g, 60% suspension in mineral oil, 159 mmol). The mixture was stirred for 13 h at room temperature. The reaction mixture was then quenched with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine. After being dried over $MgSO_4$, the solution was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/EtOAc=3:1) to give 57.0 g (110.0 mol, 83%) of **9** as a yellow oil. $[\alpha]_D^{29}=+9.1°$ (*c* 1.0, $CHCl_3$); IR (film) ν 3098, 3034, 2864, 1644, 1497, 1209 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.32 (1H, dt, *J*=14.0, 7.5 Hz), 2.56–2.62 (1H, m), 3.19 (1H, t, *J*=9.0 Hz), 3.30 (1H, ddd, *J*=9.0, 7.5, 3.0 Hz), 3.40 (1H, ddd, *J*=9.0, 4.5, 2.0 Hz), 3.56 (1H, t, *J*=9.0 Hz), 3.63 (1H, t, *J*=9.0 Hz), 3.67 (1H, dd, *J*=11.0, 4.5 Hz), 3.72 (1H, dd, *J*=11.0, 2.0 Hz), 4.15 (1H, dd, *J*=12.0, 6.0 Hz), 4.34 (1H, dd, *J*=12.0, 6.0 Hz), 4.57 (1H, d, *J*=12.0 Hz), 4.57 (1H, d, *J*=11.0 Hz), 4.62 (1H, d, *J*=12.0 Hz), 4.81 (1H, d, *J*=11.0 Hz), 4.87 (2H, s), 5.08 (1H, dd, *J*=10.0, 1.5 Hz), 5.14 (1H, dd, *J*=17.0, 1.5 Hz), 5.17 (1H, dd, *J*=10.0, 1.0 Hz), 5.26 (1H, dd, *J*=17.0, 1.0 Hz), 5.88–5.99 (2H, m), 7.16–7.19 (2H, m), 7.26–7.37 (13H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 36.03, 69.02, 73.40, 73.98, 74.96, 75.51, 78.49, 78.77, 79.04, 81.57, 87.19, 116.89, 117.09, 127.51, 127.60, 127.70, 127.76, 127.90, 128.31, 128.40, 134.78, 134.85, 138.20, 138.34, 138.64; MALDI-TOF MS calcd for $C_{33}H_{38}O_5Na$ ($M+Na^+$) 537.26, found 537.19.

4.1.2. Bicyclic system (10). To a stirred solution of **9** (57.0 g, 111.0 mmol) in CH_2Cl_2 (2.8 L) was added Grubbs catalyst (1.4 g, 1.7 mmol), and the resultant solution was stirred at room temperature for 3 h. The reaction mixture was treated with triethyl amine (16 mL) and stirred for 20 h at room temperature. The mixture was then concentrated under reduced pressure. The resultant residue was purified by flash silica gel column chromatography (hexane/EtOAc=3:1) to give 52.0 g (107.0 mmol, 97%) of **10** as a brown oil. $[\alpha]_D^{28}=+13.2°$ (*c* 1.0, $CHCl_3$); IR (film) ν 3064, 3032, 2866, 1605, 1497, 1210 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.44 (1H, ddd, *J*=16.0, 9.5, 3.0 Hz), 2.71 (1H, ddd, *J*=16.0, 8.0, 4.0 Hz), 3.26 (1H, td, *J*=9.5, 4.0 Hz), 3.44 (1H, t, *J*=9.5 Hz), 3.48 (1H, dd, *J*=9.5, 5.0 Hz), 3.57 (1H, t, *J*=9.5 Hz), 3.64 (1H, dd, *J*=10.0, 5.0 Hz), 3.65 (1H, t, *J*=9.5 Hz), 3.73 (1H, d, *J*=10.0 Hz), 4.03 (1H, dd, *J*=15.0, 1.5 Hz), 4.29 (1H, dd, *J*=15.0, 6.0 Hz), 4.53 (1H, d, *J*=10.5 Hz), 4.56 (1H, d, *J*=12.0 Hz), 4.61 (1H, d, *J*=12.0 Hz), 4.81 (1H, d, *J*=11.0 Hz), 4.85 (1H, d, *J*=10.5 Hz), 5.85–5.95 (1H, m), 7.14–7.42 (15H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 35.08, 68.34, 69.73, 73.98, 75.52, 76.15, 76.47, 78.22, 78.90, 86.25, 88.62, 127.94, 128.01, 128.13, 128.18, 128.38, 138.50, 128.87, 138.65, 139.64; MALDI-TOF MS calcd for $C_{31}H_{34}O_5Na$ ($M+Na^+$) 509.23, found 509.28.

4.1.3. Alcohol (11). To a solution of **10** (26.5 g, 54.5 mmol) in THF/EtOH (5:1, 240 mL) at −78°C was added liquid NH_3 (ca. 50 mL). Then sodium (8.1 g, 0.35 mol) was added, and the resultant mixture was stirred for 2 h. The reaction mixture was quenched with solid NH_4Cl (50 g) and allowed to warm to room temperature. After removal of ammonia completely, salt was filtered and washed with EtOH. Filtration and concentration of the resultant solution gave crude mixture of the triol along with the monocyclic tetraol. The ratio of products was determined by ^{1}H NMR analysis (triol/tetraol=79:21).

The above residue was dissolved in DMF (50.0 mL). The solution was treated with 4-methoxybenzylaldehyde dimethylacetal (14.9 mL, 81.8 mmol) and 4-toluenesulfonic acid monohydrate (1.0 g, 5.5 mmol) at 0°C. The mixture was stirred at room temperature for 1 day. The reaction mixture was quenched with triethylamine (50 mL) and saturated aqueous $NaHCO_3$, and diluted with CH_2Cl_2. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were washed with brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The resultant precipitate was recrystalized from EtOAc to give 10.8 g (32.3 mmol, 59%) of **11** as colorless plates, and the concentration of mother liquor gave mixture of **11** and **14** (1:10, 3.3 g, 22%). Data for **11**: $[\alpha]_D^{29}=-14.4°$ (*c* 1.0, $CHCl_3$); IR (film) ν 3493, 3028, 2873, 1614, 1515, 1215 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.38 (1H, ddq, *J*=16.0, 9.5, 3.0 Hz), 2.63 (1H, ddd, *J*=16.0, 8.0, 3.0 Hz), 2.76 (1H, d, *J*=2.0 Hz), 3.30 (1H, t, *J*=9.5 Hz), 3.37 (1H, td, *J*=9.5, 3.0 Hz), 3.46 (1H, td, *J*=9.5, 5.0 Hz), 3.55 (1H, t, *J*=9.5 Hz), 3.68 (1H, t, *J*=9.5 Hz), 3.80 (3H, s), 3.84 (1H, td, *J*=9.5, 2.0 Hz), 4.05 (1H, dq, *J*=16.0, 3.0 Hz), 4.30 (1H, dd, *J*=9.5, 5.0 Hz), 4.36 (1H, td, *J*=16.0, 6.0 Hz), 5.50 (1H, s), 5.83 (1H, ddt, *J*=11.5, 8.0, 3.0 Hz), 5.93 (1H, ddt, *J*=11.5, 6.0, 3.0 Hz), 6.88 (2H, m), 7.43 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 34.26, 55.28, 68.42, 68.77, 69.85, 73.58, 76.37, 80.76, 87.66, 101.70, 113.62, 127.19, 127.62, 129.60, 131.59, 160.16; MALDI-TOF MS calcd for $C_{18}H_{22}O_6Na$ ($M+Na^+$) 357.13, found 357.13.

4.1.4. Benzyl ether (12). To a solution of **11** (5.3 g, 15.8 mmol) in THF/DMF (4:1, 51 mL) was added sodium hydride (1.0 g, 60% mineral oil, 23.7 mmol) and then benzylbromide (2.3 mL, 18.9 mmol) dropwise at 0°C. After being stirred at room temperature for 3 h, the reaction mixture was quenched with MeOH (10 mL) and diluted with EtOAc and water. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine. After

being dried over Na_2SO_4, the mixture was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/EtOAc=4:1) to give 5.7 g (13.3 mmol, 84%) of **12** as a colorless oil. $[\alpha]_D^{29}=-27.4°$ (*c* 1.0, $CHCl_3$); IR (film) ν 2892, 1616, 1517, 1254 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.29 (1H, m), 2.65 (1H, ddd, *J*=16.0, 8.0, 3.0 Hz), 3.40 (1H, td, *J*=9.0, 3.0 Hz), 3.67 (1H, dd, *J*=10.0, 9.0 Hz), 3.69 (1H, t, *J*=9.0 Hz), 3.81 (3H, s), 4.05 (1H, dq, *J*=15.5, 3.0 Hz), 4.30 (1H, dd, *J*=10.0, 5.0 Hz), 4.32 (1H, dd, *J*=15.5, 6.0 Hz), 4.84 (1H, d, *J*=11.5 Hz), 4.90 (1H, d, *J*=11.5 Hz), 5.53 (1H, s), 5.77 (1H, ddt, *J*=11.5, 8.0, 3.0 Hz), 5.87 (1H, ddt, *J*=11.5, 6.0, 3.0 Hz), 6.90 (2H, d, *J*=8.0 Hz), 7.26 (1H, t, *J*=8.0 Hz), 7.31 (1H, t, *J*=8.0 Hz), 7.39 (1H, d, *J*=8.0 Hz), 7.41 (1H, d, *J*=8.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 34.50, 55.16, 68.46, 68.69, 69.89, 74.91, 77.10, 81.16, 81.24, 87.34, 100.97, 113.43, 126.21, 127.27, 127.34, 127.69, 128.09, 129.87, 131.20, 138.91, 159.86; MALDI-TOF MS calcd for $C_{25}H_{28}O_6Na$ ($M+Na^+$) 447.18, found 447.17.

4.1.5. Alcohol (13). To a solution of **12** (5.7 g, 13.2 mmol, 89.3 mmol) in CH_2Cl_2 (27 mL) at −78°C was added DIBALH (94 mL, 0.95 M hexane, 36 mmol) dropwise. The reaction mixture was allowed to warm to −20°C, and stirred for 6 h. The reaction mixture was then quenched with EtOAc (20 mL). Saturated aqueous solution of potassium sodium (+)-tartrate was added, and the resultant mixture was stirred for 2 h. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine. After being dried over Na_2SO_4, the solution was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/EtOAc=6:1) to give 4.6 g (10.8 mmol, 82%) of **13** as a colorless solid. $[\alpha]_D^{28}=+7.93°$ (*c* 1.0, $CHCl_3$); IR (film) ν 3480, 3029, 2885, 1613, 1514, 1249 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.83 (1H, bs), 2.35 (1H, ddq, *J*=16.0, 9.5, 3.0 Hz), 2.64 (1H, ddd, *J*=16.0, 8.0, 4.0 Hz), 3.28 (1H, td, *J*=9.5, 4.0 Hz), 3.30 (1H, ddd, *J*=9.5, 5.0, 3.0 Hz), 3.37 (1H, t, *J*=9.5 Hz), 3.48 (1H, t, *J*=9.5 Hz), 3.59–3.66 (1H, m), 3.64 (1H, t, *J*=9.5 Hz), 3.78–3.85 (1H, m), 3.79 (3H, s), 4.02 (1H, bq, *J*=16.0, 3.0 Hz), 4.29 (1H, dd, *J*=16.0, 6.0 Hz), 4.57 (1H, d, *J*=10.5), 4.81 (1H, d, *J*=10.5 Hz), 4.83 (1H, d, *J*=11.0 Hz), 4.97 (1H, d, *J*=11.0 Hz), 5.79 (1H, ddt, *J*=11.5, 8.0, 3.0 Hz), 5.90 (1H, ddt, *J*=11.5, 6.0, 3.0 Hz), 6.86 (2H, m), 7.22 (2H, m), 7.29 (1H, m), 7.35 (2H, m), 7.40 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 34.47, 55.18, 62.35, 67.86, 74.57, 75.52, 75.80, 77.21, 78.50, 85.51, 88.05, 113.82, 126.88, 127.43, 127.75, 128.26, 129.70, 130.31, 131.49, 139.07, 159.31; MALDI-TOF MS calcd for $C_{25}H_{30}O_6Na$ ($M+Na^+$) 449.19, found 449.21.

4.1.6. Structure determination of the monocyclic product (15). A mixture of **11** and **14** (1:10, 5.3 g, 15.8 mmol) was dissolved in THF/DMF (4:1, 44 mL). The solution was treated with sodium hydride (1.2 g, 60% mineral oil, 29.2 mmol) and benzylbromide (2.3 mL, 19.4 mmol) at 0°C. After being stirred at room temperature for 3 h, the reaction mixture was quenched with MeOH (10 mL), and diluted with EtOAc and water. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine. After being dried over Na_2SO_4, the mixture was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/EtOAc=4:1) to give 690 mg (1.6 mmol, 3%) of **12** and 5.8 g (11.3 mmol, 21% from **10**) of **15** as a colorless oil. Data for **15**: IR (film) ν 3029, 2866, 1615, 1518, 1454, 1103 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.61 (3H, d, *J*=6.0 Hz), 2.28 (1H, dt, *J*=15.0, 8.0 Hz), 2.56 (1H, dt, *J*=15.0, 3.0 Hz), 3.38 (1H, t, *J*=9.0 Hz), 3.42 (1H, td, *J*=10.0, 5.0 Hz), 3.46 (1H, tdd, *J*=10.0, 8.0, 3.0 Hz), 3.66 (1H, t, *J*=9.0 Hz), 3.70 (1H, t, *J*=10.0 Hz), 3.82 (3H, s), 3.84 (1H, t, *J*=9.0 Hz), 4.33 (1H, dd, *J*=10.0, 5.0 Hz), 4.63 (1H, d, *J*=11.0 Hz), 4.79 (1H, d, *J*=11.0 Hz), 4.97 (1H, d, *J*=11.0 Hz), 5.00 (1H, d, *J*=11.0 Hz), 5.51 (1H, dtd, *J*=10.5, 6.0, 1.5 Hz), 5.55 (1H, s), 5.58 (1H, m), 6.92 (2H, d, *J*=9.0 Hz), 7.28–7.38 (10H, m), 7.43 (2H, d, *J*=9.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.22, 29.36, 55.43, 69.08, 70.33, 75.13, 77.36, 79.75, 81.23, 82.68, 83.47, 101.16, 113.72, 125.81, 126.25, 127.43, 127.79, 127.92, 128.09, 128.19, 128.22, 128.51, 128.56, 130.12, 138.36, 138.72, 160.10; MALDI-TOF MS calcd for $C_{32}H_{36}O_6Na$ ($M+Na^+$) 539.24, found 539.25.

4.1.7. Iodide (5). A solution of **13** (5.29 g, 12.4 mmol) was treated with imidazole (2.53 g, 37.2 mmol) and PPh_3 (6.5 g, 24.8 mmol) in toluene (50 mL) at room temperature. To this mixture was added I_2 (9.44 g 18.6 mmol) portionwise. The resulting mixture was stirred for 90 min and quenched by saturated aqueous $Na_2S_2O_3$. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with saturated aqueous $NaHCO_3$, saturated aqueous NH_4Cl and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=16:1–12:1) to give **5** (5.36 g, 10.1 mmol, 82%) as a white powder. $[\alpha]_D^{30}=+23.8°$ (*c* 1.0, $CHCl_3$); IR (film) ν 3031, 2868, 1517, 1253, 1180 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.39 (1H, ddq, *J*=16.0, 9.0, 3.0 Hz), 2.68 (1H, ddd, *J*=16.0, 8.0, 4.0 Hz), 3.04 (1H, ddd, *J*=9.0, 6.0, 2.5 Hz), 3.30 (1H, td, *J*=9.0, 4.0 Hz), 3.30 (1H, dd, *J*=11.0, 6.0 Hz), 3.38 (1H, t, *J*=9.0 Hz), 3.40 (1H, t, *J*=9.0 Hz), 3.47 (1H, dd, *J*=11.0, 2.5 Hz), 3.66 (1H, t, *J*=9.0 Hz), 3.80 (3H, s), 4.02 (1H, dq, *J*=16.0, 3.0 Hz), 4.28 (1H, dd, *J*=16.0, 6.0 Hz), 4.64 (1H, d, *J*=10.5 Hz), 4.81 (1H, d, *J*=11.0 Hz), 4.87 (1H, d, *J*=10.5 Hz), 4.97 (1H, d, *J*=11.0 Hz), 5.80 (1H, ddt, *J*=11.0, 8.0, 3.0 Hz), 5.89 (1H, ddt, *J*=11.0, 6.0, 3.0 Hz), 6.86 (2H, m), 7.21 (2H, m), 7.29 (1H, m), 7.35 (2H, m), 7.39 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 7.81, 34.36, 55.28, 67.94, 75.00, 75.61, 75.72, 76.30, 76.84, 80.73, 85.19, 88.15, 113.92, 127.15, 127.57, 127.86, 128.37, 129.75, 130.30, 131.44, 138.94, 159.40; MALDI-TOF MS calcd for $C_{25}H_{29}NaO_5I$ ($M+Na^+$) 559.10, found 559.06.

4.1.8. Ester (18). To a solution of the triol (**16**) (150.0 g, 503.1 mmol) in MeOH (2.0 L) and H_2O (150 mL) was added $NaOAc{\cdot}3H_2O$ (205.4 g, 1.5 mol), acetic acid (4.3 mL, 75.5 mmol) and then $NaIO_4$ (322.8 g, 1.6 mol) at 0°C. The resultant mixture was stirred for 2 h at room temperature. The solution was then cooled to 0°C, and the reaction was quenched with saturated aqueous $NaHCO_3$ (100 mL) and $NaHCO_3$ (95 g). After the filtration, the organic layer was separated, and the aqueous layer was

extracted with EtOAc. The combined organic extracts were washed with brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure to give 128.4 g of the crude aldehyde.

A solution of the above aldehyde in THF (900 mL) was added to a slurry of methyltriphenylphosphonium bromide (539.2 g, 1.5 mol) and *t*-BuOK (84.7 g, 754.8 mmol) in THF (1 L) at 0°C and stirred for 2 h. The reaction mixture was quenched with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine. The solution was concentrated under reduced pressure. The resultant precipitate was recrystalized from hexane/EtOAc (2:1) to give 85.5 g (362.1 mmol, 72%) of **17** as a colorless solid.

A solution of **17** (13.2 g, 55.8 mmol) in THF (200 mL) and DMF (80 mL) was treated with NaH (2.7 g of 60% in oil, 66.9 mmol) at 0°C. The reaction mixture was stirred for 20 min at room temperature, and then cooled to 0°C before the addition of *t*-butyl bromoacetate (10.7 mL, 72.5 mmol). The mixture was allowed to warm to room temperature and stirred for 1 day. The reaction was quenched with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by open silica gel column chromatography (hexane/EtOAc=20:1–14:1) to give 19.3 g (55.2 mmol, 99%) of **18** as a colorless oil. $[\alpha]_D^{24}=-29.6°$ (*c* 1.04, $CHCl_3$); IR (film) ν 1035, 1139, 1250, 1519, 1748, 2978 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.47 (9H, s), 3.36 (1H, ddd, *J*=10.0, 9.4, 5.0 Hz), 3.69 (1H, dd, *J*=10.9, 10.0 Hz), 3.79 (3H, s), 4.01 (1H, d, *J*=16.3 Hz), 4.08 (1H, d, *J*=16.3 Hz), 4.12 (1H, ddd, *J*=9.4, 6.2, 1.0 Hz), 4.48 (1H, dd, *J*=10.9, 5.0 Hz), 5.31 (1H, ddd, *J*=10.6, 1.5, 1.2 Hz), 5.48 (1H, s), 5.51 (1H, ddd, *J*=17.2, 1.5, 1.3 Hz), 6.07 (1H, ddd, *J*=17.2, 10.6, 6.2 Hz), 6.86–6.90 (2H, m), 7.40–7.43 (2H, m); ^{13}C NMR (150 MHz, $CDCl_3$) δ 28.07, 55.27, 68.77, 69.38, 74.53, 81.20, 100.71, 113.58, 118.19, 127.46, 130.49, 134.86, 160.01, 169.26; HRMS (EI, 70 eV) calcd for $C_{19}H_{26}O_6$ 350.1728, found 350.1728.

4.1.9. Aldol adduct (19). A solution of *n*-butyllithium (7.6 mL, 1.56 M in hexane, 11.8 mmol) in THF (30 mL) was treated with diisopropylamine (2.2 mL, 15.7 mmol) at −78°C, and the resultant solution was stirred for 15 min. To a solution mixture was added dropwise a solution of **18** (2.8 g, 7.9 mmol) in THF (10 mL) through cannula and then a solution of 3-butenal (10.2 mmol) in CH_2Cl_2 (80 mL) dropwise through cannula over 5 min. After being stirred for 5 min, the reaction mixture was quenched with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=12:1–8:1) to give 3.0 g (7.2 mmol, 91%) of **19** as a colorless oil. IR (film) ν 3483, 2979, 2360, 2341, 1742, 1616, 1519, 1393, 1369, 1250, 1137, 1034, 924, 831 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.49–1.50 (9H, m), 2.26–2.34 (3H, m), 3.37 (0.25H, td, *J*=9.4, 4.8 Hz), 3.41 (0.25H, td, *J*=9.4, 5.2 Hz), 3.51 (0.25H, td, *J*=9.3, 4.6 Hz), 3.54 (0.25H, td, *J*=9.1, 4.5 Hz), 3.61 (0.25H, t, *J*=10.8 Hz), 3.63 (0.25H, t, *J*=10.8 Hz), 3.72 (0.25H, t, *J*=10.8 Hz), 3.73 (0.25H, t, *J*=10.8 Hz), 3.78 (1.5H, s), 3.79 (1.5H, s), 3.80 (0.25H, d, *J*=6.8 Hz), 3.83 (0.25H, d, *J*=12.4 Hz), 3.89 (0.25H, d, *J*=5.2 Hz), 3.87–3.91 (1H, m), 3.96 (0.25H, d, *J*=4.2 Hz), 4.10–4.17 (1H, m), 4.39 (0.25H, dd, *J*=10.8, 4.8 Hz), 4.42 (0.25H, dd, *J*=10.8, 4.8 Hz), 4.45 (0.5H, dd, *J*=10.8, 5.2 Hz), 5.11–5.18 (2H, m), 5.27 (0.25H, dt, *J*=10.5, 1.6 Hz), 5.28 (0.25H, dt, *J*=12.4, 1.6 Hz), 5.34 (0.25H, dd, *J*=9.8, 1.0 Hz), 5.36 (0.25H, dd, *J*=9.6, 1.0 Hz), 5.45 (0.125H, t, *J*=1.4 Hz), 5.46 (0.125H, t, *J*=1.3 Hz), 5.46–5.50 (0.5H, m), 5.48–5.50 (1H, m), 5.51 (0.125H, t, *J*=1.2 Hz), 5.53 (0.125H, t, *J*=1.3 Hz), 5.78–5.89 (1H, m), 5.59 (0.2H, dd, *J*=17.0, 6.5 Hz), 6.01 (0.2H, td, *J*=10.6, 6.3 Hz), 6.03 (0.2H, dd, *J*=17.0, 6.5 Hz), 6.16 (0.2H, td, *J*=11.5, 5.2 Hz), 6.20 (0.2H, td, *J*=10.0, 5.2 Hz), 6.86–6.89 (2H, m), 7.39–7.43 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.25, 28.29, 37.09, 37.19, 37.77, 37.83, 55.49, 55.80, 60.61, 69.04, 69.15, 69.93, 71.68, 71.98, 72.25, 72.35, 72.52, 72.78, 74.69, 74.83, 79.69, 80.36, 80.43, 80.52, 81.82, 81.86, 82.42, 82.76, 82.84, 82.90, 100.93, 101.02, 113.83, 114.53, 117.33, 117.47, 118.24, 118.37, 118.69, 119.49, 119.89, 127.69, 130.19, 130.24, 132.23, 134.04, 134.18, 134.29, 134.39, 134.88, 135.27, 135.34, 160.27, 169.31, 169.56, 170.06, 170.48, 171.38; HRMS (EI, 70 eV) calcd for $C_{23}H_{32}O_7$ 420.2148, found 420.2149.

4.1.10. Ring-closing metathesis of diene 19. To a stirred solution of **19** (1.4 g, 3.2 mmol) in CH_2Cl_2 (500 mL, 0.006 M) was added Grubbs catalyst (79.3 mg, 96.4 μmol), and the resultant solution was stirred at reflux for 36 h. The reaction mixture was quenched with triethylamine (10 mL), and stirred for 20 h at room temperature. The mixture was concentrated under reduced pressure. The resultant residue was purified by flash silica gel column chromatography (hexane/EtOAc=15:1–6:1) to give 352 mg (897.5 mmol, 28%) of desired **20** as colorless plates, along with 477 mg (1.2 mmol, 38%) of **21** as a colorless oil, and 238 mg (608 mmol, 19%) of undesired **22** as a colorless oil. Data for **20**: mp 130–132°C; $[\alpha]_D^{28}=-57.3°$ (*c* 1.01, $CHCl_3$); IR (film) ν 3510, 2976, 1736, 1616, 1518, 1250, 1105, 832 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.50 (9H, s), 2.41–2.46 (1H, m), 2.65–2.68 (1H, m), 3.06 (1H, t, *J*=2.0 Hz), 3.53 (1H, ddd, *J*=10.5, 9.2, 5.0 Hz), 3.67 (1H, t, *J*=10.5 Hz), 3.80 (3H, s), 3.87 (1H, d, *J*=9.5 Hz), 4.15 (1H, ddd, *J*=9.5, 3.0, 2.7 Hz), 4.33 (1H, dd, *J*=10.5, 5.0 Hz), 4.45 (1H, ddd, *J*=9.2, 3.5, 1.0 Hz), 5.46 (1H, s), 5.85–5.88 (2H, m), 6.88–6.90 (2H, m), 7.40–7.42 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.96, 31.45, 55.25, 69.09, 72.28, 76.43, 79.23, 80.75, 82.79, 100.81, 113.62, 126.64, 127.38, 129.87, 133.37, 160.05, 172.20; HRMS (EI, 70 eV) calcd for $C_{21}H_{28}O_7$ 392.1835, found 392.1829. Data for **21**: $[\alpha]_D^{28}=-2.3°$ (*c* 1.00, $CHCl_3$); IR (film) ν 3456, 2933, 1749, 1616, 1518, 1250, 1126, 831, 731 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.49 (9H, s), 2.44–2.54 (2H, m), 3.39–3.45 (1H, td, *J*=9.4, 5.0 Hz), 3.79 (3H, s), 3.79 (1H, d, *J*=11.0 Hz), 4.20 (1H, d, *J*=2.4 Hz), 4.23 (1H, ddd, *J*=10.6, 5.7, 2.4 Hz), 4.42 (1H, dd, *J*=11.0, 5.0 Hz), 4.56 (H, dd, *J*=9.0, 5.0 Hz), 5.46 (1H, s), 5.72–5.79 (1H, m),

5.81 (1H, dd, J=11.0, 4.8 Hz), 6.86–6.90 (2H, m), 7.39–7.43 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.05, 33.28, 55.28, 69.23, 73.42, 75.83, 79.28, 81.22, 82.23, 100.79, 113.62, 126.43, 127.40, 129.87, 131.97, 134.03, 160.04, 170.08; HRMS (EI, 70 eV) calcd for $C_{21}H_{28}O_7$ 392.1835, found 392.1833. Data for **22**: $[\alpha]_D^{29}$=−84.2° (c 0.66, $CHCl_3$); IR (film) ν 3490, 2695, 1735, 1617, 1518, 1251, 1105, 832 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (9H, s), 2.35–2.39 (1H, m), 2.52 (1H, ddd, J=13.5, 8.7, 2.8 Hz), 3.14 (1H, d, J=3.3 Hz), 3.60 (1H, ddd, J=10.8, 10.0, 5.0 Hz), 3.80 (3H, s), 3.85 (1H, d, J=11.5 Hz), 3.85–3.88 (1H, m), 3.99 (1H, t, J=10.8 Hz), 4.38 (1H, dd, J=10.8, 5.5 Hz), 4.61 (1H, ddd, J=10.0, 7.0, 1.0 Hz), 5.54 (1H, s), 5.75 (1H, ddd, J=11.0, 7.0, 1.5 Hz), 5.87–5.91 (1H, m), 6.87–6.90 (2H, m), 7.42–7.45 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.93, 34.41, 55.26, 68.48, 70.32, 70.39, 76.88, 78.54, 82.92, 101.22, 113.64, 126.13, 127.40, 126.69, 130.73, 160.09, 170.70; HRMS (EI, 70 eV) calcd for $C_{21}H_{28}O_7$ 392.1835, found 392.1838.

4.1.11. Ketone (23). To a solution of **22** (331.3 mg, 844.7 μmol) in Et_2O (6.0 mL) at 0°C was added $LiAlH_4$ (64.0 mg, 1.7 mmol) in two equal portions over 7 min, and the resultant mixture was stirred for 30 min at room temperature. The reaction mixture was quenched with H_2O (64 μL), and then 15% NaOH aqueous (128 μL) and H_2O (64 μL) was added. The mixture was filtered through a sintered glass funnel, and washed with EtOAc. The filtrate was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (hexane/EtOAc=5:1–1:8) to give 257.2 mg (798.4 μmol, 95%) of the diol as a colorless oil.

To a solution of the above diol (379.0 mg, 1.1 mmol) in CH_2Cl_2 (6.0 mL) was added TBDPSCl (310.0 μL, 1.7 mmol), triethylamine (247.0 μL, 1.7 mmol) and DMAP (15.0 mg, 120.0 μmol) at 0°C, and the resultant mixture was stirred for an hour at room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=18:1–14:1) to give 560.0 mg (1.0 mmol, 85%) of the mono TBDPS ether as a colorless oil.

A solution of the above mono TBDPS ether (2.8 g, 5.0 mmol) in CH_2Cl_2 (25 mL) was treated with Dess–Martin reagent (4.3 g, 10.0 mmol) at 0°C. The mixture was warmed to room temperature and stirred for 40 min. Then the reaction was quenched with saturated aqueous $Na_2S_2O_3$. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=20:1–16:1) to give 2.2 g (4.2 mmol, 83%) of **23** as a colorless oil. $[\alpha]_D^{28}$=−243.7° (c 1.00, $CHCl_3$); IR (film) ν 2931, 2360, 1720, 1518, 1428, 1251, 1113, 824, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.04 (9H, s), 2.88 (1H, dd, J=11.0, 7.8 Hz), 3.55 (1H, ddd, J=9.7, 9.4, 5.3 Hz), 3.79 (1H, dd, J=11.0, 9.4 Hz), 3.82 (3H, s), 3.83 (1H, dd, J=11.2, 6.8 Hz), 3.95 (1H, dd, J=11.2, 2.5 Hz), 4.03 (1H, ddd, J=8.7, 4.4, 2.0 Hz), 4.16 (1H, dd, J=6.8, 2.5 Hz), 4.44 (1H, dd, J=11.0, 5.3 Hz), 4.63 (1H, ddd, J=8.7, 4.4, 2.0 Hz), 5.52 (1H, s), 5.61 (1H, dddd, J=11.0, 9.4, 7.8, 2.0 Hz), 5.95 (1H, ddd, J=10.8, 4.9, 1.3 Hz), 6.90–6.92 (2H, m), 7.40–7.42 (2H. m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.17, 26.54, 26.76, 41.72, 55.31, 65.26, 69.99, 77.19, 79.54, 86.56, 100.56, 113.70, 121.43, 127.44, 127.82, 129.64, 134.78, 135.25, 135.54, 135.59, 177.29, 209.06; HRMS (EI, 70 eV) calcd for $C_{33}H_{38}O_6Si$ (M^+) 558.2448, found 558.2448.

4.1.12. Ketone (24). Compound **24** was synthesized by the same three-step sequence as that for **23** (73% from **21**). $[\alpha]_D^{28}$=−243.7° (c 1.00, $CHCl_3$); IR (film) ν 702, 824, 1113, 1251, 1428, 1518, 1720, 2360, 2931 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.04 (9H, s), 2.88 (1H, dd, J=11.0, 7.8 Hz), 3.55 (1H, ddd, J=9.7, 9.4, 5.3 Hz), 3.79 (1H, dd, J=11.0, 9.4 Hz), 3.82 (3H, s), 3.83 (1H, dd, J=11.2, 6.8 Hz), 3.95 (1H, dd, J=11.2, 2.5 Hz), 4.03 (1H, ddd, J=11.0, 9.4, 1.5 Hz), 4.16 (1H, dd, J=6.8, 2.5 Hz), 4.44 (1H, dd, J=11.0, 5.3 Hz), 4.63 (1H, ddd, J=8.7, 4.4, 2.0 Hz), 5.52 (1H, s), 5.61 (1H, dddd, J=11.0, 9.4, 7.8, 2.0 Hz), 5.95 (1H, ddd, J=10.8, 4.9, 1.3 Hz), 6.90–6.92 (2H, m), 7.40–7.42 (8H, m), 7.65–7.68 (4H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.17, 26.54, 26.76, 41.72, 55.31, 65.26, 69.99, 77.19, 79.54, 86.56, 100.56, 113.70, 121.43, 127.44, 127.82, 129.64, 134.78, 135.25, 135.54, 135.59, 177.29, 209.06; MALDI-TOF MS calcd for $C_{33}H_{38}O_6Si_2Na$ ($M+Na^+$) 581.23, found 581.14.

4.1.13. Epimerization of ketone (23→24). A solution of **23** (30.9 mg, 57.8 μmol) in toluene (3.0 mL) was treated with imidazole (19.6 mg, 289.0 μmol) at room temperature, and the resultant mixture was heated to 70°C for 20 h. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane/EtOAc=20:1–16:1) to give 30.9 mg (57.8 μmol, 100%) of **24** as a colorless oil.

4.1.14. Olefin (25) from 20. To a solution of **20** (545.6 mg, 1.39 mmol) in DMF (14.0 mL) was added TBSCl (629.3 mg, 4.17 mmol) and imidazole (378.1 mg, 5.56 mmol) at 0°C, and the resultant mixture was stirred for 9 h at room temperature. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (hexane/EtOAc=30:1–16:1) to give 653.8 mg (1.29 mmol, 93%) of the TBS ether as a colorless solid.

A solution of the above TBS ether (653.8 mg, 1.29 mmol) in CH_2Cl_2 (8.0 mL) was treated with DIBALH (2.72 mL, 0.95 M in hexane, 2.58 mmol) at −78°C∼−50°C for 35 min. The reaction mixture was quenched with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the solution was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=16:1–12:1) to give the aldehyde as a colorless oil.

A solution of the above aldehyde in THF (5 mL) was added to a slurry of methyltriphenyl phosphonium bromide (4.61 g, 12.9 mmol) and *t*-BuOK (724.0 mg, 6.45 mmol) in THF (16.0 mL) at 0°C, and stirred for 10 min. Then, the reaction mixture was quenched with H_2O. The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed with NH_4Cl and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=30:1–12:1) to give 293 mg (678.5 μmol, 53%) of **25** as a colorless oil, along with over-reduced primary alcohol 223.0 mg (511.2 μmol, 40%). Data for **25**: $[\alpha]_D^{28}=-121.2°$ (*c* 1.65, $CHCl_3$); IR (film) ν 2931, 2361, 1250, 1101, 832 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ −0.03 (3H, s), 0.02 (3H, s), 0.82 (9H, s), 2.18–2.21 (1H, m), 2.64–2.66 (1H, m), 3.36 (1H, ddd, *J*=10.7, 8.5, 4.8 Hz), 3.59 (1H, t, *J*=10.7 Hz), 3.64–3.66 (1H, m), 3.73 (3H, s), 3.77–3.80 (1H, m), 4.24 (1H, dd, *J*=10.7, 4.8 Hz), 4.36–4.39 (1H, m), 5.05 (1H, dd, *J*=10.5, 1.5 Hz), 5.18 (1H, dd, *J*=16.8, 1.5 Hz), 5.38 (1H, s), 5.70–5.74 (1H, m), 5.80–5.82 (1H, m), 5.84 (1H, dd, *J*=16.8, 10.5, 4.9 Hz), 6.80–6.85 (2H, m), 7.42–7.46 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.46, 17.95, 25.74, 33.39, 55.29, 69.56, 75.05, 75.86, 79.94, 82.75, 100.83, 113.63, 114.72, 126.67, 127.45, 130.12, 133.09, 137.16, 160.03; HRMS (EI, 70 eV) calcd for $C_{24}H_{36}O_5Si$ (M^+) 432.2332, found 432.2324.

4.1.15. Olefin (25) from ketone 24. A solution of **24** (108.5 mg, 194 μmol) in THF (1.0 mL) was treated with TBAF (291 μL, 1.0 M in THF, 291 μmol) and acetic acid (1.7 μL, 291.5 μmol) at 0°C, and stirred at room temperature for 50 min. The reaction mixture was concentrated under reduced pressure, and the residue was purified by flash silica gel chromatography (hexane/EtOAc=10:1–6:1) to give 40.0 mg (124.9 μmol, 64%) of the alcohol as a colorless oil.

The solution of the above alcohol (13.5 mg, 42.2 μmol) in CH_3CN (3.0 mL) was treated with $NaBH(OAc)_3$ (44.7 mg, 211.0 μmol) and acetic acid (43.5 mL, 759.6 μmol) at −45°C. The solution was allowed to warm to −10°C and stirred for an hour. Then, the reaction mixture was quenched with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=6:1–1:8) to give 12.7 mg (39.4 μmol, 93%) of the diol as a colorless oil.

To a solution of the above diol (369.8 mg, 1.14 mmol) in DMF (6.0 mL) was added TBSCl (1.73 g, 11.48 mmol) and imidazole (310.0 mg, 4.56 mmol) at 0°C, and the resultant mixture was stirred at room temperature for 10 h. Then, the reaction mixture was quenched with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=100:1–50:1) to give 849.6 mg (1.13 mmol, 98%) of the bis-TBS ether as a colorless solid.

To a solution of the above bis-TBS ether (780.7 mg, 1.44 mmol) in hexane (300 mL) was added activated neutral alumina. The slurry was stirred at room temperature for 2 days. The mixture was filtered through a sintered glass funnel and washed with EtOAc. The filtrate was concentrated under reduced pressure, and residue was purified by silica gel column chromatography (hexane/EtOAc=100:1–10:1) to give 513.7 mg (1.18 mmol, 81%) of the mono-TBS ether along with 93.9 mg (215.2 μmol, 15%) of recovered the bis-TBS ether.

A solution of the above mono-TBS ether (513.7 mg, 1.18 mmol) in CH_2Cl_2 (5.0 mL) was treated with Dess–Martin reagent (1.0 g, 2.36 mmol) at 0°C. The reaction mixture was allowed to warm to room temperature. After being stirred for 40 min, the mixture was diluted with Et_2O (2.0 mL), and saturated aqueous $Na_2S_2O_3$ was added. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine, and dried over $MgSO_4$. Concentration and filtration through a plug of florisil (hexane/EtOAc=10:1–6:1) gave the aldehyde.

A solution of the above aldehyde in THF (5.0 mL) was added to a slurry of methyltriphenylphosphonium bromide (4.2 g, 6.61 mmol) and *t*-BuOK (661.0 mg, 5.89 mmol) in THF (16.0 mL) at 0°C, and the resultant mixture was stirred for 3 min. Then, the reaction mixture was quenched with H_2O. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with NH_4Cl and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc =30:1–12:1) to give 438.2 mg (1.00 mmol, 85%) of **25** as a colorless oil.

4.1.16. *tert*-Butyl ester (6). A solution of **25** (438.2 mg, 1.01 mmol) in THF (5.0 mL) was treated with TBAF (1.32 mL, 1.0 M in THF, 1.32 mmol) at room temperature for 90 min. The solvent was removed under reduced pressure, and the resultant residue was purified by silica gel column chromatography (hexane/EtOAc=14:1–6:1) to give 317.7 mg (998.5 μmol, 99%) of the alcohol as a colorless oil.

A solution of the above alcohol (312.1 mg, 980.9 μmol) in THF (5.0 mL) and DMF (2.0 mL) was treated with NaH (40.5 mg of 98% in oil, 1.5 mmol) at 0°C. The mixture was stirred for 20 min at room temperature, and then cooled to 0°C before the addition of *t*-butyl bromoacetate (192 μL, 1.3 mmol). The solution was allowed to warm to room temperature and stirred for 1 day. The reaction was then quenched with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the solution was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=20:1–10:1) to give 319.6 mg (739.4 μmol, 75%) of **6** as a colorless oil. $[\alpha]_D^{28}=-92.4°$ (*c* 1.00,

$CHCl_3$); IR (film) ν 2977, 2360, 1748, 1518, 1250, 830 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.48 (9H, s), 2.56 (1H, ddd, J=13.0, 6.2, 3.0 Hz), 2.63 (1H, ddd, J=13.0, 9.8, 3.0 Hz), 3.44 (1H, dt, J=9.0, 3.0 Hz), 3.46 (1H, dd, J=8.3, 5.2 Hz), 3.66 (1H, t, J=10.5 Hz), 3.80 (3H, s), 3.97–3.90 (1H, m), 4.02 (2H, d, J=1.3 Hz), 4.31 (1H, dd, J=10.5, 5.2 Hz), 4.46 (1H, ddd, J=8.3, 4.7, 2.0 Hz), 5.16 (1H, dt, J=10.4, 1.6 Hz), 5.31 (1H, dt, J=16.7, 1.6 Hz), 5.44 (1H, s), 5.82 (1H, dddd, J=11.6, 9.8, 6.2, 2.0 Hz), 5.90 (1H, dd, J=11.6, 4.7 Hz), 6.09 (1H, ddd, J=16.7, 10.4, 4.3 Hz), 6.88–6.91 (2H, m), 7.40–7.42 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 28.04, 28.85, 55.23, 68.08, 69.42, 75.48, 79.73, 80.78, 81.66, 84.42, 100.75, 113.58, 114.52, 126.17, 127.40, 130.01, 135.52, 136.99, 159.99, 169.35; HRMS (EI, 70 eV) calcd for $C_{24}H_{32}O_7$ (M^+) 432.2148, found 432.2149.

4.2. Synthesis of ABCDE ring fragment

4.2.1. Coupling adduct (26). A solution of *n*-butyllithium (1.09 mL, 1.56 M hexane, 1.69 mmol) in THF (4.0 mL) was treated with diisopropylamine (475.0 μL, 3.39 mmol) at −78°C, and the resultant solution was stirred for 30 min. Then, a solution of **6** (488.1 mg, 1.13 mmol) in THF (3.0 mL) was added dropwise through cannula over 4 min. After being stirred for 11 min, a solution of **5** (667.6 mg, 1.24 mmol) in THF (3.0 mL) and HMPA (1.3 mL) was added to the solution dropwise through cannula over 5 min, and the resultant solution was stirred for 15 min. The reaction was quenched with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/EtOAc=12:1–8:1) to give 487.4 mg (579.9 μmol, 51%) of **26** as a colorless oil, along with recovered **5** 195.5 mg (354.4 μmol, 29%) and **6** 107.8 mg (249.5 μmol, 22%). IR (film) ν 2933, 2360, 1742, 1515, 1250, 1098, 828 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.48 (9H, s), 2.11 (1H, ddd, J=13.8, 11.0, 2.2 Hz), 2.33 (1H, ddd, J=15.5, 13.6, 2.5 Hz), 2.43 (1H, ddd, J=13.5, 5.0, 2.5 Hz), 2.56 (1H, ddd, J=11.0, 7.8, 3.7 Hz), 2.61 (1H, ddd, J=13.4, 6.0, 3.0 Hz), 3.15 (1H, td, J=9.3, 4.0 Hz), 3.17 (1H, t, J=9.0 Hz), 3.36 (1H, dd, J=9.4, 2.8 Hz), 3.37 (1H, t, J=9.0 Hz), 3.40–3.46 (1H, m), 3.43 (1H, t, J=9.2 Hz), 3.59 (1H, t, J=8.7 Hz), 3.66 (1H, t, J=10.0 Hz), 3.78 (3H, s), 3.94 (1H, dd, J=11.0, 2.5 Hz), 3.96–3.99 (1H, m), 4.00 (1H, dd, J=15.0, 2.7 Hz), 4.29 (1H, dd, J=15.0, 5.7 Hz), 4.30 (1H, dd, J=11.0, 5.2 Hz), 4.43 (1H, dd, J=9.0, 2.7 Hz), 4.55 (1H, d, J=10.5 Hz), 4.77 (1H, d, J=10.3 Hz), 4.80 (1H, d, J=10.3 Hz), 4.95 (1H, d, J=11.0 Hz), 5.13 (1H, dt, J=10.6, 1.5 Hz), 5.32 (1H, dt, J=17.0, 1.7 Hz), 5.44 (1H, s), 5.75–5.82 (2H, m), 5.88–5.98 (3H, m), 6.81–6.84 (2H, m), 6.87–6.90 (2H, m), 7.18–7.21 (2H, m), 7.32–7.36 (2H, m), 7.38–7.44 (5H, m). ^{13}C NMR (50 MHz, $CDCl_3$) δ 28.29, 30.66, 34.98, 36.52, 55.69, 55.78, 68.29, 68.98, 74.02, 75.01, 75.91, 75.95, 76.09, 76.19, 76.74, 77.71, 80.32, 81.18, 81.55, 85.85, 86.24, 86.31, 88.75, 101.30, 114.14, 114.22, 114.80, 115.22, 127.27, 127.63, 127.95, 128.02, 128.28, 128.29, 128.38, 128.76, 128.83, 130.40, 130.61, 130.80, 132.20, 132.47, 133.71, 137.65, 139.59, 159.75, 160.54, 173.42; MALDI-TOF MS calcd for $C_{49}H_{60}O_{12}Na$ ($M+Na^+$) 863.94, found 863.27.

4.2.2. TIPDS ether (27). A solution of **26** (277.4 mg, 330.0 μmol) in MeOH (10.0 mL) was treated with pyridinium *p*-toluenesulfonate (91.2 mg, 363.0 μmol), and stirred at room temperature for 20 h. The mixture was concentrated, and the residue was purified by silica gel column chromatography (hexane/EtOAc=3:1–1:5) to give 197.1 mg (272.8 μmol, 83%) of the diol as a colorless oil.

To a solution of the above diol (271.1 mg, 375.3 μmol) in pyridine (3.0 mL) was added 1,3-dichlorotetraisopropyldisiloxane (600 μL, 1.88 mmol) at −40°C. After being stirred for 1 day at room temperature, the reaction mixture was quenched by the addition of MeOH (1.0 mL), diluted with Et_2O, and washed with saturated aqueous $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed with saturated aqueous NH_4Cl and brine. After being dried over $MgSO_4$, the solution was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/EtOAc=15:1–10:1) to give 333.0 mg (345.0 μmol, 92%) of **27** as a colorless oil. IR ν 697, 885, 1089, 1250, 1746, 2360, 2944 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, major isomer) δ 1.02–1.06 (28H, m), 1.47 (9H, s), 2.08 (1H, ddd, J=13.7, 11.2, 2.0 Hz), 2.26–2.35 (2H, m), 2.55 (1H, td, J=8.0, 4.0 Hz), 2.59 (1H, dd, J=10.5, 2.8 Hz), 3.13 (1H, td, J=10.2, 4.0 Hz), 3.14 (1H, t, J=9.0 Hz), 3.23 (1H, d, J=9.0 Hz), 3.35 (1H, t, J=8.7 Hz), 3.40 (1H, dt, J=9.2, 3.0 Hz), 3.44 (1H, dd, J=9.0, 2.5 Hz), 3.57 (1H, t, J=8.3 Hz), 3.78 (3H, s), 3.88–3.93 (3H, m), 3.97–4.02 (1H, m), 4.16 (1H, dd, J=11.0, 1.6 Hz), 4.27 (1H, dd, J=15.0, 5.8 Hz), 4.53 (1H, d, J=11.0 Hz), 4.72 (1H, d, J=9.0, 4.4 Hz), 4.74 (1H, d, J=10.4 Hz), 4.78 (1H, d, J=11.0 Hz), 4.93 (1H, d, J=11.3 Hz), 5.12 (1H, dt, J=10.4, 1.2 Hz), 5.32 (1H, dt, J=16.7, 1.7 Hz), 5.74–5.81 (2H, m), 5.74–5.81 (2H, m), 5.81 (1H, dd, J=10.5, 4.3 Hz), 5.88–5.94 (1H, m), 5.93 (1H, ddd, J=17.5, 10.2, 5.4 Hz), 6.80–6.83 (2H, m), 7.16–7.20 (2H, m), 7.32–7.36 (2H, m), 7.37–7.40 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.17, 12.40, 13.02, 13.17, 13.29, 17.05, 17.09, 17.24, 17.29, 17.40, 27.95, 28.01, 29.68, 29.78, 34.47, 36.09, 55.18, 63.73, 67.22, 67.79, 73.37, 74.43, 75.28, 75.68, 76.14, 81.12, 81.21, 81.36, 84.46, 84.64, 85.79, 88.40, 113.69, 115.84, 125.59, 127.41, 127.47, 127.86, 128.30, 129.01, 130.35, 131.62, 137.49, 139.14, 159.20, 173.17: MALDI-TOF MS calcd for $C_{53}H_{80}O_{12}Si_2Na$ ($M+Na^+$) 987.51, found 987.31.

4.2.3. Alcohol (28). A solution of **27** (63.5 mg, 65.8 μmol) in CH_2Cl_2 (1.0 mL) and H_2O (50 μL) was treated with DDQ (22.4 mg, 98.7 μmol) at 0°C. The reaction mixture was allowed to warm to room temperature, and stirred for 1 h. The solution was diluted with Et_2O (1.0 mL) and saturated aqueous $Na_2S_2O_3$ was added. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine. After being dried over $MgSO_4$, the solution was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=10:1–6:1) to give

41.8 mg (49.5 μmol, 76%) of **28** ($C_{11}R/C_{11}S$=6:1) as a colorless oil. Analytical sample of **28-*R*** was obtained by the further purification with silica gel column. Data for **28-*R***: $[\alpha]_D^{29}=-77.6°$ (*c* 1.00, $CHCl_3$); IR (film) ν 3437, 2943, 2867, 2361, 1745, 1367, 1090, 885, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.04–1.06 (28H, m), 1.47 (9H, s), 2.16 (1H, ddd, *J*=13.0, 10.8, 1.8 Hz), 2.21 (1H, d, *J*=1.4 Hz), 2.31–2.38 (2H, m), 2.57 (1H, dd, *J*=8.0, 3.0 Hz), 2.60 (1H, dd, *J*=8.0, 4.2 Hz), 3.18 (1H, td, *J*=9.0, 4.0 Hz), 3.24 (1H, t, *J*=8.0 Hz), 3.34–3.40 (1H, dd, *J*=9.0, 2.9 Hz), 4.71 (1H, d, *J*=11.6 Hz), 4.99 (1H, d, *J*=11.3 Hz), 5.09 (1H, d, *J*=11.2 Hz), 5.64 (1H, d, *J*=17.0 Hz), 5.73–5.83 (3H, m), 5.89–5.93 (1H, m), 5.90 (1H, ddd, *J*=15.6, 10.2, 4.3 Hz), 7.35–7.37 (5H, m). ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.17, 12.40, 17.41, 29.88, 34.49, 60.38, 63.73, 67.21, 67.74, 67.77, 73.67, 75.20, 76.15, 76.37, 77.37, 77.64, 81.33, 84.39, 85.12, 87.99, 112.34, 115.93, 125.65, 127.61, 127.80, 128.54, 129.10, 131.61, 137.46, 137.59, 173.05; MALDI-TOF MS calcd for $C_{45}H_{72}O_{11}Si_2Na$ ($M+Na^+$) 867.45, found 867.21.

4.2.4. Lactone (29). A solution of **28** ($C_{11}R/C_{11}S$=6:1, 41.8 mg, 49.5 μmol) in toluene (1.0 mL) was treated with CSA (11.5 mg, 49.5 μmol) at room temperature. The mixture was heated to 70°C for 15 h. The reaction mixture was quenched with a saturated aqueous $NaHCO_3$, and diluted with EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with saturated aqueous NH_4Cl and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was quickly purified by open silica gel column chromatography (hexane/EtOAc=15:1–10:1) to give 31.3 mg (40.6 μmol, 82%) of **29** ($C_{11}R/C_{11}S$=6:1) as a colorless oil.

4.2.5. Epimerization of lactone 29. A solution of **29** ($C_{11}R/C_{11}S$=6:1, 31.3 mg, 40.6 μmol) in toluene (2.5 mL) was treated with imidazole (27.6 mg, 406 μmol) at room temperature. The mixture was heated to 110°C for 14 h. The reaction mixture was quenched with saturated aqueous NH_4Cl, and diluted with EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The isomer ratio was determined by ^1H NMR analysis of crude mixture ($C_{11}R/C_{11}S$=1.8:1). The residue was purified by preparative TLC (hexane/EtOAc=4:1) to give 15.0 mg (19.4 μmol, 48%) of **29-*R*** as a colorless oil and 7.5 mg (9.7 μmol, 24%) of **29-*S*** as a colorless oil. Data for **29-*R***: $[\alpha]_D^{27}=-121.8°$ (*c* 1.00, $CHCl_3$); IR (film) ν 2944, 2867, 1771, 1464, 1090, 886, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.03–1.06 (28H, m), 1.57–1.63 (1H, m), 2.14–2.19 (2H, m), 2.31 (1H, ddd, *J*=16.2, 9.5, 2.6 Hz), 2.62–2.66 (2H, m), 3.25 (1H, d, *J*=9.0 Hz), 3.30 (1H, td, *J*=9.5, 4.0 Hz), 3.35 (1H, t, *J*=8.2 Hz), 3.51 (1H, dd, *J*=8.7, 2.7 Hz), 3.51–3.54 (1H, m), 3.61 (1H, t, *J*=8.2 Hz), 3.85 (1H, dd, *J*=8.7, 6.7 Hz), 3.89 (1H, d, *J*=11.4 Hz), 3.96–3.90 (2H, m), 4.15–4.18 (2H, m), 4.29 (1H, dd, *J*=15.3, 5.9 Hz), 4.71 (1H, dd, *J*=9.5, 4.0 Hz), 4.84 (1H, d, *J*=11.0 Hz), 4.87 (1H, d, *J*=11.0 Hz), 5.14 (1H, dd, *J*=10.0, 1.5 Hz), 5.28 (1H, dd, *J*=16.8, 1.5 Hz), 5.75–5.91 (4H, m), 5.92 (1H, ddd, *J*=16.8, 10.0, 6.5 Hz), 7.28–7.30 (1H, m), 7.34–7.36 (2H, m), 7.39–7.41 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.38, 13.11, 17.08, 17.23, 30.25, 31.89, 34.28, 63.73, 67.16, 68.34, 70.22, 72.18, 75.57, 76.70, 78.21, 81.43, 81.69, 82.21, 84.43, 86.87, 116.58, 125.68, 126.32, 127.72, 127.95, 128.33, 128.55, 131.38, 137.32, 137.72, 138.37, 171.39; MALDI-TOF MS calcd for $C_{41}H_{62}O_{10}Si_2Na$ ($M+Na^+$) 793.38, found 793.30. Data for **29-*S***: $[\alpha]_D^{28}=-105.0°$ (*c* 1.00, $CHCl_3$); IR (film) ν 2944, 2867, 1759, 1465, 1089, 787, 748 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.03–1.06 (28H, m), 1.91 (1H, ddd, *J*=14.8, 9.0, 3.0 Hz), 2.30–2.41 (2H, m), 2.55–2.67 (3H, m), 3.25 (1H, d, *J*=9.0 Hz), 3.29 (1H, td, *J*=9.2, 4.0 Hz), 3.34 (1H, t, *J*=8.0 Hz), 3.48 (1H, dd, *J*=18.0, 8.2 Hz), 3.56 (1H, t, *J*=8.2 Hz), 3.77–3.81 (2H, m), 3.90 (1H, dd, *J*=11.6, 1.0 Hz), 4.01 (1H, dd, *J*=15.0, 2.5 Hz), 4.10 (1H, dd, *J*=7.0, 3.4 Hz), 4.15 (1H, dd, *J*=11.6, 1.4 Hz), 4.30 (1H, dd, *J*=15.0, 5.5 Hz), 4.48 (1H, t, *J*=9.3 Hz), 4.71–4.73 (1H, m), 4.81 (1H, d, *J*=11.5 Hz), 4.87 (1H, d, *J*=11.5 Hz), 5.09 (1H, dd, *J*=10.2, 1.5 Hz), 5.26 (1H, dd, *J*=16.5, 1.5 Hz), 5.57 (1H, dddd, *J*=17.0, 10.5, 6.5, 2.0 Hz), 5.75–5.78 (1H, m), 5.84 (1H, dd, *J*=10.5, 4.8 Hz), 5.86–5.90 (1H, m), 5.95 (1H, ddd, *J*=16.5, 10.2, 5.7 Hz), 7.35–7.38 (2H, m), 7.38–7.42 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.42, 13.29, 17.24, 17.29, 28.00, 33.15, 34.33, 63.60, 70.92, 72.06, 75.27, 76.53, 78.93, 81.66, 81.73, 81.88, 84.06, 86.63, 117.26, 124.41, 126.34, 127.50, 127.75, 128.19, 128.55, 131.45, 136.39, 138.38, 138.59, 168.27; MALDI-TOF MS calcd for $C_{41}H_{62}O_{10}Si_2Na$ ($M+Na^+$) 793.30, found 793.21.

4.2.6. Diene (32). To a solution of **29-*S*** (9.9 mg, 12.8 μmol) in Et_2O (700 μL) at −78°C was added vinylmagnesium bromide (79.0 μL, 1.0 M in THF, 79.0 μmol) dropwise over 70 min. The reaction mixture was quenched with saturated aqueous NH_4Cl, and diluted with EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine. After being dried over $MgSO_4$, the solution was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=15:1–10:1) to give 8.0 mg (10.0 μmol, 78%) of **30** as a colorless oil.

A solution of **30** (15.8 mg, 19.7 μmol) in CH_2Cl_2 (700 μL) was treated with methyl orthoformate (32.3 μL, 295.5 μmol) and CSA (2.3 mg, 9.9 μmol), and stirred for 11 h at room temperature. The reaction mixture was quenched by saturated aqueous $NaHCO_3$ and diluted with Et_2O. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=20:1–16:1) to give 13.7 mg (16.8 μmol, 86%) of **31** as a colorless oil.

A solution of **31** (13.7 mg, 16.8 μmol) and triethylsilane (108.0 μL, 674 μmol) in CH_2Cl_2 (1.0 mL) was treated with boron trifluoride diethyl etherate (12.8 μL, 112 μmol) at −50°C. The mixture was allowed to warm to −30°C, and stirred for 30 min. The reaction mixture

was quenched with triethylamine (5.0 μL), and diluted with Et_2O and saturated aqueous $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=20:1–16:1) to give 10.5 mg (13.4 μmol, 87%) of **32** as a colorless oil. $[\alpha]_D^{30}=-58.0°$ (*c* 0.53, $CHCl_3$); IR (film) ν 2945, 2868, 2361, 1465, 1087, 913, 788, 747 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.03–1.06 (28H, m), 1.62–1.69 (1H, m), 2.25–2.37 (2H, m), 2.29 (1H, td, *J*=6.2, 4.0 Hz), 2.46 (1H, dt, *J*=11.3, 3.8 Hz), 2.60–2.66 (2H, m), 3.14 (1H, dd, *J*=10.6, 3.8 Hz), 3.16–3.23 (2H, m), 3.31 (1H, dd, *J*=8.7, 4.7 Hz), 3.34 (1H, t, *J*=7.2 Hz), 3.49 (1H, t, *J*=8.2 Hz), 3.54 (1H, dt, *J*=8.2, 2.4 Hz), 3.65 (1H, dd, *J*=9.2, 4.9 Hz), 3.80 (1H, dd, *J*=9.0, 5.6 Hz), 3.91 (1H, dd, *J*=11.6, 4.4 Hz), 4.03 (1H, dt, *J*=15.3, 2.6 Hz), 4.16 (1H, dd, *J*=11.2, 1.4 Hz), 4.30 (1H, dd, *J*=14.0, 5.6 Hz), 4.72 (1H, ddd, *J*=9.0, 4.3, 2.1 Hz), 4.80 (1H, d, *J*=11.3 Hz), 4.89 (1H, d, *J*=11.3 Hz), 5.12 (1H, dd, *J*=11.0, 1.4 Hz), 5.20 (1H, dd, *J*=10.0, 1.3 Hz), 5.30 (1H, dd, *J*=17.0, 1.6 Hz), 5.37 (1H, dd, *J*=17.0, 1.2 Hz), 5.58–5.65 (1H, m), 5.74–5.90 (4H, m), 5.97 (1H, ddd, *J*=17.0, 10.3, 5.0 Hz), 7.30–7.34 (3H, m), 7.38–7.41 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.43, 13.26, 17.24, 17.31, 30.49, 34.66, 63.63, 67.23, 68.41, 73.11, 74.99, 75.39, 75.79, 76.18, 76.76, 80.34, 81.06, 81.94, 87.18, 112.30, 115.77, 124.91, 126.55, 127.39, 127.85, 128.16, 131.37, 135.39, 137.22, 137.96, 139.12; MALDI-TOF MS calcd for $C_{43}H_{66}O_9Si_2Na$ ($M+Na^+$) 805.41, found 805.12.

4.2.7. Diacetate (33). A solution of **32** (6.9 mg, 8.82 μmol) in THF (700 μL) was treated with TBAF (27.0 μL, 1.0 M in THF, 27.0 μmol) and stirred for 20 min at room temperature. The reaction mixture was concentrated under reduced pressure, and dissolved in pyridine (500 μL). The solution was then treated with acetic acid anhydride (80.0 μL), and stirred at room temperature for an hour. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/EtOAc=10:1–6:1) to give 4.5 mg (7.20 μmol, 82%) of **33** as a colorless oil. $[\alpha]_D^{29}=-67.1°$ (*c* 0.35, $CHCl_3$); IR (film) ν 2983, 1745, 1598, 1244, 1101 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.70 (1H, q, *J*=11.6 Hz), 2.05 (3H, s), 2.06 (3H, s), 2.32–2.39 (2H, m), 2.47 (1H, dt, *J*=11.6, 3.9 Hz), 2.65 (1H, ddd, *J*=15.9, 8.2, 3.7 Hz), 2.73 (1H, ddd, *J*=11.7, 9.8, 2.4 Hz), 3.13–3.17 (2H, m), 3.21 (1H, t, *J*=9.6 Hz), 3.30 (1H, td, *J*=9.7, 4.0 Hz), 3.35 (1H, t, *J*=8.0 Hz), 3.48 (1H, t, *J*=8.2 Hz), 3.54 (1H, dt, *J*=9.1, 2.7 Hz), 3.63–3.68 (2H, m), 3.79 (1H, dd, *J*=8.6, 4.2 Hz), 4.03 (1H, ddd, *J*=15.6, 5.0, 2.4 Hz), 4.20–4.24 (1H, m), 4.31 (1H, dd, *J*=11.0, 4.8 Hz), 5.74–5.79 (3H, m), 5.87 (1H, ddd, *J*=11.3, 5.5, 2.8 Hz), 5.97–5.99 (2H, m), 7.29–7.34 (2H, m), 7.38–7.41 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.86, 30.70, 36.64, 37.38, 64.49, 68.43, 70.49, 73.00, 75.09, 76.16, 76.79, 80.35, 81.04, 81.18, 81.90, 81.97, 82.93, 87.18, 115.39, 116.76, 126.41, 127.85, 128.17, 131.31, 131.37, 132.80, 135.27, 136.74, 139.07, 169.61, 170.83; MALDI-TOF MS calcd for $C_{35}H_{44}O_{10}Si_2Na$ ($M+Na^+$) 647.28, found 647.17.

4.2.8. ABCDE ring system (34). To a solution of **33** (4.5 mg, 7.2 μmol) in $CDCl_3$ (800 μL, 0.009 M) in NMR tube was added Grubbs catalyst 16.6 mg (20.1 μmol) in nine equal portions over 11 h at 45°C, and the reaction mixture was quenched with triethylamine (100 μL) in $CHCl_3$ (1.0 mL). Concentration and silica gel column chromatography (hexane/EtOAc=16:1–12:1) gave 4.2 mg (7.04 μmol, 98%) of **34** as a colorless oil. $[\alpha]_D^{29}=-54.0°$ (*c* 0.28, $CHCl_3$); IR (film) ν 2932, 1749, 1508, 1243, 1092 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.43 (1H, q, *J*=11.3 Hz), 2.05 (3H, s), 2.06 (3H, s), 2.30 (1H, dt, *J*=11.3, 3.8 Hz), 2.30–2.35 (1H, m), 2.33 (1H, dd, *J*=14.0, 9.0 Hz), 2.64 (1H, ddd, *J*=16.1, 7.8, 3.5 Hz), 2.80 (1H, ddd, *J*=14.0, 10.0, 3.3 Hz), 3.06 (1H, t, *J*=9.0 Hz), 3.11 (1H, dt, *J*=9.0, 3.6 Hz), 3.28 (1H, td, *J*=9.2, 3.8 Hz), 3.28–3.33 (1H, m), 3.33 (1H, t, *J*=8.3 Hz), 3.47 (1H, t, *J*=8.3 Hz), 3.67 (1H, dt, *J*=9.0, 3.0 Hz), 3.71 (1H, ddd, *J*=10.0, 6.3, 2.1 Hz), 3.80 (1H, ddd, *J*=9.2, 4.3, 2.5 Hz), 4.01 (1H, ddd, *J*=15.4, 6.2, 3.0 Hz), 4.11 (1H, dt, *J*=9.0, 2.2 Hz), 4.16 (1H, dd, *J*=10.9 Hz), 4.22 (1H, dt, *J*=10.9, 6.3 Hz), 4.29 (1H, dd, *J*=15.4, 5.8 Hz), 4.82 (2H, d, *J*=11.6 Hz), 4.87 (2H, d, *J*=11.6 Hz), 5.57 (1H, dd, *J*=11.0, 5.2 Hz), 5.62 (1H, dt, *J*=12.5, 2.4 Hz), 5.75–5.79 (2H, m), 5.80 (1H, dt, *J*=12.5, 2.7 Hz), 5.83–5.89 (2H, m), 7.30–7.35 (3H, m), 7.38–7.41 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.91, 21.03, 32.58, 34.64, 36.82, 64.67, 68.37, 70.48, 73.15, 74.81, 75.17, 75.49, 75.69, 75.96, 80.51, 81.76, 81.82, 82.08, 84.39, 87.39, 126.50, 126.73, 127.42, 127.52, 127.73, 128.19, 131.08, 131.34, 132.16, 134.42, 139.15, 168.61, 169.56; MALDI-TOF MS calcd for $C_{33}H_{40}O_{10}Si_2Na$ ($M+Na^+$) 619.25, found 619.18.

4.3. Modification of the construction of CD ring system

4.3.1. Aldehyde (35). A solution of **27** (331.8 mg, 344.0 μmol) in CH_2Cl_2 (7.0 mL) was treated with DIBALH (398.0 μL, 0.95 M in hexane, 378.4 μmol) at −78°C, and stirred for an hour at −60°C. Then, the reaction mixture was quenched with EtOAc. A saturated aqueous solution of potassium sodium (+)-tartrate was added to the mixture, and the resultant solution was stirred vigorously for an hour. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=16:1–8:1) to give 273.2 mg (306.1 μmol, 89%) of **35** ($C_{11}R/C_{11}S$=6:1) as a colorless oil. IR (film) ν 699, 1028, 1090, 1250, 1466, 1514, 1736, 2867, 2944 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, major isomer) δ 1.05 (28H, m), 1.49 (1H, ddd, *J*=14.7, 10.8, 3.8 Hz), 2.00 (1H, ddd, *J*=13.8, 10.8, 2.0 Hz), 2.24 (1H, ddd, *J*=14.2, 7.0, 2.9 Hz), 2.27–2.33 (1H, m), 2.55 (1H, ddd, *J*=15.9, 8.0, 4.0 Hz), 2.66 (1H, ddd, *J*=14.2, 10.7, 2.1 Hz), 3.13 (1H, td, *J*=10.0, 4.0 Hz), 3.17 (1H, t, *J*=9.0 Hz), 3.26 (1H, bd, *J*=8.9 Hz), 3.35 (1H, t, *J*=8.7 Hz), 3.40–3.46 (2H, m), 3.57 (1H, t, *J*=8.7 Hz), 3.89 (1H, dd, *J*=9.0, 5.8 Hz), 3.92 (1H, dd, *J*=11.6, 1.0 Hz), 3.96 (1H, ddd, *J*=15.2, 3.8, 2.0 Hz), 4.00 (1H, dd, *J*=15.4, 2.8 Hz), 4.17 (1H, dd, *J*=11.6, 1.7 Hz), 4.28 (1H, dd, *J*=15.4, 5.8 Hz), 4.51 (1H, d, *J*=10.5 Hz), 4.73 (1H, ddd, *J*=8.9, 5.0, 2.1 Hz), 4.79 (2H, d, *J*=10.5 Hz), 4.95 (1H, d, *J*=10.8 Hz), 5.15 (1H, d, *J*=10.4 Hz), 5.33 (1H, d, *J*=16.9 Hz), 5.66–5.73 (1H, m), 5.81 (1H, ddt, *J*=11.3, 8.0, 2.8 Hz), 5.87 (1H, dd, *J*=11.0, 5.0 Hz), 5.91 (1H,

ddd, J=11.0, 5.8, 2.8 Hz), 5.94 (1H, ddd, J=16.9, 10.4, 5.8 Hz), 6.82–6.86 (2H, m), 7.15–7.18 (2H, m), 7.28–7.31 (1H, m), 7.32–7.36 (2H, m), 7.37–7.40 (2H, m), 9.66 (1H, d, J=2.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.43, 12.66, 13.41, 13.54, 30.42, 33.48, 34.68, 55.49, 63.93, 67.47, 68.12, 73.57, 74.95, 75.65, 75.92, 81.57, 81.81, 81.83, 84.78, 84.84, 85.85, 88.59, 114.03, 116.44, 125.10, 127.43, 127.78, 128.09, 128.58, 129.94, 130.53, 131.87, 137.45, 138.46, 139.31, 159.58, 203.05; MALDI-TOF MS calcd for $C_{49}H_{72}O_{11}Si_2Na$ ($M+Na^+$) 915.45, found 915.36.

4.3.2. Epimerization of aldehyde 35. A solution of **35** ($C_{11}R/C_{11}S$=6:1, 115.6 mg, 129.5 μmol) in toluene (16 mL) was treated with imidazole (132 mg, 1.94 mmol), and heated to 100°C for 16 h. The reaction mixture was poured into a vigorously stirred solution of saturated aqueous NH_4Cl (100 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=16:1–8:1) to give 114.4 mg (128.2 μmol, 99%) of **35** ($C_{11}R/C_{11}S$=3:1) as a colorless oil.

4.3.3. Diene (36). A solution of tetravinyltin (32.0 μL, 176 μmol) in Et_2O (1.0 mL) was treated with methyllithium (460.0 μL, 1.14 M hexane, 847 μmol) at −78°C, and stirred for 1 min. Then, a solution of **35** ($C_{11}R/C_{11}S$=3:1, 125.5 mg, 140.6 μmol) in Et_2O (1.0 mL) was added dropwise through cannula over 1 min. After being stirred for 13 min, the reaction mixture was quenched with saturated aqueous NH_4Cl, and diluted with EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/EtOAc=16:1–8:1) to give 121.5 mg (131.9 μmol, 94%) of **36** as a colorless oil as a mixture of four diastereomers. IR (film) ν 698, 1090, 1249, 1466, 1514, 1612, 2338, 2362, 2867, 2943, 3377 cm^{-1}; MALDI-TOF MS calcd for $C_{51}H_{76}O_{11}Si_2Na$ ($M+Na^+$) 943.48, found 943.32.

4.3.4. Ring-closing metathesis reaction of diene 36. To a solution of **36** (140.6 mg, 152.7 μmol) in CH_2Cl_2 (16 mL, 0.009 M) was added Grubbs catalyst (8.8 mg, 10.7 μmol, 7 mol%) at 35°C, and the resultant mixture was stirred for 2.5 h. The reaction was then quenched with triethylamine (100 μL). Concentration and silica gel column chromatography (hexane/EtOAc=16:1–6:1) gave 40.9 mg (45.87 μmol, 30%) of **37** as a colorless oil, along with 90.2 mg (101.0 μmol, 66%) of **38** as a mixture of three diastereomers. Data for **37**: $[\alpha]_D^{29}$=−99.5° (c 0.892, $CHCl_3$); IR (film) ν 1090, 1249, 1466, 1612, 2338, 2868, 2943, 3378 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.04–1.06 (28H, m), 1.80 (1H, ddd, J=15.4, 8.8, 3.2 Hz), 2.16 (1H, dd, J=15.4, 3.4 Hz), 2.21 (1H, ddd, J=13.2, 6.7, 2.2 Hz), 2.30–2.37 (1H, m), 2.60 (1H, ddd, J=15.3, 8.0, 3.9 Hz), 2.70 (1H, ddd, J=13.2, 9.3, 3.9 Hz), 3.20 (1H, t, J=9.4 Hz), 3.28 (1H, bd, J=8.9 Hz), 3.32 (1H, td, J=9.7, 3.9 Hz), 3.37 (1H, t, J=9.0 Hz), 3.41 (1H, dt, J=8.8, 3.4 Hz), 3.62 (1H, dt, J=8.7, 2.9 Hz). 3.66 (1H, t, J=8.4 Hz), 3.68 (1H, bt, J=9.8 Hz), 3.80 (3H, s), 3.92 (1H, bd.J=11.0 Hz), 4.00 (1H, dd, J=14.9, 2.0 Hz), 4.12–4.16 (3H, m, H12), 4.20 (1H, d, J=11.0 Hz), 4.29 (1H, dd, J=15.6, 6.0 Hz), 4.57 (1H, d, J=10.5 Hz), 4.71 (1H, dd, J=8.9, 4.2 Hz), 4.81 (1H, d, J=11.3 Hz), 4.84 (1H, d, J=10.5 Hz), 4.96 (1H, d, J=11.3 Hz), 5.64 (1H, dt, J=12.6, 2.4 Hz), 5.68–5.72 (1H, m), 5.76 (1H, dd, J=11.0, 4.8 Hz), 5.78 (1H, dt, J=8.3, 2.6 Hz), 5.84 (1H, dt, J=12.6, 2.4 Hz), 5.92 (1H, ddd, J=11.0, 5.8, 2.0 Hz), 6.86–6.89 (2H, m), 7.23–7.26 (2H, m), 7.29–7.31 (1H, m), 7.34–7.38 (2H, m), 7.39–7.42 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.09, 12.40, 13.18, 13.29, 29.68, 32.65, 34.56, 34.93, 55.27, 64.08, 67.07, 67.86, 72.47, 74.55, 75.69, 80.80, 80.91, 81.59, 83.98, 84.96, 85.31, 88.03, 113.79, 125.96, 126.61, 127.53, 127.83, 128.34, 129.30, 130.45, 131.62, 131.83, 133.29, 135.13, 136.95, 139.09, 139.57, 159.24; MALDI-TOF MS calcd for $C_{49}H_{72}O_{11}Si_2Na$ ($M+Na^+$) 915.45, found 915.31.

4.3.5. Enone (39-*S*) from 37. A solution of $(COCl)_2$ (52.0 μL, 599.0 μmol) in CH_2Cl_2 (1.0 mL) was treated with DMSO (68.0 μL, 960.0 μmol) at −78°C for 10 min. A solution of **37** (10.7 mg, 12.0 μmol) in CH_2Cl_2 (1.0 mL) was added dropwise through cannula over 1 min. After an hour at −78°C, Et_3N (200 μL, 1.4 mmol) was added at −47°C. After being stirred at −35°C for 30 min, the reaction was quenched with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/EtOAc=20:1–14:1) to give 8.3 mg (9.3 μmol, 78%) of **39-*S*** as a colorless oil. $[\alpha]_D^{29}$=−31.7° (c 0.91, $CHCl_3$); IR (film) ν 698, 1089, 1249, 1514, 1665, 2360, 1867, 1944 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (28H, m), 1.88 (1H, ddd, J=13.4, 9.2, 3.3 Hz), 2.20–2.26 (1H, m), 2.29 (1H, ddd, J=13.4, 6.2, 3.1 Hz), 2.39 (1H, ddd, J=12.8, 5.3, 1.2 Hz), 2.51 (1H, ddd, J=16.3, 7.7, 4.0 Hz), 2.68 (1H, ddd, J=12.8, 10.0, 3.0 Hz), 3.11 (1H, td, J=9.9, 4.0 Hz), 3.22 (1H, t, J=8.8 Hz), 3.30 (1H, t, J=8.7 Hz), 3.42 (1H, bd, J=9.2 Hz), 3.48 (1H, td, J=9.5, 3.1 Hz), 3.56 (1H, t, J=8.8 Hz), 3.71 (1H, dt, J=8.9, 3.0 Hz), 3.94 (1H, bd, J=12.2 Hz), 3.98 (1H, bd, J=15.3 Hz), 4.22–4.28 (4H, m), 4.55 (1H, d, J=10.3 Hz), 4.69–4.73 (1H, m), 4.79 (2H, bd, J=10.7 Hz), 4.93 (1H, d, J=11.0 Hz), 5.70–5.78 (2H, m), 5.82–5.88 (3H, m), 6.46 (1H, dd, J=12.3, 1.9 Hz), 6.84–6.87 (2H, m), 7.19–7.22 (2H, m), 7.27–7.31 (1H, m), 7.32–7.35 (2H, m), 7.37–7.39 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.12, 12.41, 13.12, 13.29, 31.59, 34.23, 35.87, 55.25, 63.67, 67.02, 67.97, 69.24, 74.75, 75.55, 75.93, 79.65, 81.06, 83.19, 84.63, 85.76, 88.21, 113.82, 125.61, 126.92, 127.09, 127.48, 127.83, 128.31, 129.75, 130.36, 131.27, 138.08, 139.12, 145.62, 159.29, 203.97; MALDI-TOF MS calcd for $C_{49}H_{70}O_{11}Si_2Na$ ($M+Na^+$) 913.44, found 913.81.

4.3.6. Enone (39-*S*) from 38. A solution of $(COCl)_2$ (194.0 μL, 2.2 mmol) in CH_2Cl_2 (2.0 mL) was treated with DMSO (252.0 μL, 3.5 mmol) at −78°C, and stirred for 10 min. Then, a solution of **38** (39.6 mg, 44.4 μmol) in CH_2Cl_2 (2.0 mL) was added dropwise through cannula over 1 min. After an hour at −78°C, Et_3N (743.0 μL, 5.3 mmol)

was added to this mixture at −50°C, and the resultant solution was stirred at −35°C for 30 min. The reaction was quenched with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/EtOAc=20:1–14:1) to give 34.9 mg (39.2 μmol, 88%) of **39** (C_{11}***R***/C_{11}***S***=5:1) as a colorless oil. Data for **39**-***R***: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (28H, m), 1.95 (1H, ddd, *J*=14.7, 10.7, 1.9 Hz), 2.07 (1H, ddd, *J*=14.7, 12.2, 1.9 Hz), 2.29–2.42 (2H, m), 2.60 (1H, ddd, *J*=16.6, 9.2, 4.4 Hz), 2.70 (1H, ddd, *J*=13.8, 10.9, 4.0 Hz), 3.24 (1H, btd, *J*=9.7, 4.9 Hz), 3.26 (1H, t, *J*=9.8 Hz), 3.40 (1H, t, *J*=8.9 Hz), 3.41–3.44 (1H, m), 3.51 (1H, bt, *J*=9.2 Hz), 3.65 (1H, t, *J*=8.9 Hz), 3.79 (3H, s), 3.78–3.81 (1H, m), 3.96 (2H, bd, *J*=11.0 Hz), 4.02 (1H, dd, *J*=15.3, 2.7 Hz), 4.23 (1H, bd, *J*=11.0 Hz), 4.29 (1H, dd, *J*=15.3, 4.9 Hz), 4.36–4.41 (2H, m), 4.55 (2H, d, *J*=10.5 Hz), 4.72 (1H, dd, *J*=7.8, 4.0 Hz), 4.80 (2H, d, *J*=11.0 Hz), 4.83 (2H, d, *J*=10.5 Hz), 4.98 (2H, d, *J*=11.0 Hz), 5.72–5.76 (1H, m), 5.77–5.82 (1H, m), 5.85–5.92 (2H, m), 5.92 (1H, dd, *J*=12.3, 2.3 Hz), 6.63 (1H, dd, *J*=12.3, 2.8 Hz), 6.81–6.84 (2H, m), 7.15–7.17 (2H, m), 7.29–7.31 (1H, m), 7.34–7.37 (2H, m), 7.39–7.42 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.11, 12.39, 13.08, 13.27, 31.83, 32.85, 34.49, 55.20, 63.62, 67.00, 67.84, 74.27, 74.95, 75.59, 75.71, 78.72, 79.25, 79.97, 81.25, 84.68, 85.87, 88.24, 113.81, 125.33, 127.12, 127.25, 127.50, 127.81, 128.32, 129.53, 130.31, 138.16, 139.08, 131.51, 147.66, 159.29, 203.12; MALDI-TOF MS calcd for $C_{49}H_{70}O_{11}Si_2Na$ ($M+Na^+$) 913.44, found 913.79.

A solution of **39** (C_{11}***R***/C_{11}***S***=5:1, 76.8 mg, 86.2 μmol) in toluene (50 mL) was treated with DBU (177 μL, 1.18 mmol) at room temperature, and heated to 95°C for 14 h. The solution was poured into a vigorously stirred solution of saturated aqueous NH_4Cl (140 mL) at 0°C. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The epimers ratio of the crude mixture was determined by ^{1}H NMR analysis (**39**-***R***/**39**-***S***=1:4). The residue was purified by flash silica gel column chromatography (hexane/ether=6:1–4:1) to give 32.0 mg (**39**-***R***/**39**-***S***=1:12, 35.9 μmol, 42%), 10.0 mg (**39**-***R***/**39**-***S***=1:6, 11.2 μmol, 13%), and 25.8 mg (**39**-***R***/**39**-***S***=1:1, 29.0 μmol, 40%) as colorless oil.

4.3.7. Alcohol (40). A solution of **39**-***S*** (65.0 mg, 73.0 μmol) in CH_2Cl_2 (8.0 mL) and H_2O (400 μL) was treated with DDQ (40.0 mg, 175.2 μmol) at 0°C, and stirred for 10 min. The mixture was allowed to warm to room temperature, and stirred for 10 min. The solution was diluted with Et_2O (5.0 mL) and saturated aqueous $Na_2S_2O_3$. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=16:1–8:1) to give 52.8 mg (68.5 μmol, 94%) of **40** as a colorless oil. $[\alpha]_D^{29}$=−47.4° (*c* 0.57, $CHCl_3$); IR (film) ν 886, 1027, 1089, 1466, 1665, 2364, 2867, 2944, 3469 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (28H, m), 1.91 (1H, ddd, *J*=14.0, 8.6, 4.6 Hz), 2.30 (1H, ddd, *J*=14.0, 5.6, 2.5 Hz), 2.30–2.35 (1H, m), 2.41 (1H, ddd, *J*=13.2, 6.2, 2.0 Hz), 2.52 (1H, ddd, *J*=11.2, 7.9, 4.0 Hz), 2.70 (1H, ddd, *J*=13.2, 10.0, 3.7 Hz), 3.15 (1H, td, *J*=9.4, 3.8 Hz), 3.31 (1H, t, *J*=8.6 Hz), 3.32 (1H, r, *J*=8.3 Hz), 3.38 (1H, t, *J*=8.5 Hz), 3.40–3.44 (2H, m), 3.74 (1H, ddd, *J*=8.6, 3.7, 2.0 Hz), 3.94 (1H, dd, *J*=11.4, 1.6 Hz), 3.98 (1H, dd, *J*=15.3, 3.0 Hz), 4.22–4.30 (4H, m), 4.71 (1H, d, *J*=11.3 Hz), 4.73 (1H, ddd, *J*=9.1, 4.9, 1.8 Hz), 4.97 (1H, d, *J*=11.3 Hz), 5.75–5.79 (2H, m), 5.83–5.89 (3H, m), 6.48 (1H, dd, *J*=12.5, 2.4 Hz), 7.35–7.37 (5H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.12, 12.42, 13.13, 13.31, 31.56, 34.26, 36.02, 63.67, 67.03, 67.89, 73.38, 74.31, 75.06, 75.97, 79.60, 82.83, 83.25, 84.61, 84.92, 87.76, 125.53, 126.98, 127.19, 127.76, 127.82, 128.53, 131.31, 138.18, 138.97, 145.82, 203.78; MALDI-TOF MS calcd for $C_{41}H_{62}O_{10}Si_2Na$ ($M+Na^+$) 793.39, found 793.26.

4.3.8. The ABCDE ring fragment of CTX3C (3). A solution of **40** (6.3 mg, 8.2 μmol) in CH_2Cl_2 (1 mL) was treated with methyl orthoformate (18.0 μL, 163.0 μmol) and CSA (6.6 mg, 28.6 μmol), and stirred for an hour at room temperature. The reaction mixture was quenched with saturated aqueous $NaHCO_3$, and diluted with Et_2O. The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=20:1–14:1) to give 4.1 mg (5.3 μmol, 64%) of methyl acetal **41** as a colorless oil. $[\alpha]_D^{29}$=−91.3° (*c* 1.01, $CHCl_3$). IR (film) ν 697, 886, 1028, 1090, 1457, 2867, 2944 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (28H, m), 1.81 (1H, q, *J*=11.2 Hz), 2.03 (1H, dt, *J*=10.3, 4.1 Hz), 2.24 (1H, ddd, *J*=12.9, 5.8, 1.7 Hz), 2.34 (1H, ddd, *J*=16.0, 10.0, 2.7 Hz), 2.64 (1H, ddd, *J*=15.0, 12.3, 3.7 Hz), 2.69 (1H, ddd, *J*=12.9, 8.2, 3.0 Hz), 3.14 (1H, td, *J*=10.2, 4.2 Hz), 3.23 (3H, s), 3.27 (1H, td, *J*=10.0, 3.7 Hz), 3.33 (1H, t, *J*=7.7 Hz), 3.34 (1H, d, *J*=9.0 Hz), 3.35 (1H, t, *J*=8.9 Hz), 3.45 (1H, t, *J*=8.7 Hz), 3.47 (1H, dd, *J*=12.0, 4.1 Hz), 3.73 (1H, dt, *J*=8.4, 2.7 Hz), 3.93 (1H, d, *J*=11.0 Hz), 4.01 (1H, dd, *J*=15.3, 1.7 Hz), 4.21 (1H, d, *J*=11.3 Hz), 4.30 (1H, dd, *J*=15.3, 5.6 Hz), 4.30–4.34 (1H, m), 4.70 (1H, dd, *J*=9.0, 3.5 Hz), 4.84 (1H, d, *J*=13.0 Hz), 4.86 (1H, d, *J*=13.0 Hz), 5.51 (1H, dd, *J*=12.0, 2.0 Hz), 5.76–5.81 (3H, m), 5.86 (1H, ddd, *J*=10.7, 5.3, 2.8 Hz), 6.07 (1H, ddd, *J*=12.0, 2.2, 0.8 Hz), 7.24–7.27 (1H, m), 7.30–7.34 (2H, m), 7.38–7.41 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.09, 12.39, 13.13, 13.29, 32.38, 32.83, 34.61, 48.70, 64.10, 67.00, 68.39, 72.88, 73.26, 73.28, 75.20, 79.33, 80.28, 81.83, 84.72, 85.45, 87.59, 98.64, 125.75, 126.84, 127.38, 127.67, 128.15, 129.70, 131.28, 137.08, 139.22, 140.63; MALDI-TOF MS Calcd for $C_{42}H_{64}O_{10}Si_2Na$ ($M+Na^+$) 807.39, found 807.29.

A solution of methyl acetal **41** (43.5 mg, 55.5 μmol) and triethylsilane (85.0 μL, 529.2 μmol) in CH_2Cl_2 (3.0 mL) was treated with boron trifluoride diethyl etherate (17.0 μL, 112.0 μmol) at −78°C. The mixture was allowed

to warm to −30°C, and stirred for 15 min. The reaction mixture was quenched with triethylamine (60.0 μL), and diluted with Et_2O and saturated aqueous $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed with $NaHCO_3$ and brine. After being dried over $MgSO_4$, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=20:1–10:1) to give 41.1 mg (54.4 μmol, 98%) of **3** as a colorless oil. $[\alpha]_D^{29}=-96.6°$ (*c* 1.00, $CHCl_3$); IR (film) ν 698, 1027, 1087, 1467, 2868, 2944 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (28H, m), 1.51 (1H, q, *J*=11.8 Hz), 2.24 (1H, ddd, *J*=13.3, 6.2, 2.7 Hz), 2.29 (1H, dt, *J*=11.8, 4.1 Hz), 2.30–2.37 (1H, m), 2.64 (1H, ddd, *J*=16.0, 7.8, 3.8 Hz), 2.71 (1H, ddd, *J*=13.3, 9.9, 4.0 Hz), 3.05 (1H, t, *J*=9.2 Hz), 3.11 (1H, td, *J*=9.1, 4.1 Hz), 3.22 (1H, ddd, *J*=11.4, 9.1, 4.3 Hz), 3.27 (1H, td, *J*=9.6, 3.8 Hz), 3.30 (1H, d, *J*=8.6 Hz), 3.33 (1H, t, *J*=8.3 Hz), 3.46 (1H, t, *J*=8.2 Hz), 3.65 (1H, dt, *J*=8.9, 3.7 Hz), 3.78 (1H, ddd, *J*=9.1, 3.7, 2.3 Hz), 3.93 (1H, d, *J*=11.6 Hz), 4.01 (1H, dd, *J*=15.2, 2.2 Hz), 4.16 (1H, ddd, *J*=8.9, 4.8, 2.6 Hz), 4.21 (1H, dd, *J*=11.6, 1.5 Hz), 4.28 (1H, dd, *J*=15.2, 5.4 Hz), 4.70 (1H, ddd, *J*=8.6, 4.6, 1.7 Hz), 4.81 (1H, d, *J*=11.5 Hz), 4.87 (1H, d, *J*=11.5 Hz), 5.55 (1H, dt, *J*=12.7, 3.6 Hz), 5.67–5.73 (1H, m), 5.76–5.81 (2H, m), 5.84–5.88 (1H, m), 5.87 (1H, dt, *J*=12.7, 2.3 Hz), 7.26–7.29 (1H, m), 7.31–7.34 (2H, m), 7.38–7.42 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.09, 12.40, 13.14, 13.29, 31.57, 32.48, 34.61, 64.05, 67.03, 68.33, 73.21, 75.17, 78.02, 80.53, 80.83, 80.98, 82.16, 84.41, 84.42, 85.07, 87.38, 125.68, 126.76, 127.38, 127.72, 128.16, 130.04, 131.34, 135.66, 137.25, 139.36; MALDI-TOF MS calcd for $C_{41}H_{62}O_9Si_2Na$ ($M+Na^+$) 777.38, found 777.28.

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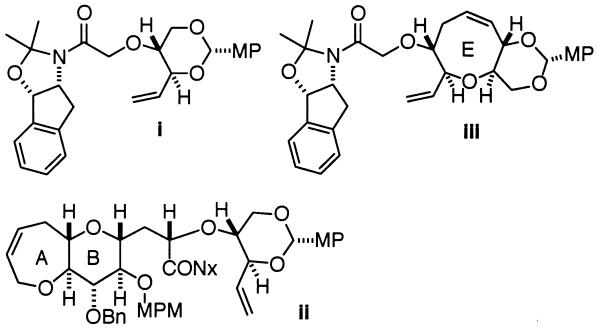
27. We successfully constructed the ABCD ring system using chiral auxiliary in a highly stereocontrolled manner (**5**+**i**→**ii**, Ref. 8e). In sharp contrast to this result, the coupling between **5** and **iii** did not produce the alkylated adduct.



28. The small amount (<10%) of byproduct **iv** was isolated, which was presumably resulted from the 1,4-addition of vinylmagnesium bromide to **30**.