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STEREOSELECTIVE SYNTHESIS OF THE A-RING OF ARMATOL A FROM A BROMO-SUBSTITUTED CHIRAL BUILDING BLOCK BASED ON IRELAND-CLAISEN REARRANGEMENT AND RING-CLOSING OLEFIN METATHESIS

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Abstract – The stereoselective synthesis of the A-ring of armatol A, a natural polycyclic ether triterpene from the red alga *Chondria armata,* was achieved in a non-biomimetic way. The synthesis employed Ireland-Claisen rearrangement of an ester, prepared from a bromo-substituted chiral building block, for the construction of C6 and C7 stereocenters and a relay ring-closing olefin metathesis for the seven-membered ring formation.

INTRODUCTION

Armatol A (Figure 1) and five other congeners, armatols B–F, were isolated from the red alga *Chondria armata* by Ciavatta and co-workers.[1] All the armatols have a solitary bromo-substituted oxepane (A-ring), a fused tricyclic ether moiety (BCD-ring), and a triterpene framework in common. The partial relative configurations of the A-ring and the BCD-ring of each armatol congener were determined by NMR analysis, and the partial absolute configuration of the A-ring of armatol A was confirmed via chemical degradation. However, the relative relationship between the A- and the BCD-rings and the configuration at C10 were unclear until Jamison and co-workers determined the full absolute configuration of armatol A, shown in Figure 1, by total synthesis in 2013.[2]

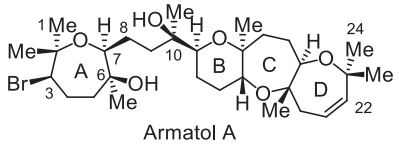
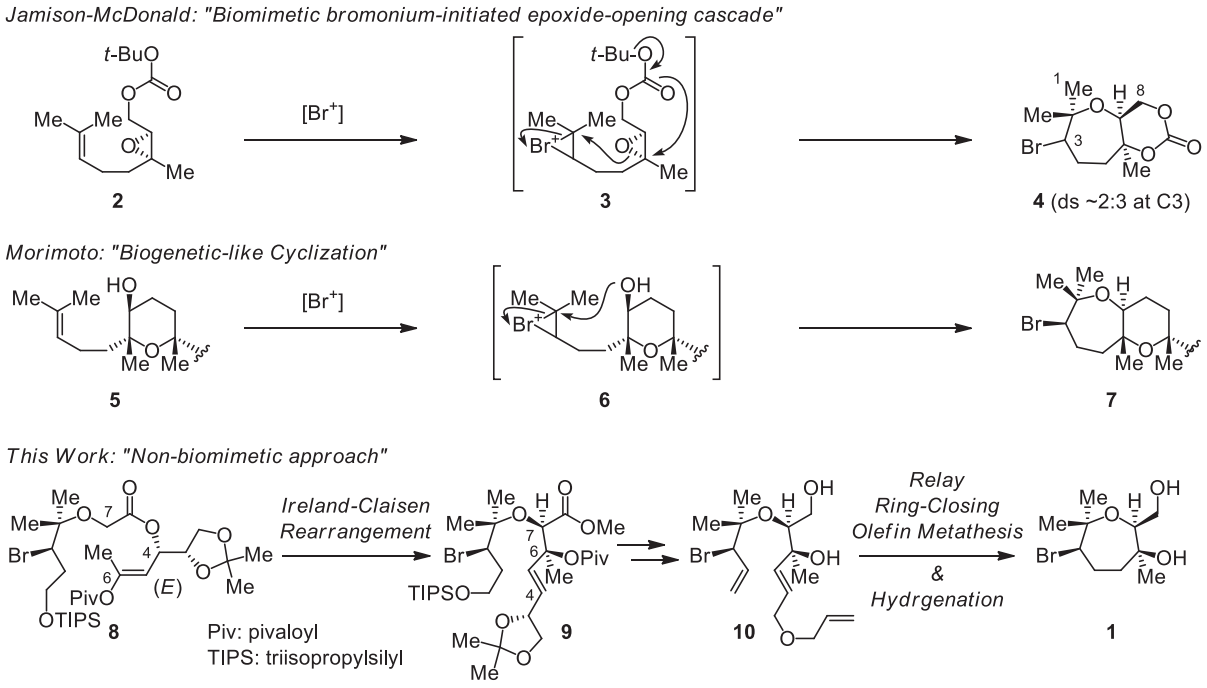


Figure 1

It is remarkable that the hydroxy group at the C6 tetrasubstituted carbon in the common A-ring of armatols A, B, D, and F is in a *cis*-relationship to the carbon chain at C7, because the *cis*-configuration is unusual among natural oxepanes possessing similar substituents.[3] The bromo-substitution at the congested C3 position in the solitary oxepane (A-ring) is also an unprecedented feature of armatols. In addition to these structural characteristics of the A-ring, the structural complexity in the fused tricyclic ether system[4] of the BCD ring of armatols prompted us to initiate a program toward their total synthesis.[5,6] As part of this program, the synthesis of the A-ring of armatol A was studied.

The A-ring was synthesized by Jamison's group through a biomimetic bromonium-initiated epoxide-opening cascade with modification of McDonald's procedure (Scheme 1).[2,7] An alternative biogenetic-like cyclization of a 6-methyl-hept-5-en-1-ol system initiated by *N*-bromosuccinimide was also reported by Morimoto for the construction of the related bromo-substituted oxepanes.[8] In contrast, we have studied a non-biomimetic synthetic route to the A-ring in expectation of the successful establishment of the bromo-substituted C3-stereocenter, which was not necessarily effective in the biomimetic synthesis. We describe herein the stereoselective synthesis of the A-ring (**1**) of armatol A from a bromo-substituted chiral building block via a route including the Ireland-Claisen rearrangement[9] of ester **8** and the relay ring-closing olefin metathesis[10,11] of triene **10**.

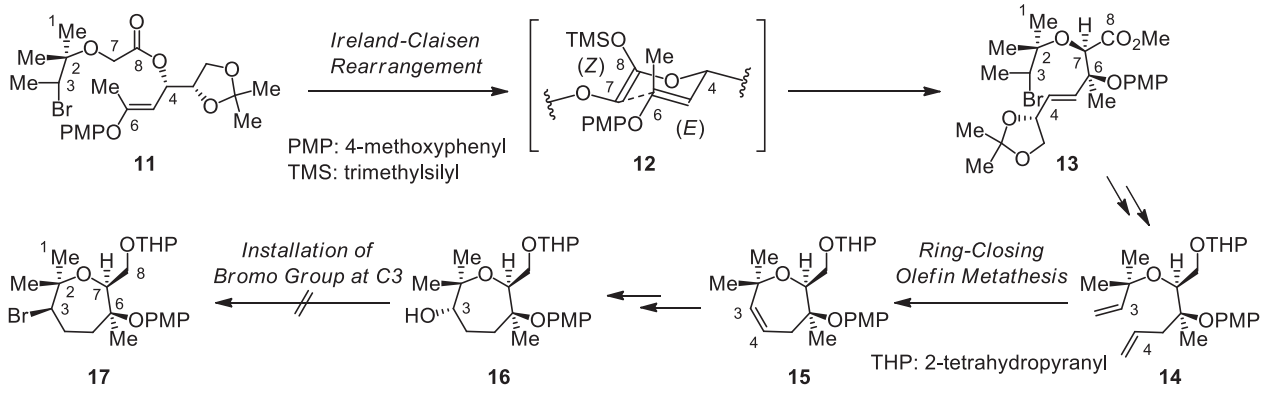


Scheme 1

RESULTS AND DISCUSSION

Previously, we reported the synthesis of oxepane **16** having the same framework as the A-ring of armatol A through a process involving the Ireland-Claisen rearrangement of ester **11** via (*Z*)-ketene silyl acetal **12** to produce **13**.[12] Conversion of **13** to diene **14**, cyclization of **14** by ring-closing olefin metathesis (RCM), and transformation of the resulting **15** produced **16**, which has a hydroxy group at C3 as a possible footing for the installation of a bromo group (Scheme 2).[5] However, all efforts for the final establishment of the bromo group at C3 were in vain.[13] Therefore, we revised the synthetic route to the A-ring in order to circumvent the late stage installation of the C3 bromo group.

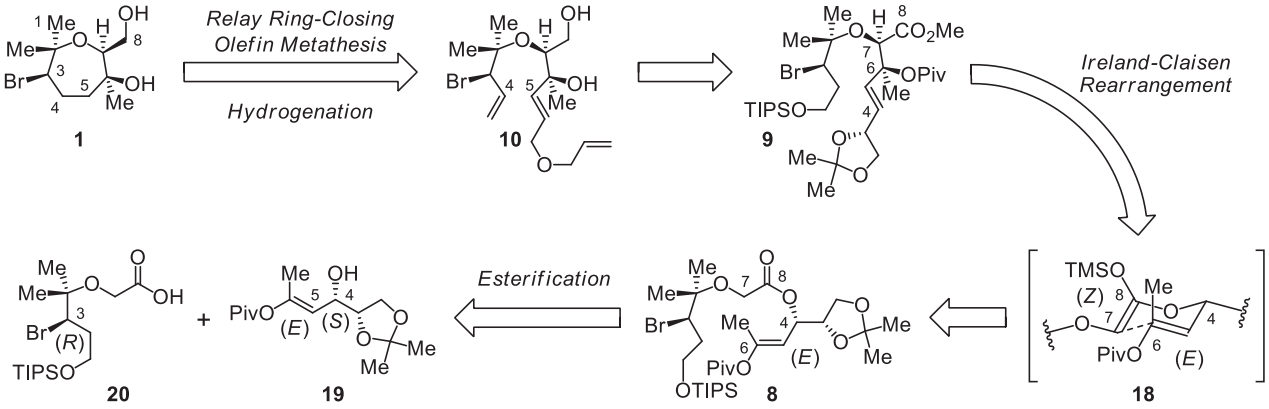
Our previous route also included several successful processes that should be retained in the revised route. In the synthesis of **16**, the establishment of the C6 and C7 stereocenters and the formation of the oxepane skeleton were successfully achieved by Ireland-Claisen rearrangement and RCM, respectively. Accordingly, we applied these two key reactions in the revised route. The previous route also showed that the bromo group at C3 of **11**, which was introduced in a non-stereoselective manner as a protecting group for the olefin group at C3 to be used for RCM, was not affected in the Ireland-Claisen rearrangement reaction. Therefore, we planned to install the bromo group at C3 stereoselectively at an earlier stage of the synthesis, and not to tamper with it later.



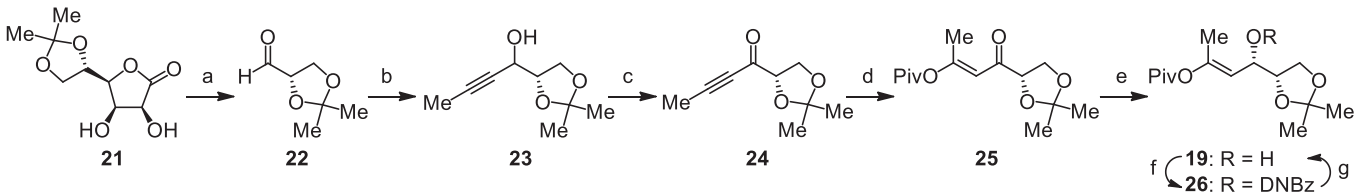
Scheme 2

The revised retrosynthetic route to the A-ring of armatol A is shown in Scheme 3. The construction of the A-ring was planned for the final stage of the synthesis via C4-C5 double bond formation from triene **10** by relay RCM followed by hydrogenation of the double bond.[14] We expected smooth ring closure at the sterically congested reactive sites (C4 and C5) by applying relay RCM, which was reported to be effective for preparing sterically hindered cyclic alkenes.[6,11] The establishment of stereocenters C6 and C7 relied on the Ireland-Claisen rearrangement of ester **8**, which would be transformed to **9** stereoselectively via (*Z*)-ketene silyl acetal **18**.[6,12] The resulting **9** would be converted to triene **10** by a

conventional process. To prevent the elimination of the oxygen functional group at C4, the electron-withdrawing pivaloyl (Piv) group was selected to stabilize ester **8** by suppressing electron donation from O6 to the adjacent double bond. The synthesis of **8** was undertaken from allylic alcohol **19** having (4*S*,5*E*)-stereochemistry and chiral carboxylic acid **20** having a bromo group at C3 with (*R*)-configuration. Alcohol **19** would be synthesized according to the previous study[6] with small modification. Carboxylic acid **20**, a bromo-substituted chiral building block, would be prepared from a chiral alcohol available from L-malic acid.



Scheme 3

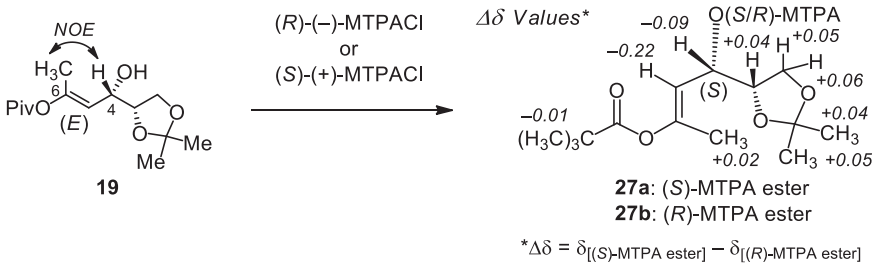


Scheme 4. Reagents and conditions: (a) $NaIO_4$, $KHCO_3$, H_2O, CH_2Cl_2, 23 °C; (b) 1-bromoprop-1-ene, BuLi, THF, –78 °C, then $MgBr_2$, –20 °C, then **22**, –20 → 0 °C; (c) DMPI, CH_2Cl_2, 23 ºC, 51% from **21**; (d) pivalic acid, DABCO, CH_2Cl_2, 25 °C, 72%; (e) $NaBH_4$, $CeCl_3$•$7H_2O$, MeOH, –78 °C, 96% (8:1 mixture of **19** and *epi*-**19**); (f) 3,5-dinitrobenzoyl chloride, Et_3N, DMAP, CH_2Cl_2, 25 °C, then separation, 88%; (g) K_2CO_3, MeOH, –20 °C, 92%.

Allylic alcohol **19** was synthesized from 5,6-*O*-isopropylidene-L-gulonic acid γ-lactone **21** (Scheme 4). Oxidative cleavage of **21** with $NaIO_4$ produced aldehyde **22**,[15] which was reacted with 1-propynyllithium, derived from 1-bromoprop-1-ene, in the presence of $MgBr_2$ to give alcohol **23**. The alcohol was oxidized with Dess-Martin periodinane (DMPI) to afford acetylene ketone **24** in 51% yield from **21**.[16] The hetero-Michael reaction of **24** with pivalic acid was successfully catalyzed by 1,4-diazabicyclo[2.2.2]octane (DABCO)[17] to furnish acyloxyvinyl ketone **25** with (*E*)-geometry in 72% yield. The diastereoselective reduction of **25**, assisted by the neighboring 2,2-dimethyl-1,3-dioxolan-4-yl

group,[18] produced the desired alcohol **19** as a major component (**19**:*epi*-**19** = 8:1, 96% combined yield) under Luche conditions,[19] though the epimers were inseparable. For the isolation of **19**, the mixture of **19** and *epi*-**19** was reacted with 3,5-dinitrobenzoyl chloride to produce a mixture of 3,5-dinitrobenzoate (DNBz) esters, which were separated by HPLC to give pure DNBz ester **26** (88%). The DNBz group of **26** was selectively removed with K_2CO_3 in MeOH at –20 °C to afford **19** in pure form (92%).

The stereochemistry of **19** was determined by NMR analysis (Scheme 5). The (*E*)-geometry of the double bond of **19** was confirmed by the presence of an NOE correlation between H4 and protons of the methyl group at C6. The (*S*)-configuration of C4 was established by application of the modified Mosher's method to **19**.[20]

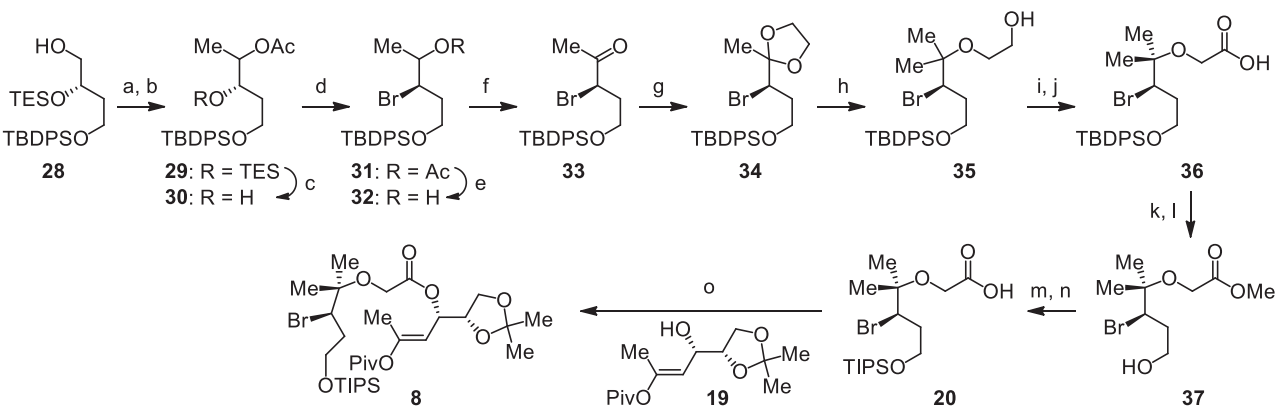


Scheme 5

The synthesis of bromo-substituted chiral building block **20** from alcohol **28**, available from L-malic acid,[21] is shown in Scheme 6. After alcohol **28** was oxidized under Swern conditions,[22] the resulting aldehyde was reacted with MeMgBr followed by Ac_2O to give acetate **29**. The triethylsilyl (TES) ether of **29** was selectively removed using pyridinium *p*-toluenesulfonate (PPTS) to produce alcohol **30** in 39% overall yield from **28**. Treatment of **30** with CBr_4 and Bu_3P in toluene at 70 °C afforded bromide **31** with inversion of stereochemistry in 84% yield without formation of byproducts caused by neighboring participation of the acetate group.[23] Next, the acetate group was removed with diisobutylaluminum hydride (DIBALH) (94%), and the resulting alcohol **32** was oxidized with Dess-Martin periodinane (DMPI)[16] to give ketone **33** (98%). The unstable ketone **33** was immediately reacted with 1,2-bis(trimethylsiloxy)ethane in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) under Noyori's conditions to furnish cyclic acetal **34** quantitatively.[24] Methylation of **34** was successfully achieved by the reaction with Me_3Al in toluene under reflux conditions (87%).[25] The resulting alcohol **35** was then subjected to Parikh-Doering oxidation[26] followed by Lindgren oxidation[27] to produce carboxylic acid **36** (83% from **35**). The optical purity of the compound was determined at this stage by HPLC analysis using a chiral column. The optical purity varied significantly according to the reaction conditions employed for the oxidation of alcohol **32**. While Dess-Martin oxidation resulted in 100–82.4% ee, Swern

oxidation showed at most 67% ee. The reaction scale of the Dess-Martin oxidation also affected the optical purity. The sub-gram scale oxidation gave a better result (~100% ee) than the gram scale oxidation (82.4% ee). The *tert*-butyldiphenylsilyl group (TBDPS) of **36** was converted to a triisopropylsilyl (TIPS) group through a process including methyl ester formation, removal of the TBDPS group, attachment of a TIPS group, and hydrolysis of the methyl ester to produce **20** in 56% yield from **36**. Thus, bromo-substituted chiral building block **20** was obtained with good optical purity.

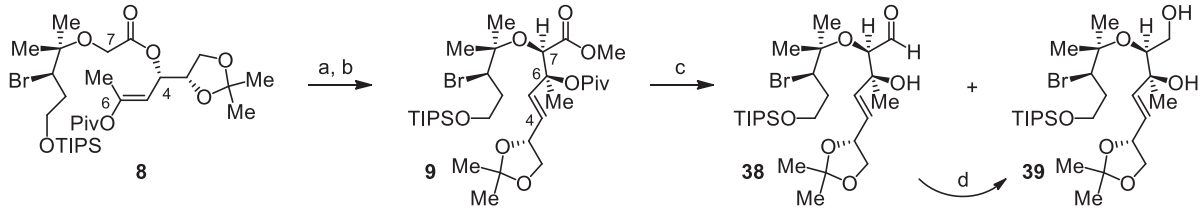
Next, ester **8** was synthesized from allylic alcohol **19** and carboxylic acid **20** by condensation with 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI•HCl) in the presence of 4-dimethylaminopyridine (DMAP) (89%) (Scheme 6). Thanks to the pivaloyl group, the stability of **8** was significantly improved over that of ester **11**, which was found to be labile in the previous study.[6] Ester **8** was stable under refrigeration for several months without decomposition.



Scheme 6. Reagents and conditions: (a) $(COCl)_2$, DMSO, CH_2Cl_2, –78 °C, then Et_3N, –78 → 0 °C; (b) MeMgBr, THF, –40 °C, then Ac_2O, –40 → 0 °C; (c) PPTS, EtOH, 0 °C, 39% from **28**; (d) CBr_4, Bu_3P, toluene, 70 °C, 84%; (e) DIBALH, CH_2Cl_2, –78 °C, 94%; (f) DMPI, CH_2Cl_2, 23 °C, 98%; (g) $(TMSOCH_2)_2$, TMSOTf, CH_2Cl_2, –20 °C, 100%; (h) Me_3Al, toluene, reflux, 87%; (i) SO_3•Py, Et_3N, DMSO, CH_2Cl_2, 0 °C; (j) $NaClO_2$, NaH_2PO_4, 2-methylbut-2-ene, *t*-BuOH, H_2O, 83% from **35**, 82.4% ee; (k) $TMSCHN_2$, MeOH, benzene, 26 °C; (l) Bu_4NF, THF, 26 °C; (m) TIPSCl, imidazole, DMAP, DMF, 25 °C; (n) K_2CO_3, MeOH, 26 °C, 56% from **36**; (o) **19**, EDCI•HCl, DMAP, CH_2Cl_2, 23 °C, 89%.

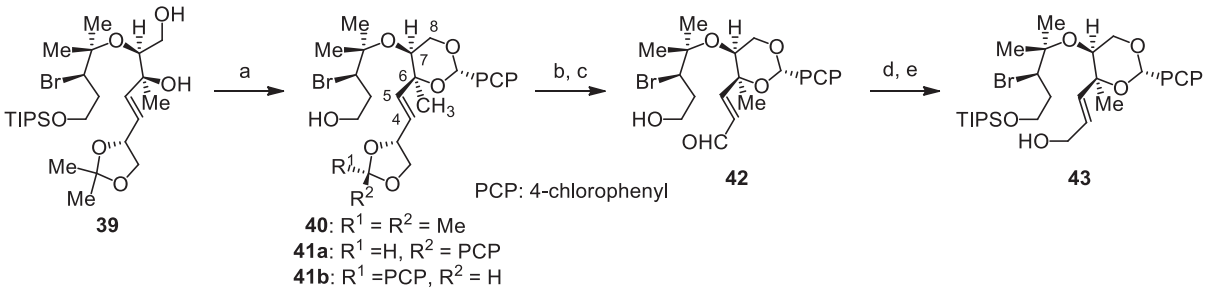
The establishment of stereocenters C6 and C7 was accomplished with ester **8** by Ireland-Claisen rearrangement (Scheme 7). After intensive optimization of reaction conditions, ester **8** was reacted with potassium bis(trimethylsilyl)amide (KHMDS) in the presence of chlorotrimethylsilane (TMSCl) in toluene at –78 °C for 30 min. The reaction mixture was treated with diethyl malonate at –78 °C to scavenge unreacted KHMDS and then warmed to 0 °C to complete the rearrangement. The resulting carboxylic acid was esterified with $TMSCHN_2$[28] to afford an 8:1 mixture of **9** and 7-*epi*-**9** in 91% yield from **8**. Interestingly, ester **8** showed reduced reactivity with lithium diisopropylamide (LDA) in toluene, which caused a low yield of products. Although the reactivity of **8** to LDA was increased in

tetrahydrofuran (THF), the rearrangement proceeded with reversed stereoselectivity. Thus, the Ireland-Claisen rearrangement of **8** using KHMDS/TMSCl in toluene was found to produce the desired **9** selectively in good yield.



Scheme 7. Reagents and conditions: (a) KHMDS, TMSCl, toluene, –78 °C, then diethyl malonate, –78 → 0 °C; (b) $TMSCHN_2$, MeOH, benzene, 26 °C, 91% from **8** (8:1 mixture of **9** and 7-*epi*-**9**); (c) DIBALH, CH_2Cl_2, –20 °C, **38**: 27%, **39**: 50%; (d) $NaBH_4$, MeOH, 26 °C, 86%.

Next, the conversion of **9** to diol **39**, including removal of the pivaloyl group and reduction of the methyl ester, was examined under reductive conditions (Scheme 7). The reduction of **9** with an excess amount of DIBALH in CH_2Cl_2 at –20 °C removed the pivaloyl group completely, but the methyl ester was only partly reduced to give aldehyde **38** (27%) and alcohol **39** (50%). Several attempts to improve the yield of **39** were unsuccessful; prolonged reaction time or warmed conditions only led to the reductive cleavage of the acetonide group. Therefore, the synthesis of **39** employed stepwise reduction via **38**, i.e., treatment of **38** with $NaBH_4$ in MeOH gave **39** in 86% yield, thereby furnishing **39** in 73% total yield from **9**. Other stereoisomers were also removed at this stage.



Scheme 8. Reagents and conditions: (a) 4-chlorobenzaldehyde dimethyl acetal, CSA, CH_2Cl_2, 26 °C; (b) 0.5 mol/L aq. HCl, MeCN, 0 °C; (c) $NaIO_4$, pH 7 buffer, MeCN, 27% from **39**; (d) TIPSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C; (e) $NaBH_4$, $CeCl_3$•$7H_2O$, MeOH, –78 °C, 94% from **42**.

The protection of the 1,3-diol moiety of **39** and the subsequent transformation of the 2,2-dimethyl-1,3-dioxolanyl group to a hydroxymethyl group were examined next (Scheme 8). A 4-chlorobenzylidene acetal was selected as a protecting group for the 1,3-diol moiety because of its expected resistance to the acidic conditions needed for the hydrolysis of the acetonide group. However, the protection of the 1,3-diol moiety with 4-chlorobenzaldehyde dimethyl acetal in the presence of

10-camphorsulfonic acid (CSA) was very slow, and therefore the removal of the TIPS group and the partial exchange of the acetonide group for a 4-chlorobenzylidene acetal group competed under these conditions. As a result, a mixture of acetal alcohols **40**, **41a** and **41b** was obtained. Fortunately, selective hydrolysis of the five-membered cyclic acetal group of each compound was achieved with 0.5 mol/L aq. HCl in MeCN at 0 °C to give the same triol. The 1,2-diol moiety of the triol was then oxidatively cleaved to give aldehyde alcohol **42** in 27% total yield from **39**. The protection of the alcohol of **42** as a TIPS ether and the subsequent Luche reduction[19] of the aldehyde group gave allylic alcohol **43** in 94% yield over two steps.

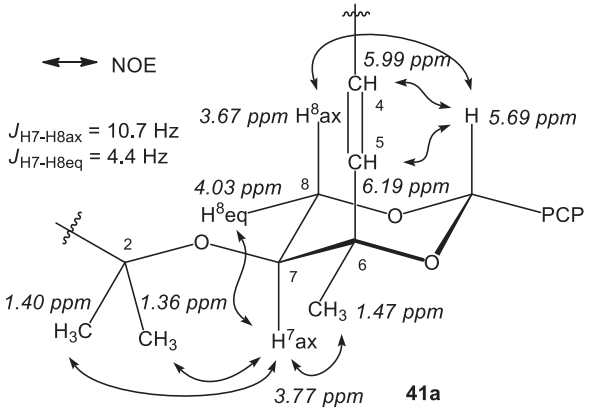
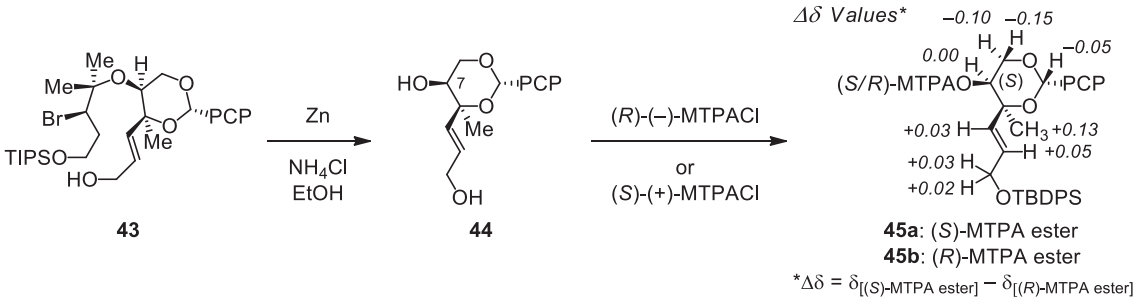


Figure 2

The relative stereochemical relationship between C6 and C7, which were constructed by the Ireland-Claisen rearrangement of **8**, was determined by NMR analysis of **41a**, which was separated from the above mixture of alcohols **40**, **41a** and **41b** by HPLC (Figure 2). The axial proton at C8 (H^8ax) of the 1,3-dioxane ring, which has a large $J_{H7-H8ax}$ value (10.7 Hz) indicating the *trans*-diaxial relationship between H^7ax and H^8ax, shows an NOE correlation with the acetal proton of the 1,3-dioxane indicating the proximate 1,3-diaxial relationship between H^8ax and the acetal proton. The axial acetal proton also shows NOE correlations with H4 and H5, which indicates that the alkenyl group at C6 is in an axial position and is proximate to the acetal proton. Accordingly, the *trans*-diaxial relationship between the alkenyl group and H^7ax is suggested. This is also supported by the absence of an NOE correlation between H^7ax and H5 or H4, which suggests that H^7ax and the alkenyl group are remote from each other. Thus, the (6*S**,7*S**) relative configuration, which originated from **9**, was determined by NMR analysis of **41a**.

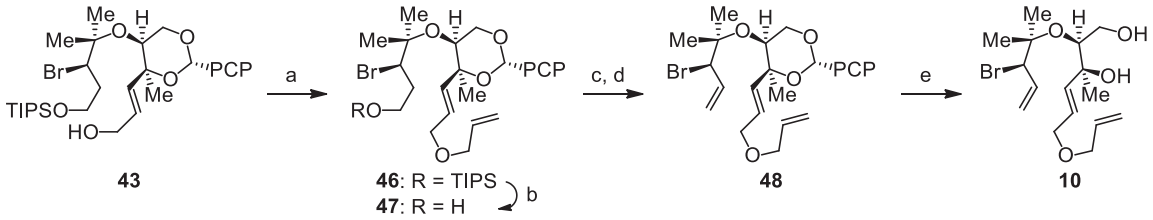
The absolute configuration of C7 was determined to be (*S*) by NMR analysis applying the modified Mosher's method[20] to alcohol **44**, which was prepared by the reductive degradation of **43** with Zn

(Scheme 9). Accordingly, from the above relative stereochemical relationship between C6 and C7, the (6*S*,7*S*) absolute stereochemistry was confirmed.



Scheme 9

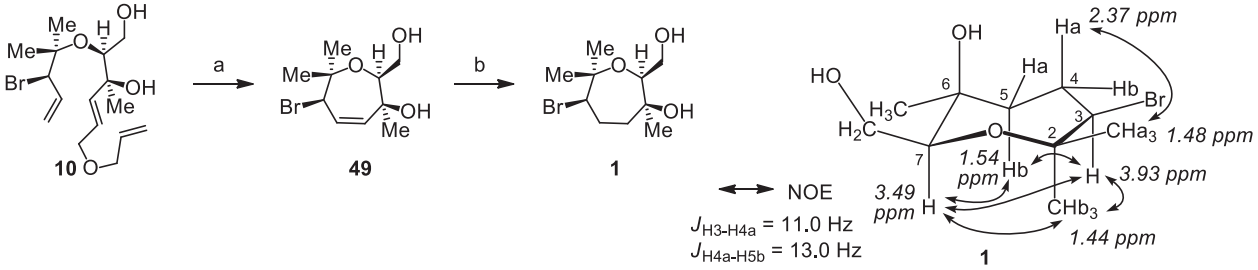
Triene **10**, a substrate for seven-membered ring formation by relay RCM at the final stage, was then synthesized from **43** (Scheme 10). After allylation of alcohol **43** under conventional conditions, the resulting **46** was desilylated with Bu_4NF to give alcohol **47** (76% from **43**). The application of Grieco-Nishizawa elimination conditions[29] to alcohol **47** successfully produced allylic bromide **48** (87%), of which the 4-chlorobenzylidene acetal was hydrolyzed under acidic conditions to afford **10** (92%).



Scheme 10. Reagents and conditions: (a) NaH, Bu_4NI, allyl bromide, DMF, 27 °C; (b) Bu_4NF, THF, 28 °C, 76% from **43**; (c) 2-nitrophenylselenocyanate, Bu_3P, THF, 28 °C; (d) 30% aq. H_2O_2, THF, 28 °C, 87% from **47**; (e) 2 mol/L aq. HCl, EtOH, 25 °C, 92%.

The completion of the synthesis of A-ring **1** is shown in Scheme 11. The successful cyclization of **10** by relay RCM with the second generation Hoveyda-Grubbs catalyst[30] required heating at reflux in xylenes and produced 7-membered ring ether **49** in 35% yield along with some oligomeric byproducts. It is notable that the treatment of **48** with the second generation Grubbs[31] or the second generation Hoveyda-Grubbs catalyst only promoted oligomerization, which rationalized the removal of the 1,3-dioxane moiety from **48** before performing relay RCM. The hydrogenation of the double bond of **49**, which employed a diimide generated in situ from 2-nitrobenzenesulfonylhydrazide (NBSH), produced A-ring **1** (≤ 43% yield).[32] The reduction was slow and required three days for completion even with an excess amount of NBSH, which was attributable to the steric congestion around the double bond.

The stereochemistry of the bromo-substituted C3 stereocenter, which originated from building block **20**, was confirmed by NMR analysis. The presence of NOE correlations H3/H7, H3/H5b, H5b/H7, H3/2-CHb$_3$, and H7/2-CHb$_3$, suggests that H3, H5b, H7, and 2-CHb$_3$ are in proximity to each other and are located on the same side of the oxepane ring with *cis*-relationships. On the other hand, H4a, which is suggested to be *anti* to both H3 and H5b by the large $J_{H3\text{-}H4a}$ (11.0 Hz) and $J_{H4a\text{-}H5b}$ (13.0 Hz), only shows an NOE enhancement with 2-CHa$_3$ at 1.48 ppm. This suggests that H4a and 2-CHa$_3$ are on the other side of the oxepane ring. Thus, the (3*R*) configuration was confirmed based on its relative relationship with the (7*S*) stereocenter, thereby completing the synthesis of the A-ring (**1**) of armatol A.



Scheme 11. Reagents and conditions: (a) the second generation Hoveyda-Grubbs catalyst, xylenes, reflux, 35%; (b) NBSH, KHCO$_3$, MeCN, 23 °C, ≤43%.

In conclusion, the stereoselective synthesis of the A-ring of armatol A, a natural polycyclic ether triterpene from the red alga *Chondria armata,* was achieved in a non-biomimetic way. The synthesis employed the Ireland-Claisen rearrangement of ester **8**, prepared from bromo-substituted chiral building block **20**, for the construction of C6 and C7 stereocenters and the relay ring-closing olefin metathesis of triene **10** for the seven-membered ring formation. Further studies toward the total synthesis of armatols are in progress in our laboratory.

EXPERIMENTAL

All air sensitive reactions were carried out under Ar atmosphere in oven-dried glassware using standard syringe, cannula and septa techniques. THF was prepared by Glass Contour Solvent Dispensing System (Nikko Hansen & Co., Ltd.). Other anhydrous solvents were purchased from commercial sources. All reactions were monitored by thin-layer chromatography (TLC) with precoated silica gel plates (Merck, silica gel 60 F_{254}). Plates were visualized by ultraviolet light and by treatment with acidic anisaldehyde or phosphomolybdic acid stain followed by heating. Chromatographic purifications were performed on silica gel (YMC, Silica Gel 60, 63–210 μm) columns with indicated eluents. Optical rotations were recorded on a JASCO P-1020 digital polarimeter at 589 nm. IR spectra were recorded on a JEOL JIR-WINSPEC100 Fourier-transform infrared spectrometer in noted states. NMR spectra were recorded on a JEOL

JNM-AL300 (^{1}H at 300 MHz, ^{13}C at 75 MHz) or a JEOL JNM-α-400 (^{1}H at 400 MHz, ^{13}C at 100 MHz) magnetic resonance spectrometer at ambient temperature. Chemical shifts (δ) are reported in ppm based on the resonance of tetramethylsilane (0 ppm for ^{1}H NMR in $CDCl_3$) or the respective solvent (^{1}H NMR: 7.15 ppm in C_6D_6; ^{13}C NMR: 77.0 ppm in $CDCl_3$, 128.0 ppm in C_6D_6) as the internal standard. High resolution mass spectra (HRMS) were measured on a JEOL JMS-T100GCV (under field desorption [FD] or field ionization (FI) conditions) or a JEOL JMS-SX102A (under chemical ionization [CI] conditions) double focusing magnetic sector mass spectrometer or a Thermo Scientific Exactive Fourier transform ion cyclotron resonance mass spectrometer (under electrospray ionization (ESI) conditions).

(*S*)-1-(2,2-Dimethyl-1,3-dioxolan-4-yl)but-2-yn-1-one (24). To a solution of **21** (8.57 g, 39.3 mmol) in CH_2Cl_2 (100 mL) and H_2O (10 mL) were added $KHCO_3$ (9.83 g, 98.2 mmol) and $NaIO_4$ (21.12 g, 98.74 mmol) at 23 ºC, and the mixture was stirred overnight. Then, anhydrous $MgSO_4$ was added to the mixture to remove H_2O. The mixture was filtered, and concentrated under reduced pressure to give crude aldehyde **22**, which was immediately used in the next reaction without further purification. To a stirred suspension of magnesium (2.86 g, 118 mmol) in THF (65 mL) was added dropwise 1,2-dibromoethane (10.1 mL, 118 mmol) via a dropping funnel. The ethene evolving reaction was exothermic, and the reaction temperature was maintained below the boiling point of THF. The mixture was further stirred at ambient temperature for 1 h. After the resulting suspension of $MgBr_2$ was cooled to –20 ºC, a solution of 1-propynyllithium, prepared by the reaction of 1-bromoprop-1-ene (6.4 mL, 75 mmol) with BuLi (1.62 mol/L in hexane, 92.0 mL, 149 mmol) in THF (65 mL) at –78 ºC for 20 min, was added to the suspension, and the mixture was stirred for 30 min at –20 ºC. To the mixture were added a solution of the above crude **22** in THF (65 mL) at –20 ºC via cannula, and the mixture was stirred at 0 ºC for 30 min. Then, the reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was roughly purified by column chromatography (silica gel, hexane/EtOAc = 5) to give crude **23** (3.79 g), which was used immediately in the next reaction. To a solution of the above crude **23** in CH_2Cl_2 (110 mL) were added DMPI (18.9 g, 44.6 mmol) at 23 ºC, and the mixture was stirred for 3 h. Then, saturated aq. $NaHCO_3$ (50 mL) and saturated aq. Na_2SO_3 (50 mL) were added, and the mixture was extracted with CH_2Cl_2 several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 8) to give **24** (3.36 g, 20.0 mmol, 51% over 3 steps); a colorless oil; $[\alpha]_D^{26}$ –30 (*c* 0.72, $CHCl_3$); IR (neat) ν 2989, 2938, 2890, 2217, 1673, 1385, 1372, 1258, 1216, 1150, 1103, 1067, 912, 845 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.42 (3H, s), 1.52 (3H, s), 2.08 (3H, s), 4.16 (1H, dd, *J* = 5.0, 8.8 Hz), 4.24 (1H, dd, *J* = 7.4, 8.8 Hz), 4.53 (1H, dd, *J* = 5.0, 7.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.3 (CH_3), 25.3 (CH_3), 26.0 (CH_3), 66.6 (CH_2), 78.2 (C),

80.9 (CH), 95.2 (C), 111.6 (C), 186.5 (C); FI-HRMS (*m*/*z*) calcd for $C_9H_{12}O_3$ [M^+]: 168.0786, found: 168.0788.

(*S*,*E*)-4-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4-oxobut-2-en-2-yl pivalate (25). To a solution of **24** (1.96 g, 11.7 mmol) in CH_2Cl_2 (120 mL) were added pivalic acid (2.0 mL, 18 mmol), DABCO (1.31 g, 11.7 mmol) at 25 ºC, and the mixture was stirred at 25 ºC for 14 h. Then, H_2O was added, and the mixture was extracted with hexane several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 15) to give **25** (2.28 g, 8.43 mmol, 72%); a pale yellow oil; $[\alpha]_D^{24}$ –52.0 (*c* 1.12, $CHCl_3$); IR (neat) ν 2983, 2938, 2916, 2876, 1753, 1700, 1624, 1481, 1465, 1458, 1384, 1373, 1274, 1213, 1152, 1107, 1084, 1062, 1032, 902, 885, 843 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$) δ 1.27 (9H, s), 1.41 (3H, s), 1.47 (3H, s), 2.35 (3H, d, *J* = 0.8 Hz), 4.06 (1H, dd, *J* = 5.5, 8.5 Hz), 4.21 (1H, dd, *J* = 7.5, 8.5 Hz), 4.46 (1H, dd, *J* = 5.5, 7.5 Hz), 6.44 (1H, q, *J* = 0.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.7 (CH_3), 25.0 (CH_3), 25.8 (CH_3), 26.6 (CH_3 × 3), 39.0 (C), 66.4 (CH_2), 80.3 (CH), 110.7 (C), 111.1 (CH), 165.7 (C), 175.3 (C), 198.5 (C); FD-HRMS calcd for $C_{14}H_{22}O_5$ [M^+]: 270.1467, found: 270.1430.

(*S*,*E*)-4-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-4-hydroxybut-2-en-2-yl pivalate (19) from 25. To a solution of **25** (2.28 g, 8.43 mmol) in MeOH (100 mL) were added $CeCl_3 \cdot 7H_2O$ (9.42 g, 25.3 mmol) and $NaBH_4$ (957 mg, 25.3 mmol) at –78 ºC, and the mixture was stirred for 20 min. Then, the reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5) to give an 8:1 mixture of **19** and its epimer at the allylic stereocenter (2.20 g, 8.08 mmol, 96% combined yield).

(*S*,*E*)-1-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-3-(pivaloyloxy)but-2-en-1-yl 3,5-dinitrobenzoate (26). After two batches of the reaction of a mixture of **19** and its epimer with 3,5-dinitrobenzoyl chloride were performed, the crude products of the two batches were combined and purified to give pure **26** as follows. To a solution of a mixture of **19** and its epimer (batch-1: 2.76 g, 10.1 mmol; batch-2: 1.29 g, 4.74 mmol) in CH_2Cl_2 (batch-1: 100 mL; batch-2: 40 mL) were added 3,5-dinitrobenzoyl chloride (batch-1: 3.50 g, 15.2 mmol; batch-2: 1.65 g, 7.16 mmol), Et_3N (batch-1: 4.3 mL, 31 mmol; batch-2: 2.0 mL, 14 mmol) and DMAP (each batch: a catalytic amount) at 25 ºC, and the mixture was stirred at 25 ºC for 10 h. Then, the reaction was quenched with H_2O, and the mixture was extracted with Et_2O several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was roughly purified by column chromatography (silica gel, hexane/EtOAc = 15) to give a mixture of **26** and its epimer at the allylic stereocenter. The

diastereomeric mixtures from batches-1 and -2 were combined and purified by preparative HPLC (YMC-Pack SIL-06, 5 μm, 500 mm × 20 mm ID, 2% EtOH in hexane; flow rate: 20 mL/min, UV 254 nm detection) to give pure **26** (5.80 g, 13.0 mmol, 88% combined yield of batches-1 and -2); a colorless amorphous; $[\alpha]_D^{24}$ +0.68 (*c* 0.925, $CHCl_3$); IR (neat) ν 3101, 2982, 2917, 2881, 2849, 1738, 1629, 1547, 1481, 1461, 1383, 1371, 1345, 1275, 1227, 1167, 1143, 1109, 1072, 919, 842, 731, 721 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$) δ 1.24 (9H, s), 1.38 (3H, s), 1.50 (3H, s), 2.11 (3H, d, *J* = 1.1 Hz), 3.88 (1H, dd, *J* = 4.9, 9.2 Hz), 4.14 (1H, dd, J = 6.6, 9.2 Hz), 4.41 (1H, ddd, *J* = 4.9, 6.6, 7.5 Hz), 5.23 (1H, qd, *J* = 1.1, 10.4 Hz), 5.77 (1H, dd, *J* = 7.5, 10.3 Hz), 9.19 (2H, d, *J* = 2.1 Hz), 9.23 (1H, t, *J* = 2.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.3 (CH_3), 25.1 (CH_3), 26.6 (CH_3), 26.9 (CH_3 × 3), 38.8 (C), 65.7 (CH_2), 74.4 (CH), 76.6 (CH), 110.6 (C), 111.4 (CH), 122.3 (CH), 129.6 (CH × 2) 133.8 (C), 148.6 (C × 2), 153.7 (C), 161.8 (C), 176.4 (C); FD-HRMS (*m*/*z*) calcd for $C_{20}H_{23}N_2O_{10}$ $[M^+–CH_3]$: 451.1353, found: 451.1380.

(*S*,*E*)-4-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-4-hydroxybut-2-en-2-yl pivalate (19) from 26. To a solution of **26** (5.26 g, 11.8 mmol) in MeOH (100 mL) and THF (100 mL) was added K_2CO_3 (1.63 g, 11.8 mmol) at –20 ºC, and the mixture was stirred for 30 min. Then, the reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with Et_2O several times. The combined organic layers were washed with saturated aq. $NaHCO_3$ and then with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5) to give pure **19** (2.96 g, 10.9 mmol, 92%); a colorless oil; $[\alpha]_D^{21}$ +6.3 (*c* 0.84, $CHCl_3$); IR (neat) ν 3466, 2983, 2936, 2909, 2876, 1743, 1700, 1481, 1457, 1437, 1383, 1371, 1280, 1258, 1215, 1135, 1066, 1035, 904, 887, 852, 834, 764 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$) δ 1.24 (9H, s), 1.37 (3H, s), 1.48 (3H, s), 1.95 (3H, d, *J* = 1.0 Hz), 2.36 (1H, d, *J* = 3.5 Hz, -OH), 3.73-3.80 (1H, m), 3.99-4.09 (2H, m), 4.22 (1H, ddd, *J* = 3.5, 6.6, 9.5 Hz), 5.11 (1H, qd, *J* = 1.0, 9.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.0 (CH_3), 25.2 (CH_3), 26.8 (CH_3), 26.9 (CH_3 × 3), 38.7 (C), 65.8 (CH_2), 69.5 (CH), 79.0 (CH), 109.9 (C), 115.7 (CH), 150.4 (C), 176.7 (C); FD-HRMS (*m*/*z*) calcd for $C_{14}H_{24}O_5$ $[M^+]$: 272.1624, found: 272.1599.

(*S*)-MTPA ester 27a. To a solution of **19** (14.5 mg, 0.0532 mmol), DMAP (a catalytic amount) and Et_3N (0.026 mL, 0.19 mmol) in CH_2Cl_2 (1 mL) was added (*R*)-(–)-MTPACl (0.030 mL, 0.16 mmol) at 24 ºC, and the mixture was stirred for 10 h. Then, the reaction was quenched with 0.2 M aq. HCl, and the mixture was extracted with Et_2O several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 30) to give (*S*)-MTPA ester **27a** (23.3 mg, 0.0477 mmol, 90%); a colorless oil; ^1H NMR (300MHz, $CDCl_3$) δ 1.24 (9H, s), 1.34 (3H, s), 1.44 (3H, s), 2.06 (3H, brs), 3.62 (3H, brs), 3.79 (1H, dd, *J* = 4.9, 9.0 Hz), 4.04 (1H, dd, J = 6.6, 9.0 Hz), 4.23 (1H, brddd, *J* = 4.9, 6.6, 8.0 Hz), 4.94 (1H, brd, *J* = 10.3 Hz), 5.63 (1H, dd, J = 8.0, 10.3 Hz), 7.34-7.43 (3H, m), 7.54-7.60 (2H, m); FD-HRMS (*m*/*z*) calcd for $C_{24}H_{31}O_7F_3$ $[M^+]$: 488.2022, found: 488.2004.

(*R*)-MTPA ester 27b. According to the preparation procedure for **27a**, (*R*)-MTPA ester **27b** was prepared from **19** (17.5 mg, 0.0642 mmol), DMAP (a catalytic amount), Et_3N (0.032 mL, 0.23 mmol), and (*S*)-(+)-MTPACl (0.036 mL, 0.19 mmol); a colorless oil; ^{1}H NMR (300MHz, $CDCl_3$) δ 1.25 (9H, s), 1.30 (3H, s), 1.39 (3H, s), 2.04 (3H, d, *J* = 1.0 Hz), 3.56 (3H, brs), 3.74 (1H, dd, *J* = 5.0, 9.0 Hz), 3.98 (1H, dd, *J* = 6.6, 9.0 Hz), 4.19 (1H, brddd, J = 5.0, 6.6, 7.0 Hz), 5.16 (1H, qd, *J* = 1.0, 10.3 Hz), 5.72 (1H, dd, *J* = 7.0, 10.3 Hz), 7.36-7.43 (3H, m), 7.49-7.60 (2H, m); FD-HRMS (*m*/*z*) calcd for $C_{24}H_{31}O_7F_3$ [M^+]: 488.2022, found: 488.2004.

(3*S*)-5-[(*tert*-Butyldiphenylsilyl)oxy]-3-hydroxypentan-2-yl acetate (30). To a solution of $(COCl)_2$ (2.87 mL, 32.9 mmol) in CH_2Cl_2 (110 mL) was added DMSO (3.11 mL, 43.8 mmol) at –78 ºC, and the mixture was stirred for 10 min. Then, to the stirred mixture was added slowly a solution of **28** (5.03 g, 11.0 mmol) in CH_2Cl_2 (22 mL) via cannula, and the mixture was stirred for 15 min. Then, to the mixture was added dropwise Et_3N (12.2 mL, 87.5 mmol) at –78 ºC, and the mixture was stirred for 30 min at 0 ºC. Then, H_2O was added, and the mixture was extracted with hexane several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude aldehyde, which was immediately used in the next reaction. To a solution of the crude aldehyde in THF (110 mL) was added MeMgBr (3.0 mol/L in THF, 11.0 mL, 33.0 mmol) at –40 ºC, and the mixture was stirred for 1 h. Then, to the mixture was added Ac_2O (6.22 mL, 65.8 mmol) at –40 ºC, and the mixture was stirred for 3 h at 0 ºC. Then, the reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was roughly purified by column chromatography (silica gel, hexane/EtOAc = 50) to give an inseparable mixture of **29** and small amounts of byproducts, which was used in the next reaction without further purification. To a solution of the above mixture of **29** and byproducts in EtOH (70 mL) was added PPTS (10 mg) at 0 ºC, and the mixture was stirred for 10 h. Then, saturated aq. $NaHCO_3$ was added, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 10) to give **30** (1.74 g, 4.34 mmol, 39% from **28**, a 9:5 mixture of diastereomers); a colorless oil; IR (neat) ν 3494, 3071, 3050, 3015, 2957, 2931, 2885, 2858, 1737, 1472, 1463, 1428, 1372, 1244, 1112, 1028, 938, 823, 738, 702, 688, 614 cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$) δ 1.05 (9H, s), 1.25 (3H×9/14, d, *J* = 6.4 Hz), 1.26 (3H×5/14, d, *J* = 6.4 Hz), 1.64-1.75 (2H, m), 2.06 (3H×9/14, s), 2.08 (3H×5/14, s), 2.99 (1H×5/14, brd, *J* = 3.8 Hz), 3.25 (1H×9/14, brd, *J* = 2.8 Hz), 3.80-3.99 (3H, m), 4.82-4.95 (1H, m), 7.34-7.48 (6H, m), 7.62-7.70 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.7 (CH_3 × 9/14), 16.0 (CH_3×5/14), 19.0 (C), 21.22 (CH_3 × 5/14), 21.27 (CH_3 × 9/14), 26.8 (CH_3 × 3), 34.1 (CH_2 × 9/14), 34.7 (CH_2 × 5/14), 62.4 (CH_2 × 5/14), 62.9 (CH_2 × 9/14), 72.6 (CH × 5/14),

72.9 (CH × 9/14), 73.2 (CH × 5/14), 73.5 (CH × 9/14), 127.8(CH × 4), 129.8 (CH × 2), 132.8 (C), 132.9 (C), 135.5 (CH × 4), 170.5 (C × 9/14), 170.6 (C × 5/14); FD-HRMS (*m*/*z*) calcd for $C_{23}H_{33}O_4Si$ [M+H$^+$]: 401.2148, found: 401.2177.

(3*R*)-3-Bromo-5-[(*tert*-butyldiphenylsilyl)oxy]pentan-2-yl acetate (31). To a solution of **30** (247.6 mg, 0.618 mmol) in toluene (9 mL) were added CBr_4 (1.04 g, 3.14 mmol) and Bu_3P (1.55 mL, 6.28 mmol) at 27 ºC, and the mixture was heated to 70 ºC and stirred for 3.5 h. Then, H_2O was added, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 70) to give **31** (241.6 mg, 0.521 mmol, 84%, a 9:5 mixture of diastereomers); a pale yellow oil; IR (neat) ν 3071, 3050, 3014, 2958, 2931, 2881, 2858, 1743, 1472, 1463, 1428, 1372, 1234, 1186, 1112, 1030, 1009, 957, 936, 823, 738, 702, 688, 614 cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$) δ 1.049 (9H × 9/14, s), 1.054 (9H × 5/14, s), 1.32 (3H × 5/14, d, *J* = 6.3 Hz), 1.35 (3H × 9/14, d, *J* = 6.3 Hz), 1.79-1.96 (1H, m), 2.02-2.17 (1H, m), 2.06 (3H × 9/14, s), 2.09 (3H × 5/14, s), 3.76-3.91 (2H, m), 4.31-4.45 (1H, m), 4.99-5.14 (1H, m), 7.34-7.47 (6H, m), 7.61-7.71 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.7 (CH_3 × 5/14), 17.5 (CH_3 × 9/14), 19.2 (C), 21.0 (CH_3 × 9/14), 21.1 (CH_3 × 5/14), 26.8 (CH_3 × 3), 37.1 (CH_2 × 5/14), 37.2 (CH_2 × 9/14), 54.0 (CH × 9/14), 54.9 (CH × 5/14), 61.0 (CH_2 × 9/14), 61.1 (CH_2 × 5/14), 72.0 (CH × 9/14), 72.5 (CH × 5/14), 127.7 (CH × 4), 129.7 (CH × 2), 133.4 (C), 133.5 (C), 135.47 (CH × 2), 135.54 (CH × 2), 170.06 (C × 9/14), 170.10 (C × 5/14); FD-HRMS (*m*/*z*) calcd for $C_{19}H_{22}O_3Si^{79}Br$ [M$^+$–*t*-Bu]: 405.0522, found: 405.0531.

(3*R*)-3-Bromo-5-[(*tert*-butyldiphenylsilyl)oxy]pentan-2-ol (32). To a solution of **31** (2.83 g, 6.11 mmol) in CH_2Cl_2 (60 mL) was added DIBALH (1.02 mol/L in hexane, 18.0 mL, 18.4 mmol) at –78 ºC, and the mixture was stirred at –78 ºC for 1 h. Then, the reaction was quenched with saturated aq. potassium sodium tartrate, and the mixture was stirred at ambient temperature for 2 h. Then, the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 20) to give **32** (2.41 g, 5.72 mmol, 94%, a 9:5 mixture of diastereomers); a colorless oil; IR (neat) ν 3423, 3071, 3050, 2958, 2930, 2858, 1472, 1463, 1428, 1389, 1362, 1259, 1185, 1112, 1009, 933, 823, 738, 702, 688, 614 cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$) δ 1.05 (9H, s), 1.29 (3H × 5/14, d, *J* = 6.2 Hz), 1.32 (3H × 9/14, d, *J* = 6.2 Hz), 1.97-2.22 (2H, m), 2.28 (1H × 9/14, brd, *J* = 6.9 Hz, OH), 2.50 (1H × 5/14, brd, *J* = 6.5 Hz, OH), 3.72-4.02 (3H, m), 4.32 (1H × 9/14, brtd, *J* = 4.2, 9.0 Hz), 4.42 (1H × 5/14, brtd, *J* = 4.3, 8.1 Hz), 7.34-7.48 (6H, m), 7.62-7.70 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1 (C), 19.4 (CH_3 × 5/14), 21.3 (CH_3 × 9/14), 26.8 (CH_3 × 3), 36.4 (CH_2 × 5/14), 38.3 (CH_2 × 9/14), 61.2 (CH_2 × 5/14), 61.40 (CH × 5/14), 61.45 (CH_2 × 9/14), 62.4 (CH × 9/14), 70.1 (CH × 9/14), 70.6 (CH × 5/14), 127.7(CH × 4), 129.7 (CH ×2), 133.3 (C), 133.4 (C),

135.47 (CH × 2), 135.53 (CH × 2); FD-HRMS (*m*/*z*) calcd for $C_{21}H_{30}O_2Si^{79}Br$ [M+H$^+$]: 421.1198, found: 421.1185.

(*R*)-3-Bromo-5-[(*tert*-butyldiphenylsilyl)oxy]pentan-2-one (33). To a solution of **32** (530 mg, 1.26 mmol) in CH_2Cl_2 (15 mL) was added DMPI (1.18 g, 2.78 mmol) at 23 ºC, and the mixture was stirred for 1 h. Then, $NaHCO_3$ (1.0 g) and saturated aq. $Na_2S_2O_3$ (10 mL) were added, and the mixture was extracted with hexane several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 50) to give **33** (515 mg, 1.23 mmol, 98%). Ketone **33** was immediately used in the next reaction due to instability; a colorless oil; $[\alpha]_D^{24}$ +59.6 (*c* 0.810, $CHCl_3$); IR (neat) ν 3071, 3050, 3014, 2999, 2958, 2931, 2884, 2858, 1720, 1472, 1463, 1428, 1390, 1361, 1257, 1230, 1146, 1112, 1008, 998, 926, 823, 738, 702, 688, 615 cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$) δ 1.05 (9H, s), 2.06 (1H, tdd, *J* = 4.5 8.6, 14.5 Hz), 2.30 (1H, tdd, *J* = 5.6, 8.1, 14.5 Hz), 2.37 (3H, s), 3.72-3.85 (2H, m), 4.61 (1H, dd, *J* = 5.6, 8.6 Hz), 7.34-7.48 (6H, m), 7.60-7.69 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.2 (C), 26.6 (CH_3), 26.8 (CH_3 × 3), 36.1 (CH_2), 51.0 (CH), 60.8 (CH_2), 127.7 (CH × 4), 129.8 (CH × 2), 133.18 (C), 133.23 (C), 135.44 (CH × 2), 135.51 (CH × 2), 201.6 (C); FD-HRMS (*m*/*z*) calcd for $C_{21}H_{28}O_2Si^{79}Br$ [M+H$^+$]: 419.1042, found: 419.1069.

(*R*)-[3-Bromo-3-(2-methyl-1,3-dioxolan-2-yl)propoxy](*tert*-butyl)diphenylsilane (34). To a solution of **33** (492 mg, 1.17 mmol) and $(TMSOCH_2)_2$ (2.88 mL, 11.7 mmol) in CH_2Cl_2 (10 mL) was added TMSOTf (0.113 mL, 0.587 mmol) at –20 ºC, and the mixture was stirred for 18 h. Then, saturated aq. $NaHCO_3$ (10 mL) was added, and the mixture was extracted with hexane several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 50) to give **34** (552 mg, 1.18 mmol, 100%); a colorless oil; $[\alpha]_D^{25}$ +22.9 (*c* 0.910, $CHCl_3$); IR (neat) ν 3071, 3049, 2957, 2930, 2883, 2858, 1472, 1463, 1446, 1428, 1380, 1362, 1307, 1274, 1252, 1218, 1188, 1145, 1112, 1057, 1038, 1008, 998, 949, 937, 874, 823, 738, 702, 688, 614 cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$) δ 1.05 (9H, s), 1.50 (3H, s), 1.81 (1H, tdd, *J* = 3.6, 11.3, 14.4 Hz), 2.32 (1H, dddd, *J* = 2.0, 6.1, 9.6, 14.4 Hz), 3.79-3.93 (2H, m), 3.96-4.07 (4H, m), 4.29 (1H, dd, *J* = 2.0, 11.3 Hz), 7.34-7.47 (6H, m), 7.64-7.72 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.2 (C), 20.8 (CH_3), 26.8 (CH_3 × 3), 36.7 (CH_2), 55.8 (CH), 61.2 (CH_2), 65.3 (CH_2), 65.4 (CH_2), 109.7 (C), 127.7 (CH × 4), 129.6 (CH × 2), 133.5 (C), 133.6 (C) 135.5 (CH × 2), 135.6 (CH × 2); FD-HRMS (*m*/*z*) calcd for $C_{23}H_{32}O_3Si^{79}Br$ [M$^+$–H]: 463.1304, found: 463.1278.

(*R*)-2-({3-Bromo-5-[(*tert*-butyldiphenylsilyl)oxy]-2-methylpentan-2-yl}oxy)ethanol (35). To compound **34** (9.10 g, 19.6 mmol) was added Me_3Al (1.8 mol/L in toluene, 70 mL, 126 mmol) at ambient temperature, and the mixture was refluxed for 18 h. Then, the mixture was cooled to ambient temperature

and diluted with hexane (100 mL). To the mixture was added 1 M aq. HCl (150 mL) carefully. The mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5) to give **35** (8.15 g, 17.0 mmol, 87%); a colorless oil; $[\alpha]_D^{24}$ +21.0 (*c* 0.990, $CHCl_3$); IR (neat) ν 3446, 3071, 3049, 2957, 2930, 2858, 1472, 1428, 1385, 1366, 1233, 1188, 1133, 1112, 1051, 1008, 998, 940, 893, 823, 738, 702, 688, 665, 614 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$) δ 1.06 (9H, s), 1.32 (3H, s), 1.35 (3H, s), 1.80 (1H, tdd, *J* = 3.4, 11.1, 14.6 Hz), 2.09 (1H, brs, OH), 2.24 (1H, dddd, *J* = 1.4, 6.2, 9.4, 14.6 Hz), 3.51 (2H, brt, *J* = 4.4 Hz), 3.69 (2H, brs), 3.80-3.95 (2H, m), 4.39 (1H, dd, *J* = 1.4, 11.1 Hz), 7.33-7.48 (6H, m), 7.61-7.73 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.2 (C), 22.6 (CH_3), 23.9 (CH_3), 26.9 (CH_3 × 3), 36.5 (CH_2), 60.0 (CH), 61.6 (CH_2), 62.1 (CH_2), 62.6 (CH_2), 76.6 (C), 127.7 (CH × 4), 129.7 (CH × 2), 133.5 (C), 133.6 (C), 135.5 (CH × 2), 135.6 (CH × 2); FD-HRMS (*m*/*z*) calcd for $C_{24}H_{36}O_3Si^{79}Br$ [M+H^+]: 479.1617, found: 479.1601.

(*R*)-2-({3-Bromo-5-[(*tert*-butyldiphenylsilyl)oxy]-2-methylpentan-2-yl}oxy)acetic acid (36). To a solution of **35** (8.15 g, 17.0 mmol), Et_3N (11.8 mL, 85.0 mmol), and DMSO (65 mL) in CH_2Cl_2 (100 mL) was added SO_3·pyridine complex (8.12 g, 51.0 mmol) at 0 ºC, and the mixture was stirred for 1.5 h. Then, H_2O (100 mL) was added, and the mixture was extracted with hexane several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was roughly purified by column chromatography (silica gel, hexane/EtOAc = 20) to give an aldehyde (6.77 g). To a solution of the aldehyde and 2-methylbut-2-ene (7.2 mL, 86 mmol) in *t*-BuOH (80 mL) and H_2O (40 mL) were added NaH_2PO_4 (10.2 g, 85.0 mmol) and $NaClO_2$ (3.84 g, 42.5 mmol) at 0 ºC, and the mixture was stirred at 21 ºC for 10 h. Then, the mixture was extracted with $CHCl_3$ several times. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5) to give **36** (6.95 g, 14.1 mmol, 83%). Optical purity of **36** was able to be determined by chiral HPLC analysis using a pre-packed column supplied by Daicel Corporation (Chiralpak IA, 250 mm × 4.6 mm ID, hexane:CH_2Cl_2:TBME:TFA = 200:86:4:1; flow rate: 1.0 mL/min, UV 254 nm detection). (*R*)-**36**: t_R =10.1 min; (*S*)-**36**: t_R = 12.5 min. The enantiomeric excess of **36** obtained here was 82.4%ee; a colorless oil; $[\alpha]_D^{22}$ +23 (*c* 0.15, $CHCl_3$); IR (neat) ν 3500-2400 (broad), 3071, 3050, 2957, 2931, 2884, 2857, 1732, 1471, 1428, 1386, 1370, 1236, 1188, 1133, 1112, 1053, 1008, 998, 939, 911, 890, 823, 738, 703, 688, 614 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$) δ 1.06 (9H, s), 1.36 (3H, s), 1.37 (3H, s), 1.81 (1H, tdd, *J* = 3.4, 11.3, 14.6 Hz), 2.15 (1H, dddd, *J* = 1.7, 6.2, 9.4, 14.6 Hz), 3.81-3.95 (2H, m), 4.06 (2H, s), 4.35 (1H, dd, *J* = 1.7, 11.3 Hz) 7.34-7.48 (6H, m), 7.61-7.70 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1 (C), 22.7 (CH_3), 23.1 (CH_3), 26.8 (CH_3 × 3), 36.4 (CH_2), 59.5 (CH), 60.0 (CH_2),

61.3 (CH_2), 78.6 (C), 127.7 (CH×4), 129.7 (CH × 2), 133.3 (C), 133.4 (C), 135.4 (CH × 2), 135.5 (CH × 2), 173.0 (C); FD-HRMS (*m*/*z*) calcd for $C_{24}H_{34}O_4Si^{79}Br$ [M+H^+]: 493.1410, found: 493.1380.

(*R*)-2-({3-Bromo-2-methyl-5-[(triisopropylsilyl)oxy]pentan-2-yl}oxy)acetic acid (20). To a solution of **36** (2.13 g, 4.32 mmol) in MeOH (10 mL) and benzene (30 mL) was added $TMSCHN_2$ (2 mol/L in Et_2O, 4.32 mL, 8.64 mmol) at 26 ºC, and the mixture was stirred for 15 min. Then, the mixture was concentrated under reduced pressure to give a crude methyl ester, which was used in the next reaction without purification. To a solution of the crude methyl ester in THF (40 mL) was added Bu_4NF (1 mol/L in THF, 8.6 mL, 8.6 mmol) at 26 ºC, and the mixture was stirred for 1 h. Then, saturated aq. NH_4Cl was added, and the mixture was extracted with hexane several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 10 → 5 → 2 → 1) to give **37** (993 mg, a colorless oil), which was used immediately in the next reaction. To a solution of the above **37**, imidazole (680 mg, 9.99 mmol), and DMAP (a catalytic amount) in DMF (30 mL) was added TIPSCl (1.05 mL, 4.96 mmol) at 25 ºC, and the mixture was stirred for 3 h. Then, saturated aq. $NaHCO_3$ was added, and the mixture was extracted with hexane several times. The combined organic layers were washed with 1 mol/L aq. HCl and then with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was roughly purified by column chromatography (silica gel, hexane/EtOAc = 50) to give a mixture of a TIPS ether and TIPSOH. The mixture was dissolved in MeOH (30 mL), and to the stirred mixture was added 1 mol/L aq. K_2CO_3 (10 mL, 10 mmol) at 26 ºC. After the mixture was stirred for 3 d, the mixture was acidified with 1 mol/L aq. HCl and extracted with $CHCl_3$ several times. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5) to give **20** (998.6 mg, 2.427 mmol, 56% over 4 steps); a colorless oil; $[\alpha]_D^{23}$ +20.3 (*c* 0.105, $CHCl_3$); IR (neat) ν 3600-2400 (broad), 2926, 2867, 1737, 1463, 1426, 1385, 1369, 1246, 1134, 1110, 1071, 1057, 1014, 996, 883, 745, 681, 659, 642 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$) δ 0.98-1.18 (21H, m), 1.38 (3H, s), 1.39 (3H, s), 1.86 (1H, tdd, *J* = 3.3, 11.1, 14.5 Hz), 2.13 (1H, dddd, *J* = 1.7, 7.1, 8.6, 14.5 Hz), 3.85-3.94 (2H, m), 4.06 (2H, s), 4.35 (1H, dd, *J* = 1.7, 11.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.9 (CH × 3), 18.0 (CH_3 × 6), 22.8 (CH_3), 22.9 (CH_3), 36.9 (CH_2), 59.8 (CH), 59.9 (CH_2), 60.7 (CH_2), 78.8 (C), 172.0 (C); FD-HRMS (*m*/*z*) calcd for $C_{17}H_{36}O_4Si^{79}Br$ [M+H^+]: 411.1566, found: 411.1576.

(1*S*,2*E*)-1-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-3-(pivaloyloxy)but-2-en-1-yl 2-[{(*R*)-3-bromo-2-methyl-5-[(triisopropylsilyl)oxy]pentan-2-yl}oxy]acetate (8). To a stirred solution of **19** (96.0 mg, 0.353 mmol), **20** (131 mg, 0.318 mmol), and DMAP (a catalytic amount) in CH_2Cl_2 (5 mL) was added EDCI·HCl (122 mg, 0.638 mmol) at 23 ºC, and the mixture was stirred for 10 h. Then, H_2O was added, and the mixture was extracted with Et_2O several times. The combined organic layers were washed with

brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 20) to give **8** (189 mg, 0.284 mmol, 89%); a colorless oil; $[\alpha]_D^{21}$ +22.5 (*c* 0.815, $CHCl_3$); IR (neat) ν 2960, 2942, 2868, 1747, 1696, 1481, 1464, 1384, 1370, 1281, 1258, 1228, 1193, 1109, 1071, 1014, 998, 968, 940, 920, 883, 847, 746, 681, 659, 638 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$) δ 0.98-1.18 (21H, m), 1.23 (9H, s), 1.35 (3H, s), 1.37 (3H, s), 1.40 (3H, s), 1.44 (3H, s), 1.82 (1H, brtdd, *J* = 3.3, 11.3, 14.5 Hz), 2.01 (3H, s), 2.31 (1H, brtd, *J* = 7.8, 14.5 Hz), 3.79 (1H, dd, *J* = 5.1, 9.0 Hz), 3.84-3.91 (2H, m), 4.03 (1H, dd, *J* = 6.5, 9.0 Hz), 4.05 (1H, d, *J* = 15.5 Hz), 4.15 (1H, d, *J* = 15.5 Hz), 4.15-4.23 (1H, m), 4.29 (1H, brd, *J* = 11.3 Hz), 5.00 (1H, d, *J* = 10.2 Hz), 5.48 (1H, dd, *J* = 7.3, 10.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.8 (CH × 3), 16.2 (CH_3), 17.9 (CH_3 × 6), 22.4 (CH_3), 23.9 (CH_3), 25.3 (CH_3), 26.5 (CH_3), 26.9 (CH_3×3), 36.5 (CH_2), 38.7 (C), 58.9 (CH), 60.4 (CH_2), 60.8 (CH_2), 65.7 (CH_2), 71.9 (CH), 76.6 (CH), 78.0 (C), 110.2 (C), 111.8 (CH), 152.7 (C), 169.7 (C), 176.4 (C); CI-HRMS (*m*/*z*) calcd for $C_{34}H_{67}NO_8Si^{79}Br$ [M+*i*-$PrNH_3^+$]: 724.3819, found: 724.3810.

(2*R*,3*S*,*E*)-Methyl 2-({(*R*)-3-bromo-2-methyl-5-[(triisopropylsilyl)oxy]pentan-2-yl}oxy)-5-[(*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-3-methyl-3-(pivaloyloxy)pent-4-enoate (9). To a solution of **8** (196 mg, 0.294 mmol) in toluene (5 mL) was added TMSCl (0.375 mL, 2.95 mmol) at –78 ºC, and the mixture was stirred for 5 min. To the mixture was added KHMDS (0.5 mol/L in toluene, 5.90 mL, 2.95 mmol), and the mixture was stirred for 30 min. Then, diethyl malonate (0.90 mL, 5.9 mmol) was added, and the mixture was warmed to 0 ºC and stirred for 1 h. Then, saturated aq. NH_4Cl was added, and the mixture was extracted with $CHCl_3$ several times. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was roughly purified by short column chromatography (silica gel, hexane/EtOAc = 10 → $CHCl_3$) to give a crude carboxylic acid. To a solution of the crude carboxylic acid in benzene (3.75 mL) and MeOH (1.25 mL) was added $TMSCHN_2$ (2 mol/L in Et_2O, 0.44 mL, 0.88 mmol) at 26 ºC, and the mixture was stirred for 15 min. Then, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 30) to give an 8:1 mixture of **9** and its C7-epimer (181.3 mg, 0.267 mmol, 91% over 2 steps); a colorless oil; $[\alpha]_D^{21}$ –4.88 (*c* 1.00, $CHCl_3$); IR (neat) ν 2943, 2868, 1755, 1737, 1480, 1463, 1435, 1390, 1380, 1370, 1282, 1254, 1210, 1157, 1130, 1107, 1063, 1030, 1014, 996, 967, 939, 918, 902, 882, 864, 877, 768, 749, 681, 660, 645 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$) δ 0.98-1.18 (21H, m), 1.18 (3H, s), 1.19 (9H, s), 1.37 (3H, s), 1.38 (3H, s), 1.43 (3H, s), 1.64 (3H, s), 1.77 (1H, tdd, *J* = 3.6, 11.3, 14.8 Hz), 2.46 (1H, brtd, *J* = 8.2, 14.8 Hz), 3.55 (1H, t, *J* = 7.8 Hz), 3.63 (3H, s), 3.82-3.97 (2H, m), 4.09 (1H, dd, *J* = 6.3, 8.2 Hz), 4.20 (1H, brd, *J* = 11.3 Hz), 4.52 (1H, brq, *J* = 7.1 Hz), 4.88 (1H, s), 5.64 (1H, dd, *J* = 7.7, 15.7 Hz), 5.98 (1H, d, *J* = 15.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.9 (CH × 3), 17.9 (CH_3 × 6), 20.8 (CH_3), 21.1 (CH_3), 23.6 (CH_3), 25.7 (CH_3), 26.6 (CH_3), 27.1 (CH_3 × 3), 36.6 (CH_2), 39.4 (C), 51.4 (CH_3),

61.0 (CH_2), 61.1 (CH), 69.4 (CH_2), 74.6 (CH), 76.6 (CH), 79.3 (C), 81.4 (C), 109.3 (C), 127.5 (CH), 133.6 (CH), 171.4 (C), 177.0 (C); FD-HRMS (*m*/*z*) calcd for $C_{32}H_{59}O_8Si^{79}Br$ [M^+]: 678.3163, found: 678.3172.

(2*S*,3*S*,*E*)-2-({(*R*)-3-Bromo-2-methyl-5-[(triisopropylsilyl)oxy]pentan-2-yl}oxy)-5-[(*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-3-methylpent-4-ene-1,3-diol (39). To a solution of a mixture of **9** and its C7-epimer (181 mg, 0.266 mmol) in CH_2Cl_2 (4 mL) was added DIBALH (1.02 mol/L in hexane, 2.61 mL, 2.66 mmol) at –20 ºC, and the mixture was stirred at –20 ºC for 1 h. Then, MeOH was added dropwise, and then saturated aq. potassium sodium tartrate was added. The mixture was stirred for 1 h. Then, the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5 → 2) to give **39** (a colorless oil, 75.7 mg, 0.133 mmol, 50%) and **38** (a colorless oil, 39.9 mg, 0.0705 mmol, 27%). The products from C7-epimeric **9** were separable at this stage. Aldehyde **38** was immediately reduced to **39** as follows. To a solution of the above **38** (39.9 mg, 0.0705 mmol) in MeOH (1 mL) was added $NaBH_4$ (8.0 mg, 0.21 mmol) at 26 ºC, and the mixture was stirred for 30 min. Then, saturated aq. NH_4Cl was added, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5 → 2) to give **39** (a colorless oil, 34.3 mg, 0.0604 mmol, 86% from **38**). The combined yield of **39** from **9** was 73% (total amount of **39**: 110.0 mg, 0.194 mmol); a colorless oil; $[\alpha]_D^{21}$ +14 (*c* 0.22, $CHCl_3$); IR (neat) ν 3416, 2926, 2867, 1463, 1454, 1381, 1370, 1246, 1222, 1156, 1128, 1107, 1061, 1013, 996, 978, 939, 919, 882, 865, 745, 681 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$) δ 1.00-1.20 (21H, m), 1.35 (6H, s), 1.38 (3H, s), 1.39 (3H, s), 1.43 (3H, s), 1.87 (1H, tdd, *J* = 3.6, 11.2, 14.5 Hz), 2.23 (1H, dddd, *J* = 1.6, 6.7, 8.9, 14.5 Hz), 2.42 (1H, t, *J* = 5.8 Hz, OH), 2.77 (1H, brs, OH), 3.51 (1H, t, *J* = 4.3 Hz), 3.61 (1H, t, *J* = 8.0 Hz), 3.66-3.76 (2H, m), 3.85-3.94 (2H, m), 4.10 (1H, dd, *J* = 6.1, 8.1 Hz), 4.24 (1H, dd, *J* = 1.6, 11.2 Hz), 4.54 (1H, ddd, *J* = 6.1, 7.3, 8.1 Hz), 5.77 (1H, dd, *J* = 7.3, 15.5 Hz), 5.90 (1H, d, *J* = 15.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.9 (CH × 3), 18.0 (CH_3 × 6), 23.5 (CH_3), 24.6 (CH_3), 25.0 (CH_3), 25.9 (CH_3), 26.7 (CH_3), 37.1 (CH_2), 61.1 (CH_2), 63.4 (C), 63.8 (CH), 69.5 (CH_2), 75.3 (C), 76.5 (CH), 76.7 (CH), 78.2 (C), 109.4 (C), 127.1 (CH), 138.5 (CH); FD-HRMS (*m*/*z*) calcd for $C_{26}H_{52}O_6Si^{79}Br$ [$M+H^+$]: 567.2717, found: 567.2723.

(*E*)-3-[(2*S*,4*S*,5*S*)-5-{[(*R*)-3-Bromo-5-hydroxy-2-methylpentan-2-yl]oxy}-2-(4-chlorophenyl)-4-methyl-1,3-dioxan-4-yl]acrylaldehyde (42). To a solution of **39** (110 mg, 0.194 mmol) in CH_2Cl_2 (4 mL) were added 4-chlorobenzaldehyde dimethyl acetal (0.0640 mL, 0.387 mmol) and CSA (a catalytic amount) at 26 ºC, and the mixture was stirred for 13 h. Then, saturated aq. $NaHCO_3$ was added, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine,

dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was roughly purified by column chromatography (silica gel, hexane/EtOAc = 30) to give a crude mixture of **40**, **41a**, and **41b** (49.5 mg). [Acetals **41a** and **41b** were partly separable from the crude mixture by HPLC (YMC-Pack SIL-06, 5 μm, 250 mm × 10 mm ID, hexane/CH_2Cl_2 = 1; flow rate: 5.0 mL/min, UV254 detection), and their ^{1}H NMR spectra were measured. **41a**: ^{1}H NMR (400MHz, $CDCl_3$) δ 1.36 (3H, s), 1.40 (3H, s), 1.47 (3H, s), 1.87 (1H, tdd, *J* = 4.1, 11.5, 14.7 Hz), 2.26 (1H, dddd, *J* = 2.0, 6.2, 9.0, 14.7 Hz), 3.67 (1H, t, *J* = 10.7 Hz), 3.73 (1H, dd, *J* = 7.3, 8.2 Hz), 3.77 (1H, dd, *J* = 4.4, 10.7 Hz), 3.79-3.94 (2H, m), 4.03 (1H, dd, *J* = 4.4, 10.7 Hz), 4.13 (1H, dd, *J* = 2.0, 11.5 Hz), 4.34 (1H, dd, *J* = 6.3, 8.2 Hz), 4.74 (1H, brq, *J* = 6.9 Hz), 5.69 (1H, s), 5.96 (1H, s), 5.99 (1H, dd, *J* = 7.3, 16.2 Hz), 6.19 (1H, dd, *J* = 0.9, 16.2 Hz), 7.34 (2H, d, *J* = 8.4 Hz), 7.36 (2H, d, *J* = 8.4 Hz), 7.42 (2H, d, *J* = 8.4 Hz), 7.43 (2H, d, *J* = 8.4 Hz); **41b**: ^{1}H NMR (400MHz, $CDCl_3$) δ 1.35 (3H, s), 1.39 (3H, s), 1.45 (3H, s), 1.84 (1H, tdd, *J* = 4.1, 11.5, 14.6 Hz), 2.21 (1H, dddd, *J* = 2.0, 7.0, 8.2, 14.6 Hz), 3.66 (1H, t, *J* = 10.7 Hz), 3.76 (1H, dd, *J* = 4.5, 10.7 Hz), 3.76 -3.84 (2H, m), 3.80 (1H, dd, *J* = 6.4, 7.9 Hz), 4.02 (1H, dd, *J* = 4.5, 10.7 Hz), 4.10 (1H, dd, *J* = 2.0, 11.5 Hz), 4.21 (1H, dd, *J* = 6.9, 7.9 Hz), 4.76 (1H, brq, *J* = 6.8 Hz), 5.66 (1H, s), 5.87 (1H, s), 5.99 (1H, dd, *J* = 7.2, 16.2 Hz), 6.17 (1H, dd, *J* = 0.8, 16.2 Hz), 7.34 (2H, d, *J* = 8.4 Hz), 7.36 (2H, d, *J* = 8.4 Hz), 7.39 (2H, d, *J* = 8.4 Hz), 7.45 (2H, d, *J* = 8.4 Hz).] The above crude mixture was divided into two batches (31.0 mg and 18.5 mg), and each batch was subjected to the following procedure. To a solution of the crude mixture of **40**, **41a**, and **41b** in MeCN (1.5 mL) was added 0.5 mol/L aq. HCl (0.5 mL) at 0 ºC, and the mixture was stirred for 36 h. Then, pH 7 buffer (1 mL) and $NaIO_4$ (more than 2 equiv.) were added, and the mixture was stirred for 2 h at 26 ºC. Then, saturated aq. $NaHCO_3$ was added, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with saturated aq. $Na_2S_2O_3$ and then with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 15) to give **42** (total production of two batches: 24.5 mg, 0.0531 mmol, 27% from **39**); a pale yellow oil; $[\alpha]_D^{22}$ +2.46 (*c* 0.820, $CHCl_3$); IR (neat) ν 3446, 3060, 2981, 2933, 2875, 2733,1689, 1633, 1603, 1494, 1464, 1418, 1404, 1389, 1371, 1301, 1240, 1220, 1192, 1160, 1139, 1129, 1089, 1031, 1016, 986, 949, 914, 871, 820, 805, 787, 733, 671, 647, 622 cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$) δ 1.39 (3H, s), 1.42 (3H, s), 1.52 (3H, s), 1.88 (1H, tdd, *J* = 4.0, 11.6, 14.6 Hz), 2.24 (1H, dddd, *J* = 1.9, 6.4, 9.0, 14.6 Hz), 3.56 (1H, t, *J* = 11.0 Hz), 3.84-3.98 (2H, m), 3.85 (1H, dd, *J* = 4.8, 10.9 Hz), 4.11 (1H, dd, *J* = 4.8, 11.2 Hz), 4.19 (1H, dd, *J* = 1.9, 11.6 Hz), 5.59 (1H, s), 6.48 (1H, dd, *J* = 7.9, 16.4 Hz), 7.24 (1H, d, *J* = 16.4 Hz), 7.35 (2H, d, *J* = 8.5 Hz), 7.42 (2H, d, *J* = 8.5 Hz), 9.67 (1H, d, *J* = 7.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.0 (CH_3), 24.4 (CH_3), 28.0 (CH_3), 36.1 (CH_2), 60.7 (CH_2), 62.2 (CH), 69.0 (CH_2), 70.0 (CH), 78.7 (C), 79.2 (C), 95.6 (CH), 127.5 (CH × 2), 128.5 (CH × 2), 133.5 (CH), 134.9 (C), 135.9 (C), 156.4 (CH), 193.5 (CH); FD-HRMS (*m*/*z*) calcd for $C_{20}H_{27}O_5{}^{35}Cl^{79}Br$ [M+H$^+$]: 461.0730, found: 461.0701.

(*E*)-3-[(2*S*,4*S*,5*S*)-5-({(*R*)-3-Bromo-2-methyl-5-[(triisopropylsilyl)oxy]pentan-2-yl}oxy)-2-(4-chlorophenyl)-4-methyl-1,3-dioxan-4-yl]prop-2-en-1-ol (43). To a solution of **42** (23.8 mg, 0.0515 mmol) and 2,6-lutidine (0.037 mL, 0.32 mmol) in CH_2Cl_2 (1 mL) was added TIPSOTf (0.042 mL, 0.16 mmol) at 0 ºC, and the mixture was stirred for 1 h. Then, saturated aq. $NaHCO_3$ was added, and the mixture was extracted with hexane several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude TIPS ether, which was used in the next reaction without purification. To a solution of the crude TIPS ether in MeOH (1 mL) were added $CeCl_3 \cdot 7H_2O$ (59 mg, 0.16 mmol) and $NaBH_4$ (6.0 mg, 0.16 mmol) at –78 ºC, and the mixture was stirred for 30 min. Then, saturated aq. NH_4Cl was added, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 10) to give **43** (29.9 mg, 0.0482 mmol, 94% over 2 steps); a colorless oil; $[\alpha]_D^{22}$ +6.46 (c 0.465, $CHCl_3$); IR (neat) ν 3422, 2941, 2926, 2866, 1494, 1464, 1419, 1387, 1369, 1234, 1130, 1104, 1088, 1016, 986, 882, 813, 744 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$) δ 0.98-1.18 (21H, m), 1.35 (3H, s), 1.38 (3H, s), 1.43 (3H, s), 1.82 (1H, brtdd, *J* = 3.7, 11.3, 14.5 Hz), 2.25 (1H, brdddd, *J* = 1.0, 6.8, 8.9, 14.5 Hz), 3.66 (1H, brt, *J* = 10.4 Hz), 3.74 (1H, dd, *J* = 3.6, 10.7 Hz), 3.83-3.96 (2H, m), 4.02 (1H, dd, *J* = 3.6, 9.9 Hz), 4.15 (1H, brdd, *J* = 1.0, 11.3 Hz), 4.24 (2H, d, *J* = 3.3 Hz), 5.74 (1H, s), 5.98-6.12 (2H, m), 7.33 (2H, d, *J* = 8.5 Hz), 7.43 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, C_6D_6) δ 12.3 (CH × 3), 18.2 (CH_3 × 6), 23.5 (CH_3), 23.9 (CH_3), 29.5 (CH_3), 37.2 (CH_2), 61.6 (CH_2), 62.7 (CH), 63.3 (CH_2), 68.5 (CH_2), 70.7 (CH), 78.1 (C), 78.7 (C), 94.8 (CH), 128.1 (CH × 2), 128.5 (CH × 2), 130.0 (CH), 132.3 (CH), 134.6 (C), 137.9 (C); FD-HRMS (*m*/*z*) calcd for $C_{29}H_{49}O_5Si^{35}Cl^{79}Br$ [M+H$^+$]: 619.2221, found: 619.2184.

(*R*)-MTPA ester 45b. To a solution of **43** (16.8 mg, 0.0271 mmol) in EtOH (3 mL) were added excess amount of Zn and NH_4Cl and reflux for 8 h. Then, the mixture was filtered through a Celite pad. The filtrate was diluted with H_2O and extracted with EtOAc several times. The combined organic layers were washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 2) to give **44** (7.4 mg, 0.026 mmol, 96%) as a colorless oil. [^1H NMR data of **44**: ^1H NMR (300 MHz, $CDCl_3$) δ 1.49 (3H, s), 3.65 (1H, t, *J* = 10.7 Hz), 3.80-3.91 (1H, m), 4.02 (1H, dd, *J* = 5.0, 10.7 Hz), 4.29 (2H, brd, *J* = 4.3 Hz), 5.75 (1H, s), 6.08 (1H, brtd, *J* = 4.3, 16.1 Hz), 6.17 (1H, brd, *J* = 16.1 Hz), 7.33 (2H, d, *J* = 8.6 Hz), 7.43 (2H, d, *J* = 8.6 Hz).] Compound **44** was immediately used in the next reaction. To a solution of **44** (6.0 mg, 0.021 mmol), DMAP (a catalytic amount) and Et_3N (0.020 mL, 0.210 mmol) in CH_2Cl_2 (1 mL) was added TBDPSCl (0.009 mL, 0.035 mmol), and the mixture was stirred for 4 h at 25 ºC. Then, (*S*)-(+)-MTPACl (0.012 mL, 0.064 mmol) was added at 25 ºC, and the mixture was stirred for 10 h. Then, 0.2 M aq. HCl was added, and the mixture was extracted with Et_2O several times. The combined organic

layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 30) to give (*R*)-MTPA ester **45b** (9.8 mg, 0.013 mmol, 62%); a colorless oil; ^{1}H NMR (300MHz, $CDCl_3$) δ 1.04 (9H, s), 1.26 (3H, s), 3.51 (3H, s), 3.69 (1H, brt, *J* = 10.7 Hz), 4.17 (1H, dd, *J* = 5.1, 10.5 Hz), 4.22 (1H, brddd, *J* = 1.0, 3.3, 14.5 Hz), 4.27(1H, brddd, *J* = 1.0, 3.3, 14.5 Hz), 5.16 (1H, dd, *J* = 5.1, 10.8 Hz), 5.67 (1H, s), 5.86 (1H, brtd, *J* = 3.3, 16.1 Hz), 5.94 (1H, brd, *J* = 16.1 Hz), 7.28-7.51 (11H, m), 7.60-7.69 (4H, m); FD-HRMS (*m*/*z*) calcd for $C_{40}H_{41}O_6F_3Si^{35}Cl$ [M^+–H]: 737.2313, found: 737.2345.

(*S*)-MTPA ester 45a. According to the preparation procedure for **45b**, (*S*)-MTPA ester **45a** was prepared from **44** (4.8 mg, 0.016 mmol), DMAP (a catalytic amount), Et_3N (0.016 mL, 0.17 mmol), TBDPSCl (0.0070 mL, 0.026 mmol), and (*R*)-(–)-MTPACl (0.011 mL, 0.059 mmol); a colorless oil; ^{1}H NMR (300MHz, $CDCl_3$) δ 1.04 (9H, s), 1.39 (3H, s), 3.49 (3H, s), 3.54 (1H, brt, *J* = 10.9 Hz), 4.07 (1H, dd, *J* = 5.2, 10.8 Hz), 4.25 (1H, brdd, J = 3.5, 14.4 Hz), 4.29 (1H, brdd, *J* = 3.5, 14.4 Hz), 5.16 (1H, dd, *J* = 5.2, 10.9 Hz), 5.62 (1H, s), 5.91 (1H, brtd, *J* = 3.5, 16.3 Hz), 5.97 (1H, brd, *J* = 16.3 Hz), 7.27-7.51 (11H, m), 7.60-7.68 (4H, m); FD-HRMS (*m*/*z*) calcd for $C_{40}H_{41}O_6F_3Si^{35}Cl$ [M^+–H]: 737.2313, found: 737.2305.

(*R*)-4-({(2*S*,4*S*,5*S*)-4-[(*E*)-3-(Allyloxy)prop-1-en-1-yl]-2-(4-chlorophenyl)-4-methyl-1,3-dioxan-5-yl}-oxy)-3-bromo-4-methylpentan-1-ol (47). To a solution of **43** (13.0 mg, 0.0210 mmol) in DMF (1 mL) were added NaH (60% in mineral oil, 6.7 mg, 0.17 mmol), allyl bromide (0.018 mL, 0.21 mmol) and Bu_4NI (a catalytic amount) at 27 ºC, and the mixture was stirred for 8 h. Then, saturated aq. NH_4Cl was added, and the mixture was extracted with hexane several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give crude allyl ether **46**, which was used in the next reaction without purification. To a solution of the above crude **46** in THF (1 mL) was added Bu_4NF (1.0 mol/L in THF, 0.063 mL, 0.063 mmol) at 28 ºC, and the mixture was stirred for 1 h. Then, saturated aq. NH_4Cl was added, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 3 → 2) to give **47** (8.0 mg, 0.016 mmol, 76% over 2 steps); a colorless oil; $[\alpha]_D^{23}$ +5.46 (*c* 0.675, $CHCl_3$); IR (neat) ν 3444, 3078, 2978, 2929, 2858, 1602, 1494, 1465, 1419, 1387, 1370, 1300, 1239, 1197, 1130, 1087, 1028, 1016, 988, 921, 816, 796, 757, 723, 666, 639 cm^{-1}; ^{1}H NMR (300MHz, C_6D_6) δ 0.87 (3H, s), 0.97 (3H, s), 1.42 (3H, s), 1.56 (1H, tdd, *J* = 3.9, 11.3, 14.6 Hz), 1.92 (1H, dddd, *J* = 1.8, 5.7, 8.0, 14.6 Hz), 3.45-3.66 (4H, m), 3.83 (1H, td, *J* = 1.2, 5.4 Hz), 3.86-3.95 (3H, m), 4.00 (1H, dd, *J* = 1.8, 11.3 Hz), 5.04 (1H, brd, *J* = 10.4 Hz), 5.25 (1H, brqd, *J* = 1.5, 17.2 Hz), 5.84 (1H, s), 5.85 (1H, brtdd, *J* = 5.4, 10.4, 17.2 Hz), 6.07 (1H, td, *J* = 5.3, 16.3 Hz), 6.22 (1H, brd, *J* = 16.3 Hz), 7.16 (2H, d, *J* = 8.6 Hz), 7.45 (2H, d, *J* = 8.6 Hz); ^{13}C NMR (75 MHz, C_6D_6) δ 23.4 (CH_3), 23.5 (CH_3), 29.3 (CH_3), 36.5 (CH_2), 60.5 (CH_2), 62.6 (CH), 68.5 (CH_2), 70.6 (CH), 70.7 (CH_2),

71.3 (CH_2), 78.1 (C), 78.7 (C), 94.9 (CH), 116.5 (CH_2), 128.1 (CH × 2), 128.5 (CH × 2), 129.6 (CH), 131.7 (CH), 134.6 (C), 135.3 (CH), 137.8 (C);FD-HRMS (*m*/*z*) calcd for $C_{23}H_{33}O_5{}^{35}Cl^{79}Br$ [M+H^+]: 503.1200, found: 503.1189.

(2*S*,4*S*,5*S*)-4-[(*E*)-3-(Allyloxy)prop-1-en-1-yl]-5-{[(*R*)-3-bromo-2-methylpent-4-en-2-yl]oxy}-2-(4-chlorophenyl)-4-methyl-1,3-dioxane (48). To a solution of **47** (17.5 mg, 0.0347 mmol) and 2-nitrophenylselenocyanate (19.7 mg, 0.0868 mmol) in THF (0.2 mL) was added Bu_3P (0.022 mL, 0.089 mmol) at 28 ºC, and the mixture was stirred for 1 h. Then, H_2O was added, and the mixture was extracted with hexane several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 20) to give a selenide, which was immediately used in the next reaction. To a solution of the selenide in THF (1 mL) was added 30% aq. H_2O_2 (0.1 mL) at 28 ºC, and the mixture was stirred for 12 h in the dark. Then, H_2O was added, and the mixture was extracted with hexane several times. The combined organic layers were washed with saturated aq. Na_2SO_3 and then with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/benzene = 3 → hexane/EtOAc = 3) to give **48** (14.7 mg, 0.0303 mmol, 87% over 2 steps); a pale yellow oil; $[\alpha]_D^{22}$ +21.0 (*c* 0.505, $CHCl_3$); IR (neat) ν 3083, 2979, 2927, 2855, 1494, 1462, 1417, 1386, 1368, 1300, 1282, 1238, 1225, 1198, 1171, 1131, 1087, 1016, 988, 926, 883, 815, 722, 666 cm^{-1}; ^1H NMR (300MHz, C_6D_6) δ 0.84 (3H, s), 0.91 (3H, s), 1.46 (3H, s), 3.56 (1H, dd, *J* = 4.7, 10.6 Hz), 3.71 (1H, t, *J* = 10.7 Hz), 3.85 (2H, td, *J* = 1.4, 5.4 Hz), 3.91-4.00 (3H, m), 4.04 (1H, d, *J* = 10.0 Hz), 4.74 (1H, brdd, *J* = 1.2, 10.0 Hz), 4.83 (1H, brd, *J* = 17.0 Hz), 5.05 (1H, brqd, *J* = 1.5, 10.4 Hz), 5.28 (1H, brqd, *J* = 1.7, 17.2 Hz), 5.76-5.93 (2H, m), 5.87 (1H, s), 6.13 (1H, td, *J* = 5.4, 16.3 Hz), 6.31 (1H, td, *J* = 1.4, 16.3 Hz), 7.16 (2H, d, *J* = 8.5 Hz), 7.46 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, C_6D_6) δ 22.3 (CH_3), 24.9 (CH_3), 29.5 (CH_3), 65.2 (CH), 68.6 (CH_2), 70.4 (CH), 70.7 (CH_2), 71.3 (CH_2), 77.1 (C), 78.8 (C), 95.0 (CH), 116.4 (CH_2), 117.9 (CH_2), 128.1 (CH × 2), 128.5 (CH × 2), 129.7 (CH), 131.7 (CH), 134.6 (C), 135.4 (CH), 136.1 (C), 137.8 (C); FD-HRMS (*m*/*z*) calcd for $C_{23}H_{29}O_4{}^{35}Cl^{79}Br$ [M^+–H]: 483.0938, found: 483.0910.

(2*S*,3*S*,*E*)-6-(Allyloxy)-2-{[(*R*)-3-bromo-2-methylpent-4-en-2-yl]oxy}-3-methylhex-4-ene-1,3-diol (10). To a solution of **48** (57.5 mg, 0.118 mmol) in EtOH (4 mL) was added 2 mol/L aq. HCl (2 mL) at 25 ºC, and the mixture was stirred for 6 h in the dark. Then, $NaHCO_3$ was added, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 2) to give **10** (39.1 mg, 0.108 mmol, 92%); a colorless oil; $[\alpha]_D^{21}$ +49 (*c* 0.22, $CHCl_3$); IR (neat) ν 3383, 3083, 2979, 2934, 2852, 1462, 1453, 1417, 1386, 1367, 1282, 1223, 1172, 1127, 1066, 987, 928, 878, 784, 721 cm^{-1}; ^1H NMR (300MHz, C_6D_6) δ

0.99 (3H, s), 1.01 (3H, s), 1.30 (3H, s), 2.02 (1H, brs, OH), 2.59 (1H, brs, OH), 3.29 (1H, dd, *J* = 3.5, 5.6 Hz), 3.50-3.67 (2H, m), 3.79-3.84 (2H, m), 3.86 (2H, d, *J* = 4.4 Hz), 4.16 (1H, d, *J* = 10.0 Hz), 4.73 (1H, brdd, *J* = 1.2, 9.8 Hz), 4.83 (1H, brd, *J* = 16.9 Hz), 5.04 (1H, brd, *J* = 10.4 Hz), 5.26 (1H, brqd, *J* = 1.7, 17.2 Hz), 5.77-6.05 (4H, m); ^{13}C NMR (75 MHz, C_6D_6) δ 22.6 (CH_3), 24.8 (CH_3), 26.2 (CH_3), 64.0 (CH_2), 66.4 (CH_2), 70.5 (CH_2), 71.2 (CH_2), 75.6 (C), 77.09 (CH), 77.12 (C), 116.4 (CH_2), 118.0 (CH_2), 126.1 (CH), 135.4 (CH), 136.3 (CH), 136.9 (CH); FD-HRMS (*m*/*z*) calcd for $C_{16}H_{28}O_4{}^{79}Br$ [M+H$^+$]: 363.1171, found: 363.1195.

(2*S*,3*S*,6*R*)-6-Bromo-2-(hydroxymethyl)-3,7,7-trimethyl-2,3,6,7-tetrahydrooxepin-3-ol (49). To a solution of **10** (12.6 mg, 0.0347 mmol) in xylenes (15 mL) was added the second generation Hoveyda-Grubbs catalyst (6.5 mg, 0.010 mmol), and the mixture was refluxed for 1 h in the dark. Then, the mixture was cooled to 25 ºC and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 2) to give **49** (3.2 mg, 0.012 mmol, 35%); a colorless amorphous; $[\alpha]_D^{22}$ –100 (*c* 0.060, $CHCl_3$); IR (neat) ν 3450, 3026, 2974, 2922, 2850, 1462, 1453, 1377, 1264, 1230, 1170, 1137, 1090, 1060, 1034, 969, 843, 795, 720 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$) δ 1.23 (3H, s), 1.46 (6H, s), 2.00-2.11 (1H, m, OH), 2.93 (1H, brs, OH), 3.67-3.88 (3H, m), 4.60 (1H, d, *J* = 6.0 Hz), 5.53 (1H, d, *J* = 11.8 Hz), 5.85 (1H, dd, *J* = 6.0, 11.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.0 (CH_3), 24.2 (CH_3), 28.3 (CH_3), 56.1 (CH), 61.3 (CH_2), 74.4 (C), 76.6 (CH), 78.9 (C), 128.4 (CH), 139.2 (CH); Under MS measurement conditions, a significant elimination of bromine atom of **49** occurred, and therefore HRMS of [M$^+$] or [M+H$^+$] peak was not obtained.

(2*S*,3*S*,6*R*)-6-Bromo-2-(hydroxymethyl)-3,7,7-trimethyloxepan-3-ol (1). To a solution of **49** (2.3 mg, 0.0087 mmol) in MeCN (3 mL) was added excess amount of NBSH and $KHCO_3$ at 23 ºC, and the mixture was stirred for 3 days in the dark. Then, $NaHCO_3$ was added, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 2) and HPLC (JAIGEL 0A2000-10, 250 mm × 10 mm ID, hexane/EtOAc = 4; flow rate: 3.0 mL/min, RI detection) to give **1** (≤ 1.0 mg, ≤43%); a colorless amorphous; $[\alpha]_D^{23}$ +6.3 (*c* 0.10, $CHCl_3$); IR (KBr) ν 3422, 2996, 2986, 2975, 2959, 2941, 2926, 2900, 2854, 1461, 1383, 1367, 1343, 1333, 1320, 1294, 1216, 1174, 1158, 1139, 1102, 1076, 1034, 1025, 970, 946, 795, 712, 599, 533 cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$) δ 1.12 (3H, s), 1.44 (3H, s), 1.48 (3H, s), 1.54 (1H, brddd, J = 3.2, 13.0, 14.7 Hz), 1.75 (brddd, J= 2.3, 5.2, 14.7 Hz), 1.91 (1H, brs, OH), 2.06 (1H, brddd, J = 3.2, 5.2, 14.8 Hz), 2.37 (1H, brdddd, J = 2.3, 11.0, 13.0, 14.8 Hz), 3.04 (1H, brs, OH), 3.49 (1H, brt, *J* = 5.9 Hz), 3.65 (2H, m), 3.93 (1H, d, *J* = 11.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.0 (CH_3), 25.1 (CH_3), 25.6 (CH_3), 30.3 (CH_2), 44.2 (CH_2), 58.2 (CH), 61.4 (CH_2), 71.5 (C), 75.7 (CH), 78.7 (C); ESI-HRMS (*m*/*z*) calcd for $C_{10}H_{19}O_3{}^{79}BrNa$ [M+Na$^+$]: 289.04098, found: 289.04105.

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